

STUDIES ON SOLUBILITY AND SOLUBILITY RELATED PROCESSES

**A Thesis presented to the University of London in partial fulfilment of the
requirements for the degree of Doctor of Philosophy in the Faculty of Science**

**By
Gary Stephen Whiting**

**Sir Christopher Ingold Laboratory
Chemistry Department
University College London**

March 1991

ProQuest Number: 10610889

All rights reserved

INFORMATION TO ALL USERS

The quality of this reproduction is dependent upon the quality of the copy submitted.

In the unlikely event that the author did not send a complete manuscript and there are missing pages, these will be noted. Also, if material had to be removed, a note will indicate the deletion.



ProQuest 10610889

Published by ProQuest LLC (2017). Copyright of the Dissertation is held by the Author.

All rights reserved.

This work is protected against unauthorized copying under Title 17, United States Code
Microform Edition © ProQuest LLC.

ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

ABSTRACT

A general description is given of solubility and solubility related processes, including the solubility of gases and vapours in liquids, and the partition of solutes between two condensed phases. Particular attention is devoted to gas-liquid chromatography (GLC) and reverse-phase high performance liquid chromatography (RP-HPLC). Theories of solubility are surveyed, including Hildebrand's theory, the scaled particle theory, and theories based on linear regression analysis. The latter requires a knowledge of characteristic parameters of solutes (solvation parameters), and solvents (solvatochromic parameters), and the determination of these is discussed.

It is shown that the method of multiple linear regression analysis is very useful in the study of solution and solubility related processes, and the aim of the work in the thesis is to set out characteristic solute parameters, and apply them to a wide range of processes.

Methods are given for the determination of solute solvation parameters based on experimental procedure. A collection of parameters (R_2 - an excess molar refraction, π^*_2 - dipolarity, α^H_2 - hydrogen bond acidity, β^H_2 - hydrogen bond basicity, $\log L^{16}$ - Ostwald solubility coefficient on n-hexadecane, V_X - size parameter) is assembled for a wide range of solutes. The construction of a solute parameter database, and its associated programs is also discussed.

A thermodynamically consistent set of explanatory variables, all related to Gibbs energy are determined. New scales of multifunctional solvation parameters reflecting real solubility situations are developed ($\Sigma\pi^H_2$, $\Sigma\alpha^H_2$ and $\Sigma\beta^H_2$). These, and the older parameters, above, are applied to various processes using equations 1 and 2 (where SP is the dependant solute variable);

$$\log SP_{(gas \rightleftharpoons condensed \text{ phase})} = c + r.R_2 + s.\Sigma\pi^H_2 + a.\Sigma\alpha^H_2 + b.\Sigma\beta^H_2 + l.\log L^{16} \quad [1]$$

$$\log SP_{(within \text{ condensed phase})} = c + r.R_2 + s.\Sigma\pi^H_2 + a.\Sigma\alpha^H_2 + b.\Sigma\beta^H_2 + m.V_X \quad [2]$$

Equations 1 and 2 are shown to be extremely useful for the prediction of physicochemical and biochemical data, and for the interpolation of factors influencing solubility and solubility related processes.

CONTENTS

Abstract	I

SECTION 1

1.1	An Introduction to Chromatography	1
1.11	Gas Chromatography	2
1.12	An Assessment of the Gas Chromatographic Method	4
1.2	Partition	6
1.21	Partition Coefficients From Headspace Analysis	8
1.22	Partition Coefficients From GLC	10
1.3	The Theoretical Basis of Chromatography	14
1.31	Considerations for GLC Efficay and Optimisation	20
1.4	A Comparison of Headspace Analysis and Dynamic GLC	25
1.5	High Performance Liquid Chromatography	26
1.51	Reversed-Phase HPLC	29

SECTION 2

2.1	Theories of Solubility	31
2.11	The Hildebrand Solubility Parameter	31
2.12	The Scaled Particle Theory and Linear Solvation Energy Relationship	32
2.13	Linear Free Energy Relationships	35
2.14	Quantitative Structure Activity Relationships	36
2.2	Prediction of Vapour-Liquid Equilibria by Group Contribution Methods	37
2.3	Multiple Linear Regression Analysis with LSER and QSAR	41
2.31	Application of MLRA in This Work	43

SECTION 3

3.1	Solvatochromic Parameters for Solvents	48
3.2	Solvatochromic Parameters for Solutes	52
3.21	The Solute Cavity Size/Dispersion Parameter	56
3.22	The Importance of Hydrogen Bonding Parameters	60

SECTION 4

4.1	Charcterisation of Stationary Phase Solvent Properties	61
4.2	Surface Acoustic Wave Chemical Sensors	69
4.21	Introduction to Piezoelectric Sorption Detectors and SAW devices	69
4.22	Selection of Suitable SAW Coating Materials	75
4.23	SAW Devices Used in Sensor Arrays	77

SECTION 5

5.1	Aims of the Present Work	81

SECTION 6

6.1	Determination and Calculation of New Solvation Parameters	87
6.11	Analysis of the Laffort Data	87
6.12	Analysis of the McReynolds Data	101
6.13	Calculation of Effective Hydrogen Bond Basicity, $\Sigma\beta^H_2$, from HPLC Data	116
6.14	Parameter Back-Calculation from GLC Data	125
6.20	The Log L ¹⁶ Parameter	149
6.30	The Construction of a New Solute Parameter Database	164

SECTION 7

7.0	Application of Solvation Equations	173
7.10	Characterisation of Some <i>N</i> -Substituted Amides as Solvents and Comparison With Some GLC Stationary Phases	173
7.20	Application to QSAR Construction for Upper Respiratory Tract Irritation by Airborne Chemicals in Mice	184
7.30	Application to Transfer of Solutes from Hexadecane to Water	193
7.40	Application to the Characterisation of Solvents and Solvent/Water Partition Coefficients	203
7.50	Characterisation of Candidate SAW Phases	224
7.60	Application to Characterisation of GLC Phases Studied by Poole	241

SECTION 8

8.10	Summary Discussion, Conclusions and Future Work	252
8.11	Future Work	255

SECTION 9

9.10	Experimental	257
9.11	Dynamic GLC Experimental	257
9.12	Static Headspace Experimental	279

SECTION 10

10.1	Appendix 1	281
10.11	The Params Database and the Fortran 77 Programs Used	281
10.12	The MhaBase1 and MhaBase2 Database and SmartII 4GL Programs	282
	Appendix 2 - Published work - bound in at end of thesis.	
10.2	References	286

Errata

Throughout the text, read physicochemical for physiochemical

ACKNOWLEDGEMENTS

My sincere thanks to Mike Abraham for his help over the last three years of this project. His enthusiasm and intimate knowledge of the subject ensured that I learnt a great deal and enabled the research to proceed without too many problems. I am extremely grateful for his encouragement, particularly on the computing side of the work, and for kindly providing suitable equipment on which to carry it out.

I was greatly helped in the early stages of the project by 'Rodge' Andrew McGill, whose work I followed on from. My thanks to him for patiently explaining the rudiments, and imparting his knowledge of the practical side of chromatography to me.

Thanks are also due to Jenik Nazari-Dehnari and Johnathan W. Steed for carrying out some of the chromatographic measurements used in the characterisation of candidate surface acoustic wave phases. Thanks to David Walsh for some headspace measurements used in the characterisation of solvents, and the contribution he has undoubtedly made to the lab since joining two years ago. All the best to him with the rest of his research. Good luck also to Harpreet Chadha, who is continuing work along similar lines.

In addition, I would like to thank all those who helped me in the early days during my time at the Chemistry Department at the University of Surrey, especially Vic Zettel, Priscilla Grel lier, Gabriel Buist, and Professor Jones for his support. My thanks to the many who have helped me at University College London and made my time there so enjoyable.

I am grateful to the US Army Research Development and Standardization Group for support of this work under Contract DAJA 45-87-C-0004.

1.10 An Introduction to Chromatography

The technique of chromatography constitutes the majority of the experimentation carried out in this work, so a generalised introduction and detailed discussion of the theoretical basis of it is therefore appropriate.

Chromatography is derived from Greek, "khroma" meaning colour, and "grafein" meaning written. The technique as such and the word "chromatography" was first used in 1906 by Tswett¹ to detail the separation he carried out when percolating coloured plant pigments through a column of calcium carbonate (the stationary phase), with a mobile phase of petroleum. The process can be defined then as a physical method of separation, in which the components to be separated are distributed between two phases, the stationary phase and the mobile phase, the latter being either a gas or a liquid.

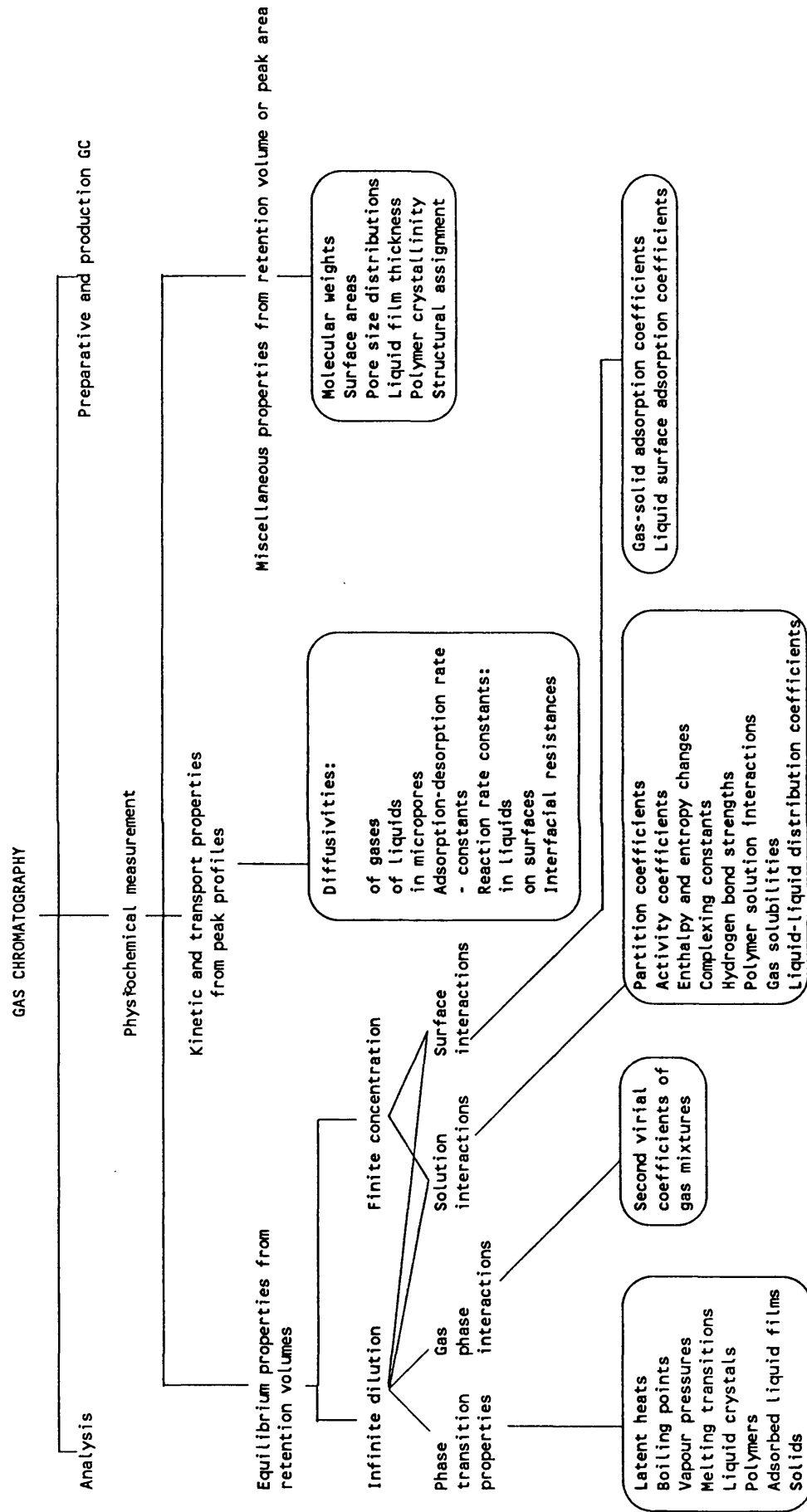
Tswett's work¹ was liquid-solid chromatography (LSC). There are three other basic forms of chromatography, classified according to the nature of the stationary and mobile phase. Liquid liquid chromatography was first used by Martin and Synge² in 1941, and here both phases are liquid. Also in 1941 gas solid chromatography (GSC) was introduced by Hesse et al³, and by Tiselius⁴ and Claesson⁵ in 1943 and 1946 respectively. The work presented here is mostly concerned with gas liquid chromatography (GLC), introduced in 1952 by James and Martin⁶, and to a lesser extent, high performance liquid chromatography (HPLC). This is a variant on liquid chromatography, the emergence of which is usually considered to have started with the publication by Huber and Hulsman⁷ in 1967, although Giddings⁸ had already shown the potential advantage in terms of column efficiencies and speed of analysis of liquid chromatography over gas chromatography, (GC).

Many physical properties can be determined from GC work, and Figure 1 shows a general classification of these. They are of three basic types. Firstly, equilibrium properties such as parameters for distribution of a volatile solid between gas and fixed phase can be obtained by measuring the retention time. Secondly kinetic and transport processes can be investigated by virtue of the fact that they determine the concentration - time profile of the migrating peak, and the extent to which it broadens as it moves towards the column outlet. Finally, there are many other miscellaneous properties, such as molecular weight and surface areas that can be investigated using the retention volume, the area under the peak, or the peak profile. In all three categories the physiochemical property studied is derived directly from measurements based on the chromatographic processes occurring in the column. Particular features of the GC approach to physical measurement are its essential simplicity, and the speed with which large amounts of data can be obtained. However, an analytical approach is also well established as a method of physiochemical study, for example in gas kinetic studies, or vapour - liquid equilibria (VLE) by head space analysis ⁹⁻¹¹.

1.11 Gas Chromatography

In GLC the liquid stationary phase is coated onto an "inert" porous solid support, typically a diatomite (kieselguhr), and then used to pack a long narrow column. A layer of stationary phase then exists at the surface of the support, and in its pores. The mobile carrier gas containing the vapour (or solute) can then flow all around and through the coated support, as it travels through the column. The two phases are mutually well dispersed with a very large area of interaction. GSC differs from GLC in that the stationary phase in GSC is in fact a solid adsorbent of a suitably fine mesh size (to give a large enough surface area for vapour/adsorbent interaction). The carrier gas containing solute vapour will

FIGURE 1: The Uses Of Gas Chromatography



similarly flow around and/or through the solid, depending on pore size.

There are three distinctive techniques to obtain measurements from a typical GC set-up. To carry out a measurement using the *elution* method a discrete sample of solute is introduced batchwise into the column at the inlet. The solute concentration or peak is then carried through the column by the mobile phase, and its emergence at the other end observed with a suitable detector.

Another mode of operation is termed *frontal analysis* chromatography. The column is first subjected to a steady stream of carrier gas and solute vapour at a fixed concentration. The solute concentration is then instantaneously altered (either positively or negatively) to a new steady value, thereby forming a frontal boundary with a step-shaped concentration profile into the column.

In addition to frontal and elution analysis the third technique is called *displacement development*¹², which relies on the competitive adsorption between two sorbates. It is occasionally used for separating mixtures and has some application to studying on-column reactions and finite solute concentration work.

1.12 An Assessment of the Gas Chromatographic Method

Conventional methods for studying solution phenomena which depend on the measurement of vapour pressure, suffer from the disadvantage that the percentage error of measurement at low concentrations is usually very much greater than at high concentrations¹³⁻¹⁵. There is a further difficulty, in that conventional vapour pressure measurements on systems of the type volatile solute and involatile solvent are usually very time consuming, and necessitate very pure solvent and solute. Gas chromatography is a very convenient way of

studying the interaction of vapours and gaseous solutes in liquids, and adsorption onto solids. The technique is simplest to operate if the solute component is at infinite dilution, the solvent is involatile, the system is a binary one, and the solute does not undergo adsorption at the gas-liquid surface, and/or support surface. It offers an alternative to other methods of obtaining physiochemical data, with a different scope and suitability of application.

For either GSC or GLC the amount of solute required is usually small, detectors of the ionization type being able to respond to quantities of down to 10^{-4} or 10^{-5} μg . It is more usual to inject samples of around 100 μg for infinite dilution studies. The amount of stationary phase required for GC is also relatively small.

A GC measurement is relatively quick, typically taking just a few minutes. This is possible because of the highly dispersed nature of the stationary phase, offering a massive area to interact with the gas. It is also possible to inject several solutes simultaneously, if their retention times differ sufficiently. Also because of the techniques' inherent ability to separate compounds, absolute solute purity is not a prerequisite (assuming the measurement required is not a quantitative one). Temperature regulation is a simple matter, as the GC column will normally be in a compact shape such as a coil, housed in a thermostatted enclosure. Any temperature within the equipments' ability can be achieved and effectively maintained. Chromatographic measurement methods are often preferred for reactive or thermally unstable solutes, as non-chromatographic techniques are often unsuitable. Reaction of the gas with traces of impurities or the vessel itself can lead to spurious pressure changes and fabrication of the experimental conditions. In GC, quantities are small, contact time short, any exposed parts of the apparatus can be made of inert compounds, and if any reaction should occur, the products are separated from the solute by the action of the column.

GC is also particularly adaptable to extremes of temperature and pressure. For low or high temperature work only the walls of the column need be exposed to the necessary temperature.

Other methods for studying solution or adsorption properties often require vacuum techniques, which leaves an experimental set-up prone to leaks. Since chromatographic methods involve pressurizing the system to above atmospheric pressure this problem is completely avoided. Systems are reasonably cheap, and (especially in the case of the older ones), are flexible. The injector and detector unit (or head) can for instance, be removed from the supplied air thermo-stat and placed over a water bath, and gas flow regulators easily replaced with higher precision models etc.

The major weakness of the GC method is the possibility of multiplicity of physiochemical processes which sometimes affect the chromatogram. Typically a gas-liquid chromatographic system contains a total of five or more phases at least: three bulk and two interfacial. The measurements may reflect equilibrium interactions or transport processes in more than one phase. A study of one interaction may be subject to interference from other interactions in the system. A common interfering process (if not itself the object of study) is the adsorption on the solid "inert" support, especially prevalent with polar solutes.

1.2 Partition

To investigate the energetics of solvation, some particular thermodynamic process must be defined. A suitable process involving only interactions between the non-electrolyte solute and the bulk solvent is that of transfer from the ideal gas state to infinite dilution in the bulk solvent¹⁶. Solvation in this way can be

investigated quantitatively using the Gibbs energy of solvation ΔG° , or the equilibration constant $\log K$ for the process



Gas chromatography is the ideal technique for measuring solvent/solute interactions for vapour-liquid equilibrium, in the form of the partition coefficient K , (equivalent to the Ostwald absorption coefficient L). K is defined as the ratio of concentration of solute distributed between gas and liquid phase, according to equation 2.

$$K = \frac{\text{concentration of solute in liquid phase}}{\text{concentration of solute in gas phase}} = \frac{C_L}{C_G} \quad [2]$$

The Gibbs energy of solvation is then related to the partition coefficient K by:

$$\Delta G^\circ = -RT \ln K \quad [3]$$

where R is the universal gas constant, ($8.31441 \text{ J K}^{-1} \text{ mol}^{-1}$). Classical vapour-liquid equilibrium experiments, or more conveniently, headspace analysis, will yield K values¹⁷⁻²³. In GLC work, as sample amounts involved are so small, K will effectively be measured at infinite dilution, and be equal to K° , the value at zero concentration.

The distribution of a solute between two mutually immiscible solvents can also be studied by GC. As there is a great deal of interest in modelling the partition processes involved in biological membranes, much work is done with water as one solvent, and an immiscible organic one as the other. A typical partition often measured is that between water and *n*-octanol. The coefficient of partition of a solute between two solvents, P , can be determined by two methods. The solute and both solvents can be shaken together in a flask, allowed to equilibrate, and

then the concentration of the solute in either phase determined, - the traditional shake-flask analysis method. For a given solute, if the gas-solvent Ostwald solubility coefficients in each solvent are known, P can be calculated by the following equation.

$$P = L_2/L_1 \quad [4]$$

L_1 is the Ostwald solubility coefficient for a given solute in the first solvent, L_2 for the second. For solvents with very low mutual miscibilities, P by either method will be identical^{24,25}. However, values of P are method dependant for partitions between solutes with slight mutual miscibility, ie. in this case the system should not be considered as a system containing two pure solvents.

1.21 Partition Coefficients From Headspace Analysis

The technique of headspace analysis is an static analytical GLC approach to making physiochemical measurements. A dilute solution of a standard and a test solute is made in the chosen solvent. The solution is left to equilibrate in a thermostatted bath (Figure 2), and samples of the liquid and vapour phase withdrawn separately, and analysed by GLC as detailed by Abraham et al^{17,19}.

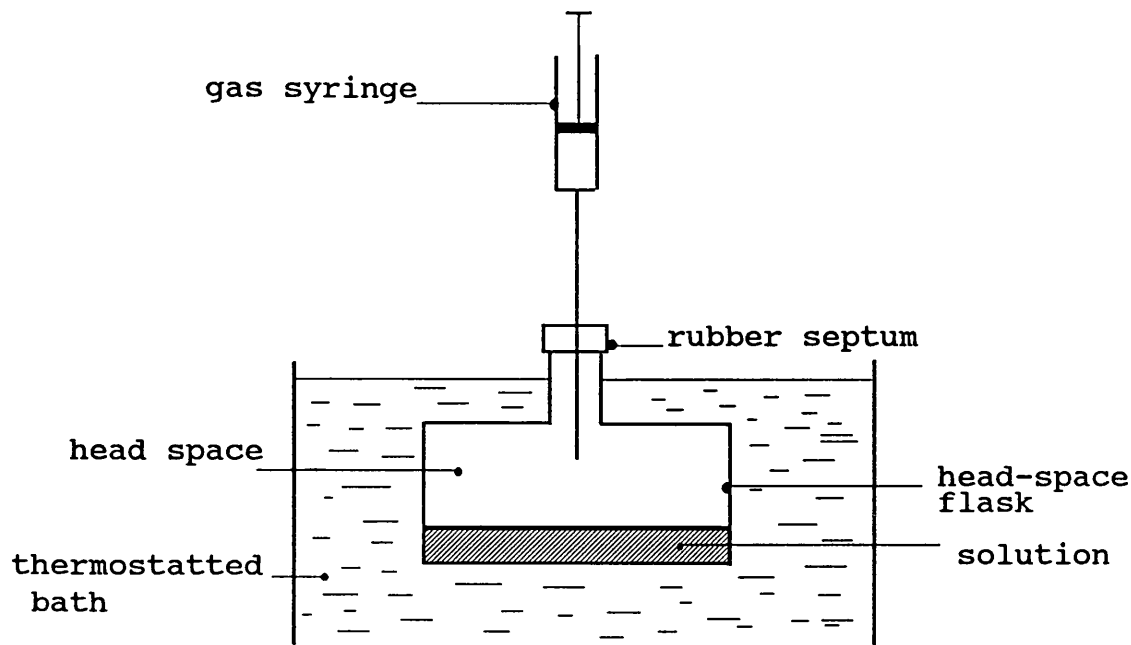
The partition of the standard solute, K^R , is known, so that of the test solute, K^T , can be calculated from the following, (where R indicates the reference solute, and T the test):

$$\frac{K^T}{K^R} = \frac{C_L^T \cdot C_G^R}{C_L^R \cdot C_G^T} \quad [5]$$

$$\text{since } K^R = \frac{C_L^R}{C_G^R} \text{ and } K^T = \frac{C_L^T}{C_G^T}$$

The area of the chart recorder response or integrator attached to the detector is

FIGURE 2: Head-Space Apparatus



assumed to vary linearly with the concentrations in gas and liquid phase, so area, (A), can be substituted for the concentration terms in equation [2]. Note that A_L will not be equal to C_L . Similarly A_L/A_G is not equal to C_L/C_G . But $A_L^T/A_L^R = C_L^T/C_L^R$ and $A_G^T/A_G^R = C_G^T/C_G^R$ from the above assumption.

$$\frac{K^T}{K^R} = \frac{A_L^T}{A_L^R} \cdot \frac{A_G^R}{A_G^T} \quad [6]$$

If the standard K value used in the equation has been corrected for vapour phase non-ideality, then the experimentally determined value will be approximately corrected.

Problems can occur when the solvent used is viscous or a solid, making the withdrawing of liquid sample impossible. A modified procedure of head space analysis is necessary in such circumstances, as detailed by Rohrschneider ²⁷. If the total amount of solute introduced into the head space flask is known, (m), and

the volume of liquid phase, V_{liq} , and the volume of the gaseous phase, V_{gas} , are also known then the concentration of solute in the liquid phase can be eliminated from the calculation procedure. The concentration of the solute in the gas phase is calculated as a product of the measured peak height, (h), and a proportionality factor (r), specific to each substance.

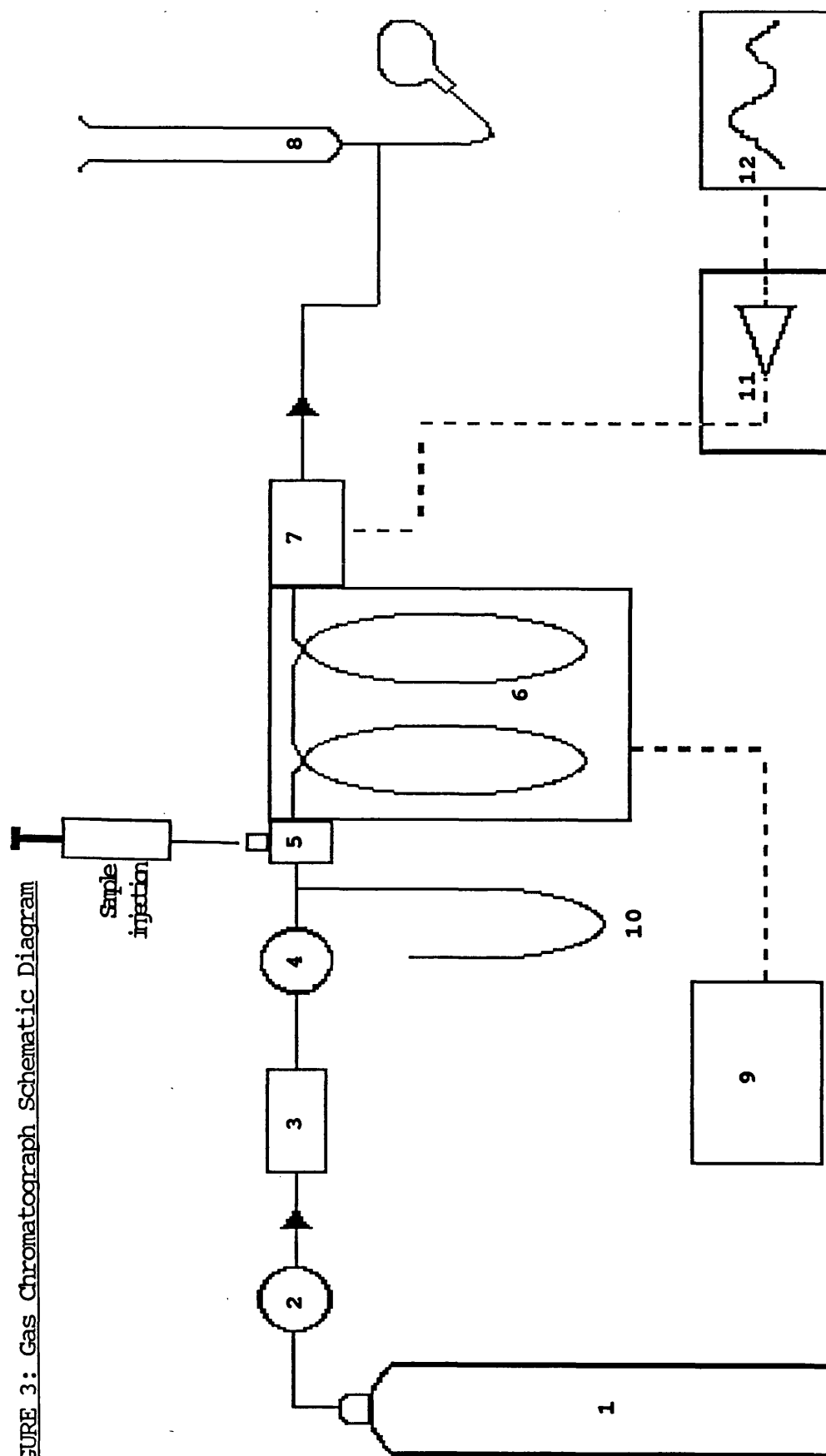
$$K = [m/(C_G - V_{\text{gas}})] \cdot V_{\text{liq}} \quad [7]$$

Solutes with unusually large partition coefficients (very involatile) are also problematic, as C_G will be small and difficult to determine accurately. Another drawback, especially with volatile solutes/solvents is absorption onto the rubber septum caps, which can only be partially resolved by covering them in foil, teflon, or heating them ²⁸.

1.22 Partition Coefficients From GLC

Dynamic GLC is the main method used in this work to obtain physiochemical parameters. So-called "inverse" GLC is also used, in that the area of investigation in this case is the nonvolatile or stationary phase and not the solute or vapour. This would be the case when chromatographing a series of solutes on a single stationary phase, in an attempt to characterise it. The layout of the basic gas chromatographic apparatus is shown in Figure 3. This consists of a column packed with stationary phase coated on the "inert" support, thermostatted with an air or liquid thermostat (for a greater degree of accuracy in temperature control) to the required temperature. Packed columns are usually constructed from glass, stainless steel or copper. Glass has the obvious advantage that the packing can be viewed while filling the column, and when in use in the GC. GLC packings, even at high loading levels, are normally completely free flowing, and may be poured into the column, or helped by application of slight pressure at

FIGURE 3: Gas Chromatograph Schematic Diagram



- 1 - carrier gas supply 2 - pressure regulator 3 - silica gel drying tube 4 - Negretti Zambra flow controller 5 - heated injector port 6 - column in water or air thermostat
7 - detector 8 - detector port 9 - chart recorder 10 - mercury manometer 11 - amplifier 12 - computer interface

one end, and vacuum at the other. The column is tapped or vibrated to settle and consolidate its contents. Excessive mechanical consolidation is deterring since diatomaceous supports tend to break down. The inert carrier gas is typically nitrogen, helium, argon, or hydrogen, supplied at around 50 psi, regulated to operating conditions using pressure controlling/reducing valves. A flow regulator preceding the column inlet governs the experimental gas flow rate, normally depending on the optimum conditions between 20 - 60 cm³ min⁻¹. The injection of a liquid sample, or a solid one dissolved in a suitably volatile solvent, is made with a microsyringe into the injection port, normally heated to instantly volatilize the sample. The carrier gas then transports the vapour onto the head of the column where it will interact with the stationary phase. The detector, which could be one of several different types, is at the outlet of the column. The most commonly used detector is the flame ionization type (FID) with a sensitivity of about 10⁻⁴ µg for a signal to noise ratio of 10² at a flow rate of 50 cm³ min⁻¹. Others include the thermal conductivity detector or katharometer, and electron capture detector (ECD). Detector output signal is amplified and measured on a chart recorder, special peak integration unit, or by computer.

An FID consists of a hydrogen flame burning at a jet in a supply of filtered air. Changes in ionization current due to components in the gas stream are detected and fed to the amplifier, which converts the impedance to a value matching that of the recording device. A katharometer is a dual channel Wheatstone bridge device, responding to the difference in thermal conductivity of the sample channel against the reference side upon emergence of components in the gas stream.

The sensitivity of an FID is some four to six orders of magnitude larger than that of a katharometer, even when the latter is used with hydrogen as the carrier gas. The signal from a katharometer depends on the difference in thermal

conductivity between carrier and solute vapour. Since organic solutes have thermal conductivities very much closer to heavy carrier gases such as nitrogen or argon, sensitivity is one to two orders of magnitude greater using the two light carrier gases (helium, hydrogen). For physiochemical work with a katharometer as a detector, helium or hydrogen are much to be preferred to nitrogen. Sensitivity of ionization type detectors such as the FID diminishes with decreasing flow rate, as they are of the mass flow type, This contrasts with the katharometer whose response is proportional to concentration rather than mass flow²⁹.

The katharometer is virtually a universal detector since it will respond to any material whose thermal conductivity differs from the carrier gas. The FID is not universal, and is by and large restricted to organic solutes, though its scope is extendible to cover inorganic gases as well³⁰. An FID cannot be used to detect water; a katharometer is essential here for physiochemical measurements. When the experimental flowrate has to be accurately known, for instance when measuring absolute partition coefficients, a katharometer is also used. It is simply a matter of connecting a soap-bubble flow meter to the gas outlet. Accurate measurement of flow rate using an FID is far less easy, as it dilutes or consumes the gas stream. It is possible to arrange for the carrier flow to be divertable at a point between the pressure gauge and sample injector, to a soap-bubble meter via a needle valve or restrictor adjusted to match the main flow line in pneumatic impedance³¹. It is also possible to measure the flow rate directly through the detector jet outlet, sealed to the flow-meter, with the flame out and the air supply switched off. If the carrier gas is diluted with hydrogen before passing through the jet, the hydrogen must also be switched off. The jet must be then left for some while to cool. This somewhat involved procedure is only satisfactory if switching off the ancillary gas produces no significant pressure change at the jet.

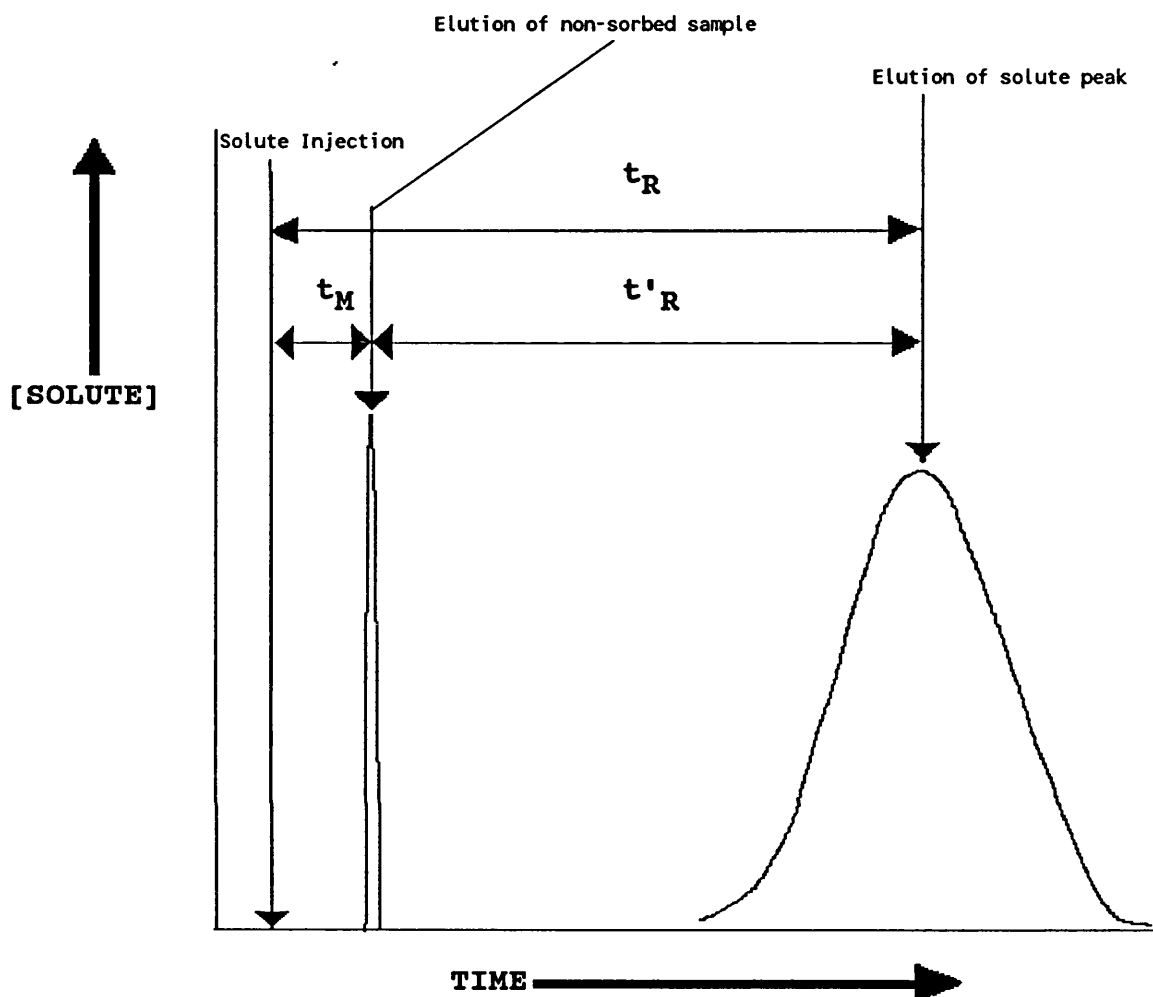
Commercial gas chromatographs usually require modifications to ensure accurate reproducible measurements. Thermostatting is often not satisfactory, especially at or near ambient temperatures, as desired in this work. In this case, the air oven is replaced by a liquid filled thermostat in which the column (to the level of the packing inside it), is completely immersed. Flow controllers supplied with commercial units are commonly unable to ensure steady gas flow rates, and so are replaced with much more sensitive units.

1.3 The Theoretical Basis of Chromatography

The chromatogram may be regarded as the solute concentration - time profile observed by the detector from introduction of solute to its emergence at the outlet. A typical elution chromatogram is shown in Figure 4. The measurement and calculation procedures outlined below use similar nomenclature and methodology as Conder and Young³². The crucial data measured from the chromatogram is the retention time, t_R , the time taken for the average molecule of solute to travel the length of the column, and is measured at the midpoint of the symmetrical breakthrough curve, or the highest point if the peak is asymmetrical. The solute will take a measurable amount of time merely to pass through the mobile phase from inlet to outlet without interaction with the stationary phase, - t_M . If these two times, t_R and t_M , are multiplied by the mobile phase flow rate F observed at the pressure at the column outlet, the product is the retention volume V_R , and the mobile phase or gas holdup volume V_M , respectively. The contribution to retention created by the stationary phase alone is the adjusted retention volume V'_R .

$$V'_R = V_R - V_M \quad [8]$$

FIGURE 4: Chromatogram obtained by elution chromatography



Owing to the compressibility of the carrier gas and the pressure drop across the column, the carrier gas flow rate differs from inlet to outlet and gradually rises from inlet to outlet as the carrier gas expands with the pressure drop. The volumes V_R , V_M , and V'_R can be corrected to mean column pressure by multiplying by a pressure-gradient correction factor J^2_3 . This factor is always less than or equal to unity, and is defined below, where P_i and P_o are the inlet and outlet pressures of the packed column:

$$J^m_n = \frac{n \cdot [(P_i/P_o)^m - 1]}{m [(P_i/P_o)^n - 1]} \quad [9]$$

$$V_N = J^2_3 \cdot V'_R \quad [10]$$

where V_N is the net retention volume.

The flow rate F is determined using a soap bubble meter, which obligates a correction for the difference between column temperature (T_c) and flowmeter (T_f), and for the vapour pressure of the soap solution, taken as the vapour pressure of pure water, P_w , at the temperature of the solution. Net retention volume then becomes:

$$V_N = J^2_3 \cdot V'_R \cdot \frac{(P_o - P_w)}{P_o} \cdot \frac{T_c}{T_f} \quad [11]$$

V_N is the chromatographic parameter from which the equilibrium thermodynamic parameters, such as partition or activity coefficients are calculated. The absolute partition coefficient K , which is dimensionless, and the net retention volume V_N are related by equation 12, where V_L is the volume of stationary phase liquid at the operating column temperature.

$$K = \frac{V_N}{V_L} \quad [12]$$

A slightly more complicated expression for an absolute K value may be derived if gas imperfections (interactions of solute vapour and carrier gas) are also accounted for.

$$\ln K^\circ = \ln(V_N/V_L) - (2B_{23} - V_2)P_o \cdot J^4_3/RT \quad [13]$$

B_{23} is the cross second virial coefficient between the solute vapour and carrier gas, J^4_3 is defined by equation 9, V_2 is the solute molar volume, an approximation for the partial molar volume V^∞_2 in the stationary phase. Even with the largest values of B_{23} and V^∞_2 usually encountered, the correction term never equates to no more than about 0.03 P_o , so unless the outlet pressure is very much greater

than atmospheric, the correction will be less than 3% of V_N .

Relative K values can be determined by chromatographing 2 or more solutes simultaneously. Where R again refers to the reference solute, and T to the test :

$$\frac{K^R}{K^T} = \frac{t_{R_R}^R - t_m}{t_{R_R}^T - t_m} \quad [14]$$

Many equilibrium properties can be determined from either the specific retention volume or the relative retention volume. The specific retention volume V_g° is characteristic of a particular solute, stationary phase and carrier gas. It is the net retention volume at 0°C for unit weight of stationary phase and is given by:

$$V_g^\circ = \frac{273 V_N}{W_S T} \quad [15]$$

where W_S is the mass of stationary phase in grams used in the column, and T is the column temperature in degrees Kelvin.

The relative retention volume is defined as the retention volume of the test solute divided by the retention volume of the reference solute:

$$\frac{V_g^T}{V_g^R} = \frac{V_{R_R}^T}{V_{R_R}^R} = \frac{t_{R_R}^T - t_m}{t_{R_R}^R - t_m} = \frac{K^T}{K^R} \quad [16]$$

The properties of solutions are usually described in terms of their derivations from the properties attached to an ideal solution. An ideal solution is defined as one in which the chemical potential of the components varies linearly with the logarithm of composition throughout the whole composition range. The chemical potential of a solute, μ_s , at any given composition X_s , is given by

$$\mu_s = \mu_s^\circ + RT \ln X_s \quad [17]$$

where μ_s° is the chemical potential of the pure component. For a solution behaving in an ideal manner, Raoult's Law states that the partial pressure of a solute, P_2 , is related to the mole fraction of the solute in the liquid solvent, X_2 , by the following relationship:

$$P_2 = P_2^\circ \cdot X_2 \quad [18]$$

where P_2° is the saturated vapour pressure of the pure solute. Deviations from Raoult's Law occur if the partial pressure of the solute is greater or less than equation 18 dictates, and a term will be required to correct for this non-ideality. The activity coefficient of the solute, Φ_2 , is required to give equation 19.

$$P_2 = P_2^\circ \cdot X_2 \cdot \Phi_2 \quad [19]$$

The solute activity coefficient at infinite dilution can be related to the partition coefficient, assuming the ideal gas law applies:

$$\Phi_2 = \frac{\rho_1 \cdot R \cdot T}{K \cdot P_2^\circ \cdot M_1} \quad [20]$$

So activity coefficients can be calculated from partition coefficients knowing the stationary phase (or solvent) molecular weight, M_1 , and density, ρ_1 at the column temperature T .

If a column behaved ideally at infinite dilution, an infinitely narrow injected peak would be infinitely narrow upon elution, and the height equivalent to theoretical plate (H) would be zero. In practice, peak spreading processes operate to broaden the peak as it travels the length of the column, reducing peak height and solute concentration. The maximum amplitude, A , of the peak is inversely related to the square root of the column length, l .

The cause of non-ideal peak band spreading may be loosely classified in two groups. The first involves processes occurring in every column, so-called "normal" processes. These are axial diffusion, spreading due to non-equivalent flow paths in the packing, and non-equilibrium due to resistance to mass transfer between phases. These three processes are responsible for the terms in the van Deemter³³ expression for H in the simplified equation below.

$$H = A + B/u + Cu \quad [22]$$

Term A represents band spreading due to eddy diffusion, purely a random effect of some molecules migrating down the column more directly than others, independently of carrier gas velocity, u. Longitudinal diffusion, B/u, is the band spreading associated with diffusion lengthwise in the column, although usually only significant solely in the gas phase. It occurs only where a concentration gradient exists, and is therefore inherently associated with an elution peak, or frontal boundary. Mass transfer, term Cu, is not instantaneous in either the stationary or mobile phases, which are not consequently in complete equilibrium. Solute molecules migrate along the column in an erratic manner, constantly sorbing on the stationary phase, and then revolatilising. The result is that the solute concentration profile in the stationary phase is always slightly displaced behind the equilibrium position, and the mobile phase profile is similarly slightly in advance. The combined peak observed at the exit is spread, but the mass centre is where it would have been for instantaneous equilibrium.

The second group of effects are not inherent in the chromatographic process, but are none the less quite common. They can be generally described as slow kinetic processes, such as slow desorption from sites of high adsorption energy, slow reactions involving the solute on the column, and very slow diffusion-controlled

mass transfer between phase.

Another band spreading process is the sorption effect, which results in areas of high solute concentration in the column moving slower than low concentration areas. Littlewood³⁴ describes a simple way of expressing this. The total pressure inside a peak in a column is not different from the total pressure elsewhere in the column, neglecting the overall pressure gradient. Since the solute has a finite vapour pressure, the partial pressure of carrier is correspondingly reduced. Mass flow rate of carrier gas in the column must remain constant along its length, so it follows that the carrier velocity is greater inside the peak than elsewhere. This causes the centre of the peak through the column to move more rapidly than other parts, so that it becomes skewed towards the end of the column, and a slight asymmetry is imposed upon the peak. The front profile will therefore be sharper than the back one. Retention volumes can be slightly reduced by this effect, but working at, or near to infinite dilution will minimize this.

1.31 Considerations for GLC Efficacy and Optimisation

A GLC system is best used with the flow rate giving minimum height equivalent to theoretical plate, (H). This will maximize the ratio of retention time to peak width, and therefore the precision with which the chromatogram is interpreted. To ensure this, H at several different flow rates can be plotted against the rates, and the flow rate for minimum H determined³⁵. Typically, optimum flow rates will be between 20 and 60 cm³ min⁻¹. The number of plates, n, for a given column can be determined from:

$$n = 5.545(t'r/W_H)^2 \quad [23]$$

where t'r is the adjusted retention time, and W_H the peak width at half height in

the same units of time. H can then be calculated by dividing column length, L, by n.

$$H = \frac{L}{n} \quad [24]$$

Since katharometers are less sensitive than FID systems, significantly more solute needs to be chromatographed to obtain a discernible peak. This might lead to adsorption effects in practice, so katharometers are only used where the solute dictates this, (eg. for water), and to obtain absolute partition coefficients, where accurate flow rate measurement is essential. Usually absolute partition coefficients of n-alkanes are measured using a katharometer system, and then an FID system is used to obtain coefficients for other compounds, relative to these.

For accurate measurement of partition coefficients the stationary phase loading on the support must be known. K is related to the volume of stationary phase liquid at experimental temperature by equation 12, where V_N is retention volume.

$$K = \frac{V_N}{V_L} \quad [12]$$

Stationary phases in most cases can simply be coated by rotary evaporation of a slurry of support and stationary phase, dissolved in a suitable volatile solvent. This technique sometimes proves unsuitable with high molecular weight compounds, as they may be thrown to the side of the flask upon evaporation. In these cases, the slurry is left to slowly coat in a beaker at room temperature, with slight mechanical agitation. If the stationary phase coats easily, and it all can be assumed to have successfully covered the support, accurate weighing is all that is needed to calculate the percentage loading, - see the experimental section, p. 260, for further details. In cases where the complete interaction of the

stationary phase and the support is in doubt, ie. a residual amount of phase is left after effecting a coating on a chosen support, other methods are necessary^{35,36}. These include possible elementary analysis, Soxhlet extraction of the stationary phase, or combustive (and subsequent weighing) techniques. Silanised supports will require a correction for the organic methylsilyl layer that will be burnt off together with the stationary phase in question if the combustive technique is used. Martire and Riedl³⁷ have found the combustion method to be more reproducible than Soxhlet extraction.

The "inert" support chosen for use in GLC is an important consideration to ensure the data recorded is meaningful. The liquid stationary phase should coat the surface of the support evenly, providing a very large interface for interaction with solute vapour.

If the support was totally inert, the phase would not be able to coat it, merely forming globules on the surface, so some degree of activity is desirable. If 100 % uniform coating of a support does not occur, the support may well be active enough to establish an equilibrium between it and the solute in the carrier gas. This will obviously effect physiochemical measurements such as partition coefficients, as the only equilibrium considered here is between solute in the gas phase and liquid stationary phase.

There are many different types of commercial support available, but most are based on diatomite (kieselguhr). It originated from one celled algae, and consists of amorphous silica with small amounts of impurities.

Chromosorb G was the main support used in this work, due to the fact that its geometry means a smaller amount of stationary phase is required to produce a suitable thickness of the surface layer, as compared to other supports. This

means that a 10% w/w (a typical loading level) coating of stationary phase on Chromosorb G is equivalent to a about a 20% w/w coating on a support such as Chromosorb W. Horváth³⁸ showed that a 2% w/w coating gives a relative surface layer thickness of 4, 1.65 and 0.5 respectively on Chromosorb G, W and P respectively. Conversely, if great problems were experienced in coating Chromosorb G, Chromosorb W was then used at the same loading level, the smaller thickness of the surface level making this easier.

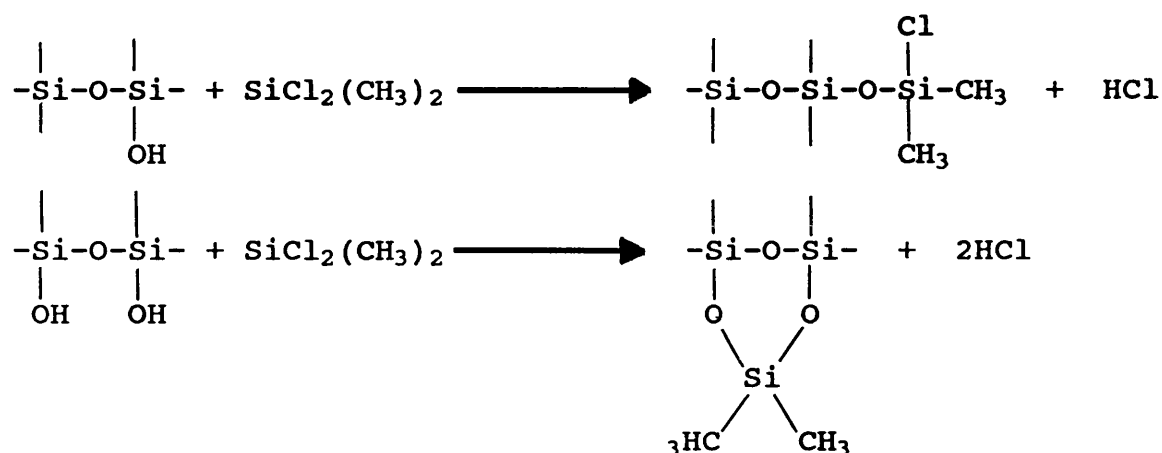
If values of partition coefficients obtained by static techniques, such as headspace analysis, agree reasonably closely with those obtained from dynamic GLC, this points to the fact that solute equilibrium effects other than partition between gas and liquid are negligible. Adsorption effects on the support are frequently shown by excessive peak tailing in the chromatogram (though this is by no means always an effect caused by the support). Solutes, especially polar ones, will interact with the active sites of the support. This effect is minimized in practice by using sufficient quantities of the stationary phase to be sure of coating all the support active sites, using a loading level of usually no less than 10% w/w³⁹. Disagreement between values of partition coefficients from static methods and dynamic GLC means the support is not completely coated, or not inert enough, and another term must be introduced into equation 12:

$$V_N = K \cdot V_L + K_S \cdot A_S \quad [25]$$

where K_S is the support adsorption coefficient, and A_S the uncoated support surface area.

Commercial supports have usually been treated in some way to minimize adsorption effects, yet still leave them sufficiently active to allow coating to occur. Any trace iron present in the support can be removed by a thorough acid washing. Diatomite supports are made up of a network of siloxane groups, which

may also contain silanol groups. Interactions between the support and stationary phase will be of the dipole and dispersion type, hydrogen-bonding, and capillary forces. These interactions hold the liquid on the surface of the support. Activity of the silanol groups in the support can be reduced by use of a silanizing agent, such as dimethyldichlorosilane (DMCS). Two reactions are suggested to be involved⁴⁰ for a single silanol group and two adjacent silanol groups:



Silanisation will therefore eliminate hydroxyl functionality and the ability of any uncoated support to act as a hydrogen-bond acid towards any hydrogen-bond base solutes. Very many solutes act as hydrogen-bond bases.

Theoretically it is desirable to use the most inert support for non-polar stationary phases, and non-silanised ones for polar stationary phases. Thus Chromosorb G AW DMCS (acid washed, and silanised) might be used for non-polar phases, and to ensure a polar phase actually coated properly, - Chromosorb G AW. In practice though, Chromosorb G AW DMCS was found suitable for almost every phase.

1.4 A Comparison of Headspace Analysis and Dynamic GLC

The obvious difference between the two methods is that headspace analysis achieves solute equilibration between vapour and liquid in a completely static manner. The system is enclosed, and there is no agitation to either phase. GLC is a dynamic method, ie. there is a mobile phase. In both cases care must be taken to make sure equilibration is complete. Sufficient time must be allowed for a static headspace experiment to reach equilibrium, especially where the solution under investigation is viscous. Similarly in GLC, carrier gas flow rate must not be too fast, and preferably the optimum setting for the system, (see section 1.31).

Dynamic GLC is far less susceptible to solute impurity problems, and providing that the solute under investigation is the largest constituent in a sample and its retention time is clearly discernible, accurate results are obtainable. Far smaller samples can be dealt with by the process of GLC, almost invariably working at infinite dilution, where solute-solute interactions can be discounted. The physiochemical parameter obtained is then a function of solute-solvent interactions only.

Speed of data acquisition is the largest advantage dynamic GLC has over the headspace technique. Instrumental and experimental variations are small giving more reproducible results, and homologues can be simultaneously injected. Headspace analysis is still an invaluable technique for corroborating GLC results, and when dynamic GLC proves impractical.

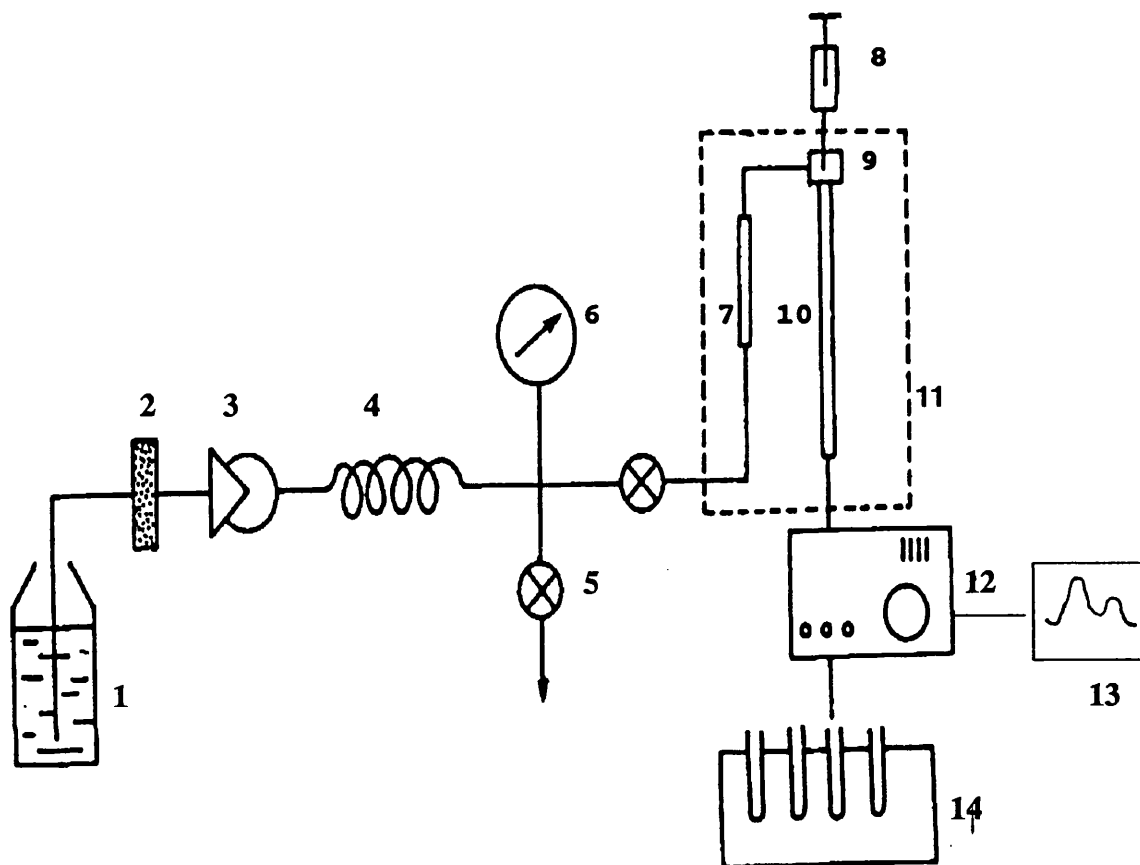
1.5 High Performance Liquid Chromatography

A limited discussion of HPLC and its applications is also appropriate, as numerical analysis was performed on data measured on HPLC systems.

The most important difference between GC and HPLC is that GC can only cope with substances which are volatile or can be evaporated intact at elevated temperatures, or from which volatile derivatives can be readily obtained. In fact, only approximately 20% of known organic compounds can be analysed by GC without prior treatment. For liquid chromatography, the sample must be dissolved in a solvent and apart from cross-linked, high molecular mass compounds, all organic and ionic inorganic products satisfy this condition. There are three important differentiations to point out when comparing the methods. Firstly, the compressibility of the mobile phase under pressure is negligibly small in HPLC (an advantage), but not in GC. The viscosity of the mobile phase is higher in HPLC (a drawback), and lastly, the diffusion coefficient of the sample in the mobile phase is much smaller in HPLC, (also a drawback). Typically, the number of separation plates in a metre of packed HPLC column is 50,000, whereas in GC this is only 1,000. A schematic of a representative HPLC unit is shown in Figure 5.

Classical liquid chromatography uses simple apparatus: a solvent reservoir, a wide bore glass column, a relatively large diameter particle packing, and collection tubes for the effluent. To increase the speed of analysis and resolving power to match that of GC, it is necessary to increase the relatively low liquid flow rates used (which are due to the high viscosity of liquids compared with gases), and to obtain faster sample equilibration between mobile and stationary phase. These two aims are achieved by pressurizing the mobile phase, (up to a limit of around 5000 psi), and by using packings of small particle size. Column

FIGURE 5: Schematic diagram of HPLC unit



- 1 - solvent reservoir 2 - sintered metal frit 3 - high-pressure pump 4 - pulse damper
 5 - drain valve 6 - manometer 7 - pre-column (optional) 8 - injection syringe
 9 - injection valve 10 - column 11 - thermostat oven (optional) 12 - detector
 13 - recorder, integrator or computer via interface 14 - fraction collector (optional)

permeability decreases with smaller particle size, so to avoid excessively high pressures, smaller column lengths must be used.

Phase preference is similarly expressed in HPLC by the partition coefficient K^{41} . This is exactly equivalent to equation 2 for GC, (written in a more generalised manner).

$$K = \frac{\text{concentration of solute in static phase}}{\text{concentration of solute in mobile phase}} = \frac{C_{\text{stat}}}{C_{\text{mob}}} \quad [26]$$

A fundamental chromatographic parameter, especially in HPLC is the capacity factor k' , where:

$$k' = \frac{n_s}{n_m} \quad [27]$$

and n_s and n_m are the number of moles of solute in the stationary and mobile phases respectively. The partition coefficient K can be related to k' as follows:

$$k' = K \cdot \frac{V_S}{V_M} \quad [28]$$

where V_S is the volume of the stationary phase, and V_M is the volume of mobile phase. In liquid chromatography the mobile phase may be considered to be incompressible, and the pressure and flow rate are constant throughout the column. Therefore, in contrast to GC, no compressibility correction has to be made to flow measurements taken at the column outlet to obtain the mean flow through the column.

The capacity factor can also be calculated from:

$$k' = \frac{t'_r}{t_o} = \frac{t_r - t_o}{t_o} \quad [29]$$

where t_r is peak retention time, and t_o is the dead time, or the time required by the mobile phase to pass through the column, (retention time of unretained solute).

Capacity factors of between 1 and 5 are preferred. If k' values are too low, the level of separation may be inadequate (if the compounds pass too quickly through the column, no stationary phase interaction occurs and hence no chromatography). High k' times are accompanied by long analysis times. The capacity factor k' , is directly proportional to the volume occupied by the

stationary phase, and more especially to its specific surface area (m^2g^{-1}) in the case of adsorbents. A column packed with porous-layer beads produces lower k' values and hence shorter analysis times than a column containing completely porous particles if the other conditions remain constant. Silica with narrow pores produces larger k' values than a wide pore material.

Two components in a mixture cannot be separated unless they have different k' values, the means of assessment being provided by the relative retention value, α , also known as the separation factor.

$$\alpha = \frac{k'_2}{k'_1} = \frac{t_{R2} - t_o}{t_{R1} - t_o} = \frac{K_2}{K_1} \quad [30]$$

If $\alpha = 1$, no separation will take place, as the retention times for both solutes will be identical. Relative retention is a measure of the selectivity of a chromatographic system, ie. its ability to separate two or more compounds. The stationary and mobile phases chosen can affect the value of α .

1.51 Reversed-phase HPLC

Reversed-phase chromatography can be classified as a special type of either adsorption or partition chromatography⁴². It is a term used to describe the state in which the stationary phase is less polar than the mobile phase. In normal phase LLC the stationary phase would be a polar liquid such as water, glycol or β,β' -oxydipropionitrile. The mobile phase is relatively non-polar, e.g. hexane, chloroform or benzene. This mode of operation is used to separate polar compounds which would be distributed preferentially in the polar stationary phase.

Reversed-phase chromatography involves a non-polar stationary phase, e.g. a hydrocarbon-bonded silica, and a polar mobile phase such as water. Water is often described as the strongest elution medium for liquid chromatography, but this is only true for adsorption processes. Water may interact so strongly with the active centres in silica gel and alumina that adsorption of sample molecules becomes highly restricted, and they are rapidly eluted as a result. Exactly the opposite applies in a reversed-phase system. Water is unable to wet the hydrophobic alkyl groups of the stationary phase, and does not interact with them in any way. Water is therefore the weakest mobile phase of all, and gives the slowest elution rate. The mobile phase generally consists of mixtures of water or aqueous buffer solutions with various water-miscible solvents. Increasing polarity leads to decreasing elution power, for example: tetrahydrofuran > propan-1-ol > acetonitrile > methanol. The greater the amount of water in the eluent, the longer is the retention time.

Sample compounds are better retained by the non-polar reversed-phase surface the less water soluble (i.e. the more non-polar) they are. The more polar the solute, and in particular the more basic the solute, the more affinity it will have for the polar (and highly acidic) aqueous eluate.

Aqueous solutions, such as those of biological origin and pharmaceutical formulations are common samples for analysis. As water is the weakest eluent, aqueous solutions may be injected directly without any specialist treatment. However, reversed-phase chromatography is not just suitable for polar compounds alone. For example, the seventeen polycyclic aromatic hydrocarbons (PAH) which are referred to by environmental analysts as 'priority pollutants' can be completely separated using this technique in 15 minutes.

2.1 Theories of Solubility

2.11 The Hildebrand Solubility Parameter

The solubility parameter δ_H (given the subscript $_H$ to distinguish it from another parameter, δ , used in this work), first introduced by Hildebrand and Scott⁴³, is defined as:

$$\delta_H = \left(\frac{\Delta H_v^\circ}{V} \right)^{0.5} \quad [31]$$

The expression $\Delta H_v^\circ/V$ is known as the solute cohesive energy density, where ΔH_v° is the enthalpy of vapourisation at 298K, and V is the molar volume. It was considered that compounds with equal or similar solubility parameters would form ideal solutions. However, the shortcoming of this single parameter is that vapours with obvious dissimilarities are sometimes ranked equally; for example, polarisable, non-hydrogen-bonding toluene has a similar parameter to dipolar, hydrogen bond basic ethyl acetate. The initial theory dealt with the solution of non-electrolyte solids in non-polar solvents, but was developed and refined⁴⁴ to extend its range of applications to common systems such as polar solvents, polymers etc. A multicomponent solubility parameter was proposed by Hansen⁴⁵ made up of contributions from non-polar dispersion forces (δ_d), permanent dipole-dipole interactions (δ_p) and hydrogen bonding interactions (δ_h).

$$\delta_H^2 = \delta_d^2 + \delta_p^2 + \delta_h^2 \quad [32]$$

This can be further extended⁴⁶ to take into account all the solubility interactions relevant to the solvation of non-ionic compounds (subscripts identify terms in equation 33), namely:

- a) induced-dipole/induced dipole interactions (dispersion) δ_d
- b) dipole/induced-dipole interactions (dipole induction) δ_{ind}
- c) dipole/dipole interactions (dipole orientation) δ_o
- d) hydrogen bonding interactions - acid δ_a base δ_b

$$\delta^2_H = \delta^2_d + \delta^2_o + 2\delta_{ind}\delta_d + 2\delta_a\delta_b \quad [33]$$

For molecules that are not too involatile, the solute cohesive energy density can be determined from:

$$\delta^2_H = (\Delta H^{\circ}_v - RT)/V \quad [34]$$

It is defined from equation 34 as the heat of vapourisation at 298K per unit volume of solvent. In the correlation and prediction of the solubility of gases and vapours the Hildebrand cohesive energy density can be used as a measure of the energy required to form a cavity in the solvent.

2.12 The Scaled Particle Theory & Linear Solvation Energy Relationship (LSER)

Abraham, Kamlet, and Taft, (AKT) ^{47,48} have developed a methodology over the past few years for modelling the process of solution, based on a scaled particle theory, (in the explanation that follows, subscript 1 refers exclusively to solvent and subscript 2 to solute). The process of dissolution of a solute in a solvent is broken down into three hypothetical steps.

- 1) A cavity of a suitable size must be formed in the bulk solvent - an endoergic process
- 2) The solvent molecules reorganize around the cavity. The Gibbs energy change is probably small, or zero.

3) The introduction of the solute into the cavity, then sets up various exoergic solvent-solute interactions

As the Gibbs energy change involved in step two is assumed to be zero for practical purposes, only steps one and three need be modelled.

The energy needed for the formation of a cavity in the bulk solvent can be taken as proportional to the Hildebrand cohesive energy density^{43,49}, and to some function of the solute size or volume. A term $(\delta_H^2)_1 \cdot V_2$, with units of energy, will account for step one, where V_2 is the solute molecular volume.

Introduction of the solute into the solvent cavity can set up (depending on the nature of both solvent and solute) various solvent-solute interactions, which will normally be exoergic. If the solvent and solute are polar or polarisable dipolar interactions may be set up, of the type dipole-dipole (dipole orientation interactions), or dipole-induced dipole (dipole induction interactions), π^*_1 representing the solvents' contribution and π^*_2 the solute. The combined term corresponding to polar interactions will then be $\pi^*_1 \cdot \pi^*_2$. Hydrogen bond acid /hydrogen bond base interactions may be set up if the solvent is a hydrogen bond acid, represented by α_1 , and the solute a hydrogen bond base, represented by β_1 , or the solvent a base and the solute an acid. This leads to the terms $\alpha_1 \cdot \beta_2$ or $\beta_1 \cdot \alpha_2$ respectively.

For solubility or a solubility related process, SP, a generalised equation can now be formulated.

$$\text{Log SP} = \text{SPo} + A\pi^*_1 \cdot \pi^*_2 + B\alpha_1 \cdot \beta_2 + C\beta_1 \cdot \alpha_2 + D \cdot (\delta_H^2)_1 \cdot V_2 \quad [35]$$

SPo is a constant, while A,B,C, and D are constants which will be entirely

dependant on the solvent property or solute property being modelled.

For a single solute property in a series of solvents, the solute parameters in the equation are also constants, and can be subsumed into A,B,C, and D, giving equation coefficients s,a,b and h. These coefficients can be obtained by the technique of multiple linear regression analysis (MLRA). Equation 35 is rewritten as:

$$\text{Log SP} = \text{SPo} + s\pi^*_1 + a\alpha_1 + b\beta_1 + h.(\delta_H^2)_1 \quad [36]$$

Alternatively, if a given property of a series of solutes in one solvent is being modelled, all the solvent parameters can be taken as constant. In this case equation 35 can be written as:

$$\text{Log SP} = \text{SPo} + s\pi^*_2 + a\alpha_2 + b\beta_2 + m.V_2 \quad [37]$$

An extra term is sometimes necessary in this equation with certain types of properties to give improved multiple linear regression analysis. If there are aromatic or polyhalogenated compounds included in the solute set, a polarisability correction term is included⁵⁰, d. δ_2 . The δ_2 parameter is a trivial one, being 0.0 for all nonpolyhalogenated aliphatics, 0.5 for polyhalogenated aliphatics, and 1.0 for all aromatics.

$$\text{Log SP} = \text{SPo} + d.\delta_2 + s\pi^*_2 + a\alpha_2 + b\beta_2 + m.V_2 \quad [38]$$

Kamlet et al⁴⁶ have taken the cavity term for a series of solutes in the same solvent as being proportional to either the intrinsic volume, V_I , of Leahy⁵¹, or the characteristic volume, V_X , of McGowan⁵². Equation 38 works very well when applied to processes in condensed phases, for example when SP is a liquid-liquid

partition coefficient. But for processes of the type gas $\rightarrow$ condensed phase, it is clear that equation 38 is deficient in that there is no explicit term to describe solute-solvent dispersion interaction. A solute parameter, denoted $\log L^{16}$, was therefore devised, where L^{16} is the Ostwald solubility coefficient on n-hexadecane at 298.15K²⁴. The term in solute volume is then redundant, and equation 39 can be used as a revised version of equation 38.

$$\text{Log SP} = \text{SPo} + d.\delta_2 + s\pi_2^* + a.\alpha_2 + b.\beta_2 + 1.\log L^{16} \quad [39]$$

The varying solute properties that give rise to interaction terms are now included in this equation (solute dipolarity, hydrogen-bond acidity and basicity, and a solute size/dispersion term). This is typical of the type of LSER used in this work.

2.13 Linear Free Energy Relationships (LFER)

In organic chemistry a number of empirical models for the description of relationships between structure and reactivity have emerged. The most successful and intensively investigated are LFER⁵³, with the Hammett equation⁵⁴⁻⁵⁶ as the most prominent example. The term LFER derives from the major use of these relationships as mathematical tools for correlating changes in free energy in different reaction series. Relationships of the same mathematical form as LFER can however be used to correlate the change of any property measured on any ensemble of similar processes, systems or objects. The terms correlation analysis or quantitative analogy models⁵⁷ are somewhat more appropriate. The term LFER in practice refers to a mathematical relationship of a special form used to correlate any type of observed quantity regardless of whether they are proportional to free energies or not⁵⁸. LFER are tools of chemical pattern recognition⁵⁹, whereby the behavioural pattern of similar chemical systems is

given a mathematical representation. Provided certain continuity assumptions are valid, generalised LFER describe the variation of any measurement made on similar systems. Due to their wide scope of application, LFER are found in a large number of areas in chemistry^{53,60,61}. The important point for the chemist is probably the close connection of the LFER to classical chemical reasoning in terms of classification and analogies within classes, which makes LFER uniquely suitable for the analysis of chemical data. LFER can handle information that is contained in several variables. LFER are not however substitutes for chemical knowledge, but rather a quantitative support for chemical reasoning. To summarise they are quantitative models of similarity that can be used in chemical pattern recognition for (a) finding the typical data structures for groups of similar systems - reactions, compounds, spectra, mixtures, etc., (b) utilising these data structures either for the classification of new, unassigned systems or for constructing new systems with desired properties.

2.14 Quantitative Structure Activity Relationships (QSARs)

It has long been desirable to be able to predict the biological effect of a given substance from its chemical constitution, or have methods for the analysis of biological activities, which would provide insight into the mechanism of action of a given drug. QSARs correlate chemical structure with biological activity⁶², ie., they are a specialised LFER. The application of QSARs is growing out of the interaction of the fields of physical organic chemistry, statistics, computer science, quantum chemistry, biomedical and pesticide chemistry, and molecular biology. Structure activity relationship models are constructed using regression analysis with physiochemical constants and indicator variables. Once some kind of abstract relationship between chemical structure and activity has been developed, it must be examined from a variety of all points of view to be

sure the model conforms with known chemistry and physical organic chemistry⁶³. There is great interest in the application of QSAR techniques especially in the pharmaceutical industry. Early work concentrated on the correlation of biological activity with oil/water partition coefficients, P_{OIL} . With the recognition of its importance in hydrophobic interactions of ligands and macromolecules and biological membranes, the octanol/water partition coefficient, $\log P_{OCT}$, has become a subject for structure-activity studies⁶⁴.

Using the AKT methodology, equations can be constructed to correlate and predict a large number of physiochemical and biochemical phenomena, ie. LSER and QSAR equations. Kamlet et al⁴⁸ have reviewed the principle of LSER, and its applications (up to about 1985) are reviewed by Kamlet and Taft⁶⁵. Multiple linear regression analyses of measured solubility or solubility related processes will lead to characteristic LSER or QSAR equations for the phenomena under investigation.

LSER and QSAR are the principal tools used in this work to quantify these processes, generating equation coefficients that uniquely characterise the process under investigation in terms of fundamental interactions. Prediction and calculation of solubility and various solubility related processes and vapour-liquid equilibria is of course also possible through the use of these equations.

2.2 Prediction of Vapour-Liquid Equilibria by Group Contribution Methods

Estimation of thermodynamic properties of liquid mixtures from group contributions was first suggested by Langmuir⁶⁶. This suggestion however, received little attention until Derr et al^{67,68} used group contribution methods to

correlate heats of mixing, followed by Wilson and Deal⁶⁹ who developed the solution of groups method for activity coefficients. The UNIFAC (Unified Functional Group Activity Coefficient) method for the calculation of activity coefficients⁷⁰ is based on the group contribution concept, which has been successful for estimating a variety of pure component properties such as liquid densities, heat capacities, and critical constants. The fundamental idea behind this approach is that whereas there are many thousands of chemical compounds of interest in chemical technology, the number of functional groups which constitute these compounds is very much smaller. Therefore, if it is assumed that a physical property of a compound is the sum of the contribution made by the molecules' functional groups, it becomes possible to correlate the properties of a large number of compounds in terms of a much smaller number of parameters which characterise the contributions of individual groups. In addition, the method provides a technique for predicting phase equilibria in systems where no data exist. For example, it is possible using the group contribution approach to predict the equilibrium composition in all ketone/alkane mixtures from data on just one representative example, such as acetone/cyclohexane.

Any group contribution method is by nature an approximation, because the contribution of a given group in one molecule is not necessarily the same as that in another molecule. The fundamental assumption behind the use of the group contribution method is additivity, and the contribution made by one group is assumed to be totally independent of that of another group. This assumption will be valid only when the influence of any one group in a molecule is not affected by the nature of other groups in that molecule.

Accuracy of correlation improves with increasing distinction in groups. For example, in a first approximation no distinction might be made between the

position of the hydroxyl group in an alcohol, but in a second approximation such a distinction might be desirable. As more distinctions are made, the ultimate group is recovered, that of the entire molecule itself. So, for practical purposes a compromise must be attained. The number of distinct groups must remain small, but not too small as to neglect significant effects of molecular structure on physical properties.

The aim of the UNIFAC method is to provide an accurate and reliable method for predicting vapour-liquid equilibria, and the present table of group contribution parameters is based wherever possible on vapour-liquid equilibria data only⁷¹. The equations in the UNIFAC method may also be used to predict liquid-liquid equilibria and excess enthalpies. However, in the present development of the UNIFAC method, accurate prediction of these has been second priority.

The basic assumption behind the UNIFAC model is that the logarithm of the activity coefficient is assumed to be the sum of two contributions: a combinatorial part,^C, essentially due to differences in size or shape of the molecules in the mixture, and a residual part,^R, due to energy interactions. Thus for any molecule, m:-

$$\ln \Phi_m = \ln \Phi_m^C + \ln \Phi_m^R \quad [40]$$

The residual part is assumed to be the sum of the individual contributions of each solute group in the solution less the sum of the individual contributions in the pure solvent environment. The individual group contributions in any environment are assumed to be only a function of group concentrations and temperature.

In its present state of development, the UNIFAC method may be used to predict

the phase equilibria in the non-electrolyte mixtures for temperatures in the range of 300-425 K and pressures up to a few atmospheres. All components must be condensable. UNIFAC is well used for several reasons:-

- 1) Flexibility; it has a well founded basis for establishing group sizes and shapes.
- 2) Simplicity; UNIFAC parameters are nearly independent of temperature for the range 300 - 425 K.
- 3) Larger range of applicability; as parameters are available for a large number of functional groups.

A major disadvantage of UNIFAC is that it is only an approximation, and this is also true of the group contribution method as a whole. UNIFAC cannot predict differences in behaviour of a *sub* group between slightly differing environments. For example, a carbonyl group in a ketone and an aldehyde is expected to behave in a similar manner, but the same can not be said of a carbonyl group in a carboxylic acid and a ketone. If too many distinctions are made between functional groups are made however, its usefulness is also limited, as the whole procedure becomes very complicated as a far greater number of parameters are necessary to define the functional groups.

Other group contribution methods are UNIQUAC⁷², ASOG (Analytical Solution Of Groups),^{69,73-75} and MOSCED. All these methods are well established in the calculation of infinite dilution activity coefficients, Φ^∞ , but there is always an overriding difficulty in the interpretation of parameters referring to Φ^∞ . Since Φ^∞ is an equilibrium constant (or partition coefficient) between the bulk liquid solute and the solute at infinite dilution in the solvent, Φ^∞ will contain not only

solute-solvent interactions, but solute-solute interactions as well. Gas-liquid partition coefficients contain only solute-solvent interaction terms¹⁶, and hence are inherently easier to interpret than quantities that refer to partition between the bulk liquid and the solvent.

2.3 Multiple Linear Regression Analysis (MLRA) with LSER & QSAR

Back in 1966 a paper was written on the use and abuse of regression techniques⁷⁶, and for accurate results to be obtained from LFER equations (LSER & QSAR), the correct interpretation and use of MLRA is an important consideration. One can be virtually certain of the interpretation of the points that are well fitted by a simple LSER, but deviations can be due to a large number of causes. In the application of MLRA to quantify LSER and QSAR, certain precautions must apply.

MLRA is a heavily used technique in statistics⁷⁷, and unfortunately the technique is often abused, because of two contributory factors:

- 1) The basic mathematics is simple, leading to the idea that all that is necessary to use multiple regression is to program some standard formulae.
- 2) There are many computer programs enabling the unwary to proceed with the regression analysis calculations, whether or not the analysis fits.

A frequent problem with data in regression analyses is caused by near linear relationships between two or more explanatory variables. If the relationships are exact then the regression estimates cannot be formed. When these linear relationships are not exact, the variance of the regression estimates can be

grossly inflated due to their presence - this problem is termed *multicollinearities* amongst the explanatory variables. The multiple regression program used in this work routinely checks for the presence of such a relationship. The effect of multicollinearity is to inflate the variance of the least squares estimator and possibly any predictions made, and to restrict the generality and applicability of the estimated model. Nesting is another problem, caused by the explanatory variable data having a crossed or nested design. In an extreme form of crossed structure the design of the data points may be such that the variables are orthogonal to each other and so a completely different form of analysis is therefore appropriate.

Frequently data sets contain one or more outliers, points which are separated in some way from the remainder of the data. They may be individual observations or groups of two or more points. Such outliers need to be investigated and identified thoroughly. There are several reasons for such outliers - accidental digit transposition, incorrectly entered values for a variate or individual observation, or experimental errors. If data has not been recorded with sufficient accuracy, the whole data set may be rendered useless. It may be that certain data points just do not fit the overall analysis, reasons for this need to be identified. Outlying observations cannot be removed from all further analyses purely because they seem discordant. For example, in some biological applications, an outlier may indicate that sporadically an entirely different type of response is given, and in this case the outlier may be more informative than the rest of the observations. It is usual with an outlier to:

- 1) Use some statistical technique to see how discrepant they are
- 2) Check the source of the data to see if any reason can be found for the outliers, such as misrecording or unexpected experimental conditions. If a

suitable explanation for the suspect data can be found, it may be modified or dropped from the overall analysis.

3) Carry out the analysis with and without the suspect data to see what effect this will have.

Multiple outliers are another difficulty and sometimes the data set can be separated into two or more sets of points or clumps. These clumps may pull the fitted equation around through themselves. Various theoretical difficulties arise in such a case^{78,79}. The existence of clumps in the data set also implies there are regions of sparse density of points in which the fitted model cannot be validated with any degree of confidence. It is also possible that two or more discrete lines of data might be apparent upon analysis of the data. For instance, a data set might be separated by the regression process into two classes, aliphatic organic compounds and aromatic, that need their own unique equations to accurately form representative LSER. Care must also be taken in forcing the regression equation through the origin, as it is the case in most instances that the overall correlation coefficient will be improved. However this approach is only valid in special cases, such as when the equation constant is known to be zero.

2.31 Application of MLRA in this work

The favoured multiple regression equation in the past few years has been equation 39, consisting of four major terms and the trivial polarity correction term, $d.\delta_2$. These correspond to the various processes and interactions that arise in the dissolution of a gaseous solute.

$$\text{Log SP} = \text{SPo} + d.\delta_2 + s\pi^*_2 + a.\alpha_2 + b.\beta_2 + l.\log L^{16} \quad [39]$$

Part of the aim of this work has been to calculate or measure better parameters for use in this equation, or investigate alternative ones. More generally, (especially with regard to seeking suitable substitutes in this equation), equation 39 can be written as:

$\text{Log SP} = \text{[1] Log SPo (equation constant)} + \text{[2] a correction term for quantitative indication of polarizable } n \text{ and } \pi \text{ electrons} + \text{[3] dipolarity or dipolarity/polarisability term} + \text{[4] hydrogen-bond acidity term} + \text{[5] hydrogen-bond basicity term} + \text{[6] solute size \& dispersion interaction term}$

Multiple regression of the logged solubility property against the four major solute parameters will generate a characteristic equation, with coefficients for terms 2 to 6. This LSER and the magnitude of the coefficients will provide an understanding of the process under investigation. Constants generated characterise the process in terms of fundamental interactions with which chemists are familiar. For instance, in the study of a gas chromatographic stationary phase which is basic and polar, one might reasonably expect large coefficients in s and a . The term $b.\beta_2$ would be expected to be zero (as no interactions with hydrogen-bond bases would be expected). For many solubility processes all the terms would not be required, resulting in a zero or statistically insignificant parameter coefficient. The magnitude of the coefficients is proportional to the solute-solvent interaction that the coefficient and solute parameter refer to. A large coefficient in the equation for hydrogen-bond acidity would give a measure of the solutes hydrogen-bond basicity, but it will not be equal to the solute basicity. This is because in studying the interactions of a set of solutes on one solvent, constants are subsumed into the equation coefficients.

Not only do the above constants characterise the phase in a chemically related way, they provide information as to separations. Thus a large value of s

indicates that solutes can be separated on the basis of dipolarity, or a large value of L shows that separation between members of homologous series is favoured.

Requirements: retention data obtained isothermally are needed for about thirty assorted solutes, chosen to provide a suitable range of parameters. Note that it is *not* necessary to choose the same solute set for each phase.

Advantages: (a) the method is very easy to apply, and requires a knowledge of only relative retention times.

(b) the constants obtained relate to specific stationary phase properties that can be comprehended by any chemist.

(c) because the method can be applied to any liquid phase, including common organic solvents, stationary phase constants can be related to the sets of constants that can be obtained for common solvents.

(d) the method is very general and can cover GLC stationary phases, capillary columns, ordinary solvents, *etc.*

Not all the solute parameters used to generate regression coefficients have values in the same range. The $\log L^{16}$ parameter can in theory vary from $-\infty$ to $+\infty$, whereas the other parameters are generally in the range of 0 to 1. So if the coefficient for any term in the equation seems small, it is worth considering the size of corresponding solute parameter, and calculating the contribution of a particular term to a LSER. When comparing coefficient size of one solubility parameter regression with another one, certain precautions must apply. To make a good comparison, the properties must have been similarly obtained, and corrected *etc.*, ideally under identical experimental conditions. Temperature can make a large difference, even when comparing the same solubility parameter measured at different temperatures. Increased kinetic motion at higher temperatures may reduce the degree of polar or hydrogen-bond interactions ^{80,81}.

The general form of a typical MLRA result (using equation 39 in this case), is shown below in Table 1 for diethylene glycol succinate, data regressed taken from Laffort et al ⁸².

Table 1: Typical MLRA Output

CORRELATION COEFFICIENT BETWEEN VARIABLES

	δ	π	α	β	$\log L^{16}$
π	0.302				
α	-0.188	0.059			
β	-0.164	0.673	0.373		
$\log L^{16}$	0.052	0.073	-0.032	0.075	
Y obs.	0.172	0.644	0.394	0.574	0.675

		d	s	a	b	l	SPo
①	Coeffs	0.120	1.757	1.839	0.115	0.400	-1.810
②	St Dev	0.047	0.089	0.088	0.125	0.010	0.044
③	TTest	0.998	1.000	1.000	0.630	1.000	1.000

Overall Correlation Coefficient R: 0.9784
S.D. Yobs. - Ycalc.: 0.163
Number of data points N: 168

LSER Equation Generated

$$\log L = 1.81 + 0.12\delta_2 + 1.76\pi_2^* + 1.84\alpha_2 + (0.12)\beta_2 + 0.40\log L^{16}$$

Firstly the correlation coefficients between the various independent variables are shown, and if these are high, variables are obviously not mutually independent, and must be examined further. The dependant variable $\log L - \log L^{\text{DECANE}}$ (SP), was used to generate these MLRA coefficients, for a data set of 168 compounds, (N). The coefficients for δ_2 , π_2^* , α_2 , β_2 , $\log L^{16}$, and SPo (the constant), are highlighted in row 1. Row 2 shows the standard deviation of each coefficient generated, and row 3 the Students Ttest. The Ttest gives confidence levels of the coefficients, and it is usual to disregard any coefficient whose Ttest value is less

than 0.950. A confidence level of less than 95% is not considered statistically significant and so if it is quoted in this work, will be parenthesized. As the Ttest value decreases so the standard deviation of a coefficient increases, until it becomes unreliable to use in an equation. The overall correlation coefficient (R) is also quoted, as is the overall standard deviation of Y observed from Y calculated (S.D.). Obviously, the higher the R value, and the lower the S.D., the more reliable a result is. The number of data points to perform a satisfactory and statistically reliable regression is around 5 times the number of explanatory variables. So for example, in the application of equation 39, when all terms are shown to be statistically significant, 25 data points would be considered to be a reasonable amount.

For the LSER equation to be meaningful, chemically sensible coefficients must be generated for each variable. Exoergic processes should give *positive* coefficients, and endoergic processes *negative* coefficients in equations 38 and 39[±]. If they are significant, coefficients for solute polarity, hydrogen-bond acidity and basicity must be positive, although the coefficient for the solute size/dispersion parameter may be positive or negative, depending on the energy required to form a cavity in the solute, and the energy released from solute/solvent dispersion interactions.

Although Table 1 shows results obtained using equation 39 using the solute parameters as shown, this should be regarded as a generalised account of the format of an LSER equation. Many of the various solute parameters have been modified and/or substituted with others, during the course of this work.

[±] Note that if equations are set up in terms of ΔG° rather than log SP, then exoergic processes will give negative coefficients, and endoergic processes will give positive coefficients, as required on thermodynamic grounds.

3.1 Solvatochromic Parameters for Solvents

The solvent parameters used in this work are summarised as follows (where subscript 1 refers specifically to solvent):

δ_1 Solvent polarisability correction parameter, $\delta_1 = 1.00$ for aromatic solvents, 0.50 for polyhalogenated, and 0.0 for all others ⁵⁰.

π^*_1 Solvent dipolarity/polarisability parameter which measures the solvent's ability to stabilise a charge or a dipole ⁸³⁻⁸⁷.

α_1 Solvent hydrogen bond acidity parameter, measuring the solvent's ability to donate a hydrogen bond ^{24,83,88-90}.

β_1 Solvent hydrogen bond basicity parameter, measuring the solvent's ability to accept a hydrogen bond ^{83,91-95}.

$(\delta_H^2)_1$ Hildebrand solvent cohesive energy density, a measure of the energy required to form a cavity in the solvent ^{43,49}. See section 2.11, p. 31.

The solvatochromic principle was first introduced by Kamlet and Taft⁹¹ in 1977 when a paper was published on the determination of the β_1 scale for hydrogen bond basicity using the solvatochromic comparison method. Solvatochromic literally means *solvent colour*, and is derived from the effect the solvent has on the colour of an indicator used in the parameter determination. The principle is based on the fact that the wavelength of maximum absorption of specific indicators in the UV and visible region is measurably shifted when the indicators are dissolved in different solvents. The extent of the wavelength shift is

determined by the degree and the type of solvent-solute indicator interactions taking place, especially polar/polarisable and hydrogen bonding interactions. Study of such wavelength shifts enabled initial scales of π^*_1 , α_1 , and β_1 to be set up.

The solvatochromic comparison principle^{83,84,88,91} measures the polarity or dipolarity (π^*_1) of a solvent by its bathochromic shift relative to cyclohexane ($\pi^*_1 = 0.0$) of the π - π^* transition of the greatest wavelength of *non* hydrogen bond donor indicators. Examples of suitable indicators are 4-nitroanisole or 4-(dimethylamino)benzophenone. To measure the solvent hydrogen bond basicity another bathochromic shift is measured using the hydrogen bond acid form (homomorph) of the *non* hydrogen bond donor indicator, eg. if 4-nitroanisole was used to measure solvent polarity, 4-nitrophenol would be used to measure the basicity. To get the sensitivity required in π^*_1 measurement, it was necessary to use indicator solutes which were capable of behaving as hydrogen bond bases. Non hydrogen bond base solutes and hydrogen bond base solutes present no problem, but to measure π^*_1 values of hydrogen bond acid solvents, indicators were chosen which were least effected by hydrogen bond effects in hydrogen bond acidic solutes

For some classes of solvents, the π^*_1 parameter is not fully capable of accounting for polarity and polarisability effects, so a polarisability correction parameter, δ_1 was introduced by Kamlet et al⁵⁰. Both δ_1 and δ_2 (the parameter for solutes) are equal to 0.0 for all non-chlorinated aliphatic compounds, 0.50 for polyhalogenated aliphatics, and 1.0 for aromatics. The δ values are supposed to reflect the difference in solvent or solute polarisability between these classes of compounds (expressed in terms of the refractive index function, $f(n^2) = [n^2-1]/[2n^2+1]$).

The original β_1 scale^{83,91-95} was determined by averaging up to 5 β values obtained from 5 different properties. 1) Solvatochromic properties using - a) a nitrogen acid indicator b) an oxygen acid indicator and 2) three properties involving solute basicity towards oxygen acids; ^{19}F nmr shifts and formation constants which were determined in dilute solutions in carbon tetrachloride solvent. So the average value for β_1 obtained by Kamlet and Taft are a mixture of solvent and solute basicity measurements. There are some shortcomings in this method of measuring solute basicity values. β_1 values of amphiprotic solvents will depend on the extent of self-association, which in a dilute solution of CCl_4 will of course be quite different. So calculating accurate values of β_1 by this method is unsatisfactory for self-associated solvents. Kamlet et al also transferred this scale of β_1 values directly to the β_2 scale for solutes⁹⁶⁻⁹⁹, which might be considered theoretically possible for some solvents, but not for amphiprotic ones.

The Kamlet and Taft method has been criticised by Nicolet and Lawrence^{80,81}. They point out that there are too few solvents used to fix a reference homomorphic line to back off hydrogen bonding effects from polar effects with non hydrogen bonding solvents. They also criticise the use of toluene, benzene and CCl_4 as non hydrogen bonding solvents (as they have measurable hydrogen bond properties), and the need for accurate temperature control when making these measurements. Abraham et al¹⁰⁰ later re-evaluated the β_1 scale, using only aniline and its derivatives as indicators. This leads to a reasonably general pure solvatochromic scale for hydrogen bond basicity of non-associated solvents. It was noted that β_1 even for non-associated compounds is only an approximation to the solute basicity, β_2 .

The solvent hydrogen bond acid scale, α_1 ^{83,88-90}, was introduced at the same time as the β_1 scale, measured similarly by the solvatochromic comparison method. Likewise however, there are shortcomings in the α_1 scale. A complication is that

the hydrogen bond base homomorphs used for non hydrogen bond solute 4-nitroanisole were completely different in their structure from 4-nitroanisole itself. This may make the separation of hydrogen bond acidity from polarity difficult, and introduce significant additional effects. Kamlet and Taft used two sets of homomorphs with *nitro* group functionality in measuring β_1 , which means if that there is any solvent interaction at the *nitro* group, this effect cancels out when the homomorphic pairs of indicators are compared. This is not the case when measuring α_1 , as the homomorphic pairs are quite different in structure. So, if there is any solvent interaction at the *nitro* group of 4-nitroanisole, this will influence the α_1 measurement. In spite of all these drawbacks, there is presently no better way of assessing solvent hydrogen bond acidity.

The solute scale of hydrogen bond acidity⁹⁶⁻⁹⁹, α_2 , has like β_2 , been formulated from values taken from the solvent scale, and cannot be seen as very satisfactory. Abraham et al have formulated new scales for hydrogen bond acidity¹⁰¹ and hydrogen bond basicity¹⁰² to overcome this problem, and they will be described later, (section 3.2, p. 52).

3.2 Solvatochromic Parameters for Solutes

The solute parameters initially used in this work in LSER and QSAR are summarised as follows (where subscript 2 refers specifically to solute):

δ_2 Solute polarisability correction parameter, $\delta_2 = 1.00$ for aromatic solutes, 0.50 for polyhalogenated solutes, and 0.0 for all others ⁵⁰.

π^*_2 Solute dipolarity/polarisability parameter which measures the solute's ability to stabilise a charge or dipole ^{47,48,85,96-99}.

α_2 Solute hydrogen bond acidity parameter, measuring the solute's ability to donate a hydrogen bond ⁹⁶⁻⁹⁹.

β_2 Solute hydrogen bond basicity parameter, measuring the solute's ability to accept a hydrogen bond ⁹⁶⁻⁹⁹.

α^H_2 Solute hydrogen bond acidity parameter as developed by Abraham et al¹⁰¹, from log K values for hydrogen bond complexation. Even for amphiprotic solutes, this is the hydrogen-bond acidity of the *monomer* solute.

β^H_2 Solute hydrogen bond basicity parameter as developed by Abraham et al¹⁰², from log K values for hydrogen bond complexation. Even for amphiprotic solutes, this is the hydrogen-bond basicity of the *monomer* solute.

V_I Computer-calculated solute intrinsic volume for specific solute conformations as derived by x-ray structure ^{51,52}.

V_X Characteristic molar volume, trivially calculable by adding atomic volumes for each constituent solute element, and subtracting a constant term for each bond present, (whatever the nature of the bond, - single, double etc.), in the molecule^{52,103-105}.

$\text{Log } L_2^{16}$ (Normally written as $\text{Log } L^{16}$, the subscript 2 referring to solute is assumed as there is no comparable solvent parameter). $\text{Log } L^{16}$ is the log of the solute Ostwald solubility coefficient¹⁰⁶, L , on n-hexadecane at 298.15 K^{24,107}.

This work is mainly concerned with LSER of the type represented by the general equations 38 and 39, specifically studying a series of *solutes* in one fixed system:-

$$\text{Log SP} = \text{SPo} + d.\delta_2 + s.\pi_2^* + a.\alpha_2 + b.\beta_2 + m.V_2 \quad [38]$$

$$\text{Log SP} = \text{SPo} + d.\delta_2 + s.\pi_2^* + a.\alpha_2 + b.\beta_2 + l.\log L^{16} \quad [39]$$

Initially π_2^* , α_2 , β_2 as a first approximation were taken to be identical to the corresponding solvent parameters, as no solute parameters were available. This may be true for simple non-associating compounds, such as aliphatic ethers, but there is underlying difficulty in that these solute parameters will not be equal to the solvent parameters where the solute is amphiprotic and/or self-associated. Most α_2 and β_2 parameters were in fact estimated using a set of rules (on the basis of some chemical intuition) or calculated from correlation and/or backcalculation techniques.

Kamlet et al^{83,108} have related the π_1^* parameter to such fundamental physical properties of solvent as their dipole moment and noted it is a linear function of the Block and Walker¹⁰⁹ reaction field function when the solvent set is limited to non-hydrogen bonding, aliphatic liquids, which have only one dominant bond

dipole, such as ethers, sulfoxides, and aldehydes. These are known as the so-called "select solvents"⁸³. Carr and Brady¹¹⁰ have also carried out similar correlations. For these compounds π^*_1 can be assumed to be identical to π^*_2 , and so correlations such as these can be used to obtain π^*_2 values, (π^*_1 values), for other important classes of compounds, (such as alcohols).

Abraham et al^{101,102} developed two new empirical solute scales for hydrogen bond acidity (α^H_2), and hydrogen bond basicity (β^H_2) in an attempt to overcome some of the problems previously associated with the Kamlet and Taft scale (α_2 and β_2), especially those problems due to amphiprotic solutes. The two new scales were constructed purely on a *thermodynamic* basis.

The scale of hydrogen bond acidity¹⁰¹ was formulated using log K equilibrium constants for the 1:1 complexation for a series of monomeric acids with a series of reference bases in tetrachloromethane solvent at 298 K.



When log K values for a series of acids (hydrogen bond donors) against a reference base are plotted versus log K values for the acid series against any other reference base, there results a set of lines that intersect at a point where $\log K = -1.1$ (equilibrium constants expressed in molar concentration units). It is then possible to obtain an average hydrogen bond acidity (with some exceptions) for solutes in CCl_4 , denoted as $\log K^H_A$. These values are then simply transformed into a solute hydrogen bond acidity scale via equation 41.

$$\alpha^H_2 = (\log K^H_A + 1.1)/4.636 \quad [41]$$

It can be similarly shown¹⁰² than when log K values for a series of bases against a

given reference acid are plotted versus log K values for the base series against any other reference acid, a set of lines is obtained that also intersect at a point where $\log K = -1.1$. Similarly to the case above, it is possible to obtain an average hydrogen bond basicity for solutes in CCl_4 , denoted as $\log K^{\text{H}_\text{B}}$, and then to transform them into a basicity scale using equation 42, where the factor 4.636 is chosen to initialise the scale so that β^{H_2} is equal to 1.0 for the base hexamethylphosphortriamide. The factor has no physical significance other than yielding a convenient working range of α^{H_2} and β^{H_2} values.

$$\beta^{\text{H}_2} = (\log K^{\text{H}_\text{B}} + 1.1)/4.636 \quad [42]$$

The α^{H_2} and β^{H_2} values so obtained (referring specifically to solute hydrogen bond complexation in CCl_4 at 298 K), can be combined in a general equation that can be used to predict a vast number of Log K values¹¹¹. From the original matrix of 89 primary α^{H_2} and 215 primary β^{H_2} , (containing 1312 experimental log K values), many more α^{H_2} and β^{H_2} values can be calculated from:

$$\log K = (7.354 \pm 0.019)\alpha^{\text{H}_2} \cdot \beta^{\text{H}_2} - (1.094 \pm 0.007) \quad [43]$$

$$R = 0.9956 \text{ S.D.} = 0.093 \text{ N} = 1312$$

This equation has been used to considerably extend the database for α^{H_2} and β^{H_2} parameters. Equations 41 - 43 are not completely general, in that some particular acid-base combinations are excluded, specifically weak acids such as pyrrole, etc. with bases such as pyridine, amines and ethers¹¹². These hydrogen bond acids give rise to a different electrostatic:covalent ratio in their complexes, with a Maria-Gal¹¹³ Θ value larger than about 75° . The combination of these acids with other bases is however included.

3.21 The Solute Cavity Size/Dispersion Parameter

In the solution of a liquid solute in a liquid solvent, dispersion forces are not considered important¹¹⁴. This is because any solute-solvent dispersion interactions will tend to cancel out with the loss of solvent-solvent dispersion interactions in forming the cavity in the solvent. The cavity size can be taken as being proportional to the solute molar volume^{114,115}, V_2 at 298 K. This is calculated as the bulk molar volume - the ratio of the solute molecular weight divided by the solvent density. The product is then divided by 100 merely to scale the value off into the same sort of range as the polarity and hydrogen bonding parameters. $10 \text{ cm}^3\text{mol}^{-1}$ was added to V_2 for aromatic and acyclic compounds, leading to $V_{2\text{adj}}$. These two cavity size parameters are not strictly solute parameters as they are measured as bulk solvent properties. For instance, for amphiprotic compounds which are self-associated they will not only reflect the *intrinsic* solute molecular volume of the monomer solute, but also the bulk structure. These two parameters are also inconvenient when considering solid solutes.

The computer-calculated intrinsic volume of Leahy⁵¹ is therefore preferable. It is measured from specific solute conformations as derived from x-ray structures, and can be measured for any solute. It also leads to improved MLRA correlations when used as the cavity term instead of V_2 or $V_{2\text{adj}}$ ^{51,116}. McGowan¹⁰³⁻¹⁰⁵ has developed another method of calculating solute intrinsic molar volumes by the addition of characteristic atomic volumes for the constituent elements of the solute molecule, and subtracting $6.56 \text{ cm}^3\text{mol}^{-1}$ for each bond. The same constant term is subtracted for any bond whether it is single, double or triple etc. There is a very good correlation between V_I and V_X ⁵² (both in $\text{cm}^3\text{mol}^{-1}$):

$$V_I = 0.597 + 0.628V_X$$

$$R = 0.9988 \quad \text{S.D.} = 1.24 \quad N = 209$$

Use of either term as a cavity term in the general LSER used (equation 37), should give completely interchangeable results. However, as V_X is so trivially calculable, this is usually the cavity size parameter employed.

V_X , (or V_I) is the preferred parameter for LSER to quantify the solubility properties of liquid solutes within condensed phases, where the nett dispersion forces will be small, or at least by no means as important a consideration as for the dissolution of a gaseous solute in a solvent¹¹⁴. A typical condensed phase process is the partition of solutes between octanol and water, the $\log P_{\text{OCT}}$ values measured being important for the modeling of biological membranes.

In the gaseous state, there will be no dispersion interaction of solute molecules with each other. Upon dissolution into a solvent, dispersion interactions, (or van der Waals interactions), will be set up between the solute and solvent, and there will be no nett tendency for a canceling out effect, as has been previously described for condensed phases. The $\log L^{16}$ parameter was formulated to provide a parameter that was a measure of cavity size and solute-solvent dispersion interactions. $\log L^{16}$ is the log of the Ostwald solubility coefficient¹⁰⁶, L , on n-hexadecane at 298.15 K^{24,107}. As it is a parameter directly measured from the dissolution of a gaseous solute into a solvent (n-hexadecane), it will automatically be a measure of cavity size and dispersion interactions. For all LSER not concerned with processes in condensed phases, (ie. gas-liquid partition coefficients), $\log L^{16}$ is preferred to V_X or V_I , as it gives consistently better results from MLRA. Coefficients generated for $\log L^{16}$ for the process gaseous solute $\Rightarrow$ solute (in solution) are invariably positive, indicating that

energy released from dispersion interactions between the solute and solvent is greater than that required in cavity formation. As a comparison, the $\log L^{16}$ coefficient from an MLRA analysis of solutes on n-hexadecane itself would be unity, so other solubility processes can be quantified by reference to this.

Abrahams and Fuchs¹⁰⁷ have used the $\log L^{16}$ parameter *itself* as the study of a MLRA to try to unravel its constituent properties. The following equation was used as the object of study:

$$\log L^{16} = \text{SPo} + b.V + c.MR + d.\mu^2 \quad [44]$$

$\log L^{16}$ is the solubility process, SPo is the equation constant, V is $V_{2\text{adj}}$, V_I , or V_X , MR is the solute molar refraction, μ is the solute dipole moment, and b, c, and d are the coefficients produced by the MLRA. The endoergic work of creating a cavity is given by the term b.V, and the exoergic solute-hexadecane interactions are given by c.MR (dispersion interactions) and d. μ^2 (dipole-induced dipole interactions). Using $V_{2\text{adj}}$ as the cavity term, the following MLRA equation was obtained.

$$\log L^{16} = 0.293 - 0.026.V_{2\text{adj}} + 0.198.MR + 0.045.\mu^2$$

$$R = 0.986 \quad \text{S.D.} = 0.185 \quad N = 84$$

(Confidence levels for all parameters > 99.9999%)

This analysis shows the $\log L^{16}$ term is made up of two contributory terms, a cavity term (b. $V_{2\text{adj}}$), and a dispersion or van der Waals interaction term (c.MR).

The term $d.\mu^2$ if calculated as a check for several solutes is comparatively very small to the other two contributory terms in equation 44, and can for all practical purposes be ignored. The contributions to the $\log L^{16}$ term from equation 44 using the coefficients generated by the MLRA are shown in Table 2 for several important and representative solutes .

Table 2: Contributions to $\log L^{16}$ from:
 (1) Cavity Formation ($-0.026.V_{2adj}$)
 (2) Dispersion Interactions ($0.198.MR$)
 (3) Dipole-Induced Dipole Interactions ($0.045.\mu^2$)

Solute	(1)	(2)	(3)
	(values in log units)		

n-hexane	-3.43	5.90	0.00
propanone	-1.93	3.20	0.37
2-heptanone	-3.70	6.87	0.31
ethyl acetate	-2.57	4.39	0.14
methanol	-1.07	1.63	0.13
1-octanol	-4.14	8.03	0.13
nitropropane	-2.35	4.29	0.60

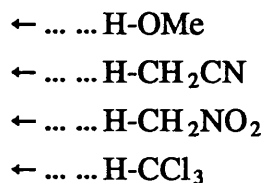
The signs of the terms also show that cavity formation opposes solute dissolution in n-hexadecane, and dispersion forces favour it, the dispersion term always being of a greater magnitude than the cavity formation term.

3.22 The Importance of Hydrogen Bonding Parameters

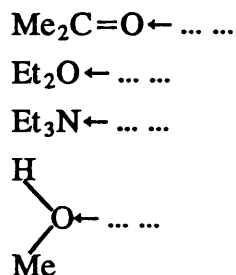
A quantitative measure of the relative strength of a 'traditional' acid is its degree of dissociation, measured in aqueous solution¹¹⁷. Similarly, the relative strength of a base can be measured¹¹⁷ by either its pK_b value, or the pK_a value of its conjugate acid. The generally accepted alternative to the proton-transfer theory is that proposed by Lewis¹¹⁸, based on electron pair acceptance (acids), or electron pair donation (bases). However, for many chemical structures and processes, including all the ones studied in this work, a proton-transfer approach is not relevant or applicable. A large number of processes, such as the solubility of non-electrolytes in water or organic solvents, or the distribution of non-electrolytes between two solvent phases, do not depend upon the actual transfer of protons, rather the ability of the solute to take part in hydrogen bonding processes. Thus, a hydrogen bond acid will not actually donate a proton (or accept an electron pair), - it will donate a hydrogen bond, and a hydrogen bond base will in the same way receive a hydrogen bond. These processes are of the upmost importance in nature as well; the three-dimensional structure of water is based on hydrogen bond networks, the secondary structure of proteins are held in place by hydrogen bonds of the type $>N-H \cdots O=C<$. An example of hydrogen bond acids and bases is given below in Table 3.

Table 3: Hydrogen bond acids and bases

Hydrogen bond acids



Hydrogen bond bases



4.1 Characterisation Of Stationary Phase Solvent Properties

The retention index system as proposed by Kovats (originally as a method of substance identification), is widely used in studies of liquid phase characterisation¹¹⁹⁻¹²¹. The retention index, I , of a substance is equivalent to 100 times the carbon number of a hypothetical n -alkane with the same adjusted retention time, adjusted retention volume, or specific retention volume, *etc.*. The retention index of any substance X , can be calculated from equation 45 by coinjection of X with two bracketing n -alkanes usually differing by one carbon number^{122,123}.

$$I = 100n + 100 \left[\frac{\log R_X - \log R_n}{\log R_{n+1} - \log R_n} \right] \quad [45]$$

R is the adjusted retention time (or adjusted retention volume, specific retention volume, *etc.*), n is the carbon number of the n -alkane eluting before substance X , and $n + 1$ is the carbon number of the substance eluting after substance X .

Efforts to characterise chromatographic stationary phases (or solvents) can generally be divided into attempts to do so in terms of their solvent strength (or more accurately, polarity), and solvent selectivity, (eg. see the review by C. Poole and S. Poole¹²⁴). Solvent strength can be defined as the capacity of a solvent for various intermolecular interactions, and solvent selectivity the relative capacity of compared solvents for a particular intermolecular interaction. Our approach is representative of the latter case. Characterisation is usually by studying the retention information, (typically retention indices), obtained experimentally on a particular stationary phase of a number of test solutes. However, most attempts are of little general use, as they are restricted to specific classes of solute¹²⁵.

The most widely used method for stationary phase characterisation is that

proposed by Rohrschneider ¹²⁶, and later modified by McReynolds ¹²⁷. It is now common for stationary phase suppliers to publish McReynolds constants to aid phase selection. When McReynolds published results for over 200 phases, the most immediate impact was to demonstrate the great similarity of the solvent properties of stationary phases commonly in use. Using this data with various statistical techniques, a much smaller group of "preferred stationary phases" could be selected that could adequately represent the full selectivity range of the original data collection ¹²⁸⁻¹³⁰.

Rohrschneider ¹²⁶ divided the free energy of solution of a solute dissolving into the stationary phase into a series of terms representing the individual contributions of molecular interactions, which were assumed to be additive and composed of two terms, a solute specific term $a...e$, and a stationary phase characteristic term $x...s$. Using this method of phase characterisation, a number of test solutes, with the characteristics a, b, c, d, e are chromatographed on a series of stationary phases with characteristics X, Y, Z, U , and S . This leads to the construction of regression equations of the type below, in equation 46:

$$I \text{ (or } \Delta I) = aX + bY + cZ + dU + eS \quad [46]$$

ΔI refers to the difference in retention indices between I values obtained for a given solute on the stationary phase being considered, and the I value on a standard apolar phase. The set of test solutes must adequately characterise the principal interactions responsible for retention in gas chromatography: dispersion, orientation, induction and donor-acceptor complexation. Rohrschneider ¹²⁶ suggested that just benzene, ethanol, 2-butanone, nitromethane and pyridine be used for this purpose. McReynolds ¹²⁷ extended the solute set used in this characterisation method to 10 solutes, and other workers ^{131,132} have used different test sets of solutes. Most stationary phase classification schemes

and models to predict retention as a function of sample properties are now based on the original experimental data published by McReynolds^{127,133}, and to a lesser extent that of Rohrschneider¹²⁶, or Rohrschneider parameters determined by Supina^{134,135}.

However, although the Rohrschneider-McReynolds method is the basis of most approaches to the classification of stationary phases, quite recently Poole et al.¹²⁴ have severely criticised the method on a number of technical and theoretical grounds. Their main technical objection is that alkanes (necessary for the determination of I values) are sorbed onto polar stationary phases mainly by interfacial adsorption, rather than by true gas-liquid partitioning. If the I values are incorrect for the phase under investigation, then the whole procedure is invalid (for polar phases). A theoretical objection is that the 'overall' polarity, defined as above cannot be a true measure of polarity, since it depends principally on the solubility of the n-alkanes in the stationary phase¹²⁴.

There are other difficulties over the Rohrschneider-McReynolds method. Firstly, the method is entirely restricted to GLC retention data, so that there is no possibility of comparing GLC stationary phases with common solvents. Secondly, the method is far too coarse to allow any analysis of solute-solvent interactions, which are actually the basis of gas-liquid partition, and hence of retention data.

Snyder has proposed the characterisation of chromatographic solvents by the relative strength of hydrogen bonding interactions and orientation interactions^{136,137}. The test solutes ethanol, dioxane and nitromethane were selected to measure the relative strength of the three intermolecular forces determined as the retention index difference of the test solute on a polar phase and on squalane as a nonpolar reference phase in a manner similar to that of

Rohrscneider. Selectivity coefficients x_i , are then calculated and plotted on the face of a solvent selectivity triangle, using equation 47,

$$x_i = \Delta I_i / \Sigma \Delta I_i \text{ for } i = e, d, \text{ or } n \quad [47]$$

x_i is the selectivity parameter, where $i = e$ - proton acceptor interactions, d - proton donor interactions, n - orientation interactions, with corresponding retention index differences of ΔI_i (where $i = e, d, n$), and the denominator $\Sigma \Delta I_i$ reflects the excess retention index due to polar interactions. The most selective stationary phases will have large $\Sigma \Delta I_i$ values, and a large value of one of the x_i coefficients. Nonselective phases have small values of $\Sigma \Delta I_i$ and x_i values close to 0.3. This approach again is of very little general use, as the position of a given phase in the selectivity triangle is purely a function of the particular test solutes used for the species concerned.

Poole et al.,¹³⁸ following several other workers,¹³⁹⁻¹⁴² suggested that the methylene increment to the gas $\rightarrow$ stationary phase transfer, as $\Delta G_s^\circ(\text{CH}_2)$ could be taken as a better measure of the overall polarity. Since $\Delta G_s^\circ(\text{CH}_2)$ can be obtained from a variety of homologous series, the difficulty over retention processes of alkanes is avoided. However, it is by no means obvious what a general polarity based on $\Delta G_s^\circ(\text{CH}_2)$ means. Abraham¹⁴³ has published data from which values of $\Delta G_s^\circ(\text{CH}_2)$ can be obtained for the n-alkanes in a number of common solvents, in Table 4. Note that since the original measurements were non-chromatographic, the n-alkane difficulty does not arise. The $\Delta G_s^\circ(\text{CH}_2)$ values can be matched against various solvent polarity parameters, and give simple regression constants, (Table 5).

Table 4. Some values of the gas $\rightarrow$ solvent methylene increment, $\Delta G_s^\circ(\text{CH}_2)$, in kcal mol⁻¹ at 298K^a.

Solvent	$\Delta G_s^\circ(\text{CH}_2)$	Solvent	$\Delta G_s^\circ(\text{CH}_2)$
Cyclohexane	-0.76	Propanone	-0.62
Hexadecane	-0.74	Ethanol	-0.61
Decane	-0.74	Dimethylformamide	-0.60
Hexane	-0.74	N-Methylpyrrolidinone	-0.56
Benzene	-0.74	Methanol	-0.56
Chlorobenzene	-0.73	Propylene carbonate	-0.48
Tetrachloromethane	-0.71	Dimethylsulphoxide	-0.48
1-Octanol	-0.68	Ethylene glycol	-0.35
1-Butanol	-0.66	Water	+0.18
Nitrobenzene	-0.64		

^a All values from data in ref. 143.

Table 5. Correlations of $\Delta G_s^\circ(\text{CH}_2)$ against some solvent parameters ^a.

(A). All Solvents in Table 4

Intercept	Slope	N	R	SD
-0.862	$0.188 \delta_H^2/100$	19	0.981	0.04
-0.804	$0.370 \pi_1^*$	19	0.673	0.17
-0.671	$0.043 \mu_1$	19	0.328	0.21
-0.955	$0.949 f(\epsilon)$	19	0.554	0.19
-1.396	$0.019 E_T$	16 ^b	0.786	0.15
0.058	$-2.529 f(\eta)$	19	0.376	0.21
-0.399	-0.089MR	19	0.530	0.19

(B). Nonhydroxylic solvents in Table 4

-0.890	$0.230 \delta_H^2/100$	13	0.941	0.04
-0.758	$0.189 \pi_1^*$	13	0.772	0.07
-0.746	$0.046 \mu_1$	13	0.911	0.04
-0.877	$0.636 f(\epsilon)$	13	0.859	0.05
-1.273	$0.016 E_T$	11 ^c	0.911	0.04
-0.679	$0.082 f(\eta)$	13	0.024	0.11
-0.570	-0.035MR	13	0.437	0.10

^a These are δ_H^2 the Hildebrand cohesive energy density, π_1^* the Kamlet-Taft solvent dipolarity, μ_1 the dipole moment,

$f(\epsilon)$ the dielectric constant function $(\epsilon-1)/(2\epsilon+1)$, E_T the Reichardt solvent parameter, $f(\eta)$ the refractive index function

$(\eta^2-1)/(\eta^2+2)$, and MR a molar refraction we define as $10.f(\eta).V_X$ where V_X is the intrinsic volume.

^b Excluding values for hexadecane, decane, and 1-octanol.

^c Excluding values for hexadecane and decane.

For the nonhydroxylic solvents, there are reasonable correlations of $\Delta G_s^\circ(\text{CH}_2)$ with solvent dipole movement (μ), or with dielectric constant function $(\epsilon-1)/(2\epsilon+1)$, or with Reichardt's E_T parameter. But none of these are as good as the solvent cohesive energy density, as $\delta_H^2/100$, and for the total solvent list in Table 4A, only the latter yields a reasonable correlation*. The correlation below in equation 48 is significantly better than the single correlation in $\delta_H^2/100$, for nonhydroxylic solvents, where the correlation coefficient, R , between δ_H^2 and $f(\eta)$ is only 0.265.

$$\Delta G_s^\circ(\text{CH}_2) = -0.679 + 0.246\delta_H^2/100 - 0.847f(\eta) \quad [48]$$

$$R = 0.970 \quad SD = 0.03 \quad N = 13$$

Equation 48 can be rationalised using a cavity theory of solution. In order to create a cavity in a solvent, solvent-solvent bonds must be broken in an endoergic process, modelled by δ_H^2 . Then on insertion of the solute CH_2 group into the cavity, exoergic CH_2 -solvent general dispersion interactions will be set up, modelled at least roughly by $f(\eta)$. The $\Delta G_s^\circ(\text{CH}_2)$ increment is therefore not a general polarity parameter in the sense of, say, π_1^* or E_T , but reflects a combination of solvent-solvent bond breaking and CH_2 -solvent dispersion interactions.

Other workers have moved away from the Rohrschneider-McReynolds method and have attempted to account for retention data on the basis of specific solute-solvent interactions. Ecknig et al.¹⁴⁴ characterised solute-solvent interactions in terms of two energy parameters, a nonpolar or dispersion parameter and a polar parameter that includes hydrogen-bonding as an electrostatic effect. The calculation of these parameters, however, is not trivial,

*The units of δ_H^2 are cal cm^{-3} , 1 cal = 4.184 J, and the units of μ are Debyes, 1D = $3.336 \times 10^{-30} \text{C m}$.

and application seems to be restricted to aliphatic solutes only¹⁴⁵. The UNIFAC solution-of-groups method has been investigated also, but yielded only rough estimates of retention data¹⁴⁶. A few workers have attempted to characterise stationary phases using indices that include stationary phase acidity and basicity as such. Burns and Hawkes,¹⁴⁷ for example, used retention data on the 1-butanol/ethyl acrylate pair of solutes to obtain stationary phase basicities, and on pyridine/benzene to obtain stationary phase acidities, but conceded that the obtained indices were rather "shaky". Hawkes et al.¹⁴⁸ later carried out various spectroscopic studies of solutes in stationary phases and tabulated indices of dispersion forces, polarity, acidity, and basicity for a number of stationary phases (but note that acidity was obtained from retention data on the n-butylamine/n-butyl chloride pair of solutes).

One of the most detailed attempts at stationary phase solvent classification is by Laffort et al⁸², who have used the linear equation below to predict retention indices. Solute factors are represented by α , ω , ϵ , π , and β (note, none of these symbols are equivalent to those used in this work), and solvent properties by A, O, E, P and B.

$$I = \alpha A + \omega O + \epsilon E + \pi P + \beta B + 100 \quad [49]$$

Several of the solute factors are easily measurable; α or the apolar factor, is proportional to mole volume at boiling point, ω or the orientation factor, is proportional to the square of the dipole moment for simple molecules, ϵ or the electron factor is proportional (for molecules with fairly regular electron distribution) to the ratio between molar refraction and mole volume at boiling point, π is a proton donor or acidity factor and β a basicity factor proportional to the ability to receive protons. This approach was used to characterise 240 solutes and 207 stationary phases.

Even from this fairly thorough analysis, the solvent factors may not be comparable with any others, for example the term P may or may not be comparable with the solvatochromic parameter β_1 that refers to solvent basicity. The set of 240 solutes studied does not contain certain key solutes, such as ones with a large hydrogen bond basicity, (dimethylformamide, dimethylsulphoxide, *etc.*). When attempting to classify a solvent, it is important for the solute set used to have a wide range in values of all the relevant solute/solvent interaction terms, eg. a wide range of hydrogen bond acid and base strengths.

Derived solute parameters for monomeric solutes do not match those already obtained by other methods, for example, in the case of pyridine, $\beta^{H_2} = 0.63^{102}$, and $\beta = 0.40^{82}$, and similar discrepancies are apparent for the majority of solutes. There is no fundamental requirement that the β^{H_2} and β values be identical for every solute, but they should both show the same overall trends in proton acceptor strengths, which is simply not the case.

It seems, therefore, to be acknowledged that factors such as dispersion, polarity, acidity, and basicity are important in solute-stationary phase interactions^{145,147,148}. In order to quantify these effects, some general system in which both solute and stationary phase are characterised is necessary. One of the purposes of this work is to develop and refine such a system that can be used for GLC stationary phases, common solvents, and, indeed, any condensed phase.

4.2 Surface Acoustic Wave Chemical Sensors

4.21 Introduction to Piezoelectric Sorption Detectors and SAW Devices

The classification of chromatographic stationary phases is an important technique for the evaluation of the suitability of a phase for use in a surface acoustic wave, (or SAW), chemical sensors. Some of the present work has been involved in doing this, and therefore an introduction to the methodology of SAW devices follows.

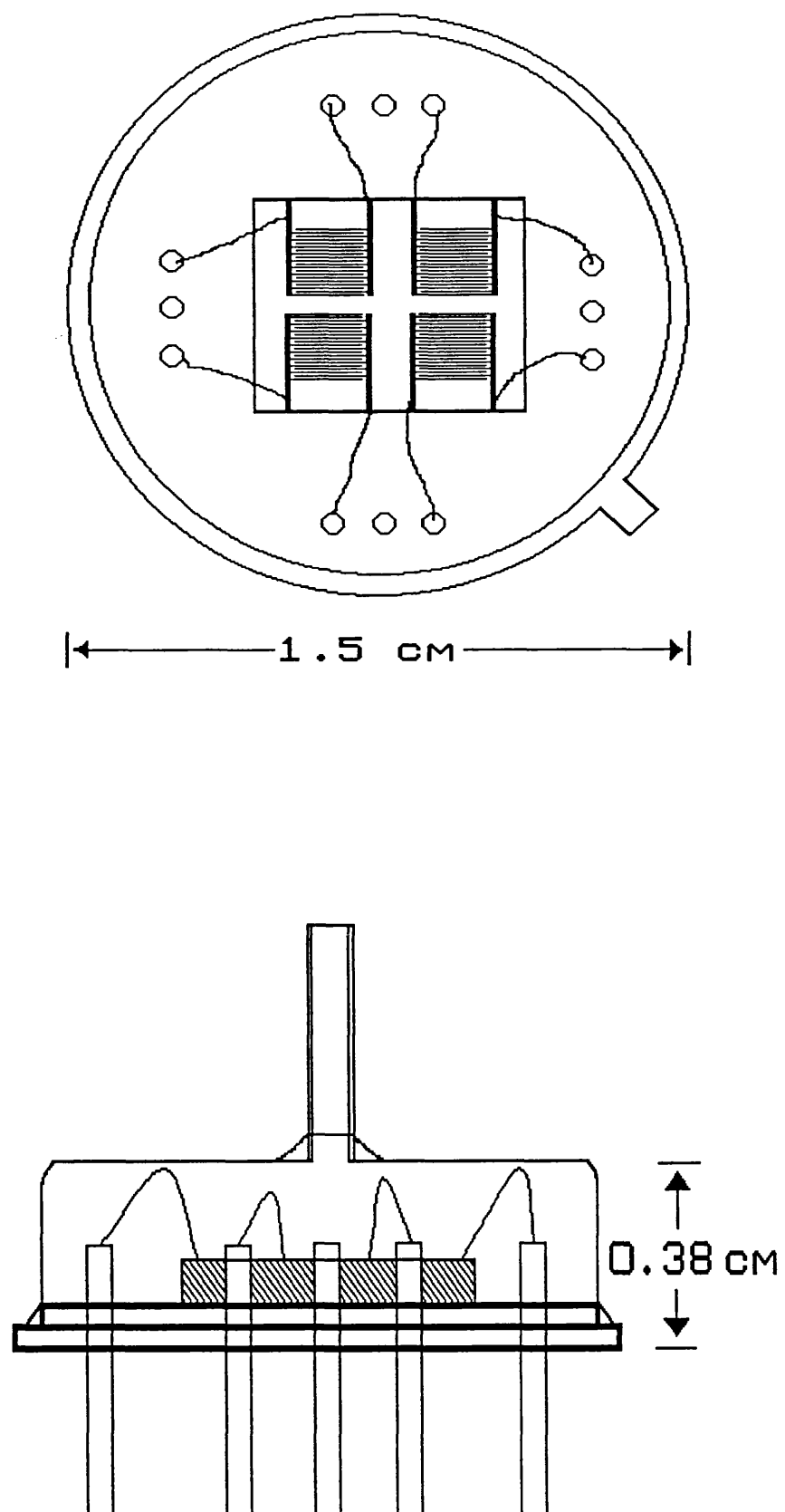
Designing and developing microsensor and microsensor-based detectors with high selectivities is a continual challenge in the field of chemical detection. This is because of the number and variety of analytes to be detected, the choice of materials which can be used to interact with the chemical environment, and the numerous transducers available to convert physicochemical interactions into electrical or optical signals.

Chemosensors transduce chemical signals into appropriate electrical or optical signals. They are used for example to warn or protect by measuring the concentration of corrosive, explosive or toxic compounds, to signal when preselected concentrations are exceeded. It has long been desired to develop small, robust, relatively cheap and reliable chemosensors.

King first introduced the concept of a piezoelectric sorption device in 1964, using bulk acoustic wave crystals¹⁴⁹, such detectors frequently referred to as quartz crystal microbalances, (QCM)¹⁵⁰⁻¹⁵³. Other acoustic wave and device configurations have since been utilized to create piezoelectric chemical sensors, such as flexural plate devices^{154,155}, and SAW devices¹⁵⁶⁻¹⁶¹.

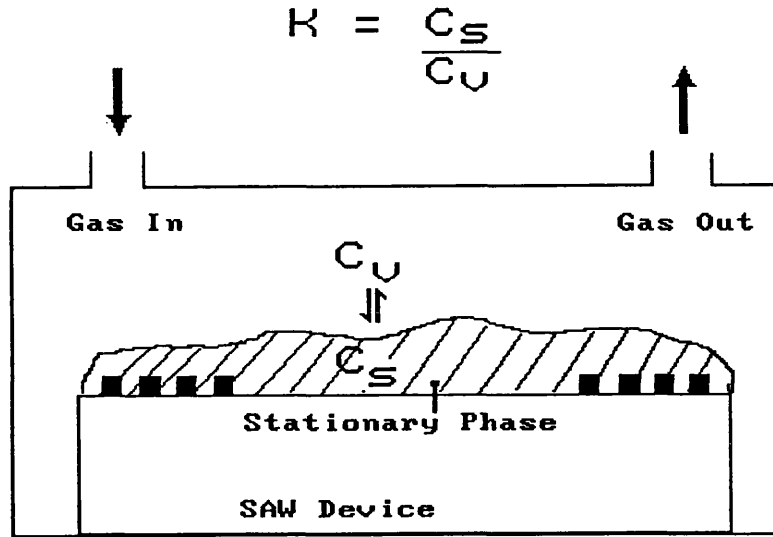
The use of SAW devices for sensing chemical vapours were first reported in 1979¹⁵⁶, and has since been thoroughly investigated by several groups^{154,157,160,161-166}. Saw devices function by generating mechanical Rayleigh surface waves on a thin slice of quartz and oscillate at a characteristic frequency when placed in a feedback circuit with an rf amplifier. The oscillator frequency is measurably altered by small changes in mass or elastic modulus at the surface of the SAW device. Sensitivity to vapour is achieved by coating the surface of the device with a thin film of a stationary phase which will specifically and reversibly interact with the target vapour, by absorption into the stationary phase. In so doing, the mass of the surface film increases, and a shift in the oscillator frequency will be observed. SAW devices are ideal in many respects as chemosensors, as they are small, reliable, rugged and cheap. They are also sensitive, the detection limit estimated to be 10^{-12} gram¹⁴⁹. They are also flexible in that a particular stationary phase can be selected or designed and used for selective sorption in a particular gas-phase analytical problem. Figure 6 shows a typical SAW sensor device. Methods to quantify vapour sorption, and to interpret the solubility interactions responsible will obviously facilitate development of suitable stationary phases.

FIGURE 6: 158 MHz Dual Saw Device



Equilibrium sorption of ambient vapour onto the SAW device coating denotes the partitioning of solute vapour between the gas phase and the stationary phase, illustrated in Figure 7.

FIGURE 7: Schematic Diagram of a SAW Sensor



This distribution can be quantified by the partition coefficient K in equation 2.

$$K = \frac{C_S}{C_G} \quad [2]$$

Considering a QCM device, perturbations on the mass, Δm , on the surface causes a shift in the oscillator frequency, Δf (in Hz), according to the following relationship^{149,150}.

$$\Delta f = k F^2 \Delta m / A \quad [50]$$

The variable A is the active area of the device, F is the fundamental resonant frequency of the oscillator, and k is a constant related to the crystal material and thickness. This relationship shows that the mass of vapour sorbed by a coating can be measured by the change in frequency.

The response of SAW devices to surface mass changes can be expressed similarly, assuming the surface film is soft and non-conducting. However, changes in the elastic properties of stiff films, or changes in the resistance of conducting films (whose sheet conductivities fall in a particular range) can also agitate the frequency. The influence of the mass and elastic properties of a thin isotropic non-conducting film on the frequency of a SAW device has been expressed according to equation 51, where Δf_s is the change in frequency caused by the film¹⁵⁷.

$$\Delta f_s = (k_1 + k_2) F^2 h \rho - k_2 F^2 h (4\mu/V_R^2)[(\lambda + \mu)/\lambda + 2\mu] \quad [51]$$

The values for k_1 and k_2 are material constants for the piezoelectric substrate, F is the fundamental resonant frequency of the oscillator, h is the coating thickness, ρ is coating density, λ and μ are the Lamé' constant and shear modulus of the coating material, and V_R is the Rayleigh wave velocity in the piezoelectric substrate. The first term represents mass effects, since $h\rho$ has the same units as $\Delta m/A$. Thus the first term in equation 51 has the same form as equation 50 for the QCM.

The second term in equation 51 represents the effects of the elastic properties of the surface coating on the frequency of the surface acoustic wave. For soft materials, e.g. $\mu = 10^7$ dynes/cm² (a value typical of elastomeric polymers, ie. amorphous polymers above their glass transition temperature), the second term is negligible compared to the first. For stiffer materials, such as glassy materials with $\mu = 10^{10}$ dynes/cm² and densities near 1g/cm³, the second term is 10 to 15% of the value of the first term.

In summary, the important features of piezoelectric detectors are that they are mass-sensitive and the quantity of vapour sorbed by the chemically selective surface film is measured by the frequency shift. In some cases such as the SAW

device, the frequency can also be influenced by other properties such as changes in stiffness or conductivity, which must be considered in coating material selection.

As has previously been said, the partition coefficient, K , is defined as the ratio of the concentration of the solute in the stationary phase (or sensor thin film coating material), C_s , to the concentration of the solute in the vapour, or gas phase C_v . K is related to the standard Gibb's free energy of solution of a gaseous solute, ΔG°_s , by:

$$\Delta G^\circ_s = -RT \ln K \quad [3]$$

where the standard states are unit concentration in the gas phase and unit concentration in solution.

The partition coefficient is particularly useful when applied to piezoelectric sorption detectors because it can be directly related to the frequency shifts determined when vapours sorb into the coatings¹⁶⁷⁻¹⁷⁰. The equation derived for SAW delay lines is as follows¹⁷⁰, where K_{SAW} is the partition coefficient between gas and the SAW coating,

$$\Delta f_v = \Delta f_s C_v K_{SAW} / \rho \quad [52]$$

This simple relationship relates the frequency shift caused by the vapour sorption, Δf_v , to the partition coefficient and experimentally determined sensor characteristics. The variable ρ is the density of the coating material as before. The variable Δf_s represents the frequency shift observed when the sorbent coating was applied to the bare SAW device, and provides a measure of the amount of material on the sensor. Δf_v is measured when the sensor is exposed to a calibrated stream of concentration C_v . The relationship is independent of the specific SAW substrate, having no dependence on SAW device frequency F , or

piezoelectric material constants.

There are several presuppositions in the use of equation 52. The mechanical effects in the functioning of the SAW device are assumed to be negligible, and the mass change observed is assumed to be due solely to the partition of analyte between the gas phase and the stationary phase coating. The density of the coating is taken as that of the pure coating, rather than that of the coating plus analyte. As long as mass loading of the coating by the analyte vapour is low, which would be the case in normal working conditions with low vapour concentrations or weakly sorbed vapours, this approximation is perfectly valid. It should also be noted that partition coefficients are strongly temperature dependent, and sorption normally decreases with increasing temperature. The more strongly sorbed a vapour is, the greater the decrease as the temperature rises¹⁷⁰. Piezoelectric sorption detectors will become less sensitive and less selective as the temperature rises because of this effect. This result also indicates that if partition coefficients measured by techniques such as GLC are to be used to evaluate a stationary phase for use in a SAW device, the measurements should be made at near identical temperatures to which the sensor device will operate, which is usually room temperature. Partition coefficients measured at higher temperatures underestimate both the selectivity and sensitivity with which vapours can be absorbed on sensors operating at room temperature.

4.22 Selection Of Suitable SAW Coating Materials

The essential physical properties of the coating are that it be non-volatile, so that it stays in place on the sensor, that its' physical state should not change, and that it allows facile diffusion of vapours, (ie. completely reversible, and non-reactive diffusion) to and from sites of selective interaction. These requirements are

satisfied by non-volatile liquids, and by amorphous oligomers or polymers. Ideally amorphous polymers should be elastomeric, i.e. above their glass transition point, T_g . In this state, constant thermal motion of the polymer chains allows rapid vapour diffusion¹⁷¹. After a vapour has sorbed, and then desorbed, the material is left in essentially the same state as it was prior to sorption. Overall, sorption in elastomers is greater than in glassy materials^{172,173}, resulting in more sensitive sensors. Glassy materials have a number of potential disadvantages as sensors^{171,173,174}. Vapour diffusion is slower than in elastomers, which can result in slower sensor response and recovery times. The diffusion process is frequently complex because increases in chain segmental motion and free volume can occur simultaneously with vapour transport, so that the diffusion rate increases as the concentration in the polymer increases. and upon desorption some vapour may become indefinitely retained. Adsorption in microvoids and microcracks may further complicate matters, and the interpretation of vapour sorption from sensor frequency shifts may not be simple if changes in polymer stiffness during the sorption process contribute to the signal.

The softness of elastomeric materials has an additional advantage on SAW devices, which are sensitive to changes in material stiffness. The frequency shift, Δf , observed when the material is applied is not significantly affected by the materials elastic properties, (in equation 51). This frequency shift is then a reasonable measure of the amount of material applied. Similarly, when a challenge vapour is sorbed, any further softening of the material will not affect the frequency shift, Δf_v , to any great degree. Soft materials will thus allow a more straightforward interpretation of sorption from frequency shifts, using eqn. 52.

4.23 SAW Devices used in Sensor Arrays

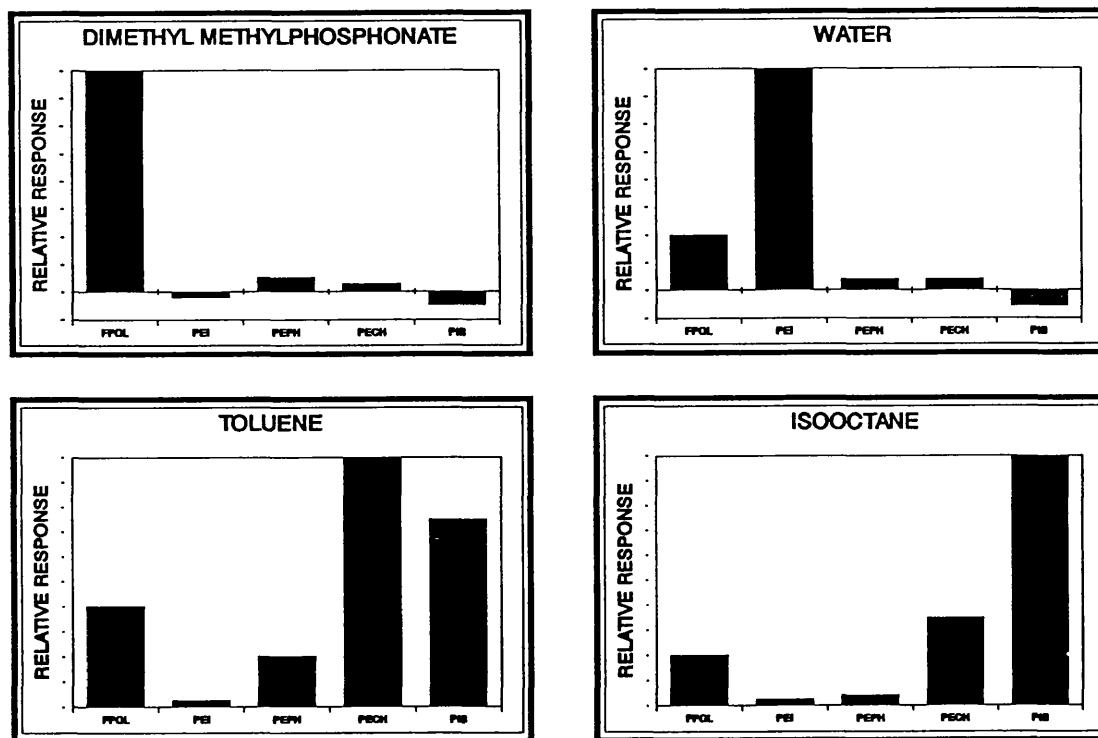
SAW devices can provide much more reliable information about the analyte if used in the form of array. This is a series of SAW devices, each coated with different stationary phases, which possess different sorption properties. Differences in selectivities of the separate sensors, and their degree of interaction with the target analyte vapour will enable a unique positive identification of the vapour, using pattern recognition techniques. Bar graphs showing typical pattern responses from experimental data¹⁷⁵ are shown in Figure 8.

The chemical structure of the coating will determine its solubility properties, and hence the sensor sensitivity and selectivity. The greatest sensitivity to target analyte will be achieved by including structural elements in the coating material which will maximize the solubility properties that will interact with the analyte vapour. All interactions that will enhance sensitivity to the vapour should be included, provided that they do not cause strong self-association of the coating material itself.

The selectivity of a coating material will be greatest if it can be designed to interact with vapours by only a single type of solubility interaction, and the coating solubility property associated with that interaction should be incorporated at maximum strength. The logical approach to obtaining the greatest selectivity from an array of sensors is then to include individual coatings for each solubility interaction. These would be in addition to the sensor(s) which maximize sensitivity to the target analyte(s).

However, it is not practical to make a material which will interact only according to a single solubility property. For example, hydrogen bond acids usually are

FIGURE 8: SAW Array Pattern Responses



Bar graphs, illustrating how different vapours give rise to different patterns when detected by a sensor array. Each graph illustrates the relative response of five dual delay line SAW vapour sensors, normalised to the highest response.

Coating Materials

FPOL - fluoropolyol

PEI - poly(ethyleneimine)

PEPH - poly(ethylenephthalate)

PECH - poly(epichlorohydrin)

PIB - poly(isobutylene)

capable of acting as hydrogen bond bases as well, and basic materials are often polar. In light of this, the selection strategy is to select a particular solubility property and incorporate it into a coating material at maximum strength, while minimizing all others. Unique combinations of solubility properties can also be prepared in a single material. The following summary lists the selection strategy:-

- ❑ Maximize dispersion interactions
- ❑ Maximize polarizability
- ❑ Maximize dipolarity (while minimizing hydrogen bond basicity)
- ❑ Maximize hydrogen bond basicity (while minimizing dipolarity)
- ❑ Maximize both hydrogen bond basicity and dipolarity
- ❑ Maximize hydrogen bond acidity (while minimizing basicity)

In selecting suitable coatings for an array it is important to remember that pattern recognition techniques are information processing methods¹⁷⁶⁻¹⁷⁹, and like all such methods they rely on the quality and quantity of the information supplied. A randomly chosen set of coatings for a sensor array is unlikely to provide optimum information, and a set of sensors in which each sensor emphasizes a particular solubility interaction will provide a lot more information than a set probing the same solubility interaction. The most general type of array could contain at least six coatings, which would maximize solubility interactions. A representative six polymers (the number referring to the category of interaction most prominent, as listed above), might be:

- ❑ poly(isobutylene)
- ❑ a phenylmethyl-diphenylsiloxane copolymer
- ❑ polybis(cyanopropyl)siloxane
- ❑ poly(ethyleneimine)
- ❑ poly(ethylene maleate)
- ❑ fluoropolyol

This is by no means an optimal set, the materials having been previously used on SAW sensors, or being well known GLC stationary phases. There is substantial room for innovation to produce materials that better maximize the particular interactions, (1) to (6).

It can immediately be seen, a quantitative method for the evaluation of each of the various types of solubility interactions for a candidate phase, (and to better understand the nature of materials already in use in SAW devices), is very desirable. Consider the LSER equation 39:

$$\text{Log SP} = \text{SPo} + d.\delta_2 + s.\pi_2^* + a.\alpha_2 + b.\beta_2 + l.\log L^6 \quad [39]$$

The application of LSER techniques using multiple regression through the use of equation 39, (and others developed during the course of this work), can be used to evaluate stationary phase properties, and to sort out the relative strengths of multiple simultaneous interactions. In addition to this, equation 39 can be used to estimate partition coefficients and hence sensor responses, via equation 52. Any vapour whose solvation parameters are known can be evaluated in this way.

5.1 Aims of the Present Work

The four major objectives during the course of this work can be summarised as below:-

- 1) To apply our LSER equations to as many solubility and solubility related processes as possible. This would test the scope of their application, and uniquely characterise in terms of our physiochemical solute parameters as many solvents as is feasible, whether the solvent be a GLC stationary phase, or a more 'typical' solvent, (such as ethanol *etc*). Solubility related processes would also be quantified in the same manner, such as partitions between immiscible solvents (condensed systems), or the upper respiratory tract irritation by airborne chemicals in mice.
- 2) To vastly extend our database of solute physiochemical parameters, and 'firm-up' these parameters by their successful application in quantifying numerous varied solubility and solubility related phenomena. Where possible parameters would be directly measured, or if not, back-calculated, or estimated by extrapolation techniques *etc*.
- 3) To investigate the use of alternative and/or improved physiochemical solute parameters for use in our LSER equations, to backcalculate improved parameters from derived LSER characterisation equations and to use MLRA techniques to calculate solute parameters from sets of numerous LSER equations.
- 4) To construct a new solute parameter database with improved interactive multiple regression programs *etc.*, on an IBM compatible personal computer (as opposed to a PRIME Mainframe), and to introduce a computer-based solute parameter value reference system, to indicate the parameter value origin.

The use of LSERs via the general equation below leads to a remarkably simple model for solubility and solubility related processes.

Log SP = [1] Log SP_o (equation constant) + [2] a correction term for quantitative indication of polarizable π and π electrons + [3] dipolarity or dipolarity/polarisability term + [4] hydrogen-bond acidity term + [5] hydrogen-bond basicity term + [6] solute size & dispersion interaction term

The two general equations that can be used for the characterisation of solutes and of a wide variety of solvent phases or solvent-like phases are:

$$\log SP = c + d.\delta_2 + s.\pi_2^* + a.\alpha_2 + b.\beta_2 + m.V_2 \quad [38]$$

$$\log SP = c + d.\delta_2 + s.\pi_2^* + a.\alpha_2 + b.\beta_2 + l.\log L^{16} \quad [39]$$

The equations can be recast to include the hydrogen bonding parameters as derived by Abraham et al ^{101,102}.

$$\log SP = c + d.\delta_2 + s.\pi_2^* + a.\alpha^H_2 + b.\beta^H_2 + m.V_x \quad [53]$$

$$\log SP = c + d.\delta_2 + s.\pi_2^* + a.\alpha^H_2 + b.\beta^H_2 + l.\log L^{16} \quad [54]$$

At the start of this work, $\log L^{16}$ values were reported for 240 solutes²⁴. We had available a large data base on π_2^* , α_2 , and β_2 values for monofunctional compounds, and a smaller data base on $\log L^{16}$ values for monofunctional, and some other compounds. The parameters α_2 and β_2 used from our database for MLRA analysis were in fact averaged or 'taken' α^H_2 and β^H_2 values respectively, and **not** the Kamlet and Taft values, although in many cases the two values are identical. The Kamlet and Taft values were not used in this work. Although this

was sufficient to be able to use equations 53 and 54 to characterise solvent phases, it was not sufficient to be able to deal with the many important classes of polyfunctional solutes. One of the main aims was therefore to extend the data base to include polyfunctional compounds, and to incorporate further monofunctional compounds. Note that there is no difficulty over V_2 ; we generally use McGowan's characteristic volumes for solutes, these being calculable for any solute simply from molecular structure^{52,103-105}.

Primary $\log L^{16}$ values can simply be measured from retention information gathered for solutes on n-hexadecane at 298.15K²⁴, so it was desirable to carry out chromatographic experiments that could be used to extend our list of $\log L^{16}$ values. Additional $\log L^{16}$ values can rather easily be predicted, for example along homologous series. Secondary values can also be calculated by correlation of primary $\log L^{16}$ values with retention data on other apolar stationary phases, such as Apiezon or Squalane. There is a wealth of such data in the literature.

We were already in a position to apply equations 53 and 54 to phenomena involving monofunctional solutes. However, there are two interrelated problems in the general application of these equations to multifunctional solutes. Firstly, the α_2 and β_2 values can be experimentally obtained^{101,102} from hydrogen bond complexation constants, only for monofunctional solutes. There seemed no practical possibility of obtaining direct experimental complexation constants for multifunctional solutes, and hence some indirect method of evaluation of α_2 and β_2 was required. Secondly, when equations 53 and 54 are applied to practical solubility situations, a given solute will be surrounded by an excess of solvent molecules, and hence multiple hydrogen bonding involving a number of solvent molecules can take place. This will not only take place with multifunctional solutes, but can also occur with certain solutes that are normally regarded as monofunctional. For example, anisole has $\beta_2 = 0.26$, derived from hydrogen bond

complexation constants ¹⁰², but when surrounded by an excess of solvent, the solute might act as a base both at the ether linkage and via the benzene ring. Indeed, any "monofunctional" solute that is an activated aromatic compound might have an enhanced effective β_2 value in a bulk solvent. Examples could be aromatic ethers, phenols, and aromatic amines.

One method of dealing with both of these problems involves back-calculation of β_2 values via equations 53 and 54. In order to back-calculate β_2 via, for example, equation 53, a number of conditions are necessary:

- (i) the experimental variable, SP, must be easily and accurately measurable,
- (ii) the coefficient of b in $b.\beta_2$ must be as large as possible, and
- (iii) the coefficients of π^*_2 and α_2 must be as small as possible.

The method of reversed-phase HPLC leads to capacity factors, $\log k'$, that can rather easily be measured for a range of solutes. It was known from preliminary correlations ¹⁸⁰ that by suitable choice of mobile phase and bonded phase, the coefficient of β_2 can be quite large, whilst those of π^*_2 and α_2 are generally small. HPLC affords data for important classes of compound, such as phenols, which is not very easily obtainable by GLC methods, as these solutes are generally retained too long on the column (especially at ambient temperature). $\log k'$ capacity factors for a variety of reversed-phase HPLC processes can be analyzed using equation 55, where α_2 and β_2 are known for monofunctional compounds. Then using the coefficients c, d, s, a, b, and m, back-calculations can be carried out to determine β_2 for multifunctional solutes.

$$\log k' = c + d.\delta_2 + s.\pi^*_2 + a.\alpha_2 + b.\beta_2 + m.V_2 \quad [55]$$

This approach, however, is not quite as easy as it seems at first sight. Although the

coefficient of α_2 may be small, it cannot be ignored. When solutes such as phenols are involved, these solutes must be counted in the actual regression equation, in order to obtain the α_2 term. But β_2 for phenols (as multifunctional bases) is not known. An iterative method must then be devised, in which certain effective β_2 values are first estimated, correlation equations are set up which yield better back-calculated effective β_2 values, and these are then incorporated into new correlation equations which in turn yield better β_2 values. The entire process is very time consuming since most of the calculations have to be done by hand. We planned to initiate the system of correlations using monofunctional known β_2 values plus estimated values for alkyl benzoic acids (0.45) and alkyl phenols (0.40). Values obtained by this method for phenols, anilines, and aromatic ethers might be expected to be appreciably higher than the "monofunctional" β_2 values. We hoped it was practical to obtain β_2 values for multifunctional solutes, and for other solutes for which direct measurements are not possible, by the technique of back-calculation. However, considerable care has to be taken, and results for important compounds must be obtained as the average of several results.

At the same time it was desired to obtain effective π^*_2 and α_2 values for multifunctional compounds. Note that an extra difficulty with polyfunctional acids is that any solute that is a hydrogen bond acid will also be a hydrogen bond base. Apart from the examination and subsequent back-calculation of 'effective' solvation parameters from HPLC data, much GLC data was available for analysis, notably the extensive data of McReynolds¹³³ and Laffort⁸². Apart from thoroughly characterising the stationary phases of McReynolds, (77 phases, approximately 350 solutes), and Laffort, (5 phases, 240 solutes), using our LSER equations and MLRA analysis, this would also enable back-calculation of 'effective' parameters, for monofunctional and multifunctional solutes alike. Any parameters calculated directly from GLC retention data can indeed be called effective values, as they should quantify accurately the degree and type of solute interaction taking place.

It was hoped to take data from many varying sources and for many different phases to calculate values for the solvation parameters which would have the widest and most accurate scope of application.

While α^H_2 and β^H_2 have a sound thermodynamic background, many π^*_2 values and δ_2 as a whole do not, so it would be preferable to investigate the use of other terms, or improved terms. Solute dipolarity was often estimated or obtained from simple correlations with dipole moments. An effective back-calculated solute dipolarity value would be an improvement over π^*_2 , and other replacement terms were also investigated. Attempts would also be made to replace the trivial parameter δ_2 with a parameter that could more accurately represent the degree of solute dipolarisability. This parameter should ideally be easily calculated and have some sort of rationale behind it.

6.1 Determination and Calculation of New Solvation Parameters

Our work to characterise the stationary phases of Laffort⁸² and McReynolds¹³³ proved to be the starting point for the realisation of the need to implement new (replacement) and/or improved solvation parameters, and describes the rationale behind these parameters. This work also afforded the opportunity to backcalculate an extensive set of improved 'effective' parameters. A summary of our work on the Laffort data^{181, see Appendix 2} and on the McReynolds data^{182, see Appendix 2} appears below.

6.11 Laffort Data

One of the most extensive and carefully determined sets of data is that of Laffort et al.⁸² who listed retention indices of 240 compounds on five stationary phases at 393K. Since Laffort et al.⁸² gave the necessary B-values¹⁸³, the reported values of I can be converted into log L values via equation 56,

$$\log L - \log L^{\text{Decane}} = \log L' = \left(\frac{I - 1000}{100} \right) B \quad [56]$$

The constant c in our general LSER equations 53 and 54 is now of little significance, but all the other constants are unaffected by the use of log L' rather than log L itself. The five Laffort phases are Carbowax, diethyleneglycol succinate (DEGS), polyphenyl ether (PPE), tricyanoethoxypropane (TCEP), and an ester of "pyromellitic acid and trihydrofluoro alcohol", known as Zonyl E-7 (ZE7).

A complete set of explanatory variables was available for 168 solutes out of the 240. For details of these solutes and parameters, please refer to Table 3¹⁸¹ in Appendix 2. The solute parameters used are all as have been described

previously for use in the two preferred equations 53 and 54, (where V_x is used for the solute volume term in equation 53). For a few difunctional bases such as anisole, 'effective' or summation $\Sigma\beta^H_2$ values were used, calculated from HPLC data as has been briefly described in section 5.1, and will be discussed in more detail in section 6.13.

$$\log SP = c + d.\delta_2 + s.\pi^*_2 + a.\alpha^H_2 + b.\beta^H_2 + m.V_x \quad [53]$$

$$\log SP = c + d.\delta_2 + s.\pi^*_2 + a.\alpha^H_2 + b.\beta^H_2 + 1.\log L^{16} \quad [54]$$

The regressions based on equations 53 and 54 are summarised in Tables 6 and 7. The overall correlation coefficients, R , and standard deviations, SD , are not particularly good, but note these refer to "all solute" regressions. The purpose of constructing these regressions was to characterise the stationary phases, and not to provide equations that can be used to predict further retention values. The obtained regression equations summarised in Tables 6 and 7 are adequate for the former, but not for the latter, purpose. It is of interest to note that as has been found before¹⁸⁴, equation 54 yields much better regressions than does equation 53 for gas/liquid partition coefficients⁺.

Examination of the constants in equations 53 and 54 reveals whether they are chemically reasonable. All five phases are to some extent dipolar, so that the s -constant in $s.\pi^*_2$ should be positive, as observed. The order of stationary phase dipolarity, as measured by the s -constant, is TCEP > DEGS > Carbowax > ZE7 $\geq$ PPE on equation 54, and almost the same on equation 53; this seems chemically quite reasonable. Again, all five phases are hydrogen bond bases, so that the a -constant in $a.\alpha^H_2$ should be positive. The order of stationary phase basicity is Carbowax > DEGS $\geq$ TCEP > ZE7 $\geq$ PPE on both equation 53

⁺ Except for gas/water partitions, but in this case neither V_x nor $\log L^{16}$ are very significant¹⁸⁴.

Table 6. Regression analysis using equation 53, n=168

$$\log L' = c + d.\delta_2 + s.\pi_2^* + a.\alpha^H_2 + b.\beta^H_2 + m.V_x$$

Phase	c	d	s	a	b	m	SD ^a	R ^b
Carbowax	-2.33	0.20	2.29	2.37	-0.53	1.57	0.22	0.960
SD ^c	0.07	0.06	0.12	0.12	0.17	0.05		
CL ^d	1.00	0.99	1.00	1.00	0.99	1.00		
DEGS	-2.04	0.25	2.41	2.05	-0.20	1.40	0.24	0.955
SD	0.07	0.07	0.13	0.13	0.18	0.05		
CL	1.00	0.00	1.00	1.00	0.74	1.00		
PPE	-2.90	0.22	1.93	0.84	-0.38	1.98	0.22	0.959
SD	0.07	0.06	0.12	0.12	0.17	0.05		
CL	1.00	1.00	1.00	1.00	0.97	1.00		
TCEP	-1.95	0.20	2.67	2.02	-0.02	1.32	0.23	0.961
SD	0.07	0.07	0.13	0.13	0.18	0.05		
CL	1.00	1.00	1.00	1.00	0.08	1.00		
ZE7	-2.43	0.09	1.91	0.81	0.21	1.59	0.16	0.975
SD	0.05	0.04	0.09	0.08	0.12	0.04		
CL	1.00	0.96	1.00	1.00	0.91	1.00		

^a Overall standard deviation. ^b Overall correlation coefficient.

^c Standard deviation in the constant. ^d Confidence level: 1.00 signifies > 0.99

Table 7. Regression analysis using equation 54, n=168

$$\log L' = c + d.\delta_2 + s.\pi_2^* + a.\alpha^H_2 + b.\beta^H_2 + l.\log L^{16}$$

A. Phase	c	d	s	a	b	l	SD	R
Carbowax	-2.07	0.05	1.55	2.13	-0.17	0.446	0.14	0.985
SD	0.04	0.04	0.07	0.07	0.10	0.008		
CL	1.00	0.83	1.00	1.00	0.89	1.00		
DEGS	-1.81	0.12	1.76	1.84	0.11	0.399	0.16	0.978
SD	0.04	0.05	0.09	0.09	0.12	0.010		
CL	1.00	0.99	1.00	1.00	0.64	1.00		
PPE	-2.54	0.04	1.01	0.53	0.08	0.554	0.11	0.990
SD	0.03	0.03	0.06	0.06	0.08	0.007		
CL	1.00	0.77	1.00	1.00	0.66	1.00		
TCEP	-1.74	0.07	2.06	1.82	0.28	0.380	0.16	0.981
SD	0.04	0.05	0.09	0.09	0.12	0.010		
CL	1.00	0.88	1.00	1.00	0.98	1.00		
ZE7	-2.10	-0.05	1.17	0.56	0.59	0.434	0.13	0.984
SD	0.03	0.04	0.07	0.07	0.10	0.008		
CL	1.00	0.84	1.00	1.00	1.00	1.00		

Table 7. (continued)

B ^a .Phase	c	d	s	a	l	SD	R
Carbowax	-2.06	0.08	1.46	2.08	0.445	0.14	0.985
SD	0.04	0.03	0.05	0.07	0.008		
CL	1.00	0.98	1.00	1.00	1.00		
DEGS	-1.81	0.10	1.82	1.87	0.400	0.16	0.978
SD	0.04	0.04	0.06	0.08	0.010		
CL	1.00	0.98	1.00	1.00	1.00		
PPE	-2.54	0.02	1.05	0.55	0.555	0.11	0.990
SD	0.03	0.03	0.04	0.05	0.007		
CL	1.00	0.61	1.00	1.00	1.00		
TCEP	-1.73	0.02	2.21	1.90	0.382	0.16	0.981
SD	0.04	0.04	0.06	0.08	0.010		
CL	1.00	0.40	1.00	1.00	1.00		
ZE7	-2.09	-0.16	1.50	0.72	0.438	0.14	0.980
SD	0.04	0.03	0.05	0.07	0.009		
CL	1.00	0.99	1.00	1.00	1.00		

^a These are the preferred equations

and equation 54. As might be expected, the fluoroester ZE7 is both less dipolar and less basic than the ester DEGS. Nominally, the five phases are all non-hydrogen-bond acids, so that the b-constant in $b.\beta^H_2$ should be near zero. There is a difficulty here, in that over the 168 solute set, the explanatory variable β^H_2 is not independent, there being a cross correlation coefficient of 0.673 between β^H_2 and π^*_2 . The total correlation matrix in terms of R is,

	δ_2	π^*_2	α^H_2	β^H_2
π^*_2	0.302			
α^H_2	-0.188	0.059		
β^H_2	-0.164	0.673	0.373	
$\log L^{16}$	0.052	0.073	-0.032	0.075

The regressions were therefore repeated, excluding the β^H_2 parameter, and it was concluded that none of the stationary phases has any significant hydrogen-bond acidity (see Tables 7(a) and 7(b)).

The l -constants in $l \cdot \log L^{16}$ are all much lower than unity. Part of this will certainly be due to the operating temperature of 393K instead of 298K, but part is probably also due to the lessening of general solute-solvent dispersion interactions by comparison to n-hexadecane solvent (at 298K).

Equation 53 and particularly equation 54 prove suitable for the characterisation of GLC stationary phases through a set of constants c , d , s , a , b , and l . Unlike Rohrschneider-McReynolds constants, however, those derived from equation 54 will yield quantitative information on the propensity of the phase to take part in given solute-stationary phase interactions. The difficulty over n-alkanes on polar phases does not apply to the application of equation 54, because incorporation of alkanes into the solute data set is not essential. Furthermore, an additional advantage of the present method is that it is now possible to compare GLC stationary phases with other condensed phases, for example common solvents. From preliminary regressions¹⁸⁴, the s -constant for ethyl acetate is known to be around 1.8, so that the dipolarity of tricyanoethoxypropane at 393K is no more than that of a simple ester at 298K.

An important disadvantage in the use of equations 53 and 54 is revealed by an examination of the origin of the explanatory variables. The dependent variable is ideally $\log L$ (or $\log K$), that is a Gibbs energy related quantity via an equilibrium constant. If $\log V_G$, $\log L'$ or $\log \tau$ are used, these quantities are still equivalent to the use of $\log L$ as far as all the terms except the c -constant are concerned. Hence for thermodynamic consistency, all the explanatory variables should be Gibbs energy related. There is no difficulty over α^H_2 , β^H_2 , and $\log L^{16}$ since these are all derived from equilibrium constants, as $\log K$ values^{24,101,102,185,186}. The variable V_x is not a Gibbs energy term, but since equation 54 is preferable to equation 53, this is not of any concern. A more pressing problem is the δ_2/π^*_2 formalism: the δ_2 parameter is simply an

empirical correction factor, whilst the π^*_2 parameter originates as a spectroscopically determined solvent π^*_1 parameter, and is certainly not a Gibbs energy related quantity. Furthermore, π^*_1 can only be determined for compounds that are liquids at room temperature, and can be equated to π^*_2 only for nonassociated liquids. All other π^*_2 values have either been estimated or have been obtained via various π^*_2 /dipole moment correlations¹⁸⁷. Due to the indeterminate nature of π^*_2 , it becomes impossible to connect the $s.\pi^*_2$ term in a regression equation with any specific solute-solvent interaction. The s -constant is more correctly representative of some blend of polarisability and dipolarity, rather than just dipolarity. These difficulties can only be resolved by replacing the δ_2 and π^*_2 parameters in equation 54.

The α^{H_2} and β^{H_2} parameters take care of hydrogen-bond interactions, and will be retained in any new equation. The $\log L^{16}$ parameter is very useful in that it accounts for cavity effects, together with general dispersion interactions of the solute-nonpolar solvent (hexadecane) type. This leaves solute-solvent dipole-dipole and dipole-induced dipole effects, together with additional dispersion interactions that may loosely be described as polarisability effects. The obvious solute parameter needed to describe dipole-dipole type interactions is the dipole moment (μ_2). Following Kirkwood¹⁸⁸, it was decided to use μ_2^2 , which has the advantage that it is very nearly a free energy related quantity⁺. Various physical quantities can be used to model dispersion/polarisability interactions. Both the solute molar refraction, MR, and the solute polarisability were briefly investigated, but neither were found satisfactory when used in combination with μ_2^2 , α^{H_2} , β^{H_2} , and $\log L^{16}$. The refractive index function, $f(\eta)$, has been used by Fuchs et al.¹⁸⁹ with some success, and in Table 8 are details of regressions using equation 57, with $f(\eta)$ defined by equation 58.

⁺Kirkwood¹⁸⁸ showed that the Gibbs energy of a dipole in a dielectric continuum was proportional to μ^2/r^3 where r is the radius of a sphere containing the dipole. Now many functional groups contain a dipole within a sphere of not-too-dissimilar radius, so that the Gibbs energy is approximately proportional to μ^2 .

$$\log L' = c + f.f(\eta) + q.\mu_2^2 + a.\alpha^H_2 + b.\beta^H_2 + l.\log L^{16} \quad [57]$$

$$f(\eta) = (\eta^2 - 1)/(\eta^2 + 2) \quad [58]$$

Table 8. Regression analysis using equation 57, n=168

$$\log L' = c + f.f(\eta) + q.\mu_2^2 + a.\alpha^H_2 + b.\beta^H_2 + l.\log L^{16}$$

Phase	c	f	q	a	b	l	SD	R
Carbowax	-3.48	7.61	0.059	2.34	0.55	0.370	0.19	0.971
SD	0.16	0.67	0.005	0.11	0.12	0.014		
CL	1.00	1.00	1.00	1.00	1.00	1.00		
DEGS	-3.62	9.56	0.067	2.06	0.92	0.304	0.22	0.961
SD	0.18	0.77	0.006	0.13	0.14	0.016		
CL	1.00	1.00	1.00	1.00	1.00	1.00		
PPE	-3.56	5.37	0.038	0.66	0.56	0.500	0.14	0.985
SD	0.11	0.48	0.004	0.08	0.09	0.010		
CL	1.00	1.00	1.00	1.00	1.00	1.00		
TCEP	-3.67	10.26	0.080	2.09	1.21	0.278	0.23	0.961
SD	0.19	0.81	0.006	0.13	0.15	0.017		
CL	1.00	1.00	1.00	1.00	1.00	1.00		
ZE7	-2.55	2.84	0.051	0.72	1.04	0.409	0.17	0.972
SD	0.14	0.58	0.005	0.10	0.11	0.012		
CL	1.00	1.00	1.00	1.00	1.00	1.00		

The regression equations based on equation 57 are appreciably poorer than those using equation 54. Not only are R and SD poorer, but significant b-constants are produced, surely as artifacts. Part of this difficulty may well be due to cross-correlations between μ_2^2 and β^H_2 ($R = 0.556$) and also between $f(\eta)$ and $\log L^{16}$ ($R = 0.534$), that could be overcome by a more suitable selection of solutes. But $f(\eta)$ must include interactions already dealt with by the $\log L^{16}$ parameter, hence the coefficients of $\log L^{16}$ in equation 57 are always less than those in equation 54. What is required is a parameter that is more specifically related to the polarisability of the solute as regards interactions due to the presence of polarisable electrons. Consider the solute molar refraction, but for convenience defined in terms of the characteristic volume,

$$MR_x = 10.(\eta^2-1)V_x/(\eta^2+2) = 10f(\eta).V_x \quad [59]$$

With V_x in units of $(\text{cm}^3 \text{ mol}^{-1})/100$, equation 59 will yield MR_x in the more convenient units of $(\text{cm}^3 \text{ mol}^{-1})/10$. Note that η is taken at 293K with the sodium-D line. Unlike $f(\eta)$ itself, the molar refraction has the interesting property of being the same (within a few per cent) for a given solute in the gas phase and in solution. Hence although $f(\eta)$ is most conveniently measured on bulk liquids, MR (and MR_x) can be taken as a property of an isolated molecule⁺. In order to remove the dispersive part already incorporated in $\log L^{16}$, the value of MR_x for an alkane of the same characteristic volume can be subtracted out,

$$R_2 = MR_x(\text{observed}) - MR_x(\text{alkane of same } V_x) \quad [60]$$

The latter quantity is readily obtained through an excellent linear regression for the n-alkanes,

$$MR_x(\text{alkane}) = -0.52553 + 2.83195V_x \quad [61]$$

$$R = 0.99999, \text{ SD} = 0.0078 \text{ N} = 13$$

Hence knowing $f(\eta)$ and V_x for any solute, MR_x and then R_2 can be calculated via equations 59-61. For convenience R_2 is tabulated in units of $\text{cm}^3/10$, and a number of typical values are in Table 9. Note that by definition $R_2 = 0$ for all n-alkanes, and by calculation R_2 is also zero for branched chain alkanes and for the rare gases as well.

⁺ We have confirmed that MR is essentially the same in the gas phase and bulk liquid even for associated compounds such as water and alcohols. The one exception we have noted is acetic acid, probably due to the extensive dimerisation that takes place in the gas phase.

Table 9. Some values of the molar refraction parameter, R_2 , and the "correction factor", δ_2 .

Solute	$R_2/10^{-1}\text{cm}^3$	δ_2
rare gases	0	0
alkanes	0	0
diethyl ether	0.041	0
but-1-ene	0.100	0
ethyl acetate	0.106	0
butanone	0.166	0
but-1-yne	0.178	0
1-chlorobutane	0.210	0
1-butanol	0.224	0
n-butylamine	0.224	0
cyclohexane	0.305	0
1-bromobutane	0.360	0
dimethylformamide	0.367	0
dichloromethane	0.387	0.5
tetrachloromethane	0.458	0.5
benzene	0.610	1
1-iodobutane	0.628	0
ethyl benzoate	0.663	1
methylphenylether	0.708	1
phenol	0.805	1
acetophenone	0.818	1
aniline	0.955	1

Substituting the new polarisability parameter, R_2 , for δ_2 , in conjunction with μ_2^2 , constructs equation 62,

$$\log L' = c + r.R_2 + q.\mu_2^2 + a.\alpha^{H_2} + b.\beta^{H_2} + l.\log L^{16} \quad [62]$$

that can be applied to the same set of 168 solutes as before. Details are in Table 10. The quality of the regressions in Table 10 is slightly better than those in Table 8, based on equation 57, but significantly poorer than those in Table 7, based on equation 54. For purposes of characterisation, this might not matter overmuch, but unfortunately the regressions in Table 10(a) show larger dependences on β^{H_2} that are probably artifacts (compare Table 10(a) with Table 10(b)).

Table 10. Regression analysis using equation 62, n=168

$$\log L' = c + r.R_2 + q.\mu_2^2 + a.\alpha^{H_2} + b.\beta^{H_2} + 1.\log L^{16}$$

A. Phase	c	r	q	a	b	l	SD	R
Carbowax	-1.98	0.86	0.052	2.30	0.53	0.438	0.17	0.976
SD	0.05	0.06	0.005	0.10	0.10	0.011		
CL	1.00	1.00	1.00	1.00	1.00	1.00		
DEGS	-1.74	1.10	0.059	2.03	0.89	0.389	0.19	0.971
SD	0.05	0.07	0.005	0.11	0.12	0.012		
CL	1.00	1.00	1.00	1.00	1.00	1.00		
PPE	-2.50	0.62	0.033	0.64	0.55	0.548	0.12	0.988
SD	0.03	0.04	0.003	0.07	0.08	0.008		
CL	1.00	1.00	1.00	1.00	1.00	1.00		
TCEP	-1.67	1.16	0.071	2.05	1.19	0.369	0.20	0.970
SD	0.05	0.07	0.006	0.12	0.13	0.013		
CL	1.00	1.00	1.00	1.00	1.00	1.00		
ZE7	-1.99	0.34	0.048	0.71	1.04	0.434	0.16	0.974
SD	0.04	0.06	0.004	0.09	0.10	0.010		
CL	1.00	1.00	1.00	1.00	1.00	1.00		
B. Phase	c	r	q	a	l	SD	R	
Carbowax	-1.92	0.85	0.068	2.56	0.444	0.18	0.972	
SD	0.05	0.07	0.004	0.09	0.011			
CL	1.00	1.00	1.00	1.00	1.00			
DEGS	-1.63	1.08	0.084	2.47	0.398	0.22	0.961	
SD	0.06	0.08	0.005	0.11	0.014			
CL	1.00	1.00	1.00	1.00	1.00			
PPE	-2.44	0.61	0.049	0.91	0.553	0.14	0.984	
SD	0.03	0.05	0.003	0.07	0.009			
CL	1.00	1.00	1.00	1.00	1.00			
TCEP	-1.50	1.14	0.105	2.64	0.382	0.25	0.954	
SD	0.06	0.09	0.005	0.12	0.016			
CL	1.00	1.00	1.00	1.00	1.00			
ZE7	-1.88	0.32	0.078	1.22	0.445	0.21	0.956	
SD	0.05	0.07	0.004	0.10	0.013			
CL	1.00	1.00	1.00	1.00	1.00			

Although there is no significant cross-correlation between R_2 and any other explanatory variable in equation 62, there still remains the connection between μ_2^2 and β^{H_2} , $r = 0.556$, referred to above. Finally, we can use calculated R_2 values (Table 9) to replace the empirical δ_2 values in equation 54 to yield,

$$\log L' = c + r.R_2 + s.\pi_2^* + a.\alpha^H_2 + b.\beta^H_2 + 1.\log L^{16} \pm \quad [63]$$

Details of regressions using equation 63 are in Table 11. In terms of overall standard deviation and correlation coefficient, these regressions are the best obtained, being slightly better than those given in Table 6. Replacement of δ_2 by R_2 in equation 53 has also been investigated, but, as usual, equations using V_x are considerably poorer than those using $\log L^{16}$.

Equation 63 represents the most satisfactory regression equation we have been able to construct. Analysis of the constants follows closely the analysis using equation 54. Although the analysis via equation 63 is only slightly better than that through equation 54, the former is to be preferred because the R_2 parameter is a well defined explanatory variable that refers to a specific type of solute-solvent phase interaction. From the method of determination of R_2 , as well as from inspection of R_2 values, it follows that the $r.R_2$ term in equation 63 is a quantitative measure of the ability of a solute to interact with the solvent through solute π (mainly) - or n-electron pairs. Furthermore, R_2 is a reasonably independent explanatory variable; cross-correlation coefficients between R_2 and the other explanatory variables in equations 62 and 63 are,

$$\pi_2^* \quad \mu_2^2 \quad \alpha^H_2 \quad \beta^H_2 \quad \log L^{16}$$

$$0.503 \quad 0.175 \quad -0.152 \quad 0.025 \quad 0.124$$

There is bound to be some correlation between R_2 and π_2^* because we have still not succeeded in subtracting all the polarisability contribution from π_2^* . However, equation 63 does go some way to so doing.

$\pm$ This is general solvation equation 63, where $\log SP$ (in this particular case) = $\log L'$.

Table 11. Regression analysis using equation 63, n=168

$$\log L' = c + r.R_2 + s.\pi_2^* + a.\alpha^H_2 + b.\beta^H_2 + 1.\log L^{16}$$

A. Phase	c	r	s	a	b	l	SD	R
Carbowax	-2.07	0.25	1.40	2.13	-0.05	0.442	0.13	0.986
SD	0.03	0.06	0.08	0.07	0.10	0.008		
CL	1.00	1.00	1.00	1.00	0.42	1.00		
DEGS	-1.84	0.43	1.53	1.83	0.28	0.393	0.15	0.982
SD	0.04	0.07	0.09	0.08	0.11	0.009		
CL	1.00	1.00	1.00	1.00	0.98	1.00		
PPE	-2.56	0.25	0.85	0.53	0.21	0.550	0.10	0.991
SD	0.03	0.05	0.06	0.05	0.08	0.006		
CL	1.00	1.00	1.00	1.00	0.99	1.00		
TCEP	-1.76	0.36	1.84	1.81	0.45	0.374	0.15	0.984
SD	0.04	0.07	0.09	0.08	0.11	0.009		
CL	1.00	1.00	1.00	1.00	1.00	1.00		
ZE7	-2.08	-0.24	1.31	0.56	0.48	0.438	0.12	0.985
SD	0.03	0.06	0.07	0.06	0.09	0.008		
CL	1.00	1.00	1.00	1.00	1.00	1.00		

B ^a . Phase	c	r	s	a	l	SD	R
Carbowax	-2.07	0.26	1.37	2.11	0.442	0.13	0.986
SD	0.03	0.05	0.05	0.06	0.008		
CL	1.00	1.00	1.00	1.00	1.00		
DEGS	-1.83	10.35	1.70	1.92	0.396	0.15	0.981
SD	0.04	0.06	0.06	0.07	0.009		
CL	1.00	1.00	1.00	1.00	1.00		
PPE	-2.55	0.19	0.98	0.59	0.552	0.11	0.991
SD	0.03	0.04	0.04	0.05	0.007		
CL	1.00	1.00	1.00	1.00	1.00		
TCEP	-1.75	0.23	2.12	1.94	0.379	0.16	0.982
SD	0.04	0.06	0.06	0.08	0.010		
CL	1.00	1.00	1.00	1.00	1.00		
ZE7	-2.07	-0.38	1.61	0.70	0.442	0.13	0.983
SD	0.03	0.05	0.05	0.06	0.008		
CL	1.00	1.00	1.00	1.00	1.00		

^a These are the preferred equations.

This characterisation process showed that a number of equations can be constructed for the characterisation of gas chromatographic phases, and, indeed, any solvent phase, through a series of constants that refer to specific solute-solvent interactions. Our preferred equation 63 leads to a set of constants c , r , s , a , b , and l of which r refers to interactions through solute π - and n - electron pairs, s to interactions of the dipole/dipole and dipole/induced dipole type (together with some polarisability effects), a to solute hydrogen bond acid/solvent hydrogen bond base interactions, b to solute hydrogen bond base/solvent hydrogen bond acid interactions and l to a combination of general dispersion forces plus cavity effects. The methodology does not suffer from the technical deficiencies of the Rohrschneider-McReynolds method, as outlined by Poole et al.¹³⁸, and can be applied to any condensed phase. Listed in Table 12 are the characteristic constants for the Laffort phases, using equations that omit the β^{H_2} explanatory variable. The dipolarity of the three phases, using either π^*_2 or μ_2^2 as a probe, is always in the order,

$$\text{TCEP} > \text{DEGS} > \text{ZE7} > \text{Carbowax} > \text{PPE}$$

and the hydrogen bond acidity of the phases, as given by the a -constant, is best represented by the order,

$$\text{Carbowax} > \text{TCEP} \geq \text{DEGS} > \text{ZE7} > \text{PPE}$$

The ability of the phase to interact with solutes specifically through π - and n -solute electron pairs is given by the r -constant in the $r.R_2$ term. There is not very good quantitative agreement between equations 62 and 63 on the solvent phase order, but both equations show that the fluorinated solvent ZE7 has the least ability to take part in π - and n - interactions.

Table 12. The characterisation of stationary phases at 393K

Phase	c ^a	d	s	a	l
Carbowax	-2.06	0.08	1.46	2.08	0.445
DEGS	-1.81	0.10	1.82	1.87	0.400
PPE	-2.54	0.02	1.05	0.55	0.555
TCEP	-1.73	0.02	2.21	1.90	0.382
ZE7	-2.09	-0.16	1.50	0.72	0.438
	c	r	s	a	l
Carbowax	-2.07	0.26	1.37	2.11	0.442
DEGS	-1.83	0.35	1.70	1.92	0.396
PPE	-2.55	0.19	0.98	0.59	0.552
TCEP	-1.75	0.23	2.12	1.94	0.379
ZE7	-2.07	-0.38	1.61	0.70	0.442
	c	r	q	a	l
Carbowax	-1.92	0.85	0.068	2.56	0.444
DEGS	-1.63	1.08	0.084	2.47	0.398
PPE	-2.44	0.61	0.049	0.91	0.553
TCEP	-1.50	1.14	0.105	2.64	0.382
ZE7	-1.88	0.32	0.078	1.22	0.445

^a Note that this constant includes the term $\log L^{\text{Decane}}$, see equation 56.

6.12 McReynolds Data

A substantial part of our work has been the characterisation of the stationary phases of McReynolds¹³³ purely in terms of our LSER equations. This would enable comparison of our derived phase classification with other workers who have attempted McReynolds phase characterisation over the years, and more importantly, 'firm up' our LSER equations and allow backcalculation of a very substantial set of effective solvation parameters. The largest sets of gas-chromatographic retention data are those of McReynolds, who determined retention volumes (V_G^0) and retention indices (I) of 376 solutes on 77 phases at two temperatures¹³³ and retention indices of 10 solutes on 226 phases at 120°C¹²⁷. Numerous workers have classified both the 77 phase set and the 226 phase set by various methods. McReynolds himself¹²⁷, assigned a single polarity index to the 226 stationary phases, using the sum of the ΔI values for benzene, butanol, 2-pentanone, nitropropane, and pyridine. Later workers refined this method¹⁹⁰, and also calculated a polarity index from the Gibbs energy of solvation of the methylene increment, $\Delta G_s^0(\text{CH}_2)$, on a given stationary phase¹³⁸. Other workers assigned a number of characteristic parameters to phases. Thus Risby et al.¹⁹¹ derived ΔG_s^0 values for six functional groups on 75 of the 226 phase set, and Fellous et al.¹⁹² assigned a polarity index (ρ^*) to the same six functional groups on 72 of the 226 phase set.

Various sophisticated methods have been used to classify the McReynolds phases into groups. They include nearest neighbour techniques¹⁹³, information theory¹⁹⁴, numerical taxonomy^{194,195}, principal components analysis¹⁹⁶, pattern cognition methods^{130,197}, and factor analysis¹⁹⁸. All these methods reduce the 226 phase set or the 77 phase set to a smaller number of clusters each of which represents a collection of similar phases. This is a very useful and helpful outcome, but, in addition, several of these methods lead to the estimation of the

number of factors that influence chromatographic retention data. Wold and Andersson¹⁹⁶ suggested three main factors, (1) polarity, (2) a factor difficult to identify, and (3) a factor that was due to hydrogen-bonding of the phase with alcohols. Chastrette¹⁹⁸ showed that five factors accounted for 99% of the total variance: three factors were difficult to account for, and the other two were polarity and a factor connected to, but not identical with, hydrogen-bonding. A polarity factor was identified by McCloskey and Hawkes¹⁹⁹, who also suggested that a factor related to the ability of a phase to retain cis-hydrindane was important.

It seems, therefore, that although a single "polarity" parameter is still often used to characterise stationary phases^{131,138}, analytical methods suggest that a number of factors must be involved, perhaps three¹⁹⁶ to five¹⁹⁸, although identification of these factors with particular chemical interactions has not proved possible. Our analysis starts with a model for solvation of a solute, (as has been described in detail in section 2.12), and then deduces from the model various possible interactions. Once these interactions are set out, the necessary parameters required to quantify these interactions have to be obtained (from data other than the chromatographic results to be analysed). These parameters then, in effect, take the place of the various factors identified by methods such as principal components analysis¹⁹⁶ or factor analysis¹⁹⁸.

Equations 54, 62 and 63 were applied¹⁸² to the data of McReynolds¹³³ on 367 solutes on 77 phases.

$$\log SP = c + r.R_2 + s.\pi_2^* + a.\alpha^H_2 + b.\beta^H_2 + l.\log L^{16} \quad [63]$$

$$\log SP = c + d.\delta_2 + s.\pi_2^* + a.\alpha^H_2 + b.\beta^H_2 + l.\log L^{16} \quad [54]$$

$$\log SP = c + r.R_2 + q.\mu_2^2 + a.\alpha^H_2 + b.\beta^H_2 + l.\log L^{16} \quad [62]$$

That up to five constants are needed to characterise a given stationary phase again reflects the complexity of solute/solvent interactions. The number of constants in equations 54, 62 and 63 however, is certainly in accord with principal components analysis of these phases¹⁹⁶, and factor analysis¹⁹⁸, which both show that several factors are required to account for retention data. Of the solutes studied, the necessary parameters were available for about 160, and our analysis uses up to 157 solutes on the 77 phases at two temperatures ⁺, in terms of the $\log V_G^0$ values reported by McReynolds¹³³. Again, as a necessary preliminary, the solute parameters used as explanatory variables were tested to validify their independance. In Table 13 are given the correlation constants, R, between the explanatory variables in equation 63. It can be seen that the intercorrelations are insignificant, with the possible exception of that between π_2^* and β^{H_2} for which R = 0.474 (and $R^2 = 0.225$ only).

Table 13. Correlation coefficients between the explanatory variables ^a.

	R_2	π_2^*	α^{H_2}	β^{H_2}
π_2^*	0.295			
α^{H_2}	0.111	-0.210		
β^{H_2}	-0.243	0.474	0.247	
$\log L^{16}$	0.016	-0.171	-0.061	-0.169

^a For the 155 solute data set used for flexol

Equations 54, 62 and 63 were first tested for two typical phases, ethyleneglycol adipate and dibutyltetrachlorophthalate; results are in Table 14. Both the overall correlation coefficient and the standard deviation, SD, are almost identical for equation 54 and equation 63. Since the molar refraction parameter R_2 can be identified with a specific type of solute/solvent interaction, whereas the empirical δ_2 parameter cannot, our final results are listed in

⁺McReynolds studied a large number of difunctional compounds for which most of the required parameters in equation 54 and equation 62 were not available; these include many formals, acetals, dihydric alcohols, etc. Note that not all solutes were studied on all phases, so that the number of solutes used in our regressions varied from 130 to 157.

terms of the preferred equation 63 only, see Appendix 2. Although the correlations in terms of equation 62 are quite useful, they are in all cases not as good as equation 63, so not all the details of equation 62 are given in the Appendix, only values of the q- constant where necessary.

Table 14. Comparison of equations 63, 54 and 62 in Regressions of $\log V_G^\circ$ at 120°C

A. Ethyleneglycol adipate

Eqn. 63	c -0.900 0.038 ^d	r 0.357 0.048	s 1.425 0.048	a 1.720 0.053	l 0.443 0.007	SD ^a 0.093	R ^b 0.9857	n ^c 143
Eqn. 54	c -0.871 0.038	d 0.116 0.030	s 1.480 0.047	a 1.867 0.053	l 0.438 0.007	SD 0.094	R 0.9849	n 143
Eqn. 62	c -0.360 0.055	r 0.784 0.079	q 0.073 0.006	a 1.405 0.089	l 0.394 0.013	SD 0.160	R 0.9476	n 143

B. Dibutyltetrachlorophthalate

Eqn. 63	c -0.615 0.019	r 0.249 0.025	s 0.692 0.025	a 0.600 0.028	l 0.600 0.004	SD 0.048	R 0.9969	n 150
Eqn. 54	c -0.615 0.020	d 0.112 0.016	s 0.752 0.025	a 0.687 0.029	l 0.599 0.004	SD 0.050	R 0.9967	n 150
Eqn. 62	c -0.410 0.024	r 0.547 0.039	q 0.038 0.003	a 0.420 0.040	l 0.586 0.006	SD 0.070	R 0.9920	n 150

^a Overall standard deviation. ^b Overall correlation coefficient.

^c Number of solutes. ^d These are the standard deviations in the constants.

The results of application of equation 63 to the entire set of stationary phases at 120° are summarised in Table III¹⁸², (please see Appendix 2), where also the q- constant in equation 62 is given. For a few phases, data were available at 80°C

and 100°C only, and the various constants at 120°C have been estimated from values at the lower temperatures. For completeness, the various equations have been applied to results at the other given temperatures used in the work of McReynolds¹³³, and details are shown in Table IV¹⁸², (please see Appendix 2). Before attempting to classify the phases, it is apparent that the correlation eqn. 63 yields results that are reasonably good for "all solute" correlations, and these results are chemically sensible. Thus the s-, a-, and b- constants, when statistically significant, are always positive, because increase in solute/solvent interactions must lead to an increase in solubility of the gaseous solute, and hence to an increase in V_G^0 . The r- constant is nearly always positive, except in the case of fluorinated phases, e.g. Dow fluid 1265, where the polarisability is even less than in hydrocarbon systems. The l- constant reflects a combination of an endoergic cavity term and an exoergic solute/solvent general dispersion interaction term. The latter always dominates, giving rise to positive l- constants.

The effect of temperature is very important with regard to characterisation of solubility-related phenomena, although it has generally been overlooked as regards characterisation of stationary phases. In general, the main characteristic constants s, a, b, and l, all decrease, often quite markedly, with temperature. Now if the relevant solute/solvent interactions are not only exoergic but are exothermic as well, the van't Hoff equation requires that these interactions will decrease with increase in temperature, hence leading to a decrease in the numerical values of the characteristic constants. On thermodynamic grounds it thus follows that any correlation equation set up in terms of solute/solvent or solute/stationary phase interactions must incorporate this temperature dependence. Our equation 63 does so via the characteristic constants. As a final check on our method of analysis, regression equations obtained from the set of solutes used by McReynolds¹³³ can be compared with those¹⁸¹ from the quite

different set of solutes used by Laffort et al.⁸² for Carbowax 1540, diethyleneglycolsuccinate, polyphenylether, and zonyl-E7. Details are in Table 15, and show that there is very good agreement between the two sets of regressions using equation 63.

Table 15. Characterisation of Phases using Equation 63 with McReynold's and Laffort's Data at 120°C

Stationary phase	Set	r	s	a	l
Carbowax 1540	M ^a	0.31	1.34	1.87	0.457
	L ^b	0.26	1.37	2.11	0.442
Diethyleneglycolsuccinate	M ^a	0.43	1.74	1.68	0.379
	L ^b	0.35	1.70	1.92	0.396
Polyphenylether, 6 rings	M ^a	0.21	0.90	0.56	0.563
	L ^b	0.19	0.98	0.59	0.552
Zonyl E-7	M ^a	-0.28	1.63	0.69	0.449
	L ^b	-0.38	1.61	0.70	0.442

^a McReynold's set, reference 133. ^b Laffort's set, reference 82.

CHARACTERISATION OF PHASES

Details of the application of equation 63 to the 77 McReynolds phases are given in Tables III^{182,Appendix 2}, IV^{182,Appendix 2}, 16, and 17. In Table III are results at a common temperature of 120°C, with values for squalane and citroflex A4 extrapolated from those at 80°C and 100°C. Table IV contains results at temperatures other than 120°C, usually at 100°C or at 140°C/160°C, so that all of McReynolds data sets have been analysed. The chemical formulation of the 77 phases is not listed, even though some of them are rather obscure, because Fellous et al.¹⁹² have detailed the 77 stationary phases already. It should be noted that many of these phases contain a nonionic surfactant (2%, w/w), and

hence the obtained constants, Table III, refer to the phases as specifically formulated by McReynolds¹³³. Although many of the McReynolds phases are no longer in current use, results are listed for all the phases in order to show the utility of our method and in order to compare our classification with previous characterisation¹³⁰ of the total 77 phase set.

Table 16. Stationary Phases with significant Hydrogen Bond Acidity

Stationary phase	<i>c</i>	<i>r</i>	<i>s</i>	<i>a</i>	<i>b</i>	<i>l</i>	SD	R	No	t/°C
Docosanol ^a	-0.41	0.13	0.29	0.75	0.34	0.603	-	-	-	120
	-0.37	0.15	0.30	1.13	0.39	0.657	0.061	0.9951	148	100
	-0.33	0.16	0.31	1.56	0.45	0.717	0.077	0.9925	134	80
Diglycerol	-1.26	0.55	1.63	2.77	0.52	0.225	0.148	0.9589	146	120
Sorbitol	-1.72	0.35	0.81	1.77	0.34	0.360	0.161	0.9217	130	120

^a Extrapolated from results at 80° and 100°.

Table 17. Test for Stationary Phase Hydrogen Bond Acidity

Stationary phase	<i>c</i>	<i>r</i>	<i>s</i>	<i>a</i>	<i>b</i>	<i>l</i>	SD	R
Castorwax	-0.47	0.13	0.59	1.06	0.08	0.563	0.059	0.9945
	-0.45	0.10	0.63	1.09	-	0.562	0.060	0.9944
Flexol 8N8	-0.49	0.12	0.71	1.25	0.03	0.573	0.065	0.9932
	-0.48	0.11	0.73	1.27	-	0.573	0.065	0.9932
Hyprose SP80	-0.86	0.09	1.56	2.42	0.05	0.414	0.103	0.9835
	-0.87	0.11	1.53	2.40	-	0.414	0.103	0.9835
Quadrol	-0.77	0.08	1.45	2.37	0.03	0.472	0.103	0.9858
	-0.77	0.07	1.47	2.38	-	0.471	0.103	0.9858

Furthermore, no corrections were made by McReynolds for effects such as interfacial adsorption, and his results for solutes such as alkanes in the more

polar phases may be subject to additional error. There was no way available to correct the raw data of McReynolds, and rather than exclude particular subsets of compounds on some arbitrary basis, all the available results were used. This may well account for part of the large standard deviations observed for regressions with phases such as diglycerol and sorbitol, and suggests also that the obtained constants for these phases should be viewed with some caution.

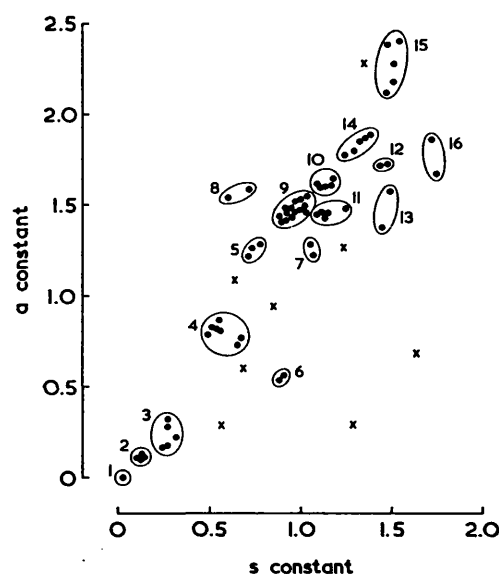
In principle, a given stationary phase at a given temperature is characterised by the six constants in equation 63. However, the constant c , although important as regards the absolute values of $\log V_G^0$, is not a very useful characteristic constant, whilst the constant r plays only a minor role, at least for the present data set. Thus four constants are left, s , a , b , and l . But we can effect further simplification by noting that only three out of the 77 phases give rise to statistically significant b -constants, and hence show hydrogen-bond acidity. These are docosanol, diglycerol and sorbitol with b -values of 0.34, 0.52, and 0.34 respectively at 120°C, see Table 16. A number of the other phases might be expected to show hydrogen-bond acidity, but the analysis given in Table 17 reveals that the $b.\beta H_2$ term is not significant.

Docosanol, diglycerol and sorbitol can be regarded as singular phases, and analyses of the remaining 74 phases can proceed with the omission of the $b.\beta H_2$ term altogether, see Tables III^{182, Appendix 2} and IV^{182, Appendix 2}. For these 74 phases, the three major characteristic constants are thus s , a , and l only.

The analysis of the 74 phases in Table III^{182, Appendix 2} can be started by noting that there is some connection between s , a , and l . In general, basic phases will also be dipolar, so that a and s will tend to run together. Furthermore, solvent/solvent interactions will be greater in dipolar, basic phases, thus giving rise to a larger endoergic cavity term, leading to a smaller value of the

l -constant. Since a and s are likely to be related, the 74 phases can be grouped through a plot of a against s , shown in Figure 9.

FIGURE 9. Classification of the stationary phases according to the a constant and the s constant in equation 63. ● = Groups as shown in Table III^{182, Appendix 2}; x = singular phases.



Quite clearly, there are several groups or clusters of phases with about the same a and s values, and Table III^{182, Appendix 2} has been drawn up to show the 16 clusters indicated in figure 9. Of course, there is an arbitrary element in the choice of clusters. Thus groups 9 and 11 might be subsumed into a common group, or group 4 might be divided into two groups, but this is a feature of any method that reduces the 77 phases down to a relatively small number of clusters. We can then examine the 16 groups to see if any further subdivision is necessary on the basis of the r and l constants. However, within each group, the r and l constants do not vary overmuch. Only in the case of group 7 and group 16 is there a clear subdivision into high and low values of l , although groups 10 and 15 do contain a rather wide spread of l -values.

An analysis in terms of s and a (and also b for phases that are hydrogen bond acids) enables grouping of the 74 McReynolds phases into a number of clusters of similar phases, leaving some 11 stationary phases (8 in Table III^{182,Appendix 2} plus the three acidic phases) as singular phases that cannot be substituted by any other of the 77 phase set. This grouping is based entirely on chemical principles, and it is very instructive to compare results with other work carried out on more mathematical lines. Huber and Reich¹³⁰ have analysed the 77 phase set, using both hierarchical clustering and the minimum spanning tree method. Their results, especially by the latter technique, are almost identical to those we have obtained. Differences, such as there are, are trivial. For example Huber and Reich¹³⁰ class Castorwax and our groups 5 and 8 together, but reference to Table III^{182,Appendix 2} and Figure 9 shows that this is quite reasonable on our analysis as well. Wold¹⁹⁶ used a pattern cognition method to group the 226 phase set into clusters. Where there are common phases between the 226 and the 77 phase sets, there is again excellent agreement between our results and those of Wold¹⁹⁶. As pointed out by Wold, the nearest neighbour technique used by Leary¹⁹³ leads to a rather peculiar set of clusters. However, the numerical taxonomy method of Massart¹⁹⁴ applied to the 226 phase set leads to groups not too dissimilar to those in Table III^{182,Appendix 2}, although there are some outstanding exceptions. Thus Massart et al.¹⁹⁴ class didecylphthalate and Flexol 8N8 in the same group, whereas we found the latter to be considerably more basic ($a = 1.27$ as against $a = 0.73$ for di-isodecylphthalate). Our method of clustering, therefore, is in excellent agreement with results of Huber and Reich¹³⁰ and of Wold¹⁹⁶, but not so much with results of Leary et al.¹⁹³ or of Massart et al.¹⁹⁴.

A general survey of our classification, Table III^{182,Appendix 2}, shows that it is completely consistent with the chemical formulation of the phases. Thus group 1 contains the saturated hydrocarbon squalane, and would include other

hydrocarbons such as hexadecane (by definition), octacosane, $C_{87}H_{176}$ etc. The apiezons in group 2 are slightly dipolar and basic due to the presence of some aromatic groups, whilst the silicones in group 3 are rather more dipolar and basic through the silicon-oxygen bond. Thus the hydrogen-bond basicity of $Me_3SiOSiMe_3$ as a solute, $\beta^{H_2} = 0.16$, can be compared to values of β^{H_2} for di-t-butylether of 0.38, and values of around 0.45 for straight-chain aliphatic ethers¹⁸⁶. All the simple esters of carboxylic acids cluster in group 4, the two amides appear in group 8, and so forth. The Carbowaxes fall into an exact sequence from Carbowax 20M to Carbowax 300, with values of s and a monotonically increasing along the series, where the cut-off point between groups 14 and 15 is clearly arbitrary.

The constant r does not vary widely over the particular set of 77 phases, but, significantly, the r -constant is negative in the case of the only fluorinated stationary phases in the set, viz. Dow Corning Fluid FS 1265 and Zonyl E-7. The ability of these phases to interact with solute π - and n -electron pairs is even less than that of a simple alkane.

Finally, consider the characteristic constant l , a resultant of an endoergic solvent cavity term tending to decrease the value of l and an exoergic general dispersion interaction term tending to increase the value of l . It has been shown previously¹⁸¹ that the methylene increment for solvation of a homologous series of gaseous solutes in a given solvent, $\Delta G_s^0(CH_2)$, depends on a combination of a solvent cavity term and a general dispersion interaction term. $\Delta G_s^0(CH_2)$ is related to $\Delta \log V_G^0$, since $\Delta G_s^0(CH_2) = -2.303RT\Delta \log V_G^0$, where $\Delta \log V_G^0$, is the average increase in $\log V_G^0$, along an homologous series. It therefore follows that the constant l must also be related to the important term $\Delta \log V_G^0$, or $\Delta G_s^0(CH_2)$.

In Table 18 are given values of $\Delta \log V_G^0$, for the homologous series of 1-alkanols in a few representative stationary phases covering the range of l -constants encountered. A regression of $\Delta \log V_G^0$, against the l -constant yields the equation,

$$\Delta \log V_G^0 = 0.022 + 1.814 \log l^6 \quad [64]$$

$$R = 0.9988 \quad SD = 0.009 \quad N = 8$$

where the intercept is close to zero, as required.

Table 18. Values of $\Delta \log V_G^0$ for 1-alkanols on some Stationary Phases

Stationary phase	$t/^\circ\text{C}$	l	$\log V_G^0$	R^a	No ^a
Squalane	80	0.735	0.398	0.9991	5
Squalane	100	0.674	0.358	0.9988	7
Squalane ^b	120	0.619	0.322	-	-
Apiezon N	120	0.601	0.314	0.9993	7
SE 30	120	0.523	0.280	0.9996	7
Carbowax 400	120	0.440	0.235	0.9998	7
Diethyleneglycol - succinate	120	0.379	0.198	0.9989	7
Diglycerol	120	0.225	0.110	0.9987	7

^a Correlation coefficients and number of points in plots of $\log V_G^0$ against carbon number of the 1-alkanols. ^b Extrapolated values.

Thus, one can show from experiment, as well as theory, that the l -constant in equation 63 is a measure of the ability of a stationary phase to separate members of an homologous series. The l -constant is entirely equivalent to $\Delta G_s^0(\text{CH}_2)$, so that equation 63 actually incorporates this latter parameter.

Equation 54 offers no advantage over equation 63 and suffers from the disadvantage of containing the empirical parameter δ_2 . Equation 62, although giving rise to significantly worse fits than equation 63 has the advantage that the

q -constant, especially, can be related to a theoretical model of solute dipole/solvent interactions via the Kirkwood equation. However, in practice the correlation constant between q and s is so high, 0.970 for the 77 stationary phases at 120°, that no extra information is contained in q . At present, therefore, equation 62 is not necessary for the characterisation of stationary phases. However, the dipole moment term is theoretically very useful, and it might be possible to incorporate other solute parameters, and to obtain an improved version of equation 62 that retains the dipole moment as a dipolarity parameter.

In Table 19 is a selection of phases characterised^{181,182,200} to show how the characteristic constants s , a , b , and l relate to the chemical nature of the stationary phase. From such a list, it is easy to select a phase that will effect separations mainly through dipole/dipole interactions (e.g. Zonyl E7), or a phase that will effect separations mainly through interactions of the type solute hydrogen bond acid/solvent hydrogen bond base (e.g. Hallcomid M18 or M180L). From the McReynolds¹³³ set of phases, there is no phase that leads mainly to interactions of the type solute hydrogen bond base/solvent hydrogen bond acid. The most acidic phase encountered is diglycerol with $b = 0.52$ at 120°, but this phase is actually the strongest hydrogen bond base of all the phases listed. In any case, diglycerol is unsuitable as a general stationary phase because of the very low l -constant. There is considerable scope to synthesise phases that are strong hydrogen bond acids but weak hydrogen bond bases.

Table 19. Chemical Characteristics of Some Phases

Phase	Polarity	Basicity	Acidity	Separation of Homologues
Hexadecane } Squalane }	Zero	Zero	Zero	High
Apiezon	Low	Low	Zero	High
Polyphenylether	Medium	Low	Zero	High
Hallcomid } Kroniflex THFP }	Medium	High	Zero	Medium
Carbowax 300 } Quadrol }	High	High	Zero	Medium
Hyprose SP80 }	High	Low	Zero	Medium
Zonyl E7	Very high	High	Zero	Low
Tricyanoethoxypropane	High	Very High	Zero	Medium
N-Methylpyrrolidinone	Low	Medium	Low	High
Docosanol	High	Very high	Medium	Very low
Diglycerol				

Our main aim in analysing McReynold's data was to characterise the set of 77 McReynolds phases in terms of equation 63, where $SP = V_G^0$. Results given in Tables III^{182, Appendix 2}, IV^{182, Appendix 2}, 15 and 16, can be used to analyse the factors that influence solute retention on stationary phases. In Table 20 is given a breakdown of equation 63, term-by-term for two typical solutes, butanone and 1-butanol, in a variety of stationary phases. In the less polar phases, where the s -constant is quite small, by far the main term is $l \cdot \log L^{16}$. The term $a \cdot \alpha^H_2$ can be substantial for the combination of a hydrogen bond acidic solute and a hydrogen bond basic phase, but for the present set of solutes and phases the $b \cdot \beta^H_2$ term is never substantial. Of course, for more acidic phases than diglycerol, the $b \cdot \beta^H_2$ term could be much more significant. In equation 63, the $l \cdot \log L^{16}$ term covers both general dispersion interactions that lead to positive values of $\log V_G^0$, and the endoergic solvent/solvent cavity term that leads to negative values of $\log V_G^0$. These two effects are very difficult to unravel quantitatively, hence we had to use a combined term in equation 63. Abraham and Fuchs¹⁰⁷, however, managed to dissect the $\log L^{16}$ values themselves into mainly a cavity term and a

general dispersion interaction term. If it is assumed¹⁸⁴ that the ratio of these two terms remains the same, then the total $l.\log L^{16}$ term can be roughly separated, as shown in Table 20, into cavity and general dispersion effects. Given that these are only approximations, especially in the case of diglycerol, we can still see that the largest interaction term corresponds to general solute/solvent dispersion effects. It is these that control the separation of members of an homologous series. Equation 63 incorporates such an effect in the $l.\log L^{16}$ term. Although dipolar and acid/base interactions tend to be smaller than the general dispersion interactions, they control separations of dissimilar solutes. Equation 63 incorporates these effects in the first four terms. Thus our preferred equation 63 not only forms the basis of a classification of stationary phases, but also leads to a rationale for the separation of solutes, based on a number of possible solute/solvent interactions.

Table 20. Analysis of the Factors that Influence $\log V_G^\circ$, using Eqn. 63 at 120°

Term	$r.R_2$	$s.\pi_2^*$	$a.\alpha^H_2$	$b.\beta^H_2$	$l.\log L^{16}$	dispersion ^a	cavity ^a
A. Solute butanone							
Apiezon M	0.04	0.07	0	0	1.37	3.36	-1.93
Hallcomid M18	0.02	0.40	0	0	1.35	3.26	-1.88
Zonyl E-7	-0.05	1.09	0	0	1.03	1.90	-1.09
Diglycerol	0.09	1.09	0	0.25	0.52	(0.48)	(-0.28)
B. Solute 1-butanol							
Aplezon M	0.06	0.40	0.04	0	1.56	4.10	-2.25
Hallcomid M18	0.03	0.24	0.52	0	1.54	4.00	-2.20
Zonyl E-7	-0.06	0.65	0.23	0	1.17	2.31	-1.27
Diglycerol	0.12	0.65	0.91	0.23	0.59	(0.59)	(-0.32)

^a These do not add up to the $l.\log L^{16}$ term because of a constant term and a small dipole/induced dipole term that have not been included.

6.13 Calculation of Effective Hydrogen Bond Basicity, $\Sigma\beta^H_2$, from HPLC Data

As has been described in section 5.1, an 'effective' hydrogen bond basicity, $\Sigma\beta^H_2$, can be calculated from chromatographic retention data, and some of these values were used in our characterisation of the Laffort phases¹⁸¹. At present, there seems no practical possibility of obtaining direct experimental complexation constants for multifunctional solutes, and hence some indirect method of evaluation of α_2 and β_2 is required. In addition, when LSER equations are applied to practical solubility situations, a given solute will be surrounded by an excess of solvent molecules, and hence multiple hydrogen bonding involving a number of solvent molecules can take place. This will not only take place with multifunctional solutes, but can also occur with certain solutes that are normally regarded as monofunctional. There are a very large number of literature reports of the determination of reversed phase HPLC (RP-HPLC) capacity factors, k' . Table 21 lists the variety of reversed-phase HPLC processes used in one of the first analyses attempted²⁰¹. A number of series were analysed, where, in each case, the solvent composition is constant, and the general equation 55 (or the preferred equation 65, since the development of the R_2 parameter) were applied, where SP in this case is $\log k'$. The use of δ_2 or R_2 in this analysis is to a great extent academic, because neither term is very important.

$$\log k' = c + d.\delta_2 + s.\pi^*_2 + a.\alpha^H_2 + b.\beta^H_2 + m.V_2 \quad [55]$$

$$\log k' = c + r.R_2 + s.\pi^*_2 + a.\alpha^H_2 + b.\beta^H_2 + m.V_2 \quad [65]$$

One method of dealing with the above problems of effective basicities involves back-calculation of β_2 values via equations 65 and 55. $\Sigma\beta^H_2$ values can be back-calculated for solutes and $\Sigma\beta^H_2$ can be averaged for each solute where there are two or more values. These averaged $\Sigma\beta^H_2$ values are then used to generate a new set of equations of type 65 or 55, $\Sigma\beta^H_2$ are back-calculated, averaged, and

the cycle repeated. This work is still continuing, but as an example, some work already done²⁰¹ is presented here. The final result is the set of correlation equations, using equation 55 in this case, which are given in Table 22, (note that the term $d.\delta_2$ is either not significant or small). Derived $\Sigma\beta^{H_2}$ values are given in Table 23. In addition, numerous $\Sigma\beta^{H_2}$ values calculated from only one result can be obtained, but these were not used to obtain the regression equations in Table 22.

Just as expected, the effective basicities values for phenols, anilines, and aromatic ethers are appreciably higher than the "monofunctional" β^{H_2} values, (see Table 24 for a comparison of $\Sigma\beta^{H_2}$ from RP-HPLC back-calculations, and β^{H_2} for representative solutes). It is rather unlikely that further cycles of this iterative process will appreciably alter the values listed in the final column of Table 23. However, it is possible to incorporate more solutes into the set of equations, and also to specify more exactly the HPLC solutes that are preferred for the back-calculation. A typical equation is that for system no. 33 (from Table 21) using equation 55, and V_X as a solute size term,

$$\log k' = -0.311 - 0.647\delta_2 + 0.308\pi_2^* - 0.082\alpha^{H_2} - 2.599\beta^{H_2} + 1.4071V_X \quad [66]$$

$$R = 0.9981 \quad SD = 0.042 \quad N=48$$

The coefficient of β^{H_2} in equation 66 is some eight times as large as that of π_2^* , with that of α^{H_2} being negligible (the coefficient of the rather trivial δ_2 term is also small). Hence if π_2^* or α^{H_2} values have to be estimated, not much error in the back-calculated β^{H_2} values will be introduced.

Such a method of calculation is an on-going project, since further literature data can be incorporated into a system of equations. However, results indicate that

$\Sigma\beta^{\text{H}_2}$ values are firmly established for a number of key series of aromatic compounds where $\beta^{\text{H}_2} \neq \Sigma\beta^{\text{H}_2}$. These include phenols, benzoic acids, benzyl alcohols, anilines, and aromatic ethers. In addition, $\Sigma\beta^{\text{H}_2}$ values have been established for a few aliphatic carboxylic acids, for which β^{H_2} cannot be derived directly.

The list of $\Sigma\beta^{\text{H}_2}$ values in Table 23 represents a very important advance in the characterisation of solutes, and enables us to extend considerably the nature of various regressions. It is still desirable to confirm and extend $\Sigma\beta^{\text{H}_2}$ values through back-calculations involving other processes. In particular, the pyridines still need to be further investigated, as so far, reliable values of $\Sigma\beta^{\text{H}_2}$ values have been difficult to obtain.

All in all, it is quite practical to obtain β^{H_2} values for multifunctional solutes, and for other solutes for which direct measurements are not possible, by the technique of back-calculation. However, considerable care has to be taken, and results for important compounds must be obtained as the average of several determinations.

In Table 24 is given a comparison of $\Sigma\beta^{\text{H}_2}$ with β^{H_2} , the latter obtained¹⁰² from 1:1 complexation constants for hydrogen bonding. Nearly all the 'activated' aromatics have $\Sigma\beta^{\text{H}_2} > \beta^{\text{H}_2}$, no doubt because in solution the aromatic ring can also function as a basic site, as well as the functional group. Deactivated aromatics, however, such as nitrobenzene and benzonitrile seem to retain the same β^{H_2} in bulk solution. Indeed such compounds are used as 'standard solutes' in setting up the regression equations for the RP-HPLC log k' values.

Table 21. Typical Reversed-phase HPLC Systems Used in the Analysis.

<u>Number</u>	<u>Bonded phase</u>	<u>Mobile phase</u>	<u>Reference</u>
1	Hypersil ODS	75 % methanol	a
2		50 % methanol	
3		55 % methanol	
4	Octadecyl	90 % acetonitrile	c
5		80 % acetonitrile	
6		70 % acetonitrile	
7	Hypersil ODS	60 % acetonitrile	d
8		90 % methanol	
9		75 % methanol	
10		60 % methanol	
11		45 % methanol	
12		30 % methanol	
13	Porous polymer gel	methanol pH 11	e
14		acetonitrile pH 11	
15		methanol pH 2	
16	Phospholipid-coated - silica gel	acetonitrile pH 2	f
17		30 % acetonitrile	
18		20 % acetonitrile	
19	Octadecyl	10 % acetonitrile	g
20		75 % methanol	
21		65 % methanol	
22		60 % methanol	
23		55 % methanol	
24		50 % methanol	
25	Glyceryl-coated - glass beads	40 % methanol	g
26		25 % methanol	
27		20 % methanol	
28		15 % methanol	
29		10 % methanol	
30		5 % methanol	
31	Octadecyl	30 % acetonitrile	h
32		32.5 % tetrahydrofuran	
33		50 % methanol	
34	LiChrosorb Octadecyl	Aqueous methanol	i
35		80 % acetonitrile	
36		70 % acetonitrile	
37		60 % acetonitrile	
38		50 % acetonitrile	
39		Aqueous methanol	
40	Octadecyl	75 % methanol	k
41		50 % acetonitrile	
42		30 % acetonitrile	
43	Octadecyl	70 % methanol	n
44		60 % methanol	
45		50 % methanol	
46		40 % methanol	
47		60 % acetonitrile	
48		50 % acetonitrile	
49		30 % acetonitrile	

^a T. L. Hafkenschied and E. Tomlinson, *Int. J. Pharmaceutics*, 1983, 17, 1. ^b J. E. Haky and A. M. Young, *J. Liq. Chromatogr.*, 1984, 7, 675. ^c T. Hanai and J. Hubert, *J. Chromatogr.*, 1984, 302, 89. ^d T. L. Hafkenschied, *J. Chromatogr. Sci.*, 1986, 24, 307. ^e K. Miyate, F. Kitaura, N. Mizuno, and H. Terada, *Chem. Pharm. Bull.*, 1987, 35, 377. ^f K. Miyate, F. Kitaura, N. Mizuno, and H. Terada, *J. Chromatogr.*, 1988, 389, 47. ^g K. Miyate, N. Mizuno, and H. Terada, *J. Chromatogr.*, 1989, 439, 227. ^h M. C. Spanier and C. L. de Ligny, *Chromatographia*, 1985, 20, 120; *J. Chromatogr.*, 1982, 253, 23. ⁱ N. El Tayar, A. Tsantili-Kakoulidou, T. Roethlisberger, B. Testa, and J. Gal, *J. Chromatogr.*, 1988, 439, 237. ^j Y. Arai, M. Hirukawa, and T. Hanai, *J. Liq. Chromatogr.*, 1987, 10, 635. ^k A. Tsantili-Kakoulidou, N. El Tayar, H. Van de Waterbeemd, and B. Testa, *J. Chromatogr.*, 1987, 389, 33. ^l F. Gago, J. Alvarez-Builla, and J. Elguero, *J. Liq. Chromatogr.*, 1987, 10, 1031. ^m M. Bogusz and R. Aderjan, *J. Chromatogr.*, 1988, 435, 43. ⁿ F. Yugi, Z. Pengling, and H. Zhide, *Chromatographia*, 1988, 25, 382.

Table 22. Summary of Correlations Giving Data in Table 23.

SET											---- CONFIDENCE LEVEL % ----					
	c	d.δ2	s.π*2	a.α2	b.β2	m.Vx	r	n	s.d.	c	d	s	a	b	m	
1	-0.637	0.038	-0.453	-0.367	-1.461	1.384	0.9958	61	0.049	100	94.4	100	100	100	100	
2	-0.378	0.079	-0.572	-0.320	-2.128	2.229	0.9968	61	0.063	100	99.7	100	100	100	100	
3	-0.023	0.332	-0.769	-0.524	-1.993	1.862	0.9933	47	0.071	100	100	100	100	100	100	
4	-0.383	-0.096	-0.311	-0.283	-1.142	0.873	0.9981	81	0.025	100	100	100	100	100	100	
5	-0.248	-0.037	-0.396	-0.309	-1.374	1.025	0.9979	79	0.028	100	99.0	100	100	100	100	
6	-0.086	0.015	-0.471	-0.303	-1.572	1.143	0.9970	76	0.033	99.9	61.9	100	100	100	100	
7	0.082	0.060	-0.509	-0.301	-1.741	1.232	0.9953	68	0.036	98.5	99.7	100	100	100	100	
8	-0.825	-	-0.510	-0.374	-1.221	1.078	0.9967	30	0.038	100	-	100	100	100	100	
9	-0.580	-	-0.520	-0.366	-1.558	1.441	0.9974	30	0.041	100	-	100	100	100	100	
10	-0.368	-	-0.600	-0.370	-1.871	1.888	0.9983	30	0.041	100	-	100	100	100	100	
11	-0.237	-	-0.652	-0.334	-2.270	2.452	0.9985	30	0.047	100	-	100	100	100	100	
12	-0.245	-	-0.739	-0.278	-2.590	3.145	0.9975	30	0.074	99.6	-	100	100	100	100	
13	0.228	-	-0.326	-1.109	-1.441	1.599	0.9853	26	0.088	93.4	-	97.8	100	100	100	
14	0.783	-	-0.526	-1.115	-1.703	1.560	0.9757	26	0.127	100	-	98.8	100	100	100	
15	0.142	-	-0.438	-0.735	-1.645	1.872	0.9649	31	0.137	61.8	-	98.7	100	100	100	
16	0.447	-	-0.436	-0.780	-1.854	1.854	0.9824	31	0.098	99.9	-	99.9	100	100	100	
17	-1.079	-	-0.125	-0.106	-1.847	1.510	0.9875	38	0.048	100	-	99.5	99.9	100	100	
18	-0.897	-	-0.112	0.118	-2.991	2.317	0.9864	45	0.081	100	-	91.7	98.9	100	100	
19	-0.892	-	-0.120	0.162	-3.063	2.567	0.9837	41	0.076	100	-	89.0	99.9	100	100	
20	-0.462	-	-0.046	-0.404	-1.086	0.657	0.9887	19	0.037	100	-	37.4	100	100	100	
21	-0.442	-	-0.124	-0.363	-1.571	1.060	0.9913	19	0.039	100	-	77.5	100	100	100	(a)
22	-0.453	-	-0.009	-0.366	-1.676	1.163	0.9876	19	0.049	100	-	5.6	100	100	100	(a)
23	-0.439	-	-0.166	-0.347	-2.004	1.482	0.9954	19	0.034	100	-	92.8	100	100	100	
24	-0.491	-	0.023	-0.404	-2.158	1.598	0.9935	19	0.044	100	-	15.8	100	100	100	
25	-0.539	-	-0.125	-0.378	-2.357	2.220	0.9924	19	0.057	100	-	60.4	100	100	100	
26	-0.177	-	-0.198	-0.660	-2.031	2.027	0.9920	65	0.051	99.2	-	99.8	100	100	100	
27	0.109	-	0.188	-0.270	-1.976	1.240	0.9700	62	0.085	67.9	-	92.0	100	100	100	
28	-0.309	-	-0.525	-0.453	-2.005	2.181	0.9983	79	0.052	100.0	-	100	100	100	100	
29	-1.721	-	-0.206	-0.205	-3.847	3.507	0.9923	24	0.113	100	-	82.5	80.7	100	100	
30	-0.819	-0.663	0.502	0.034	-2.641	0.998	0.9973	50	0.047	100	100	100	49.1	100	100	(b)
31	-0.595	-0.729	0.536	-0.092	-2.448	1.063	0.9954	48	0.057	100	100	100	85.5	100	100	(b)
32	-0.473	-0.637	0.359	-0.057	-2.543	1.224	0.9973	48	0.046	100	100	100	73.4	100	100	(b)
33	-0.311	-0.647	0.308	-0.082	-2.599	1.407	0.9981	48	0.042	100	100	100	91.9	100	100	(b)
34	0.523	-	-0.635	-0.171	-3.617	3.695	0.9902	57	0.118	99.9	-	100	99.4	100	100	
35	-0.342	-	-0.417	-0.371	-1.085	1.043	0.9913	47	0.042	100	-	100	100	100	100	
36	-0.165	0.179	0.025	0.330	-1.992	1.457	0.9992	14	0.019	92.7	99.9	14.7	97.1	100	100	
37	-0.527	0.325	0.533	0.102	-3.695	2.541	0.9989	13	0.034	97.7	99.9	91.0	31.7	100	100	
38	-0.287	-	-0.602	-0.502	-1.655	1.737	0.9963	23	0.040	99.9	-	100	100	100	100	
39	-0.131	-	-0.668	-0.551	-1.890	2.063	0.9972	23	0.039	90.9	-	100	100	100	100	
40	0.052	-	-0.715	-0.587	-2.164	2.373	0.9970	23	0.045	45.5	-	100	100	100	100	
41	0.191	-	-0.682	-0.605	-2.323	2.586	0.9961	22	0.052	93.0	-	100	100	100	100	
42	0.111	-	-0.361	-0.553	-1.316	1.135	0.9962	23	0.033	90.4	-	100	100	100	100	
43	0.125	-	-0.385	-0.628	-1.633	1.485	0.9960	23	0.041	87.5	-	100	100	100	100	
44	0.139	-	-0.387	-0.716	-2.011	1.890	0.9936	23	0.062	75.1	-	100	100	100	100	
45	1.320	-	-1.291	-0.256	-2.841	1.015	0.9811	30	0.032	100	-	100	96.3	100	100	
46	1.485	-	-1.403	-0.268	-2.980	1.145	0.9732	30	0.042	100	-	100	91.1	100	100	
47	1.614	-	-1.560	-0.174	-3.213	1.339	0.9844	30	0.036	100	-	100	81.6	100	100	
48	1.711	-	-1.711	-0.056	-3.430	1.565	0.9857	30	0.037	100	-	100	32.0	100	100	
49	1.655	-	-1.747	0.104	-3.478	1.803	0.9881	30	0.038	100	-	100	56.4	100	100	

(a) Omit 3-nitro- and 4-nitroaniline

(b) Omit phenol

Table 23. Some Backcalculated ΣBH_2 Values From HPLC Data (Table 21).

<u>General compounds</u>	<u>Average</u>	<u>SD</u>	<u>No</u>	<u>Taken</u>
benzyl bromide	0.250	0.074	10	0.25
diphenylether	0.231	0.058	5	0.24
3-methylanisole	0.352	0.009	2	0.35
1,2-dimethoxybenzene	0.648	0.013	2	0.65
1,4-dimethoxybenzene	0.578	0.014	8	0.58
phthalaldehyde	0.653	0.098	2	0.65
4-methoxybenzaldehyde	0.614	0.018	8	0.61
benzophenone	0.538	0.033	16	0.54
bromomethylphenylketone	0.552	0.018	2	0.55
methyl benzoate	0.475	0.038	28	0.47
ethyl benzoate	0.461	0.026	13	0.47
propyl benzoate	0.477	0.026	2	0.47
phenyl benzoate	0.455	0.013	3	0.47
dimethylphthalate	0.986	0.013	2	1.05
diethylphthalate	1.068	0.038	8	1.05
1-nitropropane	0.250	0.005	12	0.25
4-bromomethylnitrobenzene	0.406	0.085	9	0.41
1,3-dinitrobenzene	0.539	0.028	2	0.54
1,4-dinitrobenzene	0.548	0.013	7	0.55
1-MeO-4-nitrobenzene	0.416	0.044	3	0.42
2,4-dinitrotoluene	0.549	0.021	7	0.55
phenylacetonitrile	0.442	0.024	9	0.44
<u>Anilines</u>	<u>Average</u>	<u>SD</u>	<u>No</u>	<u>Taken</u>
aniline	0.544	0.021	17	0.53
diphenylamine	0.351	0.030	2	0.35
2-methylaniline	0.566	0.008	2	0.57
3-methylaniline	0.558	0.019	3	0.55
4-methylaniline	0.565	0.013	12	0.57
N-methylaniline	0.467	0.015	4	0.47
N,N-dimethylaniline	0.380	0.031	2	0.38
3-cyanoaniline	0.668	0.056	2	0.67
4-cyanoaniline	0.703	0.060	2	0.70
3-fluoroaniline	0.462	0.054	2	0.40
4-fluoroaniline	0.532	0.023	2	0.51
2-chloroaniline	0.438	0.004	2	0.44
3-chloroaniline	0.401	0.036	4	0.40
4-chloroaniline	0.462	0.032	11	0.45
3-bromoaniline	0.394	0.047	2	0.39
4-bromoaniline	0.419	0.036	2	0.44
3-iodoaniline	0.391	0.040	2	0.39
4-iodoaniline	0.402	0.033	2	0.42
3-methoxyaniline	0.760	0.010	4	0.76
4-methoxyaniline	0.831	0.002	3	0.83
methyl 4-aminobenzoate	0.775	0.040	6	0.78
3-nitroaniline	0.550	0.049	2	0.55
4-nitroaniline	0.599	0.035	11	0.60
3-aminoacetophenone	0.920	0.031	2	0.92
4-aminoacetophenone	0.946	0.068	3	0.95
acetanilide	0.689	0.012	3	0.69
benzamide	0.681	0.025	4	0.68
<u>Pyridines, etc.</u>	<u>Average</u>	<u>SD</u>	<u>No</u>	<u>Taken</u>
pyridine	0.63	0.01	4	0.62
3-methylpyridine	0.63	0.01	2	0.62
4-methylpyridine	0.63	0.01	2	0.65
2-chloropyridine	0.49	0.07	3	0.49
3-chloropyridine	0.49	0.01	4	0.49
4-chloropyridine	0.52	0.01	2	0.53
3-bromopyridine	0.50	0.01	4	0.50
4-bromopyridine	0.53	0.01	2	0.53
3-acetylpyridine	0.94	0.01	2	0.94
4-acetylpyridine	0.95	0.01	2	0.95
3-cyanopyridine	0.79	0.01	2	0.79
4-cyanopyridine	0.82	0.01	2	0.82
2-aminopyridine	0.61	0.02	3	0.61
3-aminopyridine	0.78	0.02	3	0.78
quinoline	0.63	0.01	2	0.63
isoquinoline	0.60	0.01	2	0.60
acridine	0.52	0.02	2	0.52

Table 23 (cont). Some Backcalculated ΣBH_2 Values From HPLC Data.

<u>Carboxylic acids</u>	<u>Average</u>	<u>SD</u>	<u>No</u>	<u>Taken</u>
2-methylpropanoic acid	0.420	0.003	2	0.42
3-methylbutanoic acid	0.423	0.003	2	0.41
hexanoic acid	0.383	0.001	2	0.39
octanoic acid	0.357	0.009	2	0.36
decanoic acid	0.332	0.011	2	0.33
benzoic acid	0.424	0.023	24	0.42
3-fluorobenzoic acid	0.363	0.012	2	0.36
2-chlorobenzoic acid	0.387	0.010	9	0.39
3-chlorobenzoic acid	0.305	0.019	8	0.29
4-chlorobenzoic acid	0.309	0.018	24	0.31
2,4-dichlorobenzoic acid	0.206	0.005	5	0.21
2,5-dichlorobenzoic acid	0.229	0.017	5	0.23
2,6-dichlorobenzoic acid	0.340	0.020	5	0.34
3,4-dichlorobenzoic acid	0.103	0.003	5	0.10
3,5-dichlorobenzoic acid	0.102	0.006	5	0.10
2-bromobenzoic acid	0.362	0.008	4	0.36
3-bromobenzoic acid	0.274	0.014	7	0.29
4-bromobenzoic acid	0.294	0.013	16	0.31
4-fluorobenzoic acid	0.380	0.002	2	0.38
3-iodobenzoic acid	0.292	0.011	8	0.29
4-iodobenzoic acid	0.303	0.037	5	0.30
2-methylbenzoic acid	0.448	0.002	4	0.45
3-methylbenzoic acid	0.436	0.012	7	0.43
4-methylbenzoic acid	0.427	0.020	23	0.43
2,4-dimethylbenzoic acid	0.457	0.004	4	0.46
2,5-dimethylbenzoic acid	0.462	0.002	4	0.46
2,6-dimethylbenzoic acid	0.582	0.014	5	0.58
3,4-dimethylbenzoic acid	0.458	0.019	8	0.46
3,5-dimethylbenzoic acid	0.452	0.003	4	0.45
2,4,6-trimethylbenzoic acid	0.588	0.010	5	0.59
4-ethylbenzoic acid	0.447	0.016	8	0.45
4-isopropylbenzoic acid	0.408	0.007	3	0.41
4-t-butylbenzoic acid	0.411	0.146	2	0.41
4-phenylbenzoic acid	0.429	0.002	2	0.43
3-nitrobenzoic acid	0.609	0.004	2	0.61
4-nitrobenzoic acid	0.544	0.028	11	0.54
3-cyanobenzoic acid	0.636	0.035	2	0.64
4-cyanobenzoic acid	0.640	0.001	2	0.64
phenylacetic acid	0.552	0.005	5	0.55
2-methylphenylacetic acid	0.565	0.008	5	0.56
3-methylphenylacetic acid	0.552	0.012	5	0.55
2-chlorophenylacetic acid	0.473	0.004	5	0.47
4-chlorophenylacetic acid	0.424	0.005	5	0.42
3-phenylpropionic acid	0.549	0.005	5	0.55
4-phenylbutyric acid	0.556	0.005	5	0.56
t-cinnamic acid	0.459	0.004	5	0.46
t-4-methylcinnamic acid	0.447	0.004	5	0.45
<u>Phenols</u>	<u>Average</u>	<u>SD</u>	<u>No</u>	<u>Taken</u>
phenol	0.363	0.020	31	0.36
2-methylphenol	0.371	0.022	9	0.37
3-methylphenol	0.388	0.010	3	0.39
4-methylphenol	0.383	0.016	25	0.40
2,3-dimethylphenol	0.384	0.012	7	0.38
2,4-dimethylphenol	0.390	0.007	8	0.39
2,5-dimethylphenol	0.387	0.004	9	0.39
2,6-dimethylphenol	0.387	0.004	8	0.39
3,4-dimethylphenol	0.434	0.017	11	0.43
3,5-dimethylphenol	0.426	0.019	8	0.43
2,3,5-trimethylphenol	0.415	0.019	8	0.41
2,3,6-trimethylphenol	0.410	0.026	8	0.41
2,4,6-trimethylphenol	0.406	0.017	8	0.41
2-ethylphenol	0.396	0.014	8	0.40
3-ethylphenol	0.409	0.015	9	0.39
4-ethylphenol	0.414	0.017	11	0.40
2,3,5,6-tetramethylphenol	0.457	0.017	9	0.46
4-t-butylphenol	0.408	0.008	3	0.41
2,6-di-t-butylphenol	0.595	0.015	2	0.60
3-fluorophenol	0.246	0.024	2	0.24
4-fluorophenol	0.322	0.013	2	0.32
2-chlorophenol	0.291	0.025	12	0.29

Table 23 (cont). Some Backcalculated $\Sigma\beta H_2$ Values From HPLC Data.

<u>Phenols (cont).</u>	<u>Average</u>	<u>SD</u>	<u>No</u>	<u>Taken</u>
3-iodophenol	0.210	0.014	2	0.23
3-chlorophenol	0.229	0.025	14	0.23
4-iodophenol	0.226	0.009	5	0.24
2,3-dichlorophenol	0.228	0.025	8	0.23
4-chlorophenol	0.261	0.025	26	0.25
3-bromophenol	0.234	0.015	9	0.23
4-bromophenol	0.244	0.027	19	0.25
2,6-dichlorophenol	0.281	0.017	11	0.28
2,5-dichlorophenol	0.205	0.002	8	0.21
3,4-dichlorophenol	0.188	0.018	8	0.19
3,5-dichlorophenol	0.128	0.011	8	0.13
2,4-dichlorophenol	0.195	0.013	8	0.20
2,4,5-trichlorophenol	0.138	0.007	8	0.14
3,4,5-trichlorophenol	0.113	0.010	8	0.11
2,3,4-trichlorophenol	0.171	0.011	8	0.17
2,3,5-trichlorophenol	0.167	0.043	8	0.17
2,3,6-trichlorophenol	0.239	0.011	8	0.24
2,4,6-trichlorophenol	0.192	0.013	7	0.19
2,3,4,5-tetrachlorophenol	0.106	0.028	8	0.11
2,3,5,6-tetrachlorophenol	0.188	0.030	8	0.19
pentachlorophenol	0.145	0.030	10	0.15
2-chloro-5-methylphenol	0.308	0.004	4	0.31
4-chloro-2-methylphenol	0.298	0.003	4	0.30
4-chloro-3-methylphenol	0.327	0.013	7	0.33
2,4-dibromophenol	0.189	0.006	8	0.19
2,6-dibromophenol	0.276	0.008	4	0.28
3-methoxyphenol	0.560	0.029	3	0.56
4-methoxyphenol	0.626	0.029	4	0.63
4-hydroxybenzaldehyde	0.538	0.013	7	0.54
3-acetylphenol	0.667	0.017	2	0.67
4-acetylphenol	0.708	0.023	2	0.71
3-CO ₂ Me-phenol	0.630	0.005	2	0.63
4-CO ₂ Me-phenol	0.631	0.012	9	0.63
2-nitrophenol	0.269	0.016	7	0.27
3-nitrophenol	0.310	0.028	6	0.31
4-nitrophenol	0.330	0.006	22	0.33
2,4-dinitrophenol	0.341	0.023	3	0.34
2-methyl-4,6-dinitrophenol	0.331	0.004	3	0.33
3-cyanophenol	0.400	0.029	2	0.40
4-cyanophenol	0.422	0.043	8	0.42
<u>Benzyl alcohols</u>	<u>Average</u>	<u>SD</u>	<u>No</u>	<u>Taken</u>
benzyl alcohol	0.498	0.044	15	0.50
2-chlorobenzyl alcohol	0.456	0.007	3	0.46
2,6-dichlorobenzyl alcohol	0.480	0.023	3	0.48
2-phenyl ethanol	0.534	0.043	2	0.53
4-phenylbenzyl alcohol	0.541	0.036	3	0.54
4-methylbenzyl alcohol	0.551	0.018	5	0.55
3,4-dimethylbenzyl alcohol	0.567	0.018	3	0.57
4-chlorobenzyl alcohol	0.453	0.007	5	0.45
3,5-dichlorobenzyl alcohol	0.341	0.008	6	0.34
3-iodobenzyl alcohol	0.427	0.025	6	0.42
4-methoxybenzyl alcohol	0.722	0.032	7	0.72
<u>Sulphur compounds</u>	<u>Average</u>	<u>SD</u>	<u>No</u>	<u>Taken</u>
PhSO ₂ Me	0.786	0.002	2	0.79
PhSO ₂ Et	0.855	0.012	2	0.85
PhSO ₂ NH ₂	0.739	0.011	2	0.74
PhSO ₂ NHMe	0.767	0.006	2	0.77

Table 24. Comparison of $\Sigma\beta^{\text{H}_2}$ Back-Calculated from RP-HPLC Data²⁰¹, and β^{H_2} ¹⁰² Values

Compound Name	$\Sigma\beta^{\text{H}_2}$	β^{H_2}
Acetic Acid	0.41	-
Butanoic Acid	0.43	-
4-Methoxybenzaldehyde	0.61	0.47
1,4-Benzoquinone	0.59	0.34
Phenyl benzoate	0.47	0.39
Aniline	0.53	0.38
2-Methylaniline	0.57	0.38
3-Methylaniline	0.55	0.40
4-Methylaniline	0.57	0.42
4-Ethylaniline	0.57	0.42
4-Fluoroaniline	0.51	0.36
2-Chloroaniline	0.44	0.33
3-Chloroaniline	0.40	0.29
4-Chloroaniline	0.45	0.34
3-Bromoaniline	0.39	0.27
4-Iodoaniline	0.42	0.31
3-Methoxyaniline	0.76	0.40
4-Methoxyaniline	0.83	0.45
N,N-Dimethylaniline	0.38	0.35
4-Fluorophenol	0.32	0.21
2-Phenylethanol	0.53	0.45
Methylphenylsulphoxide	0.79	0.70
3-Cyanopyridine	0.79	0.44
4-Cyanopyridine	0.82	0.47

6.14 Parameter Back-Calculation from GLC Data

Having examined the extensive GLC data of McReynolds¹³³, and Laffort⁸², (see sections 6.11 and 6.12), this data, along with other extensive chromatographic data, could then be used to back-calculate a large number of solvation parameters for a huge set of solutes. Recommended values for solvation parameters will be presented in a summary table later, (see Table 28). Additionally, the opportunity arises to set up a coherent scale for the π^*_2 parameter, which had hitherto been a problem. Values of R_2 , α^H_2 , β^H_2 , and $\log L$ ¹⁶ can be obtained through various approximations and estimations, all based on the original experimentally determined values. There are, however, difficulties over the solute parameter π^*_2 . Originally^{115,202} π^*_2 was taken as identical to the Kamlet-Taft solvatochromic solvent parameter π^*_1 for non-associated liquids only. Since π^*_1 is experimentally accessible only for compounds that are liquid at 298K, values of π^*_2 had then to be estimated, not only for all associated compounds (including acids, alcohols, phenols, amides, *etc.*) but also for all compounds that are solid (or gaseous) at 298K. In addition, there is present the inherent assumption that π^*_1 is identical to π^*_2 for non-associated liquids. The Kamlet-Taft solvatochromic solvent basicity parameter β_1 is not exactly equivalent to the solute parameter β^H_2 even for non-associated liquids²⁰³, and it is possible that whilst π^*_2 can be taken as equal to π^*_1 for non-associated liquids as a generality, there may be a number of exceptions to this rule.

It seems necessary to set up a scale of solute dipolarity/polarisability based on some experimental procedure that will include, at least in principle, all types of solute molecule. The data of McReynolds¹³³ and of Laffort⁸² can be used to construct a new solute dipolarity/polarisability scale π^H_2 for use in our solvation equations. Since this work was started, Carr et al.²⁰⁴ have also concluded that

the π^*_2 scale derived from π^*_1 is not very suitable for use in solvation equations, and have constructed an alternative π^{C_2} scale of solute dipolarity. This scale will be discussed later.

McReynolds¹³³ determined V_G^0 values for up to 376 solutes on up to 77 stationary phases. Nearly all the phases were examined at a common temperature of 120°C. Of these 77 phases, 75 were found (see section 6.12) to have no hydrogen bond acidity at all, hence the $b.\beta^{H_2}$ term in general solvation equation 63 drops out, and the $\log V_G^0$ values can be correlated by equation 67.

$$\log V_G^0 = c + r.R_2 + s.\pi^*_2 + a.\alpha^{H_2} + l.\log L^{16} \quad [67]$$

It is possible to set up a series of equations ($n = 1$ to $n = 75$), one for each stationary phase, where the constants c , r , s , a , and l have been determined by MLRA, using known values of the solute parameters R_2 , π^*_2 , α^{H_2} , and $\log L^{16}$ for as many solutes as possible. Typically, around 150 solutes were included in each regression equation 67, generalised as equation 68.

$$\log V_{G(n)}^0 = c_n + r_n.R_2 + s_n.\pi^*_2 + a_n.\alpha^{H_2} + l_n.\log L^{16} \quad [68]$$

It is convenient to subsume the constant c_n into the dependent variable to give 75 equations,

$$\begin{aligned} V_{n=1} &= r_{n=1}.R_2 + s_{n=1}.\pi^*_2 + a_{n=1}.\alpha^{H_2} + l_{n=1}.\log L^{16} \\ &\vdots \\ V_{n=75} &= r_{n=75}.R_2 + s_{n=75}.\pi^*_2 + a_{n=75}.\alpha^{H_2} + l_{n=75}.\log L^{16} \end{aligned} \quad [69]$$

$$\text{where } V_n = \log V_{G(n)}^0 - c_n \quad [70]$$

The matrix defined by equation 69 can be used in a vertical format, by regarding V_n for a given solute as the dependent variable, and the constants r_n , s_n , a_n and l_n

as four explanatory variables. In this new (vertical) MLR equation, R_2 , π_2^* , α^H_2 , and $\log L^{16}$ for the particular solute now become the unknown coefficients to be evaluated by MLRA. Since all the input data is now related purely to properties of the solute, π_2^* can be replaced by an experimentally determined parameter, π^H_2 :

$$V(\text{solute}) = V_n = R_2 \cdot r_n + \pi^H_2 \cdot s_n + \alpha^H_2 \cdot a_n + \log L^{16} \cdot l_n \quad [71]$$

A thorough analysis was carried out using equation 71, where the regression equation was forced through the origin, (purely because the constant should be equal to zero), and obtained reasonable values of R_2 , π^H_2 , α^H_2 , and $\log L^{16}$ for the various solutes studied. However, since R_2 is either known or can very easily be calculated for any solute, the number of explanatory variables can be reduced by incorporating R_2 into the dependent variable,

$$[\log V_{G(n)}^0 - c_n - r_n \cdot R_2] = V' = \pi^H_2 \cdot s_n + \alpha^H_2 \cdot a_n + \log L^{16} \cdot l_n \quad [72]$$

Again, the regression equation 72 is constrained to pass through the origin: results were found to be much more self-consistent than when a constant term was allowed to float. Results obtained using the preferred equation 72 can be checked by comparison of calculated solute parameters with known values, where available. Some typical results are given in Table 25 together with the standard deviation (S.D.) of the parameter, the number of stationary phases in the set (always less than 75, because not all solutes were examined on all phases by McReynolds), and the overall S.D. in the dependent variable V' . Correlation coefficients are not listed, because these have little meaning for a regression equation forced through the origin.

Table 25. Some Calculated Parameters Using equation 72.

Solute	π^{H_2}	α^{H_2}	$\log L^{16}$	n	S.D.
Pent-1-ene	0.09 ± 0.004 *0.08	0.00 ± 0.007 0.00	2.040 ± 0.007 2.013	36	0.014
Toluene	0.47 ± 0.004 *0.55	-0.01 ± 0.007 0.00	3.327 ± 0.008 3.344	73	0.017
Diethyl ether	0.27 ± 0.004 *0.27	-0.02 ± 0.007 0.00	1.975 ± 0.008 2.061	71	0.017
Butanone	0.69 ± 0.004 *0.67	0.00 ± 0.007 0.00	2.282 ± 0.007 2.287	71	0.016
n-Propyl acetate	0.61 ± 0.004 *0.55	0.00 ± 0.007 0.00	2.847 ± 0.007 2.878	73	0.016
Propan-1-ol	0.41 ± 0.009 *0.40	0.37 ± 0.006 0.33	2.060 ± 0.006 2.097	72	0.016

* Previous values, see ref. 181.

There are a number of deficiencies in McReynolds' experimentation (see section 6.12), and it is quite possible that for certain combinations of solute and stationary phase, the retention data are inexact due to sorption at the liquid interface. Note though, that the vertical or "inverse" MLRA procedure yields solvation parameters that are effectively averages for a given solute over some 30-70 stationary phases, see Table 25. In the event, hydrocarbons such as alkanes and alkenes behave quite normally in the inverse MLRA, see Table 26.

Listed in Table 26 are the π^{H_2} values obtained through equation 72. The π^{H_2} values in Table 26 are effective or 'summation' π^{H_2} values for a situation in which a solute molecule is surrounded by an excess of solvent molecules, and so in a similar manner to $\Sigma\beta^{\text{H}_2}$, may be more correctly denoted as $\Sigma\pi^{\text{H}_2}$. Before discussing these $\Sigma\pi^{\text{H}_2}$ values from the McReynolds' data¹³³, the extensive GLC data of Laffort⁸² can also be analysed, and many parameters back-calculated. The methodology of this follows after listing the $\Sigma\pi^{\text{H}_2}$ values in Table 26.

TABLE 26. CALCULATED VALUES OF π_2^H

		π_2^H		
	Equation :	72	81	73
<u>Alkanes</u>				
Ethane			0.03	0.11
Propane			0.03	0.08
Butane			0.03	0.05
2-Methylpropane			0.07	0.07
Pentane			0.03	0.03
Hexane		0.02	0.03	0.02
2,3-Dimethylbutane		-0.01		
Heptane			0.03	0.01
2,4-Dimethylpentane			-0.04	-0.02
Octane		0.01	0.03	0.00
2-Methylheptane			0.08	0.01
3-Methylheptane			0.07	0.03
Nonane			0.03	0.00
2,2,5-Trimethylhexane			0.16	
Decane		0.03	0.03	-0.01
Undecane			0.03	-0.02
Dodecane		0.03	0.03	0.03
Tridecane			0.03	-0.04
Tetradecane		0.05	0.03	-0.03
Hexadecane		0.07		
Octadecane		0.05		
Cyclohexane			0.08	0.14
Hydrindane			0.19	0.22
Decalin			0.23	0.27
<u>Alkenes</u>				
Ethene			-0.13	0.32
Propene			-0.09	0.25
But-1-ene			-0.05	0.21
Pent-1-ene		0.09	-0.05	0.19
Hex-1-ene			0.00	0.11
Hept-1-ene			0.06	0.11
Oct-1-ene			0.08	0.09
cis-Oct-2-ene			0.11	0.12
2-Ethylhex-1-ene			0.16	0.13
α -Pinene			0.30	0.18
<u>Alkynes</u>				
But-2-yne			0.17	0.37
Oct-1-yne			0.19	0.23
Oct-2-yne			0.16	0.31
<u>Haloaliphatics</u>				
1-Fluoro-octane			0.30	
Dichloromethane		0.66		
Trichloromethane		0.65	0.25	0.36
Tetrachloromethane		0.35	0.28	0.35
1,2-Dichloroethane		0.74	0.35	0.55
1,1,2,2-Tetrachloroethane			0.32	0.65
1-Chlorohexane			0.27	0.36
Trichloroethene			0.34	0.33
Hexachlorobutadiene			0.62	
Bromoethane			0.30	0.42
1-Bromopentane			0.30	0.39
2-Bromo-octane			0.33	0.28
Iodomethane			0.35	0.44
1-Iodobutane			0.38	0.39
2-Iodobutane			0.40	0.39
1,1-Difluorotetrachloroethane			0.41	
1,2-Difluorotetrachloroethane			0.41	0.33
<u>Aromatic hydrocarbons</u>				
Benzene		0.48	0.53	0.47
Toluene		0.47	0.57	0.46
Ethylbenzene		0.47	0.56	0.46
o-Xylene		0.50	0.63	0.43
m-Xylene		0.47	0.60	0.46
p-Xylene		0.46	0.61	0.46
1,3,5-Trimethylbenzene			0.64	0.46
1,2-Diethylbenzene		0.50		
1,3-Diethylbenzene		0.48		
1,4-Diethylbenzene		0.47		

TABLE 26. CALCULATED VALUES OF π_2^H

Equation :	π_2^H		
	72	81	73
<u>Aromatic hydrocarbons (continued)</u>			
Styrene		0.70	0.55
Phenylethyne		0.55	0.68
<u>Haloaromatics</u>			
1,2-Dichlorobenzene		0.65	0.70
Benzyl chloride		0.69	0.78
<u>Ethers</u>			
Dimethyl ether	0.36		
Diethyl ether	0.27	0.19	0.27
Dipropyl ether	0.23		
Di-isopropyl ether	0.16		
Dibutyl ether	0.24	0.16	0.18
Dipentyl ether	0.27		
Di-isopentyl ether	0.21		
Di-hexyl ether	0.27		
Di-2-ethyl-1-butyl ether	0.17		
Methyl propyl ether	0.30		
Methyl butyl ether	0.30		
Methyl isobutyl ether	0.25		
Methyl t-butyl ether	0.29		
Ethyl butyl ether	0.26		
Ethyl t-butyl ether	0.20		
Propyl isopropyl ether	0.19		
Isopropyl t-butyl ether	0.16		
Bis(2-ethoxyethyl)ether	0.79		
Ethyl vinyl ether	0.37		
Butyl vinyl ether	0.34		
Isobutyl vinyl ether	0.29		
2-Ethyl-1-hexyl vinyl ether	0.32		
2-Methoxyethyl vinyl ether	0.68		
Diallyl ether	0.38		
Ethylene oxide	0.59		
1,2-Propylene oxide	0.57		
1,2-Butylene oxide	0.55		
2-Methyl-1,2-Propylene oxide	0.52		
trans-2,3-Butylene oxide	0.52		
cis-2,3-Butylene oxide	0.55		
1,3-Propylene oxide	0.61		
1,3-Butylene oxide	0.52		
Furan	0.54	0.39	0.51
2-Methylfuran	0.50		
2-Acetyl-3-methylfuran		1.17	
2-Acetyl-5-methylfuran		1.19	
2-Propanoyl-3-methylfuran		0.91	
Tetrahydrofuran	0.55		
2-Methyltetrahydrofuran	0.47		
2,5-Dimethyltetrahydrofuran	0.38		
Dioxan	0.75	0.69	0.74
Tetrahydropyran	0.49		
3,4-Dihydropyran	0.51		
Trioxane	1.02		
Trimethyltrioxane (paraldehyde)	0.68		
2-Methyl-2-ethyl-1,3-dioxolane	0.58		
Anethole		1.02	
Dimethoxymethane	0.52		
Methoxyethoxymethane	0.49		
Methoxyisopropoxymethane	0.45		
Diethoxymethane	0.45		
Ethoxypropoxymethane	0.44		
Ethoxyisopropoxymethane	0.41		
Ethoxy-s-butyloxymethane	0.41		
Dipropyloxymethane	0.42		
Propoxy-s-butyloxymethane	0.40		
Di-isopropoxymethane	0.37		
Dibutyloxymethane	0.43		
Di-isobutyloxymethane	0.37		
Di-s-butyloxymethane	0.37		
1,1-Dimethoxyethane	0.49		
1,1-Diethoxyethane	0.41		
1,1-Dipropoxyethane	0.37		
1,1-Di-isobutyloxyethane	0.26		

TABLE 26. CALCULATED VALUES OF π_2^H

Equation :	π_2^H		
	72	81	73
<u>Ethers (continued)</u>			
1,1-Dimethoxypropane	0.46		
1,1-Diethoxypropane	0.38		
1,1-Dimethoxybutane	0.47		
1,1-Dimethoxy-2-methylpropane	0.42		
2,2-Dimethoxypropane	0.43		
2,2-Diethoxypropane	0.32		
1,1,3-Trimethoxybutane	0.69		
Methylphenylether		0.73	0.70
1,8-Cineole		0.47	
<u>Aldehydes</u>			
Formaldehyde	0.73		
Acetaldehyde	0.70	0.63	0.65
Propanal	0.65	0.59	0.62
Butanal	0.63	0.61	0.61
2-Methylpropanal	0.58	0.59	0.59
Pentanal	0.63		
2-Methylbutanal	0.58		
3-Methylbutanal	0.60	0.62	0.58
2,2-Dimethylpropanal	0.49		
Hexanal	0.64	0.59	0.59
Heptanal	0.65	0.58	0.59
Octanal		0.57	0.57
2-Ethylhexanal	0.56		
Prop-2-ene-1-al (acrolein)	0.74	0.68	0.58
trans-But-2-ene-1-al	0.81	0.85	0.75
2-Methylprop-2-ene-1-al (methacrolein)	0.62		
trans-Hex-2-ene-1-al		0.88	0.85
2-Ethylbut-2-ene-1-al	0.68		
trans-Hept-2-ene-1-al		0.85	0.84
trans-Oct-2-ene-1-al		0.55	
2-Ethylhex-2-ene-1-al	0.62		
Hexa-2,4-dienal	0.90		
Furfural		0.97	1.05
Benzaldehyde		0.99	0.94
3-Methoxybutanal	0.85		
<u>Ketones</u>			
Propanone	0.73	0.77	0.66
Butanone	0.69	0.72	0.66
Pentan-2-one	0.66	0.70	0.66
Pentan-3-one	0.64		
3-Methylbutan-2-one	0.63		
Hexan-2-one	0.67	0.71	0.65
Hexan-3-one	0.62	0.65	0.58
3-Methylpentan-2-one	0.62		
4-Methylpentan-2-one	0.62		
3,3-Dimethylbutan-2-one	0.58		
Heptan-2-one	0.67	0.69	0.64
Heptan-3-one	0.62		
Heptan-4-one	0.61		
4,4-Dimethylpentan-2-one	0.57		
2,4-Dimethylpentan-3-one	0.52		
Octan-2-one	0.68	0.68	0.65
Nonan-2-one	0.68	0.69	0.64
Nonan-5-one	0.61		
Decan-2-one		0.67	0.65
Undecan-2-one		0.67	0.64
Dodecan-2-one		0.67	0.64
Cyclopentanone	0.84	0.83	0.86
Cyclohexanone	0.84	0.87	0.87
Cycloheptanone		0.84	0.86
Cyclo-octanone		0.83	0.85
Cyclononanone		0.83	0.84
Cyclodecanone		0.83	0.84
Cycloundecanone		0.83	0.83
Cyclododecanone		0.83	0.83
Cyclotridecanone		0.82	0.82
Cyclotetradecanone		0.82	0.82
Carvone		0.86	0.98
But-3-ene-2-one	0.76		
3-Methylbut-3-ene-2-one	0.68		

TABLE 26. CALCULATED VALUES OF π_2^H

Equation :	π_2^H		
	72	81	73
<u>Ketones (continued)</u>			
Hex-5-ene-2-one	0.75		
4-Methylpent-3-ene-2-one	0.70		
Butan-2,3-dione	0.52	0.71	0.74
Pentan-2,3-dione	0.47		
Pentan-2,4-dione	0.56		
Acetophenone		1.09	0.99
<u>Esters</u>			
Methyl formate	0.72		
Ethyl formate	0.67		
Propyl formate	0.65	0.56	0.60
Isopropyl formate	0.62		
Butyl formate	0.66		
Isobutyl formate	0.62		
sec-Butyl formate	0.61		
Pentyl formate	0.66		
2-Pentyl formate	0.60		
3-Pentyl formate	0.60		
Hexyl formate	0.67		
Methyl acetate	0.67	0.63	0.61
Ethyl acetate	0.62	0.60	0.59
Propyl acetate	0.61	0.60	0.57
Isopropyl acetate	0.57		
Butyl acetate	0.61	0.59	0.58
Isobutyl acetate	0.58		
sec-Butyl acetate	0.56		
tert-Butyl acetate	0.50		
Pentyl acetate	0.62	0.58	0.59
Isopentyl acetate	0.60	0.59	0.53
2-Pentyl acetate	0.56		
3-Pentyl acetate	0.56		
2-Methyl-2-butyl acetate	0.51		
Hexyl acetate	0.63		
4-Methyl-2-pentyl acetate	0.55		
2-Ethyl-1-butyl acetate	0.60		
Heptyl acetate	0.63		
2-Ethyl-1-hexyl acetate	0.60		
Cyclohexyl acetate	0.69		
Methyl propanoate	0.62	0.56	0.58
Ethyl propanoate	0.58		
Propyl propanoate	0.57		
Isopropyl propanoate	0.52		
Butyl propanoate	0.57		
Isobutyl propanoate	0.54		
Pentyl propanoate	0.58		
Isopentyl propanoate	0.56		
2-Pentyl propanoate	0.52		
2-Ethyl-1-hexylpropanoate	0.55		
Methyl butanoate	0.61		
Ethyl butanoate	0.56		
Propyl butanoate	0.56	0.54	0.51
Isopropyl butanoate	0.51		
Butyl butanoate	0.56		
Isobutyl butanoate	0.54		
Pentyl butanoate	0.57		
Isopentyl butanoate	0.55		
2-Pentyl butanoate	0.51		
2-Ethyl-1-hexyl butanoate	0.57		
Methyl isobutanoate	0.56		
Butyl isobutanoate	0.51		
Isobutyl isobutanoate	0.49	0.56	0.46
Isopentyl isopentanoate		0.55	0.55
Allyl formate	0.76		
Allyl acetate	0.72		
Allyl propanoate	0.67		
Vinyl acetate	0.66		
Vinyl butanoate	0.56		
1-Propenyl acetate	0.67		
Isopropenyl acetate	0.68		
Methyl acrylate	0.68		
Ethyl acrylate	0.64		
2-Ethyl-1-hexyl acrylate	0.61		

TABLE 26. CALCULATED VALUES OF π_2^H

Equation :	π_2^H		
	72	81	73
<u>Esters (continued)</u>			
Propyl acrylate	0.62		
Butyl acrylate	0.62		
Methyl methacrylate	0.62		
Allyl acrylate	0.72		
2-Methoxyethyl acetate	0.93		
2-Ethoxyethyl acetate	0.87	0.68	0.79
3-Methoxy-1-butyl acetate	0.83		
3-Methoxy-1-butyl acrylate	0.83		
Methylene diacetate	1.16		
Ethylene diacetate	1.20		
Ethylene dipropionate	1.05		
Propylene diacrylate	1.10		
Benzyl acetate		1.19	0.95
Methyl benzoate		0.77	1.11
Methyl salicylate		0.82	
<u>Nitrocompounds</u>			
Nitromethane		0.73	0.86
Nitroethane		0.74	0.87
1-Nitropropane		0.71	0.86
2-Methyl-2-nitropropane		0.82	0.82
3-Nitrotoluene		1.08	1.05
<u>Nitriles</u>			
Acetonitrile		0.80	0.85
1-Cyanopropane		0.78	0.84
1-Cyanobutane		0.80	0.83
Benzonitrile		1.05	1.04
<u>Amines</u>			
n-Butylamine		0.21	0.47
Allylamine		0.29	
Trimethylamine		0.47	
<u>Heterocyclics</u>			
Pyridine		0.80	0.80
2,3,6-Trimethylpyridine		0.71	
Pyrrole		0.61	0.65
Trimethylpyrazine		0.77	
2-Methyl-3-ethylpyrazine		0.73	
2-Methoxy-3-isobutylpyrazine		0.56	
2,4,5-Trimethyloxazole		0.68	
<u>Carboxylic acids</u>			
Acetic acid		0.68	
Propanoic acid		0.60	
Butanoic acid		0.56	
2-Methylpropanoic acid		0.58	
Pentanoic acid		0.58	
2-Methylbutanoic acid		0.55	
3-Methylbutanoic acid		0.56	
Hexanoic acid		0.62	
2-Methylpentanoic acid		0.68	
Heptanoic acid		0.58	
Octanoic acid		0.56	
Nonanoic acid		0.53	
Decanoic acid		0.50	
Undecanoic acid		0.46	
Dodecanoic acid		0.43	
3-Butenoic acid		0.62	
<u>Phenols</u>			
2-Chlorophenol		0.66	
Salicylaldehyde		0.98	
<u>Hydroxylic compounds</u>			
Water	0.40		
Methanol	0.39	0.46	
Ethanol	0.40	0.41	
Propan-1-ol	0.41	0.42	
Butan-1-ol	0.42	0.41	
2-Methylpropan-1-ol	0.38	0.42	

TABLE 26. CALCULATED VALUES OF π_2^H

Equation :	π_2^H		
	72	81	73
<u>Hydroxylic compounds (continued)</u>			
Pentan-1-ol		0.41	
2-Methylbutan-1-ol	0.39	0.41	
3-Methylbutan-1-ol	0.39	0.42	
2,2-Dimethylpropan-1-ol	0.33		
Hexan-1-ol	0.42	0.40	
2-Methylpentan-1-ol	0.40		
3-Methylpentan-1-ol	0.44		
4-Methylpentan-1-ol	0.43		
2-Ethylbutan-1-ol	0.40		
2,2-Dimethylbutan-1-ol	0.37		
Heptan-1-ol	0.43	0.39	
2,2-Dimethylpentan-1-ol	0.37		
Octan-1-ol	0.43	0.39	
2-Ethylhexan-1-ol	0.41		
2-Ethyl-4-methylpentan-1-ol	0.39		
Nonan-1-ol	0.39	0.39	
Decan-1-ol		0.39	
Undecan-1-ol		0.39	
Dodecan-1-ol		0.38	
Propan-2-ol	0.39	0.42	
Butan-2-ol	0.41	0.44	
Pentan-2-ol	0.40		
Pentan-3-ol	0.40		
3-Methylbutan-2-ol	0.39		
Hexan-2-ol	0.40	0.44	
Hexan-3-ol	0.39	0.41	
3-Methylpentan-2-ol	0.40		
4-Methylpentan-2-ol	0.38		
2-Methylpentan-3-ol	0.39		
2,3-Dimethylbutan-2-ol	0.41		
3,3-Dimethylbutan-2-ol	0.37		
Heptan-2-ol	0.40		
Heptan-3-ol	0.40		
Heptan-4-ol	0.39		
2,4-Dimethylpentan-3-ol	0.40		
Octan-2-ol	0.41		
2-Methylpropan-2-ol	0.38	0.50	
2-Methylbutan-2-ol	0.41	0.47	
2-Methylpentan-2-ol	0.40	0.48	
3-Methylpentan-3-ol	0.45	0.47	
2-Methylheptan-2-ol		0.47	
3-Methylheptan-3-ol		0.46	
3-Ethylpentan-3-ol	0.47		
Cyclopropylcarbinol	0.57		
Cyclopentanol	0.55	0.47	
Cyclohexanol	0.57		
2-Methylcyclohexanol	0.52		
cis,cis-2,6-Dimethylcyclohexanol		0.43	
cis,trans-2,6-Dimethylcyclohexanol		0.45	
trans,trans-2,6-Dimethylcyclohexanol		0.51	
dl- α -Terpineol		0.57	
exo-Ethylfenchol		0.52	
1,2-Ethane diol	0.50		
1,2-Propane diol	0.49		
1,2-Butane diol	0.63		
2-Methyl-1,2-propane diol	0.60		
dl-2,3-Butane diol	0.62		
meso-2,3-Butane diol	0.65		
1,3-Propane diol	0.46		
1,3-Butane diol	0.68		
1,4-Butane diol	0.46		
Prop-2-ene-1-ol (allyl alcohol)	0.44	0.46	
But-2-ene-1-ol	0.49		
But-3-ene-1-ol	0.47		
But-3-ene-2-ol	0.43		
2-Methylprop-2-ene-1-ol	0.45		
Pent-3-ene-1-ol	0.50		
Pent-4-ene-1-ol	0.46		
Pent-1-ene-3-ol	0.43		
2-Methylbut-3-ene-2-ol	0.41		
trans-Hex-2-ene-1-ol		0.43	
trans-Hept-2-ene-1-ol		0.40	

TABLE 26. CALCULATED VALUES OF π_2^H

Equation :	π_2^H		
	72	81	73
<u>Hydroxylic compounds (continued)</u>			
trans-Oct-2-ene-1-ol		0.41	
Prop-2-yne-1-ol	0.46		
2-Methylbut-3-yne-2-ol	0.47		
2-Chloroethanol	0.54		
2-Methoxyethanol	0.59		
2-Ethoxyethanol	0.56		
2-Butoxyethanol	0.57		
2-Allyloxyethanol	0.64		
2-Methoxypropan-1-ol	0.58		
2-Ethoxypropan-1-ol	0.56		
3-Ethoxypropan-1-ol	0.57		
1-Methoxypropan-2-ol	0.61		
1-Propoxypropan-2-ol	0.57		
3-Methoxybutan-1-ol	0.66		
1-Ethoxypentan-3-ol	0.60		
4-Methyl-4-methoxypentan-2-ol	0.65		
3-Hydroxybutan-2-one	0.78		
4-Hydroxybutan-2-one	0.85		
3-Methyl-4-hydroxybutan-2-one	0.81		
3-Methyl-3-hydroxybutan-2-one	0.75		
4-Methyl-4-hydroxypentan-2-one	0.83		
<u>Thiols</u>			
Ethylthiol	0.26	0.34	
Propylthiol	0.25	0.34	
Isopropylthiol	0.30	0.32	
Butylthiol	0.28	0.33	
Isobutylthiol	0.30	0.37	
t-Butylthiol	0.28	0.29	
Pentylthiol	0.27	0.34	
Isopentylthiol	0.27	0.18	
Hexylthiol	0.26	0.35	
Heptylthiol	0.27	0.33	
Octylthiol	0.26	0.33	
Nonylthiol	0.26	0.33	
Decylthiol	0.25	0.33	
Thiophenol	0.70	0.84	
1,2-Ethanedithiol	0.43		
Benzylthiol	0.71		
Allylthiol	0.35	0.44	
<u>Sulphides</u>			
Dithiapentane	0.68		
Dimethyl sulphide	0.40	0.37	
Diethyl sulphide	0.37	0.34	
Dipropyl sulphide	0.36	0.31	
Methylethyl sulphide	0.28		
Methylpropyl sulphide	0.38	0.34	
Diisopentyl sulphide	0.44	0.28	
Dibutyl sulphide	0.38	0.33	
Diallyl sulphide	0.49		
Propylene sulphide	0.39		
Tetrahydrothiophene	0.47	0.50	
Thiophene	0.50	0.50	
2-Methylthiophene	0.55	0.53	
2,5-Dimethylthiophene	0.60	0.49	
Dimethyl disulphide	0.47	0.41	
Diethyl disulphide	0.49	0.44	
Dimethyl trisulphide	0.53		
Methylthioacetate	0.65		
Methylthiopropionate	0.61		
Methylthiobutanoate	0.59		
Methylthiopentanoate	0.61		
<u>Thiocyanates and isothiocyanates</u>			
Phenyl isothiocyanate	1.00		
Allyl isothiocyanate	0.60		
Ethyl isothiocyanate	0.61		
Methyl thiocyanate	0.76		

Laffort⁸² obtained retention data for 240 solutes on five stationary phases. All these phases are nonacidic, and so five regression equations can be obtained (see section 6.11) of the following type, one for each phase:

$$\log L' = c + r.R_2 + s.\pi_2^* + a.\alpha^H_2 + l.\log L^{16} \quad [73]$$

In equation 73, $\log L' = \log L - \log L(\text{decane})$, but this affects only the constant in the regression equations. The "reverse" MLRA cannot be applied as used for the McReynolds data set, because there would be only five data points in each regression, and no less than four explanatory variables. In principle, since there are five equations and (for each solute) four unknowns, viz. R_2 , π_2^* , α^H_2 , and $\log L^{16}$, these unknowns could be determined through a set of simultaneous equations. This procedure proved to be quite useless, probably because there is not a wide enough range of constants in the five equations of type equation 73. However, Laffort⁸² did manage to analyse the 240 x 5 data matrix to yield five characteristic solute parameters denoted as α , w , ϵ , π , and β . In order to avoid confusion with our own parameters, the Laffort set is referred to as α_L , w_L , ϵ_L , π_L , and β_L . Each of these parameters for the 240 solute set can be examined via general solvation equation 63, where $\log SP = \alpha_L$, w_L , etc. α_L was found to be mainly a size factor and β_L was a general combination of factors. For the other three Laffort solute parameters the following regressions were obtained,

$$\pi_L = -0.040 + 0.342R_2 - 0.265\pi_2^* + 2.540\alpha^H_2 \quad [74]$$

$$\epsilon_L = 0.165 + 2.796R_2 - 0.602\pi_2^* - 1.426\alpha^H_2 \quad [75]$$

$$w_L = -0.081 - 1.700R_2 + 2.490\pi_2^* + 0.561\alpha^H_2 \quad [76]$$

These equation (74-76) can be re-arranged to yield,

$$\alpha^H_2 = 0.0218 + 0.0335w_L - 0.0251\epsilon_L + 0.3722\pi_L \quad [77]$$

$$\pi_2^*(\pi^{H_2}) = -0.0060 + 0.4755wL + 0.2826\epsilon L + 0.0536\pi L \quad [78]$$

$$R_2 = 0.0492 + 0.1195wL + 0.4057\epsilon L + 0.2014\pi L \quad [79]$$

If R_2 is known, as it usually is, then any two equations out of equation (74-76) will yield α^{H_2} and π_2^* . But the best pair of equations to use is clearly equation 74 and equation 76 which yield,

$$\alpha^{H_2} = 0.0187 - 0.0620R_2 + 0.0409wL + 0.3847\pi L \quad [80]$$

$$\pi_2^*(\pi^{H_2}) = 0.0287 + 0.6954R_2 + 0.3932wL - 0.0789\pi L \quad [81]$$

Values of π^{H_2} calculated via equation 81 are listed in Table 26. Also, it is possible to simply take the set of five equations, equation 73, and, knowing R_2 , $\log L^{16}$, and where necessary α^{H_2} , back-calculate values of π^{H_2} . For each solute the five back-calculated π^{H_2} values can be averaged, and this average is also given in Table 26. The error in π^{H_2} as between the five equations is around 0.03 units. There are a few omissions in this set of π^{H_2} values: these arise through lack of one or another of the remaining solute parameters.

Although the combination of solutes in the McReynolds and Laffort sets numbers several hundred, there are some notable omissions. Firstly, the great majority of solutes are aliphatic, so that some of the simplest functionally substituted aromatic solutes are missing. Secondly, many of the polyhalogenated aliphatic solutes are either missing, or have π^{H_2} values that are discordant when calculated from the McReynolds or Laffort set. And finally, a number of important solutes such as nitroalkanes and nitriles need to be further studied.

Fellous et al²⁰⁵ have listed GLC data for 17 aromatic solutes on a number of stationary phases. In order to back-calculate π^{H_2} using the general solvation

equation 63, it is essential that the s -coefficient be as large as possible, i.e. that the stationary phase be quite polar. Results from the seven most polar phases used by Fellous are in Table 27. There is generally good agreement with values listed in Table 26.

Table 27. Values Of π_2^H For Some Aromatic Compounds Calculated From Results Of Fellous et al. ²⁰⁵.

X in PhX	π_2^H	S.D. ^a	π_2^H (Table 26)		
H	0.53	0.02	0.48	0.47	
CF ₃	0.45	0.02			
Me	0.52	0.01	0.47	0.57	0.46
OMe	0.73	0.02		0.73	0.70
F	0.57	0.02			
Cl	0.67	0.01			
Br	0.73	0.01			
I	0.79	0.01			
CHO	0.99	0.01		0.99	0.94
SH	0.78	0.01		0.70	0.84
CO ₂ Me	0.85	0.01		0.77	1.11
CN	1.07	0.01		1.05	1.04
COMe	0.98	0.01		1.09	0.99
NH ₂	0.96	0.02			
NO ₂	1.10	0.01		1.08 ^b	1.05 ^b
CH ₂ OH	0.85	0.01			
OH	0.88	0.01			

^a Average deviation from 7 results. ^b For 3-nitrotoluene

Several workers have examined sets of halogenated or polyhalogenated solutes on various stationary phases²⁰⁶⁻²⁰⁹. In Table 28 are given π_2^H values back-calculated from the general solvation regression equation, equation 63, as well as from results obtained on a variety of polar stationary phases.

TABLE 28. RECOMMENDED SOLVATION PARAMETERS^a
FOR USE IN EQUATION 63^b

Solute	$\Sigma\pi_2^H$	$\Sigma\alpha_2^H$	$\Sigma\beta_2^H$
Rare gas	0.00	0.00	0.00
Hydrogen	0.00	0.00	0.00
Oxygen	0.00	0.00	0.00
Nitrogen	0.00	0.00	0.00
Nitrous Oxide	0.35	0.00	0.10
Carbon Monoxide	0.00	0.00	0.04
Carbon Dioxide	0.42	0.00	0.10
Alkane	0.00	0.00	0.00
Cycloalkane	0.10	0.00	0.00
Decalin	0.25	0.00	0.00
Hydrindane	0.20	0.00	0.00
Ethene	0.10	0.00	0.07
Other alkene	0.08	0.00	0.07
Cycloalkene	0.20	0.00	0.10
α -Pinene	0.24	0.00	0.10
Diene	0.23	0.00	0.10
Ethyne	0.25	0.15	0.15
Propyne	0.25	0.13	0.15
But-1-yne	0.25	0.13	0.15
Other alk-1-yne	0.23	0.13	0.10
Alk-2-yne	0.30	0.00	0.10
Benzene	0.52	0.00	0.14
Toluene	0.52	0.00	0.14
o-Xylene	0.54	0.00	0.17
m-Xylene	0.52	0.00	0.17
p-Xylene	0.52	0.00	0.17
Ethylbenzene	0.52	0.00	0.15
n-Propylbenzene	0.52	0.00	0.15
Isopropylbenzene	(0.51)	0.00	0.15
1,2,3-Trimethylbenzene	0.54	0.00	0.20
1,2,4-Trimethylbenzene	0.52	0.00	0.20
1,3,5-Trimethylbenzene	0.52	0.00	0.20
n-Alkylbenzene	0.52	0.00	0.15
Styrene	0.63	0.00	0.18
Phenylethyne	0.58	0.12	0.21
Naphthalene	0.90	0.00	0.21
Fluoroalkane	0.35 ^c	0.00	0.10
Chloromethane	0.43 ^c	0.00	0.08
Chloroalkane	0.40 ^c	0.00	0.10
Bromomethane	0.43 ^c	0.00	0.10
Bromoalkane	0.40 ^c	0.00	0.12
Iodomethane	0.43 ^c	0.00	0.13
Iodoalkane	0.40 ^c	0.00	0.15
s-Chloroalkane	0.35 ^c	0.00	0.12
s-Bromoalkane	0.35 ^c	0.00	0.14
s-Iodoalkane	0.35 ^c	0.00	0.17
t-Chloroalkane	0.25 ^c	0.00	0.12
t-Bromoalkane	0.25 ^c	0.00	0.12
t-Iodoalkane	0.25 ^c	0.00	0.10
Dichloromethane	0.57 ^c	0.10	0.05
Trichloromethane	0.49	0.15	0.02
Tetrachloromethane	0.38	0.00	0.00
1,1-Dichloroethane	0.49	0.10	0.10
1,2-Dichloroethane	0.64	0.10	0.11
1,1,1-Trichloroethane	0.41	0.00	0.09
1,1,2-Trichloroethane	0.68	0.13	0.08
1,1,1,2-Tetrachloroethane	0.63	0.10	0.08
1,1,2,2-Tetrachloroethane	0.76	0.16	0.12
Dibromomethane	0.67	0.10	0.10
Tribromomethane	0.68	0.15	0.09
Fluorobenzene	0.57	0.00	0.10
Chlorobenzene	0.67	0.00	0.09
1,2-Dichlorobenzene	0.79	0.00	0.03
1,3-Dichlorobenzene	0.74	0.00	0.03
1,4-Dichlorobenzene	0.69	0.00	0.03
2-Chlorotoluene	0.66	0.00	0.09
3-Chlorotoluene	0.67	0.00	0.09

TABLE 28. RECOMMENDED SOLVATION PARAMETERS^a
FOR USE IN EQUATION 63^b

Solute	$\Sigma\pi_2^H$	$\Sigma\alpha_2^H$	$\Sigma\beta_2^H$
4-Chlorotoluene	0.67	0.00	0.09
2,4-Dichlorotoluene	0.73	0.00	0.03
2,6-Dichlorotoluene	0.73	0.00	0.03
3,4-Dichlorotoluene	0.79	0.00	0.03
Bromobenzene	0.73	0.00	0.09
1,2-Dibromobenzene	0.89	0.00	0.03
1,3-Dibromobenzene	0.84	0.00	0.03
1,4-Dibromobenzene	0.79	0.00	0.03
Iodobenzene	0.79	0.00	0.09
Dimethylether	0.27	0.00	0.41
Di-n-alkylether	0.25 ^c	0.00	0.45
Furan	0.53	0.00	0.15
2-Methylfuran	0.50	0.00	(0.15)
Tetrahydrofuran	0.52	0.00	0.48
2-Methyltetrahydrofuran	0.48	0.00	0.55
3,5-Dimethyltetrahydrofuran	0.38	0.00	0.55
Tetrahydropyran	0.47	0.00	0.55
1,4-Dioxane	0.75	0.00	0.64
Paraldehyde	0.68	0.00	
Methylphenylether	0.73	0.00	(0.33)
Ethylphenylether	0.72	0.00	(0.33)
Benzodioxane	1.01	0.00	
Formaldehyde	0.70	0.00	(0.33)
Acetaldehyde	0.67	0.00	0.45
n-Alkanal	0.65 ^c	0.00	0.45
Prop-2-en-1-al	0.74	0.00	0.45
trans-Alk-2-en-1-al	0.80	0.00	0.45
Benzaldehyde	0.99	0.00	(0.42)
2-, 3-, or 4-Methylbenzaldehyde	0.95	0.00	(0.44)
Propanone	0.70	0.04	0.51
Butanone	0.70	0.00	0.51
Alkan-2-one	0.68 ^c	0.00	0.51
Alkan-(3,4,5)-one	0.66 ^c	0.00	0.51
Cycloalkanone	0.86 ^c	0.00	0.52
Acetophenone	0.98	0.00	(0.51)
Methyl formate	0.68	0.00	0.38
Ethyl formate	0.66	0.00	0.38
n-Alkyl formate	0.63 ^c	0.00	0.38
Methyl acetate	0.64	0.00	0.45
Ethyl acetate	0.62	0.00	0.45
n-Alkyl acetate	0.60 ^c	0.00	0.45
Methyl propanoate	0.60	0.00	0.45
Ethyl propanoate	0.58	0.00	0.45
n-Alkyl propanoate	0.56 ^c	0.00	0.45
Vinyl acetate	0.64	0.00	0.42
Methyl acrylate	0.66	0.00	0.42
Ethyl acrylate	0.64	0.00	0.42
n-Alkyl acrylate	0.62 ^c	0.00	0.42
Methyl benzoate	0.85	0.00	0.50
n-Alkyl benzoates	0.80	0.00	0.50
Nitromethane	0.95	0.12	0.27
Nitroethane	0.95	0.05	0.27
1-Nitropropane	0.95	0.02	0.27
1-Nitroalkane	0.95 ^c	0.00	0.27
Nitrobenzene	1.10	0.00	0.27
2-, 3- or 4-Nitrotoluene	1.10	0.00	0.27
Acetonitrile	0.90	0.09	0.30
Propionitrile	0.90	0.02	0.35
n-Alkyl cyanide	0.90 ^c	0.00	0.36
Benzonitrile	1.07 ^c	0.00	(0.30)

TABLE 28. RECOMMENDED SOLVATION PARAMETERS^a
FOR USE IN EQUATION 63^b

Solute	$\Sigma\pi_2^H$	$\Sigma\alpha_2^H$	$\Sigma\beta_2^H$
Ammonia	0.35 ^d	0.10	0.62
Primary n-alkylamines	0.35 ^d	0.10	0.64
Dimethylamine	0.30 ^d	0.08	0.67
Sec di-alkylamines	0.30 ^d	0.08	0.70
Triethylamine	0.15 ^d	0.00	0.81
Aniline	0.96 ^d	0.26	(0.53)
o-Toluidine	0.94	0.23	(0.57)
m-Toluidine	0.94	0.23	(0.55)
p-Toluidine	0.94	0.23	(0.57)
2,6-Dimethylaniline	0.93	0.20	(0.60)
N-Methylaniline	0.94	0.17	(0.47)
N,N-Dimethylaniline	0.82	0.00	(0.48)
Pyridine	0.82	0.00	
2-Methylpyridine	0.80	0.00	
3-Methylpyridine	0.80	0.00	
4-Methylpyridine	0.80	0.00	
2,4,6-Trimethylpyridine	0.72	0.00	
Acetic acid	0.65	0.61	0.41
Propanoic acid	0.65	0.60	0.43
Butanoic Acid	0.62	0.60	0.43
n-Alkanoic Acids	0.60 ^c	0.60	0.43
Water	0.45	0.82	0.35
Methanol	0.44	0.43	0.47
Ethanol	0.42	0.37	0.48
Primary Alcohols	0.42 ^c	0.37	0.48
Secondary Alcohols	0.36 ^c	0.33	0.56
Tertiary Alcohols	0.30 ^c	0.31	0.60
Trifluoroethanol	0.60	0.57	(0.15)
Hexafluoropropan-2-ol	0.55	0.77	(0.03)
Decafluoroheptan-1-ol	0.55	0.60	0.22
Phenol	0.88	0.60	
o-Cresol	0.86	0.52	
m-Cresol	0.87	0.57	
p-Cresol	0.87	0.57	
2,3-Dimethylphenol	0.82	0.53	
2,4-Dimethylphenol	0.82	0.53	
2,5-Dimethylphenol	0.82	0.54	
2,6-Dimethylphenol	0.82	0.39	
3,4-Dimethylphenol	0.87	0.56	
3,5-Dimethylphenol	0.87	0.57	
2,4,6-Trimethylphenol	0.83	0.37	
Benzyl alcohol	0.85	0.39	
Carbon disulphide	0.21	0.00	0.07
Methanethiol	(0.35)	0.00	
n-Alkylthiol	0.35 ^c	0.00	0.24
Isopentylthiol	0.18 ^c	0.00	
Thiophenol	0.78	0.12	(0.15)
Di-n-alkylsulphide	0.38 ^c	0.00	0.32
Tetra-alkyltin	0.00	0.00	0.00

^a Values of $\Sigma\pi_2^H$ (this work) derived from those in Table 26 and 27, plus other calculated values. Values of $\Sigma\alpha_2^H$ and $\Sigma\beta_2^H$ are based on those given in references 185 and 186, and back-calculated where necessary or feasible. Note $\Sigma\beta_2^H$ may not necessarily be identical to values presented previously in section 6.13, Table 23, pages 121-123. Subsequent back-calculation of $\Sigma\beta_2^H$ using improved solvation parameters such as $\Sigma\pi_2^H$, and averaging of $\Sigma\beta_2^H$ for a wide range of systems may have altered the provisional values in Table 23.

^b General solvation equation 63, $\log SP = c + r.R_2 + s.\pi_2^* + a.\alpha_2^H + b.\beta_2^H + 1.\log L^{16}$.

^c Subtract 0.03 from $\Sigma\pi_2^H$ for each additional branch.

^d Provisional values

^e See text.

McReynolds¹³³ did not examine any aliphatic nitro compounds or nitriles, but in Table 26 are given values of π^{H_2} for a few such compounds, obtained from the Laffort data set. Both series of solutes on a number of stationary phases have been carefully examined, and it is apparent that π^{H_2} is even larger than the values given in Table 26. These results suggest that for 1-nitroalkanes π^{H_2} is 0.95 and that for n-alkyl cyanides π^{H_2} is around 0.90 units, see Table 28.

The α^{H_2} (or more correctly $\Sigma\alpha^{H_2}$) values calculated from equation 72 or equation 80 have not been detailed because these follow quite closely the original hydrogen bond α^{H_2} values as described before¹⁸⁵. Only in the case of the carboxylic acids do the new effective or $\Sigma\alpha^{H_2}$ values (0.60 units) differ markedly from α^{H_2} (0.54 units). In Table 28 are collected all the $\Sigma\alpha^{H_2}$ values that correspond to the $\Sigma\pi^{H_2}$ values set out.

The "inverse matrix" method used to analyse the data of McReynolds is a quite novel approach to the extraction of solvation parameters from data on a large number of stationary phases. The method works very well indeed, but is limited in scope to results for a given set of solutes on at least 15 phases. Back-calculation of parameters from regression equations based on Laffort's data set, equation 73, is likely to be the most common procedure. In principle, as pointed out above, if three solvation parameters are unknown (*e.g.* π^{H_2} , α^{H_2} and $\log L^{16}$ in equation 63), it is possible to calculate all three using three simultaneous equations derived from retention data on three phases. In practice, this method can hardly ever be used unless the three phases are specifically chosen to give rise to solvation equations with very different coefficients. In the event, all of the new π^{H_2} values have been obtained by either the inverse matrix method or simple back-calculation and averaging. By and large, the π^{H_2} values listed in Table 28 are good to about 0.02 units, not more.

As can be seen from the data collected in Table 26, there is a compelling need to correlate and to interpret π^{H_2} values in order to codify existing data and to help in the estimation of further values. An analysis of all these results has led to two very simple rules governing π^{H_2} values for aliphatic solutes:

Rule 1: In any homologous series of functionally substituted aliphatic compounds, π^{H_2} is constant except for the first one or two members of the series.

Rule 2: In any given series of functionally substituted aliphatic compounds, π^{H_2} decreases by 0.03 units for each branch in a carbon chain.

Rule 1 would be extremely valuable in the estimation of π^{H_2} values, since if π^{H_2} was known for a few members of an homologous series, then the same value could be applied to all other members. Unfortunately, Carr²⁰³ apparently finds that his own π^{C_2} parameter varies quite markedly along homologous series. Thus along the homologous series of n-alkyl carboxylic acids, π^{C_2} increases from 0.50 (acetic acid) to 0.72 (nonanoic acid), see Table 29, whereas π^{H_2} is set constant at 0.62 units after the first few members of the series. Note that π^{C_2} and π^{H_2} are "scaled" differently, so that for the present discussion only trends in these parameters are important. How the two sets of π_2 values in Table 29 both result in good fits to experimental data can be seen by inspection of the corresponding $\Sigma\alpha^{\text{H}_2}$ values, also in Table 29. A constant π^{H_2} value is accompanied by a constant $\Sigma\alpha^{\text{H}_2}$ value, whereas Carr's increase in π^{C_2} is counteracted by a decrease in $\Sigma\alpha^{\text{H}_2}$, so that both combinations of $\pi_2/\Sigma\alpha^{\text{H}_2}$ fit experimental data with respect to the solvation equation 63. However, other experimental evidence supports the constancy of π^{H_2} and $\Sigma\alpha^{\text{H}_2}$. Thus the dipole moment of the n-alkyl carboxylic acids (except for formic acid) remains constant²¹¹, the gas phase proton transfer acidity of acetic acid, propanoic acid,

and butanoic acid is almost the same (if anything, there is a slight increase in acidity along this series)²¹², and the gas phase hydrogen bond acidity of propanoic acid is slightly less than that of acetic acid²¹³, not larger. Since retention data can as well be accommodated by the constant π^{H_2} and $\Sigma\alpha^{\text{H}_2}$ values as by the variable parameters of Carr, Rule 1 is here operative.

Table 29. Comparison Of π^{H_2} With π^{C_2} For Carboxylic Acids

R in ROC_2H	- This work -		- Carr ²⁰⁴ -	
	π_2^{H}	α_2^{H}	π_2^{C}	α_2^{H}
Me	0.65	0.61	0.50	0.72
Et	0.65	0.60	0.61	0.67
n-Pr	0.62	0.60	0.57	0.62
n-Bu	0.60	0.60	0.56	0.62
n-Pe	0.60	0.60	0.60	0.52
n-Hex	0.60	0.60	0.64	0.47
n-Hept	0.60	0.60	0.68	0.41
n-Oct	0.60	0.60	0.72	0.35

There are other homologous series for which Carr finds π^{C_2} as a variable quantity, but for which $\Sigma\alpha^{\text{H}_2} = 0$, for example the alkan-2-ones or the cycloalkanones where π^{C_2} increases quite sharply along the series. In some other series, however, π^{C_2} decreases slightly (the alk-1-ene series), or remains approximately constant (the alkanal series or the alkylbenzene series). For the cycloalkanone series, as an example, the difference between Carr's result and the findings here is not fundamental at all, but is probably due to small but systematic differences in the $\log L^{16}$ values. Since the sign of the $s.\pi_2$ and $l.\log L^{16}$ coefficients is always positive, a systematic trend in π^{C_2} increasing, together with a trend in $\log L^{16}$ becoming slightly smaller than expected, would tend to cancel out. This can be seen by comparison of the figures in Table 30.

Table 30. Comparison Of π^{H_2} With π^{C_2} For Cycloalkanones

n in (CH ₂) _n CO	- This work -		- Carr ²⁰⁴ -	
	π_2^H	log L ¹⁶	π_2^C	log L ¹⁶
4	0.86	3.221	0.58	3.120
5	0.86	3.792	0.59	3.616
6	0.86	4.376	0.66	4.110
7	0.86	4.981	0.69	4.610
8	0.86	5.537	0.72	5.110
9	0.86	6.063	0.75	5.610
10	0.86	6.621	0.78	6.110
11	0.86	7.226	0.81	6.600

Just as for the carboxylic acid results, the combination of π^{C_2} with Carr's calculated log L¹⁶ values will lead to very nearly the same goodness-of-fit as the combination of π^{H_2} and log L¹⁶. Since it is always found that solute dipolarity, as the dipole moment, is constant along any homologous series, it is felt that Rule 1 applies to the various homologous series considered.

Rule 2 is not so well founded, and it quite possible that there will be exceptions or amendments to the rule. But at the moment, application of Rule 2 does allow a very large number of π^{H_2} values to be estimated for aliphatic compounds. Note that the starting point for application of the rule is not always the simplest member of any series.

According to the results in Table 26, the alkanols are a significant exception to Rule 2, since π^{H_2} seems roughly constant over nonbranched and branched members. However, because the coefficients of π^{H_2} and α^{H_2} are both positive, and, indeed, follow each other for most stationary phases, there will be various combinations of π^{H_2} and α^{H_2} that give rise to the same (or very similar) goodness-of-fit in any given solvation equation. As a check, if π^{H_2} values for

alkanols calculated using Rules 1 and 2, are used together with the α^{H_2} values listed in Table 28, regression equations are yielded that are just as good as if π^{H_2} and α^{H_2} are allowed to "float". In summary Table 28, are suggested π^{H_2} and α^{H_2} values for alkanols, with deliberate amendments to the first-calculated values in Table 26.

There are also a few minor anomalies with respect to Rule 2. Thus π^{H_2} for isopentylthiol is 0.18 (using the Laffort set) rather than 0.32 as calculated by Rule 2. Whether or not this is the result of a systematic experimental error, or even of an incorrectly named compound is not clear. Interestingly, Carr²⁰⁴ also finds an anomalously low π^{C_2} value for isopentylthiol.

Finally, the new π^{H_2} scale, as summarised in Table 28, can be compared with the π^{C_2} scale of Carr. As Carr obviously agrees, there is a need for a new π_2 scale in place of π^*_2 . Apart from the difference in treatment of homologous series, the two scales are in approximate agreement. For 198 out of the 203 compounds listed by Carr²⁰⁴, there are π^{H_2} values, and a correlation equation yields the relationship,

$$\pi^{\text{C}_2} = -0.103 + 0.845 \pi^{\text{H}_2} \quad [82]$$

with $r = 0.944$ and S.D. = 0.083 units. The intercept of -0.103 arises because Carr takes cyclohexane as the zero ($\pi^{\text{C}_2} = 0.00$), but the π^{H_2} scale is originated with alkanes taken as zero. On the π^{H_2} scale, cyclohexane has $\pi^{\text{H}_2} = 0.10$ units. Carr records π^{C_2} for a few compounds not included in Table 28, and as a first approximation equation 82 can be used to estimate π^{H_2} values for dimethylformamide and dimethylacetamide (approx. 1.10 in each case) and also for DMSO (approx. 1.30 units).

Included in summary Table 28, are a provisional set of $\Sigma\beta^{\text{H}_2}$ values to use with

the new π^{H_2} and $\Sigma\alpha^{H_2}$ scale. It is most important that these three scales are constructed more-or-less simultaneously in order that they all be compatible. As has been said in section 6.13, HPLC data affords the opportunity to calculate new $\Sigma\beta^{H_2}$ values, and/or review old values of β^{H_2} . Reliable GLC data for basic compounds on acidic phases is rare, and crucial compounds (such as phenols) prove to be remarkably difficult to elute. HPLC data analysed by an iterative MLRA process may well prove to be one of the only suitable methods to obtain 'effective' β^{H_2} values. Note, $\Sigma\beta^{H_2}$ values listed in Table 28 may not be identical to values of $\Sigma\beta^{H_2}$ set out in section 6.13, Table 23, pages 121-123. Subsequent back-calculation of $\Sigma\beta^{H_2}$ using improved solvation equations containing parameters R_2 and π^{H_2} *etc.*, and averaging of $\Sigma\beta^{H_2}$ values over a wide range of systems studied may have altered the provisional values in Table 23.

How well the parameters listed in Table 28 deal with various processes remains to be seen, but at the moment, regressions of the Laffort data using the Table 28 values can be compared with original regression equations. Details are in Table 31, and show that the new equations are very much better than the old ones in terms of the correlation constant and standard deviation. However, the characteristic constants, r , s , a and l are almost unchanged. Similarly, regression equations using McReynolds data are much better than the original ones, whilst still giving very similar characteristic constants. Hence the analysis of the McReynolds phases into clusters or groups remains unchanged, and it is not necessary to repeat the 75 regressions. Given in Table 31 are a few comparisons to show exactly the connection between the old and the new equations.

The new π^{H_2} scale is based only on solute properties. Since the dependent variable, $\log L'$ or $\log V_G$, in the equations used to calculate π^{H_2} is a free energy related term, then π^{H_2} will also be related to Gibbs energy. The main terms in a new solvation equation, *viz.* π^{H_2} , $\Sigma\alpha^{H_2}$, $\Sigma\beta^{H_2}$, and $\log L^{16}$, are all related to Gibbs

energy and hence form a thermodynamically consistent set of explanatory variables. The new π_2^H scale has an advantage in that the characteristic constants in all previous equations remain the same, within any reasonable experimental error, so that previous analyses and conclusions are unchanged.

Table 31. Comparison Of New And Old Regressions ^a

Phase	<i>c</i>	<i>r</i>	<i>s</i>	<i>a</i>	<i>l</i>	S.D.	R	No.
A. The Laffort set								
Carbowax	-2.01	0.25	1.26	2.07	0.429	0.07	0.997	199
	-2.07	0.26	1.37	2.11	0.442	0.13	0.986	168
DEGS ^b	-1.77	0.35	1.58	1.84	0.383	0.07	0.997	199
	-1.83	0.35	1.70	1.92	0.396	0.15	0.981	168
PPE (6 rings) ^b	-2.51	0.14	0.89	0.67	0.547	0.06	0.997	199
	-2.55	0.19	0.98	0.59	0.552	0.11	0.991	168
TCEP ^b	-1.69	0.26	1.93	1.88	0.365	0.06	0.998	199
	-1.75	0.23	2.12	1.94	0.379	0.16	0.982	168
ZE7 ^b	-1.99	-0.41	1.46	0.77	0.432	0.07	0.995	199
	-2.07	-0.38	1.61	0.70	0.442	0.13	0.983	168
B. The McReynolds set at 120°C								
Apiezon J	-0.48	0.24	0.15	0.13	0.596	0.02	0.999	165
	-0.48	0.27	0.13	0.13	0.594	0.03	0.998	148
PPE (5 rings)	-0.69	0.14	0.92	0.61	0.560	0.02	0.999	168
	-0.70	0.21	0.88	0.54	0.564	0.06	0.994	155
Pluronic L72	-0.54	0.09	0.93	1.42	0.529	0.03	0.998	163
	-0.54	0.17	0.89	1.41	0.531	0.08	0.992	153
Carbowax 1540	-0.75	0.22	1.37	1.92	0.456	0.04	0.998	169
	-0.75	0.31	1.34	1.87	0.457	0.09	0.987	151
DEGS ^b	-0.97	0.26	1.76	1.80	0.375	0.05	0.995	158
	-0.99	0.43	1.74	1.68	0.379	0.11	0.975	145
ZE7 ^b	-0.76	-0.42	1.55	0.78	0.448	0.07	0.991	170
	-0.82	-0.28	1.63	0.69	0.449	0.07	0.990	150

^a The new constants in equation 63 are on the top lines, and the old constants are on the bottom lines; in all cases *b* = 0.

^b These abbreviations are: DEGS, diethyleneglycol succinate; PPE, polyphenyl ether; TCEP, tricyanoethoxypropane; ZE7, zonyl E-7.

6.20 The Log L¹⁶ Parameter

The characterisation of solvent phases using the general solvation equation 63 (first derived during the analysis of the Laffort data, where $SP = \log L'$, see section 6.11), nearly always produces superior results to using a solute volume term, such as V_X , in place of $\log L^{16}$, when processes involving gas $\rightleftharpoons$ condensed phase transfer are considered.

$$\log SP = c + r.R_2 + s.\pi_2^* + a.\alpha^{H_2} + b.\beta^{H_2} + 1.\log L^{16} \quad [63]$$

Equation 63 can be re-cast using the improved parameters discussed in section 6.14.

$$\log SP = c + r.R_2 + s.\pi^{H_2} + a.\Sigma\alpha^{H_2} + b.\Sigma\beta^{H_2} + 1.\log L^{16} \quad [83]$$

Use of equation 83 will give improved results over equation 63 (see section 6.14), but the various parameters are all interchangeable, and where a 'summation' or 'effective' value is not known, the corresponding monofunctional value can be used; additionally for many solutes, the 'summation' value and the monofunctional one are identical. Parameters R_2 , π_2^* ($\Sigma\pi^{H_2}$), α^{H_2} ($\Sigma\alpha^{H_2}$), and β^{H_2} ($\Sigma\beta^{H_2}$) are now known for many hundreds of solutes, and application of the solvation equations to processes requiring the use of $\log L^{16}$ would be severely limited if this term is not known for a great many solutes. Originally²⁴, solvation equations were restricted to those solutes for which $\log L^{16}$ values were experimentally available (240), and those for which values could be estimated, giving a total of not more than 300. At present, $\Sigma\pi^{H_2}$ values are available for 1008 compounds, $\Sigma\alpha^{H_2}$ for 2064, and $\Sigma\beta^{H_2}$ values for 1439. Clearly, the scope of application for the solvation equations will be severely limited if the number of $\log L^{16}$ values are not of the same order as other parameters.

To do this, a major aim during the course of this work was to obtain $\log L^{16}$ values to ensure a database as large as, or exceeding the other parameters. A secondary aim was to reference these values so their origin was known along with their accuracy. $\log L^{16}$ values were also required for polyfunctional molecules, to enable the solvation equations to deal with the many important polyfunctional solutes (this stipulation applied to the other solvation parameters as well). Primary experimental values where possible are to be preferred, and these have been obtained on n-hexadecane at 298.15K by the gas-chromatographic method (see section 9.11 for more details). Many compounds will either elute far too quickly (such as CFCs), or too slowly (*eg.* phenols and large and/or polyfunctional molecules generally) on n-hexadecane at 298.15K. Longer or shorter gas-chromatographic columns can be used to alleviate this problem to some extent, and the temperature can be raised or lowered to affect solute elution rate (and the obtained value later corrected to 298.15K). However n-hexadecane freezes at 18.17°C, and tends to 'bleed' off the column if temperatures exceed about 40°C. In light of these drawbacks, $\log L^{16}$ values for rare or difficult compounds have to be obtained by other means.

Secondary values (*i.e.* values not directly obtained on n-hexadecane at 298.15K) can also be obtained either experimentally, or from the literature. Using phases which are similar in nature to n-hexadecane, *i.e.* non-polar hydrocarbon stationary phases, retention information can be correlated with $\log L^{16}$, providing equations which can be used to back-calculate further $\log L^{16}$ values. Published or experimentally determined retention data can be in the form of log relative retention times (relative to a standard), retention indices (I), or log retention volumes *etc.* Typical forms of the correlations that can be used to back-calculate $\log L^{16}$ values are,

$$\log (\text{relative retention time, or volume}) = c + 1.\log L^{16} \quad [84]$$

$$\log (\text{relative retention time, or volume}) = c + r.R_2 + 1.\log L^{16} \quad [85]$$

$$I = c + 1.\log L^{16} \quad [86]$$

$$I = c + r.R_2 + 1.\log L^{16} \quad [87]$$

The values of $\log L^{16}$ obtained can be assumed to be fairly accurate if a number of conditions are met;-

(1) The correlation of $\log L^{16}$ and the published (or experimental) data must be good, $R > 0.99$, and the standard deviation must be low.

(2) Data must be obtained from a non-polar stationary phase, similar to n-hexadecane.

(3) Data must all be measured at the same temperature, and ideally be as near 298.15K as is possible. Frequently, published retention indices are presented with a $\delta I/\delta T$ factor, so they can be corrected to 298.15K.

It is useful to carry out a preliminary plot by hand of data against $\log L^{16}$, to show outliers, or to show if separate correlation equations are necessary for different classes of compounds. For example, in the correlation of retention indices on Apiezon L at 403K provided from data of Kovats and Wehrli²¹⁴, two distinct correlation equations become apparent, one for aliphatic compounds and one for aromatic (the quality and form of these equations is fairly typical),

$$I/1000_{\text{ALIPHATIC}} = 0.071 + 0.202 \log L^{16} \quad [88]$$

$$R = 0.9977 \quad SD = 0.012 \quad N = 44$$

$$I/1000_{\text{AROMATIC}} = -0.22 + 0.246 \log L^{16} \quad [89]$$

$$R = 0.9919 \quad SD = 0.019 \quad N = 20$$

Outliers observed from plots of retention data against $\log L^{16}$ were further examined as follows. For a homologous series, or a series of structurally related compounds, plots of $\log L^{16}$ against $\log P$ (solute vapour pressure at 298K), or of retention data against $\log P$ are always excellent straight lines. Use of $\log P$ plots can therefore determine whether $\log L^{16}$ values used to generate a regression or the published retention data are inaccurate. In all cases, these plots showed that published data was at fault, (very possibly due to misprints *etc*).

Correlations of $\log P$ against $\log L^{16}$ can also be used to obtain additional values, as can various other correlations (such as along homologous series). Many $\log L^{16}$ values were calculated from the data of McReynolds¹³³, (see section 6.14), using the novel 'inverse' MLRA technique. Additionally, some $\log L^{16}$ values are available directly from the literature.

As a result of this, the database on important $\log L^{16}$ values has now been raised to 936 compounds. Many more values have been assimilated, but have not been inputted into the database, because they are merely extensions along homologous series, or are not compounds in common use, isomers *etc*. Rather than detail here every method that has been used to obtain solute $\log L^{16}$ values, the entire set of $\log L^{16}$ values currently in the solute database are presented in Table 32, together with comprehensive footnote references, which exactly indicate their origin and/or method of calculation.

Table 32. Log L16 Values in the Solute Database

No	Compound Name	Log L16 Ref	No	Compound Name	Log L16 Ref
1	Helium	-1.741 L4	145	n-Nonane	4.182 L18
2	Neon	-1.575 L5	146	2-Methyloctane	3.966 L62
3	Argon	-0.688 L5	147	3-Methyloctane	3.998 L62
4	Krypton	-0.211 L7	148	4-Methyloctane	3.961 L62
5	Xenon	0.378 L9	149	3-Ethylheptane	3.992 L62
6	Radon	0.877 L9	150	4-Ethylheptane	3.944 L62
11	Hydrogen	-1.200 L4	151	2,2-Dimethylheptane	3.739 L62
12	Deuterium	-1.200 L4	152	2,3-Dimethylheptane	3.925 L62
13	Oxygen	-0.723 L5	153	2,4-Dimethylheptane	3.758 L62
15	Nitrogen	-0.978 L10	154	2,5-Dimethylheptane	3.822 L62
16	Nitrous oxide	0.164 L10	155	2,6-Dimethylheptane	3.780 L18
21	Carbon monoxide	-0.836 L6	156	3,3-Dimethylheptane	3.833 L62
22	Carbon dioxide	0.057 L10	157	3,4-Dimethylheptane	3.935 L62
26	Sulphur dioxide	0.700 L22	158	3,5-Dimethylheptane	3.826 L62
101	Methane	-0.323 L23	159	4,4-Dimethylheptane	3.770 L18
102	Ethane	0.492 L13	160	2-Methyl-3-ethylhexane	3.850 L18
103	Propane	1.050 L14	161	2-Methyl-4-ethylhexane	3.760 L18
104	n-Butane	1.615 L15	162	3-Methyl-3-ethylhexane	3.890 L18
105	2-Methylpropane	1.409 L12	163	3-Methyl-4-ethylhexane	3.900 L18
106	n-Pentane	2.162 L3	164	2,2,3-Trimethylhexane	3.762 L62
107	2-Methylbutane	2.013 L16	165	2,2,4-Trimethylhexane	3.605 L62
108	2,2-Dimethylpropane	1.820 L3	166	2,2,5-Trimethylhexane	3.567 L62
109	n-Hexane	2.668 L3	167	2,3,3-Trimethylhexane	3.832 L62
110	2-Methylpentane	2.503 L62	168	2,3,4-Trimethylhexane	3.882 L62
111	3-Methylpentane	2.581 L62	169	2,3,5-Trimethylhexane	3.724 L62
112	2,2-Dimethylbutane	2.352 L62	170	2,4,4-Trimethylhexane	3.683 L62
113	2,3-Dimethylbutane	2.495 L18	171	3,3,4-Trimethylhexane	3.891 L62
114	n-Heptane	3.173 L3	172	3-Ethyl-2,2-dimethylpentane	3.740 L18
115	2-Methylhexanee	3.001 L9	173	3-Ethyl-2,3-dimethylpentane	3.970 L18
116	3-Methylhexane	3.044 L17	174	3-Ethyl-2,4-dimethylpentane	3.828 L18
117	3-Ethylpentane	3.091 L9	175	2,2,3,3-Tetramethylpentane	3.880 L18
118	2,2,-Dimethylpentane	2.791 L9	176	2,2,3,4-Tetramethylpentane	3.738 L62
119	2,3-Dimethylpentane	3.016 L9	177	2,2,4,4-Tetramethylpentane	3.512 L62
120	2,4-Dimethylpentane	2.809 L62	178	2,3,3,4-Tetramethylpentane	3.910 L18
121	3,3-Dimethylpentane	2.946 L9	179	3,3-Diethylpentane	4.013 L62
122	2,2,3-Trimethylbutane	2.844 L9	180	n-Decane	4.686 L3
126	n-Octane	3.677 L3	181	2-Methylnonane	4.453 L62
127	2-Methylheptane	3.480 L18	182	3-Methylnonane	4.486 L62
128	3-Methylheptane	3.510 L18	183	4-Methylnonane	4.441 L62
129	4-Methylheptane	3.483 L62	184	5-Methylnonane	4.432 L62
130	2,2-Dimethylhexane	3.261 L62	185	2,2-Dimethyloctane	4.225 L62
131	2,3-Dimethylhexane	3.451 L62	186	2,3-Dimethyloctane	4.401 L62
132	2,4-Dimethylhexane	3.319 L62	189	2,6-Dimethyloctane	4.304 L62
133	2,5-Dimethylhexane	3.308 L62	190	2,7-Dimethyloctane	4.282 L62
134	3,3-Dimethylhexane	3.359 L62	191	3,3-Dimethyloctane	4.307 L62
135	3,4-Dimethylhexane	3.495 L62	192	3,4-Dimethyloctane	4.324 L62
136	3-Ethylhexane	3.519 L62	193	3,5-Dimethyloctane	4.259 L62
137	2-Methyl-3-ethylpentane	3.459 L62	194	3,6-Dimethyloctane	4.331 L62
138	3-Methyl-3-ethylpentane	3.502 L62	195	4,4-Dimethyloctane	4.236 L62
139	2,2,3-Trimethylpentane	3.325 L62	197	3-Ethylloctane	4.467 L62
140	2,2,4-Trimethylpentane	3.106 L62	198	4-Ethylloctane	4.409 L62
141	2,3,3-Trimethylpentane	3.428 L62	201	3-Ethyl-2-methylheptane	4.337 L62
142	2,3,4-Trimethylpentane	3.403 L62	203	3-Methyl-3-ethylheptane	4.368 L62
143	2,2,3,3-Tetramethylbutane	3.265 L62	225	3,4,5-Trimethylheptane	4.361 L62

Table 32. Log L16 Values in the Solute Database

No	Compound Name	Log L16 Ref	No	Compound Name	Log L16 Ref
262	4-Propylheptane	4.359 L62	1004	Iso-butene	1.560 L19
265	n-Undecane	5.191 L20	1005	Pent-1-ene	2.047 L53
266	n-Dodecane	5.696 L20	1006	cis-Pent-2-ene	2.211 L18
267	n-Tridecane	6.200 L20	1007	trans-Pent-2-ene	2.180 L19
268	n-Tetradecane	6.705 L20	1008	2-Methylbut-1-ene	2.125 L53
269	n-Pentadecane	7.209 L20	1009	3-Methylbut-1-ene	1.910 L18
270	n-Hexadecane	7.714 L20	1010	2-Methylbut-2-ene	2.262 L18
271	n-Heptadecane	8.218 L20	1015	Hex-1-ene	2.572 L18
272	n-Octadecane	8.722 L20	1016	2-Methylpent-1-ene	2.567 L18
273	n-Nonadecane	9.226 L20	1019	4-Methylpent-2-ene	2.485 L18
274	Eicosane C20H42	9.731 L20	1030	Hept-1-ene	3.063 L26
275	Heneicosane C21H44	10.236 L20	1040	Oct-1-ene	3.568 L18
276	Docosane C22H46	10.740 L20	1041	cis-Oct-2-ene	3.683 L18
286	Dotriacontane C32H66	15.785 L20	1048	2-Ethylhex-1-ene	3.510 L18
501	Cyclopropane	1.314 L9	1051	2,4,4-Trimethylpent-2-ene	3.249 L18
601	Cyclopentane	2.515 L62	1100	Non-1-ene	4.073 L18
602	Methylcyclopentane	2.816 L53	1150	Buta-1,3-diene	1.543 L12
603	1,1-Dimethylcyclopentane	3.029 L62	1152	2-Methylbuta-1,3-diene	2.101 L53
604	1,2-cis-Dimethylcyclopentane	3.273 L62	1153	2,3-Dimethylbuta-1,3-diene	2.690 L19
605	1,2-trans-Dimethylcyclopentane	3.099 L62	1180	cis-Penta-1,3-diene	2.280 L19
606	1,3-cis-Dimethylcyclopentane	3.065 L62	1181	Trans-penta-1,3-diene	2.250 L19
607	1,3-trans-Dimethylcyclopentane	3.075 L62	1300	Cyclopentene	2.402 L53
608	Ethylcyclopentane	3.324 L62	1301	1-Methylcyclopentene	2.864 L53
609	1-Methyl-1-ethylcyclopentane	3.612 L62	1340	Cyclohexene	3.021 L53
701	Cyclohexane	3.007 L55	1341	1-Methylcyclohexene	3.483 L53
702	Methylcyclohexane	3.278 L62	1350	Cycloheptene	3.626 L53
703	1,1-Dimethylcyclohexane	3.582 L62	1351	1-Methylcycloheptene	3.957 L53
704	1,2-cis-Dimethylcyclohexane	3.795 L62	1360	Cyclooctene	4.119 L53
705	1,2-trans-Dimethylcyclohexane	3.634 L62	1361	1-Methylcyclo-octene	4.487 L53
706	1,3-cis-Dimethylcyclohexane	3.533 L62	1400	Cyclopentadiene	2.222 L3
707	1,3-trans-Dimethylcyclohexane	3.655 L62	1500	Limonene	4.500 L28
708	1,4-cis-Dimethylcyclohexane	3.661 L62	1501	α -Pinene	4.200 L29
709	1,4-trans-Dimethylcyclohexane	3.538 L62	1701	Ethyne	0.150 L30
710	Ethylcyclohexane	3.812 L62	1702	Propyne	1.025 L12
711	n-Propylcyclohexane	3.930 L24	1703	But-1-yne	1.520 L20
712	n-Butylcyclohexane	4.270 L18	1704	But-2-yne	1.856 L1
800	Cycloheptane	3.706 L55	1705	Pent-1-yne	2.010 L31
801	Methylcycloheptane	4.034 L53	1720	Hex-1-yne	2.510 L31
820	Cyclooctane	4.314 L55	1740	Hept-1-yne	3.000 L31
821	Cyclononane	4.862 L53	1760	Oct-1-yne	3.480 L31
822	Cyclodecane	5.353 L53	1761	Oct-2-yne	3.850 L32
823	Cycloundecane	5.791 L53	1800	Non-1-yne	3.960 L31
824	Cyclododecane	6.218 L53	1850	Dodec-1-yne	5.657 L32
830	Methylcyclo-octane	4.548 L53	2200	Tetrafluoromethane	-0.800 L34
900	trans-Hydrindane	4.450 L24	2201	Perfluoroethane	-0.230 L20
901	cis-Hydrindane	4.610 L24	2202	Perfluoropropane	0.100 L20
902	Hydrindane	4.530 L25	2203	Perfluoro-n-butane	0.380 L20
903	Adamantane	4.768 L3	2205	Perfluoropentane	0.690 L33
904	trans-Decalin	4.987 L53	2206	Perfluoro-n-hexane	0.924 L33
905	cis-Decalin	5.167 L53	2207	Perfluoro-n-heptane	1.121 L33
906	Decalin	5.077 L53	2208	Perfluoro-n-octane	1.464 L33
1001	Ethene	0.289 L16	2209	Perfluoro-n-nonane	1.771 L33
1002	Propene	0.946 L6	2500	Hydrogen chloride	0.277 L11
1003	But-1-ene	1.491 L20	2501	Chloromethane	1.163 L20

Table 32. Log L16 Values in the Solute Database

No	Compound Name	Log L16 Ref	No	Compound Name	Log L16 Ref
2502	Dichloromethane	2.019 L3	3081	2-Bromooctane	5.110 L19
2503	Trichloromethane	2.480 L3	3090	1-Bromononane	5.560 L31
2504	Tetrachloromethane	2.823 L3	3219	Bromocyclopentane	3.841 L53
2505	Chloroethane	1.678 L20	3220	Bromocyclohexane	4.401 L53
2506	1,1-Dichloroethane	2.316 L51	3221	Bromocycloheptane	5.021 L53
2507	1,2-Dichloroethane	2.573 L3	3222	Bromocyclo-octane	5.485 L53
2508	1,1,1-Trichloroethane	2.733 L51	3302	cis-1,2-Dibromoethene	3.227 L51
2509	1,1,2-Trichloroethane	3.290 L35	3303	trans-1,2-Dibromoethene	3.132 L51
2510	1,1,2,2-Tetrachloroethane	3.803 L3	3306	1-Bromoprop-2-ene	2.510 L3
2511	1,1,1,2-Tetrachloroethane	3.641 L50	3501	Iodomethane	2.106 L3
2512	Pentachloroethane	4.267 L51	3502	Diiodomethane	3.857 L51
2513	Hexachloroethane	4.808 L51	3505	Iodoethane	2.573 L3
2514	1-Chloropropane	2.202 L36	3514	1-Iodopropane	3.130 L38
2515	2-Chloropropane	1.970 L3	3515	2-Iodopropane	2.900 L34
2517	1,2-Dichloropropane	2.857 L37	3530	1-Iodobutane	3.628 L1
2518	1,3-Dichloropropane	3.101 L37	3532	2-Iodobutane	3.390 L19
2530	1-Chlorobutane	2.722 L3	3550	1-Iodopentane	4.130 L31
2531	1-Chloro-2-methylpropane	2.566 L36	3560	1-Iodohexane	4.620 L31
2532	2-Chlorobutane	2.540 L19	3806	1-Iodoprop-2-ene	3.010 L40
2533	2-Chloro-2-methylpropane	2.217 L3	4004	Bromochloromethane	2.445 L51
2550	1-Chloropentane	3.223 L26	4005	Chloriodomethane	2.947 L51
2552	1-Chloro-3-methylbutane	3.094 L50	4040	Bromodichloromethane	2.891 L51
2553	2-Chloro-2-methylbutane	2.858 L50	4042	Dibromochloromethane	3.304 L51
2555	1,5-Dichloropentane	4.632 L65	4050	Fluorotrichloromethane Freon 11	1.930 L34
2560	1-Chlorohexane	3.710 L31	4051	Difluorodichloromethane Freon 1	1.050 L34
2570	1-Chloroheptane	4.210 L31	4052	Trifluorochloromethane Freon 13	0.145 L34
2719	Chlorocyclopentane	3.436 L53	4055	Tribromofluoromethane	3.206 L3
2720	Chlorocyclohexane	3.988 L53	4059	Bromotrichloromethane	3.294 L51
2721	Chlorocycloheptane	4.667 L53	4105	1-Chloro-2-bromoethane	2.982 L51
2722	Chlorocyclo-octane	5.262 L53	4258	Halothane CF3CHBrCl	2.177 L3
2801	1,1-Dichloroethene	2.110 L3	4260	CF3CHFBr teflurane	1.370 L33
2802	cis-1,2-Dichloroethene	2.439 L3	4304	1,1,2-Trifluorotrichloroethane	2.123 L3
2803	trans-1,2,-Dichloroethene	2.278 L3	4306	1,2-Difluorotetrachloroethane	3.000 L34
2804	Trichloroethene	2.997 L3	4501	Dimethylether	1.285 L63
2805	Tetrachloroethene	3.584 L3	4502	Diethylether	2.015 L63
2806	1-Chloroprop-2-ene	2.109 L3	4503	Di-n-propylether	2.954 L63
2807	2-Chloroprop-1-ene	1.729 L50	4504	Di-isopropylether	2.482 L63
2901	1-Chloroprop-2-yne	2.080 L34	4505	Di-n-butylether	3.924 L53
3001	Bromomethane	1.630 L60	4510	Di-n-pentylether	4.875 L53
3002	Dibromomethane	2.855 L51	4511	Di-isopentylether	4.538 L63
3003	Tribromomethane	3.719 L51	4520	Di-n-hexylether	5.938 L27
3004	Tetrabromomethane	4.557 L51	4553	Methyl-n-propyl ether	2.090 L42
3005	Bromoethane	2.120 L3	4554	Methyl-n-butylether	2.630 L19
3007	1,2-Dibromoethane	3.382 L51	4555	Methyl-isobutyl ether	2.442 L63
3014	1-Bromopropane	2.620 L38	4557	Methyl-t-butylether	2.378 L63
3015	2-Bromopropane	2.390 L36	4582	Ethyl-n-butylether	2.989 L63
3030	1-Bromobutane	3.105 L3	4585	Ethyl-t-butylether	2.611 L63
3031	1-Bromo-2-methylpropane	2.960 L36	4601	Propyl-isopropyl ether	2.771 L62
3032	2-Bromobutane	2.933 L36	4620	Isopropyl-t-butyl ether	2.896 L62
3033	2-Bromo-2-methylpropane	2.616 L36	4703	Ethylvinyl ether	1.910 L42
3050	1-Bromopentane	3.611 L1	4706	n-Butylvinyl ether	2.970 L42
3060	1-Bromohexane	4.130 L31	4707	Isobutyl-vinyl ether	2.746 L63
3070	1-Bromoheptane	4.600 L31	4710	2-Ethyl-1-hexyl vinyl ether	4.682 L62
3080	1-Bromooctane	5.090 L31	4722	Ethyl-allyl ether	2.417 L63

Table 32. Log L16 Values in the Solute Database

No	Compound Name	Log L16 Ref	No	Compound Name	Log L16 Ref
4730	Di(2-ethoxyethyl) ether	4.592 L63	5320	Heptanal	3.860 L20
4735	2-Methoxyethyl vinyl ether	2.932 L63	5330	Octanal	4.380 L20
4750	Dimethoxymethane	1.894 L63	5335	2-Ethylhexanal	4.179 L62
4751	Methoxyethoxymethane	2.371 L63	5340	Nonanal	4.900 L20
4752	Diethoxymethane	2.789 L63	5401	Propenal , acrolein	1.656 L63
4754	Methoxyisopropoxymethane	2.697 L63	5402	trans-But-2-ene-1-al (crotonalde	2.570 L29
4759	Ethoxy-n-propoxymethane	3.280 L63	5403	2-Methylpropenal (methacrolein)	2.180 L62
4760	Ethoxyisopropoxymethane	3.093 L63	5415	2-Ethyl-2-butenal	3.436 L62
4761	Di-n-propoxymethane	3.762 L63	5435	2-Ethyl-2-hexenal	4.371 L62
4762	Di-isopropoxymethane	3.376 L63	5450	Hexa-2,4-dienal	3.800 L62
4772	Ethoxy-s-butoxymethane	3.609 L63	5501	Propanone	1.696 L63
4776	n-Propoxy-s-butoxymethane	4.037 L63	5502	Butanone	2.287 L1
4782	Di-n-butoxymethane	4.726 L63	5503	Pentan-2-one	2.755 L1
4783	Di-isobutoxymethane	4.331 L63	5504	Pentan-3-one	2.811 L1
4784	Di-s-butoxymethane	4.380 L63	5505	3-Methylbutan-2-one	2.692 L53
4800	1,1-Dimethoxyethane	2.334 L63	5506	Hexan-2-one	3.262 L20
4801	1,1-Diethoxyethane	3.066 L63	5507	Hexan-3-one	3.271 L53
4802	1,1-Di-n-propoxyethane	3.964 L63	5508	3-Methylpentan-2-one	3.163 L62
4805	1,1-Di-isobutoxyethane	4.491 L63	5509	4-Methylpentan-2-one	3.089 L53
4810	1,1-Dimethoxypropane	2.841 L63	5511	3,3-Dimethylbutan-2-one	2.928 L53
4811	1,1,-Diethoxypropane	3.498 L63	5512	Heptan-2-one	3.760 L3
4820	1,1-Dimethoxybutane	3.313 L63	5513	Heptan-3-one	3.776 L53
4830	2,2-Dimethoxypropane	2.699 L63	5514	Heptan-4-one	3.705 L56
4831	2,2-Diethoxypropane	3.304 L63	5517	5-Methylhexan-2-one	3.605 L53
4851	1,2-Dimethoxyethane	2.565 L63	5525	4,4-Dimethylpentan-2-one	3.344 L53
4855	1,2-Di-n-butoxyethane	5.176 L63	5530	2,4-Dimethylpentan-3-one	3.403 L62
5001	Ethylene oxide	1.371 L63	5535	Octan-2-one	4.257 L3
5002	1,2-Propylene oxide	1.775 L42	5536	Octan-3-one	4.264 L53
5003	2-Methyl-1,2-propylene oxide	2.050 L42	5544	5-Methylheptan-3-one	4.200 L20
5004	1,3-Propylene oxide	2.086 L63	5552	Nonan-2-one	4.735 L90
5005	1,2-Butylene oxide	2.350 L42	5553	Nonan-3-one	4.720 L28
5006	cis-2,3-Butylene oxide	2.290 L42	5555	Nonan-5-one	4.698 L53
5007	trans-2,3-Butylene oxide	2.140 L42	5560	2,6-Dimethylheptan-4-one	4.244 L53
5008	1,3-Butylene oxide	2.360 L42	5570	Decan-2-one	5.245 L53
5090	Methoxyflurane CHCl2CF2OCH3	2.864 L3	5580	Undecan-2-one	5.732 L53
5091	Isoflurane CF3CHClOCF2H	1.576 L3	5584	Undecan-6-one	5.677 L53
5092	Enflurane CHFClCF2OCF2H	1.653 L9	5590	Dodecan-2-one	6.167 L90
5094	Fluroxene CF3CH2OCH=CH2	1.400 L9	5600	Nonadecan-2-one	9.554 L91
5100	[CH2]3 O	2.140 L42	5705	Cyclopentanone	3.221 L55
5110	Tetrahydrofuran [CH2]4 O	2.636 L53	5710	Cyclohexanone	3.792 L53
5111	2-Methyltetrahydrofuran	2.820 L42	5711	2-Methylcyclohexanone	4.055 L53
5113	2,5-Dimethyltetrahydrofuran	2.980 L42	5712	3-Methylcyclohexanone	4.093 L53
5160	Tetrahydropyran [CH2]5 O	3.057 L53	5713	4-Methylcyclohexanone	4.129 L53
5165	Dihydropyran	2.910 L42	5720	Cycloheptanone	4.376 L53
5200	Dioxan	2.892 L63	5725	Cyclooctanone	4.981 L40
5301	Formaldehyde	0.730 L33	5730	Cyclononanone	5.537 L40
5302	Acetaldehyde	1.230 L3	5735	Cyclodecanone	6.063 L40
5303	Propionaldehyde	1.815 L3	5740	Cycloundecanone	6.621 L40
5304	Butyraldehyde	2.270 L3	5745	Cyclododecanone	7.222 L40
5305	Iso-butyraldehyde	2.120 L63	5750	Cyclotridecanone	7.783 L40
5306	Pentanal	2.851 L63	5755	Cyclotetradecanone	8.344 L40
5308	3-Methylbutanal	2.620 L19	5760	Carvone	5.330 L28
5309	2,2-Dimethylpropanal	2.406 L62	5770	But-1-ene-3-one	2.330 L19
5310	Hexanal	3.370 L20	5775	3-Methyl-but-3-ene-2-one	2.691 L63

Table 32. Log L16 Values in the Solute Database

No	Compound Name	Log L16 Ref	No	Compound Name	Log L16 Ref
5780	Hex-5-ene-2-one	3.181 L63	6152	Ethyl butanoate	3.271 L53
5785	Mesityl oxide	3.300 L1	6153	Propyl butanoate	3.783 L53
5800	Butan-2,3-dione (biacetyl)	1.639 L63	6154	Isopropyl butanoate	3.482 L53
5801	Pentan-2,3-dione	2.209 L63	6155	Butyl butanoate	4.275 L53
5802	Acetylacetone , pentan-2,4-dione	2.772 L63	6156	Isobutyl butanoate	4.097 L53
5971	g-Butyrolactone	3.600 L27	6157	s-Butyl butanoate	3.989 L53
6001	Methyl formate	1.285 L63	6158	t-Butyl butanoate	3.695 L53
6002	Ethyl formate	1.845 L53	6159	Pentyl butanoate	4.764 L53
6003	Propyl formate	2.433 L53	6160	2-Pentyl butanoate	4.472 L63
6004	Isopropyl formate	2.230 L24	6162	Isopentyl butanoate	4.597 L53
6005	n-Butyl formate	2.958 L53	6170	2-Ethyl-1-hexyl butanoate	5.856 L63
6006	Isobutyl formate	2.789 L53	6180	Vinyl butanoate	3.191 L63
6007	s-Butyl formate	2.730 L42	6201	Methyl pentanoate	3.442 L45
6008	t-Butyl formate	2.546 L53	6251	Methyl hexanoate	3.984 L45
6009	Pentyl formate	3.488 L53	6252	Ethyl hexanoate	4.194 L60
6010	2-Pentyl formate	3.250 L42	6301	Methyl heptanoate	4.761 L60
6011	3-Pentyl formate	3.266 L62	6365	Methyl isobutanoate	2.636 L53
6012	Isoamyl formate	3.306 L53	6366	Ethyl isobutanoate	3.072 L53
6015	n-Hexyl formate	3.970 L62	6367	n-Propyl isobutanoate	3.555 L53
6030	Allyl formate	2.256 L62	6368	Isopropyl isobutanoate	3.249 L53
6051	Methyl acetate	1.911 L53	6369	n-Butyl isobutanoate	4.068 L53
6052	Ethyl acetate	2.314 L53	6370	Isobutyl isobutanoate	3.885 L53
6053	n-Propyl acetate	2.819 L53	6371	s-Butyl isobutanoate	3.772 L53
6054	Isopropyl acetate	2.546 L53	6372	t-Butyl isobutanoate	3.471 L53
6055	n-Butyl acetate	3.353 L53	6373	n-Pentyl isobutanoate	4.539 L53
6056	Isobutyl acetate	3.161 L53	6380	Isoamyl isopentanoate	4.371 L53
6057	s-Butyl acetate	3.054 L54	6390	Methyl trimethylacetate	2.932 L1
6058	t-Butyl acetate	2.802 L53	6401	Methyl acrylate	2.360 L42
6059	n-Pentyl acetate	3.844 L53	6402	Ethyl acrylate	2.758 L63
6061	3-Pentyl acetate	3.679 L53	6403	Propyl acrylate	3.260 L42
6062	Isoamyl acetate	3.740 L24	6404	Isopropyl acrylate	2.950 L20
6063	2-Methyl-2-butyl acetate	3.340 L62	6405	Butyl acrylate	3.790 L42
6065	n-Hexyl acetate	4.351 L63	6406	Isobutyl acrylate	3.600 L20
6068	4-Methyl-2-pentyl acetate	3.822 L62	6408	2-Ethyl-1-hexyl acrylate	5.445 L63
6069	2-Ethyl-1-butyl acetate	4.178 L62	6410	Allyl acrylate	3.160 L63
6079	2-Ethylhexyl acetate	5.025 L62	6421	Methyl methacrylate	2.880 L42
6080	Vinyl acetate	2.152 L63	6422	Ethyl methacrylate	3.255 L1
6081	Allyl acetate	2.723 L63	6423	n-Propyl methacrylate	3.770 L20
6082	1-Propenyl acetate	2.741 L63	6424	Isopropyl methacrylate	3.460 L20
6083	Isopropenyl acetate	2.611 L63	6425	n-Butyl methacrylate	4.280 L20
6101	Methyl propanoate	2.431 L53	6426	Isobutyl methacrylate	4.090 L20
6102	Ethyl propanoate	2.807 L53	6432	Cyclohexyl acetate	4.454 L63
6103	n-Propyl propanoate	3.338 L53	6451	2-Methoxyethylacetate	3.290 L42
6104	Isopropyl propanoate	3.028 L53	6452	2-Ethoxyethylacetate	3.747 L1
6105	n-Butyl propanoate	3.833 L53	6461	Ethyl acetoacetate	3.752 L1
6106	Isobutyl propanoate	3.635 L63	6470	Methylene diacetate	3.419 L63
6107	s-Butyl propanoate	3.524 L53	6472	Ethylene diacetate	3.937 L63
6108	t-Butyl propanoate	3.244 L53	6474	Ethylene dipropanoate	4.914 L62
6109	n-Pentyl propanoate	4.331 L63	6480	Propylene diacrylate	4.979 L62
6110	2-Pentyl propanoate	4.024 L63	6547	Ethyl chloroacetate	2.559 L3
6112	Isopentyl propanoate	4.153 L53	6601	Acetonitrile	1.739 L53
6130	2-Ethyl-1-hexyl propanoate	5.486 L63	6602	Propionitrile	2.154 L53
6141	Allyl propanoate	3.241 L63	6603	1-Cyanopropane	2.604 L53
6151	Methyl butanoate	2.893 L53	6605	1-Cyanobutane	3.108 L53

Table 32. Log L16 Values in the Solute Database

No	Compound Name	Log L16 Ref	No	Compound Name	Log L16 Ref
6609	1-Cyanopentane	3.608 L53	7616	Octanoic acid	5.000 L46
6610	1-Cyanoheptane	3.980 L31	7617	Nonanoic acid	5.550 L46
6611	1-Cyanoheptane	4.480 L31	7618	Decanoic acid	6.090 L46
6612	1-Cyanooctane	4.970 L31	7619	Undecanoic acid	6.640 L46
6613	1-Cyanononane	5.460 L31	7620	Dodecanoic acid	7.180 L46
6614	1-Cyanodecane	5.940 L31	8000	Water	0.260 L47
6706	Trichloroacetoneitrile	3.677 L1	8001	Methanol	0.970 L64
6800	Ammonia	0.680 L22	8002	Ethanol	1.485 L3
6801	Methylamine	1.300 L19	8003	Propan-1-ol	2.031 L63
6802	Ethylamine	1.677 L3	8004	Propan-2-ol	1.764 L63
6803	n-Propylamine	2.141 L3	8005	Butan-1-ol	2.601 L3
6804	Isopropylamine	1.908 L19	8006	2-Methylpropan-1-ol	2.413 L63
6805	n-Butylamine	2.618 L3	8007	Butan-2-ol	2.338 L17
6806	Isobutylamine	2.469 L19	8008	2-Methylpropan-2-ol	1.963 L63
6807	s-Butylamine	2.410 L3	8009	Pentan-1-ol	3.106 L3
6808	t-Butylamine	2.493 L3	8010	Pentan-2-ol	2.840 L3
6809	n-Pentylamine	3.086 L20	8011	Pentan-3-ol	2.860 L42
6811	n-Hexylamine	3.557 L20	8012	2-Methylbutan-1-ol	3.011 L1
6812	n-Heptylamine	4.050 L20	8013	3-Methylbutan-1-ol	3.011 L1
6813	n-Octylamine	4.520 L20	8014	2-Methylbutan-2-ol	2.630 L1
6831	Allylamine	2.268 L19	8015	3-Methylbutan-2-ol	2.793 L63
6842	Cyclohexylamine	3.574 L19	8016	2,2-Dimethylpropan-1-ol	2.650 L42
6851	Dimethylamine	1.600 L17	8017	Hexan-1-ol	3.610 L3
6852	Diethylamine	2.395 L17	8018	Hexan-2-ol	3.340 L3
6853	Di-n-propylamine	3.372 L17	8019	Hexan-3-ol	3.343 L63
6854	Di-isopropylamine	2.893 L17	8020	2-Methylpentan-1-ol	3.530 L42
6855	Di-n-butylamine	4.349 L19	8022	4-Methylpentan-1-ol	3.500 L20
6882	Methyl-n-propylamine	2.487 L17	8023	2-Methylpentan-2-ol	3.081 L1
6883	Methyl-isopropylamine	2.293 L17	8025	4-Methylpentan-2-ol	3.179 L63
6884	Methyl-n-butylamine	3.049 L17	8026	2-Methylpentan-3-ol	3.240 L42
6901	Trimethylamine	1.620 L3	8027	3-Methylpentan-3-ol	3.277 L1
6902	Triethylamine	3.077 L3	8028	2-Ethylbutan-1-ol	3.523 L53
6904	Tri-n-butylamine	6.050 L19	8029	2,2-Dimethylbutan-1-ol	3.320 L42
6921	Ethyldimethylamine	2.125 L19	8032	2,3-Dimethylbutan-2-ol	3.167 L63
7101	Nitromethane	1.892 L3	8033	3,3-Dimethylbutan-2-ol	3.090 L42
7102	Nitroethane	2.414 L53	8041	Heptan-1-ol	4.115 L3
7103	1-Nitropropane	2.894 L53	8042	Heptan-2-ol	3.842 L3
7104	2-Nitropropane	2.550 L3	8043	Heptan-3-ol	3.860 L42
7105	1-Nitrobutane	3.415 L54	8044	Heptan-4-ol	3.850 L42
7108	2-Methyl-2-nitropropane	2.710 L19	8054	3-Ethylpentan-3-ol	3.785 L63
7109	1-Nitropentane	3.938 L54	8055	2,2-Dimethylpentan-1-ol	3.780 L42
7115	Nitrocyclohexane	4.733 L53	8065	2,4-Dimethylpentan-3-ol	3.603 L63
7251	N,N-Dimethylformamide	3.173 L3	8071	Octan-1-ol	4.619 L3
7261	N,N-Dimethylacetamide	3.717 L3	8072	Octan-2-ol	4.343 L20
7602	Acetic acid	1.750 L46	8078	2-Methylheptan-2-ol	3.990 L40
7603	Propanoic acid	2.290 L46	8088	3-Methyl-3-heptanol	4.000 L19
7604	Butanoic acid	2.830 L46	8091	2-Ethylhexan-1-ol	4.433 L53
7605	2-Methylpropanoic acid	2.670 L63	8092	2-Ethyl-4-methylpentan-1-ol	4.266 L63
7606	Pentanoic acid	3.380 L46	8100	Nonan-1-ol	5.124 L20
7607	2-Methylbutanoic acid	3.260 L63	8130	Decan-1-ol	5.628 L20
7608	3-Methylbutanoic acid	3.140 L63	8131	Decan-2-ol	5.356 L20
7610	Hexanoic acid	3.920 L46	8140	Undecan-1-ol	6.130 L20
7611	2-Methylpentanoic acid	3.680 L63	8145	Dodecan-1-ol	6.640 L20
7615	Heptanoic acid	4.460 L46	8191	Cyclopentanol	3.241 L53

Table 32. Log L16 Values in the Solute Database

No	Compound Name	Log L16 Ref	No	Compound Name	Log L16 Ref
8192	Cyclohexanol	3.758 L53	8502	Ethanthiol	2.173 L47
8193	Cycloheptanol	3.801 L63	8503	n-Propylthiol	2.685 L47
8194	Cyclooctanol	5.054 L53	8504	Isopropylthiol	2.406 L47
8200	1-Methylcyclopentanol	3.279 L53	8505	n-Butylthiol	3.243 L47
8201	1-Methylcyclohexanol	3.806 L53	8506	Isobutylthiol	3.091 L63
8202	2-Methylcyclohexanol	4.110 L42	8508	t-Butylthiol	2.558 L47
8210	1-Methylcycloheptanol	4.402 L53	8509	n-Pentylthiol	3.720 L47
8211	1-Methylcyclo-octanol	4.916 L53	8510	Isopentylthiol	3.360 L47
8251	Prop-2-yne-1-ol	2.050 L42	8511	n-Hexylthiol	4.220 L47
8252	Prop-2-en-1-ol (allyl alcohol)	1.951 L63	8512	n-Heptylthiol	4.720 L47
8253	But-2-en-1-ol (Crotyl alcohol)	2.618 L63	8513	n-Octylthiol	5.270 L28
8254	But-3-ene-1-ol	2.422 L63	8514	n-Nonylthiol	5.790 L28
8255	But-3-ene-2-ol	2.206 L63	8515	n-Decylthiol	6.318 L63
8256	Pent-3-ene-1-ol	3.064 L63	8520	Allyl thiol	2.654 L63
8260	Pent-1-en-3-ol	2.752 L63	8551	Dimethyl sulphide	2.238 L47
8265	Pent-1-ene-4-ol	2.710 L42	8552	Diethyl sulphide	3.104 L47
8266	2-Methylprop-2-ene-1-ol	2.509 L63	8553	Di-n-propyl sulphide	4.120 L47
8267	2-Methyl-but-3-ene-2-ol	2.376 L63	8554	Di-isopropyl sulphide	3.600 L47
8271	Hex-2-ene-1-ol	3.510 L20	8555	Di-n-butyl sulphide	4.950 L47
8281	trans-Hept-2-ene-1-ol	4.010 L20	8557	Di-s-butyl sulphide	4.490 L28
8291	trans-Oct-2-ene-1-ol	4.520 L20	8558	Di-t-butyl sulphide	4.160 L47
8295	2-Methylbut-3-yne-2-ol	2.209 L63	8560	Di-isoamyl sulphide	5.540 L47
8303	2,2,2-Trifluoroethanol	1.224 L3	8571	Methylethyl sulphide	2.730 L47
8323	1,1,1,3,3,3-Hexafluoropropan-2-o	1.392 L3	8572	Methyl-n-propyl sulphide	3.240 L47
8335	Dodecafluoroheptan-1-ol	3.089 L20	8573	Methyl isopropyl sulphide	2.920 L28
8351	2-Chloroethanol	2.630 L42	8574	Methyl n-butyl sulphide	3.590 L28
8431	2-Methoxyethanol	2.490 L42	8581	Ethyl-n-propylsulphide	3.540 L47
8432	2-Ethoxyethanol	2.815 L63	8582	Ethylisopropyl sulphide	3.350 L28
8434	2-Butoxyethanol	3.806 L63	8583	Ethyl n-butyl sulphide	4.030 L28
8436	2-Allyloxyethanol	3.283 L63	8585	Ethyl s-butyl sulphide	3.800 L28
8440	2-Methoxypropan-1-ol	2.793 L63	8586	ETHyl t-butyl sulphide	3.630 L28
8441	2-Ethoxypropan-1-ol	3.115 L63	8610	Diallyl sulphide	3.750 L40
8442	3-Ethoxypropan-1-ol	3.426 L63	8615	Propylene sulphide	2.870 L40
8443	1-Methoxypropan-2-ol	2.655 L63	8622	Tetrahydrothiophen	3.660 L47
8445	1-Propoxypropan-2-ol	3.495 L63	8681	Dimethyl disulphide	3.550 L20
8446	3-Methoxybutan-1-ol	3.398 L63	8682	Diethyl disulphide	4.210 L20
8447	1-Ethoxypentan-3-ol	4.102 L63	8685	Di-n-butyl disulphide	6.030 L47
8448	4-Methoxy-4-methylpentan-2-ol	3.963 L63	8701	Dimethylsulphoxide	3.437 L3
8451	Ethan-1,2-diol	2.661 L62	8790	Sulphur hexafluoride	-0.120 L34
8452	Propan-1,2-diol	2.918 L62	8795	Carbon disulphide	2.353 L3
8453	Propan-1,3-diol	3.263 L62	9112	Triethyl phosphate	4.750 L2
8454	Butan-1,2-diol	3.525 L62	9131	Dimethylmethanephosphonate	3.977 L3
8455	Butan-1,3-diol	3.642 L62	9151	Hexamethylphosphotriamide	5.110 L48
8456	dl-Butan-2,3-diol	3.250 L62	9501	Tetramethylsilane	2.140 L48
8457	meso-Butan-2,3-diol	3.291 L62	9502	Tetraethylsilane	4.330 L48
8458	Butan-1,4-diol	3.795 L62	9521	Tetramethyltin	2.920 L48
8459	2-Methyl-propan-1,2-diol	3.190 L62	9522	Tetraethyltin	5.080 L48
8470	3-Hydroxybutan-2-one	2.771 L63	9542	Tetraethyllead	5.200 L48
8471	4-Hydroxybutan-2-one	3.160 L63	9990	Mercury	1.620 L34
8472	1-Hydroxy-2-methylbutan-3-one	3.573 L63	10001	Benzene	2.803 L3
8473	2-Hydroxy-2-methylbutan-3-one	2.951 L63	10002	Toluene	3.344 L3
8474	4-Hydroxy-4-methylpentan-2-one	3.475 L63	10003	Ethylbenzene	3.789 L62
8490	Geraniol	5.020 L28	10004	o-Xylene	3.942 L62
8500	Hydrogen sulphide	0.529 L10	10005	m-Xylene	3.864 L3

Table 32. Log L16 Values in the Solute Database

No	Compound Name	Log L16 Ref	No	Compound Name	Log L16 Ref
10006	p-Xylene	3.836 L62	11603	1,3-Dichlorobenzene	4.419 L21
10007	n-Propylbenzene	4.229 L62	11604	1,4-Dichlorobenzene	4.446 L53
10008	Isopropylbenzene	4.082 L62	11613	2-Chlorotoluene	4.168 L53
10009	1,2,3-Trimethylbenzene	4.563 L62	11614	3-Chlorotoluene	4.176 L53
10010	1,2,4-Trimethylbenzene	4.438 L62	11615	4-Chlorotoluene	4.197 L53
10011	1,3,5-Trimethylbenzene (mesitylene)	4.316 L62	11617	2,4-Dichlorotoluene	5.008 L60
10012	2-Ethyltoluene	4.362 L49	11619	2,6-Dichlorotoluene	5.026 L60
10013	3-Ethyltoluene	4.274 L62	11620	3,4-Dichlorotoluene	5.089 L60
10014	4-Ethyltoluene	4.285 L49	11650	Benzyl chloride	4.320 L60
10015	n-Butylbenzene	4.686 L20	11651	2-Chlorobenzyl chloride	5.101 L60
10016	Isobutylbenzene	4.486 L62	11661	2-Chloroethylbenzene(b)	4.600 L19
10017	s-Butylbenzene	4.505 L62	11671	2-Chlorostyrene	4.785 L60
10018	t-Butylbenzene	4.427 L62	12601	Bromobenzene	4.035 L3
10019	1,2-Diethylbenzene	4.690 L42	12613	2-Bromotoluene	4.542 L53
10020	1,3-Diethylbenzene	4.680 L19	12614	3-Bromotoluene	4.576 L53
10021	1,4-Diethylbenzene	4.680 L19	12615	4-Bromotoluene	4.581 L53
10022	1,2,4,5-Tetramethylbenzene	5.063 L49	12650	Benzyl bromide	4.660 L3
10023	1,2,3,5-Tetramethylbenzene	5.092 L49	12662	2-Bromo-1-phenylethane	5.134 L53
10024	1,2,3,4-Tetramethylbenzene	5.246 L49	13601	Iodobenzene	4.454 L53
10028	2-n-Propyltoluene	4.579 L49	14001	Methylphenylether	3.859 L53
10029	3-n-Propyltoluene	4.678 L49	14002	Ethylphenylether	4.198 L53
10030	4-n-Propyltoluene	4.703 L49	14150	1,2-Dimethoxybenzene	4.967 L3
10031	2-Isopropyltoluene	4.597 L49	14151	1,3-Dimethoxybenzene	5.022 L3
10032	3-Isopropyltoluene	4.499 L49	14152	1,4-Dimethoxybenzene	5.044 L3
10033	4-Isopropyltoluene	4.534 L53	14401	Benzaldehyde	3.985 L1
10050	n-Pentylbenzene	5.152 L20	14403	3-Methylbenzaldehyde	4.508 L53
10060	t-Pentylbenzene	4.910 L60	14404	4-Methylbenzaldehyde	4.536 L53
10061	Pentamethylbenzene	5.847 L49	14470	Furfural	3.262 L1
10070	4-t-Butyltoluene	4.870 L19	14480	Phenylacetaldehyde	4.287 L53
10080	n-Hexylbenzene	5.617 L20	14481	3-Phenylpropanal	4.861 L53
10085	1,2-Di-isopropylbenzene	5.172 L49	14501	Acetophenone	4.483 L3
10087	1,4-Di-isopropylbenzene	5.240 L49	14601	Ethylphenylketone	4.937 L53
10092	1,3,5-Triethylbenzene	5.375 L49	14602	n-Propylphenylketone	5.312 L53
10180	n-Dodecylbenzene	8.600 L20	14619	Benzylmethylketone	4.628 L53
10300	Styrene	3.863 L61	14625	1-Phenylbutan-2-one	5.085 L53
10301	a-Methylstyrene, PhMeCCH ₃	4.322 L1	14626	4-Phenylbutan-2-one	5.188 L53
10302	trans-b-Methylstyrene	4.559 L49	14801	Methyl benzoate	4.634 L1
10305	4-Vinyltoluene	4.480 L28	14951	Benzyl acetate	4.991 L1
10308	1,4-Divinylbenzene	4.900 L28	15201	Benzonitrile	4.004 L1
10310	Phenylethyne	3.715 L1	15252	Phenylacetonitrile	4.578 L53
10340	Allyl benzene	4.227 L20	15301	Aniline	3.993 L3
10400	Naphthalene	5.149 L53	15302	o-Toluidine	4.494 L60
10440	Tetrahydronaphthalene	5.303 L49	15303	m-Toluidine	4.474 L60
10445	Indene	4.670 L49	15304	p-Toluidine	4.449 L60
10446	1-Methylindene	4.802 L49	15583	2,6-Dimethylaniline	5.037 L19
10449	Indane	4.580 L60	15601	N-Methylaniline	4.494 L1
10450	1-Methylindane	4.884 L49	15602	N-Ethylaniline	4.846 L60
10490	Azulene	5.993 L53	15603	N-Propylaniline	5.338 L60
11501	Fluorobenzene	2.786 L53	15651	N,N-Dimethylaniline	4.754 L2
11504	1,4-Difluorobenzene	2.766 L3	15652	N,N-Diethylaniline	5.343 L60
11510	Hexafluorobenzene	2.528 L3	15662	3-Methyl-N,N-dimethylaniline	5.332 L60
11530	Benzotrifluoride	2.987 L52	15663	4-Methyl-N,N-dimethylaniline	5.287 L60
11601	Chlorobenzene	3.640 L3	15801	Nitrobenzene	4.511 L53
11602	1,2-Dichlorobenzene	4.489 L53	15802	2-Nitrotoluene	4.841 L53

Table 32. Log L16 Values in the Solute Database

No	Compound Name	Log L16 Ref	No	Compound Name	Log L16 Ref
15803	3-Nitrotoluene	5.062 L53	19501	Pyrrole	2.865 L1
15804	4-Nitrotoluene	5.117 L53	19562	N-Methyl-2-pyrrolidinone	4.320 L27
15901	b-Nitrostyrene	6.600 L28	19802	N-Methylimidazole	3.805 L3
15902	b-Methyl-b-nitrostyrene	6.900 L28	20501	Thiophene	2.943 L1
16501	Phenol	3.897 L52	20502	2-Methylthiophen	3.302 L1
16502	o-Cresol	4.242 L3	20505	2,5-Dimethylthiophen	3.806 L1
16503	m-Cresol	4.329 L3			
16504	p-Cresol	4.307 L3			
16505	2,3-Dimethylphenol	4.957 L60			
16506	2,4-Dimethylphenol	4.762 L60			
16508	2,6-Dimethylphenol	4.667 L60			
16509	3,4-Dimethylphenol	4.935 L60			
16516	2,4,6-Trimethylphenol	5.185 L1			
16528	2-Isopropylphenol	4.921 L3			
16544	4-t-Butylphenol	5.340 L1			
16652	3-Fluorophenol	3.844 L3			
16654	2-Chlorophenol	4.937 L1			
16655	3-Chlorophenol	4.650 L1			
16656	4-Chlorophenol	4.630 L46			
16658	3-Bromophenol	5.050 L46			
16659	4-Bromophenol	5.030 L46			
16671	2,6-Difluorophenol	3.693 L3			
16771	3-Cyanophenol	5.020 L46			
16772	4-Cyanophenol	5.000 L46			
16776	2-Nitrophenol	4.684 L3			
16777	3-Nitrophenol	5.470 L46			
16778	4-Nitrophenol	5.450 L46			
16831	Salicylaldehyde	4.750 L24			
17001	Benzyl alcohol	4.249 L52			
17080	1-Phenylethanol	4.362 L53			
17081	2-Phenylethanol	4.578 L53			
17082	3-Phenylpropanol	5.149 L53			
17083	2-Phenylpropan-2-ol	4.504 L53			
17151	Thiophenol	4.118 L1			
18501	Furan	1.830 L1			
18502	2-Methylfuran	2.430 L42			
18551	Benzofuran	4.393 L49			
18651	Benzodioxan	4.985 L32			
18761	Trioxan	2.650 L42			
18762	Paraldehyde	3.169 L63			
19001	Pyridine	3.003 L3			
19002	2-Methylpyridine	3.437 L3			
19003	3-Methylpyridine	3.603 L3			
19004	4-Methylpyridine	3.593 L3			
19006	2,4-Dimethylpyridine	4.050 L31			
19007	2,5-Dimethylpyridine	4.050 L31			
19008	2,6-Dimethylpyridine	3.860 L31			
19009	3,4-Dimethylpyridine	4.360 L31			
19010	3,5-Dimethylpyridine	4.250 L31			
19015	2,4,6-Trimethylpyridine	4.200 L1			
19016	2-Ethylpyridine	3.900 L31			
19017	3-Ethylpyridine	4.130 L31			
19018	4-Ethylpyridine	4.140 L31			
19052	4-t-Butylpyridine	4.750 L31			

References For Table 32.

Ref Code	Reference
L1	Value measured by G. S. Whiting directly on n-hexadecane at 298.15 K.
L2	Retention data measured by G. S. Whiting on Apiezon L at 298.15 K, correlated to give Log L16 value.
L3	Value measured directly on n-hexadecane at 298.15 K by R. A. McGill; M. H. Abraham, P. L. Grellier, R. A. McGill, J. Chem. Soc., Perkin Trans. 2, 1987, 287.
L4	M. H. Abraham and E. Matteoli, survey of results.
L5	Solubility Data Project Series, vols. 1-10, Pergamon, Oxford.
L6	P. J. Lin and J. F. Parcher, J. Chromatogr. Sci., 1982, 20, 33.
L7	L5 and L6.
L8	L4 and L5.
L9	Estimated value using Abraham's Rg parameter.
L10	K. K. Tremper and J. M. Prausnitz, J. Chem. Eng. Data, 1976, 21, 295.
L11	D. Richon and H. Renon, J. Chem. Eng. Data, 1980, 25, 59.
L12	J.-Y. Lenoir, P. Renault, and H. Renon, J. Chem. Eng. Data, 1971, 16, 340.
L13	L4, L6, L11, and L12.
L14	L4, L11, L12, L21 and I. Kikic and H. Renon, Sep. Science, 1976, 11, 45.
L15	L11 and L12.
L16	A. Kwantes and G. W. A. Rijnders in 'Gas Chromatography 1958', ed. D. H. Desty, Butterworths, London, 1958.
L17	D. E. Martire and P. Riedl, J. Phys. Chem., 1968, 72, 3478; J. P. Sheridan, D. E. Martire, and Y. B. Tewari, J. Am. Chem. Soc., 1972, 94, 3294.
L18	N. Dimov, J. Chromatogr., 1985, 347, 366-374, (data corrected to 298 K using dI/dT given). Calculated value from correlation of Log L16 with retention data.
L19	Estimated from vapour pressure/log L16 correlations for closely similar compounds.
L20	Estimated from a correlation of log L with carbon number, for a homologous series.
L21	W. Hayduk and R. Castenada, Can. J. Chem. Eng., 1973, 51, 353; W. Hayduk, E. B. Walter, and P. Simpson, J. Chem. Eng. Data, 1972, 17, 59.
L22	From data in cyclohexane.
L23	L4 and L11.
L24	A. Wehrli and E. Kovats, Helv. Chim. Acta., 1959, 42, 2709-36. Calculated value from correlation of log L16 with retention data.
L25	L24, - the average of the cis and trans isomers.
L26	P. Alessi, I. Kikic, A. Alessandri and M. Fermeglia, J. Chem. Eng. Data, 1982, 24, 445, 448.
L27	Back-calculated from data in iso-octane by - D. J. W. Grant, T. Higuchi, Y. T. Hwang, and J. H. Rytting, J. Solution Chem., 1984, 13, 297.
L28	Approximate estimation.
L29	U. Weldlich and J. Grehling, J. Chem. Eng. Data, 1987, 32, 138-142. Calculated value from correlation of log L16 with retention data.
L30	Y. Miyano and W. Hayduk, Can. J. Chem. Eng., 1981, 59, 746.
L31	F. Riedo, D. Fritz, G. Tarjan, and E. Kovats, J. Chromatogr., 1976, 126, 63-83, (data corrected to 343 K using dI/dT given). Calculated value from correlation of log L16 with retention data.
L32	C. F. Poole, R. M. Pomaville, and T. A. Dean, Analyt. Chim. Acta., 1989, 225, 193.
L33	Estimated from log L olive oil/log L16 correlations for closely similar compounds.
L34	From log L values in alkanes.
L35	L19 and L33.
L36	M. Laffosse and M. Dreux, J. Chromatogr., 1980, 193, 9-18. Calculated value from correlation of log L16 with retention data.
L37	From data by P. Perez, J. Valero, M. Gracia and C. G. Losa, J. Chem. Thermodyn., 1989, 21, 259.
L38	L31 and L36. Average or adjusted value of 2 or more values.
L39	A. Lebert and D. Richon, J. Food Sci., 1984, 39, 1301.
L40	P. Laffort and F. Patte, J. Chromatogr., 1987, 406, 51-74. Calculated value from correlation of log L16 with retention data.
L41	A. Ya. Aarna, L. J. Melder, and A. V. Ebber, Zhur. Prikl. Khim., 1979, 52, 1640 (English Translation p. 1558).
L42	W. O. McReynolds in 'Gas Chromatographic Retention Data', Preston Technical Abstracts Company, USA, 1966. Calculated value from correlation of log L16 with retention data on Squalane at 80°C.

References For Table 32.

Ref Code	Reference
L43	R. I. Sidorov, A. A. Khvostikova, and G. I. Vakhursheva, <i>J. Anal. Chem. USSR</i> , 1973, 28, 1420-1424. Calculated value from the correlation of log L16 with retention data.
L44	L24 corrected slightly to be more in line with homologous series.
L45	R. N. Featherstone, C. Muehlbaeher, F. L. De Bon, and J. A. Forsaith, <i>Anesthesiology</i> , 1961, 22, 977.
L46	From log L (water) plus log P for partition between water and n-hexadecane.
L47	R. V. Golovnya and Y. N. Arsen'ev, <i>Bull. Acad. Sci. USSR, Div. Chem. Sci.</i> , 1972, 1350-52; R. V. Golovnya, V. G. Garbuzov, and T. A. Misharina, <i>Bull. Acad. Sci. USSR, Div. Chem. Sci.</i> , 1976, 2114-2117. Data corrected to 333 K using dI/dT given. Value calculated from log L16 correlation.
L48	From data by M. H. Abraham, P. L. Grellier, and R. A. McGill, <i>J. Chem. Soc., Perkin Trans. 2</i> , 1988, 339.
L49	T.-C. L. Chang and C. Karr, Jr., <i>Analyt. Chim. Acta</i> , 1959, 21, 474 (Calculated from a correlation for aromatic hydrocarbons on Apiezon)
L50	G.f.Harrison, in <i>Vapour Phase Chromatography</i> , ed by D.L.Desty, Butterworths, London, 1957. Calculated through a number of regressions.
L51	G. Castello and T.C.Gerbino, <i>J.Chromatogr.</i> , 1988, 437, 33, using a correlation for a nonpolar phase.
L52	R. Fellous, L. Lizzani-Cuvelier, and R. Luft, <i>Analyt. Chim. Acta</i> . 1985 174, 53. Calculated through a number of regressions.
L53	A. Wehrli and E. Kovats, <i>Helv. Chim. Acta</i> , 1959, 42, 2709, from a regression equation for apiezon.
L54	Average values from ref L31 and L53
L55	P. Urone, J. E. Smith, and R. J. Katnik, <i>Anal. Chem.</i> , 1962, 34, 476, from several regression equations.
L56	D. H. Desty and C. L. Harbourn, <i>Anal. Chem.</i> , 1959, 31, 1965 from the average of two regressions.
L57	E. F. Meyer, K. S. Stec, and R. D. Hotz, <i>J.Phys.Chem.</i> , 1973, 77, 2140, from a correlation with n-tetracosane.
L58	Average of values from regressions using data in ref 51, and J. P. Sheridan, D. E. Martire, and Y. B. Tewari, <i>J. Am. Chem. Soc.</i> , 1972, 94, 3294.
L59	Average of values in ref L3, and from D. E. Martire and L. Z. Pollara, <i>J. Chem. Eng. Data</i> , 1965, 10, 40.
L60	Correlations using data in 'Gas Chromatography Data Compilation', ed O. E. Schupp and J. S. Lewis, ASTM series DS 25A, Philadelphia, 1967.
L61	Average of values in L3, L53, and L60.
L62	A. J. Lubeck and D. L. Sutton, <i>J. High Res. Chromatog</i> , 1983, 6, 328.
L63	Calculated using the inverse matrix method on McReynolds data set, ref 133.
L64	Average of ten back-calculated values, M. H. Abraham and G. S. Whiting, unpublished work.
L65	Value obtained using a correlation with retention data on Apiezon at various temperatures, this work.

6.30 The Construction of a New Solute Parameter Database

The original solute and solvent parameter database, called Params, (a simple layout is shown below in Figure 10), was designed and implemented on the Prime® Mainframe at the University of Surrey.

FIGURE 10. The Layout of the 'Params' Database

1	delta	9	17	-log P	25	R
2	Pi*1	10	beta2	18	log L16	
3	alpha1	11	betaH2	19	μ^2	
4	beta1	12		20	$f(\eta^2)$	
5	deltHsq	13	V25	21	MR	
6	Pi*2	14	V20	22	$f(e)$	
7	alpha2	15	VI	23	μ	
8	alphaH2	16	Vx	24	$\Sigma\beta H2$	

Since the database has now been extensively restructured (please see later in this section), the individual parameters and layout of the Params database will not be further commented on here.

There were only three resident programs used with it, Mreg - a unique multiple regression program specially written for use with the parameter database, Update - to input and/or alter parameters and compounds, and Print - to print out or list on screen and/or printer, compound names and/or parameters. These programs were all written in the Fortran 77 language.

When the research group transferred to University College London (UCL), it was decided to download the database and its' associated programs onto IBM compatible personal computers. This decision was taken for a number of reasons.

① A method was needed of transferring all the information to UCL, and unfortunately the resident Mainframe at UCL was notoriously unreliable, and being replaced at the time.

② It was desired to have the database on computers that would not rely on the performance of the Mainframe, (it was often 'down'). A PC allowed the flexibility of using the database wherever there was an IBM compatible computer. This would necessitate considerable rewriting of the programs associated with the database, as no Fortran compiler could be found directly compatible with that used on the Prime system, but the advantages far outweighed this.

The data was transferred from the Prime Mainframe onto several IBM compatibles using the Kermit® file transfer package. The Ryan-McFarland® Fortran system v.2.43 was subsequently used to compile the extensively rewritten programs on the PCs. Several new programs were also written to increase the flexibility of the database and overcome several of its' major shortcomings. For full working details of these programs, and additional detail on the others previously mentioned, please see Appendix 1.

The system performed satisfactorily initially, but as the database became larger, both in terms of the number of compounds and parameters used, many problems became apparent:-

① As a Fortran 'driven' database with fixed length records, every new compound entered required the same amount of disk space, whether or not every parameter field contained data. As many more compounds were entered Params soon became very large. The larger the file, the more likely that disk write errors, and data corruption would occur. The ease of transfer of

information became more and more difficult, as Params became too big to fit on the floppy disks used (3.5", 720 Kb).

② A 'relational' database system was desirable. That is, the data is no longer stored in one large file, but several smaller ones, linked together by a common field. This allows far greater speed of data processing, flexibility, and data security.

③ There was no real flexibility in adding or deleting data (parameter) fields in Params or entire records (compounds). Many of the solvent and solute parameters were no longer used, and those that were needed extensive referencing to record the parameter origins.

④ The compound numbering system was hopelessly inadequate. For instance, there was not enough space to enter all the phenols, biphenyls etc. that were needed, as all the compound numbers in this region had already been allocated. The numbering system ran from 1 to 4700 uniquely identifying each compound when using the relevant programs, but it needed extending.

⑤ Only rudimentary error checking could be performed to make sure that the correct type of data was entered into each field. This was a frequent cause of data-file corruption.

⑥ The ability to exchange our data with others was limited. We needed to provide data in standard text or Ascii format, or in a widely used database format, such as Dbase III. Exchange of information via a communications package would also be advantageous.

⑦ Display and manipulation of our data was also limited. A great advantage would be to sort the database alphabetically by name, or compound number, or the magnitude of a certain parameter *etc.*

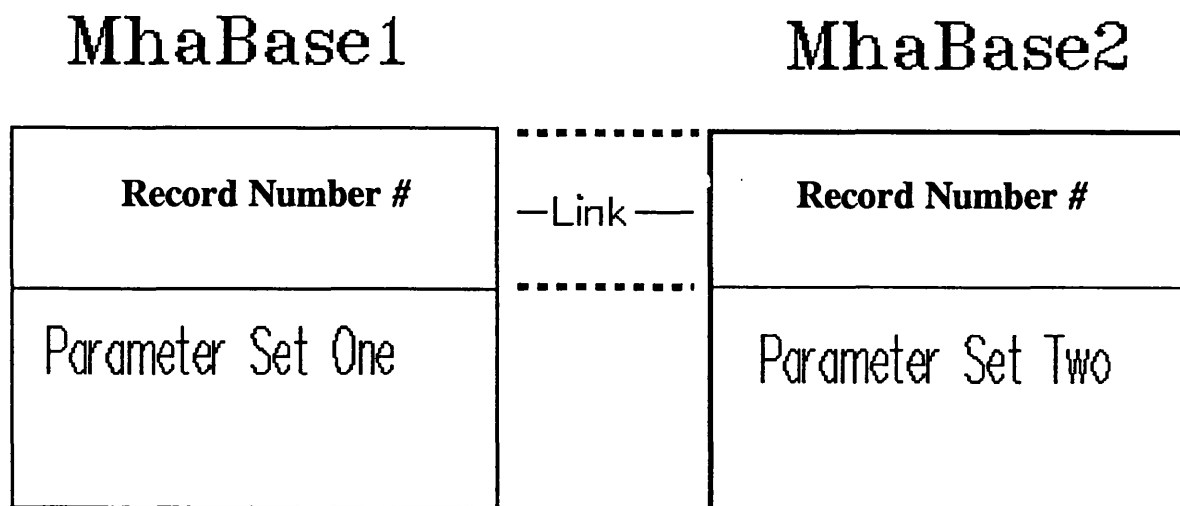
⑧ Integration of data into word-processor packages for reports, or into spreadsheet packages for calculations was difficult.

⑨ Simultaneously, an interactive parameter *reference* database could be designed and implemented.

In the light of these difficulties, it was decided to read the database into a suitable commercially available package that would fulfil all our future requirements. The software chosen was the SmartWare © II integrated package (containing spreadsheet, word-processor, database and communications modules), as this was already in use by us.

A fully relational database system was designed and implemented using Smartware II. Important parameters most often used in were placed in one database file (MhaBase1), and other less important parameters in the other file (MhaBase2), linking the two by the record number, Figure 11.

FIGURE 11. Relational Database Structure - Linking MhaBase1 & MhaBase2



Two data-files in a simple relational database such as this are linked by fields that they both have in common, in this case the field is [Record Number]. This enables viewing of both data-files simultaneously through the link field, and also means that if anything in MhaBase1 is altered that affects Mhabase2 (such as field [Compound Name], MhaBase2 will also be automatically updated (or vice-versa). In effect then, we have two independent databases, which can be updated autonomously, but can link to each other when necessary. Parameters most often used are in MhaBase1, so obviously it is more convenient to work on this database without having to involve other parameters, in MhaBase2. Previously, the whole large database, Params, had to be loaded to make changes to any parameter.

Figure 12 shows the entire database, as it would appear when linked, and then collectively known as MhaBase. There are three distinct parts to it, information contained within the box labeled *MBASE1* (MhaBase1), that within *MBASE2* (MhaBase2), and common information outside these boxes. In the explanation of fields within the database that follows, fields are shown in square brackets, [], and data referred to is from Figure 12, shown in *italics*.

FIELD IDENTITIES IN MhaBase (refer to Figure 12)

Common Data To Both MhaBase1 & Mhabase2

- (1) [Compound Number] - A unique reference number for interactive programs to identify and refer to a particular compound (record): *8002*. Can be altered. If altered, automatic update occurs in both MhaBase1 & Mhabase2.
- (2) [Compound Name]: *Ethanol*. Again, alteration results in update in Mhabase1 & Mhabase2.
- (3) [Old List Number] - As (1), but used in the old Params system. If a

FIGURE 12. Solute Parameter Database, MhaBase (Consisting of MhaBase1 & MhaBase2).

Compound Number 8002 Compound Name Ethanol			
Old List Number 3353	RECORD NUMBER 1 536	RECORD NUMBER 2 536	
Delta 0.0	MBASE1	Log P 1.110	Log P Ref
R 0.246	R Ref R1	Dipole 1.690	Dip Sq 2.856
PiH2* 0.43	PiH2* Ref I1	f(N) 0.221	f(N) Ref
AlphaH2* 0.36	AlH2* Ref A3	MR 0.992	MR Ref
BetaH2* 0.44	BeH2* Ref B1		
Vx 0.4490	Mol Wt 46.0700	Log Poct	Poct Ref
Log L16 1.485	L16 Ref L17	AlphaH2 0.333	AlH2 Ref W1
		Alpha Av	Al Av Ref
		BetaH2 0.440	BeH2 Ref Y4
		Beta Av 0.44	Be Av Ref
		Pi*2 0.40	Pi*2 Ref

compound has on Params list number it is kept, as we have a large number of old compound number files, used to extract information from the parameter database to generate regressions. Its' presence also enables a specially written program to convert old compound number files to the new compound numbering system: 3353. Read only (cannot be edited).

(4) [RECORD NUMBER 1] - Physical record number of record from MhaBase1. This is the order in which records were actually entered into the data-file. In the linked view (MhaBase), this checks that the link is performing properly, as [RECORD NUMBER 1] must equal [RECORD NUMBER2]: 536. Read only. LINK FIELD.

(5) [RECORD NUMBER 2] - Physical record number of record from MhaBase2: 536. Read only. LINK FIELD.

When looking solely at MhaBase1 or only MhaBase2, fields available are (1) to (3), the corresponding [RECORD NUMBER], eg., [RECORD NUMBER 1] if viewing MhaBase1, and the appropriate parameter set, as described below. All parameters following can be edited.

Mhabase1 (MBASE1 in Figure 12)

- (1) [Delta] - δ_2 : 0.0
- (2) [R] - R_2 : 0.246
- (3) [PiH2*] - $\Sigma\pi^H_2$: 0.42
- (4) [AlphaH2*] - $\Sigma\alpha^H_2$: 0.37
- (5) [BetaH2*] - $\Sigma\beta^H_2$: 0.48
- (6) [Vx] - $V_x / 100$: 0.4490
- (7) [Log L16] - $\text{Log } L^{16}$: 1.485

The right-hand side of MBASE1 mainly consists of references for the solute parameters, that refer to the reference database, RefMbase. [Mol Wt] is the solute molecular weight: 46.0700.

Mhabase2 (MBASE2 in Figure 12)

- (1) [Log P] - Minus log solute vapour pressure at 298.15K: 1.110
- (2) [Dipole] - Solute dipole moment (μ), in Debyes: 1.690
- (3) [Dip Sq] - Solute dipole moment squared (μ^2): 2.856
- (4) [f(N)] - Refractive index function, $f(\eta) = (\eta^2-1)/(\eta^2+2)$: 0.221
- (5) [MR] - molar refraction = $10 \cdot f(\eta^2) \cdot [V_X]$: 0.992
- (6) [Log Poct] - log octanol/water partition coefficient.
- (7) [AlphaH2] - Experimentally determined hydrogen bond acidity¹⁰¹: 0.333
- (8) [Alpha Av] - Averaged value of [AlphaH2], actually used in regressions *etc.*
- (9) [BetaH2] - Experimentally determined hydrogen bond basicity¹⁰²: 0.440
- (10) [Beta Av] - Averaged value of [BetaH2], actually used in regressions *etc.*: 0.44
- (11) [Pi*2] - Old solute dipolarity/polarisability parameter⁹⁶⁻⁹⁹: 0.40

Again the right-hand side of MBASE2 mainly consists of references for the solute parameters, references contained in RefMbase.

The solute parameter reference database, RefMbase, is a separate database that is referred to from MhaBase. Every parameter used has a reference to indicate its' origin, where this is appropriate. Some parameters do not need referencing, such as dipole moment, molecular weight, delta and V_X , as these are easily available, or in the case of delta and V_X , trivially calculable. Reference codes are entered into the solute database, where the first character is a mandatory letter, that identifies a reference code to a specific parameter. For instance L identifies a log L^{16} reference, (L3), or A a $\Sigma\alpha^H_2$ reference (A4). References corresponding to these codes are then entered into the solute database RefMbase, where there

are only two fields available, [Ref Code], and [Reference]. Specific references can then be extracted for particular data as necessary. An example of this, for the $\log L^{16}$ parameter, is in section 6.20. See Table 32, pages 153-161, references from RefMbase, pages 162-163.

Smartware II also has fourth generation language (4GL) capabilities, and many programs have been written, for example, to send data across to our modified multiple regression program, SMreg, (Smart parameter database specific). Again, see Appendix 1 for details of these programs. Since we now have a new extended compound numbering system, a program has also been written to convert any old compound number files into new ones, (compound number files are used as the search field in the database to extract information for use in multiple regression).

Currently, the database contains some 2300 compounds, but it is continuously being extended with important monofunctional and multifunctional compounds, and additional key parameters (MhaBase1), to enable wider application of the solvation equations.

7.0 Applications of Solvation Equations

Presented in this section are some of the key and representative applications of the solvation parameters and equations set up during the course of this work. Sections 7.10 to 7.30 are all published work, and are concerned with application of solvation equations using the older parameter set, viz. δ_2 (or in the case of section 7.10, R_2), π_2^* , α^H_2 , β^H_2 , (and V_X and $\log L^{16}$) - not the newer parameters referred to in sections 6.11 to 6.14. Equations generated are therefore presented in sections 7.10 to 7.30 exactly as published. Recasting of the solvation equations using R_2 , $\Sigma\pi^H_2$, $\Sigma\alpha^H_2$, $\Sigma\beta^H_2$, (and V_X and $\log L^{16}$) would not produce very significant changes in the generated coefficients, - see section 6.30, Table 31. Sections 7.40 to 7.60 are concerned with solvation equations using the new parameter set where available, viz. R_2 , $\Sigma\pi^H_2$, $\Sigma\alpha^H_2$, $\Sigma\beta^H_2$, (V_X and $\log L^{16}$), with parameters taken from Table 28.

7.10 Characterisation of Some N-Substituted Amides as Solvents And Comparison With Some GLC Stationary Phases

A number of amides are industrially important solvents, and there are several reports dealing with vapour-liquid equilibria (VLE) of N-substituted amides, especially²¹⁵⁻²²⁰. A particularly convenient method of obtaining VLE data for a series of solutes in a given amide is the gas-chromatographic procedure in which the amide acts as the stationary phase^{215,217-220}. The obtained specific retention volumes, either at the column temperature (V_G) or corrected to 273K (V_G°) can be converted into infinite dilution activity coefficients of the solute in the amide solvent, Φ_2^∞ , at the column temperature, through well-established equations^{215,217-219}. Alternatively, values of V_G can be transformed into Ostwald solubility coefficients, L_2 (equivalent to K), through the very simple equation 90 in which ρ_1 is the density of the amide at the column temperature.

$$L_2 = V_G \cdot \rho_1$$

[90]

For measurements at essentially zero solute concentration, L_2 is effectively L_2^0 , and the concentration of solute in solution becomes identical with the concentration of solute in the pure solvent.

Medina et al.²¹⁷ used both their own GLC measurements and literature data to obtain Φ^∞_2 values for hydrocarbons in N-methylpyrrolidinone (NMP) and were able to account rather well for these Φ^∞_2 values using the group contribution method, UNIFAC. A much more extensive set of solutes was studied by Gmehling et al.^{218,220} with both the amides NMP and N-formylmorpholine (NFM). They obtained V_G° values for a set of hydrocarbons, esters, aldehydes, ketones, and alcohols at various temperatures, and listed both V_G° and Φ^∞_2 values.

Although the calculation of Φ^∞_2 values using methods such as UNIFAC, UNIQUAT, and ASOG is well-established, there is always an over-riding difficulty in the interpretation of parameters that refers to Φ^∞_2 : since Φ^∞_2 is an equilibrium constant (or partition coefficient) between the bulk liquid solute and the solute at infinite dilution in the solvent, Φ^∞_2 will contain not only solute-solvent interactions, but solute-solute interactions as well. As has been pointed out before in section 2.2, gas-liquid partition coefficients contain only the solute-solvent interaction terms, and hence are inherently easier to interpret than quantities that refer to partition between the bulk liquid and the solvent. Since gas-liquid partition coefficients, either as values of L or as Henrys constants, K^H , are convertible into Φ^∞_2 values through the solute vapour pressure, P^0 , and since, in any case, P^0 values are needed to obtain Φ^∞_2 from V_G , it seems a theoretically simpler matter to deal with gas-liquid parameters (such as L , K^H , or V_G) than with Φ^∞_2 .

A start was made with the results of Gmehling et al. on NFM²¹⁸, where V_G^0 values were obtained for 45 solutes at various temperatures, ranging from 303.4K to 373.4K. Not all solutes were studied at all temperatures, and so values have been interpolated, and extrapolated from either 303.4K or 313.3K down to 298.15K to obtain a coherent set of $\log V_G^0$ values at five given temperatures. Explanatory variables are available for all 45 solutes and so the usual general solvation equations 54, 63, and 62 can be applied at each temperature.

$$\log SP = c + d.\delta_2 + s.\pi_2^* + a.\alpha^H_2 + b.\beta^H_2 + 1.\log L^{16} \quad [54]$$

$$\log SP = c + r.R_2 + s.\pi_2^* + a.\alpha^H_2 + b.\beta^H_2 + 1.\log L^{16} \quad [63]$$

$$\log SP = c + r.R_2 + q.\mu^2 + a.\alpha^H_2 + b.\beta^H_2 + 1.\log L^{16} \quad [62]$$

Preliminary results suggested that the solute hydrogen bond basicity, β^H_2 , was not important, as expected on general chemical grounds⁺, and so the equations can be reduced to four explanatory variables.

In the event, neither δ_2 in equation 54 nor R_2 in equation 63 were significant, and so both equations reduce to a three parameter equation in π_2^* , α^H_2 , and $\log L^{16}$. The 45 solutes studied are listed in Table 1^{200, Appendix 2}, and a summary of the regressions is in Table 33. Gmehling et al.²²⁰ repeated some of their measurements of V_G^0 but since there is excellent agreement between the old²¹⁸ and the new²²⁰ sets, V_G^0 values used were all from the earlier set, (for convenience). The use of equation 62 was also investigated, and details are collected in Table 34.

⁺ Neither NFM nor NMP can act as hydrogen bond acids, and hence solute hydrogen bond basicity plays no part in any solute-solvent interactions.

Table 33. Correlations of $\log V_G^0$ for 45 solutes in N-formylmorpholine ²¹⁸ using equations 54 and 63

T/K	c	s	a	l	SD ^a	R ^b
298.2	-0.313	2.311	4.335	0.708	0.122	0.985
	0.107 ^c	0.069	0.216	0.031		
313.3	-0.349	2.153	3.916	0.656	0.114	0.985
	0.101	0.065	0.204	0.029		
332.7	-0.386	1.966	3.430	0.594	0.104	0.985
	0.091	0.059	0.184	0.026		
352.5	-0.425	1.811	2.998	0.536	0.099	0.983
	0.088	0.056	0.177	0.025		
373.4	-0.459	1.645	2.582	0.487	0.094	0.982
	0.083	0.053	0.167	0.024		

^a Overall standard deviation in $\log V_G^0$.

^b Overall correlation coefficient.

^c These are the standard deviations in the various constants.

Table 34. Correlations of $\log V_G^0$ for 45 solutes in N-formylmorpholine ²¹⁸ using equation 62.

T/K	c	r	q	a	l	SD	R
298.2	-0.040	1.756	0.159	4.156	0.621	0.330	0.890
313.3	-0.095	1.659	0.149	3.742	0.572	0.302	0.892
332.7	-0.155	1.534	0.136	3.266	0.516	0.271	0.895
352.5	-0.215	1.432	0.126	2.843	0.464	0.245	0.897
373.4	-0.264	1.337	0.114	2.425	0.417	0.217	0.902

Equations 54 and 63, with δ_2 , R_2 , and β^{H_2} nonsignificant, reproduce the $\log V_G^0$ values with an overall standard deviation of 0.1 log units, at the various temperatures given. Considering that this represents "all solute" correlations, with no outliers, agreement between observed and calculated $\log V_G^0$ is quite satisfactory. These equations could therefore be used to predict further $\log V_G^0$ values for a large number of solutes for which the parameters are available.

Gmehling et al²¹⁸ also reported V_G^0 values in NMP for 31 solutes at 323.4, 333.2 and 343.4K. This data has been similarly analysed, as $\log V_G^0$, and additionally the V_G^0 values were extrapolated down to 298.2K to obtain another regression equation. As with N-formylmorpholine, the parameters δ_2 , R_2 , and β^{H_2} in equations 54 and 63 were not significant, and the latter parameter was not significant in equation 62. Details are in Tables 35 and 36.

Table 35. Correlations of $\log V_G^0$ for 31 solutes on N-methylpyrrolidinone ²¹⁸ using equations 54 and 63.

T/K	c	s	a	l	SD	R
298.2	-0.159 ^a	2.103	5.049	0.779	0.107	0.988
	0.141	0.073	0.241	0.046		
323.4	-0.212	1.883	4.298	0.680	0.096	0.987
		0.126	0.066	0.216	0.041	
333.2	-0.220	1.803	4.016	0.644	0.093	0.986
	0.121	0.063	0.208	0.040		
343.4	-0.246	1.730	3.777	0.612	0.092	0.986
	0.120	0.063	0.206	0.039		

^a For $\log L_{NMP}$, this constant takes the value -0.110

Table 36. Correlations of $\log V_G^0$ for 31 solutes on N-methylpyrrolidinone ²¹⁸ using equation 62.

T/K	c	r	q	a	l	SD	R
298.2	-0.094 ^a	1.422	0.142	5.172	0.785	0.300	0.902
323.4	-0.151	1.300	0.127	4.397	0.683	0.268	0.900
333.2	-0.164	1.254	0.121	4.109	0.647	0.255	0.900
343.4	-0.189	1.215	0.116	3.860	0.613	0.246	0.898

^a For $\log L_{NMP}$, this constant takes the value -0.045

Once again equations 54 and 63 reproduce the $\log V_G^0$ values to about 0.1 log unit, with again no solutes being excluded. Thus equations 54 and 63 with the constants in Table 35 can be used to predict $\log V_G^0$ for further solutes.

In the case of NMP, there is a very considerable quantity of literature data available, mostly on vapour-liquid equilibria^{23,221-232}, and this data can be recast in terms of $\log L_{\text{NMP}}$ at 298K, (where L_{NMP} refers to the Ostwald solubility coefficient of a solute in NMP solvent). Some of this data overlaps with that of Gmehling et al.^{218,220} but in order to have as independent a set of results as possible, Gmehling's data is used as an additional source only[±]. Details of the $\log L_{\text{NMP}}$ values are in Table 6^{200, Appendix 2}, and a summary of our obtained regression equations is in Table 37. Bearing in mind the different set of solutes studied, there is quite good agreement between the various equations in Table 37 and those given before in Tables 35 and 36 (the 31 solutes of Tables 35 and 36 are a subset of the 60 solutes in Table 37).

Table 37. Correlations of $\log L$ for 60 solutes in NMP at 298K ^a

Equation 54	c	d	s	a	l	SD	R
	-0.276	-0.170	2.157	5.134	0.870	0.148	0.995
	0.043	0.089	0.072	0.229	0.017		
Equation 63	c	r	s	a	l	SD	R
	-0.283	0.454	1.998	5.085	0.851	0.137	0.996
	-0.040	0.121	0.072	0.212	0.016		
Equation 62	c	r	q	a	l	SD	R
	-0.195	1.458	0.126	5.676	0.839	0.247	0.985
	0.071	0.198	0.009	0.377	0.029		

^a These are the 60 data entries in Table 6^{200, Appendix 2}.

The constants listed in Table 37 are considered later. Values of $\log L$ for a range of solutes in N,N-dimethylformamide (DMF) and in N,N-dimethylacetamide (DMA) are presented in Table 6^{200, Appendix 2}. These are two additional N-substituted amides for which there are a large number of $\log L$ values at 298K that can be obtained from a variety of additional literature sources^{107,143,233-239}. Values of $\log L_{\text{DMF}}$ and $\log L_{\text{DMA}}$ are collected in

[±] Values of $\log L_{\text{NMP}}$ at 298K were calculated using the equation $\log L_{\text{NMP}} = \log V_G^0 + 0.0499$

Table 6^{200, Appendix 2}. Although there are a reasonable number of hydrogen bond bases in these two sets, there are but few hydrogen bond acids. Since these are very important in characterising phases or solvents that are themselves hydrogen bond bases, a few values of $\log L_{\text{DMF}}$ and $\log L_{\text{DMA}}$ were determined for alcohols by headspace analysis as has been done before ²⁴, see section 1.21.

Log L values for 53 assorted solutes in DMF and for 27 solutes in DMA are available (Table 6^{200, Appendix 2}), and summaries of the obtained regression equations are given in Tables 38 and 39. Bearing in mind the diverse sources of the data used, the correlation equations 54 and 63 lead to quite satisfactory results. These equations could be used as "all solute" correlations to predict further log L values for a variety of solutes. For both DMF and DMA the $r.R_2$ term in equation 63 is not significant, but this may be due to lack of solutes with high R_2 values in the correlations. In general, however, the correlation equations for DMF and DMA follow closely those for NMP, compare Tables 38 and 39 with Table 37. This is exactly as expected, because all three of these amides are quite dipolar and all three are quite strong hydrogen bond bases. From the results shown in Tables 37-39, the amides NMP, DMF, and DMA are of quite similar dipolarity with s-constants 2.00, 2.48, and 2.20 respectively in equation 63, and q-constants 0.126, 0.119, and 0.115 respectively in equation 62. The hydrogen bond basicities of these amides are also very similar being for NMP, DMF, and DMA in the sequence of a-values 5.09, 4.58, and 4.86 (compare the solvent hydrogen bond β_1 basicity values of 0.77, 0.69, and 0.76 respectively) ²³⁹. The other amide studied, NFM, is of about the same dipolarity but of somewhat less basicity than NMP, DMF, and DMA, see Table 40.

Table 38. Correlations of log L for 53 solutes in DMF at 298K ^a

Equation 54	c	d	s	a	l	SD	R
	-0.231	-0.366	2.561	4.612	0.839	0.149	0.994
	0.047	0.109	0.090	0.165	0.021		
Equation 63	c	r	q	a	l	SD	R
	-0.207	-	2.482	4.585	0.829	0.164	0.993
	0.051	-	0.096	0.182	0.023		
Equation 62	c	r	q	a	l	SD	R
	-0.145	1.387	0.119	5.830	0.823	0.233	0.986
	0.072	0.193	0.008	0.244	0.034		

^a These are the 53 data entries in Table 6 ²⁰⁰, Appendix 2.

Table 39. Correlations of log L for 27 solutes in DMA at 298K ^a

Equation 54	c	d	s	a	l	SD	R
	-0.045	-0.346	2.229	4.984	0.802	0.169	0.992
	0.114	0.168	0.128	0.261	0.052		
Equation 63	c	r	s	a	l	SD	R
	-0.001	-	2.196	4.864	0.782	0.181	0.991
	0.120	-	0.136	0.271	0.054		
Equation 62	c	r	q	a	l	SD	R
	-0.003	1.158	0.115	6.222	0.796	0.145	0.994
	0.096	0.153	0.006	0.201	0.044		

^a These are the 27 data entries in Table 6 ²⁰⁰, Appendix 2.

In section 6.11, a number of stationary phases used in GLC were characterised, and it would be of considerable interest to compare such phases with common solvents. The GLC phases were studied at 393K, but the constants in equation 63 obtained for NFM and NMP at lower temperatures can be extrapolated to 393K through excellent plots against 1/T(K), see Table 40.

Table 40. Comparison of characteristic constants for solvents and GLC stationary phases, equation 63.

Solvent	T/K	$r.R_2$	$s.\pi_2^*$	$a.\alpha^H_2$	$l.\log L^{16}$
NFM ^a	298	-	2.31	4.33	0.708
NMP ^b	298	0.45	2.00	5.09	0.851
DMF ^c	298	-	2.48	4.58	0.829
DMA ^d	298	-	2.20	4.86	0.782
NFM ^e	393	-	1.52	2.24	0.442
NMP ^e	393	-	1.42	2.70	0.472
Carbowax ^f	393	0.26	1.37	2.11	0.442
DEGS ^f	393	0.35	1.70	1.92	0.396
PPE ^f	393	0.19	0.98	0.59	0.552
TCEP ^f	393	0.23	2.12	1.94	0.379
ZE7 ^f	393	-0.38	1.61	0.70	0.442

^a Table 33. ^b Table 37. ^c Table 38. ^d Table 39.

^e Extrapolated data from results in Tables 33 and 35. ^f From ref. 181.

It is quite clear from results in Table 40, and from results in Tables 33-36, that characteristic constants in equations such as 63 alter markedly with temperature. In general, it is to be expected that solute-solvent interactions would decrease with rise in temperature, simply as a result of increased thermal motion. Hydrogen bond complexation constants between a given acid and a given base do invariably decrease with increase in temperature. Any decrease in solute-solvent interactions could be due both to effects on the solute and on the solvent. At present, there is no means of separating these, and so the convention used is that any change in a characteristic constant with temperature is due to a change in solvent property only. This does not matter as regards inter-solvent comparisons, but it would be important if absolute values of solvent properties were required.

In Table 40 the constants are listed in equation 63 at 393K for NFM and NMP, together with those for five GLC phases, (see section 6.11). Comments detailed

above on temperature effects are very relevant: at 298K both NFM and NMP appear to be more dipolar and very much more basic than any of the GLC phases. But at a common temperature of 393K, NFM and NMP are somewhat less dipolar than tricyanoethoxypropane (TCEP), diethyleneglycol succinate (DEGS), and zonyl E-7 (ZE7), although more dipolar than polyphenylether (PPE). At 393K, the hydrogen bond basicity of NFM and NMP is not a great deal larger than that of the more basic GLC phases: Carbowax, TCEP, and DEGS. There are no very remarkable values of the l -constant in Table 40: as might be expected, PPE has a reasonably high value of 0.55, DEGS and TCEP the lowest values, with the amides and the other GLC phases in between.

All the solute parameters used in this regression analysis are listed in Table 11^{200, Appendix 2}, (where for 1,4-dioxane, 'effective' values were taken as $\mu^2_2 = 8.5$, and $\pi^*_2 = 0.67$).

In conclusion, application of solvation equations 54, 62 and 63 yield useful information on solute-solvent interactions and the constants in the preferred equation 63, especially, can be used to characterise solvents in terms of such interactions. Previous results, section 6.11, demonstrate that the constants in equation 63 are useful in a general method for characterising condensed phases, and lead, for the first time, to a comparison of GLC stationary phases with common solvents.

Preferred equation 63 can also be used to separate out the various contributions to the observed $\log L$ values for any particular solute. Details for solutes in DMF at 298K are in Table 41, with a number of compounds taken as examples. The $l \cdot \log L^{16}$ term is always very large, and only if the solute π^*_2 value or α^H_2 value is substantial do the $s \cdot \pi^*_2$ and $a \cdot \alpha^H_2$ terms make comparable contributions. Abraham and Fuchs¹⁰⁷ separated out various contributions to the $\log L^{16}$ term,

the two main ones being an exoergic dispersion interaction that leads to an increase in $\log L^{16}$, and an endoergic cavity term that leads to a decrease in $\log L^{16}$. If it is assumed that as a first approximation, the relative sizes of these effects is the same in DMF, the $l.\log L^{16}$ term can be further subdivided into dispersion and cavity effects, Table 41. The results show very clearly that of the exoergic solute-solvent effects considered, the general dispersion interaction is always the most important. In terms of GLC analyses, separations of adjacent members of an homologous series will be governed by differences in dispersion interactions and cavity effects. These two influences are together contained in the $l.\log L^{16}$ term - the larger the value of l , the greater will be the separation between members of an homologous series. Interactions of the dipole-dipole and hydrogen-bonding types will obviously influence separations of solutes of different functionalities, even though in general they are not so large as general dispersion effects.

Table 41. Calculation of the solute-solvent interactions that influence $\log L$ values in DMF at 298K, via equation 63.

Solute	$s.\pi_2^*$	$a.\alpha^H_2$	$l.\log L^{16}$	dispersion ^a	cavity ^a
Butane	0	0	1.34	3.38	-1.47
Octane	0	0	3.05	6.42	-2.69
Benzene	1.46	0	2.32	4.29	-1.56
Propanone	1.76	0	1.46	2.65	-1.19
Propan-1-ol	0.99	1.51	1.74	2.86	-1.29

^a Obtained by analysis of the $l.\log L^{16}$ term according to Abraham and Fuchs¹⁰⁷. The two effects do not exactly add up to $l.\log L^{16}$ because of omission of a constant term, and a small dipole-induced dipole term.

7.20 Application to QSAR Construction for Upper Respiratory Tract Irritation by Airborne Chemicals in Mice.

The most common basis for the establishment of threshold limit values (TLVs) for exposure to airborne chemicals is that of sensory irritation of the eyes, nose, and throat. Many years ago, Alarie^{243,244} used an animal bioassay to evaluate sensory irritating properties of airborne chemicals, and later suggested that TLVs for industrial exposure to airborne chemicals could be recommended on the basis of animal bioassay²⁴⁵. Alarie²⁴⁵ and DeCeaurreiz *et al.*²⁴⁶ both stressed this suggestion in subsequent studies. It is therefore of considerable importance to establish QSARs for results of animal bioassays in the hope that such QSARs will be applicable to TLVs for industrial exposure to airborne chemicals.

A first attempt was made by Muller and Greff²⁴⁷ who analysed the sensory irritation of the upper respiratory tract in male Swiss OF₁ mice by 59 airborne chemicals, using results by DeCeaurreiz *et al.*^{246,248}. These were given in terms of $\log 1/\text{FRD}_{50}$, where FRD_{50} is the concentration in mg/m^3 required to elicit a 50% decrease in respiratory rate. Muller and Greff²⁴⁷ were able to establish correlations between $\log 1/\text{FRD}_{50}$ and such physico-chemical properties as the normal boiling point, but only within families of compound, for example, saturated aliphatic alcohols, or aliphatic ketones. Roberts²⁴⁸ then re-analysed the results used by Muller and Greff²⁴⁷ by first of all recalculating FRD_{50} in units of mmol/m^3 . Using a modified $\log M/\text{FRD}_{50}$, Roberts did manage to establish a general QSAR for non-reactive compounds, equation 91, where M is the irritant molecular weight.

$$\log M/\text{FRD}_{50} = 0.0173T_B - 4.090 \quad [91]$$

$$R = 0.987 \quad \text{SD} = 0.119 \quad N = 42$$

In equation 91, the explanatory variable T'_B is a modified normal boiling point in which T'_B for alcohols is taken as $(26.5T_B/22)-8$ and in which T'_B for phenol is taken as $(24T_B/22)-4$, where T_B is the normal boiling point in °C. Roberts²⁴⁹ explicitly described equation 91 as a QSAR for nonreactive compounds, and excluded all the twelve alkyl acetates studied, as well as methylvinylketone, allyl alcohol, crotyl alcohol, mesityl oxide, and vinyl toluene. Although equation 91 is statistically a good correlation, bearing in mind that the expected error in $\log M/FRD_{50}$ must be around 0.1 log units, it suffers from two marked deficiencies. First of all, the calculation of T'_B is simply a mathematical transformation that displaces parallel lines to the same position. Secondly, and very importantly, equation 91 provides no information at all about the mechanism of toxicity of nonreactive compounds. That is, although equation 91 was referred to as a QSAR²⁴⁹, it actually involves no connection at all between structural features of the irritants and their toxicity.

If only the toxicity of nonreactive compounds are considered, then the process leading to upper respiratory tract irritation may be regarded as akin to a form of partition of a given compound or solute between air and some condensed phase. The general solvation equations 53 and 54 that have already been employed to model the partition behaviour of a series of solutes can then be used. It is worth noting that for compounds that conform to a simple partition model, activity must be proportional to the concentration of the solute in the biophase. All such solutes will bind to the target receptor site with the same intrinsic potency, and the biological effect will be given by the fraction of receptor occupied.

$$\log SP = c + d.\delta_2 + s.\pi_2^* + a.\alpha H_2 + b.\beta H_2 + m.V_x \quad [53]$$

$$\log SP = c + d.\delta_2 + s.\pi_2^* + a.\alpha H_2 + b.\beta H_2 + l.\log L^{16} \quad [54]$$

The FRD₅₀ values of Muller and Greff²⁴⁷ have been recalculated in units of mol l⁻¹ (or mol dm⁻³) and lead to values of log10⁶M/FRD₅₀, denoted as -logFRD'₅₀, in Table 1^{250,Appendix 2}; also given are the parameters used in the calculations that follow. Except for twelve acetate esters, all the compounds studied by Muller and Greff are listed in Table 1^{250,Appendix 2}, *i.e.* 47 compounds.

Applications of equations 53 and 54, where log SP = -logFRD'₅₀, to all 47 compounds leads to regressions with overall correlation coefficients, *r*, of only 0.510 on equation 53 and 0.568 on equation 54. The reason for these poor correlations is obvious - there must be included in the data set compounds that cannot be regarded as nonreactive toxicants. These compounds can be identified as "outliers" because their observed sensory irritation is much larger than values calculated through equation 53 or equation 54. If eight outliers are excluded, then the following regressions are obtained, with V_X in units of cm³ mol⁻¹/100:

$$\begin{aligned} -\log\text{FRD}'_{50} = & -(0.685 \pm 0.236) + (0.768 \pm 0.055)\delta_2 + (2.812 \pm 0.304)\pi_2^* \\ & + (4.929 \pm 0.300)\alpha^{\text{H}_2} + (2.820 \pm 0.090)V_X \quad [92] \end{aligned}$$

$$R = 0.9845 \quad \text{SD} = 0.136 \quad N = 39$$

$$\begin{aligned} -\log\text{FRD}'_{50} = & (0.596 \pm 0.165) + (1.354 \pm 0.224)\pi_2^* + (3.188 \pm 0.209)\delta_2 \\ & + (0.775 \pm 0.019)\log I^6 \quad [93] \end{aligned}$$

$$R = 0.9902 \quad \text{SD} = 0.103 \quad N = 39$$

Equation 93 with three explanatory parameters is clearly superior to equation 92, although the two equations lead to closely similar conclusions. However, in some circumstances, equation 92 might be preferred simply because it is easy to calculate V_X for any compound. The outliers to equation 92 and equation 93 are shown in Tables 42 and 43.

Table 42. Outliers using equation 92, in V_x

Outlier	Obs	-logFRD ₅₀	
		Calc	Δ
methylvinylketone	6.67	3.10	3.57
mesityl oxide	5.60	3.90	1.70
cyclohexanone	4.51	3.88	0.63
allyl alcohol	7.18	3.75	3.43
crotyl alcohol	6.44	4.15	2.29
phenol	5.16	7.25	-2.09
4-vinyltoluene	6.20	4.72	1.48
1,4-divinylbenzene	5.49	5.00	0.49
Included			
β -2-chloroethylbenzene	5.47	5.21	0.36
styrene	4.62	4.32	0.30
α -methylstyrene	4.95	4.78	0.17

Table 43. Outliers using equation 93, in log L ¹⁶

Outlier	Obs	-logFRD ₅₀	
		Calc	Δ
methylvinylketone	6.67	3.35	3.32
mesityl oxide	5.60	4.10	1.50
allyl alcohol	7.18	3.80	3.38
crotyl alcohol	6.44	4.19	2.25
phenol	5.16	6.47	-1.31
4-vinyltoluene	6.20	4.81	1.39
1,4-divinylbenzene	5.49	5.14	0.35
β -2-chloroethylbenzene	5.47	5.11	0.36
Included			
cyclohexanone	4.51	4.43	0.08
styrene	4.62	4.37	0.25
α -methylstyrene	4.95	4.69	0.26

Methylvinylketone, allyl alcohol, crotyl alcohol, mesityl oxide and 4-vinyltoluene are all much more toxic than calculated, by some 1½ to 3½ log units. These five compounds were considered by Roberts ²⁴⁹ also to be outliers, to equation 91, possibly due to their reactive electrophilic character. In the case of 4-vinyltoluene, Roberts ²⁴⁹ suggested the oxidation of the methyl group to an aldehyde group aided by the electrophilic character of the 4-vinyl group. The present analysis suggests that on equation 92 cyclohexanone and

1,4-divinylbenzene are slightly more toxic than calculated and that phenol is much less toxic than calculated. However, on equation 93, the compounds 1,4-divinylbenzene and β -chloroethylbenzene are slightly more toxic than calculated and phenol is, again, decidedly less toxic than calculated. Since equation 93 is theoretically and practically the better equation, cyclohexanone can be discounted as an outlier, and it is suggested that possibly the two compounds 1,4-divinylbenzene and β -chloroethylbenzene may be outliers. The position of these two compounds is marginal as can be seen from a plot of equation 93, shown in Figure 13. If 1,4-divinylbenzene and β -chloroethylbenzene are included, then application of equation 54 yields the regression,

$$\begin{aligned} -\log\text{FRD}'_{50} &= 0.597 \pm 0.199 + (1.287 \pm 0.267)\pi^*_2 + (3.110 \pm 0.251)\alpha^H_2 \\ &\quad + (0.794 \pm 0.022)\log E^6 \quad [94] \\ R &= 0.9860 \quad SD = 0.127 \quad N = 41 \end{aligned}$$

There is not a great deal of difference between equation 93 and equation 94, and it is a moot point whether or not 1,4-divinylbenzene and β -chloroethylbenzene are considered to be slightly reactive toxicants or not.

Phenol, however, is anomalous on all the equations used. It is possible that there is a rather large experimental error associated with phenol. On the other hand, phenols can be efficiently removed from the system by diffusion from the receptor compartment to the blood compartment where the concentration is kept low via conjugation with glucoronides or by sulphation.

A class of compounds not yet considered is that of the alkyl acetates. Roberts²⁴⁹ noted that alkyl acetates did not conform to his QSAR, equation 91, and suggested that the acetates were at least partially hydrolysed under the test

conditions. Analysis of the sensory irritant properties of the alkyl acetates is given in Table 44, and illustrated in Figure 14. As the acetates become less susceptible to hydrolysis along the series MeCO_2R where $\text{R} = \text{Me}, \text{Et}, \text{Pr}^n, \text{Pr}^{\text{iso}}, \text{Bu}^{\text{tert}}$, for example, so do the observed and calculated $-\log\text{FRD}'_{50}$ converge. The hydrolysis products, viz. acetic acid and alcohol, will together certainly be more potent than the ester itself. Thus for ethyl acetate, where the observed value is 4.62 and the calculated value on equation 93 is 3.18 log units, the calculated value for the hydrolysis product is 4.52, and an observed value is 5.18²⁴⁶.

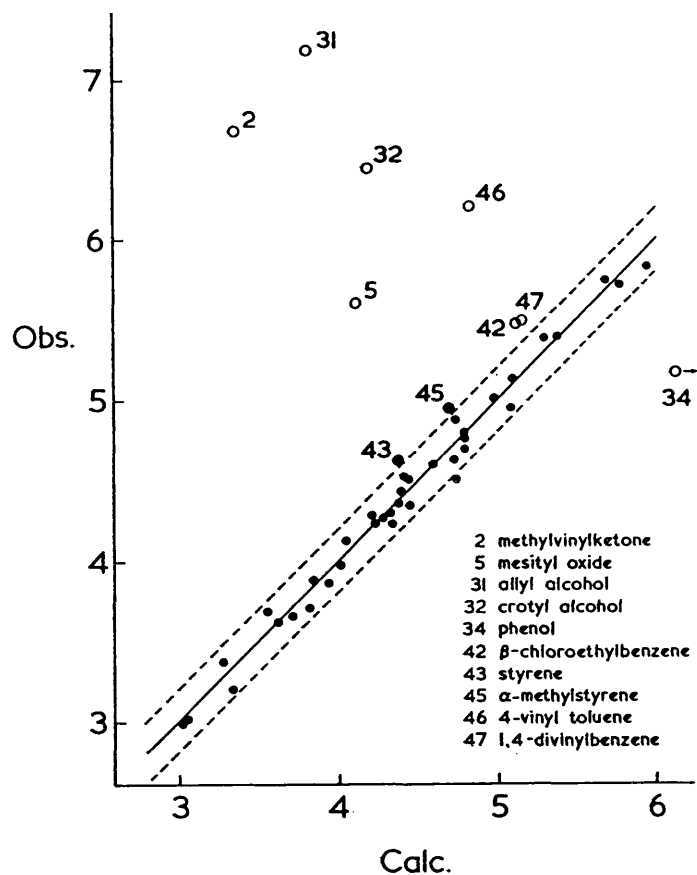
Table 44. Calculations on Alkyl acetates.

R in $\text{CH}_3\text{CO}_2\text{R}$	$-\log\text{FRD}_{50}$		
	Obs	Calc ^a	Δ
Me	4.47	2.93	1.54
Et	4.62	3.18	1.44
n-Pr	4.49	3.57	0.92
iso-Pr	3.76	3.38	0.38
n-Bu	4.52	3.96	0.56
iso-Bu	4.47	3.81	0.66
t-Bu	3.18	3.51	-0.33
n-Pe	4.19	4.29	-0.10
iso-Pe	4.36	4.24	0.12
n-Hexyl	4.52	4.65	-0.13
2-Methoxyethyl	4.63	-	-
2-Ethoxyethyl	4.53	-	-

^a Using equation 93.

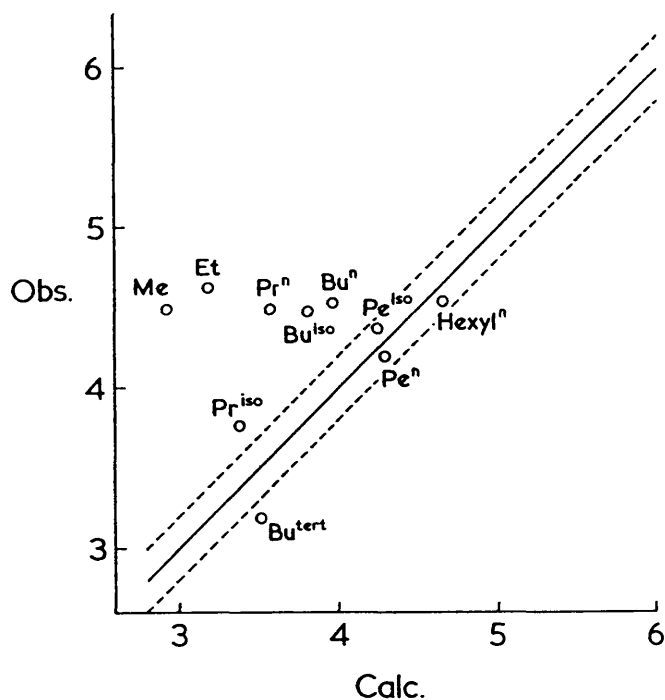
QSAR equation 93 thus seems to provide the basis for a reasonable analysis of the sensory irritation of the upper respiratory tract in male Swiss OF_1 mice by nonreactive compounds. If this model of such nonreactive toxicity as taking place via a process akin to partitioning is in any way realistic, an attempt can be made to interpret the process using equation 93. The partition referred to is simply that of airborne chemicals between the vapour phase and some condensed phase. Now since the hydrogen bond basicity of the solutes is not

FIGURE 13. Observed and Calculated $-\log \text{FRD}\%$ According to Equation 93.



• Included points, ° outliers. The dashed lines show $\pm$ two standard deviations.

Figure 14. Deviations of Alkyl Acetates, $\text{CH}_3\text{CO}_2\text{R}$, from Equation 93.



The dashed lines show two $\pm$ standard deviations.

significant on equation 93, the inference is that the condensed phase, whatever its nature, does not act as a hydrogen bond acid. On the other hand, the coefficient of α^{H_2} in equation 93 is quite large, and hence the condensed phase behaves as a hydrogen bond base.

To provide a point of reference, the coefficients of equation 93 can be compared with those obtained for the partition of vapors between the gas phase and some particular solvent phase. Abraham *et al.*¹⁸⁴ have shown how the general equation 54, where $\log \text{SP} = \log \text{L}$) can be applied to gas-liquid partitions. They gave as an example the solvent tricresylphosphate (TCPH), taking $\log \text{L}(\text{TCPH})$ values at 298 K from Alessi *et al.*²⁵¹.

$$\log \text{L}(\text{TCPH}) = -0.35 - 0.25\delta_2 + 1.71\pi_2^* + 2.98\alpha^{\text{H}_2} + 0.911 \log \text{L}^6 \quad [95]$$

$$R = 0.991 \quad \text{SD} = 0.09 \quad N = 22$$

The analysis of $\log \text{L}$ values for the gas/N-methylpyrrolidinone (NMP) partition using results of Weidlich *et al.*²¹⁸ extrapolated to 298 K, see section 7.10, provides equation 96.

$$\log \text{L}(\text{NMP}) = -0.11 + 2.10\pi_2^* + 5.05\alpha^{\text{H}_2} + 0.779 \log \text{L}^6 \quad [96]$$

$$R = 0.988 \quad \text{SD} = 0.11 \quad N = 31$$

Comparison with equation 93 suggests that the general receptor site acts as a reasonably polar area ($s = 1.354$) and has hydrogen bond basicity about the same as TCPH but less than NMP, with $a = 3.188$ in equation 93. The receptor site is still reasonably hydrophobic with $l = 0.775$ (note that for the gas/hexadecane partition $l = 1$, by definition). Abraham *et al.*¹⁸⁴ also listed a provisional equation for gas/water partition, equation 97. It is very clear, by inspection, that equation 93 resembles equations for gas/organic solvent partitions, as in

equations 95 and 96, but bears little resemblance to equation 97. The main differences are the minor dependence on $\log L^{16}$ and the dependence on β^H_2 in equation 97, the latter dependence due to the strong hydrogen bond acidity of water.

$$\log L(\text{water}) = -1.46 + 3.99\pi^*_2 + 6.10\alpha^H_2 + 3.22\beta^H_2 - 0.060\log L^{16} \quad [97]$$

$$R = 0.989 \quad SD = 0.33 \quad N = 59$$

To conclude, solvation equations can be used to construct a QSAR for nonreactive upper respiratory tract irritation in male Swiss OF₁ mice by airborne chemicals, equation 93, that will allow predictions of $-\log FRD'_{50}$ to be made. It must be noted, however, that predictions may be hazardous if the explanatory variables for the solutes concerned fall outside the range of those studied. Thus Franks and Lieb²⁵² have shown that in the inhibition of firefly luciferase activity by aqueous solutes, there is a definite "cut-off" effect in terms of solute size. Such an effect could not have been predicted by the analysis of a series of solutes all below the critical size. QSAR equation 93 is additionally valuable in that it leads to some understanding of the partition mechanism of toxicity of nonreactive compounds.

7.30 Application to Transfer of Solutes from Hexadecane to Water

The use of water-octanol partition coefficients is widespread in medicinal and pharmaceutical chemistry and, indeed, forms part of the general rational governing most QSAR's^{63,64}. Although water-saturated octanol, according to this rational, is a suitable model for biological membranes, other solvents, and hence other water-solvent partition coefficients, have also been used in QSAR's. For example, Finkelstein²⁵³ and later, Franks and Lieb²⁵² used water-hexadecane partition coefficients, the latter workers specifically to test for hydrophobic binding sites in the luciferase enzyme. In these studies the required water-hexadecane partition coefficients were obtained by the traditional "shake-flask" method. Unlike the water-octanol system, in which the mutual miscibility of the two solvents is quite high, the water-hexadecane system can be regarded as a system containing the two pure solvents (the solubility of water in n-hexadecane is $2 \cdot 10^{-3}$ mol dm⁻³ and that of n-hexadecane in water is $4 \cdot 10^{-9}$ mol dm⁻³)²⁴. Hence water-hexadecane partition coefficients can be determined indirectly using equation 98, where L_W and L_H are the respective gas-solvent Ostwald solubility coefficients $\pm$.

$$P_H = L_H / L_W \quad \text{or} \quad \log P_H = \log L_H - \log L_W \quad [98]$$

Abraham *et. al.*²⁴ and Schantz and Martire²⁵, have shown, almost simultaneously, that values of P_H obtained indirectly via equation 98 are, indeed, identical to values determined by the direct "shake-flask" method. Since values of L_H can be measured very accurately by a gas-chromatographic method using hexadecane as the stationary phase^{24,25}, it is possible from known aqueous solubilities of gases^{16,240,254-256}, to obtain P_H values relatively simply for a wide range of not-too-involatile solutes.

$\pm$ Note that L_H is identical to the symbol L ¹⁶ is the general solvation equation.

One of the aims of this section is to set out values of P_H for water-hexadecane partition of neutral, monomeric solutes, either as $\log P_H$ or as transfer Gibbs energies, ΔG°_{tr} , for as wide a range of solutes as possible. The second aim is to present values for the enthalpy, and hence the entropy, of transfer of examples of these solutes. To date there have been very few sets of ΔG°_{tr} , ΔH°_{tr} , and ΔS°_{tr} values for partition from water to a given solvent. The most substantial set of data is that of Riebesehl and Tomlinson²⁵⁷ who used a direct flow-microcalorimetric method to obtain ΔH°_{tr} values for transfer of 25 solutes from water to 2,2,4-trimethyloctane. Later workers analysed the thermodynamic results of Tomlinson and co-workers^{257,258}, but it was found²⁵⁹ that the data was not extensive enough to examine aliphatic and aromatic solutes separately. Dr. Fuchs²⁶⁰ has obtained ΔH°_{tr} values through a combination of enthalpies of solution in water and in hexadecane, so that values of ΔG°_{tr} , ΔH°_{tr} , and ΔS°_{tr} can be set out for as many solutes as possible. Dr. Fuchs has also used literature data on ΔH°_s values, in water and hexadecane, where possible selecting calorimetrically determined values. Of course, for solutes that are gaseous at room temperature and pressure, ΔH°_s values have nearly always been obtained through the temperature variation of solubility - the so called van't Hoff method - but the method of direct calorimetry is to be preferred.

Values of L_H (L^{16}) for solutes on n-hexadecane at 298.15 were obtained as usual²⁴, see experimental section 9.11). The instruments used were either a Pye-Unicam 104 chromatograph fitted with a katharometer detector, for the determination of absolute L_H values, or a Perkin-Elmer F11 chromatograph fitted with a flame ionisation detector, for the determination of relative L_H values. Suitable calibration then enabled the relative L_H values to be converted into absolute values. All the calorimetric quantities have been determined by Fuchs and Chambers, using the calorimetric equipment and procedure described before²⁶⁰.

Most of the gas solubility data on water were taken from key references ^{16,240,254}, two of which^{16,240} include values for the enthalpy of solution of gases in water. The L_H values used were mostly those determined either previously²⁴ or in this work, but a number of values were also calculated using literature data for closely related solvents such as squalane ²⁶¹⁻²⁶³, $C_{87}H_{176}$ ^{264,265}, octacosane ²⁶⁶, and heptadecane ²⁶⁷. In Table 1^{241,Appendix 2} are collected values of $\log L_W$ and $\log L_H$, together with the calculated $\log P_H$ values, via equation 98. The $\log P_H$ values all refer to the molar concentration scale, as is usual for partition coefficients.

It is trivial to convert $\log P_H$ into the Gibbs energy of transfer, ΔG_{tr} , through

$$\Delta G_{tr}^{\circ}/\text{kcalmol}^{-1} = -1.364 \log R_H \quad [99]$$

Fuchs and Chambers (personal communication) have determined enthalpies of solution of solutes in hexadecane and also in water, and literature data on enthalpies of solution in water has been sourced. Then ΔH_{tr}° is given by,

$$\Delta H_{tr}^{\circ} = \Delta H^{\circ}_{\text{, (in hexadecane)}} - \Delta H^{\circ}_{\text{, (in water)}} \quad [100]$$

Finally, ΔS_{tr}° is obtained by combination of ΔG_{tr}° and ΔH_{tr}° . values of $\log P_H$ are available for some 300 solutes, and values of ΔG_{tr}° , ΔH_{tr}° , and ΔS_{tr}° for a smaller number of solutes for which the necessary data is available, all in Table 1^{241,Appendix 2}. Additional $\log P_H$ values are given in Table 45.

Where necessary, recalculated gas solubilities have been recalculated using standard states of 1 atm (gas) and unit mole fraction (solution), so the ΔG_{tr}° values in Table 1^{241,Appendix 2} refer to the mole fraction concentration scale, a more appropriate scale when calorimetrically determined enthalpies of solution are involved. Enthalpies of solution of liquid solutes were converted into $\Delta H^{\circ}_{\text{,}}$ values for gaseous solutes, using enthalpies of vaporisation at 298K, while ensuring the same $\Delta H^{\circ}_{\text{,}}$ values were used for solution into water and hexadecane.

Table 45^a. Directly determined log P_H values for compounds not in Table 1 ^{241,Appendix 2}.

SOLUTE	$\Delta G^{\circ}_{tr}/\text{kcal mol}^{-1}$	log P _H	Ref.
1,4-Butandiol	4.30	-4.37	253
1,6-Hexandiol	2.80	-3.27	253
Formamide	5.31	-5.10	253
Acetamide	4.73	-4.68	253
n-Butyramide	3.05	-3.44	253
Isobutyramide	3.03	-3.43	253
Urea	5.79	-5.46	253
4-n-Pentylpyridine	-5.26	2.64	b
4-n-Hexylpyridine	-6.12	3.27	b
4-n-Heptylpyridine	-7.00	3.92	b
4-n-Octylpyridine	-7.89	4.57	b
4-n-Nonylpyridine	-8.76	5.21	b
4-n-Decylpyridine	-9.62	5.84	b
Paraldehyde	-1.98	0.24	252
2-Chlorophenol	(-1.52) -1.45	-0.15	c
4-Chlorophenol	(-0.70) -0.63	-0.75	c
4-Chloro-3-methylphenol	(-2.14) -2.07	0.31	c
2-Iodophenol	(-2.28) -2.21	0.41	c
o-Toluidine	-2.17	0.38	d
p-Toluidine	-2.14	0.36	d
2-Methoxyaniline	-2.10	0.33	d
4-Methoxyaniline	-0.92	-0.54	d
2-Chloroaniline	-3.11	1.07	d
3-Chloroaniline	-2.53	0.64	d
4-Chloroaniline	-2.42	0.56	d
2-Nitroaniline	-1.95	0.22	e
Acetophenone	-3.18	1.12 ^g	f
4-Methoxyacetophenone	-2.88	0.90	f
3-Methylacetophenone	-4.00	1.72	f
4-Methylacetophenone	-3.88	1.63	f
4-Fluoroacetophenone	-3.29	1.20	f
3-Chloroacetophenone	-4.40	2.01	f
4-Chloroacetophenone	-3.89	1.85	f
3-Trifluoromethylacetophenone	-4.49	2.08	f
3-Nitroacetophenone	-2.38	0.53	f
4-Nitroacetophenone	-2.59	0.69	f
Biphenyl	-7.37	4.10	25

^a Values of log P_H on the molar scale and ΔG°_{tr} on the mol fraction scale, as in Table 1, reference 241, Appendix 2. ^b K. C. Yeh and W. I. Higuchi, *J. Pharm. Sci.*, 1976, 65, 82. ^c Parenthesised values are for transfer to n-dodecane from D. E. Burton, K. Clarke, and G. W. Gray, *J. Chem. Soc.*, 1964, 1314. The listed values for ΔG°_{tr} and log P_H have been slightly adjusted to correspond to transfer to n-hexadecane, by comparison for phenols for which both transfers were known. ^d W. Kemula, H. Buchowski and W. Pawlowski, *Roczniki Chem.*, 1968, 48, 1951. ^e W. Kemula, H. Buchowski, and J. Terepak, *Bull. Acad. Sci., Polon.*, 1961, 9, 595. ^f Values for transfer to dodecane, J. Toullec, M. El-Alaoui, and P. Kleffert, *J. Org. Chem.*, 1983, 48, 4808. ^g Note the same value (Table 1, reference 241, Appendix 2) for transfer to hexadecane.

The expected error in the log L_H values is very small, probably no more than 0.03 log units. However, there are substantial differences in recorded values for log L_W , even for moderately volatile solutes. Thus for halogenated alkanes, the log L_W values given by Hine and Mookerjee²⁵⁴ and by Mackay and Shiu²⁵⁶ differ randomly by around 0.1 log units, and for hexachloroethane the two recorded values differ by a full log unit (2.87 and 3.89 respectively). Enthalpies of solution, although in the best instances⁺ are capable of leading to ΔH°_{tr} values with an error of only some 0.05 kcal mol⁻¹, can also be subject to very large errors. It is probable that the expected error in ΔG°_{tr} will be around 0.2 kcal mol⁻¹, that in ΔH°_{tr} around 0.5 kcal mol⁻¹, and that in ΔS°_{tr} about 2 cal K⁻¹ mol⁻¹. However, occasionally much larger errors may arise, and this should be borne in mind when results are discussed. The thermodynamics of transfer from water to n-hexadecane are in fact very similar to those for transfer to 2,2,4-trimethylpentane (iso-octane), as found by Tomlinson *et. al.*²⁵⁸. A number of representative solutes are compared in Table 46. Within reasonable error limits, it would seem as though ΔH°_{tr} values are identical for the two transfers, and ΔG°_{tr} average at about the same, although there is more random variation. It would seem that without introducing too much error, values of ΔH°_{tr} and ΔG°_{tr} for transfer to 2,2,4-trimethylpentane, Table 46, could be taken as those for transfer to n-hexadecane.

Tomlinson *et. al.*²⁵⁸ evaluated enthalpy-entropy correlations for transfer to 2,2,4-trimethylpentane through the statistically correct method of plotting ΔG°_{tr} vs. ΔH°_{tr} . Although linear relationships were observed for various homologous series, no general correlation was found between ΔG°_{tr} and ΔH°_{tr} . Using a rather more extended data set the findings of Tomlinson *et. al.*²⁵⁸ were confirmed in this respect. Aliphatic series such as the alkanes, alcohols and ketones form separate linear plots, but aromatic or halogeno-substituted compounds always lie off

⁺ These are nearly always with calorimetrically determined enthalpies of solution of liquid solutes that dissolve readily in water and hexadecane, and not subject to extensive self-association. Note, any error in ΔH°_v cancels out. 1 kcal = 4.184 kJ

the plots for the unsubstituted series. In view of the varied solute-solvent interactions there are possible, it is hardly surprising that the enthalpy-Gibbs energy relationship is rather complicated.

Table 46. Comparison of Thermodynamics of Transfer from Water to Hexadecane and to 2,2,4-Trimethylpentane, molar scale at 298K.

Solute	Hexadecane ^a			2,2,4-Trimethylpentane ^{257,258}		
	ΔG°_{tr}	ΔH°_{tr}	ΔS°_{tr}	ΔG°_{tr}	ΔH°_{tr}	ΔS°_{tr}
Butanone	0.59	4.58	13	0.25	4.54	14
Ethanol	2.99	8.68	19	2.72	8.36	19
Hexan-1-ol	-0.52	6.77	24	-0.74	6.57	24
Aniline	0.05	2.88	9	0.28	3.25	10
Nitrobenzene	-1.96	0.69	9	-1.95	0.67	9
Methyl Benzoate	-2.03	0.88	10	-2.49	0.82	11
Phenol	1.01			1.31	4.64	11
<i>p</i> -Cresol	0.26			0.54	4.51	13
4-Chlorophenol	1.02			0.66	4.11	12
3-Methoxyphenol				1.48	4.46	10
4-Methylaniline				-0.46	3.53	13
4-Chloroaniline				-0.65	2.46	10
N-Methylaniline				-1.41	2.52	13
Methyl phenyl sulphone				1.25	3.21	7
Methyl phenyl sulfoxide				2.03	5.60	12
Ethyl benzoate				-2.76	0.74	12
Benzyl alcohol	0.29	5.87	19	1.04	6.15	17
2-Phenylethanol				0.49	6.03	19
3-Phenylpropan-1-ol				-0.25	6.41	22
Acetophenone	-1.53	1.32	10	-1.52	2.11	12
Benzaldehyde	-1.41	0.95	8	-1.43	0.99	8
Anisole	-2.90	0.00	10	-2.76	0.00	9
Pyridine	0.60	4.13	12	0.56	4.08	12

^a From Tables 1 ²⁴¹, Appendix 2 and 45, after conversion into the molar scale.

Application of general equation 53 to the water-hexadecane partition coefficients leads to the regression equations summarised in Table 47. Note the preferred use of equation 53, as the process examined is one within condensed phases.

$$\log SP = c + d.\delta_2 + s.\pi_2^* + a.\alpha_H + b.\beta_H + v.V_X \quad [53]$$

Table 47. Regression Analysis of Water-Hexadecane Partition Coefficients Using Equation 53 ^a.

Solute Set	<i>c</i>	<i>d</i>	<i>s</i>	<i>a</i>	<i>b</i>	<i>v</i>	<i>R</i>	<i>SD</i>	<i>N</i>
All Solutes	0.26 ±0.06	0.51 ±0.05	-1.45 ±0.09	-3.92 ±0.11	-5.21 ±0.09	4.32 ±0.06	0.9984	0.28	270
Aliphatics only	0.27 ±0.07	0.48 ±0.17	-1.45 ±0.10	-4.11 ±0.14	-5.39 ±0.13	4.39 ±0.07	0.9890	0.28	203
Aromatics only	0.94 ±0.19	-	-1.31 ±0.17	-3.65 ±0.13	-4.74 ±0.17	3.85 ±0.16	0.9913	0.21	67

^a Compounds listed in Tables 1 ²⁴¹, Appendix 2, 45 and 46, with log P_H on the molar scale.

Data analysed includes that of Tomlinson *et. al.*²⁵⁸, to give a total set of 270 compounds, for which all the explanatory variables were available. The probable average experimental error in log P_H is about 0.1, and also the experimental error in the various explanatory variables, an overall correlation coefficient of no more than *ca.* 0.20 log units is all that can be expected. The regression for a total of 270 compounds gives *R* = 0.9984, and *SD* = 0.28, - quite reasonable values. The generated constants are all chemically sensible. Thus, *s*, *a*, and *b* are all very negative, and *v* very positive. This corresponds to solute dipolarity, hydrogen bond acidity, and hydrogen bond basicity leading to a marked preference to water, and solute volume leading to a preference for hexadecane. The total compound set was also analysed in two smaller subsets, aliphatics and aromatics, Table 47. Comparison of the *aliphatic* regression with the *aromatic* reveals there all small, but possibly significant differences between the two, the *aromatic* regression producing smaller constants in *a*, *b* and *v*. Kamlet *et. al.*^{99,268} found that for the aqueous solubility of liquids and solids, different regression equations were required for aliphatic and aromatic compounds⁹⁸, but for water-octanol partition coefficients, log P_{OCT}²⁶⁸, the same regression equation, equation 101, could accommodate both types of solute.

$$\log P_{\text{OCT}} = 0.35 + 0.36\delta_2 - 1.04\pi_2^* + 0.10\alpha_2 - 3.84\beta_2 + 5.35V_t \quad [101]$$

Equation 101 is cast in terms of α_2^{96-99} , β_2^{96-99} and $V_I^{51,52}$, so it would be useful to examine $\log P_{OCT}$ for the same set of solutes in Tables 1^{241,Appendix 2}, 52 and 53, using equation 53. Results are presented in Table 48.

Table 48. Regression Analysis of Water-Octanol Partition Coefficients Using Equation 53 ^a.

Solute Set	<i>c</i>	<i>d</i>	<i>s</i>	<i>a</i>	<i>b</i>	<i>v</i>	<i>R</i>	<i>SD</i>	<i>N</i>
<i>All Solutes</i>	0.20 ±0.06	0.49 ±0.04	-1.24 ±0.08	-0.28 ±0.08	-3.32 ±0.08	3.85 ±0.06	0.9790	0.26	307
<i>Aliphatics only</i>	0.28 ±0.06	0.24 ±0.15	-1.28 ±0.09	-0.48 ±0.13	-3.42 ±0.11	3.84 ±0.06	0.9740	0.27	215
<i>Aromatics only</i>	0.53 ±0.17	-	-0.91 ±0.15	-0.17 ±0.09	-3.30 ±0.14	3.74 ±0.14	0.9782	0.22	92

^a Compounds listed in Tables 1^{241,Appendix 2}, 45 and 46, with $\log P_{OCT}$ on the molar scale.

Results are in reasonable agreement with equation 101, as found by Kamlet *et. al.*²⁶⁸, and there is little difference between the aliphatic and aromatic regression. Note the *v*-constant in Table 48 is much smaller than that in equation 101, since V_X/V_I is *ca.* 0.68⁵².

Comparing the *all solutes* constants in equation 53 obtained for water-hexadecane with water-octanol is quite instructive. The dipolarity of wet octanol is very small, *s*(octanol) is surprisingly almost as negative as *s*(hexadecane). The basicity of wet octanol must be comparable to water, since *a*(octanol) is only -0.28 as compared with *a*(hexadecane) of -3.92. The hydrogen bond acidity of wet octanol is appreciably less than water: *cf.* *b*(hexadecane) = -5.21, *b*(octanol) = -3.21. Finally, the cavity effect, (probably a combined cavity effect plus dispersion interactions) for wet octanol is not far removed from that for hexadecane. To accurately quantify these effects, results on more water-solvent partitions will be needed, (see section 7.40 for more

water-solvent partition analysis), but it can be seen that equation 53 will yield information about various solute-solvent interactions.

A unified set of transfer parameters, ΔG°_{tr} , ΔH°_{tr} , and ΔS°_{tr} were also regressed. 86 such solutes were available for which all the explanatory variables were known, and the summarised regressions using equation 53 are presented in Table 49. Note, constants in the ΔG°_{tr} regression yield the $\log P_H$ constants on division by -1.364, and there is reasonable agreement between the 86 solute correlation in Table 49 and the 270 solute correlation in Table 47.

Table 49. Regression Analysis of ΔG°_{tr} , ΔH°_{tr} , and ΔS°_{tr} for the Water-Hexadecane Partition, Mole Fraction Scale at 298K ^a.

Solute Set	<i>c</i>	<i>d</i>	<i>s</i>	<i>a</i>	<i>b</i>	<i>v</i>	<i>R</i>	<i>SD</i>	<i>N</i>
ΔG°_{tr}	-1.90 ±0.11	-0.69 ±0.12	1.63 ±0.23	5.44 ±0.23	7.06 ±0.25	-5.78 ±0.15	0.9896	0.35	86
ΔH°_{tr}	2.81 ±0.30	-1.73 ±0.33	-2.08 ±0.60	8.11 ±0.62	10.05 ±0.67	-2.43 ±0.41	0.9451	0.94	86
ΔS°_{tr}	15.80 ±0.17	-3.55 ±0.95	-12.84 ±0.15	9.23 ±0.09	10.34 ±0.14	11.28 ±0.14	0.8766	2.73	86
$-T\Delta S^\circ_{tr}$ ^b	-4.71	1.06	3.83	-2.75	-3.08	-3.36			

^a Values from Tables 1²⁴¹, Appendix 2 and 46, ΔG°_{tr} and ΔH°_{tr} in kcal mol⁻¹, ΔS°_{tr} in cal K⁻¹ mol⁻¹. ^b Calculated from the constants in the ΔS°_{tr} regression. The values do not quite yield the $\Delta H^\circ_{tr} - \Delta G^\circ_{tr}$ constants due to rounding-off errors.

The results summarised in Table 49 are somewhat extraordinary. The *s*-constants, viewed as dipolarity effects cannot be easily interpreted on their own, not even in conjunction with the 'correction' constant, *d*. On the one hand, an increase in π^*_2 reduces transfer to hexadecane in terms of ΔG°_{tr} , (or $\log P_H$), but on the other actually aids transfer in terms of ΔH°_{tr} . A difficulty here is that the π^*_2 parameter involves not only dipolarity but also polarisability effects, and that there is an interplay between δ_2 and π^*_2 . The solute hydrogen bond acidity

term, $a.\alpha^H_2$, is rather more straight-forward and can be interpreted as follows. Hydrogen bonding from the solute acid to water base will be exothermic, so ΔH°_{tr} should be positive, as observed. Creation of hydrogen bonds will decrease entropy, resulting in a positive ΔS°_{tr} value, and a ΔG°_{tr} that is still positive, but less so than ΔH°_{tr} . Positive b -constants in ΔG°_{tr} , ΔH°_{tr} , and ΔS°_{tr} can be accounted for by employing exactly the same argument.

Breaking down the $v.V_X$ term into enthalpic and entropic contributions is especially enlightening, as any *hydrophobic* effect must be encompassed by the $v.V_X$ term. According to the scaled particle theory²⁶⁹, the free energy of cavity formation in water, G^W_{CAV} , is much more positive than the corresponding value in a solvent such as hexadecane, G^H_{CAV} . Therefore $G^H_{CAV} - G^W_{CAV}$ is a negative quantity, and will contribute a negative quantity to ΔG°_{tr} . However, the enthalpy of cavity formation in water is smaller than in solvents such as hexadecane, so that $H^H_{CAV} - H^W_{CAV}$ is positive²¹. If the $v.V_X$ term in equation 53 includes not only cavity effects, but also general dispersion interactions, an explanation for its magnitude can be offered. Cavity effects and dispersion interactions will always be more exoergic and exothermic in hexadecane than in water, (note that water has a particularly low refractive index and molar refraction). A combination of an exoergic interaction transfer *with* an exoergic cavity transfer will lead to a very negative $v.V_X$ term in ΔG°_{tr} . But, the combination of an exothermic interaction transfer *with* an endothermic cavity transfer can still result in a negative $v.V_X$ term, but not greatly so. Table 49 shows this trait exactly.

All in all, the rather complicated interplay of the coefficients in the Gibbs energy and enthalpy of transfer indicate that no simple relationship between ΔG°_{tr} and ΔH°_{tr} can be elucidated. This is exactly the same observation as Tomlinson *et al.*²⁵⁸.

7.40 Application to the Characterisation of Solvents and Solvent/Water Partition Coefficients

One of the major undertakings of this work has been to characterise important solvents and to analyse water to solvent partitions. As well as the detailed characterisation of some N-substituted amides, by analysing $\log L$ and V°_G for the partition process $\text{gas} \rightleftharpoons \text{solvent}$ (see section 7.10), other solvents were also characterised in this way, using $\log L$ ($\text{gas} \rightleftharpoons \text{solvent}$). The partition between water and these solvents has also been examined, using $\log P$ ($\text{water} \rightleftharpoons \text{solvent}$). Some of the amides examined in section 7.10 are again presented here. The solvents have been analysed using equations 102 and 103; where the new solvation parameters (π^{H_2} , $\Sigma\alpha^{H_2}$ and $\Sigma\beta^{H_2}$) are available, they have been used.

$$\log L (\text{gas} \rightleftharpoons \text{solvent}) = c + r.R_2 + s.\pi^{H_2} + a.\Sigma\alpha^{H_2} + b.\Sigma\beta^{H_2} + l.\log L^{16} \quad [102]$$

$$\log P (\text{water} \rightleftharpoons \text{solvent}) = c + r.R_2 + s.\pi^{H_2} + a.\Sigma\alpha^{H_2} + b.\Sigma\beta^{H_2} + v.V_X \quad [103]$$

Application of these equations using MLRA is entirely straightforward, yielding coefficients in the usual way. Note the use of preferred equation 103 (with the term $v.V_X$), for processes occurring within condensed phases. Values of $\log L$ for the solubility of gases or vapours in solvents have been extensively collected⁺, along with $\log L_W^\pm$. If $\log L$ for water and solvent is known, then from $P = L_2/L_1$ (section 1.2), where $\log L_W$ is the $\text{gas} \rightleftharpoons \text{water}$ value of $\log L$, the value of P ($\text{water} \rightleftharpoons \text{solvent}$) can be found,

$$P (\text{water} \rightleftharpoons \text{solvent}) = L_{\text{SOLVENT}}/L_W \quad [104]$$

$$\therefore \log P (\text{water} \rightleftharpoons \text{solvent}) = \log L_{\text{SOLVENT}} - \log L_W \quad [105]$$

⁺ The Solubility Data Project Series referenced in Tables 52,54 and 55 for values of $\log L$, published by Pergamon Press, Oxford. Vol 1: Helium & Neon, ed. H. L. Clever, 1979. Vol 2: Krypton, Xenon & Radon, ed. H. L. Clever, 1979. Vol 4: Argon, ed. H. L. Clever, 1980. Vol 6: Oxygen & Ozone, ed. R. Battino, 1981. Vol 8: Oxides of Nitrogen, ed. C. L. Young, 1981. Vol 9: Ethane, ed. W. Hayduk, 1982. Vol 10: Nitrogen & Air, ed. R. Battino, 1982. Vol 21: Ammonia, Amines, Phosphine, Arsine, Stibine, Silane, Germane & Stannane in Organic Solvents, ed. C. L. Young and P. G. T. Fugg, 1985. Vol 27,28: Methane, ed. H. L. Clever and C. L. Young, 1987. Vol 12: Sulphur Dioxide, Chlorine, Fluorine & Chlorine Oxides, ed. C. L. Young, 1983. Vol 24: Propane, Butane and 2-Methylpropane, ed. W. Hayduk, 1986. [±] All values of $\log L_W$ are taken from references 16, 240 and 241.

AMIDES

Solvents examined were N,N-dimethylacetamide (DMA), N,N-dimethylformamide (DMF), N-methylpyrrolidinone (NMP), and N-formylmorpholine (NFM). Summaries of the obtained regression equations are given in Table 50.

Table 50. Characterisation of Amide Solvents.

(A) Correlations of log L (gas $\rightleftharpoons$ solvent) Using Equation 102.

	c	r	s	a	b	l	R	SD	N
DMA ^a	-0.032	0.138	2.020	5.070	-	0.787	0.9987	0.063	28
NMP ^a	-0.306	0.351	2.098	4.975	-	0.838	0.9969	0.107	61
DMF ^a	-0.239	0.084	2.259	4.362	-	0.827	0.9929	0.159	55
NFM ^b	-0.439	0.008	2.567	4.324	-	0.730	0.9955	0.069	45

(B) Correlations of log P (water $\rightleftharpoons$ solvent) Using Equation 103.

	c	r	s	a	b	v	R	SD	N
DMA ^a	0.142	0.535	0.030	0.880	-4.590	3.944	0.9960	0.120	26 ^c
NMP ^a	-0.019	0.885	0.209	1.314	-4.889	3.859	0.9958	0.146	55 ^c
DMF ^a	0.018	0.566	0.386	0.588	-4.791	3.845	0.9924	0.193	51 ^c
NFM ^b	0.017	0.457	0.390	0.418	-4.713	3.389	0.9977	0.115	45

^a Values from reference 200, with additional values for 2-chloro-2-methylpropane and 2-bromo-2-methylpropane from reference 242.

^b Same compound set as in reference 200.

^c N for log P is less than N for log L because some values of log L_w are not available.

From the log L analysis, see Table 50(a), the $b.\Sigma\beta^H_2$ term is shown to be insignificant. All the amides are shown to be reasonably dipolar, s ranging from 2.57 for NFM to 2.02 for DMA, and are strong hydrogen bond bases, DMA being the strongest hydrogen bond base, $a = 5.07$. They are all medium dispersion interactors, with $l < 1.00$ (by definition, $l = 1.00$ for n-hexadecane).

Equation 103 gives constants that are generally chemically reasonable and might be expected, Table 50(b). All the amides have a v -constant around + 4, showing solute volume leads to a preference for amides. The b -constant is large, $b = -4.59$ for DMA to -4.89 for NMP, leading to solute preference, as might be expected, for water. The s -constant is small but positive (solute preference for amide), and r -constants are reasonably large and positive. The a -constants range from 0.42 (NFM) to 1.31 (NMP), showing solute preference for amide; amides are stronger hydrogen bond bases than water. Comparing solvent β_1 values²³⁹, β_1 for water is 0.18, β_1 for DMF and DMA is 0.69 and 0.76 respectively.

ALKANES

The alkanes examined were pentane, hexane, heptane, octane, decane, *iso*-octane and cyclohexane. All these solvents should be reasonably close to our standard non-polar solvent n-hexadecane, but application of equation 102 can still yield useful information, and additionally serve as a check on the method. Summaries of the obtained regression coefficients are in Table 51, and the log L and log P values for alkane solvents are set out in Table 52.

Table 51. Characterisation of Alkane Solvents.

(A) Correlations of log L (gas $\rightleftharpoons$ solvent) Using Equation 102.

	c	r	s	l	R	SD	N
Pentane	0.376	-0.130	-0.229	0.969	0.9989	0.071	30
Hexane	0.313	-0.127	-0.153	0.978	0.9977	0.098	83 ^a
Heptane	0.283	-0.193	-0.271	1.032	0.9991	0.093	78 ^a
Octane	0.238	-0.103	-0.156	0.988	0.9990	0.062	59
Decane	0.168	-0.104	-0.071	0.993	0.9995	0.053	40
Iso-octane	0.283	-0.138	-0.135	0.977	0.9983	0.078	63 ^a
Cyclohexane	0.206	-0.022	-0.040	1.031	0.9983	0.090	71
Cyclohexane	0.203	-	-	1.024	0.9983	0.089	71

(B) Correlations of log P (water $\rightleftharpoons$ solvent) Using Equation 103.

	c	r	s	a	b	v	R	SD	N
Pentane	0.344	0.145	-1.478	-3.419	-5.299	4.631	0.9989	0.108	30
Hexane	0.369	0.635	-1.699	-3.410	-5.034	4.362	0.9971	0.175	81 ^b
Heptane	0.267	0.560	-1.771	-3.439	-5.032	4.594	0.9980	0.120	76 ^b
Octane	0.210	0.574	-1.775	-3.215	-4.954	4.563	0.9978	0.132	58 ^b
Decane	0.099	0.446	-1.496	-3.417	-4.935	4.676	0.9989	0.118	40
Hexadecane ^c	0.076	0.887	-1.773	-3.605	-4.805	4.422	0.9965	0.158	256
Iso-octane	0.273	0.341	-1.580	-3.444	-5.152	4.527	0.9982	0.125	62 ^b
Cyclohexane	0.162	0.847	-1.750	-3.411	-4.773	4.683	0.9967	0.167	66 ^b

^a Less than the number of solutes given in Table 52, as there are still a few log L¹⁶ values missing.

^b Less than the log L regression, as some log L_w values are not available

^c Data from reference 241, provisional regression equation.

In equation 102, the coefficients obtained are all similar to those for solvent n-hexadecane, see Table 51(a), for which *r*, *s*, *a*, and *b* are zero and *l* is 1 by definition. Two regressions have been generated for cyclohexane, the first in *r*, *s*, and *l*, the second in solely *l*. The correlation coefficient and standard deviation are virtually identical, showing clearly that *l*.log L¹⁶ is the only relevant term, as might be expected. Equation 103, see Table 51(b), which in effect compares the (zero) coefficients for alkanes from equation 102 with those of water, again gives coefficients of similar magnitude to those for n-hexadecane. Solute dipolarity, hydrogen bond acidity and basicity favour partition to water, and solute volume partition to alkane solvent.

Table 52. Log L and Log P For Alkane Solvents.

	Pentane		Hexane		Heptane		Octane	
	log L	Log P	Log L	Log P	Log L	Log P	Log L	Log P
Helium	-1.26 ^a	0.76	-1.315 ^a	0.71	-1.38 ^a	0.64	-1.45 ^{a,b}	0.57
Neon	-1.06 ^a	0.90	-1.162 ^a	0.80	-1.23 ^a	0.73	-1.27 ^{a,b}	0.69
Argon	-0.22 ^a	1.25	-0.328 ^a	1.14	-0.38 ^a	1.09	-0.44 ^{a,b}	1.03
Krypton	0.22 ^a	1.44	0.110 ^a	1.32	0.07 ^a	1.28	0.02 ^b	1.23
Xenon	0.71 ^c	1.68	0.683 ^a	1.65	0.64 ^{a,c}	1.61	0.51 ^{a,c}	1.48
Radon			1.137 ^a	1.78				
Hydrogen	-0.85 ^a	0.87	-0.909 ^a	0.81	-0.94 ^a	0.78	-0.99 ^a	0.73
Deuterium					-0.93 ^a	0.80	-0.98 ^a	0.75
Oxygen	-0.36 ^d	1.15	-0.419 ^d	1.09	-0.47 ^d	1.04	-0.50 ^{b,d}	1.01
Nitrogen	-0.53 ^d	1.27	-0.588 ^d	1.21	-0.65 ^d	1.15	-0.71 ^b	1.09
Nitrous oxide	0.61 ^a		0.540 ^a	0.77	0.48 ^a	0.71	0.44 ^a	0.67
Nitric oxide								
Carbon monoxide			-0.494 ^e	1.14	-0.54 ^f	1.09	-0.59 ^b	1.04
Carbon dioxide					0.30 ^g	0.38	0.26 ^b	0.34
Sulphur dioxide					1.00 ^h	-0.55		
Methane			-0.012 ⁱ	1.44			-0.12 ^b	1.33
Ethane	0.74 ^k	2.08	0.76 ^{i,k}	2.10	0.73 ^k	2.07	0.70 ^k	2.04
Propane	1.33 ^k	2.77	1.31 ^{i,k}	2.75	1.30 ^k	2.74	1.28 ^k	2.72
n-Butane	1.91 ^k	3.43	1.84 ^{i,k}	3.39	1.96 ^{k,m}	3.48	1.83 ^k	3.35
2-Methylpropane	1.75 ^k	3.45	1.71 ^{i,k}	3.41	1.69 ^k	3.39	1.68 ^k	3.38
n-Pentane	2.49 ^o	4.19	2.43 ⁱ	4.13	2.36 ^p	4.06	2.30 ^q	4.00
2,2-Dimethylpropane			2.12 ^a	3.96				
n-Hexane	3.02 ^o	4.84	3.02 ⁱ	4.84	2.91 ^p	4.73	2.83 ^q	4.65
2,2-Dimethylbutane			2.67 ^a	4.57				
n-Heptane			3.45 ⁱ	5.41	3.44 ^o	5.40	3.39 ^o	5.35
n-Octane	3.99 ^u	6.10	4.00 ⁱ	6.11	3.95 ^{p,u}	6.06	3.91 ^o	6.02
2,2,4-Trimethylpentane							3.27 ^q	5.44
3,3-Diethylpentane			4.31 ⁱ	5.94				
n-Decane								
Cyclopropane			1.45 ^v	2.00				
Cyclopentane			2.71 ⁱ	3.59				
Methylcyclopentane								
Cyclohexane			3.24 ⁱ	4.14	3.12 ^s	4.02	3.03 ^w	3.93
Methylcyclohexane								
Ethene	0.51 ^k	1.45	0.53 ^{k,x}	1.47	0.52 ^x	1.46	0.44 ^k	1.38
Propene	1.31 ^k	2.28	1.29 ^k	2.26	1.28 ^k	2.25	1.26 ^k	2.23
But-1-ene	1.85 ^k	2.86	1.83 ^k	2.84	1.82 ^k	2.83	1.80 ^k	2.81
Iso-butene	1.82 ^k	2.68	1.78 ^k	2.63	1.79 ^k	2.65	1.77 ^k	2.63
Pent-1-ene					2.31 ^s	3.54	2.27 ^s	3.50
Buta-1,3-diene					1.96 ^y	2.41		
2-Methylbuta-1,3-diene					2.36 ^s	2.86	2.33 ^s	2.83
Ethyne			0.38 ⁿ	0.37				
Fluoroethane					1.06 ^z			
Tetrafluoromethane			-0.40 ^e	1.88	-0.45 ^s	1.83	-0.52 ^b	1.76
Perfluoroethane								
Perfluoropropane								
Perfluorocyclobutane								
Dichloromethane	2.13 ^w	1.17			2.13 ^s	1.17	2.10 ^s	1.14
Trichloromethane			2.65 ^s	1.86	2.65 ^s	1.86	2.58 ^{s,aa}	1.79
Tetrachloromethane			3.03 ^s	3.09	3.00 ^s	3.06	2.92 ^{ab}	2.98
Chloroethane			1.91 ^{ad}	1.45				
1,2-Dichloroethane			2.74 ^{ae,af}	1.43	2.71 ^{s,ag}	1.40	2.71 ^s	1.40
1-Chloropropane			2.47 ^{ad}	2.23	2.41 ^s	2.17	2.36 ^s	2.12
1,2-Dichloropropane			3.05 ^{ah}	2.12				
1,3-Dichloropropane			3.25 ^{ah}	1.86				

Table 52 (cont). Log L and Log P For Alkane Solvents.

	Decane		Iso-octane		Cyclohexane	
	Log L	Log P	Log L	Log P	Log L	Log P
Helium	-1.53 ^b	0.49	-1.34 ^a	0.68	-1.561 ^a	0.47
Neon	-1.37 ^b	0.59	-1.17 ^a	0.79	-1.382 ^a	0.58
Argon	-0.51 ^b	0.96	-0.37 ^a	1.10	-0.475 ^a	0.99
Krypton	-0.03 ^b	1.18	0.07 ^a	1.28	0.025 ^a	1.24
Xenon	0.57 ^c	1.54	0.60 ^a	1.57	0.673 ^a	1.65
Radon						
Hydrogen	-1.09 ^a	0.63	-0.94 ^a	0.78	-1.031 ^a	0.69
Deuterium			-0.93 ^a	0.80		
Oxygen	-0.56 ^b	0.95	-0.41 ^a	1.10	-0.556 ^d	0.95
Nitrogen	-0.82 ^b	0.98	-0.64 ^a	1.15	-0.760 ^d	1.04
Nitrous oxide	0.36 ^a	0.59	0.49 ^a	0.72	0.283 ^a	0.51
Nitric oxide					-0.350 ^a	
Carbon monoxide	-0.68 ^b	0.95			-0.652 ^g	0.98
Carbon dioxide	-0.20 ^b	-0.12			0.233 ^g	0.31
Sulphur dioxide			0.86 ^a	-0.69	0.900 ^a	-0.65
Methane	-0.18 ^b	1.27	-0.10 ^j	1.35	-0.133 ^g	1.32
Ethane	0.65 ^k	1.99	0.65 ^a	1.98	0.72 ^a	2.06
Propane	1.25 ^k	2.69	1.25 ^l	2.69	1.35 ^a	2.79
n-Butane	1.79 ^k	3.31	1.79 ^l	3.30	1.95 ⁿ	3.47
2-Methylpropane	1.64 ^k	3.34			1.71 ^e	3.41
n-Pentane	2.28 ^r	3.98	2.35 ^{s,t}	4.05	2.42 ^e	4.12
2,2-Dimethylpropane						
n-Hexane	2.82 ^r	4.64	2.82 ^t	4.64	2.99 ^e	4.81
2,2-Dimethylbutane	2.48 ^r	4.38				
n-Heptane	3.33 ^r	5.29	3.38 ^t	5.34	3.53 ^e	5.49
n-Octane	3.82 ^u	5.93	3.89 ^u	6.00	4.09 ^{e,u}	6.20
2,2,4-Trimethylpentane			3.36 ^s	5.53		
3,3-Diethylpentane						
n-Decane	4.84 ^o	7.16				
Cyclopropane					1.50 ^v	2.05
Cyclopentane	2.54 ^r	3.42			2.73 ^e	3.61
Methylcyclopentane	2.88 ^r	4.05				
Cyclohexane	3.02 ^r	3.92			3.24 ^o	4.14
Methylcyclohexane	3.35 ^r	4.60				
Ethene	0.42 ^k	1.36				
Propene	1.23 ^k	2.20				
But-1-ene	1.77 ^k	2.78				
Iso-butene	1.73 ^k	2.59				
Pent-1-ene			2.25 ^s	3.48		
Buta-1,3-diene						
2-Methylbuta-1,3-diene			2.33 ^s	2.83		
Ethyne					0.33 ⁿ	0.32
Fluoroethane						
Tetrafluoromethane	-0.63 ^b	1.65	-0.37 ^g	1.92	-0.63 ^g	1.65
Perfluoroethane					-0.26 ^g	2.62
Perfluoropropane					0.14 ^g	3.34
Perfluorocyclobutane					0.69 ^g	3.22
Dichloromethane			2.09 ^s	1.13		
Trichloromethane			2.59 ^s	1.80		
Tetrachloromethane					3.06 ^{ac}	3.12
Chloroethane						
1,2-Dichloroethane					2.83 ^{ac}	1.52
1-Chloropropane			2.36 ^s	2.12	2.52 ^{ac}	2.28
1,2-Dichloropropane					3.15 ^{ah}	2.23
1,3-Dichloropropane					3.31 ^{ah}	1.92

Table 52 (cont). Log L and Log P For Alkane Solvents.

	Pentane		Hexane		Heptane		Octane	
	log L	Log P	Log L	Log P	Log L	Log P	Log L	Log P
1-Chlorobutane	2.99 ^{ai}	2.87	2.94 ^a	2.82	2.91 ^{ag}	2.79		
2-Chloro-2-methylpropane			2.46 ^{ae,aj}	3.26	2.48 ^s	3.28		
1-Chloropentane			3.51 ^{ad}	3.46				
Bromoethane			2.27 ^{s,ad}	1.73	2.23 ^s	1.69	2.19 ^s	1.65
2-Bromo-2-methylpropane			2.75 ^{aj}	3.37				
Iodomethane					2.22 ^s	1.57	2.19 ^s	1.54
Iodoethane			2.72 ^{s,ad,ak}	2.18	2.70 ^s	2.16	2.68 ^s	2.14
1-Iodopropane								
1-Iodobutane								
Difluorodichloromethane Freon 12					1.32 ^g	2.46	1.29 ^g	2.43
Trifluorochloromethane Freon 13					0.44 ^g	2.15	0.39 ^g	2.10
1,2-Difluorotetrachloroethane			3.25 ⁿ		3.20 ^{al}	3.80		
Diethylether								
Di-n-propylether								
Di-n-butylether								
Methyl-n-butylether								
Ethyl-n-butylether								
Dimethoxymethane								
Diethoxymethane								
1,2-Dimethoxyethane								
1,2-Diethoxyethane								
Diethyleneglycol dimethylether								
Tetrahydrofuran [CH ₂] ₄ O	2.62 ^{ao}	0.07	2.69 ^{s,ao}	0.14	2.55 ^{ao}	0.00	2.68 ^s	0.13
Dioxan	2.96 ^u	-0.75	2.98 ^v	-0.73	2.95 ^{u,ao}	-0.76		
Acetaldehyde								
Propionaldehyde							1.86 ^q	-0.66
Butyraldehyde							2.37 ^q	0.04
Pentanal							2.91 ^q	0.69
Hexanal							3.49 ^q	1.43
Propanone							1.85 ^q	-0.94
Butanone	2.51 ^u	-0.21	2.54 ^{s,u}	-0.18	2.52 ^u	-0.20	2.37 ^q	-0.35
Pentan-2-one							2.84 ^q	0.26
4-Methylpentan-2-one							3.18 ^q	0.94
Cyclopentanone					3.32 ^{ar}	-0.13		
Cyclohexanone			3.65 ^s	0.05	3.80 ^{ar}	0.20		
Methyl formate								
Ethyl formate								
Propyl formate								
Ethyl acetate			2.64 ^s	0.48	2.59 ^{s,as}	0.43	2.56 ^{q,s}	0.40
n-Butyl acetate					3.61 ^{as}	1.67		
Acetonitrile			1.77 ^{s,ad}	-1.08	1.62 ^{s,as}	-1.23	1.58 ^{s,aa}	-1.27
Propionitrile			2.22 ^{s,ad}	-0.60	2.10 ^{s,as}	-0.72	2.08 ^s	-0.74
1-Cyanopropane			2.75 ^{ad}	0.08				
1-Cyanobutane			3.26 ^{ad}	0.68				
Ammonia			0.433 ^a	-2.72				
Methylamine			1.20 ^a	-2.14				
Ethylamine			1.68 ^{af}	-1.62				
n-Propylamine			2.26 ^{af}	-0.96				
Isopropylamine			2.04 ^{af}					
n-Butylamine	2.71 ^{at}	-0.40			2.98 ^p	-0.13		
n-Pentylamine					3.48 ^p	0.48		
n-Hexylamine					3.99 ^p	1.09		
n-Heptylamine					4.52 ^p	1.74		
n-Octylamine					5.04 ^p	2.36		
Dimethylamine			1.82 ^a	-1.33				

Table 52 (cont). Log L and Log P For Alkane Solvents.

	Decane		Iso-octane		Cyclohexane	
	Log L	Log P	Log L	Log P	Log L	Log P
1-Chlorobutane					3.05 ^{ac}	2.93
2-Chloro-2-methylpropane					2.47 ^{ac}	3.27
1-Chloropentane						
Bromoethane			2.18 ^s	1.64		
2-Bromo-2-methylpropane					2.84 ^{ac}	3.46
Iodomethane			2.16 ^s	1.50		
Iodoethane			2.66 ^s	2.12	2.97 ^{ak}	2.43
1-Iodopropane					3.39 ^{ac}	3.00
1-Iodobutane					3.77 ^{ac}	3.59
Diffuorodichloromethane Freon 12					1.32 ^g	2.46
Trifluorochloromethane Freon 13					0.35 ^g	2.06
1,2-Difluorotetrachloroethane					3.31 ^{am}	
Diethylether					2.29 ^{an}	1.12
Di-n-propylether					3.36 ^{an}	2.51
Di-n-butylether					4.35 ^{an}	3.74
Methyl-n-butylether					2.88 ^{an}	1.75
Ethyl-n-butylether					3.36 ^{an}	2.06
Dimethoxymethane					2.16 ^{an}	0.01
Diethoxymethane					3.20 ^{an}	
1,2-Dimethoxyethane					2.75 ^{an}	-0.79
1,2-Diethoxyethane					3.40 ^{an}	0.82
Diethyleneglycol dimethylether					4.12 ^{an}	
Tetrahydrofuran [CH ₂] ₄ O			2.71 ^s	0.16	2.66 ^{ao,ap}	0.11
Dioxan	2.91 ^u	-0.80	2.93 ^u	-0.78	3.04 ^{ap,aq}	-0.67
Acetaldehyde			1.38 ^t	-1.19		
Propionaldehyde			1.95 ^t	-0.57		
Butyraldehyde			2.42 ^t	0.09		
Pentanal						
Hexanal						
Propanone			1.84 ^s	-0.95		
Butanone	2.40 ^u	-0.32	2.47 ^u	-0.25	2.55 ^{aq}	-0.17
Pentan-2-one						
4-Methylpentan-2-one						
Cyclopentanone					3.39 ^{ar}	-0.06
Cyclohexanone					3.93 ^{ar}	0.33
Methyl formate			1.53 ^t	-0.51		
Ethyl formate			2.12 ^t	0.24		
Propyl formate			2.68 ^t	0.86		
Ethyl acetate			2.59 ^s	0.43	2.69 ^{ao}	0.53
n-Butyl acetate						
Acetonitrile			1.60 ^s	-1.25		
Propionitrile			2.10 ^s	-0.72		
1-Cyanopropane						
1-Cyanobutane						
Ammonia					0.896 ^a	-2.25
Methylamine						
Ethylamine			1.72 ^t	-1.58		
n-Propylamine			2.22 ^t	-1		
Isopropylamine						
n-Butylamine			2.83 ^t	-0.28		
n-Pentylamine						
n-Hexylamine						
n-Heptylamine						
n-Octylamine						
Dimethylamine	1.69 ^a	-1.46				

Table 52 (cont). Log L and Log P For Alkane Solvents.

	Pentane		Hexane		Heptane		Octane	
	Log L	Log P	Log L	Log P	Log L	Log P	Log L	Log P
Diethylamine			2.62 ^{at}	-0.37				
Trimethylamine			1.93 ^a	-0.42	1.79 ^a	-0.56		
Triethylamine			3.30 ^{s,ak}	0.94	3.28 ^{at}	0.92		
Nitromethane	1.97 ^u	-0.98	2.00 ^{s,u}	-0.95	1.92 ^{s,as}	-1.03	1.99 ^{s,aa}	-0.96
Nitroethane			2.51 ^s	-0.21	2.45 ^{s,as}	-0.27	2.47 ^s	-0.25
1-Nitropropane			2.97 ^s	0.52	2.91 ^{as}	0.46		
2-Nitropropane					2.79 ^{as}	0.49		
Water	0.50 ^{au}	-4.14	0.54 ^{au}	-4.10	0.43 ^{av}	-4.21	0.50 ^{aw}	-4.14
Methanol			1.15 ^{ad}	-2.59	1.20 ^{p,s}	-2.54	1.06 ^{s,aa}	-2.68
Ethanol	1.63 ^{az}	-2.04	1.63 ^u	-2.02	1.64 ^{p,u}	-2.03	1.61 ^{s,aa}	-2.06
Propan-1-ol			2.21 ^{s,ad}	-1.35	2.20 ^{p,ba}	-1.36		
Propan-2-ol			2.02 ^{am}	-1.46	1.91 ^{p,ba}	-1.57		
Butan-1-ol			2.74 ^{ad}	-0.72	2.75 ^p	-0.71		
2-Methylpropan-1-ol					2.58 ^p	-0.72		
Butan-2-ol					2.39 ^p	-1.00		
2-Methylpropan-2-ol					2.21 ^p	-1.07		
Pentan-1-ol					3.33 ^p	-0.02		
Hexan-1-ol			3.55 ^{bd}	0.32	3.87 ^p	0.64		
2-Methylpentan-3-ol								
Decan-1-ol			5.64 ^{bd}	2.97				
Sulphur hexafluoride			0.28 ^s	2.51	0.22 ^g	2.45	0.15 ^s	2.38
Carbon disulphide					2.44 ^s		2.41 ^s	
Hexamethylphosphotriamide			5.41 ^{bg}		5.33 ^{bg}		5.10 ^{bg}	
Tetramethylsilane			2.32 ⁱ	4.55				
Tetraethylsilane			4.64 ⁱ	6.67				
Tetramethyltin			3.03 ⁱ	4.65				
Tetraethyltin			5.14 ⁱ	6.96				
Mercury	1.74 ^a	1.28	1.78 ^a	1.32	1.79 ^a	1.33	1.79 ^a	1.33
Benzene	2.94 ^w	2.29	3.00 ^{w,ac}	2.35	2.93 ^{bh}	2.28	2.88 ^{q,w,bi}	2.23
Toluene	3.46 ^u	2.88	3.48 ^{u,ac}	2.90	3.47 ^u	2.89		
Hexafluorobenzene								
Chlorobenzene					3.79 ^{bk}	2.95		
Pyridine			3.07 ^{ac}	-0.37				
2-Methylpyridine								
3-Methylpyridine								
4-Methylpyridine								
2,6-Dimethylpyridine								

Table 52 (cont). Log L and Log P For Alkane Solvents.

	Decane		Iso-octane		Cyclohexane	
	Log L	Log P	Log L	Log P	Log L	Log P
Diethylamine						
Trimethylamine						
Triethylamine					3.39 ^{ar}	1.03
Nitromethane	1.92 ^u	-1.03	1.97 ^u	-0.98	2.02 ^{aq}	-0.93
Nitroethane			2.47 ^u	-0.25		
1-Nitropropane						
2-Nitropropane					2.84 ^{ae}	0.54
Water	0.35 ^{au}	-4.29	0.26 ^{aw}	-4.38	0.37 ^{aw}	-4.27
Methanol	1.03 ^{ax}	-2.71	1.06 ^s	-2.68	1.50 ^{ay}	-2.24
Ethanol	1.58 ^u	-2.09	1.63 ^s	-2.04	1.80 ^{e,am}	-1.87
Propan-1-ol			2.24 ^l	-1.32		
Propan-2-ol					2.08 ^{e,am}	-1.40
Butan-1-ol			2.75 ^{bb}	-0.71	2.80 ^{e,am}	-0.66
2-Methylpropan-1-ol			2.60 ^{bb}	-0.7		
Butan-2-ol			2.47 ^{bb}	-0.92	2.59 ^{bc}	-0.80
2-Methylpropan-2-ol			2.19 ^{bb}	-1.09	2.24 ^{bc}	-1.04
Pentan-1-ol					3.37 ^{e,am}	0.02
Hexan-1-ol						
2-Methylpentan-3-ol			3.31 ^{bc}	0.46		
Decan-1-ol						
Sulphur hexafluoride	0.04 ^b	2.27	0.35 ^g	2.58	0.09 ^h	2.32
Carbon disulphide			2.38 ^s		2.55 ^{bf}	
Hexamethylphosphotriamide						
Tetramethylsilane						
Tetraethylsilane						
Tetramethyltin					3.10 ^c	4.72
Tetraethyltin						
Mercury	1.81 ^a	1.35	1.60 ^a	1.14	2.05 ^a	1.59
Benzene	2.92 ^r	2.27	2.91 ^l	2.26	3.04 ^{ac,ae}	2.39
Toluene	3.42 ^u	2.84	3.40 ^u	2.82	3.58 ^{aq}	3.00
Hexafluorobenzene			2.75 ^{bj}			
Chlorobenzene						
Pyridine			3.10 ^{bc}	-0.34	3.23 ^{bm}	-0.21
2-Methylpyridine			3.44 ^{bc}	0.05		
3-Methylpyridine			3.64 ^{bc}	0.14		
4-Methylpyridine			3.63 ^{bc}	0.02		
2,6-Dimethylpyridine			3.88 ^{bc}	0.51		

^a Solubility Data Project Series. ^b R. J. Wilcock, R. Battino, W. F. Danforth and E. Wilhelm, *J. Chem. Thermodyn.*, **10**, 817 (1978). ^c G. L. Pollack and J. F. Hinn, *J. Chem. Phys.*, **77**, 3221 (1982). ^d R. Battino, T. R. Rettich and T. Tominaga, *J. Phys. Chem. Ref. Data*, **12**, 163 (1983); **13**, 563 (1984). ^e M. H. Abraham, *J. Am. Chem. Soc.*, **104**, 2085 (1982). ^f R. G. Linford and D. G. T. Thornhill, *J. Appl. Chem. Biotech.*, **27**, 479 (1977). ^g E. Wilhelm and R. Battino, *Chem. Rev.*, **73**, 1 (1973). ^h R. L. Benoit and E. Milanova, *Can. J. Chem.*, **57**, 1319 (1979). ⁱ M. H. Abraham, P. L. Grellier and R. A. McGill, *J. Chem. Soc., Perkin Trans. 2*, 339 (1989). ^j W. Gerrard, *J. Appl. Chem. Biotechnol.*, **23**, 1 (1973). ^k R. Jadot, *J. Chim. Phys.*, 1036 (1972). ^l Interpolated value. ^m W. Hayduk and R. Castenada, *Can. J. Chem. Eng.*, **51**, 353 (1973). ⁿ Y. Miyano and W. Hayduk, *J. Chem. Eng. Data*, **31**, 77 (1986). ^o Using $\Phi^\infty = 1$. ^p J. H. Rytting, L. P. Huston and T. Higuchi, *J. Pharm. Sci.*, **67**, 615 (1978). ^q D. W. Arnold, R. A. Greenkorn and K. -C. Chao, *J. Chem. Eng. Data*, **27**, 123 (1982). ^r T. Hofstee, A. Kwantes and G. W. A. Rijnders, *International Sym. on Distillation*, Brighton, 1960. ^s E. R. Thomas, B. A. Newman, T. C. Long, D. A. Wood and C. A. Eckert, *J. Chem. Eng. Data*, **27**, 399 (1982). ^t R. E. Pecsar and J. J. Martin, *Anal. Chem.*, **38**, 1661 (1966), from Φ^∞ at 293K and 303K in 2,3,4-trimethylpentane. ^u J. H. Park, A. Hussam, P. Couasnan, D. Fritz and P. W. Carr, *Anal. Chem.*, **59**, 1970 (1987). ^v C. L. de Ligny and J. C. Van Houwelingen, *Fluid Phase Eq.*, **27**, 263 (1986). ^w T. M. Letcher and P. J. Jerman, *J. South Afr. Chem. Inst.*, **29**, 55 (1976). ^x A. Sahgal, H. M. La and W. Hayduk, *Canad. J. Chem. Eng.*, **56**, 354 (1978). ^y W. Hayduk and B. S. Minhas, *J. Chem. Eng. Data*, **32**, 285 (1987). ^z R. G. Makitra, T. I. Politanskaya, F. B. Moin, Y. W. Pirig and S. T. Politanskaya, *Zhur. Priklad Khim.*, **56**, 2205 [Eng. Transl., 2048] (1983). ^{aa} A. J. Belfer and D. C. Locke, *Anal. Chem.*, **56**, 2485 (1984). ^{ab} D. V. S. Jain and B. S. Lark, *J. Chem. Thermodyn.*, **5**, 455 (1975). ^{ac} J. A. V. Butler and P. Harrower, *Trans. Faraday Soc.*, **33**, 171 (1937). ^{ad} I. Itsuki, S. Terasawa, N. Yamana and S. Ohotaka, *Anal. Chem.*, **59**, 2918 (1987). ^{ae} E. R. Thomas, B. A. Newman, G. L. Nicolaidis and C. A. Eckert, *J. Chem. Eng. Data*, **27**, 233 (1982). ^{af} H. Wolff, A. Hopfner and H. -M. Hopfer, *Ber. Bunsenges Phys. Chem.*, **68**, 410 (1964). ^{ag} B. Gutsche and H. Knapp, *Fluid Phase Eq.*, **8**, 285 (1982). ^{ah} P. Perez, J. Valero, M. Gracia and C. G. Losa, *J. Chem. Thermodyn.*, **21**, 259 (1989). ^{ai} J. R. Khurma, O. Muthu, S. Munjal and B. D. Smith, *J. Chem. Eng. Data*, **28**, 93 (1983). ^{aj} M. H. Abraham, A. Nasehzadeh and R. A. C. Walker, *J. Chem. Soc., Perkin Trans 2*, 1717 (1988). ^{ak} M. H. Abraham and P. L. Grellier, *J. Chem. Soc., Perkin Trans 2*, 1737 (1976). ^{al} V. Dohnal and M. Novotna, *Fluid Phase Eq.*, **23**, 303 (1985). ^{am} D. M. Trampe and C. A. Eckert, *J. Chem. Eng. Data*, **35**, 156 (1990). ^{an} L. Lepori, E. Matteoli and B. Marongiu, *Fluid Phase Eq.*, **42**, 229 (1988). ^{ao} K. A. Pividal and S. I. Sandler, *J. Chem. Eng. Data*, **33**, 438 (1988). ^{ap} H. Arm and D. Bánkay, *Helv. Chim. Acta.*, **52**, 279 (1969). ^{aq} J. Park, T. R. Rettich, R. Battino, D. Peterson and E. Wilhelm, *J. Chem. Eng. Data*, **27**, 324 (1982). ^{ar} E. Matteoli and L. Lepori, *J. Chem. Eng. Data*, **33**, 247 (1988). ^{as} S. Afrashehfar and G. C. B. Cave, *Can. J. Chem.*, **64**, 198 (1986). ^{at} R. Siedler and H. -J. Bittrich, *J. Prakt. Chem.*, **311**, 721 (1969). ^{au} W. F. Hoot, A. Azarnoosh and J. J. McKetta, *Petroleum Ref.*, **36**, 255 (1957). ^{av} P. Schatzberg, *J. Phys. Chem.*, **67**, 776 (1963). ^{aw} S. Goldman, *Can. J. Chem.*, **52**, 1668 (1974). ^{ax} Z. S. Kooner and W. A. Van Hook, *Fluid Phase Eq.*, **27**, 81 (1986). ^{ay} S. -C. Hwang and R. L. Robinson, *Canad. J. Chem. Eng. Data*, **22**, 319 (1977). ^{az} L. Cori and P. Deloga, *Fluid Phase Eq.*, **27**, 103 (1986). ^{ba} H. C. Van Ness, C. A. Soczek, C. L. Peloquin and R. L. Machado, *J. Chem. Eng. Data*, **12**, 217 (1967). ^{bb} J. H. Rytting, B. D. Anderson and T. Higuchi, *J. Phys. Chem.*, **82**, 2240 (1978). ^{bc} H. T. French, *J. Soln. Chem.*, **12**, 869 (1983). ^{bd} S. A. Wieczorek and J. Steki, *J. Chem. Therm.*, **10**, 177, 187 (1978). ^{be} S. A. Wieczorek, *J. Chem. Therm.*, **11**, 239 (1979). ^{bf} J. H. Rytting, D. R. McHan, T. Higuchi and D. J. W. Grant, *J. Soln. Chem.*, **15**, 693 (1986). ^{bg} S. Bernatova and T. Boublik, *Coll. Czech. Chem. Comm.*, **42**, 2615 (1977), with the given value for P^0 of 0.4755 atm. ^{bh} M. -A. Michou-Saucet, J. Jose, C. Michou-Saucet and J. C. Merlin, *Thermochim. Acta*, **75**, 85 (1984). ^{bi} C. H. Deal and E. L. Derr, *Ind. Eng. Chem., Process Des. Dev.*, **3**(4), 394 (1964). ^{bj} D. V. S. Jain, V. K. Gupta and B. S. Lark, *J. Chem. Therm.*, **5**, 451 (1973). ^{bk} J. Arancil, R. G. Rubro, M. Caceres, M. D. Pena and J. A. R. Renuncio, *J. Chem. Soc., Faraday Trans. 1*, **84**, 539 (1988). ^{bl} H. J. Paul, J. Krug and H. Knapp, *Fluid Phase Eq.*, **39**, 307 (1988). ^{bm} S. Warycha and J. H. Rytting, *J. Soln. Chem.*, **13**, 589 (1984). ^{bn} S. Malanowski, R. Patz, M. T. Ratzsch and C. Wohlfarth, *Fluid Phase Eq.*, **3**, 291 (1979).

METHANOL AND ETHANOL

The application of equations 102 and 103 are summarised in Table 53, and log L and log P values for methanol and ethanol are set out in Table 54.

Table 53. Characterisation of Methanol and Ethanol.

(A) Correlations of log L (gas $\rightleftharpoons$ solvent) Using Equation 102.

	c	r	s	a	b	l	R	SD	N
Methanol	-0.059	0.304	0.823	3.753	1.717	0.778	0.9963	0.140	73
Ethanol	-0.004	0.033	0.738	3.662	1.295	0.838	0.9968	0.136	60

(B) Correlations of log P (water $\rightleftharpoons$ solvent) Using Equation 103.

	c	r	s	a	b	v	R	SD	N
Methanol	0.302	0.694	-0.997	0.177	-3.048	3.517	0.9934	0.170	71 ^a
Ethanol	0.205	0.575	-0.904	0.056	-3.530	3.829	0.9939	0.120	59 ^a

^a Less than the log L regression, as some log L_w values are not available

In equation 102, both alcohols are shown to be strong hydrogen bond bases, $a = 3.75$ for methanol, and 3.67 for ethanol, whilst being somewhat weaker hydrogen bond acids, $b = 1.72$ and 1.30 for methanol and ethanol respectively. Both alcohols are reasonably dipolar, and are weaker dispersion interactors than n-hexadecane. Equation 103 gives s -constants which show solute preference for water, which suggests that any dipolarity parameter, π^*_1 , for water should be larger than π^*_1 for methanol and ethanol. This is the case²³⁹, $\pi^*_1 = 1.09$ for water, and 0.60 and 0.54 for methanol and ethanol. The a -coefficients obtained for either alcohol are very small, which indicates that the alcohols are of about the same basicity as water and is quite contrary to the solvatochromic β_1 values of 0.18 for water and 0.62 and 0.77 for methanol and ethanol²³⁹. The b -coefficients are large, -3.05 for methanol and -3.53 for ethanol, showing hydrogen bond base solute preference for water, suggesting that water is more acidic than methanol or ethanol, (compare α_1 of 1.17 for water with α_1 of 0.93 and 0.83 for methanol and ethanol²³⁹). The v -coefficients show solute preference for the alcohols.

Table 54. Log L and Log P For Methanol and Ethanol

	log L _{meoh}	log P _{meoh}	log L _{etoh}	log P _{etoh}
Helium	-1.447 ^a	0.58	-1.481 ^a	0.55
Neon	-1.314 ^a	0.64	-1.342 ^a	0.62
Argon	-0.571 ^a	0.90	-0.583 ^a	0.88
Krypton	-0.264 ^b	0.95	-0.210 ^b	1.00
Xenon	0.319 ^c	1.29	0.371 ^c	1.34
Radon	0.684 ^a	1.33	0.745 ^a	1.39
Hydrogen	-1.015 ^a	0.70	-1.066 ^a	0.65
Oxygen	-0.603 ^d	0.90	-0.614 ^c	0.89
Nitrogen	-0.785 ^f	1.01	-0.827 ^c	0.97
Nitrous oxide	0.507 ^a	0.74	0.449 ^a	0.68
Carbon monoxide	-0.644 ^g	0.99	-0.695 ^h	0.93
Carbon dioxide	0.524 ^h	0.60	0.424 ^h	0.50
Methane	-0.27 ^g	1.18	-0.278 ^g	1.17
Ethane	0.37 ^g	1.71	0.44 ^a	1.78
Propane	0.83 ^g	2.26	0.91 ^g	2.35
n-Butane	1.27 ^g	2.79	1.40 ^g	2.92
2-Methylpropane	1.07 ^g	2.77	1.20 ^g	2.90
n-Pentane	1.54 ^g	3.24	1.78 ^{g,i}	3.48
2,2-Dimethylpropane	1.40 ^g	3.24	1.61 ^g	3.45
n-Hexane	2.09 ^g	3.91	2.25 ^{g,i}	4.07
n-Heptane	2.52 ^g	4.48	2.72 ^{g,i}	4.68
n-Octane	2.82 ^{g,j}	4.93	3.20 ^{i,j}	5.31
n-Nonane			3.51 ^{i,j}	5.82
3,3-Diethylpentane	3.15 ^g	4.78	3.49 ^g	5.12
n-Decane			3.91 ^k	6.23
Cyclopentane	1.92 ^g	2.80	2.04 ^g	2.92
Cyclohexane	2.43 ^g	3.33	2.55 ^g	3.45
Ethene	0.39 ^l	1.33	0.41 ^h	1.35
Ethyne	1.04 ^m	1.03		
Dichloromethane	2.55 ⁿ	1.59		
Trichloromethane			3.06 ^o	2.27
Tetrachloromethane	2.70 ^p	2.76	2.75 ^p	2.81
2-Chloro-2-methylpropane	2.19 ^g	2.99	2.22 ^g	
1,1-Dichloroethene	2.16 ^q	2.34	2.38 ^q	2.56
Bromoethane			2.22 ^r	1.68
2-Bromo-2-methylpropane	2.36 ^g	2.98	2.49 ^g	
Iodomethane	2.35 ^g	1.69	2.19 ^s	1.53
Iodoethane	2.62 ^g	2.08	2.59 ^s	2.05
2-Iodopropane			2.92 ^t	2.58
1,2-Difluorotetrachloroethane	2.76 ^r			
1,2-Dichlorotetrafluoroethane			2.87 ^r	4.57
Diethylether	2.39 ^u	1.22		
Methyl-t-butylether	2.77 ^v			
Dioxan	3.56 ^w	-0.14	3.44 ^{g,j}	-0.26
Propionaldehyde	2.79 ^v	0.27		
Butyraldehyde	3.18 ^x	0.85		
Pentanal	3.57 ^v	1.35		
Propanone	2.77 ^v	-0.02	2.77 ^{s,t}	-0.02
Butanone	3.31 ^{j,y}	0.59	3.16 ^{g,j}	0.44
Pentan-2-one	3.43 ^v	0.85		
Hexan-2-one	3.82 ^v	1.41		
Heptan-2-one	4.38 ^{v,z}	2.33		
Heptan-3-one	4.26 ^z	2.12		
Heptan-4-one	4.23 ^z	2.09		
Methyl acetate	2.92 ^v	0.62		
Methyl propanoate	3.17 ^{v,aa}	1.02	3.04 ^{aa}	0.89
Methyl butanoate	3.55 ^v	1.47		
Methyl pentanoate	3.91 ^v	2.03		
Methyl hexanoate	4.28 ^v	2.45		
Acetonitrile	2.81 ^{ab}	-0.04	2.90 ^{ac,ad}	0.05
Ammonia	2.26 ^a	-0.89	2.01 ^a	-1.14
Dimethylamine	2.57 ^a	-0.58	2.40 ^a	-0.75
Diethylamine	3.73 ^{ac}	0.74		
Trimethylamine	2.85 ^g	0.50	2.67 ^{af}	0.32
Triethylamine	3.84 ^g	1.48	3.57 ^{ag}	1.21
Tri-n-propylamine			4.10 ^t	
Nitromethane	3.35 ^{j,n,y}	0.40	3.12 ^{g,j,n}	0.17
Water	4.07 ^{ah}	-0.57	3.72 ^{ah}	-0.92
Methanol	3.55 ^{ai}	-0.19	3.40 ^{aj}	-0.34
Ethanol	3.89 ^{ai}	0.22	3.73 ^{ai}	0.06
Propan-1-ol	4.36 ^{ai}	0.80	4.20 ^{ak}	0.64
Propan-2-ol			3.86 ^{ak}	0.38

Table 54 (cont). Log L and Log P For Methanol and Ethanol

	log Lmeoh	log Pmeoh	log Letoh	log Petoh
Ethanthiol	2.20 ^{al}	1.36		
Dimethylsulphoxide	6.52 ^w			
Carbon disulphide			2.27 ^o	
Tetramethylsilane	1.47 ^g	3.70		
Tetraethylsilane	3.30 ^g	5.33	3.62 ^g	5.65
Tetramethyltin	2.13 ^g	3.75	2.28 ^g	3.90
Tetraethyltin	3.90 ^g	5.72	4.13 ^g	5.95
Mercury	1.43 ^a	0.97		
Benzene	2.79 ^g	2.14	2.78 ^{am}	2.13
Toluene	3.20 ^{j,y}	2.62	3.28 ^j	2.70
p-Xylene			3.73 ^{an}	3.19
Chlorobenzene	3.67 ^{ao}	2.83	3.68 ^{n,t}	2.84
Benzyl chloride			4.63 ^g	3.22
Benzyl bromide			4.85 ^g	3.11
Pyridine	4.40 ^{ap}	0.96	4.18 ^{g,t}	0.74
2-Methylpyridine	4.78 ^{ap}	1.39		
2,6-Dimethylpyridine	5.05 ^{ap}	1.68		

^a Solubility Data Project Series. ^b V. N. Prorokov, V. V. Dolatov and G. A. Krestov, *Zhur. Fiz. Khim.*, **58**, 1888 [Eng. 1153] (1984). ^c G. L. Pollack, J. F. Hinn and J. J. Enyeart, *J. Chem. Phys.*, **81**, 3239 (1984). ^d Y. Miyano and W. Hayduk, *J. Chem. Eng. Data*, **31**, 77 (1986). ^e R. Battino, T. R. Rettich and T. Tominaga, *J. Phys. Chem. Ref. Data*, **12**, 163 (1983); **13**, 563 (1984). ^f I. Endler, G. Hradetzky and H. -J. Bittrich, *J. Prakt. Chem.*, **327**, 693 (1985). ^g M. H. Abraham and P. L. Grellier, *J. Chem. Soc., Perkin Trans. 2*, 1856 (1975); M. H. Abraham, P. L. Grellier and R. A. McGill, *J. Chem. Soc., Perkin Trans. 2*, 339 (1988). ^h E. Wilhelm and R. Battino, *Chem. Rev.*, **73**, 1 (1973). ⁱ L. Cori and P. Deloga, *Fluid Phase Eq.*, **27**, 103 (1986). ^j J. H. Park, A. Hussam, P. Cousasnun, D. Fritz and P. W. Carr, *Anal. Chem.*, **59**, 1970 (1987). ^k C. J. Pierotti, C. H. Deal and E. L. Durr, *Ind. Eng. Chem.*, **51**, 95 (1959). ^l S. Zeck and H. Knapp, *fluid Phase Eq.*, **20**, 37 (1986). ^m Y. Miyano and W. Hayduk, *Canad. J. Chem. Eng.*, **59**, 746 (1981). ⁿ J. R. Kharma, O. Mutha, S. Munjal and B. D. Smith, *J. Chem. Eng. Data*, **28**, 110, 113, 119, 412 (1983). ^o I. M. Barclay and J. A. V. Butler, *Trans. Faraday Soc.*, **34**, 1445 (1938). ^p E. Matteoli and L. Lepori, *J. Chem. Thermodyn.*, **18**, 1065 (1986). ^q A. Kovac, J. Svoboda and L. Ondrus, *Chem. Zvesti*, **39**, 729 (1985). ^r V. Dohnal and M. Novotna, *Fluid Phase Eq.*, **23**, 303 (1985). ^s E. R. Thomas, B. A. Newman, T. C. Long, D. A. Wood and C. A. Eckert, *J. Chem. Eng. Data*, **27**, 399 (1982). ^t E. R. Thomas, B. A. Newman, G. L. Nicolaides and C. A. Eckert, *J. Chem. Eng. Data*, **27**, 233 (1982). ^u R. Srivasteva, G. Natarajan and B. D. Smith, *J. Chem. Eng. Data*, **31**, 89 (1986); R. Srivasteva and B. D. Smith, idem p.94. ^v R. A. Djerki and R. J. Laub, *J. Liq. Chromatog.*, **11**, 585 (1988). ^w K. Quitzch, H. Ulbrecht and G. Geiseler, *Z. Phys. Chem.*, **234**, 33 (1967). ^x Interpolated value. ^y D. M. Trampe and C. A. Eckert, *J. Chem. Eng. Data*, **35**, 156 (1990). ^z R. G. Rubin, J. A. R. Renuncio and M. D. Pena, *J. Chem. Thermodyn.*, **15**, 779 (1983). ^{aa} J. Polak and B. C. -Y. Lu, *J. Chem. Eng. Data*, **17**, 457 (1972). ^{ab} B. G. Cox, A. J. Parker and W. E. Waghorne, *J. Am. Chem. Soc.*, **95**, 1010 (1973). ^{ac} V. Dohnal, F. Vesely, R. Hobab and J. Pick, *Coll. Czech. Chem. Comm.*, **47**, 3177 (1982). ^{ad} O. Muthu, P. J. Maher and B. D. Smith, *J. Chem. Eng. Data*, **25**, 163 (1980). ^{ae} Activity coefficient (no temperature given) quoted by K. Nakanishi, R. Toba and H. Shirai, *J. Chem. Eng. Japan*, **2**(1), 4 (1969). ^{af} M. H. Abraham, *J. Chem. Soc. (B)*, 299 (1971). ^{ag} M. H. Abraham and P. L. Grellier, *J. Chem. Soc., Perkin Trans. 2*, 1735 (1976). ^{ah} J. A. V. Butler, D. W. Thomson and W. H. MacLennan, *J. Chem. Soc.*, 674 (1933). ^{ai} From $\Phi^\infty = 1$. ^{aj} A. C. Morris, L. T. Munn and G. Anderson, *Canad. J. Research*, **20B**, 207 (1942). ^{ak} G. S. Parks and K. K. Kelly, *J. Phys. Chem.*, **29**, 727 (1925). ^{al} P. W. Rousseau and J. Y. Kim, *AIChE Symposium*, **83**, 42 (1987). ^{am} S. -C. Hwang and R. L. Robinson, *J. Chem. Eng. Data*, **22**, 319 (1977). ^{an} R. H. Stokes and H. T. French, *J. Chem. Soc., Faraday Trans. 1*, **76**, 537 (1980). ^{ao} P. J. Maher and B. D. Smith, *J. Chem. Eng. Data*, **24**, 363 (1979). ^{ap} C. H. Rochester and J. A. Waters, *J. Chem. Soc., Faraday Trans. 1*, **78**, 631 (1982).

BUTANONE

Log L and log P values for butanone are set out in Table 55. Application of equation 102 to log L (gas $\rightleftharpoons$ butanone) yields the relationship,

$$\text{Log L} = 0.171 - 0.453R_2 + 1.694\pi^H_2 + 2.699\Sigma\alpha^H_2 + 0.891\log L^6 \quad [104]$$

$$R = 0.9898 \quad \text{SD} = 0.134 \quad N = 34$$

Equation 103 applied to log P (water $\rightleftharpoons$ solvent) on butanone gives equation 105.

$$\log P = 0.354 + 0.003R_2 - 0.164\pi^H_2 - 0.979\Sigma\alpha^H_2 - 4.706\Sigma\beta^H_2 + 4.160V_X \quad [105]$$

$$R = 0.9985 \quad \text{SD} = 0.115 \quad N^+ = 32$$

Equation 104 shows butanone to be a solvent of moderate dipolarity ($s = 1.70$), and a medium to strong hydrogen bond base ($a = 2.70$). As is required on chemical grounds, no statistically significant coefficient in b is generated, as of course, butanone can have no hydrogen bond acidity at all. Butanone is a medium dispersion interactor, somewhat less so than n-hexadecane. V_X in equation 105 favours solute partition to butanone, but all other coefficients of significance favour partition to water, especially solute basicity. Again this is chemically sensible, as water is a hydrogen bond acid, and butanone is not.

WATER

Extensive data in log L_w (gas $\rightleftharpoons$ water) is available²⁴¹, and this was analysed using equation 102.

$$\text{Log } L_w (\text{gas} \rightleftharpoons \text{water}) = -1.217 + 0.743R_2 + 2.729\pi^H_2 + 3.984\Sigma\alpha^H_2 + 4.781\Sigma\beta^H_2 - 0.210\log L^6 \quad [106]$$

$$R = 0.9895 \quad \text{SD} = 0.238 \quad N = 256$$

⁺ Less than regression in log L, as some log L_w values not available.

Table 55. Log L and Log P For Butanone

	log L	log P
Oxygen	-0.562 ^a	0.95
n-Butane	1.70 ^b	3.25
n-Pentane	2.06 ^{c,d,e}	3.76
n-Hexane	2.53 ^{c,d}	4.35
n-Heptane	3.01 ^{c,e}	4.97
n-Octane	3.42 ^{c,f}	5.53
n-Decane	4.40 ^e	6.72
Cyclohexane	2.79 ^e	3.69
Methylcyclohexane	3.02 ^g	4.27
Pent-1-ene	2.11 ^d	3.34
3-Methylbut-1-ene	1.99 ^d	3.33
2-Methylbuta-1,3-diene	2.41 ^d	2.91
Dichloromethane	2.98 ^d	2.02
Tetrachloromethane	3.07 ^d	3.13
1,2-Dichloroethane	3.55 ^g	2.24
1-Chloropropane	2.72 ^d	2.48
Bromoethane	2.60 ^{d,g}	2.06
Iodomethane	2.56 ^d	1.90
Iodoethane	3.01 ^d	2.47
1,2-Difluorotetrachloroethane	3.31 ^h	
Dioxan	3.68 ^f	-0.03
Propanone	2.94 ^d	0.15
Butanone	3.36 ⁱ	0.64
Ethyl acetate	3.29 ^g	1.13
Acetonitrile	3.25 ^g	0.40
Nitromethane	3.66 ^g	0.71
Water	3.04 ^j	-1.60
Methanol	2.81 ^g	-0.93
Ethanol	3.17 ^f	-0.50
2,2,2-Trifluoroethanol	4.29 ^k	1.14
Carbon disulphide	2.29 ^d	
Benzene	3.29 ^e	2.64
Toluene	3.73 ^f	3.15
Ethylbenzene	4.09 ^e	3.61

^a R. Battino, T. R. Rettich and T. Tominaga, *J. Phys. Chem. Ref. Data*, **12**, 163 (1983). ^b Solubility Data Project Series. ^c M. H. Abraham, *J. Am. Chem. Soc.*, **104**, 2085 (1982). ^d E. R. Thomas, B. A. Newman, T. C. Long, D. A. Wood and C. A. Eckert, *J. Chem. Eng. Data*, **27**, 399 (1982). ^e G. J. Pierotti, C. H. Deal and E. L. Durr, *Ind. Eng. Chem.*, **51**, 95 (1959). ^f J. H. Park, A. Hussam, P. Couasnon, D. Fritz and P. W. Carr, *Anal. Chem.*, **59**, 1970 (1987). ^g E. R. Thomas, B. A. Newman, G. L. Nicolaides and C. A. Eckert, *J. Chem. Eng. Data*, **27**, 233 (1982). ^h V. Dohnal and M. Novotna, *Fluid Phase Eq.*, **23**, 303 (1985). ⁱ Taking $\Phi^\infty = 1$. ^j K. Tochigi and K. Kojima, *J. Chem. Eng. Japan*, **9**, 267 (1976). ^k This work by headspace analysis.

None of these coefficients are unexpected. The s -coefficient at 2.729 shows water solvent to be of medium to high dipolarity. With $a = 3.984$ and $b = 4.781$, while water is both a hydrogen bond acid and base, its hydrogen bond acid strength is the greater of the two. Abraham *et. al.*²³⁹ list β_1 for water of 0.18, and α_1 of 1.17. The coefficients from equation 106 suggest there is a difference between the hydrogen bond acid and base strength of water, but not of the large magnitude previously found²³⁹. Water is the only solvent characterised with a negative l -coefficient, -0.210, indicating that the exoergic solvent-solute dispersion interactions set up in the dissolution of the solute do not compensate for, or exceed the energy required for the endoergic formation of a cavity in the solvent. This again is not surprising, considering the very extensive self-association of water because of its high degree of inter-molecular hydrogen bonding and dipolar interactions.

As can be seen, the application of equation 102 can usefully characterise common solvents in terms of the solvation parameters. The analysis of $\log P$ (water $\rightleftharpoons$ solvent) via equation 103 in the cases of the amides, methanol, ethanol and butanone is a 'hypothetical' or 'theoretical' procedure, as water and these solvents are in fact completely miscible in all proportions. However, application of equation 103 to $\log P$ (water $\rightleftharpoons$ solvent) values for these solvents can still usefully characterise them, as in effect, equation 103 will compare the solvents to water in terms of the solvation parameters. The alkanes are to all extents and purposes insoluble in water, so equation 103 provides information about a 'real' partition process between water and alkane. This partition process is akin to that in biological membranes⁶⁴, between water and a phospholipid layer. The correlations of all the solvents studied using equations 102 and 103 are summarised for ease of comparison in Table 56.

Table 56. Summary of Solvent Characterisation

(A) Correlations of log L (gas $\rightleftharpoons$ solvent) Using Equation 102.

	c	r	s	a	b	l	R	SD	N
DMA	-0.03	0.14	2.02	5.07	-	0.787	0.9987	0.063	28
NMP	-0.31	0.35	2.10	4.98	-	0.838	0.9969	0.107	61
DMF	-0.24	0.08	2.26	4.36	-	0.827	0.9929	0.159	55
NFM	-0.44	0.01	2.57	4.32	-	0.730	0.9955	0.069	45
Pentane	0.38	-0.13	-0.23	-	-	0.969	0.9989	0.071	30
Hexane	0.31	-0.13	-0.15	-	-	0.978	0.9977	0.098	83
Heptane	0.28	-0.19	-0.27	-	-	1.032	0.9991	0.093	78
Octane	0.24	-0.10	-0.16	-	-	0.988	0.9990	0.062	59
Decane	0.17	-0.10	-0.07	-	-	0.993	0.9995	0.053	40
Hexadecane ^a	0	0	0	0	0	1	-	-	-
Isooctane	0.28	-0.14	-0.13	-	-	0.977	0.9983	0.078	63
Cyclohexane	0.21	-0.02	-0.04	-	-	1.031	0.9983	0.090	71
Methanol	-0.06	0.30	0.82	3.75	1.73	0.778	0.9963	0.140	73
Ethanol	0	0.03	0.738	3.66	1.30	0.838	0.9968	0.136	60
Butanone	0.17	-0.45	1.69	2.70	-	0.891	0.9898	0.134	34
Water	-1.22	0.74	2.73	3.98	4.78	-0.210	0.9895	0.238	256

^a By definition.(B) Correlations of log P (water $\rightleftharpoons$ solvent) Using Equation 103.

	c	r	s	a	b	v	R	SD	N
DMA	0.14	0.53	0.03	0.88	-4.59	3.94	0.9960	0.120	26
NMP	-0.02	0.88	0.21	1.31	-4.89	3.86	0.9958	0.146	55
DMF	0.02	0.56	0.39	0.59	-4.79	3.85	0.9924	0.193	51
NFM	0.02	0.46	0.39	0.42	-4.71	3.39	0.9977	0.115	40
Pentane	0.34	0.15	-1.48	-3.42	-5.30	4.63	0.9989	0.108	30
Hexane	0.37	0.04	-1.70	-3.41	-5.03	4.36	0.9971	0.175	81
Heptane	0.27	0.56	-1.77	-3.44	-5.03	4.59	0.9980	0.120	76
Octane	0.21	0.57	-1.75	-3.22	-4.95	4.56	0.9978	0.132	58
Decane	0.10	0.45	-1.50	-3.42	-4.94	4.68	0.9989	0.118	40
Hexadecane	0.08	0.89	-1.77	-3.60	-4.81	4.42	0.9965	0.158	256
Isooctane	0.27	0.34	-1.58	-3.44	-5.15	4.53	0.9982	0.125	62
Cyclohexane	0.16	0.85	-1.75	-3.41	-4.77	4.68	0.9967	0.167	66
Methanol	0.30	0.69	-1.00	0.18	-3.05	3.52	0.9934	0.170	71
Ethanol	0.21	0.58	-0.90	0.06	-3.53	3.83	0.9939	0.210	59
Butanone	0.35	0.00	-0.16	-0.98	-4.71	4.16	0.9985	0.115	32

The generation of coefficients from equation 102 and 103 also provides the opportunity to assess the validity of solvent parameters ²³⁹ π^*_1 , β_1 , and α_1 , by comparison with coefficients s , a and b respectively, Table 57.

Table 57. Comparison of Coefficients S , A , and B With Solvent Parameters π^*_1 , β_1 and α_1 .

(A) Comparison of Coefficients From Equation 102.

Solvent	s	π^*_1	a	β_1	b	α_1
Alkanes	≈ 0	0	(0)	0	(0)	0
DMA	2.02	0.88	5.07	0.76	(0)	0
NMP	2.10	0.92	4.98	0.77	(0)	0
DMF	2.26	0.88	4.36	0.69	(0)	0
NFM	2.57	-	4.32	-	(0)	0
Methanol	0.82	0.60	3.75	0.62	1.73	0.93
Ethanol	0.74	0.54	3.66	0.77	1.30	0.83
Butanone	1.69	0.67	2.70	0.48	(0)	0
Water	2.73	1.09	3.98	0.18	4.78	1.17

(B) Comparison of Coefficients From Equation 103.

Solvent	s	π^*_1	a	β_1	b	α_1
n-Alkanes (av.)	-1.66	0	-3.42	0	-5.01	0
DMA	0.03	0.88	0.88	0.76	-4.59	0
NMP	0.21	0.92	1.31	0.77	-4.89	0
DMF	0.39	0.88	0.59	0.69	-4.79	0
NFM	0.39	-	0.42	-	-4.71	0
Methanol	-1.00	0.60	0.18	0.62	-3.05	0.93
Ethanol	-0.90	0.54	0.06	0.77	-3.53	0.83
Butanone	-0.16	0.67	-0.98	0.48	-4.71	0
Water	0	1.09	0	0.18	0	1.17

There are sufficient data points in s and π^*_1 , and a and β_1 to generate informative XY-plots. The s -coefficients in log L and log P can be plotted against the solvent parameter π^*_1 , Figure 15, and the a -coefficient in log L and log P similarly plotted against β_1 , Figure 16.

Figure 15. Plot of S in Log L and Log P against Π^*1

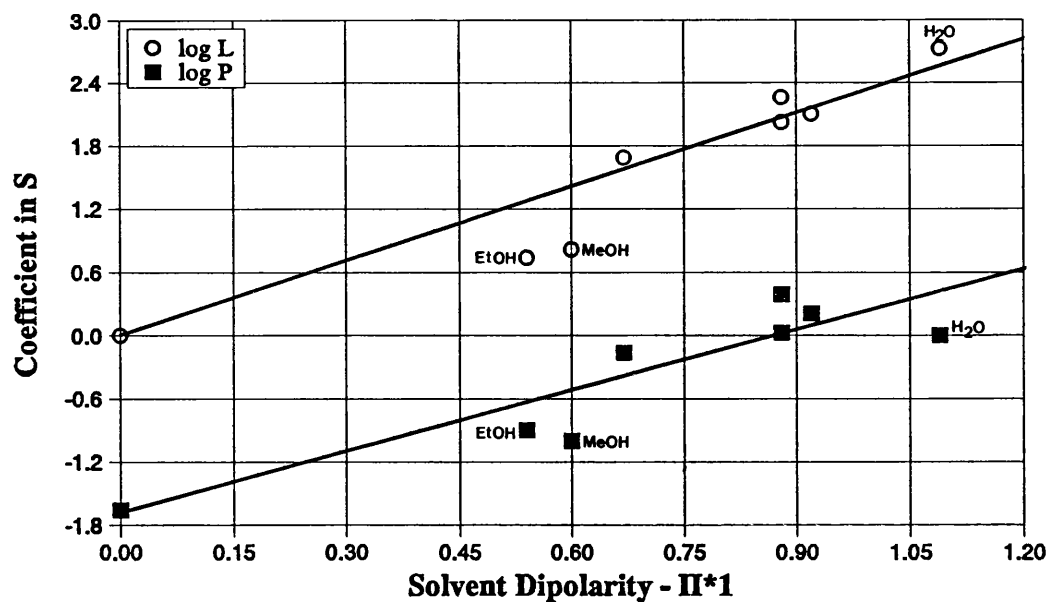
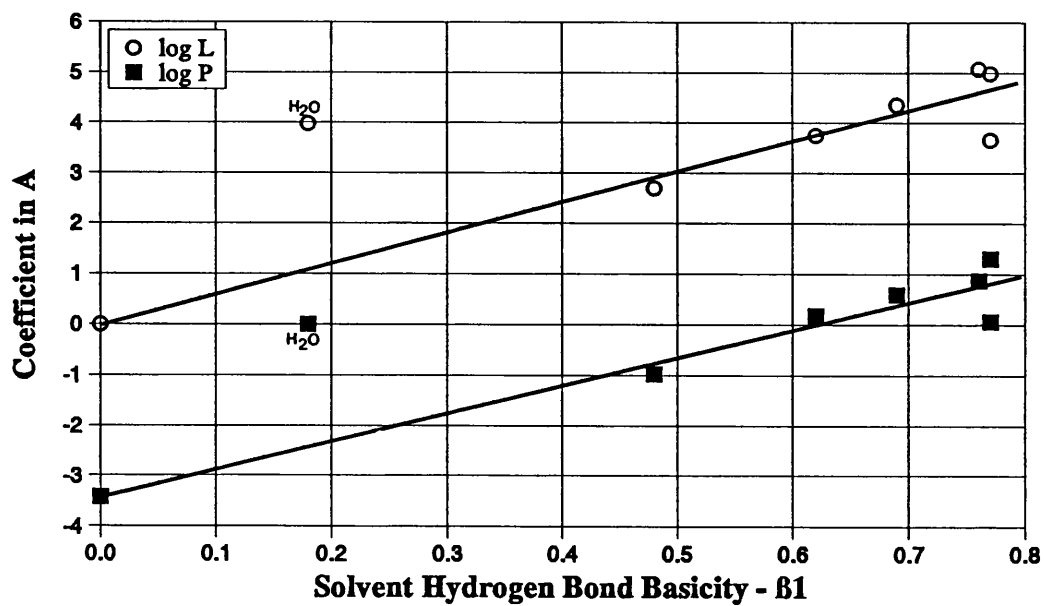


Figure 16. Plot of A in Log L and Log P against β_1



S-coefficients for amides for the log L (gas $\rightleftharpoons$ solvent) process, Table 57(a), show that amides are all a bit less dipolar than water, and that methanol and ethanol are much less dipolar than either amides or water, see also Figure 15. However, *s*-coefficients for the log P (water $\rightleftharpoons$ solvent) process, Table 57(b), suggest amides are rather *more* dipolar than water, although again, methanol and ethanol are quite a bit less dipolar than water, Figure 15. There is in general reasonable agreement between the *s*-coefficient and π^* .

Amide *a*-coefficients for the log L (gas $\rightleftharpoons$ solvent) and log P (water $\rightleftharpoons$ solvent) process show they are more basic than water. From log L (gas $\rightleftharpoons$ solvent), methanol and ethanol are slightly less basic than water, but *a*-coefficients from log P (water $\rightleftharpoons$ solvent) suggest methanol and ethanol are very slightly more basic than water. The $\beta_1 = 0.18$ for water is very considerably out of line with the other coefficients for either process, see Figure 16, suggesting β_1 for water to be far too low. A more reasonable value would seem to be no less than around 0.65 units.

The *b*-coefficients for methanol and ethanol for log L (gas $\rightleftharpoons$ solvent) are considerably less than for water, showing some agreement here with the α_1 values. Again, *b*-coefficients for log P (water $\rightleftharpoons$ solvent) for methanol and ethanol, Table 57(b), show they are considerably less acidic than water. The *b*-coefficients for amides and butanone are quite near those of the alkanes, as would be expected since these solvents have no hydrogen bond acidity at all.

7.50 Characterisation of Candidate SAW Phases.

The aim of this part of the project was to characterise a number of candidate phases for use in chemical sensors. The method, as usual, consists of setting up the linear solvation energy equation or "solvation" equation, number 83, using parameters from Table 28, pages 139-141.

$$\log SP = c + r.R_2 + s.\pi^H_2 + a.\Sigma\alpha^H_2 + b.\Sigma\beta^H_2 + l.\log L^{16} \quad [83]$$

The dependant variable in equation 83 is L (or K) for a series of solutes on a given phase. In GLC, SP can also be the specific retention volume at the column temperature, V_G , or can even be the relative retention time (τ) adjusted for dead space. Note, if V_G or τ are used instead of L, the c -constant in equation 83 will alter, although all the other constants will remain unchanged.

The method of characterisation of phases thus consists of determining $\log L$ or $\log \tau$ values for a series of solutes on a given phase, usually at 298K, obtaining the characteristic constants in equation 83, and then comparing these constants with other phases or materials. Thus a phase with a particularly large a -constant will have a large affinity for solutes that are hydrogen bond acids, and will be a strong hydrogen bond base.

In order to verify McGill's²⁷⁰ original comparison of L values obtained by the GLC method with L values obtained using a SAW device, values of $\log V_G$, τ , or L were redetermined by GLC using samples of fluoropolyol (FPOL), polyepichlorohydrin (PECH), and polyisobutylene (PIB) sent by Dr. J. W. Grate, of the Naval Research Laboratory, Washington DC. Additionally further measurements on FPOL, PIB and PECH were made in order to obtain regression equations using the latest solvation equation 83. A number of

materials as candidate phases for SAW devices were investigated. These phases had all to be above their T_G at room temperature, which was to be the operating temperature. A poly(diphenyl phenylmethyl siloxane), denoted as SXPH, was chosen as a possible phase that might interact with solutes selectively through general dispersion interactions. As a phase that might be highly polar but with a minimal basicity, poly(biscyanopropyl)siloxane denoted as SXCN was chosen, whilst for a phase that might be, conversely, of low dipolarity but of high basicity poly(ethyleneimine), or PEI, was chosen. A sample of a polysiloxane containing fluoroacidic groups was provided by Dr. J. W. Grate, and it was hoped that this material would prove to be a strongly acidic phase; this phase is denoted as SXFA. Figure 17 shows the structure of FPOL, PECH, PEI and PIB. The structures of the other three phases investigated are somewhat less definite, so a description (above) of their chemical nature will suffice.

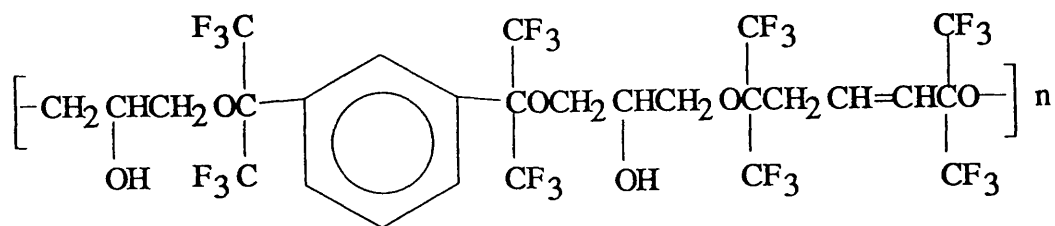
The equation used to calculate absolute log L values can be given as,

$$L = \tau \cdot F_w (P_o - P_w) T \cdot J_2^3 / (P_o \cdot T_w \cdot W_1 / \rho_1) \quad [107]$$

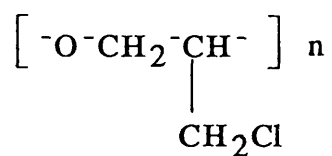
where τ is the retention time of a solute corrected for dead space, F_w is the gas flow rate at the column outlet, P_o is the outlet pressure, P_w is the vapour pressure of water at the temperature of the soap-bubble flow meter (T_w), T is the column temperature, J_2^3 is the pressure drop correction factor (equation 108), W_1 is the weight of the stationary phase on the column, (i.e. the actual weight of the candidate stationary phase), and ρ_1 is the density of the stationary phase at the column temperature. Absolute values of log L at 298K were determined on a thermal conductivity detector. Relative values were obtained using an FID detector, and were all placed on an absolute scale by matching with the absolute values. McGill's²⁷⁰ original values were obtained in a similar way, but alkanes were taken as absolute standards.

FIGURE 17: Polymer Repeat Units for Some Candidate SAW Phases.

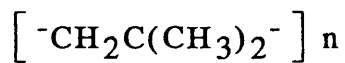
Fluoropolyol (FPOL)



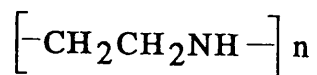
Polyepichlorohydrin (PECH)



Polyisobutylene (PIB)



Poly(ethyleneimine) (PEI)



The pressure correction term is defined as,

$$J^2_3 = \frac{3}{2} \left[\frac{(P_i/P_o)^2 - 1}{(P_i/P_o)^3 - 1} \right] \quad [108]$$

where P_i is the inlet pressure.

In addition to the pressure correction term, there is a correction term for gas imperfection,

$$\log L^o = \log L - (2B_{12} - V_2) P_o J_3 / RT \quad [109]$$

where B_{12} is the solute/carrier gas second virial coefficient and V_2 is taken as the solute molar volume. However, with helium as the carrier gas in the thermal conductivity determinations, the correction term is negligible. If nitrogen is used as the carrier gas, then the correction term is still small, amounting to around 0.005 log units to be added to log L.

Full details of the phases used, the polymer characteristics, GC conditions, and details of their construction into GLC packed columns are given in the experimental section, Table 65, page 267. Additionally, comprehensive tables of log τ , log V_G , or log L values are set out, Tables 66-74, pages 268-278. If N in the MLRA equations generated for the candidate SAW phases is less than the number of solutes in the relevant table from Tables 66-74, this is because some solvation parameters are missing (unless stated otherwise).

(i) **FPOL**

FPOL was originally studied²⁷⁰ as it was one of the few hydrogen bond acidic phases (high selectivity for hydrogen bond bases) considered for use in a SAW array. A column of McGill's was used to measure log L values at 298K, and these are set out in Table 66, section 9.11. A regression according to the full equation 83 yields,

$$\log L_{\text{FPOL}} = -1.221 (\pm 0.247) - 0.207R_2 (\pm 0.256) + 2.251H_2 (\pm 0.222) + 1.752\Sigma\alpha^H_2 (\pm 0.195) + 2.600\Sigma\beta^H_2 (\pm 0.228) + 0.736\log L^6 (\pm 0.050) \quad [110]$$

$$R = 0.9448 \quad SD = 0.243 \quad N = 50$$

A regression of McGill's²⁷⁰ original log L values on FPOL using improved solvation equation 83 gives,

$$\log L_{\text{FPOL}} = -1.490 (\pm 0.182) - 1.120R_2 (\pm 0.191) + 1.903H_2 (\pm 0.177) + 2.239\Sigma\alpha^H_2 (\pm 0.205) + 3.797\Sigma\beta^H_2 (\pm 0.188) + 0.874\log L^6 (\pm 0.047) \quad [111]$$

$$R = 0.9905 \quad SD = 0.135 \quad N = 26$$

There are some noticable differences between equations 110 and 111. The *s*-coefficient in equation 110 is larger than that in equation 111 by about 0.4 units, whereas the *a* and *b* coefficients in equation 111 are larger than equation 110, *b* by over a full unit. Recasting of equation 110 using a limited set from Table 66 using far fewer alcohols (in case their presence biases the coefficients) produces no significant change. It must be assumed that the FPOL has changed chemically in some way since initial retention measurements were taken on it²⁷⁰. It has been used at higher temperatures than 298K (such as 333K and higher) and it has

possibly degraded in some way, either through use at elevated temperatures, or a slow degradation with time. There is no easy way to check this, as first the stationary phase must be extracted in sufficient quantity from the support for analysis without further altering the phase nature. Unfortunately, there was not enough coated support available to attempt this procedure.

Either equation does not show FPOL to be a very selective candidate SAW phase, as it is reasonably dipolar, and there is little difference between the *a* and *b* coefficients. It is very likely there will be better phases for maximizing hydrogen bond acidity (while minimizing basicity).

(ii) PECH

Absolute values of log L on a new PECH column were determined at 298.15K and 312.95K, see Table 58. If the 298K values are compared with those of McGill²⁷⁰, it can be seen that the new values are systematically lower than those of McGill for all polar compounds, not just for alcohols. This is very unlikely to be due to adsorption on the solid support, since this seems to selectively affect retention of alcohols. It is likely these systematic differences are due to the different samples of PECH used in the experiments. If this is so, then the two sets of results cannot be combined, but must be treated separately. Results are:

$$\log L_{\text{PECH}}^{\text{This Work}} = -0.550 (\pm 0.076) + 0.153R_2 (\pm 0.075) + 1.463\pi_2^H (\pm 0.073) + 1.499\Sigma\alpha^H_2 (\pm 0.102) + 0.598\Sigma\beta^H_2 (\pm 0.081) + 0.792\log L^6 (\pm 0.017) \quad [112]$$

$$R = 0.9912 \quad SD = 0.110 \quad N = 54$$

$$\log L_{\text{PECH}}^{\text{McGill}} = -0.853 (\pm 0.081) - 0.063R_2 (\pm 0.122) + 1.928\pi_2^H (\pm 0.131) + 2.296\Sigma\alpha^H_2 (\pm 0.145) + 0.580\Sigma\beta^H_2 (\pm 0.131) + 0.863\log L^6 (\pm 0.020) \quad [113]$$

$$R = 0.9932 \quad SD = 0.092 \quad N = 34$$

There is little difference in the quality of the regressions, given that $N = 54$ and $N = 34$ respectively. Water has been left out from both regressions, because this seems to be at least partially retained by the water/support effects. Thus, comparing observed and calculated log L values for water:

	OBS	CALC
This work	2.41	1.75
McGill's results	2.69	2.32

Table 67, pages 269-270, contains all the results on PECH at 298K; these could then be compared with any new SAW data using the same sample of PECH.

The temperature variation of log L on PECH is not large. On average a 15° rise in temperature reduces log L by about 0.24 log units, according to data on the new PECH sample.

Table 58. Absolute Values of log L on PECH. Comparison of Results.

Solute	McGill ²⁷⁰	This Work	
	298.15K	298.15K	312.95K
Octane	2.304	2.303	(2.151) ^b
Nonane	2.717	2.721	(2.509) ^b
Decane	3.300	3.174	2.835
Undecane	3.712	(3.558) ^c	3.241
Dodecane	4.168		3.647
Tridecane			3.894
Water ^a	2.694	2.407	2.34
Ethanol	2.405	2.148	
Propan-1-ol	2.784	2.555	
Butan-1-ol	3.227	(3.003) ^c	2.660
Butanone ^d	2.73	2.61	
Methyl acetate ^d	2.36	2.21	
Acetonitrile ^d	2.72	2.57	

^a These results seem too high, possibly due to adsorption on the solid support.

^b Extrapolation of the homologous series.

^c Calculated from the final regression of values (this work).

^d From Table 67, page 269.

(iii) PIB

Absolute values of log L at 298K were determined on a thermal conductivity detector. Details are given in Table 68. It can be seen for nonprotonic compounds there is excellent agreement between the two sets of results. However, this is not so for the alcohols, where McGill's²⁷⁰ log L values are systematically larger than recent values. The result of this is that when McGill's²⁷⁰ results are taken on their own, there appears to be a dependency (although small) on $\Sigma\alpha_{H_2}$ and $\Sigma\beta_{H_2}$ that is significant at the 99.97% and 94.73% CL respectively:

$$\log L_{PIB}^{McGill} = -0.566 (\pm 0.152) - 0.044R_2 (\pm 0.177) + 0.044\pi^H_2 (\pm 0.177) + 0.979\Sigma\alpha^H_2 (\pm 0.229) + 0.414\Sigma\beta^H_2 (\pm 0.203) + 0.955\log L^6 (\pm 0.042) \quad [114]$$

$$R = 0.9833 \quad SD = 0.138 \quad N = 30$$

but, when recent results are taken separately, there is no or little dependence on $\Sigma\alpha_{H_2}$ (94.11%) or $\Sigma\beta_{H_2}$ (83.03%):

$$\log L_{PIB}^{This Work} = -0.693 (\pm 0.127) - 0.318R_2 (\pm 0.145) + 0.626\pi^H_2 (\pm 0.106) + 0.306\Sigma\alpha^H_2 (\pm 0.153) - 0.176\Sigma\beta^H_2 (\pm 0.124) + 0.975\log L^6 (\pm 0.041) \quad [115]$$

$$R = 0.9892 \quad SD = 0.097 \quad N = 27$$

An explanation is that McGill's²⁷⁰ results suffer from sorption of alcoholic solutes on the solid support - this would have the effect of increasing log L and giving rise to an *apparent* dependency on $\Sigma\alpha_{H_2}$ and $\Sigma\beta_{H_2}$. The two sets of results can be combined by averaging the very close results for aprotic solutes and by then including McGills²⁷⁰ values for aprotic solutes only. The final suggested

regressions are then:

$$\log L_{\text{PIB}}^{\text{ALL}} = -0.880 (\pm 0.104) - 0.256R_2 (\pm 0.120) + 0.568\pi^{\text{H}}_2 (\pm 0.102) + 0.077\Sigma\alpha^{\text{H}}_2 (\pm 0.129) - 0.074\Sigma\beta^{\text{H}}_2 (\pm 0.106) + 1.047\log L^{16} (\pm 0.030) \quad [116]$$

$$R = 0.9913 \quad \text{SD} = 0.099 \quad N = 36$$

$$\log L_{\text{PIB}}^{\text{ALL}} = -0.890 (\pm 0.099) - 0.205R_2 (\pm 0.097) + 0.531\pi^{\text{H}}_2 (\pm 0.081) + 1.048\log L^{16} (\pm 0.028) \quad [117]$$

$$R = 0.9911 \quad \text{SD} = 0.096 \quad N = 36$$

Equation 117 shows the $\log L^{16}$ term to be the most significant, as might be expected, PIB being a suitable phase to maximize dispersion interactions.

Water has again (see PECH) been left out from these regressions because of the possibility of adsorption on the solid support. Indeed, the calculated value for water using the combined equation is only $\log L = -0.38$ whereas $\log L$ was found to be 2.0 units.

The only compound (other than alcohols) for which there is disagreement is DMMP where $\log L = 3.55$ (McGill²⁷⁰) or $\log L = 4.23$ (this work). A new π^{H}_2 value is not available as yet, so no check by calculation can be performed. The recent value of 4.23 log units would seem to be the better.

A few absolute $\log L$ values at 312.85K were obtained using the thermal conductivity detector. These are given in Table 59, together with absolute values at 298.15K from the last column in Table 68. The values at 298.15K have been calculated using $\rho = 0.918$ which is a given value. The density at 312.85K was

estimated at 0.905, but if a more substantiated value is available, the 312.85K values could be amended.

Table 59. Absolute Values of log L on PIB at Two Temperatures. Comparison of Results.

Solute	298.15K	312.85K
Hexane	1.87	1.83
Heptane	2.46	2.35
Octane	2.99	2.86
Benzene	2.20	2.13
Toluene	2.75	2.68
Water	(2.01)	(1.94)

It can be seen that a 15° rise in column temperature reduces log L^{PIB} by only around 0.1 log units - this might be valuable information when comparing GLC with SAW results for PIB.

(iv) SXPB

The sample provided by Dr. J. W. Grate is referred to as SXPHA. The total list of log τ and log L values at 298K is in Table 69. A regression according to the full equation 83 yields,

$$\log L_{\text{SXPHA}} = -0.482 (\pm 0.061) + 0.210R_2 (\pm 0.070) + 0.962H_2 (\pm 0.093) + 0.680\Sigma\alpha^H_2 (\pm 0.093) + 1.214\Sigma\beta^H_2 (\pm 0.071) + 0.813 \log L^6 (\pm 0.014) \quad [118]$$

$$R = 0.9929 \quad SD = 0.115 \quad N = 77$$

The point for water is excluded, which has log L values obs = 2.34 and calc = 1.41, out by over 5 standard deviations. Regression equation 118 is reasonably

good, but shows disappointing little dependence of $\log L$ on π^H_2 or on $\log L^{16}$. Hence SXPHA is not particularly useful as a phase that interacts with solutes by polarisability/general dispersion reactions. A very odd feature of equation 118 is the strong dependence of $\log L$ on solute basicity (the $b.\Sigma\beta^H_2$ term). SXPH would be expected to be somewhat polarisable and basic (through the benzene rings and the siloxane backbone) but not to be acidic. It is possible that the $b.\Sigma\beta^H_2$ term arises through interaction of solutes with the support, rather than with the coating phase, but a simple IR spectrum of the original material clearly shows the presence of -OH groups, from the bands at around 3600 cm^{-1} , see Figure 18(a). The conclusion must be that material SXPHA contains OH groups, probably as SiOH, and that equation 118 reflects the acidity of the material, due to these SiOH groups.

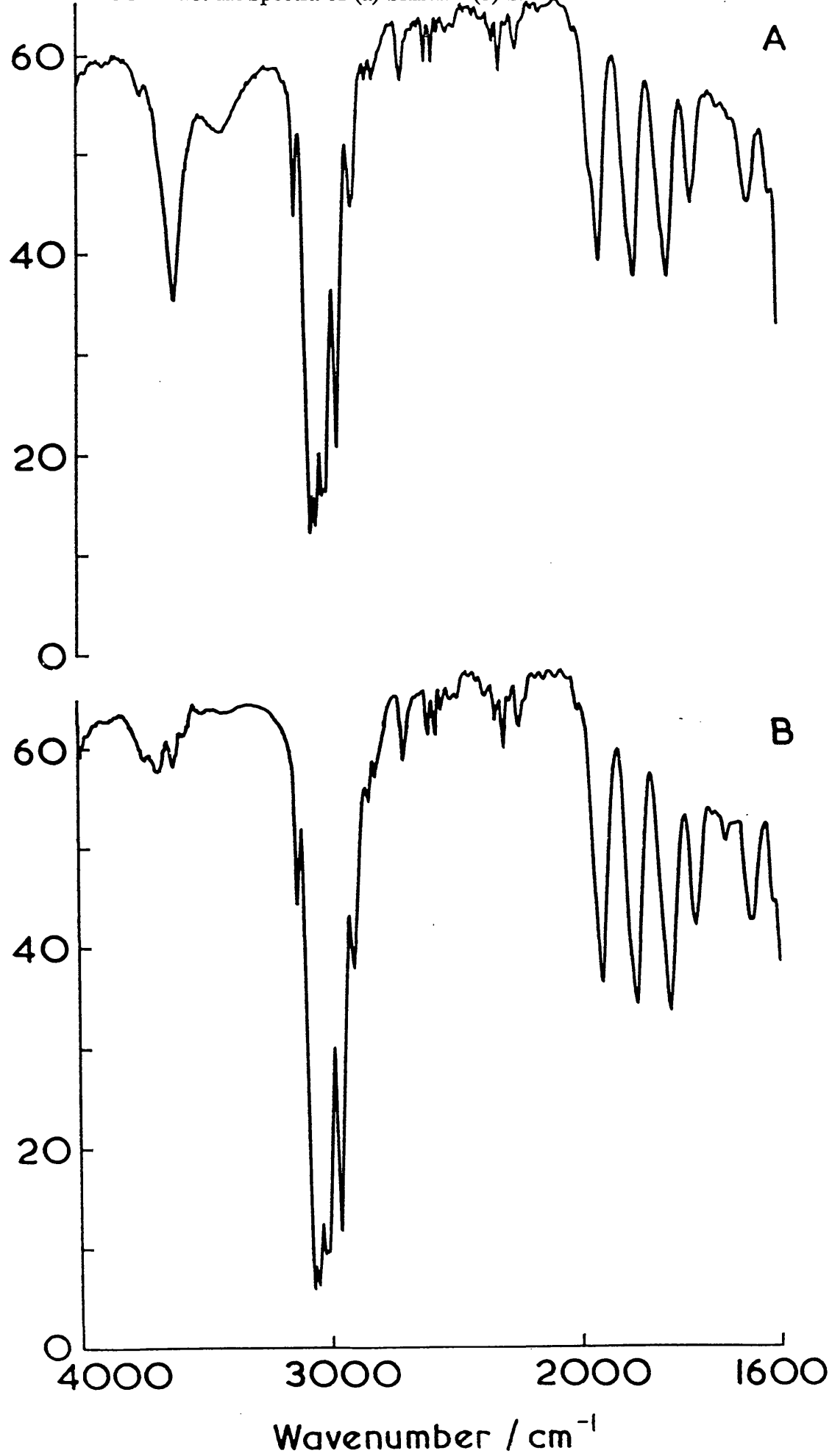
Another commercial sample of SXPH was therefore examined, denoted as SXPHB, that seemed to have appreciably less SiOH groups, see Figure 18(b), where the OH band at 3600 cm^{-1} is quite small. The full set of $\log \tau$ and $\log L$ values is in Table 70. A regression using equation 83 gives,

$$\log L_{\text{SXPHB}} = -0.801 (\pm 0.080) + 0.238R_2 (\pm 0.081) + 1.238\pi^H_2 (\pm 0.082) + 0.638\Sigma\alpha^H_2 (\pm 0.092) + 0.482\Sigma\beta^H_2 (\pm 0.084) + 0.869\log L^{16} (\pm 0.020) \quad [119]$$

$$R = 0.9932 \quad SD = 0.097 \quad N = 42$$

As suggested by the IR spectrum, SXPHB contains much less SiOH than does SXPHA, hence the much lower b -constant of 0.48 as compared to 1.21 in equation 118. The s -term is larger, at 1.24 units, but there is nothing in equation 118 to suggest that SXPH would be a useful phase in a SAW device.

FIGURE 18: IR Spectra of (a) SXPHA (b) SXPHB



Finally, to reduce the SiOH groups in SXPHA *in situ*, injections of quantities of Me₃SiCl were made, in order to convert SiOH to SiOSiMe₃. Absolute log L values were not determined, but the relative log τ values will still lead to correct characterisation constants, except for the *c*-constant. Values of log τ relative to n-octane are in Table 71 and give the regression equation,

$$\log \tau^{(\text{REL})}_{\text{SXPHC}} = -2.970 (\pm 0.109) + 0.202R_2 (\pm 0.105) + 1.032H_2 (\pm 0.092) + 0.617\Sigma\alpha^H_2 (\pm 0.114) + 0.791\Sigma\beta^H_2 (\pm 0.101) + 0.801\log L^6 (\pm 0.030) \quad [120]$$

$$R = 0.9919 \quad SD = 0.095 \quad N = 24$$

These results fit in quite well with those shown in equations 118 and 119: the *b*-constant has been reduced from 1.21 in equation 118 to 0.79 in equation 120 due to the Me₃SiCl treatment, as expected if the acidity of the phase is due to SiOH groups.

Generally, equations 118-120 show that SXPH will not be a very suitable selective phase for use in any SAW array.

(v) SXCN

Examination of this phase proved more straightforward. Details of the the entire set of log τ and log L values is in Table 72. Regressions were carried out both with and without the $b.\Sigma \beta^H_2$ term,

$$\log L_{\text{SXCN}} = -1.638 (\pm 0.084) + 0.079R_2 (\pm 0.088) + 2.311H_2 (\pm 0.105) + 3.145\Sigma\alpha^H_2 (\pm 0.133) + 0.402\Sigma\beta^H_2 (\pm 0.114) + 0.772\log L^6 (\pm 0.019) \quad [121]$$

$$R = 0.9890 \quad SD = 0.116 \quad N = 56$$

$$\log L_{\text{SXCN}} = -1.630 (\pm 0.093) - 0.085R_2 (\pm 0.082) + 2.550\pi^H_2 (\pm 0.089) + 3.364\Sigma\alpha^H_2 (\pm 0.130) + 0.776\log I^6 (\pm 0.020) \quad [122]$$

$$R = 0.9863 \quad SD = 0.129 \quad N = 56$$

It can be seen that there is a small but significant *b*-constant, possibly the result of a slightly acidic hydrogen atom in SXCN itself. As expected, SXCN is a quite dipolar material, but (unexpectedly) it is also quite a strong base. Hence SXCN will not *selectively* sorb dipolar/polarisable solutes, but will also sorb hydrogen bond acidic solutes as well.

Water was not included in regressions 121 or 122 because the calculated and observed values are totally out-of-line. This seems to be due to a particular mode of interaction between SXCN and water. The value of $\Sigma\alpha^H_2 = 0.82$ for water arises because when water is surrounded by solvent molecules, both hydrogen atoms act as acid sites, c.f. $\Sigma\alpha^H_2 = 0.43$ for methanol. A back-calculated value of $\Sigma\alpha^H_2$ for water using equation 121 is 0.50 and using equation 122 is 0.47, which suggests that only one hydrogen atom in the water molecule interacts with the solvent SXCN.

(vi) SXFA

The final siloxane examined was a novel acidic phase supplied by Dr. J. W. Grate. The total set of $\log \tau$ and $\log L$ values is in Table 73.

$$\log L_{\text{SXFA}} = -0.033 (\pm 0.097) - 0.691R_2 (\pm 0.098) + 0.853\pi^H_2 (\pm 0.095) + 0.876\Sigma\alpha^H_2 (\pm 0.134) + 4.037\Sigma\beta^H_2 (\pm 0.125) + 0.702\log I^6 (\pm 0.028) \quad [123]$$

$$R = 0.9876 \quad SD = 0.126 \quad N = 47$$

Interaction of water with the support does not seem to be significant, and water is therefore included in the regression. This is one of the most selective phases examined. It will absorb hydrogen bond bases very strongly indeed ($b = 4.04$) and yet has a rather low affinity for dipolar solutes or for hydrogen bond acids ($a = 0.88$). Hence SXFA is an extremely beneficial addition to the range of phases that can usefully make up a SAW array. Its performance is clearly very superior to FPOL.

(vii) PEI

The density of PEI at 298K was not known, so the determination of absolute values of $\log L$ is not possible. However, absolute values of $\log V_G$ can be obtained and these can be converted to $\log L$ whenever the density ρ_1 is available, from

$$L = V_G \cdot \rho_1 \quad [90]$$

The total set of $\log \tau$ and $\log V_G$ values is in Table 74. Preliminary regressions showed the $b \cdot \Sigma \beta^H_2$ term was not significant and it was then found that,

$$\log V_{G \text{ PEI}} = -1.683 (\pm 0.136) + 0.506 R_2 (\pm 0.108) + 1.524 H_2 (\pm 0.121) + 7.157 \Sigma \alpha^H_2 (\pm 0.233) + 0.789 \log L^6 (\pm 0.031) \quad [124]$$

$$N = 43 \quad R = 0.9851 \quad SD = 0.151 \quad N = 43$$

Again, it was not necessary to exclude water from the regression. As in the case of SXFA, PEI is an extraordinarily selective phase, but now for hydrogen bond acids. PEI is the most basic phase ever investigated. It seems to have little or no

hydrogen bond acidity, but this is not too surprising because secondary amines (at least as solutes) have only feebly acidic character with $\Sigma\alpha^H_2 \approx 0.05$ units only. Although PEI is also dipolar ($s = 1.52$), the very high value of the a -constant makes it a very selective phase indeed, and one that might find useful application in SAW arrays.

The characteristic constants for a number of candidate phases can now be compared, as listed in Table 60. The present work has shown that two particular phases, SXFA, and PEI have notable characteristics that could be used to advantage in SAW arrays. The former phase is very selective towards challenge vapours that are hydrogen bond bases, but has only a moderate affinity towards dipolar solutes or towards hydrogen bond acids. SXFA could usefully replace FPOL as the "base sensitive" phase in a SAW array, On the other hand, PEI (which is commercially available) is by far the most selective phase towards challenge vapours which are hydrogen bond acids. PEI is extraordinarily basic, but has zero acidic properties and hence has no affinity towards hydrogen bond bases, although it has a moderate to large affinity towards dipolar solutes. The SXPH phases do not seem to be particularly useful as phases in SAW arrays. Furthermore, this work has shown that extreme care must be taken over commercial (and other) siloxanes, which may contain unsuspected SiOH groups. Thus both commercial samples of SXPH function as hydrogen bond acids and have a moderate affinity for challenge vapours that are basic. If not detected, this could give rise to considerable difficulties in the interpretation of results from SAW arrays that contained such siloxanes.

Table 60. Comparison of Characteristic Constants For Some Candidate Phases
For Sensor Arrays at 298K.

Phase	c	r	s	a	b	l
FPOL	-1.22	-0.21	2.25	1.75	2.60	0.736
PECH	-0.54	0.16	1.45	1.48	0.62	0.789
PIB	-0.89	-0.21	0.53	(0)	(0)	1.048
SXPHA	-0.48	0.21	0.96	0.68	1.21	0.813
SXPHB	-0.80	0.24	1.24	0.64	0.48	0.869
SXCN	-1.64	0.08	2.31	3.15	0.40	0.772
SXFA	-0.03	-0.69	0.85	0.88	4.04	0.702
PEI	-1.68	0.51	1.52	7.16	(0)	0.789

7.60 Application to Characterisation of GLC Phases Studied by Poole *et. al*²⁷¹.

There have been a number of interesting new developments in recent years on the characterisation of gas-liquid chromatographic (GLC) stationary phases. Poole and his co-workers^{124,138} have pointed out several deficiencies in the McReynolds system of classification (see sections 4.1 and 6.12), and have suggested that the use of McReynolds numbers be abandoned. Following several other workers¹³⁹⁻¹⁴¹, Poole suggested that the Gibbs energy of solvation of a gaseous methylene increment into a stationary phase, $\Delta G_s^\circ(\text{CH}_2)$, could be used as a measure of the 'polarity' of the phase^{124,138}, see section 6.12. More recently, Poole^{271,272} defined a solvent strength parameter, SSP, as $\text{SSP} = \Delta G_s^\circ(\text{CH}_2)/\rho_1$ where ρ_1 is the density of the stationary phase at the column temperature. Although $\Delta G_s^\circ(\text{CH}_2)$, or alternatively SSP, might well be the best "single parameter" that can be used to classify stationary phases, it cannot possibly reflect the various solute/solvent interactions that determine the retention of a solute by a given stationary phase. The use of various test solutes as probes cannot be used to identify such interactions either, because there are no test solutes that possess, for example, a singular quality of "polarity" without also possessing some other quality. Thus a test solute such as 1-nitropropane, although certainly dipolar, is also quite basic, whereas a test solute like butan-1-ol is acidic, basic, and dipolar! Poole^{138,271,272} recognised this difficulty, although no easy solution to the problem seemed to be available.

It has already been shown how solvation equations can be used to characterise stationary phases in the McReynolds and Laffort series (sections 6.11 and 6.12), and how retention data in these two series may then be used to obtain π^{H_2} and $\Sigma\alpha^{\text{H}_2}$ solute parameters, section 6.14. Since these two activities are interdependent, it seems obligatory to test equation 83 with a quite independent set of retention data.

$$\log SP = c + rR_2 + s\pi^H_2 + a\Sigma\alpha^H_2 + b\Sigma\beta^H_2 + l\log L^{16} \quad [83]$$

The retention data, as $\log K$ values, obtained by Poole and his colleagues²⁷¹ on 24 stationary phases at 121.4°C can be used as a first test for solvation equation 83. There are two main reasons for this choice. Firstly, the data obtained by Poole²⁷¹ is amongst the most reliable GLC data ever reported, with considerable care being taken to exclude contributions from interfacial adsorption. Secondly, the stationary phases studied by Poole include seven molten salts, and it is of some interest to analyse results on these novel stationary phases using the general solvation equation 83.

The stationary phases used by Poole are shown in Table 61, together with $\Delta G_s^\circ(\text{CH}_2)$ and SSP values given by Poole²⁷¹. Solute parameters were all taken from section 6.14; for convenience they are set out in Table 62.

Note that not all solutes were examined on all phases, so that for any particular phase the number of solutes studied (N) is less than 42. When equation 83 was first applied to the Poole data set, it was noted that one of the Poole solutes, oct-1-yne, was always out of line, and consistently behaved in a manner more expected of oct-2-yne. On contacting Professor Poole over this problem, it was gratifying to receive confirmation that compound oct-1-yne in the Poole data set was indeed oct-2-yne²⁷³. Hence, oct-2-yne is listed in Table 62.

For each stationary phase, regression coefficients were generated using exactly the solutes studied by Poole²⁷¹. Of the 24 phases with an average of some 35 solutes each, only one data point was excluded. The result for 2,6-dimethylaniline on phase V was out-of-line by over four standard deviations, with $\log K(\text{obs}) = 2.947$ and $\log K(\text{calc}) = 3.416$ units.

Table 61. The Stationary Phases Examined by Poole at 121.4°C.

Code	Stationary phase	$\Delta G S^{\circ}(\text{CH}_2)$ SSP	
A	Squalane	-530	-728
B	SE-30	-463	-578
C	OV-3	-458	-523
D	OV-7	-467	-504
E	OV-11	-475	-478
F	OV-17	-470	-463
G	OV-22	-458	-439
H	OV-25	-431	-396
I	OV-105, poly (cyanopropylmethyl dimethylsiloxane)	-461	-523
J	OV-225, poly (cyanopropylmethyl phenyl methylsiloxane)	-418	-410
K	OV-275, poly (dicyanoallylsiloxane)	-265	-243
L	OV-330, a poly (dimethylsiloxane)-carbowax copolymer	-418	-407
M	Poly (trifluoropropylmethylsiloxane), QF-1	-393	-337
O	Carbowax 20M	-400	-387
P	Poly (diethyleneglycol succinate), DEGS	-324	-275
Q	1,2,3-Tris(2-cyanoethoxy)propane, TCEP	-280	-273
R	Poly (phenylether) five rings, PPE-5	-487	-436
S	Tetraethylammonium 4-toluenesulphonate	-286	-267
T	Tributylammonium 4-toluenesulphonate	-384	-384
U	Tetrabutylammonium 4-toluenesulphonate	-377	-377
V	Tetrabutylammonium picrate	-411	-381
W	Tetrabutylammonium methanesulphonate	-398	-406
X	Tetrabutylammonium N-(2-acetamido)- 2-aminoethanesulphonate	-319	-312
Y	Tetrabutylammonium 3-[tris(hydroxymethyl) methylamino]-2-hydroxy-1-propanesulphonate	-290	-276

As a necessary preliminary, the full equation 83 was applied to all 24 phases, and it was found that in no case was the b -coefficient statistically significant as judged by the t -test. The simpler equation, equation 125, can then be used. The solute parameters used in regression equation 125 follow, Table 62.

$$\log K = c + rR_2 + s\pi^H_2 + a\Sigma\alpha^H_2 + l\log L^{16} \quad [125]$$

Table 62. Solute Parameters Used In The Regression Equation 125.

Solute	R_2	π^{H_2}	$\Sigma\alpha^{H_2}$	$\log L^{16}$
n-Heptane	0.000	0.00	0.00	3.173
n-Octane	0.000	0.00	0.00	3.677
n-Nonane	0.000	0.00	0.00	4.182
n-Decane	0.000	0.00	0.00	4.686
n-Undecane	0.000	0.00	0.00	5.191
n-Dodecane	0.000	0.00	0.00	5.696
n-Tridecane	0.000	0.00	0.00	6.200
n-Tetradecane	0.000	0.00	0.00	6.705
n-Pentadecane	0.000	0.00	0.00	7.209
n-Hexadecane	0.000	0.00	0.00	7.714
Butanone	0.166	0.70	0.00	2.287
Pentan-2-one	0.143	0.68	0.00	2.755
Hexan-2-one	0.136	0.68	0.00	3.262
Heptan-2-one	0.123	0.68	0.00	3.760
Octan-2-one	0.108	0.68	0.00	4.257
Nonan-2-one	0.119	0.68	0.00	4.735
Benzene	0.610	0.52	0.00	2.803
n-Butylbenzene	0.600	0.52	0.00	4.686
cis-Hydrindane	0.439	0.20	0.00	4.610
Oct-2-yne	0.225	0.30	0.00	3.850
Dodec-1-yne	0.133	0.23	0.13	5.657
Butan-1-ol	0.224	0.42	0.37	2.601
2-Methylpentan-2-ol	0.169	0.30	0.31	3.081
Dodecafluoroheptan-1-ol	-0.640	0.55	0.60	3.089
Octan-1-ol	0.199	0.42	0.37	4.619
Phenol	0.805	0.88	0.60	3.897
2,4,6-Trimethylphenol	0.860	0.83	0.37	5.185
Benzonitrile	0.742	1.07	0.00	4.004
1-Nitropropane	0.242	0.95	0.02	2.894
1-Nitropentane	0.210	0.95	0.00	3.938
Nitrobenzene	0.871	1.10	0.00	4.511
1,1,1,2-Tetrachlorethane	0.542	0.63	0.10	3.641
Pyridine	0.631	0.82	0.00	3.003
2,4,6-Trimethylpyridine	0.634	0.72	0.00	4.200
Aniline	0.955	0.96	0.26	3.993
N-Methylaniline	0.948	0.94	0.17	4.494
N,N-Dimethylaniline	0.957	0.82	0.00	4.754
2,6-Dimethylaniline	0.967	0.93	0.20	5.037
Dioxan	0.329	0.75	0.00	2.892
Methylphenylether	0.708	0.73	0.00	3.859
Di-n-hexylether	0.000	0.25	0.00	5.938
Benzodioxan	0.874	1.01	0.00	4.985
Nonanal	0.150	0.65	0.00	4.900

Results of application of equation 125 to all 24 phases are summarised in Table 63, As judged by the values of S.D. and R, the regression equations for the 24 phases are of excellent quality. Most values of S.D. are below 0.08 log units, and in the case of the four phases with S.D. larger than 0.08, viz. P, U, W, and X,

errors in log K quoted by Poole²⁷¹ are much larger than for the other phases. It can therefore be concluded that the solvation parameters obtained previously, can, indeed, be used to characterise other GLC stationary phases. Whether such characterisation is useful or not, will depend at least in part on whether the characteristic constants r , s , a , and l in equation 125 make general chemical sense.

Table 63. Regression Equations For The Phases In Table 61.

Code	c	r	s	a	l	SD	R	N
A	-0.202	0.125	0.018	-0.097	0.581	0.033	0.9985	39
B	-0.194	0.024	0.190	0.125	0.498	0.022	0.9989	39
C	-0.181	0.033	0.328	0.152	0.503	0.021	0.9992	39
D	-0.231	0.056	0.433	0.165	0.510	0.025	0.9989	39
E	-0.303	0.097	0.544	0.174	0.516	0.029	0.9985	39
F	-0.326	0.128	0.612	0.147	0.509	0.036	0.9978	38
G	-0.328	0.201	0.664	0.190	0.489	0.034	0.9979	38
H	-0.273	0.277	0.644	0.182	0.472	0.042	0.9973	39
I	-0.212	-0.038	0.395	0.368	0.499	0.026	0.9987	39
J	-0.509	0.015	1.214	0.964	0.462	0.035	0.9979	39
K	-0.635	0.388	1.902	1.644	0.241	0.080	0.9935	32
L	-0.430	0.104	1.056	1.419	0.481	0.051	0.9954	36
M	-0.251	-0.362	1.101	0.054	0.416	0.077	0.9853	39
O	-0.558	0.285	1.292	1.803	0.450	0.059	0.9957	39
P	-0.498	0.351	1.683	1.718	0.311	0.096	0.9899	38
Q	-0.489	0.278	1.913	1.679	0.290	0.056	0.9972	40
R	-0.395	0.230	0.829	0.337	0.527	0.044	0.9972	39
S	-1.008	0.362	2.059	3.609	0.340	0.076	0.9941	29
T	-0.717	0.110	1.546	2.917	0.466	0.069	0.9922	30
U	-0.617	0.009	1.659	3.360	0.440	0.106	0.9885	34
V	-0.542	0.100	1.557	1.424	0.445	0.061	0.9935	36 ^a
W	-0.631	0.095	1.595	3.408	0.437	0.097	0.9895	34
X	-0.666	0.283	1.809	3.417	0.329	0.100	0.9902	34
Y	-0.690	0.281	1.821	2.859	0.305	0.080	0.9932	29

^a Excluding solute 2,6-dimethylaniline that is out by over four standard deviations, calc. log K = 3.416, obs. log K = 2.947

The $r.R_2$ term generally makes only a minor contribution, but nevertheless the r -constant seems well-behaved. Phases with a substantial proportion of phenyl groups lead to an increase in the r -constant, as expected if this is an index of π - and n - electron pair interaction. Thus along the OV series of poly (methylphenylsiloxane), the r -constant increases as the % phenyl group increases. The only substantially negative value of the r -constant, with phase M, corresponds to the only phase that contains fluorine, again as expected.

More important is the $s.\pi^H_2$ term in which the s -constant reflects dipole/dipole and dipole/induced dipole interactions, and so may be taken as a measure of stationary phase dipolarity. Of the conventional phases, phase K (OV-275), P(DEGS), and Q(TCEP) have the largest s -constants of around 1.7-1.9 units. The ionic salts (S - Y) all have s -constants that approach or equal those for the most dipolar conventional phases, and which are very much larger than the unsubstituted poly (methylphenylsiloxane) phases (C - H). The SSP parameter, see Table 61, is very nearly the same, however, for phase H as for phases (T - W).

All the phases in Tables 61 and 63, other than Squalane (A), are hydrogen bond bases and so give rise to significant values of the a -constant. Of the conventional phases K, L, O, P, and Q are the most basic, and hence will preferentially interact with solutes that are hydrogen bond acids. But all the ionic salts except phase V are significantly stronger hydrogen bond bases than any of the conventional phases. This is clearly due to the negatively charged counter-anions. It is not coincidental that where charge dispersion in the anion is very large, as with phase V, the a -constant decreases considerably.

The l -constant, on its own, is equivalent to $\Delta G_s^\circ(\text{CH}_2)$ in that both quantities describe the ability of a phase to separate adjacent members of an homologous

series. For the 24 phases, a regression of $\Delta G_s^\circ(\text{CH}_2)$ against l gives,

$$\Delta G_s^\circ(\text{CH}_2) = -44.9 - 816l \quad [126]$$

with S.D. = 17 cal mol⁻¹, R = 0.9739, and N = 24. Thus general solvation equations 83 or 125, includes, via the l -constant, all the information contained in $\Delta G_s^\circ(\text{CH}_2)$.

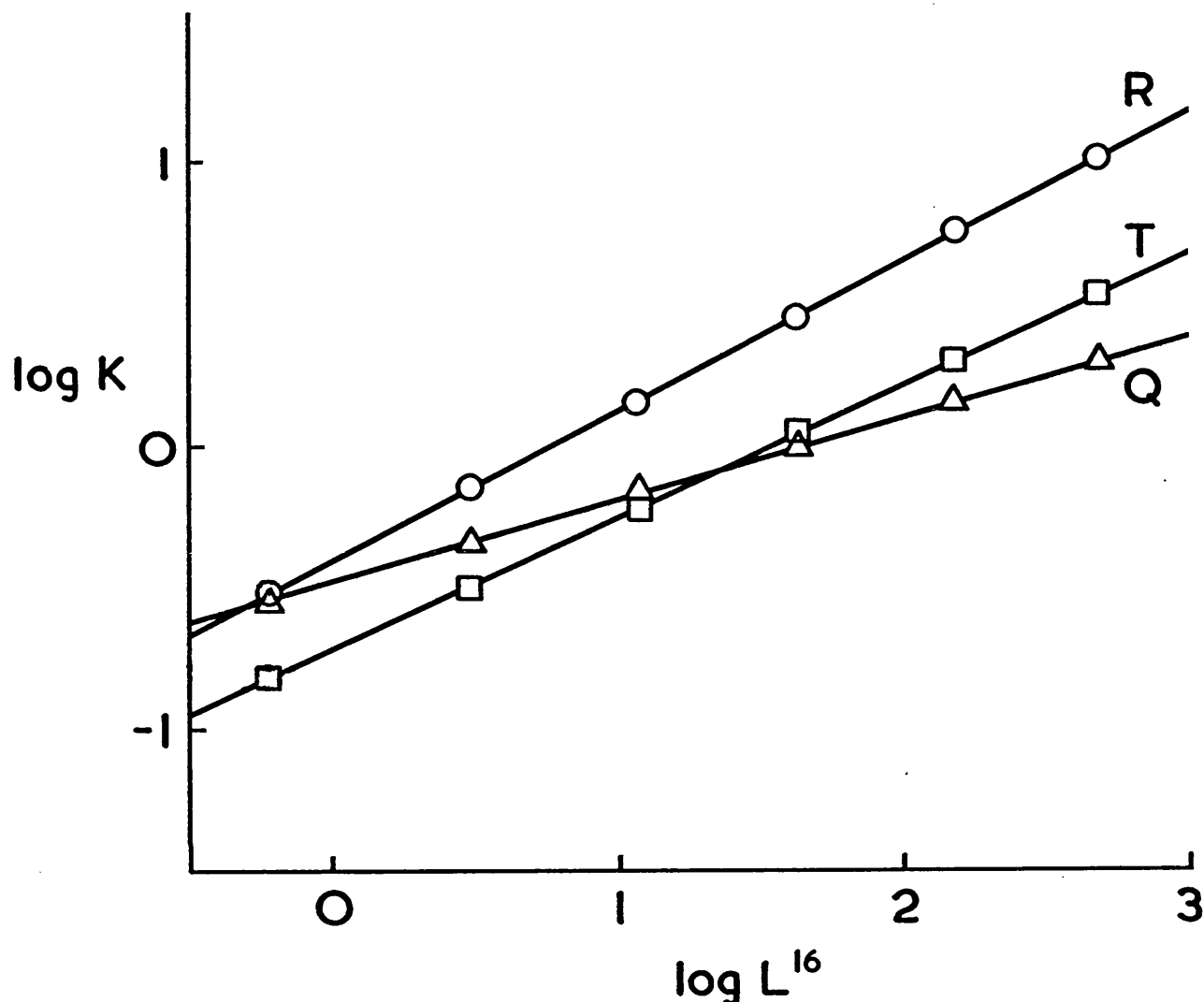
If the dependent variable, log SP, in equation 83 is based on retention times, then the characteristic constants r , s , a , b , and l will be the same as if log K had been used as the dependent variable. Only the c -constant will change. For many purposes, the c -constant is not needed in the set of characteristic constants, but if log K is used as the dependent variable, combination of the c -constant and the l -constant can lead to extra information.

Considering only the rare gases and the alkanes, for which $R_2 = \pi^{\text{H}_2} = \Sigma \alpha^{\text{H}_2} = \Sigma \beta^{\text{H}_2} = 0$, so that equation 125 will then become,

$$\log K (\text{inert solute}) = c + l \cdot \log L^{16} \quad [127]$$

The value of c is now identical to log K for an inert solute with $\log L^{16} = 0$, i.e. a rare gas between krypton (-0.211) and xenon (0.378) or an alkane between methane (-0.323) and ethane (0.492). It is now possible to combine the c -constant and the l -constant, via equation 127, to show exactly how the affinity of a stationary phase for an inert solute depends on the L^{16} value of the solute. In Figure 19 is a plot of log K calculated through equation 127 against $\log L^{16}$ for a series of n -alkanes on phases R, T, and Q. For any alkane, phase R always has the highest log K value, i.e. highest affinity, of the three phases. But for phases T and Q there is a "cross-over" point between propane and n -butane, so that for small alkanes phase Q has more affinity, but for larger alkanes phase T has the greater affinity.

FIGURE 19: Plot of Log K Against Log L^{16} for the N-Alkanes Methane to Hexane on Phases R, T and Q.



The l -constant, as with $\Delta G_s^\circ(\text{CH}_2)$, gives only the slopes of the lines in Figure 19. Combination of the l -constant with the c -constant leads to extra information on the affinity of the stationary phase for inert solutes.

The interaction of solutes with stationary phases can be quantified by calculating each term in equation 83, or, for the present purpose, each term in equation 125. The results are given in Table 64, using three particular solutes suggested by Poole²⁷¹ as test probes. *n*-Butylbenzene was used as a test probe for dispersive interactions, octan-1-ol for solvent basicity, benzodioxan for solvent acidity (not relevant here), and nitrobenzene for 'orientation

interactions'. However, examination of Table 64 shows that it is not possible to define a set of test probes in which each probe corresponds to a unique interaction. Thus octan-1-ol, the test probe for solvent basicity (the $a.\Sigma\alpha^{\text{H}_2}$ term) actually interacts with most solvents more through dipolar interactions (the $s.\pi^{\text{H}_2}$ term) than through solute hydrogen bond acid/solvent hydrogen bond base interactions.

Table 64. A Term-By-Term Quantitative Evaluation Of The Solute/Stationary Phase Interactions That Contribute to Log K In Equation 125.

Phase	c	$r.R_2$	$s.\pi^{\text{H}_2}$	$a.\alpha^{\text{H}_2}$	$l.\log L^{16}$	Dispersion ^a	Cavity ^a
Solute n-butylbenzene							
C	-0.18	0.02	0.17	0	2.36	4.63	-2.27
K	-0.64	0.23	0.99	0	1.13	2.22	-1.09
M	-0.25	-0.22	0.57	0	1.95	3.83	-1.88
Q	-0.49	0.17	0.99	0	1.36	2.67	-1.31
R	-0.40	0.14	0.43	0	2.47	4.85	-2.38
T	-0.72	0.07	0.80	0	2.18	4.28	-2.10
Solute octan-1-ol							
C	-0.18	0.01	0.14	0.06	2.32	4.79	-2.47
K	-0.64	0.08	0.80	0.61	1.11	2.29	-1.18
M	-0.25	-0.07	0.46	0.02	1.92	3.96	-2.04
Q	-0.49	0.06	0.80	0.62	1.34	2.77	-1.43
R	-0.40	0.05	0.35	0.12	2.43	5.02	-2.59
T	-0.72	0.02	0.65	1.08	2.15	4.44	-2.29
Solute nitrobenzene							
C	-0.18	0.03	0.36	0	2.27	4.16	-1.89
K	-0.64	0.34	2.09	0	1.09	2.00	-0.91
M	-0.25	-0.32	1.21	0	1.88	3.45	-1.57
Q	-0.49	0.24	2.10	0	1.31	2.40	-1.09
R	-0.40	0.20	0.91	0	2.38	4.36	-1.98
T	-0.72	0.10	1.70	0	2.10	3.85	-1.75

^a These represent a breakdown of the $l.\log L^{16}$ term according to reference 107.

It is useful to break down the $l \cdot \log L^{16}$ term into an exoergic dispersion contribution to the Gibbs energy of solution, leading to a positive contribution to $\log K$, and an endoergic cavity contribution to the Gibbs energy of solution, leading to a negative contribution to $\log K$. Abraham and Fuchs¹⁰⁷ dissected $\log L^{16}$ values into various contributions, and if these contributions are calculated for the test solutes in hexadecane, assuming that the proportions are relatively the same in the phases studied here, the results in the last two columns of Table 64 are obtained. Now even if these dispersive and cavity interactions are only very approximate, they do show, as suggested before in section 7.10, that the main exoergic contribution to solution of gaseous solutes in nearly all liquid phases (except water perhaps) is through solute/solvent dispersion interactions. Unfortunately it is very difficult to devise a simple experimental solute parameter that will reflect only the ability of a solute to interact via dispersion forces. Hence the combined dispersion plus cavity term, $\log L^{16}$, has to be used in the general solvation equation, and then broken down approximately into its constituents.

Finally, considering a few individual phases, it can be shown how the characteristic constants can be used to select phases for particular separations. Phases A - J are not exceptional; their dipolarity and hydrogen bond basicity gradually increase along the series. Phase K has a very high dipolarity and basicity but the very low value of the l -constant would tend to reduce the general usefulness of the phase. Phase M is exceptional, in that it has a moderate dipolarity ($s = 1.101$) but has effectively zero basicity, a most unusual occurrence. Of the molten salts, the tributylammonium salt, phase T, is of interest in that the Bu_3NH^+ group would be expected to be a powerful hydrogen bond acid, but for this phase, as with all others, the b -constant turns out to be zero. No doubt intramolecular hydrogen bonding between the Bu_3NH^+ group and the counter-anion takes place, so that the potential for

intermolecular hydrogen bonding is reduced to zero. A comparison of the phases S, T, and U shows that the a -constant is somewhat reduced in phase T even though all three phases contain the 4-toluenesulphonate anion. This would be the result if there were intramolecular hydrogen bonding in phase T, because the anion would not then be totally available for intermolecular hydrogen bonding to a solute that was a hydrogen bond acid.

For the separation of rather nonpolar solutes, the only relevant characteristic constant is l . Phases A-F and phase R all have $l \geq 0.50$ and will be the best phases in the set to use. In order to separate compounds that are dipolar and nonacidic, a phase with a large s -constant (and preferably a large l -constant) is required. Phases J, L, M, O, and the molten salts T, U, V, and W satisfy these criteria. These phases, except phase M, will also selectively absorb hydrogen-bond acids because they all have large a -constants. To absorb acids rather than simply dipolar compounds requires a $\gg s$, if possible, and here the molten salts seem to be preferred, see Table 64.

Again, this analysis shows that general solvation equation 83 (or 125), can be used to analyse GLC retention data, both to classify stationary phases and to select phases for particular separations. The method is quantitative in that specific solute/stationary phase interactions can be identified and their contribution to the overall retention process can be evaluated, Table 64.

8.10 Summary Discussion, Conclusions and Future Work

A much improved solvation equation, equation 83, has successfully been developed, and already applied to a variety of solubility and solubility related processes.

$$\log SP = c + r.R_2 + s.\pi^H_2 + a.\Sigma\alpha^H_2 + b.\Sigma\beta^H_2 + l.\log L^{16} \quad [83]$$

For processes occurring within condensed phases, *ie.* $\log P$ (solvent1 $\rightleftharpoons$ solvent2), a substitute term $m.V_X$, instead of $l.\log L^{16}$, has been found to give improved results over equation 83.

$$\log P \text{ (solvent1 } \rightleftharpoons \text{ solvent2)} = c + r.R_2 + s.\pi^H_2 + a.\Sigma\alpha^H_2 + b.\Sigma\beta^H_2 + v.V_X \quad [103]$$

By relating solubility and solubility related processes to solute characteristics, a wide range of processes can be characterised, and the contributions of the individual terms in equation 83 (or 103) quantified in a way which has previously been rather difficult. No attempt has, or should be made to simplify these equations, as they reflect the complexity of the solute-solvent interactions which are possible in the solvation of a solute. A single solvent strength parameter^{271,272} cannot successfully model all the possible interactions in a solubility or solubility related process.

Solvation equations have enabled the characterisation of a large number of 'typical' GLC stationary phases, other more unusual GLC phases (such as molten salts, section 7.60), polymers, more 'typical' solvents, and partition processes - some akin to those taking place inside living organisms. The systematic evaluation of gas-liquid stationary phases has been one of the largest ever attempted, notably looking at the phases of McReynolds¹³³ and Laffort⁸².

Application of solvation equations to these and other GLC phases has shown just how similar many of these phases are. GLC phases can now be chosen in a very precise way for their solute selectivity ability. The equations have also assessed the suitability of candidate phases for use in SAW devices. Solvation equations are also invaluable for the calculation or estimation of solubility and solubility related phenomena. The scope of their application is clearly wide-ranging, sections 7.40 to 7.60 specifically giving examples of applications of the improved solvation equations, 83 and 103. It has also been noted, section 6.14, Table 31, that the newer solvation equations will give essentially the same value of the coefficients as older equations for a given solubility process, but correlation coefficients and standard deviation will be improved using the newer equations.

Substitute parameters for δ_2 and π^*_2 have been investigated, $f(\eta)$ and μ^2 respectively. The use of these two parameters has been dismissed, as their use not only generates poorer standard deviation and correlation coefficients, but leads to cross-correlations between $f(\eta)$ and $\log L^{16}$, and μ^2 and β^{H_2} .

The back-calculation techniques developed during the course of this work, including the novel 'inverse' MLRA approach has been very effective in calculating new parameters, and firming up existing ones. A major aim of the project has been achieved in extending the application of the solvation equations by vastly increasing the database on $\log L^{16}$ for mono- and multifunctional compounds, to a point where the lack of a $\log L^{16}$ value is no longer a major consideration. The development and extension of the database on the effective or 'summation' solvation parameters for mono- and multifunctional compounds, π^{H_2} , $\Sigma\alpha^{H_2}$ and $\Sigma\beta^{H_2}$ clearly improves the ability of the solvation equations to reflect solute-solvent interactions in real solubility situations. The π^{H_2} scale has been set up based on an experimental procedure and is no longer based on the solvent π^*_1 value as it used to be. The $\Sigma\alpha^{H_2}$ and $\Sigma\beta^{H_2}$ scales are also based on

experimental procedure, and while they may be very similar or identical to α^H_2 and β^H_2 values for non-associated liquids, many important molecules are multifunctional in real solubility situations and the $\Sigma\alpha^H_2$ and $\Sigma\beta^H_2$ values reflect this fact. The main terms in the solvation equations, viz. π^H_2 , $\Sigma\alpha^H_2$, $\Sigma\beta^H_2$ and $\log L^{16}$ are all related to Gibbs energy, and form a thermodynamically consistent set of explanatory variables.

The molar refraction parameter developed, R_2 , is a substantial improvement over the trivial polarisability 'correction factor', δ_2 , more especially since R_2 has a degree of rationale behind it and is calculable for any molecule (knowing $f(\eta)$ and V_X). The refractive index is either known, or can be measured or estimated for the majority of molecules that might be encountered, and V_X can be easily calculated for any molecule if its constituent atoms and number of bonds are known^{52,103-105}.

The implementation of a PC-based solute parameter database has been successfully achieved. The database, and the programs specific to it (notably the multiple regression program) can now be used on any IBM compatible personal computer. Any computer with access to the SmartWare II computer package is able to run the self-contained database and programs, generating solvation equations using a selection of parameters from within the database. The limitations in flexibility and performance of the database and its programs are no longer related to the constraints and abilities of the Fortran 77 language; the performance of the database is only limited by the abilities and integral functions of the SmartWare II package, which itself is continually being improved and updated. Accessibility, the 'professional' appearance and user-friendliness of the database have all improved since transferring to Smart.

8.11 Future Work

The systematic evaluation of gas chromatographic stationary phases using extensive collections of retention data has largely been completed during the course of this work, and there is no longer any great collection of retention data left to characterise. McReynold's data¹³³ is on a large number of the common stationary phases, but of course, there are others, and new phases are constantly being developed. Characterisation of any other phases can continue in the same manner, using either published or experimentally determined data. However, one of the major conclusions from the analysis of McReynold's¹³³ and Laffort's⁸² data is that for a given phase, it is very likely there will be at least one, or more, very similar to it, (see section 6.12 especially). Also, the majority of gas chromatographic stationary phases are either hydrogen bond bases, or are neutral. There remains significant scope for development of a number of hydrogen bond acidic and other novel stationary phases for general GLC and SAW sensor use. SXFA (section 7.50) is a hydrogen bond acidic phase, and may turn out to be extremely useful. Selectivity for hydrogen bond bases is an advantageous property, as there are a vast number of important solutes with hydrogen bond base activity.

It is of considerable importance and interest to continue the characterisation of solvents and solvent/water partitions (section 7.40). There remains a wealth of values for many important solvents on $\log L$ (gas $\rightleftharpoons$ solvent) in the literature. For solvents where there is either no, or limited information, $\log L$ (gas $\rightleftharpoons$ solvent) values can be measured by the technique of headspace analysis.

Having developed a satisfactory π^{H_2} scale, it is very important to continue the calculation of π^{H_2} values, and develop the $\Sigma\alpha^{H_2}$ and $\Sigma\beta^{H_2}$ scales at the same time. $\Sigma\alpha^{H_2}$ values can be back-calculated from suitable GLC retention data; it is

relatively easy to find data on basic GLC phases. Effective $\Sigma\alpha^{\text{H}_2}$ values do not differ markedly from α^{H_2} values, and so far, only in the case of carboxylic acids has any substantial difference been noted. The calculation of $\Sigma\beta^{\text{H}_2}$ values is altogether more difficult. Reliable retention data has to be gathered for solutes on RP-HPLC systems, and any $\Sigma\beta^{\text{H}_2}$ values back-calculated by a very time-consuming iterative process, (see section 6.13). A matrix of up to 200 solutes on up to 100 different systems is being constructed, and only when suitable back-calculation computer programs have been completed, will this process be attempted. This process will make available a large database on $\Sigma\beta^{\text{H}_2}$ values, firming up provisional values and filling in the gaps for important solutes in the database such as phenols, aromatic alcohols and ethers, anilines, and pyridines.

No further work on the computing or layout side of the solute parameter database is envisaged, although if any is needed, it is a fairly simple process to develop applications and database constructions within the framework of SmartWare II.

9.10 Experimental

9.11 Dynamic GLC Experimental

The Measurement of Relative Partition Coefficients

Relative partition coefficients were measured on several specially adapted Perkin-Elmer F11 and F33 flame ionisation detector (FID) gas chromatographs, the flow controllers supplied with the machines having been replaced by high precision Negretti and Zambra M2545 units, to guarantee readily reproducible and stable gas flow rates of around 40ml/minute. Where work was to be carried out at 298.15K (or near enough to ambient temperature to make regulation by air oven inaccurate) it was preferable to use a liquid bath thermostat. The head of the gas chromatograph was simply placed over a thermostat water bath such as a Grant SE-50, and the columns completely immersed in water. Accurate temperature regulation to within $\pm 0.05\text{K}$ is possible using this method. Note, this is a distinct advantage of using older equipment such as the Perkin-Elmer F11 and F33, as opposed to modern gas chromatographs, in that they can be easily modified, taken apart, and used in this way. If room temperature strayed close to, or exceeded 298.15K, cooling units such as the Townson & Mercer Laboratory Refrigeration Unit, along with the water bath heater could also be used to ensure isothermal conditions and minimize effects due to laboratory temperature variations. A special customised water bath, with simultaneous heating and cooling facilities was also available for this purpose.

The majority of this work consisted of obtaining relative retention information, as absolute values need only be obtained for a few key solutes, and relative values converted to absolute values by matching up with an absolute experimental standard.

The Measurement of Absolute Partition Coefficients

Absolute partition coefficients were measured using a Pye-Unicam 104 chromatograph with heated katharometer detector, and also on a basic Pye-Unicam 104 system, with a replacement amplifier and detector by AMS Ltd. Flow controllers were again Negretti and Zambra M2545 units, and column temperatures were thermostatted exactly as that described for relative partition coefficients. Column temperatures were measured using mercury thermometers ($\pm 0.05\text{K}$) calibrated against some from the National Physical Laboratory, Teddington.

Exit carrier gas flow rates were measured using a soap bubble flow meter, and readings subsequently corrected for the temperature differences between the chromatograph column and the meter, and the vapour pressure of water at the flow meter temperature. A digital hand held thermometer ($\pm 0.1\text{K}$, type Tempcon TC1100) was used to measure the temperature of the soap solution and carrier gas in the flow meter for two reasons. Water saturated carrier gas will condense on a mercury bulb thermometer, (the resultant latent heat effect giving very slight inaccuracies) and simply because it was easier to introduce a thermocouple into the narrow flow meter than a thermometer. The thermocouple was previously calibrated at the experimental temperature using the accurate mercury thermometers. The inlet and outlet gas pressures were measured using manometers filled with mercury, and a correction for the pressure drop across the column also applied.

One disadvantage of a system using a katharometer detector is the low detector sensitivity compared to an FID. Hence comparatively large quantities of solutes need to be chromatogrammed, with the concurrent possibility of adsorption on to the 'inert' support. However, the use of a katharometer is desirable for

absolute measurements, as its very design enables the accurate measurement of flowrates. The method used to overcome this difficulty is to use a katharometer detection system to obtain absolute K values for a number of unreactive inert solutes, such as alkanes, and then use the FID system to obtain K values relative to the alkane standards, thereby indirectly obtaining absolute values for the unknown. As an example, for n-hexadecane many absolute K values have already been determined ²⁴. So to get an absolute L^{16} value for an unknown solute, it need only be chromatogrammed on n-hexadecane at 298.15K with a solute for which L^{16} is already known, such as octane, and from the following relationship (recasting equation 14, section 1.3), L^{16} can be easily calculated.

$$\frac{L^{16}(\text{UNKNOWN})}{L^{16}(\text{STANDARD})} = \frac{T_R'(\text{UNKNOWN})}{T_R'(\text{STANDARD})} \quad [128]$$

Experimental Details

Flame ionisation detector systems were used exclusively with moisture free nitrogen as carrier gas (dried by passing the source gas for the chromatograph through a special silica gel/molecular sieve absorbent column). Thermal conductivity detector or katharometer systems were used with helium as carrier gas, dried in the same manner. Gas flowrates were typically 40ml/minute.

For all the experimental work carried out, it was desirable to introduce a sample size as small as possible into the chromatograph for a discernible peak. Measurements obtained, such as solute partition coefficient, would then be obtained in the region of infinite dilution. Generally, sample size injected was 0.02 μ l, and even in the case of solutes which were difficult to detect or slow to elute, rarely was more than 0.1 μ l used. Samples were injected using a Hamilton 7001N 1.0 μ l syringe, into a column injection heater at a temperature sufficiently high to volatilize the solute, ensuring that the solute interacts with the column

head as a vapour. Partition coefficients calculated in this work are for the equilibrium between gas (vapour) and solvent. Relative partition coefficient work involved the use of an experimental standard all solutes were compared to, which was usually an n-alkane, such as octane. The test solute was drawn up into the syringe, the plunger then pulled back slightly, the needle wiped, and then 0.02 μ l of the standard drawn into the syringe. Solid solutes were dissolved in a suitably volatile solvent, and the required amount of the resulting solution used. Thus the test and standard solute could be simultaneously injected into the chromatograph. If the test and standard solute elution time were thought to overlap, either the standard was introduced afterward, or another standard, higher or lower in the homologous series, whose relative retention to the first standard was known could be used.

Chromatograms were displayed on a number of chart recorders, *eg.* Goerz Electronic RE 511, Perkin Elmer model 1002 and Philips PM 8251. Retention measurements were made either directly from the chart paper (especially where retention time was very large), from a Spectra-Physics minigrator (model 23000-011), or using an Amstrad 2286 IBM compatible personal computer, running Unkelscope Level II data acquisition software with a Metrabyte DAS-8 PGA analogue/digital conversion board.

Packing and Column Preparation

Usually the stationary phase could be simply coated onto the chosen support by rotary evaporation of a solution/slurry of stationary phase and support respectively, in a suitable volatile solvent. However, several high molecular weight stationary phases, such as polyisobutylene with a molecular weight of around 380,000, would not coat by this particular method, (see later). The

stationary phase is accurately weighed out into a round-bottomed flask, along with the chosen 'inert' support. If any absolute partition coefficients are to be measured, it is important that the volume of the stationary phase at column temperature is known, (equation 12, section 1.3), so all such weighings are taken to 4 decimal places in grammes. Sufficient suitable solvent is then added to completely dissolve the stationary phase, and produce a slurry of support. The same flask is used throughout the coating procedure, to avoid any errors in phase/support/solvent transfer. Depending on the estimated ease with which the phase will coat the support, the procedure now varies.

If there are no perceived problems with coating the support, the mixture is slowly agitated by turning with vacuum off on a rotary evaporator for about an hour. Care is taken here to joint all glass joints with PTFE tape, to avoid vacuum grease contamination of the mixture, and weighing errors. The solvent is then slowly extracted using vacuum over the course of the next hour. Depending on solvent volatility, heat can also applied to the bottom of the flask from a heated water bath. When all solvent has been removed, as checked by repeated weighings, the coated support is sieved to ensure a uniform mesh range, typically mesh 40/60. Care with the support is necessary throughout the whole coating procedure to ensure the particle size is not significantly decreased through attrition. The resulting coated support can now be used to pack a column.

The static procedure for coating the support in the case of high molecular weight or 'problem' stationary phases merely differs after all the weighing out procedure. Instead of turning on a rotary evaporator and then extracting the solvent, the beaker containing the stationary phase/support/solvent slurry is left to stand, with a piece of permeable paper over its top. The slurry in the beaker can be agitated using a magnetic stirrer, or even just shaken once in a while, and the solvent is left to slowly evaporate.

The static or the rotary evaporation coating procedure does not necessarily guarantee 100% coating of the support, especially with difficult phases. Where absolute L values are to be measured, the volume of phase in a given column must be known. If there was any doubt on the stationary phase loading, to determine the exact level of phase loading on a support, it was found that the ashing procedure was the most accurate and gave reproducible results. The extraction procedure using Soxhlet apparatus was not attempted, as the quantities of coated support dealt with were small, and in any case, the combustion method has been found to be more reproducible than Soxhlet extraction³⁷. Using the combustion procedure, a thoroughly dry coated support is weighed, and then 'ashed' by heating in a crucible to constant weight. The difference between initial and final weight is then calculated. The dry support is then ashed in exactly the same way, as it will have an organic methylsilyl surface layer content which can be volatilised by heating. The difference in weight obtained by the first ashing is then corrected for the volatile constituent of the support, and then the accurate loading of the stationary phase on support can be calculated.

There are two equations often used to calculate the loading of stationary phase on inert support. It can be expressed as the ratio,

$$\lambda' = \frac{\text{mass of stationary liquid phase}}{\text{mass of (support + stationary liquid phase)}} \quad [129]$$

This ratio is usually expressed as a percentage. The more useful ratio, which is linearly proportional to the amount of liquid present is,

$$\lambda = \frac{\text{mass of stationary liquid phase}}{\text{mass of support}} \quad [130]$$

The ratio defined by equation 130 was exclusively used (as a percentage) in this work.

In GLC the quantity of liquid stationary phase coated on a support can have any value up to the limit of the support's capacity, *i.e.* the loading at which the packing becomes sticky instead of free running. If no other criteria govern the percentage loading it is convenient to choose a loading which gives a high column efficiency, and minimizes support adsorption effects. Typically in physiochemical work, loadings on pink and white diatomite supports are around 20%, and 5-7% on high density diatomites such as Chromosorb G. Typically in this work, the support used was Chromosorb G with loadings of around 10%, specifically to try and minimize adsorption effects, (see section 7.50).

Columns and Packing

A variety of column lengths were employed, from 0.14m up to around 3m. This is because strongly retained solutes can be injected into the shorter columns, and the less retained solutes into the longer columns. Longer columns give improved separation of mixtures, but this is not an important consideration in this work. Often two lengths of columns were packed with the same stationary phase, so a broad range of solutes could be employed. Short columns are very advantageous when injecting very strongly retained solutes. Longer columns would necessitate the injection of larger amounts of solute, which would invalidate the infinite dilution assumption of the measurements obtained. As a rough guide, if the corrected retention time, t'_R , is 10 times or more greater than the unretained gas holdup time, t_M , a solute can be assumed to be interacting sufficiently with the stationary phase. Less than this factor, the solute will not be interacting sufficiently, and the measurement will be suspect. At the other end of the

spectra, if the chromatogram peak is extremely broad, the solute is being retained very strongly, the column is too long, and it is very difficult to measure an accurate retention time. If two different column lengths are employed to measure retention information for the same stationary phase, it is good practice to match up several solutes which will elute satisfactorily on both columns, to ensure that the calculated partition coefficients are in fact comparable.

Prior to column packing, columns are cleaned in a dilute soap solution and then rinsed through with acetone, and then dried. The columns are filled by attaching the detector end to a vacuum pump if the length of the column necessitates this, and the other end to a reservoir of coated support, which is forced into the column with dry nitrogen at about 10 psi. Figure 20 shows this apparatus, and explains the column packing procedure in detail.

Prior to any retention measurements being made on a packed GLC column, the column is conditioned by placing it in the chromatograph and heating at, or slightly above operating temperature for a number of hours (usually overnight) in a stream of carrier gas. This removes the small amount of solvent remaining from the coating process, along with water and any other volatiles. It is also believed to help achieve a more even distribution of liquid on the support. Columns are reweighed after this process to check for any decrease in weight. After this conditioning process, a stable baseline should easily be attained.

Assessment Of The Errors Involved In Partition Coefficient Determination By GLC

① Errors in the determination of retention time, volume *etc.* These can be put down to measurement error, the influence of sample size and flow rate, and

operator error. Sensitive calibrated chart recorders, integrators and computers via interfaces have minimized the error in time measurement. Accurate flow controllers and sample injections of the smallest amount of solute possible have ensured reproducibility of results.

② Errors due to insufficient and unhomogenous coatings on the supports, and active supports. The use of relatively non-adsorptive supports coated with the maximum recommended loadings where possible, ensured the minimisation of these possible errors.

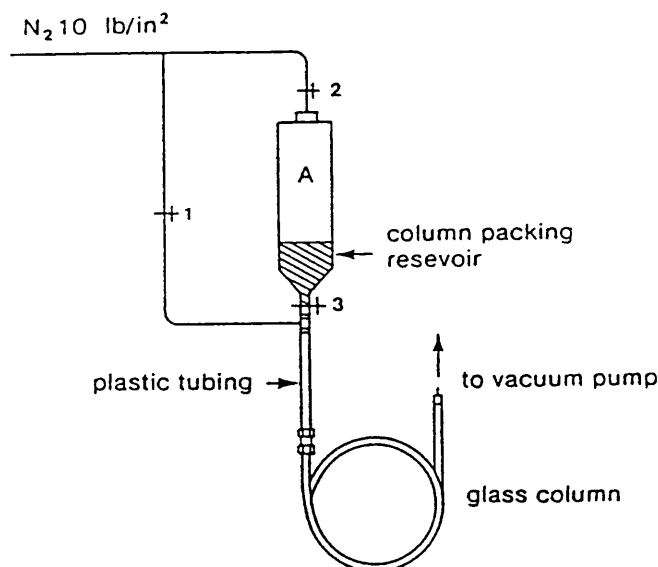
③ Fluctuation of instrumental conditions. The main parts in the chromatograph that could lead to variance were replaced. High precision flow controllers were used, and air thermostats replaced with liquid ones.

④ Calculation of stationary phase loading was done to the maximum accuracy, and checked, if need be, by the preferred procedure of ashing.

Stationary Phases Studied

Dynamic GLC was used to obtain $\log \tau$, $\log L$, or $\log V_G$ measurements on 8 stationary phases in all. One phase was n-hexadecane, in the continuing program to obtain primary $\log L^{16}$ values. The other 7 were all candidate SAW phases, (section 7.50), and for one phase, SXPH, retention measurements were taken on three variants of it. Details of these phases and their construction into GLC columns are given in Table 65, and $\log \tau$ relative to a standard (identified by $\log \tau$ (relative) = 0.00), and $\log V_G$ or $\log L$ are given in Tables 66-74.

FIGURE 20: Apparatus and Method of Column Packing



- 1 Weigh clean dry glass column empty.
- 2 Transfer sieved (for appropriate mesh size) packing into A.
- 3 Attach one end of column to vacuum pump (if length necessitates it), other end to 3.
- 4 Switch vacuum on and turn N_2 pressure up to about 10 psi. with 1 & 3 closed, 2 open.
- 5 Rotate 3 by 180° quickly (from the closed position to the open and back to closed). This allows a small amount of packing to enter the column.
- 6 Open 1, which forces packing round the column.
- 7 Close 1 to build up some pressure and reopen to force packing round the column further. Tapping the column with a metal rod facilitates packing down coated support in the column.
- 8 Repeat 5 to 7 until column is full.
- 9 Insert *preweighed* PTFE plugs to hold packing in place, and weigh the column to determine the mass of packing.

Table 65. Particulars of Phases Used and GC Conditions.

Phase	Col Length (metres)	Weight of Packing (grams)	% Loading +	Weight of Phase on Column (grams)	Phase Density (g/cm ³)	Source of Phase
n-Hexadecane	0.50	1.3708	8.340	0.11432	0.773	Aldrich
n-Hexadecane	1.50	5.6547	8.340	0.47160	0.773	Aldrich
FPOL	0.72	2.7094	4.060	0.11000	1.653	Dr. J. W. Grate
PECH (this work)	0.50	1.2498	7.574	0.09466	1.360	Dr. J. W. Grate
PECH (McGill)	1.50	9.3968	4.725	0.44400	1.360	Aldrich
PIB (this work)	1.00	5.6527	6.547	0.37008	0.918	Dr. J. W. Grate
PIB (McGill)	1.50	9.1333	6.000	0.54800	0.918	Aldrich
SXPHA	0.14	0.3232	9.994	0.03230	1.150	Dr. J. W. Grate
SXPHA	0.72	1.5447	9.994	0.15433	1.150	Dr. J. W. Grate
SXPHB	0.72	1.5396	9.928	0.15285	1.150	Phase Separations Ltd.
SXPHC	As SXPHA, length = 0.72m, modified by successive injections of Me ₃ SiCl, absolute values not calculated.					
SXCN	1.05	4.1613	7.140	0.29712	1.120	Dr. J. W. Grate
SXFA	0.76	2.9596	10.000	0.29596	1.480	Dr. J. W. Grate
PEI	0.18	0.2951	10.642	0.03140	Not known	Phase Separations Ltd.

+ % loading calculated by accurate weighing of support and phase except in the case of PECH and PIB, where ashing procedure was used.

PHASE SOURCES: [1] Dr J. W. Grate, Chemistry Division, Naval Research Laboratory (NRL), Washington, DC. USA.
[2] Aldrich Chemical Company Ltd., Gillingham, Dorset, UK. [3] Phase Separations Ltd, Deeside, Clwyd, UK.

COLUMN PARTICULARS: Material - glass, lengths as in Table above, i.d. 2mm-4mm, o.d. 6mm.

SUPPORT: Chromosorb G AW DMCS for all phases except PECH, for which Chromosorb W AW DMCS was used.

MESH SIZE (BS): All supports in the range 40/60 except FPOL, mesh range 60/80.

GAS CHROMATOGRAPH: Absolute values of log L measured on modified Pye 104 system (katharometer detector), relative log τ values measured on modified Perkin Elmer F11 and F33 (FID detector). Operating temperature of Pye 104 and F11 & F33 detectors typically $\approx$ 500K.

MODIFICATIONS: Negretti & Zambra carrier gas flow controllers, liquid (water bath) column thermostats $\pm$ 0.05K. Some measurements taken on Pye 104 with replacement amplifier and detector from AMS Ltd.

INJECTION METHOD: Heated on-column injector, typically $\approx$ 450K.

SAMPLE SIZE: Typically 0.02 μ l.

CARRIER GAS & FLOWRATE: Pye 104 - helium, ca. 40cm³/min. F11 & F33 - nitrogen, ca. 40cm³/min.

FID GASES: H₂ $\approx$ 40cm³/min., air $\approx$ 400cm³/min.

FLOW RATE MEASUREMENT: Soap-bubble meter.

GAS HOLD UP: Measured from unretained methane peak. Thus, τ = T (sample) - T (methane).

DATA RECORDING: Spectra-Physics Minigrator (model 23000-011), Perkin Elmer chart recorder 1002, Philips PM 8251, Goerz Electronic RE511, Servoscribe RE541.

Table 66. Absolute values of Log L on FPOL at 298.15K.

Solute	Log L
n-Nonane	2.17
n-Decane	2.69
1,3-Dichloropropane	2.46
1,4-Dichlorobutane	3.18
1,5-Dichloropentane	3.86
Diethylether	1.81
Di-isopropylether	1.89
Di-n-butylether	3.10
Ethylvinyl ether	1.01
n-Butylvinyl ether	1.98
Ethyl-allyl ether	2.30
Dimethoxymethane	2.32
2,2-Dimethoxypropane	2.67
1,2-Dimethoxyethane	3.73
1,2-Butylene oxide	2.82
Propenal (acrolein)	2.73
trans-But-2-ene-1-al (crotonal)	3.90
2-Methylpropenal (methacrolein)	2.78
Propanone	3.21
Butanone	3.48
Pentan-2-one	3.78
4-Methylpentan-2-one	3.83
Cyclopentanone	4.54
But-1-ene-3-one	3.46
Hex-5-ene-2-one	4.18
Methyl formate	2.02
Propyl formate	2.82
Ethyl acetate	3.26
Allyl acetate	3.57
Isopropenyl acetate	3.29
Ethyl acrylate	3.47
Methanol	2.76
Ethanol	2.86
Propan-1-ol	3.34
Propan-2-ol	2.80
Butan-1-ol	3.84
Butan-2-ol	3.28
2-Methylpropan-2-ol	2.69
Pentan-1-ol	4.32
Pentan-2-ol	3.71
Pentan-3-ol	3.71
2-Methylbutan-1-ol	3.85
2-Methylbutan-2-ol	3.17
2,2-Dimethylpropan-1-ol	3.20
Hexan-2-ol	4.23
Hexan-3-ol	4.02
2-Methylpentan-2-ol	3.64
3-Methylpentan-2-ol	3.98
4-Methylpentan-2-ol	3.84
2-Methylpentan-3-ol	3.69
3-Methylpentan-3-ol	3.70
2-Ethylbutan-1-ol	4.23
2,4-Dimethylpentan-3-ol	3.74
Prop-2-yne-1-ol	3.48
Prop-2-en-1-ol (allyl alcohol)	3.23
2-Methylprop-2-ene-1-ol	3.49
3-Methylbut-3-ene-1-ol	3.98
2,2,2-Trifluoroethanol	2.08
1,1,1,3,3,3-Hexafluoropropan-2-ol	2.40
2-Chloroethanol	3.69
α -Methylstyrene, PhMeCCH ₂	3.54
Methylphenylether	3.88
2-Methylfuran	1.91

Table 67. Absolute values of log L on PECH at 298.15K

Solute	a	b	c
Hexane			1.38
Heptane			1.86
Octane	2.303	2.31	2.30
2,2,4-Trimethylpentane			1.72
Nonane	2.721	2.72	2.72
Decane	3.174	3.17	3.30
Undecane		3.55	3.71
Dodecane			4.17
Cyclohexane			1.89
Dichloromethane		2.05	2.20
Trichloromethane		2.39	2.48
Tetrachloromethane		2.12	2.26
1,1-Dichloroethane		2.12	
1,2-Dichloroethane	2.730	2.74	2.82
1,1,2,2-Tetrachloroethane		4.06	
1-Chlorobutane		2.23	
2-Chloro-2-methylpropane			1.72
1-Chloropentane		2.74	
1,5-Dichloropentane		4.45	
Trichloroethene		2.56	
Tetrachloroethene		2.91	
Dibromomethane		3.06	
1-Bromobutane		2.70	
1-Bromo-octane		4.34	
Diethyl ether			1.54
Di-n-butyl ether		2.99	
Tetrahydrofuran			2.65
1,4-Dioxane			3.30
Acetaldehyde			1.86
Propanone			2.38
Butanone	2.610	2.61	2.73
Nonan-2-one		4.65	
Methyl formate		1.62	
Ethyl formate			2.25
n-Butyl formate		2.99	
Methyl acetate		2.21	2.36
Ethyl acetate			2.61
n-Propyl acetate			2.98
n-Pentyl acetate		3.65	
n-Butyl propanoate		3.75	
Acetonitrile		2.57	2.72
n-Propylamine		2.40	
Nitromethane		2.89	
Nitroethane		3.22	
Dimethylformamide		4.14	
Methanol			2.29
Ethanol	2.148	2.15	2.40
Propan-1-ol	2.555	2.55	2.78
Propan-2-ol		2.17	
Butan-1-ol		3.02	3.23
2-Methylpropan-1-ol		2.80	
Butan-2-ol		2.55	
Pentan-1-ol		3.44	
Hexan-1-ol		3.87	4.07
Heptan-1-ol		4.27	
Octan-1-ol		4.52	
Trifluoroethanol		2.21	
Hexafluoropropan-2-ol		2.48	
Benzene		2.61	2.65
Toluene		3.03	3.08
Ethylbenzene		3.39	
n-Propylbenzene		3.77	
Chlorobenzene		3.49	3.50
1,2-Dichlorobenzene		4.33	

Table 67 (continued). Absolute values of log L on PECH at 298.15K

Solute	a	b	c
2-Chlorotoluene		3.89	
Bromobenzene		3.91	
Methylphenyl ether		4.04	4.19
Methyl benzoate		4.45	
Pyridine		3.47	
Water (d)	2.407	2.41	2.69
1,2-Dimethoxyethane (e)			2.95
Methoxyflurane		2.89	
Methyl trimethylacetate		2.70	
Dimethylacetamide		4.48	4.75
Triethylphosphate			4.75
Dimethylmethanephosphonate		4.74	4.96

a. Absolute values, this work.

b. Values calculated from (a) and relative values, this work.

c. Absolute values by R. A. McGill:²⁷⁰

d. Not used in the regressions.

e. Parameters not available for these compounds.

Table 68. Absolute values of log L on PIB at 298K

Solute	a	b	c	d
Hexane	1.96	1.87	1.88	1.87
Heptane	2.30	2.46	2.46	2.46
Octane		2.96	3.03	2.99
2,2,4-Trimethylpentane	2.26	2.28	2.34	2.31
Nonane			3.58	3.58
Decane			4.12	4.12
Cyclohexane		2.14	2.18	2.16
Dichloromethane		1.46	1.46	1.46
Trichloromethane			1.88	1.88
Tetrachloromethane		2.10	2.11	2.10
1,2-Dichloroethane			2.07	2.07
1-Chloropentane		2.67		2.67
Tetrahydrofuran			2.10	2.10
Butanone		1.80	1.83	1.81
Pentan-2-one		2.23	2.26	2.24
4-Methylpentan-2-one		2.54		2.54
Ethyl formate			1.33	1.33
n-Butyl formate		2.33		2.33
Methyl acetate		1.44	1.46	1.45
Ethyl acetate			1.87	1.87
n-Propyl acetate			2.38	2.38
Ethyl propanoate		2.30	2.37	2.33
Diethyl malonate		3.82		3.82
Acetonitrile		1.64		1.64
Nitromethane		1.55	1.60	1.57
Nitroethane		2.23	1.98	2.00
Dimethylacetamide			3.51	3.51
Methanol			1.36	
Ethanol			1.63	
Propan-1-ol			1.91	
Butan-1-ol		2.20	2.33	2.20
Pentan-1-ol		2.61	2.85	2.61
Pentan-3-ol		2.32		2.32
2-Methylbutan-2-ol		1.80		1.80
Hexan-1-ol		3.08	3.28	3.08
Cyclohexanol		3.22		3.22
Triethylphosphate			4.29	4.29
Dimethylmethanephosphonate		4.23	3.55	4.23
Benzene	2.26	2.22	2.17	2.20
Toluene	2.81	2.76	2.74	2.75
Methylphenyl ether			3.55	3.55
Phenol		3.43		3.43
o-Cresol		3.82		3.82
Water	2.01	2.01	2.09	
n-Propylamine			2.52	
Ethylamine			2.32	

a. Absolute values by G.S. Whiting.

b. Values calculated using relative values and those in (a).

c. Absolute values by R. A. McGill.²⁷⁰

d. Combined values; all alcohols from (b).

Table 69. Values of log τ and log L on SXPH(A) at 298.15K.

Compound	log τ (Rel)			log L (Abs)		
	Short Column	Long Column	Taken	GSW [•]	JND [★]	Taken
Hexane	-0.99		-0.99			1.52
Heptane	-0.49		-0.49			2.02
Octane	0.00		0.00		2.525	2.51
Nonane	0.42		0.42	2.852	3.005	2.93
Decane	0.88		0.88	3.399	3.471	3.39
Undecane		1.30	1.30			3.81
Dodecane		1.54	1.54			4.05
Tetradecane		2.47	2.47			4.98
Cyclohexane		-0.65	-0.65			1.86
Dichloromethane	-0.53		-0.53			1.98
Trichloromethane	-0.19		-0.19			2.32
Tetrachloromethane	-0.21		-0.21			2.30
1,1-Dichloroethane	-0.42		-0.42			2.09
1,2-Dichloroethane	0.09		0.09			2.60
1,1,2,2-Tetrachloroethane		1.36	1.36			3.87
1-Chlorobutane	-0.20		-0.20			2.31
1-Chloropentane	0.26	0.29	0.27			2.78
1,5-Dichloropentane		1.82	1.82			4.33
Trichloroethene	0.05		0.05			2.56
Tetrachloroethene	0.55		0.55			3.06
Dibromomethane	0.40		0.40			2.91
1-Bromobutane	0.24		0.24			2.75
1-Bromo-octane	1.83		1.83			4.34
Benzene	0.03	-0.02	0.00			2.51
Toluene	0.48	0.50	0.49	2.861	3.057	3.00
o-Xylene	1.01	1.01	1.01			3.52
1,2,3,4-Tetramethylbenzene		2.12	2.12			4.63
Ethylbenzene	0.89	0.87	0.88			3.39
Propylbenzene		1.20	1.20			3.71
Butylbenzene		1.62	1.62			4.13
Phenylethyne	1.07		1.07			3.58
Chlorobenzene		0.86	0.86			3.37
1,2-Dichlorobenzene		1.68	1.68			4.19
1,4-Dichlorobenzene	1.65		1.65			4.16
2-Chlorotoluene	1.31	1.28	1.30			3.81
Bromobenzene	1.25		1.25			3.76
Diethyl ether	-0.54		-0.54			1.97
Di-n-butyl ether	0.86	0.84	0.85			3.36
Methylphenyl ether	1.36		1.36			3.87
1,3-Dimethoxybenzene	2.08		2.08			4.59
Propanone	-0.22		-0.22		2.313	2.29
Butanone	0.18		0.18		2.743	2.69
Pentan-2-one	0.50		0.50			3.01
Pentan-3-one	0.54	0.51	0.52			3.03
Heptan-2-one		1.38	1.38	3.885	4.013	3.89
Octan-2-one		1.75	1.75			4.26
Nonan-2-one		2.16	2.16			4.67
Cyclohexanone		1.70	1.70			4.21
Acetophenone		2.39	2.39			4.90
Methylbenzyl ketone		2.68	2.68			5.19
Methyl formate	-0.91		-0.91			1.60
Propyl formate		-0.01	-0.01			2.50
Butyl formate		0.44	0.44			2.95
Methyl acetate	-0.24		-0.24			2.27
Methyl trimethylacetate		0.18	0.18			2.69
Pentyl acetate		1.13	1.13			3.64
Ethyl propanoate	0.53	0.55	0.54			3.05
Butyl propanoate		1.33	1.33			3.84
Methyl benzoate		2.35	2.35			4.86
Nitromethane	0.04		0.04			2.55
Nitroethane	0.39		0.39			2.90
Di-isobutylamine	1.72		1.72			4.23
Triethylamine	0.98		0.98			3.49
Aniline	2.00		2.00			4.51
N,N-Dimethylaniline	2.16		2.16			4.67
Pyrrole	0.79		0.79			3.30

Table 69 (continued). Values of log τ and log L on SXPH(A) at 298.15K.

Compound	log τ (Rel)			log L (Abs)		
	Short Column	Long Column	Taken	GSW [•]	JND [★]	Taken
Water				2.336		2.34
Methanol	-0.69		-0.69			1.82
Ethanol	-0.36		-0.36		2.193	2.15
Propan-1-ol	0.07		0.07		2.638	2.58
Propan-2-ol	-0.27		-0.27		2.245	2.24
Butan-1-ol	0.55	0.46	0.50	2.942	3.137	3.01
Butan-2-ol	0.21	0.11	0.16		2.743	2.67
2-Methylpropan-1-ol		0.16	0.16			2.67
2-Methylpropan-2-ol		-0.39	-0.39			2.12
Pentan-1-ol		0.92	0.92	3.440		3.43
Hexan-1-ol		1.35	1.35			3.86
Heptan-1-ol		1.77	1.77			4.28
Octan-1-ol		2.13	2.13			4.64
Trifluoroethanol	-0.91		-0.91			1.60
Hexafluoropropan-2-ol	-0.98		-0.98			1.53
Methylamine	0.63		0.63			3.14
Ethylamine	0.38		0.38			2.89
n-Propylamine	1.14		1.14			3.65

• Value measured by G. S. Whiting.

★ Value measured by J. -N. Dehnari.

Table 70. Absolute values of $\log \tau$ and $\log L$ on SXPH(B) at 298.15K

Solute	$\log \tau$ (Rel)	$\log L$ (Abs)	$\log L$ Abs (taken)
Hexane	-0.54		1.38
Heptane	0.00		1.92
Octane	0.48	2.368	2.37
Nonane	0.98	2.901	2.90
Decane	1.49	3.366	3.37
Perfluorohexane	-0.84		1.08
Dichloromethane	0.01		1.93
Trichloromethane	0.32		2.24
Tetrachloromethane	0.27		2.19
1-Chlorobutane	0.29		2.21
1-Chloropentane	0.74		2.66
1-Bromobutane	0.75		2.67
Diethyl ether	-0.49		1.43
Di-n-butyl ether	1.20		3.12
1,2-Dimethoxyethane	0.67		2.59
1,4-Dioxane	0.93		2.85
Propanone	-0.03	1.820	1.82
Butanone	0.37	2.282	2.28
Pentan-2-one	0.73	2.666	2.67
Heptan-2-one		3.573	3.57
Octan-2-one		3.990	3.99
Ethyl formate	-0.10		1.82
n-Butyl formate	0.79		2.71
Ethyl propanoate	0.77		2.69
n-Butyl propanoate	1.61		3.53
Acetonitrile	0.24		2.16
Nitromethane	0.48		2.40
Nitroethane	0.86		2.78
Methanol	-0.50		1.42
Propan-1-ol	0.16	2.033	2.03
Butan-1-ol	0.59	2.529	2.53
2-Methylpropan-1-ol	0.39		2.31
2-Methylpropan-2-ol	-0.28		1.64
Pentan-1-ol	1.04	2.984	2.98
Hexan-1-ol	1.47	3.448	3.45
Heptan-1-ol	1.89	3.875	3.87
2,2,2-Trifluoroethanol	-0.58		1.34
1,1,1,3,3,3-Hexafluoropropan-2-ol	-0.56		1.36
Benzene	0.53		2.45
Toluene	0.98	2.924	2.92
o-Xylene	1.54		3.46
n-Butylbenzene	2.19		4.11
2-Chlorotoluene	1.85		3.77
Bromobenzene	1.86		3.78

Table 71. Values of $\log \tau$ (rel) on SXPH(C) (modified with Me₃SiCl).

Solute	$\log \tau$ (rel)
Pentane	-1.13
Hexane	-0.86
Heptane	-0.48
Octane	0.00
Decane	0.86
Benzene	0.00
Toluene	0.40
Methanol	-0.90
Ethanol	-0.59
Propan-1-ol	-0.18
Butan-1-ol	0.28
2-Methylpropan-1-ol	-0.05
2-Methylpropan-2-ol	-0.54
Propanone	-0.39
Diethyl ether	-0.83
Di-n-butyl ether	0.75
1,4-Dioxane	0.66
1,2-Dimethoxyethane	0.35
Ethyl formate	-0.56
Ethyl propanoate	0.38
Nitromethane	-0.10
Nitroethane	0.30
2,2,2-Trifluoroethanol	-1.02
1,1,1,3,3,3-Hexafluoropropan-2-ol	-0.86
Bromobenzene	1.27

Table 72. Values of log τ and log L on SXCN at 298.15K

Compound	log τ (Rel)	log L (Abs), taken
Hexane	-1.85	0.23
Heptane	-1.24	0.84
Octane	-0.85	1.23
Nonane	-0.45	1.63
Decane	0.00	2.08
Undecane	0.41	2.49
Dodecane	0.81	2.89
Tetradecane	1.60	3.68
Cyclohexane	-1.24	0.84
Dichloromethane	-0.51	1.57
Trichloromethane	-0.22	1.86
Tetrachloromethane	-0.79	1.29
1,1-Dichloroethane	-0.65	1.43
1,2-Dichloroethane	0.13	2.21
1-Chlorobutane	-0.72	1.36
1-Chloropentane	-0.31	1.77
Trichloroethene	-0.23	1.85
Tetrachloroethene	-0.11	1.97
1-Bromobutane	-0.26	1.82
Benzene	-0.18	1.90
Toluene	0.12	2.20
o-Xylene	0.68	2.76
Ethylbenzene	0.66	2.74
Propylbenzene	0.74	2.82
Butylbenzene	1.11	3.19
Phenylethyne	1.26	3.34
2-Chlorotoluene	0.96	3.04
Bromobenzene	1.14	3.22
Methylphenyl ether	1.26	3.34
Propanone	-0.40	1.68
Butanone	-0.04	2.04
Pentan-2-one	0.23	2.31
Pentan-3-one	0.19	2.27
4-Methylpentan-2-one	0.30	2.38
Heptan-2-one	0.91	2.99
Octan-2-one	1.28	3.36
Methyl formate	-0.86	1.22
Methyl acetate	-0.44	1.64
Methyl trimethylacetate	-0.29	1.79
Pentyl acetate	0.58	2.66
Ethyl propanoate	0.02	2.10
Butyl propanoate	0.69	2.77
Nitromethane	0.66	2.74
Nitroethane	0.77	2.85
Di-isobutylamine	0.48	2.56
Tri-n-butylamine	1.29	3.37
Pyrrole	1.57	3.65
Methanol	-0.28	1.80
Ethanol	-0.14	1.94
Propan-1-ol	0.20	2.28
Propan-2-ol	-0.19	1.89
Butan-1-ol	0.58	2.66
Butan-2-ol	0.18	2.26
2-Methylpropan-1-ol	0.52	2.60
2-Methylpropan-2-ol	-0.30	1.78
Pentan-1-ol	0.93	3.01
Hexan-1-ol	1.26	3.34
2,2,2-Trifluoroethanol	0.44	2.52

Table 73. Values of log τ and log L on SXFA at 298.15K

Solute	log τ (Rel)	log L (Abs), taken
Hexane	-0.82	1.74
Heptane	-0.40	2.16
Octane	0.00	2.56
2,2,4-Trimethylpentane	-0.45	2.11
Nonane	0.40	2.96
Decane	0.79	3.35
Cyclohexane	-0.52	2.04
Heptadecafluorooctane	-0.11 a	2.45
Dichloromethane	-0.75	1.81
Trichloromethane	-0.48	2.08
Tetrachloromethane	-0.39	2.17
1,1-Dichloroethane	-0.49	2.07
1,2-Dichloroethane	-0.11	2.45
1-Chlorobutane	-0.14	2.42
2-Chloro-2-methylpropane	-0.48	2.08
1-Chloropentane	0.27	2.83
1,5-Dichloropentane	1.23	3.79
Trichloroethene	-0.14	2.42
Dibromomethane	-0.10	2.46
Tribromomethane	0.47	3.03
1-Bromobutane	0.13	2.69
Halothane	-0.64	1.92
Benzene	-0.12	2.44
Toluene	0.34	2.90
o-Xylene	0.55	3.11
Ethylbenzene	0.66	3.22
Propylbenzene	1.00	3.56
Butylbenzene	1.38	3.94
Chlorobenzene	0.59	3.15
2-Chlorotoluene	1.01	3.57
Diethyl ether	0.65	3.21
Methylphenyl ether	1.53	4.09
Methoxyflurane	0.31 a	2.87
Enflurane	-0.53	2.03
Propanone	1.40	3.96
Butanone	1.60	4.16
Methyl formate	0.27	2.83
Butyl formate	1.51	4.07
Methyl acetate	1.13	3.69
Methyl trifluoroacetate	-0.44 a	2.12
Isopropyl trifluoroacetate	0.14 a	2.70
Nitromethane	0.49	3.05
Nitroethane	0.91	3.47
Nitrobenzene	1.84	4.40
Methanol	0.66	3.22
Ethanol	0.98	3.54
Propan-1-ol	1.33	3.89
Propan-2-ol	1.14	3.70
Butan-1-ol	1.74	4.30
Trifluoroethanol	-0.07	2.49
Hexafluoropropan-2-ol	-0.25	2.31

a Solutes for which parameters are not available.

Table 74. Values of $\log \tau$ and $\log V_g$ on PEI at 298K

Solute	$\log \tau$ (Rel)	$\log V_g$, taken
Heptane	-1.58	0.90
Octane	-1.37	1.11
Decane	-0.42	2.06
Undecane	0.00	2.48
Dodecane	0.40	2.88
Dichloromethane	-0.88	1.60
Trichloromethane	-0.05	2.43
Tetrachloromethane	-1.13	1.35
1-Chlorobutane	-1.38	1.10
1-Chloropentane	-0.84	1.64
1,5-Dichloropentane	1.02	3.50
Dibromomethane	0.22	2.70
1-Bromobutane	-0.89	1.59
Di-n-butyl ether	-0.72	1.76
Dioxane	-0.58	1.90
Butanone	-1.12	1.36
Pentan-2-one	-0.99	1.49
n-Propyl formate	-1.27	1.21
n-Butyl formate	-0.67	1.81
n-Pentyl acetate	-0.37	2.11
Ethyl propanoate	-1.00	1.48
n-Butyl propanoate	-0.14	2.34
Diethylmalonate	0.59	3.07
Acetonitrile	-0.73	1.75
n-Propylamine	-1.21	1.27
Di-isobutylamine	-0.75	1.73
Nitromethane	-0.06	2.42
N,N-Dimethylacetamide	0.89	3.37
Methanol	0.42	2.90
Ethanol	0.76	3.24
Propan-1-ol	1.13	3.61
Propan-2-ol	0.24	2.72
2,2,2,-Trifluoroethanol	1.46	3.94
Benzene	-0.98	1.50
Toluene	-0.57	1.91
Ethylbenzene	-0.19	2.29
o-Xylene	0.01	2.49
n-Propylbenzene	0.11	2.59
n-Butylbenzene	0.50	2.98
Phenylethyne	0.73	3.21
Chlorobenzene	0.16	2.64
2-Chlorotoluene	0.53	3.01
Bromobenzene	0.63	3.11
Benzophenone	0.44	2.92
Methyl benzoate	1.47	3.95
N,N-Dimethylaniline	1.23	3.71
4-Methylpyridine	0.52	3.00

9.12 Static Head-Space Experimental

Several solvents were studied by this method, including hexadecane, and some $\log L(\text{gas} \rightleftharpoons \text{solvent})$ values used in the characterisation of solvents (section 7.40) were measured using this technique.

Solutions of the solvent were prepared in 50cm³ head-space flasks. To approximately 5cm³ of accurately pipetted solvent in the flask, were added 30 μ l of the solute under investigation and 30 μ l of reference solute, using a 100 μ l syringe. The head-space flask was sealed with a rubber septum cap and the flask suspended in a water thermostat at 298.15K. Each septum cap was pierced with a small needle to avoid pressure build up, and a sheet of polythene placed over the flasks to reduce heat loss. The flasks were then left to equilibrate for around an hour, after which the analysis of the vapour in the head-space could be carried out by analytical GLC.

The chromatograph used was the Perkin Elmer F11 or F33, set up in the same way as described in section 9.11. The phase used to effect the analysis depended on the nature of the analytes in question, but experimental conditions were similar to those described in section 9.11 (summarised in Table 65), excepting that the column temperature was not necessarily as low as 298K and air thermostats could therefore be used. A typical system is Carbowax 20m (a good 'all-round' analytical GLC stationary phase), 10% on Chromosorb W AW, operating temperature around 400K.

Prior to the analysis of each solution, the retention time of each solute (reference and sample) was measured on the chosen phase. Solution analysis then proceeds as follows. Firstly, using a 2.5cm³ glass gas-tight syringe, about 1cm³ of the vapour above the solution was removed and then injected into the

column. Head-space analysis was carried out in each solution in turn, allowing the solutions time to re-equilibrate before repeating the procedure. A note was made of the areas under the two solute peaks for each solution, (the areas were obtained either from an integrator, via computer, or simply by cutting out and weighing the chromatogram obtained on a chart recorder, the weight of the paper being directly proportional to peak area). When head-space analysis had been carried out three consecutive times to produce consistent ratios to within $\pm 5\%$ of sample to standard solute areas, the liquid solutions were sampled, and the rubber septum caps replaced by glass stoppers. Using a 7001N $1\mu\text{l}$ Hamilton microsyringe, $0.5\mu\text{l}$ samples were removed from each solution in turn and injected into the column. Again the areas under the two solute elution peaks were recorded for each solution and the analysis repeated several times. In analysing the liquid, the solvent was also eluted (the stationary phase would be chosen to make sure the solvent elution process was slow), and the column was periodically heated up to around its maximum operating temperature to remove the solvent from the column.

Head-space analysis of vapour and liquid samples is sometimes difficult or impossible for a number of reasons. Solute involatility can mean that no vapour phase peak can be obtained. Some solutes, if not sufficiently pure, can have volatile impurities that can give numerous peaks in the vapour sample, and invalidate any area calculations. Solution concentrations were about 0.01 molar (near to infinite dilution), but the solubility of some solutes in the solvent was so low, more dilute solutions were required, making detection of these solutes difficult.

Having measured the areas of solute and standard in both the vapour, and the liquid phase, partition coefficients can be calculated using equation 6, section 1.2, page 9.

10.1 Appendix 1

Full listings of any of the programs discussed in this section are available upon request from the author. Fortran 77 programs written in standard Fortran 77, using extensions allowed by the Ryan-McFarland compiler.

10.11 The Params Database and the Fortran 77 Programs Used.

PARAMS - The database itself was a fixed length structure, 284 characters wide, containing:-

- ▣ Compound number field, 4 characters long.
- ▣ Compound name, 30 characters long.
- ▣ 25 parameter data fields, each 10 characters long.

Access Mode:- Direct. Compound number used as search field to extract desired compounds and parameters.

MREG - Multiple linear regression program specifically written to interact with the Params database. Up to seven parameters can be extracted from database (X-columns) to regress against a logged solubility property (Y-column). Limited to 500 data sets.

UPDATE - Program to alter compound names, parameters, and add new compounds.

PRINT2 - Called Print2 to avoid conflict with the DOS facility, Print. Allows print out of compound name and/or parameters of whole database, between two compound numbers, or of a set of compounds designated by an external (text) compound numbers file.

WRITER - Prints out as Print2, but only if a parameter exists for a compound. If not, compound not printed. For example, useful for listing all the $\log L^{16}$ values from database, ignoring compounds for which $\log L^{16}$ not known.

RUBOUT - Deletes unwanted compounds from Params database.

RENUM - Renumbers the compound number field in Params database.

10.12 The MhaBase1 and Mhabase2 Database and SmartII 4GL Programs.

Table 75 shows information on Mhabase (MhaBase1 & MhaBase2), printed out using the SmartWare II database facility, 'Data-Utilities-Information'. The table is in two parts. The first is concerned with general information on the 'view' MhaBase that links database files MhaBase1 and MhaBase2, and information on these two files.

The latter part of Table 75 gives a breakdown of the database files. The constituent fields in the two databases are shown, and database specifications on these fields. A key field is used to organise the database (such as compound number), and additionally the link fields (record number 1 & record number 2) must be key fields.

Data Type: A - Alphanumeric data
C - Counter (automatically incremented by database)
N - Numeric

Length: Maximum length in characters allowed for field.
A - Signifies automatic advance when field is full.

Entry Status: Dupes - yes or no - states whether two identical values allowed in a field
M - Mandatory entry. For the record number fields, this as automatically done by the database for every new compound.
R - Read only
R/W - Read and write status

Display Format: Digit signifies number of decimal places, L - left format.

Input Mask: Will only allow input of data satisfying certain criteria. For example, R{##} - will automatically make sure that R is entered in that field, followed by at least one, and up to a maximum of two digits.

PROGRAMS

MREGLINK - Linker program written in SmartWare II 4GL language. Extracts information from MhaBase databases using a compound number text file as search field. The information (a listing of compound numbers, compounds & solute parameters) is then stored as an X-columns text file ready for use by the multiple

Table 75. Database Information On Mhabase (Mhabase1 & MhaBase2).

View: c:\smartii\dbase\mhabase.vw
 Date Created: 25/07/1990
 Last Edited: 03/11/1990
 Field Count: 38
 Record Count: 2234
 Encrypted: No

Data-file: c:\smartii\dbase\MHABASE1.db
 Total Fields: 17
 Record Length: 164
 Last Add Date: 28/12/1990
 File Format: Variable
 Password: No
 Encrypted: No

Data-file: c:\smartii\dbase\MHABASE2.db
 Links: RECORD NUMBER 1->MHABASE2:RECORD NUMBER
 Total Fields: 22
 Record Length: 157
 Last Add Date: 28/12/1990
 File Format: Variable
 Password: No
 Encrypted: No

Field	Data-file Table	Data Type	Length	Entry Status	Display Format	Input Mask
RECORD NUMBER 1	MHABASE1	C	8	M	OR	
Key:RECORD NUMBER 1		Len: 8	Type:A	Dupes:Yes		
RECORD NUMBER 2	MHABASE2	C	8	M	OR	
Key:RECORD NUMBER		Len: 8	Type:A	Dupes:Yes		
Compound Number	MHABASE1	N	8	R/W	OL	
Key:Compound Number		Len: 8	Type:A	Dupes:Yes		
Compound Name	MHABASE1	A	40	R/W	OL	
Delta	MHABASE1	N	8	R/W	1L	
R	MHABASE1	N	8	R/W	3L	
PiH2*	MHABASE1	N	8	R/W	2L	
AlphaH2*	MHABASE1	N	8	R/W	2L	
BetaH2*	MHABASE1	N	8	R/W	2L	
Vx	MHABASE1	N	8	R/W	4L	
Log L16	MHABASE1	N	8	R/W	3L	
R Ref	MHABASE1	A	3	R/W	OL	R{#{#}}
PiH2* Ref	MHABASE1	A	3	R/W	OL	I{#{#}}
AlH2* Ref	MHABASE1	A	3	R/W	OL	\A{#{#}}
BeH2* Ref	MHABASE1	A	3	R/W	OL	B{#{#}}
Mol Wt	MHABASE1	N	8	R/W	4	
L6 Ref	MHABASE1	A	3	R/W	OL	\L{#{#}}

Table 75. Database Information On Mhabase (Mhabase1 & MhaBase2).

Field	Data-file Table	Data Type	Length	Entry Status	Display Format	Input Mask
Log P	MHABASE2	N	8	R/W	3L	
Dipole	MHABASE2	N	8	R/W	3L	
f(N)	MHABASE2	N	8	R/W	3L	
MR	MHABASE2	N	8	R/W	3L	
Log Poct	MHABASE2	N	8	R/W	3L	
AlphaH2	MHABASE2	N	8	R/W	3L	
Alpha Av	MHABASE2	N	8	R/W	2L	
BetaH2	MHABASE2	N	8	R/W	3L	
Beta Av	MHABASE2	N	8	R/W	2L	
Pi*2	MHABASE2	N	8	R/W	2L	
Log P Ref	MHABASE2	A	3	R/W	0L	P{#{#}}
Dip Sq	MHABASE2	N	8	R/W	3L	
f(N) Ref	MHABASE2	A	3	R/W	0L	\N{#{#}}
MR Ref	MHABASE2	A	3	R/W	0L	M{#{#}}
Poct Ref	MHABASE2	A	3	R/W	0L	O{#{#}}
AlH2 Ref	MHABASE2	A	3	R/W	L	W{#{#}}
Al Av Ref	MHABASE2	A	3	R/W	0L	\X{#{#}}
BeH2 Ref	MHABASE2	A	3	R/W	L	Y{#{#}}
Be Av Ref	MHABASE2	A	3	R/W	0L	Z{#{#}}
Pi*2 Ref	MHABASE2	A	3	R/W	0L	E{#{#}}
Old List Number	MHABASE1	N	8	R	0L	
Key:Old List Number		Len: 8	Type:A	Dupes:Yes		

Table 76. Typical Output From Mreglink.

19:10:27 Monday 25/02/1991 - Time and date file extracted by Mreglink

86 - Total number of compounds in compound number file used by Mreglink

5 - Number of solute parameters selected

R Solute parameter 1, column 3

PiH2* Solute parameter 2, column 4

AlH2* Solute parameter 3, column 5

BeH2* Solute parameter 4, column 6

LogL16 Solute parameter 5, column 7

126	n-Octane	0.000	0.000	0.000	0.000	3.677
140	2,2,4-Trimethylpentane	0.000	0.000	0.000	0.000	3.106
145	n-Nonane	0.000	0.000	0.000	0.000	4.182
180	n-Decane	0.000	0.000	0.000	0.000	4.686
2507	1,2-Dichloroethane	0.416	0.640	0.100	0.110	2.573
2518	1,3-Dichloropropane	0.408	999.000	0.000	999.000	3.101
999		999.000	999.000	999.000	999.000	999.000

Compound number in first column, solute name in second, solute parameters in columns 3 to 7. 999 is the 'no search' compound number, indicating there is solubility information in a corresponding Smreg Y-column file, but this compound does not exist in the parameter database. 999.000 shows NO parameter is available. Only first 7 compounds are shown above, the original compound number file used to create Mreglink file contained 86 numbers.

regression program Smreg. 999 in a compound number text file signifies that while retention or solubility property information is available on a compound, the compound is not in MhaBase. This facility is allowed to be able to match up the Y column and X columns for use by the multiple regression program Smreg. A 999 in a compound number file will not extract any information from the database, but will also fill parameter fields in the text files created by Mreglink with 999.000 (999.000 in parameter fields signifies that no parameter is available). The text file created by Mreglink can be edited using any text editor, so parameters and compounds etc. can be altered, added or removed. This in effect allows the construction of a miniature database that can be specifically used for regression purposes. It is usually the case that an identical set of compounds need to be regressed against various sets of solubility data, and so a miniature database will be more convenient for this purpose. Table 76 shows a portion of a typical text file extracted from the main database by Mreglink, with comments in *italics*.

CONVERT - 4GL program that converts old compound number files to new compound number files. The implementation of a new compound numbering system has necessitated converting the large number of compound number files constructed over the years (if any further regression work is to be carried out using them).

SMREG - Fortran 77 multiple regression program. Exactly the same as Mreg, but it specifically uses a file containing X-columns created by Mreglink, see Table 76.

All other facilities needed for running and updating the database are provided by the internal functions of SmartWare II, doing away completely with the need for external programs such as Print2, Renum, Update etc.

10.2 References

- 1 M. Tswett, *Ber. deut. botan. Ges.*, **24**, 316 (1906).
M. Tswett, *Ber. deut. botan. Ges.*, **24**, 384 (1906).
- 2 A. J .P. Martin and R. L. M. Synge, *J.Biochem.*, **35**, 1358 (1941).
- 3 G. Hesse, H. Eilbrecht and F. Reicheneder, *Liebigs Ann. Chem.*, **546**, 23 (1941).
- 4 A. Tiselius, *Arkiv. Kemi, Mineral. Geol.*, **16A**, No.18, 11 (1943).
- 5 S. Claesson, *Arkiv. Kemi. Mineral. Geol.*, **23A**, No.1, 133 (1946).
- 6 A. T. James and A. J. P. Martin, *J.Biochem.*, **50**, 679 (1952).
- 7 A. T. Huber and Y. A. R. J. Hulsman, *Anal. Chim. Acta*, **38**, 405 (1967).
- 8 J. C. Giddings, *Dynamics of Chromatography*, Marcel Dekker, New York (1965).
- 9 H. Hachenberg and A. P. Schmidt, *Gas Chromatographic Headspace Analysis*, Heyden & Son Ltd., London (1977).
- 10 B. Kolb, *J. Chromatog.*, **112**, 287 (1975).
- 11 A. G. Vitenberg, B. V. Ioffe, Z. St. Dimitrova and I. L. Butaeva, *J. Chromatog.*, **112**, 319 (1975).
- 12 J. H. Purnell, *Gas Chromatography*, p.78, John Wiley & Sons, New York (1962).
- 13 A. J. Ashworth and D. H. Everett, *Trans. Faraday Soc.*, **56**, 1609 (1960).
- 14 M. L. McGlashan and A. G. Williamson, *Trans. Faraday Soc.*, **57**, 588 (1961).
- 15 D. H. Everett and M. F. Penney, *Proc. Roy. Soc. A*, **212**, 164 (1952).
- 16 M. H. Abraham, *J. Chem. Soc., Faraday Trans. 1*, **80**, 153 (1984).
- 17 M. H. Abraham, *J. Chem. Soc. A*, 1061 (1971).
- 18 M. H. Abraham, *J. Chem. Soc., Perkin Trans. 2*, 1343 (1972)
- 19 M. H. Abraham, P. L. Grellier and J. Mana, *J. Chem. Thermodyn.*, **6**, 1175 (1974).
- 20 M. H. Abraham and P. L. Grellier, *J. Chem. Soc., Perkin Trans 2*, 1735 (1976).
- 21 M. H. Abraham and A. Nasehzadeh, *J. Chem. Soc., Faraday Trans 1*, **77**, 321 (1981).
- 22 M. H. Abraham and A. Nasehzadeh, *J. Chem. Thermodyn.*, **13**, 549 (1981).

- 23 J. H. Park, A. Hussam, P. Couasnon, D. Fritz and P. W Carr, *Anal. Chem.*, **59**, 1970 (1987).
- 24 M. H. Abraham, P. L. Grellier and R. A. McGill, *J. Chem. Soc. Perkin Trans.2*, 797, (1987).
- 25 M. M. Schantz and D. E. Martire, *J. Chromatogr.*, **391**, 35 (1987).
- 26 M. H. Abraham, P. L. Grellier and J. Mana, *J. Chem. Thermodynamics*, **6**, 1175 (1974).
- 27 L. Rohrschneider, *Anal. Chem.*, **45**, 1241 (1973).
- 28 H. G. Maier, *J. Chromatog.*, **50**, 329 (1970).
- 29 D. W. Grant, *Gas Liquid Chromatography*, Van Nostrand Reinhold, London (1971).
- 30 P. Russev, T. A. Gough and C. J. Wollam, *J. Chromatog.*, **119**, 461 (1976).
- 31 B. Smith and R. Ohlson, *Acta. Chem. Scand.*, **16**, 351 (1962).
- 32 J. R. Conder and C. L. Young, *Physiochemical Measurements by Gas Chromatography*, Wiley, New York, 1979.
- 33 J. J. van Deemter, F. J. Zuiderweg and A. Klinkenberg, *Chem. Eng. Sci.*, **5**, 271 (1956).
- 34 A. B. Littlewood, *Gas Chromatography*, 2nd ed., pp. 18-23, Academic Press, New York, 1970.
- 35 R. H. Perrett and J. H. Purnell, *Anal. Chem.*, **35**, 430 (1963).
- 36 E. C. Pease and S. Thorburn, *J. Chromatog.*, **30**, 344, (1967).
- 37 D. E. Martire and P. Riedl, *J. Phys. Chem.*, **72**, 3478, (1968).
- 38 C. Horváth, *The Practice of Gas Chromatography*, ed L. S. Ettre and A. Zlatkis, Interscience, New York, pp. 188-189 (1967).
- 39 J. R. Conder, D. C. Locke, and J. H. Purnell, *J. Phys. Chem.*, **73**, 700 (1969).
- 40 J. Bohemen, S. H. Langer, R. H. Perrett and J. H. Purnell, *J. Chem. Soc.*, 2444 (1960).
- 41 V. R. Meyer, *Practical High-performance Liquid Chromatography*, Wiley, New York, 1988.
- 42 H. Colin and A. M. Krstulović, *Liquid Chromatography in Pharmaceutical Development*, ed. I. W. Wainer, Aster, Springfield, p. 189 (1985).
- 43 J. H. Hildebrand, J. M. Prausnitz and R. L. Scott, *Regular and Related Solutions*, Van Nostrand Reinhold, New York, 1970.
- 44 H. Burrell, *J. Paint Technol.*, **40**, 197 (1968).

- 45 C. M. Hansen, *J. Paint Technol.*, **39**, 104 (1967).
- 46 P. J. Schoenmakers, *Optimisation of Chromatographic Selectivity*, Elsevier, New York, 1986.
- 47 M. J. Kamlet, R. M. Doherty, J. -L. M .Abboud, M. H. Abraham and R. W. Taft, *Chemtech.*, 566 - 576 (1986).
- 48 M. H. Abraham, R. M. Doherty, M. J. Kamlet and R. W. Taft, *Chem. Brit.*, **75**, 629 (1986).
- 49 J. H. Hildebrand and R. L. Scott, *The Solubility Of Non-Electrolytes*, Dover publications, New York, 1964.
- 50 M. J. Kamlet, P. W. Carr, R. W. Taft and M. H. Abraham, *J. Amer. Chem. Soc.*, **103**, 6062 (1981).
- 51 D. E. Leahy, *J. Pharm. Sci.*, **75**, 629 (1986).
- 52 M. H. Abraham and J. C. McGowan, *Chromatographia*, **23**, 243 (1987).
- 53 N. B. Chapman and J. Shorter, eds., *Advances in Linear Free Energy Relationships*, Plenum, London, 1972.
- 54 L. P. Hammett, *Physical Organic Chemistry*, McGraw-Hill, New York, 1940.
- 55 O. Chalvet, J. Hoarau, J. Joussot-Dubien, and J. C. Rayez, *J. Chim. Phys.*, **69**, 630 (1972).
- 56 D. S. Noyce and R. W. Nichols, *J. Org. Chem.*, **37**, 4306 (1972).
- 57 S. Wold, *Chem. Scripta*, **5**, 97 (1974).
- 58 N. B. Chapman and J. Shorter, *Correlation Analysis in Chemistry*, Plenum, New York, Chapter 1, 1978
- 59 G. S. Hammond, *J. Chem. Educ.*, **51**, 559 (1974).
- 60 L. P. Hammett, *Physical Organic Chemistry*, 2nd edition, McGraw-Hill, New York, p.347, 1970.
- 61 J. E. Leffler and E. Grunwald, *Rates and Equilibrium of Organic Reactions*, Wiley, New York, p.128, 1963.
- 62 N. B. Chapman and J. Shorter, *Correlation Analysis in Chemistry*, Plenum, New York, Chapter 9, 1978
- 63 S. H. Unger and C. Hansch, *J. Med. Chem.*, **16**, 745 (1973).
- 64 A. Leo, C. Hansch, and D. Elkins, *Chem. Rev.*, **71**, 525 (1971).
- 65 M. J. Kamlet and R. W. Taft, *Acta Chemica Scandinavica*, B **39**, 611 (1985).

- 66 I. Langmuir, *The Disribution and Orientation of Molecules*, Third Colloid Symp. Monograph, The Chem. Cat. Company Inc., New York, 1925.
- 67 O. Redlich, E. L. Derr and G. Pierotti, *J. Am. Chem. Soc.*, **81**, 2283 (1959).
- 68 E. L. Derr and M. Papadopoulos, *J. Am. Chem. Soc.*, **81**, 2285 (1959).
- 69 G. M. Wilson and C. H. Deal, *Ind. Eng. Chem., Fundamentals*, **1**, 20, (1962).
- 70 A. Fredenslund, R. L. Jones and J. M. Prausnitz, *AIChE Journal*, **21**, 1086 (1975).
- 71 A. Fredenslund, J. Gmehling and P. Rasmussen, *Vapor-Liquid Equilibria using UNIFAC*, Elsevier Scientific, New York, 1977.
- 72 D. S. Abrams and J. M. Prausnitz, *AIChE Journal*, **21**, 116 (1975).
- 73 E. L. Derr and C. H. Deal, *J. Chem. Eng. Symp. Ser. No 32 (Instn. Chem. Engrs. London)*, **3**, 40 (1969).
- 74 E. L. Derr and C. H. Deal, *Adv. In Chemistry Series 124, Am. Chem. Soc.*, **11** (1973).
- 75 K. Tochigi and K. Kopina, *J. Chem. Eng. Japan*, **9**, 267 (1976).
- 76 G. E. P. Box, *Technometrics*, **8**, 625 (1966).
- 77 G. B. Wetherill, P. Duncombe, M. Kenward, J. Köllerström, S. R. Paul, B. J. Vowden, *Regression Analysis with Applications*, Chapman & Hall, London, 1986.
- 78 V. Barnett and T. Lewis, *Outliers in Statistical Data*, Wiley, New York, 1978.
- 79 D. A. Belsey, E. Kuh and R. E. Welsch, *Regression Diagnostics: Identifying Influential Data and Source Collinearity*, Wiley, New York, 1980.
- 80 P. Nicolet and C. Laurence, *J. Chem. Soc., Perkin Trans 2*, 1071 (1986).
- 81 C. Laurence, P. Nicolet and M. Helbert, *J. Chem. Soc., Perkin Trans 2.*, 1081 (1986).
- 82 F. Patte, M. Etcheto and P. Laffort, *Anal. Chem.*, **54**, 2239 (1982).
- 83 M. J. Kamlet, J. -L. M. Abboud and R. W. Taft, *Prog. Phys. Org. Chem.*, **13**, 485 (1981).
- 84 M. J. Kamlet, J. -L. M. Abboud and R. W. Taft, *J. Amer. Chem. Soc.*, **99**, 6027 (1977).
- 85 M. J. Kamlet, J. -L. M. Abboud and R. W. Taft, *J. Amer. Chem. Soc.*, **99**, 8325 (1977).

- 86 B. Chawla, S. K. Pollack, C. B. Lebrilla, M. J. Kamlet and R. W. Taft, *J. Amer. Chem. Soc.*, **103**, 6924 (1981).
- 87 M. J. Kamlet, T. N. Hall, J. Boykin and R. W. Taft, *J. Org. Chem.*, **44**, 2599 (1979).
- 88 R. W. Taft and M. J. Kamlet, *J. Amer. Chem. Soc.*, **98**, 2866 (1976).
- 89 M. J. Kamlet and R. W. Taft, *J. Chem. Soc., Perkin Trans.2.*, 349 (1979).
- 90 M. J. Kamlet and R. W. Taft, *J. Chem. Soc., Perkin Trans.2.*, 1723, (1979).
- 91 R. W. Taft and M. J. Kamlet, *J. Amer. Chem. Soc.*, **98**, 377 (1976).
- 92 T. Yokoyama, R. W. Taft and M. J. Kamlet, *J. Amer. Chem. Soc.*, **98**, 3233 (1976).
- 93 M. J. Kamlet, M. E. Jones, R. W. Taft and J. -L. M. Abboud, *J. Chem. Soc., Perkin Trans. 2*, 342 (1979).
- 94 M. J. Kamlet, A. Solomonovici and R. W. Taft, *J. Amer. Chem. Soc.*, **101**, 3734 (1979).
- 95 R. W. Taft, N. J. Pienta, M. J. Kamlet and E. M. Arnett, *J. Org. Chem.*, **46**, 661 (1981).
- 96 M. J. Kamlet, R. M. Doherty, G. D. Veith, R. W. Taft and M. H. Abraham, *Envir. Sci. Tech.*, **20**, 690 (1986).
- 97 M. J. Kamlet, R. M. Doherty, R. W. Taft, M. H. Abraham, G. D. Veith and D. J. Abraham, *Envir. Sci. Tech.*, **21**, 149 (1987).
- 98 M. J. Kamlet, R. M. Doherty, J. -L. M. Abboud, M. H. Abraham and R. W. Taft, *J. Pharm. Sci.*, **75**, 338 (1986).
- 99 M. J. Kamlet, R. M. Doherty, M. H. Abraham, P. W. Carr, R. M. Doherty and R. W. Taft, *J. Phys. Chem.*, **91**, 1996 (1987).
- 100 M. H. Abraham, P. L. Grellier, R. A. McGill, J. -L. M. Abboud, M. J. Kamlet, W. J. Schuely, and R. W. Taft, Faraday Discussions '88 (March 1988)
- 101 M. H. Abraham, P. P. Duce, P. L. Grellier, D. V. Prior, J. J. Morris and P. J. Taylor, *Tetrahedron Letters*, **29**, 1587 (1988).
- 102 M. H. Abraham, P. L. Grellier, D. V. Prior, J. J. Morris, P. J. Taylor, C. Laurence and M. Berthelot, *Tetrahedron Lett.*, **29**, 1587 (1988).
- 103 J. C. McGowan, *J. Appl. Chem. Biotechnol.*, **28**, 599 (1978).
- 104 J. C. McGowan, P. Ahmad and A. Mellors, *Canad. J. Pharm. Sci.*, **14**, 72 (1979).
- 105 J. C. McGowan, *J. Appl. Chem. Biorechnol.*, **34A**, 38 (1984).

- 106 R. Battino, *Fluid Phase Equilibria*, **15**, 231 (1984).
- 107 M. H. Abraham and R. Fuchs, *J. Chem. Soc. Perkin Trans. 2*, 523 (1988).
- 108 M. J. Kamlet, J. -L. M. Abboud, M. H. Abraham and R. W. Taft, *J. Org. Chem.*, **48**, 2877 (1983)
- 109 H. Block and S. M. Walker, *Chem. Phys. Lett.*, **19**, 363 (1973).
- 110 J. E. Brady and P. W. Carr, *J. Phys. Chem.*, **89**, 1813 (1985).
- 111 M. H. Abraham, P. L. Grellier, D. V. Prior, R. W. Taft, J. J. Morris, P. J. Taylor, C. Laurence, M. Berthelot, R. M. Doherty, M. J. Kamlet, J. -L. M. Abboud, K. Sraidi and G. Guihéneuf, *J. Amer. Chem. Soc.*, **110**, 8534 (1988).
- 112 M. H. Abraham, P. L. Grellier, D. V. Prior, J. J. Morris, P. J. Taylor, P. -C. Maria and J. -F. Gal, *J. Phys. Org. Chem.*, **2**, 243 (1989).
- 113 P. -C. Maria, J. -F. Gal, J. de Franceschi and J. Fargin, *J. Amer. Chem. Soc.*, **109**, 483 (1987).
- 114 M. J. Kamlet, M. H. Abraham, R. M. Doherty and R. W. Taft, *J. Amer. Chem. Soc.*, **106**, 464 (1984).
- 115 R. W. Taft, M. H. Abraham, G. R. Famini, R. M. Doherty, J. -L. M. Abboud and M. J. Kamlet, *J. Pharm. Sci.*, **74**, 807 (1985).
- 116 D. E. Leahy, P. W. Carr, R. S. Pearlman, R. W. Taft and M. J. Kamlet, *Chromatographia*, **21**, 473 (1986).
- 117 R. P. Bell, *The Proton in Chemistry*, , Methuen, London, 1959; J. R. Jones, *The Ionisation of Carbon Acids*, Academic, London, 1973.
- 118 G. N. Lewis, *J. Franklin Inst.*, **226**, 293 (1938).
- 119 J. K. Haken, *Adv. Chromatog.*, **14**, 366 (1976).
- 120 L. S. Ettre, *Chromatographia*, **6**, 489 (1973).
- 121 L. Blomberg, *Adv. Chromatog.*, **26**, 229 (1987).
- 122 R. J. Smith, J. K. Haken, M. S. Wainwright and B. G. Madden, *J. Chromatog.*, **328**, 11 (1985).
- 123 R. J. Smith, J. K. Haken and M. S. Wainwright, *J. Chromatog.*, **334**, 95 (1985).
- 124 C. F. Poole and S. K. Poole, *Chem. Rev.*, **89**, 377 (1989).
- 125 W. Ecknig, *Z. Chem.*, **25**, 240 (1985).
- 126 L. Rohrschneider, *J. Chromatog.*, **15**, 1 (1965).
L. Rohrschneider, *J. Chromatog.*, **22**, 6 (1966).
- 127 W. O. McReynolds, *J. Chromatogr. Sci.*, **8**, 685 (1970).
- 128 J. R. Mann and S. T. Preston, *J. Chromatogr. Sci.*, **11**, 216 (1973).

- 129 L. V. Semenchenko and M. S. Vigdergauz, *J. Chromatog.*, **245**, 177 (1982).
- 130 J. F. K. Huber and G. Reich, *J. Chromatog.*, **294**, 15 (1984).
- 131 J. A. Garcia-Dominguez, J. Garcia-Munoz, V. Menendez, M. J. Molera, J. M. Santiuste, *J. Chromatog.*, **393**, 309 (1987).
- 132 K. Grob and G. Grob, *Chromatographia.*, **4**, 422 (1971).
K. Grob and G. Grob, *J. Chromatog.*, **156**, 1 (1978).
- 133 W. O. McReynolds, *Gas Chromatographic Retention Data*, Preston Technical Abstracts Co., Evanston, IL, 1966.
- 134 W. R. Supina and L. P. Rose, *J. Chromatog. Sci.*, **8**, 214 (1970).
- 135 W. R. Supina, *The Packed Column in Gas Chromatography*, Supelco, Inc., Bellefonte, PA, p.61, 1974.
- 136 L. R. Snyder, *J. Chromatog.*, **92**, 223 (1974).
- 137 L. R. Snyder, *J. Chromatogr. Sci.*, **16**, 223 (1978).
- 138 S. K. Poole, B. R. Kersten, R. M. Pomaville and C. F. Poole, *LC-GC*, **6**, 401 (1989); B. R. Kersten, C. F. Poole and K. G. Furton, *J. Chromatog.*, **411**, 43 (1987); S. K. Poole, B. R. Kersten and C. F. Poole, *J. Chromatog.*, **471**, 91 (1989).
- 139 J. Novak, *J. Chromatog.*, **78**, 269 (1973).
- 140 J. Novak, J. Ruzickova, S. Wicar and J. Janak, *Anal. Chem.*, **45**, 1365 (1973).
- 141 R. V. Golovnya and T. A. Misharina, *Chromatographia*, **10**, 658 (1977).
- 142 R. I. Sidarov, *Zh. Fiz. Khim.*, **54**, 1997 (1980) (*Engl. Trans. p.1136*).
- 143 M. H. Abraham, *J. Am. Chem. Soc.*, **104**, 2085 (1982).
- 144 Th. Kleinert and W. Ecknig, *J. Chromatog.*, **315** 75 (1984).
- 145 Th. Kleinert, W. Ecknig and J. Novak, *J. Chromatog.*, **315**, 85 (1984).
- 146 M. Roth and J. Novak, *J. Chromatog.*, **258**, 23 (1983).
- 147 W. Burns and S. J. Hawkes, *J. Chromatogr. Sci.*, **15**, 185 (1977).
- 148 E. Chong, B. deBriceno, G. Miller and S. Hawkes, *Chromatographia*, **20**, 293 (1985).
- 149 W. H. King, *Anal. Chem.*, **36**, 1735 (1964).
- 150 J. F. Alder and J. J. McCallum, *J. J. Analyst (London)*, **108**, 1169 (1983).
- 151 J. J. McCallum, *J. J. Analyst (London)*, **114**, 1173 (1989).

- 151 J. J. McCallum, *J. J. Analyst (London)*, **114**, 1173 (1989).
- 152 G. G. Guilbault and J. M. Jordan, *CRC Critical Reviews in Analytical Chemistry*, **19**(1), 1 (1988).
- 153 A. Mierzwinski and Z. Witkiewicz, *Z. Environmental Pollution*, **57**, 181 (1989).
- 154 C. T. Chuang, R. M. White and J. J. Bernstein, *IEEE Electron. Device Lett.*, EDL-3, 145 (1982).
- 155 R. M. White, P. J. Wicher, S. W. Wenzel and E. T. Zellers, *IEEE Trans. Ultrason., Ferroelectrics, Freq. Contr.*, UFFC-34, 162 (1987).
- 156 H. Wohltjen and R. E. Dessy, *Anal. Chem.*, **51**, 1458 (1979).
- 157 H. Wohltjen, *Sens. Actuators*, **5**, 307 (1984).
- 158 D. S. Ballantine Jr. and H. Wohltjen, *Anal. Chem.*, **61**, 704A-617A (1989).
- 159 G. J. Bastians, *Chemical Sensors*, Ed. T. E. Edwards, Blackie, Glasgow & London, 295-319, 1988.
- 160 A. Venema, E. Nieuwkoop, M. J. Vellekoop, M. S. Nieuwenhuizen and A. W. Barendsz, *Sens. Actuators*, **10**, 47 (1986).
- 161 M. S. Nieuwenhuizen and A. W. Barendsz, *Sens. Actuators*, **11**, 45 (1987).
- 162 J. W. Grate, A. W. Snow, D. S. Ballantine, H. Wohltjen, M. H. Abraham, R. A. McGill and P. Sasson, *Proc. of the 4th Int. Conf. on Solid-State Sensors and Actuators, Transducers '87, Tokyo*, 579 (1987).
- 163 J. W. Grate, A. W. Snow, D. S. Ballantine, H. Wohltjen, M. H. Abraham, R. A. McGill and P. Sasson, *NRL Memorandum Report*, 6024 (1987) NTIS ADA 183694.
- 164 A. Bryant, M. Poirer, G. Riley, D. L. Lee and J. F. Vetelino, *Sens. Actuators*, **4**, 105 (1983).
- 165 A. J. Ricco, S. J. Martin and T. E. Zipperian, *Sens. Actuators*, **8**, 319 (1985).
- 166 J. F. Vetelino, R. K. Lade and R. S. Falconer, *IEEE Trans. Ultrason. Ferroelectrics. Freq. Contr.*, UFFC-34, 156 (1987).
- 167 M. Janghorbani and H. Freund, *Anal. Chem.*, **45**, 325 (1973).
- 168 T. E. Edmunds and T. S. West, *Anal. Chim. Acta.*, **117**, 147 (1980).
- 169 J. J. McCallum, P. R. Fielden, M. Volkan and J. F. Alder, *Anal. Chim. Acta*, **162**, 75 (1984).
- 170 J. W. Grate, A. W. Snow, D. S. Ballantine, H. Wohltjen, M. H. Abraham, R. A. McGill and P. Sasson, *Anal. Chem.*, **60**, 869 (1988).

- 171 C. E. Rodgers, *Polymer Permeability*, Ed. J. Comyn, Elsevier, New York, pp. 29-34, 1985.
- 172 J. E. Guillet, *Advan. Anal. Chem. Instrument.*, **11**, 187 (1973).
- 173 C. H. M. Jacques and H. B. Hobfenberg, *Polym. Eng. Sci.*, **14**, 441 (1974).
- 174 H. B. Hobfenberg and V. Stanuet, *The Physics of Glassy Polymers*, Ed. R. N. Hayward, Applied Science Publishers Ltd, London, pp. 504-546, 1973.
- 175 S. L. Rose-Pehrsson, J. W. Grate, D. S. Ballantine Jr. and P. C. Jurs, *Anal. Chem.*, **60**, 2801 (1988).
- 176 J. T. Tou and R. C. Gonzalez, *Pattern Recognition Principles*, Addison-Welsey, Reading, MA, 1974.
- 177 W. T. Williams and G. N. Lance, *Statistical Methods for Digital Computers*, Ed. K. Enslein, A. Ralston and R. Wilif, Wiley Interscience, New York, 1975.
- 178 A. J. Stuper, W. E. Brugger and P. C. Jurs, *Computer Assisted Studies of Chemical Structure and Biological Function*, Wiley-Interscience, New York, 1979.
- 179 D. L. Massart and L. Kaufman, *The Interpretation of Analytical Chemical Data by the Use of Cluster Analysis*, Wiley, New York, 1983.
- 180 P. C. Sadek, P. W. Carr, R. M. Doherty, M. J. Kamlet, P. W. Taft and M. H. Abraham, *Anal. Chem.*, **57**, 2971 (1985).
- 181 M. H. Abraham, G. S. Whiting, R. M. Doherty and W. J. Schuely, *J. Chem. Soc. Perkin Trans. 2*, 1451 (1990).
- 182 M. H. Abraham, G. S. Whiting, R. M. Doherty and W. J. Schuely, *J. Chromatog.*, **518**, 329 (1990).
- 183 These are the *b*-values given in Table III of reference 82 under the row equation 5, personal communication from Professor Laffort.
- 184 M. H. Abraham, P. L. Grellier, I. Hamerton, R. A. McGill, D. V. Prior and G. S. Whiting, *Faraday Discuss. Chem. Soc.*, **85**, 107 (1988).
- 185 M. H. Abraham, P. L. Grellier, D. V. Prior, P. P. Duce, J. J. Morris and P. J. Taylor, *J. Chem. Soc., Perkin Trans. 2*, 699 (1989).
- 186 M. H. Abraham, P. L. Grellier, D. V. Prior, J. J. Morris and P. J. Taylor, *J. Chem. Soc., Perkin Trans 2*, 521 (1990).
- 187 M. J. Kamlet, R. M. Doherty, M. H. Abraham and R. W. Taft, *Quant. Struct. -Act. Relat.*, **7**, 71 (1988).
- 188 J. G. Kirkwood, *J. Chem. Phys.*, **2**, 351 (1934).
- 189 R. Fuchs, M. H. Abraham, M. J. Kamlet and R. W. Taft, *J. Phys. Org. Chem.*, **2**, 559 (1982).

- 190 G. Tarján, A. Kiss, G. Kocsis, S. Mészáros and J. M. Takács, *J. Chromatog.*, **119**, 327 (1976); and references cited therein.
- 191 C. E. Figgins, T. H. Risby and P. C. Jurs, *J. Chromatogr. Sci.*, **14**, 453 (1976).
- 192 R. Fellous, L. Luft, and J. -P. Rabine, *J. Chromatog.*, **160**, 117 (1978); **166**, 383 (1978).
- 193 J. J. Leary, J. B. Justice, S. Tsuge, S. R. Lowry and T. L. Isenhour, *J. Chromatogr. Sci.*, **11**, 201 (1973).
- 194 A. Eskes, F. Dupuis, A. Dijkstra, H. De Clercq and D. L. Massart, *Anal. Chem.*, **47** 2168 (1973).
- 195 D. L. Massart, P. Lenders and M. Lauwereys, *J. Chromatogr., Sci.*, **12**, 617 (1974).
- 196 S. Wold and K. Andersson, *J. Chromatogr.*, **80**, 43 (1973).
- 197 S. Wold, *J. Chromatogr. Sci.*, **13**, 525 (1975).
- 198 M. Chastrette, *J. Chromatogr. Sci.*, **14**, 357 (1976).
- 199 D. H. McCloskey and S. J. Hawkes, *J. Chromatogr. Sci.*, **13**, 1 (1975).
- 200 M. H. Abraham, G. S. Whiting, R. M. Doherty and W. J. Schuely, *J. Chem. Soc., Perkin Trans. 2*, 1851 (1990).
- 201 M. H. Abraham and G. S. Whiting, unpublished work.
- 202 M. J. Kamlet, M. H. Abraham, R. M. Doherty and R. W. Taft, *Nature*, **106**, 464 (1984).
- 203 M. H. Abraham, G. J. Buist, P. L. Grellier, R. A. McGill, D. V. Prior, S. Oliver, E. Turner, J. J. Morris, P. J. Taylor, P. Nicolet, P. -C. Maria, J. -F. Gal, J. -L. M. Abboud, R. M. Doherty, M. J. Kamlet, W. J. Schuely and R. W. Taft, *J. Phys. Org. Chem.*, **2**, 540 (1989).
- 204 J. Li, Y. Zhang, A. J. Dallas and P. W. Carr, *J. Chromatogr.*, in the press.
- 205 R. Fellous, L. Lizzani-Cuvelier and R. Luft, *Analyt. Chim. Acta*, **174**, 53 (1985).
- 206 P. Urone, J. E. Smith and R. J. Katnik, *Anal. Chem.*, **34**, 476 (1962).
- 207 D. E. Martire and L. Z. Pollara, *J. Chem. Eng. Data*, **10**, 40 (1965).
- 208 J. P. Sheridan, D. E. Martire and Y. B. Tewari, *J. Am. Chem. Soc.*, **94**, 3294 (1972).
- 209 E. F. Meyer, K. S. Stec and R. D. Hotz, *J. Phys. Chem.*, **77**, 2140 (1973).
- 210 G. Castello and T. C. Gerbino, *J. Chromatogr.*, **437**, 33 (1988).

- 211 A. L. McClellan, *Tables of Experimental Dipole Moments*, Vol. 2, Rahara Enterprises, Calafornia, 1974.
- 212 J. E. Bartmess, *The Gas Acidity Scale*, personal communication from Professor John E. Bartmess.
- 213 G. Caldwell and P. Kebarle, *J. Am. Chem. Soc.*, **106**, 967 (1984).
- 214 A. Wehrli and E. Kovats, *Helv. Chim. Acta.*, **42**, 2709 (1959).
- 215 H. M. Smiley, *J. Chem. Eng. Data*, **15**, 413 (1970).
- 216 N. N. Kedrina, L. V. Semenov, A. A. Gaile and T. A. Bispen, *Zh. Fiz. Khim.*, **57**, 2930 (1983) [*Russ. J. Phys. Chem. (Engl. Transl.)*, **57**, 1776 (1983)].
- 217 P. O. Ferreira, J. C. Bastos and A. G. Medina, *J. Chem. Eng. Data*, **32**, 25 (1987).
- 218 U. Weidlich, H. -J. Röhm and J. Gmehling, *J. Chem. Eng. Data*, **32**, 450 (1987).
- 219 A. O. Bender, H. A. Zainel, T. M. Sarkissian and E. K. Talib, *J. Pet. Res. Iraq*, **7**, 131 (1988).
- 220 C. Knoop, D. Tiegs and J. Gmehling, *J. Chem. Eng. Data*, **34**, 240 (1989).
- 221 *Solubility Data Project Series*; vol 9, ed. W. Hayduk, 1982; vol. 21, eds. C. L. Young and P. G. T. Fogg, 1985; ed. W. Hayduk, 1986, Pergamon, Oxford.
- 222 R. Battino, T. R. Rettich and T. Tominaga, *J. Phys. Chem. Ref. Data*, **13**, 563 (1984).
- 223 S. Wu, S. Zeck and H. Knapp, *Ber. Bunsenges. Phys. Chem.*, **89**, 1009, 1013 (1985).
- 224 S. F. Shakova and Yu. P. Zubchenko, *Khim. Prom. (Moscow)*, **49**, 595 (1973).
- 225 J. -Y. Lenoir, P. Renault and H. Renon, *J. Chem. Eng. Data*, **16**, 340 (1971).
- 226 M. H. Abraham, P. L. Grellier and R. A. McGill, *J. Chem. Soc. Perkin Trans. 2*, 339 (1988).
- 227 I. Kikic and H. Renon, *Sep. Sci.*, **11**, 45 (1976).
- 228 P. Vernier, C. Raimbault and H. Renon, *J. Chim. Phys.*, **66**, 429 (1969).
- 229 R. Alexander, E. C. F. Ko, A. J. Parker and T. J. Broxton, *J. Am. Chem. Soc.*, **90**, 5049 (1968).
- 230 W. V. Wilding, L. C. Wilson and G. M. Wilson, in *American Institute of Chemical Engineers Symposium Series*, No. 256, vol. 83, p. 49 (1987).
- 231 W. V. Wilding, L. C. Wilson and G. M. Wilson, ref. 230, p. 80.

- 232 R.Schmidt, M. Geis and H. Kelm, *Z. Phys. Chem. (Frankfurt am Main)*, **92**, 223 (1974).
- 233 E. Brunner, *Ber. Bunsenges. Phys. Chem.*, **82**, 798 (1978); **83**, 715 (1979).
- 234 H. Itsuki, H. Shigeta and S. Terasawa, *Chromatographia*, **27**, 359 (1989).
- 235 E. R. Thomas, B. A. Newman, T. C. Long, D. A. Wood and C. A. Eckert, *J. Chem. Eng. Data*, **27**, 399 (1982).
- 236 C. H. Deal and E. L. Derr, *Ind. Eng. Chem., Process Des. Dev.*, **3**, 394 (1964).
- 237 W. Gerrard, *J. Appl. Chem. Biotechnol.*, **22**, 623 (1972).
- 238 B. G. Cox, A. J. Parker and W. E. Waghorne, *J. Am. Chem. Soc.*, **95**, 1010 (1973).
- 239 M. H. Abraham, P. L. Grellier, J. -L. M. Abboud, R. M. Doherty and R. W. Taft, *Can. J. Chem.*, **66**, 2673 (1988).
- 240 S. Cabani, P. Gianni, V. Mollica and L. Lepori, *J. Solution Chem.*, **10**, 563 (1981).
- 241 M. H. Abraham, G. S. Whiting, R. Fuchs and E. J. Chambers, *J. Chem. Soc., Perkin Trans. 2*, 291 (1990).
- 242 M. H. Abraham, P. L. Grellier, A. Nasehzadeh and R. A. C. Walker, *J. Chem. Soc., Perkin Trans. 2*, 1717 (1988).
- 243 Y. Alarie, *Arch. Environ. Health*, **13**, 433 (1966).
- 244 Y. Alarie, *Toxicol. Appl. Pharmacol.*, **24**, 279 (1973).
- 245 Y. Alarie, *Food Cosmet. Toxicol.*, **19**, 623 (1981).
- 246 J. C. DeCaurriz, J. C. Miccicino, P. Bonnett and J. P. Guenier, *Toxicol. Lett.*, **9**, 137 (1981).
- 247 J. Muller and G. Greff, *Fd. Chem. Toxicol.*, **22**, 661 (1984).
- 248 J. C. DeCaurriz, J. P. Desiles, P. Bonnett, J. P. Guenier and J. Muller, unpublished results, quoted in reference 247.
- 249 D. W. Roberts, *Chem. -Biol. Interactions*, **57**, 325 (1986).
- 250 M. H. Abraham, G. S. Whiting, Y. Alarie, J. J. Morris, P. J. Taylor, R. M. Doherty, R. W. Taft and G. D. Nielsen, *Quant. Struct. -Act. Relat.*, **9**, 6 (1990).
- 251 P. Alessi, I. Kikic, A. Papo and G. Torriano, *J. Chem. Eng. Data*, **23**, 29 (1978).
- 252 N. P. Franks and W. R. Lieb, *Nature*, **316**, 349 (1985).
- 253 A. Finkelstein, *J. Gen. Physiology*, **68**, 127 (1976).

- 254 J. Hine and P. K. Mookerjee, *J. Org. Chem.*, **40**, 292 (1975).
- 255 M. H. Abraham and E. Matteoli, *J. Chem. Soc., Faraday Trans 1*, **84**, 1985 (1988).
- 256 D. Mackay and W. Y. Shiu, *J. Phys. Chem. Ref. Data*, **10**, 1175 (1981); **15**, 911 (1986).
- 257 W. Riebesehl and E. Tomlinson, *J. Phys. Chem.*, **88**, 4770 (1984).
- 258 W. Riebesehl, E. Tomlinson and H. J. M. Grünbauer, *J. Phys. Chem.*, **88**, 4775 (1984).
- 259 R. Fuchs, M. H. Abraham, M. J. Kamlet and R. W. Taft, *J. Phys. Org. Chem.*, **2**, 559 (1989).
- 260 R. Fuchs, E. J. Chambers and W. K. Stephenson, *Canad. J. Chem.*, **65**, 2624 (1987).
- 261 R. S. Siderov, A. A. Khvostikova and G. I. Vakhursheva, *J. Anal. Chem. USSR (Engl. Trans.)*, **28**, 1420 (1973).
- 262 N. Dimov, *J. Chromatog.*, **347**, 366 (1985).
- 263 L. Sojak, J. Rumen and J. Janak, *J. Chromatog.*, **406**, 51 (1987).
- 264 F. Riedo, D. Fritz, G. Tarjan, and E. Kovats, *J. Chromatog.*, **126**, 63 (1976).
- 265 P. Laffort and F. Patte, *J. Chromatog.* **406**, 51 (1987).
- 266 U. Weldlich and J. Grehling, *J. Chem. Eng. Data*, **32**, 138 (1987).
- 267 M. Laffosse and M. Dreux, *J. Chromatog.*, **193**, 9 (1980).
- 268 M. J. Kamlet, R. M. Doherty, M. H. Abraham, Y. Marcus and R. W. Taft, *J. Phys. Chem.*, **92**, 5244 (1988).
- 269 R. A. Pierotti, *Chem. Rev.*, **76**, 717 (1976).
- 270 R. A. McGill, Ph.D. Thesis - *Physicochemical Measurements by Gas Chromatography*, University of Surrey, March 1988.
- 271 B. R. Kersten, S. K. Poole and C. F. Poole, *J. Chromatog.*, **468**, 235 (1989).
- 272 S. K. Poole and C. F. Poole, *J. Chromatog.*, **500**, 329 (1990).
- 273 Personal communication from Professor Colin F. Poole.

Hydrogen bonding

XV. A new characterisation of the McReynolds 77-stationary phase set

MICHAEL H. ABRAHAM* and GARY S. WHITING

Department of Chemistry, University College London, 20 Gordon Street, London WC1H 0AJ (U.K.)

RUTH M. DOHERTY

Naval Surface Warfare Center, White Oak Laboratory, Silver Spring, MD 20910 (U.S.A.)

and

WENDEL J. SHUELY

U.S. Army Chemical Research, Development and Engineering Center, Aberdeen Proving Ground, MD 21010 (U.S.A.)

(First received March 20th, 1990; revised manuscript received June 20th, 1990)

ABSTRACT

The following equation has been applied to all the phases in the McReynolds 77-stationary phase set.

$$\log V_G^0 = c + rR_2 + s\pi_2^* + a\alpha_2^H + b\beta_2^H + l \log L^{16}$$

In this equation, V_G^0 is the specific retention volume for a series of solutes on a given stationary phase, and the explanatory variables are R_2 , a modified solute molar refraction, π_2^* the solute dipolarity, α_2^H the solute hydrogen-bond acidity, β_2^H the solute hydrogen-bond basicity, and $\log L^{16}$ where L^{16} is the solute Ostwald absorption coefficient on hexadecane at 25°C. The constants in the equation are obtained by multiple linear regression analysis, using about 150 data points in each regression, and values of r , s , a , b and l are regarded as characteristic constants of the phases that serve to classify the 77-phase set. It is shown that the classification of the phases into clusters is in accord with chemical principles, and is in excellent agreement with previous work using hierarchical clustering, minimum spanning tree techniques, and pattern cognition methods. The above equation allows the factors that lead to gas-liquid chromatographic separations to be identified, and provides quantitative information on the various solute-solvent interactions that give rise to these factors.

INTRODUCTION

The largest sets of gas chromatographic retention data are those of McReynolds, who determined retention volumes (V_G^0) and retention indices (I) of 376 solutes on 77 phases at two temperatures [1], and retention indices of 10 solutes on 226 phases at 120°C [2]. Numerous workers have classified both the 77-phase set and the 226-phase set by various methods. McReynolds himself [2] assigned a single polarity index to the 226 stationary phases, using the sum of the ΔI values for benzene, butanol,

2-pentanone, nitropropane and pyridine. Later workers refined this method [3] and also calculated a polarity index from the Gibbs energy of solvation of the methylene increment, $\Delta G_s^0(\text{CH}_2)$, on a given stationary phase [4]. Other workers assigned a number of characteristic parameters to phases. Thus Figgins *et al.* [5] derived ΔG_s^0 values for six functional groups on 75 of the 226-phase set, and Fellous *et al.* [6] assigned a polarity index (p^*) to the same six functional groups on 72 of the 226-phase set.

Various sophisticated methods have been used to classify the McReynolds phases into groups. They include nearest neighbour techniques [7], information theory [8], numerical taxonomy [8,9], principal components analysis [10], pattern cognition methods [11,12] and factor analysis [13]. All these methods reduce the 226-phase set or the 77-phase set to a smaller number of clusters each of which represents a collection of similar phases. This is a very useful and helpful outcome, but, in addition, several of these methods lead to the estimation of the number of factors that influence chromatographic retention data. Wold and Andersson [10] suggested three main factors, (1) polarity, (2) a factor difficult to identify and (3) a factor that was due to hydrogen-bonding of the phase with alcohols. Chastrette [13] showed that five factors accounted for 99% of the total variance: three factors were difficult to account for, and the other two were polarity and a factor connected to, but not identical with, hydrogen-bonding. A polarity factor was identified by McCloskey and Hawkes [14], who also suggested that a factor related to the ability of a phase to retain *cis*-hydrindane was important.

It seems, therefore, that although a single "polarity" parameter is still often used to characterise stationary phases [4,15], analytical methods suggest that a number of factors must be involved, perhaps three [10] to five [13], although identification of these factors with particular chemical interactions has not proved possible. Our analysis starts with a model for solvation of a solute, and then deduces from the model various possible interactions. Once these interactions are set out, the necessary parameters required to quantify these interactions have to be obtained (from data other than the chromatographic results to be analysed). These parameters then, in effect, take the place of the various factors identified by methods such as principal components analysis [10] or factor analysis [13].

On our model, the process of dissolution of a gaseous solute into a liquid stationary phase or solvent can conceptually be broken down into a number of stages, *viz.* (1) the creation of a cavity in the phase of suitable size, (2) reorganisation of solvent molecules round the cavity and (3) introduction of the solute into the cavity. The first stage involves the endoergic breaking of solvent-solvent bonds: the larger the solute, the more bonds are broken to create a cavity, and the more endoergic is the process. On this step alone, the larger the solute the less soluble it would be, and the smaller would be the retention volume (V_G^0) or the Ostwald solubility coefficient (L). The second stage is not very important in terms of Gibbs energy, although it probably is in terms of enthalpy and entropy. In the third stage, various solute-solvent interactions will be set up, all of which will be exoergic and will lead to increased solubility of the solute. Possible interactions include: (i) General dispersion interactions that will invariably be larger or more exoergic the larger is the solute. It is these interactions that account for the solubility of inert solutes such as the alkanes. And since such solutes are more soluble the larger they are, these dispersion interactions must be

strong enough to overcome the endoergic cavity effect. (ii) Dipolar interactions, including dipole–dipole or dipole–induced dipole effects. (iii) Hydrogen-bonding interactions between solute acid–solvent base and solute base–solvent acid. (iv) Possible specific interactions involving π - or n -electron pairs. In view of this complexity of solute–solvent systems, it is not surprising that only limited identification of the factors governing such systems has hitherto been made, but it is clearly of considerable importance if stationary phases could be characterised in terms of these fundamental interactions.

We have now developed solute parameters that, we believe, correspond to either simple fundamental properties, or to known combinations of properties [16–23]. These are as follows: R_2 a modified polarisability parameter that characterises the ability of a solute to interact via π - or n -electron pairs [16,17], δ_2 a polarisability correction term [18–20] taken as zero except for polyhalogenated aliphatics (0.5) or aromatics (1.0) and which is probably an approximation to R_2 , π_2^* the solute dipolarity^a [18–20], α_2^H the solute hydrogen-bond acidity [21], β_2^H the solute hydrogen-bond basicity [22] and $\log L^{16}$ where L^{16} is the solute Ostwald solubility coefficient on hexadecane at 25°C [23]. This latter parameter is a combination of a cavity term and a general dispersion interaction term [24]. Various multiple linear regression equations can then be constructed to account for solubility-related properties (SP) of a series of solutes in a given solvent or stationary phase, eqns. 1–3, where SP can be V_G^0 , L (or K , the gas–liquid partition coefficient), but *cannot* be the retention index.

$$\log \text{SP} = c + rR_2 + s\pi_2^* + a\alpha_2^H + b\beta_2^H + l \log L^{16} \quad (1)$$

$$\log \text{SP} = c + d\delta_2 + s\pi_2^* + a\alpha_2^H + b\beta_2^H + l \log L^{16} \quad (2)$$

$$\log \text{SP} = c + rR_2 + q\mu_2^2 + a\alpha_2^H + b\beta_2^H + l \log L^{16} \quad (3)$$

In eqn. 3, μ_2 is the solute dipole moment. We have applied eqns. 1–3 to a number of sets of gas chromatographic retention data, and also to the solubility of gases and vapours in some common solvents, with considerable success [16,17,25]. Now since the parameters, or explanatory variables, in eqns. 1–3 represent solute properties, the various constants found by multiple linear regression analyses, will represent solvent or stationary phase properties. The most useful equation in this respect is eqn. 1 for which we have r the tendency of the phase to interact with π - and n -solute electron pairs, s the phase dipolarity, a the phase hydrogen-bond basicity (because basic phases will interact with acidic solutes), b the phase hydrogen-bond acidity, and l representing a combination of general dispersion interactions and cavity effects. These constants r , s , a , b and l (together with possibly q , another measure of phase dipolarity) thus serve to characterise the phase in terms of particular chemical interactions. That up to five constants are needed to characterise a given stationary phase reflects the complexity of solute–solvent interactions. The number of constants,

^a We use this term in the Kamlet–Taft sense [18], namely the ability of a molecule to undergo molecular interactions of a dipole–dipole or a dipole–induced dipole nature. Thus dioxane and 1,4-dichlorobenzene are regarded as “dipolar”, even though they have no permanent dipole moment.

however, is certainly in accord with principal components analysis [10] and factor analysis [13], which both show that several factors are required to account for retention data.

RESULTS

We now apply eqns. 1–3 to the data of McReynolds [1] on 367 solutes on 77 phases. Of the solutes studied, we have all the necessary parameters for about 160, and our analysis uses up to 157 solutes on the 77 phases at two temperatures^a. As pointed out, above, retention indices are not suitable for use as SP values in eqns. 1–3, and all our analyses are in terms of the $\log V_G^0$ values reported by McReynolds [1]. We first test, as a necessary preliminary, whether the solute parameters used as explanatory variables are, indeed, independent. In Table I are given the correlation constants, R , between the explanatory variables in eqn. 1. It can be seen that the intercorrelations are insignificant, with the possible exception of that between π_2^* and β_2^H for which $R = 0.474$ (and $R^2 = 0.225$ only). We also test eqns. 1–3 for two typical phases, ethyleneglycol adipate and dibutyltetrachlorophthalate; results are in Table II. Both the overall correlation coefficient and the standard deviation, S.D., are almost identical for eqn. 1 and eqn. 2. Since the molar refraction parameter R_2 can be identified with a specific type of solute–solvent interaction, whereas the empirical δ_2 parameter cannot, we shall list results in terms of the preferred eqn. 1 only. Although the correlations in terms of eqn. 3 are quite useful, they are in all cases not as good as eqn. 1, and so we shall not give all the details of eqn. 3, but list where necessary values of the q constant only.

TABLE I

CORRELATION COEFFICIENTS BETWEEN THE EXPLANATORY VARIABLES, FOR THE 155-SOLUTE DATA SET USED FOR FLEXOL

	R_2	π_2^*	α_2^H	β_2^H
π_2^*	0.295			
α_2^H	0.111	−0.210		
β_2^H	−0.243	0.474	0.247	
$\log L^{16}$	0.016	−0.171	−0.061	−0.169

The results of application of eqn. 1 to the entire set of stationary phases at 120°C are summarised in Table III, where also the q constant in eqn. 3 is given. For a few phases, data were available at 80 and 100°C only, and we have estimated the various constants at 120°C from values at the lower temperatures. For completeness, we applied the various equations to results at the other given temperatures used in the work of McReynolds [1], and details are shown in Table IV. Before attempting to

^a McReynolds studied a large number of difunctional compounds for which we lack most of the required parameters in eqns. 1 and 2; these include many formals, acetals, dihydric alcohols, etc. Note that not all solutes were studied on all phases, so that the number of solutes used in our regressions varies from 130 to 157.

TABLE II

COMPARISON OF EQNS. 1-3 IN REGRESSIONS OF $\log V_G^0$ AT 120°CS.D. = Overall standard deviation; R = overall correlation coefficient; n = number of solutes.

Eqn.	c	r	d	s	q	a	l	S.D.	R	n
Ethyleneglycol adipate										
1	-0.900	0.357		1.425		1.720	0.443	0.093	0.9857	143
	0.038 ^a	0.048		0.048		0.053	0.007			
2	-0.871		0.116	1.480		1.867	0.438	0.094	0.9849	143
	0.038		0.030	0.047		0.053	0.007			
3	-0.360	0.784			0.073	1.405	0.394	0.160	0.9476	143
	0.055	0.079			0.006	0.089	0.013			
Dibutyltetrachlorophthalate										
1	-0.615	0.249		0.692		0.600	0.600	0.048	0.9969	150
	0.019	0.025		0.025		0.028	0.004			
2	-0.615		0.112	0.752		0.687	0.599	0.050	0.9967	150
	0.020		0.016	0.025		0.029	0.004			
3	-0.410	0.547			0.038	0.420	0.586	0.070	0.9920	150
	0.024	0.039			0.003	0.040	0.006			

^a These are the standard deviations in the constants.

classify the phases, we note that the correlation eqn. 1 yields results that are reasonably good for "all solute" correlations, and, as we shall see, these results are chemically sensible. Thus the s , a and b constants, when statistically significant, are always positive, because increase in solute-solvent interactions must lead to an increase in solubility of the gaseous solute, and hence to an increase in V_G^0 . The r constant is nearly always positive, except in the case of fluorinated phases, *e.g.* Dow fluid 1265, where the polarisability is even less than in hydrocarbon systems. As mentioned in the introduction, the l constant reflects a combination of an endoergic cavity term and an exoergic solute-solvent general dispersion interaction term. The latter always dominates, giving rise to positive l constants.

The effect of temperature is very important with regard to characterisation of solubility-related phenomena, although it has generally been overlooked as regards characterisation of stationary phases. In general, the main characteristic constants s , a , b and l , all decrease, often quite markedly, with temperature. Now if the relevant solute-solvent interactions are not only exoergic but are exothermic as well, the Van 't Hoff equation requires that these interactions will decrease with increase in temperature, hence leading to a decrease in the numerical values of the characteristic constants. On thermodynamic grounds it thus follows that any correlation equation set up in terms of solute-solvent or solute-stationary phase interactions must incorporate this temperature dependence. Our eqn. 1 does so via the characteristic constants.

As a final check on our method of analysis, we can compare regression equations obtained from the set of solutes used by McReynolds [1] with those [16] from the quite different set of solutes used by Patte *et al.* [26] for Carbowax 1540, diethyleneglycolsuccinate, polyphenyl ether and Zonyl-E7. Details are in Table V, and show that there is very good agreement between the two sets of regressions using eqn. 1.

TABLE III

CLASSIFICATION OF PHASES AT 120 °C

S.D. and R are the overall deviation and correlation coefficient on application of eqn. 1 to $\log V_G^0$. The number of data points is No. q = The coefficient of μ_2^2 in eqn. 3.

Group	Stationary phase	Characteristic constants in eqn. 1							S.D.	R	No	q
		c	r	s	a	l						
1	Squalane ^a	-0.33	0.12	0.02	0.00	0.619		0.026	0.9990			0.001
2	Apiezon M	-0.45	0.26	0.10	0.11	0.600		0.035	0.9982		147	0.006
	Apiezon N	-0.48	0.27	0.12	0.10	0.601		0.037	0.9978		149	0.008
	Apiezon J	-0.48	0.27	0.13	0.13	0.594		0.034	0.9984		148	0.010
	Apiezon L	-0.48	0.27	0.14	0.13	0.596		0.036	0.9982		149	0.006
3	Versilube P50	-0.37	0.03	0.25	0.17	0.538		0.036	0.9978		149	0.010
	SE-31	-0.36	0.03	0.24	0.17	0.520		0.039	0.9971		156	0.012
	SE-30	-0.32	0.03	0.27	0.29	0.523		0.040	0.9971		152	0.014
	SE-30 NPGA	-0.40	0.06	0.27	0.33	0.525		0.042	0.9969		152	0.016
4	SE-52	-0.38	0.06	0.32	0.22	0.532		0.041	0.9971		155	0.018
	Diocetylsebacate	-0.35	0.12	0.49	0.79	0.594		0.047	0.9967		153	0.029
	Di-2-ethylhexylsebacate	-0.36	0.13	0.51	0.83	0.591		0.045	0.9969		153	0.028
	Tripelargonate	-0.42	0.16	0.53	0.82	0.583		0.051	0.9964		151	0.032
	Isooctyldecyladipate	-0.37	0.13	0.55	0.81	0.586		0.048	0.9964		154	0.031
	Di-2-ethylhexyladipate	-0.36	0.13	0.55	0.87	0.590		0.047	0.9967		150	0.030
	Diisodecylphthalate	-0.52	0.13	0.65	0.73	0.589		0.055	0.9958		155	0.038
	Diocetylphthalate	-0.52	0.14	0.67	0.77	0.587		0.053	0.9960		153	0.039
5	Ucon LB-1715	-0.56	0.18	0.71	1.22	0.543		0.072	0.9923		153	0.038
	Flexol 8N8	-0.48	0.11	0.73	1.27	0.573		0.065	0.9932		155	0.043
	Pluronic L81	-0.49	0.20	0.77	1.29	0.537		0.075	0.9913		152	0.040
6	Polyphenyl ether, 5 rings	-0.70	0.21	0.88	0.54	0.564		0.064	0.9940		155	0.048
	Polyphenyl ether, 6 rings	-0.74	0.21	0.90	0.56	0.563		0.066	0.9935		155	0.048
7	Tricresylphosphate	-0.68	0.15	1.06	1.23	0.550		0.074	0.9930		154	0.057
	Sucrose acetate isobutanoate	-0.56	0.05	1.05	1.29	0.509		0.071	0.9928		157	0.056
8	Hallecomid M18	-0.35	0.11	0.60	1.55	0.592		0.062	0.9947		154	0.037
	Hallecomid M180L	-0.45	0.10	0.71	1.59	0.592		0.068	0.9930		153	0.040

9	Pluronic L42	-0.52	0.21	0.88	1.45	0.529	0.081	0.9898	154	0.045
	Pluronic L72	-0.54	0.17	0.89	1.41	0.531	0.077	0.9917	153	0.042
	Pluronic L61	-0.53	0.20	0.91	1.42	0.526	0.079	0.9905	151	0.044
	Pluronic L63	-0.54	0.24	0.92	1.46	0.519	0.080	0.9900	153	0.046
	Polytergent J300	-0.55	0.16	0.94	1.49	0.536	0.081	0.9901	154	0.052
	Pluronic P84	-0.57	0.20	0.94	1.44	0.516	0.079	0.9908	152	0.047
	Pluronic P85	-0.57	0.28	0.94	1.46	0.512	0.082	0.9902	153	0.052
	Pluronic L44	-0.56	0.26	0.96	1.52	0.515	0.084	0.9899	154	0.049
	Oronite NIW	-0.62	0.25	0.96	1.46	0.524	0.085	0.9898	155	0.053
	Ucon HB-2000	-0.60	0.28	0.97	1.48	0.514	0.081	0.9907	154	0.053
	Ethofat 60-25	-0.60	0.26	0.99	1.54	0.523	0.078	0.9916	154	0.052
	Pluronic P65	-0.60	0.28	1.01	1.50	0.513	0.086	0.9893	155	0.050
	Pluronic P46	-0.61	0.30	1.02	1.56	0.505	0.085	0.9893	154	0.052
	Tergitol NPX	-0.57	0.19	1.02	1.47	0.518	0.078	0.9917	154	0.058
10	Neopentylglycoladipate, term	-0.68	0.21	1.08	1.45	0.510	0.070	0.9929	152	0.057
	Ethylene glycolsebacate	-0.78	0.27	1.10	1.44	0.518	0.078	0.9911	145	0.054
	Diethyleneglycolsebacate	-0.76	0.32	1.14	1.45	0.498	0.074	0.9910	141	0.052
	Neopentylglycoladipate	-0.67	0.24	1.14	1.47	0.491	0.073	0.9916	150	0.060
	Neopentylglycolsuccinate	-0.71	0.23	1.24	1.49	0.466	0.082	0.9884	153	0.065
11	Pluronic F88	-0.63	0.34	1.10	1.60	0.483	0.086	0.9887	153	0.058
	Pluronic F68	-0.66	0.35	1.13	1.61	0.485	0.087	0.9884	154	0.059
	Pluronic F77	-0.63	0.32	1.09	1.61	0.496	0.083	0.9897	151	0.051
	Igepal CO 880	-0.66	0.28	1.16	1.61	0.488	0.084	0.9885	152	0.059
	Triton X 305	-0.83	0.29	1.17	1.65	0.492	0.086	0.9894	154	0.059
12	Ethylene glycoladipate	-0.90	0.36	1.43	1.72	0.443	0.093	0.9857	143	0.073
	Diethyleneglycoladipate	-0.91	0.40	1.46	1.73	0.438	0.089	0.9847	139	0.065
13	XF-1150	-0.69	0.06	1.44	1.38	0.417	0.084	0.9856	150	0.092
	Sucrose octaacetate	-0.73	0.12	1.48	1.59	0.426	0.090	0.9852	154	0.071
14	Carbowax 20M	-0.73	0.40	1.23	1.78	0.465	0.091	0.9880	153	0.059
	Carbowax 6000	-0.75	0.40	1.28	1.80	0.469	0.090	0.9878	150	0.059
	Carbowax 4000	-0.76	0.32	1.31	1.85	0.470	0.090	0.9867	149	0.059
	Carbowax 1540	-0.75	0.31	1.34	1.87	0.457	0.093	0.9866	151	0.069
	Carbowax 1000	-0.76	0.29	1.37	1.89	0.457	0.094	0.9867	152	0.071

(Continued on p. 336)

TABLE III (continued)

Group	Stationary phase	Characteristic constants in eqn. 1					S.D.	R	No	q
		c	r	s	a	l				
15	Carbowax 600	-0.82	0.31	1.46	2.12	0.455	0.093	0.9847	149	0.073
	Carbowax 400	-0.77	0.28	1.50	2.18	0.440	0.090	0.9883	149	0.077
	Carbowax 300	-0.79	0.33	1.50	2.28	0.434	0.093	0.9877	149	0.074
	Quadrol	-0.77	0.07	1.47	2.38	0.471	0.103	0.9858	153	0.087
	Hyprose SP80	-0.87	0.11	1.53	2.40	0.414	0.103	0.9835	151	0.088
16	Triethyleneglycolsuccinate	-1.05	0.39	1.71	1.87	0.416	0.090	0.9858	145	0.078
	Diethyleneglycolsuccinate	-0.99	0.43	1.74	1.68	0.379	0.114	0.9755	145	0.073
	Dow Corning Fluid 550	-0.46	0.09	0.56	0.29	0.547	0.047	0.9963	152	0.032
	Casterwax	-0.45	0.10	0.63	1.09	0.562	0.060	0.9944	150	0.040
	Dibutyltetrachlorophthalate	-0.62	0.25	0.69	0.60	0.600	0.048	0.9969	150	0.038
	Citroflex A4 ^a	-0.43	0.12	0.85	0.94	0.552	0.061	0.9951		0.046
	Bis(2-ethoxyethyl)phthalate	-0.64	0.13	1.23	1.25	0.529	0.074	0.9923	152	0.067
	Dow Corning Fluid FS 1265	-0.76	-0.25	1.29	0.29	0.451	0.083	0.9851	153	0.086
	Kroniflex THPP	-0.72	0.22	1.34	2.28	0.498	0.083	0.9913	152	0.071
	Zonyl E-7	-0.82	-0.28	1.63	0.69	0.449	0.071	0.9902	150	0.083

^a Values extrapolated from 80 and 100 °C.

CHARACTERISATION OF PHASES

Details of the application of eqn. 1 to the 77 McReynolds phases are given in Tables III, IV, VI and VII. In Table III are results at a common temperature of 120°C, with values for squalane and Citroflex A4 extrapolated from those at 80 and 100°C. Table IV contains results at temperatures other than 120°C, usually at 100 or at 140/160°C, so that all of McReynolds data sets have been analysed. We do not list the chemical formulation of the 77 phases, even though some of them are rather obscure, because Fellous *et al.* [6] have detailed the 77 stationary phases already. It should be noted that many of these phases contain a non-ionic surfactant (2%, w/w), and hence our obtained constants, Table III, refer to the phases as specifically formulated by McReynolds [1]. Although many of the McReynolds phases are no longer in current use, we list results for all the phases in order to show the utility of our method and in order to compare our classification with previous characterisation [12] of the total 77-phase set.

Furthermore, no corrections were made by McReynolds for effects such as interfacial adsorption, and his results for solutes such as alkanes in the more polar phases may be subject to additional error. We have no way of correcting the raw data of McReynolds, and rather than exclude particular subsets of compounds on some arbitrary basis, we have chosen to use all the available results. This may well account for part of the large standard deviations observed for regressions with phases such as diglycerol and sorbitol, and suggests also that the obtained constants for these phases should be viewed with some caution.

In principle, a given stationary phase at a given temperature is characterised by the six constants in eqn. 1. However, the constant c , although important as regards the absolute values of $\log V_G^0$, is not a very useful characteristic constant, whilst the constant r plays only a minor role, at least for the present data set. We are thus left with the four constants s , a , b and l . But we can effect further simplification by noting that only three out of the 77 phases give rise to statistically significant b constants, and hence show hydrogen-bond acidity. These are docosanol, diglycerol and sorbitol with b values of 0.34, 0.52 and 0.34 respectively at 120°C (see Table VI). A number of the other phases might be expected to show hydrogen-bond acidity, but the analysis given in Table VIII reveals that the $b\beta_2^H$ term is not significant. We can therefore regard docosanol, diglycerol and sorbitol as singular phases, and analyse the remaining 74 phases with the omission of the $b\beta_2^H$ term altogether (see Tables III and IV). For these 74 phases, the three major characteristic constants are thus s , a and l only.

We begin the analysis of the 74 phases in Table III by noting that there is some connection between s , a and l . In general, basic phases will also be dipolar, so that a and s will tend to run together. Furthermore, solvent-solvent interactions will be greater in dipolar, basic phases, thus giving rise to a larger endoergic cavity term, leading to a smaller value of the l constant. Since a and s are likely to be related, we can first group the 74 phases through a plot of a against s , shown in Fig. 1. Quite clearly, there are several groups or clusters of phases with about the same a and s values, and we have drawn up Table III to show the 16 clusters indicated in Fig. 1. Of course, there is an arbitrary element in the choice of clusters. Thus groups 9 and 11 might be subsumed into a common group, or group 4 might be divided into two groups, but this is a feature of any method that reduces the 77 phases down to a

TABLE IV
REGRESSIONS AT VARIOUS TEMPERATURES

Stationary phase	<i>c</i>	<i>r</i>	<i>s</i>	<i>a</i>	<i>l</i>	S.D.	<i>R</i>	No	Temperature (°C)
Squalane	{ -0.21 -0.27	0.11 0.12	0.08 0.05	- -	0.735 0.674	0.043 0.034	0.9970 0.9983	133 147	80 100
Apiezon M	-0.57	0.28	0.13	0.06	0.504	0.044	0.9971	153	160
Apiezon N	-0.62	0.28	0.15	0.09	0.504	0.045	0.9969	153	160
Apiezon J	-0.62	0.28	0.17	0.11	0.501	0.038	0.9977	150	160
Apiezon L	-0.57	0.29	0.10	0.05	0.502	0.037	0.9975	151	160
Versilube F50	-0.48	0.08	0.22	0.09	0.444	0.037	0.9972	152	160
SE-31	-0.48	0.05	0.22	0.14	0.430	0.038	0.9968	157	160
SE-30	-0.45	0.06	0.23	0.18	0.441	0.036	0.9968	154	160
SE-30 NPGA	-0.50	0.05	0.30	0.28	0.486	0.039	0.9970	139	140
SE-52	-0.51	0.07	0.29	0.17	0.442	0.040	0.9966	157	160
Diocetylsebacate	-0.31	0.13	0.55	0.94	0.646	0.049	0.9969	154	100
Di-2-ethylhexylsebacate	-0.31	0.13	0.55	0.95	0.646	0.050	0.9969	154	100
Trielargonate	-0.53	0.15	0.49	0.65	0.486	0.051	0.9957	154	160
Isooctyldecyladipate	-0.33	0.11	0.60	0.96	0.645	0.054	0.9964	155	100
Di-2-ethylhexyladipate	-0.31	0.11	0.61	1.04	0.644	0.052	0.9966	152	100
Diisodecylphthalate	-0.55	0.14	0.59	0.62	0.537	0.050	0.9964	156	140
Diocetylphthalate	-0.55	0.15	0.61	0.64	0.532	0.052	0.9960	155	140
Ucon LB-1715	-0.69	0.20	0.61	0.88	0.459	0.061	0.9924	152	160
Flexol 8N8	-0.54	0.07	0.69	1.09	0.524	0.057	0.9953	157	140
Pluronic L81	-0.44	0.18	0.84	1.56	0.589	0.081	0.9910	151	100
Polyphenyl ether, 5 rings	-0.86	0.23	0.82	0.44	0.482	0.060	0.9936	156	160
Polyphenyl ether, 6 rings	-0.87	0.24	0.82	0.46	0.478	0.063	0.9929	156	160
Tricresylphosphate	-0.62	0.15	1.14	1.44	0.600	0.078	0.9920	142	100
Sucrose acetate isobutanoate	-0.65	0.06	0.86	0.99	0.429	0.060	0.9925	155	160
Hallcomid M18	-0.31	0.11	0.65	1.89	0.649	0.066	0.9943	141	100
Hallcomid M180L	-0.38	0.10	0.74	1.90	0.646	0.069	0.9934	141	100

Pluronic L42	-0.59	0.20	0.82	1.26	0.486	0.074	0.9902	155	140
Pluronic L72	-0.61	0.23	0.81	1.23	0.489	0.072	0.9917	140	140
Pluronic L61	-0.50	0.21	1.02	1.67	0.581	0.088	0.9890	141	100
Pluronic L63	-0.47	0.17	1.01	1.71	0.571	0.083	0.9890	140	100
Polytergent J300	-0.49	0.15	1.01	1.76	0.584	0.089	0.9901	155	100
Pluronic P84	-0.52	0.25	1.00	1.70	0.564	0.090	0.9893	153	100
Pluronic P85	-0.52	0.27	1.03	1.71	0.562	0.091	0.9892	154	100
Pluronic L44	-0.62	0.25	0.89	1.31	0.473	0.078	0.9899	155	140
Oronite NIW	-0.81	0.20	0.90	1.12	0.458	0.071	0.9906	154	160
Ucon HB-2000	-0.52	0.29	1.03	1.67	0.560	0.094	0.9884	153	100
Ethofat 60-25	-0.57	0.19	1.08	1.78	0.575	0.086	0.9909	151	100
Pluronic P65	-0.50	0.27	1.05	1.76	0.560	0.090	0.9881	143	100
Pluronic P46	-0.46	0.30	0.94	1.38	0.466	0.079	0.9893	156	140
Tergitol NPX	-0.66	0.24	0.86	1.13	0.437	0.066	0.9916	152	160
Neopentylglycoladipate, term	-0.76	0.16	1.03	1.31	0.475	0.065	0.9928	140	140
Ethylene glycolsebacate	-0.81	0.22	1.02	1.32	0.478	0.067	0.9930	132	140
Diethyleneglycolsebacate	-0.83	0.27	1.06	1.34	0.460	0.073	0.9909	136	140
Neopentylglycoladipate	-0.67	0.18	1.02	1.32	0.444	0.064	0.9926	140	140
Neopentylglycolsuccinate	-0.72	0.16	1.15	1.39	0.418	0.070	0.9905	139	140
Pluronic F88	-0.58	0.28	1.21	1.83	0.531	0.095	0.9878	153	100
Pluronic F68	-0.60	0.29	1.24	1.81	0.530	0.098	0.9878	156	100
Pluronic F77	-0.57	0.32	1.19	1.87	0.547	0.094	0.9871	141	100
Igepal CO 880	-0.66	0.27	1.28	1.88	0.540	0.096	0.9890	152	100
Triton X 305	-0.86	0.31	0.94	1.26	0.407	0.072	0.9890	152	160
Ethylene glycoladipate	-0.97	0.24	1.37	1.68	0.412	0.083	0.9868	129	140
Diethyleneglycoladipate	-0.92	0.30	1.34	1.61	0.399	0.079	0.9865	130	140
XF-1150	-0.82	0.06	1.30	1.12	0.344	0.076	0.9843	152	160
Sucrose octaacetate	-0.84	0.12	1.29	1.30	0.362	0.076	0.9852	154	160
Carbowax 20M	-0.82	0.37	1.07	1.36	0.392	0.076	0.9879	151	160
Carbowax 6000	-0.79	0.40	1.15	1.56	0.431	0.083	0.9877	152	140
Carbowax 4000	-0.81	0.37	1.18	1.64	0.431	0.080	0.9889	150	140
Carbowax 1540	-0.71	0.38	1.42	2.17	0.499	0.100	0.9874	150	100
Carbowax 1000	-0.73	0.30	1.49	2.24	0.500	0.100	0.9875	149	100

(Continued on p. 340)

TABLE IV (continued)

Stationary phase	<i>c</i>	<i>r</i>	<i>s</i>	<i>a</i>	<i>l</i>	S.D.	<i>R</i>	No	Temperature (°C)
Carbowax 600	-0.78	0.29	1.61	2.39	0.496	0.104	0.9866	148	100
Carbowax 400	-0.73	0.28	1.60	2.44	0.481	0.104	0.9867	150	100
Carbowax 300	-0.76	0.26	1.64	2.56	0.476	0.106	0.9866	149	100
Quadrol	-0.72	0.12	1.50	2.76	0.521	0.106	0.9879	152	100
Hyprose SP80	-0.84	0.09	1.61	2.77	0.461	0.110	0.9848	150	100
Triethyleneglycolsuccinate	-1.06	0.33	1.57	1.67	0.381	0.086	0.9840	133	140
Diethyleneglycolsuccinate	-1.07	0.35	1.60	1.77	0.342	0.099	0.9746	133	140
Dow Corning Fluid 550	-0.56	0.11	0.47	0.20	0.456	0.041	0.9967	154	160
Casterwax	-0.56	0.13	0.60	0.93	0.519	0.053	0.9953	152	140
Dibutyltetrachlorophthalate	-0.57	0.24	0.75	0.68	0.658	0.057	0.9956	142	100
Citroflex A4	-0.29	-0.06	1.05	1.47	0.658	0.072	0.9923	136	80
	-0.36	0.04	0.94	1.19	0.602	0.066	0.9938	150	100
Bis(2-ethoxyethyl)phthalate	-0.58	0.18	1.29	1.46	0.575	0.085	0.9899	143	100
Dow Corning Fluid FS 1265	-0.86	-0.21	1.13	0.27	0.367	0.071	0.9853	155	160
Kroniflex THFP	-0.79	0.23	1.25	2.02	0.461	0.082	0.9901	153	140
Zonyl E-7	-0.78	-0.29	1.78	0.78	0.494	0.077	0.9905	138	100

TABLE V

CHARACTERISATION OF PHASES USING EQN. 1 WITH McREYNOLD'S AND LAFFORT'S DATA AT 120 °C

M = McReynold's set, this work; L = Laffort's set, ref. 16.

Stationary phase	Set	<i>r</i>	<i>s</i>	<i>a</i>	<i>l</i>
Carbowax 1540	M	0.31	1.34	1.87	0.457
	L	0.26	1.37	2.11	0.442
Diethyleneglycolsuccinate	M	0.43	1.74	1.68	0.379
	L	0.35	1.70	1.92	0.396
Polyphenyl ether, 6 rings	M	0.21	0.90	0.56	0.563
	L	0.19	0.98	0.59	0.552
Zonyl E-7	M	-0.28	1.63	0.69	0.449
	L	-0.38	1.61	0.70	0.442

TABLE VI

STATIONARY PHASES WITH SIGNIFICANT HYDROGEN-BOND ACIDITY

Stationary phase	<i>c</i>	<i>r</i>	<i>s</i>	<i>a</i>	<i>b</i>	<i>l</i>	S.D.	<i>R</i>	No	Temperature (°C)
Docosan ^a	-0.41	0.13	0.29	0.75	0.34	0.603	—	—	—	120
	-0.37	0.15	0.30	1.13	0.39	0.657	0.061	0.9951	148	100
	-0.33	0.16	0.31	1.56	0.45	0.717	0.077	0.9925	134	80
Diglycerol	-1.26	0.55	1.63	2.77	0.52	0.225	0.148	0.9589	146	120
Sorbitol	-1.72	0.35	0.81	1.77	0.34	0.360	0.161	0.9217	130	120

^a Extrapolated from results at 80 and 100 °C.

TABLE VII

TEST FOR STATIONARY PHASE HYDROGEN-BOND ACIDITY

Stationary phase	<i>c</i>	<i>r</i>	<i>s</i>	<i>a</i>	<i>b</i>	<i>l</i>	S.D.	<i>R</i>
Castorwax	-0.47	0.13	0.59	1.06	0.08	0.563	0.059	0.9945
	-0.45	0.10	0.63	1.09	—	0.562	0.060	0.9944
Flexol 8N8	-0.49	0.12	0.71	1.25	0.03	0.573	0.065	0.9932
	-0.48	0.11	0.73	1.27	—	0.573	0.065	0.9932
Hyprose SP80	-0.86	0.09	1.56	2.42	0.05	0.414	0.103	0.9835
	-0.87	0.11	1.53	2.40	—	0.414	0.103	0.9835
Quadrol	-0.77	0.08	1.45	2.37	0.03	0.472	0.103	0.9858
	-0.77	0.07	1.47	2.38	—	0.471	0.103	0.9858

TABLE VIII

EFFECT OF CHAIN LENGTH ON THE CHARACTERISTIC CONSTANTS FOR SOME STATIONARY PHASE ESTERS

Stationary phase	<i>r</i>	<i>s</i>	<i>a</i>	<i>l</i>
Dioctylsebacate	0.12	0.49	0.79	0.594
Ethyleneglycolsebacate	0.27	1.10	1.44	0.518
Diethyleneglycolsebacate	0.32	1.14	1.45	0.498
Isooctyldecyladipate	0.13	0.55	0.81	0.586
Ethyleneglycoladipate	0.36	1.43	1.72	0.443
Diethyleneglycoladipate	0.40	1.46	1.73	0.438
Diethyleneglycolsebacate	0.32	1.14	1.45	0.498
Diethyleneglycoladipate	0.40	1.46	1.73	0.438
Diethyleneglycolsuccinate	0.43	1.74	1.68	0.379

relatively small number of clusters. We can then examine the 16 groups to see if any further subdivision is necessary on the basis of the *r* and *l* constants. However, within each group, the *r* and *l* constants do not vary overmuch. Only in the case of group 7 and group 16 is there a clear subdivision into high and low values of *l*, although groups 10 and 15 do contain a rather wide spread of *l* values.

We can conclude that an analysis in terms of *s* and *a* (and also *b* for phases that are hydrogen-bond acids) enables us to group the 74 McReynolds phases into a number of clusters of similar phases, leaving some 11 stationary phases (8 in Table III plus the three acidic phases) as singular phases that cannot be substituted by any other of the 77-phase set. Our grouping is based entirely on chemical principles, and it

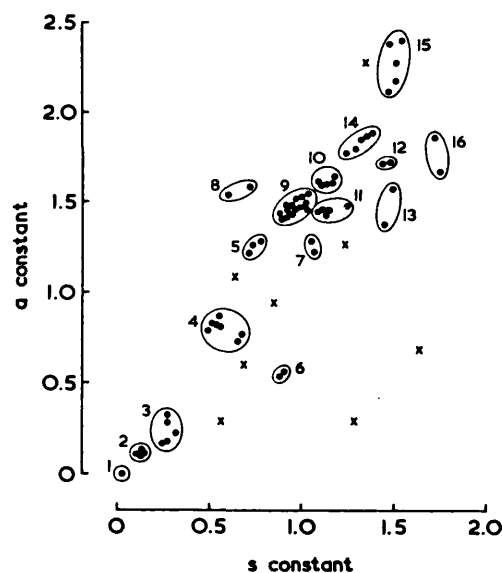


Fig. 1. Classification of stationary phases according to the *a* constant and the *s* constant in eqn. 1. ● = Groups as shown in Table III; × = singular phases.

is very instructive to compare results with other work carried out on more mathematical lines.

Huber and Reich [12] have analysed the 77-phase set, using both hierarchical clustering and the minimum spanning tree method. Their results, especially by the latter technique, are almost identical to those we have obtained. Differences, such as there are, are trivial. For example Huber and Reich [12] class Castorwax and our groups 5 and 8 together, but reference to Table III and Fig. 1 shows that this is quite reasonable on our analysis as well. Wold [11] used a pattern cognition method to group the 226-phase set into clusters. Where there are common phases between the 226- and the 77-phase sets, there is again excellent agreement between our result and those of Wold [11]. As pointed out by Wold, the nearest neighbour technique used by Leary *et al.* [7] leads to a rather peculiar set of clusters. However, the numerical taxonomy method of Massart *et al.* [9] applied to the 226-phase set leads to groups not too dissimilar to those in Table III, although there are some outstanding exceptions. Thus Massart *et al.* [9] class didecylphthalate and Flexol 8N8 in the same group, whereas we find the latter to be considerably more basic ($a = 1.27$ as against $a = 0.73$ for diisodecylphthalate). Our method of clustering, therefore, is in excellent agreement with results of Huber and Reich [12] and of Wold [11], but not so much with results of Leary *et al.* [7] or of Massart *et al.* [9].

A general survey of our classification, Table III, shows that it is completely consistent with the chemical formulation of the phases. Thus group 1 contains the saturated hydrocarbon squalane, and would include other hydrocarbons such as hexadecane (by definition), octacosane, $C_{87}H_{176}$ etc. The apiezons in group 2 are slightly dipolar and basic due to the presence of some aromatic groups, whilst the silicones in group 3 are rather more dipolar and basic through the silicon-oxygen bond. Thus the hydrogen-bond basicity of $(CH_3)_3SiOSi(CH_3)_3$ as a solute, $\beta_2^H = 0.16$, can be compared to values of β_2^H for di-*tert.*-butylether of 0.38, and values of around 0.45 for straight-chain aliphatic ethers [22]. All the simple esters of carboxylic acids cluster in group 4, the two amides appear in group 8, and so forth. The Carbowaxes fall into an exact sequence from Carbowax 20M to Carbowax 300, with values of s and a monotonically increasing along the series, where the cut-off point between groups 14 and 15 is clearly arbitrary. The sebacates (C_{10}), adipates (C_6) and succinates (C_4) are worthy of attention (see Table VIII). The sebacates are always less dipolar and less basic than the adipates or succinates, and the simple dialkylesters are always less dipolar and less basic than the corresponding ethyleneglycol or diethyleneglycol ester.

The constant r does not vary widely over the particular set of 77 phases, but, significantly, the r constant is negative in the case of the only fluorinated stationary phases in the set, *viz.* Dow Corning Fluid FS 1265 and Zonyl E-7. The ability of these phases to interact with solute π - and n -electron pairs is even less than that of a simple alkane.

Finally, we consider the characteristic constant l , a resultant of an endoergic solvent cavity term tending to decrease the value of l and an exoergic general dispersion interaction term tending to increase the value of l . We have previously shown [16] that the methylene increment for solvation of a homologous series^a of gaseous

^a That is a series in which CH_2 groups are successively inserted at the same part of the molecule.

TABLE IX

VALUES OF $\Delta \log V_G^0$ FOR 1-ALKANOLS ON SOME STATIONARY PHASES R and No = Correlation coefficients and number of points in plots of $\log V_G^0$ against carbon number of the 1-alkanols.

Stationary phase	Temperature / (°C)	l	$\Delta \log V_G^0$	R	No
Squalane	80	0.735	0.398	0.9991	5
Squalane	100	0.674	0.358	0.9988	7
Squalane ^a	120	0.619	0.322	—	—
Apiezon N	120	0.601	0.314	0.9993	7
SE-30	120	0.523	0.280	0.9996	7
Carbowax 400	120	0.440	0.235	0.9998	7
Diethyleneglycolsuccinate	120	0.379	0.198	0.9989	7
Diglycerol	120	0.225	0.110	0.9987	7

^a Extrapolated values.

solutes in a given solvent, $\Delta G_s^0(\text{CH}_2)$, depends on a combination of a solvent cavity term and a general dispersion interaction term. Now $\Delta G_s^0(\text{CH}_2)$ is related to $\Delta \log V_G^0$, since $\Delta G_s^0(\text{CH}_2) = -2.303RT \Delta \log V_G^0$, where $\Delta \log V_G^0$ is the average increase in $\log V_G^0$, along an homologous series. It therefore follows that the constant l must also be related to the important term $\Delta \log V_G^0$, or $\Delta G_s^0(\text{CH}_2)$.

In Table IX are given values of $\Delta \log V_G^0$, for the homologous series of 1-alkanols in a few representative stationary phases covering the range of l constants we have encountered. A plot of $\Delta \log V_G^0$, against the l constant (Fig. 2) yields an excellent straight line passing through the origin, since $\Delta \log V_G^0$ must approach zero as l approaches zero. We can thus show from experiment, as well as theory, that the l constant in eqn. 1 is a measure of the ability of a stationary phase to separate mem-

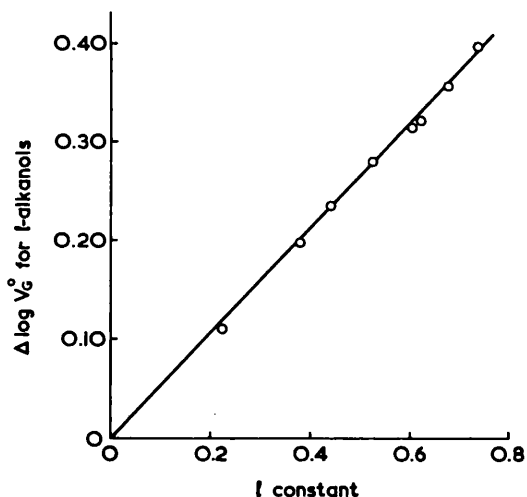
Fig. 2. Plot of $\Delta \log V_G^0$ against the l constant.

TABLE X

CHARACTERISTIC CONSTANTS FOR OTHER PHASES AT 120°C

Phase	<i>r</i>	<i>s</i>	<i>a</i>	<i>l</i>
N-methylpyrrolidinone [17]	—	1.42	2.70	0.472
N-Formylmorpholine [17]	—	1.52	2.24	0.442
Tricyanoethoxypropane [16]	0.23	2.12	1.94	0.379

bers of an homologous series. The *l* constant is entirely equivalent to $\Delta G_s^0(\text{CH}_2)$, so that eqn. 1 actually incorporates this latter parameter.

We have not considered eqns. 2 and 3 other than to compare them with eqn. 1 in Table II. Eqn. 2 offers no advantage over eqn. 1 and suffers from the disadvantage of containing the empirical parameter δ_2 . Eqn. 3, although giving rise to significantly worse fits than eqn. 1 has the advantage that the *q* constant, especially, can be related to a theoretical model of solute dipole-solvent interactions via the Kirkwood equation [27]. However, in practice the correlation constant between *q* and *s* is so high, 0.970 for the 77 stationary phases at 120°C, that no extra information is contained in *q*. At present, therefore, eqn. 3 is not necessary for the characterisation of stationary phases. However, the dipole moment term is theoretically very useful, and it might be possible to incorporate other solute parameters, and to obtain an improved version of eqn. 3 that retains the dipole moment as a dipolarity parameter.

In Table X we list a few phases that we have previously [16,17] characterised through eqn. 1. The two amides are highly basic, whilst tricyanoethoxypropane is the most dipolar phase we have examined to date. Finally, we give in Table XI a selection of phases to show how the characteristic constants *s*, *a*, *b* and *l* relate to the chemical

TABLE XI

CHEMICAL CHARACTERISTICS OF SOME PHASES

Phase	Polarity	Basicity	Acidity	Separation of homologues
Hexadecane } Squalane }	Zero	Zero	Zero	High
Apiezon	Low	Low	Zero	High
Polyphenylether	Medium	Low	Zero	High
Hallcomid } Kroniflex THFP }	Medium	High	Zero	Medium
Carbowax 300 } Quadrol }	High	High	Zero	Medium
Hyprose SP80 }				
Zonyl E-7	High	Low	Zero	Medium
N-Methylpyrrolidinone	High	Very high	Zero	Medium
Tricyanoethoxypropane	Very high	High	Zero	Low
Docosanol	Low	Medium	Low	High
Diglycerol	High	Very high	Medium	Very low

nature of the stationary phase. From such a list, it is easy to select a phase that will effect separations mainly through dipole-dipole interactions (*e.g.* Zonyl E-7), or a phase that will effect separations mainly through interactions of the type solute hydrogen-bond acid-solvent hydrogen-bond base (*e.g.* Hallcomid M18 or M180L). We have not been able to list any phase that leads mainly to interactions of the type solute hydrogen-bond base-solvent hydrogen-bond acid. The most acidic phase we have encountered is diglycerol with $b = 0.52$ at 120°C, but this phase is actually the strongest hydrogen-bond base of all the phases listed. In any case, diglycerol is unsuitable as a general stationary phase because of the very low l constant. We hope to report in the near future on our attempts to synthesise phases that are strong hydrogen-bond acids but weak hydrogen-bond bases.

In conclusion, we have been able to set up a new classification of stationary phases, based on fundamental chemical interactions. The characteristic constants r , s , a , b and l provide information on the propensity of a given phase to undergo specific interactions with solutes, and hence lead to criteria for the choice of a phase to effect particular separations. The method does not have the disadvantages of the McReynolds-Rohrschneider procedures, and although retention data on not less than about 25 solutes are required, it is necessary only to determine relative retention times. Another advantage of the present method is that eqn. 1 can be applied to equilibria involving any condensed phase, for example the solubility of gaseous solutes in simple organic solvents [17], or even the adsorption of gases on solids. We hope to report on these processes in the near future.

SOLUTE-SOLVENT INTERACTIONS

Our main aim in this paper has been to characterise the set of 77 McReynolds phases in terms of eqn. 1, where $SP = V_G^0$. However, we can now use the results given in Tables III-VI to analyse the factors that influence solute retention on stationary phases. We give in Table XII a breakdown of eqn. 1, term-by-term for two typical solutes, butanone and 1-butanol, in a variety of stationary phases. In the less polar

TABLE XII
ANALYSIS OF THE FACTORS THAT INFLUENCE $\log V_G^0$, USING EQN. 1 AT 120°C

Solute	Phase	Term					Dispersion ^a	Cavity ^a
		rR_2	$s\pi_2^*$	$a\alpha_2^H$	$b\beta_2^H$	$l \log L^{16}$		
Butanone	Apiezon M	0.04	0.07	0	0	1.37	3.36	-1.93
	Hallcomid M18	0.02	0.40	0	0	1.35	3.26	-1.88
	Zonyl E-7	-0.05	1.09	0	0	1.03	1.90	-1.09
	Diglycerol	0.09	1.09	0	0.25	0.52	(0.48)	(-0.28)
1-Butanol	Apiezon M	0.06	0.40	0.04	0	1.56	4.10	-2.25
	Hallcomid M18	0.03	0.24	0.52	0	1.54	4.00	-2.20
	Zonyl E-7	-0.06	0.65	0.23	0	1.17	2.31	-1.27
	Diglycerol	0.12	0.65	0.91	0.23	0.59	(0.59)	(-0.32)

^a See text. These do not add up to the $l \log L^{16}$ term because of a constant term and a small dipole-induced dipole term that have not been included.

phases, where the s constant is quite small, by far the main term is $l \log L^{16}$. The term $a\alpha_2^H$ can be substantial for the combination of a hydrogen-bond acidic solute and a hydrogen-bond basic phase, but for the present set of solutes and phases the $b\beta_2^H$ term is never substantial. Of course, for more acidic phases than diglycerol, the $b\beta_2^H$ term could be much more significant.

In eqn. 1, the $l \log L^{16}$ term covers both general dispersion interactions that lead to positive values of $\log V_G^0$, and the endoergic solvent-solvent cavity term that leads to negative values of $\log V_G^0$. These two effects are very difficult to unravel quantitatively, hence we have had to use a combined term in eqn. 1. Abraham and Fuchs [24], however, managed to dissect the $\log L^{16}$ values themselves into mainly a cavity term and a general dispersion interaction term. If we assume, as before [25], that the ratio of these two terms remains the same, then we can roughly separate the total $l \log L^{16}$ term shown in Table XII into cavity and general dispersion effects. Given that these are only approximations, especially in the case of diglycerol, we can still see that the largest interaction term corresponds to general solute-solvent dispersion effects. It is these that control the separation of members of an homologous series. Eqn. 1 incorporates such an effect in the $l \log L^{16}$ term. Although dipolar and acid-base interactions tend to be smaller than the general dispersion interactions, they control separations of dissimilar solutes. Eqn. 1 incorporates these effects in the first four terms.

Thus our preferred eqn. 1 not only forms the basis of a classification of stationary phases, but also leads to a rationale for the separation of solutes, based on a number of possible solute-solvent interactions.

ACKNOWLEDGEMENTS

We thank the U.S. Army Research, Development, and Standardisation Group for support under Contract DAJA 45-87-C-0004.

REFERENCES

- 1 W. O. McReynolds, *Gas Chromatographic Retention Data*, Preston Technical Abstracts, Evanston, IL, 1966.
- 2 W. O. McReynolds, *J. Chromatogr. Sci.*, 8 (1970) 685.
- 3 G. Tarján, A. Kiss, G. Kocsis, S. Mészáros and J. M. Takács, *J. Chromatogr.*, 119 (1976) 327; and references cited therein.
- 4 S. K. Poole, B. R. Kersten and C. F. Poole, *J. Chromatogr.*, 471 (1989) 91.
- 5 C. E. Figgins, T. H. Risby and P. C. Jurs, *J. Chromatogr. Sci.*, 14 (1976) 453.
- 6 R. Fellous, L. Luft and J.-P. Rabine, *J. Chromatogr.*, 160 (1978) 117; 166 (1978) 383.
- 7 J. J. Leary, J. B. Justice, S. Tsuge, S. R. Lowry and T. L. Isenhour, *J. Chromatogr. Sci.*, 11 (1973) 201.
- 8 A. Eskes, F. Dupuis, A. Dijkstra, H. De Clercq and D. L. Massart, *Anal. Chem.*, 47 (1973) 2168.
- 9 D. L. Massart, P. Lenders and M. Lauwereys, *J. Chromatogr. Sci.*, 12 (1974) 617.
- 10 S. Wold and K. Andersson, *J. Chromatogr.*, 80 (1973) 43.
- 11 S. Wold, *J. Chromatogr. Sci.*, 13 (1975) 525.
- 12 J. F. K. Huber and G. Reich, *J. Chromatogr.*, 294 (1984) 15.
- 13 M. Chastrette, *J. Chromatogr. Sci.*, 14 (1976) 357.
- 14 D. H. McCloskey and S. J. Hawkes, *J. Chromatogr. Sci.*, 13 (1975) 1.
- 15 J. A. Garcia-Dominguez, J. Garcia-Munoz, V. Menendez, M. J. Molera and J. M. Santiuste, *J. Chromatogr.*, 393 (1987) 209.
- 16 M. H. Abraham, G. S. Whiting, R. M. Doherty and W. J. Shuely, *J. Chem. Soc., Perkin Trans. 2*, in press.

- 17 M. H. Abraham, G. S. Whiting, R. M. Doherty and W. J. Shuely, *J. Chem. Soc., Perkin Trans. 2*, in press.
- 18 M. J. Kamlet, R. M. Doherty, J.-L. M. Abboud, M. H. Abraham and R. W. Taft, *Chemtech*, 16 (1986) 566.
- 19 M. H. Abraham, R. M. Doherty, M. J. Kamlet and R. W. Taft, *Chem. Britain*, 22 (1986) 551.
- 20 M. J. Kamlet, R. M. Doherty, M. H. Abraham and R. W. Taft, *Quant. Struct.-Act. Relat.*, 7 (1988) 71.
- 21 M. H. Abraham, P. L. Grellier, D. V. Prior, P. P. Duce, J. J. Morris and P. J. Taylor, *J. Chem. Soc., Perkin Trans. 2*, (1989) 699.
- 22 M. H. Abraham, P. L. Grellier, D. V. Prior, J. J. Morris and P. J. Taylor, *J. Chem. Soc., Perkin Trans. 2*, (1990) 521.
- 23 M. H. Abraham, P. L. Grellier and R. A. McGill, *J. Chem. Soc., Perkin Trans. 2*, (1987) 797.
- 24 M. H. Abraham and R. Fuchs, *J. Chem. Soc., Perkin Trans. 2*, (1988) 523.
- 25 M. H. Abraham, P. L. Grellier, I. Hamerton, R. A. McGill, D. V. Prior and G. S. Whiting, *Faraday Disc. Chem. Soc.*, 85 (1988) 107.
- 26 F. Patte, M. Etcheto and P. Laffort, *Anal. Chem.*, 54 (1982) 2239.
- 27 J. G. Kirkwood, *J. Chem. Phys.*, 2 (1934) 351.

Hydrogen Bonding. Part 13.† A New Method for the Characterisation of GLC Stationary Phases—The Laffort Data Set

Michael H. Abraham* and Garry S. Whiting

Department of Chemistry, University College London, 20 Gordon Street, London WC1H 0AJ

Ruth M. Doherty

Naval Surface Warfare Centre, White Oak Laboratory, Silver Spring, Maryland 20910, USA

Wendel J. Shuely

US Army Chemical Research, Development and Engineering Centre, Aberdeen Proving Ground, Maryland

21010, USA

A number of equations for the correlation of retention data for a series of solutes on a given stationary phase (or solvent) have been investigated with the aim of characterising stationary phases. The two most successful equations are,

$$SP = c + d\delta_2 + s\pi_2^* + a\alpha_2^H + b\beta_2^H + l \log L^{16} \quad (a)$$

$$SP = c + rR_2 + s\pi_2^* + a\alpha_2^H + b\beta_2^H + l \log L^{16} \quad (b)$$

In the present case the dependent variable SP is $\log L - \log L^{\text{Decane}}$ and the explanatory variables are solute parameters as follows: δ_2 is an empirical polarisability correction term, R_2 is a polarisability parameter that reflects the ability of a solute to interact with a solvent through π and n electron pairs, α_2^H is the solute hydrogen-bond acidity, β_2^H is the solute hydrogen-bond basicity, π_2^* is the solute dipolarity/polarisability, and L^{16} is the Ostwald solubility coefficient of the solute on *n*-hexadecane at 298 K. The constants c , r , s , a , b , and l in the more useful equation (b) are found by the method of multiple linear regression analysis, and serve to characterise a solvent phase in terms of specific solute/solvent interactions. Application of equation (b) to the five stationary phases examined by Laffort *et al.* shows that the magnitude of these constants is in accord with general chemical principles, and that the present procedure constitutes a new, general method for the characterisation of gas chromatographic stationary phases.

The most widely used method for the classification of stationary phases in gas-liquid chromatography (GLC), is that due to Rohrschneider,¹ either as such, or as subsequently modified by McReynolds.² Retention data of solutes are first expressed as Kovats retention indices³ calculated according to equation (1):

$$I^i = 100 \left(\frac{\log \tau^i - \log \tau^m}{\log \tau^{m+1} - \log \tau^m} \right) + 100m \quad (1)$$

Here, I^i is the retention index of solute i on a given stationary phase at a given temperature, τ^i is the adjusted retention time of solute i , and τ^{m+1} and τ^m are the adjusted retention times of *n*-alkanes of carbon number $m+1$ and m , respectively. Rohrschneider¹ determined values of I^i for the selected solutes benzene, ethanol, butanone, nitromethane, and pyridine, on squalane (SQ), and on a stationary phase to be investigated (P), and defined a differential set of I^i values through equation (2),

$$\Delta I^i = I_P^i - I_{SQ}^i \quad (2)$$

Then five 'Rohrschneider constants', x , y , z , u , and s , one for each of the selected solutes, can be used to characterise the stationary phase, P, according to equation (3), illustrated for the selected solute benzene.

$$x = \Delta I^{\text{benzene}}/100 \quad (3)$$

An 'overall' stationary phase polarity can also be obtained as the sum of the ΔI^i values for the five test solutes.

McReynolds² suggested the use of ten test solutes, rather than five, these being benzene (x'), butan-1-ol (y'), pentan-2-one (z'), nitropropane (u'), pyridine (s'), 2-methylpentan-2-ol (h'), 1-iodobutane (j'), oct-2-yne (k'), dioxane (l'), and *cis*-hydrindane (m'). Later workers tended to reduce the number of McReynolds test solutes, for example to the first five solutes.⁴ An overall stationary phase polarity can again be calculated as the sum of ΔI^i values ($i = x', y', z', u', \text{ and } s'$); for an account of work in this area, the comprehensive review of Budahegyi *et al.*⁵ is available.

However, although the Rohrschneider–McReynolds method is the basis of most approaches to the classification of stationary phases, quite recently Poole *et al.*⁶ have severely criticised the method on a number of technical and theoretical grounds. Their main technical objection is that alkanes (necessary for the determination of I values) are sorbed onto polar stationary phases mainly by interfacial adsorption, rather than by true gas-liquid partitioning. If the I_P values are incorrect, then the whole procedure is invalid (for polar phases). A theoretical objection is that the 'overall' polarity, defined as above cannot be a true measure of polarity, since it depends principally on the solubility of the *n*-alkanes in the stationary phase.⁶

There are other difficulties over the Rohrschneider–McReynolds method. Firstly, the method is entirely restricted to GLC retention data, so that there is no possibility of

† Part 12: M. H. Abraham, G. S. Whiting, Y. Alarie, J. J. Morris, P. J. Taylor, R. M. Doherty, R. W. Taft, and G. O. Nielsen, *QSAR*, 1990, 9, 6.

Table 1. Some values of the gas $\rightarrow$ solvent methylene increment, $\Delta G_s^\circ(\text{CH}_2)$, in kcal mol $^{-1}$ at 298 K.^a

Solvent	$\Delta G_s^\circ(\text{CH}_2)$	Solvent	$\Delta G_s^\circ(\text{CH}_2)$
Cyclohexane	-0.76	Propanone	-0.62
Hexadecane	-0.74	Ethanol	-0.61
Decane	-0.74	Dimethylformamide	-0.60
Hexane	-0.74	N-Methylpyrrolidi-2-none	-0.56
Benzene	-0.74	Methanol	-0.56
Chlorobenzene	-0.73	Propylene carbonate	-0.48
Tetrachloromethane	-0.71	Dimethyl sulphoxide	-0.48
Octan-1-ol	-0.68	Ethane-1,2-diol	-0.35
Butan-1-ol	-0.66	Water	+0.18
Nitrobenzene	-0.64		

^a All values from data in ref. 11.**Table 2.** Correlations of $\Delta G_s^\circ(\text{CH}_2)$ against some solvent parameters.^a

Intercept	Slope	<i>n</i>	<i>R</i>	SD
(a) All solvents in Table 1				
-0.862	0.188 $\delta_H^2/100$	19	0.981	0.04
-0.804	0.370 π_1^*	19	0.673	0.17
-0.671	0.043 μ_1	19	0.328	0.21
-0.955	0.949 $f(\epsilon)$	19	0.554	0.19
-1.396	0.019 E_T	16 ^b	0.786	0.15
0.058	-2.529 $f(\eta)$	19	0.376	0.21
-0.399	-0.089 MR	19	0.530	0.19
(b) Nonhydroxylic solvents in Table 1				
-0.890	0.230 $\delta_H^2/100$	13	0.941	0.04
-0.758	0.189 π_1^*	13	0.772	0.07
-0.746	0.046 μ_1	13	0.911	0.04
-0.877	0.636 $f(\epsilon)$	13	0.859	0.05
-1.273	0.016 E_T	11 ^c	0.911	0.04
-0.679	0.082 $f(\eta)$	13	0.024	0.11
-0.570	-0.035 MR	13	0.437	0.10

^a These are δ_H^2 the Hildebrand cohesive energy density, π_1^* the Kamlet-Taft solvent dipolarity, μ_1 the dipole moment, $f(\epsilon)$ the dielectric constant function $(\epsilon - 1)/(2\epsilon + 1)$, E_T the Reichardt solvent parameter, $f(\eta)$ the refractive index function $(\eta^2 - 1)/(\eta^2 + 2)$, and MR a molar refraction we define as $10/(\eta)V_x$ where V_x is the intrinsic volume.

^b Excluding values for hexadecane, decane, and octan-1-ol. ^c Excluding values for hexadecane and decane.

comparing GLC stationary phases with common solvents. Secondly, the method is far too coarse to allow any analysis of solute-solvent interactions, which are actually the basis of gas-liquid partition, and hence of retention data.

Poole *et al.*,⁶ following several other workers,⁷⁻¹⁰ suggested that the methylene increment to the gas $\rightarrow$ stationary phase transfer, as $\Delta G_s^\circ(\text{CH}_2)$ could be taken as a better measure of the overall polarity. Since $\Delta G_s^\circ(\text{CH}_2)$ can be obtained from a variety of homologous series, the difficulty over retention processes of alkanes is avoided. However, it is by no means obvious what a general polarity based on $\Delta G_s^\circ(\text{CH}_2)$ means. Abraham¹¹ has published data from which values of $\Delta G_s^\circ(\text{CH}_2)$ can be obtained for the n-alkanes in a number of common solvents (see Table 1). Note that since the original measurements were non-chromatographic, the n-alkane difficulty does not arise. We can match the $\Delta G_s^\circ(\text{CH}_2)$ values against various solvent polarity parameters, and give simple regression constants in Table 2. For the nonhydroxylic solvents, there are reasonable correlations of $\Delta G_s^\circ(\text{CH}_2)$ with solvent

dipole movement (μ), or with dielectric constant function $(\epsilon - 1)/(2\epsilon + 1)$, or with Reichardt's E_T parameter. But none of these are as good as the solvent cohesive energy density, as $\delta_H^2/100$, and for the total solvent list in Table 2(a), only the latter yields a reasonable correlation.* We have examined various double correlations amongst parameters that are not self-correlated, but the only one that is significantly better than the single correlation in $\delta_H^2/100$ is that in equation (4), for nonhydroxylic solvents, where the correlation coefficient, *R*, between δ_H^2 and $f(\eta)$ is only 0.265. Equation (4) can be

$$\Delta G_s^\circ(\text{CH}_2) = -0.679 + 0.246 \delta_H^2/100 - 0.847/f(\eta) \quad (4)$$

$$n = 13 \quad R = 0.970 \quad \text{SD} = 0.03$$

rationalised using a cavity theory of solution. In order to create a cavity in a solvent, solvent-solvent bonds must be broken in an endoergic process, modelled by δ_H^2 . Then on insertion of the solute CH_2 group into the cavity, exoergic CH_2 -solvent general dispersion interactions will be set up, modelled at least roughly by $f(\eta)$. The $\Delta G_s^\circ(\text{CH}_2)$ increment is therefore not a general polarity parameter in the sense of, say π_1^* or E_T , but reflects a combination of solvent-solvent bond breaking and CH_2 -solvent dispersion interactions.

Other workers have moved away from the Rohrschneider-McReynolds method and have attempted to account for retention data on the basis of specific solute-solvent interactions. Ecknig *et al.*¹² characterised solute-solvent interactions in terms of two energy parameters, a nonpolar or dispersion parameter and a polar parameter that includes hydrogen-bonding as an electrostatic effect. The calculation of these parameters, however, is not trivial, and application seems to be restricted to aliphatic solutes only.¹³ The UNIFAC solution-of-groups method has been investigated also, but yielded only rough estimates of retention data.¹⁴ A few workers have attempted to characterise stationary phases using indices that include stationary phase acidity and basicity as such. Burns and Hawkes,¹⁵ for example, used retention data on the butan-1-ol-ethyl acrylate pair of solutes to obtain stationary phase basicities, and on pyridine-benzene to obtain stationary phase acidities, but conceded that the obtained indices were rather 'shaky.' Hawkes *et al.*¹⁶ later carried out various spectroscopic studies of solutes in stationary phases and tabulated indices of dispersion forces, polarity, acidity, and basicity for a number of stationary phases (but note that acidity was obtained from retention data on the n-butylamine-n-butyl chloride pair of solutes).

It seems, therefore, to be acknowledged that factors such as dispersion, polarity, acidity, and basicity are important in solute-stationary phase interactions.^{13,15,16} In order to quantify these effects, some general system in which both solute and stationary phase are characterised is necessary. The pur-

* The units of δ_H^2 are cal cm $^{-3}$, where 1 cal = 4.184 J, and the units of μ are Debyes, where 1 D $\equiv 3.336 \times 10^{-30}$ C m.

pose of this paper is to give one set of examples of such a system that can be used for GLC stationary phases, common solvents, and, indeed, any condensed phase.

We start with two equations suggested by Abraham, Doherty, Kamlet, and Taft, and their co-workers,¹⁷⁻²⁰

$$SP = c + d\delta_2 + \pi_2^* + a\alpha_2 + b\beta_2 + mV_2 \quad (5)$$

$$SP = c + d\delta_2 + \pi_2^* + a\alpha_2 + b\beta_2 + l \log L^{16} \quad (6)$$

In equations (5) and (6),* SP denotes some property of a series of solutes, for example $\log V_G$ or $\log \tau$ for solutes on a given stationary phase under the same set of conditions. The explanatory variables are δ_2 , a polarisability correction term taken as zero except for polyhalogenated aliphatic compounds (0.5) and for aromatic compounds (1.0), π_2^* the solute dipolarity, α_2 the solute hydrogen-bond acidity, β_2 the solute hydrogen-bond basicity, V_2 the solute volume, and $\log L^{16}$ where L^{16} is the solute Ostwald solubility coefficient on n-hexadecane at 298 K.²¹ The constants c, d, s, a, b, m , and l are found by multiple linear regression analysis of SP against as many explanatory variables as are statistically significant.

The terms in equations (5) and (6) can be, for the most part, directly identified with particular solute-solvent interactions.^{17,18} The π_2^* term arises through solute-solvent dipole-dipole or dipole-induced dipole interactions, and hence the magnitude of the s -constant will reflect the solvent (or stationary phase) dipolarity. The $a\alpha_2$ term reflects interactions between hydrogen-bond solute acids and a hydrogen-bond solvent base, so that the a -constant will now be a measure of the solvent hydrogen-bond basicity. Conversely, the b -constant in the $b\beta_2$ term will be a measure of hydrogen-bond solvent acidity. The V_2 and $\log L^{16}$ terms both involve composite interactions, and will include both an endoergic cavity term and an exoergic solute-solvent general dispersion interaction.

There are a number of GLC retention parameters that could be used as the dependent variable (SP) in equations (5) and (6). The standard Gibbs energy of solution of a gaseous solute is given by equation (7), where L is the Ostwald solubility

$$-\Delta G_s^\circ = RT \ln L = RT \ln (V_G \rho_1) = RT \ln V_G + RT \ln \rho_1 \quad (7)$$

coefficient of the solute in the given solvent, often referred to as K the gas-liquid partition coefficient; V_G is the retention volume of the solute at the column temperature,[†] and ρ_1 is the solvent or stationary phase density. The standard states for ΔG_s° are unit concentration in the gas phase and unit concentration in solution. The most useful dependent variable is $\log L$; not only can this be obtained from $\log V_G$ values by GLC, but $\log L$ values can be derived for solution of gaseous solutes in simple solvents. If values of ρ_1 are unavailable so that $\log V_G$ itself must be used, there is little problem—all the constants in equations (5) and (6) remain the same except for c which will alter by $\log \rho_1$. Unfortunately, much retention data in GLC is expressed only as the retention index I , equation (1), which on its own is not connected directly to any physicochemical parameter such as $\log L$ (or $\log K$). Only if the so-called b -coefficient, herein designated as B , is specified for the variation of

$\log V_G$ with carbon number for n-alkanes can the retention index be reconverted into a suitable parameter for use in equations (5) and (6). Even adjusted retention times, such as $\log \tau$ values, can be used in these equations since $\log L = \log \tau + \text{constant}$.

Results and Discussion

One of the most extensive and carefully determined sets of data is that of Laffort *et al.*²² who listed retention indices of 240 compounds on five stationary phases at 393 K. Since Laffort *et al.*²² gave the necessary B -values,²³ we can convert the reported values of I into $\log L$ values via equation (8),

$$\log L - \log L^{\text{Decane}} = \log L' = \left(\frac{I - 1000}{100} \right) B \quad (8)$$

The constant c in equations (5) and (6) is now of little significance, but all the other constants are unaffected by the use of $\log L'$ rather than $\log L$ itself. The five Laffort phases are Carbowax, diethyleneglycol succinate (DEGS), polyphenyl ether (PPE), tricyanoethoxypropane (TCEP), and an ester of 'pyromellitic acid and trihydrofluoro alcohol,' known as Zonyl E-7 (ZE7).

Of the explanatory variables, δ_2 is trivial, π_2^* the Kamlet-Taft dipolarity parameter was as before,¹⁷⁻²⁰ whilst for α_2 and β_2 we used our new α_2^H and β_2^H hydrogen-bond solute parameters.²⁴⁻²⁷ For a few difunctional bases such as anisole we used recently determined 'effective' or 'summation' $\Sigma\beta_2^H$ values.²⁸ The solute volume was taken as McGowan's intrinsic volume,²⁹ V_x , which has the merit that it can be calculated for any compound of known structure, and values of L^{16} were as before, supplemented by a number of additional values.²⁸ The general equations (5) and (6) thus take the specific formulation,

$$\log L' = c + d\delta_2 + \pi_2^* + a\alpha_2^H + b\beta_2^H + mV_x \quad (9)$$

$$\log L' = c + d\delta_2 + \pi_2^* + a\alpha_2^H + b\beta_2^H + l \log L^{16} \quad (10)$$

We had available a complete set of explanatory variables for 168 solutes out of the 240. Details of the solutes and parameters are in Table 3, and the regressions based on equations (9) and (10) are summarised in Tables 4 and 5. The overall correlation coefficients, R , and standard deviations, SD, are not particularly good, but we stress that these refer to 'all solute' regressions. We wish to point out that the purpose of constructing these regressions is to characterise the stationary phases, and not to provide equations that can be used to predict further retention values. The obtained regression equations summarised in Tables 4 and 5 are adequate for the former, but not for the latter, purpose. We note also that as we have found before,²⁰ equation (10) yields much better regressions than does equation (9) for gas/liquid partition coefficients.[‡]

We can now examine the constants in equations (9) and (10) to check whether they are chemically reasonable. All five phases are to some extent dipolar, so that the s -constant in π_2^* should be positive, as observed. The order of stationary phase dipolarity, as measured by the s -constant, is TCEP > DEGS > Carbowax > ZE7 ≥ PPE on equation (10), and almost the same on equation (9); this seems chemically quite reasonable. Again, all five phases are hydrogen-bond bases, so that the a -constant in $a\alpha_2^H$ should be positive. The order of stationary phase basicity is Carbowax > DEGS ≥ TCEP > ZE7 ≥ PPE on both equation (9) and equation (10). As might be expected, the fluoroester ZE7 is both less dipolar and less basic than the ester DEGS. Nominally, the five phases are all non-hydrogen-bond acids, so that the b -constant in $b\beta_2^H$ should be near zero.

* We denote solute properties by subscript 2 and solvent properties by subscript 1.

† It is of no value to use V_G° , the specific retention volume corrected to 273 K, because V_G° must be converted back to V_G for use in equation (7).

‡ Except for gas/water partitions, but in this case neither V_x nor $\log L^{16}$ are very significant.²⁰

There is a difficulty here, in that over the 168 solute set, the explanatory variable β_2^H is not independent, there being a cross correlation coefficient of 0.673 between β_2^H and π_2^* . The total correlation matrix in terms of R is as follows:

	δ_2	π_2^*	α_2^H	β_2^H
π_2^*	0.302			
α_2^H	-0.188	0.059		
β_2^H	-0.164	0.673	0.373	
$\log L^{16}$	0.052	0.073	-0.032	0.075

We therefore repeated the regressions, excluding the β_2^H parameter, and we conclude that none of the stationary phases has any significant hydrogen-bond acidity [see Tables 5(a) and 5(b)].

The l -constants in $\log L^{16}$ are all much lower than unity. Part of this will certainly be due to the operating temperature of 393 K instead of 298 K, but part is probably also due to the lessening of general solute-solvent dispersion interactions by comparison to *n*-hexadecane solvent (at 298 K).

We can conclude that equation (9) and particularly equation (10) are suitable for the characterisation of GLC stationary phases through a set of constants c , d , s , a , b , and l . Unlike Rohrschneider-McReynolds constants, however, those derived from equation (10) yield quantitative information on the propensity of the phase to take part in given solute-stationary phase interactions. The difficulty over *n*-alkanes on polar phases does not apply to the application of equation (10), because incorporation of alkanes into the solute data set is not essential. Furthermore, an additional advantage of the present method is that it is now possible to compare GLC stationary phases with other condensed phases, for example common solvents. From preliminary regressions²⁰ we know that the s -constant for ethyl acetate is *ca.* 1.8, so that the dipolarity of tricyanoethoxypropane at 393 K is no more than that of a simple ester at 298 K. We hope to apply equation (10) to a variety of solvents, as well as to other GLC stationary phases, in order to obtain a general classification of condensed phases.

There are disadvantages in the use of equations (9) and (10). In order to obtain suitably firm regressions with five explanatory variables, it is necessary to obtain retention data for not less than about 30 solutes. However, since only $\log t$ values are needed in order to determine all the constants except c , this is not an onerous task. A more important disadvantage is revealed by an examination of the origin of the explanatory variables in equations (9) and (10). The dependent variable is ideally $\log L$ (or $\log K$), *i.e.*, a Gibbs energy related quantity *via* an equilibrium constant. If $\log V_G$, $\log L'$ or $\log t$ are used, these quantities are still equivalent to the use of $\log L$ as far as all the terms except the c -constant are concerned. Hence for thermodynamic consistency, all the explanatory variables should be Gibbs energy related. There is no difficulty over α_2^H , β_2^H , and $\log L^{16}$ since these are all derived from equilibrium constants, as $\log K$ values.^{21,24-27} The variable V_X is not a Gibbs energy term, but since we prefer equation (10) to equation (9) this does not concern us overmuch. A more pressing problem is

the δ_2/π_2^* formulism: the δ_2 parameter is simply an empirical correction factor, whilst the π_2^* parameter originates as a spectroscopically determined solvent π_1^* parameter, and is certainly not a Gibbs energy related quantity. Furthermore, π_1^* can only be determined for compounds that are liquids at room temperature, and can be equated to π_2^* only for nonassociated liquids. All other π_2^* values have either been estimated or have been obtained *via* various π_2^* /dipole moment correlations.¹⁹ Because of the indeterminate nature of π_2^* , it becomes impossible to connect the $s\pi_2^*$ term in a regression equation with any specific solute-solvent interaction. In the above discussion we have used the s -constant as a measure of 'dipolarity', but more correctly it will represent some blend of polarisability and dipolarity. We set out now our attempts to resolve these difficulties by replacement of the δ_2/π_2^* parameters in equation (10).

Construction of a New General Equation.—We first examine the terms in equation (10), in order to specify more exactly the parameters required to take the place of δ_2 and π_2^* . The α_2^H and β_2^H parameters take care of hydrogen-bond interactions, as spelt out above, and will be retained in any new equation. As we have seen in the introduction, the $\log L^{16}$ parameter is very useful in that it accounts for cavity effects, together with general dispersion interactions of the solute-nonpolar solvent (hexadecane) type. We are then left with solute-solvent dipole-dipole and dipole-induced dipole effects, together with additional dispersion interactions that may loosely be described as polarisability effects. The obvious solute parameter needed to describe dipole-dipole type interactions is the dipole moment (μ_2). Following Kirkwood,³⁰ we use μ_2^2 , which has the advantage that it is very nearly a free energy related quantity.[†] Various physical quantities can be used to model dispersion/polarisability interactions. We have briefly investigated both the solute molar refraction, MR , and the solute polarisability, but found neither satisfactory when used in combination with μ_2^2 , α_2^H , β_2^H , and $\log L^{16}$. The refractive index function, $f(\eta)$, has been used by Fuchs *et al.*³¹ with some success, and we give in Table 6 details of regressions using equation (11), with $f(\eta)$ defined by equation (12).

$$\log L' = c + ff(\eta) + q\mu_2^2 + a\alpha_2^H + b\beta_2^H + l\log L^{16} \quad (11)$$

$$f(\eta) = (\eta^2 - 1)/(\eta^2 + 2) \quad (12)$$

The regression equations based on equation (11) are appreciably poorer than those using equation (10). Not only are R and SD poorer, but significant b -constants are produced, surely as artifacts. Part of this difficulty may be due to cross-correlations between μ_2^2 and β_2^H ($R = 0.556$) and also between $f(\eta)$ and $\log L^{16}$ ($R = 0.534$), that could be overcome by a more suitable selection of solutes. But $f(\eta)$ must include interactions already dealt with by the $\log L^{16}$ parameter, hence the coefficients of $\log L^{16}$ in equation (11) are always less than those in equation (10). What is required is a parameter that is more specifically related to the polarisability of the solute as regards interactions due to the presence of polarisable electrons. We start with the solute molar refraction, but for convenience defined in terms of

$$MR_X = 10(\eta^2 - 1)V_X/(\eta^2 + 2) = 10f(\eta)V_X \quad (13)$$

the characteristic volume. With V_X in units of $(\text{cm}^3 \text{ mol}^{-1})/100$, equation (13) will yield MR_X in the more convenient units of $(\text{cm}^3 \text{ mol}^{-1})/10$. Note that η is taken at 293 K with the sodium-D line. Unlike $f(\eta)$ itself, the molar refraction has the interesting property of being the same (within a few per cent) for a given solute in the gas phase and in solution. Hence although $f(\eta)$ is most conveniently measured on bulk liquids, MR (and MR_X) can be taken as a property of an isolated molecule.[‡] In order to

[†] Kirkwood³⁰ showed that the Gibbs energy of a dipole in a dielectric continuum was proportional to μ^2/r^3 where r is the radius of a sphere containing the dipole. Now many functional groups contain a dipole within a sphere of a similar radius, so that the Gibbs energy is approximately proportional to μ^2 .

[‡] We have confirmed that MR is essentially the same in the gas phase and bulk liquid even for associated compounds such as water and alcohols. The one exception we have noted is acetic acid, probably due to the extensive dimerisation that takes place in the gas phase.

Table 3. The 168 compounds and the parameters used in the regressions.

No.	Compound	δ_2	$f(n)$	R_2	π_2^*	μ_2^2	α_2^H	β_2^H	V_x	$\log L^{16}$
3352	Methanol	0.00	0.203	0.278	0.40	2.890	0.37	0.41	0.308	0.922
3353	Ethanol	0.00	0.221	0.246	0.40	2.856	0.33	0.44	0.449	1.485
3354	Propan-1-ol	0.00	0.234	0.236	0.40	2.822	0.33	0.45	0.590	2.097
3355	Propan-2-ol	0.00	0.230	0.212	0.40	2.756	0.32	0.47	0.590	1.821
3473	Prop-2-en-1-ol, allyl-OH	0.00	0.250	0.341	0.45	2.560	0.33	0.41	0.547	1.996
3356	Butan-1-ol	0.00	0.242	0.224	0.40	2.756	0.33	0.45	0.731	2.601
3358	2-Methylpropan-1-ol	0.00	0.240	0.217	0.40	2.670	0.33	0.45	0.731	2.399
3357	Butan-2-ol	0.00	0.241	0.217	0.40	2.723	0.32	0.47	0.731	2.338
3359	t-Butyl alcohol	0.00	0.236	0.180	0.40	2.657	0.32	0.49	0.731	2.018
3360	Pentan-1-ol	0.00	0.248	0.219	0.40	2.756	0.33	0.45	0.872	3.106
3361	2-Methylbutan-1-ol	0.00	0.248	0.219	0.40	2.890	0.33	0.45	0.872	3.011
3362	3-Methylbutan-1-ol	0.00	0.245	0.192	0.40	2.560	0.33	0.45	0.872	3.011
3440	Cyclopentanol	0.00	0.270	0.427	0.40	2.890	0.32	0.48	0.763	3.270
3368	Hexan-1-ol	0.00	0.252	0.210	0.40	2.890	0.33	0.45	1.013	3.610
3490	(E)-Hex-2-en-1-ol	0.00	0.263	0.294	0.45	2.560	0.33	0.41	0.970	3.510
3369	Hexan-2-ol	0.00	0.250	0.187	0.40	2.890	0.32	0.47	1.013	3.340
3370	Hexan-3-ol	0.00	0.251	0.200	0.40	2.890	0.32	0.47	1.013	3.440
3372	2-Methylpentan-2-ol	0.00	0.248	0.169	0.40	2.890	0.32	0.49	1.013	3.181
3374	3-Methylpentan-3-ol	0.00	0.252	0.210	0.40	2.890	0.32	0.49	1.013	3.277
3389	Heptan-1-ol	0.00	0.256	0.211	0.40	2.924	0.33	0.45	1.154	4.115
3492	(E)-Hept-2-en-1-ol	0.00	0.267	0.281	0.45	2.560	0.33	0.41	1.111	4.010
3405	Octan-1-ol	0.00	0.258	0.199	0.40	2.958	0.33	0.45	1.295	4.619
3494	(E)-Oct-2-en-1-ol	0.00	0.273	0.270	0.45	2.560	0.33	0.41	1.252	4.520
3410	2-Methylheptan-2-ol	0.00	0.256	0.169	0.40	2.890	0.32	0.49	1.295	3.990
3416	Nonan-1-ol	0.00	0.260	0.193	0.40	2.958	0.33	0.45	1.435	5.124
3426	Decan-1-ol	0.00	0.262	0.191	0.40	2.592	0.33	0.45	1.576	5.628
3429	Undecan-1-ol	0.00	0.263	0.181	0.40	2.890	0.33	0.45	1.717	6.130
3430	Dodecan-1-ol	0.00	0.265	0.175	0.40	2.890	0.33	0.45	1.858	6.640
1551	Acetaldehyde	0.00	0.205	0.208	0.67	7.236	0.00	0.40	0.406	1.230
1552	Propionaldehyde	0.00	0.223	0.196	0.65	6.350	0.00	0.40	0.547	1.815
1569	Propenal, acrolein	0.00	0.243	0.324	0.65	9.734	0.00	0.40	0.504	2.110
1553	Butyraldehyde	0.00	0.234	0.187	0.65	7.398	0.00	0.40	0.688	2.270
1554	Isobutyraldehyde	0.00	0.228	0.146	0.65	7.290	0.00	0.40	0.688	2.060
1570	(E)-But-2-en-1-al	0.00	0.262	0.387	0.75	12.532	0.00	0.40	0.645	2.570
1556	3-Methylbutanal	0.00	0.237	0.144	0.65	6.859	0.00	0.40	0.829	2.620
1558	Hexanal	0.00	0.244	0.146	0.65	7.290	0.00	0.40	0.970	3.370
1560	Heptanal	0.00	0.248	0.140	0.65	7.290	0.00	0.40	1.111	3.860
1561	Octanal	0.00	0.254	0.160	0.65	7.398	0.00	0.40	1.252	4.380
1590	Benzaldehyde	1.00	0.317	0.820	0.92	7.563	0.00	0.42	0.873	3.985
1651	Propan-2-one	0.00	0.220	0.179	0.71	8.294	0.04	0.50	0.547	1.760
1652	Butan-2-one	0.00	0.231	0.166	0.67	7.618	0.00	0.48	0.688	2.287
1653	Pentan-2-one	0.00	0.237	0.143	0.65	7.290	0.00	0.48	0.829	2.755
1706	Cyclopentanone	0.00	0.262	0.373	0.76	10.890	0.00	0.52	0.720	3.120
1659	Hexan-2-one	0.00	0.243	0.136	0.65	7.023	0.00	0.48	0.970	3.262
1660	Hexan-3-one	0.00	0.243	0.136	0.65	7.290	0.00	0.48	0.970	3.310
1708	Cyclohexanone	0.00	0.269	0.403	0.76	9.000	0.00	0.52	0.861	3.615
1664	Heptan-2-one	0.00	0.247	0.123	0.65	6.812	0.00	0.48	1.111	3.760
1712	Cycloheptanone	0.00	0.274	0.436	0.76	9.610	0.00	0.52	1.002	4.110
1675	Octan-2-one	0.00	0.250	0.108	0.65	7.398	0.00	0.48	1.252	4.257
1713	Cyclo-octanone	0.00	0.279	0.474	0.76	8.762	0.00	0.52	1.143	4.610
1750	Acetophenone	1.00	0.312	0.818	0.90	9.000	0.00	0.51	1.014	4.483
1685	Nonan-2-one	0.00	0.254	0.119	0.65	7.301	0.00	0.48	1.392	4.755
1714	Cyclononanone	0.00	0.280	0.490	0.76	8.123	0.00	0.52	1.284	5.110
1690	Decan-2-one	0.00	0.256	0.108	0.65	7.290	0.00	0.48	1.533	5.260
1715	Cyclodecanone	0.00	0.284	0.527	0.76	7.840	0.00	0.52	1.425	5.610
1722	Carvone	0.00	0.294	0.674	0.80	10.049	0.00	0.49	1.339	5.330
1691	Undecan-2-one	0.00	0.258	0.101	0.65	7.290	0.00	0.48	1.674	5.760
1716	Cycloundecanone	0.00	0.288	0.557	0.76	7.840	0.00	0.52	1.566	6.110
1692	Dodecan-2-one	0.00	0.260	0.103	0.65	7.290	0.00	0.48	1.815	6.260
1717	Cyclododecanone	0.00	0.293	0.588	0.76	7.840	0.00	0.52	1.707	6.600
1352	Diethyl ether	0.00	0.217	0.041	0.27	1.323	0.00	0.45	0.731	2.061
1355	Di-n-butyl ether	0.00	0.242	0.000	0.27	1.369	0.00	0.45	1.294	4.001
1414	Furan	1.00	0.254	0.369	0.50	0.436	0.00	0.15	0.536	1.830
1450	Methyl phenyl ether	1.00	0.303	0.708	0.73	1.904	0.00	0.33	0.916	3.926
2101	Nitromethane	0.00	0.233	0.313	0.85	11.972	0.12	0.25	0.424	1.892
2102	Nitroethane	0.00	0.238	0.270	0.80	13.323	0.00	0.25	0.565	2.367
2103	1-Nitropropane	0.00	0.243	0.242	0.79	13.396	0.00	0.25	0.706	2.850
2143	3-Nitrotoluene	1.00	0.317	0.874	0.97	16.000	0.00	0.34	1.032	4.970
2201	Acetonitrile	0.00	0.212	0.237	0.75	15.366	0.09	0.44	0.404	1.560
2203	1-Cyanopropane	0.00	0.234	0.188	0.68	16.557	0.00	0.44	0.586	2.540

Table 3 (continued)

No.	Compound	δ_2	$f(n)$	R_2	π_2^*	μ_2^2	α_2^H	β_2^H	V_K	$\log L^{16}$
2205	1-Cyanobutane	0.00	0.241	0.177	0.68	16.974	0.00	0.44	0.827	3.057
2241	Benzonitrile	1.00	0.308	0.742	0.90	17.472	0.00	0.42	0.871	4.004
2701	Pyridine	1.00	0.299	0.794	0.87	4.796	0.00	0.62	0.675	3.003
2952	Acetic acid	0.00	0.227	0.265	0.60	2.890	0.55	0.43	0.465	1.750
2953	Propanoic acid	0.00	0.235	0.233	0.60	2.890	0.54	0.43	0.606	2.290
2954	Butanoic acid	0.00	0.241	0.210	0.60	2.820	0.54	0.42	0.747	2.830
2956	Pentanoic acid	0.00	0.247	0.205	0.60	2.590	0.54	0.41	0.887	3.380
2957	3-Methylbutanoic acid	0.00	0.244	0.178	0.60	2.790	0.54	0.41	0.887	3.300
2959	Hexanoic acid	0.00	0.251	0.174	0.60	2.490	0.54	0.39	1.028	3.920
2964	Heptanoic acid	0.00	0.251	0.149	0.60	2.790	0.54	0.38	1.169	4.460
2969	Octanoic acid	0.00	0.258	0.150	0.60	2.890	0.54	0.36	1.310	5.000
2975	Nonanoic acid	0.00	0.261	0.132	0.60	2.790	0.54	0.34	1.451	5.550
1860	Methyl acetate	0.00	0.220	0.142	0.60	2.958	0.00	0.40	0.606	1.960
1861	Ethyl acetate	0.00	0.227	0.106	0.55	3.168	0.00	0.45	0.747	2.376
1881	Methyl propanoate	0.00	0.230	0.128	0.55	2.890	0.00	0.45	0.747	2.459
1853	Propyl formate	0.00	0.230	0.132	0.61	3.648	0.00	0.38	0.747	2.413
1862	n-Propyl acetate	0.00	0.234	0.092	0.55	3.419	0.00	0.45	0.887	2.878
1864	n-Butyl acetate	0.00	0.239	0.071	0.55	3.240	0.00	0.45	1.028	3.379
1889	Propyl butanoate	0.00	0.249	0.068	0.55	3.063	0.00	0.45	1.169	3.810
1867	Pentyl acetate	0.00	0.244	0.067	0.55	3.063	0.00	0.45	1.169	3.810
1870	Isopentyl acetate	0.00	0.240	0.051	0.55	3.312	0.00	0.45	1.169	3.740
1892	Isobutyl isobutanoate	0.00	0.242	0.000	0.55	3.240	0.00	0.45	1.310	3.880
1896	Isopentyl isopentanoate	0.00	0.248	0.000	0.55	3.240	0.00	0.45	1.592	4.580
553	Trichloromethane	0.50	0.267	0.425	0.58	1.020	0.20	0.02	0.617	2.480
554	Tetrachloromethane	0.50	0.274	0.458	0.28	0.000	0.00	0.00	0.739	2.823
557	1,2-Dichloroethane	0.50	0.266	0.416	0.81	1.638	0.10	0.05	0.635	2.573
586	1,1,2-Trichloroethene	0.50	0.283	0.524	0.53	0.721	0.12	0.03	0.715	2.997
1038	Benzyl chloride	1.00	0.313	0.821	0.71	3.385	0.00	0.31	0.980	4.290
579	1-Chlorohexane	0.00	0.253	0.201	0.39	3.803	0.00	0.15	1.077	3.710
1002	1,2-Dichlorobenzene	1.00	0.319	0.870	0.80	5.153	0.00	0.03	0.961	4.405
605	Bromoethane	0.00	0.255	0.366	0.48	4.121	0.00	0.17	0.565	2.120
624	1-Bromopentane	0.00	0.266	0.356	0.48	4.840	0.00	0.17	0.988	3.611
637	2-Bromo-octane	0.00	0.267	0.322	0.48	4.000	0.00	0.17	1.411	5.110
651	Iodomethane	0.00	0.313	0.675	0.40	2.624	0.00	0.18	0.508	2.106
670	1-Iodobutane	0.00	0.294	0.628	0.50	4.494	0.00	0.18	0.930	3.628
671	2-Iodobutane	0.00	0.294	0.610	0.50	4.000	0.00	0.18	0.930	3.390
3552	Ethanethiol	0.00	0.259	0.392	0.35	2.459	0.00	0.16	0.554	2.172
3553	n-Propylthiol	0.00	0.263	0.385	0.35	2.280	0.00	0.16	0.695	2.685
3554	Isopropylthiol	0.00	0.256	0.336	0.35	2.560	0.00	0.16	0.695	2.406
3569	Prop-2-en-1-thiol	0.00	0.285	0.542	0.40	2.403	0.00	0.20	0.652	2.510
3555	n-Butylthiol	0.00	0.266	0.382	0.35	2.369	0.00	0.16	0.836	3.243
3556	Isobutylthiol	0.00	0.260	0.356	0.35	2.403	0.00	0.16	0.836	2.880
3558	t-Butylthiol	0.00	0.254	0.281	0.35	2.403	0.00	0.16	0.836	2.558
3601	Thiophene	1.00	0.308	0.684	0.60	0.325	0.00	0.16	0.641	2.943
3559	n-Pentylthiol	0.00	0.269	0.369	0.35	2.403	0.00	0.16	0.977	3.720
3560	Isopentylthiol	0.00	0.272	0.343	0.35	2.403	0.00	0.16	0.977	3.360
3602	2-Methylthiophene	1.00	0.304	0.688	0.40	0.449	0.00	0.14	0.782	3.302
3561	n-Hexylthiol	0.00	0.271	0.361	0.35	2.403	0.00	0.16	1.118	4.220
3603	2,5-Dimethylthiophene	1.00	0.301	0.690	0.40	0.260	0.00	0.16	0.923	3.806
3550	n-Heptanethiol	0.00	0.273	0.357	0.35	2.403	0.00	0.16	1.258	4.720
3562	n-Octylthiol	0.00	0.271	0.353	0.35	2.403	0.00	0.16	1.399	5.310
3563	n-Nonylthiol	0.00	0.271	0.347	0.35	2.403	0.00	0.16	1.540	5.890
3564	n-Decylthiol	0.00	0.270	0.342	0.35	2.403	0.00	0.16	1.681	6.480
3579	Dimethyl sulphide	0.00	0.261	0.404	0.36	2.250	0.00	0.29	0.554	2.238
3580	Diethyl sulphide	0.00	0.265	0.373	0.36	2.310	0.00	0.29	0.836	3.104
3581	Di-n-propyl sulphide	0.00	0.268	0.358	0.36	2.430	0.00	0.29	1.117	4.120
3587	Isopentyl sulphide	0.00	0.272	0.300	0.36	2.560	0.00	0.29	1.681	5.540
3610	Diethyl disulphide	0.00	0.298	0.670	0.64	3.960	0.00	0.22	0.999	4.210
3589	Di-n-butyl sulphide	0.00	0.290	0.345	0.36	2.592	0.00	0.29	1.400	4.950
3585	Methyl-n-propyl sulphide	0.00	0.266	0.380	0.36	2.560	0.00	0.29	0.836	3.240
371	Propene	0.00	0.196	0.103	0.08	0.134	0.00	0.07	0.488	0.946
373	But-1-ene	0.00	0.216	0.100	0.08	0.116	0.00	0.07	0.629	1.491
380	Pent-1-ene	0.00	0.277	0.093	0.08	0.116	0.00	0.07	0.770	2.013
392	Hex-1-ene	0.00	0.234	0.078	0.08	0.116	0.00	0.07	0.911	2.547
406	Hept-1-ene	0.00	0.242	0.092	0.08	0.116	0.00	0.07	1.052	3.063
409	Oct-1-ene	0.00	0.247	0.094	0.08	0.116	0.00	0.07	1.192	3.591
412	(Z)-Oct-2-ene	0.00	0.250	0.135	0.08	0.090	0.00	0.07	1.192	3.650
413	2-Ethylhex-1-ene	0.00	0.251	0.139	0.08	0.116	0.00	0.07	1.192	3.510
468	Oct-1-yne	0.00	0.251	0.155	0.20	0.656	0.13	0.20	1.150	3.480
469	Oct-2-yne	0.00	0.257	0.226	0.20	0.656	0.00	0.20	1.150	3.850

Table 3 (continued)

No.	Compound	δ_2	$f(\eta)$	R_2	π_2^*	μ_2^2	α_2^H	β_2^H	V_X	$\log L^{16}$
751	Benzene	1.00	0.295	0.610	0.59	0.000	0.00	0.14	0.716	2.803
752	Toluene	1.00	0.292	0.601	0.55	0.130	0.00	0.14	0.857	3.344
766	Ethylbenzene	1.00	0.292	0.613	0.53	0.348	0.00	0.15	0.998	3.765
843	Styrene	1.00	0.317	0.848	0.55	0.063	0.00	0.18	0.955	3.908
795	Phenylethyne	1.00	0.300	0.679	0.55	0.533	0.12	0.21	0.912	3.715
753	2-Xylene	1.00	0.297	0.663	0.51	0.384	0.00	0.17	0.998	3.937
754	3-Xylene	1.00	0.293	0.623	0.51	0.160	0.00	0.17	0.998	3.864
755	4-Xylene	1.00	0.292	0.613	0.51	0.000	0.00	0.17	0.998	3.858
758	Mesitylene	1.00	0.294	0.649	0.47	0.000	0.00	0.20	1.139	4.399
442	α -Pinene	0.00	0.277	0.446	0.10	0.130	0.00	0.10	1.257	4.200
52	Propane	0.00	0.181	0.000	0.00	0.000	0.00	0.00	0.531	1.050
53	n-Butane	0.00	0.205	0.000	0.00	0.000	0.00	0.00	0.672	1.615
54	Isobutane	0.00	0.197	0.000	0.00	0.000	0.00	0.00	0.672	1.409
55	n-Pentane	0.00	0.219	0.000	0.00	0.000	0.00	0.00	0.813	2.162
58	n-Hexane	0.00	0.229	0.000	0.00	0.000	0.00	0.00	0.954	2.688
287	Cyclohexane	0.00	0.257	0.305	0.00	0.000	0.00	0.00	0.845	2.913
63	n-Heptane	0.00	0.236	0.000	0.00	0.000	0.00	0.00	1.095	3.173
73	2-Methylheptane	0.00	0.240	0.000	0.00	0.000	0.00	0.00	1.236	3.480
74	3-Methylheptane	0.00	0.242	0.000	0.00	0.000	0.00	0.00	1.236	3.510
69	2,3-Dimethylpentane	0.00	0.232	0.000	0.00	0.000	0.00	0.00	1.095	2.841
72	n-Octane	0.00	0.241	0.000	0.00	0.000	0.00	0.00	1.236	3.677
91	n-Nonane	0.00	0.245	0.000	0.00	0.000	0.00	0.00	1.377	4.182
112	2,2,5-Trimethylhexane	0.00	0.242	0.000	0.00	0.000	0.00	0.00	1.377	3.530
126	n-Decane	0.00	0.248	0.000	0.00	0.000	0.00	0.00	1.518	4.686
162	n-Undecane	0.00	0.263	0.000	0.00	0.000	0.00	0.00	1.658	5.191
168	n-Dodecane	0.00	0.254	0.000	0.00	0.000	0.00	0.00	1.799	5.696
174	n-Tridecane	0.00	0.256	0.000	0.00	0.000	0.00	0.00	1.940	6.200
180	n-Tetradecane	0.00	0.258	0.000	0.00	0.000	0.00	0.00	2.081	6.705

Table 4. Regression analysis using equation (9), $n = 168$; $\log L' = c + d\delta_2 + s\pi_2^* + a\alpha_2^H + b\beta_2^H + mV_X$.

Phase	c	d	s	a	b	m	SD^a	R^b
Carbowax	-2.33	0.20	2.29	2.37	-0.53	1.57	0.22	0.960
	SD ^c	0.07	0.06	0.12	0.12	0.17	0.05	
	CL ^d	1.00	0.99	1.00	1.00	0.99	1.00	
DEGS	-2.04	0.25	2.41	2.05	-0.20	1.40	0.24	0.955
	SD	0.07	0.07	0.13	0.13	0.18	0.05	
	CL	1.00	1.00	1.00	1.00	0.74	1.00	
PPE	-2.90	0.22	1.93	0.84	-0.38	1.98	0.22	0.959
	SD	0.07	0.06	0.12	0.12	0.17	0.05	
	CL	1.00	1.00	1.00	1.00	0.97	1.00	
TCEP	-1.95	0.20	2.67	2.02	-0.02	1.32	0.23	0.961
	SD	0.07	0.07	0.13	0.13	0.18	0.05	
	CL	1.00	1.00	1.00	1.00	0.08	1.00	
ZE7	-2.43	0.09	1.91	0.81	0.21	1.59	0.16	0.975
	SD	0.05	0.04	0.09	0.08	0.12	0.04	
	CL	1.00	0.96	1.00	1.00	0.91	1.00	

^a Overall standard deviation. ^b Overall correlation coefficient. ^c Standard deviation in the constant. ^d Confidence level: 1.00 signifies > 0.99.

remove the dispersive part already incorporated in $\log L^{16}$, we then subtract out the value of MR_X for an alkane of the same

$$R_2 = MR_X(\text{observed}) - MR_X(\text{alkane of same } V_X) \quad (14)$$

characteristic volume, equation (4). The latter quantity is readily obtained through an excellent linear regression for the n-alkanes,

$$MR_X(\text{alkane}) = -0.525\,53 + 2.831\,95V_X \quad (15)$$

$n = 13, R = 0.999\,99, SD = 0.0078$

Hence knowing $f(\eta)$ and V_X for any solute, MR_X and then R_2 can be calculated via equations (13)–(15). For convenience we tabulate R_2 in units of 10^{-1} cm^3 , and give a number of typical values in Table 7. Note that by definition $R_2 = 0$ for all n-alkanes, and by calculation R_2 is also zero for branched chain alkanes and for the rare gases as well.

We now use the new polarisability parameter, R_2 , in conjunction with μ_2^2 , to construct equation (16), that we apply to the same set of 168 solutes as before. Details are in Table 8.

$$\log L' = c + rR_2 + q\mu_2^2 + a\alpha_2^H + b\beta_2^H + l\log L^{16} \quad (16)$$

The quality of the regressions in Table 8 is slightly better than those in Table 6, based on equation (11), but significantly poorer than those in Table 5, based on equation (10). For purposes of characterisation, this might not matter too much, but unfortunately the regressions in Table 8(a) show larger dependences on β_2^H that are probably artifacts [compare Table 8(a) with Table 8(b)]. Although there is no significant cross-correlation between R_2 and any other explanatory variable in equation (16), there still remains the connection between μ_2^2 and β_2^H , $r = 0.556$, referred to above. It is possible that for a better selection of solutes without the μ_2^2/β_2^H cross-correlation, equation (16) might perform as well as equation (10), and we intend to investigate this further.

Finally, we suggest that our calculated R_2 values (Table 7) can replace the empirical δ_2 values in equation (10) to yield equation (17). Details of regressions using equation (17) are in

$$\log L' = c + rR_2 + s\pi_2^* + a\alpha_2^H + b\beta_2^H + l\log L^{16} \quad (17)$$

Table 9. In terms of overall standard deviation and correlation coefficient, these regressions are the best we have obtained, being slightly better than those given in Table 5. We have also investigated replacement of δ_2 by R_2 in equation (9), but, as usual, find that equations using V_X are considerably poorer than those using $\log L^{16}$.

Table 5. Regression analysis using equation (10), $n = 168$; $\log L' = c + d\delta_2 + s\pi_2^* + a\alpha_2^H + b\beta_2^H + l\log L^{16}$.

Phase	c	d	s	a	b	l	SD	R
(a) Carbowax	-2.07	0.05	1.55	2.13	-0.17	0.446	0.14	0.985
SD	0.04	0.04	0.07	0.07	0.10	0.008		
CL	1.00	0.83	1.00	1.00	0.89	1.00		
DEGS	-1.81	0.12	1.76	1.84	0.11	0.399	0.16	0.978
SD	0.04	0.05	0.09	0.09	0.12	0.010		
CL	1.00	0.99	1.00	1.00	0.64	1.00		
PPE	-2.54	0.04	1.01	0.53	0.08	0.554	0.11	0.990
SD	0.03	0.03	0.06	0.06	0.08	0.007		
CL	1.00	0.77	1.00	1.00	0.66	1.00		
TCEP	-1.74	0.07	2.06	1.82	0.28	0.380	0.16	0.981
SD	0.04	0.05	0.09	0.09	0.12	0.010		
CL	1.00	0.88	1.00	1.00	0.98	1.00		
ZE7	-2.10	-0.05	1.17	0.56	0.59	0.434	0.13	0.984
SD	0.03	0.04	0.07	0.07	0.10	0.008		
CL	1.00	0.84	1.00	1.00	1.00	1.00		
(b) Carbowax	-2.06	0.08	1.46	2.08		0.446	0.14	0.985
SD	0.04	0.03	0.05	0.07		0.008		
CL	1.00	0.98	1.00	1.00		1.00		
DEGS	-1.81	0.10	1.82	1.87		0.400	0.16	0.978
SD	0.04	0.04	0.06	0.08		0.010		
CL	1.00	0.98	1.00	1.00		1.00		
PPE	-2.54	0.02	1.05	0.55		0.555	0.11	0.990
SD	0.03	0.03	0.04	0.05		0.007		
CL	1.00	0.61	1.00	1.00		1.00		
TCEP	-1.73	0.02	2.21	1.90		0.382	0.16	0.981
SD	0.04	0.04	0.06	0.08		0.010		
CL	1.00	0.40	1.00	1.00		1.00		
ZE7	-2.09	-0.16	1.50	0.72		0.438	0.14	0.980
SD	0.04	0.03	0.05	0.07		0.009		
CL	1.00	0.99	1.00	1.00		1.00		

* These are the preferred equations.

Table 6. Regression analysis using equation (11), $n = 168$; $\log L' = c + f f(n) + q\mu_2^2 + a\alpha_2^H + b\beta_2^H + mV_X$.

Phase	c	f	q	a	b	l	SD	R
Carbowax	-3.48	7.61	0.59	2.34	0.55	0.370	0.19	0.971
SD	0.16	0.67	0.005	0.11	0.12	0.014		
CL	1.00	1.00	1.00	1.00	1.00	1.00		
DEGS	-3.62	9.56	0.67	2.06	0.92	0.304	0.22	0.961
SD	0.18	0.77	0.006	0.13	0.14	0.016		
CL	1.00	1.00	1.00	1.00	1.00	1.00		
PPE	-3.56	5.37	0.038	0.66	0.56	0.500	0.14	0.985
SD	0.11	0.48	0.004	0.08	0.09	0.010		
CL	1.00	1.00	1.00	1.00	1.00	1.00		
TCEP	-3.67	10.26	0.080	2.09	1.21	0.278	0.23	0.961
SD	0.19	0.81	0.006	0.13	0.15	0.017		
CL	1.00	1.00	1.00	1.00	1.00	1.00		
ZE7	-2.55	2.84	0.051	0.72	1.04	0.409	0.17	0.972
SD	0.14	0.58	0.005	0.10	0.11	0.012		
CL	1.00	1.00	1.00	1.00	1.00	1.00		

Table 7. Some values of the molar refraction parameter, R_2 , and the 'correction factor', δ_2 .

Solute	$R_2/10^{-1} \text{ cm}^3$	δ_2
Rare gases	0	0
Alkanes	0	0
Cyclohexane	0.305	0
But-1-ene	0.100	0
But-1-yne	0.178	0
Benzene	0.610	1
1-Chlorobutane	0.210	0
1-Bromobutane	0.360	0
1-Iodobutane	0.628	0
Dichloromethane	0.387	0.5
Tetrachloromethane	0.458	0.5
Chlorobenzene	0.718	1
Butan-2-one	0.166	0
Diethyl ether	0.041	0
Ethyl acetate	0.106	0
Dimethylformamide	0.367	0
Butan-1-ol	0.224	0
n-Butylamine	0.224	0
Acetophenone	0.818	1
Methyl phenyl ether	0.708	1
Ethyl benzoate	0.663	1
Phenol	0.805	1
Aniline	0.955	1

Table 8. Regression analysis using equation (16), $n = 168$; $\log L' = c + rR_2 + q\mu_2^2 + a\alpha_2^H + b\beta_2^H + l\log L^{16}$.

Phase	c	r	q	a	b	l	SD	R
(a) Carbowax	-1.98	0.86	0.052	2.30	0.53	0.438	0.17	0.976
SD	0.05	0.06	0.005	0.10	0.10	0.011		
CL	1.00	1.00	1.00	1.00	1.00	1.00		
DEGS	-1.74	1.10	0.059	2.03	0.89	0.389	0.19	0.971
SD	0.05	0.07	0.005	0.11	0.12	0.012		
CL	1.00	1.00	1.00	1.00	1.00	1.00		
PPE	-2.50	0.62	0.033	0.64	0.55	0.548	0.12	0.988
SD	0.03	0.04	0.003	0.07	0.08	0.008		
CL	1.00	1.00	1.00	1.00	1.00	1.00		
TCEP	-1.67	1.16	0.071	2.05	1.19	0.369	0.20	0.970
SD	0.05	0.07	0.006	0.12	0.13	0.013		
CL	1.00	1.00	1.00	1.00	1.00	1.00		
ZE7	-1.99	0.34	0.048	0.71	1.04	0.434	0.16	0.974
SD	0.04	0.06	0.004	0.09	0.10	0.010		
CL	1.00	1.00	1.00	1.00	1.00	1.00		
(b) Carbowax	-1.92	0.85	0.068	2.56		0.444	0.18	0.972
SD	0.05	0.07	0.004	0.09		0.011		
CL	1.00	1.00	1.00	1.00		1.00		
DEGS	-1.63	1.08	0.084	2.47		0.398	0.22	0.961
SD	0.06	0.08	0.005	0.11		0.014		
CL	1.00	1.00	1.00	1.00		1.00		
PPE	-2.44	0.61	0.049	0.91		0.553	0.14	0.984
SD	0.03	0.05	0.003	0.07		0.009		
CL	1.00	1.00	1.00	1.00		1.00		
TCEP	-1.50	1.14	0.105	2.64		0.382	0.25	0.954
SD	0.06	0.09	0.005	0.12		0.016		
CL	1.00	1.00	1.00	1.00		1.00		
ZE7	-1.88	0.32	0.078	1.22		0.445	0.21	0.956
SD	0.05	0.07	0.004	0.10		0.013		
CL	1.00	1.00	1.00	1.00		1.00		

Table 9. Regression analysis using equation (17), $n = 168$; $\log L' = c + rR_2 + s\pi_2^* + a\alpha_2^H + b\beta_2^H + l\log L^{16}$

Phase	c	r	s	a	b	l	SD	R
(a) Carbowax	-2.07	0.25	1.40	2.13	-0.05	0.442	0.13	0.986
SD	0.03	0.06	0.08	0.07	0.10	0.008		
CL	1.00	1.00	1.00	1.00	0.42	1.00		
DEGS	-1.84	0.43	1.53	1.83	0.28	0.393	0.15	0.982
SD	0.04	0.07	0.09	0.08	0.11	0.009		
CL	1.00	1.00	1.00	1.00	0.98	1.00		
PPE	-2.56	0.25	0.85	0.53	0.21	0.550	0.10	0.991
SD	0.03	0.05	0.06	0.05	0.08	0.006		
CL	1.00	1.00	1.00	1.00	0.99	1.00		
TCEP	-1.76	0.36	1.84	1.81	0.45	0.374	0.15	0.984
SD	0.04	0.07	0.09	0.08	0.11	0.009		
CL	1.00	1.00	1.00	1.00	1.00	1.00		
ZE7	-2.08	-0.24	1.31	0.56	0.48	0.438	0.12	0.985
SD	0.03	0.06	0.07	0.06	0.09	0.008		
CL	1.00	1.00	1.00	1.00	1.00	1.00		
(b) ^a Carbowax	-2.07	0.26	1.37	2.11		0.442	0.13	0.986
SD	0.03	0.05	0.05	0.06		0.008		
CL	1.00	1.00	1.00	1.00		1.00		
DEGS	-1.83	0.35	1.70	1.92		0.396	0.15	0.981
SD	0.04	0.06	0.06	0.07		0.009		
CL	1.00	1.00	1.00	1.00		1.00		
PPE	-2.55	0.19	0.98	0.59		0.552	0.11	0.991
SD	0.03	0.04	0.04	0.05		0.007		
CL	1.00	1.00	1.00	1.00		1.00		
TCEP	-1.75	0.23	2.12	1.94		0.379	0.16	0.982
SD	0.04	0.06	0.06	0.08		0.010		
CL	1.00	1.00	1.00	1.00		1.00		
ZE7	-2.07	0.38	1.61	0.70		0.442	0.13	0.983
SD	0.03	0.05	0.05	0.06		0.008		
CL	1.00	1.00	1.00	1.00		1.00		

^a These are the preferred equations.

In our view, equation (17) represents the most satisfactory regression equation we have been able to construct. Analysis of the constants follows closely our analysis using equation (10). Although the analysis *via* equation (17) is only slightly better than that through equation (10), we prefer the former because the R_2 parameter is a well-defined explanatory variable that refers to a specific type of solute-solvent phase interaction. From the method of determination of R_2 , as well as from inspection of R_2 values, it follows that the rR_2 term in equation (17) is a quantitative measure of the ability of a solute to interact with the solvent through solute π (mainly) or n -electron pairs. Furthermore, R_2 is a reasonably independent explanatory variable; cross-correlation coefficients between R_2 and the other explanatory variables in equations (16) and (17) are:

π_2^*	μ_2^2	α_2^H	β_2^H	$\log L^{16}$
0.503	0.175	-0.152	0.025	0.124

There is bound to be some correlation between R_2 and π_2^* because we have still not succeeded in subtracting all the polarisability contribution from π_2^* . However, equation (17) does go some way to so doing.

Table 10. The characterisation of stationary phases at 393 K.

Phase	c^a	d	s	a	l
Carbowax	-2.06	0.08	1.46	2.08	0.445
DEGS	-1.81	0.10	1.82	1.87	0.400
PPE	-2.54	0.02	1.05	0.55	0.555
TCEP	-1.73	0.02	2.21	1.90	0.382
ZE7	-2.54	0.16	1.50	0.72	0.438
	c	r	s	a	l
Carbowax	-2.07	0.26	1.37	2.11	0.442
DEGS	-1.83	0.35	1.70	1.92	0.396
PPE	-2.55	0.19	0.98	0.59	0.552
TCEP	-1.75	0.23	2.12	1.94	0.379
ZE7	-2.07	-0.38	1.61	0.70	0.442
	c	r	q	a	l
Carbowax	-1.92	0.85	0.068	2.56	0.444
DEGS	-1.63	1.08	0.084	2.47	0.398
PPE	-2.44	0.61	0.049	0.91	0.553
TCEP	-1.50	1.14	0.105	2.64	0.382
ZE7	-1.88	0.32	0.078	1.22	0.445

^a Note that this constant includes the term $\log L^{\text{Decane}}$, see equation (8).

Conclusions

A number of equations can be constructed for the characterisation of gas chromatographic phases, and, indeed, any solvent phase, through a series of constants that refer to specific solute-solvent interactions. Our preferred equation (17) leads to a set of constants c , r , s , a , b , and l of which r refers to interactions through solute π - and n -electron pairs, s to interactions of the dipole-dipole and dipole-induced dipole type (together with some polarisability effects), a to solute hydrogen-bond acid/solvent hydrogen-bond base interactions, b to solute hydrogen-bond base/solvent hydrogen-bond acid interactions and l to a combination of general dispersion forces plus cavity effects. The methodology does not suffer from the technical deficiencies of the Rohrschneider-McReynolds method, as outlined by Poole *et al.*,⁶ and can be applied to any condensed phase. We list in Table 10, the characteristic constants for the Laffort phases, using equations that omit the β_2^H explanatory variable. The dipolarity of the three phases, using either π_2^* or μ^2 as a probe, is always in the order:



and the hydrogen-bond basicity of the phases, as given by the a -constant, is best represented by the order,



The ability of the phase to interact with solutes specifically through π - and n -solute electron pairs is given by the r -constant in the rR_2 term. There is not very good quantitative agreement between equations (16) and (17), but both equations show that the fluorinated solvent ZE7 has the least ability to take part in π - and n -interactions.

We aim to extend this method of characterisation to other stationary phases and to common solvents, and hope to report further in the near future.

Acknowledgements

We thank the US Army Research, Development, and Standardisation Group for support under Contract DAJA 45-87-C-0004, and we are grateful to Professor Paul Laffort for his advice on the b -values.

References

- 1 L. Rohrschneider, *J. Chromatogr.*, 1966, **22**, 6.
- 2 W. O. McReynolds, *J. Chromatogr. Sci.*, 1970, **8**, 685.
- 3 E. Sz. Kovats, *Helv. Chim. Acta*, 1958, **41**, 1915.
- 4 G. Tarján, A. Kiss, G. Kocsis, S. Mészáros, and J. M. Takács, *J. Chromatogr.*, 1976, **119**, 327.
- 5 M. V. Budahegyi, E. R. Lombosi, T. S. Lombosi, S. Y. Mészáros, Sz. Nyiredy, G. Tarján, I. Timár, and J. M. Takács, *J. Chromatogr.*, 1983, **271**, 213.
- 6 S. K. Poole, B. R. Kersten, R. M. Pomaville, and C. F. Poole, LC-GC, 1989, **6**, 401; B. R. Kersten, C. F. Poole, and K. G. Furton, *J. Chromatogr.*, 1987, **411**, 43; S. K. Poole, B. R. Kersten, and C. F. Poole, *J. Chromatogr.*, 1989, **471**, 91.
- 7 J. Novak, *J. Chromatogr.*, 1973, **78**, 269.
- 8 J. Novak, J. Ruzickova, S. Wicar, and J. Janak, *Anal. Chem.*, 1973, **45**, 1365.
- 9 R. V. Golovnya and T. A. Misharina, *Chromatographia*, 1977, **10**, 658.
- 10 R. I. Sidarov, *Zh. Fiz. Khim.*, 1980, **54**, 1997 (*Engl. Transl.* p. 1136).
- 11 M. H. Abraham, *J. Am. Chem. Soc.*, 1982, **104**, 2085.
- 12 Th. Kleinert and W. Ecknig, *J. Chromatogr.*, 1984, **315**, 75.
- 13 Th. Kleinert, W. Ecknig, and J. Novak, *J. Chromatogr.*, 1984, **315**, 85.
- 14 M. Roth and J. Novak, *J. Chromatogr.*, 1983, **258**, 23.
- 15 W. Burns and S. J. Hawkes, *J. Chromatogr. Sci.*, 1977, **15**, 185.
- 16 E. Chong, B. deBriceno, G. Miller, and S. Hawkes, *Chromatographia*, 1985, **20**, 293.
- 17 M. J. Kamlet, R. M. Doherty, J.-L.M. Abboud, M. H. Abraham, and R. W. Taft, *Chemtech.*, 1986, **16**, 566.
- 18 M. H. Abraham, R. M. Doherty, M. J. Kamlet, and R. W. Taft, *Chem. Brit.*, 1986, **22**, 551.
- 19 M. J. Kamlet, R. M. Doherty, M. H. Abraham, and R. W. Taft, *QSAR*, 1988, **7**, 71.
- 20 M. H. Abraham, P. L. Grellier, I. Hamerton, R. A. McGill, D. V. Prior, and G. S. Whiting, *Faraday Discuss. Chem. Soc.*, 1988, **85**, 107.
- 21 M. H. Abraham, P. L. Grellier, and R. A. McGill, *J. Chem. Soc., Perkin Trans. 2*, 1987, 797.
- 22 F. Patte, M. Etcheto, and P. Laffort, *Anal. Chem.*, 1982, **54**, 2239.
- 23 These are the *b*-values given in Table III of ref. 22 under the row equation 5, personal communication from Professor Laffort.
- 24 M. H. Abraham, P. P. Duce, P. L. Grellier, D. V. Prior, J. J. Morris, and P. J. Taylor, *Tetrahedron Lett.*, 1988, **29**, 1587.
- 25 M. H. Abraham, P. L. Grellier, D. V. Prior, P. P. Duce, J. J. Morris, and P. J. Taylor, *J. Chem. Soc., Perkin Trans. 2*, 1989, 699.
- 26 M. H. Abraham, P. L. Grellier, D. V. Prior, J. J. Morris, P. J. Taylor, C. Lawrence, and M. Berthelot, *Tetrahedron Lett.*, 1989, **30**, 2571.
- 27 M. H. Abraham, P. L. Grellier, D. V. Prior, J. J. Morris, and P. J. Taylor, *J. Chem. Soc., Perkin Trans. 2*, 1990, 521.
- 28 M. H. Abraham and G. S. Whiting, unpublished work.
- 29 M. H. Abraham and J. C. McGowan, *Chromatographia*, 1987, **23**, 243.
- 30 J. G. Kirkwood, *J. Chem. Phys.*, 1934, **2**, 351.
- 31 R. Fuchs, M. H. Abraham, M. J. Kamlet, and R. W. Taft, *J. Phys. Org. Chem.*, 1982, **2**, 559.

Paper 0/00007H

Received 2nd January 1990

Accepted 26th April 1990

Hydrogen Bonding. Part 14.† The Characterisation of Some *N*-Substituted Amides as Solvents: Comparison with Gas-Liquid Chromatography Stationary Phases

Michael H. Abraham* and Gary S. Whiting

Department of Chemistry, University College London, 20 Gordon Street, London WC1H 0AJ

Ruth M. Doherty

Naval Surface Warfare Center, White Oak Laboratory, Silver Spring, Maryland 20910, USA

Wendel J. Shuely

US Army Chemical Research, Development and Engineering Center, Aberdeen Proving Ground, Maryland 21010, USA

Equations previously used for the characterisation of GLC stationary phases have been found to be equally suitable for the characterisation of common solvents. Thus equation (a) has been applied to solubility data for series of solutes on *N*-formylmorpholine (NFM), *N*-methylpyrrolidinone (NMP), *N,N*-dimethylformamide (DMF), and *N,N*-dimethylacetamide (DMA).

$$SP = c + r \cdot R_2 + s \cdot \pi_2^* + a \cdot \alpha_2^H + b \cdot \beta_2^H + l \cdot \log L^{16} \quad (a)$$

In equation (a), SP can be $\log V_G^\circ$ or $\log L$ for a series of solutes on a given solvent where V_G° is the specific retention volume and L is the Ostwald solubility coefficient. The solute parameters are R_2 , a polarisability parameter; π_2^* , the solute dipolarity; α_2^H , the solute hydrogen-bond acidity; β_2^H , the solute hydrogen-bond basicity; and $\log L^{16}$ where L^{16} is the solute Ostwald solubility coefficient on *n*-hexadecane at 298 K.

It is shown that at 298 K all four amides have about the same dipolarity, as judged by the s -constant, and have nearly the same hydrogen-bond basicity, as judged by the $a \cdot \alpha_2^H$ term: all have zero hydrogen-bond acidity so that $b = 0$ in equation (a). Comparison can be made between results for NFM and NMP at 393 K and results for some GLC stationary phases. The two amides are less dipolar than tricyano(ethoxy)propane and diethyleneglycol succinate, about the same as Zonyl E-7® and Carbowax®, and more dipolar than poly(phenyl ether). The amides, however, have rather more hydrogen-bond basicity than any of the above five GLC phases. It is suggested that equation (a) can be used as the basis of method for characterising condensed phases, such that common solvents as well as GLC stationary phases can be included within the scope of the method.

A number of amides are industrially important solvents, and there are several reports dealing with vapour-liquid equilibria (VLE) of *N*-substituted amides, especially.¹⁻⁶ A particularly convenient method of obtaining VLE data for a series of solutes in a given amide is the gas-chromatographic procedure in which the amide acts as the stationary phase.^{1,3-6} The obtained specific retention volumes, either at the column temperature (V_G) or corrected to 273 K (V_G°), can be converted into infinite dilution activity coefficients of the solute in the amide solvent, γ_2^∞ , at the column temperature, through well established equations.^{1,3-5} Alternatively, values of V_G can be transformed into Ostwald solubility coefficients, L_2 , defined by equation (1), through the very simple equation (2) in which ρ_1 is the density

$$L_2 = \frac{\text{concentration of solute in solution}}{\text{concentration of solute in the gas phase}} \quad (1)$$

$$L_2 = V_{G, \rho 1} \quad (2)$$

of the amide at the column temperature. For measurements at essentially zero solute concentration, L_2 is effectively L_2° , and the concentration of solute in solution becomes identical with the concentration of solute in the pure solvent.

Medina and co-workers³ used both their own gas-liquid chromatographic (GLC) measurements and literature data to

obtain γ^∞ -values for hydrocarbons in *N*-methylpyrrolidinone (NMP) and were able to account rather well for these γ^∞ -values using the group contribution method, UNIFAC. A much more extensive set of solutes was studied by Gmehling and co-workers^{4,6} with both the amides NMP and *N*-formylmorpholine (NFM). They obtained V_G° -values for a set of hydrocarbons, esters, aldehydes, ketones, and alcohols at various temperatures, and listed both V_G° - and γ^∞ -values.

Now although the calculation of γ^∞ -values using methods such as UNIFAC, UNIQUAT, and ASOG is well established, there is always an over-riding difficulty in the interpretation of parameters that refer to γ^∞ : since γ^∞ is an equilibrium constant (or partition coefficient) between the bulk liquid solute and the solute at infinite dilution in the solvent, γ^∞ will contain not only contributions from solute-solvent interactions, but also those from solute-solute interactions. As has been pointed out before,⁷ gas-liquid partition coefficients contain only the solute-solvent interaction terms, and hence are inherently easier to interpret than quantities that refer to partition between the bulk liquid and the solvent. Since gas-liquid partition coefficients, either as values of L or as Henry's constants K^H , are convertible into γ^∞ -values through the solute vapour pressure, P° , and since, in any case, P° -values are needed to obtain γ^∞

† Part 13 is ref. 10.

Table 1. Solutes used in the correlations with V_G° , Tables 2–5.

NFM	NMP
n-Pentane	n-Pentane
n-Hexane	n-Hexane
n-Heptane	n-Heptane
n-Octane	n-Octane
2,2,4-Trimethylpentane	2,2,4-Trimethylpentane
n-Decane	Cyclopentane
Cyclopentane	Cyclohexane
Methylcyclopentane	Methylcyclopentane
Cyclohexane	Methylcyclohexane
Methylcyclohexane	Benzene
Ethylcyclohexane	Toluene
1,4- <i>trans</i> -Dimethylcyclohexane	Hex-1-ene
1,4- <i>cis</i> -Dimethylcyclohexane	Oct-1-ene
1,2- <i>trans</i> -Dimethylcyclohexane	Methanol
1,2- <i>cis</i> -Dimethylcyclohexane	Ethanol
Benzene	Propan-2-ol
Toluene	t-Butyl alcohol
2-Xylene	Methyl acetate
3-Xylene	n-Propyl acetate
4-Xylene	Ethyl propanoate
Ethylbenzene	Ethyl butanoate
Isopropylbenzene	Vinyl acetate
Hex-1-ene	Acetone
Oct-1-ene	Butan-2-one
Methanol	Pentan-2-one
Ethanol	Pentan-3-one
Propan-2-ol	Butanal
Propan-1-ol	2-Methylpropanal
t-Butyl alcohol	Pentanal
Methyl acetate	(<i>E</i>)-But-2-enal
Ethyl acetate	Thiophene
n-Propyl acetate	
Ethyl propanoate	
Ethyl butanoate	
Vinyl acetate	
Acetone	
Butan-2-one	
Pentan-2-one	
Pentan-3-one	
4-Methylpentan-2-one	
Butanal	
2-Methylpropanal	
Pentanal	
(<i>E</i>)-But-2-enal	
Thiophene	

from V_G , it seems a theoretically simpler matter to deal with gas-liquid parameters (such as L , K^H , or V_G) than with γ^∞ .

A number of equations have already been derived for the correlation of gas-liquid partition coefficients, as $\log L$ or $\log V_G$, for a series of solutes in a given liquid phase.^{8–10}

$$SP = c + d \cdot \delta_2 + s \cdot \pi_2^* + a \cdot \alpha_2^H + b \cdot \beta_2^H + l \cdot \log L^{16} \quad (3)$$

$$SP = c + r \cdot R_2 + s \cdot \pi_2^* + a \cdot \alpha_2^H + b \cdot \beta_2^H + l \cdot \log L^{16} \quad (4)$$

$$SP = c + r \cdot R_2 + q \cdot \mu_2^2 + a \cdot \alpha_2^H + b \cdot \beta_2^H + l \cdot \log L^{16} \quad (5)$$

In these equations SP can be $\log L$ or $\log V_G$, etc.,† and the various explanatory variables are as follows: δ_2 is an empirical solute polarisability correction term taken as zero except for aromatic solutes ($\delta_2 = 1$) and polyhalogenated solutes ($\delta_2 = 0.5$), π_2^* is the solute dipolarity/polarisability, α_2^H and β_2^H are

† Note that $\log L$ and $\log V_G$ give rise to exactly the same constants in equations (3), (4), and (5) except for the c -constant which will differ by $\log \rho_1$.

Table 2. Correlations of $\log V_G^\circ$ for 45 solutes in NFM⁴ by using equations (3) and (4).

T/K	c	s	a	l	SD^a	R^b
298.2	−0.313	2.311	4.335	0.708	0.122	0.985
	0.107 ^c	0.069	0.216	0.031		
313.3	−0.349	2.153	3.916	0.656	0.114	0.985
	0.101	0.065	0.204	0.029		
332.7	−0.386	1.966	3.430	0.594	0.104	0.985
	0.091	0.059	0.184	0.026		
352.5	−0.425	1.811	2.998	0.536	0.099	0.983
	0.088	0.056	0.177	0.025		
373.4	−0.459	1.645	2.582	0.487	0.094	0.982
	0.083	0.053	0.167	0.024		

^a Overall standard deviation in $\log V_G^\circ$. ^b Overall correlation coefficient.

^c These are the standard deviations in the various constants.

Table 3. Correlations of $\log V_G^\circ$ for 45 solutes in NFM⁴ by using equation (5).

T/K	c	r	q	a	l	SD	R
298.2	−0.040	1.756	0.159	4.156	0.621	0.330	0.890
313.3	−0.095	1.659	0.149	3.742	0.572	0.302	0.892
332.7	−0.155	1.534	0.136	3.266	0.516	0.271	0.895
352.5	−0.215	1.432	0.126	2.843	0.464	0.245	0.897
373.4	−0.264	1.337	0.114	2.425	0.417	0.217	0.902

Table 4. Correlations of $\log V_G^\circ$ for 31 solutes in NMP⁴ by using equations (3) and (4).

T/K	c	s	a	l	SD	R
298.2	−0.159 ^a	2.103	5.049	0.779	0.107	0.988
	0.141	0.073	0.241	0.046		
323.4	−0.212	1.883	4.298	0.680	0.096	0.987
	0.126	0.066	0.216	0.041		
333.2	−0.220	1.803	4.016	0.644	0.093	0.986
	0.121	0.063	0.208	0.040		
343.4	−0.246	1.730	3.777	0.612	0.092	0.986
	0.120	0.063	0.206	0.039		

^a For $\log L_{NMP}$, this constant takes the value −0.110.

Table 5. Correlations of $\log V_G^\circ$ for 31 solutes in NMP⁴ by using equation (5).

T/K	c	r	q	a	l	SD	R
298.2	−0.094 ^a	1.422	0.142	5.172	0.785	0.300	0.902
323.4	−0.151	1.300	0.127	4.397	0.683	0.268	0.900
333.2	−0.164	1.254	0.121	4.109	0.647	0.255	0.900
343.4	−0.189	1.215	0.116	3.860	0.613	0.246	0.898

^a For $\log L_{NMP}$, this constant takes the value −0.045.

respectively the solute hydrogen-bond acidity and hydrogen-bond basicity, L^{16} is the solute Ostwald solubility coefficient on n-hexadecane at 298.15 K, R_2 is the solute molar refraction less that of an alkane of the same characteristic volume, and μ_2 is the solute dipole moment.¹⁰ Equations (3) and (4) have usually given better correlations than has equation (5).

We start with the results of Gmehling and co-workers on NFM,⁴ where V_G° -values were obtained for 45 solutes at various temperatures, ranging from 303.4 to 373.4 K. Not all solutes were studied at all temperatures, and so we have interpolated values, and have also extrapolated values from either 303.4 K or 313.3 K down to 298.15 K to obtain a

Table 6. Values of log L at 298 K for solutes in NMP, DMF, and DMA.

Solute	NMP	DMF	DMA
Argon	-0.98 ^{19,†}	-0.86 ¹⁹	
Hydrogen	-1.46 ²⁷	-1.35 ^{26,27}	
Nitrogen	-1.25 ¹⁵		
Ammonia	1.34 ¹⁴		
Carbon monoxide		-1.06 ²⁸	
Methane	-0.61 ¹⁶⁻¹⁹	-0.52 ¹⁹	
Ethane	0.19 ^{16,17,19}	0.22 ^{14,19}	0.35 ²⁹
Propane	0.65 ^{14,16,17,19}	0.64 ¹⁴	0.81 ²⁹
n-Butane	1.14 ^{16,17,19}	1.08 ¹⁴	1.28 ²⁹
Isobutane	0.88 ^{14,16,17,19}		
n-Pentane	1.56 ^{3,16,19}	1.51 ¹⁹	1.70 ²⁹
2-Methylbutane	1.32 ³	1.39 [†]	1.45 [†]
n-Hexane	2.03 ^{3,16,19}	1.99 ¹⁹	2.10 ²⁹
n-Heptane	2.34 ^{3,16,19}	2.36 ¹⁹	
n-Octane	2.77 ^{3,16,19,20}	2.81 ^{19,20}	2.90 ²⁰
2,2,4-Trimethylpentane	2.29 ^{3,21}	2.22 ³⁰	
n-Nonane	3.05 ³		
Cyclopentane	1.92 ³		
Methylcyclopentane	2.20 ³		
Cyclohexane	2.33 ^{3,16,21,22}	2.31 ^{2,19}	
Methylcyclohexane	2.64 ^{3,16}	2.58 ^{19,30}	
Ethylcyclohexane	3.02 ³		
n-Propylcyclohexane	3.35 ³		
n-Butylcyclohexane	3.73 ³		
Ethene	0.29 ^{16,18}		
Propene	0.91 ¹⁸		
But-1-ene		1.30 ²⁵	
Pent-1-ene	1.65 ¹	1.70 ^{1,2,30}	1.72 ¹
3-Methylbut-1-ene	1.50 ¹	1.53 ¹	1.56 ¹
2-Methylbut-2-ene	1.86 ^{1,22}	1.88 ¹	1.89 ¹
Hex-1-ene	2.06 ⁴	2.21 ²	
Oct-1-ene	2.91 ⁴		
Cyclopentene		2.22 ²	
Cyclohexene		2.68 ²	
Buta-1,3-diene	1.73 ¹⁸	1.68 ²⁴	
2-Methylbuta-1,3-diene	2.14 ^{1,22}	2.11 ^{1,2}	2.12 ¹
2,3-Dimethylbuta-1,3-diene		2.63 ²	
(E)-Penta-1,3-diene	2.24 ¹	2.23 ¹	2.25 ¹
(Z)-Penta-1,3-diene	2.29 ¹	2.27 ¹	2.29 ¹
Cyclopenta-1,3-diene		2.50 ²	
Pent-1-yne		2.54 ²	
Benzene	3.30 ^{21,22}	3.26 ³¹	
Toluene	3.71 ²⁰	3.64 ²⁰	3.64 ²⁰
Chloromethane		1.74 ³²	
Chloroethane		2.01 ²⁹	2.16 ²⁹
Trichloromethane	3.84 ²⁴		
Bromoethane		2.45 ^{29,30}	2.53 ²⁹
Iodomethane	2.76 ²³	2.56 ³⁰	2.66 ²³
Iodoethane		2.86 ^{29,30,33}	2.91 ²⁹
Dimethyl ether		1.56 ³²	
1,4-Dioxane	3.66 ²⁰	3.72 ²⁰	3.66 ²⁰
Butanal	3.05 ⁴		
2-Methylpropanal	2.78 ⁴		
Pentanal	3.42 ⁴		
(Z)-But-2-enal	3.66 ⁴		
Acetone	2.77 ⁴		
Butan-2-one	3.42 ²⁰	3.36 ²⁰	3.28 ²⁰
Pentan-2-one	3.47 ⁴		
Pentan-3-one	3.49 ⁴		
Methyl acetate	2.72 ⁴		
n-Propyl acetate	3.39 ⁴		
Ethyl propanoate	3.29 ⁴		
Ethyl butanoate	3.59 ⁴		
Vinyl acetate	3.05 ⁴		
Acetonitrile		3.41 ³⁴	
Propanonitrile		3.67 ²⁹	3.66 ²⁹
Nitromethane		4.07 ²⁰	4.02 ²⁰
Methylamine		1.95 ¹⁴	
Dimethylamine		2.11 ¹⁴	
Trimethylamine		1.77 ¹⁴	
Triethylamine		2.62 ³³	

Table 6 (continued).

Solute	NMP	DMF	DMA
Thiophene	3.43 ⁴		
Tetramethyltin	2.19 ¹⁹	2.15 ¹⁹	
Water		4.07 ³⁴	
Methanol	3.43 ⁴		
Ethanol	3.78 ²⁰	3.73 ²⁰	3.82 ²⁰
Propan-1-ol		4.08 ^a	
Propan-2-ol	3.73 ⁴		
Butan-1-ol			4.84 ^a
Butan-2-ol		4.16 ^a	4.32 ^a
t-Butyl alcohol	3.75 ⁴		
2,2,2-Trifluoroethanol		5.08 ^a	4.99 ^a
NMP	5.63§		
DMF		4.72§	
DMA			4.69§

^a This work, see the text. †, § — see footnotes in the text.

coherent set of log V_G° -values at five given temperatures. Explanatory variables are available for all 45 solutes,⁹⁻¹³ and so we can apply equations (3), (4), and (5) at each temperature. Preliminary results suggested that the solute hydrogen-bond basicity, β_2^H was not important, as expected on general chemical grounds,[†] and so we can reduce the equations to four explanatory variables.

In the event, neither δ_2 in equation (3) nor R_2 in equation (4) were significant, and so both equations reduce to a three-parameter equation in π_2^* , α_2^H , and $\log L^{16}$. The 45 solutes studied are listed in Table 1, and a summary of the regressions is in Table 2. Gmehling and co-workers⁶ repeated some of their measurements of V_G° but since there is excellent agreement between the old⁴ and the new⁶ sets, we took V_G° all from the earlier set, for convenience. We also investigated use of equation (5), and details are collected in Table 3.

Equations (3) and (4), with δ_2 , R_2 , and β_2^H non-significant, reproduce the log V_G° -values with an overall standard deviation of 0.1 log units, at the various temperatures given. Considering that this represents 'all solute' correlations, with no outliers at all, agreement between observed and calculated log V_G° is quite satisfactory. These equations could therefore be used to predict further log V_G° -values for a large number of solutes for which the necessary parameters are available.

Gmehling and co-workers also reported V_G° -values in NMP for 31 solutes at 323.4, 333.2, and 343.4 K. We have similarly analysed these data, as log V_G° , and have also extrapolated the V_G° -values down to 298.2 K to obtain another regression equation. As with NFM, the parameters δ_2 , R_2 , and β_2^H in equations (3) and (4) were not significant, and the latter parameter was not significant in equation (5). Details are in Tables 4 and 5. Once again equations (3) and (4) reproduce the log V_G° -values to ca. 0.1 log unit, with again no solutes being excluded. Thus equations (3) and (4) with the constants in Table 4 can be used to predict log V_G° for further solutes.

In the case of NMP, there is a very considerable quantity of literature data available, mostly on vapour-liquid equilibria,¹⁴⁻²⁴ and we have recast these data in terms of log L_{NMP} at 298 K. Here, L_{NMP} refers to the Ostwald solubility coefficient of a solute in NMP solvent, see equation (1). Some of these data overlap with those of Gmehling and co-workers,^{4,6} but in order to have as independent a set of results as possible,

† Neither NFM nor NMP can act as hydrogen-bond acids, and hence solute hydrogen-bond basicity plays no part in any solute-solvent interactions.

‡ Calculated from high pressure data given in ref. 14.

§ Taking $\gamma^\infty = 1$, by definition.

Table 7. Correlations of log *L* for 60 solutes^a in NMP at 298 K.

	<i>c</i>	<i>d</i>	<i>r</i>	<i>s</i>	<i>q</i>	<i>a</i>	<i>l</i>	<i>SD</i>	<i>R</i>
Equation (3)	-0.276 0.043	-0.170 0.089		2.157 0.072		5.134 0.229	0.870 0.017	0.148	0.995
Equation (4)	-0.283 0.040		0.454 0.121	1.998 0.072		5.085 0.212	0.851 0.016	0.137	0.996
Equation (5)	-0.195 0.071		1.458 0.198		0.126 0.009	5.676 0.377	0.839 0.029	0.247	0.985

^a These are the 60 data entries in Table 6.**Table 8.** Correlations of log *L* for 53 solutes^a in DMF at 298 K.

	<i>c</i>	<i>d</i>	<i>r</i>	<i>s</i>	<i>q</i>	<i>a</i>	<i>l</i>	<i>SD</i>	<i>R</i>
Equation (3)	-0.231 0.047	-0.366 0.109		2.561 0.090		4.612 0.165	0.839 0.021	0.149	0.994
Equation (4)	-0.207 0.051			2.482 0.096		4.585 0.182	0.829 0.023	0.164	0.993
Equation (5)	-0.145 0.072		1.387 0.193		0.119 0.008	5.830 0.244	0.823 0.034	0.233	0.986

^a These are the 53 data entries in Table 6.**Table 9.** Correlations of log *L* for 27 solutes^a in DMA at 298 K.

	<i>c</i>	<i>d</i>	<i>r</i>	<i>s</i>	<i>q</i>	<i>a</i>	<i>l</i>	<i>SD</i>	<i>R</i>
Equation (3)	-0.045 0.114	-0.346 0.168		2.229 0.128		4.984 0.261	0.802 0.052	0.169	0.992
Equation (4)	-0.001 0.120			2.196 0.136		4.864 0.271	0.782 0.054	0.181	0.991
Equation (5)	-0.003 0.096		1.158 0.153		0.115 0.006	6.222 0.201	0.796 0.044	0.145	0.994

^a These are the 27 data entries in Table 6.**Table 10.** Comparison of characteristic constants for solvents and GLC stationary phases, equation (4).

Solvent	<i>T</i> /K	<i>r</i> · <i>R</i> ₂	<i>s</i> · π ₂ [*]	<i>a</i> · α ₂ ^H	<i>l</i> · log <i>L</i> ¹⁶
NFM ^a	298		2.31	4.33	0.708
NMP ^b	298	0.45	2.00	5.09	0.851
DMF ^c	298		2.48	4.58	0.829
DMA ^d	298		2.20	4.86	0.782
NFM ^e	393		1.52	2.24	0.442
NMP ^e	393		1.42	2.70	0.472
Carbowax ^f	393	0.26	1.37	2.11	0.442
DEGS ^f	393	0.35	1.70	1.92	0.396
PPE ^f	393	0.19	0.98	0.59	0.552
TCEP ^f	393	0.23	2.12	1.94	0.379
ZE7 ^f	393	-0.38	1.61	0.70	0.442

^a Table 2. ^b Table 7. ^c Table 8. ^d Table 9. ^e Extrapolated data from results in Tables 2 and 4. ^f From ref. 10.

we have used Gmehling's data as an additional source only.* Details of the log *L*_{NMP}-values are in Table 6, and a summary of our obtained regression equations is in Table 7. Bearing in mind

* We calculated log *L*_{NMP} at 298 K by using the equation log *L*_{NMP} = log *V*_G⁰ + 0.0499.

the different set of solutes studied, there is quite good agreement between the various equations in Table 7 and those given before in Tables 4 and 5 (the 31 solutes of Tables 4 and 5 are a subset of the 60 solutes in Table 7).

We shall consider in more detail the actual constants listed in Table 7, but now set out values of log *L* for a range of solutes in *N,N*-dimethylformamide (DMF) and in *N,N*-dimethylacetamide (DMA). These are two additional *N*-substituted amides for which there are a large number of log *L*-values at 298 K that can be obtained from a variety of additional literature sources.²⁵⁻³⁴ Values of log *L*_{DMF} and log *L*_{DMA} are collected in Table 6. Although there are a reasonable number of hydrogen-bond bases in these two sets, there are but few hydrogen-bond acids. Since these are very important in characterising phases or solvents that are themselves hydrogen-bond bases, we determined a few values of log *L*_{DMF} and log *L*_{DMA} for alcohols by the method of headspace analysis, exactly as we have detailed before.¹¹

We have to hand log *L*-values for 53 assorted solutes in DMF and for 27 solutes in DMA (Table 6), and give summaries of the obtained regression equations in Tables 8 and 9. Bearing in mind the diverse sources of the data used, the correlation equations (3) and (4) lead to quite satisfactory results. These equations could be used as 'all solute' correlations to predict further log *L*-values for a variety of solutes. For both DMF and DMA the *r* · *R*₂ term in equation (4) is not significant, but this

Table 11. Solute parameters used in the regressions.

No.	Compound	δ_2	R_2	μ_2^2	π_2^*	α_2^H	$\log L^{16}$
3	Argon	0.00	0.000	0.000	0.00	0.00	-0.688
11	Hydrogen	0.00	0.000	0.000	0.00	0.00	-1.200
15	Nitrogen	0.00	0.000	0.000	0.00	0.00	-0.978
18	Ammonia	0.00	0.139	2.074	0.34	0.10	0.680
21	Carbon monoxide	0.00	0.000	0.010	0.02	0.00	-0.812
50	Methane	0.00	0.000	0.000	0.00	0.00	-0.323
51	Ethane	0.00	0.000	0.000	0.00	0.00	0.492
52	Propane	0.00	0.000	0.000	0.00	0.00	1.050
53	n-Butane	0.00	0.000	0.000	0.00	0.00	1.615
54	Isobutane	0.00	0.000	0.000	0.00	0.00	1.409
55	n-Pentane	0.00	0.000	0.000	0.00	0.00	2.162
56	2-Methylbutane	0.00	0.000	0.000	0.00	0.00	2.013
58	n-Hexane	0.00	0.000	0.000	0.00	0.00	2.668
63	n-Heptane	0.00	0.000	0.000	0.00	0.00	3.173
72	n-Octane	0.00	0.000	0.000	0.00	0.00	3.677
86	2,2,4-Trimethylpentane	0.00	0.000	0.000	0.00	0.00	3.120
91	n-Nonane	0.00	0.000	0.000	0.00	0.00	4.182
126	n-Decane	0.00	0.000	0.000	0.00	0.00	4.686
284	Cyclopentane	0.00	0.263	0.000	0.00	0.00	2.447
288	Methylcyclopentane	0.00	0.225	0.000	0.00	0.00	2.771
287	Cyclohexane	0.00	0.305	0.000	0.00	0.00	2.913
293	Methylcyclohexane	0.00	0.244	0.000	0.00	0.00	3.252
308	1,2-trans-Dimethylcyclohexane	0.00	0.227	0.000	0.00	0.00	3.550
307	1,2-cis-Dimethylcyclohexane	0.00	0.281	0.000	0.00	0.00	3.760
312	1,4-trans-Dimethylcyclohexane	0.00	0.191	0.000	0.00	0.00	3.550
311	1,4-cis-Dimethylcyclohexane	0.00	0.204	0.000	0.00	0.00	3.700
313	Ethylcyclohexane	0.00	0.263	0.000	0.00	0.00	3.590
314	n-Propylcyclohexane	0.00	0.257	0.000	0.00	0.00	3.930
315	n-Butylcyclohexane	0.00	0.255	0.000	0.00	0.00	4.270
370	Ethene	0.00	0.107	0.000	0.08	0.00	0.289
371	Propene	0.00	0.103	0.134	0.08	0.00	0.946
373	But-1-ene	0.00	0.100	0.116	0.08	0.00	1.491
380	Pent-1-ene	0.00	0.093	0.116	0.08	0.00	2.013
383	3-Methylbut-1-ene	0.00	0.063	0.250	0.08	0.00	1.910
379	2-Methylbut-2-ene	0.00	0.159	0.116	0.08	0.00	2.190
392	Hex-1-ene	0.00	0.078	0.116	0.08	0.00	2.547
409	Oct-1-ene	0.00	0.094	0.116	0.08	0.00	3.591
387	Buta-1,3-diene	0.00	0.320	0.068	0.20	0.00	1.543
389	2-Methylbuta-1,3-diene	0.00	0.313	0.144	0.20	0.00	2.130
390	2,3-Dimethylbuta-1,3-diene	0.00	0.352	0.270	0.20	0.00	2.690
385	(E)-Penta-1,3-diene	0.00	0.385	0.342	0.20	0.00	2.250
384	(Z)-Penta-1,3-diene	0.00	0.345	0.250	0.20	0.00	2.280
427	Cyclopentadiene	0.00	0.417	0.281	0.35	0.00	2.222
454	Pent-1-yne	0.00	0.172	0.740	0.20	0.13	2.010
751	Benzene	1.00	0.610	0.000	0.59	0.00	2.803
752	Toluene	1.00	0.601	0.130	0.55	0.00	3.344
753	2-Xylene	1.00	0.663	0.384	0.51	0.00	3.937
754	3-Xylene	1.00	0.623	0.160	0.51	0.00	3.864
755	4-Xylene	1.00	0.613	0.000	0.51	0.00	3.858
766	Ethylbenzene	1.00	0.613	0.348	0.53	0.00	3.765
768	Isopropylbenzene	1.00	0.602	0.152	0.53	0.00	4.105
551	Chloromethane	0.00	0.249	3.764	0.40	0.00	1.163
552	Dichloromethane	0.50	0.387	2.624	0.82	0.13	2.019
553	Trichloromethane	0.50	0.425	1.020	0.58	0.20	2.480
605	Bromoethane	0.00	0.366	4.121	0.48	0.00	2.120
651	Iodomethane	0.00	0.676	2.624	0.40	0.00	2.106
655	Iodoethane	0.00	0.640	2.924	0.50	0.00	2.573
1351	Dimethyl ether	0.00	0.000	1.664	0.27	0.00	1.090
1421	1,4-Dioxane	0.00	0.329	8.500	0.67	0.00	2.797
1553	Butanal	0.00	0.187	7.398	0.65	0.00	2.270
1554	2-Methylpropanal	0.00	0.144	7.290	0.65	0.00	2.060
1555	Pentanal	0.00	0.163	6.760	0.65	0.00	2.770
1570	(E)-But-2-enal	0.00	0.387	12.530	0.75	0.00	2.570
1651	Acetone	0.00	0.179	8.294	0.71	0.04	1.760
1653	Pentan-2-one	0.00	0.143	7.290	0.65	0.00	2.755
1654	Pentan-3-one	0.00	0.154	7.398	0.65	0.00	2.811
1662	4-Methylpentan-2-one	0.00	0.111	7.290	0.65	0.00	3.050
1860	Methyl acetate	0.00	0.142	2.958	0.60	0.00	1.960
1861	Ethyl acetate	0.00	0.106	3.168	0.55	0.00	2.376
1862	n-Propyl acetate	0.00	0.092	3.420	0.55	0.00	2.878
1882	Ethyl propanoate	0.00	0.087	3.240	0.55	0.00	2.881

Table 11 (continued).

No.	Compound	δ_2	R_2	μ_2^2	π_2^*	α_2^H	$\log L^{16}$
1888	Ethyl butanoate	0.00	0.106	3.240	0.55	0.00	3.379
1880	Vinyl acetate	0.00	0.223	2.890	0.55	0.00	2.600
2201	Acetonitrile	0.00	0.237	15.366	0.75	0.09	1.560
2202	Propanonitrile	0.00	0.162	16.000	0.70	0.00	2.050
2101	Nitromethane	0.00	0.313	11.972	0.85	0.12	1.892
2301	Methylamine	0.00	0.250	1.664	0.32	0.00	1.300
2321	Dimethylamine	0.00	0.189	0.941	0.25	0.00	1.600
2340	Trimethylamine	0.00	0.140	0.375	0.15	0.00	1.620
2346	Triethylamine	0.00	0.101	0.490	0.15	0.00	3.077
3601	Thiophene	1.00	0.687	0.325	0.60	0.00	2.943
4561	Tetramethyltin	0.00	0.000	0.000	0.00	0.00	2.920
3351	Water	0.00	0.000	3.497	0.43	0.65	0.260
3352	Methanol	0.00	0.278	2.890	0.40	0.37	0.922
3353	Ethanol	0.00	0.246	2.856	0.40	0.33	1.485
3354	Propan-1-ol	0.00	0.236	2.822	0.40	0.33	2.097
3355	Propan-2-ol	0.00	0.212	2.756	0.40	0.32	1.821
3356	Butan-1-ol	0.00	0.224	2.756	0.40	0.33	2.601
3357	Butan-2-ol	0.00	0.217	2.723	0.40	0.32	2.338
3359	t-Butyl alcohol	0.00	0.180	2.657	0.40	0.32	2.018
3497	2,2,2-Trifluoroethanol	0.50	0.015	4.121	0.73	0.57	1.224
2854	N-methylpyrrolidin-2-one	0.00	0.481	16.728	0.92	0.00	4.320
2503	N,N-dimethylformamide	0.00	0.367	14.900	0.88	0.00	3.173
2509	N,N-dimethylacetamide	0.00	0.363	13.838	0.88	0.00	3.717

may be due to lack of solutes with high R_2 -values in the correlations. In general, however, the correlation equations for DMF and DMA follow closely those for NMP (*cf.* Tables 8 and 9 with Table 7). This is exactly as expected, because all three of these amides are quite dipolar and all three are quite strong hydrogen-bond bases. From the results shown in Tables 7–9, the amides NMP, DMF, and DMA are of quite similar dipolarity with s -constants 2.00, 2.48, and 2.20, respectively, in equation (4), and q -constants 0.126, 0.119, and 0.115, respectively, in equation (5). The hydrogen-bond basicities of these amides are also very similar, being for NMP, DMF, and DMA in the sequence of a -values 5.09, 4.58, and 4.86 (compare the solvent hydrogen-bond β_1 basicity values of 0.77, 0.69, and 0.76, respectively).³⁵ The other amide studied, NFM, is of about the same dipolarity but of somewhat lower basicity than NMP, DMF, and DMA; see the collected results in Table 10.

We have previously¹⁰ characterised a number of stationary phases used in gas-liquid chromatography (GLC), and it would be of considerable interest to compare such phases with common solvents. The GLC phases were studied at 393 K, but we have found that the constants in equation (4) obtained for NFM and NMP at lower temperatures can be extrapolated to 393 K through excellent plots against $1/T(K)$; see Table 10.

It is quite clear from results in Table 10, and from results in Tables 2–5, that characteristic constants in equations such as (4) alter markedly with temperature. In general, it is to be expected that solute-solvent interactions would decrease with a rise in temperature, simply as a result of increased thermal motion. Indeed, hydrogen-bond complexation constants between a given acid and a given base do invariably decrease with increase in temperature. In the present case, any decrease in solute-solvent interactions could be due both to effects on the solute and on the solvent. We have no means of separating these, and hence adopt the convention that any change in a characteristic constant with temperature is due to a change in solvent property only. This does not matter as regards inter-solvent comparisons, which is what we are concerned with, but it would be important if absolute values of solvent properties were required.

In Table 10 we report constants in equation (4) at 393 K for NFM and NMP, together with those for five GLC phases.¹⁰

Table 12. Calculation of the solute-solvent interactions that influence $\log L$ -values in DMF at 298 K, *via* equation (4).

Solute	$s \cdot \pi_2^*$	$a \cdot \alpha_2^H$	$l \cdot \log L^{16}$	Dis- persion ^a	Cavity ^a
Butane	0	0	1.35	3.38	–1.47
Octane	0	0	3.05	6.42	–2.69
Benzene	1.46	0	2.32	4.29	–1.56
Propanone	1.76	0	1.46	2.65	–1.19
Propan-1-ol	0.99	1.51	1.74	2.86	–1.29

^a Obtained by analysis of the $l \cdot \log L^{16}$ term according to Abraham and Fuchs.³⁶ The two effects do not exactly add up to $l \cdot \log L^{16}$ because of omission of a constant term, and a small dipole-induced dipole term.

Our above-stated comments on temperature effects are very relevant: at 298 K both NFM and NMP appear to be more dipolar and very much more basic than any of the GLC phases. However, at a common temperature of 393 K, NFM and NMP are somewhat less dipolar than tricyano(ethoxy)propane (TCEP), diethyleneglycol succinate (DEGS), and Zonyl E-7® (ZE7), although more dipolar than poly(phenyl ether) (PPE). At 393 K, the hydrogen-bond basicity of NFM and NMP is not a great deal larger than that of the more basic GLC phases: Carbowax®, TCEP, and DEGS. The l -constant represents a combination of cavity effects and general dispersion interactions,¹⁰ but as regards GLC separations its importance lies in the separation of members of homologous series. The larger the l -constant, the greater will be the separation. There are no very remarkable values of the l -constant in Table 10: as might be expected, PPE has a reasonably high value of 0.55, DEGS and TCEP the lowest values, with the amides and the other GLC phases in between.

We can conclude that equations (3)–(5) yield useful information on solute-solvent interactions and that the constants in equation (4), especially, can be used to characterise solvents in terms of such interactions. Together with previous results,¹⁰ we can demonstrate that the constants in equation (4) are useful in a general method for characterising condensed phases, and lead, for the first time, to a comparison of GLC stationary phases with common solvents.

Finally, we collect in Table 11 all the solute parameters used in the regression analysis. Note that, for 1,4-dioxane, an 'effective' value of 8.5 is used for μ_2^H and one of 0.67 for π_2^H .

Solute-Solvent Interactions.—Our preferred equation (4) can be used to separate out the various contributions to the observed $\log L$ -values for any particular solute. Details for solutes in DMF at 298 K are in Table 12, with a number of compounds taken as examples. The $l \cdot \log L^{16}$ term is always very large, and only if the solute π_2^H -value or α_2^H -value is substantial do the $s \cdot \pi_2^H$ and $a \cdot \alpha_2^H$ terms make comparable contributions. Abraham and Fuchs³⁶ separated out various contributions to the $\log L^{16}$ term itself, the two main ones being an exoergic dispersion interaction that leads to an increase in $\log L^{16}$, and an endoergic cavity term that leads to a decrease in $\log L^{16}$. If we assume that, as a first approximation, the relative sizes of these effects is the same in DMF, we can further subdivide the $l \cdot \log L^{16}$ term into dispersion and cavity effects; see Table 12. The results show very clearly that, of the exoergic solute-solvent effects we have considered, the general dispersion interaction is always the most important.

In terms of GLC analyses, separations of adjacent members of an homologous series will be governed by differences in dispersion interactions and cavity effects. These two influences are together contained in the $l \cdot \log L^{16}$ term—the larger the value of l , the greater will be the separation between members of a homologous series. Interactions of the dipole-dipole and hydrogen-bonding types will obviously influence separations of solutes of different functionalities, even though in general they are not so large as general dispersion effects.

Acknowledgements

We thank the US Army Research Development, and Standardisation Group for support under Contract DAJA 45-87-C-0004, and David Walsh for help with the headspace analyses.

References

- 1 H. M. Smiley, *J. Chem. Eng. Data*, 1970, **15**, 413.
- 2 N. N. Kedrina, L. V. Semenov, A. A. Gaile, and T. A. Bispen, *Zh. Fiz. Khim.*, 1983, **57**, 2930 [*Russ. J. Phys. Chem. (Engl. Transl.)*, 1983, **57**, 1776].
- 3 P. O. Ferreira, J. C. Bastos, and A. G. Medina, *J. Chem. Eng. Data*, 1987, **32**, 25.
- 4 U. Weidlich, H.-J. Röhm, and J. Gmehling, *J. Chem. Eng. Data*, 1987, **32**, 450.
- 5 A. O. Bender, H. A. Zainel, T. M. Sarkissian, and E. K. Talib, *J. Pet. Res. Iraq*, 1988, **7**, 131.
- 6 C. Knoop, D. Tiegs, and J. Gmehling, *J. Chem. Eng. Data*, 1989, **34**, 240.
- 7 M. H. Abraham, *J. Chem. Soc., Faraday Trans. 1*, 1984, **80**, 153.
- 8 M. H. Abraham, P. L. Grellier, R. A. McGill, R. M. Doherty, M. J. Kamlet, T. N. Hall, R. W. Taft, P. W. Carr, and W. J. Koros, *Polymer*, 1987, **28**, 1363.
- 9 M. H. Abraham, P. L. Grellier, I. Hamerton, R. A. McGill, D. V. Prior, and G. S. Whiting, *Faraday Discuss. Chem. Soc.*, 1988, **85**, 107.
- 10 M. H. Abraham, G. S. Whiting, R. M. Doherty, and W. J. Schuele, *J. Chem. Soc., Perkin Trans. 2*, 1990, 1451.
- 11 M. H. Abraham, P. L. Grellier, and R. A. McGill, *J. Chem. Soc., Perkin Trans. 2*, 1987, 797.
- 12 M. H. Abraham, P. P. Duce, P. L. Grellier, D. V. Prior, J. J. Morris, and P. J. Taylor, *Tetrahedron Lett.*, 1988, **29**, 1587.
- 13 M. H. Abraham, P. L. Grellier, D. V. Prior, P. P. Duce, J. J. Morris, and P. J. Taylor, *J. Chem. Soc., Perkin Trans. 2*, 1989, 699.
- 14 Solubility Data Project Series; vol. 9, ed. W. Hayduk, 1982; vol. 21, eds. C. L. Young and P. G. T. Fogg, 1985; vol. 24, ed. W. Hayduk, 1986, Pergamon, Oxford.
- 15 R. Battino, T. R. Rettich, and T. Tominaga, *J. Phys. Chem. Ref. Data*, 1984, **13**, 563.
- 16 S. Wu, S. Zeck, and H. Knapp, *Ber. Bunsenges. Phys. Chem.*, 1985, **89**, 1009, 1013.
- 17 S. F. Shakova and Yu. P. Zubchenko, *Khim. Prom. (Moscow)*, 1973, **49**, 595.
- 18 J.-Y. Lenoir, P. Renault, and H. Renon, *J. Chem. Eng. Data*, 1971, **16**, 340.
- 19 M. H. Abraham, P. L. Grellier, and R. A. McGill, *J. Chem. Soc., Perkin Trans. 2*, 1988, 339.
- 20 J. H. Park, A. Hussam, P. Couasnon, D. Fritz, and P. W. Carr, *Anal. Chem.*, 1987, **59**, 1970.
- 21 I. Kikic and H. Renon, *Sep. Sci.*, 1976, **11**, 45.
- 22 P. Vernier, C. Raimbault, and H. Renon, *J. Chim. Phys.*, 1969, **66**, 429.
- 23 R. Alexander, E. C. F. Ko, A. J. Parker, and T. J. Broxton, *J. Am. Chem. Soc.*, 1968, **90**, 5049.
- 24 W. V. Wilding, L. C. Wilson, and G. M. Wilson, in American Institute of Chemical Engineers Symposium Series, No. 256, 1987, vol. 83, p. 49.
- 25 W. V. Wilding, L. C. Wilson, and G. M. Wilson, ref. 24, p. 80.
- 26 R. Schmidt, M. Geis, and H. Kelm, *Z. Phys. Chem. (Frankfurt am Main)*, 1974, **92**, 223.
- 27 E. Brunner, *Ber. Bunsenges. Phys. Chem.*, 1978, **82**, 798; 1979, **83**, 715.
- 28 M. H. Abraham, *J. Am. Chem. Soc.*, 1982, **104**, 2085.
- 29 H. Itsuki, H. Shigeta, and S. Terasawa, *Chromatographia*, 1989, **27**, 359.
- 30 E. R. Thomas, B. A. Newman, T. C. Long, D. A. Wood, and C. A. Eckert, *J. Chem. Eng. Data*, 1982, **27**, 399.
- 31 C. H. Deal and E. L. Derr, *Ind. Eng. Chem., Process Des. Dev.*, 1964, **3**, 394.
- 32 W. Gerrard, *J. Appl. Chem. Biotechnol.*, 1972, **22**, 623.
- 33 M. H. Abraham and P. L. Grellier, *J. Chem. Soc., Perkin Trans. 2*, 1976, 1735.
- 34 B. G. Cox, A. J. Parker, and W. E. Waghorne, *J. Am. Chem. Soc.*, 1973, **95**, 1010.
- 35 M. H. Abraham, P. L. Grellier, J.-L. M. Abboud, R. M. Doherty, and R. W. Taft, *Can. J. Chem.*, 1988, **66**, 2673.
- 36 M. H. Abraham and R. Fuchs, *J. Chem. Soc., Perkin Trans. 2*, 1988, 523.

Paper 0/00782J

Received 20th February 1990

Accepted 31st May 1990

Michael H. Abraham,
 Gary S. Whiting, Yves Alarie,[○]
 Jeffrey J. Morris⁺,
 Peter J. Taylor⁺,
 Ruth M. Doherty^Δ,
 Robert W. Taft[▼] and
 Gunnar D. Nielsen[□]

Department of Chemistry,
 University College London,
 London WC1H 0AJ, UK

Hydrogen Bonding 12. A New QSAR for Upper Respiratory Tract Irritation by Airborne Chemicals in Mice.

Abstract

Upper respiratory tract irritation of male Swiss OF₁ mice by airborne chemicals is well correlated by the following equations for the toxicity of nonreactive compounds,

$$-\log \text{FRD}'_{50} = -0.69 + 0.77\delta_2 + 2.81\pi_2^* + 4.93\alpha_2^{\text{H}} + 2.82V_x$$

n = 39 r = 0.985 sd = 0.14

$$-\log \text{FRD}'_{50} = 0.60 + 1.35\pi_2^* + 3.19\alpha_2^{\text{H}} + 0.77 \log L^{16}$$

n = 39 r = 0.990 sd = 0.10

FRD'₅₀ is the concentration in mol l⁻¹ of the airborne chemical required to elicit a 50% decrease in respiratory rate, and the explanatory variables are δ_2 a polarisability correction term, π_2^* the solute dipolarity, α_2^{H} the solute hydrogen-bond acidity, V_x the characteristic volume, and L^{16} the gas/hexadecane partition coefficient. These equations considerably resemble corresponding equations for gas/liquid partition coefficients into organic bases such as tricesylphosphate, but do not resemble an equation for gas/water partition coefficients.

Correspondence: Dr. M.H. Abraham, Department of Chemistry, University College London, London WC1H 0AJ, UK.

[○] The Toxicology Laboratory, Department of Industrial Environmental Health Sciences, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, Pennsylvania 15261, USA

⁺ ICI Pharmaceutical Division, Mereside Alderly Park, Macclesfield, SK10 4TG, UK

^Δ Naval Surface Warfare Center, White Oak Laboratory, Silver Spring, Maryland 20903-5000, USA

[▼] Department of Chemistry, University of California, Irvine, California 92717, USA.

[□] Danish National Institute of Occupational Health, Lersø Parkallé 105, DK-2100, København Ø, Denmark

Abbreviations and Symbols: QSAR – quantitative structure-activity relationship; SP – the dependent variable; δ_2 – a polarisability correction term; π_2^* – the solute dipolarity; α_2^{H} – the solute hydrogen-bond acidity; β_2^{H} – the solute hydrogen-bond basicity; V_x – characteristic volume; L – a gas/liquid partition coefficient; L^{16} – a gas/hexadecane partition coefficient.

Key words: Upper respiratory tract irritation, toxicity, hydrogen-bond acidity, hydrogen-bond basicity, dipolarity, gas/liquid partition coefficients.

1 Introduction

The most common basis for the establishment of threshold limit values (TLVs) for exposure to airborne chemicals is that of sensory irritation of the eyes, nose, and throat. Many years ago, Alarie [1, 2] used an animal bioassay to evaluate sensory irritating properties of airborne chemicals, and later suggested that TLVs for industrial exposure to airborne chemicals could be recommended on the basis of animal bioassay [3]. Alarie [3] and DeCeaurrez *et al.* [4] both stressed this suggestion in subsequent studies. It is therefore of considerable importance to establish quantitative structure-activity relationships (QSARs) for result of animal bioassays in the hope that such QSARs will be applicable to TLVs for industrial exposure to airborne chemicals.

A first attempt was made by Muller and Greff [5] who analysed the sensory irritation of the upper respiratory tract in male Swiss OF₁ mice by 59 airborne chemicals, using results by DeCeaurrez *et al.* [4, 6]. These were given in terms of $\log 1/\text{FRD}_{50}$, where FRD_{50} is the concentration in mg/m³ required to elicit a 50% decrease in respiratory rate. Muller and Greff [5] were able to establish correlations between $\log 1/\text{FRD}_{50}$ and such physico-chemical properties as the normal boiling point, but only within families of compound, for example, saturated aliphatic alcohols, or aliphatic ketones. Roberts [7] then re-analysed the results used by Muller and Greff [5] by first of all recalculating FRD_{50} in units of mmol/m³. Using a modified $\log M/\text{FRD}_{50}$, Roberts did manage to establish a general QSAR for non-reactive compounds, Eq. (1), where M is the irritant molecular weight.

$$\log M/\text{FRD}_{50} = 0.0173T'_B - 4.090$$

n = 42 r = 0.987 s = 0.119

In Eq. (1), the explanatory variable T'_B is a modified normal boiling point in which T'_B for alcohols is taken as $(26.5T_B/22) - 8$ and in which T'_B for phenol is taken as $(24T_B/22) - 4$, where T_B is the normal boiling point in °C. As usual, n is the number of data points, r the correlation coefficient, and s the standard deviation. Roberts [7] explicitly described Eq. (1) as a QSAR for nonreactive compounds, and excluded all the twelve alkyl acetates studied, as well as methylvinylketone, allyl alcohol, crotyl alcohol, mesityl oxide, and vinyl toluene. Although Eq. (1) is statistically a good correlation, bearing in mind that the expected error in $\log M/\text{FRD}_{50}$

must be around 0.1 log units, it suffers from two marked deficiencies. First of all, the calculation of T'_B is simply a mathematical transformation that displaces parallel lines to the same position. Secondly, and very importantly, Eq. (1) provides no information at all about the mechanism of toxicity of nonreactive compounds. That is, although Eq. (1) was referred to as a QSAR [7], it actually involves no connection at all between structural features of the irritants and their toxicity.

We have approached this problem in a quite different way. If we deal only with toxicity of nonreactive compounds then the process leading to upper respiratory tract irritation may be regarded as akin to a form of partition of a given compound or solute between air and some condensed phase. We can then use equations that have already been employed to model the partition behaviour of a series of solutes, or the toxicity effects of a series of solutes. Equation (2) has been used to correlate both partition of solutes between water and octanol, and the nonreactive toxicity of aqueous solutes towards a variety of organisms [8], whilst both Eq. (2) and Eq. (3) have been used to analyse the gas/liquid partition of series of solutes [9, 10]. It is worth noting that for compounds that conform to a simple partition model, activity must be proportional to the concentration of the solute in the biophase. All such solutes will bind to the target receptor site with the same intrinsic potency, and the biological effect will be given by the fraction of receptor occupied.

$$SP = c + d.\delta_2 + s.\pi_2^* + a.\alpha_2 + b.\beta_2 + m.V_2 \quad (2)$$

$$SP = c + d.\delta_2 + s.\pi_2^* + a.\alpha_2 + b.\beta_2 + 1.\log L^{16} \quad (3)$$

In these equations, SP is the dependent variable, e.g. $\log FRD_{50}$ or a partition coefficient as $\log P$, and the explanatory variables are δ_2 a rather trivial polarisability correction term, π_2^* the solute dipolarity, α_2 the solute hydrogen-bond acidity, β_2 the solute hydrogen-bond basicity, V_2 the solute volume, and $\log L^{16}$ where L^{16} is the solute Ostwald solubility coefficient (or gas-liquid partition coefficient) on *n*-hexadecane at 298 K. As before, [8], δ_2 is taken as zero except for aromatic solutes ($\delta_2 = 1$), and polyhalogenated aliphatic solutes ($\delta_2 = 0.5$), and the dipolarity parameter π_2^* is also as before [8]. However, we now have to hand the extended results of Abraham and coworkers on a solute hydrogen-bond acidity scale, α_2^H , and a solute hydrogen-bond basicity scale, β_2^H [11–14]; we use McGowan's characteristic volume V_x as the solute size [15], and the $\log L^{16}$ values as determined before [16]. We have recalculated the FRD_{50} values of Muller and Greff [5] in units of mol l^{-1} (or mol dm^{-3}) and give values of $\log 10^6 M / FRD_{50}$, denoted as $-\log FRD'_{50}$, in Table 1 together with the parameters used in the calculations that follow. Except for twelve acetate esters, all the compounds studied by Muller and Greff are listed in Table 1, i.e. 47 compounds.

2 Results and Discussion

Applications of Eq. (2) and (3), where $SP = -\log FRD'_{50}$, to all 47 compounds leads to regressions with overall correlation coefficients, r , of only 0.510 on Eq. (2) and 0.568 on Eq. (3). The reason for these poor correlations is obvious – we have

included in the data set compounds that cannot be regarded as nonreactive toxicants. These compounds can be identified as “outliers” because their observed sensory irritation is much larger than values calculated through Eq. (2) or Eq. (3). If eight outliers are excluded, then the following regressions are obtained, with V_x in units of $\text{cm}^3 \text{mol}^{-1}/100$:

$$-\log FRD'_{50} = -(0.685 \pm 0.236) + (0.768 \pm 0.055)\delta_2 + (2.812 \pm 0.304)\pi_2^* + (4.929 \pm 0.300)\alpha_2^H + (2.820 \pm 0.090)V_x \quad (4)$$

$$n = 39 \quad r = 0.9845 \quad s = 0.136$$

$$-\log FRD'_{50} = (0.596 \pm 0.165) + (1.354 \pm 0.224)\pi_2^* + (3.188 \pm 0.209)\alpha_2^H + (0.775 \pm 0.019)\log L^{16} \quad (5)$$

$$n = 39 \quad r = 0.9902 \quad s = 0.103$$

Eq. (5) with three explanatory parameters is clearly superior to Eq. (4), although the two equations lead to closely similar conclusions. However, in some circumstances, Eq. (4) might be preferred simply because it is easy to calculate V_x for any compound. The outliers to Eq. (4) and Eq. (5) are shown in Tables 2 and 3. Methylvinylketone, allyl alcohol, crotyl alcohol, mesityl oxide and 4-vinyltoluene are all much more toxic than calculated, by some $1\frac{1}{2}$ to $3\frac{1}{2}$ log units.

These five compounds were considered by Roberts [7] also to be outliers, to Eq. (1), possibly due to their reactive electrophilic character. In the case of 4-vinyltoluene, Roberts [7] suggested the oxidation of the methyl group to an aldehyde group aided by the electrophilic character of the 4-vinyl group. The present analysis suggests that on Eq. (4) cyclohexanone and 1,4-divinylbenzene are slightly more toxic than calculated and that phenol is much less toxic than calculated. However, on Eq. (5), the compounds 1,4-divinylbenzene and β -chloroethylbenzene are slightly more toxic than calculated and phenol is, again, decidedly less toxic than calculated. Since Eq. (5) is theoretically and practically the better equation, we discount cyclohexanone as an outlier, and suggest that possibly the two compounds 1,4-divinylbenzene and β -chloroethylbenzene may be outliers. The position of these two compounds is marginal as can be seen from a plot of Eq. (5), shown in Fig. 1. If 1,4-divinylbenzene and β -chloroethylbenzene are included, then application of Eq. (3) yields the regression,

$$-\log FRD'_{50} = (0.597 \pm 0.199) + (1.287 \pm 0.267)\pi_2^* + (3.110 \pm 0.251)\alpha_2^H + (0.794 \pm 0.022)\log L^{16} \quad (6)$$

$$n = 41 \quad r = 0.9860 \quad sd = 0.127$$

There is not a great deal of difference between Eq. (5) and Eq. (6), and it is a moot point whether or not 1,4-divinylbenzene and β -chloroethylbenzene are considered to be slightly reactive toxicants or not.

Phenol, however, is anomalous on all the equations we have used. It is possible that there is a rather large experimental error associated with phenol. On the other hand, phenols can be efficiently removed from the system by diffusion from the receptor compartment to the blood compartment where the concentration is kept low via conjugation with glucoronides or by sulphation.

Table 1. Parameters used in the calculations

Solute	δ_2	π_2^*	α_2^H	β_2^H	$\log L^{16}$	V_x	$-\log FRD'_{50}$
2-propanone	0.00	0.71	0.04	0.50	1.760	0.547	3.01
but-1-ene-3-one	0.00	0.70	0.00	0.48	2.330	0.645	6.67
2-butanone	0.00	0.67	0.00	0.48	2.287	0.688	3.36
2-pentanone	0.00	0.65	0.00	0.48	2.755	0.829	3.61
mesityl oxide	0.00	0.70	0.00	0.55	3.300	0.927	5.60
cyclohexanone	0.00	0.76	0.00	0.52	3.616	0.861	4.51
2-hexanone	0.00	0.65	0.00	0.48	3.262	0.970	3.98
4-methyl-2-pentanone	0.00	0.65	0.00	0.48	3.050	0.970	3.88
3,3-dimethyl-2-butanone	0.00	0.65	0.00	0.48	2.887	0.970	3.64
2-heptanone	0.00	0.65	0.00	0.48	3.760	1.111	4.44
4-heptanone	0.00	0.65	0.00	0.48	3.820	1.111	4.35
5-methyl-2-hexanone	0.00	0.65	0.00	0.48	3.670	1.111	4.30
2-octanone	0.00	0.65	0.00	0.48	4.257	1.252	4.71
5-methyl-3-heptanone	0.00	0.65	0.00	0.48	4.200	1.251	4.51
5-nonanone	0.00	0.65	0.00	0.48	4.640	1.392	4.95
2,6-dimethyl-4-heptanone	0.00	0.65	0.00	0.48	4.180	1.392	4.88
2-undecanone	0.00	0.65	0.00	0.48	5.760	1.674	5.83
methanol	0.00	0.40	0.37	0.41	0.922	0.308	2.99
ethanol	0.00	0.40	0.33	0.44	1.485	0.449	3.21
1-propanol	0.00	0.40	0.33	0.45	2.097	0.590	3.71
2-propanol	0.00	0.40	0.32	0.47	1.821	0.590	3.69
1-butanol	0.00	0.40	0.33	0.45	2.601	0.731	4.29
2-methyl-1-propanol	0.00	0.40	0.33	0.45	2.399	0.731	4.13
1-pentanol	0.00	0.40	0.33	0.45	3.106	0.872	4.60
3-methyl-1-butanol	0.00	0.40	0.33	0.45	3.011	0.872	4.52
1-hexanol	0.00	0.40	0.33	0.45	3.610	1.013	5.01
4-methyl-2-pentanol	0.00	0.40	0.32	0.47	3.400	1.013	4.76
1-heptanol	0.00	0.40	0.33	0.45	4.115	1.154	5.39
1-octanol	0.00	0.40	0.33	0.45	4.619	1.295	5.71
2-ethyl-1-hexanol	0.00	0.40	0.33	0.45	4.500	1.295	5.74
prop-2-en-1-ol, allyl-OH	0.00	0.45	0.33	0.41	1.996	0.547	7.18
but-2-en-1-ol, crotyl-OH	0.00	0.45	0.33	0.41	2.500	0.688	6.44
toluene	1.00	0.55	0.00	0.14	3.344	0.857	3.86
phenol	1.00	0.72	0.60	0.36	3.856	0.775	5.16
chlorobenzene	1.00	0.71	0.00	0.09	3.640	0.839	4.36
bromobenzene	1.00	0.79	0.00	0.09	4.035	0.891	4.78
1,2-dichlorobenzene	1.00	0.80	0.00	0.03	4.405	0.961	5.13
2-chlorotoluene	1.00	0.67	0.00	0.08	4.160	0.980	4.63
acetophenone	1.00	0.90	0.00	0.51	4.483	1.014	5.38
2-xylene	1.00	0.51	0.00	0.17	3.937	0.998	4.23
4-xylene	1.00	0.51	0.00	0.17	3.858	0.998	4.27
β -chloroethylbenzene	1.00	0.70	0.00	0.25	4.600	1.121	5.47
styrene	1.00	0.55	0.00	0.18	3.908	0.955	4.62
ethylbenzene	1.00	0.53	0.00	0.15	3.765	0.998	4.24
α -methylstyrene, PhMeCCH ₂	1.00	0.55	0.00	0.18	4.322	1.118	4.95
4-vinyltoluene	1.00	0.55	0.00	0.20	4.480	1.096	6.20
4-divinylbenzene	1.00	0.55	0.00	0.20	4.900	1.194	5.49

A class of compounds we have not yet considered is that of the alkyl acetates. Roberts [7] noted that alkyl acetates did not conform to his QSAR, Eq. (1), and suggested that the acetates were at least partially hydrolysed under the test conditions. Our analysis of the sensory irritant properties of the alkyl acetates is given in Table 4, and illustrated in Fig. 2. As the acetates become less susceptible to hydrolysis along the series MeCO₂R where R = Me, Et, Prⁿ, Pr^{iso}, Bu^{tert}, for example, so do the observed and calculated $-\log FRD'_{50}$ converge. The hydrolysis products, viz. acetic acid and alcohol, will together certainly be more potent than the ester itself. Thus for ethyl acetate, where

the observed value is 4.62 and the calculated value on Eq. (5) is 3.18 log units, our calculated value for the hydrolysis product is 4.52, and an observed value is 5.18 [4].

Our suggested QSAR, Eq. (5), thus seems to provide the basis for a reasonable analysis of the sensory irritation of the upper respiratory tract in male Swiss OF₁ mice by nonreactive compounds. If our model of such nonreactive toxicity as taking place via a process akin to partitioning is in any way realistic, we can go further and attempt to interpret the process using Eq. (5). The partition we refer to is simply that of airborne

Table 2. Outliers using the equation in V_x

$-\log\text{FRD}'_{50}$			
Outlier	Obs	Calc	Δ
methylvinylketone	6.67	3.10	3.57
mesityl oxide	5.60	3.90	1.70
cyclohexanone	4.51	3.88	0.63
allyl alcohol	7.18	3.75	3.43
crotyl alcohol	6.44	4.15	2.29
phenol	5.16	7.25	-2.09
4-vinyltoluene	6.20	4.72	1.48
1,4-divinylbenzene	5.49	5.00	0.49
Included			
β -chloroethylbenzene	5.47	5.21	0.36
styrene	4.62	4.32	0.30
α -methylstyrene	4.95	4.78	0.17

$-\log\text{FRD}'_{50} = -0.658 + 0.768\delta_2 + 2.812\pi_2^* + 4.929\alpha_2^H + 2.820 V_x$
 $r = 0.984 \quad s = 0.136 \quad n = 39$

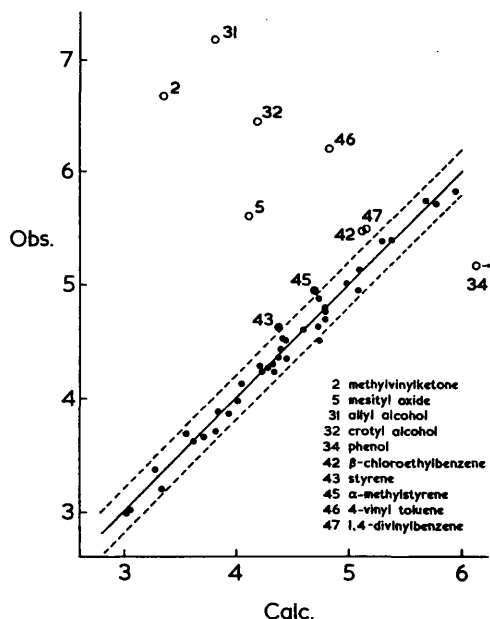
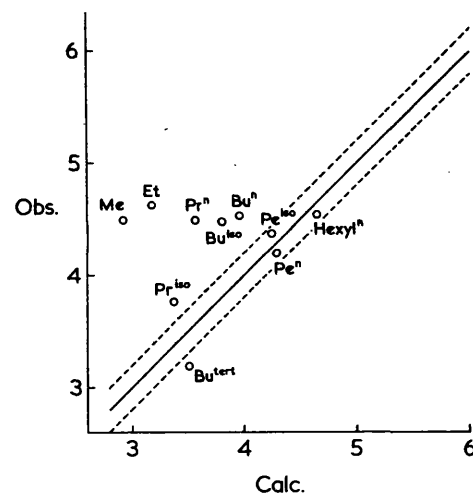
Table 3. Outliers using the equation in $\log L^{16}$

$-\log\text{FRD}'_{50}$			
Outlier	Obs	Calc	Δ
methylvinylketone	6.67	3.35	3.32
mesityl oxide	5.60	4.10	1.50
allyl alcohol	7.18	3.80	3.38
crotyl alcohol	6.44	4.19	2.25
phenol	5.16	6.47	-1.31
4-vinyltoluene	6.20	4.81	1.39
1,4-divinylbenzene	5.49	5.14	0.35
β -chloroethylbenzene	5.47	5.11	0.36
Included			
cyclohexanone	4.51	4.43	0.08
styrene	4.62	4.37	0.25
α -methylstyrene	4.95	4.69	0.26

$-\log\text{FRD}'_{50} = -0.596 + 1.354\pi_2^* + 3.188\alpha_2^H + 0.775\log L^{16}$
 $r = 0.990 \quad s = 0.103 \quad n = 39$

Table 4. Calculations on alkyl acetates.

$-\log\text{FRD}'_{50}$			
R in $\text{CH}_3\text{CO}_2\text{R}$	Obs	Calc ^a	Δ
Me	4.47	2.93	1.54
Et	4.62	3.18	1.44
n-Pr	4.49	3.57	0.92
iso-Pr	3.76	3.38	0.38
n-Bu	4.52	3.96	0.56
iso-Bu	4.47	3.81	0.66
t-Bu	3.18	3.51	-0.33
n-Pe	4.19	4.29	-0.10
iso-Pe	4.36	4.24	0.12
n-Hexyl	4.52	4.65	-0.13
2-Methoxyethyl	4.63	—	—
2-Ethoxyethyl	4.53	—	—

^a Using equation (5).**Figure 1.** Observed and calculated $-\log\text{FRD}'_{50}$ according to Eq. (5): • included points, o outliers. The dashed lines show $\pm$ two standard deviations.**Figure 2.** Deviations of alkyl acetates, $\text{CH}_3\text{CO}_2\text{R}$, from Eq. (5). The dashed lines show $\pm$ two standard deviations.

chemicals between the vapour phase and some condensed phase. Now since the hydrogen-bond basicity of the solutes is not significant on Eq. (5), we can infer that the condensed phase, whatever its nature, does not act as a hydrogen-bond acid. On the other hand, the coefficient of α_2^H in Eq. (5) is quite large, and hence we infer that the condensed phase behaves as a hydrogen-bond base.

We can place the coefficients of Eq. (5) in context, by comparison with those obtained for the partition of vapors between the gas phase and some particular solvent phase. Abraham *et al.* [10] have shown how the general equation (3; $\text{SP} = \log L$) can be applied to gas-liquid partitions. They gave as an example

the solvent tricresylphosphate (TCPH), taking logL (TCPH) values at 298 K from Alessi *et al.* [17].

$$\log L(\text{TCPH}) = -0.35 - 0.25\delta_2 + 1.71\pi_2^* + 2.98\alpha_2^H + 0.911 \log L^{16} \quad (7)$$

$$n = 22 \quad r = 0.991 \quad s = 0.09$$

Abraham and Whiting [18] have recently analysed logL values for the gas/N-methylpyrrolidinone (NMP) partition using results of Weidlich *et al.* [19] extrapolated to 298 K, Eq. (8).

$$\log L(\text{NMP}) = -0.11 + 2.10\pi_2^* + 5.05\alpha_2^H + 0.779 \log L^{16} \quad (8)$$

$$n = 31 \quad r = 0.988 \quad s = 0.11$$

Comparison with Eq. (5) suggests that the general receptor site acts as a reasonably polar area ($s = 1.354$) and has hydrogen-bond basicity about the same as TCPH but less than NMP, with $a = 3.188$ in Eq. (5). The receptor site is still reasonably hydrophobic with $l = 0.775$ (note that for the gas/hexadecane partition $l = 1$, by definition). Abraham *et al.* [10] also listed a provisional equation for gas/water partition, Eq. (9). It is very clear, by inspection, that Eq. (5) resembles equations for gas/organic solvent partitions, as in Eqs (7) and (8), but bears little resemblance to Eq. (9). The main differences are the minor dependence on $\log L^{16}$ and the dependence on β_2^H in Eq. (9), the latter dependence due to the strong hydrogen-bond acidity of water.

$$\log L(\text{water}) = -1.46 + 3.99\pi_2^* + 6.10\alpha_2^H + 3.22\beta_2^H - 0.060 \log L^{16} \quad (9)$$

$$n = 59 \quad r = 0.989 \quad s = 0.33$$

In conclusion, we have been able to construct a QSAR for nonreactive upper respiratory tract irritation in male Swiss OF₁ mice by airborne chemicals, Eq. (5), that will allow predictions of $-\log \text{FRD}'_{50}$ to be made. It must be noted, however, that predictions may be hazardous if the explanatory variables for the solutes concerned fall outside the range of those studied. Thus Franks and Lieb [20] have shown that in the inhibition of firefly luciferase activity by aqueous solutes, there is a definite "cut-off" effect in terms of solute size. Such an effect could not have been predicted by the analysis of a series of solutes all below the critical size. Our QSAR is additionally valuable in that it leads to some understanding of the partition mechanism of toxicity of nonreactive compounds. In future we hope to analyse results on Swiss-Webster male mice for which, at the moment, we are gathering relevant data.

3 Acknowledgements

MHA and GSW thank the US Army Research Development and Standardisation Group for support under Contract DAJA 45-87-C-0004.

Received on August 16th 1989; accepted on November 12th 1989

4 References

- [1] Alarie, Y., *Arch. Environ. Health* 13, 433 (1966).
- [2] Alarie, Y., *Toxicol. Appl. Pharmacol.* 24, 279 (1973).
- [3] Alarie, Y., *Food Cosmet. Toxicol.* 19, 623 (1981).
- [4] DeCaurriz, J.C., Micillino, J.C., Bonnet, P., and Guenier, J.P., *Toxicol. Lett.* 9, 137 (1981).
- [5] Muller, J., and Greff, G., *Fd. Chem. Toxicol.* 22, 661 (1984).
- [6] DeCaurriz, J.C., Desiles, J.P., Bonnet, P., Guenier, J.P., and Muller, J., unpublished results, quoted in ref. [5].
- [7] Roberts, D.W., *Chem.-Biol. Interactions* 57, 325 (1986).
- [8] Kamlet, M.J., Doherty, R.M., Abraham, M.H., and Taft, R.W., *Quant. Struct.-Act. Relat.* 7, 71 (1988).
- [9] Abraham, M.H., Grellier, P.L., McGill, R.A., Doherty, R.M., Kamlet, M.J., Hall, T.N., Taft, R.W., Carr, P.W., and Koros, W.J., *Polymer* 28, 1363 (1987).
- [10] Abraham, M.H., Grellier, P.L., Hamerton, I., McGill, R.A., Prior, D.V. and Whiting, G.S., *Faraday Discuss. Chem. Soc.* 85, 107 (1988).
- [11] Abraham, M.H., Duce, P.P., Grellier, P.L., Prior, D.V., Morris, J.J., and Taylor, P.J., *Tetrahedron Letters* 19, 1587 (1988).
- [12] Abraham, M.H., Grellier, P.L., Prior, D.V., Duce, P.P., Morris, J.J., and Taylor, P.J., *J. Chem. Soc. Perkin Trans. 2*, 699 (1989).
- [13] Abraham, M.H., Grellier, P.L., Prior, D.V., Morris, J.J., Taylor, P.J., Laurence, C., and Berthelot, M., *Tetrahedron Letters* 30, 2571 (1989).
- [14] Abraham, M.H., Grellier, P.L., Prior, D.V., Morris, J.J., and Taylor, P.J., *J. Chem. Soc. Perkin Trans. 2*, submitted.
- [15] Abraham, M.H. and McGowan, J.C., *Chromatographia* 23, 243 (1987).
- [16] Abraham, M.H., Grellier, P.L., and McGill, R.A., *J. Chem. Soc. Perkin Trans. 2*, 797 (1987).
- [17] Alessi, P., Kikic, I., Papo, A., and Torriano, G., *J. Chem. Eng. Data* 23, 29 (1978).
- [18] Abraham, M.H. and Whiting, G.S., unpublished work.
- [19] Weidlich, U., Rohm, H.-J. and Gmehling, J., *J. Chem. Eng. Data* 32, 450 (1987).
- [20] Franks, N.P., and Lieb, W.R., *Nature* 316, 349 (1985).

Thermodynamics of Solute Transfer from Water to Hexadecane

Michael H. Abraham* and Gary S. Whiting

Chemistry Department, University College London, 20 Gordon St., London WC1H 0AJ

Richard Fuchs* and Eric J. Chambers

Department of Chemistry, University of Houston, Houston, Texas 77204-5641, USA

New measurements of enthalpies of solution in hexadecane and in water (ΔH_s°), and gas-hexadecane Ostwald solubility coefficients (L_H) of neutral monomeric organic solutes are reported. These values, together with literature values of ΔH_s° , L_H , and gas-water Ostwald solubility coefficients (L_W), have been used to derive the Gibbs energies, enthalpies, and entropies of solute transfer from water to hexadecane (ΔG_{tr}° , ΔH_{tr}° , and ΔS_{tr}°), as well as water-hexadecane partition coefficients (as $\log P_H$). Results have been examined by the method of multiple linear regression analysis, using the equation,

$$SP = c + d\delta_2 + s\pi_2^* + a\alpha_2 + b\beta_2 + vV_2$$

The $s\pi_2^*$ term is difficult to interpret, but the $a\alpha_2$ and $b\beta_2$ terms can be shown to arise through hydrogen bonding of solute molecules to the bulk water that is exothermic but rather disfavoured entropically. It is shown also that the vV_2 term arises due to a combination of cavity effects and general dispersion interactions in bulk water and bulk hexadecane.

The use of water-octanol partition coefficients is widespread in medicinal and pharmaceutical chemistry, and, indeed, forms part of the general rationale governing most quantitative structure-activity relationships (QSARs).¹ Although water-saturated octanol, according to this rationale, is a suitable model for biological membranes, other solvents, and hence other water-solvent partition coefficients, have also been used in QSARs. For example, Finkelstein² and, later, Franks and Lieb³ used water-hexadecane partition coefficients, the latter workers specifically to test for hydrophobic binding sites in the luciferase enzyme. In these studies the required water-hexadecane partition coefficients were obtained by the traditional 'shake-flask' method. Unlike the water-octanol system, in which the mutual miscibility of the two solvents is quite high, the water-hexadecane system can be regarded as a system containing the two pure solvents (the solubility of water in hexadecane is 2×10^{-3} mol dm⁻³ and that of hexadecane in water is 4×10^{-4} mol dm⁻³).⁴ Hence water-hexadecane partition coefficients can be determined indirectly using equation (1), where L_W and L_H are the respective gas-solvent

$$P_H = L_H/L_W \quad (1)$$

Ostwald solubility coefficients.† We,⁴ and Shantz and Martire,⁵ have shown almost simultaneously that values of P_H obtained indirectly *via* equation (1) are, indeed, identical with values determined by the direct 'shake-flask' method. Since the values of L_H can be measured very accurately by a gas-chromatographic method using hexadecane as the stationary phase,^{4,5} it is possible from known aqueous solubilities of gases⁶⁻¹⁰ to obtain P_H values relatively simply for a wide range of not-too-involatile solutes.

One of the aims of the present work is to set out values of P_H for the water-hexadecane partition of neutral, monomeric solutes, either as $\log P_H$ or as transfer Gibbs energies, ΔG_{tr}° , for as wide a range of solutes as possible. The second aim is to present values for the enthalpy, and hence the entropy, of transfer of examples of these solutes. To date, there have been very few sets of ΔG_{tr}° , ΔH_{tr}° , and ΔS_{tr}° values for partition from

water to a given solvent. The most substantial set of data is that of Riebeschl and Tomlinson,¹¹ who used a direct flow-microcalorimeter method to obtain ΔH_{tr}° values for transfer of 29 solutes from water to 2,2,4-trimethylpentane. We later analysed the thermodynamic results of Tomlinson and co-workers,^{11,12} but found¹³ that the data were not extensive enough to examine aliphatic and aromatic solutes separately. We have therefore obtained ΔH_{tr}° values through a combination of enthalpies of solution in water and in hexadecane separately, and set out ΔG_{tr}° , ΔH_{tr}° , and ΔS_{tr}° values for as many solutes as possible. We have, as well as our own calorimetrically determined ΔH_s° values, used literature data on ΔH_s° values in water and hexadecane, where possible, selecting calorimetrically determined values. Of course, for solutes that are gaseous at room temperature and pressure, ΔH_s° values have nearly always been obtained through the temperature variation of solubility—the so called van't Hoff method—but the method of direct calorimetry is to be preferred.

Experimental

Values of L_H for solutes on hexadecane at 298.15 K were obtained as described before.⁴ The instruments used were either a Pye-Unicam 104 chromatograph fitted with a katharometer detector, for the determination of absolute L_H values, or a Perkin-Elmer F-11 chromatograph fitted with a flame detector, for the determination of relative L_H values to be converted into absolute values.

Enthalpies of solution in hexadecane and in water were measured as described previously,¹⁴ with liquid solute samples of 10, 20, or 50 mm³ injected through Teflon-faced silicone septa into vapour-tight, vacuum-jacketed solution calorimeters containing 80–110 cm³ of solvent. For solutes which dissolve slowly the normal stirring speed of 300 rpm was increased to 600 rpm. Solutes and solvents, all of >99% purity, were dried with 4A molecular sieve, with the ex-

† Note that L_H is the same as L ,¹⁶ the symbol we previously used.⁴

Table 1. Thermodynamics of transfer of solutes from water to hexadecane, and calculation of ΔG_{tr}° (mole fraction scale) and $\log P_{Hl}$ (molar scale) for water to hexadecane at 298 K.

Solute	Water ^a		Hexadecane ^b		Water $\longrightarrow$ Hexadecane			$\log L_w$	$\log L_H$	$\log P_{Hl}$
	ΔG_s°	ΔH_s°	ΔG_s°	ΔH_s°	ΔG_{tr}°	ΔH_{tr}°	ΔS_{tr}°			
Helium	7.03	-0.16	4.99	1.97 ^c	-2.04	2.13	14.0	-2.023	-1.741	0.28
Neon	6.94	-0.92	4.77	1.62 ^c	-2.17	2.54	15.8	-1.958	-1.575	0.38
Argon	6.27	-2.93	3.56	-0.19 ^c	-2.71	2.74	18.3	-1.467	-0.688	0.78
Krypton	5.93	-3.74	2.91	-1.20 ^c	-3.02	2.54	18.6	-1.213	-0.211	1.00
Xenon	5.60	-4.63	2.10	-2.41 ^c	-3.50	2.22	19.2	-0.972	0.378	1.35
Radon	5.15	-5.74	1.42	-3.39 ^c	-3.73	2.35	20.4	-0.646	0.877	1.52
Methane	6.27	-3.15	3.06	-0.95 ^c	-3.21	2.20	18.1	-1.452	-0.323	1.14
Ethane	6.09	-4.66	1.95	-2.75 ^c	-4.14	1.91	20.3	-1.336	0.492	1.83
Propane	6.23	-5.56	1.19	-3.81 ^c	-5.04	1.75	22.8	-1.436	1.050	2.49
Butane	6.34	-6.20	0.42	-4.97 ^c	-5.92	1.23	24.0	-1.518	1.615	3.13
2-Methylpropane	6.59	-5.78 ^d	0.70	-4.48 ^c	-5.89	1.30	24.1	-1.70	1.409	3.11
Pentane	6.60	-6.76	-0.33	-6.20	-6.93	0.56	25.1	-1.704	2.162	3.87
Hexane	6.76	-7.65	-1.02	-7.42	-7.78	0.23	26.9	-1.821	2.668	4.49
Heptane	6.95	-8.13	-1.71	-8.64	-8.66	-0.51	27.3	-1.962	3.173	5.14
Octane	7.15	-8.60	-2.40	-9.83	-9.55	-1.23	27.9	-2.109	3.677	5.79
Cyclopropane	5.02	-5.56 ^d	0.83		-4.19			-0.55	1.314	1.86
Cyclopentane	5.48	-7.25	-0.72	-6.61 ^e	-6.20	0.64	22.9	-0.88	2.447	3.33
Cyclohexane	5.50	-7.84 ^d	-1.35	-7.53 ^e	-6.85	0.31	24.0	-0.90	2.913	3.81
2,2-Dimethylpropane ^f	6.78		0.14		-6.64			-1.84	1.82	3.66
3,3-Diethylpentane ^f	6.50		-2.59		-9.09			-1.63	3.82	5.45
Tetramethylsilane ^f	7.32		-0.30		-7.62			-2.23	2.14	4.37
Tetraethylsilane ^f	7.04		-3.24		-10.33			-2.03	4.33	6.36
Tetramethyltin ^f	6.48		-1.36		-7.84			-1.62	2.92	4.54
Tetraethyltin ^f	6.75		-4.31		-11.06			-1.82	5.08	6.90
Ethene	5.55	-3.93 ^d	2.23	-2.67 ^g	-3.32	1.26	15.4	-0.94	0.289	1.23
Propene	5.59	-5.17 ^d	1.33	-3.19 ^h	-4.26	1.98	20.9	-0.97	0.946	1.92
But-1-ene	5.65	-5.77 ^d	0.59		-5.06			-1.01	1.491	2.50
Pent-1-ene	5.94		-0.13		-6.07			-1.23	2.013	3.24
Hex-1-ene	5.85		-0.86		-6.71			-1.16	2.547	3.71
Hept-1-ene	5.93		-1.56		-7.49			-1.22	3.063	4.28
Oct-1-ene	6.19		-2.28		-8.47			-1.41	3.591	5.00
Non-1-ene	6.33		-2.84		-9.17			-1.51	4.00	5.51
Ethyne	4.26	-3.49 ^d	2.41	1.67 ⁱ	-1.85	5.16	23.5	0.01	0.150	0.14
Propyne	3.79	-3.73 ^j	1.22		-2.57			0.35	1.025	0.68
But-1-yne	4.11	-3.71 ^j	0.55		-3.56			0.12	1.52	1.40
Pent-1-yne	4.29		-0.12		-4.41			-0.01	2.01	2.02
Hex-1-yne	4.56		-0.80		-5.36			-0.21	2.51	2.72
Hept-1-yne	4.87		-1.47		-6.34			-0.44	3.00	3.44
Oct-1-yne	4.98		-2.13		-7.11			-0.52	3.48	4.00
Non-1-yne	5.32		-2.78		-8.10			-0.77	3.96	4.73
Benzene	3.39	-7.59	-1.20	-7.26	-4.59	0.33	16.5	0.65	2.803	2.15
Toluene	3.48	-8.67	-1.94	-8.58	-5.42	0.09	18.3	0.58	3.344	2.76
Ethylbenzene	3.61	-9.62	-2.52	-9.59	-6.13	0.03	20.7	0.48	3.765	3.28
Propylbenzene	3.75	-10.50	-3.14	-10.55	-6.89	-0.05	22.9	0.38	4.221	3.84
Butylbenzene	3.91	-10.55 ^m	-3.17		-7.68			0.27	4.686	4.42
Pentylbenzene	4.04	-11.82 ^m	-4.41		-8.45			0.17	5.152	4.98
Hexylbenzene	4.23	-12.60 ^m	-5.04		-9.27			0.03	5.617	5.59
<i>o</i> -Xylene	3.36 ^k	-9.01 ⁿ	-2.75		-6.11			0.67	3.937	3.27
<i>m</i> -Xylene	3.56 ^l	-9.37 ⁿ	-2.65	-9.89	-6.21	-0.52	19.2	0.52	3.864	3.34
<i>p</i> -Xylene	3.54 ^{k,l}	-9.49 ⁿ	-2.64	-9.92	-6.18	-0.43	19.3	0.54	3.858	3.32
1,2,3-Trimethylbenzene	3.30 ^{k,l}	-8.96 ⁿ						0.71		
1,2,4-Trimethylbenzene	3.47 ^{k,l}	-9.54 ⁿ						0.59		
1,3,5-Trimethylbenzene	3.59 ^k	-9.36 ⁿ	-3.38	-11.13	-6.97	-1.77	17.4	0.50	4.399	3.90
Isopropylbenzene	3.81 ^{k,l}	-9.46 ⁿ	-2.98		-6.79			0.34	4.105	3.77
Naphthalene	1.87 ^{k,o}	-11.20 ^o	-4.67		-6.54			1.76	5.34	3.58
Fluorene	0.92 ^k							2.46		
Phenanthrene	0.41							2.83		
Pyrene	-0.30							3.35		
Propanone	0.46	-9.90 ^p	0.22	-5.14	-0.24	4.76	16.8	2.79	1.760	-1.03
Butanone	0.56	-10.91 ^p	-0.50	-6.33	-1.06	4.58	18.9	2.72	2.287	-0.43
Pentan-2-one	0.75	-11.63 ^p	-1.14	-7.42	-1.89	4.21	20.5	2.58	2.755	0.18
Hexan-2-one	0.98	-12.57 ^p	-1.83	-8.55 ^q	-2.81	4.02	22.9	2.41	3.262	0.85
Heptan-2-one	1.23	-13.43 ^p	-2.51	-9.67	-3.74	3.76	25.1	2.23	3.760	1.53
Octan-2-one	1.39	-14.15 ^q	-3.19	-10.73 ^q	-4.58	3.42 ^q	26.8	2.11	4.257	2.15
Nonan-2-one	1.78	-14.90 ^j	-3.87	-11.80 ^q	-5.65	3.10 ^q	29.3	1.83	4.755	2.92
Decan-2-one	1.92		-4.56		-6.48			1.72	5.260	3.54
Undecan-2-one	2.11		-5.24		-7.35			1.58	5.760	4.18
Pentan-3-one	0.86 ^j	-11.82 ^j	-1.22		-2.08			2.50	2.811	0.31

Table 1 (continued)

Solute	Water ^a		Hexadecane ^b		Water $\rightarrow$ Hexadecane			log L_w	log L_H	log P_H
	ΔG°	ΔH°	ΔG°	ΔH°	ΔG°_{tr}	ΔH°_{tr}	ΔS°_{tr}			
Heptan-4-one	1.35 ^j	-14.40 ^j	-2.59		-3.94			2.14	3.820	1.68
Nonan-5-one	1.63 ^j	-16.04	-3.71		-5.34			1.94	4.64	2.70
3-Methylbutan-2-one	1.03 ^j		-1.01		-2.04			2.38	2.66	0.28
4-Methylpentan-2-one	1.21 ^j		-1.54		-2.75			2.24	3.05	0.81
Cyclopentanone	-0.43 ^r	-12.36	-1.64		-1.21			3.45	3.120	-0.33
Cyclohexanone	-0.64 ^s	-12.90 ^t	-2.31	-8.72	-1.67	4.18	19.6	3.60	3.616	0.02
Acetophenone	-0.31 ^j	-12.64 ^t	-3.50	-11.32	-3.19	1.32	15.1	3.36	4.483	1.12
Formaldehyde	1.52 ^u		1.62		0.10			2.02	0.73	-1.29
Acetaldehyde	0.77 ^v		0.94		0.17			2.57	1.230	-1.34
Propanal	0.83 ^v		0.14		-0.69			2.52	1.815	-0.70
Butanal	1.09 ^v		-0.48		-1.57			2.33	2.270	-0.06
Pentanal	1.24 ^v		-1.16		-2.40			2.22	2.770	0.55
Hexanal	1.46 ^v		-1.98		-3.44			2.06	3.370	1.31
Heptanal	1.60 ^v		-2.65		-4.25			1.96	3.86	1.90
Octanal	1.98 ^v		-3.35		-5.33			1.68	4.38	2.70
Nonanal	2.20 ^v		-4.07		-6.27			1.52	4.90	3.38
2-Methylpropanal	1.41 ^w		-0.19		-1.60			2.10	2.06	-0.04
Benzaldehyde	0.25 ^j	-10.79 ^t	-2.82	-9.84	-3.07	0.95	13.5	2.95	3.985	1.03
(E)-But-2-enal	0.05 ^j		-0.89		-0.94			3.10	2.57	-0.53
Dimethyl ether	2.38 ^j		1.33					1.39	1.09	-0.30
Diethyl ether	2.68 ^j	-11.20 ^t	-0.19	-6.02	-2.87	5.18	27.0	1.17	2.061	0.89
Dipropyl ether	3.11 ^j		-1.46		-4.57			0.85	2.989	2.14
Di-isopropyl ether	3.74 ^x		-0.87		-4.61			0.39	2.559	2.17
Dibutyl ether	3.44 ^x		-2.84		-6.28			0.61	4.001	3.39
Tetrahydrofuran	0.80 ^j	-11.31 ^t	-0.84	-6.82	-1.64	4.49	20.6	2.55	2.534	-0.02
Tetrahydropyran	1.15 ^j	-11.68 ^j	-1.46					2.29	2.99	0.70
Anisole	1.82 ^y	-9.90 ^t	-2.74	-9.90	-4.56	0.00	15.3	1.80	3.926	2.13
Phenetole	2.05 ^y		-3.03		-5.08			1.63	4.14	2.51
Methyl formate	1.49		0.63		-0.86			2.04	1.459	-0.58
Methyl acetate	1.13	-9.44 ^t	-0.05		-1.18			2.30	1.960	-0.34
		-10.16 ^j								
Methyl propanoate	1.34		-0.74		-2.08			2.15	2.459	0.31
Methyl butanoate	1.44	-11.50 ^j	-1.40		-2.84			2.08	2.943	0.86
Methyl pentanoate	1.70	-12.33 ^j	-2.08		-3.78			1.88	3.442	1.56
Methyl hexanoate	1.78		-2.81		-4.59			1.83	3.984	2.15
Ethyl formate	1.70		0.03		-1.67			1.88	1.901	0.02
Ethyl acetate	1.33	-10.78 ^t	-0.62	-6.69	-1.95	4.09	20.3	2.16	2.376	0.22
Ethyl propanoate	1.59		-1.31		-2.90			1.97	2.881	0.91
Ethyl butanoate	1.77		-1.99		-3.76			1.83	3.379	1.55
Ethyl pentanoate	1.77							1.83		
Ethyl hexanoate	2.03							1.64		
Ethyl heptanoate	1.95							1.70		
Propyl formate	1.79 ^x		-0.67		-2.46			1.82	2.413	0.59
Propyl acetate	1.48		-1.31		-2.79			2.05	2.878	0.83
Propyl propanoate	1.83		-1.98		-3.81			1.79	3.370	1.58
Propyl butanoate	1.99 ^x		-2.58		-4.57			1.67	3.81	2.14
Butyl acetate	1.63	-12.36 ^t	-1.99	-9.20	-3.62	3.16	22.7	1.94	3.379	1.44
Pentyl acetate	1.76		-2.58		-4.34			1.84	3.81	1.97
Pentyl propanoate	2.16		-3.32		-5.60			1.55	4.350	2.80
Hexyl acetate	2.01 ^x		-3.21		-5.22			1.66	4.27	2.61
Isopropyl formate	2.25 ^x		-0.42		-2.67			1.48	2.23	0.75
Isopropyl acetate	1.63 ^x		-0.97		-2.60			1.94	2.633	0.69
Isopropyl propanoate	2.05 ^x		-1.51		-3.56			1.63	3.03	1.40
Isobutyl formate ^z	2.05 ^x		-1.24		-3.29			1.63	2.83	1.20
Isobutyl acetate ^z	1.91 ^x		-1.72		-3.63			1.73	3.180	1.45
Isoamyl formate ^z	2.14 ^x		-1.95		-4.09			1.56	3.35	1.79
Isoamyl acetate ^z	2.06 ^x		-2.48		-4.54			1.62	3.74	2.12
Isobutyl isobutyrate ^z	2.59 ^w		-2.67		-5.25			1.24	3.88	2.64
Methyl benzoate	-0.01 ^x	-12.44 ^t	-3.70	-11.56	-3.69	0.88	15.3	3.14	4.634	1.49
Ethyl benzoate	0.63 ^y							2.67		
Propylene carbonate	-3.29 ^{aa}	0.39 ^{ab}						5.54		
Water	-2.05 ^{ac}	-10.51 ^{ac}	2.26 ^{ad}	-8.44 ^{ae}	4.31	2.07	-7.5	4.64	0.260	-4.38
Methanol	-0.83	-10.78 ^p	1.36	-3.19	2.19	7.59	18.1	3.74	0.922	-2.82
Ethanol	-0.73	-12.58 ^p	0.59	-3.90	1.32	8.68	24.7	3.67	1.485	-2.19
Propan-1-ol	-0.58	-13.77 ^p	-0.24	-5.06	0.34	8.71	28.1	3.56	2.097	-1.46
Butan-1-ol	-0.45	-14.75 ^p	-0.93	-6.71	-0.48	8.04	28.6	3.46	2.601	-0.86
Pentan-1-ol	-0.30	-15.48 ^p	-1.62	-7.46	-1.32	8.02	31.3	3.35	3.106	-0.24
Hexan-1-ol	-0.14	-16.28 ^p	-2.31	-9.51	-2.17	6.77	30.0	3.23	3.610	0.38
Heptan-1-ol	0.06	-17.24 ^p	-2.99	-10.62 ^q	-3.05	6.62	32.4	3.09	4.115	1.02

Table 1 (continued)

Solute	Water ^a		Hexadecane ^b		Water → Hexadecane			log L_w	log L_H	log P_H
	ΔG°_i	ΔH°_i	ΔG°_i	ΔH°_i	ΔG°_{tr}	ΔH°_{tr}	ΔS°_{tr}			
Octan-1-ol	0.18	-17.72 ^p	-3.68	-11.73	-3.86	5.99	33.0	3.00	4.619	1.62
Nonan-1-ol	0.39		-4.37		-4.76			2.85	5.124	2.27
Decan-1-ol	0.63		-5.06		-5.69			2.67	5.628	2.96
Propan-2-ol	-0.48 ^{ef}	-14.05 ⁱ	0.14	-5.35	0.62	8.70	27.1	3.48	1.821	-1.66
Butan-2-ol	-0.35 ^{ef}	-15.00 ^j	-0.57		-0.22			3.39	2.338	-1.05
2-Methylpropan-1-ol	-0.23 ^{ef}	-14.38 ^j	-0.65		-0.42			3.30	2.339	-0.90
2-Methylpropan-2-ol	-0.20 ^{ef}	-15.39 ^j	-0.13	-5.50	0.07	9.89	32.9	3.28	2.018	-1.26
Pentan-2-ol	-0.12 ^x		-1.26		-1.14			3.22	2.840	-0.38
2-Methylbutan-1-ol	-0.15 ^x		-1.49		-1.34			3.24	3.011	-0.23
2-Methylbutan-2-ol	-0.16 ^x	-16.44 ^{ag}	-0.97		-0.86			3.25	2.630	-0.62
Pentan-3-ol	-0.08 ^j	-15.77 ^j						3.19		
3-Methylbutan-1-ol	-0.15 ^j		-1.49					3.24	3.011	-0.23
Hexan-3-ol	0.20 ^j	-16.63 ^j	-2.07					2.98	3.440	0.46
4-Methylpentan-2-ol	0.53 ^x							2.74		
2-Methylpentan-2-ol	0.34 ^x		-1.72					2.88	3.181	0.30
2-Methylpentan-3-ol	0.38 ^x							2.85		
Cyclopentanol	-1.22 ^j	-15.98 ^j	-1.84		-0.62			4.03	3.270	-0.76
Cyclohexanol	-1.20 ^j	-16.85 ^j	-2.39		-1.19			4.01	3.671	-0.34
Cycloheptanol	-1.21 ^j	-17.82 ^j						4.02		
Allyl alcohol	-0.76 ^x		-0.10		0.66			3.69	1.996	-1.69
2,2,2-Trifluoroethanol	-0.03 ^j	-12.01 ⁱ	0.95	-4.99	0.98	7.02	20.3	3.15	1.224	-1.93
Hexafluoropropan-2-ol	0.51 ^j	-13.65 ^j	0.72	-5.28	0.21	8.37	27.4	2.76	1.392	-1.37
Benzyl alcohol	-2.07 ^y	-16.00 ⁱ	-3.44	-10.13	-1.37	5.87	24.3	4.65	4.443	-0.21
Phenol	-2.00 ^{ah}	-13.65 ^{ai}	-2.64		-0.64			4.60	3.856	-0.74
<i>o</i> -Cresol	-1.60 ^{ai}	-14.52 ^{ai}	-3.17		-1.57			4.30	4.242	-0.06
<i>m</i> -Cresol	-1.23 ^{aj}		-3.29		-2.06			4.03	4.329	0.30
<i>p</i> -Cresol	-1.86 ^{ai}	-14.29 ^{ai}	-3.26		-1.40			4.50	4.307	-0.19
4- <i>t</i> -Butylphenol	-1.65 ^{ai}	-15.25 ^{ai}						4.34		
4-Bromophenol	-2.86 ^{ai}	-16.27 ^{ai}						5.23		
2-Nitrophenol	-0.15 ^{ak}	-11.47 ^{ak}	-3.77		-3.62			3.24	4.684	1.44
3-Nitrophenol	-5.36 ^j	-16.18 ^j						7.06		
4-Nitrophenol	-6.38 ^{ai}	-18.04 ^{ai}						7.81		
		-16.40 ^j								
3-Cyanophenol	-5.24 ^j	-16.90 ^j						6.97		
4-Cyanophenol	-5.90 ^j	-16.80 ^j						7.46		
3-Hydroxybenzaldehyde	-5.24 ^j	-16.00 ^j						6.97		
4-Hydroxybenzaldehyde	-6.20 ^j	-16.30 ^j						7.68		
2-Chlorophenol									4.937	
3-Chlorophenol		-12.03 ^j								
4-Chlorophenol		-8.58 ^j								
Formic acid		-11.09								
Acetic acid	-2.43 ^{ai}	-12.28	0.23		2.66			4.91	1.75	-3.16
Propanoic acid	-2.20 ^{ai}	-13.45	-0.50		1.70			4.74	2.29	-2.45
Butanoic acid	-2.08 ^{ai}	-14.50	-1.24		0.84			4.66	2.83	-1.83
Pentanoic acid	-1.90 ^{am}	-15.32	-1.99		-0.09			4.52	3.38	-1.14
Hexanoic acid	-1.95 ^{an}	-16.08	-2.72		-0.77			4.56	3.92	-0.64
Heptanoic acid	-1.89 ^{an}	-16.96	-3.47		-1.58			4.52	4.46	-0.06
Octanoic acid	-1.78 ^q	-17.75	-4.20		-2.42			4.44	5.00	0.56
3-Methylbutanoic acid	-1.82 ^w		-1.88		-0.06			4.47	3.30	-1.17
Ammonia	-0.03 ^{ao}	-8.42 ^{ao}	2.25		2.28			3.15	0.269	-2.88
Methylamine	-0.29	-10.82						3.34		
Ethylamine	-0.23	-12.83	0.33		0.56			3.30	1.677	-1.62
Propylamine	-0.12	-13.38	-0.30	-5.73	-0.18	7.65	26.3	3.22	2.141	-1.08
Butylamine	0.03	-14.15	-0.95	-7.03	-0.98	7.12	27.2	3.11	2.618	-0.49
Pentylamine	0.18	-14.85	-1.59		-1.77			3.00	3.086	0.09
Hexylamine	0.32	-15.76	-2.23	-9.43	-2.55	6.33	29.8	2.90	3.557	0.66
Heptylamine	0.48		-2.91		-3.39			2.78	4.050	1.27
Octylamine	0.62		-3.55		-4.17			2.68	4.520	1.84
Isopropylamine		-13.37 ^{ao}								
<i>t</i> -Butylamine		-14.16 ^{ao}	-0.78	-6.25		7.91			2.493	
Cyclohexylamine	-0.32 ^w							3.37		
Dimethylamine	-0.03 ^{ao}	-12.69 ^{ao}	0.44		0.47			3.15	1.60 ^q	-1.55
Diethylamine	0.19 ^{ao}	-15.37 ⁱ	-0.65	-5.88	-0.84	9.49	34.6	2.99	2.395	-0.60
Dipropylamine	0.62 ^{ao}	-17.26 ^{ao}	-1.98		-2.60			2.68	3.372	0.69
Dibutylamine	1.03 ^{ao}	-18.89 ^{ao}						2.38		
Di-isopropylamine	1.06 ^{ao}	-16.81 ^{ao}	-1.33		-2.39			2.36	2.893	0.53
Trimethylamine	1.03 ^{ao}	-12.60 ^{ao}	0.41		-0.62			2.35	1.620	-0.73
Triethylamine	1.05 ^{ap}	-16.64 ^{ap}	-1.58	-8.16	-1.58	8.48	33.7	2.36	3.077	0.72
Aniline	-1.23 ^y	-12.87 ⁱ	-2.83	-9.99	-1.60	2.88	15.0	4.03	3.993	-0.04

Table 1 (continued)

Solute	Water ^a		Hexadecane ^b		Water $\rightarrow$ Hexadecane			log L_w	log L_H	log P_H
	ΔG_s°	ΔH_s°	ΔG_s°	ΔH_s°	ΔG_{tr}°	ΔH_{tr}°	ΔS_{tr}°			
<i>N,N</i> -Dimethylaniline	0.82 ^y		-3.87	-11.56	-4.69			2.53	4.754	2.22
Pyridine	-0.42 ^{aq}	-11.93 ^j	-1.48	-7.80	-1.06	4.13	17.4	3.44	3.003	-0.44
2-Methylpyridine	-0.35 ^{aq}	-13.18 ^j	-2.07	-8.58	-1.72	4.60	21.2	3.39	3.437	0.05
3-Methylpyridine	-0.50 ^{aq}	-13.08 ^j	-2.30	-8.96	-1.80	4.12	19.9	3.50	3.603	0.10
4-Methylpyridine	-0.66 ^{aq}	-13.15 ^j	-2.28	-8.79	-1.62	4.36	20.1	3.61	3.593	-0.02
2-Ethylpyridine	-0.05 ^{aq}	-13.31 ^{aq}	-2.70		-2.65			3.17	3.90	0.73
3-Ethylpyridine	-0.33 ^{aq}	-12.78 ^{aq}	-3.01		-2.68			3.37	4.13	0.76
4-Ethylpyridine	-0.46 ^{aq}	-12.48 ^{aq}	-3.03		-2.57			3.47	4.14	0.67
2,3-Dimethylpyridine	-0.55 ^{aq}	-13.79 ^{aq}						3.53		
2,4-Dimethylpyridine	-0.59 ^{aq}	-14.51 ^j	-2.91		-2.32			3.56	4.05	0.49
2,5-Dimethylpyridine	-0.44 ^{aq}	-14.54 ^j	-2.91		-2.47			3.45	4.05	0.60
2,6-Dimethylpyridine	-0.32 ^{aq}	-14.81 ^j	-2.65		-2.33			3.37	3.86	0.49
3,4-Dimethylpyridine	-0.94 ^{aq}	-13.54 ^{aq}	-3.33		-2.35			3.82	4.36	0.54
3,5-Dimethylpyridine	-0.56 ^{aq}	-14.46 ^j	-3.18		-2.62			3.54	4.25	0.71
4- <i>n</i> -Butylpyridine	-0.19 ^j	-13.83 ^j	-3.86		-3.67			3.27	4.75	1.48
Nitromethane	0.25 ^{ar}	-8.54 ^j	0.04	-6.06	-0.21	2.48	9.0	2.95	1.892	-1.06
Nitroethane	0.56 ^x		-0.61		-1.17			2.72	2.367	-0.35
1-Nitropropane	0.93 ^x		-1.27		-2.20			2.45	2.85	0.40
1-Nitrobutane	1.18		-1.92		-3.10			2.27	3.33	1.06
1-Nitropentane	1.45 ^w		-2.59		-4.04			2.07	3.82	1.75
2-Nitropropane	1.14		-0.86		-2.00			2.30	2.550	0.25
Nitrobenzene	0.15 ^x	-11.60 ^t	-3.46	-10.91	-3.61	0.69	14.4	3.02	4.460	1.44
2-Nitrotoluene	0.68 ^x		-3.90		-4.58			2.63	4.78	2.15
3-Nitrotoluene	0.82		-4.16		-4.98			2.53	4.97	2.44
4-Nitrotoluene			-4.23						5.02	
Acetonitrile	0.38 ^x	-8.37 ^t	0.49	-4.56	0.11	3.81	12.4	2.85	1.560	-1.29
Propanonitrile	0.43 ^x	-9.48 ^j	-0.18		-0.61			2.82	2.050	-0.77
Butanonitrile	0.63 ^x	-10.15 ^t	-0.85		-1.48			2.67	2.540	-0.13
Pentanonitrile	0.75 ^w		-1.55		-2.30			2.58	3.057	0.48
Benzonitrile	0.16 ^y	-11.59 ^t	-2.84	-9.86	-3.00	1.73	15.9	3.01	4.004	0.99
Chloromethane	3.72	-5.53 ^{as}	1.03		-2.69			0.40	1.163	0.76
Chloroethane	3.64		0.33		-3.31			0.46	1.678	1.22
1-Chloropropane	3.94		-0.38		-4.32			0.24	2.202	1.96
1-Chlorobutane	4.11	-6.92 ^{at}	-1.09	-7.38	-5.20	-0.46	15.9	0.12	2.722	2.60
1-Chloropentane	4.21	-9.39 ^{at}	-1.78		-5.99			0.05	3.223	3.17
1-Chlorohexane	4.27	-8.86 ^{at}	-2.44		-6.71			0.00	3.71	3.71
1-Chloroheptane	4.56		-3.12		-7.68			-0.21	4.21	4.42
2-Chloropropane	4.03 ^x		-0.07		-4.10			0.18	1.970	1.79
2-Chlorobutane	4.27 ^{at}	-8.94 ^{at}						0.00		
1-Chloro-2-methylpropane			-0.88						2.566	
2-Chloro-2-methylpropane	5.36 ^{au}	-4.88 ^{au}	-0.41		-5.77			-0.80	2.217	3.02
2-Chloropentane	4.34 ^x							-0.05		
3-Chloropentane	4.31 ^x							-0.03		
Dichloromethane	2.96 ^{k,x,at}	-7.24 ^{av}	-0.14	-5.54	-3.10	1.70	16.1	0.96	2.019	1.06
Trichloromethane	3.20 ^{k,x,at}	-7.99 ^f	-0.76	-6.71	-3.96	1.28	17.6	0.79	2.480	1.69
Tetrachloromethane	4.35 ^{at}	-8.77 ^{av}	-1.23	-7.39	-5.58	1.38	23.3	-0.06	2.823	2.88
1,2-Dichloroethane	2.48 ^{at,aw}	-8.54 ^{av}	-0.89		-3.37			1.31	2.573	1.26
1,1-Dichloroethane	3.42 ^{k,x,aw}		-0.59		-4.01			0.62	2.350	1.73
1,1,1-Trichloroethane	4.08 ^{x,at,aw}		-1.05		-5.20			0.14	2.690	2.55
1,1,2-Trichloroethane	2.28 ^{x,at}		-1.87		-4.15			1.46	3.29	1.83
1,1,2,2-Tetrachloroethane	1.80 ^{at,aw}		-2.60		-4.48			1.81	3.826	2.02
1,1,1,2-Tetrachloroethane	2.99 ^k		-2.22		-5.21			0.94	3.55	2.61
Pentachloroethane	2.88 ^{k,x}							1.02		
Hexachloroethane	2.87 ^x									
	3.89 ^k									
1,2-Dichloropropane	3.01 ^{x,at}	-8.61 ^{at}	-1.27		-4.28			0.93	2.85	1.92
1,3-Dichloropropane	2.38 ^{x,at}	-7.78 ^{at}	-1.74		-4.12			1.39	3.194	1.80
1,4-Dichlorobutane	1.95 ^{at}	-6.22 ^{at}	-2.53		-4.48			1.70	3.775	2.08
Bromomethane	3.46	-6.10 ^{as}						0.60		
Bromoethane	3.54		-0.14		-3.68			0.54	2.020	1.48
1-Bromopropane	3.71		-0.95		-4.66			0.41	2.620	2.21
1-Bromobutane	3.87		-1.62		-5.49			0.29	3.105	2.82
1-Bromopentane	4.18		-2.31		-6.49			0.07	3.611	3.54
1-Bromohexane	4.45		-3.01		-7.46			-0.13	4.13	4.26
1-Bromoheptane	4.61		-3.66		-8.27			-0.25	4.60	4.85
1-Bromo-octane	4.79		-4.32		-9.11			-0.38	5.09	5.47
2-Bromopropane	3.79 ^x		-0.64		-4.43			0.35	2.391	2.04
2-Bromobutane			-1.38						2.933	
1-Bromo-2-methylpropane	4.24 ^x		-1.42		-5.66			0.02	2.961	2.94

Table 1 (continued)

Solute	Water ^a		Hexadecane ^b		Water → Hexadecane			log <i>L_w</i>	log <i>L_H</i>	log <i>P_H</i>
	ΔG°_s	ΔH°_s	ΔG°_s	ΔH°_s	ΔG°_{tr}	ΔH°_{tr}	ΔS°_{tr}			
2-Bromo-2-methylpropane	5.12 ^{au}	-6.07 ^{au}	-0.95		-6.07			-0.62	2.616	3.24
Dibromomethane	2.31 ^x		-1.27		-3.58			1.44	2.849	1.41
Tribromomethane	2.14 ^y		-2.51		-4.65			1.56	3.747	2.19
1,2-Dibromoethane	1.94 ^x		-2.01		-3.95			1.71	3.999	1.69
Iodomethane	3.37	-6.19 ^j								
Iodoethane	3.54		-0.89		-4.43			0.54	2.573	2.04
1-Iodopropane	3.74		-1.65		-5.39			0.39	3.130	2.74
1-Iodobutane	4.03		-2.33		-6.36			0.18	3.628	3.45
1-Iodopentane	4.14		-3.01		-7.15			0.10	4.13	4.03
1-Iodohexane	4.35		-3.68		-8.03			-0.06	4.62	4.68
1-Iodoheptane	4.54		-4.32		-8.86			-0.20	5.09	5.29
Di-iodomethane	1.77 ^y		-2.64	-9.31	-4.41			1.84	3.853	2.01
Fluoromethane	4.06 ^{as}	-4.33 ^{as}								
CCl ₂ FCClF ₂	6.05 ^x		-0.28		-6.33			-1.30	2.123	3.42
CF ₃ CHFBr (Tefluorane)	4.78 ^{ax}		0.74		-4.04			-0.37	1.37	1.74
CF ₃ CHClBr (Halothane)	4.13 ^{ax}		-0.35		-4.51			0.08	2.177	2.10
CHF ₂ OCF ₂ CHFCI (Enfluorane)			0.36						1.653	
CH ₃ OCF ₂ CHCl ₂ (Methoxyfluorane)	3.15 ^{ax}		-1.29		-4.44			0.82	2.864	2.04
CHF ₂ OCHClCF ₃ (Isofluorane)	4.37 ^{ax}		0.47		-3.90			-0.07	1.576	1.65
CF ₃ CH ₂ OCH=CH ₂ (Fluoroxene)	4.14 ^{ax}		0.71		-3.43			0.10	1.40	1.30
Chloroethene	4.20 ^{as}	-5.87 ^{as}						0.05		
1,1-Dichloroethene	4.52 ^{at}	-9.18 ^{at}	-0.26		-4.78			-0.18	2.110	2.29
cis-1,2-Dichloroethene	3.57 ^{ax}		-0.72		-4.29			0.51	2.450	1.94
trans-1,2-Dichloroethene	3.50 ^{ax}		-0.59		-4.09			0.57	2.350	1.78
Trichloroethene	3.83 ^{ax}	-9.23 ^{at}	-1.47		-5.30			0.32	2.997	2.68
Tetrachloroethene	4.37 ^{ax}	-9.41 ^{at}	-2.27	-9.18	-6.64	0.23	23.0	-0.07	3.584	3.65
Allyl chloride	3.69 ^x		-0.26		-3.95			0.42	2.109	1.69
Allyl bromide	3.42 ^y		-0.80		-4.22			0.63	2.510	1.88
Allyl iodide			-1.49						3.01	
Benzyl chloride	2.35 ^y	(3.47) ^{ay}	-3.23	(1.62)	-5.58	-1.85	12.5	1.41	4.290	2.88
Benzyl bromide	1.90 ^y		-3.74		-5.64			1.74	4.66	2.92
Fluorobenzene	3.48 ^{az}	-7.53 ⁱ	-1.26	-7.42	-4.74	0.11	16.3	0.58	2.84	2.26
Chlorobenzene	3.13 ^k	-10.40 ^{ap}	-2.35	-9.14	-5.48	1.26	22.6	0.84	3.640	2.80
2-Chlorotoluene	3.13 ^{at}		-3.06		-6.19			0.84	4.16	3.32
3-Chlorotoluene									4.16	
4-Chlorotoluene									4.19	
1,2-Dichlorobenzene	2.77 ^k		-3.39		-6.16			1.10	4.405	3.30
1,3-Dichlorobenzene	3.14 ^k		-3.37		-6.51			0.83	4.39	3.56
1,4-Dichlorobenzene	2.95 ^{k,x}		-3.38		-6.33			0.97	4.40	3.43
Bromobenzene	2.81 ^k		-2.89		-5.80			1.07	4.035	2.97
2-Bromotoluene			-3.55						4.52	
3-Bromotoluene			-3.57						4.54	
4-Bromotoluene	2.88 ^x		-3.57		-6.45			1.02	4.54	3.52
Iodobenzene	2.53 ^k		-3.63		-6.16			1.28	4.58	3.30
Methanethiol ^{ba}	2.91	-6.16						1.00		
Ethanethiol ^{ba}	3.13	-6.80	-0.34		-3.47			0.84	2.173	1.34
Propanethiol ^{ba}	3.21	-7.10	-1.04		-4.25			0.78	2.685	1.91
Butanethiol ^{ba}	3.27	-7.58	-1.31		-4.58			0.73	2.880	2.15
Dimethyl sulphide ^{ba}	2.72	-7.49	-0.43		-3.15			0.63	2.238	1.61
Diethyl sulphide ^{ba}	2.81	-8.87	-1.62		-4.43			1.07	3.104	2.03
Dipropyl sulphide ^{ba}	2.99	-7.58	-3.00		-5.99			0.94	4.120	3.18
Di-isopropyl sulphide ^{ba}	3.06	-9.56	-2.29		-5.35			0.89	3.600	2.71
Dimethyl disulphide ^{ba}	2.43	-7.58	-2.22		-4.65			1.35	3.549	2.20
Diethyl disulphide ^{ba}	2.63	-7.36	-3.12		-5.75			1.20	4.210	3.01
Thiophene ^{ba}	2.85	-7.15	-1.40	-7.15	-4.25	0.00	14.3	1.04	2.943	1.90
2-Methylthiophene ^{ba}	2.90	-7.55	-1.89		-4.79			1.01	3.302	2.30
Thiophenol	1.72 ^x		-3.00		-4.72			1.87	4.118	2.25

^a Values of ΔG°_s and ΔH°_s in kcal mol⁻¹ mole fraction scale, for gaseous solutes taken from refs. 8 and 9 unless shown otherwise. ^b This work, or from ref. 4, unless shown otherwise. ^c M. H. Abraham and E. Matteoli, unpublished survey. ^d S. F. Dec and S. J. Gill, *J. Solution Chem.*, 1984, 13, 27. ^e Note that van't Hoff enthalpies from A. Kuantas and G. W. A. Rijnders in 'Gas Chromatography 1958,' ed. D. H. Desty, Butterworths, London, 1958, are -5.95 and -6.87, respectively. ^f From data given by M. H. Abraham, P. L. Grellier, and R. A. McGill, *J. Chem. Soc., Perkin Trans. 2*, 1987, 797. ^g Value for solution in dodecane by the van't Hoff method. Data from A. Sahgad, H. M. La, and W. Hayduk, *Can. J. Chem. Eng.*, 1978, 56, 354. ^h By the van't Hoff method, P. J. Lin and J. F. Parcher, *J. Chromatogr. Sci.*, 1982, 20, 33. ⁱ By the van't Hoff method, data from Y. Migano and W. Hayduk, *Can. J. Chem. Eng.*, 1981, 59, 746. ^j Ref. 7. ^k Ref. 10. ^l G. L. Amidon and S. T. Anik, *J. Chem. Eng. Data*, 1981, 26, 28. ^m J. W. Owens, S. P. Wasik, and H. De Voe, *J. Chem. Eng. Data*, 1986, 31, 47. ⁿ I. Sanemasa, M. Araki, T. Deguchi, and H. Nagai, *Bull. Chem. Soc. Jpn.*, 1982, 55, 1054. ^o R. D. Wauchope and R. Haque, *Can. J. Chem.*, 1972, 50, 133. ^p Data from ref. 8 slightly adjusted using more recent ΔH°_v values from V. Majer and V. Svoboda, 'Enthalpies of Vaporization of Organic Compounds,' Blackwell, Oxford, 1985. ^q Estimated

Table 1 (continued)

value, this work. ^a Estimated value by J. P. Guthrie and P. A. Cullimore, *Can. J. Chem.*, 1979, 57, 240. ^b K. R. Brower, J. Peslak, and J. Elrod, *J. Phys. Chem.*, 1969, 73, 207. ^c This work. ^d C. J. Marsh and R. C. Pemberton, *National Physical Laboratory, Report Chem. III*, 1980. ^e R. G. Buttery, L. C. Ling, and D. G. Guadagni, *J. Agric. Food Chem.*, 1969, 17, 385. These values are for the unhydrated aldehydes; see ref. in footnote u. ^f J. E. Amoure and R. G. Buttery, *Chem. Senses Flavour*, 1978, 3, 57. ^g Ref. 6. ^h From liquid solubilities and vapour pressures as calculated in this work. ⁱ Isobutyl is 2-methylpropyl; isoamyl is 3-methylbutyl; isobutyrate is 2-methylpropanoate. ^{aa} Calculated from vapour-liquid equilibria. ^{ab} Enthalpy of solution of the pure liquid from B. C. Cox, A. J. Parker, and W. E. Waghorne, *J. Am. Chem. Soc.*, 1973, 95, 1010. ^{ac} Parameters for the vaporisation of pure water. ^{ad} Value from ref. 2. Other values that may be calculated are 2.17 from S. D. Christian, R. French, and K. O. Yeo, *J. Phys. Chem.*, 1973, 74, 813, and 2.27 from P. Schatzberg, *J. Phys. Chem.*, 1963, 67, 776. ^{ae} H. Saito and K. Shinoda, *J. Colloid Interfac. Chem.*, 1970, 32, 647. ^{af} J. H. Rytting, L. P. Huston, and T. Higuchi, *J. Pharm. Sci.*, 1978, 67, 615. ^{ag} K. Boccek, *J. Chromatogr.*, 1979, 162, 209. ^{ah} M. F. Abd-El-Bary, M. F. Hamoda, S. Tanisho, and N. Wakao, *J. Chem. Eng. Data*, 1986, 31, 229. ^{ai} G. H. Parsons, C. H. Rochester, and C. E. Wood, *J. Chem. Soc., Perkin Trans. 2*, 1972, 136. ^{aj} Calculated from the known partition coefficient and log L_H values. ^{ak} K. Schoene and J. Steinhanses, *Fresenius Z. Anal. Chem.*, 1985, 321, 538. The ΔH° value is by the van't Hoff method. ^{al} J. A. V. Butler and C. N. Ramchandani, *J. Chem. Soc.*, 1935, 952. ^{am} Average of values from ref. in footnote w (−1.88) and calculated from partition coefficients of R. Aveyard and R. W. Mitchell, *Trans. Faraday Soc.*, 1970, 66, 37, corrected in this work for dimerization in hexadecane (−1.92). ^{an} From partition coefficients, see ref. in footnote am. ^{ao} E. M. Arnett and F. M. Jones, *Prog. Phys. Org. Chem.*, 1974, 11, 263. ^{ap} M. H. Abraham and A. Naschzadeh, *J. Chem. Thermodyn.*, 1981, 13, 549. ^{aq} R. J. L. Andon, J. D. Cox, and E. F. G. Herington, *J. Chem. Soc.*, 1954, 3118. ^{ar} J. H. Park, A. Hussam, P. Couasnon, D. Fritz, and P. W. Carr, *Anal. Chem.*, 1987, 59, 1970. ^{as} E. Wilhelm, R. Battino, and R. J. Wilcock, *Chem. Rev.*, 1977, 77, 219. ^{at} D. L. Leighton and J. M. Cole, *J. Chem. Eng. Data*, 1981, 26, 382. ^{au} M. H. Abraham, P. L. Grellier, A. Naschzadeh, and R. A. C. Walker, *J. Chem. Soc., Perkin Trans. 2*, 1988, 1717. ^{av} From ΔH°_{tr} (liq) by J. W. Larsen and L. Magid, *J. Phys. Chem.*, 1974, 78, 834, and R. de Lisi, M. Goffredi, and V. T. Liveri, *J. Chem. Soc., Faraday Trans. 1*, 1980, 1660, together with ΔH°_{tr} . ^{aw} R. S. Barr and D. M. T. Newshan, *Fluid Phase Eq.*, 1987, 35, 189. ^{ax} M. H. Abraham, M. J. Kamlet, R. W. Taft, R. M. Doherty, and P. K. Weathersby, *J. Med. Chem.*, 1985, 28, 865. ^{ay} This is ΔH°_{tr} (liq) from R. Ohnishi and K. Tanabe, *Bull. Chem. Soc. Jpn.*, 1971, 44, 2647, by the van't Hoff method. Our own listed value for ΔH°_{tr} in hexadecane is also for the liquid solute. ^{az} P. Bernal, S. D. Christian, and E. E. Tucker, *J. Solution Chem.*, 1986, 15, 947. ^{ba} A. Przyjazny, W. Janicki, W. Chrzanowski, and R. Staszewski, *J. Chromatogr.*, 1983, 280, 249.

ception of methanol (3A), nitromethane (3A), and water. ΔH°_{tr} values were independent of concentration in the measurement range.

Discussion

Most of the gas solubility data in water were taken from key references,^{6–8} two of which^{7,8} include values for the enthalpy of solution in water. The L_H values used were mostly those we have determined either previously⁴ or in this work, but we also calculated a number of values using literature data for closely related solvents such as squalane,^{15–17} $C_{27}H_{54}$,^{18,19} octacosane,²⁰ and heptadecane.²¹ In Table 1 are collected values of log L_w and log L_H , together with the calculated log P_H values, via equation (1). The log P_H values all refer to the molar concentration scale, as is usual for partition coefficients. We have, where necessary, recalculated gas solubilities using standard states of 1 atm (gas) and unit mole fraction (solution), so that the ΔG°_{tr} values in Table 1 refer to the mole fraction concentration scale, a more appropriate scale when calorimetrically determined enthalpies of solution are involved. Our enthalpies of solution of liquid solutes were converted into ΔH°_{tr} values for gaseous solutes, using enthalpies of vaporization at 298 K, care being taken to ensure that the same ΔH°_{tr} values were used for solution into water and hexadecane. The observed ΔH°_{tr} values, and the deduced ΔH°_{tr} and ΔS°_{tr} are collected in Table 1. Additional log P_H values are given in Table 2.

The expected error in the log L_H values is very small, probably no more than 0.03 log unit. However, there are substantial differences in recorded values for log L_w , even for moderately volatile solutes. Thus for halogenated alkanes, the log L_w values given by Hine and Mookerjee⁶ and by Mackay and Shiu¹⁰ differ randomly by ca. 0.1 log unit, and for hexachloroethane the two recorded values differ by a full log unit (2.87 and 3.89, respectively). Enthalpies of solution, although in the best instances* capable of leading to ΔH°_{tr} values with an error of only some 0.05 kcal mol^{−1}, can also be subject to very large errors.

We can suggest that the expected error in ΔG°_{tr} will be ca. 0.2 kcal mol^{−1}, that in ΔH°_{tr} around 0.5 kcal mol^{−1}, and that in ΔS°_{tr} ca. 2 cal K^{−1} mol^{−1}. However, occasionally much larger experimental errors may arise, and this should be borne in mind when results are discussed. We note that the thermodynamics of transfer from water to hexadecane are very similar to those for transfer to 2,2,4-trimethylpentane, as found by Tomlinson *et al.*¹² A comparison for a number of solutes is in Table 3. Within any reasonable error, it seems as though ΔH°_{tr} values are identical for the two transfers, and that ΔG°_{tr} values average at about the same, with rather more random variation. It seems that without introducing too much error, values of ΔH°_{tr} and ΔG°_{tr} for transfer to 2,2,4-trimethylpentane, Table 3, could be taken as those for transfer to hexadecane.

Tomlinson *et al.*¹² examined the possibility of enthalpy-entropy correlations for transfer to 2,2,4-trimethylpentane through the statistically correct method of plotting ΔG°_{tr} vs. ΔH°_{tr} . They found that there was no general correlation between ΔG°_{tr} and ΔH°_{tr} , although linear relationships were observed for various homologous series. Using a more extended data set, we can confirm the findings of Tomlinson *et al.*¹² Aliphatic series such as the alkanes, ketones, and alcohols form separate linear plots. However, aromatic or halogeno-substituted compounds always lie off the plots for the unsubstituted series. This rather complicated enthalpy-Gibbs energy interplay is hardly surprising in view of the varied solute-solvent interactions that are possible.

One method for the examination of solute-solvent interactions is that of multiple linear regression analysis, especially as developed by Abraham, Doherty, Kamlet, Taft, and their co-workers.^{22–25} The solubility of a gaseous solute in a solvent is regarded as being made up of an endoergic cavity term, that arises through breaking of solvent-solvent interactions, together with a number of exoergic terms that arise through different solute-solvent interactions. For a number of solutes in a given solvent phase, equations (2) and (3) are valid.^{22–25}

$$SP = c + d\delta_2 + s\pi_2^* + a\alpha_2 + b\beta_2 + vV_2 \quad (2)$$

$$SP = c + d\delta_2 + s\pi_2^* + a\alpha_2 + b\beta_2 + l\log L_H \quad (3)$$

Equation (2) is recommended for processes within condensed phases, such as the water-hexadecane partition coefficients we

* These are nearly always with calorimetrically determined enthalpies of solution of liquid solutes that dissolve readily in water and hexadecane and are not subject to extensive self-association. Note that any error in ΔH°_{tr} cancels out. 1 kcal = 4.184 kJ.

Table 2. Directly determined log P_H values for compounds not in Table 1.^a

Solute	$\Delta G_{tr}^\circ/\text{kcal mol}^{-1}$	log P_H	Ref.
Butane-1,4-diol	4.30	-4.37	2
Hexane-1,6-diol	2.80	-3.27	2
Formamide	5.31	-5.10	2
Acetamide	4.73	-4.68	2
Butyramide	3.05	-3.44	2
Isobutyramide	3.03	-3.43	2
Urea	5.79	-5.46	2
4-Pentylpyridine	-5.26	2.64	b
4-Hexylpyridine	-6.12	3.27	b
4-Heptylpyridine	-7.00	3.92	b
4-Octylpyridine	-7.89	4.57	b
4-Nonylpyridine	-8.76	5.21	b
4-Decylpyridine	-9.62	5.84	b
Paraldehyde	-1.98	0.24	3
2-Chlorophenol	(-1.52) -1.45	-0.15	c
4-Chlorophenol	(-0.70) -0.63	-0.75	c
4-Chloro-3-methylphenol	(-2.14) -2.07	0.31	c
2-Iodophenol	(-2.28) -2.21	0.41	c
<i>o</i> -Toluidine	-2.17	0.38	d
<i>p</i> -Toluidine	-2.14	0.36	d
2-Methoxyaniline	-2.10	0.33	d
4-Methoxyaniline	-0.92	-0.54	d
2-Chloroaniline	-3.11	1.07	d
3-Chloroaniline	-2.53	0.64	d
4-Chloroaniline	-2.42	0.56	d
2-Nitroaniline	-1.95	0.22	e
Acetophenone	-3.18	1.12 ^g	f
4-Methoxyacetophenone	-2.88	0.90	f
3-Methylacetophenone	-4.00	1.72	f
4-Methylacetophenone	-3.88	1.63	f
4-Fluoroacetophenone	-3.29	1.20	f
3-Chloroacetophenone	-4.40	2.01	f
4-Chloroacetophenone	-3.89	1.85	f
3-Trifluoromethylacetophenone	-4.49	2.08	f
3-Nitroacetophenone	-2.38	0.53	f
4-Nitroacetophenone	-2.59	0.69	f
Biphenyl	-7.37	4.19	5

^a Values of log P_H on the molar scale and ΔG_{tr}° on the mol fraction scale as in Table 1. ^b K. C. Yeh and W. I. Higuchi, *J. Pharm. Sci.*, 1976, 65, 82. ^c Parenthesised values are for transfer to dodecane, from D. E. Burton, K. Clarke, and G. W. Gray, *J. Chem. Soc.*, 1964, 1314. The listed values for ΔG_{tr}° and log P have been slightly adjusted to correspond to transfer to hexadecane, by comparison for phenols for which both transfers are known. ^d W. Kemula, H. Buchowski, and W. Pawlowski, *Rocz. Chem.*, 1968, 48, 1951. ^e W. Kemula, H. Buchowski, and J. Terepat, *Bull. Acad. Sci. Polon.*, 1961, 9, 595. ^f Values for transfer to dodecane, from J. Toullec, M. El-Alaoui, and P. Kleffert, *J. Org. Chem.*, 48, 4808. ^g Note the same value (Table 1) for transfer to hexadecane.

wish to analyse. We shall therefore consider only equation (2) and not equation (3), preferred for gas-solvent partition coefficients. In equation (2), δ_2 is a solute polarisability correction term taken as zero except for polyhalogeno aliphatics (0.5) and aromatics (1.0), π_2^* is the solute dipolarity, α_2 the solute hydrogen-bond acidity, β_2 the solute hydrogen-bond basicity, and V_2 is the solute volume. The constants c , d , s , a , b , and v are found by multiple linear regression analysis, and can be used to deduce the factors that are important in the particular process. If we consider specifically the water-hexadecane partition, with $SP = \log P_H$ as defined *via* equation (1), then the values of the s -constant will depend on the differences in dipolarity between water and hexadecane; a negative s -constant will indicate that water is more dipolar than hexadecane and hence more able to undergo solvent-solute dipole-dipole interactions. In a similar vein, the a -constant will reflect the hydrogen-bond basicity of water, that is its ability to hydrogen bond with solutes that

are hydrogen-bond acids (hexadecane cannot), whilst the b -constant will reflect the hydrogen-bond acidity of water. The vV_2 term covers cavity effects, the larger the solute the more solvent-solvent interactions must be broken to make a suitably sized cavity. Hence the v -constant should provide an assessment of the difference in cavity effects between water and hexadecane.

In equation (2), the solute explanatory variables were taken as follows: δ_2 defined as above; π_2^* as listed before;²²⁻²⁵ α_2 as α_2^H , the new solute hydrogen-bond acidity parameter;²⁶ β_2 as β_2^H , the new solute hydrogen-bond basicity parameter,^{27,28} supplemented by a few recently determined²⁹ 'effective' or 'summation' β_2^H values for multifunctional bases; V_2 as McGowan's intrinsic volume V_x .³⁰ The equation that we use to correlate log P_H and also the thermodynamic functions of transfer is therefore as follows, where V_x is in units of ($\text{cm}^3 \text{mol}^{-1}$)/100.

$$SP = c + d\delta_2 + s\pi_2^* + a\alpha_2^H + b\beta_2^H + vV_x \quad (4)$$

If we include all of the data of Tomlinson *et al.*¹² in Table 3, as well as our calculated values in Tables 1 and 2, we have 270 compounds for which we have all the required explanatory variables. Details of the regression equations are in Table 4, where n is the number of solutes, r the overall correlation coefficient, and sd the standard deviation. Bearing in mind the probable average experimental error in log P_H of about 0.1, and also the experimental errors in the various explanatory variables, an overall standard deviation of *ca.* 0.2 log units is as good as can be expected. Thus the regression equation for 270 compounds, with $r = 0.9884$ and $sd = 0.28$, is quite acceptable. The constants in equation (4) are all chemically reasonable, with s , a , and b all being very negative, and v being very positive. Thus solute dipolarity, hydrogen-bond acidity, and hydrogen-bond basicity, all lead to a preference for water, whereas solute volume leads to a preference for hexadecane. As mentioned in the introduction, we were interested in results for aliphatic compounds and aromatic compounds taken separately; details of the found regressions are also in Table 4. A comparison of the 'aliphatics only' with the 'aromatics only' regression does suggest that there are small, but possibly significant differences, with the constants a , b , and v all being numerically smaller for the aromatic regression. Interestingly, Kamlet and co-workers^{31,32} found that for aqueous solubility of liquids and solids, different regression equations were required for aliphatic and aromatic compounds,³¹ but for water-octanol partition coefficients (log P_{OCT})³² the same regression equation could accommodate both types of solutes [equation (5)].

$$\log P_{OCT} = 0.35 + 0.36\delta_2 - 1.04\pi_2^* + 0.10\alpha_m - 3.84\beta_m + 5.35V_I \quad (5)$$

Because equation (5) is cast in terms of α_m and β_m (related to α_2^H and β_2^H but not entirely equivalent) and also of Leahy's intrinsic volume, V_I ,³³ we felt it useful to examine log P_{OCT} for the set of solutes assembled in Tables 1-3 using equation (4). The results are in Table 5. The v -constant in Table 5 is much smaller than in equation (5), but this is to be expected since V_x/V_I is only *ca.* 0.68.³⁰ The other constants in Table 5 are all reasonably consistent with those in equation (5), and, as found by Kamlet and co-workers,³² there is little difference between aliphatic and aromatic solutes.

It is instructive to compare the constants in equation (4) for water-hexadecane with water-octanol, for the 'all solutes' correlations:

	c	d	s	a	b	v
water-hexadecane	0.26	0.51	-1.45	-3.92	-5.21	4.32
water-octanol	0.20	0.49	-1.24	-0.28	-3.32	3.85

Table 3. Comparison of thermodynamics of transfer from water to hexadecane and to 2,2,4-trimethylpentane, molar scale at 298 K.

Solute	Hexadecane ^a			2,2,4-Trimethylpentane ^{11,12}		
	ΔG_{tr}°	ΔH_{tr}°	ΔS_{tr}°	ΔG_{tr}°	ΔH_{tr}°	ΔS_{tr}°
Butanone	0.59	4.58	13	0.25	4.54	14
Ethanol	2.99	8.68	19	2.72	8.36	19
Hexan-1-ol	-0.52	6.77	24	-0.74	6.57	24
Aniline	0.05	2.88	9	0.28	3.25	10
Nitrobenzene	-1.96	0.69	9	-1.95	0.67	9
Methyl benzoate	-2.03	0.88	10	-2.49	0.82	11
Phenol	1.01			1.31	4.64	11
<i>p</i> -Cresol	0.26			0.54	4.51	13
4-Chlorophenol	1.02			0.66	4.11	12
3-Methoxyphenol				1.48	4.46	10
4-Methylaniline				-0.46	3.53	13
4-Chloroaniline				-0.65	2.46	10
<i>N</i> -Methylaniline				-1.41	2.52	13
Methyl phenyl sulphone				1.25	3.21	7
Methyl phenyl sulphoxide				2.03	5.60	12
Ethyl benzoate				-2.76	0.74	12
Benzyl alcohol	0.29	5.87	19	1.04	6.15	17
2-Phenylethanol				0.49	6.03	19
3-Phenylpropan-1-ol				-0.25	6.41	22
Acetophenone	-1.53	1.32	10	-1.52	2.11	12
Benzaldehyde	-1.41	0.95	8	-1.43	0.99	8
Anisole	-2.90	0.00	10	-2.76	0.00	9
Pyridine	0.60	4.13	12	0.56	4.08	12

^a From Tables 1 and 2, after conversion into the molar scale.**Table 4.** Regression analysis of water-hexadecane partition coefficients, using equation (4).^a

Solute set	<i>c</i>	<i>d</i>	<i>s</i>	<i>a</i>	<i>b</i>	<i>v</i>	<i>n</i>	<i>r</i>	sd
All solutes	0.26 ± 0.06	0.51 ± 0.05	-1.45 ± 0.09	-3.92 ± 0.11	-5.21 ± 0.09	4.32 ± 0.06	270	0.9884	0.28
Aliphatics only	0.27 ± 0.07	0.48 ± 0.17	-1.45 ± 0.10	-4.11 ± 0.14	-5.39 ± 0.13	4.39 ± 0.07	203	0.9890	0.28
Aromatics only	0.94 ± 0.19	—	-1.31 ± 0.17	-3.65 ± 0.13	-4.74 ± 0.17	3.85 ± 0.16	67	0.9913	0.21

^a Compounds listed in Tables 1-3, with log P_H on the molar scale.**Table 5.** Regression analysis of water-octanol partition coefficients,^a using equation (4).

Solute set	<i>c</i>	<i>d</i>	<i>s</i>	<i>a</i>	<i>b</i>	<i>v</i>	<i>n</i>	<i>r</i>	sd
All solutes	0.20 ± 0.06	0.49 ± 0.04	-1.24 ± 0.08	-0.28 ± 0.08	-3.32 ± 0.08	3.85 ± 0.06	307	0.9790	0.26
Aliphatic only	0.28 ± 0.06	0.24 ± 0.15	-1.28 ± 0.09	-0.48 ± 0.13	-3.42 ± 0.11	3.84 ± 0.06	215	0.9740	0.27
Aromatic only	0.53 ± 0.17	—	-0.91 ± 0.15	-0.17 ± 0.09	-3.30 ± 0.14	3.74 ± 0.14	92	0.9782	0.22

^a Compounds listed in Tables 1-3, with log P_{OCT} on the molar scale.

The most striking features of the two sets of constants are (i) the dipolarity of wet octanol is surprisingly small, with *s* (octanol) almost as negative as *s* (hexadecane); (ii) the basicity of wet octanol must be almost the same as that of water, since *a* (octanol) is only -0.28 as compared with *a* (hexadecane) of -3.92; (iii) the hydrogen-bond acidity of wet octanol is appreciably less than that of water: *cf.* *b* (hexadecane) = -5.21, *b* (octanol) = -3.21; and (iv) the cavity effect (or probably a combined cavity effect plus dispersion interactions) for wet octanol is not far away from that for hexadecane. Obviously, results on more water-solvent partitions are needed to quantify these effects, but already it can be seen that equation (4) will yield information about various solute-solvent interactions.

Having now to hand not only values of log P_H (equivalent to ΔG_{tr}° on the molar scale) but also ΔH_{tr}° , we can now set out ΔG_{tr}° , ΔH_{tr}° , and ΔS_{tr}° on the mole fraction scale, Table 1, and regress a unified set of transfer parameters for the same solutes. We have 86 such solutes for which the required explanatory variables are

known, and summarise results of the regressions in Table 6. The constants in the ΔG_{tr}° regression (other than *c*) then yield the log P_H constants on division by -1.364; there is reasonable agreement between the 86 solute correlation in Table 6 and the 270 solute correlation in Table 4. The sd values in Table 6 are roughly as expected for correlations of ΔH_{tr}° (± 0.5 kcal mol⁻¹) and ΔS_{tr}° (± 2 kcal K⁻¹ mol⁻¹), being 0.94 kcal mol⁻¹ and 2.7 cal K⁻¹ mol⁻¹ respectively.

There are a number of extraordinary features of the results given in Table 6; it is useful to take the main parameters in turn. The *s*-constants, viewed as dipolarity effects, are almost impossible to interpret. Whereas an increase in solute dipolarity (π_2^*) reduces transfer to hexadecane in terms of ΔG_{tr}° or log P_H , it actually aids transfer in terms of ΔH_{tr}° . One difficulty here is that the π_2^* parameter involves not only dipolarity, but also polarisability effects; furthermore, there is an interplay between δ_2 , the polarisability correction term, and π_2^* . The solute hydrogen-bond acidity term, $\alpha\alpha_2^H$, can be plausibly interpreted

Table 6. Regression analysis of ΔG_{tr}° , ΔH_{tr}° , and ΔS_{tr}° for the water-hexadecane partition, mole fraction scale at 298 K.^a

Parameter	c	d	s	a	b	v	n	r	sd
ΔG_{tr}°	-1.90 ± 0.11	-0.69 ± 0.12	1.63 ± 0.23	5.44 ± 0.23	7.06 ± 0.25	-5.78 ± 0.15	86	0.9896	0.35
ΔH_{tr}°	2.81 ± 0.30	-1.73 ± 0.33	-2.08 ± 0.60	8.11 ± 0.62	10.05 ± 0.67	-2.43 ± 0.41	86	0.9451	0.94
ΔS_{tr}°	15.80 ± 0.88	-3.55 ± 0.95	-12.84 ± 1.74	9.23 ± 1.80	10.34 ± 1.95	11.28 ± 1.19	86	0.8766	2.73
$-T\Delta S_{tr}^\circ$ ^b	-4.71	1.06	3.83	-2.75	-3.08	-3.36			

^a Values from Tables 1 and 3, ΔG_{tr}° and ΔH_{tr}° in kcal mol⁻¹; ΔS_{tr}° in cal K⁻¹ mol⁻¹. ^b Calculated from the constants in the ΔS_{tr}° regression. The values do not quite yield the $\Delta H_{tr}^\circ - \Delta G_{tr}^\circ$ constants due to rounding-off errors.

as follows. Hydrogen-bonding from the solute acid to water base will be exothermic, and hence ΔH_{tr}° will be positive (as observed). But the creation of hydrogen bonds will be somewhat disfavoured in terms of entropy, leading to a positive ΔS_{tr}° value and to a ΔG_{tr}° value that is still positive, but less so than ΔH_{tr}° . An exactly similar argument can account for the positive b -constants in ΔG_{tr}° , ΔH_{tr}° , and ΔS_{tr}° . The breakdown of the vV_x 'cavity' term into enthalpic and entropic contributions is especially interesting in that any so-called 'hydrophobic effect' must reside in this vV_x term. Now on the scaled particle theory (SPT),³⁴ the free energy of cavity formation in water, G_{cav}^w , is much more positive than the corresponding value in a solvent such as hexadecane, G_{cav}^h . Hence $G_{cav}^h - G_{cav}^w$ is negative and will correspondingly contribute a negative quantity to ΔG_{tr}° . But the enthalpy of cavity formation in water is smaller than in solvents such as hexadecane, so that $H_{cav}^h - H_{cav}^w$ is actually positive.³⁵ We suggest that the vV_2 term in equation (2) and the vV_x term in equation (4) include not only cavity effects, but general dispersion interactions as well. These will always be more exoergic and exothermic in hexadecane than in water (note that water has a particularly low refractive index and molar refraction). Hence a combination of an exoergic interaction transfer with an exoergic cavity transfer will lead to a very negative vV_x term in ΔG_{tr}° . But combination of an exothermic interaction transfer with an endothermic cavity transfer can result in a vV_x term that is still negative, but not greatly so. This is exactly as observed, Table 6.

Our thermodynamic analysis thus reveals that the $\pi\pi_2^*$ term in equation (2) and equation (4) cannot easily be interpreted on its own, not even in conjunction with the correction term $d\delta_2$. The hydrogen-bond terms, however, seem to be quite straightforward, but the so-called cavity term vV_x (or vV_2) must include not only cavity effects but also general dispersion interactions as well. Our analysis also shows that because of the rather complicated interplay of the coefficients in the Gibbs energy and enthalpy of transfer, no simple relationship between ΔG_{tr}° and ΔH_{tr}° across families of solutes is expected. This is in agreement with the findings of Tomlinson *et al.*¹² and also our own observations.

Acknowledgements

The studies at the University of Houston were supported by the Welch Foundation, and those at University College London by the United States Army Research, Development and Standardisation Group. We thank Dr. Albert Leo for providing us with a number of water-octanol partition coefficients.

This paper is dedicated to the memory of Mortimer J. Kamlet.

References

- C. Hansch and A. Leo, 'Substituent Constants for Correlation Analysis in Chemistry and Biology,' Wiley-Interscience, New York, 1974.
- A. Finkelstein, *J. Gen. Physiol.*, 1976, 68, 127.
- N. P. Franks and W. R. Lieb, *Nature (London)*, 1978, 274, 339.
- M. H. Abraham, P. L. Grellier, and R. A. McGill, *J. Chem. Soc., Perkin Trans. 2*, 1987, 747.
- M. M. Schantz and D. E. Martire, *J. Chromatogr.*, 1987, 391, 35; M. M. Schantz and D. E. Martire, *J. Res. Nat. Bur. Stand., Sect. A*, 1988, 93, 161.
- J. Hine and P. K. Mookerjee, *J. Org. Chem.*, 1975, 40, 292.
- S. Cabani, P. Gianni, V. Mollica, and L. Lepore, *J. Solution Chem.*, 1981, 10, 563.
- M. H. Abraham, *J. Chem. Soc., Faraday Trans. 1*, 1984, 80, 153.
- M. H. Abraham and E. Matteoli, *J. Chem. Soc., Faraday Trans. 1*, 1988, 84, 1985.
- D. Mackay and W. Y. Shiu, *J. Phys. Chem. Ref. Data*, 1981, 10, 1175; 1986, 15, 911.
- W. Riebesehl and E. Tomlinson, *J. Phys. Chem.*, 1984, 88, 4770.
- W. Riebesehl, E. Tomlinson, and H. J. M. Grünbauer, *J. Phys. Chem.*, 1984, 88, 4775.
- R. Fuchs, M. H. Abraham, M. J. Kamlet, and R. W. Taft, *J. Phys. Org. Chem.*, in the press.
- R. Fuchs, E. J. Chambers, and W. K. Stephenson, *Can. J. Chem.*, 1987, 65, 2624.
- R. S. Siderov, A. A. Khvostikova, and G. I. Vakhursheva, *J. Anal. Chem. USSR (Engl. Transl.)*, 1973, 28, 1420.
- N. Dimov, *J. Chromatogr.*, 1985, 347, 366.
- L. Sojak, J. Rumen, and J. Janak, *J. Chromatogr.*, 1987, 391, 79.
- F. Riedo, D. Fritz, G. Tarjan, and E. Kovats, *J. Chromatogr.*, 1976, 126, 63.
- P. Laffort and F. Patte, *J. Chromatogr.*, 1987, 406, 51.
- U. Weldlich and J. Grehling, *J. Chem. Eng. Data*, 1987, 32, 138.
- M. Laffosse and M. Dreux, *J. Chromatogr.*, 1980, 193, 9.
- M. J. Kamlet, R. M. Doherty, J.-L. M. Abboud, M. H. Abraham, and R. W. Taft, *Chemtech.*, 1986, 16, 566.
- M. H. Abraham, R. M. Doherty, M. J. Kamlet, and R. W. Taft, *Chem. Br.*, 1986, 22, 551.
- M. J. Kamlet, R. M. Doherty, M. H. Abraham, and R. W. Taft, *Quant. Struct. Act. Relat.*, 1988, 7, 71.
- M. H. Abraham, P. L. Grellier, I. Hamerton, R. A. McGill, D. V. Prior, and G. S. Whiting, *Faraday Discuss. Chem. Soc.*, 1988, 85, 107.
- M. H. Abraham, P. L. Grellier, D. V. Prior, P. P. Duce, J. J. Morris, and P. J. Taylor, *J. Chem. Soc., Perkin Trans. 2*, 1989, 699.
- M. H. Abraham, P. L. Grellier, D. V. Prior, J. J. Morris, P. J. Taylor, C. Laurence, and M. Berthelot, *Tetrahedron Lett.*, 1989, 30, 9571.
- M. H. Abraham, P. L. Grellier, D. V. Prior, J. J. Morris, and P. J. Taylor, *J. Chem. Soc., Perkin Trans. 2*, submitted for publication.
- M. H. Abraham and G. S. Whiting, unpublished work.
- M. H. Abraham and J. C. McGowan, *Chromatographia*, 1987, 23, 243.
- M. J. Kamlet, R. M. Doherty, M. H. Abraham, P. W. Carr, R. F. Doherty, and R. W. Taft, *J. Phys. Chem.*, 1987, 91, 1996.
- M. J. Kamlet, R. M. Doherty, M. H. Abraham, Y. Marcus, and R. W. Taft, *J. Phys. Chem.*, 1988, 92, 5244.
- D. E. Leahy, *J. Pharm. Sci.*, 1986, 75, 629.
- R. A. Pierotti, *Chem. Rev.*, 1976, 76, 717.
- M. H. Abraham and A. Nasehzadeh, *J. Chem. Soc., Faraday Trans. 1*, 1981, 77, 321.

Paper 9/01419E

Received 6th April 1989

Accepted 20th October 1989