*Acta Cryst.* (1990). B46, 426–431

# X-ray Structural Studies on Three Analogues of the α-Anomer of the Antitumour Antibiotic Showdomycin. Differential Ring-Puckering Effects of Hydroxyl Sugar Substituents in *lyxo* and *arabino* Configurations

BY STEPHEN NEIDLE*

*Cancer Research Campaign Biomolecular Structure Unit, The Institute of Cancer Research, Sutton, Surrey SM2 5NG, England*

AND ANDREW KAYE AND COLIN B. REESE

*Department of Chemistry, King's College London, Strand, London WC2R 2LS, England*

(*Received* 29 *September* 1989; *accepted* 10 *January* 1990)

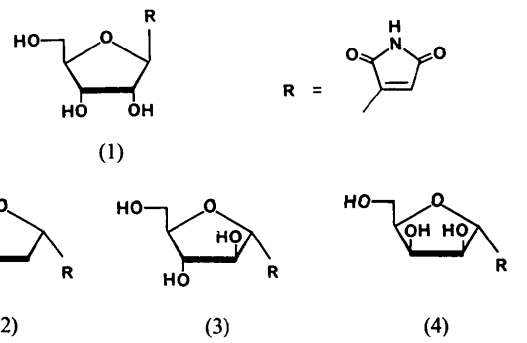
## Abstract

The crystal structures of three α-analogues of the anititumour antibiotic showdomycin (1) have been determined at room temperature. They are 2-(α-D-2′-deoxyribofuranosyl)maleimide (2), 2-(α-D-arabinofuranosyl)maleimide (3) and 2-(α-D-lyxofuranosyl)maleimide (4). The structures were refined to *R* factors of 0·039, 0·042 and 0·029 for 971, 1025 and 716 observed reflections. The conformational properties of the sugar rings are discussed in detail, in relation to the differing hydroxyl group substitutions. Compounds (2) and (3) have C3′-*endo*, C4′-*exo* and C3′-*endo* ring puckers, whereas (3) has C2′-*endo*, C1′-*exo* puckers. Compound (3) has an intramolecular hydrogen bond between the O5′ and O2′ hydroxyl groups. This and the sugar pucker difference are in accord with NMR chemical shift data for the O5′ and O2′ protons. Crystal data: compound (2), $C_9H_{11}NO_5$, orthorhombic, $P2_12_12_1$, $a$ = 5·916 (1), $b$ = 8·191 (1), $c$ = 19·691 (3) Å, $Z$ = 4; compound (3), $C_9H_{11}NO_6$, orthorhombic, $P2_12_12_1$, $a$ = 6·785 (1), $b$ = 8·006 (1), $c$ = 17·564 (2) Å, $Z$ = 4; compound (4), $C_9H_{11}NO_6$, monoclinic, $P2_1$, $a$ = 8·681 (1), $b$ = 5·135 (1), $c$ = 11·364 (1) Å, $Z$ = 2.

## Introduction

Showdomycin (1) is a naturally occurring β-*C*-nucleoside with a maleimide group replacing a normal nucleobase (Suhadolnik, 1979). It is moderately active against gram-positive and gram-negative bacteria and shows some cytotoxic activity against HeLa cells; it is highly active against ascites tumours in rats, probably by means of inhibition of nucleic acid synthesis.

There is considerable current interest in nucleoside analogues, in large part because of the antiviral activity shown by compounds such as 2′,3′-dideoxycytidine and 3′-azido-3′-deoxythymidine against human immunodeficiency virus (HIV) (Mitsuya & Broder, 1986; DeClercq, 1986). The latter compound has been established to act by blocking the action of the reverse transcriptase enzyme, RNA-dependent DNA polymerase (Furman *et al.*, 1986). Nucleosides with the unnatural α-configuration have also been reported to show this action, and some have potent experimental antitumour activity. This paper reports on the crystal structures of three showdomycin analogues, all of which have an α-configuration at C1′. The compounds studied are: 2-(α-D-2′-deoxyribofuranosyl)-maleimide (2), 2-(α-D-arabinofuranosyl)maleimide (3) and 2-(α-D-lyxofuranosyl)maleimide (4). The effects of systematic changes of hydroxyl group configuration on nucleoside conformation are detailed here; synthetic studies on these compounds have been published elsewhere (Kaye, Neidle & Reese, 1988*a*,*b*).




## Experimental

Colourless prismatic crystals of all three compounds were grown by slow evaporation from ethanol/water solutions. Preliminary cell dimensions and space-

* Address correspondence to this author.

0108-7681/90/030426-06$03.00

group assignments were obtained from oscillation and Weissenberg photographs. Accurate cell dimensions were obtained by least-squares refinement of sets of 25 $\theta$ values in the range of 17–32° measured on an Enraf–Nonius CAD-4 diffractometer with graphite-monochromated Cu $K\alpha$ radiation. These are given in Table 1, which also contains numerical details of the data collection and structure refinement.

Intensity data for all three compounds were collected on the diffractometer at room temperature using the $\omega$–$2\theta$ scan method. The scan rate was varied during the data collections from 1·0 to 4·0° $min^{-1}$, so as to ensure good counting statistics for weak reflections, for which a slow scan speed was employed. A variable scan width was used, with $\omega = (1{\cdot}0 + 0{\cdot}140\tan\theta)°$. Background counts were made by scanning an additional 25% above and below this range. This gave a ratio of 2:1 for peak:background counting times. The data collections were monitored with three standard reflections for each hour of X-ray exposure time; in no case was any significant crystal decay noted. Lorentz and polarization corrections were applied to the data sets, together with empirical absorption corrections (Walker & Stuart, 1983).

Structures (2) and (4) were solved by routine application of the multisolution direct-methods program *MULTAN*82 (Main *et al.*, 1982). In both cases, solutions with the highest combined figure of merit resulted in *E* maps that revealed all the non-H atoms. Structure (3) was eventually solved only after a starting set of origin-defining and permuting reflections was chosen by hand. This has a wider range of *hkl* index values than the set chosen by *MULTAN*82: the resulting phase set with the highest combined figure of merit produced an *E* map that showed all the non-H atoms. All previous attempts at solving this structure resulted in trial structures that would not refine below $R = 0{\cdot}12$. These were related to the eventual correct structure by half-cell translations in *a*, *b* or *c* directions.

All three structures were refined by full-matrix least-squares techniques, minimizing $\sum w(\Delta F)^2$ with weights $w = 1/[\sigma^2(F) + 0{\cdot}04F^2]$. Non-H atoms were refined anisotropically. The positions of all H atoms in the three structures were located in difference Fourier syntheses. These, together with individual isotropic temperature factors, were also included in the later stages of the least-squares refinements. The final refinement statistics are given in Table 1.

Atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1974). All calculations were performed on a VAX 11/750 computer, using the *SDP* program system (Frenz, 1981) together with programs developed at the Institute of Cancer Research.

Table 1. *Crystallographic data for compounds* (2)–(4)

| | (2) | (3) | (4) |
|---|---|---|---|
| $a$ (Å) | 5·916 (1) | 6·785 (1) | 8·681 (1) |
| $b$ (Å) | 8·191 (1) | 8·006 (1) | 5·135 (1) |
| $c$ (Å) | 19·691 (3) | 17·564 (2) | 11·364 (1) |
| $\beta$ (°) | | | 109·75 (1) |
| Space group | $P2_12_12_1$ | $P2_12_12_1$ | $P2_1$ |
| $Z$ | 4 | 4 | 2 |
| Formula | $C_9H_{11}NO_5$ | $C_9H_{11}NO_6$ | $C_9H_{11}NO_6$ |
| $\mu$ ($cm^{-1}$) | 10·0 | 11·3 | 11·3 |
| $D_x$ (g $cm^{-3}$) | 1·484 | 1·584 | 1·596 |
| Crystal size (mm) | 0·35 × 0·15 × 0·10 | 0·30 × 0·15 × 0·08 | 0·20 × 0·10 × 0·05 |
| $\theta$ range (°) | $1{\cdot}5 \le \theta \le 70$ | $1{\cdot}5 \le \theta \le 70$ | $1{\cdot}5 \le \theta \le 70$ |
| *hkl* range | $h$ 0→7 | 0→8 | 0→10 |
| | $k$ 0→9 | 0→9 | 0→6 |
| | $l$ 0→24 | 0→21 | −13→13 |
| Max. scan time (s) | 90 | 90 | 90 |
| $T_{min}/T_{max}$ (° $min^{-1}$) | 0·93/1·23 | 0·91/1·15 | 0·88/1·07 |
| No. of observations | 1077 | 1082 | 969 |
| No. of reflections > $n\sigma(I)$ | 971 ($n$ = 3) | 1025 ($n$ = 3) | 716 ($n$ = 2) |
| E.s.d. of observation of unit weight | 2·00 | 3·01 | 1·02 |
| Max. $\Delta/\sigma$ | 0·09 | 0·16 | 0·06 |
| $R$ | 0·039 | 0·042 | 0·029 |
| $wR$ | 0·055 | 0·069 | 0·033 |
| Max., min. $\Delta\rho$ (e $Å^{-3}$) | ±0·18 | ±0·28 | ±0·25 |

## Results and discussion

The molecular structures of the compounds (2)–(4) are shown in Figs. 1–3. Their absolute configurations have been defined with reference to the known absolute configurations of their sugar precursors; hence in all three cases the maleimide group is in an $\alpha$-configuration with respect to the sugar ring. Atomic coordinates for structures (2)–(4) are given in Table 2,* and bond lengths and angles in Table 3. Relevant derived conformational parameters are given in Table 4.

### *Conformational features*

The 2′-deoxyribofuranosyl sugar in (2) and the lyxofuranose in (4) are both in the C3′-*endo* pucker class (Figs. 1, 3), with the former having the more pronounced pucker, as shown by the difference in calculated maximum angles of pseudorotation. The C3′-*endo* family and the closely related C2′-*exo* pucker are frequently found in crystal structures of $\alpha$-nucleosides, especially in those with a carbon–carbon glycosidic bond. Thus, $\alpha$-pseudouridine (Rohrer & Sundaralingam, 1970) has a C2′-*exo* sugar pucker, and 1′-(3-pyridyl)-2′-deoxy-$\alpha$-D-ribofuranose (Ford, Neidle, Eaton, Millican & Mann, 1987) is C2′-*exo*–C1′-*endo*. Similar puckers have been observed for 1-$\alpha$-D-xylofuranosylcytosine and its hydrochloride salt (Post, Huber, Birnbaum & Shugar, 1981) and in the $\alpha$-anomer of the *C*-nucleoside liazofurin (Goldstein, Takusagawa,

* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 52637 (42 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Berman, Srivastava & Robins, 1985). The $\alpha$-anomer of showdomycin (Barrett & Broughton, 1984) has a C2′-*exo* sugar pucker, whereas showdomycin itself is C2′-*endo* (Tsukuda & Koyama, 1970). The model compound methyl $\alpha$-D-lyxofuranoside (Groth & Hammer, 1968), which is analogous to (4), has pure C3′-*endo* pucker. A recent combined NMR and molecular-mechanics study (Raap, van Boom, van Lieshout & Hassnoot, 1988) of the conformations adopted by methyl 2′-deoxy-D-ribofuranoside in both the $\alpha$- and $\beta$-configurations has relevance to the conformation of compound (2); this analysis showed a strong preference for C2′-*endo* pucker in the case of the $\alpha$-anomer, although this is clearly dependent on the nature of the substituent at C1′, with the —OMe group in this analysis (Raap *et al.*, 1988) producing a substantial anomeric effect. The *gauche* effect (Birnbaum & Shugar, 1987) may well play a role in the preference shown by compounds (2) and (4) (at least in the solid state) for the C3′-*endo* form. This effect tends to stabilize the conformation that has the maximum number of *gauche* interactions, thus favouring the observed puckers for the 2′-deoxy (2) and *lyxo* (4) sugars – C2′-*endo* puckers would result in one less *gauche* interaction for each one.

By contrast, arabinosyl sugars would be expected to favour C2′-*endo* puckers. This is indeed observed here for compound (3), although the existence of an intramolecular hydrogen bond between O2′ and O5′ is probably a more important factor in the stabilization of this pucker. This hydrogen bond is of length 2·788 (4) Å, with O2′ acting as donor. The O5′···H2′ distance is 1·88 (3) Å and the angle O5′···H2′—O2′ is 162·6 (21)°. NMR chemical shift data (Kaye & Reese, 1989) show that the resonance signals of the 2′- and 5′-hydroxyl protons of the *ara* compound (3) are 0·28 and 0·24 p.p.m. respectively downfield from the corresponding signals in the NMR spectrum of the *lyxo* compound (4), and the resonance signal of the 5′-hydroxyl proton in (3) is 0·14 p.p.m. downfield from the corresponding signal in the deoxy compound (2). These data are in accordance with hydrogen bonding in the *ara* compound (3). Such intramolecular hydrogen bonding has frequently been observed in the *arabino* series, for example in the crystal structure of 1-($\beta$-D-arabinosyl)cytosine (Chwang & Sundaralingam, 1973). By contrast, its 5-methyl derivative does not have this interaction, even though C2′-*endo* puckering was still observed (Birnbaum & Gentry, 1983).

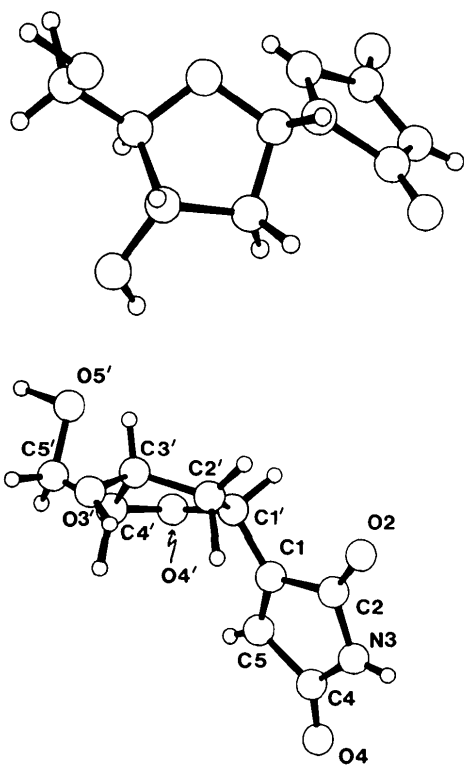



Fig. 1. Computer-drawn plots of compound (2). The top figure is drawn projected onto the mean plane of the ribose ring. The bottom figure is drawn at right-angles to this.

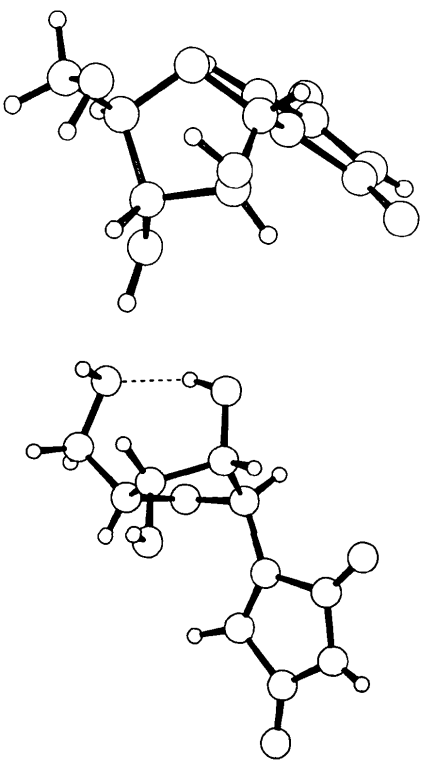


Fig. 2. Computer-drawn plots of compound (3). The intramolecular hydrogen bond between O2′ and O5′ is shown by a dashed line.

The *C*-glycosidic angles for all three structures are very similar (Table 4), with no clear relationship between sugar pucker and value. There is thus a *cis* relationship between the O4′ ring sugar atom and C5/H5 of the pyrrolidine ring. A *trans* orientation, with $\chi = 180°$, would bring the O2 carbonyl atom into close contact with the $\alpha$-H atom attached to C2′, in the case of both structures (2) and (4). A $\chi$ of 180° for (3) would result in a clash with O3′, or with the $\alpha$-H atom of C2′ if compound (3) adopted a C3′-*endo* pucker. The epi-showdomycin structure (Barrett & Broughton, 1984) has a $\chi$ of $-14{\cdot}5°$.

The conformations about the exocyclic C5′—C4′ bonds can be described as *gauche*$^+$, *gauche*$^-$ for structures (2) and (3), and the more unusual *trans*, *gauche* for (4). The intramolecular hydrogen bonding in (3) between O2′ and O5′ of the arabinosyl ring is responsible for its conformation, which has also been found in $\beta$-arabinosyl nucleosides (see, for example; Chwang, Sundaralingam & Hanessian, 1974; Ekiel, Darzynkiewicz, Birnbaum & Shugar, 1979; Ekiel, Remin, Darzynkiewicz & Shugar, 1979) both in solution and in the solid state. The *trans* conformation in (4) can be correlated with C3′-*endo* sugar pucker (Berman, 1981).

### *Bond geometry*

Examination of bond lengths and angles for the sugar rings of (2)–(4) (Table 3) shows that there are some small but statistically significant differences between them. In particular, the C1′—O4′ bond is 0·03 Å (7$\sigma$) shorter in (4) than in (2); the corresponding bond in the furanose sugar of epi-showdomycin (Barrett & Broughton, 1984) is 1·432 Å. This difference between (2) and (4) is probably not ascribable to conformational effects since they have very similar sugar ring puckers (Table 4), but possibly to a transmitted electronic effect of the hydroxyl group at C2′ in (4). The averaged O4′—C1′ bond length of 1·433 Å is significantly longer than in normal *N*-nucleosides (Saenger, 1983), and is similar to those observed in other *C*-nucleosides (Goldstein, Takusagawa, Berman, Srivastava & Robins, 1983, 1985; and references therein). The C1′—C1 glycosi-

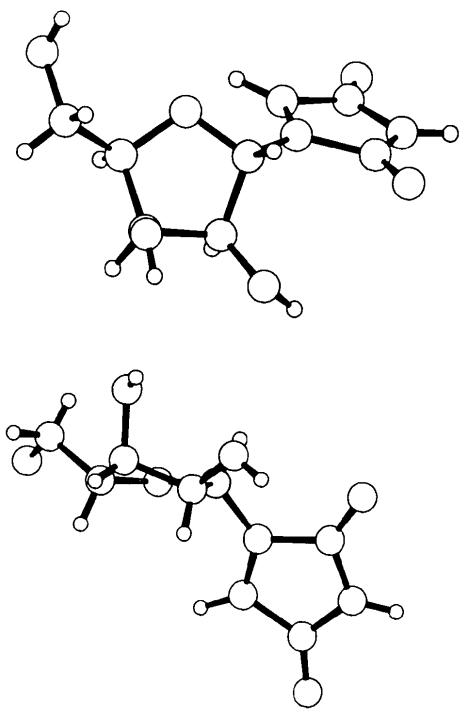


Fig. 3. Computer-drawn plots of compound (4).

Table 2. *Positional parameters and equivalent isotropic thermal parameters for the non-*H *atoms with e.s.d.'s in parentheses*

$B = (8\pi^2/3)(U_{11} + U_{22} + U_{33})$ where $U_{11}$, $U_{22}$ and $U_{33}$ are the principal components of the mean-square-displacement matrix **U**.

| | *x* | *y* | *z* | *B* (Å$^2$) |
|---|---|---|---|---|
| (*a*) Compound (2) | | | | |
| C1′ | 1·0756 (8) | 1·3727 (6) | 0·6427 (2) | 2·04 (8) |
| C2′ | 1·1074 (9) | 1·1867 (6) | 0·6359 (2) | 2·26 (9) |
| C3′ | 0·9445 (8) | 1·1185 (6) | 0·6887 (2) | 2·02 (8) |
| O3′ | 0·8513 (6) | 0·9617 (4) | 0·6697 (2) | 2·49 (6) |
| C4′ | 0·7574 (8) | 1·2442 (6) | 0·6910 (2) | 2·17 (8) |
| C5′ | 0·6230 (9) | 1·2510 (7) | 0·7557 (2) | 2·8 (1) |
| O5′ | 0·7741 (7) | 1·2634 (7) | 0·8117 (2) | 3·32 (7) |
| O4′ | 0·8730 (6) | 1·3984 (4) | 0·6827 (2) | 2·52 (6) |
| C1 | 1·0529 (9) | 1·4561 (6) | 0·5757 (2) | 2·04 (8) |
| C2 | 1·2304 (9) | 1·4396 (6) | 0·5238 (2) | 2·50 (9) |
| O2 | 1·4096 (6) | 1·3661 (5) | 0·5279 (2) | 3·68 (8) |
| N3 | 1·1562 (8) | 1·5251 (5) | 0·4666 (2) | 2·61 (8) |
| C4 | 0·952 (1) | 1·5980 (6) | 0·4803 (2) | 2·8 (1) |
| O4 | 0·8463 (8) | 1·6853 (5) | 0·4426 (2) | 4·04 (8) |
| C5 | 0·8931 (9) | 1·5497 (7) | 0·5513 (2) | 2·45 (9) |
| (*b*) Compound (3) | | | | |
| O2 | 0·7828 (4) | −0·0135 (4) | −0·5114 (2) | 2·49 (4) |
| O4 | 0·2942 (4) | −0·2296 (3) | 0·3628 (1) | 2·88 (5) |
| N3 | 0·5766 (5) | −0·1496 (4) | 0·4264 (2) | 2·20 (5) |
| C1 | 0·4258 (4) | 0·0286 (4) | 0·5114 (2) | 1·48 (5) |
| C2 | 0·6202 (5) | −0·0406 (4) | 0·4860 (2) | 1·78 (5) |
| C4 | 0·3774 (5) | −0·1508 (4) | 0·4132 (2) | 1·88 (5) |
| C5 | 0·2840 (5) | −0·0392 (4) | 0·4693 (2) | 1·90 (5) |
| C1′ | 0·4052 (5) | 0·1634 (4) | 0·5696 (2) | 1·58 (5) |
| C2′ | 0·4751 (5) | 0·1251 (4) | 0·6511 (2) | 1·57 (5) |
| C3′ | 0·2976 (5) | 0·0321 (4) | 0·6845 (2) | 1·46 (5) |
| C4′ | 0·1224 (5) | 0·1094 (4) | 0·6425 (2) | 1·44 (5) |
| O4′ | 0·2017 (3) | 0·2046 (3) | 0·5795 (1) | 1·68 (4) |
| C5′ | −0·0018 (5) | 0·2264 (4) | 0·6894 (2) | 2·04 (5) |
| O5′ | 0·1156 (4) | 0·3557 (3) | 0·7230 (1) | 2·36 (5) |
| O3′ | 0·3099 (4) | −0·1408 (3) | 0·6676 (1) | 2·06 (4) |
| O2′ | 0·5072 (4) | 0·2775 (3) | 0·6910 (1) | 2·22 (4) |
| (*c*) Compound (4) | | | | |
| C1′ | 0·5188 (4) | 0·446 | 0·7661 (3) | 2·06 (7) |
| C2′ | 0·6344 (4) | 0·5464 (8) | 0·8935 (3) | 2·02 (7) |
| O2′ | 0·5717 (3) | 0·5077 (6) | 0·9929 (2) | 2·75 (5) |
| C3′ | 0·7904 (4) | 0·3932 (8) | 0·9125 (3) | 2·24 (8) |
| O3′ | 0·7788 (3) | 0·1398 (6) | 0·9599 (2) | 2·87 (5) |
| C4′ | 0·7921 (4) | 0·3666 (8) | 0·7804 (3) | 2·02 (7) |
| C5′ | 0·8811 (4) | 0·1340 (9) | 0·7567 (3) | 2·64 (8) |
| O5′ | 0·8851 (3) | 0·1296 (6) | 0·6324 (2) | 2·55 (5) |
| O4′ | 0·6223 (3) | 0·3552 (6) | 0·7012 (2) | 2·91 (6) |
| C1 | 0·4085 (4) | 0·6545 (8) | 0·6924 (3) | 2·04 (7) |
| C2 | 0·2513 (4) | 0·7250 (8) | 0·7148 (3) | 2·33 (8) |
| O2 | 0·1919 (3) | 0·6179 (6) | 0·7844 (2) | 3·09 (6) |
| N3 | 0·1874 (3) | 0·9368 (7) | 0·6398 (2) | 2·62 (7) |
| C4 | 0·2864 (4) | 1·0015 (8) | 0·5706 (3) | 2·35 (7) |
| O4 | 0·2617 (3) | 1·1862 (6) | 0·5000 (2) | 3·11 (6) |
| C5 | 0·4240 (4) | 0·8137 (8) | 0·6051 (3) | 2·22 (7) |

Table 3. *Bond lengths* (Å) *and angles* (°) *for non*-H *atoms in compounds* (2)–(4)

| | (2) | (3) | (4) |
|---|---|---|---|
| C1—C2′ | 1·541 (3) | 1·539 (3) | 1·545 (6) |
| C1′—O4′ | 1·449 (3) | 1·431 (2) | 1·419 (4) |
| C2′—C3′ | 1·525 (3) | 1·535 (3) | 1·518 (7) |
| C2′—O2′ | — | 1·432 (2) | 1·425 (5) |
| C3′—C4′ | 1·512 (3) | 1·532 (3) | 1·513 (6) |
| C3′—O3′ | 1·447 (3) | 1·429 (2) | 1·425 (6) |
| C4′—O4′ | 1·445 (3) | 1·451 (2) | 1·446 (5) |
| C4′—C5′ | 1·503 (3) | 1·509 (3) | 1·496 (6) |
| C5′—O5′ | 1·423 (3) | 1·439 (3) | 1·424 (5) |
| C1′—C1 | 1·491 (3) | 1·499 (3) | 1·491 (6) |
| C1—C2 | 1·471 (3) | 1·500 (3) | 1·514 (5) |
| C1—C5 | 1·308 (3) | 1·331 (3) | 1·328 (6) |
| C2—O2 | 1·222 (3) | 1·201 (3) | 1·211 (5) |
| C2—N3 | 1·398 (3) | 1·385 (3) | 1·379 (6) |
| N3—C4 | 1·373 (3) | 1·372 (3) | 1·387 (5) |
| C4—O4 | 1·207 (3) | 1·227 (3) | 1·214 (5) |
| C4—C5 | 1·495 (3) | 1·478 (3) | 1·481 (6) |
| C2′—C1′—O4′ | 107·0 (2) | 103·4 (2) | 105·8 (4) |
| C1′—C2′—C3′ | 103·0 (2) | 102·2 (2) | 103·1 (4) |
| C1′—C2′—O2′ | — | 109·3 (2) | 113·3 (4) |
| C3′—C2′—O2′ | — | 110·6 (2) | 112·1 (4) |
| C2′—C3′—C4′ | 103·5 (2) | 103·1 (2) | 102·3 (4) |
| C2′—C3′—O3′ | 112·9 (2) | 110·6 (2) | 110·7 (4) |
| C4′—C3′—O3′ | 109·5 (2) | 110·0 (2) | 105·6 (4) |
| C3′—C4′—O4′ | 104·2 (2) | 107·1 (2) | 105·7 (4) |
| C3′—C4′—C5′ | 115·9 (2) | 115·2 (2) | 115·4 (4) |
| O4′—C4′—C5′ | 106·3 (2) | 107·0 (2) | 109·6 (4) |
| C1′—O4′—C4′ | 109·0 (2) | 109·1 (2) | 110·8 (3) |
| C4′—C5′—O5′ | 109·1 (2) | 111·6 (2) | 112·2 (4) |
| C1′—C1′—C2′ | 112·7 (2) | 117·4 (2) | 112·1 (4) |
| C1′—C1′—O4′ | 109·8 (2) | 110·0 (2) | 110·1 (4) |
| C2—C1—C5 | 108·3 (2) | 108·5 (2) | 107·6 (4) |
| C2—C1—C1′ | 120·5 (2) | 123·7 (2) | 121·4 (4) |
| C5—C1—C1′ | 131·2 (2) | 127·5 (2) | 130·9 (4) |
| O2—C2—N3 | 124·9 (2) | 125·8 (2) | 126·2 (4) |
| O2—C2—C1 | 128·2 (2) | 128·7 (2) | 127·4 (1) |
| C1—C2—N3 | 106·9 (2) | 105·5 (2) | 106·3 (4) |
| C2—N3—C4 | 109·6 (2) | 110·6 (2) | 110·1 (4) |
| N3—C4—O4 | 126·4 (2) | 126·0 (2) | 123·8 (4) |
| O4—C4—C5 | 127·6 (2) | 126·8 (2) | 129·1 (4) |
| N3—C4—C5 | 106·0 (2) | 107·2 (2) | 107·0 (4) |
| C1—C5—C4 | 109·2 (2) | 108·1 (2) | 108·8 (1) |

Table 4. *Torsion angles* (°) *and conformational parameters for compounds* (2)–(4)

| | | (2) | (3) | (4) |
|---|---|---|---|---|
| $\gamma_0$ | (C4′—O4′—C1′—C2′) | −9·7 (3) | −32·2 (3) | 5·4 (6) |
| $\gamma_1$ | (O4′—C1′—C2′—C3′) | −13·5 (3) | 39·0 (3) | −25·1 (6) |
| $\gamma_2$ | (C1′—C2′—C3′—C4′) | 30·4 (3) | −30·9 (3) | 34·2 (6) |
| $\gamma_3$ | (C2′—C3′—C4′—O4′) | −36·9 (3) | 12·8 (3) | −31·9 (6) |
| $\gamma_4$ | (C3′—C4′—O4′—C1′) | 29·2 (3) | 12·3 (3) | 16·8 (6) |
| | (O5′—C5′—C4′—C3′) | 51·3 (3) | 54·5 (3) | −176·8 (6) |
| | (O5′—C5′—C4′—O4′) | −65·3 (3) | −64·4 (3) | 63·9 (6) |
| $\delta$ | (C5′—C4′—C3′—O3′) | 83·6 (3) | 135·9 (3) | −36·1 (6) |
| | (O4′—C1′—C1—C5) | 4·0 (3) | 4·6 (3) | −23·4 (6) |
| Pseudorotation phase angle, $P$ (°) | | 33·6 | 143·4 | 9·8 |
| Sugar pucker* | | C3′-*endo* C4′-*exo* | C2′-*endo* C1′-*exo* | C3′-*endo* |
| Maximum angle of pseudorotation (°) | | 11·6 | −40·1 | 5·4 |

* The sugar-pucker parameters were calculated according to Altona & Sundaralingam (1972).

dic bond-length invariance here suggests an insensitivity to sugar pucker or hydroxy group differences. On the other hand, the small ring angle at C1′ in (3) and the larger ring angle at C4′ in (3) may be a result of the C2′-*endo* sugar pucker of (3) compared to the C3′-*endo* of (2) and (4). It is notable that these differences are not paralleled by theoretical studies of angular dependence on pseudorotational value in both $\alpha$- and $\beta$-nucleosides (Olson & Sussman, 1982; Serianni & Chipman, 1987).

Table 5. *Intermolecular hydrogen bonds*

| | Distance (Å) | Symmetry operation* |
|---|---|---|
| Compound (2) | | |
| O3′···O5′ | 2·780 (2) | 4 2 −1 1 |
| O3′···N3 | 2·934 (2) | 3 −1 2 1 |
| Compound (3) | | |
| O4···O5′ | 2·728 (3) | 2 0 0 −1 |
| N3···O3′ | 2·837 (2) | 3 0 −1 1 |
| O3′···O2′ | 2·853 (3) | 4 1 −1 1 |
| Compound (4) | | |
| O2′···O2′ | 2·882 (4) | 2 1 −1 2 |
| O3′···O2′ | 2·832 (4) | 2 1 −1 2 |
| O5′···N3 | 2·780 (4) | 1 1 −1 0 |
| O5′···O4 | 2·788 (4) | 2 1 −2 1 |

* The first digit in each symmetry operation refers to the standard space-group symmetry (below); the other three give $x$, $y$ and $z$ translations. For compounds (2) and (3) the space-group symmetry elements are: (1) $x, y, z$; (2) $\frac{1}{2}-x, -y, \frac{1}{2}+z$; (3) $\frac{1}{2}+x, \frac{1}{2}-y, -z$; (4) $-x, \frac{1}{2}+y, \frac{1}{2}-z$. For compound (4) they are: (1) $x, y, z$; (2) $-x, \frac{1}{2}+y, -z$.

Crystal packing in all three structures (Table 5) involves hydrogen bonding, with the hydroxyl groups participating in every interaction. There are no direct base···base hydrogen bonds.

We are grateful to the Cancer Research Campaign for support (to SN and CBR) and to the SERC and Roche Products Ltd for a Case studentship (to AK).

## References


ALTONA, C. L. & SUNDARALINGAM, M. (1972). *J. Am. Chem. Soc.* **94**, 8205–8212.

BARRETT, A. G. M. & BROUGHTON, H. B. (1984). *J. Org. Chem.* **49** (19), 3674.

BERMAN, H. M. (1981). In *Topics in Nucleic Acid Structure*, Part 1, edited by S. NEIDLE. London: Macmillan Press.

BIRNBAUM, G. I. & GENTRY, G. A. (1983). *J. Am. Chem. Soc.* **105**, 5398–5402.

BIRNBAUM, G. I. & SHUGAR, D. (1987). In *Topics in Nucleic Acid Structure*, Part 3, edited by S. NEIDLE. London: Macmillan Press.

CHWANG, A. K. & SUNDARALINGAM, M. (1973). *Nature (London)*, **243**, 78–80.

CHWANG, A. K., SUNDARALINGAM, M. & HANESSIAN, S. (1974). *Acta Cryst.* B**30**, 2273–2276.

DECLERCQ, E. (1986). *J. Med. Chem.* **29**, 1561–1569.

EKIEL, I., DARZYNKIEWICZ, E., BIRNBAUM, G. I. & SHUGAR, D. (1979). *J. Am. Chem. Soc.* **101** (16), 4724–4729.

EKIEL, I., REMIN, M., DARZYNKIEWICZ, E. & SHUGAR, D. (1979). *Biochim. Biophys. Acta*, **562**, 177–191.

FORD, K. G., NEIDLE, S., EATON, M. A. W., MILLICAN, T. A. & MANN, J. (1987). *Acta Cryst.* C**43**, 1988–1989.

FRENZ, B. A. (1981). *Enraf–Nonius Structure Determination Package*. Enraf–Nonius, Delft, The Netherlands.

FURMAN, P. A., FYKE, J. A., ST CLAIR, M. H., WEINHOLD, K., RIDEOUT, J. L., FREEMAN, G. A., LEHRMAN, S. N., BOLOGNESI, D. P., BRODER, S., MITSUYA, H. & BARRY, D. W. (1986). *Proc. Natl Acad. Sci. USA*, **83**, 8333–8337.

GOLDSTEIN, B. M., TAKUSAGAWA, F., BERMAN, H. M., SRIVASTAVA, P. C. & ROBINS, R. K. (1983). *J. Am. Chem. Soc.* **105**, 7416–7422.

GOLDSTEIN, B. M., TAKUSAGAWA, F., BERMAN, H. M., SRIVASTAVA, P. C. & ROBINS, R. (1985). *J. Am. Chem. Soc.* **107**(5), 1394–1400.

GROTH, P. & HAMMER, H. (1968). *Acta Chem. Scand.* **22**, 2059–2070.
*International Tables for X-ray Crystallography* (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)
KAYE, A., NEIDLE, S. & REESE, C. B. (1988*a*). *Tetrahedron Lett.* **29**, 1841–1844.
KAYE, A., NEIDLE, S. & REESE, C. B. (1988*b*). *Tetrahedron Lett.* **29**, 2711–2714.
KAYE, A. & REESE, C. B. (1989). Unpublished data.
MAIN, P., FISKE, S. J., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1982). *MULTAN82. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data.* Univs. of York, England, and Louvain, Belgium.
MITSUYA, H. & BRODER, S. (1986). *Proc. Natl Acad. Sci. USA*, **83**, 1511–1516.
OLSON, W. K. & SUSSMAN, J. L. (1982). *J. Am. Chem. Soc.* **104** (1), 270–278.
POST, M. L., HUBER, C. P., BIRNBAUM, G. I. & SHUGAR, D. (1981). *Can. J. Chem.* **59**, 238–245.
RAAP, J., VAN BOOM, J. H., VAN LIESHOUT, H. C. & HAASNOOT, A. G. (1988). *J. Am. Chem. Soc.* **110**, 2736–2743.
ROHRER, D. C. & SUNDARALINGAM, M. (1970). *J. Am. Chem. Soc.* **92** (16), 4950–4955.
SAENGER, W. (1983). *Principals of Nucleic Acid Structure.* Berlin: Springer-Verlag.
SERIANNI, A. S. & CHIPMAN, D. M. (1987). *J. Am. Chem. Soc.* **109** (18), 5297–5303.
SUHADOLNIK, R. J. (1979). *Nucleosides as Biological Probes.* New York: John Wiley.
TSUKUDA, BY. & KOYAMA, H. (1970). *J. Chem. Soc. B*, pp. 1709–1712.
WALKER, N. & STUART, D. (1983). *Acta Cryst.* A**39**, 158–166.

*Acta Cryst.* (1990). B**46**, 431–440

# Crystal Structures and Solid-State Photochemistry of Dimorphic Dibenzobarrelenes: Enantioselectivity of the Di-$\pi$-methane Rearrangement in the Solid State

BY MIGUEL GARCIA-GARIBAY, JOHN R. SCHEFFER, JAMES TROTTER AND FRED C. WIREKO

*Department of Chemistry, University of British Columbia, Vancouver, BC, Canada V6T 1Y6*

(*Received* 6 *July* 1989; *accepted* 15 *January* 1990)

## Abstract

The diisopropyl diester derivative of dibenzobarrelene is dimorphic; one of the dimorphs crystallizes in a chiral space group ($P2_12_12_1$), while the other crystallizes in an achiral space group (*Pbca*). The chiral crystal undergoes a stereospecific photorearrangement to yield the corresponding dibenzosemibullvalene in near-quantitative enantiomeric excess, and the absolute configurations of the starting material and the product have been determined (with reasonable, although not complete certainty). Steric arguments, coupled with the absolute configurational relationship between the starting material and its photoproduct, have been used to rationalize the enantioselective pathway of the rearrangement in the solid state. Crystal data are: $T = 295$ K, Mo $K\alpha_1$, $\lambda = 0{\cdot}70930$ Å, or Cu $K\alpha_1$, $\lambda = 1{\cdot}54056$ Å; diisopropyl 9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylate (form *a*, $^i$Pr/$^i$Pr-*a*), $C_{24}H_{24}O_4$, $M_r = 376{\cdot}45$, orthorhombic, $P2_12_12_1$, $a = 8{\cdot}3488$ (9), $b = 11{\cdot}7036$ (9), $c = 21{\cdot}8060$ (13) Å, $V = 2130{\cdot}7$ (3) Å$^3$, $Z = 4$, $D_x = 1{\cdot}173$ g cm$^{-3}$, $\mu$(Cu) = 6·0 cm$^{-1}$, $F(000) = 800$, $R = 0{\cdot}069$ for 3101 observed reflections; diisopropyl 9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylate (form *b*, $^i$Pr/$^i$Pr-*b*), $C_{24}H_{24}O_4$, $M_r = 376{\cdot}45$, orthorhombic, *Pbca*, $a = 9{\cdot}738$ (2), $b = 17{\cdot}092$ (3), $c = 25{\cdot}080$ (5) Å, $V = 4174$ (1) Å$^3$, $Z = 8$, $D_x = 1{\cdot}198$ g cm$^{-3}$, $\mu$(Mo) = 0·75 cm$^{-1}$, $F(000) = 1600$, $R = 0{\cdot}044$ for 1299 observed reflections; diisopropyl 4b,8b,8c,8d-tetrahydrodibenzo[*a,f*]cyclopropa[*cd*]pentalene-8c,8d-dicarboxylate ($^i$Pr/$^i$Pr-*ap*), $C_{24}H_{24}O_4$, $M_r = 376{\cdot}45$, tetragonal, $P4_32_12$, $a = 10{\cdot}1889$ (2), $c = 38{\cdot}6347$ (5) Å, $V = 4010{\cdot}8$ (1) Å$^3$, $Z = 8$, $D_x = 1{\cdot}247$ g cm$^{-3}$, $\mu$(Cu) = 6·4 cm$^{-1}$, $F(000) = 1600$, $R = 0{\cdot}036$ for 2879 observed reflections. The molecular structures of the dimorphs are similar to each other, except in the region of the $\alpha,\beta$-unsaturated carbonyl system where the extents of conjugation of the ester groups to the central double bond are different in the two dimorphs. The ring skeletons of the dibenzobarrelenes and the dibenzosemibullvalene are similar to the corresponding units of the unsymmetrical 11,12-diester derivatives in previous work. The enantioselective pathway leading to the formation of $^i$Pr/$^i$Pr-*ap* is consistent with steric packing effects, estimated from qualitative visual inspection of the packing environment around the ester groups, and from van der Waals intermolecular steric energy changes resulting from the movement of the ester groups.

## Introduction

Previous crystal structure studies of 11,12-diester derivatives of dibenzobarrelene with non-equivalent ester groups ($E' \neq E$, Fig. 1) (Garcia-Garibay,

0108-7681/90/030431-10$03.00