Gold Catalysed Reactions of Propargylic Alcohols

A dissertation presented by

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Declaration

I, Matthew Pennell, confirm that the work presented in this thesis is my own. Where information is derived from other sources, I confirm that it has been indicated and acknowledged.

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Abstract

Propargylic alcohols are easily accessed through the reaction of alkynes with aldehydes and ketones. The 1,3-isomerisation of propargylic alcohols to enones is known as the Meyer-Schuster rearrangement. [1] We have demonstrated efficient room temperature reaction conditions for the Au-catalysed Meyer-Schuster rearrangement (>30 examples) of a wide array of secondary and tertiary propargylic alcohols to the corresponding enones in generally excellent yields and with high *E*-selectivity (**A**). [2,3]

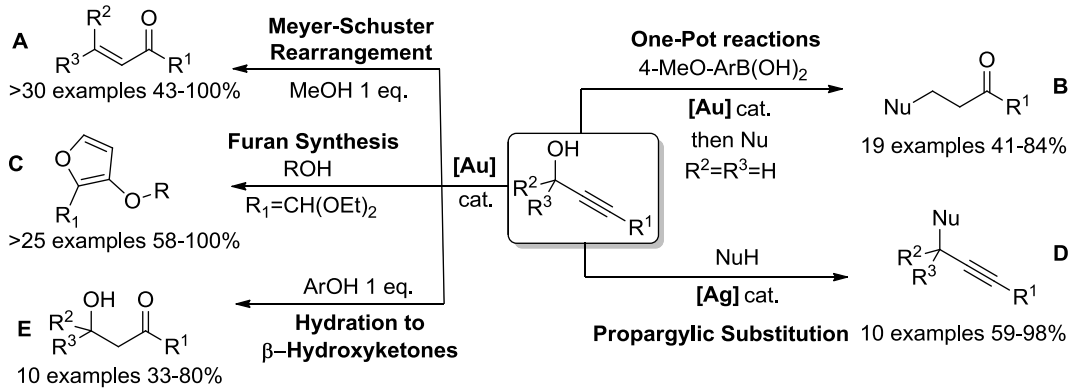


Figure 1: Reactions of Propargylic alcohols

Primary propargylic alcohols rearrange to give highly reactive terminal enones, which can undergo conjugate addition reactions with nucleophiles to access β-substituted products through suitable one-pot procedures (**B**). [2,3] Diethyl acetal substituted propargylic alcohols can be used to access synthetically useful 3-alkoxy furans in the presence of Au in high yield (**C**). The use of silver as a catalyst promotes substitution of the propargylic alcohol with various oxygen, carbon and nitrogen nucleophiles (**D**). [3] β-Hydroxyketones can be accessed *via* a Au-catalysed hydration, employing phenols or acidic alcohols as the reaction additive (**E**).

Contents

Abbreviations

AcOH	Acetic acid
MeCN	Acetonitrile
Ac	Acetyl
Bn	Benzyl
bp	Boiling point
Bu	Butyl
Cat.	Catalytic
X	Counter ion
Cy	Cyclohexyl
Et_2O	Diethyl ether
DIPEA	N,N-Diisopropylethylamine
DMF	N,N-Dimethylformamide
DMSO	Dimethyl sulfoxide
EI	Electron impact
EWG	Electron withdrawing group
E	Electrophile
ES	Electrospray ionisation
ee	Enantiomeric excess
er	Enantiomeric ratio
EtOH	Ethanol
Et	Ethyl
EtOAc	Ethyl acetate

Eq. or equiv.	Equivalents
g	Grams
HRMS	High resolution mass spectrometry
h	Hour(s)
IR	Infrared spectroscopy
n	Integer number
i	Iso
LA	Lewis acid
L	Ligand
LHMDS	Lithium bis(trimethylsilyl)amide
LDA	Lithium diisopropylamide
mp	Melting point
m-	Meta
MeOH	Methanol
Me	Methyl
mg	Miligram
mL	Millilitre
mmol	Millimole
nm	Nanometre
NHC	N-Heterocylic carbene
NMR	Nuclear magnetic resonance spectroscopy
Nu	Nucleophile
o-	Ortho

p-	Para
ppm	Parts per million
Ph	Phenyl
Pr	Propyl
Ref.	Reference
rt	Room temperature
Temp	Temperature
t or tert	Tertiary
TBS	tert-Butyl dimethylsilyl
TBME	tert-Butyl methyl ether
THF	Tetrahydrofuran
TLC	Thin layer chromatography
PhMe	Toluene
Et_3N	Triethylamine
UV	Ultraviolet
UCL	University College London
υ	Wavenumber cm^{-1}
IPR	2,6-bis(disopropylphenyl)imidazol-2-ylidene;

Acknowledgements

First of all I need to thank Tom whose brilliant ideas, infectious enthusiasm and capacity for daytime drinking have made the project so enjoyable throughout my time at UCL. I doubt I will ever, in my working life, have such an excellent boss again. I also need to thank my industrial supervisor Peter who helped make my time at GSK both enjoyable and productive.

I have thoroughly enjoyed working in the Sheppard Group and a large proportion of that is down to the company. I would in particular like to thank Osman (the 'wonderful p'), Lauren, Sam, Fav, Fil and Rhian for making the lab such a welcoming, curiosity driven and entertaining working environment, despite far too many lunchtime crosswords for my liking. Thanks also need to go to Sheppard group members past and present including Laure, Samantha, Emily, and Jarryl who have all been led astray from time to time. In that category I must also include Roomi, Sally, Rosemary, Dan, Liz and the rest of the Baker, Wilden and Caddick groups. A big thank you must also go to Jamie, Jon, Mark and Richard.

From day one I was joined by the fabulous Vincent Gray, whose quick wit and ever increasing array of talents continue to astound me and to whom I wish the very best for the future. Rachel, once approved by Vincent, joined us a year later and I am not sure how we ever coped without her. Rachel's generosity is a constant source of admiration, as are her fabulous dance moves and snail-like drinking pace. Rachel and Vincent have always been their to celebrate, commiserate and savage, when required, and for this and many other things I am truly grateful.

My parents unwavering support and encouragement appears limitless despite turning there much loved dining room into my thesis office, which I promise to tidy away in the near future. Also to my friends away from chemistry a big thank you for providing welcome distractions.

Finally and by no means least, I would like to thank my girlfriend Eddie, without whom I would never have had the work ethic to embark on my PhD and without her love and support I would never have finished it.

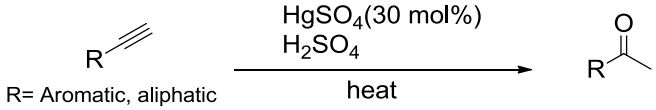
"Like all young men I set out to be a genius, but mercifully laughter intervened"

Lawrence Durrell - *Clea* (1960)

1. Introduction

I aim to provide a brief introduction as to what makes Au an effective homogeneous catalyst and discuss its role in activating alkynes towards a variety of nucleophiles for synthesis of substrates and also towards natural products. I will then give a background into the synthesis and reactions of propargylic alcohols. This will build towards discussion of the Meyer-Schuster rearrangement and also the Rupe rearrangement. Following the background discussion of propargylic alcohol reactions and Au catalysis I will go on to talk through the Sheppard group's previous work in the area of Au catalysis. I will then focus on my own research into the Meyer-Schuster rearrangement of various propargylic alcohols with a commercially available Au catalyst and how the research has developed to include one-pot reactions, propargylic substitution, hydration to β-hydroxyketones and furan synthesis. I will then look to draw some conclusions and make some recommendations for future work.

The Hg(II)-catalysed addition of alcohols to alkynes has been known for almost three-quarters of a century (Scheme 1). [4] Given the toxicity of Hg, a range of alternate transition-metal catalysts have been developed. [5] Over the last decade Au has emerged as an important synthetic tool exhibiting mild and chemoselective catalytic activation of alkynes. [6,7,8,9,10,11,12,13,14,15] Au has become the transition metal of choice to replace Hg in reactions such as hydrations, allowing alkynes to be viewed as masked carbonyls under benign conditions in many cases. [16] Importantly Au is employed catalytically in the hydration reaction at significantly lower levels than Hg (see section 1.3. Au activation of alkynes).



Scheme 1: Hg hydration of a terminal alkyne [17]

Advantages of Au include air stability, due to the high oxidation potential of Au(I) to Au(III) which provides a sufficient barrier to oxidation. Relative non-toxicity and lowered oxophilicity and thus tolerance towards water and alcohols.

Plus carbon-Au bonds that favour protodemetallation over beta-hydride elimination. [6,7,8,9,10,11,12,13,14,15]

1.1. Gold catalysts

Au can exist in three different oxidation states Au(0), Au(I), and Au(III). In aqueous solutions, in the absence of stabilising ligands, Au(I) spontaneously disproportionates to Au(III) and Au(0). [18] Au(I) usually exists as adducts of the form LAuX, where L is a ligand such as a triphenylphosphine or an isocyanide, and X is usually a halide or methyl. The presence of a ligand prevents reduction of Au(I) to metallic Au(0) *via* dimerisation of the organic residue. Au(I) complexes are 2-coordinate, linear, diamagnetic, 14 electron species, whereas Au(III) complexes are 4 coordinate, square planar, diamagnetic, 16 electron species and tend to exist in the form L_3AuX (Figure 1). [19]

Figure 1: Main structures of simple Au(I) and Au(III) complexes

In general commercially available Au salts and complexes for catalysis range from simple Au(I) and Au(III) halides (**1-2**) to more elaborate cationic Au complexes employing spectator ligands such as phosphines (**3-4**) and *N*-heterocyclic carbenes (**5**) (Figure 2). In the case of Au(III) when the formal coordination number is less than four, ligands such as chlorine can form a bridging ligand or intramolecular chelation can occur (**6**, Figure 2).

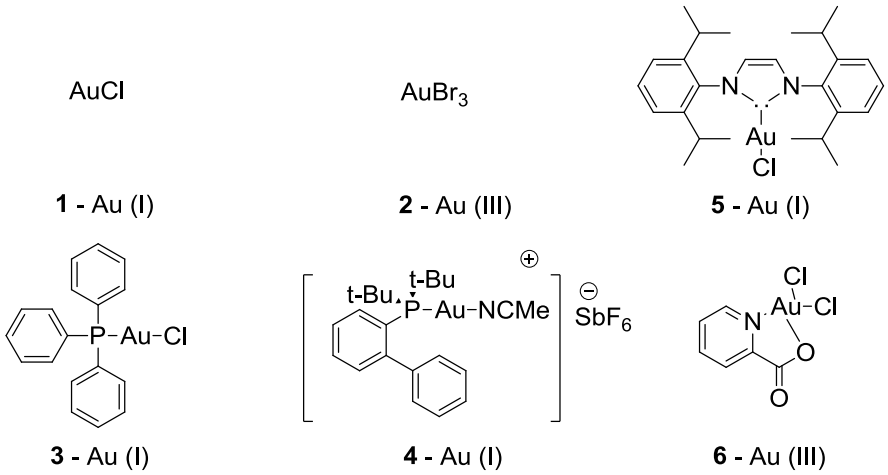
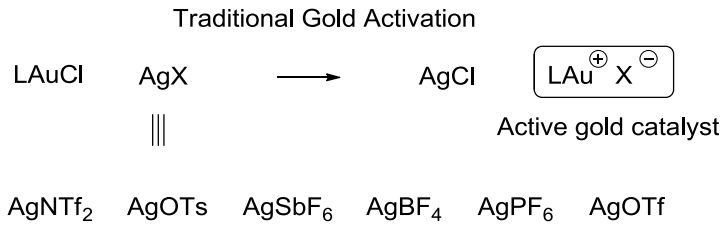


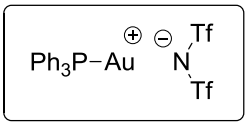
Figure 2: Selection of commercially available Au catalysts

Traditionally, a Ag co-catalyst is required to activate Au catalysts that have bonding or intermolecular chelation with halides (Scheme 2). Silver is well known for its high affinity towards halides. The presence of the silver halide had for a long time been considered to have little effect on the reaction with the silver playing a supporting role, although more recently there has been a greater focus on the 'silver effect' in Au catalysed reactions, which in some cases has been to shown to help promote the reaction. [20]



Scheme 2: Activating the Au catalyst

Gagosz and co-workers have developed an air and moisture stable silver free system, $LAuNTf_2$, where the bistrifluoromethanesulfonylimidate (NTf_2) moiety is a weakly coordinating counter-ion, which can easily dissociate in organic solution (Figure 3). [21] This is the catalyst we have employed for our Au transformations; it is commercially available, tolerant towards open flask conditions and does not require additional silver activation.



Au (I)

Figure 3: Commercially available Gagosz catalyst [21]

Au is less expensive than the platinum group metals (platinum, palladium, iridium, rhodium, ruthenium). [22,23] The price of catalysis is often dominated by the ligand choice rather than by the metal, the Gagosz catalyst employ involves a simple and cheap triphenylphosphine ligand and counter ion. Au has also been shown to be a low risk metal by the British Geological Risk List 2012 for elements of economic value. The list is based on a number of criteria including the scarcity, production concentration, reserve distribution, recycling rate, substitutability and governance (top producing nation and top reserve-hosting nation). The risk scale runs from high (10) to low (1) with Au determined to be a relatively low risk compared to the platinum group elements and Hg (Table 1). [24]

Table 1: British Geological Risk List 2012 [24]

Element	Symbol	Risk index
Hg	Hg	**8.6**
Platinum, Rhodium, Ruthenium, Iridium, Palladium	Pt, Rh, Ru, Ir, Pd	**7.6**
Tin	Sn	**6.7**
Silver and Nickel	Ag, Ni	**6.2**
Gold	Au	**5.7**
Iron	Fe	**5.2**
Copper	Cu	**4.3**

1.2. Homogeneous gold catalysis

Relativistic effects are significant when considering why Au is a good catalyst. The contracted 6s orbital and expanded 5d orbitals account for the attributes of Au catalysts and the relativistic effects provide a theoretical frame-work for rationalising the observed reactivity. [25] In the simplest terms, relativistic effects in chemistry can be considered to be small corrections to the non-relativistic theory of chemistry, which is developed from the solutions of the Schrödinger equation. These corrections, such as contraction or expansion have differential effects on the electrons in various atomic orbitals within the atom, according to the speed of these electrons relative to the speed of light. When the relativistic radial velocity ν (relative to the speed of light c) increases then the mass of the 6s electrons (m: relativistic, m_0: non-relativistic) significantly increase as described by the Bohr equation (Equation 1). [23]

$$m = m_o\sqrt{(1-(\nu/c)^2} \quad \{\nu_r\} = Z;$$

when $\nu \rightarrow c$: relativistic effects

Equation 1: Bohr Radius [23]

Relativistic effects are more prominent in heavy elements, because only in these elements do electrons attain relativistic speeds. Down groups in the periodic table, where the nuclei get heavier, the relativistic effects will get larger and can eventually dominate the chemical processes. Contraction of the 6s (and 6p) orbital occurs in those elements with atomic number Z>70, for Au the atomic number Z=79 (Figure 4). [25,23]

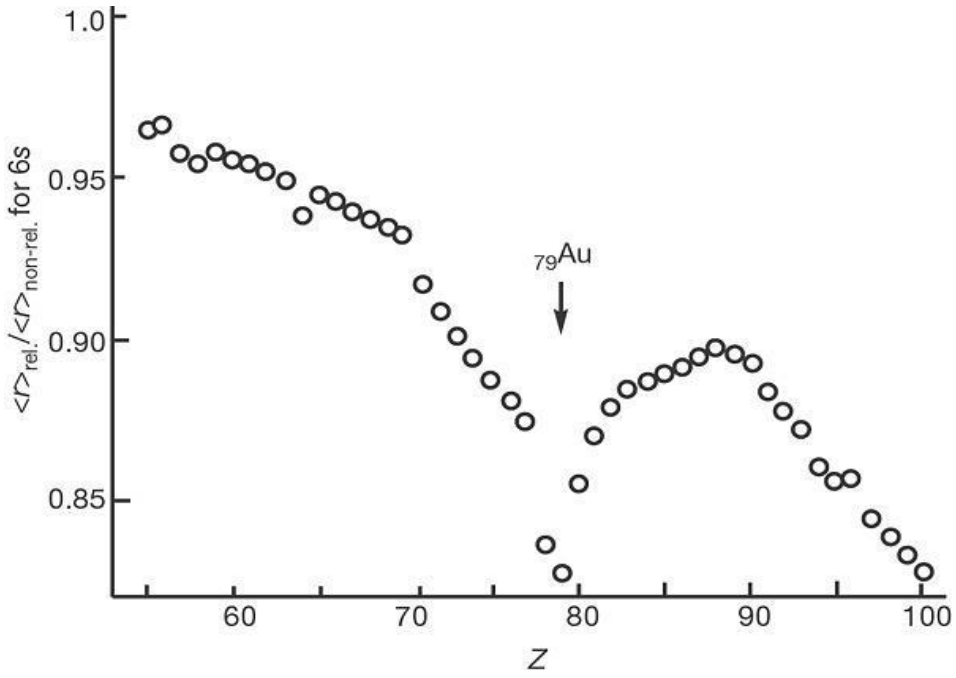


Figure 4: Calculated relativistic contraction of the 6s orbital [25]

Relativistic effects are more significant for electrons held close to the nucleus, the contraction of core s and p orbitals leads to contraction of higher s orbitals since the Bohr radius of an s orbital is inversely proportional to the mass m. Whereas d and f orbitals will expand due to more effective nuclear screening by the contracted s and p orbitals. From a reactivity point of view, the orbital contraction leaves the LUMO (lowest unoccupied molecular orbital) in a low-lying level of energy in comparison with other transition metals of the same group, therefore elements with Z>70 have a higher Lewis acidity. [25,23]

Au(I) coordinates preferentially to alkene or alkyne bonds, interacting according to the Dewar-Chatt-Duncanson model. [25] Several metal ions isolobal with the simple proton including Hg(II) and Pt(II) also show this type of bonding and reactivity. The Dewar-Chatt-Duncanson model treats π systems as a σ donor with complimentary back bonding from the metal to the π* orbital. Calculations suggest alkynes are strong two-electron σ donors but fairly weak π-acceptors when bound to Au(I) (Figure 5). [25]

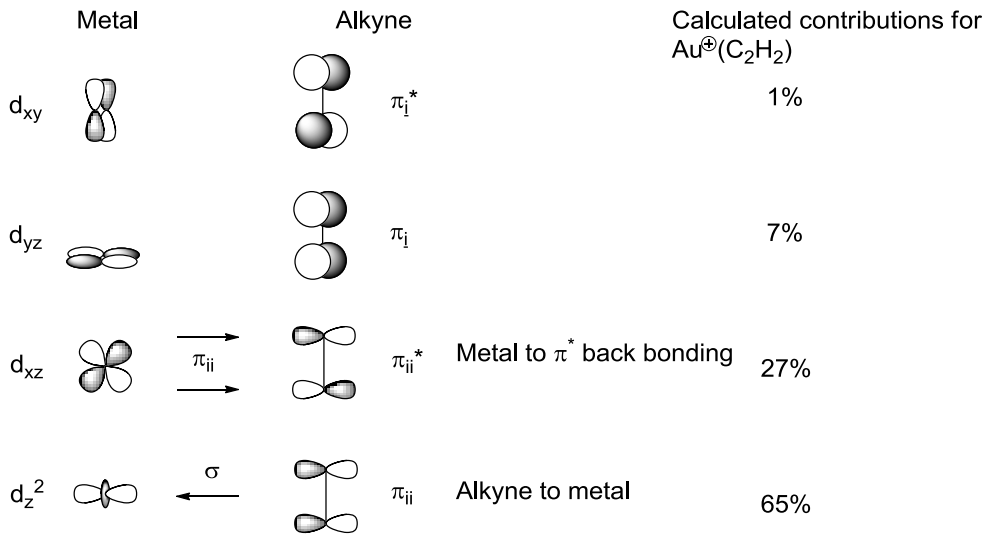
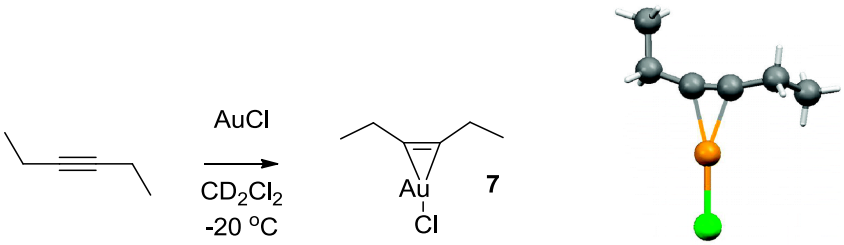


Figure 5: Dewar-Chatt-Duncanson model [25]

More electron density is lost by the alkyne through σ bonding to Au than is gained through back donation from the Au d_{xz} orbital (Figure 5). [26] This renders the π-system of the alkyne electrophilic and as a result open to nucleophillic attack. A complementary viewpoint is to consider the LUMO for Au(I), which is the stabilised 6s orbital, thus the corresponding cationic metal salt can be considered as an extremely "soft" Lewis acid species. [26] In general 'hard' applies to species which are small, have high charge states, and are weakly polarisable. Whereas, 'soft' applies to species which are big, have low charge states and are strongly polarisable. [27] Therefore, "soft" nucleophiles such as C≡C bonds would be preferentially activated in the presence of the "soft" Au(I) ion. The 'soft' character of Au(I) as a large and polarisable cation ensures a much greater affinity to the alkyne, which ultimately translates into mild reaction conditions and high yields of the desired addition products. [15]

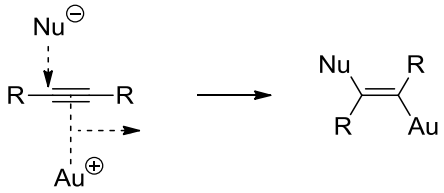
1.3. Gold activation of alkynes

A linear Au(I) complex featuring a simple, unstrained alkyne has been synthesised from AuCl and 3-hexyne, and characterised using X-ray crystallography (Scheme 3). [28] Density functional theory calculations show that σ donation from the alkyne to Au dominates over the Au to alkyne π back-donation.[28] Au chlorides are widely used as effective π-activation catalysts for alkynes, and Au(η^2-EtC≡CEt)Cl (**7**) may be viewed as a good model for the likely intermediate in some of these processes.



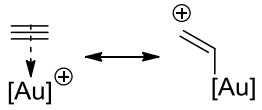
Scheme 3: Simple Au(I) chloride-alkyne complex [28]

In the presence of a nucleophile the activation of the alkyne is thought to occur by 'slippage' of the Au catalyst (Scheme 4). [26] The concept of slippage involves the relaxation of symmetry in bonding orbitals which then allows mixing of previous orthogonal orbitals and facilitates charge transfer from the nucleophile to the π ligand, and finally to the metal centre.



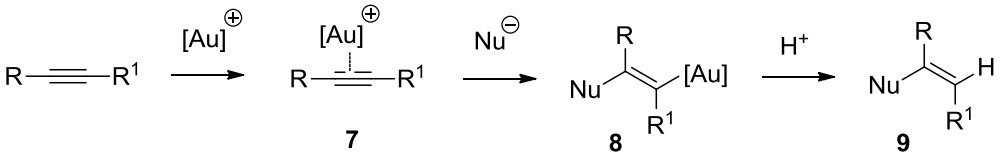
Scheme 4: Electrophilicity is enhanced upon η^2 → η^1 deformation [26]

In 2007 Furstner and Davies proposed the term π-acid as a description of Au as a catalyst. [26] A π-acid is a metal fragment that binds to a C-C multiple bond and deprives the C-C multiple bond of a part of its electron density, inducing a positive charge (scheme 5). [26]



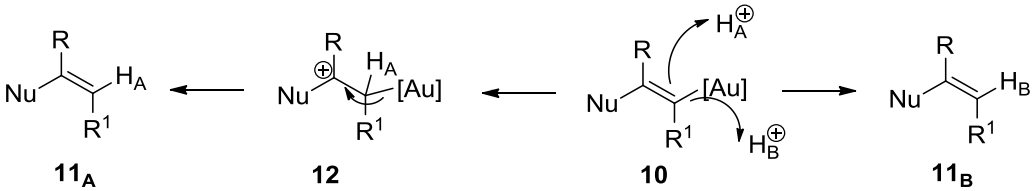
Scheme 5: Au as a π-acid, depriving an alkyne of electron density

A diverse range of transformations have been developed based on the activation of alkynes by Au salts and complexes. [6,7,8,9,10,11,12,13,14,15] In a simplified form, the Au interacts with the π-system of the substrate to form intermediate **7**, the resulting metal-multiple bond complex is electrophilic in nature and therefore activated for nucleophilic attack. The nucleophile can then attack the electron deficient alkyne to form the vinylAu **8**. There is strong evidence that the nucleophile adds anti to Au. [6,7,8,9,10,11,12,13,14,15] The vinylAu intermediate **8** then liberates the addition product **9** and the Au catalyst by proto-demetallation (Scheme 6). In oxymercuration the resultant organomercurial species is generated stoichiometrically and requires an additional step to liberate the product, protodemetallation of the Au-C bond enables catalysis to occur.



Scheme 6: General reaction scheme for homogeneous Au catalysed activation of alkynes

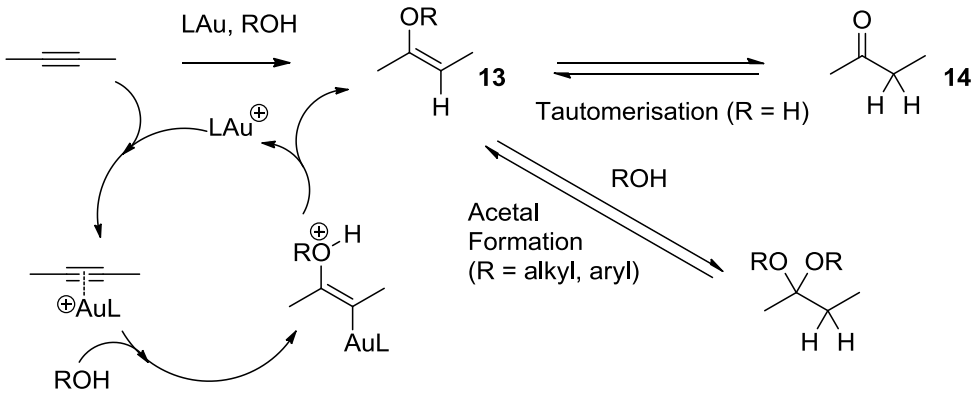
Au is known to favour protodemetallation over β-hydride elimination and this process could occur by two possible mechanisms (Scheme 7). [6,7,8,9,10,11,12,13,14,15] Electrophilic cleavage leads from **10** directly to $\mathbf{11_B}$, whereas alkene protonation gives intermediate **12** which can then undergo elimination of the gold $\mathbf{11_A}$.



Scheme 7: Possible protodemetallation mechanism routes

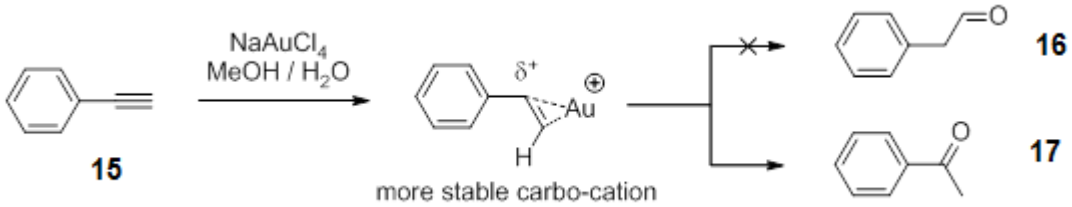
Alkyne hydration, or the addition of an equivalent of water across a carbon–carbon triple bond, is a one of the most useful functionalisations of simple alkynes and is one of the oldest transformations in organic chemistry. [18] The

general mechanism of this transformation is shown (Scheme 8), and in many cases, alcohols can be used in place of water to provide enol ether or acetal products, depending on the conditions and the substrate. The hydration reaction of an alkyne leads to enol **13** that tautomerises to the corresponding ketone **14**. [16]



Scheme 8: Alkyne hydration mechanism [16]

The hydration of unsymmetrical phenyl acetylene **15** has two possible products, the aldehyde **16** or the methyl ketone **17**. The methyl ketone **17** is the favoured product proceeding through the more stable carbocation, providing an example of 'slippage' of the Au catalyst (Scheme 9).

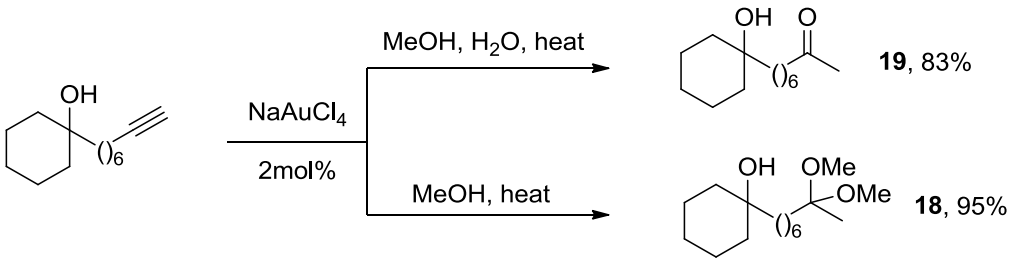


Scheme 9: Example of 'slippage' [29]

Au catalysed reactions of alkynes are in general conducted under very mild conditions, often room temperature and 'open' to the atmosphere, offering much higher functional group tolerance than Brϕnsted acid catalysis. In comparison, the addition reactions to alkynes (or olefins) catalysed by a Brϕnsted acid usually requires harsh conditions and is plagued by numerous side reactions of the carbocation intermediate formed. Chemoselectivity is highly desirable in the presence of other functional groups or in highly complex late stage intermediates to prevent unwanted side reactions. [16] Hence the exceptional chemoselectivity of Au towards alkynes under mild conditions is a powerful synthetic tool.

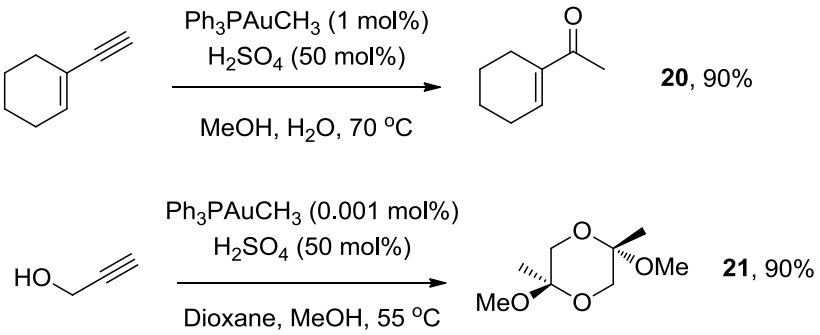
1.4. Gold catalysed reactions of alkynes

The simplest nucleophile is water leading to ketone formation. Initial methyl enol ether products are readily transformed, under the reaction conditions demonstrated by Utimoto and Fukudu in 1991, to acetals (**18**) or hydrolysed to ketones (**19**, Scheme 10). [29] This pioneering work involved low catalyst loading and required heating to produce good yields of the two examples.



Scheme 10: Addition of water to alkynes [29]

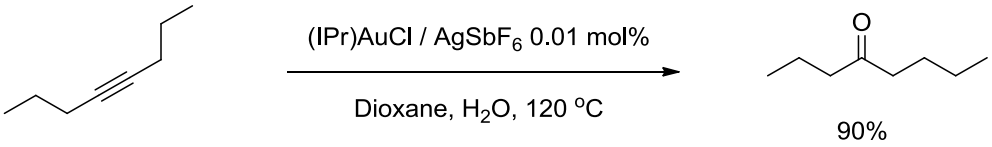
Following this work Teles and co-workers in 1998 demonstrated the hydration of alkynes by cationic Au(I) complexes (scheme 11). This publication arguably sparked the current activity in Au catalysis. [30] The Au catalyst is activated by loss of methane, promoted by the acid and heat, and depending on the solvent system the product could be directed between **20** and **21**.



Scheme 11: Low catalyst loadings for hydration of alkyne [30]

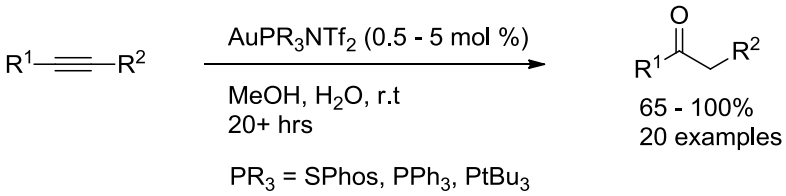
Many groups took inspiration and tried to improve upon these results and recently there have been several interesting breakthroughs (Scheme 12 and 13). [31,32,33] In 2009, Nolan and co-workers published a report of an Au *N*-heterocyclic carbene (NHC) catalysed hydration under essentially acid-free conditions that was demonstrated at low catalyst loadings at elevated temperatures (Scheme 12). The

extremely high stability and activity of the catalyst complex provides a turnover number in excess of 84000, thus allowing extremely low catalyst loadings (50 ppm or lower). [34]



Scheme 12: NHC-catalysed hydration [34]

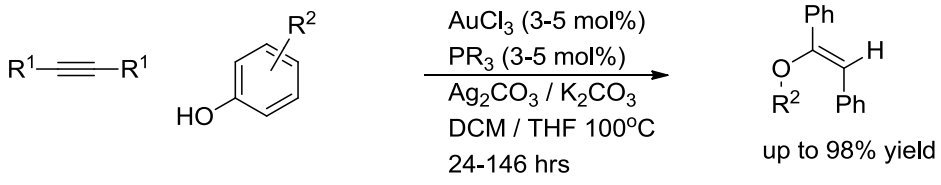
Also in 2009, Leyva and Corma made further improvements and managed to lower the temperature of the hydration reaction to room temperature using Au bistrifluoromethylsulfonimide complexes. The catalytic activity of the Au(I) catalyst is strongly dependant on both the nature of the coordinated phosphine ligand and the softness of the counterion (Scheme 13). [23] However, the reaction time even for simple terminal alkynes is 20 hours and the majority of the reactions take over 24 hours without reaching completion. Overall this method provides extremely mild access to a variety of ketones, though the selectivity on unsymmetrical internal alkynes remains problematic, unless driven by cation stability.



Scheme 13: Room temperature Au catalysed hydration of alkynes

The addition of various heteroatom nucleophiles across an alkyne is also effectively catalysed by Au and is now widely used. [6,7,8,9,10,11,12,13,14,15] The nucleophiles that can be applied include nitrogen nucleophiles (hydroamination, Schmidt reaction),[35,36] oxygen nucleophiles (hydration,[35,36] hydroalkoxylation,[37] carboalkoxylation,[38] carbonyl oxygens, sulfur nucleophiles (carbothiolation)[39] and carbon nucleophiles (enolates, enol ethers and silyl enol ethers, hydroarylation, enyne cycloisomerisation). As the π-system is only partially transformed during these reactions, valuable functional groups including ketones, acetals, enol ethers or enol esters, imines, enamines, and enamides can be

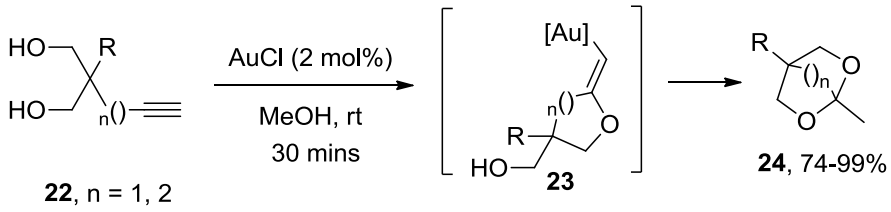
accessed depending on the nucleophile present. Alcohols can be readily employed as nucleophiles demonstrated by an intermolecular Au-catalysed phenol addition across symmetrical alkynes (Scheme 14).[37] The reaction conditions for the hydrophenoxylation are reasonably harsh, requiring high temperatures and with relatively high Au(III) catalyst loadings. The yields vary from very poor to excellent. Electron rich phenols give better yields in a shorter reaction time than more electron deficient phenols, the sterically encumbered 2,6-dimethylphenol is the only example shown that does not take part in hydrophenoxylation. In terms of the alkyne the more electron rich the alkyne, the more susceptible the alkyne to lewis acid activation and hence the higher the yield of the reaction; electron deficient alkynes give moderate yields in comparison.



R^1 = Ph, *n*-C_2H_5, *n*-C_3H_7, 4-MeO-C_6H_4, 4-Cl-C_6H_4, TMS
R^2 = H, Ph, 4-MeO-C_6H_4, 4-Cl-C_6H_4, 4-F_3C-C_6H_4, 4-O_2N-C_6H_4, *i*-C_4H_9
2,5-Me-C_6H_3, 2-F-C_6H_4, 3-F-C_6H_4, 2-Ph-C_6H_4, 2-O_2N-C_6H_4

Scheme 14: Hydrophenoxylation of Au activated alkynes. [37]

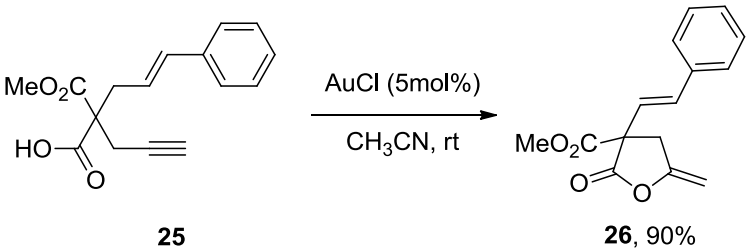
In 2005 Michelet and co-workers demonstrated cycloisomerisation of bis-homopropargylic diols **22** with terminal alkynes resulting in the formation of strained bicyclic ketals **24**. This most likely occurs *via* trapping of the intermediate enol ether **23**. The reaction employs a simple Au(I) catalyst, with a free coordination site, in low catalyst loadings and results in excellent yields at room temperature in 30 minutes (Scheme 15). [40]



R = Bn, Ph, *n*-Bu, cinnamyl n=1 and 2, allyl n=2,

Scheme 15: Cycloisomerisation of bis-homopropargylic diols [40]

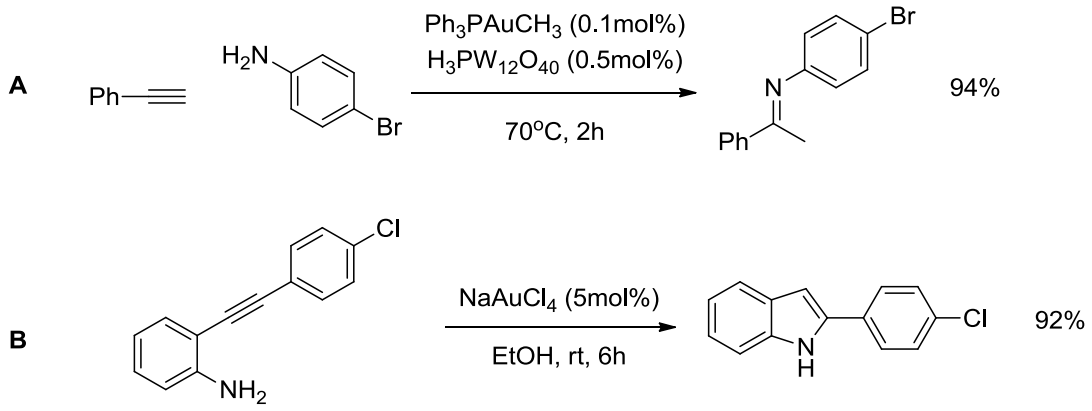
In a very similar transformation Michelet and co-workers demonstrated the synthesis of lactones **26** *via* cyclisation of carboxylic acid **25** in excellent yield (scheme 16). [38] This reaction demonstrates the excellent functional group tolerance and chemoselectivity of the Au catalyst towards the alkyne, which is favoured over the alkene and the ester group remains untouched (scheme 16).



25 **26**, 90%

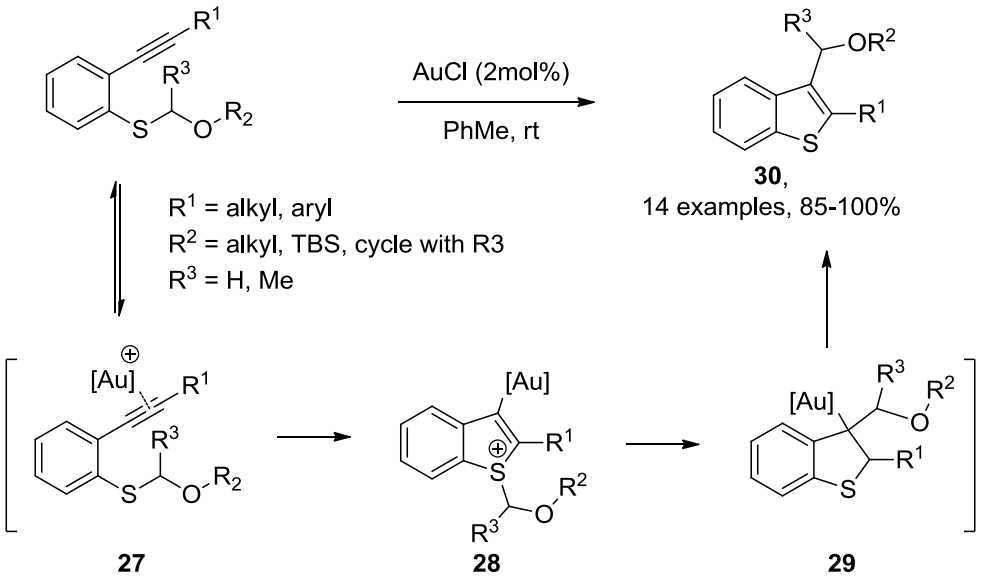
Scheme 16: Au-catalysed reaction of carboxylic acid with alkynes [38]

Hydroamination is a challenging transformation as the Au has an affinity for free amines inhibiting catalytic activation of the alkyne. However both intermolecular and intramolecular amines have been utilised in some cases.[35,36] This is a difficult transformation to achieve through traditional chemistry, commonly requiring a nitrogen protecting group. There is no requirement for a protecting group in either of these examples, demonstrating excellent step economy. The intermolecular example (**A**) requires a higher temperature (similar to that of hydration) and requires a tungsten co-catalyst, as the acidic promoter, but the reaction time is relatively short. Whereas the intramolecular example (**B**) cyclises readily at room temperature with a 'hard' Au(III) catalyst in a polar solvent (scheme 17).[35,36]



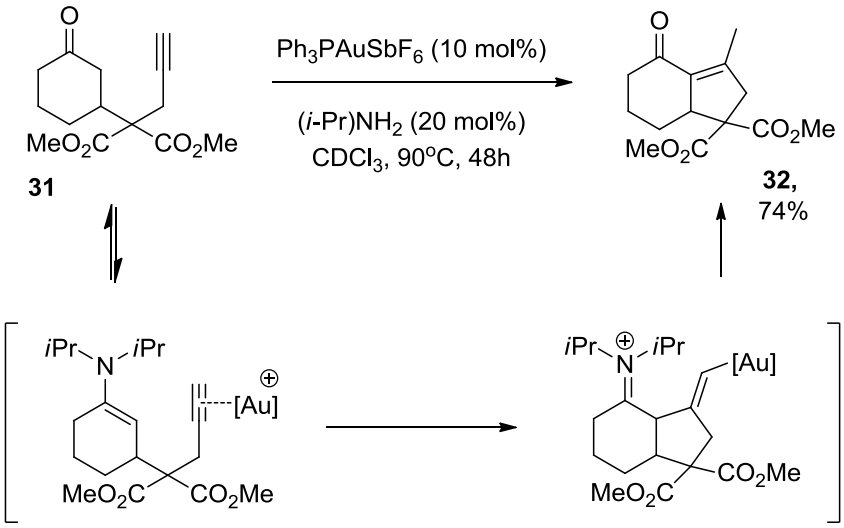
Scheme 17: Au-Catalysed hydroamination of alkyne [35,36]

Nakamura and co-workers have demonstrated intramolecular carbothiolation at room temperature with a readily available simple Au(I) chloride catalyst (scheme 18). [39] The reaction most likely proceeds *via* Au activation of the alkyne (**27**) followed by nucleophillic attack of the sulfur lone pair to give the 5-membered ring vinyl Au intermediate (**28**). This then undergoes a 1,3 shift to give **29**, which proto-demetallates to give **30** in excellent yield. In general this mild reaction produces good to excellent yields, however limited functional group tolerance has been investigated.



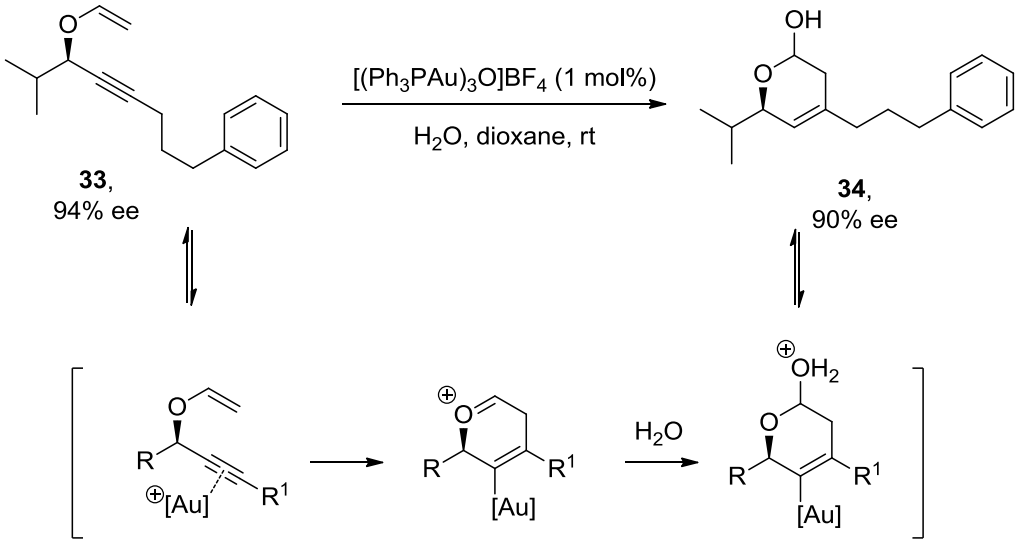
Scheme 18: Au-catalysed carbothiolation [39]

Unactivated enolisable carbonyls (**31**) can undergo α-functionalisation with alkynes under Au catalysis in the presence of an amine to access iminium-enamine tautomerisation to give **32** (Scheme 19). [41] Analagous cyclisations are observed in the absence of an amine at room temperature, but these are likely to proceed *via* alkyne hydration/aldol dehydration processes. [41] This example of dual organo and metal catalysis requires fairly high catalyst loading at elevated temperature.



Scheme 19: α-Functionalisation with alkynes under Au catalysis [41]

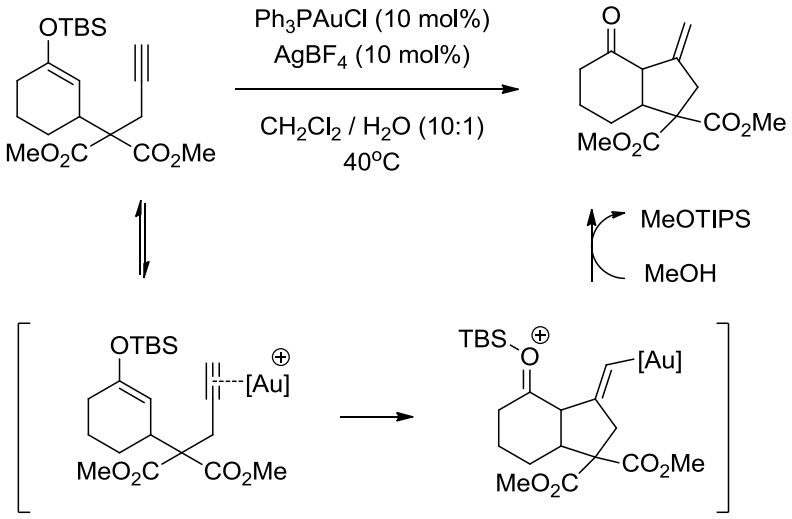
Toste and co-workers have demonstrated the cyclisation of enol ether **33** onto an alkyne catalysed by Au in the presence of water. Water is vitally important for the reaction to proceed to the formation of dihydropyran derivative **34** (Scheme 20).[42] In the absence of water allenes are produced. A weakly coordinating counter ion allows for silver free conditions and the reaction proceeds with low catalyst loadings and without racemisation of the propargylic alcohol.



Scheme 20: Au-catalysed cyclisations of enol ethers [42]

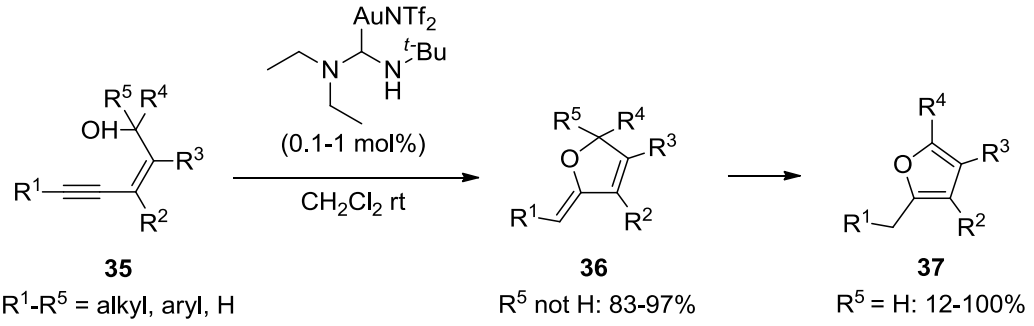
The cyclisation of silyl enol ethers onto alkynes, catalysed by Au, is a powerful methodology for the formation of carbon-carbon bonds. Cleavage of the oxygen-

silicon bond occurs in the presence of alcohol/water additives (Scheme 21). [43] High catalyst loading is required but the reaction benefits from a fairly low operating temperature.



Scheme 21: Au-catlaysed cyclisation of silyl enol ethers [43]

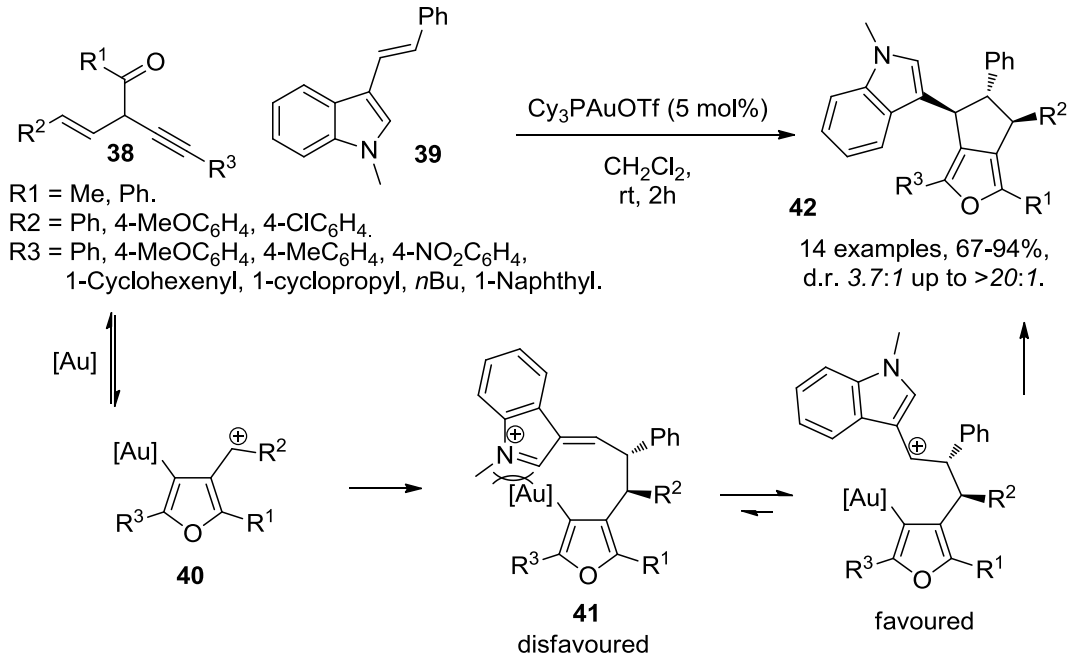
Furan synthesis has been demonstrated by Hashmi and co-workers, who showed that allyl alcohols **35** can efficiently undergo intramolecular cyclisation to furans **37** *via* intermediate **36**, which tautomerises to the thermodynamically more stable furan (Scheme 22). [44] Low catalyst loadings at room temperature, are used to give poor to excellent yields of some highly functionalised tetrasubstituted furans.



Scheme 22: Intramolecular alcohol cyclisation to furans [44]

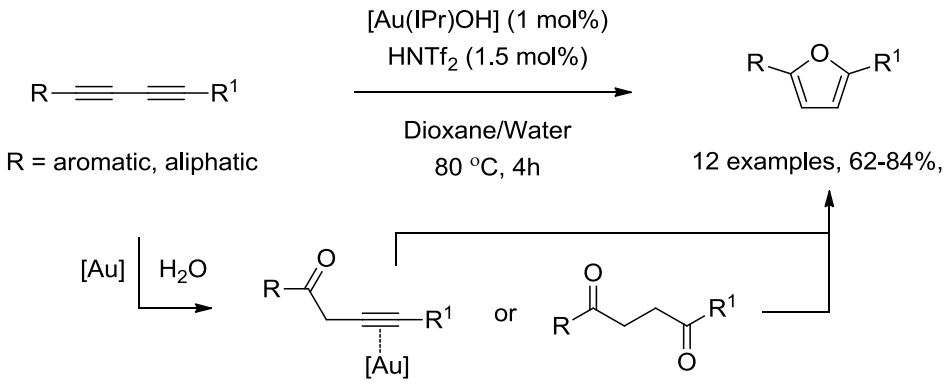
Highly substituted fused cyclopentylfurans (**42**) can be efficiently constructed through a Au(I)-catalysed tandem [3+2] cycloaddition bicyclisation method from simple starting materials (Scheme 23).[45] The furan core (**40**) is constructed from readily available 2-(1-alkynyl)-2-alken-1-ones (**38**) and 3-styrylindoles (**39**) in a one-pot manner by employing an Au-catalysed tandem cyclisation. The high

diastereoselectivities are rationalised through the disfavoured steric clash of the Au catalyst and the *N*-methyl of the styrylindole (**41**). The reaction also benefits from mild reaction conditions, good to excellent yields, and a reasonably wide functional-group tolerance. [45]



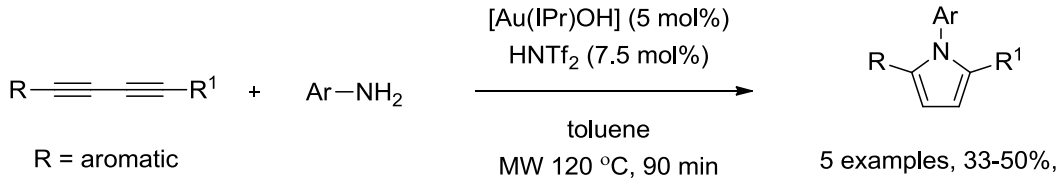
Scheme 23: Au-catalysed tandem [3+2] cycloadditon bicyclisation [45]

Nolan and co-workers showed in 2011 that the Au carbene catalyst [Au(IPr)OH] is a very convenient catalyst for heterocycle synthesis. [9] Furans were prepared in high yields, although the conditions are not as mild as with some other Au(I) catalysts, with small equivalents of an acid additive and elevated temperatures required (Scheme 24). Two intermediates were proposed, although the diketone route appears unlikely as it does not cyclise under Au catalysed hydration conditions. [46]



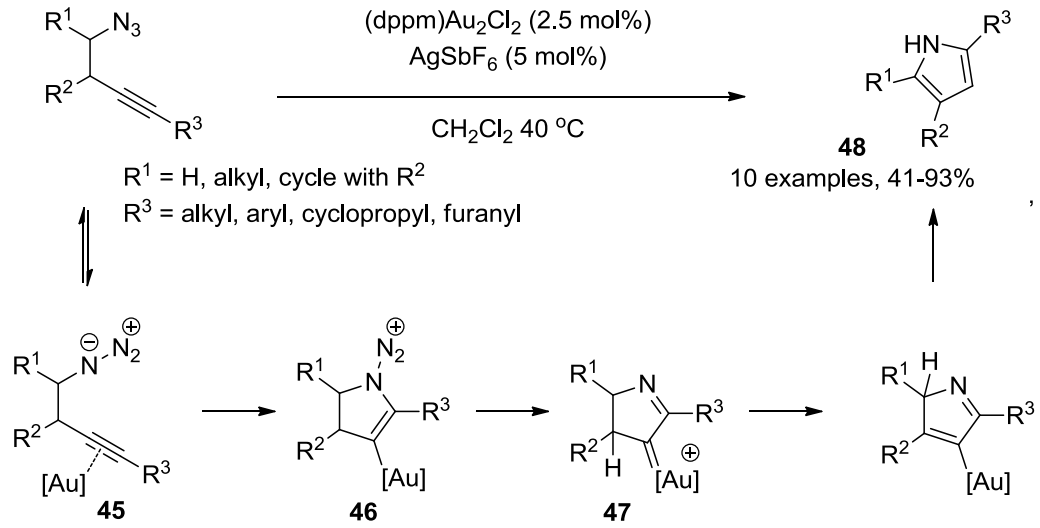
Scheme 24: Furan synthesis [46]

The strength of the Nolan procedure is that pyrroles were also prepared *via* the Au(I)-catalysed alkyne hydration of diynes illustrating the diversity of heterocycle synthesis (Scheme 25). [46] The use of NHC-Au catalyst [Au(IPr)OH] in a silver-free protocol permits low catalyst loadings and *in situ* generation of the active cationic Au species. Instead of thermal heating, the reaction was conducted under microwave conditions and for a relatively short period of time. Amines showed a lower reactivity under the optimised reaction conditions with poor to moderate yields of a smaller selection of examples than the corresponding furan synthesis.



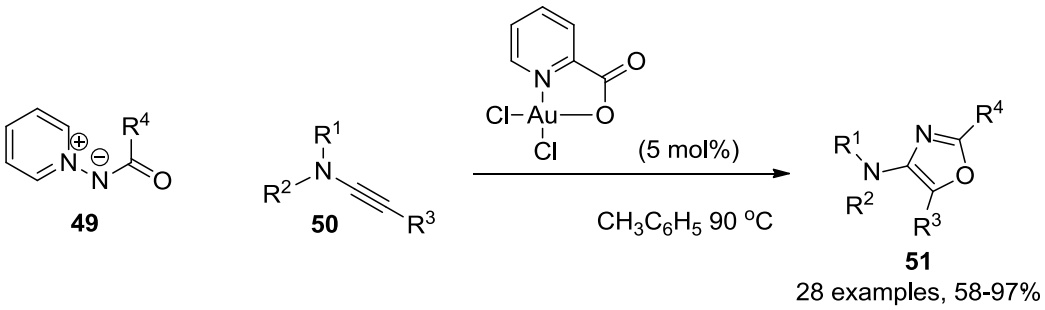
Scheme 25: Au-catalysed pyrrole synthesis [46]

Toste and co-workers have demonstrated pyrrole synthesis by using an azide nucleophile in an intramolecular acetylenic Schmidt reaction (Scheme 26). [47] The mechanism is proposed to proceed *via* Au activation of the alkyne (**45**) and nucleophillic attack of the azide to generate the vinylgold intermediate **46**. Elimination of nitrogen gives **47**, which aromatises and proto-demetallates to give pyrrole **48** in moderate to excellent yield. The reaction boasts mild reaction conditions and promising initial functional group tolerance.



Scheme 26: Intramolecular acetylenic Schmidt reaction [47]

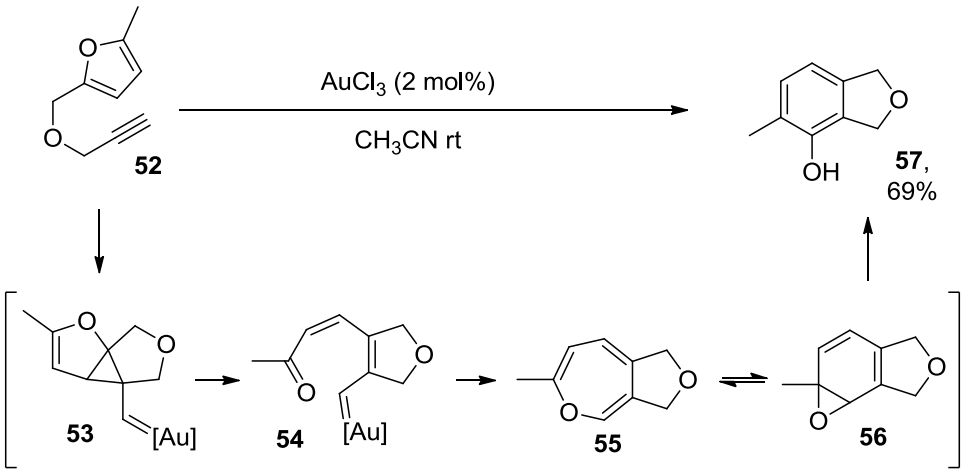
An Au-catalysed intermolecular reaction of pyridine-*N*-aminides (**49**) with ynamides (**50**) can be used to prepare trisubstituted 1,3-oxazoles (**51**) with a variety of functional groups (scheme 27). This formal [3+2] cycloaddition employs robust conjugated *N*-ylides as *N*-nucleophilic *N*-acyl nitrene equivalents for a highly chemoselective and regioselective addition across electron-rich ynamides. The reaction requires 5 mol% of the Au(III) catalyst, the 'harder' Au catalyst is employed whenever amines are present in the reaction and the high temperatures facilitate a fairly extensive range of examples in good to excellent yield.



Scheme 27: Au-catalysed synthesis of oxazoles [48]

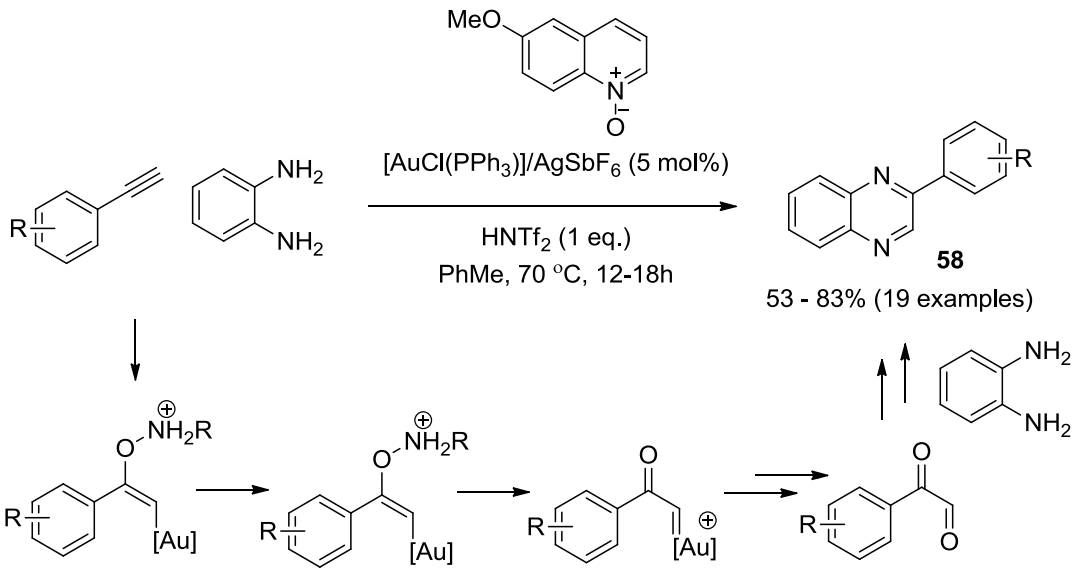
The intramolecular reaction of a furan **52** with a terminal alkyne was reported by Hashmi and co-workers in 2000, demonstrating the synthesis of phenols (Scheme 28). [49] Intramolecular migration of the oxygen atom was supported by isotopic labelling. Computational studies by Echavarren and co-workers revealed the

initial formation of a cyclopropyl carbenoid intermediate **53**. [50,51,52] Ring opening then gives **54** and this vinylcarbenoid intermediate can react with the carbonyl to access the oxepin/arene tautomer **55**/**56**. Ring opening of the arene oxide gives access to the phenol **57**.



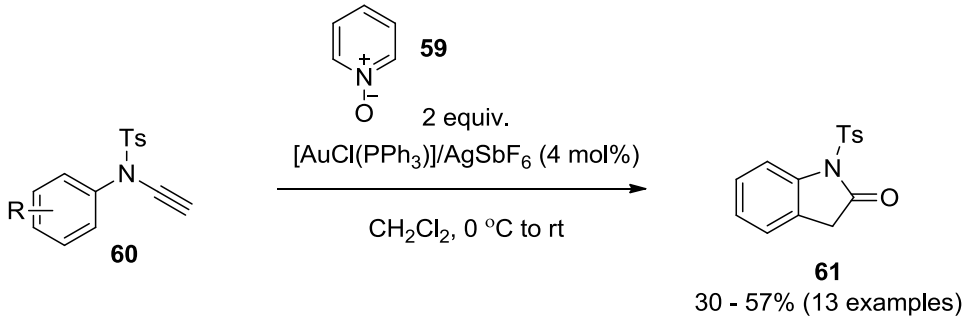
Scheme 28: Au catalysed phenol synthesis

Oxidation with pyridine *N*-oxide and its derivatives has become much more prevalent in the last few years.[53 54] Hashmi and co-workers very recently reported an Au catalysed oxidation of a broad range of aromatic and aliphatic alkynes that can be used to access a wide variety of quinoxaline derivatives (**58**) in moderate to good yields, in a one-pot tandem procedure (scheme 29). [53] This is another example of the tolerance of Au towards free amines, the simple Au(I) catalyst is activated by a Ag co-catalyst in conjunction with 1 equivalent of acid and heating.



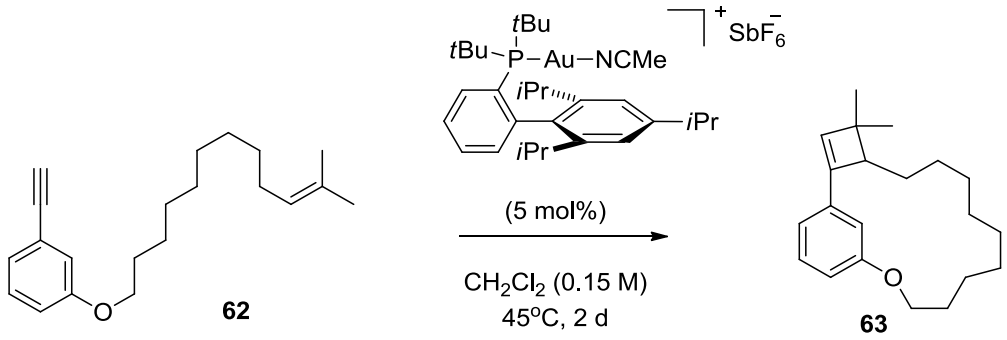
Scheme 29: One-pot synthesis of quinoxalines [53]

Oxidation with pyridine *N*-Oxide (**59**) has also been demonstrated on tosyl protected *N*-arylynamides (**60**), which can be trapped by the ortho position of the ring to give functionalised oxindoles (**61**) in low to moderate yields under mild reaction conditions and relatively low catalyst loading (Scheme 30). [54]



Scheme 30: Au-catalysed synthesis of oxindoles [54]

Au(I) catalysed macrocyclisation has been reported *via* a [2+2] cycloaddition of large 1,n-enynes (**62**, n = 10–16), which provides access to 9- to 15-membered rings incorporating a cyclobutene moiety (**63**). The reaction requires the use of an Au(I) catalyst bearing a sterically hindered biphenylphosphine ligand, under mild conditions (Scheme 31). However the reaction requires 2 days, although this is not unusual where macrocycle synthesis is concerned. [55]

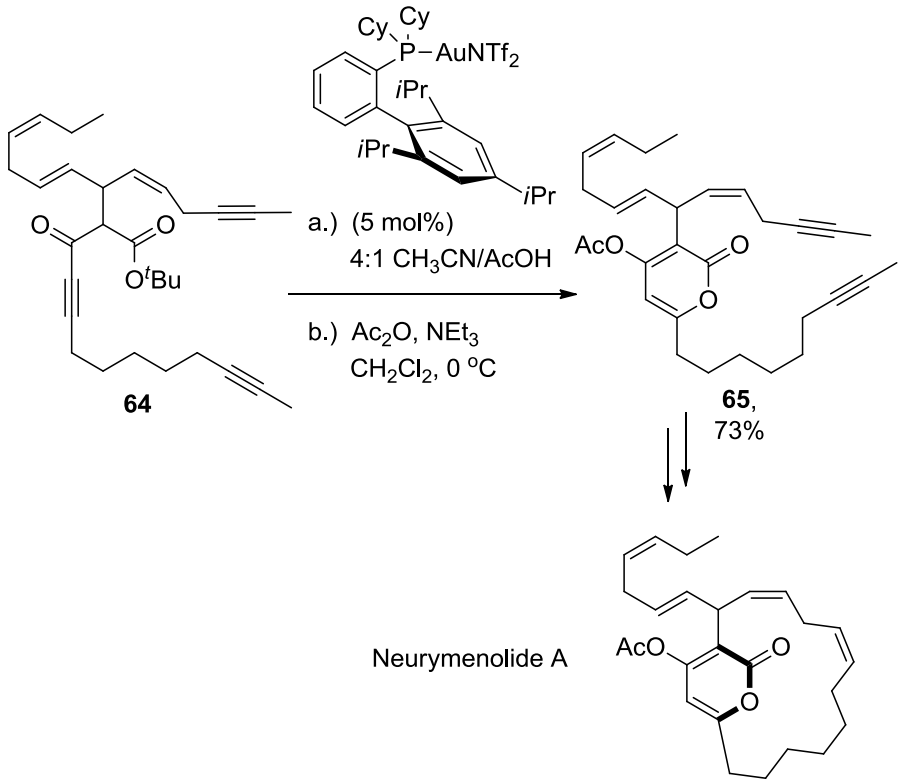


Scheme 31: Au-catalysed macrocyclisation [55]

1.5. Applications in total synthesis

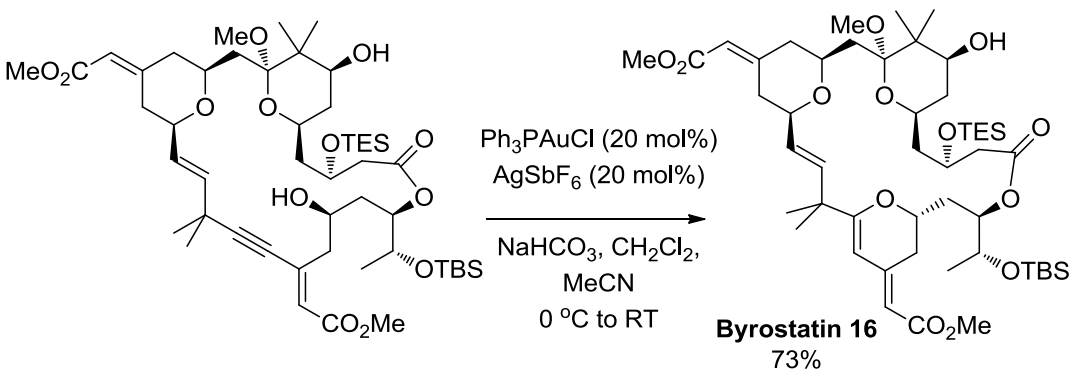
The direct alkyne hydration to provide ketones has been employed several times in total synthesis with great success. [56,57] More recently there have been a growing number of publications employing Au for key roles in late stage total syntheses, benefiting from the mild reaction conditions and the chemoselectivity demonstrated by Au thus providing additional flexibility when planning synthetic routes. [16] The stability and ease of installation of the alkyne allows the Au catalysed activation to be exploited at almost any stage in a synthetic route, such that the alkyne can be considered a masked carbonyl. [16] More traditional Brϕnsted acid approaches to carbonyls in the presence of acid-sensitive functionalities would most likely be destructive to highly complex synthetic intermediates. Fürstner and co-workers reported in 2012 the total synthesis of the highly sensitive pyrone-containing cyclophane, Neurymenolide A (Scheme 32) without unwanted isomerisations, eliminations, or side reactions which can plague other methods. [58] Synthesis of this compound *via* the dehydration of a 1,3,5-tricarbonyl unit would require potentially disruptive reactions conditions. Treatment of the polyenyne **64** with 5 mol% of the Au(I) catalyst, under mild conditions, led to the facile formation of the desired pyrone core **65**, this occurred without the disruption of the stereochemistry and the position of the remaining unsaturation was unchanged in this high-yielding process (scheme 32). This transformation is highly chemoselective occurring in the presence of a series of sensitive skipped *cis* dienes which are prone towards isomerisation. This transformation provides

further evidence of the potential application of Au-catalysed procedures for total synthesis.



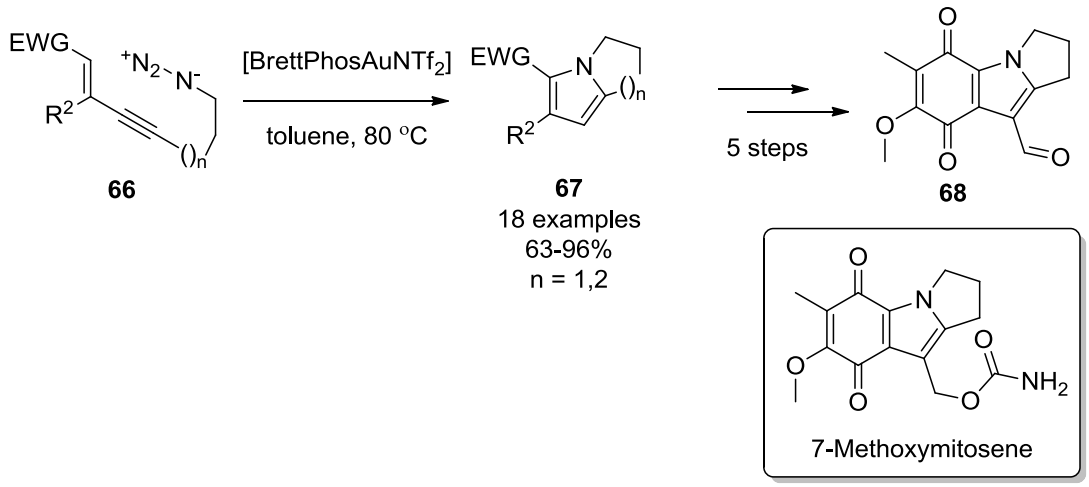
Scheme 32: Synthesis of Neurymenolide A [58]

In 2008, Trost and co-workers further demonstrated the excellent functional group tolerance of Au for the synthesis of Byrostatin 16. [59] The key Au-catalysed cyclisation occurs in the presence of acetals, activated alkenes and unprotected alcohols but remains chemoselective towards the desired alcohol cyclisation (Scheme 33). Although the catalyst loading is fairly high at 20 mol% the reaction is high yielding and conducted under mild conditions.



Scheme 33: Byrostatin 16 synthesis involving Au-catalysed cyclisation [59]

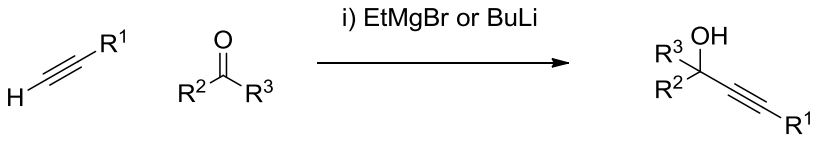
A formal synthesis of 7-methoxymitosene was reported recently by Zhang and co-workers in 2012, where Au was employed to form the key intermediate (**67**). Bicyclic dihydropyrrolizines (**67**) with an electron-withdrawing group (EWG) at the 5-position are formed in one step from linear azidoenynes (**66**) under Au catalysis (Scheme 34). This novel route involves the use of an azide as a nitrene precursor that in the presence of the Au(I) catalyst generates the substituted pyrrole **67** *via* generation of destabilised a 1-azapentadienium ion. [60] A number of examples were demonstrated in good to excellent yield and the target molecule **68** containing the core of 7-Methoxymitosene could be accessed in 5 steps.



Scheme 34: Synthesis of 7-Methoxymitosene [60]

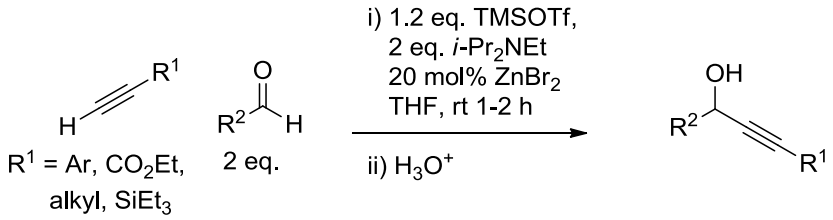
1.6. Synthesis of propargylic alcohols

Propargylic alcohols have two functional groups, an alcohol and an alkyne, which makes them highly attractive as building blocks. Propargylic alcohols are highly versatile and amenable to many catalytic transformations that have greatly expanded the synthetic chemist's toolbox. [61,26,62,63,64,65] Well-established and robust strategic bond-forming reactions exist for generating propargylic alcohols (Scheme 35). [66,67] Propargylic alcohols can be synthesised from a broad range of terminal alkynes and aldehydes or the more sterically encumbered ketones. The traditional method involves stoichiometric deprotonation of an alkyne *via* Grignard formation or by lithiation to access the metallated alkyne, which can then be used as a nucleophile to add into the electrophilic carbonyl (Scheme 35). [66,67]



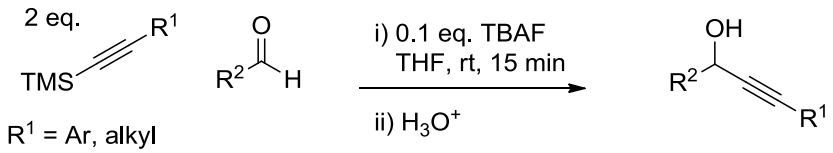
Scheme 35: Organometallic synthesis of propargylic alcohols

Modern methods for propargylic alcohol synthesis have been focused on catalytic approaches that allow a broad range of terminal alkynes to add rapidly and efficiently to aldehydes, one method involves zinc acetylide generation in the presence of trimethylsilyl trifluoromethanesulfonate (TMSOTf) (Scheme 36). [68] However 1.2 equivalents of TMSOTf are required for the reaction to proceed and in the absence of TMSOTf no reaction is observed. [68]



Scheme 36: Zinc catalysed synthesis of propargylic alcohols [68]

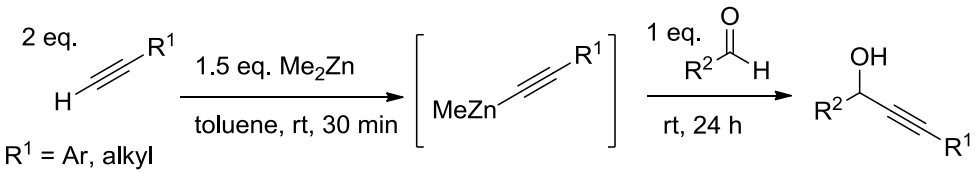
Tetrabutylammonium fluoride (TBAF) is a very efficient catalyst for the mild and operationally simple addition of trialkylsilylalkynes to aldehydes, ketones, and trifluoromethyl ketones in THF at room temperature (Scheme 37). [69] The reaction conditions are mild and various aryl functional groups are tolerated, such as chloro, trifluoromethyl, bromo, and fluoro groups. [69] Although the reaction only requires 0.1 equivalents of TBAF, the silyated alkyne (2 equivalents) is essential for the reaction to proceed.



Scheme 37: TBAF mediated synthesis of propargylic alcohols

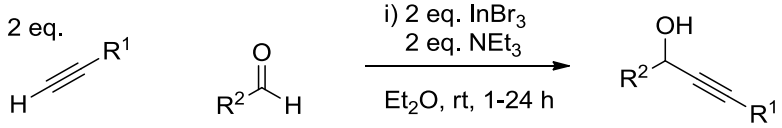
Commercially available 2M dimethylzinc in toluene is able to promote the addition of phenylacetylene to aldehydes and ketones (Scheme 38). [70] Broad scope, high tolerance to functional groups and a simple room temperature

procedure make this method highly interesting, although greater than stoichiometric equivalents of dimethylzinc are required. [70]



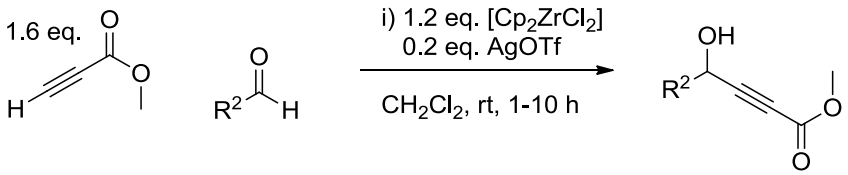
Scheme 38: Dimethyl zinc mediated synthesis of propargylic alcohols

An $InBr_3$-NEt_3 reagent system promotes the alkynylation of not only a variety of aromatic/heterocyclic or bulky aliphatic aldehydes but also N,O- or N,S-acetals (Scheme 39). [71] Although the reaction is not catalytic it does proceed mildly at room temperature.



Scheme 39: Indium mediated synthesis of propargylic alcohols

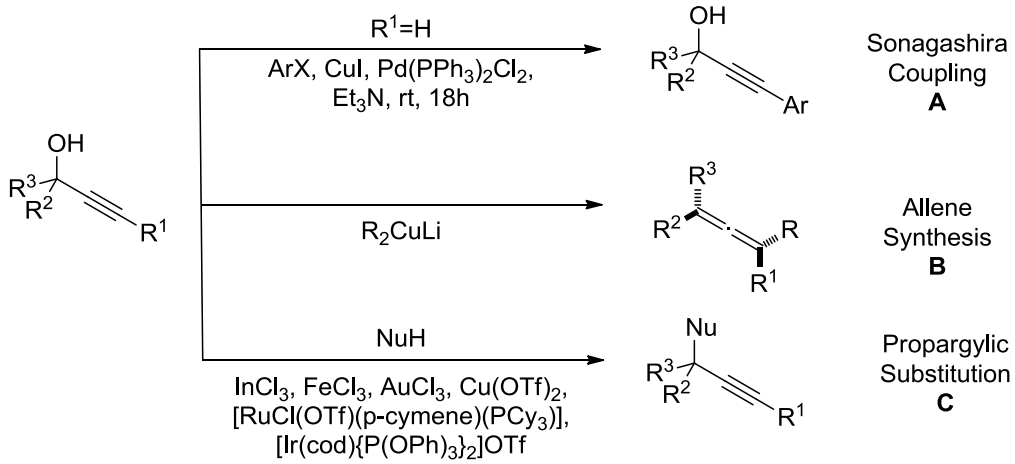
A zirconium based method for the coupling of aldehydes or ketones with alkynyl propiolates in the absence of a base was developed by Koide and Shahi in 2004. [72] The reagents involved in this coupling reaction are easy to handle and tolerate various functional groups but are limited by the alkynyl propiolate which reduces the possible functionalisation of the propargylic alcohol (Scheme 40). [72]



Scheme 40: Zirconium based synthesis of propargylic alcohols

1.7. Reactions of propargylic alcohols

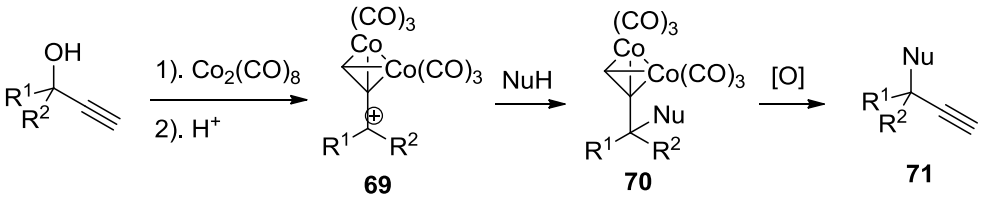
Propargylic alcohols undergo a variety of Pd-catalysed transformations and Songashira coupling makes up one important class of these reactions (A, scheme 41). [61] Propargylic alcohols have provided a fertile testing ground upon which to explore new catalytic activation pathways. Chiral propargylic ethers react with organocopper reagents to afford optically active allenes by addition to the terminal triple bond followed by an anti elimination of the resulting alkenyl copper species (B, Scheme 41). [63] S_N1 type propargylic substitution reactions (such as the Nicholas reaction) have been demonstrated with various metals (C, Scheme 41). [62]



Scheme 41: Reactions of propargylic alcohols

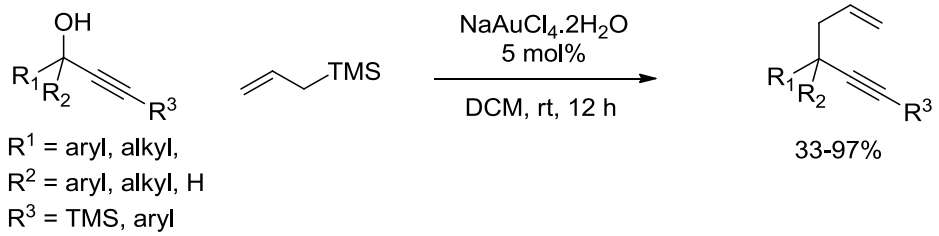
The nucleophilic substitution of propargylic alcohols was first demonstrated by the Nicholas reaction, an established multistep process first reported in the early 1970s (Scheme 42). [73,74,75] In this approach, the triple bond is first stoichiometrically coordinated to cobalt carbonyl [$Co_2(CO)_8$]. The hydroxy group is then removed under acidic conditions to give the dicobalt-stabilized carbenium ion **69**. It can be attacked by a nucleophile to give **70** and oxidative removal of the cobalt 'protecting group' gives the corresponding substitution product **71**. The protocol suffers from several drawbacks; a stoichiometric amount of toxic cobalt carbonyl is required for the reaction, which then must be oxidatively removed at the termination of the synthetic pathway, thus adding steps to the transformation. Nevertheless, the Nicholas reaction is frequently applied in natural product

syntheses [76,77,78] and enantioselective versions have been reported, [79] outlining the importance of propargylic substitution in organic transformations.



Scheme 42: Nicholas reaction

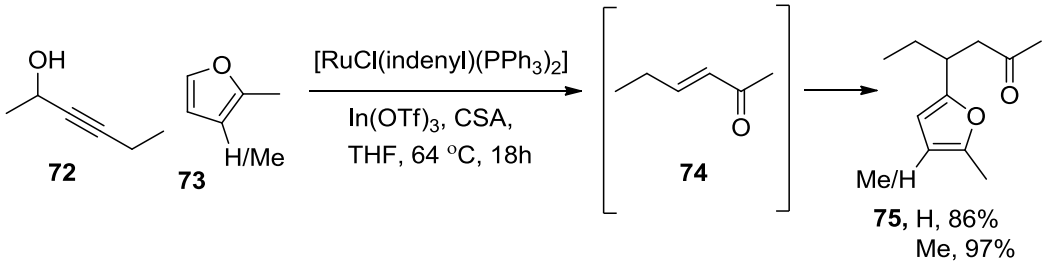
There are several metals that can be used as catalysts in propargylic substitutions. This includes Au, Ru, Fe, Mo, Ag, Sn, Al, Yt and Bi, amongst others. [80] There are varying compatibilities of the metals with different nucleophiles. The main nucleophiles that have been researched are carbon, nitrogen and oxygen nucleophiles, however, research has also been done with phosphorus and sulfur centred nucleophiles. When the nucleophile used is in the form NuH (as opposed to NuTMS), the only by-product is water which makes this method environmentally friendly and eliminates waste by-products. The substituents on the propargylic alcohol can also affect the reactivity of the compound and the reaction with the nucleophile and catalyst. In some cases, a propargylic alcohol with an electron deficient group will not react with a nucleophile in the presence of a catalyst. [81] In 2005, Campagne and co-workers reported the Au(III) catalysed S_N1 type substitution of propargylic alcohols (Scheme 43). [81] In addition to allyl silane several other nucleophiles were demonstrated including alcohols, dimethoxybenzene, furan heterocycles and thiols. [81,82]



Scheme 43: Au catalysed propargylic substitution [81]

Pt, Au and Rh salts, amongst others, can activate the alkyne of the propargylic alcohol towards reactivity. [26] Isomerisation reactions comprise another synthetically useful transformation of propargylic alcohols. There are three major types of isomerisations that propargylic alcohols can undergo; the Meyer–

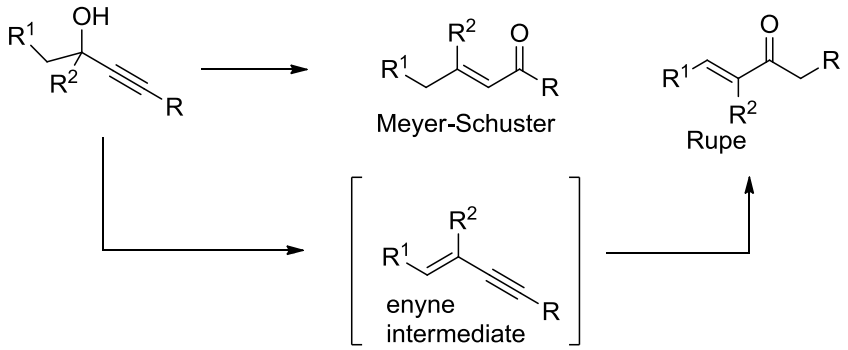
Schuster rearrangement, [83] the Rupe rearrangement, [84,85] and redox isomerisations. [84] Redox isomerisations are less common than the other transformations. [86] Trost reported a reaction sequence suggested to proceed through the enone intermediate **74**, which is formed from the propargylic alcohol **72** by redox isomerisation. Conjugate addition with furan **73** to **74** gave the corresponding products **75** in excellent yield (Scheme 44). [87]



Scheme 44: Redox isomerisation followed by conjugate addition [87]

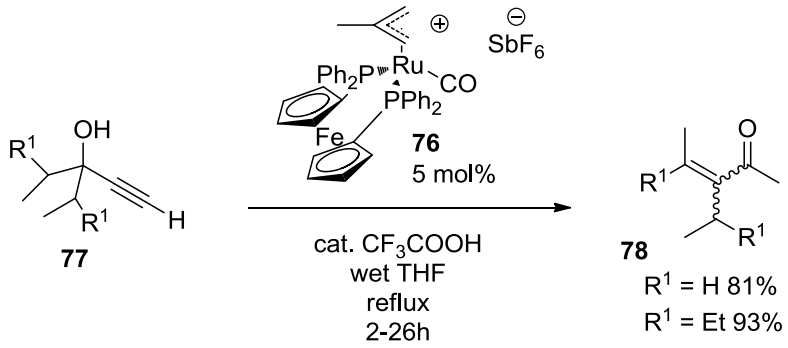
1.8. The Meyer-Schuster rearrangement and the Rupe rearrangement

The 1,3-rearrangement of propargylic alcohols to enones is known as the Meyer-Schuster rearrangement. [1] Discovered in 1922, the original conditions involved high temperature and an acid-catalyst to promote the 1,3 isomerisation of propargylic alcohols. The reaction was extensively reviewed in the 1970's, [88] and it was found that there are many competing reaction pathways for propargylic alcohols and the Meyer-Schuster rearrangement was typically only favoured in the absence of β-hydrogens in the starting material (Scheme 45). In the case of tertiary propargylic alcohols containing an α-acetylenic group the competing pathway gives α,β-unsaturated methyl ketones *via* an enyne intermediate. This competing reaction is known as the Rupe rearrangement. [89]



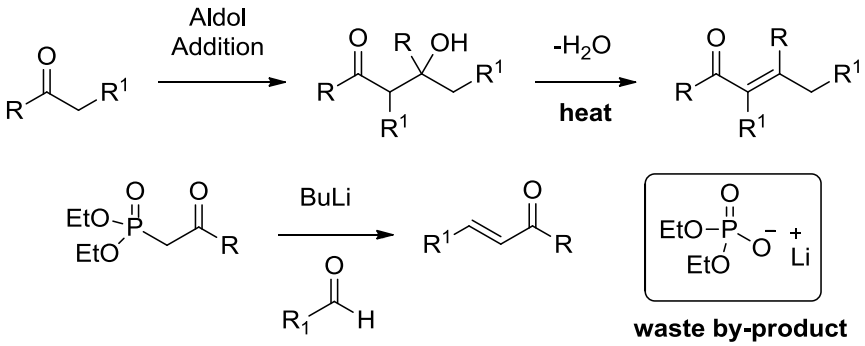
Scheme 45: Meyer-Schuster and Rupe rearrangements [89]

Cadierno and Gimeno have utilised the ruthenium complex **76** for the Rupe rearrangement of terminal propargylic alcohols **77** with hydrogen atoms in the β-position, which gave the corresponding methyl ketones **78** in good to excellent yield (Scheme 46). [90] This protocol was also successfully employed in the functionalisation of steroids. [90]



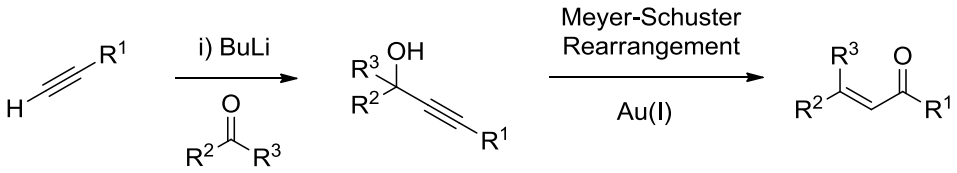
Scheme 46: Ru catalysed Rupe rearrangement [90]

The synthesis of enones (α,β-unsaturated carbonyl compounds) is traditionally achieved *via* aldol condensation [91] or *via* a Wittig, [92] Horner-Wadsworth-Emmons, [93] or Petersen olefination reaction, [94] methods that have been highly successful in organic synthesis. Some limitations of these methods include elevated temperatures for the aldol condensation and sometimes only modest yields (Scheme 47). Olefination methods often produce higher yields (Scheme 47) however waste by-products are incurred that are difficult to remove and the reactions are often highly sensitive to steric congestion around the aldehyde or ketone.



Scheme 47: Traditional methods for access to α,β-unsaturated carbonyls

In the last five years there has been a marked increase in the application of the Meyer-Schuster rearrangement. [85,83] This increase in interest is due to the employment of 'soft' Lewis acid catalysts such as Au(I), which are used for activating sp-hybridised systems, subsequently lowering the energy of the Meyer-Schuster reaction pathway and promoting the formation of enones. A potentially useful alternative strategy to access highly congested unsaturated carbonyls can be achieved in two steps from simple commercially available starting materials: The simple and well known addition of an alkynyl anion to an aldehyde or ketone followed by the mild, chemoselective and atom economic Au catalysed Meyer-Schuster rearrangement (Scheme 48).



Scheme 48: Meyer-Schuster rearrangement to access α,β-unsaturated carbonyls

The Meyer–Schuster rearrangement of propargylic alcohols frequently requires high reaction temperatures, but the isomerisation can be performed at lower temperatures when activated propargylic alcohols are used for the transformation. The first reports required conversion of the alcohol to the corresponding acetate, including early work by Dudley and co-workers in 2006 using Au(III) in the presence of 5 equivalents of ethanol to catalyse the Meyer-Schuster rearrangement (Scheme 49). [95] Dudley showed that the ethoxy acetylenes **79** can rearrange to the corresponding α,β-unsaturated esters **80** in >95% conversion using 5 mol% Au(III) chloride as catalyst (Scheme 49). [95] The ethoxy group

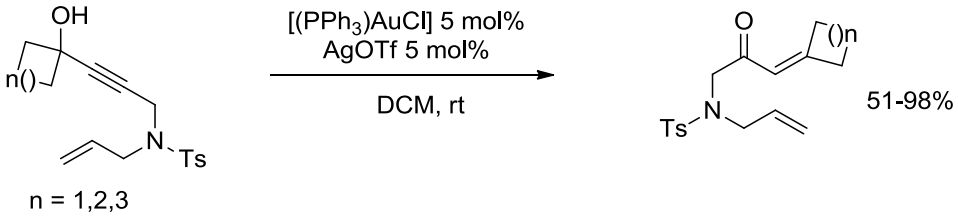
increases the electron density of the triple bond, making it more susceptible to activation by the Lewis acidic Au(III) chloride catalyst. In addition, Au is known to have an affinity for acetylenic π electrons. [96,97,8,98] Both factors result in a reaction time of only five minutes at room temperature, but no *E/Z* selectivity was reported.

Scheme 49: Meyer–Schuster rearrangement of activated substrates [95]

Dudley investigated other Lewis acid catalysts for the transformation and found that scandium(III) triflate performed better than other Lewis acids including gold (Scheme 50). [99] The corresponding unsaturated esters **81** were obtained in good to excellent yield (63 to 97% yield), and the *E*-isomer was typically obtained in 4:1 selectivity. Dudley also investigated the use of a mixture of Au(I) chloride and silver hexafluoroantimonate(V) for the rearrangement of **81**, and observed *E/Z* selectivities up to 30:1 for enone **82**. [100]

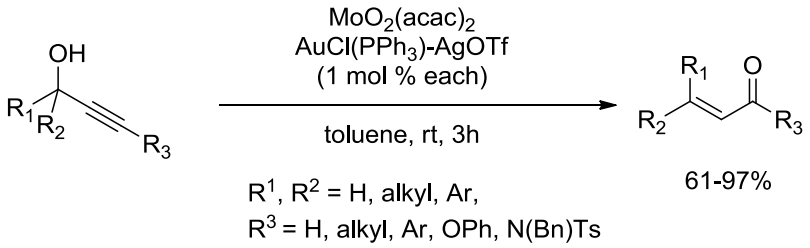
Scheme 50: Meyer–Schuster rearrangement of activated substrates [99]

In 2007 Chung and co-workers reported Au(I)-catalysed Meyer–Schuster rearrangement of specific substrates using [(PPh_3)AuCl] and AgOTf (Scheme 51), with moderate to good yields. [101]



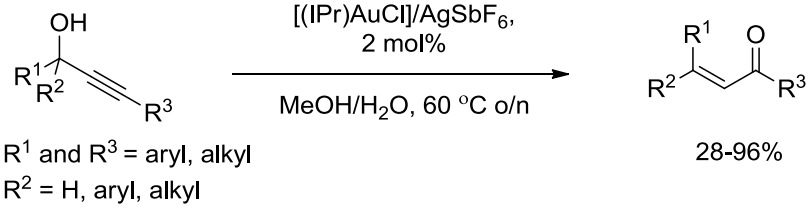
Scheme 51: Au(I)-catalysed Meyer-Schuster rearrangement [101]

In 2008 Akai and co-workers demonstrated the first room temperature Meyer-Schuster rearrangement requiring a molybdenum, Au, and silver catalyst mixture (scheme 52). [102] Good to excellent yields were achieved with this catalytic system on an array of alkyl and aromatic substituents.



Scheme 52: Room temperature Meyer-Schuster rearrangement [102]

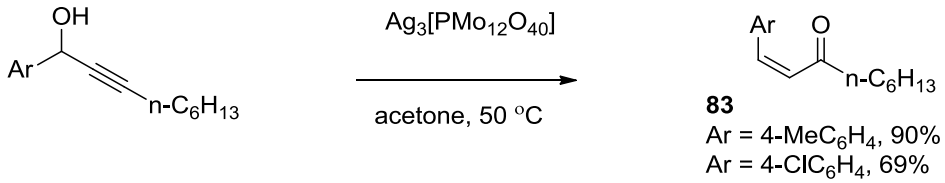
Following this Nolan and co-workers in 2009 investigated the Meyer-Schuster rearrangement with an Au NHC complex and silver hexafluoroantimonate(V) co-catalyst, reporting smooth transformation at 60 ˚C of a range of secondary and tertiary propargylic alcohols (Scheme 53). [103]



Scheme 53: Au carbene catalysed Meyer-Schuster rearrangement [103]

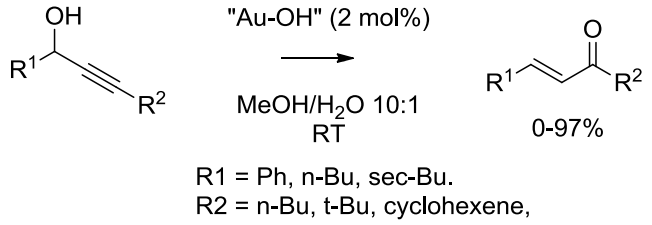
Typically, Meyer–Schuster rearrangements afford the thermodynamically more stable *E*-isomers. Akai demonstrated that the thermodynamically less favoured *Z*-isomers can be accessed when the heteropoly salt $Ag_3[PMo_{12}O_{40}]$ was employed as catalyst. [104] The corresponding *Z*-enones **83** were isolated in good to excellent yields (Scheme 54). When the heteropoly acid $H_3[PMo_{12}O_{40}]$ was used as

catalyst, the corresponding *E*-isomers were obtained; these formed through isomerization of the initially formed *Z*-isomers, as shown by ^{1}H NMR experiments. [104] Thus, the counterion of the heteropoly compound determines the stereochemical outcome of the reaction.



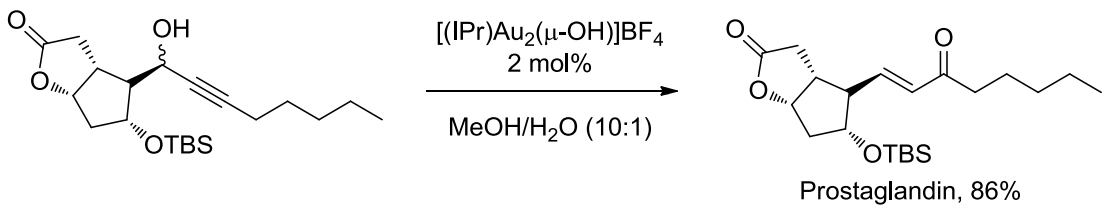
Scheme 54: Selective synthesis of *Z*-enones through Meyer–Schuster rearrangement [104]

Nolan more recently demonstrated the use of an NHC Au catalyst, which required a multistep synthesis, at room temperature in a methanol and water solvent system with mixed yields (Scheme 55). Only four examples are demonstrated with moderate to excellent yields depending on the catalyst and conditions; the reaction times were between 1 and 24 hours (Scheme 55). [105]



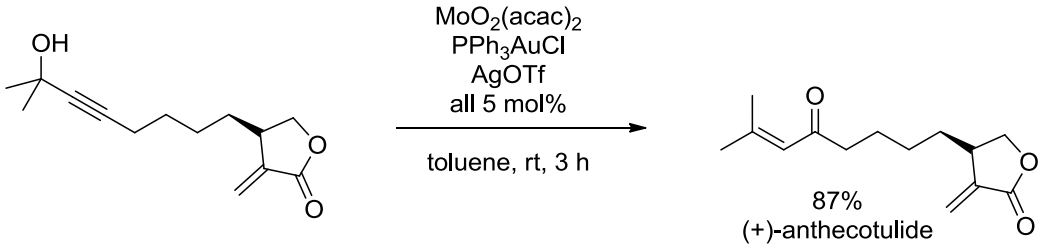
Scheme 55: Au Carbene Catalyst for Meyer-Schuster Rearrangement

Nolan also demonstrated, in the same publication, the utilisation of the Au-catalysed Meyer–Schuster rearrangement for the synthesis of Prostaglandin (Scheme 5). [105] The natural product was synthesised in excellent yield, employing the Meyer-Schuster rearrangement in the final step.



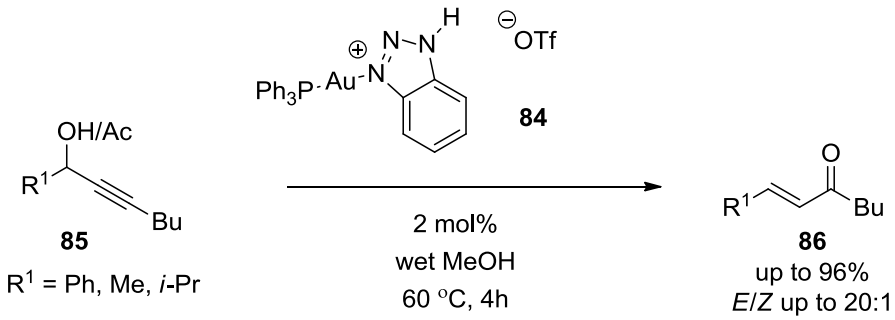
Scheme 56: Prostaglandin synthesis *via* Meyer-Schuster rearrangement [105]

The variety of catalysts systems now available for the Meyer–Schuster rearrangement has led to a number of applications in the synthesis of complex natural products. [83,84,85] Hodgson utilised this rearrangement as the key step in the first synthesis of the sesquiterpene lactone (+)-anthecotulide (Scheme 57). [106]



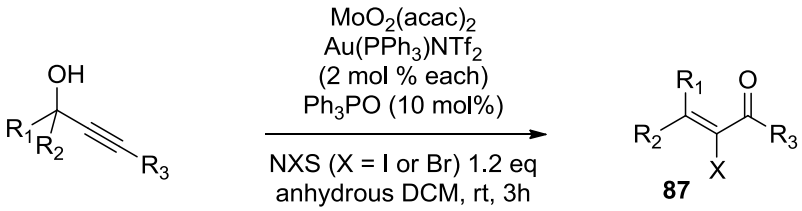
Scheme 57: Meyer–Schuster Rearrangement in the synthesis of (+)-anthecotulide[106]

Shi and co-workers in 2011 reported Au(I) triazole complex **84** as a good candidate for transformations involving alkyne units. The Au triazole complex **84** catalysed the rearrangement of internal propargylic acetates or alcohols **85** to give **86** in good to excellent yields with *E/Z* selectivity up to 20:1 (Scheme 58). [107]



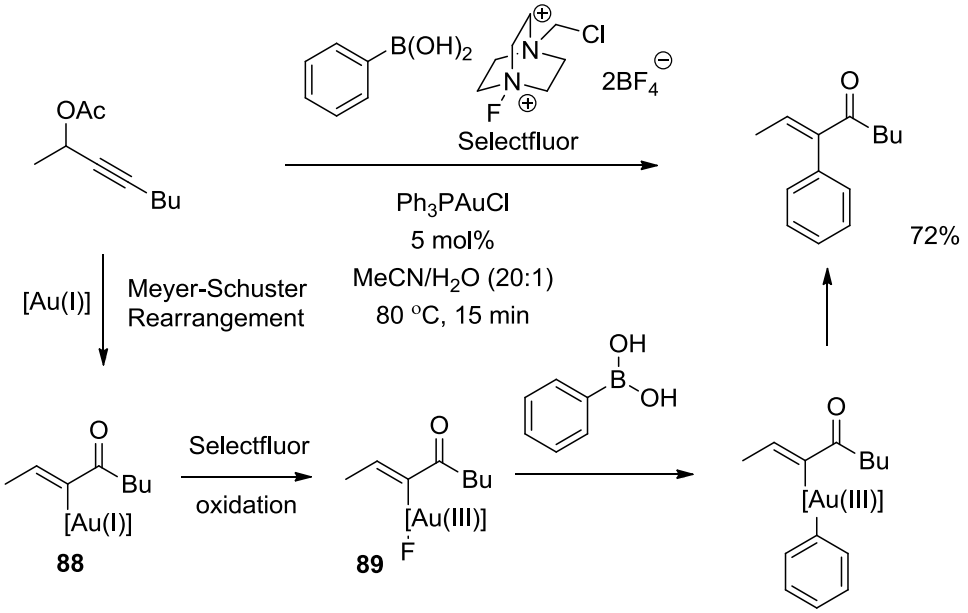
Scheme 58: Au triazole catalyst meyer-schuster rearrangement

Zhang and co-workers demonstrated a Meyer-Schuster rearrangement followed by a second step to introduce iodine or bromine, which occurs before proto-demetallation removes the Au (scheme 59). [108] This one-pot procedure was able to generate excellent yields of halogen substituted enones **87**, allowing a highly functionalised molecule to be accessed quickly and simply from the propargylic alcohol.



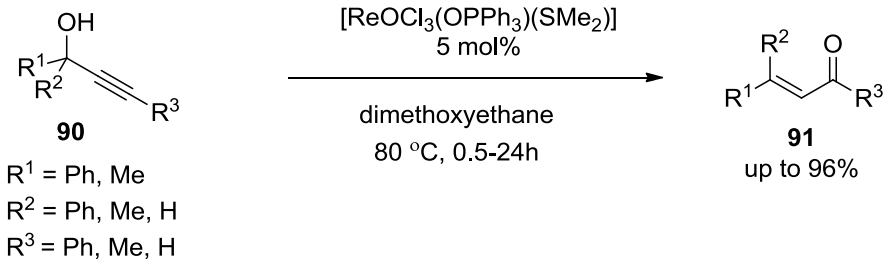
Scheme 59: One-pot Meyer-Schuster Rearrangement and halogen incorporation

The Zhang group also demonstrated that Selectfluor could be also used with the Au catalyst to effectively cross-couple with aryl boronic acids *via* an oxidative Au-catalysed reaction of propargylic acetates with arylboronic acids to provide a range of simple trisubstituted enones in reasonable yields (scheme 60). [109] The Selectfluor is postulated to oxidise the vinyl Au(I) **88** to Au(III) **89**, which then cross couples with the aryl boronic acid.



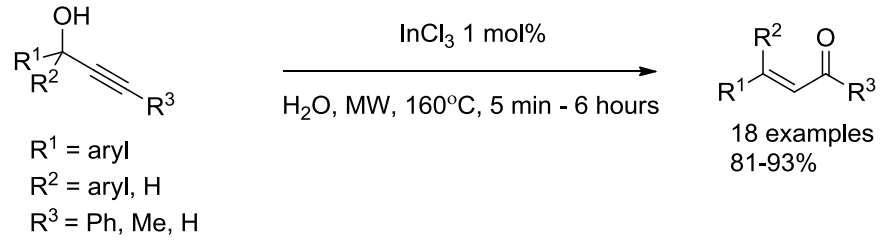
Scheme 60: One-pot Meyer-Schuster rearrangement and aryl substitution

Other Lewis acids such as iron(III) trichloride are catalytically active for the Meyer-Schuster rearrangement as well, [110] as are certain metal–oxo compounds. [85] For example, the rhenium complex $[ReOCl_3(OPPh_3)(SMe_2)]$ gave virtually complete *E* selectivities in the conversion of **90** into **91**, as shown by Vidari (Scheme 61). [111]



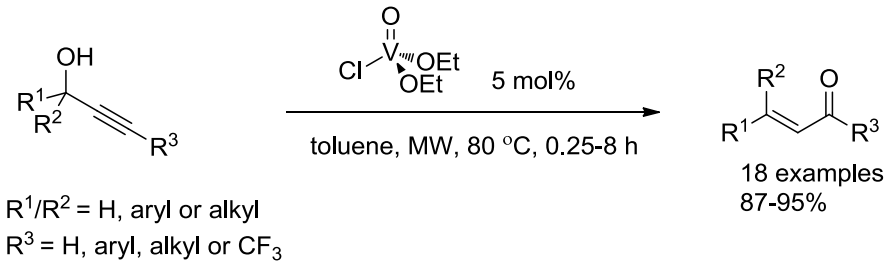
Scheme 61: Rhenium catalysed Meyer-Schuster rearrangement

The rearrangement can be greatly accelerated when performed under microwave irradiation. Cadierno showed that an aqueous solution of indium(III) chloride catalyzed the microwave-assisted rearrangement of various secondary and tertiary terminal propargylic alcohols in times ranging between five minutes and six hours (scheme 62). [112]



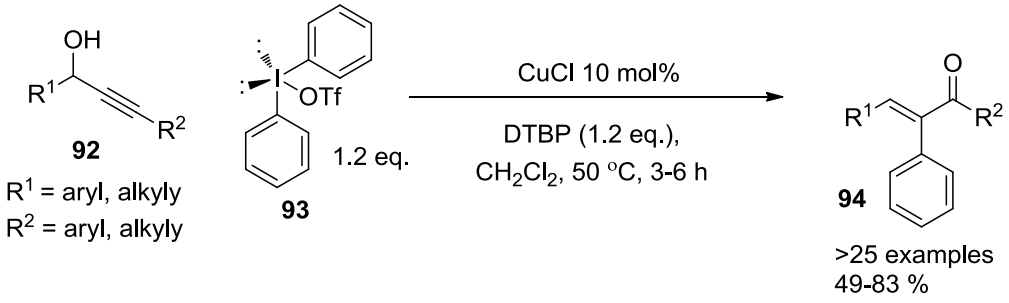
Scheme 62: Microwave assisted $InCl_3$ catalysed Meyer-Schuster Rearrangement[112]

Carrilo-Hermosilla and García-Álvarez demonstrated the catalytic activity of a vanadate $V(O)Cl(OEt)_2$ in the rearrangement of internal and terminal propargylic alcohols under microwave irradiation (scheme 63). [113] Compared to other systems, significantly reduced reaction times – typically below one hour – were sufficient to give the rearranged products in >90% yields. The vanadate $V(O)(OSiPh_3)_3$ was very recently employed by Alibés as the catalyst for a microwave-assisted Meyer–Schuster rearrangement in the synthesis of sesquiterpenes. [114]



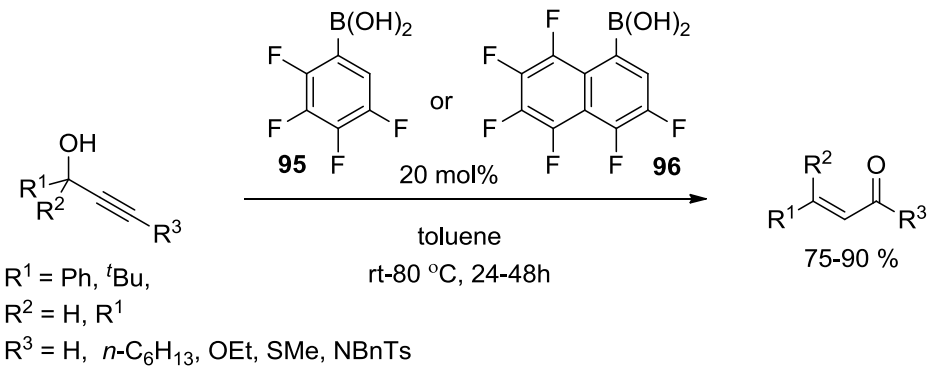
Scheme 63: Vanadate catalysed microwave assisted Meyer-Schuster rearrangement [113]

Gaunt and co-workers in 2013 developed a new approach to transform readily accessible propargylic alcohols (**92**) into α-aryl-α,β-unsaturated carbonyls (**94**) using diaryliodonium salts (**93**) and copper catalysis (Scheme 64). [115] This protocol operates under mild conditions and provides a broad scope of the desired enone products in good yields and high selectivity for the *E*-isomer. The highly functionalised *E*-trisubstituted enone products (**94**) are versatile synthetic intermediates and can be readily transformed into important heterocyclic motifs



Scheme 64: Cu catalysed Meyer-Schuster rearrangement and arylation [115]

In 2011, Hall and co-workers demonstrated the metal free boronic acid catalysed Meyer-Schuster rearrangement in good to excellent yield (Scheme 65). [116] Although the scope is limited and the reaction conditions and choice of boronic acid **95** or **96** need to be tailored to each substituent. The propargylic alcohol examples are generally activated with a terminal ethoxy group at R^3, making the alkyne more electron rich. The aromatic groups at R^1 and R^2 also stabilise the formation of the carbo-cation, lowering the energy of the Meyer-Schuster pathway for tertiary propargylic alcohols.



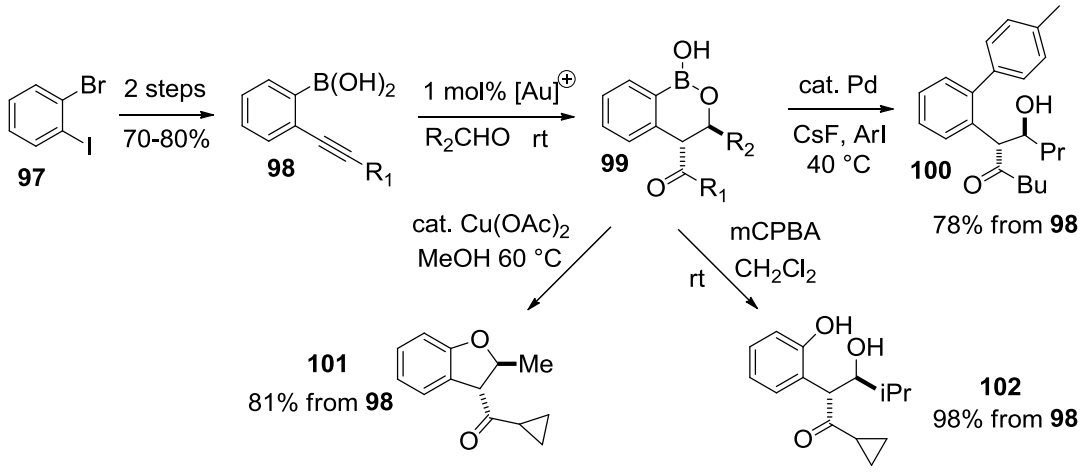
Scheme 65: Boronic acid **95**/**96** catalysed Meyer-Schuster rearrangement [116]

2. Results and Discussion

The initial aim of the research project was to develop an intermolecular aldol reaction utilising various propargylic alcohols in the presence of a Au catalyst. Although it ws quickly established that we had developed some very efficient conditions for the Meyer-Scjhuster rerrnagemnent. The scope and limitations of our developed Meyer-Schuster rearrgangement conditions have been explored and will be discussed, along with other transformations discovered along the way.

2.1. Previous Work: Gold catalysed enolate formation from alkynes

The Sheppard group has developed an efficient catalytic method for generating boron enolates from alkynes and demonstrated the feasibility of a combined Au/boronic acid catalysed intermolecular aldol reaction (scheme 66). [117] The enolate formation is exceptionally mild (the enolate is stable to column chromatography) and the enolates can be trapped by aldehydes present in the reaction mixture.



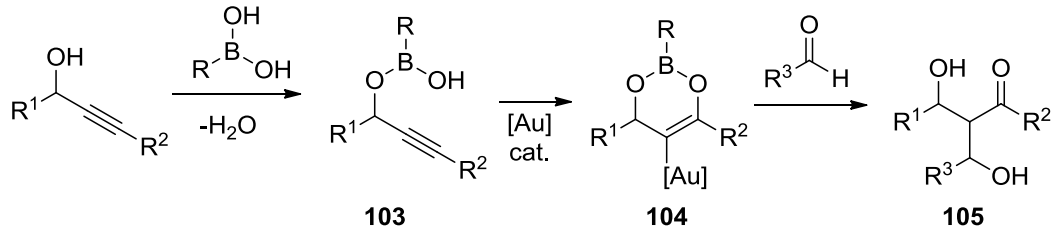
Scheme 66: Au-catalysed boron enolate formation and reactions [117]

Intramolecular enolate formation and subsequent transformation of the boronic acid from the aldol product (**99**) are achieved *via* Chan-Lam coupling (**101**), Suzuki reactions (**100**) or oxidation (**102**) and can provide access to a range of

functionalised scaffolds. [117] Eleven examples of products (**100**-**102**) were synthesised in excellent yield with moderate diastereoselectivity achieved in most cases. [117]

2.2. Secondary propargylic alcohols: Meyer-Schuster rearrangement and reaction optimisation

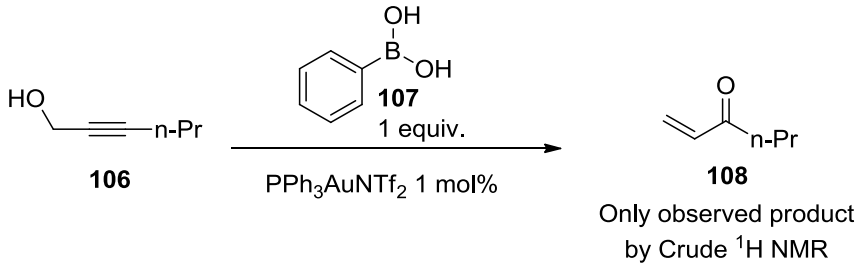
We began by investigating the reaction profile of propargylic alcohols in the presence of a Au(I) catalyst and boronic acid. Gagosz's [Bis(trifluoromethanesulfonyl)imidate] (triphenylphosphine)Au(I) (2:1) toluene adduct was the commercially available Au catalyst used for the reaction. [21] Initially we anticipated boronic acid condensation [118] to create an intermediate similar to boronic acid [103] which could then potentially undergo Au activation of the alkyne promoting attack of the boronic acid to give boron enolate **104**, followed by aldol reaction to give **105** (Scheme 67). [117]



Scheme 67: Proposed condensation, boronic acid cyclisation and aldol reaction

However, the only product observed when propargylic alcohol **106** was treated with Au catalyst and phenylboronic acid (**107**) was the enone **108** (Scheme 68). Formation of Enone **108** proceeded rapidly at room temperature, however **108** was only observed by ^{1}H NMR and is unstable to column chromatography (see section 2.6). The observed enone was a product of the Au catalysed Meyer-Schuster rearrangement and we reasoned that the room temperature boronic acid mediated approach could provide a superior method for access to synthetically useful enones. Existing Meyer-Schuster rearrangement procedures (at that time) generally involved high temperature, the use of co-catalysts such as molybdenum, and long reaction times or a combination of the above. [102,103] Our preliminary

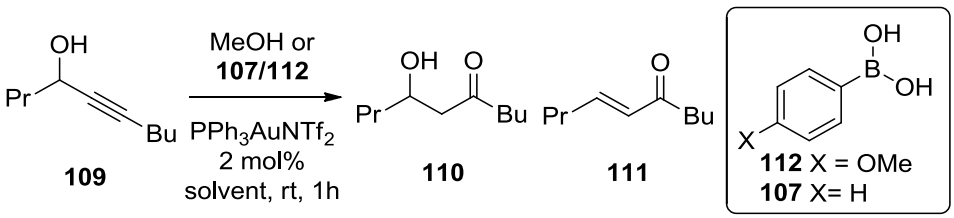
result, however, was at room temperature and proceeded efficiently in the presence of phenyl boronic acid.



Scheme 68: Meyer-Schuster rearrangement of a primary propargylic alcohol

At this point due to the instability of enone **108** towards column chromatography, the secondary propargylic alcohol **109** was chosen as a test substrate for a brief condition screen to optimise the Meyer-Schuster rearrangement (table 2). Interestingly, a β-hydroxyketone side product **110** was also observed as well as the expected enone **111**, which was not the case for the primary propargylic alcohol **106** where only the enone **108** was observed (see hydration section 2.7).

Table 2: Optimisation of the Meyer-Schuster rearrangement



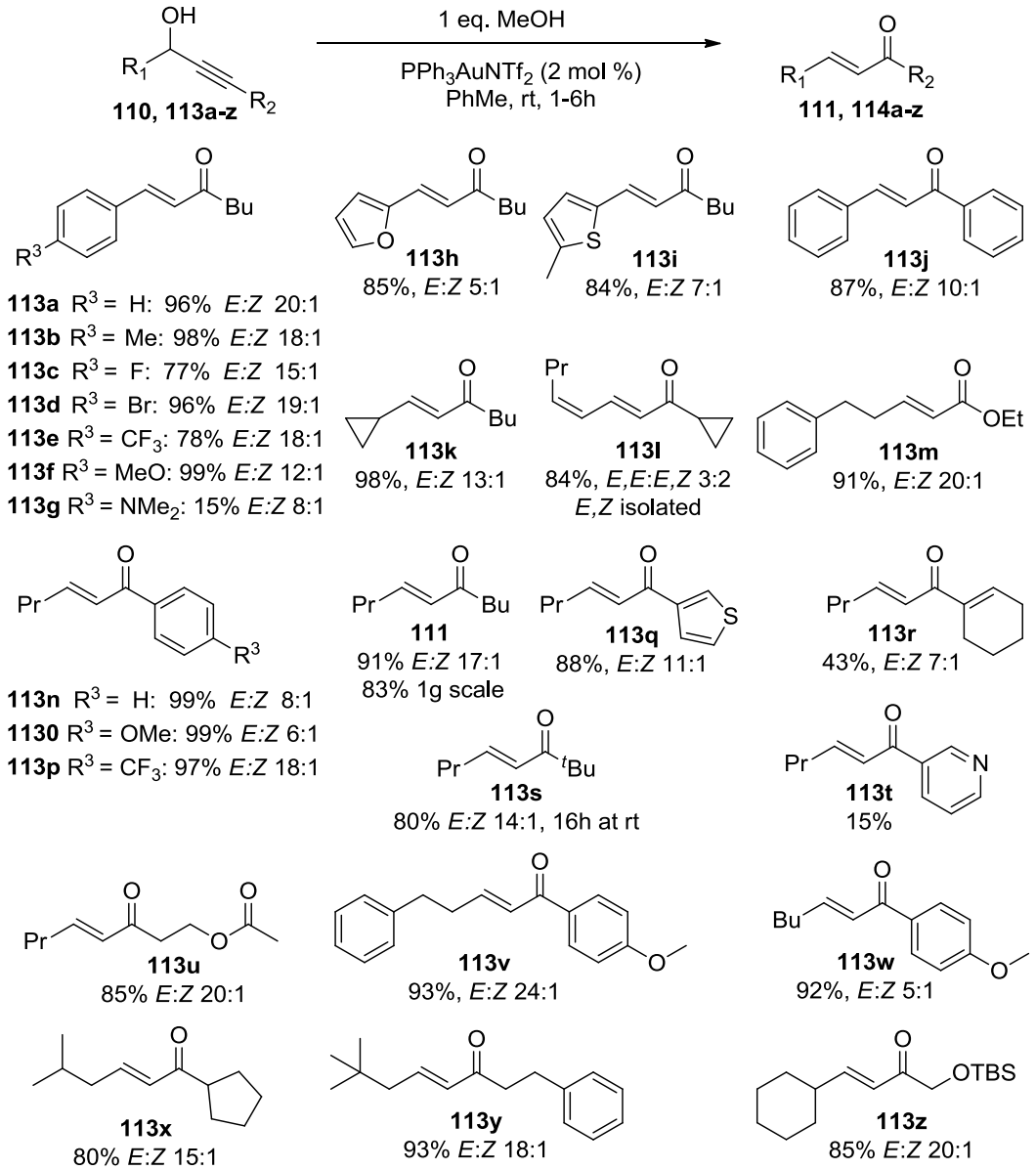
Entry	Solvent	Additive	Conversion	**111:110**	*E:Z*
1	CH_2Cl_2	0.1 eq. **112**	43%	*1.2:1*	*10.5:1*
2	MeOH	0.1 eq. **112**	58%	*4.3:1*	*>30:1*
3	THF	0.1 eq. **112**	46%	*1.6:1*	*27:1*
4	Acetone	0.1 eq. **112**	28%	*3.0:1*	*20:1*
5	PhMe	0.1 eq. **112**	76%	*1.8:1*	*20:1*
6	PhMe	0.2 eq. **112**	99%	*2.0:1*	*27:1*
7	PhMe	1 eq. **112**	99%	*1.8:1*	*>30:1*
8	PhMe	0.2 eq. **107**	54%	*1.8:1*	*7.8:1*
9	PhMe	-	64%	*1.1:1*	*5.6:1*
10	MeOH	-	43%	*>36:1*	*5.1:1*

11	PhMe	0.1 eq. MeOH	98%	*2.6:1*	*5.1:1*
12	PhMe	1 eq. MeOH	100%	**111** only	*17:1*

The Meyer-Schuster rearrangement was most efficient in non-polar solvents in the presence of a protic additive, such as methanol or phenyl boronic acid (Entries 1-5).[2] The more electron rich 4-methoxyphenylboronic acid **112** gave a higher conversion than the same number of equivalents of phenyl boronic acid **107** (Entries 6 and 8). The conversion to enone **111** decreased when the equivalents of boronic acid **112** were reduced from 0.2 to 0.1 equivalents and this also adversely affected the *E:Z* selectivity (Entries 6 and 5, respectively). Conversely there was no benefit in using a stoichiometric quantity of boronic acid **112** when compared with 0.2 equivalents (Entries 6 and 7). In the absence of boronic acid, a lower conversion was observed, suggesting that the boronic acid co-catalyses the Meyer-Schuster rearrangement (Entry 9). However, the presence of β-hydroxyketone **110** as a by-product in the reaction (entries 1-9) posed a problem for achieving the desired high conversions and suggested that the reaction could be going *via* an intermediate or potentially a divergent reaction pathway. This promoted our curiosity in the role of the reaction additive and the potential formation of β-hydroxyketone products (See section 2.7). Interestingly, when using methanol as solvent the formation of β-hydroxyketone **110** was supressed, with enone **111** being obtained as the sole product. This suppression of β-hydroxyketone in methanol was irrespective of the presence (Entry 2) or absence of boronic acid 50 (Entry 10). This led to the examination of small quantities of methanol as an additive (Entries 11-12). The use of 1 equivalent of methanol, with toluene as the solvent, led to rearrangement of propargylic alcohol **109** to enone **111** with excellent conversion and very high selectivity in favour of the *E* isomer (Entry 12).

Following the optimisation a wide range of secondary propargylic alcohols were subjected to this Meyer-Schuster rearrangement, generally on a 100 mg scale, with 2 mol% commercially available Au(I) catalyst. The reactions were conducted at room temperature in the presence of just 1 equivalent of methanol

(Scheme 69) in toluene as the solvent. In nearly all cases the reaction proceeded to completion within an hour, and the pure *E* isomer of the enone was obtained after purification (see Experimental Section). The *E:Z* ratios were obtained from the crude ^{1}H NMR before purification.

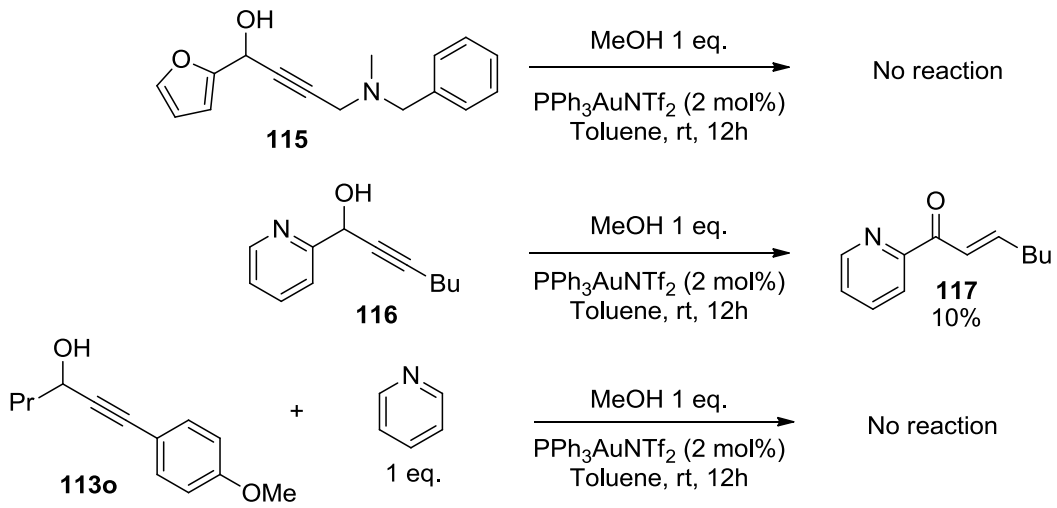


Scheme 69: Meyer-Schuster rearrangement

A variety of substituents can be incorporated at the R^{1} position of the propargylic alcohol (**113a-m**). Benzylic alcohols rearrange efficiently (**113a-g**) with substrates containing electron deficient (substrates **113c-e**) or moderately electron-donating (**113a**) substituents giving excellent yields. Whilst electron-rich alcohol **113f** gave the corresponding enone **114f** in excellent yield, dimethylaniline **113g** gave only a 15% yield of the corresponding enone **114g**.

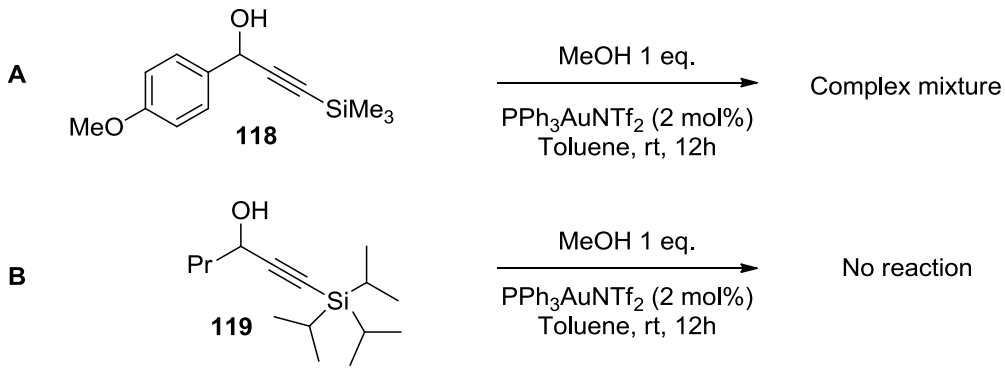
This may be due to the presence of the co-ordinating nitrogen atom which can (potentially) inhibit the Au catalyst. [119] Propargylic alcohols containing electron-rich heterocycles gave the corresponding enones in good yield (Entries **114h-i**) and there was no evidence for Au-catalysed reaction of the electron-rich heterocycle with the pendant enone in the product as reported by Hashmi and co-workers. [120] Meyer-Schuster rearrangement is favoured over possible nucleophillic attack of the furan ring onto the alkyne, proceeding smoothly without any oxygen coordination problems. [49,121] At the R^2 position of the alkyne a wide variety of alkyl, alkenyl and aryl substituents were tolerated (**113j**, **113m-n**, and **113v**) and the reaction could also be run on a 1 g scale using 1 mol% Au catalyst (**111**). An alkoxy group could be incorporated at R^2 of the alkyne to give access to an *α,β*-unsaturated ester (**114m**). Compounds containing both electron rich aromatic groups (**114o**, **114v**, **114w**) and electron deficient aromatic groups (**114p**) at R^2 rearranged smoothly, as did a substrate containing a thiophene ring (**114q**). The sulfur of the thiophene ring causing no coordination issues with the Au catalyst. [122,21] Pyridine substituted example **113t** proceeded in very low yield, suggesting that the nitrogen lone pair may be coordinating to the Au catalyst and inhibiting the reaction. The sterically congested substrate containing a tertiary butyl substituent (**113s**) rearranged to the corresponding enone in very good yield, but required a prolonged reaction time of 16 hours. This was a vast improvement on the reported 28% yield achieved by Nolan and co-workers reacting overnight at 60^{o}C. [103] A substrate containing a conjugated alkene at R^2 (**113r**) gave a lower yield, but this probably reflects the relative instability of the dienone product **113r** rather than the yield of the reaction itself. Silyl protected alcohols can be tolerated (**113z**) without incurring any problems. Further combinations of substituents could also be incorporated (**113u**-1**13z**) including cyclopropanes (**113k**, **113l**), which did not undergo ring-expansion during the rearrangement reaction. [123,124] The dienone (**114l**) can be generated in excellent yield from the corresponding propargylic alcohol **113l**. Interestingly the initial major product observed in the crude ^{1}H NMR from the rearrangement was the *E*,*E* isomer. However after purification the pure *E*,*Z* isomer **113l** was obtained cleanly in good yield, which presumably is the thermodynamically more stable isomer in this case.

As mentioned above, propargylic alcohols containing nitrogen functionality either proceed poorly or do not proceed at all to the desired enone when submitted to our standard Meyer-Schuster rearrangement conditions (Scheme 70). Tertiary amine **115** was completely unreactive, whereas pyridine **116** gave the abnormal migration product **117** in 10% yield (scheme 70). The low reactivity of these substrates is presumably a consequence of the ability of the basic nitrogen atom to co-ordinate to the Au-catalyst and deactivate it. Addition of 1 eq. of pyridine to alcohol **113o** completely inhibited the Meyer-Schuster rearrangement of this otherwise reactive substrate. It should be noted that there are virtually no reports of the Au-catalyzed Meyer-Schuster rearrangement of nitrogen containing compounds in the literature to the best of our knowledge. Recently Lee and co-workers were able to show the deactivation of Au(I) catalysts caused by thiols and amines. [122]



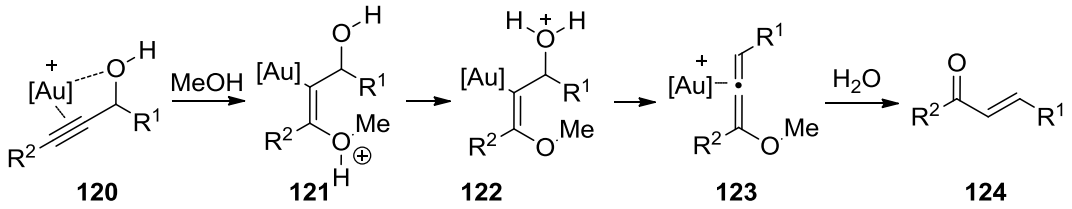
Scheme 70: Basic nitrogen reaction isssues [3]

Other propargylic alcohols that did not proceed as desired under our Meyer-Schuster rearrangement conditions include the terminal silicon substituted substrates **118** and **119** (Scheme 71), resulting in either a complex mixture (A) or no reaction at all (B). It should be noted that the TBS protection of a beta alcohol (**113z**) within the molecule did not hinder the reaction, which proceeded smoothly to the desired product, so it is unlikely that it is due to the silicon coordinating to the Au. It may be that the silicon is sufficiently electron withdrawing to deactivate the alkyne towards catalyst activation or possibly the steric clash of the terminal silicon substituent and the Au catalyst is prohibitive.



Scheme 71: Other problematic examples

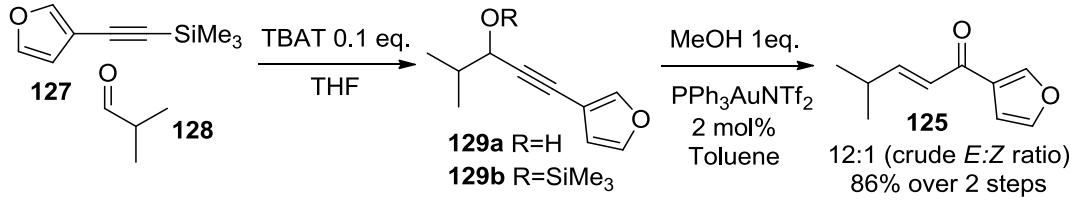
In the presence of alcohols, the Meyer-Schuster rearrangement has been proposed to proceed *via* the formation of an allenyl ether (**121**). [102,103] For our methanol containing reaction system the allenyl ether **121** could be generated by an addition of methanol to the Au-activated alkyne (**120**), followed by proton transfer (**121**-**122**) and elimination of water (**122**-**123**) (Scheme 72). The allenyl ether **123** could then undergo hydrolysis and proto-demetallation to give the enone **124** and subsequently release the Au catalyst. Methanol as a reaction additive does not promote early proto-demetallation of (**121**), therefore this could be the reason no β-hydroxyketone is observed (see section 2.7). [125]



Scheme 72: Meyer-Schuster rearrangement via allenyl ether nn [2]

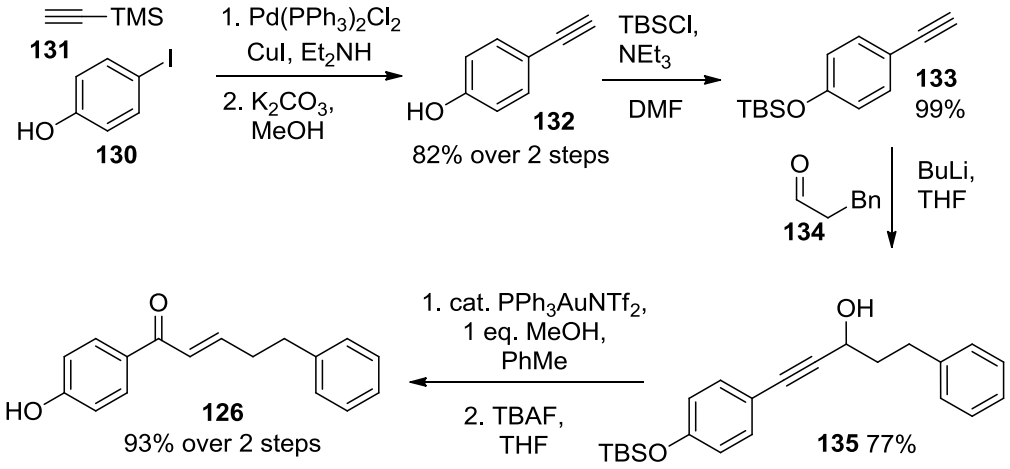
We have applied our Meyer-Schuster rearrangement conditions to the synthesis of two small natural products Isoegomaketone (**125**) and Daphenone (**126**). Isoegomaketone **125** is an essential oil component of *Perilla Frutescens Britt* and has been shown to exhibit anti-inflammatory properties. [126,127,128] The natural product **125** was synthesised in two steps *via* fluoride-mediated addition of commercially available silylacetylene **127** to aldehyde **128**, [129] followed by Meyer-Schuster rearrangement of the resulting mixture of alcohol **129a** and its corresponding TMS ether **129b**, with simultaneous silyl deprotection. (Scheme

73). Isoegomaketone **125** was obtained in 86% overall yield with high *E:Z* selectivity from the two-step sequence.



Scheme 73: Isoegomaketone synthesis [3]

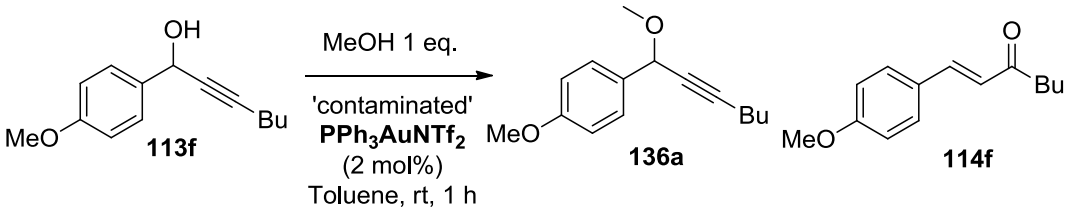
We also carried out a short synthesis of Daphenone **126** (Scheme 74), a natural product isolated from *daphne odora* which showed cytotoxicity against five human tumor cell lines. [130] Sonigashira coupling of 4-iodophenol **130** with TMS-acetylene **131** gave phenol **132** after desilylation. [131] After protection of the phenol as a silyl ether, alkyne **133** was lithiated and reacted with dihydrocinnamaldehyde **134** to give access to the propargylic alcohol **135** in good yield. Meyer-Schuster rearrangement of **135** proceeded cleanly and efficiently but without concomitant deprotection of the bulkier silyl ether, which was cleaved in an additional step with fluoride to give Daphenone **126** in 58% yield over 6 steps from **130** (Scheme 74).



Scheme 74: Synthesis of Daphenone [3]

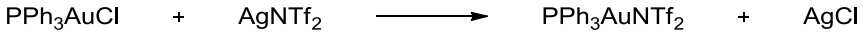
2.3. Silver catalysed propargylic alcohol substitution

During the course of evaluation of the substrate scope of the Meyer-Schuster rearrangement (M-S scheme 69), the formation of propargylic substitution product **136a** was initially observed in 54% yield when rearrangement of electron rich propargylic alcohol **113f** was attempted, with enone **114f** being produced only as a minor product (Scheme 75). It subsequently transpired that the formation of the substituted product **136a** was not reproducible, and appeared to be dependent on the batch of Au catalyst used in the reaction. With a new batch of catalyst (batch 2) the Meyer-Schuster rearrangement proceeded cleanly in good yield (Scheme 75). [3]



Scheme 75: Inconsistent reactions from different batches of Au catalyst [3]

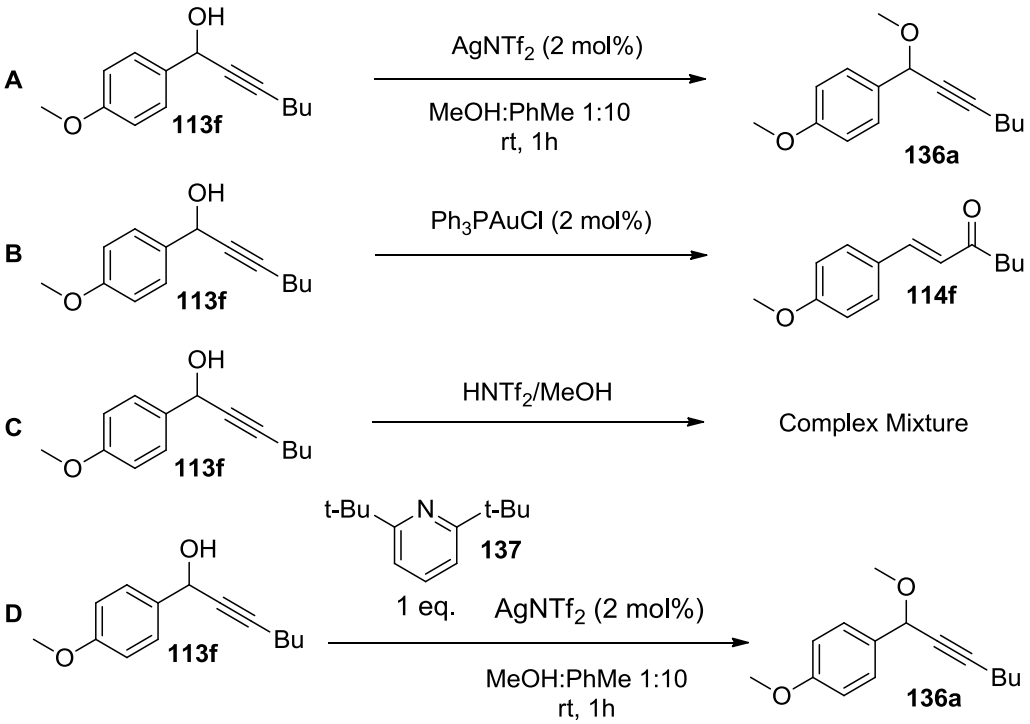
We hypothesised that the propargylic substitution reaction was probably mediated by an impurity present in the original batch of Au catalyst (scheme 76).



Scheme 76: Catalyst activation

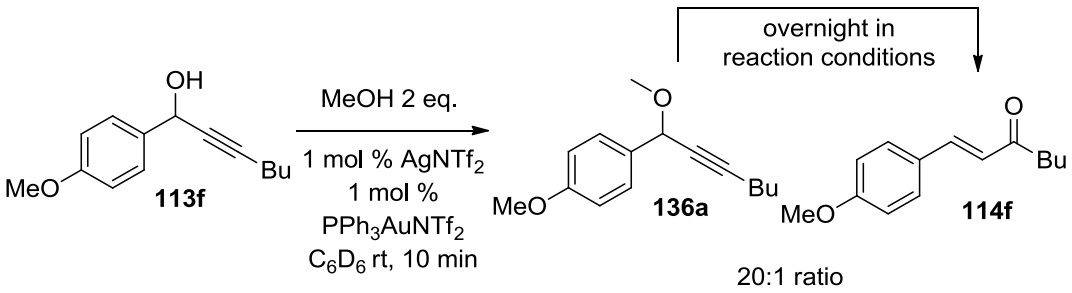
The most likely candidate seemed to be the Silver bis(trifluoromethanesulfonyl)imide ($AgNTf_2$), [132,133] used during the preparation of the catalyst. [21] Treatment of propargylic alcohol **113f** with $AgNTf_2$ and methanol in toluene led to the formation of substitution product **136a** in good yield (scheme 77, A). Reaction with PPh_3AuCl and methanol in toluene gave slow conversion to the enone **114f**, with no substitution product **136a** observed (scheme 77, B). Reaction of alcohol **113f** with the acid $HNTf_2$ and methanol in toluene led to a complex mixture of products (Scheme 77, C). [134,32,18] The reaction

still proceeds in the presence of 1 equivalent of base **137**, albeit more slowly, giving evidence that Ag is catalysing or playing a key role in the substitution reaction and suggesting that this is not simply an acid-catalysed process (Scheme 77, D).



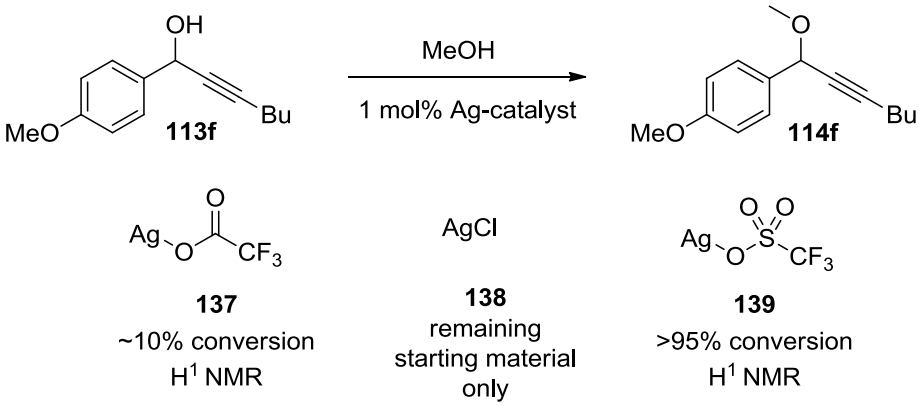
Scheme 77: Propargylic substitution investigation reactions

The quantity of silver present in the original reaction as an impurity in the 2 mol% Au catalyst used must have been very small suggesting that the silver-catalysed substitution reaction must be highly efficient as it was the dominant reaction pathway (batch screen 1). The reaction was conducted in deuterated benzene and monitored by ^{1}H NMR to determine the relative rates of the silver and Au catalysed reactions (Scheme 78). Treatment of alcohol **113f** with 1 mol% of each of the catalysts in the presence of 2 eq. MeOH in C_6D_6 gave a 20:1 ratio of substitution product **136a** to Meyer-Schuster rearrangement product **114f** after 10 minutes at room temperature, illustrating that the substitution reaction is considerably faster than the Meyer-Schuster rearrangement. Over time the methanol substituted product underwent Meyer-Schuster rearrangement, such that overnight the enone **114f** was the major product.



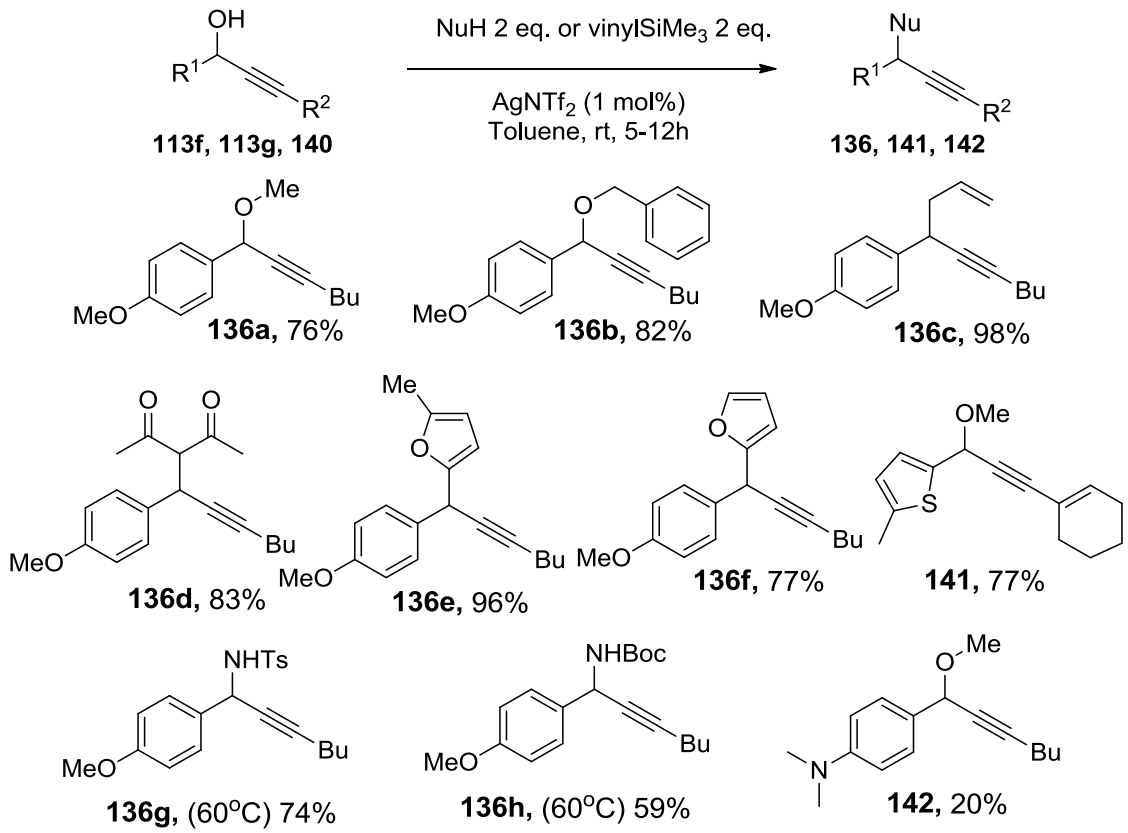
Scheme 78: Relative rates of the silver and Au catalysed reactions

A small range of silver catalysts were investigated (Scheme 79). Silver trifluoroacetate (**137**) and silver chloride (**138**) promoted minor conversion or no conversion respectively, whereas silver trifluoromethane sulfonate (**139**) gave conversion comparable to $AgNTf_2$ (Scheme 79).



Scheme 79: Range of Ag catalysts

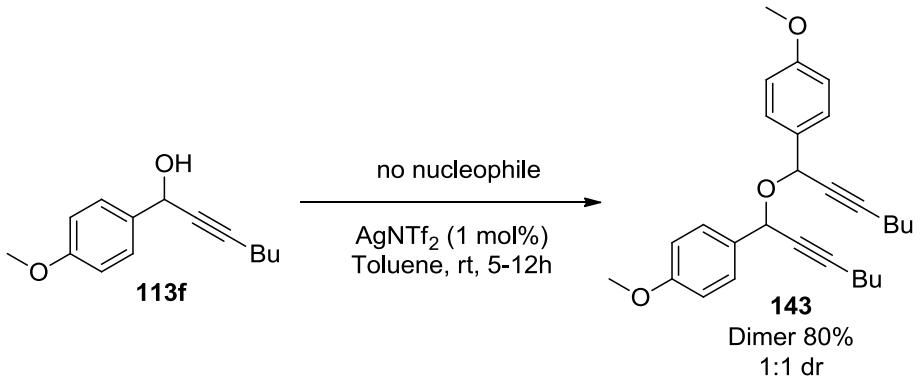
Propargylic alcohols **113f**, **113g** and **140** were submitted to 1 mol% $AgNTf_2$ in the presence of 2 equivalents of a selected nucleophile in toluene to help establish the potential scope of the substitution reaction (scheme 80).



Scheme 80: Silver catalysed propargylic alcohol substitution

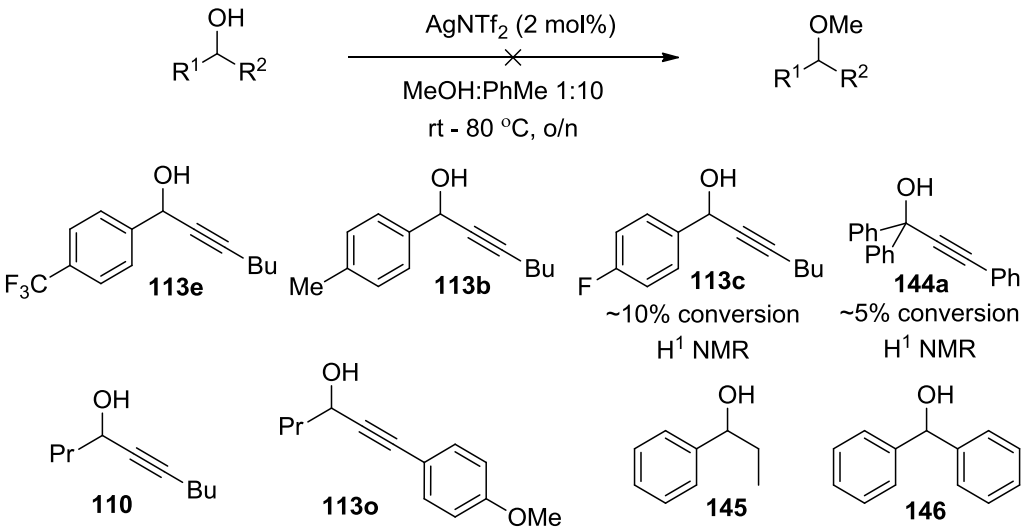
Substitution reactions with oxygen, (**136a-b**, **141**, **142**) carbon (**136c-f**), and nitrogen nucleophiles (**136g**, **136h**) were all possible, although the nitrogen nucleophiles required heating to 60 °C. Propargylic alcohol **113g** with 4-dimethylamine substitution gave a dramatically decreased yield under the silver substitution conditions, proceeding in a modest 20% yield (**142**). Otherwise good conversion was achieved for the majority of entries. The presence of both an alkyne and an electron rich aromatic ring at the R^1 position seem to be necessary for the substitution reaction to take place. The R^2 position remains relatively unexplored with the butyl chain suitable in all examples.

In the absence of an external nucleophile, dimerisation of the propargylic alcohol (**113f**) took place to form the symmetrical ether (**143**) as a mixture of diastereoisomers (Scheme 81).



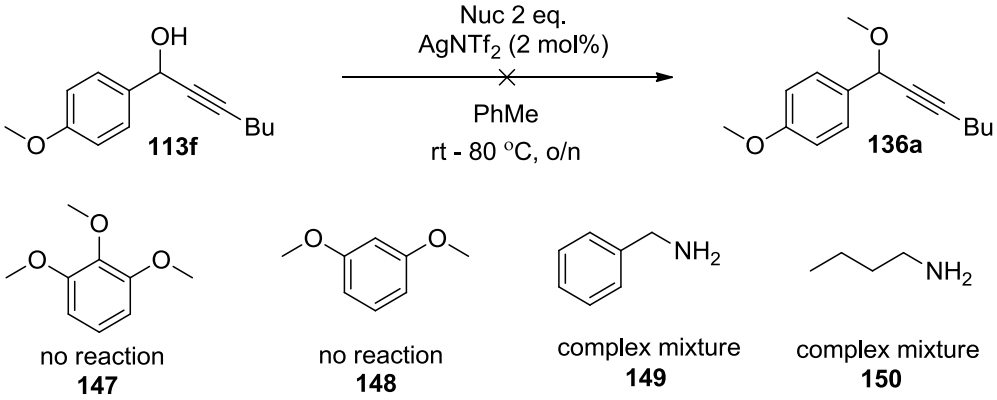
Scheme 81: Dimerisation of propargylic alcohol **113f**

Propargylic alcohols with electron withdrawing group at R^1 (**113e**), alkyl substituted (**110**) and electron rich group at R^2 (**113o**) did not react in the presence of silver catalyst ($AgNTf_2$) and methanol, heating to 60 °C; similarly, benzhydrol **146** (Ph_2CHOH) and 1-phenylethanol **145** were also unreactive (Scheme 82). The unreactivity of benzhydrol was particularly surprising as it was anticipated the two aromatic rings would facilitate substitution, indicating that the alkyne along with an electron rich group at R^1 are vital for the silver catalysed reaction to proceed. Small conversions were noted with secondary propargylic alcohol **113c** and tertiary propargylic alcohol **144a**, but no significant conversion was observed (Scheme 82).



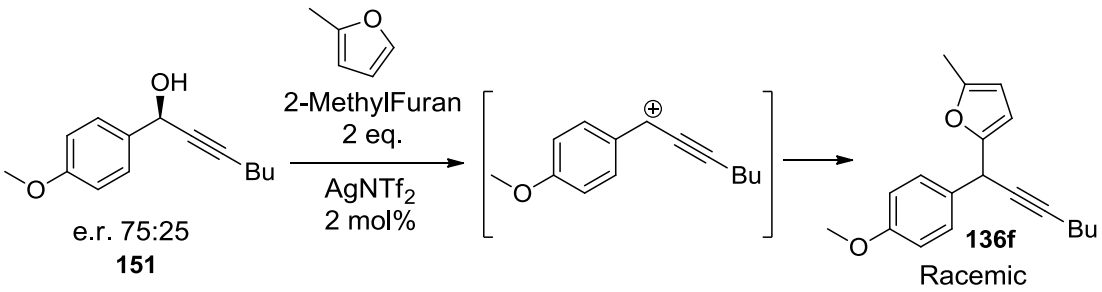
Scheme 82: Unsuccessful substitution reactions

Some of the nucleophiles attempted did not work including electron rich aromatics **147** and **148**, also primary amines **149** and **150** gave a complex mixture which did not appear to contain the expected yield (Scheme 83).



Scheme 83: Other nucleophiles attempted

The mechanism of the reaction most likely involves going through a carbo-cation intermediate as opposed to a direct substitution mechanism (scheme 84). This is reinforced by the complete racemisation of alcohol **151** when submitted to the reaction conditions; the carbon nucleophile at room temperature should give a sufficiently stable product not to itself racemise by repeated S_N2 reactions, after the initial substitution (scheme 84).

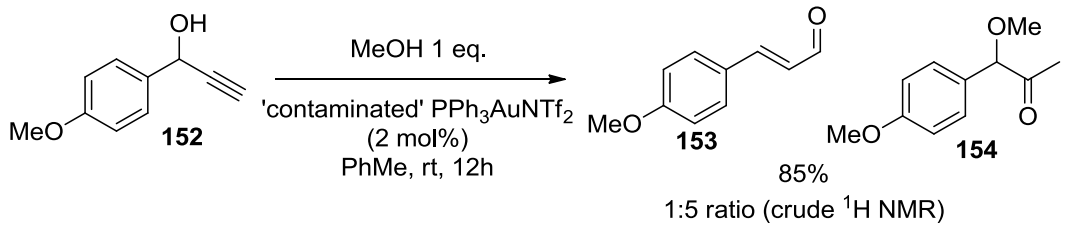


Scheme 84: Racemisation of enatio-enriched alcohol **151**

It is possible that some of the several reports in the literature of metal-catalysed substitution reactions of alcohols [132,133,80,135,82,81] may actually be mediated or assisted by trace quantities of silver salts that are present in the reaction mixture, particularly where silver salts have been added as a co-catalyst. [136] However substitution reactions of propargylic alcohols which do not contain an electron-rich aromatic substituent have been reported with Au(III)-catalysts. [81]

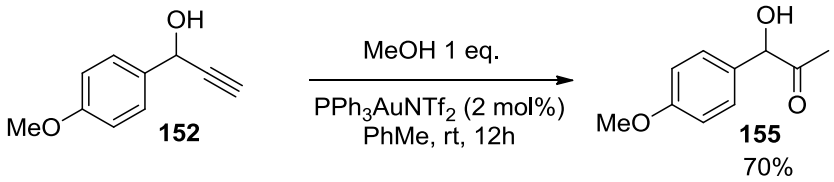
2.4. Terminal propargylic alcohols: Hydration versus Meyer-Schuster rearrangement

Terminal propargylic alcohols were explored with the aim of utilising a Meyer-Schuster rearrangement to obtain α,β-unsaturated aldehydes. The initial reactions were carried out by treatment of alcohol **152** with the contaminated Au catalyst batch that led to the discovery of the silver catalysed substitution (Scheme 85). This gave a mixture of the desired aldehyde **153** and α-methoxyketone **154**.



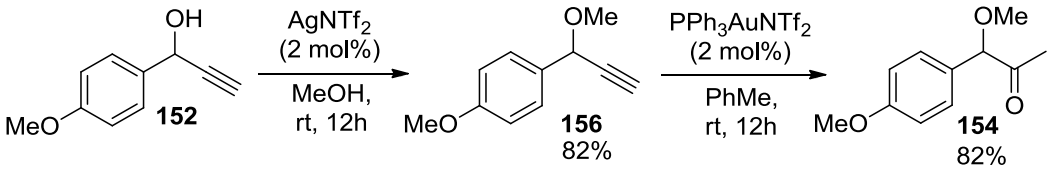
Scheme 85: Initial reaction with terminal propargylic alcohol **152**

Treatment of alcohol **152** with a new batch of uncontaminated Au catalyst gave the hydration product **155** over the desired Meyer-Schuster rearrangement, suggesting that for terminal alkynes, hydration of the alkyne is faster than the Meyer-Schuster reaction (scheme 86).



Scheme 86: Hydration faster than Meyer-Schuster rearrangement

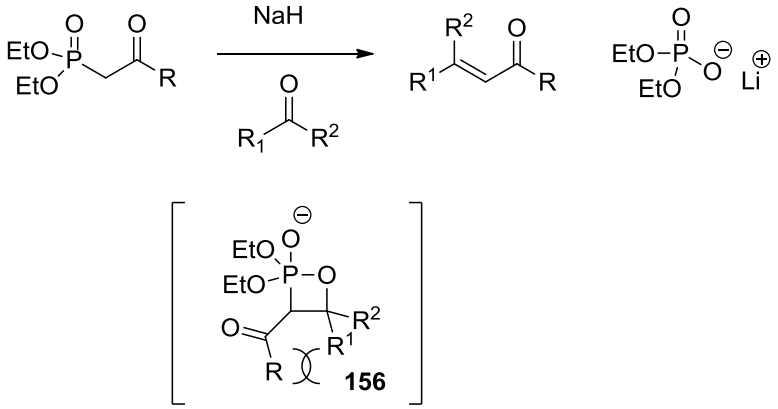
Treatment of alcohol **152** with silver catalyst in the presence of methanol gave the expected substitution product **156** cleanly and in good yield (scheme 87). Treatment of **156** with catalytic Au gave ketone **154**, providing evidence that product **154** was formed in our original experiment by two separate steps catalysed by the two different metals. [136]



Scheme 87: Ag catalysed substitution followed by Au hydration

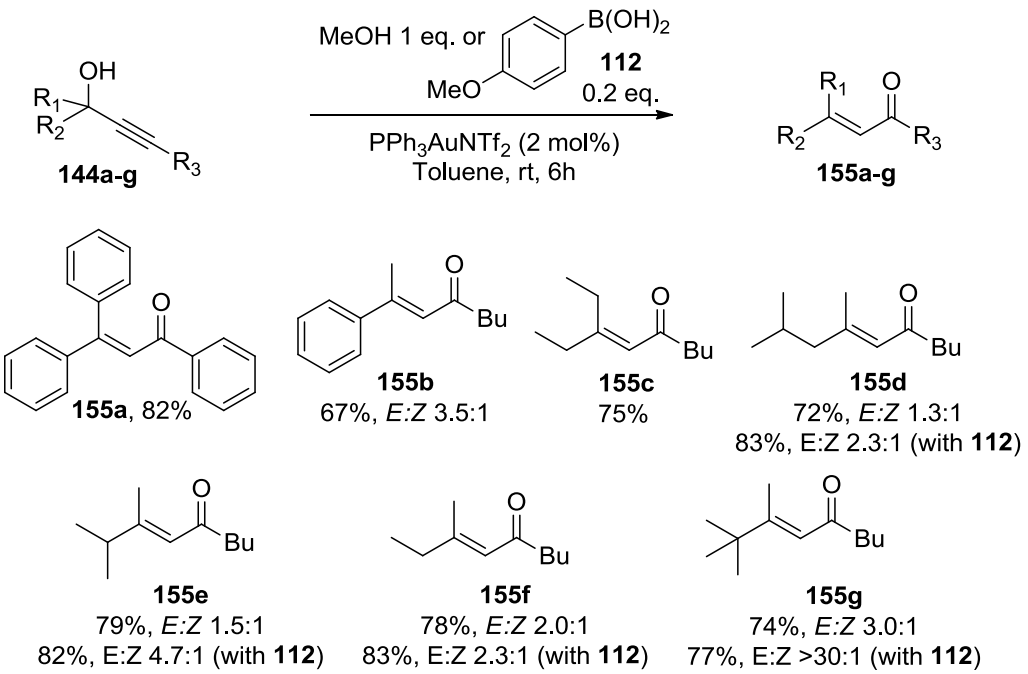
2.5. Tertiary propargylic alcohols: Meyer-Schuster rearrangement

Tertiary propargylic alcohols **144a-g** can be easily prepared by addition of alkynyl anions to ketones; and following a Meyer-Schuster rearrangement can provide access to sterically congested trisubstituted enones **155a-g**. The strength of this two-step approach from simple alkynes and ketones is the synthesis of products with bulky substituents, which could prove challenging to synthesise by conventional aldol or Horner-Wadsworth-Emmons procedures due to steric clashes (Scheme 88).



Scheme 88: Steric congestion in the Horner-Wadsworth-Emmons reaction

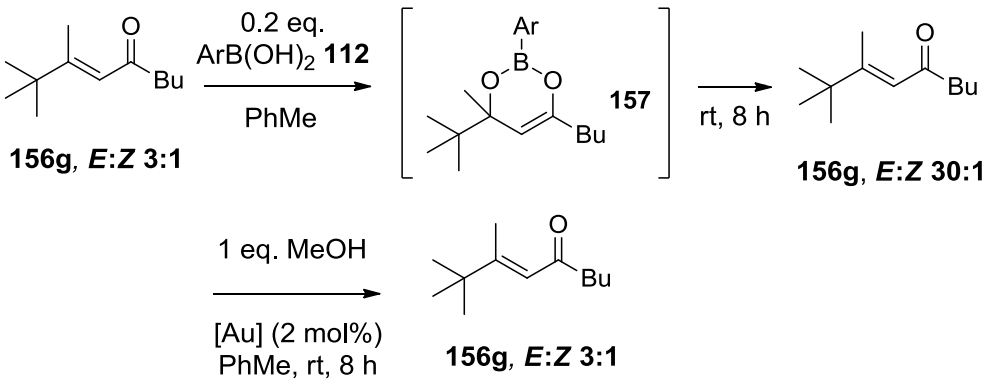
With our Meyer-Schuster rearrangement conditions in hand the formation of a range of symmetrically and unsymmetrically substituted enones **155a-g** proceeded in good to excellent yield and exhibiting high levels of geometric control in some cases (Scheme 89).



Scheme 89: Tertiary propargylic alcohol Meyer-Schuster rearrangement

In general, the Meyer-Schuster rearrangement of tertiary propargylic alcohols required longer reaction times than those of secondary propargylic alcohols. Highly congested enone **155a** was formed in high yield illustrating the steric tolerance of this approach. Where there are groups are of similar size moderate *E/Z* selectivity is obtained (**155d-f**), when there is a large difference in the size of the propargylic substituents more impressive selectivity is observed (**155g**). Interestingly the use of p-methoxyphenyl boronic acid **112** rather than methanol as the reaction additive was found to give higher yields and higher *E:Z* selectivity in many cases, though longer reaction times were necessary (**155d-g**). [116]

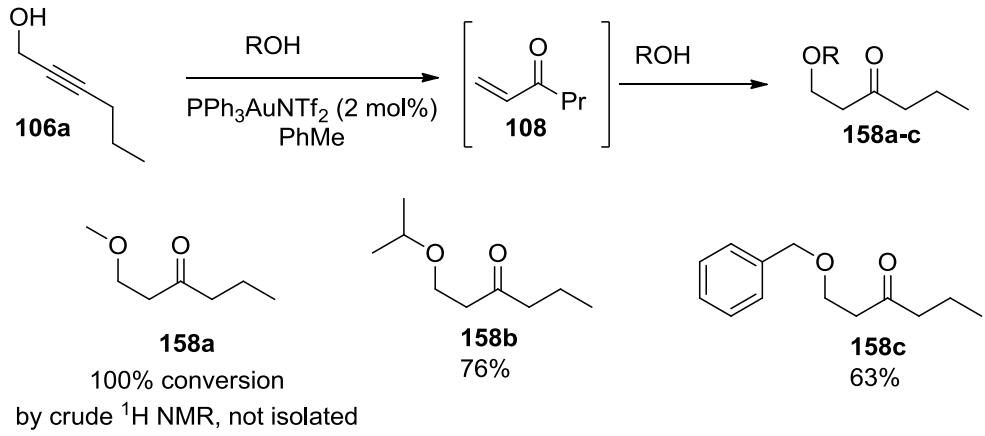
If we took the 3:1 ratio of enone **155g** obtained from Au/methanol catalysed rearrangement and introduced boronic acid **112** to the reaction. This led to further isomerisation of the product to give an enhanced *E:Z* ratio (Scheme 90). Extending the reaction time with methanol as the additive did not increase the *E:Z* selectivity. This indicates that the boronic acid is involved in the isomerisation of the alkene, possibly *via* an addition process to give cyclic boronate **157**.



Scheme 90: Possible boronic acid isomerisation of the alkene

2.6. Primary propargylic alcohols: One-pot Meyer-Schuster rearrangement and additions

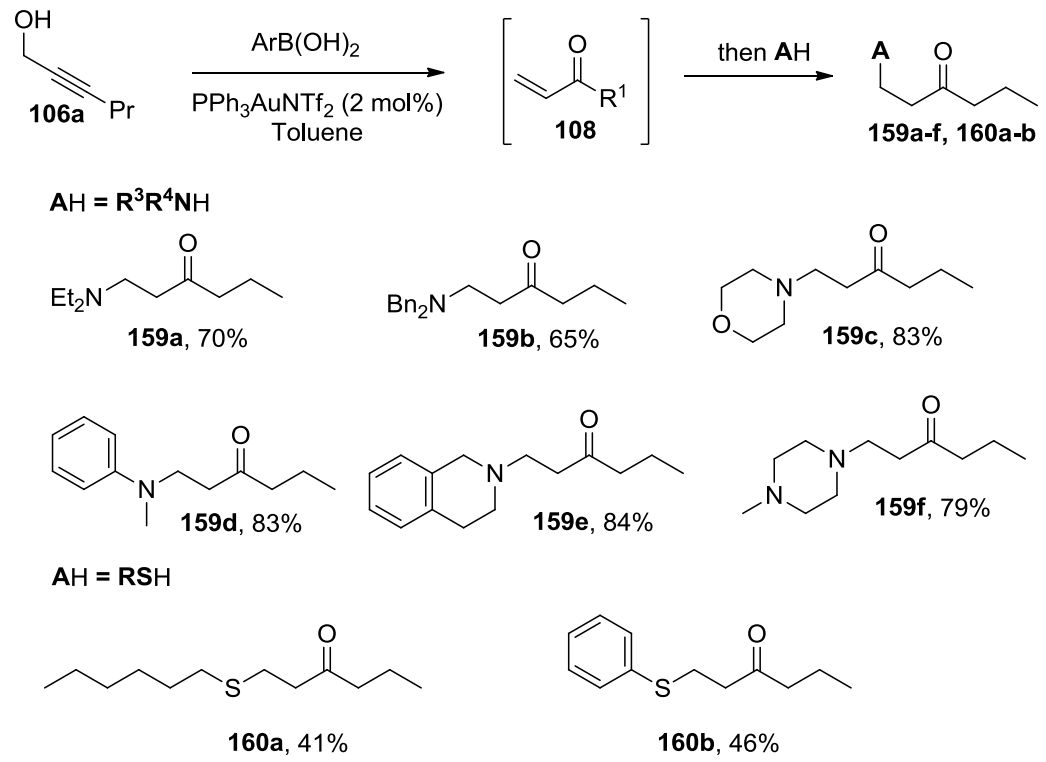
When primary propargylic alcohols were submitted to our Meyer-Schuster rearrangement conditions the methanol additive reacted with terminal enone **108** to give 1,4 addition resulting in β-methoxyketone **158a** (scheme 91).



Scheme 91: One-pot formation of β-alkoxyketones

This reactivity can be exploited with other alcohols such benzyl alcohol (**158c**) and isopropanol (**158b**) to give a small range of β-alkoxyketones (**158**) in a concerted one-pot procedure. The use of alcohol additive limits the reaction with terminal enones, however boronic acid **112** allowed clean formation of the terminal enone (Scheme 68) without further reaction. This terminal enone could then be reacted with a wider range of nucleophiles (scheme 92). We therefore

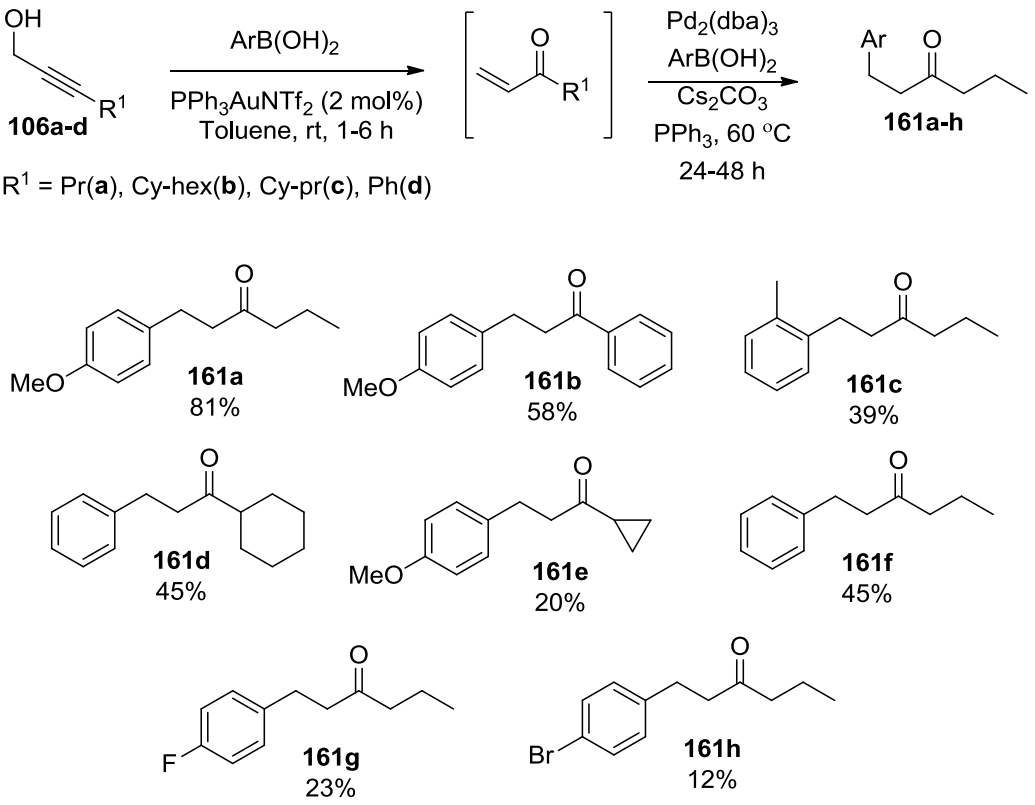
developed reaction conditions for the synthesis of a range of functionalised products by addition of different nucleophiles to the crude enone, generated in-situ from the propargylic alcohol (scheme 92).



Scheme 92: One-pot synthesis of β-aminoketones and β-sulfidoketones

The boronic acid reaction additive in the Meyer-Schuster rearrangement provides a mild method for generating highly reactive terminal enones, which can be reacted *in-situ* allowing access to β-aminoketones **159** and β-sulfidoketones **160**. [3] For amine examples a range of different alkyl and aromatic substituents are incorporated in good to excellent yield, the major limitation is that only secondary amines could be utilised. Primary amines were unsuccessful under the reaction conditions, leading to complex mixtures, and tertiary amines are obviously incompatible. The yields were much lower for the thiols, probably due to sulfide formation, and in all cases the nucleophile has to be added after the Au step to avoid deactivating the Au catalyst. [119]

β-Aryl ketones **161** could be accessed in a one-pot dual metal catalysis procedure. After Au catalysed Meyer-Schuster rearrangement, palladium-catalysed addition of boronic acids [137] could be used to access β-aryl ketones **161** in poor to good yield (scheme 93). [2]



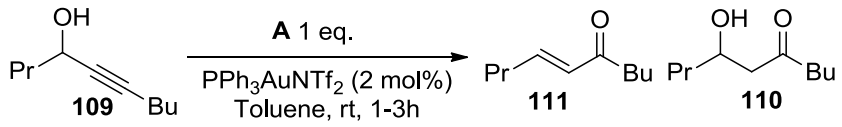
Scheme 93: One-pot synthesis of β-arylketones

It is worth noting that the same boronic acid is used throughout the reaction sequence. Overall the reaction produced poor to good yields. The electron rich boronic acid **112** gave the highest yield, with the reaction being adversely affected by steric congestion (**161c**) or less electron rich boronic acids (**161g-h**).

2.7. Influence of the reaction additive: Hydration of propargylic alcohols

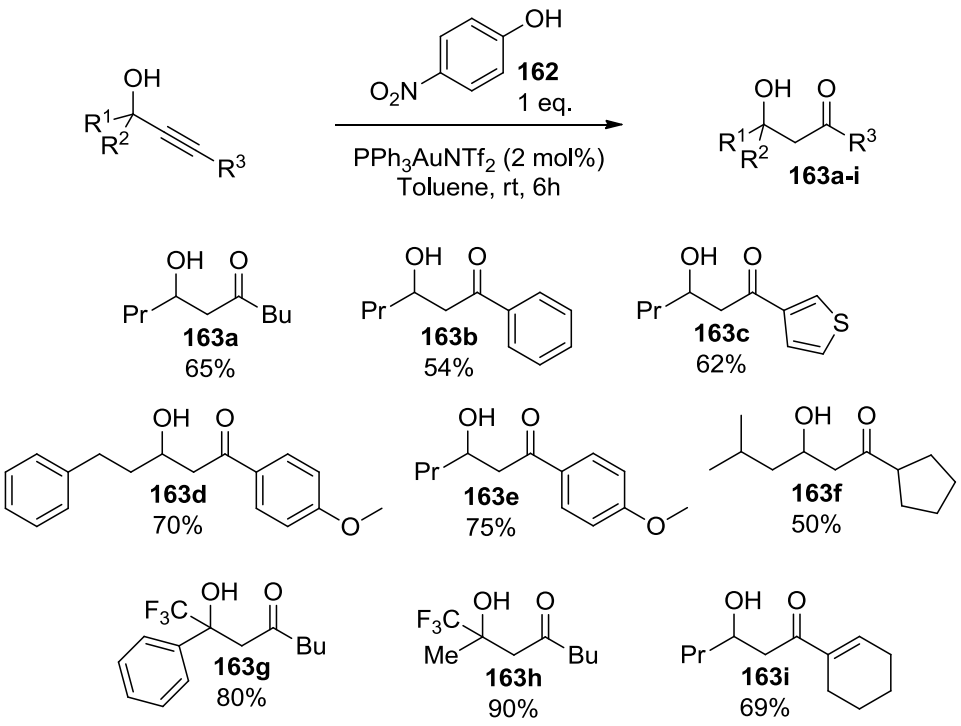
During the Meyer-Schuster rearrangement screen (table 3), varying amounts of the β-hydroxyketone **110** side product were noted. In the presence of methanol the β-hydroxyketone **110** was not observed, yet in the presence of the more acidic boronic acid additives **107** and **112** the β-hydroxyketone 110 was observed. This led us to consider the influence of the acidity of the additive (Methanol, aryl boronic acid, etc) on the reaction pathway, and we carried out a study of the rearrangement of propargylic alcohol **109** in the presence of a variety of additives of differing acidity (Table 3).

Table 3: Reaction additive screen determined by crude ^{1}H NMR ratios



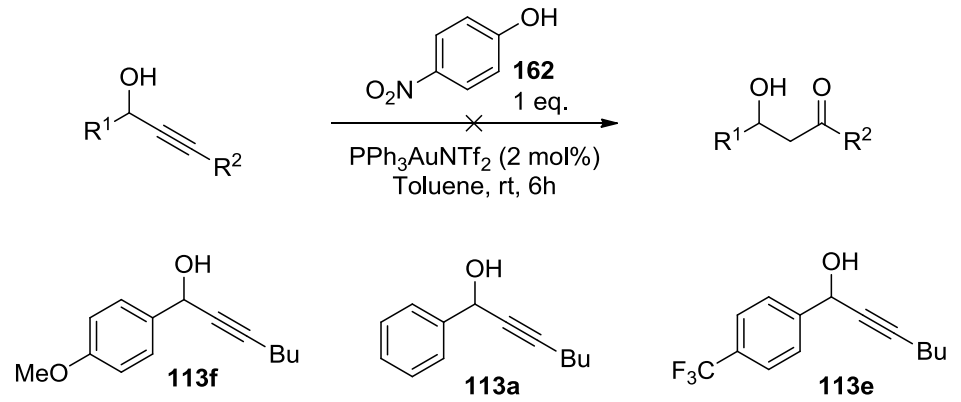
Entry	A	pk_a	110:111
1	MeOH	15.7	0:1
2	TFE	12.5	1:1
3	Phenol	9.95	3:2
4	Boric acid	9.23	3:2
5	Para-nitro phenol (**162**)	7.10	3:1
6	Pentafluorophenol	5.50	1:1
7	Pentachlorophenol	4.74	1:1
8	Acetic acid	4.76	2:3
9	TFA	0.25	1:3

Increasing the acidity of the alcohol additive led to an increase in the proportion of the β-hydroxyketone **110** formed up to a maximum of pK_a ~7, with 4-nitrophenol as the additive (entries 1-5). Interestingly increasing the acidity of the alcohol further by using pentaflurophenol or pentachlorophenol (entries 6 and 7), reduced the proportion of β-hydroxyketone formed. Increasing the acidity still further led to increasing quantities of enone **111** (entries 8 and 9). This seems to demonstrate the existence of an 'acidity window' where the formation of the β-hydroxyketone **110** is favoured over the enone **111**. We therefore examined the synthetic potential of the 4-nitrophenol reaction additive by applying these conditions to a number of different secondary propargylic alcohols (Scheme 94).



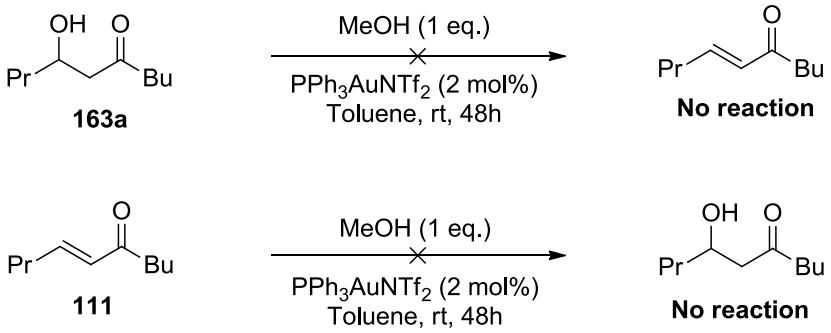
Scheme 94: β-Hydroxyketone synthesis

Pleasingly we were able to demonstrate the formation of a range of β-hydroxyketones in moderate to excellent yield, with the electron rich propargylic alcohol **163e** produced the best yield. Alkyl examples, including alkene functionality, are also tolerated (**113a**, **113f** and **113i**). With benzylic alcohols (**113a**, **113e-f**), no β-hydroxyketone product was observed by crude ^{1}H NMR (scheme 95). This may be due to the fact that there is a greater driving force for the formation of the enone with these substrates, driven by the R^1 group stabilising the carbo-cation formed during alcohol elimination.



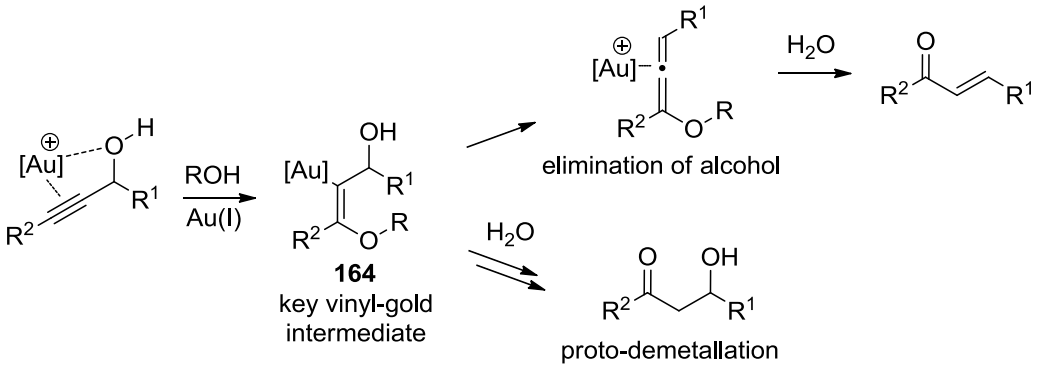
Scheme 95: Unsuccessful hydration substrates

Generally, when methanol is the reaction additive, most propargylic alcohols proceed smoothly to the corresponding enone. We have shown that through the addition of 4-nitrophenol (**162**), as a reaction additive, you can access β-hydroxyketones as well as enone products. The β-hydroxyketone **163a** is not converted into the enone **111** or vice versa under the standard methanol Meyer-Schuster rearrangement conditions (scheme 96).



Scheme 96: Resubmitting to Meyer-Schuster rearrangement conditions

This would suggest a divergent reaction pathway that could possibly occur through a common vinylgold intermediate **164** (scheme 97).

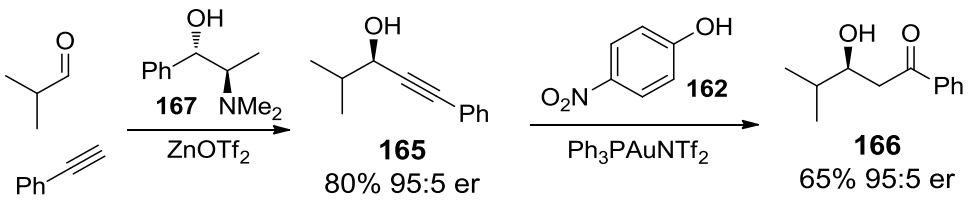


Scheme 97: Possible divergent reaction mechanism

The β-hydroxyketone pathway could be due to an increased rate of proto-demetallation of the key vinylgold intermediate **164** facilitated by the more acidic additive. A recent study into the rates of proto-demetallation with various alcohols concurs with our findings that with methanol proto-demetallation of an sp^2 Au-C bond is negligible, but when a more acidic additive is used the proto-demetallation becomes more evident. [125] From our investigations it appears to be the case that the acidity of the reaction additive can play a key role in the reaction

pathway taken and hence play a key role in the outcome of the reaction. Increasing the acidity of the additive opens up the proto-demetallation pathway, which can then compete with the enone pathway. When the additive is too acidic elimination of the alcohol is most likely promoted *via* an $E1_{cb}$ mechanism.

Enantiomerically enriched β-hydroxyketones (**165**) can also be accessed in two steps by utilising Carriera and co-workers procedure for synthesising enantiomerically enriched propargylic alcohols, followed by the above hydration reaction (Scheme 98). [138] This mild and convenient two-step process for access to enantiomerically enriched β-hydroxyketones could provide a useful alternative to aldol procedures, particularly when the molecule contains other enolisable centres. The ability to completely retain the enantiomerically enriched centre could offer a powerful route towards β-hydroxyketones.



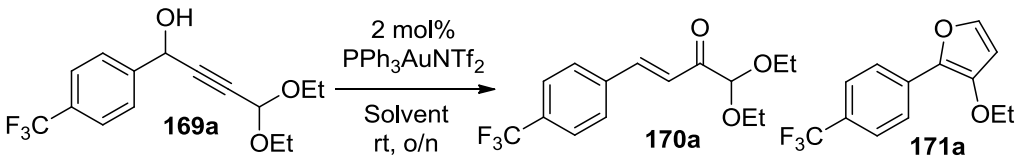
Scheme 97: Synthesis of enantiomerically enriched β-hydroxyketones

2.8. Synthesis and reactions of 3-alkoxyfurans

3-Alkoxyfurans such as the simple 3-methoxyfuran are highly electron rich systems that show useful reactivity. [140,141] However, largely as a consequence of their synthetic inaccessibility the chemistry of more complex 3-alkoxyfurans has not been widely explored. 3-Methoxyfurans have found application in natural product synthesis,[142,143,144,145] as well as in the construction of polysubstituted tetrahydrofurans. [146] Existing procedures for 3-methoxyfuran synthesis and related derivatives involve multistep reaction sequences which proceed in only moderate overall yield. [147,148,149]

During the course of studying the scope of the Meyer-Schuster rearrangement, attempted rearrangement of acetal-containing propargylic alcohol **169a** gave a mixture of the expected enone **170a** and the 3-ethoxyfuran **171a** (Table 4). [150] Given the importance of polysubstituted furans and the lack of reliable and viable synthetic routes for the synthesis of alkoxyfurans we sought to optimise this transformation to provide furan **171a** selectively.

Table 4: Optimisation of furan synthesis



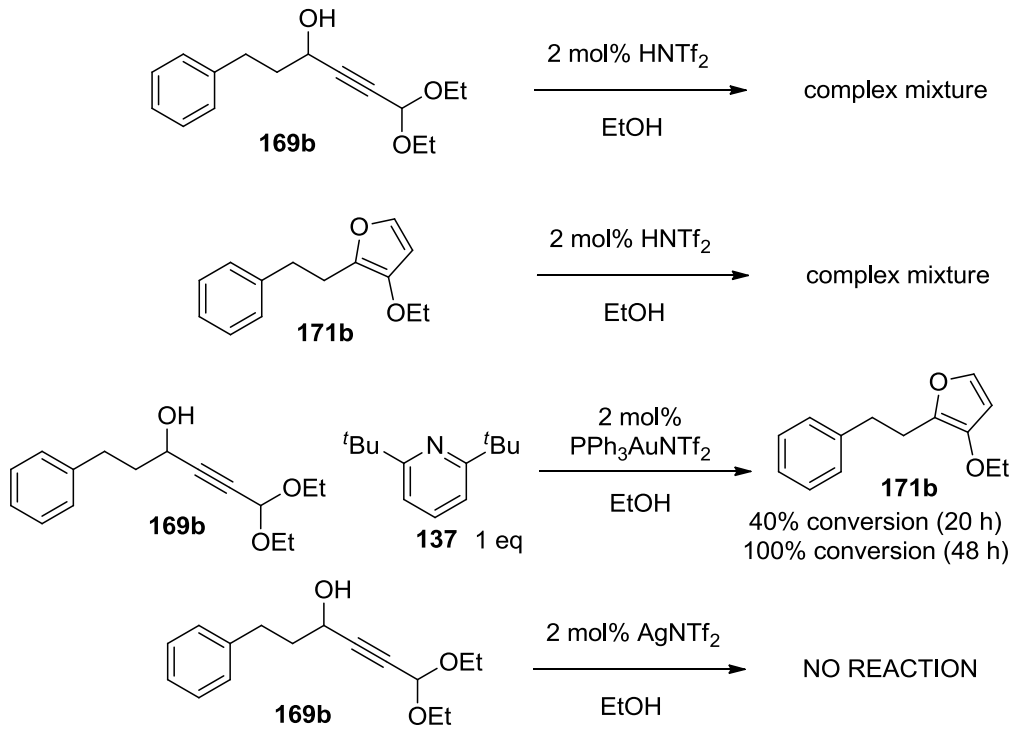
Entry	Solvent[a]	Yield of 170a[b]	Yield of 171a[b]
1	PhMe:EtOH	35%	65%
2	Petrol:EtOH	12%	18%
3	CH_2Cl_2:EtOH	35%	47%
4	THF:EtOH	18%	71%
5	Et_2O:EtOH	24%	65%
6	1,4-Dioxane:EtOH	35%	65%
7	EtOAc:EtOH	24%	53%
8	MeCN:EtOH	18%	35%
9	EtOH only	<5%	94% (89%[c])
10	CH_2Cl_2 only	45% (40%[c])	55%

[a]5:1 ratio solvent:EtOH unless otherwise stated. [b] Yield calculated using C_6Cl_5H as an internal standard. [c] Isolated yield.

In a wide range of solvents containing ethanol (5:1 ratio), mixtures of the two products **170a** and **171a** were obtained (Table 1, entries 1-8), with toluene and ethereal solvents offering the highest selectivity in favour of 3-ethoxyfuran **171a**. However, on switching the solvent to neat ethanol, the furan **171a** was formed in high yield, with complete selectivity over the enone **170a** (entry 9). We were also able to isolate highly functionalised enone **170a** in 40% isolated yield by performing the reaction in CH_2Cl_2 as solvent, in the absence of added ethanol (entry 10). It is likely that ethanol released from the acetal can react with the

propargylic alcohol **169a** to give access to furan **171a**, which is why the yield is low for the enone.

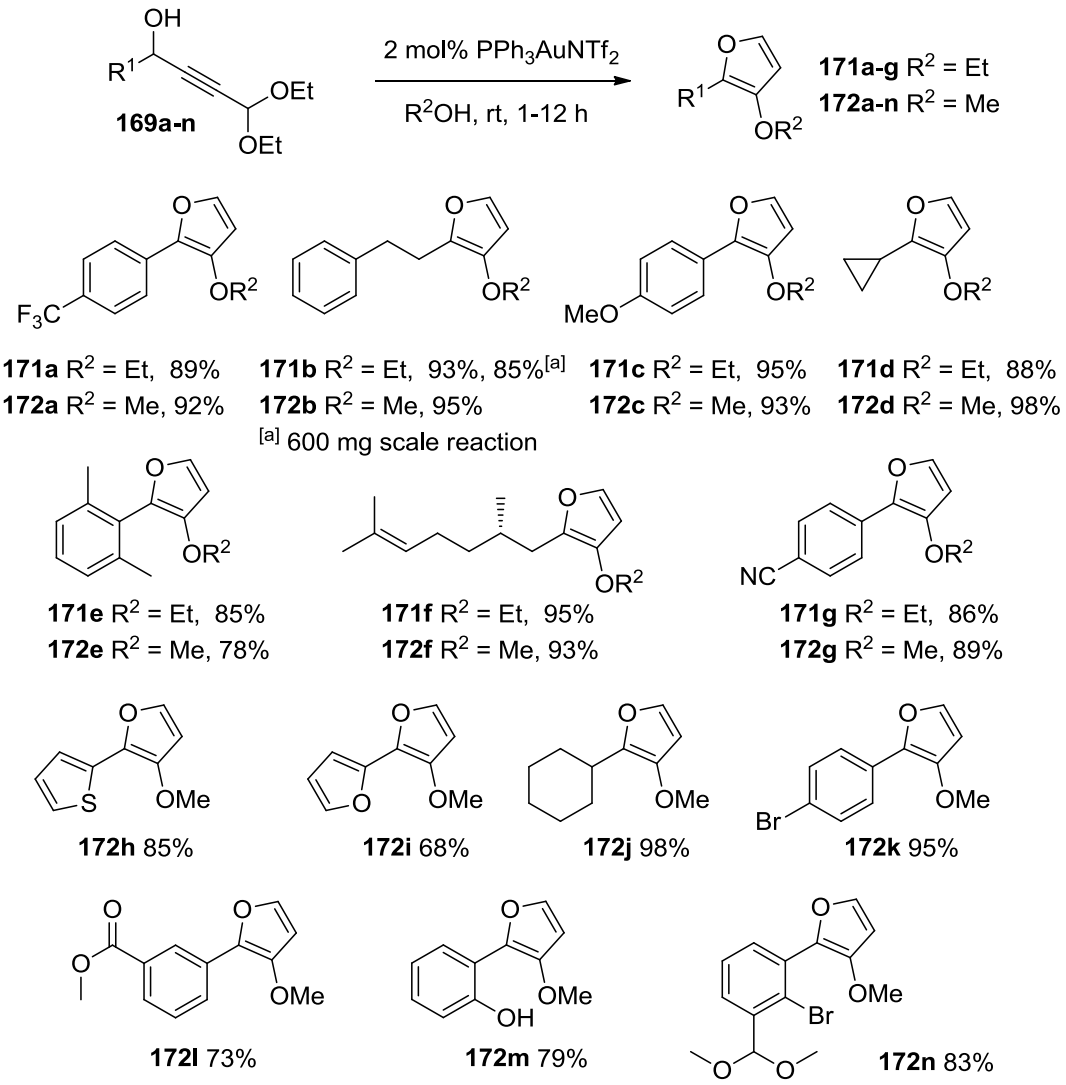
Control experiments were performed to confirm that the Au catalyst was involved in the furan formation reaction (Scheme 99). Reaction of alcohol **169b** with Au catalyst and ethanol in the presence of 10 mol% Tf_2NH, the most likely acidic source in our reaction scheme, gave a complex mixture with no discernible furan product. Furan **171b** was also stirred in 10 mol% of triflimide, which resulted in rapid degradation of the furan to a complex mixture. In the presence of one equivalent of the hindered base 2,6-di-*tert*-butylpyridine the reaction still proceeded to formation of furan **171b**, although it required a longer reaction time to achieve full conversion.[151] This suggests that the furan formation is not a simple acid catalysed process. [32,18,134,152] Treatment of **169b** with 2 mol% $AgNTf_2$ in ethanol did not lead to furan formation, demonstrating that this reaction is not likely to be catalysed by Ag impurities in the Au catalyst. [3,136,20].



Scheme 99: Control experiments

With these optimised conditions in hand, we then went on to explore the synthesis of a wide range of 3-ethoxyfurans and 3-methoxyfurans (Scheme 100). High yields of the furan were obtained with a selection of propargylic alcohols **169a-n**

using only 2 mol% Au catalyst at room temperature in the presence of either methanol or ethanol, which were incorporated into the furan at the 3-position (Scheme 100).

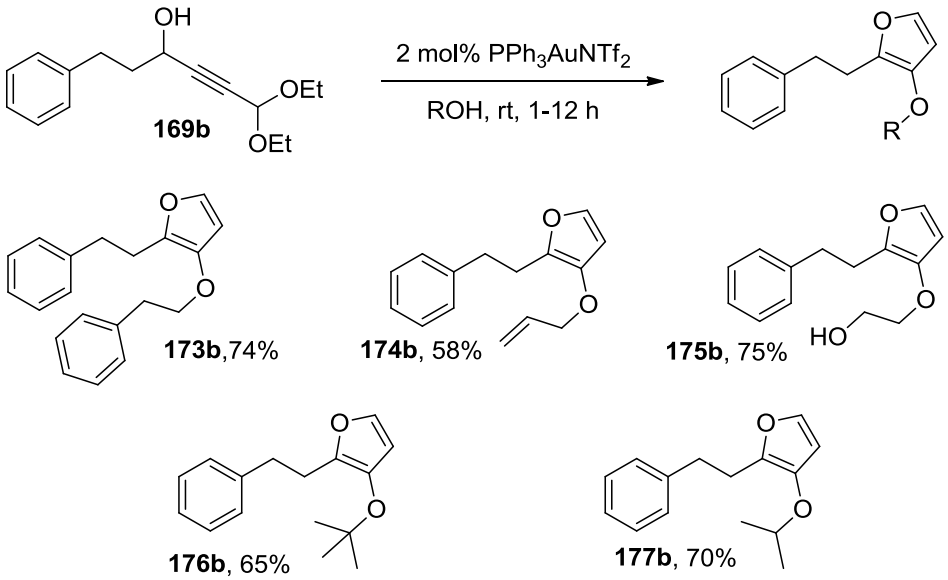


Scheme 100: Au-catalysed synthesis of 3-ethoxyfurans and 3-methoxyfurans

The reaction responded well to scaling for the synthesis of furan **171b**, which was performed on a 600 mg scale, with only a small drop in yield (85% vs 93% on a 100 mg scale). However, the corresponding scale up reaction with methanol resulted in a drop off in yield (63% vs 97% on a 100 mg scale). This could be due to competition with ethanol released from the diethyl acetal unit, which provides a competing nucleophile. At the 2-position of the furan ring a wide range of aromatic groups could be incorporated, comprising electron deficient (**171a, 171g, 171l**), electron rich (**169c, 169m**) and sterically encumbered (**169e**)

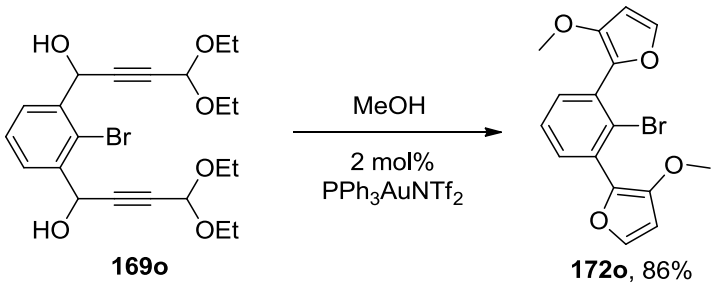
benzene rings as well as thiophene (**169h**) and furan (**169i**) rings. Reactions with aliphatic groups at the 2-position of the furan ring also proceeded efficiently (**169b, 169f, 169j**), including systems with a cyclopropane (**169d**) directly attached to the alkyne. Many functional groups including halides (**169k**), an ester (**169l**), a nitrile (**169g**) and an alkene (**169f**) were compatible with the reaction with either methanol or ethanol. A free phenol (**169m**) is also tolerated and this is particularly significant as the reaction is chemoselective for furan formation over cyclisation of the phenol onto the nearby alkyne. [153,154] In the case of aldehyde containing substrate **169n**, parallel formation of the corresponding dimethylacetal was observed during the formation of the 3-methoxyfuran **172n**.

After the exploration of methanol and ethanol the next step was to investigate the incorporation of other alcohols in the furan formation reaction to synthesise more complex 3-alkoxyfurans (Scheme 101). Primary (**173b, 174b, 175b**), secondary (**177b**) and tertiary (**176b**) alcohols were incorporated efficiently in good yields. Examples included more functionalised alcohols such as allyl alcohol (**174b**) and ethylene glycol (**175b**), creating options for further reaction steps.



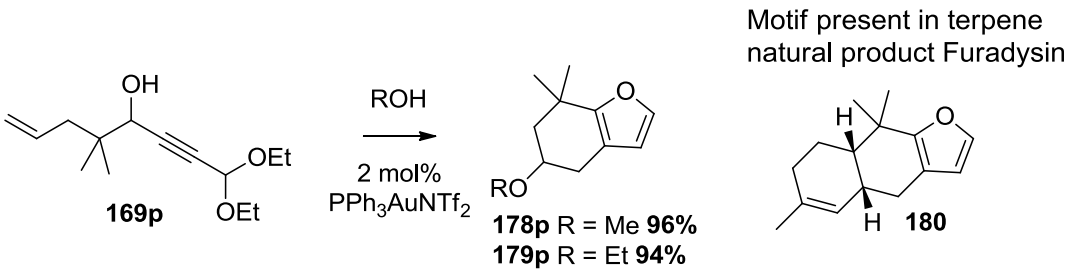
Scheme 101: Synthesis of various 3-alkoxyfurans from propargylic alcohol **169b**

We were also able to demonstrate a double cyclisation within the same molecule to construct a conjugated bis-(3-alkoxy-2-furyl)benzene **172o** in excellent yield, proceeding *via* the Au-catalysed reaction of bis-propargylic alcohol **169o** with methanol (Scheme 102).



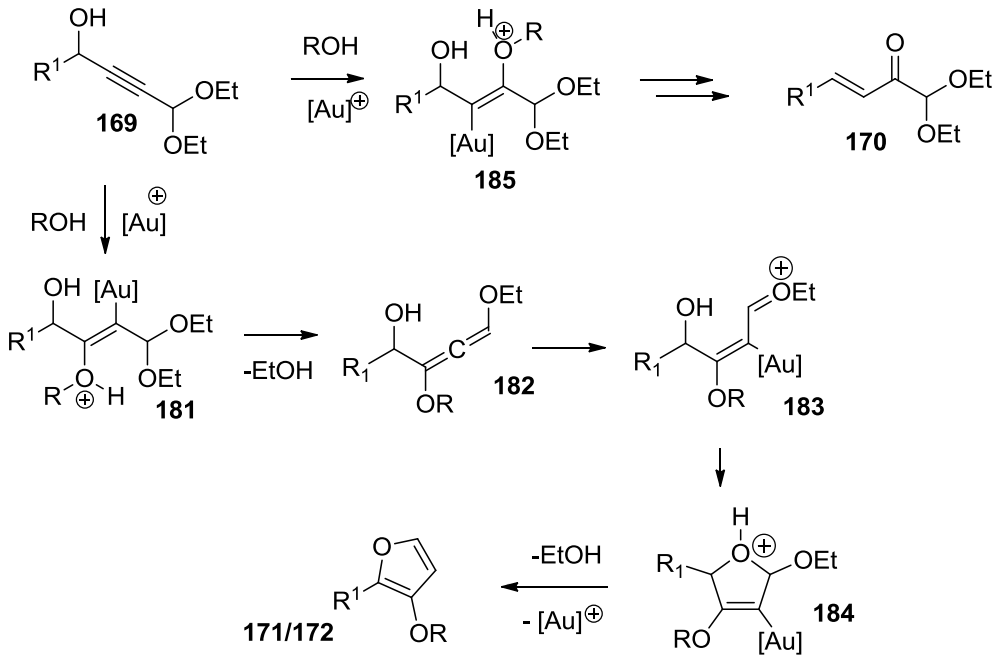
Scheme 102: Double furan synthesis

Interestingly we were able to demonstrate the rapid assembly of the fused furan-cyclohexane motif present in the terpene natural product furadysin (scheme 103). [155] Propargylic alcohol **169p** containing a nearby alkene unit underwent tandem ene-yne cyclisation [156,157] and furan formation to give fused cyclohexylfurans **178p** and **179p** in excellent yield with incorporation of either methanol or ethanol on the cyclohexane ring (Scheme 103).



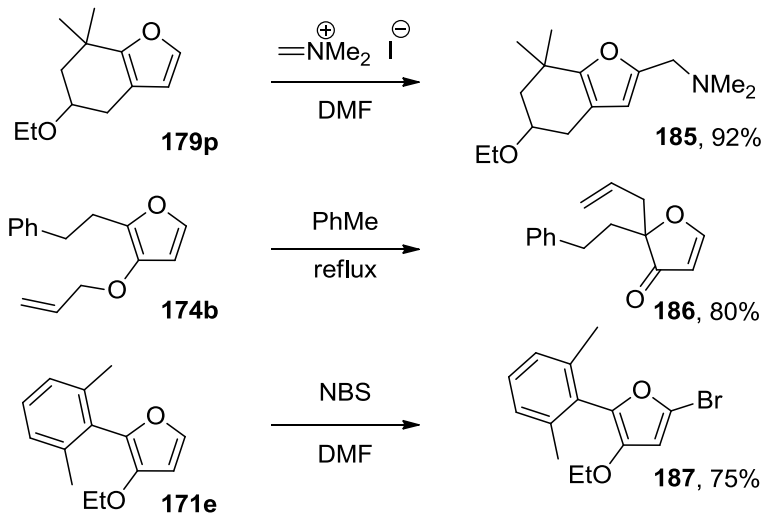
Scheme 103: Tandem ene-yne cyclisation/furan synthesis.

The mechanism of the furan formation reaction could presumably proceed *via* regioselective Au-catalysed addition of the alcohol to the alkyne in the propargylic alcohol to generate vinyl Au intermediate **181** (Scheme 104). Loss of ethanol gives allenyl ether **182** that can undergo further activation by Au to give oxonium ion **183**. Attack of the nearby intramolecular alcohol on oxonium ion **183** could generate dihydrofuran intermediate **184**. Protodeauration and loss of ethanol would then give access to furan **171/172**. The competing Meyer-Schuster rearrangement observed in other solvents presumably occurs *via* Au-catalysed addition of ethanol (or water or a second molecule of 1) to give the vinyl Au species **185**. It is not clear at this stage why the regioselectivity of addition is altered so significantly by changing the reaction solvent.



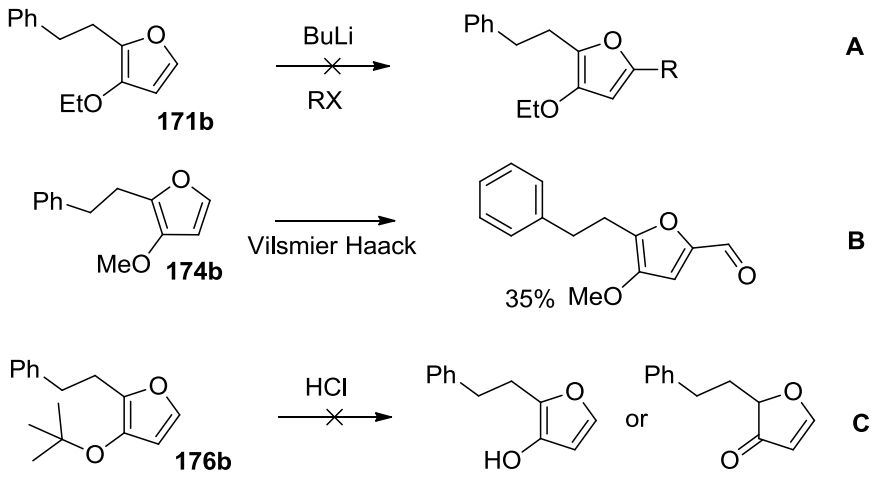
Scheme 104: Possible mechanism for the Au-catalysed furan synthesis.

The reactivity of these potentially highly reactive 3-alkoxyfurans has not been widely explored, as electron rich aromatics they proved amenable to a number of potentially useful transformations (Scheme 105). The first transformation involved cyclohexyl fused furan **179p**, which exhibited substitution with Eschenmoser's salt to give the tertiary amine **185** in excellent yield. [158] Claisen rearrangement of allyloxyfuran **174b** to generate disubstituted 3-furanone **186** was facilitated by heating at reflux in toluene. **159** Also electrophilic bromination of furan **171e** proceeded in high yield to give access to the bromide **187**. [160]



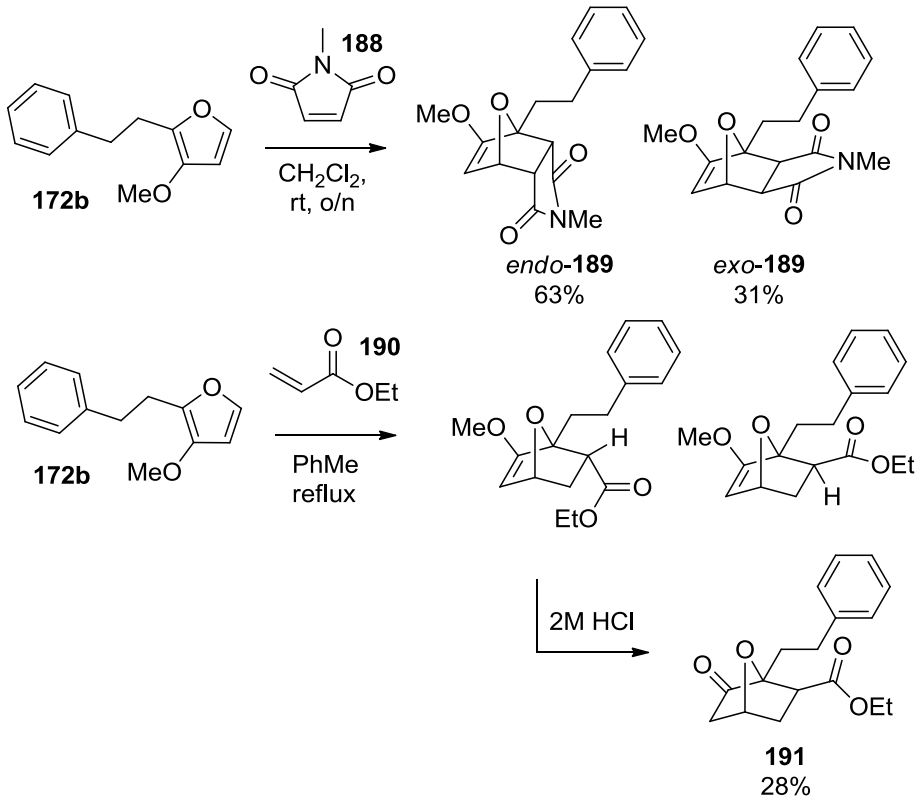
Scheme 105: Reactions of the furan products

An attempted deprotonation of C5 and alkylation with ^{n}BuLi did not proceed as anticipated, although the starting material was recovered (scheme 106, A). The Vilsmeir-Haack gave a low yield of 15%, but this remains un-optimised and may be due to the quality of reagents used (Scheme 106, B). Acid removal of tertiary butyl substituent did not proceed as desired, with the acid leading to a complex mixture. Owing to the stability towards acid, it was not possible to deprotect **176b** using HCl (Scheme 106, C).



Scheme 106: Selected attempted reactions of the furan products

Furan **172b** smoothly underwent a Diels-Alder reaction at room temperature with *N*-methylmaleimide (**188**) to generate the cycloadduct **189** as a 2:1 mixture of separable stereoisomers in excellent overall yield (Scheme 107). Furan **172b** also underwent a Diels-Alder reaction with ethyl acrylate (**190**). The dienophile is less reactive hence the reaction required heating to reflux in toluene. The crude mixture was then treated with acid in an attempt to ring open the oxygen bridge, with the aim of forming a substituted aromatic. However, the major product was ketone **191**, a product of hydrolysis of the enol ether.

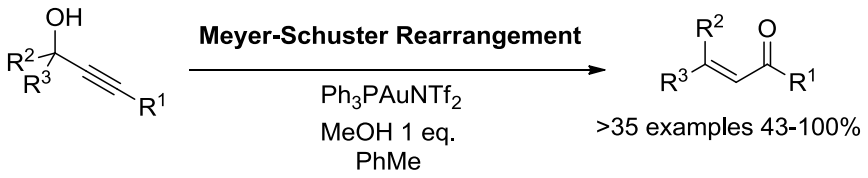


Scheme 107: Diels-Alder reactions

A wide variety of 3-alkoxyfurans can be synthesised utilising a mild Au-catalysed method in good to excellent yields. These useful molecules can be accessed in just two steps from readily available aldehydes, alkynes and alcohols. The 3-alkoxyfuran products can then be used to access more complex structures through a range of subsequent transformations.

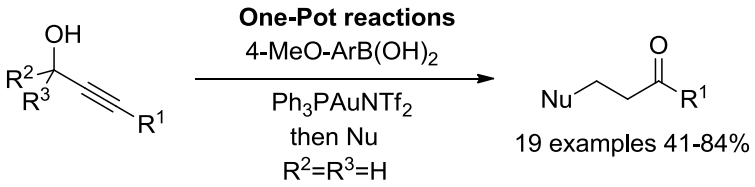
3. Conclusions

Propargylic alcohols can allow access to a diverse range of products and have been at the core of all the transformations we have developed.For the synthesis of enones we have been able to demonstrate the efficiency of Au-based catalysts, utilising the commercially available PPh_3AuNTf_2 for the Meyer–Schuster rearrangement of internal propargylic alcohols without an activating ethoxy group on the alkyne unit and at room temperature. [2,3] Secondary and tertiary propargylic alcohols were converted into the corresponding enones in up to 99% yields with moderate to high *E/Z* selectivity for over 35 examples (Scheme 108).



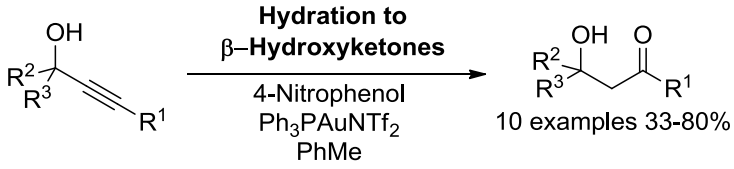
Scheme 108: Meyer-Schuster Rearrangement

Primary propargylic alcohols were utilised in one-pot procedures to take advantage of the highly reactive terminal enones accessed from the Meyer-Schuster rearrangement (Scheme 109).



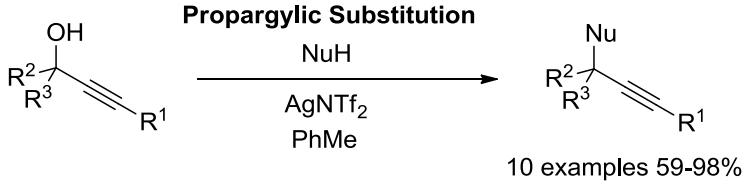
Scheme 109: One pot reactions of primary propargylic alcohols

The investigation of different reaction additives unearthed the hydration of propargylic alcohols to β-hydroxyketones, showing the key role a reaction additive can play (Scheme 110). Although the reaction has been capricious with respect to the transformation, it yielded some interesting examples and could still prove a potentially useful route to enantiomerically enriched β-hydroxyketones, particularly in the presence of other enolisable centres.



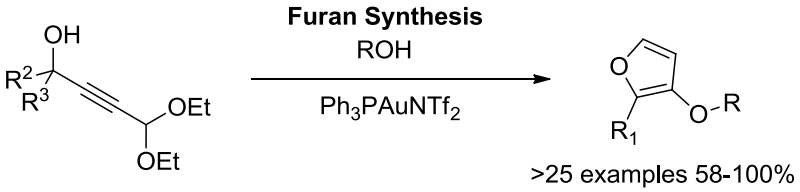
Scheme 110: Hydration of propargylic alcohols to β-hydroxyketones

During the course of investigating the scope of the Meyer-Schuster rearrangement a silver-catalysed propargylic alcohol substitution with various nucleophiles was developed. We have demonstrated over 10 examples of C-C, C-O and C-N bond formation in good to excellent yields, and provided evidence that the mechanism of the reaction proceeds through a carbocation intermediate.



Scheme 111: Ag catalysed substitution of propargylic alcohols

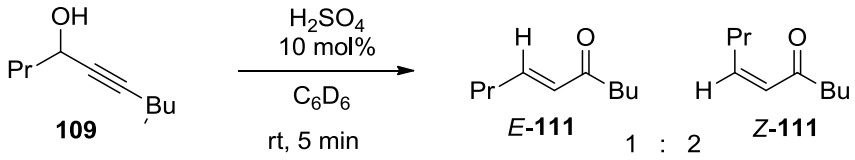
More recently we have developed an efficient route to synthetically useful 3-alkoxyfurans with >30 examples. Currently there are very few 3-alkoxyfuran synthesis procedures in the literature, and the existing methods require many steps to access the target. Whereas, our simple two step procedure has allowed a diverse set of products to be synthesised. Subsequently we have explored their inherent reactivity, with a number of transformations leading to a diverse range of interesting products.



Scheme 112: 3-Alkoxyfuran synthesis

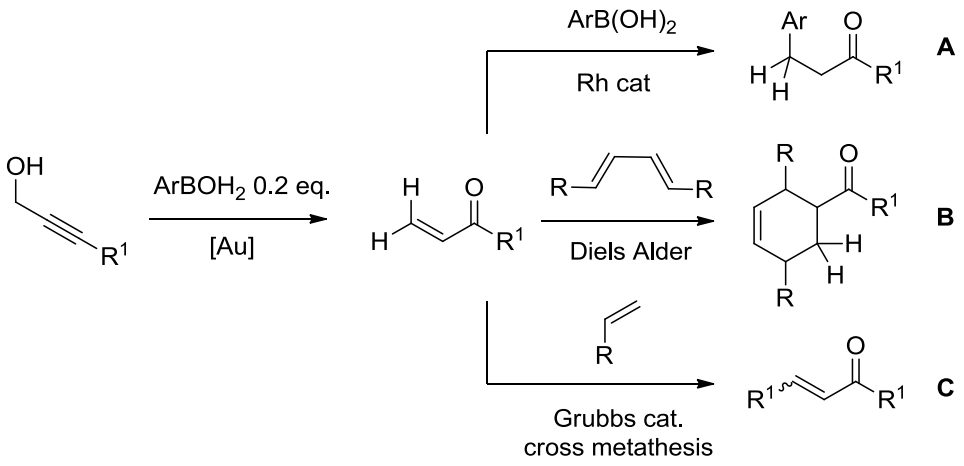
4. Future Work

The Meyer-Schuster rearrangement under our Au reaction conditions gave the *E*-enone preferentially over the *Z*-enone in nearly all cases. Interestingly, small quantities of H_2SO_4 appeared to favour rapid preferential formation of the Z-enone over the *E*-enone (Scheme 113). Other acids including HCl, acetic acid and H_3PO_4 gave no reaction. Methane sulphonic acid also gave the Z-enone but in a slower conversion than H_2SO_4. Access to both geometries would be desirable and could possibly be achieved with small quantities of acid.



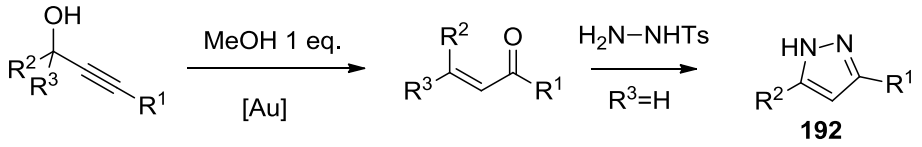
Scheme 113: Preferential formation of the Z-enone

Beyond the Meyer-Schuster rearrangement the methodology could be expanded to utilise the enone in a range of transformations. For primary propargylic alcohols the enones formed are highly reactive at the β-position, hence additional reactions are a logical next step. The terminal enones (**108**) are excellent Michael acceptors and should be able to react with a variety of nucleophiles (Scheme 114, A). Other possibilities could include Diels Alder cyclisation (scheme 114, B), [161] cross metathesis with various alkenes (scheme 114, C), [162] or improvement on the palladium catalysed 1,4-addition to give β-arylketones. 1,4-Additions have been shown to work more efficiently with a rhodium-catalyst in the literature, [163] and also with a platinum catalyst. [164]



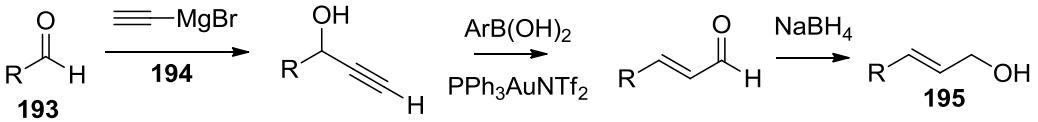
Scheme 114: Possible advancements involving one-pot procedures

Secondary Propargylic alcohols give access to more stable enones but they are themselves useful synthetic intermediates and could be utilised as reactive intermediates, such as in the synthesis of substituted pyrazoles **192** (scheme 115).[165]



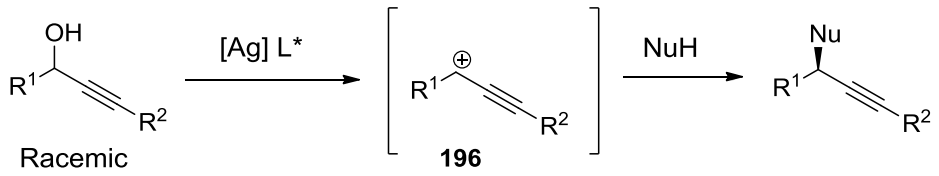
Scheme 115: Proposed Meyer-Schuster rearrangement and subsequent enone cyclisation

Propargylic alcohols with a terminal alkyne potentially generate an aldehyde as the product of a Meyer-Schuster rearrangement. Reduction of the aldehydes (**193**) can provide a quick and easy route to synthetically useful allylic alcohols **195** (scheme 116). In conjunction with the coupling of ethynyl magnesium bromide (**194**) and various aldehydes this may provide a viable alternative to existing literature procedures for generating allylic alcohols, although initial attempts were unsuccessful.



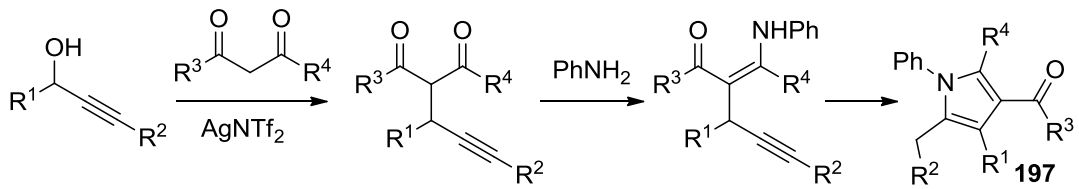
Scheme 116: Propargylic alcohol route to allylic alcohols

The Ag catalysed propargylic substitution chemistry is very likely to proceed through a carbocation intermediate **196**, which provides the opportunity to influence the enantiomeric ratio of the substituted product through the use of a chiral ligand (Scheme 117).



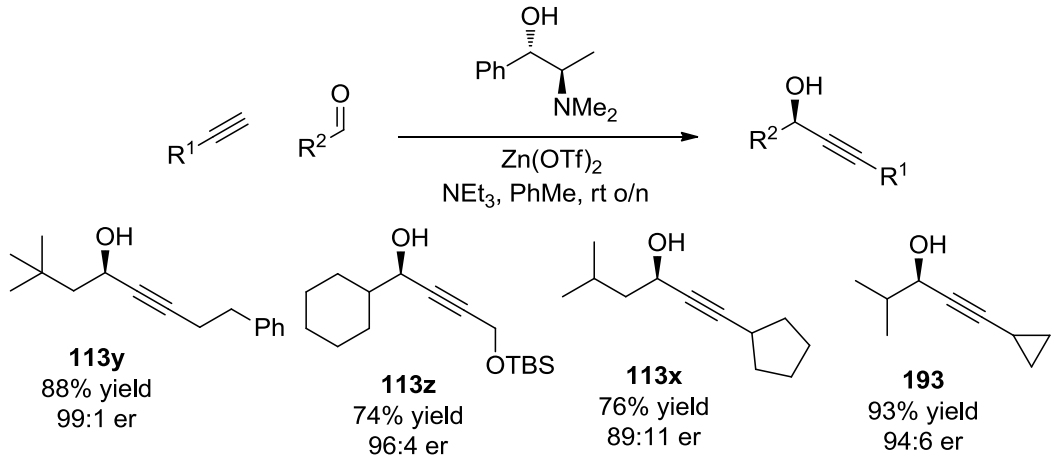
Scheme 117: Enantioselective propargylic alcohol substitution

The products of this reaction are also suitable for further functionalisation and could be applied to heterocycle synthesis, such as pyrrole (**197**) syntheses (scheme 118). [166]



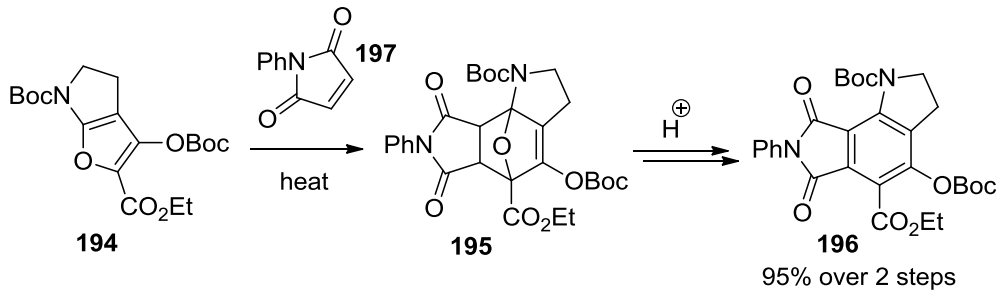
Scheme 118: Pyrrole synthesis through Ag-catalysed substitution

The conversion of propargylic alcohols to β-hydroxyketones requires further investigation and a wider selection of enantioenriched alcohols have been synthesised. The generation of enantiomerically enriched β-hydroxyketones have been demonstrated and **113x** proceeded smoothly under racemic conditions and could provide further enantiomerically enriched examples (Scheme 119).



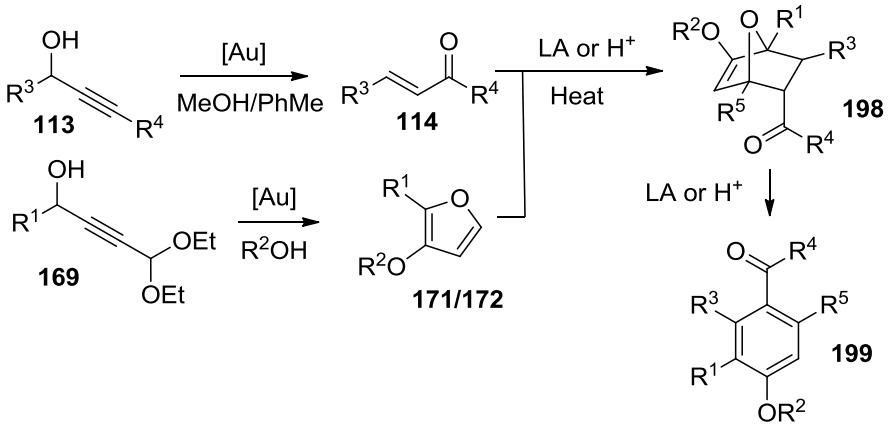
Scheme 119: Enantiomerically enriched propargylic alcohols

Having demonstrated the 3-alkoxyfuran synthesis on a reasonably wide selection of substrates the next step could involve the further exploration of the reactivity of these potentially powerful synthetic intermediates. The 3-alkoxyfurans are quite reactive in Diels-Alder reactions, even without a catalyst, and there is literature precedent for elimination of the oxygen-bridge from the adducts. *N*-Phenyl maleimide (**197**) has also been used as a dienophile (scheme 120). Treatment with furan **194** resulted in formation of adduct **195**, which could be readily aromatised in the presence of acid to **196**. [167]



Scheme 120: Diels Alder with *N*-phenyl maleimide and ring opening [167]

The Diels-Alder reaction of furan **171**/**172** could be employed with dienophile **114**, utilising the Meyer-Schuster rearrangement and the furan formation. The resultant product **198** could then be ring opened to provide the highly substituted aromatic **199**. This could allow us to very quickly build up a library of compounds based on two key reactions we have developed providing both the diene and dienophile for the Diels Alder reaction (Scheme 121).



Scheme 121: Synthesis of substituted aromatics

5. Experimental

Tetrahydrofuran was used following purification from a zeolite drying apparatus. All other chemicals were used as supplied unless otherwise indicated. Column chromatography was carried out using silica gel (40-60 μm) and analytical thin layer chromatography was carried out using aluminium-backed plates coated with silica gel. Components were visualised using combinations of ultra-violet lights, iodine, ceric ammonium molybdate, phosphomolybdic acid and potassium permanganate. ^{1}H NMR spectra were recorded at at 400, 500 MHz or at 600 MHz on a spectrometer in $CDCl_3$ using residual protic solvent $CHCl_3$ (δ = 7.26 ppm, s) as the internal standard. Chemical shifts are quoted in ppm using the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; qn, quintet; sx, sextet; m, multiplet; br, broad; Ar, aromatic; Cp, cyclopropane or a combination of these. The coupling constants (*J*) are measured in Hertz. ^{13}C NMR spectra were recorded at 100, 125 MHz or at 150 MHz in $CDCl_3$ using the central reference of $CHCl_3$ (δ = 77.0 ppm, t) as the internal standard.

1. General Procedures for the Preparation of Propargylic Alcohols

General Procedure A: *n*-Butyllithium (1.6M in hexanes, 1.2 eq.) was added dropwise to a stirred solution of alkyne (1 eq.) in dry THF (1 $mLmmol^{-1}$) at –78 ˚C under an argon atmosphere. After 30 min aldehyde or ketone (1 eq.) was added and the resulting solution was stirred for 5 min at 0 ˚C and 30 min at rt. The reaction was quenched with aq. $NaHCO_3$ and the organic phase extracted with Et_2O. The combined organic phases were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by flash column chromatography to give the propargylic alcohol.

General Procedure B: Ethylmagnesium bromide (1M in THF, 1 eq.) was added dropwise to a stirred solution of alkyne (1 eq.) in dry THF (1 $mLmmol^{-1}$) at rt under an argon atmosphere. After 30 min the solution was cooled to -78 °C and the aldehyde or ketone (1 eq.) was added dropwise and the reaction stirred for 1 h before the solution was allowed to warm to rt. The reaction was quenched with aq. $NaHCO_3$ and the organic phase extracted with Et_2O. The combined organic phases were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by flash column chromatography to give the propargylic alcohol.

General Procedure C: The reaction flask was charged with $Zn(OTf)_2$ (1.1 eq.) and *N*-methylephedrine (1.2 eq.) and purged with argon for 15 mins, after this time toluene (0.75 $mLmmol^{-1}$) and triethylamine (1.2 eq.) were added and the mixture stirred at room temperature for 2 hrs. The acetylene (1.2 eq.) was then added to the stirred solution and sfter 15 mins the aldehyde (1.2 eq.) was also added to the solution. The reaction was stirred o/n at room temperature. The reaction was quenched with aq. NH_4Cl and the organic phase extracted with Et_2O. The combined organic phases were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by flash column chromatography to give the propargylic alcohol.

General Procedure D: $[Ph_3PAuNTf_2]_2PhMe$ (1-2 mol%) and methanol (1 eq.) or 4-methoxyboronic acid (0.2 eq.) were added to a solution of propargylic alcohol

in toluene (10 mL/g) and the solution stirred magnetically at room temperature until starting material had disappeared (TLC). The solvent was removed *in vacuo* and the crude product purified by column chromatography.

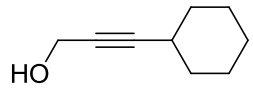
General Procedure E: $[Ph_3PAuNTf_2]_2PhMe$ (1 mol%) and alcohol (2 eq.) or 4-methoxyphenylboronic acid (0.2 eq.) were added to a solution of propargylic alcohol in toluene ($10\ mLg^{-1}$) and the solution stirred magnetically at room temperature until starting material had disappeared (TLC). After this time nucleophile (2 eq.) was added to the solution and it was stirred overnight at room temperature. The solvent was removed *in vacuo* and the crude product purified by column chromatography to give the β-substituted ketone.

General Procedure F: $[Ph_3PAuNTf_2]_2PhMe$ (2 mol%) added to a solution of propargylic alcohol (1 eq.) and 4-Nitrophenol (1eq.) dissolved in toluene (10 mL/g) and the solution stirred magnetically at room temperature until starting material had disappeared (TLC). The reaction was quenched with aq. NH_4Cl and the organic phase extracted with Et_2O. The combined organic phases were washed with brine, dried ($MgSO_4$), concentrated *in vacuo*, and the crude product was purified by column chromatography to give β-hydroxyketone.

General Procedure G: $AgNTf_2$ (1 mol%) and nucleophile (2 eq.) were added to a solution of propargylic alcohol in toluene (10 mL/g) and the solution stirred magnetically at rt until the starting material has disappeared (TLC) or at 60 °C overnight. The reaction was quenched with aq. $NaHCO_3$ and the organic phase extracted with diethyl ether. The combined organic phases were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by flash column chromatography to give the product.

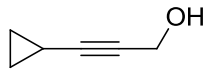
General Procedure H: $[Ph_3PAuNTf_2]_2PhMe$ (1-2 mol%) was added to a solution of propargylic alcohol in alcohol (10 mL/g) and the solution stirred magnetically at rt until starting material had disappeared (TLC). The solvent was removed *in vacuo* and the crude product purified by column chromatography.

106b: 3-Cyclohexyl-prop-2-yn-1-ol [168]



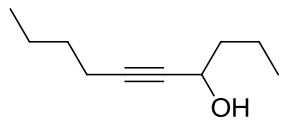
General Procedure A: 0.36 g, 70% yield; ν_{max} (film/cm^{-1}) 3354 (O-H), 2900, 2853 (C-H); δ_H (500 MHz, $CDCl_3$) 1.27 (2H, m, cyclohexyl CH_2), 1.40 (2H, m, cyclohexyl CH_2), 1.51 (2H, m, cyclohexyl CH_2), 1.68 (2H, m, cyclohexyl CH_2), 1.78 (2H, m, cyclohexyl CH_2), 1.93 (1H, br s, OH), 2.37 (1H, m, cyclohexyl CH), 4.25 (2H, d, *J* 1.9, C*H*$_2$OH); δ_C (125 MHz, $CDCl_3$) 25.1, 26.0, 29.2, 32.8, 51.5, 78.4, 90.9.

106c: 3-Cyclopropyl-prop-2-yn-1-ol [169]



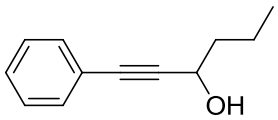
General Procedure A: 300 mg, 60% yield; ν_{max} (film/cm^{-1}) 3436 (O-H), 2935, 2926 (C-H); δ_H (500 MHz, $CDCl_3$) 0.67 (2H, m, cyclopropane CH_2), 0.77 (2H, m, cyclopropane CH_2), 1.25 (1H, m, cyclopropane CH), 1.77 (1H, br s, OH), 4.21 (2H, d, *J* 2.1, C*H*$_2$OH); δ_C (125 MHz, $CDCl_3$) -0.5, 8.3, 51.5, 73.7, 89.8.

110: Dec-5-yne-4-ol [170]



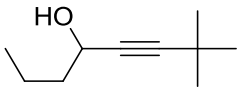
General Procedure A: 3.99 g, 75% yield; ν_{max} (film/cm^{-1}) 3331 (O-H), 2958, 2933, 2873 (C-H), 2231 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.89 (3H, t, *J* 7.2, C≡C$(CH_2)_3$C*H*$_3$), 0.91 (3H, t, *J* 7.3, HOCH$(CH_2)_2$C*H*$_3$), 1.43 (4H, m, 2 x CH_2), 1.64 (4H, m, 2 x CH_2), 1.93 (1H, br s, OH), 2.20 (2H, td, *J* 7.2, 1.9, C≡CCH_2), 4.35 (1H, m, C*H*OH); δ_C (150 MHz, $CDCl_3$) 13.7, 13.9, 18.5, 18.6, 22.0, 30.9, 40.4, 62.6, 81.4, 85.6.

113n: 1-Phenyl-hex-1-yn-3-ol [171]



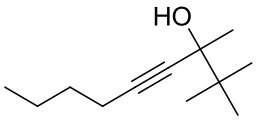
General Procedure A: 3.22 g, 63% yield; ν_{max} (film/cm^{-1}) 3315 (O-H), 2959, 2934, 2873 (C-H), 2227 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.98 (3H, t, *J* 7.4, CH_3), 1.55 (2H, sx, *J* 7.4, C*H*$_2$CH$_3$), 1.74-1.84 (2H, m, CHC*H*$_2$), 2.37 (1H, br s, OH), 4.61 (1H, t, *J* 6.6, CH), 7.27-7.31 (3H, m, Ar-H), 7.42-7.45 (2H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.9, 18.7, 40.1, 62.8, 84.9, 90.4, 122.8, 128.4, 128.5, 131.8.

113s: 7,7-Dimethyl-oct-5-yn-4-ol [172]



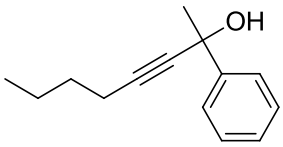
General Procedure A: 3.10 g, 76% yield; ν_{max} (film/cm^{-1}) 3336 (O-H), 2965, 2933, 2872 (C-H), 2234 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.92 (3H, t, *J* 7.4, CH$_2$C*H*$_3$), 1.19 (9H, s, CC*H*$_3$), 1.39-1.48 (2H, m, CHCH$_2$C*H*$_2$), 1.55-1.68 (2H, m, CHC*H*$_2$), 2.38 (1H, s, OH); δ_C (150 MHz, $CDCl_3$) 13.9, 18.6, 27.3, 40.3, 62.3, 79.9, 93.6.

144g: 2,2,3-Trimethyl-non-4-yn-3-ol [173]



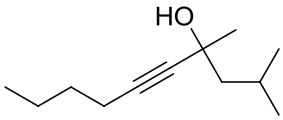
General Procedure A: 5.38 g, 68% yield; ν_{max} (film/cm^{-1}) 3476 (O-H), 2959, 2935, 2874 (C-H), 2242 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.89 (3H, t, *J* 7.3, CH$_2$C*H*$_3$), 1.00 (9H, s, 3 x CH_3), 1.36-1.41 (5H, m, CH_2+CH_3C), 1.43-1.49 (2H, m, CH_2), 1.86 (1H, br s, OH), 2.18 (2H, t, CCH_2); δ_C (150 MHz, $CDCl_3$) 13.7, 18.4, 22.1, 25.1, 25.3, 31.0, 38.3, 74.0, 83.8, 84.2.

144b: 2-Phenyl-oct-3-yn-2-ol [173]



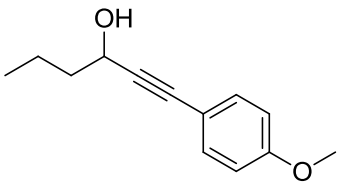
General Procedure A: 4.55 g, 52% yield; ν_{max} (film/cm^{-1}) 3405 (O-H), 2959, 2932, 2872 (C-H), 2245 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.93 (3H, t, *J* 7.4, CH_2CH_3), 1.40-1.47 (2H, app sx, *J* 7.4, CH_2CH_3), 1.50-1.56 (2H, app qn, *J* 7.3, $CH_2CH_2CH_3$), 1.75 (3H, s, CCH_3), 2.27 (2H, t, *J* 7.1, CCH_2), 2.48 (1H, br s, OH), 7.25-7.29 (1H, m, Ar-H), 7.33-7.37 (2H, m, Ar-H), 7.65-7.67 (2H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.8, 18.6, 22.1, 30.9 33.8, 70.1, 83.9, 85.8, 125.1, 127.6, 128.5, 146.4.

144d: 2,4-Dimethyl-5-decyn-4-ol [174]



General Procedure A: 7.00 g, 96% yield; ν_{max} (film/cm^{-1}) 3389 (O-H), 2956, 2931, 2871 (C-H), 2239 (C≡C); δ_H (500 MHz, $CDCl_3$) 0.89 (3H, t, *J* 7.3, CH_2CH_3), 0.99 (6H, t, *J* 7.0, $(CH_3)_2CH_2$), 1.3-1.50 (7H, m, 2 x CH_2, CH_3C), 1.55 (2H, d, *J* 6.1 $(CH_3)_2CHCH_2$), 1.88 (1H, s, OH), 1.91 (1H, m, $(CH_3)_2CH$), 2.18 (2H, t, *J* 7.0, $C{\equiv}CCH_2(CH_3)_2CH_3$); δ_C (125 MHz, $CDCl_3$)13.6, 18.4, 22.0, 24.2, 24.4, 25.2, 30.8, 31.3, 52.2, 68.3, 83.9, 84.5.

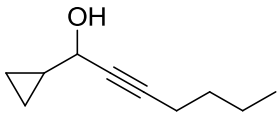
113o: 1-(4-Methoxy-phenyl)-hex-1-yn-3-ol



General Procedure A: 2.36 g, 75% yield: ν_{max} (film/cm^{-1}) 3347 (O-H), 2959, 2935, 2872 (C-H) 2224 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.97 (3H, t, *J* 7.5, CH_3),

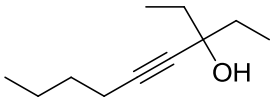
1.50-1.57 (2H, m, C*H*$_2$CH$_3$), 1.72-1.81 (2H, m, C*H*$_2$CH$_2$CH$_3$), 2.04 (1H, br s, OH), 3.80 (3H, s, OMe), 4.59 (1H, t, *J* 6.5, C*H*OH), 6.81-6.84 (2H, m, Ar-H), 7.34-7.37 (2H, m, Ar-H); δ_C (150 MHz, CDCl$_3$) 13.9, 18.7, 40.2, 55.4, 62.9, 84.8, 88.9, 114.0, 114.9, 133.2, 159.7; Found (EI): [M] 204.11418, $C_{13}H_{16}O_2$ requires 204.11447.

113k: 1-Cyclopropyl-hept-2-yn-1-ol



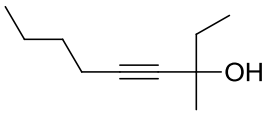
General Procedure A: 3.42 g, 86% yield; ν_{max} (film/cm^{-1}) 3343 (O-H), 2958, 2932, 2864 (C-H), 2224 (C≡C); δ_H (600 MHz, CDCl$_3$) 0.32-0.50 (4H, m, 2 × cyclopropane CH$_2$), 0.85 (3H, t, *J* 7.4, CH$_3$), 1.13-1.19 (1H, m, cyclopropane CH), 1.31-1.38 (2H, m C*H*$_2$CH$_3$), 1.39-1.45 (2H, m, C*H*$_2$CH$_2$CH$_3$), 2.14 (2H, td, *J* 7.2, 1.9, C≡CCH$_2$), 2.30 (1H, br s, OH), 4.17 (1H, dt, *J* 6.2, 1.9, C*H*OH); δ_C (150 MHz, CDCl$_3$) 1.4, 3.2, 13.7, 17.3, 18.4, 22.0, 30.8, 65.8, 78.9, 85.7; Found (CI): [M+H] 153.12811, $C_{10}H_{17}O$ requires 153.12811.

144c: 3-Ethyl-non-4-yn-3-ol



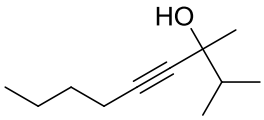
General Procedure A: 3.81 g, 65% yield; ν_{max} (film/cm^{-1}) 3387 (O-H), 2964, 2935, 2877 (C-H), 2241 (C≡C); δ_H (600 MHz, CDCl$_3$) 0.87 (3H, t, *J* 7.3, CH$_2$CH$_2$C*H*$_3$), 0.97 (6H, t, *J* 7.3, 2×CH$_3$), 1.37 (2H, app sx, *J* 7.3, C*H*$_2$CH$_3$), 1.44 (2H, qn, *J* 7.3, C*H*$_2$CH$_2$CH$_3$), 1.58 (4H, m, 2 × CCH$_2$), 2.05 (1H, br s, OH), 2.16 (2H, t, *J* 7.3, C≡CCH$_2$); δ_C (150 MHz, CDCl$_3$) 8.7, 13.7, 18.4, 22.0, 31.0, 34.7, 72.3, 82.7, 84.8; Found (EI): [M-OH] 151.14762, $C_{11}H_{19}$ requires 151.14813.

144f: 3-Methyl-non-4-yn-3-ol



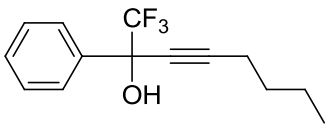
General Procedure A: 6.00 g, 90% yield; ν_{max} (film/cm^{-1}) 3370 (O-H), 2964, 2933, 2875 (C-H), 2237 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.84 (3H, t, *J* 7.2, $(CH_2)_3CH_3$), 0.95 (3H, t, *J* 7.4, CCH_2CH_3), 1.35-1.44 (7H, m, 2 × CH_2, CH_3C), 1.52-1.64 (2H, m, CH_2), 2.12 (2H, t, *J* 7.0, C≡CCH_2), 2.38 (1H, s, OH); δ_C (150 MHz, $CDCl_3$) 9.1, 13.6, 18.3, 21.9, 29.6, 30.9, 36.8, 68.7, 83.5, 83.9; Found (EI): [M-H] 153.12667, $C_{10}H_{17}0$ requires 153.12739.

144e: 2,3-Dimethyl-non-4-yn-3-ol



General Procedure A: 6.60 g, 92% yield; ν_{max} (film/cm^{-1}) 3381 (O-H), 2961, 2933, 2875 (C-H), 2235 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.86 (3H, t, *J* 7.3, $(CH_2)_3CH_3$), 0.92 (3H, d, *J* 6.7, $CHCH_3$), 0.95 (3H, d, *J* 6.7, $CHCH_3$), 1.31-1.47 (7H, m, 2 x CH_2, CH_3COH), 1.66-1.76 (1H, septuplet, *J* 6.7, C*H*), 2.14 (2H, t, *J* 7.0, C≡CCH_2), 2.15 (1H, br s, OH); δ_C (150 MHz, $CDCl_3$) 13.6, 17.5, 18.0, 18.3, 21.9, 27.5, 30.9, 38.1, 71.7, 83.1, 84.2; Found (EI): [M-OH] 151.14883, $C_{11}H_{19}$ requires 151.14867.

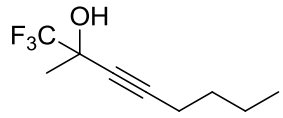
1,1,1-Trifluoro-2-phenyl-oct-3-yn-2-ol [175]



General Procedure A: 9.44g, 85% yield; ν_{max} (film/cm^{-1}) 3464 (O-H), 2961, 2936, 2875 (C-H), 2245 (C≡C); δ_H (500 MHz, $CDCl_3$) 0.97 (3H, t, *J* 7.3, CH_3), 1.43-1.52 (2H, m, CH_2CH_3), 1.56-1.53 (2H, m, $CH_2CH_2CH_3$), 2.35 (2H, t, *J* 7.0,

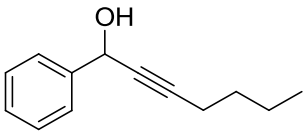
C≡CCH_2), 3.3 (1H, s, OH), 7.42 (3H, m, Ar-H), 7.78 (2H, m, Ar-H); δ_C (125 MHz, $CDCl_3$) 13.6, 18.4, 22.0, 30.2, 73.0 (q, *J* 32.4), 78.4, 89.7, 123.5 (q, *J* 286.1), 127.3, 128.1, 129.3, 135.9.

1,1,1-Trifluoro-2-methyl-oct-3-yn-2-ol



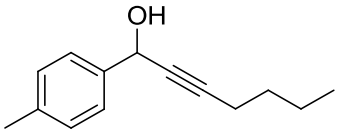
General Procedure A: 6.13 g, 87% yield; ν_{max} (film/cm^{-1}) 3408 (O-H), 2962, 2938, 2877 (C-H), 2256 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.90 (3H, t, *J* 7.3, CH_2CH_3), 1.35-1.42 (2H, app sx, *J* 7.3, C*H2*CH_3), 1.46-1.51 (2H, qn, *J* 7.3, C$H_2CH_2CH_3$), 1.58 (3H, s, CCH_3), 2.21 (2H, t, *J* 7.3, C≡CCH_2), 2.86 (1H, s, OH); δ_C (150 MHz, $CDCl_3$) 13.5, 18.2, 21.9, 23.3, 30.2, 68.6 (q, *J* 32.5), 76.5, 87.6, 124.1 (q, *J* 282.7); Found (CI): $[M+H]^+$ 177.08874, $C_9H_{12}F_3$ requires 177.08911.

113a: 1-Phenylhept-2-yn-1-ol [173]



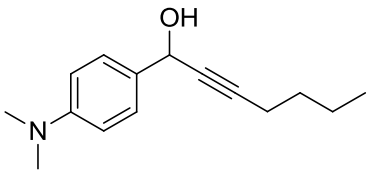
General Procedure A: 1.39 g, 85% yield; δ_H (600 MHz, $CDCl_3$) 0.92 (3H, t, *J* 7.3, CH_2CH_3), 1.43 (2H, sx, *J* 7.3, CH_2CH_3), 1.53 (2H, app qn, *J* 7.3, C$H_2CH_2CH_3$), 2.28 (2H, td, *J* 7.3, 2.2, CCH_2), 2.33 (1H, d, *J* 6.0, OH), 5.44 (1H, d, *J* 6.0, C*H*OH), 7.32 (1H, m, Ar-H), 7.34 (2H, app. t, *J* 7.8, Ar-H), 7.54 (2H, d, *J* 7.8, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.7, 18.6, 22.1, 30.8, 64.9, 80.0, 87.8, 126.8, 128.3, 128.6, 141.4; Found (EI): [M] 188.11894, $C_{13}H_{16}O$ requires 188.11956.

113b: 1-(4-Tolyl)hept-2-yn-1-ol [173]



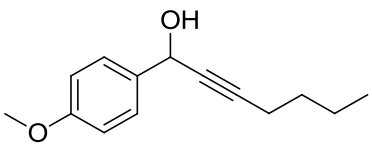
General Procedure A: 1.26 g, 72% yield; δ_H (600 MHz, $CDCl_3$) 0.92 (3H, t, *J* 7.4, CH_2CH_3), 1.43 (2H, sx, *J* 7.4, CH_2CH_3), 1.53 (2H, qn, *J* 7.4, $CH_2CH_2CH_3$), 2.18 (1H, d, *J* 6.1, OH), 2.27 (2H, td, *J* 7.4, 1.9, $C{\equiv}CCH_2$), 2.36 (3H, s, Ar-CH_3), 5.41 (1H, d, *J* 6.1, C*H*OH), 7.18 (2H, d, *J* 8.0, Ar-H), 7.43 (2H, d, *J* 8.0, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.7, 18.6, 21.3, 22.1, 30.8, 64.8, 80.1, 87.6, 126.7, 129.3, 138.1, 138.6; Found (EI): [M] 202.13450, $C_{14}H_{18}O$ requires 202.13521.

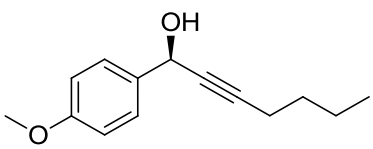
113g: 1-(4-(Dimethylamino)phenyl)hept-2-yn-1-ol



General Procedure A: 1.48 g, 74% yield; ν_{max} (film/cm^{-1}) 3400 (O-H), 2956, 2931, 2871, 2800 (C-H); δ_H (600 MHz, $CDCl_3$) 0.94 (3H, t, *J* 7.4, CH_3), 1.45 (2H, sx, *J* 7.4, CH_2CH_3), 1.54 (2H, qn, *J* 7.4, $CH_2CH_2CH_3$), 2.29 (2H, td, *J* 7.4, 2.2, CCH_2), 2.34 (1H, s, OH), 2.96 (6H, s, $N(CH_3)_2$), 5.36 (1H, br s, C*H*OH), 6.73 (2H, d, *J* 8.7, Ar-H), 7.41 (2H, d, *J* 8.7, Ar-H); δ_C (150 MHz, $CDCl_3$) 14.0, 18.7, 22.2, 30.9, 40.8, 64.7, 80.5, 87.0, 112.6, 127.9, 129.6, 150.7; Found (EI): $[M]^+$ 231.16240, $C_{15}H_{21}ON$ requires 231.16176.

113f and 151: 1-(4-Methoxyphenyl)hept-2-yn-1-ol [173]

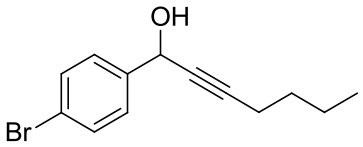




General Procedure A (1.40 g, 74% yield) and General Procedure C (25 mg, 17% yield 75:25 er), respectively: δ_H (600 MHz, $CDCl_3$) 0.92 (3H, t, *J* 7.4, CH_2CH_3),

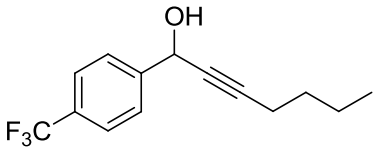
1.42 (2H, sx, *J* 7.4, C*H*$_2$CH$_3$), 1.53 (2H, qn, *J* 7.4, C*H*$_2$CH$_2$CH$_3$), 2.27 (2H, td, *J* 7.4, 1.9, C≡CCH$_2$), 2.47 (1H, d, *J* 6.0, OH), 3.79 (3H, s, OCH$_3$), 5.38 (1H, d, *J* 6.0, C*H*OH), 6.88 (2H, d, *J* 8.7, Ar-H), 7.45 (2H, d, *J* 8.7, Ar-H); δ_C (150 MHz, CDCl$_3$) 13.7, 18.6, 22.1, 30.8, 55.4, 64.5, 80.3, 87.5, 113.9, 128.2, 133.8, 159.6; Found (EI): $[M]^+$ 218.13027, $C_{14}H_{18}O_2$ requires 218.13012.

113d: 1-(4-Bromophenyl)hept-2-yn-1-ol [173]



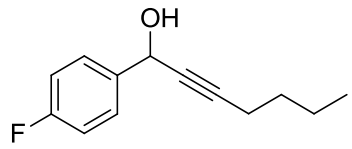
General Procedure A: 1.40 g, 74% yield; δ_H (600 MHz, CDCl$_3$) 0.91 (3H, t, *J* 7.4, CH$_3$), 1.40 (2H, sx, *J* 7.4, C*H*$_2$CH$_3$), 1.51 (2H, qn, *J* 7.4, C*H*$_2$CH$_2$CH$_3$), 2.25 (2H, td, *J* 7.4, 2.0, C≡CCH$_2$), 2.53 (1H, d, *J* 6.0, OH), 5.37 (1H, d, *J* 6.0, C*H*OH), 7.39 (2H, d, *J* 8.4, Ar-H), 7.48 (2H, d, *J* 8.4, Ar-H); δ_C (150 MHz, CDCl$_3$) 13.7, 18.6, 22.1, 30.7, 64.2, 79.6 88.2, 122.2, 128.5, 131.7, 140.4; Found (EI): [M] 266.02898, $C_{13}H_{15}OBr$ requires 266.03007.

113e: 1-(4-(Trifluoromethyl)phenyl)hept-2-yn-1-ol



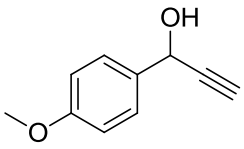
General Procedure A: 1.71 g, 76% yield; ν_{max} (film/cm^{-1}) 3327 (O-H), 2961, 2936, 2875 (C-H), 2226, 2207 (C≡C), 1305 (C-F); δ_H (600 MHz, CDCl$_3$) 0.91 (3H, t, *J* 7.4, CH$_3$), 1.41 (2H, sx, *J* 7.4, C*H*$_2$CH$_3$), 1.52 (2H, qn, *J* 7.4, C*H*$_2$CH$_2$CH$_3$), 2.26 (2H, td, *J* 7.4, 2.0, C≡CCH$_2$), 2.80 (1H, d, *J* 5.8, OH), 5.48 (1H, d, *J* 5.8, C*H*OH), 7.61 (2H, d, *J* 8.3, Ar-H), 7.63 (2H, d, *J* 8.3, Ar-H); δ_C (150 MHz, CDCl$_3$) 13.6, 18.5, 22.1, 30.7, 64.1, 79.4, 88.5, 124.0 (q, *J* 271.3), 125.5 (q, *J* 3.8), 127.0, 130.3 (q, *J* 31.4), 145.1; Found (EI): $[M]^+$ 256.10743, $C_{14}H_{15}OF_3$ requires 256.10694.

113c: 1-(4-Fluorophenyl)hept-2-yn-1-ol



General Procedure A: 1.55 g, 86% yield; ν_{max} (film/cm^{-1}) 3326 (O-H), 2959, 2934, 2873 (C-H), 2226 (C≡C) 1220 (C-F); δ_H (600 MHz, $CDCl_3$) 0.91 (3H, t, *J* 7.3, CH_3), 1.41 (2H, app. sx, *J* 7.3, C*H*$_2$CH$_3$), 1.52 (2H, app. qn, *J* 7.3, C*H*$_2$CH$_2$CH$_3$), 2.26 (2H, td, *J* 7.3, 2.0, CCH$_2$), 2.59 (1H, d, *J* 6.0, OH), 5.40 (1H, d, *J* 6.0, C*H*OH), 7.03 (2H, m,Ar-H), 7.46-7.50 (2H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.7, 18.6, 22.1, 30.7, 64.2, 79.9, 88.0, 115.4 (d, *J* 21.9), 128.6 (d, *J* 7.9), 137.2 (d, *J* 3.3), 162.7 (d, *J* 243.8); Found (EI): [M]$^+$ 206.10970, $C_{13}H_{15}OF$ requires 206.11014.

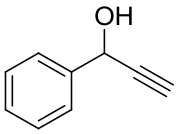
152: 1-(4-Methoxyphenyl)prop-2-yn-1-ol [176]



p-Anisaldehyde (1.2 mL, 9.8 mmol) was added to a solution of ethynylmagnesium bromide (0.5 M in THF, 20 mL, 10 mmol) at 0 °C and the reaction was then stirred for 30 mins at room temperature. The reaction was quenched with aq. $NaHCO_3$ and the organic phase extracted with Et_2O. The combined organic phases were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by flash column chromatography to give the propargylic alcohol (1.53 g, 9.4 mmol, 96%).

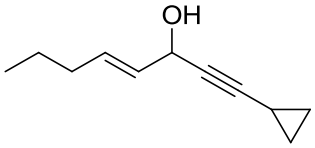
δ_H (500 MHz, $CDCl_3$) 2.25 (1H, br d, *J* 6.0, OH), 2.66 (1H, d, *J* 2.2, C≡CH), 3.82 (3H, s, OCH_3), 5.42 (1H, br dd, *J* 6.0, 2.2, C*H*OH), 6.91 (2H, d, *J* 8.7, Ar-H), 7.48 (2H, d, *J* 8.7, Ar-H); δ_C (125 MHz, $CDCl_3$) 55.4, 64.1, 74.7, 83.8, 114.1, 128.2, 132.5 159.9; Found (EI): [M]$^+$ 162.06768, $C_{10}H_{10}O_2$ requires 162.06753.

1-Phenylprop-2-yn-1-ol [177]



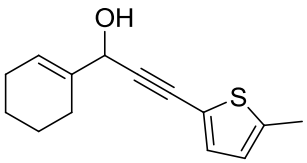
Same Procedure as above: 392 mg, 30% yield; δ_H (500 MHz, $CDCl_3$) 2.64 (1H, br d, *J* 6.2, OH), 2.67 (1H, d, *J* 2.2, C≡CH), 5.45 (1H, br dd, *J* 6.2, 2.2, C*H*OH), 7.33-7.37 (1H, m, Ar-H), 7.39-7.42 (2H, m, Ar-H), 7.53-7.57 (2H, m, Ar-H); δ_C (125 MHz, $CDCl_3$) 64.5, 75.0, 83.6, 126.8, 128.7, 128.8, 140.1; Found (CI): $[M+H]^+$ 133.06588, C_9H_9O requires 133.06534.

113l: (*E*)-1-Cyclopropyloct-4-en-1-yn-3-ol



General Procedure B: 1.20 g, 65% yield; ν_{max} (film/cm^{-1}) 3362 (O-H), 2960, 2931, 2873 (C-H), 2243 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.70 (2H, m, cyclopropane), 0.77 (2H, m, cyclopropane), 0.90 (3H, t, *J* 7.3, CH_3), 1.28 (1H, m, cyclopropane), 1.42 (2H, app sx, *J* 7.3, C*H*$_2$$CH_3$), 1.76 (1H, br s, OH), 2.03 (2H, app q, *J* 7.3, C*H*$_2$$CH_2CH_3$), 4.77 (1H, br s, C*H*OH), 5.57 (1H, dd, *J* 15.3, 6.4, C*H*CHOH), 5.82 (1H, dt, *J* 15.3, 6.8, CH_2C*H*=CH); δ_C (150 MHz, $CDCl_3$) -0.4, 8.39, 8.40, 13.8, 22.2, 34.1, 63.4, 75.0, 89.9, 129.7, 133.6; Found (CI): $[M-OH]^+$ 147.11724, $C_{11}H_{15}$ requires 147.11683.

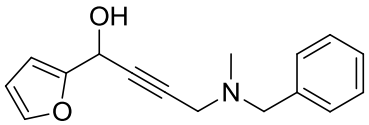
140: 1-(Cyclohex-1-en-1-yl)-3-(5-methylthiophen-2-yl)prop-2-yn-1-ol



General Procedure B: 1.80 g, 77% yield; ν_{max} (film/cm^{-1}) 3387 (O-H), 2932, 2860, 2836 (C-H), 2187 (C≡C); δ_H (600 MHz, $CDCl_3$) 1.56-1.61 (2H, m, CH_2),

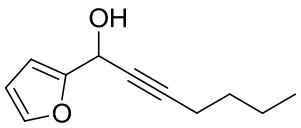
1.61-1.66 (2H, m, CH_2), 2.08-2.12 (2H, m, CH_2), 2.13-2.17 (2H, m, CH_2), 2.27 (1H, br d, *J* 7.0, OH), 2.46 (3H, br s, CH_3), 5.67 (1H, br d, *J* 7.0, C*H*OH), 6.15-6.22 (1H, m, HC=C), 6.58-6.63 (1H, m, Ar-H), 6.95 (1H, br d, *J* 3.4, Ar-H); δ_C (150 MHz, $CDCl_3$) 15.6, 21.5, 22.3, 25.8, 29.1, 60.9, 85.5, 87.9, 120.0, 124.8, 125.6, 136.2, 140.9, 142.7; Found (EI): $[M]^+$ 232.09147, $C_{14}H_{16}OS$ requires 232.09164.

115: 4-(Benzyl(methyl)amino)-1-(furan-2-yl)but-2-yn-1-ol



General Procedure B: 1.0 g 39% yield; ν_{max} (film/cm^{-1}) 3354 (O-H), 2947, 2841, 2800 (C-H), 2247 (C≡C); δ_H (600 MHz, $CDCl_3$) 2.34 (3H, s, CH_3), 3.25 (1H, br s, OH), 3.37 (2H, br d, *J* 1.8, C≡CCH_2), 3.58 (2H, br s, NCH_2), 5.53 (1H, br s, C*H*OH), 6.36 (1H, br dd, *J* 3.2, 1.8, furan-H), 6.47 (1H, br d, *J* 3.2, furan-H), 7.25-7.35 (5H, m, Ar-H), 7.40-7.44 (1H, m, furan-H); δ_C (150 MHz, $CDCl_3$) 42.0, 45.1, 58.2, 60.2, 80.8, 83.4, 107.7, 110.5, 127.5, 128.5, 129.4, 138.0, 143.0, 153.5; Found (EI): $[M+H]^+$ 256.13371, $C_{16}H_{18}O_2N$ requires 256.13375.

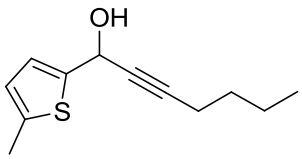
113h: 1-(Furan-2-yl)hept-2-yn-1-ol



General Procedure B: 1.40 g, 86% yield; ν_{max} (film/cm^{-1}) 3419 (O-H), 2965, 2934, 2873 (C-H), 2212 (C≡C); δ_H (500 MHz, $CDCl_3$) 0.91 (3H, t, *J* 7.4, CH_3), 1.41 (2H, app sx, *J* 7.4, C$H_2$$CH_3$), 1.52 (2H, app qn, *J* 7.4, C$H_2$$CH_2$$CH_3$), 2.26 (2H, td, *J* 7.4, 2.0, C≡CCH_2), 2.51 (1H, br s, OH), 5.43 (1H, br s, C*H*OH), 6.34 (1H, br dd, *J* 3.1, 1.9, furan-H), 6.43 (1H, br d, *J* 3.1, furan-H), 7.38 (1H, br d, *J* 1.9, furan-H); δ_C (125 MHz, $CDCl_3$) 13.7, 18.5, 22.1, 30.6, 58.4, 77.5, 87.1,

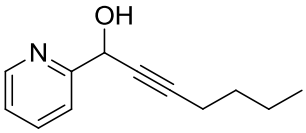
107.6, 110.4, 143.0, 153.8; Found (EI): $[M]^+$ 178.09826, $C_{11}H_{14}O_2$ requires 178.09883.

113i: 1-(5-Methylthiophen-2-yl)hept-2-yn-1-ol



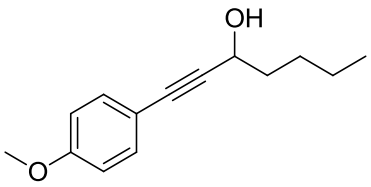
General Procedure B: 1.16 g, 56% yield; ν_{max} (film/cm^{-1}) 3345 (O-H), 2962, 2933, 2872 (C-H), 2232 (C≡C); δ_H (500 MHz, $CDCl_3$) 0.92 (3H, t, *J* 7.3, CH_2CH_3), 1.39-1.48 (2H, m, CH_2CH_3), 1.49-1.56 (2H, m, $CH_2CH_2CH_3$), 2.27 (2H, td, *J* 7.3, 2.0, $C{\equiv}CCH_2$), 2.46 (3H, s, thiophene-CH_3), 2.51 (1H, br s, OH), 5.53 (1H, br d, *J* 6.3, CHOH), 6.59 (1H, m, thiophene-H), 6.92 (1H, br d, *J* 3.5, thiophene-H); δ_C (125 MHz, $CDCl_3$) 13.7, 15.5, 18.5, 22.0, 30.6, 72.0, 79.6, 86.9, 124.7, 125.3, 140.6, 143.1; Found (EI): $[M]^+$ 208.09199, $C_{12}H_{16}OS$ requires 208.09164.

116: 1-(Pyridin-2-yl)hept-2-yn-1-ol



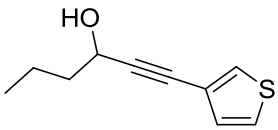
General procedure B: 1.40 g, 74% yield; ν_{max} (film/cm^{-1}) 3340 (O-H), 2959, 2932, 2872 (C-H), 2352 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.88 (3H, t, *J* 7.3, CH_3), 1.38 (2H, app sx, *J* 7.3, CH_2CH_3), 1.45-1.52 (2H, m, $CH_2CH_2CH_3$), 2.34 (2H, td, *J* 7.2, 2.1, $C{\equiv}CCH_2$), 4.88 (1H, br s, OH), 5.49 (1H, br s, CHOH), 7.20-7.25 (1H, m, Ar-H), 7.53 (1H, br d, *J* 7.8, Ar-H), 7.70-7.75 (1H, m, Ar-H), 8.50-8.56 (1H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.7, 18.6, 22.1, 30.7, 63.9, 79.5, 86.8, 121.0, 123.1, 137.3, 148.2, 158.9; Found (EI): $[M]^+$ 189.11425, $C_{12}H_{15}ON$ requires 189.11482.

113w: 1-(4-Methoxyphenyl)hept-1-yn-3-ol



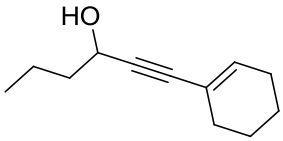
General Procedure B: 1.7 g, 78% yield; ν_{max} (film/cm^{-1}) 3383 (O-H), 2957, 2862, 2839 (C-H), 2541 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.93 (3H, t, *J* 7.3, CH_3), 1.38 (2H, app sx, *J* 7.3, C*H*$_2$CH$_3$), 1.46-1.52 (2H, m, C*H*$_2$CH$_2$CH$_3$), 1.74-1.82 (2H, m, C*H*$_2$CH$_2$CH$_2$CH$_3$), 1.84 (1H, br s, OH), 3.80 (3H, s, OMe), 4.57 (1H, br t, *J* 6.5, C*H*OH), 6.83 (2H, d, *J* 8.8, Ar-H), 7.36 (2H, d, *J* 8.8, Ar-H); δ_C (150 MHz, $CDCl_3$) 14.2, 22.5, 27.5, 37.8, 55.4, 63.1, 84.8, 88.9, 114.0, 114.8, 133.3, 159.7; Found (EI): $[M]^+$ 218.13087, $C_{14}H_{18}O_2$ requires 218.13013.

113q: 1-(Thiophen-3-yl)hex-1-yn-3-ol



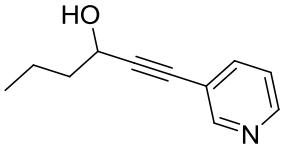
General Procedure B: 900 mg, 46% yield; ν_{max} (film/cm^{-1}) 3353 (O-H), 2959, 2934, 2872 (C-H), 2226 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.97 (3H, t, *J* 7.4, CH_3), 1.53 (2H, app sx, *J* 7.4, C*H*$_2$CH$_3$), 1.72-1.81 (2H, m, C*H*$_2$CH$_2$CH$_3$), 2.07 (1H, br s, OH), 4.58 (1H, t, *J* 6.5, C*H*OH), 7.09 (1H, dd, *J* 5.0, 1.1, thiophene-H), 7.25 (1H, dd, *J* 5.0, 3.0, thiophene-H), 7.42 (1H, dd, *J* 3.0, 1.1, thiophene-H); δ_C (150 MHz, $CDCl_3$) 13.9, 18.6, 40.0, 62.9, 80.1, 90.0, 121.8, 125.4, 129.0, 130.0; Found (EI): [M] 180.06034, $C_{10}H_{12}OS$ requires 180.06081.

113r: 1-(Cyclohex-1-en-1-yl)hex-1-yn-3-ol [178]



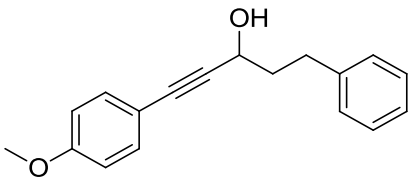
General Procedure B: 1.10g , 62% yield; ν_{max} (film/cm^{-1}) 3391 (O-H), 2940, 2938, 2873 (C-H), 2187 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.94 (3H, t, *J* 7.4, CH_3), 1.47 (2H, app sx, *J* 7.4, C*H*$_2$$CH_3$), 1.53-1.74 (6H, m, CH_2), 2.04-2.12 (5H, m, 2×CH_2, OH), 4.47 (1H, br t, *J* 6.6, C*H*OH), 6.09 (1H, m, C=CH); δ_C (150 MHz, $CDCl_3$) 13.9, 18.6, 21.6, 22.4, 25.7, 29.3, 40.2, 62.8, 86.7, 87.6, 120.2, 135.3; Found (EI): $[M]^+$ 178.13569, $C_{12}H_{18}O$ requires 178.13522.

133t: 1-(Pyridin-3-yl)hex-1-yn-3-ol



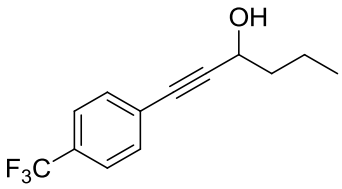
General Procedure B: 950 mg, 51% yield; ν_{max} (film/cm^{-1}) 3254 (O-H), 2959, 2935, 2873 (C-H), 2233 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.95 (3H, t, *J* 7.4, CH_3), 1.53 (2H, app sx, *J* 7.4, C*H*$_2$$CH_3$), 1.71-1.82 (2H, m, C*H*$_2$$CH_2CH_3$), 4.59 (1H, t, *J* 6.6, C*H*OH), 4.78 (1H, br s, OH), 7.21-7.25 (1H, m, Ar-H), 7.67-7.72 (1H, m, Ar-H), 8.45-8.48 (1H, m, Ar-H), 8.72-8.74 (1H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.9, 18.7, 39.9, 62.2, 80.8, 95.2, 120.5, 123.3, 139.1, 148.2, 152.1; Found (EI): $[M]^+$ 175.09977, $C_{11}H_{13}ON$ requires 175.09917.

113v: 1-(4-Methoxyphenyl)-5-phenylpent-1-yn-3-ol



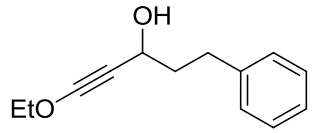
General Procedure B: 2.0 g, 75% yield; ν_{max} (film/cm^{-1}) 3364 (O-H), 3063, 2933, 2876 (C-H), 2255 (C≡C); δ_H (500 MHz, $CDCl_3$) 2.09-2.16 (2H, m, CH_2CHOH), 2.19 (1H, br s, OH), 2.87 (2H, t, *J* 7.8, Ar-CH_2), 3.81 (3H, s, OCH_3), 4.60 (1H, t, *J* 6.5, C*H*OH), 6.85 (2H, d, *J* 8.7, Ar-H), 7.21 (1H, t, *J* 7.5, Ar-H), 7.25 (2H, d, *J* 7.5, Ar-H), 7.31 (2H, t, *J* 7.5, Ar-H), 7.39 (2H, d, *J* 8.7, Ar-H); δ_C (150 MHz, $CDCl_3$) 31.7, 39.5, 55.4, 62.4, 85.3, 88.6, 114.1, 114.8, 126.1, 128.6, 128.7, 133.3, 141.5, 159.8; Found (EI): $[M]^+$ 266.12974, $C_{18}H_{18}O_2$ requires 266.13013.

133p: 1-(4-(Trifluoromethyl)phenyl)hex-1-yn-3-ol [178]



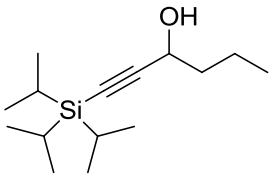
General Procedure A: 1.74 g, 72% yield; ν_{max} (film/cm^{-1}) 3338 (O-H), 2963, 2937, 2876 (C-H); δ_H (600 MHz, $CDCl_3$) 0.96 (3H, t, *J* 7.5, CH_3), 1.53 (2H, app sx, *J* 7.5, C$H_2$$CH_3$), 1.74-1.84 (2H, m, CHC$H_2$), 2.93 (1H, d, *J* 5.1, OH), 4.63 (1H, m, C*H*OH), 7.48 (2H, d, *J* 8.3, Ar-H), 7.52 (2H, d, *J* 8.3, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.8, 18.6, 39.9, 62.7, 83.5, 92.9, 124.0 (q, *J* 271.1), 125.3 (q, *J* 3.7), 126.7, 130.1 (q, *J* 33.0), 132.0; Found (EI): $[M-H]^+$ 241.08310, $C_{13}H_{12}OF_3$ requires 241.08348.

113m: 1-Ethoxy-5-phenylpent-1-yn-3-ol



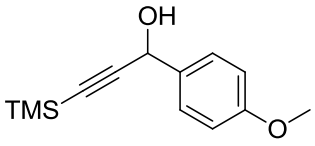
General Procedure A: 694 mg, 68% yield; ν_{max} (film/cm^{-1}) 3394 (O-H), 3027, 2942, 2934 (C-H), 2161 (C≡C); δ_H (600 MHz, $CDCl_3$) 1.39 (3H, t, *J* 7.3, OCH_2CH_3), 1.59 (1H, br s, OH), 2.04-1.93 (2H, m, CH_2CH_2), 2.78 (2H, m, CH_2CH_2), 4.11 (2H, q, *J* 7.3, OCH_2), 4.40-4.44 (1H, m, CHOH), 7.19 (1H, t, *J* 7.3, Ar-H), 7.22 (2H, d, *J* 7.3, Ar-H), 7.29 (2H, t, *J* 7.5, Ar-H); δ_C (150 MHz, $CDCl_3$) 14.5, 31.5, 39.5, 40.3, 61.9, 74.8, 94.2, 126.0, 128.5, 128.6, 141.7, Found (EI): $[M\text{-}OH]^+$ 187.11203, $C_{13}H_{15}O$ requires 187.11174.

119: 1-(Triisopropylsilyl)hex-1-yn-3-ol



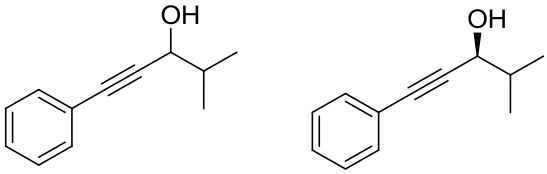
General Procedure A: 1.86 g, 82% yield; ν_{max} (film/cm^{-1}) 3321 (O-H), 2958, 2942, 2866 (C-H), 2171 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.93 (3H, t, *J* 7.4, CH_2CH_3), 1.05 (21H, m, 3 × SiCH(CH_3)$_2$), 1.48 (2H, app sx, *J* 7.4, CH_2CH_3), 1.62-1.72 (2H, m, $CHCH_2CH_2$), 2.14 (1H, br s, OH), 4.37 (1H, t, *J* 6.6, CHOH); δ_C (150 MHz, $CDCl_3$) 11.2, 13.9, 18.5, 18.6, 40.1, 62.8, 85.3, 109.1; Found (EI): $[M]^+$ 254.20650, $C_{15}H_{30}OSi$ requires 254.20603.

118: 1-(4-Methoxyphenyl)-3-(trimethylsilyl)prop-2-yn-1-ol



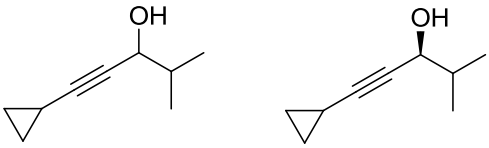
General procedure A: 1.80 g, 94% yield; ν_{max} (film/cm^{-1}) 3394 (O-H), 2959, 2901, 2837 (C-H), 2173 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.00 (9H, s, $SiMe_3$), 2.35 (1H, br s, OH), 3.59 (3H, s, OMe), 5.18 (1H, d, *J* 6.2, C*H*OH), 6.68 (2H, d, *J* 8.7, Ar-H), 7.25 (2H, d, *J* 8.7, Ar-H); δ_C (150 MHz, $CDCl_3$) 0.0, 55.4, 64.6, 91.3, 105.5, 114.1, 128.3, 132.9, 159.8; Found (EI): $[M]^+$ 234.106664, $C_{13}H_{18}O_2Si$ requires 234.10706.

165: 4-Methyl-1-phenylpent-1-yn-3-ol



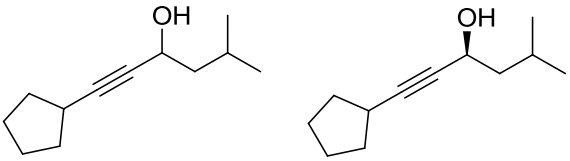
General Procedure B (1.53 g, 88% yield) and General Procedure C (70 mg, 80% yield, 95:5 er) respectively: ν_{max} (film/cm^{-1}) 3351 (O-H), 2961, 2928, 2872 (C-H), 2219 (C≡C); δ_H (600 MHz, $CDCl_3$) 1.06 (3H, d, *J* 6.8, CH_3), 1.08 (3H, d, *J* 6.8, CH_3), 1.96-2.01 (1H, m, C*H*CH_3), 2.25 (1H, br s, OH), 4.41 (1H, d, *J* 5.7, C*H*OH), 7.28-7.32 (3H, m, Ar-H), 7.43-7.45 (2H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 17.7, 18.4, 32.8, 68.5, 85.7, 89.1, 122.9, 128.4, 128.5, 131.8; Found (EI): $[M]^+$ 174.10447, $C_{12}H_{14}O$ requires 174.10391. $[\alpha]_D^{22}$ –0.010 (c 1 in $CHCl_3$).

193: 1-Cyclopropyl-4-methylpent-1-yn-3-ol



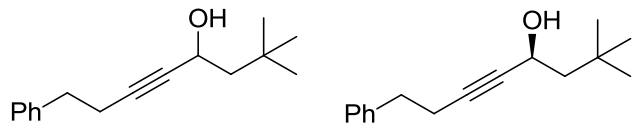
General Procedure B (4.50 mmol, 90%) and General Procedure C (0.56 mmol, 93%, 94:6 er) respectively: ν_{max} (film/cm^{-1}) 3380 (O-H), 2961, 2931, 2873 (C-H), 2247 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.63-0.66 (2H, m, CH_2), 0.73-0.77 (2H, m, CH_2), 0.93 (3H, d, *J* 6.8, CH_3), 0.95 (3H, d, *J* 6.8, CH_3), 1.21-1.26 (1H, m, C*H*(CH_2)$_2$), 1.75-1.83 (1H, m, C*H*(CH_3)$_2$), 1.85 (1H, br s, OH), 4.09 (1H, br s, C*H*OH); δ_C (150 MHz, $CDCl_3$) -0.50, 8.37, 8.38, 17.6, 18.2, 34.8, 68.2, 75.1, 89.4; Found (EI): $[M]^+$ 138.103596, $C_9H_{14}O$ requires 138.10392.

113x: 1-Cyclopentyl-5-methylhex-1-yn-3-ol



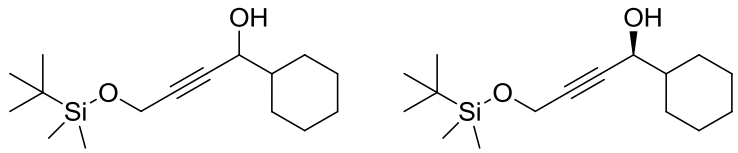
General Procedure A (1.68 mmol, 78%) and General Procedure C (0.47 mmol, 76%, 89:11 er) respectively: ν_{max} (film/cm^{-1}) 3317 (O-H), 2965, 2870 (C-H), 2230 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.90 (3H, d, *J* 6.7, CH_3), 0.92 (3H, d, *J* 6.7, CH_3), 1.46-1.61 (6H, m, 3 x CH_2), 1.67-1.72 (2H, m, CH_2), 1.76-1.84 (2H, m, C*H*(CH_3)$_2$, OH), 1.85-1.92 (2H, m, CH_2), 2.57-2.63 (1H, m, $CH_2CH_2CHC{\equiv}C$), 4.38 (1H, br t, *J* 7.0, C*H*OH); δ_C (150 MHz, $CDCl_3$) 22.6, 22.7, 24.9, 25.0, 30.2, 33.91, 33.93, 47.4, 61.3, 81.1, 89.7; Found (CI): $[M\text{-}OH]^+$ 163.14810, $C_{12}H_{19}$ requires 163.14868.

113y: 2,2-Dimethyl-8-phenyloct-5-yn-4-ol [179]



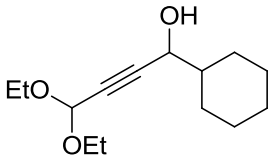
General procedure A and General Procedure C (98:2 er): δ_H (600 MHz, $CDCl_3$) 0.97 (9H, s, 3 × CH_3), 1.65 (2H, d, *J* 6.5, C*H*$_2$C(CH_3)$_3$), 1.66 (1H, br s, OH), 2.50 (2H, td, *J* 7.6, 1.8, C≡CCH_2), 2.82 (2H, t, *J* 7.6, Ar-CH_2), 4.42 (1H, tt, *J* 6.5, 1.8, C*H*OH), 7.20-7.23 (3H, m, Ar-H), 7.28-7.31 (2H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 21.1, 30.1, 30.2, 35.1, 51.9, 60.5, 83.6, 84.6, 126.4, 128.5, 128.6, 140.7; Found (EI): [M]+ 230.168024, $C_{16}H_{22}O$ requires 230.16707.

113z: 4-((*tert*-Butyldimethylsilyl)oxy)-1-cyclohexylbut-2-yn-1-ol [179]



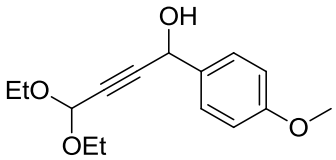
General procedure A (2.10 mmol, 88%) and General Procedure C (0.60 mmol, 74%, 96:4 er): δ_H (600 MHz, $CDCl_3$) 0.10 (6H, s, Si(CH_3)$_2$), 0.90 (9H, s, SiC(CH_3)$_3$), 0.99-1.27 (5H, m, cyclohexane-H), 1.48-1.56 (1H, m, cyclohexane-H), 1.63-1.68 (1H, m, cyclohexane-H), 1.72-1.77 (2H, m, cyclohexane-H), 1.81-1.85 (2H, m, cyclohexane-H), 1.89 (1H, br s, OH), 4.16 (1H, br d, *J* 6.1, C*H*OH), 4.34 (2H, s, C≡CCH_2); δ_C (150 MHz, $CDCl_3$) -5.0, 18.4, 25.91, 25.95, 26.0, 26.5, 28.2, 28.6, 44.1, 51.9, 67.3, 84.4, 84.9; Found (CI): $[M+H]^+$ 283.20930, $C_{16}H_{31}O_2Si$ requires 283.20878.

169j: 1-Cyclohexyl-4,4-diethoxybut-2-yn-1-ol [179]



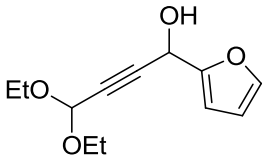
General procedure A: 625 mg, 75% yield; ν_{max} (film/cm^{-1}) 3417 (O-H), 2925 (C-H); δ_H (600 MHz, $CDCl_3$) 0.96-1.27 (5H, m, cyclohexane-H), 1.21 (6H, t, *J* 7.1, 2 × CH_3), 1.50-1.58 (1H, m cyclohexane-H), 1.60-1.68 (1H, m cyclohexane-H), 1.71-1.78 (2H, m cyclohexane-H), 1.79-1.87 (2H, m cyclohexane-H), 2.07 (1H, br s, OH), 3.53-3.61 (2H, m, OCH_2), 3.68-3.75 (2H, m, OCH_2), 4.19 (1H, br d, *J* 6.6, C*H*OH), 5.29 (1H, s, $CH(OEt)_2$); δ_C (150 MHz, $CDCl_3$) 15.2, 25.91, 25.94, 26.4, 28.3, 28.6, 43.9, 60.9, 61.0, 67.1, 81.0, 85.6, 91.4; Found (EI): $[M-H]^+$ 239.16446, $C_{14}H_{23}O_3$ requires 239.16417.

169c: 4,4-Diethoxy-1-(4-methoxyphenyl)but-2-yn-1-ol



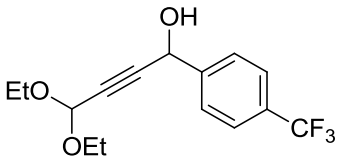
General procedure A: 1.20 g, 55% yield; ν_{max} (film/cm^{-1}) 3412 (O-H), 2976, 2933, 2889 (C-H), 2243 (C≡C); δ_H (400 MHz, $CDCl_3$) 1.23 (6H, t, *J* 7.1, CH_2CH_3), 2.53 (1H, br s, OH), 3.55-3.65 (2H, m, CH_2CH_3), 3.70-3.79 (2H, m, CH_2CH_3), 3.80 (3H, s, OCH_3), 5.34 (1H, s, $CH(OEt)_2$), 5.46 (1H, d, *J* 6.0, C*H*OH), 6.89 (2H, d, *J* 8.7, Ar-H), 7.44 (2H, d, *J* 8.7, Ar-H); δ_C (100 MHz, $CDCl_3$) 15.1, 55.3, 60.96, 61.03, 64.0, 81.7, 85.3, 91.4, 114.0, 128.1, 132.4, 159.8; Found (EI): $[M]^+$ 264.135933, $C_{15}H_{20}O_4$ requires 264.13561.

169i: 4,4-Diethoxy-1-(furan-2-yl)but-2-yn-1-ol



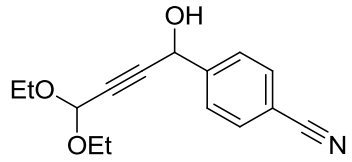
General procedure A: 2.10 g, 94% yield; ν_{max} (film/cm^{-1}) 3404 (O-H), 2977, 2933, 2890 (C-H), 2240 (C≡C); δ_H (400 MHz, $CDCl_3$) 1.23 (6H, t, *J* 7.1, 2×CH_2CH_3), 3.27 (1H, br s, OH), 3.55-3.65 (2H, m, CH_2CH_3), 3.70-3.80 (2H, m, CH_2CH_3), 5.34 (1H, s, $CH(OEt)_2$), 5.51 (1H, d, *J* 6.8, CHOH), 6.32-6.35 (1H, m, furan-H), 6.44 (1H, d, *J* 3.3, furan-H), 7.39-7.41 (1H, m, furan-H); δ_C (100 MHz, $CDCl_3$) 15.0, 57.8, 61.0, 61.1, 80.9, 82.9, 91.2, 107.9, 110.4, 143.0, 152.5; Found (EI): $[M]^+$ 224.104178, $C_{12}H_{16}O_4$ requires 224.10431.

169: 4,4-Diethoxy-1-(4-(trifluoromethyl)phenyl)but-2-yn-1-ol



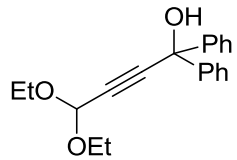
General procedure A: 2.20 g, 99% yield; ν_{max} (film/cm^{-1}) 3404 (O-H), 2980, 2936, 2888 (C-H), 2246 (C≡C); δ_H (400 MHz, $CDCl_3$) 1.21 (6H, t, *J* 7.1, 2×CH_2CH_3), 3.41 (1H, br s, OH), 3.54-3.63 (2H, m, CH_2CH_3), 3.68-3.77 (2H, m, CH_2CH_3), 5.33 (1H, s, $CH(OEt)_2$), 5.56 (1H, d, *J* 5.7, CHOH), 7.59-7.66 (4H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 15.0, 61.1, 63.5, 65.8, 82.3, 84.5, 91.2, 124.3 (q, *J* 272.0), 125.5 (q, *J* 3.7), 126.9, 130.5 (q, *J* 32.3), 143.9; Found (ES): $[M-H]^+$ 301.1051, $C_{15}H_{16}O_3F_3$ requires 301.1052.

169g: 4-(4,4-Diethoxy-1-hydroxybut-2-yn-1-yl)benzonitrile



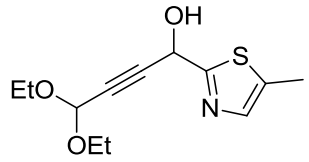
General procedure A: 850 mg, 43% yield; ν_{max} (film/cm^{-1}) 3423 (O-H), 2977, 2932, 2888 (C-H), 2230 (C≡N); δ_H (400 MHz, $CDCl_3$) 1.22 (6H, t, *J* 7.1, 2×$CH_2C\mathit{H}_3$), 3.47 (1H, br s, OH), 3.54-3.64 (2H, m, $C\mathit{H}_2CH_3$), 3.68-3.78 (2H, m, $C\mathit{H}_2CH_3$), 5.32 (1H, s, $CH(OEt)_2$), 5.57 (1H, d, *J* 5.8, C*H*OH), 7.64-7.67 (4H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 15.0, 61.2, 63.3, 65.8, 82.6, 84.1, 91.2, 112.0, 118.6, 127.2, 132.4, 154.2; Found (ES): $[M-H]^+$ 258.1130, $C_{15}H_{16}NO_3$ requires 258.1130.

4,4-Diethoxy-1,1-diphenylbut-2-yn-1-ol



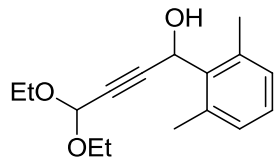
General procedure A: 1.60 g, 94% yield; ν_{max} (film/cm^{-1}) 3417 (O-H), 2976, 2931, 2897 (C-H), 2250 (C≡C); δ_H (400 MHz, $CDCl_3$) 1.17 (6H, t, *J* 7.1, 2×$CH_2C\mathit{H}_3$), 3.52 (1H, br s, OH), 3.53-3.61 (2H, m, $C\mathit{H}_2CH_3$), 3.66-3.75 (2H, m, $C\mathit{H}_2CH_3$), 5.34 (1H, s, $CH(OEt)_2$), 7.18-7.30 (6H, m, Ar-H), 7.54-7.59 (4H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 15.1, 61.1, 74.3, 82.7, 88.0, 91.5, 126.1, 127.8, 128.3, 144.7; Found (CI): $[M-OH]^+$ 293.152248, $C_{20}H_{21}O_2$ requires 293.15361.

4,4-Diethoxy-1-(5-methylthiazol-2-yl)but-2-yn-1-ol



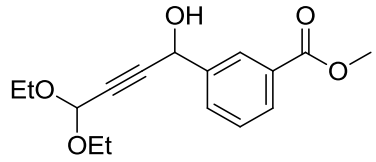
General procedure A: 1.4 g, 70% yield; ν_{max} (film/cm^{-1}) 3400 (O-H), 2976, 2929, 2886 (C-H), 2248 (C≡C); δ_H (400 MHz, $CDCl_3$) 1.22 (6H, t, *J* 7.1, CH_2CH_3), 2.44 (3H, s, Ar-CH_3), 3.54-3.62 (2H, m, CH_2CH_3), 3.68-3.76 (2H, m, CH_2CH_3), 4.99 (1H, br s, OH), 5.30 (1H, s, $CH(OEt)_2$), 5.75 (1H, s, CHOH), 8.66 (1H, s, Ar-H); δ_C (100 MHz, $CDCl_3$) 15.0, 31.9, 56.9, 61.0, 61.1, 81.2, 84.5, 91.2, 132.5, 149.6, 151.6; Found (ES): $[M-H]^+$ 254.0849, $C_{12}H_{16}NO_3S$ requires 254.0851.

169e: 1-(2,6-Dimethylphenyl)-4,4-diethoxybut-2-yn-1-ol



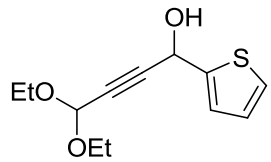
General procedure A: 1.9 g, 97% yield; ν_{max} (film/cm^{-1}) 3424 (O-H), 2976, 2930, 2890 (C-H), 2248 (C≡C); δ_H (400 MHz, $CDCl_3$) 1.18 (3H, t, *J* 7.1, CH_2CH_3), 1.20 (3H, t, *J* 7.1, CH_2CH_3), 2.49 (6H, s, Ar-Me), 2.60 (1H, br s, OH), 3.50-3.60 (2H, m, CH_2CH_3), 3.65-3.75 (2H, m, CH_2CH_3), 5.26 (1H, s, $CH(OEt)_2$), 5.94 (1H, s, CHOH), 6.97-7.01 (2H, m, Ar-H), 7.05-7.10 (1H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 15.0, 57.8, 61.0, 61.1, 80.9, 82.9, 91.2, 107.9, 110.4, 143.0, 152.4; Found (CI): $[M]^+$ 261.148379, $C_{16}H_{22}O_3$ requires 261.14852.

169l: Methyl 3-(4,4-diethoxy-1-hydroxybut-2-yn-1-yl)benzoate



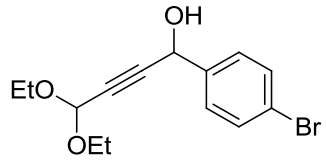
General procedure A: 1.20 g, 67% yield; ν_{max} (film/cm^{-1}) 3429 (O-H), 2977, 2934, 2888 (C-H), 2240 (C≡C), 1722 (C=O); δ_H (600 MHz, $CDCl_3$) 1.21 (6H, t, *J* 7.1, 2×CH_2CH_3), 2.40 (1H, br s, OH), 3.55-3.63 (2H, m, CH_2CH_3), 3.68-3.79 (2H, m, CH_2CH_3), 3.90 (3H, s, OCH_3), 5.32 (1H, s, $CH(OEt)_2$), 5.56 (1H, br s, CHOH), 7.35-7.39 (1H, m, Ar-H), 7.70-7.75 (1H, m, Ar-H), 7.94-8.00 (1H, m, Ar-H), 8.18 (1H, s, Ar-H); δ_C (150 MHz, $CDCl_3$) 15.0, 52.2, 61.0, 61.1, 63.7, 81.9, 84.9, 91.2, 127.8, 128.7, 129.5, 130.3, 131.2, 140.8, 166.8; Found (CI): $[M\text{-}OEt]^+$ 247.095983, $C_{14}H_{15}O_4$ requires 247.09649.

169h: 4,4-Diethoxy-1-(thiophen-2-yl)but-2-yn-1-ol



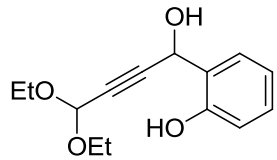
General procedure A: 900 mg, 51% yield; ν_{max} (film/cm^{-1}) 3395 (O-H), 2976, 2930, 2888 (C-H), 2243 (C≡C); δ_H (400 MHz, $CDCl_3$) 1.22 (6H, t, *J* 7.1, CH_2CH_3), 3.44 (1H, br s, OH), 3.55-3.65 (2H, m, CH_2CH_3), 3.70-3.80 (2H, m, CH_2CH_3), 5.33 (1H, s, $CH(OEt)_2$), 5.69 (1H, d, *J* 6.7, CHOH), 6.93-6.97 (1H, m, Ar-H), 7.13-7.16 (1H, m, Ar-H), 7.26-7.29 (1H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 15.0, 60.0, 61.0, 61.1, 81.1, 84.7, 91.2, 125.7, 126.0, 126.7, 144.1; Found (CI): $[M\text{-}OH]^+$ 223.078664, $C_{12}H_{15}O_2S$ requires 223.07873.

169k: 1-(4-Bromophenyl)-4,4-diethoxybut-2-yn-1-ol



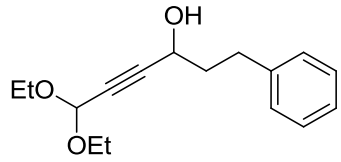
General procedure A: 800 mg, 48% yield; ν_{max} (film/cm^{-1}) 3397 (O-H), 2976, 2930, 2887 (C-H), 2242 (C≡C); δ_H (400 MHz, $CDCl_3$) 1.22 (6H, t, *J* 7.1, 2×CH_2CH_3), 2.76 (1H, br s, OH), 3.55-3.63 (2H, m, CH_2CH_3), 3.68-3.77 (2H, m, CH_2CH_3), 5.33 (1H, s, $CH(OEt)_2$), 5.47 (1H, br s, CHOH), 7.39 (2H, d, *J* 8.3, Ar-H), 7.49 (2H, d, *J* 8.3, Ar-H); δ_C (100 MHz, $CDCl_3$) 15.1, 61.06, 61.11, 63.7, 82.2, 84.6, 91.3, 122.5, 128.4, 131.7, 139.0; Found (EI): $[M\text{-}OEt]^+$ 267.000941, $C_{12}H_{12}O_2Br$ requires 267.00152.

169m: 2-(4,4-Diethoxy-1-hydroxybut-2-yn-1-yl)phenol



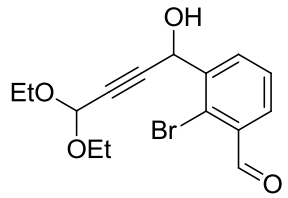
General procedure A: 400 mg, 22% yield; ν_{max} (film/cm^{-1}) 3326 (O-H), 2977, 2931, 2892 (C-H), 2246 (C≡C); δ_H (400 MHz, $CDCl_3$) 1.21 (6H, t, *J* 7.1, 2×CH_2CH_3), 3.54-3.63 (2H, m, CH_2CH_3), 3.69-3.78 (2H, m, CH_2CH_3), 4.32 (1H, br s, OH), 5.32 (1H, s, $CH(OEt)_2$), 5.70 (1H, s, CHOH), 6.82-6.88 (2H, m, Ar-H), 7.17 (1H, t, *J* 7.8, Ar-H), 7.30 (1H, d, *J* 7.8, Ar-H), 7.70 (1H, s, Ar-OH); δ_C (100 MHz, $CDCl_3$) 15.0, 61.25, 61.27, 62.9, 82.3, 84.1, 91.3, 116.9, 120.2, 124.6, 127.7, 130.0, 154.9; Found (ES): $[M\text{-}H]^+$ 249.1125, $C_{14}H_{17}O_4$ requires 249.1127.

169b: 6,6-Diethoxy-1-phenylhex-4-yn-3-ol



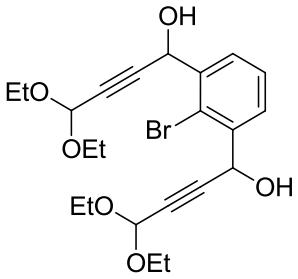
General procedure A: 2.00 g, 75% yield; ν_{max} (film/cm^{-1}) 3418 (O-H), 2977, 2930, 2885 (C-H), 2248 (C≡C);δ_H (400 MHz, $CDCl_3$) 1.22 (6H, t, *J* 7.1, 2×CH_2CH_3), 1.98-2.07 (2H, m, $CHCH_2$), 2.78 (2H, t, *J* 7.9, Ar-CH_2), 2.89 (1H, br s, OH), 3.54-3.62 (2H, m, CH_2CH_3), 3.70-3.77 (2H, m, CH_2CH_3), 4.40 (1H, br s, $CH(OEt)_2$), 5.30 (1H, s, CHOH), 7.15-7.28 (5H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 15.1, 31.4, 39.0, 60.9, 61.0, 61.3, 80.3, 86.5, 91.3, 126.0, 128.46, 128.51, 141.2; Found (CI): $[M\text{-}OEt]^+$ 217.12276, $C_{14}H_{17}O_2$ requires 217.12231.

169n: 2-Bromo-3-(4,4-diethoxy-1-hydroxybut-2-yn-1-yl)benzaldehyde



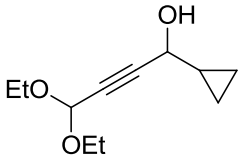
General procedure A: 150 mg, 15% yield; ν_{max} (film/cm^{-1}) 3408 (O-H), 2975, 2925 (C-H), 2248 (C≡C), 1690 (C=O); δ_H (400 MHz, $CDCl_3$) 1.03 (6H, t, *J* 7.1, 2×CH_2CH_3), 2.98 (1H, br d, *J* 4.8, OH), 3.35-3.45 (2H, m, CH_2CH_3), 3.49-3.60 (2H, m, CH_2CH_3), 5.13 (1H, s, $CH(OEt)_2$), 5.78 (1H, d, *J* 4.8, CHOH), 7.29 (1H, t, *J* 7.6, Ar-H), 7.68 (1H, d, *J* 7.6, Ar-H), 7.82 (1H, d, *J* 7.6, Ar-H), 10.24 (1H, s, OCH); δ_C (100 MHz, $CDCl_3$) 14.1, 61.1, 61.2, 63.2, 82.3, 83.7, 91.2, 127.1, 128.1, 130.1, 133.9, 134.1, 140.7, 191.9; Found (CI): $[M+H]^+$ 341.07010, $C_{15}H_{18}O_4Br$ requires 341.03102.

169o: 1,1'-(2-Bromo-1,3-phenylene)bis(4,4-diethoxybut-2-yn-1-ol)



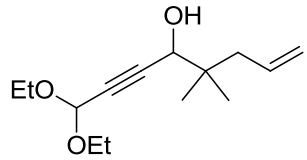
General procedure A: 700 mg 51% yield; ν_{max} (film/cm^{-1}) 3409 (O-H), 2977, 2931, 2887 (C-H), 2248 (C≡C); δ_H (400 MHz, $CDCl_3$) 1.21 (12H, t, *J* 7.1, 2×CH_2CH_3), 3.02 (2H, br d, *J* 5.5, 2×OH), 3.54-3.63 (4H, m, 2×CH_2CH_3), 3.68-3.77 (4H, m, 2×CH_2CH_3), 5.32 (2H, s, 2×C*H*$(OEt)_2$), 5.90 (2H, d, *J* 5.5, 2×C*H*OH), 7.39 (1H, t, *J* 7.6, Ar-H), 7.73 (2H, d, *J* 7.6, Ar-H); δ_C (100 MHz, $CDCl_3$) 15.0, 61.0, 61.1, 64.1, 81.9, 84.2, 91.3, 123.0, 128.1, 128.6, 139.9; Found (ES): $[M-H]^+$ 467.1075, $C_{22}H_{28}O_6Br$ requires 467.1069.

169d: 1-Cyclopropyl-4,4-diethoxybut-2-yn-1-ol



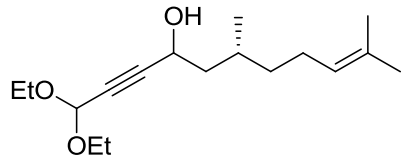
General procedure A: 1.19 g, 86% yield; ν_{max} (film/cm^{-1}) 3410 (O-H), 2978, 2932, 2890 (C-H), 2248 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.38-0.45 (2H, m, HCCH_2), 0.47-0.56 (2H, m, HCCH_2) 1.19 (3H, t, *J* 7.2, OCH_2CH_3), 1.20-1.25 (1H, m, *H*C$(CH_2)_2$), 2.46 (1H, br s, OH), 3.52-3.57 (2H, m, OCH_2), 3.65-3.72 (2H, m, OCH_2), 4.18 (1H, t, *J* 6.0, C*H*OH), 5.26 (1H, s, $(EtO)_2CH$); δ_C (150 MHz, $CDCl_3$) 1.76, 3.34, 15.1, 17.0, 60.9, 61.0, 65.5, 80.2, 84.6, 91.3; Found (CI): $[M-OEt]^+$ 153.10159, $C_9H_{13}O_2$ requires 153.09101.

169p: 1,1-Diethoxy-5,5-dimethyloct-7-en-2-yn-4-ol



General procedure A: 1.25 g, 78% yield; ν_{max} (film/cm^{-1}) 3466 (O-H), 2977, 2932, 2892 (C-H), 2249 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.89 (3H, s, CCH_3), 0.91 (3H, s, CCH_3), 1.16 (6H, t, *J* 7.2, 2×OCH_2CH_3), 2.03 (1H, dd, *J* 13.6, 7.2, C*H*HCH=C), 2.10 (1H, dd, *J* 13.6, 7.5, CH*H*CH=C), 2.66 (1H, br s, OH), 3.50-3.55 (2H, m, OCH_2), 3.64-3.70 (2H, m, OCH_2), 4.06 (1H, s, $HC(OEt)_2$), 4.97-5.02 (2H, m, $CH=CH_2$), 5.25 (1H, s, C*H*OH), 5.75 (1H, m, *H*C=CH_2); δ_C (150 MHz, $CDCl_3$) 15.1, 22.5, 22.7, 38.6, 42.7, 60.8, 61.0, 69.7, 81.4, 85.2, 91.3, 117.8, 134.8; Found (EI): [M-OEt] 195.16034, $C_{12}H_{19}O_2$ requires 195.13796.

169f: (6*R*)-1,1-Diethoxy-6,10-dimethylundec-9-en-2-yn-4-ol

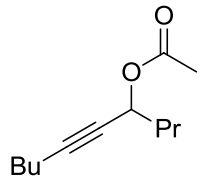


General procedure A: Synthesised from commercially available (*R*)-(+)-Citronellal purchased from Sigma Aldrich $[\alpha]_D^{20}$ 1.448. [180]

1.72 g, 88% yield; ν_{max} (film/cm^{-1}) 3388 (O-H), 2974, 2913 (C-H), 2236 (C≡C), 1480 (C=C); δ_H (600 MHz, $CDCl_3$) 0.88 (3H, dd, *J* 6.4, 4.5, $CHCH_3$), 1.10-1.17 (1H, m, C*H*CH_2C=C), 1.19 (6H, t, *J* 7.2, 2 × OCH_2CH_3), 1.27-1.37 (1H, m, C*H*HCH_2C=C), 1.42-1.47 (0.5H, m C*H*CH_3), 1.50-1.56 (1H, m, C*H*HCHOH), 1.56 (3H, s, C=CCH_3), 1.63 (3H, s, C=CCH_3), 1.64-1.69 (1H, m, C*H*HCHOH), 1.70-1.77 (0.5H, m C*H*CH_3), 1.88-2.01 (2H, m, CH_2C=C), 2.46 (0.4H, d, *J* 5.7 OH), 2.54 (0.6H, d, *J* 5.3 OH), 3.51-3.57 (2H, m, OCH_2), 3.66-3.72 (2H, m, OCH_2), 4.42-4.46 (1H, m, *H*COH), 5.04 (1H, t, J 5.7, C*H*C=C), 5.26 (1H, s, *H*CO$(Et)_2$); δ_C (150 MHz, $CDCl_3$) 15.1, 17.7, 19.2, 19.7, 25.38, 25.41, 25.8 29.0, 29.4, 37.1, 37.2, 44.8, 44.9, 60.3, 60.9, 61.0, 79.7 80.0, 86.9, 87.2, 91.3, 124.6,

124.7, 131.3, 131.4; Found (CI): [M-OEt] 237.184928, $C_{15}H_{25}O_2$ requires 237.18491; $[\alpha]_D^{20}$ -1.7 (c 0.71 in $CHCl_3$).

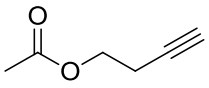
Dec-5-yn-4-yl acetate [181]



Propargylic alcohol **109** (250 mg, 1.6 mmol, 1 eq.) was dissolved in 1,2-dichloroethane (15 ml) followed by the addition of DMAP (0.06 g, 0.48 mmol, 0.3 eq.), triethylamine (1.8 mL, 6.4 mmol, 4 eq.) and acetic anhydride (290 mg, 3.2 mmol, 2 eq.). The reaction was heated to reflux o/n. The reaction was quenched with aq. $NaHCO_3$ and the organic phase extracted with diethyl ether. The combined organic phases were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography to give the ester (302 mg, 1.54 mmol, 96%).

δ_H (600 MHz, $CDCl_3$) 0.87 (3H, t, *J* 7.3, C≡C$(CH_2)_3$CH_3), 0.90 (3H, t, *J* 7.4, OCH$(CH_2)_2$CH_3), 1.32-1.47 (6H, m, 3 x CH_2), 1.62-1.71 (2H, m, CH_2), 2.00 (3H, s, O=CCH_3), 2.17 (2H, td, *J* 7.1, 1.9, C≡CCH_2), 5.32 (1H, td, *J* 6.6, 1.9 CHOC=O); δ_C (150 MHz, $CDCl_3$) 13.65, 13.71, 18.5, 21.2, 22.0, 30.7, 37.3, 64.5, 77.7, 86.2, 170.2; Found (EI): $[M]^+$ 196.14669, $C_{12}H_{20}O_2$ requires 196.14578.

But-3-yn-1-yl acetate

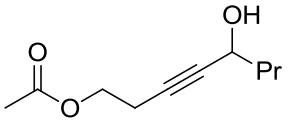


Same procedure as above.

7.3 g, 98% yield; ν_{max} (film/cm^{-1}) 2967 (C-H), 1735 (C=O); δ_H (600 MHz, $CDCl_3$) 1.89 (3H, s, CH_3), 1.90 (1H, t, *J* 2.7, C≡CH), 2.35 (2H, td, *J* 6.8, 2.7,

$CH_2C{\equiv}C$), 3.98 (2H, t, *J* 6.8, OCH_2); δ_C (150 MHz, $CDCl_3$) 18.8, 20.6, 62.0, 70.0, 80.0, 170.5; Found (CI): [M] 112.05330, $C_6H_8O_2$ requires 112.05243.

113u: 5-Hydroxyoct-3-yn-1-yl acetate

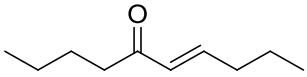


$ZnMe_2$ (2M in toluene, 30 mL, 1.6 eq.) was added dropwise to a solution of alkyne (6.2 g, 1.5 eq.) in toluene (50 mL) and stirred for 30 mins. After this time butraldehyde (2.60 g, 1 eq.) was added and the reaction mixture stirred overnight. The reaction was quenched with aq. $NaHCO_3$ and the organic phase extracted with diethyl ether. The combined organic phases were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography to give the alcohol **113u** (1.50g, 22% yield)

ν_{max} (film/cm^{-1}) 3436 (O-H), 2960, 2875 (C-H), 2217 (C≡C), 1740 (C=O); δ_H (600 MHz, $CDCl_3$) 0.88 (3H, t, *J* 7.3, CH_2CH_3), 1.39 (2H, app sx, *J* 7.3, CH_2CH_3), 1.53-1.64 (2H, m, CH_2), 2.01 (3H, s, $O{=}CCH_3$), 2.46-2.52 (3H, m, CH_2, OH), 4.09 (2H, t, *J* 7.0, OCH_2), 4.29 (1H, t, *J* 6.6, C*H*OH); δ_C (150 MHz, $CDCl_3$) 13.8, 18.5, 19.3, 20.9, 40.1, 62.2, 62.5, 80.5, 83.2, 171.1; Found (CI): [M-OH] 167.10764, $C_{10}H_{15}O_2$ requires 167.10720.

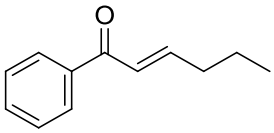
2. Meyer-Schuster Rearrangement

111: (*E*)-Dec-6-en-5-one [181]



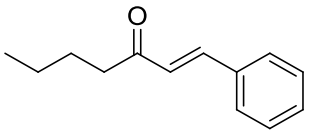
General Procedure D: 77 mg, 91% yield, crude *E:Z* 17:1; 830 mg, 83% yield; ν_{max} (film/cm^{-1}) 2933, 2873 (C-H), 1712 (C=O); δ_H (500 MHz, $CDCl_3$) 0.91 (3H, t, *J* 7.5, $(CH_2)_3CH_3$), 0.93 (3H, t, *J* 7.4, $CC(CH_2)_2CH_3$), 1.29-1.37 (2H, sx, *J* 7.5, $OC(CH_2)_2CH_2$), 1.45-1.53 (2H, sx, J 7.4, $CCCH_2CH_2$), 1.55-1.61 (2H, qn, *J* 7.5, $OCCH_2CH_2$), 2.16-2.20 (2H, td, *J* 7.4, 1.4, $CCHCH_2$), 2.52 (2H, t, *J* 7.5, $OCCH_2$), 6.08 (1H, dt, *J* 15.8, 1.4, OCCH), 7.09 (1H, dt, *J* 15.8, 7.0, CH); δ_C (125 MHz, $CDCl_3$) 13.8, 14.0, 21.5, 22.5, 26.4, 34.3, 39.8, 130.7, 147.1, 201.1.

114n: (*E*)-1-Phenyl-hex-2-en-1-one [181]



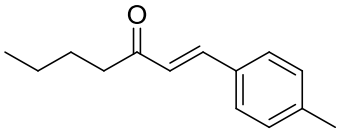
General Procedure D: 99 mg, 99% yield crude *E:Z* 8:1; ν_{max} (film/cm^{-1}) 2961, 2932, 2873 (C-H), 1669 (C=O); δ_H (600 MHz, $CDCl_3$) 0.97 (3H, t, *J* 7.3, CH_3), 1.55 (2H, app sx, *J* 7.3, CH_2CH_3), 2.30 (2H, tdd, *J* 7.5, 7.0, 1.4, $CCCH_2$), 6.87 (1H, dt, *J* 15.4, 1.4, OCC*H*), 7.06 (1H, dt, *J* 15.4, 7.0, C*H*CH_2) 7.44-7.47 (2H, m, Ar-H), 7.54 (1H, tt, *J* 7.3, 1.2, Ar-H) 7.91-7.94 (2H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.9, 21.6, 35.0, 126.1, 128.6, 128.7, 132.7, 138.1, 150.0, 191.1.

114a: (*E*)-1-Phenylhept-1-en-3-one [182]



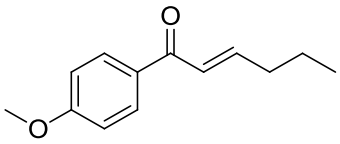
General Procedure D: 96 mg, 96% yield, crude *E:Z* 20:1; mp 38-39˚C; ν_{max} (film/cm^{-1}) 2955, 2942, 2926, 2866 (C-H), 1649 (C=O); δ_H (500 MHz, $CDCl_3$) 0.94 (3H, t, *J* 7.5, CH_3), 1.39 (2H, sx, *J* 7.5, C*H*$_2$CH$_3$), 1.64-1.69 (2H, m, C*H*$_2$CH$_2$CH$_3$), 2.64 (2H, t, *J* 7.5, OCCH$_2$), 6.75 (1H, d, *J* 16.3, OCC*H*), 7.38-7.41 (3H, m, Ar-H) 7.53-7.56 (2H, m, Ar-H), 7.55 (1H, d, *J* 16.3, ArCH); δ_C (150 MHz, $CDCl_3$) 14.1, 22.6, 26.6, 40.8, 126.4, 128.4, 129.1, 130.5, 134.7, 142.4, 200.9.

114b: (*E*)-1-(4-Tolyl)hept-1-en-3-one [182]



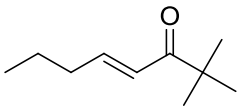
General Procedure D: 98 mg, 98% yield, crude *E:Z* 18:1; mp 38-40˚C (EtOH); ν_{max} (film/cm^{-1}) 2955, 2930, 2862 (C-H), 1648 (C=O); δ_H (500 MHz, $CDCl_3$) 0.94 (3H, t, *J* 7.5, CH_3), 1.39 (2H, sx, *J* 7.5, C*H*$_2$CH$_3$), 1.65 (2H, qn, *J* 7.5, C*H*$_2$CH$_2$CH$_3$), 2.38 (3H, s, ArCH$_3$), 2.65 (2H, t, *J* 7.5, OCCH$_2$), 6.70 (1H, d, *J* 16.3, OCC*H*), 7.20 (2H, d, *J* 8.0, Ar-H) 7.45 (2H, d, *J* 8.0, Ar-H), 7.53 (1H, d, *J* 16.3, OCCHC*H*); δ_C (150 MHz, $CDCl_3$) 14.1, 21.6, 22.6, 26.7, 40.7, 125.5, 128.4, 129.8, 131.9, 141.0, 142.5, 201.0.

114o: (*E*)-1-(4-Methoxyphenyl)hex-2-en-1-one



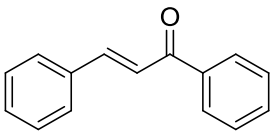
General Procedure D: 99 mg, 99% yield, crude *E:Z* 6:1; mp 56-58˚C (EtOH); ν_{max} (film/cm^{-1}) 2961, 2933, 2873 (C-H), 1664 (C=O); δ_H (600 MHz, $CDCl_3$) 0.97 (3H, t, *J* 7.5, CH_2CH_3), 1.55 (2H, sx, *J* 7.5, CH_2CH_3), 2.29 (2H, dtd, *J* 7.5, 7.0, 1.5, $CCCH_2$), 3.86 (3H, s, OCH_3), 6.89 (1H, dt, *J* 15.5, 1.5, OCC*H*), 6.94 (2H, d, *J* 8.8, Ar-H), 7.04 (1H, dt, *J* 15.5, 7.0, C*H*CH_2) 7.94 (2H, d, *J* 8.8, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.9, 21.6, 35.0, 55.6, 113.8, 125.7, 130.9, 131.0, 148.9, 163.4, 189.3; Found (EI): $[M]^+$ 204.11405, $C_{13}H_{16}O_2$ requires 204.11447.

114s: (*E*)-2,2-Dimethyl-oct-4-en-3-one



General Procedure D: 16 h at rt: 80 mg, 80% yield crude *E:Z* 14:1; ν_{max} (film/cm^{-1}) 2963, 1933, 2873 (C-H), 1689 (C=O); δ_H (600 MHz, $CDCl_3$) 0.92 (3H, t, *J* 7.3, CH_3), 1.13 (9H, s, $(CH_3)_3$), 1.47 (2H, app sx, *J* 7.3, CH_2CH_3), 2.17 (2H, tdd, *J* 7.4, 7.0, 1.5, $CCCH_2$), 6.48 (1H, dt, *J* 15.2, 1.5, OCC*H*) 6.92 (1H, dt, *J* 15.2, 7.0, C*H*CH_2); δ_C (150 MHz, $CDCl_3$) 13.8, 21.6, 26.3, 34.6, 42.9, 124.4, 147.5, 204.5; Found (EI): $[M]^+$ 154.13498, $C_{10}H_{18}O$ requires 154.13522.

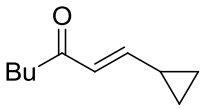
114j: (*E*)-1,3-Diphenyl-propenone [183]



General Procedure D: 87 mg, 87% yield, crude *E:Z* 10:1; mp 56-58˚C (EtOH); ν_{max} (film/cm^{-1}) 3059, 3027 (C-H), 1662 (C=O); δ_H (500 MHz, $CDCl_3$) 7.40-7.45 (3H, m, Ar-H), 7.49-7.54 (2H, m, Ar-H), 7.54 (1H, d, *J* 15.8, C*H*CO), 7.60 (1H,

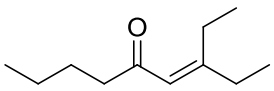
tt, *J* 7.4, 2.0, Ar-H), 7.63-7.67 (2H, m, Ar-H), 7.82 (1H, d, *J* 15.8, OCCHC*H*), 8.01-8.05 (2H, m, Ar-H); δ_C (125 MHz, $CDCl_3$) 122.2, 128.5, 128.6, 128.7, 129.1, 130.6, 132.9, 135.0, 138.3, 144.9, 190.6.

114k: (*E*)-1-Cyclopropylhept-1-en-3-one



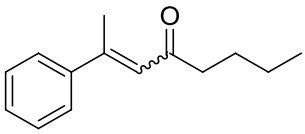
General Procedure D: 98 mg, 98% yield, crude *E:Z* 13:1; ν_{max} (film/cm^{-1}) 2957, 2932, 2872 (C-H), 1662 (C=O); δ_H (600 MHz, $CDCl_3$) 0.62-0.66 (2H, m, Cp-H), 0.90 (3H, t, *J* 7.5, CH_3), 0.93-0.98 (2H, m, Cp-H), 1.31 (2H, app sx, *J* 7.5, C*H*$_2$CH$_3$), 1.54-1.58 (3H, m, OCCH$_2$C*H*$_2$, Cp-H), 2.46 (2H, t, *J* 7.5, OCC*H*$_2$), 6.20 (1H, d, *J* 15.4, OCC*H*) 6.28 (1H, dd, *J* 15.4, 9.6, CC*H*Cp); δ_C (150 MHz, $CDCl_3$) 9.0, 14.0, 14.8, 22.6, 26.6, 40.2, 127.3, 152.4, 200.2; Found (CI): $[M+H]^+$ 153.12811, $C_{10}H_{17}O$ requires 153.12793.

155c: 3-Ethyl-non-3-en-5-one



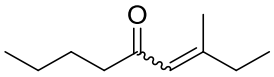
General Procedure D: 75 mg, 75% yield, crude *E:Z*; ν_{max} (film/cm^{-1}) 2962, 2934, 2875 (C-H), 1686 (C=O); δ_H (500 MHz, $CDCl_3$) 0.89 (3H, t, *J* 7.4, $CH_2CH_2CH_3$), 1.03 (3H, t, *J* 7.5, CCH_2CH_3), 1.05 (3H, t, *J* 7.5, CCH_2CH_3), 1.30 (2H, sx, *J* 7.4, C*H*$_2$CH$_3$), 1.54 (2H, qn, *J* 7.5, C*H*$_2$CH$_2$CH$_3$), 2.14 (2H, qd, *J* 7.5, 1.3, CCH_2), 2.40 (2H, t, *J* 7.5, O=CCH_2), 2.54 (2H, qd, *J* 7.5, 1.3, CCH_2), 5.97 (1H, s, CH); δ_C (150 MHz, $CDCl_3$) 12.2, 13.1, 14.0, 22.5, 25.9, 26.6, 31.1, 44.3, 121.2, 165.5, 201.4; Found (EI): $[M]^+$ 168.15087, $C_{11}H_{20}O$ requires 168.15043.

155b: (*E*/*Z*)-2-Phenyl-oct-2-en-4-one



General Procedure D: 67 mg, 67% yield, crude *E:Z* 3.5:1; ν_{max} (film/cm^{-1}) 2957, 2930, 2871 (C-H), 1681 (C=O); ***E*-isomer** δ_H (600 MHz, $CDCl_3$) 0.93 (3H, t, *J* 7.5, CH_2CH_3), 1.33-1.39 (2H, m, CH_2CH_3), 1.60-1.66 (2H, m, $CH_2CH_2CH_3$), 2.53 (2H, t, *J* 7.4, $OCCH_2$), 2.54 (3H, d, *J* 1.1, $C=CCH_3$), 6.50 (1H, d, *J* 1.1, C=C*H*), 7.35-7.40 (3H, m, Ar-H), 7.47-7.50 (2H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 14.1, 18.5, 22.6, 26.6, 44.8, 124.4, 126.6, 128.6, 129.1, 142.8, 153.7, 201.9; ***Z*-isomer** δ_H (600 MHz, $CDCl_3$) 0.77 (3H, t, *J* 7.4, CH_2CH_3), 1.10-1.16 (2H, m, CH_2CH_3), 1.39-1.45 (2H, m, $CH_2CH_2CH_3$), 2.14 (2H, t, *J* 7.4, $OCCH_2$), 2.18 (3H, d, *J* 1.5, $C=CCH_3$), 6.13 (1H, d, *J* 1.5, C=C*H*), 7.17-7.20 (2H, m, Ar-H), 7.31-7.36 (3H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.9, 22.3, 26.5, 27.3, 42.7, 127.2, 127.5, 128.2, 128.4, 141.1, 151.9, 202.8; Found (EI): $[M]^+$ 202.13490, $C_{14}H_{18}O$ requires 202.13521.

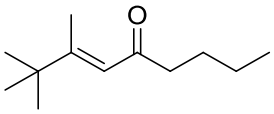
155f: *E*/*Z*)-3-Methyl-non-3-en-5-one



General procedure D: 78 mg, 78% yield crude *E:Z* 2:1; ν_{max} (film/cm^{-1}) 2960, 2934, 2874 (C-H), 1686 (C=O); ***E*-isomer** δ_H (600 MHz, $CDCl_3$) 0.89 (3H, t, *J* 7.4, $CH_2CH_2CH_3$), 1.05 (3H, t, *J* 7.4, $C=CCH_2CH_3$), 1.26-1.33 (2H, m, $CH_2CH_2CH_3$), 1.51-1.58 (2H, m, $OCCH_2CH_2$), 2.11 (3H, d, *J* 1.1, $C=CCH_3$), 2.13 (2H, qd, *J* 7.4, 0.8, $C=CCH_2$), 2.40 (2H, t, *J* 7.4, $O=CCH_2$), 6.03 (1H, br s, CH); δ_C (150 MHz, $CDCl_3$) 12.2, 14.0, 19.4, 22.6, 26.5, 34.1, 44.3, 122.1, 159.9, 201.8; ***Z*-isomer** δ_H (600 MHz, $CDCl_3$) 0.88 (3H, t, *J* 7.4, $CH_2CH_2CH_3$), 1.03 (3H, t, *J* 7.4, $C=CCH_2CH_3$), 1.26-1.33 (2H, m, $CH_2CH_2CH_3$), 1.51-1.58 (2H, m, $OCCH_2CH_2$), 1.85 (3H, d, *J* 1.2, $C=CCH_3$), 2.38 (2H, t, *J* 7.4, $O=CCH_2$), 2.56 (2H, q, *J* 7.4, $C=CCH_2$), 6.00 (1H, br s, CH); δ_C (150 MHz, $CDCl_3$) 12.6, 14.0,

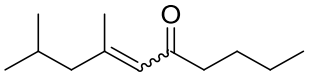
22.5, 25.0, 26.4, 26.9, 44.2, 123.3, 160.6, 201.1; Found (CI): $[M+H]^+$ 155.14380, $C_{10}H_{19}O$ requires 155.14358.

155g: (*E*)-2,2,3-Trimethyl-3-nonen-5-one [184]



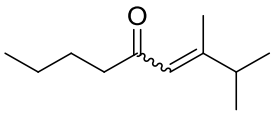
General Procedure D: 73 mg, 73% yield crude *E:Z* 3:1; ν_{max} (film/cm^{-1}) 2958, 2873 (C-H), 1687 (C=O); δ_H (500 MHz, $CDCl_3$) 0.88 (3H, t, *J* 7.3, CH_2CH_3), 1.07 (9H, s, $C(CH_3)_3$), 1.29 (2H, sx, *J* 7.5, CH_2CH_3), 1.54 (2H, qn, *J* 7.5, $CH_2CH_2CH_3$), 2.08 (3H, d, *J* 1.0, CCH_3), 2.41 (2H, t, *J* 7.5, $O=CCH_2$), 6.08 (1H, s, CH); δ_C (125 MHz, $CDCl_3$) 14.0, 15.7, 22.4, 26.5, 28.6, 37.8, 44.5, 120.2, 165.2, 202.5.

155d: (*E*/*Z*)-7,9-Dimethyl-dec-6-en-5-one



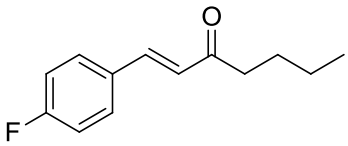
General Procedure D: 72 mg, 72% yield, crude *E:Z* 1.3:1; ν_{max} (film/cm^{-1}) 2957, 2931, 2871 (C-H), 1686 (C=O); ***E*-isomer** δ_H (600 MHz, $CDCl_3$) 0.84-0.90 (9H, m, 2 x $CHCH_3$, CH_2CH_3), 1.26-1.33 (2H, m, CH_2CH_3), 1.50-1.58 (2H, m, $CH_2CH_2CH_3$), 1.82-1.88 (1H, m, $CH(CH_3)_2$), 1.95 (2H, d, *J* 7.2, $C=CCH_2$), 2.08 (3H, d, *J* 1.1, $C=CCH_3$), 2.39 (2H, t, *J* 7.3, $O=CCH_2$), 6.00 (1H, d, *J* 1.1, C=CH); ***Z*-isomer** δ_H (600 MHz, $CDCl_3$) 0.84-0.90 (9H, m, 2 x $CHCH_3$, CH_2CH_3), 1.26-1.33 (2H, m, CH_2CH_3), 1.50-1.58 (2H, m, $CH_2CH_2CH_3$), 1.82-1.88 (1H, m, $CH(CH_3)_2$), 1.83 (3H, d, *J* 1.5, $C=CCH_3$), 2.37 (2H, t, *J* 7.3, $O=CCH_2$), 2.51 (2H, d, *J* 7.5, $C=CCH_2$), 6.07 (1H, s, C=CH); δ_C (150 MHz, $CDCl_3$) 14.0 & 19.3, 22.49 & 22.51, 22.54 & 22.56, 22.8 & 25.8, 26.3 & 27.6, 26.4 & 26.5, 42.0 & 44.30, 44.31 & 51.0, 124.4 & 124.9, 157.5 & 158.0, 201.1 & 201.6; Found (CI): $[M+H]^+$ 183.17454, $C_{12}H_{23}O$ requires 183.17488.

155e: (*E*/*Z*)-2,3-Dimethyl-non-3-en-5-one



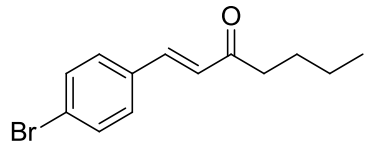
General Procedure D: 79 mg, 79% yield, crude *E:Z* 1.5:1; ν_{max} (film/cm^{-1}) 2958, 2930, 2872 (C-H), 1725 (C=O); ***E*-isomer** δ_H (600 MHz, $CDCl_3$) 0.89 (3H, t, *J* 7.4, CH_2CH_3), 1.04 (6H, d, *J* 6.9, $CH(CH_3)_2$), 1.26-1.34 (2H, m, CH_2CH_3), 1.51-1.58 (2H, m, $CH_2CH_2CH_3$), 2.08 (3H, d, *J* 1.1, $C=CCH_3$), 2.31 (1H, septet, *J* 6.9, $CH(CH_3)_2$), 2.41 (2H, t, *J* 7.4, $O=CCH_2$), 6.04 (1H, s, C=CH); δ_C (150 MHz, $CDCl_3$) 14.0, 16.9, 21.0, 26.5, 29.4, 38.4, 44.3, 121.2, 163.8, 202.2; ***Z*-isomer** δ_H (600 MHz, $CDCl_3$) 0.88 (3H, t, *J* 7.3, CH_2CH_3), 0.98 (6H, d, *J* 7.0, $CH(CH_3)_2$), 1.26-1.33 (2H, m, CH_2CH_3), 1.51-1.58 (2H, m, $CH_2CH_2CH_3$), 1.76 (3H, d, *J* 1.3, $C=CCH_3$), 2.38 (2H, t, *J* 7.3, $O=CCH_2$), 3.89 (1H, septet, *J* 7.0, $CH(CH_3)_2$), 5.95 (1H, s, C=CH); δ_C (150 MHz, $CDCl_3$) 14.0, 19.5, 20.7, 26.4, 29.4, 38.4, 44.3, 123.4, 163.9, 201.3. Found (EI): $[M]^+$ 168.15099, $C_{11}H_{20}O$ requires 168.15086.

114c: (*E*)-1-(4-Fluorophenyl)hept-1-en-3-one [181]



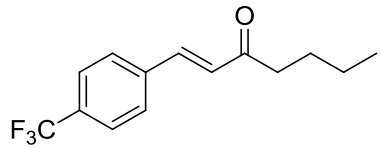
General procedure D: 77 mg, 77% yield, crude *E:Z* 15:1; mp 39-40˚C (EtOH); δ_H (500 MHz, $CDCl_3$) 0.94 (3H, t, *J* 7.4, CH_3), 1.38 (2H, sx, *J* 7.4, CH_2CH_3), 1.65 (2H, qn, *J* 7.4, $CH_2CH_2CH_3$), 2.65 (2H, t, *J* 7.4, $OCCH_2$), 6.67 (1H, d, *J* 16.2, CHCO), 7.08 (2H, t, *J* 8.6, Ar-H), 7.50 (1H, d, *J* 16.2, *HC*=CHCO), 7.53 (2H, br dd, *J* 8.6, 5.4, Ar-H). δ_C (125 MHz, $CDCl_3$) 14.0, 22.5, 26.5, 40.9, 116.1 (d, *J* 22.0), 126.0 (d, *J* 1.9), 130.2 (d, *J* 8.6), 130.9 (d, *J* 3.8), 141.0, 162.2 (d, *J* 250.7), 200.5; Found (CI): $[M+H]^+$ 207.11852, $C_{13}H_{16}OF$ requires 207.11806.

114d: (*E*)-1-(4-Bromophenyl)hept-1-en-3-one



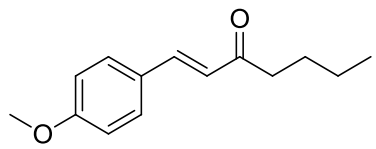
General procedure D: 96 mg, 96% yield, crude *E:Z* 19:1; mp 56-57˚C; ν_{max} (film/cm^{-1}) 2964, 2951, 2930, 2868 (C-H), 1685 (C=O); δ_H (500 MHz, $CDCl_3$) 0.94 (3H, t, *J* 7.4, CH_3), 1.38 (2H, sx, *J* 7.4, C*H*$_2$CH$_3$), 1.65 (2H, qn, *J* 7.4, C*H*$_2$CH$_2$CH$_3$), 2.65 (2H, t, *J* 7.4, OCC*H*$_2$), 6.72 (1H, d, *J* 16.1, C*H*CO), 7.40 (2H, d, *J* 8.5, Ar-H), 7.50 (1H, d, *J* 16.1, *HC*=CHCO), 7.52 (2H, d, *J* 8.5, Ar-H). δ_C (125 MHz, $CDCl_3$) 14.0, 22.5, 26.5, 41.0, 124.7, 126.8, 129.7, 132.2, 133.6, 140.9, 200.4; Found (CI): $[M+H]^+$ 267.03824, $C_{13}H_{16}OBr$ requires 267.03845.

114e: (*E*)-1-(4-(Trifluoromethyl)phenyl)hept-1-en-3-one [181]



General procedure D: 78 mg, 78% yield, crude *E:Z* 18:1; δ_H (500 MHz, $CDCl_3$) 0.95 (3H, t, *J* 7.4, CH_3), 1.39 (2H, sx, *J* 7.4, C*H*$_2$CH$_3$), 1.66 (2H, qn, *J* 7.4, C*H*$_2$CH$_2$CH$_3$), 2.68 (2H, t, *J* 7.4, OCC*H*$_2$), 6.80 (1H, d, *J* 16.3, C*H*CO), 7.56 (1H, d, *J* 16.3, *HC*=CHCO), 7.63 (4H, s, Ar-H). δ_C (125 MHz, $CDCl_3$) 14.0, 22.5, 26.3, 41.1, 123.9 (q, *J* 271.6), 125.6 (q, *J* 3.8), 128.3, 128.4, 131.9 (q, *J* 32.7), 138.1, 141.3, 200.2; Found (CI): $[M+H]^+$ 257.11501, $C_{14}H_{16}OF_3$ requires 257.11532.

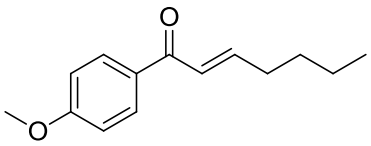
114f: (*E*)-1-(4-Methoxyphenyl)hept-1-en-3-one [181]



General Procedure D: 99 mg, 99%, crude *E:Z* 12:1 yield; ν_{max} (film/cm^{-1}) 2958, 2934, 2872 (C-H), 1685 (C=O); δ_H (600 MHz, $CDCl_3$) 0.94 (3H, t, *J* 7.4, CH_3),

1.37 (2H, app sx, *J* 7.5, C*H*$_2$CH$_3$), 1.66 (2H, app qn, *J* 7.5, C*H*$_2$CH$_2$CH$_3$), 2.64 (2H, t, *J* 7.5, OCC*H*$_2$), 3.84 (3H, s, OCH$_3$), 6.63 (1H, d, *J* 16.0, C*H*CO), 6.91 (2H, d, *J* 8.6, Ar-H), 7.50 (2H, d, *J* 8.6, Ar-H), 7.51 (1H, d, *J* 16.0, *H*C=CHCO); δ_C (150 MHz, $CDCl_3$) 14.1, 22.6, 26.8, 40.7, 55.5, 114.5, 124.2, 127.3, 130.1, 142.2, 161.6, 200.9;

114w: 1-(4-Methoxyphenyl)hept-2-en-1-one



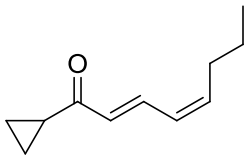
General Procedure D: 93 mg, 92% yield, crude *E*:*Z* 5:1;

E-Enone: ν_{max} (film/cm^{-1}) 2962, 2935 (C-H), 1600 (C=O); δ_H (600 MHz, $CDCl_3$) 0.93 (3H, t, *J* 7.5, CH$_2$C*H*$_3$), 1.38 (2H, app sx, *J* 7.5, C*H*$_2$CH$_3$), 1.51 (2H, app qn, *J* 7.5, C*H*$_2$CH$_2$CH$_3$), 2.31 (2H, qd, *J* 7.5, 1.5, OCC*H*$_2$), 3.87 (3H, s, OCH$_3$) 6.89 (1H, dt, *J* 15.5, 1.5, C*H*CO), 6.95 (2H, d, *J* 8.9, Ar-H), 6.75 (1H, dt, *J* 15.5, 7.5, OCC=CH), 7.95 (2H, d, *J* 8.7, Ar-H); δ_C (150 MHz, $CDCl_3$) 14.0, 22.5, 30.5, 32.7, 55.6, 113.8, 125.6, 130.9, 131.0, 149.2, 163.3, 189.3;

Z-Enone: ν_{max} (film/cm^{-1}) 2962, 2935 (C-H), 1600 (C=O); δ_H (600 MHz, $CDCl_3$) 0.90 (3H, t, *J* 7.5, CH$_2$C*H*$_3$), 1.35 (2H, app sx, *J* 7.5, C*H*$_2$CH$_3$), 1.44 (2H, app qn, *J* 7.5, C*H*$_2$CH$_2$CH$_3$), 2.60 (2H, qd, *J* 7.5, 1.5, OCC*H*$_2$), 3.87 (3H, s, OCH$_3$), 6.26 (1H, dt, *J* 11.6, 7.5, OCC=CH), 6.75 (1H, dt, *J* 11.6, 1.5 C*H*CO), 6.90 (2H, d, *J* 8.6, Ar-H) 7.94 (2H, d, *J* 8.6, Ar-H); δ_C (150 MHz, $CDCl_3$) 14.1, 22.6, 29.7, 31.6, 55.6, 113.8, 124.5, 130.8, 131.7, 148.7, 163.3, 191.1;

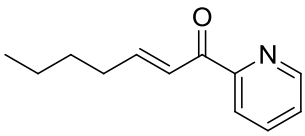
Found (CI): $[M+H]^+$ 219.13812, $C_{14}H_{19}O_2$ requires 219.13850.

114l: (2*E*,4*Z*)-1-Cyclopropylocta-2,4-dien-1-one



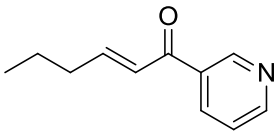
General Procedure D: 84 mg, 84% yield, crude *E,E:E,Z* 3:2; ν_{max} (film/cm^{-1}) 2965, 2936, 2876 (C-H), 1704 (C=O); δ_H (600 MHz, $CDCl_3$) 0.87-0.91 (2H, m, cp-CH_2) 0.92 (3H, t, *J* 7.4, CH_3), 1.06-1.10 (2H, m, cp-CH_2), 1.46 (2H, app sx, *J* 7.4, C*H*$_2$CH$_3$), 2.10-2.14 (1H, m, cp-CH), 2.14-2.18 (2H, m, C=CCH_2), 6.15-6.21 (2H, m, *H*C=C*H*CH_2), 6.21 (1H, d, *J* 15.4, O=CCH) 7.20 (1H, dd, *J* 15.4, 9.6, O=CC(H)=C*H*); δ_C (150 MHz, $CDCl_3$) 11.1, 13.8, 19.3, 22.0, 35.3, 128.1, 129.2, 142.8, 145.6, 200.6; Found (EI): $[M]^+$ 164.11993, $C_{11}H_{16}O$ requires 164.11957.

117: (*E*)-1-(Pyridin-2-yl)hept-2-en-1-one



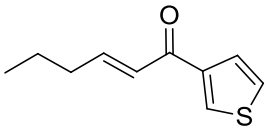
General Procedure D: 10 mg, 10% yield, crude *E:Z* 8:1; ν_{max} (film/cm^{-1}) 2960, 2933, 2831 (C-H), 1621 (C=O); δ_H (600 MHz, $CDCl_3$) 0.93 (3H, t, *J* 7.4, CH_3), 1.35-1.41 (2H, m, C*H*$_2$CH$_3$), 1.48-1.55 (2H, m, C*H*$_2$CH$_2$CH$_3$), 2.35 (2H, br qd, *J* 7.0, 1.2, C=CC*H*$_2$), 7.24 (1H, dt, *J* 15.6, 7.0, *H*C=C(H)CO) 7.45-7.49 (1H, m, Ar-H), 7.58 (1H, dt, *J* 15.6, 1.2, HCCO), 7.85 (1H, td, *J* 7.9, 1.5, Ar-H), 8.12 (1H, d, *J* 7.9 Ar-H), 8.70-8.73 (1H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 14.0, 22.5, 30.4, 32.8, 123.0, 124.5, 126.9, 137.1, 148.9, 150.8, 154.3, 189.7; Found (CI): $[M+H]^+$ 190.12364, $C_{12}H_{16}ON$ requires 190.12319.

114g: (*E*)-1-(Pyridin-3-yl)hex-2-en-1-one



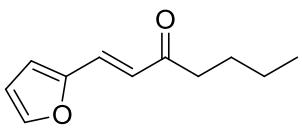
General Procedure D: 15 mg, 15% yield; ν_{max} (film/cm^{-1}) 3054, 2988, (C-H), 1635 (C=O); δ_H (600 MHz, $CDCl_3$) 0.98 (3H, t, *J* 7.4, CH_3), 1.58 (2H, app sx, *J* 7.4, C*H*$_2$CH$_3$), 2.33 (2H, br qd, *J* 7.3, 1.5, C=CC*H*$_2$), 6.85 (1H, dt, *J* 15.6, 1.5, *H*CCO), 7.11 (1H, dt, *J* 15.6, 7.3, *H*C=CCO), 7.43-7.45 (1H, m, Ar-H), 8.22 (1H, dt, *J* 8.0, 2.0, Ar-H), 8.76-8.79 (1H, m, Ar-H), 9.11-9.14 (1H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.9, 21.5, 35.1, 123.8, 125.7, 134.3 136.3, 149.7, 151.7, 152.9, 189.6; Found (EI): $[M]^+$ 176.1080, $C_{11}H_{13}ON$ requires 176.1075.

114q: (*E*)-1-(Thiophen-3-yl)hex-2-en-1-one



General Procedure D: 88 mg, 88% yield, crude *E:Z* 11:1; ν_{max} (film/cm^{-1}) 2963, 2933, 2874 (C-H), 1665 (C=O); δ_H (600 MHz, $CDCl_3$) 0.96 (3H, t, *J* 7.4, CH_3), 1.54 (2H, app sx, *J* 7.4, C*H*$_2$CH$_3$), 2.25-2.30 (2H, m, C*H*$_2$CH$_2$CH$_3$), 6.77 (1H, br d, *J* 15.5, HCCO), 7.08 (1H, dt, *J* 15.5, 7.1, HC=C(H)CO), 7.31-7.33 (1H, m, thiophene-H), 7.59 (1H, br d, *J* 4.9, thiophene-H), 8.03-8.07 (1H, m, thiophene-H); δ_C (150 MHz, $CDCl_3$) 13.9, 21.6, 34.9, 126.4, 126.7, 127.6, 132.1, 142.9, 149.1, 184.4; Found (EI): $[M]^+$ 180.06071, $C_{10}H_{12}OS$ requires 180.06034.

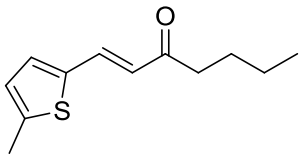
114h: (*E*)-1-(Furan-2-yl)hept-1-en-3-one



General Procedure D: 45 mg, 45% yield, crude *E:Z* 5:1; ν_{max} (film/cm^{-1}) 2961, 2934, 2875 (C-H), 1611 (C=O); δ_H (600 MHz, $CDCl_3$) 0.93 (3H, t, *J* 7.4, CH_3),

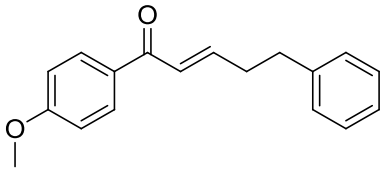
1.36 (2H, app sx, *J* 7.4, C*H*$_2$CH$_3$), 1.61-1.67 (2H, m, C*H*$_2$CH$_2$CH$_3$), 2.60 (2H, t, *J* 7.5, OCCH$_2$) 6.47 (1H, br dd, *J* 3.4, 1.5, furan-H), 6.64 (1H, d, *J* 15.8, HCCO), 6.65 (1H, d, *J* 3.4, furan-H), 7.31 (1H, d, *J* 15.8, HC=C(H)CO), 7.49 (1H, br d, *J* 1.5, furan-H); δ_C (150 MHz, $CDCl_3$) 14.0, 22.6, 26.6, 41.3, 112.6, 115.7, 123.5, 128.6, 144.9, 151.3, 200.4; Found (EI): $[M]^+$ 178.09903, $C_{11}H_{14}O_2$ requires 178.09883.

114 l: (*E*)-1-(5-Methylthiophen-2-yl)hept-1-en-3-one



General Procedure D: 84 mg, 84% yield, crude *E:Z* 7:1; ν_{max} (film/cm^{-1}) 2960, 2932, 2873 (C-H), 1651 (C=O); δ_H (600 MHz, $CDCl_3$) 0.93 (3H, t, *J* 7.4, CH$_2$C*H*$_3$), 1.36 (2H, app sx, *J* 7.4, C*H*$_2$CH$_3$), 1.63 (2H, app qn, *J* 7.4, C*H*$_2$CH$_2$CH$_3$), 2.50 (3H, s, thiophene-CH$_3$), 2.59 (2H, t, *J* 7.4, OCCH$_2$), 6.41 (1H, dd, *J* 15.8, HCCO), 6.72 (1H, br d, *J* 3.6, thiophene-H), 7.08 (1H, br d, *J* 3.6, thiophene-H), 7.58 (1H, d, *J* 15.8, HC=C(H)CO); δ_C (150 MHz, $CDCl_3$) 14.1, 16.0, 22.6, 26.7, 40.9, 123.9, 126.8, 132.5, 135.4, 138.1, 144.4, 200.4; Found (EI): $[M]^+$ 208.09115, $C_{12}H_{16}OS$ requires 208.09164.

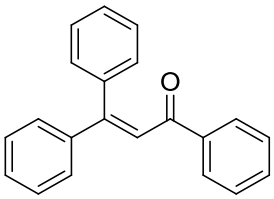
114 v: (*E*)-1-(4-Methoxyphenyl)-5-phenylpent-2-en-1-one



General Procedure D: 93 mg, 93% yield, crude *E:Z* 6:1; ν_{max} (film/cm^{-1}) 2965, 2938 (C-H), 1618 (C=O); δ_H (600 MHz, $CDCl_3$) 2.63-2.65 (2H, m, C=C(H)C*H*$_2$), 2.85 (2H, t, *J* 7.5, Ar-CH$_2$), 3.05 (3H, s, OCH$_3$), 6.88 (1H, dt, *J* 15.4, 1.3, HCCO), 6.94 (2H, d, *J* 8.9, Ar-H), 7.07 (1H, dt, *J* 15.4, 6.9, HC=C(H)CO), 7.20-7.23 (3H, m, Ar-H), 7.31 (2H, t, *J* 7.6, Ar-H), 7.91 (2H, d, *J* 8.9, Ar-H); δ_C (150 MHz,

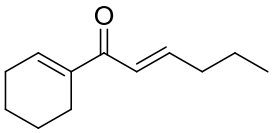
$CDCl_3$) 34.66, 34.69, 55.6, 113.9, 126.3, 128.55, 128.63, 130.83, 131.0, 141.1, 147.5, 163.4, 189.2; Found (EI): $[M]^+$ 266.13090, $C_{18}H_{18}O_2$ requires 266.13013.

155a: 1,3,3-Triphenylprop-2-en-1-one [185]



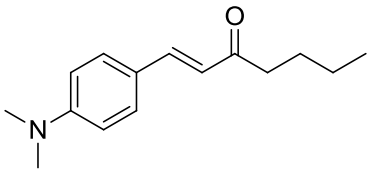
General procedure D: 82 mg, 82% yield; mp 85-87˚C (CH_2Cl_2/Hexane); δ_H (600 MHz, $CDCl_3$) 7.12 (1H, s, C=CH), 7.17-7.20 (2H, m, Ar-H), 7.25-7.29 (3H, m, Ar-H), 7.36-7.41 (7H, m, Ar-H), 7.48 (1H, br t, *J* 7.3, Ar-H), 7.91 (2H, br d, *J* 7.3, Ar-H); δ_C (150 MHz, $CDCl_3$) 124.1, 128.2, 128.49, 128.51, 128.58, 128.7, 128.9, 129.5, 129.9, 132.8, 138.3, 139.1, 141.5, 154.9, 192.8; Found (CI): $[M+H]^+$ 283.11288, $C_{21}H_{16}O$ requires 283.1174.

114r: (*E*)-1-(Cyclohex-1-en-1-yl)hex-2-en-1-one [181]



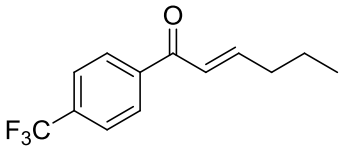
General Procedure D: 65 mg, 43% yield, crude *E*:*Z* 7:1; ν_{max} (film/cm^{-1}) 2962, 2936, 2875 (C-H), 1711 (C=O); δ_H (600 MHz, $CDCl_3$) 0.94 (3H, t, *J* 7.4, CH_3), 1.50 (2H, app sx, *J* 7.4, CH_2), 1.56-1.68 (4H, m CH_2), 2.19 (2H, app q, *J* 7.4, C=CCH_2), 2.24-2.30 (4H, m, CH_2), 6.63 (1H, br d, *J* 15.4, O=CCH), 6.84 (1H, dt, *J* 15.4, 7.4, O=CCHC=C*H*CH_2) 6.88-6.91 (1H, m, HC=C); δ_C (150 MHz, $CDCl_3$) 13.9, 21.6, 21.7, 22.1, 23.5, 26.3, 34.8, 125.0, 139.96, 140.00, 147.0, 191.6; Found (EI): $[M]^+$ 178.13492, $C_{12}H_{18}O$ requires 178.13522.

114g: (*E*)-1-(4-(Dimethylamino)phenyl)hept-1-en-3-one



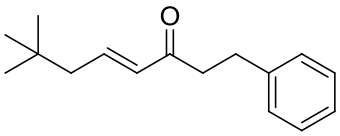
General Procedure D: 15 mg, 15% yield, crude *E:Z* 8:1; mp 70-72˚C (hexane); ν_{max} (film/cm^{-1}) 2956, 2931, 2871 (C-H), 1646 (C=O); δ_H (600 MHz, $CDCl_3$) 0.94 (3H, t, *J* 7.5, CH_3), 1.38 (2H, app sx, *J* 7.5, C*H*$_2$CH$_3$), 1.65 (2H, app qn, *J* 7.5, C*H*$_2$CH$_2$CH$_3$), 2.62 (2H, t, *J* 7.5, OCCH$_2$), 3.03 (6H, s, NMe$_2$), 6.56 (1H, d, *J* 16.0, *H*CCO), 6.68 (2H, d, *J* 8.8, Ar-H), 7.45 (2H, d, *J* 8.8, Ar-H), 7.50 (1H, d, *J* 16.0, *H*C=CCO); δ_C (150 MHz, $CDCl_3$) 14.1, 22.7, 27.1, 40.3, 40.4, 112.0, 121.7, 122.3, 130.1, 143.3, 152.0, 201.1; Found (EI): $[M]^+$ 231.16240, $C_{15}H_{21}ON$ requires 231.16176.

114p: (*E*)-1-(4-(Trifluoromethyl)phenyl)hex-2-en-1-one



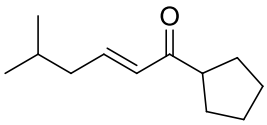
General Procedure D: 97 mg, 97% yield, crude *E:Z* 18:1; ν_{max} (film/cm^{-1}) 2964, 2935, 2877 (C-H), 1736 (C=O); δ_H (600 MHz, $CDCl_3$) 0.98 (3H, t, *J* 7.4, CH_3), 1.56 (2H, app sx, *J* 7.4, C*H*$_2$CH$_3$), 2.33 (2H, br qd, *J* 7.4, 1.5, C=CC*H*$_2$), 6.84 (1H, br dt, *J* 15.4, 1.5, *H*CCO), 7.09 (1H, dt, *J* 15.4, 7.2, *H*C=CCO), 7.73 (2H, d, *J* 8.3, Ar-H), 8.00 (2H, d, *J* 8.3, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.9, 21.5, 35.1, 123.9 (q, *J* 274,) 125.7 (q, *J* 3.7), 125.9, 128.9, 134.0 (q, *J* 32.5), 141.0, 151.6, 190.2; Found (EI): $[M]^+$ 242.09084, $C_{13}H_{13}OF_3$ requires 242.09130.

114y: (*E*)-2,2-Dimethyl-8-phenyloct-5-en-4-one



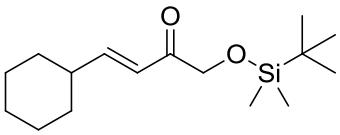
General Procedure D: 28 mg, 93%, crude *E:Z* 18:1; ν_{max} (film/cm^{-1}) 2957, 2867 (C-H), 1672 (C=O); δ_H (600 MHz, $CDCl_3$) 0.92 (9H, s, $C(CH_3)_3$), 2.08 (2H, dd, *J* 7.9, 1.0, $(CH_3)_3CCH_2$), 2.86-2.90 (2H, m, CH_2), 2.92-2.97 (2H, m, CH_2), 6.08 (1H, dt, *J* 15.7, 1.0, OCCH), 6.85 (1H, dt, *J* 15.7, 7.9, OCCH=C*H*), 7.18-7.22 (3H, m, Ar-H), 7.29 (2H, app t, *J* 7.5, Ar-H); δ_C (150 MHz, $CDCl_3$) 29.5, 30.3, 31.6, 41.9, 47.1, 126.2, 128.5, 128.6, 132.4, 141.4, 145.3, 196.6; Found (EI): $[M]^+$ 230.166881, $C_{16}H_{22}O$ requires 230.16652.

114x: (*E*)-1-Cyclopentyl-5-methylhex-2-en-1-one



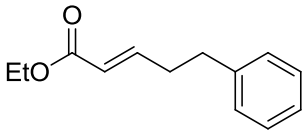
General Procedure D: 15 mg, 80% yield, crude *E:Z* 15:1; ν_{max} (film/cm^{-1}) 2305, 2873 (C-H), 1702 (C=O); δ_H (600 MHz, $CDCl_3$) 0.92 (6H, d, *J* 6.6, 2 × CH_3), 1.54-1.84 (9H, m, C*H*$(CH_3)_2$, 4 × cyclopentane-CH_2), 2.09 (2H, app t, *J* 7.2, CH_2CH=CH), 3.08 (1H, app. qn, *J* 7.9, cyclopentane-CH), 6.12 (1H, d, *J* 15.8, HC=C*H*CO), 6.82 (1H, d, *J* 15.8, 7.2, *H*C=CHCO); δ_C (150 MHz, $CDCl_3$) 22.5, 26.3, 28.0, 29.3, 41.9, 48.9, 130.8, 146.2, 202.9; Found (CI): $[M]^+$ 181.157951, $C_{12}H_{20}O$ requires 181.15869.

114z: (*E*)-1-((tert-Butyldimethylsilyl)oxy)-4-cyclohexylbut-3-en-2-one



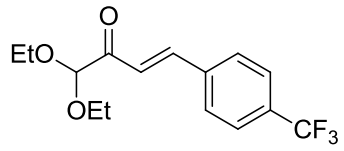
General Procedure D: 17 mg, 85% yield, crude *E:Z* 20:1; ν_{max} (film/cm^{-1}) 2995, 2880 (C-H), 1715 (C=O); δ_H (600 MHz, $CDCl_3$) 0.09 (6H, s, $Si(CH_3)_2$), 0.93 (9H, s, $SiC(CH_3)_3$), 1.10-1.34 (6H, m, 3 × cyclohexane-CH_2), 1.73-1.79 (4H, m, cyclohexane-CH_2), 2.11-2.17 (1H, m, cyclohexane-CH), 4.31 (2H, s, CH_2OSi), 6.34 (1H, dd, *J* 16.1, 1.4, HC=C*H*CO), 6.92 (1H, dd, *J* 16.1, 6.7, *H*C=CHCO); δ_C (150 MHz, $CDCl_3$) -5.3, 18.5, 25.8, 25.9, 26.0, 31.7, 40.9, 68.8, 122.8, 153.5, 199.4;

114m: (*E*)-Ethyl 5-phenylpent-2-enoate [186]



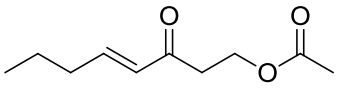
General Procedure D: Ethanol instead of methanol: 68 mg, 91% yield, crude *E:Z* 20:1; δ_H (600 MHz, $CDCl_3$) 1.08 (3H, t, *J* 7.4, CH_3), 2.51-2.56 (2H, m, $C=CCH_2$), 2.54 (2H, q, *J* 7.4, OCH_2), 2.78 (2H, t, *J* 7.6, Ar-CH_2), 6.11 (1H, dt, *J* 16.0, 1.5, O=CCH), 6.85 (1H, dt, *J* 16.0, 6.8, C=C*H*CH_2), 7.18 (2H, d, *J* 7.5, Ar-H), 7.21 (1H, t, *J* 7.5, Ar-H), 7.29, (2H, t, *J* 7.5, Ar-H); δ_C (150 MHz, $CDCl_3$) 8.2, 33.4, 34.3, 34.6, 126.3, 128.5, 128.6, 130.6, 140.9, 145.8, 201.3; Found (EI): $[M\text{-}OEt]^+$ 159.08083, $C_{11}H_{11}O$ requires 159.08044.

170a: (*E*)-1,1-Diethoxy-4-(4-(trifluoromethyl)phenyl)but-3-en-2-one



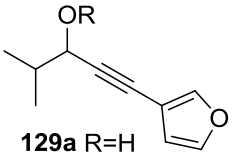
General procedure D – no methanol and DCM as solvent:40 mg, 40% yield; ν_{max} (film/cm^{-1}) 2980, 2933, 2884 (C-H), 1702 (C=O), 1615 (C=C), 1321 (C-F); δ_H (600 MHz, $CDCl_3$) 1.28 (6H, t, *J* 7.2, 2 × OCH_2CH_3), 3.63 (2H, q, *J* 7.2, OCH_2), 3.75 (2H, q, *J* 7.2, OCH_2), 4.80 (1H, s, OCH), 7.17 (1H, d, *J* 16.2, OCCH), 7.64 (2H, d, *J* 8.7, Ar-H), 7.70 (2H, d, *J* 8.7, Ar-H), 7.77 (1H, d, *J* 16.2, OCHC=C*H*); δ_C (150 MHz, $CDCl_3$) 15.3, 63.5, 102.7, 122.9, 123.8 (q, *J* 271.7), 125.9 (q, *J* 4.0), 128.8, 132.1 (q, *J* 32.1), 138.1, 142.9, 194.0; Found (CI): $[M\text{-}OEt]^+$ 257.09021, $C_{13}H_{12}F_3O_2$ requires 257.07839.

114a: (*E*)-3-Oxooct-4-en-1-yl acetate

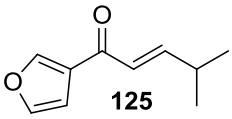


85 mg, 85% yield, crude *E:Z* 20:1; ν_{max} (film/cm^{-1}) 2961, 2933 (C-H), 1737 (C=O), 1230 (C-O); δ_H (600 MHz, $CDCl_3$) 0.93 (3H, t, *J* 7.3, CH_2CH_3), 1.49 (2H, sx, *J* 7.3, CH_2CH_3), 2.01 (3H, s, $OCCH_3$), 2.20 (2H, app q, *J* 7.3, $CH_2CH_2CH_3$), 2.87 (2H, t, *J* 6.4, CH_2), 4.36 (2H, t, *J* 6.4, CH_2), 6.10 (1H, d, *J* 16.0, OCCH), 6.85 (1H, dt, *J* 16.0, 6.9 CH_2CH); δ_C (150 MHz, $CDCl_3$)13.8, 21.0, 21.4, 34.6, 38.5, 59.7, 130.5, 148.6, 171.1, 197.3; Found (CI): $[M+H]^+$ 185.11805, $C_{10}H_{17}O_3$ requires 185.11805.

Isoegomaketone:



129a R=H
129b R=$SiMe_3$



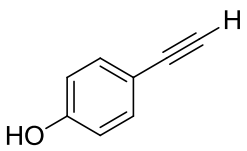
125

Isobutraldehyde (1.52 mmol, 1eq.), (furan-3-ylethynyl)trimethylsilane (3.65 mmol, 2 eq.), and tetrabutylammonium triphenyldifluorosilicate (TBAT 0.15 mmol, 0.1 eq.) were dissolved in dry THF (10 mL). The resultant solution was stirred for 20 min at 0 °C. The reaction was quenched with aq. $NaHCO_3$ and the organic phase extracted with diethyl ether. The combined organic phases were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo* to give **129a** and **129b** as a mixture of products. **129** was submitted without further purification to general reaction conditions D to give *E*-Isoegomaketone (86% yield over two steps).

ν_{max} (film/cm^{-1}) 2966, 2934, 2873 (C-H), 1667 (C=O); δ_H (600 MHz, $CDCl_3$) 1.11 (6H, d, *J* 6.8, $CH(CH_3)_2$), 2.53 (1H, m, $CH(CH_3)_2$), 6.49 (1H, dd, *J* 15.4, 1.5, HCCO), 6.83 (1H, br dd, *J* 1.7, 0.8, furan-H), 7.02 (1H, dd, *J* 15.4, 6.8, HC=C(H)CO), 7.45 (1H, br t, *J* 1.7 furan-H), 8.02-8.05 (1H, m, furan-H); δ_C (150 MHz, $CDCl_3$) 21.5, 31.4, 109.3, 124.1, 128.3, 144.3, 147.2, 154.7, 185.0; Found (EI): $[M]^+$ 164.08354, $C_{10}H_{12}O_2$ requires 164.08318.

Daphnenone synthesis:

132: (4-Hydroxyphenyl)acetylene [131]



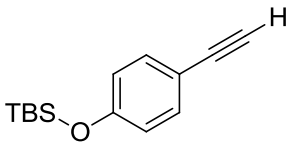
$Pd(PPh_3)_2Cl_2$ (0.40 g, 2 mmol%) Copper iodide (0.055 g, 2 mmol%), and Para-Iodophenol (2.50 g, 11.35 mmol) were dissolved in diethylamine (100 mL) under argon and stirred for 10 mins. Ethynyltrimethylsilane (3.86 mL, 27.3 mmol) was added dropwise with a syringe pump over two hours and the reaction stirred for a

futher 12 h. Sat. NH_4Cl solution (30 ml) was added to the reaction mixture and the aq. layer extracted with Et_2O (3 × 20 ml). The combined organic layers were washed with brine (50 ml) and dried (anh. $MgSO_4$). The solvent was removed *in vacuo* to give the crude product which was then filtered through a plug of silica and celite (1.95g, 10.3 mmol, 91%).

The filtered product (2.9 mmol, 1 eq.) was then dissolved in methanol with Potassium Carbonate (5.7 mmol, 3 eq.) and stirred at RT for 2 hours. After this time the reaction was neutralised with 2M HCl (10 mL) and the aq. layer extracted with EtOAc (3 ×10 mL). The combined organic layers were washed with NaHCO3 (10 mL) and brine (10 mL) and dried (anh. $MgSO_4$). The solvent was removed *in vacuo* to give the crude product without further purification (307 mg, 2.60 mmol, 90%, 82% yield over two steps).

δ_H (600 MHz, $CDCl_3$) 2.99 (1H, s, C≡CH), 5.25 (1H, br s, OH), 6.78 (2H, d, *J* 8.6, Ar-H), 7.38 (2H, d, *J* 8.6, Ar-H);

133: *tert*-Butyl(4-ethynylphenoxy)dimethylsilane [189]

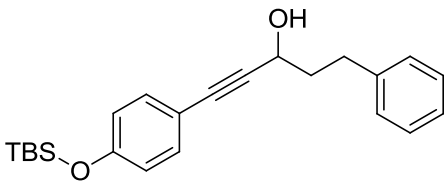


(4-Hydroxyphenyl)acetylene (400 mg, 3.43 mmol, 1 eq.) was mixed with imidazole (230 mg, 3.43 mmol 1eq.) in DMF (10 mL). To the mixture was added TBSCl (510 mg 3.43 mmol, 1 eq.). The reactants were stirred at room temperature overnight and then quenched with the addition of water. The resultant slurry was extracted with diethyl ether, the combined organic phases were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by flash column chromatography to give the protected acetylene (790 mg, 3.40 mmol, 99%).

ν_{max} (film/cm^{-1}) 2957, 2930, 2896, 2860 (C-H), 2157 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.20 (6H, s, $Si(CH_3)_2$), 0.98 (9H, s, $SiC(CH_3)_3$), 2.99 (1H, s, C≡CH), 6.78 (2H, d, *J* 8.6, Ar-H), 7.38 (2H, d, *J* 8.6, Ar-H); δ_C (150 MHz, $CDCl_3$) -4.3, 0.17,

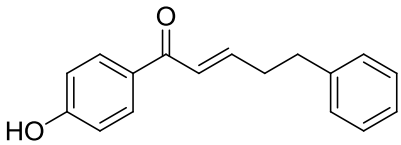
25.7, 76.0, 83.8, 114.9, 120.3, 133.7, 156.4; Found (EI): $[M]^+$ 233.12850, $C_{14}H_{20}OSi$ requires 232.12779.

135: 1-(4-((*tert*-Butyldimethylsilyl)oxy)phenyl)-5-phenylpent-1-yn-3-ol



General Procedure B: 169 mg, 77% yield; ν_{max} (film/cm^{-1}) 3650 (O-H), 3007, 2944 (C-H), 2293 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.20 (6H, s, $Si(CH_3)_2$), 0.98 (9H, s, $SiC(CH_3)_3$), 1.96 (1H, br s, OH), 2.08-2.14 (2H, m, CHC*H*$_2$), 2.86 (2H, t, *J* 7.5, Ar-CH_2), 4.59 (1H, br t, *J* 5.5, C*H*OH), 6.79 (2H, d, *J* 8.6, Ar-H), 7.19-7.22 (1H, m, Ar-H), 7.24-7.26 (2H, m, Ar-H), 7.28-7.31 (2H, m, Ar-H), 7.32 (2H, d, *J* 8.6, Ar-H); δ_C (150 MHz, $CDCl_3$) -4.3, 18.3, 25.8, 31.6, 39.5, 62.5, 85.4, 88.6, 115.4, 120.3, 126.1, 128.6, 128.7, 133.3, 141.5, 156.2; Found (EI): $[M]^+$ 366.20131, $C_{23}H_{30}O_2Si$ requires 366.20096.

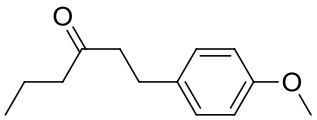
126: Daphnenone



General Procedure D: 78 mg, 93% yield; ν_{max} (film/cm^{-1}) 2954, 2926, 2856 (C-H), 1737 (C=O); δ_H (600 MHz, $CDCl_3$) 2.62-2.66 (2H, m, C=C(H)C*H*$_2$), 2.84 (2H, t, *J* 7.5, Ar-CH_2), 6.44 (1H, br s, OH), 6.88 (1H, dt, *J* 15.3, 1.3, HCCO), 6.89 (2H, d, *J* 8.8, Ar-H), 7.07 (1H, dt, *J* 15.3, 6.8, HC=C(H)CO), 7.20-7.22 (3H, m, Ar-H), 7.28-7.31 (2H, m, Ar-H), 7.85 (2H, d, *J* 8.8, Ar-H); δ_C (150 MHz, $CDCl_3$) 34.6, 34.7, 115.5, 126.26, 126.30, 128.5, 128.6, 130.6, 131.4, 141.0, 148.1, 160.4, 189.7; Found (EI): $[M]^+$ 252.11537, $C_{17}H_{16}O_2$ requires 252.11448.

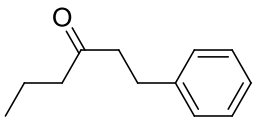
3. One-Pot Reactions of Primary Propargylic Alcohols

161a: 1-(4-Methoxyphenyl)-hexan-3-one [190]



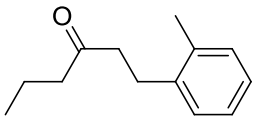
General Procedure E: 170 mg, 81% yield; ν_{max} (film/cm^{-1}) 2960, 2835 (C-H), 1710 (C=O), 1511 (Ar-OMe); δ_H (500 MHz, $CDCl_3$) 0.89 (3H, t, *J* 7.4, CH_2CH_3), 1.58 (2H, app sx, *J* 7.4, CH_2CH_3), 2.35 (2H, t, *J* 7.4, $CH_3CH_2CH_2$), 2.68 (2H, t, *J* 7.6, CH_2CH_2Ar), 2.83 (2H, t, *J* 7.6, CH_2CH_2Ar), 3.77 (3H, s, OMe), 6.81 (2H, d, *J* 8.5, Ar-H) 7.09 (2H, d, *J* 8.5, Ar-H); δ_C (125 MHz, $CDCl_3$) 13.8, 17.3, 29.1, 44.4, 44.7, 55.4, 114.3, 129.5, 133.4, 158.0, 210.5; Found (EI): $[M]^+$ 206.13054, $C_{13}H_{18}O_2$ requires 206.13012.

161f: 1-Phenyl-hexan-3-one [191]



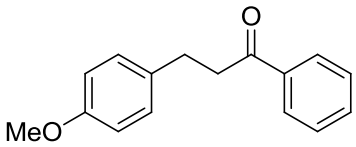
General Procedure E: 80 mg, 45% yield; ν_{max} (film/cm^{-1}) 3027, 2961, 2932, 2875 (C-H), 1712 (C=O), 1604 (Ar-H); δ_H (500 MHz, $CDCl_3$) 0.88 (3H, t, *J* 7.5, CH_3), 1.56 (2H, app sx, *J* 7.5, CH_2CH_3), 2.36 (2H, t, *J* 7.5, $CH_2CH_2CH_3$), 2.71 (2H, t, *J* 7.6, CH_2CH_2Ar), 2.90 (2H, t, *J* 7.6, CH_2CH_2Ar), 7.16-7.30 (5H, m, Ar-H); δ_C (125 MHz, $CDCl_3$) 13.8, 17.3, 29.9, 44.4, 45.0, 125.5, 127.91, 128.5, 141.3, 210.5; Found (CI): $[M+H]^+$ 177.12758, $C_{12}H_{16}0$ requires 176.12012.

161c: 1-Tolyl-hexan-3-one



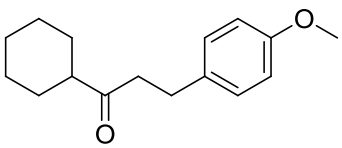
General procedure E: 72 mg, 37% yield; ν_{max} (film/cm^{-1}) 2932 (C-H), 1682 (C=O); δ_H (600 MHz, $CDCl_3$) 0.91 (3H, t, *J* 7.5, CH_3), 1.61 (2H, sx, *J* 7.4, CH_2), 2.31 (3H, s, Ar-Me), 2.39 (2H, t, *J* 7.4, CH_2), 2.66-2.69 (2H, m, CH_2), 2.87-2.90 (2H, m, CH_2), 7.09-7.15 (4H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.9, 17.4, 19.4, 27.2, 43.0, 44.9, 126.2, 126.4, 128.7, 130.4, 136.0, 139.4, 210.5; Found (EI): $[M]^+$ 191.14384, $C_{13}H_{19}O$ requires 191.14359.

161b: 3-(4-Methoxy-phenyl)-1-phenyl-1-propan-1-one [192]



General Procedure E: 100 mg, 58% yield; mp 61-63˚C (hexane); ν_{max} (film/cm^{-1}) 3061, 3029, 3000, 2931, 2834 (C-H), 1682 (C=O), 1510 (Ar-OMe); δ_H (600 MHz, $CDCl_3$) 3.00-3.04 (2H, m, O=CCH_2), 3.26-3.30 (2H, m, ArCH_2), 3.79 (2H, s, OMe), 6.85 (2H, d, *J* 8.6, Ar-H), 7.18 (2H, d, *J* 8.6, Ar-H), 7.45-7.48 (2H, m, Ar-H), 7.54-7.57 (2H, m, Ar-H), 7.95-7.99 (1H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 29.5, 41.1, 55.5, 114.2, 128.2, 128.7, 129.5, 133.2, 133.4, 137.0, 158.1, 199.6.

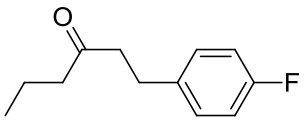
1-Cyclohexyl-3-(4-methoxy-phenyl)-propan-1-one [193]



General Procedure E: 51 mg, 29% yield; ν_{max} (film/cm^{-1}) 2927, 2853 (C-H), 1705 (C=O) 1512 (1,4-Ar); δ_H (600 MHz, $CDCl_3$) 1.13-1.34 (5H, m, Cyclohexane), 1.62-1.82 (5H, m, Cyclohexane), 2.30 (1H, tt, *J* 11.2, 3.3, CH), 2.72 (2H, t, *J* 7.5,

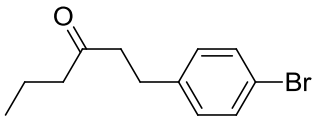
CH_2), 2.81 (2H, t, *J* 7.5, CH_2), 3.77 (2H, s, OMe), 6.81 (2H, d, *J* 8.5, Ar-H) 7.10 (2H, d, *J* 8.5, Ar-H); δ_C (150 MHz, $CDCl_3$) 25.8, 26.0, 28.5, 29.0, 52.6, 51.1, 55.4, 113.9, 119.4, 133.6, 158.0, 213.5.

161g: 1-(4-Fluoro-phenyl)-hexan-3-one [190]



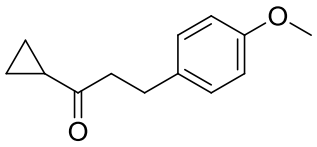
General Procedure E: 46 mg, 23% yield; ν_{max} (film/cm^{-1}) 2962, 2933, 2876 (C-H), 1712 (C=O), 1510 (1,4-Ar); δ_H (600 MHz, $CDCl_3$) 0.89 (3H, t, *J* 7.4 CH_3), 1.58 (2H, sx, *J* 7.4, CH_2), 2.35 (2H, t, *J* 7.4, CH_2), 2.69 (2H, t, *J* 7.4, CH_2), 2.86 (2H, t, *J* 7.4, CH_2), 6.95 (2H, t, *J* 8.6, Ar-H) 7.13 (2H, dd, *J* 8.6, 5.3, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.8, 17.3, 29.0, 44.4, 55.1, 115.3 (d, *J* 21.0), 129.8 (d, *J* 7.3), 136.9 (d, *J* 3.3), 161.4 (d, *J* 245.0), 210.2.

161h: 1-(4-Bromo-phenyl)-hexan-3-one [194]



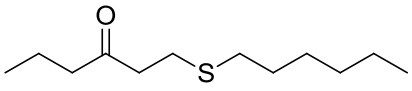
General Procedure E: 31 mg, 12% yield; δ_H (500 MHz, $CDCl_3$) 0.89 (3H, td, *J* 7.4, 2.0, CH_3), 1.54-1.64 (2H, m, $COCH_2CH_2$), 2.36 (2H, td, *J* 7.3, 1.9, Ar-CH_2), 2.69 (2H, td, *J* 7.4, 1.8, $COCH_2$), 2.84 (2H, td, *J* 7.4, 1.6, $COCH_2$), 7.05 (2H, dd, *J* 8.5, 1.8, Ar-H), 7.39 (2H, dd, *J* 8.5, 1.8, Ar-H); δ_C (125 MHz, $CDCl_3$) 13.8, 17.3, 29.2, 44.0, 45.0, 119.9, 130.3, 131.6, 140.3, 209.9; Found (EI): $[M]^+$ 254.03086, $C_{12}H_{15}OBr$ requires 254.03008.

161e: 1-Cyclopropyl-3-(4-methoxy-phenyl)-propan-1-one [195]



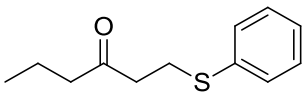
General Procedure E: 25 mg, 20% yield; ν_{max} (film/cm^{-1}) 3006, 2931, 2836 (C-H), 1696 (C=O); δ_H (500 MHz, $CDCl_3$) 0.83-0.86 (2H, m, cyclopropane CH_2), 0.99-1.04 (2H, m, cyclopropane CH_2), 1.88-1.93 (1H, m, CH), 2.84-2.89 (4H, m, $COCH_2CH_2$), 3.78 (3H, s, OMe), 6.83 (2H, d, *J* 8.5, Ar-H), 7.11 (2H, d, *J* 8.5, Ar-H); δ_C (125 MHz, $CDCl_3$) 10.9, 20.7, 29.2, 45.4, 55.8, 114.0, 128.5, 133.4, 158.0, 210.4.

160a: 1-Hexylsulfanyl-hexan-3-one [196]



General Procedure E: 130 mg, 41% yield; ν_{max} (film/cm^{-1}) 2958, 2926, 2857 (C-H), 1710 (C=O); δ_H (600 MHz, $CDCl_3$) 0.88 (3H, t, *J* 7.0, CH_3), 0.91 (3H, t, *J* 7.2 CH_3), 1.22-1.39 (6H, m, CH_2), 1.53-1.65 (4H, m, CH_2), 2.40 (2H, t, *J* 7.5, CH_2), 2.50 (2H, t, *J* 7.5, CH_2), 2.66-2.69 (2H, m, SCH_2), 2.71-2.74 (2H, m, SCH_2); δ_C (150 MHz, $CDCl_3$) 13.8, 14.2, 17.3, 22.7, 25.9, 28.7, 29.7, 31.5, 32.6, 42.9, 45.1, 209.5.

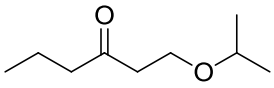
160b: 1-(Phenylthio)hexan-3-one [197]



General Procedure E: 140 mg, 46 % yield; ν_{max} (film/cm^{-1}) 2961, 2933, 2875 (C-H), 1710 (C=O); δ_H (600 MHz, $CDCl_3$) 0.90 (3H, t, *J* 7.4, CH_3), 1.53-1.58 (2H, m, CH_2), 2.37 (2H, t, *J* 7.4, $O=CCH_2$), 2.72 (2H, t, *J* 7.4, $O=CCH_2$), 3.14 (2H, t, *J* 7.4, SCH_2), 7.18-7.21 (1H, m, Ar-H) 7.27-7.31 (2H, m, Ar-H) 7.32-7.35 (2H, m,

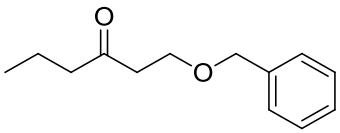
Ar-H); δ_C (150 MHz, $CDCl_3$) 13.8, 17.3, 27.6, 42.2, 45.1, 126.4, 129.1, 129.5, 135.9, 209.2.

158b: 1-Isopropoxyhexan-3-one



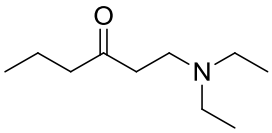
General Procedure E: 76% yield; ν_{max} (film/cm^{-1}) 2966, 2935, 2875 (C-H), 1710 (C=O); δ_H (600 MHz, $CDCl_3$) 0.86 (3H, t, *J* 7.4, CH_3), 1.08 (6H, d, *J* 6.1, $CH(CH_3)_2$), 1.60 (2H, app sx, *J* 7.4, CH_2), 2.37 (2H, t, *J* 7.4, $O{=}CCH_2$), 2.58 (2H, t, *J* 6.5, OCH_2CH_2), 3.51 (2H, septuplet, *J* 6.1, CH), 3.62 (2H, t, *J* 6.5, OCH_2CH_2); δ_C (150 MHz, $CDCl_3$) 13.8, 17.1, 22.1, 43.2, 45.4, 63.2, 71.8, 209.9; Found (EI): $[M+H]^+$ 159.13881, $C_9H_{19}O_2$ requires 159.13850.

158c: 1-(Benzyloxy)hexan-3-one



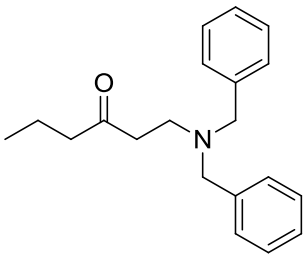
General Procedure E: 190 mg, 63% yield; ν_{max} (film/cm^{-1}) 2963, 2935, 2875 (C-H), 1712 (C=O); δ_H (600 MHz, $CDCl_3$) 0.91 (3H, t, *J* 7.4, CH_3), 1.59 (2H, app sx, *J* 7.4, CH_2), 2.43 (2H, t, *J* 7.3, $O{=}CCH_2$), 2.69 (2H, t, *J* 6.3, OCH_2CH_2), 3.74 (2H, t, *J* 6.3, OCH_2CH_2), 4.51 (2H, s, OCH_2Ar), 7.25-7.36 (5H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.8, 17.1, 43.0, 45.5, 65.5, 73.4, 127.77, 127.81, 128.5, 138.2, 209.6; Found (EI): $[M+H]^+$ 207.13812, $C_{13}H_{19}O_2$ requires 207.13850.

159a: 1-(Diethylamino)hexan-3-one



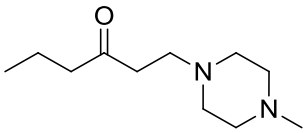
General Procedure E: 176 mg, 70% yield; ν_{max} (film/cm^{-1}) 2962, 2928, 2876 (C-H), 1713 (C=O); δ_H (600 MHz, $CDCl_3$) 0.91 (3H, t, *J* 7.4, CH_3), 1.01 (6H, t, *J* 7.3, NCH_2CH_3), 1.59 (2H, app sx, *J* 7.4, CH_2), 2.40 (2H, t, *J* 7.4, $O{=}CCH_2$), 2.50 (4H, q, *J* 7.3, 4H), 2.55 (2H, t, *J* 7.5, NCH_2CH_2), 2.74 (2H, t, *J* 7.5, NCH_2CH_2); δ_C (150 MHz, $CDCl_3$) 11.8, 13.9, 17.3, 40.5, 45.3, 47.0, 47.4, 210.9; Found (EI): $[M]^+$ 171.16234, $C_{10}H_{21}ON$ requires 171.16177.

159b: 1-(Dibenzylamino)hexan-3-one



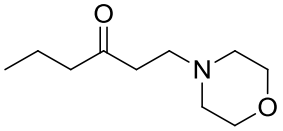
General Procedure E: 65% yield; ν_{max} (film/cm^{-1}) 2961, 2932, 2874 (C-H), 1708 (C=O); δ_H (600 MHz, $CDCl_3$) 0.85 (3H, t, *J* 7.4, CH_3), 1.53 (2H, app sx, *J* 7.4, CH_2), 2.23 (2H, t, *J* 7.4, $O{=}CCH_2$), 2.56 (2H, t, *J* 7.2, NCH_2CH_2), 2.76 (2H, t, *J* 7.2, NCH_2), 3.55 (4H, s, NCH_2Ar), 7.22-7.33 (10H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.8, 17.2, 41.0, 44.6, 48.7, 58.4, 127.1, 128.3, 129.0, 139.5, 210.6; Found (EI): $[M]^+$ 295.19352, $C_{20}H_{25}NO$ requires 295.19307.

159f: 1-(4-Methylpiperazin-1-yl)hexan-3-one



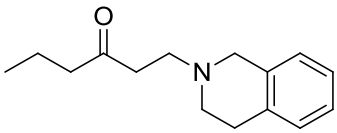
General Procedure E: 230 mg, 79% yield; ν_{max} (film/cm^{-1}) 2961, 2936, 2876, 2794 (C-H), 1711 (C=O); δ_H (600 MHz, $CDCl_3$) 0.89 (3H, t, *J* 7.4, CH_3), 1.58 (2H, app sx, *J* 7.4, CH_2), 2.20-2.71 (8H, m, 4 × CH_2), 2.26 (3H, s, CH_3), 2.39 (2H, t, *J* 7.4, CH_2), 2.58 (2H, t, *J* 7.1, CH_2), 2.65 (2H, t, *J* 7.1, CH_2); δ_C (150 MHz, $CDCl_3$) 13.9, 17.3, 40.4, 45.1, 46.1, 52.8, 53.1, 55.2, 210.2; Found (EI): $[M]^+$ 198.17302, $C_{11}H_{22}ON_2$ requires 198.17266.

159c: 1-Morpholinohexan-3-one



General Procedure E: 226 mg, 83% yield; ν_{max} (film/cm^{-1}) 2960, 2855, 2809 (C-H), 1709 (C=O); δ_H (600 MHz, $CDCl_3$) 0.90 (3H, t, *J* 7.4, CH_3), 1.60 (2H, app sx, *J* 7.4, CH_2), 2.40 (2H, t, *J* 7.4, C*H*$_2$CH$_2$CH$_3$), 2.42 (4H, br s, 2 × CH_2), 2.55-2.67 (4H, m, 2 × CH_2), 3.68 (4H, br t, *J* 4.6, 2 × CH_2); δ_C (150 MHz, $CDCl_3$) 13.8, 17.2, 40.1, 45.1, 53.2, 53.7, 67.0, 209.9; Found (EI): $[M]^+$ 186.15011, $C_{10}H_{20}O_2N$ requires 186.14940.

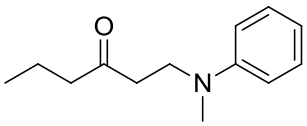
159e: 1-(3,4-Dihydroisoquinolin-2(1H)-yl)hexan-3-one



General Procedure E: 282 mg, 84% yield; ν_{max} (film/cm^{-1}) 2960, 2931, 2874 (C-H), 1709 (C=O); δ_H (600 MHz, $CDCl_3$) 0.91 (3H, t, *J* 7.4, CH_3), 1.61 (2H, app sx, *J* 7.4, CH_2), 2.44 (2H, t, *J* 7.4, C*H*$_2$CH$_2$CH$_3$), 2.71 (2H, t, *J* 7.3, CH_2), 2.74 (2H, t,

J 6.0, CH_2), 2.84 (2H, t, *J* 7.3, CH_2), 2.89 (2H, br t, *J* 6.0, CH_2), 3.63 (2H, br s, CH_2), 6.99-7.03 (1H, m, Ar-H), 7.07-7.13 (3H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.9, 17.3, 29.2, 40.8, 45.2, 51.1, 52.7, 56.2, 125.8, 126.3, 126.7, 128.7, 134.2, 134.5, 210.2; Found (EI): $[M]^+$ 232.1707, $C_{15}H_{22}ON$ requires 232.1701.

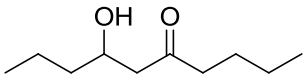
159d: 1-(Methyl(phenyl)amino)hexan-3-one



General Procedure E: 156 mg, 52% yield; ν_{max} (film/cm^{-1}) 2963, 2951, 2810 (C-H), 1710 (C=O); δ_H (600 MHz, $CDCl_3$) 0.89 (3H, t, *J* 7.4, CH_3), 1.54-1.63 (2H, m, CH_2), 2.38 (2H, t, *J* 7.4, $CH_2CH_2CH_3$), 2.67 (2H, t, *J* 6.9, CH_2), 2.92 (3H, br s, CH_3), 3.64 (2H, t, *J* 6.9, CH_2) 6.69-6.72 (3H, m, Ar-H), 7.22-7.25 (2H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.8, 17.2, 38.6, 39.4, 45.6, 47.5, 112.5, 116.7, 128.7, 129.4, 210.5; Found (EI): $[M]^+$ 205.14639 $C_{13}H_{19}ON$ requires 205.14612.

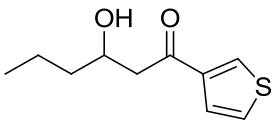
4. β-hydroxyketone products

163a: 7-Hydroxydecan-5-one [198]



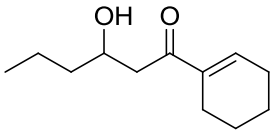
General procedure F: 65% yield; ν_{max} (film/cm^{-1}) 3429 (O-H), 2958, 2932, 2873 (C-H), 1704 (C=O); δ_H (600 MHz, $CDCl_3$) 0.90 (3H, t, *J* 7.4, $OC(CH_2)_3CH_3$), 0.92 (3H, t, *J* 7.2, $HOCH(CH_2)_2CH_3$) 1.25-1.59 (8H, m, 2 × CH_2CH_3, 2 × $CH_2CH_2CH_3$), 2.42 (2H, t, *J* 7.4, $OCCH_2$), 2.49 (1H, dd, *J* 17.6, 8.4, $HOCHCH_2CO$), 2.59 (1H, dd, *J* 17.6, 2.7, $HOCHCH_2CO$), 4.02-4.06 (1H, m, CHOH); δ_C (150 MHz, $CDCl_3$) 13.9, 14.1, 18.7, 22.3, 25.8, 38.6, 43.5, 49.0, 67.4, 212.7.

163c: 3-Hydroxy-1-(thiophen-3-yl)hexan-1-one



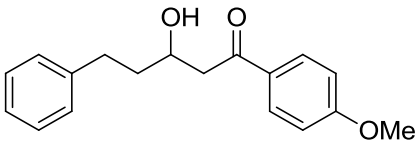
General procedure F: 62% yield; ν_{max} (film/cm^{-1}) 3505 (O-H), 2962, 2933, 2875 (C-H), 1667 (C=O); δ_H (600 MHz, $CDCl_3$) 0.95 (3H, t, *J* 7.3, CH_3), 1.36-1.63 (4H, m, $CH_2CH_2CH_3$), 2.95 (1H, dd, *J* 17.4, 9.1, CH_2CO), 3.08 (1H, dd, *J* 17.4, 2.6, CH_2CO), 3.24 (1H, br s, OH) 4.19-4.23 (1H, m, CHOH), 7.33 (1H, dd, *J* 5.2, 2.8, Thiophene-H), 7.54 (1H, dd, *J* 5.2, 1.2, Thiophene-H), 8.07 (1H, dd, *J* 2.8, 1.2, Thiophene-H); δ_C (150 MHz, $CDCl_3$) 14.2, 18.9, 38.8, 46.3, 67.7, 126.7, 126.8, 132.7, 142.3, 195.4; Found (CI): $[M+H]^+$ 199.07955, $C_{10}H_{15}O_2S$ requires 199.07928.

163i: 1-(Cyclohex-1-en-1-yl)-3-hydroxyhexan-1-one



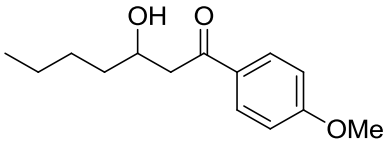
General procedure F: 69% yield; ν_{max} (film/cm^{-1}) 3502 (O-H), 2961, 2935, 2875 (C-H), 1710 (C=O); δ_H (600 MHz, $CDCl_3$) 0.93 (3H, t, *J* 7.3, CH_3), 1.35-1.42 (2H, m, C*H*$_2$CH$_3$), 1.46-1.54 (2H, m, CHC*H*$_2$), 1.59-1.67 (4H, m, cyclohexyl-CH_2), 2.21-2.28 (4H, m, cyclohexyl-CH_2), 2.66 (1H, dd, *J* 17.3, 9.4, OCCH$_2$), 2.85 (1H, dd, *J* 17.3, 2.4, OCCH$_2$), 3.34 (1H, br s, OH), 4.04-4.09 (1H, br m, C*H*OH), 6.92-6.95 (1H, m, HC=C); δ_C (150 MHz, $CDCl_3$) 14.2, 18.9, 21.6, 21.9, 23.0, 26.3, 38.8, 43.3, 67.8, 139.5, 141.5, 202.3; Found (CI): $[M+H]^+$ 197.15389, $C_{12}H_{21}O_2$ requires 197.15415.

163d: 3-Hydroxy-1-(4-methoxyphenyl)-5-phenylpentan-1-one



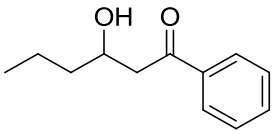
General procedure F:70% yield; ν_{max} (film/cm^{-1}) 3542 (O-H), 3054, 2987 (C-H), 1712 (C=O); δ_H (600 MHz, $CDCl_3$) 1.76-1.83 (1H, m, CHC*H*$_2$CH$_2$), 1.90-1.97 (1H, m, CHC*H*$_2$CH$_2$), 2.72-2.78 (1H, m, CHCH$_2$C*H*$_2$), 2.86-2.92 (1H, m, CHCH$_2$C*H*$_2$), 3.00 (1H, dd, *J* 17.5, 9.2, OCCH$_2$), 3.12 (1H, dd, *J* 17.5, 2.4, OCCH$_2$), 3.50 (1H, br d, *J* 2.78, OH), 3.87 (3H, s, OMe), 4.19-4.24 (1H, br m, C*H*OH), 6.93 (2H, d, *J* 8.9, Ar-H), 7.19 (1H, t, *J* 7.2, Ar-H), 7.23 (2H, d, *J* 7.0, Ar-H), 7.29 (2H, t, *J* 7.6, Ar-H), 7.92 (2H, d, *J* 8.9, Ar-H); δ_C (150 MHz, $CDCl_3$) 32.0, 38.3, 44.6, 55.7, 67.3, 113.9, 126.0, 128.5, 128.6, 129.9, 130.5, 142.1, 164.0, 199.6; Found (EI): $[M+Na]^+$ 307.1306, $C_{18}H_{20}O_3Na$ requires 307.1310.

163e: 3-Hydroxy-1-(4-methoxyphenyl)heptan-1-one



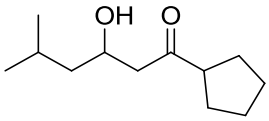
General Procedure F: 75%; ν_{max} (film/cm^{-1}) 3500 (O-H), 3003, 2958, 2933 (C-H), 1713 (C=O); δ_H (600 MHz, $CDCl_3$) 0.92 (3H, t, J 7.3, CH3), 1.33-1.66 (6H, m, CH2CH2CH2CH3), 2.97 (1H, dd, J 17.5, 9.2, OCCH2), 3.14 (1H, dd, J 17.5, 2.4, OCCH2), 3.39 (1H, s, OH), 3.88 (3H, s, OMe), 4.16-4.22 (1H, m, HOCH), 6.94 (2H, d, J 8.8, Ar-H), 7.95 (2H, d, J 8.8, Ar-H); δ_C (150 MHz, $CDCl_3$) 14.1, 22.7, 27.8, 36.3, 44.6, 55.6, 68.0, 113.9, 130.0, 130.5, 163.9, 199.7; Found (EI): $[M+H]^+$ 249.14714, $C_{14}H_{21}O_3$ requires 249.14852.

163b: 3-Hydroxy-1-phenylhexan-1-one



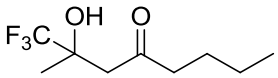
General procedure F: 54% yield; ν_{max} (film/cm^{-1}) 3451 (O-H), 2959, 2928, 2871 (C-H), 1710 (C=O); δ_H (600 MHz, $CDCl_3$) 0.96 (3H, t, *J* 7.3, CH_3), 1.40-1.50 (2H, m, C*H*$_2$CH$_3$), 1.57-1.66 (2H, m, C*H*$_2$CH$_2$CH$_3$), 3.05 (1H, dd, *J* 17.6, 9.1, OCCH$_2$), 3.17 (1H, d, *J* 17.6, 2.4, OCCH$_2$), 4.21-4.26 (1H, m, HOC*H*), 7.48 (2H, t, *J* 7.6, Ar-H), 7.59 (1H, bt t, *J* 7.6, Ar-H), 7.95-7.97 (1H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 14.2, 18.9, 38.7, 45.1, 67.6, 128.2, 128.8, 133.7, 136.9, 201.2; Found (CI): $[M+H]^+$ 193.12337, $C_{12}H_{17}O_2$ requires 193.12285.

163f: 1-Cyclopentyl-3-hydroxy-5-methylhexan-1-one



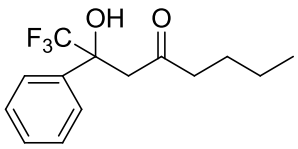
General Procedure F: 50% yield; ν_{max} (film/cm^{-1}) 3480 (O-H), 2980, 2945, 2898 (C-H), 1700 (C=O); δ_H (600 MHz, $CDCl_3$) 0.91 (6H, dd, *J* 6.8, 2.3, 2×CH_3), 1.10-1.15 (1H, m, CH), 1.44-1.49 (1H, m, CH), 1.57-1.84 (9H, m, CH, 4×CH_2), 2.52 (1H, dd, *J* 17.7, 9.0, OCCH_2), 2.62 (1H, dd, *J* 17.7, 2.6, OCCH_2), 2.85 (1H, qn, *J* 7.9, CH), 3.13 (1H, br s, OH), 4.11 (1H, br m, C*H*OH); δ_C (150 MHz, $CDCl_3$) 22.1, 23.5, 24.5, 26.1, 28.8, 28.9, 45.6, 48.5, 52.1, 65.9, 215.0; Found (CI): $[M+H]^+$ 199.17059, $C_{12}H_{23}O_2$ requires 199.16980.

163h: 1,1,1-Trifluoro-2-hydroxy-2-methyl-octan-4-one



General Procedure F (heated to 80˚C): 90% yield; ν_{max} (film/cm^{-1}) 3446 (O-H), 2960, 2930, 2873 (C-H), 1725 (C=O); δ_H (600 MHz, $CDCl_3$) 0.91 (3H, t, *J* 7.5, CH_2CH_3), 1.32 (2H, sx, *J* 7.5, CH_2CH_3), 1.39 (3H, s, CCH_3), 1.53-1.59 (2H, m, $CH_2CH_2CH_3$), 2.47-2.50 (2H, m, OCCH_2), 2.55 (1H, d, *J* 16.8, HOCCH_2CO), 2.92 (1H, d, *J* 16.8, HOCCH_2CO) 5.2 (1H, s, OH); δ_C (150 MHz, $CDCl_3$) 13.9, 22.2, 25.3, 44.4, 44.6, 73.2 (q, *J* 29.0), 125.8 (q, *J* 287.4), 212.0; Found (CI): $[M+H]^+$ 213.11064, $C_9H_{16}O_2F_3$ requires 213.11024.

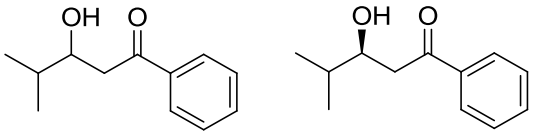
163g: 1,1,1-Trifluoro-2-hydroxy-2-phenyl-octan-4-one



General procedure F (heated to 80˚C): 80% yield; ν_{max} (film/cm^{-1}) 3395 (O-H), 2961, 2935, 2875 (C-H), 1702 (C=O); δ_H (600 MHz, $CDCl_3$) 0.85 (3H, t, *J* 7.4,

C*H*$_3$), 1.21 (2H, sx, *J* 7.4, C*H*$_2$CH$_3$), 1.48 (2H, qn, *J* 7.4, C*H*$_2$CH$_2$CH$_3$), 2.39 (1H, dt, *J* 17.3, 7.3, OCC*H*$_2$CH$_2$), 2.50 (1H, dt, *J* 17.3, 7.3, OCC*H*$_2$CH$_2$), 3.16 (1H, d, *J* 17.3, HOCC*H*$_2$CO), 3.32 (1H, d, *J* 17.3, HOCC*H*$_2$CO), 5.62 (1H, s, OH), 7.34-7.42 (3H, m, Ar-H), 7.56 (2H, d, *J* 7.7, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.8, 22.1, 25.2, 44.4, 44.8, 76.2 (q, *J* 29.3), 124.6 (q, *J* 282.5), 126.3, 128.6, 128.9, 137.6, 211.7; Found (CI): $[M+H]^+$ 275.12623, $C_{14}H_{18}O_2F_3$ requires 275.12589.

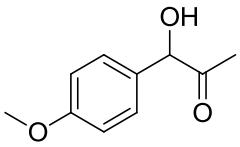
166: 3-Hydroxy-4-methyl-1-phenylpentan-1-one



General procedure F : 65% yield, 95:5 er; ν_{max} (film/cm^{-1}) 3472 (O-H), 2960, 2928, 2874 (C-H), 1676 (C=O); δ_H (600 MHz, $CDCl_3$) 0.99 (3H, d, *J* 6.8, CH_3), 1.02 (3H, d, *J* 6.8, CH_3), 1.77-1.83 (2H, m, C*H*CH$_3$), 3.03 (1H, dd, *J* 17.4, 9.5, CH_2), 3.17 (1H, dd, *J* 17.4, 2.2, CH_2), 3.19 (1H, br s, OH), 3.98-4.01 (1H, m, C*H*OH), 7.45 (2H, t, *J* 7.6, Ar-H), 7.59 (1H, t, *J* 7.6, Ar-H), 7.95-7.98 (2H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 18.0, 18.7, 33.2, 42.0, 72.5, 128.2, 128.8, 133.6, 137.0, 201.5; Found (EI): $[M]^+$ 193.12302, $C_{12}H_{17}O_2$ requires 193.12285. $[\alpha]_D^{22}$ – 0.20 (c 1 in $CHCl_3$).

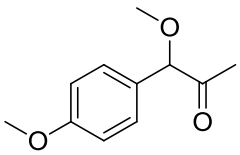
5. Terminal Alkyne Hydration

155: 1-Hydroxy-1-(4-methoxyphenyl)propan-2-one



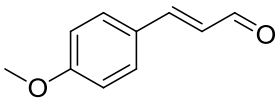
General Procedure D: 70% yield; ν_{max} (film/cm^{-1}) 3465 (O-H), 3055, 2988 (C-H), 1712 (C=O); δ_H (600 MHz, $CDCl_3$) 2.07 (3H, s, $OCCH_3$) 3.81 (3H, s, OCH_3), 4.24 (1H, br d, *J* 3.5, OH), 5.05 (1H, br d, *J* 3.5, C*H*OH), 6.91 (2H, d, *J* 8.9, Ar-H), 7.23 (2H, d, *J* 8.9, Ar-H); δ_C (150 MHz, $CDCl_3$) 25.4, 55.4, 114.1, 114.5, 128.8, 130.1, 160.0, 207.5; Found (EI): $[M]^+$ 180.07883, $C_{10}H_{12}O_3$ requires 180.07810.

154: 1-Methoxy-1-(4-methoxyphenyl)propan-2-one [199]



General Procedure D: 98 mg, 82% yield; ν_{max} (film/cm^{-1}) 3002, 2937, 2909 (C-H), 1716 (C=O); δ_H (600 MHz, $CDCl_3$) 2.10 (3H, s, CH_3), 3.35 (3H, s, CHOC*H*$_3$), 3.81 (3H, s, $ArOCH_3$), 4.61 (1H, s, CH), 6.91 (2H, d, *J* 8.5, Ar-H), 7.29 (2H, d, *J* 8.5, Ar-H); δ_C (150 MHz, $CDCl_3$) 25.4, 55.4, 57.1, 89.0, 114.4, 128.5, 130.5, 160.1, 206.8;

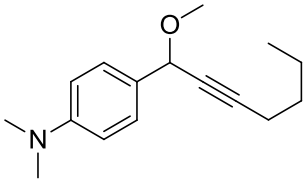
153: (*E*)-3-(4-Methoxyphenyl)acrylaldehyde



δ_H (600 MHz, $CDCl_3$) 3.86 (3H, s, OCH_3), 6.62 (1H, dd, *J* 15.8, 7.6, HC=C-Ar), 6.95 (2H, d, *J* 8.8, Ar-H), 7.43 (1H, d, *J* 15.8, Ar-CH), 7.53 (2H, d, *J* 8.8, Ar-H), 9.65 (1H, d, *J* 7.6, O=CH); δ_C (150 MHz, $CDCl_3$) 55.6, 114.7, 126.7, 126.9, 127.9, 152.9, 162.3, 193.9.

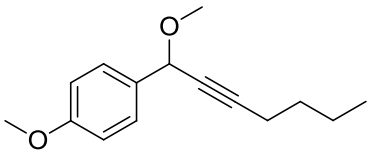
6. Ag catalysed Nucleophillic Substitution

142: 4-(1-Methoxyhept-2-yn-1-yl)-N,N-dimethylaniline



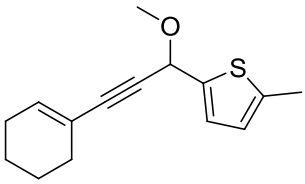
General Procedure G: 21 mg, 20% yield; ν_{max} (film/cm^{-1}) 2956, 2930, 2871 (C-H), 2245 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.92 (3H, t, *J* 7.3, CH_3), 1.40-1.47 (2H, m, C*H*$_2$CH$_3$), 1.51-1.56 (2H, m, C*H*$_2$CH$_2$CH$_3$), 2.29 (2H, td, *J* 7.1, 2.0, C≡CC*H*$_2$), 2.95 (6H, s, NMe_2), 3.34 (3H, s, OMe), 4.99 (1H, br t, *J* 2.0, CHOMe), 6.71 (2H, d, *J* 8.7, Ar-H), 7.35 (2H, d, *J* 8.7, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.8, 18.7, 22.1, 30.9, 40.7, 55.2, 73.1, 78.2, 88.0, 112.4, 126.9, 128.7, 150.7; Found (EI): $[M]^+$ 245.17828, $C_{16}H_{23}ON$ requires 245.17742.

136a: 1-Methoxy-4-(1-methoxyhept-2-yn-1-yl)benzene [200]



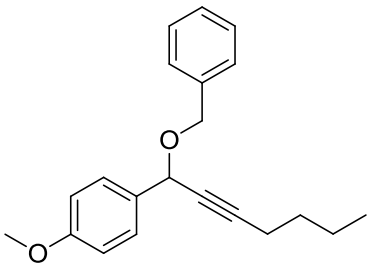
General Procedure G: 58 mg, 54% yield; δ_H (600 MHz, $CDCl_3$) 0.92 (3H, t, *J* 7.3, CH_3), 1.40-1.47 (2H, m, C*H*$_2$CH$_3$), 1.51-1.56 (2H, m, C*H*$_2$CH$_2$CH$_3$), 2.29 (2H, td, *J* 7.2, 1.9, C≡CC*H*$_2$), 3.37 (3H, s, OMe), 3.81 (3H, s, OMe), 5.02 (1H, br t, *J* 1.9, CHOMe), 6.89 (2H, d, *J* 8.6, Ar-H), 7.42 (2H, d, *J* 8.6, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.7, 18.7, 22.1, 30.9, 55.4, 55.5, 72.9, 77.8, 88.5, 113.8, 128.9, 131.5, 159.7; Found (EI): $[M]^+$ 232.14620, $C_{15}H_{20}O_2$ requires 232.14578.

141: 2-(3-(Cyclohex-1-en-1-yl)-1-methoxyprop-2-yn-1-yl)-5-methylthiophene



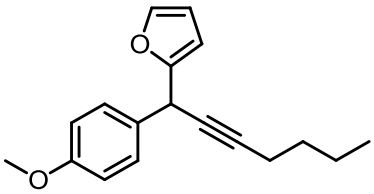
General Procedure G: 89 mg, 77% yield; ν_{max} (film/cm^{-1}) 3007, 2958 (C-H), 1637 (C=C); δ_H (600 MHz, $CDCl_3$) 1.55-1.61 (2H, m, CH_2), 1.61-1.66 (2H, m, CH_2), 2.08-2.12 (2H, m, CH_2), 2.14-2.19 (2H, m, CH_2), 2.46 (3H, s, thiophene-CH_3), 3.39 (3H, s, OCH_3), 5.37 (1H, s, C*H*OCH_3), 6.17-6.20 (1H, m, CH), 6.58-6.61 (1H, m, thiophene-H), 6.94 (1H, d, *J* 3.4, thiophene-H); δ_C (600 MHz, $CDCl_3$) 15.6, 21.5, 22.3, 25.7, 29.2, 55.0, 68.8, 83.3, 89.0, 120.1, 124.6, 126.5, 136.0, 139.9, 141.1; Found (EI): $[M]^+$ 246.10810, $C_{15}H_{18}OS$ requires 246.10729.

136b: 1-(1-(Benzyloxy)hept-2-yn-1-yl)-4-methoxybenzene



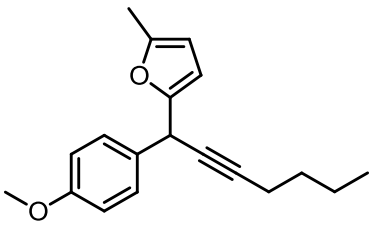
General Procedure G: 116 mg, 82% yield; ν_{max} (film/cm^{-1}) 2958, 2933, 2872 (C-H), 2230 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.93 (3H, t, *J* 7.4, CH_3), 1.45 (2H, app sx, *J* 7.4, C*H*$_2$$CH_3$), 1.55 (2H, app qn, *J* 7.4, C*H*$_2$$CH_2CH_3$), 2.31 (2H, td, *J* 7.1, 1.9, C≡CC*H*$_2$), 3.81 (3H, s, OMe), 4.63 (2H, dd, *J* 12.1, 11.8, OCH_2), 5.16 (1H, br t, *J* 1.9, CHOMe), 6.89 (2H, d, *J* 8.6, Ar-H), 7.26-7.29 (1H, m, Ar-H), 7.33-7.39 (4H, m, Ar-H), 7.45 (2H, d, *J* 8.6, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.8, 18.7, 22.1, 30.9, 55.4, 69.6, 70.4, 78.0, 88.6, 113.8, 127.7, 128.2, 128.5, 129.0, 131.6, 138.2, 159.6; Found (EI): $[M]^+$ 308.17794, $C_{21}H_{24}O_2$ requires 308.17708.

136f: 2-(1-(4-Methoxyphenyl)hept-2-yn-1-yl)furan



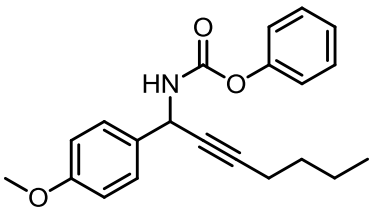
General Procedure G: 28 mg, 77% yield; ν_{max} (film/cm^{-1}) 2957, 2930, 2871 (C-H) 2265 (C≡C), 1607 (C=C); δ_H (600 MHz, $CDCl_3$) 0.91 (3H, t, *J* 7.4, CH_3), 1.42 (2H, app sx, *J* 7.4, C*H*$_2$CH$_3$), 1.52 (2H, app qn, *J* 7.4, C*H*$_2$CH$_2$CH$_3$), 2.26 (2H, td, *J* 7.1, 2.2, C≡CC*H*$_2$), 3.79 (3H, s, OMe), 4.96 (1H, br t, *J* 2.2, CH), 6.16 (1H, br dt, *J* 3.2, 0.9, Furan-H), 6.28 (1H, br dd, *J* 3.2, 1.9, Furan-H), 6.86 (2H, d, *J* 8.7, Ar-H), 7.28-7.31 (1H, m, Furan-H), 7.32 (2H, d, *J* 8.7, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.8, 18.7, 22.1, 31.1, 36.6, 55.4, 78.2, 84.2, 106.1, 110.3, 114.0, 128.9, 131.8, 142.1, 155.1, 158.8; Found (EI): $[M]^+$ 268.14630, $C_{18}H_{20}O_2$ requires 268.14577.

136e: 2-(1-(4-Methoxyphenyl)hept-2-yn-1-yl)-5-methylfuran



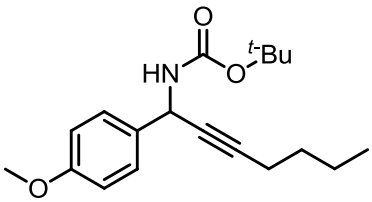
General Procedure G: 59 mg, 96% yield; ν_{max} (film/cm^{-1}) 2956, 2932, 2871, 2837 (C-H), 2249 (C≡C), 1609 (C=C); δ_H (600 MHz, $CDCl_3$) 0.92 (3H, t, *J* 7.4, CH_3), 1.43 (2H, app sx, *J* 7.4, C*H*$_2$CH$_3$), 1.53 (2H, app qn, *J* 7.4, C*H*$_2$CH$_2$CH$_3$), 2.23 (3H, s, Furan-CH_3), 2.26 (2H, td, *J* 7.1, 2.2, C≡CC*H*$_2$), 3.79 (3H, s, OMe), 4.91 (1H, br s, CH), 5.86 (1H, br dd, *J* 2.9, 1.1, Furan-H), 6.02 (1H, br d, *J* 2.9, Furan-H), 6.86 (2H, d, *J* 8.7, Ar-H), 7.32 (2H, d, *J* 8.7, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.76, 13.77, 18.7, 22.1, 31.1, 36.6, 55.4, 78.5, 84.0, 106.2, 106.8, 113.9, 128.9, 132.1, 151.7, 153.2, 158.7; Found (EI): $[M]^+$ 282.16170, $C_{19}H_{22}O_2$ requires 282.16142.

Phenyl (1-(4-methoxyphenyl)hept-2-yn-1-yl)carbamate



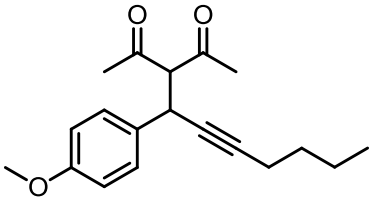
General Procedure G: 35 mg, 59% yield; ν_{max} (film/cm^{-1}) 3335 (N-H), 2959, 2932, 2871 (C-H), 2251 (C≡C), 1732 (C=O); δ_H (600 MHz, $CDCl_3$) 0.93 (3H, t, *J* 7.3, CH_3), 1.44 (2H, app sx, *J* 7.3, C*H*$_2$CH$_3$), 1.54 (2H, app qn, *J* 7.3, C*H*$_2$CH$_2$CH$_3$), 2.28 (2H, td, *J* 7.3, 2.1, C≡CC*H*$_2$), 3.80 (3H, s, OMe), 5.45 (1H, br d, *J* 8.6, NH), 5.68 (1H, br d, *J* 8.6, C*H*NH), 6.90 (2H, d, *J* 8.7, Ar-H), 7.13 (2H, d, *J* 7.9, Ar-H), 7.19 (1H, br t, *J* 7.9, Ar-H), 7.35 (2H, br t, *J* 7.9, Ar-H), 7.49 (2H, br d, *J* 8.7, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.8, 18.6, 22.1, 30.8, 46.9, 55.5, 77.9, 86.2, 114.1, 121.7, 125.5, 128.5, 129.4, 131.8, 151.0, 153.7, 159.5; Found (EI): $[M]^+$ 337.16787, $C_{21}H_{23}O_3N$ requires 337.16723.

136h: *tert*-Butyl (1-(4-methoxyphenyl)hept-2-yn-1-yl)carbamate



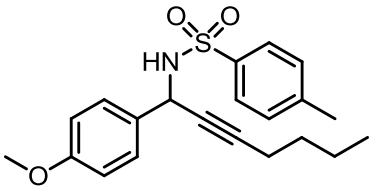
General Procedure G: 42 mg, 59% yield; ν_{max} (film/cm^{-1}) 3351 (N-H), 2959, 2933, 2870 (C-H), 2250 (C≡C), 1699 (C=O); δ_H (600 MHz, $CDCl_3$) 0.91 (3H, t, *J* 7.4, CH_3), 1.40 (2H, app sx, *J* 7.4, C*H*$_2$CH$_3$), 1.44 (9H, s, C(CH$_3$)$_3$), 1.51 (2H, app qn, *J* 7.4, C*H*$_2$CH$_2$CH$_3$), 2.24 (2H, td, *J* 7.1, 2.1, C≡CC*H*$_2$), 3.80 (3H, s, OMe), 4.96 (1H, br s, NH), 5.57 (1H, br s, C*H*NH), 6.86 (2H, d, *J* 8.7, Ar-H), 7.41 (2H, br d, *J* 8.7, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.7, 18.6, 22.1, 28.5, 30.8, 46.0, 55.4, 78.6, 80.0, 85.3, 113.9, 128.2, 132.6, 154.9, 159.2; Found (EI): $[M+Na]^+$ 340.1881, $C_{19}H_{27}O_3NNa$ requires 340.1889.

136d: 3-(1-(4-Methoxyphenyl)hept-2-yn-1-yl)pentane-2,4-dione



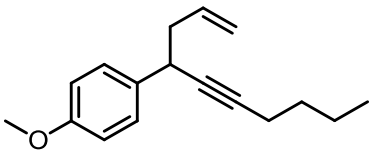
General Procedure G: 57 mg, 83% yield; ν_{max} (film/cm^{-1}) 2957, 2928, 2871 (C-H), 2160 (C≡C), 1700 (C=O); δ_H (600 MHz, $CDCl_3$) 0.88 (3H, t, *J* 7.4, CH_3), 1.35 (2H, app sx, *J* 7.4, C*H*$_2$CH$_3$), 1.41-1.47 (2H, m, C*H*$_2$CH$_2$CH$_3$), 1.89 (3H, s, O=CCH$_3$), 2.16 (2H, td, *J* 7.1, 2.3, C≡CC*H*$_2$), 2.30 (3H, s, O=CCH$_3$), 3.78 (3H, s, OMe), 4.05 (1H, d, *J* 10.8, O=CC*H*C=O), 4.36 (1H, dt, *J* 10.8, 2.3, CHC≡C), 6.83 (2H, d, *J* 8.7, Ar-H), 7.23 (2H, d, *J* 8.7, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.7, 18.5, 22.0, 28.6, 30.9, 31.4, 37.1, 76.4, 79.0, 85.3, 113.9, 114.2, 129.1, 130.9, 158.9, 202.29, 202.31; Found (EI): $[M]^+$ 300.17241, $C_{19}H_{24}O_3$ requires 300.17200.

136g: *N*-(1-(4-Methoxyphenyl)hept-2-yn-1-yl)-4-methylbenzenesulfonamide



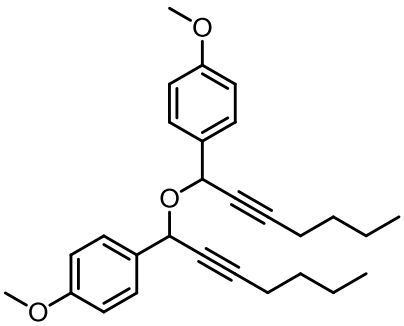
General Procedure G: 64 mg, 74% yield; ν_{max} (film/cm^{-1}) 3270 (N-H), 2958, 2933, 2872 (C-H), 2251 (C≡C); δ_H (600 MHz, $CDCl_3$) 0.85 (3H, t, *J* 7.4, CH_3), 1.22-1.30 (4H, m, C*H*$_2$C*H*$_2$CH$_3$), 1.96 (2H, td, *J* 7.0, 2.1, C≡CC*H*$_2$), 2.42 (3H, s, Ar-CH$_3$), 3.78 (3H, s, OMe), 4.79 (1H, br d, *J* 8.8, NH), 5.24 (1H, br dt, *J* 8.8, 2.1, C*H*NH), 6.82 (2H, d, *J* 8.8, Ar-H), 7.28 (2H, br d, *J* 8.1, Ar-H), 7.37 (2H, d, *J* 8.8, Ar-H), 7.76 (2H, br d, *J* 8.1, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.7, 18.3, 21.7, 22.0, 30.5, 49.1, 55.4, 76.9, 87.4, 114.0, 127.6, 128.7, 129.5, 130.4, 137.7, 143.3, 159.6; Found (ES): $[M+Na]^+$ 394.1446, $C_{21}H_{25}NO_3SNa$ requires 394.1453.

136c: 1-(Dec-1-en-5-yn-4-yl)-4-methoxybenzene [82]



General Procedure G: 98% yield; ν_{max} (film/cm^{-1}) 2958, 2933, 2873 (C-H), 2250 (C≡C) 1641 (C=C); δ_H (600 MHz, $CDCl_3$) 0.92 (3H, t, *J* 7.4, CH_3), 1.42 (2H, app sx, *J* 7.4, C*H*$_2$CH$_3$), 1.48-1.55 (2H, m, C*H*$_2$CH$_2$CH$_3$), 2.25 (2H, td, *J* 7.0, 2.3, C≡CC*H*$_2$), 2.45 (2H, app t, *J* 7.0, C=CCH$_2$), 3.68 (1H, m, CHC≡C), 3.79 (3H, s, OCH_3), 5.05-5.09 (2H, m, C=CH$_2$), 5.85-5.88 (1H, m, *H*C=CH$_2$), 6.86 (2H, d, *J* 8.8, Ar-H), 7.27 (2H, d, *J* 8.8, Ar-H); δ_C (150 MHz, $CDCl_3$) 13.8, 18.7, 22.1, 31.3, 37.6, 43.3, 55.4, 81.5, 84.0, 113.9, 116.3, 128.5, 134.2, 136.0, 158.4; Found (CI): $[M+H]^+$ 243.17533, $C_{17}H_{22}O$ requires 243.17489.

143: 4,4'-(Oxybis(hept-2-yne-1,1-diyl))bis(methoxybenzene)



General Procedure G: Mixture of distereoisomers A and B. 80% yield, crude ratio of A:B is 1.3:1.

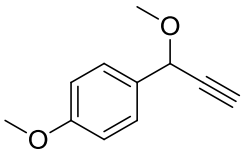
ν_{max} (film/cm^{-1}) 2956, 2932, 2871 (C-H), 2238 (C≡C);

A: δ_H (600 MHz, $CDCl_3$) 0.93 (6H, t, *J* 7.4, 2 × CH_3), 1.46 (4H, app sx, *J* 7.4, 2 × C*H*$_2$CH$_3$), 1.54-1.59 (4H, m, 2 × C*H*$_2$CH$_2$CH$_3$), 2.32 (2H, td, *J* 7.2, 1.9, 2 × C≡CC*H*$_2$), 3.79 (6H, s, 2 × OMe), 5.53 (2H, br t, *J* 1.9, 2 × OCH), 6.86 (4H, d, *J* 8.7, 2 × Ar-H), 7.47 (4H, d, *J* 8.7, 2 × Ar-H); δ_C (150 MHz, $CDCl_3$) 13.8, 18.7, 22.1, 30.9, 57.4, 69.2, 78.1, 88.5, 113.7, 129.2, 131.8, 159.5.

B: δ_H (600 MHz, $CDCl_3$) 0.91 (6H, t, *J* 7.4, 2 × CH_3), 1.41 (4H, app sx, *J* 7.4, 2 × C*H*$_2$CH$_3$), 1.49-1.54 (4H, m, 2 × C*H*$_2$CH$_2$CH$_3$), 2.26 (2H, td, *J* 7.2, 1.9, 2 × C≡CC*H*$_2$), 3.8 (6H, s, 2 × OMe), 5.14 (2H, br t, *J* 1.9, 2 × OCH), 6.88 (4H, d, *J* 8.7, 2 × Ar-H), 7.41 (4H, d, *J* 8.7, 2 × Ar-H); δ_C (150 MHz, $CDCl_3$) 13.8, 18.8, 22.2, 30.8, 55.4, 68.5, 78.4, 88.3, 113.9, 129.4, 131.5, 159.7.

Found (ES): $[M+H]^+$ 419.2600, $C_{28}H_{35}O_3$ requires 419.2586.

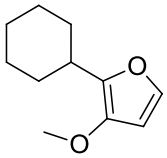
156: 1-Methoxy-4-(1-methoxyprop-2-yn-1-yl)benzene



General Procedure G: 82% yield; ν_{max} (film/cm^{-1}) 2995, 2936, 2904 (C-H), 2174 (C≡C); δ_H (600 MHz, $CDCl_3$) 2.65 (1H, br d, *J* 2.1, C≡CH), 3.42 (3H, s, CHOC*H*$_3$), 3.81 (3H, s, OCH_3), 5.04 (1H, br d, *J* 2.1, C*H*O), 6.91 (2H, d, *J* 8.7, Ar-H), 7.44 (2H, d, *J* 8.7, Ar-H); δ_C (150 MHz, $CDCl_3$) 55.4, 55.8, 72.5, 75.7, 81.6, 114.0, 128.9, 130.3, 159.9; Found (EI): $[M]^+$ 176.08350, $C_{11}H_{12}O_2$ requires 176.08318.

7. Furan Synthesis

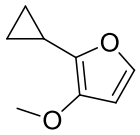
172j: 2-Cyclohexyl-3-methoxyfuran



General procedure H: Structure comparison reference for furan substitution [201]

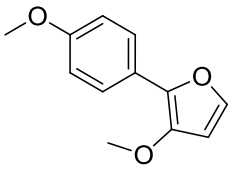
22 mg, 98% yield; ν_{max} (film/cm^{-1}) 2927, 2895 (C-H), 1629 (C=C), 1274 (C-O); δ_H (600 MHz, $CDCl_3$)1.20-1.38 (5H, m, CH_2), 1.65-1.85 (5H, m, CH_2), 2.66-2.73 (1H, m, CH), 3.72 (3H, s, OMe), 6.26 (1H, d, *J* 1.9, Furan-H), 7.09 (1H, d, *J* 1.9, Furan-H); δ_C (150 MHz, $CDCl_3$) 26.1, 26.5, 31.3, 35.4, 59.7, 103.2, 138.6, 142.1, 144.1; Found (CI): $[M]^+$ 180.114359, $C_{11}H_{16}O_2$ requires 180.1144857.

172d: 2-Cyclopropyl-3-methoxyfuran



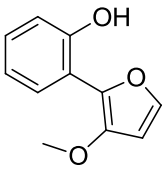
General procedure H: 98% yield; ν_{max} (film/cm^{-1}) 2957, 2924, 2855 (C-H), 1667 (C=C), 1230 (C-O); δ_H (600 MHz, $CDCl_3$) 0.82-0.85 (4H, m, 2 × CH_2), 1.85 (1H, qn, *J* 7.2, CH), 3.75 (3H, s, OMe), 6.25 (1H, br s, Furan-H), 7.03 (1H, br s, Furan-H); δ_C (150 MHz, $CDCl_3$) 5.5, 6.4, 59.5, 103.5, 138.3, 139.9, 143.7; Found (CI): $[M]^+$ 138.07201, $C_8H_{10}O_2$ requires 138.06808.

172c: 3-Methoxy-2-(4-methoxyphenyl)furan



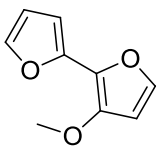
General procedure H: 43 mg, 93% yield; ν_{max} (film/cm^{-1}) 2979, 2935, 2838 (C-H), 1672 (C=C), 1247 (C-O); δ_H (600 MHz, $CDCl_3$) 3.82 (3H, s, OMe), 3.86 (3H, s, OMe), 6.41 (1H, d, *J* 2.1, furan-H), 6.92 (2H, d, *J* 8.9, Ar-H), 7.23 (1H, d, *J* 2.1, furan-H), 7.71 (2H, d, *J* 8.9, Ar-H); δ_C (150 MHz, $CDCl_3$) 55.4, 58.9, 103.5, 114.1, 124.2, 124.6, 136.8, 139.4, 144.1, 157.9; Found (EI): $[M]^+$ 204.077876, $C_{12}H_{12}O_3$ requires 204.07864.

172m: 2-(3-Methoxyfuran-2-yl)phenol



General procedure H: 30 mg, 79% yield; ν_{max} (film/cm^{-1}) 3333 (O-H), 2968, 2944 (C-H), 1606 (C=C), 1287 (C-O); δ_H (600 MHz, $CDCl_3$) 3.94 (3H, s, OMe), 6.46 (1H, d, *J* 2.1, furan-H), 6.92-6.98 (2H, m, Ar-H), 7.18 (1H, t, *J* 8.4, Ar-H), 7.37 (1H, d, *J* 2.1, furan-H), 7.61 (1H, t, *J* 8.8, Ar-H), 7.99 (1H, s, OH); δ_C (150 MHz, $CDCl_3$) 60.2, 103.5, 117.3, 117.9, 120.4, 126.2, 128.9, 136.1, 141.5, 142.7, 152.1; Found (EI): $[M+H]^+$ 190.062865, $C_{11}H_{10}O_3$ requires 190.06299.

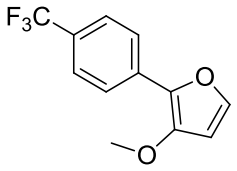
172i: 3-Methoxy-2,2'-bifuran



General procedure H: 35 mg, 68% yield; ν_{max} (film/cm^{-1}) 2972 (C-H), 1741 (C=C), 1370 (C-O); δ_H (600 MHz, $CDCl_3$) 3.87 (3H, s, OMe), 6.40 (1H, d, *J* 2.1,

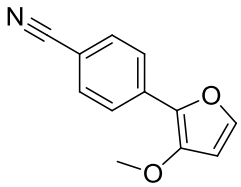
furan-H), 6.45-6.48 (2H, m, furan-H), 7.26 (1H, d, *J* 2.1, furan-H), 7.43 (1H, br s, furan-H); δ_C (150 MHz, $CDCl_3$) 59.0, 103.1, 104.4, 111.2, 130.8, 140.5, 141.1, 144.3, 145.5; Found (EI): $[M]^+$ 164.04811, $C_9H_8O_3$ requires 164.04734.

172a: 3-Methoxy-2-(4-(trifluoromethyl)phenyl)furan



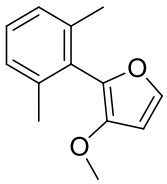
General procedure H: 44 mg, 92% yield; ν_{max} (film/cm^{-1}) 2944 (C-H), 1677 (C=C), 1270 (C-O); δ_H (600 MHz, $CDCl_3$) δ_H (600 MHz, $CDCl_3$) 3.91 (3H, s, OMe), 6.45 (1H, d, *J* 2.1, furan-H), 7.33 (1H, d, *J* 2.1, furan-H), 7.59 (2H, d, *J* 8.2, Ar-H), 7.85 (1H, d, *J* 8.2, Ar-H); δ_C (150 MHz, $CDCl_3$) 58.7, 103.2, 122.8, 124.4 (q, *J* 270), 125.5 (q, *J* 4.0), 127.1 (q, *J* 32.1), 134.1, 135.2, 141.4, 147.4; Found (EI): $[M]^+$ 242.055390, $C_{12}H_9O_2F_3$ requires 242.05546.

172g: 4-(3-Methoxyfuran-2-yl)benzonitrile



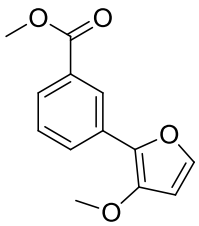
General procedure H: 35 mg, 89%; ν_{max} (film/cm^{-1}) 2944 (C-H), 2232 (C≡N), 1601 (C=C), 1225 (C-O); δ_H (600 MHz, $CDCl_3$) 3.92 (3H, s, OMe), 6.46 (1H, d, *J* 2.1, furan-H), 7.36 (1H, d, *J* 2.1, furan-H), 7.61 (2H, d, *J* 8.6, Ar-H), 7.83 (1H, d, *J* 8.6, Ar-H); δ_C (150 MHz, $CDCl_3$) 58.8, 103.3, 108.1, 119.7, 122.9, 132.4, 134.7, 134.8, 142.2, 148.4 Found (CI): $[M]^+$ 200.069819, $C_{12}H_{10}NO_2$ requires 200.07061.

172e: 2-(2,6-Dimethylphenyl)-3-methoxyfuran



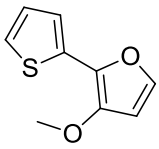
General procedure H: 36 mg, 78% yield; ν_{max} (film/cm^{-1}) 2979, 2942 (C-H), 1626 (C=C), 1282 (C-O); δ_H (600 MHz, $CDCl_3$) 2.19 (6H, s, Ar-Me), 3.70 (3H, s, OMe), 6.40 (1H, d, *J* 2.1, furan-H), 7.07 (2H, d, *J* 7.5, Ar-H), 7.17 (1H, d, *J* 7.5, Ar-H), 7.33 (1H, d, *J* 2.1, furan-H); δ_C (150 MHz, $CDCl_3$) 20.3, 58.8, 103.0, 127.4, 128.9, 129.4, 136.0, 139.3, 140.7, 144.7; Found (EI): $[M]^+$ 202.098693, $C_{13}H_{14}O_2$ requires 202.09938.

172l: Methyl 3-(3-methoxyfuran-2-yl)benzoate



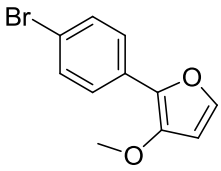
General procedure H: 29 mg, 73% yield; ν_{max} (film/cm^{-1}) 2953, 2846 (C-H), 1721 (C=O), 1673 (C=C), 1206 (C-O); δ_H (600 MHz, $CDCl_3$) 3.90 (3H, s, OMe), 3.93 (3H, s, OMe), 6.45 (1H, d, *J* 2.1, furan-H), 7.30 (1H, d, *J* 2.1, furan-H), 7.43 (1H, t, *J* 7.8, Ar-H), 7.83 (1H, d, *J* 7.8, Ar-H), 7.96 (1H, d, *J* 7.8, Ar-H), 8.42 (1H, br s, Ar-H); δ_C (150 MHz, $CDCl_3$) 52.1, 58.7, 103.2, 124.0, 126.6, 127.2, 128.5, 130.4, 131.2, 135.5, 140.6, 146.2, 167.3; Found (EI): [M+H]+ 233.08138, $C_{13}H_{13}O_4$ requires 233.08084.

172h: 3-Methoxy-2-(thiophen-2-yl)furan



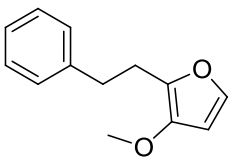
General procedure H: 32 mg, 85% yield; ν_{max} (film/cm^{-1}) 2937 (C-H), 1624 (C=C), 1283 (C-O); δ_H (600 MHz, $CDCl_3$) 3.88 (3H, s, OMe), 6.40 (1H, d, *J* 2.1, furan-H), 7.04 (1H, dd, *J* 4.9, 3.6, thiophene-H), 7.18 (1H, dd, *J* 4.9, 1.1, thiophene-H), 7.22 (1H, d, *J* 2.1, furan-H), 7.24-7.27 (1H, m, thiophene-H); δ_C (150 MHz, $CDCl_3$) 59.0, 103.3, 120.8, 122.7, 127.4, 132.5, 134.4, 140.0, 143.9; Found (EI): $[M]^+$ 180.24207, $C_9H_8O_2S$ requires 180.22362.

172k: 2-(4-Bromophenyl)-3-methoxyfuran



General procedure H: 46 mg, 95% yield; ν_{max} (film/cm^{-1}) 2939, 2850 (C-H), 1672 (C=C), 1217 (C-O); δ_H (600 MHz, $CDCl_3$) 3.88 (3H, s, OMe), 6.42 (1H, d, *J* 2.1, furan-H), 7.28 (1H, d, *J* 2.1, furan-H), 7.47 (2H, d, *J* 8.6, Ar-H), 7.64 (2H, d, *J* 8.6, Ar-H); δ_C (150 MHz, $CDCl_3$) 58.7, 103.3, 119.1, 124.5, 129.8, 131.5, 135.6, 140.5, 145.9; Found (EI): $[M]^+$ 251.977808, $C_{11}H_9O_2Br$ requires 251.97859.

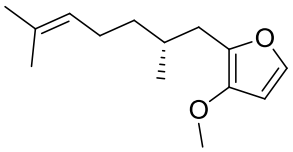
172b: 3-Methoxy-2-phenethylfuran



General procedure H: 55 mg, 95% yield; 500mg scale: 250mg 1.24 mmol, 65% yield; ν_{max} (film/cm^{-1}) 2980, 2931 (C-H), 1638 (C=C), 1277 (C-O); δ_H (600 MHz, $CDCl_3$) 2.90-2.98 (4H, m, 2 × CH_2), 3.64 (3H, s, OMe), 6.29 (1H, d, *J* 2.1, furan-

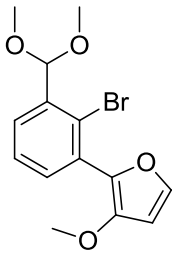
H), 7.17 (1H, d, *J* 2.1, furan-H), 7.18-7.24 (3H, m, Ar-H), 7.28-7.32 (2H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 27.1, 34.3, 59.5, 103.2, 125.9, 128.3, 128.4, 128.6, 139.18, 139.21, 141.5; Found (EI): $[M]^+$ 202.099153, $C_{13}H_{14}O_2$ requires 202.09938.

172f: (*R*)-2-(2,6-Dimethylhept-5-en-1-yl)-3-methoxyfuran



General procedure H: 93% yield; ν_{max} (film/cm^{-1}) 2958, 2913 (C-H), 1635 (C=C), 1279 (C-O); δ_H (600 MHz, $CDCl_3$) 0.88 (3H, d, *J* 6.7, CHC*H*$_3$), 1.14-1.23 (1H, m, C=CCH$_2$CH*H*), 1.31-1.41 (1H, m, C=CCH$_2$CH*H*), 1.60 (3H, s, C=C(CH$_3$)$_2$), 1.68 (3H, s, C=C(CH$_3$)$_2$), 1.77-1.86 (1H, m, C*H*CH$_3$), 1.93-2.08 (2H, m, CH$_2$C=C), 2.42 (1H, dd, *J* 14.8, 7.8, Furan-C*H*H), 2.56 (1H, dd, *J* 14.8, 6.1, Furan-C*H*H), 3.73 (3H, s, OCH$_3$), 5.09 (1H, m, HC=C), 6.28 (1H, d, *J* 2.1, Furan-H), 7.12 (1H, d, *J* 2.1, Furan-H); δ_C (150 MHz, $CDCl_3$) 17.7, 19.6, 25.7, 25.9, 32.3, 32.4, 36.8, 59.5, 102.9, 124.9, 131.3, 139.0, 139.4, 144.0; Found (CI): $[M]^+$ 222.161292, $C_{14}H_{22}O_2$ requires 222.16143.

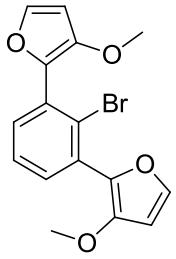
172n: 2-(2-Bromo-3-(dimethoxymethyl)phenyl)-3-methoxyfuran



General procedure H: 80 mg, 83% yield; ν_{max} (film/cm^{-1}) 2935, 2832 (C-H), 1668 (C=C), 1235 (C-O); δ_H (600 MHz, $CDCl_3$) 3.41 (6H, s, 2 × OMe), 3.77 (3H, s, OMe), 5.66 (1H, s, C*H*(OMe)$_2$), 6.43 (1H, d, *J* 2.1, furan-H), 7.33-7.39 (2H, m, furan-H, Ar-H), 7.45 (1H, dd, *J* 7.6, 1.7 Ar-H), 7.58 (1H, dd, *J* 7.6, 1.7 Ar-H); δ_C (150 MHz, $CDCl_3$) 54.1, 58.8, 103.1, 103.5, 123.7, 126.8, 127.8, 131.9, 132.3,

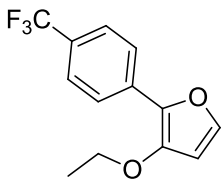
136.1, 138.1, 141.0, 145.5; Found (CI): $[M]^+$ 326.014436, $C_{14}H_{15}BrO_4$ requires 326.01482.

172o: 2,2'-(2-Bromo-1,3-phenylene)bis(3-methoxyfuran)



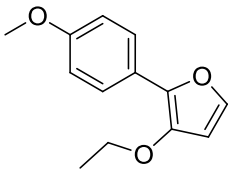
General procedure H: 32 mg, 86% yield; ν_{max} (film/cm^{-1}) 2960, 2932 (C-H), 1245 (C-O); δ_H (600 MHz, $CDCl_3$) δ_H (600 MHz, $CDCl_3$) 3.78 (6H, s, 2 × OMe), 6.43 (2H, d, *J* 2.1, furan-H), 7.33-7.37 (1H, m, Ar-H), 7.36 (2H, d, *J* 2.1, furan-H), 7.44 (2H, d, *J* 7.2, Ar-H); δ_C (150 MHz, $CDCl_3$) 58.9, 103.2, 123.5, 126.7, 131.1, 132.9, 136.4, 140.9, 145.5; Found (CI): $[M]^+$ 347.999242, $C_{16}H_{13}BrO_4$ requires 347.99917.

171a: 3-Ethoxy-2-(4-(trifluoromethyl)phenyl)furan



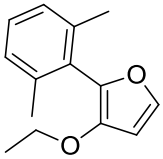
General procedure H: 89% yield; ν_{max} (film/cm^{-1}) 2979, 2929 (C-H), 1615 (C=C), 1322 (C-F); δ_H (600 MHz, $CDCl_3$) 1.45 (3H, t, *J* 6.8, CH_3), 4.12 (2H, q, *J* 6.8, C*H*$_2$CH$_3$), 6.42 (1H, d, *J* 2.3, Furan-H), 7.32 (1H, d, *J* 2.3, Furan-H), 7.60 (2H, d, *J* 7.9, Ar-H), 7.88 (2H, d, J 7.9, Ar-H); δ_C (150 MHz, $CDCl_3$) 15.3, 67.3, 103.9, 122.8, 124.5 (q, *J* 271), 125.5 (q, *J* 4.0 Hz), 127.0 (q, *J* 32.1), 134.2, 135.5, 141.4, 146.3; Found (CI): $[M]^+$ 256.070568, $C_{13}H_{11}O_2F_3$ requires 256.07057.

171c: 3-Ethoxy-2-(4-methoxyphenyl)furan



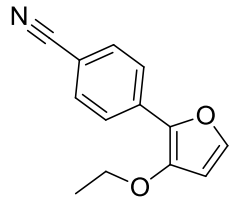
General procedure H: 76% yield; ν_{max} (film/cm^{-1}) 2976, 2936, 2895 (C-H), 1600 (C=C), 1254 (C-O); δ_H (600 MHz, $CDCl_3$) 1.42 (3H, t, *J* 7.0, CH_2CH_3), 3.38 (3H, s, OMe), 4.07 (2H, q, *J* 7.0, CH_2CH_3), 6.38 (1H, d, *J* 2.1, furan-H), 6.92 (2H, d, *J* 8.9, Ar-H), 7.22 (1H, d, *J* 2.1, furan-H), 7.74 (2H, d, *J* 8.9, Ar-H); δ_C (150 MHz, $CDCl_3$) 15.4, 55.4, 67.3, 104.3, 114.0, 124.3, 124.5, 137.2, 139.4, 142.9, 157.8; Found (EI): $[M]^+$ 218.09347, $C_{13}H_{14}O_3$ requires 218.09429.

171e: 2-(2,6-Dimethylphenyl)-3-ethoxyfuran



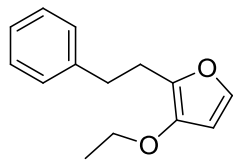
General procedure H: 85% yield; ν_{max} (film/cm^{-1}) 2979, 2925 (C-H), 1623 (C=C), 1283 (C-O); δ_H (600 MHz, $CDCl_3$) 1.27 (3H, t, *J* 7.2, CH_2CH_3), 2.23 (6H, s, 2 × Ar-Me), 3.92 (2H, q, *J* 7.2, CH_2CH_3), 6.40 (1H, br s, Furan-H), 7.09 (2H, d, *J* 7.5, Ar-H), 7.19 (1H, t, *J* 7.5, Ar-H), 7.35 (1H, br s, Furan-H); δ_C (150 MHz, $CDCl_3$) 15.3, 20.4, 67.0, 103.8, 127.4, 128.8, 129.6, 136.5, 139.2, 140.6, 143.6; Found (CI): $[M]^+$ 216.113848, $C_{14}H_{16}O_2$ requires 216.11448.

171g: 4-(3-Ethoxyfuran-2-yl)benzonitrile



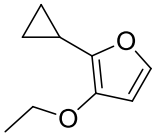
General procedure H: 86% yield; ν_{max} (film/cm^{-1}) 2986, 2971, 2899 (C-H), 2219 (C≡N); δ_H (600 MHz, $CDCl_3$) 1.46 (3H, t, *J* 7.2, CH_3), 4.13 (2H, q, *J* 7.2, CH_2), 6.42 (1H, d, *J* 1.9, Furan-H), 7.34 (1H, d, *J* 1.9, Furan-H), 7.60 (2H, d, *J* 8.7, Ar-H), 7.84 (2H, d, *J* 8.7, Ar-H); δ_C (150 MHz, $CDCl_3$) 15.3, 67.4, 103.8, 108.0, 119.7, 122.9, 132.4, 134.9, 135.0, 142.2, 147.4; Found (CI): $[M]^+$ 214.085614, $C_{13}H_{12}NO_2$ requires 214.08626.

171b: 3-Ethoxy-2-phenethylfuran



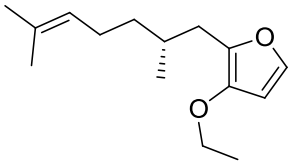
General procedure H: 52 mg, 84% yield; ν_{max} (film/cm^{-1}) 2979, 2930 (C-H), 1636 (C=C), 1275 (C-O); δ_H (600 MHz, $CDCl_3$) 1.23 (3H, t, *J* 7.0, CH_2CH_3), 2.85-2.97 (4H, m, Ar-CH_2CH_2), 3.78 (2H, q, *J* 7.0, CH_2CH_3), 6.21 (1H, d, *J* 2.1, furan-H), 7.12 (1H, d, *J* 2.1, furan-H), 7.15-7.20 (3H, m, Ar-H) 7.23-7.29 (2H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 15.1, 27.1, 34.3, 67.9, 104.1, 125.9, 128.3, 128.5, 139.1, 139.9, 141.6, 142.2; Found (CI): $[M+H]^+$ 217.121850, $C_{14}H_{17}O_2$ requires 217.12285.

171d: 2-Cyclopropyl-3-ethoxyfuran



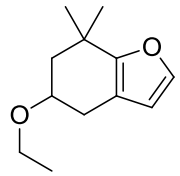
General procedure H: 88% yield; ν_{max} (film/cm^{-1}) 2958, 2927, 2870 (C-H), 1667 (C=C), 1219 (C-O); δ_H (600 MHz, $CDCl_3$) 0.81-0.85 (4H, m, 2 × CH_2), 1.33 (3H, t, J 7.2, CH_3), 1.83-1.89 (1H, m, CH), 3.95 (2H, q, *J* 7.2, C*H*$_2$CH$_3$), 6.22 (1H, d, *J* 1.8, Furan-H), 7.02 (1H, d, *J* 1.8, Furan-H); δ_C (150 MHz, $CDCl_3$) 5.6, 6.6, 15.3, 67.9, 104.5, 138.3, 140.7, 142.3; Found (CI): $[M]^+$ 152.083284, $C_{14}H_{12}O_2$ requires 152.08318.

171f: (*R*)-2-(2,6-Dimethylhept-5-en-1-yl)-3-ethoxyfuran



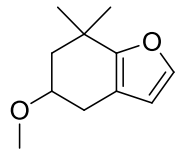
General procedure H: 95% yield; ν_{max} (film/cm^{-1}) 2966, 2914 (C-H), 1634 (C=C), 1278 (C-O); δ_H (600 MHz, $CDCl_3$) 0.88 (3H, d, *J* 6.4, CHC*H*$_3$), 1.13-1.23 (1H, m, C=CCH$_2$CH*H*), 1.31 (3H, t, *J* 7.2, CH$_2$C*H*$_3$), 1.32-1.41 (1H, m, C=CCH$_2$CH*H*), 1.60 (3H, s, C=C(CH$_3$)$_2$), 1.68 (3H, s, C=C(CH$_3$)$_2$), 1.77-1.86 (1H, m, C*H*CH$_3$), 1.93-2.08 (2H, m, CH$_2$C=C), 2.42 (1H, dd, *J* 14.7, 7.9, Furan-C*H*H), 2.56 (1H, dd, *J* 14.7, 6.0, Furan-C*H*H), 3.92 (2H, q, *J* 7.2, OCH$_2$), 5.09 (1H, m, HC=C), 6.24 (1H, d, *J* 1.9, Furan-H), 7.11 (1H, d, *J* 1.9, Furan-H); δ_C (150 MHz, $CDCl_3$) 15.3, 17.8, 19.7, 25.7, 25.9, 32.3, 32.4, 36.8, 67.8, 103.8, 124.9, 131.2, 139.0, 140.2, 142.7; Found (CI): $[M]^+$ 236.17704, $C_{15}H_{24}O_2$ requires 236.17708.

179p: 5-Ethoxy-7,7-dimethyl-4,5,6,7-tetrahydrobenzofuran



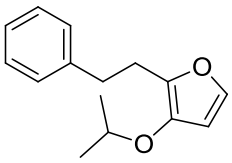
General procedure H: 76 mg 94% yield; ν_{max} (film/cm^{-1}) 2967, 2929, 2867 (C-H), 1161 (C-O); δ_H (600 MHz, $CDCl_3$) 1.23 (3H, t, *J* 7.2, CH_2CH_3), 1.25 (3H, s, CCH_3), 1.29 (3H, s, CCH_3), 1.69 (1H, app t, *J* 12.0, C*H*HC$(CH_3)_2$), 1.93 (1H, br d, *J* 12.0, CH*H*C$(CH_3)_2$), 2.33 (1H, dd, *J* 15.1, 9.0, Furan-C*H*H), 2.85 (1H, dd, *J* 15.1, 5.3, Furan-CH*H*), 3.53-3.63 (2H, m, OCH_2), 3.72-3.78 (1H, m, CHOEt), 6.13 (1H, d, *J* 1.9, Furan-H), 7.23 (1H, d, *J* 1.9, Furan-H); δ_C (150 MHz, $CDCl_3$) 15.9, 28.3, 28.5, 29.5, 32.9, 45.1, 63.9, 73.5, 110.3, 112.8, 141.2, 156.6; Found (CI): $[M]^+$ 194.130165, $C_{12}H_{18}O_2$ requires 194.13013.

178p: 5-Methoxy-7,7-dimethyl-4,5,6,7-tetrahydrobenzofuran



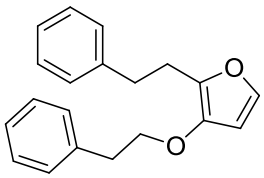
General procedure H: 72 mg, 96% yield; ν_{max} (film/cm^{-1}) 2964, 2928, 2863 (C-H), 1161 (C-O); δ_H (600 MHz, $CDCl_3$) 1.26 (3H, s, CCH_3), 1.30 (3H, s, CCH_3), 1.67 (1H, app t, *J* 12.0, C*H*HC$(CH_3)_2$), 1.94 (1H, br d, *J* 12.0, CH*H*C$(CH_3)_2$), 2.32 (1H, dd, *J* 14.8, 9.1, Furan-C*H*H), 2.86 (1H, dd, *J* 14.8, 5.4, Furan-CH*H*), 3.40 (3H, s, OMe), 3.62-3.69 (1H, m, CHOMe), 6.14 (1H, d, *J* 1.9, Furan-H), 7.24 (1H, d, *J* 1.9, Furan-H); δ_C (150 MHz, $CDCl_3$) 28.3, 28.4, 28.9, 32.8, 44.4, 56.2, 75.2, 110.2, 112.5, 141.2, 156.5; Found (CI): $[M]^+$ 180.114054, $C_{11}H_{16}O_2$ requires 180.11448.

177b: 3-Isopropoxy-2-phenethylfuran



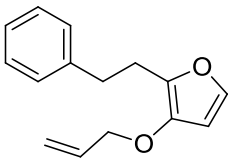
General procedure H: 45 mg, 70% yield; ν_{max} (film/cm^{-1}) 2975, 2933 (C-H), 1634 (C=C), 1274 (C-O);); δ_H (600 MHz, $CDCl_3$) 1.18 (6H, d, *J* 6.2, CH_2CH_3), 2.84-2.95 (4H, m, Ar-CH_2CH_2), 3.98 (1H, septet, *J* 6.2, $CH(CH_3)_2$), 6.19 (1H, d, *J* 2.1, furan-H), 7.14 (1H, d, *J* 2.1, furan-H), 7.15-7.20 (3H, m, Ar-H) 7.23-7.30 (2H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 22.2, 27.0, 34.4, 74.4, 105.3, 125.9, 128.3, 128.4, 139.1, 140.9, 141.2, 141.6; Found (CI): $[M+H]^+$ 231.136913, $C_{15}H_{19}O_2$ requires 231.13850.

173b: 3-Phenethoxy-2-phenethylfuran



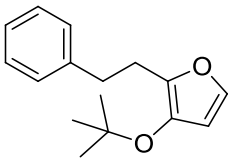
General procedure H: 58 mg, 74% yield; ν_{max} (film/cm^{-1}) 2979, 2869 (C-H), 1636 (C=C), 1275 (C-O); δ_H (600 MHz, $CDCl_3$) 2.82-2.92 (4H, m, Ar-CH_2CH_2-Furan), 2.91 (2H, t, *J* 7.5, Ar-CH_2CH_2O), 3.92 (2H, t, *J* 7.5, Ar-CH_2CH_2O), 6.20 (1H, d, *J* 1.9, Furan-H), 7.12-7.32 (10H, m, Ar-H), 7.13 (1H, d, *J* 1.9, Furan-H); δ_C (150 MHz, $CDCl_3$) 27.2, 34.4, 36.2, 73.1, 104.1, 126.0, 126.5, 128.4, 128.5, 128.6, 129.0, 138.4, 139.3, 140.0, 141.6, 142.4 Found (CI): $[M+H]^+$ 293.153275, $C_{20}H_{21}O_2$ requires 293.15415.

174b: 3-(Allyloxy)-2-phenethylfuran



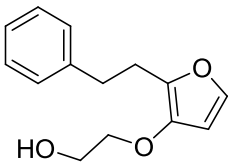
General procedure H: 25 mg, 58% yield; ν_{max} (film/cm^{-1}) 2926, 2858 (C-H), 1636 (C=C), 1276 (C-O);); δ_H (600 MHz, $CDCl_3$) 2.86-2.96 (4H, m, Ar-CH_2CH_2), 4.23 (2H, dt, *J* 5.5, 1.5, CH_2O), 5.19 (1H, dd, *J* 10.6, 1.5, *H*HC=CH), 5.28 (1H, dd, *J* 17.4, 1.5, H*H*C=CH), 5.90 (1H, ddd, *J* 17.4, 10.6, 1.5, HHC=C*H*), 6.22 (1H, d, *J* 2.1, furan-H), 7.13 (1H, d, *J* 2.1, furan-H), 7.15-7.20 (3H, m, Ar-H) 7.23-7.29 (2H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 27.1, 34.3, 73.1, 104.2, 117.5, 125.9, 128.3, 128.5, 133.9, 139.1, 140.0, 141.5, 142.3; Found (CI): $[M+H]^+$ 229.12213, $C_{15}H_{17}O_2$ requires 229.12285.

176b: 3-(*tert*-Butoxy)-2-phenethylfuran



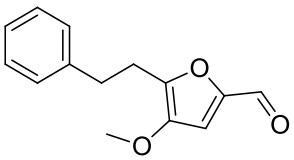
General procedure H: 30 mg, 65% yield; ν_{max} (film/cm^{-1}) 2977, 2933 (C-H), 1624 (C=C), 1273 (C-O); δ_H (600 MHz, $CDCl_3$) 1.25 (9H, s, CCH_3), 2.83-2.96 (4H, m, Ar-CH_2CH_2), 6.15 (1H, d, *J* 2.1, furan-H), 7.15 (1H, d, *J* 2.1, furan-H), 7.17-7.22 (3H, m, Ar-H) 7.24-7.31 (2H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 27.3, 28.4, 34.1, 78.5, 109.3, 126.0, 128.3, 128.4, 137.1, 138.7, 141.7, 144.8; Found (CI): $[M+H]^+$ 245.15352, $C_{16}H_{21}O_2$ requires 245.15415.

175b: 2-((2-Phenethylfuran-3-yl)oxy)ethanol



General procedure H: 75% yield; ν_{max} (film/cm^{-1}) 3420 (O-H), 2928, 2871 (C-H), 1660 (C=C), 1275 (C-O); δ_H (600 MHz, $CDCl_3$) 1.79 (1H, br s, OH), 2.88-2.96 (4H, m, Ar-CH_2CH_2), 3.69-3.78 (4H, m, HOCH_2CH_2), 6.22 (1H, d, *J* 1.9, furan-H), 7.12 (2H, d, *J* 7.2, Ar-H), 7.15 (1H, d, *J* 1.9, furan-H), 7.19 (1H, t, *J* 7.2, Ar-H), 7.24-7.30 (2H, m, Ar-H); δ_C (150 MHz, $CDCl_3$) 27.2, 34.4, 61.7, 73.6, 104.0, 126.1, 128.4, 128.6, 139.4, 139.9, 141.5, 142.4; Found (CI): $[M]^+$ 233.116954, $C_{14}H_{17}O_3$ requires 233.11722.

4-Methoxy-5-phenethylfuran-3-carbaldehyde

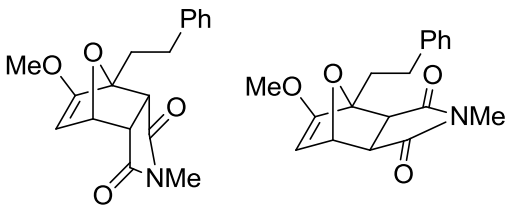


$POCl_3$ (0.04 mL, 0.42 mmol) and DMF (2 mL) at 0 ˚C for 5 min then added furan (100mg, 0.38 mmol) in DMF. Stirred overnight at rt. The reaction was quenched with aq. $NaHCO_3$ and the organic phase extracted with diethyl ether. The combined organic phases were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo* to give the aldehyde (30 mg, 35% yield);

ν_{max} (film/cm^{-1}) 2929, 2856 (C-H), 1675 (C=O), 1609 (C=C), 1229 (C-O); δ_H (600 MHz, $CDCl_3$) 2.99 (4H, s, Ar-CH_2CH_2), 3.68 (3H, s, OMe), 7.05 (1H, s, furan-H), 7.15-7.21 (3H, m, Ar-H), 7.26-7.29 (1H, m, Ar-H), 9.45 (1H, s, OCH); δ_C (150 MHz, $CDCl_3$) 27.6, 33.6, 59.2, 126.4, 128.45, 128.53, 128.55, 140.7, 146.3, 147.4, 148.9, 177.0; Found (CI): $[M]^+$ 231.101465, $C_{14}H_{15}O_3$ requires 231.10157.

(3aR,4S,7S,7aS)-5-Methoxy-2-methyl-4-phenethyl-3a,4,7,7a-tetrahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione

(4S,7S,7aR)-5-Methoxy-2-methyl-4-phenethyl-3a,4,7,7a-tetrahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione



endo-**189** 63%

exo-**189** 31%

3-Methoxy furan **172b** and N-methylmaleimide **188** were dissolved in CH_2Cl_2 and stirred overnight at rt. The product was purified by column chromatography.

Endo:Exo Crude ratio 2:1. Single distereoisomers isolated: 63% endo, 31% exo.

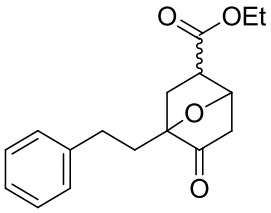
ν(film/cm^{-1}) 3025, 2930 (C-H), 1697 (C=O), 1625 (C=C);

Endo: δ_H (600 MHz, $CDCl_3$) 2.22-2.29 (1H, m, Ar-CH_2C*H*H), 2.55-2.62 (1H, m, Ar-CH_2CH*H*), 2.80 (2H, t, *J* 8.5, Ar-CH_2), 2.85 (3H, s, OMe), 3.21 (1H, d, *J* 7.5, H_B), 3.53 (3H, s, NMe), 3.70 (1H, dd, *J* 7.5, 5.3, H_A), 5.02 (1H, br s, C=CH), 5.20 (1H, dd, *J* 5.3, 1.9, H_C), 7.19 (1H, t, *J* 7.5, Ar-H), 7.24 (H, d, *J* 7.5, Ar-H), 7.29 (2H, t, *J* 7.5, Ar-H); δ_C (150 MHz, $CDCl_3$) 24.6, 30.5, 31.9, 49.8, 51.3, 58.2, 78.2, 89.7, 96.9, 126.1, 128.49, 128.52, 141.6, 165.4, 174.3, 175.6;

Exo: δ_H (600 MHz, $CDCl_3$) 2.20-2.29 (1H, m, Ar-CH_2C*H*H), 2.33-2.39 (1H, m, Ar-CH_2CH*H*), 2.73-2.83 (2H, m, Ar-CH_2), 2.93 (1H, d, *J* 6.4, H_B), 2.96 (3H,s, OMe), 3.14 (1H, d, *J* 6.4, H_A), 3.66 (3H, s, NMe), 5.16 (1H, br s, C=CH), 5.19 (1H, d, *J* 1.9, H_C), 7.18 (1H, t, *J* 7.5, Ar-H), 7.23 (H, d, *J* 7.5, Ar-H), 7.28 (2H, t, *J* 7.5, Ar-H); δ_C (150 MHz, $CDCl_3$) 25.0, 29.4, 30.8, 49.2, 54.4, 58.3, 79.9, 89.3, 99.6, 126.0, 128.4, 128.5, 141.9, 168.4, 174.9, 176.4;

Found (CI): $[M]^+$ 313.132190, $C_{18}H_{19}NO_4$ requires 313.13086.

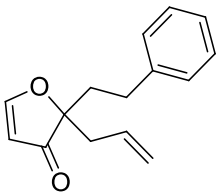
191: Ethyl 5-oxo-4-phenethyl-7-oxabicyclo[2.2.1]heptane-2-carboxylate



Same Procedure as above, except in toluene at reflux, followed by addition of 2M HCl. Crude ratio 3:1. Single distereoisomer isolated: 80 mg, 0.8 mmol 28%.

ν_{max} (film/cm^{-1}) 2980, 2937 (C-H), 1726 (C=O); δ_H (600 MHz, $CDCl_3$) 1.27 (3H, t, *J* 7.2, CH_3), 2.00 (1H, t, *J* 12.0), 2.09 (2H, td, *J* 13.9, 5.7), 2.24 (1H), 2.33 (1H, d, *J* 17.7), 2.53 (1H, dd, *J* 17.7, 6.0), 2.65 (1H, td, *J* 12.4, 4.9), 2.80 (1H, td *J* 12.8, 4.9), 3.35 (1H,), 4.16 (2H, q, *J* 7.2, C*H*$_2$CH$_3$), 4.97 (1H, t, *J* 5.7), 7.19 (2H, t, *J* 7.2, Ar-H), 7.22 (2H, d, *J* 7.2, Ar-H), 7.29 (1H, t, *J* 7.2, Ar-H); δ_C (150 MHz, $CDCl_3$) 14.3, 30.4, 31.1, 32.9, 41.6, 47.4, 61.4, 75.7, 89.0, 126.2, 128.4, 128.6, 141.7, 171.4, 210.4; Found (CI): $[M]^+$ 289.143412, $C_{17}H_{21}O_4$ requires 289.14344.

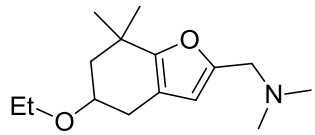
186: 2-Allyl-2-phenethylfuran-3(2H)-one



Procedure: **174b** (50mg, 0.219 mmol) was dissolved in toluene (2ml) and heated to reflux for 6h. The reaction was then allowed to cool before it was concentrated in vacuo to give the crude product. This was purified by flash column chromatography to give **186** (40mg, 0.176 mmol 80%); ν(film/cm^{-1}) 3064, 3028, 2920 (C-H), 1697 (C=O), 1559 (C=C); δ_H (600 MHz, $CDCl_3$) 2.05-2.10 (2H, m, C*H*$_2$CH$_2$Ar), 2.44-2.58 (2H, m, CH$_2$C*H*$_2$Ar), 2.50 (H, d, *J* 7.2, C=CHC*H*$_2$), 5.11 (1H, d, *J* 11.3, HC=C*H*H), 5.13 (1H, d, *J* 18.8, HC=CH*H*), 5.63-5.69 (1H, m, *H*C=CH$_2$), 5.70 (1H, d, *J* 2.3, O*H*C=CH), 7.14 (2H, d, *J* 7.5, Ar-H), 7.18 (1H, d, *J* 7.5, Ar-H), 7.26 (2H, d, *J* 7.5, Ar-H), 8.25 (1H, d, *J* 2.3, OHC=C*H*CO); δ_C (150

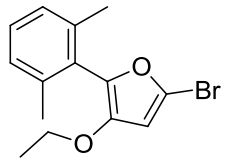
MHz, $CDCl_3$) 29.1, 37.2, 40.4, 91.5, 107.7, 119.9, 126.2, 128.4, 128.6, 130.4, 141.0, 177.3, 206.4; Found (CI): [M] 229.122392, $C_{15}H_{17}O_2$ requires 229.12231.

185: 1-(5-Ethoxy-7,7-dimethyl-4,5,6,7-tetrahydrobenzofuran-2-yl)-N,N-dimethylmethanamine



Procedure: N-Methyl-N-methylenemethanaminium iodide (Eschenmoser's salt, 2 eq.), was added to a solution of **179p** (20 mg, 0.103 mmol) in DMF (1ml). The solution was stirred at rt for 12h. The reaction was then concentrated in *vacuo* to give the crude product. This was purified by flash column chromatography to give **185** (24 mg, 0.095 mmol 92%); ν(film/cm^{-1}) 2964, 2926, 2866 (C-H), 1456 (C=C), 1362 (C-N); δ_H (600 MHz, $CDCl_3$) 1.22 (3H, t, *J* 7.2, OCH_2CH_3), 1.24 (3H, s, CCH_3), 1.28 (3H, s, CCH_3), 1.66 (1H, t, *J* 12.1, C*H*HC$(CH_3)_2$), 1.91 (1H, br d, *J* 12.0, CH*H*C$(CH_3)_2$), 2.27 (6H,s NMe_2), 2.29 (1H, dd, *J* 15.1, 9.4, Furan-C*H*H), 2.80 (1H, dd, *J* 15.1, 4.9, Furan-CH*H*), 3.43 (1H, d, *J* 14.0, C*H*HNMe_2), 3.47 (1H, d, *J* 14.0, CH*H*NMe_2), 3.53-3.62 (2H, m, OCH_2), 3.70-3.77 (1H, m, CHOEt), 5.97 (1H, s, Furan-H); δ_C (150 MHz, $CDCl_3$) 15.8, 28.3, 28.5, 29.5, 32.9, 44.9, 45.1, 55.9, 63.9, 73.4, 109.9, 113.4, 150.1, 156.5; Found (CI): [M] 251.187845, $C_{15}H_{25}NO_2$ requires 251.18798.

187: 5-Bromo-2-(2,6-dimethylphenyl)-3-ethoxyfuran



Procedure: N-Bromo-succinimide (2 eq.) was added to a solution of **174b** (20 mg, 0.09 mmol) in DMF (1ml). The solution was stirred at rt for 6h. The reaction was then concentrated in *vacuo* to give the crude product. This was purified by flash column chromatography to give **187** (18 mg, 0.061 mmol 68%); δ_H (600 MHz,

$CDCl_3$) 1.16 (3H, t, *J* 7.2, OCH_2CH_3), 2.27 (6H, s, 2 × Ar-Me), 3.80 (2H, q, *J* 7.2, OCH_2CH_3), 6.27 (1H, s, Furan-H), 7.02 (2H, d, *J* 7.5, Ar-H), 7.20 (1H, t, *J* 7.5, Ar-H); δ_C (150 MHz, $CDCl_3$) 15.2, 20.4, 67.3, 105.6, 119.7, 127.5, 128.5, 129.2, 139.0, 139.3, 144.7; Found (EI): [M] 294.024760, $C_{14}H_{15}BrO_2$ requires 294.02499.

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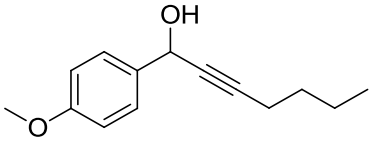
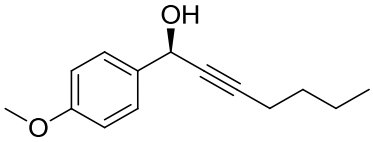
8. Appendix

1-(4-Methoxyphenyl)hept-2-yn-1-ol





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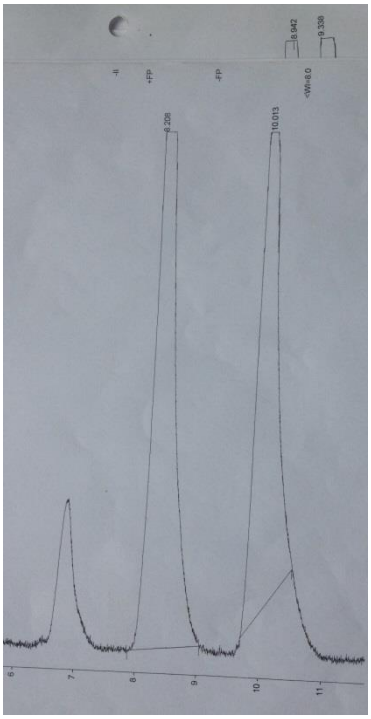

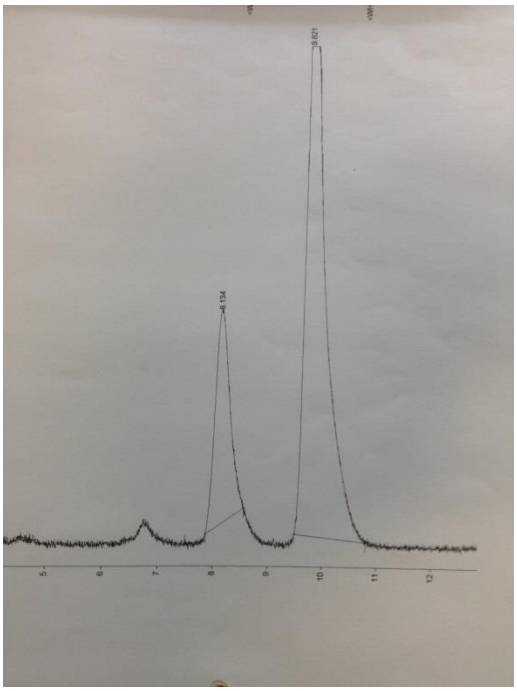

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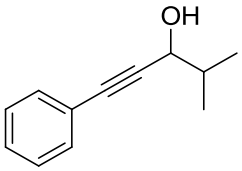
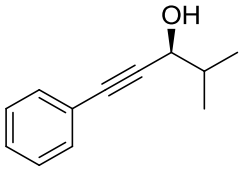
Enantiomenriched: HPLC (Daicel Chiralpack AD, hexane/i-PrOH, 80/20, flow rate 1 mL/min λ = 254 nm), t_R=8.1 min (minor), t_R=9.8 min (major)

4-Methyl-1-phenylpent-1-yn-3-ol





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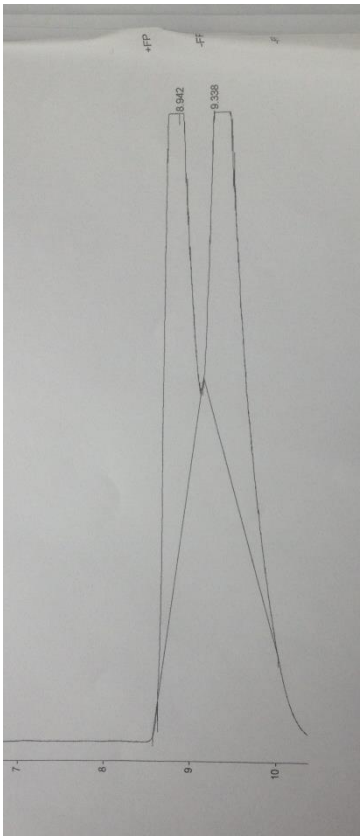
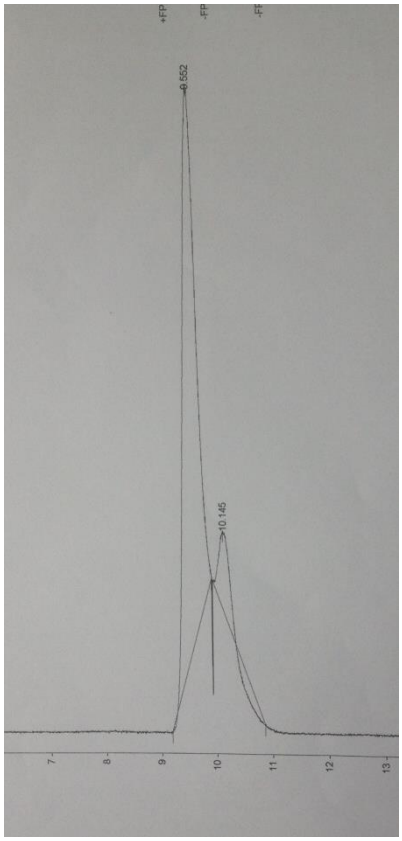
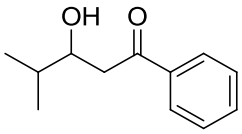


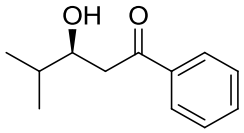


Racemic: HPLC (Daicel Chiralpack AD, hexane/i-PrOH, 80/20, flow rate 1 mL/min λ = 254 nm), t_R=8.9 min, t_R=9.4 min

Enantiomenriched: HPLC (Daicel Chiralpack AD, hexane/i-PrOH, 80/20, flow rate 1 mL/min λ = 254 nm), t_R=9.5 min (Major), t_R=10.1 min (minor)

3-Hydroxy-4-methyl-1-phenylpentan-1-one





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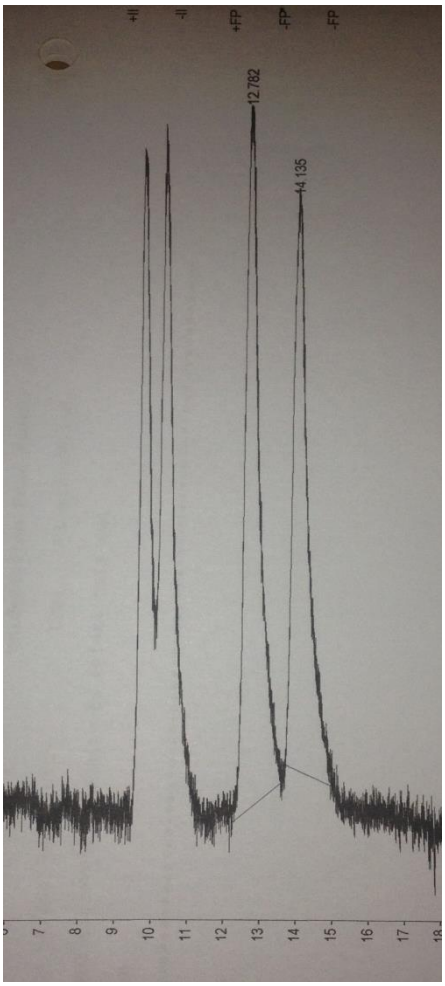

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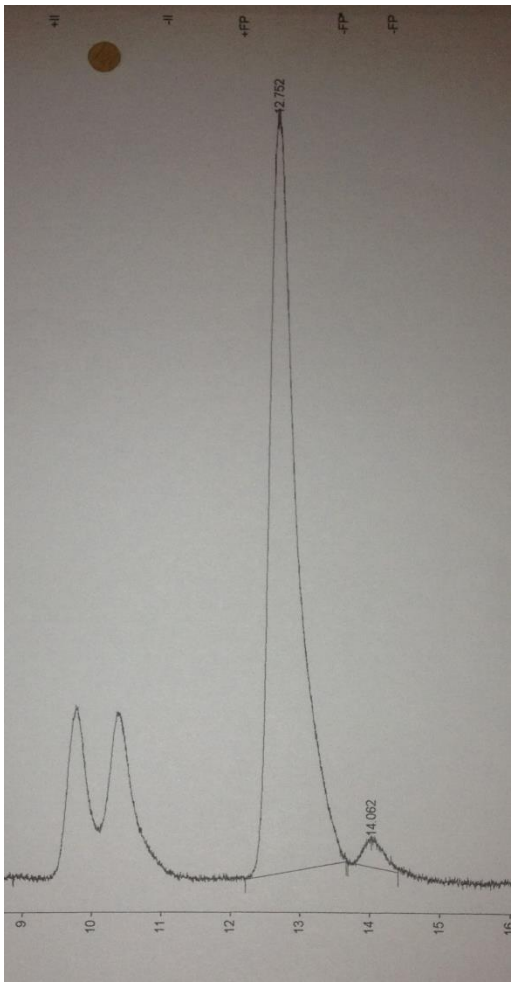

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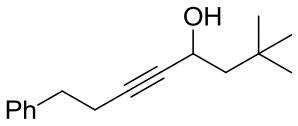
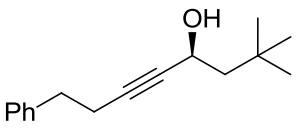
Enantiomenriched: HPLC (Daicel Chiralpack AD, hexane/i-PrOH, 80/20, flow rate 1 mL/min λ = 254 nm), t_R=12.8 min (major), t_R=14.1 min (minor)

2,2-Dimethyl-8-phenyloct-5-yn-4-ol





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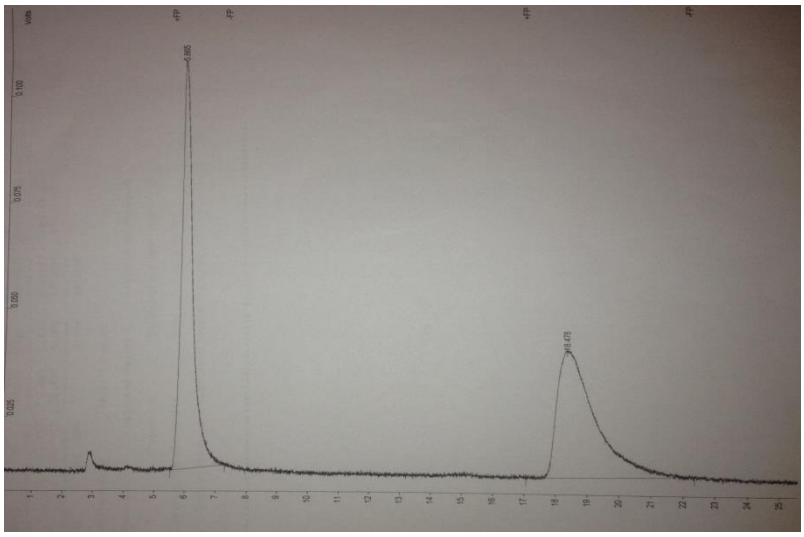

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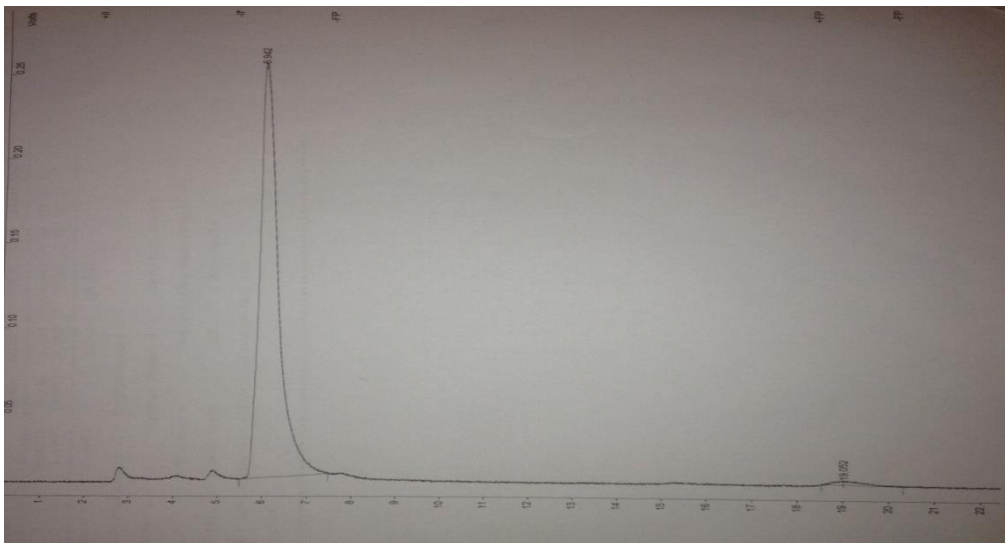
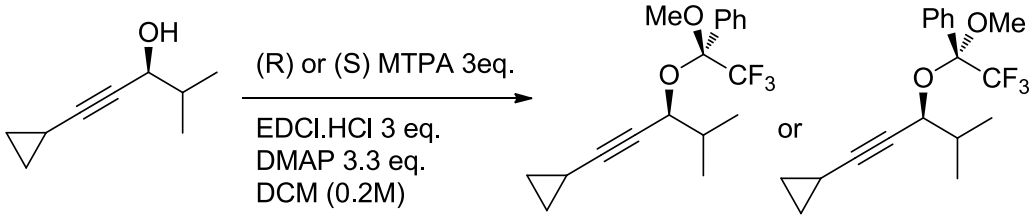
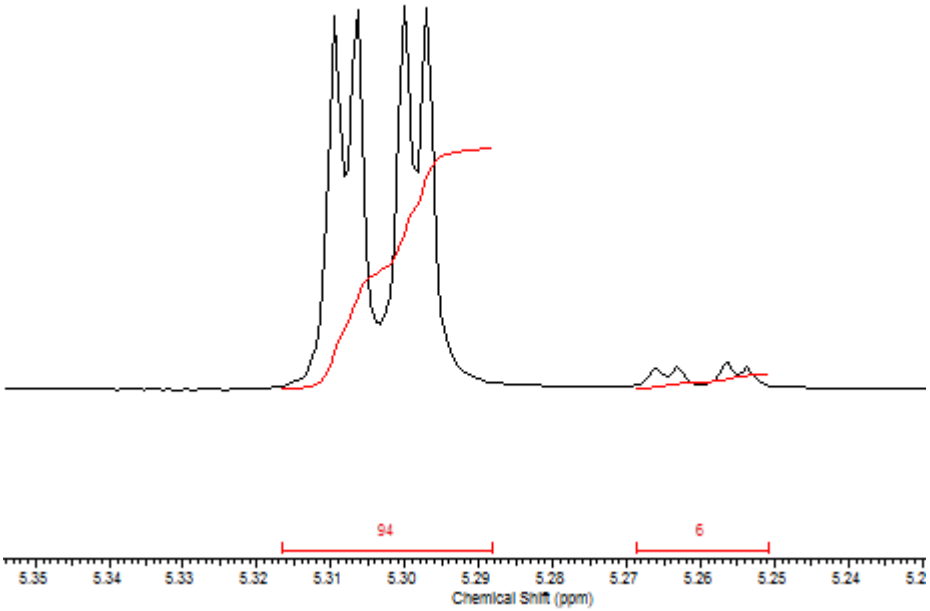


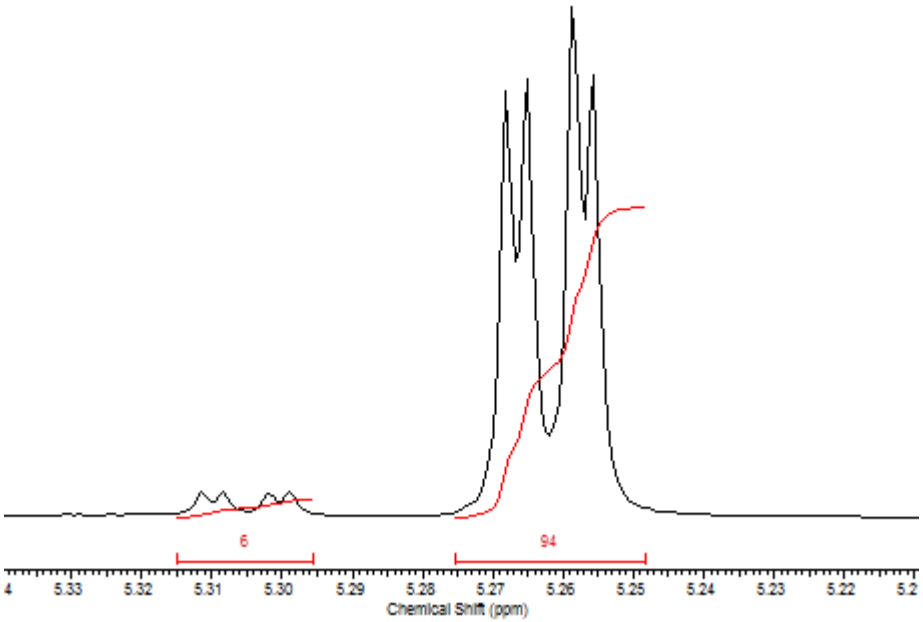
Racemic: HPLC (Daicel Chiralpack AD, hexane/i-PrOH, 80/20, flow rate 1 mL/min λ = 254 nm), t_R=5.9 min, t_R=18.5 min

Enantiomenriched: HPLC (Daicel Chiralpack AD, hexane/i-PrOH, 80/20, flow rate 1 mL/min λ = 254 nm), t_R=5.9 min (major), t_R=19.0 min (minor)

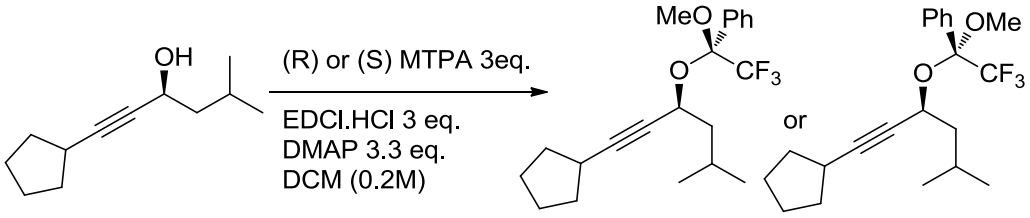
1-Cyclopropyl-4-methylpent-1-yn-3-ol

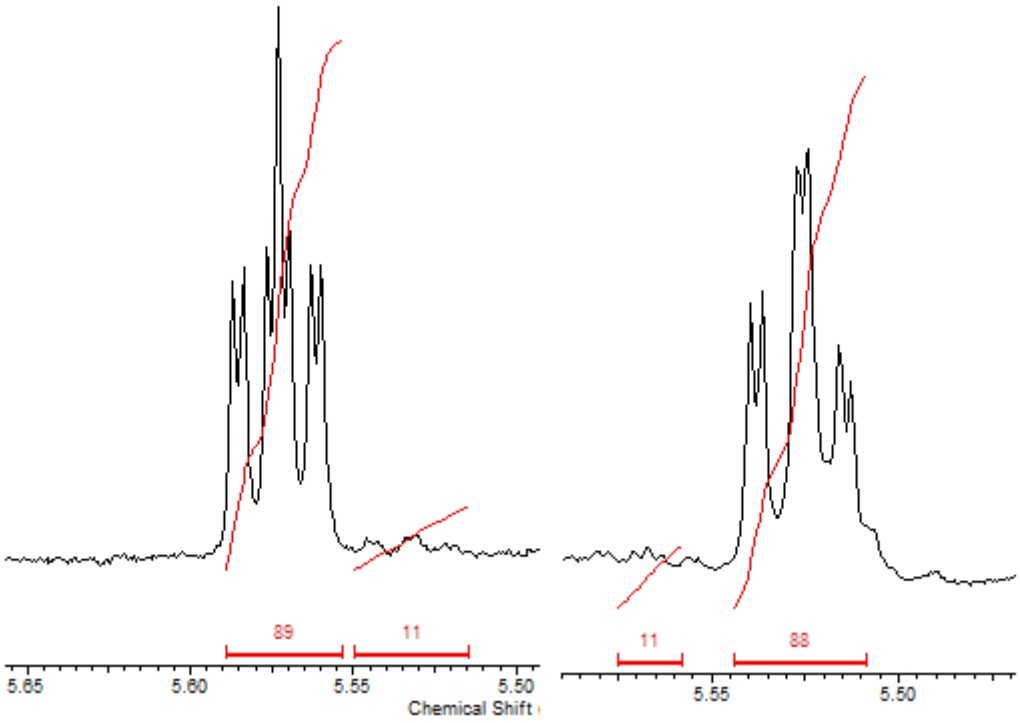






1-Cyclopentyl-5-methylhex-1-yn-3-ol





4-((*tert*-Butyldimethylsilyl)oxy)-1-cyclohexylbut-2-yn-1-ol