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Expedient Syntheses of β-Iodofurans by 5-*endo-dig* Cyclisations

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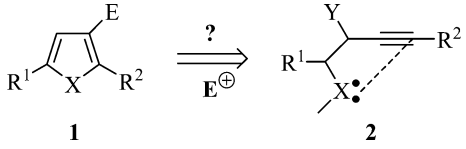
5-*endo-dig* cyclisations of 3-alkyne-1,2-diols using iodine as the electrophile proceed smoothly to deliver excellent yields of the corresponding β-iodofurans. The necessary precursors are available from a number of different approaches, notably regioselective bis-hydroxylation of conjugated enynes and the addition of acetylides to α-hydroxy carbonyl groups. The initial iodofurans can be homologated using a number of strategies, ranging from various transition metal-catalysed couplings to halogen–metal exchange and subsequent coupling with an electrophile. Hence, this method overall represents a flexible, relatively brief and very efficient approach to a variety of highly substituted furans.

Introduction

Despite enormous advances in drug development and in other endeavours involving applications of previously unknown structures, such as in the design of new materials and effect chemicals in general, heteroaromatic residues still occupy a central position in all of these areas. Perhaps even more surprising is that, even after over one hundred years of development, there is still room and indeed a need for the definition of more efficient or operationally simpler routes to these important heterocycles. The current and future demands of a more environmentally demanding population on the chemical industry in general only serve to emphasise this. In broad terms, heteroaromatic targets are obtained either by late formation of the heteroaromatic ring from a complex acyclic precursor or by (multiple) functionalisation of a simple or even parent heteroaromatic predominantly by using some of the myriad of electrophilic substitution methods or by metallation strategies.[1] In this respect, halogen substituents have always occupied a special position by, for example, facilitating regioselective metallation using halogen–metal exchange.[2] However, this status has been enhanced enormously by the development of a whole host of predominantly palladium-catalysed coupling methods which, collectively, represent a paradigm shift in synthetic design over the past twenty years or so.[3] A most attractive tactic in heteroaromatic synthesis therefore would be to create the heterocycle at the same time as incorporating a halogen atom. We reasoned that this might be achievable using 5-*endo-dig* halocyclisations of homopropargylic systems, based on an extrapolation of what was emerging as a useful synthetic strategy for the stereoselective synthesis of saturated heterocycles, that of overall 5-*endo-trig* cyclisations.[4] Although highly successful in many cases, the latter type of cyclisation is disfavoured according to Baldwin's rules;[5] by contrast, 5-*endo-dig* processes are favoured.

Despite this, and perhaps because at first sight, such cyclisations do not look viable because of the distance between the necessary reacting centres (Figure 1), there was little activity in this area until very recently, notwithstanding the existence of some earlier reports hinting at their viability and potential.[6]



1 **2**

Figure 1. Electrophile-driven 5-*endo-dig* cyclisation.

Results and Discussion

We were also inspired to investigate the general area of 5-*endo-dig* cyclisations by what seemed to us to be a remarkable key step in a synthesis of the antifungal pyrrolidine (+)-preussin (**5**), which involved a mercury(II)-induced conversion of the ynone **3** into the pyrrolone **4**, subsequent reductions of which led to the target **5** (Scheme 1).[7] The very fact that this central 5-*endo-dig* cyclisation works with an electron-deficient alkyne and also that the single stereogenic centre in the precursor **3** remained unmolested as far as the target **5** attested to a cyclisation procedure which was both mild and favoured, a conclusion further supported by the survival of the *N*-Boc group. The latter function is, of course, well positioned to compete with nitrogen

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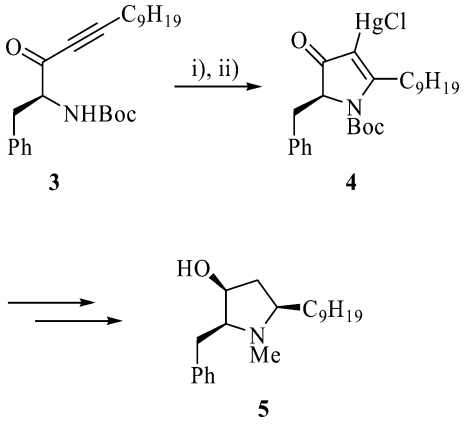
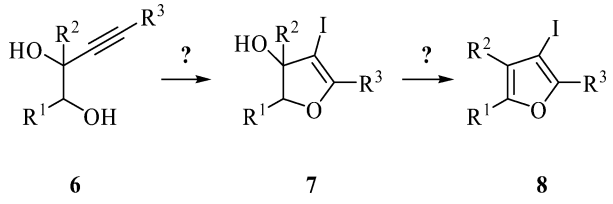
in a 6-*exo* reaction mode when presented with the nearby electron-deficient centre; the fact that it does not participate boded well for further developments of such 5-*endo* cyclisations.



Scheme 1. i) $Hg(OAc)_2$, ii) NaCl.

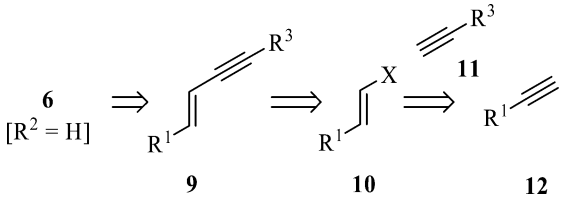
A few isolated examples of similar, mercury(II)-induced furan syntheses from related 3-alkyne-1,2-diols have also previously been reported in the Russian literature.[6] For a viable furan synthesis, we needed to look beyond using mercury(II) salts as the source of the necessary electrophilic trigger for reasons of toxicity and practicality and obviously we needed an alcohol group to act as a nucleophile in place of the NHBoc function used in Scheme 1. Incorporation of an additional hydroxy group, which we hoped would be lost as water during an aromatisation step subsequent to cyclisation, then led to this idea of obtaining the iodofurans **8** from the 3-alkyne-1,2-diols **6**, presumably via the dihydrofuran species **7**, as shown in Scheme 2.



Scheme 2.

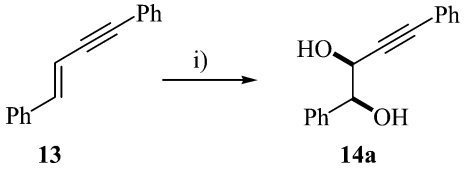
We chose to use iodine, partly because it had been so successful in triggering our 5-*endo-trig* cyclisations leading to β-iodotetrahydrofurans[4] and partly because, if the proposed cyclisations proved successful, then the iodofuran products **8** would be highly amenable to subsequent homologation using a wide range of metallation reactions, as argued above. Herein, we report in full the successful outcome of the chemistry shown in Scheme 2, a few of its limitations and its application to the formation of highly substituted furans.[8]

Although there are many possibilities for the synthesis of the necessary starting diols **6**, initially we chose to employ a single approach, that of the highly regioselective bis-hydroxylation of a disubstituted conjugated enyne **9**, a very useful method highlighted by the Sharpless group.[9] Within obvious limitations, an attraction of this approach is the availability of the enynes **9** from Sonogashira coupling[10] between a 1-alkyne **11** and a 1-halo-1-alkene **10**, which can often be derived most expediently from a second 1-alkyne **12**, as well as using many other methods (Scheme 3).



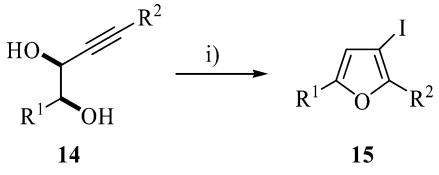
Scheme 3.

This is illustrated by the efficient conversion of the diphenyl butenyne **13** into the *syn*-diol **14a** in 78% isolated yield (Scheme 4), which also provided some useful stereochemical insights into the cyclisation (see below).



Scheme 4. i) $K_2OsO_4{\cdot}2H_2O$ (cat.), $K_3Fe(CN)_6$ (xs), K_2CO_3 (xs), $MeSO_2NH_2$, quinuclidine (cat.), *t*BuOH/H_2O (1:1), 20 °C, 96 h (78%).

All the diols shown in Scheme 5 were prepared in the same manner from the corresponding (*E*)-enynes, specifically using the non-enantiomeric recipe for bis-hydroxylation developed by the Warren group.[11] The enynes were obtained in turn from Sonogashira couplings of a 1-alkyne and a 1-bromoalkene, all of which are commercially available.



a: $R^1 = R^2 = Ph$ [60 %]
b: $R^1 = Ph$; $R^2 = Bu$ [71 %]
c: $R^1 = Bu$; $R^2 = Ph$ [77 %]
d: $R^1 = Me$; $R^2 = Ph$ [88 %]
e: $R^1 = Me$; $R^2 = Bu$ [65 %]
f: $R^1 = CO_2Me$; $R^2 = Ph$ [47 %]

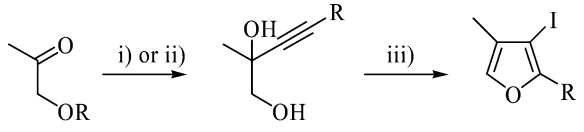
Scheme 5. i) I_2 (3.3 equiv.), $NaHCO_3$ (3.3 equiv.), MeCN, 0–20 °C, 1 h.

Success in the key cyclisation step (Scheme 5) turned out to be readily achieved using conditions employed previously in our 5-*endo-trig* cyclisations.[4] The diols **14** were stirred with slightly over three equivalents of iodine in acetonitrile containing three equivalents of sodium hydrogen carbonate, initially with ice-water cooling but subsequently without cooling. Under these conditions, the cyclisations were com-

plete in around one hour and delivered good to excellent isolated yields of the β-iodofurans **15**. In subsequent experiments, we found that dichloromethane or tetrahydrofuran could equally well be used as the solvent. Workup consisted of reduction of the excess iodine using aqueous sodium sulfite (or, less conveniently due to its substantially lower solubility in water, thiosulfate), followed by an aqueous wash and straightforward chromatography. Isolated yields were generally in excess of 80%, with the major losses largely due to product volatility.

The requirement for at least three equivalents of iodine is essential; using less results in incomplete conversion. This is a common phenomenon throughout these and related iodolactonisations and iodoetherifications in general when using molecular iodine and has, to the best of our knowledge, not been explained.[12] We assume that such an excess is necessary to generate a particularly reactive and/or suitable electrophilic species, perhaps iodonium pentaiodide, $I{\cdot}I_5$, based on the need for three equivalents. Of course, this requirement does rather detract from the overall efficiency of the scheme, especially seriously if it were to be applied on a large scale. However, this brief sequence does otherwise arrive at useful substituted furans, which would usually be tricky to prepare in comparable yields and in so few steps using alternative methods.

While these examples all worked well, we were however concerned that each contained a secondary alcohol group that underwent (eventual) elimination to give the heteroaromatic system (Scheme 5). This was evidently an extremely facile step under the condition used as, despite many attempts using ^{1}H NMR monitoring, we were never able to obtain any unambiguous evidence for the existence of the dihydrofurans **7** (Scheme 2). In view of this, we were somewhat concerned that a tertiary alcohol might be too sensitive to allow smooth cyclisation as shown in Scheme 2. To test this, we used an alternative general approach for precursor synthesis, that of the addition of an acetylide to an *O*-protected α-hydroxy ketone or aldehyde, which of course also served the purpose of adding flexibility to this overall approach to iodofurans (Scheme 6).



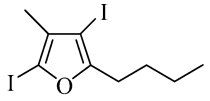
16 **17** **18**

a: R = $OSiPh_2Me$;
b: R = OThP

a: R = Bu;
b: R = Ph

Scheme 6. i) [**17a**] RCCLi, THF, 0 °C, 2 h then TBAF, THF [89%]; ii) [**17b**] as i) then *p*TSA, MeOH, 20 °C, 2 h [71%]; iii) as Scheme 5 [**18a**: 82%; **18b**: 61%].

In the first examples aimed at extending the range to substrates having tertiary alcohol functions, lithiated alkynes were added to the protected hydroxyacetone derivatives **16**; subsequent standard deprotection then gave the alkynediols **17** in good yields. Our fears proved groundless, as both substrates **17a** and **17b** underwent equally smooth iodocyclisation to give the iodofurans **18a** and **18b** in excellent yields; again, losses due to product volatility were a factor. However, the fact that these two products both contained an α-free position meant that they were more prone to subsequent electrophilic substitution by the residual molecular iodine. For example, when a cyclisation reaction of the hexynyl-derived diol **17a** was stirred for three hours rather than the usual one hour, significant quantities (ca. 20% of the total product) of the diiodofuran **19** were detected by both GC-MS and ^{1}H NMR analysis. This was almost completely avoided by reaction workup as soon as the cyclisation was completed.



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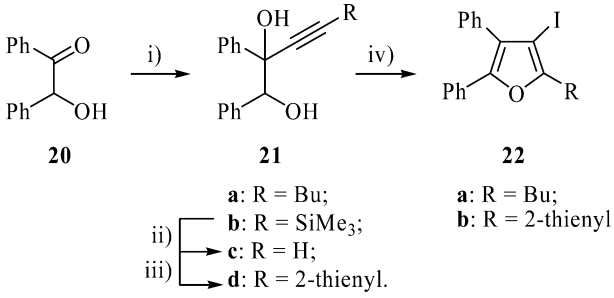
We were also successful in extending the methodology to include fully substituted examples. Thus, the adduct **21a**, formed as essentially a single diastereoisomer by the addition of 2.1 equivalents of lithiated 1-hexyne directly to benzoin **20**, underwent similarly smooth cyclisation upon exposure to three equivalents each of iodine and sodium hydrogen carbonate to give an excellent yield of the fully substituted iodofuran **22a** (Scheme 7).



20 **21** **22**

a: R = Bu;
b: R = $SiMe_3$;
c: R = H;
d: R = 2-thienyl.

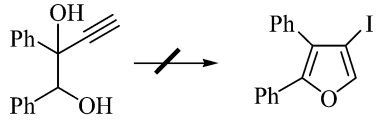
a: R = Bu;
b: R = 2-thienyl

Scheme 7. i) [**21a**, **21b**] 2.1 equiv. RCCLi, THF, –78 °C to 0 °C [68%; 77%]; ii) [**21c**] TBAF, THF, 0 °C, 20 min. [80%]; iii) 2-iodothiophene, $Pd(PPh_3)_4$, Et_2NH, 20 °C, 16 h [81%]; iv) as Scheme 5 [**22a**: 93%; **22b**: 71%].

A similarly stereoselective addition of lithiated trimethylsilylacetylene to benzoin (**20**) also gave a decent yield of the expected adduct **21b**, which was desilylated by brief exposure to tetrabutylammonium fluoride (TBAF) in tetrahydrofuran. The resulting diol **21c** then underwent a smooth Sonogashira coupling with 2-iodothiophene to give the anticipated homologue **21d**, which then also underwent smooth conversion into the corresponding β-iodofuran **22b** under the same conditions.

Two caveats follow: firstly, it was both more time- and atom-efficient to employ one equivalent of acetylide to deprotonate the benzoin prior to addition of the second equivalent to the ketone than to protect the benzoin hydroxy as, for example, a *tert*-butyldimethylsilyl ether. This is generally true in cases where the acetylene is reasonably

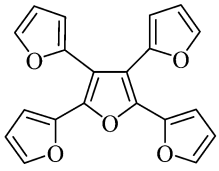
volatile and completely removed upon evaporation of the final reaction workup; presumably, on a large scale, this excess could even be recovered and recycled. A second caveat concerns the diol stereochemistry: we were surprised to note that the diol **21a** was isolated as essentially a single diastereoisomer (ca. 99:1). We have not yet determined the stereochemistry of the major isomer, as this was not especially irrelevant to the central iodocyclisation (but see below). We are currently following up this observation in a separate study, which will be reported shortly. The presence of the thiophene residue evidently had no deleterious effect upon the iodocyclisation, as far as we could tell. However, we did uncover one limitation of the present iodocyclisation methodology: it appears that terminal alkyne groups do not participate. Thus, attempts to cyclise the terminal alkyne **21c** failed to provide the iodofuran **23** (Scheme 8).



21c **23**

Scheme 8.

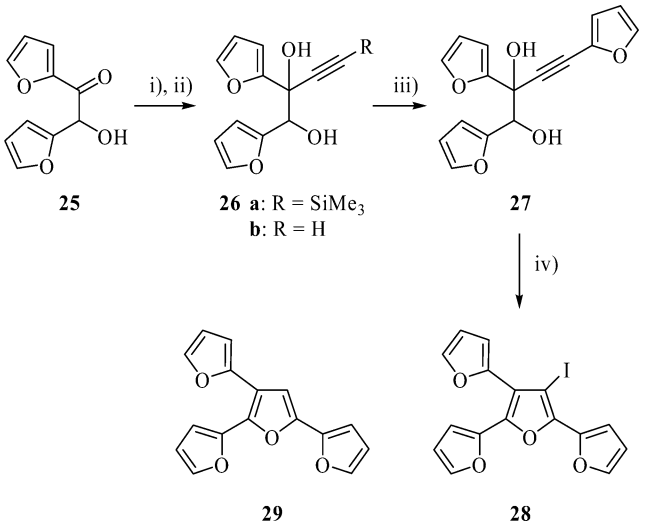
It occurred to us that a continuation of this theme of incorporating heterocycles onto the furan could be taken to an interesting extreme by a synthesis of tetra(2-furyl)furan (**24**), a novel chromophore, which might display some useful properties; it would also be interesting to determine its lower energy conformations, both in the solid state and in solution. Obviously, the conformation shown (**24**) is drawn simply for style and may well not represent the real orientation of the furan rings.



24

In the event, condensation of furoin (**25**) with lithiated trimethylsilylacetylene followed by desilylation gave a respectable return of the alkyne diol **26** (Scheme 9).

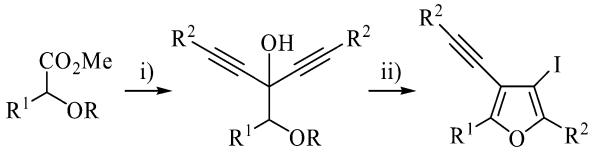
This proved to be a rather delicate molecule which nevertheless underwent smooth Sonogashira coupling with 2-iodofuran, fortunately at ambient temperature, to give the trifuryl derivative **27**. The key 5-*endo-dig* iodocyclisation was successful after a fashion and gave the expected iodofuran **28** but as a very unstable oil in poor yield, almost certainly due to product decomposition during both the cyclisation and purification steps. Unfortunately, a number of attempts at a final Suzuki coupling step using 2-furylboronic acid gave variable yields of the deiodinated trifurylfuran **29** as the only isolable product. In retrospect, perhaps a more successful strategy to obtain the target chromophore **24** would have been to use 5-substituted furans throughout the sequence, as the unsubstituted furan α-positions render



Scheme 9. i) TMSCCLi, THF, –78 °C to 0 °C [78%]; ii) TBAF, THF, 20 min. [68%]; iii) 2-iodofuran, CuI (cat.), $Pd(PPh_3)_4$ (cat.), Et_2NH, 20 °C, 16 h [74%]; iv) $3I_2$, $3NaHCO_3$, dry EtOAc, 20 °C, 1 h [25%].

the intermediates and final product just too sensitive. Future efforts in this direction will therefore begin with the furoins derived from precursors such as 5-phenyl- or 5-alkyl-2-furancarboxaldehydes.

A final idea was to attempt to obtain iodofurans **32** from the 2-silyloxy or 2-hydroxy esters **30**, as shown in Scheme 10. Clearly, the intermediate diols **31** will contain two identical alkyne substituents and hence the products **32** will be "pseudosymmetrical". At the outset, it was far from clear if the second alkyne unit would survive or would interfere with the cyclisation in some way.



30 **31** **32**

Entry	R	R^1	R^2	**31**	**32**
1	TBS	Me	Bu	**a**: 78	**a**: 82
2	TBS	Ph	Bu	**b**: 83	**b**: –
3	TBS	Me	Ph	**c**: 74	**c**: 82
4	TBS	Ph	Ph	**d**: 80	**d**: 89
5	H	Me	Bu	**e**: 86	**a**: 93
6	H	Ph	Bu	**f**: 72	**b**: 87
7	H	Me	Ph	**g**: 66	**c**: 93
8	H	Ph	Ph	**h**: 76	**d**: 94

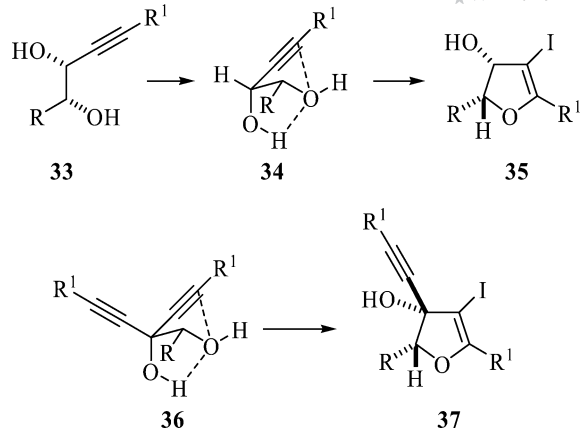
Scheme 10. i) 2 (R = TBS) or 3 (R = H) equiv. R^2CCLi, THF, –78 °C, 1 h; ii) 3 I_2, 3 $NaHCO_3$, MeCN, 20 °C, 1 h.

In the event, both the acetylide condensations with the 2-substituted esters **30** and the key iodocyclisations worked very smoothly in most examples carried out; the results are summarised in Scheme 10. Once again, the seemingly wasteful tactic of reacting some 2-hydroxy esters directly with, now, just over three equivalents of an acetylide, proved viable and arguably more atom efficient that employing a protecting group strategy. However, when an *O*-silyl group such as *tert*-butyldimethylsilyl was used, the finding that its presence hardly affected the rate of the iodocyclisation step obviated the requirement for a separate deprotection step, thereby offering an alternative method for abbreviating the overall sequence.

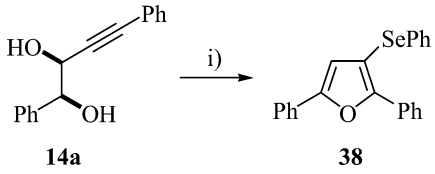
This in situ deprotection tactic will very likely be successful in the case of a number of alternative hydroxy protecting groups, such as other silyl functions, *O*-benzyl, OPMB and possibly *O*-allyl, amongst others. Overall, however, the yields of iodofurans recovered from cyclisations of dialkynyl diols (Entries 5–8, Scheme 10) were up to 10% higher that the corresponding reactions of the *O*-silyl derivatives, possibly due to some removal of the necessary excess of iodine by reaction(s) with the silicon residues. This not unreasonable observation came to an extreme in the case of the adduct formed between *O*-silylmandelate and 1-hexyne (Entry 2), when the *O*-silyl derivative refused to cyclise; in contract, the corresponding diol underwent highly efficient cyclisation (Entry 6). No products resulting from the addition of iodine or from any other reactions with the remaining alkyne group were observed in any of the examples quoted.

Some comments on the stereochemistry of these cyclisations are perhaps appropriate. Our first reactions were carried out using single *syn*-diastereoisomers of the alkynediols derived from stereochemically pure (*E*)-enynes. However, subsequently some examples, such as diols **14d** and **14e** were prepared as diastereoisomeric mixtures when we started with a commercial *E*/*Z* mixture of 1-bromopropene [ca. 2:1 in favour of the (*Z*)-isomer]. We were therefore able to correlate and confirm which isomer was which in the diol mixture. We noted that the *syn*-isomers **33** underwent significantly faster cyclisation in a mixed sample, by stopping the reaction before completion. This is consistent with the intermediacy of conformation **34**, wherein hydrogen bonding may also assist in the cyclisation process (Scheme 11). The resulting unobserved dihydrofurans **35** are then especially well set up for the final E_2 elimination of water, which may also contribute to faster formation of the final iodofuran from these *syn*-isomers. Similarly, we would therefore anticipate that the related geometry **36** might be involved in cyclisations of the bis-alkynes **31**, which might therefore proceed via the dihydrofurans **37**.

There may, of course, be other electrophiles which could be equally successful in inducing such 5-*endo* cyclisations. A single example, albeit not an especially efficient one, indicates that selenocyclisations could be developed into useful transformations in this area (Scheme 12). When the alkynyl diol **14a** was treated with phenylselanyl chloride at –78 °C for five hours in tetrahydrofuran-containing potassium carbonate, the β-selanylfuran **37** was isolated in 29% yield. We suggest that optimisation will prove feasible.



Scheme 11.



Scheme 12. i) PhSeCl, K2CO3, THF, –78 0C, 5 h [29%].

Since our initial report of this type of cyclisation,[8] there has been considerable activity in the general area of 5-*endo*-*dig* cyclisations[4] triggered by halogens in particular. Related iodocyclisations using different precursors leading to furans and ring-fused derivatives have been developed.[13] Unassisted by a subsequent dehydration step, 5-*endo*-*dig* cyclisations have also proven especially effective in the direct synthesis of β-iodo-benzothiophenes,[14] -benzofurans[15] and -indoles.[16] Similarly, β-iododihydropyrroles and iodopyrroles can be obtained from homopropargylic sulfonamides by iodocyclisation followed by various elimination steps.[17] Two further and very significant development have been the use of aryl rings as the nucleophilic components of such cyclisations and the general usage of metallic species to trigger 5-*endo*-*dig* cyclisations in general. These now form a considerable body of methodology, very recently exemplified and summarised by the Larock group.[18] Hence, this general type of cyclisation can now be regarded as a generally useful synthetic method. The present approach to β-iodofurans exemplifies this and has potential as a general furan synthesis. The necessary precursors can be readily obtained by at least two distinct and direct routes: the regiospecific bis-hydroxylation of enynes or the addition of acetylides to α-alkoxycarbonyls. Of course, alternatives exist for the synthesis of such 3-alkyne-1,2-diols, the viability of which will often depend on the desired substitution pattern. The β-iodofurans themselves are best viewed as intermediates towards many types of highly substituted derivatives, accessible by replacing the iodine using a Pd^0- or Ni^0-catalysed coupling reaction,[3] by halogen–metal exchange or by radical generation.

Experimental Section

General Remarks: NMR spectra were recorded with a Bruker WM or DPX spectrometers, operating at 250 MHz or 400 MHz respectively for ^{1}H spectra and at 67.5 MHz or 100.6 MHz for ^{13}C spectra respectively. Unless stated otherwise, NMR spectra were measured using dilute solutions in deuteriochloroform. All NMR measurements were carried out at 30 °C and chemical shifts are reported as ppm on the delta scale downfield from tetramethylsilane (TMS: δ = 0.00 ppm) or relative to the resonances of $CHCl_3$ (δ_H = 7.27 ppm in proton spectra and δ_C = 77.0 ppm for the central line of the triplet in carbon spectra respectively). Coupling constants (*J*) are reported in Hz. Infrared spectra were recorded as thin films for liquids and as nujol mulls for solids, using a Perkin–Elmer 1600 series FTIR spectrophotometer and sodium chloride plates. Low resolution mass spectra were obtained using a VG Platform II Quadrupole spectrometer operating in the electron impact (EI; 70 eV) or atmospheric pressure chemical ionisation (ApcI) modes, as stated. High resolution mass spectrometric data was obtained from the EPSRC Mass Spectrometry Service, University College, Swansea, using the ionisation modes specified. Melting points were determined with a Kofler hot-stage apparatus and are uncorrected. Elemental analyses were obtained using a Perkin–Elmer 240C Elemental Microanalyser.

All reactions were conducted in oven-dried apparatus under dry nitrogen unless otherwise stated. All organic solutions from aqueous workups were dried by brief exposure to dried magnesium sulfate, followed by gravity filtration. The resulting dried solutions were evaporated using a Büchi rotary evaporator under water aspirator pressure and at ambient temperature unless otherwise stated. Column chromatography was carried out using Merck Silica Gel 60 (230–400 mesh). TLC analyses were carried out using Merck silica gel 60 F254 pre-coated, aluminium-backed plates, which were visualized using ultraviolet light or potassium permanganate or ammonium molybdenate sprays.

"Ether" refers to diethyl ether and petroleum ether to the fraction with boiling range 60–80 °C, unless stated otherwise.

The enynes **13** were prepared by Sonogashira coupling,[10,19] followed by regiospecific bis-hydroxylation, using the method developed by Sharpless,[9] to obtain the 3-alkyne-1,2-diols **14**. As an alternative in the latter step, the "racemic" method reported by the Warren group[11] was also used in some cases. A typical example of the latter method is as described below.

(1*RS*,2*RS*)-1,4-Diphenylbut-3-yne-1,2-diol (14a): Potassium ferricyanide (9.72 g, 29.62 mmol), potassium osmate(IV) dihydrate (0.08 g), potassium carbonate (4.08 g, 29.56 mmol), methanesulfonamide (0.946 g, 9.94 mmol) and quinuclidine (0.07 g)[11] were added to a stirred mixture of *tert*-butyl alcohol (50 mL) and water (50 mL), followed by the (*E*)-1,4-diphenylbut-1-en-3-yne (**13**) (2.01 g, 9.85 mmol). The resulting mixture was stirred at ambient temperature for 96 h, then sodium sulfite (15.05 g, 5.96 mmol) was added and stirring continued for 1 h. The bulk of *tert*-butyl alcohol was then evaporated and the residual slurry extracted with dichloromethane (3 × 100 mL). The combined extracts were washed with 2 M aqueous potassium hydroxide (20 mL), water (20 mL) and brine (20 mL) then dried and evaporated to leave a solid yellow residue which was purified by short column chromatography (5% MeOH in chloroform) and crystallisation from $CHCl_3$/petroleum ether to give the diol **14a** (1.83 g, 78%) as a pale yellow solid, m.p. 125–6 °C. ^{1}H NMR: δ = 4.38 (d, *J* = 8.0 Hz, 1 H), 4.61 (d, *J* = 8.0 Hz, 1 H), 7.00–7.21 (m, 8 H), 7.30 (d, *J* = 6.5 Hz, 2 H) ppm. ^{13}C NMR: δ = 68.4 (CHOH), 77.9 (CHOH), 86.9 (C), 87.5 (C), 122.5 (C), 127.6 (2 CH), 128.7 (4 CH), 132.0 (2 CH), 139.5 (C) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3440, 2940, 1650, 1444, 1380, 1080 cm^{-1}. HRMS: (APCI): calcd. for $C_{16}H_{15}O_2$ 239.1072 (M^+ + H); found 239.1076. $C_{16}H_{14}O_2$ (238.29): calcd. C 80.65, H 5.9; found C 80.65, H 6.1.

Iodocyclisation: General Procedure for Scales Less Than ca. 2 g of Alkynediol: Sodium hydrogen carbonate (3.3 equiv.) was added to dry acetonitrile (3 mL/mmol^{-1} of alkynediol), stirred under dry nitrogen and cooled in an ice-water bath, followed by the alkynediol (1 equiv.). After stirring for 5 min, solid iodine (3.3 equiv.) was added in one portion and, after a further 5 min, the cooling bath was removed and stirring continued until tlc analysis indicated complete reaction (ca. 1 h). Aqueous 10% sodium sulfite was then added dropwise until the excess iodine colour was completely discharged (ca. 3 mL/mmol of iodine), followed by ether (5 mL/mmol of alkynediol). The two layers were separated and the aqueous layer extracted with diethyl ether (2 × 5 mL/mmol of alkynediol). The combined organic solutions were washed with water (2× equal volume) and brine (1× equal volume) then dried ($MgSO_4$), filtered and carefully evaporated. The essentially pure product could then be further purified by filtration through silica gel using 5% ether in pentane, distillation or crystallisation, as appropriate.

On scales larger than around two grams, the production of heat caused by the sudden single addition of solid iodine should be controlled either by portionwise addition of the solid with temperature monitoring or by adding the halogen dropwise after dissolution in a minimum of acetonitrile.

All of the following preparations of iodofurans **15** were carried out on 3–5 mmol scales a number of times in each case. Yields quoted are an average of those obtained using the specified conditions; variations were typically around 5–8%.

3-Iodo-2,5-diphenylfuran (15a): By the foregoing general procedure, the alkynediol **14a** was converted into the iodofuran **15a** (60%), a yellow crystalline solid (from ether/hexane), m.p. 84 °C. ^{1}H NMR: δ = 6.88 (s, 1 H, 4-H), 7.30–7.62 (m, 6 H), 7.77 (dd, *J* = 7.0, 1.8 Hz, 2 H), 8.15 (dd, *J* = 7.0, 1.8 Hz, 2 H) ppm. ^{13}C NMR: δ = 62.8 (3-CI), 115.8 (4-CH), 123.9 (2 CH), 126.1 (2 CH), 128.1 (CH), 128.2 (CH), 128.4 (2 CH), 128.8 (2 CH), 129.6 (C), 130.2 (C), 151.1 (C), 154.0 (C) ppm. IR (film): $\tilde{\nu}$ = 3081, 3065, 1606, 1585, 1489, 1440, 1117, 946, 762, 688 cm^{-1}. MS (EI): *m*/*z* (%) = 346 (65) [M^+], 202 (23), 191 (38), 113 (20), 105 (73), 77 (100), 57 (61). $C_{16}H_{11}IO$ (346.17): calcd. C 55.5, H 3.2; found C 55.7, H 3.2.

2-Butyl-3-iodo-5-phenylfuran (15b): By the general procedure, iodocyclisation of the alkynediol **14b** gave the expected product [71%] as a yellow oil, which could be distilled with some loss to give the iodofuran **15b** as a pale yellow oil, b.p. 70–85 °C (oven temp.) at 1 Torr. ^{1}H NMR: δ = 0.90 (t, *J* = 7.3 Hz, 3 H, 4′-Me), 1.32 (hex, *J* = 7.3 Hz, 2 H, 3′-CH_2), 1.63 (pent, *J* = 7.3 Hz, 2 H, 2′-CH_2), 2.69 (t, *J* = 7.3 Hz, 2 H, 1′-CH_2), 6.56 (s, 1 H, 4-H), 7.18–7.23 (m, 1 H), 7.29–7.35 (m, 2 H), 7.51 (dd, *J* = 7.0, 1.2 Hz, 2 H, 2 *o*-H) ppm. ^{13}C NMR: δ = 13.9 (Me), 22.2, 27.2, 30.3, 64.0 (3-CI), 112.4 (4-CH), 123.5 (2 CH), 127.5 (CH), 128.7 (2 CH), 130.2 (C), 153.4 (C), 156.6 (C) ppm. IR (film): $\tilde{\nu}$ = 1555, 1483, 1441, 1009, 747 cm^{-1}. MS (EI): *m*/*z* (%) = 326 (1) [M^+], 286 (5), 285 (18), 131 (12), 105 (92), 84 (20), 77 (100), 57 (48). $C_{14}H_{15}IO$ (326.18): calcd. C 51.55, H 4.6; found C 51.6, H 4.6.

5-Butyl-3-iodo-2-phenylfuran (15c): By the general procedure, iodocyclisation of the isomeric alkynediol **15c** gave the iodofuran **15c** [77%] as a yellow oil which showed ^{1}H NMR: δ = 0.99 (t, *J* = 7.4 Hz, 3 H, 4′-Me), 1.43 (hex, *J* = 7.4 Hz, 2 H, 3′-CH_2), 1.71 (pent, *J* = 7.4 Hz, 2 H, 2′-CH_2), 2.76 (t, *J* = 7.4 Hz, 2 H, 1′-CH_2),

6.64 (s, 1 H, 4-H), 7.27 (app. t, J = 7.4 Hz, 1 H, *p*-CH), 7.39 (app. t, J = 7.9 Hz, 2 H, 2 *m*-H), 7.61 (dd, J = 7.1, 1.3 Hz, 2 H, 2 *o*-H) ppm. ^{13}C NMR: δ = 13.7 (4′-Me), 22.1, 27.2, 30.3, 64.0 (3-CI), 112.4 (4-CH), 123.4 (2 CH), 127.4 (2 CH), 128.6 (CH), 130.1 (C), 153.4 (C), 156.5 (C) ppm. IR (film): $\tilde{\nu}$ = 1560, 1490, 1450, 1020, 750 cm^{-1}. *m*/*z* 326 (M^+, 7%), 285 (31), 131 (21), 105 (100), 77 (94), 57 (56).

3-Iodo-5-methyl-2-phenylfuran (15d): By the general procedure, iodocyclisation of the alkynediol **14d**[20] gave the iodofuran **15d** as a yellow oil [88%]. ^{1}H NMR: δ = 2.36 (s, 3 H, 5-Me), 6.25 (s, 1 H, 4-H), 7.28–7.34 (m, 1 H, *p*-CH), 7.38–7.48 (m, 2 H, 2 *m*-H), 7.94–8.02 (m, 2 H, 2 *o*-H) ppm. ^{13}C NMR: δ = 13.4 (5-Me), 61.2 (3-CI), 116.4 (4-CH), 125.8 (2 CH), 127.7 (CH), 128.3 (2 CH), 130.4 (C), 150.3 (C), 152.8 (C) ppm. IR (film): $\tilde{\nu}$ = 3081, 3052, 1593, 1544, 1483, 1448, 1221, 1083, 1071 cm^{-1}. MS (EI): *m*/*z* (%) = 285 (18) [M^+ + H], 284 (100), 157 (10), 129 (35), 128 (17), 114 (15). MS (CH_4-CI): *m*/*z* (%) = 285 (100) [M^+ + H], 159 (85), 58 (83). HRMS: calcd. for $C_{11}H_{10}IO$ 284.9776; found 284.9772.

2-Butyl-3-iodo-5-methylfuran (15e): By the general procedure, iodocyclisation of the alkynediol **14e** gave the iodofuran **15e** [65%] as a pale yellow oil. ^{1}H NMR: δ = 0.88 (t, J = 7.3 Hz, 3 H, 4′-Me), 1.28 (hex, J = 7.3 Hz, 2 H, 3′-CH_2), 1.50 (pent, J = 7.3 Hz, 2 H, 2′-CH_2), 2.19 (s, 3 H, 5-Me), 2.54 (t, J = 7.3 Hz, 2 H, 1′-CH_2), 5.86 (s, 1 H, 4-H) ppm. ^{13}C NMR: δ = 13.5 (Me), 13.8 (Me), 22.1, 27.0, 30.4, 62.1 (3-CI), 112.8 (4-CH), 151.6 (C), 155.1 (C) ppm. IR (film): $\tilde{\nu}$ = 1600, 1542, 1455, 1380, 1265, 1130, 1020, 960, 910, 735 cm^{-1}. MS (EI): *m*/*z* (%) = 264 (77) [M^+], 221 (100), 137 (70), 95 (20), 77 (10), 66 (40), 65 (73). HRMS: calcd. for $C_9H_{13}IO$ 264.0011; found 264.0012.

Methyl 4-Iodo-5-phenylfuran-2-carboxylate (15f): By the general procedure, iodocyclisation of alkynediol **14f** gave the iodofuran **15f** [47%] as a yellow oil. ^{1}H NMR: δ = 3.91 (s, 3 H, OMe), 7.35 (s, 1 H, 3-H), 7.40–7.49 (m, 3 H), 8.04–8.08 (m, 2 H) ppm. ^{13}C NMR: δ = 52.1 (OMe), 61.7 (4-CI), 127.1 (2 CH), 127.8 (CH), 128.5 (2 CH), 129.0 (C) ppm. 129.5 (CH), 144.2 (C), 155.3 (C), 158.3 (C) ppm. IR (film): $\tilde{\nu}$ = 1695 cm^{-1}. MS (EI): *m*/*z* (%) = 328 (53) [M^+], 241 (14), 173 (13), 145 (54), 114 (100), 113 (43). HRMS: calcd. for $C_{12}H_9IO_3$ 327.9596; found 327.9599.

2-Methyl-3-octyne-1,2-diol (17a): Butyllithium (11.3 mL of a 1.6 M solution in hexanes, 18.1 mmol) was added dropwise to a stirred solution of 1-hexyne (1.48 g, 18.1 mmol) in tetrahydrofuran (80 mL) cooled in an ice-water bath. After 0.5 h, 1-(*tert*-butyldiphenylsilyloxy)-2-propanone (**16a**, 4.57 g, 18.1 mmol)[21] diluted with tetrahydrofuran (3 mL) was slowly added and the resulting solution stirred for a further 2 h, then quenched by the addition of water (20 mL). The resulting mixture was extracted with diethyl ether (3 × 50 mL) and the combined extracts washed with water (40 mL) and brine (40 mL) then dried, filtered and the solvents evaporated. The residue, a dark yellow liquid (5.6 g), was immediately dissolved in a 1 M solution of tetrabutylammonium fluoride (20 mL) and the resulting solution stirred at ambient temperature for 48 h then evaporated. The residue was separated using silica gel column chromatography, eluting with 5% methanol in chloroform to give the diol **17a** (2.50 g, 89%)[22] as a colourless oil. ^{1}H NMR: δ = 0.85 (t, J = 7.0 Hz, 3 H, 8-Me), 1.33–1.40 (m, 2 H, 7-CH_2), 1.43–1.51 (m, 2 H, 6-CH_2), 1.80 (s, 3 H, 2-Me), 2.25 (t, J = 7.0 Hz, 2 H, 5-CH_2), 3.38 (d, J = 11.0 Hz, 1 H, 1-H_a), 3.52 (d, J = 11.0 Hz, 1 H, 1-H_b) ppm. ^{13}C NMR: δ = 13.9 (8-Me), 18.6 (7-CH_2), 22.3 (6-CH_2), 25.9 (2-Me), 31.0 (5-CH_2), 69.0 (1-CH_2), 69.9 (C), 81.9 (C), 85.7 (C) ppm. IR (film): $\tilde{\nu}$ = 3400, 2962, 2933, 2246, 1652, 1458, 1373, 1158, 1115, 1050, 950, 914, 728 cm^{-1}. MS (EI): *m*/*z* (%) = 156 (18) [M^+], 84 (40), 77 (70), 76 (100), 68 (42). HRMS: calcd. for $C_9H_{16}O_2$ 156.1150; found 156.1150.

2-Butyl-3-iodo-4-methylfuran (18a): Iodocyclisation of the foregoing diol **17a** (0.78 g, 5.0 mmol) using the general procedure gave the iodofuran **18a** (1.09 g, 82%) as a volatile, yellow oil. ^{1}H NMR: δ = 0.82 (t, J = 7.0 Hz, 3 H, 4′-Me), 1.12–1.28 (m, 2 H), 1.50–1.58 (m, 2 H), 1.85 (d, J = 1.0 Hz, 4-Me), 2.59 (distorted t, J = 7.0 Hz, 1′-CH_2), 7.11 (q, J = 1.0 Hz, 5-H) ppm. ^{13}C NMR: δ = 11.7 (Me), 14.3 (Me), 22.5 (CH_2), 27.9 (CH_2), 30.5 (CH_2), 70.0 (3-CI), 123.7 (4-C), 137.6 (5-CH), 157.0 (2-C) ppm. IR (film): $\tilde{\nu}$ = 2954, 1602, 1551, 1458, 1380, 1272, 1122, 1022, 957, 907, 735 cm^{-1}. MS (EI): *m*/*z* (%) = 264 (50) [M^+], 221 (100), 137 (55), 95 (30), 77 (10), 66 (34), 65 (63). HRMS: calcd. for $C_9H_{13}IO$ 264.0011; found 264.0009.

After a longer reaction time, beyond 2 h, significant quantities of the iodination product, 2-butyl-3,5-diiodo-4-methylfuran (**19**) began to be formed, according to GC-MS analysis: MS (EI): *m*/*z* (%) = 390 (58) [M^+], 347 (100) [M^+ – Pr], 319 (43) [M^+ – Pr – CO], 263 (5) [M^+ – I], 235 (19) [M^+ – ICO], 192 (16) [M^+ – Pr – ICO], 136 (82) [M^+ – 2I], 93 (22) [M^+ – 2I – Pr], 77 (30), 65 (96). Its presence could also be detected by ^{1}H NMR analysis of the crude product and was best quantified by the reduced integration of the 5-H resonance, relative to that of the combined integration of its 4-Me resonance and that of **18a**.

2-Methyl-4-phenylbut-3-yne-1,2-diol (17b): Butyllithium (34.4 mL of a 1.6 M solution in hexanes, 55 mmol) was added dropwise to a stirred solution of phenylacetylene (5.10 g, 50 mmol) in tetrahydrofuran (80 mL) maintained at 0 °C. After 0.5 h, 1-(tetrahydropyran-2-yloxy)-2-propanone (**16b**) (9.48 g, 60 mmol) was added and the resulting mixture stirred at 0 °C for 2 h then quenched by the careful addition of water (20 mL). The resulting mixture was extracted with diethyl ether (3 × 50 mL) and the combined extracts washed with water (40 mL) then dried, filtered and the solvents evaporated. The residue was dissolved in methanol (20 mL) containing *p*-toluenesulfonic acid monohydrate (1.0 g) and the resulting solution stirred at ambient temperature for 2 h, then diluted with diethyl ether (20 mL), washed with brine (40 mL), dried, filtered through a small plug of silica gel and the solvents evaporated. Crystallisation of the residue from hexane/ether gave the alkynediol **17b** (7.50 g, 71%) as a pale yellow, crystalline solid, m.p. 105–106 °C [ref.[22] m.p. 109.5 °C]. ^{1}H NMR: δ = 1.55 (s, 3 H, 2-Me), 3.62 (d, J = 11.0 Hz, 1 H, 1-H_a), 3.80 (d, J = 11.0 Hz, 1 H, 1-H_b), 7.25–7.35 (m, 3 H), 7.42 (d, J = 6.4 Hz, 2 H) ppm. ^{13}C NMR: δ = 19.6 (Me), 68.1 (C), 71.0 (1-CH_2), 84.7 (C), 90.9 (C), 122.0 (C), 127.4 (2 CH), 127.7 (CH), 131.2 (2 CH) ppm. IR (film): $\tilde{\nu}$ = 3556, 1339, 1460, 1401, 1287, 1050, 972, 778 cm^{-1}. MS (EI): *m*/*z* (%) = 176 (8) [M^+], 158 (28), 145 (100), 129 (35), 115 (45), 102 (35), 84 (45), 71 (42). $C_{11}H_{12}O_2$ (176.21): calcd. C 75.0, H 6.9; found C 75.0, H 7.1.

3-Iodo-4-methyl-2-phenylfuran (18b): Iodocyclisation of the alkynediol **17b** (0.85 g, 4.82 mmol) following the general procedure, but with tetrahydrofuran (10 mL) as solvent in place of acetonitrile and the usual workup provided the iodofuran **18b** (0.83 g, 61%) as a colourless crystalline solid, m.p. 83–4 °C (ether/hexane). ^{1}H NMR: δ = 2.05 (d, J = 1.0 Hz, 1 H, 4-Me), 7.34–7.41 (m, 2 H, *p*-H, 5-H), 7.45–7.51 (m, 2 H, 2 *m*-H), 8.05 (d, J = 7.0 Hz, 2 *o*-H) ppm. ^{13}C NMR: δ = 12.3 (4-Me), 69.4 (3-CI), 126.2 (C), 126.6 (2 CH), 128.5 (CH), 128.9 (2 CH), 131.0 (C), 138.6 (5-CH), 152.1 (C) ppm. IR (film): $\tilde{\nu}$ = 3062, 1587, 1537, 1473, 1380, 1272, 1129, 1022, 914, 764 cm^{-1}. MS (EI): *m*/*z* (%) = 284 (88) [M^+], 157 (15), 129 (85), 128 (95), 127 (100), 102 (45), 76 (62), 73 (42). $C_{11}H_9IO$ (284.10): calcd. C 46.5, H 3.2; found C 46.9, H 3.2.

1,2-Diphenyloct-3-yne-1,2-diol (21a): 1-Hexyne (2.3 mL, 20 mmol) and butyllithium (13.8 mL of a 1.6 M solution in hexanes, 22.0 mmol) were added sequentially to tetrahydrofuran (30 mL) maintained at –78 °C. After stirring at the temperature for 2 h, a solution of benzoin **20** (2.12 g, 10 mmol) in tetrahydrofuran (2 mL) was added dropwise and the resulting solution stirred for 16 h without further cooling. Saturated aqueous ammonium chloride (20 mL) was then carefully added followed by dichloromethane (20 mL). The two layers were separated and the aqueous layer extracted with dichloromethane (2 × 20 mL). The combined organic solutions were dried, filtered and the solvents evaporated. Column chromatography of the waxy residue (5% MeOH/$CHCl_3$) separated the diol **21a** (2.0 g, 68%) m.p. 96 °C (from $CHCl_3$/hexanes). ^{1}H NMR: δ = 0.82 (t, J = 7.2 Hz, 3 H, 8-Me), 1.30–1.60 (m, 4 H), 2.25 (t, J = 7.2 Hz, 2 H, 5-CH_2), 2.68 (br. s, 2 H, 2 OH), 4.78 (s, 1 H, 1-H), 7.00–7.45 (m, 10 H) ppm. ^{13}C NMR: δ = 14.2 (8-Me), 18.1 (CH_2), 28.3 (CH_2), 31.2 (CH_2), 76.0 (2-C), 76.5 (1-CH), 78.5 (C), 86.1 (C), 127.7 (2 CH), 128.1 (2 CH), 128.4 (CH), 128.6 (CH), 129.0 (CH), 129.5 (2 CH), 130.0 (C), 133.2 (C), 134.3 (CH) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3445, 2923, 1679, 1458, 1377, 1059 cm^{-1}. MS (EI): m/z (%) = 294 (3) [M^+], 277 (28), 195 (35), 187 (40), 146 (28), 108 (52), 107 (88), 105 (98), 79 (93), 76 (100). $C_{20}H_{22}O_2$ (294.39): calcd. C 81.6, H 7.5; found C 81.9, H 7.6.

1,2-Diphenyl-4-(trimethylsilyl)but-3-yne-1,2-diol (21b): Butyllithium (9.0 mL of a 2.3 M solution in hexanes, 20.7 mmol) was added dropwise to a stirred solution of (trimethylsilyl)acetylene (2.66 mL, 18.8 mmol) in dry tetrahydrofuran (50 mL) stirred and maintained at –78 °C. After 1 h, benzoin **20** (2.00 g, 9.4 mmol) was added in one portion and stirring continued without further cooling for 1 h. Saturated aqueous ammonium chloride (80 mL) was then added and the resulting two layers separated. The aqueous layer was extracted with diethyl ether (3 × 50 mL) and the combined organic solutions washed with brine (2 × 100 mL), then dried and the solvents evaporated. Column chromatography of the residue (20% EtOAc/petroleum ether) separated the alkynediol **21b** (2.26 g, 77%), which separated from petroleum ether as a colourless solid, m.p. 104–105 °C. ^{1}H NMR: δ = 0.01 (s, 9 H, 3 Me), 2.74 (br. s, 1 H, OH), 2.84 (br. s, 1 H, OH), 4.89 (s, 1 H, 1-H), 7.18–7.46 (m, 10 H) ppm. ^{13}C NMR: δ = 0.0 (3 Me), 81.1 (1-CH), 81.2 (C), 93.2 (C), 105.9 (C), 126.8 (PhCH), 126.9 (PhCH), 127.7 (PhCH), 127.9 (PhCH), 128.3 (PhCH), 129.3 (PhCH), 139.8 (C), 141.6 (C) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3378, 2925, 2274, 1602, 1453, 1377, 1250, 1192, 1062, 954, 838 cm^{-1}. MS (APCI): m/z = 293 [M^+ + H – H_2O]. $C_{19}H_{22}O_2Si$ (310.47): calcd. C 73.5, H 7.1; found C 73.2, H 6.9.

1,2-Diphenylbut-3-yne-1,2-diol (21c): Tetrabutylammonium fluoride (4.9 mL of a 1.0 M solution in tetrahydrofuran, 4.9 mmol) was added dropwise to a stirred solution of the foregoing silylated alkyne **21b** (1.51 g, 4.9 mmol) in tetrahydrofuran (20 mL), cooled in an ice-water bath. After 20 min, during which time the colour of the solution changed from yellow to brown, the bulk of the tetrahydrofuran was evaporated and the residue taken up in ether and water (1:1, 20 mL). The resulting layers were separated and the aqueous layer extracted with diethyl ether (3 × 20 mL). The combined organic solutions were dried, filtered and evaporated to leave a dark oil, which was purified by column chromatography (20% EtOAc/petroleum ether) to give the alkynediol **21c**, which crystallised from EtOAc/petroleum ether as a colourless crystalline solid (0.93 g, 80%), m.p. 98–99 °C [ref.[23] m.p. 112–113 °C]. ^{1}H NMR: δ = 2.67 (s, 1 H, 4-H), 2.71 (br. s, 1 H, OH), 2.94 (br. s, 1 H, OH), 4.82 (s, 1 H, 1-H), 7.06–7.22 (m, 8 H), 7.35–7.45 (m, 2 H) ppm. ^{13}C NMR: δ = 76.2 (4-CH), 76.5 (C), 81.2 (1-CH), 85.0 (C), 126.9 (PhCH), 128.2 (PhCH), 128.4 (PhCH), 128.6 (PhCH), 129.1 (PhCH), 137.5 (C), 139.9 (C) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3405, 3269, 2918, 1456, 1377, 1216, 1193, 1137, 1082, 1060, 954, 833, 757 cm^{-1}. MS (APCI): m/z = 221 [M^+ + H – H_2O]. HRMS: (NH_4CI): calcd. for $C_{16}H_{18}NO_2$ 256.1338 (M^+ + NH_4); found 256.1337. $C_{16}H_{14}O_2$ (238.29): calcd. C 80.65, H 5.9; found C 80.2, H 5.7.

1,2-Diphenyl-4-(thien-2-yl)but-3-yne-1,2-diol (21d): Copper(I) iodide (26 mg, 0.14 mmol) was added to a stirred solution of 2-iodothiophene (Aldrich; 0.31 mL, 2.81 mmol), 1,2-diphenylbut-3-yne-1,2-diol **21c** (0.67 g, 2.81 mmol) and tetrakis(triphenylphosphane)-palladium(0) (0.16 g, 0.14 mmol) in dry, degassed diethylamine (10 mL) and the resulting mixture stirred under argon at ambient temperature overnight. The bulk of the diethylamine was then evaporated and the residue separated by column chromatography (20% EtOAc/petroleum ether) to give the thienyl alkynediol **21d** (0.69 g, 81%) as a yellow crystalline solid, m.p. 119–120 °C (from hexane/ether). ^{1}H NMR: δ = 2.61 (br. d, J = 3.2 Hz, 1 H, 1-OH), 2.83 (br. s, 1 H, 2-OH), 4.88 (d, J = 3.2 Hz, 1 H, 1-H), 6.92 (dd, J = 5.2, 3.8 Hz, 1 H, 3′-H), 7.16–7.25 (m, 10 H), 7.41–7.45 (m, 2 H) ppm. ^{13}C NMR: δ = 77.3 (C), 81.4 (1-CH), 81.6 (C), 93.7 (C), 122.5 (C), 127.1, 127.4, 127.8, 127.9, 128.1, 128.3, 128.4, 128.6, 133.0 (all ArCH), 137.9 (C), 140.1 (C) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3416, 2170, 1461, 1376, 1171, 1041, 926, 851, 832, 759, 698 cm^{-1}. MS (APCI): m/z (%) = 321 (11) [M^+ + H], 303 (100) [M^+ + H – H_2O]. HRMS: calcd. for $C_{20}H_{17}O_2S$ 321.0949; found 321.0948.

2-Butyl-4,5-diphenyl-3-iodofuran (22a): By the general iodocyclisation procedure, the alkynediol **21a** was converted into the iodofuran **22a** (93%), as a pale yellow crystalline solid, m.p. 60–61 °C (from hexane). ^{1}H NMR: δ = 0.91 (t, J = 7.4 Hz, 3 H, 4′-Me), 1.38 (hex, J = 7.4 Hz, 2 H, 3′-CH_2), 1.66 (pent, J = 7.4 Hz, 2 H, 2′-CH_2), 2.74 (t, J = 7.4 Hz, 2 H, 1′-CH_2), 7.05–7.40 (m, 10 H) ppm. ^{13}C NMR: δ = 14.0 (Me), 22.4, 27.9, 30.4, 71.8 (3-CI), 125.4 (2 PhCH), 126.8 (PhCH), 127.4 (PhCH), 127.8 (2 PhCH), 128.2 (2 PhCH), 130.4 (2 PhCH), 130.6 (C), 134.1 (C), 147.8 (C), 155.9 (C) (one quaternary obscured) ppm. IR (film): $\tilde{\nu}$ = 3086, 2923, 2854, 1679, 1458, 1377, 1059 cm^{-1}. MS (EI): m/z (%) = 402 (100) [M^+], 360 (22), 359 (95), 105 (95), 77 (92). $C_{20}H_{19}IO$ (402.27): calcd. C 59.7, H 4.8; found C 59.7, H 4.8.

3-Iodo-4,5-diphenyl-2-(thien-2-yl)furan (22b): Following the general iodocyclisation procedure, reaction between the alkynediol **21d** (0.20 g, 0.62 mmol), sodium hydrogen carbonate (0.166 g, 1.98 mmol) and iodine (0.500 g, 1.98 mmol) gave, after purification by column chromatography (5% EtOAc/petroleum ether), the thienyl-iodofuran **22b** (0.20 g, 71%) as a pale brown, crystalline solid, m.p. 158–159 °C (from ether/petroleum ether). ^{1}H NMR: δ = 7.07 (d, J = 0.8 Hz, 1 H, 3′-H), 7.12–7.17 (m, 3 H), 7.26–7.40 (m, 8 H), 7.75 (d, J = 3.5 Hz, 1 H, 5′-H) ppm. ^{13}C NMR: δ = 71.5 (3-CI), 125.6 (CH), 125.9 (CH), 127.8 (overlapping CH), 128.0 (C), 128.1 (CH), 128.6 (CH), 128.8 (CH), 129.2 (CH), 130.1 (C), 130.8 (CH), 132.7 (C), 133.9 (C), 148.2 (C), 148.4 (C) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1462, 1376, 1061, 905, 846, 823, 767, 694 cm^{-1}. UV (EtOH): λ_{max} = 343 nm. MS (APCI): m/z = 429 [M^+ + H]. HRMS: calcd. for $C_{20}H_{14}IOS$ 428.9810; found 428.9811. $C_{20}H_{13}IOS$ (428.29): calcd. C 56.1, H 3.1; found C 56.2, H 3.2.

1,2-Di(furan-2-yl)-4-(trimethylsilyl)but-3-yne-1,2-diol (26a): Using exactly the same method for the preparation of the alkynediol **21b** from benzoin and (trimethylsilyl)acetylene, addition of the latter alkyne to furoin **25** (5.00 g, 26 mmol) with scaling of all the remaining quantities of reactants and solvents, gave the alkynediol **26a** (5.85 g, 78%) as a yellow oil and a single diastereoisomer. ^{1}H NMR: δ = 0.00 (s, 9 H, 3 MeSi), 2.60 (d, J = 7.5 Hz, 1 H, 1-OH), 2.96 (br. s, 1 H, 2-OH), 4.93 (d, J = 7.5 Hz, 1 H, 1-H), 6.12–6.14 (m, 3 H, 3 furyl-β-H), 6.27 (d, J = 2.7 Hz, 1 H, furyl-β-H), 7.15 (d, J = 0.8 Hz, 1 H, furyl-α-H), 7.20 (d, J = 0.8 Hz, 1 H, furyl-α-

H) ppm. ^{13}C NMR: δ = 0.0 (3 MeSi), 71.8 (2-C), 73.6 (1-CH), 92.7 (C), 102.5 (C), 108.8 (2 CH), 109.6 (CH), 110.6 (CH), 142.5 (CH), 143.2 (CH), 151.8 (C), 152.5 (C) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3455, 2959, 2899, 2176, 1655, 1500, 1374, 1224, 1065, 927, 700 cm^{-1}. MS (APCI): *m*/*z* = 273 [M^+ + H – H_2O]. $C_{15}H_{18}O_4Si$ (290.39): calcd. C 62.0, H 6.25; found C 62.4, H 6.4.

1,2-Di(furan-2-yl)but-3-yne-1,2-diol (26b): Tetrabutylammonium fluoride (7.8 mL of a 1 M solution in tetrahydrofuran, 7.8 mmol) was added dropwise to a stirred solution of the foregoing silylated alkynediol **26a** (2.25 g, 7.8 mmol) in tetrahydrofuran (30 mL) cooled in an ice-water bath. After 20 min, during which time the solution colour changed from yellow to black, the bulk of the solvent was evaporated and the residue partitioned between ether (20 mL) and water (20 mL). The resulting two layers were separated and the aqueous layer extracted with diethyl ether (2 × 20 mL). The combined organic solutions were dried and evaporated and the dark green oily residue separated by column chromatography (20% EtOAc/petroleum ether) to give the alkynediol **26b** (1.15 g, 68%) as a dark, unstable oil and a single diastereoisomer. ^{1}H NMR: δ = 2.61 (s, 1 H, 4-H), 2.80 (br. s, 1 H, OH), 3.20 (br. s, 1 H, OH), 5.06 (d, *J* = 7.0 Hz, 1 H, 1-H), 6.25–6.28 (m, 3 H, 3 furyl-β-H), 6.42 (d, *J* = 3.2 Hz, 1 H, furyl-β-H), 7.29 (d, *J* = 0.8 Hz, 1 H, furyl-α-H), 7.34 (d, *J* = 0.8 Hz, 1 H, furyl-α-H) ppm. ^{13}C NMR: δ = 71.6 (2-C), 73.6 (CH), 75.5 (CH), 81.7 (C), 109.2 (CH), 109.5 (CH), 110.8 (CH), 110.9 (CH), 142.9 (CH), 143.3 (CH), 151.5 (C), 152.3 (C) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3438, 3290, 2983, 2118, 1567, 1462, 1375, 1258, 1151, 926, 819 cm^{-1}. MS (APCI): *m*/*z* (%) = 201 (100) [M^+ + H – H_2O], 187 (90). HRMS: (NH_4CI): calcd. for $C_{12}H_{14}NO_4$ 236.0923 (M^+ + NH_4); found 236.0922.

1,2,4-Tri(furan-2-yl)but-3-yne-1,2-diol (27): Copper(I) iodide (21 mg, 0.11 mmol) was added to a stirred solution of 2-iodofuran (0.42 g, 2.29 mmol),[24] the foregoing alkyne-1,2-diol **26b** (0.50 g, 2.29 mmol) and tetrakis(triphenylphosphane)palladium(0) (0.132 g, 0.11 mmol) in dry, degassed diethylamine (10 mL) at ambient temperature and the resulting mixture stirred overnight then evaporated. Column chromatography of the residue (20% EtOAc/petroleum ether) gave the trifuryl-alkynediol **27** (0.483 g, 74%) as a red oil. ^{1}H NMR: δ = 2.63 (d, *J* = 7.2 Hz, 1 H, 1-OH), 3.03 (br. s, 1 H, 2-OH), 5.01 (d, *J* = 7.2 Hz, 1 H, 1-H), 6.14–6.20 (m, 4 H, 4 furyl-β-H), 6.33 (d, *J* = 3.0 Hz, 1 H, furyl-β-H), 6.46 (d, *J* = 3.0 Hz, 1 H, furyl-β-H), 7.18 (d, *J* = 1.8 Hz, 1 H, furyl-α-H), 7.20 (d, *J* = 0.8 Hz, 1 H, furyl-α-H), 7.22 (d, *J* = 0.9 Hz, 1 H, furyl-α-H) ppm. ^{13}C NMR: δ = 72.7 (2-C), 74.1 (1-CH), 91.4 (C), 102.5 (C), 109.5 (CH), 110.0 (CH), 111.2 (CH), 111.3 (CH), 111.7 (C), 117.3 (CH), 136.8 (C), 143.3 (CH), 143.8 (CH), 144.8 (CH), 151.9 (C), 153.2 (C) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3525, 2229, 1573, 1483, 1375, 1212, 1149, 1011, 922, 884, 818 cm^{-1}. MS (APCI): *m*/*z* (%) = 267 (100) [M^+ + H – H_2O]. HRMS: (APCI + aq. NaCl) calcd. for $C_{16}H_{12}NaO_5$ 307.0582 (M^+ + Na), found 307.0583.

2,4,5-Tri(furan-2-yl)-3-iodofuran (28): Sodium hydrogen carbonate (0.35 g, 4.22 mmol) was added to a stirred solution of the foregoing trifuryl-alkyne **27** (0.40 g, 1.40 mmol) in dry ethyl acetate (10 mL) at ambient temperature. After 10 min, iodine (1.07 g, 4.22 mmol) was added in one portion and the resulting mixture stirred for 1 h then quenched by the addition of 10% aqueous sodium sulfite (10 mL). The organic layer was separated and the aqueous layer extracted with ethyl acetate (3 × 10 mL). The combined organic solutions were washed with brine (20 mL) then dried, filtered through a pad of silica and evaporated to leave the iodofuran **28** (0.14 g, 25%) as an unstable red oil. ^{1}H NMR: δ = 6.38 (dd, *J* = 3.5, 1.6 Hz, 1 H, furyl-4-H), 6.47 (dd, *J* = 3.5, 2.0 Hz, 1 H, furyl-4-H), 6.49 (dd, *J* = 3.5, 2.0 Hz, 1 H, furyl-4-H), 6.58 (d, *J* = 3.5 Hz, 1 H, furyl-3-H), 6.69 (d, *J* = 3.5 Hz, 1 H, furyl-3-H), 7.04 (d, *J* = 3.5 Hz, 1 H, furyl-3-H), 7.40 (d, *J* = 2.0 Hz, 1 H, furyl-2-H), 7.49 (d, *J* = 1.6 Hz, 1 H, furyl-2-H), 7.50 (d, *J* = 2.0 Hz, 1 H, furyl-2-H) ppm. ^{13}C NMR: δ = 68.6 (3-CI), 111.6 (CH), 111.7 (CH), 113.4 (CH), 113.5 (CH), 113.9 (C), 114.0 (CH), 119.5 (C), 128.3 (C), 145.0 (CH), 145.3 (CH), 145.4 (CH), 146.7 (C), 146.9 (C), 147.4 (C), 147.9 (C) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 1537, 1502, 1217, 1148, 1071, 1011, 986, 914, 807 cm^{-1}. UV (EtOH): λ_{max} = 277.3, 338.9 nm. MS (APCI): *m*/*z* (%) = 393 (100) [M^+ + H]. HRMS: (EI): calcd. for $C_{16}H_9IO_4$ 391.9546 (M^+); found 391.9550.

2,3,5-Tri(furan-2-yl)furan (29): Sodium carbonate (20 mg, 0.18 mmol) was added to a stirred mixture of 2-furanboronic acid (10 mg, 0.09 mmol), the iodofuran **28** (37 mg, 0.09 mmol) and tetrakis(triphenylphosphane)palladium(0) (10 mg, 9 μmol) in 90% aqueous ethanol (2 mL). The resulting mixture was refluxed overnight then evaporated. Column chromatography of the residue (1% EtOAc/petroleum ether) separated the trifurylfuran **29** (ca. 9 mg, ca. 40%) as a colourless oil. ^{1}H NMR: δ = 6.42–6.44 (m, 2 H, 2 furyl-4-H), 6.47 (dd, *J* = 3.5, 1.8 Hz, 1 H, furyl-4-H), 6.61 (d, *J* = 3.5 Hz, 1 H, furyl-3-H), 6.79–6.83 (m, 3 H), 7.39 (d, *J* = 1.4 Hz, 1 H, furyl-2-H), 7.42 (d, *J* = 1.8 Hz, 1 H, furyl-2-H), 7.47 (d, *J* = 1.4 Hz, 1 H, furyl-2-H) ppm. MS (APCI): *m*/*z* (%) = 267 (100) [M^+ + H]. HRMS: calcd. for $C_{16}H_{11}O_4$ 267.0657; found 267.0657.

Acetylide Additions to 2-Silyloxy Esters. General Procedure: Butyllithium (2.2 equiv. of a 2.5 M solution in hexanes) was added slowly to a stirred solution of a 1-alkyne (2.0 equiv.) in dry tetrahydrofuran (4 mL/mmol of butyllithium) at –78 °C. After 20 min, the protected hydroxy ester (1.0 equiv.) was added, diluted with a minimum of tetrahydrofuran. The progress of the reaction was monitored by tlc at –78 °C. When complete, typically after ca. 1 h, the mixture was quenched by the addition of saturated aqueous ammonium chloride (4 mL/mmol of butyllithium) and the organic layer separated. The aqueous layer was extracted with diethyl ether (3×) and the combined organic solutions washed with brine then dried and the solvents evaporated.

Acetylide Additions to 2-Hydroxy Esters. General Procedure: Butyllithium (3.3 equiv. of a 2.5 M solution in hexanes) was added slowly to a stirred solution of a 1-alkyne (3.0 equiv.) in dry tetrahydrofuran (4 mL/mmol of butyllithium) at –78 °C. After 0.5 h, the hydroxy ester (1.0 equiv.) was added and the foregoing general procedure followed.

7-[(1-*tert*-Butyldimethylsilyloxy)ethyl]trideca-5,8-diyn-7-ol (31a): Following the general procedure, condensation between methyl 2-(*tert*-butyldimethylsilyloxy)propanoate (**30a**)[25] (2.00 g, 9.17 mmol) and 1-hexyne (2.10 mL, 18.3 mmol) gave the *O*-silyl diol **31a** (3.21 g, 78%) as a pale yellow oil. ^{1}H NMR: δ = 0.00 (s, 6 H, 2 MeSi), 0.78–0.84 (m, 15 H, *t*BuSi, 2 Me), 1.20 (d, *J* = 6.2 Hz, 3 H, 2′-Me), 1.25–1.40 (m, 8 H), 2.08–2.14 (m, 4 H), 2.92 (br. s, 1 H, OH), 3.76 (q, *J* = 6.2 Hz, 1 H, 1′-H) ppm. ^{13}C NMR: δ = 14.0 (Me), 14.1 (Me), 18.4 (CSi), 18.8 (CH_2), 18.9 (CH_2), 19.2 (2′-Me), 22.2 (CH_2), 22.4 (CH_2), 26.1 (3 Me), 30.8 (CH_2), 30.9 (CH_2), 68.0 (7-C), 75.7 (1′-CH), 78.7 (C), 80.0 (C), 84.6 (C), 85.5 (C) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3549, 2239, 1631, 1463, 1362, 1255, 1189, 1009, 954, 811 cm^{-1}. MS (APCI): *m*/*z* (%) = 333 (100) [M^+ + H – H_2O].

2-Butyl-4-(hex-1-ynyl)-3-iodo-5-methylfuran (32a): Using the general iodocyclisation procedure, but carried out entirely at ambient temperature, cyclisation of the *O*-silyl diol **31a** (1.00 g, 2.85 mmol) using iodine (2.17 g, 8.57 mmol), followed by workup after 1 h and column chromatography (10% EtOAc/petroleum ether) gave the iodofuran **32a** (0.94 g, 82%) as a yellow oil. ^{1}H NMR: δ = 0.86 (t, *J* = 7.5 Hz, 3 H, Me), 0.92 (t, *J* = 7.3 Hz, 3 H, Me), 1.25–1.31 (m, 2 H), 1.39–1.41 (m, 2 H), 1.50–1.57 (m, 4 H), 2.08 (s, 3 H, 5-Me),

2.54 (t, J = 7.4 Hz, 2 H, CH_2), 2.68–2.74 (m, 2 H, CH_2) ppm. ^{13}C NMR: δ = 13.7 (Me), 14.3 (Me), 14.6 (Me), 22.0 (CH_2), 22.5 (CH_2), 27.8 (CH_2), 30.6 (CH_2), 31.1 (CH_2), 49.9 (CH_2), 65.8 (3-CI), 87.3 (C), 110.9 (C), 131.2 (4-C), 147.7 (C), 155.2 (C) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 2954, 2869, 1639, 1565, 1428, 1381, 1137, 1109, 961, 886, 789 cm^{-1}. MS (APCI): m/z (%) = 345 (100) [M^+ + H]. HRMS: calcd. for $C_{15}H_{22}IO$ 345.0715; found 345.0711.

7-[(*tert*-Butyldimethylsilyloxy)phenylmethyl]trideca-5,8-diyn-7-ol (31b): Following the general procedure, condensation between methyl 2-(*tert*-butyldimethylsilyloxy)-2-phenylacetate (**30b**)[26] (1.00 g, 3.57 mmol) and 1-hexyne (0.82 mL, 7.14 mmol) gave the *O*-silyl diol **31b** (1.23 g, 83%) as a pale yellow oil. ^1H NMR: δ = –0.01 (s, 3 H, MeSi), 0.00 (s, 3 H, MeSi), 0.77–0.84 (m, 15 H, *t*BuSi, 2 Me), 1.24–1.41 (m, 8 H), 2.05–2.14 (m, 4 H), 4.84 (s, 1 H, 1′-H), 7.11–7.19 (m, 3 H), 7.36–7.38 (m, 2 H) ppm. ^{13}C NMR: δ = 14.0 (Me), 14.1 (Me), 18.3 (CSi), 18.8 (CH_2), 18.9 (CH_2), 22.3 (CH_2), 22.4 (CH_2), 26.1 (3 Me), 30.6 (CH_2), 30.7 (CH_2), 68.5 (7-C), 78.7 (C), 79.5 (C), 81.6 (1′-CH),85.8 (C), 86.6 (C), 127.5 (2 CH), 128.5 (*p*-CH), 128.9 (2 CH), 139.4 (C) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3552, 2956, 2859, 2235, 1463, 1361, 1252, 1102, 1069, 836, 778, 700 cm^{-1}. MS (APCI): m/z (%) = 396 (100) [M^+ + H – H_2O]. HRMS: (NH_4CI): calcd. for $C_{26}H_{44}NO_2Si$ 430.3141 (M^+ + NH_4); found 430.3147.

3-[(*tert*-Butyldimethylsilyloxy)ethyl]-1,5-diphenylpenta-1,4-diyn-3-ol (31c): Following the general procedure, condensation between methyl 2-(*tert*-butyldimethylsilyloxy)propanoate **30a**[25] (2.00 g, 9.17 mmol) and phenylacetylene (2.01 mL, 18.3 mmol) and column chromatography (5% EtOAc/petroleum ether) gave the *O*-silyl diol **31c** (2.63 g, 74%) as a pale yellow oil. ^1H NMR: δ = 0.00 (s, 6 H, 2 MeSi), 0.77 (s, 9 H, *t*BuSi), 1.30 (d, J = 6.2 Hz, 3 H, 2′-Me), 3.16 (br. s, 1 H, OH), 4.00 (q, J = 6.2 Hz, 1 H, 1′-H), 7.11–7.18 (m, 6 H), 7.30–7.34 (m, 4 H) ppm. ^{13}C NMR: δ = 17.0 (CSi), 17.8 (2′-Me), 24.7 (3 Me), 67.4 (7-C), 74.1 (1′-CH), 82.7 (C), 83.7 (C), 85.7 (C), 87.2 (C), 121.1 (C), 121.2 (C), 127.1 (2 CH), 127.2 (2 CH), 127.5 (CH), 127.6 (CH), 130.7 (2 CH), 130.8 (2 CH) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3536, 3057, 2929, 2885, 2230, 1671, 1573, 1471, 1361, 1255, 1140, 1062, 943, 836 cm^{-1}. MS (APCI): m/z (%) = 373 (100) [M^+ + H – H_2O].. HRMS: (NH_4CI): calcd. for $C_{25}H_{34}NO_2Si$ 408.2359 (M^+ + NH_4); found 408.2356.

3-Iodo-5-methyl-2-phenyl-4-phenylethynylfuran (32c): Using the general iodocyclisation procedure, but carried out entirely at ambient temperature, cyclisation of the *O*-silyl diol **31c** (0.51 g, 1.27 mmol) using iodine (0.97 g, 3.82 mmol), followed by workup after 1 h and column chromatography (10% EtOAc/petroleum ether) gave the iodofuran **32c** (0.94 g, 82%) as a yellow solid, which crystallised from dichloromethane/petroleum ether as needles, m.p. 104–105 °C. ^1H NMR: δ = 2.37 (s, 3 H, 5-Me), 7.17–7.19 (m, 3 H), 7.24–7.27 (m, 3 H), 7.38–7.41 (m, 2 H), 7.81–7.86 (m, 2 H) ppm. ^{13}C NMR: δ = 13.8 (5-Me), 67.8 (3-CI), 81.7 (C), 95.5 (C), 112.9 (C), 123.6 (C), 126.3 (CH), 126.4 (CH), 128.5 (CH), 128.7 (CH), 130.2 (C), 131.9 (CH), 147.2 (C), 155.9 (C) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 2921, 1584, 1555, 1463, 1377, 1265, 1082, 1066, 1022, 985, 916, 758, 670 cm^{-1}. MS (APCI): m/z = 385 [M^+ + H]. HRMS: calcd. for $C_{19}H_{14}IO$ 385.0089 (M^+ + H); found 385.0090. $C_{19}H_{13}IO$ (384.22): calcd. C 59.4, H 3.4; found C 59.2, H 3.5.

3-[(*tert*-Butyldimethylsilyloxy)phenylmethyl]-1,5-diphenyl-1,4-pentadiyn-3-ol (31d): Following the general procedure, condensation between methyl 2-(*tert*-butyldimethylsilyloxy)phenylacetate (**30b**)[26] (2.00 g, 7.14 mmol) and phenylacetylene (1.56 mL, 14.3 mmol) gave the *O*-silyl diol **31d** (2.59 g, 80%) as a pale yellow oil. ^1H NMR: δ = –0.01 (s, 3 H, MeSi), 0.00 (s, 3 H, MeSi), 0.79 (s, 9 H, *t*BuSi), 3.16 (s, 1 H, OH), 4.85 (s, 1 H, 1′-H), 7.13–7.23 (m, 11 H), 7.29–7.31 (m, 2 H), 7.44–7.52 (m, 2 H) ppm. ^{13}C NMR: δ = 18.6 (CSi), 26.2 (3 Me), 69.3 (3-C), 81.6 (1′-CH), 85.2 (C), 86.0 (C), 87.3 (C), 88.1 (C), 122.6 (C), 122.7 (C), 127.8 (CH), 128.5 (CH), 128.6 (CH), 128.7 (CH), 128.9 (CH), 129.0 (CH), 129.1 (CH), 132.1 (CH), 132.2 (CH), 139.1 (C) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3545, 3062, 2928, 2885, 2232, 1573, 1471, 1361, 1176, 1072, 938, 669 cm^{-1}. MS (APCI): m/z (%) = 435 (100) [M^+ + H – H_2O]. HRMS: (NH_4CI): calcd. for $C_{30}H_{36}NO_2Si$ 470.2515 (M^+ + NH_4); found 470.2515.

3-Iodo-2,5-diphenyl-4-(phenylethynyl)furan (32d): Using the general iodocyclisation procedure, but carried out entirely at ambient temperature, cyclisation of the *O*-silyl diol **31d** (1.00 g, 2.21 mmol) using iodine (1.68 g, 6.63 mmol), followed by workup after 1 h and column chromatography (5% EtOAc/petroleum ether) gave the iodofuran **32d** (0.88 g, 89%) as a yellow solid, which crystallised from dichloromethane/petroleum ether as needles, m.p. 112–113 °C. ^1H NMR: δ = 7.50–7.52 (m, 5 H), 7.57–7.61 (m, 4 H), 7.74–7.76 (m, 2 H), 8.23 (d, J = 7.6 Hz, 2 H), 8.30 (d, J = 7.6 Hz, 2 H) ppm. ^{13}C NMR: δ = 70.9 (3-CI), 83.2 (C), 97.6 (C), 111.8 (C), 123.4 (C), 125.3 (CH), 126.7 (CH), 128.8 (CH), 128.9 (CH), 129.0 (CH), 129.1 (CH), 129.8 (C), 130.0 (C), 131.9 (CH), 150.9 (C), 154.3 (C) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 2923, 1595, 1479, 1377, 1132, 1067, 1026, 940, 911, 764, 672 cm^{-1}. MS (APCI): m/z (%) = 447 (100) [M^+ + H]. HRMS: calcd. for $C_{24}H_{16}IO$ 447.0246 (M^+ + H); found 447.0235. $C_{24}H_{15}IO$ (446.29): calcd. C 64.6, H 3.4; found C 64.3, H 3.2.

3-(Hex-1-ynyl)nona-4-yne-2,3-diol (31e): Following the general procedure for condensations between α-hydroxy esters and acetylides, reaction between methyl 2-hydroxypropanoate (**30e**) (2.00 g, 19.21 mmol) and 1-hexyne (6.62 mL, 57.63 mmol), followed by column chromatography (20% EtOAc/petroleum ether), gave the diynyl diol **31e** (3.92 g, 86%) as a pale yellow oil. ^1H NMR: δ = 0.84 (t, J = 7.2 Hz, 3 H, Me), 0.85 (t, J = 7.2 Hz, 3 H, Me), 1.28 (d, J = 6.3 Hz, 3 H, 1-Me), 1.30–1.35 (m, 4 H), 1.42–1.51 (m, 4 H), 2.15–2.28 (m, 4 H, 3′-, 6-CH_2), 3.75 (q, J = 6.3 Hz, 1 H, 2-H) ppm. ^{13}C NMR: δ = 13.8 (Me), 13.9 (Me), 17.8 (1-Me), 18.7 (CH_2), 18.8 (CH_2), 22.3 (CH_2), 22.4 (CH_2), 30.7 (CH_2), 30.8 (CH_2), 68.4 (3-C), 74.8 (2-CH), 77.9 (C), 79.1 (C), 85.0 (C), 86.0 (C) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3405, 2958, 2872, 2236, 1465, 1378, 1268, 1187, 1119, 930 cm^{-1}. MS (APCI): m/z (%) = 219 (100) [M^+ + H – H_2O]. HRMS: (NH_4CI): calcd. for $C_{15}H_{28}NO_2$ 254.2120 (M^+ + NH_4); found 254.2125.

2-Butyl-4-(hex-1-ynyl)-3-iodo-5-methylfuran (32a) from Diol 31e: Using the general iodocyclisation procedure, but carried out entirely at ambient temperature, cyclisation of the diynyl diol **31e** (0.20 g, 0.84 mmol) using iodine (0.64 g, 2.54 mmol), followed by workup after 1 h and column chromatography (10% EtOAc/petroleum ether) gave the iodofuran **32a** (0.27 g, 93%) as a yellow oil, which showed spectroscopic and analytical data identical to the foregoing sample of iodofuran **32a** derived from the corresponding *O*-silyl ether **31a**.

2-(Hex-1-ynyl)-1-phenyloct-3-yne-1,2-diol (31f): Following the general procedure for condensations between α-hydroxy esters and acetylides, reaction between methyl 2-hydroxy-2-phenylacetate (**30f**) (0.50 g, 3.00 mmol) and 1-hexyne (1.03 mL, 9.02 mmol), followed by column chromatography (20% EtOAc/petroleum ether), gave the diynyl diol **31f** (0.64 g, 72%) as a pale yellow oil. ^1H NMR: δ = 0.80–0.83 (m, 6 H, 2 Me), 1.25–1.32 (m, 4 H), 1.36–1.44 (m, 4 H), 2.12–2.15 (m, 4 H), 2.77 (br. s, 1 H, OH), 2.92 (d, J = 3.2 Hz, 1 H, 1-OH), 4.70 (d, J = 3.2 Hz, 1 H, 1-H), 7.24–7.29 (m, 3 H), 7.44–7.49 (m, 2 H) ppm. ^{13}C NMR: δ = 13.8 (Me), 13.9 (Me), 18.8 (CH_2), 18.9 (CH_2), 22.3 (CH_2), 22.4 (CH_2), 30.6 (CH_2), 30.7 (CH_2), 68.4 (2-C), 78.1 (2-CH), 78.8 (C), 80.4 (1-CH), 87.3 (C), 87.5 (C), 127.8 (2 CH), 128.5 (*p*-CH), 128.6 (2 CH), 137.8 (C) ppm. IR

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($CHCl_3$): $\tilde{\nu}$ = 3417, 3062, 3032, 2956, 2871, 2235, 1605, 1494, 1378, 1299, 1175, 1087, 903, 766 cm^{-1}. MS (APCI): *m*/*z* (%) = 281 (100) [$M^+ + H - H_2O$].

2-Butyl-4-(hex-1-ynyl)-3-iodo-5-phenylfuran 32b from Diol 31f: Using the general iodocyclisation procedure, but carried out entirely at ambient temperature, cyclisation of the diynyl diol **31f** (0.50 g, 0.84 mmol) using iodine (1.27 g, 5.03 mmol), followed by workup after 1 h and column chromatography (5% EtOAc/petroleum ether) gave the iodofuran **32b** (0.59 g, 87%) as a yellow oil. ^1H NMR: δ = 0.98 (t, *J* = 7.3 Hz, 3 H, Me), 1.04 (t, *J* = 7.3 Hz, 3 H, Me), 1.40–1.46 (m, 2 H), 1.53–1.59 (m, 2 H), 1.69–1.75 (m, 4 H), 2.76 (t, *J* = 7.6 Hz, CH_2), 2.84–2.90 (m, 2 H), 7.34–7.35 (m, 1 H, *p*-H), 7.40–7.44 (m, 2 *m*-H), 7.69–7.72 (m, 2 *o*-H) ppm. ^{13}C NMR: δ = 14.1 (Me), 14.5 (Me), 22.4 (CH_2), 22.6 (CH_2), 28.0 (CH_2), 30.5 (CH_2), 30.8 (CH_2), 49.8 (CH_2), 69.2 (3-CI), 88.8 (C), 97.3 (C), 111.8 (4-C), 125.3 (CH), 128.2 (CH), 128.3 (CH), 128.9 (CH), 129.1 (CH), 131.2 (C), 147.2 (C), 156.5 (C) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 2954, 2869, 1632, 1602, 1583, 1428, 1378, 1248, 1142, 1070, 929, 879 cm^{-1}. MS (APCI): *m*/*z* (%) = 407 (100) [$M^+ + H$]. HRMS: calcd. for $C_{20}H_{24}IO$ 407.0872 ($M^+ + H$); found 407.0870. $C_{20}H_{23}IO$ (406.31): calcd. C 59.1, H 5.7; found C 59.4, H 5.9.

5-Phenyl-3-(phenylethynyl)pent-4-yne-2,3-diol (31g): Following the general procedure for condensations between α-hydroxy esters and acetylides, reaction between methyl 2-hydroxypropanoate (**30e**) (1.00 g, 9.6 mmol) and phenylacetylene (3.16 mL, 28.8 mmol) followed by column chromatography (20% EtOAc/petroleum ether), gave the diynyl diol **31g** (1.78 g, 66%) as a pale yellow, crystalline solid, m.p. 106–107 °C (from petroleum ether/dichloromethane). ^1H NMR: δ = 1.35 (d, *J* = 6.3 Hz, 3 H, 1-Me), 2.61 (br. s, 1 H, OH), 3.52 (br. s, 1 H, OH), 3.94 (q, *J* = 6.3 Hz, 1 H, 2-H), 7.12–7.16 (m, 6 H), 7.29–7.34 (m, 4 H) ppm. ^{13}C NMR: δ = 18.2 (1-Me), 69.1 (3-C), 74.9 (2-CH), 85.4 (C), 85.9 (C), 86.3 (C), 87.4 (C), 122.1 (C), 122.2 (C), 128.2 (CH), 128.7 (CH), 129.3 (CH), 129.5 (CH), 132.5 (CH), 133.4 (CH) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3478, 2929, 2875, 2241, 1636, 1475, 1140, 966, 862 cm^{-1}. MS (APCI): *m*/*z* (%) = 259 (100) [$M^+ + H - H_2O$]. $C_{19}H_{16}O_2$ (276.33): calcd. C 82.6, H 5.8; found C 82.6, H 5.9.

3-Iodo-5-methyl-2-phenyl-4-(phenylethynyl)furan 32c from Diol 31g: Using the general iodocyclisation procedure, but carried out entirely at ambient temperature, cyclisation of the diynyl diol **31g** (1.00 g, 3.62 mmol) using iodine (2.75 g, 10.86 mmol), followed by workup after 1 h and column chromatography (5% EtOAc/petroleum ether) gave the iodofuran **32c** (1.29 g, 93%) as a yellow solid, m.p. 104–105 °C, which showed other spectroscopic and analytical data identical to the foregoing sample of iodofuran **32c** derived from the corresponding *O*-silyl ether **31c**.

1,4-Diphenyl-2-(phenylethynyl)-3-butyne-1,2-diol (31h): Following the general procedure for condensations between α-hydroxy esters and acetylides, reaction between methyl 2-hydroxy-2-phenylacetate (**30f**) (2.00 g, 12.03 mmol) and phenylacetylene (3.96 mL, 36.1 mmol) followed by column chromatography (20% EtOAc/petroleum ether), gave the diynyl diol **31h** (3.10 g, 76%) as a pale yellow, crystalline solid, m.p. 160–162 °C (from petroleum ether/dichloromethane). ^1H NMR: δ = 3.13 (br. s, 1 H, OH), 3.24 (br. s, 1 H, OH), 4.97 (s, 1 H, 1-H), 7.21–7.23 (m, 13 H), 7.58–7.60 (m, 2 H) ppm. ^{13}C NMR: δ = 69.2 (2-C), 80.5 (1-CH), 86.4 (C), 86.5 (C), 86.7 (C), 87.0 (C), 122.0 (C), 122.1 (C), 128.1 (CH), 128.5 (CH), 128.7 (CH), 128.8 (CH), 129.0 (CH), 129.3 (CH), 132.2 (CH), 132.3 (CH), 137.3 (C) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3503, 2914, 2227, 1596, 1487, 1326, 1220, 1194, 1156, 1095, 992, 850 cm^{-1}. MS (APCI): *m*/*z* (%) = 321 (100) [$M^+ + H - H_2O$]. $C_{24}H_{18}O_2$ (338.41): calcd. C 85.2, H 5.4; found C 85.4, H 5.6.

3-Iodo-2,5-diphenyl-4-(phenylethynyl)furan 32d from Diol 31h: Using the general iodocyclisation procedure, but carried out entirely at ambient temperature, cyclisation of the diynyl diol **31h** (0.20 g, 0.59 mmol) using iodine (0.45 g, 1.77 mmol), followed by workup after 1 h and column chromatography (5% EtOAc/petroleum ether) gave the iodofuran **32d** (0.245 g, 94%) as a yellow solid, m.p. 112–113 °C, which showed other spectroscopic and analytical data identical to the foregoing sample of iodofuran **32d** derived from the corresponding *O*-silyl ether **31d**.

2,5-Diphenyl-3-(phenylselanyl)furan (33): The diol **14a** (0.70 g, 2.9 mmol) and anhydrous potassium carbonate (0.48 g, 3.48 mmol) were added to dry tetrahydrofuran (5 mL) and the resulting suspension stirred and cooled to –78 °C. Phenylselanyl chloride (0.609 g, 3.19 mmol) was added in one portion and stirring continued at this temperature for 5 h. Most of the solvent was then evaporated and the residue dissolved in a mixture of water (20 mL) and ether (20 mL). The separated aqueous layer was then extracted with diethyl ether (2 × 20 mL) and the combined organic solutions dried, filtered and the solvents evaporated. Column chromatography of the residue (5% ether in pentane) separated the selanylfuran **33** (0.32 g, 29%) as a pale yellow solid, m.p. 52–53 °C (ether/hexane). ^1H NMR: δ = 6.65 (s, 1 H, 4-H), 7.15–7.45 (m, 11 H), 7.62 (dd, *J* = 7.0 and ca. 1 Hz, 2 *o*-H), 8.05 (dd, *J* = 7.5 and ca. 1 Hz, 2 *o*-H) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3020, 1666, 1466, 1430, 1351, 1215, 1101, 1015, 735, 685 cm^{-1}. MS (EI): *m*/*z* (%) = 376 (15) [M^+], 296 (12), 202 (8), 191 (20), 105 (78), 77 (100). $C_{22}H_{16}OSe$ (375.33): calcd. C 70.4, H 4.2; found C 70.2, H 4.3.

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