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# Cyclic Enol Ether Synthesis *via* Arenesulfonyl Iodide Additions to Alkynols

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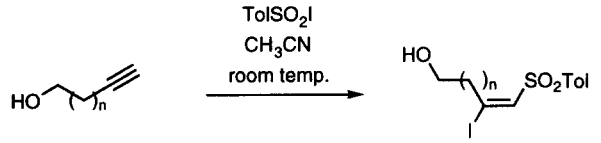
**Abstract:** The reaction of arenesulfonyl iodides with alkynols generally provides adducts in good yields. Treatment of these adducts with $KN(SiMe_3)_2$ gives enol ethers; cyclisation of the functionalised pentenol (**5**) results in formation of the *exo*-alkylidene tetrahydrofuran (**7**), whereas the homologous hexenol (**6**) gives the dihydropyran (**8**). Attempts to cyclise the hexenol (**6**) with potassium *t*-butoxide under the conditions reported by Short and Ziegler generally gave the endocyclic ether (**8**).


The discovery of a diversity of oxygenated natural products such as the polyether marine toxins ciguatoxin[1] and maitotoxin[2] has stimulated much interest in the development of new methods that could be directed towards their total syntheses.[3] One challenge in the development of such a strategy has been the requirement for a heterocyclic ring synthesis that preserves a degree of functionality for further elaboration and, where appropriate, gives good stereocontrol α to the heteroatom. Sulfonyl radical chemistry suggested itself as an attractive means for the achievement of this outcome with concomitant introduction of an activating functional group; we have recently shown that a two step procedure (radical addition to an alkenol followed by cyclisation of the intermediate β-iodosulfone) provides heterocycles in acceptable yields,[4] and that excellent *cis*-diastereoselectivity in the synthesis of 2,6-dihydropyrans can be obtained.[5] A logical extension of this method would involve the addition of *para*-toluenesulfonyl iodide (tosyl iodide) to an alkynol producing an intermediate β-iodo vinyl sulfone;[6] subsequent cyclisation should, possibly by an addition-elimination mechanism,[7] give access to a range of unsaturated oxygenated heterocycles. This general concept has been used recently for synthesis of a range of cyclic structures.[8-10] After the conclusion of our studies into the tosyl iodide reactions, a communication by Short and Ziegler[11] on similar chemistry using benzenesulfonyl iodide leading to oxygen heterocycles has prompted us to report details of our research in this field.

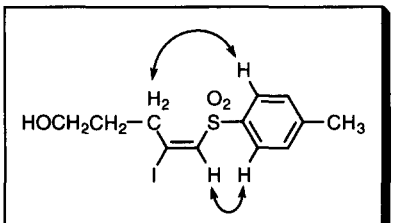
In additions of a sulfonyl iodide to alkenes and alkynes, we have found that tosyl iodide is a satisfactory reagent for this purpose: it can be prepared[12] on a multigram scale, recrystallised (by dissolution in $CCl_4$ at room temperature and chilling in a freezer at *ca.* -20 °C overnight, typically giving yields >70% on a multigram scale) and stored in a conventional freezer protected from light for several months without noticeable decomposition. In recent times, we have also developed an alternative procedure where the sulfonyl iodide is prepared in a toluene / water mixture, and crystallised by addition of hexane to the dried toluene solution; this modification avoids use of carbon tetrachloride. Alkynols (**1**) to (**3**) were then stirred with equimolar quantities of tosyl iodide at room temperature *without irradiation*, giving the β-iodo vinyl sulfones (**4**) to (**6**) in 58 to 71% yields (not optimised) respectively following purification. [Use of diethyl

ether as solvent and illumination for the addition to hexynol (**3**), after the method of Truce and Wolf,[11] gave a reduced yield of 52%.] Whereas chromatography of saturated β-iodosulfones led to significant decomposition,[4] the vinyl analogues were quite stable on silica. (*E*)-Stereochemistry was assigned with the aid of a two-dimensional nOe experiment.



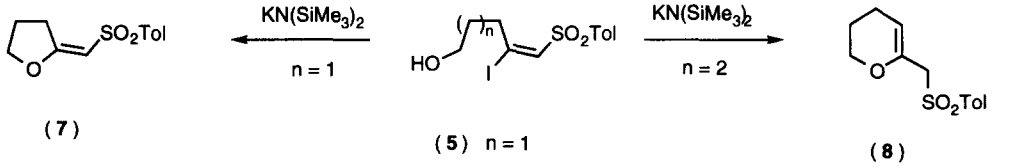

(**1**) n = 1
(**2**) n = 2
(**3**) n = 3

(**4**) n = 1
(**5**) n = 2
(**6**) n = 3




Key nuclear Overhauser enhancements for iodosulfone (**5**)

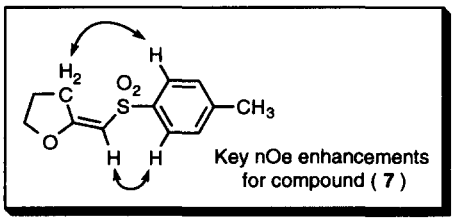
While sodium hydride initially proved satisfactory for the cyclisation of saturated iodosulfones,[4] its use with the unsaturated analogues was unreliable, and this led us to examine other possibilities; potassium hexamethyldisilazide [bis(trimethylsilyl)amide] is now our reagent of choice for this step. Cyclisation of the iodosulfone (**5**) was effected by treatment with 1.5 equivalents of $KN(SiMe_3)_2$ in toluene/THF at 0 °C, giving the (*E*)-exocyclic enol ether (**7**) in 62% yield as a single stereo- and regio-isomer. Comparison of the $^1H$ n.m.r. spectrum [$\delta_H$(=CH) 5.79 p.p.m.] with published data[13] for the analogous phenyl sulfone [$\delta_H(=CH_E)$ 5.8 p.p.m., and $\delta_H(=CH_Z)$ 5.5 p.p.m.] suggested (*E*)-stereochemistry, and difference nOe spectroscopy confirmed the assignment. A similar cyclisation of the iodosulfone (**6**) gave instead the endocyclic dihydropyran (**8**) in 65% yield, as the sole isomer. When a similar reaction was attempted using the tosyl iodide adduct (**4**) of 3-butyn-1-ol (**1**), only insoluble polymeric material was isolated along with some unchanged starting material; to date, we have found no evidence for the formation of either an oxetane or an alkynyl sulfone (resulting from elimination of HI from the iodosulfone). Variation of the reaction conditions for the cyclisation of the hexenol (**6**) gave a modest increase in yield (71%) (Table). On no occasion was any exocyclic alkene detected. In this way, our method using $KN(SiMe_3)_2$ now provides a simple method for synthesis of endocyclic dihydropyrans.

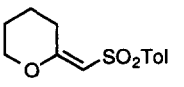



(**7**)

(**5**) n = 1
(**6**) n = 2

(**8**)




(**9**)

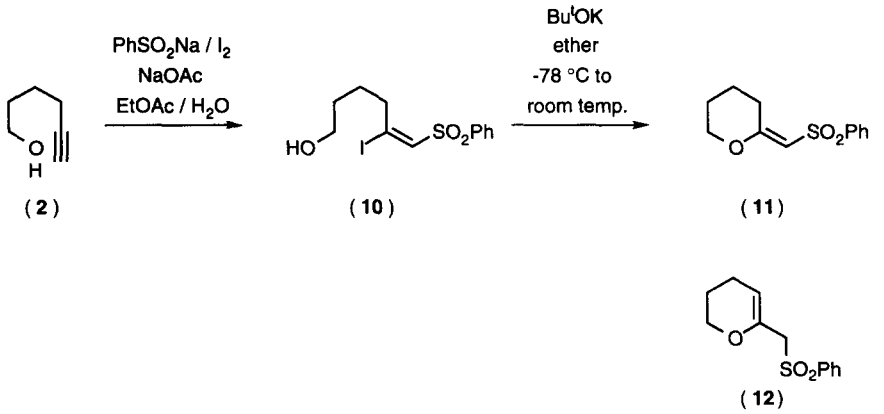
TABLE: CYCLISATION OF IODOSULFONE (**6**)

| BASE | SOLVENT | TEMPERATURE[a] | YIELD[b] |
|---|---|---|---|
| $KN(SiMe_3)_2$;[c] 1.5 equiv. | toluene/THF (3:1) | 0 °C, then room temp. | 65% |
| $KN(SiMe_3)_2$;[c] 1.5 equiv. | THF | 0 °C, then room temp. | 60% |
| $KN(SiMe_3)_2$;[c] 1.1 equiv. | toluene/THF (3:1) | 0 °C, then room temp. | 63%[d] |
| $KN(SiMe_3)_2$;[c] 1.1 equiv. | toluene/THF (4:1) | room temp. | 71%[d] |
| $KN(SiMe_3)_2$;[c] 1.1 equiv. | toluene/THF (3:1) | room temp, then reflux | 60% |

**a**. Where two temperatures are specified, the base was added at the first temp., then the reaction was allowed to warm (or was heated) to the second temp.; all reactions were quenched at 0 °C. **b**. Isolated yield (following chromatography). **c**. Aldrich reagent: 0.5M solution in toluene. **d**. Cleaner crude product (300 MHz $^1$H n.m.r. spectroscopy).

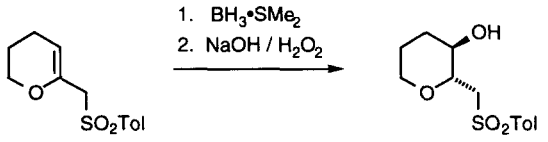
At this stage, we proceeded to investigate the intriguing formation of the exocyclic isomer (**11**) by cyclisation of the iodosulfone (**10**) using potassium *t*-butoxide in ether, as reported by Short and Ziegler.[11,14] Initially, we carried out the analogous reaction of the tosyl derivative (**6**) with commercial (Aldrich) Bu$^t$OK in ether at -78 °C; addition of the iodosulfone to a slurry of the base in ether followed by an acetic acid quench at -78 °C, gave a poor yield (< 10%) of the **endocyclic** isomer (**8**) accompanied by some unchanged starting material. Repetition of the reaction but using an inverse mode of addition, or substitution of the solvent by THF, led to similar outcomes. If the iodosulfone (**6**) was added to Bu$^t$OK in ether at -78 °C, and then allowed to warm to room temperature before work-up, only the endocyclic enol ether (**8**) was isolated, in 51% yield. Evidence for the intermediacy of the exocyclic ether (**9**) was obtained when the iodosulfone (**6**) was treated with $KN(SiMe_3)_2$ in THF at -78 °C and quenched at that temperature by the addition of AcOH ($^1$H n.m.r.: δ 5.76 p.p.m. tentatively assigned to $=CHSO_2$ for the exocyclic isomer), however the endocyclic isomer was still the major product [ratio of (**8**) : (**9**) ≈ 95 : 5] and we were unable to isolate the exocyclic isomer (**9**) in a pure form.

This disappointing outcome prompted us to repeat the experiments using the benzenesulfonyl reagent. Addition of benzenesulfonyl iodide (formed *in situ*) to 5-hexyn-1-ol (**3**) under the conditions described by Short and Ziegler[11,14] proceeded smoothly, giving the iodo vinyl sulfone (**10**) in 68% yield. Attempted cyclisation using commercial Bu$^t$OK gave similar results to those described above, however use of a freshly sublimed sample of the base gave samples that appeared to contain the exocyclic isomer (**11**) in addition to the exocyclic compound (**12**). In the $^1$H n.m.r. spectrum of the crude reaction mixture, an absorption at δ 4.63 p.p.m. can be assigned to the endocyclic isomer, and signals at δ 5.49 and 5.68 p.p.m. could represent isomeric exocyclic enol ethers. Unfortunately, chromatographic purification of the reaction mixture caused extensive isomerisation of the postulated exocyclic isomer(s) to the dihydropyran (**12**); in our experience, this has been an extremely capricious reaction and the exocyclic compound is extremely reactive, readily converting to the more stable endocyclic form.



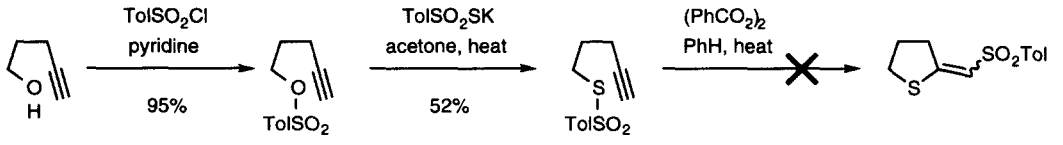

(2) (10) (11) (12)

While the exocyclic enol ether (**7**) is a crystalline solid and thus quite stable, the dihydropyran (**8**) is often isolated as an oil and has proved to be liable to partial hydration on storage at room temperature (this undesirable reaction can be considerably suppressed by refrigeration). After storage of a sample that had failed to crystallise for a week at room temperature, evidence for the hydrated form is readily apparent: the lactol / hydroxyketone isomerisation is observed by both infrared and $^{13}C$ n.m.r. spectroscopy [$\nu_{OH}$ 3490 and $\nu_{C=O}$ 1740 $cm^{-1}$; $\delta_C$(p.p.m.) 198.1 (C=O) and 96.5/94.7 (C2 of anomers of lactol)]. Once crystalline, the enol ether (**8**) exhibits greater stability. Hydroboration of a pure sample of the dihydropyran (**8**) gave the desired 3-hydroxy pyran (**13**) in 59% yield. We are currently investigating other aspects of the reactivity of these interesting dihydropyrans.




(8) (13)

Our preliminary investigations on routes to analogous sulfur heterocycles have been less encouraging. 4-Pent-1-enyl thiotosylate has been shown by Serra and da Silva Corrêa[15] to rearrange readily to the 2-(*para*-toluenesulfonylmethyl)tetrahydrothiophen, and we considered that a similar cyclisation may be possible with the 4-pentynyl analogue (**15**), prepared from commercially available 4-pentyn-1-ol (**2**). However attempted cyclisation (benzoyl peroxide, benzene, reflux) gave unchanged starting material contaminated with only traces (<5%) of by-products.




(2) (14) (15) (16)

## EXPERIMENTAL

### General

$^1$H n.m.r. spectra were recorded as deuterochloroform solutions on a Bruker AC300F (300 MHz) spectrometer and a Bruker AM 500 (500 MHz) spectrometer. Chemical shifts are measured in parts per million (δ, p.p.m.) downfield from tetramethyl silane (TMS) relative to chloroform ($\delta_H$ = 7.26 p.p.m.) as an internal reference. Coupling constants (*J*) are reported in hertz (Hz). Multiplicities are designated as follows: singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br). $^{13}$C n.m.r. spectra were recorded as deuterochloroform solutions on a Bruker AC300F (75.5 MHz) spectrometer. Chemical shifts are reported in parts per million downfield from TMS relative to the central peak of the $CDCl_3$ signal ($\delta_C$ = 77.04 p.p.m.). Infrared spectra were obtained on a Perkin Elmer 298 Infrared spectrophotometer either as thin films of liquids or paraffin mulls of solids. Absorptions of medium or strong intensity are reported in $cm^{-1}$. Mass spectra, in electron ionisation mode, were obtained on a VG Quattro mass spectrometer at 70 eV ionising potential and with an ion source of 210 °C. Melting points were determined on a Mel-Temp melting point apparatus and are uncorrected. Elemental analyses were performed by the School of Chemistry Microanalysis Service, UNSW.

Flash chromatography[16] was carried out using Merck Kieselgel 60 (230-400 mesh; No. 9385), using analytical reagent grade or distilled solvents. Reagents and solvents were purified by standard procedures. Acetone refers to May and Baker analytical grade solvent; acetonitrile was distilled from calcium hydride and stored over 4A molecular sieves; benzene and carbon tetrachloride were dried with calcium chloride, distilled, and stored over 5A molecular sieves; ethyl acetate was distilled before use; light petroleum refers to the hydrocarbon fraction boiling in the range 60 to 80 °C; pyridine was dried with KOH, distilled, and stored over fresh KOH; tetrahydrofuran (THF) was distilled under an argon atmosphere, from sodium/benzophenone; toluene was distilled from sodium metal, and stored over sodium wire. All other chemicals were used without further purification.

### *para*-Toluenesulfonyl iodide (Tosyl iodide)

***Method A*** A solution of iodine (8.50 g, 33.5 mmol) in ethanol (100 ml) was added slowly to a vigorously stirred solution of sodium *para*-toluenesulfinate (8.90 g, 50 mmol) in water (750 ml). The mixture was stirred for a further 5 min, and the precipitate was collected by filtration. The solid was dissolved in the minimum volume of carbon tetrachloride **at room temperature** and the solution was dried ($MgSO_4$) and then stored overnight at -20 °C. *para*-Toluenesulfonyl iodide was isolated as yellow needles (6.99 g, 74%), m.p. 88-89 °C (lit.[17] 88-90 °C ). $\delta_H$ (300 MHz) 2.47, s, 3H, $ArCH_3$; 7.34, d, *J* 8.5 Hz, 2H, ArH; 7.75, d, *J* 8.5 Hz, 2H, ArH.

***Method B*** A solution of iodine (17.0 g, 67 mmol) in toluene (150 ml) was added to a solution of sodium *para*-toluenesulfinate (17.8 g, 0.10 mol) in water (200 ml), and the mixture was stirred vigorously at room temperature and with the exclusion of light for 1 h. The organic layer was then separated, washed with water, and dried ($MgSO_4$). An equal volume of hexane was added, and the resulting solution was stored overnight at -20 °C. The product was separated by filtration and washed with hexane to give tosyl iodide as a yellow crystalline solid (13.3 g, 70%).

**3-Iodo-4-(*para*-toluenesulfonyl)-3-buten-1-ol (4)**

A solution of 3-butyn-1-ol (**1**) (0.62 g, 8.8 mmol) and tosyl iodide (2.50 g, 8.9 mmol) in dry acetonitrile (50 ml) was stirred under an argon atmosphere for 72 h. The solvent was removed under reduced pressure to give an orange oil which was dissolved in diethyl ether and washed twice with aqueous sodium thiosulfate (5% w/v) and then with water. Evaporation of the dried ($MgSO_4$) solution gave the crude product as a viscous colourless oil that slowly crystallised (3.02 g, 97%). Recrystallisation from diethyl ether / hexane gave the *title compound* (**4**) as fine colourless needles (1.80 g, 58%), m.p. 76-77 °C (Found; C, 37.9; H, 4.1. $C_{11}H_{13}IO_3S$ requires C, 37.5; H, 3.7%). $\nu_{max}$ 3300, 1600, 1320, 1145, 1080, 1040 $cm^{-1}$. $\delta_H$(300 MHz; $CDCl_3$) 2.15, s br, 1H, OH; 2.45, s, 3H, $ArCH_3$; 3.37, t, *J* 5.9 Hz, 2H, $CH_2C(I)$=; 3.86, t br, *J* 5.9 Hz, 2H, $CH_2O$; 7.13, s, 1H, =$CHSO_2$; 7.37, d, *J* 8.2 Hz, 2H, ArH; 7.81, d, *J* 8.2 Hz, 2H, ArH. $\delta_C$(75.5 MHz, $CDCl_3$) 21.7 ($ArCH_3$), 43.3 (C2), 61.0 (C1), 119.6 (C3), 127.6 (Ar C3 and C5), 130.2 (Ar C2 and C6), 137.4 (Ar C4), 141.1 (C4), 145.1 (Ar C4).

**4-Iodo-5-(*para*-toluenesulfonyl)-4-penten-1-ol (5)**

A solution of 4-pentyn-1-ol (**2**) (0.61 g, 7.2 mmol) in dry acetonitrile (10 ml) was added to a stirred solution of tosyl iodide (2.04 g, 7.2 mmol) in acetonitrile (40 ml) under an argon atmosphere. After 17 h the solvent was removed under reduced pressure, and the residue was dissolved in dichloromethane and washed twice with sodium thiosulfate (5% w/v), then water, and dried ($MgSO_4$). Evaporation of the solvent under reduced pressure and purification of the crude product by flash chromatography (40% ethyl acetate/light petroleum) gave the *title compound* (**5**) as pale yellow crystals (1.54 g, 58%), m.p. 81-83 °C (Found: C, 39.7; H, 4.3. $C_{12}H_{15}IO_3S$ requires C, 39.4; H, 4.1%).

$\nu_{max}$ (paraffin) 3530, 1600, 1310, 1140, 1080 $cm^{-1}$. $\delta_H$(300 MHz, $CDCl_3$) 1.87, pentet, *J* 6.3 Hz, 2H, H2; 2.41, t, *J* 6.2 Hz, 1H, OH; 2.45, s, 3H, $ArCH_3$; 3.14, t, *J* 6.8 Hz, 2H, H3; 3.67, q, *J* 5.9 Hz, 2H, H1; 7.07, s, 1H, H5; 7.37, d, *J* 8.5 Hz, 2H, ArH; 7.80, d, *J* 8.5 Hz, 2H, ArH. $\delta_C$(75.5 MHz, $CDCl_3$) 21.6 ($ArCH_3$), 32.2 (C2), 36.5 (C3), 60.1 (C1), 124.4 (C4), 127.4 (Ar C3 and C5), 130.2 (C2 and C6), 137.4 (Ar C4), 139.8 (C5), 145.1 (Ar C1).

*m/z* 367 [(M+1), <1%], 239 (M-I, 27%), 91 (100%).

**(*E*)-5-Iodo-6-(*para*-toluenesulfonyl)-5-hexen-1-ol (6)**

A solution of 5-hexyn-1-ol (**3**) (1.00 g, 10.2 mmol) in dry acetonitrile (10 ml) was added to a stirred solution of tosyl iodide (2.87 g, 10.2 mmol) in acetonitrile (40 ml) under an argon atmosphere. After 21 h at room temperature the solvent was removed under reduced pressure, and the residue was dissolved in dichloromethane (50 ml) and washed twice with sodium thiosulfate (2 x 25 ml, 5% aq.) and then water (30 ml), and dried ($MgSO_4$). Flash chromatography (40% ethyl acetate/light petroleum) of the crude product gave the *(E)-5-iodo-6-(*para*-toluenesulfonyl)-5-hexen-1-ol* (**6**) as a colourless microcrystalline solid (2.73 g, 71%), m.p. 50-52 °C (Found: C, 40.9; H, 4.8. $C_{13}H_{17}IO_3S$ requires C, 41.1; H, 4.5%).

$\nu_{max}$(neat) 3560, 3400, 1600, 1315, 1150, 1080 $cm^{-1}$; $\delta_H$(300 MHz, $CDCl_3$) 1.55-1.71, m, 4H, H2 and H3; 1.93, s, 1H, OH; 2.42, s, 3H, $ArCH_3$; 3.05, t, *J* 7.1 Hz, 2H, H4; 3.66, t, *J* 5.9 Hz, 2H, H1; 6.99, s, 1H, H6; 7.34, d, J 8.2 Hz, 2H, ArH; 7.78, d, *J* 8.2 Hz, 2H, ArH. $\delta_C$(75.5 MHz, $CDCl_3$) 21.6 ($ArCH_3$) 26.0 (C3), 31.0 (C2), 39.5 (C4), 62.0 (C1), 124.6 (C5), 127.4 (Ar C3 and C5), 130.1 (Ar C2 and C6), 137.7 (Ar C4), 138.9 (C6), 144.9 (Ar C1). *m/z* 381 (M+1), 253 (M–I).

**(*E*)-5-Iodo-6-benzenesulfonyl-5-hexen-1-ol (10)**

Iodine (2.80 g, 11.0 mmol) was added in a single portion to a mixture of sodium acetate (1.39 g, 17 mmol), sodium benzenesulfinate (3.60 g, 22 mmol) and 5-hexyn-1-ol (**3**) (1.00 g, 10 mmol) in ethyl acetate (20 ml) and water (10 ml). The resulting dark red mixture was stirred rapidly under an argon atmosphere with irradiation (100 W) for 17 h, during which time the colour faded to pale yellow. The reaction was quenched by the addition of sodium thiosulfate (5% w/v, aq.) until no further colour change occurred, whereupon the aqueous layer was separated and extracted with ethyl acetate (4 x 8 ml). The combined organic extracts were dried ($MgSO_4$) and evaporated, and the residue was purified by flash chromatography (40% ethyl acetate : light petroleum) to give (*E*)- 5-iodo-6-benzenesulfonyl-5-hexen-1-ol (**10**)[14] as a pale yellow powder (2.49 g, 68 %), m.p 50-52 °C. (lit.[14] 49–51 °C).

$\nu_{max}$(paraffin) 3200 br, 1440, 1300, 1140, 775, 745, 730, 710, 680, 660, 640 $cm^{-1}$.

$\delta_H$ (300 MHz, $CDCl_3$) 1.53-1.70, m, 4H, H2 and H3; 1.98, s, 1H, OH; 3.06, t, *J* 7.2 Hz, 2H, H4; 3.65, t, *J* 5.9 Hz, 2H, H1; 7.01, s, 1H, H6; 7.53-7.59, m, 2H, Ph; 7.62-7.68, m, 1H, Ph; 7.87-7.91, m, 2H, Ph.

$\delta_C$ (75.5 MHz, $CDCl_3$) 26.0 (C3), 31.1 (C2), 39.6 (C4), 62.0 (C1), 125.4 (C5), 127.4 (Ar), 129.5 (Ar), 133.8 (Ar), 138.6 (C6), 140.6 (Ar).

**(E)-Tetrahydro-2-[(*para*-toluenesulfonyl)methylene]furan (7)**

A solution of 4-iodo-5-(*para*-toluenesulfonyl)-4-penten-1-ol (**5**) (0.47 g, 1.28 mmol) in dry toluene (30 ml) and THF (10 ml) was placed under an argon atmosphere at 0 °C and a solution of potassium bis(trimethylsilyl)amide (4.0 ml of a 0.5 M solution in toluene, 2.0 mmol) was added over 15 min. The solution was allowed to warm to room temperature with continuous stirring. After 2 h the solution was cooled in ice and quenched with water. The aqueous layer was removed and washed twice with diethyl ether. The combined organic extracts were washed with water, dried ($MgSO_4$), and the solvent was evaporated. Purification of the crude product by flash chromatography (40% ethyl acetate : light petroleum) gave *(E)-tetrahydro-2-[(*para*-toluenesulfonyl)methylene]furan* (**7**) as colourless crystals, m.p. 100-102 °C, (Found: C, 60.2; H, 6.2. $C_{12}H_{14}O_3S$ requires C, 60.5; H, 5.9%). $\nu_{max}$ 1630, 1285, 1140, 1080, 660 $cm^{-1}$. $\delta_H$(300 MHz; $CDCl_3$) 2.13, pentet, *J* 7.4 Hz, 2H, H4; 2.45, s, 3H, $ArCH_3$; 3.15, dt, *J* 8.0, 1.8 Hz, 2H, H3; 4.26, t, *J* 6.9 Hz, 2H, H5; 5.79, t(br), *J* 1.8 Hz, 1H, $CHSO_2$; 7.33, d, *J* 8.2 Hz, 2H, ArH; 7.79, d, *J* 8.2 Hz, 2H, ArH. $\delta_C$(75.5 MHz; $CDCl_3$) 21.4 ($ArCH_3$), 23.7 (C4), 29.2 (C3), 72.3 (C5), 100.1 ($CHSO_2$), 126.3 (Ar C3 and C5), 129.5 (Ar C2 and C6), 141.0 (Ar C4), 143.1 (Ar C1), 173.4 (C2).

*m/z* 238 (M, 59%), 174 (M-$SO_2$, 24), 155 ($TolSO_2^+$•, 37), 131 (33), 91 (100).

**3,4-Dihydro-6-[(*para*-toluenesulfonyl)methyl)]-2*H*-pyran (8)**

A solution of 5-iodo-6-(*para*-toluenesulfonyl)-5-hexen-1-ol (**6**) (1.00 g, 2.64 mmol) in dry toluene (80 ml) and THF (20 ml) was placed under an argon atmosphere and potassium bis(trimethylsilyl)-amide (6.0 ml of a 0.5 M solution in toluene, 3.0 mmol) was added over 15 min. The solution was stirred at room temperature for 2 h; water (50 ml) was added, and the aqueous layer was separated and washed twice with ether (2 x 25 ml). The combined organic extracts were washed with water (2 x 50 ml) and dried ($MgSO_4$), and the crude product was purified by flash chromatography (20% ethyl acetate/light petroleum) giving *3,4-dihydro-6-[(*para*-toluenesulfonyl)methyl)]-2H-pyran* (**8**) as a colourless oil (0.47 g, 71%), that slowly crystallised, m.p. 56-58 °C (Found: C, 61.7; H, 6.4; $C_{13}H_{16}O_3S$ requires: C, 61.9; H, 6.4%). $\nu_{max}$ 1680, 1320, 1150, 1085,

1070 $cm^{-1}$. $\delta_H$(300 MHz, $CDCl_3$) 1.64-1.74, m, 2H, H3; 1.90-2.00, m, 2H, H4; 2.43, s, 3H, $ArCH_3$; 3.72, s, 2H, $CH_2SO_2$; 3.79, t, *J* 5.1 Hz, 2H, H2; 4.71, t, *J* 3.9 Hz, 1H, H5; 7.31, d, *J* 8.2 Hz, 2H, ArH; 7.76, d, *J* 8.2 Hz, 2H, ArH. $\delta_C$(75.5 MHz, $CDCl_3$) 20.3 (C3), 21.5 (C4), 21.6 ($ArCH_3$), 62.0 ($CH_2SO_2$), 66.4 (C2), 104.7 (C5), 128.5 (Ar C3 and C5), 129.3 (Ar C2 and C6), 136.0 (Ar C4), 143.4 (C6), 144.4 (Ar C1).
*m/z* 252 ($M^+$).

**3,4-Dihydro-6-[(benzenesulfonyl)methyl)]-2*H*-pyran (12)**

A solution of 5-iodo-6-(benzenesulfonyl)-5-hexen-1-ol (**10**) (2.00 g, 5.47 mmol) in dry toluene (160 ml) and THF (40 ml) was placed under an argon atmosphere and potassium bis(trimethylsilyl)amide (12.0 ml of a 0.5 M solution in toluene, 6.0 mmol) was added over 15 min. The solution was stirred at room temperature for 2 h; water (100 ml) was added, and the aqueous layer was separated and washed twice with ether (2 x 50 ml). The combined organic extracts were washed with water (2 x 100 ml) and dried ($MgSO_4$), and the crude product was purified by flash chromatography (20% ethyl acetate/light petroleum) giving 3,4-dihydro-6-(benzenesulfonyl)-methyl-2*H*-pyran (**12**)[13] as a colourless microcrystalline solid (1.00 g, 74%), m.p. 60-61 °C (lit.[13] oil) (Found: C, 60.3; H, 6.1; $C_{12}H_{14}O_3S$ requires: C, 60.5; H, 5.9%).
$\delta_H$(300 MHz) 1.64-1.73, m, 2H, H3; 1.94-1.99, m, 2H, H4; 3.77, t br, $J_{av}$ 6.4 Hz, 4H, $CH_2SO_2$ and H2; 4.73, t, *J* 3.6 Hz, 1H, H5; 7.53, t, *J* 7.4 Hz, 2H, Ph; 7.63, t, *J* 7.2 Hz, 1H, Ph; 7.90, d, *J* 7.2 Hz, 2H, Ph [lit.[13] $\delta_H$ 1.8, 4H, alicyclic; 3.75, 4H, $CH_2O$ and $CH_2SO_2$; 4.7, 1H, vinylic; 7.5-8.1, 5H, aromatic]. $\delta_C$(75.5 MHz) 20.3 (C3), 21.5 (C4), 62.0 ($CH_2SO_2$), 66.4 (C2), 104.9 (C5), 128.5 (Ph), 128.8 (Ph), 138.8 (Ph), 143.3 (C6).

**(2R*,3R*)-3-Hydroxy-2-[(*para*-toluenesulfonyl)methyl]-tetrahydropyran (13)**

A solution of borane•dimethyl sulfide complex (0.75 ml, 2.0 M solution in THF, 1.5 mmol) was added over a period of 30 min to a solution of the dihydropyran (**8**) (0.25 g, 1.0 mmol) in dry tetrahydrofuran (13 ml) under an argon atmosphere. The resulting solution was stirred for 18 h then cooled to 0 °C. Aqueous sodium hydroxide (1.5 ml of a 3.0 M solution, 4.5 mmol) and hydrogen peroxide (0.45 ml of a 30% w/v solution, 4.0 mmol) were added dropwise, then the reaction was allowed to warm to room temperature. After 1 h, diethyl ether was added and the mixture was washed with water (40 ml). The organic layer was dried ($MgSO_4$), and the solvent was removed under reduced pressure. Purification by flash chromatography (50% ethyl acetate : light petroleum) gave the *title compound* (**13**) as a colourless oil (0.16 g, 59%) that slowly crystallised, m.p. 87-89 °C (Found: C, 57.6; H, 6.95. $C_{13}H_{18}O_4S$ requires C, 57.8%; H, 6.7%.)
$\nu_{max}$ (neat) 3460br, 2920, 2860, 1280, 1135, 1115, 1080, 1030, 805, 760, 720, 700, 650 $cm^{-1}$.
$\delta_H$(500 MHz, $CDCl_3$) 1.41, ddt (br), *J* 12.4, 10.7, 6.7 Hz, 1H, $H4_{ax}$; 1.61-1.67, m, 3H, H5 and OH; 2.14, ddq (br), *J* 14.5, 4.0, 1.5 Hz, 1H, $H4_{eq}$; 2.44, s, 3H, $ArCH_3$; 3.24-3.29, m, 1H, $H6_{ax}$; 3.29, dd, *J* 14.5, 8.3 Hz, 1H, $CH_aSO_2$; 3.34, ddd, *J* 9.3, 4.6, 4.5 Hz, 1H, H3; 3.57, dt, *J* 8.7, 2.6 Hz, 1H, H2; 3.66, dd, *J* 14.5, 2.6 Hz, 1H, $CH_bSO_2$; 3.76, doublet of pentets (br), *J* 11.8, 2.0 Hz, 1H, $H6_{eq}$; 7.33, d, *J* 8.1 Hz, 2H, ArH; 7.80, d, *J* 7.9 Hz, 2H, ArH. $\delta_C$(75.5 MHz, $CDCl_3$) 21.6 ($ArCH_3$), 25.1 (C5), 32.9 (C4), 59.0 ($CH_2SO_2$), 67.6 (C6), 69.0 (C2), 77.3 (C3), 128.1 (Ar C3 and C5), 129.6 (Ar C2 and C6), 137.3 (Ar C4), 144.5 (Ar C1).
*m/z* 271 (M+1, 10%), 253 (M-OH, 6), 155 ($TolSO_2^+$•, 18), 139 (19), 115 (75), 92 (43), 91 (100).

**4-Pentyn-1-yl *para*-toluenesulfonate (14)**

A solution of *para*-toluenesulfonyl chloride (3.40 g, 17.9 mmol) in dry pyridine (6 ml) was added dropwise to 4-pentyn-1-ol (**2**) (1.00 g, 11.9 mmol) while the temperature was kept below 0 °C (ice/salt bath). When addition was complete the flask was stored at -20 °C for 17 h. The reaction mixture was poured into cold water and extracted with ether. The organic extract was washed with cold hydrochloric acid (1M), saturated $NaHCO_3$, and water, and dried ($MgSO_4$). Flash chromatography (10% ethyl acetate : light petroleum) gave the title compound (**14**)[18] as a colourless oil (2.69 g, 95%).

$\nu_{max}$ 3300, 1360, 1190, 1175, 660 $cm^{-1}$. $\delta_H$(300 MHz, $CDCl_3$) 1.80-1.89, m, 3H, H2 and H5; 2.25, dt, *J* 6.9, 2.7 Hz, 2H, H3; 2.44, s, 3H, $ArCH_3$; 4.13, t, *J* 6.2 Hz, 2H, H1; 7.34, d, *J* 8.2 Hz, 2H, ArH; 7.79, d, *J* 8.2 Hz, 2H, ArH. $\delta_C$(75.5 MHz, $CDCl_3$) 14.6 (C3), 21.6 ($ArCH_3$), 27.6 (C2), 68.7 (C1), 69.4 (C5), 82.1 (C4), 127.9 (Ar C3 and C5), 129.8 (Ar C2 and C6), 132.8 (Ar C4), 144.8 (Ar C1).

*m/z* 237 (M-1, <1%), 174 (M-$SO_2$, 28), 155 ($TolSO_2^+$•, 62), 92 (43), 91 (100).

**4-Pentyn-1-yl *para*-toluenethiosulfonate (15)**

Potassium *para*-toluenethiosulfonate (0.62 g, 2.7 mmol) was added to a solution of 4-pentyn-1-yl *para*-toluenesulfonate (**14**) (0.50 g, 2.1 mmol) in acetone (10 ml), and the solution was heated under reflux for 24 h. The solvent was removed under reduced pressure and the residue was dissolved in ether, washed with water and dried ($MgSO_4$). Evaporation of the solvent and purification of the crude product by flash chromatography (10% ethyl acetate : light petroleum) gave starting material (0.01 g, 2%), followed by *4-pentyn-1-yl* para-*toluenethiosulfonate* (**15**) as a colourless oil (0.28 g, 52%), (Found: C, 56.4%; H, 5.8%; $C_{12}H_{14}O_2S_2$ requires C, 56.7%; H, 5.6%). $\nu_{max}$ 3300, 2120, 1320, 1140, 650 $cm^{-1}$. $\delta_H$(300 MHz, $CDCl_3$) 1.85, pentet, *J* 7.0 Hz, 2H, H2; 1.95, t, *J* 2.7 Hz, 1H, H5; 2.25, dt, *J* 6.7, 2.6 Hz, 2H, H3; 2.45, s, 3H, $ArCH_3$; 3.10, t, *J* 7.2 Hz, 2H, H1; 7.34, d, *J* 8.2 Hz, 2H, ArH; 7.82, d, *J* 8.2 Hz, 2H, ArH. $\delta_C$(75.5 MHz, $CDCl_3$) 17.2 (C3), 21.6 ($ArCH_3$), 27.5 (C2), 34.6 (C1), 69.7 (C5), 82.2 (C4), 127.0 (Ar C3 and C5), 129.9 (Ar C2 and C6), 141.9 (Ar C4), 144.8 (Ar C1). *m/z* 254 (M, <1%), 190 (M-$SO_2$, 32), 162 (25), 155 ($TolSO_2^+$•, 29), 99 (39), 91 (100).

**Attempted preparation of tetrahydro-2-[(*para*-toluenesulfonyl)methylene]thiophen (16)**

A solution of 4-pentyn-1-yl *para*-toluenethiosulfonate (**15**) (100 mg, 0.39 mmol) in dry benzene (10 ml) was placed under an argon atmosphere and heated to boiling. A solution of benzoyl peroxide (10 mg) in dry benzene was added at a rate of 1.0 ml $h^{-1}$ (syringe pump), and heating was continued for a further 15.5 h after addition was complete. The reaction mixture was washed with aqueous sodium bisulfite (5%), dried ($MgSO_4$), and the solvent removed under reduced pressure. The crude product was identified ($^1H$ n.m.r.) as recovered starting material contaminated with minor byproduct(s), as shown by the presence of absorptions (triplets) at 5.45, 6.24 and 6.26 p.p.m. (integration <5%).

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