# Approaches to 2,6-Diaryl-3,7-Dioxabicyclo[3.3.0]Octane Lignans *via* Asymmetric Synthesis of Dihydro- and Tetrahydro-furan Derivatives

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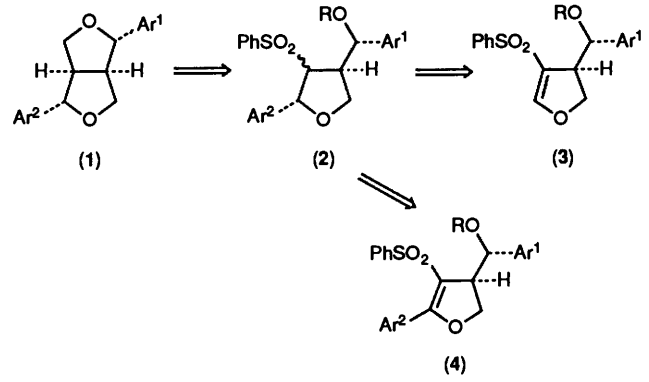
Cyclisation of chiral non-racemic phenylsulphonylvinyl epoxy ethers, produced using the Sharpless epoxidation reaction, has been used to prepare a series of enantiomerically enriched 2-aryl-4-(α-hydroxybenzyl)-4,5-dihydrofuran derivatives. Reduction of these compounds using triethylsilane and $BF_3$–diethyl ether gave the corresponding tetrahydrofuran derivatives stereoselectively. Attempts to convert either the dihydro- or tetrahydro-furan derivatives into lignans belonging to the 2,6-diaryl-3,7-dioxabicyclo[3.3.0]octane series have so far proved unsuccessful.

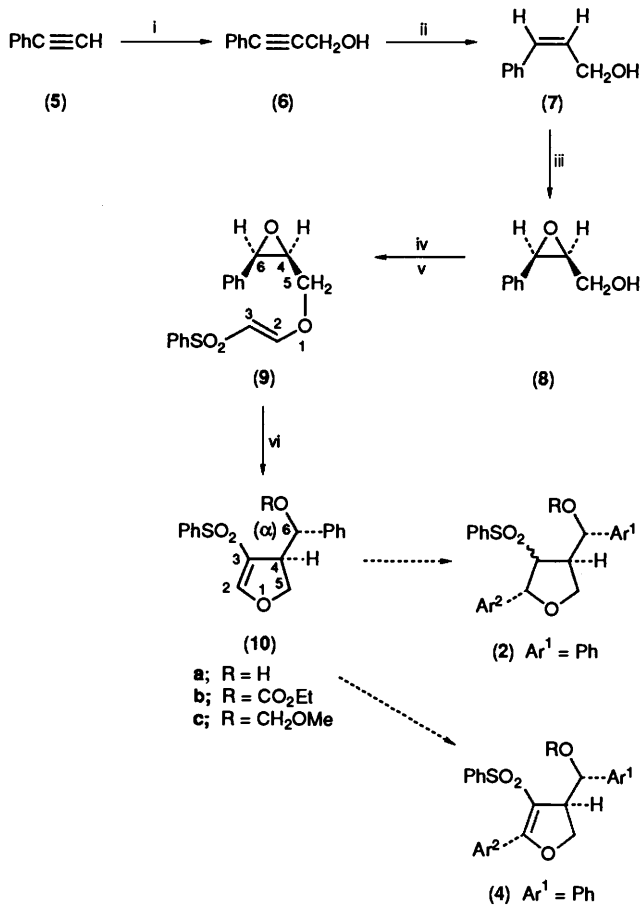
While several routes for the synthesis of racemic lignans of the 2,6-diaryl-3,7-dioxabicyclo[3.3.0]octane type have been reported[1–8] only one lengthy asymmetric synthesis of these compounds has been reported.[9] As a first step towards devising an asymmetric synthesis of such compounds we have investigated the synthesis of a series of enantiomerically enriched dihydro- and tetrahydro-furan derivatives which were seen as possible precursors for the eventual asymmetric synthesis of the natural products (Scheme 1). The original route envisaged for




**Scheme 1.**

the synthesis of the tetrahydrofurans (**2**) is shown in Scheme 2. This strategy employs the Sharpless epoxidation reaction[10–12] to introduce two of the required chiral centres into the target molecule. Coupling of the epoxy alcohol (**8**) with (*E*)-1-chloro-2-phenylsulphonylethene or (*E*)-1,2-bisphenylsulphonylethene followed by cyclisation would yield the dihydrofuran (**10a**).[13] Conjugate addition of an arylcopper reagent to a suitable derivative of (**10a**) would afford the required tetrahydrofuran (**2**). Alternatively, oxidative coupling of (**10a**) to an aryl halide would afford the 2-aryl-4,5-dihydrofuran (**4**) which could also serve as a precursor of (**2**). It was expected that the epoxide ring opening would be both regioselective and stereospecific leading to (**10a**)[13] and further that the conjugate addition or reduction step leading to (**2**) would be stereoselective, allowing the controlled production of four contiguous chiral centres in the tetrahydrofuran (**2**). Subsequent cyclisation of a suitable derivative of (**2**) or addition of a one-carbon unit followed by removal of the phenylsulphonyl group would afford access to compounds belonging to the 2,6-diaryl-3,7-dioxabicyclo[3.3.0]-octane series.

(*Z*)-3-Phenylprop-2-en-1-ol (**7**) was prepared from phenylacetylene as indicated in Scheme 2.[14] Sharpless epoxidation of



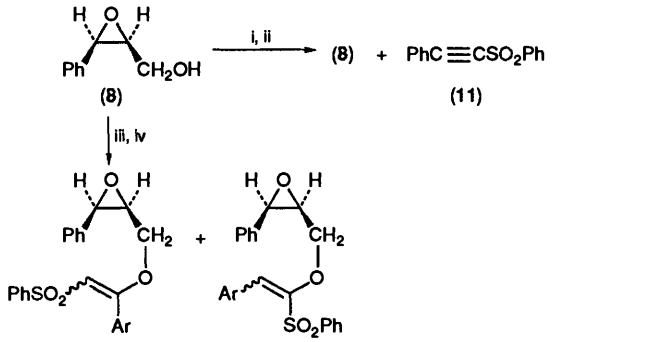

**Scheme 2.** *Note:* Dihydrofuran numbering used in NMR tables. The α position is equivalent to the 6-position. *Reagents and conditions:* i, EtMgBr, $CH_2O$; ii, $H_2$; iii, Sharpless oxidation, L-(+)-DET; iv, NaH; v, $PhSO_2CH{=}CHX$ (X = Cl or $SO_2Ph$); vi, LDA.

(**7**)[15–17] using (+)-diethyl (L)-tartrate (DET) gave the epoxy alcohol (**8**). However, removal of the diethyl tartrate from the product posed a major problem. This was eventually overcome by using flash chromatography on base-treated silica which gave a 70% yield of the epoxy alcohol (**8**) having $[\alpha]_D^{20}$ −44° (*c* 0.30 in $CHCl_3$). This purification procedure may be generally applicable in instances where separation of the diethyl tartrate from the epoxy alcohol proves difficult. The enantiomeric purity of the epoxy alcohol was determined by reaction with (*S*)-(−)-

methoxy(trifluoromethyl)phenylacetyl chloride[17,18] followed by analysis of the $^1H$ NMR spectrum of the Mosher ester in the presence of a europium shift reagent. This analysis indicated an enantiomeric excess of 78% for (**8**). Reaction of (**8**) with (*E*)-1-chloro-2-phenylsulphonylethene[13] gave the phenylsulphonyl vinyl ether (**9**) as a crystalline product in 72% yield. Subsequent treatment with lithium di-isopropylamide (LDA) gave the dihydrofuran (**10a**) in 68% yield.[13] The enantiomeric purity of this product was determined by again preparing the Mosher ester of (**10a**) followed in this case by examination of the $^{19}F$ NMR spectrum. This indicated an e.e. of *ca.* 88% for (**10a**).

Compound (**10a**) was converted into the carbonate (**10b**) and the methoxymethyl ether (**10c**) by reaction with butyl-lithium followed by ethyl chloroformate and chloromethyl methyl ether respectively. The $^1H$ and $^{13}C$ NMR spectra of these compounds are listed in Tables 1 and 2. However, despite attempts using a wide variety of organocopper reagents (*e.g.* $ArCu{\cdot}BF_3$, $Ar_2CuLi$, $Ar_3CuLi_2$)[19,20] in no case could the conjugate addition leading to (**2**) be achieved. As an alternative approach the addition of an aryl radical to the αβ-unsaturated sulphone was considered. However, reaction of (**10b**) with triphenylborane also proved unsuccessful.

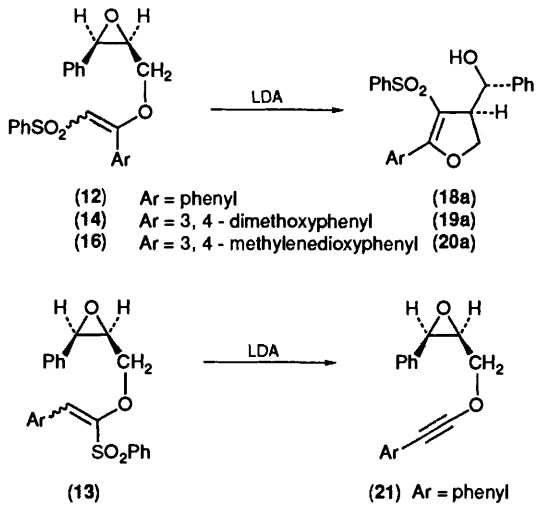
Furthermore, although the vinyl-lithium derivative of (**10a**) could be prepared (as shown by quenching with $D_2O$) reaction with zinc chloride to give the corresponding organozinc compound followed by reaction with 4-bromoanisole in the presence of either bistriphenylphosphinenickel(II) chloride or tetrakis(triphenylphosphine)palladium as catalyst[21] gave only starting materials with no sign of the cross-coupling product (**4**) even after prolonged reflux. It was, therefore, decided to introduce the second aryl group ($Ar^2$) at an earlier stage in the synthesis in order to avoid the need for the conjugate addition or cross-coupling step. Attempts to bring about reaction of the epoxy-alcohol (**8**) with (*E*)-1-(4-methoxyphenyl)-2-phenylsulphonylethene[22–24] and 2-phenylsulphonyl-1-chlorostyrene[25] were unsuccessful. Similarly, reaction of the epoxy alcohol with 2-phenylsulphonyl-1-bromostyrene[25] gave only 2-phenylsulphonyl-1-phenylethyne (**11**) (Scheme 3). However, reaction




**Scheme 3.** *Reagents and conditions:* i, NaH; ii, $PhSO_2CH{=}CH(Br)Ph$; iii, NaH; iv, (**11**).

of (**8**) with 2-phenylsulphonyl-1-phenylethyne (**11**) gave two products in approximately equal proportions. One of these was the required vinyl ether (**12**) whilst the other was identified as the regioisomer (**13**). The $^1H$ and $^{13}C$ NMR spectra of (**12**) and (**13**) are listed in Tables 3 and 4.

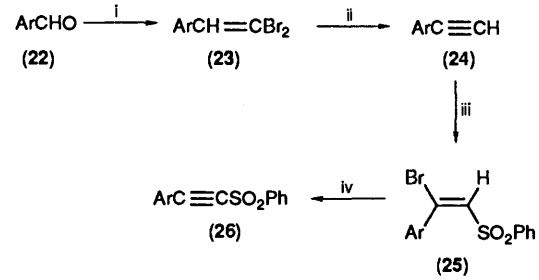
Not surprisingly, the two isomers behaved very differently in their reaction with LDA. Treatment of (**12**) with LDA afforded the required dihydrofuran (**18a**) as a crystalline product in 85% yield. However, reaction of (**13**) with LDA resulted in




**Scheme 4.**

elimination of the phenylsulphonyl group to give the acetylene (**21**) as the major product (Scheme 4).

In view of the low yield of (**12**) obtained in the above reaction, due to the formation of (**13**), it was decided to change the aryl group (Ar) in such a way as to discourage the formation of (**13**) by introducing electron donating substituents into Ar. Such substituents are invariably present in the natural lignans. The required arylacetylenes (**24**) were prepared in high yields by the route outlined in Scheme 5.[26] These were then converted into the corresponding 1-phenylsulphonyl-2-arylalkynes (**26**) using a modification of the route used to prepare 2-phenylsulphonyl-1-phenylethyne (**11**).[25]




**Scheme 5.** *Reagents and conditions:* i, $Ph_3P$, $CBr_4$; ii, BuLi, iii, $PhSO_2Br$; iv, $Et_3N$.

Reaction of (**26**) (Ar = 3,4-dimethoxyphenyl and Ar = 3,4-methylenedioxyphenyl) with the sodium salt of the epoxy alcohol (**8**) gave the adducts (**14**) and (**16**) as the major products respectively with minor amounts of the corresponding regioisomers (**15**) and (**17**) (see Scheme 3). Examination of the major products (**14**) and (**16**) by HPLC and NMR indicated that, in each case, two geometrical isomers were present in a 4:1 ratio. The $^1H$ and $^{13}C$ NMR data for these compounds are listed in Tables 3 and 4. The two stereoisomers were not separated as they were to be used as the anions. Instead they were treated with LDA leading to the formation of the dihydrofurans (**19a**) and (**20a**) in 92 and 84% yield respectively (see Scheme 4). The optical purities of (**18a**) and (**19a**) were determined by converting them into their Mosher esters followed by examination of their $^{19}F$ NMR spectra which indicated an approx. 88% e.e. and 90% e.e. for (**18a**) and (**19a**) respectively.

A number of derivatives of the dihydrofurans (**18a**) and (**19a**) have been prepared with a view to attempting to bring about cyclisation to the 2,6-diaryl-3,7-dioxabicyclo[3.3.0]octane

**Table 1.** $^1$H NMR spectra of dihydrofurans.[a]

| | (10a) | (10b) | (10c) | (18a) | (18b) | (18c) |
|---|---|---|---|---|---|---|
| 2-H | 7.2–7.6 | 7.08s | 6.98s | — | — | — |
| 4-H | 3.32m | 3.53m | 3.40m | 3.60m | 3.74m | 3.67m |
| 5-H | 4.0–4.4m | 4.61dd (4, 10) | 4.68dd (4, 10) | 4.66dd (3, 10) | 4.73dd (3, 10) | 4.75dd (3, 10) |
| | | 4.27t (10) | 4.23t (10) | 4.30t (10) | 4.23t (10) | 4.25t (10) |
| 6-H (α) | 4.87d (8) | 6.03d (5) | 5.12d (4) | 5.15d (5) | 6.22d (5) | 5.26d (4) |
| Arom | 7.27s | | | | | |
| | 7.55m | 7.2–7.6m | 7.1–7.6m | 7.1–7.8m | 7.1–7.8m | 7.0–7.8m |
| | 7.93m | 8.0m | 7.94m | | | |
| $CO_2Et$ | — | 1.26t (7) | — | — | 1.23t (7) | — |
| | — | 4.12q (7) | — | — | 4.14q (7) | — |
| $OCH_2X$ | — | — | 4.48s | — | — | 4.61s |
| $OCH_2XMe$ | — | — | 3.20s | — | — | 3.32s |
| OH | — | — | — | 3.4br | — | — |
| OMe | — | — | — | — | — | — |
| | **(19a)** | **(19b)** | **(19c)** | **(19d)**[b] | **(19e)** | **(19f)**[c] |
| 2-H | — | — | — | — | — | — |
| 4-H | 3.56m | 3.76m | 3.70m | 3.75m | 3.63m | 3.80m |
| 5-H | 4.49dd (3, 10) | 4.76dd (3, 10) | 4.75dd (2, 10) | 4.82dd (2, 10) | 4.70m | 4.70dd (2, 10) |
| | 4.16t (10) | 4.26t (10) | 4.26t (10) | 4.27t (10) | 4.23t (10) | 4.27t (10) |
| 6-H (α) | 5.17d (6) | 6.22d (5) | 5.26d (4) | 5.35d (4) | 5.32d (4) | 5.21d (5) |
| Arom | 6.8–7.7m | 6.8–7.7m | 6.7–7.7m | 6.7–7.7m | 6.7–7.7m | 6.7–7.7m |
| $CO_2Et$ | — | 1.30t (7) | — | — | — | — |
| | — | 4.21q (7) | — | — | — | — |
| $OCH_2X$ | — | — | 4.66s | — | 4.45d (11) | 4.47s |
| | | | | | 4.70d (11) | |
| $OCH_2XMe$ | — | — | 3.37s | — | 2.14s | 2.60s |
| OH | | — | — | — | — | — |
| OMe | 3.84s | 3.84s | 3.79s | 3.81s | 3.78s | 3.81s |
| | 3.85s | 3.86s | 3.80s | 3.82s | | 3.84s |
| | **(19g)** | **(19h)** | **(20a)**[d] | | | |
| 2-H | — | — | — | | | |
| 4-H | 3.55m | 3.75m | 3.50m | | | |
| 5-H | 4.71dd (3, 10) | 4.70dd (3, 10) | 4.48dd (3, 10) | | | |
| | 4.19t (10) | 4.26t (10) | 4.11t (10) | | | |
| 6-H (α) | 5.51d (4) | 5.40d (4) | 5.17d (6) | | | |
| Arom | 6.7–7.7m | 6.8–8.0m | 6.7–7.7m | | | |
| $CO_2Et$ | — | — | — | | | |
| | — | — | — | | | |
| $OCH_2X$ | 5.16d (12) | 4.70d (12) | — | | | |
| | 4.77d (12) | 4.59d (12) | — | | | |
| $OCH_2XMe$ | — | — | — | | | |
| OH | — | — | 3.8br | | | |
| OMe | 3.82s | 3.87s | — | | | |
| | 3.84s | 3.91s | — | | | |

[a] All spectra recorded in $CDCl_3$ except **(18a)** which was in [$^2H_6$]-DMSO. [b] Signals at 5.13s and 3.33s due to $CH(OMe)_2$ group. [c] Signals due to major diastereoisomer only recorded. [d] Signal at 5.90s due to $OCH_2O$ group.

skeleton (Scheme 6). Treatment of **(18a)** and **(19a)** with butyllithium followed by ethyl chloroformate or chloromethyl methyl ether gave the corresponding carbonates **(18b)** and **(19b)** and the methoxymethyl ethers **(18c)** and **(19c)** respectively. Similarly, treatment of **(19a)** with a large excess of trimethyl orthoformate in the presence of magnesium chloride[27] under reflux in dichloromethane gave a 91% yield of the orthoester **(19d)**. Attempted cyclisation of **(19d)** using $BF_3$–diethyl ether followed by treatment with L-Selectride or triethylsilane was unsuccessful. In both cases, a complex mixture of products was obtained which could not be satisfactorily separated and, therefore, could not be identified, but gave no indication of the required product.

Similarly, the methylthiomethyl ether **(19e)** was prepared in 93% yield by treating the alcohol **(19a)** with sodium hydride, sodium iodide, and chloromethyl methyl sulphide.[28] Attempts to cyclise **(19e)** using mercury salts or methylating agents followed by reaction with hydride gave only the starting material or the parent alcohol **(19a)**. The sulphoxide **(19f)** was also prepared with a view to carrying out a Pummerer reaction to give the bicyclic system.[29] The sulphoxide was obtained as a mixture of two diastereoisomers (ratio 5:2) in 78% yield by oxidation of the methylthiomethyl ether **(19e)** with *m*-chloroperbenzoic acid (MCPBA). Treatment of **(19f)** with trifluoroacetic anhydride followed by sodium borohydride gave the alcohol **(19a)** as the major product with no indication of the formation of a bicyclic product. The phenylthiomethyl ether **(19g)** was prepared from **(19a)** using the same method as that employed to make the methylthiomethyl ether **(19e)**. Oxidation with excess MCPBA gave the phenylsulphonylmethyl ether **(19h)**. Attempted cyclisation of **(19h)** by reaction with the sodium salt of thiophenol was unsuccessful. The $^1$H and $^{13}$C NMR spectra of these derivatives are included in Tables 1 and 2.

Attempts to remove the phenylsulphonyl group from **(19a)** using sodium dithionite[30] gave only the starting material. The use of aluminium or sodium amalgam[31–33] did lead to removal

**Table 2.** $^{13}C$ NMR spectra of dihydrofurans.[a]

| | (10a) | (10b) | (10c) | (18a) | (18b) | (18c) | (19a) | (19b) | (19c) | (19d)[b] | (19e) | (19f)[c] | (19g) | (19h) | (20a)[d] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| C-2 | 160.63 | 160.15 | 159.69 | 166.35 | 167.67 | 167.05 | 167.32 | 167.32 | 166.70 | 166.97 | 166.65 | 166.94 | 166.82 | 167.18 | 167.03 |
| C-3 | 119.55 | 117.94 | 118.06 | 111.69 | 110.98 | 111.76 | 111.24 | 110.01 | 110.39 | 109.87 | 110.25 | 110.07 | 109.84 | 109.57 | 111.33 |
| C-4 | 49.29 | 46.05 | 47.29 | 51.29 | 49.17 | 50.54 | 52.11 | 49.40 | 50.73 | 50.58 | 50.64 | 50.31 | 50.47 | 50.08 | 51.88 |
| C-5 | 76.54 | 74.95 | 75.02 | 70.96 | 70.78 | 71.07 | 71.37 | 70.31 | 70.57 | 70.47 | 70.61 | 70.27 | 70.49 | 70.01 | 71.37 |
| C-6 (α) | 75.62 | 77.55 | 76.15 | 70.90 | 77.66 | 76.73 | 74.75 | 77.64 | 76.90 | 75.26 | 77.35 | 83.42 | 77.54 | 82.44 | 74.46 |
| | — | 153.82 | — | — | 153.77 | — | — | 153.88 | — | — | — | — | — | — | — |
| $CO_2Et$ | — | 64.29 | — | — | 64.27 | — | — | 64.34 | — | — | — | — | — | — | — |
| | — | 14.18 | — | — | 14.22 | — | — | 14.23 | — | — | — | — | — | — | — |
| $OCH_2X$ | — | — | 94.78 | — | — | 94.78 | — | — | 94.80 | — | 73.22 | 86.10 | 73.83 | 83.86 | — |
| $OCH_2XMe$ | — | — | 55.49 | — | — | 55.62 | — | — | 55.64 | — | 10.43 | 35.46 | — | — | — |
| OMe | — | — | — | — | — | — | 55.87 | 55.88 | 55.79 | 55.81 | 55.79 | 55.77 | 55.82 | 55.89 | — |
| | | | | | | | 55.93 | 55.93 | 55.84 | 55.87 | | | 55.87 | | |

[a] All spectra run in $CDCl_3$ except (**18a**) which was run in [$^2H_6$]-DMSO. [b] Signals at 112.83, 52.14, and 50.34 due to $CH(OMe)_2$ group. [c] Signals due to major diastereoisomer only shown. [d] Signal at 101.54 due to $OCH_2O$ group.

**Table 3.** $^1H$ NMR spectra of epoxides.[a]

| | (9) | (12) | (13) | (14)[b] | (15) | (16)[b] |
|---|---|---|---|---|---|---|
| 2-H | 7.48m | — | — | — | — | — |
| 3-H | 5.58d (12) | 6.05s | 7.2–7.6 | 6.12s | 7.1–8.0 | 6.05s |
| 4-H | 3.40m | | 3.50m | 3.60m | 3.60m | 3.54dt (4, 6) |
| 5-H | 3.77dd (4, 11) | 3.4–3.7m | 4.11dd (4, 10) | 3.68dd (6, 11) | 4.30m | 3.68d (6) |
| | 3.55m | | 3.80dd (7, 10) | 3.75dd (5, 11) | 3.80m | |
| 6-H (α) | 4.11d (4) | 4.06d (4) | 4.06d (4) | 4.13d (4) | 4.14m | 4.13d (4) |
| Arom H | 7.24s | 6.9–7.6m | 7.16s | 6.7–7.6m | 7.21s | 6.6–7.6m |
| | 7.48m | | 7.2–7.6m | | 7.1–7.5m | |
| | 7.78m | 8.03m | 7.88m | 8.06m | 7.92m | 8.05m |
| OMe | — | — | — | 3.86s | 3.81s | — |
| | | | | 3.80s | 3.84s | |
| $OCH_2O$ | — | — | — | — | — | 5.95s |

**Table 4.** $^{13}C$ NMR spectra of epoxides.[a]

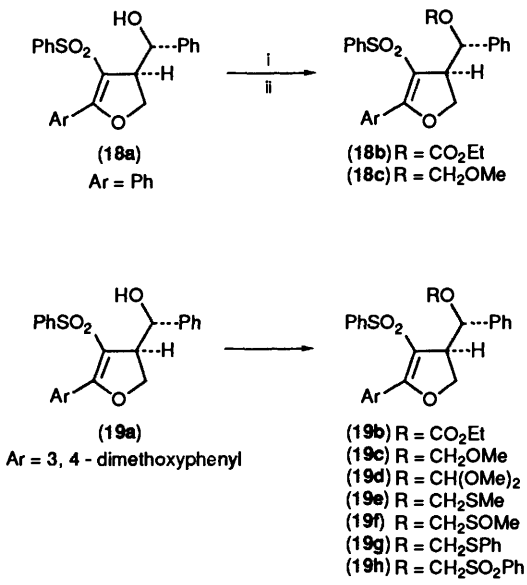
| | (9) | (12) | (13) | (14)[b] | (15) | (16)[b] |
|---|---|---|---|---|---|---|
| C-2 | 160.24 | 165.98 | 151.61 | 165.98 | 150.39 | 165.49 |
| C-3 | 107.68 | 114.28 | 123.28 | 113.01 | 123.61 | 113.21 |
| C-4 | 56.17 | 56.48 | 56.29 | 56.28 | 56.09 | 56.43 |
| C-5 | 69.75 | 69.50 | 72.14 | 69.86 | 72.41 | 69.48 |
| C-6 | 55.45 | 56.16 | 56.07 | 55.93 | 56.03 | 55.99 |
| OMe | — | — | — | 56.02 | 55.55 | — |
| $OCH_2O$ | — | — | — | — | — | 101.78 |

[a] All spectra run in $CDCl_3$ solution. [b] Signals for major diastereoisomer only given.

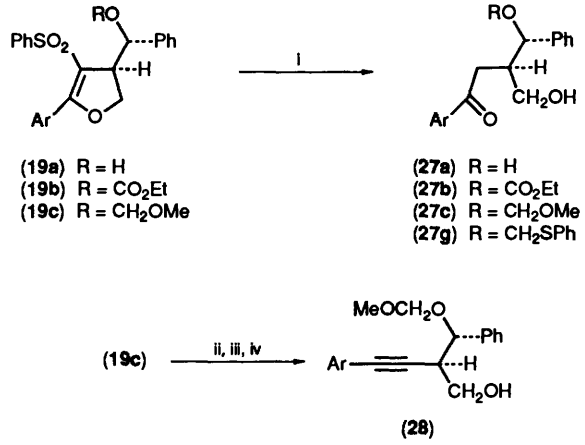
of the phenylsulphonyl group from (**19a**), (**19b**), and (**19c**) but also resulted in opening of the dihydrofuran ring to give the hydroxy ketones (**27a–c**) (Scheme 7). Removal of the phenylsulphonyl group could also be achieved by treating (**19c**) with tributyltin lithium[34] but the reaction again involved opening of the dihydrofuran ring leading to the acetylene (**28**). Finally, treatment of the phenylthiomethyl ether (**19g**) with lithium naphthalenide[35] gave the hydroxy ketone (**27g**; R = $CH_2SPh$). The $^1H$ and $^{13}C$ NMR spectra of (**27b**), (**27c**), and (**27g**) are listed in Tables 5 and 6.

We next investigated the reduction of the various dihydrofurans to the corresponding tetrahydrofurans with a view to achieving one of the main objectives outlined in Scheme 1. It was hoped that this could be carried out stereoselectively in order to generate four contiguous chiral centres in a controlled manner. Catalytic hydrogenation of (**18b**) and (**18c**) using a variety of catalysts and conditions gave only the starting materials even when high pressure was used. Reduction of (**18c**) with lithium aluminium hydride gave only the ring opened product (**29**) (Scheme 8). However, reduction of the double bond was readily achieved by treating (**18c**) with triethylsilane and $BF_3$–diethyl ether giving the alcohol (**30a**) in 83% yield. Similarly, the tetrahydrofurans (**30b**) and (**31a**) could be prepared in 75 and 85% yield respectively starting from (**18b**) and (**19a**). In each case only one stereoisomer of the product was selectively produced. The $^1H$ and $^{13}C$ NMR spectra of these compounds are listed in Tables 7 and 8.

NOE experiments on the methoxymethyl ether (**31c**) prepared from (**31a**) showed a significant interaction between the *ortho* protons of the phenylsulphonyl group and 2-H suggesting that the phenylsulphonyl group is *cis*- to 2-H. There was, however, no NOE effect between the phenylsulphonyl group and 4-H. In order to establish beyond doubt the configuration of the newly created chiral centres, compound (**31c**) was subjected to X-ray analysis. The resulting structure (Figure) reveals that the aryl group at C-2 is indeed *trans* to the




**Scheme 6.** *Reagents and conditions:* i, BuLi; ii, RCl.




**Scheme 7.** *Reagents and conditions:* i, AlHg or Na(Hg), 2% aqueous THF; ii, $Bu_3SnLi$; iii, $H^+$ or $CH_2O$; iii, $SiO_2$.

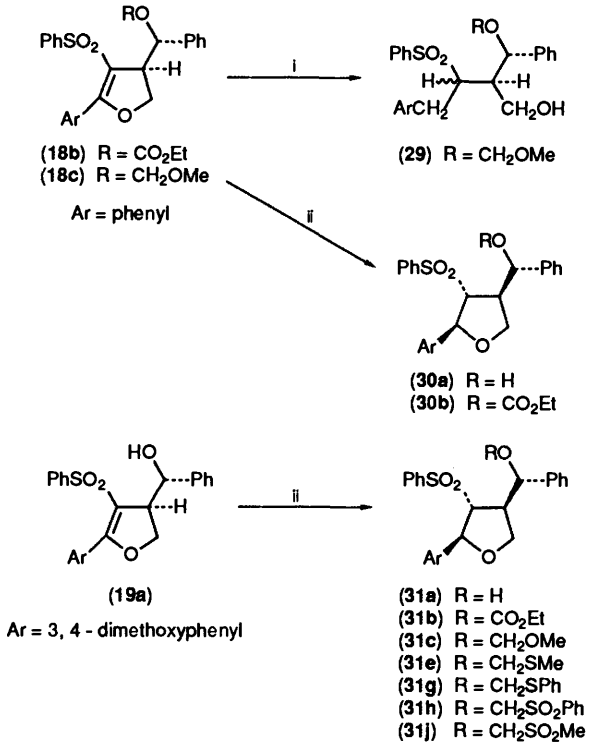
**Table 5.** $^1H$ NMR spectra of hydroxy ketones.[a]

| | (27b) | (27c) | (27g) |
|---|---|---|---|
| 3-H | 3.12m | 3.20dd (4, 17)<br>3.04dd (9, 17) | 3.19dd (4, 17)<br>3.00dd (9, 17) |
| 4-H | 2.82m | 2.66m | 2.62m |
| 5-H | 3.51dd (5, 11)<br>3.62dd (6, 11) | 3.55dd (5, 11)<br>3.68dd (6, 11) | 3.40dd (5, 11)<br>3.58dd (6, 11) |
| 6-H (α) | 5.92dd (7) | 4.93d (6) | 5.01d (7) |
| $CO_2Et$ | 4.15q (7)<br>1.24t (7) | —<br>— | —<br>— |
| $OCH_2X$ | — | 4.53d (6)<br>4.58d (6) | 4.61d (12)<br>5.20d (12) |
| $OCH_2OMe$ | — | 3.37s | — |
| OMe | 3.91s<br>3.94s | 3.90s<br>3.93s | 3.85s<br>3.91s |

[a] All spectra were run in $CDCl_3$.

phenylsulphonyl group at C-3 but that the phenylsulphonyl group is also *trans* to the hydroxybenzyl group at C-4.

Various derivatives of (**30a**) and (**31a**) were prepared in order to attempt to achieve cyclisation to the 2,6-diaryl-3,7-




**Scheme 8.** *Reagents and conditions:* i, $LiAlH_4$; $Et_3SiH$, $BF_3{\cdot}Et_2O$.

**Table 6.** $^{13}C$ NMR spectra of hydroxy ketones.[a]

| | (27b) | (27c) | (27g) |
|---|---|---|---|
| C-2 | 198.14 | 198.85 | 198.98 |
| C-3 | 35.26 | 35.53 | 35.85 |
| C-4 | 43.26 | 43.90 | 43.74 |
| C-5 | 64.31 | 63.28 | 63.15 |
| C-6 (α) | 79.39 | 78.69 | 79.28 |
| $CO_2Et$ | 154.82 | — | — |
| | 62.36 | — | — |
| | 14.18 | — | — |
| $OCH_2X$ | — | 94.89 | 73.11 |
| $OCH_2OMe$ | — | 55.95 | — |
| OMe | 56.10 | 56.04 | 56.01 |
| | 56.02 | | 56.12 |

[a] All spectra were run in $CDCl_3$.

dioxabicyclo[3.3.0]octane framework. Attempts to cyclise the carbonate (**30b**) using a number of bases (LDA, LHDS, NaH) gave only the corresponding alcohol (**30a**). The methylthiomethyl ether (**31e**) was prepared in 90% yield by treating the sodium salt of the alcohol (**31a**) with sodium iodide and chloromethyl methyl sulphide. Attempted cyclisation of (**31e**) using butyl-lithium as base was unsuccessful giving as the major product the ring opened compound (**32e**). Oxidation of (**31e**) with an excess of MCPBA gave the methylsulphonylmethyl ether (**31j**) in 78% yield. Attempts to cyclise this compound using LDA or NaH gave only the starting material. The phenylthiomethyl ether (**31g**) and the phenylsulphonylmethyl ether (**31h**) were also prepared but again failed to react with LDA. Treatment of (**31h**) with KHDS gave a complex mixture of six or seven products which could not be separated by chromatography and were, therefore, not identified.

Attempts were also made to attach a one-carbon unit at C-3 of the tetrahydrofuran ring. Thus, reaction of the alcohol (**31a**) with two equivalents of butyl-lithium followed by an excess of ethyl chloroformate gave only the carbonate (**31b**) in 80% yield.

**Table 7.** $^1$H NMR spectra of tetrahydrofurans.

| | (30a) | (30b) | (31a) | (31b) | (31c) | (31e) | (31j) | (31g) | (31h) |
|---|---|---|---|---|---|---|---|---|---|
| 2-H | 5.23d (6) | 5.35d (6) | 5.17d (6) | 5.29d (7) | 5.33d (6) | 5.33d (6) | 5.05d (7) | 5.28d (6) | 5.40d (7) |
| 3-H | 4.01dd (2, 6) | 3.76dd (2, 6) | 4.01dd (3, 6) | 3.76dd (3, 7) | 3.92dd (2, 6) | 3.90m | 4.45dd (3, 7) | 3.75m | 3.87m |
| 4-H | 3.05m | 3.20m | 3.06m | 3.20m | 3.00m | 3.03m | 3.43m | 2.93m | 2.83m |
| 5-H | 3.80m | 3.94m | 3.82m | 3.89m | 3.80m | 3.90m | 3.80m | 3.75m | 3.82m |
| 6-H (α) | 4.45d (10) | 5.44dd (9) | 4.52d (9) | 5.55d (9) | 4.40d (10) | 4.61d (10) | 4.90d (10) | 4.65d (11) | 4.98d (11) |
| OH | 2.40m | — | 3.00m | — | — | — | — | — | — |
| $CO_2Et$ | — | 3.96q (7) | — | 4.00q (7) | — | — | — | — | — |
| | — | 1.15t (7) | — | 1.18t (7) | — | — | — | — | — |
| $OCH_2X$ | — | — | — | — | 4.07d (7) | 3.98d (12) | 4.08d (13) | 4.22d (12) | 3.68d (10) |
| | — | — | — | — | 4.20d (7) | 4.32d (12) | 4.45d (13) | 4.82d (12) | 3.83d (10) |
| $OCH_2XMe$ | — | — | — | — | 3.00s | 1.83s | 3.02s | — | — |
| OMe | — | — | 3.73s | 3.87s | 3.83s | 3.86s | 3.91s | 3.85s | 3.99s |
| | — | — | 3.78s | 3.84s | | 3.88s | 3.92s | 3.86s | 3.90s |
| Arom H | 7.0–7.9m | 7.0–7.9m | 7.2–7.8m | 6.7–7.8m | 6.7–7.9m | 6.75–7.9m | 7.4–7.9m | 6.7–7.6m | 6.9—7.7m |
| | | | 6.69s | | | | 6.75m | | |

**Table 8.** $^{13}$C NMR spectra of tetrahydrofurans.

| | (30a) | (30b) | (31a) | (31b) | (31c) | (31e) | (31j) | (31g) | (31h) |
|---|---|---|---|---|---|---|---|---|---|
| C-2 | 72.50 | 72.47 | 72.25 | 72.26 | 72.84 | 73.02 | 71.91 | 72.34 | 71.90 |
| C-3 | 81.31 | 81.18 | 81.17 | 81.33 | 80.52 | 80.81 | 82.81 | 80.37 | 82.48 |
| C-4 | 50.00 | 48.57 | 49.82 | 48.46 | 49.64 | 49.64 | 48.58 | 49.44 | 49.81 |
| C-5 | 70.49 | 69.85 | 70.40 | 69.79 | 69.96 | 70.16 | 69.85 | 69.86 | 69.58 |
| C-6 (α) | 74.87 | 79.39 | 74.84 | 79.40 | 77.66 | 77.45 | 85.34 | 77.72 | 80.47 |
| | — | 154.12 | — | 154.27 | — | — | — | — | — |
| $CO_2Et$ | — | 64.12 | — | 64.18 | — | — | — | — | — |
| | — | 14.07 | — | 14.09 | — | — | — | — | — |
| $OCH_2X$ | — | — | — | — | 93.72 | 72.60 | 81.60 | 72.39 | 81.52 |
| $OCH_2XMe$ | — | — | — | — | 55.81 | 14.29 | 38.46 | — | — |
| OMe | — | — | 55.89 | 55.93 | 55.87 | 56.05 | 55.90 | 55.87 | 55.99 |
| | | | | | 55.93 | | | 55.99 | 56.08 |

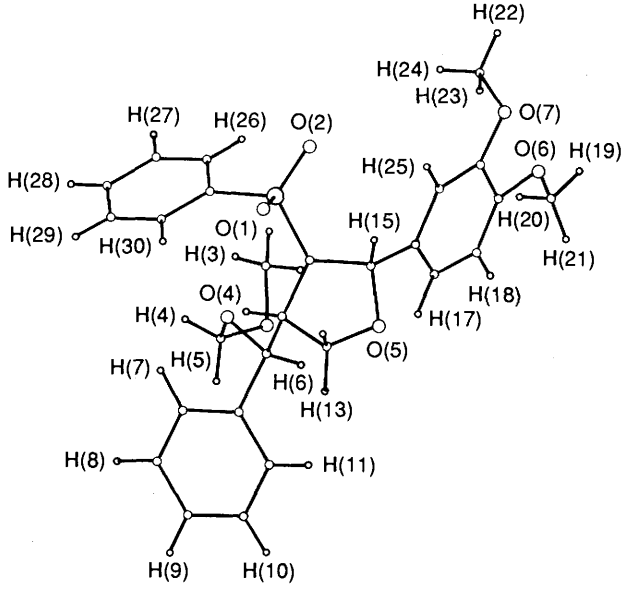
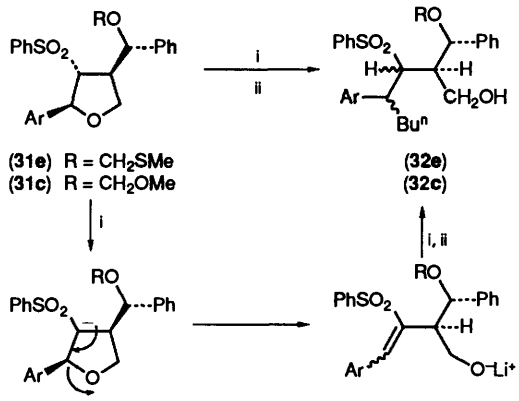



**Figure.**

Reaction of the methoxymethyl ether (**31c**) with LDA followed by quenching with $D_2O$ showed significant deuterium incorporation at C-3. A number of other bases (KH, NaH, Bu$^t$Li) gave no detectable anion formation (as demonstrated by lack of deuterium incorporation with $D_2O$) while with butyl-lithium a product (**32c**) resulting from ring opening of the heterocyclic ring was formed (Scheme 9 ). Treatment of (**31c**) with LDA followed by various electrophiles gave no products resulting from

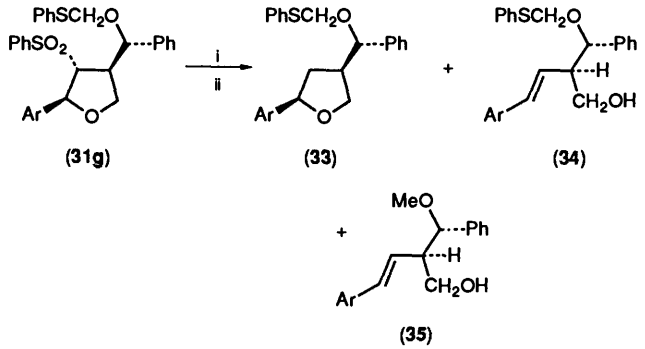



**Scheme 9.** *Reagents and conditions:* i, BuLi, ii, $H_2O$.

electrophilic attack at C-3. Finally, reaction of (**31g**) with lithium naphthalenide gave a mixture of three products all of which had lost the phenylsulphonyl group but two of which had involved opening of the tetrahydrofuran ring (Scheme 10).

## Experimental

IR spectra were recorded on a Pye Unicam SP1050 spectrometer. UV spectra were recorded on a Philips PU8720 scanning spectrophotometer. $^1$H NMR spectra were recorded on a Hitachi Perkin-Elmer R24B spectrometer at 60 MHz, a Varian HA-100 or a Varian XL-100 instrument at 100 MHz and a Bruker 250 WM spectrometer at 250 MHz. $^{13}$C NMR spectra were obtained from a Varian XL-100 instrument at 25 MHz and a Bruker 250 WM spectrometer at 62.5 MHz. All spectra used




**Scheme 10.** *Reagents and conditions:* i, lithium naphthalenide; ii, $H_2O$ or PhCHO.

tetramethylsilane as the internal standard and all samples were run in deuteriated chloroform unless otherwise stated. Mass spectra were recorded on a VG-12-250 low resolution quadruple mass spectrometer. Accurate mass measurements were obtained from a ZAB-E, high-resolution double focussing mass spectrometer. M.p.s were recorded on a Gallenkamp hot-stage instrument and are uncorrected. Optical rotation measurements were obtained from a Perkin-Elmer 141 polarimeter using a sodium lamp at 589 nm. All analytical HPLC work was carried out on an LDC gradient elution instrument, linked to an LDC CI-10 integrator, using an ODS-Hypersil 5μm packed column. Thin layer chromatography was carried out on Merck 5735 Kieselgel 60 $F_{254}$ fluorescent plates. Column chromatography was performed with silica gel (Merck 9385, Kieselgel 60, 230–400 Mesh). Base-treated silica was prepared by washing successively with 0.1M NaOH, water, and methanol, followed by drying at 120 °C and deactivation by addition of 5% water. Small-scale purifications were carried out on a chromatotron 7924 using 1, 2, or 4 mm plates prepared from silica gel (Merck 7749, Kieselgel 60 $PF_{254}$).

Reactions carried out under a nitrogen atmosphere refer to 'white spot' nitrogen used directly from the cylinder. Diethyl ether, glyme, and dichloromethane were dried by passage down an alumina column and then by distillation from calcium hydride. Tetrahydrofuran was dried by passage down an alumina column and then distillation from sodium wire and benzophenone. Dry toluene and benzene were prepared by distillation from calcium hydride and then storage over sodium wire. Dimethylformamide was distilled from calcium hydride. Solutions of butyl-lithium in hexane were obtained from Aldrich and were estimated before use. Anhydrous t-butyl hydroperoxide was prepared as a solution in toluene as described by Sharpless[12,15] and estimated using potassium iodide and sodium thiosulphate titration. Low-temperature baths were prepared by making a slurry of solid carbon dioxide with acetone (−78 °C) or with carbon tetrachloride (−23 °C).

*Preparation of* 3-*Phenylprop*-2-*yn*-1-*ol* (**6**).—Phenylacetylene (10.93 ml, 0.1 mol) was added, from a pressure equalizing dropping funnel, to a stirred solution of ethylmagnesium bromide (0.1 mol) in diethyl ether (75 ml) over a period of 1.5 h, under a static pressure of nitrogen. The mixture was heated under reflux for an additional hour. The reaction was then cooled to 0 °C and formaldehyde gas, generated from paraformaldehyde (5 g) by heating with a bunsen burner, was passed directly into the reaction mixture, *via* a wide glass inlet tube, with vigorous stirring. When addition of formaldehyde was complete, the contents of the reaction mixture were poured onto crushed ice (30 g) and sufficient sulphuric acid was added to decompose the magnesium hydroxide. The layers were separated and the aqueous layer was saturated with potassium carbonate. The aqueous solution was extracted with ether (3 × 40 ml), and the organic extracts were combined, dried ($MgSO_4$), filtered, and evaporated to give a yellow liquid. Distillation yielded the alkyne (**6**) (8.9 g, 68%) as a colourless liquid, b.p. 95 °C/0.2 mmHg (lit.,[14] 114–115 °C/3 mmHg); $\nu_{max}$(neat) 3 350 (OH) and 2 250 $cm^{-1}$ (C≡C); $\delta_H$(100 MHz) 4.08 (1 H, br s, $D_2O$ exchange, OH), 4.43 (2 H, s, 1-H), 7.1–7.5 (5 H, nı, aromatic H); *m/z* 132 ($M^+$, 55%) and 131 (100).

*Preparation of* (Z)-3-*Phenylprop*-2-*en*-1-*ol* (**7**).—3-Phenylprop-2-yn-1-ol (**6**) (5 g, 0.038 mol) was dissolved in dry methanol (70 ml) to which Lindlar catalyst (0.85 g) was added. The resultant mixture was then stirred vigorously under hydrogen using an atmospheric pressure hydrogenator, on which 860 ml (0.038 mol) of hydrogen were absorbed over a period of *ca.* 2 h. The catalyst was filtered off and the methanol evaporated. The resultant yellow liquid was distilled to give (**7**) (4.97 g, 98%) as a colourless liquid, b.p. 62 °C/0.07 mmHg (lit.,[14] 115 °C/5 mmHg); $\nu_{max}$(neat), 3 350 $cm^{-1}$ (OH): $\delta_H$(100 MHz), 2.94 (1 H, br s, $D_2O$ exchange, OH), 4.33 (2 H, d, *J* 6 Hz, 1-H), 5.78 (1 H, m 2-H), 6.46 (1 H, d, *J* 12 Hz, 3-H), 7.0–7.4 (5 H, m, aromatic H); *m/z* 134 ($M^+$, 63%).

*Preparation of* (2S,3R)-3-*Phenyl*-2,3-*epoxypropan*-1-*ol* (**8**).—A 500 ml round-bottomed flask was charged with dry $CH_2Cl_2$ (200 ml) and cooled to −23 °C under argon. To this was added titanium tetraisopropoxide (5.94 ml, 0.02 mol), followed by a solution of L-(+)-diethyl tartrate (4.12 g, 0.02 mol) in $CH_2Cl_2$ (5 ml). The resultant mixture was stirred for 5 min before the addition of (*Z*)-3-phenylprop-2-en-1-ol (**7**) (2.68 g, 0.02 mol) followed by t-butyl hydroperoxide (2.5M; 0.04 mol, 16 ml) *via* syringe. The resultant solution was stored in a freezer at −23 °C for 20 h. After this time aqueous tartaric acid (10% solution; 50 ml) was added, stirring was continued at −23 °C for 30 min, and the reaction mixture was then allowed to warm to room temperature. After 2–3 h the layers were separated and the organic layer cooled in an ice bath. Sodium borohydride (1.0 g, 0.03 mol) was added to the stirred mixture and vigorous stirring was continued for 30 min; after this time aqueous sodium sulphite (0.50 M; 50 ml) was added. The layers were rapidly separated. The organic layer was dried ($MgSO_4$), filtered, and evaporated. Toluene (10 ml) was added to the remaining oil and the resultant solution evaporated; this process was repeated twice. Purification of the crude product by column chromatography on base-treated silica (10% EtOAc in $CH_2Cl_2$), yielded the pure *epoxy alcohol* (**8**) (2.1 g, 70%), as a colourless oil; $[\alpha]_D^{20}$ −44.24° (*c* 0.300 in $CHCl_3$); $\nu_{max}$(neat), 3 420 $cm^{-1}$ (OH); $\lambda_{max}$ ($CH_2Cl_2$) 227.6 nm (ε 1 015); $\delta_H$(100 MHz) 3.02 (1 H, br s, $D_2O$ exchange, OH), 3.2–3.5 (3 H, m, 1-H and 2-H), 4.09 (1 H, d, *J* 4 Hz, 3-H), 7.24 (5 H, s, aromatic H); *m/z*(CI) 168 $(M + NH_4)^+$ (100%) [Found: $(M + NH_4)^+$, 168.102 83. $C_9H_{10}O_2$ requires $(M + NH_4)^+$, 168.102 46].

*Preparation of* (*E*)-1-*Chloro*-2-*phenylsulphonylethene*.—(*a*) Sodium methoxide (12 g, 0.22 mol) was stirred in dry DMF (200 ml) in a cooling bath at 15 °C. To this was added, *via* syringe, thiophenol (22 ml, 0.214 mol), and the mixture stirred for 15 min at 15 °C. 1,1,2-Trichloroethane (60 ml, 0.65 mol) was then added in one portion, and the reaction mixture stirred in a water-bath at 60 °C for 3–4 h, to give a greyish-white precipitate. The mixture was poured into water (350 ml) and to this was added light petroleum (b.p. 40–60 °C) (350 ml). The aqueous layer was extracted with light petroleum (3 × 200 ml). The combined organic extracts were washed with 5% aqueous sodium hydroxide (2 × 250 ml), dried ($MgSO_4$), filtered, and evaporated to yield 2,2-dichloroethyl phenyl sulphide as a

colourless oil (42.95 g, 95%) $\delta_H$(60 MHz; $CDCl_3$) 3.45 (2 H, d, *J* 8 Hz, $CH_2$), 5.5 (1 H, t, *J* 8 Hz, C*H*), and 7.0–7.4 (5 H, m, aromatic H).

(*b*) The crude sulphide (42.05 g, 0.203 mol) was stirred in glacial acetic acid (200 ml) and conc. sulphuric acid (3 ml). To this was added 30% $H_2O_2$ (23 ml) over a period of 20 min without cooling. A reflux condenser was fitted to the flask and additional 30% $H_2O_2$ (30 ml) was added in portions (6 × 5 ml), the boiling being allowed to subside before each subsequent addition. The resultant mixture was stirred for a further 30 min before addition to cold water (1 l) without stirring. A white crystalline solid was precipitated and this was filtered off washed with water (100 ml), and then thoroughly dried to constant weight (47.06 g, 97%) to give 2,2-dichloroethyl phenyl sulphone.

(*c*) The sulphone (46.15 g, 0.197 mol), was stirred in a mixture of dry ether (600 ml) and $CH_2Cl_2$ (60 ml) in a water cooling bath at 15 °C. Triethylamine (32 ml, 0.23 mol) was added with stirring over a period of 20 min and stirring continued for a further 30 min. The resultant mixture was washed with 0.5M sulphuric acid (500 ml). The organic layer was dried ($MgSO_4$), filtered, and evaporated to yield a white solid (39.81 g). Recrystallization of the crude product from ether–light petroleum (b.p. 40–60 °C) yielded the required chlorovinyl phenyl sulphone (38.70 g, 97%) as white crystals, m.p. 50–52 °C (lit.,[13] 50–51 °C) (Found: C, 47.5; H, 3.5; Calc. for $C_8H_7ClO_2S$: C, 47.41; H, 3.46%); $\nu_{max}$(KBr) 1 320 and 1 150 $cm^{-1}$ ($SO_2$); $\lambda_{max}(CH_2Cl_2)$ 231.9 nm (ε, 25 800); $\delta_H$(100 MHz; $CDCl_3$). 6.74 (1 H, d, *J* 13 Hz, H-1), 7.41 (1 H, d, *J* 13 Hz, H-2), 7.4–8.0 (5 H, m, aromatic H); *m/z* 202 ($M^+$, 9.7%), 125 (100%) (Found: $M^+$, 201.985 84. Calc. for $C_8H_7ClO_2S$: $M^+$, 201.985 53).

*Preparation of Compound* (**9**) *from* (2S,3R)-3-*Phenyl*-2,3-*epoxypropan*-1-*ol* (**8**).—A solution of the epoxy alcohol (**8**) (4.90 g, 33 mmol) in THF was added to a stirred suspension of sodium hydride (1.35 g, 39.6 mmol) in dry THF (20 ml) at −23 °C under argon. Stirring was continued at −23 °C for 30 min, before the addition of a solution of the chlorovinyl phenyl sulphone (8.1 g, 40 mmol) in THF (40 ml). The reaction was allowed to warm to 0 °C over a period of 30 min. It was then quenched with saturated aqueous $(NH_4)_2SO_4$ (40 ml) and extracted with ether (3 × 50 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to yield a brown solid (10.93 g). Purification of the crude product by flash column chromatography on silica ($CH_2Cl_2$) yielded the required compound (**9**) (7.5 g, 72%) as white crystals, m.p. 103–105 °C (Found: C, 64.8; H, 5.2. Calc. for $C_{17}H_{16}O_4S$: C, 64.6; H, 5.1%); $[\alpha]_D^{20}$ −56.17° (*c* 0.251 in $CHCl_3$); $\nu_{max}$(KBr) 1 310 and 1 145 $cm^{-1}$ ($SO_2$); $\lambda_{max}(CH_2Cl_2)$ 232.8 nm (ε 17 300); see Tables 3 and 4 for $^1H$ and $^{13}C$ NMR data; *m/z* ($M^+$, 4%) and 91 (100%) (Found: $M^+$, 316.077 24. $C_{17}H_{16}O_4S$ requires $M^+$, 316.076 93).

*Preparation of* (4R,αS)-4-(α-*Hydroxybenzyl*)-3-*phenylsulphonyl*-4,5-*dihydrofuran* (**10a**).—A solution of LDA (4.1 mmol, 1.3 equiv) in THF (10 ml) was added to a stirred solution of compound (**9**) (1.0 g, 3.16 mmol) in dry THF (10 ml) at −78 °C under nitrogen. A deep red colouration was observed. The reaction mixture was allowed to warm to 0 °C over a period of 20 min, and then quenched with saturated aqueous $(NH_4)_2SO_4$ (15 ml) and extracted with ether (3 × 20 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to yield a brown gum. Purification of the crude product by flash column chromatography on silica (5% EtOAc in $CH_2Cl_2$) yielded the required dihydrofuran (**10a**) (0.69 g, 68%) as a white solid, m.p. 119–121 °C (lit.,[13] *racemic* 120–122 °C); $[\alpha]_D^{20}$ + 39.84 (*c* 0.31 in $CHCl_3$) (Found: C, 64.6; H, 5.1. Calc. for $C_{17}H_{16}O_4S$: C, 64.6; H, 5.1%); $\nu_{max}$(KBr) 3 525 (OH), 1 310, and 1 145 $cm^{-1}$ ($SO_2$); $\lambda_{max}(CH_2Cl_2)$ 254.1 nm; see Tables 1 and 2 for $^1H$ and $^{13}C$ NMR data *m/z* (CI) 334 $(M + NH_4)^+$ (35%) [Found: $(M + NH_4)^+$ 334.1113. Calc. for $C_{17}H_{16}O_4S$: $(M + NH_4)^+$, 334.1113].

*Preparation of* (4R,αS)-4-(α-*Ethoxycarbonyloxybenzyl*)-3-*phenylsulphonyl*-4,5-*dihydrofuran* (**10b**).—Butyl-lithium (2.1M; 2.0 ml, 4.15 mmol) was added to a stirred solution of (**10a**) (1.31 g, 4.15 mmol) in dry THF (40 ml) at −78 °C under nitrogen and stirring was continued at −78 °C for 45 min. After this time, freshly distilled ethyl chloroformate (0.55 ml, 9.30 mmol) was added from a syringe, and the reaction mixture was allowed to warm up to room temperature over a period of 1.5 h. It was then quenched with saturated aqueous $(NH_4)_2SO_4$ (30 ml) and extracted with ether (3 × 30 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to give a yellow gum (1.63 g). Purification of the crude product by column chromatography on silica ($CH_2Cl_2$) yielded the required *carbonate* (**10b**) as a white solid (1.31 g, 82%), m.p. 153–154 °C; $[\alpha]_D^{20}$ +4.68° (*c* 0.30 in $CHCl_3$) (Found: C, 61.85; H, 5.3. $C_{20}H_{20}O_6S$ requires C, 61.9; H, 5.2%); $\nu_{max}$(KBr) 1 770 (carbonate), and 1 315 and 1 150 $cm^{-1}$ ($SO_2$); $\lambda_{max}(CH_2Cl_2)$. 251.5 nm (ε 10 300); see Tables 1 and 2 for $^1H$ and $^{13}C$ NMR data; *m/z* (CI) 406 $(M + NH_4)^+$ (100%) [Found: $(M + NH_4)^+$, 406.1324, $C_{20}H_{20}O_6S$ requires $(M + NH_4)^+$, 406.132 43].

*Preparation of* (4R,αS)-4-(α-*Methoxymethoxybenzyl*)-3-*phenylsulphonyl*-4,5-*dihydrofuran* (**10c**).—Butyl-lithium (1.2M; 1.0 ml, 2.12 mmol) was added to a stirred solution of (**10a**) (0.67 g, 2.12 mmol) in dry THF (20 ml) at −78 °C under nitrogen and stirring was continued at −78 °C for 45 min. Freshly distilled chloromethyl methyl ether (0.51 ml, 6.36 mmol) was then added, *via* syringe, and the reaction mixture allowed to warm to room temperature over a period of 1 h; it was then stirred for a further 4 h. The solvent was removed by rotary evaporation and the resultant yellow gum was dissolved in a minimum amount of THF. Lithium chloride was precipitated by the addition of pentane and the mixture filtered and solvent removed. Purification by column chromatography on basic silica ($CH_2Cl_2$) yielded *compound* (**10c**) as white crystals (0.482 g, 63%), m.p. 136–137 °C; $[\alpha]_D^{20}$ −62.00 (*c* 0.50 in $CHCl_3$) (Found: C, 63.1; H, 5.7. $C_{19}H_{20}O_5S$ requires C, 63.3; H, 5.8%); $\lambda_{max}(CH_2Cl_2)$ 227.1 nm; see Tables 1 and 2 for $^1H$ and $^{13}C$ NMR data; *m/z* (CI) 378 $(M + NH_4)^+$ (3%).

*Typical Procedure for the Preparation of a Mosher Ester.*[18]—The epoxy alcohol (**8**) (24 mg, 0.16 mmol) was mixed with (*S*)-(−)-methoxy(trifluoromethyl)phenylacetyl chloride (409 mg, 0.162 mmol) and $CCl_4$ (5 drops) and pyridine (5 drops) were added. The flask was stoppered and left at room temperature for 12 h. Water (1 ml) was then added, followed by ether (20 ml). The organic extract was washed with 2M HCl (10 ml), followed by saturated aqueous $Na_2CO_3$ (10 ml); it was then dried ($MgSO_4$), filtered, and evaporated to yield the Mosher ester as a colourless gum (52 mg).

*Typical Procedure for the Reaction of an Arylcopper Reagent with the* α,β-*Unsaturated Sulphone* (**10b**).—4-Methoxybromobenzene (0.3 ml, 2.5 mmol) was dissolved in dry THF (5 ml) at −78 °C under argon and to this was added, *via* syringe, t-butyl-lithium (2.0M; 2.5 ml, 5.00 mmol). Stirring was continued at −78 °C for 15 min, after which the cooling bath was removed and the reaction mixture stirred for a further 40 min. The resultant 4-methoxyphenyl-lithium was cooled to −30 °C and added, *via* a double ended needle, to a suspension of anhydrous CuI (either 0.33, 0.5, or 1 equiv. as required) in THF (5 ml). The mixture was stirred at −30 °C for a further 30 min before it was cooled to −78 °C. At this stage $BF_3$·$Et_2O$ (1 equiv.) was

added if required. To the stirred reaction mixture was added, *via* a double ended needle, a solution of the required amount of the carbonate (**10b**) in THF (10 ml). The reaction mixture was allowed to warm up to 0 °C, room temperature or reflux. After the required time at the appropriate temperature, the reaction mixture was quenched with saturated aqueous $(NH_4)_2SO_4$ and extracted with ethyl acetate. The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated, and the crude products were analysed by HPLC, $^1H$ NMR, IR and mass spectrometry.

*Reaction of the Carbonate* (**10b**) *with Triphenylborane*.—The carbonate (**10b**) (170 mg, 0.438 mmol) was dissolved in dry THF (15 ml) at room temperature and to this was added, *via* a double ended needle, a solution of triphenylborane (0.312 g, 0.876 mmol) in THF (10 ml) with vigorous stirring. A small quantity of air was injected by syringe, through a septum cap, onto the surface of the reaction mixture. Stirring was continued at room temperature for 18 h with small amounts of air being injected periodically into the reaction vessel, and the reaction was then heated under reflux for 4 h. Finally water (2 mmol) was injected in and the reaction mixture was refluxed for a further 2 h. At this point examination of the reaction mixture by HPLC showed that no reaction had occurred, so the reaction was quenched with brine and (**10b**) (150 mg) was recovered.

*Attempted Cross-coupling of* (**10c**) *with* 4-*Methoxybromobenzene*.—t-Butyl-lithium (1.5M; 0.38 ml, 0.57 mmol, 1.2 equiv.) was added to a stirred solution of (**10c**) (170 mg, 0.472 mmol) in THF (10 ml) at −78 °C under nitrogen after which stirring was continued at −78 °C for 15 min. The mixture was allowed to warm to room temperature for 15 min and then stirred for a further 30 min. Zinc chloride (65 mg, 0.472 mmol) (which had been dried in a pistol over $P_2O_5$ at 140 °C), was dissolved in THF (5 ml) and then added, by double ended needle, to the stirred solution of the lithium derivative of (**10c**). Stirring was continued at room temperature for 1 h after which the reaction mixture was transferred by double ended needle into a stirred suspension of $[Ni(PPh_3)_2Cl_2]$ (0.015 g, 0.024 mmol) in a solution of 4-methoxybromobenzene (0.07 ml, 0.567 mmol) in THF (10 ml). The reaction mixture was then heated under reflux for 24 h after which it was quenched with saturated aqueous $(NH_4)_2SO_4$ and extracted with ether (3 × 10 ml); the combined organic extracts were dried ($MgSO_4$), filtered, and evaporated. Examination of the crude product by HPLC and $^1H$ NMR showed that the methoxymethyl ether (**10c**) was still present, with no evidence of cross coupled products formed.

*Preparation of* 1-*Bromo*-2-*phenylsulphonylstyrene*.—Benzenesulphonyl bromide (8.99 g, 0.040 mol), phenylacetylene (4.54 g, 0.044 mol), and acetonitrile (10 ml) were introduced into a Carius tube and cooled in liquid nitrogen. The tube was degassed at 0.1 mmHg, sealed, and then heated to 100 °C for 5 h. After this time the tube was cooled in liquid nitrogen and opened. The contents were evaporated to dryness to yield a brown solid, crystallization of which from methanol yielded the desired product (10.51 g, 80%) as white crystals, m.p. 82 °C (lit.,[25] 82 °C) (Found: C, 52.2; H, 3.4. Calc. for $C_{14}H_{11}BrO_2S$: C, 52.0; H, 3.4%); $\lambda_{max}(CH_2Cl_2)$ 232 nm (ε 17 810); $\delta_H$(100 MHz; $CDCl_3$) 7.1–7.6 (6 H, m, aromatics and 2-H); *m/z* 322/324 ($M^+$, 4.1%, 4.2%) (Found: $M^+$, 321.9659. Calc. for $C_{14}H_{11}BrO_2S$: $M^+$, 321.9666).

*Preparation of* 2-*Phenylsulphonyl*-1-*phenylethyne* (**11**).—2-Phenylsulphonyl-1-bromostyrene (1.40 g, 4.33 mol) was dissolved in dry benzene (4 ml) and triethylamine (4 ml). The solution was stirred at room temperature for 17 h, during which time a precipitate slowly accumulated. This was filtered off and the residue was washed with benzene (2 × 5 ml). The organic extracts were combined and evaporated. The resultant crude product was crystallized from methanol to yield (**11**) as white crystals (1.01 g, 96%), m.p. 72–73 °C (lit.,[25] 74 °C) (Found: C, 69.2; H, 4.4. Calc. for $C_{14}H_{10}O_2S$: C, 69.4; H, 4.1%); $\nu_{max}$(KBr) 2 230 (C≡C), and 1 355 and 1 185 $cm^{-1}$ ($SO_2$); $\lambda_{max}(CH_2Cl_2)$ 261 nm (ε 27 590); $\delta_H$(100 MHz; $CDCl_3$) 7.2–7.7 and 8.0–8.2 (10 H, m, aromatics); *m/z* 242 ($M^+$, 35%) (Found: $M^+$, 242.041 295. Calc. for $C_{14}H_{10}O_2S$: $M^+$, 242.040 15).

*Reaction of* 1-*Bromo*-2-*phenylsulphonylstyrene with the Epoxy Alcohol* (**8**).—Sodium hydride (41 mg, 1.3 equiv) was stirred in THF (10 ml) at −20 °C under a nitrogen atmosphere and to this was added a solution of (**8**) (0.15 g, 1 mmol) in THF (8 ml). Stirring was continued at −20 °C for 30 min before the addition of 1-bromo-2-phenylsulphonylstyrene (0.355 g, 1.1 mol) in THF (10 ml). The reaction was allowed to warm to room temperature for 1 h and then stirred for a further 3 h. After this time the reaction was quenched with saturated aqueous $(NH_4)_2SO_4$ (15 ml) and extracted with ether (3 × 10 ml). The organic extracts were dried ($MgSO_4$), filtered, and evaporated. Analysis of the crude product (HPLC and NMR) revealed the presence of 2-phenylsulphonyl-1-phenylethyne (**11**).

*Coupling Reaction of* 2-*Phenylsulphonyl*-1-*phenylethyne* (**11**) *with the Epoxy Alcohol* (**8**).—To a stirred suspension of NaH (0.247 g, 7.2 mmol) in dry THF (20 ml), at −23 °C under a nitrogen atmosphere was added a solution of the epoxy alcohol (**8**) (0.90 g, 6 mmol) in THF (20 ml). Stirring was continued at −20 °C for 30 min before the addition of a solution of 2-phenylsulphonyl-1-phenylethyne (**11**) (1.74 g, 7.2 mmol) in THF (20 ml). The reaction mixture was allowed to warm up to 0 °C over a period of 45 min, after which it was stirred at 0 °C for 30 min and then quenched with saturated aqueous $(NH_4)_2SO_4$ (40 ml) and extracted with ether (3 × 35 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to yield a brown gum (2.66 g). Purification of the crude product by column chromatography on silica ($CH_2Cl_2$) first yielded (**13**) as a flaky, off-white solid (0.89 g, 38%), $\nu_{max}$(neat) 1 305 and 1 145 $cm^{-1}$ ($SO_2$); see Tables 3 and 4 for $^1H$ and $^{13}C$ NMR data; *m/z*(CI) 410 $(M + NH_4)^+$ (100%) [Found: $(M + NH_4)^+$, 410.143 15. $C_{23}H_{20}O_4S$ requires $(M + NH_4)^+$, 410.1621]; and then (**12**) as a flaky off-white solid (0.87 g, 37%), $[\alpha]_D^{20}$ −28.11 (*c* 0.37 in $CHCl_3$); $\nu_{max}$(neat) 1 315 and 1 145 $cm^{-1}$ ($SO_2$); $\nu_{max}(CH_2Cl_2)$ 262 nm (ε 15 150); see Tables 3 and 4 for $^1H$ and $^{13}C$ NMR data; *m/z*(CI) 410 $(M + NH_4)^+$ (100%) [Found: $M + NH_4)^+$, 410.143 15. $C_{23}H_{20}O_4S$ requires $(M + NH_4)^+$, 410.142 61].

*Preparation of* (4R,αS)-4-(α-*Hydroxybenzyl*)-2-*phenyl*-3-*phenylsulphonyl*-4,5-*dihydrofuran* (**18a**).—Compound (**12**) (170 mg, 0.43 mmol) was dissolved in dry THF (10 ml) and cooled to −78 °C under nitrogen. To this was added, *via* a double ended needle, a solution of LDA (0.56 mmol) in THF (5 ml). The reaction mixture was allowed to warm to 0 °C for 15 min after which it was stirred at 0 °C for a further 30 min. After this time the reaction mixture was quenched with saturated aqueous $(NH_4)_2SO_4$ (10 ml) and extracted with ether (3 × 10 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to yield a yellow solid (181 mg). Purification of the crude product on a chromatotron (silica, 4% EtOAc in $CH_2Cl_2$) gave (**18a**) as white crystals (145 mg, 85%), m.p. 177–178 °C (Found: C, 70.25; H, 5.1. $C_{23}H_{20}O_4S$ requires C, 70.4; H, 5.1%); $\nu_{max}$(KBr) 3 540 (OH) and 1 305 and 1 155 $cm^{-1}$ ($SO_2$); $\lambda_{max}(CH_2Cl_2)$ 230 nm (ε 19 520); see Tables 1 and 2 for $^1H$ and $^{13}C$ NMR data; *m/z*(CI) 410 $(M + NH_4)^+$ (2%) [Found: $(M + NH_4)^+$, 410.143 15. $C_{23}H_{20}O_4S$ requires $(M + NH_4)^+$, 410.142 61].

*Reaction of* (**13**) *with LDA*.—Compound (**13**) (200 mg, 0.51 mmol) was dissolved in dry THF (10 ml) and cooled to −78 °C under argon. To this was added a solution of LDA (0.66 mmol) in THF (7 ml). The reaction was allowed to warm to 0 °C for 15 min and then stirred at 0 °C for 1.5 h. Saturated aqueous $(NH_4)_2SO_4$ (10 ml) was then added and the solution extracted with ether (3 × 10 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to yield a brown gum. Purification of the crude product on a chromatotron (silica) [$CH_2Cl_2$–light petroleum (b.p. 40–60 °C) (1:1)] yielded 2 fractions. The first was identified as (**21**) (70 mg, 54%) as a viscous *oil*, $\nu_{max}$(neat) 2 270 $cm^{-1}$ (C≡C); $\delta_H$(60 MHz; $CDCl_3$) 3.5 (1 H, m, 2-H), 3.8 (2 H, m, 1-H), 4.1 (1 H, d, *J* 5 Hz, 3-H), and 7.1–7.2 (10 H, m, aromatic H); *m/z*(CI) 268 $(M + NH_4)^+$ (100%) [Found: $(M + NH_4)^+$, 268.136 00. $C_{17}H_{14}O_2$ requires $(M + NH_4)^+$ 268.133 75]; and the second was identified as the starting material (**13**) (60 mg, 30%).

*Preparation of* (4R,αS)-2-*Phenyl*-3-*phenylsulphonyl*-4-(α-*ethoxycarbonyloxybenzyl*)-4,5-*dihydrofuran* (**18b**).—BuLi (2.2M; 0.45 ml, 1.0 mmol) was added to a stirred solution of (**18a**) (390 mg, 1.0 mmol) in dry THF (20 ml) at −78 °C under nitrogen, and stirring continued at −78 °C for 45 min. After this time, freshly distilled ethyl chloroformate (0.20 ml, 2.0 mmol) was added from a syringe. The reaction mixture was allowed to warm to room temperature over a period of 1.5 h. It was then quenched with saturated aqueous $(NH_4)_2SO_4$ (10 ml) and extracted with ether (3 × 10 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to yield a flaky white solid. Purification of the crude product on a chromatotron (silica, $CH_2Cl_2$) yielded the required *carbonate* (**18b**) (410 mg, 89%) as a flaky solid, $\nu_{max}$(KBr) 1 760 (carbonate) and 1 310 and 1 150 $cm^{-1}$ ($SO_2$); $\lambda_{max}$($CH_2Cl_2$) 230.4 nm; see Tables 1 and 2 for $^1H$ and $^{13}C$ NMR data; *m/z*(CI), 482 $(M + NH_4)^+$ (100%) [Found: $(M + NH_4)^+$, 482.162 71. $C_{26}H_{24}O_6S$ requires $(M + NH_4)^+$ 482.163 69].

*Preparation of* (4R,αS)-2-*phenyl*-3-*phenylsulphonyl*-4-(α-*methoxymethyloxybenzyl*)-4,5-*dihydrofuran* (**18c**).—BuLi (2.2M; 0.90 ml, 1.91 mmol) was added to a stirred solution of (**18a**) (750 mg, 1.91 mmol) in dry THF (20 ml) at −78 °C under nitrogen, and stirring was continued at −78 °C for 45 min. Freshly distilled chloromethyl methyl ether (0.5 ml, 5.73 mmol) was then added. The reaction mixture was allowed to warm to room temperature over a period of 1 h and then stirred for a further 4 h, after which the solvent was evaporated. The resultant product was dissolved in the minimum amount of THF, and lithium chloride was precipitated by the addition of pentane. The precipitate was filtered off and the filtrate evaporated to yield a yellow gum (0.91 g). Purification of the crude product on a chromatotron (silica, 3% EtOAc in $CH_2Cl_2$), yielded the desired *product* (**18c**) (0.76 g, 82%) as a white solid, m.p. 135–137 °C; $[\alpha]_D^{20}$ −47.93° (*c* 0.29 in $CHCl_3$) (Found: C, 68.9; H, 5.4. $C_{25}H_{24}O_5S$ requires C, 68.9; H, 5.5%); $\nu_{max}$(KBr) 1 305 and 1 150 $cm^{-1}$ ($SO_2$); $\lambda_{max}$($CH_2Cl_2$) 230.9 nm; see Tables 1 and 2 for $^1H$ and $^{13}C$ NMR data; *m/z* 437 $(M + H)^+$ (3%) and 285 (100).

*Preparation of* 2,2-*Dibromo*-1-(3,4-*dimethoxyphenyl*)*ethene*.—To a well stirred solution of carbon tetrabromide (2.99 g, 9 mmol) in dry $CH_2Cl_2$ (20 ml) at 0 °C, was added triphenylphosphine (4.74 g, 18 mmol), and then 3,4-dimethoxybenzaldehyde (1.5 g, 9 mmol). The resultant solution was stirred for 10 min, washed with water (20 ml), dried ($MgSO_4$), filtered, and evaporated to give an orange solid. Purification of this by column chromatography on silica ($CH_2Cl_2$) afforded a colourless *oil* (2.72 g, 94%); $\lambda_{max}$($CH_2Cl_2$) 277.6 nm (ε 13830); $\delta_H$(250 MHz; $CDCl_3$) 3.87 [6 H, s, 2 × ($OCH_3$)], 6.82 (1 H, d, *J* 8 Hz, 5′-H), 7.07 (1 H, dd, *J* 2 and 8 Hz, 6′-H), 7.17 (1 H, d, *J* 2 Hz, 2′-H), and 7.38 (1 H, s, 1-H); *m/z* 322 ($M^+$, 100%) (Found: $M^+$, 321.902 65. $C_{10}H_{10}Br_2O_2$ requires $M^+$, 321.902 67).

*Preparation of* 2,2-*Dibromo*-1-(3,4-*methylenedioxyphenyl*)-*ethene*.—To a well stirred solution of $CBr_4$ (6.62 g, 0.02 mol) in $CH_2Cl_2$ (45 ml) at 0 °C, was added triphenylphosphine (10.48 g, 0.04 mol), and then 3,4-methylenedioxybenzaldehyde (3.0 g, 0.02 mol). Stirring was continued at 0 °C for 10 min at which point the reaction mixture was washed with water (30 ml). The organic layer was dried ($MgSO_4$), filtered, and evaporated to leave an orange gum. Purification of this by column chromatography on silica ($CH_2Cl_2$) afforded a colourless *oil* (5.10 g, 84%); $\lambda_{max}$($CH_2Cl_2$) 276.8 nm (ε 10 035); $\delta_H$(250 MHz; $CDCl_3$) 5.96 (2 H, s, $OCH_2O$), 6.78 (1 H, d, *J* 8 Hz, 5′-H), 6.92 (1 H dd, *J* 2 and 8 Hz, 6′-H), 7.16 (1 H, d, *J* 2 Hz, 2′-H), and 7.34 (1 H, s, 1-H); *m/z* 306 ($M^+$, 43%) (Found: $M^+$, 305.872 33. $C_9H_6Br_2O_2$ requires $M^+$, 305.871 41).

*Preparation of* 3,4-*Dimethoxyphenylethyne*.—2,2-Dibromo-1-(3,4-dimethoxyphenyl)ethene (16.08 g, 0.05 mol) was dissolved in dry THF (300 ml) and the solution cooled to −78 °C under nitrogen. Butyl-lithium (1.9M; 52.6 ml, 0.1 mol) was added to the stirred solution, by syringe, over a period of 0.5 h. Stirring was continued at −78 °C for 1 h, after which time the cooling bath was removed and the reaction mixture stirred for 1.5 h at room temperature. The reaction was quenched with saturated aqueous $(NH_4)_2SO_4$ (250 ml) and extracted with ether (3 × 200 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated. Purification of the residue by column chromatography on silica ($CH_2Cl_2$) yielded the *title ethyne* (7.20 g, 90%) as a pale yellow solid, m.p. 76 °C (Found: C, 74.1; H, 6.2. $C_{10}H_{10}O_2$ requires C, 74.1; H, 6.2%); $\lambda_{max}$($CH_2Cl_2$) 258.9 nm (ε 19 834); $\delta_H$(250 MHz; $CDCl_3$) 3.04 (1 H, s, 2-H), 3.86 (6 H, s, $OCH_3$), 6.78 (1 H, d, *J* 8 Hz, 5′-H), 6.98 (1 H, d, *J* 2 Hz, 2′-H), and 7.08 (1 H, dd, *J* 2 and 8 Hz, 6′-H); *m/z* ($M^+$, 100%) (Found: $M^+$, 162.0671. $C_{10}H_{10}O_2$ requires $M^+$, 162.068 08).

*Preparation of* 3,4-*Methylenedioxyphenylethyne*.—2,2-Dibromo-1-(3,4-methylenedioxyphenyl)ethene (4.65 g, 0.15 mol) was dissolved in dry THF (70 ml) and the solution cooled to −78 °C under nitrogen. Butyl-lithium (1.6M; 18.5 ml, 0.03 mol) was added to the stirred solution, by syringe, over a period of 15 min. Stirring was continued at −78 °C for 1 h, after which time the cooling bath was removed and the reaction mixture stirred for 1.5 h at room temperature. The reaction was quenched with saturated aqueous $(NH_4)_2SO_4$ extracted with ether (3 × 50 ml), and the organic extracts dried ($MgSO_4$), filtered, and evaporated. Purification of the residue by column chromatography on silica ($CH_2Cl_2$) yielded the ethyne (2.11 g, 95%) as a pale yellow *oil*, $\nu_{max}$(neat) 2 100 $cm^{-1}$ (C≡C); $\lambda_{max}$($CH_2Cl_2$) 261 nm (ε 10 995); $\delta_H$(250 MHz; $CDCl_3$) 2.97 (1 H, s, 2-H), 5.92 (2 H, s, $OCH_2O$), 6.72 (1 H, d, *J* 8 Hz, 5′-H), 6.98 (1 H, d, *J* 5 Hz, 2′-H), 7.01 (1 H, dd, *J* 1.5 and 8 Hz, 6′-H); *m/z* 146 ($M^+$, 98%), 145 (100) (Found: $M^+$, 146.039 15. $C_9H_6O_2$ requires $M^+$, 146.036 78).

*Preparation of* 1-*Bromo*-1-(3,4-*dimethoxyphenyl*)-2-*phenylsulphonylethene*.—3,4-Dimethoxyphenylethyne (5.52 g, 0.034 mol) was dissolved in acetonitrile (11 ml) and to this was added benzenesulphonyl bromide (7.85 g, 0.035 mol). The reaction mixture was heated under reflux for 3 h, allowed to cool and then evaporated. Purification by column chromatography on silica ($CH_2Cl_2$) yielded the product (11.82 g, 91%) as a white *solid*, m.p. 89–91 °C (Found: C, 50.2; H, 4.1. $C_{16}H_{15}BrO_4S$ requires C, 50.1; H, 3.9%); $\nu_{max}$(KBr) 1 325 and 1 140 $cm^{-1}$ ($SO_2$); $\lambda_{max}$($CH_2Cl_2$) 233.3 nm (ε 19 824); $\delta_H$(250 MHz; $CDCl_3$), 3.80 (3 H, s, OMe), 3.89 (3 H, s, OMe), and 6.7–7.6 (9 H, m, 2-H and

aromatic H); *m/z* 382/384 ($M^+$, 7%/7%) and 162 (100) (Found: $M^+$, 383.985 41. $C_{16}H_{15}BrO_4S$ requires $M^+$, 383.985 38).

*Preparation of* 1-*Bromo*-1-(3,4-*methylenedioxyphenyl*)-2-*phenylsulphonylethene*.—3,4-Methylenedioxyphenylethyne (1.3 g, 8.9 mmol) was dissolved in acetonitrile (4 ml) and to this was added benzenesulphonyl bromide (1.96 g, 8.9 mmol). The reaction mixture was heated under reflux for 2 h, after which the solvent was evaporated. Purification of the crude product by column chromatography on silica ($CH_2Cl_2$) afforded the desired product (1.98 g, 61%) as an off-white *solid*, m.p. 132–133 °C (Found: C, 49.0; H, 3.1. $C_{15}H_{11}BrO_4S$ requires C, 49.05; H, 3.0%); $\nu_{max}$(KBr), 1 320 and 1 140 $cm^{-1}$ ($SO_2$); $\lambda_{max}$($CH_2Cl_2$) 236.8 nm (ε 18 840); $\delta_H$(250 MHz; $CDCl_3$) 6.01 (2 H, s, $OCH_2O$), 6.7–8.1 (8 H, m, aromatic H), and 7.24 (1 H, s, 2-H); *m/z*(CI) 384/386 $(M + NH_4)^+$ (45%) [Found: $(M + NH_4)^+$ 383.9905. $C_{15}H_{11}BrO_4S$ requires $(M + NH_4)^+$, 383.990 52].

*Preparation of* 1-(3,4-*Dimethoxyphenyl*)-2-*phenylsulphonylethyne*.—1-Bromo-1-(3,4-dimethoxyphenyl)-2-phenylsulphonylethene (9.99 g, 0.026 mol) was dissolved in dry benzene (28 ml) and triethylamine (28 ml) at room temperature and the solution stirred at room temperature for 54 h. After this time the precipitate of triethylamine hydrobromide was filtered off and washed with benzene (2 × 10 ml). The organic layers were combined and the solvent evaporated. Crystallization from methanol yielded the *product* (7.16 g, 91%) as white crystals, m.p. 139 °C (Found: C, 63.25; H, 4.6. $C_{16}H_{14}O_4S$ requires C, 63.6; H, 4.6%); $\nu_{max}$(KBr), 2 170 (C≡C) and 1 325 and 1 145 $cm^{-1}$ ($SO_2$); $\lambda_{max}$($CH_2Cl_2$) 232.5 nm (ε 19 819); $\delta_H$(250 MHz; $CDCl_3$), 3.83 (3 H, s, OMe), 3.88 (3 H, s, OMe), 6.84 (1 H, d, *J* 8 Hz, 5′-H), 6.96 (1 H, d, *J* 2 Hz, 2′-H), 7.16 (1 H, dd, *J* 2 and 8 Hz, 6′-H), and 7.5–8.1 (5 H, m, remaining aromatic H); *m/z*, 302 ($M^+$, 80%) (Found: $M^+$, 302.056 82. $C_{16}H_{14}O_4S$ requires $M^+$, 302.061 28).

*Preparation of* 1-(3,4-*Methylenedioxyphenyl*)-2-*phenylsulphonylethyne*.—1-Bromo-1-(3,4-methylenedioxyphenyl)-2-phenylsulphonylethene (1.3 g, 3.54 mmol) was dissolved in dry $CH_2Cl_2$ (20 ml) and triethylamine (5 ml) and the mixture stirred at room temperature for 60 h after which time the triethylamine hydrobromide was filtered off. The precipitate was washed with $CH_2Cl_2$ (2 × 5 ml) and the organic extracts were combined and evaporated. Crystallization of the residue from methanol yielded the product (0.88 g, 87%) as an off-white *solid*, $\nu_{max}$(KBr) 2 210 (C≡C) and 1 365 and 1 185 $cm^{-1}$ ($SO_2$); $\lambda_{max}$($CH_2Cl_2$) 231.3 nm (ε 22 920); $\delta_H$(250 MHz; $CDCl_3$) 6.00 (2 H, s, $OCH_2O$), 6.76 (1 H, d, *J* 8 Hz, 5′-H), 6.87 (1 H, d, *J* 2 Hz, 2′-H), and 7.06 (1 H, dd, *J* 2 and 8 Hz, 6′-H); *m/z* 286 ($M^+$, 100%) (Found: $M^+$, 286.031 64. $C_{15}H_{10}O_4S$ requires $M^+$, 286.029 37).

*Coupling of* 1-(3,4-*Dimethoxyphenyl*)-2-*phenylsulphonylethyne with the Epoxy Alcohol* (**8**).—A solution of the epoxy alcohol (**8**) (0.98 g, 6.53 mmol) in THF was added *via* a double ended needle to a suspension of NaH (0.29 g, 1.3 equiv.) in dry THF (20 ml) at −23 °C under argon. Stirring was continued at −23 °C for 30 min before the addition of a solution of the alkyne (2.17 g, 7.18 mmol) in THF (40 ml). The mixture was allowed to warm to 0 °C over a period of 30 min, after which it was stirred at 0 °C for 2 h, then quenched with saturated aqueous $(NH_4)_2SO_4$ (50 ml) and extracted with ether (3 × 50 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to yield a brown gum (3.32 g). Purification of the crude product by column chromatography on silica (2% EtOAc in $CH_2Cl_2$) yielded two *fractions*. The first was (**15**) (0.28 g, 9.5%); $\delta_H$(250 MHz; $CDCl_3$), 3.60 (1 H, m, 4-H), 3.81/4.30 (2 H, m, 5-H), 4.14 (1 H, m, 6-H), 3.81/3.82 (6 H, s, OMe), 7.1–7.9 (14 H, m, aromatic H and 3-H); *m/z* 452 ($M^+$, 4%) (Found: $M^+$, 452.1291. $C_{25}H_{24}O_6S$ requires $M^+$, 452.129 36). The second *fraction* was (**14**) (1.79 g, 61%) as a mixture of the *cis* and *trans* isomers, $[\alpha]_D^{20}$ 20.52 (*c*, 0.38 in $CHCl_3$); $\nu_{max}$(KBr) 1 310 and 1 140 $cm^{-1}$ ($SO_2$); $\lambda_{max}$($CH_2Cl_2$) 228 nm (ε 14 580); see Tables 3 and 4 for $^1H$ and $^{13}C$ NMR data; *m/z* 452 ($M^+$, 9%) (Found: $M^+$, 452.127 93. $C_{25}H_{24}O_6S$ requires $M^+$, 452.129 36.

*Coupling of* 1-(3,4-*Methylenedioxyphenyl*)-2-*phenylsulphonylethyne with the Epoxy Alcohol* (**8**).—To a stirred suspension of NaH (63 mg, 1.60 mmol) in dry THF (5 ml) at −23 °C under argon was added *via* double ended needle, a solution of the epoxy alcohol (**8**) (185 mg, 1.23 mmol) in THF (10 ml). Stirring was continued at −23 °C for 30 min before the addition of a solution of (**11c**) (385 mg, 1.35 mmol) in THF (15 ml). The reaction mixture was allowed to warm up to 0 °C over a period of 45 min and it was then stirred at 0 °C for a further 2.5 h. After this time the reaction mixture was quenched with saturated aqueous $(NH_4)_2SO_4$ (20 ml) and extracted with ether (3 × 15 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to yield a brown gum. Purification of the crude product on a chromatotron (silica, 2% EtOAc in $CH_2Cl_2$) yielded (**17**) (45 mg, 9%) and also (**16**) (356 mg, 66%) as a white *solid*, m.p. 123 °C [Found for (**16**): C, 66.2; H, 4.8. $C_{24}H_{20}O_6S$ requires C, 66.1; H, 4.6%]; $\nu_{max}$(KBr) 1 310 and 1 145 $cm^{-1}$ ($SO_2$); $\lambda_{max}$($CH_2Cl_2$) 229.1 nm (ε 21 288); see Tables 3 and 4 for $^1H$ and $^{13}C$ NMR data; *m/z*(CI), 437 $(M + H)^+$ (45%) [Found: $(M + H)^+$, 437.113 85. $C_{24}H_{20}O_6S$ requires $(M + H)^+$, 437.105 89].

*Preparation of* (4R,αS)-2-(3,4-*Dimethoxyphenyl*)-4-(α-*hydroxybenzyl*)-3-*phenylsulphonyl*-4,5-*dihydrofuran* (**19a**).—A solution of LDA (1.52 mmol) in THF (10 ml) was added *via* a double ended needle to a solution of (**14**) (0.52 g, 1.15 mmol) in dry THF (10 ml) at −78 °C under nitrogen. The reaction mixture was allowed to warm up to 0 °C over a period of 15 min after which it was stirred at 0 °C for 30 min, and then quenched with saturated aqueous $(NH_4)_2SO_4$ (10 ml), and extracted with ether (3 × 10 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to yield a yellow solid (0.63 g). Purification of the crude product by column chromatography on silica (4% EtOAc in $CH_2Cl_2$) yielded (**19a**) (0.48 g, 92%), m.p. 194–195 °C, $[\alpha]_D^{20}$ −100° (*c* 0.24 in $CHCl_3$) (Found: C, 66.3; H, 5.5. $C_{25}H_{24}O_6S$ requires C, 66.4; H, 5.3%); $\nu_{max}$(KBr) 3 510 (OH) and 1 305 and 1 155 $cm^{-1}$ ($SO_2$); $\lambda_{max}$ ($CH_2Cl_2$) 227.5 nm (ε 21 880); for $^1H$ and $^{13}C$ NMR data see Tables 1 and 2; *m/z*(CI) 453 $(M + H)^+$ (50%) [Found: $(M + H)^+$, 453.137 720. $C_{25}H_{24}O_6S$ requires $(M + H)^+$, 453.137 19].

*Preparation of* (4R,αS)-4-(α-*Hydroxybenzyl*)-2-(3,4-*methylenedioxyphenyl*)-3-*phenylsulphonyl*-4,5-*dihydrofuran* (**20a**).—A solution of LDA (0.75 mmol) in THF (5 ml) was added to a solution of (**16**) (250 mg, 0.57 mmol) in dry THF (10 ml) at −78 °C under argon. The reaction mixture was allowed to warm to 0 °C over a period of 45 min and then stirred at 0 °C for 1 h. After this time, the reaction was quenched with saturated aqueous $(NH_4)_2SO_4$ (10 ml) and extracted with ether (3 × 10 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to yield a brown gum (290 mg). Purification of the crude product on a chromatotron yielded (**20a**) (0.21 g, 84%) as a white *solid*, $\nu_{max}$(KBr) 3 510 (OH) and 1 310 and 1 155 $cm^{-1}$ ($SO_2$). For $^1H$ and $^{13}C$ NMR data see Tables 1 and 2; *m/z*(CI) 437 $(M + H)^+$ (48%) [Found: $(M + H)^+$, 437.105 89. $C_{24}H_{20}O_6S$ requires $(M + H)^+$, 437.105 89].

*Preparation of* (4R,αS)-2-(3,4-*Dimethoxyphenyl*)-4-(α-*ethoxycarbonyloxybenzyl*)-3-*phenylsulphonyl*-4,5-*dihydrofuran* (**19b**).—BuLi (2.1M; 0.44 ml, 0.93 mmol) was added to a stirred solution of (**19a**) (420 mg, 0.93 mmol) in dry THF (30 ml) at −78 °C under argon. Stirring was continued at −78 °C for 45 min after which freshly distilled ethyl chloroformate (0.25 ml, 2.77 mmol) was added. The reaction mixture was allowed to warm to room temperature over a period of 1 h and then stirred for a further 30 min before being quenched with saturated aqueous $(NH_4)_2SO_4$ (15 ml) and extracted with ether (3 × 20 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to yield a flaky solid (480 mg). Purification of the crude product on a chromatotron (silica, $CH_2Cl_2$) yielded (**19b**) (420 mg, 82%) as a flaky white *solid*, m.p. 57–58 °C $[\alpha]_D^{20}$ −20.75° (*c* 0.35 in $CHCl_3$); $\nu_{max}$(KBr) 1 760 (carbonate) and 1 310 and 1 155 $cm^{-1}$ ($SO_2$); $\lambda_{max}$($CH_2Cl_2$) 228 nm (ε 18 500); see Tables 1 and 2 for $^1H$ and $^{13}C$ NMR data; *m/z* (CI) 525 $(M + H)^+$ (65%) [Found: $(M + H)^+$, 525.158 315. $C_{28}H_{28}O_8S$ requires $(M + H)^+$, 525.158 32].

*Preparation of* (4R,αS)-2-(3,4-*Dimethoxyphenyl*)-4-(α-*methoxymethoxybenzyl*)-3-*phenylsulphonyl*-4,5-*dihydrofuran* (**19c**).—BuLi (2.1M; 0.48 ml, 1.01 mmol) was added to a stirred solution of (**19a**) (456 mg, 1.01 mmol) in dry THF (30 ml) at −78 °C under argon and stirring was continued at the same temperature for 45 min. After this time freshly distilled chloromethyl methyl ether (0.35 ml, 4.04 mmol) was added. The reaction mixture was allowed to warm up to room temperature over a period of 1 h and then stirred for a further 3 h; it was then evaporated. The resultant product was dissolved in a minimum amount of THF and pentane was added to precipitate out the lithium chloride. The precipitate was filtered off and the solvent evaporated to yield a yellow gum. Purification of the crude product on a chromatotron (silica, 2% EtOAc in $CH_2Cl_2$) yielded (**19c**) as a white *solid*, m.p. 107–108 °C; $[\alpha]_D^{20}$ −61.18 °C (*c* 0.51 in $CHCl_3$) (Found: C, 65.4; H, 5.8. $C_{27}H_{28}O_7S$ required C, 65.3; H, 5.6%); $\nu_{max}$(KBr) 1 305 and 1 150 $cm^{-1}$ ($SO_2$); $\lambda_{max}$($CH_2Cl_2$) 229.1 nm (ε 19 890); see Tables 1 and 2 for $^1H$ and $^{13}C$ NMR data; *m/z*(CI) 497 $(M + H)^+$ (100%) [Found: $(M + H)^+$, 497.166 50. $C_{27}H_{28}O_7S$ requires $(M + H)^+$, 497.163 40].

*Preparation of* (4R,αS)-2-(3,4-*dimethoxyphenyl*)-4-(α-*dimethoxymethoxybenzyl*)-3-*phenylsulphonyl*-4,5-*dihydrofuran* (**19d**).—Trimethyl orthoformate (1.21 ml, 11 mmol) was added to a stirred suspension of $MgCl_2$ (10.5 mg, 0.11 mmol) (which had been dried *in vacuo* in a pistol over $P_2O_5$ for 16 h) in dry $CH_2Cl_2$ (10 ml) at room temperature and stirring was continued at this temperature for 10 min. At this point a solution of (**19a**) (190 mg, 0.42 mmol) in $CH_2Cl_2$ (10 ml) was added *via* a double ended needle. The resultant mixture was heated under reflux for 24 h, after which a second portion of anhydrous $MgCl_2$ (10.5 mg, 0.11 mmol) was added, and the reaction mixture was heated under reflux for a further 24 h. The $MgCl_2$ was then filtered off and the solvent evaporated to yield (**19d**) (0.201 g, 91%) as a flaky solid, $\nu_{max}$(KBr) 1 350 and 1 155 $cm^{-1}$ ($SO_2$); see Tables 1 and 2 for $^1H$ and $^{13}C$ NMR data.

*Preparation of* (4R,αS)-2-(3,4-*Dimethoxyphenyl*)-4-(α-*methylthiomethoxybenzyl*)-3-*phenylsulphonyl*-4,5-*dihydrofuran* (**19e**).—To a stirred suspension of NaH (30 mg, 0.88 mmol) in dry monoglyme (5 ml) at 0 °C under nitrogen, was added a solution of (**19a**) (200 mg, 0.44 mmol) in monoglyme (10 ml). The resultant mixture was stirred at 0 °C for 10 min and then NaI (66 mg, 0.44 mmol), followed by freshly distilled chloromethyl methyl sulphide (0.05 ml, 0.44 mmol) were added. The reaction mixture was stirred at 0 °C for 1 h and then at room temperature for 5 h. It was then poured into water (10 ml) and extracted with ether (3 × 15 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to yield a yellow solid (245 mg). Purification of the crude product on a chromatotron (silica, $CH_2Cl_2$) yielded the desired *product* (**19e**) (210 mg, 93%) as a white solid, m.p. 120–121 °C; $[\alpha]_D^{20}$ −89.3° (*c* 0.4 in $CHCl_3$) (Found: C, 63.15; H, 5.7. $C_{27}H_{28}O_6S_2$ requires C, 63.3; H, 5.5%); $\nu_{max}$(KBr) 1 305 and 1 150 $cm^{-1}$ ($SO_2$); $\nu_{max}$($CH_2Cl_2$) 229.1 nm (ε 18 140); see Tables 1 and 2 for $^1H$ and $^{13}C$ NMR data; *m/z*(CI) 513 $(M + H)^+$ (100%) [Found: $(M + H)^+$, 513.135 60. $C_{27}H_{28}O_6S_2$ requires $(M + H)^+$, 513.140 54].

*Preparation of* (4R,αS)-2-(3,4-*Dimethoxyphenyl*)-4-(α-*methylsulphinylmethoxybenzyl*)-3-*phenylsulphonyl*-4,5-*dihydrofuran* (**19f**).—Freshly sublimed MCPBA (70 mg, 0.41 mmol) was added to a stirred solution of (**19e**) (210 mg, 0.41 mmol) in dry $CH_2Cl_2$ (10 ml) at −10 °C under argon. Stirring was continued at −10 °C for 1 h and then at room temperature for 16 h. The reaction mixture was quenched with saturated aqueous sodium bisulphite (10 ml) and extracted with $CH_2Cl_2$ (2 × 10 ml). The combined organic extracts were washed with 1M $NaHCO_3$ (10 ml), dried ($MgSO_4$), filtered, and evaporated to leave a yellow gum. Purification by chromatotron (silica, 2% EtOAc in $CH_2Cl_2$) yielded the desired *product* (**19f**) (162 mg, 78%) as a flaky fibrous solid, m.p. 70–72 °C, $[\alpha]_D^{20}$ −52.8° (*c* 0.4 in $CH_2Cl_2$); $\nu_{max}$(KBr) 1 025 $cm^{-1}$ (sulphoxide); $\lambda_{max}$($CH_2Cl_2$) 228.7 nm (ε 19 500); see Tables 1 and 2 for $^1H$ and $^{13}C$ NMR data; *m/z*(CI), 529 $(M + H)^+$ (52%) [Found: $(M + H)^+$, 529.135 470. $C_{27}H_{28}O_7S_2$ requires $(M + H)^+$, 529.135 470].

*Preparation of* (4R,αS)-2-(3,4-*Dimethoxyphenyl*)-3-*phenylsulphonyl*-4-(α-*phenylthiomethoxybenzyl*)-4,5-*dihydrofuran* (**19g**).—To a stirred suspension of NaH (21 mg, 0.59 mmol) in dry monoglyme (10 ml) at 0 °C under argon, was added, *via* a double ended needle, a solution of the alcohol (**19a**) (133 mg, 0.29 mmol) in monoglyme (10 ml). The mixture was stirred at 0 °C for 10 min after which NaI (44 mg, 0.29 mmol) and chloromethyl phenyl sulphide (0.04 ml, 0.29 mmol) were added. The reaction mixture was then stirred at 0 °C for 1 h and finally at room temperature for 16 h. After this time the reaction was quenched with water (10 ml) and extracted with ether (3 × 10 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to yield a white solid (181 mg). Purification of the crude product on a chromatotron (silica, $CH_2Cl_2$) yielded (**19g**) (139 mg, 83%) as a white *solid*, m.p. 130–131 °C (Found: C, 66.7; H, 5.27. $C_{32}H_{30}O_6S_2$ requires C, 66.7; H, 5.2%); $\nu_{max}$(KBr) 1 320 and 1 155 $cm^{-1}$ ($SO_2$); $\lambda_{max}$($CH_2Cl_2$) 228.3 nm (ε 22 000); see Tables 1 and 2 for $^1H$ and $^{13}C$ NMR data; *m/z*(CI) 575 $(M + H)^+$ (75%) [Found: $(M + H)^+$, 575.156 21. $C_{32}H_{30}O_6S_2$ requires $(M + H)^+$, 575.156 21].

*Preparation of* (4R,αS)-2-(3,4-*Dimethoxyphenyl*)-3-*phenylsulphonyl*)-4-(α-*phenylsulphonylmethoxybenzyl*)-4,5-*dihydrofuran* (**19h**).—MCPBA (275 mg, 1.68 mmol) was added to a stirred solution of (**19g**) (0.48 g, 0.84 mmol) in dry $CH_2Cl_2$ (50 ml) at −23 °C under argon. The reaction mixture was stirred at −23 °C for 1 h and then at room temperature for 16 h. After this time the reaction mixture was quenched with saturated aqueous sodium bisulphite (30 ml), the layers were separated, and the aqueous layer was extracted with $CH_2Cl_2$ (2 × 20 ml). The organic layers were combined, washed with 1M aqueous $NaHCO_3$ (50 ml), dried ($MgSO_4$) filtered, and evaporated. Purification of the crude product on a chromatotron (silica, 2% EtOAc in $CH_2Cl_2$) afforded (**19h**) (0.43 g, 84%) as a flaky solid, $\nu_{max}$(KBr) 1 305 and 1 150 $cm^{-1}$ ($SO_2$); $\lambda_{max}$($CH_2Cl_2$) 228.7 nm (ε 21 420); for $^1H$ and $^{13}C$ NMR data see Tables 1 and 2; *m/z*(CI) 607 $(M + H)$ (28%) [Found: $(M + H)^+$, 607.146 04. $C_{32}H_{30}O_8S_2$ requires $(M + H)^+$, 607.146 04].

*Desulphonylation of the Alcohol* (**19a**) *using Aluminium*

*Amalgam.*—The alcohol (**19a**) (0.18 g, 0.40 mmol) was dissolved in 2% aqueous THF (20 ml) at 0 °C. Aluminium foil strips (0.56 g, 20.7 mmol) were dipped into 2% aqueous $HgCl_2$ for 15 s. The strips were then washed with ethanol, followed by ether and cut, in 1 cm squares, directly into the vigorously stirred alcohol solution. Stirring was continued at 0 °C for 2 h and then room temperature for 2 h. During this time the aluminium squares had disintegrated into a fine powder. The solid inorganic material was filtered off and washed with ether (10 ml). The combined organic extracts were washed with brine (15 ml), dried ($MgSO_4$), filtered, and evaporated to yield a yellow gum. Purification of the crude product on a chromatotron (silica, 50% EtOAc in $CH_2Cl_2$) yielded the hydroxy ketone (**27a**) (99 mg, 77%); $\nu_{max}$(neat) 3 510 (OH) and 1 690 $cm^{-1}$ (ketone); *m/z* 312 $(M - H_2O)^+$ (15%) and 281 (100).

When this reaction was repeated using 3 equiv. of water in THF or 3 equiv. of methanol in THF rather than 2% aqueous THF, no reaction was observed.

*Desulphonylation of the Carbonate* (**19b**) *using Aluminium Amalgam.*—The carbonate derivative (**19b**) (197 mg, 0.38 mmol) was dissolved in 2% aqueous THF (30 ml) at 0 °C. To this was added aluminium amalgam (500 mg, 190 mmol). Stirring was continued at 0 °C for 2 h and then at room temperature for 4 h. After this time the solid inorganic material was filtered off and washed with ether (15 ml). The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and evaporated to yield a yellow gum (185 mg). Purification of the crude product on a chromatotron [silica, ether–light petroleum (3:2)] yielded the hydroxy ketone (**27b**) (113 mg, 75%) as a colourless gum, $\nu_{max}$(neat) 3 495 (OH), 1 760 (carbonate) and 1 685 $cm^{-1}$ (ketone); see Tables 5 and 6 for $^1H$ and $^{13}C$ NMR data; *m/z*(CI) 385 $(M - 18 + H)^+$ (75%).

The methoxymethyl ether derivative (**19c**) was treated in the same fashion to that described above. In this experiment there was no observed reaction and the starting material was recovered.

*Desulphonylation of the Methoxymethyl Ether* (**19c**) *using Sodium Amalgam.*—The methoxymethyl ether (**19c**) (150 mg, 0.30 mmol) was dissolved in a solution of THF/MeOH (3:2) (40 ml) and $NaH_2PO_4 \cdot H_2O$ (1 g) was added as a buffering agent. To the resultant mixture was added sodium amalgam (2.78 g, 8 equiv. of sodium). The reaction mixture was stirred at room temperature for 5 h, after which it was poured into brine (20 ml), and extracted with ether (3 × 25 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to yield a white gum (85 mg). Purification of the crude product on a chromatotron [silica, EtOAc–$CH_2Cl_2$ (1:1)] yielded the hydroxy ketone (**27c**) (55 mg, 49%) as a colourless gum, $\nu_{max}$(neat), 3 500 (hydroxy), and 1 680 $cm^{-1}$ (ketone); see Tables 5 and 6 for $^1H$ and $^{13}C$ NMR; *m/z*(CI) 357 $(M - 18 + H)^+$ (100%).

*Reaction of* (**19c**) *with Tributylstannyl-lithium.*—A solution of $Bu_3SnLi$ (3.87 mmol) in THF (15 ml) was added to a stirred solution of (**19c**) (160 mg, 0.32 mmol) in dry THF (10 ml) at −78 °C under argon, and stirring was continued at −78 °C for 20 min. Analysis of the reaction mixture by HPLC showed the formation of approximately 33% of a new product. Since after the mixture had been stirred for a further 1 h at −78 °C the reaction had not progressed, a further portion of $Bu_3SnLi$ (3.87 mmol) in THF (5 ml) was added. Analysis of the reaction mixture after it had been stirred for a further 30 min at −78 °C showed the reaction to be *ca.* 70% complete. A final portion of $Bu_3SnLi$ (3.87 mmol) in THF (5 ml) was added and the reaction mixture stirred for a further 20 min at −78 °C. After this time saturated aqueous $(NH_4)_2SO_4$ (15 ml) was added and the reaction mixture allowed to warm to room temperature over a period of 45 min. The resultant mixture was extracted with ether (3 × 20 ml), dried ($MgSO_4$), filtered, and evaporated to yield a yellow oil. Purification of the crude product on a chromatotron (silica, 3% EtOAc in $CH_2Cl_2$) yielded (**28**) (85 mg, 75%) as a colourless *gum*, $\nu_{max}$(neat) 3 510 $cm^{-1}$ (OH); $\delta_H$(250 MHz; $CDCl_3$) 3.16 (1 H, q, C*H*$CH_2$), 3.42 (3 H, s, $OCH_3$), 3.63 (1 H, dd, *J* 5.7 and 10.8 Hz, C*H*$_2$OH), 3.77 (1 H, dd, *J* 6.5 and 10.9 Hz, C*H*$_2$OH), 3.84/3.85 (6 H, s, 2 × $OCH_3$), 4.59 (1 H, d, *J* 5.7 Hz, $OCH_2O$), 4.65 (1 H, d, *J* 5.7 Hz, $OCH_2O$), 4.93 (1 H, d, *J* 6.1 Hz, PhCH), 6.7–7.5 (8 H, m, aromatic H); *m/z*(CI) 357 $(M + H)^+$ (100%) [Found: $(M + H)^+$, 357.171 40. $C_{21}H_{24}O_5$ requires $(M + H)^+$, 357.170 20].

*Reaction of* (4R,αS)-2-(3,4-*Dimethoxyphenyl*)-3-*phenylsulphonyl*-4-(α-*phenylthiomethoxybenzyl*)-4,5-*dihydrofuran* (**19g**) *with Lithium Naphthalenide.*—(*a*) Lithium naphthalenide (0.5M; 1.42 ml, 0.71 mmol) (prepared by the addition of lithium metal to a solution of naphthalene in THF) was added to a stirred solution of (**19g**) (135 mg, 0.24 mmol) in THF (10 ml) at −78 °C under nitrogen. The reaction mixture was stirred at −78 °C for 20 min before the addition of a further portion of lithium naphthalenide (0.5M; 0.47 ml, 0.24 mmol). The reaction mixture was allowed to warm to 0 °C over a period of 30 min and stirring was continued for a further 30 min, after which the reaction mixture was poured into water (10 ml) and extracted with ether (3 × 20 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to yield an off-white solid. Purification of the crude product on a chromatotron (silica, $CH_2Cl_2$) yielded two fractions. The first was identified as the starting phenylsulphide (**19g**) (45 mg, 33%), and the second was identified as the hydroxy ketone (**27g**) (61 mg, 56%); $\nu_{max}$(neat), 3 510 (OH), and 1 680 $cm^{-1}$ (C=O); see Tables 5 and 6 for $^1H$ and $^{13}C$ NMR data; *m/z*(CI) 435 $(M - 18 + H)^+$ (19%). This reaction was repeated, the reaction mixture being heated under reflux for 3 h; this gave a similar result to that described above.

(*b*) Lithium naphthalenide (0.5M; 1.56 ml, 0.78 mmol) was added to a stirred solution of (**19g**) (150 mg, 0.26 mmol) in dry THF (15 ml) at −78 °C under nitrogen. The reaction mixture was stirred at −78 °C for 20 min and then a further portion of lithium naphthalenide (0.5M; 0.52 ml, 0.26 mmol) was added. The reaction mixture was allowed to warm to 0 °C over a period of 30 min and then a final addition of lithium naphthalenide (0.5M; 0.52 ml, 0.26 mmol) was made. The reaction mixture was stirred for 1 h at 0 °C and then a solution of TFA (0.1 ml, 1.31 mmol) in THF (10 ml) was added. Stirring was continued for 1.5 h with the reaction mixture being allowed to warm to room temperature. It was then quenched with water (15 ml) and extracted with ether (3 × 15 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to yield an off-white solid. Purification of the crude product on a chromatotron (silica, $CH_2Cl_2$) yielded (**27g**) (104 mg, 88%).

*Reaction of* (**19g**) *with Lithium Naphthalenide and an Electrophile.*—(*a*) Lithium naphthalenide (0.5M; 1.45 ml, 0.73 mmol) was added to a stirred solution of (**19g**) (140 mg, 0.24 mmol) in dry THF (20 ml) at −78 °C under argon. Stirring was continued at −78 °C for 20 min after which a further portion of lithium naphthalenide (0.49 ml, 0.24 mmol) was added; the reaction mixture was allowed to warm up to 0 °C over a period of 30 min, when a final portion of lithium naphthalenide (0.49 ml, 0.24 mmol) was added. Stirring was continued at 0 °C for 1 h at which point benzaldehyde (0.5 ml, 4.9 mmol) was added. The reaction mixture was then allowed to warm to room temperature and stirred for a further 2.5 h. The reaction mixture was then quenched with water (15 ml) and extracted with ether

(3 × 15 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated. The crude product was purified on a chromatotron (silica, $CH_2Cl_2$) to yield the hydroxy ketone (**27g**) (88 mmg, 80%) and benzyl alcohol.

(*b*) The above reaction was repeated, the benzaldehyde being replaced by ethyl chloroformate (3 ml); once again the hydroxy ketone (**27g**) was obtained as the only product.

(*c*) The above reaction was repeated except DMEU (8 ml) was added to the reaction mixture and stirred for 1 h prior to the addition of ethyl chloroformate. This again produced (**27g**) (85%) as the only product.

(*d*) A final reaction was performed using sodium naphthalenide in place of lithium naphthalenide, followed by the addition of ethyl chloroformate. This yielded a complex mixture of products which were not identified.

*Reaction of* (**18c**) *with Lithium Aluminium Hydride.*—A solution of lithium aluminium hydride (1.49M; 0.27 ml, 0.40 mmol) was added to a stirred solution of (**18c**) (140 mg, 0.32 mmol) in dry THF (20 ml) at −25 °C under nitrogen. Stirring was continued at −25 °C for 1 h and then at 0 °C for 4 h. The reaction mixture was then quenched with water (10 ml) and extracted with ether (3 × 10 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to give a yellow gum (133 mg). Purification of the crude product on the chromatotron (silica, 2% EtOAc in $CH_2Cl_2$) yielded (**29**) (77 mg, 55%) as a colourless *gum*, $\nu_{max}$(neat) 3 520 (OH) and 1 310 and 1 145 $cm^{-1}$ ($SO_2$); $\lambda_{max}$($CH_2Cl_2$) 229.7 nm; $\delta_H$(100 MHz; $CDCl_3$) 2.3–2.6 (1 H, m, 4-H), 3.0–3.2 (2 H, m, 2-H), 3.24 (3 H, s, OMe), 3.4–3.9 (2 H, m, 5-H), 4.3–4.5 (1 H, m, 3-H), 4.4 (2 H, s, $OCH_2O$), 5.1 (1 H, d, *J* 10 Hz, 6-H), and 6.8–8.1 (10 H, m, aromatic H); $\delta_C$(25.2 MHz; $CDCl_3$) 34.81 (t, C-2), 48.28 (d, C-4), 56.28 (q, OMe) 59.86 (t, C-5), 63.64 (d, C-3), 77.93 (d, C-6), and 95.21 (t, $OCH_2O$); *m/z*(CI) 458 $(M + NH_4)^+$ [Found: $(M + NH_4)^+$, 458.201 260. $C_{25}H_{28}O_5S$ requires $(M + NH_4)^+$, 458.200 12].

*Preparation of* (2S,3S,4R,αS)-4-(α-*Hydroxybenzyl*)-2-*phenyl*-3-*phenylsulphonyltetrahydrofuran* (**30a**).—Compound (**18c**) (105 mg, 0.24 mmol) was dissolved in dry $CH_2Cl_2$ (15 ml) and stirred at −78 °C under argon. $BF_3$·$Et_2O$ (0.06 ml, 0.48 mmol) was added and stirring continued at −78 °C for 10 min before the addition of $Et_3SiH$ (0.40 ml, 2.52 mmol). The reaction mixture was stirred at −78 °C for 1 h and then at room temperature for 3 h. After this time the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (10 ml) and extracted with $CH_2Cl_2$ (2 × 15 ml). The combined organic extracts were washed with brine (20 ml), dried ($MgSO_4$), filtered, and evaporated to give a yellow flaky solid (150 mg). Purification of the crude product on a chromatotron (silica, $CH_2Cl_2$) yielded (**30a**) (79 mg, 83%) as a flaky white *solid*, $\nu_{max}$(KBr), 3 520 (OH) and 1 310 and 1 160 $cm^{-1}$ ($SO_2$); $\lambda_{max}$($CH_2Cl_2$) 230.9 nm (ε 3 241); see Tables 7 and 8 for $^1H$ and $^{13}C$ NMR data; *m/z*(CI) 412 $(M + NH_4)^+$ (22%) [Found: $(M + NH_4)^+$, 412.158 84. $C_{23}H_{22}O_4S$ requires $(M + NH_4)^+$, 412.158 26].

This reaction was repeated omitting the $BF_3$·$OEt_3$, and in this case unchanged starting material was recovered. The reaction was repeated, the reaction mixture being quenched with $D_2O$. Analysis of the resultant product by $^1H$ NMR showed no deuterium incorporation at C-2 or C-3.

*Preparation of* (2S,3S,4R,αS)-2-*Phenyl*-3-*phenylsulphonyl*-4-(α-*ethoxycarbonyloxybenzyl*)*tetrahydrofuran* (**30b**).—Compound (**18b**) (137 mg, 0.295 mmol) was dissolved in dry $CH_2Cl_2$ (15 ml) and stirred at −78 °C under argon. $BF_3$·$Et_2O$ (0.08 ml, 0.59 mmol) was added and stirring was continued at −78 °C for 10 min before the addition of $Et_3SiH$ (0.47 ml, 2.95 mmol). The reaction mixture was stirred at −78 °C for 1 h and then at room temperature for 3 h. After this time the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (10 ml) and extracted with $CH_2Cl_2$ (2 × 10 ml). The combined organic extracts were washed with brine (15 ml), dried ($MgSO_4$), filtered, and evaporated to yield a yellow gum (161 mg). Purification of the crude product on a chromatotron (silica, $CH_2Cl_2$) yielded (**30b**) (103 mg, 75%), as a flaky white *solid*, $[\alpha]_D^{20}$ +20.06° (*c* 0.94 in $CHCl_3$); $\nu_{max}$(KBr) 1 755 $cm^{-1}$ (carbonate) and 1 310 and 1 155 $cm^{-1}$ ($SO_2$); $\lambda_{max}$($CH_2Cl_2$) 230 nm (ε 2 415); see Tables 7 and 8 for $^1H$ and $^{13}C$ NMR data; *m/z*(CI) 484 $(M + NH_4)^+$ (1%) [Found: $(M + NH_4)^+$, 484.184 14. $C_{26}H_{26}O_6$ requires $(M + NH_4)^+$, 484.179 39].

*Preparation of* (2S,3S,4R,αS)-2-(3,4-*Dimethoxyphenyl*)-3-*phenylsulphonyl*-4-(α-*hydroxybenzyl*)*tetrahydrofuran* (**31a**).—Compound (**19a**) (196 mg, 0.434 mmol) was dissolved in dry $CH_2Cl_2$ (20 ml) and stirred at −78 °C under argon. $BF_3$·$Et_2O$ (0.11 ml, 0.868 mmol) was added and stirring was continued at −78 °C for 10 min before the addition of $Et_3SiH$ (0.69 ml, 8.68 mmol). The reaction mixture was stirred at −78 °C for 1 h and then at room temperature for 3 h. After this time it was quenched with saturated aqueous $NaHCO_3$ (15 ml) and extracted with $CH_2Cl_2$ (2 × 20 ml). The combined organic extracts were washed with brine (20 ml), dried ($MgSO_4$), filtered, and evaporated to yield a flaky white solid (230 mg). Purification of the crude product on the chromatotron (silica, 3% EtOAc in $CH_2Cl_2$) yielded (**31a**) (170 mg, 85%), m.p. 59–61 °C; $[\alpha]_D^{20}$ +1.38° (*c* 0.55 in $CHCl_3$) (Found: C, 65.85; H, 5.6. $C_{25}H_{26}O_6S$ requires C, 66.1; H, 5.7%); $\nu_{max}$(KBr) 3 510 (OH) and 1 305 and 1 150 $cm^{-1}$ ($SO_2$); $\lambda_{max}$($CH_2Cl_2$) 232.5 nm (ε 11 910); see Tables 7 and 8 for $^1H$ and $^{13}C$ NMR data; *m/z* 454 ($M^+$, 2%) and 205 (100) (Found: $M^+$, 454.145 73. $C_{25}H_{26}O_6S$ requires $M^+$, 454.145 01).

*Preparation of* (2S,3S,4R,αS)-2-(3,4-*Dimethoxyphenyl*)-3-*phenylsulphonyl*-4-(α-*ethoxycarbonyloxybenzyl*)*tetrahydrofuran* (**31b**).—The alcohol (**31a**) (168 mg, 0.37 mmol) was dissolved in dry THF (15 ml) and cooled to −78 °C under argon. To this was added, *via* a syringe, BuLi (1.9M; 0.39 ml, 0.74 mmol). Stirring was continued at −78 °C for 40 min, after which freshly distilled ethyl chloroformate (0.03 mmol) was added. The reaction mixture was allowed to warm to −20 °C over a period of 45 min, after which it was recooled to −78 °C. A precooled solution of TFA (0.37 mmol) in THF (5 ml) was then added *via* a double ended needle. The reaction mixture was stirred at −78 °C for 30 min and then allowed to warm to room temperature over a period of 1.5 h. After this time the reaction mixture was quenched with 1M aqueous $Na_2CO_3$ (15 ml) and extracted with ether (2 × 15 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to yield an orange gum (172 mg). Purification of the crude product on a chromatotron (silica, $CH_2Cl_2$) yielded the *carbonate* (**31b**) (149 mg, 77%) as a flaky white solid, m.p. 53–55 °C $[\alpha]_D^{20}$ −27.5° (*c* 0.45 in $CHCl_3$); $\nu_{max}$(KBr) 1 755 (carbonate) and 1 310 and 1 150 $cm^{-1}$ ($SO_2$); $\nu_{max}$($CH_2Cl_2$) 229.2 nm (ε, 8 001); see Tables 7 and 8 for $^1H$ and $^{13}C$ NMR data; *m/z* 526 ($M^+$, 10%) and 205 (100) (Found: $M^+$, 526.164 14. $C_{28}H_{30}O_8S$ requires $M^+$, 526.166 13).

This reaction was repeated using an excess (10 equiv.) of ethyl chloroformate. This resulted in the formation of the carbonate (**31b**) in an 80% yield.

*Preparation of* (2S,3S,4R,αS)-2-(3,4-*Dimethoxyphenyl*)-3-*phenylsulphonyl*-4-(α-*methoxymethyloxybenzyl*)*tetrahydrofuran* (**31c**).—Compound (**31a**) (0.34 g, 0.749 mmol) was dissolved in dry THF (20 ml) and stirred at −78 °C under nitrogen. BuLi (2.0M; 0.37 ml, 0.794 mmol) was added and stirring was continued at −78 °C for 45 min before the addition of freshly

distilled chloromethyl methyl ether (0.28 ml, 3.00 mmol). The reaction mixture was allowed to warm to room temperature over a period of 1 h and then stirred for 3 h, after which the solvent was evaporated. The resultant crude product was dissolved in a minimum amount of THF and pentane was added to precipitate out the LiCl. The precipitate was filtered off and the solvent evaporated to yield a yellow gum (0.41 g), which was purified on a chromatotron (silica, $CH_2Cl_2$) to give (**31c**) (0.33 g, 88%) as a white solid, m.p. 124–125 °C; $[\alpha]_D^{20}$ −42.3° (*c* 0.30 in $CHCl_3$) (Found: C, 65.2; H, 6.15. $C_{27}H_{30}O_7S$ requires C, 65.1; H, 6.0%); $\nu_{max}$(KBr) 1 310 and 1 155 $cm^{-1}$ ($SO_2$); $\lambda_{max}$($CH_2Cl_2$) 230.7 nm (ε 10 475); see Tables 7 and 8 for $^1H$ and $^{13}C$ NMR data; *m/z* 498 ($M^+$, 2%) and 205 (100) (Found: $M^+$, 498.168 152. $C_{27}H_{30}O_7S$ requires $M^+$, 498.171 22).

*Preparation of* (2S,3S,4R,αS)-2-(3,4-*Dimethoxyphenyl*)-3-*phenylsulphonyl*-4-(α-*methylthiomethoxybenzyl*)*tetrahydrofuran* (**31e**).—To a stirred suspension of NaH (22 mg, 0.634 mmol) in dry monoglyme (5 ml) at 0 °C under argon was added a solution of (**31a**) (144 mg, 0.319 mmol) in monoglyme (15 ml). Stirring was continued at 0 °C for 10 min before the addition of NaI (47.5 mg, 0.317 mmol) and freshly distilled chloromethyl methyl sulphide (0.03 ml, 0.319 mmol). The reaction mixture was stirred at 0 °C for 1 h and then at room temperature for 5 h, after which water (10 ml) was added, and the resultant solution was extracted with ether (3 × 15 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to yield a yellow solid. This was purified on a chromatotron (silica, 5% EtOAc in $CH_2Cl_2$) to yield (**31e**) (146 mg, 90%) as a white *solid*, m.p. 110–111 °C; $[\alpha]_D^{20}$ −67.1° (*c* 0.8 in $CHCl_3$): $\nu_{max}$(KBr) 1 330 and 1 170 $cm^{-1}$ ($SO_2$); $\lambda_{max}$($CH_2Cl_2$) 228.5 nm (ε 7 633); for $^1H$ and $^{13}C$ NMR data see Tables 7 and 8; *m/z* 514 ($M^+$, 15%) (Found: $M^+$, 514.148 60. $C_{27}H_{30}O_6S_2$ requires 514.148 48).

*Preparation of* (2S,3S,4R,αS)-2-(3,4-*Dimethoxyphenyl*)-3-*phenylsulphonyl*-4-(α-*methylsulphonylmethoxybenzyl*)*tetrahydrofuran* (**31j**).—A solution of MCPBA (91 mg, 0.524 mmol) in $CH_2Cl_2$ (10 ml) was added to a stirred solution of (**31e**) (135 mg, 0.262 mmol) in dry $CH_2Cl_2$ (15 ml) at −10 °C under argon. Stirring was continued at <0 °C for 1 h and then at room temperature for 12 h, after which the reaction mixture was quenched with saturated aqueous sodium bisulphite and extracted with $CH_2Cl_2$ (2 × 15 ml). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (15 ml), dried ($MgSO_4$), and evaporated to yield a white solid (151 mg). Crystallization of the crude product from methanol yielded (**31j**) (112 mg, 78%) as white crystals, m.p. 89–90 °C; $[\alpha]_D^{20}$ −47.2° (*c* 0.42 in $CHCl_3$); $\nu_{max}$(KBr) 1 305 and 1 140 $cm^{-1}$ ($SO_2$); $\lambda_{max}$($CH_2Cl_2$) 229.1 nm (ε 7 261); see Tables 7 and 8 for $^1H$ and $^{13}C$ NMR data; *m/z* 546 ($M^+$, 6%) and 205 (100) (Found: $M^+$, 546.132 33. $C_{27}H_{30}O_8S_2$ requires $M^+$, 546.1382).

*Preparation of* (2S,3S,4R,αS)-2-(3,4-*Dimethoxyphenyl*)-3-*phenylsulphonyl*-4-(α-*phenylthiomethoxybenzyl*)*tetrahydrofuran* (**31g**)—To a stirred suspension of NaH (20 mg, 0.54 mmol) in dry monoglyme (5 ml) at 0 °C under argon, was added, *via* a double ended needle, a solution of the saturated alcohol (**31a**) (123 mg, 0.27 mmol) in monoglyme (10 ml) The resultant mixture was stirred at 0 °C for 10 min before the addition of NaI (40 mg, 0.27 mmol) and chloromethyl phenyl sulphide (0.05 ml, 0.27 mmol). Stirring was continued at 0 °C for 1 h and then at room temperature for 16 h, after which the reaction mixture was quenched with water (10 ml) and extracted with ether (3 × 15 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to yield a white solid (160 mg). Crystallization of the crude product from methanol yielded (**31g**) (119 mg, 76%) as white *crystals*, m.p. 164–165 °C; $[\alpha]_D^{20}$ −267.8 (*c* 1.0 in $CHCl_3$) (Found: C, 66.8; H, 5.75. $C_{32}H_{32}O_6S_2$ requires C, 66.7; H, 5.6%); $\nu_{max}$(KBr) 1 305 and 1 145 $cm^{-1}$ ($SO_2$); $\lambda_{max}$($CH_2Cl_2$) 229 nm; see Tables 7 and 8 for $^1H$ and $^{13}C$ NMR data; *m/z*(CI) 594 $(M + NH_4)^+$ (100%) [Found: $(M + NH_4)^+$, 594.198 410. $C_{32}H_{32}O_6S_2$ requires $(M + NH_4)^+$, 594.198 41].

*Preparation of* (2S,3S,4R,αS)-2-(3,4-*Dimethoxyphenyl*)-3-*phenylsulphonyl*-4-(α-*phenylsulphonylmethoxybenzyl*)*tetrahydrofuran* (**31h**)—A solution of MCPBA (120 mg, 0.66 mmol) in $CH_2Cl_2$ (10 ml) was added to a stirred solution of (**31g**) (188 mg, 0.33 mmol) in dry $CH_2Cl_2$ (10 ml) at −23 °C under argon. Stirring was continued at −20 °C for 1 h and then at room temperature for 16 h, after which the reaction mixture was quenched with aqueous $NaHCO_3$ (10 ml) and extracted with $CH_2Cl_2$ (2 × 15 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to yield a white solid (219 mg). Crystallization of this from methanol yielded the *phenylsulphone* (**31h**) (163 mg, 82%) as white crystals, m.p. 149–150 °C; $[\alpha]_D^{20}$ −52.43° (*c* 0.7 in $CHCl_3$) (Found: C, 63.1; H, 5.35. $C_{32}H_{32}O_8S_2$ requires C, 63.2; H, 5.3%); $\nu_{max}$(KBr) 1 305 and 1 150 $cm^{-1}$ ($SO_2$); $\lambda_{max}$($CH_2Cl_2$) 228.2 (ε 11 010); see Tables 7 and 8 for $^1H$ and $^{13}C$ NMR data; *m/z* 608 ($M^+$, 9%) and 205 (100) (Found: $M^+$, 608.150 74. $C_{32}H_{32}O_8S_2$ requires $M^+$, 608.153 86).

*Attempted Cyclization of the Methylthiomethyl Ether* (**31e**).—The methylthiomethyl ether (**31e**) (146 mg, 0.284 mmol) was dissolved in dry THF (15 ml) and cooled to −78 °C under a nitrogen atmosphere. To this was added, *via* a syringe, BuLi (2.0M; 0.14 ml, 0.248 mmol). The reaction mixture was stirred at −78 °C for 1 h, and then allowed to warm to 0 °C over a period of 2 h. After this time it was quenched with saturated $(NH_4)_2SO_4$ (10 ml) and extracted with ether (3 × 10 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to yield a brown gum (157 mg). Purification of the crude product on a chromatotron yielded two fractions. The first contained a mixture of products which were not identified, whilst the second was identified as the ring-opened product (**32e**) (79 mg, 50%); $\nu_{max}$(neat) 3 520 (OH) and 1 300 and 1 130 $cm^{-1}$ ($SO_2$); $\delta_H$(250 MHz; $CDCl_3$) 0.26–1.2 (9 H, m, butyl), 2.25 (3 H, s, $SCH_3$), 3.1 (1 H, m, 4-H), 3.6 (3 H, m, 3-H and 5-H), 3.72 (3 H, s, $OCH_3$), 3.84 (3 H, s, $OCH_3$), 4.14 (1 H, d, *J* 8.2 Hz, 2-H), 4.31 (1 H, d, *J* 9.4 Hz, $OCH_2S$), 4.96 (1 H, d, *J* 8.3 Hz, 6-H), and 6.5–7.4 (13 H, m, aromatic H); *m/z* 572 ($M^+$, 15%).

*Reaction of the Phenylthiomethyl Ether* (**31g**) *with Lithium Naphthalenide*.—The phenylthiomethyl ether derivative (**31g**) (147 mg, 0.25 mmol) was dissolved in dry THF (20 ml) and stirred at −78 °C under argon. To this was added lithium naphthalenide (0.5M; 1.5 ml, 0.75 mmol). Stirring was continued for 20 min after which a further portion of lithium naphthalenide (0.5M; 0.5 ml, 0.25 mmol) was added. The reaction mixture was allowed to warm to room temperature over a period of 1 h and stirred for a further 3 h. It was then heated under reflux for 1 h, before being quenched with saturated aqueous $(NH_4)_2SO_4$ (10 ml) and extracted with ether (3 × 10 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to give a brown solid, which was purified on a chromatotron (silica, $CH_2Cl_2$) to give first (**33**) (22 mg, 20%); $\delta_H$(250 MHz; $CDCl_3$) 1.84 (1 H, m, 4-H), 2.4 and 2.8 (2 H, m, 3-H), 3.76 (2 H, m, 5-H), 3.85 (3 H, s, OMe), 3.87 (3 H, s, OMe), 4.69 (1 H, d, *J* 8.8 Hz, 6-H), 4.78 (1 H, dd, *J* 6.10 Hz, 2-H), 4.54 and 5.01 (2 H, d, *J* 11.9 Hz, $SCH_2O$), and 6.8–7.5 (13 H, m, aromatic H); *m/z*(CI) 436 ($M^+$, 5%); and then compound (**34**) (33 mg, 30%); $\delta_H$(250 MHz, $CDCl_3$) 2.72 (1 H, m, 4-H), 3.65 (2 H, m, 5-H), 3.80 (3 H, s, OMe), 3.87 (3 H, s, OMe), 5.05 (1 H, d, *J* 6 Hz, 6-H), 5.99 (1 H, dd, *J* 9, 16 Hz, 3-H), 6.30 (1 H, d, *J* 16 Hz, 2-H), 4.40 and 5.10 (2 H, d, *J* 11.9, $SCH_2O$), and 6.8–7.5 m (13 H, m, aromatic H); *m/z*(CI) 419 ($M$ − 18 + H, 5%); and compound

(**35**) (24 mg, 29%); $\delta_H$(250 MHz; $CDCl_3$), 2.74 (1 H, m, 4-H) 3.25 (3 H, s, $OCH_3$) 3.52 (2 H, m, 5-H), 3.86 (3 H, s, OMe), 3.88 (3 H, s, OMe), 4.43 (1 H, d, *J* 5 Hz, 6-H), 3.98 (1 H, dd, *J* 9, 16 Hz, 3-H), 6.28 (1 H, d, *J* 16 Hz, 2-H), and 6.6–7.4 m (8 H, m, aromatic H); *m*/*z*(CI) 329 $(M + H)^+$ (5%).

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36 Details of the X-ray determination may be obtained from Prof. M. Hursthouse, Queen Mary College.

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