Synthesis of Enantiomerically Pure 2,5-Disubstituted Tetrahydrofurans Using Readily Prepared (2*S*)-1-Phenylsulphonylalkan-2-ols

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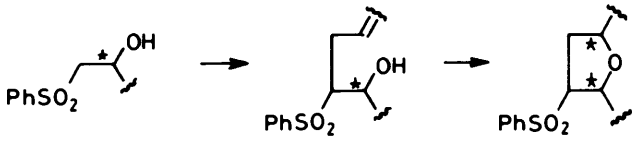
Enantiomerically pure (2*S*)-1-phenylsulphonylalkan-2-ols [*S*—(**1**)] have been prepared from 1-chloro-3-phenylsulphonylpropan-2-one (**2**) by the following successive procedures: reduction with baker's yeast, epoxidation with silver(I) oxide, and alkylation with a Grignard reagent. Alkylation of dianions of *S*—(**1**), followed by phenylselenocyclization gave enantiomerically pure 2,5-disubstituted tetrahydrofurans [*S*—(**8**)] with high regioselectivity.

Enantiomerically pure 2,5-disubstituted tetrahydrofuran units are found in many natural products, including polyether antibiotics[1] and furanoterpenes,[2] and there has been increasing interest in the synthesis of the tetrahydrofuran ring system.[3–5] One of the most effective ways to construct this ring system is electrophilic cyclization[6] of a γ,δ-unsaturated alcohol by use of iodine, *N*-bromosuccinimide, mercury(II) acetate, benzeneselenenyl chloride, *etc.*, but an enantiomerically pure γ,δ-unsaturated alcohol is not readily available. The central features of the present synthetic strategy are: (*a*) preparation of enantiomerically pure (2*S*)-1-phenylsulphonylalkan-2-ols [*S*—(**1**)] by asymmetric reduction with baker's yeast; (*b*) introduction of an allyl group in enantiomerically pure form; and (*c*) construction of the tetrahydrofuran ring system *via* phenylselenocyclization (Scheme 1).

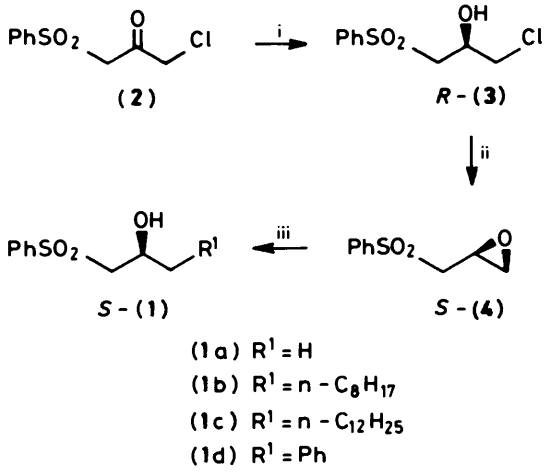


Scheme 1.

Asymmetric reduction of ketones with baker's yeast is increasingly being recognized as a valuable approach to organic synthesis.[7,8] Since reduction of 1-phenylsulphonylpropan-2-one with baker's yeast resulted in formation of (2*S*)-1-phenylsulphonylpropan-2-ol [*S*—(**1a**)] in 100% enantiomeric excess (e.e.),[9] it is interesting to see whether a similar reduction is widely applicable to other 1-phenylsulphonylalkan-2-ones. Treatment of a dianion of 1-phenylsulphonylalkan-2-ol (**1**) with sodium iodoacetate leads to carbon-carbon bond formation.[10] It is also worthwhile clarifying whether an allyl group can be introduced on a dianion of *S*—(**1**) to yield enantiomerically pure γ,δ-unsaturated alcohols.

Results and Discussion

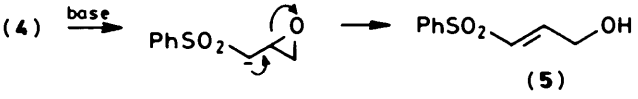
Since there have been many reports relating to enantioselective reduction of ketones containing a sulphur atom with baker's yeast,[11] we first tried to prepare *S*—(**1**) directly from 1-phenylsulphonylalkan-2-ones. However, the reduction of 1-phenylsulphonylpentan-2-one afforded the corresponding alcohol only in 53% yield and 46% e.e., and 1-phenylsulphonyloctan-2-one was found to be unreactive towards baker's yeast. In order to obtain an alcohol with enantiomerically high purity in considerable yield the following must be taken into consideration: (*a*) the ketone, in which one of the groups bonded to a carbonyl group is much smaller than the other,[7] must be employed as a starting substrate; (*b*) the alcohol must be easily separable from an aqueous reaction mixture; and (*c*) recrystallization can enhance the enantiomeric excess. Hence we tried to obtain *S*—(**1**) from 1-chloro-3-phenylsulphonylpropan-2-one (**2**) (Scheme 2).



Scheme 2. *Reagents:* i, Baker's yeast; ii, Ag_2O; iii, R^1MgBr/CuI

Compound (**2**) was synthesized by condensation of sodium benzenethiolate and 1,3-dichloropropan-2-one in water, followed by oxidation. A suspension of (**2**), baker's yeast, and sucrose in water was stirred at 20 °C for 2 days. After extraction of the produced alcohol with dichloromethane, chromatography on silica gel gave (2*R*)-1-chloro-3-phenylsulphonylpropan-2-ol [*R*—(**3**)] as a solid in 85% yield (84% e.e.), and recrystallization from ethanol readily yielded *R*—(**3**) in enantiomerically pure form *i.e.*, use of the sulphone overcomes the difficulty in isolation and recrystallization. The (*R*)-configuration was determined by comparison of authentic (2*S*)-1-phenylsulphonylpropan-2-ol[9] [*S*—(**1a**)] with the alcohol formed by reduction of *R*—(**3**) with tributyltin hydride and azoisobutyronitrile (AIBN).

On the other hand, use of the sulphone causes other problems, *i.e.*, the epoxide (**4**) containing an electron-withdrawing sulphonyl group at the β-position readily undergoes eliminative ring fission even under mildly basic conditions giving 3-phenylsulphonylprop-2-en-1-ol (**5**).[12,13]



This problem was solved in the following manner. Treatment of *R*—(**3**) with silver(I) oxide[14] in heated 1,2-dimethoxyethane (DME) generated (2*S*)-1,2-epoxy-3-phenylsulphonylpropane

Table 1. Preparation of compounds (6)

(6a)[a]	R^1	R^2	R^3	Yield (%)[b]	(6A):(6B)
S—(6a)	H	Me	H	74	73:27
(6b)	Et	Me	H	82	87:13
(6c)	Pr^i	Me	H	74	79:21
(6d)	$-(CH_2)_5CH-$[c]	Me	H	72	100:0
(6e)	$n\text{-}C_8H_{17}$	H	H	79	87:13
S—(6f)	$n\text{-}C_8H_{17}$	Me	H	80	88:12
(6g)	$n\text{-}C_8H_{17}$	Me	Me	76	90:10
S—(6h)	$n\text{-}C_{12}H_{25}$	Me	H	81	90:10
(6i)	Ph	H	H	69	100:0
S—(6j)	Ph	Me	H	75	100:0
(6k)	Ph	Me	Me	66	100:0

[a] Enantiomerically pure *S*—(6) was obtained from *S*—(1) and racemic (6) from racemic (1). [b] Isolated yield. [c] R^1CH_2 (not R^1).

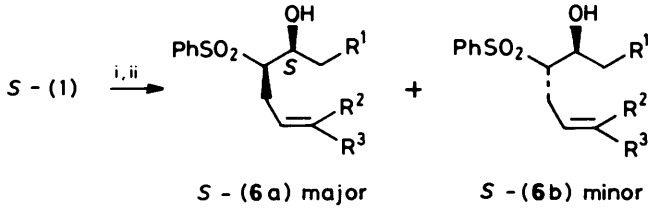
Table 2. Preparation of compounds (7) and (8)

(7)[a,b]	Yield (%)[c]	(8)[a,b]	Yield (%)[c]	(8A):(8B)
S—(7a)	90	*S*—(8a)	90	43:57
(7b)	90	(8b)	92	50:50
(7c)	90	(8c)	99	48:52
(7d)	84	(8d)	88	63:37
(7e)	70	(8e)	(93)[d]	
S—(7f)	90	*S*—(8f)	76	55:45
(7g)	89	(8g)	75	60:40
S—(7h)	88	*S*—(8h)	78	58:42
(7i)	61	(8i)	(89)[d]	
S—(7j)	81	*S*—(8j)	82	58:42
(7k)	72	(8k)	92	64:36

[a] Enantiomerically pure *S*—(7) and *S*—(8) were obtained from *S*—(6), and racemic (7) and (8) from racemic (6). [b] R^1, R^2, R^3 are as shown in Table 1. [c] Isolated yield. [d] Thermally stable selenoxide was obtained.

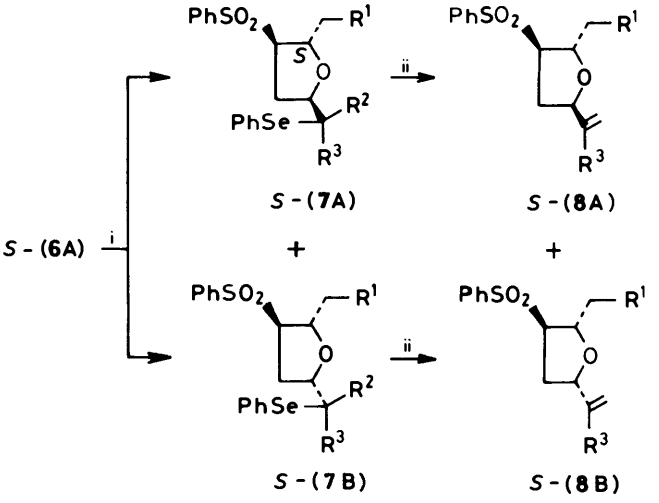
[*S*—(4)] in 85% yield. To a suspension of copper(I) iodide in diethyl ether was added a solution of a Grignard reagent in tetrahydrofuran (THF) at −60 °C, followed by prompt addition of a solution of *S*—(4) in ether–THF.[15] The reaction was completed in 1 min. giving (2*S*)-1-phenylsulphonylundecan-2-ol [*S*—(1b)], (2*S*)-1-phenylsulphonylpentadecan-2-ol [*S*—(1c)], and (2*S*)-1-phenylsulphonyl-3-phenylpropan-2-ol [*S*—(1d)] in 83, 72, and 95% yields, respectively. Although the specific optical rotation of *S*—(1) was in some cases found to be 0°, the enantiomeric excess was 100% as measured by ^{19}F n.m.r. after converting *S*—(1) into the ester of (+)-α-methoxy-α-(trifluoromethyl)phenylacetic acid [(+)-MTPA].

Treatment of a dianion of *S*—(1) with allyl bromide, but-2-enyl bromide, or 3-methylbut-2-enyl bromide at −78 °C produced a diastereoisomeric mixture of the alkylated products [*S*—(6)], which were chromatographed on silica-gel column yielding diastereoisomers [*S*—(6A) and *S*—(6B)] in enantiomerically pure forms (Scheme 3). The configuration of *S*—(6A) and *S*—(6B) will be determined in further work. The ratio of (6A):(6B) increases with the bulkiness of the group R^1. The results obtained from *S*—(1a—d) and other racemic compounds (1) are given in Table 1.



Scheme 3. *Reagents:* i, 2 BuLi; ii, $BrCH_2CH{=}CR^2R^3$

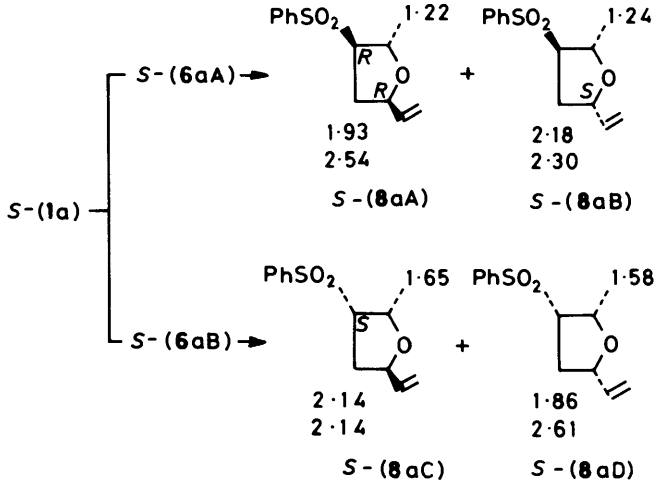
The problem encountered in electrophilic cyclization is that it sometimes provides both the five- and the six-membered rings. We adopted phenylselenocyclization[16,17] because of the ease of removal of a phenylselenenyl group.[18,19] Phenylselenocyclization carried out with *S*—(6A) and benzeneselenenyl chloride in dichloromethane at −78 °C took place regioselectively giving the 2,5-disubstituted tetrahydrofuran [*S*—(7)] in high yields, but not generating the six-membered ring (Scheme 4). A diastereoisomeric mixture of *S*—(7A) and *S*—(7B) in dichloromethane was oxidized with *m*-chloroperbenzoic acid (MCPBA) at −78 °C, quenched with aqueous sodium hydrogen carbonate, and then warmed to room temperature. Work-up and subsequent chromatography on silica-gel column gave the optically active 2,5-disubstituted tetrahydrofurans [*S*—(8A) and *S*—(8B)] (Scheme 4). Although the enantiomeric



Scheme 4. *Reagents:* i, PhSeCl; ii, MCPBA

excess was not determined, it is improbable that the present cyclization resulted in a lowering of the enantiomerical purity.

In order to elucidate the stereochemical problem of the two reactions [(1)→(6) and (6)→(7)], four possible isomeric products [*S*—(8aA) to *S*—(8aD)] generated by the reaction of *S*—(1a) and but-2-enyl bromide were isolated, and some of their ^1H n.m.r. data are shown in Scheme 5.



Scheme 5. $\delta_H(CDCl_3)$ from ^1H n.m.r. spectra

In the minor products [*S*—(**8aC**) and *S*—(**8aD**)] the methyl group must be *cis* to the sulphonyl group because its proton signal appeared at lower field *i.e.* the major isomer *S*—(**6aA**) has the (*R*) configuration at the alkylated carbon atom. In the *trans* 2,5-disubstituted tetrahydrofurans [*S*—(**8aA**) and *S*—(**8aC**)] one of the proton signals of the methylene group in the ring appeared at lower field owing to the deshielding effects of both sulphonyl and vinyl groups *cis* to that proton.[20] These findings suggest that the introduction of a sulphonyl group facilitates the separation and the identification of the products. Some results are given in Table 2.

Although according to the present procedure both the *cis*- and the *trans*-tetrahydrofurans [*S*—(**8B**) and *S*—(**8A**)] were obtained in enantiomerically pure forms, the *cis*-tetrahydrofuran may be synthesized selectively by employing benzyl ethers in the cyclization.[21] Since a sulphonyl and selenenyl groups would be converted into other functional groups, the present strategy may be widely applicable to organic synthesis. A study of the replacement of a sulphonyl group by hydrogen atom[22,23] and another method for cyclization will be presented in a subsequent paper.

Experimental

^1H and ^{19}F N.m.r. spectra were determined at 100 MHz with a JEOL JNM-PS-100 or at 400 MHz with a JEOL JNM-GX-400 spectrometer, and refer to deuteriochloroform solutions with tetramethylsilane as internal standard. I.r. spectra were determined with a Hitachi 215 spectrometer, and mass spectra with a JEOL JMX-DX-300. Column chromatography was performed with Wakogel 200 silica gel, and t.l.c. with Merck plastic sheet silica gel 60 F_{254}.

1-*Chloro*-3-*phenylsulphonylpropan*-2-*one* (**2**).—A suspension of sodium benzenethiolate prepared from benzenethiol (11.0 g, 0.1 mol) and sodium hydroxide (4.0 g, 0.1 mol) in water (100 ml) was added to a stirred solution of 1,3-dichloropropan-2-one (12.7 g, 0.1 mol) in methanol–water (1:3) (100 ml) at 0 °C. The mixture was stirred at 0 °C for 7 h and then at room temperature for a further 10 h. The precipitated product was extracted with chloroform and the extract was washed with water, dried (Na_2SO_4), and evaporated to give a residue. This was recrystallized from ethanol to afford 1-chloro-3-phenylthiopropan-2-one (16.1 g, 80%) as a solid, m.p. 47 °C (lit.,[24] m.p. 47 °C). A solution of MCPBA (80%) (34.5 g, 0.16 mol) in chloroform (300 ml) was added to a stirred solution of this ketone in chloroform (100 ml) at 0 °C, and stirring was continued at room temperature for 30 h. The organic phase was washed with aqueous sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated. The residual solid was recrystallized from ethanol to give compound (**2**) (17.7 g, 76% overall yield) as a solid, m.p. 103 °C (lit.,[24] m.p. 99 °C).

(2R)-1-*Chloro*-3-*phenylsulphonylpropan*-2-*ol* [*R*—(**3**)].—A suspension of compound (**2**) (4.65 g, 20 mmol), baker's yeast (Oriental Yeast Co.) (80 g), and sucrose (20 g) in water was stirred at 20 °C for 2 days. After extraction with dichloromethane the extract was washed with water, dried (Na_2SO_4) and evaporated to dryness. Chromatography of the residue on silica gel with hexane–ethyl acetate (4:1) as eluant yielded the *alcohol* [*R*—(**3**)] (3.99 g, 85%) in 84% e.e. Recrystallization from ethanol gave *R*—(**3**) (2.95 g, 63%) as a solid in 100% e.e., m.p. 89 °C, $[\alpha]_D^{24}$ +10.15° (*c* 1.00 in MeOH); $\nu_{max.}$(Nujol) 3 490 (OH), 1 310, and 1 160 cm^{-1} (SO_2); δ_H($CDCl_3$) 3.34 (1 H, m, CH), 3.36 (2 H, d, *J* 6 Hz, 3-H_2), 3.60 (2 H, d, *J* 6 Hz, 1-H_2), 4.40 (1 H, br s, OH), and 7.5—8.0 (5 H, m, Ph) (Found: C, 46.2; H, 4.8. $C_9H_{11}ClO_3S$ requires C, 46.1; H, 4.7%).

A solution of *R*—(**3**) (84% e.e.) (0.23 g, 1 mmol), tributyltin hydride (1.46 g, 5 mmol), and AIBN (0.16 g, 1 mmol) in benzene (10 ml) was refluxed for 3 h, and worked up in the usual way. Chromatography on silica gel furnished (2*S*)-1-phenylsulphonylpropan-2-ol [*S*—(**1a**)] (0.16 g, 80%), $[\alpha]_D^{23}$ +13.3° (*c* 1.03 in MeOH) {lit.,[9] $[\alpha]_D^{28.5}$ +15.8° (*c* 1.03 in MeOH)}.

(2S)-1,2-*Epoxy*-3-*phenylsulphonylpropane*[*S*—(**4**)].—A suspension of *R*—(**3**) (2.35 g, 10 mmol) and silver(I) oxide (4.63 g, 20 mmol) in DME (30 ml) was stirred at 85 °C for 60 h under an argon atmosphere. Work-up and chromatography of the crude product on silica gel with hexane–ethyl acetate (4:1) as eluant gave the *epoxide* [*S*—(**4**)] (1.66 g, 84%) as a liquid, $[\alpha]_D^{25}$ −3.4° (*c* 1.02 in 1,4-dioxane); $\nu_{max.}$(neat) 1 310 and 1 150 cm^{-1} (SO_2); δ_H($CDCl_3$) 2.42 (1 H, m, 1-H), 2.80 (1 H, m, 1-H), 3.30 (3 H, m, 2-H, CH_2), and 7.4—8.0 (5 H, m, Ph); *m/z* 198.0 (M^+, 15%), 169 (43), and 77 (100) (Found: M^+ 198.0349. $C_9H_{10}O_3S$ requires *M*, 198.0350).

(2S)-1-*Phenylsulphonylalkan*-2-*ols* [*S*—(**1**)].—A solution of a Grignard reagent (15 mmol) in THF (15 ml) was added dropwise to copper(I) iodide (2.86 g, 15 mmol) in ether (15 ml) at −60 °C under an argon atmosphere, and to the resulting mixture was added quickly a solution of (**4**) (1.98 g, 10 mmol) in THF–ether (1:1) (20 ml). The resulting mixture was stirred for 5 min., and then quenched with saturated aqueous ammonium chloride. The organic extract was washed with 5% hydrochloric acid and water, dried (Na_2SO_4), and evaporated to dryness. Chromatography of the residue on silica gel with hexane–ethyl acetate (4:1) as eluant yielded the alcohol [*S*—(**1**)] in enantiomerically pure form. (2S)-1-*Phenylsulphonylundecan*-2-*ol* [*S*—(**1b**)] (2.59 g, 83%); a liquid; $[\alpha]_D^{22}$ 0°, $[\alpha]_{365}^{22}$ −2.7° (*c* 1.15 in MeOH); $\nu_{max.}$(neat) 3 450 (SO_2), 1 310, and 1 160 cm^{-1} (OH); δ_H($CDCl_3$) 0.86 (3 H, t, *J* 6 Hz, Me), 1.0—1.6 (16 H, m, CH_2), 3.20 (2 H, m, 1-H_2), 3.40 (1 H, m, CH), 4.16 (1 H, br s, OH), and 7.4—8.0 (5 H, m, Ph); *m/z* 312 (M^+, 4%), 295 (M^+ — OH, 8), and 185 (M^+ − C_9H_{19}, 100). (2S)-1-*Phenylsulphonylpentadecan*-2-*ol* [*S*—(**1c**)] (2.65 g, 72%), m.p. 76 °C; $[\alpha]_D^{22}$ 0°, $[\alpha]_{365}^{22}$ −2.0° (*c* 1.10 in MeOH); $\nu_{max.}$(Nujol) 3 500 (OH), 1 310, and 1 160 cm^{-1} (SO_2); δ_H($CDCl_3$) 0.86 (3 H, t, *J* 6 Hz, Me). 1.0—1.6 (24 H, m, CH_2), 3.20 (2 H, m, 1-H_2), 3.40 (1 H, m, CH), 4.16 (1 H, m, OH), and 7.4—8.0 (5 H, m, Ph); *m/z* 369 (M^+, 3%) and 185 (M^+ − $C_{13}H_{27}$, 100). (2S)-1-*Phenylsulphonyl*-3-*phenylpropan*-2-*ol* [*S*—(**2d**)] (2.62 g, 95%), m.p. 105 °C; $[\alpha]_D^{22}$ 0°, $[\alpha]_{365}^{22}$ −31.3° (*c* 1.04 in MeOH); $\nu_{max.}$(Nujol) 3 500 (OH), 1 310, and 1 160 cm^{-1} (SO_2); δ_H($CDCl_3$) 2.84 (2 H, m, 3-H_2), 3.25 (2 H, m, 1-CH_2), 3.43 (1 H, m, CH), 4.42 (1 H, m, OH), 7.0—7.4 (5 H, m, Ph), and 7.4—8.0 (5 H, m, Ph); *m/z* 185 (M^+ − $PhCH_2$, 100%).

(2S)-1-Phenylsulphonylpropan-2-ol [*S*—(**1a**)] was prepared by the reduction of 1-phenylsulphonylpropan-2-one with baker's yeast.[9] 1-Phenylsulphonylpentan-2-ol, 1-phenylsulphonyl-5-methylhexane-2-ol, 1-cyclohexyl-2-phenylsulphonyl-5-methylhexan-2-ol, 1-cyclohexyl-2-phenylsulphonylethanol were prepared in racemic forms by the condensation of an anion of methyl phenyl sulphone with the corresponding aldehyde,[10] and similarly racemic (**2b—d**) were synthesized.

(2S,3R)-3-*Phenylsulphonylhept*-4-*en*-2-*ol* [S—(**6aA**)] *and* (2S,-3S)-3-*Phenylsulphonylhept*-4-*en*-2-*ol* [*S*(**6aB**)].—A solution of butyl-lithium (15%; 6.80 ml, 11 mmol) in hexane was added to a stirred solution of *S*—(**1a**) (1.00 g, 5 mmol) in THF (25 ml) at −78 °C under argon. After 30 min, *trans*-but-2-enyl bromide (0.74 g, 5.5 mmol) was added dropwise and the resulting solution was allowed to warm to room temperature. After being stirred for 30 min at room temperature the solution was quenched with aqueous ammonium chloride and extracted with ethyl acetate. The extract was washed with water, dried (Na_2SO_4), and evaporated to dryness. Chromatography on silica gel with hexane–ethyl acetate (4:1) as eluant yielded the *alcohols* [*S*—

(**6aA**) (0.69 g, 54%) and *S*—(**6aB**) (0.25 g, 20%)]; their physical data were found to be very similar. *S*—(**6aA**) and *S*—(**6aB**), liquid; $[a]_D^{25}$ 0° (*c* 1.00 in MeOH); $\nu_{max.}$(neat) 3 500 (OH), 1.320, and 1 160 cm^{-1} (SO_2); $\delta_H(CDCl_3)$ 1.27 (3 H, d, *J* Hz, 1-Me), 1.52 (3 H, d, *J* 6 Hz, 7-Me), 2.50 (2 H, t, *J* 6 Hz, CH_2), 2.9—3.2 (2 H, m, 2-H, 3-H), 4.35 (1 H, br s, OH), 5.2—5.4 (2 H, m, 5-H, 6-H), and 7.4—8.0 (5 H, m, Ph) [Found for *S*—(**6aA**): C, 61.7; H, 7.0. $C_{13}H_{18}O_3S$ requires C, 61.4; H, 7.1%]. Both *S*—(**6aA**) and *S*—(**6aB**) were found to be enantiomerically pure by ^{19}F n.m.r. observation of their (+)-MTPA esters.

Similar treatment of (**1**) with allyl bromide, *trans*-but-2-enyl bromide, or 3-methylbut-2-enyl bromide gave 5-phenylsulphonylnon-2-en-6-ols (**6b**) [(**6bA**); (5*R*,6*S*) + (5*S*,6*R*) and (**6bB**); (5*R*,6*R*) + (5*S*,6*S*)], 2-methyl-5-phenylsulphonylnon-7-en-4-ols (**6c**) [(**6cA**); (4*R*,5*S*) + (4*S*,5*R*) and (**6cB**); (4*R*,5*R*) + (4*S*,5*S*)], 1-cyclohexyl-2-phenylsulphonylhex-4-en-1-ol [(**6dA**); (1*R*,2*S*) + (1*S*,2*R*)], 4-phenylsulphonyltetradec-1-en-5-ols (**6e**) [(**6eA**); (4*R*,5*S*) + (4*S*,5*R*) and (**6eB**); (4*R*,5*R*) + (4*S*,5*S*)], (6*S*)-5-phenylsulphonylpentadec-2-en-6-ols [*S*—(**6f**)] [*S*—(**6fA**); (5*R*) and *S*—(**6fB**); (5*S*)], 2-methyl-5-phenylsulphonylpentadec-2-en-6-ols (**6g**) [(**6gA**); (5*R*,6*S*) + (5*S*,6*R*) and (**6gB**); (5*R*,6*R*) + (5*S*,6*S*)], (6*S*)-5-phenylsulphonylnonadec-2-en-6-ol [*S*—(**6h**)] [*S*—(**6hA**); (5*R*) and *S*—(**6hB**); (5*S*)], 1-phenyl-3-phenylsulphonylhex-5-en-2-ol [(**6iA**); (2*R*,3*S*) + (2*S*,3*R*)], (2*S*)-1-phenyl-3-phenylsulphonylhept-5-en-2-ol [*S*—(**6jA**); (3*R*)], and 6-methyl-1-phenyl-3-phenylsulphonylhept-5-en-2-ol [(**6kA**); (2*R*,3*S*) + (2*S*,3*R*)] (Table 1). Physical data as shown below were almost the same between diastereoisomers (**6A**) and (**6B**). Mass spectra of (**6**) were too complicated to be explained.

Alcohol (**6b**) liquid; $\nu_{max.}$(neat) 3 510 (OH), 1 310, and 1 510 cm^{-1} (SO_2); $\delta_H(CDCl_3)$ 0.84 (3 H, t, *J* 7 Hz, 9-Me), 1.0—1.8 (7 H, m, 1-Me, CH_2), 2.58 (2 H, m, 4-H_2), 3.0—3.2 (2 H, m, 5-H, 6-H), 4.24 (1 H, br s, OH), 5.1—5.6 (2 H, m, 2-H, 3-H), and 7.4—8.0 (5 H, m, Ph).

Alcohol (**6c**) liquid; $\nu_{max.}$(neat) 3 500 (OH), 1 310, and 1 510 cm^{-1} (SO_2); $\delta_H(CDCl_3)$ 0.81 (6 H, m, 1-Me), 1.0—2.0 (6 H, m, 2-H, 3-H_2, 9-Me) 2.54 (2 H, m, 6-H_2), 3.0—3.2 (2 H, m, 4-H, 5-H), 4.34 (1 H, br s, OH), 5.0—5.6 (2 H, m, 7-H, 8-H), and 7.4—8.1 (5 H, m, Ph).

Alcohol (**6dA**) liquid; $\nu_{max.}$(neat) 3 500 (OH), 1 310, and 1 510 cm^{-1} (SO_2); $\delta_H(CDCl_3)$ 0.6—2.0 (14 H, m, cyclohexene, Me), 2.60 (2 H, m, 3-H_2), 2.96 (1 H, m, 1-H), 3.16 (1 H, m, 2-H), 3.86 (1 H, br s, OH), 5.2—5.6 (2 H, m, 4-H, 5-H), and 7.4—8.1 (5 H, m, Ph).

Alcohol (**6e**) liquid; $\nu_{max.}$(neat) 3 500 (OH), 1 310, and 1 100 cm^{-1} (SO_2); $\delta_H(CDCl_3)$ 0.86 (3 H, t, *J* 6 Hz, 14-Me), 1.0—1.9 (16 H, m, CH_2), 2.62 (2 H, m, 3-H_2), 3.0—3.3 (2 H, m, 4-H, 5-H), 4.17 (1 H, br s, OH), 4.9—5.2 (2 H, m, 1-H), 5.72 (1 H, m, 2-H), and 7.4—8.0 (5 H, m, Ph).

Alcohol *S*—(**6f**) liquid; $\nu_{max.}$(neat) 3 500 (OH), 1 310, and 1 100 cm^{-1} (SO_2); $\delta_H(CDCl_3)$ 0.7—1.0 (6 H, m, Me), 1.0—1.9 (16 H, m, CH_2), 2.26 (2 H, m, 4-H_2), 2.9—3.3 (2 H, m, 5-H, 6-H), 4.22 (1 H, br s, OH), 5.2—5.6 (2 H, m, 2-H, 3-H), and 7.4—8.0 (5 H, m, Ph); $[\alpha]_D^{25}$ 0° (*c* 1.00 in MeOH); (+)-MTPA ester 100% e.e.

Alcohol (**6g**) liquid; $\nu_{max.}$(neat) 3 500 (OH), 1 310, and 1 100 cm^{-1} (SO_2); $\delta_H(CDCl_3)$ 0.86 (3 H, t, *J* 6 Hz, 15 Me), 1.0—1.9 (19 H, m, 1-Me, CH_2), 2.30 (2 H, m, 4-H_2), 2.9—3.3 (2 H, m, 5-H, 6-H), 4.30 (1 H, br s, OH), 4.80 (1 H, m, 2-H), and 7.4—8.0 (5 H, m, Ph).

Alcohol *S*—(**6h**) liquid; $\nu_{max.}$(neat) 3 500 (OH), 1 310, and 1 100 cm^{-1} (SO_2); $\delta_H(CDCl_3)$ 0.7—1.0 (6 H, m, Me), 1.0—2.0 (24 H, m, CH_2), 2.28 (2 H, m, 4-H_2), 2.9—3.3 (2 H, m, 5-H, 6-H), 4.40 (1 H, br s, OH), 5.2—5.6 (2 H, m, 2-H, 3-H), and 7.4—8.0 (5 H, m, Ph); $[\alpha]_D^{22}$ 0° (*c* 1.03 in MeOH).

Alcohol (**6iA**) liquid; $\nu_{max.}$(neat) 3 500 (OH), 1 300, and 1 150 cm^{-1} (SO_2); $\delta_H(CDCl_3)$ 2.2—3.4 (6 H, m, 1-H_2, 2-H, 3-H, 4-H_2), 4.30 (1 H, m, br s, OH), 4.8—5.2 (2 H, m, 6-H),5.60 (1 H, m 5-H), 7.0—7.4 (5 H, m, Ph), and 7.4—8.0 (5 H, m, Ph).

Alcohol *S*—(**6jA**) liquid; $\nu_{max.}$(neat) 3 500 (OH), 1 300, and 1 150 cm^{-1} (SO_2); $\delta_H(CDCl_3)$ 1.56 (3 H, m, Me), 2.4—3.2 (6 H, m, 1-H_2, 2-H, 3-H, 4-H_2), 4.50 (1 H, br s, OH), 5.2—5.7 (2 H, m, 5-H, 6-H), 7.0—7.4 (5 H, m, Ph), and 7.4—8.0 (5 H, m, Ph); (+)-MTPA ester 100% e.e.

Alcohol (**6kA**) liquid; $\nu_{max.}$(neat) 3 500 (OH), 1 300, and 1 150 cm^{-1} (SO_2); $\delta_H(CDCl_3)$ 1.60 (6 H, d, *J* 6 Hz, Me), 2.4—3.2 (6 H, m, 1-H_2, 2-H, 3-H, 6-H_2), 4.50 (1 H, br s, OH), 5.2—5.4 (1 H, m, 5-H), 7.0—7.4 (5 H, m, Ph), and 7.4—8.0 (5 H, m, Ph).

(2S)-2,5-*Epoxy*-3-*phenylsulphonylhept*-6-*enes** [S—(**8aA**) to S—(**8aD**)].—A solution of benzeneselenenyl chloride (98%; 0.70 g, 3.6 mmol) in dry dichloromethane (10 ml) was added to a stirred solution of *S*—(**6aA**) (0.76 g, 3 mmol) in dry dichloromethane (20 ml) at −78 °C under an argon atmosphere. After 1 h the resulting solution was allowed to warm to room temperature when it was neutralized with aqueous sodium hydrogen carbonate. The organic extract was washed with water and dried (Na_2SO_4). After removal of the solvent, the residue was chromatographed on silica gel with hexane–ethyl acetate (4:1) as eluant, giving a diastereoisomeric mixture of (2*S*,3*R*,5*R*)— and (2*S*,3*R*,5*S*)—2,5 epoxy-6-phenylselenenyl-3-phenylsulphonylnonanes [*S*—(**7aA**)] and [*S*—(**7aB**)] (1.10 g, 90%) as a liquid, $\nu_{max.}$(neat) 1 310 and 1 160 cm^{-1} (SO_2); $\delta_H(CDCl_3)$ 1.0—1.5 (6 H, m, Me),2.0—2.4 (2 H, m, CH_2), 3.1—3.5 (2 H, m, 2-H, 5-H), 3.8—4.6 (2 H, m, 3-H, 6-H), and 7.2—8.0 (10 H, m, Ph).

MCPBA (80%) (0.86 g, 4 mmol) was added to a stirred solution of a mixture (1.10 g, 2.7 mmol) of [*S*—(**7aA**)] and [*S*—(**7aB**)] at −78 °C under argon and stirring was continued for 1 h. After addition of aqueous sodium carbonate at −78 °C the resulting mixture was allowed to warm to room temperature and extracted with dichloromethane. The extract was washed with water, dried (Na_2SO_4), and evaporated to dryness. Chromatography of the residue on silica gel with hexane–ethyl acetate (4:1) as eluant gave (2S,3R,5R)—2,5-*epoxy*-3-*phenylsulphonylhept*-6-*ene* [*S*—(**8aA**)] (0.26 g, 39%) and (2S,3R,5S)-2,5-*epoxy*-3-*phenylsulphonylhept*-6-*ene* [*S*—(**8aB**)] (0.35 g, 51%). Compound [*S*—(**8aA**)] m.p. 119 °C; $[\alpha]_D^{23}$ −29.8° (*c* 1.08 in $CHCl_3$); $\nu_{max.}$(Nujol) 1 310 and 1 150 cm^{-1} (SO_2); $\delta_H(CDCl_3)$ 1.22 (3 H, d, *J* 6 Hz, Me), 1.93 (1 H, m, 4-H_2), 2.54 (1 H, m, 4-H_2), 3.32 (1 H, m, 3-H), 4.36 (2 H, m, 2-H, 5-H), 5.17 (1 H, d, *J* 10 Hz, 7-H_2), 5.30 (1 H, d, *J* 17 Hz, 7-H_2), 5.78 (1 H, m, 6-H), and 7.5—8.0 (5 H, m, Ph); *m*/*z* 110 (M^+ − $PhSO_2H$, 100%) (Found: C, 61.8; H, 6.4. $C_{13}H_{16}O_3S$ requires C, 61.9; H, 6.4%). Compound [*S*—(**8aB**)], m.p. 91 °C; $[\alpha]_D^{23}$ +5.6° (*c* 1.23 in $CHCl_3$); $\nu_{max.}$(Nujol) 1 310 and 1 150 cm^{-1} (SO_2); $\delta_H(CDCl_3)$ 1.24 (3 H, d, *J* 6 Hz, Me), 2.18 (1 H, m, 4-H_2), 2.30 (1 H, m, 4-H_2), 3.42 (1 H, m, 3-H), 4.43 (1 H, m, 2-H), 4.54 (1 H, m, 5-H), 5.13 (1 H, d, *J* 10 Hz, 7-H_2), 5.18 (1 H, d, *J* 17 Hz, 7-H_2), and 7.5-8.0 (5 H, m, Ph); *m*/*z* 110 (M^+ − $PhSO_2H$, 100%) (Found: C, 61.7; H, 6.4. $C_{13}H_{16}O_3S$ requires C, 61.9; H, 6.4%).

Similar treatment of *S*—(**6aB**), (**6bA**), (**6cA**), (**6dA**), *S*—(**6fA**), (**6gA**), *S*—(**6hA**), (**6iA**), *S*—(**6jA**), and (**6kA**) gave (2*S*,-3*S*,5*R*)- and (2S,3S,5S)-2,5-*epoxy*-3-*phenylsulphonylhept*-6-*enes* [*S*—(**8aC**)] and [*S*—(**8aD**)], (3R)- and (3S)-3,6-*epoxy*-5-*phenylsulphonylnon*-1-*enes* [(**8bA**) and (**8bB**)], (3R)- and (3S)-3,6-*epoxy*-8-*methyl*-5-*phenylsulphonylnon*-1-*enes* [(**8cA**) and (**8cB**)], (2R,4R)- and (2R,4S)-1-*cyclohexyl*-1,4-*epoxy*-2-*phenylsulphonylhex*-5-*enes* [(**8dA**) and (**8dB**)], (3R,5R,6S)- and (3S,5R,6S)-3,6-*epoxy*-5-*phenylsulphonylpentadec*-1-*enes* [*S*—(**8fA**) and *S*—(**8fB**)], (3R,5R), and (3S,5R)-3,6-*epoxy*-2-*methyl*-5-*phenylsulphonylpentadec*-1-*enes* [(**8gA**) and (**8gB**)], (3R,5R,6S)- and

* These compounds [(**7**) and (**8**)] can also be named as derivatives of furan; *e.g.* (**8aA**) would be named as 5-methyl-4-phenylsulphonyl-2-vinyltetrahydrofuran.

(3S,5R,6S)-3,6-*epoxy*-5-*phenylsulphonylnonadec*-1-*enes* [*S*—(**8hA**) and *S*—(**8hB**)], (2S,3R,5R)- and (2S,3R,5S)-2,5-*epoxy*-1-*phenyl*-3-*phenylsulphonylhept*-6-*enes* [(**8jA**) and (**8jB**)], and (3R,5R)- and (3R,5S)-2,5-*epoxy*-6-*methyl*-1-*phenyl*-3-*phenylsulphonylhept*-6-*enes* [(**8kA**) and (**8kB**)] (Table 2).

The selenoxides obtained by the oxidation of the (**7e**) and (**7i**) were so stable that they did not furnish (**8e**) or (**8i**) by thermolysis.

^{1}H N.m.r. spectra were almost identical for (**8A**) and (**8B**). I.r. spectra of (**8**) indicated peaks due to SO_2Ph at 1 310 and 1 150 cm^{-1}, and their mass spectra revealed no molecular peak, but the maximum peak due to $M^+ - PhSO_2H$. The results of their elemental analyses were satisfactory; C, ±0.3% and H, ±0.2%.

Compound *S*—(**8aC**), liquid; $[\alpha]_D^{24}$ −13.7° (*c* 1.22 in $CHCl_3$); $\delta_H(CDCl_3)$ 1.65 (3 H, d, *J* 7 Hz, Me), 2.14 (2 H, m, 4-H_2), 3.75 (1 H, m, 3-H_2), 4.17 (1 H, m, 2-H), 4.35 (1 H, m, 5-H), 5.20 (1 H, d, *J* 10 Hz, 7-H), 5.20 (1 H, d, *J* 17 Hz, 7-H), 5.89 (1 H, m, 6-H), and 7.5—8.0 (5 H, m, Ph).

Compound *S*—(**8aD**), liquid; $[\alpha]_D^{24}$ −3.9° (*c* 0.42 in $CHCl_3$); $\delta_H(CDCl_3)$ 1.58 (3 H, d, *J* 7 Hz, Me), 1.86 (1 H, m, 4-H_2), 2.61 (1 H, m, 4-H_2), 3.75 (1 H, m, 3-H), 4.55 (1 H, m, 2-H), 4.71 (1 H, m, 5-H), 5.20 (1 H, d, *J* 10 Hz, 7-H), 5.20 (1 H, d, *J* 17 Hz, 7-H), 5.75 (1 H, m, 6-H), and 7.5—8.0 (5 H, m, Ph).

Compound (**8b**), liquid; $\delta_H(CDCl_3)$ 0.93 (3 H, t, *J* 6 Hz, Me), 1.6 (2 H, m, 8-H_2), 1.8—2.7 (4 H, m, 4-H_2, 7-H_2), 3.49 (1 H, m, 5-H), 4.2—4.6 (2 H, m, 3-H, 6-H), 5.1—5.5 (2 H, m, 1-H), 5.82 (1 H, m, 2-H), and 7.5—8.1 (5 H, m, Ph).

Compound (**8c**), liquid; $\delta_H(CDCl_3)$ 0.80 (6 H, m, Me), 1.0—2.7 (5 H, m, CH_2, 8-H), 3.4 (1 H, m, 5-H), 4.2—4.6 (2 H, m, 3-H, 6-H), 5.0—5.4 (2 H, m, 1-H), 5.8 (1 H, 2-H), and 7.4—8.0 (5 H, m, Ph).

Compound (**8d**), m.p. 90 °C; $\delta_H(CDCl_3)$ 0.8—2.0 (11 H, m, cyclohexene), 2.2 (2 H, m, 3-H_2), 3.75 (1 H, m, 2-H), 4.2—4.7 (2 H, m, 1-H, 4-H), 5.1—5.5 (2 H, m, 6-H), 5.8 (1 H, m, 5-H), and 7.4—8.2 (5 H, m, Ph).

Compound *S*—(**8fA**), liquid; $[\alpha]_D^{22}$ −18.7° (*c* 1.13 in $CHCl_3$); $\delta_H(CDCl_3)$ 0.86 (3 H, t, *J* 6 Hz, Me), 1.0—1.6 (16 H, m, CH_2), 1.8—2.6 (2 H, m, 4-H_2), 3.65 (1 H, m, 5-H), 4.2—4.6 (2 H, m, 3-H, 6-H), 5.1—5.5 (2 H, m, 1-H), 5.8 (1 H, m, 2-H) and 7.5—8.1 (5 H, m, Ph).

Compound *S*—(**8fB**), liquid; $[\alpha]_D^{22}$ −3.7° (*c* 1.06 in $CHCl_3$); $\delta_H(CDCl_3)$ were similar to those of *S*—(**8fA**).

Compound (**8g**), liquid; $\delta_H(CDCl_3)$ 0.86 (3 H, t, *J* 6 Hz, 15-Me), 1.0—1.6 (16 H, m, CH_2), 1.70 (3 H, s, 1′-Me), 1.8—2.6 (2 H, m, 4-H_2), 3.6 (1 H, m, 5-H), 4.2—4.6 (2 H, m, 3-H, 6-H), 4.8—5.1 (2 H, m, 1-H), and 7.5—8.1 (5 H, m, Ph).

Compound *S*—(**8hA**), liquid; $[\alpha]_D^{25}$ −18.0° (*c* 1.00 in $CHCl_3$); $\delta_H(CDCl_3)$ 0.86 (3 H, t, *J* 6 Hz, Me), 1.0—1.6 (24 H, m, CH_2), 1.8—2.6 (2 H, m, 4-H_2), 3.6 (1 H, m, 5-H), 4.2—4.6 (2 H, m, 3-H, 6-H), 5.1—5.5 (2 H, m, 1-H), 5.8 (1 H, m, 2-H), and 7.5—8.1 (5 H, m, Ph).

Compound *S*—(**8hB**), liquid; $[\alpha]_D^{25}$ −3.5° (*c* 0.88 in $CHCl_3$); δ_H were similar to those of *S*—(**8hA**).

Compound *S*—(**8jA**), m.p. 112 °C; $[\alpha]_D^{22}$ −29.1° (*c* 1.10 in $CHCl_3$); $\delta_H(CDCl_3)$ 2.3 (2 H, m, 1-H_2), 2.8 (2 H, m, 4-H_2), 3.51 (1 H, m, 3-H), 4.2—4.8 (2 H, m, 2-H, 5-H), 5.0—5.4 (2 H, m, 7-H), 5.8 (1 H, m, 6-H), 7.0—7.4 (5 H, m, Ph), and 7.4—8.0 (5 H, m, $PhSO_2$).

Compound *S*—(**8jB**), m.p. 113 °C; $[\alpha]_D^{22}$ −19.4° (*c* 0.99 in $CHCl_3$); δ_H were similar to those of *S*—(**8jA**).

Compound (**8k**), m.p. 94 °C; $\delta_H(CDCl_3)$ 1.65 (3 H, s, Me), 2.0—3.0 (4 H, m, CH_2), 3.44 (1 H, m, 3-H), 4.1—4.4 (2 H, m, 2-H, 5-H), 4.7—5.1 (2 H, m, 7-H), 7.0—7.4 (5 H, m, PH), and 7.4—8.1 (5 H, m, $PhSO_2$).

Determination of Enantiomeric Excess.—Treatment of an alcohol with (+)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride and 4-dimethylaminopyridine[25] gave its ester in a quantitative yield. Enantiomeric excess was determined by measuring the ^{19}F n.m.r. spectra.

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