Asymmetric Selection *via* Addition.   Optically Active Allenic Sulphones

By **Mauro Cinquini, Stefano Colonna,** and **Franco Cozzi,** Centro C.N.R. e Istituto di Chimica Industriale dell'Università, Via Golgi 19, 20133 Milano, Italy

Racemic allenic sulphones can be partially resolved by reaction with a deficiency of optically active amines; a catalytic kinetic resolution is also described.

OPTICALLY active allenic sulphones (1) can be obtained either *via* thermal rearrangement of optically active prop-2-ynyl sulphinates [1] or *via* reaction of prop-2-ynyl Grignard reagents with optically active sulphinates and subsequent oxidation of the resulting allenic sulphoxides.[2]

A direct approach to the optically active compounds (1) is, in principle, made possible by the fact that the unsaturated system is strongly activated by the sulphonyl group towards nucleophilic addition [3] and thus furnishes a 'handle' for kinetic resolution. We report that asymmetric selection is, indeed, at work in the reaction of chiral allenic sulphones with optically active primary and secondary amines.

Buta-1,2-dienyl *p*-tolyl sulphone (1a), whose optical purity had previously been evaluated,[1,2] was chosen as reference compound.   Reaction of (1a) with a deficiency of the chiral bases (2)—(5) afforded the corresponding enamine (6) and allowed the recovery of partially resolved (1a).   The choice of solvent is crucial, since a competitive allene–acetylene rearrangement may occur, the extent of the latter process increasing in the series Et_2O, tetrahydrofuran $< C_6H_6 <$ MeOH.   From the results (see Table 1) it appears that the absolute configuration and the optical purity of the recovered sulphone (1a) depend on the amine used, the enantioselectivity of the chiral base being in the order (2) > (5) > (4) > (3).   The best result, corresponding to an enantiomeric excess of 70%,[1,2] was achieved with (1a) and (2) in a 2 : 1 ratio, in diethyl ether as solvent.   Higher conversion or a change of the solvent resulted either in lower values of optical rotation or in the formation of substantial amounts of the acetylenic isomer (7).

The enamine adducts (6) † were not isolated as such, being hydrolyzed, during work up, to the oxo-sulphone (8).   The ready transformation of (6) into (8) suggested the possibility of a 'catalytic kinetic resolution' of allenic sulphones by reaction with catalytic amounts of a chiral base in the presence of water; the latter continuously destroys the adduct and thus regenerates the chiral agent.   Indeed when (1a) was treated with 0.05 molar equivalents of (R)-(+)-(2) and 0.45 mol of water in tetrahydrofuran (THF) as solvent at 25 and 70 °C, the recovered buta-1,2-dienyl *p*-tolyl sulphone had optical purities of 40 and 10%, respectively.   Under the same conditions, when methanol was used as solvent, (1a) was quantitatively converted into (7).

Kinetic resolution of the allenic sulphones (1b—d) was also investigated.   Reaction of (1b—d) with a deficiency of the chiral bases (2)—(5) resulted in most cases in the recovery of optically active allenic sulphones (see Table 2), whose absolute configuration was assigned on the basis of Brewster's rule.[2,4]   Allene–acetylene rearrangement was observed in the case of (1b), the amount of acetylene formed depending on the reaction conditions.   On the other hand, in the case of the trisubstituted allenes (1c and d) no detectable amount of acetylenic sulphone was obtained.   The value of enantiomeric enrichment of the recovered sulphones (1b—d) could be roughly estimated only in the case of (1c), the best value being *ca.* 30%, on the basis of the maximum value of its optical rotation, $[\alpha]_D^{25}$ $-18°$ (CHCl₃), previously reported.[2]   Attempts to determine the optical purity of (1b—d) with the aid of chiral shift reagent $Eu(tfc)_3$ were unsuccessful.

Kinetic resolution constitutes a very simple method of obtaining optically active allenic sulphones, and is

† The extensive work by Stirling [3] indicates that reaction of amines with allenic and acetylenic sulphones affords the conjugated enamine adduct.

[1] G. Smith and C. J. M. Stirling, *J. Chem. Soc.* (C), 1971, 1530.

[2] M. Cinquini, S. Colonna, F. Cozzi, and C. J. M. Stirling, *J.C.S. Perkin I*, 1976, 2061.

[3] (a) S. T. McDowell and C. J. M. Stirling, *J. Chem. Soc.* (B), 1967, 351; (b) G. D. Appleyard and C. J. M. Stirling, *J. Chem. Soc.* (C), 1967, 2686; (c) W. E. Truce and L. D. Markley, *J. Org. Chem.*, 1970, **35**, 3275.

[4] (a) G. Lowe, *Chem. Comm.*, 1965, 411; (b) G. Krowe, *Topics in Stereochem.*, 1970, **5**, 31.

particularly useful in the case of phenyl substituted derivatives, which are difficult to obtain *via* the Andersen synthesis.[2]

It must be mentioned that in all cases examined the absolute configuration of the resolved allene is related to that of the resolving amines (2)—(5), and is in-dependent of the solvent used. The amines used can be represented by the stereoformula (9) and by its mirror image (10) in the case of compounds (R)-$(+)$-(2), (R)-$(-)$-(4) and (S)-$(+)$-(3), (S)-$(-)$-(5), respectively, on the assumption that the relative effective bulk is Ph > $PhCH_2$ > Me.

$$p\text{-MeC}_6H_4 \cdot SO_2 \cdot C \equiv C = CR^2R^3 \qquad\qquad R^1\text{-CH-} NHR^3$$

(1a) R¹ = R² = H; R³ = Me   (2) R¹ = Ph; R² = Me; R³ = H

(1b) R¹ = R² = H; R³ = Ph   (3) R¹ = PhCH₂; R² = Me; R³ = H

(1c) R¹ = H; R² = Me; R³ = Et   (4) R¹ = PhCH₂; R² = Ph; R³ = H

(1d) R¹ = H; R² = Me; R³ = Ph   (5) R¹ = Ph; R² = Me ; R³ = PhCH₂

$$p\text{—MeC}_6H_4 \cdot SO_2 \cdot CH = C = CHMe \xrightarrow{\;>NH\;} p\text{—MeC}_6H_4 \cdot SO_2 \cdot CH = CEt + p\text{—MeC}_6H_4 \cdot SO_2 \cdot CH_2 C \equiv CMe$$

(1a)   (6)   (7)

$$\downarrow H_2O$$

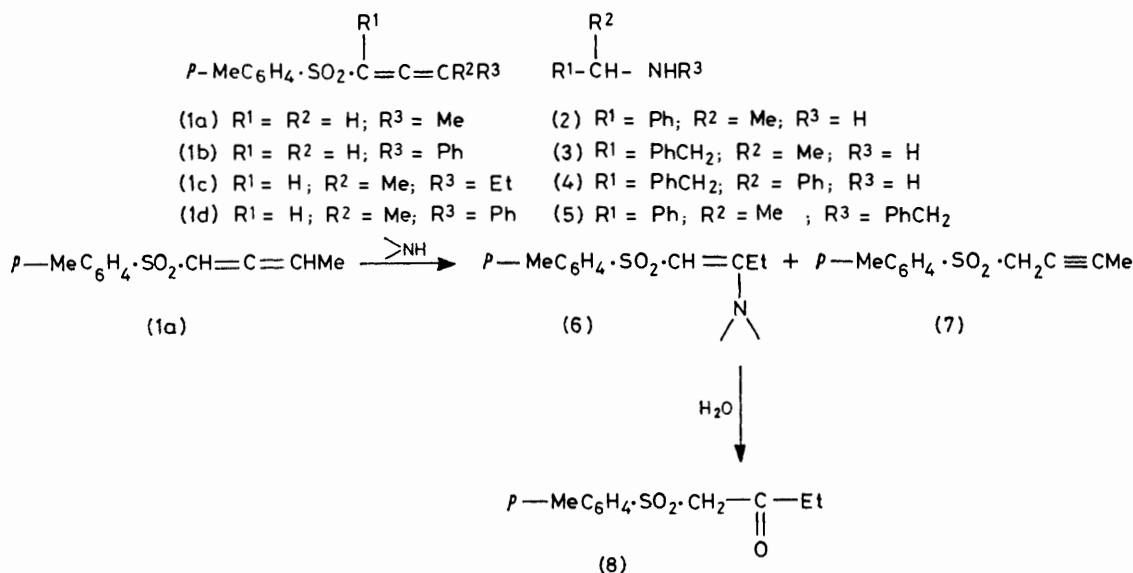$$p\text{—MeC}_6H_4 \cdot SO_2 \cdot CH_2 - C - Et$$
(8)

TABLE 1

Kinetic resolution of the sulphone (1a)

| Amine	Mol. equiv. of amine	Solvent	Time (h) [a]	Acetylene (7),[b] %	Recovered sulphone (1a)	
					$[\alpha]_D^{25}$ [c]	Absolute configuration
(R)-$(+)$-(2)	0.5	Et₂O	15	0	−43.3	R
(R)-$(+)$-(2)	0.5	Et₂O	15 [d]	0	−37.0	R
(R)-$(+)$-(2)	0.5	THF	15	0	−29.5	R
(R)-$(+)$-(2)	0.5	MeOH	15	100		
(R)-$(+)$-(2)	0.75	Et₂O	15	0	−33.5	R
(R)-$(+)$-(2)	0.75	C₆H₆	15	20	−36.4 [e]	R
(R)-$(+)$-(2)	0.05 [f]	THF	600	0	−25.8	R
(R)-$(+)$-(2)	0.05 [f]	THF	27 [g]	0	−6.2	R
(S)-$(+)$-(3)	0.5	Et₂O	15	⩽5	+8.9 [e]	S
(R)-$(-)$-(4)	0.5	Et₂O	48	0	−16.0	R
(S)-$(-)$-(5)	0.5	Et₂O	15	0	+29.4	S

[a] The reactions were carried on at 25 °C, unless otherwise stated.   [b] By ¹H n.m.r. spectroscopy.   [c] c 1, in Me₂CO.   [d] At 0 °C.   [e] Optical rotation of the acetylene–allene mixture.   [f] In the presence of 0.45 mol equiv. of H₂O; 50% of the starting sulphone was recovered.   [g] At 70 °C.

TABLE 2

Sulphone	Amine	Mol equiv. of amine	Solvent	Time (h) [a]	Acetylene % [b]	Recovered sulphone	
						$[\alpha]_D^{25}$ [c]	Absolute configuration
(1b)	(R)-$(+)$-(2)	0.5	THF	15	10	−111.2 [d]	R
(1b)	(R)-$(+)$-(2)	0.5	C₆H₆	15	40	−86.8 [d]	R
(1b)	(R)-$(+)$-(2)	0.05 [e]	THF	600	0	−37.2	R
(1b)	(S)-$(-)$-(5)	0.5	THF	72	50	+62.6 [d]	S
(1c)	(R)-$(+)$-(2)	0.5	Et₂O	15	0	−3.1	R
(1c)	(R)-$(+)$-(2)	0.9	Et₂O	15	0	−7.0	R
(1c)	(S)-$(+)$-(3)	0.5	MeOH	75	0	0	
(1c)	(R)-$(-)$-(4)	0.5	Et₂O	72	0	0	
(1d)	(R)-$(+)$-(2)	0.5	THF	15	0	−16.3	R
(1d)	(R)-$(+)$-(2)	0.9	THF	15	0	−32.1	R
(1d)	(R)-$(-)$-(4)	0.5	THF	48	0	−20.7	R

[a] The reactions were carried out at 25 °C.   [b] By ¹H n.m.r. spectroscopy.   [c] c 1, in Me₂CO.   [d] Optical rotation of the allene–acetylene mixture; 50% of the starting sulphone was recovered.   [e] In the presence of 0.45 mol equiv. of H₂O.

On this basis the chirality of the resolved sulphone can be inferred from that of the optically active amine.
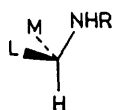
(9)

EXPERIMENTAL

General.—Light petroleum had b.p. 40—60 °C. Ether and benzene were dried over sodium, and tetrahydrofuran was distilled from lithium aluminium hydride. Extractions were performed with dichloromethane and extracts were dried over Na_2SO_4. ^1H N.m.r. spectra were recorded with a Varian A-60 and/or a Varian HA 100 instruments; i.r. spectra were recorded on a Perkin-Elmer 377 spectrometer. Optical rotations were measured with a Perkin-Elmer 141 polarimeter. (R)-α-Phenylethylamine, $[\alpha]_D^{20}$ $+40.1°$ (neat), (S)-amphetamine, $[\alpha]_D^{15}$ $+40.2°$ (c 9 in C_6H_6), and (S)-N-benzyl-α-phenethylamine, $[\alpha]_D^{25}$ $-39.8°$ (neat), were commercial products. (R)-1,2-Diphenylethylamine, resolved [5] with $(+)$-tartaric acid, had $[\alpha]_D^{25}$ $-45°$ (c 2 in EtOH), lit.,[6] $[\alpha]_D^{25}$ $-45°$ (c 2 in EtOH).

Racemic Allenic Sulphones.—Prop-2-ynyl toluene-p-sulphinates were prepared by reaction of toluene-p-sulphinyl chloride with 1-methylprop-2-ynyl, 1-phenylprop-2-ynyl, 1-ethyl-1-methylprop-2-ynyl, and 1-methyl-1-phenylprop-2-ynyl alcohol, according to literature methods,[1,7] and purified by column chromatography (silica; light petroleum–ether).

1-Methylprop-2-ynyl toluene-p-sulphinate had n_D^{25} 1.5412 (lit.,[1] n_D^{25} 1.5410). When heated in chlorobenzene it afforded buta-1,2-dienyl p-tolyl sulphone (1a), m.p. 47—48 °C (lit.,[1] m.p. 47—48 °C).

1-*Phenylprop-2-ynyl toluene*-p-*sulphinate* had n_D^{21} 1.5894 (Found: C, 71.1; H, 5.2. $C_{16}H_{14}O_2S$ requires C, 71.1; H, 5.2%). When heated in acetonitrile as solvent in the

[5] D. Pitre and L. Fumagalli, *Farmaco Ed. Sci.*, 1962, **17**, 130.
[6] H. E. Smith and T. Chad Willis, *J. Amer. Chem. Soc.*, 1971, **93**, 2282.

presence of $CaCO_3$ [7] at 81 °C for 5 h it afforded in 40% yield 1-p-*tolylsulphonyl-3-phenylpropadiene*, m.p. 89—90 °C, after purification from column chromatography (silica; light petroleum–ether) (Found: C, 71.1; H, 5.3. $C_{16}H_{14}O_2S$ requires C, 71.1; H, 5.2%).

3-*Methylpenta*-1,2-*dienyl* p-*tolyl sulphone* was obtained in 60% yield by heating at 81 °C for 30 min a solution of the crude 1-ethyl-1-methyl-prop-1-ynyl toluene-p-sulphinate in cyclohexane. It had m.p. 70—71 °C (from cyclohexane) (Found: C, 66.0; H, 6.8. $C_{13}H_{16}O_2S$ requires C, 66.1; H, 6.8%).

3-*Phenylbuta*-1,2-*dienyl* p-*tolyl sulphone* was obtained in 50% yield through column chromatography (silica; light petroleum–ether) of the crude product of the reaction of toluene-p-sulphinyl chloride with 1-methyl-1-phenylprop-2-ynyl alcohol. It had m.p. 99—100 °C (Found: C, 71.9; H, 5.6. $C_{17}H_{16}O_2S$ requires C, 71.8; H, 5.7%).

Resolution of Allenic Sulphones.—In a typical run 0.121 g (1 mmol) of $(+)$-(R)-α-phenylethylamine were added to a solution of 0.416 g (2 mmol) of buta-1,2-dienyl p-tolyl sulphone in anhydrous ether (6 ml). After 15 h at 25 °C the solvent was evaporated and the crude product was separated by column chromatography (silica, light petroleum–ether) to give 0.208 g of the optically active sulphone (1a) and 0.226 g of 1-p-*tolylsulphonylbutan-2-one*, m.p. 46—47 °C (Found: C, 58.5; H, 6.3. $C_{11}H_{14}O_3S$ requires C, 58.4; H, 6.25%).

Under the same conditions, reaction of 2 mmol of racemic 1-p-tolylsulphonyl-3-phenylpropadiene and 1 mmol of $(+)$-(R)-(2) afforded 1 mmol of optically active (1b) and 1 mmol of 1-p-*tolylsulphonyl-3-phenylpropan-2-one*, m.p. 75—76 °C (Found: C, 66.6; H, 5.6. $C_{16}H_{16}O_3S$ requires C, 66.65; H, 5.6%).

Starting from racemic sulphones (1c and d), inseparable mixtures of the corresponding enamine and ketone were obtained together with the optically active sulphone. Optical rotations of the resolved sulphones (1a—d) are reported in Tables 1 and 2.

[7] S. Braverman and H. Mechoulam, *Tetrahedron*, 1974, **30**, 3883.