

Elimination and Addition Reactions. Part XXVI.¹⁻³ Asymmetric Induction in Additions of Nucleophiles and Electrophiles to $\alpha\beta$ -Unsaturated Sulphoxides

By Douglas J. Abbott, Esso Research, Abingdon, Berkshire,
Stefano Colonna (in part), Università di Milano, Istituto di Chimica Industriale, Via C. Golgi 19, 20133
Milano, Italy
Charles J. M. Stirling,* School of Physical and Molecular Sciences, University College of North Wales,
Bangor, Gwynedd

Optically pure $\alpha\beta$ -unsaturated sulphoxides have been synthesised.

Addition of piperidine to (-)-(R)-(Z)-propenyl *p*-tolyl sulphoxide gives a quantitative yield of adduct with an optical yield of 70%. The absolute configuration of the asymmetric carbon centre (β -induction) of the major diastereoisomer is assigned by comparison of the rotation of the derived sulphide with that of a specimen synthesised from (+)-alanine. A lower optical yield is obtained in addition of piperidine to (+)- α -methylvinyl *p*-tolyl sulphoxide (α -induction). No discernible α -induction is found in additions of PhSD to *p*-tolyl vinyl sulphoxide.

Addition of bromine to (+)-*p*-tolyl vinyl sulphoxide gives the dibromide with an optical yield (α -induction) of 32%. The absolute configuration of the new asymmetric centre at carbon is assigned by using Brewster's rules. (+)- α -Methylvinyl *p*-tolyl sulphoxide gives a higher degree of asymmetric induction but yields of dibromide are low.

The relationship of the optical yields and absolute configurations of the adducts obtained in these nucleophilic and electrophilic additions is discussed with respect to the mechanisms and steric courses of the reactions.

ADDITIONS of nucleophiles and of electrophiles to alkenes have been extensively studied^{4,5} but few instances of asymmetric induction resulting from additions to alkenes bearing directly connected chiral groups have been reported.^{6,7} The reason for the paucity of relevant studies is that the ideal system requires an alkene bearing a chiral group which is configurationally homogeneous, of known absolute configuration which will permit both nucleophilic and electrophilic additions to proceed, and whose structure will enable investigation of induction both α and β to the chiral substituent to the exclusion of other reactions. We report the results of such a study in this paper.

The System.—The foregoing criteria are met in every

¹ Part XXV, M. J. van der Sluijs and C. J. M. Stirling, *J.C.S. Perkin II*, 1974, 1268.

² Preliminary communication, D. J. Abbott, S. Colonna, and C. J. M. Stirling, *Chem. Comm.*, 1971, 471.

³ Preliminary communication, D. J. Abbott and C. J. M. Stirling, *Chem. Comm.*, 1971, 472.

⁴ 'Organic Reaction Mechanisms,' eds. B. Capon and C. W. Rees, Wiley, London, 1970—1973.

respect by $\alpha\beta$ -unsaturated sulphoxides (Scheme 1). Treatment of (-)-menthyl toluene-*p*-sulphinate (2) with vinyl-, (Z)-propenyl-, or α -methylvinyl-magnesium bromide according to Andersen's procedure⁸ yielded the $\alpha\beta$ -unsaturated sulphoxides (1) (see Table 1). The sulphinate ester (2) is of known absolute configuration⁹ and the steric course of replacement by an alkyl or aryl group in the Andersen synthesis is authenticated by many examples.¹⁰

Nucleophilic Addition— β -Induction.—Treatment of the sulphoxide (1a) with an excess of piperidine in methanol at 60 °C for 24 h gave a quantitative yield of

⁵ 'Comprehensive Chemical Kinetics,' vol. 9, eds. C. H. Bamford and C. F. H. Tipper, Elsevier, London, 1973.

⁶ H. Felkin, G. Swierczewski, and A. Tambuté, *Tetrahedron Letters*, 1969, 707.

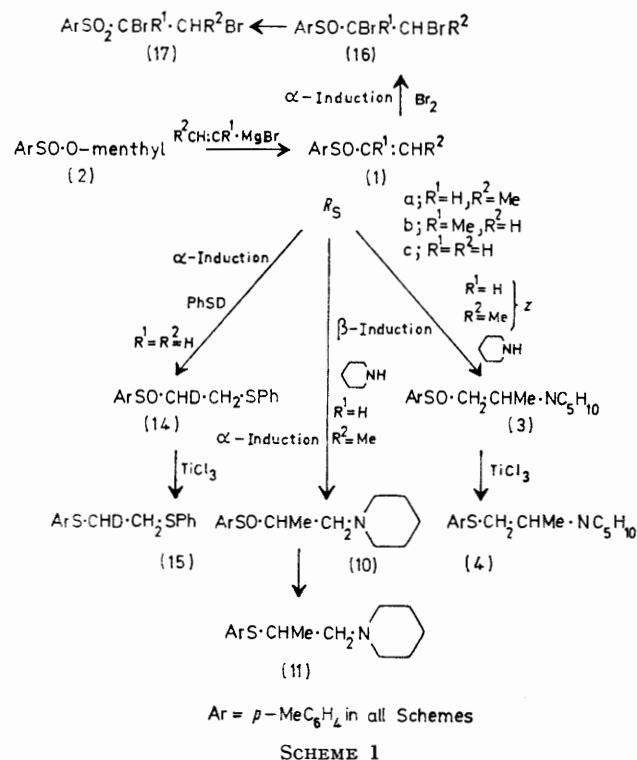
⁷ D. R. Boyd and M. A. McKerverey, *Quart. Rev.*, 1968, 22, 95.

⁸ K. K. Andersen, *Tetrahedron Letters*, 1962, 93.

⁹ Cf. E. B. Fleischer, M. Axelrod, M. Green, and K. Mislow, *J. Amer. Chem. Soc.*, 1964, 86, 3395.

¹⁰ M. Axelrod, P. Bickart, J. Jacobus, M. Green, and K. Mislow, *J. Amer. Chem. Soc.*, 1968, 90, 4835.

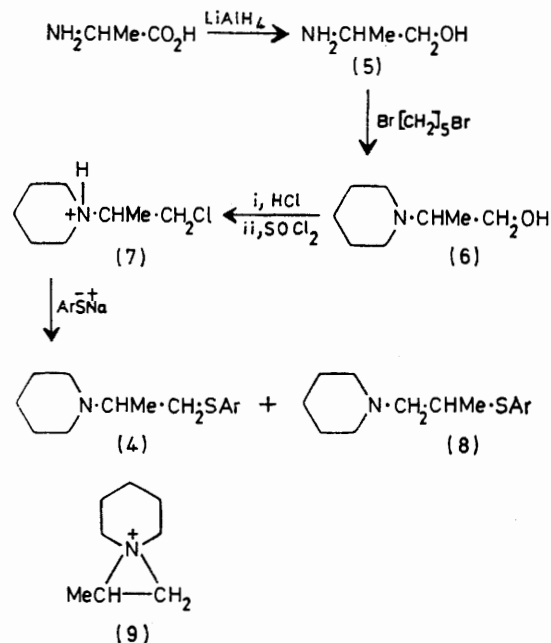
a mixture of the diastereoisomeric piperidino-sulphoxides (3). (The solvent is important; in chlorobenzene at 100 °C only 10% of adduct is obtained; the main



products result from interception of a sulphoxide-sulphenate ester interconversion.¹¹) From the 80:20 mixture the major component was obtained pure by crystallization. The minor (liquid) isomer was separated by chromatography. Both diastereoisomers were characterised as picrates.

pure diastereoisomer showed that the degree of asymmetric induction (optical yield) was 74%.

Absolute Configuration of the Major Diastereoisomer.—The sulphide (4) was synthesised from (+)-(*S*)-alanine according to Scheme 2. Reduction of alanine with lithium aluminium hydride gave the alcohol (5), which, with 1,5-dibromopentane, gave the piperidino-alcohol (6), treatment of which with thionyl chloride gave the chloride hydrochloride (7). Reaction of the salt (7) with sodium thiophenolate in ethanol gave a mixture of



the sulphides (4) and (8) which result from attack at either carbon atom of the intermediate aziridinium ion

TABLE 1

Chiral $\alpha\beta$ -unsaturated sulphoxides				
	B.p. (°C) [Torr]	n_D (°C)	Yield (%)	$[\alpha]$ (°) [λ /nm]
(1; $R^1 = R^2 = H$) ^a	88 [0.05]	1.5776(18)	88	+396 [589] +416 [578] +488 [546]
(1; $R^1 = H, R^2 = Me$) (<i>Z</i>)	(M.p. 54—55)		95	-306 [589] -321 [578] -373 [546]
(1; $R^1 = Me, R^2 = H$)	98 [0.1]	1.5674(22)	70	+126 [589] +131 [578] +153 [546]

^a Found: C, 64.6; H, 6.1; S, 19.4. $C_9H_{10}OS$ requires C, 65.1; H, 6.0; S, 19.3%; $\tau(CCl_4)$ 2.4—2.9 (4 H, m), 3.1—4.3 (3 H, m), and 7.68 (3 H, s). ^b Found: C, 66.7; H, 6.6; $C_{10}H_{12}OS$ requires C, 66.7; H, 6.7%; $\tau(CDCl_3)$ 2.4—2.8 (4 H, m), 3.6—3.9 (2 H, m), 7.64 (3 H, s), and 7.9 (3 H, d). ^c Found: C, 66.1; H, 6.4; S, 17.7. $C_{10}H_{12}OS$ requires C, 66.7; H, 6.7; S, 17.8%; $\tau(CCl_4)$ 2.4—2.8 (4 H, m), 4.05 (1 H, q), 4.47 (1 H, q), 7.65 (3 H, s), and 8.35 (3 H, d).

In separate experiments, reduction of the diastereoisomer mixture and of the pure (major) crystalline diastereoisomer with titanium(III) chloride¹² gave the sulphide (4). Comparison of the rotation of the sulphide obtained from the mixture with that obtained from the

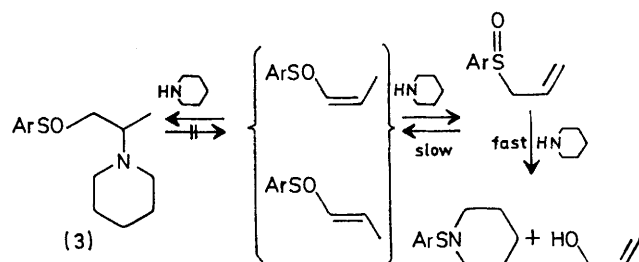
(9). Separation of the isomeric sulphides by preparative g.l.c. caused partial decomposition but gave the slightly impure, optically active sulphide (4) with the same sign of rotation as that obtained by the reduction of the pure crystalline diastereoisomeric sulphoxide (3). Picrates

¹¹ D. J. Abbott and C. J. M. Stirling, *J. Chem. Soc. (C)*, 1969, 818.

¹² D. Barnard and K. R. Hargrave, *Analyt. Chim. Acta*, 1951, 536.

obtained from the two sulphides were identical. The absolute configuration at carbon in the major diastereoisomer from the mixture of β -piperidino-sulphoxides (3) is, therefore, the same as in (+)-(*S*)-alanine. The complete specification of the absolute configuration of the major sulphoxide-piperidine adduct is thus $R_S S_C$.

The degree of asymmetric induction is sufficiently great to warrant tentative interpretation of the steric course of the addition of piperidine to the sulphoxide. Addition of amines to $\alpha\beta$ -unsaturated sulphones is known to be reversible¹³ under basic conditions in which protonation at nitrogen by solvent can occur.¹⁴ These conditions exist in principle (Scheme 3) in the sulphoxide-piperidine additions, notwithstanding the fact that the sulphinyl group is a much less potent activator of β -elimination than is the sulphonyl group.¹⁵ It was essential to establish, therefore, whether the addition was reversible under the reaction conditions and, therefore, whether the asymmetric induction was thermodynamically or kinetically determined. A specimen of the major diastereoisomer with $[\alpha]_{589}^{25} +208^\circ$ (diastereoisomer mixture $[\alpha]_{589}^{25} +184^\circ$) was heated with piperidine in methanol under conditions simulating those of the addition reaction. The 'specific rotation' of the



SCHEME 3

reaction mixture changed from 156 to 153° in this period showing that either decomposition or epimerisation of the diastereoisomer does occur but much more slowly than the addition reaction.

A further possibility exists, namely that the (*Z*)-sulphoxide (Scheme 3) is converted into (*E*)-sulphoxide *via* equilibration with the allylic sulphoxide. Treatment of the allylic sulphoxide with piperidine in methanol under the conditions used for additions to the (*Z*)-propenyl sulphoxide yields¹¹ only 10% of the adduct (3). Formation of allyl alcohol and *p*-tolylsulphenyl-piperidine by sulphenate interception is much faster. We conclude, therefore, that the reaction is not reversible under the conditions used and that the steric course is kinetically determined.

The steric course of the reaction is represented in Scheme 4. It may be presumed¹⁶ that the nucleophile

¹³ A. S. Angeloni, P. De Maria, A. Fini, and G. Salvadori, *Tetrahedron*, 1970, **26**, 5601.

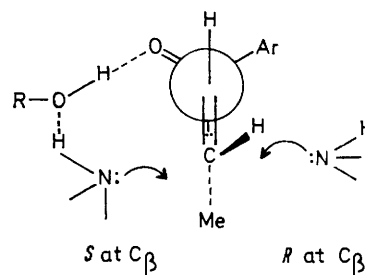
¹⁴ K. N. Barlow, D. R. Marshall, and C. J. M. Stirling, unpublished observations.

¹⁵ J. Crosby and C. J. M. Stirling, *J. Chem. Soc. (B)*, 1970, 671.

¹⁶ Cf. E. Toromanoff, *Bull. Soc. chim. France*, 1962, 1190.

¹⁷ S. T. McDowell and C. J. M. Stirling, *J. Chem. Soc. (B)*, 1967, **343**, 348, 351.

approaches perpendicular to the plane containing the substituents attached to the carbon-carbon double bond. Detailed mechanistic studies^{17,18} of additions of



SCHEME 4

amines to $\alpha\beta$ -unsaturated sulphones suggest the occurrence of a concerted process in which a proton is conveyed to the α -carbon atom either *via* a solvent molecule or, in the case of reactions in aprotic solvents (which are second order to an amine) *via* a second molecule of amine. We have considered the alternative approaches to the sulphoxide in its most populated conformation, denoted in Scheme 4. The approach which is least sterically hindered (O less bulky than Ar) and which allows hydrogen bonding from amino nitrogen to sulphinyl oxygen (probably *via* an eight-membered ring¹⁹ which includes a solvent molecule) is to be preferred. This direction is that which produces the major diastereoisomer.

Since our preliminary announcement,² Tschushihashi and his collaborators²⁰ have made elegant synthetic use of α - and β -induction in additions to chiral β -styryl sulphoxides.

α -Induction in Nucleophilic Addition.—Two reactions were examined in order to assess the possibility of induction of asymmetry at carbon adjacent to the sulphinyl group. In the first, addition of piperidine to α -methylvinyl *p*-tolyl sulphoxide, the prochiral atom becomes chiral by addition of a hydrogen atom. In the second, addition of benzene- $[^2\text{H}]$ thiol to *p*-tolyl vinyl sulphoxide, the addition of a deuterium at C_α produces the chiral centre.

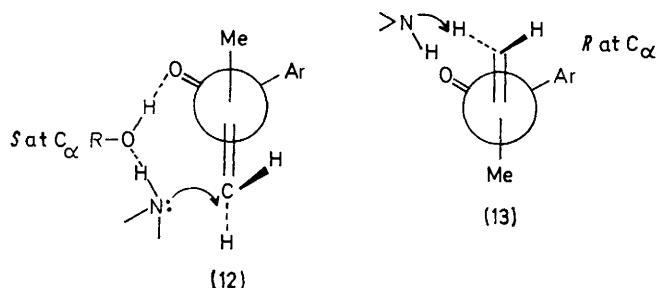
*Addition of Piperidine to (+)- α -Methylvinyl *p*-Tolyl Sulphoxide.*—Reaction with the sulphoxide (1b) was very much slower than that with the β -methyl isomer (1a), in accord with the reactivities of the corresponding sulphones towards amines.¹⁷ Further, the yield of adduct (10) (Scheme 1) obtained from reactions at 80°C in ethanol for 1 week was 55%, the remainder of the product being unchanged sulphoxide, together with optically inactive compounds which were not sulphoxides. The products were separated chromatographically, with special care to prevent separation of the

¹⁸ W. G. Davies, E. W. Hardisty, T. P. Nevell, and R. H. Peters, *J. Chem. Soc. (B)*, 1970, 1004.

¹⁹ For a discussion of proton transfer in cyclic transition states see J. Hine, M. S. Cholod, and R. A. King, *J. Amer. Chem. Soc.*, 1974, **96**, 835.

²⁰ G. Tschuchihashi, S. Mitamura, and K. Ogura, *Tetrahedron Letters*, 1974, 455 and earlier references.

diastereoisomeric adducts (10). ^1H N.m.r. spectroscopy on the adduct mixture showed that the diastereoisomers were present in a ratio 1.8:1, corresponding to an optical yield of 29%. They were readily separated by chromatography and, as before, the major diastereoisomer was a solid which was crystallised to constant rotation. Reduction with titanium(III) chloride yielded the enantiomerically pure sulphide (11) and comparison of the rotation of this sulphide with that of the sulphide obtained by reduction of the diastereoisomer mixture showed that the optical yield was 30%, in excellent agreement with the spectroscopic analysis. This figure is a tentative one because of the modest yield of adducts obtained and the lack of information on whether there is any selectivity between diastereoisomers in formation of by-products. If it is assumed that further reaction does not greatly affect the diastereoisomer ratio, the stereospecificity of the reaction is much lower than for β -induction. If we adopt the same model for the steric course of the reaction which was used for the β -methyl isomer (Scheme 5) it can be seen that no clear-cut choice



SCHEME 5

between conformations (12) and (13) of the sulfoxide can be made. The lower degree of asymmetric induction reflects this uncertainty. The asymmetric

hydrogen has been extensively investigated, particularly by Streitwieser and Wolfe²¹ and Eliel.²² We considered it possible that in an aprotic solvent, addition of a nucleophile bearing a deuterium would lead to the formation of a chiral centre adjacent to the sulphinyl group. *N*-Deuteriodibenzylamine had been found useful in earlier studies of addition reactions²³ but was unreactive towards the vinyl sulfoxide (1c) even on protracted heating in benzene or chlorobenzene. Addition of [^2H]thiol to the sulfoxide (1c) was catalysed by triethylamine and the adduct (14) was recrystallised to constant m.p. Reduction with titanium(III) chloride gave the bis-sulphide (15) whose isotopic composition was verified by ^1H n.m.r. spectroscopy. After rigorous purification by g.l.c., however, the sulphide showed no measurable optical activity. Specific rotations of optically pure compounds which are optically active by virtue of H-D dissymmetry are typically in the range 0.1–0.7°.^{21,22} Lack of optical activity of the product from this reaction suggests that the degree of asymmetric induction is less than ca. 10%.

Electrophilic Addition— α -Induction in Additions of Bromine to $\alpha\beta$ -Unsaturated Sulfoxides.— α -Methylvinyl and vinyl *p*-tolyl sulfoxides reacted with bromine to give mixtures of diastereoisomeric dibromo-sulfoxides (16) (Scheme 1) which were separated from various amounts of toluene-*p*-sulphonyl bromide and an unidentified carbonyl compound. Care was taken to prevent separation of diastereoisomers during purification. The degree of asymmetric induction was assigned by oxidation of the mixture of diastereoisomers and comparison of the rotation of the dibromo-sulphone mixture (17) obtained with that of the sulphone obtained from oxidation of the pure major diastereoisomer. Alternatively, in the case of the α -methyl sulfoxide (1; $\text{R}^1 = \text{Me}$, $\text{R}^2 = \text{H}$) where diastereoisomers were not

TABLE 2
Asymmetric induction in electrophilic addition to $\alpha\beta$ -unsaturated sulfoxides

Sulfoxide	Adduct (16) yield	$[\alpha]_{546}^{25}$ of mixture of sulphone enantiomers	$[\alpha]_{546}^{25}$ of major sulphone enantiomer	Absolute configuration	Optical yield (%)
(1; $\text{R}^1 = \text{R}^2 = \text{H}$)	92	-21.8	-66.7	S	32 *
(1; $\text{R}^1 = \text{Me}$, $\text{R}^2 = \text{H}$)	50	†	-20.6	S	43 ‡

* Calc. from optical rotation ratio. † See text. ‡ Calc. from ^1H n.m.r. C-Me signal integral ratio.

induction in this case is determined by the proton transfer, and a concerted process involving hydrogen bonding between the nucleophile, solvent molecule, and perhaps the sulphinyl group as before, is suggested. We consider that reaction *via* (12) is more probable and this pathway leads to the prediction that the new asymmetric centre has the S-configuration. The configuration of the major diastereoisomeric adduct is, therefore, tentatively assigned as $\text{R}_\text{S}\text{S}_\text{C}$.

Addition of Benzene- ^2H thiol to p-Tolyl Vinyl Sulfoxide.—Optical activity due to isotopic dissymmetry of

²¹ A. Streitwieser and J. R. Wolfe, *J. Amer. Chem. Soc.*, 1959, **81**, 4912 and earlier papers.

²² E. L. Eliel, *J. Amer. Chem. Soc.*, 1949, **71**, 3970.

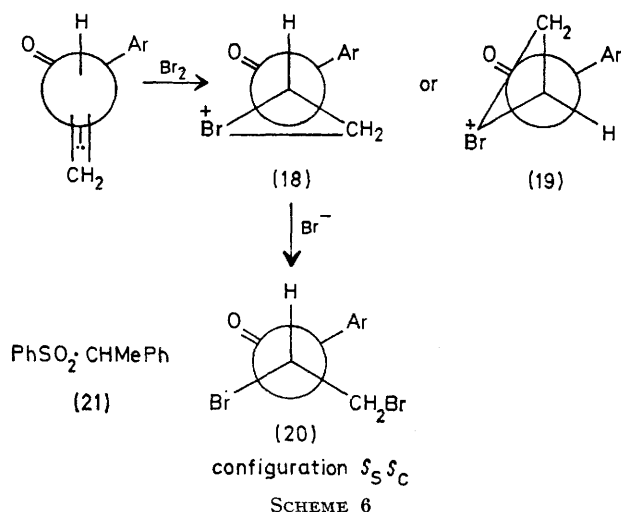
chromatographically separable, the diastereoisomer ratio was calculated from the integral ratio of the ^1H n.m.r. C-Me signals. Results are in Table 2.

It seems probable that the bromonium ion intermediate in the electrophilic addition is symmetrical.²⁴ A high degree of carbocation character would place a positive charge either on carbon adjacent to the electro-negative sulphinyl group or on a primary carbon atom. Examination of the possible conformations of the intermediate bromonium ion formed in reactions with the vinyl sulfoxide leads to the preference for structures

²³ C. J. M. Stirling, *J. Chem. Soc.*, 1964, 5863.

²⁴ P. B. de la Mare and R. Bolton, 'Electrophilic Additions to Unsaturated Systems,' Elsevier, London, 1966.

(18) and (19) (Scheme 6) in which gauche interactions between the bromine atom and the aryl group are avoided. The preferred conformation is (18) and attack of bromide ion leads to the dibromide (20) with absolute configuration $S_S S_C$. Robertson and his co-workers^{25,26} have suggested that formation of loose complexes between two molecules of bromine and one of alkene precedes reaction to give dibromide when bromine concentrations are high. The concentrations of bromine



used in the present study were about three times as great as those used in Robertson's work and any such molecular association would have the effect of accentuating the energy differences between those conformations which do and do not have bromine gauche to the aryl group.

This description can be tested with a knowledge of the absolute configuration of the sulphone (17) derived from the sulphoxide (16). Brewster's rules²⁷ allow the prediction of absolute configuration from sign of rotation (or *vice versa*). In this case, the appropriate polarisability sequence²⁸ is $Br > CH_2Br > H$, and placement of $ArSO_2$ in this sequence is required for a prediction of absolute configuration. No polarisability value is available for an arylsulphonyl group but Corey and Lowry²⁹ find (*R*)-1-phenylethyl phenyl sulphone (21) to be dextrorotatory and Brewster's rules therefore require the polarisability sequence $PhSO_2 > Ph > Ne > H$. As bromine has a very high polarisability²⁷ it appears reasonable to assign the polarisability sequence $Br > ArSO_2 > CH_2Br > H$ which also leads to the designation of the (*S*)-configuration to the laevorotatory enantiomer.

In reactions with (+)-(*S*)- α -methylvinyl *p*-tolyl sulphoxide, the optical yield determined by ¹H n.m.r. spectroscopy was 43%. Examination of the most probable conformations of the bromonium ion does not allow

²⁵ P. W. Robertson, N. T. Clare, K. J. McNaught, and G. W. Paul, *J. Chem. Soc.*, 1937, 335.

²⁶ B. W. Swedlund and P. W. Robertson, *J. Chem. Soc.*, 1945, 131; 1947, 630.

²⁷ J. H. Brewster, *Topics Stereochem.*, 1967, 2, ch. 1.

confident prediction of absolute configuration at the new asymmetric carbon centre produced. The yields of adduct obtained in reactions with this sulphoxide are, however, much lower, and the possibility exists that degradation of the initial product affects one diastereoisomer preferentially.

EXPERIMENTAL

General.—Light petroleum had b.p. 40–60°, ether was dried over sodium, and tetrahydrofuran was distilled from lithium aluminium hydride. Titanium(III) chloride solution was aqueous 15% w/v. N.m.r. spectra were recorded on instruments operating at 60 MHz. Optical rotations were determined on a Perkin-Elmer 141 polarimeter (1 ml 1 dm cell; solvent $CHCl_3$; wavelengths 589, 578, and 546 nm, unless otherwise stated).

(-)-Menthyl toluene-*p*-sulphinic acid was prepared as previously described;³⁰ the desired diastereoisomer (product of thermodynamic control) was obtained from mother liquors by treatment with dry hydrogen chloride at 0 °C; m.p. 104–105°, $[\alpha]_D^{25} -198^\circ$ (*c* 2 in Me_2CO) [lit.,³⁰ m.p. 105–106°, $[\alpha]_D^{21} -202^\circ$ (*c* 2 in Me_2CO)].

Synthesis of $\alpha\beta$ -Unsaturated Sulphoxides.—The following description exemplifies the procedure generally used. 1-Bromopropene was first distilled from a trace of sodium and the *Z*-isomer, b.p. 58°, was separated from the *E*-isomer, b.p. 63°, by using a spinning-band column. The i.r. spectrum of the *Z*-isomer in hexane showed that less than 10% of the *E*-isomer was present.³¹

(*Z*)-1-Bromopropene (5 g) was added to magnesium turnings (3.6 g, 0.144 g atom) suspended in tetrahydrofuran (50 ml) under argon. After the vigorous reaction had started, further bromide (17.4 g, 0.144 mol) in tetrahydrofuran (100 ml) was added at a rate sufficient to maintain gentle refluxing. The solution was then forced through a sintered glass filter under nitrogen pressure and added dropwise, with stirring, to a solution of menthyl toluene-*p*-sulphinic acid (44 g, 0.15 mol) in sodium-dried benzene (200 ml) at 20 °C. After addition was complete (1 h), the mixture was stirred for 1 h and was then added to saturated aqueous ammonium chloride (200 ml). The mixture was extracted with chloroform (800 ml) and the residue from evaporation was chromatographed on alumina (Spence type H) to remove unchanged menthyl toluene-*p*-sulphinic acid (14 g; m.p. 75–80°) which was eluted with light petroleum together with most of the menthol produced. The sulphoxide (18.7 g, 95%), slightly contaminated with menthol, was recovered by elution with benzene. Recrystallisation of the sulphoxide from light petroleum afforded pure (-)-(*Z*)-propenyl *p*-tolyl sulphoxide, m.p. 54–55°, $[\alpha]_{546}^{25} -387^\circ$ (*c* 0.2) (Found: C, 66.7; H, 6.6. $C_{10}H_{12}OS$ requires C, 66.7; H, 6.7%, $\nu_{s, O} 1050\text{ cm}^{-1}$; τ ($CDCl_3$) 2.4–2.8 (4 H, m), 3.6–3.9 (2 H, m), 7.64 (3 H, s), and 7.9 (3 H, d).

(*Z*)-Propenyl *p*-Tolyl Sulphone.—The preceding sulphoxide (0.418 g) in acetic acid (5 ml) was heated with hydrogen peroxide (1 g; 30% w/v; 5 mol) at 90 °C for 1 h. Water was added and the solution was extracted with

²⁸ E. L. Eliel, 'Stereochemistry of Carbon Compounds,' McGraw-Hill, New York, 1962, p. 151.

²⁹ E. J. Corey and T. H. Lowry, *Tetrahedron Letters*, 1965, 803.

³⁰ C. J. M. Stirling, *J. Chem. Soc.*, 1963, 5741.

³¹ D. Y. Curtin and J. W. Crump, *J. Amer. Chem. Soc.*, 1958, 80, 1922.

chloroform. The extracts were washed with aqueous sodium hydrogen carbonate and water; evaporation gave the *sulphone*, m.p. 44–45°, $[\alpha]_{546}^{25}$ 0.00° (c 4) (Found: C, 61.3; H, 6.1. $C_{10}H_{12}O_2S$ requires C, 61.2; H, 6.1%); τ (CCl_4) 2.0–2.7 (4 H, m), 2.6–2.8 (2 H, m), 7.6 (3 H, s), and 7.85 (3 H, d).

Additions of Piperidine to Sulphoxides.—(a) (–)-(Z)-*Propenyl p-tolyl sulphoxide*. The sulphoxide (0.90 g) was treated with piperidine (2.2 mol. equiv.) in reagent grade methanol (15 ml) at reflux for 24 h. The solvent and excess of piperidine was distilled off and the residue (1.33 g, 100%) had m.p. 87–89°, $[\alpha]_{546}^{25}$ +200° (c 1.5). Recrystallisation from light petroleum gave the pure *diastereoisomer*, m.p. 98–99°, $[\alpha]_{546}^{25}$ +226° (c 0.4) (Found: C, 67.7; H, 8.5; S, 12.5. $C_{15}H_{23}NOS$ requires C, 67.9; H, 8.7; S, 12.1%).

The pure diastereoisomer (0.328 g) was reduced¹² by treatment with acetic acid (50 ml), titanium(III) chloride (5 ml), and sodium acetate (5 g) at 90 °C for 1 h under nitrogen. The mixture was adjusted to pH 12 with aqueous sodium hydroxide and diluted with water (200 ml). Extraction with dichloromethane and evaporation gave a residue (0.315 g, >100%), $[\alpha]_{546}^{25}$ –17° (c 7). The reduction procedure was repeated; the residue then had $[\alpha]_{546}^{25}$ –12.0° (c 8). Distillation gave (–)-2-*piperidino-propyl p-tolyl sulphide*, b.p. 120° at 0.05 mmHg, n_D^{20} 1.5495, $[\alpha]_{546}^{25}$ –24.0° (c 1) (Found: C, 72.3; H, 9.2. $C_{15}H_{23}NS$ requires C, 72.3; H, 9.25%).

Repetition of this procedure with the mixture of diastereoisomers gave a sample of 2-piperidinopropyl *p*-tolyl sulphide, b.p. 120° at 0.05 mmHg, n_D^{15} 1.5558, $[\alpha]_{546}^{25}$ –17.7° (c 1). The i.r. spectra of the two samples (liquid films) were identical.

(+)-2-Piperidinoethyl *p*-tolyl sulphoxide, $[\alpha]_{589}^{25}$ +208°, m.p. 100–102° (20.1 mg), was kept in a sealed tube with methanol (1.5 ml) containing piperidine (7.8 mg) (1.2 mol. equiv.) at 60 °C. The initial rotation of the solution (2.082°) had changed to 2.043° after 24 h and to 1.934° after 72 h.

Absolute configuration of 2-piperidinoethyl p-tolyl sulphide. (+)-Alanine (8.01 g) was reduced with lithium aluminium hydride (10.5 g) in tetrahydrofuran (120 ml) according to Vogel and Pohn's³² procedure. The resulting hydroxyamine (70%) had b.p. 85° at 10 mmHg, $[\alpha]_D^{25}$ +19° (c 6.0 in 96% EtOH) {lit.,³² b.p. 67° at 8 mmHg, $[\alpha]_D^{25}$ +22.0° (c 6.45 in 96% EtOH)}. The amino-alcohol (2 g) was boiled under reflux with 1,5-dibromopentane (6.15 g, 1 mol. equiv.) in toluene (40 ml). After 3 h, sodium hydrogen carbonate (4.5 g, 2 mol. equiv.) was added and the mixture was boiled with stirring for an additional 18 h. The mixture was cooled and after the addition of 50% aqueous sodium hydroxide (10 ml) continuous extraction with ether gave the crude piperidino-alcohol (89%), b.p. 98° at 15 mmHg, $[\alpha]_D^{25}$ +7.2 (c 0.42 in 96% EtOH), n_D^{19} 1.4839, which was converted into the hydrochloride with gaseous hydrogen chloride in methanol. Removal of the solvent and treatment of the crude amino-alcohol hydrochloride with thionyl chloride (3.5 ml) in chloroform (40 ml) gave 2-*piperidinopropyl chloride hydrochloride* (7) (65%), m.p. 194.5° (from ethanol-ethyl acetate), $[\alpha]_D^{25}$ –8.7° (c 0.5 in 96% EtOH) (Found: C, 48.5; H, 8.8; N, 7.1. $C_8H_{17}Cl_2N$ requires C, 48.7; H, 8.6; N, 7.1%).

The chloride hydrochloride (1 g) was treated with a solution of sodium toluene-*p*-thiolate obtained by addition

of toluene-*p*-thiol (0.75 g, 1.2 mol. equiv.) and sodium ethoxide (0.27 g) in ethanol (50 ml). The mixture was boiled under reflux for 4 h and, after addition of water, extraction with dichloromethane gave the product (79%), b.p. 128–130° at 0.4 mmHg, $[\alpha]_{546}^{20}$ –25.8° (c 5 in $CHCl_3$). The product was a ca. 80:20 mixture of 2-piperidino-propyl *p*-tolyl sulphide (4) and 1-methyl-2-piperidinoethyl *p*-tolyl sulphide (8). These were separated by g.l.c. on an SE30 column at 210 °C. The specimen of 2-piperidino-propyl *p*-tolyl sulphide, $[\alpha]_{546}^{20}$ –16.1°, was converted into the picrate, m.p. 122–123° alone or mixed with a specimen of the picrate of the material, m.p. 122–124°, obtained from the sulphoxide addition–reduction route.

(b) (+)- α -Methylvinyl *p*-tolyl sulphoxide. The sulphoxide (2.79 g) and piperidine (10 mol. equiv.) were refluxed in reagent grade ethanol (75 ml). The reaction was monitored by decrease in the intensity of the i.r. bands at 1 635 and 920 cm^{-1} (samples of the mixture were removed and evaporated and the residue was redissolved in benzene). After 114 h, solvent and the excess of piperidine were removed by distillation and the residue was chromatographed on alumina. Elution with benzene gave an unidentified compound (0.8 g), $[\alpha]_{546}^{25}$ 0.00° (c 5), whose i.r. spectrum showed that it was not a sulphoxide; b.p. 116° at 0.5 mmHg, n_D^{22} 1.5582; τ (CCl_4) 2.5–3.0 (4 H, m), 4.8 (1 H, s), 5.3 (1 H, s), 7.0 (2 H, s), 7.8 (9 H, s), and 8.6br (6 H, s). Elution with ether gave unchanged α -methylvinyl *p*-tolyl sulphoxide (0.90 g) followed by the adduct (2.27 g, 55%), $[\alpha]_{546}^{25}$ +134° (c 2); τ (CCl_4) 2.4–2.8 (4 H, m), 7.0–8.0 (10 H, m + s), 8.5br (6 H, s), and 9.0 (d) and 9.25 (d) (3 H). The ratio of the intensities of the two α -C-methyl doublets was taken as the ratio of the diastereoisomers and was 1.8:1, indicating an optical yield of 29%.

One portion (1.415 g) of the adduct was chromatographed on alumina; elution with benzene gave one *diastereoisomer*, which was crystallised from light petroleum to constant m.p. 85–86° and rotation $[\alpha]_{546}^{25}$ +207° (c 9.5), τ 9.25 (Found: C, 68.2; H, 8.9. $C_{15}H_{23}NOS$ requires C, 67.9; H, 8.7%). Subsequent elution with ethanol-ether gave the other diastereoisomer, $[\alpha]_{546}^{25}$ +78° (c 0.5), τ 9.0. Attempts to crystallise this diastereoisomer failed.

The second portion (0.756 g) of the adduct mixture was reduced with titanium(III) chloride (10 ml) in acetic acid (15 ml) and sodium acetate (1 g) at 90 °C for 1 h under nitrogen. The mixture was treated as above to give a residue (0.553 g, 77%), $[\alpha]_{546}^{25}$ –5.30° (c 5), which was reduced by the same procedure, $[\alpha]_{546}^{25}$ –5.1° (c 5). Distillation gave 1-methyl-2-*piperidinoethyl p-tolyl sulphide*, b.p. 118° at 0.1 mm, n_D^{19} 1.5456, $[\alpha]_{546}^{25}$ –6.3° (c 4) (Found: C, 72.1; H, 9.0; S, 13.6. $C_{15}H_{23}NS$ requires C, 72.3; H, 9.2; S, 12.9%). The pure diastereoisomer of m.p. 85–86° was also reduced to constant rotation by the same procedure; the sulphide obtained had n_D^{23} 1.5438, $[\alpha]_{546}^{25}$ –20.8° (c 6), i.r. spectrum identical with that of the enantiomeric mixture of sulphides.

The other diastereoisomer, $[\alpha]_{546}^{25}$ +78°, was also reduced and gave the sulphide, n_D^{23} 1.5420, $[\alpha]_{546}^{25}$ +17.7° (c 2), the lower rotation showing that this specimen was not entirely free of the other diastereoisomer. The rotation ratio gives the optical yield as 30%, in good agreement with that from n.m.r. measurements (29%).

³² O. Vogl and M. Pohn, *Monatsh.*, 1952, **83**, 541.

Addition of Benzene-²H-thiol to (+)-p-Tolyl Vinyl Sulphoxide.—Benzenethiol (2 g) was shaken with deuterium oxide (99.7%; 4 g, 12 mol. equiv.) for 15 h. The benzenethiol was separated; repetition of the procedure gave the exchanged product which was distilled in apparatus which had been used to distil deuterium oxide and then dried. The product had b.p. 167° at 760 mmHg, and the ¹H n.m.r. spectrum showed that it contained less than 1% [¹H]-analogue.

(+)-*p*-Tolyl vinyl sulphoxide (1.044 g) and benzene-²H-thiol (0.747 g, 1.1 mol. equiv.) were kept in sodium-dried benzene (20 ml) containing triethylamine (2 drops) at 25 °C. The reaction was monitored by observing the disappearance of the i.r. band at 960 cm⁻¹, and was complete after 65 h. Solvent was distilled off and a portion of the sulphide (1.803 g, 100%), [α]_D²⁵ +132° (*c* 1 in EtOH) was crystallised to constant m.p. 79–80°, [α]_D²⁵ +145° (*c* 1 in EtOH) (Found: C, 65.0; H, 6.1; S, 23.3. C₁₅H₁₅DOS₂ requires C, 65.0; H, 6.1; S, 23.1%).

The adduct was reduced with titanium(III) chloride as before to give the bis-sulphide (100%), m.p. 45–46°, raised to 48–49° (from ethanol), [α]₅₄₆²⁵ +0.04° (*c* 14). The specimen was re-reduced and the product then had m.p. 48–49°, [α]₅₄₆²⁵ +0.05° (*c* 10), τ (CCl₄) 2.5–2.8 (9 H, m), 6.9 (3 H, s), and 7.6 (3 H, s). G.l.c. of the material (5 ft SE30; 190 °C; H₂ carrier gas) gave the bis-sulphide, [α]₅₄₆²⁵ 0.00° (*c* 12 in CHCl₃), m.p. 42–43° alone or on admixture with an authentic specimen (above).

Addition of Bromine to $\alpha\beta$ -Unsaturated Sulphoxides.—(a) *Reactions with p-tolyl vinyl sulphoxide.* Bromine (2.1 g, 1.1 mol. equiv.) in acetic acid (10 ml) was added dropwise with stirring to (+)-*p*-tolyl vinyl sulphoxide (2.0 g) in acetic acid (10 ml) at 25 °C. After 16 h, water (1 ml) was added and sulphur dioxide was passed through the solution till it was colourless. Water (50 ml) was added and the mixture was extracted with chloroform. Evaporation of the extracts gave an oil (4.25 g), [α]₅₄₆²⁵ +81.3° (*c* 0.6). The product was chromatographed on silica gel; elution with benzene gave, first, toluene-*p*-sulphonyl bromide (0.50 g), m.p. 91–92° (from light petroleum) alone or mixed with an authentic specimen prepared by treatment of sodium toluene-*p*-sulphinate in water with bromine at 0 °C (lit.,³³ m.p. 96°). The crude specimen also contained a compound which showed i.r. absorption at 1760 cm⁻¹ but which could not be purified. Elution with ether gave the diastereoisomeric 1,2-dibromo-1-*p*-tolylsulphinyethanes (3.7 g, 92%), [α]₅₄₆²⁵ +93.6° (*c* 0.6); τ (CDCl₃) 2.2–2.7 (4 H, m), 5.2 (1 H, q), 6.05 (2 H, m), and 7.6 (3 H, s). The i.r. spectrum showed that it was free from toluene-*p*-sulphonyl bromide (no bands at 1350 and 1150 cm⁻¹) and of the carbonyl compound (no bands at 1760 cm⁻¹), and t.l.c. (benzene) showed two, closely spaced, slow-running spots.

The mixture of diastereoisomers (2.0 g) in acetic acid (20 ml) was kept with hydrogen peroxide (30%; 10 mol. equiv.) at 60 °C for 1 h. Water was added and extraction of the mixture with chloroform and evaporation gave a residue (1.9 g), [α]₅₄₆²⁵ –20.1° (*c* 1) with no i.r. absorption at 1050 cm⁻¹ (vs. O). Re-oxidation gave material (1.9 g), [α]₅₄₆²⁵ –21.1° (*c* 2), and a third oxidation gave material (1.9 g), [α]₅₄₆²⁵ –21.8° (*c* 2), m.p. 67–70°. Recrystallisation

of this material (light petroleum) raised the m.p. to 73–74° but the rotation decreased { $[\alpha]_{546}^{25}$ –15.9° (*c* 2.5)} (Found: C, 32.1; H, 3.0. C₉H₁₀Br₂O₂S requires C, 31.6; H, 2.9%).

A portion of the diastereoisomeric mixture obtained by column chromatography was crystallised (light petroleum) to give the major diastereoisomer, m.p. 74–75°, [α]₅₄₆²⁵ +142° (*c* 1.5) (Found: C, 33.2; H, 3.2. C₉H₁₀Br₂O₂S requires C, 33.1; H, 3.1%). I.r. (CHCl₃) spectra were identical with those of the mixture of diastereoisomers.

The pure diastereoisomer was oxidised and reoxidised (4 times) as already described until the rotation was constant. The pure sulphone had m.p. 83–83.5°, [α]₅₄₆²⁵ –66.7° (*c* 4) (Found: C, 32.1; H, 2.5; S, 9.5. C₉H₁₀Br₂O₂S requires C, 31.6; H, 2.9; S, 9.4%). The optical yield was taken as the ratio of the rotation of the sulphone obtained directly from the diastereoisomer mixture to that of the sulphone obtained from the pure diastereoisomer. The i.r. spectrum was identical with that of a racemic sample (below).

1,2-Dibromo-1-p-tolylsulphonyethane. *p*-Tolyl vinyl sulphone (1 g) and bromine (1.1 mol. equiv.) in acetic acid (10 ml) were kept for 2 h at 25°. Water (1 ml) was added and sulphur dioxide was passed until the solution became colourless. Addition of water and extraction with dichloromethane gave 1,2-dibromo-1-*p*-tolylsulphonyethane (78%), m.p. 72–75°, raised to 76–77° (from benzene–light petroleum) (Found: C, 32.2; H, 2.5. C₉H₁₀Br₂O₂S requires C, 31.6; H, 2.9%); τ (CDCl₃) 2.0–2.7 (4 H, m), 5.0 (1 H, q), 5.7 (1 H, q), 6.42 (1 H, q), and 7.51 (3 H, s).

(b) (+)- α -Methylvinyl *p*-tolyl sulphoxide. Bromine (3.7 g, 1.2 mol. equiv.) in acetic acid (25 ml) was added to (+)- α -methylvinyl *p*-tolyl sulphoxide (3.47 g) in acetic acid (25 ml). After 15 h, more bromine (0.20 g) was added, followed after a further 3 h by water (1 ml), and sulphur dioxide was passed until the solution was colourless. Water (100 ml) was then added and the mixture was extracted with dichloromethane. Evaporation of the extracts gave a residue (6.9 g, >100% calculated as adduct), [α]₅₄₆²⁵ +36.9° (*c* 2.5). The i.r. spectrum showed the presence of toluene-*p*-sulphonyl bromide and a carbonyl compound. Chromatography on silica gel gave a mixture of diastereoisomeric dibromo-sulphoxides (3.29 g, 50%), [α]₅₄₆²⁵ +73° (*c* 1). The ¹H n.m.r. spectrum showed that contaminants were present in negligible amounts, and from the ratio of the *C*-methyl group signal intensities (20:8) the optical yield is calculated as 43%. The diastereoisomers could not be separated by chromatography and a portion of the adduct (1.10 g) in acetic acid was oxidised with hydrogen peroxide in acetic acid as before to give 1,2-dibromo-1-methyl-1-*p*-tolylsulphonyethane (85%), m.p. 81–85°, [α]₅₄₆²⁵ –16.0° (*c* 5). Repetition of the oxidation procedure gave sulphone of m.p. 89–90° (from benzene–light petroleum), [α]₅₄₆²⁵ –20.6° (*c* 1) (Found: C, 33.8; H, 3.6; S, 9.5. C₁₀H₁₂Br₂O₂S requires C, 33.7; H, 3.4; S, 9.0%); τ (CHCl₃) 1.9–2.6 (4 H, m), 6.0 (2 H, q), 7.5 (3 H, s), and 7.9 (3 H, s).

We thank the S.R.C. for a maintenance grant (to D. J. A.), the Leverhulme Foundation for a European Fellowship (to S. C.), and Mr. G. Griffiths for technical assistance.

³³ C. J. M. Stirling, *J. Chem. Soc.*, 1957, 3597.