Stereochemistry and Reactivity in Interconversions of Three- and Fourco-ordinate Imino-derivatives of Sulphur †

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Optically pure sulphoxides have been converted into N-phthalimidosulphoximides by treatment with N-aminophthalimide and lead tetra-acetate. Sulphoxides are regenerated in high yields and optical purities on treatment with sodium ethoxide or hydrazine in ethanol and it is suggested that each step in these two-step cycles occurs with retention of configuration at sulphur. No attack occurs at the carbon-carbon double bond in formation of the sulphoximide from *p*-tolyl vinyl sulphoxide.

Reactions of S-vinyl- and of S- β -substituted-ethyl-sulphimides have been briefly investigated in a qualitative evaluation of the activating effects of the sulphonylimino-sulphur group on elimination and addition reactions.

THE reactivity and stereochemistry of simple iminoderivatives of sulphur has been widely investigated.¹ Much attention has been focused on the interchange of ligands at sulphur and rather less on the effect of iminosulphur groups on reactivity at more distant molecular sites. In this paper we report on two aspects of iminosulphur chemistry: first, the stereochemistry of formation of N-phthalimidosulphoximides (1) from optically active sulphoxides and the subsequent regeneration of the sulphoxides; and secondly, the effect of the threeco-ordinate imino-sulphur group in sulphimides on the reactivity of leaving groups situated β to it and upon the electrophilic reactivity of an adjacent carbon-carbon double bond.

$$(1)$$

$$a; R^{1}=CH_{2}CH, R^{2}=p-MeC_{6}H_{4}$$

$$b; R^{1}=CH_{2}CH, R^{2}=p-MeC_{6}H_{4}$$

$$d; R^{1}=CH_{2}CH, R^{2}=p-MeC_{6}H_{4}$$

$$d; R^{1}=CH_{2}CH, R^{2}=cH_{2}CH_{2}CL$$

$$e; R^{1}=CH_{2}CH, R^{2}=cH_{2}CH_{2}CL$$

Sulphoximides.-Several methods are available for the conversion of sulphoxides into sulphoximides. These include treatment with a sulphonyl azide and copper,² with hydrazoic acid,³ and with a sulphonamide together with lead tetra-acetate and a mild base such as triethylamine.⁴ A particularly simple procedure has been reported by Rees and his collaborators⁵ which involves treatment of the sulphoxide with N-aminophthalimide

† Part of this work has been reported in a preliminary communication: S. Colonna and C. J. M. Stirling, Chem. Comm., 1971, 1591.

¹ T. R. Williams, R. E. Booms, and D. J. Cram, J. Amer.

Chem. Soc., 1971, 93, 7338. ² D. J. Cram, J. Day, D. R. Rayner, D. M. von Schriltz, D. J. Duchamp, and D. C. Garwood, J. Amer. Chem. Soc., 1970, **91**, 7369.

⁸ R. Fusco, and A. Tenconi, Chimica e Industria, 1965, 1, 61.

and lead tetra-acetate in dichloromethane; a synthesis which probably involves nitrene intermediates.⁶ We have now applied this procedure to a number of sulphoxides including three optically active compounds; the results are in the Table; yields are excellent and the sulphoximides obtained from the active sulphoxides are themselves optically active. Particularly interesting in this respect is the conversion of optically active p-tolyl vinyl sulphoxide ⁷ into the $\alpha\beta$ -unsaturated sulphoximide (1b). No competing reactions were observed which could have been associated with the carbon-carbon double bond which, in this case, is susceptible to electrophilic,⁷ nucleophilic,⁸ and radical⁹ addition. Nitrene addition is a familiar reaction type for alkenes.¹⁰

The N-phthalimidosulphoximides (e.g. S-p-tolyl-Svinyl-) were stable to concentrated sulphuric acid for short periods (ca. 30 min) at room temperature; conditions in which N-p-tolylsulphonylsulphoximides are readily hydrolysed² to the simple sulphoximides. With longer reaction times, however, decomposition occurred. Treatment of the N-phthalimidosulphoximides with sodium ethoxide or with hydrazine in ethanol, however, regenerated the sulphoxide with concurrent formation, in the case of sodium ethoxide, of the half-ester of phthalic acid. In the case of the S-vinylsulphoximide, the adduct with ethanol, 2-ethoxyethyl p-tolyl sulphoxide, was isolated as the regeneration product. When optically active sulphoximides were used, the sulphoxides were obtained in good yield and with high optical purity (Table). These observations established that both formation of the sulphoximides from the sulphoxides and their regeneration occurs with high stereospecificity. Clearly, in this two-reaction cycle, both reactions occur with retention or both with inversion of configuration. We favour double retention in the cycle; Cram and his co-workers,² have shown that treatment of methyl p-tolyl sulphoxide with toluene-p-sulphonyl

⁴ T. Ohashi, K. Matsunaga, M. Okalhara, and S. Koniori, Synthesis, 1971, 96, and references cited.
 ⁵ C. W. Rees and M. Yelland, J.C.S. Perkin I, 1972, 77.

 D. S. Atkinson and C. W. Rees, Chem. Comm., 1967, 1230.
 D. J. Abbott and C. J. M. Stirling, Chem. Comm., 1971, 472.
 D. J. Abbott, S. Colonna, and C. J. M. Stirling, Chem. Comm., 1971. 471.

⁹ C. Walling, ' Free Radicals in Solution,' Wiley, New York, 1957.

¹⁰ H. Kwart and A. A. Khan, J. Amer. Chem. Soc., 1967, 89, 1951.

azide and copper give the sulphoximide with retention of configuration. For these reactions, copper-nitrene complexes¹¹ are probably involved and the mechanism is formally similar to that of the N-aminophthalimide reaction. The ethoxide reaction probably occurs in several stages and the yields of sulphoxide obtained are virtually quantitative

with triethylamine in toluene. As would be expected from this observation, a three-co-ordinate imino-sulphur group activates the adjacent carbon-carbon double bond of the $\alpha\beta$ -unsaturated sulphimide towards nucleophilic addition. The sulphimide (3b) on treatment with ethanolic sodium ethoxide gave the ethoxy-derivative (4a), which is also formed directly by similar treatment

Interconversion of sulphoxides and N-phthalimidosulphoximides

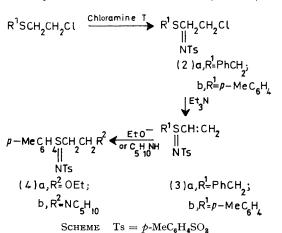
	X7: 11 Course										sulp	ohoxide	
	Yield from sulphoxide			Fou	und (°	6)		Requ	aired	(%)	Yield	Optical	
Compound	(%)	M.p. (°C)	[α] _D (°)	c	H	Ň	Formula	c –	H H	Ň	(%)	purity (%)	
(la)	89	137		67.2	4.6	7.3	$C_{22}H_{13}N_2O_3S$	67.7	4.6	$7\cdot 2$	88	75 %	
(1b)	70	163 $^{\circ}$	+30 a	$62 \cdot 2$	4.4	8.6	$C_{17}H_{14}N_{2}O_{3}S$	62.5	4 ·3	8.6	75 d		
(lc)	92	184	-26·8 °	69.3	$4 \cdot 3$	6.5	$C_{25}H_{18}N_2O_3S$	70.0	$4 \cdot 2$	6.6	80	96 ^f , 95	
(1d)	80	113		56.2	$4 \cdot 0$	$8 \cdot 0$	$C_{17}H_{15}ClO_3N_2S$	56.3	4.1	7.7			
(l e)	100	143		56.5	$4 \cdot 3$	7.5	$C_{17}H_{15}ClO_3N_2S$	56.3	4.1	7.7			
^a c 1, CHCl ₃ .	^b Before purification.		[¢] Racemic m.p. 191·5°.			^{<i>d</i>} 2-Ethoxyethyl p -tolyl sulphoxide.				^e $[\alpha]_{546} - 17.6^{\circ}$ (c 1, acetone).			

، ول ^f Hydrazine reaction.

In correction of our earlier report,* nitrogen is evolved in the ethoxide reactions. These were carried out under oxygen at 1 atm. and treatment of samples of the gas space with alkaline pyrogallol showed that stoicheiometric quantities of nitrogen were obtained. Hydrazine was sought by a procedure which would have detected its formation in yields >5%. None was found.

In relation to these results, it has been shown that alkaline hydrolysis of a sulphimide involves inversion of configuration at sulphur.²

Sulphimides .--- A qualitative examination has been made of the electronic effects of three- and four-co-ordinate imino-sulphur groups, with particular reference to the comparison of the electronic effects of these groups with sulphinyl and sulphonyl groups. We prepared the Np-tolylsulphonylsulphimides (2) from 2-halogenoethyl sulphides by reaction with chloramine T (Scheme). The



imino-sulphur group activates elimination of chloride

under very mild conditions; formation of the $\alpha\beta$ unsaturated sulphimides occurs rapidly on treatment * See footnote to title.

¹¹ H. Kwart and A. A. Khan, J. Amer. Chem. Soc., 1967, 89, 1950.
 ¹² C. J. M. Stirling, J. Chem. Soc., 1962, 3676.
 ¹³ C. J. M. Stirling, J. Chem. Soc., 1963, 5741.

of the chloride (2b). This latter reaction is probably an elimination-addition process 12 and with piperidine, the chloride (2b) gives the piperidinosulphimide (4b), which is also obtained by addition of piperidine to the sulphimide (3b).

Electronic effects of three-co-ordinate sulphur groups in this context will obviously vary considerably with the precise structure of the sulphimido-group and we propose to examine this aspect further.

Examination of the effect on elimination-addition reactions of the N-phthalimidosulphoximido-group was frustrated by the lability of the sulphoximido-group towards bases. Investigation of less labile sulphoximidoderivatives is planned.

EXPERIMENTAL

Sulphoxides.--p-Tolyl benzyl,¹³ vinyl,⁷ and *a*-naphthyl sulphoxides¹⁴ were obtained by literature methods.

2-Chloroethyl sulphoxides were obtained by periodate oxidation 15 of the 2-chloroethyl sulphides. Benzyl 2chloroethyl sulphoxide (60%) had m.p. 91° (from ethanol) (Found: C, 52.9; H, 5.5. C₉H₁₁ClOS requires C, 53.3; H, 5.4%). 2-Chloroethyl p-tolyl sulphoxide (81%) had b.p. 131° at 0.15 mmHg (lit.,¹⁶ boils with decomposition).

Preparation of N-Phthalimidosulphoximides.-The sulphoxide, in dry chloroform, was treated with N-aminophthalimide 17 (1.2 mol) and to the clear solution was added lead tetra-acetate (1.3 mol. equiv.). The mixture was kept at 20° for 30 min, then water was added and the organic layer separated and dried. Evaporation under reduced pressure gave the sulphoximide which was purified by recrystallisation from ethanol. Details are in the Table.

Treatment of Racemic S-p-Tolyl-S-vinyl-N-phthalimidosulphoximide (1b) with Sulphuric Acid.-The N-phthalimidosulphoximide (1 g) was treated with concentrated sulphuric acid (d 1.84; 5 mol, equiv.) at 20° for 30 min. The mixture was rapidly diluted with ice-water and filtration gave the recovered sulphoximide (97%), m.p. and mixed m.p. 189°.

 K. K. Andersen, J. Amer. Chem. Soc., 1964, 86, 5637.
 N. J. Leonard and C. R. Johnson, J. Amer. Chem. Soc., 1962, ¹⁶ R. J. Leonard 4. **84**, 3701.
¹⁶ E. Fromm and A. Kohn, *Ber.*, 1921, **54**, 326.
¹⁷ H. D. K. Drew and H. H. Hatt, *J. Chem. Soc.*, 1937, 16.

Regenerated

Reaction of N-Phthalimidosulphoximides with Bases.— (a) With sodium ethoxide in ethanol. Sodium ethoxide (0.15 mol) was added to a stirred solution of the sulphoximide (1c) (0.01 mol) in ethanol (100 ml). The mixture was stirred for 4 h, poured into water, acidified with dilute sulphuric acid, and extracted with chloroform. The organic layer was washed with water and evaporated. The residue, on treatment with ether-light petroleum (b.p. $40-60^{\circ}$) gave, after filtration, (-)- α -naphthyl *p*-tolyl sulphoxide (96%), m.p. and mixed m.p. 135-136°, [α]_D -398° (c 1, acetone) (lit.,¹⁴ - 414°). Evaporation of the filtrate yielded monoethyl phthalate (80%) as an oil whose spectral properties (i.r., n.m.r.) were identical with those of an authentic sample.¹⁸

The reaction was repeated in a two-necked flask attached to a vacuum line. The solution of the sulphoximide in ethanol was degassed by freeze-thaw cycles and oxygen was admitted at 1 atm. with a levelling bulb. Degassed ethanolic sodium ethoxide was added by syringe through a serum cap and after 4 h, samples of the gas space were removed by syringe and shaken in a gas burette with alkaline pyrogallol. The yield of nitrogen calculated from seven determinations was $100 \pm 2\%$. It was confirmed that the products of the reaction under oxygen were as obtained from reactions under air.

Separate experiments showed that had hydrazine been liberated in the reactions, even in small amounts, it could have been isolated as the NN-dibenzoyl derivative by addition of benzoyl chloride and triethylamine to the reaction mixture. None was detected in this way.

(b) With hydrazine and ethanol. Hydrazine hydrate (0.04 mol) was added to a stirred suspension of the sulphoximide (1c) (0.001 mol) in ethanol (10 ml). After 30 min at 40°, the mixture was diluted with ether (100 ml), water was added, and the organic layer separated, dried, and evaporated to give α -naphthyl *p*-tolyl sulphoxide (80%), m.p. and mixed m.p. 135°, $[\alpha]_{\rm p} - 398^{\circ}$ (c 1, acetone).

Reactions with the other sulphoximides were carried out similarly.

Preparation of Sulphimides.—2-Chloroethyl p-tolyl sulphide (0.01 mol) in ethanol (20 ml) was added dropwise, with stirring, to chloramine τ (0.015 mol) in ethanol (100 mol). After 20 h, water (100 ml) was added to precipitate S-2-chloroethyl-S-p-tolyl-N-p-tolylsulphonylsulph

imide (2b) (60%), m.p. 125° (from ethanol) (Found: C, 54·1; H, 5·3; N, 4·1. $C_{16}H_{18}ClNO_2S_2$ requires C, 54·0; H, 5·1; N, 3·9%).

S-Benzyl-S-2-chloroethyl-N-p-tolylsulphonylsulphimide (2a) (67%), m.p. 135° (from ethanol) was obtained in a similar way (lit.,¹⁹ m.p. 133—134°).

Elimination Reactions with S-2-Halogenoethylsulphimides. —The S-p-tolylsulphimide (2b) (1·4 g) in toluene (170 ml) was treated with triethylamine (0·3 g). After 24 h at 25°, the mixture was kept at 50° for 30 h and the precipitate of triethylammonium hydrochloride was filtered off. Evaporation of the solvent gave S-p-tolyl-S-vinyl-N-p-tolylsulphonylsulphimide (3b) (87%), m.p. 129° (from methanol) (Found: C, 60·1; H, 5·2; N, 4·4. $C_{16}H_{17}NO_2S_2$ requires C, 60·2; H, 5·3; N, 4·4%).

Formation of S- β -Substituted-ethyl-S-p-tolyl-N-p-tolylsulphonylsulphimides.—(a) The S-vinylsulphimide (3b) (0.01 mol) in ethanol (60 ml) was treated with ethanolic sodium ethoxide (0.03 mol). After 24 h, the mixture was poured into acidified saturated brine and extracted with chloroform. Evaporation of the extract gave S-2-ethoxyethyl-S-p-tolyl-N-p-tolylsulphonylsulphimide (100%), m.p. 114° (from ethanol) (Found: C, 59.3; H, 6.4; N, 3.9. C₁₈H₂₃NO₃S₂ requires C, 59.2; H, 6.3; N, 3.8%).

(b) The S-2-chloroethylsulphimide (2b) (0.01 mol) in ethanol (60 ml) was treated with piperidine (0.05 mol). After 6 h at 50°, the mixture was evaporated and extraction of the residue with ether gave S-2-piperidinoethyl-S-p-tolyl-N-p-tolylsulphonylsulphimide (4b) which readily formed an unstable *carbonate* (Found: C, 56·1; H, 5·7; N, 6·1. C₂₂H₃₀N₂O₂S₂ requires C, 56·5; H, 6·4; N, 6·0%). This product was converted into the *picrate* (98%), m.p. 128° (from ethanol) (Found: C, 50·1; H, 5·0; N, 11·8. C₂₀H₂₅N₄O₈S requires C, 50·0; H, 5·2; N, 11·6%).

The same product (4b) was obtained in quantitative yield by direct addition of piperidine to the S-vinylsulphimide (3b).

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¹⁸ K. von Auwers and A. Heinze, Ber., 1919, 52, 600.

¹⁹ T. P. Dawson, J. Amer. Chem. Soc., 1947, 69, 968.