

Mechanism and Stereochemistry of Nucleophilic Substitutions in Alkoxy-sulphonium Salts

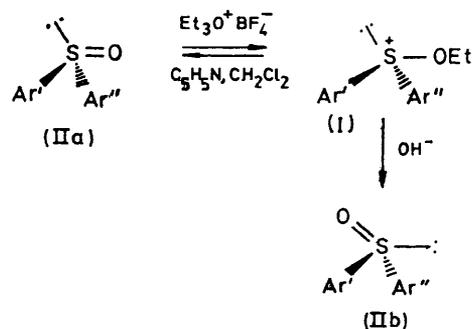
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Optically active diarylethoxysulphonium salts react with pyridine to afford the corresponding diaryl sulphoxides with retention of configuration at sulphur. The reaction of sulphoxonium salts bearing at least one hydrogen atom bonded to the α -carbon leads, in contrast, to α -pyridinio-sulphides.

ALKOXY-SULPHONIUM salts react with nucleophiles to give a variety of products, depending on the nature of the nucleophile and of the substrate. In the case of hydroxide ions, rear-side attack on tetrahedral sulphur gives the sulphoxide of the reverse configuration.¹ Attack at sulphur also occurs in reactions with organo-metallic reagents^{2,3} to give sulphonium salts, in alkoxy-interchange,⁴ in reduction to sulphides by sodium borohydride,⁵ and in the formation of sulphur ylides and of aminosulphonium salts by interaction with carbanions or aliphatic amines, respectively.⁶ Although attack at sulphur seems to be the common pathway in reactions of alkoxy-sulphonium salts with nucleophiles, attack at carbon is also possible, as illustrated by the formation, in low yield, of sulphoxides of retained configuration in reactions of ethoxysulphonium salts with bromide ions.²

We have investigated the stereochemical course and

the influence of structural factors in the reaction of alkoxy-sulphonium salts with pyridine. Optically active diarylethoxysulphonium fluoroborates (I), obtained



according to Johnson's procedure,¹ reacted with pyridine in refluxing anhydrous methylene chloride (20 h) to

¹ C. R. Johnson and D. McCants, *J. Amer. Chem. Soc.*, 1965, **87**, 5404.

² K. K. Andersen, M. Cinquini, and N. E. Papanikolaou, *J. Org. Chem.*, 1970, **35**, 706.

³ (a) K. K. Andersen, *Chem. Comm.*, 1971, 1051; (b) K. K. Andersen, Abstracts of Papers, 163rd A.C.S. National Meeting, Boston, April 1972.

⁴ C. R. Johnson and W. G. Phillips, (a) *J. Amer. Chem. Soc.*, 1969, **91**, 682; (b) *J. Org. Chem.*, 1967, **32**, 1926.

⁵ C. R. Johnson and W. G. Phillips, *J. Org. Chem.*, 1967, **32**, 3233.

⁶ R. M. Acheson and J. K. Stubbs, *J.C.S. Perkin I*, 1972, 899.

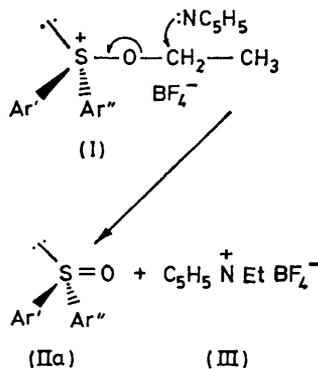
afford the corresponding optically active diaryl sulphoxides (IIb) with retention of configuration at sulphur, while the pyridine was converted into *N*-ethylpyridinium fluoroborate (III). Hydrolysis of the salt (I) with sodium hydroxide¹ gives the sulphoxide of inverted configuration (IIb); thus both the enantiomeric sulphoxides can be obtained from the same alkoxy-sulphonium salt. Yields and optical purity of compounds (IIa and b) are reported in the Table.

| Sulphoxide | [α] _D ^a | Reaction with pyridine | | Reaction with OH ⁻ | |
|--|--|------------------------|---------------|-------------------------------|---------------|
| | | Yield (%) ^b | Retention (%) | Yield (%) ^b | Inversion (%) |
| <i>p</i> -MeC ₆ H ₄ ·SO·C ₁₀ H ₇ - α | -416° | 95 | 100 | 80 | 99 |
| <i>p</i> -MeC ₆ H ₄ ·SOPh | +22° | 79 | 93 | 81 | 93 |
| <i>p</i> -MeC ₆ H ₄ ·SO·C ₆ H ₄ Me- <i>o</i> | -86° | 77 | 97 | 77 | 93 |

^a In acetone; see K. K. Anderson, W. Gaffield, N. E. Papanikolaou, J. W. Foley, and R. I. Perkins, *J. Amer. Chem. Soc.*, 1964, **86**, 5637. ^b For the conversion from sulphoxide back into sulphoxide.

The stereochemistry at sulphur and the formation of salt (III) in the reactions of compounds (I) with pyridine are in agreement with an S_N2 substitution at carbon, where the sulphoxide is the leaving group. Similar mechanisms have been postulated in the reaction of oxosulphonium salts with iodide ions⁷ and in the reaction of *NS*-dimethyl-*S*-*p*-tolylsulphoximide with tosyl chloride in pyridine,⁸ where the sulphoxide and the sulphinamide are the leaving groups, respectively.

It has been shown⁹ that in hindered sulphoxides steric effects can favour attack on carbon over displacement at sulphur in the reaction of alkoxy-sulphonium salts with base; in fact total retention of the original oxygen

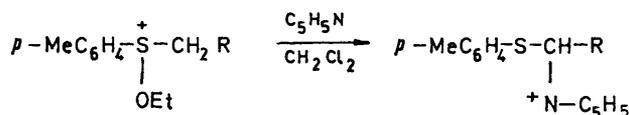


bonded to sulphur has been found.⁹ This, together with the close parallelism between the stereospecificity of the reactions with pyridine and with hydroxide ions (see Table) seems to indicate that the small amount of racemization observed occurs during the preparation of

* Compound (IVb) is not thermally stable and when heated in methylene chloride is converted into pyridinium fluoroborate, benzaldehyde *p*-tolyl thioacetal, and benzaldehyde. Although the mechanism of this reaction has not been investigated, the nature of the products gives an idea of the type of fragmentation of (IVb). Formation of the analogous $\alpha\alpha$ -bisbenzylthiotoluene has been observed¹⁰ in the Pummerer reaction of dibenzyl sulphoxide.

the salt (I), either at the sulphoxide or at the ethoxy-sulphonium salt level.

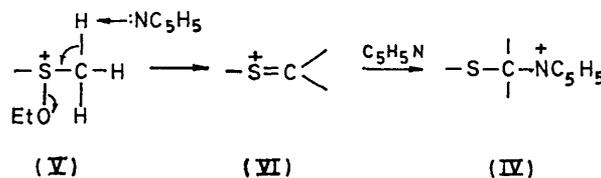
A different behaviour is observed in the reaction of pyridine with alkoxy-sulphonium salts bearing at least one hydrogen atom bonded to the carbon α to the sulphur atom. The reaction, carried out in refluxing methylene chloride for 4 min, leads to α -pyridinio-sulphides (IV).^{*} No asymmetric induction from sulphur to carbon occurs during the rearrangement: from optically active alkoxy-sulphonium salt (Vb), racemic sulphide (IVb) was



(V) a; R = H
b; R = Ph

(IV) a; R = H
b; R = Ph

obtained. This suggests the formation of an ylide intermediate (VI) analogous to that involved in the Pummerer rearrangement undergone by alkoxy-sulphonium salts in the reactions⁴ with alkoxides or carboxylate ions.



Structural factors are important in determining the course of the reaction between nucleophiles and sulphoxonium salts, apart from the intervention of steric effects. In diarylethoxy-sulphonium salts, attack occurs at sulphur with strong nucleophiles²⁻⁶ (carbanions, hydroxide ions, aliphatic amines) but at carbon with weak nucleophiles (bromide ions,² pyridine), in agreement with the 'hard' electrophilic character of a positively charged sulphur atom.¹¹ In the case of alkoxy-sulphonium salts having at least one α -hydrogen atom abstraction of the proton is preferred with pyridine as nucleophile, and is the product-determining step when the initial attack on sulphur only exchanges the groups bonded to this atom (reactions with alkoxides or carboxylate ions),⁴ leaving unaltered the structure of the alkoxy-sulphonium salt.

EXPERIMENTAL

Alkoxy-sulphonium Fluoroborates.—Alkoxy-sulphonium salts were prepared by the general method described by

⁷ M. Kobayashi, K. Kamiyama, H. Minato, Y. Oishi, Y. Takada, and Y. Hattori, *Chem. Comm.*, 1971, 1577.

⁸ (a) T. R. Williams, R. E. Booms, and D. J. Cram, *J. Amer. Chem. Soc.*, 1971, **93**, 7338; (b) T. R. Williams, A. Nudelman, R. E. Booms, and D. J. Cram, *ibid.*, 1972, **94**, 4684.

⁹ M. Kishi and T. Komeno, *Internat. J. Sulphur Chem. (A)*, 1972, **2**, 1.

¹⁰ G. E. Wilson and C. J. Strong, *J. Org. Chem.*, 1972, **37**, 2376.

¹¹ J. L. Kice, *Mech. Reactions Sulphur Comp.*, 1968, **3**, 91.

Johnson.¹ In the case of diaryl derivatives (I) the reaction time was 48 h, and the products were isolated as oils and used as such. Optical purities were checked by hydrolyses with sodium hydroxide;¹ the results are reported in the Table. (*R*)-Benzyl(ethoxy)-*p*-tolylsulphonium fluoroborate had m.p. 115—116°, $[\alpha]_D^{25} +205^\circ$ (CHCl₃) {lit.,¹ m.p. 115—117°, $[\alpha]_D^{22} +202^\circ$ (CHCl₃)}. (*R*)-Ethoxy(methyl)-*p*-tolylsulphonium fluoroborate had m.p. 69°, $[\alpha]_D^{20} +149^\circ$ (acetone) (Found: C, 44.6; H, 5.7. C₁₀H₁₅BF₄OS requires C, 44.5; H, 5.6).

Reaction of Diarylethoxysulphonium Salts (I) with Pyridine.—A solution of diarylethoxysulphonium salt (I) (2 mmol) and pyridine (0.2 ml) in methylene chloride (5 ml) was refluxed for 20 h. Addition of anhydrous diethyl ether at 0° precipitated *N*-ethylpyridinium fluoroborate, m.p. 59—60° (lit.,¹² 58.5—59.5°). Evaporation of the solvent afforded the optically active sulphoxide (see Table).

Reaction of Alkylarylethoxysulphonium Salts (Va and b) with Pyridine.—Pyridine (0.2 ml) was added to a solution of sulphonium salt (Va or b) (2 mmol) in methylene chloride (5 ml) and the mixture was kept at room temperature for

4 min. Addition of anhydrous diethyl ether at 0° precipitated the α -pyridinio-sulphide (IVa or b) in 60—70% yield. *N*-(*p*-Tolylthiomethyl)pyridinium fluoroborate (IVa) had m.p. 110—111° (Found: C, 51.3; H, 4.7; N, 4.7. C₁₃H₁₄BF₄NS requires C, 51.5; H, 4.7; N, 4.6%). *N*-[α -(*p*-Tolylthio)benzyl]pyridinium fluoroborate (IVb) had m.p. 122—123° (Found: C, 59.9; H, 4.7; N, 3.8. C₁₉H₁₈BF₄NS requires C, 60.2; H, 4.8; N, 3.7). The latter is thermally unstable: on heating in methylene chloride under reflux for 3 h, pyridinium fluoroborate is precipitated (95%), m.p. 219—221° (lit.,¹³ 220—222°). Evaporation of the solvent affords a mixture whose n.m.r. and i.r. spectra indicate the presence of benzaldehyde [δ (CDCl₃) 9.92 (s), ν_{max} (CCl₄) 1710 cm⁻¹] together with benzaldehyde di-*p*-tolyl thioacetal. The last compound was isolated by column chromatography (SiO₂; eluant diethyl ether) in 90% yield [based on (IVb)]. *Benzaldehyde di-p-tolyl thioacetal* had m.p. 80° (Found: C, 75.0; H, 6.2. C₂₁H₂₀S requires C, 74.9; H, 6.0%).

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¹² H. Meerwein, G. Hinz, P. Hofman, E. Kroning, and E. Pfeil, *J. prakt. Chem.*, 1937, **147**, 257.

¹³ R. Daniels and C. G. Kormendy, *J. Org. Chem.*, 1962, **27**, 1860.