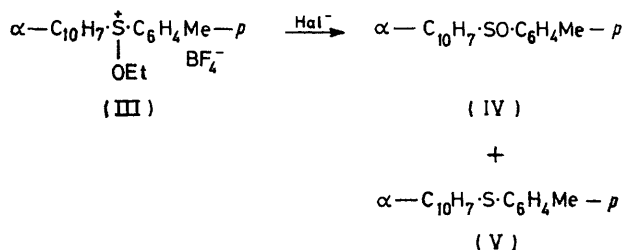
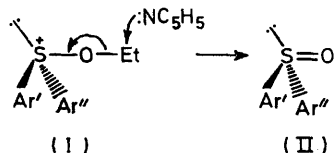
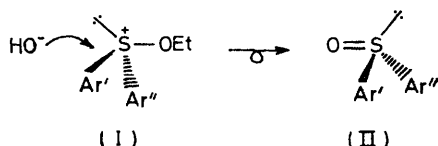


Mechanism and Stereochemistry of Nucleophilic Substitutions in Alkoxy-sulphonium Salts. Part II.¹ Competitive Attack at Sulphur and Carbon in the Reaction of Alkoxydiarylsulphonium Salts with Halide Ions

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

The stereochemical course of the reaction of optically active diarylethoxysulphonium salts with halide ions to give sulphoxides depends on the nature of the halide. For chloride, bromide, and iodide ions the reaction proceeds with retention of configuration at sulphur, whereas for fluoride ions net inversion is observed; this is tentatively explained on the basis of nucleophilic substitution involving apical attack by fluoride ion and equatorial departure of the leaving group, or of Berry pseudorotation.

ALKOXYDIARYLSULPHONIUM salts (I) are ambident electrophiles and, depending on the nature of the nucleophile and of the substrate, attack can occur at sulphur or at carbon.^{1,2} In the reaction of optically active diarylethoxysulphonium salts with hydroxide ions³ and with pyridine,¹ diaryl sulphoxides (II) are formed with inversion and with retention of chirality at sulphur, respectively, by initial attack at the different reaction centres.



We decided to establish the preferred pathway when a series of related nucleophiles is used, and treated (*S*)-ethoxy-(α -naphthyl)-*p*-tolylsulphonium fluoroborate (III) with tetraethylammonium iodide, bromide, chloride, and fluoride. From the results we could determine a relative order of nucleophilicity and of thiophilicity. Reaction in anhydrous acetonitrile at room temperature gave the corresponding sulphoxide (IV), of variable optical activity, together with minor amounts of α -naphthyl *p*-tolyl sulphide (V) (see the Table). Further information was obtained with the aid of a 10% ¹⁸O-enriched (*R*)-(III).

¹ Part I, R. Annunziata, M. Cinquini, and S. Colonna, *J.C.S. Perkin I*, 1973, 1231; see also references therein.

² M. A. Khuddus and D. Swern, *J. Amer. Chem. Soc.*, 1973, **95**, 8393.

DISCUSSION

The stereochemical results, and the isotopic content of the products, clearly indicate that reaction of (III)

Reaction of the sulphonium salt (III) with halide ions in acetonitrile at 25°

Halide	Mol. equiv.	Yield (%)	Sulphoxide			Yield (%)
			$[\alpha]_D^{25}$ ^a (°)	Retention (%)	¹⁸ O Content ^b (%)	
I ⁻	2	95	-410	100	100	3
Br ⁻	2	86	-410	100	100	5
Cl ⁻	2	74	-405	99	100	18
F ⁻	2	70	+144	32	<i>c</i>	14
I ⁻	1	85	-380	96	<i>c</i>	3
Br ⁻	1	80	-354	93	<i>c</i>	10
Cl ⁻	1	66	-156	69	44	30
F ⁻	1	65	+129	35	10	25

^a In acetone. ^b With respect to the starting material. ^c Not examined.

with an excess of I⁻, Br⁻, or Cl⁻ occurs only *via* nucleophilic attack at carbon by the halide ion, without affecting the chirality at sulphur.

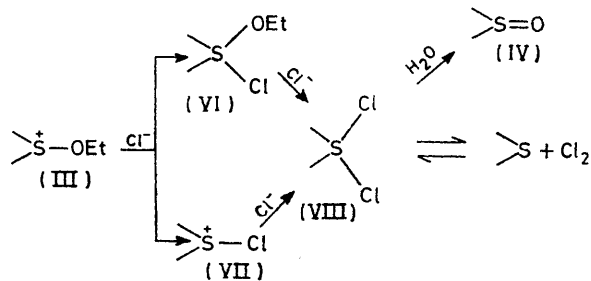
Nucleophilic displacement at carbon is still largely preferred in the reaction with equimolecular amounts of I⁻ and Br⁻, but with 1 mol. equiv. of Cl⁻ the sulphoxide (IV) obtained is substantially racemized. In the latter case, attack at carbon, the extent of which can be measured from the isotopic content of (IV) (44%), must be accompanied by a competitive process involving achiral intermediates. Indeed the amount of retention based on the optical rotation of (IV) (69%) is in good agreement with the value (72%) obtained from the isotopic content, on the assumption that attack at sulphur leads to fully racemic material.

It seems likely that racemization derives from substitution at sulphur by Cl⁻ in the alkoxy-sulphonium salt (III), since both (III) and (IV) are optically stable in the reaction medium (see Experimental section). A possible mechanism is shown in Scheme 1.

This mechanism involves the intervention of either a tetraco-ordinate intermediate (VI) or a chlorosulphonium salt (VII). Loss of chirality could be due either to formation of a diarylsulphur dichloride (VIII) or to halide exchange on (VII). Similar pathways have been proposed for the racemization of sulphoxides

³ C. R. Johnson and D. McCants, *J. Amer. Chem. Soc.*, 1965, **87**, 5404.

by chloride ions.^{4,5} Furthermore the occurrence of intermediates such as (VI) and (VIII) has been proved in the reaction of sulphides with organic hypochlorites.⁶ Isolation of bis-(*p*-chlorophenyl)sulphur dichloride has



SCHEME 1

been reported⁷ and its crystal structure has been determined.⁸

The presence of sulphide (V) in the reaction mixture could be accounted for on the basis of the equilibrium between (VIII) and the corresponding sulphide.^{4,9}

When the alkoxy-sulphonium salt (III) is treated with tetraethylammonium fluoride the stereochemical result is different: the sulphoxide obtained (*ca.* 30% optically pure) is of opposite chirality to the starting material. Its isotopic content, 10% with respect to (III), indicates that the reaction proceeds only to a limited extent *via* attack at carbon, *i.e.* with retention of configuration. Two competitive pathways, *viz.* racemization and inversion, must operate, both involving sulphur as the reaction centre.

In blank experiments it was shown that under the reaction conditions (i) the sulphoxide (IV) is chemically and optically stable in the presence of fluoride ions; and (ii) the alkoxy-sulphonium salt (III) in solvent alone is transformed, after the usual work-up, only to a very limited extent into (IV) which is almost racemic: assuming that the reaction of (III) with fluoride ions proceeds through formation of a fluorosulphonium salt (X) followed by hydrolysis to sulphoxide (IV), one of the two steps must occur with retention and the other with inversion of configuration.

A possible explanation involves apical attack by fluoride ion on (III) to give the intermediate (IX) and equatorial displacement of the ethoxy-group to afford (X) with retention of configuration at sulphur (Scheme 2).

Other examples of nucleophilic substitutions at sulphur which proceed with retention of chirality are known.¹⁰ An alternative explanation is that the

* Similar assumptions are required if conversion (III) \rightarrow (X) occurs with inversion and hydrolysis of (X) occurs with retention of configuration.

† In the reaction of 1-ethoxy-3-methylthietanium salts with hydroxide ion pseudorotation has been disproved.¹²

⁴ R. H. Rymbrandt, *Tetrahedron Letters*, 1971, 3553, and references therein.

⁵ K. Mislow, *Record Chem. Progr.*, 1967, 28, 217, and references therein.

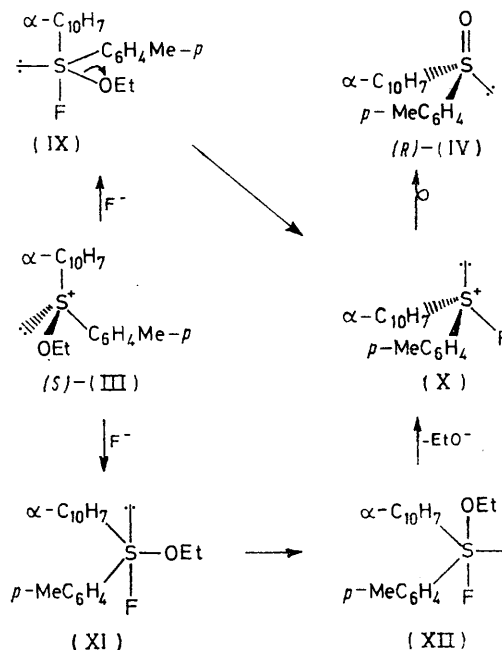
⁶ (a) C. R. Johnson and J. J. Rigau, *J. Amer. Chem. Soc.*, 1969, 91, 5398; (b) R. J. Arhart and J. C. Martin, *ibid.*, 1972, 94, 4997, 5003.

incoming fluoride ion approaches the tetrahedral sulphonium salt from the side opposite to the lone pair (Scheme 2) to give a trigonal bipyramidal intermediate (XI).

On energetic grounds (XI) could rearrange through a Berry pseudorotation,¹¹ to the more stable form (XII), where the more electronegative groups (F, EtO) both occupy the favourable axial positions. Assuming that loss of ethoxide ion is slower than pseudorotation, the fluorosulphonium salt (X) is formed from (III) with net retention of configuration, and then collapses to sulphoxide (IV) with inversion.* It should be noted that no example of pseudorotation in sulphur compounds has yet been reported.†

The racemization process as well as the formation of sulphide (V) could be rationalized, as in the case of chloride ions, by formation of difluorosulphuranes, which have recently been investigated.¹³

Two features of the present work should be emphasized: (i) under our experimental conditions, the relative order of nucleophilicity of the halide ions towards



SCHEME 2

alkoxy-sulphonium salts is $I^- > Br^- > Cl^- \gg F^-$, while the thiophilicity order is reversed; and (ii) reduction to sulphide occurs more readily with chloride and

⁷ R. J. Maver, *Diss. Abs.*, 1967, 29, 2B, S 48.

⁸ N. C. Baenziger, R. E. Buckles, R. J. Maner, and T. D. Simpson, *J. Amer. Chem. Soc.*, 1969, 93, 5749.

⁹ G. Wilson and M. Chang, *Tetrahedron Letters*, 1971, 875.

¹⁰ (a) S. Oae, M. Yokoyama, M. Kise, and N. Furukawa, *Tetrahedron Letters*, 1968, 4131; (b) B. U. Christensen and A. Kjaer, *Chem. Comm.*, 1969, 934.

¹¹ (a) K. Mislow, *Accounts Chem. Res.*, 1970, 3, 321, and references therein; (b) E. L. Muetterties and R. A. Schunn, *Quart. Rev.*, 1966, 20, 245.

¹² R. Tang and K. Mislow, *J. Amer. Chem. Soc.*, 1969, 91, 5644.

¹³ D. B. Denney, D. Z. Denney, and Y. F. Hsu, *J. Amer. Chem. Soc.*, 1973, 95, 4064.

fluoride ions and is clearly related to their higher thiophilicity with respect to bromide and iodide. In each case it is lowered by using an excess of reagent, which leads to increased attack at carbon.

As previously discussed for other nucleophiles,¹ preferential attack by halide ions at sulphur or carbon in alkoxy-sulphonium salts can be explained by a positively charged sulphur being a 'harder' electrophilic centre than carbon and fluoride being the 'hardest' nucleophile among the halide ions.

A comparison can be made between our results and the acid-catalysed reaction of sulphoxide with halide ions in protic solvents,¹⁴ which has been shown to involve the protonated sulphoxide, which is similar to an alkoxy-sulphonium salt. In this case iodide ion leads to reduction whereas bromide and chloride ion give only racemization, both reactions proceeding *via* attack at sulphur with formation of a halogenosulphonium salt.¹⁴ In different conditions, *i.e.* in anhydrous medium, reduction of sulphoxide is a side reaction, and may become dominant, depending on the medium and the substrate.⁵

It remains to be explained why the use of an excess of halide ions leads in the case of Br⁻ and Cl⁻ to a different ratio of attack at sulphur and carbon. Work is in progress to define the kinetics of the two processes.

EXPERIMENTAL

(R)-(+)- α -Naphthyl *p*-Tolyl [¹⁸O]Sulphoxide (IV).—This was prepared, according to the procedure previously described,¹⁵ *via* hydrolysis of the corresponding ethoxy-

¹⁴ D. Landini, G. Modena, F. Montanari, and G. Scorrano, *J. Amer. Chem. Soc.*, 1970, **92**, 7168, and references therein.

sulphonium salt with sodium [¹⁸O] deuterioxide [from D₂¹⁸O (10% ¹⁸O) and sodium], and had m.p. 136°, [α]_D²⁵ +410° (*c* 1, acetone), 10% ¹⁸O (mass spectrum).

(S)-Ethoxy-(α -naphthyl)-*p*-Tolylsulphonium Fluoroborate (III).—This was prepared by the method previously reported¹ from (S)-(IV), [α]_D²⁵ -410° (*c* 1, acetone), and was isolated as an oil and used as such.

Reactions of the Ethoxysulphonium Salt (III) with Tetraethylammonium Halides.—Anhydrous tetraethylammonium halide (1 or 2 mmol) was dissolved in anhydrous acetonitrile (10 ml) and added at room temperature to a solution of (III) (1 mmol) in the same solvent (10 ml). After a suitable reaction time (12 h for I⁻ and Br⁻, 24 h for Cl⁻, and 48 h for F⁻) the mixture was diluted with water and extracted several times with chloroform. After evaporation of the solvent the crude product was purified by column chromatography (SiO₂; diethyl ether-light petroleum 3 : 7). Yields and optical rotations are reported in the Table. The result from the reaction with fluoride ion did not change on working in a glass vessel or in a steel bomb.

Blank Experiments.—(a) A solution of the sulphoxide (IV), [α]_D²⁵ -410° (*c* 1, acetone), and the tetraethylammonium halide (2 equiv.) in acetonitrile was kept at room temperature for 48 h. Work-up as previously described afforded the sulphoxide (IV) with unaltered optical rotation.

(b) The (S)-ethoxysulphonium salt (III) was kept in acetonitrile for 48 h at room temperature. Half the solution after the usual work-up afforded the sulphoxide (IV) (10% yield), [α]_D²⁵ +14° (*c* 3, acetone). The optical stability of (III) was checked by hydrolysis of the remaining solution with sodium hydroxide¹ to afford a practically quantitative yield of the sulphoxide (IV), [α]_D²⁵ +410° (*c* 1, acetone).

[4/1217 Received, 21st June, 1974]

¹⁵ R. Annunziata, M. Cinquini, and S. Colonna, *J.C.S. Perkin I*, 1972, 2057.