Nucleophilic Substitution of α-Chloro-sulphoxides

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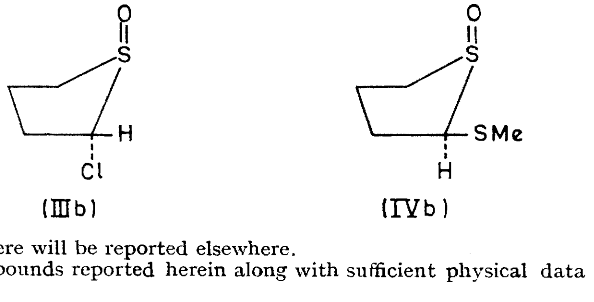
Summary Chloromethyl methyl sulphoxide reacts with alcohols, phenol, and thiophenols in the presence of potassium hydroxide to yield the corresponding displacement products, and several other α-chloro-sulphoxides undergo the S_N2 substitution with MeS^-.

NUCLEOPHILIC substitution of α-chloro-derivatives of organosulphur compounds (sulphides, sulphoxides, and sulphones) has been investigated,[1-4] and the mechanisms seem to be established for the reaction of α-chloro-sulphides and -sulphones, on the basis of both product analyses and kinetic studies. The Finkelstein reaction of aryl chloromethyl sulphoxides appears to proceed quite slowly,[5,6] but no research has been reported on the products for the displacement reaction of α-chloro-sulphoxides. We report a study on the nucleophilic substitutions of α-chloro-sulphoxides, *i.e.*, the substitutions of chloromethyl methyl sulphoxide by alkoxide, phenoxide, and thiophenoxide ions and the S_N2-type displacements of several α-chloro-sulphoxides by MeS^-.

$$\underset{\text{(I)}}{MeSOCH_2Cl} + ROH \xrightarrow{KOH} \underset{\text{(II)}}{MeSOCH_2OR} \quad \begin{array}{l} a;\ R = Et \\ b;\ R = Me \\ c;\ R = Pr^i \\ d;\ R = Ph \end{array}$$

A solution containing 1·00 g of chloromethyl methyl sulphoxide (I)[7]† and 2·0 g of potassium hydroxide in 15 ml of ethanol was warmed at 50° for 18 h and the reaction mixture was separated by column chromatography (silica gel) to afford 816 mg (77%) of ethoxymethyl methyl sulphoxide (IIa) as a colourless oil (b.p. 85°/5 mmHg). The structure was confirmed by its i.r. spectrum (ν_{SO}1038 cm^{-1}), n.m.r. spectrum [δ in $CDCl_3$:4·45s (2H), 3·85q (2H, *J* 7·2 Hz), 2·57s (3H), 1·26t (3H, *J* 7·2 Hz)] and mass spectrum [*m/e* 122 (M^+) and 59 (base peak)]. The analogous treatment of (I) in methanol and isopropyl alcohol yielded new sulphoxides, (IIb) (75%) and (IIc) (55%),‡ respectively, but the same treatment of (I) in t-butyl alcohol did not give the corresponding substitution product. Methyl phenoxymethyl sulphoxide (IId) was also obtained in 64% yield by warming a solution of (I) (647 mg), phenol (707 mg), potassium hydroxide (580 mg), and water (1 ml), at 60° for 11 h. Thiophenol also reacted with (I) under similar conditions to phenol, affording methyl phenylthiomethyl sulphoxide (87%).

The reaction of (I) with MeSNa in water occurred instantaneously and gave methyl methylthiomethyl sulphoxide quantitatively. Moreover, chloromethyl phenyl sulphoxide, which was shown to be resistant to S_N2 reactions, [5,6] was quantitatively converted into the displacement product by treatment with MeS^- in water–acetonitrile at 60° for 80 min. On the other hand, 68% of the starting material was recovered on similar treatment of 1-chloroethyl phenyl sulphoxide, even after prolonged



(IIIa) (IVa)

(IIIb) (IVb)

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† The novel preparative method for other α-chloro-sulphoxides used here will be reported elsewhere.

‡ Satisfactory elemental analyses have been obtained for all new compounds reported herein along with sufficient physical data (i.r., n.m.r., and mass spectra) to determine the structures.

heating (at 60° for 33 h), and the substitution product was obtained in only 25% yield. The introduction of a methyl group at the α-position considerably retards the reaction. This fact, as well as the fact that (I) is much more susceptible to the displacement than chloromethyl phenyl sulphoxide and that t-butoxide anion does not react with (I), clearly indicates that the steric factor plays an important role.

The reaction of *cis*- and *trans*-2-chlorothiolan 1-oxides (IIIa) and (IIIb) with MeS^- are instructive as regards the steric course of the reaction. The reaction of (IIIa) with MeS^- gave *trans*-2-methylthiothiolan 1-oxide (IVa)§ in 40% yield along with the unreacted starting material (30%), in water–acetonitrile at room temperature over 4 h. No trace of the isomer (IVb) was observed in the reaction mixture. The *trans*-isomer (IIIb) was, however, completely unreactive under the same conditions. Apparently, the nucleophile attacks at the chlorine-bearing carbon atom from the back side, and the substitution proceeds *via* inversion of configuration. The reaction of (IIIb) is hampered by an electrostatic repulsion between the incoming nucleophile anion and the sulphinyl oxygen atom.

All results obtained here are compatible with the S_N2 mechanism of the reaction, making a striking contrast with the S_N1 mechanism established for the substitution of α-chloro-sulphides.[2] The α-substituted sulphoxides reported here are of new type.

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§ The configuration of (IVa) was assigned by n.m.r. The aromatic solvent-induced shifts [$\Delta = \delta(CCl_4) - \delta(PhH)$][8] of the methine and the *S*-methyl protons are 0·22 and 0·57 p.p.m., respectively. For the α-protons *cis* and *trans* to the sulphinyl oxygen in thiolan 1-oxide, the values of Δ have been reported to be 0·36 (*cis*) and 0·78 (*trans*), respectively.[9] The coupling constants of the methine proton of (IVa) (*J* 3·0 and 7·0 Hz) are similar to those of (IIIb).

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