Stereoselective Synthesis of α-Chloro-sulphoxides from Sulphoxides or Sulphides and Iodobenzene Dichloride

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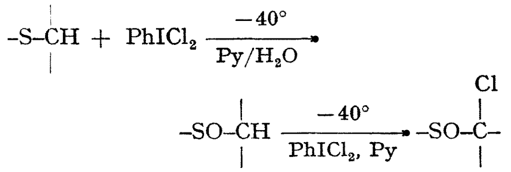
Summary α-Chlorination of dialkyl and aryl alkyl sulphoxides by iodobenzene dichloride is highly stereospecific, and in benzyl methyl sulphoxide involves the proton diastereotopic to that which is preferentially exchanged by deuterium in NaOD–D_2O.

Dialkyl and aryl alkyl sulphoxides react with equimolecular amounts of iodobenzene dichloride in pyridine at −40° to give α-chloro-sulphoxides. The same compounds are also obtained from sulphides and 2 moles of reagent, provided that the reaction is carried out in aqueous pyridine to ensure the formation of the sulphoxide.



$$-\mathrm{S{-}CH} + \mathrm{PhICl_2} \xrightarrow[\mathrm{Py/H_2O}]{-40^\circ}$$

$$-\mathrm{SO{-}CH} \xrightarrow[\mathrm{PhICl_2,\ Py}]{-40^\circ} -\mathrm{SO{-}}\overset{\mathrm{Cl}}{\mathrm{C}}-$$

The reaction, already described in the case of benzyl *p*-tolyl and dibenzyl sulphides,[1] can be applied to sulphides and sulphoxides with at least one hydrogen atom bonded to the α-carbon. The reaction is usually fast, and takes place with 60—80% yield.

In the aromatic series the use of a second mole of iodobenzene dichloride leads to sulphones.[1] Both the oxidation[1] and the chlorination of sulphoxides are slowed down, or prevented, by the presence of electron-withdrawing groups or by steric hindrance. Sulphones do not react with iodobenzene dichloride.

Recently, a few other methods of synthesis of α-chloro-sulphoxides have been reported.[2,3] These compounds are remarkable for the extraordinary inertness of the halogen atom towards both nucleophilic and electrophilic reagents.[2–4]

We have found that, when the α-carbon is a prochiral centre, only one of the two diastereomeric α-chloro-sulphoxides is obtained. This behaviour tallies with the extreme stereospecificity of other electrophilic substitutions α to the sulphinyl group.[3–7] When optically active benzyl methyl sulphoxide (Ia) ($[\alpha]_D^{20}$ + 96°, EtOH; −55°, $CHCl_3$)[8] was chlorinated with iodobenzene dichloride, α-chlorobenzyl methyl sulphoxide (IIa) (30%) m.p. 50—51°, $[\alpha]_D^{20}$ + 10·8° (*c* 1, $CHCl_3$) and benzyl chloromethyl sulphoxide (IIIa) (32%), m.p. 54—55°, $[\alpha]_D^{20}$ −23° (*c* 1, $CHCl_3$) were isolated.† Oxidation of (IIa) afforded α-chlorobenzyl methyl sulphoxide, m.p. 111—112°, $[\alpha]_D^{20}$ −17·1° (*c* 2, $CHCl_3$).

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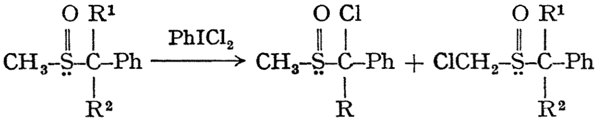
† In some experiments during separation of (II) and (III) a partial racemisation took place, probably catalysed by chloride ion.

Chlorination of the (*SS*, *RR*) α-deuteriobenzyl methyl sulphoxide (Ib) and of the diastereomeric (*SR*, *RS*) (Ic)‡ gave α-chloro-α-deuteriobenzyl methyl sulphoxide (IIb) and α-chlorobenzyl methyl sulphoxide (IIc), respectively, together with the corresponding chloromethyl benzyl sulphoxides (IIIb) and (IIIc). No contamination from (IIc) and (IIb), respectively, could be detected in either case.



$$\mathrm{CH_3{-}\overset{O}{\underset{\cdot\cdot}{S}}{-}\overset{R^1}{\underset{R^2}{C}}{-}Ph} \xrightarrow{\mathrm{PhICl_2}} \mathrm{CH_3{-}\overset{O}{\underset{\cdot\cdot}{S}}{-}\overset{Cl}{\underset{R}{C}}{-}Ph} + \mathrm{ClCH_2{-}\overset{O}{\underset{\cdot\cdot}{S}}{-}\overset{R^1}{\underset{R^2}{C}}{-}Ph}$$

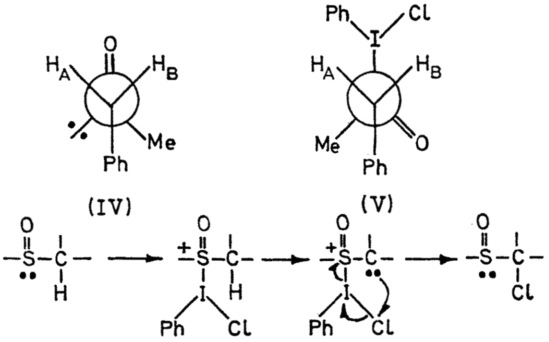
(I) (II) (III)

(Ia), (IIIa) $R^1, R^2 = H$
(Ib), (IIIb) $R^1 = H, R^2 = D$
(Ic), (IIIc) $R^1 = D, R^2 = H$
(Id), (IIId) $R^1, R^2 = D$

(IIa) = (IIc) $R = H$
(IIb) = (IId) $R = D$

The latter reactions define the stereochemistry of the chlorination of sulphoxides. This involves the proton (H_B), diastereotopic to the proton (H_A) which is preferentially exchanged by deuterium[5b] in NaOD–D_2O, as in conformation (IV). The yields in (II) and (III) were 30 and 32% from (Ib), and 54 and 8% from (Ic), respectively. Percentages of (II) and (III) analogous to those obtained from (Ib) and (Ic), were obtained by chlorination of benzyl methyl sulphoxide (Ia) and αα-dideuteriobenzyl methyl sulphoxide (Id), respectively.

The large isotope effect strongly suggests the formation of an intermediate α-carbanion. This must derive from a primary adduct between the sulphoxide and the reagent, as indicated by stereochemical and electronic effects. If Wolfe's conclusions[9] concerning proton exchange in sulphoxides are extended to chlorination, one is led to suppose that the carbanion has a pyramidal structure, and is formed through abstraction of the proton situated on the bisector of the oxygen–iodine angle, conformation (V). The carbanion is finally converted into the α-chloro-sulphoxide by intramolecular attack at the chlorine atom.



This work was supported by a grant from the Consiglio Nazionale delle Ricerche, Rome.

(*Received, April* 14*th*, 1969; *Com.* 506.)

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‡ Obtained *via* stereoselective H–D exchange from benzyl methyl sulphoxide (Ia) and αα-dideuteriobenzyl methyl sulphoxide (Id), respectively.[5a]

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