Inversion of Chirality at Sulphinyl Sulphur in a Reaction not Involving Breaking of Bonds of the Chiral Sulphur Atom

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Summary Conversion of (+)-methyl *p*-tolyl sulphoxide into the corresponding (−)- or (+)-α-halogenomethyl derivatives in the presence or in the absence of silver nitrate, respectively, involves inversion of configuration at sulphur in one of the two reactions; the inversion was proved to occur without any breaking of bonds at the chiral centre or any diastereomeric interaction in the transition state.

α-HALOGENO-SULPHOXIDES are obtained from dialkyl and aryl alkyl sulphoxides and iodobenzene dichloride or bromine in the presence of pyridine.[1,2] The reaction is highly stereospecific: when the α-carbon is a prochiral centre, only one of the two diastereomeric α-halogeno-sulphoxides is obtained.[1,2] Preliminary kinetic data indicate that iodobenzene dichloride only acts as a controlled source of chlorine and that the rate-determining step of the α-chlorination is the abstraction of a proton from an initially formed chlorosulphoxonium salt.[1c,3]

The (−)-α-chloromethyl *p*-tolyl sulphoxide (IVa), $[\alpha]_D^{25}$ −81° (*c* 1, acetone) and the corresponding α-bromo-derivative (IVb), $[\alpha]_D^{25}$ −155° (*c* 1, acetone), were converted, by reaction with sodium methoxide in boiling methanol, into the (−)-α-methoxymethyl *p*-tolyl sulphoxide (V), $[\alpha]_D^{25}$ −171° and −72° (*c* 1, acetone), respectively.† This means that (−)-(IVa) and (−)-(IVb) have the same absolute configuration.

Since either the (+)- or the (−)-α-halogenomethyl derivative is obtained from the (+)-methyl *p*-tolyl sulphoxide, depending on the reaction conditions, one of the two reactions must involve inversion of configuration at sulphur; which it is, we are not as yet in a position to decide, although the c.d. curves of compounds (I), (IVa), (IVb) suggest that it might be the reaction in the presence of silver nitrate. In fact, compounds (I), (IVa), and (IVb) with the same sign of optical rotation exhibit Cotton effects of the same sign, the effects being centred at 240—245 nm in EtOH and attributed to the *n*–π* transition of the SO group.

TABLE 1

α-Halogenation of (+)*-alkyl* p*-tolyl sulphoxides*

	Sulphoxide, $[\alpha]_D^{25a}$	α-Chloro-sulphoxide, $[\alpha]_D^{25a}$		α-Bromo-sulphoxide, $[\alpha]_D^{25a}$	
		b	c	b	c
(I)	+144°	+92°	−106°	+153°	−196°
(II)	+189°	−7°	−153°	−83°	−101°
(III)	+176°	−23°	−119°	−84°	−88°

[a] In acetone; [b] in the absence of $AgNO_3$; [c] in the presence of $AgNO_3$.

Under the conditions described, α-halogenation of (*R*)-(+)-methyl *p*-tolyl sulphoxide (I) affords the corresponding (+)-α-halogeno-sulphoxides (IVa) and (IVb), but in the presence of silver(I) nitrate (2 moles per mole of halogenating agent), the (−)-enantiomers are obtained (Table 1). Similar stereospecificity is observed in the chlorination of (I) by 1-chlorobenzotriazole. Nickel(II) nitrate behaves like silver nitrate in the reaction of (I) with iodobenzene dichloride. In the presence of silver nitrate, sulphoxide (I) and the corresponding (+)- and (−)-α-chloro-sulphoxides (IVa) are recovered without any loss of optical purity in the reaction conditions. Water has no effect on the stereochemical result of the chlorination, whether in the presence or absence of silver nitrate. In both cases, chlorination of ^{18}O-enriched sulphoxide (I) in the presence of isotopically normal water proceeds with complete retention of the isotopic content.

$p\text{-}CH_3\cdot C_6H_4\cdot SO\cdot R$

(I) $R = Me$ (IVa) $R = CH_2Cl$
(II) $R = Et$ (IVb) $R = CH_2Br$
(III) $R = Pr^i$ (V) $R = CH_2OMe$

The halogenation of (*R*)-(+)-ethyl and of (*R*)-(+)-isopropyl *p*-tolyl sulphoxides (II) and (III) is also influenced by the presence of silver ions. The results seem to indicate that the inversion of chirality at sulphur is favoured by the steric hindrance of the alkyl groups and of the halogen.‡

Oxidation of α-halogenoethyl *p*-tolyl sulphoxides (VI) affords the corresponding optically active sulphones (VII) (Table 2).

TABLE 2

Hal	$p\text{-}CH_3\cdot C_6H_4\cdot\overset{*}{S}O\cdot\overset{*}{C}HHal\cdot CH_3$ (VI) $[\alpha]_D^{25a}$	$p\text{-}CH_3\cdot C_6H_4\cdot SO_2\cdot\overset{*}{C}HHal\cdot CH_3$ (VII) $[\alpha]_D^{25a}$
Cl	−153°	−6·9°
Cl	−7°	−0·5°
Br	−101°	−12·9°

[a] In acetone.

The fact that the ^1H n.m.r. spectra of samples of compound (VI; Hal = Cl) with various optical activities are identical shows that we are dealing with enantiomers of

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† The yields in the methoxy-derivative (V) were 80% from (IVb) and 40% from (IVa) after 24 and 75 h, respectively. In both cases unreacted α-halogenosulphoxide was recovered.

‡ The yields of α-chlorination are in the range 70—80% after 1 h at −40° in CH_2Cl_2–Py 3 : 1; in the presence of silver nitrate the yields drop to 50—60% owing to C–S bond cleavage. α-Bromination is much slower and yields of 40—60% can only be reached after 20 h at r.t. in MeCN–Py 3 : 1; the recovered starting sulphoxide retains a high optical purity. The reaction is strongly accelerated by silver nitrate, 70% yields being achieved after 30 min. at r.t. in the same solvent.

different optical purity, and not with mixtures of diastereomers in different ratios. This is confirmed by the ^{1}H n.m.r. spectrum of the mixture of diastereomeric α-chloroethyl *p*-tolyl sulphoxides obtained[4] *via* t-butyl hypochlorite, a spectrum which shows two different quartets for the methine protons. Thus the stereochemical course at carbon is influenced by the stereochemical course at sulphur: if retention at sulphur is accompanied by retention at carbon, inversion at sulphur must be accompanied by inversion at carbon.§

Collapse of the initially formed halogeno-sulphoxonium salt to α-halogeno-sulphoxide, by migration of the halogen from the sulphinyl group to the α-carbon, should proceed by two competitive mechanisms, both highly stereospecific.

To the best of our knowledge, the conversion of (+)-methyl *p*-tolyl sulphoxide into the (−)- or (+)-α-halogenomethyl derivatives is the first example of a reaction in which inversion of chirality occurs without any breaking of bonds at the chiral centre or any diastereomeric interaction in the transition state.

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§ The only possible alternative is that retention at sulphur is accompanied by inversion at carbon, and that inversion at sulphur is accompanied by retention at carbon.

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[2] M. Cinquini and S. Colonna, *Boll. sci. Fac. Chim. ind. Bologna*, 1969, **27**, 201.

[3] D. Landini, unpublished results from this laboratory.

[4] S. Iriuchijima and G. Tsuchihashi, *Tetrahedron Letters*, 1969, 5259.