Synthesis of α-Halogeno-sulphoxides

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Reaction of sulphoxides with (dichloroiodo)benzene or with bromine in the presence of pyridine affords the corresponding α-halogeno-sulphoxides. Some reactions of α-halogeno-sulphoxides are here described.

CHLORINE and bromine can be used as halogenating agents to convert dialkyl and aryl alkyl sulphoxides into the corresponding α-halogeno-sulphoxides, provided that the reaction is carried out in the presence of pyridine. While bromine can be used as such, we have found that (dichloroiodo)benzene, $PhICl_2$, which acts as a controlled source of chlorine,[1] is more convenient to work with than chlorine itself. Preliminary results have been previously reported.[2] Recently other methods of α-halogenation of sulphoxides have been described.[3]

Reaction of sulphoxides with electrophilic agents results in Pummerer-type rearrangements[4] giving α-substituted sulphides instead of α-substituted sulphoxides. α-Halogeno-sulphoxides are more or less as unreactive towards nucleophiles such as alkoxides[5,6] as are α-halogeno-sulphones, whose reactivity is known to be very low.[6] The most relevant feature of α-halogenation of sulphoxides by chlorine and bromine, and generally by halonium ions, is the high stereospecificity of the reaction in the presence of base. When the α-carbon atom is a chiral or prochiral centre, only one, or predominantly one, of the two possible α-halogeno-sulphoxides is obtained.[1,2] While the stereochemical

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[1] M. Cinquini, S. Colonna, and D. Landini, *J.C.S. Perkin II*, 1972, 296.

[2] (*a*) M. Cinquini, S. Colonna, and F. Montanari, *Chem. Comm.*, 1969, 607; (*b*) M. Cinquini, S. Colonna, and D. Iarossi, *Boll. sci. Fac. Chim. ind. Bologna*, 1969, **27**, 197; (*c*) M. Cinquini and S. Colonna, *ibid.*, p. 201.

[3] (*a*) M. Cinquini and S. Colonna, *Synthesis*, 1972, in the press, and references therein; (*b*) S. Iriuchijima and G. Tsuchihashi, *ibid.*, 1970, 588.

[4] T. Durst, *Adv. Org. Chem.*, 1969, **6**, 285, and references therein.

[5] Unpublished results from this laboratory.

[6] K. Ogura and G. Tsuchihashi, *Chem. Comm.*, 1970, **1689**, and references therein.

aspect is discussed elsewhere,[7] we describe here the synthesis and reactions of these compounds.

Treatment of sulphoxides with (dichloroiodo)benzene or with bromine in the presence of pyridine at −40° affords the corresponding α-halogeno-sulphoxides. α-Halogeno-sulphoxides can also be obtained directly from sulphides, provided that the reaction is carried out with 2 mol of (dichloroiodo)benzene or bromine in aqueous pyridine to ensure the formation of the intermediate sulphoxides. The reaction is applicable only to substrates bearing at least one α-proton (see Table 1).

TABLE 1

Yields of α-halogeno-sulphoxides

	X = Cl (Yield %)		X = Br (Yield %)	
α-Halogeno-sulphoxide	*a*	*b*	*b*	*c*
PhSO·CH$_2$X (1)	75			
PhSO·CHXMe (2)	77	65	76	
PhSO·CXMe$_2$ (3)	73			
p-MeC$_6$H$_4$·SO·CH$_2$X (4)	79	75	86	84
p-MeC$_6$H$_4$·SO·CXMe$_2$ (5)	70	70	70	80
PhCH$_2$·SO·CHXPh (6)	63	67	73	
{PhCH$_2$·SO·CH$_2$X (7)	33	32	44	
PhCHX·SO·Me (8)	37	30	29	
PhCHX·SOPh (9)	40		25	
PhCHX·SO·C$_6$H$_4$·NO$_2$-*p* (10)	39			
PhCHX·SO·C$_6$H$_4$Me-*p* (11)	80			
{PhCH$_2$·SO·CHXBz (12)	29			
PhCH$_2$·SO·CHX$_2$ (13)	38			
PhSO·CHX·C$_6$H$_4$·NO$_2$-*p* (14)	69			
PhSO·CHXBz (15)	60			

[a] From the sulphide. [b] From the sulphoxide. [c] From the sulphoxide in the presence of silver ions.

The α-halogeno-sulphoxides were identified from the ^{1}H n.m.r. spectra and by oxidation to the corresponding sulphones.

α-Halogenation of sulphoxides followed by oxidation to α-halogeno-sulphones constitutes a useful synthesis of the latter. Diaryl sulphoxides react with (dichloroiodo)benzene in the presence of aqueous pyridine to give the corresponding sulphones.[8] In the absence of pyridine and water, sulphides with at least one α-proton give α-chlorosulphides or products derived from breaking of the C–S bond.[9] Sulphones are recovered unchanged under these conditions.

α-Chlorination is slowed down by the presence of electron-withdrawing groups and by steric hindrance:[1] 2,4-dinitrophenyl ethyl and benzyl 2,4-dinitrophenyl sulphoxide do not react at all, the starting material being quantitatively recovered. In the case of α-benzylthioacetophenone, α-chlorination is accompanied by a haloform reaction which gives benzyl dichloromethyl sulphoxide.

α-Bromination of alkyl aryl sulphoxides is catalysed by the presence of silver ion; the time of reaction can be reduced and the yields improved (see Experimental section).

When the α-carbon is a prochiral centre, only one of the two diastereomeric α-halogeno-sulphoxides is obtained [(2), (6), (8)—(12), (14), (15), see Table 1]. This behaviour has been confirmed by the halogenation of optically active sulphoxides [2a,10] and α-deuteriobenzyl methyl sulphoxides.[2a]

A few examples of nucleophilic substitution of α-halogeno-sulphoxides have been reported.[2b,6,10] Halogenomethyl *p*-tolyl sulphoxides react with sodium methoxide in boiling methanol by S_N2 substitution to give the corresponding methoxymethyl *p*-tolyl sulphoxide which is not stable and on standing is converted into *p*-tolyl toluene-*p*-thiosulphinate.

α-Halogenoethyl phenyl sulphoxide yields the β-methoxyethyl phenyl sulphoxide on treatment with sodium methoxide, *i.e.* the product being derived from elimination–addition. This is confirmed by the identity of the compound with that obtained from addition of methanol to phenyl vinyl sulphoxide (see Scheme).

$$\begin{tikzcd}
\mathrm{PhSO{\cdot}CHXMe} \arrow[r, "\mathrm{MeONa}", "\mathrm{MeOH}"'] & \mathrm{PhSO{\cdot}CH_2{\cdot}CH_2{\cdot}OMe} \\
 & \mathrm{PhSO{\cdot}CH{:}CH_2} \arrow[u, "\mathrm{MeONa{-}MeOH}"']
\end{tikzcd}$$

Nucleophilic substitutions are faster with bromo- than with chloro-sulphoxides.

EXPERIMENTAL

α-Chloro-sulphoxides.—(a) *From sulphides*. A solution of (dichloroiodo)benzene (5·5 g, 0·02 mol) in anhydrous pyridine (10 ml) was added dropwise at −40° to a stirred solution of the sulphide (0·01 mol) in 20% (v/v) aqueous pyridine (15 ml). The mixture was kept at −40° for 1 h away from direct sunlight, then at room temperature overnight. Chloroform (50 ml) was added and pyridine was removed with aqueous sulphuric acid; the chloroform solution was then washed with water, dried, and evaporated to give the product, which was purified by column chromatography [silica; ether–light petroleum (1 : 1, v/v)]. Data of the products are summarised in Table 1 and 2.

(b) *From sulphoxides*. A solution of (dichloroiodo)benzene (2·75 g, 0·01 mol) in anhydrous pyridine (5 ml) and anhydrous dichloromethane (10 ml) was added dropwise at −40° to a stirred solution of the sulphoxide (0·01 mol) in anhydrous dichloromethane (10 ml). The mixture was kept at −40° for 1 h, then at room temperature for 1 h. Work-up as described in (a) afforded the α-chloro-sulphoxides.

α-Bromo-sulphoxides.—A solution of bromine (3·2 g, 0·02 mol) in anhydrous acetonitrile (20 ml), cooled to −20°, was added dropwise to a stirred solution of the sulphoxide (0·01 mol) and anhydrous pyridine–acetonitrile (25 ml; 1 : 4, v/v) at −40°. After 1 h at −40°, the mixture was kept at room temperature for 20 h. Acetonitrile was removed under reduced pressure, the residue was dissolved in chloroform (50 ml), washed with an aqueous solution of sodium thiosulphate, and then with aqueous sulphuric acid. Evaporation gave the α-bromo-sulphoxide (see Tables 1 and 2), which was purified by column chromatography [silica; ether–light petroleum (1 : 1)].

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TABLE 2

Physical properties and analytical data of α-halogeno-sulphoxides

α-Halogeno-sulphoxide	M.p. (b.p./mmHg) (°C)	Formula	Found (%) C	Found (%) H	Required (%) C	Required (%) H
(1; X = Cl)	(78—79/0·02) [a]	C_7H_7ClOS	48·25	4·1	48·15	4·05
(2; X = Cl)	(82/0·03) [b]	C_8H_9ClOS	51·05	4·75	50·9	4·8
(3; X = Cl)	64—65 [c]	$C_9H_{11}ClOS$	53·2	5·45	53·35	5·45
(4; X = Cl)	61·5—62 [d]	C_8H_9ClOS	50·8	4·85	50·9	4·8
(5; X = Cl)	40—41	$C_{10}H_{13}ClOS$	55·5	5·95	55·4	6·05
(6; X = Cl)	120 [e]					
(7; X = Cl)	63·5—64	C_8H_9ClOS	50·95	4·75	50·9	4·8
(8; X = Cl)	58·5—59	C_8H_9ClOS	50·8	4·75	50·9	4·8
(9; X = Cl)	122—123	$C_{13}H_{11}ClOS$	62·0	4·25	62·4	4·4
(10; X = Cl)	151—152	$C_{13}H_{10}ClNO_3S$	53·1	3·4	52·8	3·35
(11; X = Cl)	154—155					
(12; X = Cl)	166—167	$C_{15}H_{13}ClO_2S$	61·55	4·45	61·55	4·5
(13; X = Cl)	92—93	$C_8H_8Cl_2OS$	42·7	3·65	43·05	3·6
(14; X = Cl)	125—126	$C_{13}H_{10}ClNO_3S$	52·5	3·35	52·8	3·35
(15; X = Cl)	120—121	$C_{14}H_{11}ClO_2S$	59·85	3·8	60·3	4·0
(2; X = Br)	*g*					
(4; X = Br)	64—65	C_8H_9BrOS	40·95	4·0	41·2	3·9
(5; X = Br)	59—60	$C_{10}H_{13}BrOS$	45·75	4·95	46·0	5·0
(6; X = Br)	110·5—112 [h]	$C_{14}H_{13}BrOS$	54·4	4·3	54·4	4·25
(7; X = Br)	78	C_8H_9BrOS	41·0	4·05	41·2	3·9
(8; X = Br)	62—63	C_8H_9BrOS	41·0	4·0	41·2	3·9
(9; X = Br)	125—126·5	$C_{13}H_{11}BrOS$	53·75	3·85	54·1	3·8

[a] Lit.,[12] b.p. 134—137° at 1 mmHg. [b] Lit.,[12] b.p. 90° at 0·2 mmHg. [c] Lit.,[12] 64·5—65·5°. [d] Lit.,[13] 61·5°—62. [e] Lit.,[8] 120°. [f] Lit.,[8] 154—155°. [g] n_D^{20} 1·5995, purified by column chromatography and identified by oxidation to the corresponding sulphone. [h] Lit.,[3b] 110·5—112°.

TABLE 3

α-Halogeno-sulphones, $R^1SO_2{\cdot}CR^2R^3X$

R^1	R^2	R^3	X	M.p. (°C)	Lit. m.p. (°C)	Ref.
Ph	H	H	Cl	52—53	52—53	14
Ph	H	Me	Cl	53—54	53—54	15
p-MeC_6H_4	H	H	Cl	87—89	87—89	16
p-MeC_6H_4	Me	Me	Cl	102—104	102—104	15
$PhCH_2$	H	Ph	Cl	119—120	119—120	8
$PhCH_2$	H	H	Cl	103—104	103—104	17
Me	H	Ph	Cl	111	111	18
Ph	H	Ph	Cl	185—186	185—186	19
p-MeC_6H_4	H	Ph	Cl	205—205·5	205—205·5	8
$PhCH_2$	H	Bz	Cl	155—156 [a]		
$PhCH_2$	H	Cl	Cl	104	104	20
Ph	H	$C_6H_4{\cdot}NO_2$-*p*	Cl	168—169	168—169	19
Ph	H	Bz	Cl	128—129	126	21
Ph	H	Me	Br	49—50	49—50	22
p-MeC_6H_4	H	H	Br	90—92	90—92	22
p-MeC_6H_4	Me	Me	Br	105—106 [b]		
$PhCH_2$	H	Ph	Br	107—108	106—108	23
$PhCH_2$	H	H	Br	142—143 [c]		
Me	H	Ph	Br	98 [d]		
Ph	H	Ph	Br	193—194	193—194	24

[a] From methanol (Found: C, 58·0; H, 4·1. $C_{15}H_{13}ClO_3S$ requires C, 58·35; H, 4·25%). [b] From ether–light petroleum (1 : 3) (Found: C, 43·5; H, 4·8. $C_{10}H_{13}BrO_2S$ requires C, 43·35; H, 4·75%). [c] From methanol (Found: C, 38·3; H, 3·6. $C_8H_9BrO_2S$ requires C, 38·55; H, 3·65%). [d] From methanol (Found: C, 38·4; H, 3·65. $C_8H_9BrO_2S$ requires C, 38·55; H, 3·65%).

The reaction was repeated in the presence of silver(I) nitrate. In a typical procedure, a solution of bromine (1·9 g, 0·012 mol) in anhydrous acetonitrile (20 ml) at −20° was added dropwise to a stirred solution of the sulphoxide (0·01 mol), silver(I) nitrate (4·1 g, 0·024 mol), and anhydrous pyridine (5 ml) in anhydrous acetonitrile (20 ml) at −40°. After 1 h at −40° and 30 min at room temperature, the mixture was filtered to remove the silver bromide, and then worked-up as described before.

Oxidation of α-Halogeno-sulphoxides to α-Halogeno-sulphones.—α-Halogeno-sulphoxides (0·01 mol) in dichloromethane (30 ml) were oxidised with a slight excess of *m*-chloroperbenzoic acid at 0 °C for 24 h. Work-up afforded the sulphones (see Table 3), which were purified by column chromatography [silica; ether–light petroleum (1 : 1)] and/or by crystallisation. Yields were 90—100%.

Reaction of Aryl α-Halogenomethyl Sulphoxides with Sodium Methoxide.—(a) A solution of the α-chloro- or α-bromo-methyl sulphoxide (0·01 mol) and sodium methoxide (0·03 mol) in methanol (50 ml) was heated under reflux for 75 or 24 h, respectively. The solvent was then evaporated in vacuum and the residue was dissolved in chloroform. The chloroform solution was washed with water, dried, and evaporated to leave the product, which was purified by column chromatography (silica; ether). *α-Methoxymethyl* p-*tolyl sulphoxide* was obtained in 80 or 40% yield from the α-chloro- or α-bromo-derivative, respectively (in both cases unchanged α-halogeno-sulphoxide was recovered), m.p. 47° (from n-hexane) (Found: C, 58·6; H, 6·5. $C_9H_{12}O_2S$ requires C, 58·7; H, 6·55%).

The product is not stable and on standing turns into p-*tolyl toluene-*p*-thiosulphinate*, m.p. 113° [from ether–light petroleum (1 : 1) (lit.,[11] 102°) (Found: C, 63·85; H, 5·35. $C_{14}H_{14}OS_2$ requires C, 64·05; H, 5·4%).

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(b) A solution of α-chloro- or α-bromo-ethyl phenyl sulphoxide (0·01 mol) and sodium methoxide (0·03 mol) in methanol (50 ml) was heated under reflux for 90 and 24 h, respectively. Work-up as described before afforded β-*methoxyethyl phenyl sulphoxide*, b.p. 87—90° at 0·025 mmHg, n_D^{26} 1·5492 (32 and 52%, respectively) (Found: C, 58·75; H, 6·6. $C_9H_{12}O_2S$ requires C, 58·7; H, 6·55%), δ ($CHCl_3$) 2·87 (2H, m), 3·35 (3H, s), 3·65 (2H, m), and 7·50 p.p.m. (5H, m). In both cases unchanged α-halogeno-sulphoxide was recovered.

The *methoxy-derivative* is identical to that obtained from addition of methanol in the presence of sodium methoxide (0·05 mol) to phenyl vinyl sulphoxide (0·01 mol) in methanol (25 ml) under reflux. After 1 h, the product was isolated by the normal work-up in 60% yield.

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