Intramolecular Reactions. Part XI.[1] Cyclisation of ω-Halogenoalkyl Sulphides: the Significance of Bromide:Chloride Ratios in Displacement Reactions

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Solvolysis of ω-halogenoalkyl sulphides has been investigated. Under appropriate conditions, the rate-limiting step is formation of a cyclic sulphonium salt. Three-membered cyclic sulphonium salts are formed more rapidly than their five-membered analogues and the enthalpy of activation for three-membered ring formation is *lower* than that for five-membered ring formation. Attachment of a phenyl group adjacent to the leaving group accelerates formation of rings of both sizes but the three-membered ring is favoured to a considerably greater extent by an entropic and not an *enthalpic* change. The results are discussed in terms of special conjugative effects of three-membered rings. Bromide:chloride ratios have been measured for reactions giving three- and five-membered ring sulphonium salts. The relevance of bromide:chloride ratios in assessment of bond extension in transition states is considered.

EARLIER papers [1-4] dealt with comparisons of cyclisation rates in which a nucleophilic atom displaces intramolecularly a leaving group such as halide. The results, together with literature information, showed that in formation of three-membered rings, as compared with other sizes, two generalisations emerged. (i) In formation of carbocyclic rings when the internal nucleophile is a resonance-stabilised carbanion, three-membered rings are formed much more rapidly than those of any other size. (ii) In formation of azacycloalkanes from ω-halogenoalkylamines, three-membered rings are formed much more slowly than five-membered rings and if an aryl group is placed on nitrogen or on carbon adjacent to nitrogen, no effect on relative rates (and indeed very little effect on absolute rates) is discernible.

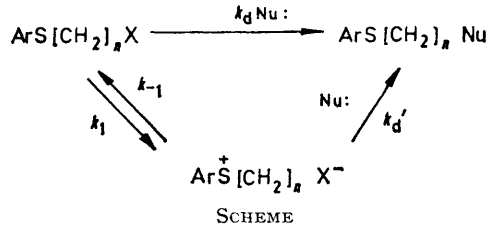
It has been suggested [3] that in formation of carbocyclic rings, conjugation of the incipient three-membered ring with the group stabilising the carbanion increases *selectively* the rate of three-membered ring formation. This hypothesis requires that there should be a high degree of C–C bond formation in the transition state and the lack of response of the rate of formation of aziridines to attachment of aryl groups is attributed to a low degree of bond formation in the transition state.[1] This is judged from a ' normal ' chloride : bromide ratio and the low β values obtained for the intramolecular nucleophiles which vary in basicity by factors of 10^6.

Several studies [5,6] of cyclisation of ω-halogenoalkylsulphides to sulphonium salts show striking contrasts to the analogous reactions with amines. It has been shown that in reactions of ω-halogenoalkyl sulphides with nucleophiles, formation of the cyclic sulphonium salts is rate determining and is followed by rapid attack of nucleophiles with ring opening.[2,7] For ethyl ω-halogenoalkyl sulphides, rate of formation of the three-membered ring sulphonium salt is much less than for the five-membered ring sulphonium salt. For phenyl ω-halogenoalkyl sulphides, however, relative rates are *reversed*, an observation that is interesting *per se* but which is also compatible with the hypothesis of conjugative control of the formation of three-membered rings.[3] It must also be stressed that in contrast with behaviour in the amine series, replacement of an *S*-ethyl group by an *S*-phenyl group lowers [7] cyclisation rate for a three-membered ring by a factor of *ca.* 40. Furthermore, it appears that the PhS:EtS ratio is very much higher for three- than for five-membered rings. Replacement of an alkyl group by a conjugative phenyl group accelerates formation of the three-membered ring *selectively*.

We have investigated the solvolysis of a series of ω-halogenoalkyl sulphides (Table 1) to which mechanisms involving rate-limiting formation of cyclic sulphonium salts have been assigned. Activation parameters for cyclisation have been determined and the results are discussed in terms of the relevance of conjugative effects in the formation of small rings.

RESULTS

It was essential for the objective of the investigation to be able to examine cyclisation apart from any competing process. Two principal routes for solvolysis of ω-halogenoalkyl sulphides are likely (Scheme). The process k_1 whose



SCHEME

rate constant is required competes with direct nucleophilic displacement k_d in which the solvent or added nucleophile participates, and with k_{-1}, the reversion process.

Sulphonium Intermediates.—In preliminary experiments, reactions with 2-halogenoalkyl sulphides in ethanol came to equilibrium at *ca.* 10% conversion to ionic halide. When

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[1] Part X, R. Bird, A. C. Knipe, and C. J. M. Stirling, preceding paper.
[2] A. C. Knipe and C. J. M. Stirling, *J. Chem. Soc.* (*B*), 1967, 808.
[3] A. C. Knipe and C. J. M. Stirling, *J. Chem. Soc.* (*B*), 1968, 67.
[4] R. Bird and C. J. M. Stirling, *J. Chem. Soc.* (*B*), 1968, 111.
[5] Summarised by B. Capon, *Quart. Rev.*, 1964, **18**, 45.
[6] F. Gundermann, *Angew. Chem. Internat. Edn.*, 1963, **2**, 674.
[7] H. Bohme and K. Sell, *Chem. Ber.*, 1948, **81**, 123.

water or a strong base, *e.g.* ethoxide ion, was added, reaction proceeded to completion. This behaviour is consistent [8] with formation of intimately associated sulphonium–halide ion pairs which are separated on addition of water. Rapid solvolysis of the episulphonium ion follows. Spectroscopic observation [8] of formation of larger ring, *e.g.* tetrahydrothiophenonium salts, was made directly but no spectroscopic changes occur during solvolysis of 2-halogenoethyl sulphides. U.v. spectra of starting materials and products are very similar and any intermediate formed was evidently in too low a concentration to produce a spectral change. While there is no direct evidence for formation of episulphonium ions [9] in these reactions, two indirect lines of evidence are indicative. Rates of solvolysis are very much greater than for simple halides,[10] pointing to participation of neighbouring sulphur, and this effect is not simply due to induction by the arylthio-group, as authenticated direct displacement processes are little affected.[2] Further evidence for the intermediacy of episulphonium ions was obtained from solvolyses run in the presence of aniline. Anilino-sulphide was the sole product in spite of the fact that the major component of the rate was a first-order process. As ethoxy-sulphide (the product from solvolyses in the absence of aniline) was stable to aniline it can be concluded that the rate-limiting step in solvolysis is formation of the episulphonium ion and that the second-order component in the aniline reactions results from direct substitution (k_d).

For solvolyses in aqueous ethanol without added aniline, apparent first-order rate constants decreased as reactions proceeded. This behaviour is consistent with formation of an episulphonium ion which is slowly attacked by solvent and by halide ion. As the concentration of the latter rises so the reversion rate increases and the forward *rate*, as measured by halide ion release, decreases. This result implies that water competes inefficiently with halide ion (*i.e.* $k_{-1}/k_{d'}$ is high). Bartlett and Swain [11] found however that this is unimportant.[12] Further, the equilibrium position between 4-chlorobutyl *p*-tolyl sulphide and the cyclic sulphonium salt is concentration dependent as expected for forward and back reactions of different orders. This would not be the case if ion pairs, behaving kinetically as a single species [8] were formed. A possible explanation is that protons released in the initially neutral solvolyses protonate

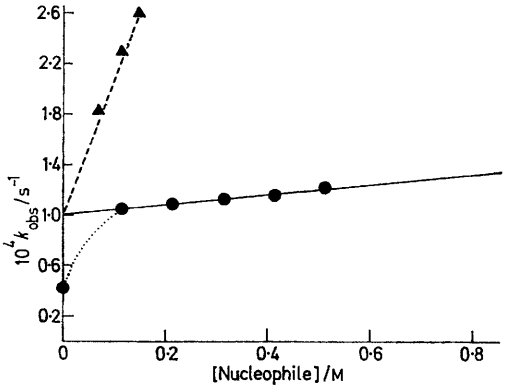

FIGURE 1 Solvolysis of 2-chloroethyl *p*-tolyl sulphide in 80% EtOH–MeOH in the presence of added nucleophiles: ▲, hydroxide: ●, aniline

the product ether and cause reversion to sulphonium salt. Nucleophilic displacement of halide (Br^-) and water from sp^3 carbon occur with about equal facility.[13] At all events, in the presence of an excess of aniline or of hydroxide ion, pseudo-first-order rate constants increased with increasing concentration of added nucleophile. This behaviour is attributable to the superimposition of the direct second-order displacement process k_d on the first-order process k_1.

$$k_{obs} = k_1 + k_d[Nu] \quad (1)$$

Plots of observed rate constant against [Nu] gave k_1 and k_d according to the expression (1). A typical plot is in Figure 1.

As expected, k_d for OH^- is much greater than for aniline

TABLE 1

Solvolysis rates of ω-halogenoalkyl sulphides in ethanol–water [a]

	Substrate	*t*/°C	$10^5 k_1/s^{-1}$	$10^5 k_{d(aniline)}$/l mol^{-1} s^{-1}	Product (%)
(1)	*p*-TolylS[CH_2]$_2$Cl	40·3	1·16 ± 0·04	0·39	
		54·9	4·43 ± 0·20	1·45	95 [d]
		65·0	10·1 ± 0·5	4·00 (79) [b]	
(2)	*p*-TolylS[CH_2]$_4$Cl	45·5	1·26 ± 0·02 (0·21) [c]	—	
		55·3	3·24 ± 0·05	—	96 [d]
		64·9	7·69 ± 0·2	—	
(3)	*p*-TolylS[CH_2]$_2$Br	54·2	157 ± 10	258	92 [d]
(4)	*p*-TolylS[CH_2]$_4$Br	54·2	180 ± 2 (9·8) [c]	—	92 [d]
(5)	*p*-TolylSCH_2CHPhCl	9·8	317 ± 4	—	
		20·1	878 ± 6	330	90 [e]
		29·8	2060 ± 40	—	
(6)	*p*-TolylS[CH_2]$_3$CHPh·Cl	29·7	18·1 ± 0·3 (11) [c]	—	
		39·7	47·9 ± 0·4	—	90 [e]
		49·5	109 ± 8	—	

[a] 80% w/w. [b] k_d for OH^-. [c] Spectroscopically determined at 25°. [d] Anilino-sulphide. [e] Ethoxy-sulphide.

solvolysis of *S*-alkylepisulphonium ions was much preferred to halide ion reversion. This difference may be intrinsic; we do not favour an explanation based on ion pair equilibria as, under similar conditions, other evidence suggests that

[8] A. C. Knipe and C. J. M. Stirling, *J. Chem. Soc.* (*B*), 1968, 1218.
[9] W. H. Mueller, *Angew. Chem. Internat. Edn.*, 1969, **8**, 482.
[10] F. G. Bordwell and W. T. Brannen, *J. Amer. Chem. Soc.*, 1964, **86**, 4645.
[11] P. D. Bartlett and C. G. Swain, *J. Amer. Chem. Soc.*, 1949, **71**, 1406.
[12] A. L. Jacobson and J. B. Hine, *J. Amer. Chem. Soc.*, 1960, **82**, 2418.
[13] A. Streitwieser, 'Solvolytic Displacement Reactions,' McGraw-Hill, New York, 1962.

but the intercept value, giving k_1, is the same for both nucleophiles. $k_{d(aniline)}$ Has been evaluated for all the 2-halogenoalkyl sulphides examined. Values are in Table 1.

An interesting aspect of the kinetic behaviour in the presence of added nucleophile is the sharp initial increase in k_{obs} produced by 0·1M-aniline. This is attributable to suppression of the reversion reaction caused by rapid removal of the episulphonium salt in reaction with the external nucleophile (Figure 1).

For the 4-halogenobutyl halides, rates were unaffected by addition of aniline. Reversion is very slow, *i.e.* the equilibrium constant for sulphonium salt formation is much greater for the five-membered ring even in pure ethanol [8] and the forward rate is obtained directly. With aniline present, however, the products from substrates (1)—(4) were the anilino-sulphides. It had been shown earlier [8] that rates of reaction of 4-bromobutyl *p*-tolyl sulphide with ethoxide and t-butoxide ion were very nearly independent of nucleophile concentration and there is little doubt that the rate-limiting step is formation of the cyclic sulphonium salt. Further evidence for this conclusion is provided by spectroscopic observation of solvolysis of substrates (2), (4), and (6). In all cases absorption maxima at *ca.* 224 and 258 nm were replaced by a single maximum at 242 nm consistent with conversion to the cyclic salt.[8]

Attempted preparations of the sulphides (7) and (8) also suggested the ready involvement of cyclic sulphonium salts in reactions of ω-halogenoalkyl sulphides. When the

p-TolylSCHPhCH$_2$Cl (7) *p*-TolylSCHPh[CH$_2$]$_3$Cl (8)

alcohols (7; OH for Cl) and (8; OH for Cl) were treated with thionyl chloride in dichloromethane under very mild conditions, the sole products were the isomeric chlorides (5) and (6) respectively. This finding is consistent with formation of a cyclic sulphonium ion from the initially formed chlorosulphite which suffers subsequent attack at the benzylic carbon atom by chloride ion which is highly nucleophilic in this non-solvating medium.[14]

DISCUSSION

We conclude that the rate-limiting step is formation of a cyclic sulphonium salt in all the solvolytic reactions desribed. Our reults thus allom comparison of the formation of three- and of five-memberad rings in this type of system.

A striking feature of these results, and a contrast to the behaviour of the ω-halogenoalkylamines,[1] is that the rates of formation of three member rings are *greater* than for five-membered rings. It might be argued that this is simply a reflection of the lower excess of enthalpy associated with the episulphonium ring [15] (for thiiren the value is *ca.* 9 compared with 14 kcal mol^{-1} for the aziridine ring) but cyclisation rates in the sulphide series respond differently from those in the amine series in a number of significant respects. As mentioned earlier, replacement of an *S*-alkyl by an *S*-aryl group appears to promote cyclisation to form a three-membered ring *selectively*. Accurate data are not available because of the extremely rapid formation of *S*-alkyltetrahydrothiophenonium salts.[7] When an *S*-alkyl is replaced by an *S*-aryl group, the cyclisation rate is markedly decreased; thus for episulphonium salt (three-membered ring) formation the SEt : SPh ratio is 40. The present results also show the expected result that placement of a conjugative phenyl group on carbon adjacent to the leaving group raises cyclisation rates for both three- and five-membered systems, but the ratio is 45 for the five-membered ring system and 5400 for the three-membered ring system. These values are to be compared with the effects for the analogous amines where phenyl substitution α to the *nucleophilic* atom accelerates three-membered ring formation by a factor of 1·35 (1·22 when the leaving group is sulphate [16]).

Structural comparisons with the amines have also included comparison of the chloride : bromide ratios for both three- and five-membered ring systems [substrates (1)—(4)]. These are 35 and 56 respectively. The ratio for *N*-phenylaziridine formation [1] is 28.

Activation Parameters.—Values in Table 2 show that, for the three-membered ring systems, enthalpies of activation are lower than for five-membered ring systems in both the pairs of substrates for which comparison is possible. Furthermore, the entropy of activation for formation of the *S*-*p*-tolylepisulphonium [from (1)] ion is *more* negative than for the related tetrahydrothiophenonium system [from (2)]. These results are again contrary to the view that formation of three-membered rings is favoured by the less negative entropy change associated with less restriction of the rotamer population [17] but disfavoured by an enthalpy change associated with ring strain.

TABLE 2

Activation parameters * and relative rates for solvolysis reactions

	Substrate	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$	$\Delta G^{\ddagger}_{25}$	$k_{rel.}^{25°}$	$k_{rel.}^{54.2°}$
(1)		17·8 ±0·3	−24 ±0·5	24·9 ±0·5	1 [a]	1
(1)	+ $PhNH_2$ [b]	19·1 ±0·2	−22 ±0·4	25·6 ±0·4		(1) [c]
(2)		19·4 ±0·3	−20 ±0·5	25·3 ±0·5	0·53 [a]	0·73
(3)						35(178) [c]
(4)						41
(5)		15·4 ±0·3	−13 ±0·5	19·3 ±0·5	5,400	
(6)		17·0 ±1·1	−19 ±1·5	22·8 ±1·6	45 [a]	

* $\Delta H^{\ddagger}$ and $\Delta G^{\ddagger}$ in kcal mol^{-1}; $\Delta S^{\ddagger}$ in cal mol^{-1} K^{-1}.

[a] Calculated from data obtained at higher temperatures. [b] Displacement reaction. [c] k_{rel} For displacement.

Placement of a phenyl group on carbon adjacent to the leaving group causes reduction of 2·4 kcal mol^{-1} in the enthalpy of activation for *both* three- and five-membered ring systems. There is, therefore, no *prima facie* evidence for conjugative control in these cyclisations. An intriguing aspect of the activation parameters,

[14] A. J. Parker, *Adv. Phys. Org. Chem.*, 1967, **5**, 173.
[15] R. A. Nelson and R. S. Jessup, *J. Res. Nat. Bur. Stand.*, 1952, **48**, 206.
[16] C. S. Dewey and R. A. Bafford, *J. Org. Chem.*, 1967, **32**, 3108.
[17] N. L. Allinger and V. Zalkow, *J. Org. Chem.*, 1960, **25**, 701.

however, is the large positive change in the entropy of activation for the episulphonium salt caused by introduction of the *C*-phenyl group. It is this change that is responsible for the widening of the rate differential between three- and five-membered rings that *C*-phenylation produces. By contrast, for the amines [1] enthalpies of activation are increased by α-*C*-phenylation.

Charged intermediates are formed in both types of reaction and we tentatively suggest that the degree of ring formation in the transition state is greater for sulphonium salts than for amines. This suggestion is consistent with the much greater effect on atom nucleophilicity occasioned by attachment of a phenyl group. For the sulphides, the *C*-phenyl group increases reactivity because of stabilisation of the displacement transition state as in general experience of benzylic compounds. The *C*-phenyl group probably exerts an adverse steric effect on solvation. The small ring sulphonium salt is probably more efficiently solvated and hence more adversely affected by steric repression of solvation so that $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ terms are more positive on this account than for the five-membered ring series. To the extent that this supposition is valid, behaviour in this system is consistent with conjugative control of three-membered ring formation.

It is also relevant to the comparison of transition states for three- and five-membered ring formation that, for three-membered ring formation, the product is much less stable than the starting material and reacts much more rapidly with solvent or with chloride ion than the thiophenonium salts. In the latter case the product is of stability comparable to starting material (equilibrium constant near unity). The Hammond postulate thus suggests greater sulphonium salt character in the transition state leading to the episulphonium intermediate.

Bromide : Chloride Ratios.—The difference in reactivities between bromides and chlorides has been regarded as an index of the degree of bond extension to the leaving group in a number of systems [18,19] with the implication that the greater the bromide : chloride ratio, the greater the extent of leaving group bond cleavage in the transition state. As the extent of bond formation in the transition state of three-membered ring closure is crucial to the operation of any p(C–C)–π conjugative effect, we have reconsidered this ' element effect ' because of probable inverse relationship between extension of the bond to the leaving group and C–C bond formation.

For displacement at saturated carbon, a change of leaving group from bromide to chloride results in changes of at least three parameters, (i) the differential in C–X bond energy, ΔD(C–X), (ii) the differential in electron affinity of the atom, ΔI(X), and (iii) the differential in solvation energy, ΔSOLV(X^-) giving equation (2).

$$\Delta\Delta G(\mathrm{Br:Cl}) = \Delta\Delta D(\mathrm{C{-}X}) - \Delta\Delta I(\mathrm{X}) - \Delta\Delta\mathrm{SOLV}(\bar{\mathrm{X}}) \quad (2)$$

This simple treatment takes electron affinities for gaseous atoms, and thus assumes that desolvation and vaporisation energies of alkyl bromides and chlorides are the same. In fact, alkyl chlorides are more solvated in protic media than are alkyl bromides [20] (making Br : Cl higher). Values of parameters are in Table 3. It can

TABLE 3

Energetics * of nucleophilic displacements of bromide and chloride ion

	D(C–X)	I(X)	$\Delta\Delta G_{\mathrm{solvation}}$	$\Delta\Delta G^{\mathrm{total}}_{\mathrm{cleavage}}$
Br	+60	−81·6	−77·8	−99·4
Cl	+73	−88·2	−84·2	−99·4

* In kcal mol^{-1}.

be seen that the value of $\Delta\Delta G$ for complete bond cleavage in water is zero implying that under these conditions a bromide : chloride ratio of unity should be observed.

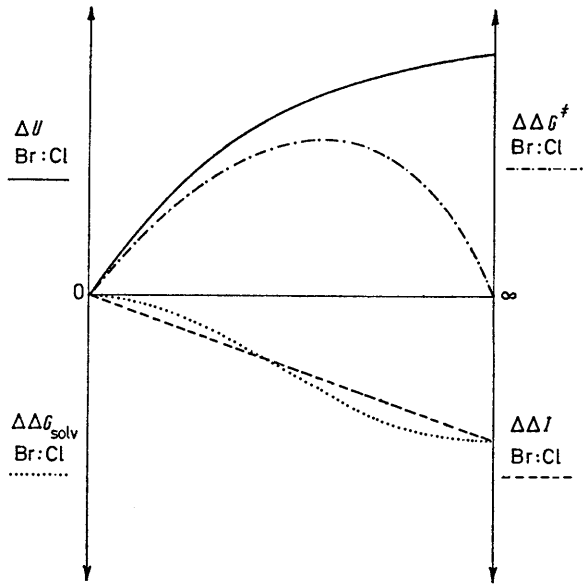

FIGURE 2 Factors determining relative reactivities of bromides and chlorides in nucleophilic displacement reactions at a function of C–X extension in the transition state

For most intermolecular displacement reactions in solvents such as methanol, bromide : chloride ratios vary from 30 to *ca.* 150 although very large values are sometimes observed.[21] These values are consistent with partial cleavage of the C–X bond, because under these conditions, the dominant factor which favours bromide over chloride is the bond dissociation energy differential. This rises steeply (Figure 2) with bond extension in the initial stages of bond cleavage according to a Morse-curve dependence. The compensating factor (for chloride) of solvation has the form of the Born equation (3), where e is the charge on the ion and r the bond

$$\Delta\Delta\mathrm{SOLV} = \alpha\frac{e^2}{r} \quad (3)$$

extension, and if, in the absence of any certain evidence,

[18] G. Modena, *Accounts Chem. Res.*, 1971, **4**, 73 and refs. cited.
[19] H. M. R. Hoffmann, *J. Chem. Soc.*, 1965, 6753.
[20] R. Alexander, E. C. F. Ko, A. J. Parker, and T. J. Broxton, *J. Amer. Chem. Soc.*, 1968, **90**, 5049.
[21] F. G. Bordwell and J. M. Williams, *J. Amer. Chem. Soc.*, 1968, **90**, 435.

it is assumed that electron affinity rises linearly with bond extension, superimposition of the three factors (Figure 2) gives a bell-shaped dependence of bromide : chloride ratio on bond extension for a solvent *in which solvation of halide ions is important.**

In earlier work [2,4] on intramolecular displacement leading to small rings, cyclisation of ω-halogenoalkyl sulphones was shown to give a $k_{3\text{-ring}} : k_{5\text{-ring}}$ ratio of 100, associated with a chloride : bromide ratio of only 2. The coincidence of preferred three-membered ring closure and low bromide : chloride ratio is, of course, consistent with the operation of conjugative control of cyclisation in that system.

The present results show for three-membered ring cyclisation, a bromide : chloride ratio similar to the amine systems [1] in which no evidence of the conjugative control was obtained. The amine systems, however, are insensitive to solvent change and we suggested that the bromide : chloride ratio represents a degree of bond extension less than that observed at the maximum of the ratio. For sulphonium salts, the value may correspond with the ratio obtained at greater than the ratio maximum and in this connection it is perhaps significant that the bromide : chloride ratio for sulphonium salts is greater for the five- than for the three-membered ring system. The differential found in entropies of activation is consistent with this idea.

The large value (178) for the chloride : bromide ratio in the direct displacement reactions with aniline makes a notable contrast with the intramolecular reactions.

Conclusions.—Cyclisation of ω-halogenoalkyl sulphides differs markedly from cyclisation of ω-halogenoamines in terms of the response of rate towards structural change. While the effect on relative rates of formation of three- and five-membered rings is correctly predicted by the hypothesis of conjugative control, activation parameters show that enthalpy differences considered *alone* are not consistent with this interpretation. Activation parameters, however, do not accord with any simple ideas of the factors which control rates of cyclisation. Further work is being concentrated on assessing degrees of bond formation in cyclisation transition states.

EXPERIMENTAL

For general directions see Part X.[1] ^{1}H N.m.r. and i.r. spectra of substrates were consistent with the structures assigned.

Substrates.—*2-Bromoethyl* p-*tolyl sulphide.* Toluene-*p*-thiol (18 g) was added to potassium t-butoxide (12 g) in t-butyl alcohol (200 ml) and the mixture was added to 1,2-dibromoethane (390 g) in t-butyl alcohol (150 ml). The mixture was boiled under reflux for 4 h and poured into saturated brine. Extraction and distillation of the extracts gave the *sulphide* (80%), b.p. 118° at 0·1 mmHg, n_D^{22} 1·5947, m.p. 24—25° (Found: C, 46·6; H, 4·7. $C_9H_{11}BrS$ requires C, 46·6; H, 4·8%).

2-Chloroethyl p-*tolyl sulphide.* The chloro-analogue (85%) was obtained as for the bromide using 1,2-dichloroethane. It had b.p. 90° at 0·1 mmHg, n_D^{25} 1·5728 (lit.,[22] b.p. 132° at 10 mmHg, n_D^{20} 1·5728).

4-Bromobutyl p-*tolyl sulphide.* The same procedure using 1,4-dibromobutane gave the bromo-sulphide (65%), b.p. 148° at 0·1 mmHg, n_D^{22} 1·5756 (lit.,[23] 1·5746).

4-Chlorobutyl p-*tolyl sulphide.* Treatment of toluene-*p*-thiol with 4-chlorobutan-1-ol and potassium t-butoxide in t-butyl alcohol gave 4-hydroxybutyl *p*-tolyl sulphide (57%), b.p 134° at 0·1 mmHg, n_D^{17} 1·5663 (lit.,[24] b.p. 139° at 4 mmHg, n_D^{20} 1·5656). The alcohol (0·08 mol) was refluxed in chloroform (250 ml) with thionyl chloride (0·15 mol) for 30 min. Distillation of the mixture gave the *chloro-sulphide* (93%), b.p. 120° at 0·05 mmHg, n_D^{20} 1·5603 (Found: C, 61·5; H, 6·8. $C_{11}H_{16}ClS$ requires C, 61·5; H, 7·0%).

1-Chloro-1-phenyl-2-(p-tolylthio)ethane. 2-Chloro-1-phenylethanol (72%) was obtained by reduction of phenacyl chloride with lithium borohydride in tetrahydrofuran. It had b.p. 76° at 0·8 mmHg, n_D^{25} 1·5505 (lit.,[25] b.p. 88° at 0·3 mmHg, n_D^{20} 1·5525).

Treatment of the chlorohydrin (0·13 mol) with toluene-*p*-thiol (0·14 mol) and sodium ethoxide (0·14 mol) in ethanol (230 ml) at reflux for 3 h gave *1-phenyl-2-(p-tolylthio)ethanol* (79%), b.p. 155° at 0·02 mmHg, n_D^{23} 1·6079 (Found: C, 73·8; H, 6·9. $C_{15}H_{16}OS$ requires C, 72·7; H, 6·6%).

The hydroxy-sulphide (0·05 mol) was kept with thionyl chloride (0·06 mol) in chloroform (100 ml) at 30° for 30 min. Solvent and excess of thionyl chloride were removed to give the *chloro-sulphide* which decomposed on attempted distillation. Freshly prepared sulphide was solvolysed in ethanol–water and chloride liberated was titrated potentiometrically (Found: ionic Cl, 13·4. $C_{15}H_{15}ClS$ requires ionic Cl, 13·4%).

1-Chloro-1-phenyl-4-(p-tolylthio)butane. 4-Bromobutyrophenone (85%) was obtained by treatment of benzene with 4-bromobutyryl bromide and aluminium chloride in dichloromethane. It had b.p. 162° at 13 mmHg, m.p. 35° (lit.,[26] b.p. 157° at 15 mmHg, m.p. 38°). Treatment of the bromo-ketone (0·09 mol) with toluene-*p*-thiol (0·09 mol) in ethanolic 0·36M-sodium ethoxide (250 ml) at reflux for 3 h gave the *keto-sulphide* (72%), b.p. 176° at 0·05 mmHg, n_D^{23} 1·5972 (Found: C, 75·3; H, 7·0. $C_{17}H_{18}OS$ requires C, 75·5; H, 6·7%).

The keto-sulphide (0·1 mol) in tetrahydrofuran was added slowly to potassium borohydride (0·1 mol) in tetrahydrofuran (100 ml). The mixture was stirred at 25° for 24 h when ice and dilute aqueous hydrochloric acid were added. Extraction gave *1-phenyl-4-(p-tolylthio)butan-1-ol* (90%), b.p. 178° at 0·05 mmHg, n_D^{22} 1·5923 (Found: C, 75·3; H, 7·6. $C_{17}H_{20}OS$ requires C, 75·0; H, 7·4%).

Treatment of the alcohol with thionyl chloride in chloroform at 25° as before gave the *chloride* which decomposed on attempted distillation (Found: C, 69·8; H, 6·5. $C_{17}H_{19}ClS$ requires C, 70·3; H, 6·6%).

* Comparison of toluene-*p*-sulphonate and bromide as leaving groups as a function of bond extension has been considered by A. F. Cockerill (*Tetrahedron Letters*, 1969, 4913) from a different point of view. His treatment takes into account electronegativity differences between the leaving groups at low extents of bond cleavage which can be ignored for the bromide : chloride comparison.

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Attempted Preparation of 2-*Chloro*-1-*phenyl*-1-(p-*tolylthio*)-*ethane*.—Methyl α-(*p*-tolylthio)phenylacetate (0·05 mol) was reduced with lithium aluminium hydride (0·08 mol) in ether to give 2-*phenyl*-2-(p-*tolylthio*)*ethanol* (69%), b.p. 146° at 0·1 mmHg, n_D^{18} 1·6130 (Found: C, 73·5; H, 6·4. $C_{15}H_{16}OS$ requires C, 73·8; H, 6·6%).

Treatment of the hydroxy-sulphide with thionyl chloride in dichloromethane gave 2-chloro-1-phenyl-1-(*p*-tolylthio)-ethane identical (n.m.r. and i.r. spectra) with a specimen described above.

Attempted Preparation of 4-*Chloro*-1-*phenyl*-1-(p-*tolylthio*)-butane.—Butyl-lithium in hexane was added to benzyl *p*-tolyl sulphide (0·11 mol) and 2-(3-chloropropoxy)tetrahydropyran (0·1 mol) until the deep red colour of the benzylic carbanion persisted for 1 h. The mixture was quenched with water and extraction gave the crude pyranyl ether which was hydrolysed during 48 h with 0·25% ethanolic toluene-*p*-sulphonic acid. After addition of brine and neutralisation with Na_2CO_3 methylene chloride gave 1-*phenyl*-1-(p-*tolylthio*)*butan*-1-*ol* (53%), b.p. 170° at 0·1 mmHg, n_D^{18} 1·5963 (Found: C, 75·0; H, 7·35. $C_{17}H_{20}OS$ requires C, 75·0; H, 7·4%).

Treatment of the hydroxy-sulphide with thionyl chloride in dichloromethane as before gave 1-chloro-1-phenyl-4-(*p*-tolylthio)butane identical with that obtained by the alternative route above.

Kinetics.—Solvolyses in 5 : 1 w/w ethanol–water were followed by titration at intervals of halide ion liberated. Typically, thermally equilibrated solvent and sulphide were mixed and aliquot parts were withdrawn at intervals. Titration of halide ion was carried out either potentiometrically or, for the fastest reactions, polarographically at +0·25 V, using an Amel 462 multipurpose instrument with lithium perchlorate as supporting electrolyte under an atmosphere of nitrogen. When solvolysis of the sulphides occurred appreciably during the titration procedure, the titration curves showed an initial steep section (halide initially present) and a more gently sloping section indicating solvolysis. The latter sections of the curves were extrapolated to zero time to obtain the true initial titres.

Product Analyses.—(a) 2-*Halogenoethyl* p-*tolyl sulphides*. The chloro-sulphide (9·4 mmol) was treated with aniline (60 mmol) in aqueous ethanol (200 ml). The mixture was kept at 65° for 24 h and was then reduced in volume to 50 ml. After addition of brine and extraction, distillation of the extracts gave N-(2-p-*tolylthio*)*aniline* (95%), b.p. 160° at 0·05 mmHg, n_D^{21} 1·6205 (Found: C, 73·9; H, 7·1. $C_{15}H_{17}NS$ requires C, 74·1; H, 7·1%). The same procedure with the bromo-sulphide gave the anilino-sulphide (92%). When aniline was added to the solvolysis mixture of the chloro-sulphide after 48 h and the mixture was kept at 65° for a further 24 h, extraction, as before, gave 2-ethoxyethyl *p*-tolyl sulphide (87%), b.p. 145° at 13 mmHg, n_D^{25} 1·5300 (lit.,[27] b.p. 145° at 12 mmHg, n_D^{22} 1·5340).

(b) 4-*Halogenobutyl* p-*tolyl sulphides*. Treatment of the chloro-sulphide with aniline as in the ethyl series gave N-(4-p-*tolylthioethyl*)*aniline* (96%), b.p. 181° at 0·1 mmHg, m.p. 37—38° (Found: C, 75·0; H, 7·6. $C_{17}H_{21}NS$ requires C, 75·3; H, 7·8%). The bromide gave the same anilino-sulphide in 92% yield.

(c) 1-*Chloro*-1-*phenyl*-2-(p-*tolylthio*)*ethane*. The sulphide (12·7 mmol) was kept for 1 h in aqueous ethanolic 0·05M-lithium perchlorate (800 ml) at 25°. Addition of brine followed by extraction and distillation of the extracts gave 1-*ethoxy*-1-*phenyl*-2-(p-*tolylthio*)*ethane* (90%), b.p. 158° at 0·1 mmHg, n_D^{21} 1·5827 (Found: C, 74·6; H, 7·3. $C_{17}H_{20}OS$ requires C, 74·9; H, 7·4%).

(d) 1-*Chloro*-1-*phenyl*-4-(p-*tolylthio*)*butane*. The sulphide (9·2 mmol) was kept in ethanol–water (200 ml) at 50° for 48 h. Extraction as before gave 1-*ethoxy*-1-*phenyl*-4-(p-*tolylthio*)*butane* (99·5%), b.p. 158° at 0·1 mmHg, n_D^{21} 1·5649 (Found: C, 75·9; H, 7·7. $C_{19}H_{24}OS$ requires C, 75·9; H, 8·0%).

We thank the S.R.C. for a maintenance grant (to R. B.)

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[2/2691 *Received*, 28*th November*, 1972]