THE ELIMINATION REACTION OF VICINAL DISULPHONYLOXY COMPOUNDS WITH SODIUM IODIDE

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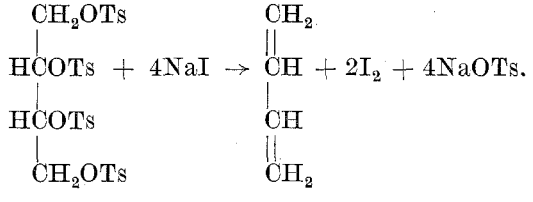
Summary

The elimination of two tosyloxy groups from vicinal ditosyloxy compounds by reaction with sodium iodide has been investigated. The reaction involves nucleophilic displacement of one tosyloxy group; this is followed by the simultaneous elimination of the second tosyloxy group and iodine, if the steric arrangement is favourable; if it is unfavourable, a second displacement by an iodide ion probably occurs to give substituents having a *trans*-arrangement suitable for elimination.

In one case, that of the ditosyl derivative of *trans*-cyclohexane-1,2-diol, the intermediate *cis*-2-iodocyclohexyl toluene-*p*-sulphonate was isolated.

I. INTRODUCTION

Sulphonyloxy groups, when attached to saturated carbon atoms, behave like halogen atoms toward nucleophilic reagents. Thus, a vicinal disulphonyloxy compound reacts with iodide ion by elimination of the sulphonyloxy groups with the establishment of an ethylenic linkage and the formation of molecular iodine. Tipson and Cretcher (1943) were the first to recognize this reaction clearly when they found that sodium iodide in acetone removed all four tosyloxy groups from 1,2,3,4-tetra-*O*-tosylerythritol, with the production of butadiene:



The reaction has since been used for the preparation of unsaturated sugar derivatives (for a review, see Tipson 1953) but in carbohydrate chemistry it was found applicable only to cases where one of the sulphonyloxy groups was primary. On the other hand, two secondary sulphonyloxy groups were eliminated from cyclitol derivatives by Angyal and Gilham (1958); the greater stability of cyclitols, compared to that of sugars, allowed here the use of more vigorous conditions.

Two applications of this reaction have been described, which possess stereochemical interest. Slates and Wendler (1955, 1956) applied the reaction to the 2,3-disulphonyloxy derivatives of an *allo*-steroid; they found that two of the diastereomers (the 2α,3β- and the 2α,3α-isomers) gave the Δ^2-olefin in good yield, whereas the other two (the 2β,3β and the 2β,3α) were recovered unchanged.

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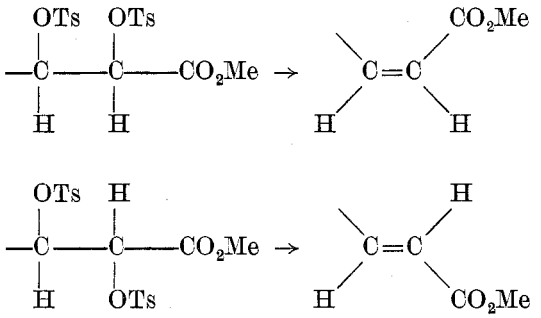
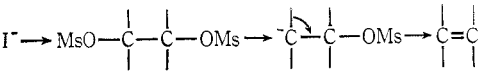
Previously Linstead, Owen, and Webb (1953) had shown that esters of *erythro*- and *threo*-αβ-dimesyloxy acids react with sodium iodide in acetone, with overall *cis*-elimination, to give the corresponding *cis*- and *trans*-unsaturated esters. This behaviour is opposite to that of the αβ-dibromo acids which undergo *trans*-elimination with sodium iodide :



In order to explain these cases of stereochemical specificity it seemed desirable to study the course of the reaction. Several suggestions have previously been advanced. Bladon and Owen (1950) proposed a course comprising independent displacement of each sulphonyloxy group by iodide ion to give a di-iodo compound which would be unstable and would decompose to iodine and an olefin. Foster and Overend (1951*b*) suggested an alternative mechanism in which the first step is the displacement (S_N^-2) by iodide ion of one sulphonyloxy group (a primary one, which is well known to undergo this reaction readily), followed by a concerted elimination (*E*2), of the remaining sulphonyloxy group and the iodine atom. In support of this suggestion these authors showed that 3,6-anhydro-1-deoxy-1-iodo-4,5-*O*-isopropylidene-2-*O*-tosyl-D-mannitol reacts more readily with sodium iodide in acetone than does the corresponding ditosyl compound. Newth (1956) produced evidence in support of this mechanism by showing that methyl 4,6-*O*-benzylidene-3-deoxy-3-iodo-2-*O*-tosyl-α-D-glucoside reacts quantitatively with sodium iodide in acetone in 10 min at 100 °C, whereas the corresponding ditosyl compound is unaffected by the same reagent during 24 hr at 100 °C. It is evident therefore that vicinal *trans*-iodosulphonyloxy compounds undergo elimination readily with sodium iodide ; but it has not been proven that such a compound is an intermediate in the reaction of vicinal disulphonyloxy compounds with sodium iodide.

A completely different course for the reaction was proposed by James, Rees, and Shoppee (1955) to explain the results obtained by Slates and Wendler. They suggested that the reaction proceeds by the mechanism—designated as *ElcB* (Ingold 1953)—where the first step is the formation of a carbanion as a result of the removal of one sulphonyloxy group by combination with the iodide ion :



the anion then would lose a sulphonate ion to give the olefin.

II. The Reaction of Cyclic *cis*- and *trans*-Isomers

It is well known that the reaction of *trans*-1,2-dibromocyclohexanes with sodium iodide is much faster than that of the *cis*-isomers (Barton and Rosenfelder 1951; Alt and Barton 1954); this fact indicates the concerted nature of the former reaction. The ditosyloxycyclohexanes behave differently: preliminary experiments (Gilham 1956) have shown that the yield of sodium toluene-*p*-sulphonate is approximately the same, after a given time, from either the *cis*- or the *trans*-isomer. On repetition of these experiments it was observed, however, that the colour of iodine appeared much earlier in the reaction mixture containing the *cis*-isomer. It was then decided to determine the yield of sodium toluene-*p*-sulphonate (by filtration) and of iodine (by titration) formed from each isomer at intervals: the results are shown in Table 1.

Table 1

Reaction of 1,2-ditosyloxycyclohexanes with sodium iodide in acetone at 78 °C

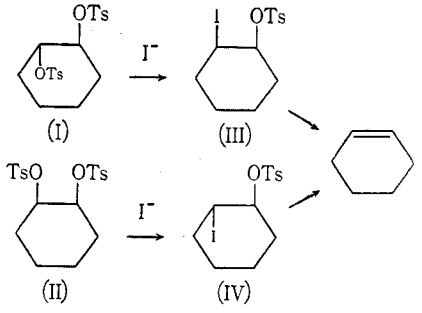
Time (hr)	*cis*-Isomer (II)		*trans*-Isomer (I)	
	NaOTs (moles)	Iodine (equiv.)	NaOTs (moles)	Iodine (equiv.)
4	0·20	0·19	0·14	0·06
8	0·31	0·27	0·26	0·16
16	0·61	0·50	0·58	0·34
32	1·02	0·77	1·04	0·71

The analysis for iodine is not accurate because iodine reacts slowly with acetone under the conditions of the experiment and is gradually removed thereby. The results in Table 1 nevertheless show that iodine is formed initially at the same rate as sodium toluenesulphonate from the *cis*-isomer (II), but at a much lower rate from the *trans*-compound (I). The reaction in the latter case therefore proceeds by a first step—in which iodine is *not* produced—giving an intermediate which releases iodine by a subsequent reaction. Formation of an intermediate in the reaction of the *trans*-compound is also shown by the fact that the starting material recovered (by dilution with water), after the reaction was allowed to proceed for some time, had a low melting point and was, therefore, contaminated. On the other hand pure starting material was recovered by the same procedure from the reaction of the *cis*-isomer indicating the absence of an intermediate in substantial amounts.

Subsequently, the intermediate was isolated in 10% yield from a 28-hr run of the *trans*-derivative (I), and gave correct analyses for an iodotosyloxycyclohexane. It was not identical with the known (Winstein, Grunwald, and Ingraham 1948) *trans*-2-iodocyclohexyl toluene-*p*-sulphonate (IV) and is therefore assigned the corresponding *cis*-structure (III). It reacts with sodium iodide in acetone, with the formation of equimolecular amounts of iodine and sodium toluenesulphonate, approximately five times faster than the ditosyl compounds (I) and (II). The *trans*-iodo compound (IV), on the other hand, reacts very rapidly

with sodium iodide even at room temperature (Winstein, Grunwald, and Ingraham 1948), obviously by a concerted mechanism.

Either of the two tosyloxy groups of the *trans*-isomer therefore react with iodide ion independently from each other by inversion to give the *cis*-iodo-intermediate. The mechanism by which the *cis*-iodotosyloxy compound (III) reacts further with iodide ion is not known : probably either the tosyloxy group or the iodine atom is displaced by inversion, giving a *trans*-compound which can undergo *E*2 elimination with ease. It can be assumed that the *cis*-ditosyloxy compound behaves in the same way (the initial rates being similar) but here the intermediate *trans*-iodo derivative reacts so rapidly with iodide ion that it cannot be isolated ; appearance of iodine is therefore at the same rate as that of sodium toluenesulphonate. These results vindicate the mechanism suggested by Foster and Overend (1951*b*) but are incompatible with that proposed by James, Rees, and Shoppee (1955).



This stepwise course of the reaction clearly explains its stereochemical outcome in the aliphatic series, as exemplified by the dimesyloxy compounds of Linstead, Owen, and Webb (1953). After the displacement of one group by inversion, elimination will occur in that conformation in which the C—O and the C—I bonds are antiparallel ; the overall result is *cis*-elimination. It is to be expected that this stereochemical outcome of the reaction will be general in all compounds where rotation is not constricted. However, Slates and Wendler's (1956) experiments do not appear to be explained by this mechanism.

The reaction of the ditosyloxycyclopentanes with iodide ion was investigated in a similar manner ; the results are shown in Table 2. These compounds react more rapidly than the cyclohexane derivatives, a general phenomenon for S_N2 reactions in these cyclic systems (Brown, Fletcher, and Johannsen 1951). The reaction of the *trans*-isomer is distinctly slower, probably because backside attack of the iodide ion is hindered by the adjacent tosyloxy group. There is no lag in the appearance of iodine from the *trans*-ditosyloxy compound ; nevertheless it is assumed that *cis*-iodocyclopentyl toluene-*p*-sulphonate is an intermediate and that it reacts much faster with iodide ion (being a *cis*-derivative of cyclopentane) ; therefore it does not appear in substantial concentrations.

The ditosyl esters of the four camphane-2,3-diols (Angyal and Young 1959) were also investigated, because the ring system in these compounds is rigid and nucleophilic attack on the *endo*-substituents is strongly hindered. It was indeed

found that 2-*endo*,3-*endo*-ditosyloxycamphane was very resistant to attack by iodide ion, being recovered unchanged after 94 hr at 100 °C. Each of the other three isomers reacted with iodide ion with the formation of sodium toluene-*p*-sulphonate and an amount of iodine much less than theoretical. It appears that

TABLE 2

REACTION OF 1,2-DITOSYLOXYCYCLOPENTANES WITH SODIUM IODIDE IN ACETONE AT 78 °C

Time (hr)	*cis*-Isomer		*trans*-Isomer	
	NaOTs (moles)	Iodine (equiv.)	NaOTs (moles)	Iodine (equiv.)
0·5	0·34	0·31		
1	0·47	0·44		
2	0·76	0·74		
4	1·25	1·23	0·41	0·39
8	1·90	1·67	0·71	0·70
16	1·98	1·90	1·40	1·01

these reactions are not straightforward eliminations but may be accompanied by skeletal rearrangements. Attempts to isolate a camphane derivative from the reactions were unsuccessful.

The reaction of tosyloxy groups with iodide ion is often inconveniently slow. Following a suggestion by Tipson (1953), Angyal and Gilham (1958) have shown

TABLE 3

REACTION OF DISULPHONYL COMPOUNDS WITH SODIUM IODIDE IN ACETONE

Compound	Time (hr)	Temp. (°C)	Yield of Sodium Salt (%)
trans-Cyclohexane-1,2-diol di-*p*-nitrobenzenesulphonate ..	1·25	78	66·5
ditoluene-*p*-sulphonate	32	78	51·5
ditoluene-*p*-sulphonate	8	78	13
dimethanesulphonate	8	78	25
Camphane-2*endo*,3-*exo*-diol di-*p*-nitrobenzenesulphonate ..	1	78	79
ditoluene-*p*-sulphonate	2	100	70

that vicinal *p*-nitrobenzenesulphonyl groups are eliminated more rapidly by iodide ion than are tosyl groups. It was found that the di-*p*-nitrobenzenesulphonyl esters of *trans*-cyclohexane-1,2-diol and of camphane-2-*endo*,3-*exo*-diol also react much faster than the corresponding tosyl compounds (see Table 3). The dimesyl ester of *trans*-cyclohexane-1,2-diol was also found to react somewhat

faster than the corresponding ditosyl compounds; in other cases, however, the opposite had been reported (Foster *et al.* 1949; Foster and Overend 1951*a*; Angyal and Gilham 1958).

III. Experimental

All melting points are corrected.

(*a*) *Preparation of the Disulphonyl Compounds.*—(i) *trans*-1,2-Ditosyloxycyclohexane, m.p. 110·5–111·5 °C, and its *cis*-isomer, m.p. 129 °C, were prepared according to Criegee and Stanger (1936); the *cis*- and *trans*-1,2-ditosyloxycyclopentanes, m.p. 89–90 °C and 109·5 °C, respectively, according to Owen and Smith (1952); *trans*-1,2-dimethanesulphonyloxycyclohexane, m.p. 132·5–133·5 °C, according to Clarke and Owen (1949).

(ii) trans-1,2-*Di*-p-*nitrobenzenesulphonyloxycyclohexane*. *trans*-Cyclohexane-1,2-diol (1 g) and *p*-nitrobenzenesulphonyl chloride (5·8 g), dissolved in anhydrous pyridine (10 ml), were allowed to stand at room temperature for 20 hr. Addition of ice precipitated a solid which was crystallized from ethanol to give needles of the *diester* (2·16 g, 51%), m.p. 147·5 °C (Found: C, 44·5; H, 3·5%. Calc. for $C_{18}H_{18}O_{10}N_2S_2$: C, 44·5; H, 3·7%).

(iii) *The 2,3-Ditosyloxycamphanes*. Each of the four camphane-2,3-diols (Angyal and Young 1959) (0·3 g) was allowed to stand for 2 weeks with toluene-*p*-sulphonyl chloride (1·1 g) in anhydrous pyridine (3 ml). Crushed ice was added and the precipitated solid was crystallized from methanol. The 2-*endo*,3-*exo*-diol gave an oily product which was extracted by chloroform; evaporation of the solvent left an oil which crystallized from light petroleum (b.p. 40–60 °C). Thus were obtained: (—)-2-exo,3-exo-*ditosyloxycamphane*, m.p. 139·5–140·5 °C, $[\alpha]_D^{20}$ —21° (*c*, 1·1 in chloroform) (Found: C, 60·4; H, 6·1%. Calc. for $C_{24}H_{30}O_6S_2$: C, 60·2; H, 6·3%); the (+)-2-endo,3-endo-*isomer*, m.p. 166·5–167·5 °C, $[\alpha]_D^{20}$ +42·6° (*c*, 1·1 in chloroform) (Found: C, 60·5; H, 6·2%); the (+)-2-exo,3-endo-*isomer*, m.p. 99·5–100·5 °C (decomp.), $[\alpha]_D^{20}$ +15° (*c*, 1·2 in chloroform) (Found: C, 60·5; H, 6·2%); and the (+)-2-endo,3-exo-*isomer*, m.p. 92–93 °C (decomp.), $[\alpha]_D^{20}$ +15·3° (*c*, 1·5 in chloroform) (Found: C, 60·6; H, 6·4%). The yield was about 90% in each case.

(iv) (+)-2-endo,3-exo-*Di*-p-*nitrobenzenesulphonyloxycamphane*. (+)-Camphane-2-*endo*,3-*exo*-diol (1 g) and *p*-nitrobenzenesulphonyl chloride (3·9 g), dissolved in anhydrous pyridine (10 ml), were allowed to stand at room temperature for 8 days. Crushed ice was added and the precipitated solid material was crystallized from acetone–methanol to give needles of the *camphane diester* (1·87 g, 59%), m.p. 121 °C (decomp.), $[\alpha]_D^{20}$ +25·3° (*c*, 0·6 in chloroform) (Found: C, 48·5; H, 4·75%. Calc. for $C_{22}H_{24}O_{10}N_2S_2$: C, 48·9; H, 4·5%).

(*b*) *Reactions with Sodium Iodide.*—(i) *Cyclohexane and Cyclopentane Derivatives*. Sulphonyl compound (0·212 g of the ditosyloxycyclohexanes, 0·103 g of the ditosyloxycyclopentanes, 0·136 g of the dimethanesulphonate, and 0·243 g of the di-*p*-nitrobenzenesulphonate of *trans*-cyclohexane-1,2-diol), sodium iodide (0·75 g), and anhydrous acetone (5 ml) were heated (in a sealed tube) immersed in the vapours of boiling ethanol. After intervals, the tubes were cooled in a dry ice-ethanol mixture and opened. After warming to room temperature to redissolve the precipitated iodine, the sodium salt was collected by filtration, washed with acetone (5 ml), dried at 150 °C, and weighed. A correction was applied for the solubility of sodium toluene-*p*-sulphonate in acetone (1·2 mg/ml; 1·9 mg/ml for the *p*-nitrobenzenesulphonate). The filtrate was titrated with standard sodium thiosulphate solution. After removal of the acetone by distillation the mixture was diluted with much water and starting material recovered by filtration. The results are shown in the tables. The recovered *trans*-1,2-ditosyloxycyclohexane had m.p. 100–106 °C (after 8 hr), 98–106 °C (16 hr), 102–105 °C (32 hr); the other recovered compounds had substantially unchanged melting points.

(ii) *Camphane Derivatives*. The ditoluene-*p*-sulphonates (0·239 g) were treated as under (i) but were submerged in boiling water. The following results were obtained by the methods described under (i), the figures showing moles of NaOTs and equivs. of iodine: 2-*endo*,3-*exo*-isomer, 0·25 hr, 0·45, 0·08; 0·5 hr, 0·65, 0·10; 1 hr, 0·93, 0·17; 2 hr, 1·39, 0·24; 2-*exo*,3-*exo*-isomer: 4·25 hr, 0·37, 0·09; 8·5 hr, 0·65, 0·18; 17 hr, 0·83, 0·37; 34 hr, 0·97, 0·59; 2-*exo*,3-

endo-isomer: 0·5 hr, 1·06, 0·56. The 2-*endo*,3-*endo*-isomer was recovered in 97% yield after 94 hr at 100 °C. For the di-*p*-nitrobenzenesulphonate of camphane-2-*endo*,3-*exo*-diol (0·2705 g) at 78 °C: 1 hr, 1·58, 0·53.

(*c*) *Isolation of* cis-2-*Iodocyclohexyl Toluene*-p-*sulphonate* (III).—*trans*-1,2-Ditosyloxycyclohexane (3 g), sodium iodide (11·25 g), and anhydrous acetone (75 ml) were heated in a sealed tube at 78 °C for 28 hr. The precipitated sodium toluene-*p*-sulphonate (1·06 g, 39%) was collected by filtration; iodine was titrated (19%), and acetone removed by distillation (the distillate readily decolorized bromine in chloroform). The remaining oil solidified and was crystallized from methanol to give starting material, m.p. 108–109 °C (1·91 g, 63%). The mother liquors were evaporated and the residue crystallized from light petroleum (60–80 °C) to give prisms of the *iodo compound* (0·28 g, 10·5%), m.p. 89·5–90·5 °C. Recrystallization from methanol raised the m.p. to 90–91 °C (Found: C, 41·2; H, 4·5; I, 33·0%. Calc. for $C_{13}H_{17}O_3SI$: C, 41·1; H, 4·5; I, 33·4%).

This compound (0·063 g) was heated with sodium iodide (0·25 g) and anhydrous acetone (1·6 ml) at 78 °C. Results, obtained as under (*b*), were: 3 hr, 0·33, 0·51; and 6 hr, 0·54, 0·94.

IV. Acknowledgments

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V. References

Alt, G. H., and Barton, D. H. R. (1954).—*J. Chem. Soc.* **1954**: 4284.
Angyal, S. J., and Gilham, P. T. (1958).—*J. Chem. Soc.* **1958**: 375.
Angyal, S. J., and Young, R. J. (1959).—*J. Amer. Chem. Soc.* **81**: 5467.
Barton, D. H. R., and Rosenfelder, W. J. (1951).—*J. Chem. Soc.* **1951**: 1048.
Bladon, P., and Owen, L. N. (1950).—*J. Chem. Soc.* **1950**: 598.
Brown, H. C., Fletcher, R. S., and Johannsen, R. B. (1951).—*J. Amer. Chem. Soc.* **73**: 212.
Clarke, M. F., and Owen, L. N. (1949).—*J. Chem. Soc.* **1949**: 315.
Criegee, R., and Stanger, H. (1936).—*Ber. dtsch. chem. Ges.* B **69**: 2753.
Foster, A. B., and Overend, W. G. (1951*a*).—*J. Chem. Soc.* **1951**: 680.
Foster, A. B., and Overend, W. G. (1951*b*).—*J. Chem. Soc.* **1951**: 3452.
Foster, A. B., Overend, W. G., Stacey, M., and Wiggins, L. F. (1949).—*J. Chem. Soc.* **1949**: 2542.
Gilham, P. T. (1956).—Ph.D. Thesis, N.S.W. University of Technology.
Ingold, C. K. (1953).—"Structure and Mechanism in Organic Chemistry." p. 422. (G. Bell & Sons: London.)
James, D. R., Rees, R. W., and Shoppee, C. W. (1955).—*J. Chem. Soc.* **1955**: 1370.
Linstead, R. P., Owen, L. N., and Webb, R. F. (1953).—*J. Chem. Soc.* **1953**: 1218.
Newth, F. H. (1956).—*J. Chem. Soc.* **1956**: 471.
Owen, L. N., and Smith, P. N. (1952).—*J. Chem. Soc.* **1952**: 4026.
Slates, H. L., and Wendler, N. L. (1955).—*Chem. & Ind.* **1955**: 167.
Slates, H. L., and Wendler, N. L. (1956).—*J. Amer. Chem. Soc.* **78**: 3749.
Tipson, R. S. (1953).—*Advanc. Carbohyd. Chem.* **8**: 201.
Tipson, R. S., and Cretcher, L. H. (1943).—*J. Org. Chem.* **8**: 95.
Winstein, S., Grunwald, E., and Ingraham, L. L. (1948).—*J. Amer. Chem. Soc.* **70**: 821.