Solvolytic Fragmentation Studies on 7-Substituted *exo*- and *endo*-5,6-(*o*-Phenylene)-2-norbornyl Toluene-*p*-sulphonates

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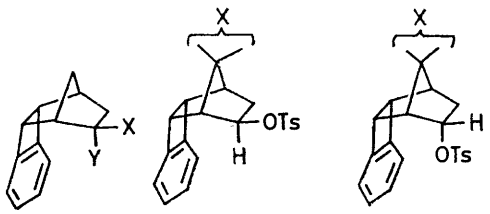
Toluene-*p*-sulphonates (3)—(12) have been prepared and their rates and products of solvolysis in acetic acid studied. Enhanced solvolysis rates were found for (4) and (6) which, together with exclusive formation of fragmentation product, are explained in terms of a synchronous fragmentation process. The effect of non-bonded interactions on the alignment of participating bonds has been suggested to be important. Neighbouring-group participation has been demonstrated in reaction of (10) but free rotation of the C–OMe bond makes a synchronous process unimportant. Although some fragmentation product is formed in solvolysis of (3), (5), (9), (11), and (12), the presence of other products, and absence of enhanced solvolysis rates establishes the mechanism as ionisation to a carbonium ion, followed by fragmentation mainly due to relief of strain. No fragmentation was observed in solvolysis of (7) and (8) but interesting rearrangements involving the carbon–sulphur bond are observed.

ALTHOUGH the importance of σ bond participation in the ionisation process could not be assessed, C(1)–C(6) bond migration was observed in solvolysis of *endo*-5,6-(*o*-phenylene)-*exo*-2-norbornyl toluene-*p*-sulphonate (1).[1] Ion-pair return led to rapid accumulation of *exo*-5,6-(*o*-phenylene)-*exo*-2-norbornyl toluene-*p*-sulphonate (13) in the reaction mixture and the rate of solvolysis fell rapidly to that obtained for this latter derivative after *ca.* 15% reaction. To obtain information on possible steric or electronic origins for the rearrangement, studies have been made on the solvolysis of derivatives with an isopropylidene [2] or carbonyl group [3] at the bridge position. Compound (4) was found to undergo a fragmentation and the rate of reaction was markedly accelerated compared to (2). In contrast, although some fragmentation was observed in solvolysis of (3), no rate acceleration was observed. We now report studies on a number of similar systems with acetal substituents at the bridge positions (5)—(12) which have yielded substantial insight into the nature of fragmentation reactions of these derivatives. The preferred stereochemistry for a synchronous fragmentation reaction involving *anti*-periplanar arrangement of the lone-electron-pair on the γ-substituent and the carbon-leaving group bond to the fragmenting C(β)–C(γ) bond has previously been clearly established.[4] In the present studies it has been shown that non-bonded interactions within the molecule can have a marked influence in affecting the alignment of participating bonds in the fragmentation process.

Synthesis.—The essential synthetic steps are illustrated in Scheme 1 following the addition of fulvene to benzocyclobutene prepared from the di-iodo-precursor; [2] acetalisation of (3)-OAc and (4)-OAc was by standard procedures, followed by reduction with lithium aluminium hydride to yield the corresponding alcohols.

A more complex route was required for (11) and (12), summarised in Scheme 2. Treatment of the olefin prepared from cyclopentadiene and benzocyclobutene [5] with *m*-chloroperbenzoic acid gave the epoxide, n.m.r. (CCl_4), τ 2·97 (4, m, aromatic), 7·37 (2, m, α to epoxide), 6·30 (2, m, benzylic), 7·33 (2, s, bridgehead), and 8·27 and 8·80 (2, d, *J* 16·5 Hz, bridge). The position of the signal for protons α to an epoxide normally occurs at *ca.* τ 6·9, so that, in the present case, shielding of the *endo*-protons by the benzene ring indicates *exo*-configuration of the epoxide. Opening of the epoxide with 50% aqueous hydrobromic acid yielded mainly a mixture of the *exo*- and *endo*-bromo-alcohols (Scheme 3) which could not be separated by chromatography. Although the stereochemistry of these compounds was not confirmed by n.m.r. spectroscopy, the *exo*-benzo-stereochemistry was



(1) X = OTs, Y = H

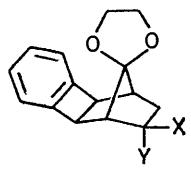
(2) X = H, Y = OTs

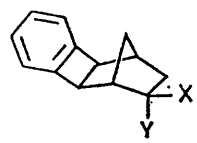
(3) X = O = (4)

(5) X = O O = (6)

(7) X = S S = (8)

(9) X = MeO OMe = (10)





(11) X = OTs, Y = H

(12) X = H, Y = OTs

(13) X = OTs, Y = H

(14) X = H, Y = OTs

[1] R. Baker and T. J. Mason, *J.C.S. Perkin II*, 1972, 18; R. Baker and J. Hudec, *Chem. Comm.*, 1967, 929.

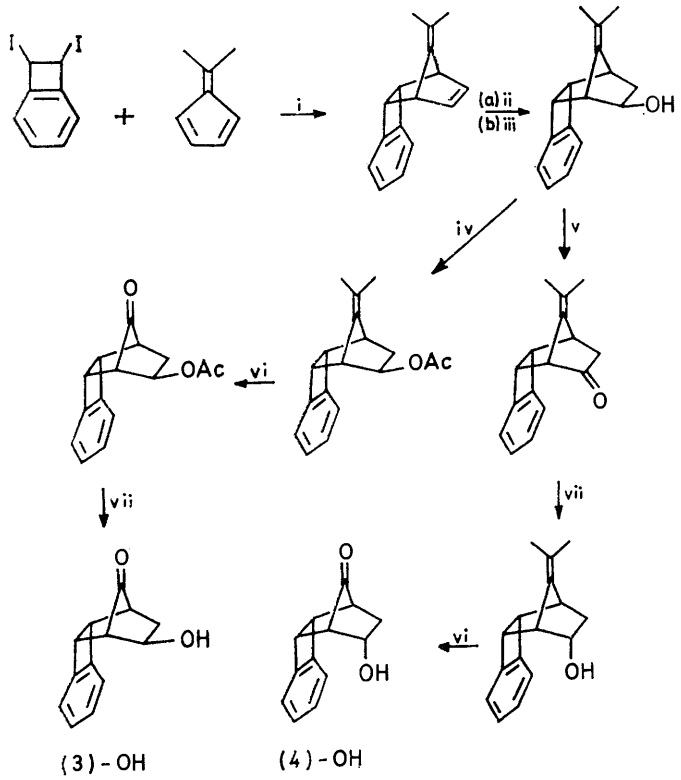
[2] R. Baker and J. C. Salter, *J. Chem. Soc.*, 1971, 757.

[3] R. Baker, T. J. Mason, and J. C. Salter, *Chem. Comm.*, 1970, 509.

[4] C. A. Grob, *Angew. Chem. Internat. Edn.*, 1969, **8**, 535; C. A. Grob and P. W. Scheiss, *ibid.*, 1967, **6**, 1; C. A. Grob, R. M. Hoegerle, and M. Ohta, *Helv. Chim. Acta*, 1962, **45**, 1823; C. A. Grob and W. Schwarz, *ibid.*, 1964, **47**, 1870; A. T. Bottini C. A. Grob, E. Schumacher, and J. Zergenyi, *ibid.*, 1966, **49**, 2516; U. Burckhardt, C. A. Grob, and H. R. Kiefer, *ibid.*, 1967, **50**, 231; R. D'Arcy, C. A. Grob, T. Kaffenberger, and V. Krasnobajew, *ibid.*, 1966, **49**, 185; C. A. Grob, H. R. Kiefer, H. J. Lutz, and H. J. Wilkens, *ibid.*, 1967, **50**, 416; C. A. Grob, K. Kostka, and F. Kuhnen, *ibid.*, 1970, **53**, 608.

[5] R. Baker and T. J. Mason, *J. Chem. Soc.*, 1970, 596.

assigned on the basis of the structure of the dehydrobrominated product, n.m.r. ($CDCl_3$), τ 2·87 (4, m, aromatic), 3·78 (2, s, vinylic), 6·54 (1, s, α-OH), 6·83 (2, s, benzylic), 7·18 (2, s, bridgehead), and 8·03 (1, m, OH). In particular the signal for the benzylic protons is strong



SCHEME 1 Reagents: i, Zn–EtOH; ii, B_2H_6; iii, H_2O_2–OH^-; iv, Ac_2O–pyridine; v, CrO_3–Et_2O; vi, O_3–MeOH; vii, $NaBH_4$–MeOH

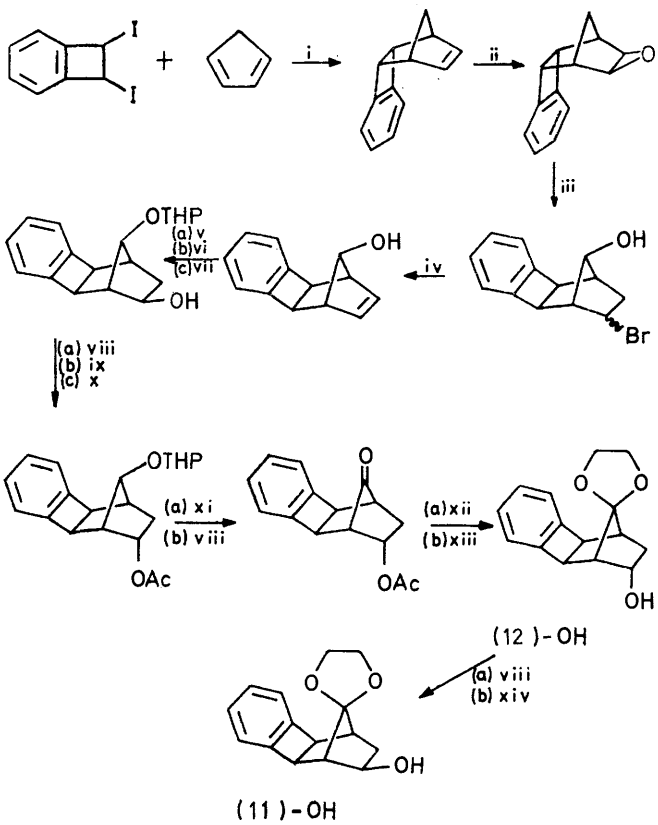
evidence for their *endo*-stereochemistry.[5] Hydroboration of the tetrahydropyranyl ether derivative yielded a mixture of *exo*- and *endo*-alcohols in the ratio 3 : 1 which were readily separated by chromatography. Oxidation of the *exo*-alcohol with chromic acid, followed by reduction with aluminium isopropoxide in isopropyl alcohol gave >99% *endo*-alcohol. Sodium borohydride reduction of the ketone obtained by oxidation of (12)-OH yielded a mixture of 95% of (11)-OH and 5% of (12)-OH; (11)-OH was obtained pure by crystallisation.

TABLE 1

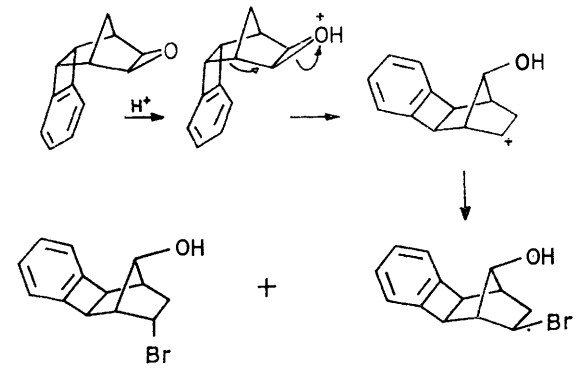
Rates of acetolysis of toluene-*p*-sulphonates [a]

Toluene-*p*-sulphonate	25°	10^7k/s^{-1} 75°	100°	ΔH kcal.mol^{-1}	ΔS e.u.
(*1*)		2675 [d]		24·0 [d]	−10·6 [d]
(*2*)		1·20	25·0	30·6	−2·5
(*3*)		22·3	360	29·0	−1·7
(*4*)		198	2550	26·8	−3·5
(*5*)		24·5	311 [c]	25·4	−11·4
(*6*)		270	2225 [c]	20·8	−19·9
(*7*)		55·4	816	26·0	−5·5
(*8*)		1·24	24·2	29·7	−5·0
(*9*)		6·3 [c]	111	28·9	−4·4
(*10*)		2·3 [c]	48·5 [c]	30·6	−0·9
(*11*)		26·4 [c]	513	30·1	+2·2
(*12*)		8·23	175	30·8	+1·9
(*13*)		79·5 [d]	1429 [d]	29·1	+1·5
(*14*)		45·8 [d]	683 [d]	27·1	−5·2
endo-Norbornyl	0·84 [e]	509 [e]		25·8	−2·5

[a] Average of two runs, accuracy ±2%. [b] Calculated using an infinity titre (theoretical). [c] These values are initial rate constants calculated by taking a tangent to the graph of log ($T_\infty - T_t$) *vs.* time at zero time (Figures 3 to 8). [d] Ref. 1. [e] P. von R. Schleyer, M. M. Donaldson, and W. E. Watts, *J. Amer. Chem. Soc.*, 1965, **87**, 375.



SCHEME 2 *Reagents*: i, Zn–EtOH; ii, *m*-$ClC_6H_4CO_3H$–CCl_4; iii, HBr; iv, Bu^tOK–Me_2SO; v, dihydropyran–PhH; vi, B_2H_6–diglyme; vii, H_2O_2–OH^-; viii, CrO_3–pyridine; ix, Pr^iOH–$Al(Pr^iO)_3$; x, Ac_2O–pyridine; xi, H^+–H_2O; xii, ethanediol–xylene–H^+; xiii, $LiAlH_4$–Et_2O; xiv, $NaBH_4$–MeOH



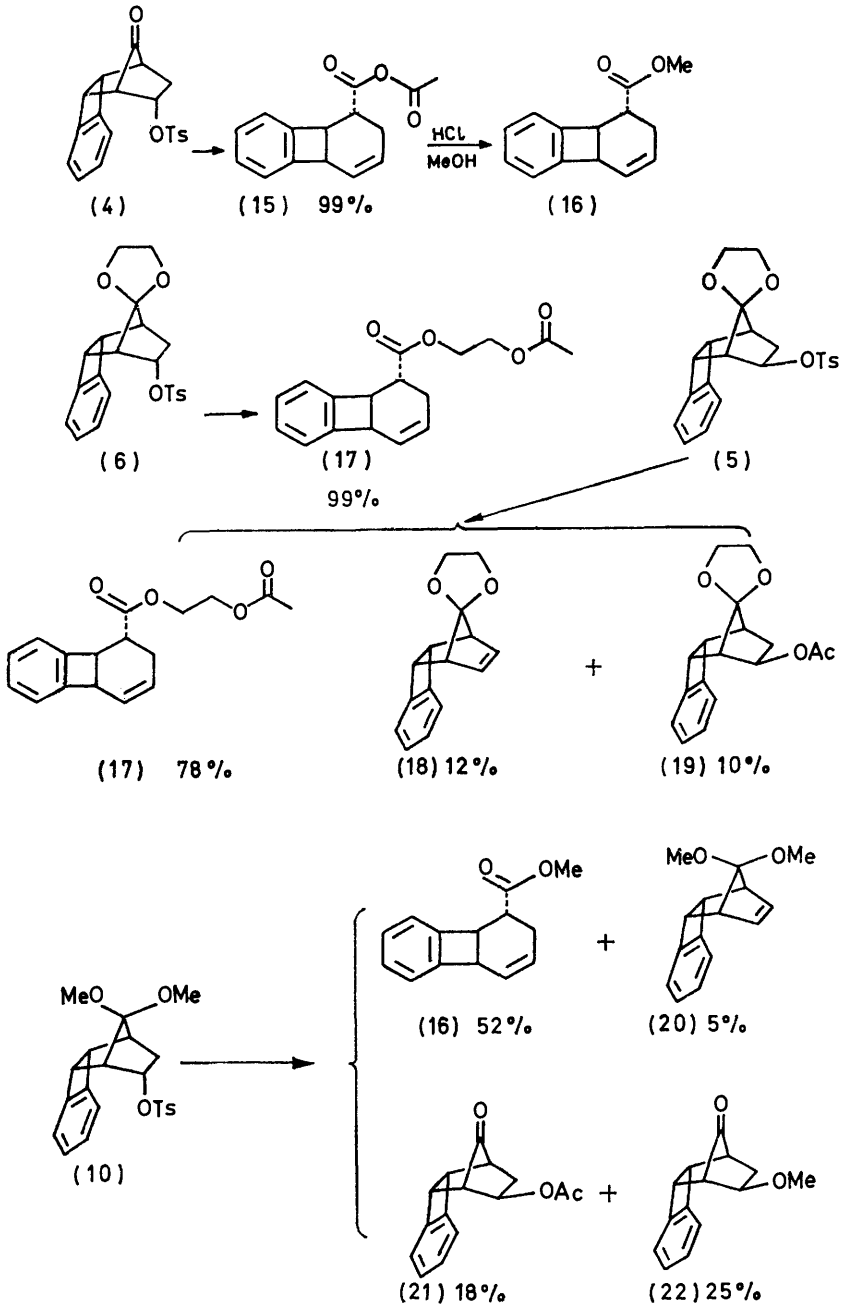
SCHEME 3

RESULTS

Acetolysis rate constants are summarised in Table 1. Product studies were carried out in anhydrous acetic acid buffered with a ten-fold excess of sodium acetate. Schemes

4a–c provide a summary of the solvolysis products which were analysed by g.l.c. and structures assigned by consideration of their n.m.r. and i.r. spectra.

Compound (4) gave exclusive formation of the anhydride (15) which was identified as the corresponding methyl ester methyl). From mechanistic considerations the diester group of (17) is assigned *trans*-stereochemistry to the benzo-group. (17) was also the predominant product in acetolysis of (5); in addition the unrearranged olefin (18), n.m.r. ($CDCl_3$), τ 2·92 (2, q, *J* 3 Hz, aromatic), 3·13 (2, q, *J* 3 Hz

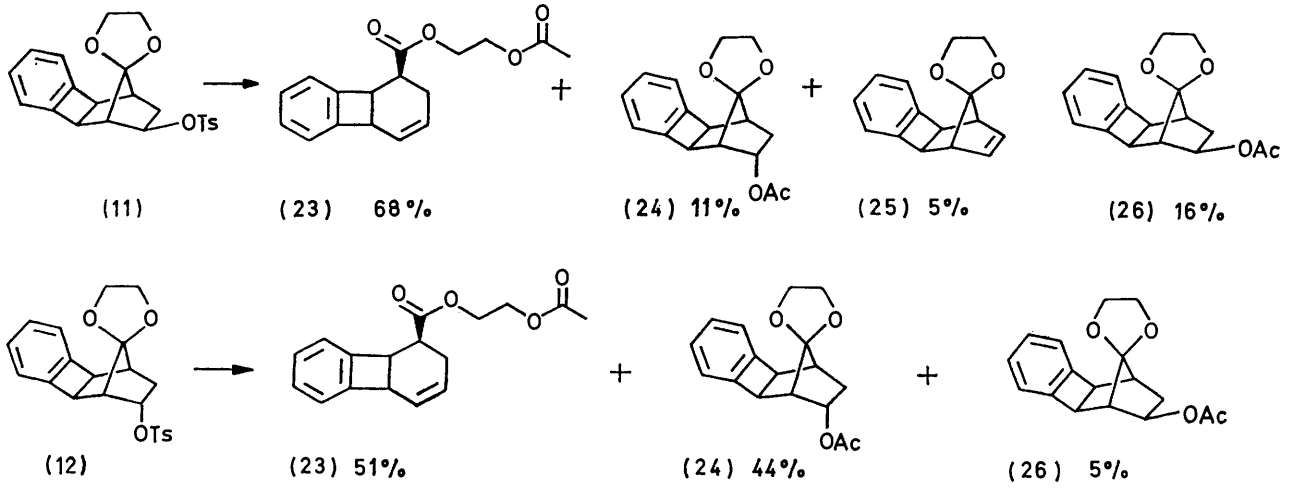


SCHEME 4a

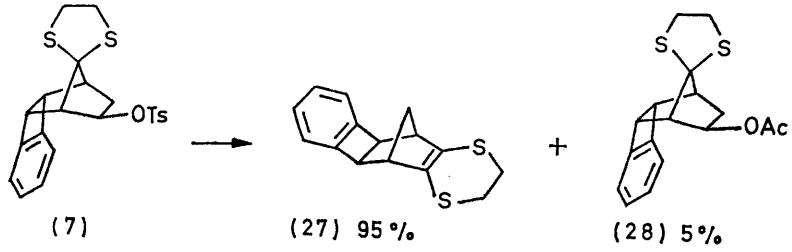
(16), n.m.r. ($CDCl_3$), τ 2·85 (4, m, aromatic), 3·89 (1, m, vinyl), 5·96 (2, m, benzylic), 6·28 (3, s, methyl), 7·13 (1, m, allylic), and 7·77 (1, m, α-ester). The sole product from the solvolysis of (6) was the diester (17), n.m.r. ($CDCl_3$); τ 2·83 (4, m, benzylic), 3·95 (1, q, *J* 6 Hz, vinylic), 4·20 (1, q, *J* 6 Hz, vinylic), 5·63 (2, s, methylene), 5·68 (2, s, methylene), 7·29 (1, m, allylic), 7·80 (1, m, α-ester), and 7·96 (3, s, aromatic), 4·28 (2, t, *J* 2 Hz, vinylic), 6·14 (6, m, acetal and benzylic H), and 7·17 (2, m, bridgehead), and *exo*-acetate (19) were formed. Solvolysis of (10) yielded the methyl ester (16) as the main product; in addition to a minor amount (5%) of unrearranged olefin, two products were formed possessing a 9-keto-function and arising from OMe participation. The predominant product from (11) was (23),

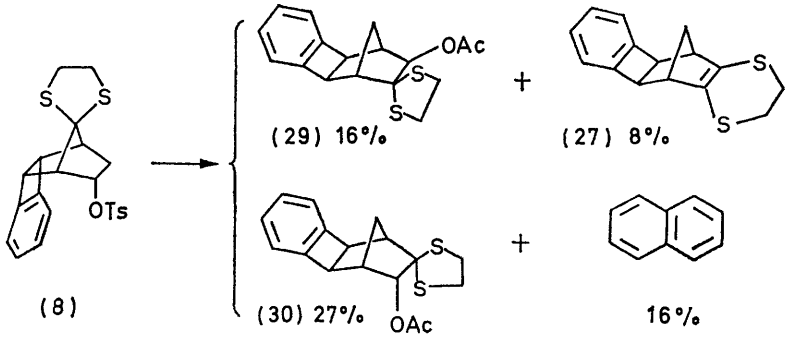
identified as isomeric with (17), but with a *cis*-configuration of diester and benzo-group; (23) was also obtained from solvolysis of (12).

The thioacetal (7) gave rise predominantly to the rearranged olefin (27), n.m.r. ($CDCl_3$), τ 2·96 (4, m, aromatic), 6·58 (2, s, benzylic), 6·95 (4, 2, α-S), 7·28 (2, t, *J* 3 Hz, bridgehead), and 8·87 (2, t, *J* 11 Hz, bridge). The *exo*-benzo-stereochemistry was assigned on the basis of the 7·25 (2, m, α-sulphur), 7·67 (2, m, bridgehead), 8·00 (3, s, methyl), 8·42 (1, m, bridge), and 8·90 (1, m, bridge). The n.m.r. spectra of (29) and (30) are substantially different from those of the acetate (28) and its epimer on three accounts: first the signal for the proton α to acetate is much higher in (29) and (30), second the benzylic protons, 5-H and 7-H absorb at different positions which suggests that they have *endo*-stereochemistry, and third the protons



SCHEME 4b





SCHEME 4c

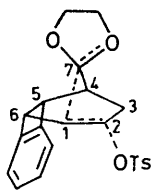
absorption for the benzylic protons, since these occur at τ 0·5 higher field than that for the equivalent protons of the *endo*-benzo-derivatives.[5] Four compounds were obtained from solvolysis of (8); naphthalene, *exo*-benzo-olefin (27), (29), n.m.r. ($CDCl_3$), τ 2·90 (4, m, aromatic), 6·25 (2, m, benzylic and α-acetate), 6·42 (1, m, benzylic), 6·83 (2, m, α-sulphur), 7·25 (2, m, α-sulphur), 7·67 (2, m, bridgehead), 8·00 (3, s, methyl), 8·42 (1, m, bridge), 8·75 (1, m, bridge), and (30), n.m.r. ($CDCl_3$), τ 2·90 (4, m, aromatic), 6·43 (2, m, benzylic and α-acetate), 6·75 (1, d, *J* 22 Hz), 6·83 (2, m, α-sulphur), α to sulphur on the acetal do not absorb as a singlet. The fact that these acetates thermally decompose to (27) (as seen by g.l.c. at 220°) suggests that they are structurally similar to (27). A large amount of deshielding for both benzylic protons of (30) indicates the *endo*-stereochemistry of the acetate group.

DISCUSSION

The acetolyses of (3) and (5) yield 85% and 78% respectively of a product due to fragmentation together

with some elimination and substitution products. These derivatives solvolyse *ca.* 10 times more slowly than their corresponding *endo*-derivatives (4) and (6) which both undergo exclusive fragmentation. Whereas (3) and (5) undergo acetolysis about 120 times slower than (1) at 75°, (4) and (6) solvolyse 165 and 220 times faster respectively than the corresponding unsubstituted derivative (2). Clearly (3) and (5) are undergoing fragmentation subsequent to initial ionisation whereas (4) and (6) are undergoing a synchronous fragmentation process providing anchimeric assistance to ionisation.

endo-*Toluene*-p-*sulphonates*.—Although the rate enhancement in solvolysis of (6) and (2) is 220 at 75°, a large rate difference is found if the rate retarding inductive effect of the 9-acetal substituent is taken into account. A factor of 7 can be utilised for this latter effect from work of Gassman [6] which would lead to an estimate of $1{\cdot}3 \times 10^3$ as the true rate difference in solvolysis of (6) and (2). The extremely slow rate of solvolysis of (2) has been previously explained [1] in terms of steric inhibition to ionisation; ionisation of the C–O bond is unfavourable due to increasing steric repulsion in the transition state between the leaving group and the *endo*-5,6-substituent (31). In the fragmentation process for solvolysis of (6), however, the leaving group departs along a different reaction path (32). Development of a π-bond between C-1 and C-2 results in gradual flattening of the ring and the departing toluene-*p*-sulphonate group moves away from the bulky *endo*-benzo-substituent with a consequent reduction in the non-bonded interaction between these substituents. Whilst this effect certainly contributes to the difference in solvolysis rates of (6) and (2), the frangomeric effect (acceleration in the rate of fragmentation) in solvolysis of (6) is apparent from comparison of the rates of (6), and (10) which differ by a factor of over 100.



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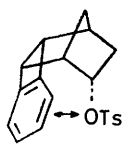

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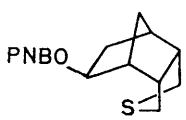

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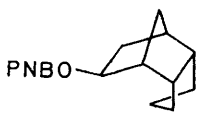


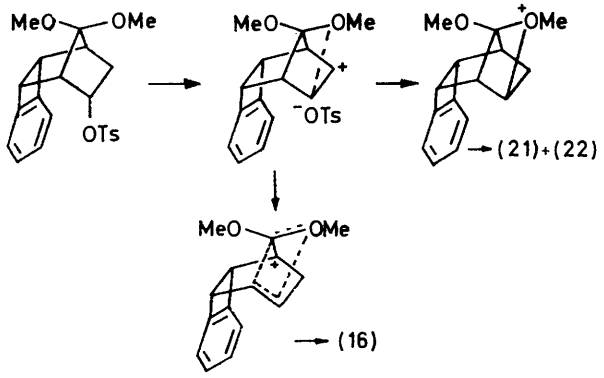
(34)

Grob has clearly shown that correct orbital alignment is required for enhanced rates in fragmentation reactions.[4] A concerted Grob fragmentation requires that the lone-pair orbital lobe on the hetero-atom on C(γ), the intervening C(β)–C(γ) bond and the bond to the leaving group must be aligned so that maximum orbital overlap can occur in the transition state.[4] This ideal situation does not apply to either (6) or (10) but different behaviour might originate from two reasons. Firstly, rotation of the C–O bond must occur in (10) so that although there is a lone-pair orbital which can adopt the required antiperiplanar geometry for fragmentation, this conformation has only a transitory existence. This effect is also found in solvolysis of 3-chloro-*NN*-trimethylbutylamine [7] which reacts by a two-step carbonium ion process even though it is capable of adopting a conformation suitable for a synchronous fragmentation. Secondly since the oxygen atoms in (6) are held in a rigid position in the acetal group the orbital alignment of the lone pair with the other bonds might be more favourable for fragmentation.

A marked difference in rates of solvolysis is found between (6) and (8); product studies confirm the absence of fragmentation in solvolysis of the latter derivative. Compound (8) is, in fact, comparable in reactivity to (2), whereas, due to the inductive effect of the thioacetal a slower rate would be anticipated. A likely explanation is that a lone-pair orbital of the sulphur atom *syn* to the toluene-*p*-sulphonate group is able to provide some anchimeric assistance to ionisation (see Scheme 13). Sulphur can be extremely effective as a neighbouring group; (33) reacts 752 times faster than the homomorphous derivative (34).[8] For (8), however, only a relatively minor amount of participation can be expected since the orbital lobe of the sulphur atom is not directed to the developing carbonium ion in the ideal way. The extent of this participation is clearly just sufficient to balance out the rate retarding inductive influence of the sulphur atoms. On the basis of this result neighbouring-group participation can be excluded as an important contributing factor in the solvolysis of (8) since, due to the relative extension of its lone pair orbitals, sulphur is more important at providing neighbouring-group participation than oxygen; β-chloroethyl sulphide solvolyses $1{\cdot}5 \times 10^4$ times faster than β-chloroethyl ether in aqueous dioxan at 100°.[9] The difference in the solvolytic behaviour of (6) and (10) is confirmed by the products from reaction of the latter. Some product resulting from fragmentation (16) (52%) is obtained, accompanied by (21) and (22) as a consequence of OMe participation (Scheme 5). Again on the basis of an inductive effect (10) would react slower than (2) so that it is evidence that this rate retarding effect is counteracted by a small neighbouring-group effect or as a result of some fragmentation with acceleration. No fragmentation was observed in acetolysis of 7-dimethoxynorbornyl *endo*-toluene-*p*-sulphonate in which ketonic products were formed exclusively (Scheme 6).[10] The rate of solvolysis was 35 times slower than that of *endo*-norbornyl toluene-

[6] P. G. Gassman and J. C. Macmillan, *J. Amer. Chem. Soc.*, 1969, **91**, 5527.
[7] C. A. Grob and F. O. Ostermayer, *Helv. Chim. Acta* **1962**, **5**, 1119.
[8] R. F. Gratz and P. Wilder, *Chem. Comm.*, 1970, 1449.
[9] H. Bohme and K. Sell, *Chem. Ber.*, 1948, **81**, 123.
[10] P. G. Gassman and J. L. Marshall, *Tetrahedron Letters*, 1968, 2429.

p-sulphonate indicating that participation occurs after the ionisation step.



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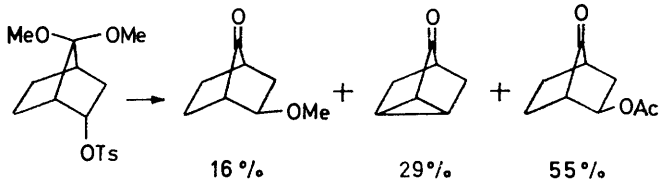

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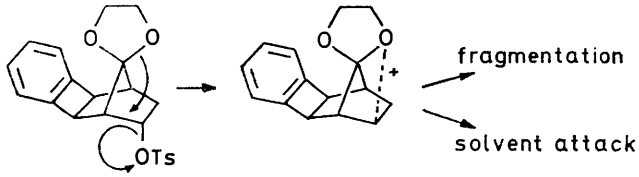
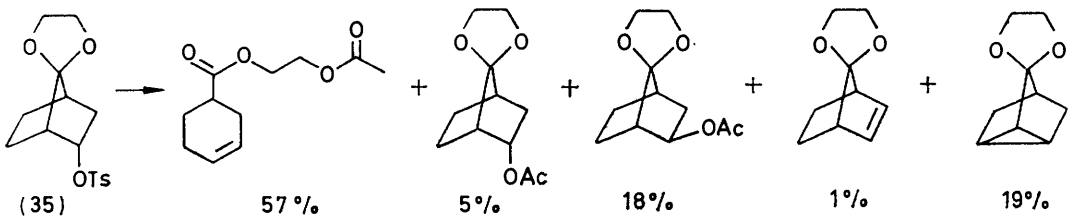


SCHEME 7

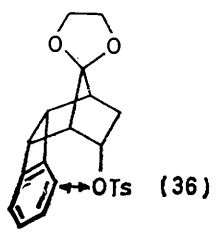
More information was obtained on the origin of the rate acceleration in solvolysis of (6) from the reactivity of (12). The rate of solvolysis was $26{\cdot}4 \times 10^{-7}$ s^{-1} compared to $45{\cdot}8 \times 10^{-7}$ s^{-1} for that of (14). It is apparent that no marked rate accelerating factor exists but both fragmentation product [(21) 51%] and that resulting from neighbouring-group participation [(24) 44%] are formed (Scheme 7). The acetolysis of (12) shows an interesting change in the product distribution from that of its norbornyl counterpart [(35) Scheme 8].[6] Unrearranged *endo*-acetate (24) accounts for 44% of the products from (12), whilst *exo*-acetate (26) is only produced in 5% yield. This is in marked contrast to the proportion of acetates arising from (35) in which over three times more *exo*- than *endo*-acetate is produced. Since solvent attack on the initially formed ion pairs from (12) and (35) would be subject to the same steric influences in both cases it appears that the former possesses a factor which enhances *endo*-attack by solvent. This may be due to a closer approach of the acetal oxygen atom in (12) due to a displacement from the *exo*-benzo-group to relieve non-bonded interactions.

A comparison of the solvolysis rates of the acetal substituted *endo*-toluene-*p*-sulphonates can then be made. Only (6) shows a marked rate acceleration over its comparable non-acetal substituted analogue. It is apparent that the *endo*-5,6-substituent is partially responsible but the explanation cannot lie simply in the possibility of following a different reaction path compared to the solvolysis of (2). We suggest an explanation based on a more favoured alignment of the bond orbitals in the fragmentation of (6) brought about by non-bonded interactions between the C–OTs bond and the *endo*-5,6-substituent (36). A similar explanation has been previously suggested for enhanced double-bond participation in solvolysis of the 7-isopropylidene derivative of (2).[2]

In general, this type of effect may be more generally important. Steric inhibition to ionisation, observed in solvolysis of (2),[1] and other systems,[11] could be partially the result of the difficulty of collinear approach of solvent from the rear as a result of the modified direction of the reaction co-ordinate in ionisation due to increasing non-bonded interactions [see (31)]. The achievement of the most effective solvation of the vacant *p* orbital is then only possible at the expense of increasing non-bonded interactions between the methylene bridge and the solvent.



SCHEME 8



[11] H. C. Brown, ' The Transition State,' *Chem. Soc. Special Publ.*, No. 6, 1962; H. C. Brown, *Chem. in Brit.*, 1966, **2**, 199; H. C. Brown, I. Rothberg, P. von R. Scheyler, M. M. Donaldson, and J. J. Harper, *Proc. Nat. Head. Sci., U.S.A.*, 1966, **56**, 1653; H. C. Brown and W. J. Hammar, *J. Amer. Chem. Soc.*, 1967, **89**, 6378; H. C. Brown, W. J. Hammar, J. H. Kawakami, I. Rothberg, and D. L. Vander Jagt, *ibid.*, 1967, **89**, 6381; H. C. Brown, I. Rothberg, and D. L. Vander Jagt, *ibid.*, p. 6380; H. C. Brown and D. L. Vander Jagt, *ibid.*, 1969, **91**, 6850.

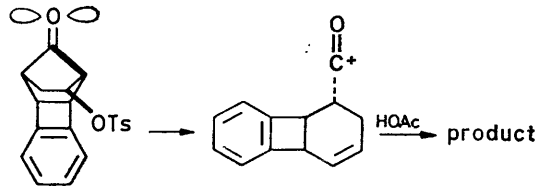
Solvolysis of these systems demonstrates that synchronous fragmentation involving oxygen as the donor substituent is subject to strict requirements. In solvolysis of (6), favourable stereoelectronic alignment together with potential relief of non-bonded interactions results in substantial frangomeric acceleration. For the dimethoxy-acetal (10) the rotational freedom of the methoxy-substituent is responsible for the absence of frangomeric acceleration although a small amount of rate enhancement over the corresponding unsubstituted compound is probably a result of methoxy-neighbouring-group participation.

exo-*Toluene*-p-*sulphonates*.—A rate retardation is found in solvolysis of (3), (5), (9), and (11) compared to the corresponding unsubstituted derivatives due to inductive withdrawal of the 7-substituent. Although fragmentation occurs, this process is clearly subsequent to ionisation. Formation of a number of other products is typical of a two-step carbonium ion process.[4]

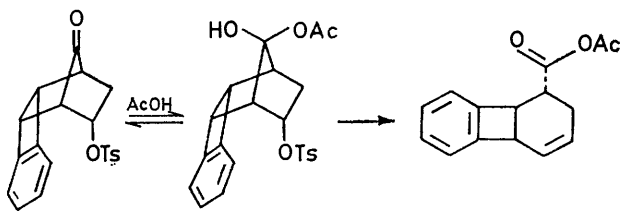
It is of interest to compare the product distribution from acetolysis of (3) and (5) with that from the corresponding norbornyl derivatives. The most striking difference is the predominance of fragmentation from (3) and (5) whereas none is obtained from acetolysis of 7-oxo-2-*exo*-norbornyl toluene-*p*-sulphonate[12] and only 15% from the 7-acetal of 2-*exo*-norbornyl toluene-*p*-sulphonate;[6] 68% fragmentation is also observed in solvolysis of (11). It is evident that fragmentation in solvolysis of (3), (5), (9), and (11) is mainly due to the additional strain imposed on the norbornyl system by substitution of the cyclobutane ring.

Solvolysis of 7-*Oxo-toluene*-p-*sulphonates* (3) *and* (4).—Acetolysis of (4) is very similar to that of (6); the anhydride (17) is formed exclusively and at 75° the rate enhancement over its 7-unsubstituted counterpart is 165-fold. If the electron withdrawing capacity of the bridge carbonyl function is taken into account the rate difference is even larger. The interpretation proposed for the concerted fragmentation of (6) applies equally well to (4) if it is assumed that the lone-pair of electrons on the carbonyl oxygen atom takes part in the synchronous mechanism (Scheme 9). The oxygen atom of a carbonyl group possesses two lone-pairs of electrons, one of which is in a highly *s* hybridised orbital, the other in a highly *p* hybridised orbital, orthogonal to the carbon–oxygen π bond.[13] This latter orbital is in antiperiplanar alignment with the C(1)–C(6) bond, thus providing an equally favourable fragmentation path as for solvolysis of (6).

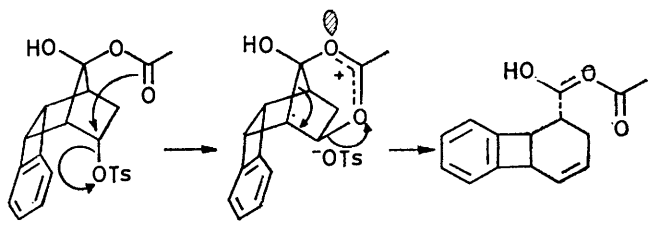
Whereas, the 7-acetal of norbornyl-*endo*-toluene-*p*-sulphonate gives rise to 57% of fragmentation product,[6] substitution products only are obtained from solvolysis of 7-oxonorbornyl *endo*-toluene-*p*-sulphonate.[12] An important difference is evident between these derivatives and the *endo*-benzo-compounds where fragmentation is observed for both the acetal and keto-derivatives. One possibility is that fragmentation from (4) may occur subsequent to attack of acetic acid at C(7) followed by fragmentation from the hemiacetal (Scheme 10). Gassman concluded that hemiacetal formation did not take place in solvolysis of the norbornyl derivatives on the basis of the absence of a significant effect of solvent change from acetic acid to ethanol.[12] Although a study of the u.v. absorption of (4) in acetic acid gave no indication of hemiacetal formation it cannot be excluded as a reactive intermediate. An increased tendency to change from sp^2 at C(7) to sp^3 for (4) compared to 7-oxonorbornyl toluene-*p*-sulphonate might arise from the greater strain inherent in the former. Favoured, hemiacetal formation



SCHEME 9



SCHEME 10



SCHEME 11

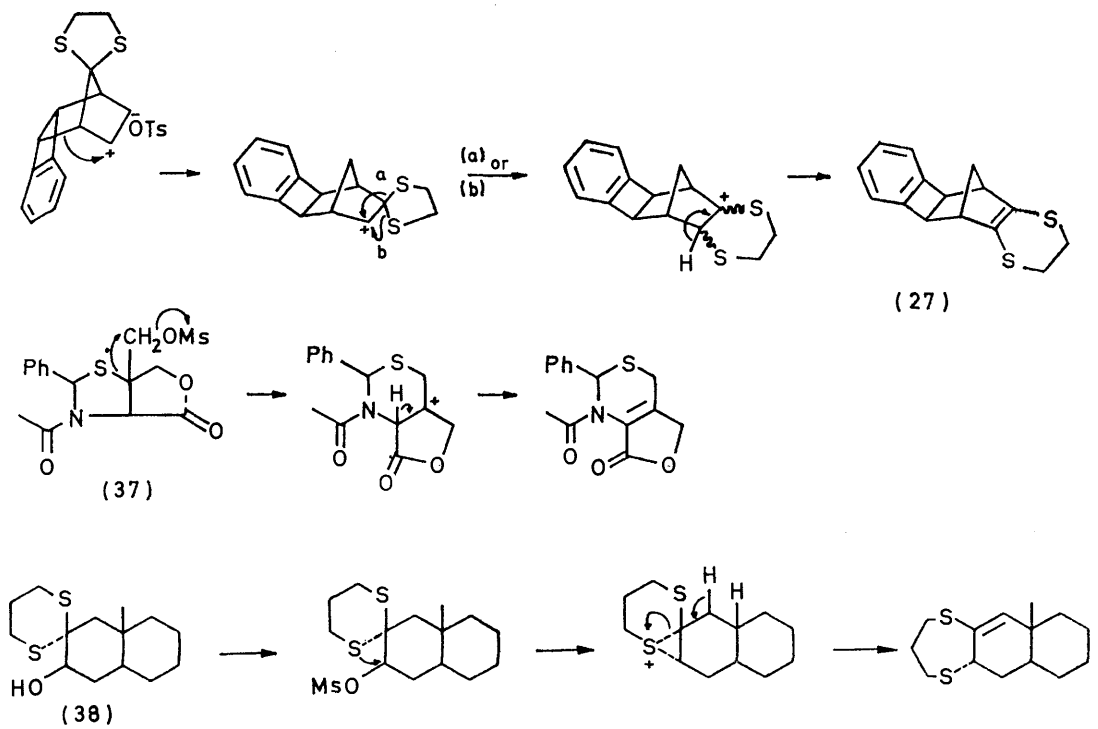
for (4) might also arise from the ability of the cyclobutane ring to stabilise a positive charge at the bridge position.[14]

If formation of a hemiacetal intermediate were to occur, it is possible that fragmentation can take place subsequent to initial nucleophilic participation by the acetoxy-group (Scheme 11). This would involve loss of rotational freedom of the acetoxy-group which would result in favourable geometrical orientation for a fragmentation process.

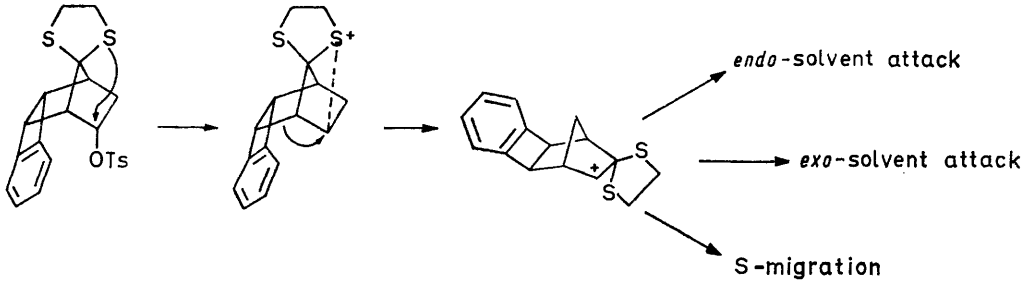
Solvolysis of the Thioacetal Toluene-p-*sulphonates* (7) *and* (8).—In complete contrast to bridge oxygenated systems neither of the 9-thioacetal derivatives (7) and (8) yield any product arising from fragmentation. Although the *exo*-toluene-*p*-sulphonate (7) undergoes acetolysis 50 times more slowly at 75° than (1), due partly to the inductive effect of the sulphur atom, C(1)–C(6) bond

[12] P. G. Gassman and J. C. Macmillan, *J. Amer. Chem. Soc.*, 1966, **88**, 2822.
[13] D. J. Pasto, *J. Amer. Chem. Soc.*, 1965, **87**, 1515.
[14] A. Diaz and S. Winstein, *J. Amer. Chem. Soc.*, 1970, **92**, 4452; M. A. Battiste and J. W. Nebzydoski, *ibid.*, p. 4450.

migration accounts for 95% of the product, comparable with 90% from (1). The major product from acetolysis of (7) is olefin (27) resulting from 1,2-sulphur shift in the intermediate carbonium ion, followed by elimination (Scheme 12). A similar sulphur shift has been reported [15] for the solvolysis of the methanesulphonate (37) in dioxan. A leaving group β to a thioacetal has also only partially effective since the orbital lobe of the sulphur atom is unable to be directed towards the developing carbonium ion in the most favourable way. The extent of this participation is clearly just sufficient to balance out the rate-retarding influence of the sulphur atoms and to exclude any *exo*-solvent attack. Normally such a stabilised intermediate would undergo solvent



SCHEME 12



SCHEME 13

been shown to be extremely labile since, on treatment of alcohol (38) with methanesulphonyl chloride at 0° for 2 h, the product isolated was that arising from a sulphur shift in the initially formed methanesulphonate.[16]

Although C(1)–C(6) bond migration is occurring in solvolysis of (7) there is a significant difference in product distribution compared to solvolysis of (8). On the basis of the inductive effect of the sulphur atoms a rate retardation would be anticipated for (8) compared with (2). In fact the rates are almost identical which suggests that there is some measure of assistance to ionisation in solvolysis of (8). A small amount of neighbouring-group participation is implicated (Scheme 13) but this can be attack from the side opposite the neighbouring group, but the presence of the bulky *endo*-benzo-substituent precludes this mode of attack. Instead, the C(1)–C(6) bond is able to provide rear-side attack on the stabilised carbonium ion to yield the rearranged carbonium ion which can be attacked by solvent to give *exo*- or *endo*-acetate or undergo sulphur migration followed by elimination. Absence of fragmentation in the solvolysis is due to the decrease in ability of the sulphur atom to

[15] G. Stork and H. T. Cheung, *J. Amer. Chem. Soc.*, 1965, **87**, 3783; J. A. Marshall and H. Roebke, *J. Org. Chem.*, 1969, **34**, 4188.

[16] S. Oae, W. Tagaki, and A. Ohno, *Tetrahedron*, 1964, 417.

donate an electron pair to an adjacent electropositive carbon atom compared to an oxygen atom. This decreased electromeric effect of the sulphur atoms in the thioacetal derivatives is insufficient to promote fragmentation in these polycyclic systems even though ring cleavage of the bicyclo[2.2.1]system would result in the relief of strain energy. Differences in other reactions, such as the rapid hydrolysis of alkan-1-ynyl ethers compared to slow hydrolysis of alkan-1-ynyl thioethers, arise from a similar origin.[17]

The formation of naphthalene from (8) involves the loss of three carbon atoms in addition to loss of the acetal function. We are unable to suggest an acceptable mechanism for this process at this stage but ionic intermediates are indicated on the basis of the intense purple colour which develops in the solvolysis solution.

EXPERIMENTAL

General.—Laport Industries activated alumina type H was used for chromatography. A Pye 104 chromatograph was employed for all g.l.c. analysis [nitrogen carrier gas flow of 60 ml min^{-1} through glass columns (5 ft × 0·25 in)]; n.m.r. spectra were obtained with tetramethylsilane as internal standard and deuteriochloroform as solvent. The purification of the acetic acid and technique for kinetic studies have been previously described.[18]

Preparation of Alcohols (3)-OH *and* (4)-OH.—All steps before the ozonolysis have been described.[2] This latter procedure involved passage of ozone through a solution of the unsaturated derivative (3 g in 25 ml methanol) at −20° for 3·3 h. Water (5 ml) was added to the resulting mixture and the solution was refluxed for 40 min. Extraction chromatography on silica gel and elution with 50% ether–benzene gave (3)-OH (1·6 g), m.p. 145—147°; $\nu_{max.}$ (Nujol), 742, 754, 1010, 1047, 1084, 1112, 1228, 1327, 1760, and 3400 cm^{-1}. Similarly, (4)-OH was obtained as an oil, which although not crystallised was employed to form a crystalline toluene-*p*-sulphonate derivative.

(3)-OAc and (4)-OAc were obtained from either (3)-OH or (4)-OH or the precursors before ozonolysis by treatment with acetic anhydride in pyridine overnight. Recrystallisation from petroleum gave (3)-OAc, m.p. 106—107·5° and (4)-OAc, m.p. 106—107°.

Acetal Alcohols (5)-OH *and* (6)-OH.—(3)-OAc and (4)-OAc (2·5 g) were dissolved in benzene (20 ml) together with ethanediol (10 ml) and toluene-*p*-sulphonic acid (5 mg) and the mixture was refluxed overnight using a water separator. The mixtures were added to a well-stirred solution of sodium hydrogen carbonate and extracted with ether. Reduction with lithium aluminium hydride (500 mg) in ether (25 ml) gave (5)-OH, m.p. 78·0—79·0° (Found: C, 73·4; H, 6·35. $C_{15}H_{16}O_3$ requires C, 73·75; H, 6·6%); $\nu_{max.}$ (Nujol), 735, 740, 1008, 1048, 1230, 1330, and 3510 cm^{-1} and (6)-OH, m.p. 116—117° (Found: C, 73·7, H, 6·4); $\nu_{max.}$ (Nujol), 760, 1028, 1058, 1083, 1088, 1093, 1314, and 3510 cm^{-1}.

Thioacetal Alcohols (7)-OH *and* (8)-OH.—(3)-OAc and (4)-OAc (2 g) were set aside overnight at room temperature with ethanedithiol (5·5 ml) and boron trifluoride–ether (11 ml) in glacial acetic acid. The crystalline thioacetals were filtered off and washed with methanol and diethyl ether to yield the acetates, m.p. 163—164·5° and 146·5—148° respectively. After reduction with lithium aluminium hydride in tetrahydrofuran and crystallisation from diethyl ether (7)-OH was obtained, m.p. 141—142·5° (Found: C, 65·3; H, 5·65. $C_{15}H_{16}OS_2$ requires C, 65·2, H, 5·85%); $\nu_{max.}$ (Nujol) 740, 755, 771, 972, 1031, 1063, 1188, 1294, and 3490 cm^{-1}; and (8)-OH, m.p. 123—124·5° (Found: C, 65·4, H, 6·0); $\nu_{max.}$ (Nujol) 713, 761, 1071, 1088, 1155, 1278, and 3510 cm^{-1}.

Alcohol (12)-OH.—Benzocyclobutene and cyclopentadiene were allowed to react following the conditions of Simmons and Cava.[19] Epoxidation with *m*-chloroperbenzoic acid gave a crystalline solid from petroleum, m.p. 60·5—61·5°; $\nu_{max.}$ (Nujol) 734, 758, 855, 962, 1380, 1461, and 2930 cm^{-1}.

48% Hydrobromic acid (75 ml) was added to the epoxide (14 g) in ether (75 ml) and the two-phase mixture was vigorously stirred for 3 h at 0 °C. After extraction a 1 : 1 mixture of bromo-alcohols was obtained in 76% yield. The crude mixture (10 g) dissolved in dimethyl sulphoxide (100 ml) was added to a vigorously stirred solution of potassium t-butoxide (15 g) in dimethyl sulphoxide (100 ml). After 2 h, the solution was poured into water and acidified with 50% sulphuric acid. Extraction and chromatography on alumina with ethyl acetate–diethyl ether as eluant gave, after crystallisation from diethyl ether–petroleum, the hydroxy-olefin (3·0 g), m.p. 94·5—96·0°, i.r. ($CDCl_3$), 708, 1047, 1085, 1099, 1212, 1277, 1458, 2900, and 3400 cm^{-1}.

Reaction with dihydropyran (10 g) in benzene (50 ml) and toluene-*p*-sulphonic acid (5 mg) gave the tetrahydropyran derivative (5·0 g), m.p. 105·5—106·5°; $\nu_{max.}$ (Nujol) 745, 979, 1032, 1055, 1064, and 1125 cm^{-1}.

Hydroboration [20] gave a 3 : 1 mixture of two alcohols which were readily separated on alumina. The *exo*-isomer (3 g), eluted with 20% ethyl acetate–diethyl ether, after crystallisation from diethyl ether–petroleum had m.p. 102—103°; $\nu_{max.}$ (Nujol) 752, 1027, 1057, 1066, 1074, 1131, 1383, and 3520 cm^{-1}. The *endo*-isomer (1 g) was eluted with 40% ethyl acetate–diethyl ether, m.p. 133·5—134·5°; $\nu_{max.}$ (Nujol) 750, 1032, 1066, 1132, 1384, and 3380 cm^{-1}.

The *exo*-alcohol derivative (3 g) was oxidised with chromium trioxide–pyridine complex (6 g) in pyridine (30 ml).[21] Recrystallisation from petroleum gave the ketone, m.p. 110—111·5°; $\nu_{max.}$ (Nujol) 754, 984, 1036, 1084, 1120, 1381, and 1740 cm^{-1}. A Meerwein–Ponndorf–Verley reduction [22] of the ketone was carried out to yield the *endo*-alcohol, m.p. 133·5—134·5°, which after conversion into the acetate was hydrolysed with 2N-hydrochloric acid to give the hydroxy-acetate; this was recrystallised from diethyl ether–petroleum and had m.p. 88—89°; $\nu_{max.}$ (Nujol) 740, 761, 1016, 1024, 1044, 1054, 1245, 1379, 1725, and 3260 cm^{-1}. Oxidation with the chromium trioxide–pyridine complex gave the keto-acetate (1·6 g) which was crystallised from petroleum; it had m.p. 106—107°; $\nu_{max.}$ (Nujol) 743, 1013, 1044, 1075, 1108, 1130, 1244, 1733, and 1773 cm^{-1}. The acetal acetate was obtained as previously described and after reduction with lithium aluminium hydride, (14)-OH was obtained; it was recrystallised from diethyl ether and had m.p. 175—176° (Found: C, 74·0; H, 6·7. $C_{15}H_{16}O_3$ requires C, 73·75; H, 6·6%).

Alcohol (11)-OH.—Oxidation of (12)-OH with chromium

[17] Z. Reyes and R. M. Silverstein, *J. Amer. Chem. Soc.*, 1958, **80**, 6367.
[18] S. Winstein, E. Grunwald, and L. L. Ingraham, *J. Amer. Chem. Soc.*, 1948, **70**, 821.
[19] H. E. Simmons, *J. Amer. Chem. Soc.*, 1961, **83**, 1657; M. P. Cava and M. J. Mitchell, *ibid.*, 1959, **81**, 5409.
[20] G. Zweifel and H. C. Brown, *Org. Reactions*, 1963, **13**, 31.
[21] R. Ratcliffe and R. Rodehorst, *J. Org. Chem.*, 1970, **35**, 4000.
[22] R. S. Tipson, *J. Org. Chem.*, 1944, **9**, 235.

trioxide–pyridine complex gave the acetal ketone which was crystallised from diethyl ether and had m.p. 195—196°; $\nu_{max.}$ ($CHCl_3$), 665, 1069, 1114, 1131, 1211, 1322, 1741, and 3070 cm^{-1}. Reduction with sodium borohydride gave (13)-OH which recrystallised from diethyl ether and had m.p. 175—176·5° (Found: C, 73·55; H, 6·55).

Toluene-p-*sulphonates*.—These derivatives were prepared by standard procedures.[22] The following lists the key numbers for the compounds prepared followed by their m.p. (in °C) and their $\nu_{max.}$ values (in cm^{-1}): (3), 132—134°, 664, 752, 862, 870, 958, 1018, 1177, 1190, 1385, and 1762; (4), 144—146°, 690, 863, 1058, 1180, 1345, 1389, and 1770; (5), 123·5—125·0°, 662, 882, 950, 1085, 1168, and 1358; (6), 153—154°, 663, 750, 819, 878, 980, 1165, 1188, 1308, and 1360; (7), 162·5—163·5°, 661, 742, 881, 913, 1176, and 1360; (8), 193·0—193·5°, 661, 750, 872, 1165, 1188, and 1360; (10), 149—150°, 663, 760, 810, 958, 1168, 1355, and 1380; (11), 151—152·5°, 663, 735, 926, 945, 1161, 1173, and 1351; (12), 166—167°, 660, 740, 812, 870, 953, 1010, 1178, and 1378.

Acetolysis Product Studies.—These reactions were conducted for six half-lives in acetic acid buffered with 0·05M-sodium acetate at 75 °C. After extraction the products were analysed by g.l.c. on a 1% cyclohexanol–dimethyl succinate column. In all cases comparisons against authentic samples were made and the products were collected and separated except when only minor amounts were formed.

The reaction product from (4) was refluxed overnight in a solution of hydrogen chloride in methanol to yield (16) in >99% yield. Similarly (17) was indicated by g.l.c. to be the only product from solvolysis of (6) and was purified by chromatography on alumina on elution with 50% diethyl ether–petroleum. In acetolysis of (5), (11), and (12) the relative g.l.c. retention times at 160° were (18) : (19) : (17) = 1 : 4·5 : 62; (25) : [(24) and (26)] : (23) = 1 : 4·8 : 7·9 and (24)-OH : (26)-OH = 1 : 1·8.

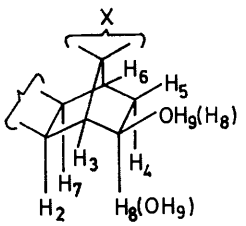
Products from solvolysis of (7) and (8) were separated by chromatography on alumina and compared to authentic samples.

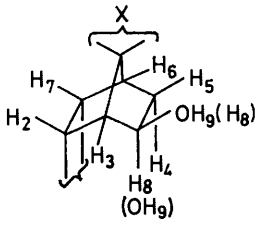
We thank the S.R.C. for a research studentship (J. C. S.).

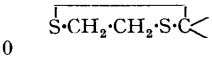
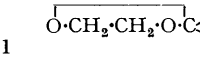
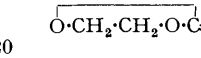
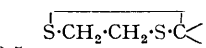
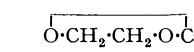
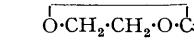
[2/1097 *Received*, 15*th May*, 1972]

TABLE 2

N.m.r. spectra of alcohols (τ values, J in Hz)





Compound	Solvent	H_1	H_2 and H_7	H_3 and H_6	H_4 and H_5	H_8	H_9	X Group	
(3)-OH	$CDCl_3$	2·91(4)m	6·42(2)m	7·68(2)m	8·57(2)m	6·52m	7·60s		
(7)-OH	$CDCl_3$	2·95(4)m	6·17(2)m	7·53(2)m	8·37(1)d J_{45} = 2 2 8·43(1)d	6·55m	7·03d J = 10		6·81(2)s 6·83(2)s
(5)-OH	CCl_4	2·94(4)m	6·33(2)m	7·92(2)m	8·49(1)d J_{45} = 4 8·59(1)d	6·86m	7·51d J = 21		6·07(4)s
(11)-OH	CCl_4	3·06(4)m	6·79(2)s	7·92(2)m	8·21(2)m	6·25m	7·27d J = 20		6·42(4)q J = 6·5
(4)-OH	$CDCl_3$	2·86(4)m	6·30(2)m	7·46(2)m	8·92(1)d J_{45} = 5 9·06(1)d	5·88m	7·82m		
(9)-OH	$CDCl_3$	2·83(4)m	6·24(2)m	7·59(2)m	9·08(1)d J_{45} = 7 9·30(1)d	5·85m	7·73s		6·78(3)s
(8)-OH	$CDCl_3$	2·78(4)m	5·93(2)m	7·50(2)m	8·88(1)d J_{45} = 7·5 9·12(1)d	5·50m	8·66d J_{89} = 18·5		6·77(4)s
(6)-OH	CCl_4	2·84(4)m	6·19(2)m	7·90(2)m	9·06(1)m 9·25(1)m	5·80m	7·96s		6·14(4)s
(12)-OH	Pyridine		5·00(1)d J = 8 6·47(1)m	7·42(1)m 7·71(1)t J = 8	8·53(1)d J_{45} = 6 8·74(1)d	5·00m	7·94s		6·47(4)m

H_1 Refers to all aromatic protons.