Solvolysis of *endo*- and *exo*-Bicyclo[3.2.1]octan-3-yl Toluene-*p*-sulphonates. Part 1. Product Analysis

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Bicyclo[3.2.1]octan-3-yl tosylates (1a) and (2a) have been solvolysed in buffered acetic and formic acids, and buffered 98 and 50% aqueous ethanol. Major reactions in all solvents are elimination and unrearranged substitution with inversion of configuration. The amount of rearrangement is solvent dependent ranging from 1.7% for (2a) in 98% aqueous ethanol to 37.4% for (1a) in formic acid, and from (1a) and (2a) comprises the *exo*-bicyclo[3.2.1]octan-2-yl and bicyclo[2.2.2]octan-2-yl compounds (3) and (5) in similar amounts with (usually) *endo*-bicyclo[3.2.1]-octan-2-yl compounds (4) in much lower yield. In all cases, the yield of unrearranged substitution product of retained configuration is very low (0.2–0.8%) and no rearranged alkene was detected at all. We suggest that whereas (1a) reacts through a chair cyclohexane conformation, (2a) reacts largely through a boat cyclohexane conformation. From both (1a) and (2a), an unsymmetrical non-classical cation (8), formed *via* classical bicyclo-[3.2.1]octan-2-yl cations, is invoked to account for the bulk of the two major rearrangement products (3) and (5), with only much smaller amounts of rearrangement occurring directly from the classical intermediates or *via* the symmetrical non-classical cation (9).

EARLIER investigators of the relationship between reactivity and conformation supposed that a t-butyl substituent remote from the reaction site acted as a conformational lock upon a chair cyclohexane without otherwise interfering with the reaction centre.[1] This view has been critically reconsidered.[2] Recent kinetic measurements [3] and product analyses [4] have shown that although *cis*-4-t-butylcyclohexyl arenesulphonates react through chair conformations, the *trans*-diastereoisomers react predominantly through non-chair flexible conformations. Several substituted cyclohexanols are now known which exist as twist-boat conformers in their ground states and their tosylates are particularly reactive.[5,6] There have nonetheless been other reports that unbridged cyclohexyl compounds undergo solvolysis through chair conformations with the leaving group departing along an equatorial direction.[7] An informative extension to these studies would be an investigation of cyclohexane systems which, though still simple secondary ones, *i.e.* without carbon branching at the β-carbons, have reduced conformational mobility.

The ethane bridge of bicyclo[3,2.1]octane derivatives (1) and (2) imposes a severe restriction upon the flexibility of the cyclohexane. The six-membered ring in (1)

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[2] J. McKenna, *Tetrahedron*, 1974, **30**, 1555; J. McKenna, J. M. McKenna, and B. G. Hutley, *J.C.S. Chem. Comm.*, 1974, 522; H. Kwart and T. Takeshita, *J. Amer. Chem. Soc.*, 1964, **86**, 1161; J. L. Mateos, C. Perez, and H. Kwart, *Chem. Comm.*, 1967, 125.

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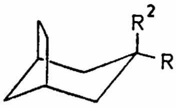
[5] D. J. Pasto and D. R. Rao, *J. Amer. Chem. Soc.*, 1970, **92**, 5151.

[6] M. Hanack and K. W. Heinz, *Annalen*, 1965, **682**, 75.

[7] J. E. Nordlander, J. M. Blank, and S. P. Jindal, *Tetrahedron Letters*, 1969, 3477; J. E. Nordlander and T. J. McCrary, *J. Amer. Chem. Soc.*, 1972, **94**, 5133; 1974, **96**, 4066; S. Hirsl-Starcevic, Z. Majerski, and D. E. Sunko, *ibid.*, 1974, **96**, 3659.

and (2) is known to be in the chair form in the ground state conformation,[8,9] though it is of course distorted.[10] Models suggest that the conformers of (1) and (2) with the cyclohexane in the boat form correspond to higher energy minima, and that in the interconversion of these two forms, the bicyclo-octane approximately maintains C_s symmetry. In other words, the potential energy hypersurfaces of (1) and (2) include no easily accessible twist-boat conformations.[11] In this respect (1) and (2) differ from unbridged cyclohexanes and cyclohexanes bridged by groups longer and more flexible than the ethano-group.[12]



(1) R^1 = H (2) R^2 = H
a; R^2 = OTs a; R^1 = OTs
b; R^2 = Cl b; R^1 = Cl
c; R^2 = OH c; R^1 = OH

There have already been reports of the kinetics of the acetolysis of (1a) and (2a),[8] and of the aqueous ethanolysis of (1b) and (2b).[13] An important aid to interpreting kinetic results is an accurate product analysis. Besides the stereochemistry of substitution at the unrearranged position, a knowledge of rearrangements can be illuminating. This ought particularly to be so for the reactions of (1a) and (2a) because 1,2-hydride shift could give either of two distinct σ-bridged (non-classical) cations which are known to be obtained stereospecifically from *endo*-bicyclo[3.2.1]octan-2-yl tosylate [14a] on the one hand, and *exo*-bicyclo[3.2.1]octan-2-yl and bicyclo[2.2.2]octan-2-yl derivatives [14] on the other.

Furthermore, products *via* these non-classical cations have already been obtained by the π-route from cyclohept-4-enylmethyl brosylates [15] and acetate,[16] 2-(cyclohex-3-enyl)ethyl brosylate [17a] and thiocyanate,[17b] by ring-opening of *exo*-tricyclo[3.2.1.$0^{2,4}$]octane,[18] by ring expansion routes from bicyclo[3.1.1]heptan-5-ylmethyl tosylates [19a] and several norbornylmethyl derivatives,[19b,c] and formally by 1,3-hydride shifts from *exo*- and *endo*-bicyclo[3.2.1]octan-6-yl tosylates.[20] Their generation *via* 1,2-hydride shifts from simple secondary carbonium ions would be an independent indirect route and could provide new knowledge of σ-bridged cations.

We report the product analyses of the solvolyses of (1a) and (2a). We have used buffered acetic acid (to facilitate comparison with results of other compounds), buffered formic acid (higher ionizing power at constant nucleophilicity), and buffered 98% aqueous ethanol (98E; higher nucleophilicity than acetic acid but similar ionizing power). With approximately the same nucleophilicity as 98E,[21] we have also used buffered 50% aqueous ethanol (50E) to compare the effect of increased ionizing power in a very nucleophilic medium. We did not include the weakly nucleophilic but strongly ionizing trifluoroacetic acid as it adds to alkenes even in the presence of sodium trifluoroacetate.[22]

Methods.—The preparation of (1a) and (2a) *via exo*-3,4-dichlorobicyclo[3.2.1]oct-2-ene and bicyclo[3.2.1]-octan-3-one were by literature methods.[8,9,23] We also obtained all probable products of solvolysis of (1a) and (2a). Bicyclo[2.2.2]octan-2-ol was prepared by the Diels–Alder reaction of cyclohexa-1,3-diene with vinyl acetate followed by hydrogenation and reduction.[14a,24] Bicyclo[3.2.1]octan-2-ols were prepared by reduction of the commercially available bicyclo[3.2.1]octan-2-one.[25] Samples of the known *exo*- and *endo*-bicyclo[3.2.1]octan-6-ols [20] were kindly supplied by Dr. A. J. Baker, Glasgow University. Bicyclo[3.2.1]oct-2-ene was prepared by sodium-induced dechlorination [26] of 3-chlorobicyclo-[3.2.1]oct-2-ene [8,23] and bicyclo[2.2.2]oct-2-ene was prepared by Wolff–Kishner reduction [27] of bicyclo[2.2.2]-oct-2-en-5-one which, in turn, was prepared by oxidation [28] of bicyclo[2.2.2]oct-2-en-5-ol.[14a]

We showed that the g.l.c. method used by earlier

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[16] R. Thies and L. E. Schick, *J. Amer. Chem. Soc.*, 1974, **96**, 456.

[17] (*a*) S. Winstein and P. Carter, *J. Amer. Chem. Soc.*, 1961, **83**, 4485; (*b*) L. A. Spurlock and R. J. Schultz, *ibid.*, 1970, **92**, 6302.

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[24] H. Maskill, *J.C.S. Perkin II*, 1975, 1850.

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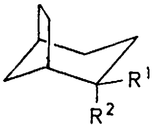
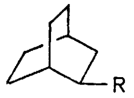
[28] H. C. Brown and C. P. Garg, *J. Amer. Chem. Soc.*, 1961, **83**, 2952.

workers[8] was incapable of resolving a mixture of up to seven bicyclo-octanyl acetates into more than two peaks. The prospects for a complete analysis appeared to be better for the bicyclo-octanols than for their acetates, so it was established that acetates (and formates), which were stable to the solvolysis conditions, could be reduced quantitatively and without rearrangement or stereomutation. However, no single set of g.l.c. conditions which we tried completely resolved a mixture of the seven bicyclo-octanols. Using a 50 ft SCOT Carbowax 20M column (1c), (2c), and *exo*-bicyclo[3.2.1]octan-2-ol (3a) were resolved from each and all others. The other four were eluted in the order bicyclo[2.2.2]octan-2-ol (5a), *endo*-bicyclo[3.2.1]octan-2-ol (4a), *exo*-bicyclo[3.2.1]octan-6-ol, and *endo*-bicyclo[3.2.1]octan-6-ol, but they were sufficiently close together that if all were present in comparable amounts, their separate analysis would be imprecise. On a 50 ft SCOT DEGS column their resolution is better and in the order *endo*-bicyclo[3.2.1]octan-6-ol, (5a), *exo*-bicyclo[3.2.1]octan-6-ol, and (4a), but still not suited to a precise analysis if all seven alcohols are present.



(3) R^1 = H (4) R^2 = H
a, R^2 = OH a, R^1 = OH
b, R^2 = OAc b, R^1 = OAc
c, R^2 = OTs c, R^1 = OTs



(5)
a, R = OH
b, R = OAc
c, R = OTs

It became clear however from preliminary work that only three of the five possible rearranged secondary alcohols were produced from (1a) and (2a). By co-injection of authentic samples, these were shown to be (3a) and (5a) in low to modest yields depending upon the solvent, and (4a) in much lower yield. Neither of the bicyclo[3.2.1]octan-6-ols was detected at all. We estimate that the upper limit of the yield of these two alcohols to be of the order of the yield of (4a) (<0.2—0.5% in acetolysis, <0.1—0.3% in aqueous ethanolysis, and <0.5—2% in formolysis). The only incompletely resolved pair of alcoholic products on the SCOT Carbowax 20M column then was (4a) and (5a) and these were adequately resolved on the SCOT DEGS column. {The absence of the bicyclo[3.2.1]octan-6-ols is also the justification for not including the bicyclo[3.2.1]octan-8-ols among possible products. Bicyclo[3.2.1]octan-1-ol and bicyclo[2.2.2]octan-1-ol were not thought to be realistic products as the formation of their cationic precursors would be strongly endothermic from relatively stable cations. Had either tertiary alcohol been present, it is unlikely that it would have co-chromatographed with the other (secondary) bicyclo-octanols.}

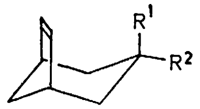
Bicyclo[2.2.2]oct-2-ene and bicyclo[3.2.1]oct-2-ene (the latter of which was shown to be stable to the acidic solvolysis conditions and work-up procedures) were well resolved by the 50 ft SCOT Carbowax 20M column. In no product mixture, however, was bicyclo[2.2.2]oct-2-ene detected ($<0.1\%$ from formolysis and 98E, $<0.3\%$ from acetolysis and 50E).

The five bicyclo-octyl ethyl ethers corresponding to the five alcohols were prepared from the individual alcohols, ethyl iodide, and silver oxide.[29] These were shown to be resolved by the g.l.c. conditions used for the alcohol analysis and by careful co-injection of authentic samples, the identities of the products were established.

The absolute yields of all identified products were calculated by using internal calibrants: n-undecane which chromatographed after the alkenes under the same conditions, and n-pentadecane which chromatographed after the ethers and before the alcohols under the conditions used for the alcohol analysis. The molar response factors (m.r.f.s) of the flame ionization detector, under the conditions used for the analyses, for the bicyclo[3.2.1]oct-2-ene to n-undecane, and *exo*-bicyclo[3.2.1]octan-3-ol to n-pentadecane were determined. An m.r.f. for the ethers to pentadecane was computed.[30] An error in this m.r.f. will not, of course, affect the relative yields of isomeric ethers.

RESULTS AND DISCUSSION

Acetolysis.—The principal features of the acetolysis of both (1a) and (2a), the details of which are shown in Tables 1—3, are substantial elimination, unrearranged substitution with strong preference for inversion, and rearrangement. These results are similar to those of the 4-t-butylcyclohexyl arenesulphonates[4] and the bicyclo[3.2.1]oct-6-en-3-yl tosylates (6) and (7),[31] and are in contrast to the earlier reports by Jefford.[8]



(6) R^1 = OTs, R^2 = H
(7) R^1 = H, R^2 = OTs

The yields of alkene from (1a) and (2a) are somewhat lower than from simpler cyclohexyl compounds (this is more pronounced in the other solvents). One possible cause is that the increase in strain[32] which accompanies elimination in the bicyclo[3.2.1]octane structure is greater than in unbridged cyclohexanes, and consequently substitution is better able to compete in the bicyclic system. There is a second possibility which may become more important when the amount of rearrangement is high. Whereas the rearranged cations from the simple cyclohexyl derivatives also yield predominantly alkenes, elimination is a very minor process from σ-bridged

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bicyclo-octyl cations,[14,24] the probable rearrangement products from (1a) and (2a) (see later).

TABLE 1

Products of solvolysis of *endo*-bicyclo[3.2.1]octan-3-yl tosylate (1a)

Products [a]	Formic acid [b] 25°	Acetic acid [c] 61°	50E [d] 36°	98E [e] 60°
2-ene	46.0	68.8 [g] (44.0)	63.3	56.3
1-OR	0.7	0.8 (21.5)	0 [f]	0.6
2-OR	15.9	16.6 (34.5)	5.6	36.5
3-OR	19.5	8.0	0.5	1.0
5-OR	16.7	5.2	0.5	0.6
4-OR	1.2	0.6	0 [f]	0 [g]
1-OH			0.4	0.1
2-OH			24.6	4.5
3-OH			3.1	0.3
5-OH			1.8	0.1
4-OH			0.2	0 [g]

[a] 2-ene = bicyclo[3.2.1]oct-2-ene. [b] Containing 0.15M-$Na^+HCO_2^-$. [c] Containing 0.15M-$K^+CH_3CO_2^-$; Jefford's[8] results in parentheses. [d] Containing 0.017M-Borax. [e] Containing 0.05M-DABCO. [f] <0.2%. [g] <0.1%.

The preference of (1a) for unrearranged substitution with inversion (inv : ret = 21) is not surprising, as nucleophilic approach to the cyclohexane from the *exo*-side is along a relatively unhindered equatorial direction. Interestingly, the *exo*-isomer (2a) shows an even stronger preference for inversion (inv : ret = 883) at the unrearranged position. These ratios are to be compared with inv : ret *ca.* 16 and *ca.* 75 at 60° from *cis*- and *trans*-4-t-butylcyclohexyl *p*-nitrobenzenesulphonates (interpolated from results at 25 and 100°[4]). LeBel and Maxwell[31] reported substitution at the unrearranged position of (6) with inv : ret *ca.* 9, and 35.8% of unrearranged substitution from (7) which was *entirely* inverted. These results for (2a) and (7) are difficult to accommodate by a mechanism involving chair cyclohexanes as proposed by Jefford[8] and implied by LeBel and Maxwell.[31] It would require a greater preference for inversion when the process involves nucleophilic approach to the chair cyclohexane from an *endo*, axial direction encumbered by the bridging ethano- (or etheno-) group. On the other hand, this very strong preference of (2a) and (7) for inversion is expected if they react through boat cyclohexane conformations.

TABLE 3

Collated results of solvolysis of *endo*- and *exo*-bicyclo[3.2.1]octan-3-yl tosylates

Reaction	Reactant	Formolysis	Acetolysis	50E		98E	
Elimination (%)	(1a)	46.0	68.8	63.3		56.3	
	(2a)	52.6	69.0	40.4		39.5	
Unrearranged substitution (%)	(1a)	16.6	17.4	30.6		41.7	
	(2a)	30.5	26.8	54.5		58.8	
Inv : ret in unrearranged substitution	(1a)	227	21	>28 [a]	62 [b]	61 [a]	45 [b]
	(2a)	60	883	>87 [a]	228 [b]	64 [a]	67 [b]
Rearrangement (%)	(1a)	37.4	13.8	6.1		2.0	
	(2a)	16.9	4.2	5.1		1.7	
Rearranged product ratios (3 : 5 : 4)	(1a)	52 : 45 : 3	58 : 38 : 4	50 : 50 [a]	63 : 37 [b]	61 : 35 : 4 [a]	75 : 25 [b]
	(2a)	47 : 50 : 3	50 : 45 : 5	44 : 56 [a]	48 : 52 [b]	46 : 54 [a]	50 : 50 [b]

[a] Ether products. [b] Alcohol products.

Rearranged products were anticipated and the yield of 13.8% from (1a) constitutes almost half the total acetolysis substitution product. The smaller yield of 4.2% from (2a) seems anomalously low especially when the results in the other solvents are considered. However, whereas the rearranged substitution products from 4-t-butylcyclohexyl arenesulphonates are modestly stereospecific (in favour of nucleophilic capture from the side of the cyclohexane opposite to that from which the leaving group departs), we find the same three products, (3b), (5b), and (4b), in very similar proportions from (1a) *and* (2a) (58 : 38 : 4 and 50 : 45 : 5 respectively) even though the total rearrangement from (1a) is more than three times that from (2a). This non-stereospecificity alone effectively rules out the intermediate formation of covalent tosylates (4c) from (1a) and (3c) from (2a).[4]

TABLE 2

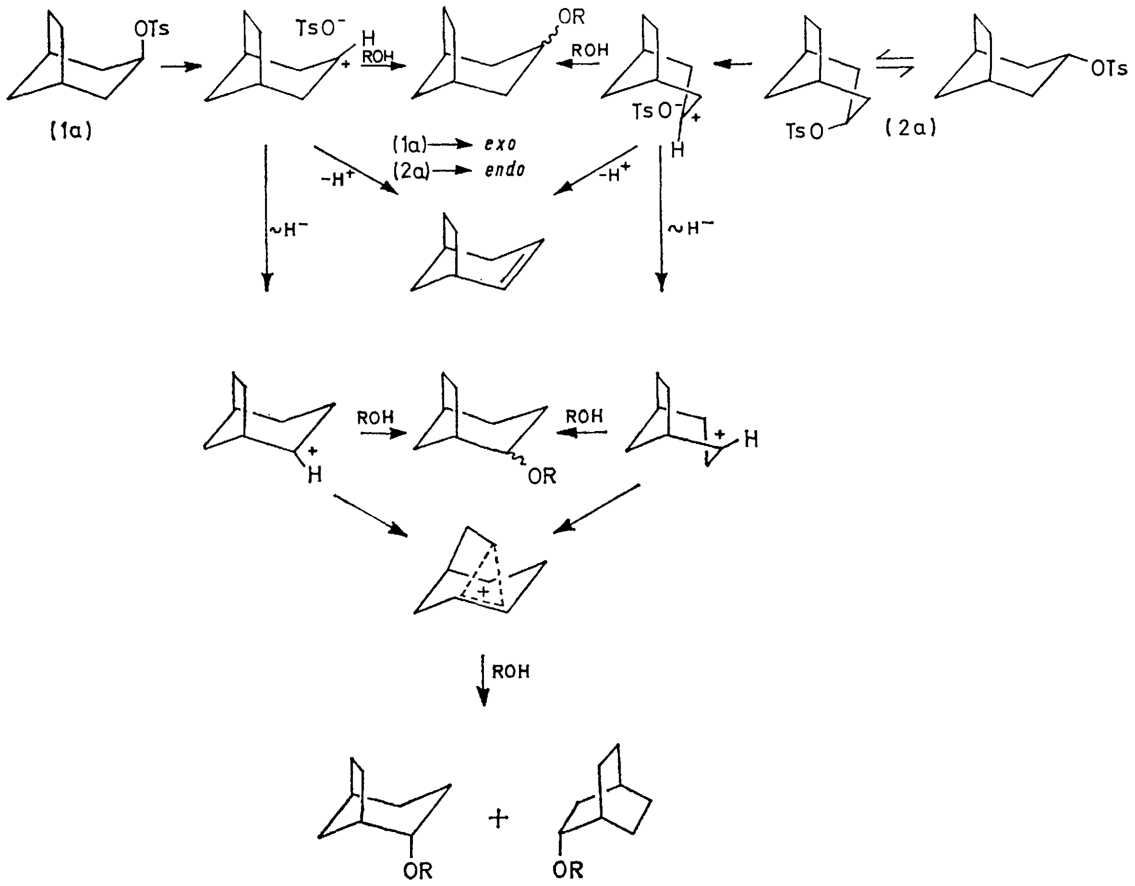
Products of solvolysis of *exo*-bicyclo[3.2.1]octan-3-yl tosylate (2a)

Products [a]	Formic acid [b] 25°	Acetic acid [c] 61°	50E [d] 36°	98E [e] 70°
2-ene	52.6	69.0 (35.8)	40.4	39.5
1-OR	30.0	26.5 (64.2)	8.7	51.2
2-OR	0.5	0.3	0 [g]	0.8
3-OR	8.0	2.1	0.4	0.6
5-OR	8.4	1.9	0.5	0.7
4-OR	0.5	0.2	0 [g]	0 [g]
1-OH			45.6	6.7
2-OH			0.2	0.1
3-OH			2.0	0.2
5-OH			2.2	0.2
4-OH			0 [h]	0 [g]

[a-g] See Table 1. [h] <0.3%.

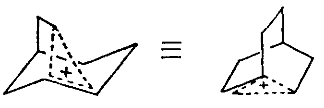
Effect of Solvent.—It is seen from the Tables that the results in other solvents are remarkable more for their similarity than their differences, and that such trends as are evident are consistent with the proposed mechanism (illustrated in the Scheme) and the known properties of the solvents, and are in accord with other results.[4] Compared with the reactions in acetic acid, the lower yields of alkene are accompanied, in the case of the weakly nucleophilic, strongly ionizing formic acid, by an increased amount of rearrangement and, in the more nucleophilic aqueous ethanol mixtures, by increased yields of unrearranged substitution products.

In all the solvents, the yield of unrearranged substitution product with retained configuration from (1a) and (2a) is exceedingly low. The small amounts which are formed are probably the result of solvolysis of inverted starting material, as internal return with some stereomutation is well known to accompany solvolyses.[33]

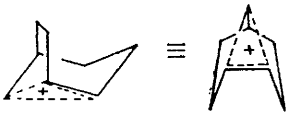


SCHEME Major routes in the solvolysis of *endo*- and *exo*-bicyclo[3.2.1]octan-3-yl tosylates

Formic acid is known to facilitate rearrangements of cations and accordingly in this solvent both (1a) and (2a), but especially the former, give substantial yields of rearranged products. The relative proportions of the same three rearranged products (3) : (5) : (4) are, however, remarkably constant [52 : 45 : 3 from (1a) and 47 : 50 : 3 from (2a)], and there is still no evidence of bicyclo[2.2.2]oct-2-ene (<0.1%). In the strongly nucleophilic, weakly ionizing 98E, there is only little rearrangement from both (1a) and (2a) and in the better ionizing, but also very nucleophilic 50E, the total yields of rearrangement are still only modest. Interestingly, the proportions of alcohols to ethers of both rearranged and unrearranged structures in the aqueous ethanolyses are always higher than the molar proportion of water in the aqueous ethanol even though ethanol is commonly believed to be more nucleophilic than water.[21] The explanation of this paradox is most likely that water, being a far better solvating species than ethanol, is at a higher concentration in the immediate vicinity of the incipient ions than in the bulk solvent.



(8)



(9)

Mechanism of Rearrangement.—The formation of (3) and (5) is compatible with the intermediacy of the σ-bridged cation (8) formed *via* hydride shift from the ion-pairs obtained from (1a) and (2a). At least one other intermediate is required from both to account for the small yield of (4), and this could be the isomeric symmetrical σ-bridged cation (9). It is unlikely however that (8) and (9) would be formed directly and in the same

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[33] A. Streitwieser and T. D. Walsh, *Tetrahedron Letters*, 1963, 27; *J. Amer. Chem. Soc.*, 1965, **87**, 3686; A. Streitwieser, T. D. Walsh, and J. R. Wolfe, *ibid.*, p. 3682.

proportions from the diastereoisomeric bicyclo[3.2.1]-octan-3-yl cation ion-pairs.[19c]

We suggest that the initially formed ion-pair from (1a) undergoes 1,2-hydride shift to the isomeric classical bicyclo[3.2.1]octan-2-yl cation tosylate ion-pair. This is exactly analogous to the proposed mechanism for rearrangement in the 4-t-butylcyclohexyl system [4] and the tosylate is still *endo*. The cation would suffer a small amount of nucleophilic capture mainly from the *exo*-direction to give (3), and also some elimination to give bicyclo[3.2.1]oct-2-ene. Predominantly however, this classical cation, which corresponds to a high energy deformation on the potential energy hypersurface which contains (8) and (9), relaxes to give largely (8) [thence (3) and (5) and much less (9) [thence (4)]. This mechanism for (1a) accounts not only for the small proportion of (4) but also, because of the two routes to (3), for the slight but consistent excess of (3) over (5), a result which is not found when (8) is generated directly from (3c), (5c),[14,24] or other precursors.[17,19c]

The first formed ion-pair from (2a) will rearrange initially to a classical ion-pair which may give some bicyclo[3.2.1]oct-2-ene and which, upon nucleophilic capture, should give (4) principally. But again, to account for the rearranged substitution products it is proposed that the predominant course for the classical rearranged cation will be relaxation to (8) and, to a much lesser extent, (9).

This non-stereospecific formation of (8) from (1a) *and* (2a) is in contrast to those reactions in which (8) is formed directly from (3c) or (5c). and (9) from (4c),[14] and to those formations of (8) and (9) by π-routes from 2-(cyclohex-3-enyl)ethyl brosylate [17a] and cyclohept-4-enylmethyl arenesulphonates [15] respectively. The results are not paradoxical since in the one case (8) is the product of relaxation of classical cations, and in the others (8) and (9) are initial products of ionizations. The direct production of the non-classical cations involves some measure of electronic delocalization and bridging during the ionization [24] and the higher energy classical cations are by-passed. In other words, in contrast to the direct routes, the formation of (8) and (9) from diastereoisomeric classical ion-pairs is not stereocontrolled by the heterolytic departure of a leaving group. This mechanism requires however that (8) is more stable than (9) or is always more easily formed in reactions of (1a) and (2a). We note that in the direct formation of (8) there is always very little leakage to (9), usually $<1\%$,[14a] whereas in the direct formation of (9) there is always a significant leakage to (8), usually 10—15% [14a] and sometimes considerably more.[19c] Furthermore, this may be related to the formation of only the symmetrical σ-bridged norbornyl cation from both *exo*- and *endo*-substrates.[34] Our mechanism is also in accord with the earlier reports that (3b) and (5b) are formed in approximately the same ratio as we find from the acetolysis of *both exo*- and *endo*-bicyclo[3.2.1]octan-6-yl tosylates,[20] and *both exo*- and *endo*-bicyclo[3.1.1]heptan-3-ylmethyl tosylates.[19a]

Scrutiny of the elimination product supports a non-classical ion mechanism for rearrangement. No bicyclo-[2.2.2]oct-2-ene was detected from any solvolysis (<0.1—0.3%), so the cationic precursor of (5) shows a strong preference for substitution rather than elimination. This is one of the principal characteristics of reactions which involve σ-bridged cations.[14,34a]

EXPERIMENTAL

Pentane and light petroleum were extracted twice with concentrated sulphuric acid, washed with aqueous sodium hydroxide then with brine, and were finally fractionally distilled from phosphorus pentaoxide. Ethyl acetate was fractionally distilled, and the diethyl ether which was used for product analysis was redistilled AnalaR grade. The 60 MHz n.m.r. spectra were recorded on Perkin-Elmer R10 or R24 instruments; i.r. spectra were recorded on a Perkin-Elmer 457 and u.v. spectra on a Unicam SP 8000 instrument. M.p.s were recorded on a Kofler apparatus or in sealed capillary tubes and are uncorrected. Routine g.l.c. analyses were done with 2 m × 1/8 in stainless steel columns packed with 15% Carbowax 20M on Chromosorb W. Solvolysis product analyses were done with a 50 ft SCOT Carbowax 20M column (A) and a 50 ft SCOT DEGS column (B). All analytical columns were used in Perkin-Elmer F11 chromatographs fitted with inlet splitters and using nitrogen (15—20 lb in^{-2}) as carrier gas. Preparative g.l.c. was performed on a Varian model 700 with nitrogen as the carrier gas.

Bicyclo[3.2.1]*octan*-3-*ols*.—Bicyclo[3.2.1]octan-3-one was prepared by literature methods [8,9,23] and reduced in several ways to give different mixtures of the corresponding *endo*- and *exo*-alcohols.

(a) Catalytic hydrogenation of a solution of the ketone in acetic acid–concentrated hydrochloric acid (*ca.* 10 : 1) over Adams catalyst at 3 atm. for 18 h at room temperature gave a mixture of alcohols and acetates. After routine work-up, this mixture was reduced with lithium aluminium hydride in the usual manner to give a 40 : 1 mixture of *endo*- and *exo*-bicyclo[3.2.1]octan-3-ols. The *endo*-isomer (1c) was purified by alumina chromatography (light petroleum–ethyl acetate) and sublimation (80° and 4 Torr), yield 64%; m.p. 204—204.5° (lit.,[9] 206—206.5°); $\tilde{\nu}_{max.}$ (CCl_4) 3 625s, 2 930s, 2 865s, 1 450m, 1 100m, 1 050m, 970m, and 920m cm^{-1}; τ (CCl_4) 6.0 (1 H, m) and 7.8—8.7 (13 H, m).

(b) Reduction of the ketone with lithium aluminium hydride in the usual way gave a 1 : 2 mixture of (1c) (30%), m.p. 204—204.5°, and (2c) (41%), m.p. 113.5—114° (lit.,[9] 114—115°); $\tilde{\nu}_{max.}$ (CCl_4) 3 620m, 2 940s, 2 870s, 1 455m, 1 100m, 1 060s, and 950m cm^{-1}; τ (CCl_4) 6.25 (1 H, m), 7.35 (1 H, s), and 7.6—9.1 (12 H, m), which were separated and purified by alumina chromatography and sublimation as described above.

(c) Reduction of the ketone with sodium borohydride gave a *ca.* 1 : 1 mixture of (1c) and (2c).

Bicyclo[3.2.1]*octan*-3-*yl Tosylates*.—These compounds were made by the Tipson [35] procedure, from the respective alcohols (which were shown by g.l.c. to contain $<0.1\%$ of

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[34] (*a*) S. Winstein, E. Clippinger, R. Howe, and E. Vogelfanger, *J. Amer. Chem. Soc.*, 1965, **87**, 376; (*b*) G. D. Sargent, *Quart. Rev.*, 1966, **20**, 301; see also Yi. Lin and A. Nickon, *J. Amer. Chem. Soc.*, 1970, **92**, 3496.

[35] R. S. Tipson, *J. Org. Chem.*, 1944, **9**, 235.

diastereoisomeric impurities) and were purified by recrystallization from light petroleum (b.p. 40—60°). Compound (1a) had m.p. 75—76° (lit.,[8] 71—73°); yield 76%; $\nu_{max.}$ (CCl_4) 1 370m, 1 190m, 1 180s, and 910s cm^{-1}; τ (CCl_4) 2.2—2.8 (4 H, ABq), 5.2—5.4 (1 H, m), and 7.6—8.7 (15 H, m); $\lambda_{max.}$ (C_2H_5OH) 273 (ε 488), 267(552), 262(615), and 257 nm (494); (2a) had m.p. 80—81° (lit,[8] 76—77°); yield 65%; $\bar{\nu}_{max.}$ (CCl_4) 1 375s, 1 190s, 1 180s, 1 100s, and 950s cm^{-1}; τ(CCl_4) 2.2—2.9 (4 H, ABq), 5.2—5.7 (1 H, m), and 7.5—8.8 (15 H, m); $\lambda_{max.}$ (C_2H_5OH) 273 nm (ε 482), 267(540), 262(604), and 257 nm (488). The tosylates were stored in a desiccator at −15° and the m.p. of each sample was checked before use.

Bicyclo[3.2.1]*octan-2-ols*.—The *endo*- and *exo*-isomers were prepared by catalytic hydrogenation (as described above) of impure bicyclo[3.2.1]octan-2-one (Aldrich) in the ratio 36 : 50 plus 14% of (5a).[24,25] By careful alumina chromatography [light petroleum (b.p. 40—60°)–ethyl acetate; automatic collection of small fractions] samples of the *exo*-isomer (3a) containing 4% (5a) and of the *endo*-isomer (4a) containing 1% (3a) were obtained. Compound (3a) had m.p. 191—192° (lit.,[14a] 194.2—195.5°); $\bar{\nu}_{max.}$ (CCl_4) 3 620m, 3 350br, 2 940s, 2 870s, 1 450m, 1 030s, 1 015s, 965s, and 930w cm^{-1}. Compound (4a) had m.p. 173—174° (lit.,[14a] 174.5—177°); $\bar{\nu}_{max.}$ (CCl_4) 3 620m, 3 350br, 2 940s, 2 870s, 1 455m, 1 065s, 1 040s, 993s, and 909w cm^{-1}.

Bicyclo[2.2.2]*octan-2-ol*.—This was prepared by a literature method,[14a,24] m.p. 216—216.5° (lit.,[14a] 216—217°).

The acetates of these alcohols were prepared from the individual alcohols (*ca.* 200 mg), acetic anhydride (1.5 cm^3), and pyridine (3 cm^3) by heating under reflux for 1 h. Work-up in ether with acidic and basic washes gave the product from which alcoholic and other minor contaminants were removed by percolation through alumina.

Formates were prepared from the individual alcohols (*ca.* 50 mg) with an excess of acetic formic anhydride [36] (*ca.* 2 cm^3) at room temperature for 1 week. Extraction between ether and dilute aqueous sodium carbonate gave, in each case, the formate contaminated with up to 5% of the corresponding acetate. This was never a complication as the formate and acetate were well separated in the g.l.c. analysis.

The ethyl ethers were prepared from the individual alcohols (*ca.* 20 mg), ethyl iodide (*ca.* 500 mg), and silver oxide (*ca.* 90 mg) in diethyl ether (2 cm^3) by stirring and heating under reflux for 48 h.[29] The cooled mixture was filtered and percolated through alumina (*ca.* 20 g) in pentane to remove unchanged alcohol.

Bicyclo[3.2.1]*oct-2-ene*.—To a stirred solution of anhydrous t-butyl alcohol (4.7 g, 0.06 mol) in absolute tetrahydrofuran (25 cm^3) under nitrogen were added small pieces of sodium (2.9 g, 0.12 mol) and the mixture was then heated under reflux. A solution of 3-chlorobicyclo[3.2.1]oct-2-ene (3 g, 0.02 mol) in absolute tetrahydrofuran (10 cm^3) was added dropwise to the boiling mixture and the heating was continued for 20 h. The cooled solution was decanted from unchanged sodium, treated with methanol, poured onto ice, and extracted three times with pentane. The combined pentane phase was dried ($MgSO_4$), filtered, and fractionally distilled to remove solvent. The residue was percolated through a column of silica impregnated with silver nitrate, elution being with pentane. The fractions containing the required alkene were combined and fractionally distilled. The product was isolated from the residue by preparative g.l.c. (10 ft × 3/8 in 10% Carbowax 20M on Chromosorb A; 100°) followed by sublimation (40° and 40 Torr) to give crystals (1.0 g, 45%), m.p. 38—38.5° (lit.,[23a] 35—36°); $\bar{\nu}_{max.}$ (CCl_4) 3 030m, 2 950s, 2 870m, 2 840m, 1 640w, 1 448m, and 685s cm^{-1}; τ(CCl_4) 3.9—4.9 (2 H, m) and 7.3—8.9 (10 H, m).

Bicyclo[2.2.2]oct-2-ene [27] was made in low yield by the Wolff–Kishner reduction of bicyclo[2.2.2]oct-2-en-5-one [14a,24,28] and was purified by preparative g.l.c. (20 ft × 3/8 in 30% SE30 on Chromosorb W; 100 cm^3 min^{-1}; 170°); $\bar{\nu}_{max.}$ (CCl_4) 3 050s, 2 945s, 2 870s, 1 618w, 1 470w, 1 455m, 1 375m, 1 250w, 1 180w, 1 165w, 865s, and 695s cm^{-1}; τ(CCl_4) 3.78 (2 H, m), 7.51 (2 H, m), and 8.63 (8 H, m).

Preparation of Solvolysis Media.—(a) Anhydrous potassium acetate (29.44 g, 0.300 mol) and acetic anhydride (AnalaR; 20 cm^3) were made up to 2 l with acetic acid (AnalaR). A standard solution (100.00 cm^3) of n-undecane, b.p. 57° at 2 Torr (156.6 mg), and n-pentadecane, b.p. 100° at 0.3 Torr (103.4 mg), in the acetolysis medium was prepared. This solution was shown to contain no impurities which gas chromatographed with any potential reaction products.

(b) Formic acid (AnalaR; 98%; 1 l) was dried over boric anhydride (80 g) for 3 days, filtered, and fractionally distilled, b.p. 38° at 100 Torr, from a fresh batch of boric anhydride. Anhydrous sodium formate (3.36 g, 0.049 mol) was dissolved in the distillate (330 cm^3) to give a solution 0.15M in sodium formate. Because of the limited solubilities of pentadecane and undecane in this formolysis medium, no stock solution of the markers was prepared.

(c) A standard solution (50.00 cm^3) of n-undecane (142.3 mg), n-pentadecane (110.8 mg), and 1,4-diazabicyclo[2.2.2]-octane [DABCO; recrystallised and sublimed (100° at 14 Torr); 286.8 mg, 0.002 56 mol] in 98 : 2 v/v ethanol (spectroscopic grade): water was prepared. This solution is 0.051M in DABCO. No stock solution of the hydrocarbons in 50E was prepared.

Solvolytic Procedures.—(a) *Acetolysis*. The tosylate (accurately *ca.* 45 mg) was made up to 5.00 cm^3 with the standard solution of markers in buffered acetic acid. The homogeneous solution was sealed in an ampoule which was then immersed in a thermostatted water-bath (61.0°) for *ca.* 15 h in the case of (1a) and 2—4 days for (2a). The ampoule was then cooled in ice, opened, and cautiously added to an ice-cold aqueous solution of tripotassium phosphate (3.5M; 25 cm^3). The mixture was extracted twice with cold ether and the combined organic phase was dried ($MgSO_4$). The cold, dry solution was decanted and one portion (*ca.* 2 cm^3) was analysed directly for alkenes and the second portion (*ca.* 8 cm^3) was reduced with an excess of lithium aluminium hydride (*ca.* 100 mg) in the usual way. The reduced product was cooled (0°), acidified, and extracted twice with ether. The combined ether phase was washed once with brine then analysed for alcohols.

(b) *Formolysis*. To the tosylate and the two hydrocarbons (accurately *ca.* 20—30 mg of each) was added the formolysis medium (*ca.* 3.5 cm^3), and the flask was tightly stoppered and shaken vigorously to dissolve the tosylate. The flask was then placed in a thermostatted water-bath (25.0°) for 1 h in the case of (1a) and 15—18 h for (2a). The flask was then cooled, ether was added, and the resultant homogeneous solution was cautiously added to the ice-cold tripotassium phosphate solution. The subsequent steps were as described above for acetolysis.

[36] W. Stevens and A. Van Es, *Rec. Trav. chim.*, 1964, **83**, 1287.

(c) *Aqueous ethanolysis* (98*E*). The tosylate (accurately *ca.* 45 mg) was made up to 5.00 cm^3 with the standard solution of markers in buffered 98% aqueous ethanol. The homogeneous solution was sealed in an ampoule and immersed in a thermostatted water-bath [60.0° for (1a) and 70.0° for (2a)] for >6 h in the case of (1a) and *ca.* 40 h for (2a). The ampoule was cooled (0°), opened, and the contents were extracted between ether and brine. The aqueous phase was extracted with a second portion of ether and the combined ether phase was then washed twice with dilute hydrochloric acid and twice with brine before being analysed by g.l.c.

(d) *Aqueous ethanolysis* (50*E*). The tosylate and two hydrocarbon markers (accurately *ca.* 30 mg of each) were dissolved in spectroscopic grade ethanol (7 cm^3) and an exactly equal volume of aqueous borax (7 cm^3; 0.034M) was added. The stoppered flask was vigorously shaken then placed in a thermostatted water-bath (36.0°) for *ca.* 15 h for (1a) and 2—4 days for (2a). The cooled solution was saturated with sodium chloride, made more basic by the addition of aqueous sodium hydroxide, and extracted twice with ether. The combined ether phase was analysed by g.l.c.

Analysis of Products.—The ether solutions of markers and products were analysed on column A at 60° for alkenes, and at 120° for ethers and alcohols. The combined yield of (4a) and (5a) was obtained in this latter analysis and their relative proportions were determined using column B at 100°.

Both tosylates were solvolysed twice in each solvent. For each run, 3—5 analyses of each product mixture were made with the area of each peak on each chromatogram being measured at least twice with a Stanley Precision Disc Planimeter. The normalized mean combined analysis for one run was combined with its duplicate to give an average normalized product analysis for each solvolysis. These are the values quoted in Tables 1 and 2. Errors are approximately ∓ 0.05 or 3% of the actual figure, whichever is the larger. Total recoveries were in the range 100—110%.

Determination of Molar Response Factors (*M.r.f.s*)—Three standard solutions of pure bicyclo[3.2.1]oct-2-ene and pure n-undecane (accurately *ca.* 20 mg of each) in pentane were prepared. Each solution was analysed not fewer than three times under the conditions of the actual product analyses, and chromatogram peak areas were measured planimetrically. M.r.f. (alkene : undecane) = 0.751($\mp$0.004) where equation (1) applies. In the same manner, four

$$\text{m.r.f.} = \frac{\text{peak area per mole of alkene}}{\text{peak area per mole of standard}} \qquad (1)$$

standard solutions containing n-pentadecane and (2c) were prepared and analysed. M.r.f. (alcohol : pentadecane) = 0.524($\mp$0.013). An m.r.f. of 0.667 was calculated for the bicyclo-octyl ethyl ethers with respect to pentadecane by formula (2). (This method gives 0.727 and 0.533 for the

$$\text{m.r.f.} = \frac{\text{carbon atoms per mole of ether}}{\text{carbon atoms per mole of standard}} \qquad (2)$$

alkene and alcohol m.r.f.s compared with the above experimental results.)

Stability of Products to Experimental Conditions.—(a) *Acetates to work-up procedure*. Compound (1c) was converted to the corresponding acetate as described above. The solution of the acetate in ether was reduced with lithium aluminium hydride at 35° for 1.5 h, cooled, and worked up in the usual manner. Analysis on column B at 100° showed that the reduction product contained no alcohol ($<0.1\%$) other than (1c). A similar experiment with (2c) confirmed that reduction of its acetate was accompanied by no inversion or rearrangement. A third experiment starting with an approximately equimolar mixture of (3a)—(5a) showed that acetylation followed by reduction gave a mixture of alcohols identical, within the precision of the method (*ca.* 2%), with the reactant mixture.

(b) *Acetates to acetolysis condition*. A mixture of (3b) and (5b) was kept at 60° for 40 h in the acetolysis medium. After work-up, g.l.c. analysis of the acetates (100m WCOT Ucon LB550X;[14a] 120°) showed that the relative amounts of the acetates were unchanged (within 2%) and no other acetates were detected.

(c) *Bicyclo*[3.2.1]*oct-2-ene to acetolysis and formolysis conditions and work-up procedures*. The alkene was kept in the acetolysis medium at 60° for 40 h; then the mixture was worked up as in an acetolysis reaction. After treatment with lithium aluminium hydride followed by the usual work-up, g.l.c. (column A; 60°) showed no bicyclo[2.2.2]oct-2-ene ($<0.4\%$), and (column A; 120°) no alcoholic products ($<1\%$). When the same alkene was treated with formolysis medium at 25° for 18 h, work-up and g.l.c. analysis (column A; 120°) showed that $<1\%$ of any formate had formed.

(d) *Formates to the formolysis medium and work-up procedure*. Both bicyclo[3.2.1]octan-3-yl formates were separately subjected to the formolysis conditions at 25° for 18 h. Reduction of the products followed by g.l.c. analysis (column A; 120°) showed that in both cases, an upper limit of 0.2% can be placed on the yield of any rearranged or inverted product. In a similar experiment starting with a mixture of (3a) and (5a), conversion to formates, formolysis, and reduction gave a mixture of two alcohols identical, within experimental error (*ca.* 3%), with the initial one.

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