Deamination of Bicyclo[2.2.2]octan-2-yl- and Bicyclo[3.2.1]octan-2-yl-amines. Evidence for Classical Precursors of Non-classical Carbonium Ions [1]

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Bicyclo[2.2.2]octan-2-yl- and *exo*-bicyclo[3.2.1]octan-2-yl-amines have been deaminated in acetic acid by nitrous acid and *via* their *N*-phenyltriazenes; their ethyl *N*-nitrosocarbamates have also been solvolysed in ethanol. Product distributions by a given method from the structurally isomeric starting materials are similar to each other and to the common product distribution obtained from bicyclo[2.2.2]-octan-2-yl and *exo*-bicyclo[3.2.1]octan-2-yl toluene-*p*-sulphonates. Each amine gives, however, a small but unmistakable excess of the structurally unrearranged product compared (in the case of substitution) with the distribution obtained from the solvolysis of the corresponding bicyclo-octyl toluene-*p*-sulphonates. *endo*-Bicyclo[3.2.1]octan-2-ylamine has also been deaminated in acetic acid by nitrous acid and *via* its ethyl *N*-nitrosocarbamate in ethanol. The product ratios of these reactions are characteristically different from those of the isomeric amines but, as far as substitution is concerned, are similar to what is obtained from *endo*-bicyclo[3.2.1]octan-2-yl toluene-*p*-sulphonate. A common mechanism describes all the deaminative reactions. We propose that classical carbonium ions are the initial products of fragmentation of diazo-intermediates. These are intercepted to only a small extent to give products structurally and stereochemically characteristic of the original amines; to an even smaller extent they rearrange to isomeric classical carbonium ions, which in turn may be intercepted. The predominant reaction of the initially formed classical carbonium ions is rearrangement to non-classical isomers. From both bicyclo[2.2.2]octan-2-yl- and *exo*-bicyclo[3.2.1]octan-2-yl-amines, the same unsymmetrical non-classical carbonium ion is produced as has been implicated in the solvolysis of the corresponding toluene-*p*-sulphonates. *endo*-Bicyclo[3.2.1]octan-2-ylamine deamination gives rise to an isomeric symmetrical non-classical carbonium ion, the same one that intervenes in the solvolysis of *endo*-bicyclo-[3.2.1]octan-2-yl toluene-*p*-sulphonate. Symmetrical and unsymmetrical non-classical carbonium ions once formed give product ratios largely independent of their origins or modes of formation although the symmetrical one appears to undergo a small extent of isomerization to the (more stable) unsymmetrical species. These results are contrasted with those obtained from simple carbocyclic systems (without branching at the β-carbon) in which deamination and toluene-*p*-sulphonate solvolysis give characteristically different and unrelated product distributions.

The relationship between so-called non-classical and classical carbonium ions is still only incompletely understood and the usual question is whether intermediates of one sort or the other are involved in a given reaction. There have been very few investigations directed towards the detection of classical precursors of non-classical carbocations where the intermediacy of the latter is purported to be established. The investigations of Corey *et al.*[2] and Berson and Remanick [3] on the norbornyl system illustrate the difficulties in dealing with such a problem using as a probe the chiral relationship between reactants and products.

We have directed our attention to the analogous problem in the bicyclo-octan-2-yl system since here we can use as the probe the structural and diastereoisomeric relationship between reactants and products. This is much more amenable to reproducible precise quantification using high-performance g.l.c.

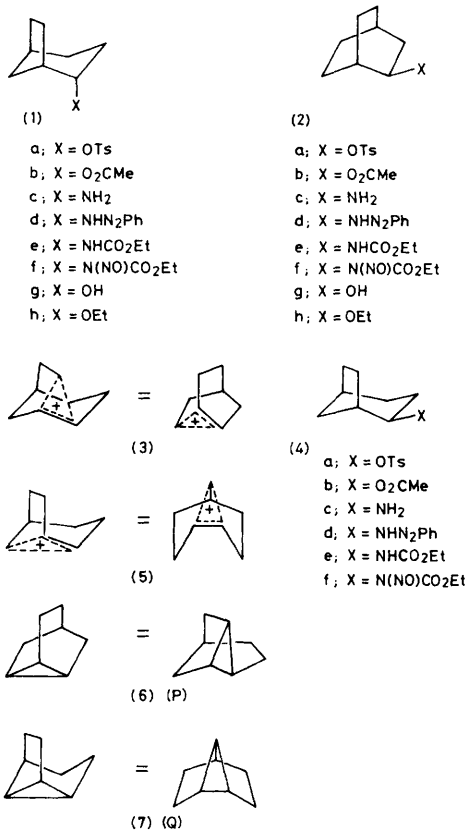
Goering and Fickes [4] have previously investigated the acetolysis of *exo*-bicyclo[3.2.1]octan-2-yl and bicyclo[2.2.2]octan-2-yl toluene-*p*-sulphonate (1a) and (2a), and found that, although the compounds react at different rates, they give identical product mixtures (Table 1). Their results were interpreted in terms of reactions through a single common unsymmetrical non-classical carbonium ion, (3). A corollary of this is that the particular ratio of bicyclo[2.2.2]octan-2-yl to *exo*-bicyclo[3.2.1]octan-2-yl substitution product obtained in each solvent is characteristic of the intermediacy of (3) in that solvent.

Acetolysis of the isomeric toluene-*p*-sulphonate (4a) gives a quite different mixture of products (Table 1). *endo*-Bicyclo-[3.2.1]octan-2-yl acetate (4b) is the single major product and this was interpreted as requiring the main reaction through the symmetrical non-classical carbonium ion (5).[4] The corresponding alcohol and formate are formed in aqueous acetone [4] and formic acid.[5]

Deamination of simple axial and equatorial cyclohexylamines has been investigated previously and compared with results from solvolysis of the corresponding toluene-*p*-sulphonates.[6,7] Deamination gives product ratios which are characteristic of the axial or equatorial disposition of the original amino group in the ground-state conformation of the six-membered carbocycle.

Axial amines give predominant elimination, non-stereoselective substitution, and a substantial proportion of rearrangement.[6b] In contrast, equatorial amines predominantly give unrearranged substitution of mainly retained configuration, a modest yield of elimination, and only very little rearrangement.[6b] These product distributions are not only different from each other, but are also characteristically different from the outcome of solvolysis of the corresponding axial and equatorial toluene-*p*-sulphonates.[6a] Regardless of whether the toluene-*p*-sulphonate group is axial or equatorial in the ground-state conformation of a cyclohexane, solvolysis gives predominant elimination, some substitution with a strong preference for inversion of configuration, and a substantial measure of rearrangement *via* 1,2-hydride shift.

The initially-formed carbonium ion intermediates invoked in these particular earlier comparative investigations of deamination and toluene-*p*-sulphonate solvolysis, however, had no



branching at the carbon β to the reaction site, and the effect of carbonium ion stabilization by carbon hyperconjugation upon their subsequent reactions was, at the beginning of our investigation, largely unexplored.

In our present work, as in other recent investigations,[6b,7] newer deaminative methods have been exploited.[8] They are much more reproducible, reliable, and mechanistically informative than the classical procedure using nitrous acid. Besides the 1-(bicyclo-octyl)-3-phenyltriazenes,[8a,9] we had intended to solvolyse the corresponding *N*-nitrosoamides to facilitate comparisons with other systems.[6b,7,8b] These compounds, however, proved too unstable. White and Dolak had reported that *N*-nitrocarbamates were somewhat more stable.[10] Indeed, we found that, in the bicyclo-octane system, such compounds were too stable, requiring inordinately long solvolysis reaction times. The *N*-nitrosocarbamates [8a,11] were much more suitable, being isolable yet appropriately reactive.

Results

Preparation of Substrates.—Bicyclo[2.2.2]octan-2-ylamine was prepared by catalytic hydrogenation of bicyclo[2.2.2]-octan-2-one oxime (obtained from the ketone [5]) and stored as its hydrochloride.

The usual method [6b] of reducing a cyclohexanone oxime stereoselectively by hydrogenation to give an axial amino group and by lithium or sodium in protic solvents to give the equatorial isomer failed for bicyclo[3.2.1]octan-2-one oxime. Catalytic hydrogenation and sodium in propan-2-ol both gave (1c) and (4c) in roughly equal amounts as also did reductive amination of the ketone with sodium cyanoborohydride and ammonium acetate,[12] and we were unable to separate the isomeric amines, their hydrochlorides, or their acetamides. (The stereoselectivity of these reactions was estimated from the integrated n.m.r. spectra of the acetylated mixtures of amines, the signals due to the methyl groups being just sufficiently resolved.) Stereospecific S_N2' reactions of *exo*-3,4-dihalogenobicyclo[3.2.1]oct-2-ene with retention of relative configuration [13] were exploited for the preparation of *exo*-3-halogenobicyclo[3.2.1]oct-2-en-4-yl azide, which gave *exo*-bicyclo[3.2.1]octan-2-ylamine (1c) upon hydrogenolysis. The *endo*-epimer (2c) was obtained in low yield from *exo*-bicyclo[3.2.1]octan-2-yl toluene-*p*-sulphonate with sodium azide in hexamethylphosphoramide followed by catalytic hydrogenolysis. The corresponding sequence starting from *endo*-bicyclo[3.2.1]octan-2-yl toluene-*p*-sulphonate provided an alternative route to (1c). Since *exo*- and *endo*-bicyclo[3.2.1]-octan-2-yl azides were separable by g.l.c., we were able to confirm their stereochemical purity and, hence, that of the subsequently formed amines. Both amines were stored as their hydrochlorides.

Table 1. Proportions of substitution products (2.2.2) : (*exo*-2) : (*endo*-2) from bicyclo-octyl toluene-*p*-sulphonate solvolysis [a,b]

	Solvent		
Reactant	Formic acid [c]	Acetic acid [d]	80% Aqueous acetone [d]
(1a)		53.9 : 45.5 : 0.6 (85)	56.7 : 43.3 : 0 (100)
(2a)		53.4 : 46.2 : 0.4 (87)	57.2 : 42.8 : 0 (100)
(3a)	1.7 : 2.2 : 96.1 (100)	4.0 : 6.6 : 89.4 (98)	1.0 : 4.1 : 94.9 (100)

[a] (2.2.2) = Bicyclo[2.2.2]octan-2-yl product; *exo*-2 = *exo*-bicyclo-[3.2.1]octan-2-yl product; *endo*-2 = *endo*-bicyclo[3.2.1]octan-2-yl product. [b] All solvents were buffered and the total substitution yield is given in parentheses. [c] Ref. 5, 30 °C, hydrocarbon yield <0.3%. [d] Ref. 4, 49 °C.

Triazenes (1d) and (2d) were prepared from the corresponding amine hydrochlorides by simple modifications to literature methods; [6b] despite repeated attempts, we were unable to prepare (4d). The crystalline ethyl carbamates (1e) and (4e) were prepared in the normal way by reaction of the amines with ethyl chloroformate in the presence of potassium carbonate. An alternative procedure was followed for the preparation of (2e). An aluminium chloride catalysed Diels–Alder reaction of cyclohexa-1,3-diene with ethyl acrylate in benzene gave ethyl bicyclo[2.2.2]oct-2-ene-5-carboxylate in good yield.[14] The ester was converted into the corresponding hydrazide which, with sodium nitrite, gave the acyl azide.[15] This was transformed without isolation into the unsaturated ethyl carbamate by being heated in ethanol. Catalytic hydrogenation gave ethyl *N*-bicyclo[2.2.2]octan-2-ylcarbamate (2e) which was purified by recrystallization. All three ethyl carbamates, which gave satisfactory elemental analysis and were pure by g.l.c., were nitrosated by a solution of dinitrogen tetraoxide in dichloromethane at low temperatures. Sodium acetate was used as the base in the preparation of (2f) and (4f) both of which were obtained as yellow oils after an aqueous work-up and characterised spectroscopically. Anhydrous sodium carbonate was used in the preparation of (1f), which appeared to be appreciably less stable than the other two and was isolated (also as a yellow oil) after a non-aqueous work-up at 0 °C, and solvolysed without further purification.

Product Analysis.—Our general methods for the analysis of bicyclo-octyl esters, alcohols, ethyl ethers, and alkenes have already been described.[16] Additional products were formed in the present investigation. *N*-(Bicyclo-octyl)anilines were

Table 2. Products of deamination of *exo*-bicyclo[3.2.1]octan-2-ylamine [a]

Product [b]	Reaction: Triazene in $MeCO_2H$ [c]	Reaction: Nitrous acid in $MeCO_2H$ [c,d]	Reaction: Nitrosocarbamate in EtOH
3.2.1-ene	10.4	1.7 (11.5)	23.1
2.2.2-ene	4.6	0.2 (2.1)	22.8
(P)	13.9 [e]	21.4 [f] (36.7) [f]	22.9 [f]
exo-2-X			8.6
2.2.2-X			11.4
endo-2-X	20.6	See text	1.6
exo-3-X			0 [g]
endo-3-X			0.1
exo-2-Y	20.3	32.1 (20.9)	3.4
2.2.2-Y	24.9	36.7 (22.4)	4.3
endo-2-Y	5.3	7.9 (6.4)	1.8
exo-3-Y	0 [g]	0 [g]	0 [h]
endo-3-Y	0 [g]	0 [g]	0 [h]
Total recovery (%)	87 ∓ 1	40 ∓ 1 (34)	100 ∓ 2 [i]

[a] Each reaction was carried out twice and 5—7 gas-chromatographic analyses of hydrocarbons, alcohols and, from the nitrosocarbamates, ethers, were obtained from both. For the duplicate nitrous acid and nitrosocarbamate reactions, the results from each were averaged and normalized and the results shown are the mean values from the duplicate runs; for the duplicate triazene reactions, the mean of the average chromatographic analysis results was combined with a single secondary amine determination prior to final normalization. These normalized deamination yields do not include denitrosation from the nitrosocarbamate but the total recovery does. [b] 3.2.1-ene = bicyclo[3.2.1]oct-2-ene; 2.2.2-ene = bicyclo[2.2.2]oct-2-ene; (P) = tricyclo[3.2.1.$0^{2,7}$]octane; (Q) = tricyclo[3.3.0.$0^{2,8}$]octane (see text); X = NHPh from triazene, OH from the nitrous acid deamination, and O_2COEt from the nitrosocarbamate, *i.e.*, the Lewis base derived from the internal nucleophile; Y = O_2CMe from acetic acid and OPh from ethanol, *i.e.*, the Lewis base derived from the solvent. Other abbreviations are given in footnote *a* to Table 1. [c] Contains 0.15 mol dm^{-3} sodium acetate. [d] Results in parentheses for 1.25 molar equivalents of $NaNO_2$ (rather than 4.5, see Experimental section). [e] May include up to 0.6% (Q). [f] May include up to 1% (Q). [g] <0.5%. [h] <0.1%. [i] Includes 1.5% denitrosation.

Table 3. Products of deamination of bicyclo[2.2.2]octan-2-ylamine [a]

Product [b]	Reaction: Triazene in $MeCO_2H$ [c]	Reaction: Nitrous acid in $MeCO_2H$ [c]	Reaction: Nitrosocarbamate in EtOH
3.2.1-ene	8.4	1.1	22.4
2.2.2-ene	9.1	0.9	23.2
(P) [d]	21.9	21.4	23.0
exo-2-X			7.5
2.2.2-X			10.9
endo-2-X	12.7	See text	0
endo-3-X			0.16
exo-3-X			0.14
exo-2-Y	17.7	28.5	5.5
2.2.2-Y	30.2	48.1	6.9
endo-2-Y	0 [e]	0 [e]	0.22
exo-3-Y	0 [f]	0 [f]	0.02
endo-3-Y	0 [f]	0 [f]	0.02
Total recovery (%)	101 ∓ 3	81 ∓ 1	102 ∓ 1 [g]

[a–c] As for Table 2. [d] Results may include up to 1% of (Q). [e] <0.4%. [f] <0.2%. [g] Includes 28 ∓ 1% denitrosation.

Table 4. Products of deamination of *endo*-bicyclo[3.2.1]octan-2-ylamine [a]

Product [b]	Reaction: Nitrous acid in $MeCO_2H$ [c]	Reaction: Nitrosocarbamate in EtOH
3.2.1-ene	0.75	24.3
2.2.2-ene	0.06	0.54
(P)	4.5	3.4
(Q)	14.7	23.1
exo-2-X		2.0
2.2.2-X		0.28
endo-2-X	See text	21.9
exo-3-X		0 [d]
endo-3-X		0.40
exo-2-Y	6.0	1.0
2.2.2-Y	3.7	0.46
endo-2-Y	70.3	22.6
exo-3-Y	0 [f]	0 [e]
endo-3-Y	0 [d]	0.01
Total recovery (%)	65, 82	91 ± 1 [g]

[a–c] As in Table 2. [d] <0.2%. [e] <0.1%. [f] <0.4%. [g] Includes 54.1% denitrosation.

produced in the acetolysis of triazenes and estimated by u.v. spectroscopy after chromatographic separation from other products; ring alkylated anilines were not estimated.[17] Results from nitrous acid deamination are less reproducible than those by other methods and the total recovery in such reactions is invariably low. In particular, the low yields of hydrocarbon that were obtained (compared with results by other methods) indicate that these compounds are not stable to the reaction conditions as was anticipated from earlier work.[6b,7] Unlike the alcohols, which also react with nitrous acid, the hydrocarbons cannot be regenerated by a subsequent step.[7] Furthermore, we were unable to estimate accurately alcohols and acetates together. Consequently, the acetates were reduced to alcohols by treatment of a portion of the total isolated products with lithium aluminium hydride followed by acidification. By this procedure and analysing total alcohols, we lost the distinction between external substitution products in the deamination (initially acetates) and the internal ones (alcohols). It follows, therefore, that the substitution products from the nitrous acid deamination included in Tables 2—4 as acetates (but analysed as alcohols) include some proportion (estimated to be *ca.* 6—8% of the total non-normalized yield) actually obtained initially as alcohols. Although this leads us to over-estimate the total solvent-derived substitution product in this reaction, it appears from the nitrosocarbamate results that the isomer distribution is not seriously distorted.

As anticipated,[18] *N*-nitrosocarbamates underwent some extent of denitrosation during solvolysis, which we were able to measure by g.l.c. and to allow for in the normalization of yields. Ethyl bicyclo-octyl carbonates, which are the internal substitution products from ethyl *N*-nitrosocarbamates, were analysed as the alcohols after hydrolysis of a portion of the reaction mixture. This procedure caused no loss of information since the solvent-derived (external) substitution products were ethyl bicyclo-octyl ethers. Unlike bicyclo-octyl acetates,

these ethyl ethers are separately estimable when present together with bicyclo-octanols.

Two hydrocarbon products were obtained in these deaminations which were not found from solvolysis of bicyclo[3.2.1]-octan-3-yl toluene-*p*-sulphonates.[16] The one of slightly shorter retention time, (P) in Tables 2—4, is a major product from (1c, d, and f) and (2c, d, and f) but formed to a much smaller extent from (4c and f); the other, (Q) in Tables 2—4, is a major product from (4c) and (4f) and possibly not formed at all from (1c, d, and f) and (2c, d, and f). (P) and (Q) were initially assumed to be tricyclic hydrocarbons, (6) and (7), formed by proton loss from the non-classical cations (3) and (5) respectively (or by 1,3-elimination from some carbonium ion precursor). Such processes are analogous to the formation of nortricyclene in the norbornyl system,[19] and of 2-t-butyl-bicyclo[3.1.0]hexane in the deamination type reactions of *trans*-4-t-butylcyclohexylamine.[6b] Subsequently, sufficient (P) was isolated from a large-scale deamination of (2c) to allow structure (6) to be assigned unambiguously.

Identification of Compound (P). Bicyclo[2.2.2]octan-2-ylamine was deaminated by nitrous acid in buffered acetic acid and the product mixture was oxidized using conditions that are known to cleave alkenes but that should leave cyclopropanes unaffected.[6b,20] Alumina chromatography separated unreacted (P) plus bicyclo[2.2.2]octan-2-yl acetate from the alkene oxidation products and other deamination products. Surprisingly, neither the alumina nor a subsequent silica column effected appreciable separation of (P) from bicyclo-[2.2.2]octan-2-yl acetate. However, (P) was isolated as a crystalline solid by preparative g.l.c. and was found to be pure by analytical g.l.c. The proton n.m.r. spectrum showed nothing but high-field signals characteristic only of hydrogens bonded to formally saturated carbons, and the mass spectrum confirmed the C_8H_{12} molecular constitution. Structural possibilities included tricyclo[3.2.1.$0^{2,4}$]octane, tricyclo[3.3.0.$0^{2,8}$]-octane (7), and tricyclo[3.2.1.$0^{2,7}$]octane (6). The symmetry of these compounds requires that their ^{13}C spectra comprise 5, 5, and 6 signals respectively. The proton-decoupled ^{13}C spectrum of (P) appeared to show only five resolved lines but partially-decoupled spectra unambiguously established that what seemed to be one high-field signal was in fact two superimposed: a doublet and a triplet. There were, therefore, six signals (three doublets and three triplets) in the H-coupled spectrum and these are compatible only with structure (6) for compound (P). Furthermore, the ^1H and ^{13}C n.m.r. spectra and mass spectrum of P are in excellent agreement with reported spectra for tricyclo[3.2.1.$0^{2,7}$]octane.[21,22]

Since (4c) and its derivatives are much less easily prepared for a comparable experiment to allow isolation and characterization of (Q), assignment of structure (7) is, strictly, unproven but almost certainly correct.

The complete analytical results are given in Tables 2—4 and compared with other results in Tables 1 and 5.

Discussion

In broad terms, the different deamination methods from a given parent amine in the present investigation gave similar product distributions indicating a similarity in mechanisms. Furthermore, the general mechanism (at least those steps up to and including the formation of carbonium ion intermediates) that was proposed earlier, on the basis of work done principally at Oxford and Bristol, accommodates our present results without drastic modification.[6,23] Identical product distributions from different reactions are powerful evidence for a common (relatively) long-lived intermediate. If, for deamination, this distribution does not include products derived from the internal nucleophile, then any intermediate lives long enough for the internal nucleophile to diffuse away. Deamination of primary alkyl amines by different methods does indeed give virtually identical product ratios with no appreciable quantities of internal substitution product.[23,24] The common intermediate in such reactions is believed to be the primary alkane diazonium ion and an analogous species from cyclopropylamine has been trapped by azide before it has time to eject nitrogen.[25] In contrast, deamination of simple secondary alkyl amines gives substantial recoveries of product derived from the internal nucleophile.[6b,23,24] In the present investigation, we also found yields of internal substitution sufficient to rule out long-lived intermediates and to suggest that the diazo-intermediates, as in the deamination of other secondary alkyl amines, undergo synchronous fragmentation directly to carbonium ions.

Table 5. Proportions of solvent-derived substitution products (2.2.2) : (*exo*-2) : (*endo*-2) from (1c), (2c), and (3c) [a]

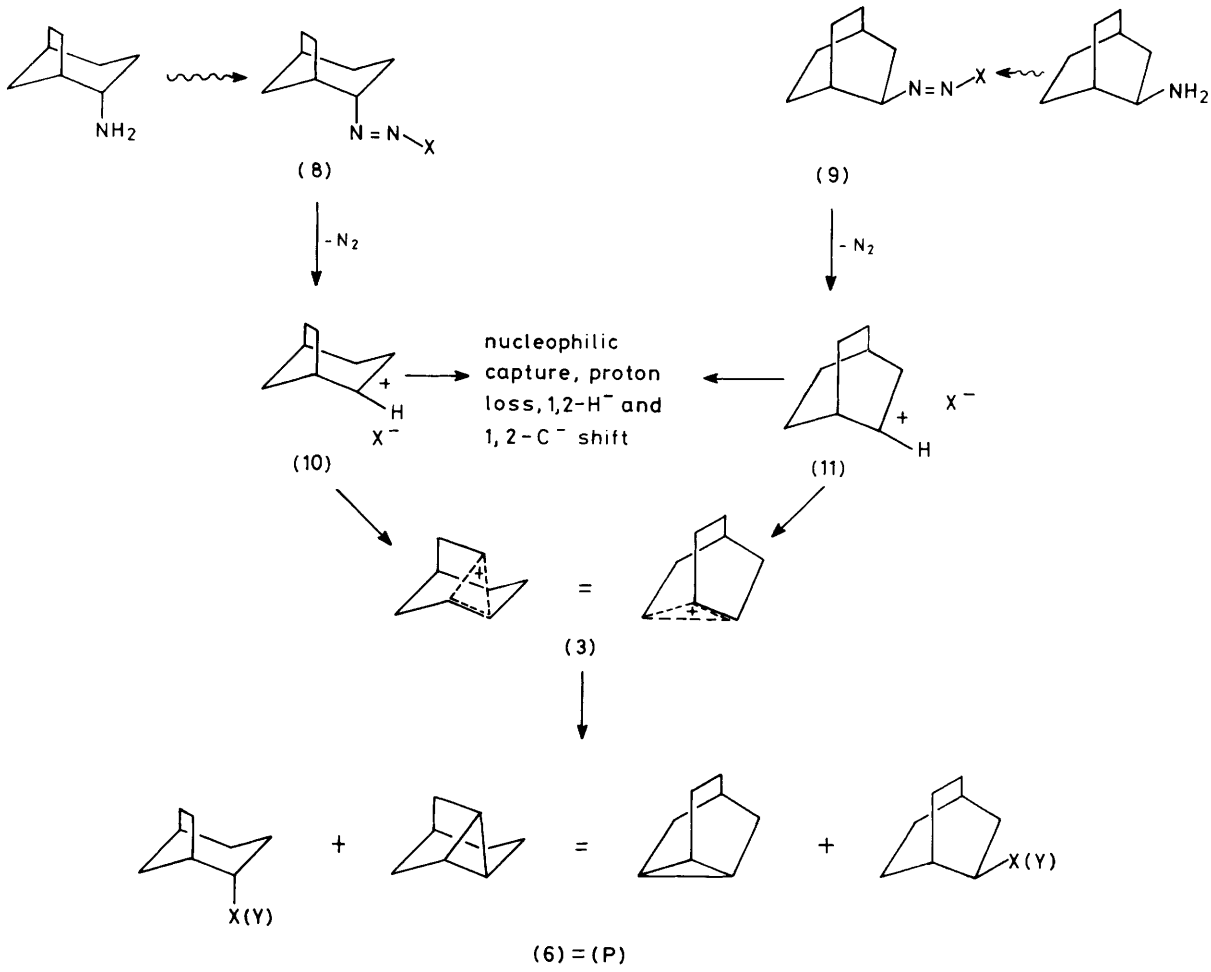
	Reaction		
Reactant	Triazene in $MeCO_2H$	Nitrous acid in $MeCO_2H$	Nitrosocarbamate in EtOH
(1c)	49 : 40 : 10 (51)	48 : 42 : 10 (77)	45 : 36 : 19 (9.5) [53 : 40 : 7 (21.6)] [b]
(2c)	63 : 37 : 0 (48)	63 : 37 : 0 (77) [c]	54 : 44 : 2 (12.6) [59 : 41 : 0 (18.4)] [b]
(4c)		4.5 : 7.5 : 88 (80)	2 : 4 : 94 (24) [1 : 8 : 91 (24)] [b]

[a] See footnotes *a* and *b* of Table 1. [b] Corresponding values for substitution by internal nucleophile. [c] This result is in excellent agreement with the earlier report by Goering and Sloan [30] of (2b) : (1b) in the ratio 64 : 36 determined by i.r. spectroscopy.

Although the products of deamination of a given amine by the different methods are obviously similar rather than identical, too detailed a comparison of results by different methods is probably not warranted in the present study. In the first place, results from the nitrous acid induced reaction are inherently imprecise and should be weighted less in forming any overall view than those from the other two reactions. Secondly, the nitrosocarbamates were solvolysed in ethanol whereas acetic acid was the solvent for the nitrous acid and triazene reactions. Deductions based upon a given deamination method for different amines are, on the other hand, much more soundly based.

As seen from Table 1, products from toluene-*p*-sulphonates (1a) and (2a) are identical in a given solvent and differences from one solvent to another are small. If we may take the common substitution product distribution from toluene-*p*-sulphonates (1a) and (2a) in each solvent as characteristic of the intermediacy of the unsymmetrical non-classical ion (3) in that solvent, we can estimate the extents of reactions of (1c, d, and f) and of (2c, d, and f) which involve this species. In all cases this is very high. There is, nevertheless, a noticeable tendency for (1c, d, and f) to give an excess of (1b), (1g), and (1 h) and for (2c, d, and f) to give an excess of (2b), (2g), and (2 h) over the proportions characteristic of reaction exclusively through (3). This observation is supported by comparison of the hydrocarbon yields from (1c, d, and f) and (to a lesser extent) (2c, d, and f) shown in Tables 2 and 3. The former give more bicyclo[3.2.1]oct-2-ene, and the latter give more bicyclo[2.2.2]oct-2-ene. In other words, both amines show an unmistakable tendency to retain their structural types.

The simplest mechanism that accommodates these results is illustrated in Scheme 1. Initial synchronous fragmentation of



Scheme 1. Principal routes in the deamination of (1c) and (2c); X = internal nucleophile and HY = solvent

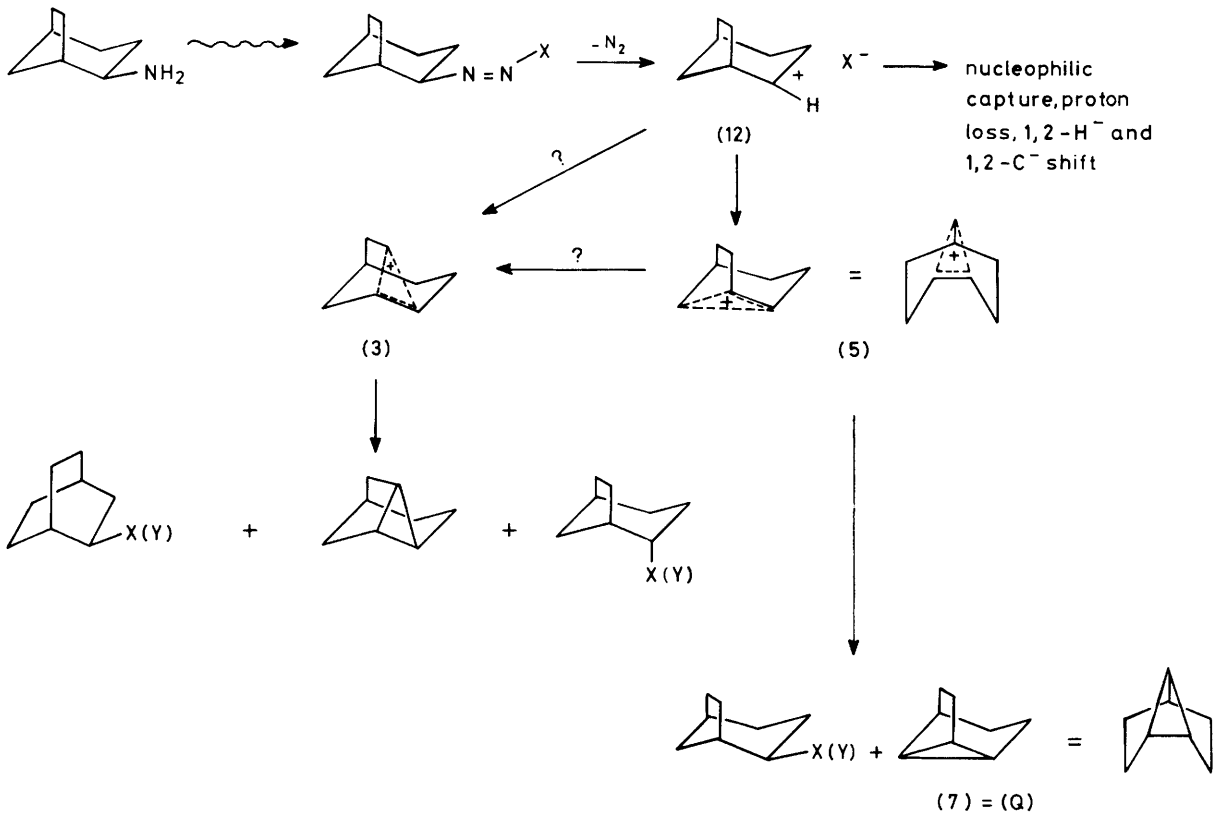
diazo-intermediates (8) and (9) produces classical carbonium ions (10) and (11), which undergo some degree of proton loss and nucleophilic capture with retention of structural identity. The predominant fate of these classical ions is isomerization to the same unsymmetrical non-classical ion (3), which goes on to suffer proton loss to give (6) and nucleophilic capture.

Since internal substitution product is obtained from (3) regardless of which amine is used, the formation of (3) from (10) or (11) must be very fast and its own lifetime very short. However, since the classical precursors of (3) have been intercepted, the conversion of (10) and (11) into (3) in these deaminative routes must be a chemical reaction with an associated standard free-energy barrier. If the unimolecular process were simply a unidirectional molecular vibration or relaxation, bimolecular nucleophilic capture and proton abstraction would be unable to compete.

Two consequences are required of this mechanism; both are found. A classical carbonium ion from (1c, d, and f) should show some vestige of the characteristics of those obtained in the deamination of other axially substituted cyclohexylamines: non-stereoselective nucleophilic capture and thermo-neutral rearrangement by 1,2-hydride shift to other classical carbonium ions. (1c, d, and f) give appreciable yields of solvent-derived *endo*-bicyclo[3.2.1]octan-2-yl substitution products, and (1f) yields a trace of *endo*-bicyclo-[3.2.1]octan-3-yl carbonate. Interestingly, (2f) also gives traces of bicyclo[3.2.1]octan-3-yl substitution products, which requires either sequential carbon and hydrogen shifts within classical carbonium ion intermediates or an equivalent single concerted process. The generation of even trace amounts of bicyclo[3.2.1]octan-3-yl substitution products is difficult to explain by any other current mechanism not involving classical carbonium ions.

The product distributions from the *endo* substrates (4c) and (4f) given in Table 4 are very different from those in Tables 2 and 3. But as far as substitution products are concerned, there is a striking resemblance to the results from the corresponding toluene-*p*-sulphonate (Tables 1 and 5). We see a significantly smaller proportion of hydrocarbon that is predominantly bicyclo[3.2.1]oct-2-ene and (Q), substitution product with only very little loss of structural type, and very little inversion of relative stereochemical configuration.

The mechanism of Scheme 2, analogous to that of Scheme 1, accommodates these results and earlier experimental findings. The difference between classical ion (12) in Scheme 2 and (10) from (1c, d, and f) in Scheme 1 is the location of the counter-ion. Like (10), however, (12) also suffers some small extent of proton loss and direct nucleophilic capture. Both modes are in competition with a very small extent of rearrangement to the classical bicyclo[3.2.1]octan-3-yl and bicyclo-[2.2.2]octan-2-yl carbonium ions, which are required to account for the small yields of bicyclo[3.2.1]octan-3-yl substitution product and bicyclo[2.2.2]oct-2-ene, respectively. The principal reaction of (12), however, is rearrangement to



Scheme 2. Principal routes in the deamination of (4c); X = internal nucleophile and HY = solvent

the symmetrical non-classical carbonium ion (5), which was implicated earlier in the solvolysis of (4a).

A small extent of leakage from either (12) or (5) to (3) is required to account for the small yield of (P) from (4c) and (4f). This small involvement of (3) could also be the source of some of the bicyclo[2.2.2]octan-2-yl and *exo*-bicyclo[3.2.1]-octan-2-yl substitution products.

A corollary of the intermediacy of the classical (12) is that nucleophilic capture will lead to an overall ratio of *exo*-bicyclo[3.2.1]octan-2-yl to bicyclo[2.2.2]octan-2-yl products, which is larger than found from (1c, d, and f) and (2c, d, and f). Our results confirm this expectation and, not surprisingly, this ratio is higher for internal than external substitution.

Experimental

exo-3-*Chloro*-4-*azidobicyclo*[3.2.1]*oct*-2-*ene*.—A suspension of sodium azide (2.0 g, 30.7 mmol) in DMSO (20 cm^3) containing *exo*-3,4-dichlorobicyclo[3.2.1]oct-2-ene (2.0 g, 11.3 mmol) was stirred at room temperature for 5 days.[13] The mixture was then quenched with water (80 cm^3) and extracted three times with ether. The combined ether phase was washed with water then brine, dried (Na_2SO_4), filtered, and evaporated to leave a brown oil (1.59 g, 76.7%) which was distilled using a Kugelrohr, b.p. 90—95 °C at 0.6 Torr; $\tilde{\nu}_{max.}$ (liquid film) 2 180, 2 100, 1 635, 1 450, 1 300, 1 050, 1 010, and 895 cm^{-1}; τ ($CDCl_3$) 3.85 (1 H, d), 6.5 (1 H, d), and 7.2—8.8 (8 H, m).

exo-*Bicyclo*[3.2.1]*octan*-2-*ylamine Hydrochloride*.—(a) A suspension of platinum oxide (0.1 g) in ethanol (150 cm^3) and chloroform (15 cm^3) containing *exo*-3-chloro-4-azidobicyclo-[3.2.1]oct-2-ene (1.5 g, 8.17 mmol) was hydrogenated at 4 atm for 3 days.[26] The solution was filtered and evaporated to leave the amine hydrochloride (1.3 g, 98%), which was recrystallized twice from ethanol–chloroform (1 : 1), m.p. >260 °C (decomp.).

(b) A suspension of sodium azide (2.0 g, 30.7 mmol) in hexamethylphosphoramide (5 cm^3) containing *endo*-bicyclo-[3.2.1]octan-2-yl toluene-*p*-sulphonate (1.7 g, 6.06 mmol) was stirred at room temperature for 3 days. The mixture was then quenched with water (40 cm^3) and extracted three times with ether. The combined ether phase was washed with water then brine, dried (Na_2SO_4), filtered, and evaporated to leave crude *exo*-bicyclo[3.2.1]octan-2-yl azide (0.51 g, 56%); $\tilde{\nu}_{max.}$ (liquid film) 2 050, 1 450, and 1 265 cm^{-1}; τ ($CDCl_3$) 6.5 (1 H, m) and 7.6—9.3 (12 H, m); g.l.c. [50 foot SCOT column, DEGS 100 °C, N_2 (20 p.s.i.)] retention time 6.6 min. A solution of the azide in ethanol (100 cm^3) and chloroform (10 cm^3) was hydrogenated over PtO_2 (0.1 g) at 1 atm for 24 h.[26] The solution was then filtered and evaporated to leave the amine hydrochloride (0.40 g, 93%), m.p. >290 °C (decomp.); $\tilde{\nu}_{max.}$ (KBr) 3 200—2 200, 2 200—1 800, 1 590, 1 459, 1 425, 1 105, 1 060, and 1 040 cm^{-1}; τ ($CDCl_3$) 1.0—2.8 (3 H, br s), 6.5 (1 H, m), and 7.5—8.9 (12 H, m).

endo-*Bicyclo*[3.2.1]*octan*-2-*yl Azide*.—A suspension of sodium azide (4.9 g, 75 mmol) in a solution of *exo*-bicyclo-[3.2.1]octan-2-yl toluene-*p*-sulphonate (4.9 g, 17.5 mmol) in dry hexamethylphosphoramide (27 cm^3) was stirred at room temperature for 7 days. The mixture was then quenched with water (200 cm^3) and extracted three times with ether. The combined ether phase was washed with water then brine, dried (Na_2SO_4), filtered, and evaporated to leave a brown oil (2.5 g). The azide was purified by chromatography on alumina (grade I, neutral), the elution being with light petroleum–

diethyl ether (9 : 1) and Kugelrohr distillation, b.p. 150 °C at 12 Torr, (0.51 g, 19.5%); $\bar{\nu}_{max.}$ (liquid film) 2 090, 1 475, 1 455, 1 255, and 950 cm^{-1}; τ ($CDCl_3$) 6.6 (1 H, m) and 7.3—9.3 (12 H, m); g.l.c. [50 foot SCOT column, DEGS, 100 °C, N_2 (20 p.s.i.)], retention time 7.0 min.

endo-*Bicyclo*[3.2.1]*octan-2-ylamine Hydrochloride*.—A suspension of 10% Pd on charcoal (0.2 g) in ethanol (100 cm^3) and chloroform (10 cm^3) containing *endo*-bicyclo[3.2.1]octan-2-yl azide (0.51 g, 3.4 mmol) was hydrogenated at 1 atm for 24 h.[26] The solution was filtered and evaporated to leave the crude amine hydrochloride (0.55 g, 100%) which was recrystallized from methanol–THF (1 : 1), m.p. >270 °C (decomp.); $\bar{\nu}_{max.}$ (KBr) 3 600—2 350, 2 100—1 850, 1 595, 1 490, 1 455, 1 395, 1 105, 1 035, and 530 cm^{-1}; τ ($CDCl_3$) 1.0—1.6 (3 H, br s), 6.4—6.9 (1 H, m), and 7.3—8.9 (12 H, m).

Bicyclo[2.2.2]*octan-2-ylamine Hydrochloride*.—A suspension of PtO_2 (0.1 g) in ethanol (110 cm^3) and chloroform (10 cm^3) containing bicyclo[2.2.2]octan-2-one oxime (0.61 g, 4.38 mmol), m.p. (re-sublimed) 118—119 °C, was hydrogenated at 3 atm for 2 days.[26] The solution was filtered and evaporated to leave the crude amine hydrochloride (0.75 g) which was recrystallized from ethanol, m.p. >320 °C (decomp.); $\bar{\nu}_{max.}$ ($CHCl_3$) 3 400—2 400, 2 050—1 850, 1 605, 1 505, 1 395, 1 210, and 1 030 cm^{-1}; τ ($CDCl_3$) 1.2—2.5 (3 H, br s), 6.55 (1 H, m), and 7.6—9.2 (12 H, m).

exo-*Bicyclo*[3.2.1]*octan-2-yl Toluene-p-sulphonate*.—A solution of toluene-*p*-sulphonyl chloride (recrystallized, 6.5 g, 23.2 mmol) in dry pyridine (29 cm^3) was added dropwise to an ice-cold solution of *exo*-bicyclo[3.2.1]octan-2-ol (2.9 g, 23.0 mmol) in dry pyridine (14.5 cm^3) over 30 min.[27] The resultant solution was kept at *ca.* −5 °C for 3 days then quenched with cold water (100 cm^3) and extracted three times with ether. The combined ether phase was washed with dilute hydrochloric acid three times, aqueous sodium carbonate, and twice with water. It was then dried (Na_2SO_4), filtered, and evaporated to leave an oil (4.69 g, 72.3%) which was dissolved in light petroleum (b.p. 40—60 °C)–diethyl ether (5 : 1). Crystals formed as the solution was cooled to −70 °C; these were recrystallized twice at low temperatures to give the product; m.p. 50—52 °C (lit.,[4] 51.8—52.8 °C); $\bar{\nu}_{max.}$ (KBr) 1 600, 1 425, 1 385, 1 375, 1 195, 1 185, 1 095, 905, 720, 710, and 660 cm^{-1}; τ ($CDCl_3$) 2.45 (4 H, q), 5.52 (1 H, m), and 7.0—9.3 (15 H, m).

Bicyclo[3.2.1]*octan-2-one*.—A solution of *exo*-bicyclo[3.2.1]-octan-2-ol (17 g, 0.13 mol) in dichloromethane (20 cm^3) was added to a stirred suspension of pyridinium chlorochromate (46.6 g, 0.22 mol) in dichloromethane (270 cm^3).[28] After 90 min, ether (150 cm^3) was added to the tar-like reaction mixture and the solution was decanted. The black residue was washed three more times with ether. The combined ether–dichloromethane solution was percolated through a short Florisil column and evaporated to leave a crude yellow oil. A portion of this oil was dissolved in light petroleum (b.p. 40—60 °C)–diethyl ether (1 : 1) and cooled slowly. Crystals (m.p. 75—80 °C) were deposited at −15 °C which were separated and sublimed, 40 °C at 0.2 Torr, to give colourless waxy crystals, m.p. 121—124 °C (lit.,[29] 127—129 °C); $\bar{\nu}_{max.}$ (CCl_4) 1 720, 1 450, 1 410, 1 240, 1 100, and 810 cm^{-1}; τ ($CDCl_3$) 7.2—7.9 (m).

endo-*Bicyclo*[3.2.1]*octan-2-ol*.[15]—A solution of bicyclo-[3.2.1]octan-2-one (3.9 g, 31.4 mmol) in dry ether (31 cm^3) was added to a mechanically stirred solution of liquid ammonia (*ca.* 300 cm^3, redistilled through NaOH) and dry methanol (52 cm^3) cooled to −78 °C. Lithium (*ca.* 4.5—5.0 g, 0.7 mol, cut into small pieces) which caused the mixture to become deep blue, was added followed, 1 h later, by ammonium chloride (35 g, 0.67 mol). The ammonia was allowed to evaporate overnight then water (300 cm^3) was added to the residue and the solution was extracted four times with ether. The combined ether phase was washed with water and brine, dried (Na_2SO_4), filtered, and evaporated to leave crystals (3.65 g, 92%) which were shown to be the desired alcohol contaminated with about 0.5% of the epimeric *exo*-alcohol and starting ketone; $\bar{\nu}_{max.}$ (KBr) 3 550—3 050, 1 505, 1 070, 1 050, and 1 000 cm^{-1}.

endo-*Bicyclo*[3.2.1]*octan-2-yl Toluene-p-sulphonate*.—This compound was prepared in 70% yield by the above-described Tipson method [27] and recrystallized at low temperatures; m.p. 79.0—80.5 °C (lit.,[30] 80.1—80.8 °C); $\bar{\nu}_{max.}$ (KBr) 1 595, 1 455, 1 345, 1 325, 1 190, 1 175, 1 100, 935, 855, 820, 670, and 560 cm^{-1}; τ ($CDCl_3$) 2.55 (4 H, q), 5.55 (1 H, m), and 7.5—9.0 (15 H, m).

1-*Phenyl*-3-(exo-*bicyclo*[3.2.1]*octan-2-yl*)*triazene*.—*exo*-Bicyclo[3.2.1]octan-2-ylamine hydrochloride (200 mg, 1.24 mmol) was extracted between pentane and freshly prepared potassium hydroxide solution. The organic phase was separated and evaporated under a stream of argon. Anhydrous sodium carbonate (2 g) and acetonitrile (redistilled, 8 cm^3) were added and the suspension was stirred at −10 °C under argon as a pre-cooled solution of benzenediazonium tetrafluoroborate (0.2 g, 1.25 mmol) [6b] in acetonitrile (redistilled, 4 cm^3) was added dropwise. The reaction mixture was stirred for 3 h at −10 °C, then allowed to come to 0 °C before being filtered and extracted five times with ice-cold pentane. The combined pentane phase was evaporated and the residual orange powder was recrystallized three times at low temperature from light petroleum (b.p. 40—60 °C). The product was finally sublimed, 70 °C at 0.1 Torr, m.p. 74—75 °C; $\bar{\nu}_{max.}$ (CCl_4) 3 440, 3 340, 3 050, 1 605, 1 510, 1 470, 1 235, and 695 cm^{-1}; τ (CCl_4) 1.3—2.3 (1 H, br s), 2.45—3.6 (5 H, m), 6.2—6.45 (1 H, m), and 7.5—9.3 (12 H, m) (Found: C, 73.43 H, 8.41; N, 18.36. $C_{14}H_{19}N_3$ requires C, 73.32; H, 8.35; N, 18.33%).

1-*Phenyl*-3-(*bicyclo*[2.2.2]*octan-2-yl*)*triazene*.—Anhydrous sodium carbonate (2.5 g) was added to a stirred solution of bicyclo[2.2.2]octan-2-ylamine hydrochloride (0.252 g, 1.56 mmol) in acetonitrile (10 cm^3). The mixture was stirred for 1 h and then cooled to −30 °C (or lower) after which a pre-cooled solution of benzenediazonium tetrafluoroborate (0.35 g, 1.82 mmol) [5b,31] in acetonitrile (5 cm^3) was added dropwise. After a further 1 h of stirring at −30 °C, the reaction mixture was filtered and extracted five times with pentane. The combined pentane phase was washed with water, percolated through a column of sodium sulphate, and evaporated. One drop of pentane was added to the residual red oil and the mixture was allowed to stand at −15 °C for 3 days, whereupon crystals formed which were separated and washed with further amounts of cold pentane, m.p. 42—44 °C; $\bar{\nu}_{max.}$ (CCl_4) 1 600, 1 500, 1 470, 1 230, 1 130, and 695 cm^{-1}; τ (CCl_4) 1.4—2.2 (1 H, br s), 2.85 (5 H, m), 6.05 (1 H, m), and 7.4—8.8 (12 H, m).

Ethyl N-(exo-*Bicyclo*[3.2.1]*octan-2-yl*)*carbamate*.—Portions of potassium carbonate (1.335 g, 13.2 mmol) and ethyl chloroformate (0.84 g, 7.9 mmol) were alternately added to a stirred slurry of *endo*-bicyclo[3.2.1]octan-2-ylamine hydrochloride (1.04 g, 6.6 mmol) in ether (15 cm^3) and water (0.5 cm^3). The mixture was then heated under reflux for 1.5 h,

cooled, filtered, washed with water and brine, then dried (Na_2SO_4), filtered, and evaporated. The solid residue (1.36 g) was recrystallized twice from light petroleum (b.p. 40—60 °C)–diethyl ether at −70 °C then sublimed (65 °C at 0.1 Torr); m.p. 53.5—55.5 °C; $\tilde{\nu}_{max.}$ (CCl_4) 3 420, 3 330, 1 720, 1 500, 1 220, 1 040, and 1 020 cm^{-1}; τ (CCl_4) 4.95 (1 H, br s), 5.9 (2 H, q), 6.45 (1 H, m), and 7.5—9.1 (15 H, m) (Found: C, 67.06; H, 9.78; N, 6.98. $C_{11}H_{19}NO_2$ requires C, 66.97; H, 9.71; N, 7.10%).

Ethyl N-(endo-*Bicyclo*[3.2.1]*octan*-2-*yl*)*carbamate*.—This compound was prepared as described above for the *exo* isomer: m.p. 78—81 °C; $\tilde{\nu}_{max.}$ (CCl_4) 3 455, 3 360, 1 725, 1 505, 1 225, 1 095, 1 065, and 1 040 cm^{-1}; τ (CCl_4) 5.6 (1 H, br s), 6.05 (2 H, q,) 6.5 (1 H, m), and 7.6—9.3 (15 H, m) (Found: C, 66.86; H, 9.76; N, 7.03%).

Ethyl N-(*Bicyclo*[2.2.2]*octan*-2-*yl*)*carbamate*.—Cyclohexa-1,3-diene (redistilled, 3.5 g, 43.6 mmol), ethyl acrylate (redistilled, 3.0 g, 30 mmol), and anhydrous aluminium trichloride (1.2 g) in dry benzene (70 cm^3) were heated under reflux for 16 h.[14] The mixture was then cooled, quenched with dilute hydrochloric acid, and extracted three times with ether. The combined organic phase was washed with water and brine, dried (Na_2SO_4), filtered, and evaporated to leave a dark brown oil which was Kugelrohr distilled (b.p. 100 °C at 20 Torr; 3.72 g, 69%). This unsaturated bicyclic ester was heated under reflux with hydrazine hydrate (4.13 g) and ethanol (6 cm^3) for 2 days, then cooled and evaporated to give the hydrazide as a yellow solid residue (3.3 g, 95%); τ ($CDCl_3$) 2.1—3.2 (1 H, br s), 3.8 (2 H, m), 5.6—6.4 (2 H, br s), and 7.0—8.9 (9 H, m). Diethyl ether (25 cm^3) was added to a stirred ice-cold solution of the hydrazide in water (30 cm^3). Concentrated hydrochloric acid (2 cm^3) followed, over 15 min, by an aqueous solution of sodium nitrite (1.52 g, 22 mmol), was added.[15] The organic phase was separated and the aqueous solution extracted three times with diethyl ether. The combined ether phase was washed with aqueous sodium carbonate (2M), dried (Na_2SO_4), and filtered; ethanol (15 cm^3) was added and the ether removed by fractional distillation from calcium sulphate. The ethanolic residue was heated under reflux for 4 h, cooled, and evaporated to yield a yellow oil which was redissolved in ethanol (400 cm^3) and hydrogenated over 10% Pd on charcoal (0.3 g) under 1 atm for 24 h. The reaction mixture was filtered and evaporated, and the residue was recrystallized from light petroleum (b.p. 40—60 °C)–diethyl ether then sublimed (60 °C at 0.1 Torr) to give the product as colourless crystals (1.8 g, 30%, based upon ethyl acrylate), m.p. 96.5—98 °C; $\tilde{\nu}_{max.}$ (CCl_4) 3 440, 1 720, 1 495, 1 210, 1 080, and 1015 cm^{-1}; τ (CCl_4) 5.3 (1 H, br s), 6.0 (2 H, q), 6.35 (1 H, m), and 7.7—9.2 (15 H, m) (Found: C, 67.05; H, 9.71; N, 7.16. $C_{11}H_{19}NO_2$ requires C, 66.97; H, 9.71; N, 7.10%).

Ethyl N-*Nitroso*-N-(endo-*bicyclo*[3.2.1]*octan*-2-*yl*)*carbamate*.—Freshly fused sodium acetate (1.74 g, 21.2 mmol) was added to a stirred solution of dinitrogen tetraoxide in anhydrous dichloromethane (12.5 cm^3 containing 15 mmol N_2O_4) cooled to −70 °C under argon followed by the dropwise addition of a solution of ethyl *N*-(*endo*-bicyclo[3.2.1]-octan-2-yl)carbamate (0.31 g, 1.57 mmol) in dichloromethane (redistilled). The temperature of the blue-green solution was allowed to rise slowly to −30 °C when the carbon dioxide–acetone bath was replaced by an ice-water bath. After about 1 h at 0 °C, the golden yellow reaction mixture was washed at 0 °C successively with water, aqueous sodium carbonate, then with water again; the solution was dried ($CaCl_2$) and filtered. Evaporation of the solvent gave a yellow oil which was not purified further (0.332 g, 93%); $\lambda_{max.}$ (C_2H_5OH) 408 and 426 nm.

Ethyl N-*Nitroso*-N-(*bicyclo*[2.2.2]*octan*-2-*yl*)*carbamate*.—This compound was prepared in the manner described above and had the same u.v. absorption spectrum.

Ethyl N-*Nitroso*-N-(exo-*bicyclo*[3.2.1]*octan*-2-*yl*)*carbamate*.—This compound, which is appreciably less stable than the two isomers described above, was made by the same general method with the following alterations: (1) anhydrous sodium carbonate was used as base rather than sodium acetate, and (2) instead of an aqueous work-up, the reaction mixture in dichloromethane at 0 °C was percolated through a column containing anhydrous sodium sulphate and sodium carbonate, the elution being with dichloromethane. The solvent was evaporated at 0 °C and the residual yellow oil was solvolysed immediately.

Preparation of G.l.c. Samples of Bicyclo-octyl Ethyl Ethers.—A stirred suspension of *exo*-bicyclo[3.2.1]octan-3-ol (50 mg, 0.4 mmol), silver oxide (0.225 g, 0.97 mmol), and ethyl iodide (1.25 g, 8 mmol) in diethyl ether (5 cm^3) was heated under reflux for 48 h. The reaction mixture was then filtered and the filtrate passed through a short column of dry alumina, the elution being with light petroleum (b.p. 40—60 °C). After combination of fractions containing the required ether, most of the solvent was evaporated and the residual concentrated solution was used directly for g.l.c. identification. The same procedure was used for the other four bicyclo-octyl ethyl ethers.

Large-scale Deamination of Bicyclo[2.2.2]*octan*-2-*ylamine and Characterization of* (*P*).—Sodium nitrite (11.3 g, 164 mmol) was added portionwise over 1.5 h to a vigorously stirred solution of bicyclo[2.2.2]octan-2-ylamine hydrochloride (8.7 g, 54 mmol) in acetic acid 0.15 molar in potassium acetate (200 cm^3) at 30 °C under a slow stream of argon. The gas flow was passed from the reaction vessel through a carbon dioxide–acetone trap at −78 °C. Effervescence ceased when the addition was about half complete and a precipitate began to be deposited. After a further 2 h, the mixture was diluted with water (100 cm^3) and extracted three times with pentane. The gas trap was also washed out with pentane. The pentane solutions were washed with aqueous sodium carbonate, combined, dried ($CaCl_2$ and K_2CO_3) at 0 °C, filtered, and fractionally distilled slowly [the distillate being tested periodically by g.l.c. to confirm the absence of (P)]. The residue (*ca.* 30 cm^3) was stirred at room temperature with pyridine (200 cm^3), sodium metaperiodate (5.0 g, 23 mmol), potassium permanganate (0.40 g, 2.5 mmol), acetone (100 cm^3), and tetrabutylammonium hydroxide (5 cm^3 of a 40% aqueous solution) for 5 h by which time g.l.c. analysis of a worked up portion confirmed the complete absence of alkenes. The reaction was diluted with water (1 dm^3) and extracted twice with pentane. The combined pentane phase was washed three times with aqueous copper sulphate, twice with aqueous sodium thiosulphate, twice with aqueous sodium hydrogensulphite, and finally with brine. It was dried ($CaCl_2$ and $MgSO_4$), filtered, and slowly fractionally distilled down to about 20 cm^3. This residue was chromatographed on alumina (300 g, activity grade 1) the elution being with pentane and fraction monitoring by g.l.c. Fractions containing (P) (which was not separated from *exo*-bicyclo-[3.2.1]octan-2-yl acetate) were combined, fractionally distilled and re-chromatographed on silica gel (t.l.c. grade). Again, (P) was not separated from *exo*-bicyclo[3.2.1]octan-2-yl acetate. All fractions containing (P) were combined and

Table 6. Analysis conditions and g.l.c. retention times

Compound [a]	Column [b]	Retention time [c] (min)
2.2.2-ene	A	5.3
3.2.1-ene	A	5.5
(P)	A	6.7
(Q)	A	6.9
n-$C_{11}H_{24}$	A	18.5
n-$C_{11}H_{24}$	B	2.5
endo-3-OEt	B	3.9
exo-2-OEt	B	5.1
2.2.2-OEt	B	5.45
endo-2-OEt	B	6.25
exo-3-OEt	B	7.05
n-$C_{15}H_{32}$	B	18.1
endo-3-OH	B	21.9
exo-2-OH	B	27.8
2.2.2-OH	B	29.8
endo-2-OH	B	31.1
exo-3-OH	B	33.8
endo-3-$NHCO_2Et$	C	21.9
exo-3-$NHCO_2Et$	C	26.7
exo-2-$NHCO_2Et$	C	28.2
2.2.2-$NHCO_2Et$	C	29.6
endo-2-$NHCO_2Et$	C	29.6

[a] *endo*-3- = *endo*-bicyclo[3.2.1]octan-3-yl; *exo*-3- = *exo*-bicyclo-[3.2.1]octan-3-yl. See footnotes *a* and *b* in Tables 1 and 2, respectively, for other abbreviations. [b] A = 50 foot SCOT column, Apiezon L, 110 °C; B = 50 foot SCOT column, DEGS, 85 °C; C = 50 foot SCOT column, DEGS, 140 °C. [c] N_2 inlet pressure = 20 p.s.i.

fractionally distilled. Compound (P) (701 mg, 12%) was isolated from the residue (*ca.* 5 cm^3) by preparative g.l.c. (manual 300 μl injections on to a 6 foot × ⅜ inch column packed with 8% Apiezon L on Phase-Prep A; 120 °C; N_2 at 8—10 p.s.i.). The sample used for characterization by n.m.r. [^1H, τ (80 MHz, CD_2Cl_2) 8.0—8.8 (11 H, m) and 9.2—9.5 (1 H, m); ^{13}C, δ (CD_2Cl_2) 30.163 (t), 29.470 (d), 27.179 (t), 16.334 (d + t), and 12.703 p.p.m. (d)] was shown to be pure by analytical g.l.c. In an earlier comparable experiment, a sample of (P) had been obtained for mass spectrometric analysis; low-resolution mode: *m/z* 108 ($M^{\cdot+}$, 51.8%), 93 ($M^{\cdot+}$ − 15, 22.8%), 79 ($M^{\cdot+}$ − 29, 100%), and 66 ($M^{\cdot+}$ −42, 71%); high-resolution mode: *m/z* ($M^{\cdot+}$) 108.0941, C_8H_{12} requires 108.0939.

Solvolysis Media.—1. *Acetolysis medium.* Approximately 250 mg of both n-undecane (distilled, b.p. 57 °C at 2 Torr, pure by g.l.c.) and n-pentadecane (distilled, b.p. 100 °C at 0.3 Torr, pure by g.l.c.) were weighed accurately and, with freshly-fused sodium acetate (1.232 g), made up to 100.0 cm^3 with acetic acid (fractionally distilled from acetic anhydride).

2. *Ethanolysis medium.* Approximately 200 mg of both n-undecane (as above) and n-pentadecane (as above), weighed accurately, were made up to 100.0 cm^3 with spectroscopic-grade absolute ethanol.

Deamination Procedures.—1. *Nitrous acid in acetic acid.* Several procedures were tried including using the free amine and the amine hydrochloride, varying the proportion of sodium nitrite, and carrying out the reaction under argon. In all cases, yields were low and variable. The following procedure was found to give the highest and most reproducible yields and was used for all three isomers. Approximately 100—150 mg of amine hydrochloride were accurately weighed and dissolved in stirred acetolysis medium (5.00 cm^3) under argon

Table 7. Molar response factors (m.r.f.)

Compound	Internal standard	M.r.f.
C_8H_{12}	n-$C_{11}H_{24}$	0.751 [a] (±0.004)
Ethyl bicyclo-octyl ethers	n-$C_{11}H_{24}$	0.909 [b]
Bicyclo-octanols	n-$C_{15}H_{32}$	0.524 [a] (±0.013)
Ethyl *N*-(bicyclo-octyl)carbamates	n-$C_{15}H_{32}$	0.611 [c] (±0.013)

[a] Ref. 16. [b] Calculated.[16] [c] Determined in the present investigation using ethyl (*exo*-bicyclo[3.2.1]octan-3-yl)carbamate.

at 25 °C. Sodium nitrite (3 molar equivalents) was added portionwise over 30 min, then the reaction vessel was stoppered and the reaction mixture under argon was stirred overnight. After about 15 h more sodium nitrite (1.5 molar equivalents) was added 1 h before the reaction was quenched with a solution of $K_3PO_4 \cdot H_2O$ (20.13 g) in water (35 cm^3) then extracted with ether (redistilled). The ether solution was washed with dilute hydrochloric acid and with water. One portion of the ether phase was analysed directly for hydrocarbons; the remainder was heated under reflux with lithium aluminium hydride (*ca.* 0.1 g) for 2 h, cooled, and quenched with dilute hydrochloric acid. The ether phase was separated, washed with brine, and analysed for bicyclo-octanols.

2. *Acetolysis of triazenes.* (i) *For analysis of hydrocarbons and acetates (as alcohols).* Approximately 30—70 mg of triazene were weighed accurately and added portionwise to stirred acetolysis medium (5.00 cm^3) at 25 °C. The stoppered flask was stirred for a further 1 h before being worked up for analysis as described above for the nitrous acid deamination.

(ii) *For determination of* N-*(bicyclo-octyl)anilines.* The method was as for the analysis of acetates and hydrocarbons except that no acid wash of the ether solution of total reaction products was included. Instead, the ether solution was water-washed, dried (Na_2SO_4), and filtered. The ether was evaporated, the total residue was taken up in pentane and chromatographed (Al_2O_3, 30 g, activity grade 2), using pentane as eluant. Those fractions containing *N*-alkylanilines were combined, evaporated, and the residue was made up to a standard volume in spectroscopic grade ethanol for measurement of the u.v. absorbance from which the total secondary amine concentration, and hence yield, were calculated.

3. *Ethanolysis of* N-*nitrosocarbamates.* Approximately 30—50 mg of the freshly prepared nitrosocarbamate were accurately weighed using a Pasteur pipette into ethanolysis medium (5.00 cm^3). The stoppered reaction vessel was maintained at 25 °C for at least 10 reaction half-lives before the contents were divided. One portion (*ca.* 1 cm^3) was analysed directly for hydrocarbons, ethers, and de-nitrosated material. The remainder was heated under reflux for 2.5 h with potassium hydroxide (*ca.* 200 mg), cooled, and extracted between ether (4 cm^3) and brine. The separated ether solution was analysed directly for bicyclo-octanols.

G.l.c. Analysis.—Table 6 shows the conditions used for gas chromatographic product analysis and approximate retention times of the various compounds. In the early stages of the investigation, chart recorder peak areas were measured by precision disc planimeter. Each peak was measured repeatedly until consistent results were obtained. In the later stages, signals were integrated electronically using a Kemtronix Supergrator. A complete analysis of products from one reaction was carried out using both methods and it was

$$\text{M.r.f.} = \frac{\text{signal per mole of compound}}{\text{signal per mole of internal standard}} \quad (1)$$

$$\text{M.r.f.} = \frac{\text{number of carbon atoms per molecule of compound}}{\text{number of carbon atoms per molecule of internal standard}} \quad (2)$$

$$\text{Yield (\%)} = \frac{\text{product signal}}{\text{internal standard signal}} \times \frac{\text{molarity of internal standard}}{\text{molarity of reactant}} \times \frac{100}{\text{m.r.f.}} \quad (3)$$

established that, within experimental error, there was no discrepancy between the two.

Molar Response Factors.—The molar response factors (m.r.f.) (Table 7) of compounds with respect to the internal standard (n-undecane or n-pentadecane) were either measured under the analytical conditions from the defining equation (1), as described previously,[16] or calculated from equation (2). From the definition of m.r.f. in equation (1) it follows that the percentage yield of any product analysed by g.l.c. from a known amount of reactant and using a known amount of internal standard is given by equation (3).

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