Deamination of *endo*- and *exo*-Bicyclo[3.2.1]octan-3-ylamines and their Derivatives

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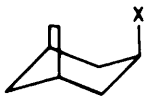
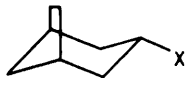
Bicyclo[3.2.1]octan-3-ylamines have been deaminated in acetic acid by nitrous acid and *via* their *N*-phenyltriazenes; their ethyl *N*-nitrosocarbamates have also been solvolysed in ethanol. The *exo*-isomers give mainly unrearranged substitution, some elimination, and very little rearrangement. The unrearranged substitution is derived from both the solvent (the external nucleophile, either acetic acid or ethanol) and the internal nucleophile liberated in the deaminative fragmentation step (water from the nitrous acid reaction, aniline from the triazene, and ethyl carbonate from the nitrosocarbamate). It is of predominantly retained configuration in all three reactions with the solvent, and, as demonstrated in the nitrosocarbamate solvolysis, with the internal nucleophile. The *endo*-isomers give mainly elimination, some unrearranged substitution, and appreciable rearrangement. The solvent-derived unrearranged substitution is with predominant inversion of configuration in all three reactions whereas that from the internal nucleophile, established by the nitrosocarbamate solvolysis, is predominantly with retention. Rearrangement from both *endo*- and *exo*-compounds is best explained in terms of hydride shift from the first formed carbonium ions (in nitrogen-separated complex ion-pairs with hydrogen-bonded anions) produced in the deaminative fragmentation. This gives rearranged classical bicyclo[3.2.1]octan-2-yl carbonium ions which, in competition with nucleophilic capture and proton loss, undergo further stepwise rearrangement to a common unsymmetrical non-classical carbonium ion. The non-classical cation and its classical precursors (which, from *exo*-and *endo*-substrates, differ in the location of the counter-anion) give rise to substitution products derived from solvent and the internal nucleophile. The non-classical carbonium ion also gives some tricyclo[3.2.1.$0^{2,7}$]octane. The high yields of internal substitution products from both *endo*- and *exo*-compounds rule out long lived intermediates such as diazonium ions.

Our studies in the recent past have been directed, on the one hand, towards learning about the relationship between stereochemistry and mechanism in solvolysis reactions, and, on the other, towards studying the phenomenon of non-classical carbonium ions. In both ventures we have used bicyclo-octanes which are bridged cyclohexanes of restricted conformational freedom. The two interests converge in the present report of product analytical results of the solvolytic deamination of *endo*- and *exo*-bicyclo[3.2.1]octan-3-yl compounds (**1a**—**c**) and (**2a**—**c**).[1] They complement our previously reported study of the deamination of *exo*- and *endo*-bicyclo[3.2.1]octan-2-yl and bicyclo[2.2.2]octan-2-yl analogues (**3a**—**c**), (**4a**, **b**), and (**5a**—**c**),[2] and relate to our earlier investigation of the solvolysis of *endo*- and *exo*-bicyclo[3.2.1]octan-3-yl tosylates (**1d**) and (**2d**).[3]

The present results extend earlier investigations[4–6] using 4-t-butylcyclohexylamine derivatives (**6a**—**c**) and (**7a**—**d**) thereby consolidating knowledge regarding the stereochemical and conformational requirements of elimination and substitution in the deamination of cyclohexylamine systems. We also provide yet more evidence that diazonium ions are not significant intermediates in such reactions. Finally, we are able to



(1) a; X = NH_2
b; X = $NHN_2C_6H_5$
c; X = $N(NO)CO_2C_2H_5$
d; X = OTs
e; X = OC_2H_5



(2) a; X = NH_2
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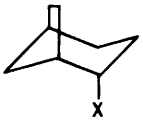
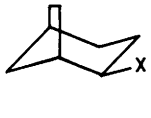
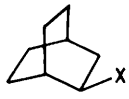
c; X = $N(NO)CO_2C_2H_5$
d; X = OTs
e; X = OC_2H_5



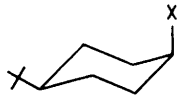
(3) a; X = NH_2
b; X = $NHN_2C_6H_5$
c; X = $N(NO)CO_2C_2H_5$
d; X = OTs
e; X = O_2CCH_3
f; X = $O_2COC_2H_5$



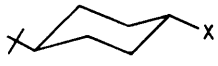
(4) a; X = NH_2
b; X = $N(NO)CO_2C_2H_5$
c; X = O_2CCH_3
d; X = $O_2COC_2H_5$



(5) a; X = NH_2
b; X = $NHN_2C_6H_5$
c; X = $N(NO)CO_2C_2H_5$
d; X = OTs
e; X = O_2CCH_3
f; X = $O_2COC_2H_5$



(6) a; X = NH_2
b; X = $NHN_2C_6H_5$
c; X = $N(NO)COCH_3$
d; X = OTs



(7) a; X = NH_2
b; X = $NHN_2C_6H_5$
c; X = $N(NO)COCH_3$
d; X = $N(NO)COC_3H_7$
e; X = OTs

contribute further to the ongoing debate concerning the nature and origin of non-classical carbonium ions, as some of the product ratios which we measure require the intervention of such intermediates formed by rearrangement of classical carbonium ions.

Methods and Procedures

Our preparative methods are based upon earlier reported work; solvolytic procedures and product analytical techniques using capillary g.l.c. and internal standards have already been described.[2,3] In order to facilitate comparison with earlier results,[4,7] we have carried out direct deaminations of the parent amines (**1a**) and (**2a**) in acetic acid using sodium nitrite to generate nitrous acid, but we weight the results from these reactions less in forming our overall view of the deaminative mechanism than those obtained by newer, indirect, and much more reproducible methods.[8,9] Triazene reactions allowed complete and reproducible analyses of hydrocarbons and external substitution products (those derived from the solvent, in this case, acetic acid). Only the unresolved internal substitution product derived by nucleophilic interception of cationic intermediates at the nitrogen of the internal nucleophile, aniline in these reactions, was measured. No attempt was made to analyse for any ring-alkylated anilines.[10] In order to estimate the bicyclo-octyl acetates which are produced in the nitrous deamination of the parent amines and in the acetolysis of the triazenes, a sample of a reaction mixture was saponified, and the yields of the bicyclo-octanols were then analysed. Possible errors in this indirect method are negligible for the triazene reactions, and those from the nitrous acid deamination in which internal and external substitution products become composited have already been discussed.[2]

Solvolysis of nitrosocarbamates in ethanol produced complex mixtures of hydrocarbons, bicyclo-octyl ethers (derived from the solvent), and bicyclo-octyl ethyl carbonates (derived from the internal nucleophile). The two former compound types were directly estimable. To estimate the last type, samples of reaction mixtures were hydrolysed thereby cleaving the carbonates to corresponding bicyclo-octanols which were in turn analysed. White and Field had reported[9] that methyl carbonate monoanion can fragment to give carbon dioxide and methoxide, $CH_3OCO_2^- \rightarrow CH_3O^- + CO_2$, and CH_3O^- acts as a trap for the carbonium ion. A corresponding reaction in our system would lead to ethoxide which could act as a source of bicyclo-octyl ethyl ether from *internal* nucleophile. We ruled out this reaction mode by showing that *N*-nitroso-*N*-(*exo*-bicyclo[3.2.1]octan-3-yl)carbamate gives no bicyclo-octyl ethyl ethers upon solvolysis in aqueous THF. Consequently, a complete analysis of hydrocarbons and internal and external substitution products was possible from these reactions which constitutes a greater volume of more reliable and reproducible information than is obtained from any of the other reactions of the present investigation.

Results and Discussion

Results of deamination of (**1a**—**c**) and (**2a**—**c**) are given in Tables 1 and 2. The former shows that the *endo*-compounds, with axial amino-functions in their conformational ground states give predominant elimination, only little unrearranged substitution, and substantial yields of rearrangement products. The nitrosocarbamate results show that the small amount of unrearranged substitution product from the internal nucleophile (ethyl carbonate) is predominantly of retained configuration (Ret/Inv = 6.6) whereas that from the solvent ethanol (the external nucleophile) is mainly inverted (Inv/Ret = 5.7). With acetic acid, which is a bidentate external nucleophile in the triazene decomposition, there is an appreciably lower selectivity, but still in favour of inversion of configuration for external substitution at the unrearranged position (Inv/Ret =

Table 1. Products of deamination of *endo*-bicyclo[3.2.1]octan-3-ylamine[a]

	Reaction		
Product[b]	Triazene in CH_3CO_2H[c]	Nitrous acid in CH_3CO_2H[c]	Nitrosocarbamate in C_2H_5OH
3.2.1-ene	50.6	39.5	64.3
2.2.2-ene	0.3	0[d]	0[d]
(**11**)	9.6	8.5	17.1
2.2.2-X			1.0
endo-2-X			1.9
exo-2-X	16.8	See text	1.1
endo-3-X			4.6
exo-3-X			0.7
2.2.2-Y	6.0	10.2	1.8
endo-2-Y	0.6	0[e]	0.4
exo-2-Y	7.4	11.0	2.4
endo-3-Y	3.2	14.7	0.7
exo-3-Y	5.5	16.1	4.0
Total recovery (%)	59—62	46,59	100—102

[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 here are the mean values from the duplicate runs; for the duplicate triazene reactions, the mean of the average chromatographic analysis results were combined with a single secondary amine determination prior to final normalization. These normalized deamination yields do not include denitrosation from the nitrosocarbamate,[2,7] 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; (**11**) = tricyclo[3.2.1.$0^{2,7}$]octane; X = NHC_6H_5 from the triazene, OH from the nitrous acid deamination, and $O_2COC_2H_5$ from the nitrosocarbamate, *i.e.* the Lewis base derived from the internal nucleophile; Y = O_2CCH_3 from acetic acid and OC_2H_5 from ethanol, *i.e.* the Lewis base derived from the solvent. [c] Contains 0.15 mol dm^{-3} sodium acetate. [d] <0.2%. [e] <0.4%.

Table 2. Products of deamination of *exo*-bicyclo[3.2.1]octan-3-ylamine[a]

	Reaction		
Product[b]	Triazene in CH_3CO_2H[c]	Nitrous acid in CH_3CO_2H[c]	Nitrosocarbamate in C_2H_5OH[g]
3.2.1-ene	22.6	13.0	40.6
2.2.2-ene	0[e]	0[e]	0[d]
(**11**)	1.1	1.5	1.1
2.2.2-X			0[e]
endo-2-X			0.2
exo-2-X	13.6	See text	0.2
endo-3-X			6.6
exo-3-X			20.9
2.2.2-Y	1.7	2.0	0.7
endo-2-Y	0.1	0[f]	0.1
exo-2-Y	2.8	3.1	1.0
endo-3-Y	6.2	11.1	2.4
exo-3-Y	51.9	69.3	26.2
Total recovery (%)	80—83	53—56	88—93

[a–d] As Table 1. [e] <0.1. [f] <0.3. [g] Unidentified peaks were also obtained, one in the hydrocarbon and one in the ethyl ether region of the chromatograms. These would constitute 0.3 and 2.3% yields if they were an isomeric hydrocarbon and an isomeric bicyclo-octyl ethyl ether, respectively.

1.7). As noted before,[6] therefore, early views that substitutions from nitrous deaminations of axial cyclohexylamines (in aqueous media) are non-stereoselective are wrong due to the compositing of rearranged and unrearranged, and internal and external-substitution products.

The *exo*-isomers with equatorial ground state amino residues (Table 2) give some elimination, very little rearrangement, and show a strong preference for unrearranged substitution. For all three deaminative methods, unrearranged external (solvent-derived) substitution is with predominant retention of configuration. Reaction of the nitrosocarbamate in ethanol demonstrates that unrearranged internal substitution is also with predominant retention, but to a somewhat lower degree than in the solvent-derived reaction (Ret/Inv = 3.2 for the ethyl carbonates compared with 11 for the ethyl ethers) and, intriguingly, only about half as stereoselective as in the corresponding process for the *endo* (axial) isomer (Ret/Inv = 6.6, see above). Stereoselectivity with a bidentate external (solvent) nucleophile in the acetolysis of the triazene is only slightly lower (Ret/Inv = 8.4) than in ethanolysis of the nitrosocarbamate. The very low measure of rearrangement, and internal and external substitution processes following qualitatively the same steric course (net retention), account for early reports being essentially correct regarding the stereochemistry of substitution in the deamination of equatorial cyclohexylamines despite the use of inadequate analytical methods.

These stereochemical results from the unrearranged substitution mode of solvolytic deamination for both *endo*- and *exo*-compounds rule out relatively long lived free (unsolvated) or symmetrically solvated carbonium ions as significant intermediates, able to react with equal facility with nucleophiles from either side regardless of the origin of the carbonium ion or the nature of the nucleophile. Furthermore, the results are stereospecific to such a degree that there can be no appreciable reaction through early intermediates common to both *exo*- and *endo*-substrates.

The nature of the stereospecificity of these deaminations is also in contrast to that encountered in the solvolysis of cyclohexyl tosylates. Such reactions give unrearranged substitution with a strong preference for inversion of configuration (implicating intimate ion-pairs as the principal intermediates from which substitution products are formed) regardless of the configuration or the conformational ground state equatorial or axial disposition of the leaving group.[3,11] In other words, the steric course of substitution in the solvolysis of *cis*- and *trans* (*exo* or *endo*)-substituted cyclohexyl tosylates, unlike those of the corresponding deaminations, is approximately the same, so substitution product distributions from diastereoisomeric reactants are themselves diastereoisomerically related.

This finding, along with secondary deuterium kinetic isotope effect determinations,[12,13] establish that the *trans*-compound (**7e**), unlike the *cis*-diastereoisomer (**6d**), actually reacts through a non-chair conformation. There is no evidence from the deaminations for invoking any appreciable extent of reaction through non-chair conformers.

Our results in general, therefore, are in broad agreement with those already reported for the 4-t-butylcyclohexylamine system, (**6a**—**c**) and (**7a**—**d**).[5,6] The mechanisms based upon the t-butylcyclohexylamine results which were essentially modifications of ones proposed earlier from deaminations in the decalin system[14] require little modification to accommodate our results as far as the initial generation of the carbonium ions is concerned. We are clearly dealing with very short lived reaction intermediates whose properties and subsequent reactions are grossly affected by the method of their generation. Best estimates from experimental results indicate that the lifetimes of simple secondary carbonium ions in acetic acid are short compared with the time for carbon–carbon bond rotation.[15]

The Putative Intermediacy of Secondary Alkanediazonium Ions.[16]—An important feature of the present results, and of earlier studies of deamination by nitroso-amide and related methods,[5,6,17] is the high ratio of internal–external substitution products, the internal ones being derived from the nucleophilic leaving group in a late step of the deamination sequence. Since the reactions are carried out at low substrate concentrations (0.04—0.2M), these results establish beyond reasonable doubt that the internal nucleophile (the leaving group generated in some heterolytic step) must be captured by an electrophile to give the substitution product before the internal nucleophile can have diffused away. In other words, the results preclude any appreciable extent of reaction *via* a relatively long lived cationic intermediate which would allow diffusional separation. To explain the substantial yields of internal substitution products, there appear to be two alternatives to the proposal of a synchronous fragmentation of the diazo-intermediates giving carbonium ions directly which then react very rapidly with either the solvent or the internal nucleophile. The fragmentation could be stepwise to give diazonium ion and internal nucleophile, then *either* the unimolecular fragmentation of the diazonium ion follows so rapidly that the internal nucleophile does not have time to diffuse away and so may be trapped by the carbonium ion, *or* the diazonium ion itself undergoes very rapid bimolecular reaction with internal nucleophile or with solvent.

A primary alkanediazo-derivative would not be expected to undergo synchronous fragmentation because of the very high instability of the primary alkyl carbonium ion that would be produced. Similarly, the primary alkanediazonium ion formed by a single heterolysis of the potentially two-step deaminative sequence would not be expected to have a facile, unimolecular nitrogen elimination as the second step for the same reason. However, being primary alkyl with an excellent leaving group (molecular nitrogen), it should undergo a very ready S_N2 reaction.

In acetic acid,[5,17] deamination of primary alkyl primary amino-derivatives gives minimal yields of internal substitution product, so we conclude that, indeed, in these cases, the diazo-intermediate does not undergo synchronous fragmentation, and the diazonium ion is sufficiently long lived for the internal nucleophile to diffuse away, so it mainly undergoes solvent-induced bimolecular substitution. Interestingly, White and Field reported[9] that deamination of n-butylamine by methyl nitrosocarbamate decomposition in ethanol gave an appreciable yield of internal substitution product (n-butyl methyl carbonate). It is unclear why the primary oxydiazonium ion in this reaction in ethanol (a medium with a higher dielectric constant than acetic acid) should be so short lived as not to allow diffusion away of the internal nucleophile. A bridgehead tertiary alkanediazo-compound (or diazonium ion) should also be inhibited from undergoing synchronous fragmentation (or unimolecular elimination of nitrogen) by the instability of the carbonium ion which would be produced. In such systems, however, there can be no rear-side S_N2 displacement by either internal or external nucleophiles. Consequently, a much longer lived bridgehead tertiary alkanediazonium ion is anticipated which should be trappable by a dilute nucleophile and, indeed, a diazo-coupling product with β-naphthol was detected in one such investigation.[18] An exactly analogous consideration accounts for the trapping by azide of the (relatively) long lived cyclopropanediazonium ion in the deamination of a cyclopropylamine.[16]

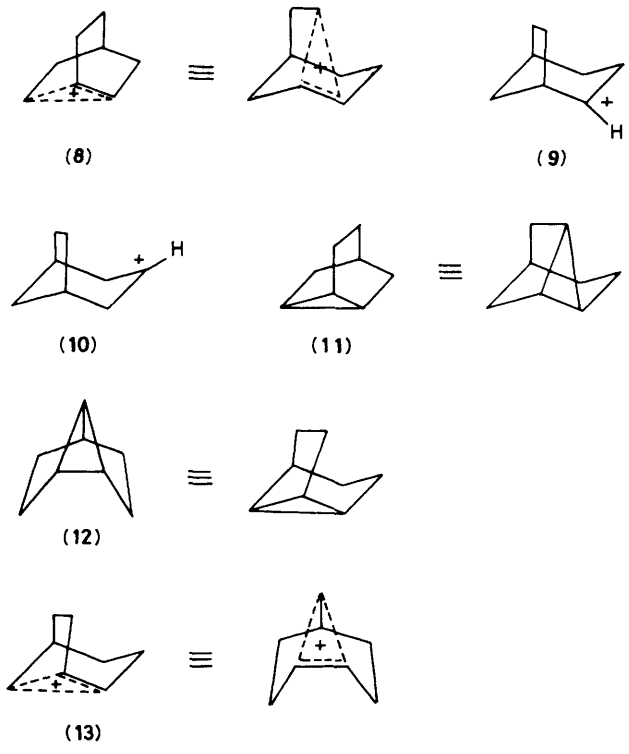
Since a secondary alkanediazonium ion would be a poorer electrophile in an S_N2 reaction than the primary analogue (for steric reasons), it too would not be expected to give internal

substitution product by the S_N2 mechanism, so this alternative may be ruled out for the production of substantial amounts of internal substitution products from (**1c**) and (**6c**). There remains as an alternative to the synchronous fragmentation mechanism, therefore, only the possibility of a stepwise process involving a diazonium ion whose own lifetime prior to its subsequent unimolecular fragmentation is very short compared with the time required for molecules to diffuse apart. The burden of proof for a mechanism involving such intermediates in favour of a synchronous fragmentation by-passing the diazonium ion altogether lies with those who wish to invoke it.[16] It also follows that any feature such as C–C hyperconjugation (σ-bridging) which stabilizes a carbonium ion but which would not be expected to have much effect upon the putative diazonium ion renders even more tenuous the case for invoking the diazonium ion as a significant intermediate.[19]

Rearrangement and the Involvent of Non-classical Carbonium Ions.—There are several questions which need to be addressed in considering the mechanism by which rearrangement products arise in reactions known to involve carbonium ions in the formation of unrearranged products. In the first place, we have to ask whether the rearranged products arise through carbonium processes at all, or by concerted alternatives by-passing high-energy intermediates. The usual test of the involvement of a reaction intermediate is to attempt to generate it from different substrates and establish common reaction product ratios. By this test, and others, the unsymmetrical non-classical bicyclo-octyl carbonium ion (**8**) is a well established species, known to give *exo*-bicyclo[3.2.1]octan-2-yl and bicyclo[2.2.2]octan-2-yl substitution products in the approximate ratio 46:54.[2,20,21]

If (**8**) is implicated in the currently reported reactions, we then have to consider whether it is formed directly from substrate by a single complicated but concerted process of leaving group departure and bond migrations, or whether it is formed *via* a classical carbonium ion precursor by step wise departure of leaving group from substrate and subsequent bond migrations. And finally, if (**8**) does have a classical precursor, is it the bicyclo[3.2.1]octan-2-yl carbonium ion formed by hydride migration from the first-formed simple classical bicyclo-[3.2.1]octan-3-yl cation, or can (**8**) be formed directly from this first formed carbonium ion by a concerted process which by-passes the classical bicyclo[3.2.1]octan-2-yl carbonium ion?

The rearranged substitution product analyses are given and compared with other results in Table 3. Total yields and relative proportions of solvent-derived substitution products are virtually the same from all three *exo* (equatorial) substrates (**2a**—**c**). Furthermore, the relative proportions of these rearrangement products are very similar to those obtained in the acetolysis of (**1d**) and (**2d**), and not very different from the distributions obtained by deamination of amines (**3a**—**c**) and (**5a**—**c**), and solvolysis of bicyclo-octyl tosylates (**3d**) and (**5d**). These results are strong evidence for the major involvement of a common intermediate, the unsymmetrical non-classical carbonium ion (**8**). On the basis of results from *trans*-4-t-butylcyclohexylamine and its derivatives,[6] a 1,2-hydride shift involving only simple secondary classical carbonium ions would lead to solvent-derived *exo*/*endo* bicyclo[3.2.1]octan-2-yl products in the ratio *ca.* 2 in acetic acid rather than 30 from (**2b**) in acetic acid and 9 from (**2c**) in ethanol. And the proportion of bicyclo[2.2.2]octan-2-yl material formed *via* a subsequent 1,2-alkide shift should be very much smaller than is actually found if it were formed from the last intermediate produced in a series of approximately thermoneutral rearrangements of very short lived species. Significantly, however, there is always a higher proportion of *exo*-bicyclo[3.2.1]octan-2-yl compounds among the rearrangement products compared with what is obtained



from reactions exclusively through (**8**).[2,20] This finding indicates that (**8**) is not the only product-forming intermediate. We propose that the small amount of *endo*- and some of the *exo*-bicyclo[3.2.1]octan-2-yl products are formed from a *classical* bicyclo[3.2.1]octan-2-yl carbonium ion (**9**). But the results above do not allow us to distinguish between sequential formation of (**8**) from (**9**), and concerted formation of (**8**) from some other source parallel with the independent formation of (**9**).

The rearrangement results from the *endo* (axial) analogues (**1a**—**c**) are more informative and resolve the above ambiguity in part because the higher proportion of rearrangement (approximately three times that from the *exo*-compounds) allowed a reliable analysis not only of solvent-derived (external) substitution products, but also of those from the internal nucleophile in the case of (**1c**). As seen in Table 3, the proportions of solvent-derived materials from (**1a**—**c**) are very similar indeed to those from the *exo*-isomers (**2a**—**c**) and we propose that they too are formed principally from the same non-classical ion (**8**) plus a small proportion from (**9**). Solvent-derived rearrangement products from deamination of bicyclo[3.2.1]octan-3-ylamines and their derivatives, therefore, are formed non-stereospecifically. This immediately distinguishes these reactions from the deaminations of (**6a**—**c**) and (**7a**—**c**) which give rearranged substitution with some degree of stereospecificity. In this important respect, therefore, the deaminations of (**1a**—**c**) and (**2a**—**c**) have more in common with the solvolyses of the corresponding tosylates (**1d**) and (**2d**). Furthermore, the same solvent-derived product distribution from *endo*- and *exo*-substrates effectively establishes not only (**8**) as a common intermediate but that it is formed by stepwise rather than concerted processes which, from different precursors in the present system, would have led to different product ratios.

The main rearranged internal substitution product from ethanolysis of (**1c**) is *endo*-bicyclo[3.2.1]octan-2-yl ethyl carbonate (**4d**), with the *exo*-diastereoisomer (**3f**) and bicyclo[2.2.2]octan-2-yl ethyl carbonate (**5f**) being formed in

Table 3. Yields and proportions of solvent-derived rearranged substitution products (2.2.2), (*exo*-2), and (*endo*-2) from (**1a**—**c**) and (**2a**—**c**) compared with results from other compounds[a]

Reactant	Solvent[b]	External substitution product: Total[c] (2.2.2) + (*exo*-2) + (*endo*-2)	Proportions[d] (2.2.2) : (*exo*-2) : (*endo*-2)	Reference
(**1a**)	A	21.2	48 : 52 : 0[e]	Present work
(**1b**)	A	14.0	42 : 54 : 4	
(**1c**)	E	4.6	40 : 52 : 8	
		(4.0)	(25) : (28) : (47)[f]	
(**2a**)	A	5.1	39 : 61 : 0[g]	
(**2b**)	A	4.6	37 : 61 : 2	
(**2c**)	E	4.1	38 : 56 : 6	
(**3a**)	A	77	48 : 42 : 10	2
(**3b**)	A	51	49 : 40 : 10	
(**3c**)	E	9.5	45 : 36 : 19	
		(21.6)	(53) : (40) : (7)[f]	
(**5a**)	A	77	63 : 37 : 0	
(**5b**)	A	48	63 : 37 : 0	
(**5c**)	E	12.6	54 : 44 : 2	
		(18.4)	(59) : (41) : (0)[f]	
(**3d**)	A	85	54 : 45 : 0.6	20
(**5d**)	A	87	53 : 46 : 0.4	20
(**1d**)	A	13.8	38 : 58 : 4	3
(**2d**)	A	4.2	45 : 50 : 5	3

[a] See footnotes to Tables 1 and 2 for abbreviations. [b] A = CH_3CO_2H, E = C_2H_5OH. [c] As % of total normalized recovery. [d] Results for (**1a**—**c**) and (**2a**—**c**) calculated from raw chromatographic data rather than from the results in Tables 1 and 2. [e] <4. [f] Results in parentheses are for internal substitution. [g] <5.

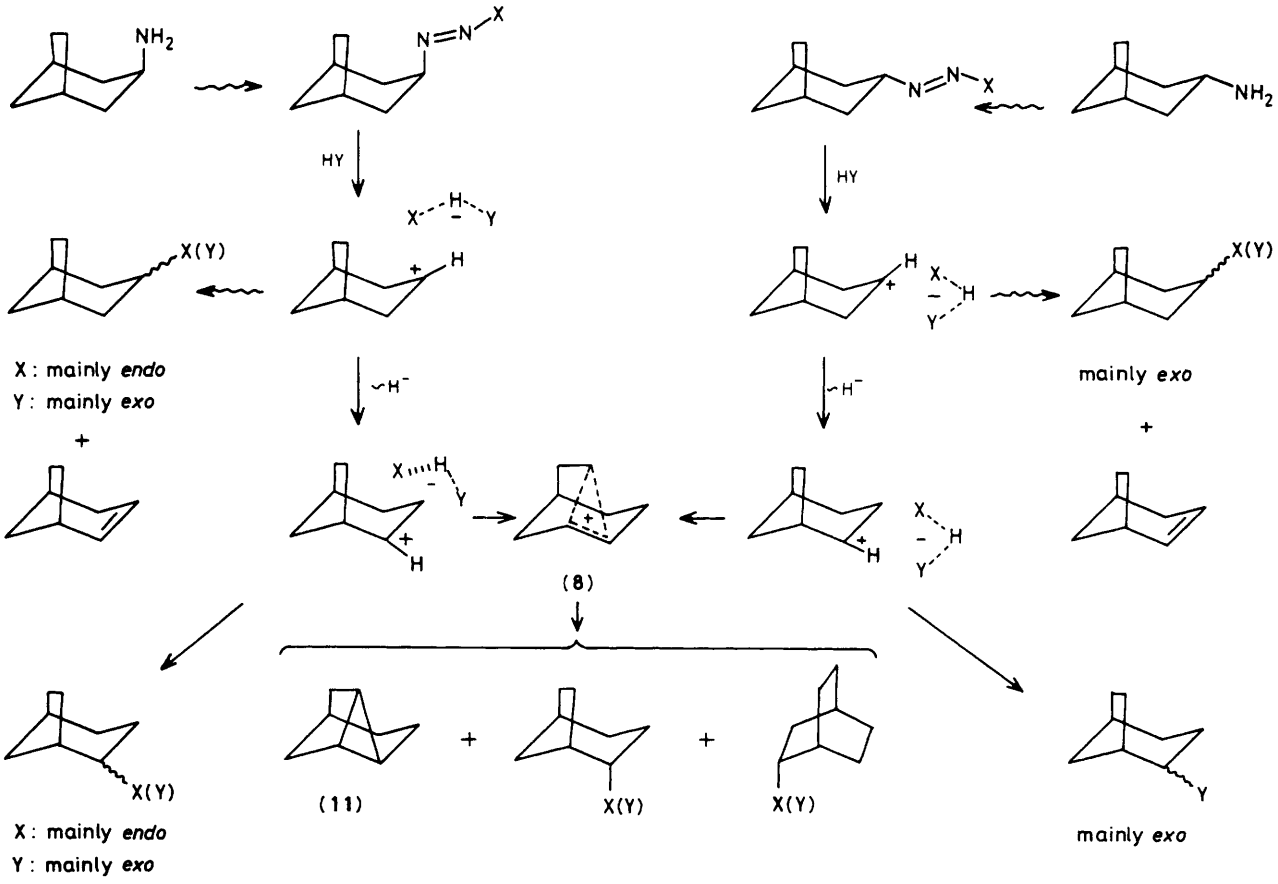
smaller but approximately equal amounts. The most economical explanation of this result, which also accommodates the solvent-derived rearranged substitution product ratios, and is in complete accord with our findings from bicyclo[3.2.1]octan-2-yl and bicyclo[2.2.2]octan-2-ylamine deaminations,[2] is that the classical bicyclo[3.2.1]octan-2-yl carbonium ion (**9**) is the precursor of (**8**). Initial fragmentation[5] of a diazo-intermediate gives the simple classical bicyclo[3.2.1]octan-3-yl carbonium ion (**10**) which undergoes some extent of 1,2-hydride shift to give (**9**). Before the counter-anion diffuses away from the *endo*-face of this classical carbonium ion they undergo some extent of combination to give principally *endo*-bicyclo[3.2.1]octan-2-yl product and a smaller amount of the *exo*-diastereoisomer. Capture of the classical cation by solvent to give mainly *exo*- but some *endo*-bicyclo[3.2.1]octan-2-yl products is less well able to compete with the very rapid rearrangement to the unsymmetrical non-classical carbonium ion (**8**). This in turn is captured to some extent by internal nucleophile, but mainly by solvent to give, in both cases, *exo*-bicyclo[3.2.1]octan-2-yl and bicyclo[2.2.2]octan-2-yl products in the ratio 46:54.

Independent supportive evidence regarding the involvement of non-classical ions comes from a comparison of the proportion of alkene from these bicyclo[3.2.1]octan-3-yl compounds and from the related 4-t-butylcyclohexyl system. Compounds (**1a**, **b**) give smaller yields of elimination in acetic acid than (**6a**, **b**) (39—51% compared with 70—74%). This is unlikely to be due to alkene formation being associated with a greater increase in strain in the bicyclic system since the effect is not found for the diastereoisomers [alkene formation: 13—23% from (**2a**, **b**) compared with 8—14% from (**7a**, **b**, **d**)]. Each alkene may, of course, be derived from both unrearranged and rearranged carbonium ions, but since compounds (**2a**, **b**) and (**7a**, **b**, **d**) give so little rearrangement, the ratio alkene–unrearranged substitution product accurately reflects the partitioning of the first-formed carbonium ion between proton loss and nucleophilic capture. Compounds (**1a**, **b**) and (**6a**, **b**), however, give substantial rearrangement by 1,2-hydride shift and, whereas the rearranged cation from (**6a**, **b**) partitions only between proton loss and nucleophilic capture (as does its unrearranged isomer), the rearranged cation from (**1a**, **b**), in competition with proton loss and nucleophilic capture, may also isomerize to give the non-classical (**8**). As has been observed previously,[21,22] such non-classical cations give very little alkene, hence the low total alkene yield from (**1a**, **b**).

Note, however, that regardless of mechanism, there are approximately equal total amounts of internal and external substitution products from (**1c**) at the rearranged position just as there are at the unrearranged position. Consequently, the rate of the overall rearrangement from the classical bicyclo[3.2.1]octan-3-yl cation must be fast compared with that of diffusion away of the internal nucleophile or, indeed, with that of any major re-orientation of the complex hydrogen-bonded anion with respect to the cation.

If we assume that (**8**) gives (**3f**) and (**5f**) in the ratio 46:54 as is found in other reactions involving (**8**), then we can estimate that (**9**), the *classical* precursor of (**8**) derived from the axial *endo*-substrate (**1c**), gives (**4d**):(**3f**) in the approximate ratio 12:1, *i.e.* strongly stereoselective in favour of retention of configuration. This is in qualitative agreement with the approximate ratio *cis*-(**3**)/*trans*-(**3**) *ca.* 27:1 for the 3-t-butylcyclohexyl acetates in the butyrolysis of (**6c**).[6] A similar calculation for solvent-derived product from the same *classical* bicyclo[3.2.1]octan-2-yl cation but from (**1b**, **c**) indicates a much lower stereoselectivity now in favour of inversion: (**3e**)/(**4c**) *ca.* 2—3. This time agreement with results from (**6b**, **c**) is better than could be expected: *trans*-(**3**)/*cis*-(**3**) *ca.* 2.[6]

Cyclopropane Formation.—Tricyclo[3.2.1.$0^{2,7}$]octane (**11**) is formed stereospecifically and in very substantial yields from (**3a**—**c**) and (**5a**—**c**), and is reasonably derived only from (**8**).[2] The structurally isomeric tricyclo[3.3.0.$0^{2,8}$]octane (**12**) is analogously formed from (**4a**, **b**) and ascribed to proton abstraction from the symmetrical non-classical cation (**13**).[2]



Scheme. Principal routes in the deamination of *endo*- and *exo*-bicyclo[3.2.1]octan-3-ylamines and their derivatives in solvent HY

However, only (**11**) was detected from either *endo*- or *exo*-series in the currently reported deamination study. This is in accord with our mechanism which includes only a single non-classical carbonium ion (**8**) common to *exo*- and *endo*-compounds. The result also establishes that, indeed, cyclopropane formation is by proton loss from the non-classical ion and not by 1,3-elimination from some diazo-precursor since such precursors would not lead to the same product from *exo*- and *endo*-substrates. The substantially higher yield of (**11**) from (**1a**—**c**) parallels the higher yield of rearranged substitution product *via* (**8**) from the *endo*-compounds and supports our view that substitution and hydrocarbon formation routes are not independent.

Mechanism.—The principal features of the mechanisms of deamination of *endo*- and *exo*-bicyclo[3.2.1]octan-3-ylamines and their derivatives are illustrated in the Scheme. These mechanisms, involving specifically solvated ion-pairs, are based upon those proposed earlier for the deamination of 4-t-butylcyclohexylamines.[6] The main difference is the non-stereospecific formation of a common non-classical carbonium ion (**8**) from both *endo*- and *exo*-compounds of the bicyclic series *via* classical precursors. The proximity of the internal nucleophile to the first formed classical carbonium ions accounts for the predominant retention of configuration in the unrearranged internal substitution products from both (**1c**) and (**2c**). The solvent has an easier approach along an equatorial direction to the first formed classical carbonium ions from both *exo*- and *endo*-substrates which leads to retention of configuration from the *exo*-diastereoisomer but inversion from the *endo* in the external substitution product. The substantially higher ratio of internal–external substitution with retention of configuration at the unrearranged position from (**1c**), 6.8 compared with 0.8 from (**2c**), suggests that (**1e**) is derived from (**1c**) *via* (**10**) virtually entirely from the hydrogen-bonded solvent molecule of the complex anion. In contrast, the much easier equatorial approach to the cation from (**2c**) allows external substitution by bulk solvent molecules to compete much more effectively with the internal process. The lower stereoselectivities of solvent-derived products from both *exo*- and *endo*-substrates with acetic acid compared with ethanol is most reasonably ascribed to the difference between bidentate and monodentate nucleophiles.

Experimental

3-Chlorobicyclo[3.2.1]*oct-2-ene.*—*exo*-3,4-Dichlorobicyclo[3.2.1]oct-2-ene[23–25] (12 g, 0.070 mol) was added dropwise to a magnetically stirred suspension of lithium aluminium hydride (3.05 g, 0.080 mol) in anhydrous ether (100 cm^3) at 0 °C. The mixture was then heated under reflux (20 h), cooled to 0 °C, and quenched by the cautious addition of wet ether followed by ice then dilute hydrochloric acid. The product was isolated by ether extraction (three times), desiccation of the solution ($MgSO_4$), filtration, evaporation of the solvent, and fractional distillation under reduced pressure (8.08 g, 81%; b.p. 90 °C at 20 Torr).

Bicyclo[3.2.1]*octan-3-one.*[24,25] Concentrated sulphuric acid (80 cm^3) was added dropwise to an ice-cold magnetically stirred solution of 3-chlorobicyclo[3.2.1]oct-2-ene (7.9 g, 0.055

mol) in dry tetrahydrofuran (25 cm^3). The mixture was stirred for a further 15 h then poured onto ice (250 g) and made alkaline by the cautious addition of aqueous sodium hydroxide. The crude crystalline product was isolated by ether extraction (×3), desiccation of the solution ($MgSO_4$), filtration, and evaporation of the solvent (4.7 g, 68%).

Bicyclo[3.2.1]*octan-3-one Oxime*.—A solution of bicyclo[3.2.1]octan-3-one (16.5 g, 0.133 mol), hydroxylamine hydrochloride (13.9 g, 0.20 mol), sodium acetate (22 g, 0.27 mol), water (170 cm^3), and methanol (70 cm^3) was gently heated under reflux for 15 h. The cooled mixture was extracted with ether (×3) and the combined ether solution was washed with brine, aqueous sodium carbonate, and water (twice), then dried (Na_2SO_4), and filtered. Evaporation of the solvent left an oil which slowly crystallized under vacuum desiccation {15.7 g, 85%; m.p. [from light petroleum (b.p. 60—80 °C)] 88—89 °C; lit.,[25] 96 °C}.

exo-*Bicyclo*[3.2.1]*octan-3-ylamine Hydrochloride*.—Sodium (40 g, 1.7 mol, cut into small pieces) was cautiously added in portions to a solution of bicyclo[3.2.1]octan-3-one oxime (15.7 g, 0.11 mol) in propan-2-ol (350 cm^3; freshly distilled) boiling under reflux.[4,6] The mixture was heated for a further 15 h, cooled, quenched with methanol–water, then extracted with ether (×3). The combined ether phase was back-extracted with dilute hydrochloric acid (×3) then evaporated to give unreacted starting material (7.5 g). Slow evaporation of the acidic solution gave off-white needles of amine hydrochloride [17.3 g, 39%; m.p. (from ethanol) > 280 °C (decomp.); $\bar{\nu}_{max.}$(KBr) 3 500—2 300 (s), 2 100—1 800 (w), 1 570 (m), 1 500 (m), 1 210 (w), 1 110 (m), 1 040 (m), and 450 (m) cm^{-1}; τ(D_2O) 6.6 (1 H, septet) and 7.2—9.2 (12 H, m)].

endo-*Bicyclo*[3.2.1]*octan-3-ylamine Hydrochloride*.—A suspension of platinum(IV) oxide (Adams' catalyst) (0.5 g) in a solution of bicyclo[3.2.1]octan-3-one oxime (2.8 g, 0.02 mol), ethanol (490 cm^3; distilled from magnesium ethoxide), and chloroform (10 cm^3) was shaken under hydrogen (3 atm.) at room temperature for 3 days.[4,6,26] The mixture was filtered and evaporated to leave a red-brown oil which crystallized upon vacuum desiccation [3.1 g, 100%; m.p. (from ethanol–chloroform) 278—285 °C (decomp.); $\bar{\nu}_{max.}$(KBr) 3 300—2 300 (s), 2 050—1 870 (w), 1 570 (m), 1 490 (s), 1 380 (m), 1 070 (s), 945 (m), 825 (m), and 335 (m) cm^{-1}; τ($CDCl_3$) 1.1—2.8 (3 H, s), 6.45 (1 H, m), and 7.4—8.9 (12 H, m)].

1-*Phenyl*-3-(*bicyclo*[3.2.1]*octan*-3-*yl*)*triazenes*.—These compounds were prepared as described previously.[2,6] Compound (**2b**) had m.p. (sublimed, 60—70 °C at 0.1 Torr) 72—73 °C; $\bar{\nu}_{max.}$(CCl_4) 1 605 (m), 1 505 (m), 1 475 (m), 1 270 (s), 1 210 (m), and 695 (m) cm^{-1}; τ(CCl_4) 1.3 (1 H, br s), 2.85 (5 H, m), 6.1 (1 H, m), and 7.3—9.0 (12 H, m). Compound (**1b**) was obtained as an oil which resisted attempts at purification by sublimation or crystallization: $\bar{\nu}_{max.}$ (liquid film) 3 300 (m), 1 600 (m), 1 505 (m), 750 (m), and 695 (m) cm^{-1}; τ(CCl_4) 0.9—1.7 (1 H, s), 2.85 (5 H, m), 6.15 (1 H, m), and 7.0—9.2 (12 H, m).

Ethyl N-*Bicyclo*[3.2.1]*octan*-3-*ylcarbamates*.—These compounds were prepared as described previously.[2] The endo-*isomer* had m.p. (sublimation, 65 °C at 0.1 Torr) 71.5—73 °C; $\bar{\nu}_{max.}$(KBr) 3 380 (m), 1 670 (s), 1 515 (s), 1 240 (s), 1 080 (m), and 1 040 (m) cm^{-1}; τ($CDCl_3$) 5.0 (1 H, br s), 5.85 (2 H, q), 6.15 (1 H, m), and 7.6—9.3 (15 H, m) (Found: C, 67.2; H, 9.7; N, 7.2. $C_{11}H_{19}NO_2$ requires C, 67.0; H, 9.7; N, 7.1%). The exo-*isomer* had m.p. [from light petroleum (b.p. 40—60 °C)] 78.5—80 °C; $\bar{\nu}_{max.}$(CCl_4) 3 400 (w), 3 320 (sh), 1 720 (s), 1 500 (m), 1 210 (m), and 1 060 (m) cm^{-1}; τ(CCl_4) 5.6 (1 H, br s), 6.05 (2 H, q), 6.3 (1 H, m), and 7.6—9.2 (15 H, m) (Found: C, 67.1; H, 9.8; N, 7.3%).

Ethyl N-*Nitroso*-N-(*bicyclo*[3.2.1]*octan*-3-*yl*)*carbamates*. These compounds were prepared as described previously[2] and were not purified. Compound (**1c**) had $\bar{\nu}_{max.}$(CCl_4) 1 740 (s), 1 515 (m), 1 315 (s), 1 140 (s), 1 040 (s), and 965 (m) cm^{-1}; τ(CCl_4) 4.95—5.85 (3 H, m) and 7.5—9.1 (15 H, m); $\lambda_{max.}$(C_2H_5OH) 408 and 426 nm. Compound (**2c**) had $\bar{\nu}_{max.}$(CCl_4) 1 745 (s), 1 520 (s), 1 315 (s), 1 130 (s), 1 030 (m), 945 (m), 905 (m), and 575 (m) cm^{-1}; τ(CCl_4) 4.7—5.4 (1 H, septet), 5.6 (2 H, q), and 7.6—9.2 (15 H, m); $\lambda_{max.}$(C_2H_5OH) 408 and 426 nm.

Solvolysis of N-*Nitroso*-N-(exo-*bicyclo*[3.2.1]*octan*-3-*yl*)*carbamate in* 80% *Aqueous Tetrahydrofuran*.—A solution of (**2c**) (*ca.* 100 mg) in 80% aqueous THF (5 cm^3) was maintained at 40 °C for 10 days. Ether (2 cm^3) was added and the solution was washed once with saturated brine prior to g.l.c. analysis. A minor peak with the retention time corresponding to *exo*-bicyclo[3.2.1]octan-3-yl ethyl ether was just detectable but corresponds to a yield of <0.01% (using the alkene peak as an internal standard).

Other solvolytic and analytical procedures were as described previously.[2,3]

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