DEAMINATION AND RELATED REACTIONS OF SOME BICYCLO-OCTYLAMINES

by

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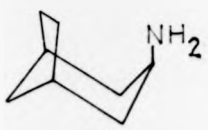
DECLARATION

This thesis has been entirely composed by myself. The work described therein is part of a research programme under the supervision of Dr. H. Maskill. Acknowledgements to results used in this work which came from other parts of the programme have been included in the text of this thesis. In all other aspects the work is my own.

Alan A. Wilson

ABSTRACT

The bicyclo-octylamines (1-5) have been deaminated by the nitrous acid method and by the decomposition of their nitrosocarbamates in ethanol. In addition, the amines (1-4) were deaminated by the decomposition of their triazenes in acetic acid. Complete quantitative analyses of the products



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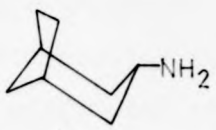

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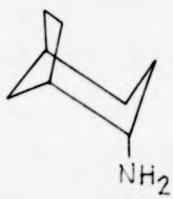

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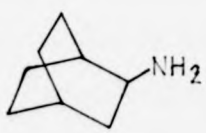

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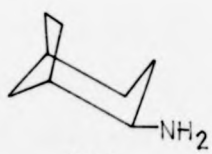

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from the nitrosocarbamate decompositions were obtained using analytical capillary column g.l.c. techniques developed by Banks.[1] Incomplete information was obtained from the nitrous acid and triazene decompositions.

The results from (1) and (2) were very different from the solvolysis products of the corresponding tosylates reported earlier by Banks[1] but broadly in agreement with the results from cis- and trans-4-t-butylcyclohexylamines.[2]

The endo-amine (1) gave large amounts of elimination and hydride shift products. At the unrearranged position, internal substitution to give R-X (Scheme) occurred with predominant retention of configuration. Unrearranged external substitution product, R-Y, was mainly of inverted configuration.

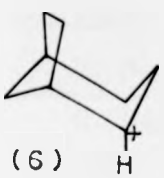
The exo-amine (2) gave less elimination and

$$R\text{-}NH_2 \rightsquigarrow \left[R\text{-}N{=}N\text{-}X\right] \xrightarrow{HY} R\text{-}X, R\text{-}Y, \text{ and hydrocarbon}$$

Scheme

rearrangement. Both internal and external substitution occurred with predominant retention of configuration at the unrearranged position. There was some evidence that this amine reacted, to a small extent, through a non-chair conformer. The model proposed by Maskill and Whiting[2] involving an ion pair separated by molecular nitrogen was used, with minor alterations, to accommodate these results.

The products of deamination of amines (3) and (4) were similar but not identical and included large amounts of hydrocarbon and products derived from carbon migration. However, both amines showed a tendency to maintain their structural identity when compared with the products of solvolysis of the corresponding tosylates.[3] The results suggest initial formation of the classical carbonium ions (6) and (7) from (3) and (4) respectively followed by relaxation to a common non-classical ion (8).



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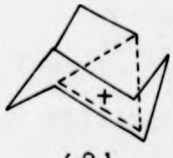

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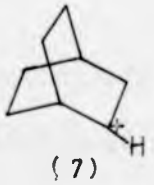
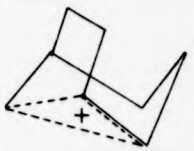


(7)

Deamination of (5) gave a very different distribution of products from (3) and (4). Very little rearranged product was observed and most of the substitution was with retention of configuration although a small but significant amount was inverted.

Initial formation of a classical carbonium ion, with nominal structure (6), followed by relaxation to the non-classical ion (9) is proposed as a possible mechanism. The different fates



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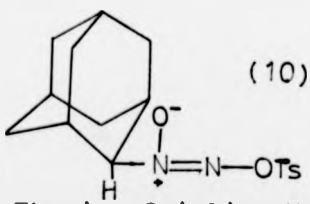
of the initially formed carbonium ions from (5) and (3) are thought to be due to the different positions of the counter-ions.

The mode of decomposition of adamant-2-yl-ONN-azoxy-tosylate (10) has been investigated as a link between deamination and tosylate solvolysis which would be amenable to kinetic studies. Preliminary results suggested that the mechanism is ionic, the activated complex having carbonium ion character. Isolation of 2-adamantyl tosylate from the ethanolysis of (10) is presented as evidence for internal return of tosylate anion in solvolysis of alkyl tosylates.



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3. H. R. Goering and G. R. Fickes, J.Amer.Chem.Soc., 1968, 90, 2848; 2856; 2862.

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CHAPTER 1

INTRODUCTION

An understanding of the detailed nature of reactive intermediates, especially those which collectively may be termed carbonium ions, has long been pursued by organic chemists. Solvolysis reactions in particular have provided much information and led to the development of such concepts as ion-pairs,[1] non-classical ions[2] and neighbouring group participation.[3] No less important an area of study for the understanding of the properties of carbonium ions is deamination reactions. Experimental difficulties and a certain lack of synthetic utility has meant that the nature of the carbonium ions derived from deamination reactions has not recently been probed as deeply or as subtly as their solvolysis counterparts. Nevertheless a comparison of these two methods of generating carbonium ions has improved our understanding of both sets of reactions.

The first part of this work, the study of

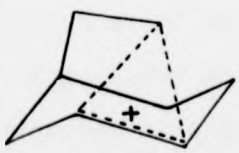
(1)

a; $R_1 = NH_2$, $R_2 = H$
b; $R_1 = H$, $R_2 = NH_2$
c; $R_1 = OTs$, $R_2 = H$
d; $R_1 = H$, $R_2 = OTs$

the deamination of (1a) and (1b) and their derivatives by product analysis, was designed to partner the work of Dr. R. M. Banks[4] on the solvolysis of the corresponding

p-toluenesulphonates (1c) and (1d). She showed that β-hydrogen participation is important in the solvolysis of both isomers and that the exo-isomer (1c) reacts through a non-chair (boat) conformation. Nitrogen is a far better leaving group than p-toluenesulphonate so it is possible that the ground-state conformation will play a more important role in the deamination reactions of (1a).

This work closely parallels the deamination of cis- and trans-4-t-butylcyclohexylamines which was investigated by Maskill[5] and Whiting[6] but has an interesting side-line. The carbonium ions formed by 1,2 hydride shift from (1a) and (1b) may be stabilised by σ participation resulting in non-classical ions (2) or (3). Such ions, which are the next higher homologues



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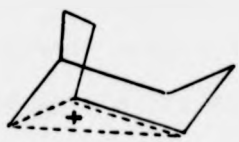
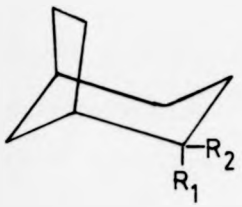


(3)

of the non-classical norbornyl ion, have been invoked as intermediates in the solvolysis reactions of (4c), (4d) and (5b).[7,8]

The second part of this work has been an investigation of the deamination reactions of (4a), (4b) and (5a). These reactions might be expected to provide direct



(4)

(5)

a; R_1 = H, R_2 = NH_2

b; R_1 = NH_2, R_2 = H

c; R_1 = H, R_2 = OTs

d; R_1 = OTs, R_2 = H

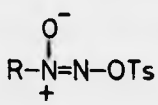
a; X = NH_2

b; X = OTs

access to species (2) and (3) in which case a comparison of non-classical ions from deamination and from solvolysis reactions might be made.

Three methods of deamination were employed, namely the "nitrous acid" method, the "triazene" method and the "nitrosocarbamate" method. The latter is a variation of the "nitrosoamide" method more commonly met in the literature.[9]

Thirdly, the desire to obtain some kinetic data on deamination reactions and the reports by Stevens[10] and White[11] that azoxytosylates (6) were stable



(6)

crystalline compounds led to a preliminary investigation of the properties of (6) with R = 2-adamantyl. It was hoped that such compounds might react in the same manner as the diazo-intermediates formed in deamination reactions.

It has been stated[12] that the failure to observe any

hydride shift products in a reaction involving an electron deficient intermediate is a consequence of inadequate experimental techniques and not because there is no product to be observed. To avoid such criticism in this work 50' SCOT capillary g.l.c. columns have been used in the detection, identification and quantification of reaction products and it was demonstrated that all probable reaction products from the corresponding tosylates could be separately analysed.

A short review of some aspects of deamination reactions is presented in Chapter 2 along with a review of the other pertinent work done on cyclohexyl systems. Chapter 3 describes the methods used to synthesise the derivatives of the five isomeric bicyclo-octylamines and the azoxytosylate. A discussion of the results from the product analyses of the deamination reactions is given in Chapter 4. The preliminary results from the azoxytosylate work are also given and examined in this section. The experimental techniques used, including analytical g.l.c., and deamination procedures are presented in Chapter 5 as well as the procedures required to prepare the compounds. Finally, the complete product analysis results and kinetic data are tabulated in the Appendices.

Abbreviations of compounds' names have been used throughout this work since to refer constantly to some compounds by their full name or by a number is either cumbersome or confusing. Table I gives a list of the abbreviations used.

TABLE I

Abbreviations

2-ene	bicyclo[2,2,2]oct-2-ene
3-ene	bicyclo[3,2,1]oct-2-ene
P,Q	unidentified hydrocarbons believed to be tricyclic with a 3-membered ring
endo-3-	endo-bicyclo[3,2,1]octan-3-yl
exo-3-	exo-bicyclo[3,2,1]octan-3-yl
endo-2-	endo-bicyclo[3,2,1]octan-2-yl
exo-2-	exo-bicyclo[3,2,1]octan-2-yl
[2,2,2]-	bicyclo[2,2,2]octan-2-yl
2° amine	N-(bicyclo-octyl)anilines
carbamate	ethyl bicyclo-octylcarbamate
tosyl chloride	p-toluenesulphonyl chloride
tosylate	p-toluenesulphonate

-OEt = ethyl ether

$-OCO_2Et$ = ethyl carbonate

-OAc = acetate

CHAPTER 2

Some previous work

DEAMINATION REACTIONS

Methods of deamination

In the past 25 years the deamination reactions of primary aliphatic amines have attracted much interest from both mechanistic and synthetic organic chemists. During this period new methods of deamination have been developed which have largely superseded the classical nitrous acid method used since 1848.[13] Some methods of deamination, pertinent to this work, are shown below:

(i) the reaction of nitrous acid with amines[14];

$$R\text{-}NH_2 + NaNO_2 + H^+ \rightarrow R\text{-}\underset{H}{\overset{N=O}{N}} \rightarrow [\,R\text{-}N{=}N\text{-}OH] \rightarrow \text{products}$$

(ii) the decomposition of N-alkyl-N-nitrosoamides[15] or nitrosocarbamates[16];

$$R\text{-}\underset{\underset{O}{\|}}{\overset{N=O}{\overset{|}{N}}}\text{-}\overset{}{C}\text{-}R' \rightarrow [\,R\text{-}N{=}N\text{-}O\text{-}\overset{O}{\overset{\|}{C}}\text{-}R'] \rightarrow \text{products}$$

(iii) the acid catalysed decomposition of 1-aryl-3-alkyltriazenes[17];

$$R\text{-}\overset{H}{\overset{|}{N}}\text{-}N{=}N\text{-}Ar \rightleftharpoons R\text{-}N{=}N\text{-}\overset{H}{\overset{|}{N}}\text{-}Ar \xrightarrow{H^+} [\,R\text{-}N{=}N\text{-}\overset{+}{N}H_2\text{-}Ar] \rightarrow \text{products}$$

Many workers have shown that every method involves a similar diazo-intermediate; the subject has been reviewed by several workers in the field.[18] Much research has been done to unravel the processes which occur after the formation of the diazo-intermediate. Since formation of this species is usually rate determining[15] kinetic studies have yielded little information. The most important tool used by chemists to

investigate deamination reactions has been product analysis.

The development of the reaction mechanism

By analogy to aromatic systems it was first thought that the aliphatic diazonium ion was an intermediate in the deamination reaction but the products were derived from a carbonium ion.[19] Some textbooks still invoke this model of

$$[R\text{-}N{=}N\text{-}OH] \rightarrow [R\text{-}\overset{+}{N}{\equiv}N] \xrightarrow{-N_2} [R^{+}] \rightarrow \text{products}$$

deamination.[20] Since then this model has undergone constant refinement. Analysis of the products from deamination reactions soon impressed that this simple model was inadequate. It was found that product fallout from other reactions generating carbonium ions such as solvolysis of alkyl halides and arene-sulphonates (in the limiting case of the SN_1 mechanism) were different from deamination reactions of the same analogue.[21]

In order to account for the extensive rearrangement accompanying deamination reactions the concept of a "hot" carbonium ion evolved.[22] These "high-energy" ions were believed to differ from ions formed in solvolysis reactions by the lesser amount of solvation experienced by the ions or by being vibrationally excited.[23] Although this refined model was sufficiently vague to explain many results it was unable to explain why diastereoisomeric amines in cyclic and acyclic systems yield different products.[21,24] The "hot" carbonium ion model predicts the same carbonium ion from such amines.

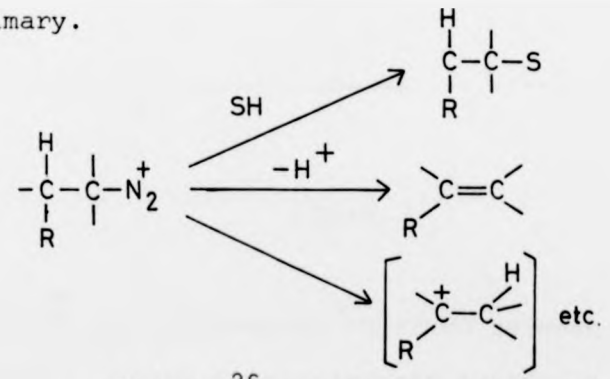
The hypothesis that the alkyldiazonium ion was the

last common intermediate in deamination reactions was invoked to explain the stereochemistry of some reactions;

$$R\text{-}NH_2 \rightarrow [R\text{-}\overset{+}{N}_2] \xrightarrow{-N_2} [R^+] \rightarrow \text{products}$$

$$SH \mid SN_2 \quad R\text{-}S$$

an SN_2 displacement of nitrogen was invoked to account for the amount of inverted product obtained, for example, from the reaction of optically active 1-aminobutane-1-d with nitrous acid in acetic acid, (69% inversion).[25] Streitwieser[31] proposed a model in which all products are directly derived from the intermediate diazonium ion even when the alkyl group is not primary.



Huisgen[26] noted that elimination of nitrogen from an sp^3 hybridised carbon atom is probably the only exothermic ionisation of this type and hence the energy scale covering the reactions of a diazonium ion is compressed when compared with that of a solvolysis reaction. In effect this is a restatement of the reactivity-selectivity principle (RSP)[27] which says that the selectivity of a chemical species (X) decreases as the reactivity of (X) increases. Rappoport[28] has recently discussed the RSP. A mode of reaction which is

unimportant in solvolysis reactions may be important therefore in deamination reactions (Fig.1). When ground state conformational control is invoked,[29] this model is capable of explaining

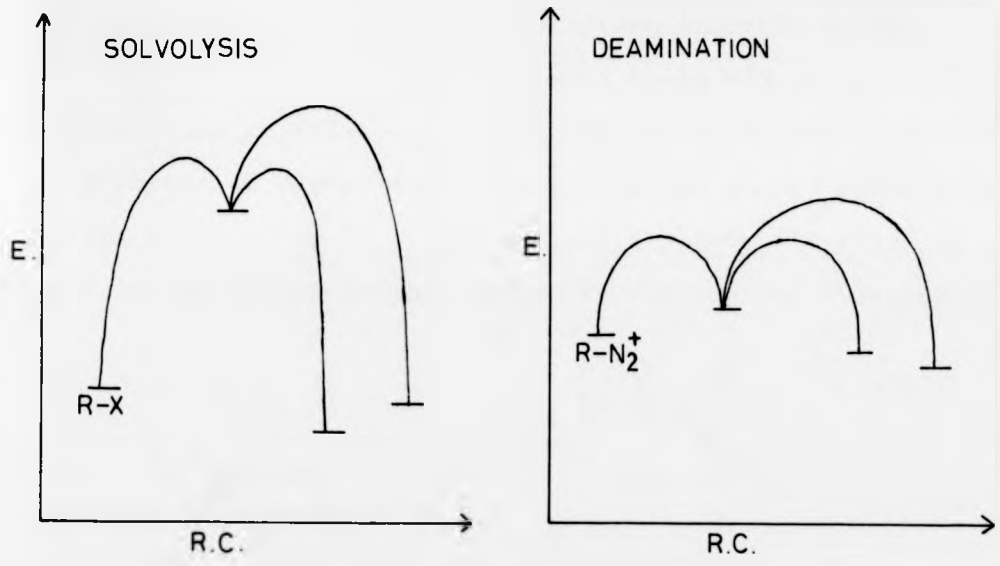
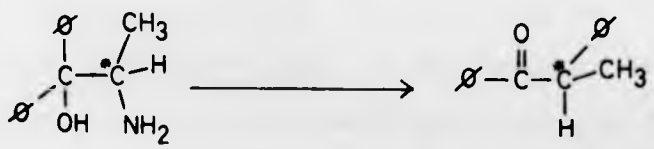


Figure 1

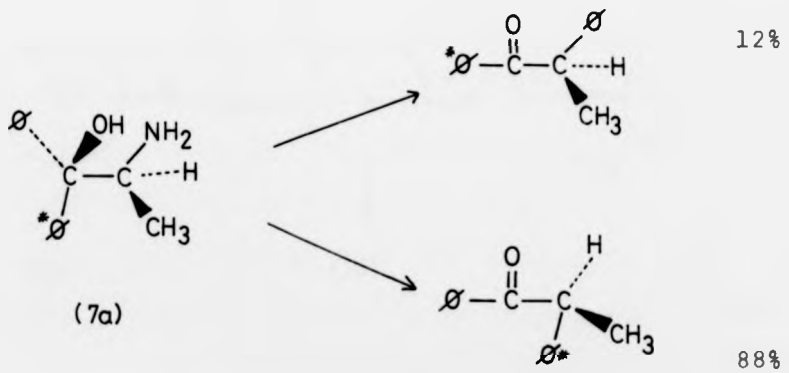
many of the differences observed between diastereoisomeric amines c.f. the Curtin-Hammett principle.

Objections to this model were soon raised[14b] on the basis of results obtained mainly from optically active amines, e.g. Bernstein and Whitmore[30] found that 1,1-diphenyl-2-aminopropanol (7) gave the ketone (8) with 88% inversion.

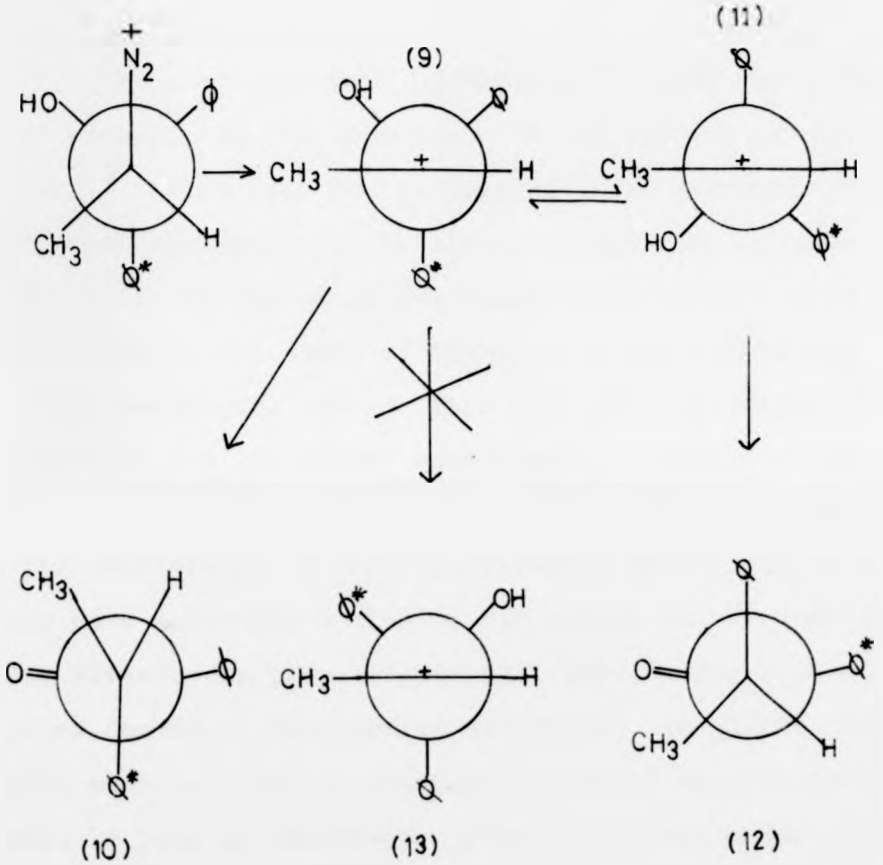


(7) (8)

Streitwieser[31] claimed this result supported his concerted rearrangement model but neglected to rationalise the formation of the 12% of product with retained configuration. Collins and coworkers[32] labelled one of the phenyl groups in (7) with ^{14}C thus producing two diastereoisomeric amines. Deamination of one of these (7a) gave again 88% of ketone with inverted configuration. However, the 12% of retained product was a result of migration of the unlabelled phenyl group only and the inverted product came exclusively from migration of the labelled phenyl group. These results can be explained by



the formation of a short lived carbonium ion (9) which either rearranges to (10) or has time to rotate slightly to give conformer (11) which results in ketone (12). The absence of unlabelled inverted phenyl migration product indicates that the carbonium ion does not live long enough for the larger rotation about the carbon-carbon bond, to give conformer (13), to occur. Huisgen[15] has pointed out that, on the basis of the P.E. diagram (Figure 1) and the Hammond postulate, at the transition state of a reacting diazonium ion the positive charge on the carbon atom is so small that help from neighbouring groups is unlikely.

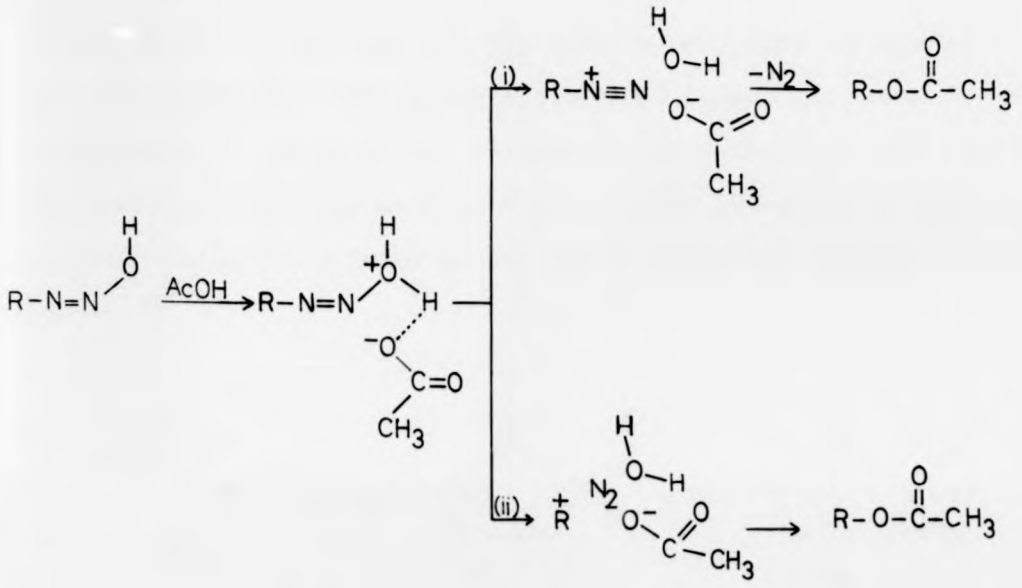


The relevance of the work by Collins to the present work is attenuated by the presence of the β-hydroxyl group in (7a) which must influence the stereochemistry of the reaction somewhat. Nevertheless the fact that migration of the phenyl group can occur from the same side of the molecule as the departing nitrogen molecule does mean that nitrogen must have departed first.

The role of the counter-ion

The classical work of Winstein[33] (from the early 1950's) established the importance of ion pairing in solvolysis reactions.[34] This work led indirectly to an awareness of the role of the counter-ion in deamination reactions and was reinforced by the advent of new deamination methods which were more amenable to the study of the role of the counter-ion. The early work developing the ion pair hypothesis in deamination reactions and the concurrent development of modern methods of deamination have been reviewed.[5a,9,18a,b] With the realisation that the counter-ion ^{-}X may significantly affect the product fallout came an understanding of the effect of the solvent. Solvent effects can play an important part in the life of the ion pairs formed in deamination reactions; in polar, nucleophilic solvents such as water or alcoholic mixtures the counter-ion does not seem to play as important a role as in less polar solvents such as acetic acid or hexane.[35] In a highly polar medium the forces of attraction between cation and counter-ion may be weakened by solvation and competing processes such as solvent attack and ion pair dissociation may dominate. The acidity of the solvent is also important; White has established[36] that if the solvent is more acidic than the conjugate acid of the counter-ion then a process called front-side exchange can occur. Some work concerning the role of the counter-ion will be summarised here.

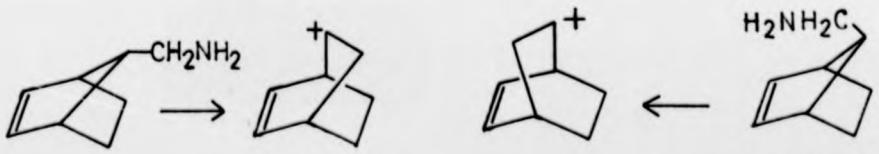
Berson[37] attributed the formation of different products from the deamination of the two amines (14) and (15) to twisted ions and called this and related phenomena "memory effects". He ruled out the possibility of ion pairs on the



(i) non-concerted
(ii) concerted

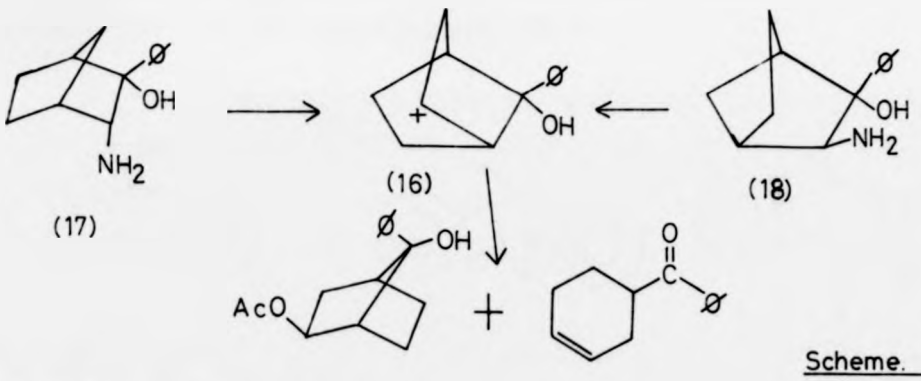
grounds that the returning group would be molecular nitrogen. However consideration of the effect of the counter-ion in these reactions could have explained the results.

Collins and coworkers have done a lot of work investigating the effects of the counter-ion upon reaction products.[38] They studied the nitrous acid deamination, in acetic acid, of 3-exo-and 3-endo-phenyl-3-hydroxy-2-endo-norbornylamines[39] (17) and (18) respectively. They cleverly



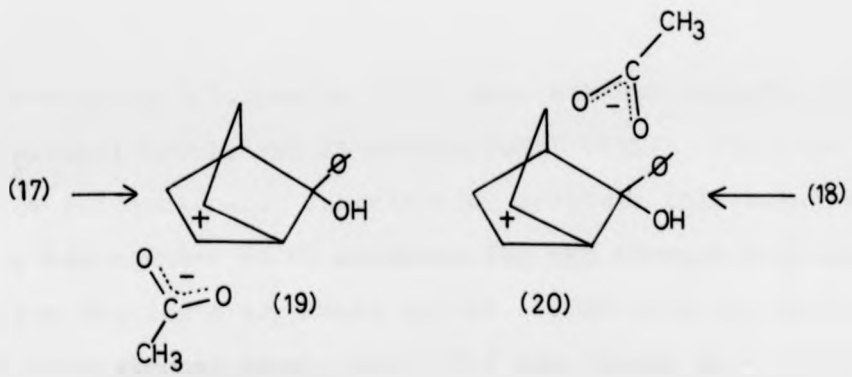
(14) (15)

showed that the ion (16) was the common precursor to two of the many products. The results shown in Scheme (1) were interpreted in terms of two different ion pairs (19) and (20). The exo-anion can collapse in (20) to give exo-product whereas the endo-anion in (19) is in the wrong position. Either solvent



Scheme. 1.

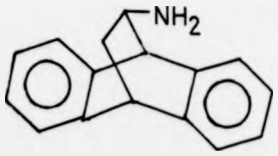
% yield from exo-phenyl	18.5	22.1
endo-phenyl	0	29.2



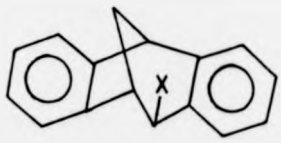
attack or competing ring opening gives the final products. The authors assume that front side exchange occurs and thus

the counter-ion becomes acetate anion. The value of their arguments should not be affected by whether or not this is completely true.

Mohrig's group have investigated the nitrous acid deamination of the three amines (21), (22a), and (23a).[40] The bicyclo[2,2,2]amine (21) and the exo-bicyclo[3,2,1]amine (22a) gave the same product mixture in acetic acid namely 76% exo-acetate (22b) and 24% exo-alcohol (22c).



(21)

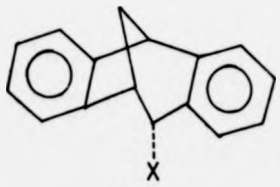


(22)

(a) X=NH_2

(b) X=OAc

(c) X=OH



(23)

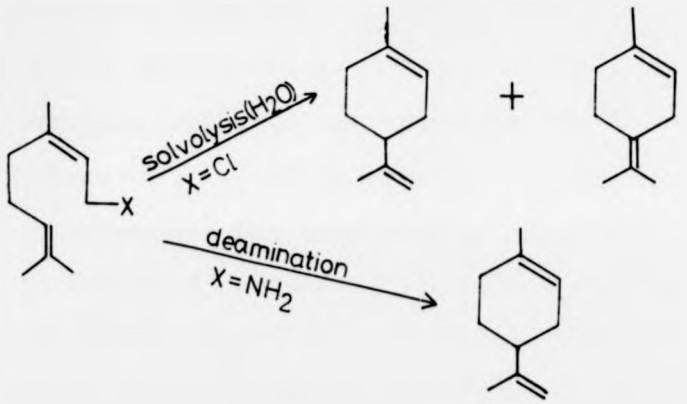
(a) X=NH_2

(b) X=OH

The endo-bicyclo[3,2,1]amine (23a) gave 87% exo-acetate (22b), 9% exo-alcohol (22c), and 3% endo-alcohol (23b). The high yields of intramolecular substitution products (alcohols) were taken by the authors to be evidence for the formation of ion pairs (see Whiting's arguments below). Similarly the formation of some endo-alcohol (23b) from (23a) was viewed as a result of the collapse of an ion pair to give product with retained configuration, a process which is in competition with cation rotation followed by attack of the counter-ion from the more favourable exo direction.

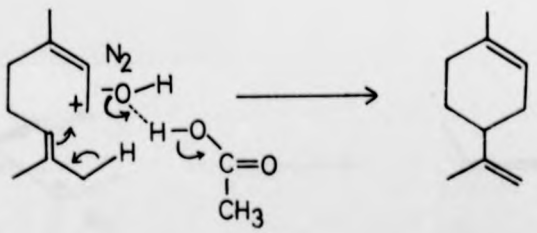
Burton[41] commented on the role of the counter-ion in

the deamination of nerylamine. Solvolysis of neryl chloride results in approximately equal amounts of limonene and terpinolene whereas the only cyclic olefin from the deamination reaction is limonene. This result was interpreted by asserting that the

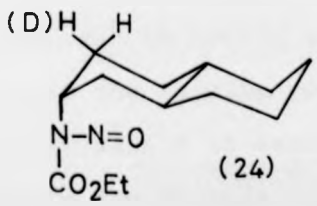


counter-ion deprotonates the allylic methyl group, thus providing assistance to the pathway leading to limonene. However, it also seems credible to suggest that the regioselectivity is due to the close proximity of the counter-ion to the methyl group after cyclisation has taken place. It is notable that the yield of limonene is less in water or aqueous acetic acid than it is in glacial acetic acid.

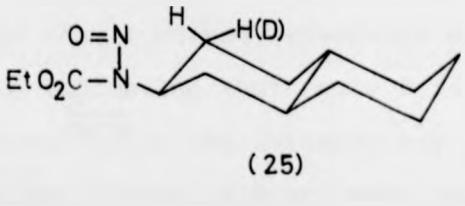
The decomposition of the nitrosocarbamates (24) and (25) in boiling cyclohexane, studied by Cohen and coworkers,[35]



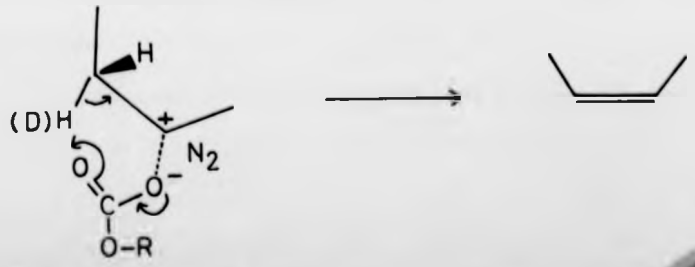
gives in both cases some 2-octalin. It was surprisingly found by deuterium labelling that cis elimination was the major mode of reaction to give 2-octalin; 94% cis elimination for the axial isomer and 84% for the equatorial isomer. The amount of cis elimination from the equatorial isomer is less surprising since in its ground state conformation it does not possess a trans coplanar hydrogen/leaving group arrangement. The axial isomer, however, exists in what is commonly regarded as the ideal conformation for elimination. To explain these results it is necessary to invoke participation of the counter-ion in the elimination reactions. In such a non-basic solvent as cyclohexane it would appear that the carbonate ion is required to act as the base, pulling off the proton (deuterium ion) on the same side of the ring as itself. It also seems that the counter-ion is important in this respect when acetic acid is solvent since in this solvent it was found that about 50% of the 2-octalin formed from the axial isomer was a result of cis elimination. The reason(s) for the greater elimination/ substitution ratios from axial amines are not clear from these results.



(24)



(25)



Concerted or non-concerted cleavage of the bonds to nitrogen?

The importance of the timing of the breaking of the C-N and N-X bonds has been stressed by Whiting and coworkers.[12,24a] They described the deamination reaction in terms of two competing pathways and noted that the two mechanisms are, in principle, distinguishable.

$$R\text{-}N{=}N\text{-}X \rightarrow R\text{-}\overset{+}{N}{=}N^{-}X \begin{cases} \nearrow R^{+} + N_2 + {}^{-}X \rightarrow \text{products} \\ \searrow \text{products} \end{cases} \qquad \text{ROUTE A}$$

$$R\text{-}N{=}N\text{-}X \rightarrow R^{+}N_2\,{}^{-}X \rightarrow \text{products} \qquad \text{ROUTE B}$$

Following route A, the counter-ion ^{-}X can undergo exchange with an external nucleophile ^{-}Y. Following route B, the carbonium ion R^{+} and the counter-ion ^{-}X are formed in close proximity (separated only by molecular nitrogen) and thus ^{-}X is in a favourable position for recombination with R^{+} or otherwise to affect the course of the reaction.

The results obtained by Huisgen and Ruchardt[15a] for the deamination of n-propylamine by various methods (i.e. ^{-}X is variable) and by Southam[42] for octylamine in acetic acid indicate that when R is primary then route A is followed. The results for 4-octylamine[42] and cis- and trans-4-t-butylcyclohexylamines[6] in acetic acid show a marked dependance on the nature of the leaving group indicating that route B is more important when R is secondary. Thus the intermediacy of the diazonium ion depends upon the nature of R or, more precisely, upon the stability of the carbonium ion R^{+} generated from the diazonium ion.

White[16] has contested this model for deamination reactions on the following grounds:

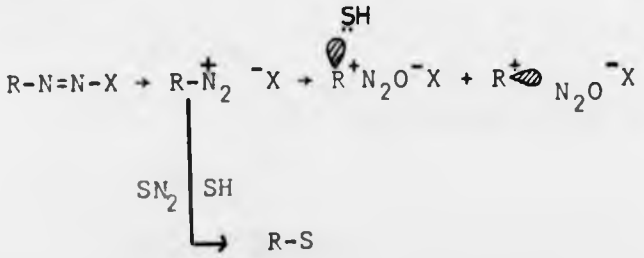
(i) trends in ratios of products are not very meaningful when more than two types of products are formed;

(ii) the use of acetic acid as solvent enables frontside exchange with the counter-ion[36] of a reaction intermediate and "complicates the picture";

(iii) the low yields of R-X found when R is primary is not due to diffusion of ^{-}X into the solvent but due to a displacement reaction by (presumably) solvent on the diazonium ion.

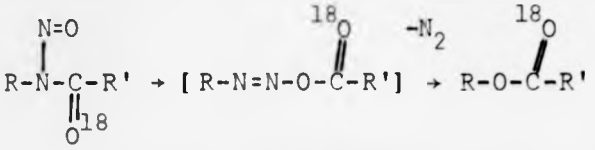
These criticisms have some validity but it should be noted that the basis for Whiting's model is not just product ratios but actual normalised product recoveries. Frontside exchange, when it occurs, can only influence the course of reaction for route B not route A - given that the diazonium ion is sufficiently long lived.

White suggests that the diazonium ion is an intermediate in all cases and this species quickly gives gas separated ion pairs some of which have the carbonium ion oriented towards solvent and some oriented towards the counter-ion. The lifetime



of the diazonium ion pair is dependant upon the structure of R and also upon the nature of the solvent. It can be seen that the two mechanisms essentially merge when the diazonium ion is short-lived with respect to diffusion processes.

The decomposition of nitrosoamides of secondary and tertiary carbinylamines which have been labelled with ^{18}O in the carbonyl group results in esters which have an excess of ^{18}O in the carbonyl group.[43] The ^{18}O distribution is remarkably insensitive to the structure of the parent amine (Table 2). If the diazonium ion pair is an intermediate in these reactions



then the amount of ^{18}O scrambling should decrease as the incipient carbonium ion becomes more stable.

Since the results are the same for two very different incipient carbonium ions such as cyclohexyl and diphenylmethyl ions then it must be concluded that the diazonium ion is not formed in these reactions or that its existence is so fleeting that the difference is not important. These results also ruled out the suggestion[36] that a concerted cyclic mechanism was responsible for the ester formation.

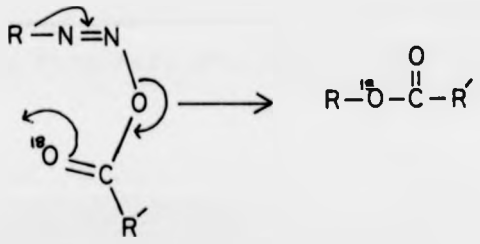
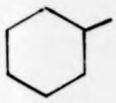
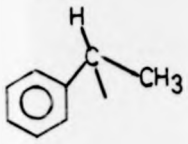
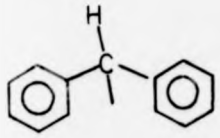
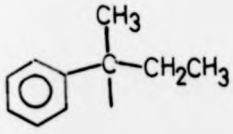
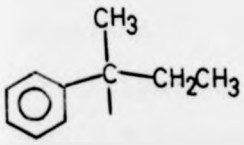


TABLE 2[a]

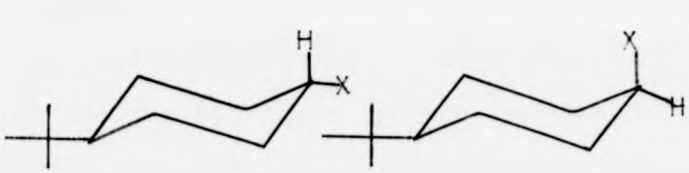
R	Solvent	^{18}O in carbonyl group (%)
	CH_3CO_2H	65
	CH_3CO_2H	69
	CH_3CO_2H	65
	CH_3OH/Et_2O (2:1)	65
	THF	63

a Data taken from Ref. No. 9 p.450 and Ref. No. 43.

Cyclohexyl systems

(a) Without β-carbon branching

It was long believed that the t-butyl group effectively locked the cyclohexane ring into one conformation; thus studies on compounds such as (26) and (27) were made to investigate the properties of axial and equatorial substituents.[29]



a - X = OTs

b - X = OBs

(26) (27)

Winstein investigated the solvolysis of compounds (26a) and (27a) and found only small differences in their rates of reaction.[44] From this finding he concluded that β-hydrogen participation was not important since only the cis-isomer (26a) has a β-hydrogen in the correct (trans,coplanar) orientation for participation. Since then cyclohexyl systems have been studied in greater detail.

The two traditional experimental techniques of the mechanistic chemist, kinetics and product analysis, have both become more sophisticated and subtle since Winstein's original investigations. Shiner and Jewett[45] investigated the solvolysis of compounds (26b) and (27b), measuring the kinetic isotope effects of deuterium substitution at C-2 and C-6 in 50% aqueous ethanol. They found, for both isomers, that substitution of deuterium trans to the leaving group gave a significant rate retardation while cis-substitution had only

a small effect on the reaction rates. In addition they noted that the olefin product from both isomers was formed with loss of the trans hydrogen. Thus trans-β-hydrogen participation is important for both isomers and, in accord with the known stereoelectronic requirements of hyperconjugation and hydrogen participation[46], they suggested that the trans-isomer (27b) reacts through a non-chair conformer.

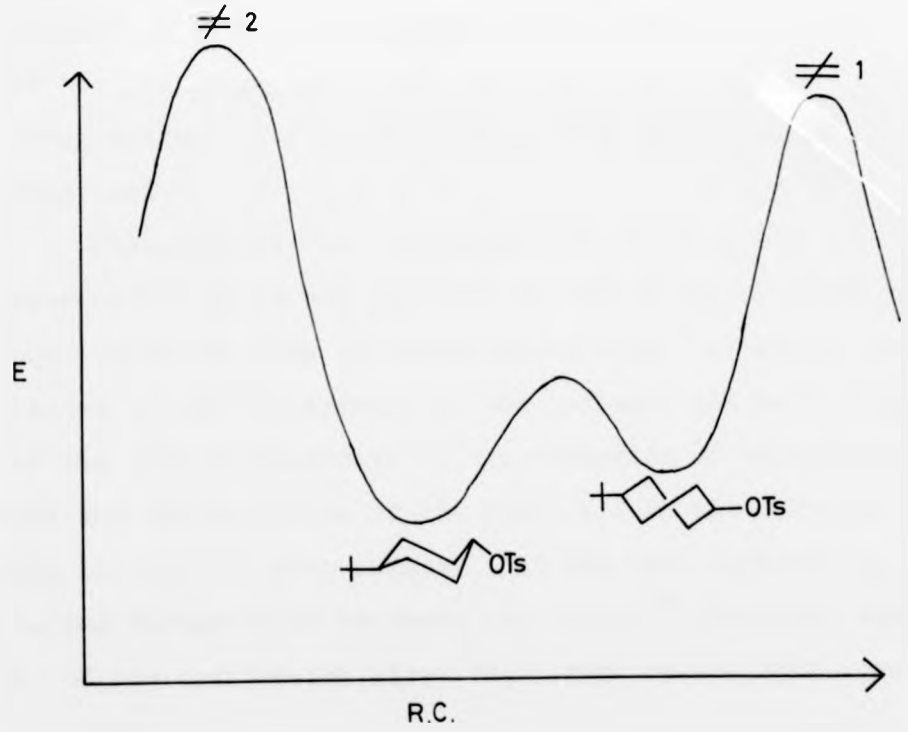
A detailed analysis of the products of acetolysis of the 4-t-butylcyclohexyl tosylates by Whiting and coworkers[47] complemented the kinetic studies of Shiner and Jewitt. From both isomers the major product was the Δ-4 olefin with similar amounts (ca. 14%) of 1,2-hydride shift products. The unrearranged substitution products were diastereoisomerically related, in both cases the major product had inverted configuration. These results indicate that the trans-isomer reacts through a non-chair conformation as suggested by Shiner and Jewitt.

Whiting explained these results in terms of a modified Winstein-Holness[44] equation (28) in which n_e, n_a, and n_T are

$$k = k_e n_e + k_a n_a + k_T n_T \qquad (28)$$

the equilibrium fractions of conformers having the tosylate group in equatorial, axial and twist (or flexible) orientations respectively. Since in the ground state the trans-isomer (27b) exists predominantly with the leaving group in an equatorial conformation and it is known that twist conformations are more stable than boat ones then $n_e >> n_T > n_a$. To explain a

substantial contribution from the term $k_T n_T$, k_T must be much larger than k_e, i.e. the twist conformer is highly reactive compared to the chair conformer. This is shown in the reaction profile diagram (Figure 2). Thus the t-butyl group does not serve its intended purpose of restricting the flexibility of the cyclohexane ring.



Maskill and Banks[48] studied the solvolysis reactions of exo- and endo-bicyclo[3,2,1]octan-3-yl tosylates (1d) and (1c) in various solvents. The ethane bridge across the six-membered ring effectively rules out any reaction through a

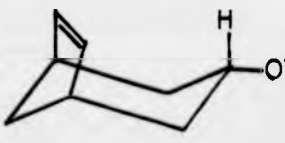
(1d)

(1c)

twist conformation for these compounds. Detailed product analyses and a study of the kinetics of solvolysis of both tosylates were carried out. High β-$^2H_4$ kinetic isotope effects and substantial elimination and hydride shift products were found for both isomers; in broad outline the same results as obtained for the 4-t-butylcyclohexyl tosylates and brosylates (Table 3). It was suggested that the exo-tosylate (1d) reacted through a boat-cyclohexane conformation in order to account for the large amount of β-hydrogen participation and the strong preference for substitution with inversion of configuration.

Unfortunately no stereospecific β-^2H k.i.e's were measured so it is not possible on this evidence alone to preclude completely some cis-elimination from (1d) which could be effected by the counter-ion at the intimate ion pair stage.[35] However the stereospecificity of the formation of substitution products and the magnitude of the α-k.i.e's in all solvents employed (1.19-1.20) both suggest that the rate determining step is the formation of intimate ion pairs;[49] therefore any effect of the counter-ion after this stage cannot influence the β-^2H k.i.e's.

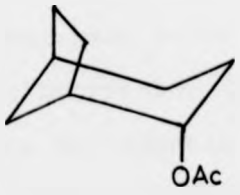
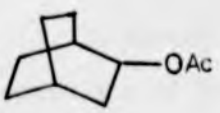
The earlier work of LeBell and Maxwell supports these conclusions.[50] Solvolysis of compound (29) gave 36% of completely inverted unrearranged substitution product.



(29)

TABLE 3[a]

Products of acetolysis of exo- and endo-bicyclo[3,2,1]-octan-3-yl tosylates

Products	exo-tosylate	endo-tosylate
	69.0	68.8
	26.5	0.8
	0.3	16.6
	2.1	8.0
	0.2	0.6
	1.9	5.2

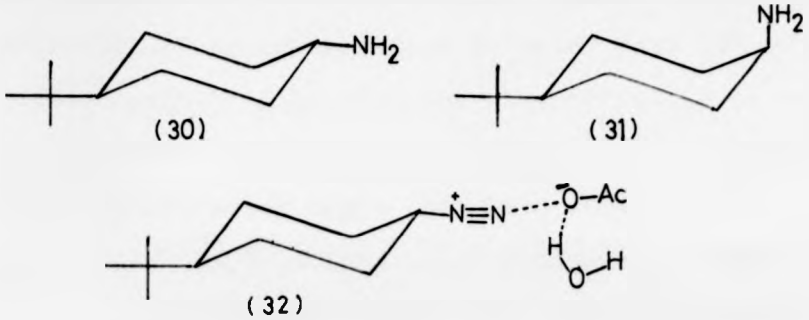
a Data taken from Ref. No. 48.

The ground state conformational preferences of a molecule need not control its mode of reaction as can readily be seen from the solvolysis work described above. This is, in effect, the Curtin-Hammett principle and is reasonable in reactions which have high activation energies and could, in principle, be even more important in solvolysis reactions which involve poorer leaving groups than the well studied sulphonate esters such as fluoride.

When nitrogen is the leaving group the activation energy for loss of nitrogen is small and therefore the Curtin-Hammett principle cannot be applied i.e. the energy barrier between conformers is comparable to the activation energy of the deamination reaction. As discussed above, the course of many deamination reactions has been rationalised on the basis of conformational preferences in the ground state.

The early deamination work on cyclohexyl systems has been reviewed and interpreted by Streitweiser[51] and summarised later by Maskill.[5b] This early work was often misinterpreted due to inadequate experimental techniques which were not capable of resolving rearranged from unrearranged products. Conflicting results were also obtained through the use of different solvent systems; the effects of solvents as different as water and acetic acid were not always appreciated. Work was done by Hückel and Heyder[52] on the nitrous acid deaminations of cis- and trans-4-t-butylcyclohexylamines (30) and (31), by Cowen and Jankowski[53] on the cis- and trans-2-amino-trans-decalins in aqueous acetic acid and by others.[5b] This work led to the formation of certain views; for those cyclohexylamines

which have the amine group in an equatorial position in the most stable conformation the key intermediate was a specifically ion paired diazonium ion (32). Collapse of (32) would give predominantly retained acetate and alcohol as is observed for



most systems. Reaction through the chair conformation accounts for the low yields of olefin obtained. The ratio n_e/n_T is large and the ratio of k_e/k_T is not so important when the rate of conformer interconversion is slow. Thus the observation of reaction through a chair conformation is simply a consequence of the ground state populations of the different conformations. Figure (3) depicts the relevant P.E. diagram.

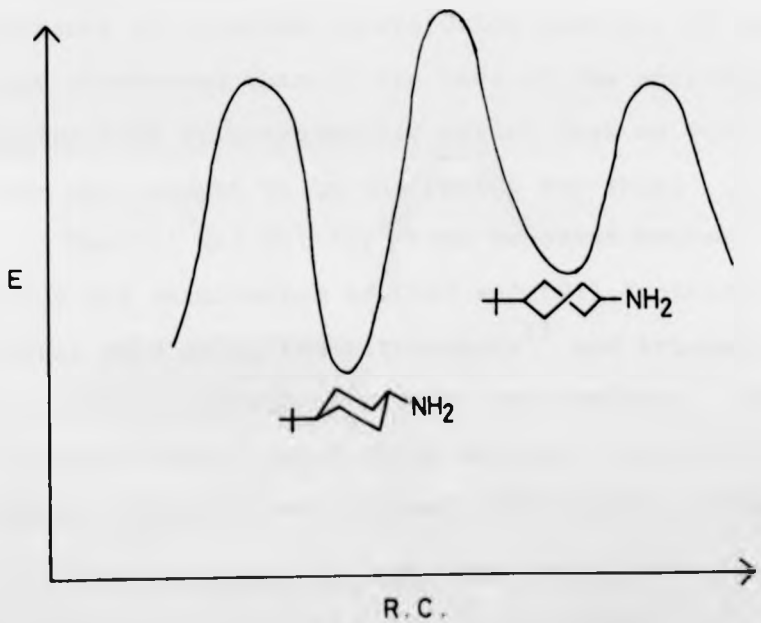


Figure. 3.

The ion pair model also provides an explanation for the insensitivity of the ratio of acetate to alcohol product to the composition of the aqueous acetic acid used as solvent.[53,40] The ^{18}O work of Boutle and Bunton[54] which showed that in the deamination of cyclohexylamine in water only 10% of the alcoholic product came from the diazohydroxide is not incompatible with this model as originally thought.[5c,55] A higher proportion of ^{18}O incorporation might have been incorporated if the reaction were carried out in a less polar medium than water.

The diastereoisomerically related diazonium ion pair intermediate has also been postulated for axial cyclohexylamines. However in this case the evidence is not so strong. Elimination is the major reaction and is easily explained on the basis of the trans-coplanar arrangement of leaving group and β-hydrogen. A variety of inconsistent results have been reported[56] for the yields of inverted and retained products, due to the reasons stated above no doubt. It was apparent, however, that the preponderance of retained substitution product, if any, was much more attenuated than in the case of the equatorial amine. The greater ease of nucleophilic attack from an equatorial direction was thought to be the reason for this.

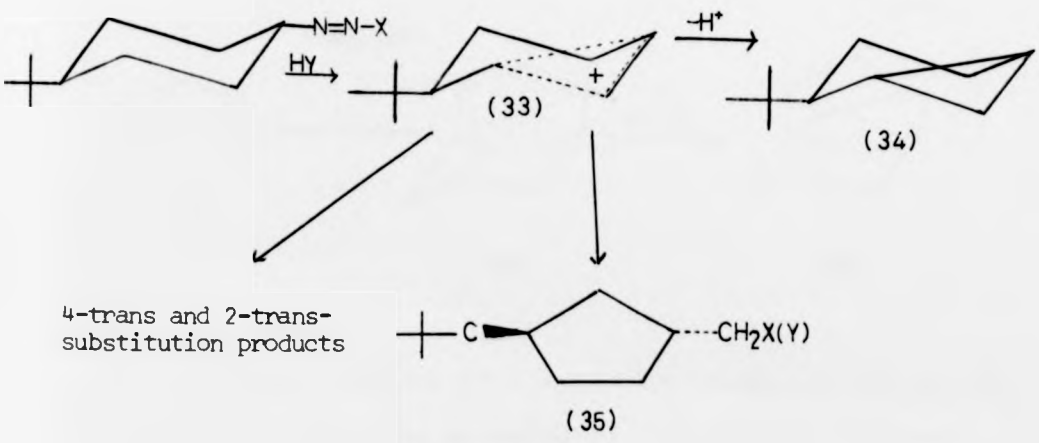
Maskill and Whiting[6] have reported recently on the results of the deamination of (30) and (31) derivatives in acetic and butyric acid using the nitrosamide[15] and triazene[17] methods as well as the conventional nitrous acid method.[14] The butyrolysis of N-nitroso-N-acetyl derivatives allowed a distinction to be made between internal and external substitution products (Table 7).

The gross differences in product fallout from the cis- and trans-amines emphatically rule out any free carbonium ion or other common intermediate which may have been postulated for deamination reactions, i.e. there is negligible crossover in the two reaction pathways. Unlike the results obtained by Whiting for the arenesulphonate analogues[47] there is no noticeable diastereoisomeric relationship between the two isomeric product distributions. The different deamination procedures result in subtle but definite differences in product fallout indicating, along with the extensive formation of intramolecular substitution products, that decomposition of the intermediate diazo-ester is concerted or nearly so.

The most noticeable feature of the cis-derivatives is the amount of hydride shift (ca. 35%) derived products and the large amount of olefin product. This implies extensive participation by the trans-coplanar β-hydrogens. The stereochemistry of the rearranged internal substitution products (mainly retained configuration) show that there was little time for diffusion processes to occur. Whiting and Maskill decided therefore that the hydride migration must occur in concert with, or very rapidly after, the C-N bond is cleaved. Internal substitution at the unrearranged position gives predominantly retained product while external substitution is non-selective.

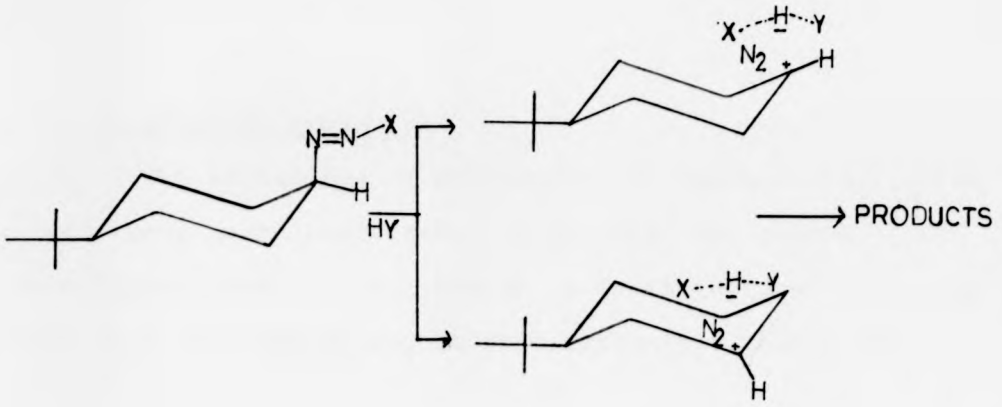
Deamination of the trans-cyclohexylamine derivatives gave much less rearrangement and elimination products. Both internal and external substitution products were of predominantly retained configuration and it was also found that internal substitution was especially selective when water was the

internal nucleophile. These results are essentially in agreement with the earlier results reported in the literature.[56] The greater amount of elimination compared with 1,2-hydride shift is in accord with the work of Cohen[53] mentioned above and of Shiner[45]. The counter-ion could be responsible for proton abstraction from the ion pair intermediate. The small amounts of 2-t-butyl-bicyclo[3,1,0]hexane (34) and trans-3-t-butylcyclopentylmethyl acetate[5] (butyrate) (35) which were obtained only from the equatorial amine were interpreted as evidence for a protonated cyclopropane intermediate (33).

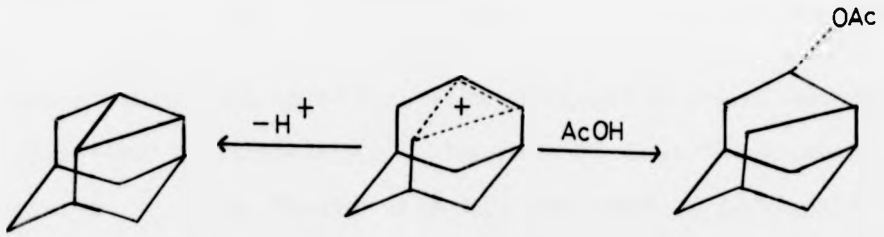


The overall mechanism for both isomers was discussed in terms of a concerted cleavage of C-N and N-X bonds to give rearranged and unrearranged ion pairs separated by ca. 60 pm as shown below for the cis-isomer. The anions are hydrogen-bonded to solvent molecules.

Whiting and coworkers have also investigated the deamination and solvolysis reactions of 2-adamantyl derivatives.[58a] A protonated cyclopropane intermediate (36) similar to (33) was



postulated as an intermediate in the deamination of 2-amino-adamantane in acetic acid to explain the formation of large amounts of skeletally rearranged, thermodynamically unfavourable products including the cyclopropane (37) and the exo-acetate (38).



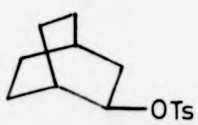
(37) (36) (38)

The exo-acetate (38) was also found, in low (0.5%) yield, in the acetolysis products of 2-adamantyl tosylate. Thus the σ participation of the anti-parallel C-C bond is weaker in the solvolysis reaction. The questions naturally arise as to whether this σ participation is helping the initial ionization or occurring after the initial formation of the classical carbonium ion and also why σ participation is more important in the deamination reactions. Whiting has suggested[58b] that anchimeric assistance does occur in the solvolysis of 2-adamantyl tosylate.

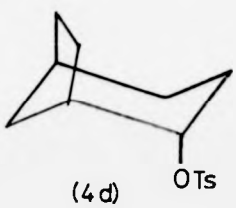
(b) With β-carbon branching

The mechanisms of solvolysis of compounds (4c), (5b) and (4d) have been investigated by Goering[8] and others.[59,7] Goering showed that the solvolysis in acetic acid of optically active (4c) gave completely racemic products; mainly the

(4c)

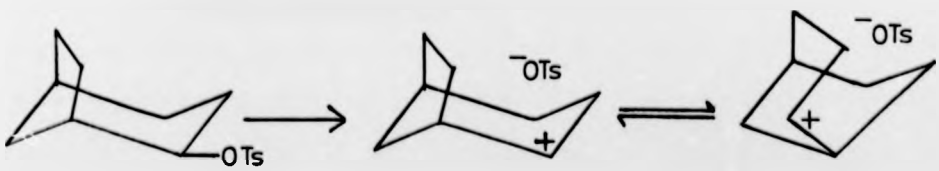


(5b)

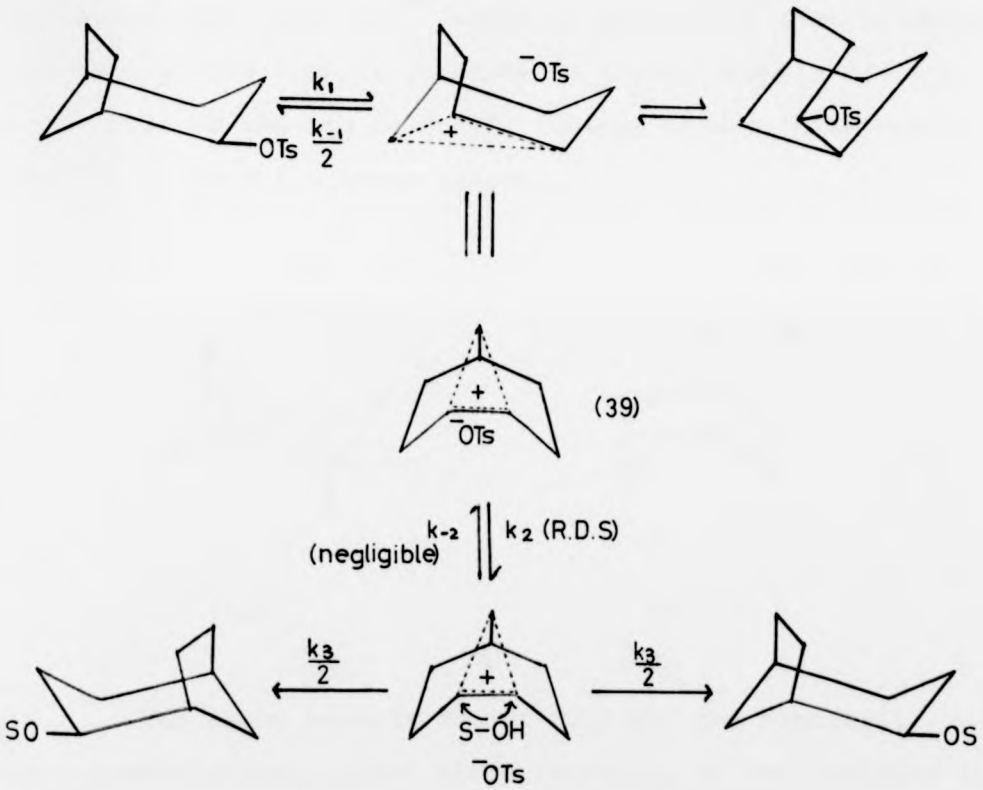


(4d)

corresponding endo-acetate, endo-2-OAc, with small amounts of [2,2,2]-OAc and exo-2-OAc. The rate of loss of optical activity, k_α, was faster than k_t, the rate of product formation. No special salt effect was observed. These results were interpreted in terms of Scheme (2). Racemization of starting material is a result of internal return since the absence of a special salt effect implies little return from solvent separated ion pairs ($k_{-2} < k_3$). Direct formation of the symmetrical non-classical ion (39) accounts nicely for the total racemization of reaction products. The alternative view of a pair of rapidly equilibrating classical carbonium ions (40) and (41) was considered by Goering but discarded since none of the initially formed optically active (40) was intercepted by solvent.

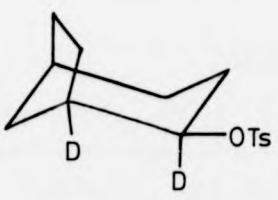


(40) (41)

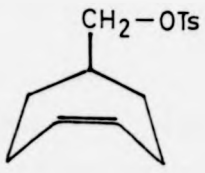

k1
k-1/2
OTs
⁻OTs
+
OTs
(39)
⁻OTs
(negligible) k-2
k2 (R.D.S)
k3/2
k3/2
SO
S–OH
⁻OTs
OS

Scheme (2)

When the classical cation (40) (disregarding the counter-ion) was generated from endo-2-aminomethylnorbornane partial interception was observed.[60] Maskill maintained that bridging is present at the transition state in the solvolysis of (42) on the basis of the low α-kinetic isotope effects observed in formic acid and 80% aqueous ethanol.[7]



(42)



(43)

The above results do not rule out the possibility that σ participation occurs after formation of the intimate ion pair (40) since the rate determining step in the reaction is formation of the solvent separated ion pair from which the products are derived. The non-interceptibility of (40) could be due to the close proximity of the counter-ion. The products of solvolysis of (4c) were shown to be similar to but not identical with the products of solvolysis of cyclohept-4-enylcarbinyl tosylate[8] (43) i.e. the σ and π routes to (3) do not produce identical results. The tosylate (43) gave less rearranged and inverted products than tosylate (4c). These subtle differences were attributed to the different locations

of the anions with respect to the electron deficient centres. Thus the anion generated from the σ route can be reversibly captured while, from the π route, the anion is generated further away from the centre(s) of positive charge. Internal return from the monocyclic ion pair to give the bicyclic tosylate was not detected.

The solvolysis of the tosylates (5b) and (4d) gave essentially identical products[8] (Table 4). Goering[8] has shown, however, that (5b) and (4d) are partially interconverted during solvolysis which dampens any difference in product distribution

TABLE 4*

Compound	exo-2-X	Products[c] [2,2,2]-X	endo-2-X	Olefins
(4d)[a]	53.4	46.2	0.4	13
(5b)[a]	53.9	45.5	0.6	15
(4d)[b]	57.2	42.8	-	-
(5b)[b]	56.7	43.3	-	-

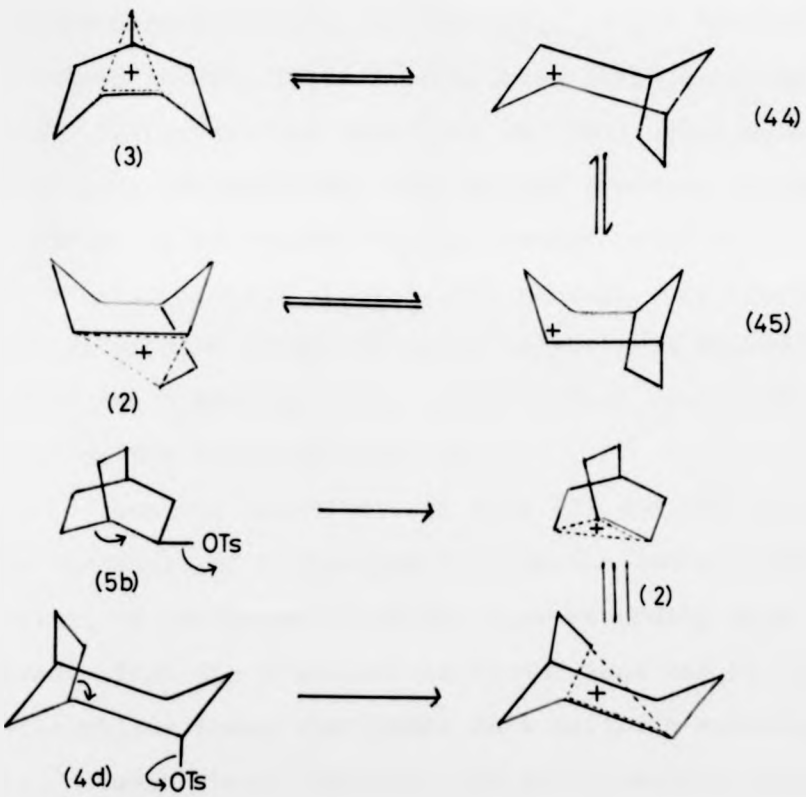
* Data taken from Ref. No. 8

a, in AcOH b, in 80% in aqueous acetone c, T = 49°C

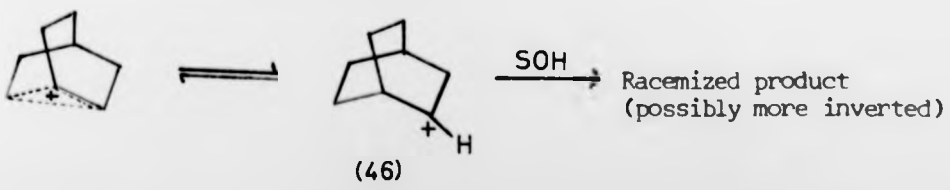
X = OAc X = OH

which might exist. Analysis of the solvolysis products after only 10% reaction however gave similar if not identical product distributions. Thus it seems that (4d) and (5b) react through the same product forming intermediate (2). Much more leakage from the endo-[3,2,1] system to the exo-[3,2,1]/[2,2,2] system was found than *vice versa*. Berson[60] and Goering[8] have presented

evidence for the leakage mechanism involving the chair and boat conformers of the classical [3,2,1] carbonium ion.



The solvolysis products of optically active (5b) and (4d) were partially racemized. The [2,2,2] product was always less optically pure than the exo-[3,2,1]product and acetolyses gave products of lower optical purity than solvolysis in the more nucleophilic 80% aqueous acetone system. Formation of the symmetrical classical carbonium ion (46) to some extent was postulated to account for these results.[8]



Finally the mode of formation of the rearranged products from the solvolysis of exo- and endo-bicyclo[3,2,1]-octan-3-yl tosylates mentioned above[48] was discussed in terms of the non-classical ions (2) and (3). It was thought that the first formed intermediates from hydride shift were the classical bicyclo[3,2,1]octan-2-yl ions (44) and (45) which subsequently relax to give predominantly (2) and the products thereof. The small amount of endo-substitution product found and the small excess exo-bicyclo[3,2,1]octan-2-yl product over bicyclo[2,2,2]-octan-2-yl product (Table 3) could result from solvent attack on one of the classical ions. endo-Product would also be formed from the non-classical ion (3).

Thus the non-classical ions (2) and (3) can be the initial products of ionization or they can result from the relaxation of preformed classical ions depending upon the system involved. That the classical carbonium ions can be intercepted by nucleophiles shows that there is a definite activation barrier between these classical and non-classical ions.

CHAPTER 3

PREPARATIVE METHODS

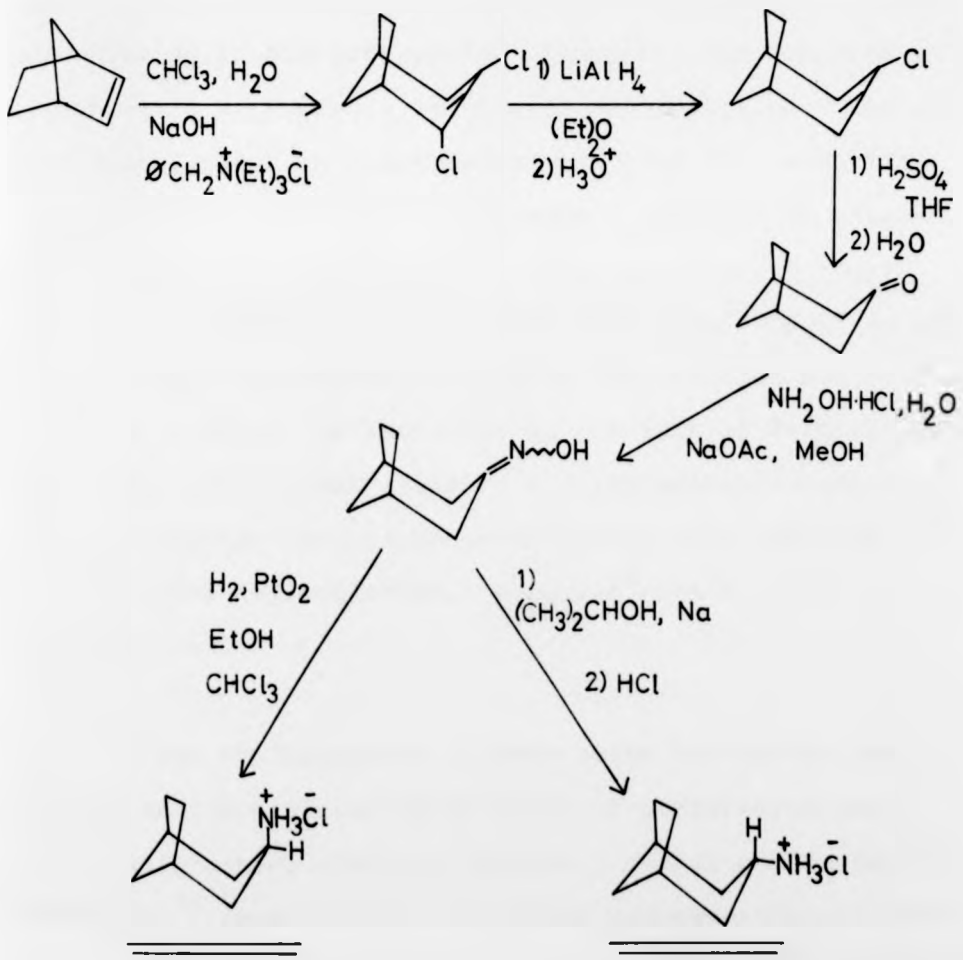
Preparation of exo- and endo-bicyclo[3,2,1]octan-3-ylamine hydrochlorides

Entry into the bicyclo[3,2,1]octyl skeleton was achieved by the addition of dichlorocarbene to norbornene and opening of the cyclopropane ring. The method described by Kraus[61] and developed by Banks[4a] was used. Benzyltriethylammonium chloride was found to be a suitable phase-transfer catalyst. Fractional distillation of the crude product gave exo-3,4-dichlorobicyclo[3,2,1]oct-2-ene in 75% yield. The dichloride was reduced with an ethereal solution of lithium aluminium hydride to give, after fractional distillation, 81% of 3-chlorobicyclo[3,2,1]oct-2-ene. A small amount of the dichloride was present in the product which was not reduced even after further treatment with lithium aluminium hydride.

Treatment of the monochloride with concentrated sulphuric acid and quenching the reaction with ice gave bicyclo[3,2,1]octan-3-one in 68% yield. Further preparations of this ketone showed that the yield was highly variable, in agreement with the observations of Banks.[4b] The oxime was prepared in high yield by refluxing a solution of the ketone, hydroxylamine hydrochloride and sodium acetate in aqueous methanol.

A variety of methods was available for the reduction of the oxime,[62] and variations of the methods employed by Maskill[5d] to reduce 4-t-butylcyclohexanone oxime were used. exo-Bicyclo[3,2,1]octan-3-ylamine hydrochloride was prepared by reducing the oxime with sodium in refluxing anhydrous isopropanol. The reaction mixture was quenched with water,

FIGURE 4



Preparative scheme for the synthesis of the bicyclo[3,2,1]-octan-3-ylamine hydrochlorides

extracted with ether and then given an acid-base workup. The ethereal solution was finally extracted with dilute hydrochloric acid and then the acidic aqueous solution was slowly reduced in volume to precipitate crystals of exo-amine hydrochloride in moderate yield. Recrystallization from ethanol gave crystals with m.p. > 280°C with decomposition. The endo-amine was prepared in quantitative yield by the catalytic hydrogenation of the oxime using Adams' catalyst in ethanol and chloroform. (Chloroform was added since under these conditions it generates the hydrochloric acid[63] required to form the amine hydrochloride.) When the reaction was complete (3 days at 3 atm.), as indicated by the lack of further hydrogen uptake, the mixture was filtered and the solvents removed. Recrystallization from ethanol/chloroform gave crystals of the endo-amine hydrochloride, m.p. 278°-285°C (with decomposition).

The configuration of both amine hydrochlorides was assigned on the basis of their modes of preparation and by analogy with other, similar, systems. Huckel and Heyder[52] and Maskill[5d] reported that catalytic hydrogenation of 4-t-butylcyclohexanone oxime gave the axial amine. They also found that reduction of this oxime by sodium in alcohol gave the equatorial amine. Kraus[61] and Banks[4b] found that catalytic hydrogenation of bicyclo[3,2,1]octan-3-one gave the endo (axial) alcohol. It was difficult to estimate the diastereoisomeric purity of the two compounds from their melting points due to the decomposition which accompanied melting. However it could be shown by g.l.c. that the carbamates prepared from both amine

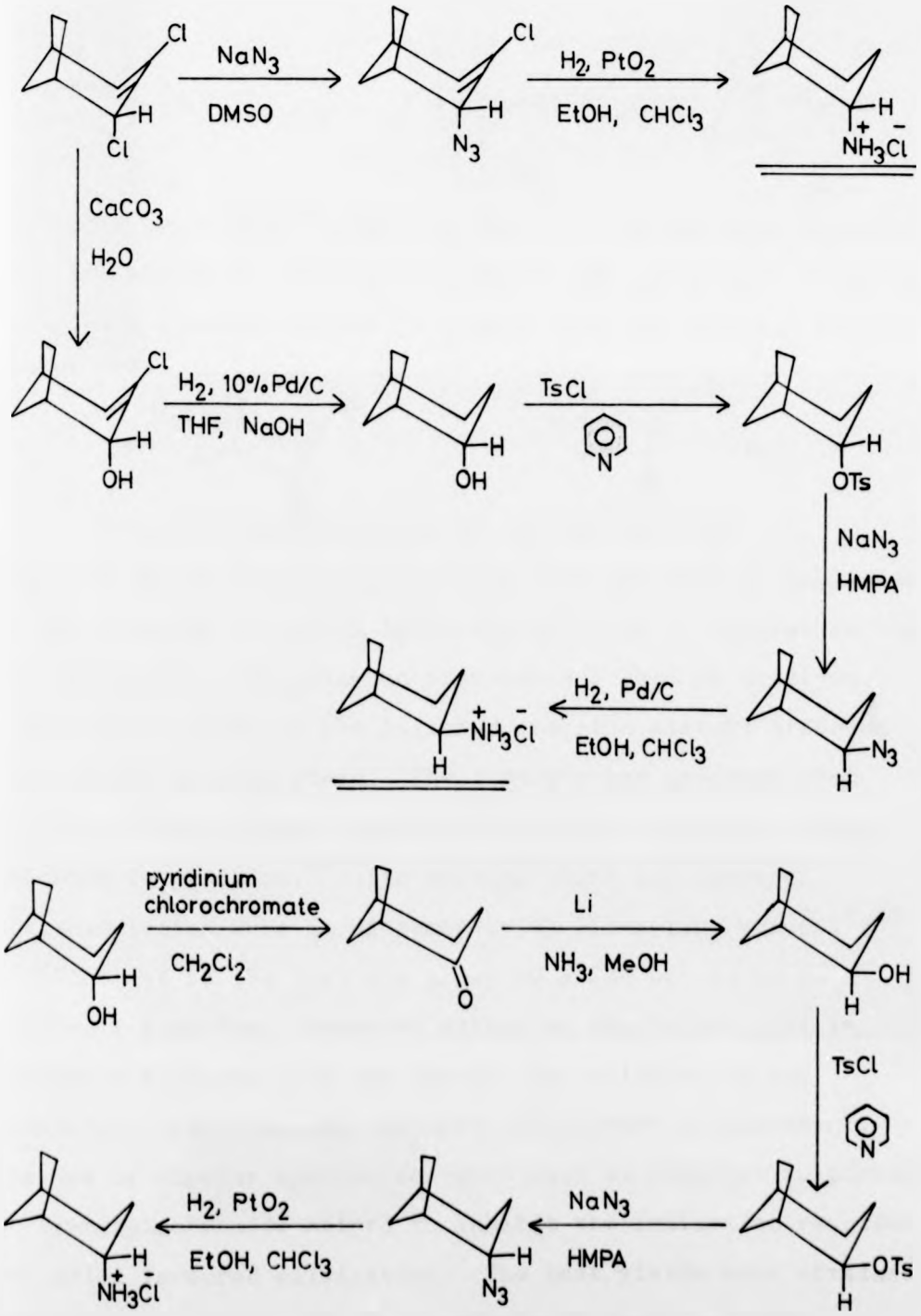
hydrochlorides (vide infra) were free from contamination. It is interesting to note here that of the five isomeric amine hydrochlorides prepared in this work only exo-bicyclo[3,2,1]-octan-3-ylamine hydrochloride was insoluble in deuterochloroform. The amines were always prepared and stored as the hydrochlorides to avoid reaction with atmospheric carbon dioxide.

Preparation of exo- and endo-bicyclo[3,2,1]octan-2-ylamine hydrochlorides

All compounds which are capable of optical isomerism were synthesised as racemic modifications. It was hoped that the reduction of bicyclo[3,2,1]octan-2-one oxime would afford the exo- and endo-amines in similar fashion to the work described above. However reduction by catalytic hydrogenation and by sodium in isopropanol gave roughly equal amounts of both isomers as did the reductive amination of the ketone with sodium cyanoborohydride and ammonium acetate.[64] (The methyl resonances of the acetylated amines were sufficiently resolved to allow a rough estimate of the isomeric ratios by n.m.r. spectroscopy.) It was not possible, in the present work, to separate roughly equal amounts of these amines, amine hydrochlorides or acetamides. The routes outlined in Figure 5 were followed, therefore, to prepare selectively the two isomeric amine hydrochlorides.

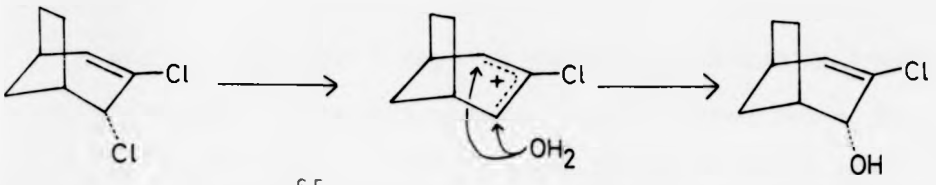
exo-3-Chloro-4-hydroxybicyclo[3,2,1]oct-2-ene was prepared by hydrolysis of the corresponding dichloride in the manner described by Kraus[61] for the dibromide analogue. The retained stereochemistry of this reaction implies the formation

FIGURE 5

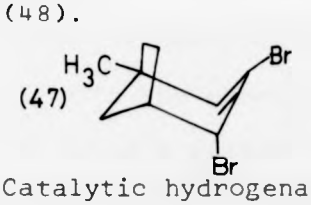


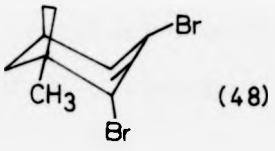
Preparative schemes for the synthesis of exo- and endo-bicyclo[3,2,1]octan-2-ylamine hydrochlorides

of an allylic carbonium ion which is specifically attacked by water or hydroxide ion from the exo-direction.



Work done by Jefford[65] suggests that this is the most favourable side for attack by nucleophiles in the SN'_2 reactions of exo-1-methyl-3,4-dibromobicyclo[3,2,1]oct-2-ene (47) and its allylic isomer (48).





(48)

Catalytic hydrogenation of the hydroxyvinyl chloride to exo-bicyclo[3,2,1]octan-2-ol was best accomplished in the presence of sodium hydroxide solution to neutralise the HCl generated. Palladium on charcoal was used as catalyst. Steam distillation of the filtered reaction mixture afforded the alcohol in good yield. The tosylate was prepared from recrystallized alcohol and recrystallized p-toluenesulphonyl chloride in pyridine.[66] Its melting point and spectral characteristics were in agreement with literature values.[8,67] Displacement of the tosylate group by azide proved to be a difficult reaction. Rearside attack by the nucleophile is extremely hindered with the result that elimination and ionization reactions are favoured over direct displacement. The use of dipolar aprotic solvents such as dimethyl sulphoxide or dimethylformamide helped to inhibit the ionization reaction but still favoured elimination. The best yields were obtained

when hexamethylphosphoramide (HMPA) was used as solvent. A mixture of the tosylate (1 mole) and sodium azide (4.3 moles) in HMPA was stirred for 7 days at room temperature and then worked up between ether and water. The isolated crude product was chromatographed on alumina; each fraction being monitored by g.l.c. The oil obtained from combination of the desired fractions and removal of solvent was then distilled to give the endo-azide in 19.5% yield. The assignment of endo-configuration was made on the basis of the mode of preparation and comparison by g.l.c. with the exo-azide (vide infra). Hydrogenation of the azide using a mixture of ethanol and chloroform as solvent and 10% palladium on charcoal as catalyst gave the endo-amine hydrochloride in quantitative yield. When purified by recrystallization from methanol/tetrahydrofuran it had m.p. > 270°C with decomposition.

Two synthetic routes were followed to prepare the exo-amine hydrochloride. The second route helped to confirm the stereochemistry of the amine hydrochloride. exo-3,4-Dichlorobicyclo[3,2,1]oct-2-ene was reacted with sodium azide in dry dimethyl sulphoxide to give the SN'_2 product[65] i.e. the exo-4-azide. Catalytic hydrogenation of this product using platinum dioxide and a mixture of ethanol and chloroform as solvent gave the exo-amine hydrochloride.

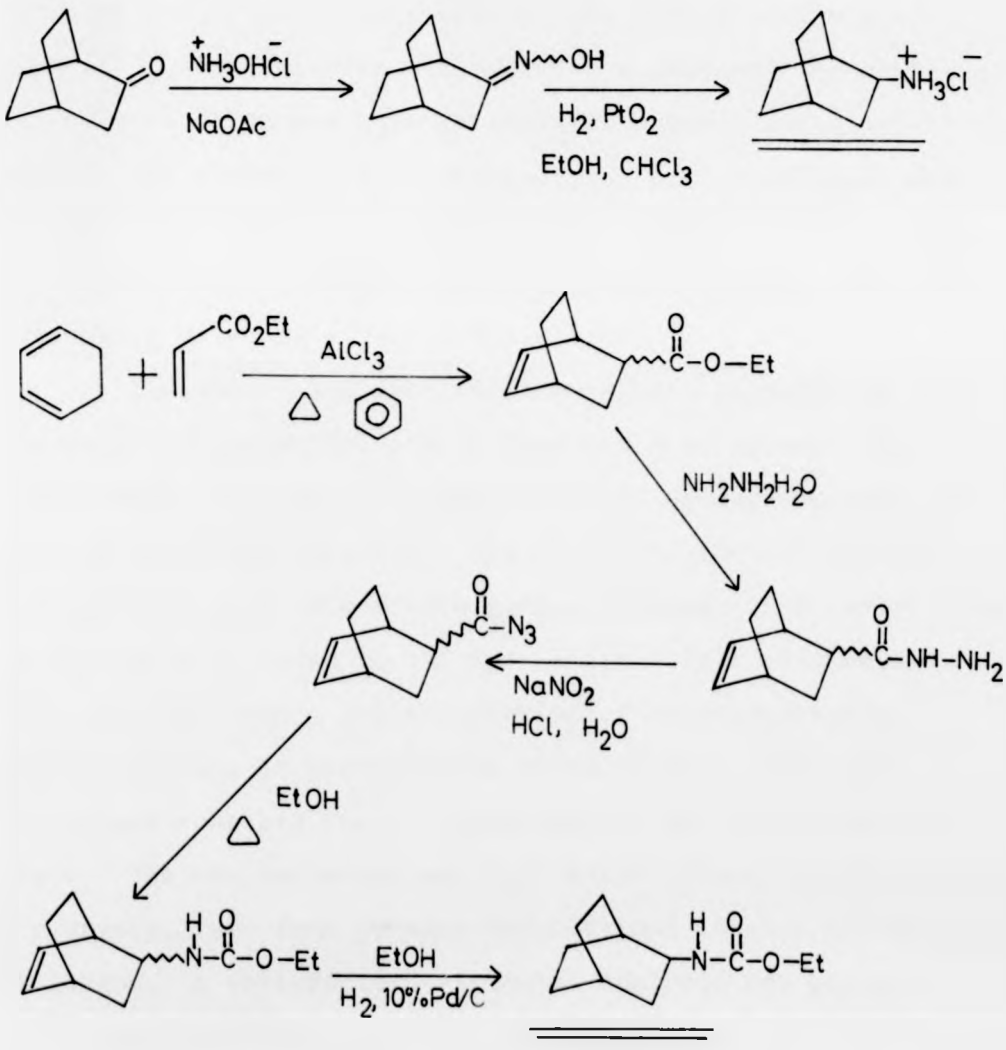
Recrystallization from ethanol/chloroform gave a solid, m.p. > 260°C with decomposition.

Bicyclo[3,2,1]octan-2-one was prepared from exo-bicyclo[3,2,1]octan-2-ol using pyridinium chlorochromate in the manner described by Corey.[68] After recrystallization and sublimation the waxy product had m.p. 121-124°C (lit.[69] 123-129°C). The ketone was then reduced to the endo-alcohol using lithium in liquid ammonia with dry ether as cosolvent and methanol as the proton donor.[70] After a normal workup the endo-alcohol was obtained in 92% yield. G.l.c. showed that approximately 0.5% of starting material and the isomeric exo-alcohol were the only impurities. The crude alcohol was tosylated in the usual manner and recrystallized to give the endo-tosylate m.p. 79-80.5°C (lit.[71] 80.1-80.8°C). The tosylate was then reacted with sodium azide in HMPA to produce the exo-2-azide. This material which did not co-chromatograph (g.l.c.) with the endo-2-azide prepared earlier gave the exo-2-amine hydrochloride after catalytic hydrogenation in the usual manner.

Preparation of bicyclo[2,2,2]octan-2-ylamine hydrochloride

The preparation of the bicyclo[2,2,2]octyl derivatives was comparatively simple since no problems of stereochemistry arise in this system. Bicyclo[2,2,2]octanone was kindly supplied by Dr. Maskill. The oxime was prepared in the same manner as bicyclo[3,2,1]octan-3-one oxime. Catalytic hydrogenation in the usual manner gave the amine hydrochloride, which had m.p. > 320°C (with decomposition) after recrystallization from ethanol.

FIGURE 6



Synthetic routes to bicyclo[2,2,2]octan-2-ylamine hydrochloride and ethyl N-(bicyclo[2,2,2]octan-2-yl)carbamate

Triazene preparations

The benzenediazonium tetrafluoroborate required to prepare the triazenes was made by the method of Roe and Hawkins.[72] Propyl nitrite was added to a stirred, ice-cold solution of aniline and aqueous tetrafluoroboric acid in ethanol. The diazonium salt precipitated out of solution and ether was added to effect further precipitation. The product was filtered off at the pump and washed with ethanol and ether before being dried in a vacuum desiccator.

The exo-3- and exo-2-triazenes were prepared as sharp melting crystalline solids from the free amines. The relevant amine hydrochloride was extracted between pentane and potassium hydroxide solution. The separated pentane solution was evaporated under argon then sodium carbonate and redistilled acetonitrile were added to the free amine. This mixture was stirred at -10°C and a cooled solution of benzenediazonium tetrafluoroborate in acetonitrile added slowly. When the reaction was complete the filtered mixture was extracted with pentane. The residue which was left after removal of the pentane was recrystallized from pentane and sublimed to give crystals of triazene. A satisfactory elemental analysis was obtained for the exo-2-triazene.

The endo-2- and the bicyclo[2,2,2]triazenes were prepared in a slightly different fashion from that described above. The amine hydrochlorides were used instead of the free amine and the petrol extracts of the reaction mixture were washed with water to remove any traces of acetonitrile. The petrol extracts were then dried with sodium sulphate and the

solvent removed. The oily residue thus produced from the endo-3-amine hydrochloride was recrystallised at -70°C but produced a glue upon warming to room temperature. The residue from the bicyclo[2,2,2]amine hydrochloride was not successfully recrystallized. However after standing at -15°C for three days with a little pentane, crystals of the triazene formed. These were separated from the oil and washed with cold pentane to give a slightly sticky solid m.p. 42-44°C. The endo-2-triazene was not successfully prepared.

Preparation of carbamates and nitrosocarbamates

It was initially planned to study the decomposition of the nitrosoacetamides of the bicyclooctylamines. However only the exo-3-derivative was successfully prepared; the other isomeric nitrosoacetamides proved to be too unstable for satisfactory studies. White[73] had reported that the nitrocarbamate derivatives of amines were more stable than the corresponding nitrosoamides. It was found that these were actually too stable, requiring long reaction times and/or high temperatures for complete reaction. The nitrosocarbamates were more suitable being more reactive than the nitrocarbamates but sufficiently stable to allow isolation and subsequent decomposition.

All four of the bicyclo[3,2,1]carbamates were prepared from the amine hydrochlorides following the procedure described below. Portions of potassium carbonate and ethyl chloroformate were added alternately to a stirred slurry of amine hydrochloride in ether and a drop of water and then the mixture was refluxed. After a normal workup the carbamate was recrystallised and sublimed.

The bicyclo[2,2,2]carbamate was prepared by the route shown in Figure 6. The Diels-Alder reaction of cyclohexadiene with ethyl acrylate in benzene was catalysed by aluminium chloride[74] and gave a 69% yield of ethyl bicyclo[2,2,2]-oct-5-ene carboxylate. From this ester the acid hydrazide was prepared which in turn was converted into the acyl azide by the action of sodium nitrite in acid solution.[75] The acyl azide was not isolated but instead extracted into ether. The ethereal solution was dried and diluted with ethanol. After removal of the ether by fractional distillation the ethanolic solution was refluxed to produce the unsaturated ethyl carbamate. Catalytic hydrogenation in ethanol with 10% palladium on charcoal as catalyst gave, after recrystallization, ethyl, N-(bicyclo[2,2,2]-octan-2-yl) carbamate in 30% yield (from ethyl acrylate). All five carbamates gave satisfactory elemental analyses.

The dinitrogen tetroxide used to nitrosate the carbamates was obtained by the pyrolysis of lead nitrate. The distilled liquid was diluted with freshly distilled, dry, dichloromethane to make up a nitrosating medium and stored at -15°C in a teflon stoppered vessel till needed. With the exception of the exo-2-carbamate the procedure described by Maskill[5e] was adopted to effect nitrosation. Fused sodium acetate and the nitrosating solution were stirred at -70°C under argon and a solution of the carbamate in dichloromethane added dropwise. The temperature was allowed to rise to 0°C and the golden yellow colour, characteristic of nitroso compounds,

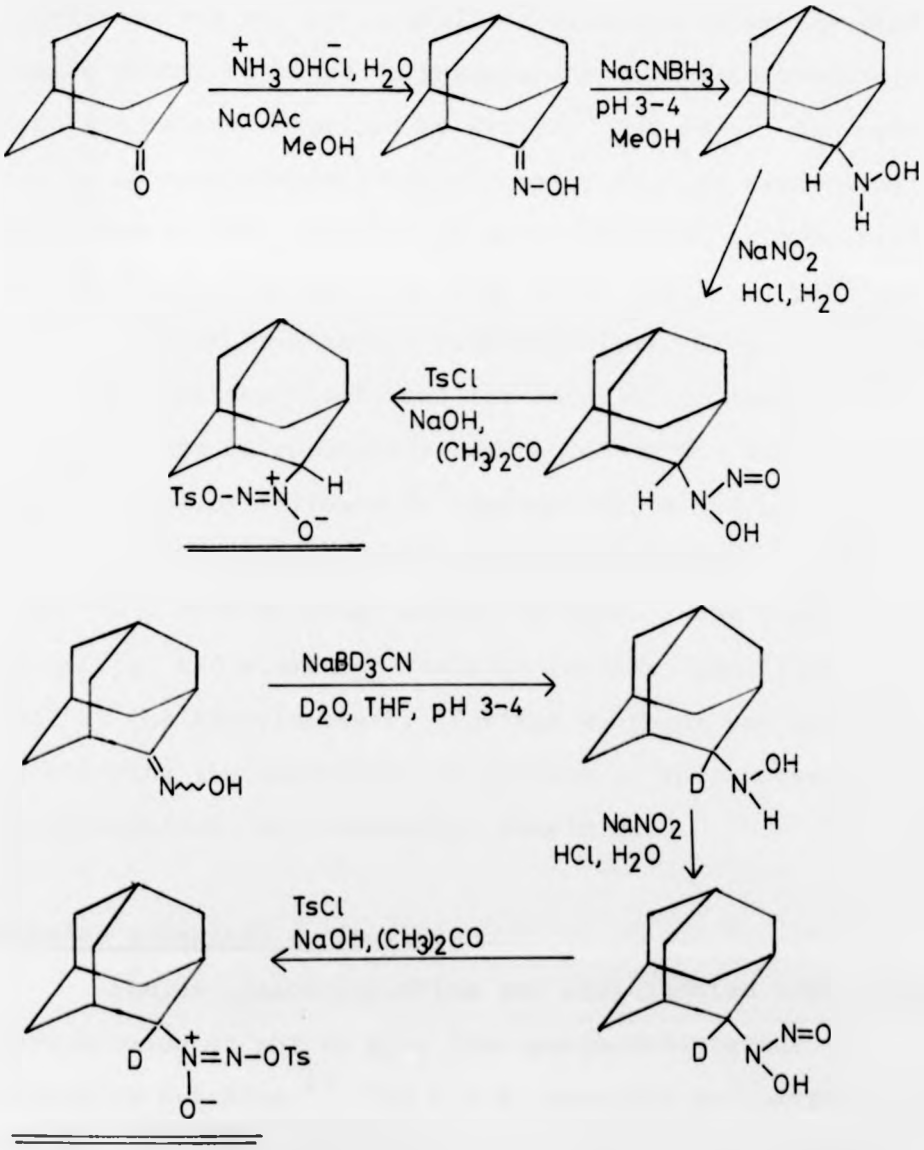
appeared. The reaction mixture was then given a cold aqueous workup and the nitrosocarbamate isolated as a yellow oil. All four nitrosocarbamates thus prepared showed a characteristic doublet in the visible spectrum at 408nm and 426nm in ethanol. Southam reported a doublet at 409nm and 429nm for N-(1-octyl)-N-nitrosobutyramide (42) in the same solvent while Maskill recorded doublets at 410nm and 429nm for N-(trans-4-t-butyl-cyclohexyl)-N-nitrosoacetamide and butyramide. The n.m.r. and i.r. spectral characteristics of these compounds were also indicative of nitrosocarbamates; in particular the i.r. spectrum showed peaks at 1740 cm^{-1} and 1515 cm^{-1} characteristic of the -N(NO)CO-group.

The exo-2-nitrosocarbamate was unstable to the workup conditions. The procedure was therefore modified accordingly. Anhydrous sodium carbonate was used as a proton acceptor instead of sodium acetate in case the nitrosocarbamate was exceptionally sensitive to acidic conditions.[76] When the reaction was complete, the mixture was passed down a column containing a mixture of sodium carbonate and sodium sulphate and eluted with dichloro-methane. Removal of the solvent at $0^{o}C$ left a yellow oil which was solvolysed immediately.

Preparation of adamantyl derivatives

Adamantanone oxime was prepared in quantitative yield from the parent ketone by the usual method. A procedure involving the use of BH_3 in tetrahydrofuran[77] was tried to reduce the oxime to the hydroxylamine without success. Reduction was effected by sodium cyanoborohydride[64] in methanol using

FIGURE 7



Preparative scheme for the synthesis of 2-adamantyl derivatives

methanolic HCl to keep the solution acidic. The hydroxylamine so obtained was purified by sublimation and identified on the basis of its n.m.r. and mass spectral properties. N-(2-Adamantyl) hydroxylamine was not successfully nitrosated using the dinitrogen tetroxide method employed to prepare the nitrosocarbamates; instead the method described by Wright[78] was used. The hydroxylamine, in aqueous ethanolic acidic solution, was treated with sodium nitrite. The addition of water resulted in precipitation of the nitrosohydroxylamine in high yield which was purified by recrystallization from carbon tetrachloride. Elemental analysis and mass spectroscopy confirmed the identity of the product. Treatment of the nitrosohydroxylamine in acetone with p-toluenesulphonyl chloride followed by aqueous sodium hydroxide solution gave the azoxytosylate in good yield which was then recrystallized at -70°C from an ether/petrol mixture. The n.m.r., mass spectroscopy, and elemental analysis results identified the product as the azoxytosylate. Further evidence was provided by identifying the decomposition product of this material, in deuterochloroform, as 2-adamantyl tosylate.

Deuterated adamantyl derivatives

Sodium cyanoborohydride was equilibrated twice with deuterium oxide at pH2 to give the cyanoborodeuteride as described by Hutchins.[64] The n.m.r. spectrum indicated approximately 3% residual protium so another equilibration was given to some of the salt. This material had about 1% residual protium and was used to prepare the α-deuterated

hydroxylamine. The parent oxime was dissolved in a tetrahydrofuran/deuterium oxide mixture and then $NaCNBD_3$ added. An acidic mixture prepared from acetyl chloride and deuterium oxide was used to maintain the solution acidic. After a normal acid-base workup the α-deuterated hydroxylamine was obtained in moderate yield. This material was then nitrosated and tosylated as previously described for the protium analogue.

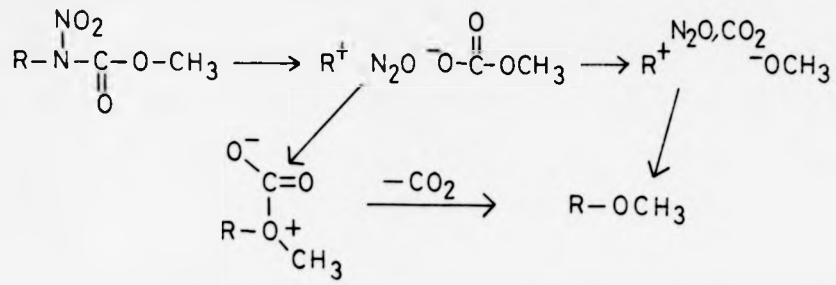
Determination of the amount of deuterium incorporation

The azoxytosylate was not suitable for an accurate estimation of the deuterium incorporation by mass spectroscopy. The intensity of the parent-ion peak was too low and all other significant peaks had M-1 and M+1 peaks flanking them. Since these flanking peaks probably arise from loss or gain of hydrogen in the mass spectrometer their intensity in the deuterated compound will be affected by isotope effects. A concentrated solution of the deuterated compound was investigated by n.m.r. using a Perkin-Elmer R24 90 mHz instrument. The quartet at 2.4τ was compared with the very weak residual signal at 4.3τ; each signal was integrated at least eight times. The measurements were consistent, and indicated a deuterium incorporation of 97.4% with a standard deviation of only 0.2%.

Deamination of Ethyl N-nitroso,N-(exo-bicyclo[3,2,1]octan-3-yl)-carbamate in 80% aqueous tetrahydrofuran

White reported that the decomposition of methyl nitrocarbamates in ethanol gave small amounts of methyl ethers either

by a "2-gas" deamination or by carbonium ion attack on the ether oxygen of the counter-ion.[16] If this process were to occur in the present investigation then the ethyl ethers formed



would be a mixture of external and internal substitution products; thus masking the differences between the two processes.

Ethyl N-nitroso,N-(exo-bicyclo[3,2,1]octan-3-yl)-carbamate was decomposed in 80% aqueous tetrahydrofuran and the product mixture analysed by g.l.c. to see if any ethyl ether was formed. A trace amount (ca. 0.01%) of a compound which co-chromatographed with exo-bicyclo[3,2,1]octan-3-yl ethyl ether was detected. This is far too small an amount to interfere with the unravelling of internal and external substitution processes.

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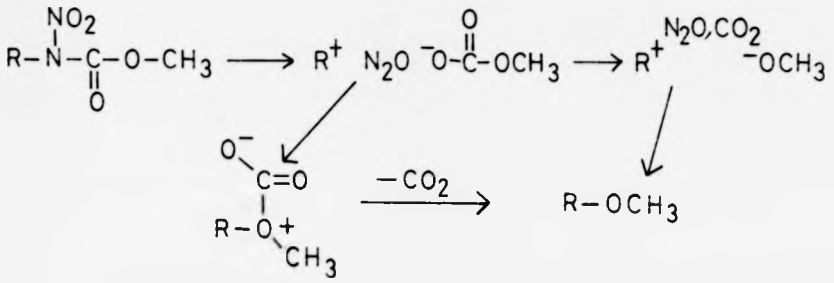

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CHAPTER 4

DISCUSSION SECTION

INTRODUCTION

The techniques used to prepare and deaminate the amines, triazenes and nitrosocarbamates of the five isomeric amines are described in Chapters 3 and 5. The triazene from endo-bicyclo[3,2,1]octan-2-ylamine was not successfully prepared and that from endo-bicyclo[3,2,1]octan-3-ylamine was only obtained as an impure oil. The amounts of N-alkylanilines produced from the triazene reactions were estimated by the method described by Maskill[5f] but the amount of ring alkylated anilines formed was not determined. The nitrous acid deaminations were the least useful for several reasons. The product yields were the least reproducible of the three methods employed and the alcohol products could not be satisfactorily separated from the acetate products. The acetates were therefore reduced to alcohols and the total substitution products then analysed as alcohols. From the low yields of olefins from some of the nitrous acid reactions and also the results of previous work[53] indicate that olefins are not stable to the conditions of the reaction. It is likely therefore that some of the substitution products from the nitrous acid deaminations are derived from olefins and not from the deamination reactions proper.

The nitrosocarbamates were obtained as yellow oils and their solvolysis gave reproducible results. Denitrosation[76] was a minor reaction from some isomers but important for others. It was possible to measure the extent of these reactions using g.l.c. and therefore to allow for this reaction pathway when product yields were normalised. The solvolysis reactions of the nitrosocarbamates in ethanol allow a distinction to be made

between the internal nucleophile (designated X or ^{-}X) and the external nucleophile (Y) and it is these reactions which have provided the most information.

Recoveries from the nitrous acid reactions ranged from 40 to 82%, from the triazene reactions, 59-103%, and from the nitrosocarbamate reactions, 88-103%. The complete results are given in the Appendices.

In gross outline the results from the various deamination methods for a given amine are not very different indicating a similarity of mechanism. A stricter comparison may not be meaningful since the nitrosocarbamate method is performed in a different solvent from the other two methods and, as noted above, the nitrous acid method has inherent errors. It is not possible therefore to distinguish between the concerted or non-concerted mechanisms depicted on page 18 on the basis of a comparison of the different methods of deamination. The results of Whiting[6,12,24a] are conclusive enough to expect confidently that the loss of nitrogen from any simple secondary carbinylamine is a concerted process, or nearly so. The large amounts of internal substitution products obtained from the triazene and nitrosocarbamate reactions are indicative of a concerted process.

Deamination of exo- and endo-bicyclo[3,2,1]octan-3-ylamine derivatives

The products of deamination of the exo- and endo-3-amine derivatives are given in Table 5 and collated in Table 6. Table 7 shows some of the results obtained by Whiting and Maskill[6]

TABLE 5

Products of deamination of exo- and endo-bicyclo[3,2,1]-octan-3-ylamines

Products	Reactant	Triazene	Nitrous acid	Nitrosocarbamate[e]
2-ene	exo	0[a]	0[a]	0[c]
	endo	0.33	0[c]	0[c]
3-ene	exo	22.7	12.9	39.5
	endo	50.8	39.4	64.4
P	exo	1.1	1.5	1.1
	endo	9.6	8.5	17.1
endo-3-X	exo		11.1	6.4
	endo		14.7	4.6
exo-3-X	exo		69.1	20.4
	endo		17.7	0.66
[2,2,2]-X	exo		2.0	0[a]
	endo		10.2	1.0
exo-2-X	exo		3.1	0.2
	endo		11.0	1.1
endo-2-X	exo		0[b]	0.2
	endo		0[d]	1.9
endo-3-Y	exo	6.2		2.3
	endo	3.2		0.68
exo-3-Y	exo	52.0		25.5
	endo	5.5		4.0
[2,2,2]-Y	exo	1.7		0.68
	endo	6.0		1.8
exo-2-Y	exo	2.8		1.0
	endo	7.4		2.4
endo-2-Y	exo	0.10		0.11
	endo	0.60		0.36

a <0.1% b <0.3% c <0.2% d <0.4%

e 2.3% of E also formed from the exo-amine. R-Y = external substitution product. R-X = internal substitution product (plus external for nitrous acid).

TABLE 6

Summary of Product Analyses from  (exo)

and  (endo)

	Reactant	Triazene	Nitrous Acid	Nitroso-carbamate
% olefin (tricyclic hydrocarbon)	exo	22.7(1.1)	12.9(1.5)	39.5(1.4)
	endo	51.1(9.6)	39.4(8.5)	64.4(17.1)
Pet:Inv (Total) in unrearranged substitution (% of total substitution)	exo	-	6.7(85.3)	5.3(59.1)
	endo	-	0.91(53.6)	1.13(18.5)
Pet:Inv (Internal) (% internal substitution)	exo	-	-	3.2(27.2)
	endo	-	-	7.0(9.3)
Pet:Inv (External) (% external substitution)	exo	8.4(62.8)	-	11.1(31.9)
	endo	0.58(22.7)	-	0.17(9.2)
% rearranged substitution (Total)	exo	-	5.1	2.2
	endo	-	21.2	8.56
% rearranged substitution (Internal)	exo	-	-	0.4
	endo	-	-	4.0
% rearranged substitution (External)	exo	4.6	-	1.8
	endo	14.0	-	4.56

TABLE 7

Product analyses[a] of deamination of cis- and trans-N-nitroso-N-(4-t-butylcyclohexyl)acetamides in butyric acid.

Product	Cis-derivative	Trans-derivative
Elimination		
4-Ene	78.4	17.3
3-Ene	7.9	0.3
1-Ene	0.3	
Cyclopropane[b]		6.0
Internal Substitution		
c-4-OAc	7.2	4.9
t-4-OAc	0.6	33.9
c-3-OAc	2.7	0.1
t-3-OAc	0.1	0.1
t-2-OAc		0.1
Cyclopentylmethyl-OAc		2.5
External Substitution		
c-4-OBt	0.7	6.7
t-4-OBt	1.0	27.0
c-3-OBt	0.3	0.1
t-3-OBt	0.8	0.2
t-2-OBt		0.2
Cyclopentylmethyl-OBt		0.6

a Data taken from Ref. No. 6.

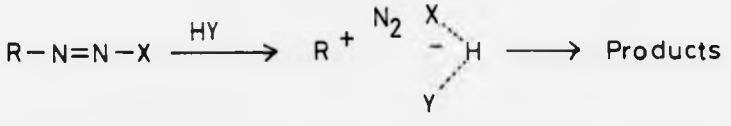
b 2-t-butylbicyclo[3,1,0]hexane

for the deamination of the closely related trans- and cis-4-t-butylcyclohexylamines.

As expected from the literature[56] the major reaction of the endo-3-amine derivatives is elimination. A substantial amount of 1,2-hydride shift was also detected. From the nitroso-carbamate reaction it can be seen that the stereochemistry of substitution in the unrearranged product is very different for the internal and external nucleophiles. The internal nucleophile $CH_3CH_2OCO_2^-$, gives predominantly retained (axial) product while the external nucleophile (EtOH) shows a strong preference for equatorial attack. The distribution of products from hydride shift will be discussed below since these results are more pertinent to the nature of the reaction intermediates derived from the endo- and exo-2-amine derivatives and the [2,2,2]-amine derivatives. An unidentified C_8H_{12} hydrocarbon P was a major product from all three endo-3-amine derivatives.

Less of compound P was formed and a reduced amount of olefin from the exo-3-amine derivatives although the latter was still an important reaction pathway. A small but definite amount of 1,2-hydride shift was detected and from the nitroso-carbamate solvolysis an unidentified external substitution product E was found in modest yield. Large amounts of substitution products were formed from all three exo-3-amine derivatives with both internal and external nucleophiles giving largely retained (equatorial) product.

Since the product fallout from these two amines is so grossly different it is clear that they do not react through the same intermediate i.e. the "free" bicyclo[3,2,1]octan-3-yl carbonium ion cannot be an important product forming intermediate for both sets of diastereoisomeric amine derivatives. The different stereochemical results from internal and external nucleophiles in the ethanolysis of the endo-3-nitrosocarbamate specifically rule out such an intermediate in this reaction. Neither are the product distributions diastereoisomerically related as found in the solvolysis of the tosylate analogues.[4,48] These results are best discussed in terms of the specifically solvated ion pair mechanism as proposed by Cohen and Jankowski[53] and modified by Whiting and Maskill.[6] The latter workers



(49)

proposed that the key intermediate in the deamination of cis- and trans-4-t-butylcyclohexylamine derivatives in acetic or butyric acid was the nitrogen separated ion pair (49) in which the counter-ion ^{-}X is specifically hydrogen bonded to one solvent molecule.

A comparison of Tables 5 and 7 shows that the results from the two sets of diastereoisomers are very similar. There are differences however. There is a smaller amount of olefin formed from the endo-3-amine derivatives compared with the

cis-4-t-butylcyclohexylamine derivatives. This could be a reflexion of the greater strain of the bicyclic olefin formed[79] although the effect is not repeated for the exo-3-amine derivatives. Here, more olefin is formed compared with the trans-4-t-butylcyclohexylamine derivatives. Another reason could be that little olefin is formed from the endo-3-amine derivatives after 1,2-hydride shift has occurred (see later) since other processes may then compete successfully with elimination.

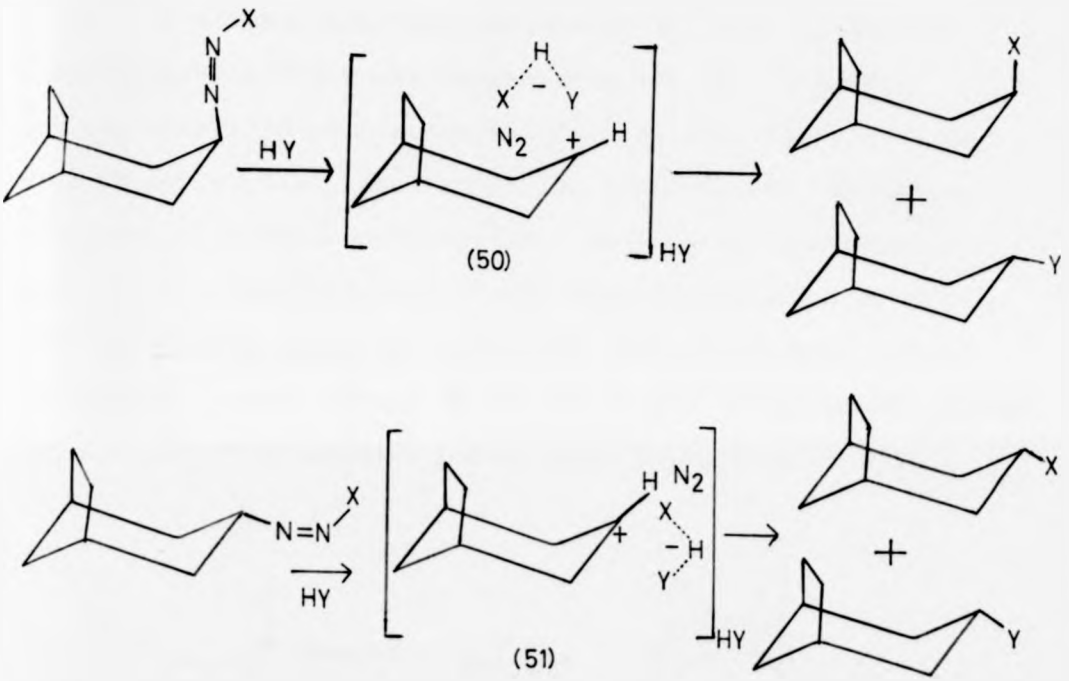
A satisfactory model for the solvolysis of the exo- and endo-3-amine derivatives has to accommodate the following observations obtained mainly from the nitrosocarbamate studies.

(i) the opposite stereochemical preferences of internal and external nucleophiles in the solvolysis of the endo-3-nitroso-carbamate and their similar preferences in the solvolysis of the exo-3-nitrosocarbamate;

(ii) the reduced stereoselectivity of the external nucleophile when acetic acid is solvent as compared to ethanol in both cases;

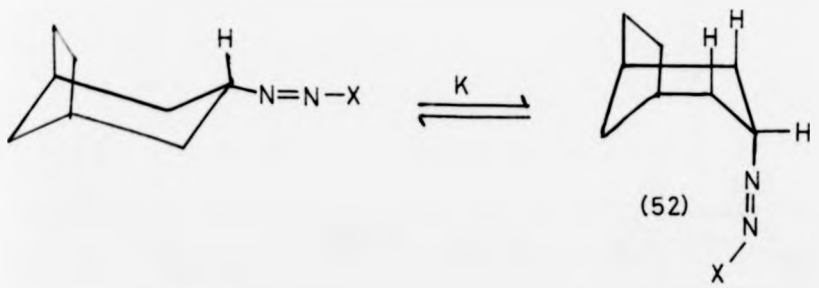
(iii) the reduced stereoselectivity of the internal nucleophile in the solvolysis of the exo-3-nitrosocarbamate compared with the endo-3-nitrosocarbamate;

(iv) the large difference in the ratio of internal/external substitution product with retained configuration from the endo- and exo-isomers. The endo-nitrosocarbamate gives a ratio of 6.8 while the exo-isomer gives a ratio of only 0.8.



The model of Whiting and Maskill[6] involving (50) and (51) as intermediates accounts for the first two points. Collapse of the ion pair (50) to give retained product competes with solvent attack from the unhindered equatorial direction. Since ethanol is more nucleophilic than acetic acid relatively more inverted external substitution product is obtained in this solvent. Collapse of the ion pair (51) to give retained product competes successfully with attack by the bulk solvent from the less accessible axial side of the molecule. The modest reduction of stereoselectivity for external substitution in acetic acid can be attributed to the differences between a monodentate and a bidentate nucleophile.[9]

The same phenomenon as stated in point (iii) was found by Maskill[5g] for the butyrolysis of the two N-(4-t-butylcyclohexyl)-N-nitrosoacetamides. It was interpreted as evidence for partial reaction of the trans-isomer through a non-chair, flexible, conformation. No flexible conformations exist in the bicyclo[3,2,1]octanyl ring system and the only other accessible conformation is the boat arrangement (52). Reaction of a small amount of the exo-3-nitrosocarbamate through (52) conveniently explains point (iii) (return of ^{-}X with

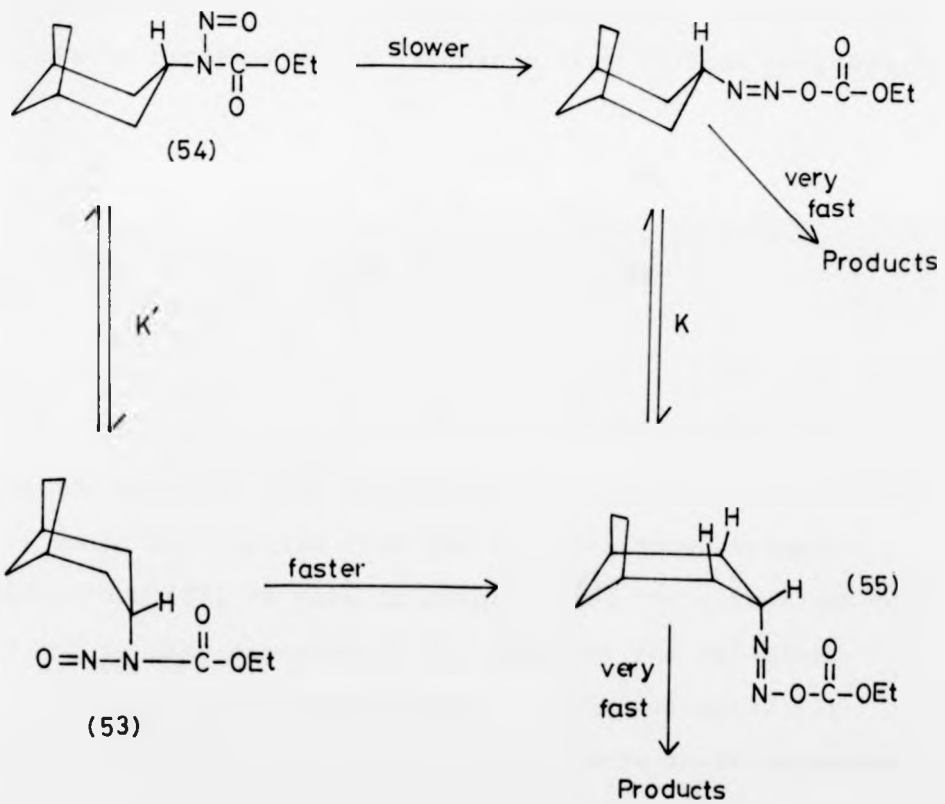


(52)

inversion is encouraged in (52) since this requires pseudo-equatorial attack) although the value of K, the equilibrium constant, will be very small.

A different way to arrive at (52) is the rearrangement of the boat conformer (53) shown in Scheme (3). Although K' will also be small it has been observed in this work and elsewhere[5,55] that axial N-nitrosocarbamates and amides react faster than equatorial ones. If it is assumed that K and K' are equal then Scheme (3) allows a greater proportion of the reaction to proceed via (55) since the Curtin-Hammett principle is applicable to this system. In any case the small amount of

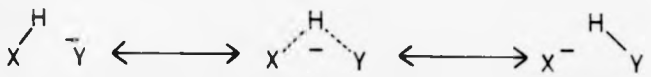
rearranged product from (54), which probably arises from a non-chair conformer, indicates that the deamination reaction occurs mainly through a chair conformation.



Scheme (3)

It is difficult to accommodate the observations in point (iv) on the basis of a specifically hydrogen bonded counter-ion unless one admits the possibility that some (if not

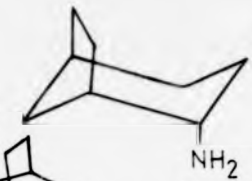
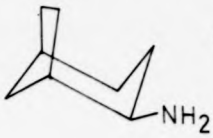
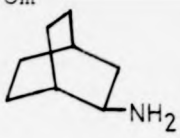
most) of the retained R-Y from the equatorial nitrosocarbamate is derived from the bulk solvent i.e. species resembling solvent separated ion pairs are important product forming intermediates in this reaction. Consideration of the three resonance forms of the paired counter-ion may explain this better. If the counter-ion exists as represented by resonance form (57) as proposed by



(56) (57) (58)

Whiting and Maskill[6] then roughly equal amounts of retained R-X and R-Y would be expected from the endo-3-nitrosocarbamate. Resonance form (58) is more in keeping with the actual amounts formed and is also expected on the basis of the relative acidities of HX and HY (when ethanol is the solvent). If resonance form (57) is not valid for the endo-3-nitrosocarbamate reaction there is no reason why it should be valid for the reaction of the exo-isomer. It follows therefore that some of the large amount of retained R-Y formed in this reaction is derived from the bulk solvent. The formation of solvent separated ion pairs is favoured here because (a) attack by solvent from an axial direction is sterically hindered and (b) ethanol is a polar solvent in which the separation of ion pairs is encouraged.

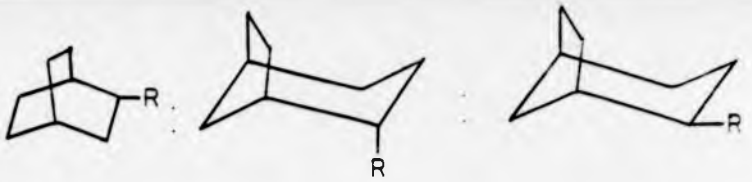
TABLE 8

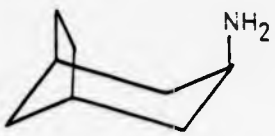
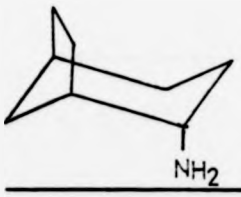
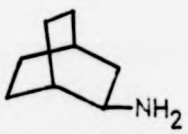
Summary of Product Analyses from  (exo),  (endo) and  (2,2,2).

	Reactant	Triazene	Nitrous Acid	Nitroso-carbamate
	exo	4.6	0.22	22.8
% 2-ene	2,2,2	9.1	0.92	22.6
	endo	-	0.06	0.54
	exo	10.4	1.7	23.1
% 3-ene	2,2,2	8.4	1.1	21.8
	endo	-	0.75	24.6
	exo	13.9	21.4	22.9
% P	2,2,2	22.0	21.4	22.4
	endo	-	4.5	3.4
	exo	up to 0.5%	up to 0.5%	up to 1%
% Q	2,2,2	0[a]	0[a]	0[a]
	endo	-	14.7	23.4
	exo	71.4	76.7	31.2
% Substitution	2,2,2	60.8	76.6	31.4
(Total)	endo	-	79.9	49.2
% Substitution	exo	20.8	-	21.7
	2,2,2	12.9	-	18.7
(Internal)	endo	-	-	24.9
	exo	50.6	-	9.5
% Substitution	2,2,2	47.9	-	12.7
(External)	endo	-	-	24.4

a <0.5%

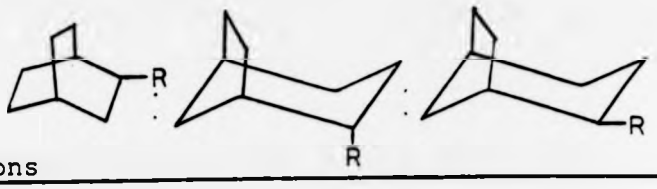
TABLE 9

Product ratios of 

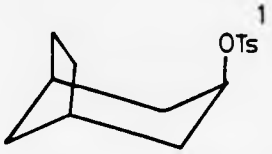
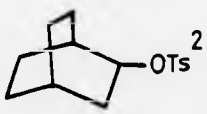
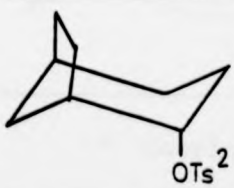
Reactant	Triazene	Nitrous acid	Nitrosocarbamate
	43:53:4	48:52	33:40:26 (Total) 25:28:47 (Internal) 39:53:8 (External)
	37:61:2	39:61	31:55:14 (Total) - (Internal) 38:56:6 (External)
	48:42:10	49:40:10	50:39:11 (Total) 53:40:7 (Internal) 45:36:19 (External)
	63:37	63:37*	57:42:1 (Total) 59:41 (Internal) 54:44:2 (External)
	-	5:8:88	2:6:92 (Total) 1:8:91 (Internal) 2:4:94 (External)

* Goering[71] reported a ratio of 64:36

TABLE 10



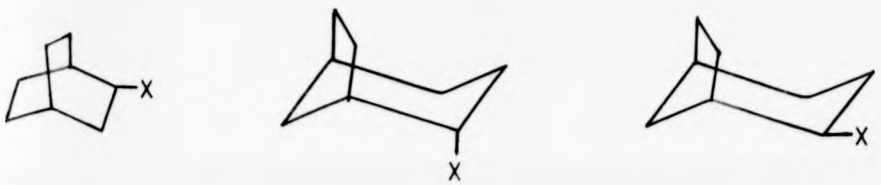
Product ratios of
from solvolysis reactions

Compound	Solvent	Ratio
	Acetic acid	38:58:4
	Formic acid	45:52:3
	50E	38:59:3
	98E	35:65
	Acetic acid	45:50:5
	Formic acid	50:47:3
	50E	53:47
	98E	53:47
	Acetic acid[2]	4:7:89
	Formic acid[3]	2:2:96
	80A[2]	1:4:95
	Acetic acid	54:46:1
	80A	57:43
	Acetic acid	53:46:1
	80A	57:43

1. Ref. No. 48 2. Ref. No. 8 3. Ref. No. 7

Deamination of Bicyclo[2,2,2]octan-2-ylamine and exo- and endo-Bicyclo[3,2,1]octan-2-ylamine Derivatives.

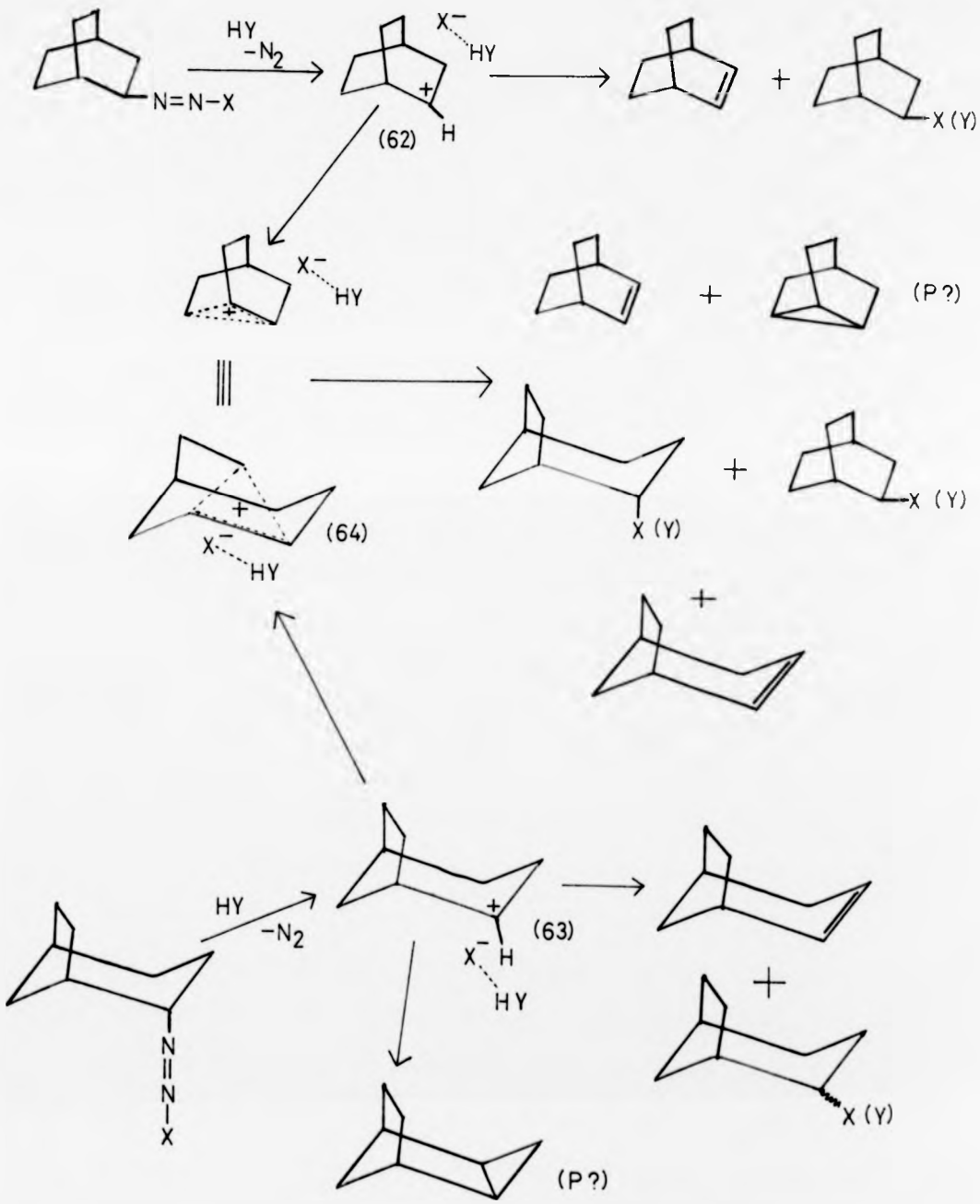
The products of deamination of the title compounds, (59), (60) and (61) X = NH_2 respectively, are given in Table 8.



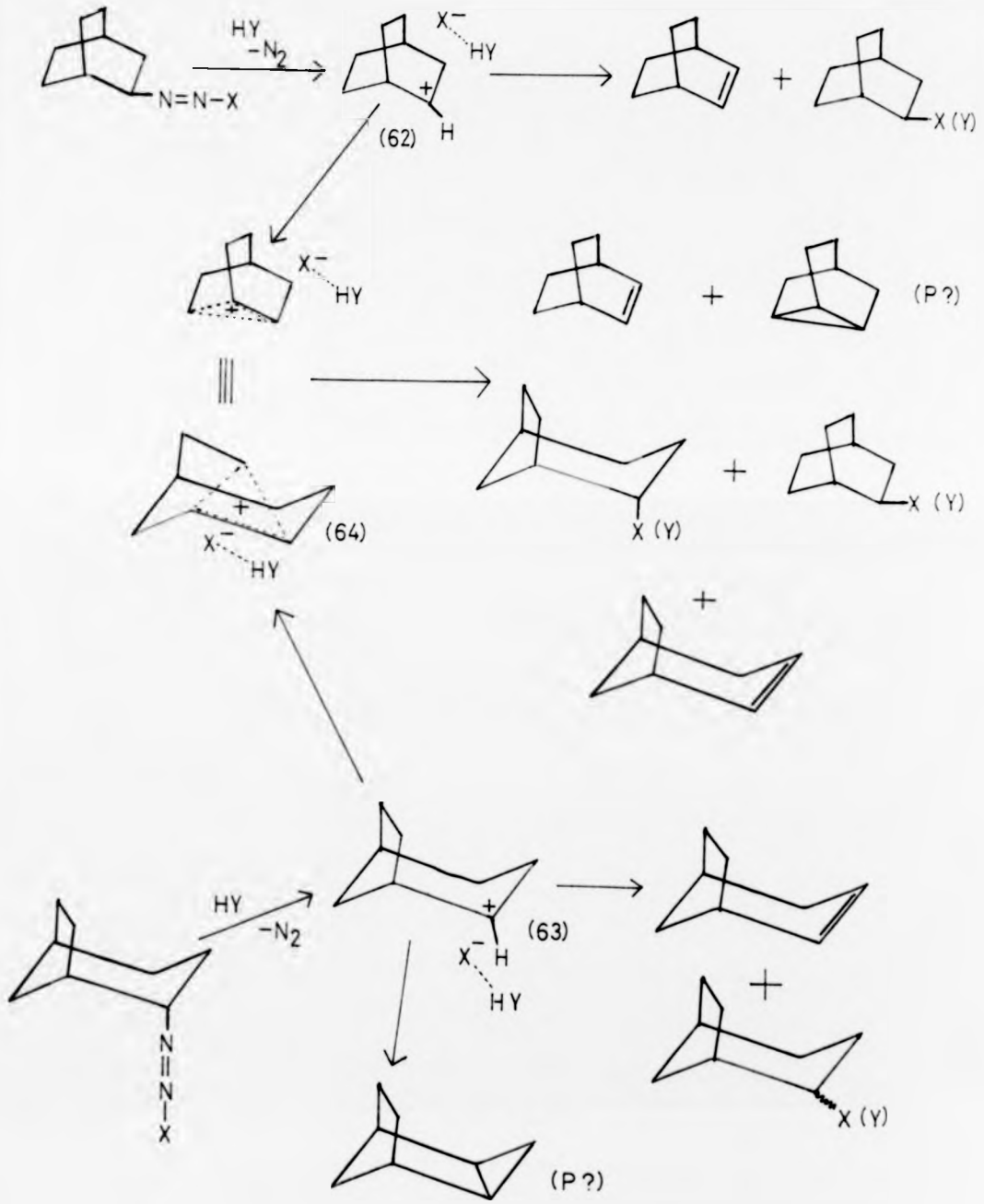
(59) (60) (61)

Tables 9 and 10 show the substitution product ratios of (59):(60):(61) obtained from deamination and from the solvolysis of p-toluenesulphonate esters of the five bicyclo-octyl isomers.

The very low yields of olefin from all three isomeric amines when deaminated by the nitrous acid method shows clearly the instability of the olefins to the reaction conditions. From both the triazene and the nitrosocarbamate deamination methods large amounts of hydrocarbon product were formed from the [2,2,2]-amine. In these reactions over twice as much olefin was formed from the nitrosocarbamate reaction as from the triazene acetolysis although the amount of P, the unidentified C_8H_{12} hydrocarbon (probably tricyclo[3,2,1,$0^{2,7}$]octane - see later) was the same from both reactions. The ratio of the two substitution products from the triazene and nitrous acid reactions (59):(60) = 63:37 is in agreement with earlier work reported by Goering.[71] A small amount of (61) X = OEt was detected from the nitrosocarbamate reaction.



Scheme 4



Scheme 4

The results from the exo-2-amine derivatives are very similar to those from the [2,2,2]-isomers. The most important difference is the detection of a significant amount of external and internal substitution product with the endo-2-configuration from the exo-2-isomer. Apparently this material was formed at the expense of some [2,2,2]-substitution product. Also, from the triazene reaction of the exo-2-amine, more bicyclo[3,2,1]oct-2-ene was formed than bicyclo[2,2,2]oct-2-ene.

The simplest mechanism which accommodates these results is represented in Scheme 4. The initial concerted fragmentation of the diazo-intermediates produce classical carbonium ions which may undergo some elimination and substitution with retention of structural identity but (in the case of the exo-2-amine derivatives) not necessarily with retention of configuration. The predominant fate of the classical ions (62) and (63) is however relaxation to the same non-classical intermediate (64) from which large quantities of products are derived.

The initial existence of the classical ion (62) is suggested to explain the excess of substitution product with retention of structural identity from the deamination of the [2,2,2]-amine derivatives. The acetolysis of [2,2,2]-p-toluene-sulphonate, which is believed to proceed directly through a non-classical ion,[9] shows a much smaller excess of product with retained structural identity (Table 10).

Similarly, an excess of substitution product with retained structural identity is formed from the deamination of

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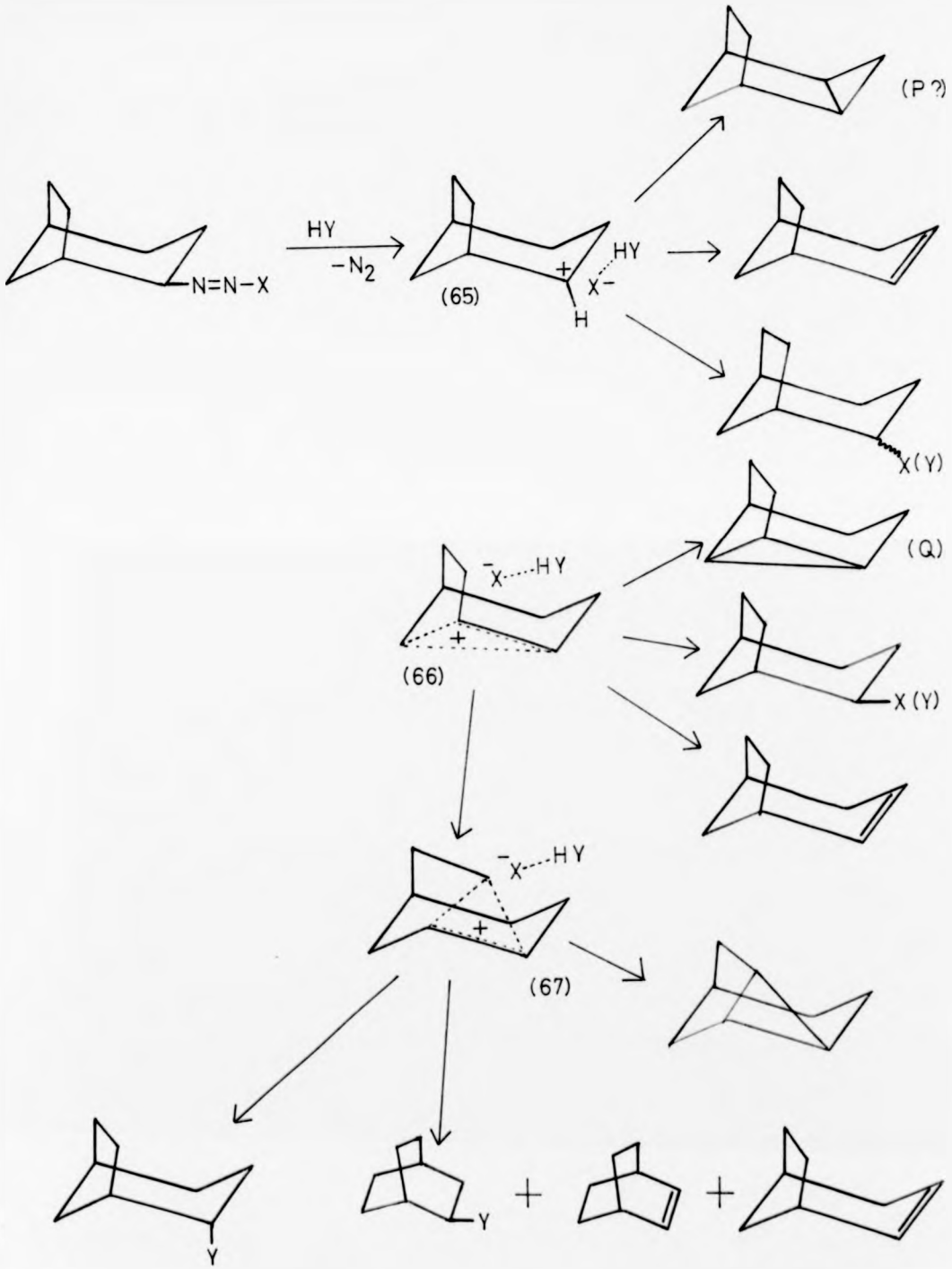
Similarly, an excess of substitution product with retained structural identity is formed from the deamination of

the exo-2-amine derivatives. Also in this case the ratio of (59):(60):(61) X = OEt from the exo-2-nitrosocarbamate shows a larger proportion of (61) when compared with the same ratio for internal substitution (X = OCO_2Et). All three methods of deamination of the exo-2-amine gave a larger proportion of (61) compared to the solvolysis of the exo-2-tosylate, which is also thought to react directly through a non-classical ion.[8] These findings can be explained by postulating that a certain amount of substitution product is derived from the initially formed classical carbonium ion (63) before it relaxes to a non-classical ion. Internal return from (63) X = OCO_2Et, Y = OEt would be expected to give mainly (60) X = OCO_2Et while attack by the external nucleophile (from an equatorial direction) leads to (61) X = OEt.

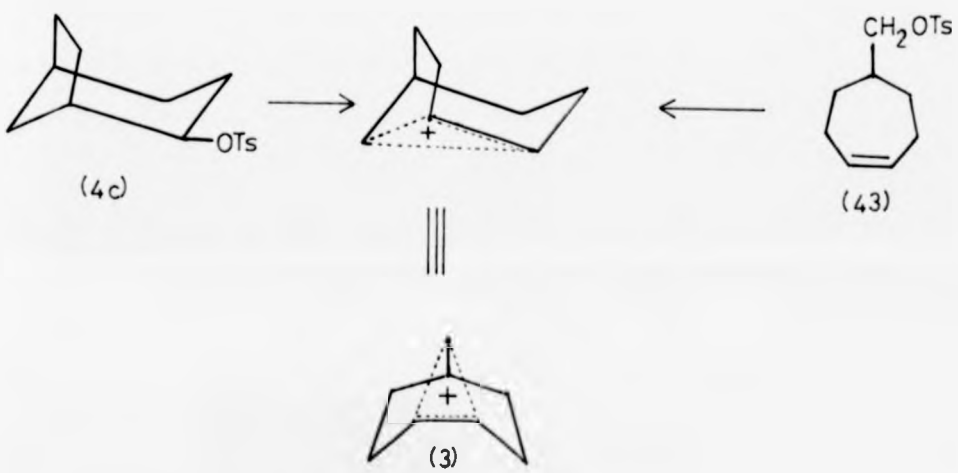
The product fallout from the endo-2-amine derivatives is very different from the exo-2- and [2,2,2]-amine derivatives. Since the results of the nitrous acid method indicate that most of the olefin products have been destroyed comments will be restricted to the nitrosocarbamate reaction only. Equal amounts of substitution product and hydrocarbon were obtained from the endo-2-nitrosocarbamate. This is ca. 1.6 times more substitution than obtained from the exo-2- and [2,2,2]-nitrosocarbamates and this excess is mainly due to substitution by the external nucleophile. Substitution occurs with predominant retention of configuration (Ret/Inv = 15.3) and, in contrast to the [2,2,2]- and exo-2-isomers, only 0.5% of the substitution



Scheme 5

product has lost its structural type. The hydrocarbon fraction consisted of equal amounts of bicyclo[3,2,1]oct-2-ene and an unidentified hydrocarbon Q as well as a small amount of hydrocarbon P and a trace of bicyclo[2,2,2]oct-2-ene.

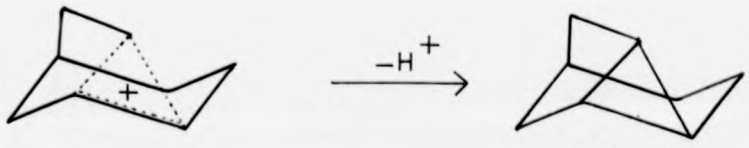
Scheme 5 depicts a possible mechanism to explain the above results. The initial concerted cleavage of the diazo-intermediate is again thought to generate the classical carbonium ion (65) which differs from ion (63) in the position of the counter-ion. This intermediate can give elimination and substitution products before it relaxes to the non-classical ion (66). This species has been proposed by other workers[7,8] as the first formed intermediate in the solvolysis of (4c) and (43). A small amount of leakage from (66) to the isomeric non-classical ion (67) is postulated to account for the formation of some [2,2,2]-substitution product and some bicyclo[2,2,2]-oct-2-ene.



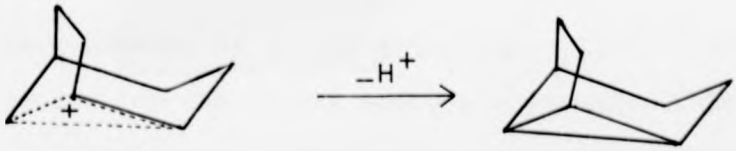
It seems reasonable to formulate (65) as the first formed intermediate in a process analogous to the deamination of the exo-2- and [2,2,2]-amine derivatives. The ratio of exo-2-/[2,2,2]-substitution product is much larger here than from the exo-2- or [2,2,2]-isomers and nucleophilic attack on (65) accounts for this extra exo-2-substitution product. As would be expected from this model the exo-2-/[2,2,2]-internal substitution ratio is larger than the external ratio.

On the nature of the unidentified hydrocarbons P and Q

An unidentified peak in the hydrocarbon region of the chromatogram from every deamination reaction was designated compound P. Another unidentified peak of slightly greater retention time, designated compound Q, was obtained only from the deamination of the endo-2-amine derivatives although small amounts were probably present in the product mixtures obtained from the exo-2- and [2,2,2]-amine derivatives. Far more P was formed from the endo-3-amine derivatives than from the exo-3-amine derivatives. This observation and the fact that large amounts of P were formed from the exo-2- and [2,2,2]-amine derivatives suggested that P might be tricyclo[3,2,1,$0^{2,7}$]octane (68). Compound P could be formed either by loss of a proton from the non-classical carbonium ion intermediate or possibly by a 1,3-elimination process.[80] It was thought that compound Q might be tricyclo[3,3,0,$0^{2,8}$]octane (69). It was found that the yields of P and Q were as high from the nitrous acid deaminations as from the other two methods, supporting the view that these compounds were not olefins.

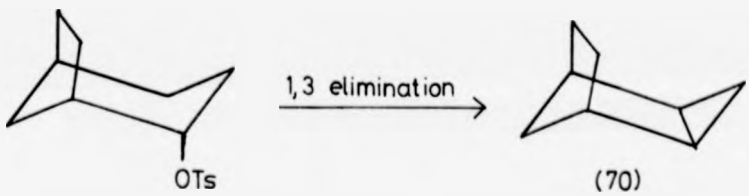


(68)



(69)

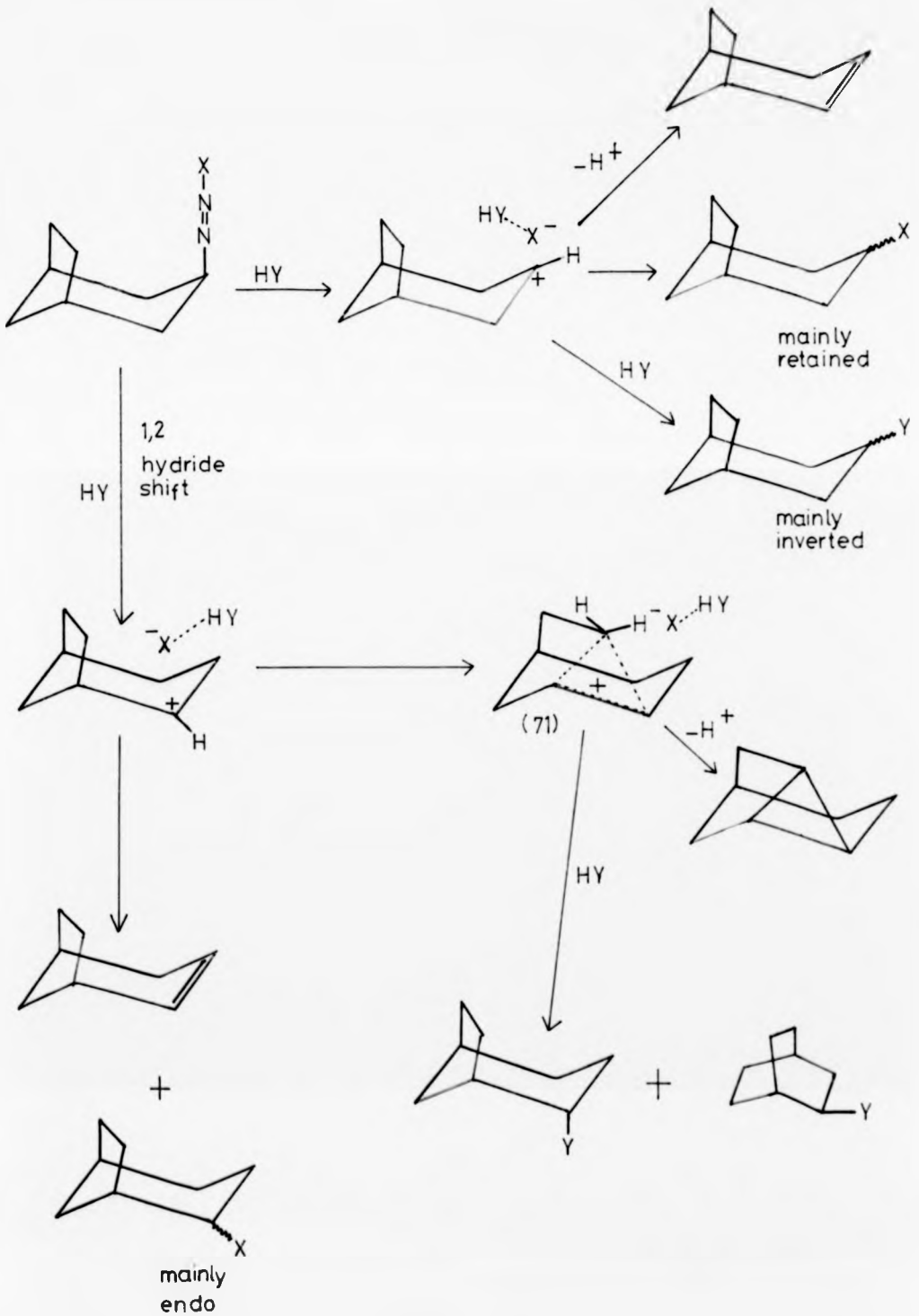
A large scale nitrous acid deamination of the exo-2-amine was done and a small amount of P isolated by preparative g.l.c. High resolution mass spectroscopy indicated that this material was a C_8H_{12} hydrocarbon. Proton magnetic resonance spectroscopy gave little structural information except that there were no signals in the olefinic region but there were signals in the cyclopropane region. Another preparation of compound P, this time by the solvolysis of exo-bicyclo[3,2,1]octan-2-yl tosylate in dimethylformamide following the procedure of Saito et al.[81], gave a very low recovery (2.1%) of P. The ^{13}C magnetic resonance spectrum of this material showed eleven signals in the aliphatic carbon region. Tricyclo[3,2,1,$0^{2,7}$]octane should give six signals and tricyclo[3,2,1,$0^{2,8}$]octane five signals. Even though only one peak was observed in the g.l.c. chromatogram of the material used for ^{13}C analysis P cannot be a single compound. Another tricyclic compound, tricyclo[3,2,1,$0^{2,4}$]octane (70) could be obtained by 1,3-elimination from the exo-2-tosylate. This compound would give rise to five signals in the ^{13}C spectrum



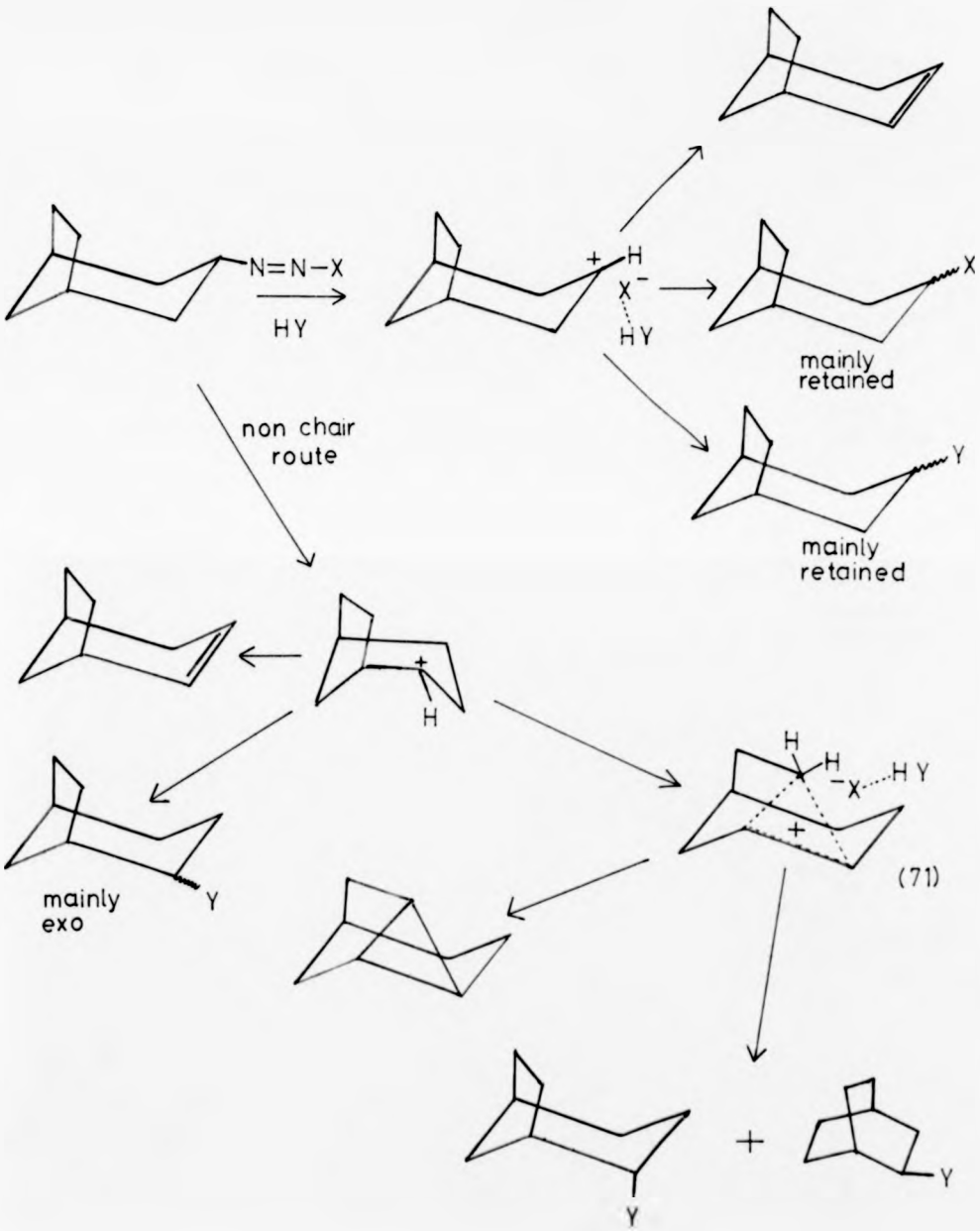
and thus a mixture of it and tricyclo[3,2,1,$0^{2,7}$]octane could also account for the eleven signals observed. Tricyclo-[3,2,1,$0^{2,7}$]octane was previously reported to be a probable

product of acetolysis of exo-2- and [2,2,2]-tosylates.[8]

The 3.5-4.5% of P found in the deamination of the endo-2-amine derivatives could possibly consist mainly of tricyclo[3,2,1,$0^{2,4}$]octane since the geometry for a 1,3 elimination is particularly favourable in this case.[80]


X-N=N
HY
HY...X⁻
H
+
-H⁺
X
mainly retained
HY
Y
mainly inverted
1,2 hydride shift
HY
⁻X...HY
+
H
H
H⁻X...HY
(71)
-H⁺
HY
Y
+
Y
+
X
mainly endo

Scheme (6)


N=N–X
HY
+
H
X⁻
HY
X
mainly
retained
non chair
route
Y
mainly
retained
H
mainly
exo
Y
H
H
–X
HY
+
(71)
Y
+
Y

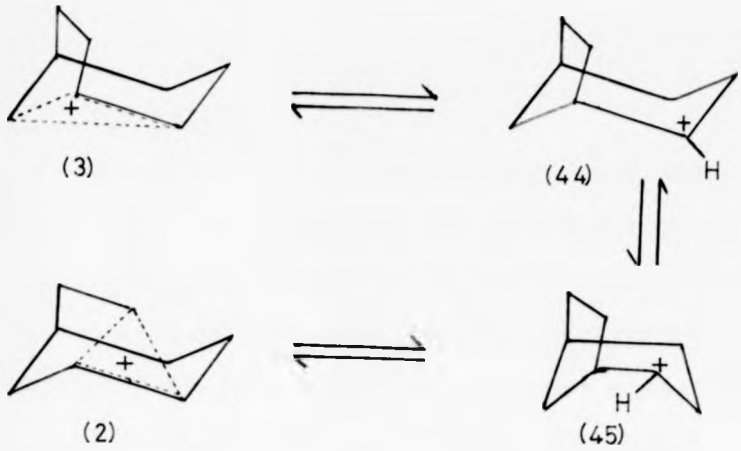
Scheme (7)

Rearrangement in the bicyclo[3,2,1]octan-3-yl system

The major rearranged internal substitution product from the deamination of endo-3-nitrosocarbamate is endo-2-OCO_2Et (Table 5). This result is in sharp contrast to the external substitution product distribution, which shows an excess of exo-2-OEt over [2,2,2]-OEt with little endo-2-OEt, and the results from the solvolysis of the corresponding tosylate.[4,48] A preference for internal substitution with retention of configuration at the rearranged position was reported in the deamination of N-(cis-4-t-butylcyclohexyl)-N-nitrosoacetamide in butyric acid.[6] This was taken to mean that the migration of hydrogen took place quickly enough to prevent diffusion of the internal nucleophile into the bulk solvent. Such an interpretation seems valid in the present case also.

The yields of rearranged internal substitution product from the exo-3-nitrosocarbamate are too small to allow any meaningful interpretation but the rearranged external substitution product shows an excess of exo-2-OEt over [2,2,2]-OEt in contrast to the substitution ratios obtained from the exo-2- and [2,2,2]-amine derivatives and tosylates. Clearly the initial products of hydride shift from both epimers are classical carbonium ions from which some product is derived before relaxation to a non-classical ion (71) occurs. Possible reaction schemes for the endo-3- and exo-3-amine derivatives are shown in Schemes (6) and (7) respectively.

Berson and co-workers[37] and Kraus[82] have proposed that the interconversion of the two non-classical ions (3) and (2) proceeds via two conformationally related classical ions (44) and (45). Berson maintains that when (44) is generated it will relax



to the non-classical ion (3) and similarly (45) leads to the formation of (2). There is no evidence for this process from the present work. The formation of (44) from the endo-3-amine derivatives by 1,2 hydride shift is followed by at least 50% relaxation to (2). This figure is even larger in the solvolysis reactions of the endo-3-tosylate.[48]

Hydrocarbon formation

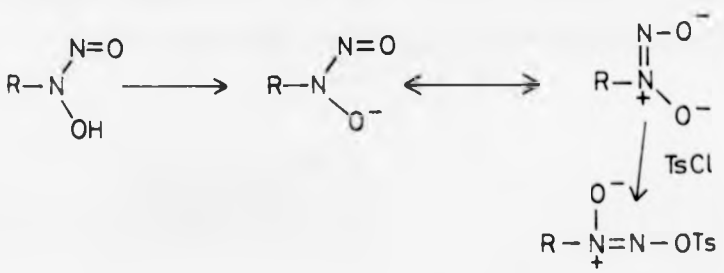
A feature of these deamination reactions not found in their solvolysis counterparts is the formation of large amounts of elimination products from what are believed to be non-classical carbonium ions e.g. the solvolysis of endo-bicyclo[3,2,1]octan-2-yl tosylate in acetic acid, aqueous acetone[8] or formic acid[7] resulted in the formation of less than 0.3% of hydrocarbon whereas deamination of the corresponding amine gave up to 52% of hydrocarbon products. A strong preference for substitution as opposed to elimination has been recognised as a characteristic of solvolysis reactions which proceed through σ-bridged intermediates.[83] In the deamination reactions studied here elimination from non-classical ions is a major reaction whether or not the non-classical ions are formed following hydride shifts. However it should be noted that despite the large amount of rearrangement from the endo-3-amine derivatives the most bicyclo[2,2,2]oct-2-ene formed was 0.2%. This could be an effect of the counter-ion which is nicely positioned to abstract a proton from (71) (Scheme 6) to form tricyclo-[3,2,1,$O^{2,7}$]octane.

It is suggested that the non-classical ions which are formed via hydride shift from the endo- and exo-3-amine derivatives are essentially no different from those formed in solvolysis reactions except perhaps for some effect of the counter-ion. The non-classical ions formed without involving hydride shift however show the propensity for non-selective reaction (compared with solvolysis reactions) which is characteristic of deamination reactions.

Solvolysis of azoxytosylates

The transient existence of the diazo-intermediates in the deamination reactions of primary aliphatic carbinylamines has meant that mechanistic studies of these processes have been confined on the whole to product analyses and labelling studies whilst the elucidation of the mechanisms of solvolysis reactions has been greatly helped by kinetic information as well. The inability of chemists to compare kinetic data from both solvolysis and deamination reactions must be considered a serious handicap. Attempts to isolate stable diazo-esters have been made without success.[84] Such efforts have been focused on involving an alkyl group which would lead to an unstable carbonium ion e.g. a bridgehead ion. If the incipient carbonium ion is very unstable then the rate of decomposition to such an unfavourable species should be (relatively) slow. However even when the incipient carbonium ion is the 1-norbornyl cation the diazo-intermediate has only a fleeting existence at -50°C.[84]

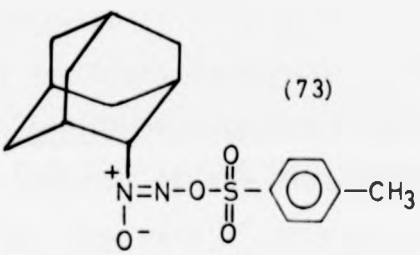
It was surprising when Stevens[10] proposed that the stable crystalline compounds formed by the reaction of nitroso-hydroxylamine salts with p-toluenesulphonyl chloride were azoxytosylates (72).



(72)

White confirmed the structure of (72) R=phenyl by X-ray crystallography[11] and drew attention to the similarity of these compounds to the diazo-intermediates in deamination reactions. Such a structure could, in principle, be formed from the acylation of salts of nitrosohydroxylamines but only typical deamination products are obtained from this reaction.[85] The stability of compounds with structure (72) then is remarkably reduced by replacing the p-toluenesulphonyl group with an acyl group. The reason for this is far from clear. These azoxytosylates should then provide the means to study some of the kinetic aspects of deamination reactions.

It was decided to investigate the chemistry of adamant-2-yl-ONN-azoxytosylate (73) since the 2-adamantyl system has been extensively studied in both solvolysis[85] and deamination[58] reactions and because of the stereochemical simplicity.



(73)

The decomposition of the azoxytosylate (73) in deuterochloroform at 60°C was monitored by n.m.r. spectroscopy. The resonance peak at 5.7τ (attributed to the hydrogen atom attached to C-2 on the adamantane ring) slowly attenuated and a new peak at 5.3τ appeared. The half-life for this process was roughly 16 hours. After 2.5 days the n.m.r. spectrum was indistinguishable from that of 2-adamantyl tosylate. The experiment was repeated on a larger scale and the product isolated in 93% yield. After recrystallisation this material was identified as 2-adamantyl tosylate by melting point, i.r. and n.m.r. spectroscopy.

Some azoxytosylate (73) was solvolysed in ethanol at 60-62°C and any volatile products were removed by prolonged pumping. The residue showed two products by t.l.c., one having the same R_F as 2-adamantyl tosylate and the other having a very low R_F. The latter compound was probably p-toluenesulphonic acid. Recrystallisation of the residue gave a white solid which was identical with authentic 2-adamantyl tosylate.

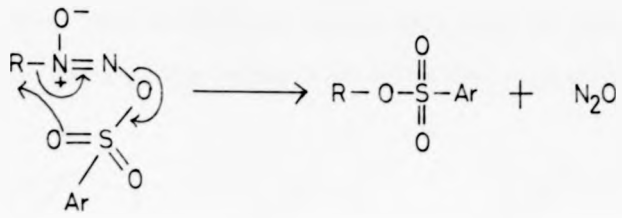
It was hoped to obtain an α-k.i.e. for the solvolysis of the azoxytosylate (73) in 97% hexafluoroisopropanol since in this solvent one might reasonably expect a limiting mechanism to occur. However 1st order kinetics were not observed probably due to the fast solvolysis of the 2-adamantyl tosylate formed during the reaction. The rate of reaction in ethanol, although faster than that in $CDCl_3$, was too slow for practical purposes so 80% aqueous ethanol (80E) was used instead. In this solvent mixture at 61.3°C good 1st order kinetics were obtained; $k_H = (3.28 \pm 0.02) \times 10^{-4}$ sec^{-1} and $k_H/k_D = 1.132 \pm 0.005$. The errors quoted are standard errors with 2/3 confidence limits.[87]

The decomposition of the azoxytosylate (73) in deuterochloroform at 60°C was monitored by n.m.r. spectroscopy. The resonance peak at 5.7τ (attributed to the hydrogen atom attached to C-2 on the adamantane ring) slowly attenuated and a new peak at 5.3τ appeared. The half-life for this process was roughly 16 hours. After 2.5 days the n.m.r. spectrum was indistinguishable from that of 2-adamantyl tosylate. The experiment was repeated on a larger scale and the product isolated in 93% yield. After recrystallisation this material was identified as 2-adamantyl tosylate by melting point, i.r. and n.m.r. spectroscopy.

Some azoxytosylate (73) was solvolysed in ethanol at 60-62°C and any volatile products were removed by prolonged pumping. The residue showed two products by t.l.c., one having the same R_F as 2-adamantyl tosylate and the other having a very low R_F. The latter compound was probably p-toluenesulphonic acid. Recrystallisation of the residue gave a white solid which was identical with authentic 2-adamantyl tosylate.

It was hoped to obtain an α-k.i.e. for the solvolysis of the azoxytosylate (73) in 97% hexafluoroisopropanol since in this solvent one might reasonably expect a limiting mechanism to occur. However 1st order kinetics were not observed probably due to the fast solvolysis of the 2-adamantyl tosylate formed during the reaction. The rate of reaction in ethanol, although faster than that in $CDCl_3$, was too slow for practical purposes so 80% aqueous ethanol (80E) was used instead. In this solvent mixture at 61.3°C good 1st order kinetics were obtained; $k_H = (3.28 \pm 0.02) \times 10^{-4}$ sec^{-1} and $k_H/k_D = 1.132 \pm 0.005$. The errors quoted are standard errors with 2/3 confidence limits.[87]

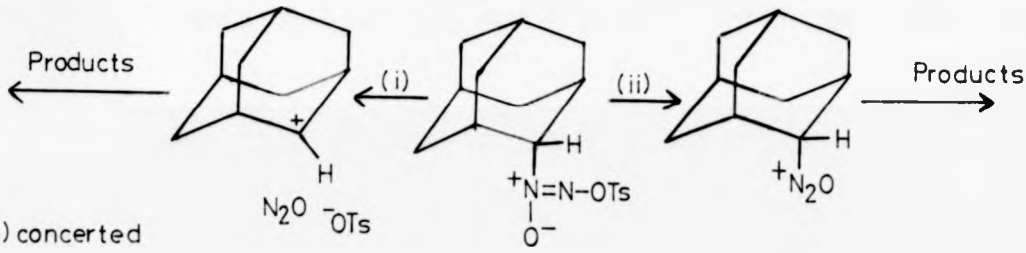
The possibility exists that the azoxytosylates react through a cyclic mechanism. A similar cyclic mechanism was at



one time proposed for the decomposition of nitrosoamides[15b] but was ruled out on the basis of some ^{18}O labelling studies.[9,43] Some evidence is available which suggests that the mechanism of reaction is not cyclic. The crystal structure of the azoxytosylate (72) R=phenyl shows that the alkyl group and the tosylate moeity are trans to each other. Such a geometrical relationship, if it holds for the 2-adamantyl analogue, rules out a concerted reaction with a cyclic six-membered transition state. The increase in reaction rate as the solvent increases in ionising ability suggests an ionic mechanism rather than a cyclic one. Also the low recovery of 2-adamantyl tosylate from the ethanolysis of (73) and the formation of some olefin from the decomposition of (72), R=isopropyl, in chloroform[11] are not compatible with a cyclic mode of decomposition.

The α-k.i.e. of 1.13 in 80E suggests an activated complex with carbonium ion character.[88] The value of the α-k.i.e. in the complete absence of nucleophilic assistance to ionisation

cannot be estimated accurately since no data are available for reactions in which nitrogen is the departing atom from the incipient carbonium ion. The result is compatible with a mechanism in which either concerted[6] decomposition of the substrate (73) or a non-concerted fragmentation if the second step is rate limiting occurs. The formation of some 2-adamantyl tosylate



(i) concerted
(ii) non concerted

(73) (74)

from the ethanolysis of (73) could be construed as evidence for some amount of concerted reaction but it should be noted that some intramolecular substitution product was formed from the deamination of ethyl N-nitroso, N-(1-norbornyl)carbamate in ethanol[84] and this reaction is believed to proceed by a step-wise decomposition of the diazoester intermediate.

The most satisfactory way to determine whether the decomposition of (73) is concerted or not would be to perform an ^{18}O labelling study. Decomposition of (73) would lead to scrambling of the ^{18}O label in the starting material if return from (74) is important i.e. if step-wise fragmentation, with the second step rate limiting, is important.

The two major schools of thought on the mechanisms of solvolysis reactions in general have different views on the solvolysis mechanism of 2-adamantyl tosylate. According to Schleyer and his co-workers[1,86,89] the rate determining process is the formation of intimate ion pairs (k_1 in (75)) while the products of the reaction are derived from solvent separated ion pairs i.e. return from the intimate ion pair, k_{-1}, to starting material is negligible. Shiner and others[90,48] have proposed

$$R\text{-}OTs \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R^+ \; \bar{O}Ts \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} R^+ \,\|\, \bar{O}Ts \qquad (75)$$

that the rate determining step is solvent separation of the intimate ion pair, k_2, and that internal return is substantial.

The formation of some 2-adamantyl tosylate in the ethanolysis of the azoxytosylate (73) is evidence for return of tosylate from an ion pair which is separated by a molecule of nitrous oxide at least. The case for return from an intimate ion pair is strengthened by this observation.

CHAPTER 5

EXPERIMENTAL PROCEDURES

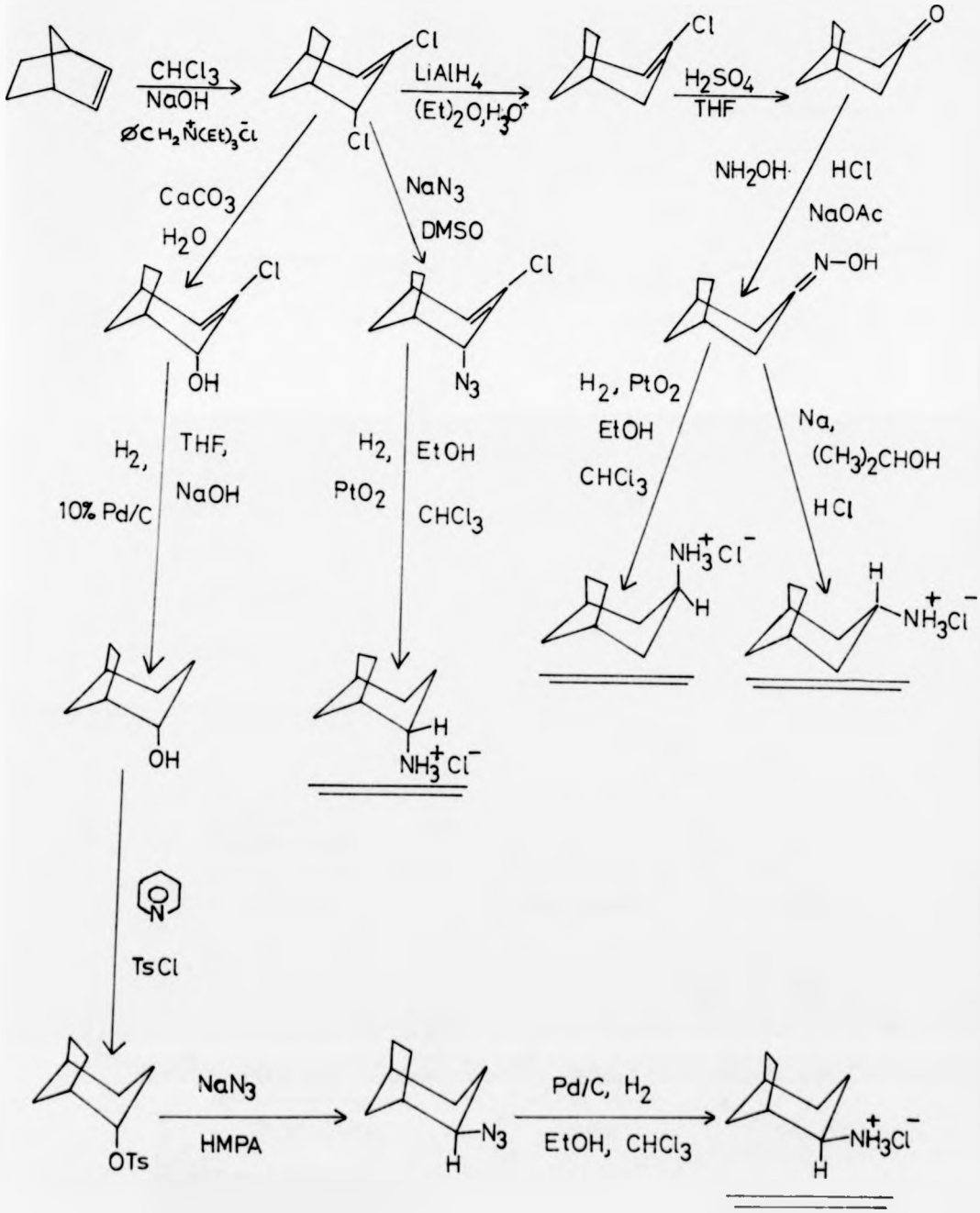
General details

Infra-red (i.r.) spectra were determined with a Perkin-Elmer 577 grating infrared spectrophotometer or with a Perkin-Elmer 197 infrared spectrophotometer. Nuclear magnetic resonance (n.m.r.) spectra were carried out on a Perkin-Elmer R24 or R32 n.m.r. spectrometer using tetramethylsilane (TMS) as internal standard except when D_2O or CD_3NO_2 were used as solvent. Ultraviolet (u.v.) spectra were carried out using either a Perkin-Elmer 402 ultraviolet-visible spectrophotometer or a Unicam SP.800A spectrophotometer. Mass spectra were determined by Mr. D. F. Dance using a Jeol D-100 double focusing mass spectrometer.

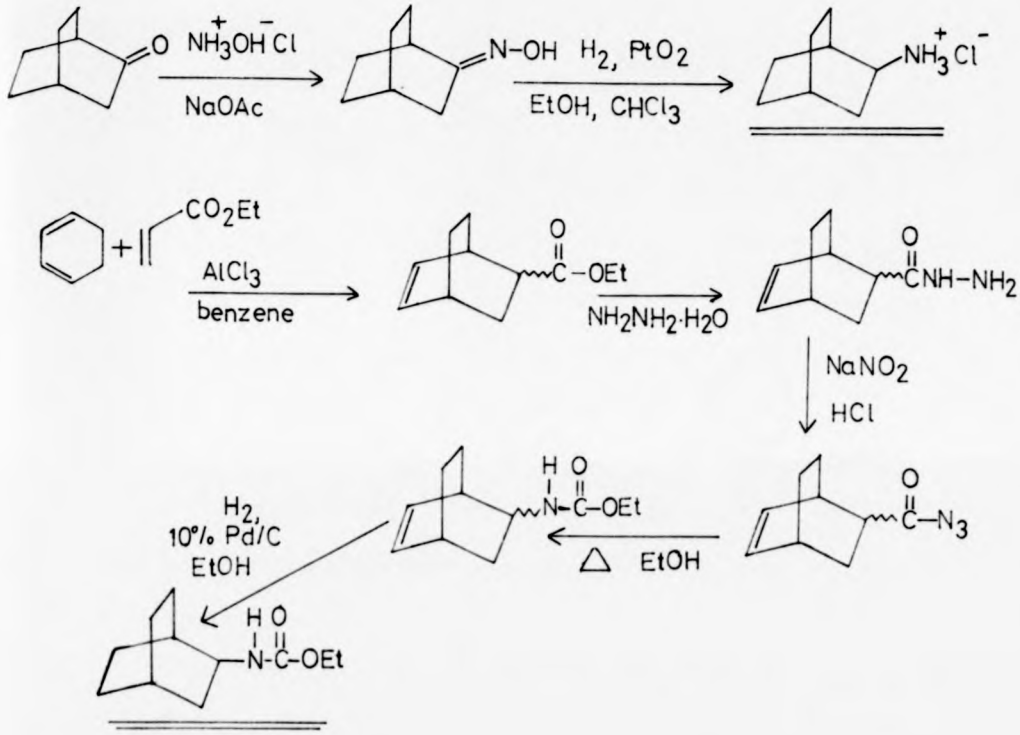
A Perkin-Elmer F30 gas chromatograph was used to run all analytical gas-liquid chromatograms (g.l.c.). Melting points were determined using a Kofler hot stage and are uncorrected.

The pentane and petroleum ether (40-60) used for recrystallisation purposes were purified by being washed three times with concentrated sulphuric acid, then with aqueous sodium carbonate solution and water, and finally being dried over calcium chloride. Fractional distillation from phosphorus pentoxide completed the purification process. The ether and tetrahydrofuran required for g.l.c. analyses and recrystallisations were refluxed with lithium aluminium hydride overnight and distilled. Dimethylsulphoxide was stirred with potassium hydroxide for 3 days then fractionally distilled, under reduced pressure, from barium oxide. Benzene was purified by passing it down a column of alumina (Grade I) prior to use. Dichloromethane was fractionally distilled from phosphorus pentoxide b.p. 40°C.

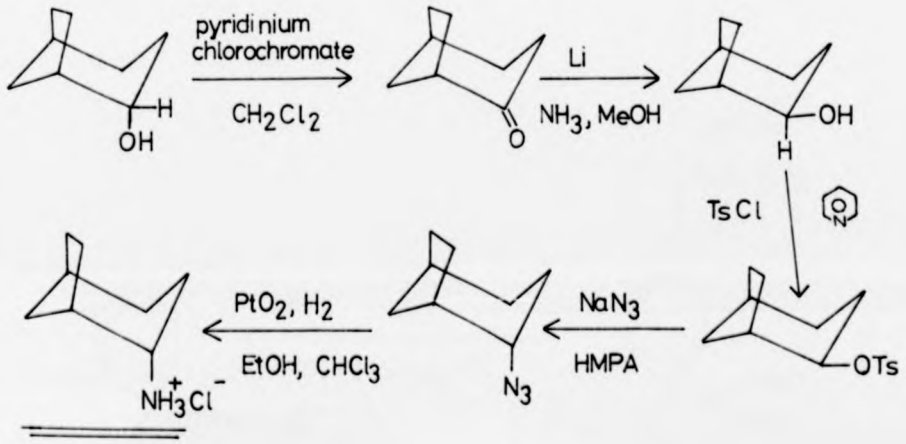
Preparative Scheme I



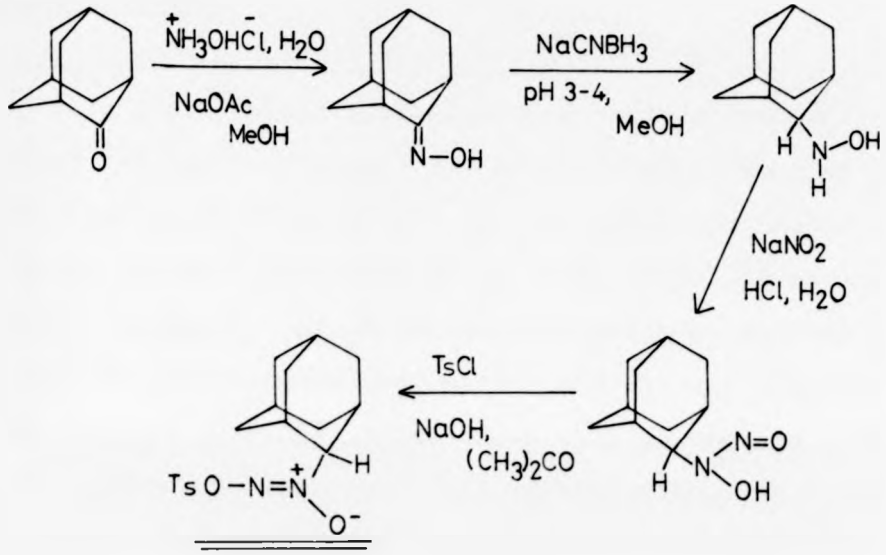
Preparative Scheme II

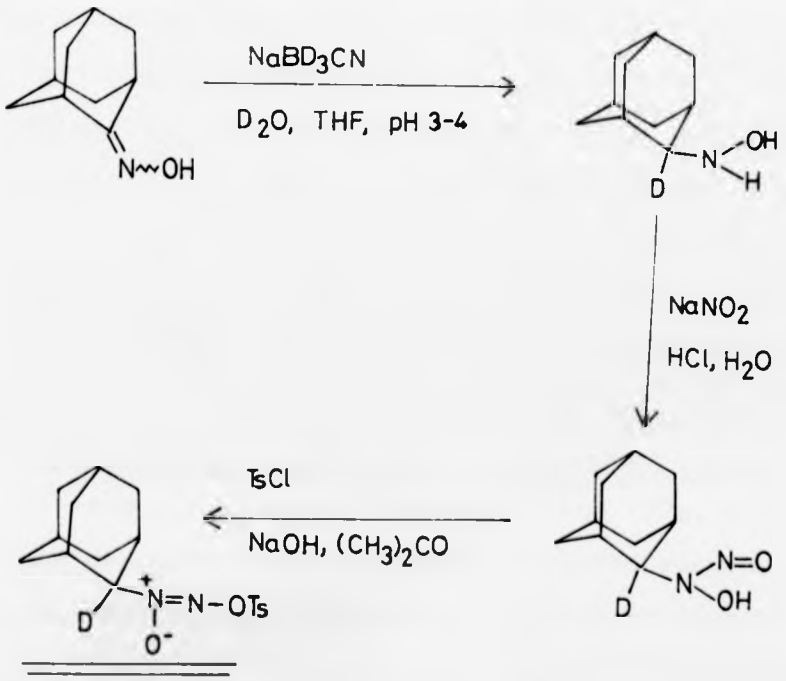


Preparative Scheme III



Preparative Scheme IV





Preparative Details

exo-3,4-Dichlorobicyclo[3,2,1]oct-2-ene[61]

To a mechanically stirred, ice-cold solution of norbornene (43.1g, 0.46 moles) and benzyltriethylammonium chloride (1g) in chloroform (214.2g, 1.8 moles) was added a solution of sodium hydroxide (146.6g, 3.66 moles) in water (250 cms^3), dropwise. After the mixture had been stirred for three days at room temperature, water (450 ml) was added and the dark mixture extracted three times with chloroform. The combined organic extracts were then washed with water (twice), dilute hydrochloric acid and brine, and dried over calcium chloride. The solution was then filtered and the solvent removed under vacuum. Fractional distillation of the dark red residue under reduced pressure gave a colourless oil. (61g, 75%) b.p. 40-45°C/0.2 mm; (lit.[91] 72-73°C/0.9mm) i.r. (FILM): $\bar{\nu}_{max}$ = 1710 (w), 1615 (m), 1420 (m), 1415 (m), 1350 (w), 1330 (m), 1300 (s), 1230 (m), 1220 (m), 1015 (m), 950 (m), 870 (m), 830 (m), 740 (m), 710 (m) and 680 (s) cm^{-1}; n.m.r. (CCl_4): τ = 4.0 (1H,d), 5.9 (1H,d) and 7.1-9.0 (8H,m); g.l.c. (50' SCOTDEGS; 20 psi, 130°C): Retention time = 5.3 mins.

3-Chlorobicyclo[3,2,1]oct-2-ene

exo-3,4-Dichlorobicyclo[3,2,1]oct-2-ene (12g, 0.07 moles) was added dropwise to a magnetically stirred suspension of lithium aluminium hydride (3.05g, 0.08 moles) in anhydrous ether (100 cms^3) at 0°C. The mixture was then refluxed for twenty hours. After being cooled in an ice bath, the reaction mixture was quenched by the addition of wet ether and ice. The reaction

mixture was poured onto ice, acidified with dilute hydrochloric acid and extracted with ether (3 times). The combined organic extracts were dried over magnesium sulphate, filtered, and the ether was removed under vacuum to leave a pale yellow oil. Fractional distillation under reduced pressure gave a colourless oil.

(8.08g, 81%); b.p. 90°C/20mm. (lit.[91] 76-77°C/21 mm).

i.r. (FILM): $\bar{\nu}_{max}$ = 1715 (w), 1620 (m), 1425 (m), 1420 (m), 1355 (w), 1335 (w), 1305 (s), 1240 (w), 1225 (w), 1040 (m), 950 (m), 870 (m), 830 (m), 780 (m), 740 (w), 710 (w), and 685 (s) cm^{-1};

n.m.r. (CCl_4): τ = 3.15 (1H,d), and 7.2-9.0 (10H,m);

g.l.c. (50' SCOTDEGS; 20 psi, 130°C): Retention time = 1.9 mins.

Bicyclo[3,2,1]octan-3-one

Typically, bicyclo[3,2,1]octan-3-one was prepared by the addition of concentrated sulphuric acid (80 cms^3) dropwise to an ice cold, magnetically stirred solution of 3-chloro-bicyclo[3,2,1]oct-2-ene (7.89g, 0.055 moles) in dry tetra-hydrofuran (25 cms^3). The mixture was stirred at 0°C for three hours, then at room temperature overnight. The solution was poured onto ice (250g) and made basic by addition of concentrated sodium hydroxide solution. The mixture was extracted with ether (3 times) and the combined organic extracts were dried over magnesium sulphate and filtered. The ether was removed by fractional distillation to leave a solid residue of crude ketone (4.72g, 68%); i.r. (CCl_4): $\bar{\nu}_{max}$ = 1715 (s), 1450 (m), 1410 (m)

1350 (m), 1220 (m) and 1075 cm^{-1};

n.m.r. (CCl_4): τ = 7.3-8.8 (m);

g.l.c. (2m 10% FFAP; 30 cms^3/min., 160°C):

Retention time = 5.8 mins.

Bicyclo[3,2,1]octan-3-one oxime

A mixture of bicyclo[3,2,1]octan-3-one (16.5g, 0.133 moles), hydroxylamine hydrochloride (13.9g, 0.2 moles), and sodium acetate (22g, 0.27 moles) was dissolved in a mixture of water and methanol (170 cms^3 and 70 cms^3 respectively) and the solution was gently refluxed overnight. The cooled reaction mixture was then extracted three times with ether. The combined organic extracts were washed with brine, sodium carbonate solution (1M) and water (twice), dried over sodium sulphate and filtered. The solvent was then removed under vacuum to leave a sticky oil which solidified upon being stored in a vacuum desiccator, (15.65g, 85%). A portion of the product was recrystallised from petroleum ether(60-80) to give white crystals m.p. 88-89°C; (lit.[91] 96°C);

i.r. (KBr): $\bar{\nu}_{max}$ = 3210 (s), 1660 (m), 1020 (m) and 950 (s) cm^{-1};

n.m.r. ($CDCl_3$): τ = 0.5 (1H,s), 6.8 (1H,m), 7.05 (1H,m), 7.75 (4H,m) and 7.8-8.7 (6H,m);

$C_8H_{13}NO$ requires C, 69.03; H, 9.41; N, 10.06:

found C, 69.0; H, 9.4; N, 10.2.

exo-3-Chloro-4-hydroxybicyclo[3,2,1]oct-2-ene

A mixture of exo-3,4-dichlorobicyclo[3,2,1]oct-2-ene

(39g, 0.22 moles), calcium carbonate (32g, 0.32 moles), acetone (75 cms^3) and water (250 cms^3) was refluxed for 3 days. When cooled, the mixture was filtered, the acetone removed on a rotary evaporator and the aqueous mixture was extracted with three portions of ether. The combined ethereal extracts were washed with hydrochloric acid (2M) and brine, and then dried over sodium sulphate and filtered. Removal of the solvent left a pale yellow oil (33.5g, 96%) which was then fractionally distilled. The fraction distilling at 74-78°C/0.3 mm was collected as a colourless oil (27.94g, 80%);
i.r. (FILM): $\bar{\nu}_{max}$ = 3600-3050 (s), 1700 (w), 1630 (w), 1450 (m), 1040 (s), 1005 (m), 895 (m), 865 (m), 760 (m), and 725 (m) cm^{-1};
n.m.r. ($CDCl_3$): τ = 3.95 (1H,d), 6.15 (1H,br s), 6.3 (1H,d), and 7.3-9.1 (8H,m);
g.l.c. (50' SCOTDEGS; 20 psi, 130°C): Retention time = 17.1 mins.

<u>exo-Bicyclo[3,2,1]octan-2-ol</u>

exo-3-Chloro-4-hydroxybicyclo[3,2,1]oct-2-ene (1.5g, 9.46 mmol) and palladium on charcoal (10%, 0.3g) were added to a mixture of tetrahydrofuran (redistilled, 150 cms^3) and aqueous sodium hydroxide solution (1M, 20 cms^3). This mixture was then shaken for 3 days under 4 atmospheres of hydrogen. After filtration of the solution, the organic solvent was distilled off and the aqueous residue was steam distilled. The distillate (600 cms^3) was extracted with ether (thrice), the combined ethereal extracts were dried over sodium sulphate, and filtered. The solvent was removed to leave pink, sticky crystals (0.95g, 80%) which were recrystallised from petroleum

ether (40-60) to leave a white solid m.p. 185-188°C (lit.[71] 194-195°C);

i.r. (KBr): $\bar{\nu}_{max}$ = 3550-3050 (s), 1450 (m), 1035 (m), 1015 (m), 965 (m) and 930 (m) cm^{-1};

n.m.r. ($CDCl_3$): τ = 6.3 (1H,m) and 7.6-9.2 (13H,m);

Low Temperature Recrystallisation

The material to be purified was dissolved in the minimum amount of solvent at room temperature and then filtered through a short column of sodium sulphate into a pear-shaped flask. The flask was then fitted with a drying tube and placed in an acetone bath, the temperature of which was slowly reduced using dry ice. If no precipitation was observed at -20 to -30°C then the sides of the flask were scratched with a glass rod. The temperature was then slowly reduced to -70°C and the mother liquors removed by pipette. The crystals were then washed with more solvent and the washings also removed by pipette. As the bath was allowed to warm up to room temperature, the last traces of solvent were removed under reduced pressure. If further recrystallisations were required then the procedure was repeated, with the omission of the filtration step.

exo-Bicyclo[3,2,1]octan-2-yl tosylate

exo-Bicyclo[3,2,1]octan-2-ol (2.9g, 22.98 mm) was dissolved in pyridine (14.5 cms^3) and stirred in an ice bath. A solution of tosyl chloride (p-toluenesulphonyl chloride) (recrystallised, 6.5g, 23.2 mmol) in pyridine (29 cms^3) was added dropwise over 30 minutes.

The mixture was left in a refrigerator over a weekend. A mass of pink crystals formed. Water (100 cms^3) was added to the mixture which was then extracted three times with ether. The ethereal washings were combined and washed with cold hydrochloric acid (3x), aqueous sodium carbonate solution (2M) and water (twice). After being dried and filtered, the ether was removed to leave a yellow oil (4.69g, 72.3%) which was taken up in a (5/1) mixture of petroleum ether (40-60) and diethyl ether and recrystallised twice at -70°C to give white crystals m.p. 50-52°C (lit.[67] 51-52.6°C);
i.r. (KBr): $\bar{\nu}_{max}$ = 1600 (m), 1425 (m), 1385 (s), 1375 (s), 1195 (s), 1185 (s), 1095 (m), 905 (s), 720 (m), 710 (m), and 660 (s) cm^{-1};
n.m.r. ($CDCl_3$): τ = 2.45 (4H,q), 5.52 (1H,m), and 7.0-9.3 (15H,m).

endo-Bicyclo[3,2,1]octan-2-yl Azide

exo-Bicyclo[3,2,1]octan-2-yl tosylate (4.9g, 17.5 mmol) was added to a mixture of hexamethylphosphoramide (27 cms^3, dried over KOH) and sodium azide (4.9g, 75 mmol). The mixture was stirred for 7 days and then water (200 cms^3) was added and the mixture extracted three times with ether. The combined ethereal extracts were washed with water and brine, dried (Na_2SO_4), and filtered. Removal of the solvent left a brown oil (2.5g). This was chromatographed on alumina (grade I; neutral), using a mixture of petroleum ether (40-60)/diethyl ether (9/1), to separate the desired azide from the other products, mainly hydrocarbons. Combination of the desired fractions, identified by g.l.c., and

evaporation of the solvent left a light brown oil which was distilled on a Kugelrohr (150°C/aspirator pressure) to give a colourless oil (0.51g, 19.5%);
i.r. (FILM): $\bar{\nu}_{max}$ = 2090 (s), 1475 (w), 1455 (m), 1255 (m), and 950 cm^{-1};
n.m.r. ($CDCl_3$): τ = 6.6 (1H,m), and 7.3-9.3 (12H,m);
g.l.c. (50' SCOTDEGS; 20 psi, 100°C): Retention time = 7.0 mins.

exo-3-Chloro-4-azidobicyclo[3,2,1]oct-2-ene

exo-3,4-Dichlorobicyclo[3,2,1]oct-2-ene (2g., 11.3 mmol) was dissolved in dry dimethylsulphoxide (20 cms^3) and sodium azide (2g, 30.7 mmol) was added. The suspension was stirred at room temperature for 5 days and then quenched with water (80 cms^3). The mixture was extracted with ether (thrice) and the combined ethereal extracts were washed with water and brine. After the solution had been dried (Na_2SO_4) and filtered the solvent was removed to leave a brown oil (1.59g, 76.7%) which was distilled on a Kugelrohr (90-95°C/0.6mm);
i.r. (FILM): $\bar{\nu}_{max}$ = 2180 (sh), 2100 (s), 1635 (w), 1450 (m), 1300 (s), 1050 (m), 1010 (m), and 895 (m) cm^{-1};
n.m.r. ($CDCl_3$): τ = 3.85 (1H,d), 6.5 (1H,d), and 7.2-8.8 (8H,m).

Bicyclo[3,2,1]octan-2-one

Chromic oxide (100g, 1 mole) was added in one portion to a stirred solution of hydrochloric acid (6M, 184 cms^3). After 5 minutes, the stirred solution was cooled in an ice bath and pyridine (79.1g, 1 mole) was added dropwise over 10 minutes. An orange precipitate formed almost immediately. After 30 minutes

the precipitate was filtered off at the pump and dried for one week in a vacuum desiccator to leave an orange brown solid, pyridinium chlorochromate[68] (150g, 70%).

To a stirred suspension of pyridinium chlorochromate (46.6g, 0.22 moles) in dichloromethane (270 cms^3, redistilled) was added quickly a solution of exo-bicyclo[3,2,1]octan-2-ol (crude, 17g, 0.13 moles) in dichloromethane (20 cms^3). The reaction mixture immediately turned black and grew noticeably warmer. After 90 minutes, ether (150 cms^3) was added and the solution decanted off. The black residue was washed three times with ether and the combined solutions were passed through a short Florisil column. The solvent was removed to leave a yellow oil (17.2g, 103%). A portion of this oil was taken up in a 50/50 mixture of petroleum ether (40-60)/diethyl ether and cooled slowly. Crystals, m.p. 75-80°C, formed at -15°C. This solid was sublimed at 40°C/0.2mm to give a waxy white solid m.p. 121-124°C (lit.[69] 123-129°C);

i.r. (CCl_4): $\bar{\nu}_{max}$ = 1720 (s), 1450 (m), 1410 (w), 1240 (m), 1100 (m), and 810 (m) cm^{-1};

n.m.r. ($CDCl_3$): τ = 7.2-9.3 (m).

g.l.c. (50' SCOTDEGS; 20 psi, 115°C): Retention time = 7.8 mins.

endo-Bicyclo[3,2,1]octan-2-yl tosylate[67]

Approximately 300 cms^3 of liquid ammonia was distilled through an NaOH drying tower into a 3-necked reaction vessel equipped with a mechanical stirrer and an air condenser and cooled to -78°C. Sodalime drying tubes were used to avoid

moisture condensation in the vessel. Methanol (52 cms^3, distilled from magnesium methoxide) was added, using a dropping funnel, to the stirred ammonia. This was followed by a solution of bicyclo[3,2,1]octan-2-one (3.9g, 31.4 mmol) in dry ether (31 cms^3). Lithium (approx. 4.5-5g, 0.7 mole) was added to the stirred solution in small pieces. An intense blue colour was generated by each piece of added lithium which quickly disappeared. One hour after all the lithium had been added, ammonium chloride was added (35g, 0.67 moles) and the ammonia allowed to evaporate off overnight. Water (300 cms^3) was added and the mixture extracted 4 times with ether. The combined organic extracts were washed with water and brine, dried over sodium sulphate and filtered. Evaporation of the solvent left a yellowish white solid (3.65g, 92%) which was shown by g.l.c. to be the desired alcohol, contaminated with approximately 0.5% of the isomeric exo alcohol and starting material;
i.r. (KBr): $\bar{\nu}_{max}$ = 3550-3050 (s), 1505 (m), 1070 (s), 1050 (s), and 1000 (m) cm^{-1};

This material was tosylated in the manner described previously to give 5.65g (70%) of a solid which was recrystallised from petroleum ether (40-60)/diethyl ether (50/50) at -70°C to give white crystals, m.p. 79-80.5°C (lit.[67] 80.1-80.8°C), of endo-bicyclo[3,2,1]octan-2-yl tosylate;
i.r. (KBr): $\bar{\nu}_{max}$ = 1595 (m), 1455 (m), 1345 (s), 1325 (m), 1190 (m), 1175 (s), 1100 (m), 935 (s), 855 (m), 820 (m), 670 (s), and 560 (s) cm^{-1};
n.m.r. ($CDCl_3$): τ = 2.55 (4H,q), 5.55 (1H,m), and 7.5-9.0 (15H,m).

Bicyclo[2,2,2]octanone Oxime

This oxime was prepared from the parent ketone in 89% yield in the same manner as bicyclo[3,2,1]octan-3-one oxime. Recrystallisation from petroleum ether (b.p. 60-80) gave shiny brownish crystals m.p. 118-119°C. Sublimation did not improve the melting point, (lit.[92] 114-118°C), i.r. (KBr): $\bar{\nu}_{max}$ = 3500-3000 (s), 1660 (m), 1470 (m), 1445 (m), 995 (s) and 960 (s) cm^{-1}; n.m.r. (CCl_4): τ = 0.1 (1H,s), 7.6 (4H,m), and 7.8-8.8 (8H,m).

exo-Bicyclo[3,2,1]octan-3-ylamine hydrochloride

Bicyclo[3,2,1]octan-3-one oxime (15.65g, 0.11 moles) was dissolved in freshly distilled anhydrous isopropanol (350 cms^3) and the solution was heated to reflux. To the boiling solution sodium ($\approx$40g, 1.7 moles) was cautiously added in small portions. The reaction mixture was refluxed overnight, cooled, and quenched with wet methanol and water. The mixture was extracted with three portions of ether and the combined organic extracts were washed with dilute hydrochloric acid (3 times). Evaporation of the ether gave a solid residue (7.5g) which was mainly starting material. The combined acid washings were made basic by the addition of concentrated sodium hydroxide solution and then extracted with ether (3 times). The ethereal extracts were then washed with water (twice) and then back extracted into acid solution by washing twice with dilute hydrochloric acid. Slow evaporation of the acidic solution gave off-white needles (7.3g, 38.8%). A portion of this

material was recrystallised from ethanol m.p. > 280°C (slow decomposition)

i.r. (KBr): $\bar{\nu}_{max}$ = 3500-2300 (s), 2100-1800 (w), 1570 (m), 1500 (m), 1210 (w), 1110 (m), 1040 (m), and 450 (m) cm^{-1};

n.m.r. (D_2O): τ = 6.6 (1H,septet), and 7.2-9.2 (12H,m).

endo-Bicyclo[3,2,1]octan-3-ylamine hydrochloride

Bicyclo[3,2,1]octan-3-one oxime (2.78g, 0.02 moles) was dissolved in absolute ethanol (distilled from magnesium ethoxide, 490 cms^3) and chloroform[63] (10 cms^3) and Adams' catalyst (PtO_2, 0.5g) was added. The mixture was shaken under three atmospheres of hydrogen at room temperature for three days and then filtered. The solvent was removed on a rotary evaporator to leave a red-brown slurry which solidified upon standing in a vacuum desiccator (3.1g, 100%). Recrystallisation from ethanol/chloroform (1:1) gave a white solid m.p. 278-285°C (decomposed).

i.r. (KBr): $\bar{\nu}_{max}$ = 3300-2300 (s), 2050-1870 (w), 1570 (m), 1490 (s), 1380 (m), 1070 (s), 945 (m), 825 (m), and 335 (m) cm^{-1};

n.m.r. ($CDCl_3$): τ = 1.1-2.8 (3H,br s), 6.45 (1H,m), and 7.4-8.9 (12H,m).

Bicyclo[2,2,2]octan-2-ylamine hydrochloride

Bicyclo[2,2,2]octanone oxime (0.61g, 4.38 millimoles) was dissolved in a mixture of ethanol (110 cms^3) and chloroform (10 cms^3) and some PtO_2 (0.1g) was added. The resultant mixture was shaken under 3 atm. of hydrogen for 2 days. After the solution had been filtered the solvent was removed on a rotary

evaporator. The cream coloured residue (0.75g, 102%) was recrystallised from ethanol, filtered at the pump, and washed with pentane to give white, flaky crystals m.p. > 320°C (decomposed);

i.r. ($CHCl_3$): $\bar{\nu}_{max}$ = 3400-2400 (s), 2050-1850 (w), 1605 (m), 1505 (s), 1395 (m), 1210 (m), and 1030 (m) cm^{-1};

n.m.r. ($CDCl_3$: τ = 1.2-2.5 (3H,br s), 6.55 (1H,m), and 7.6-9.2 (12H,m).

endo-Bicyclo[3,2,1]octan-2-ylamine hydrochloride

endo-Bicyclo[3,2,1]octan-2-yl azide (0.51g, 3.4 mmol) was dissolved in a mixture of ethanol (100 cms^3) and chloroform (10 cms^3) to which 10% Pd on charcoal (0.2g) had been added. This mixture was stirred under 1 atm. of hydrogen for 24 hours. When filtered the solvents were removed from the filtered solution on a rotary evaporator to leave a brown solid (0.55g, 100%) which was recrystallised from a 50/50 mixture of methanol and tetrahydrofuran to give a white solid m.p. > 270°C (decomposed);

i.r. (KBr): $\bar{\nu}_{max}$ = 3600-2350 (s), 2100-1850 (w), 1595 (m), 1490 (m), 1455 (m), 1295 (w), 1105 (w), 1035 (m) and 530 (w) cm^{-1};

n.m.r. ($CDCl_3$): τ = 1.0-1.6 (3H,br s), 6.4-6.9 (1H,m), and 7.3-8.9 (12H,m).

exo-Bicyclo[3,2,1]octan-2-ylamine hydrochloride

Two methods of preparation were employed.

A. exo-3-Chloro-4-azidobicyclo[3,2,1]oct-2-ene (1.5g, 8.17 mmol) was added to a mixture of ethanol (150 cms^3), chloroform (15 cms^3)

and platinum dioxide (0.1g), and was hydrogenated at 4 atm. for 3 days. After being filtered the solvents were removed on a rotary evaporator. The solid residue (1.3g, 98%) was recrystallised twice from a 50/50 mixture of ethanol and chloroform to leave a white solid m.p. > 260°C (decomposed);

B. endo-Bicyclo[3,2,1]octan-2-yl tosylate (1.7g, 6.06 mmol) was added to a suspension of sodium azide (2.0g, 30.7 mmol) in hexamethylphosphoramide (5 cms^3) and stirred at room temperature for 3 days. Water (40 cms^3) was added and the mixture extracted three times with ether. The combined ethereal extracts were washed with water and brine, dried over Na_2SO_4 and filtered. Removal of the solvent left an oil (0.51g, 55.7%), exo-bicyclo[3,2,1]octan-2-yl azide;

i.r. (FILM): $\bar{\nu}_{max}$ = 2050 (s), 1450 (m), and 1265 (s) cm^{-1};

n.m.r. ($CDCl_3$): τ = 6.5 (1H,m), and 7.6-9.3 (12H,m);

g.l.c. 50' SCOTDEGS; 20 psi, 100°C): Retention time = 6.6 mins.

The crude azide (0.4g, 2.65 mmol), was stirred with some PtO_2 (0.1g) in a mixture of ethanol (100 cms^3) and chloroform (10 cms^3) under 1 atm. of hydrogen for 24 hours. After being filtered the solvents were removed on a rotary evaporator to leave an off-white solid (0.4g, 93%), exo-bicyclo[3,2,1]octan-2-ylamine hydrochloride; m.p. > 290°C (decomposed);

i.r. (KBr): $\bar{\nu}_{max}$ = 3200-2200 (s), 2200-1800 (m), 1590 (s), 1495 (m), 1425 (m), 1105 (m), 1060 (w) and 1040 (m) cm^{-1};

n.m.r. ($CDCl_3$): τ = 1.0-2.8 (3H, br s), 6.5 (1H,m) and 7.5-8.9 (12H,m).

and platinum dioxide (0.1g), and was hydrogenated at 4 atm. for 3 days. After being filtered the solvents were removed on a rotary evaporator. The solid residue (1.3g, 98%) was recrystallised twice from a 50/50 mixture of ethanol and chloroform to leave a white solid m.p. > 260°C (decomposed);

B. endo-Bicyclo[3,2,1]octan-2-yl tosylate (1.7g, 6.06 mmol) was added to a suspension of sodium azide (2.0g, 30.7 mmol) in hexamethylphosphoramide (5 cms^3) and stirred at room temperature for 3 days. Water (40 cms^3) was added and the mixture extracted three times with ether. The combined ethereal extracts were washed with water and brine, dried over Na_2SO_4 and filtered. Removal of the solvent left an oil (0.51g, 55.7%), exo-bicyclo[3,2,1]octan-2-yl azide;
i.r. (FILM): $\bar{\nu}_{max}$ = 2050 (s), 1450 (m), and 1265 (s) cm^{-1};
n.m.r. ($CDCl_3$): τ = 6.5 (1H,m), and 7.6-9.3 (12H,m);
g.l.c. 50' SCOTDEGS; 20 psi, 100°C): Retention time = 6.6 mins.

The crude azide (0.4g, 2.65 mmol), was stirred with some PtO_2 (0.1g) in a mixture of ethanol (100 cms^3) and chloroform (10 cms^3) under 1 atm. of hydrogen for 24 hours. After being filtered the solvents were removed on a rotary evaporator to leave an off-white solid (0.4g, 93%), exo-bicyclo[3,2,1]octan-2-ylamine hydrochloride; m.p. > 290°C (decomposed);
i.r. (KBr): $\bar{\nu}_{max}$ = 3200-2200 (s), 2200-1800 (m), 1590 (s), 1495 (m), 1425 (m), 1105 (m), 1060 (w) and 1040 (m) cm^{-1};
n.m.r. ($CDCl_3$): τ = 1.0-2.8 (3H, br s), 6.5 (1H,m) and 7.5-8.9 (12H,m).

Benzenediazonium Tetrafluoroborate[72]

A solution of aniline (33.6g, 0.414 moles), aqueous tetrafluoroboric acid (160 cms^3, 40% solution) and ethanol (320 cms^3) was stirred and cooled in an ice bath till the internal temperature was lower than 2°C. Propyl nitrite (kindly supplied by Dr. Maskill, 33.3g, 0.37 moles) was added slowly over a period of fifteen minutes whilst the internal temperature rose to 9°C. The mixture was stirred for 30 minutes and a yellow precipitate suddenly formed during this period. Ether was added (320 cms^3) to reduce the solubility of the salt and the precipitate filtered off at the pump. The product was slurried with ethanol and then with ether to leave white crystals which were dried in a vacuum desiccator (44.4g, 63%); m.p. 86-88°C (with violent decomposition);

i.r. (KBr): $\bar{\nu}_{max}$ = 3090 (m), 3085 (sh), 3000 (w), 2280 (s), 1555 (m), 1455 (m), 1300 (m), 1250-850 (s), 750 (s), 655 (m), 515 (s), and 445 (w) cm^{-1};

n.m.r. (CD_3NO_2): τ = 1.95-2.9 (complex mult.)

1-Phenyl-3-(exo-bicyclo[3,2,1]oct-3'-yl)triazene[5h]

exo-Bicyclo[3,2,1]octan-3-ylamine hydrochloride (200 mg, 1.24 mmol) was extracted between pentane and freshly prepared potassium hydroxide solution. The organic phase was separated and the pentane blown off under argon. Anhydrous sodium carbonate (2g) and redistilled acetonitrile (8 cms^3) was added to the amine, still under argon. This suspension was stirred at -10°C and a solution of benzenediazonium tetrafluoroborate (0.2g, 1.25 mmol) in redistilled acetonitrile

(4 cms^3), cooled below 0°C, was added dropwise. The mixture was stirred for 3 hours at -10°C, during which time it turned red, and then allowed to warm up to 0°C. The mixture was then filtered and the filtrate extracted five times with cold pentane. The pentane was removed under reduced pressure to leave a red slurry which was recrystallised three times at low temperature from pentane to leave pale pink crystals which were then sublimed at 60-70°C/0.1 mm to give a very pale pink solid m.p. 72-73°C;

i.r. (CCl_4): $\bar{\nu}_{max}$ = 1605 (m), 1505 (m), 1475 (m), 1270 (s), 1210 (m), and 695 (m) cm^{-1}; no N-H or aryl C-H stretch were detected;

n.m.r. (CCl_4): τ = 1.3 (1H, br s), 2.85 (5H,m), 6.1 (1H,m), and 7.3-9.0 (12H,m).

1-Phenyl-3-(exo-bicyclo[3,2,1]oct-2'-yl)triazene

This triazene was prepared in the same manner as the exo-3'-isomer. The orange powder obtained was recrystallised from petroleum ether (40-60) at -70°C and then sublimed (70°C/0.1mm) to give a pale yellow solid m.p. 74-75°C;

i.r. (CCl_4): $\bar{\nu}_{max}$ = 3440 (w), 3340 (w), 3050 (w), 1605 (m), 1510 (m), 1470 (m), 1235 (m), and 695 (m) cm^{-1};

n.m.r. (CCl_4): τ = 1.3-2.3 (1H, br s), 2.45-3.6 (5H,m), 6.2-6.45 (1H,m) and 7.5-9.3 (12H,m);

$C_{14}H_{19}N_3$ requires C, 73.32%; H, 8.35; N, 18.33:

found C, 73.43%; H, 8.41; N, 18.36.

1-Phenyl-3-(endo-bicyclo[3,2,1]oct-3'-yl) triazene

endo-Bicyclo[3,2,1]octan-3-ylamine hydrochloride (0.252g, 1.56 mmol) was dissolved in acetonitrile (10 cms^3) and anhydrous sodium carbonate (2.5g) added. The mixture was stirred under argon for one hour and then cooled to below $-30^{\circ}C$. A cooled solution of benzenediazonium tetrafluoroborate (1.82 mmoles; 0.35g) in acetonitrile (5 cms^3) was added dropwise and the mixture stirred for one hour at $-30^{\circ}C$ during which time the mixture turned red. The reaction mixture was then filtered and extracted five times with cold pentane. The petrol extracts were combined, washed with cold water and dried by passing through a column of sodium sulphate. Evaporation of the pentane left a red oil which was taken up in light petroleum and cooled to effect crystallisation. The solid produced at $-70^{\circ}C$ was, after removal of the mother liquor, washed twice with cold light petroleum and pumped to dryness at $-70^{\circ}C$. As the residue warmed up to room temperature it changed into a red glue which resisted further attempts to crystallise it. Sublimation also failed.

i.r. (FILM): $\bar{\nu}_{max}$ = 3300 (m), 1600 (m), 1505 (m), 750 (m) and 695 (m) cm^{-1};

n.m.r. (CCl_4): τ = 0.9-1.7 (1H, br s), 2.85 (5H,m), 6.15 (1H,m) and 7.0-9.2 (12H,m).

1-Phenyl-3-(bicyclo[2,2,2]oct-2'-yl)triazene

This triazene was prepared in the same manner as the endo-3'-bicyclo[3,2,1]-isomer. The oil produced was not successfully recrystallised or sublimed. A drop of pentane was added to the oil which was then left in a freezer at $-15^{\circ}C$ over

a week-end. Crystals formed which were separated from the oil and washed carefully with cold pentane to give a slightly sticky pink solid which was not purified further,

m.p. 42-44°C;

i.r. (CCl_4): $\bar{\nu}_{max}$ = 1600 (m), 1500 (m), 1470 (m), 1230 (m), 1130 (m), and 695 (m) cm^{-1},

n.m.r. (CCl_4): τ = 1.4-2.2 (1H, br s), 2.85 (5H,m), 6.05 (1H,m), and 7.4-8.8 (12H,m).

Ethyl N-(bicyclo[3,2,1]octyl)carbamates

The preparation of ethyl N-(endo-bicyclo[3,2,1]octan-3-yl)carbamate was typical:

to a stirred slurry of endo-bicyclo[3,2,1]octan-3-yl-amine hydrochloride (1.04g, 6.6 mmol) in a mixture of ether (15 cms^3) and water (0.5 cms^3) were added alternately portions of potassium carbonate (1.335g, 13.2 mmol) and ethyl chloroformate (0.84g, 7.9 mmol). The mixture was refluxed for 1½ hours. When cool the reaction mixture was filtered, washed with water and brine, dried over sodium sulphate and filtered. Removal of the solvent left a yellowish solid (1.36g, 107%) which was recrystallised from petroleum ether (40-60)/diethyl ether at -70°C (twice) m.p. 71°-73°C. Sublimation of this material (65°C/0.1 mm) gave a white, pleasant smelling solid

m.p. 71.5-73°C;

g.l.c. (50' SCOTDEGS; 20 psi, 140°C): Retention time = 21.9 mins;
i.r. (KBr): $\bar{\nu}_{max}$ = 3380 (m), 1670 (s), 1515 (s), 1240 (s), 1080 (m), and 1040 (m) cm^{-1};
n.m.r. ($CDCl_3$): τ 5.0τ (1H, br s), 5.85 (2H, q), 6.15 (1H, m), and 7.6-9.3τ (15H, m);

$C_{11}H_{19}NO_2$ requires C, 66.97%; H, 9.71; N, 7.10;
found C, 67.20%; H, 9.74; N, 7.22.

In the same manner was prepared

Ethyl N-(exo-bicyclo[3,2,1]oct-3-yl)carbamate

m.p. 78.5-80°C in 94% yield;
g.l.c. (50' SCOTDEGS; 20 psi, 140°C): Retention time = 26.7 mins;
i.r. (CCl_4): $\bar{\nu}_{max}$ = 3400 (w), 3320 (sh), 1720 (s), 1500 (m), 1210 (m) and 1060 (m) cm^{-1};
n.m.r. (CCl_4): τ= 5.6 (1H, br s), 6.05 (2H,q), 6.3 (1H,m) and 7.6-9.2 (15H,m);

$C_{11}H_{19}NO_2$ requires C, 66.97%; H, 9.71; N, 7.10:
found C, 67.08%; H, 9.84; N, 7.33;

Ethyl N-(endo-bicyclo[3,2,1]oct-2-yl)carbamate

m.p. 78-81°C in 45% yield;
g.l.c. (50' SCOTDEGS; 20 psi; 140°C: Retention time = 29.6 mins.
i.r. (CCl_4): $\bar{\nu}_{max}$ = 3455 (m), 3360 (w), 1725 (s), 1505 (s), 1225 (m), 1095 (m), 1065 (m), and 1040 (m) cm^{-1};
n.m.r. (CCl_4): τ = 5.6 (1H, br s), 6.05 (2H,q), 6.5 (1H,m), and 7.6-9.3 (15H,m);

$C_{11}H_{19}NO_2$ requires C, 66.97%; H, 9.71; N, 7.10:
found C, 66.86%; H, 9.76; N, 7.03;

and

Ethyl N-(exo-bicyclo[3,2,1]oct-2-yl)carbamate

m.p. 53.5-55.5°C in 96% yield; g.l.c. (50' SCOTDEGS; 20 psi; 140°C): Retention time 2 28.2 mins.

i.r. (CCl_4): $\bar{\nu}_{max}$ = 3420 (w), 3330 (w), 1720 (s), 1500 (s), 1220 (s), 1040 (m), and 1020 (m);

i.r. (KBr): $\bar{\nu}_{max}$ = 3280 (m), 1670 (s), 1515 (s) and 1240 (s) cm^{-1};

n.m.r. ($CDCl_3$): τ = 4.95 (1H, br s), 5.9 (2H,q), 6.45 (1H,m) and 7.5-9.1 (15H,m);

$C_{11}H_{19}NO_2$ requires C, 66.97%; H, 9.71; N, 7.10:
found C, 67.06%; H, 9.78; N, 6.98.

Ethyl N-(bicyclo[2,2,2]oct-2-yl)carbamate

This carbamate was prepared by a different method from the other four isomers.

A mixture of cyclohexa-1,3-diene (redistilled, 3.5g, 0.0436 moles), ethyl acrylate (redistilled, 3.0g, 0.03 moles)

and anhydrous aluminium trichloride[74] (1.2g) in dry benzene (70 cms^3) was refluxed for 16 hours. The red reaction mixture was cooled, dilute hydrochloric acid added and then washed three times with ether. The combined ethereal washings were washed with water and brine, dried over sodium sulphate and filtered. Removal of the solvent on a rotary evaporator left a dark brown oil which was distilled (Kugelrohr, 100°C/20 mm) to give 3.72g (69%) of a sweet-smelling colourless oil. This oil was refluxed with a mixture of hydrazine hydrate (4.13g) in ethanol (6 cms^3) for 2 days. After being cooled, the solvent was removed on a rotary evaporator to leave a yellow solid (3.3g, 95%);

n.m.r. ($CDCl_3$): τ = 2.1-3.2 (1H, br s), 3.8 (2H,m), 5.6-6.4 (2H, br s) and 7.0-8.9 (9H,m).

A solution of the acid hydrazide (3.3g; 19.8 mmol) in water (30 cms^3) and conc. hydrochloric acid (2 cms^3) was cooled in an ice bath and stirred. Ether (25 cms^3) was added, followed by an aqueous solution of sodium nitrite (1.52g; 22 mmol) added over a period of 15 minutes. The organic layer was separated and the aqueous layer washed three times with ether. The combined ethereal extracts were washed with sodium carbonate solution (2M), dried over Na_2SO_4, and filtered. Ethanol (15 cms^3) was added, and the ether removed by fractional distillation from calcium sulphate. The ethanolic residue was refluxed for 4 hours, cooled, and the solvent removed to leave a yellow oil. This oil was dissolved in ethanol (400 cms^3) and 10% palladium on charcoal (0.3g) added. The mixture was stirred under 1 atm. of hydrogen for 24 hours. After the

and anhydrous aluminium trichloride[74] (1.2g) in dry benzene (70 cms^3) was refluxed for 16 hours. The red reaction mixture was cooled, dilute hydrochloric acid added and then washed three times with ether. The combined ethereal washings were washed with water and brine, dried over sodium sulphate and filtered. Removal of the solvent on a rotary evaporator left a dark brown oil which was distilled (Kugelrohr, 100°C/20 mm) to give 3.72g (69%) of a sweet-smelling colourless oil. This oil was refluxed with a mixture of hydrazine hydrate (4.13g) in ethanol (6 cms^3) for 2 days. After being cooled, the solvent was removed on a rotary evaporator to leave a yellow solid (3.3g, 95%);

n.m.r. ($CDCl_3$): τ = 2.1-3.2 (1H, br s), 3.8 (2H,m), 5.6-6.4 (2H, br s) and 7.0-8.9 (9H,m).

A solution of the acid hydrazide (3.3g; 19.8 mmol) in water (30 cms^3) and conc. hydrochloric acid (2 cms^3) was cooled in an ice bath and stirred. Ether (25 cms^3) was added, followed by an aqueous solution of sodium nitrite (1.52g; 22 mmol) added over a period of 15 minutes. The organic layer was separated and the aqueous layer washed three times with ether. The combined ethereal extracts were washed with sodium carbonate solution (2M), dried over Na_2SO_4, and filtered. Ethanol (15 cms^3) was added, and the ether removed by fractional distillation from calcium sulphate. The ethanolic residue was refluxed for 4 hours, cooled, and the solvent removed to leave a yellow oil. This oil was dissolved in ethanol (400 cms^3) and 10% palladium on charcoal (0.3g) added. The mixture was stirred under 1 atm. of hydrogen for 24 hours. After the

solution had been filtered the ethanol was removed on a rotary evaporator. The oily residue was recrystallised from petroleum ether (40-60)/diethyl ether and sublimed (60°C/0.1 mm) to give Ethyl N-(bicyclo[2,2,2]oct-2-yl) carbamate as a white solid (1.8g, 30% from ethyl acrylate); m.p. 96.5-98°C;
i.r. (CCl_4): $\bar{\nu}_{max}$ = 3440 (w), 1720 (s), 1495 (m), 1210 (m), 1080 (m), and 1015 (m) cm^{-1};
n.m.r. (CCl_4): τ = 5.3 (1H, br s), 6.0 (2H,q), 6.35 (1H,m), and 7.7-9.2 (15H,m);

$C_{11}H_{19}NO_2$ requires C, 66.97%; H, 9.71; N, 7.10:
found C, 67.05%; H, 9.71; N, 7.16.

g.l.c. (50' SCOTDEGS; 20 psi, 140°C): Retention time = 29.6 mins.

Preparation of Dinitrogen Tetroxide[5a]

Lead nitrate (80g) was pyrolysed in a test-tube fitted with a delivery tube. The brown gases evolved were passed through a Dreschel bottle cooled in an acetone-dry ice bath. The brown liquid collected was distilled into another bottle externally cooled by a freezing mixture of common salt and ice. The blue liquid obtained (≃12.5g, 56%) was diluted with freshly distilled (from P_2O_5) dichloromethane (100 cms^3). The solution was transferred to a bottle stoppered with a teflon top and stored below -10°C in a freezer. Ten cms^3 of this solution contains approximately 12 millimoles of dinitrogen tetroxide.

Ethyl N-nitroso, N-(endo-bicyclo[3,2,1]oct-3-yl) carbamate

The procedure described by Maskill[5e] was adopted. Fused sodium acetate (1.74g, 21.2 millimoles) was

added to a stirred solution of dinitrogen tetroxide in dichloromethane (12.5 cms^3, containing 15 millimoles of N_2O_4) cooled to -70°C in an acetone-carbon dioxide bath under argon. A solution of the carbamate (0.31g, 1.57 millimoles) in redistilled dichloromethane was added dropwise. The blue-green mixture was stirred as the temperature was allowed to rise to -30°C when the acetone-carbon dioxide bath was replaced by an ice bath. The reaction mixture gradually turned lime-green then yellow. After 30 minutes at 0°C, the mixture was golden yellow, the characteristic colour of N-nitroso carbonyl compounds. The mixture was stirred at 0°C for a total time of 1 hour then washed with ice-cold water, ice-cold sodium carbonate solution and ice-cold water again. The yellow solution was dried over calcium chloride at 0°C (fused gran. 8-15 mm) and filtered through some cotton wool. The solvent was removed on a rotary evaporator at 0°C to leave a yellow oil (0.332g, 93.4%) which was not purified further;

i.r. (CCl_4): $\bar{\nu}_{max}$ = 1740 (s), 1515 (m), 1315 (s), 1140 (s), 1040 (s), and 965 cm^{-1};

n.m.r. (CCl_4): τ = 4.95-5.85 (3H,m) and 7.5-9.1 (15H,m); the multiplet at 4.95-5.85τ contained a quartet at 5.65τ which could be assigned to the methylene protons of the carbethoxy group. A triplet at 8.55τ could be assigned to the methyl group of the carbethoxy moiety;

u.v. (EtOH): λ_{max} = 408nm, 426nm.

Some of this yellow oil was solvolysed immediately in ethanol.

Ethyl N-nitroso, N-(exo-bicyclo[3,2,1]oct-3-yl) carbamate

This nitrosocarbamate was prepared in the same manner as the endo-3-isomer. The yellow oil gave
i.r. (CCl_4): $\bar{\nu}_{max}$ = 1745 (s), 1520 (s), 1315 (s), 1130 (s), 1030 (m), 945 (m), 905 (m), and 575 (m) cm^{-1};
n.m.r. (CCl_4): τ = 4.7 to 5.4 (1H, septet), 5.6 (2H,q) and 7.6-9.2 (15H,m); the multiplet at 7.6-9.2τ contained a triplet at 8.55τ which could be assigned to the methyl group of the carbethoxy moiety;
u.v. (EtOH): λ_{max} = 408nm, 426nm.

Ethyl N-nitroso, N-(bicyclo[2,2,2]oct-2-yl) carbamate and Ethyl N-nitroso, N-(endo-bicyclo(3,2,1)oct-2-yl) carbamate

These two isomeric nitrosocarbamates were prepared as yellow oils in the same manner as the endo-3-isomer and had the same absorption spectra as the other isomers.

Ethyl N-nitroso, N-(exo-bicyclo[3,2,1]oct-2-yl) carbamate

This compound proved to be unstable to the work-up conditions used to prepare the other isomers.

The procedure, therefore, was as described above for the endo-3-isomer except that anhydrous sodium carbonate was used to neutralise the acid formed instead of sodium acetate. The reaction mixture, when the reaction was completed, was percolated down a column containing a mixture of anhydrous sodium carbonate and sodium sulphate and eluted with redistilled dichloromethane. The solvent was removed at $0^{\circ}C$ on a rotary evaporator and the residual yellow oil was solvolysed immediately.

Preparation of Ethers for G.L.C. Identification[4c]

A stirred suspension of exo-bicyclo[3,2,1]octan-3-ol (0.05g, 0.4 mmol), silver oxide (0.225g, 0.97 mmol) and ethyl iodide (1.25g, 8 mmol) in ether (5 cms^3) was refluxed for 48 hours. The mixture was then filtered and passed down a column of dry alumina using petroleum ether (40-60) as eluent. Most of the solvent was blown off with argon to leave a concentrated solution of the ether . This solution was used directly for g.l.c. identification. The bicyclic ether was never isolated.

The same procedure was followed to alkylate the other isomeric alcohols. In no case were the ethers isolated.

Adamantanone Oxime

A mixture of adamantanone (4.65g, 30.95 mmol), hydroxylamine hydrochloride (3.36g, 48.3 mmol) and sodium acetate (5.28g, 64.4 mmol) were refluxed in 50% aqueous methanol (80 cms^3) for four hours. After ten minutes a white precipitate was observed. The reaction mixture was cooled, some of the methanol removed on the rotary evaporator and then extracted three times with dichloromethane. The combined organic extracts were washed with brine, dried over sodium sulphate and filtered. Evaporation of the solvent left a clean, white solid (5.30g, 104%) which was not purified further, m.p. 165-166°C (Lit.[93] 162.8-163.6°C);
i.r. (KBr): $\bar{\nu}_{max}$ = 3210 (s), 3120 (s), 1675 (m), 1480 (m), 1455 (m), 965 (s), and 955 (sh) cm^{-1};
n.m.r. ($CDCl_3$): τ = 1.3 (1H, br s), 6.4 (1H,m), 7.4 (1H,m), and 7.7-8.9 (12H,m).

N(2-Adamantyl)hydroxylamine

Adamantanone oxime (1.22g, 7.38 mmol) was added to a stirred solution of sodium cyanoborohydride[64] (0.7g, 11.1 mmol) in methanol (17 cms^3) containing a trace of bromocresol green indicator. The blue-green solution was acidified with methanolic hydrochloric acid (approx. 2M) until it turned orange/yellow. More acid was added each time the colour changed back to green. After 30 minutes no more acid was required. The mixture was stirred for 3 hours and then the methanol removed on the rotary evaporator. The residue was made basic by the addition of sodium hydroxide solution and extracted three times with chloroform. The chloroform extracts were combined and washed with water and brine, dried over sodium sulphate and filtered. Removal of the solvent gave a white crystalline solid (1.18g, 95.5%). Sublimation ($130^{\circ}C/0.1$ mm) gave a white solid and a substantial residue (0.4g) which would not sublime. The sublimed material (0.78g, 63%) had m.p. 140-142°C and the following spectral characteristics;

i.r. (CCl_4): $\bar{\nu}_{max}$ = 3610 (w), 3280 (m), and 1455 (m) cm^{-1};

n.m.r. ($CDCl_3$): τ = 4.25 (2H, br s), 6.85 (1H,m) and 7.6-8.9 (14H,m)

m/e 167 (33%,M), 150 (6.7, M-OH), 136 (14), 135 (100, M-NH_2O).

N-Nitroso,N-(2-adamantyl)hydroxylamine[78]

N-(2-Adamantyl)hydroxylamine (3.5g, 20.9 mmol) was suspended in a stirred mixture of ethanol (25 cms^3) and aqueous

hydrochloric acid (2M, 9 cms^3). The reaction mixture was cooled in an ice bath till the internal temperature dropped below 5^oC. A saturated solution of sodium nitrite (1.6g, 23.2 mmol) was added over 30 minutes and the reaction mixture almost clarified. After 45 minutes there was a sudden precipitation of a white solid. The mixture was stirred for a further 15 minutes and then filtered at the pump. The precipitate was washed with water to leave a slightly yellow solid (0.98g, 23.7%). The washings were added to the filtrate and this effected further precipitation. The second crop was filtered off at the pump to give a white solid which was washed with water (2.34g, 56.7%). Water was added to the filtrate and a third batch of white solid was collected (0.55g, 13.3%). The total recovery was 3.87g, 94%. The second crop was recrystallised twice from carbon tetrachloride to give shiny needles. m.p. 137-139^oC.

i.r. (KBr): $\bar{\nu}_{max}$ = 3400 (w), 3060 (w), 1455 (m), 1085 (m), 1060 (s), 1045 (m), 980 (m), 790 (m), 715 (m), 415 (m), and 375 (m) cm^{-1};

n.m.r. ($CDCl_3$): τ = -3.4 to -1.4 (1H, s), 5.65 (1H, m), 7.3 (2H, m), and 7.5-8.8 (12H, m);

m/e 167 (12.4%), 166 (100, M-NO), 135 (25.2, $M-N_2O_2H$);

$C_{10}H_{16}N_2O_2$ requires C, 61.20%; H, 8.22; N, 14.27:

found C, 61.37%; H, 8.18; N, 14.28.

Adamant-2-yl-ONN-azoxytosylate

N-Nitroso,N-(2-adamantyl)hydroxylamine (0.29g, 1.48 mmol) in acetone (5 cms^3) was stirred at 0^oC. Tosyl chloride

(recrystallised, 0.57g, 3.67 mmol) was added, followed by 2M sodium hydroxide solution (1.5 cms^3) which was added dropwise over 15 minutes.[10] The reaction mixture cleared and then a precipitate appeared. Water was added (0.75 cms^3) and the stirred mixture was allowed to warm up to room temperature. After 30 minutes water (2.5 cms^3) was added and the mixture filtered at the pump. The filter cake was a white solid (0.38g, 73.4%). Some of the product was recrystallised from petrol (40-60)/ether at low temperature (-70°C) to give crystals m.p. 111-113°C (with some decomposition);

i.r. (KBr): $\bar{\nu}_{max}$ = 1600 (m), 1505 (m), 1455 (m), 1390 (s), 1195 (s), 1180 (s), 1090 (m), 920 (m), 900 (m), 820 (m), 805 (m), 795 (m), 770 (m), 725 (s), 665 (m), 565 (m), and 550 (s) cm^{-1};

n.m.r. ($CDCl_3$): τ = 2.4 (4H, q), 5.7 (1H, m), 7.55 (5H, m), and 7.6-9.0 (12H, m);

m/e 135 (64.3%M-$ON_2OSO_2C_7H_7$), 134 (100), 93 (40.3), 92 (85.8), 91 (62.6), 79 (44.5);

u.v. (EtOH): λ_{max} = 275 nm (ε = 830)

$C_{17}H_{22}N_2O_4S$ requires C, 58.27%; H, 6.33; N, 8.00; S, 9.15:

found C, 58.14%; H, 6.33; N, 8.19; S, 9.36.

Sodium Cyanoborodeuteride[64]

Sodium cyanoborohydride (4g, 63.6 mmol) was dissolved in deuterium oxide (30 cms^3, 99.8%D) and stirred at room temperature. A freshly prepared solution, made by the reaction

of acetyl chloride (1.6 cms^3) with deuterium oxide (8 cms^3) was added till the pH was less than 2 (pH meter used). Hydrogen was slowly evolved as the pH was kept in the range 1.8 to 2.2 for 30 minutes. Anhydrous sodium carbonate was added till the pH was greater than 6. The deuterium oxide was removed on the rotary evaporator, fresh deuterium oxide (30 cms^3) added, and the process repeated. The solid obtained was dried in a vacuum desiccator and taken up in dry tetrahydrofuran (50 cms^3) and stirred for 1 hour. The solution was filtered and the solvent evaporated off. After being dried overnight, a white solid was obtained (2.0g, 50%). The n.m.r. spectra of this material and of the protium starting material were compared and indicated that there was approximately 3% residual protium in the deuterated material. Some of this material (1g) was washed once more with deuterium oxide as described above to give a white solid (0.64g, 64%). The n.m.r. spectra indicated approximately 99% of deuterium incorporation.

N-(2-Adamantyl-2-^{2}H)hydroxylamine[64]

Adamantanone oxime (1.1g, 6.66 mmol) was added to a stirred solution of sodium cyanoborodeuteride (0.625g, 9.49 mmol, 99%D) in deuterium oxide (0.3 cms^3) and dry tetrahydrofuran (7 cms^3). A trace of bromocresol green was added and the blue solution was acidified with a mixture of acetyl chloride (1 cms^3) and deuterium oxide (1 cms^3) till the solution turned yellow. The acid solution was added as required to keep the solution yellow. After 10 minutes the reaction seemed complete. The

reaction mixture was left stirring overnight and then most of the organic solvent was removed on the rotary evaporator. The residue was made basic with sodium hydroxide solution and extracted three times with ether. The combined ethereal extracts were washed with brine, dried over sodium sulphate, filtered, and the solvent removed to leave a green oil. The oil was taken up in ether and washed twice with hydrochloric acid (2M). The combined acid washings were made basic by the addition of solid sodium hydroxide and back extracted with ether (twice). The ethereal solution was washed with brine, dried over sodium sulphate, filtered, and the solvent removed to leave a white solid (0.59g, 52.7%) which was not purified further.

i.r. (CCl_4): $\bar{\nu}_{max}$ = 3600 (w), 3260 (m), and 1450 (m) cm^{-1};

n.m.r. ($CDCl_3$): τ = 4.05 (2H, br s), and 7.3-8.7 (14H, m), the resonance peak at 6.85 observed in the ^2H compound was not detected;

m/e 168 (14.7%, M), 151 (1.5, M-OH), 137 (12), 136 (100, M-NH_2O).

N-Nitroso,N-(2-adamantyl-2-^{2}H)hydroxylamine

This compound was prepared from the deuterated hydroxylamine following the same method used for the non-deuterated hydroxylamine. The product was recrystallised from carbon tetrachloride in 65% yield,

m.p. 135-136.5°C;

i.r. (KBr): $\bar{\nu}_{max}$ = 3420 (m), 3060 (w), 1450 (m), 1425 (m), 1080 (m), 1050 (s), 1020 (m), 960 (m), 945 (m), 780 (m), 710 (m), 410 (m), and 370 (m) cm^{-1};

n.m.r. ($CDCl_3$: τ = -2 to 0.5 (1H, br s), 7.35 (2H, m) and 7.6-8.8 (12H, m);

m/e 168 (15.2%), 167 (100, M-NO), 136 (35.2, $M-N_2O_2H$).

Adamant-2-yl-2-^{2}H-ONN-azoxytosylate

This tosylate was prepared from the deuterated nitrosohydroxylamine (0.39g, 1.98 mmol) following the method used for the preparation of the non-deuterated tosylate. After two recrystallisations from ether/methylene chloride at -70°C a white solid was obtained (0.61g, 88%),

m.p. 111-112.5°C;

i.r. (KBr): $\bar{\nu}_{max}$ = 1600 (m), 1505 (m), 1455 (m), 1390 (s), 1305 (m), 1200 (s), 1190 (m), 1095 (m), 910 (s), 825 (m), 810 (sh), 795 (m), 765 (m), 725 (s), 665 (m), 565 (m), and 550 (s) cm^{-1};

n.m.r. ($CDCl_3$): τ = 2.4 (4H, q), 7.55 (5H, m) and 7.7-9.1 (12H, m);

m/e 136 (31.0%, $M-ON_2OSO_2C_7H_7$), 135 (100), 94 (15.8), 93 (45.7), 92 (22.0), 91 (26.4).

Integration of a concentrated solution, comparing the quartet at 2.4 with the small resonance peak at 4.3τ, indicated that the amount of deuterium incorporation was 97.4% ± 0.2%.

Thermal decomposition of Adamant-2-yl-ONN-azoxytosylate

A. In Deuterochloroform

(i) Adamant-2-yl-ONN-azoxytosylate (approximately 25 mg) was dissolved in deuterochloroform (0.5 cms^3) in an n.m.r. tube. The n.m.r. tube was placed in an oil bath heated to 60°C. The resonance peak at 5.7τ, due to the hydrogen at position 2 on the

adamantane ring, slowly disappeared with concomitant formation of a new resonance peak at 5.3τ. The half life of this process was approximately 16 hours. After 64 hours the n.m.r. spectrum was indistinguishable from that of 2-adamantyl tosylate. An authentic sample was available for comparison.

(ii) Adamant-2-yl-ONN-azoxytosylate (0.43g, 1.23 mmol) was dissolved in deuterochloroform (6 cms^3) and heated in an oil bath to 65°C for three days. Evaporation of the solvent gave a brown oil (0.35g, 93%) which crystallised upon standing overnight. The crude product was recrystallised from petroleum ether(40-60)/diethyl ether at low temperature to give a white solid, m.p. 81-83°C (lit.[94] 82.1-83.4°C for 2-adamantyl tosylate). i.r. (KBr): $\bar{\nu}_{max}$ = 1600 (m), 1495 (w), 1455 (m), 1335 (s), 1195 (m), 1180 (s), 1170 (sh), 1100 (m), 965 (m), 915 (s), 905 (s), 860 (m), 815 (m), 690 (m) and 570 (m) cm^{-1}; n.m.r. ($CDCl_3$): τ = 2.45 (4H,q), 5.3 (1H,m), 7.6 (5H,m) and 7.6-8.9 (12H,m).

B. Solvolysis in Ethanol

Adamant-2-yl-ONN-azoxytosylate (0.16g, 0.46 mmol) was dissolved in ethanol (5 cms^3) and stirred at 60-62°C in an oil bath for 4 days. The ethanol was removed on a rotary evaporator to leave a light brown oil. This was pumped on for 24 hours at 40°C/0.1 mm to leave an oil which crystallised upon drying in a desiccator overnight (0.07g). Thin layer chromatography on silica using a mixture of dichloromethane and methanol (9/1 v/v respectively) gave two spots, R_F = 0.7 and R_F = 0.05. 2-Adamantyl tosylate has R_F = 0.7 under the same

conditions. The crude product was recrystallised from petroleum ether (40-60)/diethyl ether at -70°C to leave a white solid m.p. 82.5-8.35°C; this material was identical in all respects (i.r., n.m.r., tlc) with 2-adamantyl tosylate.

Miscellaneous Experiments

Large scale deamination of exo-bicyclo[3,2,1]octan-2-ylamine hydrochloride and subsequent isolation of compound P.

A mixture of crude exo-bicyclo[3,2,1]octan-2-ylamine hydrochloride (11.9g, 0.074 moles) in anhydrous acetic acid (175 cms^3) was stirred under argon at ca. 22°C. Sodium nitrite (5.6g, 0.081 moles) was added over a period of one hour. After stirring for 16 hours the reaction mixture was cooled in an ice bath and poured onto a cold solution of $K_3PO_4.H_2O$ (735g) in water (900 cms^3). The cold mixture was extracted twice with pentane and the combined organic extracts washed with cold water, cold dilute hydrochloric acid and again with cold water. When most of the pentane had been removed by careful fractional distillation the hydrocarbon products were separated from the other reaction products by column chromatography (alumina grade II, 300g) using pentane as eluent. When concentrated by fractional distillation the pentane solution was added to a mixture of water (226 cms^3), pyridine (336 cms^3), sodium carbonate decahydrate (1.12g), potassium permanganate (0.1g) and sodium periodate (4.72g)[5i] and the resultant mixture stirred overnight. The reaction mixture was extracted twice with pentane and the combined organic extracts washed with dilute sulphuric acid, dilute potassium hydroxide solution and twice with concentrated sodium thiosulphate solution. The procedure of concentration,

separation of the hydrocarbon by chromatography and concentration were repeated and finally a small quantity (40 mg) of a white solid isolated by preparative g.l.c. using a 10% Carbowax 20M column at 115°C. Analytical g.l.c. indicated that this material co-chromatographed with P;

n.m.r. ($CDCl_3$): τ = 7.9-9.5m;

m/e 108 (51.8%,M); 93 (22.8, M-15), 79 (100, M-29) and 66 (71, M-42)

C_8H_{12} requires m/e = 108.0939

found m/e = 108.0941

Another preparation of P, this time by the solvolysis of exo-bicyclo[3,2,1]octan-2-yl tosylate in dimethylformamide at 100°C for 24 hours in a Karius tube was done following the procedure of Saito.[81] After a similar workup to that described above gave a waxy liquid (2.1%) which co-chromatographed with P. This material was sent for ^{13}C n.m.r. analysis.

^{13}C n.m.r. ($CDCl_3$): 134.32 ppm (Intensity = 44), 41.36(57), 36.34(49), 31.31(63), 31.18(208), 30.79(69), 30.24(77), 28.74(190), 27.98(72), 24.16(50), 16.61(157), and 12.76(48).

Deamination of Ethyl N-nitroso, N-(exo-bicyclo[3,2,1]oct-3-yl) carbamate in 80% aqueous tetrahydrofuran.

The title compound (ca. 100mg) was dissolved in 80% aqueous tetrahydrofuran (5 cms^3) and left for 10 days at 40°C. A little ether (ca. 2 cms^3) was added to the cooled solution which was then washed once with brine. G.l.c. analysis of the ethereal solution showed a trace amount of a compound which

co-chromatographed with exobicyclo[3,2,1]octan-3-yl ethyl ether. By comparison with the amount of olefin formed it was estimated that less than 0.01% of the ether was formed. It was assumed that the amount of olefin product formed was the same as that formed when ethanol was used as solvent.

G.l.c. Analysis of Reaction Products

Dr. R. M. Banks had demonstrated that all the products from the solvolysis reactions of the two bicyclo[3,2,1]-oct-3-yl tosylates were detectable and resolvable by g.l.c.[4] No other products were anticipated from the deamination reactions of the five isomeric amines studied here, even though more rearrangement was expected to occur. This is one of the features of deamination reactions. In fact two extra hydrocarbons and one ether, all of unknown identity, were found among the products of some reactions.

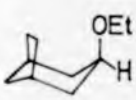
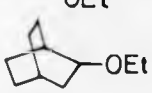
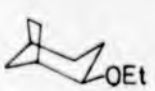
Samples of all five isomeric alcohols were kindly supplied by Dr. Maskill as were samples of the two expected hydrocarbon products; bicyclo[3,2,1]oct-2-ene and bicyclo[2,2,2]-oct-2-ene. The ethers were prepared from the corresponding alcohols as described above.

Wall coated open tubular (WCOT) columns were found to give superior resolution of products compared with support coated open tubular (SCOT) columns but the former type were highly susceptible to overloading, resulting in misshapen peaks which interfered with the resolution. SCOT columns were therefore used throughout. The g.l.c. conditions employed were different from those described by Dr. Banks as it was found that some products were not completely resolvable under her prescribed conditions. This was probably due to the different properties supposedly identical g.l.c. columns can possess.

As reported by Dr. Banks it was found that the acetate products were inadequately resolved by g.l.c. and so were reduced to the alcohols with $LiAlH_4$. Similarly the

TABLE 11

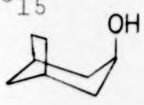
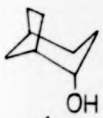
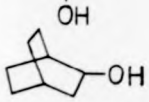
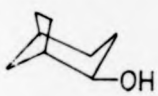
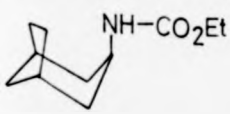
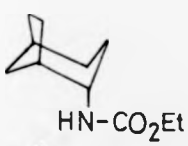
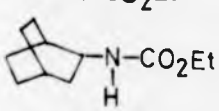
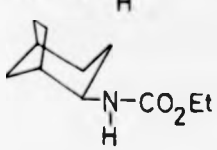
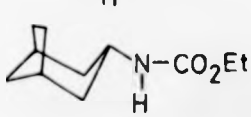
G.l.c. Retention Times; Hydrocarbons and Ethers

Compound	Column	Temperature (^{o}C)	Retention Time[a] (mins.)
			5.3
	50' SCOT APL	110^{o}C	5.5
P			6.7
Q			6.9
C_{11}			18.5
C_{11}			2.5
			3.9
	50' SCOTDEGS	85^{o}C	5.1
			5.45
			6.25
			7.05

a Carrier gas pressure = 20 psi

TABLE 12

G.l.c. Retention Times; Alcohols and Carbamates

Compound	Column	Temperature (°C)	Retention Time[a] (mins.)
C_{15}			18.1
			21.9
	50' SCOTDEGS	85°C	27.8
			29.8
			31.10
			33.8
			21.9
			28.2
	50' SCOTDEGS	140°C	29.6
			29.6
			26.7

a Carrier gas pressure = 20 psi.

carbonate products were saponified with potassium hydroxide to give the corresponding alcohols. $LiAlH_4$ was not used since the solvent here was ethanol.

The hydrocarbon products were analysed on a 50 foot SCOT Apiezon L. column (Perkin-Elmer, 110°C) using n-undecane as the internal standard. Table 11 shows the retention time of the hydrocarbons under these conditions. The ethers, Table 11, alcohols and carbamates, Table 12, were all analysed separately on a 50 foot SCOT DEGS column (Perkin-Elmer) at different temperatures due to their large differences in retention times. The ethers were analysed using n-undecane as internal standard while the alcohols and carbamates were analysed using n-pentadecane. It was found necessary to use a temperature programming procedure to estimate the amount of carbamate formed in a given reaction; initial temperature- 120°C for 4 minutes then heated at 39°C/minute to a final temperature of 180°C. The hydrocarbon standard was eluted during the first isothermal period and the carbamate during the second.

Sensitivity Optimization of the Flame Ionisation Detector (F.I.D.)

In order to obtain the best conditions possible for the product analyses the F.I.D. response was optimized w.r.t. the hydrogen and air pressures at normal operating carrier gas pressure.

Injections of ether (3 µl) were made at different pressures of hydrogen while the air pressure was kept constant. It was found that the F.I.D. response (measured as the peak height) went through a maximum at a pressure of between 12 and

carbonate products were saponified with potassium hydroxide to give the corresponding alcohols. $LiAlH_4$ was not used since the solvent here was ethanol.

The hydrocarbon products were analysed on a 50 foot SCOT Apiezon L. column (Perkin-Elmer, 110°C) using n-undecane as the internal standard. Table 11 shows the retention time of the hydrocarbons under these conditions. The ethers, Table 11, alcohols and carbamates, Table 12, were all analysed separately on a 50 foot SCOT DEGS column (Perkin-Elmer) at different temperatures due to their large differences in retention times. The ethers were analysed using n-undecane as internal standard while the alcohols and carbamates were analysed using n-pentadecane. It was found necessary to use a temperature programming procedure to estimate the amount of carbamate formed in a given reaction; initial temperature- 120°C for 4 minutes then heated at 39°C/minute to a final temperature of 180°C. The hydrocarbon standard was eluted during the first isothermal period and the carbamate during the second.

Sensitivity Optimization of the Flame Ionisation Detector (F.I.D.)

In order to obtain the best conditions possible for the product analyses the F.I.D. response was optimized w.r.t. the hydrogen and air pressures at normal operating carrier gas pressure.

Injections of ether (3 µl) were made at different pressures of hydrogen while the air pressure was kept constant. It was found that the F.I.D. response (measured as the peak height) went through a maximum at a pressure of between 12 and

14 psi. (Table 13). The same procedure was carried out to optimize the air pressure. The sensitivity of the F.I.D. increased with the air pressure but so did the background noise. A compromise of 20 psi was thought to be the best operating pressure.

TABLE 13

Flame Ionisation Detector Response Optimization

Hydrogen Pressure (psi)	Response (Peak Height)
8	22
10	29
12	32
14	32
16	30
20	24
22	21
Air Pressure (psi)	**Response (Peak Height)**
10	13
16	26
18	29
20	31
28	34

Calibration of the Detector

Introduction of a known amount of inert standard into the reaction medium along with a known amount of starting material allows calculation of the absolute yield of a product. It is known that the amplitude of response of an F.I.D. is different for different compounds. It was essential, therefore, to work out calibration factors for the different products w.r.t. their internal standards. Dr. Banks had experimentally determined the molar response factor (m.r.f.) of bicyclo[3,2,1]oct-2-ene w.r.t. n-undecane and of the alcohols exo-bicyclo[3,2,1]octan-3-ol and bicyclo[2,2,2]octan-2-ol w.r.t. n-pentadecane using the expression given below.

For a solution containing known amounts of product and standard the m.r.f. is given by the expression:

$$\text{m.r.f.} = \frac{\text{Area of Product Peak x Concentration of Standard}}{\text{Concentration of Product x Area of Standard Peak}}$$

Using this expression an m.r.f. of 0.611 ($\pm$ 0.013) was determined from three solutions containing known amounts of n-pentadecane and ethyl N-(exo-bicyclo(3,2,1)oct-2-yl) carbamate. An m.r.f. for the ether products, using n-undecane as a standard, was calculated simply by dividing the number of carbon atoms in the ether by the number in the standard i.e. m.r.f. = 10/11 = 0.909.

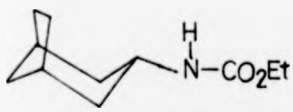
It was assumed throughout that isomeric products gave the same response in the F.I.D. and that the unexpected tricyclic products found in some reactions had the same m.r.f. as the olefin hydrocarbons. Table 14 gives a summary of the m.r.f's of the assorted products.

Calculation of Reaction Product Yields

Initially a precision disc planimeter was used to measure peak areas. Each peak area was measured repeatedly until consistent results were obtained. Later an electronic digital integrator (Kemtronix Supergrator) was used. A check was made to ensure that there was no discrepancy between the two methods. A complete analysis of products from one reaction was carried out using both methods and it was shown that within experimental error there was no discrepancy between the two methods. Appendix 2 gives details of the results.

TABLE 14

Molar Response Factors (M.R.Fs) of Deamination Products

Compound Type	Internal Standard	M.R.F.
hydrocarbons		
 etc	n-undecane	0.751[a] (±0.006)
ethers		
 etc	n-undecane	0.909[b]
alcohols		
 etc	n-pentadecane	0.524[a] (±0.016)
carbamates		
 etc	n-pentadecane	0.611[c] (±0.013)

a Determined by Dr. Banks[4]

b Calculated value

c Determined by the author

It was found later, however, that because of a partial overlap of peaks due to bicyclo[2,2,2]octan-2-ol and endo-bicyclo[3,2,1]octan-2-ol, the integrator gave an overestimated value to the latter alcohol. By inspection a correction factor of 0.33 was used i.e. one third of the value of the later peak was taken from itself and added to the value of the earlier peak. The correction factor was checked by planimeter and seemed to be very reasonable.

Each analysis was carried out four times or more depending upon the reproducibility of the results. A mean value for each product and the total recovery of products were then calculated. The product yields were then normalised by dividing each mean value by the total recovery and multiplying by 100. The solvolysis procedure was then repeated and a mean normalised value obtained for each product.

The extent of formation of a given product is given by the formula:

$$\% \text{ yield of product} = \frac{\text{Area of Product Peak} \times 100 \times \text{No. of moles of Standard}}{\text{No. of moles of starting material} \times \text{m.r.f.} \times \text{Standard Peak Area}}$$

Preparation of Standard Solutions

Purification of Internal Standards

Both hydrocarbons had been redistilled by Dr. Banks. n-Undecane had b.p. 57°C/2 mm and n-pentadecane had b.p. 100°C/ 0.3 mm. Their purity was checked by g.l.c.; no impurities were detected.

Preparation of Acetolysis Solution

Into a 100 cms^3 volumetric flask was accurately

weighed about 250 mg of both n-undecane and n-pentadecane followed by 1.232g of fused sodium acetate. The flask was then made up to the mark with acetic acid which had been purified by refluxing overnight with acetic anhydride followed by fractional distillation. Such a solution is 0.15 molar in sodium acetate.

Preparation of Ethanolysis Solution

A standard solution was prepared by accurately weighing about 200 mg of both internal standards into a 100 cms^3 volumetric flask. The flask was then made up to the mark with commercial absolute spectroscopic grade ethanol.

Preparation of 80% Aqueous Ethanol for Kinetics

20 cms^3 of water (twice distilled from potassium permanganate) was pipetted into a 100 cms^3 volumetric flask. Absolute spectroscopic grade ethanol was used to make the solution up to the mark.

Deamination Methods

Nitrous acid deamination of the amine hydrochlorides

Several variations of procedure were tried including using free amine, varying the amount of sodium nitrite added, and carrying out the reaction under argon. In most cases the yields were low and variable. The following procedure was found to give the highest yields and to be the most reproducible; it was followed for all five isomers.

Typically 100 to 150 mg of amine hydrochloride (weight accurately known) was dissolved in 5 cms^3 of acetolysis solution (described above) and stirred in a water bath at 24-25^{o}C

under argon. Sodium nitrite (3 molar equivalents) was added portionwise over 30 minutes and the mixture stirred overnight (sealed, under argon). More sodium nitrite was added (1.5 molar equivalents) and the mixture stirred for one more hour before it was added to a cold buffer solution of $K_3PO_4.H_2O$ (20.13g) in water (35 cms^3). The buffered solution was extracted once with ether (redistilled from $LiAlH_4$). The ethereal solution was washed with cold hydrochloric acid (2M) and cold water. A portion of this solution was used directly for analysis of the hydrocarbon products. The remainder was refluxed with $LiAlH_4$ (about 0.1g) for 2 hours, cooled, and quenched with hydrochloric acid (2M). The ethereal layer was separated and washed with brine and then used for analysis of the alcohol products (reduced acetates).

Deamination of Triazenes in Acetic Acid

(i) For analysis of hydrocarbon and acetate products

Conveniently 30 to 70mg of triazene (weight accurately known) was added portionwise (if solid) or dropwise (if liquid) to a flask in a water bath at 25°C, containing 5 cms^3 of stirred acetolysis solution (described above). In the two cases where the triazene was an oil, a pasteur pipette containing the triazene was weighed before and after the addition. The evolution of nitrogen ceased after a few seconds but the reaction was stoppered and stirred for an hour or thereby. The procedure was then the same as that used in the nitrous acid deaminations described above.

(ii) For determination of N-(bicyclooctyl)-anilines

The procedure was the same as for the analysis of

hydrocarbons and acetates except no acid wash of the ethereal layer was performed. Instead the ether solution was washed with water, dried over sodium sulphate, and filtered. The ether was removed on the rotary evaporator and the residue taken up in pentane (acid washed, redistilled) and chromatographed on alumina (about 30g, grade II) using pentane as eluent. Those fractions containing secondary amine (detected by u.v. spectroscopy) were combined and the solvent removed. The residue was taken up in ethanol, made up to a standard volume, and its u.v. absorption measured.[5]

Deamination of The Nitrosocarbamates in Ethanol

Immediately after their preparation the nitrosocarbamates were deaminated; 30 to 50mg was accurately weighed into a flask and 5 cms^3 of ethanolysis solution (described above) was added using a pipette. The flask was stoppered and shaken and placed in a water bath at 25°C with the exception of the exo-3-isomer which was reacted at 50°C instead. The flask was left for at least 10 half lives* then the contents were divided into two fractions. One fraction, about 1 cm^3, was used directly for analysis of the hydrocarbon, ether and denitrosated products. The other, about 4 cms^3, was refluxed for 2½ hours with potassium hydroxide (200 mg) and then cooled. Ether was added (4 cms^3) and the mixture washed with brine. The organic solution left was used to be analysed for the alcohol products (saponified carbonates).

* A u.v. cell containing some nitrosocarbamate in ethanol was immersed in the same waterbath and its spectrum recorded periodically.

Kinetics

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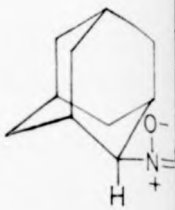

(a)

more than 0.05°C.
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Checks
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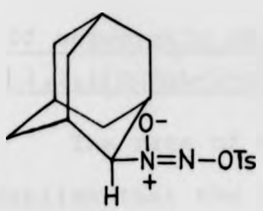
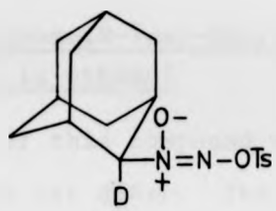
Kinetics

(i) Of solvolysis of Adamant-2-yl-ONN-azoxytosylate in 80% aqueous ethanol

All reactions were followed spectrophotometrically at 274nm using a Unicam SP500 Series 2 spectrophotometer and a thermostatted cell compartment. Compounds (a) and (b) were solvolysed simultaneously in 80% aqueous ethanol at 61.3°C in the same cell compartment to reduce the effects of any small temperature fluctuations. The temperature fluctuation was not



(a)



(b)

more than 0.05°C. After the substrates had been weighed into the silica cells (ca. 2 mg) and the solvent added prolonged and vigorous shaking of the cells was required to ensure that the azoxytosylates were completely dissolved in the solvent mixture. Three 1 cm silica cells fitted with P.T.F.E. stoppers were used in each run. The first contained solvent, the second a solution of non-deuterated azoxytosylate (a) and the third a solution of deuterated azoxytosylate (b).

Checks on the kinetic method used were carried out by Dr. Banks who established that there was no bias in the spectrophotometer. Reference No. 4 gives further details.

The reactions were monitored for a minimum of five half-lives and approximately 40 points recorded for each reaction.

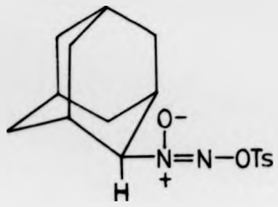
A computer program, written by Dr. R. L. Tranter of this department, using a non-linear minimisation routine was used to evaluate the 1st order rate constants. Standard deviations were in the range 0.3-0.8% showing that good 1st order kinetics were followed. Four runs were done on each of two pairs of solutions. The errors quoted are standard errors[87] and the isotope effects have not been corrected for less than 100% deuterium incorporation.

The results are given in Appendix 1.

(ii) Of solvolysis of Ethyl N-nitroso,N-(exo-bicyclo-[3,2,1]octan-3-yl)carbamate in ethanol

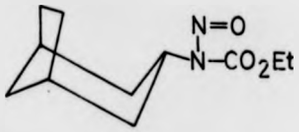
The rate of solvolysis of this compound was determined to establish that the reaction was 1st order. The conditions used were as described for the azoxytosylate work except that the reactions were monitored at 407nm and spectroscopic grade ethanol was used as solvent. Six runs were done and the results are given in Appendix 1.

APPENDIX 1

Solvolysis of  in 80% aqueous ethanol at 61.3°C

k_H (x 10^4) sec^{-1}	k_D (x 10^4) sec^{-1}	k_H/k_D
3.274	2.859	1.145
3.333	2.942	1.133
3.246	2.879	1.127
3.280	2.916	1.125

$\overline{k_H}$ = (3.28 ± 0.02) x 10^{-4} sec^{-1} $\overline{k_H/k_D}$ = 1.132 ± 0.005

Solvolysis of  in ethanol at 61.3°C

k (x 10^5) sec^{-1}
8.858
8.894
9.112
8.981
9.439
9.449

$\bar{k}$ = (9.12 ± 0.10) x 10^{-5} sec^{-1}

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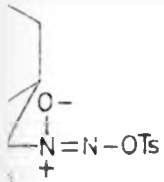

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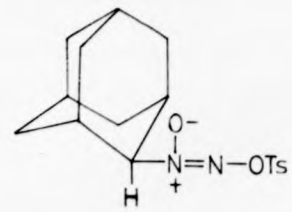
APPENDIX 1

Solvolysis of  in 80% aqueous ethanol at 61.3°C

k_H (x 10^4) sec^{-1}	k_D (x 10^4) sec^{-1}	k_H/k_D
3.274	2.859	1.145
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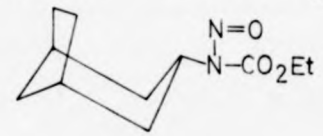
$\overline{k_H}$ = (3.28 ± 0.02) x 10^{-4} sec^{-1} $\overline{k_H/k_D}$ = 1.132 ± 0.005

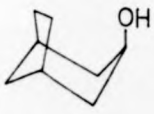
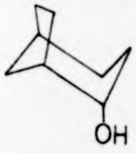
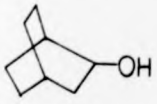
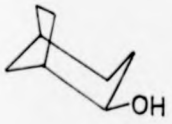
Solvolysis of  in ethanol at 61.3°C

k (x 10^5) sec^{-1}
8.858
8.894
9.112
8.981
9.439
9.449

$\overline{k}$ = (9.12 ± 0.10) x 10^{-5} sec^{-1}

APPENDIX 2

Acetolysis of 1-(exo-bicyclo[3,2,1] octan-3'-yl)-3-phenyltriazene and check on the comparability of planimeter and integrator

Product	1	2	3	4	5	Mean
	(18.54)[a]	(17.43)	(17.39)	(17.06)	(17.41)	(17.57)
	18.85[b]	18.27	17.57	17.90	17.63	18.04
P	(0.67)	(0.68)	(0.65)	(0.56)	(0.61)	0.64
	0.68	0.70	0.69	0.67	0.68	0.68
	(4.88)	-	(4.76)	(4.99)	(4.90)	(4.88)
	4.60	4.72	4.91	4.68	4.87	4.78
	(2.11)	-	(2.16)	(2.29)	(2.19)	(2.19)
	2.15	2.29	2.27	2.26	2.32	2.26
	(1.46)	-	(1.54)	(1.50)	(1.37)	(1.47)
	1.21	1.27	1.21	1.49	1.36	1.33
	(N.D.)[c]	-	(0.23)	(0.21)	(0.16)	(0.15)
	N.D.	0.04	N.D.	0.24	0.05	0.07
	(41.62)	-	(42.62)	(42.63)	(42.36)	(42.30)
	39.87	41.54	43.02	41.21	42.57	41.64

a Values in brackets are those measured by planimeter

b Values without brackets were measured by integrator

c N.D. = Not Detected

APPENDIX 3

Analysis of Products

Each reaction was done twice. The results from the repeat chromatograms from each run of each reaction were averaged. The normalised average values from each run and a mean normalised value are shown in a separate table. The ethyl bicyclo-octylcarbamates formed from the nitroso-carbamate reactions were not included among the normalised products since these compounds are not strictly deamination products. All reactions were carried out at 24-25^{o}C unless otherwise stated.

Solvolysis of 

in Acetic Acid 0.15 Molar in Sodium Acetate at 27°C

Run I

Products	1	2	3	4	5	6	7	Average
3-ene	18.85	18.27	17.61	17.57	17.90	17.63	-	17.91
X	0.91	0.93	0.84	0.92	0.89	0.91	-	0.90
endo-3-OAc	4.60	4.72	4.91	4.68	4.87	-	-	4.78
exo-2-OAc	2.15	2.29	2.27	2.26	2.32	-	-	2.26
[2,2,2]-OAc	1.21	1.27	1.21	1.49	1.36	-	-	1.33
endo-2-OAc	N.D.	0.04	N.D.	0.24	0.05	-	-	0.07
exo-3-OAc	39.87	41.54	43.02	41.21	42.57	-	-	41.64
2° amine	one determination only							10.9
Recovery								79.8

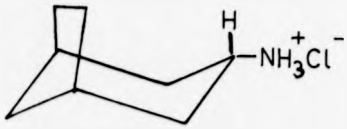
Run II

Products	1	2	3	4	5	6	7	Average
3-ene	18.81	18.85	19.05	18.58	19.53	19.05	18.65	18.93
X	0.77	0.77	0.91	0.81	0.93	0.89	0.89	0.85
endo-3-OAc	5.14	5.28	5.35	5.30	5.30	-	-	5.27
exo-2-OAc	2.32	2.41	2.28	2.39	2.35	-	-	2.35
[2,2,2]-OAc	1.24	1.54	1.42	1.59	1.50	-	-	1.46
endo-2-OAc	0.07	N.D.	0.25	0.28	0.25	-	-	0.14
exo-3-OAc	41.85	41.43	42.71	44.35	43.81	-	-	42.83
Recovery	including 2° amine product							82.7

< 0.1% 2-ene formed

N.D. = not detected

Products	Normalised Average Run I	Normalised Average Run II	Mean
3-ene	22.4	22.9	22.7
X	1.1	1.0	1.1
endo-3-OAc	6.0	6.4	6.2
exo-2-OAc	2.8	2.8	2.8
[2,2,2]-OAc	1.7	1.8	1.7
endo-2-OAc	0.1	0.2	0.1
exo-3-OAc	52.2	51.8	52.0
2° amine	13.7	-	13.7

Nitrous Acid Deamination of 

in Acetic Acid 0.15 Molar in Sodium Acetate

Run I

Products	1	2	3	4	5	6	Average
3-ene	6.39	6.07	6.69	6.32	-	-	6.37
X	0.76	0.84	0.76	0.87	-	-	0.81
endo-3-OAc	5.70	5.92	6.01	6.24	5.84	-	5.94
exo-2-OAc	1.77	1.83	1.65	1.75	1.63	-	1.72
[2,2,2]-OAc	1.35	1.31	1.00	1.01	1.00	-	1.13
exo-3-OAc	35.84	36.11	39.51	39.43	36.01	-	37.38
Recovery*							53.55

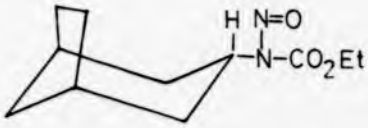
Run II

Products	1	2	3	4	5	6	Average
3-ene	7.88	7.95	7.67	8.29	7.34	7. 43	7.78
X	0.78	0.89	0.88	0.84	0.77	0.76	0.82
endo-3-OAc	5.43	6.38	6.27	6.63	6.40	-	6.22
exo-2-OAc	-	1.63	1.66	1.77	1.76	-	1.70
[2,2,2]-OAc	-	0.98	1.00	1.07	1.03	-	1.02
exo-3-OAc	35.32	38.15	37.48	42.24	39.04	-	38.44
Recovery*							

* including trace amount (ca. 0.2%) of endo-2-OAc

<0.1% 2-ene <0.3% endo-2-OAc

Products	Normalised Average Run I	Normalised Average Run II	Mean
3-ene	11.90	13.84	12.9
X	1.51	1.46	1.5
endo-3-OAc	11.09	11.07	11.1
exo-2-OAc	3.21	3.02	3.1
[2,2,2]-OAc	2.11	1.81	2.0
exo-3-OAc	69.80	68.40	69.1

Solvolysis of 

in Ethanol at 50°C

Run I

Products	1	2	3	4	5	6	Average
3-ene	33.87	33.84	32.84	34.90	34.22	-	33.93
Z	0.29	0.28	0.29	0.28	0.29	-	0.29
X	0.81	0.98	1.00	1.03	0.94	-	0.95
endo-3-OEt	1.85	2.04	2.00	1.93	1.90	-	1.94
exo-2-OEt	0.87	0.90	0.84	0.88	0.90	-	0.88
[2,2,2]-OEt	0.59	0.64	0.58	0.61	0.64	-	0.61
endo-2-OEt	N.D.	N.D.	0.13	0.12	0.13	-	0.08
E	2.08	2.23	1.93	2.01	2.00	-	2.06
exo-3-OEt	22.19	24.52	22.07	23.03	22.81	-	22.93
endo-3-OCO_2Et	6.30	5.17	4.92	6.31	5.27	5.36	5.59
exo-2-OCO_2Et	0.25	0.26	0.29	0.28	N.D.	N.D.	0.18
endo-2-OCO_2Et	0.22	0.28	N.D.	0.39	N.D.	N.D.	0.15
exo-3-OCO_2Et	18.95	16.66	16.27	19.41	-	16.98	17.65
carbamate	5.10	5.49	6.07	6.05	-	-	5.68
Recovery							92.9

Z and E are unidentified products of dubious origins.

Run II

Products	1	2	3	4	5	6	Average
3-ene	33.42	30.69	33.41	34.67	30.72	36.11	33.17
Z	0.30	0.26	0.29	0.32	0.26	0.30	0.29
X	0.87	0.65	1.00	0.85	0.77	0.93	0.84
endo-3-OEt	1.88	1.88	1.88	2.00	1.82	-	1.90
exo-2-OEt	0.78	0.78	0.80	0.85	0.80	-	0.80
[2,2,2]-OEt	0.54	0.55	0.54	0.59	0.55	-	0.55
endo-2-OEt	0.13	0.10	0.13	0.11	0.10	-	0.11
E	1.90	1.89	1.87	2.06	1.81	-	1.90
exo-3-OEt	19.95	20.05	19.90	22.55	20.15	-	20.53
endo-3-OCO_2Et	4.99	5.25	5.14	5.15	6.11	-	5.33
exo-2-OCO_2Et	N.D.	N.D.	0.28	0.25	N.D.	-	0.2
endo-3-OCO_2Et	N.D.	N.D.	0.30	0.25	N.D.	-	0.2
exo-3-OCO_2Et	17.38	16.98	16.18	15.37	18.98		16.98
carbamate	5.25	5.39	5.98	5.74	-	-	5.59
Recovery							88.4

< 0. 2% 2-ene

< 0.1% [2,2,2]-OCO_2Et

N.D. = not detected.

Products	Normalised Average Run I	Normalised Average Run II	Mean
3-ene	38.90	40.06	39.5
Z	0.33	0.35	0.34
X	1.09	1.01	1.1
endo-3-OEt	2.22	2.29	2.3
exo-2-OEt	1.01	0.97	1.0
[2,2,2]-OEt	0.70	0.66	0.68
endo-2-OEt	0.09	0.13	0.11
E	2.36	2.29	2.3
exo-3-OEt	26.29	24.79	25.5
endo-3-OCO_2Et	6.41	6.44	6.4
exo-2-OCO_2Et	0.21	0.24	0.2
endo-2-OCO_2Et	0.17	0.24	0.2
exo-3-OCO_2Et	20.24	20.50	20.4

Nitrous Acid Deamination of 

in Acetic Acid 0.15 Molar in Sodium Acetate

Run I

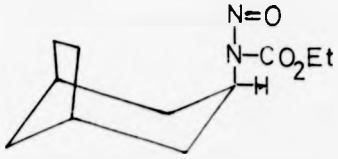
Products	1	2	3	4	5	6	Average
3-ene	27.25	22.23	25.88	25.45	25.03	-	25.17
X	5.68	4.78	4.91	4.65	4.87	-	4.98
endo-3-OAc	8.18	8.87	9.17	7.91	8.45	-	8.52
exo-2-OAc	5.62	6.07	6.19	5.89	5.88	-	5.93
[2,2,2]-OAc	5.38	5.45	5.54	5.14	5.29	-	5.36
exo-3-OAc	8.33	8.45	9.09	8.17	8.66	-	8.54
Recovery							58.5

Run II

Products	1	2	3	4	5	6	Average
3-ene	16.33	16.59	16.72	16.85	15.90	-	16.48
X	3.90	3.89	4.02	4.10	3.70	-	3.92
endo-3-OAc	6.48	6.64	7.24	6.48	6.99	6.96	6.80
exo-2-OAc	5.51	5.26	5.74	5.29	5.51	5.63	5.49
[2,2,2]-OAc	5.03	5.16	5.39	5.16	5.01	5.14	5.15
exo-3-OAc	7. 62	7.91	8.37	8.89	7.77	8.23	8.13
Recovery							46.0

< 0.2% 2-ene < 0.4% endo-2-OAc

Products	Normalised Average Run I	Normalised Average Run II	Mean
3-ene	43.03	35.83	39.4
X	8.51	8.52	8.5
endo-3-OAc	14.56	14.78	14.7
exo-2-OAc	10.14	11.93	11.0
[2,2,2]-OAc	9.16	11.20	10.2
exo-3-OAc	14.60	17.67	16.1

Solvolysis of 

in Ethanol

Run I

Products	1	2	3	4	5	6	Average
3-ene	67.30	61.03	65.73	63.55	64.30	-	64.38
X	17.96	16.36	17.43	16.85	17.11	-	17.14
endo-3-OEt	0.68	0.69	0.69	0.69	0.69	0.69	0.69
exo-2-OEt	2.34	2.40	2.36	2.35	2.40	2.43	2.38
[2,2,2]-OEt	1.82	1.79	1.82	1.85	1.75	1.80	1.81
endo-2-OEt	0.36	0.36	0.36	0.37	0.35	0.36	0.36
E	0.032	0.038	0.033	0.035	0.036	0.038	0.035
exo-3-OEt	4.03	4.15	3.97	4.25	3.99	4.13	4.09
endo-3-OCO_2Et	5.13	4.89	5.30	4.79	5.35	4.79	5.04
exo-2-OCO_2Et	1.26	1.03	1.19	1.00	1.12	1.17	1.13
[2,2,2]-OCO_2Et	1.12	0.88	0.98	0.83	0.94	1.08	0.97
endo-2-OCO_2Et	2.16	1.38	1.59	1.48	1.50	1.96	1.68
exo-3-OCO_2Et	0.72	0.52	0.61	0.66	0.71	0.78	0.67
Recovery							100.4

Run II

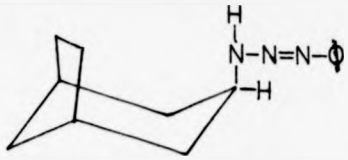
Products	1	2	3	4	5	6	Average
3-ene	63.91	66.48	65.97	66.26	68.25	-	66.17
X	17.01	17.64	17.60	17.60	17.60	-	17.57
endo-3-OEt	0.68	0.70	0.66	0.67	0.68	-	0.68
exo-2-OEt	2.43	2.57	2.31	2.37	2.47	-	2.43
[2,2,2]-OEt	1.76	1.89	1.64	1.72	1.77	-	1.76
endo-2-OEt	0.35	0.42	0.33	0.34	0.36	-	0.36
E	0.035	N.D.	0.029	0.034	0.036	-	0.027
exo-3-OEt	4.00	4.37	3.66	3.83	4.16	-	4.00
endo-3-OCO_2Et	4.27	4.32	4.57	3.80	4.64	4.59	4.37
exo-2-OCO_2Et	1.05	1.14	1.22	1.02	1.16	1.18	1.13
[2,2,2]-OCO_2Et	0.97	1.04	1.13	0.93	1.05	1.10	1.04
endo-2-OCO_2Et	1.82	2.02	2.18	1.76	1.79	1.79	2.11
exo-3-OCO_2Et	0.64	0.47	0.70	0.61	0.66	0.67	0.66
Recovery							102.3

< 0.2% 2-ene

< 0.5% carbamate

N.D. = not detected.

Products	Normalised Average Run I	Normalised Average Run II	Mean
3-ene	64.12	64.68	64.4
X	17.07	17.17	17.1
endo-3-OEt	0.69	0.66	0.68
exo-2-OEt	2.37	2.38	2.4
[2,2,2]-OEt	1.80	1.72	1.8
endo-2-OEt	0.36	0.35	0.36
E	0.035	0.026	0.03
exo-3-OEt	4.07	3.91	4.0
endo-3-OCO_2Et	5.02	4.27	4.6
exo-2-OCO_2Et	1.13	1.10	1.1
[2,2,2]-OCO_2Et	0.97	1.02	1.0
endo-2-OCO_2Et	1.67	2.06	1.9
exo-3-OCO_2Et	0.67	0.65	0.66

Solvolysis of 

in Acetic Acid 0.15 Molar in Sodium Acetate at 26°C

Run I

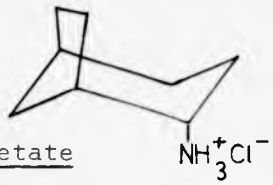
Products	1	2	3	4	5	Average
2-ene	0.25	0.23	0.21	0.19	N.D.	0.18
3-ene	29.11	30.16	30.15	29.33	30.68	29.89
X	5.57	5.66	5.63	5.61	5.85	5.66
endo-3-OAc	2.02	1.99	1.88	1.90	1.96	1.95
exo-2-OAc	4.39	4.01	4.12	4.24	4.43	4.24
[2,2,2]-OAc	3.63	3.43	2.91	3.65	3.76	3.48
endo-2-OAc	0.50	0.57	N.D.	0.61	0.06	0.35
exo-3-OAc	3.59	3.16	3.31	3.76	3.15	3.39
2° amine	one determination only					10.0
Recovery						59.1

Run II

Products	1	2	3	4	5	Average
2-ene	0.25	0.39	0.23	N.D.	-	0.22
3-ene	30.31	32.15	31.31	31.83	-	31.40
X	5.95	5.66	6.07	6.07	-	5.94
endo-3-OAc	1.88	1.87	1.86	1.91	2.0u	1.92
exo-2-OAc	4.66	4.84	4.70	4.78	4.78	4.75
[2,2,2]-OAc	3.98	3.40	3.85	3.97	3.50	3.74
endo-2-OAc	0.51	N.D.	0.50	0.45	0.45	0.38
exo-3-OAc	3.17	3.07	3.34	3.49	3.04	3.22
Recovery	including 2° amine product					61.6

Products	Normalised Average Run I	Normalised Average Run II	Mean
2-ene	0.30	0.36	0.33
3-ene	50.58	50.97	50.8
X	9.58	9.64	9.6
endo-3-OAc	3.30	3.11	3.2
exo-2-OAc	7.17	7.71	7.4
[2,2,2]-OAc	5.89	6.07	6.0
endo-2-OAc	0.59	0.62	0.60
exo-3-OAc	5.74	5.23	5.5

Nitrous Acid Deamination of



in Acetic Acid 0.15 Molar in Sodium Acetate

Run I

Products	1	2	3	4	5	Average
2-ene	0.10	0.10	0.10	0.09	0.08	0.10
3-ene	0.60	0.75	0.71	0.70	0.69	0.69
X*	8.01	9.16	8.76	8.62	9.03	8.72
exo-2-OAc	12.29	12.76	12.82	11.74	12.72	12.49
[2,2,2]-OAc	14.56	14.91	14.96	14.26	14.85	14.71
endo-2-OAc	2.69	2.91	2.96	2.65	2.85	2.81
Recovery						39.5

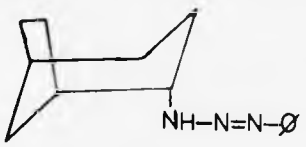
Run II

Products	1	2	3	4	5	Average
2-ene	0.08	0.08	0.08	0.08	0.07	0.08
3-ene	0.67	0.66	0.68	0.67	0.62	0.66
X*	8.63	8.32	8.53	8.23	8.46	8.43
exo-2-OAc	13.16	13.05	13.67	13.17	12.94	13.20
[2,2,2]-OAc	14.99	14.52	14.55	14.83	14.34	14.65
endo-2-OAc	3.57	3.01	3.11	4.11	3.83	3.53
Recovery						40.55

* contains up to 0.5% Y

< 0.2% endo-3-OAc and exo-3-OAc

Products	Normalised Average Run I	Normalised Average Run II	Mean
2-ene	0.25	0.20	0.22
3-ene	1.75	1.63	1.7
X	22.08	20.79	21.4
exo-2-OAc	31.57	32.55	32.1
[2,2,2]-OAc	37.24	36.13	36.7
endo-2-OAc	7.11	8.70	7.9

Solvolysis of 

in Acetic Acid 0.15 Molar in Sodium Acetate

Run I

Products	1	2	3	4	5	6	7	Average
2-ene	4.14	4.09	4.01	4.15	4.10	4.18	-	4.11
3-ene	9.04	9.19	8.86	9.11	9.05	9.28	-	9.09
X*	11.93	11.73	11.69	11.97	12.00	12.22	-	11.92
exo-2-OAc	17.29	18.50	17.53	17.86	17.52	17.52	17.23	17.64
[2,2,2]-OAc	21.13	22.15	21.35	21.56	22.15	21.09	20.85	21.47
endo-2-OAc	4.14	3.78	4.16	3.73	4.19	3.59	3.73	3.90
2^{O} amine	one determination only							17.9
Recovery								86.0

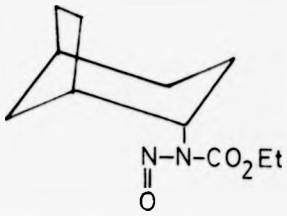
Run II

Products	1	2	3	4	5	6	7	Average
2-ene	4.09	4.04	3.99	3.85	3.92	4.04	-	3.97
3-ene	8.90	9.32	9.07	8.85	8.99	8.75	-	8.98
X*	12.45	12.10	11.86	12.03	12.55	12.27	-	12.21
exo-2-OAc	17.23	17.39	18.12	17.12	17.16	17.55	18.65	17.60
[2,2,2]-OAc	21.38	21.79	22.57	21.00	21.60	21.87	22.73	21.85
endo-2-OAc	5.22	5.27	5.53	5.03	5.71	5.27	5.54	5.37
Recovery	including 2^{O} amine product							87.9

< 0.2% endo-3-OAc and exo-3-OAc

* contains up to 0.5% of Y

Products	Normalised Average Run I	Normalised Average Run II	Mean
2-ene	4.78	4.52	4.6
3-ene	10.57	10.22	10.4
X	13.86	13.89	13.9
exo-2-OAc	20.51	20.02	20.3
[2,2,2]-OAc	24.97	24.86	25.0
endo-2-OAc	4.53	6.11	5.3
2^{O} amine	20.81	-	20.8

Solvolysis of 

in Ethanol

Run I

Products	1	2	3	4	5	Average
2-ene	22.59	22.32	22.41	22.95	22.39	22.53
3-ene	23.35	22.41	22.84	23.37	22.68	22.93
Y*	23.66	23.53	21.16	20.43	21.07	21.97
exo-2-OEt	3.71	3.48	3.07	3.50	3.60	3.47
[2,2,2]-OEt	4.76	4.43	3.90	4.27	4.53	4.38
endo-2-OEt	1.97	1.83	1.62	1.85	1.91	1.84
endo-3-OCO_2Et	N.D.	0.09	0.14	0.09	0.14	0.09
exo-2-OCO_2Et	8.56	8.56	8.99	8.81	8.64	8.71
[2,2,2]-OCO_2Et	11.23	11.21	11.58	12.17	11.65	11.57
endo-2-OCO_2Et	1.67	1.61	1.71	2.15	1.70	1.77
Recovery						99.3

Run II

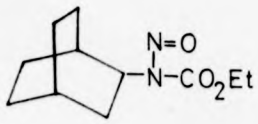
Products	1	2	3	4	5	6	Average
2-ene	23.89	21.72	24.19	23.47	22.73	23.34	23.22
3-ene	24.26	22.22	25.02	23.70	23.38	22.30	23.46
X*	25.24	23.20	23.29	24.59	24.10	24.18	24.10
exo-2-OEt	3.12	3.28	3.39	3.41	3.38	-	3.34
[2,2,2]-OEt	3.86	4.16	4.25	4.33	4.22	-	4.18
endo-2-OEt	1.63	1.80	1.86	1.81	1.80	-	1.79
endo-3-OCO_2Et	0.13	0.05	0.15	0.14	0.11	-	0.12
exo-2-OCO_2Et	8.53	8.72	8.67	8.96	8.36	-	8.65
[2,2,2]-OCO_2Et	11.20	11.53	11.32	11.69	10.98	-	11.34
endo-2-OCO_2Et	1.59	1.57	1.47	1.62	1.51	-	1.55
Recovery							101.75

* includes up to 1% of Y

< 0.1% endo-3-OEt and exo-3-OEt

< 0.2% exo-3-OCO_2Et < 1.5% carbamate

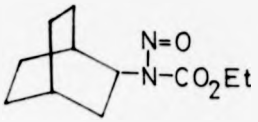
Products	Normalised Average Run I	Normalised Average Run II	Mean
2-ene	22.69	22.82	22.8
3-ene	23.09	23.06	23.1
X	22.12	23.69	22.9
exo-2-OEt	3.49	3.28	3.4
[2,2,2]-OEt	4.41	4.11	4.3
endo-2-OEt	1.85	1.76	1.8
endo-3-OCO_2Et	0.09	0.12	0.10
exo-2-OCO_2Et	8.77	8.50	8.6
[2,2,2]-OCO_2Et	11.65	11.14	11.4
endo-2-OCO_2Et	1.78	1.52	1.6

Solvolysis of 

in Ethanol

Run I

Products	1	2	3	4	5	6	7	Average
2-ene	16.70	16.47	16.91	16.73	-	-	-	16.70
3-ene	16.50	16.18	16.29	16.46	-	-	-	16.36
X	17.26	16.55	17.43	17.17	-	-	-	17.10
endo-3-OEt	0.022	0.023	0.013	N.D.	N.D.	-	-	0.012
exo-2-OEt	4.13	4.08	4.44	4.33	4.31	-	-	4.26
[2,2,2]-OEt	5.20	5.10	5.57	5.46	5.29	-	-	5.32
endo-2-OEt	0.18	0.16	0.19	0.19	0.19	-	-	0.18
endo-3-OCO_2Et	0.17	0.22	0.16	0.15	N.D.	N.D.	0.20	0.13
exo-2-OCO_2Et	6.15	6.29	5.42	5.58	6.01	5.79	6.22	5.92
[2,2,2]-OCO_2Et	9.12	9.14	8.06	8.08	8.82	8.46	8.96	8.66
exo-3-OCO_2Et	0.18	0.16	0.07	0.12	0.15	N.D.	0.12	0.11
carbamate	28.59	28.52	27.51	26.94	26.00	27.95	-	27.59
Recovery								102.3

Solvolysis of 

in Ethanol

Run I

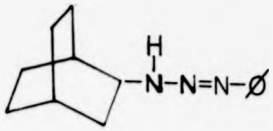
Products	1	2	3	4	5	6	7	Average
2-ene	16.70	16.47	16.91	16.73	-	-	-	16.70
3-ene	16.50	16.18	16.29	16.46	-	-	-	16.36
X	17.26	16.55	17.43	17.17	-	-	-	17.10
endo-3-OEt	0.022	0.023	0.013	N.D.	N.D.	-	-	0.012
exo-2-OEt	4.13	4.08	4.44	4.33	4.31	-	-	4.26
[2,2,2]-OEt	5.20	5.10	5.57	5.46	5.29	-	-	5.32
endo-2-OEt	0.18	0.16	0.19	0.19	0.19	-	-	0.18
endo-3-OCO_2Et	0.17	0.22	0.16	0.15	N.D.	N.D.	0.20	0.13
exo-2-OCO_2Et	6.15	6.29	5.42	5.58	6.01	5.79	6.22	5.92
[2,2,2]-OCO_2Et	9.12	9.14	8.06	8.08	8.82	8.46	8.96	8.66
exo-3-OCO_2Et	0.18	0.16	0.07	0.12	0.15	N.D.	0.12	0.11
carbamate	28.59	28.52	27.51	26.94	26.00	27.95	-	27.59
Recovery								102.3

Run II

Products	1	2	3	4	5	6	Average
2-ene	17.46	16.68	17.07	16.44	17.19	-	16.97
3-ene	17.19	16.52	16.70	16.30	16.97	-	16.74
X	16.81	17.25	-	17.20	17.88	-	17.29
endo-3-OEt	0.015	0.017	N.D.	0.019	0.024	0.025	0.017
exo-2-OEt	4.57	4.04	4.01	4.21	3.97	4.42	4.20
[2,2,2]-OEt	5.71	5.03	4.89	5.28	4.90	5.55	5.23
endo-2-OEt	0.19	0.17	0.15	0.18	0.16	0.19	0.17
exo-3-OEt	0.010	0.020	0.007	0.019	0.026	0.016	0.016
endo-3-OCO_2Et	0.12	0.12	0.11	0.12	0.12	0.13	0.12
exo-2-OCO_2Et	5.48	5.67	5.17	5.58	5.56	5.64	5.51
[2,2,2]-OCO_2Et	8.00	8.21	7.33	8.40	8.11	8.29	8.06
exo-3-OCO_2Et	0.11	0.10	0.10	0.08	0.10	0.11	0.10
carbamate	28.22	27.98	29.63	31.05	27.65	-	28.91
Recovery							103.3

< 0.2% endo-2-OCO_2Et N.D. = not detected

Products	Normalised Average Run I	Normalised Average Run II	Mean
2-ene	22.34	22.80	22.6
3-ene	21.89	21.78	21.8
X	22.35	22.49	22.4
endo-3-OEt	0.016	0.021	0.02
exo-2-OEt	5.57	5.47	5.5
[2,2,2]-OEt	6.96	6.80	6.9
endo-2-OEt	0.24	0.21	0.22
exo-3-OEt	<0.02	0.020	0.02
endo-3-OCO_2Et	0.17	0.16	0.16
exo-2-OCO_2Et	7.75	7.16	7.5
[2,2,2]-OCO_2Et	11.33	10.48	10.9
exo-3-OCO_2Et	0.15	0.13	0.14



Solvolysis of

in Acetic Acid 0.15 Molar in Sodium Acetate

Run I

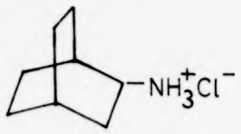
Products	1	2	3	4	5	6	7	Average
2-ene	8.52	8.89	8.12	8.65	9.48	8.60	8.78	8.72
3-ene	7.76	8.26	7.21	7.92	8.47	7.44	8.52	7.94
X	20.73	21.72	19.56	20.71	22.95	20.33	22.04	21.15
exo-2-OAc	16.95	17.01	18.21	17.47	17.37	-	-	17.40
[2,2,2]-OAc	30.14	31.58	31.34	30.92	28.21	-	-	30.44
2^{o} amine	one determination only							12.7
Recovery								98.35

Run II

Products	1	2	3	4	5	6	Average
2-ene	9.74	9.55	9.05	9.72	10.09	10.03	9.70
3-ene	8.73	8.81	8.71	9.07	9.51	9.51	9.06
X	23.29	23.14	22.23	21.64	24.56	24.52	23.23
exo-2-OAc	17.55	17.28	19.09	18.31	18.96	-	18.24
[2,2,2]-OAc	29. 51	29.86	31.70	30.07	31.50	-	30.53
Recovery	including 2^{o} amine product						103.5

< 0.2% endo-3-OAc and exo-3-OAc < 0.4% endo-2-OAc

Products	Normalised Average Run I	Normalised Average Run II	Mean
2-ene	8.87	9.37	9.1
3-ene	8.07	8.75	8.4
X	21.50	22.44	22.0
exo-2-OAc	17.69	17.62	17.7
[2,2,2]-OAc	30.95	29.50	30.2
2^{o} amine	12.91	-	12.9

Nitrous Acid Deamination of 

in Acetic Acid 0.15 Molar in Sodium Acetate

Run I

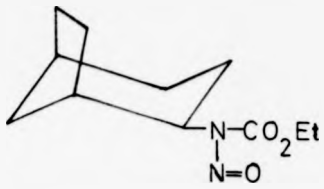
Products	1	2	3	4	5	6	Average
2-ene	1.11	1.10	1.08	1.09	1.11	1.03	1.09
3-ene	1.08	1.10	1.06	1.10	1.01	1.06	1.07
X	17.78	18.43	17.27	17.61	18.24	16.70	17.67
exo-2-OAc	22.77	22.37	25.19	23.47	22.79	22.66	23.21
[2,2,2]-OAc	41.07	37.48	40.50	39.52	38.32	38.36	39.21
Recovery							82.25

Run II

Products	1	2	3	4	5	6	Average
2-ene	0.42	0.39	0.39	0.41	0.42	0.39	0.40
3-ene	0.75	0.67	0.68	0.71	0.74	0.70	0.71
X	18.37	16.19	16.33	17.04	17.53	16.57	17.01
exo-2-OAc	22.73	23.78	21.76	23.65	24.66	22.16	23.09
[2,2,2]-OAc	38.84	40.19	35.80	39.65	41.18	37.32	38.83
Recovery							80.0

< 0.2% endo-3-OAc and exo-3-OAc < 0.4% endo-2-OAc

Products	Normalised Average Run I	Normalised Average Run II	Mean
2-ene	1.33	0.50	0.92
3-ene	1.30	0.89	1.1
X	21.48	21.26	21.4
exo-2-OAc	28.22	28.86	28.5
[2,2,2]-OAc	47.67	48.54	48.1

Solvolysis of 

in Ethanol

Run I

Products	1	2	3	4	5	6	Average
2-ene	0.20	0.22	0.20	0.22	0.20	0.17	0.20
3-ene	8.70	9.62	8.83	9.55	8.93	8.45	9.01
X	1.18	1.29	1.22	1.28	1.21	1.15	1.22
Y	8.29	9.05	8.54	9.00	8.47	8.06	8.57
endo-3-OEt	$6x10^{-3}$	$9x10^{-3}$	N.D.	$4x10^{-3}$	$6x10^{-3}$	N.D	$4x10^{-3}$
exo-2-OEt	0.45	0.40	0.38	0.40	0.35	0.39	0.39
[2,2,2]-OEt	0.18	0.17	0.17	0.18	0.16	0.17	0.17
endo-2-OEt	8.94	8.30	8.10	8.29	7.67	8.47	8.29
endo-3-OCO_2Et	0.18	0.14	0.11	0.10	0.09	0.15	0.13
exo-2-OCO_2Et	0.69	0.72	0.84	0.71	0.76	0.66	0.73
[2,2,2]-OCO_2Et	0.13	0.12	0.15	0.14	0.16	N.D.	0.12
endo-2-OCO_2Et	7.22	7.85	9.06	7.64	8.09	7.34	7.87
carbamate	53.03	53.26	57.53				54.61
Recovery							92.0

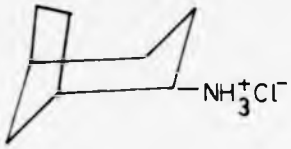
Run II

Products	1	2	3	4	5	6	Average
2-ene	0.21	0.18	0.19	0.20	0.18	0.19	0.19
3-ene	9.24	8.29	8.75	8.80	9.28	8.78	8.86
X	1.28	1.16	1.22	1.22	1.29	1.23	1.23
Y	8.73	7.89	8.29	8.29	8.75	8.34	8.38
endo-3-OEt	N.D.	N.D.	4×10^{-3}	10×10^{-3}	8×10^{-3}	8×10^{-3}	5×10^{-3}
exo-2-OEt	0.36	0.34	0.39	0.38	0.35	0.37	0.37
[2,2,2]-OEt	0.16	0.15	0.18	0.16	0.15	0.17	0.16
endo-2-OEt	7.16	6.68	8.05	7.27	7.08	8.00	7.37
endo-3-OCO_2Et	0.18	0.14	0.18	0.11	0.22	0.11	0.16
exo-2-OCO_2Et	0.78	0.72	0.80	0.79	0.71	0.71	0.75
[2,2,2]-OCO_2Et	0.12	N.D.	0.13	0.15	0.08	N.D.	0.08
endo-2-OCO_2Et	8.51	8.29	9.12	8.16	7.83	7.54	8.22
carbamate	51.33	56.65	52.80				53.60
Recovery							89.4

< 0.2% exo-3-OCO_2Et < 0.1% exo-3-OEt

N.D. = not detected

Products	Normalised Average Run I	Normalised Average Run II	Mean
2-ene	0.54	0.53	0.54
3-ene	24.53	24.75	24.6
X	3.32	3.44	3.4
Y	23.33	23.41	23.4
endo-3-OEt	0.01	0.01	0.01
exo-2-OEt	1.06	1.03	1.0
[2,2,2]-OEt	0.46	0.47	0.46
endo-2-OEt	22.57	23.16	22.9
endo-3-OCO_2Et	0.35	0.45	0.40
exo-2-OCO_2Et	1.99	2.09	2.0
[2,2,2]-OCO_2Et	0.33	0.22	0.28
endo-2-OCO_2Et	21.43	22.96	22.2

Nitrous Acid Deamination of 

in Acetic Acid 0.15 Molar in Sodium Acetate

Run I

Products	1	2	3	4	5	6	Average
2-ene	0.03	0.04	0.04	0.04	0.03	0.03	0.04
3-ene	0.56	0.54	0.57	0.58	0.54	0.55	0.56
X	)	3.40	3.62	3.59	3.35	3.41	3.47
Y	14.93)	10.93	11.55	11.66	11.16	11.25	11.31
exo-2-OAc	5.06	4.97	5.04	5.05	5.16	4.73	5.00
[2,2,2]-OAc	3.16	3.06	2.99	3.19	3.27	2.98	3.11
endo-2-OAc	59.13	58.96	59.48	59.05	60.67	56.61	58.98
Recovery							82.47

Run II

Products	1	2	3	4	5	6	Average
2-ene	0.04	0.05	N.D.	0.05	0.04	0.04	0.04
3-ene	0.54	0.53	0.50	0.56	0.54	0.52	0.53
X	3.10	3.03	3.03	3.29	3.01	3.08	3.09
Y	10.35	10.03	9.74	10.51	10.44	10.30	10.23
exo-2-OAc	3.67	3.89	3.87	3.80	3.87	-	3.82
[2,2,2]-OAc	2.21	2.46	2.41	2.50	2.42	-	2.40
endo-2-OAc	42.20	44.53	44.93	44.55	47.32	-	44.71
Recovery							64.82

< 0.2% endo-3-OAc < 0.4% exo-3-OAc

N.D. = not detected

Products	Normalised Average Run I	Normalised Average Run II	Mean
2-ene	0.05	0.06	0.06
3-ene	0.68	0.82	0.75
X	4.21	4.77	4.5
Y	13.71	15.78	14.7
exo-2-OAc	6.06	5.89	6.0
[2,2,2]-OAc	3.77	3.70	3.7
endo-2-OAc	71.52	68.98	70.2

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