Translated from *Uspekhi Khimii*, **59**, 304–331 (1990) U.D.C. 547.1

# Recent trends in the theory of the deamination of aliphatic and alicyclic amines

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ABSTRACT. The different theories that account for the stereochemical characteristics of the deamination of aliphatic and alicyclic amines compared to solvolysis of the corresponding sulphonates and halides are examined. There is a discussion on the recent hypothesis concerning the relative increase of electron demand for the participation of neighbouring groups and bonds in deamination compared to solvolysis, making it possible to predict the direction of skeletal rearrangements in reactions involving elimination of nitrogen and to carry out deliberately such rearrangements when they do not occur in reactions with classical leaving groups. Questions concerning the applicability of the extended Hammond postulate and the Curtin–Hammett principle to reactions that involve decomposition of alkyldiazonium ions are discussed.

The bibliography includes 73 references.

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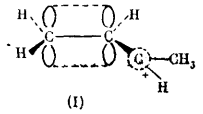
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## I. Introduction

During the past thirty years hundreds of articles devoted to a comparative study of deamination and solvolysis have been published. There have been a number of reviews in which this question has received special attention.[1–6] The present review, without claiming to be complete, makes an attempt to interpret the results reported earlier in terms of a new hypothesis that has recently been developed concerning the relative electron demand for participation of neighbouring groups and bonds in $S_N1$-decomposition of aliphatic and alicyclic diazonium ions.[7,8]

The steady interest in what appears at first glance to be a special problem is maintained not only by the contradictions existing to date in the interpretation of the experimental results but also by the close link with the basic concept of carbocations and the debate about nonclassical ions as well as with such fundamental theories as the Hammond postulate and the Curtin–Hammett principle. The above-mentioned hypothesis interprets the application of these postulates to aliphatic deamination in a new way. Moreover, for a long time the theoretical aspect of the problem has relegated the synthetic possibilities of deamination to second place. Meanwhile, the "driving force" of the rearrangements in such reactions is much higher than in traditional solvolysis and it would be tempting to learn how to regulate this process.

It may be assumed that the synthetic use of deamination has been held in check not so much by the widespread notion of the supposed low selectivity of reactions involving the elimination of nitrogen as by the long absence of an adequate theory that has predictive force in relation to stereochemistry and the composition of the products of such reactions in alicyclic compounds and particularly in aliphatic compounds. In the 1950's the concept of "hot" ions was put forward by a number of authors. This hypothesis, which qualitatively accounts for the "unconventional" rearrangements during deamination, has been followed in various forms in many publications. Various factors have been identified as the source of excess energy. Thus, the high stability of the nitrogen molecule must assist the large exothermicity of the reaction. In turn, it is possible with this hypothesis to conclude that there is "chemical activation" of the carbocations as reaction products. It was suggested that there is non-optimal solvation of the carbocations during rapid decomposition of a diazonium ion. Abnormal charge localisation in relation to the non-optimal geometry of the carbocation has also been proposed, as for example in one of the precursors of all "hot" ions—the hypothetical nonconjugated allyl cation (I):[9]



(I)

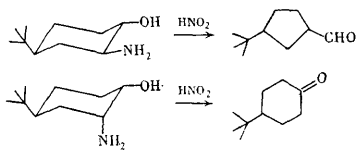
On the strength of this, the terms "localised", "free", and "open" carbocations have appeared in the literature together with the term "hot". These terms signify at the same time the classical nature of carbocations from deamination (as opposed to nonclassical cations from solvolysis) as well as the excess energy contained in them. There has been a lively discussion of the concept of "hot" ions in the literature, while, at any rate, for a long time two factors do not seem to have been in doubt—the classical nature of carbocations from deamination and the absence of any $S_N2$ activity in this reaction.

The ease in forming molecular nitrogen and the probable low energy of activation related to this led to the idea of a "compression" of the energy scale. This hypothesis, which belongs to Huisgen,[10] does not require the concept of a "hot" ion since the reduction in the difference in energies of activation between the competing routes for forming carbocations—processes involving

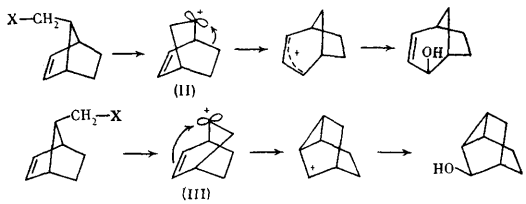
neighbouring groups and bonds ($k_\Delta$) and with assistance from the solvent ($k_s$)—favours a reduction in selectivity in the choice of routes for forming carbocations as compared to traditional solvolysis. It is easy to see that by using these concepts it is impossible to predict the stereochemical result of a reaction.

It soon became clear that one of the main problems with the idea of "hot" ions is its failure to account for the differences in product composition that occur in the deamination of cyclic diastereomeric amines. For example, if in Scheme 1 the sole intermediate species is the 2-hydroxy-5-t-butylcyclohexyl cation, the reason for such a marked difference in the results of the reaction[11] remains unclear.

Scheme 1



It was shown that this type of structural selectivity is characteristic of deamination[12] to an even greater degree than solvolysis:[13–15]

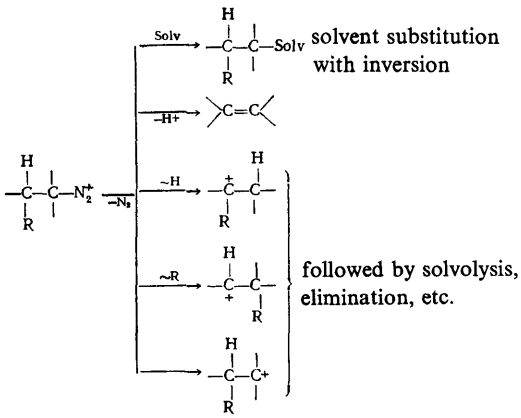


X = ONs, $NH_2$.

As a result, opinions that were developed from earlier ideas began to be formed. For example, the so-called "memory effect" is actually an extension of concepts such as the "localised" allyl cation to alicyclic ions. Structures (II) and (III) depict such "twist" cations.

However, it is not difficult to see that such a selective interaction of the cation site with a particular bond resembles anchimeric assistance. Streitwieser came closest to this standpoint when he put forward a familiar scheme of reaction pathways of the diazonium ion (Scheme 2).[16,17] However, he did not regard the synchronous shift of the periplanar group as a factor that assisted decomposition of the diazonium ion. In his opinion the shifts of the hydrogen atoms and alkyl groups cannot be regarded as participation in the sense that the neighbouring group can "push" the departing nitrogen but this process should more accurately be regarded as the neighbouring periplanar group being "pulled" by the departing nitrogen[16] or positively charged region which develops on the α-carbon atom.[17]

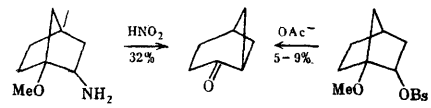
Scheme 2




The view of Streitwieser, which was developed as an alternative to the concept of "hot" ions, was criticised (see two reviews[6,18]). It is held that the scheme of Streitwieser was disproved by Collins, who demonstrated that the shift of a neighbouring group to a cation site in a number of cases occurs after the nitrogen has left the molecule (discussed in detail in Section III). In the long run Streitwieser's view was relegated to second place and for a long time was not regarded as promising. The concept of conformational control and "counterion control" became prominent (discussed in Section IV).

With the exception of the "hot" ion concept, all the remaining views are in agreement that during deamination the group that is periplanar to the nitrogen being eliminated mainly migrates. This is important in so far as it can predict the expected direction of skeletal rearrangement in relation to the configuration or conformational composition of the diazonium ion.

However, the above-mentioned concepts are insufficient because they do not shed any light on the causes of the observed rearrangements. While the concept of "hot" ions contradicts many facts and is inaccurate, it remains unclear what exactly causes the neighbouring periplanar bond to migrate during deamination. The same bond is much less prone to rearrangement in solvolysis of the analogous sulphonate:[19,20]



Facts such as these have been increasingly accumulating in the literature (see Section II), but approaches to the solution of this problem have only recently come to light—during a discussion about nonclassical carbocations, in particular, the 2-norbornyl cation.[7] The interest in deamination within the scope of this problem arises in particular because decomposition of diazonium ions was thought for a long time to be the most reliable method of generating classical ions with a "short" lifetime. However paradoxical this may be, it was the use of deamination as a model reaction for studying the property of classical cations that in the long run made it possible for serious contradictions to be revealed. The solution of these led to formulation of the hypothesis that during deamination, when compared to solvolysis, the electron demand for neighbouring group participation as a most important factor determining the stereochemistry in reactions involving elimination of nitrogen is maintained[7] or even increased.[8]

## II. Theory of the increase in electron demand for participation in $S_N1$-deamination compared to $S_N1$-solvolysis

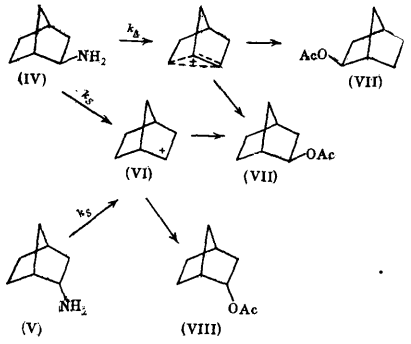
In the debate about the structure of the 2-nornbornyl cation ideas about the mechanism for deamination of epimeric 2-norbornylamines have undergone fundamental changes during the last 25 years. They can be illustrated by three studies, each of which constitutes a particular stage in the solution of the problem.

Initially Corey et al.,[21] by studying the deamination of optically active epimeric 2-norbornylamines (IV) and (V) with sodium nitrite in acetic acid, analysed the combined mixture of acetates, obtained

after reduction and acylation of the initial reaction mixtures, which contained not only acetates but also alcohols. This method of analysis, which was typical of the early studies in this area, led the authors to the mistaken conclusion that there was an approximately equal ratio of *exo*- to *endo*-products, retention of optical activity for the reactions of both amines, and hence a common intermediate—the classical cation (VI).

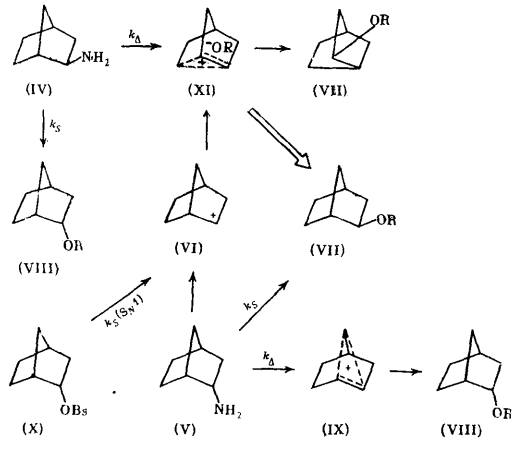
Berson et al.[22] subsequently studied in greater detail the composition of the acetate fractions that were isolated from the initial reaction mixtures, and they came to the conclusion that the assumption by Corey of a common intermediate for all products was incorrect since the degree of racemisation for *exo*-product (VII) and *endo*-product (VIII) was not the same. The values obtained for the acetate fractions were more in line with the reactions occurring according to Scheme 3. The relatively low ratios of *exo*- to *endo*-products [(VII):(VIII) ranging from 19:1 to 45:1] and the partial retention of optical activity suggest at first glance that there is a reduced degree of σ-participation in deamination compared to solvolysis, where this ratio is ~300:1 and racemisation occurs.[23]

Scheme 3




Finally, Kirmse et al.[7] recently once again carried out a similar study using a wide range of media. By varying the polarity of the medium it was possible to establish that different routes—$k_\Delta$ and $k_s$ (the latter was of two types: $S_N1$ and $S_N2$)—were competing in the decomposition of diazonium ions (Scheme 4).

Scheme 4




The formation of *endo*-alcohols (or esters) (VIII) increases for the *exo*-amine (IV) and decreases for the *endo*-amine (V) as the polarity of the medium is reduced. This is an indication that the *endo*-products (VIII) are formed from the epimeric amines by different reaction routes. The *endo*-products (VIII) are probably formed from *exo*-amine (IV) by an $S_N2$-type of route $k_s$, but they are formed from *endo*-amine (V) by the $k_\Delta$ route since an $S_N1$ mechanism is preferred when there is an increase in polarity of the medium. According to Kirmse and Siegfried[7] the classical cation (VI) can be excluded for the reason that in an aqueous medium which is favourable for an $S_N1$ mechanism there is the highest proportion of *endo*-attack on the chiral intermediate by the nucleophile. This intermediate may be the nonclassical carbocation (IX), which is formed as a result of participation of the C(1)–C(7) bond.

The question arises: what is the reason for this participation, which does not occur in solvolysis of the analogous sulphonate? Kirmse suggests that the $k_\Delta$ process usually has the lowest energy barrier and therefore frequently occurs in solvolysis. If the $k_\Delta$ route is accompanied by an increase in steric strain in the ring, as in the case of ion (IX), the $k_s$ process becomes energetically more favourable and it is the only one to take place in solvolysis of the corresponding *endo*-brosylate (X). However, *endo*-amine (V), which reacts when there is "compression" of the energy scale, proves to be capable of reacting by the less favourable $k_\Delta$ route. Although Kirmse and Siegfried[7] consider that this situation is an exception to the general rule, it should be recognised that the conclusion made by them can be formulated as a hypothesis about the increase (if only in certain cases) in the degree of σ-participation in deamination compared to solvolysis. However, the authors only note that the study they carried out does not support the idea of a classical 2-norbornyl cation as the precursor of *endo*-2-norbornyl products.

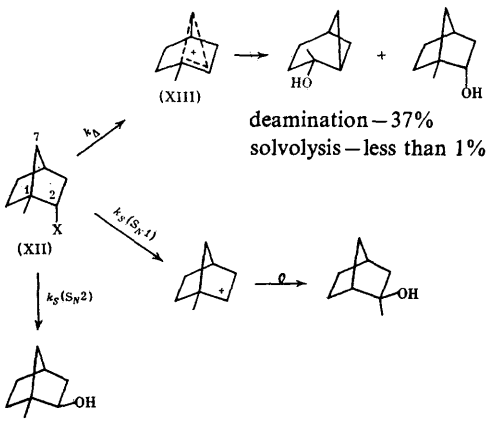
For the deamination reactions of *exo*-amine (IV), Kirmse and Siegfried[7] concluded that the reactions occur by the $k_\Delta$ route via the nonclassical carbocation (XI), which is incorporated in an asymmetric ion pair, resulting in a preferred *exo*-attack by the nucleophile on the site of nitrogen elimination. However, it is noted here[7] that from the data obtained it is not possible to make a definite choice between the nonclassical carbocation structure (XI) and a rapid equilibrium involving "*exo*-selective" classical cations.

The alternative stated above is typical of the debate about the structure of the 2-norbornyl cation and we are convinced that it is predetermined by the choice of model compound, since 2-substituted norbornanes have a number of basic disadvantages in this capacity. The most important of them are: the Wagner–Meerwein rearrangement on elimination of 2-*exo*- as well as 2-*endo*-substituents in many cases only occurs with displacement of the C(1)–C(6) bond, resulting in the initial norbornane system; the directions of attack by the nucleophile coincide for the nonclassical 2-norbornyl cation (for stereoelectronic reasons) and for the classical 2-norbornyl cation (for steric reasons); the classical cation readily changes to the nonclassical; finally, a quantitative determination of the degree of epimeric purity of the initial compounds appears quite difficult.[1,8]

However, the introduction of very simple substituents (for example, methyl groups) into the skeleton of the same norbornane makes the model more convenient. A comparison of the results of deamination and solvolysis of 1-methyl-2-*endo*-substituted norbornanes with structure (XII), as a result of the 1,2-shifts of the C(1)–C(7) bond that occur (Scheme 5), clearly indicates a considerable σ-participation of this bond in deamination (water) but not

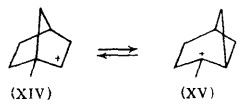
in solvolysis (aqueous acetone)†.[24]

Scheme 5



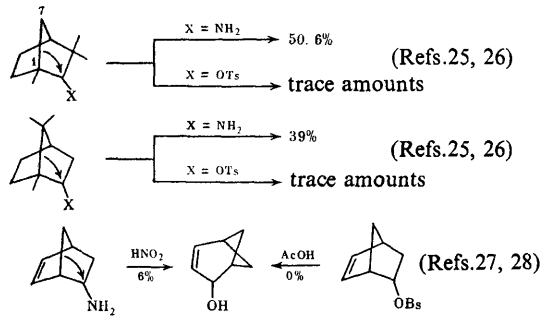

X = $NH_2$; *p*-$OSO_2C_6H_4$–...–...Me, –Br, $-NO_2$

The important role of the nonclassical carbocation (XIII) in this deamination reaction follows from the direction of attack by the nucleophile on the *endo* side and also from the very low probability of an "imitation" of cation (XIII) by rapid inter-conversion of two completely different ions—the secondary (XIV) and tertiary (XV):

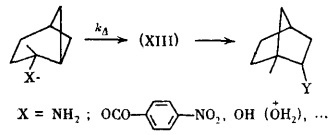



The case studied by Kirmse et al.[24] is also classed as an exception to the rule. However, 1,2-shifts of the C(1)–C(7) bond are not rare for deamination, but they hardly ever occur in solvolysis of norbornyl derivatives. Solvolysis leads to a displacement of the C(1)–C(6) bond without dependence on the configuration of the leaving group. In deamination, on the other hand, there is a clear dependence of the direction of the skeletal shift on the configuration of the leaving group, which suggests the idea of an increase in demand for the participation of neighbouring periplanar bonds in the elimination of nitrogen. A certain amount of conjecture about the change in demand for participation when going from solvolysis to deamination of compounds with a bicyclo[2.2.1]heptane skeleton gives Scheme 6,‡ which depicts a number of similar examples in outline.

Scheme 6




It should be mentioned that the reverse rearrangement of the norpinane skeleton to norbornane occurs with the same ease in both solvolysis and deamination; in this case every indication is that participation of the C(1)–C(7) bond occurs:[29]

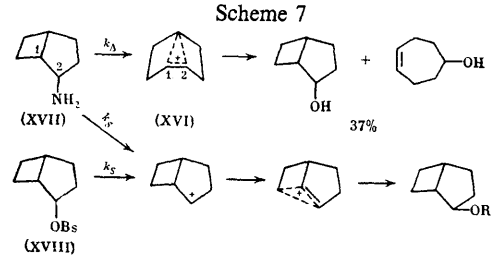



A number of problems may arise here. For example, why should the compression of the energy scale during deamination and the lack of this during solvolysis occur only in rearrangements of the type "norbornane–norpinane" and not in the reverse rearrangement or in rearrangements of *exo*-amines and sulphonates in the norbornane series. Then, if the examples of rearrangements of the type "norbornane–norpinane" given above are the exception, what should be considered the rule?

In the meantime these questions can be eliminated if it is assumed that during deamination there is an increased demand for the participation of the neighbouring periplanar band in any structures. In fact, the relative increase in the proportion of $k_\Delta$ in deamination is exhibited not only in models with a bicyclo[2.2.1]heptane skeleton.

For example, the "σ-route" to the nonclassical cation (XVI) can occur in deamination of amine (XVII) but not in solvolysis of the analogous brosylate (XVIII)[30] (Scheme 7). Kirmse et al.[30] also account for this phenomenon as an exception to the general rule. The bridging ion (XVI) is sterically unfavourable and is formed during deamination only as a result of "compression" of the energy scale together with products from the more "favourable" $k_s$ process. In the case of solvolysis, where the $k_\Delta$ and $k_s$ processes differ in energy much more considerably, it is only the $k_s$ route, which is more favourable for this structure, that occurs.

Scheme 7



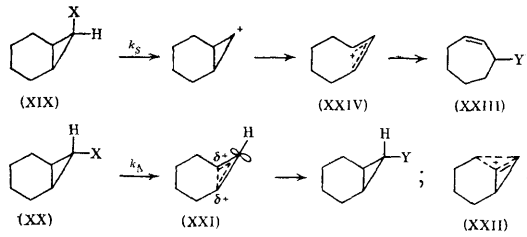

† Unfortunately, a comparison of solvolysis and deamination in the same solvents is seldom to be found in the literature. However, in our opinion, the significant differences that occur on going from solvolysis to deamination cannot solely be due to medium effects.[8]

‡ See also Scheme 5 and the reactions at the end of Section 1. The corresponding *exo*-epimers react almost exclusively with a shift of the C(1)–C(6) bond in both reactions.

It may be assumed, however, that the reason for the formation of the clearly sterically hindered carbocation (XVI) is the strong demand for participation in deamination and not "compression" of the energy scale. The latter may be illustrated by the following example.

The *endo*-tosylate (XIX), in which participation of the neighbouring carbon-carbon bonds is impossible because of the skeletal structure, reacts more rapidly than the *exo*-isomer (XX),[31] although in the latter participation of a C–C bond is probable, judging by the selectivity of nucleophilic attack (Scheme 8)§.

Scheme 8




X = $NH_2$ ; OTs, Cl, ... Y = OH, Br, OMe, OAc.

Thus, for this skeleton the barrier for the $k_\Delta$ process is definitely higher than the barrier for $k_s$, which, following the logic of Kirmse, unites this case with the previous one (Scheme 7). However, both solvolysis[31] and deamination[32] of compounds with the skeleton of (XIX) and (XX) give the same results for each of the epimers. Meanwhile, "compression" of the energy scale ought to lead to the formation of a considerable proportion of product (XXIII) in deamination of amine (XX), which in actual fact does not occur. The impression is created that participation of the neighbouring bonds assist to the same extent the "difficult" elimination of both the sulphonate group and nitrogen and starts to occur much earlier than the moment when the developing cation site may be stabilised by the formation of the allylic system (XXIV).

It is necessary to develop a more detailed hypothesis about the relative increase in demand for participation in deamination and substantiate the possible reasons for such an increase. Manuilov and Barkhash[8] made a comparative study of solvolysis and deamination of model sulphonates with tetrafluorobenzobicyclo[2.2.2]octadiene and tetrafluorobenzobicyclo[2.2.2]octene skeletal structures and obtained quantitative data that characterised the contribution of the $k_\Delta$ process in each reaction (one of the examples is shown in Scheme 9).

The following rules were established:

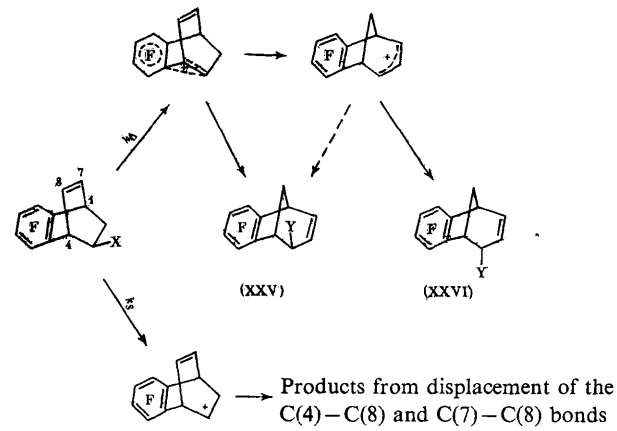
1. The preferred direction of the skeletal shift in both reactions is determined by the configuration (*exo*- or *endo*-) of the group being eliminated.

2. Selectivity in the choice of the direction of rearrangement and nucleophilic attack increases as the solvating power of the medium towards cations decreases (in the series DMSO > MeOH > AcOH). In this case the stereoselectivity of nucleophilic attack (ratio of *exo* to *endo* products) is substantially higher for deamination.

§ Sliwinski et al.[31] propose the nonclassical structure (XXI). In our opinion the nonclassical carbocation (XXII) is more probable. In any case it is significant that the *exo*-isomers (XX) react by the $k_\Delta$ route while the *endo*-isomers (XIX) react by the $k_s$ route in both reactions.

3. Comparison of the mixtures of acetates from deamination with solvolysis products generally indicates a relative decrease in the contribution of the $k_\Delta$ process in the case of deamination (agrees with Berson's results on acetate products from deamination[22]).

Scheme 9




medium—AcOH; *exo*/*endo* = (XXV)/(XXVI);
X = $NH_2$, Y = OH: $k_\Delta = 86 \pm 5\%$, *exo*/*endo* = (79%)/(2%)
X = OTs, Y = OAc: $k_\Delta = 89 \pm 6\%$, *exo*/*endo* = (51%)/(32%).

4. The alcohol fractions of the deamination products show a reverse trend. The relative contribution of the $k_\Delta$ process in deamination generally does not decrease or even increases compared to solvolysis (contradicts Berson's results but is in agreement with Kirmse's results[7,24,30]).

5. Nucleophiles have a greater tendency to attack the site of nitrogen elimination in deamination reactions, which may be due to the formation of an asymmetric ion pair (agrees with the conclusions of Kirmse and Siegfried[7]).

The rules established are interrelated and do not contradict each other as may appear at first glance. It is likely that with an $S_N1$ mechanism for the same model there cannot occur a relative decrease in the contribution of $k_\Delta$ in the case of the acetate products from deamination and at the same time an increase in contribution of this process for alcohol products. It is probable that the acetates are formed to a considerable extent by an $S_N2$ mechanism, so comparison of demand for participation should be carried out only "within" the $S_N1$ routes of solvolysis and deamination, this condition being more consistent with the alcohol fraction for the latter reaction.

In order to explain the rules propounded above from a single standpoint, it must be assumed that the observed increase in the share of the $k_\Delta$ process and the stereoselectivity of nucleophilic attack in deamination results from the increase in demand for participation in the $S_N1$ process of nitrogen elimination compared to a similar elimination of sulphonate or other group. The main reason for this may be a less favourable solvation of the transition state and carbocation (more precisely, cation site) in the more rapid process of decomposition of the diazonium ion. The idea of a less favourable solvation within the intimate ion pair is not inconsistent since at the moment that it is formed within the solvation cage the counterions

are separated by a nitrogen molecule (Scheme 10, compare with three studies[18,33,34]).

Scheme 10

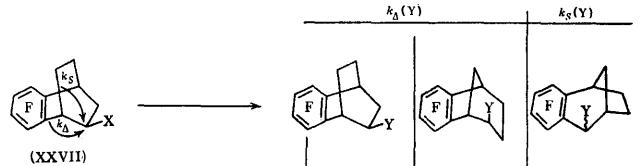
$$2HNO_2 \rightleftarrows N_2O_3 \xrightleftharpoons{Solv-OH} Solv-ONO + HNO_2;$$

$$R-NH_2 + Solv-ONO \rightarrow R-\overset{+}{N}H_2-N=O\ldots Solv-O^- \rightarrow$$

$$\xrightarrow{\sim H^+} R-\overset{+}{N}H=N-OH\ldots Solv-O^- \xrightarrow[-N_2]{\sim H^+} R^+\ldots N_2\ldots H_2O\ldots Solv-O^-.$$

The formation of a cation site in deamination as against solvolysis is comparable, if not to gas-phase conditions, at least to substantially less nucleophilic conditions, namely, it corresponds to a considerable reduction in the solvating ability of the medium. In this case deamination in AcOH, for example, should give the same stereochemical result as solvolysis does in a much more ionising and less nucleophilic medium such as $CF_3COOH$. This actually occurs (Scheme 11). In this case, as was to be expected, the reactions of the model compounds (XXVII) demonstrate the relative increase in contribution of $k_\Delta$ on going from solvolysis to deamination in the same medium ($\sim$49% $k_\Delta$ in acetolysis compared to 82% $k_\Delta$ in deamination in AcOH).[8]

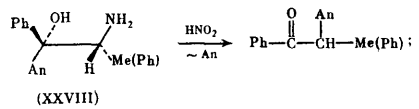
Scheme 11



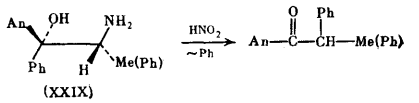

The special conditions for elimination of nitrogen probably have the result that the electrons of the neighbouring periplanar bond ("internal nucleophile") gain an advantage in attack on the cation site over any other nucleophile. In this case the demand for participation may be so great that the determining role is played not by the migrating ability of the participating group but its optimal orientation relative to the developing cation site, namely, a periplanar position in relation to the C–N bond in a given conformation or configuration.

This property of diazonium ions is widely known since it "violates" the Curtin–Hammett principle in the case of pinacolic deamination (Scheme 12).[36,37]

Scheme 12




(XXVIII)




(XXIX)

An = *p*-$MeOC_6H_4$ .

In solvolysis the ratio of products formed from the different conformations of the substrate does not depend on the relative populations of the conformations and is determined solely by the free energies of the transition states leading to these products. In deamination this rule does not apply. Thus, diastereomer (XXVIII) reacts with preferred migration of anisyl while migration of phenyl is typical for diastereomer (XXIX). As Kirmse notes,[2] the nucleophilicity of the aryl group is not a factor that regulates the choice of migrant (the migrating ability of anisyl is higher in reactions with neighbouring-group participation). The ratio of products is determined by conformational control—from the most stable conformer with a *gauche*-orientation of OH and $NH_2$ groups stabilised by intramolecular hydrogen bonding.

This definition of conformational control in deamination is typical. In our view the electronic and conformational factors are incorrectly contrasted here, which on the whole is typical for many publications¶. It is more accurate to say that electronic factors assist the exhibition of conformational control. Among the former the demand of the cation site prevails over the nucleophilicity of the migrant. The concept of conformational control in deamination acquires a logical basis from such a statement.

If it is assumed that anchimeric assistance compensates the insufficient solvation of the cation site in decomposition of a diazonium ion, the retardation of 1,2-shifts at the stage of the nonclassical ion becomes clear. It is advantageous for a poorly solvated carbocation to preserve a nonclassical delocalisation and, moreover, the lifetime of an intimate ion pair within the solvation cage (see Scheme 10) may be relatively short. This corresponds to an increase in the ratio of *exo*- to *endo*-products in the reaction mixtures. The lack of symmetry of the intimate ion pair results in preferred attack on the site of nitrogen elimination.[7,8]

This explanation does not contradict the fact that in the acetate fractions of deamination products there is sometimes a relative increase in the share of the $k_s$ process compared to solvolysis. In our opinion this occurs not because of a suppression of the $k_\Delta$ process for some reason "within" an $S_N1$ mechanism for forming acetates but is related to the increase in the relative role of an $S_N2$-type of $k_s$ process that is typical for charged nucleophiles, including the acetate anion†. Thus, the theory of the increase in demand for participation in deamination compared to solvolysis applies only to $S_N1$ routes of both reactions.

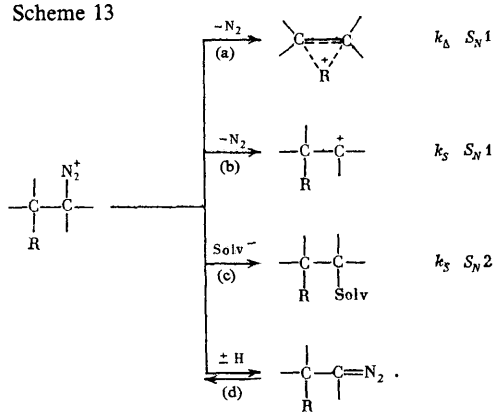
The theory advanced above can be summarised with the help of Scheme 13. The ratio of contributions of the competing routes (a)–(c) depends on the structure of the aliphatic part of the diazonium ion, the nucleophile, and the solvent. However, compared to solvolysis, the increase in demand for participation in deamination must always lead to a more effective shift of the neighbouring bond under conditions where the analogous sulphonates are often only able to react by an $S_N2$ mechanism. Hence the observed "reduction in selectivity" on going from solvolysis to deamination. On the other hand, the increase in electron demand makes it possible in deamination reactions to observe the shift of groups and bonds

¶ For example, in relation to the reactions of diastereomers (XXVIII) and (XXIX) Morrison and Boyd mention that the course of the reaction is determined more by conformational factors than electronic.[38] A similar but more expanded view is given by Bundel' et al.,[39] who assume that since the energy required for cleavage of the C–N bond is not great and lies within the conformational barriers, in the decomposition of the diazonium ion the determining factor for the choice of a particular conversion route is the initial confor-mation, in contrast to solvolytic reactions where the main role in this choice is played by the neighbouring group.

† For $S_N2$ processes in the decomposition of diazonium ions, see the studies of Kirmse[5] and Collins[6] and the references in them.

that do not migrate in solvolytic reactions. Hence, using this approach it is possible to explain satisfactorily not only the increased tendency towards rearrangements in deamination reactions, which is a well-known fact, but also to carry out rearrangements intentionally in those cases where the conformational composition (or configuration) of the initial amine is reliably known.

Scheme 13

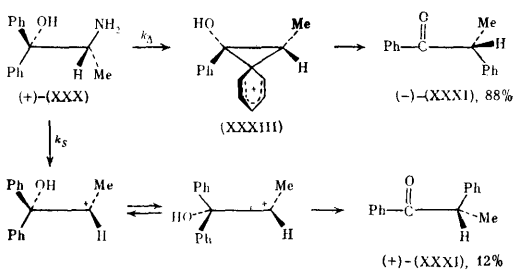


## III. A critical examination of the literature data on a comparative study of deamination and solvolysis

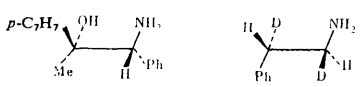
In accordance with Schemes 2 and 13 the diazonium ion is the "branching point" in the competing pathways of deamination. As was mentioned above, Collins published a number of studies (see his review[18]) in which the scheme of Streitwieser is criticised. It is therefore necessary to examine the arguments of Collins in relation to the new Scheme 13.

In deamination of the optically active amine (+)-(XXX) in acetic acid, an appreciable quantity of product (+)-(XXXI) is obtained, being formed as a result of migration of a phenyl group to the cation site obviously after the nitrogen has left the molecule (Scheme 14).[40–42]

Scheme 14



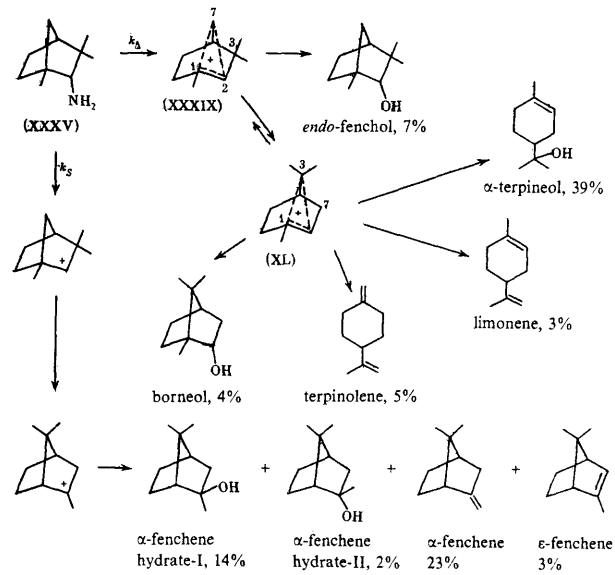
Retention of configuration is even more substantial (58%) compared to inversion in the case of the deamination of amine (XXXII) in the same medium.[42]



In the opinion of Collins these results contradict the postulate of Streitwieser that the diazonium ion prior to the carbocation serves as a branching point of the competing reactions, since the displacement of the neighbouring group occurs after the change in conformational state of the carbocation. In actual fact there is no contradiction with Scheme 13, as the formation of product (+)-(XXXI) corresponds to route $k_s$(b). However, at least a proportion of compound (−)-(XXXI) may be obtained by route $k_\Delta$(a) via the phenonium ion (XXXIII) (Scheme 14). If the amino group is situated on a benzyl carbon atom rather than a secondary carbon atom, the $k_s$(b) process successfully competes with the $k_\Delta$ process. This specific example cannot, of course, be extended to deamination as a whole as Collins has done, assuming that "migration of hydrogen or aryl... in most cases occurs after decomposition of the diazonium ion."[18] For example, it is not surprising that in the reaction of the optically active amine (XXXIV), which has an amino group on a primary carbon atom, only processes $k_\Delta$ and $k_s$(c) compete.[43,44]

The view of Collins is disproved most convincingly in those cases where comparative data on deamination and solvolysis are available. Since the increase in demand for participation on going from solvolysis to deamination occurs in $S_\Delta 1$ routes of these reactions, model compounds that mainly give rearranged products are of particular interest. The reactions of model tosylates and amines of fenchane and bornane fully satisfy this requirement.[25,26] It is worth considering these results of Hückel et al. in greater detail on the basis of Scheme 13, when it is borne in mind that previously they were of interest to Collins from the point of view of deamination only occurring via classical ions.[42] The latter approach is not able to explain certain facts that can readily be accommodated by the assumption that processes $k_\Delta$ and $k_s$ occur at the same time, as is shown in Scheme 15 for deamination of *endo*-fenchylamine (XXXV)‡.

Scheme 15

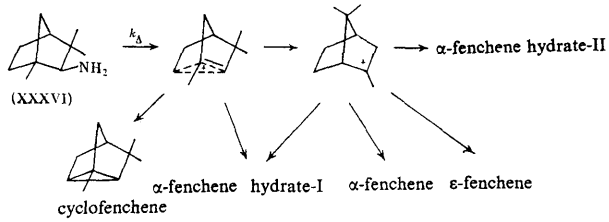


In fact, deamination of *endo*-amine (XXXV) gives in total more than half of the products from displacement of the C(1)–C(7) bond whereas the *exo*-amine (XXXVI) rearranges almost exclusively with

‡ Here and subsequently in Schemes 15–18, products with a content of less than 1% of the reaction mixtures are not given.

migration of the C(1)–C(6) bond (Scheme 16).

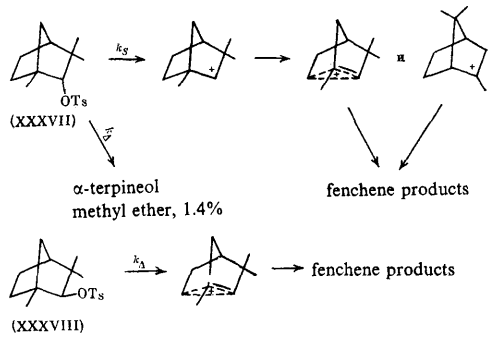
Scheme 16




At the same time, in the solvolysis of the epimeric fenchyl tosylates (XXXVII) and (XXXVIII) such a dependence of the direction of skeletal displacement on the configuration of the leaving group does not occur (Scheme 17). This indicates that deamination of amine (XXXV) occurs to a considerable extent via the $k_\Delta$ route involving the C(1)–C(7) bond whereas in solvolysis of the analogous tosylate (XXXVII) there is virtually no participation of this bond. On the basis of Scheme 15 the results of deamination via the $k_\Delta$ route conform completely with the stereoelectronic requirements of the nonclassical carbocations (XXXIX) and (XL). This idea, in contrast to the view of Collins, can be used to explain the absence of *exo*-fenchol in the mixture while the yield of *endo*-fenchol is 7%. Similarly, it must be assumed from the isolation of borneol in the absence of isoborneol (the *exo*-epimer) in the mixture that nonclassical carbocation (XXXIX) isomerises to nonclassical carbocation (XL). The interconversion of these carbocations is postulated in the decomposition of the corresponding sulphonyl hydrazones (see the review of Ando[3]).

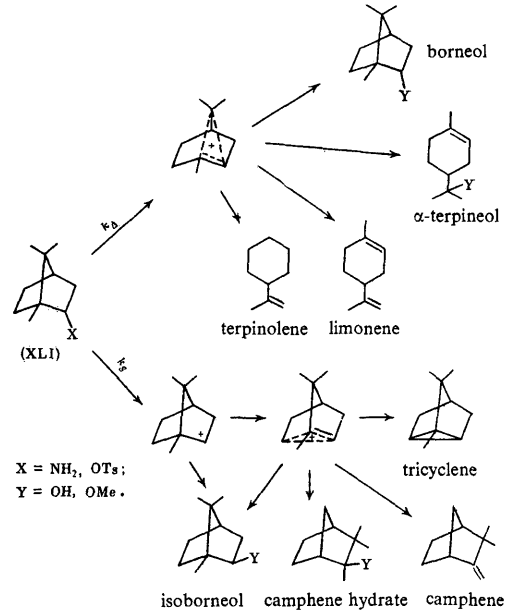
A quantitative determination of the relative contribution of the $k_\Delta$ and $k_s$ processes in deamination and solvolysis can be made from Schemes 15–17. The ratio of $k_\Delta$ to $k_s$ for the deamination of *endo*-fenchylamine (XXXV) is 1.4:1 in water and zero (in AcOH) or close to this value (in MeOH) for solvolysis reactions of *endo*-fenchyl tosylate (XXXVII). It should be emphasised that the $k_\Delta$ and $k_s$ processes are compared exclusively on the basis of the $S_Ni$ mechanism.

Scheme 17




The latter condition is not completely fulfilled for the model bornane compounds (XLI) (Scheme 18). It may be assumed, however, that the contribution of the $S_N2$-type mechanism $k_s$(c) is small, on taking into account the small content of inverted bornane products in the resulting mixtures. Assignment of the yields of products from the $k_\Delta$ and $k_s$ routes in accordance with Scheme 18 leads to the following ratios of $k_\Delta$ to $k_s$: ~0.7:1 for deamination in water and ~0.005:1 for methanolysis of the tosylate (for quantitative data on the product content, see the studies of Hückel et al.[25,26]).

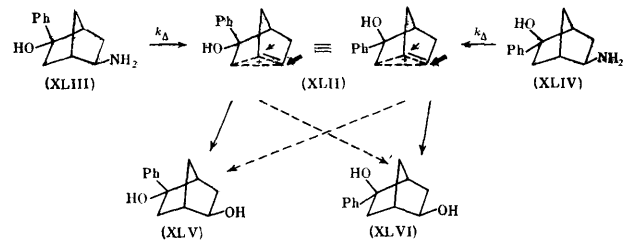
Scheme 18




In a number of alicyclic compounds one of the main arguments of Collins et al. in favour of the intermediate formation of a classical cation is as follows: the nonclassical carbocation (XLII) cannot be a common intermediate species in the reaction of amines (XLIII) and (XLIV) since each of them forms products (XLV) and (XLVI) in different ratios (2.3:1 and 1:1.7 respectively).[18,42] In the opinion of Collins, this fact suggests an equilibrium of classical cations which has not been reached, since solvolysis of the analogous sulphonates with formation of an intermediate nonclassical ion gives the same ratio of products (XLV) and (XLVI).[42]

It should be stated that the above-mentioned tendency of the regioselectivity of nucleophilic attack in deamination[7,8] to change can readily be used to explain this result with the concept of nonclassical ions. In the deamination of amines (XLIII) and (XLIV) the same nonclassical carbocation (XLII) is probably formed, being bonded in different ion pairs, in each case the nucleophile attacks the site of nitrogen elimination with a certain preference. In this connection the predominance of product (XLV) in the deamination of amine (XLIII) becomes clear, as does the predominance of product (XLVI) in the deamination of (XLIV). This is shown in Scheme 19.

Scheme 19




In the studies reviewed, Collins et al. include products whose content in the mixture is extremely small (for example, 0.114% and 0.039%) in their discussion of the mechanism, while the reaction mixtures from deamination are analysed without separating the

alcohol and acetate products.[42] The example given has been discussed since it is a good illustration of the experimental difficulties in the comparative study of solvolysis and deamination, particularly in models of norbornane compounds. An analysis of the experimental data and choice of routes for forming deamination products is often very troublesome not only because of the variety of products obtained but also as a result of possible competing reactions that take place by $S_N1$ and $S_N2$ mechanisms.[45] Berson indicates the difficulty of obtaining reproducible results.[22] There are features that are quite often ignored such as the need for a quantitative determination of the epimeric purity of the initial amines and sulphonates, the possibility of the diazonium ion epimerising via a diazoalkane, the occurrence of "internal re-entry" (trapping, Ed. of translation) of the leaving group in solvolysis, the influence of micellar effects in deamination, and the effect of temperature differences when conducting the reactions.[8] These complications to some extent help to answer the question as to why the substantial contribution of processes with anchimeric assistance in deamination often escapes the attention of research workers. Some of these factors are considered below in greater detail.

Thus, in Berson's study[22] discussed above, an analysis of a mixture of only some acetate products of deamination leads to the conclusion that there is a reduction in the degree of σ-participation compared to solvolysis, not in a "pure" $S_N1$ process but in a combination of $S_N1$ and $S_N2$ reaction routes.

Internal re-entry of a sulphonate group can only affect the comparability of results in certain cases. For many purposes titrimetric rate constants ($k_t$) rather than polarimetric rate constants ($k_\alpha$) (for optically active sulphonates) can be used, since the error introduced is small; in solvents such as water and trifluoroacetic acid the ratio of the constants $k_\alpha : k_t$ is $\sim 1:1$, in methanol it is 1.2:1, and in aqueous acetone 1.4:1.[46] However, in ethanol (2.94:1) and acetic acid (3.46:1) the difference between $k_\alpha$ and $k_t$ should probably be taken into account. On the whole this factor may result in a "thermodynamic" stereochemistry of the solvolysis products, which quite often imitates the stereochemistry of the $k_\Delta$ process. At the same time deamination, which is devoid of internal re-entry of leaving nitrogen, gives a purely "kinetic" product stereochemistry, which as a rule corresponds to competing $k_\Delta$ and $k_s$ processes.

A factor such as micellar effects in deamination should be taken into account in a comparative study of the two reactions. It may be concluded from the literature data that the formation of micelles of diazonium ions is typical for relatively stable primary diazonium ions.[47] In this case the change in the stereochemistry of nucleophilic attack on reaching a critical micellar concentration occurs only for superweak nucleophiles such as perchlorate, fluoroborate, tosylate, and camphor sulphonate anions;§ such effects do not occur in "micellar" deamination in the presence of $Cl^-$, $Br^-$, and $AcO^-$ anions.[50] In checking the reproducibility of the results it is useful to vary the concentration of the initial amine. Thus, in one study[47] micellar effects of primary diazonium ions occurred when the concentration was changed approximately by a factor of three.

The effect of temperature changes on the comparability of the results of solvolysis and deamination should also be considered. Usually deamination is carried out at temperatures close to room temperature while solvolysis occurs at an appreciable rate at higher temperatures, and the difference can reach 100 °C or more. In this connection the results of direct measurement of the rate constants of the $k_\Delta$ and $k_s$ processes in the acetolysis of β-arylethyl tosylates at different temperatures[51] are of interest. The ratio of $k_\Delta/k_s$ for the model tosylates (XLVII)–(XLIX) changes symbatically (nonlinearly) with temperature, the increase in temperature always involving a more rapid increase in $k_\Delta$ (Fig. 1). For the acetolysis of 2-phenylethyl tosylate (XLVII) extrapolation of the linear dependence of log $(k_\Delta/k_s)$ on $1/T$ to room temperature gives a lower value of the ratio of $k_\Delta/k_s$ ($\sim 0.6:1$) compared to that calculated for the deamination of 2-phenylethylamine (L) in AcOH at room temperature ($\sim 0.8:1$).[52] Despite the proximity of the extrapolation made by us, it can be qualitatively maintained from this result that the increase in the contribution of the $k_\Delta$ process in deamination compared to solvolysis does not result from the different temperature conditions for carrying out the reactions. On the other hand, the higher temperature of solvolysis levels out the differences in the ratios of $k_\Delta/k_s$ due to the properties of the leaving groups. This is probably related to a deterioration in solvation conditions of carbocations when the temperature is increased. It cannot be excluded that the $S_N2$-type $k_s$(c) processes in solvolysis are suppressed, since this mechanism requires a strict orientation of the nucleophile. Thus, the phenomenon of "temperature levelling" indirectly confirms the concept that the increase in demand for participation may be due to insufficient external solvation. It follows from the results discussed that this property of nitrogen as a leaving group may remain unnoticed in a comparative study of solvolysis and deamination if the temperature conditions for conducting the reactions differ sufficiently strongly.

## IV. The Hammond postulate and Curtin–Hammett principle applied to a comparative study of deamination and solvolysis

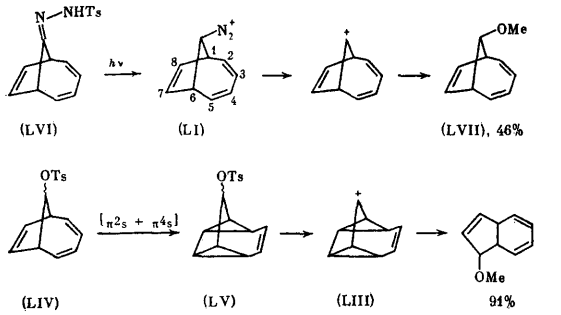
As a result of the widespread propagation of ideas about the obviously classical nature of carbocations in deamination reactions there have been attempts to use such reactions as a model for a typical process that has an "early" transition state. Extracts from many studies, including comparatively recent ones, can be quoted. For example: "deamination ... occurs with formation of an energy-rich diazonium ion, which makes the transition state of its decomposition 'early', i.e., without any change in nuclear coordinates (vertical ionisation). As a result of this, deamination may produce cations with an undistorted geometry that are not formed in solvolysis; the latter lead directly to more stable bridged forms."[3]

Another example is: "...solvolysis and deamination give a fundamentally different result. Solvolysis with its 'late' transition state on the reaction coordinate assists the transposition of the atomic nuclei in such a manner that the route is attained with the minimum of energy. On the other hand, deamination, which starts with an energy-rich diazonium ion passes through its transition state 'earlier' and without any significant distortion of the positions of the nuclei."[53] At first glance, the latter conclusion follows on logically from the stereochemical result shown in Scheme 20. The essential difference between solvolysis and deamination of compounds with the same skeleton is identified by Kirmse as the significant example

§For example, this important phenomenon as well as the possibility of reactions occurring by an $S_N2$ mechanism has not been taken into account in studies[48,49] on the deamination of alkylamines in the presence of superweak nucleophiles.

of the formation of a "free carbocation" during decomposition of a diazonium ion.[5]

Scheme 20



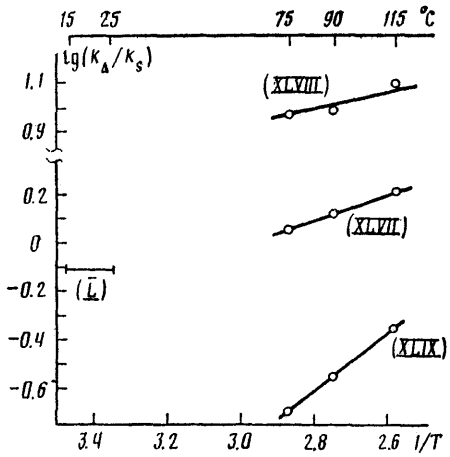
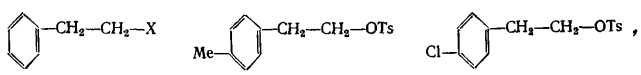
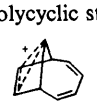




**Figure 1.** Dependence of the ratio of log ($k_\Delta/k_s$) on temperature in the solvolysis of tosylates (XLVII)–(XLIX) from the data of Jones and Coce[51] and the ratio of log ($k_\Delta/k_s$), calculated from the results of Coce,[52] in the deamination of amine (L) at room temperature; the ratio of $k_\Delta/k_s$ was obtained with the following assumptions: 1-phenylethanol (yield 18%) is formed by route $k_s(S_N1)$; the proportion of $k_\Delta$ in the formation of 2-phenylethanol (yield 82%) is approximately equal to double the percentage of migration of the label: $k_\Delta/k_s \sim 44/(38 + 18)$;




(XLVII) X = OTs, (L) X = $NH_2$. (XLVIII) (XLIX)

Meanwhile, an essentially different interpretation of Kirmse's results[53] is possible. The diazonium ion (LI) decomposes by the $k_\Delta$ route with anchimeric assistance from the C(7)–C(8) bond, giving the nonclassical carbocation (LII), whereas solvolysis occurs via the classical cation (LIII) ($k_s$), which is stabilised through the formation of a polycyclic structure.[8]



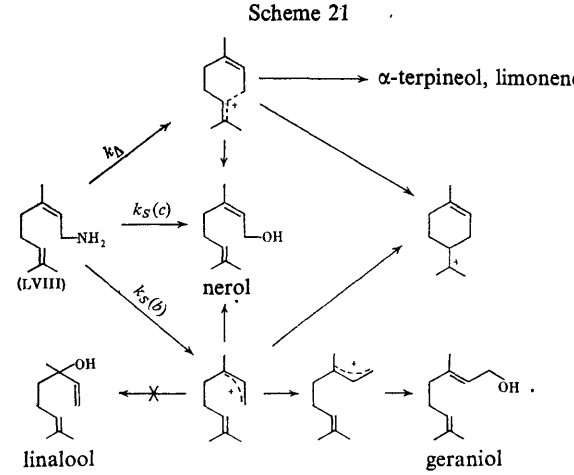
(LII)

In fact, from the equal rates of solvolysis of epimeric tosylates (LIV) and the lack of dependence of the composition of the reaction mixture on the configuration of the sulphonate group and the nature of the solvent, Kirmse and Voigt[53] correctly assume that the rate-limiting stage of solvolysis is formation of the intermediate tosylates (LV). However, no account was later taken of the essential characteristic that the formation of a similar polycyclic structure during the photochemical reaction of tosyl hydrazone (LVI) is prevented by orbital symmetry. An intramolecular Diels–Alder reaction in the rigid bicyclo[4.2.1]nona-2,4,7-triene system permits only a supra-suprasurface cycloaddition involving six electrons [$\pi 2_s + \pi 4_s$], which is photochemically forbidden. Consequently, stabilisation of the cation site during photochemical deamination cannot occur in the same way as in thermal solvolysis, and it probably occurs by intramolecular participation of the C(7)–C(8) bond to form ion (LII), which is suggested by the formation of only one of the two possible epimeric products (LVII).

The study by Bunton et al.[54] concerning a comparative deamination of nerylamine (LVIII) and solvolysis of the phosphate and chloride with the same skeleton is a similar example. The application of Scheme 13 from Section II to nerylamine gives Scheme 21, in which the $k_\Delta$ and $k_s$ routes cannot be separated quantitatively. Nevertheless, Bunton et al.,[54] by indicating the relatively lower yield of cyclisation products in deamination, conclude that π-participation is considerable in the formation of the transition state for neryl chloride and neryl phosphate whereas elimination of nitrogen from the diazonium ion does not require neighbouring-group assistance.

The following features of this deamination reaction should be mentioned. Firstly, the total yield of identified products is low but the relative proportion of cyclisation products is almost the same as in solvolysis. Secondly, in deamination there is virtually no linalool formed, which again supports the idea of a change in regioselectivity in this reaction and also indirectly suggests a lower contribution of the $k_s$(b) process, since solvolysis gives 20–25% linalool against 9–14% geraniol in deamination. However, on the whole, a conclusion about the quantitative ratio of the $k_\Delta$ to $k_s$ processes cannot be made using this model compound, as is evident from Scheme 21. Nevertheless, the results discussed by Bunton et al.[54] are used to illustrate the applicability of the Hammond postulate.

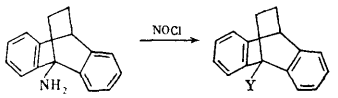
Scheme 21




The account of the different versions of the theory of an "early" transition state in deamination could be continued. However, the material presented in the previous sections suggests the reverse:

participation probably starts at the early stages of nitrogen elimination and the transition state is thus structurally similar to the final nonclassical carbocation. How can this conclusion be made to fit the generally accepted idea about the high exothermicity of this fundamental stage?

In fact, the exothermicity of nitrogen elimination from a diazonium ion is not in doubt in the majority of cases. Nitrogen is known to be eliminated with ease even from bridgehead positions. For example, amine (LIX) undergoes 47% reaction after 15 s at −70 °C, which is virtually impossible for traditional leaving groups ($\Delta\Delta F \geqslant 20$ kcal mol$^{-1}$).[55]




(LIX)

Y = Cl, OEt.

There have been various determinations of the height of the activation barrier and the heat of reaction for decomposition of an alkyldiazonium ion. Corey et al.[21] determined the heat of reaction from the sum of the ionisation potential of the sec-alkyl radical (8 eV), the energy of homolytic dissociation of the C−$N_2^+$ bond (4 eV), and the first ionisation potential of the nitrogen molecule (−15.6 eV). The value of −3.6 eV per mol obtained for $\Delta H$ is 83 kcal, which is quite unsuitable even for an approximate determination of the height of the activation barrier. This barrier is probably not as small as may be suggested from general considerations.

Direct kinetic measurements for stable diazonium ions give values in the region 10−20 kcal mol$^{-1}$. Thus, the energy of activation for elimination of nitrogen from diazonium ion (LX) is 19 ± 4 kcal mol$^{-1}$.

$$(CF_3)_2CN_2 + FSO_3H \xrightarrow{-70\ ^\circ C} \underset{(LX)}{(CF_3)_2CHN_2^+} + OSO_2F^-.$$

The very fact of the direct detection of diazonium ions (LXI)[57] and (LXII)[58] suggests that there is a perceptible activation barrier for their decomposition.

$$\underset{(LXI)}{CF_3CH_2N_2^+}\ OSO_2F^-, \quad \underset{(LXII)}{CH_3N_2^+}\ OSO_2F^-.$$

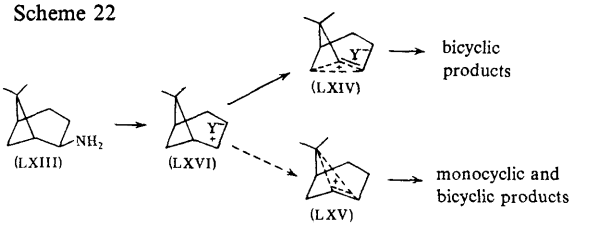
It should be mentioned here that the structure of ions (LX)−(LXII) and the conditions under which they occur (the medium) are not conducive for the elimination of nitrogen by a "pure" $S_N1$ route, namely, without any external or internal assistance.

A calculation using the MNDO method that was carried out for methyldiazonium and ethyldiazonium ions showed that $S_N2$ reactions of these ions with different nucleophiles are exothermic processes with a heat of reaction ranging from −16.5 kcal mol$^{-1}$ (reaction of the ethyldiazonium ion with water) to −64.9 kcal mol$^{-1}$ (reaction of the methyldiazonium ion with imidazole). However, decomposition of these same ions by an $S_N1$ mechanism occurs endothermically ($\Delta H$ ranging from +13.9 to +45.8 kcal mol$^{-1}$), and even when solvation effects are taken into account such endothermicity for the process largely excludes an $S_N1$ decomposition of ion (LXII).[59]

These results again support the conclusion that nitrogen has no tendency to undergo elimination without external ($S_N2$) or internal ($k_\Delta$) assistance. The high exothermicity and the low barrier in processes with such assistance together with the reverse situation for the $S_N1$ route for formation of a classical cation make deamination an "anomalous" process in relation to the extended Hammond postulate.

At first glance the contradiction that arises can be removed by rejecting the idea of anchimeric assistance as such. There is a view that the carbocation is formed without any participation and the cation site is then stabilised by a displacement of the neighbouring group. Thus, in the opinion of Collins, the intermediate carbocations in deamination reactions are classical ions and the subsequent stereoselectivity of the skeletal shifts and nucleophilic attack in an $S_N1$ reaction are determined by the position of the counterion.[42,60–63] Whittaker has expressed a similar view, according to which participation does nevertheless occur but not in the transition state for formation of a carbocation but at the subsequent stages (Scheme 22).[4,64]

Scheme 22




(LXIII) (LXVI) (LXIV) (LXV)

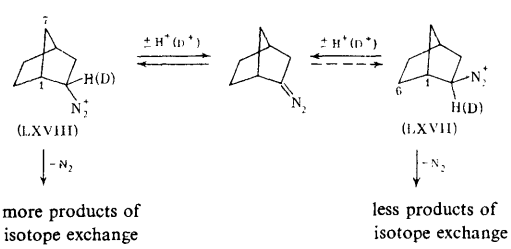
Deamination of amine (LXIII) in AcOH gives only products derived by further reactions of ion (LXIV). In water small quantities of products formed from ion (LXV) occur.

Whittaker proposes that the classical cation (LXVI) is formed at the first stage, the counterion in the intimate ion pair being positioned on the same side as the departing nitrogen. In this case delocalisation of the σ-bond is only possible on the opposite side. In water, separation of the ion pair can partly forestall this type of delocalisation, resulting in the competitive formation of ion (LXV).[4]

Nevertheless, if there is reason to suppose that in this case, as in all the other cases, ions of the type (LXVI) and (LXIV) are formed in parallel rather than successively, this conforms to the general Scheme 13. This is suggested in particular by results that can be used to determine the relative barriers of the decomposition of epimeric diazonium ions.

In the decomposition of the diazonium ions (LXVII) and (LXVIII) in aprotic media, route (d) in the general Scheme 13 starts to play a significant role (Scheme 23). It is worth noting that under these conditions significant deuterium exchange only occurs in the case of the *endo*-substrate (LXVIII).[65]

Scheme 23



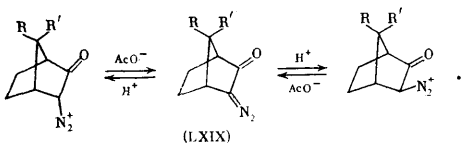

(LXVIII) (LXVII)

Hence there is a higher barrier for elimination of nitrogen for the *endo*-diazonium ion (LXVIII) than for the *exo*-diazonium ion (LXVII). Bearing in mind that participation of the C(1)−C(6) bond is much more effective than participation of the C(1)−C(7) bond, it is doubtful that the difference in the barriers should be assigned to the variable orientation of the counterion. It is more

likely due to participation of the C(1)–C(6) bond in the transition state for elimination of nitrogen from the *exo*-diazonium ion (LXVII).

Fairly recently this proposal received further experimental confirmation in a study of the acid-catalysed decomposition of diazoketones (Scheme 24).[66]

Scheme 24



(LXIX)

| | $k_{H^+}$, mol$^{-1}$ s$^{-1}$ | |
|---|---|---|
| | *exo* | *endo* |
| R = H, R′ = iso-Pr | 7.4 | 0.47 |
| R = H, R′ = t-Bu | 0.28 | 0.06 |
| R = iso-Pr, R′ = H | 55 | 0.8 |
| R = t-Bu, R′ = H | 80 | 1.2 |
| R = H, R′ = H | — | — |

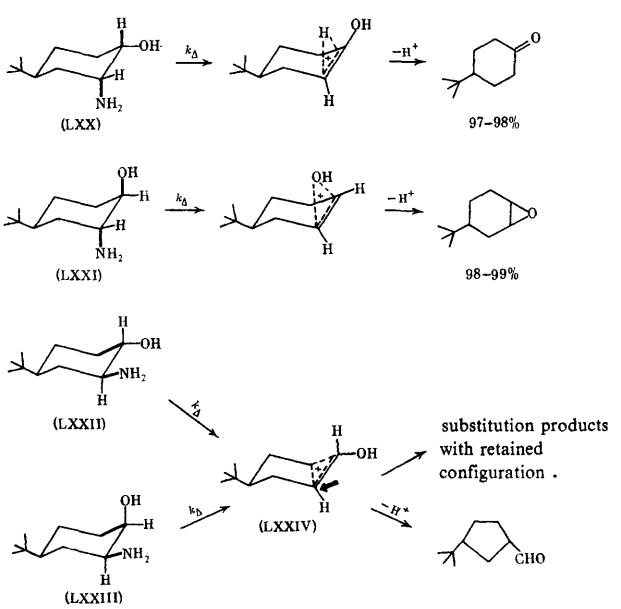
It can be seen from the results in Scheme 24 that the rate constants of reaction for the *exo*- and *endo*-epimers differ by a factor of 10–100. There is reason to suppose that in the presence of acetate anion, elimination of nitrogen in the protonation of diazoketone, is, at least in part, the rate-limiting stage.[66] This is due to the competing deprotonation of the diazonium ions. In a medium without acetate anion added the rate-limiting stage is protonation of diazoketone (but it probably has a similar rate to the nitrogen elimination stage). The enthalpy of activation of this reaction for diazoketone (LXIX), R = H, R′ = iso-Pr, in aqueous acid is 13.7 kcal mol$^{-1}$, which may be similar to the enthalpy of nitrogen elimination. The entropy of activation (–8.4 e.u.) increases the barrier by a further 2.3 kcal mol$^{-1}$ under normal conditions¶.[66]

The many illustrations of the extended Hammond postulate in the case of deamination are based on an estimate of the energy of activation for decomposition of the diazonium ion in the region of 3 to 5 kcal mol$^{-1}$ that was made by Streitwieser from general considerations.[16,17] The findings reported above confirm that this barrier usually does not exceed 10–15 kcal mol$^{-1}$ when the process is accompanied by internal or external assistance. Thus, the contradiction between the concept of the increase in demand for participation in deamination developed here and the extended Hammond postulate is retained. It may be assumed that in an exothermic reaction with assistance (which in turn gives rise to exothermicity), the "early" substrate-like transition state contains a partial displacement of the neighbouring group in so far as even when the diazonium ion exists there can arise a "low-electron, multicentred" delocalisation involving the electrons of the neighbouring periplanar bond, which is accompanied by a partial rehybridisation of the carbon atom bonded to the charged nitrogen. This specific precarbocation stage of nonclassical delocalisation in the diazonium ion does not contradict the existing facts. It may be confirmed or disproved using quantum-chemical methods, but these results have so far not appeared in the literature.

In our opinion, regardless of whether it is possible at the present time to resolve the contradiction between the Hammond postulate and the hypothesis developed here, the predictive potentialities of the latter should be utilised. It is useful to give as an example the solution of the problem relating to the reactions of diastereomeric cyclohexylamines whose conformations are stabilised by the introduction of bulky alkyl substituents.

Thus, in terms of the general Scheme 13, deamination of the diastereomeric amines (LXX)–(LXXIII) is given by Scheme 25, in which the determining factor is participation of one of the periplanar neighbouring bonds. Moreover, by using Scheme 25 it is possible to answer the question raised previously, but up to now not having received a satisfactory explanation (see the reviews of Kirmse[2] and Moss[11] and the references in them), namely: why do axial cyclohexylamines of the type (LXX) and (LXXI) give many elimination products and only a few equatorial (inverted) products while equatorial amines of the type (LXXII) and (LXXIII) mainly form substitution products with retained configuration and few elimination products?

Scheme 25



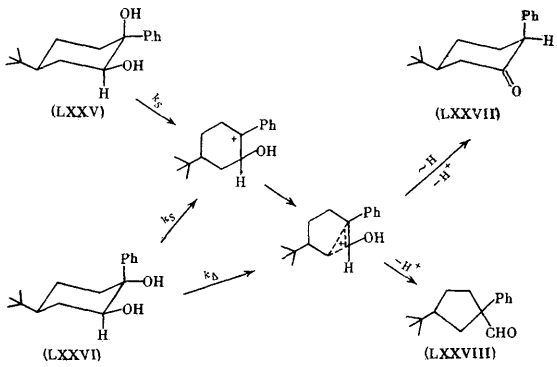

It can be seen from Scheme 25 that in the typical axial amine (LXX) participation of the C–H bond must be less effective than participation of the C–C bond of the ring in any equatorial epimer. The latter, for its part, gives nonclassical cations of the type (LXXIV), whose stereoelectronic requirements assist the formation of substitution products with retained configuration.

¶If it is assumed that the kinetic parameters for protonation of diazoketones are similar to those for the nitrogen elimination stage, the results of Kronis et al.[66] do not support the idea of the entropy factor, when there is a low enthalpy of activation, having a decisive effect in deamination.[4,67,68] According to this hypothesis the entropy factor inhibits the formation of a nonclassical carbocation as a more ordered species under conditions where the solvate shell has little effect on the degree of ordering of the transition stage. It is evident from the activation parameters stated above that the entropy contribution is not decisive.

In the meantime the lesser requirement for ordering of the solvation shell from a nonclassical cation compared to a classical cation[69] may in fact make the nonclassical cation "entropy-preferred". Thus, according to the results of two studies,[70,71] diazoalkane (LXIX), R = R′ = H, after being protonated decomposes with σ-participation.

As expected, glycols (LXXV) and (LXXVI), which are analogous in structure to the amino alcohols (LXX)–(LXXIII), do not react stereospecifically. The products—(LXXVII) and (LXXVIII)—are formed in the ratio 9 : 1 whatever the configuration of the leaving group[2,72] (Scheme 26).

Scheme 26




In this case it is worth comparing the reactions of aliphatic and alicyclic substrates. Thus, the example shown in Scheme 25 is similar to the pinacolic deamination discussed earlier (Scheme 12). In both cases the result contradicts the Curtin–Hammett principle in that the ratio of products formed from the different conformations (or diastereomers) of the substrate depends on the relative populations of the conformations (or on the configuration of the leaving group).

There is reason to suppose that the above-mentioned "violations" of the extended Hammond postulate and Curtin–Hammett principle in deamination have a common origin which should be looked for under the specific conditions of ionisation of the substrate. These conditions, which have been discussed in detail in the preceding sections, lead to the formation from different conformers (diastereomers) of different carbocations (as a rule, nonclassical) that tend not to undergo interconversions. As has already been mentioned, one of the causes may be a specific precarbocation ionisation stage which involves a partly "nonclassical" diazonium ion. Under these conditions formation of carbocations from diazonium ions is kinetically controlled and the stereospecificity is not disturbed.

In solvolysis, where anchimeric assistance in the $S_N1$ process plays a lesser role but internal re-entry plays an important part†, the composition of the intermediates is to a greater degree thermodynamically controlled. The Curtin–Hammett principle is fulfilled precisely in the "thermodynamic" region of nucleophilic substitution, which is accessible to only a limited degree for nitrogen elimination reactions (see, for example, Scheme 14). However, this fact makes deamination a convenient method for carrying out uncommon (such as the Dem'yanov rearrangement) and directed skeletal rearrangements.

† There is no information about internal re-entry of nitrogen in the decomposition of a diazonium ion in aliphatic compounds. It may be judged that this is a very insignificant process from the results on the insertion of nitrogen into the reactive phenyl cation; at 300 atm 2.46 ± 0.4% external nitrogen is inserted.[73]

On the other hand, decomposition of a diazonium ion is a single-stage fundamental process and it conforms to the Hammond postulate. In this sense the diazonium ion must also be partially stabilised through nonclassical delocalisation.

Having summarised the results of the critical examination of the literature conducted above, we consider it desirable to note the following fundamental characteristics of deamination reactions as compared to solvolysis.

1. The formation of a charged diazonium ion species at a precarbocation stage helps to develop a greater degree of anchimeric assistance in deamination as compared to traditional solvolysis. By using deamination it is possible to carry out purposefully rearrangements which are impossible or difficult in other reactions. In this case the group periplanar to the leaving nitrogen is always displaced. In a number of cases replacement of a separating sulphonate group by nitrogen is equivalent to conducting solvolysis in a much more ionising and less nucleophilic solvent.

2. The direction of nucleophilic attack in $S_N1$-deamination should be expected to correspond to the stereoelectronic requirements of the nonclassical carbocation in which participation of the neighbouring periplanar group develops. Regioselectivity must be taken into account; substitution occurs primarily on the site of nitrogen elimination.

3. In a comparative study of deamination and solvolysis, particular factors that affect the comparability of the stereochemical results of the two reactions must be taken into account:

a) the possibility of partial epimerisation of a diazonium ion via a diazoalkane;

b) internal re-entry of the leaving group in solvolysis;

c) micellar effects in deamination;

d) the difference in the temperature conditions for carrying out the reactions;

e) the necessity of making a separate analysis of deamination products that belong to different classes of compounds.

4. The observed variance of the stereochemistry of deamination products with the extended Hammond postulate and Curtin–Hammett principle probably has a common origin and can be accounted for in a similar way. The concept of nonclassical delocalisation of the positive charge in a diazonium ion itself may serve as one of the explanations.

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