INTERMEDIATES IN CARBONIUM ION REACTIONS OF METHYL-SUBSTITUTED CYCLOPROPYLCARBINYL, CYCLOBUTYL AND ALLYLCARBINYL DERIVATIVES

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The pleasure of working with Professor John D. Roberts has indeed been a great one. The author hopes he can retain a small amount of that which Dr. Roberts has taught him.

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"One must be prepared to approach the subject of this chapter philosophically, prepared to accept conclusions which are, at first thought, seemingly at variance with our senses and with a belief that has persisted almost unquestioned from the time of the Greeks. . . "

F. K. Richtmeyer, E. H. Kennard and T. Lauritsen

"Introduction to Modern Physics"

Chapter 6, Wave Mechanics

ABSTRACT

The products of the nitrous acid deamination of 2-methylcyclobutylamine, 3-methylcyclobutylamine, 2-methylcyclopropylcarbinylamine, cyclopropylmethylcarbinylamine, allylmethylcarbinylamine and crotylcarbinylamine have been determined. In addition, studies on the rates of solvolysis of suitable derivatives of the same carbon skeleton have been carried out. The experimental data are reminiscent of those reported for the reactions of unsubstituted cyclobutyl, cyclopropylcarbinyl and allylcarbinyl compounds and are interpreted in terms of cationic intermediates closely related to those proposed for the latter substances. In the present case, the intermediates are most reasonably represented as three nonclassical, unsymmetrical, non-equivalent pyramidal ions, "bicyclobutonium" ions.

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I. INTRODUCTION

The carbonium ion reactions of a family of isomeric methyl-substituted cyclopropylcarbinyl, cyclobutyl and allylcarbinyl derivatives comprise the subject matter of this thesis. The two sections of the Introduction include discussions of (a) the nature of the carbonium ion intermediates formed from unsubstituted cyclopropylcarbinyl, cyclobutyl and allylcarbinyl derivatives, and (b) the nitrous acid deaminations--such reactions providing a standard means of generation of carbonium ions under mild conditions. Cox (1) has recently considered the general theory of carbonium ion rearrangements and the amine-nitrous acid reaction in detail, so no similar comprehensive review will be attempted here.

The Interconversion of Cyclopropylcarbinyl, Cyclobutyl and Allylcarbinyl Compounds in Carbonium Ion Reactions

Much of the seemingly contradictory data on the behavior of cyclopropylcarbinyl, cyclobutyl and allylcarbinyl derivatives in carbonium ion-type reactions have been shown by Roberts and Mazur (2) to result from having either kinetic or equilibrium control over the reaction products. In an equilibrium-controlled process, the composition of the products is determined by the relative thermodynamic stabilities of the products themselves. On the other hand, the composition of the products of a kinetically-controlled carbonium ion reaction usually reflects the relative stabilities of the different intermediates involved, or the charge distribution

on a single intermediate, if such is implicated.

As an example of an equilibrium-controlled reaction, we may consider the work of Roberts and Mazur (2) on the behavior of cyclopropylcarbinyl and cyclobutyl alcohols or chlorides with Lucas reagent. Allylcarbinyl chloride was found to be the sole product.* The same reagent under milder conditions caused a 2:1 mixture of cyclopropylcarbinyl and cyclobutyl chlorides to isomerize to a 1:1 mixture of allylcarbinyl and cyclobutyl chlorides (2). Since other evidence (vide infra) shows that both cyclobutyl and cyclopropylcarbinyl chlorides lose chloride ion to form the same cationic intermediate, the disappearance of cyclopropylcarbinyl chloride from the mixture reflects the lesser stability of this chloride relative to cyclobutyl chloride. The relative thermodynamic stabilities of the products corresponding to the three isomeric carbon skeletons are therefore allylcarbinyl $\gg$ cyclobutyl $>$ cyclopropylcarbinyl. This sequence is as expected from strain considerations and provides a basis for prediction of the nature of the reaction products in reversible reactions of cyclopropylcarbinyl and cyclobutyl derivatives.

Now what is the evidence on the cationic intermediates involved in these reactions? As has been pointed out, the products formed in rapid and essentially irreversible kineti-

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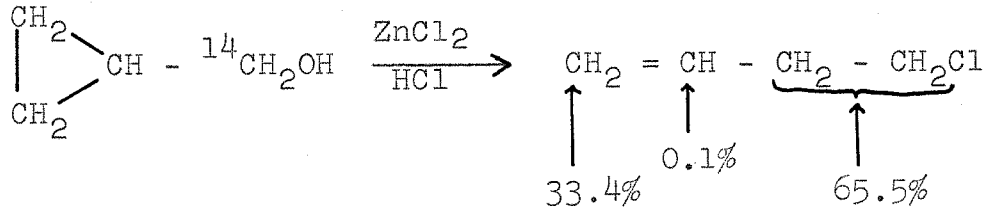
*Exchange experiments with radioactive ^{38}Cl showed that, under the reaction conditions, the small-ring compounds were in equilibrium with cationic intermediates but the allylcarbinyl compound was not.

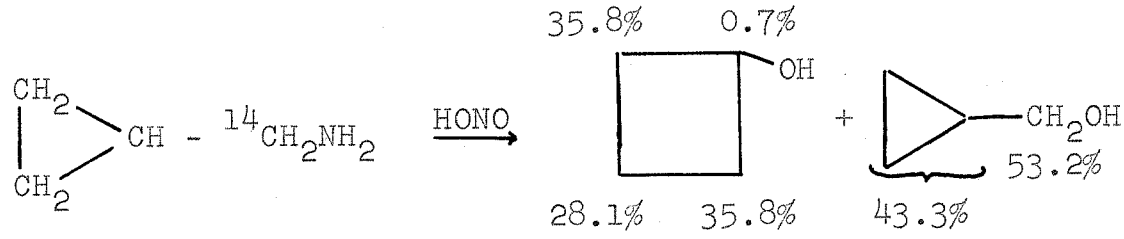
cally-controlled reactions usually reflect the nature of the intermediates. Examples of such reactions are the deamination of cyclobutylamine and cyclopropylcarbinylamine, solvolysis of cyclobutyl and cyclopropylcarbinyl derivatives and reactions of cyclobutanol and cyclopropylcarbinol with a variety of reagents, as thionyl chloride and phosphorous tribromide. Interestingly, all these reactions give similar mixtures of products, where the relative amounts of material having the cyclobutyl, cyclopropylcarbinyl and allylcarbinyl skeletons are about 10:10:1, respectively. This suggests incursion of common cationic intermediates in carbonium ion reactions of such compounds. All the data thus far introduced can be interpreted in terms of an equilibrating mixture of classical cyclobutyl, cyclopropylcarbinyl and allylcarbinyl cations and one might ask whether there is any evidence against this simple explanation. Significantly, there is. Roberts and Mazur (2) measured the solvolysis rates of several chlorides and found that, in 50% aqueous ethanol at 50°, cyclopropylcarbinyl chloride is 27 times more reactive than cyclobutyl chloride and 40 times more reactive than β-methylallyl chloride, cyclobutyl chloride is 1.5 times more reactive than β-methylallyl chloride and 15 times more reactive than isopropyl chloride and allylcarbinyl chloride is completely unreactive. The high reactivity of <u>both</u> cyclobutyl and cyclopropylcarbinyl derivatives and the similarity in the composition of the products of the reactions of these compounds can best be explained by common,

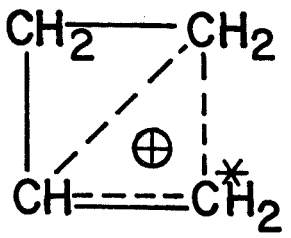
non-classical intermediate(s). Before further considering the nature of these intermediates, two intriguing pieces of data will be introduced.

Mazur (4) has treated cyclopropylcarbinol-α-^{14}C with Lucas reagent and degraded the resultant allylcarbinyl-x-^{14}C chloride. The ^{14}C was found to be distributed equally among the three methylene groups. In another experiment (4),

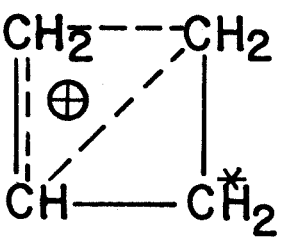


cyclopropylcarbinylamine-α-^{14}C was deaminated with aqueous nitrous acid and the cyclopropylcarbinol and cyclobutanol so formed were degraded with the results shown below.

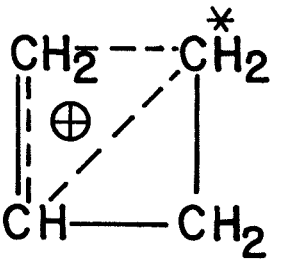




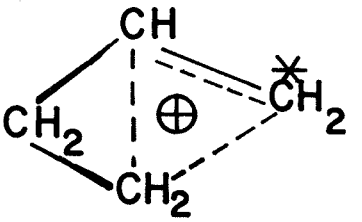
Ia



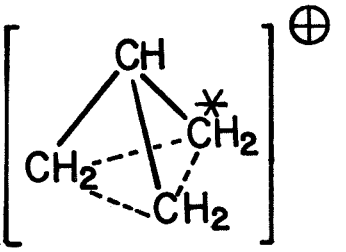
Ib



Ic



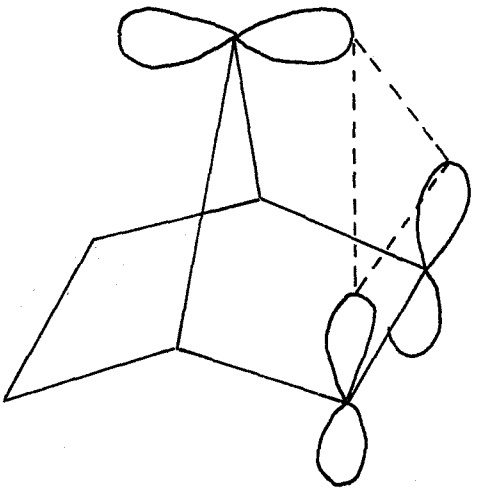
Ia



II

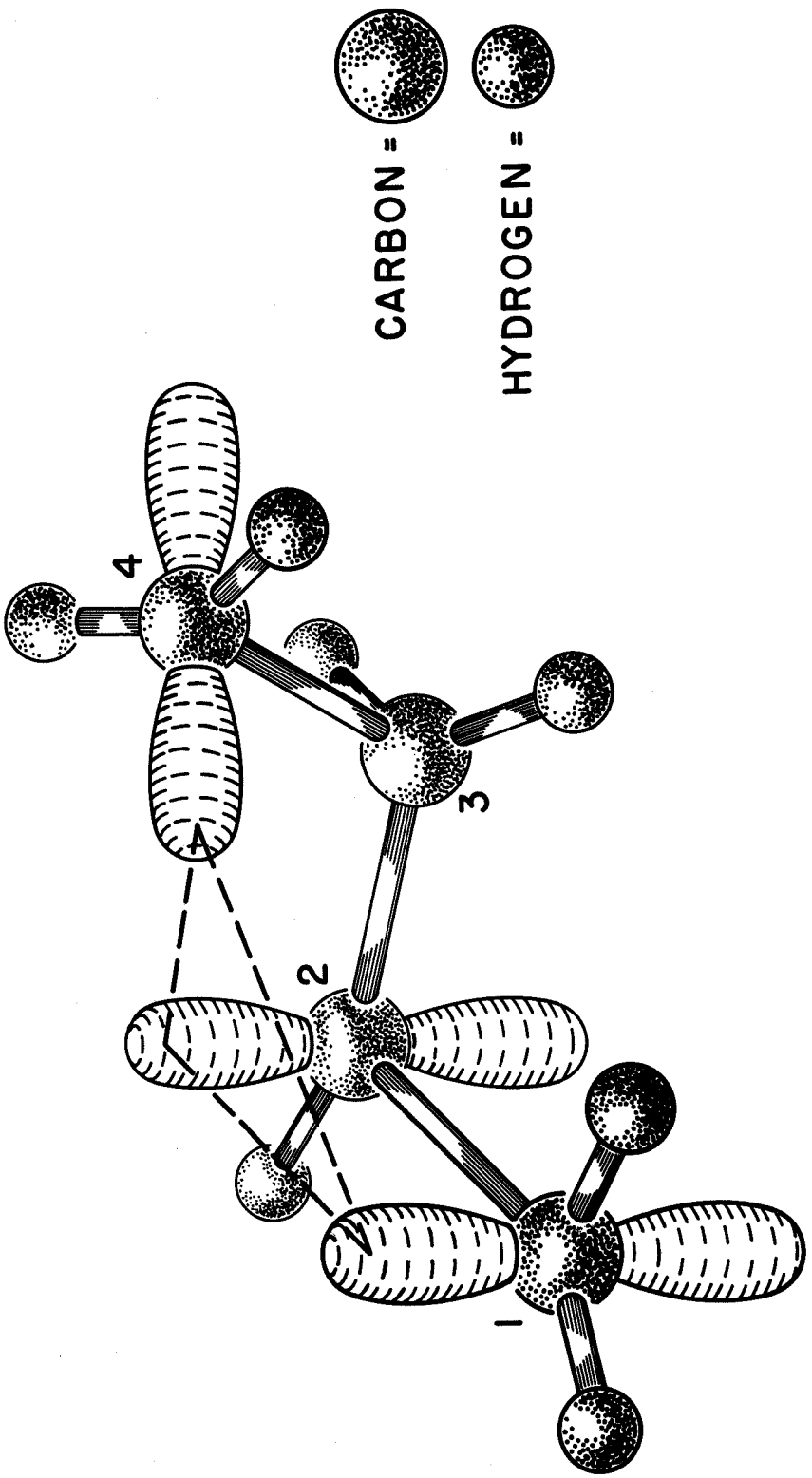
With these results in mind, we may proceed with an analysis of the nature of the common non-classical intermediates. Firstly, consideration of the previously proposed (3) completely symmetrical "tricyclobutonium" ion II leads to prediction of equivalent amounts of ^{14}C in the three methylene groups of the cyclobutanol-x-^{14}C formed in the deamination of cyclopropylcarbinylamine-α-^{14}C. Since the ^{14}C distribution approaches but does not quite reach that predicted for II as the intermediate, the best formulation for the cationic intermediates seems to be a rapid but not instantaneous equilibrium of three unsymmetrical "bicyclobutonium" ions (Ia-c). The foregoing experimental results, in conjunction with a proposed molecular model (III) for intermediates Ia-c, suggest a number of interesting possible characteristics for these intermediates.

Model III for the "bicyclobutonium" ion is based on a model derived previously for the 7-dehydronorbornyl cation, which seems, from simple molecular orbital and steric strain calculations to be the best geometric arrangement for a homoallylic cation (25). The experimental data obtained in studies of rates of carbonium ion formation with 7-dehydronorbornyl derivatives are in accord with the predicted high degree of election delocalization in the 7-dehydronorbornyl cation. A comparison of model III and the drawing below for the 7-dehydronorbornyl cation demonstrates the close relationship between the "bicyclobutonium" ion and the latter cation.

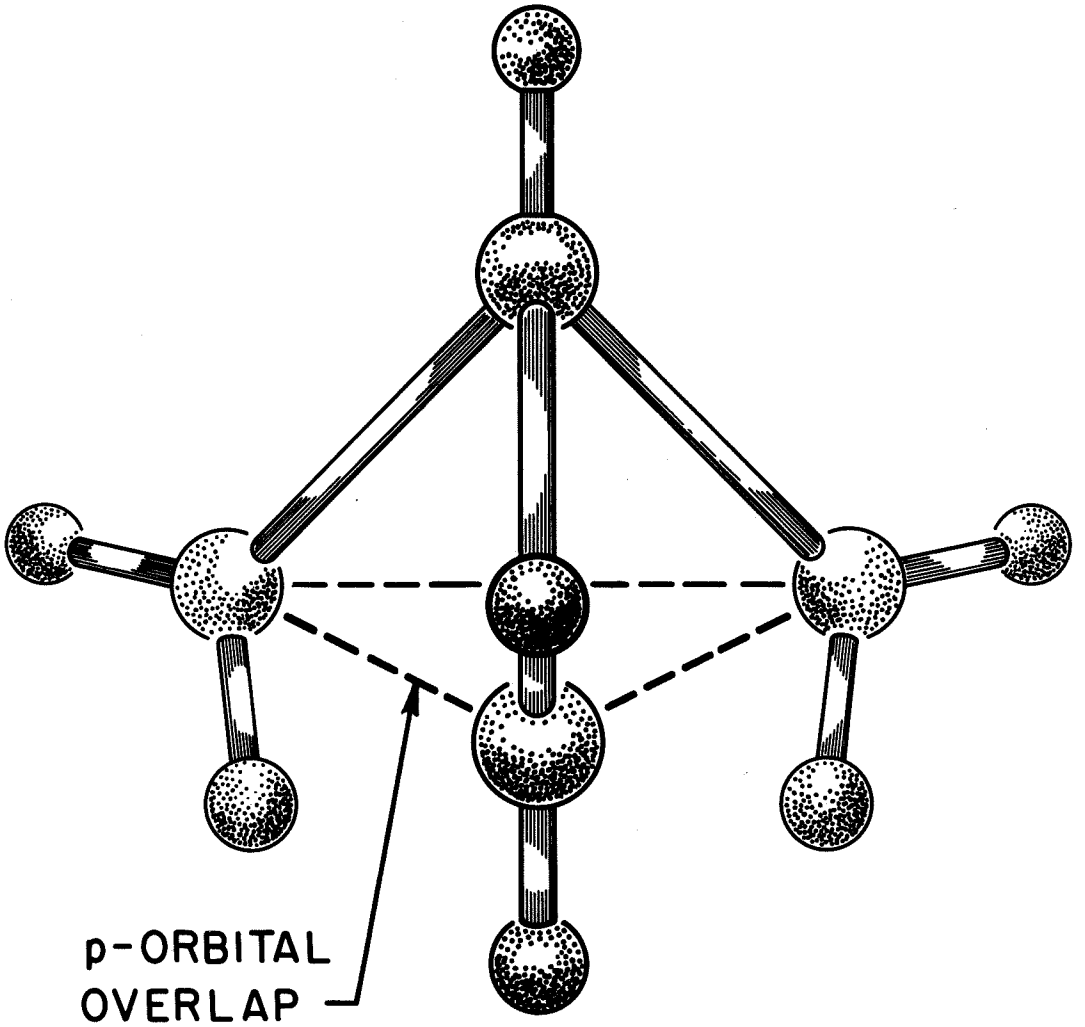


With the "bicyclobutonium" ion, the charge appears to be almost evenly distributed over the 1, 2 and 4 carbon atoms (numbering refers to III), since III reacts to give approximately equal amounts of cyclopropylcarbinyl, cyclobutyl and allylcarbinyl products (10:10:1) despite the predicted (and observed) large differences in thermodynamic stabilities.

The next question pertains to the mechanism for the interconversion of Ia-c. This may reasonably take place <u>via</u> a transition state resembling symmetrical ion II, in which case, the conformation of II illustrated by IV might well be most favorable. In IV, the plane determined by the carbon and two hydrogens of each methylene group is perpendicular to the plane determined by the carbon atoms of the three methylene groups. However, model III also shows that



III



IV

conversion of unsymmetrical ion Ia to Ib (and vice versa) entails only a slight movement of atoms (referring to the numbering on III, C_4 must be transferred from C_3 to C_1) whereas the conversion of either Ia or Ib to Ic (and vice versa) involves considerable distortion of model III (a bond must be formed between C_1 and C_3 of III). The first interconversion may thus have a lower activation energy and occur more readily. Since, in the deamination of cyclopropylcarbinylamine-α-^{14}C, Ia is the cation initially formed, such an effect might account for the lack of complete equilibration of Ia-c and explain the excess ^{14}C in the 2,4-positions of cyclobutanol and the exocyclic methylene group of cyclopropylcarbinol.* The movement of atoms in Ic corresponding to the Ia-Ib interconversion converts Ic only to its mirror image.

Experience with a variety of carbonium ion-type reactions suggests that the nearly equal rates of formation of cyclopropylcarbinyl, cyclobutyl and allylcarbinyl derivatives in kinetically-controlled reactions must arise from a rather delicate balance of steric and electrical effects in the

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*Ia and Ib, it will be observed, form cyclobutanol with ^{14}C in the 2,4-positions and, by themselves, will form cyclopropylcarbinol with 50% of the ^{14}C in the exocyclic methylene group. The large excess of ^{14}C in the latter position probably arises mainly from some special, non-rearranging cation. This process may be closely related to that which causes anionotropically related allylic amines to give different mixtures of products. The latter observations are discussed in the subsequent section of the Introduction.

unsymmetrical ions Ia-c. Consequently, substitution of a methyl group for any of the hydrogens of Ia-c might be expected to cause drastic alterations in the behavior of the intermediate cations. Cox (1) has studied 1-methylcyclopropylcarbinyl, 1-methylcyclobutyl and β-methylallylcarbinyl derivatives and has observed such effects. For instance, the amines of these structures give only one cyclic product, 1-methylcyclobutanol, upon treatment with nitrous acid, and 1-methylcyclopropylcarbinylamine-α-^{14}C gives only 3% ^{14}C in the 3-position of the 1-methylcyclobutanol. All of Cox's (1) results are readily interpretable (5) in terms of unsymmetrical cations resembling Ia-c, in which the charge is highly localized on the methinyl carbon atom (in this family, this carbon has become a potential tertiary carbonium ion center). There may be a ready "short-cut" interconversion for the unsymmetrical ions related to Ia and Ib but the conversion of either of these ions to Ic via the pertinent "tricyclobutonium" transition state (with its concomitant rearrangement of ^{14}C into the 3-position of 1-methylcyclobutanol) appears to be energetically unfavorable. The methyl group probably stabilizes the "bicyclobutonium" ions more than the "tricyclobutonium" transition state, perhaps because the more delocalized charge on the latter is less available for stabilization by the methyl group (the charge on the symmetrical transition state is spread over four carbon atoms while the charge on unsymmetrical ions Ia-c is only over three).

The introduction of a methyl group into Ia-c, as studied by Cox (1), was expected to cause a maximum perturbation, since it introduced a latent tertiary cationic center. The substitution of a methyl group on any of the methylene carbon atoms, with its potential secondary cationic center (thus, two such in the same molecule) might be expected to have less drastic effects. This has been the subject of the investigation reported in this thesis.

At the present time, Dr. E. Renk of this laboratory is studying the ^{14}C-distribution in the cyclobutanol and cyclopropylcarbinol formed in the deamination of allylcarbinylamine-1-^{14}C. This amine should first form intermediate Ic and therefore is predicted to give cyclobutanol with $>33.3\%$ ^{14}C in the 3-position and cyclopropylcarbinol with $>66.7\%$ ^{14}C in the ring positions. The experiment should be a crucial test of the proposed reaction scheme.

The Deamination of Primary Aliphatic Amines

As was seen in the previous section of the Introduction, the amine-nitrous acid reaction has been used extensively as a model carbonium ion-type reaction of cyclopropylcarbinyl, cyclobutyl and allylcarbinyl derivatives. The results so obtained have been of considerable aid in the interpretation of other carbonium ion reactions of this family of compounds. However, there are at least two important differences between the amine deamination reaction and solvolytic-type reactions.

First, while a solvolysis normally has an enthalpy of activation of order 25 kcal., the loss of nitrogen from an alkyldiazonium ion has a very low enthalpy of activation, or may even be exothermic (16,23). Second, whereas the solvolysis reaction leads to the formation of an oppositely charged ion pair,* the amine-nitrous acid reaction proceeds via the loss of a neutral nitrogen molecule from a positively charged carbocation. A serious question therefore arises as to how closely the carbonium ions formed in solvolytic-type reactions and in amine-nitrous acid reactions resemble each other. With specific reference to cyclopropylcarbinyl, cyclobutyl and allylcarbinyl derivatives, there are some data that bear directly on this question.

Significantly, the compositions of the products obtained in the deamination of cyclopropylcarbinyl- and cyclobutylamines are greatly similar to those of the mixtures obtained in other carbonium ion reactions of compounds of the same carbon skeleton (2). This would indicate that at least for these compounds, the deamination reaction is a good approximation to other carbonium ion-type reactions. In the case of the allylcarbinyl derivatives, a somewhat different situation arises. No evidence was obtained (2) for the formation of the allylcarbinyl cation in the solvolysis of allylcarbinyl

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*Of course, there are solvolyses, such as those of sulphonium salts, in which no ion pair is formed. We consider here only the most common kinds of solvolyses, where the leaving group is halide, tosylate, brosylate, etc.

chloride or in the action of Lucas reagent upon this chloride or the corresponding alcohol (Lucas reagent is an especially potent means of generating carbonium ions from such substances). On the other hand, the plethora of rearrangement products obtained in the reaction of allylcarbinylamine with nitrous acid certainly indicates formation of cationic intermediates in this last reaction. There is no direct evidence, however, that the behavior of the primary cation produced in the deamination of allylcarbinylamine is in any way more unusual than that of a primary cation formed in another manner. The need is to determine a standard for comparison, and the succeeding pages will indicate just how difficult it is to define such a standard. Before proceeding, however, we shall assume a working hypothesis as to the mechanism of the deamination reaction.

The assumed mechanism is that the alkyldiazonium ion loses a molecule of nitrogen to form a "hot" carbonium ion. This "hot" carbonium ion is non-rearranged; indeed, there is some evidence (vide infra) that the conformation of the "hot" ion, aside from that about the carbon atom which actually bears the positive charge, is nearly the same as the conformation of the alkyldiazonium ion itself. This "hot" carbonium ion can then undergo alternative reactions. It should be kept in mind that this mechanism for the amine-nitrous acid reaction is not universally accepted, and we shall give a more detailed analysis of the mechanism at the conclusion of the Introduction.

With the aid of the above mechanistic hypothesis, let us first discuss the deamination of primary aliphatic amines. Whitmore and Thorpe (10) report that methylamine gives no isolable products, ethylamine gives a 60% yield of ethanol and n-propylamine gives 7% 1-propanol, 32% 2-propanol and 28% propylene. Aside from the anomalous behavior of methylamine, these results are what one would expect if the intermediate formed were a primary cation that can subsequently react with solvent, lose a proton to form olefin or rearrange to a more stable cation (which can then react with solvent, etc.), all these reactions of carbonium ions having been established in innumerable other instances (22). Henry (11) has reported that allylamine yields only allyl alcohol and, as might be expected, shows no tendency to form acetone via the highly unfavorable isopropenyl cation (13). Likewise, cyclopropylcarbinylamine undergoes no hydrogen migration (2,4) in the amine-nitrous acid reaction. Apparently, the initial "hot" cyclopropylcarbinyl cation forms the "bicyclobutonium" ions in preference to the 1-methylcyclopropyl cation, which would be the product of hydrogen migration and which has been shown to be unusually unfavorable for a tertiary carbonium ion (1). On the other hand, the deamination of allylcarbinylamine, as has been mentioned previously, gives a highly complex mixture of products which include crotyl alcohol and α-methylallyl alcohol, formed via hydrogen migration, and cyclopropylcarbinol and cyclobutanol, formed

via the "bicyclobutonium" ions. The most reasonable explanation is that the "hot" allylcarbinyl cation, especially if formed in the extended conformation, cannot instantaneously attain the "bicyclobutonium" ion conformation. Thus, the formation of the resonance stabilized butenyl cation via hydrogen migration now competes successfully with the first-mentioned path.

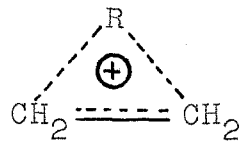
The behavior of anionotropically related allylic amines also elucidates some of the features of the amine-nitrous acid reaction. Roberts and Mazur (2) have found that the deamination of crotylamine and α-methylallylamine gives alcohol mixtures of different compositions. The first gives 47% crotyl alcohol and 53% α-methylallyl alcohol while the second gives 31% and 69% of these alcohols, respectively. This indicates that the carbonium ion formed in the amine-nitrous acid reaction is not completely "free," but, for allylic cations at least, has a tendency to react at that carbon which originally carried the amino group.

Further light is shed on the deamination reaction, and especially on the tremendous driving force associated with it, by the work of Bartlett and Knox (12). These workers showed that a bridgehead carbonium ion could be produced in an aliphatic deamination reaction whereas no such intermediate could be formed with either water or chloride ion as the leaving group, even under the most vigorous conditions. The loss of the nitrogen molecule presumably occurs, in this

case, without either solvent or neighboring group participation.

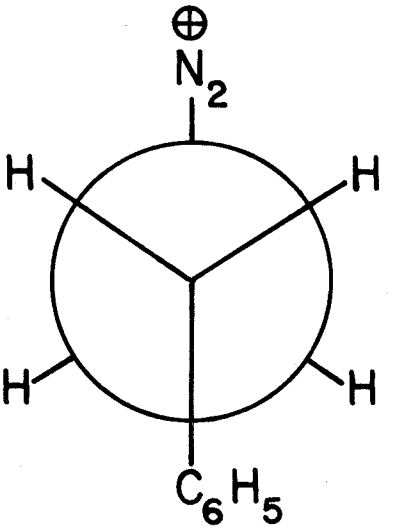
The stereochemical course of the amine-nitrous acid reaction, when not complicated by neighboring group or unusual structural effects, is racemization accompanied by inversion (14-16), in a manner reminiscent of typical S_N1-type reactions (17). The inversion observed may arise in a reaction path related to that which causes allylic isomers to give different product mixtures, and may reflect a degree of covalent bonding, in the transition state, between the solvent molecules and the developing positive carbon atom of the alkyldiazonium ion. The results of Bartlett and Knox (12) show that such bonding is not indispensable.

Many interesting experiments on the amine-nitrous acid reaction have recently been performed, utilizing ^{14}C as a tracer for carbon. In the deamination of 3-phenyl-1-propylamine-1-^{14}C, Fort and Roberts (21) found no evidence of benzyl migration but approximately 40% hydrogen migration. Roberts and Yancey (8) showed that the deamination of ethylamine-α-^{14}C gives ethanol with 1.5 ± 0.2% of the ^{14}C in the methyl group, indicating the presence of 3% of the ethylene protonium ion (V, R=H), if that is the intermediate. Roberts and Halmann (18) found that n-propylamine-1-^{14}C gives n-propyl alcohol with 8.5% of the ^{14}C in the 2-position, showing that 17% of the reaction goes by way of the methyl-bridged structure (V, $R=CH_3$). Roberts and Regan (19) studied

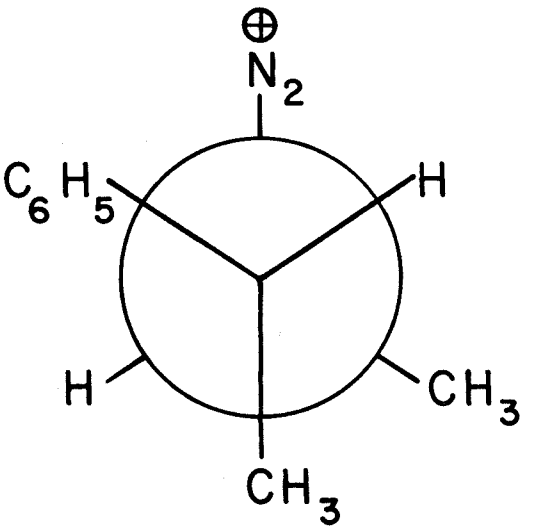


V

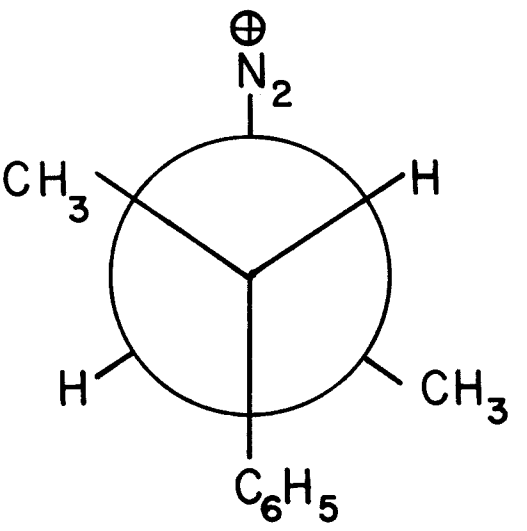
a series of para substituted β-phenylethylamines-α-^{14}C and found that p-nitrophenyl gives 12% of the bridged intermediate (V, R=p-X-phenyl), while phenyl gives 54% of V and p-methoxyphenyl, 66% of V. In this last series of compounds, the formation of the highly resonance-stabilized α-phenylethyl cation, via hydrogen migration, was not observed. The authors (18) offer two possible explanations: (a) the hydrogen-bridged intermediate preferentially gives styrene, or (b) the phenyl bridge is formed concurrently with loss of nitrogen. In support of hypothesis (b), it is apparent that the conformation of the β-phenylethyldiazonium ion with the phenyl group trans to the nitrogen molecule is highly favored (VI). The "hot" primary β-phenylethyl cation may stabilize itself so rapidly--by either forming a phenonium ion or by reacting with solvent--that the carbon-carbon single bond does not have time to rotate and bring the hydrogen atoms into position to form a hydrogen-bridged intermediate. In contrast to the results of Roberts and Regan, the deamination of either threo or erythro 3-phenyl-2-butylamine gives about



VI



VII



VIII

20% 2-phenyl-2-butanol, the result of hydrogen migration (20).* Here, the initially formed cation is a more stable secondary one, and it may last sufficiently long to allow 60° rotation about a carbon-carbon bond, with subsequent migration of hydrogen.**

A recent paper by Raaen and Collins (70) illustrates some differences between carbonium ions formed in the amine-nitrous acid reaction and those formed via another route, specifically the pinacol rearrangement. These authors found that, in the rearrangement of diphenyl-o-tolylacetaldehyde and the related glycols to the two isomeric ketones, the o-tolyl/phenyl migration ratio is 3. The results are explicable in terms of a relatively long-lived open carbonium ion intermediate in which the migration of o-tolyl is favored sterically and electronically. On the other hand, in the deamination of 2,2-diphenyl-2-o-tolylethylamine-1-^{14}C, this ratio is 0.75. If phenyl and o-tolyl have equal effective sizes, and if it is assumed that rearrangement is so rapid that no rotation of more than 60° occurs, the ratio is predicted to be 1.00.

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*It is interesting to note that Bonner and Tanner (69) have recently shown that the 3-phenyl-2-butanol-1,4-^{14}C from the deamination of 3-phenyl-2-butylamine-1-^{14}C has 50% of its ^{14}C in each of the 1 and 4 positions. This is in accord with a symmetrical phenonium ion as an intermediate in the formation of 3-phenyl-2-butanol from this amine.

**Consideration of the possible conformations of the diazonium ion shows that one diastereomer preferentially has methyl opposite to nitrogen (VII) while the other has phenyl in that position (VIII).

The value of 0.75 arises, according to the authors, from the fact that the conformation with the o-tolyl group trans to the diazonium group is less-favored.* It would be interesting to see if 2,2-diphenyl-2-p-tolylethylamine-1-^{14}C would give a migration ratio of 1.00 or even greater.

Let us now proceed to a detailed consideration of the mechanism of the amine-nitrous acid reaction. The initial step is assumed to be the formation of the alkyldiazonium ion (7). The work of Roberts and Yancey (8) rules against the incursion of a diazo compound as an intermediate, since they showed that the ethanol produced in the deamination of ethylamine in 99% deuterium oxide contained only the natural amount of deuterium. Similarly, Young and Semenow (9) have ruled out the occurrence of a diazo compound in the deamination of α- and γ-methylallylamines in deuteroacetic acid. The mechanistic problem thus centers about the mode of conversion of the alkyldiazonium ion to the final products. The most likely route is certainly by way of a carbonium ion, so the true controversy rages over the timing and intimate nature of the loss of the nitrogen molecule from the alkyl-

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*This is a very strange fact, if true, since presumably o-tolyl is the bulkiest group present and also the one of highest migration aptitude. Professor J. D. Roberts suggests that the conformation with o-tolyl trans to nitrogen is favored but that it is twisted, by the non-bonded interactions of the methyl group, out of the position of overlap most favorable to migration. Therefore, this conformation may give an unusual amount of migration with retention of configuration (via phenyl migration).

diazonium ion, and the consequent character of the carbonium ion so formed.

One possible mechanism has been already considered, i.e., the alkyldiazonium ion loses a molecule of nitrogen to form a "hot" unsolvated cation, which then undergoes the reactions characteristic of the amine-nitrous acid reaction. An opposite viewpoint maintains that any reactions unique to the deamination (as opposed to solvolysis) must occur simultaneously with the loss of nitrogen, and the cations remaining after the loss of nitrogen are to be regarded as normal, solvolytic cations.* The first interpretation has been recently defended by Cram and McCarty (20) while the second is supported by Streitwieser (16,23). These papers contain comprehensive references to previous researches.

Cram and McCarty emphasize that the driving force in the decomposition of the alkyldiazonium ion comes from formation of a nitrogen molecule and not from neighboring group or solvent participation. The open, flat carbonium ion formed by the loss of nitrogen is of such high energy that its half-life is much less than the half-life of rotation by 60° about the carbon-carbon bond. The fate of this "hot" cation is therefore determined by the proximity

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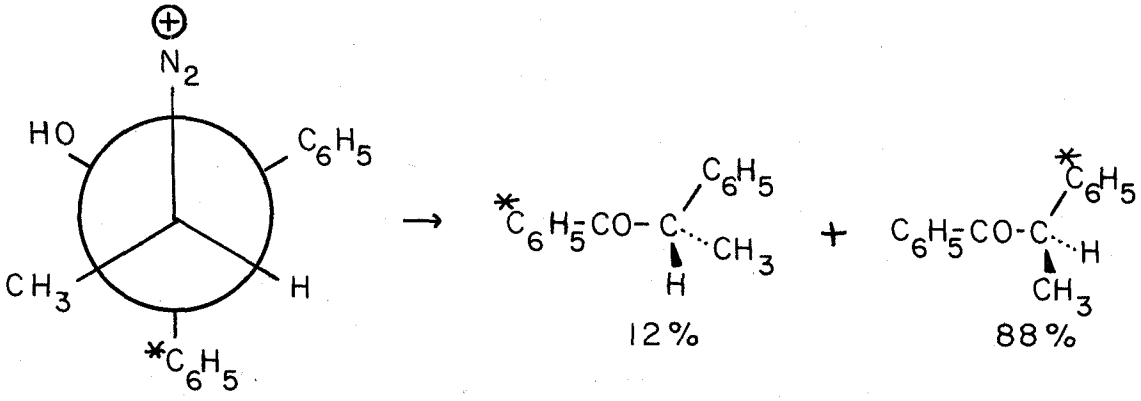
*Since there is no way to form a solvolytic primary cation, it is hard for one to predict exactly how such a cation should behave. See preceding discussion.

of its nearest neighbors, whether they be solvent molecules or neighboring atoms. If migration occurs, which group migrates is primarily determined by the conformation of the alkyldiazonium ion itself.

Recently, Benjamin, Schaeffer and Collins (24) have reported a very elegant study of the semipinacolic deamination of one optically active diastereomer of 1,1-diphenyl-2-amino-1-propanol labeled with ^{14}C in one phenyl ring. It



was found that about 25% of the phenyl α-phenylethyl ketone product was racemized, although products and reactants were stable under the reaction conditions. The racemization was explained when it was shown that almost every time the unlabeled phenyl migrated, the migration terminus had <u>retained</u> configuration. The proof consisted of showing that

about 12% of the product had rearranged unlabeled phenyl (corresponding to 24% racemization if each migration of unlabeled phenyl goes with retention of configuration). Furthermore, an almost racemic fraction, separated from the product mixture, had 44% of its ^{14}C in the phenyl bonded to the carbonyl and 53% of its ^{14}C in the α-phenylethyl group (calculated 50% of the ^{14}C in each fragment for a pure racemic mixture if all migrations of unlabeled phenyl occur with retention of configuration). These findings are the first unequivocal demonstration of a flat, open carbonium ion in deamination reactions. The time for rotation through 60° about the carbon-carbon single bond is apparently comparable to the rate of phenyl migration, and for at least 12% of the phenyl migration, a rearrangement occurring simultaneously with the loss of nitrogen is not a reasonable possibility. These last experimental data are readily accommodated in the scheme of Cram and McCarty and lend some support to the existence of a "free" cation and to the assumption of rapid migrations. As Cram and McCarty indicate, the observed small differences in migratory aptitudes in the deamination reaction, when compared to solvolyses reactions, are also in agreement with postulation of a highly reactive, relatively unselective intermediate.

A recent report by Young (80) provides still further support for the "hot" ion mechanism. An extensive study was undertaken of the previously-mentioned tendency of allylic amines to react at the same carbon atom from which the amino

group departs as nitrogen. In two experiments, pure optically active α-methylallylamine was deaminated in acetic acid in the presence of acetate ion. Although the concentration of acetate differed by 340-fold between the two experiments, the products were identical, both as to relative amounts of the two isomeric acetates and as to optical activity (slight predominance of inversion over retention). Young (80) proposes the intermediacy of a "hot" carbonium ion, "whose formation does not require a distribution of charge and which reacts with predominant racemization but no rearrangement." This "hot" carbonium ion reacts before it has a chance to change conformation and distribute its charge by resonance.*

The opposition to this "hot" carbonium ion mechanism, as exemplified by Streitwieser (16,23), agrees that the driving force for the decomposition of an alkyldiazonium ion is derived from the loss of a nitrogen molecule. However, according to this author, the alkyldiazonium ion can enter many reaction paths simultaneously with the loss of the nitrogen molecule. It can (a) undergo an S_N2 reaction with

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*In his presentation, Young (80) implies that part of the reaction goes via the "hot" ion while the rest follows another route (which apparently resembles a solvolysis). He makes no explicit mention of the possibility that all of the reaction goes via the "hot" ion, which then enters alternate pathways, one of which may be solvation. A cation of the latter kind might behave as a solvolytic cation.

solvent; (b) lose a hydrogen ion to give olefin; (c) undergo hydrogen or carbon migration to form a normal, rearranged carbonium ion; or (d) just lose nitrogen to form a normal, unrearranged carbonium ion. In this scheme, Streitwieser (16,23) believes that the migrating group is best viewed as being "pulled over" rather than supplying a "push," as in anchimeric-assisted solvolyses. Since this scheme predicts the stereochemistry of migrations in terms of relative populations of conformations of the alkyldiazonium ion, just as the "hot" atom mechanism does, it will generally be exceedingly difficult to differentiate between the two mechanisms. The work of Benjamin, Schaeffer and Collins (24) and of Young (80) are the best examples extant in which some distinction can be drawn, and in both cases, the data favor the "hot" carbonium ion mechanism.

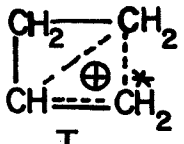
II. RESULTS AND DISCUSSION

Forward

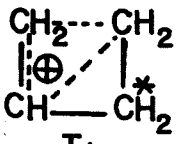
The purpose of the present research was to examine the effect of methyl groups substituted at a methylene carbon atom upon the non-classical "bicyclobutonium" ion intermediates Ia-c. There are seven isomeric five-carbon cyclopropylcarbinyl, cyclobutyl and allylcarbinyl derivatives (X-XVI) that can give rise to such intermediates (IXa-c) by processes involving only interchanges of rings and double bonds. The amines of structures X-XV have been synthesized and treated with nitrous acid and the resultant alcohol mixtures analyzed. In addition, the solvolysis rates of some esters and bromides of X-XIII have been determined and the behavior of the alcohols of structures X-XV under strongly acidic conditions has been examined. No efforts were ever made to separate cis-trans isomers, where the possibility for such exist.

Solvolyses

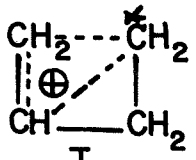
The original intent of this investigation was to synthesize and measure the rates of solvolysis of the bromides of the isomeric five-carbon compounds X-XVI. 3-Methylcyclobutyl bromide was readily prepared as a mixture of cis-trans isomers by conventional means. However, all efforts to convert cyclopropylmethylcarbinol to the corresponding bromide failed, extensive rearrangement apparently taking place. Attempts were made to determine the nature of the resultant bromides. The vapor phase chromatographic spectrum



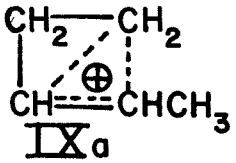
Ia



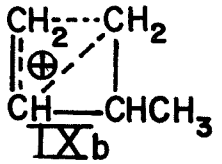
Ib



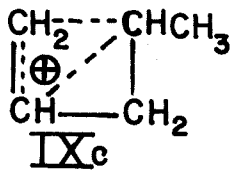
Ic



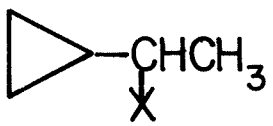
IXa



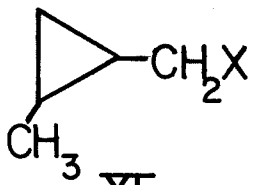
IXb



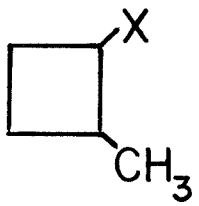
IXc



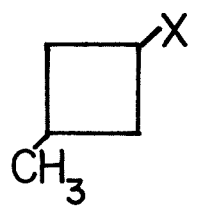
X



XI

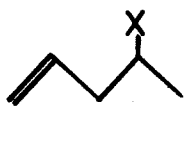


XII



XIII

XIV



XV

XVI

(hereinafter v.p.c.) showed three peaks, the relative sizes of which varied slightly depending upon the synthetic method employed.

The peak of greatest retention time and of largest size (80%) was most likely crotylcarbinyl bromide for the following reasons. Firstly, in the v.p.c.'s of alcohols X-XVI, crotylcarbinol has the longest retention time; the bromides might follow the same order of appearance as the alcohols. Also, the infrared spectrum of the bromide mixture was similar in many respects to that of crotylcarbinol. The nuclear magnetic resonance spectrum (n.m.r.) of the bromide mixture was nearly identical to that of crotylcarbinol except, of course, for the O-H proton peak. 1-Cyclopropylethanol-1-^{2}H was synthesized and converted to the bromide mixture. Qualitative n.m.r.'s of the bromides prepared from the deuterated and undeuterated alcohols, when compared, also showed the effects expected if the predominant species present was crotylcarbinyl bromide. Thus, in the spectrum of the deutero-bromide ($CH_3CD = CHCH_2CH_2Br$), the peak assigned to the methyl group was no longer split into two and the vinylic hydrogen peak was diminished by about one-half.

Referring back to the v.p.c. of the bromide mixture, the peak of medium retention time, representing 8-14% of the total peak area, was arbitrarily assigned to the desired cyclopropylmethylcarbinyl bromide. The reason for this association, aside from the relative retention time, was that the percentage approximately corresponds to that for a very reactive

bromide, as estimated from the solvolysis data (*vide infra*). The peak of shortest retention time was 3-5% of the total peak area, and had the same retention time as allylmethylcarbinyl bromide. No attempt was made to confirm this tentative assignment.

The rates of solvolysis of 3-methylcyclobutyl bromide and of the bromide mixture were measured at 25° in 50% ethanol-water. Under these conditions, cyclobutyl bromide exhibits first-order kinetics, $k_1 = 4.2 \times 10^{-6}$ sec.$^{-1}$ (2). 3-Methylcyclobutyl bromide solvolyzes with a sharply decreasing k_1. The possibility that the *cis* and *trans* isomers, which most certainly occur in the material, solvolyze at highly different rates cannot be excluded. However, since cyclobutyl bromide is so reactive under the same conditions (2), it seems unreasonable to propose that a methyl group either *cis* or *trans* to the bromine atom in the 3-position of the cyclobutyl ring could cause the compound to be essentially unreactive.

The most likely alternative explanation is that 3-methylcyclobutyl bromide undergoes two competing first-order reactions, one leading to solvolysis products and one giving rearranged, slightly reactive bromide (76). This latter might be allylmethylcarbinyl bromide, for instance. Calculations (see Experimental) based on such a reaction scheme give k_1 for the formation of products as 3.47×10^{-6} sec.$^{-1}$, while k_2 for the rearrangement equals 8.2×10^{-6} sec.$^{-1}$.

The solvolysis curves of the various bromide mixtures from the cyclopropylmethylcarbinyl bromide preparations all

indicated the presence of ca. 10% of an extremely reactive compound. After two hours, reaction essentially ceased. An estimate, probably on the low side, for cyclopropylmethylcarbinyl bromide is $k_1 = 170 \times 10^{-6}$ sec.$^{-1}$ (see Experimental).

Several p-nitrobenzoate esters were prepared, and the rates of acid-catalysed solvolysis in 80% acetone measured at 94.7° (77). Most of the plots exhibited poor first-order rate curves. The reason for this behavior is not clear but may have been tied, in some way, to instability of the solvent mixture at the elevated temperature employed. No control runs on pure solvent were made. Details for these kinetics are in the Experimental and the results are summarized in Table I. The solvolysis of some p-bromobenzenesulfonates (brosylates) at 25° in 50% ethanol-water were also carried out and these results are included in Table I.

Examination of Table I immediately reveals that the relative reactivities exhibited by the p-nitrobenzoates are far out of line with all the other results, so discussion of the former will be deferred. The salient feature of Table I is that the enhanced reactivity observed (2) for cyclobutyl and cyclopropylcarbinyl derivatives has been retained, and perhaps even increased, in the methyl-substituted compounds. Cyclopropylmethylcarbinyl derivatives (even the p-nitrobenzoate) are exceedingly reactive. Cyclobutyl and methyl-substituted cyclobutyl derivatives are all of the same order of reactivity, and are all as reactive as the corresponding allyl derivatives.

TABLE I

SOLVOLYSIS RATE CONSTANTS OF RX

R =	X = Cl[2] (10^6 sec.$^{-1}$)	Br[b] (10^6 sec.$^{-1}$)	$\underline{p}$-$NO_2C_6H_4CO_2$[c,d] (10^6 sec.$^{-1}$)	$\underline{p}$-$BrC_6H_4SO_3$[b,d] (10^4 sec.$^{-1}$)
Cyclopropylcarbinyl	125[e]	94[e]	2.8	
Cyclobutyl	4.7[e]	4.2[e]	3.3	11.8
Cyclopropylmethylcarbinyl		170[d]	110	
2-Methylcyclopropylcarbinyl			3.2	
2-Methylcyclobutyl			2.8	24[f]
3-Methylcyclobutyl		11.7[d,f]	2.6	7.0[f]
Allyl		3.6[e]		5.2
Cyclopentyl			1.2	

[a] 50% ethanol at 50°. [b] 50% ethanol at 25°. [c] 80% acetone at 94.7°, ($HClO_4$) = 0.0524 M. [d] This work. [e] Ref. 2. [f] Total rate of ionization, equal to rate of solvolysis plus rate of rearrangement.

The p-nitrobenzoates were prepared in the hope that the acid-catalysed solvolysis would resemble the deamination reaction, in that for both reactions, a neutral molecule is leaving a developing cationic center. However, all the compounds studied, with the exception of cyclopropylmethylcarbinyl, show about the same k_1. This is especially striking in comparing cyclopropylcarbinyl and cyclobutyl, for the chloride of the first-named structure is 27 times more reactive than that of the second. A possible rationalization is that in the acid-catalysed solvolysis, no ion pair is formed and no electrostatic attraction between oppositely charged entities has to be overcome. The transition state for the acid-catalysed solvolysis may therefore come at a position in the reaction coordinate* that bears greater resemblance to the starting materials, with less positive charge developed on the carbon atom. Such a factor, in turn, might decrease the necessity, or perhaps rather, the opportunity for delocalization of the positive charge (less positive charge is available for delocalization) and much of the ability of the rest of the

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*As a crude example, consider the fact that the uncatalysed solvolysis of the p-nitrobenzoates under the same conditions of solvent and temperature is immeasurably slow. This tells us that the energy of activation for the catalysed reaction is probably less than that of the uncatalysed reaction, so that, by the Hammond postulate (72), the transition state for the first reaction bears more resemblance to the starting material than does the transition state for the second reaction. However, according to the same principle, the transition state for halide solvolysis bears a greater resemblance to starting material than does that for the catalysed p-nitrobenzoate reaction, since the former presumably has a lower activation energy. Thus the alkyl halides should show even less spread in reactivity, which is not observed.

molecule to expedite the solvolysis will be lost. This hypothesis could be tested in many ways.

The important point to be derived from the kinetic data, however, is that the high reactivity of both the cyclobutyl and cyclopropylcarbinyl derivatives, as discussed in the Introduction, is best understood in terms of non-classical cationic intermediates. We shall consider, in the next section, whether the compounds at hand can be accommodated in a scheme of intermediates similar to that outlined in the Introduction for the unmethylated derivatives.

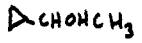
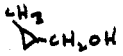
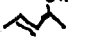
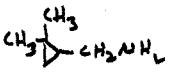
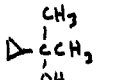
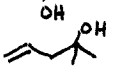
Amine-Nitrous Acid Reactions

The deamination of the amines of structures X-XV and of 2,2-dimethylcyclopropylcarbinylamine was carried out in aqueous perchloric acid, with the intent of learning something about the relative stabilities of the carbonium ion intermediates formed under these conditions of kinetic control. Table II records the results of the amine experiments and the Experimental contains the details. It was established that the alcohols were stable to the reaction conditions; analyses are good to ±2%, in general.

The great variety in both kinds and amounts of products formed rule out a common methyl-substituted "tricyclobutonium" intermediate resembling II. Let us focus our attention on the three non-classical unsymmetrical intermediates, IXa-c, which are similar to Ia-c except that the ^{14}C label has been replaced by a methyl group. The introduction of this methyl

TABLE II

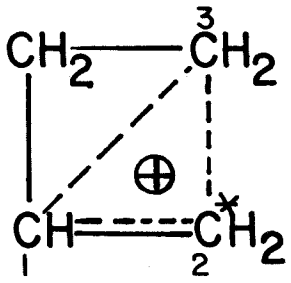
PERCENT COMPOSITION OF THE ALCOHOL MIXTURES OBTAINED IN THE DEAMINATION OF METHYL-SUBSTITUTED CYCLOBUTYL-, CYCLOPROPYLCARBINYL- AND ALLYLCARBINYLAMINES.[a]

Alcohol	Amine					
	100	51	100	47	17	74
	0	13	0	9	3[b]	0
	0	0	0	0	0	0
	0	0	0	5	0	0
	0	35	0	39	49	0
	--	--	--	--	25	--
	--	--	--	--	6[b]	--
	0	0	0	0	0[b]	10
	--	--	--	--	--	16
						
	17					
	83					

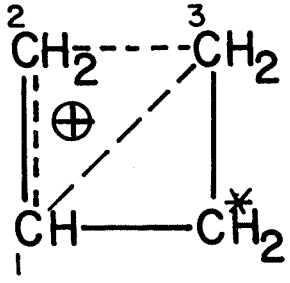
[a]A dash(--) indicates that no effort was made to identify this alcohol in the reaction mixture. As the Experimental shows, at least 90% of each product mixture was identified. [b]The identification of this alcohol was unsure (see Experimental).

group, of course, means that Ia-c are no longer equally stable and we must now consider how large the effect of the methyl will be in determining the relative stabilities of IXa-c. IXb, in which the methyl group does not help in stabilizing the positive charge, must certainly be the intermediate of highest energy. The formation of cyclopropylmethylcarbinol in the deamination of all these amines shows that IXa is more stable than IXc (see Table II and later discussion; cyclopropylmethylcarbinol is formed only from IXa) and an explanation can be offered for this. In Ia-c (the intermediates without methyl substituents), the positive charge lies primarily on the two carbon atoms at which reaction occurs to give cyclobutyl and cyclopropylcarbinyl products (C_1 and C_2 of Ia-c) (2,4). A methyl group at C_1 or C_2 can thus be more effective in stabilizing the positive charge than one at C_3. Therefore, IXa, in which the methyl group is at C_2, should be of lower energy than IXc, in which the methyl group is at C_3. The effects of a methyl group at C_1 were studied by Cox, Silver and Roberts (1,5).

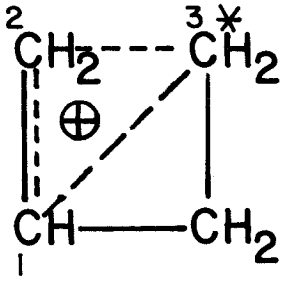
One of the most interesting properties of unsymmetrical ions IXa-c is their mode of interconversion. By analogy to Ia-c complete interconversion may occur by way of a methyl-substituted symmetrical pyramidal transition state similar to II, and some such transition state is indeed necessary to interconvert IXc with IXa or IXb (cf. Introduction). In the present case however, the symmetrical transition state may open preferentially to the most stable "bicyclobutonium"



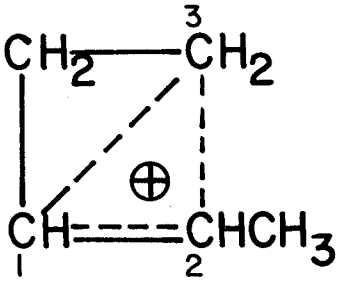
Ia



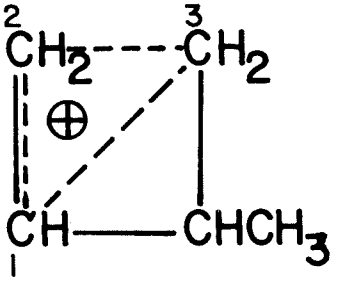
Ib



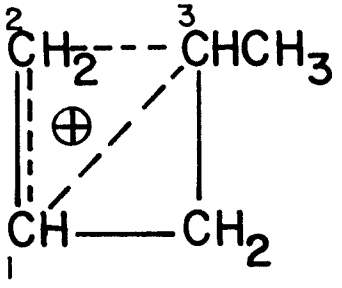
Ic



IXa



IXb



IXc

ion, IXa. In addition, the possible low-energy route previously suggested for the interconversion of "bicyclobutonium" ions Ia and Ib is available for interconverting IXa and IXb. Here again, however, the non-equivalent stability of IXa-c introduces an added degree of complexity and the previously reversible interconversions may tend, under these kinetically-controlled conditions where the stability of the cations is paramount, toward essentially one-way reactions--thus, IXb is probably converted relatively rapidly to IXa and slowly (if at all) to IXc while IXc is converted relatively slowly to IXa.

As to the products formed by reaction of these cations with water, reaction of IXa at positions 1, 2 and 3 gives 2-methylcyclobutanol, cyclopropylmethylcarbinol and crotylcarbinol respectively; reaction of IXb at positions 1, 2 and 3 gives 2-methylcyclobutanol, 2-methylcyclopropylcarbinol and α-methylallylcarbinol respectively; reaction of IXc at positions 1, 2 and 3 gives 3-methylcyclobutanol, 2-methylcyclopropylcarbinol and allylmethylcarbinol respectively (Fig. 1). In regards to formation of IXa-c, it would appear that in that fraction of each deamination which follows the scheme of Fig. 1, the "bicyclobutonium" ion initially formed is the most stable one which can be formed <u>directly</u> from the starting amine. As an example, 2-methylcyclobutylamine can close to either IXa or IXb. Since the deamination of this amine gives cyclopropylmethylcarbinol as the sole product, it appears that

only cation IXa is formed.* Presumably the same preferential formation of the most stable unsymmetrical ion occurs as well in other carbonium ion reactions of this family of compounds.

Fig. 1 has been constructed primarily on the basis of the product distributions in the amine-nitrous acid reactions. It has been assumed that the relative amounts of these products reflect the respective barrier heights for going from an intermediate to such products. For instance, 2-methylcyclopropylcarbinol and allylmethylcarbinol are both formed from intermediate IXc. Since the first alcohol is formed in consistently smaller amounts than the second, it is reasonable to assume that the activation energy for the formation of the former alcohol is larger. The possible reaction paths for each of the unsymmetrical intermediates will now be considered in detail, taking the intermediates one at a time.

The least stable intermediate, IXb, is probably only formed from α-methylallylcarbinyl derivatives, and none of these have been studied. Since the methyl group of IXb is fairly well insulated from the region of positive charge, the properties of IXb should be predictable, however, from those of unmethylated unsymmetrical ion Ib. It is known (see Introduction) that Ib gives cyclobutanol, cyclopropylcarbinol and allylcarbinol in the ratio of 10:10:1, respectively. Therefore,

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*The possibility cannot be eliminated, with the data at hand, that 2-methylcyclobutylamine also closes to IXb, but that IXb converts rapidly and exclusively to IXa. If the deamination of α-methylallylcarbinylamine afforded products derived from IXb, the latter explanation would be proven false.

IXb will probably give about equal amounts of 2-methylcyclobutanol (A) and 2-methylcyclopropylcarbinol (C) and a lesser amount of α-methylallylcarbinol (B). The barriers should therefore be in the order B > A ~ C. The barriers for conversion of IXb to the other intermediates (barrier D, for conversion to both of the other "bicyclobutonium" ions via the symmetrical transition state, and barrier E, for conversion to the "short-cut" partner IXa) must be relatively small.* If the "short-cut" path is available,** D > E and B > A ~ C > D > E.

As to intermediate IXc, the one of medium stability, since 3-methylcyclobutylamine and 2-methylcyclopropylcarbinylamine give nearly equal amounts of allylmethylcarbinol (J) and cyclopropylmethylcarbinol (via K through IXa), it appears that the barriers J and K are of about the same height (assuming all of IXa goes to cyclopropylmethylcarbinol, as is suggested by the fact that 2-methylcyclobutylamine and cyclopropylmethylcarbinylamine give only this alcohol upon deamination).

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*As will be seen immediately, the fact that the ion of intermediate stability (IXc) affords products derived both from itself and from the most stable unsymmetrical ion (IXa) indicates that the barrier to conversion of IXc to a more stable ion (IXa) is of the same order of magnitude as the barrier to the formation of product. All the barriers (D, E and K) to the formation of more stable intermediates from less stable ones should be of about the same height, the major differences arising in distinguishing between the "short-cut" path and the "tricyclobutonium" transition state.

**If such a path is available, the deamination of α-methylallylcarbinylamine would have to give more cyclopropylmethylcarbinol relative to allylmethylcarbinol than did either 2-methylcyclopropylcarbinylamine or 3-methylcyclobutylamine. However, observation of such "excess" cyclopropylmethylcarbinol would not prove the existence of an alternate low-energy path, since "excess" cyclopropylmethylcarbinol might just as well arise from preferential formation of IXa relative to IXc by way of the "tricyclobutonium" transition state.

K (for converting IXb to IXc) and D (for converting IXc to IXa) are probably nearly equal since they both apparently involve formation of the "tricyclobutonium" transition state. Barriers F and M, for reaction of IXc to form 3-methylcyclobutanol and 2-methylcyclopropylcarbinol respectively, should be relatively large, since products formed *via* these routes involve reaction at a cationic center that bears only a small amount of positive character (most of the positive charge of IXc must lie on the carbon bearing the methyl group). The formation of both 3-methylcyclobutanol and 2-methylcyclopropylcarbinol from 3-methylcyclobutylamine but of no detectable amount of 3-methylcyclobutanol from 2-methylcyclopropylcarbinylamine means that barrier F (IXc to 3-methylcyclobutanol) is greater than barrier M (IXc to 2-methylcyclopropylcarbinol). The probable formation of 2-methylcyclopropylcarbinol in the deamination of allylmethylcarbinylamine is also in accord with this idea. There is no *a priori* reason for the intrusion of this difference between the heights of F and M, since in intermediate Ic, without the methyl group, the two comparable barriers are of equal height (Ic to cyclobutanol and cyclopropylcarbinol), and it would seem that the barriers for reaction at these two positions would be affected nearly the same by the introduction of a methyl group at the third reactive position in the intermediate. One could introduce an alternate reaction sequence to explain the formation of 2-methylcyclopropylcarbinol in the deamination of 3-methylcyclobutylamine, and then attribute the formation of

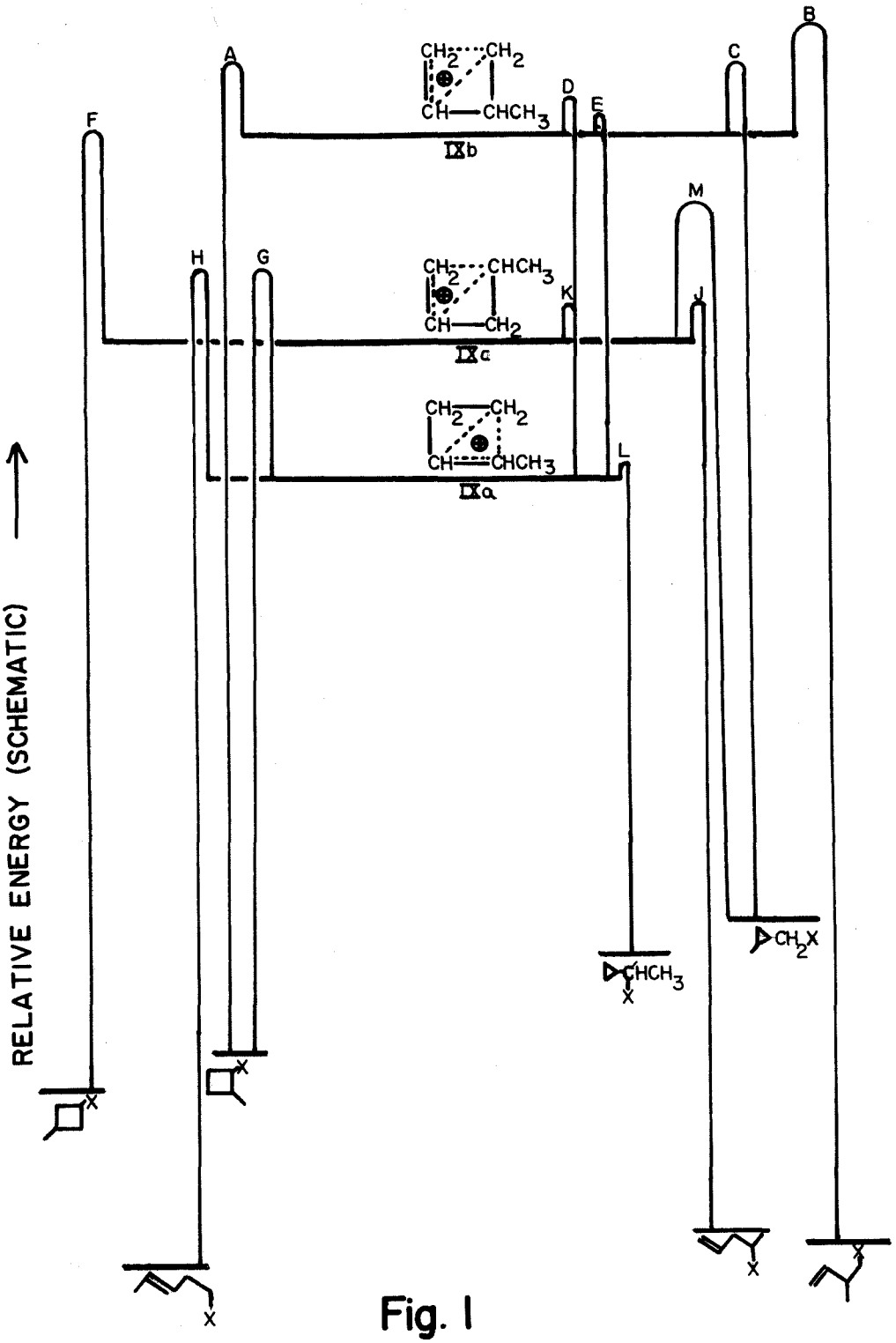
RELATIVE ENERGY (SCHEMATIC)
A
B
C
D
E
F
G
H
J
K
L
M
IXb
IXc
IXa
CH2X
CHCH3
X

Fig. 1

3-methylcyclobutanol from this amine, and of 2-methylcyclopropylcarbinol in the deamination of 2-methylcyclopropylcarbinylamine, to a non-rearranging, S_N2-type reaction (see Introduction). This picture also involves numerous assumptions and has no special merit, so the explanation based on unequal barrier heights is favored. The barriers for IXc are thus F > M > J ~ K, and combined with those for IXb F > M > B > A ~ C > D ~ J ~ K > E. Intermediate IXc is presumably formed from 3-methylcyclobutylamine, 2-methylcyclopropylcarbinylamine and allylmethylcarbinylamine.*

Only the barriers to reaction of intermediate IXa remain to be defined. IXa, formed necessarily by cyclopropylmethylcarbinylamine and crotylcarbinylamine and preferentially by 2-methylcyclobutylamine, gives only cyclopropylmethylcarbinol upon reaction with water. The barrier for formation of this product (L) must be small, perhaps about the same as E (which is the barrier to the "short-cut" interconversion). The barriers G (IXa to 2-methylcyclobutanol) and H (IXa to crotylcarbinol) must be large, since neither of these products is formed from IXa (the crotylcarbinol formed in the deamination of crotylcarbinylamine must arise from an alternate reaction path and not from IXa). Barriers G and H are

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*The deamination of the open-chain amines is more complicated than that of the small-ring amines, since the former give hydride-shift products whereas the latter do not.

probably about as large as F, which is the barrier for the conversion of IXc to 3-methylcyclobutanol, a process that was also unobserved. The final barriers are therefore

$$F \sim G \sim H > M > B > A \sim C > D \sim J \sim K > E \sim L,$$

where the height for conversion to either an intermediate or a product is measured from the level of the less stable of the two species being considered.

Nearly all the information for completing Fig. 1 has been presented. Previous studies (2) have established that the decreasing order of stability of products is allylcarbinyl $\gg$ cyclobutyl $>$ cyclopropylcarbinyl and the methyl-substituted compounds should be similarly related. Differences within the group-types are relatively small but, non-bonded interactions between 1,2-substituents may decrease the stability of 1,2-disubstituted small-ring compounds. There is some evidence that the allylmethylcarbinyl structure is less stable than the crotylcarbinyl structure under conditions of strong acidity.* In addition, a terminal double bond is less favorable than a more highly substituted one (73).

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*T. A. Favorskaya and Sh. A. Fridman, J. Gen. Chem., 20, 413 (1950); Chem. Abs., 44, 7753a (1950) report that allylmethylethylcarbinol rearranges to 4-methyl-3-hexen-1-ol at reflux temperature with 25% sulfuric acid. We observed that allylmethylcarbinol only polymerized under these conditions; no crotylcarbinol was observed.

While the results of the treatment of alcohols of structure X-XV with strong acid should not be given great weight, they are in accord with the scheme of Fig. 1. The cyclopropylcarbinols rearranged to allylmethylcarbinol extremely rapidly. The fact that cyclopropylmethylcarbinol gave no detectable 2-methylcyclobutanol or crotylcarbinol indicates G and H probably rise above J in Fig. 1. The cyclobutyl alcohols were only rearranged under more forcing conditions, the 2-methyl alcohol reacting at least five times faster than the 3-methyl alcohol (in solvolysis, the 2-methyl brosylate was three times more reactive than the 3-methyl brosylate). The open-chain alcohols were recovered unchanged in all experiments.

The behavior of 2,2-dimethylcyclopropylcarbinylamine with nitrous acid also fits the scheme of Fig. 1. The intermediate corresponding to IXc, when compared to IXc itself, is seen to have an even more highly localized charge, with a consequent greater barrier for conversion to the IXa-type intermediate and a lower barrier for reaction to give allyldimethylcarbinol. The formation of cyclopropyldimethylcarbinol shows that some of the conversion to the IXa-type intermediate still occurs. This high but not complete localization of charge is analogous to the effect wrought by one methyl group in the 1-methylcyclobutyl series of compounds (1,5). Surprisingly, the v.p.c. of the deamination product of 2,2-dimethylcyclopropylcarbinylamine showed no

peak that could be assigned to 2,2-dimethylcyclopropyl-carbinol. Assuming that the retention time of this alcohol is not identical with that of the two alcohols detected and that it is stable under the reaction conditions, the unexplained reaction of IXc to give 2-methylcyclopropyl-carbinol does not occur with the dimethyl derivative. Indeed, no detectable S_N2-type reaction takes place; substitution occurs only at the tertiary cationic center.

III. EXPERIMENTAL

All melting points and boiling points are uncorrected. Analyses by A. Elek, Los Angeles, California. Typical experiments are described for most preparations. Infrared spectra and v.p.c.'s are at the end of the Experimental. Appendix I gives detailed descriptions of all distillation columns.

Cyclopropylcarbinol was prepared in 33% yield by the reduction of cyclopropanecarboxylic acid (37) with lithium aluminum hydride in ether solution. The low yield was attributed to the poor grade of hydride used. The product had b.p. 121-122°, $n^{25}D$ 1.4300 (lit. b.p. 122-123° (26), $n^{25}D$ 1.4300 (2)).

The p-nitrobenzoate was recrystallized from hexane, m.p. 52.6-54.6°.

Anal. Calcd. for $C_{11}H_{11}O_4N$: C, 59.72; H, 5.01. Found: C, 60.00; H, 4.93.

1,1-Dicarbethoxycyclobutane was prepared according to Mariella and Raube (27), b.p. 109° (16.3 mm.), $n^{25}D$ 1.4330.

1,1-Cyclobutanedicarboxylic Acid.--To a solution of 210 g. (3.75 moles) of potassium hydroxide in 333 ml. of ethanol and 1250 ml. of water in a 2-ℓ. round-bottomed flask was added 250 g. (1.25 moles) of 1,1-dicarbethoxycyclobutane and the resultant mixture was heated under reflux for 4 hr., concentrated to about 300 ml., cooled in an ice bath and acidified with ice-cold dilute sulfuric acid. The aqueous solution

was extracted with ether, and the ether solution was dried over magnesium sulfate, filtered and concentrated. The product was filtered off, wt. 141 g. (79%). A small amount of the acid was recrystallized from benzene, m.p. 157.6-158.4° (lit. m.p. 156-158° (30)).

1,1-Cyclobutanedicarbonyl chloride was prepared in 90% yield by heating 170 g. (1.18 moles) of 1,1-cyclobutanedicarboxylic acid and 500 g. (4.2 moles) of thionyl chloride under reflux for several hours and distilling the residue. The product had b.p. 90-95° (30-40 mm., water aspirator).

Cyclobutanone.--Efforts were directed to finding a safe way of preparing this compound from cyclobutane-1,1-dicarbonyl chloride, in high yield, but no successful procedure was found (indeed, one preparation exploded). Brief descriptions are given for some of the experiments performed.

To a solution of 33 g. (0.5 mole) of sodium azide in 100 ml. of water in an 800-ml. beaker was added, with stirring, 250 ml. of acetone. The suspension was cooled to 5° in an ice bath and, with good stirring, 25 g. (0.168 mole) of 1,1-cyclobutanedicarbonyl chloride was added at such a rate that the addition was completed within 15 min. Stirring was maintained for 15 min. The solution was poured into a mixture of 1000 ml. of water and 100 ml. of ether, the ether layer separated and the aqueous phase extracted with four 100-ml. portions of ether. The combined ether layers were dried over potassium carbonate and decanted into a 1-ℓ., round-bottomed one-necked flask which contained 175 ml. of

n-butyl cellosolve and many boiling chips. To the flask there was attached a condenser positioned for downward distillation. The ether was distilled and the azide decomposed smoothly, using pans of warm water as a heat source. The solution was heated at 100° for 15 min., a solution of 12.5 ml. of sulfuric acid in 200 ml. of water was added, and the resultant solution, after being allowed to stand for 15 min., was distilled until 200 ml. of distillate had been collected. The distillate was saturated with potassium carbonate, the layers separated, and the aqueous layer extracted with an equal volume of n-butyl cellosolve. The combined organic solutions were dried over magnesium sulfate, filtered and fractionated, the material boiling between 75° and 96° being saved (two layers). This distillate was saturated with potassium carbonate, the organic phase separated, redried and redistilled and the fraction of b.p. 94.5-97.2° (2.65 g., 26.5%) taken as product.

An attempt to separate the ketone from the original steam distillate *via* the bisulfite complex gave only 1.4 g. (14%) of product, b.p. 96-98°.

Decomposition of the azide in propylene glycol gave 2.7 g. (27%) of cyclobutanone, b.p. 97-97.5°, fractionated through column 3.

Decomposition in propylene glycol, followed by heating the sulfuric acid solution under reflux for 2.5 hr. before distillation gave 5.4 g. (56%) of cyclobutanone, b.p. 97-100°, through column 3. A run on twice the usual scale was too

large to be managed conveniently, but gave 8.1 g. (42%) of cyclobutanone.

Decomposition in xylene followed by heating the sulfuric acid solution under reflux for several hr. gave yields of 30-40%. A run with xylene and immediate distillation of the sulfuric acid solution gave a 50% yield of cyclobutanone.

Some cyclobutanone was carefully fractionated through column 3 and had b.p. 96.5° (lit. b.p. 98-100° (28)).

Cyclobutanol was prepared in 80% yield by the reduction of 10 g. (0.143 mole) of cyclobutanone with 1.5 g. (0.04 mole) of lithium aluminum hydride in ether solution and had b.p. 119-120°, $n^{25}D$ 1.4333-1.4340 (lit. b.p. 125°, $n^{25}D$ 1.4347 (28)).

The p-nitrobenzoate had m.p. 84.0-85.3° after recrystallization from hexane.

Anal. Calcd. for $C_{11}H_{11}O_4N$: C, 59.72; H, 5.01. Found: C, 59.59; H, 4.98.

Cyclobutyl p-Bromobenzenesulfonate.--Sodium hydride (0.8 g.) was suspended in about 10 ml. of ether in a 100-ml. three-necked, round-bottomed flask equipped with mechanical stirrer, dropping funnel and reflux condenser. Cyclobutanol (1.24 g.) was added and the mixture heated under reflux for 30 min. A solution of 3.8 g. of p-bromobenzenesulfonyl chloride in 15 ml. of ether was added and the resultant mixture was heated under reflux for 1 hr. Water (15 ml.) was added and the layers separated. The ether solution was dried

over magnesium sulfate, filtered, the filtrate concentrated at reduced pressure at room temperature and then frozen in Dry Ice. Upon warming there was obtained a mixture of solid and liquid. The solid was removed by filtration and recrystallized with care from ether, m.p. 52.5-53.0°. This material titrated 95-96% of the theoretical amount in kinetic runs and was fairly stable at room temperature.

Cyclopropylmethylcarbinol was prepared in 71% yield by the reduction of cyclopropyl methyl ketone (62.7 g., 0.746 mole) with lithium aluminum hydride (11.4 g., 0.3 mole) in ether solution, and had b.p. 120-121°. Some of the material was redistilled through column 3, b.p. 122-124°, $n^{25}D$ 1.4292-1.4298 (lit. b.p. 123.5°, $n^{20}D$ 1.4316 (29)).

The p-nitrobenzoate was recrystallized from hexane, m.p. 54-55.5°.

Anal. Calcd. for $C_{12}H_{13}O_4N$: C, 61.27; H, 5.57. Found: C, 61.55; H, 5.46.

The p-bromobenzenesulfonate could not be prepared.

1-Cyclopropylethanol-1-^2H.--In a 100-ml., three-necked, round-bottomed flask equipped in the usual manner were placed 1.2 g. (0.0286 mole) of lithium aluminum deuteride and 50 ml. of ether. The flask was cooled in an ice bath and 9 g. (0.107 mole) of cyclopropyl methyl ketone was slowly added. The mixture was stirred at room temperature overnight and then 8 ml. of ethylene glycol was added and the mixture distilled through column 1. The product, b.p. 118-121°, weighed 7.06 g. (77%).

Attempted Preparation of Cyclopropylmethylcarbinyl Bromide.--A 100-ml., round-bottomed, three-necked flask equipped with mechanical stirrer and two calcium chloride drying tubes was flamed out and cooled in a Dry Ice-acetone bath. The drying tubes were removed and anhydrous hydrogen bromide was passed into the flask until more than 5 ml. had condensed. Cyclopropylmethylcarbinol (10 g., 0.116 mole) was added slowly with vigorous stirring and more hydrogen bromide was condensed in the flask. Stirring was maintained at this temperature for 15 min., and the solution was then slowly warmed to 0°. The material was washed with dilute sodium bicarbonate solution and water at 0°. Ether (20 ml.) was added, the solution was dried over magnesium sulfate, filtered and distilled through column 1. The middle fraction had b.p. 48-50° (115 mm.), $n^{25}D$ 1.4674, yield 32.5%. The infrared spectrum and nuclear magnetic resonance spectrum (n.m.r.) indicated it was mainly crotylcarbinyl bromide (see Discussion).

Anal. Calcd. for C_5H_9Br: C, 40.29; H, 6.09. Found: C, 40.02; H, 6.55.

A similar preparation was carried out using 1-cyclopropylethanol-1-^2H (2.3 g.) and gave 2.9 g. (74%) of deuterobromide, b.p. 122°. The various spectra of this mixture were consistent with a predominance of 3-penten-1-ol-4-^2H.

The general method of Coe, Landauer and Rydon (31) for the preparation of bromides was tried. In a 100-ml.

distilling flask was placed 18.5 g. (0.060 mole) of triphenyl phosphite. In the neck of the flask was placed a dropping funnel, and the sidearm was protected with a drying tube. Bromine (9.1 g., 0.057 mole) was slowly added to the cooled flask, and a vigorous reaction was observed. The thick yellow oily product slowly grew large, snow-white crystals of exceptional beauty. Cyclopropylmethylcarbinol (5 g., 0.058 mole) was added, the flask was corked and the sidearm of the distillation flask fitted with a test tube with sidearm. The system was evacuated to 70 mm. and the flask placed in an oil bath while the test tube was cooled in a Dry Ice bath. The temperature of the oil bath was slowly raised to 95°, distillation was halted, the distillate was washed with aqueous sodium bicarbonate, diluted with ether, dried over magnesium sulfate, filtered and distilled through column 1, wt. 2.6 g., b.p. 122.5-124°, $\underline{n}^{25}D$ 1.4650-1.4660. The preparation was also carried out on 1-cyclopropylethanol-1-^{2}H. Infrared spectra and n.m.r.'s of both products were similar to those of the corresponding materials from the hydrogen bromide preparation.

Cyclopropylmethylcarbinylamine was prepared by Dr. R. H. Mazur (32) and isolated as the amine hydrochloride in 54% yield from 20.8 g. (0.21 mole) of methyl cyclopropyl ketoxine and 11.7 g. (0.31 mole) of lithium aluminum hydride.

The benzamide had m.p. 96.8-97.6° after recrystallization from hexane-benzene.

Anal. Calcd. for $C_{12}H_{15}ON$: C, 76.15; H, 7.99. Found: C, 76.31; H, 8.00.

1-Bromo-3-chloro-2-methylpropane.--In a 1-ℓ. three-necked round-bottomed flask equipped with two gas inlet tubes and Dry Ice condenser was placed 380 g. of β-methallyl chloride. A slow stream of oxygen and a rapid stream of anhydrous hydrogen bromide were bubbled into the reaction mixture for 8 hr., at which time it appeared that gas absorption had ceased. The solution was washed with water, dried over potassium carbonate and distilled through column 5. The product (402 g., 65.5%) had b.p. 55-63° (26-28 mm.). The n.m.r. showed three main peaks and the splitting was consistent with the assigned structure. Very little of the isomeric 1-chloro-2-bromo-2-methylpropane appeared to have been formed.

1-Cyano-3-chloro-2-methylpropane.--A solution of 260 ml. of 75% aqueous ethanol, 32.5 g. (0.66 mole) of sodium cyanide and 88.5 g. (0.56 mole) of 1-bromo-3-chloro-2-methylpropane was heated under reflux for 7.5 hr., diluted to 1 ℓ. and extracted with three 170-ml. portions of chloroform. The combined organic layers were dried over calcium chloride and distilled through column 4 to give 39.6 g. (60.5%) of 1-cyano-3-chloro-2-methylpropane, b.p. 74-79° (11.7 mm.), $n^{23}D$ 1.4430 (lit. b.p. 82-83° (16 mm.), $n^{20}D$ 1.4426 (35)).

2-Methylcyclopropanecarboxylic Acid.--In a 250-ml. round-bottomed flask equipped with reflux condenser were placed 39 g. of 1-cyano-3-chloro-2-methylpropane and 46 g.

of ground sodium hydroxide flakes. Since heating on a steam bath caused no visible reaction, a Wood's Metal bath was substituted. At 150-160°, a vigorous reaction occurred, and after 30 min. a solid cake had formed in the flask. Heating was maintained at this temperature for 1 additional hr. and the flask then transferred to a steam bath. Water (150 ml.) was added over a 20 min. period and the contents of the flask heated for 3 hr., cooled to 0° and poured over a slurry of 100 g. of ice and 37 ml. of sulfuric acid. A strong smell, reminiscent of butyric acid, was observed. The layers were separated, the aqueous phase extracted with two 100-ml. portions of ether and the combined organic solutions dried over magnesium sulfate and distilled through column 4 to give 23.1 g. (68%) of product, b.p. 97-98° (17.6 mm.), $\underline{n}^{21.5}D$ 1.4384-1.4387 (lit. b.p. 98-99° (18 mm.), $\underline{n}^{15}D$ 1.4441 (33)).

4-(2-Furyl)-3-buten-2-one was prepared from furfural and acetone in 58% yield, according to Leuck and Cejka (34).

2-Methylcyclopropanecarboxylic Acid.--An attempt was made to prepare this compound by oxidation of 4-(2-furyl)-3-buten-2-one according to Kishner (33) but in our hand met with almost no success.

2-Methylcyclopropylcarbinol was prepared in 78% yield by the reduction of 23.1 g. (0.231 mole) of 2-methylcyclopropanecarboxylic acid with 7.2 g. (0.2 mole) of lithium aluminum hydride in ether, b.p. 129-134° for the crude alcohol. A portion of the product was carefully fractionated

through column 3, b.p. 133°, $n^{25}D$ 1.4283. The v.p.c. of this material showed two cleanly separated peaks that were attributed to cis-trans isomers. The peak areas were of the same order of magnitude.

Anal. Calcd. for $C_5H_{10}O$: C, 69.72; H, 11.70. Found: C, 69.75; H, 11.90.

The p-nitrobenzoate could not be obtained in crystalline form at room temperature, despite repeated attempts at recrystallization from hexane.

Anal. Calcd. for $C_{12}H_{13}O_4N$: C, 61.27; H, 5.57. Found: C, 61.14; H, 5.68.

2-Methylcyclopropylcarbonitrile.--Sodamide was prepared from 6 g. (0.522 mole) of sodium and 500 ml. of ammonia in a 1-ℓ., three-necked, round-bottomed flask equipped with Dry Ice condenser, mechanical stirrer and glass stopper. A solution of 28.8 g. (0.203 mole) of 1-cyano-3-chloro-2-methylpropane in 50 ml. of ether was added in 1 min. with good stirring. The condenser was removed and 190 ml. of ether added over 1.5 hr. Ammonium chloride (4 g.) was added and the ammonia allowed to evaporate overnight. The solution was filtered. The filter cake was dissolved in water and extracted with ether. The ether extracts were combined with the previously obtained filtrate, dried over Drierite and concentrated by removing the ether through column 2. The residue was fractionated through column 1, wt. 9.3 g. (57%), b.p. 143-146°, $n^{25}D$ 1.4242-1.4250 (lit. $n^{20}D$ 1.4259 (35)).

2-Methylcyclopropylcarbinylamine was prepared in 55% yield by the reduction of 9.3 g. (0.115 mole) of 2-methylcyclopropanecarbonitrile with 4.55 g. (0.12 mole) of lithium aluminum hydride in ether. The product was very hard to dry, and although the water did not complicate the deamination reactions, considerable purification was needed to obtain an analytical sample of the amine, b.p. 102-102.5°, $n^{25}D$ 1.4310.

Anal. Calcd. for $C_5H_{11}N$: C, 70.52; H, 13.02. Found: C, 70.37; H, 13.09.

3-Methyl-1,1-dicarbethoxycyclobutane was prepared from 1-bromo-3-chloro-2-methylpropane and malonic ester in a manner analogous to that used to synthesize 1,1-dicarbethoxycyclobutane. The yield was 34% of material of b.p. 99-116° (11 mm.).

3-Methylcyclobutanecarboxylic acid was prepared in poor yield by basic saponification of 3-methyl-1,1-dicarbethoxycyclobutane, followed by acidification and heating under reflux, b.p. 96° (13 mm.). This material had an infrared spectrum that was identical to that of 3-methylcyclobutanecarboxylic acid (b.p. 92-93° (8 mm.)) prepared by the catalytic hydrogenation of 3-methylenecyclobutanecarboxylic acid (vide infra).

3-Methylcyclobutyl bromide was prepared from the silver salt of 3-methylcyclobutanecarboxylic acid following the procedure of Cason and Way (36) for the synthesis of cyclobutyl bromide from cyclobutanecarboxylic acid. The yield was 42%, b.p. 117°.

Anal. Calcd. for C_5H_9Br: C, 40.29; H, 6.09. Found: C, 40.26; H, 6.16.

3-Methylenecyclobutanecarbonitrile was prepared from allene and acrylonitrile according to Cripps, Williams and Sharkey (37) and had b.p. 66-67° (20 mm.), $n^{25}D$ 1.4590-1.4598 (lit. b.p. 64-65° (21 mm.), $n^{25}D$ 1.4595 (37)).

3-Methylenecyclobutanecarboxylic Acid.--A solution of 300 g. (4.55 moles) of potassium hydroxide, 500 ml. of water, 500 ml. of ethanol and 161 g. (1.73 moles) of 3-methylenecyclobutanecarbonitrile was heated under reflux for 7.5 hr. and evaporated to dryness under reduced pressure. Water (200 ml.) was added and evaporated and the process was repeated again. Water (100 ml.) was added and the solution made strongly acid with concentrated hydrochloric acid. The layers were separated and the aqueous phase extracted with two 100-ml. portions of ether. The combined organic layers were dried over magnesium sulfate and distilled. The product weighed 165 g. (85%), b.p. 99-104° (11.4-15.8 mm.).

3-Methylcyclobutanecarbonyl chloride was prepared in 86% yield from 3-methylcyclobutanecarboxylic acid and thionyl chloride, b.p. 78-81° (90-91 mm.).

3-Methylenecyclobutanecarboxamide was prepared in 81% yield from 101.5 g. (0.915 mole) of 3-methylenecyclobutanecarboxylic acid, 92.5 (0.915 mole) of triethylamine, excess ammonia and 100 g. (0.922 mole) of ethyl chlorocarbonate in 3 l. of chloroform, m.p. 156.7-157.2°, after sublimation. The procedure was

analogous to that of Roberts, Moreland and Frazer (40).

Anal. Calcd. for C_6H_9ON: C, 64.82; H, 8.17. Found: C, 64.61; H, 8.08.

3-Methylcyclobutanecarboxamide was prepared in 92% yield by the low-pressure hydrogenation of 3-methylenecyclobutanecarboxamide in acetic acid over reduced platinum dioxide. A small sample was sublimed twice, m.p. 154.5-163.0° (cis-trans isomers).

Anal. Calcd. for $C_6H_{11}ON$: C, 63.68; H, 9.80. Found: C, 63.47; H, 9.64.

3-Methyl-1-acetylcyclobutane.--The procedure followed was that of Pinson and Friess (39) for the preparation of acetylcyclobutane from cyclobutanecarbonyl chloride and methylmagnesium iodide. The yield of 3-methyl-1-acetylcyclobutane, from 25 g. of 3-methylcyclobutanecarbonyl chloride, was 2.54 g. (12%), b.p. 142-143.5°, $n^{25}D$ 1.4242-1.4248.

3-Methyl-1-acetylcyclobutane was also prepared by the reaction of 3-methylcyclobutanecarboxamide with methylmagnesium iodide, following the general method of Whitmore, Noll and Meunier (40) for the conversion of an amide to a ketone. From 25 g. (0.221 mole) of 3-methylcyclobutanecarboxamide, 21.4 g. (0.884 mole) of magnesium and 128 g. (0.90 mole) of methyl iodide there was obtained 16.7 g. of 3-methyl-1-acetylcyclobutane (69%), b.p. 140-143°, $n^{25}D$ 1.4269-1.4275. The 3-methyl-1-acetylcyclobutane obtained by the two routes exhibited nearly identical infrared spectra. Part of the material from the second procedure was carefully fractionated

through column 3, b.p. 140-140.5°, $n^{25}D$ 1.4261.

Anal. Calcd. for $C_7H_{12}O$: C, 74.95; H, 10.78. Found: C, 74.90; H, 10.90.

The 2,4-dinitrophenylhydrazone was prepared, m.p. 143.0-146.6°, after recrystallization from ethanol.

Anal. Calcd. for $C_{12}H_{16}O_4N_4$: C, 53.42; H, 5.52. Found: C, 53.40; H, 5.53.

3-Methyl-1-acetoxycyclobutane was prepared in 79% yield by the oxidation of 11.2 g. (0.1 mole) of 3-methyl-1-acetylcyclobutane with peroxytrifluoroacetic acid (from 4.1 ml. of 90% hydrogen peroxide and 25.4 ml. of trifluoroacetic anhydride) in methylene chloride in the presence of anhydrous disodium hydrogen phosphate. The method was that of Emmons and Lucas (41). The product had b.p. 140-142.5°, $n^{24}D$ 1.4165-1.4170. A center cut was fractionated through column 3, b.p. 140.5, $n^{22.5}D$ 1.4172. The v.p.c. showed one broad, partially resolved peak.

Anal. Calcd. for $C_7H_{12}O_2$: C, 65.59; H, 9.44. Found: C, 65.38; H, 9.29.

3-Methylcyclobutanol was prepared in 75% yield by basic saponification of 3-methyl-1-acetoxycyclobutane, b.p. 131°, $n^{23}D$ 1.4300. Redistillation through column 3 gave material of b.p. 133-134°, $n^{25}D$ 1.4287-1.4292. The v.p.c. showed one broad, partially resolved peak.

Anal. Calcd. for $C_5H_{10}O$: C, 69.72; H, 11.70. Found: C, 69.43; H, 11.72.

The p-nitrobenzoate had m.p. 50.8-69.5° after recrystallization from hexane.

Anal. Calcd. for $C_{12}H_{13}O_4N$: C, 61.27; H, 5.57. Found: C, 61.29; H, 5.55.

The p-bromobenzenesulfonate was prepared and purified in the fashion described for the corresponding cyclobutyl derivative, m.p. 39.6-42.4°, sap. equiv. 303.5 (calcd. 301).

3-Methylcyclobutylamine was prepared by the Schmidt reaction (42) of 3-methylcyclobutanecarboxylic acid. From 27 g. (0.24 mole) of organic acid, 50 ml. of concentrated sulfuric acid, 200 ml. of chloroform and 19 g. (0.3 mole) of sodium azide, there was obtained 9.2 g. of 3-methylcyclobutylamine (distilled through column 2), b.p. 94-95°, $n^{25}D$ 1.4290-1.4293.

Anal. Calcd. for $C_5H_{11}N$: C, 70.52; H, 13.02. Found: C, 70.56; H, 13.06.

2-Methyl-1,1-dicarbethoxycyclobutane was prepared in 37% yield from 920 g. (4.25 moles) of 1,3-dibromobutane, 197 g. (8.60 moles) of sodium and 810 g. (4.3 moles) of diethyl malonate, b.p. 112-121° (17.3-28 mm.), $n^{25}D$ 1.4322-1.4343 (lit. b.p. 86-87° (2.8 mm.), $n^{20}D$ 1.4349-1.4351 (43)).

2-Methyl-1,1-cyclobutanedicarboxylic acid was prepared in 75-85% yield by basic saponification of 2-methyl-1,1-dicarbethoxycyclobutane, m.p. 161.7-162.8° (dec.) (lit. m.p. 163-164° (43)) after crystallization from chloroform.

Anal. Calcd. for $C_7H_{10}O_4$: C, 53.16; H, 6.37. Found: C, 53.28; H, 6.30.

2-Methyl-1,1-cyclobutanedicarbonyl chloride was prepared in 85% yield from 60 g. of the diacid and 150 g. of thionyl chloride, b.p. 95-100° (25-32 mm.).

2-Methylcyclobutanone.--Attempts to convert the diacid chloride to the ketone by rearrangement of the intermediate diazide (see cyclobutanone) gave poor yields. The use of xylene as a solvent for decomposition gave a product that was difficult to separate from the xylene by fractional distillation. Hydroxylic solvents were totally unsatisfactory.

Preparation of this compound by methylation of cyclobutanone also failed. 1-(N-Pyrrolidyl)-1-cyclobutene was prepared from cyclobutanone (44), but treatment of this compound with methyl iodide (45) gave no isolable product.

2-Methylcyclobutanecarboxylic Acid.--Distillation of 20-40 g. of 2-methyl-1,1-cyclobutanedicarboxylic acid at atmospheric pressure gave 92-99% yields of 2-methylcyclobutanecarboxylic acid, $n^{25}D$ 1.4380 (lit. $n^{20}D$ 1.4394 (43)). The acid was used without further purification and was converted to 2-methylcyclobutanol by a series of reactions exactly paralleling the conversion of 3-methylenecyclobutanecarboxylic acid to 3-methylcyclobutanol (except that there was no catalytic hydrogenation). The steps are outlined below.

2-Methylcyclobutanecarboxamide, m.p. 130-133° (lit. m.p. 130-131.2° (43)) from 2-methylcyclobutanecarboxylic acid in 89% yield, recrystallized from benzene.

2-Methyl-1-acetylcyclobutane was prepared in 57% yield from the above amide and had b.p. 140-145°, $n^{25}D$ 1.4290.

The v.p.c. showed two cleanly resolved peaks, attributed to cis-trans isomers. The peak of lower retention time was considerably larger than the other.

Anal. Calcd. for $C_7H_{12}O$: C, 74.95; H, 10.78. Found: C, 74.80; H, 10.82.

2-Methyl-1-acetoxycyclobutane was prepared from the acetyl analogue in 65-77% yields, b.p. 139-141°, $n^{25}D$ 1.4160-1.4180. Careful purification of a sample of this compound gave material of the correct elemental composition, b.p. 139.5°, $n^{25}D$ 1.4170. The v.p.c. showed three peaks. One specific group may not have migrated during the oxidation.

Anal. Calcd. for $C_7H_{12}O_2$: C, 65.59; H, 9.44. Found: C, 65.49; H, 9.51.

2-Methylcyclobutanol was prepared in 80% yield by saponification of 2-methyl-1-acetoxycyclobutane, b.p. 131°, $n^{25}D$ 1.4308. The v.p.c. showed two peaks. In addition the infrared spectrum of this material was nearly identical to that of a small amount of 2-methylcyclobutanol formed by the reduction of 2-methylcyclobutanone with lithium aluminum hydride (since the proportion of cis-trans isomers is presumably different, the two spectra would not be expected to be identical).

Anal. Calcd. for $C_5H_{10}O$: C, 69.72; H, 11.70. Found: C, 69.51; H, 11.73.

The p-nitrobenzoate, recrystallized from hexane, had m.p. 50.3-52.5°.

Anal. Calcd. for $C_{12}H_{13}O_4N$: C, 61.27; H, 5.57. Found: C, 61.30; H, 5.55.

The p-bromobenzenesulfonate was prepared as was described for the cyclobutyl ester but proved highly intractable. It could not be crystallized, and the oily product partly decomposed overnight at room temperature in a vacuum. Some of the dark oil was used immediately in a kinetic run. A saponification equivalent was 120% of theory, indicating the presence of p-bromobenzenesulfonyl chloride. A positive silver nitrate test confirmed this suspicion. The very rapid initial consumption of base in the kinetic run was taken as evidence that about 4% of the mixture was p-bromobenzenesulfonic acid. Assuming a mixture of the desired ester, this acid and of p-bromobenzenesulfonyl chloride, and using the saponification equivalent and the estimated amount of free acid, it was possible to estimate that the mixture contained ca. 83% of the desired ester. This figure was used in the kinetic calculations.

2-Methylcyclobutylamine was prepared from 2-methylcyclobutanecarboxylic acid in the fashion described for the 3-methyl analogue. The amine had b.p. 92°, $n^{25}D$ 1.4341.

Anal. Calcd. for $C_5H_{11}N$: C, 70.52; H, 13.02. Found: C, 70.41; H. 12.90.

Allylmethylcarbinol was prepared from zinc, acetaldehyde and allyl bromide according to Levene and Haller (46), b.p. 113.5-114.5°, $n^{25}D$ 1.4227 (lit. b.p. 114° (49)).

Allylmethylcarbinyl bromide was prepared in 57% yield from the corresponding alcohol, following the procedure of Goering, Cristol and Dittmer for an isomeric compound (47).

The product had b.p. 110.5-113°, $n^{25}D$ 1.4587 and the v.p.c. had one peak.

Allylmethylcarbinyl p-toluenesulfonate was prepared (78%) according to the general procedure of Sekera and Marvel (48). The crude ester was used in synthetic work.

2-Nitro-4-propene.--Several attempts were made to prepare this compound from allyl bromide and nitroethane, following a procedure of Hoover and Hass (50). In all runs sodium ethoxide was prepared from 5.75 g. (0.25 mole) of sodium and 100 ml. of absolute ethanol. The nitroethane (18.8 g., 0.25 mole) and allyl bromide (30 g., 0.25 mole) used were redistilled.

In run 1, the nitroethane was added to the sodium ethoxide solution. Then 150 ml. of alcohol was added and the allyl bromide was dripped in. The solution was heated under reflux for 6 hr., cooled and filtered. The filtrate decomposed into a solid cake while being distilled at atmospheric pressure. The same procedure was repeated with distillation under reduced pressure (56 mm.). Just as some distillate of the b.p. expected for 2-nitro-4-propene began coming over, a violent decomposition occurred and all the material was lost.

An identical run was made, but after heating the ethanolic solution under reflux, the reaction mixture was concentrated at room temperature under reduced pressure and 50 ml. of water was added. A small amount of a top layer separated and the aqueous phase was saturated with sodium chloride and extracted with methylene chloride. The combined organic layers were concentrated to constant weight (14.3 g.) at room temperature

under reduced pressure (water aspirator). This residue was added to 100 ml. of water, 28 ml. of concentrated hydrochloric acid and 32 g. of iron filings and heated under reflux. After 1 hr., the solution was neutral to pH paper. About 30 ml. of acid were added. The solution was still neutral or slightly alkaline. The solution was heated under reflux a total of 13.5 hr., then made strongly basic and distilled until 50 ml. of distillate was collected. The distillate was saturated with potassium carbonate and extracted with ether. The ether solution was dried and distilled; after the ether was mostly removed, less than 2 g. of material remained, containing mainly solvent but smelling strongly of amine. This synthetic approach was abandoned.

N-(Allylmethylcarbinyl)-phthalimide.--All efforts to prepare this compound in the conventional manner (51), utilizing the reaction of the corresponding bromide or tosylate with potassium phthalimide in dimethylformamide, failed.

Allylmethylcarbinylamine.--After the failure to obtain this compound via 2-nitro-4-propene, the easiest route appeared to be that involving the reaction of allylmethylcarbinylmagnesium bromide with O-methylhydroxylamine (52). The Grignard reagent (0.4 mole) was prepared and cooled to -10 to -15° while an ether solution of 0.2 mole of O-methylhydroxylamine was slowly added. The solution was stirred for 30 min. at -10 to -15°, slowly warmed to room temperature and then heated under reflux for 2 hr. The solution was made strongly alkaline and the ether layer separated, dried over barium oxide and

concentrated with the aid of column 5. The residual material was distilled through column 1, and gave a main fraction of b.p. 107-110° (2.45 g.). The residue weighed 3.2 g. A v.p.c. of the center fraction showed three peaks. One corresponded to what is believed to be genuine allylmethylcarbinylamine (see below). The other two are probably isomeric compounds, formed by some rearrangement of the Grignard reagent. As a test, this Grignard reagent was oxygenated. The product alcohol mixture gave a v.p.c. that showed three peaks that could be associated with alcohols. The largest peak had the same retention time as allylmethylcarbinol (42%). The peak of intermediate size had the same retention time as α-methylallylcarbinol (18%). The third peak could not be even tentatively identified (7%).

Recourse was then made to the method of Streitwieser and Schaeffer (53) for the preparation of 2-octylamine. A solution of 200 ml. of methanol, 40 ml. of water, 15.5 g. of sodium azide and 33 g. of allylmethylcarbinyl tosylate was heated under reflux for 22.5 hr., cooled and diluted with 200 ml. of ether and 125 ml. of water. A solution of 200 g. of calcium chloride in 500 ml. of water was added, the organic layer separated and the aqueous phase thoroughly extracted with ether. The ether extracts were dried over calcium chloride, filtered and added to a suspension of 5.5 g. of lithium aluminum hydride in ether. The resultant solution was made strongly acid and extracted with ether (the extracts were discarded). The aqueous residue was made alkaline and

extracted with ether. The combined etheral solutions were dried over barium oxide, filtered and the ether removed through column 2. The residue, 2.8 g. and still containing ether, was distilled through a micro apparatus, two fractions being taken (1.1 g. and 1.5 g.). A v.p.c. of the second fraction showed only an ether peak and a homogeneous amine peak (which was about 70% of the total peak area). This amine band had the same retention time as that of the largest amine band from the above-mentioned Grignard synthesis. Some of the material prepared *via* the azide was used in the deamination reaction, some was hydrogenated and some was converted to the phenylthiourea.

The phenylthiourea was recrystallized from ethanol-water and had m.p. 82.8-84.0°.

Anal. Calcd. for $C_{12}H_{16}N_2S$: C, 65.41; H, 7.32. Found: C, 65.44; H, 7.38.

2-Pentylamine was prepared by hydrogenating the above unsaturated amine. The phenylthiourea had m.p. 73.5-74.0° (ethanol-water) and the *p*-nitrobenzamide had m.p. 92.6-93.8° (benzene-hexane). 2-Pentylamine was also prepared from commercial 2-pentanone and ammonium formate, following the procedure of Rohrmann and Shoule (54), b.p. 89-89.5° (lit. b.p. 89° (55)). The v.p.c. of this material showed only one peak, and this peak had exactly the same retention time as that of the 2-pentylamine prepared from the unsaturated amine. The amine from 2-pentanone gave a phenylthiourea, recrystallized from ethanol-water, of m.p. 65-66.5°, mixed m.p. 65-73°.

The infrared spectra of the two phenylthioureas were identically superimposable. It seemed possible that the 2-pentanone was contaminated, perhaps with 3-pentanone (the v.p.c. showed no separation between these ketonic isomers). Therefore, the p-nitrobenzamide of the amine from 2-pentanone was prepared, and after repeated recrystallization from benzene-hexane, it had m.p. 92.0-94.0°, mixed m.p. 92.0-93.5°. The infrared spectra of the p-nitrobenzamides were identical except for two shoulders in the spectrum of the material synthesized from 2-pentanone (6.85 and 7.75 μ).

1-Penten-3-ol was prepared from ethylmagnesium bromide and acrolein according to Hunsdiecker (56), b.p. 112-114°, $n^{25}D$ 1.4221-1.4227 (lit. b.p. 114.2-114.4°, $n^{20}D$ 1.4240 (57)).

1-Cyano-2-butene was prepared from a mixture of 1-chloro-2-butene and 3-chloro-1-butene (b.p. 68-82°, prepared in 64.5% yield from hydrogen chloride and butadiene according to Hatch and Nesbitt (58)) and cuprous cyanide, following the directions of Lane, Fentress and Sherwood (59), b.p. 142-144°, $n^{25}D$ 1.4199 (lit. b.p. 146°, $n^{20}D$ 1.4228 (59)).

3-Pentenoic acid was synthesized from the cyano compound according to these same authors (59), b.p. 95-98° (35 mm.), $n^{25}D$ 1.4340 (lit. b.p. 93° (14 mm.), $n^{20}D$ 1.4362 (59)). The manometer used in this distillation was probably malfunctioning.

Crotylcarbinol was prepared in 63% yield by the lithium aluminum hydride reduction of 3-pentenoic acid, b.p. 134-134.5°, $n^{25}D$ 1.4339-1.4340. The v.p.c. indicated that this product was very pure. The pure trans alcohol is reported to have

b.p. 136-137°, $n^{25}D$ 1.4322-1.4324 (60).

Crotylcarbinylamine could be prepared in 30-40% yield by the reduction of 1-cyano-2-butene with lithium aluminum hydride provided the reduction and subsequent work-up were all at 0°. The product had b.p. 104.5-106.5°, $n^{25}D$ 1.4345-1.4350, and the v.p.c. showed one peak.

Anal. Calcd. for $C_5H_{11}N$: C, 70.52; H, 13.02. Found: C, 70.42; H, 13.20.

3-Penten-2-ol was synthesized from methylmagnesium iodide and crotonaldehyde, b.p. 117-122°, $n^{25}D$ 1.4270 (lit. $n^{19}D$ 1.4288 (61)).

1-Cyano-2,2-dimethylcyclopropane was prepared according to Nelson, Maienthal, Lane and Benderly (62) from the di-tosylate of 2,2-dimethyl-1,3-propanediol, b.p. 150-151°, $n^{25}D$ 1.4250 (lit. b.p. 154.5-155.5°, $n^{23}D$ 1.4261 (62)).

2,2-Dimethylcyclopropylcarbinylamine was prepared by the reduction of 1-cyano-2,2-dimethylcyclopropane with lithium aluminum hydride, b.p. 111.5-112.0°, $n^{25}D$ 1.4300. The v.p.c. showed one peak.

Anal. Calcd. for $C_6H_{13}N$: C, 72.66; H, 13.21. Found: C, 72.69; H, 13.29.

Cyclopropyldimethylcarbinol was prepared from methyl-magnesium iodide and methylcyclopropyl ketone and had b.p. 121-123°, $n^{25}D$ 1.4338 (lit. b.p. 123.4-123.6° (752 mm.), $n^{20}D$ 1.4326 (63)).

Allyl p-nitrobenzoate had m.p. 27.5° (lit. m.p. 28.5° (64)), recrystallized from hexane.

Allyl p-bromobenzenesulfonate was prepared by the procedure described for the cyclobutyl ester. Unfortunately, a m.p. was not taken, but the material titrated 96% of theory in a kinetic run.

Cyclopentyl p-nitrobenzoate was only recrystallized once from hexane, m.p. 59.5-61.5°.

Kinetics of the Solvolysis of the Alkyl Bromides.--The solvent used was 50% ethanol-water and was prepared by pipeting 200 ml. of conductivity water (71) and 200 ml. of purified absolute ethanol (78) into a glass-stoppered flask and shaking. The 0.01 N sodium hydroxide solution was prepared in the conventional fashion (65) and was standardized against hydrochloric acid and potassium acid phthalate. A Sargent constant temperature bath was used and the temperature was 25.0°. The kinetic procedure was to weigh out the sample in a 50-ml. volumetric flask and dilute to the mark with solvent that had already been equilibrated in the thermostat. Vigorous shaking was sometimes necessary for obtaining a homogeneous solution; zero time was taken as the point when shaking was begun. In taking a point, a 5 ml. sample was removed, and diluted to 30 ml. with 50% ethanol-water. The free acid was determined using bromthymol blue indicator.

3-Methylcyclobutyl bromide was found to exhibit a first order rate constant decreasing with time. Table III demonstrates the best run carried out and gives the k_1 calculated for some points relative to zero time. A run 0.0324 M in organic bromide and 0.0367 M in potassium bromide gave

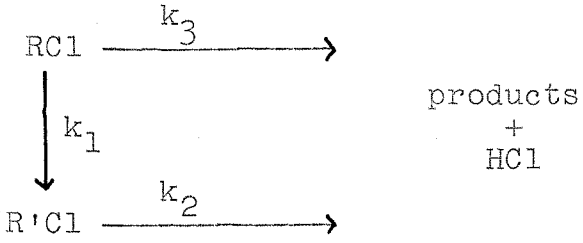
Table III

Run #3; Solvolysis of 0.0356 M 3-Methylcyclobutyl Bromide in 50% Ethanol-Water at 25.0°

Time (10^{-4} sec.)	% Unreacted	k_1 (10^6 sec.$^{-1}$)
0.36	97.0	8.47
2.16	93.4	3.17
7.64	81.4	2.72
10.75	79.0	2.19
19.2	72.2	1.69
28.0	69.1	1.33
34.8	67.4	
43.1	66.7	

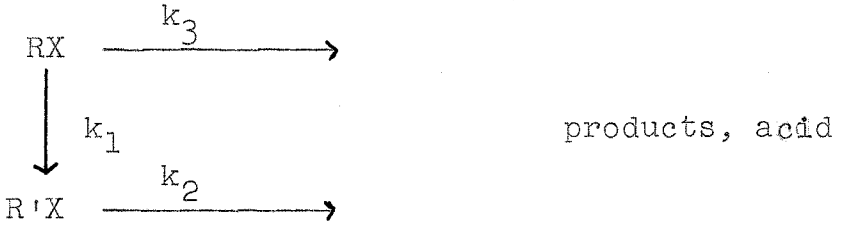
points that closely coincided with those of the run recorded in Table III, showing that the decreasing rate constant is not due to either a general salt effect or to bromide ion, specifically. As was mentioned in the Discussion, the most reasonable interpretation is that two competing first order reactions are occurring, one giving solvolysis product and the other giving rearranged, less reactive bromide. The final slope can be taken as the rate of solvolysis of the rearranged bromide. It is desirable to estimate the rate of rearrangement and the rate of solvolysis of 3-methylcyclobutyl bromide.

A similar situation has been treated by Young, Winstein and Goering (66). These authors studied the solvolysis of γ,γ-dimethylallyl chloride and α,α-dimethylallyl chloride and observed that the second of these halides exhibited a first order rate constant that decreased with time, the final value coinciding with that of the γ,γ-isomer. They ascribed this observation to an internal return isomerization to the less reactive γ,γ-isomer, which eventually is the only chloride remaining. Using graphical methods of analysis, values for three rate constants were obtained. The k_2 was measured directly by studying the solvolysis of γ,γ-dimethylallyl chloride, k_3 was estimated from the initial slope of the solvolysis curve of the α,α-isomer, and k_1 was obtained by the aforementioned graphical method.



A recent paper by Winstein and Fainberg (67) has described a more exact, analytical method of successive approximations for extracting the values of the rate constants for a solvolysis system that behaves in a similar fashion (2-p-anisyl-1-propyl and 1-p-anisyl-2-propyl). These results were reported after the completion of the calculations presented below, which also invoke successive approximations. Both methods presumably give the same results; both schemes would have to be tried on the same calculation in order to determine which is more easily handled. While the data of Winstein and Fainberg (67) could be treated by the scheme presented below in order to get a direct comparison between the two methods, the worth derived did not seem to justify the time involved.

The simplified scheme considered is:



Let RX = A, R'X = B, product acid = C

$$-d(A)/dt = k_1(A) + k_3(A) \qquad (A) = (A)_o e^{-(k_1+k_3)t}$$

$$d(B)/dt = k_1(A) - k_2(B) = k_1(A)_o e^{-(k_1+k_3)t} - k_2(B)$$

$$(B) = \frac{k_1(A)_o}{k_2-k_1-k_3} \left(e^{-(k_1+k_3)t} - e^{-k_2 t}\right)$$

$$(A) + (B) + (C) = (A)_o \qquad (B)_o = (C)_o = 0$$

where subscript o refers to concentrations at t = 0.

Substituting in the equation $(C) = (A)_o - (A) - (B)$, we get:

$$\frac{(C)}{(A)_o} = 1 - e^{-k_3 t} e^{-k_1 t} - \frac{k_1}{k_2-k_1-k_3} \left[e^{-k_3 t} e^{-k_1 t} - e^{-k_2 t}\right]$$

Let $X = 1 - \frac{(C)}{(A)_o}$ = fraction of halides unreacted

and simplify algebraically

$$X = e^{-k_3 t} e^{-k_1 t} - \frac{e^{-k_2 t} - X}{k_3-k_2} k_1$$

or

$$X = ae^{-k_1 t} - \frac{b-X}{d} k_1 \qquad (1)$$

$$a = e^{-k_3 t}$$

$$b = e^{-k_2 t}$$

$$d = k_3 - k_2$$

X = fraction unreacted

This last form of the equation is especially convenient for calculations. For each experimental point, the value of k_1 is determined that balances both sides of equation 1.

The data of Young, Winstein and Goering (66) were treated by the above technique. The value of k_2, 2.1×10^{-6} sec.$^{-1}$ had been measured directly and is presumed correct. For a first approximation the value of k_3 (16×10^{-6} sec.$^{-1}$) reported by these workers was taken, and the value of k_1 needed to balance equation 1 for each experimental point was calculated. The values of k_1 for all the points were added and the average deviation determined. This gave $k_1 = 67(\pm 24) \times 10^{-6}$ sec.$^{-1}$ A different value of k_3 (12.3×10^{-6} sec.$^{-1}$) gave $k_1 = 32(\pm 6) \times 10^{-6}$ sec.$^{-1}$, a marked improvement. Finally, assuming $k_3 = 13.2 \times 10^{-6}$ sec.$^{-1}$ gave $k_1 = 40(\pm 3) \times 10^{-6}$ sec.$^{-1}$ These values compare favorably with the graphically-derived (66) values of 16×10^{-6} sec.$^{-1}$ and 36×10^{-6} sec.$^{-1}$, respectively, and are probably more accurate.

A similar treatment was now carried out for 3-methylcyclobutyl bromide. The value of k_2 was estimated from the final slope of the solvolysis curve to be 0.15×10^{-6} sec.$^{-1}$ An assumed $k_3 = 4.70 \times 10^{-6}$ sec.$^{-1}$ gave $k_1 = 17(\pm 6.7) \times 10^{-6}$ sec.$^{-1}$; $k_3 = 3.75 \times 10^{-6}$ sec.$^{-1}$ gave $k_1 = 10.2(\pm 1.9) \times 10^{-6}$ sec.$^{-1}$; $k_3 = 3.47 \times 10^{-6}$ sec.$^{-1}$ gave $k_1 = 8.2(\pm 0.5) \times 10^{-6}$ sec.$^{-1}$ The estimated error in this last determination of k_1 is about the same as that in the analysis of the data of Young, Winstein and Goering. As a further check on the

method, one calculation was made with a $k_2 = 0.24 \times 10^{-6}$ sec.$^{-1}$, since the value of k_2 estimated from the plot was subject to much error. Assuming $k_3 = 3.47 \times 10^{-6}$ sec.$^{-1}$ gave $k_1 = 8.7(\pm 0.5) \times 10^{-6}$ sec.$^{-1}$, indicating that the values of k_3 and k_1 are not highly subject to errors in k_2. In summary, the best rate constants for 3-methylcyclobutyl bromide are 3.47×10^{-6} sec.$^{-1}$ for reaction to form acid and 8.2×10^{-6} sec.$^{-1}$ for rearrangement.

Cyclopropylmethylcarbinyl bromide was prepared in a highly impure state as described previously. Analysis of the mixtures has been described in the Discussion section where it was pointed out that the mixtures probably contained 8-14% cyclopropylmethylcarbinyl bromide. This is in accord with the kinetic experiments that showed about 10% of a highly reactive bromide (cf. Table IV). The same kinetic procedure as for 3-methylcyclobutyl bromide was employed. This was an unfortunate choice and a technique for following fast reactions should have been used. The amount of unreactive bromide in the starting material can be estimated from the place in the kinetic plot where essentially all reaction ceases. By assuming that cyclopropylmethylcarbinyl bromide does not rearrange to a less reactive species and that all other species present are very much less reactive, one can estimate k_1 as approximately 170×10^{-6} sec.$^{-1}$, which is probably a minimal value correct only to an order of magnitude.

Table IV

Run #6; Solvolysis of 0.0414 M Cyclopropylmethylcarbinyl Bromide in 50% Ethanol-Water at 25.0°.

Time (10^{-4} sec.)	% Unreacted
0.72	86.2
1.83	80.3
7.35	78.2
10.27	77.7
19.1	76.4
25.9	75.3
34.2	73.7
37.4	73.1

The kinetics of the solvolysis of the alkyl brosylates were measured in a more sophisticated manner. A water thermostat was maintained at 25.0°, and absolute ethanol and freshly boiled distilled water were equilibrated in it. At the beginning of each run, 200 ml. of each solvent were pipetted into a 1-ℓ. three-necked round-bottomed flask immersed in the water bath and equipped with mechanical stirrer, nitrogen inlet tube and burette containing 0.0529 M sodium hydroxide in 50% aqueous ethanol. The mixed solvent was allowed to reach temperature equilibrium, stirring was begun and some bromthymol blue was added. Base was added until the indicator just turned color and the burette reading was taken. Excess base was added, the burette read and the sample was introduced as stopwatch A was started. When the indicator began to turn to the acid color, stopwatch A was stopped, stopwatch B was started and some more base was added. In the interim, the burette was read, and A was read and returned to zero time. The process was then repeated as many times as was desired. Infinity titers were taken after 10 half-lifes. The only flaw in the procedure was the manner of introduction of the sample. Four procedures were tried. In runs 21-26, the sample was weighed out on a small watch glass which was dropped into the solvent at time zero. Since the esters dissolved slowly, this gave curvature in the plot of the data. If the ester solvolyzed in a well-behaved fashion, the zero time could be

taken arbitrarily and the straight line portion of the solvolysis curve considered. If internal return occurred (2- and 3-methylcyclobutyl esters), no such correction could be applied. In runs 27 and 28, the sample was dissolved in 1 ml. of ether and poured into the reaction flask. This was unsatisfactory because the ether solution ran down the side of the flask and the ether evaporated, leaving ester on the walls of the flask. In run 29, the ether solution was pipetted into the reaction flask. This procedure was quite satisfactory, but the ether solution was difficult to pipet. In runs 30 and 31, the 1-ml. volumetric flask containing the ether solution of the ester was dropped into the solvent mixture. There seemed to be some difficulty with rates of mixing and diffusion, however. The details of a few runs are given below, but the various compounds will first be discussed.

Allyl brosylate gave straight line plots, especially in run 31 if the first few points were ignored. Run 23, $k_1 = 5.1(\pm 0.2) \times 10^{-4}$ sec.$^{-1}$, run 31, $k_1 = 5.2(\pm 0.1) \times 10^{-4}$ sec.$^{-1}$; average is $k_1 = 5.2 \times 10^{-4}$ sec.$^{-1}$

Cyclobutyl brosylate gave good straight lines in individual runs, but considerable scatter from run to run. Run 27 seemed most reliable and it also falls near the average of three runs. Run 21, $k_1 = 11.1(\pm 0.1) \times 10^{-4}$ sec.$^{-1}$; run 24, $k_1 = 12.3(\pm 0.3) \times 10^{-4}$ sec.$^{-1}$; run 27, $k_1 = 11.9(\pm 0.03) \times 10^{-4}$ sec.$^{-1}$; average is $k_1 = 11.8 \times 10^{-4}$ sec.$^{-1}$

For 3-methylcyclobutyl brosylate, no corrections could be applied to individual runs since internal return to a rearranged compound apparently was occurring, and only about 40% of the theoretical amount of acid was produced. Two methods of analysis of the data were tried. First, the data were plotted and the maximum slope of the curve was determined. This gave: run 22, $k_1 = 3.0 \times 10^{-4}$ sec.$^{-1}$; run 26, $k_1 = 2.4 \times 10^{-4}$ sec.$^{-1}$; run 29, $k_1 = 2.8 \times 10^{-4}$ sec.$^{-1}$ Because of the method of sample introduction, run 29 is believed to give the most accurate value of k_1. A second treatment of the data assumed that two first order competition reactions were occurring, one leading to solvolysis products and one leading to rearranged, completely unreactive brosylate. Different values of these two rate constants were taken and a theoretical value for the amount of unreacted material calculated, for each experimental point. This value was compared to the experimental value, and the average difference between the pairs of values minimized by varying the rate constants. Values for k_1 (products) $= 2.8 \times 10^{-4}$ sec.$^{-1}$ and for k_2 (rearrangement) $= 4.2 \times 10^{-4}$ sec.$^{-1}$ gave the best fit for run 29, and the k_1 value is the same as that estimated directly from the graph of the data. The average discrepancy between theoretical and actual values for 13 points in run 29 is 0.35% (absolute).

2-Methylcyclobutyl brosylate presented the same kinetic problems as the 3-methyl derivative and, as described earlier, it was contaminated with impurities. These impurities were

assumed to be unreactive and it was indeed shown that p-bromobenzenesulfonyl chloride reacted very slowly under the reaction conditions (a saturated solution in 50% ethanol-water at room temperature showed no appreciable pH change over a period of several hours). Only one run (#30) is believed to have real validity. The data of this run were analyzed as described for the 3-methyl isomer. From the graph, k_1 was estimated as 12 x 10^{-4} sec.$^{-1}$ From calculations, k_1 = 11 x 10^{-4} sec.$^{-1}$ and k_2 (rearrangement) = 13 x 10^{-4} sec.$^{-1}$, with an average discrepancy between seven theoretical and observed points of 0.7%.

Solvolysis of the alkyl p-nitrobenzoates was carried out in 80% acetone-20% water solution, 0.0524 M in perchloric acid. Standard ampule technique (79) was used and the temperature was 94.7°. A pH meter was used to follow titrations to pH 9, which was taken as the endpoint.

Cyclopropylmethylcarbinyl p-nitrobenzoate gave a reasonable first order plot, k_1 = 11($\pm$0.6) x 10^{-5} sec.$^{-1}$

Cyclopropylcarbinyl p-nitrobenzoate did not give very good straight lines. Run 11, k_1 = 0.27($\pm$0.02) x 10^{-5} sec.$^{-1}$; run 13, k_1 = 0.29($\pm$0.02) x 10^{-5} sec.$^{-1}$; average, k_1 = 0.28 x 10^{-5} sec.$^{-1}$

2-Methylcyclopropylcarbinyl p-nitrobenzoate was even worse behaved, k_1 = 0.32($\pm$0.03) x 10^{-5} sec.$^{-1}$

Cyclobutyl p-nitrobenzoate gave a good first order plot, k_1 = 0.33($\pm$0.01) x 10^{-5} sec.$^{-1}$

Table V

Run #27; Solvolysis of 1.05×10^{-3} M Cyclobutyl Brosylate in 50% Ethanol-Water at 25.0°.

Time (10^{-3} sec.)	% Unreacted	k_1 (10^4 sec.$^{-1}$)
0.186	80.1	11.9
0.258	73.5	11.9
0.425	60.3	11.9
0.525	53.6	11.9
0.633	47.0	11.9
0.768	40.4	11.8
0.920	33.8	11.8
1.10	27.2	11.8
1.33	20.5	11.9
1.66	13.9	11.9
		Ave. 11.9 ± 0.03

$$k_1 = 11.9 \times 10^{-4} \text{ sec.}^{-1}$$

Table VI

Run #29; Solvolysis of 2.17×10^{-3} M 3-Methylcyclobutyl Brosylate in 50% Ethanol-Water at 25.0°.

Time (10^{-3} sec.)	% Unreacted	Calcd. % Unreacted for $k_1 = 2.8 \times 10^{-4}$ sec.$^{-1}$ and $k_2 = 4.2 \times 10^{-4}$ sec.$^{-1}$
0.071	97.5	98.0
0.192	94.3	94.9
0.350	91.1	91.2
0.497	88.0	88.0
0.660	84.8	85.1
0.855	81.6	81.7
1.09	78.4	78.4
1.37	75.3	75.0
1.68	72.1	71.9
2.13	68.9	68.6
2.70	65.8	65.6
3.48	62.6	63.0
4.66	59.4	61.0

$k_1 = 2.8 \times 10^{-4}$ sec.$^{-1}$

$k_2 = 4.2 \times 10^{-4}$ sec.$^{-1}$

Table VII

Run #30; Solvolysis of 1.07×10^{-3} M 2-Methylcyclobutyl Brosylate in 50% Ethanol-Water at 25.0°.

Time (10^{-3} sec.)	% Unreacted	Calcd. % Unreacted for $k_1 = 11 \times 10^{-4}$ sec.$^{-1}$ and $k_2 = 13 \times 10^{-4}$ sec.$^{-1}$
0.050	93.8	94.9
0.128	87.4	87.9
0.225	81.5	81.0
0.345	75.3	74.4
0.494	69.1	68.4
0.698	63.0	62.8
1.06	56.8	57.6

$k_1 = 11 \times 10^{-4}$ sec.$^{-1}$

$k_2 = 13 \times 10^{-4}$ sec.$^{-1}$

Table VIII

Run #31; Solvolysis of 1.16×10^{-3} M Allyl Brosylate in 50% Ethanol-Water at 25.0°.

Time (10^{-3} sec.)	% Unreacted	k_1 (10^4 sec.$^{-1}$)
0.196	90.1	5.34
0.418	80.1	5.30
0.665	70.2	5.32
0.965	60.2	5.26
1.33	50.3	5.19
1.75	40.4	5.19
2.34	30.4	5.08
		5.24 ± 0.07

$$k_1 = 5.24 \times 10^{-4} \text{ sec.}^{-1}$$

2-Methylcyclobutyl p-nitrobenzoate had k_1 = $0.28(\pm 0.01) \times 10^{-5}$ sec.$^{-1}$

3-Methylcyclobutyl p-nitrobenzoate, $k_1 = 0.26(\pm 0.02) \times 10^{-5}$ sec.$^{-1}$

Cyclopentyl p-nitrobenzoate, $k_1 = 0.12(\pm 0.006) \times 10^{-5}$ sec.$^{-1}$

Independent experiments showed that the uncatalysed reactions of the cyclobutyl and cyclopropylcarbinyl compounds were immeasurably slow under the reaction conditions.

The Deamination Reactions.--The same procedure was followed in the deamination of all amines but one. In a 500-ml., round-bottomed, three-necked flask equipped with mechanical stirrer, glass stopper and condenser position for downward distillation was placed a solution of 22-43 g. of sodium nitrite (depending on the amount of amine to be used) and of amine (1-10 g.) in 280 ml. of water. To the condenser there was attached a round-bottomed flask with sidearm that opened to the atmosphere via a Dry Ice trap and calcium chloride drying tube. The reaction flask was cooled in an ice bath, the stirrer started and 17 ml. of 60% perchloric acid added. After about 30 min., the ice bath was replaced with a heating mantle and distillation begun and continued until 75 ml. of homogeneous distillate had been collected after the initial two-phase distillate. The distillate was saturated with potassium carbonate and the organic (upper) layer separated. The aqueous phase was extracted with two 15-ml. portions of ether. The combined organic layers were dried over magnesium sulfate, filtered and the ether removed through column 2. The residue was dis-

tilled through column 1, no effort being made to cut fractions. Everything distillable was driven over, so no residue was left in the distillations. The Dry Ice trap used in the deamination reaction was never observed to collect anything but oxides of nitrogen.

The first step in performing the analysis of the alcohol mixture was to measure, on the vapor phase chromatograph, the retention time of each alcohol likely to be present. This included the six isomeric alcohols (X-XV) as well as appropriate allylic alcohols if the starting amine was olefinic. Some alcohols had identical retention times and recourse had to be made to infrared analysis, using comparisons with the spectra of known mixtures. For instance, the 2- and 3-methylcyclobutanols and 2-methylcyclopropylcarbinol fell at the same place. Also, α-methylallylcarbinol coincided with cyclopropylmethylcarbinol; there was no reason why the former alcohol should be formed from any of the amines studied so no effort was made to identify it and no ambiguities arose because of this assumption. If the retention time of an alcohol seemed to be affected by the presence of other alcohols, a synthetic mixture was run to redetermine retention times. Also, there were often peaks of minor size, generally of high retention time, that could not be identified. These presumably arose from nitro compounds, side reactions, etc. The final analysis was checked by preparing a synthetic mixture of the derived composition and comparing its infrared spectrum to that of the reaction mixture. The infrared spectra are at the end of the Experimental.

The Vapor Phase Chromatography Apparatus and its Calibration.--The apparatus was a 5 ft. column equipped with thermal conductivity cells and a Varian G-10 recorder, chart speed 1 inch = 4 min. It was surrounded by a vapor jacket that was heated by boiling toluene. The effluent gas was helium and the stationary phase dioctyl phthalate supported on Johns Manville Celite (0.45 g. of liquid/g. Celite). Peak areas were measured by counting squares or by tracing the curves on onion skin, cutting out and weighing. Both methods were accurate. Table IX shows the results obtained with standard solutions. Fig. 2, at the end of the Experimental, shows some typical v.p.c.'s.

Proof of Stability of Alcohols under Deamination Conditions.--Two g. of an alcohol mixture was substituted for the amine in the deamination procedure and the starting material and products were analyzed. There was little

Alcohol	% Taken	% Recovered
Allylmethylcarbinol	36	33
Cyclopropylmethylcarbinol	46	51
3-Methylcyclobutanol 2-Methylcyclopropylcarbinol	18	16

change in the composition of the mixture.

In a separate experiment, 2-methylcyclobutanol was tested and found to be completely stable and recoverable.

Table IX

Calibration of the Chromatography Apparatus

	Alcohol								
	Allylmethylcarbinol			Cyclopropylmethylcarbinol			3-Methylcyclobutanol		
	Cm.	%		Cm.	%		Cm.	%	
		Taken	Fd.		Taken	Fd.		Taken	Fd.
Run									
1	7.3	100							
2				9.4	100				
3	7.3	30.0	32.3	9.4	70.0	67.7			
			33.1			66.9			
4							11.7	100	
5	7.0	20.8	21.2	9.1	48.6	45.6	11.7	30.5	33.2
	7.0		22.6	9.1		47.6	11.7		29.8
			21.2			46.9			31.9
5 average		20.8	21.7		48.6	46.6		30.5	31.6
6	---	45.7	47.2	---	54.3	52.8			
7	---	38.6	38.5	---	45.2	44.7	---	16.3	16.7

Test of Isolation Procedure in Deamination.--In the deamination of crotylcarbinylamine, an analysis of the initial steam distillate was performed and compared to the final analysis.

Alcohol	%	
	Crude	Pure
3-Penten-2-ol	16.9	15.2
Cyclopropylmethylcarbinol	72.6	73.6
Crotylcarbinol	10.5	11.3

The deamination of cyclopropylmethylcarbinylamine was carried out by Dr. R. H. Mazur (32) employing a slightly different procedure from that described above. Two fractions (yield 69%) were recovered, one of which appeared to be unreacted amine and the other of which was, according to the infrared spectrum, pure cyclopropylmethylcarbinol.

The deamination of 2-methylcyclobutylamine gave a 56% yield of alcohols. The v.p.c. (q.v.) showed only one peak, corresponding to cyclopropylmethylcarbinol and the infrared spectrum was superimposable with that of this alcohol.

The deamination of 2-methylcyclopropylcarbinylamine gave a 58% yield of a mixture of alcohols. All but 5% of the total peak area of the v.p.c. was accounted for. The alcohols present were cleanly separated and infrared analysis showed that no detectable amount of 3-methylcyclobutanol lay under the 2-methylcyclopropylcarbinol peak in the v.p.c. The 8.10 μ band seemed characteristic of 3-methylcyclobutanol.

Deamination of 3-methylcyclobutylamine was carried out twice, with yields of alcohols amounting to 49% and 70%. Analysis of the first run and the second run gave: cyclopropylmethylcarbinol: 48, 45%; allylmethylcarbinol: 39, 39%; 3-methylcyclobutanol: 5, 6%; 2-methylcyclopropylcarbinol: 8, 10%. This was the only duplicate deamination carried out. Since the last two alcohols had identical retention times, infrared analysis was used on the main fraction (90% of the total distillate) of the second run to determine the relative amounts of these two alcohols. It was assumed that in all fractions of both runs, these alcohols occurred in the same ratio. There was no doubt that both alcohols were present, judging from the infrared spectra. Over 94% of the total peak areas in the v.p.c. were accounted for in the analyses.

The deamination of crotylcarbinylamine was carried out in 44% yield and the product mixture had a highly complex v.p.c. The final analysis, in which cyclopropylmethylcarbinol, crotylcarbinol and 3-penten-2-ol were detected, accounted for 92% of the total peak area of the v.p.c.

The deamination of allylmethylcarbinylamine gave a 21% yield of alcohols; only 0.8 g. of amine was available. The resultant v.p.c. had four peaks. Two peaks (91%) were assigned to cyclopropylmethylcarbinol and a mixture of allylmethylcarbinol and ethylvinylcarbinol. This last mixture was analyzed via infrared spectra. A peak, area 6%, had the same retention time as crotylcarbinol but was assigned to 2-penten-1-ol (should be present but was not synthesized). This alcohol

might be expected to have a retention time close to that of crotylcarbinol. The last remaining peak (3%) had a retention time corresponding to that of 2-methylcyclopropylcarbinol (shown by adding genuine 2-methylcyclopropylcarbinol to the reaction mixture and observing the increase in the size of this peak). However, one cannot be sure of the nature of this peak.

The deamination of 2,2-dimethylcyclopropylcarbinylamine gave a 65% yield of alcohols. The v.p.c. showed two peaks. A synthetic mixture of allyldimethylcarbinol and cyclopropyldimethylcarbinol of composition indicated by the v.p.c. had an infrared spectrum nearly identical to that of the reaction mixture.

The Behavior of the Isomeric $C_5H_{10}O$ Alcohols under Strongly Acidic Conditions.--These experiments were carried out only in an exploratory fashion and some of the results were not reproducible. Analyses were performed with vapor phase chromatography but the v.p.c.'s thus obtained were generally not of good quality. The alcohols tested were 2-methylcyclopropylcarbinol, cyclopropylmethylcarbinol, 2- and 3-methylcyclobutanol, crotylcarbinol and allylmethylcarbinol.

With 45% fluoboric acid at room temperature, both cyclopropylcarbinols rapidly rearranged to allylmethylcarbinol and variable amounts of unidentified material. The other alcohols were stable.

With 22% fluoboric acid heated under reflux for 30 min., 3-methylcyclobutanol showed approximately 80% starting material and 20% allylmethylcarbinol. Under the same conditions, 2-methylcyclobutanol was totally rearranged to allylmethylcarbinol and the olefinic alcohols were unaffected.

Allylmethylcarbinol gave only polymer and unrearranged alcohol when heated under reflux for 1 hr. with 25% sulfuric acid. Under the same conditions, it is reported that allylmethylethylcarbinol is totally rearranged to 4-methyl-3-hexen-1-ol (68). This corresponds to the rearrangement of allylmethylcarbinol to crotylcarbinol.

Fig. 2

Curve	Subject
1	The alcohols from the deamination of 2-methylcyclobutylamine.
2	The alcohols from the deamination of 3-methylcyclobutylamine.
3	The qualitative separation of a mixture of allylmethylcarbinol, cyclopropylmethylcarbinol, 2-methylcyclopropylcarbinol and crotylcarbinol. Alcohols named in order of occurrence in spectrum from left to right.
4	The alcohols from the deamination of crotylcarbinylamine.

The vapor phase chromatograms were obtained at 110°, using helium gas as carrier and dioctyl phthalate on Celite as the stationary phase. These spectra were run at different gas flows, so the retention times in different spectra are not comparable.

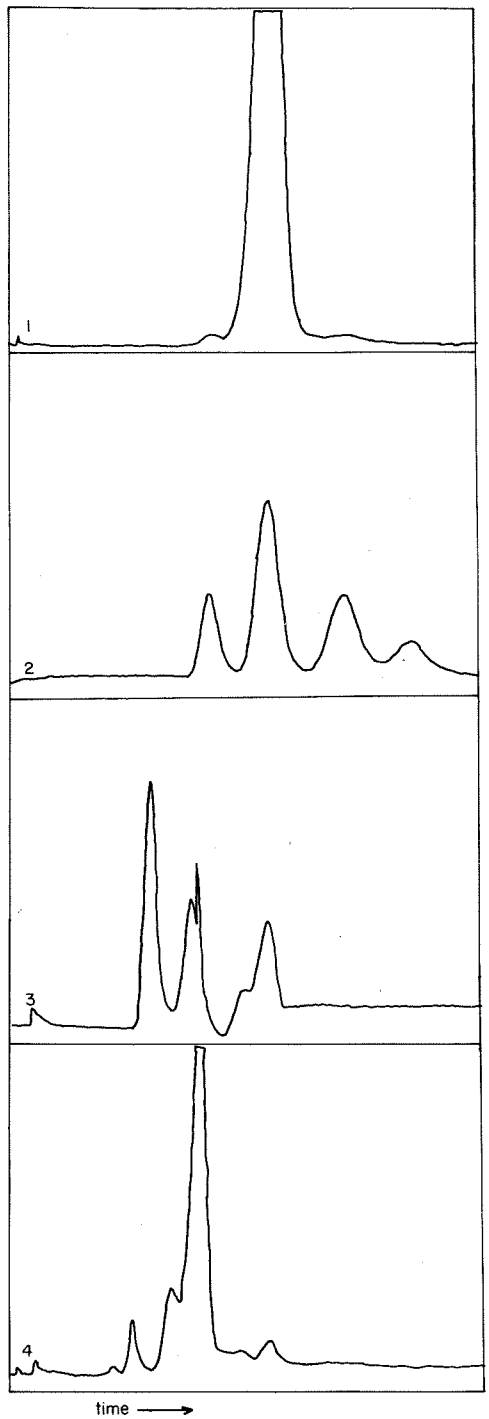
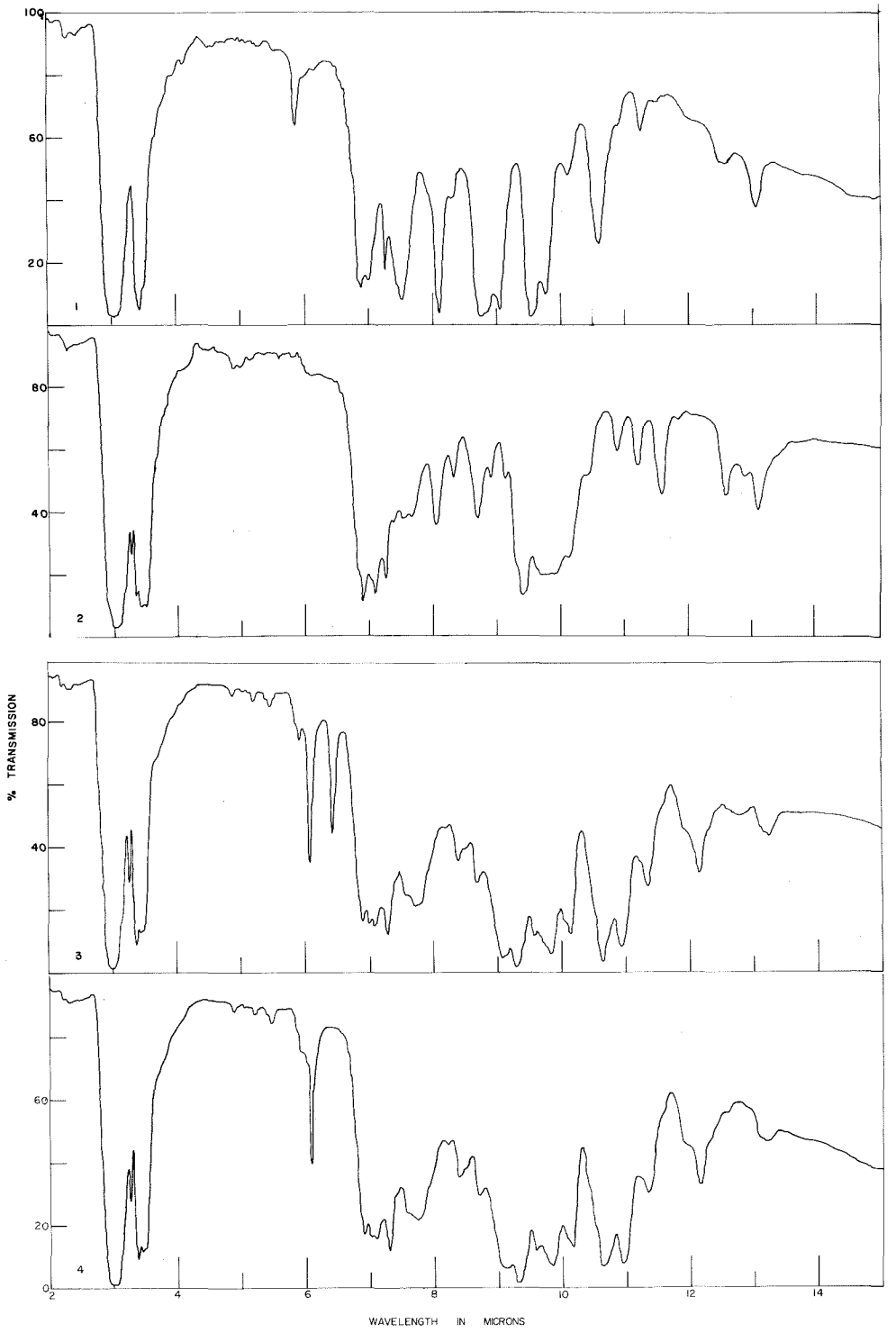


Fig. 2

Fig. 3

Curve	Compound
1	3-Methylcyclobutanol.
2	2-Methylcyclopropylcarbinol.
3	2-Methylcyclopropylcarbinylamine + HONO.
4	51% Cyclopropylmethylcarbinol, 36% allylmethylcarbinol, 13% 2-methylcyclopropylcarbinol.

The infrared spectra were obtained with a model 21 Perkin-Elmer double beam recording spectrophotometer equipped with NaCl optics, using pure liquids in an 0.025 mm. NaCl cell. The band at 6.43 μ, in the spectra of the deamination products, was assigned to small amounts of nitro compounds (74).


100
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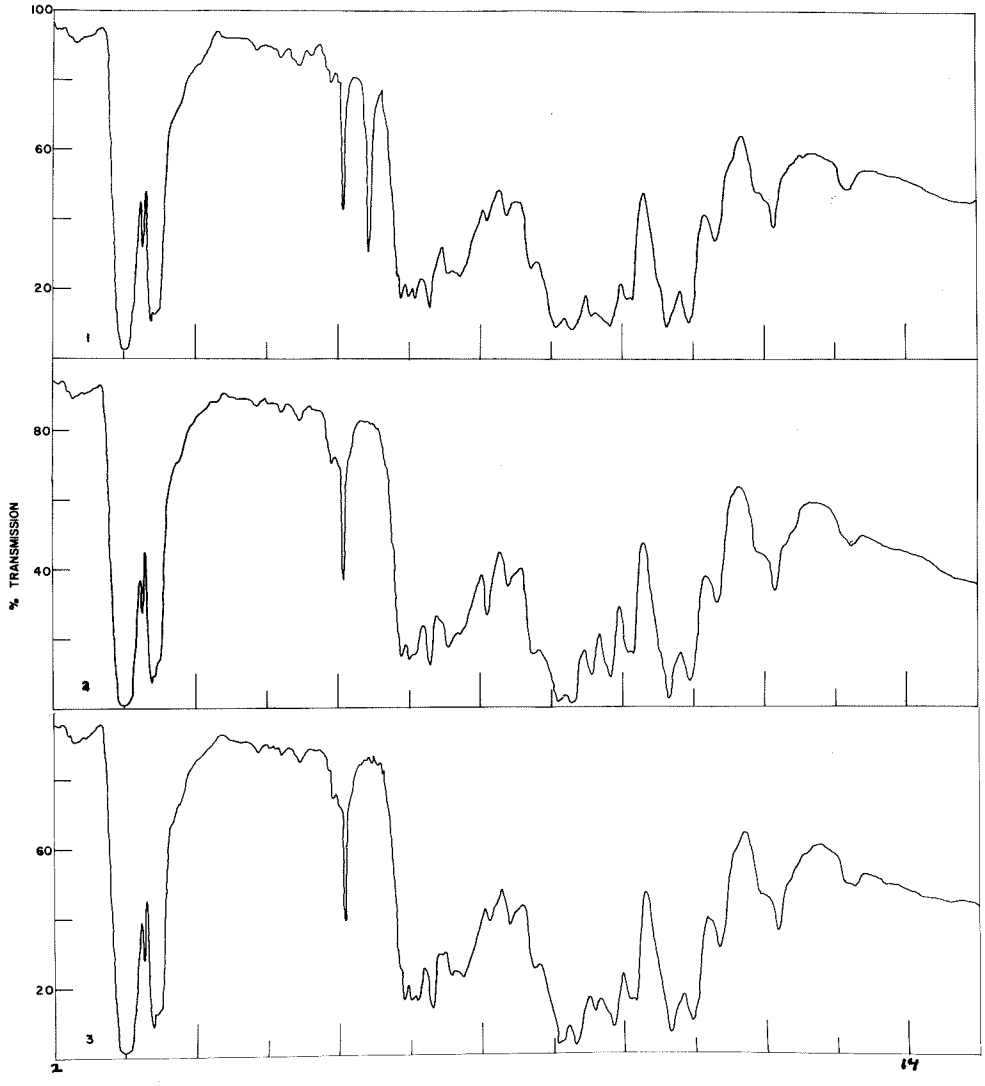
14
WAVELENGTH IN MICRONS

FIG. 3

Fig. 4

Curve	Compound
1	3-Methylcyclobutylamine + HONO.
2	45% Cyclopropylmethylcarbinol, 39% allylmethylcarbinol, 16% 3-methylcyclobutanol.
3	45% Cyclopropylmethylcarbinol, 39% allylmethylcarbinol, 10% 2-methylcyclopropylcarbinol, 6% 3-methylcyclobutanol.

The infrared spectra were obtained with a model 21 Perkin-Elmer double beam recording spectrophotometer equipped with NaCl optics, using pure liquids in an 0.025 mm. NaCl cell. The band at 6.43 μ, in the spectra of the deamination products, was assigned to small amounts of nitro compounds (74).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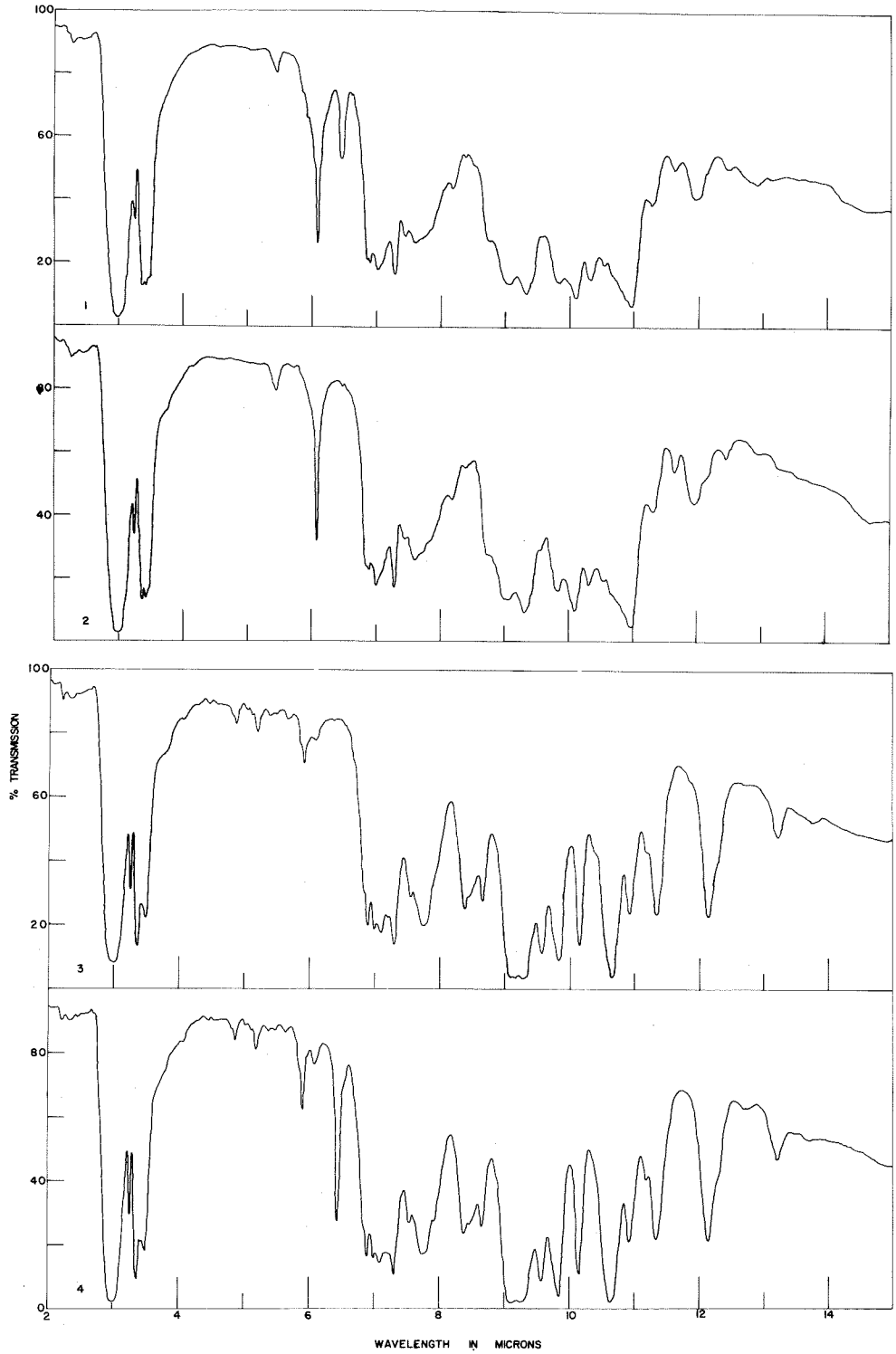
2
14
WAVELENGTH IN MICRONS

Fig. 4

Fig. 5

Curve	Compound
1	Allylmethylcarbinylamine + HONO.
2	17% Cyclopropylmethylcarbinol, 55% allylmethylcarbinol, 28% ethylvinylcarbinol.
3	Cyclopropylmethylcarbinol.
4	2-Methylcyclobutylamine + HONO.

The infrared spectra were obtained with a model 21 Perkin-Elmer double beam recording spectrophotometer equipped with NaCl optics, using pure liquids in an 0.025 mm. NaCl cell. The band at 6.43 μ, in the spectra of the deamination products, was assigned to small amounts of nitro compounds (74).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WAVELENGTH IN MICRONS

Fig. 5

IV. APPENDIX I

DESCRIPTION OF FRACTIONATING COLUMNS

Column No. 1.--A 0.8 x 26 cm. column packed with a tantalum wire coil and carrying an evacuated jacket and a partial reflux head (75).

Column No. 2.--A 1.0 x 48 cm. column packed with stainless steel Helipaks and carrying an electrically heated air jacket and a total reflux head.

Column No. 3.--A 0.8 x 30 cm. concentric tube column equipped with a vacuum jacket and total reflux, solenoid operated head. This column is rated by the manufacturer, Precision Distillation Apparatus Co., at 75 theoretical plates at total reflux.

Column No. 4.--A 0.7 x 60 cm. column packed with a tantalum wire coil and equipped with an electrically heated air jacket and a total reflux head.

Column No. 5.--A 1.3 x 80 cm. column packed with glass helices and equipped with an electrically heated air jacket and a total reflux head.

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VI. PROPOSITIONS

1. The unknown quantities in the amine-nitrous acid reaction are the nature of the cation remaining after loss of the nitrogen molecule from the alkyldiazonium ion and the nature of the cation remaining after intramolecular migration has occurred in the "hot" carbonium ion (if such is implicated). Two kinds of experiments will illuminate the nature of these cations.

(a) Shiner and others (1,2) have shown that the composition of the product mixtures obtained in S_N1-type solvolyses are markedly affected by the substitution of deuterium for beta hydrogens. The effect of beta deuterium substitution on the course of the deamination of primary aliphatic amines should be determined.

(b) While the Streitwieser mechanism (3) for the deamination reaction explicitly states that the cation formed via intramolecular hydrogen migration in this reaction is to be regarded as a solvolytic cation, the "hot" ion mechanism (4) leaves open the possibility that some of the "hotness" may be retained in the rearranged cation. A comparison of the behavior of carbonium ions formed via hydrogen migration in the deamination reaction and that of carbonium ions formed via solvolysis is proposed; there is already some evidence that differences of this type do exist (5,6).

2. Grob and Kammüller (7) have recently published persuasive evidence for an intramolecular 1,5-hydrogen migration in the 5-phenylpentyl free radical. The deamination of 5-phenylpentylamine is predicted to show a similar 1,5-migration. In view of the failure (8) to observe a 1,4-hydrogen migration in the 4-phenylbutyl free radical, it would also be interesting to study the deamination of 4-phenylbutylamine, and see if it undergoes 1,4-hydrogen migration.

3. The possibility of incorporating vapor phase chromatography into a scheme for rapid qualitative and quantitative inorganic analysis should be examined, in view of the great number of elements that form volatile hydrides, halides, etc. The great sensitivity of the chromatography process might be especially useful in the routine determination of trace amounts.

4. Striking isotope-position and structural rearrangements have been observed in the overall formation and reactions of allylcarbinyl Grignard reagents (9). A question that should be answered immediately is whether the allylcarbinyl and cyclopropylcarbinyl Grignards are best represented by one common structure that reacts to give only allylcarbinyl derivatives or by a rapid, highly one-sided equilibrium between two structures.

Striking rearrangements of phenyl groups in Grignard reactions may also occur. Thus the Grignard of 1-phenyl-2-chloropropane could yield 2-phenyl-1-propyl derivatives and that of 1-phenyl-2-methyl-2-chloropropane could yield neophyl derivatives.

5. Considerable interest on the part of the physical chemists attends homogeneous reductions with molecular hydrogen in both aqueous and non-aqueous solutions (10). Besides the reduction of inorganic ions, the reductionsof benzoquinone and of cinnamic acid have been carried out (11,12). A study of the stereochemistry of the homogeneous reduction of olefins and ketones should be feasible. This could perhaps both help elucidate the mechanism of these homogeneous reductions and develop into a useful tool for synthetic organic chemistry. For instance, variation in the size of the anion coupled with the active cationic reducing agent might permit strict stereochemical control over the course of the reduction.

6. Recently, Streitwieser (13) and others have observed small but measurable effects on solvolysis rates caused by the substitution of deuterium for an alpha hydrogen. The results were interpreted in terms of the changes in hybridization at the carbon atom undergoing substitution. If the alpha isotope effect could be measured in a free radical reaction, an indication of the as yet unknown (14) configuration of a carbon free radical could be gained.

7. The large dipole moment of acrolein is generally attributed (15) to a contribution from the resonance form

$$\overset{+}{C}H_2 - CH = CH - \overset{-}{O}$$

The fact that the dipole moment of crotonaldehyde is 0.6 D

larger than acrolein has been explained on the basis of hyperconjugation (15). If this explanation for the large moment of crotonaldehyde is correct, then it is predicted that the moments of 3-methyl-2-butenal ($CH_3CH_3C = CHCHO$) and 3-(methyl-d_3)-2-butenal-4,4,4-d_3 ($CD_3CD_3C = CHCHO$) will be measurably different.

8. Reports have accumulated on the unusually high reactivity of ferrocene in electrophilic aromatic substitution (16). No mention has been made of the mechanism of these aromatic substitution reactions, the tacit assumption apparently being that the mechanism is the same as that for benzene derivatives. A study should be made of the isotope effect on the rate of sulfonation of ferrocene-d_{10}, in order to determine whether this mechanistic assumption is, in fact, justified.

9. Few studies on the relative solvolysis rates of compounds of the types RX and R'X versus RY and R'Y have been reported (17). The nature of X is usually determined by convenience. The observations reported in this thesis indicate the need for an investigation of the effect of X upon relative reactivities. Compounds with different degrees of substitution at the alpha carbon atom should be especially carefully scrutinized. Aniontropically related allylic compounds would be an ideal case, since one can ensure observation of S_N1-type reactions for primary, secondary and tertiary derivatives.

10. Preliminary work on solutions of the interesting addition compounds formed between halogens and triphenyl phosphite has been reported (18). The properties of the pure molten compounds (19) should be examined to see if such characteristics as conductivity are exhibited outside of solution.

11. Recent years have seen the leading technical schools of this country grow increasingly aware of the need for the incorporation of a liberal arts program into their science and engineering curricula. The purpose of such a program is presumably to awaken in the students a realization of, and an appreciation for the arts, so that in future years they will make more valuable use of their leisure time. It is indeed surprising that one can obtain a Ph.D. without in any way having to demonstrate an even casual acquaintance with the arts. Some changes in the requirements for a Ph.D are advocated by the author.

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