CARBONIUM ION REARRANGEMENTS IN REACTIONS OF CYCLOPROPYLCARBINYL AND CYCLOBUTYL DERIVATIVES

Thesis by

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To My Wife

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The author wishes to express his sincere appreciation to Professor John D. Roberts for suggesting this problem and for his continued interest and enthusiasm. Association with Dr. Roberts has been both a pleasant and profitable experience.

The author also wishes to thank the U. S. Rubber Company for a fellowship.

ABSTRACT

1-Methylcyclopropylcarbinylamine and 1-methylcyclobutylamine on treatment with aqueous nitrous acid gave only 1-methylcyclobutanol, while β-methylallylcarbinylamine gave predominantly β-methylallylcarbinol and 1-methylcyclobutanol, with smaller amounts of α-methyl-β-methylallyl alcohol and β-methyl-γ-methylallyl alcohol and possibly 2-3% of 1-methylcyclopropylcarbinol. The 1-methylcyclobutanol from 1-methylcyclopropylcarbinyl-C^{14}-amine contained only 2.6% of the total C^{14}-activity in C-3. The corresponding reaction in acetic acid gave 1-methylcyclobutyl acetate with 3.1% of the C^{14} in C-3.

1-Methylcyclopropylcarbinyl chloride solvolyzes in 50% aqueous ethanol ca. 10 times faster than 1-methylcyclobutyl chloride and about as fast as t-butyl chloride.

It was concluded that the above carbonium-ion type reactions of 1-methylcyclobutyl and 1-methylcyclopropylcarbinyl derivatives are best accounted for by formation, as the important reaction intermediate, of an unsymmetrical, non-classical carbonium ion, structurally similar to the classical 1-methylcyclobutyl cation.

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I. INTRODUCTION

This thesis describes an investigation of carbonium ion reactions of some cyclopropylcarbinyl, cyclobutyl and allylcarbinyl derivatives. Before discussing this research, it will be profitable to consider some related topics and to review the previous work in this field. The following section includes (1) a general discussion of carbonium ion rearrangements, with particular emphasis on bridged or so-called 'nonclassical' carbonium ions; (2) a brief review of the reaction of aliphatic amines with nitrous acid, including Demjanow rearrangements; and (3) a report of recent work on the interconversion reactions of (a) cyclopropylcarbinyl, cyclobutyl and allylcarbinyl derivatives and (b) cyclobutylcarbinyl and cyclopentyl derivatives.

Carbonium Ion Rearrangements

Demonstration of the existence of carbonium ions came as early as 1902, when Walden[1] observed that solutions of triphenylmethyl (trityl) chloride in liquid sulfur dioxide are intensely yellow and excellent conductors,* and furthermore by the fact that ionization is induced by addition of Lewis acids to a colorless solution of triphenylmethyl chloride in a non-

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*The yellow color of these solutions may not necessarily mean that the compound is ionic in nature.[2]

ionizing solvent. The theory is adequately supported by the molar freezing-point depression of triphenylcarbinol in sulfuric acid[3] and the isolation of anhydrous triphenylmethyl perchlorate.[4]

Carbonium ions have been postulated and demonstrated as intermediates in a large number of organic reactions,[5-7] including hydration of olefins, addition of halogen acids to olefins, reactions of amines with aqueous nitrous acid, acid-catalyzed olefin polymerization, hydride transfer in isoparaffins, hydrolysis of certain esters and solvolysis of sulfonates.

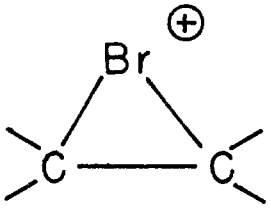
All of these reactions and many more[5-8] may, with properly constituted molecules, involve a concomitant rearrangement of the carbon skeleton, e.g., pinacol, Demjanow, Wagner-Meerwein and dienone-phenol rearrangements. The generally accepted mechanism of 1,2-shifts in carbonium-ion reactions was formulated by Whitmore.[9] According to this hypothesis an unstable cationic intermediate is formed which rearranges by the migration of an alkyl group (or hydrogen), together with its pair of electrons, from a neighboring carbon to the carbonium carbon (1,2-shift). The resulting carbonium ion may react with some nucleophilic species, lose a proton from a neighboring carbon or undergo further rearrangement.

Although the usefulness of the Whitmore mechanism has been widespread, there remain a number of phenomena associated with certain reactions which cannot be, or are inadequately explained by simple 1,2-shifts in carbonium ions. As a re-

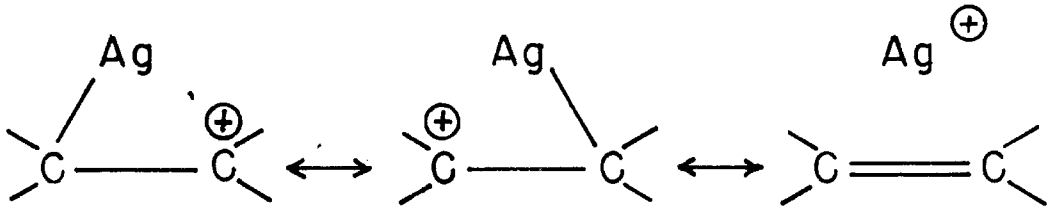
sult, the proposals and demonstrations of bridged ions or so-called non-classical carbonium ions have been important contributions to the development of carbonium ion theory.

Historically, Roberts and Kimball[10] first proposed such an intermediate to explain the trans addition of bromine and hydrogen halides to olefins. Experimental support for the bromonium ion (I) (fig. 1) came with the report that stereoisomers of 3-bromo-2-butanol react with hydrobromic acid to give dibromides with retention or inversion at both carbon atoms.[11] Previously the bridged ion II was used to explain the non-isomerization of cis- and trans-2-butenes when complexed with silver.[12]

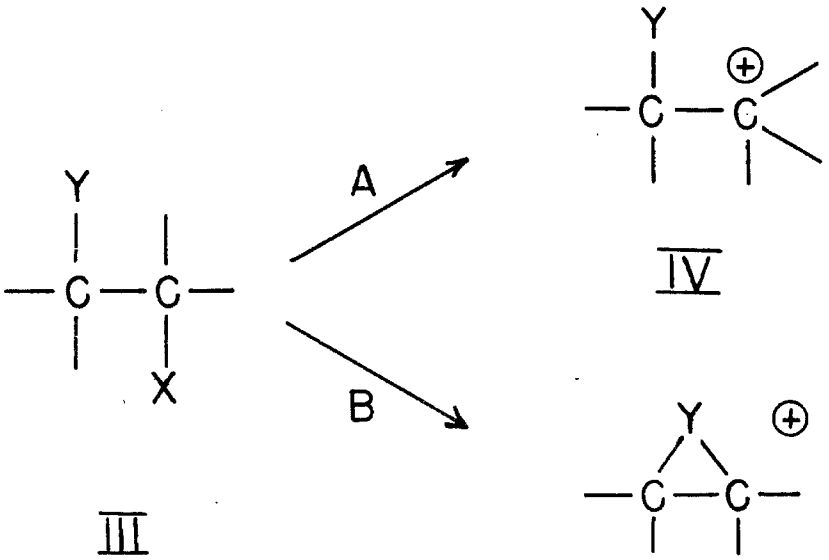
Additional evidence for cyclic intermediates comes from kinetic studies of compounds which contain substituents attached to carbon atoms adjacent to the leaving group (III). Thus a substituent Y, by its electrical effect might decrease the reaction rate of path A (compared to the unsubstituted compound), yet enhance the rate of path B by assisting the departure of the leaving group X. Such assistance has been termed "neighboring group participation."[13] It should be noted that some Y substituents (e.g., Br) may decrease the overall reaction rate ($k_A + k_B$) compared to the unsubstituted compound, yet this overall rate may be considerably larger than simple ionization (k_A), due to the participation of the neighboring group. The relative importance of paths A and B depends to a large extent upon groups X and Y and their stereo-



I



II



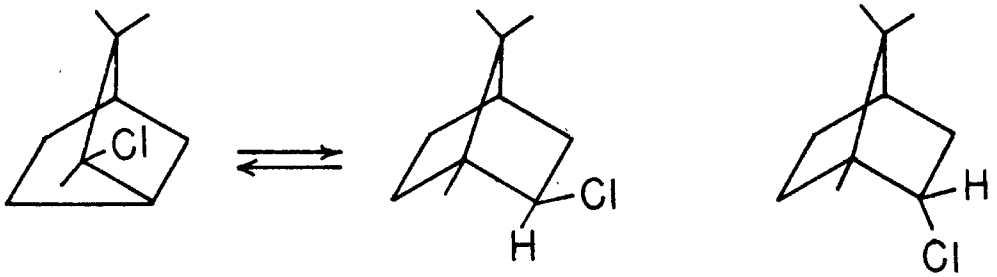
III IV V

Fig. 1

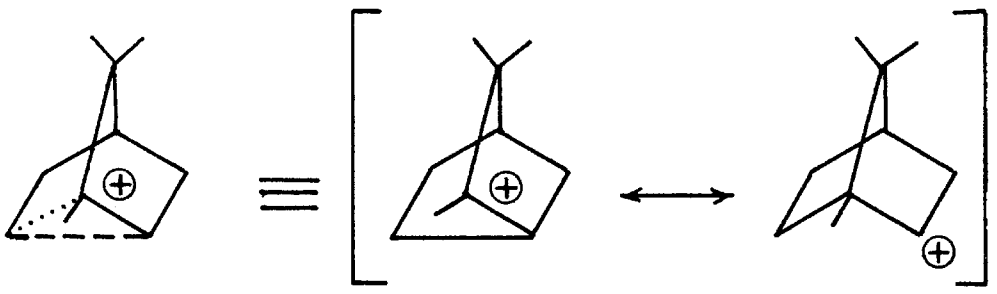
chemical relationship, the reaction type and solvent.

As a measure of the amount of neighboring group participation, a new term was introduced. The "driving force"[14] for a given substituent Y is a logarithmic measure of the ratio of reaction rates of paths B to A. Thus the "driving force" is the decrease in free energy in going from IV to V which is already realized when the transition state is reached. Some typical examples of driving force values (L_o) for Y substituents are Br, 4.6; I, 9; $O^{\ominus}$, 6; OCH_3, 1.3; NH_2, 8; C_6H_5CONH, 14 and C_6H_5, 2.0.[13,15]

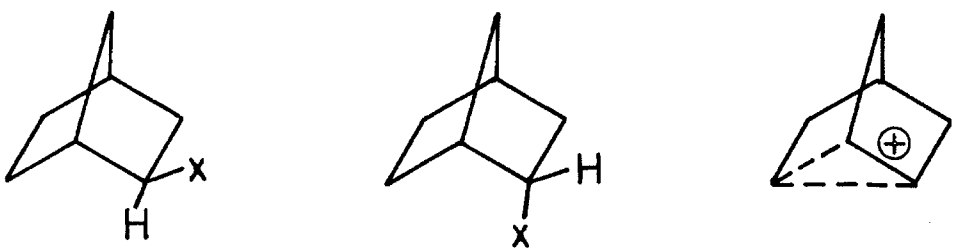
Evidence for carbon participation was first realized in the facile interconversion of camphene hydrochloride (VI) and isobornyl chloride (VII) (fig. 2). Complete stereospecificity was evident in the non-formation of the slightly more stable isomer, bornyl chloride (VIII). The postulated intermediate (IX)[16,17] may be considered as a hybrid structure of two ions which are not energetically equivalent; thus the camphenyl cation (X) is weighted more heavily than the isobornyl cation (XI). Further support for the mesomeric cation IX is available in the solvolysis rates in 80% ethanol at 80°, isobornyl chloride (VII) reacting ca. 10^5 times faster than bornyl chloride (VIII),[18,19] the latter being comparable to that of i-propyl chloride,[20] a typical secondary chloride. This example is instructive for it emphasizes the stereochemical requirements for participation of neighboring electrons. Ethanolysis of camphene hydrochloride at 0° is 6000



VI VII VIII

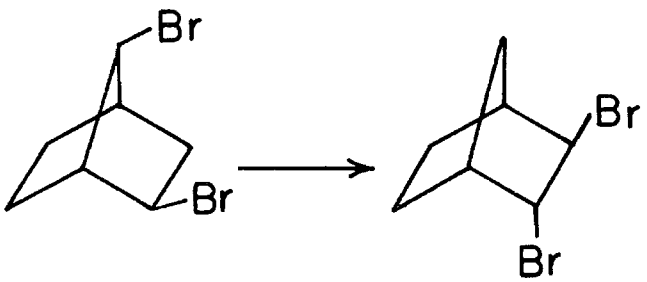


IX X XI



XII, x = p−BrC$_6$H$_4$SO$_3$ XIV XV

XIII, x = CH$_3$COO x = p−BrC$_6$H$_4$SO$_3$



XVI XVII

Fig. 2

times greater than the corresponding rate for t-butyl chloride.[18]

Acetolysis of optically active exo-norbornyl p-bromobenzenesulfonate (XII)[19,21] proceeds 350 times faster than optically active endo-norbornyl p-bromobenzenesulfonate (XIV),[21] the product from both reactions, racemic exo-norbornyl acetate (XIII),[22,23] implying a high degree of stereospecificity. About 7-8% of the product from XIV is optically active exo-norbornyl acetate (XIII) formed by nucleophilic solvent participation. Note that the suggested non-classical cationic intermediate (XV),[21] which accounts for the loss of optical activity, has a plane of symmetry (defined by C-4, C-5, C-6 and the midpoint of C-1 and C-2). The rate differences in solvolyses between isobornyl (VII) and bornyl (VIII) compounds ($\sim 2.5 \times 10^5$) and between exo-norbornyl (XII) and endo-norbornyl (XIV) compounds ($\sim$350) are noteworthy; the 1-methyl group of isobornyl compounds apparently enhances the rate by a factor of ca. 700.[19]

A similar intermediate was proposed in the acid-catalyzed isomerization of 2-exo-7-syn-dibromo-[2,2,1]-bicycloheptane (XVI) to trans-2,3-dibromo-[2,2,1]-bicycloheptane (XVII).[24]

Some of the most convincing and first concrete evidence for a bridged, non-classical carbonium ion was brought to light by the work of Cram, et al., with compounds asymmetric both at the reaction center and the adjacent carbon atom. For example, acetolysis of D- or L-threo-3-phenyl-2-butyl p-toluenesulfonate (XVIII or XIX) gave a racemic mixture of

the corresponding threo acetate (XX and XXI) (fig. 3).[25] On the other hand, optically active erythro-3-phenyl-2-butyl p-toluenesulfonate (XXIV) gave only active erythro acetate (XXV ≡ XXVIII) of retained configuration (fig. 4). The only reasonable interpretation was that the intermediate ion-pairs XXII and XXVI (or the kinetic equivalent, two unsymmetrical ion-pairs in dynamic equilibrium) reacted with solvent to give the ion-pairs XXIII and XXVII, respectively. The latter then collapsed stereospecifically to give the products. Since XXII has a plane of symmetry, it can give only racemic product. Furthermore XXII and XXVI, termed phenonium p-toluenesulfonate ion-pairs,[26] may undergo exchange with anions (e.g., p-bromobenzenesulfonate ion) to form new ion-pairs. Ion pair XXII may also collapse to give the enantiomorph (XIX) of the starting material (XVIII).

Olefins accompanied the formation of acetates, e.g., XXIV yielded the four possible 2-phenylbutenes, with cis-2-phenyl-2-butene predominating (56%); presumably the latter was formed via the hydrogen-bridged ion pair, XXIX.[27] Similar studies have been made on the 2-phenyl-3-pentyl,[27] 3-phenyl-2-pentyl,[28] 1,2-diphenyl-1-propyl[29] and 4-phenyl-3-hexyl[30] systems.

An especially interesting result was observed in the acetolysis of L-threo-4-phenyl-3-hexyl p-toluenesulfonate (XXX) (fig. 5).[30] About 12% of the product was L-threo-4-phenyl-3-hexyl acetate and 2.5% was the L-erythro isomer. This predominance of retention over inversion, the opposite of

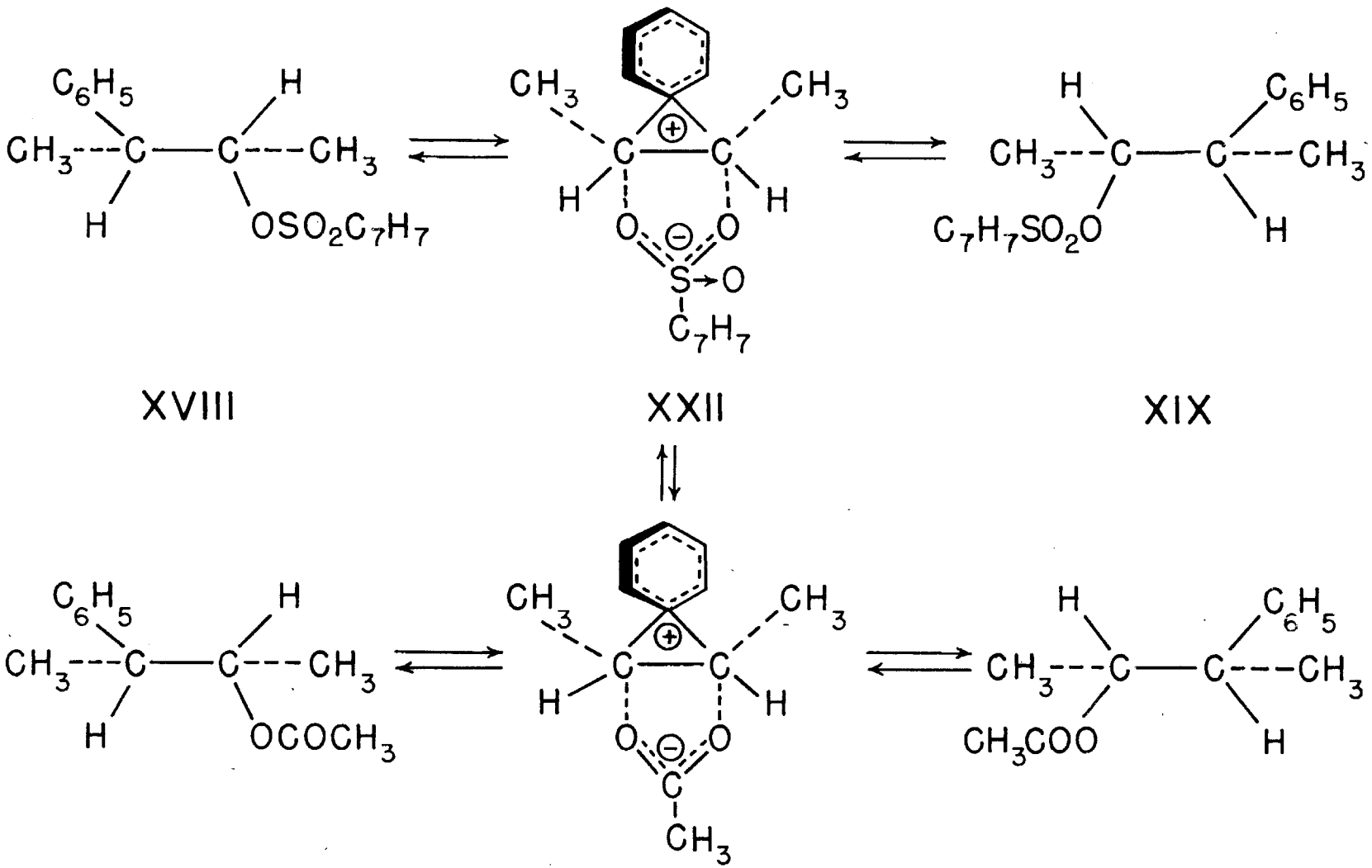


Fig. 3

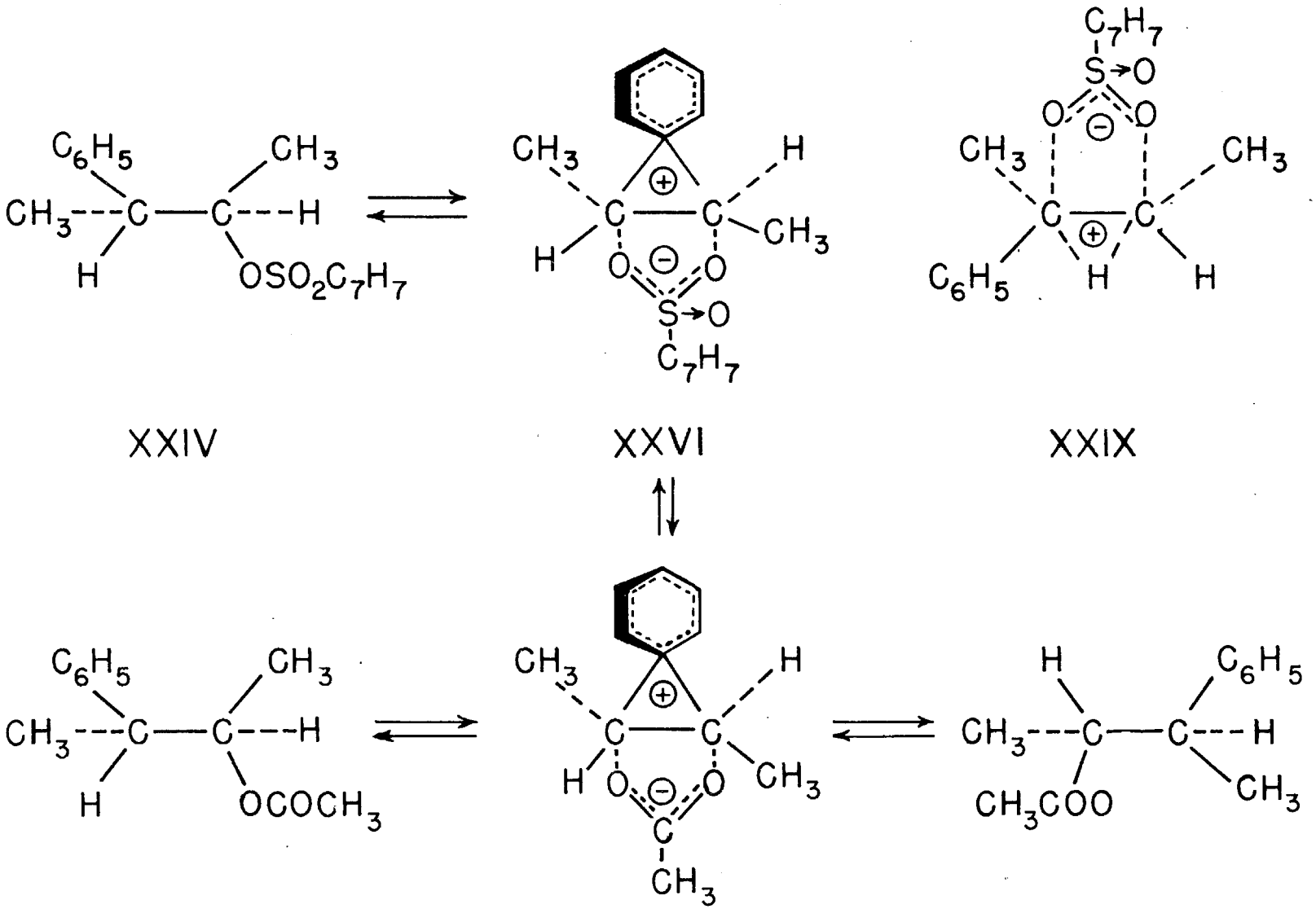
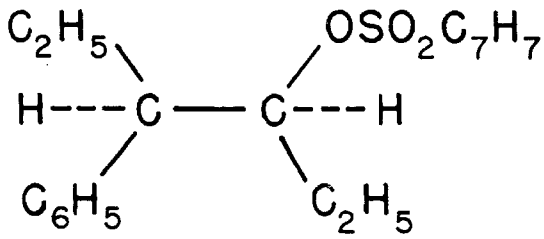
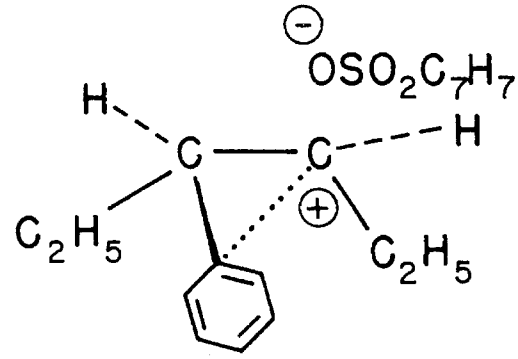


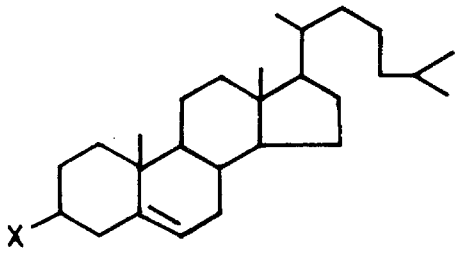
Fig. 4



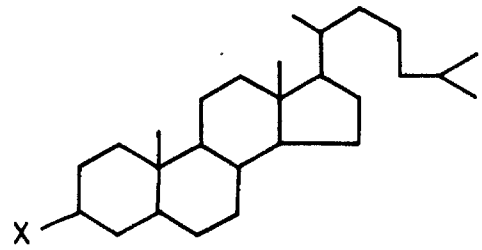
XXX



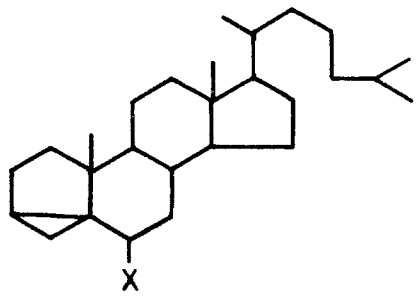
XXXI



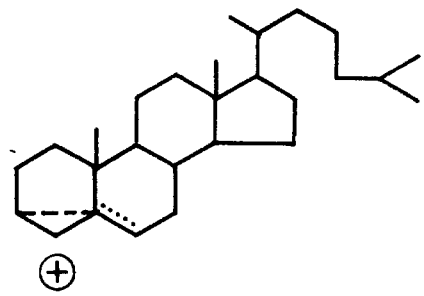
XXXII



XXXIII



XXXIV



XXXV

Fig. 5

what is usually observed in typical S_N1 (unimolecular) reactions, was explained on the basis of an unsymmetrical phenonium ion (XXXI).

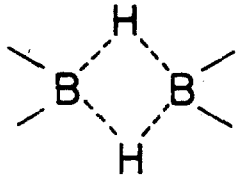
One of the most convincing examples of non-classical carbonium ions is found in the cholesteryl--i-cholesteryl (5,6-dehydrocholestanyl--3,5-cyclocholestanyl) interconversion. Cholesteryl derivatives (XXXII) undergo certain displacements (unimolecular) with retention of configuration.[31-33] Methanolysis of cholesteryl p-toluenesulfonate (XXXII, X = $CH_3C_6H_4SO_3$) in the presence of acetate ion (buffer) affords the methyl ether of i-cholesterol (XXXIV, X = OCH_3)[34] with inversion at C-3.[35] The i-cholesteryl methyl ether is extremely reactive, undergoing exchange with acidic ethanol giving i-cholesteryl ethyl ether (XXXIV, X = OC_2H_5) which then rearranges to cholesteryl ethyl ether (XXXII, X = OC_2H_5).[36]

Cholesteryl p-toluenesulfonate (XXXII, X = $CH_3C_6H_4SO_3$) undergoes ethanolysis ca. 40 times faster than cholestanyl p-toluenesulfonate (XXXIII, X = $CH_3C_6H_4SO_3$)[37] and 100 times as fast as cyclohexyl p-toluenesulfonate.[33] Strikingly, i-cholesteryl chloride (XXXIV, X = Cl) is $\sim 10^{10}$ times more reactive than cholestanyl chloride (XXXIII), rearranging to cholesteryl chloride (XXXII, X = Cl) (80% yield in acetic acid:dioxane with added sodium acetate and 25% in 90% dioxane).[38] From rough calculations,[39] i-cholesteryl methyl ether (XXXIV, X = OCH_3) exchanges (in acidic ethanol) 100 times faster than the methyl ether of methylcyclopropylcarbi-

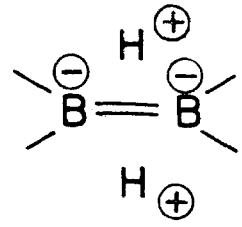
nol and rearranges to cholesteryl methyl ether (XXXII, X = OCH_3) about 10^5 times as fast as methylcyclopropylcarbinyl methyl ether rearranges to the methyl ether of 3-pentene-1-ol. The most satisfactory interpretation of the above facts is furnished by a mesomeric cationic intermediate (XXXV).

A number of structures with hydrogen bridges have been proposed for boron hydrides, among which are XXXVI[40] (which is actually a hybrid of four resonance forms, two being ionic) and XXXVII (fig. 6).[41] The most simple hydrogen-bridged non-classical cation, the 'ethyleneprotonium' ion (XXXVIII), was not found to be an important intermediate in the reaction of ethylamine-1-C^{14} with aqueous nitrous acid. The ethanol product was shown to contain 1.5% of the rearrangement product ethanol-2-C^{14}; hence XXXVIII (or an equilibrium mixture of the two ethyl cations XXXIX and XL) could have led to only 3% of the product ethanol. As a corollary, the ethyl cation, XXXIX, reacts with water considerably faster than it rearranges to XXXVIII or XL.[42] It is possible that XXXVIII represented more than 3% of the intermediate cations, but then lost a proton preferentially to form ethylene.

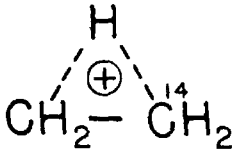
Considerably more rearrangement occurred in the reaction of 1-aminopropane-1-C^{14}, with aqueous nitrous acid.[43] The 1-propanol product contained 8.5% of 1-propanol-2-C^{14} corresponding to rearrangement either by way of 8.5% of the rearranged 1-propyl cation (XLI) (by methyl migration) or 17% of the non-classical cation XLII. The relative stability of XLII



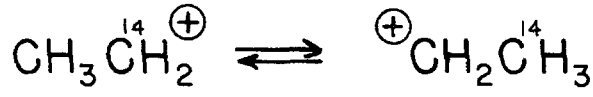
XXXVI



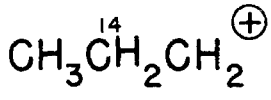
XXXVII



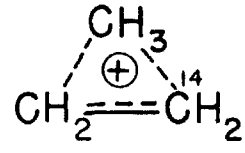
XXXVIII



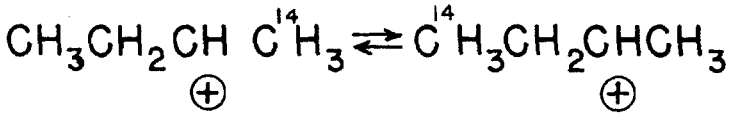
XXXIX XL



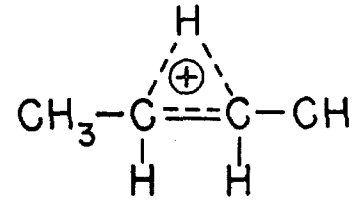
XLI



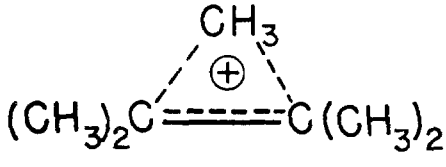
XLII



XLIII XLIV



XLV



XLVI

Fig. 6

compared to XXXVIII is reflected in the larger amount of rearrangement (8.5% by a methide shift) in the diazotization of n-propylamine than the corresponding amount of rearrangement (1.5% by hydride shift) observed with ethylamine.

Unimolecular acetolysis of 2-butyl-1-C^{14} p-toluenesulfonate in the presence of acetate ion gave 9% of rearranged product, 2-butyl-4-C^{14} acetate, which could arise from 9% of XLIV or 18% of the non-classical cation, XLV.[44] It was shown that the product was stable under the reaction conditions and that the product could not have arisen by reaction of butenes with acetic acid. XLIII, and some of XLIV, were the preferred intermediates.

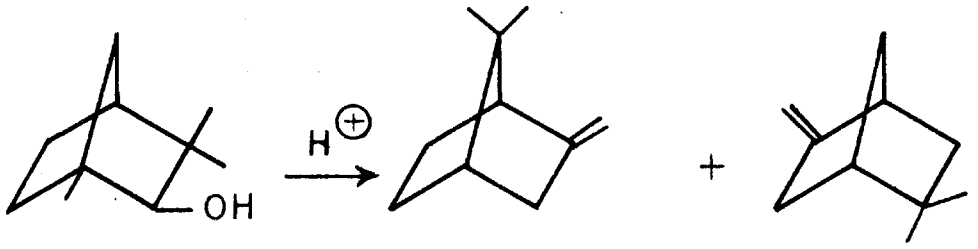
In contrast to the % migration of hydrogen and methyl in primary cations, 1,2-migration of benzyl occurred only to the extent of ca. 0.2% in the reaction with nitrous acid of 1-amino-3-phenylpropane-1-C^{14} or the corresponding p-methoxy derivative.[45] In the acetolysis and formolysis of isomers of 3,4-dimethyl-4-phenyl-3-hexyl p-bromobenzenesulfonate, the order of migratory aptitudes was phenyl > methyl > ethyl.[46] The lack of agreement between migratory aptitudes in Wagner-Meerwein and pinacol rearrangements (where benzyl > ethyl > methyl)[47] was explained on the basis of the greater relative importance of hyperconjugative resonance in the bridged intermediates in the Wagner-Meerwein rearrangements.[46]

Treatment of 2,3,3-trimethyl-2-butanol-1-C^{14} with an equimolar mixture of concentrated hydrochloric acid and zinc chloride (Lucas reagent) caused complete equilibration of the methyl

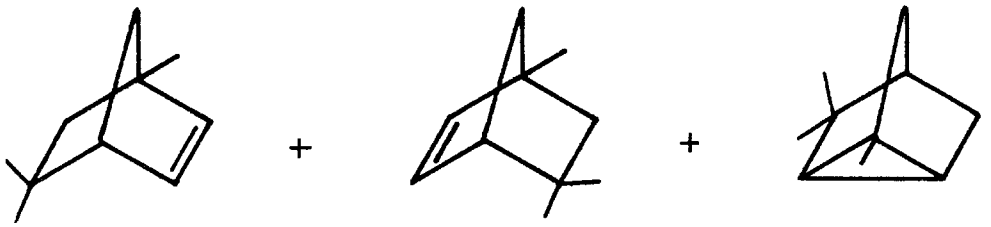
groups and complete chloride ion exchange with Lucas reagent containing radioactive chloride ion.[48] Milder conditions, e.g., concentrated hydrochloric acid at 25° for twenty minutes, gave considerably less rearrangement (36%) and no chloride exchange. These results are best explained on the basis of an equilibrium between two classical carbonium ions. It was concluded that the non-classical cation XLVI was not an important intermediate in the irreversible carbonium ion-type reactions.

A 1,3-hydride shift was suggested to explain the acid catalyzed racemization of isobornyl chloride.[49,50] Adequate support of this postulate has appeared in recent years. Rate and deuterium tracer studies indicated an intramolecular 2,6-hydride shift occurred in the formation of β- and γ-fenchenes by acid catalyzed dehydration of β-fenchol.[51] The intermediate was depicted as XLVII (fig. 7).

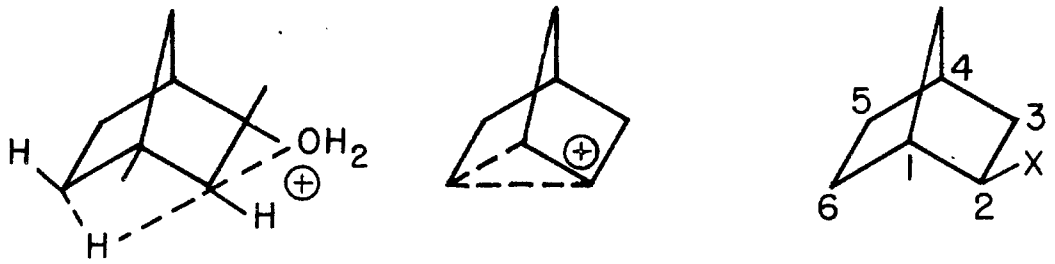
The 'norbornonium' ion (XLVIII) proposed[21] to explain the solvolytic and stereochemical behavior encountered in the solvolysis of exo- and endo-norbornyl p-toluenesulfonate (XLIX, X-p-$CH_3C_6H_4SO_3$, exo shown), fails to explain the results obtained with exo- and endo-norbornyl-2,3-C^{14} p-bromobenzenesulfonate (XLIX, X = p-$BrC_6H_4SO_3$, exo shown).[52,53] The C^{14}-distribution in the product of acetolysis of exo-norbornyl-2,3-C^{14} p-bromobenzenesulfonate indicates 58% isotope-position rearrangement, 15% in C-5 and C-6. Any of the intermediates XLVIII (fig. 7), L, LI or LII (fig. 8), or any combination of these, fails to explain the results. The only satisfactory



β-fenchol α-fenchene β-fenchene

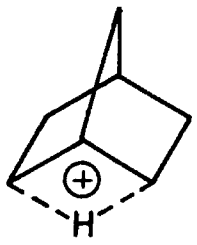


γ-fenchene δ-fenchene cyclofenchene



XLVII XLVIII XLIX

Fig. 7



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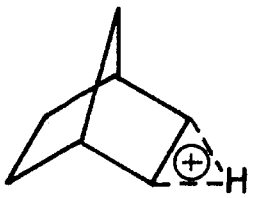
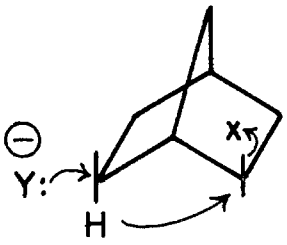
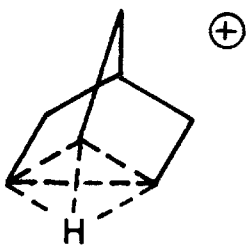


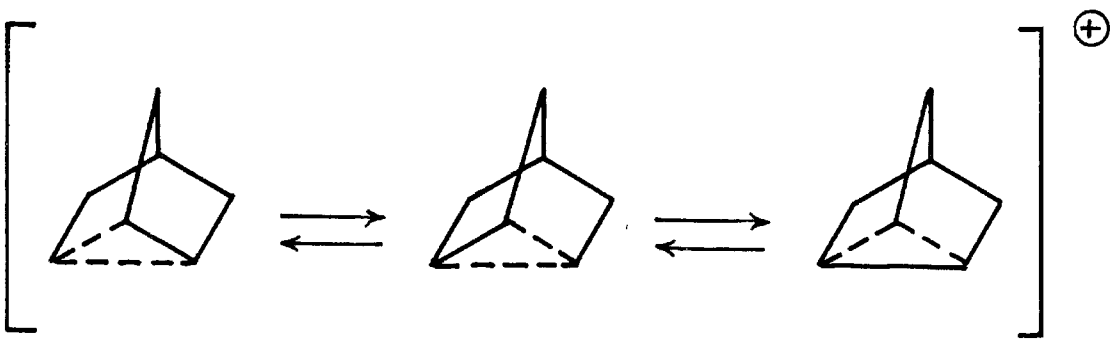
LI



LII



LIII



LIV a LIV b LIV c

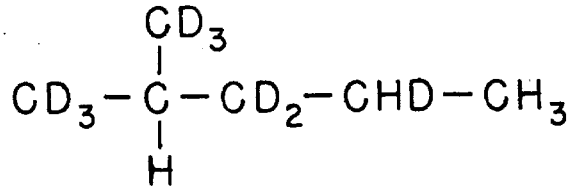
Fig. 8

explanation involves the intermediate 'nortricyclonium' ion (LIII) or its equivalent,[54] an equilibrium between the three types of LIV (LIVa-LIVc). Evidence for intermediates of type LIV has also been found in the racemization of 8-substituted camphenes[55] and camphene-8-C^{14}.[56]

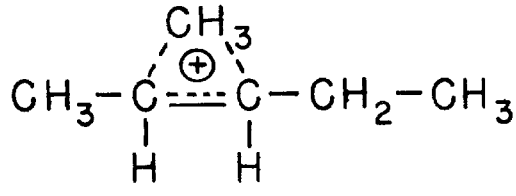
The isolation of 2,4-dimethyl-3-ethyl-2-pentene as the main product in the acid catalyzed dehydration of 4,4-dimethyl-3-ethyl-2-pentanol strongly indicated a 1,3-methide shift.[57] Another possible product, 2,3,4-trimethyl-2-hexene, which could arise by two successive alkyl shifts, was not found.

Isomerization experiments with saturated hydrocarbons in deuterated sulfuric acid have led to the postulation of bridged ions.[58] For example, 2-methylpentane exchanges to give roughly equivalent amounts of 2-methylpentane-$\underline{d}_8$, -$\underline{d}_9$, -$\underline{d}_{10}$ and -$\underline{d}_{13}$. The process of alkyl shifts did not adequately explain the exchange of non-contiguous hydrogens (cf. 2-methylpentane-$\underline{d}_9$, LV, fig. 9), hence a cyclic intermediate (LVI) was suggested. The positive charge on the center carbon of the pentane chain was believed to permit a slow exchange with the adjacent secondary hydrogens.

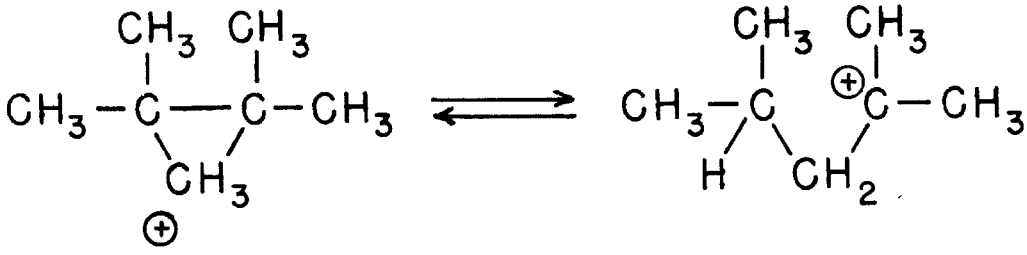
Isomerization of 2,2,3-trimethylbutane[58] in sulfuric acid led to a considerable amount of 2,4-dimethylpentane; the cyclic intermediate LVII was postulated to be formed. LVII was then assumed to undergo an intramolecular hydride shift to form the 2,4-dimethylpentyl moiety (LVIII). This mechanism obviated the necessity of postulating the formation



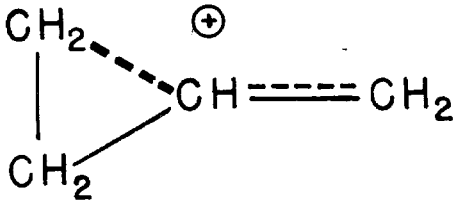
LV



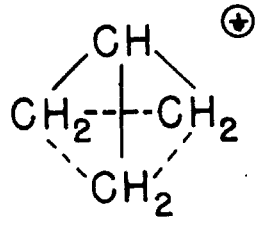
LVI



LVII LVIII



LIX



LX

Fig. 9

of a primary carbonium ion followed by (1) 1,2-alkyl shifts or (2) migration and synchronous rearrangement of the migrating group.

Cyclopropylcarbinyl benzenesulfonate solvolyzes in ethanol at 20° about 15 times as fast as allyl benzenesulfonate,[59] and cyclopropylcarbinyl chloride solvolyzes at 50° in 50% aqueous ethanol 40 times as fast as allyl chloride.[60,61] One intermediate postulated (LIX) finds an analogy in the i-sterol rearrangement.

The results of the amine-nitrous acid reaction of cyclopropylcarbinylamine-α-C^{14} disclosed that a partial equivalence of the three methylene groups was achieved during the reaction.[62,63] From these findings, together with the abnormally high solvolysis rates of cyclopropylcarbinyl and cyclobutyl derivatives,[59,60,61,64] the symmetrical intermediate LX was proposed.[62]

Among numerous symbols suggested to represent simple bridged carbonium ions are those (fig. 10) of Nevel, de Salas and Wilson[16] and Ingold[17] (LXI); Eyring[65] (LXII); Walsh[66] and Dewar[67] (LXIII) (π-complex); Price[68] (LXIV); Arcus[69] (LXV); Stevenson, Wagner, Beeck and Otvos[58] (LXVI) and Winstein, et al.,[70] (LXVII). Perhaps the charge distribution is more on the order of LXVIII.[26]

Regardless of whether the intermediate is represented by LXIX (LXIXa-LXIXc) or by an equilibrium mixture of the two canonical forms, LXX and LXXI, the essential point of dif-

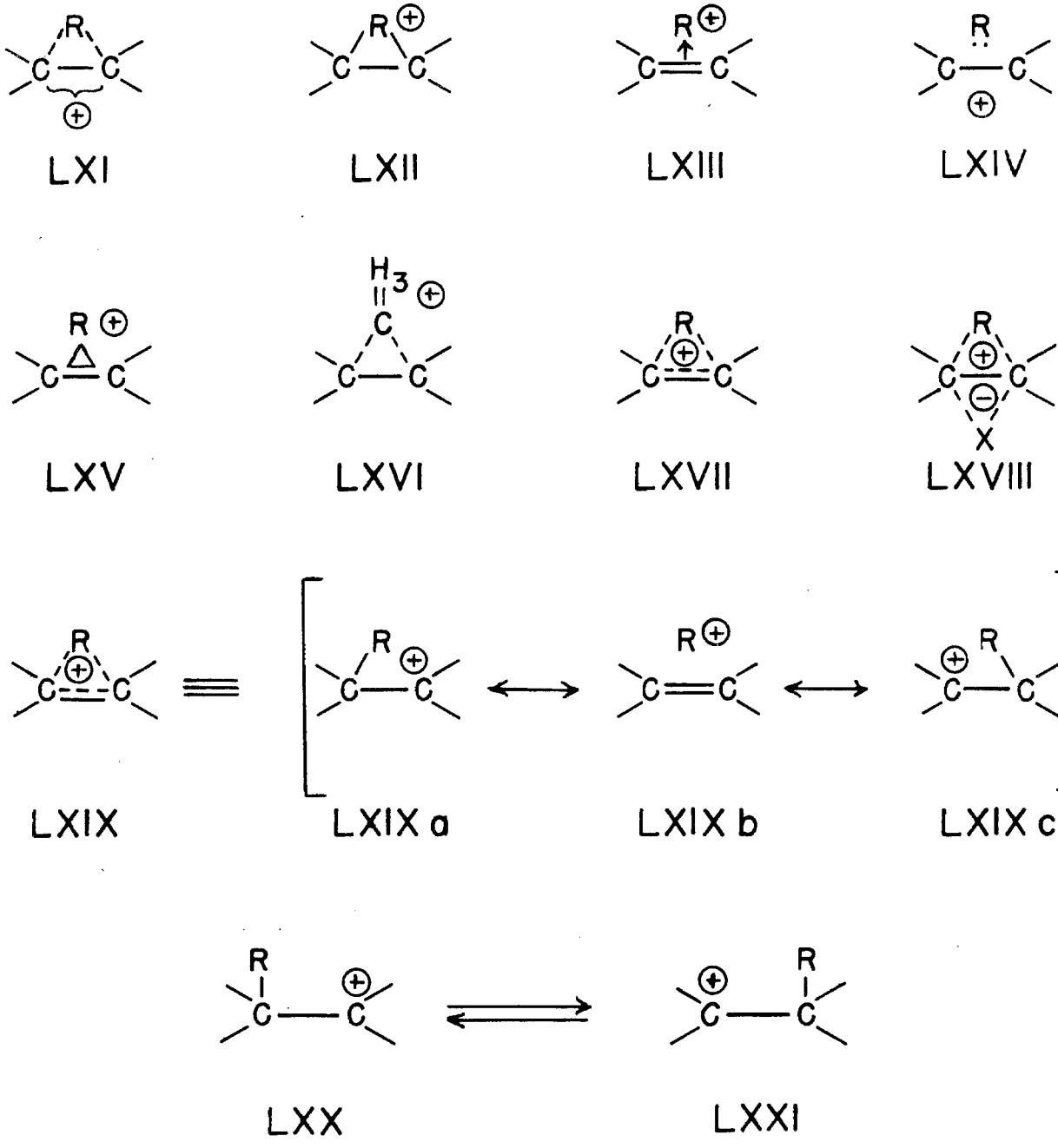

LXI
LXII
LXIII
LXIV
LXV
LXVI
LXVII
LXVIII
LXIX
LXIX a
LXIX b
LXIX c
LXX
LXXI

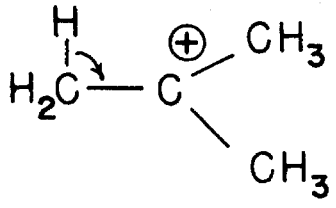
Fig. 10

ference is found in the answers to the following questions: (1) does LXIX represent a valley in the potential energy-reaction coordinate curve, lower in energy than LXX and LXXI, or (2) is LXIX better described by a potential energy valley higher in energy than LXX and LXXI, or finally (3) is LXIX an activated state (or transition state) of higher energy than LXX and LXXI?

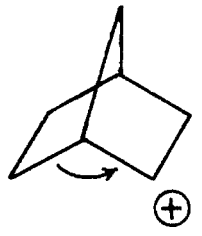
Of considerable interest is the physical interpretation of bridged intermediates and other non-classical cations. In this respect, it is noteworthy that the H_3^+ ion is most stable in the triangular configuration[71] and furthermore, it has been calculated that a proton attached to two adjacent centers is probably stable.[65]

It is generally considered that carbonium ions derive a considerable amount of their stabilization by delocalization of electrons of the adjacent carbon atom, whether these electrons be σ-bonding electrons (t-butyl cation, LXXII, or norbornyl cation, LXXIII), π-electrons (allylic cations, LXXIV, or homoallylic cations, e.g., cholesteryl cation, LXXV) or electrons of a neighboring cyclopropane ring (i-cholesteryl cation, LXXVI) (fig. 11).

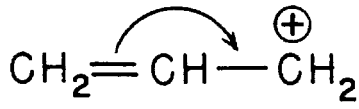
A clear interpretation of the solvolytic behavior of certain compounds has been presented,[72] with due regard to stereochemical orientation of the orbitals involved in participation. Thus the low reactivity of dehydronorbornyl halides (LXXVII), relative to cholesteryl derivatives (LXXVIII),[33] is explained



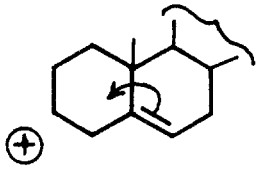
LXXII



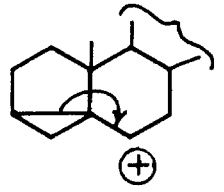
LXXIII



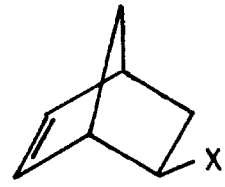
LXXIV



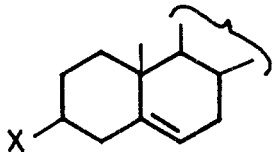
LXXV



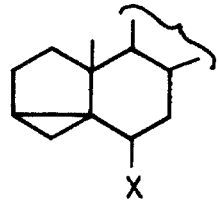
LXXVI



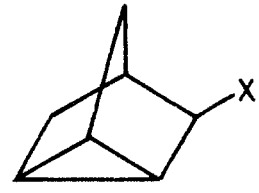
LXXVII



LXXVIII



LXXIX



LXXX

Fig. 11

partly by the spatial arrangement of the carbons holding the substituent and the double bond, the carbon atom bearing the substituent in LXXVIII being oriented more nearly endwise to the double bond than in LXXVII. The unreactivity of epi-cholesteryl derivatives relative to the cholesteryl analogues was explained in a similar fashion; the 3-substituent in epi-cholesteryl compounds is α (down with respect to the C-10 methyl) and axial (polar) and hence is not properly oriented with respect to backside participation by the 5-6 double bond.[73]

A similar interpretation was offered[72] for the extra-ordinarily high reactivity of i-cholesteryl compounds[33] (LXXIX) compared to the nortricyclyl derivatives[72] (LXXX). The vacant C-6 p-orbital in the i-cholesteryl cation is well-positioned for effective overlap of the 3-5 bond, but models show a similar situation does not exist in the nortricyclyl cation.

Semi-empirical molecular orbital calculations[74] predict considerable stabilization due to the 1,3-interaction of a cationic center and a π-electron-containing β-substituent. Estimated stabilizations of 4 and 6 kcal. for β-phenyl and β-vinyl are in agreement with the observed rate-enhancing effects of these substituents. It was concluded that the intervening methylene group in homoallylic systems is a poor insulator against 1,3-interaction.

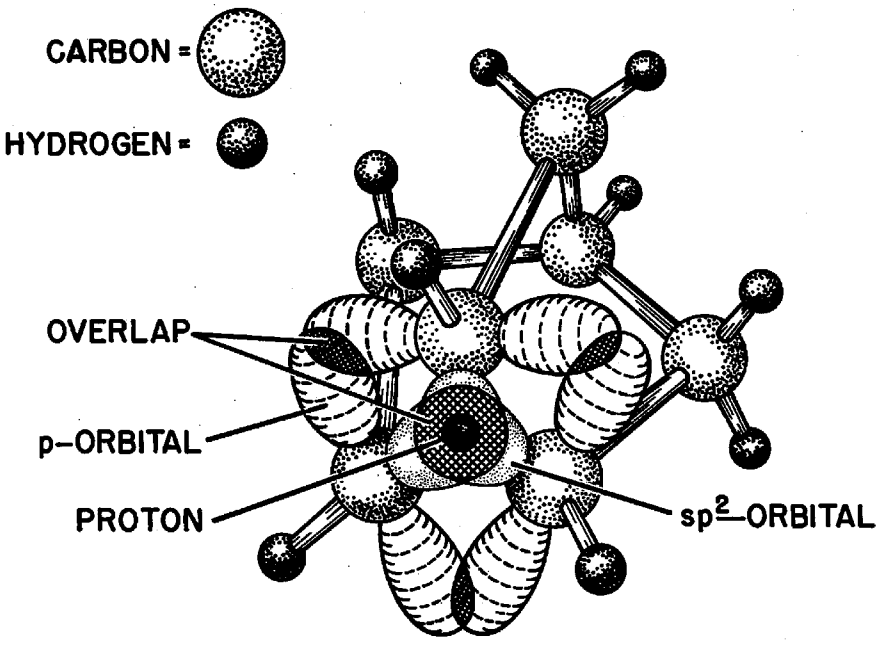
An atomic orbital representation (LXXXII) of the 'nortricyclonium' ion (LXXXI) has recently appeared,[53] based on

Walsh's[75] model of the cyclopropane ring and molecular models for boron hydrides.[76,77] A similar model has also been proposed for the 'tricyclobutonium' ion[62] (LXXXIII).

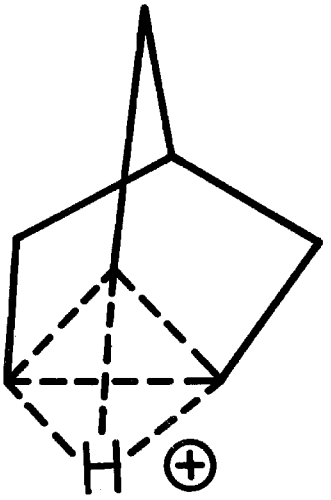
The effect of structural changes on neighboring group participation (anchimeric assistance)[78] has been discussed[13] and a convincing amount of experimental evidence presented.[79] Briefly, participation decreases in the order primary > secondary > tertiary with respect to the carbon bearing the leaving group (C-α), and alkyl or aryl substitution on C-β favors neighboring group participation.

A semi-quantitative approach has been made[13,78] which enables one to make estimations of the driving force (rate enhancement) expected for simple substituents, or conversely, if rate data are available, the driving force of a given substituent may be calculated and comparisons made with other substituents. The parallelism of values for the driving force of certain neighboring groups with the nucleophilic constants[80] of certain nucleophilic reagents is by no means accidental, since both values are derived from linear free-energy relationships.

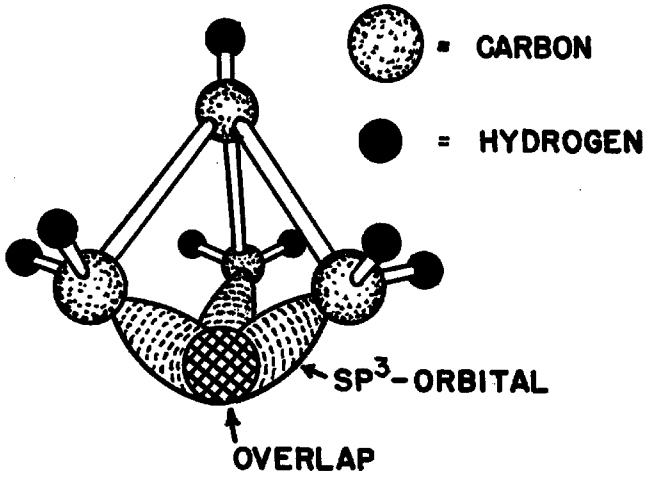
Various combinations of rate acceleration and structural change have been studied recently by Hughes, Ingold, et al.[18] Three examples will be illustrative. Neopentyl bromide undergoes unimolecular solvolysis in wet formic acid with rearrangement about one-half as fast as ethyl bromide (no rate acceleration), while 2,2,2-triphenylethyl chloride reacts with



LXXXII



LXXXI



LXXXIII

rearrangement $\sim 10^5$ times as fast as neopentyl chloride. It is noteworthy that neopentyl p-toluenesolfonate solvolyzes at the same rate as ethyl p-toluenesulfonate, even in formic acid at 75°.[81] Rate acceleration without rearrangement occurs in the ethanolysis of camphene hydrochloride, which solvolyzes ca. 6000 times as fast as t-butyl chloride.[18] Ingold[8] has termed rate acceleration (with or without rearrangement) due to neighboring methyl or phenyl as 'synartetic' acceleration; consequently, this term does not encompass the large number of reactions covered by the term 'anchimeric assistance' or 'anchimeric acceleration'.

The relative importance of solvent participation (displacement of the leaving group by solvent with no "interference" by neighboring groups) and neighboring group participation is determined to a large extent by external conditions (e.g., solvent and temperature) and the reaction type. For example, ethanolysis of benzylmethylcarbinyl p-toluenesulfonate gave the corresponding acetate with 93% inversion, acetolysis gave 65% inversion and formolysis, 15% inversion.[82] From these and other considerations, the order of nucleophilic solvent participation was derived as $C_2H_5OH > CH_3OH > H_2O > CH_3COOH > HCOOH$ and the order of phenyl participation as a function of solvent was $HCOOH > CH_3COOH > C_2H_5OH$. The relative rates of the above reactions and of i-propyl and p-methoxybenzylmethylcarbinyl p-toluenesulfonate clearly demonstrate this trend (Table I).

Table I

Comparison of Solvolysis Rates of p-Toluenesulfonates[82]

Solvent	$CH_3\underset{X}{CH}CH_3$ >	$C_6H_5CH_2\underset{X}{CH}CH_3$ by a factor of	$C_6H_5CH_2\underset{X}{CH}CH_3$ <	$p\text{-}CH_3OC_6H_4CH_2\underset{X}{CH}CH_3$ by a factor of
C_2H_5OH		5		6
CH_3COOH		3		21
HCOOH		2		32

X = p-$CH_3C_6H_4SO_3$

Caution must be exercised in predicting solvent effects. For example, the ratio of the polarimetric rates to titrimetric rates in solvolysis of exo-norbornyl p-bromobenzenesulfonate is 3.46, 2.94 and 1.40 in acetic acid, ethanol and 75% acetone, respectively.[23] The result with aqueous acetone is not well-explained on the basis of (1) the aforementioned orders of solvent participation, (2) Grunwald and Winstein's[83] Y values (ionizing power), which are meant to correlate solvolysis rates in reactions of the type, $RX \longrightarrow R^+ + X^-$, or (3) the nucleophilic (n) or electrophilic (e) solvent constants of Swain.[84] The absence of an accompanying common-ion depression in the internal return isomerization during the solvolysis of optically active exo-norbornyl p-bromobenzenesulfonate has been taken by Winstein[38] as evidence favoring return mainly

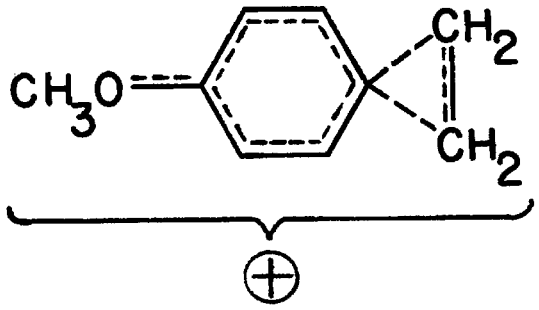
from a tight ion-pair, rather than a loose ion-pair or free cation. Thus solvents which (1) have high positive Y values (good ionizing solvents) and (2) which are very nucleophilic will lead to less return, as in the case of 75% acetone.

2-Butyl-1-C^{14} [44] and exo-norbornyl-2,3-C^{14} [53] p-toluenesulfonates undergo considerably less rearrangement in aqueous acetone than in acetic acid. In a solvent such as aqueous acetone, water molecules would be expected to be substantially covalently bonded to the reaction center; with acetic acid as solvent, this bonding should be considerably weakened, allowing a greater chance for rearrangement.

Reaction type is quite important in rearrangement studies. For instance, the ratio of p-tolyl to phenyl migration in the acid catalyzed rearrangement of 2-p-tolyl-2-phenylethanol-1-C^{14} [85] is 1.5 and the same ratio for the reaction of nitrous acid on the corresponding amine is 0.9.[86] With a p-methoxy substituent the corresponding ratios are 24 for the rearrangement of the alcohol and 1.4 for the amine. The greatly reduced selectivity toward aryl groups in the amine-nitrous acid reaction points to a relatively high energy carbonium ion in such reactions.

Likewise, the % rearrangement in the reaction of exo- and endo-norbornylamine-3-C^{14} with nitrous acid was less than that observed in the solvolysis of exo- and endo-norbornyl-2,3-C^{14} p-toluenesulfonate.[53] Furthermore the % rearrangement during the amine-nitrous acid reaction was less sensitive to

medium changes, an observation previously made in the reaction of 2-phenyl- and 2-p-nitrophenylethyl-1-C^{14}-amines.[87] Yet with 2-p-methoxyphenylethyl-C^{14}-amine, stabilization of an intermediate cation such as LXXXIV, is relatively more im-



LXXXIV

portant than with a p-H or p-NO_2, consequently the longer half life leads to considerably more (36%) rearranged product in acetic acid than in water.

Amine-Nitrous Acid Reaction

Most carbonium-ion rearrangements find analogies in the reaction of aliphatic amines with nitrous acid. Albeit little direct evidence is available concerning the exact mechanism, it is generally believed that the initial step is the formation of a diazonium ion. Such an ion in an aliphatic system is unstable and loses a molecule of nitrogen to form a carbonium ion which may (1) react with the solvent or other nucleophilic species which may be present in the solution,

(2) lose a proton, giving rise to an olefin or cyclopropane compound or (3) undergo rearrangement to another carbonium ion and then proceed as in (1) or (2).

Methylamine, on treatment with aqueous nitrous acid, behaves anomalously;[88] varying amounts of starting material were recovered, but no isolable product. When silver nitrite was used a small amount of methanol was found. It may indeed be unfortunate that methylamine is generally used in kinetic studies of the amine-nitrous acid reaction.[89-92] Ethylamine with nitrous acid gives a good yield of ethanol but no ethylene.[88] The products from n-propylamine[88] are n-propyl alcohol (7%), i-propyl alcohol (37%) and propene (28%). Other n-alkyl amines[93-95] give primary and secondary alcohols and olefins, the amount of rearranged secondary alcohol decreasing with molecular weight. i-Butylamine yields rearranged product, t-butyl alcohol, as well as i-butyl alcohol and isobutene.[96,97] Only t-amyl alcohol and some olefin were obtained from neopentylamine.[98]

Allylamine yields only allyl alcohol[99] while crotyl and α-methylallylamine gave similar, but not identical, mixtures of crotyl- and α-methylallyl alcohols.[60,61]

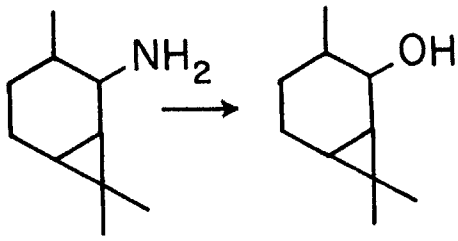
The Demjanow rearrangement usually refers to the ring expansion accompanying the reaction of nitrous acid with certain cycloalkylmethylamines (cycloalkylcarbinylamines), however the following survey encompasses ring contraction and ring closures as well. A comprehensive review of the Demjanow

ring expansion and the closely related reaction of nitrous acid with 1-aminomethylcycloalkanols (Tiffeneau-Tchoubar reaction) may be found elsewhere.[100]

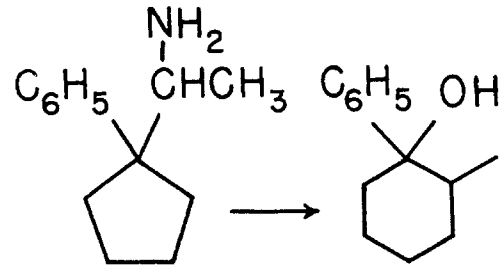
The simplest cycloalkylmethylamine, cyclopropylcarbinylamine, reacts with nitrous acid[101-103] to give cyclopropylcarbinol (48%), cyclobutanol (47%) and allylcarbinol (5%).[60,61] Cyclobutylcarbinylamine has been reported[104,105] to yield a mixture of cyclopentanol, cyclopentene, cyclobutylcarbinol and methylenecyclobutane. A recent investigation[106] reports cyclopentanol (28%) cyclopentene (27%), cyclopentyl nitrite (2%) and cyclobutylcarbinol (3%), but no methylenecyclobutane. Cyclohexanol was the only product reported from cyclopentylcarbinylamine.[107]

Substitution in the aminomethyl side chain invariably hinders the Demjanow ring-expansion and sometimes prevents it altogether. Thus methylcyclopropylcarbinylamine affords only methylcyclopropylcarbinol[108] while methylcyclobutylcarbinylamine gives a mixture of 1-ethylcyclobutanol and 1-methylcyclopentanol, a trace of 2-methylcyclopentanol and some olefin.[109] The products from methylcyclopentylcarbinylamine are methylcyclopentylcarbinol, 1-ethylcyclopentanol and 2-methylcyclohexanol.[109] Carylamine (LXXXV) was reported to yield only carol (LXXXVI) (fig. 12).[110]

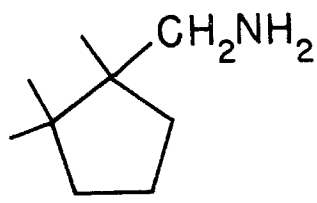
As expected, substitution of an alkyl or aryl group on the ring carbon holding the aminomethyl group facilitates ring expansion, and indeed with α-(1-phenylcyclopentyl)-



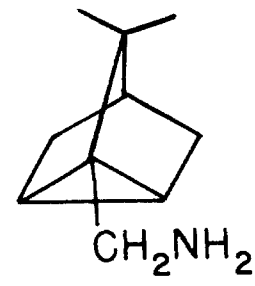
LXXXV LXXXVI



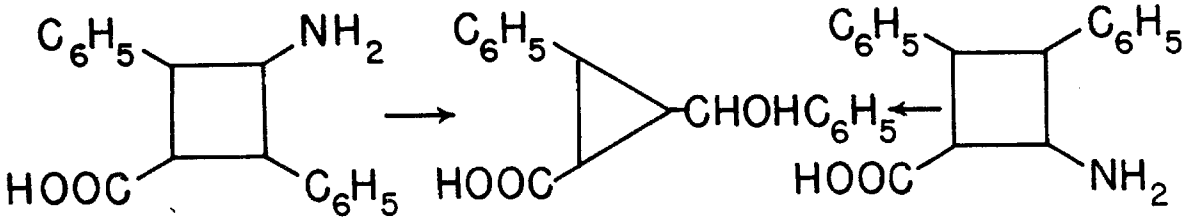
LXXXVII LXXXIX



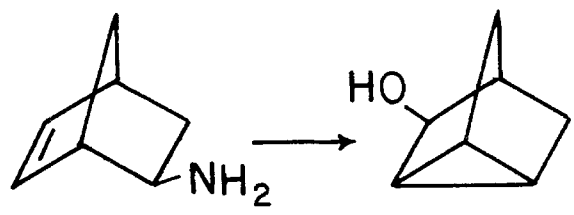
LXXXVIII



XC



XCI XCII XCIII



XCIV XCV

Fig. 12

ethylamine (LXXXVII), overcomes the hindering influence of the methyl group on the aminomethyl carbon.[109] Two further examples are 1,2,2-trimethylcyclopentylcarbinylamine[111,112] (LXXXVIII) and 1,2,2-trimethyl-3-carboxycyclopentylcarbinylamine[112,113] which apparently give only substituted 1-methylcyclohexanols.

Although it has been stated[109] that ring substituents on carbons other than the one holding the aminomethyl group do not markedly alter the usual results of the Demjanow ring expansion, 2-methylcyclopropylcarbinylamine gave a mixture of carbinols containing rearranged (but not ring-expanded product) methylcyclopropylcarbinol (85%) and methylallylcarbinol (15%).[108] None of the products from the reaction of 10-aminotricyclene (XC) with nitrous acid could be identified.[114]

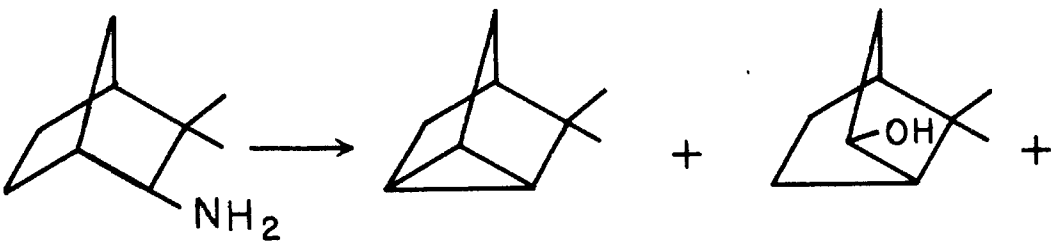
Ring contraction is here considered to come under the range of Demjanow rearrangements. Formation of allyl alcohol from cyclopropylamine has been considered a contraction of a 3- to a 2-membered ring.[115] Cyclobutylamine and nitrous acid[116,117] gave a mixture essentially identical to that obtained from cyclopropylcarbinylamine, viz., cyclobutanol (48%), cyclopropylcarbinol (48%) and allylcarbinol (4%).[60,61] Likewise cyclopentylamine gave the same mixture obtained from cyclobutylcarbinylamine (i.e., cyclobutylcarbinol and cyclopentanol, (10:90).[106] 2-Methylcyclobutylamine[108] with nitrous acid yields only methylcyclopropylcarbinol, and the isomeric 3-methylcyclobutylamine[108] gives a mixture of carbinols containing

methylcyclopropylcarbinol (75%) and methylallylcarbinol (25%). Other examples of ring contractions are truxillamic (XCI) and truxinamic (XCIII) acids which both give the same carbinol (XCII) along with the corresponding lactone.[118,119]

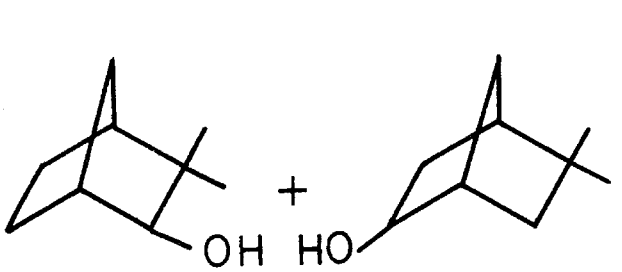
Allylcarbinylamine and nitrous acid give a varied assortment of carbinols (57%) including allylcarbinol (45%), α-methylallyl alcohol (18%), crotyl alcohol (10%) and two cyclic carbinols, cyclopropylcarbinol (14%) and cyclobutanol (13%).[60,61] However 1-amino-3-pentene yields largely methylcyclopropylcarbinol.[108] Ring closure also occurs in the reaction of 2,5-endo-methylene-1-amino-3-cyclohexene (XCIV) to give mostly 3-hydroxynortricyclene (XCV).[120]

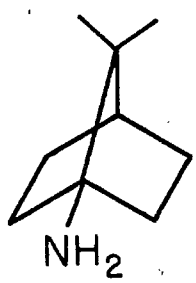
The cation obtained in the reaction of optically active camphenylamine (XCVI) with nitrous acid cannot lose a proton from the bridgehead carbon according to Bredt's rule,[121] but a 1,3-elimination does occur to form a cyclopropane compound, apocyclene (XCVII), along with apo-isoborneol (XCVIII), camphenilol (XCIX) and β-isofenchocamphorol (C), all of which were racemized (fig. 13).[122,123] α-[124,125] and β-fenchylamines[125] behave similarly.

The stereochemistry of the amine-nitrous acid reaction is not well-understood. One example studied involving a single asymmetric center is s-butylamine. Reaction of optically active s-butylamine with nitrous acid[126] gave s-butyl alcohol which was 78% racemized and 22% inverted, a result not unlike that of a typical carbonium-ion reaction.[127] The

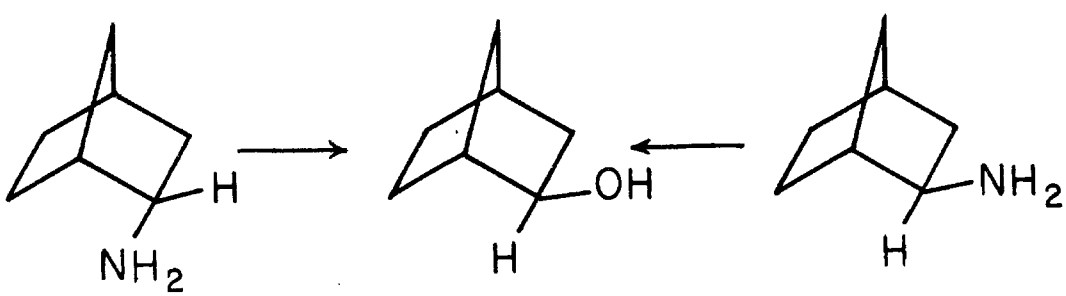


XCVI XCVII XCVIII





XCIX C CIV



CI CII CIII

Fig. 13

rotation and configuration of several amines and the corresponding carbinol products obtained in the amine-nitrous acid reactions have been correlated[128] (1) by use of the bimolecular (S_N2) reaction of corresponding halides with azide ion followed by reduction to the amines and (2) with the aid of known stereochemical correlations of halides and alcohols. Accordingly, optically active s-butylamine, s-octylamine and α-phenylethylamine all give rise to carbinol products with racemization and inversion (S_N1 rule).[127]

In cases involving neighboring group participation, e.g., α-amino acids, retention of configuration is observed. Another such example is the reaction of endo- and exo-norbornylamines (CI and CIII), both leading to exo-norborneol (CII).[129,130] The classical example of an amine-nitrous acid reaction which can proceed only with complete retention is apocamphylamine (CIV).[131] The only product is apocamphanol, since the rigid bicyclic system prohibits inversion.

In reactions of cyclic and bicyclic primary amines with nitrous acid, generalizations concerning configuration of the products should be made with caution and with due regard to conformation analysis. In general, cyclohexylamines with equatorial amino groups give carbinols with retention; axial (polar) amino groups often lead to olefin and alcohol of inverted configuration.[132] Cyclopentylamines frequently give inversion.

Interconversion of Cyclopropylcarbinyl, Cyclobutyl and Allylcarbinyl Derivatives

As part of an extensive research program concerning carbonium-ion rearrangements[42-44, 48,52,53,87,133,134] and the structure, physical properties and reactions of small-ring compounds[64,135-143] a study was made of the interconversion reactions of cyclopropylcarbinyl, cyclobutyl and allylcarbinyl compounds by Mazur.[60-62]

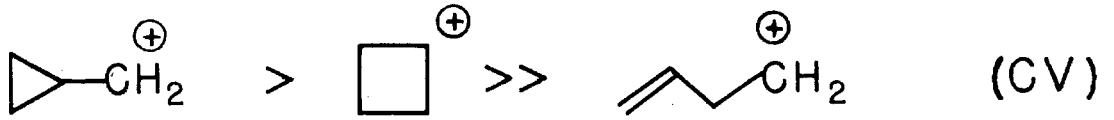
This problem arose from the scrutiny of a number of perplexing and uncorrelated examples of ring openings, closures, expansions and contractions of cyclopropylcarbinyl, cyclobutyl and allylcarbinyl derivatives, in carbonium-ion type reactions. The difficulty of judging which of several reaction paths will be most favorable in carbonium-ion reactions is exemplified in these interconversions and depends on a knowledge of (1) relative carbonium-ion stabilities, (2) the energy barriers to interconversion of carbonium ions, (3) the relative reactivity of carbonium ions toward nucleophilic agents, (4) the reversibility of the reaction in question and (5) the thermodynamic stabilities of the reactants and possible products.

Cyclopropylcarbinyl and cyclobutyl chlorides were isomerized by an equimolar mixture of anhydrous zinc chloride and concentrated hydrochloric acid (Lucas reagent) to allylcarbinyl chloride and furthermore a 2:1 mixture of cyclo-

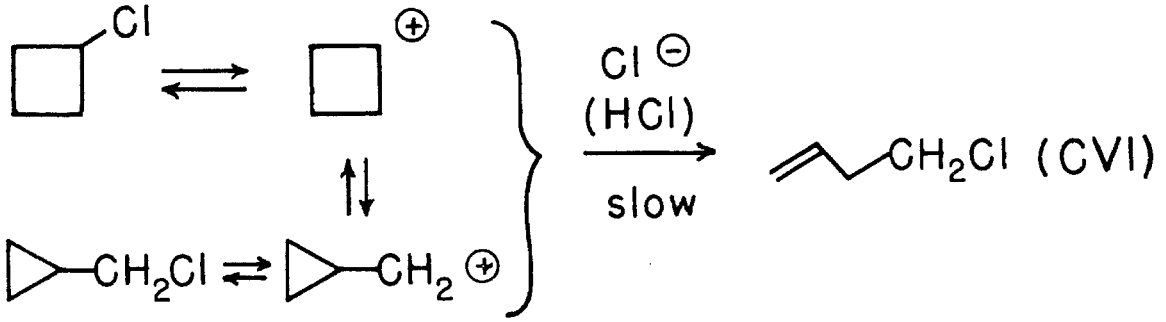
propylcarbinyl chloride and cyclobutyl chloride under milder conditions gave approximately a 1:1 mixture of cyclobutyl and allylcarbinyl chloride. In a reversible carbonium-ion reaction, the stability of the products is paramount, hence the order of increasing stability of the chlorides is cyclopropylcarbinyl < cyclobutyl ≪ allylcarbinyl.

Supporting evidence is found in the reactivity of the corresponding alcohols, cyclopropylcarbinol being the most reactive while allylcarbinol is nearly inert; thus a tentative order of carbonium-ion stabilities was advanced (CV) (fig. 14). The most attractive interpretation of these results involved an equilibrium between the cyclopropylcarbinyl and cyclobutyl cations, as well as the respective chlorides, and a slow, essentially irreversible reaction of one or both of these cations with chloride ion or hydrogen chloride as shown in the equations CVI. Evidence favoring this explanation was the lack of formation of crotyl or α-methylallyl chlorides, ruling against the allylcarbinyl cation as an intermediate. An intramolecular rearrangement was ruled out by the findings that under conditions giving 77% isomerization of a mixture of cyclopropylcarbinyl and cyclobutyl chloride, 107% of the theoretical amount of chloride-ion exchange occurred (using Lucas reagent containing Cl^{38}) while under similar conditions only 13% exchange occurred with allylcarbinyl chloride.

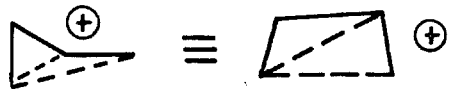
Direct evidence concerning the nature of the intermediate



(CV)

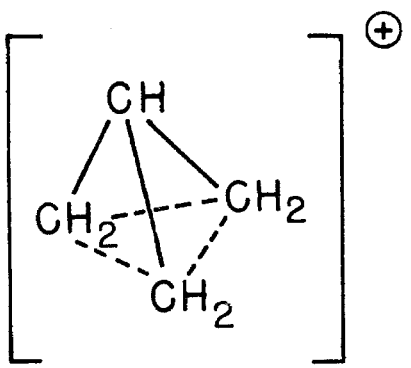


CVII

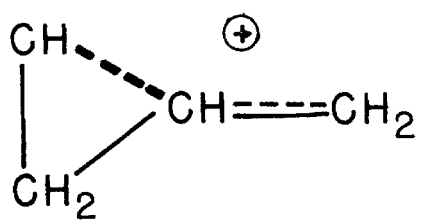


CVIII

A B C D



CIX



CX

Fig. 14

involved was obtained by the action of Lucas reagent on cyclopropylcarbinol-α-C^{14}. Degradation of the allylcarbinyl chloride by two methods and determination of the C^{14}-distribution gave essentially identical results. One-third (33%) of the total C^{14}-activity was found in the terminal methylene carbon atom, 0% in the methinyl group and two-thirds of the C^{14}-activity in the other two methylene groups (CVII). These results eliminated (1) a common intermediate (CVIII) which could give rise to the three chlorides by an attack at three different carbon atoms and (2) a concerted displacement on cyclopropylcarbinol; both of these possibilities would lead to C^{14}-acitivity only in the terminal methylene group.

Two interpretations of the data present themselves. The first involves an equilibrium between the cyclopropylcarbinyl and cyclobutyl cations (ABCD) and the second, a symmetrical, non-classical carbonium ion (CIX).

The relative solvolytic reactivities of cyclopropylcarbinyl, cyclobutyl and allylcarbinyl chlorides proved to be of particular interest. In 50% aqueous ethanol at 50° the rate constant for cyclopropylcarbinyl chloride was 27 times that of cyclobutyl chloride and 40 times that of β-methylallyl chloride, while the reaction of allylcarbinyl chloride under the same conditions was immeasurably slow. The corresponding bromides behaved similarly. The rather unexpected high reactivity of cyclopropylcarbinyl chloride, especially for a

primary chloride, was explained by the supposition of a resonance-stabilized intermediate involving extreme forms analogous to the allyl cation with the cyclopropylcarbinyl cation weighted heavier in the hybrid structure (CX). The unusually high reactivity of cyclobutyl chloride was unexplained. It is worthy of note that cyclobutyl chloride solvolyzes, in 50% ethanol at 50°, 1.5 times as fast as β-methallyl chloride[60,61] and 15 times as fast as i-propyl chloride.[144] The relative solvolytic reactivities support the predicted order of carbonium-ion stabilities, although the drawbacks of such an inference have been brought to attention.[145]

Cyclopropylcarbinyl chloride, along with allylcarbinyl chloride and some unreactive chloride of undetermined structure, was obtained by the vapor-phase chlorination of methylcyclopropane. From the solvolysis rate curve, it appeared that the cyclopropylcarbinyl chloride contained considerably more less-reactive chloride than was consistent with the infrared spectrum. Indications were that an "internal return" isomerization[23,146-149] was occurring simultaneously at a rate about one-third that of the solvolysis. Similarly, solvolysis of cyclopropylcarbinyl chloride in acetic acid was accompanied by an even more rapid rearrangement to cyclobutyl and allylcarbinyl chlorides, while cyclobutyl chloride rearranged to allylcarbinyl chloride during acetolysis.

Significantly, hydrolysis of cyclopropylcarbinyl and

cyclobutyl chlorides each led to essentially identical mixtures of alcohols consisting of ~5% of allylcarbinol and roughly equal amounts of cyclopropylcarbinol and cyclobutanol.

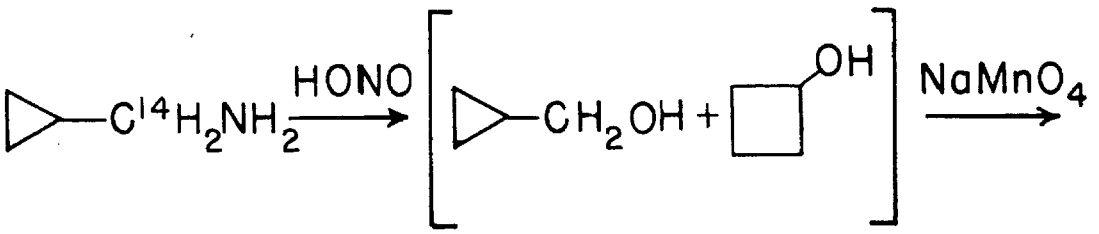
The most generally suited method of generating carbonium ions, i.e., the reaction of primary aliphatic amines with nitrous acid, was used to generate the cyclopropylcarbinyl, cyclobutyl and allylcarbinyl cations. To test the reliability of the reaction for this purpose, crotyl- and α-methylallylamines were diazotized. Crotylamine gave a mixture containing crotyl alcohol (47%) and α-methylallyl alcohol (53%), while α-methylallylamine was found to give a mixture containing α-methylallyl alcohol (69%) and crotyl alcohol (31%). The compositionsof the alcohol mixtures correspond, within experimental error, to those reported for the products of the carbonium-ion type reactions of crotyl and α-methylallyl chlorides with silver hydroxide in aqueous media.[150]

Treatment of cyclopropylcarbinyl and cyclobutylamines with sodium nitrite in dilute aqueous perchloric acid produced essentially identical mixtures of alcohols containing cyclopropylcarbinol (~48%), cyclobutanol (~47%) and allylcarbinol (~5%). The corresponding reaction of allylcarbinylamine was found to give a complex mixture of carbinols having the following approximate composition: 45% allylcarbinol, 18% α-methylallyl alcohol, 10% crotyl alcohol, 14% cyclopropylcarbinol and 13% cyclobutanol.

The amounts of various products in amine-nitrous acid

reactions appear to correspond roughly with carbonium-ion stabilities. In this respect it is noteworthy that the barrier to interconversion of cyclopropylcarbinyl and cyclobutyl cations is quite small while the energy barrier to conversion of the ions to the allylcarbinyl cation is large. The reverse process appears to be intermediate in magnitude. It is not without significance that both the amine-nitrous acid reaction and chloride solvolysis lead to nearly identical mixtures of alcohols.

Considerable interest attends the question of the nature of the intermediate or intermediates involved in the reactions of cyclopropylcarbinyl- and cyclobutylamines with nitrous acid. A number of possibilities present themselves, of which several were eliminated by the use of C^{14} as a tracer. Cyclopropylcarbinylamine-α-C^{14} was prepared and treated with sodium nitrite in dilute aqueous perchloric acid. The cyclopropylcarbinol and cyclobutanol mixture was separated from the small amount of allylcarbinol by fractional distillation and the mixture of carbinols oxidized with permanganate, giving a mixture of cyclopropanecarboxylic acid and succinic acid which were separated conveniently by fractional distillation. These acids were further degraded in the manner shown in fig. 15. A number of control experiments were conducted in order to ensure the reliability of the results.


HONO
OH
NaMnO4

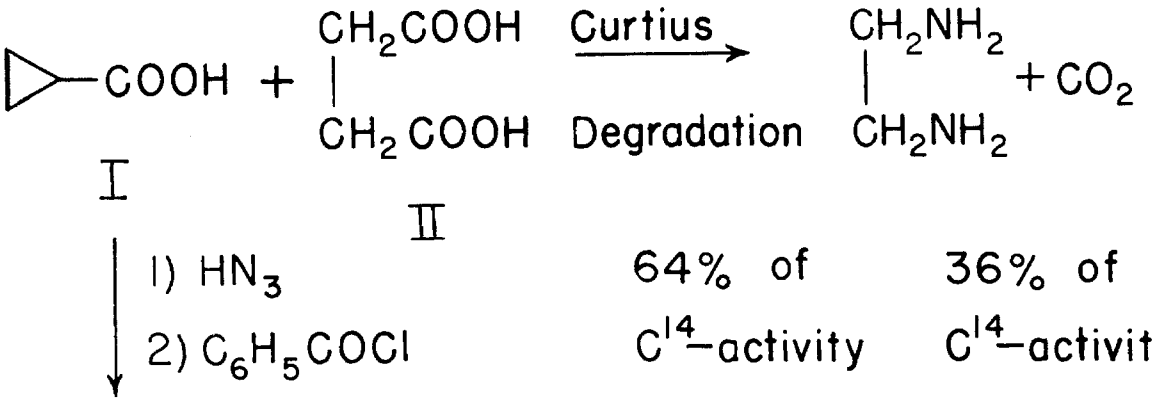
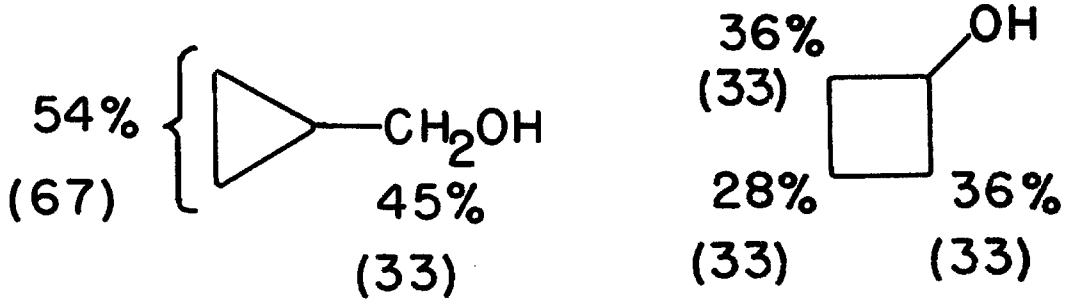
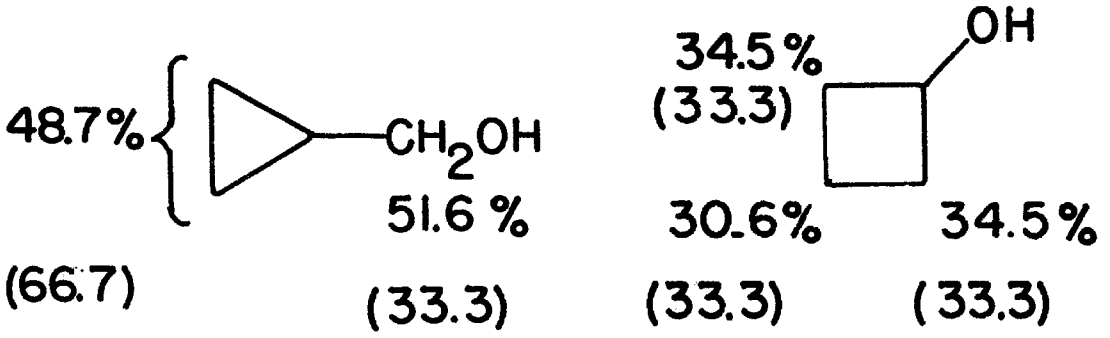

Curtius
Degradation
+CO2
I
II
1) HN3
2) C6H5COCl
64% of C14-activity of II
36% of C14-activity of II
+CO2
54% of C14-activity of I
45% of C14-activity of I

Fig. 15

At this point it is desirable to introduce some results of W. N. White[151] on the reaction of cyclopropylcarbinylamine-α-C^{14}. A different method of degradation was used which allowed more checks on the reliability of the results. Furthermore, the C^{14} counting-procedure was more accurate than that used by Mazur[60] (cf. the experimental errors, ~2 and 0.1%). The degradation procedure used is outlined in figs. 16 and 17 together with the C^{14}-activity results. A summary of the above C^{14}-results follow. (Roberts and Mazur)[60,62]



(White)[151]



Degradation of Cyclopropylcarbinol[151]

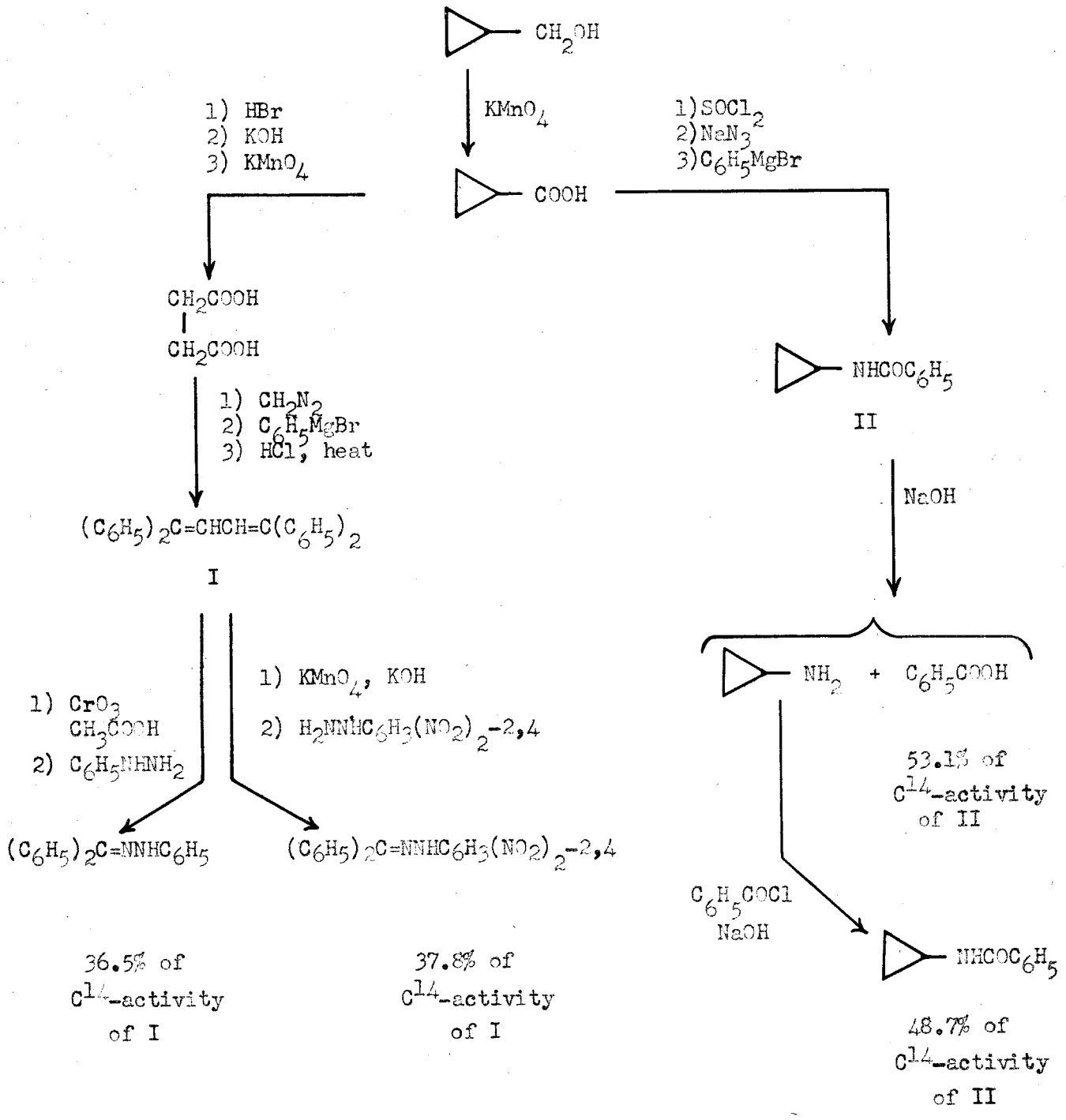


Fig. 16

Degradation of Cyclobutanol[151]

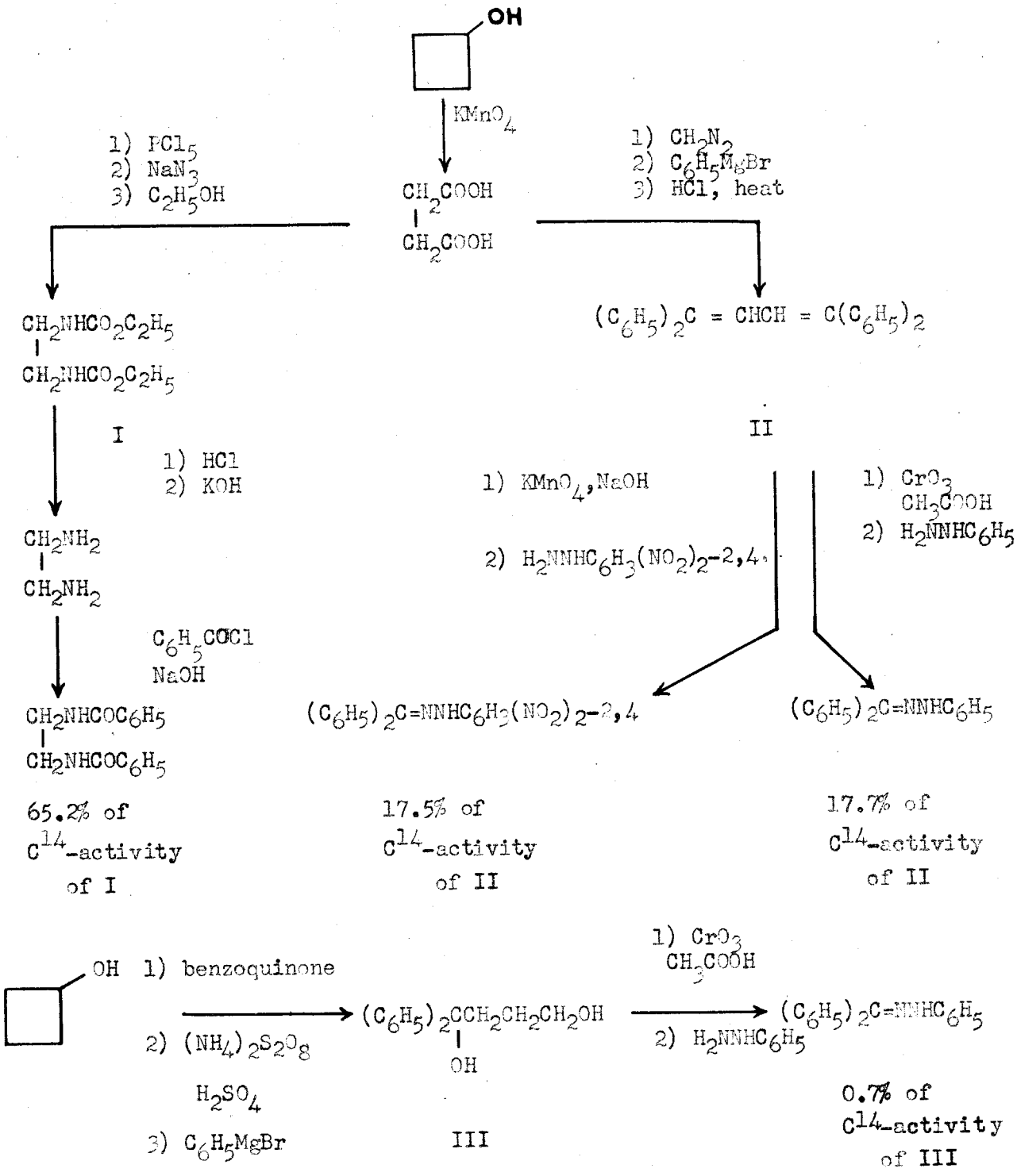


Fig. 17

The figures in parentheses are the % C^{14}-activities expected if the three methylene groups were equivalent.

Examination of the C^{14} data permits one to eliminate a number of conceivable mechanisms. A single classical carbonium ion which reacts at different carbon atoms to give the three possible products would not give rise to activity (1) in the cyclopropane ring or the 3-position of the cyclobutanol if the cyclopropylcarbinyl cation were the only intermediate or (2) in the 3-position of cyclobutanol if the cyclobutyl cation were the only real intermediate. Added refinements due to an isotope effect would not significantly alter this conclusion. Likewise, the 'common-intermediate' (CVIII) (fig. 14) suggested by Mazur[60] is eliminated on the same grounds.

One of the most obvious mechanisms involves a partially established equilibrium (ABCD) between cyclopropylcarbinyl and cyclobutyl cations, each of which reacts normally to give cyclopropylcarbinol and cyclobutanol, respectively, and an accompanying abnormal reaction leading to allylcarbinol. The results of Roberts and Mazur[62] predict that cations C and D are present to the extent of ~81 and ~84% of the equilibrium concentrations, respectively (cf. the ratio of the actual and predicted values (on the basis of complete equilibrium) for the activity of the two ring methylene groups in cyclopropylcarbinol (which derives only from C), 54:67, and the corresponding values for the C-3 carbon of cyclobutanol (which

derives only from D), 28:33). Note that the assumption of 81 and 84% of equilibrium concentration assumes, say in the case of D (84% of equilibrium), that the remaining species are present at 100% of the equilibrium concentration (an impossibility). The results of White[151] predict that cations C and D are present to the extent of 73% and 92% of the equilibrium concentrations, respectively. It must be concluded that a partially established equilibrium does not alone suffice to explain the data.

The data, however, are consistent with product formation through a partially established equilibrium mixture of the cations and, superimposed, a bimolecular reaction between solvent and the cyclopropylcarbinyldiazonium ion; the latter explains the relatively high proportion of C^{14} in the α-carbon of cyclopropylcarbinol. (The formation of ethanol with only 1.1 atom % of deuterium attached to carbon in the reaction of ethylamine with perchloric acid and sodium nitrite in 99.8% deuterium oxide[42] rules against any α-diazo-methylcyclopropane as an intermediate).

A mechanism involving (1) a bimolecular displacement of solvent on the cyclopropylcarbinyldiazonium ion and (2) a complete equilibrium of cations A, B, C and D was excluded by Mazur. Such a mechanism requires equivalence of the three methylene groups in cyclobutanol and it was felt that the difference between the observed (36:64) and predicted (33:67) values (for the ratio of C^{14} in the carboxyl and methylene

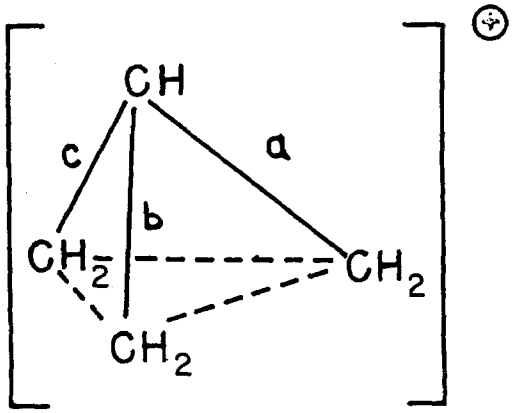
groups of succinic acid) was beyond the experimental error, especially since the observed values were from independent determinations. Although the corresponding values obtained by White[151] (34.5:65.2) are somewhat closer to those predicted (33.3:66.7), the increased accuracy of these values still places the difference slightly beyond the experimental error.

If the difference between found and predicted values (for ABCD) is compensated by a bimolecular reaction of solvent with the cyclopropylcarbinyldiazonium ion, it is conceivable that the "low" value for C-3 in cyclobutanol is due to an isotope effect. It is difficult however even to estimate the increase in the concentration of cation B relative to cation D in the equilibrium caused by a C^{14}-C^{12} isotope effect. Even though the increase in the ratio B/D would tend to compensate for the low activity for C-3 in cyclobutanol, this effect would be offset by the isotope effect in the oxidation of cyclobutanol,[60,62,151] which would increase the relative C-3 activity.

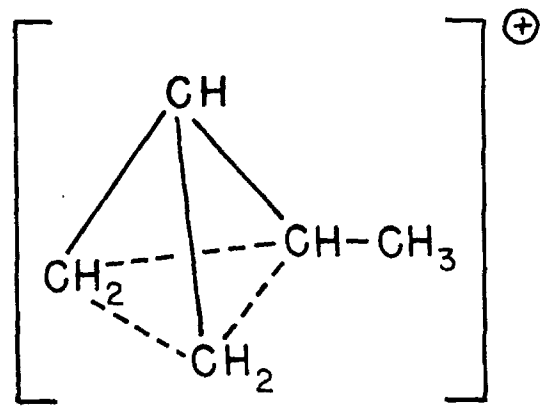
The achievement of a degree of equivalence of the methylene groups in the reaction of C^{14}-labeled cyclopropylcarbinyl derivatives, together with the abnormally high solvolytic reactivities of cyclopropylcarbinyl and cyclobutyl halides[60,61] and p-toluenesulfonates[39,59,64] and the ease of interconversion of cyclopropylcarbinyl and cyclobutyl derivatives,[60,61] have led to the suggestion[62] of a symmetrical, non-classical

cationic intermediate (CIX). CIX alone does not explain the observed distribution. The difference between the observed C^{14}-distribution for cyclopropylcarbinol and that calculated on the basis of CIX may conveniently be accounted for by a certain amount ($\sim$19%) of bimolecular displacement, but the distribution in the cyclobutanol remains unexplained. An unsymmetrical intermediate (CXI, fig. 18) similar to CIX might meet the requirements provided that the transition state for bond breaking is of lower energy when bonds b and c are broken than when bond a is broken. The former cases (b and c) lead to a greater activity in C-2 of cyclobutanol relative to C-3.

An isotope effect in the reaction of CIX (or CXI) with water to form cyclobutanol is perhaps slightly easier to estimate than in the case of an equilibrium of cyclopropylcarbinyl and cyclobutyl cations (ABCD) If, in the reaction of CIX with water to form cyclobutanol, an isotope effect of 1.11 is assumed (an average of 21 available values; standard deviation, $\pm$ 0.08), then the calculated % C^{14}-acitivity in C-3 is 32.2. (Note that the partial bonds in CIX are considered to be one-third of a full sigma bond). However, the same isotope effect in the oxidation of cyclobutanol to succinic acid changes the % C^{14}-activity in C-3 to 35.8. It can be shown that the corresponding calculations on the unsymmetrical ion, CXI, do not significantly alter these values. Apparently then, isotope effect corrections of the C^{14}-distribution expected from CIX, widen the agreement with experimental.



CXI



CXIII

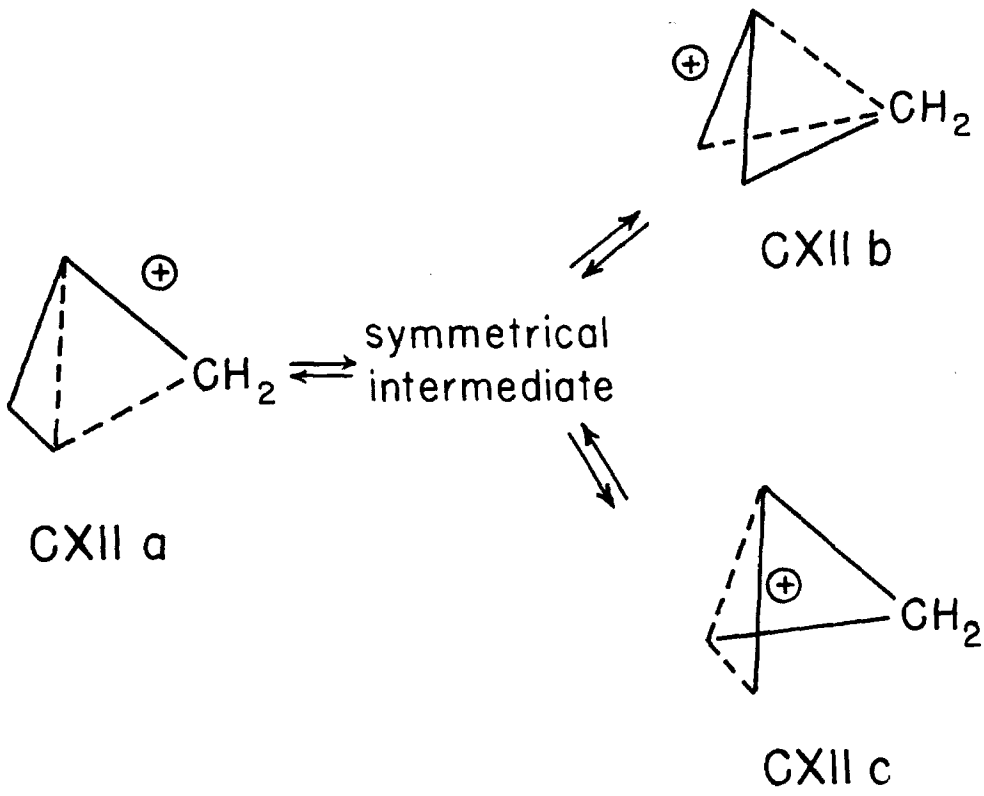


Fig. 18

Another possible interpretation is based on a proposal of a partial equilibrium between unsymmetrical 'ethylene-phenonium' ions in the reaction of 2-phenylethylamine with nitrous acid, viz., a partially established equilibrium between three unsymmetrical 'common ions' (CXIIa-CXIIc).[60] (The ions may or may not be interconverted through a symmetrical ion.) For example, if 83% equilibrium is attained, then the calculated and experimental values, respectively, for the C^{14}-distribution of the products are as follows: cyclopropylcarbinol: carboxyl group, 45:45; cyclopropane ring, 55:54; and cyclobutanol: C-3, 28:28; C-2 and C-4, 72:72.

The results of White[151] do not support this mechanism, per se. If, however, cyclobutanol and cyclopropylcarbinol are formed from a mixture of the 'common-ions' which has attained 92% equilibrium and, in addition, 21% of the total quantity of cyclopropylcarbinol arises by bimolecular substitution, then the requirements of the experimental results of White[151] are satisfied.

The general results of Roberts and Mazur[60-62] on the interconversions of cyclopropylcarbinyl, cyclobutyl and allylcarbinyl compounds suggest the logical questions: (1) What effect would substituents, e.g., methyl, suitably placed, have upon the interconversion reactions, relative reactivities and suggested intermediates? (2) Do homologous systems, e.g., cyclobutylcarbinyl and cyclopentyl derivatives, exhibit similar properties? Some answers to these questions have been found

in several current researches.

One of these investigations has been concerned with the behavior of several substituted cyclopropylcarbinyl-, cyclobutyl- and allylcarbinylamines, with methyl substituents so placed that if an intermediate similar to CIX were involved in the reaction of these amines with nitrous acid, then it would be represented by CXIII. A close examination reveals that seven amines might conceivably lead to CXIII; these are methylcyclopropylcarbinylamine, 2-methylcyclopropylcarbinylamine, 2-methylcyclobutylamine, 3-methylcyclobutylamine, methylallylcarbinylamine, crotylcarbinylamine and α-methylallylcarbinylamine. Reactions of the first five of the above mentioned amines with nitrous acid have been carried out and the product composition determined.

Surprisingly, methylcyclopropylcarbinylamine, 2-methylcyclobutylamine and crotylcarbinylamine were found to give only methylcyclopropylcarbinol, whereas mixtures of methylcyclopropylcarbinol and methylallylcarbinol were obtained from 2-methylcyclopropylcarbinylamine (85:15) and 3-methylcyclobutylamine (75:25). Unfortunately this investigation is incomplete and no other details are available, particularly concerning the stereochemistry of the starting materials and products. Since, as a general rule, the amounts of the various carbinols obtained in the reaction of aliphatic amines with nitrous acid correspond roughly to the relative carbonium-ion stabilities, it might be fruitful to first consider the

possible cationic intermediates (cf. A-G) (fig. 19).

From the results of Roberts and Mazur[60,61] and the abnormally high reactivity of methylcyclopropylcarbinyl derivatives,[39] one would clearly predict the relative order of carbonium-ion stabilities as follows: A > C > D > B > E > G > F. However the results of the reactions of amines with nitrous acid indicate that cation E is second in order of stability, i.e., A > E > C, etc. Hence if classical cations are the only intermediates involved then either (1) the correlation of carbonium-ion stability with the relative amount of carbinol product in the amine-nitrous acid reaction is invalid (not very attractive) or else (2) the order of carbonium-ion stabilities found by Roberts and Mazur[60,61] for unsubstituted cyclopropylcarbinyl, cyclobutyl and allylcarbinyl compounds does not maintain with the analogous methyl-substituted derivatives. Additional evidence against classical ions as intermediates is the complete absence of products which would be formed by solvent attack on 2- and 3-methylcyclobutyl cations and the 2-methylcyclopropylcarbinyl cations. Previous work[60,61] indicated that these ions are expected to be unusually stable.

An unsymmetrical non-classical cationic intermediate (CXIII) (fig. 18) adequately explains the results with one provision: that any attack by water molecules which leads to products, occurs only at the methyl-substituted carbon atom. From the evidence at hand, it appears that the methyl-

Possible Cationic Intermediates from Methyl-Substituted Cyclopropylcarbinyl, Cyclobutyl and Allylcarbinyl Derivatives.

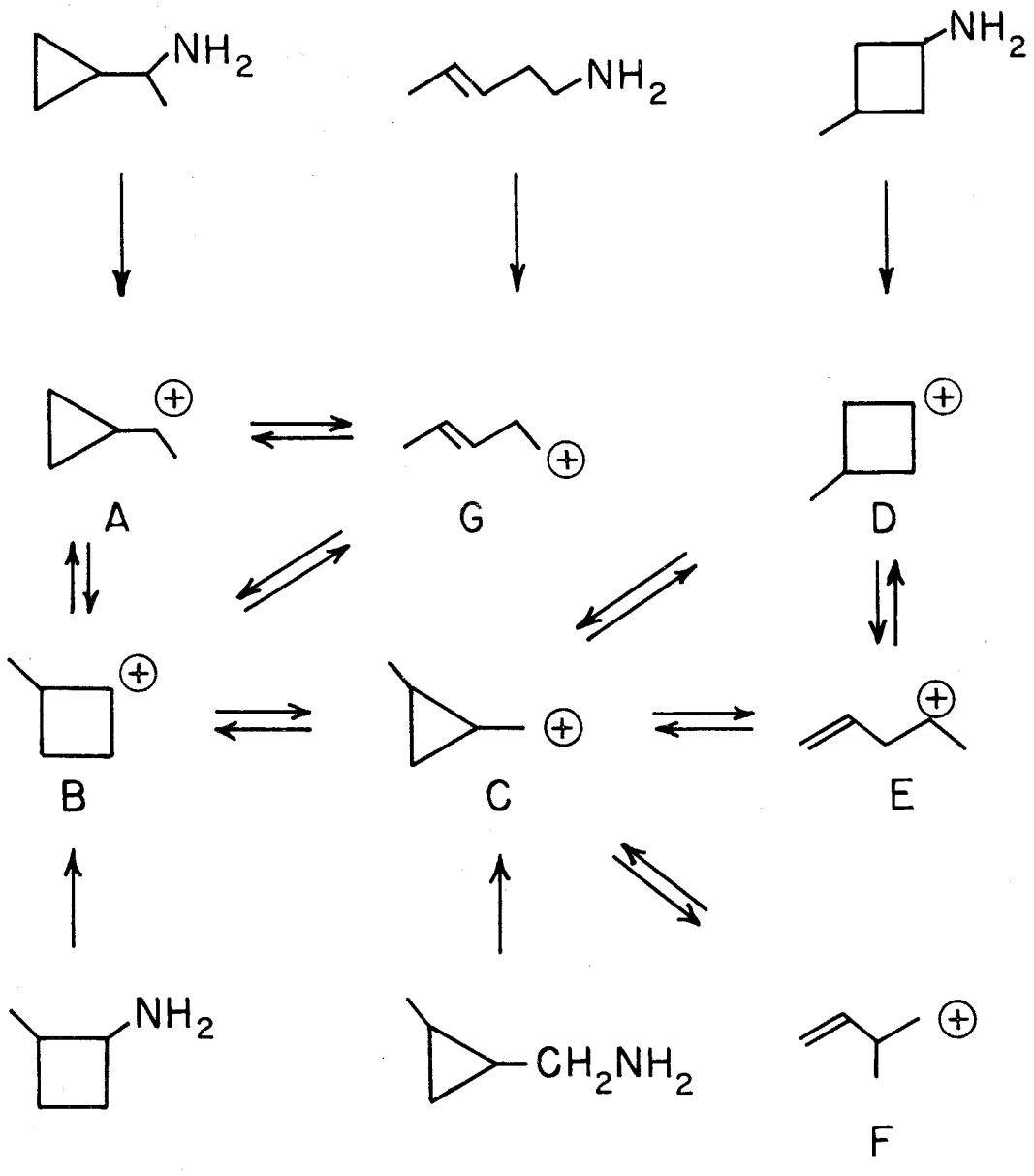


Fig. 19

substituted cyclopropylcarbinyl, cyclobutyl and allylcarbinyl derivatives in question are not as easily interconverted as are the unsubstituted analogues. However, the most convincing evidence favoring non-classical intermediates, i.e., rate enhancement, is provided in the case of one of the structures in question. Hence methylcyclopropylcarbinol reacts readily with acidic methanol giving the unrearranged methyl ether.[39] This is to be contrasted with s-butyl alcohol which reacts sluggishly under similar conditions and leads to rather poor yields.

An alternative mechanism might be considered in which methylcyclopropylcarbinol is formed solely from the unsymmetrical non-classical ion, and methylallylcarbinol arises by a concerted attack by water on the 2-methylcyclopropylcarbinyl- and 3-methylcyclobutyldiazonium cations accompanied by conventional electron shifts. Significantly, these are the only alkyldiazonium cations in this system (seven in all) which could undergo such a process.

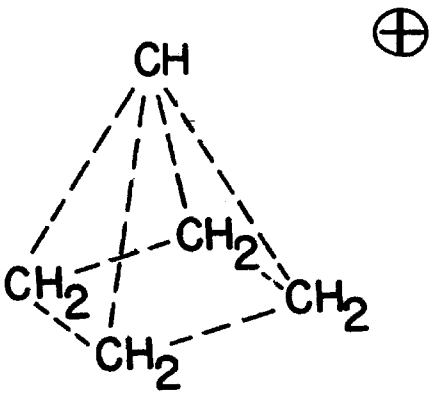
It will be noted that in the study of methyl-substituted cyclopropylcarbinyl, cyclobutyl and allylcarbinyl derivatives previously discussed, in all compounds (or cations) mentioned, the methyl group was substituted on a methylene carbon atom. The various effects of substituting a methyl group on the methinyl carbon atom in the cyclopropylcarbinyl, cyclobutyl and allylcarbinyl derivatives is the subject of the present investigation (vide infra).

Interconversion of Cyclobutylcarbinyl and Cyclopentyl Derivatives

This subject has been reviewed[106] and only the results of the amine-nitrous acid reaction will be discussed.

Sheppard[106] has initiated a study of the interconversion reactions of cyclobutylcarbinyl and cyclopentyl derivatives. Unfortunately this investigation was unavoidably interrupted, but results of the amine-nitrous acid reactions are available. It was found that the reaction of both cyclobutylcarbinyl- and cyclopentylamines with sodium nitrite in dilute aqueous perchloric acid gave an almost identical mixture of products consisting of cyclopentene (~25%), cyclopentanol (~27%), cyclobutylcarbinol (~3%) and cyclopentyl nitrite (~3%). No methylenecyclobutane, open-chain carbinol or 1-methylcyclobutanol was detected.

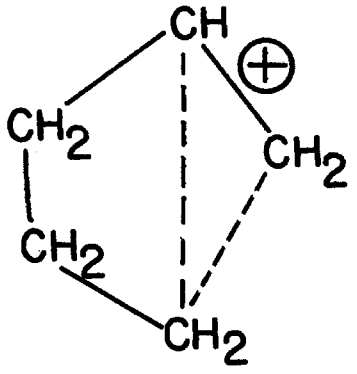
C^{14}-labeled cyclobutylcarbinylamine was used to help distinguish between four of the possible intermediates. The first mechanism considered involved an equilibrium between the cyclobutylcarbinyl and cyclopentyl cations and would lead to equal distribution of C^{14} in the four methylene groups of the carbinol products. A second mechanism considered was a symmetrical non-classical cation (CXIV) similar to that proposed by Roberts and Mazur[62] in the interconversion of cyclopropylcarbinyl, cyclobutyl and allylcarbinyl derivatives. CXIV would also lead to shuffling of C^{14} among the four methylene carbons.



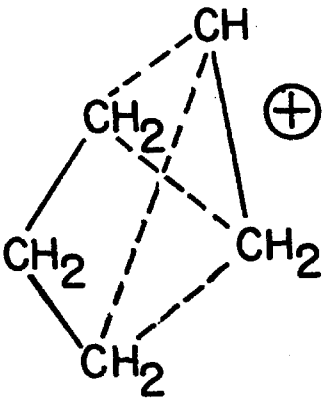
CXIV

The similarity between CXIV and the analogous structure for B_5H_9[77] is indeed striking. Recent molecular orbital calculations[152] based on the concept of the localized three-center bond satisfactorily account for the structures[77] of the boron hydrides and their dipole moments and geometry, and indeed show that the boron hydrides are not electron deficient. The location of the hydrogen atoms in CXIV may be changed to conform with the known structure of B_5H_9, but CXIV has four more electrons than B_5H_9 which could be accommodated only in two molecular orbitals of higher energy (one non-bonding and one anti-bonding orbital). This argument definitely rules against CXIV as a possible intermediate.

Another non-classical intermediate considered was CXV, which would lead to no shuffling of the carbon atoms. Finally, an intermediate such as CXVI would give the same distribution as CXV.



CXV



CXVI

The carbinol products from the reaction of cyclobutylcarbinylamine-α-C^{14} with aqueous nitrous acid were degraded to determine the C^{14}-distribution. C-1 of cyclopentanol contained 5% and the remaining four carbon atoms, 91% of the total C^{14}-activity. C-α of cyclobutylcarbinol accounted for 80% of the total activity in cyclobutylcarbinol, with 11% being found in the ring carbons.

The rather poor results obtained with cyclobutylcarbinol were attributed to radioactive contamination. The lack of extensive C^{14}-rearrangement was considered as evidence for a non-classical cationic intermediate such as CXV or CXVI.

Arguments of Sheppard supporting a non-classical intermediate which are based on abnormally high reactivities of cyclobutylcarbinyl derivatives,[153] are strengthened by the finding that the ratio of the solvolysis rate constants of cyclopentyl bromide to cyclobutylcarbinyl bromide in 60%

aqueous ethanol at 75° is 12.[154] By assuming that this same ratio holds approximately for the corresponding chlorides in 50% aqueous ethanol, and by making use of available rate constants[60,61,64,144,155] for solvolysis of some other chlorides and bromides in 50% ethanol, the following comparisons may be drawn: (1) cyclopropylcarbinyl chloride solvolyzes $\sim 10^3$-10^4 times faster than n-propyl chloride and about 27 times as fast as cyclobutyl chloride (cyclobutyl chloride[60,61] solvolyzes about 15 times faster than i-propyl chloride[144]); (2) cyclobutylcarbinyl chloride solvolyzes about 320 times faster than n-propyl chloride, but only 1/12th as fast as cyclopentyl chloride (cyclopentyl chloride reacts about 1/3 as fast as cyclobutyl chloride). Driving force values (L_o) for cyclopropylcarbinyl and cyclobutylcarbinyl derivatives of 9.0 and 4.5, respectively, have been reported.[15]

II. RESULTS AND DISCUSSION

Synthetic Procedures

Most of the substances needed in this study which contained cyclopropane rings were prepared by the addition of diazomethane to unsaturated compounds. Thus in a modification of a known procedure,[156] 1-methylcyclopropanecarbonitrile was obtained by thermolysis of the pyrazoline formed from diazomethane and α-methacrylonitrile. 1-Methylcarbomethoxycyclopropane was prepared in a similar fashion from methyl methacrylate. Unsaturated isomers invariably accompanying the cyclopropane analogues were removed by permanganate. Alkaline hydrolysis of 1-methylcarbomethoxycyclopropane gave 1-methylcyclopropanecarboxylic acid. 1,1-Dimethylcyclopropane was prepared by a published procedure starting with isobutyraldehyde.[157,158]

All compounds with cyclobutane rings, excepting one, were obtained from methylenecyclobutane.[137] For example, cyclobutanone was prepared by hydroxylation of methylenecyclobutane with performic acid, followed by cleavage of the resulting 1-hydroxymethyl-1-cyclobutanol with lead tetraacetate[137] or phenyl iodosoacetate.

Reduction of 1-methylcarbomethoxycyclopropane with lithium aluminum hydride afforded 1-methylcyclopropylcarbinol (1-methyl-

cyclopropanemethanol).[189] 1-Methylcyclobutanol was prepared by the acid-catalyzed hydration of methylenecyclobutane,[159-161] hydrolysis of 1-methylcyclobutyl chloride[162] and by reaction of methylmagnesium iodide with cyclobutanone. β-Methylallylcarbinol (3-methyl-3-butene-1-ol) was prepared from β-methylallylmagnesium chloride and formaldehyde by the known procedure for the synthesis of allylcarbinol (3-butene-1-ol).[163] The reaction of α-methacrolein and methylmagnesium iodide gave α-methyl-β-methylallyl alcohol (3-methyl-3-butene-2-ol). β-Methyl-γ-methylallyl alcohol (2-methyl-2-butene-2-ol) was obtained by lithium aluminum hydride reduction of methyl tiglate, the latter compound comprising the higher-boiling fractions of the decomposition product of the pyrazoline prepared from diazomethane and methyl methacrylate.[189]

1-Methylcyclopropylcarbinyl acetate was prepared by the action of acetyl chloride on the sodium salt of 1-methylcyclopropylcarbinol. The reaction of 1-methylcyclobutanol with acetic anhydride in dimethylaniline gave 1-methylcyclobutyl acetate.

Preparation of 1-methylcyclopropylcarbinyl chloride was attempted by the vapor-phase chlorination of 1,1-dimethylcyclopropane. Careful fractionation of the monochlorination product was only partially successful, giving a large (~50%), low-boiling fraction shown to contain ~75% 1-methylcyclopropylcarbinyl chloride, as well as smaller amounts of 1-methylcyclobutyl chloride (~6%), β-methylallylcarbinyl chloride

(1-chloro-3-methyl-3-butene) (~2%) and an unidentified unreactive chloride (~17%), presumably 2-chloro-1,1-dimethylcyclopropane. An intermediate fraction was shown to be a mixture of chlorides comprised of 43% 1-methylcyclopropylcarbinyl chloride, 29% 1-methylcyclobutyl chloride, 14% β-methylallylcarbinyl chloride and 10% of unreactive chloride. The high-boiling fraction consisted largely of β-methylallylcarbinyl chloride (48%) with smaller amounts of 1-methylcyclopropylcarbinyl chloride (12%), 1-methylcyclobutyl chloride (27%), and unreactive chloride (13%). The percentage compositions were determined from boiling points, refractive indices, and by analysis of the infrared spectra and solvolysis rate data of a number of different fractions. A graphical analysis indicated that the overall chlorination product had the following composition: 1-methylcyclopropylcarbinyl chloride (49%), 1-methylcyclobutyl chloride (16%), β-methylallylcarbinyl chloride (14%) and unreactive chloride (21%). 1-Methylcyclobutyl chloride was obtained through the reaction of methylenecyclobutane and hydrogen chloride[162] or concentrated hydrochloric acid.[161] The method used in the synthesis of allylcarbinyl chloride, i.e., treatment of allylcarbinol with thionyl chloride in the presence of pyridine,[60,61] failed when applied to β-methylallylcarbinol. Even when a large excess of pyridine was employed, no β-methylallylcarbinyl chloride was formed; the product was 1,3-dichloro-3-methylbutane (isoprene dihydrochloride). However replacement of

pyridine by tri-n-butylamine led to a good yield of β-methylallylcarbinyl chloride. Apparently pyridine hydrochloride is an acid of sufficient strength to cause addition of hydrogen chloride to the double bond of β-methylallylcarbinyl chloride (or β-methylallylcarbinol). This reaction is expected to be more facile than the corresponding addition to allylcarbinyl chloride.

1-Methylcyclopropyl bromide was obtained by the action of bromine on the silver salt of 1-methylcyclopropanecarboxylic acid in a manner similar to a published procedure[139] (71%) and offers another example of a Hunsdiecker reaction which leads to a tertiary bromide.[164] Addition of hydrogen bromide to methylenecyclobutane gave 1-methylcyclobutyl bromide.[161]

Reduction of 1-methylcyclopropanecarbonitrile with sodium in ethanol or lithium aluminum hydride and the action of lithium aluminum hydride on 1-methylcyclopropanecarboxamide gave 1-methylcyclopropylcarbinylamine. 1-Methylcyclobutylamine was prepared by the alkaline hydrolysis of N-(1-methylcyclobutyl)-acetamide or N-(1-methylcyclobutyl)-formamide; the amide was obtained, using a recently developed reaction,[165,166] by treatment of methylenecyclobutane with acetonitrile or sodium cyanide in the presence of sulfuric and acetic acids. Attempts to synthesize β-methylallylcarbinylamine by lithium aluminum hydride reduction of 3-methyl-3-butenonitrile (β-methylallylcarbonitrile) met with

little success. In one experiment, a 6% yield of an amine was obtained which gave a satisfactory boiling point, refractive index and analysis of the phenylthiourea derivative, however the product seemed likely to contain some of the isomeric γ,γ-dimethylallylamine (1-amino-3-methyl-2-butene). Several attempts to prepare β-methylallylcarbinylamine by reaction of the sodium or lithium salt of nitromethane with β-methylallyl chloride, followed by reduction of the nitro compounds with iron in hydrochloric acid, failed due to the then undiscovered facile addition of hydrogen chloride to the double bond. In one experiment a small (5%) yield of amine was obtained. The only product isolated from the reaction of potassium phthalimide with the p-bromobenzenesulfonate of β-methylallylcarbinol in dimethyl formamide was phthalimide (75%), possibly formed by elimination of a molecule of p-bromobenzenesulfonic acid to give isoprene. Another attempt to prepare β-methylallylcarbinylamine, this time from diethyl 3-methyl-3-butene-1,1-dicarboxylate, was also unsuccessful. When the corresponding dicarboxylic acid was rapidly decarboxylated, the main product was not 4-methyl-4-pentenoic acid (on which a Schmidt reaction or Curtius degradation was next intended), but the corresponding γ-lactone. A successful synthesis of β-methylallylcarbinylamine was achieved in the reaction of β-methylallylcarbinyl chloride with potassium phthalimide in dimethyl formamide followed by hydrazinolysis.

Amine-Nitrous Acid Reactions

The first problem of this research was to determine the effect of a methinyl-substituted methyl group upon the relative stabilities of the cyclopropylcarbinyl, cyclobutyl and allylcarbinyl cations or upon the relative importance of possible non-classical intermediates compared to the classical ions. The correlation of carbonium-ion stabilities with the relative amounts of the various carbinol products observed in the reaction of aliphatic amines with nitrous acid was found to be quite satisfactory in previous studies;[60-62] this mild, irreversible process appears to be the reaction of choice. The amine-nitrous acid reactions were carried out by the addition of a solution of sodium nitrite to a solution of the amine in dilute aqueous perchloric acid, thus avoiding the complication of chloride formation observed in dilute hydrochloric acid. The product compositions were determined from boiling points, refractive indices and infrared spectra.

Treatment of 1-methylcyclopropylcarbinylamine and 1-methylcyclobutylamine with sodium nitrite in dilute aqueous perchloric acid gave 1-methylcyclobutanol (64-78%) as the only product. No 1-methylcyclopropylcarbinol, β-methylallylcarbinol or olefin was detected. Evidence from infrared spectra indicates that no more than ~1-2% of these components could have been present and still undetected. In a separate experiment, it was demonstrated that 1-methylcyclopropylcarbinol is

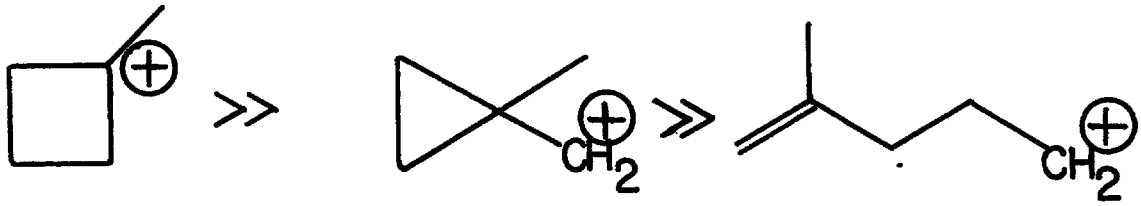
stable under the conditions of the amine-nitrous acid reaction and the product isolation procedures.

Treatment of 1-methylcyclopropylcarbinylamine and 1-methylcyclobutylamine with sodium nitrite in glacial acetic acid was found to give mainly 1-methylcyclobutyl acetate (~80%) and a smaller amount (~20%) of 1-methylcyclobutanol. The infrared spectrum of the product indicated a small amount of organic nitrite, presumably 1-methylcyclobutyl nitrite. Heating under reflux of the nitrite containing fraction with methanol caused the nitrite band in the infrared spectrum to decrease with no apparent change in other bands.

Treatment of β-methylallylcarbinylamine with sodium nitrite in dilute aqueous perchloric acid gave a complex mixture of products. Analysis of the infrared spectrum indicated the following approximate composition: 1-methylcyclobutanol (55%), β-methylallylcarbinol (33%), 1-methylcyclopropylcarbinol (2 ± 2%), α-methyl-β-methylallyl alcohol (4%) and β-methyl-γ-methylallyl alcohol (6%).

Assuming for the moment that only classical cations are involved in these amine-nitrous acid reactions, it may be concluded that conversion of the 1-methylcyclopropylcarbinyl cation to the 1-methylcyclobutyl cation requires little or no activation energy, while the conversion of the β-methylallylcarbinyl cation to the 1-methylcyclobutyl ion occurs with less facility; the reversal of these processes apparently does not take place significantly under irreversible conditions. The 1-methylcyclopropylcarbinyl cation does not re-

arrange to the β-methylallylcarbinyl cation and the reverse rearrangement was doubtful. The β-methylallylcarbinyl cation is converted, to a small extent, to the α-methyl-β-methylallyl and β-methyl-γ-methylallyl cations, although the reverse process is not expected to occur (cf. the diazotization of α-methylallyl- and crotyl amines[60,61]). These results may be summarized in the postulated order of carbonium-ion stabilities (see below). This order is to be



compared with that observed by Roberts and Mazur[60,61] for the cyclopropylcarbinyl, cyclobutyl and allylcarbinyl cations, viz., cyclopropylcarbinyl $\gtrsim$ cyclobutyl $>>$ allylcarbinyl (CV, fig. 14).

Indeed the classical carbonium-ion theory predicts this result, i.e., the effect of a methyl substituent is most pronounced when substituted at the carbonium carbon. The stabilization of the 1-methylcyclobutyl cation is derived, at least in part, from the hyperconjugative resonance structure involving delocalization of the C-H σ-electrons of the methyl group with the vacant p-orbital of the carbonium carbon. Apparently the strain involved in approaching an sp^2 configuration ($\angle$ 120°) about the carbonium carbon in a four-membered ring is

not prohibitive although this process surely requires some energy. The rearrangement of 1-methylcyclopropylcarbinylamine in aqueous nitrous acid is reminiscent of the behavior of neopentylamine under similar conditions; the two are structurally analogous.

The exact nature of the intermediate, or intermediates, involved in the interconversion of cyclopropylcarbinyl, cyclobutyl and allylcarbinyl derivatives was of considerable interest and a number of experiments successfully eliminated several mechanisms as reasonable possibilities.[60-62] The degree of equivalence attained by the three methylene groups in the diazotization of cyclopropylcarbinyl-C^{14}-amine was part of the evidence supporting the non-classical 'tricyclobutonium' ion as the actual intermediate. Would a similar result be observed with 1-methylcyclopropylcarbinyl-C^{14}-amine or does the methyl substituent radically alter the reaction path? This question obviously led to the next problem of this research, viz., the determination of the C^{14}-distribution in the 1-methylcyclobutanol obtained from the amine-nitrous acid reaction of 1-methylcyclopropylcarbinyl-C^{14}-amine.

The starting material for the synthesis of 1-methylcyclopropylcarbinyl-C^{14}-amine was 1-methylcyclopropyl bromide. The corresponding Grignard reagent was prepared and carbonated with $C^{14}O_2$ in an evacuated system at -25°.[167] Hydrolysis gave 1-methylcyclopropanecarboxylic-C^{14} acid (88% from $BaC^{14}O_3$) which on successive treatment in chloroform with triethylamine,

ethyl chloroformate and anhydrous ammonia;[164,168,169] gave 1-methylcyclopropanecarbox-C^{14}-amide (84%). Reduction of the amide with lithium aluminum hydride gave 1-methylcyclopropylcarbinyl-C^{14}-amine (51%). As was previously mentioned treatment of this amine with sodium nitrite in dilute aqueous perchloric acid gave only 1-methylcyclobutanol.

The problem of degrading 1-methylcyclobutanol-C^{14} and determining the C^{14}-distribution among the three methylene groups was an intriguing one. Certainly any conditions favoring formation of a carbonium ion, e.g., acid-catalyzed dehydration or chromic acid oxidation, had to be avoided. Oxidation of 1-methylcyclobutanol with alkaline permanganate was first considered but the complexity of the product mixture (viz., formic, acetic, oxalic, malonic and succinnic acids[170]) was discouraging. Attention was next turned to a reaction which would generate 1-methylcyclobutoxy free radicals, but the only effort in this direction was an unrewarding attempt to photolyze 1-methylcyclobutyl hypochlorite with ultra-violet light.

The next possibility considered was the Tschugaeff dehydration, a reaction involving a 'molecular mechanism.' The methyl xanthate of 1-methylcyclobutanol was prepared in the usual fashion and decomposed by dropwise addition to refluxing diphenyl (254°). The gases evolved were swept through a sodium hydroxide solution to remove most of the carbon oxysulfide and methyl mercaptan, and the vapors con-

densed. Distillation of the hydrocarbon mixture (83% from the xanthate) gave no apparent separation but analysis by infrared spectra revealed the structure and composition of the products. The percent composition calculated from the infrared spectra follows: methylenecyclobutane, 18%; 1-methylcyclobutene, 25%; and isoprene, 57%. The formation of isoprene was not unexpected since pyrolysis of the methyl xanthate of cyclobutanol has been reported to yield only 1,3-butadiene.[137] Treatment of methylenecyclobutane under the reaction conditions, i.e., one pass through refluxing diphenyl, gave no isomerization, the infrared spectrum of the product and starting material being identical. On the other hand, pyrolysis of 1-methylcyclobutene under these conditions led to a hydrocarbon mixture containing 1-methylcyclobutene (14%) and isoprene (86%), but no methylenecyclobutane. It is interesting that an isomerization of methylenecyclobutane to isoprene via 1-methylcyclobutene appears to take place in the presence of maleic anhydride and benzene at 190-195°, since the products are 4-methyl-4-cyclohexene-1,2-dicarboxylic anhydride and 4-(2,3-dicarboxypropyl)-4-cyclohexene-1,2-dicarboxylic dianhydride.[171]

At this point, isoprene was chosen as the hydrocarbon for further degradation. The reasons were threefold: (1) isoprene was present in the largest percentage in the hydrocarbon mixture, (2) many dienes are readily separated from monoolefins via the formation of cyclic sulfones and (3) isoprene appeared

to be only a step or two away from trimethylethylene, a compound for which a complete degradative procedure has been published.[133] The mixture of hydrocarbons obtained from the pyrolysis of the methyl xanthate of 1-methylcyclobutanol was heated with an excess of sulfur dioxide at 100° in a sealed tube with a small amount of hydroquinone as a polymerization inhibitor.[172-174] Recrystallization of the product from water gave an excellent yield of isoprene-C^{14} sulfone (2,5-dihydro-3-methylthiophene-1,1-dioxide) (40% from the xanthate, 84% from the calculated amount of isoprene in the hydrocarbon mixture). In separate experiments, and contrary to another report,[172] it was found that reaction of isoprene with sulfur dioxide at room temperature and in the presence of hydroquinone gave predominantly an extremely tough, yellow polymer, presumably the open-chain sulfur dioxide : isoprene polymer.

Isoprene sulfone underwent decomposition when heated at 110 to 180°.[172,174] The gases evolved were bubbled through a solution of sodium hydroxide to remove the sulfur dioxide, the vapors then passed through a drying tube and finally into a Dry Ice condenser. The isoprene thus collected (92%) needed no further purification.[172]

The initial plan was to reduce isoprene to trimethylethylene with an alkali metal in liquid ammonia. Several efforts were made in this direction, using sodium and lithium in liquid ammonia, with the intention of changing to ethyl-

amine since this combination (lithium in ethylamine) has been used successfully[175] to reduce aromatic systems to monoolefins; however before the desired procedure was developed, an entirely different route from isoprene to trimethylethylene was uncovered. This path involved the 1,4-addition of bromine to isoprene (77%)[176] and subsequent reduction of the isoprene dibromide with lithium aluminum hydride[177] (95%). The bromine addition was specific, stopping quantitatively after one molecule had added.

Trimethylethylene was degraded by a previously described procedure.[133] The first step involved hydroxylation of the double bond with performic acid followed by cleavage of the resulting diol (2-methyl-2 , 3-butanediol) with periodate, yielding acetone and acetaldehyde which were assayed as solid derivatives. The acetone was further degraded to iodoform. A pinacol rearrangement of 2-methyl-2,3-butanediol gave methyl isopropyl ketone which was also degraded to iodoform. The complete degradation scheme is described in fig. 20.

Inspection of Table II reveals that the C^{14} results are quite satisfactory. Most of the several ways of adding and subtracting the various activities give good agreement, within the limits of error. Thus the activities of acetone 2,4-dinitrophenylhydrazone (α,1,2) and acetaldehyde dimethone (3,4) total 99.8 ± 1.3%, well within the limits of error for the activity of methyl isopropyl ketone 2,4-dinitrophenylhydrazone (α,1,2,3,4), 100.0 ± 0.5%.

Degradation of 1-Methylcyclobutanol.

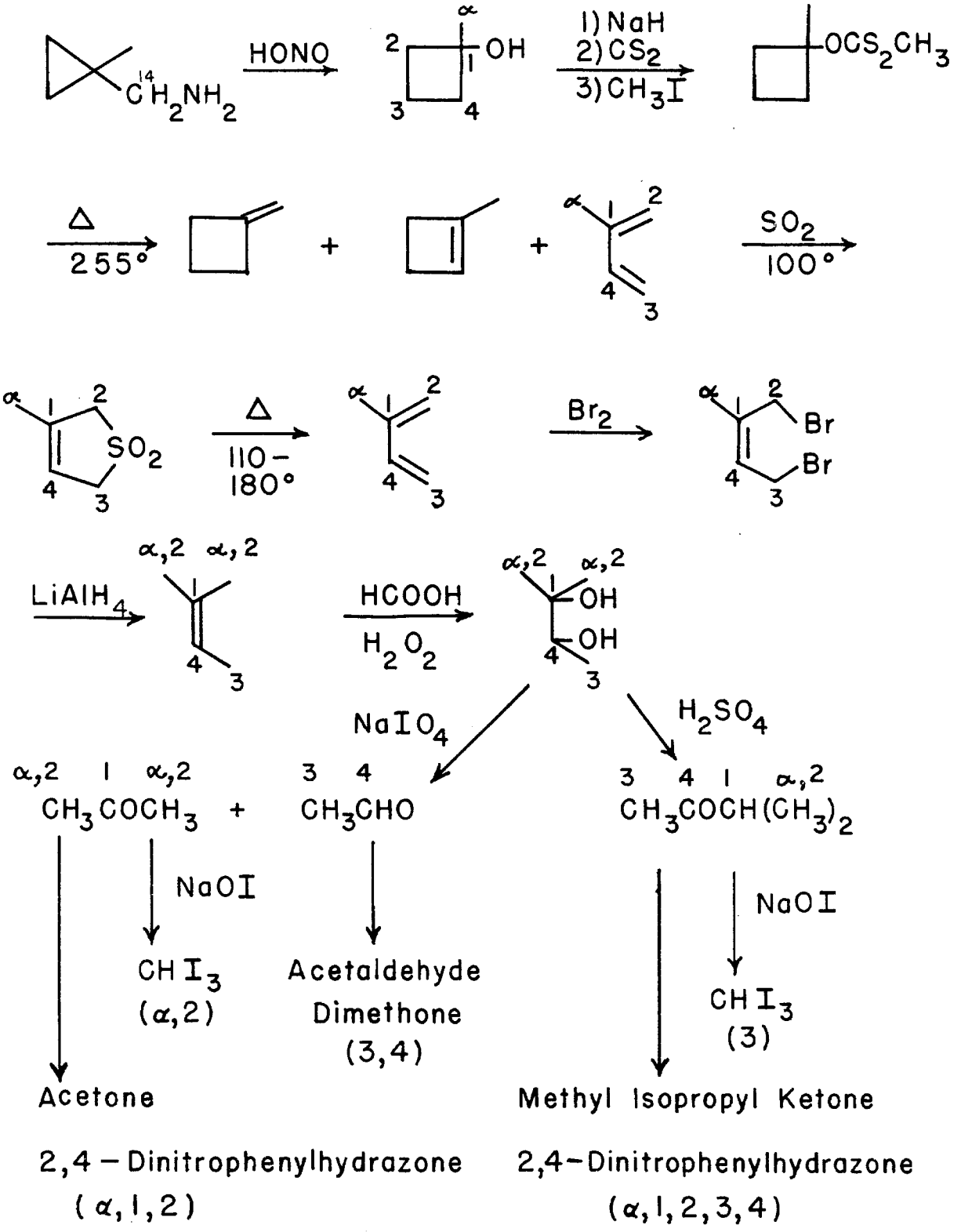


Fig. 20

Table II

Radioactivity Analyses of the Degradation Products of 1-Methylcyclobutanol-C^{14} Obtained in the Reaction of 1-Methylcyclopropylcarbinyl-C^{14}-amine with Sodium Nitrite in Dilute Aqueous Perchloric Acid

Compound	Atoms[a]	Percent of total C^{14}-activity in degradation product[b]
CHI_3, from methyl isopropyl ketone	3	2.6 ± 0.1
CHI_3, from acetone	$\frac{1}{2}[\alpha + 2]$	24.5 ± 0.1
Acetone 2,4-dinitrophenylhydrazone	α,1,2	47.9 ± 0.5
Acetaldehyde dimethone	3,4	51.9 ± 0.8
Methyl isopropyl ketone 2,4-dinitrophenylhydrazone	α,1,2,3,4	100.0 ± 0.5

[a]These numbers refer to the numbering of 1-methylcyclobutanol, where 2 = 4.

[b]The standard deviations, in %, are attached to the % C^{14}-activities.

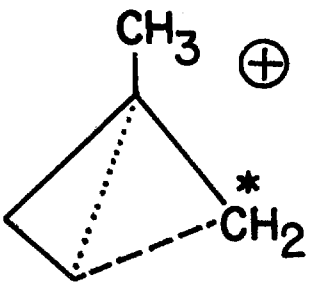
A number of control experiments were conducted to ensure the reliability of the results. The recovery of unchanged 1-methylcyclopropylcarbinol after treatment with sodium nitrite in dilute aqueous perchloric acid was strong evidence against the formation and subsequent rearrangement (to 1-methylcyclobutanol) of 1-methylcyclopropylcarbinol in the reaction of 1-methylcyclopropylcarbinylamine with sodium nitrite in dilute aqueous perchloric acid. Furthermore, permanganate oxidation of 1-methylcyclopropylcarbinyl-C^{14}-amine to 1-methylcyclopropanecarboxylic-C^{14} acid followed by a Schmidt reaction on the acid gave N-(1-methylcyclopropyl)-benzamide which possessed a maximum of 0.29% of the total activity of the original 1-methylcyclopropylcarbinyl-C^{14}-amine (actually measured as 1-methylcyclopropanecarbox-C^{14}-amide).

Actually only the activity in the 3-position of 1-methylcyclobutanol (measured as iodoform from methyl isopropyl ketone) and the total activity (measured as methyl isopropyl ketone 2,4-dinitrophenylhydrazone) need be known, the other compounds assayed for C^{14} serving merely as useful checks on the reliability of the degradative methods. The prominant feature of these results is the relatively low C^{14}-activity (2.6%) in the 3-position of 1-methylcyclobutanol compared to the corresponding activity for the 3-position of cyclobutanol observed by Roberts and Mazur[61,62] (28%) and White (30.6%).[151] Obviously, the degree of equivalence attained by the three

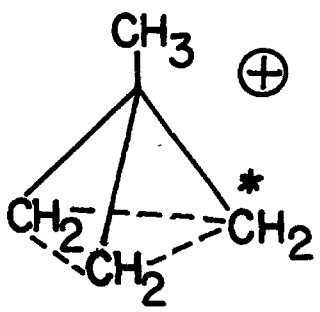
methylene groups in the amine-nitrous acid reaction changes drastically on going from cyclopropylcarbinylamine (85%[61,62] and 92%[151] equivalence in the cyclobutanol) to 1-methylcyclopropylcarbinylamine (7.8% equivalence for 1-methylcyclobutanol). The significance of these findings will now be discussed.

It is profitable to discuss the results in terms of the various possible mechanisms previously considered for interconversion reactions of other cyclopropylcarbinyl, cyclobutyl and allylcarbinyl derivatives. Certain reaction paths may be excluded from further consideration simply on the basis of the non-formation of 1-methylcyclopropylcarbinol. Thus the 1-methylcyclopropylcarbinyl cation is entirely unreasonable as the only real intermediate (this would involve a concerted attack by water at the 1-carbon of the cyclopropane ring), and bimolecular displacement on the 1-methylcyclopropylcarbinyl diazonium ion is likewise ruled out. It will be remembered that this latter process adequately accounted for the high activity observed in the α-carbon of cyclopropylcarbinol obtained in the reaction of cyclopropylcarbinyl-C^{14}-amine with nitrous acid (vide supra). A convincing argument against intermediate formation of a diazo compound (1-methyl-1-diazomethylcyclopropane) may be found in the formation of ethanol containing only 1.1 atom % of deuterium attached to carbon when ethylamine reacts with perchloric acid and sodium nitrite in 99.8% deuterium oxide.

The methylcyclobutyl cation or the non-classical ion CXVII would lead to 1-methylcyclobutanol with no activity in

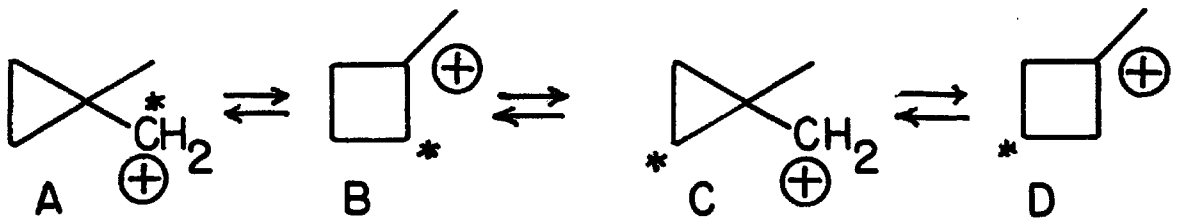


CXVII



CXVIII

the 3-position. On the other hand, the symmetrical non-classical ion CXVIII or an equilibrium mixture of the classical 1-methylcyclopropylcarbinyl and 1-methylcyclobutyl cations ABCD (CXIX) (where reaction with solvent is much faster with



CXIX

B and D than with A and C) would give rise to equal activity in the 2-, 3- and 4-positions of 1-methylcyclobutanol; hence complete equilibration of these intermediates is not in accord with the results.

A reaction scheme involving successive hydride and methide shifts in the (initially) 1-methylcyclobutyl cation

(and forming successive secondary and tertiary carbonium ions) is unlikely. Although such a mechanism could account for a small amount of activity in the 3-position of 1-methylcyclobutanol, an equal amount would also appear in the 1-position. Shuffling of the carbon atoms *via* successive 1,2-hydride shifts is expected to be more facile (successive secondary carbonium ions) in the cyclobutyl cation, yet only 0.7% of the total C^{14}-activity was found in the 1-position of the cyclobutanol.[151] Overwhelming evidence against a hydride shift in the 1-methylcyclobutyl cation (to give the 2-methylcyclobutyl cation) is the absence of any methylcyclopropylcarbinol in the product. The latter compound was the only product isolated from the reaction of 2-methylcyclobutylamine with nitrous acid.[108]

One explanation which accounts for the C^{14}-results is a partially established equilibrium of the 1-methylcyclopropylcarbinyl and 1-methylcyclobutyl cations (ABCD, CXIX). Such a mechanism requires the rate of reaction of cation B with solvent to be considerably greater than the rate at which the equilibrium of the ions is attained. A further requisite of this scheme is a negligible rate of reaction of cation A and C (compared to B and D) with solvent since the product corresponding to this reaction, *i.e.*, 1-methylcyclopropylcarbinol, was not detected. Certainly the difference between the % C^{14}-activity in the 3-position of cyclobutanol and 1-methylcyclobutanol (30.6 or 28 versus 2.6%) is in the direction ex-

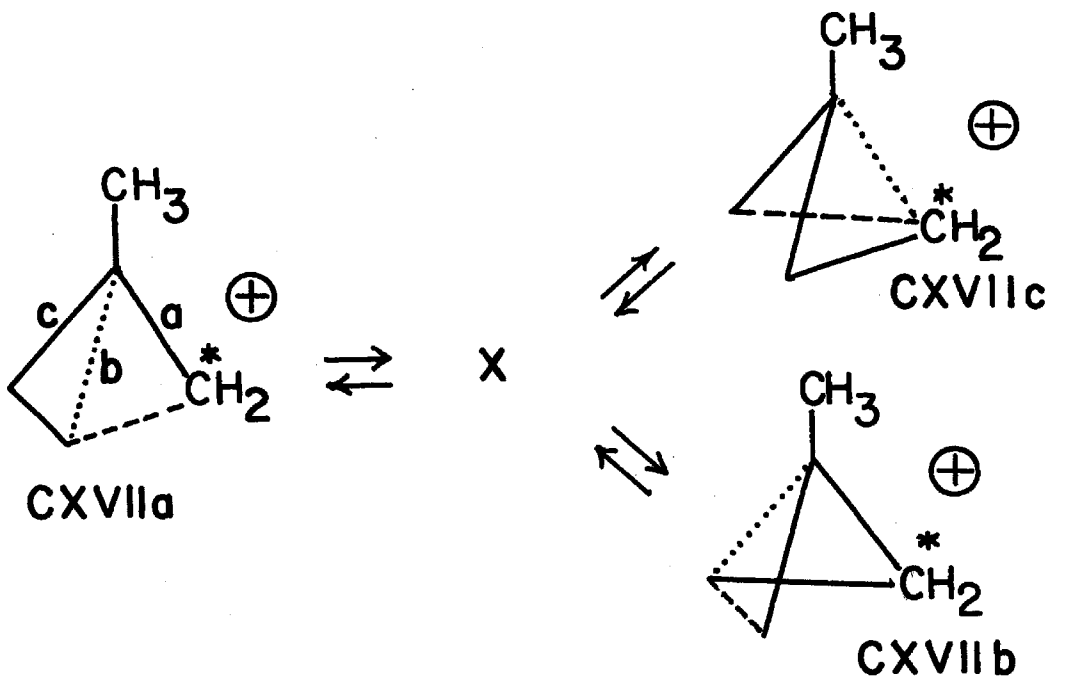
pected since stabilization of the cyclobutyl cation by the methyl group would be far more important than stabilization of the cyclopropylcarbinyl cation; the magnitude of this effect is mildly surprising. A priori, one might expect at least a small amount of 1-methylcyclopropylcarbinol to arise from the 1-methylcyclopropylcarbinyl cation in the reaction of 1-methylcyclopropylcarbinylamine with nitrous acid. Furthermore a partial equilibrium of cations ABCD leaves something to be desired to explain the unusually high reactivity of 1-methylcyclopropylcarbinyl and other cyclopropylcarbinyl derivatives (vide infra).

An intermediate non-classical 'tricyclobutonium' ion was postulated to explain (1) the C^{14}-results in the reaction of cyclopropylcarbinyl-C^{14}-amine with nitrous acid, (2) the abnormally high solvolytic reactivities of cyclopropylcarbinyl and cyclobutyl halides and sulfonate esters and (3) the ease of interconversion of cyclopropylcarbinyl and cyclobutyl derivatives. The C^{14} data in the present case are explained if 7.8% of the reaction of 1-methylcyclopropylcarbinylamine proceeds by way of the symmetrical, non-classical cation CXVIII and the remaining 92.2% via the classical 1-methylcyclobutyl cation or non-classical ion, CXVII. This mechanism does not suffer the disadvantage inherent in the intermediate 1-methylcyclopropylcarbinyl cation, i.e., the non-formation of 1-methylcyclopropylcarbinol. An essential feature of this proposal is the reaction of cation

CXVIII with solvent only at the carbon holding the methyl group (apex carbon), the position of maximum charge stabilization. With the unsubstituted non-classical 'tricyclobutonium' ion it was suggested[62] that three sp^3 atomic orbitals, one from each methylene group, overlapped to form one stable molecular orbital, holding the two electrons, and two vacant, considerably less-stable orbitals. A methyl group substituted at the apex carbon would stabilize a more or less larger proportion of the positive charge at that carbon and would tend to "push" the electrons toward the methylene groups and presumably forcing them into less-stable molecular orbitals; hence the non-classical cation CXVIII is expected to be less stable than the corresponding unsubstituted analogue. In this respect, it is noteworthy that the rate of decomposition of 2,2'-azo-bis-2-cyclopropylpropionitrile in toluene at 80.5° is from 15 to 25 times faster than the corresponding azo-bis-nitriles derived from methyl cyclobutyl, methyl cyclopentyl and methyl cyclohexyl ketones.[178] The possibility was mentioned[178] that the enhanced rate of the azo-bis nitrile from methyl cyclopropyl ketone might be due, at least partly, to stabilization of the intermediate free radical by contributing structures similar to those postulated by Roberts and Mazur[60-62] for the cyclopropylcarbinyl and 'tricyclobutonium' cations.

Another intermediate which satisfies the C^{14} results and deserves some merit is the unsymmetrical non-classical cation,

CXVIIa. The finding of 2.6% of the C^{14}-activity in the 3-



position of 1-methylcyclobutanol may be explained by the supposition of a mixture of three unsymmetrical non-classical ions (CXVIIa, CXVIIb, CXVIIc) as intermediates where CXVIIb and CXVIIc are formed to the extent of 7.8% of their equilibrium concentrations. All solvent attack which leads to products must occur at the methyl-substituted carbon and must arise by cleavage of the weakest bond shown. An alternative interpretation, with CXVIIa as the only intermediate, has 1-methylcyclobutanol being formed by solvent attack at the methyl-substituted carbon and by cleavage not only of bond b, but also an amount of cleavage of bonds a and c sufficient to explain the C^{14} data. (Note that cleavage only of bond a leads to activity in the 3-position).

It is appropriate to consider now the effect on the final C^{14} results, if any, of the difference in the reaction rates (both formation and cleavage) of C^{12} and C^{14} bonds. In making these calculations the following simplifications were made: (1) An isotope effect of 1.11 (an average of 21 available values for cleavage of C-C and C-O bonds, standard deviation $\pm$ 0.08) was assumed for k_{C12}/k_{C14} for C-C, C-H, C-O, C-N, C-S and C-Br bonds and also for transformations from a single to a double carbon-carbon bond. (2) In each reaction sequence it was considered that 2.6% of the radioactive starting material consisted of molecules which possessed activity in a carbon atom logically derived from C-3 of 1-methylcyclobutanol. (3) Intermolecular isotope effects were estimated by use of a chart published for this purpose by the Chemical Division of the Oak Ridge National Laboratory. In the reaction of 1-methylcyclopropylcarbinyl-C^{14}-amine with aqueous nitrous acid, the 1-methylcyclobutanol-C^{14}-3 was assumed to be derived from the symmetrical nonclassical cation CXVIII since the isotope effect would be larger with CXVIII than the other possible intermediates previously discussed. A simple calculation predicts an 8.7% decrease in the isotopic concentration of 1-methylcyclobutanol-C^{14}-3 over and above that expected in the amine-nitrous acid reaction had there been no isotope effect. Formation of the xanthate from 1-methylcyclobutanol would involve no isotope effect. The next two sequences, viz., forma-

tion of 1-methylcyclobutene by pyrolysis of the xanthate followed by isomerization to isoprene are expected to have equal and opposite isotope effects, thus cancelling each other. This may be clearer if a single concerted mechanism[137] is considered for the transformation of xanthate to isoprene; such a process involves cleavage and formation of the same number of C^{14} bonds regardless of the position of the C^{14}. A similar situation exists in the formation and decomposition of isoprene sulfone, i.e., C^{14} bonds are formed and broken to the same extent, independent of the C^{14} location. Since we have assumed equal reaction rates for all C^{14}-X bonds formed and cleaved, the above argument predicts no observable isotope effect in the formation of isoprene dibromide. However calculations reveal that hydroxylation of trimethylethylene and the subsequent pinacol rearrangement could lead to a 3.1% and 2.3% isotopic enrichment, respectively, of the molecules derived from 1-methylcyclobutanol-C^{14}-3. (The yield in the pinacol rearrangement of 2-methyl-2,3-butanediol was taken as the yield of the 2,4-dinitrophenylhydrazone of the resulting methyl isopropyl ketone). The formation of iodoform from methyl isopropyl ketone was assumed to involve no isotope effect since none was observed in the iodoform reaction of acetone-C^{14}.[179] From the above calculations, it can be shown that on going from 1-methylcyclopropylcarbinyl-C^{14}-amine to iodoform (from methyl isopropyl ketone) (11 steps), there occurs an overall decrease of 3.7% in the original isotopic

concentration of the 1-methylcyclobutanol-C^{14}-3. Thus from the observed value (2.6%) of the C^{14}-activity in the 3-position of 1-methylcyclobutanol as determined from the iodoform from methyl isopropyl ketone, it follows that the real C^{14}-activity is not likely to be lower than 2.7%. Thus the difference between the real (calculated) and experimental activities is only 0.1%, a value barely in the range of experimental error. Hence as a final conclusion, and even if the simplifying assumptions made are not completely valid, the isotope effect in the reactions considered may be neglected.

We have previously considered three mechanisms as reasonable possibilities in the reaction of 1-methylcyclopropylcarbinyl-C^{14}-amine with nitrous acid, viz., (1) a partially established equilibrium of 1-methylcyclopropylcarbinyl and 1-methylcyclobutyl cations (ABCD), (2) 7.8% of the symmetrical non-classical carbonium ion CXVIII plus 92.2% of the classical 1-methylcyclobutyl cation or the non-classical ion CXVII, and (3) an unsymmetrical non-classical cation CXVIIa (a) which is in partial equilibrium (7.8%) with two similar ions (CXVIIb and CXVIIc) or (b) which alone reacts to give 1-methylcyclobutanol with 2.6% of the C^{14}-activity in the 3-position. In the case of a partially established equilibrium of classical ions (ABCD), water molecules are expected to be substantially covalently bonded to the carbonium carbons in the transition state. In a less nucleophilic solvent, e.g., acetic acid, this covalent bonding should be

considerably weakened, allowing more time for rearrangement. Moreover the effect on the percent rearrangement of changing to a less nucleophilic solvent should be more noticeable in the case of an equilibrium of classical ions than with the non-classical ions, in which cases the positive charge is smeared over more than one carbon, thus demanding less nucleophilic solvation. It is entirely possible that all the cations considered here (both classical and non-classical) are of such high energy that changes in the nucleophilicity of the solvent would be relatively unimportant. Experiments to this end were carried out in a manner similar to those previously described. 1-Methylcyclopropylcarbinyl-C^{14}-amine when treated with sodium nitrite in glacial acetic acid was found to give a mixture of products consisting of 1-methylcyclobutyl acetate and 1-methylcyclobutanol in a 4:1 ratio. Lithium aluminum hydride reduction of this mixture gave 1-methylcyclobutanol which was degraded as previously described. See Table III for C^{14} results.

It may be concluded that ~20% more rearrangement of C^{14} into the C-3 position occurs in the reaction of 1-methylcyclopropylcarbinyl-C^{14}-amine with sodium nitrite in acetic acid (3.1%) than in aqueous medium (2.6%). This change is rather small, although definitely outside the limits of experimental error. The effect in changing from water to acetic acid may be taken as evidence favoring a more or less high energy cationic intermediate (classical or non-classical)

Table III

Radioactivity Analyses of the Degradation Products of 1-Methylcyclobutyl-C^{14} Acetate and 1-Methylcyclobutanol-C^{14} Obtained in the Reaction of 1-Methylcyclopropylcarbinyl-C^{14}-amine with Sodium Nitrite in Glacial Acetic Acid

Compound	Atoms[a]	Percent of total C^{14}-activity in degradation product[b]
CHI_3, from methyl isopropyl ketone	3	3.1 ± 0.1
CHI_3, from acetone	$\frac{1}{2}(\alpha + 2)$	23.6 ± 0.3
Acetone 2,4-dinitrophenylhydrazone	α,1,2	47.6 ± 1.2
Acetaldehyde dimethone	3,4	49.5 ± 1.8
Methyl isopropyl ketone 2,4-dinitrophenylhydrazone	α,1,2,3,4	100.0 ± 1.1

[a]These numbers refer to the numbering of 1-methylcyclobutanol, where 2 = 4.

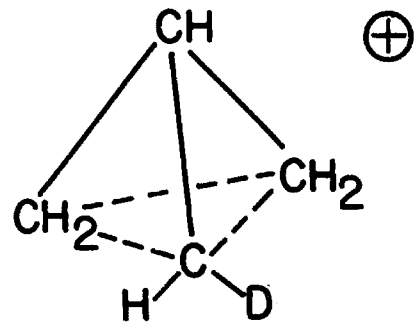
[b]The standard deviations, in %, are attached to the % C^{14}-activities.

which shows little selectivity toward the solvent. Unfortunately these results offer no compelling evidence favoring or opposing any of the postulated mechanisms. Solvent effects have been observed in other amine-nitrous acid reactions. For example the % rearrangement in the reaction of exo- and endo-norbornyl-C^{14}-amines with nitrous acid is relatively insensitive to changes in solvent compared to the % rearrangement observed in the solvolysis of the corresponding p-bromobenzenesulfonates in various solvents.[53] Furthermore both the exo and endo isomers give less rearrangement (6 and 10%, respectively) in acetic acid than in aqueous fluoboric acid. On the other hand the reaction of 2-p-methoxyphenylethylamine-1-C^{14} with nitrous acid gave 36% more rearrangement in acetic acid than in water, although the corresponding 2-phenyl- and 2-p-nitrophenylethylamine-C^{14} displayed no preference between water and acetic acid. The latter two amines presumably lead to cations of higher energy and less charge dispersal.

It is conceivable that the 1-methylcyclobutanol-C^{14} from the amine-nitrous acid reaction of 1-methylcyclopropylcarbinyl-C^{14}-amine actually contained no activity in the 3-position and that some or all the observed activity assigned to that position derived its origin in one or more of the degradative steps. Time did not permit an experimental check on this point.

Unfortunately, in this work and in the researches of

Roberts and Mazur,[60-62] White,[151] Sheppard[106] and Rice,[108] no evidence is available which permits an undeniable decision between classical and non-classical intermediates. One experiment comes to mind, viz., the reaction of optically active cyclopropylcarbinylamine-α-$\underline{d}_1$ with nitrous acid. If only intermediate classical cations are involved, all products should be inactive; however if the "symmetrical" non-classical cation CXX (or else a slightly unsymmetrical



CXX

cation) is the important intermediate, then a total of three isomers of cyclopropylcarbinol-$\underline{d}_1$ (all optically active) and four isomers of cyclobutanol-$\underline{d}_1$ (two optically active) are expected. The experimental difficulties involved in such an investigation would be numerous, but not necessarily insurmountable. Indeed the reward of some telling results would overshadow the pains taken.

The reaction of optically active 1-methylcyclopropylcarbinyl-$\underline{d}_1$-amine would lead to the same products (97.4% of diasteromers of 1-methylcyclobutanol-2-$\underline{d}_1$) whether the

intermediate is CXVII (CXVIIa-c) or CXIX-B. A classical 1-methylcyclopropylcarbinyl cation would lead only to inactive 1-methylcyclobutanol-$\underline{d}_1$.

The results of the reaction of optically active methylcyclopropylcarbinylamine and 2-methylcyclopropylcarbinylamine should be informative.

Solvolytic Reactivities of Halides

We have discussed the effect of methyl substituents in determining the products of amine-nitrous acid reactions and hence, the influence of methyl substitution upon the stability of classical and/or non-classical carbonium ions. In this connection it was of particular interest to study the solvolysis rates of cyclopropylcarbinyl, cyclobutyl and allylcarbinyl derivatives and to correlate the consequences of methyl substitution in terms of relative solvolytic reactivities. Table IV contains a compilation of data obtained in this and other work concerning solvolysis of a number of cycloalkyl and cycloalkylcarbinyl halides in aqueous ethanol. Also included for purposes of comparison are rate constants for some allyl, allylcarbinyl and alkyl halides.

The cycloalkyl chlorides have been discussed in detail elsewhere[64] but a brief mention of them is desirable. In 50% aqueous ethanol at 95° the relative solvolysis rates of the chlorides are $\underline{i}$-propyl, 1.00; cyclopropyl, < 0.005;

Table IV

Solvolysis Rate Constants in Aqueous Ethanol

No.	Radical	Halide	T °C	k_1(hr.$^{-1}$)	% EtOH	Ref.
1	Cyclopropyl	Cl	95	0.0005	50	64
2	Cyclopropyl	Br	130	.0094	50	a
3	1-Methylcyclopropyl	Cl	30	7×10^{-6}	50	b
4	1-Methylcyclopropyl	Br	130	.378	50	a
5	Cyclopropylcarbinyl	Cl	50	.45	50	60,61
6	Cyclopropylcarbinyl	Br	25	.34	50	60,61
7	Cyclopropylcarbinyl	Br	75	25.	60	c
8	1-Methylcyclopropyl-carbinyl	Cl	30	2.49	50	a
9	Cyclobutyl	Cl	50	.017	50	60,61
10	"	"	95	1.36	50	64
11	Cyclobutyl	Br	25	.015	50	60,61
12	1-Methylcyclobutyl	Cl	25	.00224	80	162
13	"	"	30	.257	50	a
14	"	"	50	2.22	50	a
15	1-Methylcyclobutyl	Br	25	6.09	50	d
16	"	"	30	11.1	50	a
17	"	"	130	79,000.	50	d
18	Cyclobutylcarbinyl	Br	75	60.	60	154
19	Cyclopentyl	Cl	85	.017	80	180
20	"	"	95	.48	50	64
21	Cyclopentyl	Br	75	732.	60	154
22	1-Methylcyclopentyl	Cl	25	1.32	80	162

Table IV (continued)

No.	Radical	Halide	T °C	k_1 (hr.$^{-1}$)	% EtOH	Ref.
23	1-Methylcyclopentyl	Cl	85	480.	80	e
24	Cyclohexyl	Cl	95	.033	50	64
25	1-Methylcyclohexyl	Cl	25	.0106	80	162
26	"	"	95	740.	50	f
27	Allyl	Cl	30	.00127	50	g
28	"	"	44.6	.00606	50	155
29	Allyl	Br	25	.013	50	60,61
30	β-Methylallyl	Cl	44.6	.00924	50	155
31	"	"	50	.011	50	60,61
32	Allylcarbinyl	Cl	90	.006	50	60,61
33	β-Methylallyl-carbinyl	Cl	130	1.05	50	a
34	n-Propyl	Cl	50	10^{-4}	50	h
35	"	"	101.6	.0348	50	155
36	i-Propyl	Cl	50	.00116	50	i
37	"	"	95	.0934	50	144
38	t-Butyl	Cl	25	.0302	80	162
39	"	"	25	1.32	50	83
40	"	"	30	3.5	50	j
41	"	"	50	26.4	50	j
42	Ethyl	Br	25	.00060	50	k
43	"	"	25	.000364	60	181
44	"	"	75	.185	60	l
45	i-Propyl	Br	25	.0026	50	m
46	"	"	25	.000950	60	181

Table IV (continued)

No.	Radical	Halide	T °C	k_1 (hr.$^{-1}$)	% EtOH	Ref.
47	t-Butyl	Br	25	24.	50	n
48	"	"	25	13.5	60	83

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[a]This work. [b]Estimated from No. 4,13 and 17 by assuming that the ratio of the rates of 1-methylcyclobutyl bromide to 1-methylcyclopropyl bromide at 130°, is roughly the same at 30°. [c]Calculated from No. 6 using E_a = 21.5 kcal. mole^{-1} (for t-butyl bromide),[83] and m = 0.917 (for t-butyl bromide) in the equation log k = mY + log k_o (or log k/k = m (Y_2-Y_1)).[83] [d]Calculated from No. 16 using E_a = 21.5 kcal. mole^{-1} (for t-butyl bromide).[83] [e]Calculated from No. 22 (E_a = 20.8 kcal. mole^{-1}). [f]Estimated from No. 25, using the equation in footnote c with m = 1.000 (for t-butyl chloride). [g]Calculated from No. 28, E_a = 20.4 kcal. mole^{-1}. [h]Approximated from No. 35 by assuming a decrease in the rate constant by a factor 10 for a 20° decrease in temperature. [i]Calculated from No. 37, E_a = 22.8 kcal. mole^{-1}. [j]Calculated from No. 39, E_a = 22.9 kcal. mole^{-1}. [k]Estimated from No. 43 (as in footnote c) using m = 0.392 (for n-butyl bromide)[83] [l]Calculated from No. 43, E_a = 23.8 kcal. mole^{-1}. [m]Estimated from No. 46 (as in footnote c) using m = 0.850 (for i-propyl p-bromobenzenesulfonate).[83] [n]Estimated from No. 48 as in footnote c.

cyclobutyl, 14.6; cyclopentyl, 5.2; and cyclohexyl, 0.35 (No. 1, 10, 20, 24 and 37). Cyclopropyl bromide has been found to be 10^5 times less reactive than i-propyl bromide (No. 2 and 45). Cyclobutyl bromide reacts 5.8 times as fast as i-propyl bromide at 25° in 50% ethanol (No. 11 and 45). The extremely low reactivity of cyclopropyl derivatives in general may be ascribed to the same factors causing the inertness of the analogous aryl and vinyl compounds. The unexpected high reactivity of cyclobutyl chloride may mean (1) that the cyclobutyl cation is unusually stable for a secondary cation, (2) that cyclobutyl chloride is exceptionally strained and this strain is released in forming the ion, or (3) that some other more stable carbonium ion, e.g., cyclopropylcarbinyl or 'tricyclobutonium' ion, is formed in the rate-determining step. The latter explanation appears to be the more attractive hypothesis. The solvolysis rates for cyclopentyl and cyclohexyl chlorides relative to i-propyl chloride are generally interpreted on grounds of hydrogen-hydrogen repulsions. These repulsions are at a maximum in cyclopentyl chloride and are relaxed somewhat at partial ionization in the transition state. However with cyclohexyl chloride, all adjacent hydrogen-hydrogen repulsions are at a minimum (skew) and ionization tends to eclipse some of the C-H bonds, thus increasing the $\Delta F^{\ddagger}$.

The 1-methylcycloalkyl chloride series has been thoroughly studied in 80% ethanol[162] and data on 1-methylcyclopropyl bro-

mide now complete the 1-methylcycloalkyl series (i.e., all small and medium rings and some large rings). Using t-butyl bromide as the standard, the relative reactivities of the bromides at 25° in 50% ethanol are t-butyl, 1.00; 1-methylcyclobutyl, 0.25; and 1-methylcyclopropyl, 10^{-6} (Nos. 4, 15, 17 and 48) (assuming the ratio of 1-methylcyclobutyl/1-methylcyclopropyl at 130°, holds at 25°). By a simple approximation (i.e., ratios in 50% ethanol and 80% ethanol are equal) the results of Brown[162] for solvolysis of chlorides in 80% ethanol at 25° may be extended: t-butyl, 1.00; 1-methylcyclopropyl, $\sim 10^{-6}$; 1-methylcyclobutyl, 0.0741; 1-methylcyclopentyl, 43.6; and 1-methylcyclohexyl, 0.350 (Nos. 12, 22, 25, 38). Indeed the qualitative order is similar to that obtained for the unmethylated cases, the notable exception being 1-methylcyclobutyl chloride. Brown[162] has interpreted these results on the basis of I-strain--the increase in internal strain in a cyclic structure, resulting from alterations in bond angles and constellations, which accompanies a change in the coordination number of a ring atom in the course of a reaction. In small rings (3 and 4 atoms) internal strain results primarily from the distortion of the bond angles from the preferred values, while in common rings (5,6 and 7 atoms) the deviation of the C-H constellations from the preferred staggered arrangement is the controlling factor. The low reactivity of 1-methylcyclobutyl chloride was explained by the increased strain attend-

ing the change in coordination number of the ring carbon from 4, in 1-methylcyclobutyl chloride, to 3 in the 1-methylcyclobutyl cation. (It was shown that this reaction led to no carbon skeletal rearrangement). We shall see later that the I-strain concept does not adequately explain the solvolytic reactivity of 1-methylcyclobutyl chloride.

A more informative comparison may be made from the ratio of the rates of 1-methylcycloalkyl to cycloalkyl halides. Two methods have been used. The first involves a comparison of a particular 1-methylcycloalkyl halide with the corresponding cycloalkyl halide under the same conditions (solvent and temperature). Then the following ratios are obtained: 1-methylcyclopropyl/cyclopropyl, 40 (No. 2 and 4); 1-methylcyclobutyl/cyclobutyl, 130 (No. 9 and 14) and 460 (No. 11 and 15); 1-methylcyclopentyl/cyclopentyl, 28,000 (No. 19 and 23); and 1-methylcyclohexyl/cyclohexyl, 22,000 (No. 24 and 26). For purposes of comparison the ratio of t-butyl/s-butyl is 23,000 for the chlorides (No. 36 and 41) and 9,200 for the bromides (No. 46 and 48). A second method of comparison is available from the cycloalkyl series and 1-methylcycloalkyl series mentioned previously. The two may be interrelated by the ratio 1-methylcyclobutyl/cyclobutyl for the chlorides at 50° in 50% ethanol (No. 9 and 14). This method leads to the following ratios: 1-methylcyclopropyl/cyclopropyl, 190; 1-methylcyclobutyl/cyclobutyl, 130; 1-methylcyclopentyl/cyclopentyl, 220,000; and 1-methylcyclohexyl/

cyclohexyl, 25,000. From consideration of the above values, the order of decreasing rate enhancement due to the methyl substituent is cyclopentyl > cyclohexyl >> cyclobutyl $\gtrsim$ cyclopropyl, with cyclohexyl being approximately normal when compared to the ratio t-butyl/s-butyl for the chlorides, 23,000 (No. 36 and 41). Although cyclobutyl chloride is $\sim$15 times more reactive than i-propyl chloride (and even slightly more reactive than β-methylallyl chloride), substitution of a methyl group at the reaction center increases the rate by a factor of only $\sim$130, with 1-methylcyclobutyl chloride being $\sim$13 times less reactive than t-butyl chloride. No single mechanism adequately explains the results from both of these chlorides. Thus formation of stabilized cyclopropylcarbinyl and 1-methylcyclopropylcarbinyl cations is rendered unlikely since no rearranged product was observed in the solvolysis of 1-methylcyclobutyl chloride.[162] Neither are symmetrical non-classical cations satisfactory to account for both cases since the symmetrical cation CXVIII was not the important intermediate in the reaction of 1-methylcyclopropylcarbinylamine with nitrous acid; the similarity of products observed in the amine-nitrous acid and chloride solvolysis reactions (see above) rules against a symmetrical ion CXVIII as the important intermediate. Although the I-strain accompanying the formation of the 1-methylcyclobutyl cation has been used[162] as an explanation for the somewhat low solvolytic reactivity of 1-methylcyclobutyl chloride, the

classical cyclobutyl cation is, by no logical reasoning, the important intermediate in solvolysis of cyclobutyl halides. An alternative explanation is found in the formation of an unsymmetrical non-classical intermediate (CXVII) in the solvolysis of 1-methylcyclobutyl halides.

Attention is now focused on the cyclopropylcarbinyl, cyclobutyl and allylcarbinyl series. Cyclopropylcarbinyl chloride has been shown to be 27 times more reactive than cyclobutyl chloride and 40 times more reactive than β-methylallyl chloride at 50° in 50% aqueous ethanol (No. 5, 9 and 31). At the same temperature the reaction of allylcarbinyl chloride was immeasurably slow. Cyclopropylcarbinyl chloride solvolyzes ca. 10^3-10^4 times faster than n-propyl chloride, a typical primary chloride (No. 5 and 34). At 25° the rate constant for cyclopropylcarbinyl bromide was 20 times that of cyclobutyl bromide and 30 times that of allyl bromide (No. 6, 11 and 29). Ethyl bromide, a typical primary bromide, reacts ~600 times slower than cyclopropylcarbinyl bromide (No. 6 and 42).

The unusually high reactivity of cyclopropylcarbinyl halides has been assigned to resonance stabilization of cyclopropylcarbinyl cation similar to that in the allyl cation.[61] However, the abnormally high reactivity of cyclobutyl chloride together with the finding that cyclopropylcarbinyl and cyclobutyl chlorides give essentially an identical mixture of carbinols (~50% cyclopropylcarbinol and 50% cyclo-

butanol) is evidence favoring the non-classical 'tricyclobutonium' cation CIX (fig. 14). This conclusion is strongly supported by the degree of equivalence of methylene groups attained in the reaction of cyclopropylcarbinyl-C^{14}-amine with nitrous acid. However, a rapid equilibration of classical cyclopropylcarbinyl and cyclobutyl cations was not eliminated as an acceptable mechanism if one assumes an order of carbonium ion stabilities with cyclopropylcarbinyl $\gtrsim$ cyclobutyl $\gg$ allylcarbinyl. It is of interest to compare the solvolytic behavior of the analogous methyl-substituted compounds. 1-Methylcyclopropylcarbinyl chloride has a solvolysis rate constant about 9.6 times that of 1-methylcyclobutyl chloride and $\sim$1300 times that of β-methylallyl chloride at 30°. As expected from consideration of the unsubstituted case, β-methylallylcarbinyl chloride was immeasurably slow under these conditions. A priori, one would predict the same order of carbonium ion stabilities as with the unmethylated substances (above),[61] i.e., 1-methylcyclopropylcarbinyl $\gtrsim$ 1-methylcyclobutyl $\gg$ β-methylallylcarbinyl. However this order is in striking contrast to that inferred from the products of the amine-nitrous acid reactions (vide supra), viz., 1-methylcyclobutyl $\gg$ 1-methylcyclopropylcarbinyl $\gg$ β-methylallylcarbinyl.

These apparent discrepancies and the problem of the significance of solvolytic reactivities will now be discussed. A general example is first considered where two chlorides

RCl and R'Cl, have different thermodynamic stabilities, this difference being ΔF (see fig. 21). The free energies of activation, to form the activated complexes RCl^* and $R'Cl^*$, are, respectively, ΔF^*_{RCl} and $\Delta F^*_{R'Cl}$. Intermediates R^+ and R'^+ (abbreviated as 1 and 2, respectively) are formed in the solvolysis of RCl and R'Cl. The assumption is now made that (1) the intermediate ions, R^+ and R'^+ (1 and 2) become equilibrated much faster than they react to give either product or starting material, or (2) that the two chlorides (RCl and R'Cl) solvolyze to give directly a common non-classical cationic intermediate. In the first case, i.e., equilibrium of classical cations, the energy difference is ΔF^*_{eq}. An example would be cyclopropylcarbinyl and cyclobutyl cations in equilibrium, or the non-classical 'tricyclobutonium' ion (CIX, fig. 14); either satisfies the C^{14} results. Second, it is assumed that the ratio of the free energies of activation of the ions R^+ and R'^+ (1 and 2) (ΔF^*_1 and ΔF^*_2) in the reverse reaction to form chloride, is practically the same as the ratio of the free energies for the reaction of the two ions to form the analogous alcohols. This assumption is supported by the nearly identical mixture of alcohols obtained in solvolysis of chlorides and in the amine-nitrous acid reactions of the structurally analogous amines.

It follows from these two assumptions, that the ratio of the products will be determined solely by the ratio of the rates of reaction of the two ions, which is given in

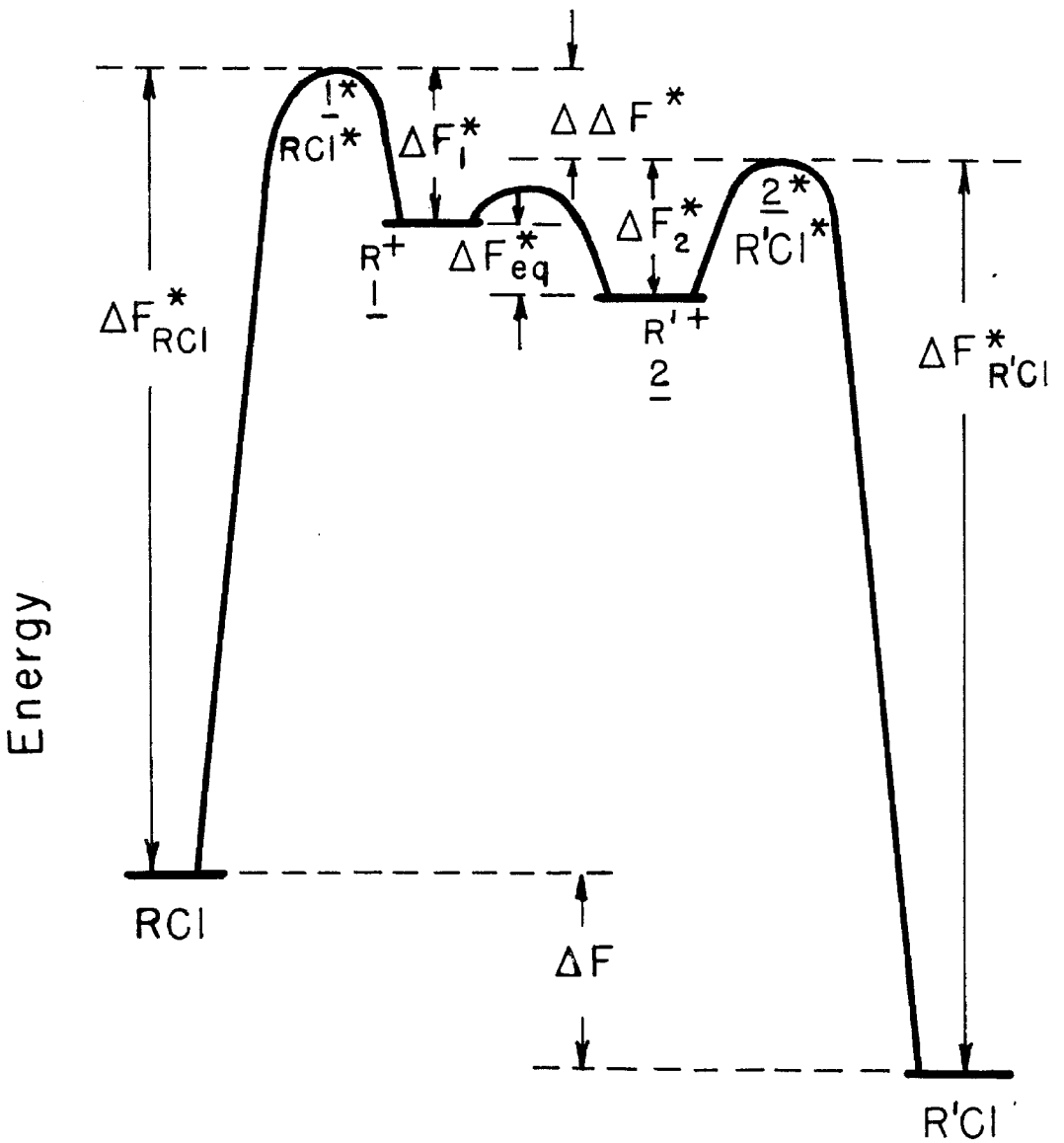

Energy
ΔF^*_{RCl}
$\overline{1}^*$
RCl^*
ΔF^*_1
$\Delta\Delta F^*$
$R^+_{\overline{1}}$
ΔF^*_{eq}
ΔF^*_2
$\overline{2}^*$
$R'Cl^*$
$R'^+_{\overline{2}}$
$\Delta F^*_{R'Cl}$
RCl
ΔF
R'Cl
Reaction Coordinate

Fig. 21

equation 1.

$$\frac{v_1}{v_2} = \frac{k_1[C_1]}{k_2[C_2]} \qquad (1)$$

From the equilibrium constant ($K = [C_1]/[C_2]$) for the interconversion of the two ions 1 and 2 (R^+ and R'^+), and the relation between free energy and equilibrium, it follows that

$$RT\ln\frac{C_1}{C_2} = -\Delta F^*_{eq.} \qquad (2)$$

where $-\Delta F^*_{eq} = RT\ln K$. The ratio of the rates of reaction of the two intermediates 1 and 2 to give product (or starting material) is obtained by combination of equation 1 and 2, to give 3.

$$\frac{v_1}{v_2} = \frac{k_1}{k_2}\, e^{-\Delta F^*_{eq}/RT} \qquad (3)$$

Combination of equation 3 with Eyring's expression for the rate constant (equation 4),

$$k_1 = \frac{RT}{Nh}\, e^{-\Delta F^*_1/RT} \qquad (4)$$

gives equation 5, for the ratio of rates, v_1/v_2.

$$\frac{v_1}{v_2} = e^{-(\Delta F^*_1 - \Delta F^*_2) - \Delta F^*_{eq}/RT} \qquad (5)$$

However, inspection of fig. 21, leads to equation 6,

$$\Delta F^*_{eq} = (\Delta F^*_2 + \Delta\Delta F^*) - \Delta F^*_1 \qquad (6)$$

where $\Delta\Delta F^*$ represents the energy difference between the transition states $\underline{1}^*$ and $\underline{2}^*$ (RCl^* and $R'Cl^*$). Combination of equations 5 and 6 gives equation 7, the ratio of the rates of reaction of the two cations.

$$\frac{v_1}{v_2} = e^{-\Delta\Delta F^*/RT} \qquad (7)$$

Thus the ratio of the rates of the reaction of the intermediates $\underline{1}$ and $\underline{2}$, and hence the ratio of the products, will be determined solely by the difference ($\Delta\Delta F^*$) in the energy of the two transition states ($\underline{1}^*$ and $\underline{2}^*$, or RCl^* and $R'Cl^*$). $\Delta\Delta F^*$ is, in turn, determined by two factors: (1) the free energies of activation (ΔF^*_{RCl} and $\Delta F^*_{R'Cl}$) of the two chlorides and (2) the relative thermodynamic stability of RCl and R'Cl, i.e., ΔF. The free energies of activation (ΔF^*_{RCl} and $\Delta F^*_{R'Cl}$) may be obtained from the solvolysis rate constants of the two chlorides, while ΔF may be determined from thermodynamic data (if available), or if ΔF is small, it may be estimated.

Thus solvolysis rates offer little information concerning carbonium ion stability (which is meaningless if a non-classical ion is the sole intermediate), but do give information about product ratios, provided data are available for corrections for the difference in thermodynamic stability of the starting

halides.

Since both cyclopropylcarbinyl and cyclobutyl chlorides give essentially equimolar amounts of cyclopropylcarbinol and cyclobutanol (ca. 48% each), it follows from the above argument that the energies of the two solvolysis transition states are approximately equal and $\Delta\Delta F^*$ (equation 7) is zero.

Inspection of fig. 21, gives equation 8.

$$\Delta F + \Delta F^*_{RCl} = \Delta\Delta F^* + \Delta F^*_{R'Cl} \qquad (8)$$

In the case just considered, $\Delta\Delta F^* = 0$, and the result is equation 9.

$$\Delta F = \Delta F^*_{RCl} - \Delta F^*_{R'Cl} \qquad (9)$$

Hence solvolysis rates of RCl and R'Cl will then reflect only the thermodynamic stability of the two halides. This includes such factors as strain energy and, to a smaller extent, H-H and H-X repulsions.

Roberts and Mazur[61] have pointed out that solvolytic reactivities of halides measure, at best, only the tendency toward partial ionization in the transition state and that carbonium ion stabilities may be safely inferred from solvolytic reactivities only if there is reasonable assurance that the substances being solvolyzed have rather similar thermodynamic stabilities. From the previous discussion the conclusion may

be reached that if an equilibrium of classical cationic intermediates is involved, then there is another requisite to the inference of carbonium ion stabilities from solvolytic reactivities; that is, the difference in energy of the two ions (ΔF^*_{eq}, which is a measure of the relative stability of the ions) must be equal to the difference in energy of the two transition states ($\Delta\Delta F^*$). This, in effect, requires equality of the free energies of activation of the two ions for the reverse reaction (i.e., $\Delta F^*_1 = \Delta F^*_2$).

If only a non-classical intermediate is involved in the solvolysis, then $\Delta F^*_{eq} = 0$, and combination of equations 6 and 8 gives equation 10.

$$\Delta F + (\Delta F^*_{RCl} - \Delta F^*_{R'Cl}) = \Delta F^*_1 - \Delta F^*_2 \qquad (10)$$

The term $\Delta F^*_{RCl} - \Delta F^*_{R'Cl}$ may be determined from the solvolysis rates of the two chlorides, and if ΔF can be estimated, then $\Delta F^*_1 - \Delta F^*_2$, which determines the product ratio, is available.

Let us try to apply these arguments to the solvolysis of 1-methylcyclopropylcarbinyl and 1-methylcyclobutyl chlorides. Unfortunately the available thermodynamic data are limited, but some crude calculations can be made. In this connection we shall see later that 1-methylcyclopropylcarbinyl chloride is thermodynamically less stable than 1-methylcyclobutyl chloride. The ratio of the solvolysis rates of cyclopropylcarbinyl chloride and cyclobutyl chloride is 26.5, or in terms of energy (Arrhenius equation), 2.1

kcal./mole. If it is assumed that the transition state energies of solvolysis of cyclopropylcarbinyl chloride and cyclobutyl chloride are equal (a reasonable supposition since roughly equal amounts of cyclopropylcarbinol and cyclobutanol are obtained as products), then the value for ΔF for cyclobutyl chloride is 2.1 kcal./mole (the value obtained kinetically). If this value of ΔF is also applicable to the energy difference between 1-methylcylopropylcarbinyl chloride and 1-methylcyclobutyl chloride, then by utilizing the ratio of the solvolysis rates of 1-methylcyclopropylcarbinyl and 1-methylcyclobutyl chlorides (9.7, or 1.5 kcal./mole = $\Delta F^*_{RCl} - \Delta F^*_{R'Cl}$), the value of $\Delta\Delta F^*$ becomes 0.6 kcal./mole (from equation 9). In terms of rate ratios this value is 2.7. In other words the predicted ratio of 1-methylcyclobutanol to 1-methylcyclopropylcarbinol is 2.7 (or 73% 1-methylcyclobutanol and 27% 1-methylcyclopropylcarbinol). This is far from the experimental observation of amine-nitrous acid reaction products, where no 1-methylcyclopropylcarbinol was detected ($2 \pm 2\%$). If our earlier assumptions are correct, then the ΔF for 1-methylcyclopropylcarbinyl and 1-methylcyclobutyl chlorides is larger than ΔF (= 2.1 kcal./mole) for cyclopropylcarbinyl and cyclobutyl chlorides. In this respect, it is noteworthy that a general characteristic of anionotropically related halides, is that the more thermodynamically stable of the two halides is the less reactive one.

Another approach to this problem may be made by assuming

that the maximum amount of 1-methylcyclopropylcarbinol in the reaction of 1-methylcyclopropylcarbinyl amine with nitrous acid is 4%. Thus (using the hypothesis of analogous product ratios in solvolyses and amine-nitrous acid reactions), the ratio of the reaction rates of the solvolysis intermediates is 24:1, or 1.9 kcal./mole ($\Delta\Delta F^{*}$). From this value and the experimental ratio of solvolysis rate constants for 1-methylcyclopropylcarbinyl and 1-methylcyclobutyl chlorides (9.7, or 1.5 kcal./mole), the value for ΔF becomes 3.4 kcal./mole.

Unfortunately no values of ΔF are available for methylcyclopropane and cyclobutane. Such data could be considered an approximation of the ΔF's for cyclopropylcarbinyl and cyclobutyl chlorides (and 1-methylcyclopropylcarbinyl and 1-methylcyclobutyl chlorides). Heats of combustion for cyclopropane and cyclobutane are available[182] and the difference between the heat of combustion of methylcyclopropane and cyclobutane may be roughly approximated as 1.4 kcal. Comparison of the difference in the heats of combustion with the expected value of ΔF (ca. 2.1 kcal./mole) gives an agreement which is likely fortuitous, since the entropy term has been neglected. Accurate measurements of thermodynamic constants for some of these compounds, e.g., methylcyclopropane and cyclobutane, would be useful in testing these concepts.

In the amine-nitrous acid reaction, two fundamentally different mechanisms may be hypothesized. First, if equili-

bration of individual cations is involved, then the ratio of carbinol products may be considered to reflect the carbonium ion stabilities, provided the activation energies for the reaction of the cations to form products are equal, or nearly so. Secondly, if only one intermediate is involved, the products are controlled by the rate of attack by solvent on the various carbon atoms of the intermediate, which in turn is governed (neglecting steric hindrance to solvent attack, i.e., F-strain) by the distribution of the positive charge.

The almost equal amounts of the two carbinols obtained in the reaction of cyclopropylcarbinyl and cyclobutylamines with nitrous acid and the solvolysis of cyclopropylcarbinyl and cyclobutyl chlorides, has been interpreted[62] as evidence favoring a single non-classical cationic intermediate. A rapid equilibrium of the two cations (cyclopropylcarbinyl and cyclobutyl) is not, however, ruled out as a possible mechanism unless it is accepted that cyclobutyl and cyclopropylcarbinyl halides solvolyze too rapidly to be accounted for by classical cations as intermediates. However, if a non-classical cation is the intermediate, then the observed products and the C^{14} results require that the positive charge be spread over all four carbon atoms.

In the amine-nitrous acid reaction of 1-methylcyclopropylcarbinylamine and 1-methylcyclobutylamine, an unusually stable symmetrical ion was not the important intermediate and evidence favored either an unsymmetrical non-classical ion or else the

classical 1-methylcyclobutyl cation, with the order of stability being 1-methylcyclobutyl >> 1-methylcyclopropylcarbinyl.

Classical carbonium ion theory predicts an overwhelming positive effect on the stabilities of cations when a methyl group is substituted at a secondary carbonium carbon compared to a β-methyl substituent in a primary carbonium ion, cf. the solvolysis rates in 50% ethanol at 25°: t-butyl bromide > s-butyl bromide by a factor of ~10^4 (No. 45 and 47), as against i-butyl bromide < n-propyl bromide by a factor of ~10 and neopentyl bromide < i-butyl bromide by a factor of ~10.[180] However 1-methylcyclobutyl chloride solvolyzes at 50° in 50% aqueous ethanol only ~10^2 times faster than cyclobutyl chloride. Rather convincing evidence has been presented which favors a non-classical cationic intermediate in the solvolysis of cyclobutyl chloride, hence comparison with 1-methylcyclobutyl chloride is perhaps unjustified.

At least two factors may be important in determining the solvolysis rate of 1-methylcyclobutyl chloride compared to t-butyl chloride. The first of these factors, I-strain (angle strain), has been considered by Brown[162] to be solely responsible for the low solvolysis rate of 1-methylcyclobutyl chloride with respect to t-butyl chloride. Another factor which may play an important role in the solvolysis of 1-methylcyclobutyl chloride, is steric inhibition to hyper-

conjugation, which may be defined as the lack of delocalization of neighboring sigma electrons with a vacant p-orbital of a carbonium carbon due to unfavorable orbital orientations. An example of where the above effect may be important is provided by the solvolysis of 7-chloronorbornane (7-chloro-[2,2,1]-bicycloheptane). This compound in 80% ethanol reacts ca. 10-100 times more slowly than cyclopentyl chloride.[184] A careful examination of models and rough calculations of angle distortions from normal, reveal that considerably less strain is involved in 7-chloronorbornane or the analogous cation than in corresponding 1-methylcyclobutyl derivatives. The relative inertness of 7-chloronorbornane in solvolysis suggests the possibility that 1-methylcyclobutyl chloride might be similarly (or indeed, because of greater strain, much more) unreactive if there were not some important compensating factor which could be participation of neighboring carbon and formation of a non-classical cation in the solvolysis transition state. In this view, the small rate ratio (13) of 1-methylcyclobutyl and t-butyl chlorides is considered to be the resultant of large opposing factors. In agreement with this idea it may be noted that a rough calculation of the I-strain involved in the formation of the 1-methylcyclobutyl cation from the chloride (using 17.5 cal./degree^2) leads to 8.6 kcal., which is a factor of 2×10^6 in the rate at 30°. This calculation may be in error for several reasons. First, the value chosen for the force constant (17.5 cal./degree^2) may

not be accurate. Second, the angle bending may be so great that the energy law for the harmonic oscillator breaks down. Another complicating factor is the possibility that the transition state may be less strained than the ion (on which the calculation was based). The distribution of the strain over all C—C—C angles has been taken into account in the above calculation. In any event, it is clear that the solvolysis product of 1-methylcyclobutyl chloride (1-methylcyclobutanol) together with the C^{14} results of the amine-nitrous reaction, surely requires that any non-classical cation in these reactions must be structurally rather similar to the classical 1-methylcyclobutyl cation. The best formulation seems to be structure CXVII (p. 81).

It is interesting that 1-methylcyclopropylcarbinyl chloride solvolyzes at 30° in 50% aqueous ethanol about 66 times faster than cyclopropylcarbinyl chloride, yet as mentioned previously the 1-methyl substituent is expected to decrease the rate by ~10 (cf. i-butyl and n-butyl). An explanation is found in the general theory of the effect of substituents on neighboring group participation. The standard driving force (L_o) of a β-substituent in the ethyl system may be calculated from the equation $L_o = RT \ln k_\Delta / k_c$, where k_Δ is the specific rate constant for the ionization involving neighboring group participation (to a bridged intermediate) and k_c is the specific rate constant for ionization without neighboring group participation (or nucleo-

philic solvent participation). In the case of cyclopropylcarbinyl halides, k_Δ has been assumed to be equal to k (the observed rate), since $k = k_\Delta + k_c$, and k_c is negligible in this case. The value of k_c has been taken as the rate constant for unimolecular solvolysis of i-butyl halides under the same conditions at which k was determined. (The ratio i-butyl/ethyl was taken as 0.08, the observed[183] value for the bromides in 50% aqueous ethanol at 95°). Thus from the rate constant for the solvolysis of cyclopropylcarbinyl bromide at 25° in 50% aqueous ethanol, the L_o value for the cyclopropylcarbinyl group (ethyl is standard) is 5.2 kcal. $mole^{-1}$. A similar value, 5.3 kcal. $mole^{-1}$ was obtained from the solvolysis rate constant of cyclopropylcarbinyl chloride in 50% aqueous ethanol at 50°. (The relative independence of L_o upon the leaving group has been noted).[13] A semi-empirical treatment of the dependence of rate of anchimerically-assisted ionization upon α- and β-methyl substitution has been presented by Winstein, et al.[78] The equation $RT \ln k/k_o = d_\alpha N_\alpha + d_\beta N_\beta$ (where k and k_o are the rate constants for methylated and unmethylated compounds) has been used successfully to correlate rate and substitution. The equation is based upon data for a large number of compounds, where the effect of methyl groups upon the rate is roughly additive. The constants d_β (we are not concerned with d_α) have been determined for a number of various compounds under a variety of conditions. The value of d_β chosen (1.75 kcal.

mole^{-1}) is the average of the values for $\underline{d}_{\beta}$ (1.74 and 1.79 kcal. mole^{-1}) for the neighboring groups p-methoxyphenyl and iodine. From the rate constant (0.45 hr.$^{-1}$) for solvolysis of cyclopropylcarbinyl chloride at 50° in 50% ethanol (No. 5), the corresponding rate constant for 1-methylcyclopropylcarbinyl chloride is calculated to be 7.1 hr.$^{-1}$, i.e., a 1-methyl substituent enhances the solvolysis rate of cyclopropylcarbinyl chloride by a factor of 15; the observed value is 50. The L_o value calculated from the data herein for the cyclopropylcarbinyl group is 5.2-5.3 kcal. mole^{-1}. A value of 9.0 has been reported[15] (possibly from i-cholesteryl derivatives) but this leads to a calculated rate constant for cyclopropylcarbinyl chloride of 130 hr.$^{-1}$ (observed, 0.45 hr.$^{-1}$). The reported[15] value for the cyclobutylcarbinyl group is only 4.5 kcal. mole^{-1}; however the value calculated from data in Table IV (No. 18 and 44) (i-butyl/ethyl = 0.08)[183] is 5.7 kcal. mole^{-1}, an L_o larger than that of the cyclopropylcarbinyl group. Direct comparison of the rate constants (No. 7 and 18) indicates that cyclobutylcarbinyl bromide solvolyzes in 60% ethanol at 75° about 3 times as fast as cyclopropylcarbinyl bromide. The accuracy of this number is somewhat uncertain, since the solvolysis rate constant for cyclopropylcarbinyl bromide at 75° in 60% ethanol was calculated from the value at 25° in 50% ethanol, using constants for t-butyl bromide (E_a and m)[83] (see Table IV). For example, using E_a and m values for neopentyl bromide,[83] a

factor of 1/3 is obtained, i.e., cyclopropylcarbinyl bromide solvolyzes faster than cyclobutylcarbinyl bromide, by a factor of 3. If an m value for n-butyl bromide[83] and E_a for ethyl bromide[181] are used, the calculated solvolysis constants for cyclopropylcarbinyl and cyclobutylcarbinyl bromide are approximately equal. Since, in general, allylic halides have Ea's more closely resembling those of t-alkyl, rather than primary or secondary halides,[83,155,181] then the original analogy (i.e., cyclopropylcarbinyl and t-butyl bromides) seems best. Nevertheless, the rate constants for cyclopropylcarbinyl bromide and cyclobutylcarbinyl bromide should not differ by more than a factor of 3-5 in either direction. The unexpected high reactivity of cyclobutylcarbinyl bromide indicates a rearrangement to the unusually stable cyclopentyl cation.

Internal return isomerization (vide supra)[60,61] as in the solvolysis of cyclopropylcarbinyl and cyclobutyl chlorides in 50% ethanol-50% water and acetic acid was also detected in the solvolysis of 1-methylcyclopropylcarbinyl chloride in 50% ethanol. In one experiment a mixture of chlorides was hydrolyzed at room temperature and the composition of both the starting material and recovered chloride mixture was determined by infrared analysis and kinetic methods. The various chlorides present and the % of each in the starting and recovered chloride mixture, respectively, are as follows: 1-methylcyclopropylcarbinyl chloride (35, 13), 1-methylcyclo-

butyl chloride (49, 65), β-methylallylcarbinyl chloride (3, 10) and unreactive chloride, including β-methylallylcarbinyl chloride, (20, 30). Close examination of these results clearly reveals significant increases in the % of 1-methylcyclobutyl chloride, β-methyallylcarbinyl chloride and total unreactive chloride, and a decrease in 1-methylcyclopropylcarbinyl chloride. The above numbers are each actually an average of several analytical determinations (from spectra and kinetics) and in each instance the change (on going from starting material to product) of a particular component is always in the direction reported above. Without additional evidence (such as increased internal return isomerization in various solvents, $C_2H_5OH < CH_3COOH < HCOOH$) the order of chloride stability may be taken as β-methylallylcarbinyl $\gg$ 1-methylcyclobutyl $>$ 1-methylcyclopropylcarbinyl. The results are not unexpected since the same order was observed with the unmethylated series and also since the solvolytic reactivities are in the reverse order.

Reversible Carbonium Ion Reactions

Initial studies of reversible reactions of 1-methylcyclopropylcarbinyl, 1-methylcyclobutyl and β-methylallylcarbinyl derivatives were unrewarding. Thus, treatment of 1-methylcyclobutyl chloride with an equimolar mixture of anhydrous zinc chloride and concentrated hydrochloric acid gave, as the only isolable product, 1,3-dichloro-3-methyl-

butane (isoprene dihydrochloride), which apparently arose by addition of hydrochloric acid to β-methylallylcarbinyl chloride. This irreversible removal of one of the three possible chlorides reveals little concerning the relative stability of 1-methylcyclopropylcarbinyl and 1-methylcyclobutyl chlorides although it is quite reasonable to assume that β-methylallylcarbinyl chloride is easily the most stable.[60,61] The action of Lucas reagent on 1-methylcyclopropylcarbinol was also unsuccessful and milder conditions for isomerization were sought. A mixture of the chlorides (obtained by chlorination of 1,1-dimethylcyclopropane, see above) was treated with concentrated hydrochloric acid at 0° for three minutes and the products analyzed. The % composition of each component in the starting material and product, respectively, are 1-methylcyclopropylcarbinyl chloride (36,35), 1-methylcyclobutyl chloride (24,49), β-methyallylcarbinyl chloride (19,3) and total unreactive (32,20). Similar results were observed in an experiment of longer duration. Removal of most of the β-methylallylcarbinyl chloride was not unexpected, especially since it is the highest boiling component; the combined % of 1-methylcyclopropylcarbinyl and 1-methylcyclobutyl chlorides correspondingly increases. The noteworthy feature is the change in the ratio of 1-methylcyclobutyl to 1-methylcyclopropylcarbinyl chloride from 0.7 to 1.4 in the starting material and final product, respectively; in an isomerization at 0-10°

for one hour, the corresponding ratios changed from 0.04 to 0.3. In summary, the decreasing thermodynamic stability of the chlorides (β-methylallylcarbinyl $\gg$ 1-methylcyclobutyl $>$ 1-methylcyclopropylcarbinyl) corresponds to increasing solvolytic reactivity (β-methylallylcarbinyl $\ll$ 1-methylcyclobutyl $<$ 1-methylcyclopropylcarbinyl).

Miscellany

A control experiment was desired in order to check the reliability of the method of degradation of 1-methylcyclobutanol-C^{14}. Cyclobutanone-C^{14} was attractive, since it is easily converted to 1-methylcyclobutanol. The synthesis of cyclobutanone-2-C^{14} via a Perkin ring closure was desirable, but involved too many steps; the synthetic method used was the well-known formation of cyclobutanone from ketene and diazomethane. N-Nitroso-N-methyl-C^{14}-urea, prepared from methyl-C^{14}-urea, was converted to diazomethane to which ketene was added.

At this point it was discovered that the planned experiments with this compound would have been of little value in revealing the amount of rearrangement, if any, in the degradation of 1-methycyclobutanol-C^{14}. Had cyclobutanone been available for conversion to 1-methylcyclobutanol-2-C^{14} and subsequent degradation, a rather large amount of rearrangement of C^{14} into the 3-position was possible (33 - 0 = 33%). However if the synthetic cyclobutanone-C^{14} were formed by an

attack of methylene radical on the intermediate cyclopropanone[185] to give the epoxide of methylenecyclopropane which then rearranged to cyclobutanone (the process may be concerted), then the resulting cyclobutanone-C^{14} should have 25% of the C^{14}-activity in the 3-position and 37.5% each in the 2- and 4-positions. An alternative mechanism has a neutral symmetrical intermediate (where the three methylenes are equivalent) formed by an attack of methylene on cyclopropanone; the result, of course, is equal activity (33.3%) in the 2-, 3- and 4-positions. Assuming the first case to hold (25% C^{14} in the 3-position) then the maximum amount of rearrangement during degradation which could be detected in the 1-methylcyclobutanol would be 3 x 0.026 x (33.3 - 25.0)% = 0.65% (2.6% is the actual observed activity in the 3-position of 1-methylcyclobutanol obtained in the reaction of 1-methylcyclopropylcarbinyl-C^{14}-amine with nitrous acid; this corresponds to 3 x 2.6 = 7.8% rearrangement). This value, 0.65%, is really the maximum possible % change in the activity of the 3-position during degradation. The experiments were discontinued at this point since the final results would have depended upon a difference between two large numbers, i.e., the 25% C^{14}-activity in the 3-position of the 1-methylcyclobutanol used, and the 25.0 + x% C^{14} activity observed in the proposed degradation; the maximum x is 0.65%. The combined experimental errors in the two rather large % activities would likely have been as large as 0.65%.

The C^{14}-distribution in the cyclobutanone-C^{14} (after reduction to cyclobutanol) was determined by White[151] by a method previously discussed (vide supra). The 3-position accounted for 30.9% of the total C^{14}-activity and the 2- and 4-positions, 35.7% each (total, 102.2%). Thus the C^{14}-activity in the 3-position is experimentally between the values predicted by the two mechanisms proposed for the formation of cyclobutanone from diazomethane and ketene. Noteworthy is the near equality of the % C^{14}-activities in the 3-position of the cyclobutanol-C^{14} derived (a) from cyclobutanone-C^{14} and (b) from the reaction of cyclopropylcarbinyl-C^{14}-amine with nitrous acid. It will be interesting to see if this result is real or inherent in the degradation scheme used by White. This can be tested experimentally by conversion of the cyclobutanone-C^{14} to 1-methylcyclobutanol-C^{14} followed by degradation using the scheme reported herein.

Of somewhat indirect interest was a recent note concerning the characteristic infrared absorption bands of the cyclopropane ring.[186] A total of 34 cyclopropane derivatives (including hydrocarbons, alcohols, ketones, chlorides and an ester) displayed strong absorption between 9.5 and 10.0 microns; of the 30 compounds with one substituent on the ring, all but two had maxima at 9.79 $\pm$ 0.04 microns. Infrared spectra taken of a number of cyclopropane compounds synthesized by J. D. Roberts and coworkers were available for such observa-

tions. Of 43 cyclopropane derivatives, all showed absorption in the 9.5 - 10.0 micron region, and of 20 compounds with one substituent on the ring, 12 possessed maxima in the 9.79 $\pm$ 0.04 micron region; 27 of the total (43) had absorption bands in this region. The derivatives included hydrocarbons, alcohols, chlorides, bromides, amines, ketones, acids, esters, nitriles, amides and an aldehyde, oxime and silyl ether.

III. EXPERIMENTAL

All melting points are corrected and were determined in a modified Hershberg apparatus using total immersion, N.B.S. calibrated thermometers; boiling points are not corrected. Analyses are by S. M. Nagy, Microchemical Laboratory, Massachusetts Institute of Technology and A. Elek, Elek Microanalytical Laboratories, Los Angeles, California.

1-Methylcyclopropanecarbonitrile.--The following experiments are illustrative of a number of preparations. Diazomethane.--To a mixture of 200 ml. of 50% potassium hydroxide and 500 ml. of ethyl ether cooled to 0° in an ice-salt bath, was added 68 g. (0.66 mole) of finely powdered N-nitroso-N-methylurea.[187] The ether layer was decanted and the aqueous layer swirled twice with two 50-ml. portions of ice-cold ether. The combined ether layers were dried over potassium hydroxide pellets for one hour at 0°, filtered, and made up to 610 ml. with anhydrous ether. A 10.00 ml. aliquot was slowly added to 1.748 g. (14.32 meq.) of benzoic acid[188] in 25 ml. of anhydrous ethyl ether at 0°. Ten milliliters of water were added and the solution warmed to remove the ether; titration of the residue required 32.94 ml. of 0.204 N sodium hydroxide (6.72 meq.). The yield of diazomethane was 0.456 mole (70%); a second preparation from 82 g. (0.79 mole) of N-nitroso-N-methylurea gave 0.519 mole (66%); the total,

0.98 mole (68%). 3-Methyl-3-cyano-1-pyrazoline.--To the ethereal solution of diazomethane (0.98 mole) in a 3-l. three-necked flask equipped with a stirrer, dropping funnel and condenser (calcium chloride tube) and immersed in an ice-salt bath, was added 67.1 g. (1.00 mole) of freshly distilled α-methacrylonitrile (courtesy of Shell Chemical Co., b.p. 90.0-90.3° at 759 mm., $n^{25}D$ 1.3982) over a period of one hour. After the yellow color of diazomethane disappeared (6-7 hours), the ether was removed in vacuo, leaving 110 g. (1.01 moles) of the pyrazoline, 102% from diazomethane. (The higher than theoretical yield is undoubtedly due to the ethanol impurity in the ether used. See also under the preparation of 1-methylcarbomethoxycyclopropane, below). Decomposition of 3-methyl-3-cyano-1-pyrazoline.--Cautious, intermittent heating of 10 g. quantitites with a free flame effected the decomposition of the pyrazoline (110 g., 1.01 moles) in a 100-ml. flask equipped with a spiral condenser and suitable attachments for measuring the nitrogen evolved by the displacement method. After decomposition in small quantities, the combined product was heated under gentle reflux for one hour. The yield of crude 1-methylcyclopropanecarbonitrile was 82.6 g. (1.01 moles), 97% calculated from the loss in weight during decomposition. The total amount of nitrogen evolved was 21 l. at 23° and 750 mm. or 18 l. at S.T.P. (82%). The crude product was dried over Drierite and distilled through a 7 x 440-mm., glass-spiral column giving 53.5 g.

(0.66 mole), b.p. 127.4-128.9° (758 mm.), $n^{25}D$ 1.4130-1.4137 (67% from diazomethane). The distillation products invariably contained some ethylenic nitriles (probably angelic and tiglic nitriles) which were removed by washing with dilute permanganate.[156] The physical properties for the purified material were b.p. 127.7-128.5° (765 mm.), $n^{25}D$ 1.4128; lit.[156] b.p. 127-127.5° (761.5 mm.), $n^{20}D$ 1.41407. The purified product did not decolorize permanganate after 10 minutes at 20°. The yield in the purification step was 54%. One preparation was carried out as described in the literature[156] using inverse addition (i.e., adding diazomethane to α-methacrylonitrile) with no significant change in the yield.

1-Methylcarbomethoxycyclopropane.--A modification of the procedure of Siegel and Bergstrom[189] was used. Diazomethane.--The procedure (above) was followed using 100 g. (0.97 mole) of N-nitroso-N-methylurea and anhydrous (ethanol-free) ethyl ether. 3-Methyl-3-carbomethoxy-1-pyrazoline.--To the filtered solution of diazomethane in a 2-l. one-necked flask was added 67.3 g. (0.67 mole) of freshly distilled methyl methacrylate (courtesy of Rohm and Haas Co., b.p. 100.0-100.4° at 756 mm., $n^{25}D$ 1.4126) in 65 ml. of anhydrous ether. After the yellow color had disappeared, the ether was removed, giving a 99% yield of pyrazoline. The above experiment was performed in two mole batches without difficulty. Decomposition of 3-methyl-3-carbomethoxyl-1-pyrazoline.--The

pyrazoline was smoothly decomposed in small quantities (as in the preparation of 1-methylcyclopropanecarbonitrile) giving 97% of crude 1-methycarbomethoxycyclopropane. Distillation of 520 g. of the crude pyrazoline decomposition product through a 11 x 1200-mm. column packed with glass helices over a period of ten days at ca. 760 mm. gave the following fractions: (1-8) 71 g., b.p. 75.0-122.1° (mostly azeotrope),[189] $n^{25}D$ 1.3680-1.4168; (9-23) 316 g., b.p. 122.3-124.3° $n^{25}D$ 1.4180-1.4211; (24-28) 69 g., b.p. 124.3-138.2°, $n^{25}D$ 1.4224-1.4320; (29-31) 29 g., b.p. 138.3-139.3°, $n^{25}D$ 1.4330-1.4336 (methyl tiglate).[189] The yield of fractions 9-23 was 60%. Fractions 9-23 all decolorized permanganate (possibly due to methyl angelate, i.e., methyl cis-α-methyl-β-methylacrylate) and further purification was necessary. A large batch (310 g.) of 1-methylcarbomethoxycyclopropane (from the above distillation), 500 ml. of petroleum ether (35-60°) and 20 ml. of sodium carbonate were cooled to 0° and washed in a separatory funnel with 0.25 M sodium permanganate solution until the violet color persisted. Chipped ice was added at intervals to keep the temperature at 0°. Approximately 1.2 l. of the permanganate solution was required. The petroleum ether layer was separated and the aqueous layer extracted three times with 300 ml. of petroleum ether and the combined layers dried over Drierite. After removal of the petroleum ether in vacuo, the residue was dis-

tilled through a 11 x 1200-mm. column packed with glass helices giving 186 g. (60%) of product (five fractions), b.p. 55.9-57.1° (60.4-65.6 mm.), $n^{25}D$ 1.4192-1.4193; lit. (1)[189] b.p. 124.5-126.0° (760 mm.), $n^{25}D$ 1.4208, (2)[190] b.p. 121-123°. The product did not decolorize permanganate even at 25° in five minutes.

An attempt to prepare 3-methyl-3-carbomethoxy-1-pyrazoline by adding N-nitroso-N-methylurea to a stirred solution at 0° of methyl methacrylate in ether over 50% potassium hydroxide was unsuccessful (19%). Apparently the concentrated alkali decomposed the pyrazoline and saponified the ester group.

1-Methylcyclopropanecarboxylic Acid.--Hydrolysis of 1-methylcarbomethoxycyclopropane gave a 90% yield of 1-methylcyclopropanecarboxylic acid, b.p. 107.8-108.9°(34.4-36.4 mm.), 111.0-112.0° (40.0-41.5 mm.), micro b.p.[191] (759 mm.), 188.7°, m.p. 32.4-34.3°, $n^{25}D$ 1.4363-1.4364; lit. (1)[189] m.p. 29.5-32.0°, (2)[190] m.p. 29-31°.

The p-bromophenacyl ester after two recrystallizations from 50% aqueous ethanol gave white leaflets, m.p. 64.1-65.0°, lit.[189] 59-60°.

Anal. Calcd. for $C_{13}H_{13}O_3Br$: C, 52.52; H, 4.41; Br, 26.89. Found: C, 52.65; H, 4.57; Br, 26.59.

The anilide was prepared and recrystallized four times from 50% ethanol as white crystals, m.p. 100.5-101.6°.

Anal. Calcd. for $C_{11}H_{13}NO$: C, 75.40; H, 7.48; N, 8.00. Found: C, 75.37; H, 7.32; N, 7.89.

1-Methylcyclopropanecarboxamide.--The procedure of Wieland,[168] Boissonnas,[169] and Roberts, Moreland and Frazer[164] was followed. A solution of 1.19 g. (0.0119 mole) of 1-methylcyclopropanecarboxylic acid, 1.20 g. (0.0119 mole) of triethylamine and 56 ml. of chloroform were cooled in an ice-salt bath, 1.29 g. (0.0119 mole) of ethyl chloroformate added rapidly with vigorous stirring, and anhydrous ammonia passed in for ten minutes. The reaction mixture was stirred for thirty minutes at room temperature, and the white suspension was filtered and washed twice with small portions of chloroform. The solution was evaporated nearly to dryness and the remainder of the chloroform removed by the aspirator. The slightly colored residue was dissolved in 12 ml. of hot benzene, filtered and 35 ml. of boiling petroleum ether (60-70°) added; the amide separated almost immediately, as white glistening plates, 0.856 g. (0.0086 mole), 72%, m.p. 140-144°. A small sample was recrystallized three times from benzene-cyclohexane (5:1), m.p. 145.7-146.9°.

Anal. Calcd. for C_5H_9ON: C, 60.58; H, 9.15; N, 14.13. Found: C, 59.74, H, 9.10; N, 14.31.

An attempt to prepare the amide by heating a solution of 1-methylcarbomethoxycyclopropane in 90% methanol saturated with ammonia in a pressure bottle led to ca. 10% of product.

1,1-Dimethylcyclopropane.--Isobutyraldehyde was converted to 2,2-dimethyl-1,3-propanediol by the action of potassium hydroxide and 36-38% aqueous formaldehyde in 95% ethanol (84%).[157,158] This diol became commercially available (Tennessee Eastman) during the later stages of the investigation. Conversion to the dibromide was effected with commercial phosphorous tribromide (39%) or thionyl bromide[192] in pyridine (54%). The necessity of preparing the thionyl bromide and the difficulty in decomposing the sulfite ester rendered this procedure more tedious than the phosphorous tribromide method. Ring closure of the dibromide was carried out by the method of Shortridge, Craig, Greenlee, Derfer and Boord,[158] b.p. 19.0-20.0° (738 mm.); lit. (1)[157] 19.9° and (2)[158] 20.63° (760 mm.).

Methylenecyclobutane.--The general method used has been described elsewhere.[137] Pentaerythrityl tetrabromide was prepared from pentaerythritol by the action of phosphorous tribromide[137] (90%) and thionyl bromide[192] (30%) and *via* the tetrabenzenesulfonate followed by the action of sodium bromide in acetone (62%).[193] The phosphorous tribromide procedure, which gave a crude, orange product, is the preferred method, but the path through pentaerythrityl tetrabenzenesulfonate leads to a purer product, m.p. 158.6-159.7°, lit.[193] 156.5-158°. About four kilograms of the crude tetrabromide was converted to methylenecyclobutane in the usual fashion[137] in an average yield of 73%. Distillation of 418 g. of the

hydrocarbon mixture gave, after early fractions, 266 g. of methylenecyclobutane, b.p. 41.0-42.0° (739 mm.) (64%), lit.[192] b.p. 41.3° (746 mm.).

Cyclobutanone.--The synthesis of cyclobutanone from methylenecyclobutane has been described.[137] Cleavage of 1-hydroxymethyl-1-cyclobutanol was effected with lead tetraacetate[137] and phenyl iodosoacetate. In the latter procedure, 1-hydroxymethyl-1-cyclobutanol (8.4 g., 0.082 mole) and 50 ml. of methylene chloride in a 200-ml. three-necked flask fitted with a stirrer, condenser and dropping funnel, were treated with a solution of phenyl iodosoacetate[195] (35 g., 0.11 mole) in 110 ml. of methylene chloride, added dropwise so as to maintain gentle reflux. The solution was refluxed an additional hour, 25 ml. of water was added and the methylene chloride separated. The aqueous solution was cooled to 0°, made basic with 50% potassium hydroxide, and about 40 ml. of steam distillate collected. Half the methylene chloride was used to extract the steam distillate, followed by an additional extraction with 10 ml. of methylene chloride. The residue remaining from the steam distillate was extracted with the second half of the methylene chloride, the combined extracts filtered and dried over Drierite. The yield of cyclobutanone, b.p. 96-99° (765 mm.), was 3.9 g. (0.055 mole, 67%).

1-Methylcyclopropylcarbinol.--A published procedure[189]

was used for the lithium aluminum hydride reduction of 1-methylcarbomethoxycyclopropane. The product, 1-methylcyclopropylcarbinol, had b.p. 125.8-126.3° (739 mm.), $n^{25}D$ 1.4290-1.4292 (63%); lit.[189] b.p. 124.5-128.0° (760 mm.), $n^{20}D$ 1.4308 (56%). The infrared spectrum is given in fig. 24, APPENDIX.

The phenylurethan was prepared and recrystallized twice from petroleum ether (35-60°) as white needles, m.p. 78.8-79.8°.

Anal. Calcd. for $C_{12}H_{15}O_2N$: C, 70.21; H, 7.36; N, 6.82. Found: C, 70.58; H, 7.06; N, 6.56.

The 3,5-dinitrobenzoate was prepared by the pyridine method. (1) Recrystallization of a portion of this sample three times from ethanol gave light yellow needles, m.p. 98.2-100.6°, lit.[189] 85.5-85.7°.

Anal. Calcd. for $C_{12}H_{12}O_6N_2$: C, 51.43; H, 4.32; N, 10.00. Found: C, 52.52; H, 4.89; N, 9.63.

(2) Recrystallization of the remaining portion of the 3,5-dinitrobenzoate from benzenecyclohexane (1:2) gave light yellow needles, m.p. 88.9-90.7°.

Anal. Calcd. for $C_{12}H_{12}O_6N_2$: C, 51.43; H, 4.32; N, 10.00. Found: C, 51.08; H, 4.39; N, 9.96.

Starting from a bath temperature of 80° gave a mixed m.p. for the samples from ethanol and benzene-cyclohexane of 90.6-101.2°. The melt was cooled from 110° and solidifica-

tion occurred anywhere from 98 to 68°; heating again gave a m.p. of 99.0-101.5°. Siegel[189] has reported a m.p. of 85.5-85.7° (from ethanol) and later[196] a m.p. of 84-85° (from ethanol), with a slight hazy cast remaining until about 96-98° (a similar observation was made in this work); recrystallization from cyclohexane gave a m.p. of 84-85°, and did not change after solidification and remelting. A sample of this ester (from cyclohexane) obtained from Siegel gave a m.p. of 88.8-90.7°. A mixed m.p. of Siegel's sample (from cyclohexane) with the one obtained in this work (from cyclohexane) gave a m.p. of 89.8-93.2° which did not change after cooling and remelting. The sample of the ester (from ethanol) reported herein is probably impure (see analysis).

1-Methylcyclobutanol. A. From Methylenecyclobutane.--The method of Fischer[197] was followed. A 2-l. three-necked flask with pressure-equalized dropping funnel, stirrer and Dry Ice condenser was immersed in an ice-salt bath and 132 g. of ice and 264 g. of concentrated sulfuric acid added. The solution was kept below 0° and 68.0 g. (1.00 mole) of methylenecyclobutane was added slowly over a period of one and a half hours. After one-half hour of stirring at 0°, the solution was made alkaline by the slow addition of 5 N sodium hydroxide solution, keeping the solution below 10°. The resulting solution was continuously extracted with ethanol-free ethyl ether for 48 hours, dried over magnesium sulfate, filtered and distilled giving 58.5 g. (0.68 mole, 68%), b.p.

117.8-118.3° (746 mm.), $n^{25}D$ 1.4332-1.4336; lit. (1)[160] b.p. 117.5-118.5° (755 mm.), $n^{22}D$ 1.4315; (2)[161,197] b.p. 115-118° (747 mm.), $n^{24}D$ 1.4333 (63%); (3)[159] b.p. 114-117°, $n^{25}D$ 1.4329; and (4)[162] b.p. 116-118° (742 mm.), $n^{25}D$ 1.4333. See APPENDIX, fig. 24, for the infrared spectrum. B. From 1-Methylcyclobutyl Chloride.--The hydrolysis procedure of Brown and Borkowski[162] gave a 40% yield of alcohol, b.p. 117.1-118.9° (756 mm.), $n^{25}D$ 1.4329. The infrared spectrum of the product was identical with the spectrum obtained in A. C. From Cyclobutanone.--Cyclobutanone (1.8 g., 0.026 mole) in 10 ml. of anhydrous ethyl ether was added slowly to methylmagnesium iodide (prepared from 1.2 g. (0.05 mole) of magnesium turnings, 3.1 ml. (0.05 mole) of methyl iodide and 20 ml. of anhydrous ethyl ether) at a rate so as to maintain gentle reflux. The mixture was refluxed one-half hour longer, then decomposed with ice and ammonium chloride. The aqueous layer was saturated with sodium carbonate and extracted twice with 10 ml. of ether. The combined extracts were dried (magnesium sulfate), the ether removed in vacuo and the product distilled giving 1.4 g. (0.016 mole, 67%), b.p. 110.8-113.9° (766 mm.), micro b.p.[191] 118.3° (765 mm.), $n^{25}D$ 1.4332. The infrared spectrum was identical to those in A and B (above).

The N-phenylcarbamates of the above samples were prepared and recrystallized from petroleum ether:

Sample	Starting material	M.p. of N-phenylcarbamate[a]	Mixed m.p.
A	Methylenecyclobutane	138.5-139.5°	138.6-140.2°
B	1-Methylcyclobutyl chloride	138.3-139.2°	138.4-139.4°
C[b]	Cyclobutanone	138.6-139.5°	

[a]Lit.[160] 139.1°. [b]Anal. Calcd. for $C_{12}H_{15}NO_2$: C, 70.19; H, 7.36; N, 6.82. Found: C, 70.08; H, 7.35; N, 7.00.

β-Methyallylcarbinol. A.--A 5-l. three-necked flask, fitted with a high speed (Morton) stirrer, a 50-cm. spiral condenser and a dropping funnel, was immersed in an ice-salt bath. The stirrer shaft, modified to form a Hershberg stirrer, was driven by a ¼-h.p., 10,000-r.p.m. 'Lightnin' motor. The top of the condenser was stoppered and a small positive pressure of nitrogen was maintained through inlets in the stirrer housing and the dropping funnel. The apparatus was thoroughly dried before assembly. Ninety-six grams (4.0 moles) of magnesium turnings (previously dried at 85° for one hour) and 1500 ml. of anhydrous ethyl ether were added and extremely vigorous stirring was started. A 1.00 M solution of β-methylallyl chloride in ether (1000 ml., total) was added at a rate of approximately 2 ml. per minute. At the end of each 250 ml. portion added, the amount of Grignard reagent was determined by titration.[198] The theoretical and experimental amounts in moles were 0.25, 0.23; 0.50, 0.41; 0.75, 0.60 and 1.00, 0.74. One-half hour after the addition, the stopper in the condenser

was replaced with a drying tube and the dropping funnel replaced with a pyrex tube (12 mm. inside diameter) which was placed about 3 cm. above the surface of the liquid. This tube led from a 500-ml. round-bottomed flask containing 50 g. (1.67 moles) of paraformaldehyde, previously dried for three days over phosphorous pentoxide in a vacuum desiccator. The paraformaldehyde was decomposed by an oil bath at 180-200°, the gaseous formaldehyde formed being carried over by a slow stream of nitrogen. This reaction required about one hour and the inlet tube had to be cleared of paraformaldehyde several times. After stirring for one-half hour, the reaction mixture was poured onto a mixture of 1000 g. of ice and 250 g. of ammonium chloride. The ether layer was separated and the aqueous layer saturated with potassium carbonate and extracted three times with 200-ml. portions of ether. The combined ether layers were dried over anhydrous magnesium sulfate, filtered and the ether removed in vacuo. The crude product was dried (Drierite) and distilled through a 7 x 440-mm. glass-spiral column giving five fractions, 24.6 g. (0.286 mole), b.p. 124.0-127.3° (750 mm.), $n^{24.2}D$ 1.4289-1.4292; lit.[199] b.p. 126-130°. The yield from the Grignard reagent was 39%; from β-methylallyl chloride, 29%. Redistillation through the same column gave b.p. 124.3-127.2° (763 mm.), $n^{25}D$ 1.4312. See APPENDIX, fig. 24, for the infrared spectrum.

An α-naphthylurethan was prepared and recrystallized twice from petroleum ether as white needles, m.p. 66.7-67.3°.

Anal. Calcd. for $C_{16}H_{17}NO_2$: C, 75.28; H, 6.71; N, 5.49. Found: C, 75.26; H, 6.81; N, 5.23.

In earlier experiments, predominantly coupling product, 2,5-dimethyl-1,5-hexadiene, was obtained, b.p. 114.9-115.3° (758 mm.), $n^{25}D$ 1.4275 (22%); lit.[200] b.p. 114.3°, $n^{20}D$ 1.4293.

B.--The method of Kharasch and Fuchs[163] for the preparation of allylcarbinol was applied to the synthesis of β-methylallylcarbinol; in this procedure a rather slow addition of the chloride is used to give a concentrated slurry of the Grignard reagent. The yield from β-methylallyl chloride was 35%, b.p. 127.9-130.4° (six fractions) (741 mm.), $n^{25}D$ 1.4305-1.4312.

α-Methyl-β-methylallyl Alcohol (3-Methyl-3-butene-2-ol).--To 16 g. (0.67 mole) of magnesium and 300 ml. of anhydrous ethyl ether in a 1-l. three-necked flask with stirrer, dropping funnel and condenser with drying tube, was added 71 g. (0.50 mole) of methyl iodide at a rate so as to maintain gentle reflux. After one hour, a solution of α-methacrolein (35 g., 0.50 mole) in 50 ml. of ether was added at gentle reflux. The solution was refluxed 30 minutes, then poured onto 150 g. of ammonium chloride and 200 g. of ice, and after the solution stood overnight it was filtered, the ether layer separated and the aqueous layer extracted with

two 100-ml. portions of ethyl ether. The ethereal layers were dried, the ether was removed through a packed column and the residue was dried over Drierite. Distillation through a Holzman[201] column gave five fractions, 6.95 g. (0.081 mole), 16%, b.p. 54.6-56.8° (59.9-60.4 mm.), $\underline{n}^{25}D$ 1.4241-1.4242; lit. (1)[202] b.p. 115-118°, (2)[203] b.p. 117-118° and (3)[204] b.p. 112-113°, $\underline{n}^{21}D$ 1.4296. See APPENDIX, fig. 24, for the infrared spectrum of the middle fraction.

β-Methyl-γ-methylallyl Alcohol (2-Methyl-2-butene-1-ol). Methyl Tiglate.--The product previously reported, i.e., the high boiling portions of the decomposition of 3-methyl-3-carbomethoxy-1-pyrazoline, was redistilled, b.p. 136.9-137.1° (740 mm.), $\underline{n}^{25}D$ 1.4338; lit.[189] b.p. 138.0-139.2°, $\underline{n}^{25}D$ 1.4338. Reduction of Methyl Tiglate.--In a 500-ml. three-necked flask with stirrer, condenser and dropping funnel were placed 250 ml. of anhydrous ethyl ether and 6.82 g. (0.180 mole) of lithium aluminum hydride. The slurry was stirred and cooled while a solution of 32.7 g. (0.286 mole) of methyl tiglate in 50 ml. of ether was added dropwise over a period of 45 minutes. After an additional hour of stirring at room temperature, the excess lithium aluminum hydride was decomposed with water and the slurry filtered. The filtrate and washings were dried overnight over anhydrous magnesium sulfate and the ether was removed through a packed column. Distillation from an 8 x 600-mm.

Podbielniak column at 739 mm. gave a 2.1 g. forerun, b.p. 60-135°; three fractions, 2.4 g., b.p. 135-137.7°, $n^{25}D$ 1.4345-1.4380; and six fractions, 11.5 g., b.p. 137.6-137.9°, $n^{25}D$ 1.4386-1.4401; lit. b.p. 136-137° [202] and 138.0°.[203] An infrared spectrum of a middle fraction with b.p. 137.7-137.9°, $n^{25}D$ 1.4398, is given in fig. 24, APPENDIX. The yield of the last six fractions was 40%.

1-Methylcyclopropylcarbinyl Acetate.--In a 200-ml. three-neck flask with a stirrer, dropping funnel and condenser (drying tube) was placed 2.6 g. (0.11 mole) of sodium hydride and 100 ml. of anhydrous ethyl ether. The slurry was stirred while 8.61 g. (0.100 mole) of 1-methylcyclopropylcarbinol in 10 ml. of anhydrous ethyl ether was added during fifteen minutes. After the initial reaction subsided, the mixture was stirred under reflux for three hours. A solution of 8.46 g. (0.108 mole) of acetyl chloride in 10 ml. of ether was added so as to maintain gentle reflux. After three more hours at reflux, 3 ml. of water, 4 ml. of 20% sodium hydroxide and 14 ml. of water were added successively. The solution was filtered and the residue washed with two 20-ml. portions of ether. The combined ether solutions were dried over anhydrous magnesium sulfate and the ether removed through a packed column. Distillation through a Holzman[201] column gave five fractions: (1) 2.38 g., b.p. 59.8-60.6° (40 mm.), $n^{25}D$ 1.4122; (2-3) 2.89 g., b.p. 60.6-60.8° (40 mm.), $n^{25}D$

1.4131; and (4-5) 5.83 g., b.p. 60.7-61.0° (40 mm.), $n^{25}D$ 1.4137-1.4139. The total yield was 11.1 g. (0.086 mole), 86%.

1-Methylcyclobutyl Acetate.--The Organic Synthesis[205] procedure for the preparation of t-butyl acetate was followed using 12.9 g. (0.150 mole) of 1-methylcyclobutanol, 20.2 g. (0.167 mole) of dimethylaniline, 12.4 g. (0.158 mole) of acetyl chloride, and 20 ml. of ethyl ether. The yield of product, b.p. 54.5-54.9° (40 mm.), $n^{25}D$ 1.4160-1.4162 (five fractions), was 14.7 g. (0.115 mole, 77%).

1-Methylcyclobutyl Chloride.--Hydrogen chloride was added to methylenecyclobutane by the procedure of Brown and Borkowski.[162] The yield of product, b.p. 90.8-91.3° (742 mm.), $n^{25}D$ 1.4283-1.4287, was 81%; lit. (1)[162] b.p. 89.5-91.4° (744 mm.), $n^{20}D$ 1.4310 (89%) and (2)[161] b.p. 90-91° (745 mm.), $n^{25}D$ 1.4288, $n^{20}D$ 1.4311 (80% from concentrated hydrochloric acid and methylenecyclobutane). For the infrared spectrum of 1-methylcyclobutyl chloride, see fig. 23, APPENDIX.

β-Methylallylcarbinyl Chloride.--In a 100-ml. flask with a dident holding a dropping funnel and drying tube was placed 8.61 g. (0.10 mole) of β-methylallylcarbinol, 25 ml. of anhydrous ethyl ether and 18.5 g. (0.10 mole) of tri-n-butylamine. The solution was stirred magnetically at 0° while 11.9 g. (0.10 mole) of thionyl chloride was added dropwise over three hours. The product was washed with water, 5% sodium hydroxide and water again, dried (Drierite) and the ether re-

moved through a packed column. Distillation through a Holzman[201] column gave five fractions: the middle three, 4.99 g. (0.048 mole, 48%), had b.p. 101.0-102.7° (739 mm.), 42.3-42.5° (80.7 mm.), $n^{25}D$ 1.4301-1.4305. An infrared spectrum of the middle fraction is shown in fig. 23, see the APPENDIX. A second experiment gave a 53% yield.

Anal. Calcd. for C_5H_9Cl: C, 57.42; H, 8.68. Found: C, 57.32; H, 8.84.

The procedure of Roberts and Mazur[61] for the synthesis of allylcarbinyl chloride (i.e., addition of thionyl chloride to allylcarbinol in pyridine) failed with β-methylallylcarbinol. The product, which had a b.p. of 141.5-143.9° (747 mm.), 45.1-45.2° (16.7-17.5 mm.), $n^{25}D$ 1.4439, gave a positive test for halogen (sodium fusion and Beilstein test) and ethanolic silver nitrate (immediate), and reacted slowly with permanganate.

Anal. Calcd. for $C_5H_{10}Cl_2$: C, 42.58, H, 7.15. Found: C, 42.66; H, 7.15.

The above data are consistent with 1,3-dichloro-3-methylbutane (isoprene dihydrochloride); lit. (1)[206] b.p. 145-146°, 52-53° (12 mm.), (2)[207] b.p. 142°, and (3)[208] b.p. 144-148°, 34-40°, (10-12 mm.), $n^{20}D$ 1.44549.

1-Methylcyclopropylcarbinyl Chloride. Chlorination of 1,1-Dimethylcyclopropane.--The apparatus and procedure described by Roberts and Mazur[61] were used. Two photoflood

lamps and a high-vacuum mercury lamp were the light sources. The flow of chlorine was controlled by a flow meter (hexachlorobutadiene) which was calibrated by displacement of water saturated with sodium chloride and chlorine (a plot of log of the flow rate versus log of the difference in height of the levels on the flow meter gave a straight line). 1,1-Dimethylcyclopropane (74.5 g., 1.06 moles) was chlorinated at an average flow rate of 2.93 l. of chlorine per hour. The time of the reaction was 9.0 hours, and the volume of chlorine used corresponded to 1.00 mole (96%) at S.T.P. The head temperature remained at 20-21° until the end of the reaction, when it rose rapidly; the pot temperature rose steadily from 20 to 92° during the reaction.

The product, 113.2 g. (1.08 moles) was rapidly distilled from a modified Claisen flask, the clear product, b.p. 80-102°, being collected, 102 g. (0.97 mole, 92%). The monochlorination product was dried over Drierite, then carefully fractionated through a 12 x 500-mm. column packed with glass helices, at 735 mm., reflux ratio, 40:1, 27 fractions. A distillation temperature versus weight of distillate plot is given in fig. 22. The best values for the liquid corresponding to the plateau of the distillation curve (later shown to be rich in 1-methylcyclopropylcarbinyl chloride) were b.p. 83.0-83.9° (735 mm.), $\underline{n}^{25}D$ 1.4045-1.4052. The spectra of three fractions of the distillation are shown in fig. 23; these will be interpreted later. All even numbered frac-

Distillation of the Chlorination Product of 1,1-Dimethylcyclopropane.

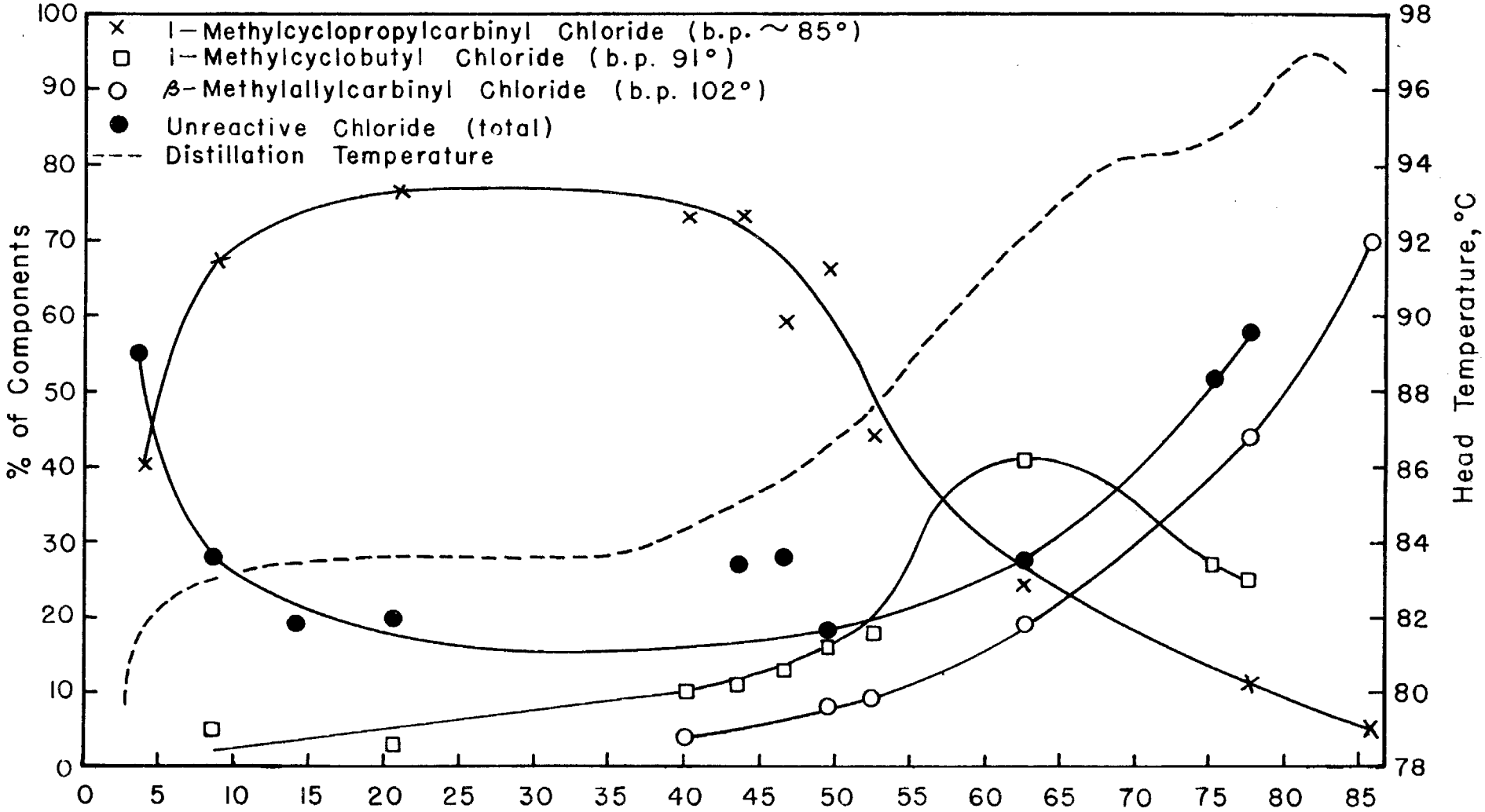


Fig.22

tions decolorized permanganate and bromine in carbon tetrachloride and gave positive silver nitrate tests. Fractions 4-10 (26 g., b.p. 82-84°), corresponding to the level portion of the distillation curve, were combined, dried (Drierite) and redistilled through the same column. Throughout the distillation, large volumes of vapors (including hydrogen chloride) were continually evolved. Apparently some decomposition occurred (this observation was not noted in the first distillation) which due to the partial pressure of hydrogen chloride, lowered the distillation temperature to 72-73°; the indices of refraction were also somewhat lower than those of the starting material. A middle fraction of this redistillation gave a micro b.p.[191] of 85.4°. Analysis of the Chlorination Product. A. β-Methylallylcarbinyl Chloride.--Analysis of the infrared spectra of mixtures of chlorides of known composition and comparison with the spectrum of authentic β-methylallylcarbinyl chloride, led to reliable values for the % β-methylallylcarbinyl chloride in the mixtures. The method was then applied to a number of fractions of the chlorination product. For results, see fig. 22. B. Reactive and Unreactive Chloride.--The % reactive chloride in a given fraction was the amount which solvolyzed in 50% aqueous ethanol at 50° in 30 or more minutes, i.e., at least 10 half-lives of 1-methylcyclobutyl chloride, which corresponds to approximately 100 half-lives of 1-methyl-

cyclopropylcarbinyl chloride, vide infra. The % unreactive chloride is (100 - % reactive chloride). This quantity (% unreactive chloride) was consistently greater than the % β-methylallylcarbinyl chloride (see fig. 22). C. 1-Methylcyclobutyl Chloride. (1) Kinetic Method.--The proportion of 1-methylcyclobutyl chloride (and hence 1-methylcyclopropylcarbinyl chloride) in the reactive chloride of a given fraction was determined by analysis of the rate curve (solvolysis in 50% ethanol at 30 and 50°) for that fraction. Three techniques were used: (a) Curve Fitting. From the rate constants of 1-methylcyclobutyl chloride and 1-methylcyclopropylcarbinyl chloride (vide infra) and the total % of reactive chloride, a series of rate curves may be calculated for varying ratios of 1-methylcyclopropylcarbinyl and 1-methylcyclobutyl chlorides and the best curve chosen by inspection. (b) Intercept Method. The analytical method of Brown and Fletcher[209] could be applied to the rate curves of a few fractions where the total % of 1-methylcyclobutyl chloride was ca. 15% or more. (c) Time Method. Using the rate constants at 30° for 1-methylcyclobutyl chloride and 1-methylcyclopropylcarbinyl chloride, the time of 0.83 hours was found to give the values 0.19 and 0.88 for the fraction of 1-methylcyclobutyl and 1-methylcyclopropylcarbinyl chloride, respectively, reacted in 0.83 hours. A crude estimate of the amount of the two components may thus be made by assuming that all the chloride which reacts in the

first 0.83 hours is 1-methylcyclopropylcarbinyl chloride, the remainder of the reactive chloride being 1-methylcyclobutyl chloride. (2) Infrared Spectra. The approximate % of 1-methylcyclobutyl chloride was determined by analysis of the infrared spectra of various fractions in the 14.40 micron region and comparing with the spectrum of authentic 1-methylcyclobutyl chloride. Other bands of doubtful value are 13.15, 8.02 and 7.88 microns. The % 1-methylcyclobutyl chloride in the chlorination mixture determined by a combination of the above methods is shown graphically in fig. 22.

D. 1-Methylcyclopropylcarbinyl Chloride.--(1) The methods used to determine 1-methylcyclobutyl chloride (kinetic method), also led to the % of 1-methylcyclopropylcarbinyl chloride in the reactive chloride, the % reactive chloride in the mixture, and hence, the % of 1-methylcyclopropylcarbinyl chloride in the mixture. (2) By assuming that the amount of 1-methylcyclopropylcarbinyl chloride, determined by the kinetic method in fractions richest in this component, was correct, the absorption for 100% 1-methylcyclopropylcarbinyl chloride in the infrared region was calculated using Beer's law. The best bands for this purpose were at 8.38 and 9.41 microns. The % of 1-methylcyclopropylcarbinyl chloride in other fractions could then be determined. For results, see fig. 22.

Graphical analysis (addition of areas) of fig. 22 leads to the following composition of the total chlorination mixture:

1-methylcyclopropylcarbinyl chloride, 49%; 1-methylcyclobutyl chloride, 16%; β-methylallylcarbinyl chloride, 14%; and total unreactive chloride, 32%. The unreactive chloride probably consists of two components. 1-Chloro-2,2-dimethylcyclopropane is likely as the lower boiling unreactive chloride (see fig. 22), and β-methylallylcarbinyl chloride is the higher boiling unreactive chloride. In the higher boiling region, the % of unreactive chloride determined by kinetics is consistently higher than the % of β-methylallylcarbinyl chloride determined from spectra, presumably due to an internal return isomerization of more reactive chloride to β-methylallylcarbinyl chloride during solvolysis (see below). The residue of the distillation was rich in β-methylallylcarbinyl chloride. The infrared spectra of three fractions from the main distillation of the chlorination product are shown in fig. 23. The approximate % of each chloride in curves No. 3, 4 and 5, respectively (fig. 23), follow: β-methylallylcarbinyl chloride (0,19,44); 1-methylcyclobutyl chloride (3,41,25); 1-methylcyclopropylcarbinyl chloride (76,24,11); and unreactive chloride (including β-methylallylcarbinyl chloride) (20,28,58).

1-Methylcyclopropyl Bromide.--The procedure of Roberts and Chambers[139] was followed. Treatment of the silver salt of 1-methylcyclopropanecarboxylic acid (79% from the acid) with bromine in Freon-12 (dichlorodifluoromethane) gave on

distillation through a Holzman[201] column, five fractions, 14.2 g. (0.105 mole, 71%) of 1-methylcyclopropyl bromide, b.p. 77.2-78.0° (740 mm.), $n^{25}D$ 1.4471-1.4474.

1-Methylcyclopropylmagnesium bromide was prepared under nitrogen from 1.12 g. (0.0083 mole) of 1-methylcyclopropyl bromide, 0.28 g. (0.012 mole) of magnesium turnings and 12 ml. of anhydrous ethyl ether (distilled from lithium aluminum hydride). Phenyl isocyanate (0.33 g., 0.0030 mole) was added slowly through a syringe, the mixture refluxed one-half hour and poured into 6 ml. of 2 N hydrochloric acid. The ether layer was separated, combined with three 8-ml. ether extracts of the aqueous layer, and the combined extracts dried. Petroleum ether was added, the solution evaporated to dryness and 10 ml. more added. The solution was evaporated to 3 ml. and still remained clear. Apparently no s-diphenylurea was present. Crystallization from cyclohexane gave 0.28 g. (0.0016 mole, 53%), m.p. 95.4-99.7°. Recrystallization from hexane gave white crystals, m.p. 99.2-100.1°. An authentic sample of 1-methylcyclopropanecarboxanilide (see above, m.p. 100.5-101.6° from 50% ethanol) when recrystallized from hexane gave a m.p. of 100.6-101.3°; mixed m.p. with the present sample, 99.3-100.7°. The infrared spectra of the two anilides were identical.

1-Methylcyclobutyl Bromide.--Synthesis from methylenecyclobutane and hydrobromic acid by the method of Shand,

Shoemaker and Fischer[161,197] gave a 55% yield of 1-methylcyclobutyl bromide, b.p. 54.3-54.9° (98 mm.), $n^{25}D$ 1.4648-1.4662; lit.[161] b.p. 55-57° (100 mm.), $n^{25}D$ 1.4673.

1-Methylcyclopropylcarbinylamine. A. Sodium in Ethanol Reduction.--The reported[61] synthesis of cyclopropylcarbinylamine from cyclopropyl cyanide was applied to 1-methylcyclopropanecarbonitrile. The yield of 1-methylcyclopropylcarbinylamine was 56%; b.p. 95.0-96.8° (764 mm.); $n^{25}D$ 1.4269. B. Lithium Aluminum Hydride Reduction.--The synthesis used was adapted from the procedure of Amundsen and Nelson.[210] To a solution of 11.4 g. of lithium aluminum hydride in 600 ml. of anhydrous ethyl ether at 0° was added 24.3 g. (0.30 mole) of 1-methylcyclopropanecarbonitrile in 30 ml. of anhydrous ether at a rate causing gentle reflux. The reaction mixture was stirred and cooled while 12 ml. of water, 9 ml. of 20% sodium hydroxide and 42 ml. of water were added in succession. The ether layer was separated and the white granular residue washed three times with 45-ml. portions of ether. After the ether solution was dried over potassium hydroxide and most of the ether removed, the product was distilled from a 7 x 440-mm. glass-spiral column, b.p. 94.3-96.1° (761 mm.), $n^{25}D$ 1.4267-1.4273, 17.9 g. (0.21 mole, 70%).

N-Phenyl-N'-(1-methylcyclopropylcarbinyl)-thiourea, recrystallized from dilute ethanol, had a m.p. of 112.7-113.5°.

Anal. Calcd. for $C_{12}H_{16}N_2S$: C, 65.42; H, 7.29; N, 12.72.

Found: C, 65.64; H, 7.38; N, 12.74.

1-Methylcyclobutylamine.--The method used was adapted from the general procedure of Ritter, et al.[165,166] (a) Via N-(1-Methylcyclobutyl)-acetamide.--In a 500 ml. flask with stirrer, dropping funnel and condenser, and immersed in an ice-salt bath, was placed 9.0 g. (0.22 mole) of acetonitrile, 100 ml. of glacial acetic acid and 20 g. of concentrated sulfuric acid. Methylenecyclobutane (13.6 g., 0.20 mole) was added slowly, and stirring continued for one hour at 20°. The solution was cooled, diluted with 300 ml. of water, made basic with sodium carbonate and extracted five times with 50-ml. portions of ethyl ether. After the ethereal solution was dried and filtered, the ether was evaporated, giving 17.7 g. (0.14 mole) of white crystals (70%). The N-(1-methylcyclobutyl)-acetamide (10.0 g., 0.078 mole) and 400 ml. of 4 N potassium hydroxide in ethylene glycol was heated at reflux for 48 hours. Continuous ether extraction of all material boiling below 180° followed by drying (potassium hydroxide) of the extract and removal of the ether, gave 3.1 g. (0.036 mole, 46%) of 1-methylcyclobutylamine, b.p. 85.5-86.0° (764 mm.), $n^{25}D$ 1.4200.

N-Phenyl-N'-(1-methylcyclobutyl)-thiourea was recrystallized from dilute ethanol, m.p. 135.3-135.8°.

Anal. Calcd. for $C_{12}H_{16}N_2S$: C, 65.42; H, 7.29; N, 12.72. Found: C, 65.23; H, 7.40; N, 12.97.

(b) Via N-(1-Methylcyclobutyl)-formamide.--A 200-ml. three-necked flask with stirrer, dropping funnel and Dry Ice condenser was cooled to 0° and 11.0 g. (0.20 mole) of 90% sodium cyanide, 13.6 g. (0.20 mole) of methylenecyclobutane and 25 ml. of glacial acetic acid were added. An ice-cold solution of 25 ml. of glacial acetic acid and 50 g. of concentrated sulfuric acid was added dropwise, with stirring, over a period of 25 minutes. The solution was stirred for three hours at 0°, one hour at room temperature, and at 55° for 45 minutes. The reaction mixture was allowed to stand overnight and an ice-cold solution of 120 g. of sodium hydroxide in 250 ml. of water was added slowly with stirring. The resulting solution was refluxed for eight hours and steam distilled until 250 ml. of distillate was collected. Titration of an aliquot indicated a 74% yield of amine. The steam distillate was continuously extracted with ether for 18 hours, dried over potassium hydroxide and the ether removed through a packed column. Distillation through a 9 x 240-mm. vacuum-jacketed Vigreux column gave, after a small forerun of impure amine, four fractions, b.p. 84.0-84.7° (745 mm.), $n^{25}D$ 1.4292-1.4293, 8.03 g. (0.094 mole, 47%).

β-Methylallylcarbinylamine. (a) The method previously described[61] for the preparation of allylcarbinylamine was used. N-1-(3-Methyl-3-butene)-phthalimide was obtained from

β-methylallylcarbinyl chloride and potassium phthalimide in dimethylformamide in 85% yield. A small sample was recrystallized from aqueous methanol, m.p. 50.6-51.8°; sublimation gave find white needles, m.p. 51.2-52.8°.

Anal. Calcd. for $C_{13}H_{13}NO_2$: C, 72.61; H, 6.07; N, 6.49. Found: C, 72.78; H, 5.73; N, 4.42.

The low value for the % nitrogen may possibly be due to the analytical method used, which was different from other analytical determinations for nitrogen, but generally suited for imides, in general. Hydrazinolysis of the phthalimide (using perchloric acid instead of hydrochloric acid) gave a 26% yield of amine, b.p. 47.6-48.5° (101 mm.), $n^{25}D$ 1.4288. (b) By the reported[211] synthesis of allyl cyanide, β-methylallyl chloride and cuprous cyanide gave β-methylallyl cyanide in 76% yield, b.p. 135.0-135.9° (760 mm.), $n^{25}D$ 1.4159-1.4162; lit. (1)[212] b.p. 134.5-136.5°, $n^{20}D$ 1.4180 (76%) and (2)[213] b.p. 136.2-136.4°, $n^{20}D$ 1.4202. Lithium aluminum hydride reduction of the nitrile (by the method used for 1-methylcyclopropanecarbonitrile, see above) gave a brilliant yellow reaction mixture throughout the reduction. Distillation gave only a few % of product, b.p. 90.8-91.9° (742 mm.), $n^{25}D$ 1.4081.

The N-phenylthiourea of the amine in part (b) was recrystallized twice from 50% ethanol and had a m.p. of 71.4-73.0°.

Anal. Calcd. for $C_{12}H_{16}SN_2$: C, 65.41; H,7.32; N, 12.72. Found: C, 64.85; H, 7.32; N, 12.20.

(c) Several attempts to prepare β-methylallylcarbinylamine by reaction of the sodium salt of nitromethane in ethanol (or lithium salt in methanol) with β-methylallyl chloride, followed by reduction[214] of the possible nitro compounds with iron and hydrochloric acid, all failed, either due to formation of a nitronic ester instead of the nitro compound, or due to addition of hydrogen chloride to the double bond. In one case a 5% yield of impure amine was obtained, b.p. 105.5-112.1° (745 mm.), $n^{25}D$ 1.4270-1.4310. (d) The reaction of crude β-methylallylcarbinyl p-toluenesulfonate (90% from β-methylallylcarbinol, sodium hydride and p-toluenesulfonyl chloride in ether via a procedure published for the preparation of cyclobutyl p-toluenesulfonate[140]) with potassium phthalimide in dimethylformamide gave only phthalimide (75%). (d) Hydrolysis of diethyl β-methylallylmalonate (prepared from β-methylallyl chloride and diethyl malonate by D. E. Applequist) gave the diacid which when decarboxylated by distillation at 187-205° (742 mm.), gave a product with b.p. 57.9-59.9° (3.3-3.4 mm.). That the product was not the desired acid (on which a Schmidt reaction or Curtius degradation was next intended), but the corresponding γ-lactone, was indicated by the decolorization of only 15% of the theoretical amount of diazomethane.

Amine-Nitrous Acid Reactions in Aqueous Media. Similar procedures were used throughout and the details are given for only one experiment. A. 1-Methylcyclopropylcarbinylamine.--A 500-ml. three-necked flask was equipped with a dropping funnel, stirrer, and Claisen head and condenser set for downward distillation. The receiver was connected to a Dry Ice trap and the latter to a water aspirator via a calcium chloride drying tube. To 1-methylcyclopropylcarbinylamine (12.8 g., 0.150 mole) in 50 ml. of water and 180 ml. of 1.0 N perchloric acid, was added, with stirring, a solution of 30 g. (0.44 mole) of sodium nitrite (95%) in 100 ml. of water over a period of thirty minutes. The temperature rose slightly during the reaction (ca. 10°) and brown nitrogen oxides were evolved. The pressure was reduced to 50-65 mm. for one hour, then 100 ml. of steam distillate was collected. The aqueous layer was saturated with potassium carbonate, extracted with four 20-ml. portions of ethanol-free ether and the extracts combined with the carbinol layer. The solution was dried over anhydrous magnesium sulfate, the ether removed in vacuo, and the product was distilled through a 7 x 440-mm. glass-spiral column. After a small forerun of ether, six fractions were obtained (9.4 g., 0.11 mole, 73%), b.p. 112.2-119.2°, $n^{25}D$ 1.4094-1.4334; the two middle fractions (4.9 g., 0.05 mole, 38%) had b.p. 118.2-119.3°, $n^{25}D$ 1.4334. The Dry Ice trap contained ca. 2 ml. of a deep

blue liquid (dinitrogen trioxide), which upon warming to 0°, turned green, then yellow with the evolution of brown gases. Two layers remained; the upper carbinol layer (the lower layer was water), 0.72 g., after drying over Drierite, gave a micro b.p.[191] of 118.4° (758 mm.). The total recovery was 10.1 g. (0.117 mole, 78%). An infrared spectrum of the middle fraction (fig. 24) and the last fraction indicated that 1-methylcyclobutanol (fig. 24) was the only carbinol product (cf. the spectra of the other possible carbinols in fig. 24). In two of these amine-nitrous acid reactions, the infrared spectrum of the product had a small band at ca. 6.5 microns (fig. 24) indicating an impurity, possibly nitrite.

B. 1-Methylcyclobutylamine.--From 6.46 g. (0.076 mole) of 1-methylcyclobutylamine, 90 ml. of 1.0 N perchloric acid (0.090 mole), 15.0 g. (0.22 mole) of sodium nitrite and 75 ml. of water were obtained five fractions by distillation through a Holzman[201] column, 4.22 g. (0.049 mole), b.p. 58.4-58.9° at 50.9-51.7 mm., $n^{25}D$ 1.4319-1.4336 (64%); three of these fractions, 2.95 g. (0.034 mole, 45%), had the same b.p. and $n^{25}D$ 1.4332-1.4336. An infrared spectrum on a middle fraction (fig. 24) and last fraction were practically identical with the spectrum of authentic 1-methylcyclobutanol (fig. 24). The other possible carbinols (fig. 24) were not present in detectable amounts.

C. β-Methylallylcarbinylamine.--The reaction of β-methylallylcarbinylamine (1.36 g., 0.016 mole) with 18.5 ml. of 1.0 N perchloric acid (0.019 mole), sodium nitrite (3.1 g., 0.045 mole) and 8.2 ml. of water yielded, after distillation through a Holzman[201] column (following a small forerun), two fractions: (1) 0.21 g. (0.0024 mole), b.p. 49.9-55.8° (38.5 mm.), $n^{25}D$ 1.4303, and (2) 0.19 g. (0.0022 mole), b.p. 51.0-55.8° (38.5 mm.), $n^{25}D$ 1.4320. The carbinol composition calculated from the infrared spectrum of fraction 2 (fig. 24) was 1-methylcyclobutanol (41%), β-methylallylcarbinol (47%) and β-methyl-γ-methyallyl alcohol (12%). The presence of very small amounts of 1-methylcyclopropylcarbinol and α-methyl-β-methyallyl alcohol in this fraction could not be excluded. The composition of the total carbinol product as calculated from infrared spectra was 1-methylcyclobutanol (55%), β-methylallylcarbinol (33%), 1-methylcyclopropylcarbinol (2 ± 2%), α-methyl-β-methylallyl alcohol (4%) and β-methyl-γ-methyallyl alcohol (6%).

1-Methylcyclobutyl Hypochlorite.--The method for the preparation of t-butyl hypochlorite was followed.[215] From 17.2 g. (0.20 mole) of 1-methylcyclobutanol, there was obtained only 5.2 g. (0.043 mole, 21%) of 1-methylcyclobutyl hypochlorite as a yellow oil which was extremely difficult to separate from the aqueous layer. Although t-butyl and t-amyl hypochlorites have specific gravities

somewhat less than that of water, the specific gravity of 1-methylcyclobutyl hypochlorite is greater than that of water.

Anal. Calcd. for C_5H_9OCl: C, 49.80; H, 7.52; Cl, 29.41. Found: C, 45.72; H, 6.4; Cl, 34.66.

If free chlorine is present to the extent of 8.00%, then the reported values change to C, 49.7; H, 7.0; Cl, 29.0.

Exposure of 1-methylcyclobutyl hypochlorite to ultraviolet light (Cenco mercury lamp) caused a slight darkening, however no chemical effects were observable. Both the starting and irradiated material gave definite positive tests with 2,4-dinitrophenylhydrazine, iodoform reagent, potassium iodide in acetone (positive halogen) and alcoholic silver nitrate. Experiments with this compound were discontinued.

1-Methylcyclopropanecarboxylic-C^{14} Acid.--A modification of the procedure and apparatus of Dauben, Reid and Yankwich was used to carbonate the Grignard reagent in an evacuated system at -25 to -20°.[167] 1-Methylcyclopropylmagnesium bromide was prepared from 1-methylcyclopropyl bromide (2.28 g., 0.0169 mole), magnesium turnings (0.486 g., 0.0200 mole) and 25 ml. of anhydrous ethyl ether (distilled from lithium aluminum hydride). Carbon dioxide-C^{14} was generated from barium carbonate (66.62 mg., 0.338 mmole, of barium carbonate-C^{14} of which 133.2 mg. contained 5.0 mc., and 405 mg. (2.06 mmole) of inactive barium carbonate) and sulfuric acid. 1-Methylcyclopropylmagnesium bromide rapidly absorbed the carbon

dioxide and the system was flushed several times with inactive carbon dioxide until all the Grignard reagent had reacted. After acidification, inactive 1-methylcyclopropanecarboxylic acid (17.21 g., 0.172 mole) was added. Distillation of the product through a Holzman[201] column gave 23.83 g. (0.238 mole) of 1-methylcyclopropanecarboxylic-C^{14} acid, b.p. 96.6-97.4° (19.2-19.4 mm.). The recovery was 97%. A radioactivity analysis of 1-methylcyclopropanecarbox-C^{14}-amide prepared from this acid (see below) indicated an activity of 9.26 μc./mmole or a total of 2.20 mc.; the radioactivity yield of the acid from barium carbonate-C^{14} was 88%.

1-Methylcyclopropanecarbox-C^{14}-amide.--The procedure described for the preparation of inactive 1-methylcyclopropanecarboxamide (vide supra) was used. 1-Methylcyclopropanecarboxylic-C^{14} acid (16.6 g., 0.166 mole) gave 13.9 g. (0.140 mole) of amide (84%) having a C^{14}-activity of 9.26 μc./mmole.

1-Methylcyclopropylcarbinyl-C^{14}-amine.--A 500-ml. three-necked flask was fitted with a stopper, stirrer and continuous flow extractor surmounted by a condenser and drying tube. An extraction thimble was filled with 13.7 g. (0.138 mole) of 1-methylcyclopropanecarbox-C^{14}-amide, and 7.9 g. (0.21 mole) of lithium aluminum hydride and 300 ml. of anhydrous ethyl ether were added to the flask. The slurry was stirred and heated at reflux until all the amide had been extracted from

the thimble (8 hours). The mixture was worked up as in the preparation of the inactive amine (see above) and the product distilled giving a 0.7 g. forerun (38-91.0°) and three fractions (6.41 g., 0.075 mole, 54%), b.p. 91.0-93.1° (735 mm.). The corresponding hydrobromide (2.35 g., 0.014 mole) was recovered from the dried ether solutions; the total yield in the reduction was 51%.

Reaction of 1-Methylcyclopropylcarbinyl-C^{14}-amine with Aqueous Nitrous Acid.--The same procedure for diazotization of the inactive amine was used. From 6.23 g. (0.073 mole) of 1-methylcyclopropylcarbinyl-C^{14}-amine, 90 ml. (0.090 mole) of 1 N perchloric acid, 15.0 g. (0.22 mole) of sodium nitrite and 75 ml. of water (plus 3.74 g. (0.043 mole) of inactive 1-methylcyclobutanol) was obtained 8.50 g. (0.099 mole, 85%) of 1-methylcyclobutanol-C^{14}, b.p. 51.8-53.3° (40.0 mm.).

Reaction of 1-Methylcyclopropylcarbinyl-C^{14}-amine with Nitrous Acid in Glacial Acetic Acid.--To a magnetically stirred solution of 10.2 g. (0.120 mole) of 1-methylcyclopropylcarbinyl-C^{14}-amine and 85 ml. of glacial acetic acid in a flask with a drying tube, was added portionwise 12.4 g. of sodium nitrite during six hours. The reaction mixture was stirred overnight at room temperature, and the solution was cooled rapidly and poured into 300 g. of ice-cold 20% sodium hydroxide with stirring. After continuous ether extraction, desiccation (Drierite), and removal of ether,

four fractions were obtained by distillation through a Holzman[201] column, b.p. 51.8-56.3° (40.2 mm.), $\underline{n}^{25}D$ 1.4193-1.4203, 9.53 g. (0.075 mole). Analysis of the infrared spectrum of the two main fractions indicated 69% 1-methylcyclobutyl acetate (bands at 11.40 and 11.63 microns) and 17% 1-methylcyclobutanol (14.02 microns). No more than 2-3% of 1-methylcyclopropylcarbinyl acetate could have been present. A nitrite band (6.13 microns) was present in the spectrum of both fractions.

A mixture of inactive 1-methylcyclopropylcarbinylamine and 1-methylcyclobutylamine with sodium nitrite in glacial acetic acid gave the same products as 1-methylcyclopropylcarbinyl-C^{14}-amine.

Reduction of 1-Methycyclobutyl-C^{14} Acetate.--A mixture (9.12 g.) of 1-methycyclobutyl-C^{14} acetate and 1-methylcyclobutanol-C^{14} in 20 ml. of anhydrous ethyl ether was added dropwise with stirring to 2.3 g. (0.060 mole) of lithium aluminum hydride in 80 ml. of anhydrous ether, then stirred under reflux for one hour. The excess lithium aluminum hydride was decomposed with water and the mixture filtered. The filtrate and ether washings were combined, dried (magnesium sulfate) and the ether removed. Distillation gave 4.75 g. (0.056 mole), of 1-methylcyclobutanol-C^{14}, b.p. 53.6-55.1° (40 mm.) (some of the product was lost accidentally).

O-1-Methylcyclobutyl-C^{14} S-Methyl Xanthate.--The procedure of Roberts and Sauer[137] was followed. In a dry 100-ml. three-necked flask fitted with a spiral condenser, stirrer and dropping funnel was placed 1.63 g. (0.068 mole) of sodium hydride and 40 ml. of anhydrous ether. The slurry was stirred while 4.25 g. (0.050 mole) of 1-methylcyclobutanol-C^{14} in 5 ml. of ether was added over a period of thirty minutes, and the reaction mixture was refluxed for three hours. Then 4.95 g. (0.065 mole) of carbon disulfide was added and the solution stirred under reflux for three hours. Finally, 9.23 g. (0.065 mole) of methyl iodide was added and the mixture refluxed an additional three hours. Water (40 ml.) was cautiously added and then 9.230 g. (0.052 mole) of inactive O-1-methylcyclobutyl S-methyl xanthate was added. The combined solutions were continuously extracted with ether, dried (Drierite) and the ether removed. Distillation through a Holzman[201] column gave 17.2 g. (0.098 mole, 95% of xanthate), b.p. 53.6-56.2° (40 mm.). Preparations in which no previously prepared xanthate was added, gave yields averaging 79%.

Thermolysis of O-1-Methycyclobutyl-C^{14} S-Methyl Xanthate.--The apparatus consisted of a 50-ml. flask (half full of diphenyl) surmounted by a straight air-condenser. To one opening of a T-tube at the top of the condenser was placed a rubber policeman and to the other opening were connected in

the following order an empty trap, a gas-washing bottle (with a fritted cylinder and containing 40% sodium hydroxide), a drying tube (Indicating Drierite), a Dry Ice condenser with receiver and finally a Dry Ice trap. All connections were of Tygon tubing. To the refluxing diphenyl was added, as rapidly as foaming permitted, 8.16 g. of O-1-methylcyclobutyl-C^{14} S-methyl xanthate through the rubber policeman and with the aid of a syringe. After completion of the addition, the system was flushed thoroughly with dry nitrogen while the apparatus was warmed with a heat lamp. The yield of hydrocarbon was 2.67 g. (0.039 mole, 85%). Analysis of the infrared spectrum of the product (fig. 25) indicated the following composition: methylenecyclobutane (18%), 1-methylcyclobutene (25%), and isoprene (57%). See fig. 25 for the infrared spectra of the pure components.

Pyrolysis of Cyclobutane-Ring Hydrocarbons.--With the aid of a slow stream of nitrogen, hydrocarbons were passed once through boiling diphenyl then through a glass-wool filter and finally condensed in a trap. The apparatus was so constructed that a fine stream of bubbles passed upward through a glass spiral containing the hot diphenyl (ca. 255°). A. Methylenecyclobutane.--No isomerization of methylenecyclobutane was apparent, the spectra of the starting material (fig. 25) and product being identical. B. 1-Methylcyclobutene.--Analysis of the infrared spectrum of the product

(fig. 25) indicated that 1-methylcyclobutene (high purity material kindly supplied by Dr. E. R. Buchman, b.p. 37.1° at 750 mm.) (fig. 25) gave a mixture of 86% isoprene and 14% 1-methylcyclobutene. C. Cyclobutene.--One pass of cyclobutene through an apparatus which assured somewhat less contact time gave a mixture of 51% 1,3-butadiene and 49% cyclobutene. The infrared spectrum of cyclobutene[137,138] and butadiene (Matheson) were taken in a 10-cm. gas cell at a pressure of 150 mm.

3-Methyl-2,5-dihydrothiophene-1,1-dioxide-C^{14} (Isoprene Cyclic Sulfone).--The following experiment is illustrative. The hydrocarbon mixture (5.46 g., 0.080 mole) obtained from the pyrolysis of O-1-methylcyclobutyl-C^{14} S-methyl xanthate, 8.0 ml. (0.10 mole) of sulfur dioxide, and 0.08 g. (0.0008 mole) of hydroquinone were heated for 12 hours at 96-102° in a sealed tube. After removal of the excess sulfur dioxide, the product was dissolved in a minimum of hot (50-60°) water, treated with Norite and filtered. The cyclic sulfone is only very slightly soluble in cold water. The yield of white, glistening plates was 5.06 g. (0.038 mole), m.p. 63.2-63.8°. (40% from O-1-methylcyclobutyl S-methyl xanthate); lit. (1)[172] m.p. 63.0-63.5°, (2)[173] m.p. 63-64°, solubility in 100 g. of water at 25°, 7.85 mg. and (3)[174] m.p. 63-63.5°. The average yield of a number of experiments starting with isoprene and synthetic mixtures of isoprene and methylenecyclobutane,

was 83%. Omission of hydroquinone led to considerable polymerization, and two experiments (with hydroquinone) at room temperature gave only a tough, yellow polymer which, when macerated and extracted with hot water, gave only 24 and 31% of isoprene cyclic sulfone.

Thermolysis of 3-Methyl-2,5-dihydrothiophene-1,1-dioxide-C^{14} (Isoprene Cyclic Sulfone).--The apparatus consisted of an 8 x 300-mm. fractionating column (with a platinum spiral) and heating jacket, with a 50-ml. flask at the lower end and on top, an inlet for dry nitrogen and an outlet which led to an empty trap, a gas-washing bottle (with fritted cylinder and containing 20% sodium hydroxide), a drying tube (Indicating Drierite), a Dry Ice condenser with receiver, and finally, a Dry Ice trap. Isoprene-C^{14} sulfone (6.61 g., 0.050 mole) was placed in the boiler and the flow of nitrogen started. The heating jacket was held at 170-180°, while a heating bath at 110° was placed around the flask and the temperature was raised to 180° in 45 minutes. Any sulfone which condensed in the neck of the flask was easily removed by a Bunsen flame, and a heat lamp was used to drive the last of the isoprene from the system. The collected isoprene-C^{14} (2.91 g., 0.043 mole, 86%) had an infrared spectrum identical to the spectrum of authentic isoprene (fig. 25). The reported rate constant for the thermolysis of isoprene sulfone is 2.64×10^{-4} sec.$^{-1}$ at 131.2°; for 95% reaction, this corresponds to 3.2 hours at 131.2°.[172] However

better yields were obtained at higher temperatures (ca. 160-180°), the average being 81%.

1,4-Dibromo-2-methyl-2-butene-C^{14} (Isoprene Dibromide).—The procedure followed is that of Sheppard and Johnson.[176] An experiment with inactive isoprene is described first. In a 100-ml. three-necked flask with stirrer, dropping funnel and Dry Ice condenser were placed 6.81 g. (0.100 mole) of isoprene and 10 ml. of chloroform. The solution was kept at -30 to -25° while a solution of 16.0 g. (0.10 mole) of bromine was added over a period of two hours. The solution was nearly colorless after the addition. Chloroform was removed at 40° and 20 mm., and the residue dried over Drierite. Distillation through a Holzman[201] column gave a small forerun (0.52 g., b.p. 37.2-55.0° at 1.5 mm., $n^{25}D$ 1.5508) and four fractions, b.p. 55.5-58.8° (1.4-1.5 mm.), $n^{25}D$ 1.5590-1.5612, 17.5 g. (0.077 mole, 77%). The product was extremely lacrymatory as reported.[176]

In experiments using isoprene-C^{14}, an excess of bromine was added (bromine addition stops sharply after one molecule has added) and inactive isoprene then added to absorb the excess bromine. The average yield in these experiments was 82%.

Reduction of 1,4-Dibromo-2-methyl-2-butene-C^{14} with Lithium Aluminum Hydride. 2-Methyl-2-butene-C^{14}.--The procedure of Trevoy and Brown for reduction of 1,4-dibromo-2-

butene[177] was used. The apparatus consisted of 100-ml. three-necked flask with stirrer, dropping funnel, and gas-exit tube connected through a drying tube (Indicating Drierite) to a Dry Ice condenser with receiver, and finally to a Dry Ice trap. Diethylcarbitol (dried over sodium) (40 ml.) and 2.01 g. (0.053 mole) of lithium aluminum hydride were stirred and heated to 70°, and a solution of 16.0 g. (0.070 mole) of isoprene-C^{14} dibromide in 12 ml. of dry diethyl-carbitol was added over a period of 65 minutes, the reaction being quite vigorous. After 20 minutes longer, 20 ml. of water were cautiously added, the evolved hydrogen driving the last traces of trimethylethylene-C^{14} (2-methyl-2-butene-C^{14}) into the Dry Ice condenser. The product, 4.74 g. (0.068 mole, 97%), had an infrared spectrum identical to the spectrum of authentic trimethylethylene (2-methyl-2-butene), prepared by heating t-amyl chloride and water, b.p. 37.6-38.5° (738 mm.).

2-Methyl-2,3-butanediol-C^{14}.--The procedure of Roberts, McMahon and Hine[133] was used to hydroxylate 4.63 g. (0.066 mole) of 2-methyl-2-butene-C^{14} with performic acid, giving 4.07 g. (0.039 mole, 59%) of the diol, b.p. 90.7-91.0° (22.9-24.5 mm.). Attempts to purify the bis-N-phenylcarbamate of 2-methyl-2,3-butanediol were not successful; the product, a tan powder, had m.p. 128-131°; lit.[216] 134.5-135.5°.

Degradation of 2-Methyl-2,3-butanediol-C^{14}.--A procedure for cleavage of the diol with periodate to give acetaldehyde and acetone, and conversion of the acetone into iodoform has been described.[133] All iodoform samples were recrystallized from methanol-water. Ether extraction of the crude acetone 2,4-dinitrophenylhydrazone was necessary to separate the unreacted 2,4-dinitrophenylhydrazine (insoluble in ether). The dimethone derivative of acetaldehyde was prepared as described.[133] 2-Methyl-2,3-butanediol-C^{14} was treated with sulfuric acid as reported,[133] however a portion of the product (methyl isopropyl ketone) was converted to the corresponding 2,4-dinitrophenylhydrazone (using the same procedure reported[133] for preparing acetone 2,4-dinitrophenylhydrazone), m.p. 121.1-122.1° from methanol-water. The radioactivity determinations of the degradation products are given in Tables V and VI.

Control Experiments. A. Attempted Isomerization of 1-Methylcyclopropylcarbinol.--The procedure used in the diazotization of 1-methylcyclopropylcarbinylamine was repeated using 1-methylcyclopropylcarbinol in place of the amine. The infrared spectrum of the product, a light yellow liquid, b.p. 25-26°(50 mm.), indicated nitrite. After refluxing this yellow liquid for three hours with excess methanol, the yellow color disappeared. Distillation gave a product which had an infrared spectrum identical with that of pure 1-methylcyclopropylcarbinol.

Table V

Radioactivity Determinations of the Degradation Products of 1-Methylcyclobutanol Obtained in the Reaction of 1-Methylcyclopropylcarbinyl-C^{14}-amine with Aqueous Nitrous Acid

Compound	Atoms[a]	C^{14}-activity[b]	Average C^{14}-activity[c]	% of C^{14}-activity in degradation products[d]
Iodoform, from methyl isopropyl ketone	3	172 152 164	163 ± 8	2.6 ± 0.1
Iodoform, from acetone	$\frac{1}{2}(\alpha + 2)$	1503 1513 1511	1509 ± 4	24.5 ± 0.1
Acetone 2,4-dinitrophenyl-hydrazone	α,1,2	2968 2977 2904[e]	2950 ± 32	47.9 ± 0.5
Acetaldehyde dimethone	3,4	3132 3243 3253 3158	3197 ± 51	51.9 ± 0.8
Methyl isopropyl ketone 2,4-dinitrophenylhydrazone	α,1,2,3,4	6109 6183 6175	6156 ± 33	100.0 ± 0.5

Footnotes to Tables V and VI

[a]Carbon atoms of 1-methylcyclobutanol (see fig. 20), where $2 \equiv 4$. [b]Measured by the procedure of Neville[217] using a vibrating reed electrometer (Applied Physics Corporation). Corrected for background. The lowest activities measured (iodoform from methyl isopropyl ketone) were ca. 10 times background. Activities are in millicuries/millimole x 10^7. [c]The standard deviation is appended to the average activity. [d]The % standard deviation is affixed to the % average activity. The activity of methyl isopropyl ketone (which contains all five of the carbon atoms of 1-methylcyclobutanol) is 100.0. [e]This value may be low since a leak in the combustion line was detected just before the residual activity was measured.

Table VI

Radioactivity Determinations of the Degradation Products of 1-Methylcyclobutanol Obtained in the Reaction of 1-Methylcyclopropylcarbinyl-C^{14}-amine with Nitrous Acid in Glacial Acetic Acid

	Atoms[a]	C^{14}-activity[b]	Average C^{14}-activity[c]	% of C^{14}-activity in degradation products[d]
Iodoform, from methyl isopropyl ketone	3	45.2 47.7 46.1 47.6	46.7 ± 1.1	3.1 ± 0.1
Iodoform, from acetone	$\frac{1}{2}(\alpha + 2)$	351 356 345 347	350 ± 4	23.6 ± 0.3
Acetone 2,4-dinitrophenyl-hydrazone	α,1,2	696 739 696 711	711 ± 18	47.8 ± 1.2
Acetaldehyde dimethone	3,4	719 713 723 733 788	735 ± 27	49.5 ± 1.8
Methyl isopropyl ketone 2,4-dinitrophenylhydrazone	α,1,2,3,4	1459 1488 1478 1519 1484	1486 ± 16	100.0 ± 1.1

White[151] has treated ethylamine with sodium nitrite in dilute aqueous perchloric acid in the presence of cyclopropylcarbinol-α-C^{14}. The initial cyclopropylcarbinol-α-C^{14} had 1.9% of its total C^{14}-activity in the ring atoms, while the recovered cyclopropylcarbinol-α-C^{14} from the above reaction had 2.1% of the C^{14}-activity in the ring.

B. Degradation of 1-Methylcyclopropylcarbinyl-C^{14}-amine Hydrobromide. Oxidation.--To a stirred solution of 0.404 g. (0.00244 mole) of 1-methylcyclopropylcarbinyl-C^{14}-amine hydrobromide and 25 ml. of 10% potassium hydroxide was added 0.642 g. (0.0041 mole) of potassium permanganate in small portions over 45 minutes. The temperature rose to 35-40° during the addition and stirring was continued for two hours. Near the end of this procedure, 7.38 g. (0.074 mole) of inactive 1-methylcyclopropanecarboxylic acid was added. Sulfur dioxide was bubbled in to destroy the excess permanganate, the solution filtered and made acidic with cold 50% sulfuric acid. The resulting solution was extracted with three 20 ml. portions of ether, the extracts dried and the ether removed. Distillation through a Holzman[201] column gave 5.02 g. (0.050 mole, 66%), b.p. 55.9-57.3° (1.5 mm.). From a portion of this acid, 1-methylcyclopropanecarboxamide was prepared as described (see above). Radioactivity analysis indicated an average activity of 128 x 10^{-6} mc./mmole. Schmidt Reaction with 1-Methylcyclopropanecarboxylic-C^{14} Acid.--A solution of

2.00 g. (0.020 mole) of 1-methylcyclopropanecarboxylic-C^{14} acid (from the oxidation of the amine hydrobromide) and 6.0 ml. of sulfuric acid were held at 45-50° by a water bath while 12.4 ml. of 1.62 N hydrazoic acid in chloroform was added over a period of 70 minutes. Gas was evolved for 75 minutes after the addition was completed. The solution was cooled to 0°, neutralized with 20% sodium hydroxide and a 5 ml. excess added. Water (30 ml.) was added and about 25 ml. of steam distillate collected. To the distillate, 0.40 g. (0.010 mole) of sodium hydroxide and 1.41 g. (0.010 mole) of benzoyl chloride were added, and the mixture shaken vigorously and placed in the refrigerator overnight. The product was dissolved in 30 ml. of benzene and washed successively with 5% sodium hydroxide, 5% hydrochloric acid and water. The benzene solution was dried, filtered, heated to boiling and hot petroleum ether (60-70°) added to the cloud point. White needles separated which after four recrystallizations from benzene-petroleum ether (60-70°), had m.p. 161.7-163.0°.

Anal. Calcd. for $C_{11}H_{13}NO$: C, 75.47; H, 7.46; N, 7.97. Found: C, 76.08; H, 7.37; N, 8.14.

Radioactivity analysis of this sample indicated a C^{14}-activity of 0.37 x 10^{-6} mc./mmole. This value corresponds to 0.29% of the activity of the 1-methylcyclopropanecarbox-C^{14}-amide (from oxidation of the amine).

Solvolysis of Halides in 50% Aqueous Ethanol. Method A.--

A sample of the halide was accurately weighed in a volumetric flask and, three minutes before the zero time, 50% aqueous ethanol (by volume) at the reaction temperature was added to the 50.0 (or 100.0) ml. mark. After thorough mixing, the volumetric flask was placed in the constant temperature bath ($\pm$ 0.01°), one minute before the zero time. At given time intervals, aliquots were withdrawn and added to approximately 10 ml. of cold ethanol and titrated with standard sodium hydroxide (in water and 50% ethanol), using bromthymol blue as the indicator. Method B.--To 500 ml. of 50% aqueous ethanol (at 30.0 or 50.0°) with bromthymol blue in a 1-l. Erlenmeyer flask immersed in a water bath at the reaction temperature and stirred magnetically, was added an accurately weighed sample of the halide (in a weighing bottle). At this instant, stopwatch A was started and an aliquot of standard base was added. As the indicator changed color, (1) stopwatch A was stopped, (2) stopwatch B started and (3) another aliquot of standard sodium hydroxide added. Before the next color change, (1) the time on stopwatch A was recorded and stopwatch A set back to zero time and (2) another aliquot made ready. This procedure was repeated at each color change. In experiments where the amount of halide was large (ca. 0.001 M) and where dilute aqueous base was used instead of base in 50% aqueous ethanol, increasing first order kinetics was observed, presumably due to the increase

in rate with increasing concentration of water. Method C.-- An accurately weighed sample of the halide was made up at room temperature to 50.0 (or 100.0) ml. with 50% aqueous ethanol and the sample thoroughly mixed. Aliquots of 5.00 ml. were pipetted into ampoules, the ampoules sealed and placed in the constant temperature bath. Beginning after a specified time (15-20 minutes at 50.0°) or after the bath had attained its original temperature in the case of reactions at 110 and 130°, the ampoules were withdrawn, cleaned, broken open, and titrated with standard alkali using bromthymol blue indicator. The baths at 110 and 130° were vapor thermostats heated by appropriate mixtures of toluene and xylene. The thermostat liquid was diethylene glycol.

The averages of the rate constants are recorded in Table VII. Data for individual runs are recorded in the APPENDIX.

Recovery of Unreacted Chloride from Partial Hydrolysis of the Chlorination Product of 1,1-Dimethylcyclopropane.-- A mixture of chlorides (1.7 g.) obtained from the chlorination of 1,1-dimethylcyclopropane was shaken with 20 ml. of distilled water at room temperature for 75 minutes. The unreacted chloride was recovered, dried and distilled through a Holzman[201] column giving three fractions, 0.5 g., b.p. 81-85° (741 mm.). Analysis of the infrared spectra of the starting material and total recovered chloride (fig. 23, curves 6 and 7, respectively) indicated the following composition, respectively: 1-methylcyclopropylcarbinyl

Table VII

Solvolysis Rate Constants of Halides in 50% Ethanol-50% Water (By Volume)

Halide	Temp., °C. (± 0.1°)	k_1 (hr.$^{-1}$)
1-Methylcyclopropylcarbinyl chloride	30	2.49
1-Methylcyclobutyl chloride	30	0.257
	50	2.22
β-Methylallycarbinyl chloride	130	1.05
Cyclopropyl bromide	130	0.0094
1-Methylcyclopropyl bromide	130	0.378
1-Methylcyclobutyl bromide	30	11.1

chloride (35,13%), 1-methylcyclobutyl chloride (49,65%), β-methylallylcarbinyl chloride (3,10%) and unreactive chloride, including β-methylallylcarbinyl chloride, (20,30%).

Isomerization of Chloride Mixture with Hydrochloric Acid.--A mixture of chlorides (4.0 g.) obtained from the chlorination of 1,1-dimethylcyclopropane was vigorously stirred with 3.2 ml. of cold (0°) concentrated hydrochloric acid for three minutes. The chloride was drawn off, dried and distilled through a Holzman[201] column, the middle fraction (1.8 g.) (the first and last fractions totaled 0.4 g.) having a b.p. of 78.9-81.6° (742 mm.). The approximate chloride composition of the starting material and recovered chloride, respectively, (by infrared analysis) was β-methylallylcarbinyl chloride (19,3%), 1-methylcyclobutyl chloride (24,49%), 1-methylcyclopropylcarbinyl chloride (36,35%), and total unreactive chloride, including β-methylallylcarbinyl chloride, (32,20%). Another isomerization at 0-10° for 60 minutes gave the following result: β-methylallylcarbinyl chloride (0,0%), 1-methylcyclobutyl chloride (3,23%), 1-methylcyclopropylcarbinyl chloride (76,77%), and total unreactive chloride (20,13%).

The reaction of 1-methylcyclopropylcarbinol and 1-methylcyclobutyl chloride with an equimolar mixture of concentrated hydrochloric acid and anhydrous zinc chloride (Lucas reagent)

were uninformative. In the latter case (1-methylcyclobutyl chloride), a small amount of 1,3-dichloro-3-methylbutane (isoprene dihydrochloride) was obtained.

Cyclobutanone-C^{14}. N-Nitroso-N-methyl-C^{14}-urea.--The procedure is a modification of that described by Heard, Jamieson and Solomon[218] for the preparation of diazomethane-C^{14} from sodium cyanide-C^{14}. A solution was prepared from 2.20 g. (0.030 mole) of inactive methylurea, 0.020 g. (0.27 mole) of methyl-C^{14}-urea (3.8 mc./mmole, 1 mc.), 2.6 g. (0.038 mole) of sodium nitrite, and 13 ml. of water. The solution was stirred at 0° while a solution of 1.30 ml. of concentrated sulfuric acid in 14 g. of ice-water was added dropwise during twenty minutes. The dry product weighed 2.14 g. (0.021 mole), 61% (from the total amount of methylurea). A radioactivity analysis indicated a C^{14}-activity of 30 μc./mmole. Diazomethane.--The Organic Synthesis procedure[188] was followed using 1.32 g. (0.0128 mole) of N-nitroso-N-methyl-C^{14}-urea and 31.3 g. (0.303 mole) of inactive N-nitroso-N-methylurea. Reaction of Diazomethane with Ketene.--The procedure is that of Kaarsemaker and Coops.[219] Ketene[220] was passed into the diazomethane solution at -75 to -70° until the bright yellow color changed to a dull, opaque brownish-yellow. The solution was filtered, dried (Drierite) and the ether removed through a packed column. Distillation from the Holzman[201] gave two fractions: (1) b.p. 35.6-39.0° (82 mm.), 2.25 g. and (2) b.p. 39.0-40.1° (82 mm.), 3.49 g. The total product amounted to 5.74 g. (0.082 mole, 26% from the the total N-nitroso-N-methylurea used).

IV. APPENDIX

Table VIII

Solvolysis of the Chlorination Product of 1,1-Dimethylcyclopropane in 50% Ethanol-50% Water (By Volume), 0.00664 M and Approximately 65% 1-Methylcyclopropylcarbinyl Chloride

Temperature: 30.0° Procedure: B (See EXPERIMENTAL)

Aliquots of 0.0700 N NaOH: 1.00 ml.

Time interval (sec.)	Total time (sec.)	% Unreacted
33.6	33.6	97.9
31.4	65.0	95.8
32.2	97.2	93.7
31.7	128.9	91.6
34.3	163.2	89.5
33.6	196.8	87.3
34.5	231.3	85.2
36.2	267.5	83.1
37.8	305.3	81.0
38.3	343.6	78.9
38.8	382.4	76.8
41.2	423.6	74.7
42.4	466.0	72.6
43.8	509.8	70.5
45.8	555.6	68.4

Table VIII (continued)

Time interval (sec.)	Total time (sec.)	% Unreacted
47.4	603.0	66.2
50.0	653.0	64.1
52.8	705.8	62.0
55.3	761.1	59.8
59.4	820.5	57.8
63.1	883.6	55.7
67.4	951.0	53.6
73.3	1024	51.5
79.7	1104	49.4
86.7	1192	47.3
114.9	1307	45.1
133.5	1441	43.0
161.3	1602	40.9
189.8	1792	38.8
235	2027	36.7
342	2369	34.6
550	2919	32.5

$k_1 = 2.49\ hr.^{-1}$

Table IX

Solvolysis of 0.0875 M 1-Methylcyclobutyl Chloride in 50% Ethanol

Temperature: 30.0° Procedure: A (See EXPERIMENTAL)

Aliquots: 5.00 ml. Normality of NaOH: 0.0700

Time (hr.)	Ml. of base	% Unreacted
0.00	0.19	97.0
0.25	0.70	88.8
0.50	1.25	80.9
0.75	1.37	78.0
1.25	2.00	68.0
1.75	2.50	60.0
2.75	3.42	45.2
4.00	4.15	33.5
5.75	4.78	23.5

$k_1 = 0.260 \text{ hr.}^{-1}$

Table X

Solvolysis of 0.001640 M 1-Methylcyclobutyl Chloride in 50% Ethanol

Temperature: 50.0° Procedure: B(See EXPERIMENTAL)

Aliquots of 0.0461 N NaOH in 50% ethanol: 1.00 ml.

Time interval (sec.)	Total time (sec.)	% Unreacted
57.3	57.3	94.4
87.0	144.3	88.7
102.9	247.2	83.1
105.9	353.1	77.5
119.6	472.7	71.8
140.3	613.0	66.2
185.1	798.1	60.6
213.8	1012	55.0
255	1267	49.3

$k_1 = 2.38 \text{ hr.}^{-1}$

Table XI

Solvolysis of 0.0272 M β-Methylallylcarbinyl Chloride in 50% Ethanol

Temperature: 130° Procedure: C (See EXPERIMENTAL)

Aliquot: 5.00 ml. 0.0461 N NaOH in 50% ethanol

Time (hr.)	Ml. of base	% Unreacted
0.00	0.19	93.6
1.00	0.46	84.4
2.00	0.71	75.9
3.00	0.93	68.6
4.17	1.17	60.4
5.00	1.32	55.3
16.00	2.29	22.5
16.50	2.31	21.7

$k_1 = 1.05 \text{ hr.}^{-1}$

Table XII

Solvolysis of 0.0239 M Cyclopropyl Bromide in 50% Ethanol

Temperature: 130° Procedure: C (See EXPERIMENTAL)

Aliquots: 5.00 ml. 0.0461 N NaOH in 50% ethanol

Time (hr.)	Ml. of base	% Unreacted
0.00	0.13	95.0
1.50	0.14	94.6
7.50	0.28	89.2
16.00	0.44	83.0
26.50	0.65	74.8
45.50	0.84	67.5

$k_1 = 0.0094 \text{ hr.}^{-1}$

Table XIII

Solvolysis of 0.0212 M 1-Methylcyclopropyl Bromide in 50% Ethanol

Temperature: 130° Procedure: C (See EXPERIMENTAL)

Aliquots: 5.00 ml. 0.0461 N NaOH in 50% ethanol

Time (hr.)	Ml. of Base	% Unreacted
0.00	0.46	80.0
0.25	0.65	71.7
0.50	0.80	65.2
0.75	0.94	59.0
1.00	1.05	54.3
1.25	1.20	47.7
1.50	1.27	44.6
1.75	1.35	41.2
2.00	1.42	38.2

$k_1 = 0.378 \text{ hr.}^{-1}$

Table XIV

Solvolysis of 0.000846 M 1-Methylcyclobutyl Bromide in 50% Ethanol

Temperature: 30.0° Procedure: B (See EXPERIMENTAL)

Aliquots of 0.0692 N NaOH in 50% ethanol: 1.00 ml.

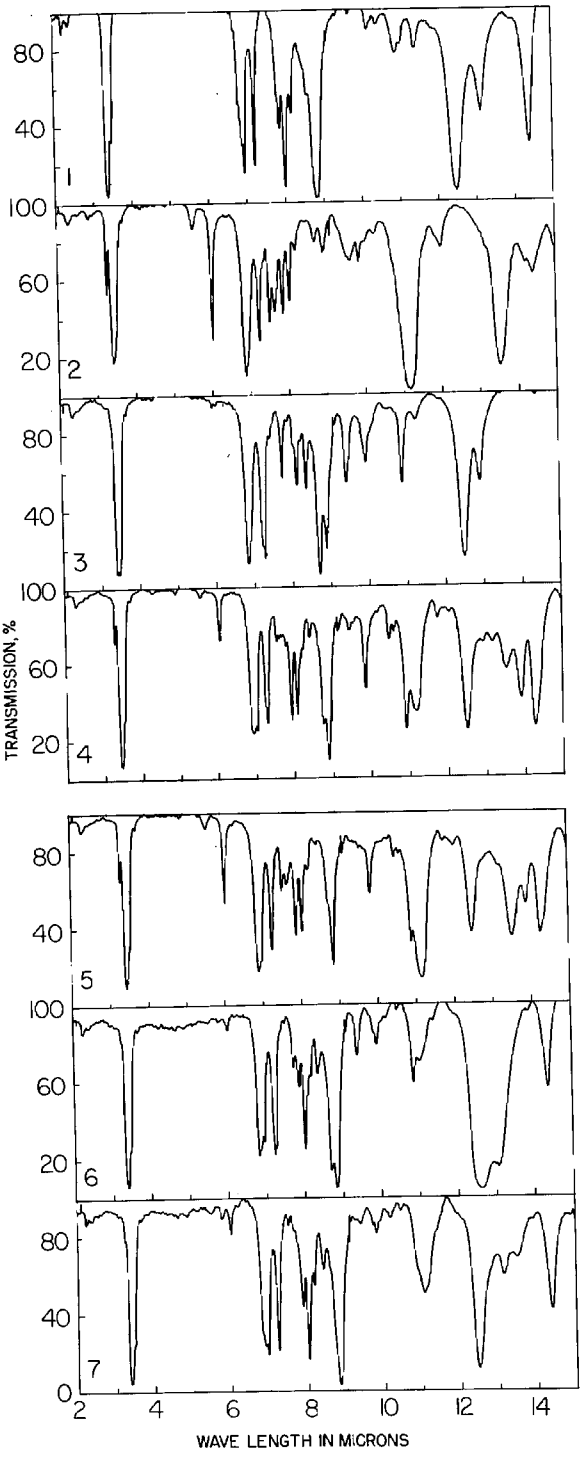
Time interval (sec.)	Total time (sec.)	% Unreacted
58.0	58.0	83.6
77.6	135.6	67.2
91.2	226.8	50.9
114.5	341.3	34.5
176.2	517.5	19.1
368	886	1.7

$k_1 = 10.4 \text{ hr.}^{-1}$

Fig. 23

Curve	Compound
1	1-Methylcyclobutyl chloride.
2	β-Methylallylcarbinyl chloride.
3	Chlorination product of 1,1-dimethylcyclopropane, rich in 1-methylcyclopropylcarbinyl chloride (76%).
4	Chlorination product of 1,1-dimethylcyclopropane, rich in 1-methylcyclobutyl chloride (41%).
5	Chlorination product of 1,1-dimethylcyclopropane, rich in β-methylallylcarbinyl chloride (58%).
6	Chlorination product of 1,1-dimethylcyclopropane.
7	Chloride mixture recovered from the partial hydrolysis of the mixture shown in curve 6.

The infrared spectra were obtained with a model 21 Perkin-Elmer double beam recording spectrophotometer, using pure liquids in a 0.028 mm. NaCl cell.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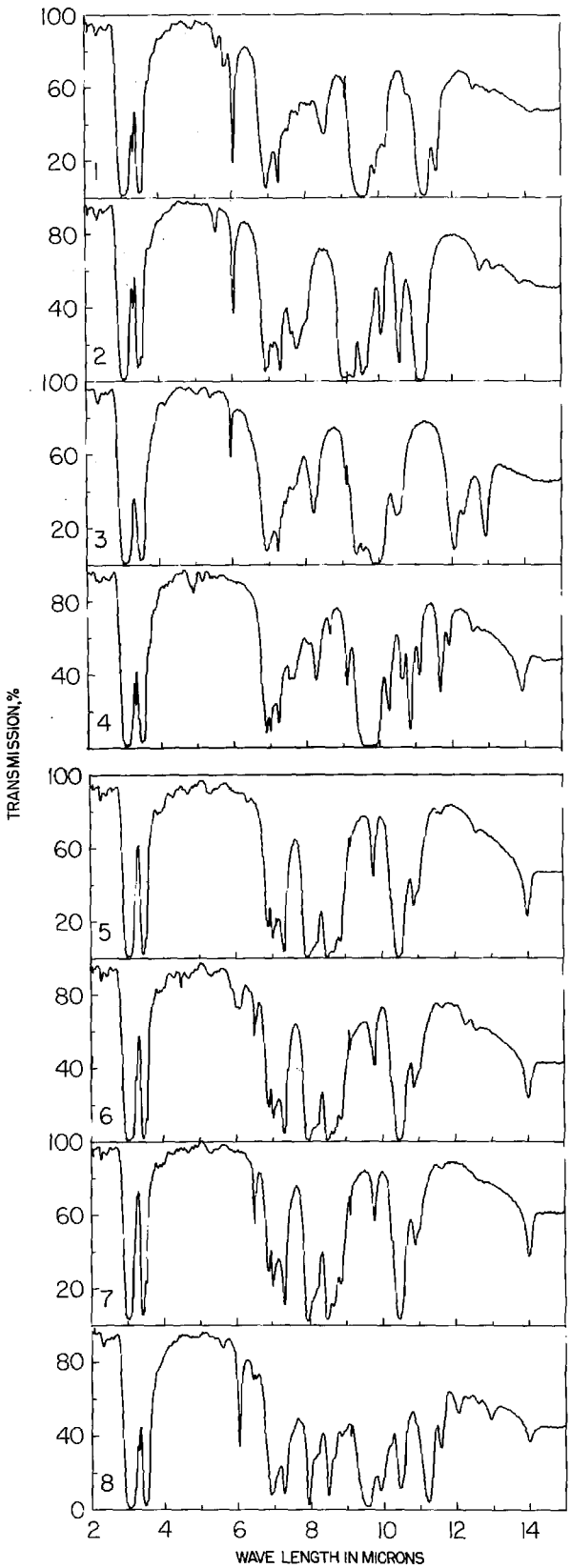
WAVE LENGTH IN MICRONS

Fig. 23

Fig. 24

Curve	Compound
1	β-Methylallylcarbinol.
2	α-Methyl-β-methylallyl alcohol.
3	β-Methyl-γ-methylallyl alcohol.
4	1-Methylcyclopropylcarbinol.
5	1-Methylcyclobutanol.
6	Product from the reaction of 1-methylcyclopropylcarbinylamine with aqueous nitrous acid.
7	Product from the reaction of 1-methylcyclobutylamine with aqueous nitrous acid.
8	Product from the reaction of β-methylallylcarbinylamine with aqueous nitrous acid.

The infrared spectra were obtained with a model 21 Perkin-Elmer double beam recording spectrophotometer, using pure liquids in a 0.028 mm. NaCl cell.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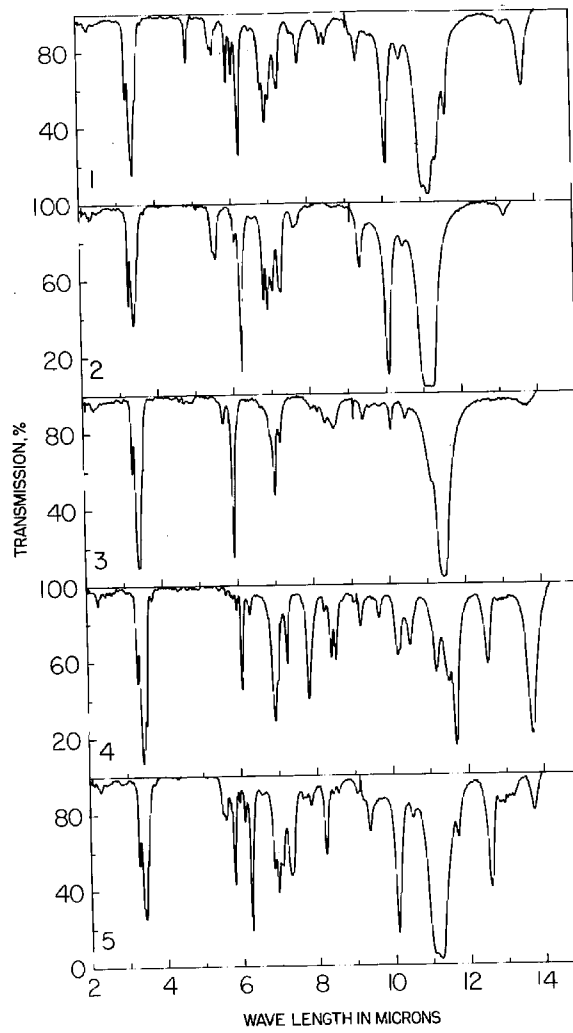
WAVE LENGTH IN MICRONS

Fig. 24

Fig. 25

Curve	Compound
1	Hydrocarbon from the thermolysis of O-1-methylcyclobutyl S-methyl xanthate.
2	Isoprene.
3	Methylenecyclobutane.
4	1-Methylcyclobutene.
5	Product from the pyrolysis of 1-methylcyclobutene.

The infrared spectra were obtained with a model 21 Perkin-Elmer double beam recording spectrophotometer, using pure liquids in a 0.025 mm. NaCl cell.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TRANSMISSION, %
WAVE LENGTH IN MICRONS

Fig. 25

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VI. PROPOSITIONS

1. Two mechanisms which satisfy the results obtained in the reaction of cyclopropylcarbinyl-C^{14}-amine with aqueous nitrous acid are (1) an equilibrium of classical cyclopropylcarbinyl and cyclobutyl cations and (2) a symmetrical 'tricyclobutonium' ion.[1] These mechanisms may be distinguished by the use of optically active cyclopropylcarbinylamine-α-$\underline{d}_1$. Stereospecific synthesis and detection of optical activity could be accomplished enzymatically by the use of diphosphopyridine nucleotide (DPN) in the presence of yeast alcohol dehydrogenase.[2]

2. Free radical rearrangements involving carbon-skeleton rearrangements with migration of aryl groups are well-known. A few examples of the rearrangement of strictly aliphatic radicals have been reported[1a,3-5] but in each of these examples either strong acids were present or high (ca. 450°) temperature was used. Attempted free radical rearrangement in the 1-methylcyclopropylcarbinyl system using mild, non-acidic conditions (e.g., di-t-butyl peroxide catalyzed decomposition of 1-methylcyclopropylcarbinylcarboxaldehyde) should be revealing.

3. The structure of sphingosine (I) has been elucidated and

$$CH_3(CH_2)_{12}CH{=}CH\text{-}\overset{3}{C}HOH\text{-}\overset{2}{C}HNH_2\text{-}\overset{1}{C}H_2OH$$

I

recent investigations indicate that the double bond is trans,[6] that the configuration about C-2 is D,[7] and that the C-2 to C-3 relation is erythro.[8] It is suggested that a stereospecific synthesis of sphingosine could be achieved starting from L-(+)-serine.

4. It has recently[9] been shown that optically active diacyl peroxides of the type $(RCO_2)_2$ decompose when heated to give optically active esters (RCO_2R) with retention of configuration in both R's. A mechanism involving a quasi, six-membered ring appears attractive. The non-exchange of esters containing O^{18} under more drastic conditions[10] suggests that evidence concerning the proposed mechanism might be obtained using diacyl peroxides with O^{18} in the carbonyl or peroxide group.

5. Calculations[11] of the rate of racemization of molecules of the type XY_3 indicate that unsymmetrically substituted organic phosphorous compounds ($PR_1R_2R_3$) should be resolvable only at low temperature while the mixed trihalides ($PX_1X_2X_3$) should be stable toward racemization; unfortunately the latter types are expected to

decompose to the simple trihalides. Of unsymmetrically substituted phosphines, it is suggested that the types PR_1R_2X[12] and PRX_1X_2 offer the best chance for resolution.

6. Relatively few researches have been concerned with the reaction of diazo compounds with dienes. 1,2-Addition is common, however 1,4-addition has been reported.[13] It is proposed that the reaction of carbenes (e.g., $:CH_2$, $:CCl_2$ and $:CHCO_2C_2H_5$) and imino radicals ($R\ddot{N}:$) with certain dienes be investigated as a possible synthetic method of preparing a variety of cyclopentenes, cyclopentadienes, bicycloheptenes, unsaturated spiro compounds and 7-azabicyclo[2,2,1]-heptenes.

7. The facile isomerization of cyclobutene to 1,3-butadiene[3,14,15] and the known reaction of cyclic dienes with ketenes[16] suggest a method of introducing an additional double bond into such cyclic dienes. For example, cycloöctatriene might be synthesized from cyclohexadiene and ketene (via bicyclo[4,2,0]-2-octene-7-one and the corresponding alcohol and xanthate).

8. Arguments[17] based on inconclusive evidence have been presented against a free radical mechanism in the light induced reaction of diazomethane with saturated hydrocarbons. It is suggested that the mechanism of this reaction could be elucidated by use of a few selected hydrocarbons and by a kinetic study.

9. A number of nitrogen containing compounds have been proposed as precursors in nicotine biosynthesis,[18] however experimental evidence supporting these compounds in toto as precursors is meager. It is suggested that some of these possibilities, e.g., nicotinic acid, be labeled with C^{14} (in a ring position least likely to be involved in ring opening or else doubly labeled) and fed to tobacco plants of low nicotine content.

10. Hydrogenation of 4-methylquinoline in acetic acid over Adam's platinum oxide catalyst at 1000 p.s.i. gives first order kinetics.[19] A plot of log p_o/p versus time gives three distinct straight lines, representing relative rates of 2,15 and 1, in that order. These results are not inconsistent with steric effects in the more generally accepted mechanism of catalytic hydrogenation, and may be explained as hydrogenation of three species.

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11. Recent investigations of the chemistry of Mo(VI) and W(VI), and their catalysis of perchlorate reduction by Sn(II) and Ti(III) suggest the following: (1) A complex of the type $[MoO_2 \cdot ClO_4]^+$ may be present in $HClO_4$ solutions of Mo(VI) and that the solubility of Mo(VI) should be studied in other acids. (2) W(VI) might exist as WO_2^{++} in strong acids and a complex of this ion with perchlorate may be active in oxidizing Sn(II). (3) A kinetic study of W(VI) catalyzed reduction of perchlorate-O^{18} with Sn(II) might be informative. (4) W(VI) may catalyze the oxidation of Ti(III) by perchlorate. (5) Some cryoscopic studies should be useful in these systems.