SMALL-RING COMPOUNDS—XXIX

A REINVESTIGATION OF THE SOLVOLYSIS OF CYCLOPROPYL-CARBINYL CHLORIDE IN AQUEOUS ETHANOL. ISOMERIZATION OF CYCLOPROPYLCARBINOL*†

Marjorie C. Caserio, William H. Graham‡ and John D. Roberts

Gates and Crellin Laboratories of Chemistry, California Institute of Technology, Pasadena, California

Abstract—The solvolysis of cyclopropylcarbinyl chloride in 80% ethanol is attended by substantial rearrangement—not only do the solvolysis products include cyclobutyl and allylcarbinyl alcohols and ethyl ethers but cyclopropylcarbinyl chloride undergoes partial rearrangement by "internal return" to cyclobutyl and allylcarbinyl chlorides. Nuclear magnetic resonance spectroscopy has been used to demonstrate that considerable isotope-position rearrangement takes place under quite mild conditions in the reactions of deuterium-labeled cyclopropylcarbinol and cyclobutanol with thionyl chloride. Isotope-position changes have been studied in the acid-induced isomerization of cyclopropylcarbinol.

INTRODUCTION

STUDIES of the solvolysis of cyclopropylcarbinyl chloride (I) in aqueous ethanol by two groups of workers have given somewhat different results. Chloride (I) was first obtained pure§ by Mazur[1] via vapor-phase photochlorination of methylcyclopropane, and he made a rather extensive investigation of its solvolysis reactions. The behavior of I in acetic acid was most unusual when viewed in the light of the knowledge of the time. In the first place, chloride I in this and other solvents was most uncommonly reactive for a saturated primary chloride; and, second, by the time 30 per cent of the theoretical amount of chloride ion was liberated, I essentially was completely converted to a mixture of substantially less reactive cyclobutyl and allylcarbinyl chlorides in a ratio of about 1·7 to 1. The acetolysis products arising from I were cyclopropyl-carbinyl and cyclobutyl acetates in the ratio of about 2·6 : 1 with perhaps a few percent of allylcarbinyl acetate as well.
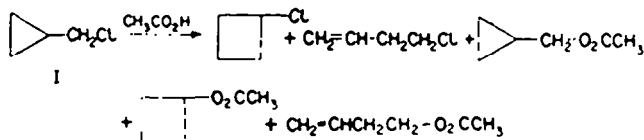
Similar, but much less extreme, behavior was noted in 50 per cent aqueous ethanol. In this solvent, rearrangement was found to occur at only about one-third the rate of

[1] J. D. Roberts and R. H. Mazur, *J. Amer. Chem. Soc.* **73**, 2509 (1951).

liberation of chloride ion. Although the reaction products were not determined in 50 per cent ethanol, the neutral heterogeneous reaction with water was found to give rearranged chlorides and a mixture of cyclopropylcarbinol cyclobutanol, and allylcarbinol in about the same proportions as formed from the treatment of either cyclopropylcarbinylamine or cyclobutylamine with nitrous acid.

The rearrangement of chloride I to cyclobutyl and allylcarbinyl chlorides in solvolytic reactions is now well understood as an example of "internal return" from an "intimate" carbocation-chloride ion pair. which phenomenon was first clearly demonstrated by Young, Winstein and Goering[2] for α,α-dimethylallyl chloride and subsequently scrutinized with great care by Winstein et al.[3] The abnormally high solvolytic reactivity of I and its tendency both to rearrange to isomeric chlorides and to form rearranged solvolysis products speak strongly for the intermediacy of a bridged, rather substantially stabilized carbonium ion embodying structural elements of the cyclopropylcarbinyl, cyclobutyl, and allylcarbinyl cations—the "non-classica" bicyclobutonium cation (II).[4]

$$
\begin{array}{c}
CH_2\!-\!CH \\
\diagdown \\
CH_2\cdots CH_2
\end{array}
$$
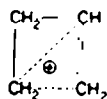
II

Chloride I has also been prepared by Brown and Borkowski[5] by liquid-phase chlorination of methylcyclopropane. The carefully purified product was judged to be 94 mole per cent I by analysis of its cooling curve. Solvolysis rate studies in 80 per cent ethanol showed the reactivity to be about 1/15 as large as t-butyl chloride, whereas a normal saturated primary chloride might be expected to form carbonium ions about 10^{10} times slower than t-butyl chloride.[6] No evidence for internal-return isomerization of chloride I can be deduced from the reported solvolysis rate measurements,[5] which were stated to be in accord with simple, first-order kinetics throughout. The solvolysis products were not investigated.

While the discrepancies between the above investigations may seem trivial, the finding of simple, first-order kinetics for the solvolysis of I[5] in aqueous ethanol, buttressed by the reported[7] formation of substantially pure cyclopropylcarbinyl ethyl ether from the solvolysis of cyclopropylcarbinyl benzenesulfonate in absolute ethanol,* has been taken as evidence for the conclusion that cyclopropylcarbinyl

* The significance of the particular experiment as a solvolysis is open to question. To be sure, Bergstrom and Siegel report an apparently insignificant increase in the first-order solvolysis rate constant of the benzenesulfonate in the presence of sodium ethoxide (from $6\cdot3 \cdot 10^{-5}$ to $7\cdot2 \cdot 10^{-5}$ sec^{-1} with 0·0266 M ethoxide) so that one might well infer a negligible contribution of non-rearranging S_N2 type substitution between the ester and ethoxide ion. However, a simple calculation shows that [benzenesulfonate]. [ethoxide] was $2\cdot1 \cdot 10^{3}$ times greater under the conditions where the reaction products were determined than under the conditions used for the kinetic runs. It should be clear that the seemingly small increase in the ethanolysis rate constant with a small amount of added ethoxide might well mean essentially exclusive S_N2 reaction where the arithmetic product of ester and ethoxide concentrations is so very high.

[2] W. G. Young, S. Winstein and H. L. Goering, J. Amer. Chem. Soc. 73, 1958 (1951).
[3] S. Winstein and A. H. Fainberg, J. Amer. Chem. Soc. 80, 459 (1958) and earlier papers.
[4] R. H. Mazur, W. N. White, D. A. Semenow, C. C. Lee, M. S. Silver and J. D. Roberts, J. Amer. Chem. Soc. 81, 4390 (1959).
[5] H. C. Brown and M. Borkowski, J. Amer. Chem. Soc. 74, 1894 (1952).
[6] L. C. Bateman, K. A. Cooper, E. D. Hughes and C. K. Ingold, J. Chem. Soc. 925 (1940); E. Grunwald and S. Winstein, J. Amer. Chem. Soc. 70, 841 (1948); S. Winstein, E. Grunwald and H. W. Jones, Ibid. 73, 2700 (1951).
[7] C. G. Bergstrom and S. Siegel, J. Amer. Chem. Soc. 74, 145 (1952).

derivatives may solvolyze by way of a cationic intermediate without formation of rearrangement products and that the enhanced rate of solvolysis may not be due to any driving force for formation of a non-classical cation.[8] It has been further maintained that the extraordinary facile interconversions of cyclopropylcarbinyl, cyclobutyl, and allylcarbinyl derivatives observed in amine-nitrous acid and many other carbonium ion type reactions[1,4] need not be typical of solvolysis or other reactions occurring under very mild conditions. The results obtained in the solvolysis of chloride I by Mazur[1] have been attributed to impurities[8] on the grounds that material of 94 per cent purity, prepared by Brown and Borkowski[5] gave a first-order rate of hydrogen chloride production.

The above criticisms of Mazur's work are important since they clearly strike at the very heart of the argument[4] for intervention of non-classical ions such as II in carbonium ion-type interconversion reactions of cyclopropylcarbinyl, cyclobutyl, and allylcarbinyl derivatives. Although, as indicated, the factual basis for the criticisms leaves much to be desired, the importance of the points in question has prompted us to repeat and extend much of the earlier work. The investigation has been greatly facilitated by the use of vapor-phase chromatography (v-p-c) which technique was not available at the time of the previous investigation. Fortunately, samples of I prepared by Mazur in 1950 were still available for analysis.

EXPERIMENTAL RESULTS

Vapor-phase chromatography is well suited for the analysis of cyclopropylcarbinyl cyclobutyl, and allylcarbinyl chlorides. Fig. 1A shows a chromatogram* for a typical chloride mixture resulting from the reaction of cyclopropylcarbinol with thionyl chloride. The composition of the mixture (69 per cent cyclopropylcarbinyl chloride, 27 per cent cyclobutyl chloride and 4 per cent allylcarbinyl chloride) agrees well with Mazur's infrared analysis of a mixture prepared in the same way (67 per cent cyclopropylcarbinyl chloride, 30 per cent cyclobutyl chloride, and 3 per cent allylcarbinyl chloride). The sample of chloride I used in Mazur's kinetic measurements[1] was found to be 99 · per cent cyclopropylcarbinyl chloride. Only a faint indication of allycarbinyl chloride was noted in the v-p-c analysis. Consequently, there seems to be no question that the internal-return mechanism must be invoked to account for the isomerization of the chloride during the solvolysis reaction because the chloride does not rearrange at the solvolysis temperature in the absence of an ionizing solvent or ionizing agent such as zinc chloride.

The internal consistency and clarity of the data reported by Mazur[1] for chloride I in acetic acid leave no room for doubt that, in acetic acid, solvolysis and rearrangement are very intimately related. The results in all respects are consistent with the formation of II (or its intimate ion-pair with chloride ion). We have seen no need to repeat this work nor the measurements of the kinetics of the solvolysis of I in 50 per cent aqueous ethanol since the essential point in question as to whether internal-return isomerization actually occurred has been answered in the affirmative by the finding that the starting chloride was even purer than advertised and by verification of the validity of the

---

* All vapor-phase chromatographic analyses reported herein were obtained with Perkin Elmer Vapor Fractometer using "A"-type packing (diisodecyl phthalate on crushed firebrick).

§ H. C. Brown, *Falk-Plaut Lecture*, Columbia University, March 6 (1957) and seminar at Harvard University, October 10 (1958).

infrared analysis used to establish the presence of rearranged chloride in the unreacted halide isolated from the reaction mixture.

We turn next to consideration of the solvolysis of I in 80 per cent ethanol for which clean, first-order kinetics are reported[5] and for which it has been inferred that no rearrangement products are formed.[8] The following technique was used in studying
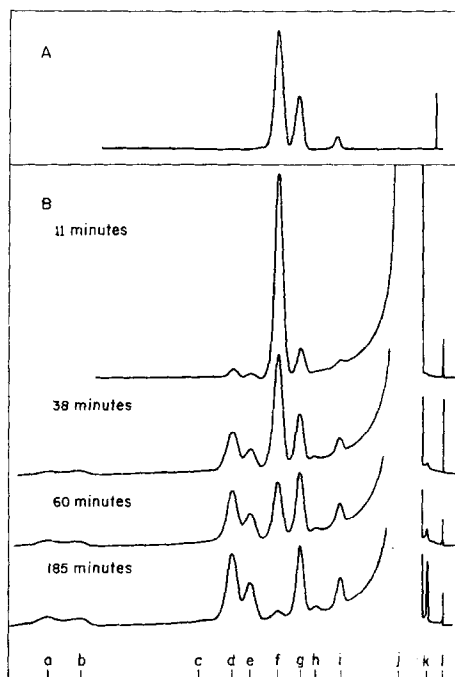

FIG. 1. A, v-p-c of chloride mixture from reaction of thionyl chloride with cyclopropyl-carbinol; B, v-p-c of mixtures from solvolysis of cyclopropylcarbinyl chloride in 80% ethanol at 97° showing the change of composition with time. Peaks were identified as: a, cyclobutanol; b, cyclopropylcarbinol; c, allylcarbinol; d, cyclopropylcarbinyl ethyl ether; e, cyclobutyl ethyl ether; f, cyclopropylcarbinyl chloride; g, cyclobutyl chloride; h, allylcarbinyl ethyl ether; i, allylcarbinyl chloride; j, solvent; k, hydrogen chloride; l, air.

this reaction and the solvolysis of cyclobutyl chloride. A few microliters of standard solutions of the chlorides in 80 per cent aqueous ethanol were sealed into melting point capillaries, heated to 97° for various periods, and then small samples of the intact reaction mixtures analyzed by v-p-c. The accuracy of the analyses was at first somewhat limited by lack of reproducibility of the size of the sample injected into the v-p-c apparatus, but this difficulty was surmounted by incorporating a few per cent of cyclohexane in the reaction mixture to act as an internal standard. The added cyclohexane made no discernible change in the results except to permit considerably greater analytical precision. Since the supply of Mazur's high-purity chloride was limited, we used a somewhat less pure material (96 per cent cyclopropylcarbinyl, 2 per cent cyclobutyl, and 2 per cent allylcarbinyl chlorides) prepared from cyclo-propylcarbinol and thionyl chloride in ether in the presence of tri-n-butylamine.[9,*]

---

* This reaction, when carried out with crotyl alcohol, gives no allylic rearrangement.

[9] R. H. DeWolfe and W. G. Young, *Chem. Rev.* **56**, 815 (1956); F. F. Caserio, Jr., Ph.D. Thesis, U.C.L.A. (1954).

The v-p-c tracings for typical solvolysis mixtures of 1 in 80 per cent ethanol are shown in Fig. 1B. The substances responsible for the various v-p-c peaks were assigned, by comparison of retention times, with those established for known samples. It is clear that solvolysis under these circumstances yields a variety of rearrangement products as chlorides, alcohols, and ethyl ethers. Fig. 2 shows the progress of the reaction as measured by the proportions of the various products formed. Again we conclude that solvolysis and rearrangement are intimately related.
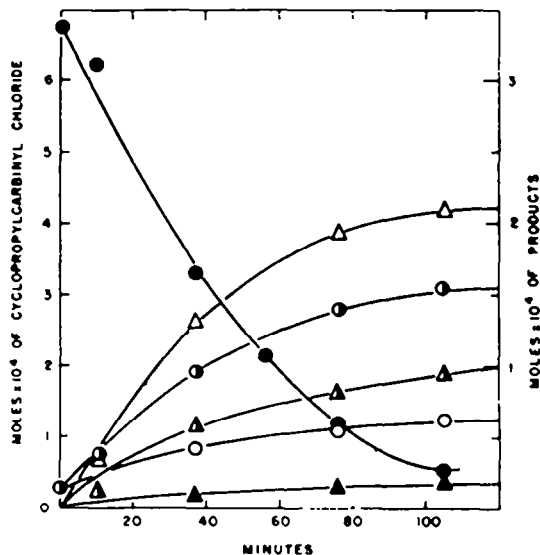

FIG. 2. Rate of change in composition of the mixture from the solvolysis of cyclopropyl-carbinyl chloride in 80% ethanol at 97°: ● cyclopropylcarbinyl chloride, ◑ cyclobutyl chloride, ○ allylcarbinyl chloride, △ cyclopropylcarbinyl ethyl ether, ▲ cyclobutyl ethyl ether, ▲ allylcarbinyl ethyl ether. Cyclopropylcarbinol, cyclobutanol and allylcarbinol are also formed in small amounts but their formation is not shown.
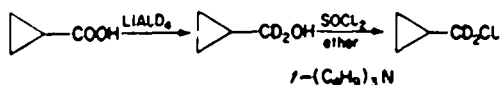
Weight has been added to the argument[4] for intervention of a common inter-mediate(s) in solvolysis reactions of cyclopropylcarbinyl and cyclobutyl chlorides by evidence for close similarity (in energy, at least) of the solvolysis transition states for these chlorides with the aid of the procedure discussed by Winstein and Kosower[10]. Thus, isomerization of cyclopropylcarbinyl chloride with zinc chloride at 25° gives a mixture of cyclobutyl-cyclopropylcarbinyl chlorides, the approximate equilibrium composition of which was determined by v-p-c as about 36/1 in favor of cyclobutyl chloride. The ratio of the total rates of disappearance of the chlorides (solvolysis plus internal-return isomerization) in 80 per cent ethanol at 97° is $1·37 \times 10^{-5}$ $\sec^{-1}/4·17 \times 10^{-4} \sec^{-1}$ equal to 1/30. Assuming that the equilibrium and relative rate data are not subject to large changes with change of media and temperature, the conclusion follows that the difference in rates between the two chlorides is not due to differences in transition-state stabilities but to differences in ground-state stabilities.*

* This possibility was suggested previously[1] but not given appropriate emphasis partly because no adequate data for the equilibrium composition was available.

[10] S. Winstein and E. M. Kosower, J. Amer. Chem. Soc. 81, 4399 (1959); see also, E. F. Cox, Ph.D. Thesis, California Institute of Technology (1955).

The isomerization of cyclopropylcarbinyl chloride to cyclobutyl and allylcarbinyl chlorides induced by ionizing solvents is an excellent example of an interconversion reaction occurring under exceptionally mild conditions. Considerable interest is therefore attached to the degree of isotope-position rearrangement which accompanies this process. Some information bearing on this point has been obtained by deuterium-labeled chloride as follows.

First of all, the synthesis of cyclopropylcarbinyl chloride labeled with deuterium in the x-position presented a considerable problem. It was known from Mazur's[1] work that the reaction of cyclopropylcarbinol with thionyl chloride, with or without pyridine, gives a mixture of isomeric chlorides which cannot be separated conveniently. Allylic alcohols behave similarly under these conditions. However, chlorides may be prepared from primary allylic alcohols and thionyl chloride without rearrangement[9] if the reaction is carried out under carefully controlled conditions in the presence of an equivalent amount of tri-n-butylamine in ether or pentane solution. Using these conditions, a typical product obtained from cyclopropylcarbinol was found to consist of 91 per cent cyclopropylcarbinyl chloride, 8 per cent cyclobutyl chloride, and 1 per cent allylcarbinyl chloride. Clearly, the propensity for rearrangement in this system is high even under mild conditions known to give no rearrangement with allyl derivatives. Despite this, the method was used reasonably successfully for the preparation of deuterium-labeled cyclopropylcarbinyl chloride as shown in the following scheme:

$$\triangleright\text{—COOH} \xrightarrow{\text{LIALD}_4} \triangleright\text{—CD}_2\text{OH} \xrightarrow[\text{ether}]{\text{SOCL}_2} \triangleright\text{—CD}_2\text{CL}$$
$$t\text{-(C}_4\text{H}_9)_3\text{N}$$

The nuclear magnetic resonance (NMR) spectra of cyclopropylcarbinyl and cyclopropylcarbinyl-x-^{2}H$_2$ chlorides are shown in Figs. 3A and 3B, respectively. The characteristic doublet of the carbinyl protons is barely evident in the labeled chloride, and it is estimated that less than 4 per cent isotopic rearrangement occurred during its formation. This estimate was made from the peak area of the carbinyl protons relative to the tertiary ring proton which, of course, is assumed to be 2:1 in the unlabeled chloride.

In an attempt to observe isotope-position rearrangement during hydrolysis, a sample of cyclopropylcarbinyl-x-^{2}H$_2$ chloride (containing 6 per cent cyclobutyl chloride) was shaken with water in a sealed tube at 97°. After 140 minutes, the unreacted chloride was separated from the aqueous layer and analyzed by v-p-c. The ratio of chlorides, cyclopropylcarbinyl:cyclobutyl:allylcarbinyl, was found to be 7·5:3·2:1·0, respectively. The hydrolysis products remained largely in aqueous solution, but small amounts of alcohols (and water) were also present in the chloride mixture. The NMR spectra of this mixture and that obtained from unlabeled chloride under the same conditions are shown in Figs. 3C and 3D, respectively. The incidence of isotopic rearrangement is evident from Fig. 3C, which shows a sharp doublet due to the carbinyl protons of cyclopropylcarbinyl chloride, the spectrum of which was barely evident initially (cf. Fig. 3B). Unfortunately, the complexity of the spectrum precluded a *precise* measurement of how much rearrangement of the deuterium label had occurred. However, it is estimated from the ratio of peak areas of the carbinyl and tertiary cyclopropylcarbinyl protons that some 24 per cent of isotopically
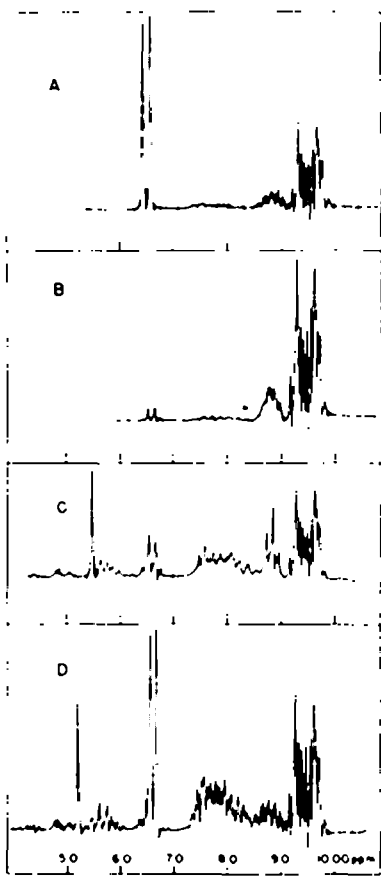
FIG. 3. NMR spectra at 60 mc in ppm relative to tetramethylsilane as internal standard (equal to 10 ppm). A, cyclopropylcarbinyl chloride from photochlorination of methylcyclopropane;[1] B, cyclopropylcarbinyl-α-²H₂ chloride from cyclopropylcarbinol-α-²H₂ and thionyl chloride in ether and tri-n-butylamine; C, chloride mixture from hydrolysis of cyclopropylcarbinyl-α-²H₂ chloride; D, chloride mixture from hydrolysis of cyclopropylcarbinyl chloride.
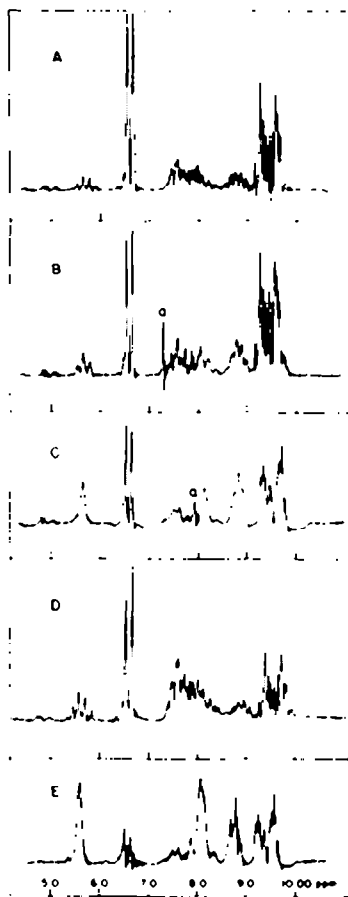
FIG. 4. NMR spectra at 60 mc in ppm relative to tetramethylsilane as internal standard (equal to 10 ppm) of chloride mixtures obtained from reaction of thionyl chloride with: A, cyclopropylcarbinol or cyclobutanol; B, cyclopropylcarbinol-α-²H₂, peak marked a is impurity; C, cyclobutanol-2,4-²H₄, peaked marked a is impurity; D, cyclobutanol in presence of tri-n-butylamine and ether; E, cyclobutanol-2,4-²H₄, conditions as in C.

rearranged cyclopropylcarbinyl chloride is present in the mixture. Further evidence for isotope-position rearrangement was obtained from other related reactions which we now describe.

It was originally observed by Mazur that chloride mixtures of the *same* composition were obtained from the reaction of cyclopropylcarbinol and cyclobutanol with thionyl chloride (no solvent). We have repeated these reactions with deuterium-labeled alcohols, using the conditions defined by Mazur, in order to observe the extent of isotope-position rearrangement in the chloride mixtures by means of NMR. The labeled alcohols required for these experiments were prepared as follows. Cyclopropylcarbinol-α-²H₂ was prepared by the reduction of cyclopropanecarboxylic acid

with lithium aluminum deuteride. To obtain deuterium-labeled cyclobutanol, cyclobutanone-2,4-$^2H_4$ was prepared to about 95 per cent isotopic purity by base-catalyzed exchange of cyclobutanone in deuterium oxide and the product was subsequently reduced to the alcohol with lithium aluminum hydride. The NMR spectrum of the crude labeled ketone is shown in Fig. 6C and may be compared to the
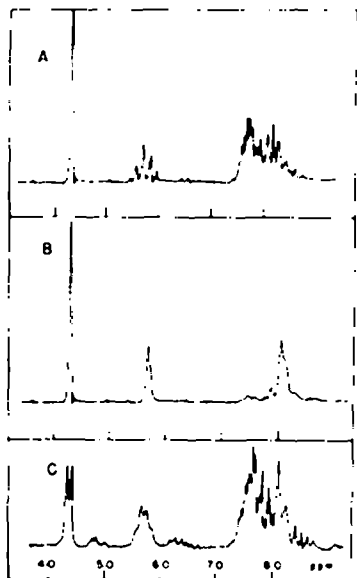

FIG. 5. NMR spectra at 60 mc in ppm relative to tetramethylsilane as internal standard (equal to 10 ppm). A, cyclobutanol from acid-catalyzed rearrangement of cyclopropylcarbinol; B, cyclobutanol-2,4-$^2H_4$; C, deuterium-labeled cyclobutanol from acid-catalyzed rearrangement of cyclopropylcarbinol-α-$^2H_2$(allylcarbinol is also present in small amounts).

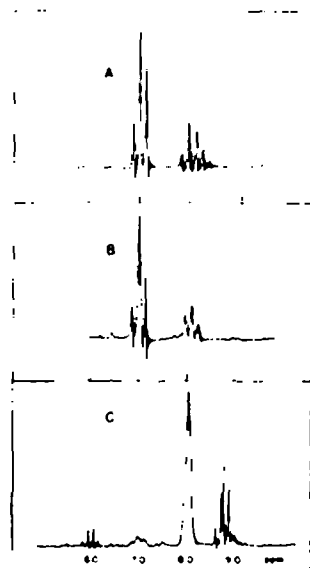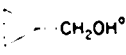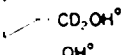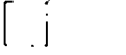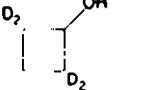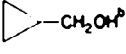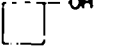FIG. 6. NMR spectra at 60 mc in ppm relative to tetramethylsilane as internal standard (equal to 10 ppm). A, cyclobutanone; B, deuterium-labeled cyclobutanone from oxidation of labeled cyclobutanol (minor peaks are due to impurities); C, cyclobutanone-2,4-$^2H_4$ (impure).

spectrum of unlabeled cyclobutanone in Fig. 6A. The spectrum of the labeled ketone was run at high gain in order to detect any residual protonation of the 2 and 4 positions. The presence of significant amounts of impurities is apparent, but it is also evident that there remains only 4–5 per cent of ketone with protons in the 2 or 4 positions. The spectra of cyclobutanol and cyclobutanol-2,4-$^2H_4$ are shown in Figs. 5A and 5B, respectively. The 3-methylene protons of the labeled alcohol appear as a rather indistinct quartet since these two protons are non-equivalent; the 4–5 per cent of 2- or 4-protonated material appears on the low field side of this quartet.

The composition of the chloride mixtures from the thionyl chloride reaction was determined by v-p-c. The results are shown in Table 1 and, clearly, they confirm that the *same* mixture of chlorides is obtained from either alcohol. The NMR spectra corresponding to the chloride mixtures obtained from cyclopropylcarbinol (or cyclobutanol), cyclopropylcarbinol-α-$^2H_2$, and cyclobutanol-2,4-$^2H_4$ are shown respectively in Figs. 4A, 4B and 4C. They are exceedingly complex, and it was not possible to determine the distribution of the deuterium label within the cyclobutyl ring with certainty. However, by focusing attention on the sharp doublet of the carbinyl protons

TABLE 1. PERCENT COMPOSITION OF CHLORIDE MIXTURES FROM REACTION OF THIONYL CHLORIDE WITH CYCLOPROPYLCARBINOL AND CYCLOBUTANOL

| Alcohol	Cyclopropylcarbinyl	Cyclobutyl	Allylcarbinyl
	%	%	%
⟋—CH$_2$OH[a]	69	27	4
⟋—CD$_2$OH[a]	67	28	5
(cyclobutanol) OH[a]	69	25	6
D$_2$ ⟋OH[a] D$_2$	67	29	4
▷—CH$_2$OH[b]	~67	~30	~3
(cyclobutyl) OH[b]	~67	~30	~3

[a] Analyzed by v-p-c.
[b] Analyzed by infrared spectrometry.[1]

of cyclopropylcarbinyl chloride, one thing becomes immediately apparent—in order for this doublet to appear at all, extensive isotope-position rearrangement must have occurred during the formation of cyclopropylcarbinyl chloride from both deuterium-labeled alcohols. Moreover, the area of this doublet relative to the area of the tertiary ring hydrogen of cyclopropylcarbinyl chloride permits a rough estimate of the percent isotopic rearrangement to be made. Such measurements reveal that 66 ± 5 per cent of the cyclopropylcarbinyl chloride obtained from cyclopropylcarbinol-α-^{2}H$_2$ has a —CH$_2$—- group in the α-position, while 33 ± 2 per cent of the chloride from cyclo-butanol-2,4-^{2}H$_4$ has a —CH$_2$—- group in the α-position. These figures closely approach the values of 67 per cent and 33 per cent, respectively, for a statistical distribution of the deuterium label in cyclopropylcarbinyl chloride derived from both labeled alcohols. Thus, the three methylene groups of cyclopropylcarbinol and cyclobutanol achieve near equivalence during reaction—a result which, in conjunction with the identity of product composition, argues for formation of the same cationic intermediates from either alcohol. As a check on the validity of area measurements, the ratio of cyclo-propylcarbinyl chloride to the cyclobutyl chloride present was estimated from the ratio of peak areas of the tertiary proton of each chloride. The results gave a ratio of cyclopropylcarbinyl to cyclobutyl of $2\cdot28 \pm 0\cdot12$ and $2\cdot26 \pm 0\cdot19$ for the chlorides from labeled cyclopropylcarbinol and cyclobutanol, respectively (cf. Figs. 3B and 3C), while analysis by v-p-c gave the ratio as $2\cdot3$ (cf. Table 1). The agreement is satisfactory.

On treating these same alcohols with thionyl chloride in the presence of tri-n-butyl-amine in a non-ionizing solvent (ether or pentane) somewhat different results were obtained as already discussed in the case of cyclopropylcarbinol. Under these conditions, cyclobutanol reacted with extensive rearrangement to give 45 per cent cyclopropylcarbinyl, 50 per cent cyclobutyl, and 5 per cent allylcarbinyl chlorides.

The NMR spectrum of the mixture is shown in Fig. 4D. If one assumes that the product distribution arising from carbonium ion intermediates is the same as that obtained in the absence of added base and solvent (cf. Table 1), then it may be estimated that 66 per cent of reaction takes an ionic path with rearrangement and 34 per cent proceeds without rearrangement probably by an S_N2 displacement.[9] The NMR spectrum of the chloride mixture from cyclobutanol-2,4-$^2H_4$ (Fig. 4E) is especially interesting since it shows that only 16·5 $\pm$ 1 per cent of the $-CH_2-$ group turns up in the α-position of cyclopropylcarbinyl chloride. Again, the area measurements were judged to be significant since the ratio of cyclopropylcarbinyl chloride to cyclobutyl chloride was determined as 1·03 $\pm$ 0·10 by NMR and 0·9 by v-p-c. In this case then, the extent of isotopic rearrangement is about one half that expected for complete equilibration of the three methylene groups. This result is highly significant in that it rules out the possibility of a symmetrical ion such as III as the sole intermediate in these interconversion reactions. The methylene groups are completely equivalent in III, which inevitably would lead to products with a random isotope distribution under any set of reaction conditions. A similar conclusion was reached from the results of nitrous-acid deamination of cyclopropylcarbinylamine-α-^{14}C[4]. The ^{14}C-distribution in the products, cyclopropylcarbinol and cyclobutanol, showed that extensive but not random ^{14}C-rearrangement had taken place. It was suggested that these results could

III
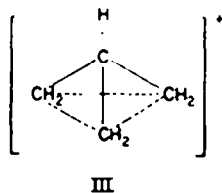
best be explained by the intermediacy of the unsymmetrical bicyclobutonium ions IIa, IIb, and IIc, which equilibrate rapidly but not instantaneously. Clearly, the present results can be rationalized by these same intermediates. The advent of less isotopic

IIa   IIb   IIc
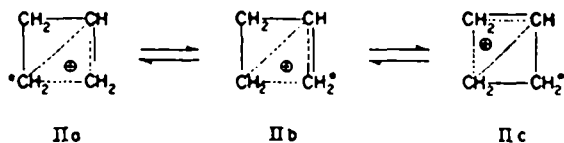
rearrangement in the reaction of cyclobutanol with thionyl chloride when carried out in the presence of tri-n-butylamine in ether solution is indicative that equilibration of IIa–c is not fully attained in this medium. Under the best ionizing conditions, when the alcohol acts as its own solvent, equilibration is attained more rapidly and results in a more nearly random isotope distribution.

Cyclopropylcarbinol has been found to undergo a facile rearrangement in dilute aqueous acid to give cyclobutanol and small amounts of allylcarbinol.[*] The rearrangement, which provides an excellent synthetic route to cyclobutanol, has been studied with the aid of cyclopropylcarbinol-α-$^2H_2$, and it was hoped that the position of the deuterium label in the resulting cylcobutanol could be observed from its NMR

* This rearrangement was first observed by Mr. David I. Schuster in these Laboratories.

spectrum. Unfortunately, the spectrum of the product turned out to be too complex to interpret (Fig. 5C). To overcome this, the labeled cyclobutanol was oxidized to cyclobutanone with chromic oxide in pyridine, and the distribution of deuterium was observed from the NMR spectrum of the cyclobutanone which is relatively simple. The spectra obtained for both labeled and unlabeled cyclobutanones are shown in Figs. 6A and 6B, respectively. The presence of 2-labeled cyclobutanone in the rearrangement product is clearly evident from Fig. 6B since the five-line spectrum of the 3-methylene protons in the unlabeled ketone is reduced to a broad triplet in the labeled material. Equally clear is the presence of 3-labeled cyclobutanone since the triplet due to the 2-methylene protons has a central peak of far greater intensity than in the unlabeled ketone. Thus, the deuterium label is found in all three methylene groups of the ring. The relative amounts of 2- and 3-labeled cyclobutanones may be roughly calculated from relative peak areas. The area of the 2- and 4-protons relative to the 3-protons was measured as $2 \cdot 1 \pm 0 \cdot 1$, which gives the composition of the mixture as 67 per cent cyclobutanone-2-^{2}H$_2$ and 33 per cent cyclobutanone-3-^{2}H$_2$. Consequently, it is inferred that cyclobutanol derived from cyclopropylcarbinol-α-^{2}H$_2$ has the deuterium-labeled methylene group statistically distributed between the 2,3- and 4-ring positions.

EXPERIMENTAL

Cyclopropylcarbinol-α-^{2}H$_2$. (b.p. 121–122·5 , 746 mm) was prepared in 75 % yield by the reduction of cyclopropanecarboxylic acid with lithium aluminum deuteride.

Cyclobutanol-2,4-^{2}H$_4$. A mixture of three parts of cyclobutanone to four parts of dueterium oxide, 0·1 M in sodium acetate, was heated in a sealed tube at 97° for 37 hr. The ketone was recovered from solution and similarly treated with fresh deuterium oxide, 0·1 M in sodium acetate. The crude, recovered cyclobutanone gave an NMR spectrum showing 95 % deuterium in the 2- and 4-positions (Fig. 6C). This material was reduced with lithium aluminum hydride, and the crude product was fractionally distilled. The purest fraction of labeled cyclobutanol obtained which was used in subsequent experiments had b.p. 122·5 123·0° at 745 mm, n_D^{23} 1·4315, and gave a single peak in the v-p-c. The NMR spectrum of this material is shown in Fig. 5B.

Cyclobutanol from cyclopropylcarbinol. A solution of cyclopropylcarbinol (30·0 g) in 280 ml water and 25 ml conc hydrochloric acid was heated on a steam bath for 100 min. Most of the acid was neutralized by the addition of 11·0 g sodium hydroxide pellets to the cooled mixture. Neutralization was completed with potassium carbonate. The mixture was continuously extracted with ether and the ether extracts were dried over magnesium sulfate, filtered, and the ether removed by distillation. The residue was distilled through a small wire spiral-packed column to give 21·6 g (72 %) material, b.p. 121 -124', which analyzed by v-p-c as 97 % cyclobutanol and 3 % allylcarbinol.

By the above procedure, 5·33 g of cyclopropylcarbinol-α-^{2}H$_2$ gave 3·73 g (70 %) deuterium-labeled material, b.p. 121·5-125 , which analysed by v-p-c as 93 % cyclobutanol and 7 % allylcarbinol.

Oxidation of deuterium-labeled cyclobutanol to cyclobutanone. The oxidizing agent employed was chromic oxide in pyridine, and the procedure was essentially that described by Poos *et al.*[11] To a stirred suspension of chromic oxide-pyridine complex in pyridine (5·0 g chromic oxide to 48 g pyridine) at 17 was added 3·53 g deuterium-labeled cyclobutanol (containing 7 % allylcarbinol) in 32 g pyridine. The mixture was allowed to stand at room temp for about 18 hr. The pyridine was converted to the hydrochloride by the addition of 98 g conc hydrochloric acid in 100 g ice water to the ice-cooled mixture. The resulting solution was evaporated immediately *in vacuo* at room temp and the vapors condensed in a series of dry ice traps. The aqueous distillate was continuously extracted with ether and the ether extracts were dried over sodium sulfate and distilled. The crude product obtained was shown by v-p-c to consist of unreacted cyclobutanol, cyclobutanone, and small amounts of allyl-carbinol. The cyclobutanone was separated from the alcohols by v.p.c. using a preparative column.

Thionyl chloride reactions. Thionyl chloride (1·65 g) was added dropwise to 1·0 g cyclopropyl-carbinol at 0' with stirring. Evolution of sulfur dioxide immediately took place. The mixture was

[11] G. I. Poos, G. E. Ayth, R. E. Beyler and L. H. Sarett, *J. Amer. Chem. Soc.* **75**, 422 (1953).

4

allowed to stand at room temp for 3·5 hr. Dissolved hydrogen chloride was neutralized by the addition of a few drops of water and solid potassium carbonate. The chloride mixture was analyzed by v-p-c and then distilled. The product composition was found not to vary with reaction time; however, on working up the mixture immediately upon addition of thionyl chloride, some unrearranged cyclopropylcarbinol was recovered. Cyclopropylcarbinol-α-$^2H_2$, cyclobutanol, and cyclobutanol-2,4-$^2H_4$ were treated with thionyl chloride exactly as described for cyclopropylcarbinol.

To a well-stirred, ice-cooled mixture of 10·0 g (0·139 mole) of cyclopropylcarbinol, 25·4 g (0·139 mole) of tri-n-butylamine (b.p. 123° at 51 mm) in 200 ml ether was added 16·5 g (0·139 mole) of thionyl chloride at such a rate that the temp did not exceed 6°. The addition took about 80 min and the precipitate which formed during the addition eventually re-dissolved to give two liquid phases, one of which was orange-yellow in color. The volatile components were flash-distilled *in vacuo* and trapped at −78°. The ether was evaporated from the distillate and the residue, after analysis by v-p-c, was fractionally distilled. There was obtained overall 10·8 g (86%) material, b.p. 82·5 85·5° at 748 mm, of which 2·9 g had b.p. 85·5° and which analyzed for 97% cyclopropylcarbinyl chloride and 3% cyclobutyl chloride.

Cyclopropylcarbinyl-α-$^2H_2$ chloride was prepared by this method. On treating cyclobutanol and cyclobutanol-2,4-$^2H_2$ with thionyl chloride as described above, the reaction was found to be appreciably slower; it was necessary to leave the reaction mixture at room temp for 3 hr before flash-distilling the products. Shorter reaction times gave poor yields, yet the product composition remained unchanged.