of fraction I in section a of the experiment entitled "Ethyl Iodide with Potassium 2,6-Di-*t*-butylphenoxide."

The light yellow solid II, m.p. 30–32°, had an infrared spectrum devoid of phenolic absorption, but showed a doublet at 6.00 and 6.06 μ (dienone). The ultraviolet spectrum exhibited a maximum at 242 mμ (cross-conjugated dienone).[15] Gas chromatographic analysis showed a single peak. *Anal.* Calcd. for $C_{18}H_{30}O$: C, 82.38; H, 11.52; mol. wt., 267. Found: C, 82.25; H, 11.71; mol. wt. (cryoscopic in camphene), 248, 250. Thus II is 2,6-di-*t*-butyl-4,4-diethyl-2,5-cyclohexadienone. A mixed m.p. with the dienone, m.p. 29–31°, isolated in section b of the experiment "Ethyl Iodide with Potassium 2,6-Di-*t*-butylphenoxide," was undepressed. Furthermore, the infrared and ultraviolet absorption spectra of these two dienones are identical.

The yellow liquid III exhibited phenolic absorption at 2.75 μ and a doublet at 6.05 and 6.10 μ (dienone). The ultraviolet spectrum showed absorption at 283 mμ (aromatic absorption) and at 318 mμ. The doublet in the infrared and the peak at 318 mμ suggest the presence of the 2,6-di-*t*-butyl-4,6-diethyl-2,4-cyclohexadienone.

Preparation of 2,6-Di-*t*-butylphenetole.—Prior to carrying out the experiment "Ethyl Iodide with Potassium 2,6-Di-*t*-butylphenoxide" as described above, a run was made with the purpose of obtaining a pure sample of 2,6-di-*t*-butylphenetole. After treatment with sodium hydride a neutral fraction corresponding to A was obtained. On chromatographing 2.00 g. of this neutral material on basic alumina (Merck) with petroleum ether (35–37°), there was isolated 0.48 g. of a white solid, m.p. 50–57°. On rechromatographing, this gave 0.12 g. of white crystals, m.p. 57–58.5°. The infrared spectrum was devoid of phenolic and dienone absorption, but exhibited ether absorption at 7.95 μ. Also, gas chromatographic analysis showed only one peak.

Anal. Calcd. for $C_{16}H_{26}O$: C, 81.99; H, 11.18. Found: C, 81.98; H, 11.12.

Isopropyl Iodide with Potassium 2,6-Di-*t*-butylphenoxide.—To 20.0 g. (0.097 mole) of 2,6-di-*t*-butylphenol dissolved in 25 ml. of *t*-butyl alcohol was added 93 ml. (0.097 mole) of a 1.05 *N* solution of potassium *t*-butoxide in *t*-butyl alcohol and 50 ml. of tetraethylene glycol dimethyl ether. To the resulting green solution was added 50.0 ml. (0.45 mole) of isopropyl iodide ($n^{20}\mathrm{D}$ 1.4994). As the reaction proceeded precipitation occurred and the solution turned orange. The reaction was allowed to proceed for 29 hours at room temperature, and a slow stream of nitrogen was bubbled through the reaction mixture. The exit gases passed, in turn, through two ice-cooled traps each containing 5 ml. (0.098 mole) of bromine in 75 ml. of methylene chloride and then an empty trap, cooled to −80°. After 29 hours the reaction mixture was poured into 250 ml. of distilled water and extracted with petroleum ether (35–37°). The extract was washed several times with distilled water and dried over anhydrous sodium sulfate. Removal of the petroleum ether gave 21.2 g. of crude product as a red liquid (I). Titration of the aqueous layer for iodide ion showed the reaction to be complete.

The contents of the traps were combined and washed with aq. sodium sulfite until the methylene chloride layer was colorless. The methylene chloride phase then was washed with aq. sodium bicarbonate, distilled water and dried over anhydrous magnesium sulfate. Removal of the solvent left 11.0 g. of a residue as a yellow liquid (II).

Gas chromatographic analysis of I showed only two peaks and quantitative studies showed that 68% of the mixture was 2,6-di-*t*-butylphenol and 32% 2,6-di-*t*-butyl-4-isopropylphenol. This corresponds to 14.4 g. (0.070 mole) of 2,6-di-*t*-butylphenol and 6.80 g. (0.027 mole) of 2,6-di-*t*-butyl-4-isopropylphenol. Thus, 28% alkylation occurred, and proceeded quantitatively to give the *p*-isopropylated phenol. Furthermore, the infrared spectrum of a synthetic mixture of these two phenols is identical with that of I. A 1.00-g. sample of I was chromatographed on silica gel (Davison 200-mesh) with petroleum ether to give 0.14 g., m.p. 39–41°, 2,6-di-*t*-butyl-4-isopropylphenol; mixed m.p. with authentic 2,6-di-*t*-butyl-4-isopropylphenol 39–41°, lit.[18] m.p. 38–42°.

Anal. Calcd. for $C_{17}H_{28}O$: C, 82.20; H, 11.36. Found: C, 82.00; H, 11.18.

Six grams of II was made up to 100 ml. in methylene chloride. Quantitative gas chromatographic analysis showed that 5.25 g. of 1,2-dibromopropane was present. Since the reaction of isopropyl iodide with potassium 2,6-di-*t*-butylphenoxide went to completion (see above), and since only 28% alkylation was achieved, 72% elimination must have occurred. The 5.25 g. of dibromopropane corresponds to 49% elimination, *i.e.*, to a 68% yield. Distillation of 5.00 g. of II gave a 0.50-g. forerun of a yellow liquid (b.p. 110–130°) and then 3.76 g. of pure 1,2-dibromopropane, b.p. 136–138°, $n^{20}\mathrm{D}$ 1.5189–1.5190; lit.[19] b.p. 139–142°, $n^{20}\mathrm{D}$ 1.5194.

Anal. Calcd. for $C_3H_6Br_2$: C, 17.84; H, 3.00; Br, 79.16. Found: C, 17.86; H, 3.17; Br, 79.15.

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[18] C. D. Cook and B. E. Norcross, *J. Am. Chem. Soc.*, **78**, 3797 (1956).

[19] M. S. Kharasch and F. R. Mayo, *ibid.*, **55**, 2468 (1953).

[CONTRIBUTION NO. 2666 FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, PASADENA, CALIF., AND THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE, MASS.]

Small-Ring Compounds. XXXV. Studies of Rearrangements in the Nitrous Acid Deaminations of Methyl-substituted Cyclobutyl-, Cyclopropylcarbinyl- and Allylcarbinylamines[1a,b]

BY MARC S. SILVER,[1c] MARJORIE C. CASERIO, HOWARD E. RICE AND JOHN D. ROBERTS

RECEIVED MARCH 3, 1961

The compositions of the alcohol mixtures formed in nitrous acid deaminations of cyclopropylmethylcarbinylamine, (2-methylcyclopropyl)-carbinylamine, 2-methylcyclobutylamine, 3-methylcyclobutylamine, crotylcarbinylamine and allylmethylcarbinylamine have been determined. These results and the behavior of the corresponding alcohols under isomerization conditions in strongly acidic media may be explained by assuming formation of three non-equivalent, unsymmetrical, non-classical cationic intermediates analogous to those previously proposed for the carbonium ion reactions of other small-ring derivatives.

Introduction

The pattern of reaction products from carbonium ion-type reactions of cyclobutyl, cyclopropylcarbinyl and allylcarbinyl derivatives cannot be satisfactorily explained by assuming formation of the highly symmetrical "tricyclobutonium ion" intermediate (I).[2] However, the experimental

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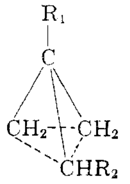
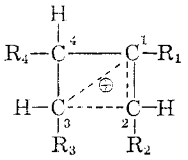
[1] (a) Supported in part by the National Science Foundation and the Petroleum Research Fund of the American Chemical Society. Grateful acknowledgment is hereby made to the Donors of this Fund. (b) Presented at the Sixteenth National Organic Chemistry Symposium of the American Chemical Society, June 15, 1959, Seattle, Wash.; *cf.* the Symposium Abstracts, p. 1-10. (c) National Science Foundation Predoctoral Fellow, 1955–1958.

[2] R. H. Mazur, W. N. White, D. A. Semenow, C. C. Lee, M. S. Silver and J. D. Roberts, *J. Am. Chem. Soc.*, **81**, 4390 (1959).

data can be correlated in terms of formation and limited interconversion of three unsymmetrical "bicyclobutonium ions" (II).[2]



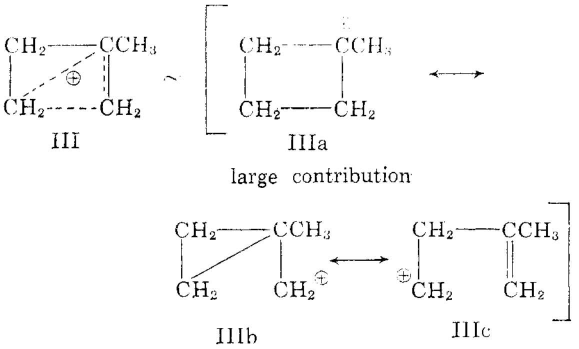
I, $R_1 = R_2 = H$
Ia, $R_1 = CH_3, R_2 = H$
Ib, $R_1 = H, R_2 = CH_3$



II, $R_1 = R_2 = R_3 = R_4 = H$
IIa, $R_1 = CH_3, R_2 = R_3 = R_4 = H$
IIb, $R_2 = CH_3, R_1 = R_3 = R_4 = H$
IIc, $R_3 = CH_3, R_1 = R_2 = R_4 = H$
IId, $R_4 = CH_3, R_1 = R_2 = R_3 = H$

An important point of difference between I and II is that I has two possible non-equivalent positions for location of a single substituent group (neglecting geometrical isomerism) that are here designated by R_1 and R_2. With II, there are four such positions, designated as R_1, R_2, R_3 and R_4.

Examination of carbonium ion-type reactions of 1-methylcyclobutyl and (1-methylcyclopropyl)-carbinyl derivatives that could afford Ia and/or IIa as intermediates has led us to the conclusion the results are best explained by assuming structures of type II are more important than those of type I.[3] In this case, a dominant resonance contribution appears to be made by a valence-bond structure corresponding to the classical 1-methylcyclobutyl cation with the result that the positive charge must be rather highly localized on the methyl-bearing carbon atom, as can be symbolized by the hybrid structure III. This picture of the intermediate III is different from the alternate and (perhaps to some readers) the more obvious representation of three classical, equilibrating ions IIIa-c with IIIa being the most favored. Either way, the result is that both (1-methylcyclopropyl)-carbinyl and 1-methylcyclobutyl derivatives react in carbonium ion-type reactions to give only 1-methylcyclobutyl products.



III

IIIa

large contribution

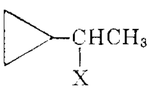
IIIb

IIIc

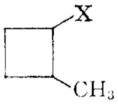
smaller contributions

The effect of methyl groups as substituents at the R_2, R_3 and R_4 positions is the subject of the present paper. The amine–nitrous acid reaction has served as the primary investigative tool.

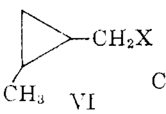
There are seven amines (IVa–Xa) that, upon deamination, might form IIb, IIc and IId by processes involving only the interchange of rings for double bonds, and *vice versa*. All of these amines



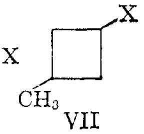
IV



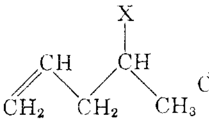
V



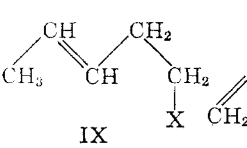
VI



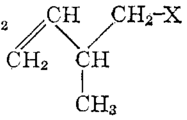
VII



VIII



IX



X

IVa–Xa, X = NH_2; IVb–Xb, X = OH

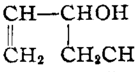
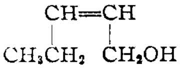
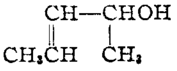
except Xa have been synthesized, treated with aqueous nitrous acid and the resulting alcohol mixtures analyzed. No effort was made to separate *cis-trans* isomers where such were possible. The expectation was that both isomers would behave similarly under the reaction conditions; no definite evidence to the contrary of this was noted.

Results and Discussion

The compositions of the alcohol mixtures resulting from the deamination of the amines IVa–IXa are listed in Table I. The analyses utilized vapor phase chromatography (v.p.c.) and infrared spectroscopy and are believed to be accurate to ±3%. The analytical procedures and some of the control experiments are described in the Experimental section. It was shown that 2-methylcyclobutanol was stable under the reaction conditions and, furthermore, that the composition of a mixture of 3-methylcyclobutanol, (2-methylcyclopropyl)-carbinol, cyclopropylmethylcarbinol and allylmethylcarbinol was not appreciably altered under the same conditions.

TABLE I

PERCENTAGE COMPOSITIONS OF ALCOHOLS FROM NITROUS ACID DEAMINATIONS OF METHYL-SUBSTITUTED CYCLOBUTYL-, CYCLOPROPYLCARBINYL- AND ALLYLCARBINYL-AMINES

Alcohol	IVa	Va	VIa	VIIa	VIIIa	IXa
IVb	100	100	51	47	17	74
Vb	0	0	0	0	0	0
VIb	0	0	13	9	3^b	0
VIIb	0	0	0	5	0	0
VIIIb	0	0	35	39	49	0
IXb	0	0	0	0	0	10
 $CH_2=CH-CH(OH)-CH_2CH_3$	..[a]	..[a]	..[a]	..[a]	25	..[a]
 $CH_3CH_2CH=CHCH_2OH$	..[a]	..[a]	..[a]	..[a]	6^b	..[a]
 $CH_3CH=CH-CH(OH)-CH_3$	..[a]	..[a]	..[a]	..[a]	..[a]	16

[a] No effort was made to determine whether or not this alcohol was in the product. [b] The identification was uncertain.

It is possible to account for the products obtained in the reactions of amines IVa–IXa with

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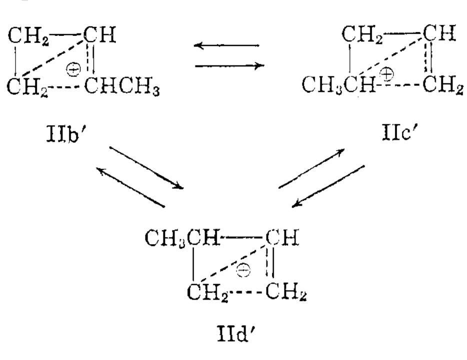
(3) E. F. Cox, M. C. Caserio, M. S. Silver and J. D. Roberts, *J. Am. Chem. Soc.*, **83**, 2719 (1961).

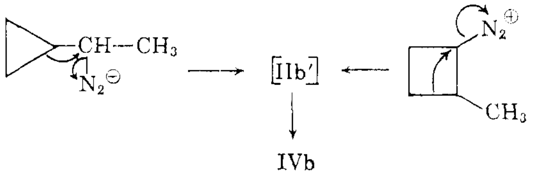
nitrous acid by assuming only the intervention of equilibrating "classical" cationic intermediates.[2] However, the weight of other evidence, particularly solvolytic reactivities for closely related systems,[2,3] indicates that this simple explanation will not suffice to accommodate all of the available information. Consequently, in this paper, we shall confine ourselves to showing the extent to which the observed product compositions can be rationalized in terms of intermediates IIb–IId. We are unable, at this time, to say whether or not relatively unstable classical ions are formed by loss of nitrogen from the presumed intermediary diazonium ions and subsequently isomerize to more stable non-classical intermediates, such as IIb–IId. We have no strong arguments for the intermediacy of classical ions ("hot" or "cold") in this work, although such might be invoked to account for the considerable yields of products of hydrogen migration observed with the open-chain amines VIIIa and IXa.

A prime feature of the results shown in Table I, which points up the problems involved, is the very considerable extent of formation of cyclopropylmethylcarbinol (IVb) in the deamination of *all* of the amines studied. Furthermore, this alcohol was the exclusive product from cyclopropylmethylcarbinylamine (IVa) and 2-methylcyclobutylamine (Va). We can understand this aspect of the results by first considering the effect of substitution of a methyl group on the "bicyclobutonium" cation (II) following the line of reasoning given earlier.[1b,3] The positive charge of II appears to be principally located at carbons 1 and 2.[2] Therefore, we expect that substitution of methyl for hydrogen will have the greatest stabilizing effect at these positions. A smaller effect would be anticipated for position 3, and an essentially negligible effect would be anticipated for position 4. Consequently, we expect the following order of bicyclobutonium ion stabilities: IIa $\sim$ IIb $>$ IIc $>$ IId. Experimental evidence for the postulated effect of a methyl at position IIa has been presented earlier.[3]

The products to be expected from IIb, IIc and IId will of course depend on how the methyl group influences the charge distribution in each. If we consider the charge to tend to be concentrated at the carbon where the methyl is located, then we can express the structures of IIb, IIc and IId, respectively, by IIb′, IIc′ and IId′. Since carbonium ions generally tend to react most rapidly with solvent at the positions where their cationic charge is greatest,[4] we expect that IIb′ would react with water to afford largely if not exclusively cyclopropylmethylcarbinol (IVb), while IIc′ would afford principally allylmethylcarbinol (VIIIb) and IId′ would afford a roughly equal mixture of (2-methylcyclopropyl)-carbinol (VIb) and 2-methylcyclobutanol (Vb).[5] These are the products to be expected for reactions subject to kinetic, not thermodynamic, control.[6] If we now consider, in addition, the relative stabilities of IIb′, IIc′ and IId′ and the expectation that they should be rapidly but not instantaneously interconverted,[2,3] perhaps by way of an intermediate or transition state like Ib,[2,3] then we have available the ingredients necessary to provide a more or less rational explanation of the pattern of deamination products shown in Table I.



The exclusive formation of cyclopropylmethylcarbinol (IVb) from cyclopropylmethylcarbinylamine (IVa) and 2-methylcyclobutylamine (Va) is seen as the consequence of IIb′ being the most stable of the three possible bicyclobutonium ions IIb′–IId′ and the fact that IIb′ can be formed *directly* from each amine (IVa and Va).



The products from (2-methylcyclopropyl)-carbinylamine (VIa) present a more complicated picture. First, we note that VIa cannot afford IIb′ directly but only IIc′ or IId′. Of these, IIc′ is clearly expected to be favored because of the more favorable location of the methyl group thereon (*vide supra*). The intermediate IIc′ could isomerize to IIb′ and thence give cyclopropylmethylcarbinol (IVb, 51% observed). However, IIc′ could also react with solvent to yield allylmethylcarbinol (VIIIb, 35% observed). The origin of (2-methylcyclopropyl)-carbinol is less clear but it may arise by attack of solvent at the 2-position of IIc′, or by direct displacement of nitrogen by hydroxyl similar to that suggested for the reaction of cyclopropylcarbinylamine with nitrous acid,[7] but since (2-methylcyclopropyl)-carbinol (VIb) is also formed in the deamination of 3-methylcyclobutylamine (VIIa) and allylmethylcarbinylamine (VIIIa), and since these amines, like (2-methylcyclopropyl)-carbinylamine, can only form IIc′ directly, then the VIb derived from VIa more likely comes from IIc′ than by direct substitution.

From the above arguments, we see that the reaction products from 3-methylcyclobutylamine

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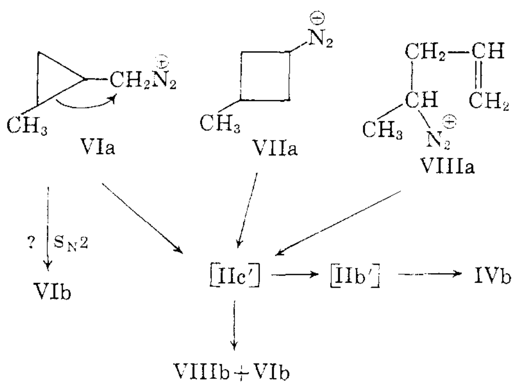
[4] This is a clear consequence of the kind of considerations that led to G. S. Hammond's thermic postulate, *J. Am. Chem. Soc.*, **77**, 334 (1955); namely, that in the highly exothermic reaction of a carbonium ion with solvent, the transition state will closely resemble the starting materials and the distribution of charge in the ion will be much more important than the ultimate thermodynamic stabilities of the possible products in determining the position of attack.

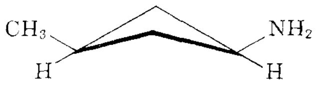
[5] Very recently, J. A. Berson, *Tetrahedron Letters*, **16**, 17 (1960), has applied the same arguments to correlate the products derived from attack of solvent on bicyclic non-classical cations.

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

[7] E. Renk and J. D. Roberts, *ibid.*, **83**, 878 (1961).



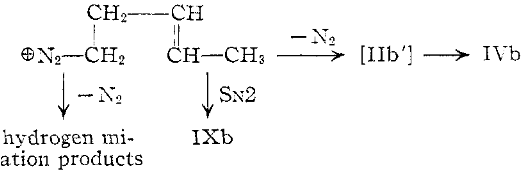
(VIIa) fit into the pattern observed for VIa, but there is one notable exception—the 5% of 3-methylcyclobutanol (VIIb). The amount of this "abnormal" product is small but a careful search showed that no detectable 3-methylcyclobutanol was formed in the deamination of VIa. The abnormal character of the non-rearranging formation of VIIb is further emphasized by the fact that neither cyclobutylamine[7] nor 2-methylcyclobutylamine (Va) appears to give any direct displacement products. This result may ultimately prove to be the Achilles' heel of our rationalization of the course of these deamination reactions. However, we would like to observe that 3-methylcyclobutylamine may possess extenuative structural features which could set its behavior apart from cyclobutyl- and 2-methylcyclobutylamines. In particular, the starting amine VIIa appeared to contain at least some of the *cis* isomer which would be expected to have as the favored conformation VIIc with the substituents in "equatorial" positions. Such a conformation might lead to some degree of simple displacement with retention of configuration and without rearrangement in a manner analogous to that observed for equatorial amines in the cyclohexane series.[8]



VIIc

The reaction of the open-chain amines, allylmethylcarbinylamine (VIIIa) and crotylcarbinylamine (IXa), with nitrous acid was complicated by about 20–25% of hydrogen migration, just as has been observed previously with allylcarbinylamine[6,7] and (β-methylallyl)-carbinylamine.[3] The formation of allylic alcohols by hydrogen migration is unexceptional. The only important message it has for us here is to provide a contrast in behavior between the first-formed intermediate from decomposition of the open-chain diazonium salts and the intermediate that ultimately leads to allylmethylcarbinol (VIIIa) starting with the cyclic amines. The point of difference is that no hydrogen migration to give allylic alcohols occurs when one starts with the cyclic amines. This can be taken to mean that the open-chain amines first yield some special variety of carbonium ion ("hot" or classical) that undergoes competitive reactions of ring closure to a bicyclobutonium cation or hydrogen migration to give an allylic cation. This situation could very reasonably obtain if the open-chain diazonium ions lose nitrogen in extended conformations having the double bond poorly disposed for participation.[9] With the cyclic amines, the conformations should in general be much more favorable for carbon participation and direct formation of the bicyclobutonium ions.

Deamination of crotylcarbinylamine (IXa) can only lead directly to the most stable of the three bicyclobutonium ions (IIb′), which affords cyclopropylmethylcarbinol (IVb, observed 74%). Other than hydrogen migration products, no other alcohol was isolated with the exception of 10% of crotylcarbinol IXb, which could reasonably arise by a small amount of an S_N2-like displacement.



Allylmethylcarbinylamine (VIIIa) on deamination and cyclization leads first to IIc′ and subsequently to IIb′. The products of the reaction other than those resulting from hydrogen migration, allylmethylcarbinol (VIIIb, 49%), cyclopropylmethylcarbinol (IVb, 17%), and possibly 3% of (2-methylcyclopropyl)-carbinol are those expected from IIc′ and IIb′. However, the amount of VIIIb formed relative to either IVb or VIb is substantially larger than from the cyclic amines VIa and VIIa. Therefore, much of VIIIb is judged to arise by a direct displacement reaction (35% S_N2, or 70% of the total amount of VIIIb).

The behavior of the alcohols IVa–Xa under the influence of strong acid is noteworthy. It would be expected that open-chain alcohols would be some 8–10 kcal. more stable than their cyclic isomers[6]; consequently, one would anticipate considerable driving force for ring opening under conditions where at least partial thermodynamic control of the products can be expected. Of the bicyclobutonium ions IIb′, IIc′ and IId′, however, only IIc′ is favorably disposed to give open-chain product, and it would give only allylmethylcarbinol (VIIIb). It seems significant, in fact, that all of the cyclic alcohols IVb–VIIb were isomerized more or less readily by fluoroboric acid to allylmethylcarbinol (VIIIb). Isomerization of allylmethylcarbinol to crotylcarbinol (IXb) or α-methylallylcarbinol (Xb) did not appear to occur, probably because competing reactions such as cyclization to tetrahydrofurans, etc., were faster than formation of bicyclobutonium ions from the open-chain alcohols.[10]

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[8] (a) J. A. Mills, *J. Chem. Soc.*, 260 (1953); (b) A. K. Bose, *Experientia*, **9**, 256 (1953); (c) W. G. Dauben, R. C. Tweit and C. Mannerskantz, *J. Am. Chem. Soc.*, **76**, 4420 (1954).

[9] *Cf.* D. Semenow, Chin-Hua Shih and W. G. Young, *ibid.*, **80**, 5472 (1958).

[10] The exclusive formation of VIIIb in the isomerizations of the cyclic alcohols is rendered all the more interesting by the fact that VIIIb is probably less stable than IXb, which has a more highly substituted double bond. In this connection, T. A. Favorskaya and Sh. A.

Experimental[11]

Cyclopropylmethylcarbinol was prepared in 71% yield by the reduction of cyclopropyl methyl ketone (62.7 g., 0.746 mole) with lithium aluminum hydride (11.4 g., 0.3 mole) in ether solution. The pure alcohol had b.p. 122–124°, $n^{25}D$ 1.4292–1.4298 (lit.[12] b.p. 123.5°, $n^{20}D$ 1.4316).

The *p*-nitrobenzoate was recrystallized from hexane; m.p. 54–55.5°.

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

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

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

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

Cyclobutanol was prepared in 80% yield by the reduction of cyclobutanone with lithium aluminum hydride in ether solution and had b.p. 119–120°, $n^{25}D$ 1.4333–1.4340 (lit.[13] b.p. 125°, $n^{25}D$ 1.4347).

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

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

3-Methylenecyclobutanecarboxamide was prepared in 81% yield from 101.5 g. (0.915 mole) of 3-methylenecyclobutanecarboxylic acid,[14] 92.5 g. (0.915 mole) of triethylamine, excess ammonia and 100 g. (0.922 mole) of ethyl chlorocarbonate[15] in 3 l. of chloroform and had m.p. 156.7–157.2°, after sublimation.

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

3-Methylcyclobutanecarboxamide was prepared in 92% yield by the low-pressure hydrogenation of 3-methylenecyclobutanecarboxamide in acetic acid over reduced platinum dioxide. A small sample was sublimed twice and had m.p. 154.5–163.0°. The sample was probably a mixture of *cis-trans* isomers.

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

3-Methyl-1-acetylcyclobutane was prepared by the reaction of 3-methylcyclobutanecarboxamide with methylmagnesium iodide, following the general method of Whitmore, Noll and Meunier[16] for the conversion of an amide to a ketone. From 25 g. (0.221 mole) of 3-methylcyclobutanecarboxamide, 21.4 g. (0.884 mole) of magnesium and 128 g. (0.90 mole) of methyl iodide there was obtained 16.7 g. of 3-methyl-1-acetylcyclobutane (69%), b.p. 140–143°, $n^{25}D$ 1.4269–1.4275. Part of the material was carefully fractionated and had b.p. 140–140.5°, $n^{25}D$ 1.4261.

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

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

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

3-Methyl-1-acetoxycyclobutane was prepared in 79% yield by the oxidation of 11.2 g. (0.1 mole) of 3-methyl-1-acetylcyclobutane with peroxytrifluoroacetic acid (from 4.1 ml. of 90% hydrogen peroxide and 25.4 ml. of trifluoroacetic anhydride) in methylene chloride in the presence of anhydrous disodium hydrogen phosphate. The method was patterned after that of Emmons and Lucas.[17] The product had b.p. 140–142.5°, $n^{24}D$ 1.4165–1.4170, and when a center cut was redistilled it had b.p. 140.5, $n^{22.5}D$ 1.4172. The v.p.c.[18] showed one broad, partially resolved peak.

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

3-Methylcyclobutanol was prepared in 75% yield by basic saponification of 3-methyl-1-acetoxycyclobutane, b.p. 133–134°, $n^{25}D$ 1.4287–1.4292. The v.p.c.[18] showed one broad, partially resolved peak.

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

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

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

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

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

2-Methyl-1,1-cyclobutanedicarboxylic acid was prepared according to Blomquist and Wolinsky[20]; m.p. 161.7–162.8° dec. (lit.[20] m.p. 163–164°) after crystallization from chloroform.

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

2-Methylcyclobutanecarboxylic Acid.—Distillation of 20–40 g. of 2-methyl-1,1-cyclobutanedicarboxylic acid at atmospheric pressure gave 92–99% yields of 2-methylcyclobutanecarboxylic acid, $n^{25}D$ 1.4380 (lit.[20] $n^{20}D$ 1.4394). The acid was used without further purification and was converted to 2-methylcyclobutanol by a series of reactions exactly paralleling the conversion of 3-methylenecyclobutanecarboxylic acid to 3-methylcyclobutanol (except that there was no catalytic hydrogenation). 2-Methylcyclobutanecarboxamide of m.p. 130–133° (lit.[20] m.p. 130–131.2°) was obtained from 2-methylcyclobutanecarboxylic acid in 89% yield and recrystallized from benzene.

2-Methyl-1-acetylcyclobutane was prepared in 57% yield from the above amide and had b.p. 140–145°, $n^{25}D$ 1.4290. The v.p.c.[18] showed two cleanly resolved peaks, attributed to *cis-trans* isomers. The peak of lower retention time was considerably larger than the other.

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

2-Methyl-1-acetoxycyclobutane was obtained from the ketone in 65–77% yields, b.p. 139–141°, $n^{25}D$ 1.4160–1.4180. Careful purification of a sample of this compound gave material of the correct elemental composition, b.p. 139.5°, $n^{25}D$ 1.4170. The v.p.c.[18] showed three peaks. With this compound methyl migration may have occurred to some extent during the oxidation.

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

2-Methylcyclobutanol was prepared in 80% yield by saponification of 2-methyl-1-acetoxycyclobutane, b.p. 131°, $n^{25}D$ 1.4308. The v.p.c. showed two peaks. In addition, the infrared spectrum was nearly identical with that of a sample of 2-methylcyclobutanol formed by the reduction of 2-methylcyclobutanone with lithium aluminum hydride

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Fridman [*J. Gen. Chem. (USSR)*, **20**, 413 (1950); *C. A.*, **44**, 7753 (1950)] report that allylmethylethylcarbinol is rearranged completely to 4-methyl-3-hexen-1-ol by 25% sulfuric acid at the reflux temperature.

(11) All b.p.'s and m.p.'s are uncorrected. The elemental analyses were performed by Dr. A. Elek, Los Angeles, Calif.

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(18) The vapor phase chromatography apparatus had a 5-ft. column equipped with thermal conductivity cells and surrounded by a vapor jacket heated by boiling toluene. The effluent gas was helium and the stationary phase was dioctyl phthalate supported on Johns-Manville Celite (0.45 g. of liquid/g. Celite). The peak areas were measured by counting squares or by tracing the curves on onion skin, cutting and weighing.

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(since the proportion of *cis-trans* isomers in the two samples was presumably different, the two spectra would not be expected to be identical).

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

The **p-nitrobenzoate** had m.p. 50.3–52.5° after recrystallization from hexane.

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

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

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

1-Bromo-3-chloro-2-methylpropane.—In a 1-l. three-necked round-bottomed flask equipped with two gas-inlet tubes and Dry Ice condenser was placed 380 g. of β-methallyl chloride. A slow stream of oxygen and a rapid stream of anhydrous hydrogen bromide were bubbled into the reaction mixture for 8 hr., at which time the gas absorption had ceased. The solution was washed with water, dried over potassium carbonate and distilled. The product (402 g., 65.5%) had b.p. 55–63° (26–28 mm.), $n^{26.5}$D 1.4800 [lit.[21] b.p. 49° (15 mm.), n^{20}D 1.4816]. The n.m.r. showed three main peaks and the splitting was consistent with the assigned structure. Very little of the isomeric 1-chloro-2-bromo-2-methylpropane appeared to be formed.

1-Cyano-3-chloro-2-methylpropane.—A solution of 260 ml. of 75% aqueous ethanol, 32.5 g. (0.66 mole) of sodium cyanide and 88.5 g. (0.56 mole) of 1-bromo-3-chloro-2-methylpropane was heated under reflux for 7.5 hr., diluted to 1 l. and extracted with three 170-ml. portions of chloroform. The combined organic layers were dried over calcium chloride and fractionally distilled to give 39.6 g. (60.5 %) of 1-cyano-3-chloro-2-methylpropane, b.p. 74–79° (11.7 mm.), n^{23}D 1.4430 [lit.[22] b.p. 82–83° (16 mm.), n^{20}D 1.4426].

2-Methylcyclopropanecarboxylic Acid.—In a 250-ml. round-bottomed flask equipped with reflux condenser were placed 39 g. of 1-cyano-3-chloro-2-methylpropane and 46 g. of ground sodium hydroxide flakes. Since heating on a steam-bath caused no visible reaction, a Woods metal-bath was substituted. At 150–160° a vigorous reaction occurred, and after 30 min. a solid cake had formed in the flask. Heating was maintained at this temperature for 1 additional hr. and the flask then transferred to a steam-bath. Water (150 ml.) was added over a 20-min. period and the contents of the flask heated for 3 hr., cooled to 0° and poured over a slurry of 100 g. of ice and 37 ml. of sulfuric acid. The layers were separated, the aqueous phase extracted with two 100-ml. portions of ether and the combined organic solutions dried over magnesium sulfate and distilled to give 23.1 g. (68%) of product, b.p. 97–98° (17.6 mm.), $n^{21.5}$ 1.4384–1.4387 [lit.[23] b.p. 98–99° (18 mm.), n^{16}D 1.4441].

(2-Methylcyclopropyl)-carbinol was prepared in 78% yield by the reduction of 23.1 g. (0.231 mole) of 2-methylcyclopropanecarboxylic acid with 7.2 g. (0.2 mole) of lithium aluminum hydride in ether. The crude product had b.p. 129–134°. A portion of the product was fractionally distilled and a center cut showed b.p. 133°, n^{25}D 1.4283.

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

The **p-nitrobenzoate** could not be obtained crystalline at room temperature.

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

(2-Methylcyclopropyl)-carbonitrile.—Sodamide was prepared from 6 g. (0.522 mole) of sodium and 500 ml. of ammonia in a 1-l. three-necked round-bottomed flask equipped with Dry Ice condenser, mechanical stirrer and glass stopper. A solution of 28.8 g. (0.203 mole) of 1-cyano-3-chloro-2-methylpropane in 50 ml. of ether was added over 1 min. with good stirring. The condenser was removed and 190 ml. of ether added over 1.5 hr. Ammonium chloride (4 g.) was added and the ammonia allowed to evaporate overnight. The solution was filtered. The filter cake was dissolved in water and extracted with ether. The ether extracts were combined with the previously obtained filtrate, dried over Drierite and concentrated by removing the ether. The residue was fractionated to yield 9.3 g. (57%) of (2-methylcyclopropyl)-carbonitrile, b.p. 143–146°, n^{25}D 1.4242–1.4250 (lit.[22] n^{20}D 1.4259).

(2-Methylcyclopropyl)-carbinylamine was prepared in 55% yield by the reduction of 9.3 g. (0.115 mole) of (2-methylcyclopropyl)-carbonitrile with 4.55 g. (0.12 mole) of lithium aluminum hydride in ether. The product was very hard to obtain anhydrous, and, although the water did not complicate the deamination reactions, several distillations were needed to obtain the analytical sample of b.p. 102–102.5°, n^{25}D 1.4310.

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

1-Cyano-2-butene was prepared from a mixture of 1-chloro-2-butene and 3-chloro-1-butene (b.p. 68–82°, prepared in 64.5% yield from hydrogen chloride and butadiene according to Hatch and Nesbitt[24]) and cuprous cyanide, following the directions of Lane, Fentress and Sherwood[25]; b.p. 142–144°, n^{25}D 1.4199 (lit.[26] b.p. 146°, n^{20}D 1.4228).

3-Pentenoic acid was synthesized from the cyano compound[25] and reduced to crotylcarbinol in 63% yield by lithium aluminum hydride, b.p. 134–134.5°, n^{25}D 1.4339–1.4340. The v.p.c. indicated that this product was quite pure. The pure *trans*-alcohol is reported[26] to have b.p. 136–137°, n^{25}D 1.4322–1.4324.

Crotylcarbinylamine could be prepared in 30–40% yield by the reduction of 1-cyano-2-butene with lithium aluminum hydride provided the reduction and subsequent work-up were all at 0°. The product had b.p. 104.5–106.5°, n^{25}D 1.4345–1.4350, and the v.p.c.[18] showed one peak.

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

3-Penten-2-ol was synthesized from methylmagnesium iodide and crotonaldehyde; b.p. 117–122°, n^{25}D 1.4270 (lit.[27] n^{19}D 1.4288).

Allylmethylcarbinol was prepared from zinc, acetaldehyde and allyl bromide according to Levene and Haller[28]; b.p. 113.5–114.5°, n^{25}D 1.4227 (lit.[29] b.p. 114°).

1-Penten-3-ol was prepared from ethylmagnesium bromide and acrolein according to Hunsdiecker[30]; b.p. 112–114°, n^{25}D 1.4221–1.4227 (lit.[31] b.p. 114.2–114.4°, n^{20}D 1.4240).

Allylmethylcarbinyl p-toluenesulfonate was prepared (78%) according to the general procedure of Sekera and Marvel.[32] The crude ester was used in synthetic work.

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

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2.8 g. and still containing some ether, was distilled through a micro apparatus, two fractions being taken (1.1 g. and 1.5 g.). The v.p.c. of the second fraction showed only an ether peak and a homogeneous amine peak (which was about 70% of the total peak area). Some of the material was used in the deamination reaction, some was hydrogenated and some was converted to the phenylthiourea.

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

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

Hydrogenation of the unsaturated amine gave 2-pentylamine, which afforded a phenylthiourea of m.p. 73.5–74.0° (ethanol–water) and a *p*-nitrobenzamide of m.p. 92.6–93.8° (benzene–hexane). The melting points of these derivatives were not depressed on admixture with authentic samples.

The Deamination Reactions.—The same procedure was followed in the deamination of all amines but one. In a 500-ml. round-bottomed three-necked flask equipped with mechanical stirrer, glass stopper and condenser position for downward distillation was placed a solution of 22–43 g. of sodium nitrite (depending on the amount of amine to be used) and of amine (1–10 g.) in 280 ml. of water. To the condenser there was attached a round-bottomed flask with sidearm that opened to the atmosphere *via* a Dry Ice trap and calcium chloride drying tube. The reaction flask was cooled in an ice-bath, the stirrer started and 17 ml. of 60% perchloric acid added. After about 30 min., the ice-bath was replaced with a heating mantle and distillation begun and continued until 75 ml. of homogeneous distillate had been collected after the initial two-phase distillate. The distillate was saturated with potassium carbonate and the organic (upper) layer separated. The aqueous phase was extracted with two 15-ml. portions of ether. The combined organic layers were dried over magnesium sulfate, filtered, the ether removed, and the residue distilled with no attempt to fractionate the various products present. The Dry Ice trap used in the deamination reaction was never observed to collect anything but oxides of nitrogen.

The first step in performing the analysis of the alcohol mixture was to measure on the vapor phase chromatograph[18] the retention time of each alcohol likely to be present. This included the six isomeric alcohols of the same structure as the amines studied as well as appropriate allylic alcohols if the starting amine was an allylcarbinylamine derivative. Some of the alcohols had identical retention times and recourse was made to concentration of the components in question by preparative v.p.c. and infrared analysis with the aid of comparisons with the spectra of known mixtures. For instance, the 2- and 3-methylcyclobutanols and (2-methylcyclopropyl)-carbinol fell at the same place. Also, α-methylallylcarbinol coincided with cyclopropylmethylcarbinol; there was no reason why the former alcohol should be formed from any of the amines studied so no effort was made to identify it and no ambiguities arose because of this assumption. If the retention time of an alcohol seemed to be affected by the presence of other alcohols, a synthetic mixture was run to redetermine retention times. Also, there were often peaks of minor size, generally of high retention time, that could not be identified. These presumably arose from nitro compounds, side reactions, etc. The final analysis was checked by preparing a synthetic mixture of the derived composition and comparing its infrared spectrum to that of the reaction mixture. The accuracy of the analyses was estimated to be ±3% on the basis of results with known mixtures.

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

Alcohol	Percentage Taken	Percentage Recovd.
Allylmethylcarbinol	36	33
Cyclopropylmethylcarbinol	46	51
3-Methylcyclobutanol (2-Methylcyclopropyl)-carbinol	18	16

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

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

Alcohol	% in crude product	% in pure product
3-Penten-2-ol	16.9	15.2
Cyclopropylmethylcarbinol	72.6	73.6
Crotylcarbinol	10.5	11.3

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

The deamination of 2-methylcyclobutylamine gave a 56% yield of alcohols. The v.p.c. showed only one peak, corresponding to cyclopropylmethylcarbinol, and the infrared spectrum was superimposable on that from an authentic sample of this alcohol.

Deamination of 3-methylcyclobutylamine was carried out twice, with yields of alcohols amounting to 49 and 70%. Analysis of the first and second runs gave cyclopropylmethylcarbinol, 48 and 45%; allylmethylcarbinol, 39 and 39%; 3-methylcyclobutanol, 5 and 6%; (2-methylcyclopropyl)-carbinol, 8 and 10%. Since the last two alcohols had very nearly identical retention times, their identity and relative amounts could not be ascertained by v.p.c. alone. Therefore, in the case of the first run, a sample of the alcohols with this retention time was isolated from the fraction having b.p. 123–124° by means of v.p.c.[34] and analyzed by infrared. The spectrum obtained corresponded to a mixture of 64% (2-methylcyclopropyl)-carbinol and 36% 3-methylcyclobutanol. In the second run, the amount of 3-methylcyclobutanol was ascertained from the intensity of the 8.10 μ band in the infrared spectrum of the main fraction (90% of the total distillate). In calculating the compositions it was assumed that in all fractions of both runs 3-methylcyclobutanol and (2-methylcyclopropyl)-carbinol occurred in the same ratio. Over 94% of the total area of the v.p.c. peaks were accounted for in the analysis.

The deamination of (2-methylcyclopropyl)-carbinylamine gave a 58% yield of a mixture of alcohols. Analysis by v.p.c. and infrared indicated a mixture composed of 51% cyclopropylmethylcarbinol, 35% allylmethylcarbinol and 13% (2-methylcyclopropyl)-carbinol. To be certain of the absence of 3-methylcyclobutanol, a sample of the alcohol(s) with retention time equal to (2-methylcyclopropyl)-carbinol and 3-methylcyclobutanol was isolated by v.p.c.[34] and its infrared spectrum taken. The spectrum was essentially that of (2-methylcyclopropyl)-carbinol, there being no evidence of any 3-methylcyclobutanol.

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

The deamination of allylmethylcarbinylamine gave a 21% yield of alcohols from 0.8 g. of amine. The resultant v.p.c. had four peaks. Two peaks (91%) were assigned to cyclopropylmethylcarbinol and a mixture of allylmethylcarbinol and ethylvinylcarbinol. This last mixture was analyzed *via* infrared spectra. A peak, area 6%, had the same retention time as crotylcarbinol and was assigned to 2-penten-1-ol. This alcohol might be expected to have a retention time close to that of crotylcarbinol. The last peak (3%) had a retention time corresponding to that of (2-methylcyclopropyl)-carbinol [shown by adding authentic (2-methylcyclopropyl)-carbinol to the reaction mixture and observing the increase in the size of this peak]; however, no other evidence was obtained for the nature of this peak.

The Behavior of the Isomeric $C_5H_{10}O$ Alcohols under Strongly Acidic Conditions.—These experiments were carried out only in an exploratory fashion. Analyses were by vapor-phase chromatography, but the curves were generally not of good quality because of formation of side products. The alcohols tested were (2-methylcyclopropyl)-carbinol,

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(34) These samples were obtained using a Perkin–Elmer Vapor Fractometer equipped with an analytical-type column packed with diisodecyl phthalate on crushed firebrick.

cyclopropylmethylcarbinol, 2- and 3-methylcyclobutanol, crotylcarbinol and allylmethylcarbinol.

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

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

Allylmethylcarbinol gave only polymer and unrearranged alcohol when heated under reflux for 1 hr. with 25% sulfuric acid. Under the same conditions it is reported[10] that allylmethylethylcarbinol is totally rearranged to 4-methyl-3-hexen-1-ol. This corresponds to rearrangement of allylmethylcarbinol to crotylcarbinol.

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Electrophilic Substitution at Saturated Carbon. XIII. Solvent Control of Rate of Acid–Base Reactions that Involve the Carbon–Hydrogen Bond[1,2]

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The base-catalyzed hydrogen–deuterium exchange reaction at carbon alpha to the nitrile, amide and ester groups has been found to occur with complete racemization in a number of systems. The kinetics of racemization of these systems has been examined with solvent composition as the main variable, and with methanol, methanol–dimethyl sulfoxide mixtures, ethylene glycol, *t*-butyl alcohol and *n*-butyl alcohol as solvents. Rate constants, kinetic order and thermodynamic activation parameters were evaluated. With potassium methoxide as base and (+)-2-methyl-3-phenylpropionitrile as substrate, the rate constant for racemization in dimethyl sulfoxide possessed a value $\sim 10^9$ times that observed in methanol. The reactivity-depressing effect of hydrogen bonds on alkoxides is emphasized.

In our previous studies of electrophilic substitution at saturated carbon,[3] carbon[4] and oxygen[5] were employed as leaving groups, and proton or deuteron donors were used as electrophiles. This and the two succeeding papers report the results of investigations of the stereochemistry and kinetics of base-catalyzed hydrogen–deuterium exchange reactions at saturated carbon. In a formal sense, these acid–base reactions are electrophilic substitutions with hydrogen or deuterium as leaving groups, and deuteron or proton donors as electrophiles.

Two previous studies of the stereochemistry of base-catalyzed hydrogen–deuterium exchange have appeared in the literature. Wilson *et al.*,[6] observed that the rates of hydrogen–deuterium exchange and of racemization of optically active 1-phenyl-2-methyl-1-butanone in a basic solution of dioxane–deuterium oxide were equal. A similar identity of rates was observed when optically active phenyl-*p*-tolyldeuterioacetic acid was heated in aqueous base.[7] These results were interpreted as involving proton abstraction by base in the rate-controlling step, followed by deuteration[6] (protonation[7]) of a symmetrical ambident anion on either oxygen[6] or carbon.[7]

Of the many investigations of the kinetics of proton abstraction from carbon, only leading references are mentioned here. Among compounds studied are nitroparaffins,[8] tris-*p*-nitrophenylmethane,[9] acetylene,[10] haloforms,[11] and a number of ketones, nitriles, carboxylic acids, sulfones and amides.[12] In many of these studies, the rates of halogenation were measured, and the rates of proton abstraction and halogenation were presumed to be identical, since in most base-catalyzed halogenations of carbon acids anion formation is rate controlling.[13]

The present study involved use of cyano, amido and ester groups to acidify hydrogen attached to asymmetric carbon. The racemization and exchange reactions of optically active compounds I–V were examined with the possibility in mind that the stereochemistry and mechanism of these electrophilic substitution processes might be solvent dependent as were those that involved carbon leaving groups.[3,5] The main objective was to obtain quantitative data concerning the dependence of the catalytic activity of bases on the character of the solvent.

Results

The preparations of optically active nitriles I[14] and II[4] have been described previously, as have the optically active acids[15,4] from which amides III and

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(1) Preliminary communications of some of the results of this paper have appeared previously: (a) D. J. Cram, B. Rickborn and G. R. Knox, *J. Am. Chem. Soc.*, **82**, 6412 (1960); (b) D. J. Cram, W. D. Nielsen and B. Rickborn, *ibid.*, **82**, 6415 (1960).

(2) This work was supported by a grant from the National Science Foundation.

(3) D. J. Cram, J. L. Mateos, F. Hauck, A. Langemann, K. R. Kopecky, W. D. Nielsen and J. Allinger, *J. Am. Chem. Soc.*, **81**, 5774 (1959), is a summarizing paper.

(4) Previous paper D. J. Cram and P. Haberfield, *ibid.*, **83**, 2363 (1961).

(5) D. J. Cram, C. A. Kingsbury and A. Langemann, *ibid.*, **81**, 5785 (1959).

(6) (a) S. K. Hsu, C. K. Ingold and C. L. Wilson, *J. Chem. Soc.*, 78 (1938); (b) C. L. Wilson, *ibid.*, 1550 (1936).

(7) D. J. G. Ives and G. C. Wilks, *ibid.*, 1455 (1938); see also D. J. G. Ives, *ibid.*, 81 (1938).

(8) O. Reitz, *Z. physik. Chem.*, **A176**, 363 (1936); (b) R. P. Bell "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, p. 109.

(9) E. F. Caldin and G. Long, *Proc. Roy. Soc. (London)*, **A228**, 263 (1955).

(10) L. H. Reyerson, *J. Am. Chem. Soc.*, **57**, 779 (1935).

(11) J. Hine, N. W. Burske, M. Hine and P. B. Langford, *ibid.*, **79**, 1409 (1957).

(12) (a) R. G. Pearson and R. L. Dillon, *ibid.*, **75**, 2441 (1953); (b) K. F. Bonhoeffer, K. H. Geib and O. Reitz, *J. Chem. Phys.*, **7**, 664 (1939).

(13) For instance, Hsu and Wilson, *J. Chem. Soc.*, 623 (1936), demonstrated that optically active 1-phenyl-2-methyl-1-butanone was racemized and brominated at identical rates, both processes being catalyzed by acetate ion.

(14) D. J. Cram and P. Haberfield, *J. Am. Chem. Soc.*, **83**, 2354 (1961).

(15) C. L. Arcus and J. Kenyon, *J. Chem. Soc.*, 916 (1939).