

IX were very similar showing ion current percentages for M^+ of 0.27 and 0.23, respectively. Both showed large $(M - 18)^+$ peaks (see text) and $C_5H_6^+$ and $C_5H_7^+$ peaks. These latter represent the base peaks in IX and IV, respectively. Both systems likewise show moderate $C_7H_7^+$ peaks. Ketone V shows a base peak at 66 ($C_5H_6^+$), a strong peak at 79, and a weak peak at 94 ($M - CO$)⁺.

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Small-Ring Compounds. XLVII. Reactions of Optically Active Cyclopropylmethylcarbinyl Derivatives^{1,2a}

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Abstract: Cyclopropylmethylcarbinylamine and cyclopropylmethylcarbinol were resolved into optical antipodes and their configurations were related. The former was deaminated with aqueous nitrous acid to give the latter with 0–4% net inversion of configuration. Solvolysis of N-methyl-4-alkoxypyridinium salts was investigated as a means of providing a leaving group which would not undergo "internal return." Solvolysis rates for N-methyl-4-(cyclopropylmethylcarbinyl)pyridinium iodide and perchlorate in water and in 80% ethanol and of N-methyl-4-(cyclopropylmethylcarbinyl)pyridinium iodide in water were measured. The first-order rate constant for the hydrolysis of N-methyl-4-(cyclopropylmethylcarbinyl)pyridinium iodide at 30° was calculated to be 6×10^3 times that of N-methyl-4-(cyclopropylcarbinyl)pyridinium iodide. The hydrolysis of optically active N-methyl-4-(cyclopropylmethylcarbinyl)pyridinium iodide produced cyclopropylmethylcarbinol with $4.4 \pm 1.5\%$ inversion of configuration. The stereochemistry of the deamination of cyclopropylmethylcarbinylamine and of the hydrolysis of N-methyl-4-(cyclopropylmethylcarbinyl)pyridinium iodide and the ratio of rate constants for the cyclopropylmethylcarbinyl and cyclopropylcarbinyl pyridinium salts are discussed with respect to the possible intervention of nonclassical carbonium ion intermediates in these reactions.

Considerable interest attends the nature of the intermediates in carbonium ion type interconversion reactions of cyclopropylcarbinyl, cyclobutyl, and allylcarbinyl derivatives. Evidence regarding these intermediates has come principally from studies of solvolysis rates and product distributions in such interconversion reactions.³

In general, carbonium ion type reactions of both cyclopropylcarbinyl and cyclobutyl derivatives give similar relative amounts of products with the cyclopropylcarbinyl, cyclobutyl, and allylcarbinyl structures, almost independently of which of the two starting structures is employed. Such reactions include the reaction of cyclopropylcarbinylamine and cyclobutylamine with nitrous acid, the solvolysis of cyclopropylcarbinyl and cyclobutyl derivatives, and the reactions of cyclopropylcarbinol and cyclobutanol with thionyl chloride and of cyclopropylcarbinol with hydrogen bromide or phosphorus tribromide. This behavior suggests that all the above reactions go through common cationic intermediates; small variations in product composition may be accounted by specific effects of each

reaction and do not require postulation of a drastic change in mechanism.

The solvolyses of cyclopropylcarbinyl and cyclobutyl derivatives are unusually fast. For instance, in 50% aqueous ethanol at 50°, cyclopropylcarbinyl chloride is 40 times more reactive than β -methylallyl chloride and cyclobutyl chloride is 15 times more reactive than isopropyl chloride.⁴ Unusually high solvolysis rates are often indicative of nonclassical cationic intermediates.⁵ The weight of the evidence is such, therefore, that the common intermediate(s) in the solvolyses of cyclopropylcarbinyl and cyclobutyl derivatives has (have) been inferred to be nonclassical in nature.⁶

The effect of methyl substitution at the methylene groups of the intermediate cations has been investigated in the deamination of the appropriate amines with aqueous nitrous acid.⁷ The results fit reasonably well into a scheme similar to that presented for the unmethylated amines with some understandable differences due to the presence of the added methyl group. The isomeric methyl-substituted ions are, of course, not equal in stability, and their order of stability appears to be $I > II \gg III$. Two of the amines studied, 2-methylcyclobutylamine and 2-methylcyclopropylcarbinylamine, could form directly either of two non-

(1) Supported in part by the National Science Foundation and the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgment is hereby made to the Donors of the Petroleum Research Fund.

(2) (a) From the Ph.D. Thesis of M. Vogel, California Institute of Technology, 1961. Presented in part at Sixteenth National Organic Chemistry Symposium of the American Chemical Society, Seattle, Washington, June 15, 1959; (b) National Science Foundation Predoctoral Fellow, 1958–1960.

(3) Cf. K. L. Servis and J. D. Roberts, *J. Am. Chem. Soc.*, **87**, 1331 (1965), and references cited therein.

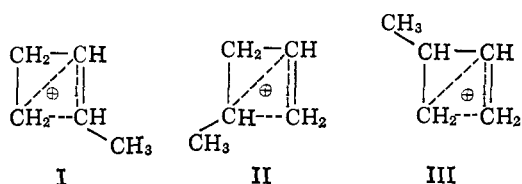
(4) J. D. Roberts and R. H. Mazur, *ibid.*, **73**, 2509 (1951).

(5) Cf. A. Streitwieser, Jr., *Chem. Rev.*, **56**, 571 (1956).

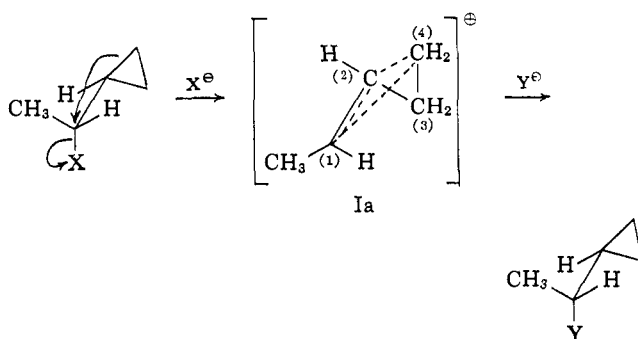
(6) (a) R. H. Mazur, W. N. White, D. A. Semenow, C. C. Lee, M. S. Silver, and J. D. Roberts, *J. Am. Chem. Soc.*, **81**, 4390 (1959); (b) M. E. H. Howden and J. D. Roberts, *Tetrahedron, Suppl.*, **2**, 403 (1963).

(7) M. S. Silver, M. C. Caserio, H. E. Rice, and J. D. Roberts, *J. Am. Chem. Soc.*, **83**, 3671 (1961).

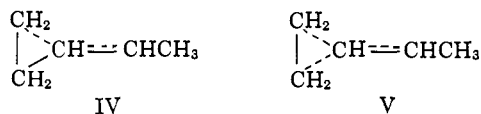
classical ions, but only the more stable of the possible ions actually appears to be formed.



The success of a scheme involving nonclassical ions in accounting for these results suggests that the added methyl group has not drastically altered the nature of the intermediates in the deaminations of the methyl-substituted compounds. However, in hope of obtaining more information, we have studied the stereochemistry of the carbonium ion type reactions of optically active cyclopropylmethylcarbinyl derivatives. Formation of a nonclassical ion of structure I without intervention of any other intermediates (such as must be invoked to account for isotope position scrambling with cyclopropylcarbinyl^{6a} and allylcarbinyl⁸ derivatives) is expected to lead to retention of configuration in S_N1-type reactions with optically active cyclopropylmethylcarbinyl derivatives. The rationale for this follows where I is shown as Ia in a three-dimensional drawing. The intermediate (Ia) clearly has no element of sym-



metry and should lead to retention of configuration provided that the C₍₁₎-C₍₄₎ bonding remains strong enough throughout to maintain the configuration at C₍₁₎. Obviously, the methyl group at C₍₁₎ will favor locating a very considerable fraction of positive charge at this position and hence weaken the C₍₁₎-C₍₄₎ binding and perhaps favor the alternate homoallylic structures (IV or V) which would be expected to have substantially less angle strain. Of these, we have favored IV pre-



viously⁴ because of an erroneous comparison⁹ of the reactivities of nortricyclyl and cyclopropylcarbinyl derivatives which did not take proper account of ground-state stabilities.^{4,10,11} Although there is strong evidence for the monohomoallylic type of structure in stereochemically restricted systems,¹⁰ Wiberg¹² and

Olah¹³ have recently provided compelling evidence for the bishomoallylic structure where stereochemical restraints do not prohibit its formation.

The stereochemical result from optically active cyclopropylmethylcarbinyl derivatives reacting through IV will depend on the nature of the dotted bond shown between the CH₂ and CH groups of the ring. If the orbitals involved are p, overlapping in the π manner, IV will have a plane of symmetry; while if the overlap is of the σ type, no symmetry elements would be present. In the first event, complete racemization would be expected; in the second, retention, if it is assumed that the antipodes of IV cannot equilibrate rapidly by way of V. Clearly, V should give complete racemization if the p orbital of C₍₁₎ is assumed to be parallel to the bond connecting the methylene groups of the three-membered ring.

The reactions chosen for the present study of the stereochemistry of reactions of cyclopropylmethylcarbinyl derivatives were not the customary solvolyses of alkyl halides and esters. For one thing, the cyclopropylmethylcarbinyl halides and sulfonate esters are very difficult to obtain pure and rearrange readily. Solvolysis of carboxylic esters always involves questions of acyl-oxygen vs. alkyl-oxygen fission and, in addition, solvolyses of both esters and halides are complicated by the problem of internal return from intimate ion pairs.¹⁴ The reactions actually employed were the deamination of cyclopropylmethylcarbinylamine with aqueous nitrous acid and the hydrolysis of N-methyl-4-(cyclopropylmethylcarbinyl)pyridinium iodide, giving in both cases cyclopropylmethylcarbinol as the product. Both of the cyclopropylmethylcarbinyl starting materials are stable and easily handled. In addition, both generate the ion(s) of interest by means of a neutral leaving group which hopefully should obviate the complication of internal return. Thus, the solvolysis of 5-methyl-2-cyclohexenyl *p*-nitrobenzoate in 80% acetone is accompanied by internal return but the acid-catalyzed solvolysis of the same substrate is not.¹⁵

The stereochemistry of the amine-nitrous acid reaction, in general, is more or less typical of S_N1 processes. Deamination in excess aqueous acid of 2-butyl-, 2-octyl-, and 1-phenylethylamines is reported to give racemization and inversion of configuration; alanine gives retention and phenylglycine gives retention and racemization.¹⁶ Wiberg¹⁷ found 22% net inversion of configuration in the deamination of 2-butylamine in excess aqueous sulfuric acid and 26% inversion in glacial acetic acid. 1-Butylamine-1-²H in glacial acetic acid gives 69% net inversion of configuration,¹⁸ while optically active α-methylallylamine is deaminated in glacial acetic acid to give a mixture of α- and γ-methylallyl acetates, wherein the α-acetate showed 16% net

(12) K. B. Wiberg, paper presented at the 19th Organic Chemistry Symposium of the American Chemical Society, Tempe, Ariz., June 17, 1965.

(13) C. U. Pittman, Jr., and G. A. Olah, *J. Am. Chem. Soc.*, **87**, 2998 (1965).

(14) Cf., S. Winstein and A. H. Fainberg, *ibid.*, **80**, 459 (1958), and many earlier papers by Winstein and co-workers.

(15) H. L. Goering and E. F. Silversmith, *ibid.*, **77**, 6249 (1955).

(16) P. Brewster, F. Hiron, E. D. Hughes, C. K. Ingold, and P. A. D. S. Rao, *Nature*, **166**, 179 (1950).

(17) K. B. Wiberg, Ph.D. Thesis, Columbia University, 1950.

(18) A. Streitwieser, Jr., and W. D. Schaeffer, *J. Am. Chem. Soc.*, **79**, 2888 (1957).

(8) E. Renk and J. D. Roberts, *J. Am. Chem. Soc.*, **83**, 878 (1961).
 (9) J. D. Roberts, W. Bennett, and R. Armstrong, *ibid.*, **72**, 3329 (1950); J. D. Roberts and W. Bennett, *ibid.*, **76**, 4623 (1954).
 (10) S. Winstein and E. M. Kosower, *ibid.*, **81**, 4399 (1959).
 (11) M. C. Caserio, W. H. Graham, and J. D. Roberts, *Tetrahedron*, **11**, 171 (1960).

inversion and neither the ratio of α - to γ -acetates nor the optical activity of the α -acetate was affected by the addition of acetate ion.¹⁹ In the case of the optically active *exo*- and *endo*-norbornylamines, deamination in acetic acid gives very largely the product expected from the nonclassical ion although some simple inversion (2% with the *exo* amine and 18% with the *endo* amine) was observed along with some retention of optical activity in the noninverted product.²⁰

The second reaction used in this work, the hydrolysis of N-methyl-4-(cyclopropylmethylcarbinyl)pyridinium iodide, is a new example of the solvolysis of a cationic substrate. Similar reactions that have been studied previously are the solvolyses of sulfonium salts and of quaternary ammonium salts. The reactions of trimethyl- and tribenzylsulfonium salts in solution are bimolecular processes,²¹ while the decomposition of *t*-butyldimethylsulfonium salts is a unimolecular solvolysis.²² Benzhydryltrimethylammonium hydroxide is reported to give benzhydrol by a first-order process and methanol by a second-order process.²³ The hydrolysis of isobornyltrimethylammonium hydroxide or iodide gives camphene and tricyclene, undoubtedly through a carbonium ion intermediate.²⁴

The stereochemistry of the solvolysis of cationic substrates is poorly documented. The decomposition of optically active 1-phenylethyltrimethylammonium iodide in methanol, ethanol, and 1-butanol gives the respective ethers of 1-phenylethanol with complete racemization.²⁵ The starting material and the products were shown to be optically stable under the reaction conditions. Although no kinetic evidence was given, the racemized products were taken as proof of a unimolecular mechanism.²⁵ The reaction of 2-benzamidoalkyldimethylsulfonium salts with water gives the products typical of a solvolysis with participation of a neighboring benzamido group, except when such participation is sterically prohibited.^{26a} Acetolysis of *sec*-butylmercuric perchlorate, an S_N1 reaction, gives mostly racemized but partially inverted *sec*-butyl acetate.^{26b}

Results and Discussion

Cyclopropylmethylcarbinylamine (VI) was resolved by means of its tartrate salt and the maximum rotation obtained was $\alpha^{23D} + 21.80^\circ$ (neat). That the resolution was complete or nearly complete was indicated by the conversion of the amine of maximum rotation to the benzamide VII in 93% yield with $[\alpha]^{29D} + 33.7^\circ$ (absolute ethanol, *c* 5.0); the melting point of the optically active benzamide VII could not be improved by recrystallization.

Cyclopropylmethylcarbinyl hydrogen phthalate (VIII) was resolved with brucine. The almost constant

(19) D. Semenow, C.-H. Shih, and W. G. Young, *J. Am. Chem. Soc.*, **80**, 5472 (1958).

(20) We have chosen here to quote the results of J. A. Berson and A. Remanick, *ibid.*, **86**, 1749 (1964), which are somewhat different from those of E. J. Corey, J. Casanova, Jr., P. A. Vatakencherry, and R. Winter, *ibid.*, **85**, 169 (1963).

(21) C. G. Swain and L. E. Kaiser, *ibid.*, **80**, 4089 (1958).

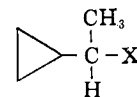
(22) C. G. Swain, L. E. Kaiser, and T. E. C. Knee, *ibid.*, **80**, 4092 (1958).

(23) E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 69 (1933).

(24) J. McKenna and J. B. Slinger, *ibid.*, 2759 (1958).

(25) D. N. Kursanov and S. V. Vitt, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 1445 (1959).

(26) (a) T. Taguchi and M. Kojima, *J. Am. Chem. Soc.*, **81**, 4318 (1959); (b) F. R. Jensen and R. J. Ouellette, *ibid.*, **85**, 363 (1963).



- VI, X = NH₂
 VII, X = NHCO₂C₆H₅
 VIII, X = O₂CC₆H₄CO₂H
 IX, X = OH
 X, X = O₂CC₆H₅

melting point and specific rotation of the resolved phthalate upon fractional recrystallization speak for its optical purity. The reduction of optically pure phthalate with lithium aluminum hydride gave cyclopropylmethylcarbinol (IX) containing impurities, but a value of $\alpha^{25D} + 20.1^\circ$ (neat) could be calculated for pure IX. The alkoxide of the optically pure alcohol with benzoyl chloride gave the optically pure benzoate X with $\alpha^{27D} + 33.82^\circ$ (neat).

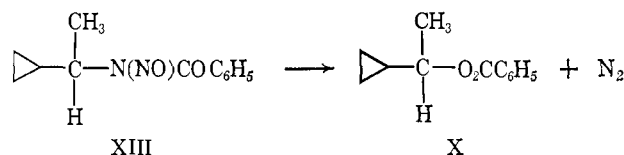
Transformation of amine VI to benzamide VII and the transformation of alcohol IX to benzoate X do not disturb the bonds attached to the asymmetric carbon atom so that amine and benzamide, which have the same sign of rotation, have the same configuration and alcohol and benzoate which also have the same sign of rotation have the same configuration. It remains to establish the relative configurations of the alcohol and amine derivatives.

There are at least 13 pairs of compounds with structures XI and XII whose relative configurations have been established.²⁷ For each pair, without excep-



tion, the amine and alcohol of the same configuration have the same sign of rotation. It seems reasonable therefore to conclude that cyclopropylmethylcarbinylamine (VI) and cyclopropylmethylcarbinol (IX) of the same sign of rotation also have the same absolute configuration, especially since the optical rotations are comparatively large.

Confirmation of the assignments of the amine VI and alcohol IX was sought from the thermal decomposition of N-nitroso-N-(cyclopropylmethylcarbinyl)benzamide (XIII) to benzoate X. In a variety of polar and nonpolar solvents, N-(1-arylethyl)nitrosamides usually decompose with predominant retention of



configuration.²⁸⁻³⁰ To be sure, with N-nitroso-N-(2-butyl)benzamide, a bimolecular inversion reaction (with benzoic acid released into the solution by an olefin-forming side reaction) competes in nonpolar solvents such as pentane, and may lead to a slight net

(27) See J. A. Mills and W. Klyne in "Progress in Stereochemistry," Vol. I, W. Klyne, Ed., Butterworth and Co. (Publishers) Ltd., London, 1954, pp 194-195, for a summary and references.

(28) R. Huisgen and C. Ruchardt, *Ann.*, **601**, 21 (1956).

(29) E. H. White, *J. Am. Chem. Soc.*, **77**, 6014 (1955).

(30) E. H. White and C. A. Aufdermarsh, Jr., *ibid.*, **83**, 1179 (1961).

inversion of configuration.²⁹ However, in dioxane, decomposition occurs with retention of configuration,²⁹ and the over-all reaction is regarded as stereochemically reliable enough to relate the configuration of at least one amine to that of the corresponding alcohol.³¹

Decomposition of the nitrosamide XIII, from the (+)-amide in dioxane and in pentane, gave (+)-benzoate with 21 and 17% retention of optical activity, respectively. It appears safe to conclude that these transformations, especially in dioxane, represent retention of configuration and therefore the (+)-alcohol and (+)-amine have the same configuration. It is perhaps significant to note that the per cent retention of configuration observed with XIII is small compared to the 40–94% (polar solvents) observed in other cases.^{28–30}

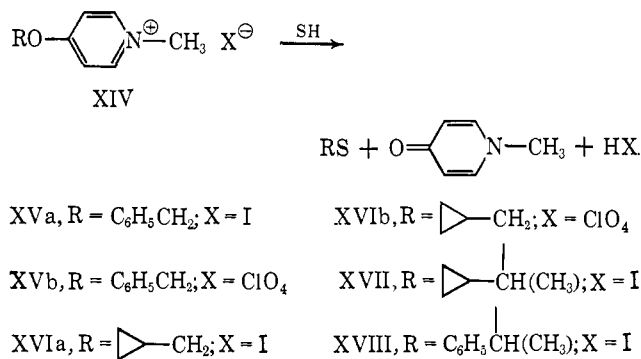
When the optically active amine VI was deaminated with aqueous nitrous acid at high pH, nearly racemic alcohol IX was obtained with a small (up to 4%), but definite, excess of inversion. The largest observed rotation of the product was $\alpha^{25D} +0.27^\circ$ (neat), starting with amine of $\alpha^{30D} -9.67^\circ$. The product contained about 1% of the amine and, if the contributions of amine and alcohol to the observed rotation are additive, then the amine-free alcohol would have $\alpha^{25D} +0.37^\circ$ which corresponds to 4% net inversion on the basis of the maximum rotations for amine and alcohol given above. The product of one deamination experiment had the same sign of rotation as the starting amine but a similar correction for amine in the product reversed the sign. Formation of significant amounts of methyl cyclopropyl ketone was also observed. The alcohol IX was shown to racemize only slightly (16%) under the reaction and isolation conditions. For one deamination experiment, the major product was bis-(cyclopropylmethylcarbonyl) ether; the formation of ethers from alcohols under mild conditions is often indicative of a highly stable carbonium ion intermediate.³²

The stereochemical result of the deamination of cyclopropylmethylcarbonylamine may be due to contributions from (1) an S_N2 displacement by water of nitrogen from the intermediate diazonium ion or (2) a "hot" classical carbonium ion which can give products directly or go over to a more stable "cold" (solvolytic), presumably nonclassical ion(s). Either of these possibilities is in accord with the nonrearranging path which is important in the deamination of cyclopropylcarbonylamine- α -¹⁴C.^{4,8} The work of Young and co-workers¹⁹ is very relevant here. These workers report that 43% of the acetate formed in the deamination of α -methylallylamine in acetic acid appears to come from a nonrearranging mechanism (and the rest from a solvolytic carbonium ion). They concluded from the stereochemistry of the nonrearranging process (40% net inversion if the solvolytic carbonium ion gives racemic product) that a "hot" carbonium ion is most likely to be involved rather than an S_N1 or S_N2 process.

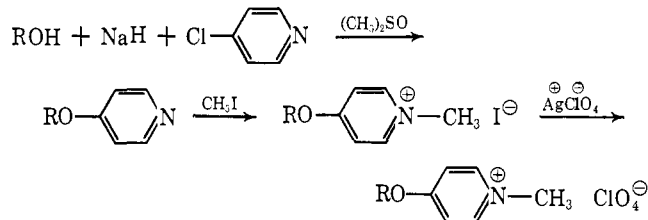
Because of the unknown relative contributions of the S_N2 mechanism and/or a "hot" carbonium ion intermediate to the observed stereochemical result of the deamination of cyclopropylmethylcarbonylamine, it is difficult to assess precisely the contribution of the solvolytic intermediate(s). However, since stereo-

chemistry is very largely lost in the reaction, it is difficult to believe that the degree of retention of configuration can be very large. Thus, if the "hot ion" were formed and gave 2–15% of clean inversion as in the norbornyl system, the degree of retention would at most be about 10%.

The next approach to the problem was to find a method of generating carbonium ions from the solvolysis of a positively charged cyclopropylmethylcarbonyl derivative. The hope was to avoid the disadvantages of the amine-nitrous acid reaction but to retain the advantages. Thus, the carbonium ion would no longer be formed in an exothermic step, obviating the problem of "hot" carbonium ions; the formation of the carbonium ion would be the slow step of the reaction and consequently accessible to kinetic investigation; and internal return might be avoided. The desirable properties of the cationic substrate would be ease of preparation and purification, ability to be obtained optically active and to be configurationally related to the solvolysis products, ability to be followed kinetically during solvolysis, and freedom from side reactions during solvolysis. After a number of abortive trials with various kinds of compounds, a class of compounds was found which generally met these qualifications, namely N-methyl-4-alkoxy-pyridinium salts (XIV).



The synthesis of these compounds was accomplished by the following route.



The yields were 86–89% for the first step, 68–100% for the second step, and 51–72% for the third step. All of the pyridinium salts were readily purified solids except for XVII and XVIII which were viscous liquids. The former was purified by low-temperature crystallization but the purification of the latter was not attempted.

The products of the solvolyses of the pyridinium salts in various solvents were determined mainly by means of vapor phase chromatography. Thus, the reaction of N-methyl-4-benzyloxy-pyridinium iodide (XVa) in glacial acetic acid at 109° gave a quantitative yield of benzyl acetate after 92 hr; the half-life of the reaction was 2–3 hr. In contrast, the corresponding perchlorate salt XVb was completely unreactive under

(31) C. J. Collins, W. A. Bonner, and C. T. Lester, *J. Am. Chem. Soc.*, **81**, 466 (1959).

(32) Cf. N. Weliky and E. S. Gould, *ibid.*, **79**, 2742 (1957).

Table I. Solvolysis of N-Methyl-4-alkoxy-pyridinium Salts

Run	Substrate	Solvent	Temp, °C	k_1 , hr ⁻¹	Infinity titer, % of theory
1	XVIa	Ethanol, 80%	98.4	0.013	89.4
2	XVIa	Water	98.6	0.20	90.7, 91.9
3	XVIa	Water	70.7	0.0065	89.4
4	XVIb	Ethanol, 80%	98.4	0.010	84.0
5	XVIb	Water	98.6	0.19	90.7
6	XVII	Water	30.0	0.16	84.5, 84.7, 86.1

the same conditions, indicating that the anion must be involved in the rate-determining step of the reaction of the iodide. The solvolysis of N-methyl-4-(cyclopropylcarbinyl)pyridinium iodide (XVIa) in 80% ethanol at 120° gave cyclopropylcarbinol, cyclobutanol, and allylcarbinol but predominantly the corresponding ethyl ethers as products. The ratio of the three ethers was cyclopropylcarbinyl/cyclobutyl/allylcarbinyl = 3.6:1.5:1.0; this ratio may be compared to the ratio observed for the ether products of the solvolysis of cyclopropylcarbinyl chloride in 80% ethanol at 97° of 5.7:2.5:1.0.¹¹ The hydrolysis of the same salt at 98.6° in the presence of lithium carbonate gave a 99% yield of cyclopropylcarbinol, cyclobutanol, and allylcarbinol; 8% of the alcohol mixture was allylcarbinol and the remaining 92% was cyclopropylcarbinol and cyclobutanol in the ratio of 1.2–1.5 to 1. The aqueous deamination of allylcarbinylamine, where cyclopropylcarbinol and cyclobutanol arise presumably only from nonclassical ions, gives a ratio of these alcohols of 1.17 to 1.⁸ Ethanolysis of N-methyl-4-(cyclopropylmethylcarbinyl)pyridinium iodide (XVII) at 98.4° gave cyclopropylmethylcarbinyl ethyl ether with no isomeric ethers; hydrolysis at room temperature in the presence of lithium carbonate gave only cyclopropylmethylcarbinol. On the other hand, the acetolysis of the same substrate at 87° gave a host of products, including cyclopropylmethylcarbinyl acetate; the product mixture obtained at 125° contained no cyclopropylmethylcarbinyl acetate, undoubtedly due to the isomerization of this substance under the conditions of the reaction. Acetolysis of the 1-phenylethyl derivative XVIII gave 1-phenylethyl acetate.

The fate of the heterocyclic ring during the solvolysis reactions was not rigorously determined. From the solvolyses of the cyclopropylmethylcarbinyl derivative XVII in acetic acid and in ethanol and the solvolysis of the 1-phenylethyl derivative XVIII in acetic acid was isolated what appeared to be the same yellow, crystalline solid. The solid could not be obtained in a pure state but contained carbon, hydrogen, nitrogen, and ionizable iodine, was very soluble in hydroxylic solvents, and insoluble in nonpolar solvents, and was very acidic. The available evidence indicates that this material was the expected, but impure, hydroiodide of N-methyl- γ -pyridone. When a solution of N-methyl- γ -pyridone in aqueous hydrogen iodide was evaporated to dryness, a yellow solid remained with a wide melting point range which appeared to be similar to the solids obtained from the solvolytic reactions.

The kinetics were measured of the solvolyses of N-methyl-4-(cyclopropylcarbinyl)pyridinium iodide (XVIa) and perchlorate (XVIb) in water and in 80% ethanol and of N-methyl-4-(cyclopropylmethylcarbinyl)pyridinium iodide (XVII) in water. The reac-

tions were followed by titration of the evolved acid, and the data are summarized in Table I. The first-order rate constants stayed relatively constant through the first or second half-life of each reaction but decreased significantly thereafter. Runs 2 and 3 gave $\Delta E^* \cong 31$ kcal/mole, and $\Delta S^* \cong 4$ eu for hydrolysis of the cyclopropylcarbinyl derivative XVIa. The rate for this compound, extrapolated to 30°, is $k_1 = 2.6 \times 10^{-5}$ hr⁻¹. The cyclopropylmethylcarbinyl derivative XVII ($k_1 = 0.16$ hr⁻¹) is, therefore, 6×10^3 more reactive than the cyclopropylcarbinyl derivative XVIa in water at 30°. ³³

The alcohols (or esters) obtained from the solvolyses of the pyridinium salts may arise by means of three reasonable mechanisms: (1) a direct solvolysis reaction (SN1), (2) an SN2 displacement by iodide to give unrearranged alkyl iodide which then solvolyzes to give the final products, and (3) displacement of the alkoxy group from the pyridine ring by an aromatic nucleophilic substitution mechanism. The solvolyses of N-methyl-4-(cyclopropylcarbinyl)pyridinium iodide in 80% ethanol and in water cannot be SN2 because the rates are virtually the same as those of the corresponding perchlorate (see Table I). Furthermore, the large rate enhancement (6×10^3) produced by α -methyl substitution on the cyclopropylcarbinyl substrate is consistent only with an SN1 solvolysis reaction. It is possible that the aromatic nucleophilic substitution may compete successfully in some of the investigated solvolyses. However, the hydrolysis of the cyclopropylcarbinyl derivative must be proceeding largely by SN1 solvolysis because the alcoholic products were a mixture of isomers typical (within the wide limits of experimental error) of carbonium ion type reactions of cyclopropylcarbinyl systems. We conclude therefore that the solvolysis of the cyclopropylmethylcarbinyl derivative proceeds essentially exclusively by the SN1 mechanism.

The observed infinity titers of the kinetic experiments presented in Table I (84–92% of theory) were somewhat low, and it is possible there is some formation of isomeric unreactive pyridinium salts by internal return.

(33) Both N-methyl-4-(cyclopropylcarbinyl)pyridinium iodide and perchlorate are about 20 times more reactive in water than in 80% ethanol. The dependence of rate on solvent is surprising compared to the 3110 times greater reactivity of *t*-butyl chloride at 25° in water than in 80% ethanol: A. H. Fainberg and S. Winstein, *J. Am. Chem. Soc.*, **78**, 2770 (1956). However, the SN1 solvolysis of *t*-butyldimethylsulfonium chloride, in a wide range of solvents and solvent mixtures, gives less than a fourfold variation in the first-order rate constants with, in general, the slowest rates in the better solvating media.²¹ This behavior has been attributed²² to an important role played by the cation-solvating power of the solvent; the better solvating media stabilize the cation with its localized charge relative to the transition state where the charge is distributed over sulfur, carbon, and nine hydrogens. It is reasonable, therefore, that the pyridinium salts, where the charge of the substrate is already delocalized over the pyridine ring and oxygen, should show behavior intermediate between that of *t*-butyl chloride and that of *t*-butyldimethylsulfonium chloride.

Streitwieser⁵ has explained the acid-catalyzed allylic rearrangements of 2-hexen-4-ol to 3-hexen-2-ol and of 1-phenyl-2-buten-1-ol to 1-phenyl-1-buten-3-ol with partial net retention of configuration on the basis of internal return from an "ion pair" with water playing the role of the anion part of a true ion pair. Thus, there is some evidence for internal return with neutral leaving groups. Cyclopropylcarbinyl chloride shows a remarkable propensity to rearrange by internal return; the acetolysis of the chloride appears to give 70% of rearranged chlorides⁴ and even the hydrolysis gives a 10% isolated yield of rearranged chlorides.⁴ However, internal return should almost certainly be much less important with a neutral rather than an anionic leaving group and in addition, the fact that the cyclopropylcarbinyl derivative XVIa gave a 99% yield of alcohols (admittedly under different conditions than those of the kinetic experiments) indicates that internal return may well be unimportant for this substrate. Another possible explanation for the low infinity titers is the consumption of the evolved acid by side reactions. When hydrogen iodide was dissolved in 80% ethanol under conditions approximating those of the rate runs 1, 15% of the initial acid disappeared after 17 hr, due, probably, to the formation of ethyl iodide and/or molecular iodine (the solution became brown). This explanation, of course, will not work for the perchlorate salt.

The ratio of rate constants for the solvolyses of N-methyl-4-(cyclopropylmethylcarbinyl)pyridinium iodide and of N-methyl-4-(cyclopropylcarbinyl)pyridinium iodide in water at 30° (6×10^3) provides the first reliable measurement of the effect of an α -methyl group upon the solvolysis rate of a cyclopropylcarbinyl derivative. Silver^{34a} found that the acid-catalyzed solvolysis of cyclopropylmethylcarbinyl *p*-nitrobenzoate is 40 times faster than that of cyclopropylcarbinyl *p*-nitrobenzoate, but there is good reason to believe that the slower of the two compounds is reacting by acyl-oxygen fission.

If the solvolysis of a cyclopropylcarbinyl derivative proceeds through the classical carbonium ion, one might expect the usual rate enhancement due to α -methyl substitution of at least 10^5 – 10^6 .^{34b} The observed effect of 6×10^3 does not speak for the classical intermediate but is large enough to lead one to question whether the intermediate would be better formulated as IV or V rather than as I. The stereochemical result of the substitution speaks for IV or V.

Thus, N-methyl-4-(cyclopropylmethylcarbinyl)pyridinium iodide synthesized with optically active cyclopropylmethylcarbinol and hydrolyzed in the presence of lithium carbonate gave the alcohol IX which was

(34) (a) M. S. Silver, Ph.D. Thesis, California Institute of Technology, 1959. (b) One may well ask whether relative rates for SN1 reactions with neutral leaving groups are directly comparable with relative SN1 rates obtained with anionic leaving groups. The rates of solvolysis of three alkyl dimethylsulfonium salts in aqueous ethanol are in nearly the same ratios as those of the corresponding alkyl chlorides. However, it is not wholly certain whether all the sulfonium salts are reacting by an SN1 mechanism: J. B. Hyne and H. S. Golinkin, *Can. J. Chem.*, **41**, 3139 (1963). Furthermore, solvolysis of alkylmercuric salts involves an SN1 mechanism with mercury as a neutral leaving group: F. R. Jensen and R. J. Ouellette, *J. Am. Chem. Soc.*, **83**, 4477, 4478 (1961), and the rate enhancements due to α -methyl substitution are larger with mercury as the leaving group than with tosylate or halide ion.^{26b} Thus, if anything, one might expect even more than a 10^5 – 10^6 rate enhancement due to α -methyl substitution with neutral N-methyl-4-pyridone as the leaving group.

$95.6 \pm 1.5\%$ racemic. The small optical activity of the product corresponded to $4.4 \pm 1.5\%$ of inversion which is in accord with a small shielding effect by the leaving group. This result in conjunction with those obtained in the decomposition of N-nitroso-N-(cyclopropylmethylcarbinyl)benzamide and the deamination of cyclopropylmethylcarbinylamine suggest either that the preferred intermediate in this system is IV or V or that there is a mechanism for facile racemization of whatever other cationic intermediates are involved.

Experimental Section

Melting points and boiling points are uncorrected. Elemental analyses were performed by Dr. Adalbert Elek, Elek Microanalytical Laboratories, Los Angeles, Calif. Infrared absorption spectra were obtained using a Perkin-Elmer double-beam recording infrared spectrophotometer, Model 21, or a Beckman infrared spectrophotometer, Model IR-7. Vapor chromatographic (vpc) analyses were obtained with a Perkin-Elmer vapor fractometer, Model 154-C, using diisodecyl phthalate (column A) as the stationary phase, unless otherwise indicated. Optical rotations were observed with a Winkel-Zeiss polarimeter relative to air or the appropriate solvent in the cases of neat liquids and solutions, respectively; the rotations were observed with a 1-dm tube and are accurate to $\pm 0.02^\circ$ unless otherwise noted.

The nmr spectra were observed at 60 Mcps with a Varian Model V4300B spectrometer equipped with a super stabilizer. The samples were either neat liquids or solutions in methylene chloride with tetramethylsilane as an internal standard.

Cyclopropylmethylcarbinylamine. In a 2-l. three-necked flask, equipped with a pressure-equalizing addition funnel, a mechanical stirrer, a nitrogen inlet, and a reflux condenser fitted with a calcium chloride drying tube, were placed 77 g (2.0 moles) of lithium aluminum hydride and 750 ml of anhydrous ether. To the stirred mixture in a nitrogen atmosphere was added dropwise 105 g (1.06 moles) of methyl cyclopropyl ketoxime dissolved in 450 ml of dry ether so as to maintain a moderate rate of reflux. The first half of the oxime solution was added over a period of 1.5 hr; the flask was cooled with an ice-water mixture and the remaining oxime was added over a 1-hr period. The mixture was stirred at room temperature for 18 hr and then under reflux for 34 hr. The condenser was replaced by a Dry Ice condenser; the flask was immersed in an ice-water bath and the reaction mixture was hydrolyzed with 500 ml of 10% aqueous sodium hydroxide. Ether (250 ml) and water (250 ml) were then added. The flask was equipped for downward distillation, and distillation was conducted until a second, aqueous phase formed in the receiver. The aqueous phase was saturated with potassium carbonate, and the ethereal phase was removed and dried over potassium carbonate. The solvent was removed and the residue was distilled through a 30-cm Vigreux column, yielding 70.0 g (78%) of material, bp 91–94° (740 mm), n_D^{25} 1.4243 (lit³⁵ bp 94.2–94.8° (745 mm), n_D^{25} 1.4265).

Resolution of Cyclopropylmethylcarbinylamine. From a solution of 108 g (1.27 moles) of amine and 190 g (1.27 moles) of *d*-tartaric acid in 300 ml of water was obtained 121 g (41%) of the amine tartrate salt. Six recrystallizations from 93% ethanol gave 69 g of salt, mp 161.8–163.0°.

Anal. Calcd for $C_9H_{17}NO_6$: C, 45.95; H, 7.29; N, 5.96. Found: C, 46.19; H, 7.23; N, 6.11.

A 15-g sample of the tartrate and 30 g of potassium hydroxide were added to 20 ml of water. The organic layer was withdrawn and repeatedly shaken with sodium hydroxide pellets until an aqueous layer no longer formed. The recovered amine was dried over barium oxide and on distillation gave 3.6 g of material, bp 88–92°. Redistillation through a packed column gave 1.15 g, bp 92–94°, α_D^{25} +21.30° (neat). Since vpc indicated about 5% impurities, the product was purified by preparative vpc. The material which collected had α_D^{25} +21.14° (neat) and contained about 5% water. Other samples from different tartrate fractions had rotations of +21.29°, +21.80°, and +21.45°.

(+)-N-(Cyclopropylmethylcarbinyl)benzamide. A mixture of 5.7 g (0.067 mole, α_D^{25} +21.80°) of (+)-cyclopropylmethylcarbinylamine, 8.3 g of sodium hydroxide, 12 g (0.085 mole) of benzoyl chloride, and 60 ml of water was stirred magnetically for 10 hr.

(35) N. J. Demjanov and S. Pinegin, *Zh. Russ. Fiz. Khim. Obshchestva*, **46**, 58 (1914); *Chem. Zentr.*, 1999 (1914).

The white precipitate which separated was collected by suction filtration and recrystallized from 50% ethanol-water and then from 50% benzene-hexane. The yield of purified benzamide was 11.0 g (93%), mp 123.4–124.0°, $[\alpha]_D^{25} + 33.7 \pm 0.2^\circ$ (c 5.0, absolute ethanol). Further recrystallization failed to raise the melting point of the product. The infrared spectrum of the optically active benzamide was identical with that of a sample of racemic benzamide, mp 96.0–97.0° (lit^{34a} mp 96.8–97.6°).

Cyclopropylmethylcarbinol was prepared in 62% yield by the reduction of methyl cyclopropyl ketone (62.7 g, 0.746 mole) with lithium aluminum hydride (11.9 g, 0.31 mole) in ether solution and had bp 119°, $n_D^{25} 1.4299$ (lit³⁶ bp 123.5°, $n_D^{20} 1.4316$).

Resolution of Cyclopropylmethylcarbinol. **A. Cyclopropylmethylcarbinyl Hydrogen Phthalate.** In a 100-ml, round-bottomed flask was placed 75 ml of reagent grade toluene and one-third was distilled to remove any moisture that may have been present. The remaining toluene was allowed to cool (protected from moist air with a calcium chloride drying tube) and 10.8 g (0.125 mole) of cyclopropylmethylcarbinol and 18.5 g (0.125 mole) of phthalic anhydride were added. The mixture was stirred magnetically and heated in an oil bath at 85–90° for 12 hr; it was then cooled and poured into a solution of 18 g of sodium carbonate in 900 ml of water. The aqueous phase was filtered and acidified with concentrated hydrochloric acid. The oil that separated solidified upon standing and was collected and, when dried, gave 20.2 g (69%) of white crystals, mp 67.8–69.4°. The analytical sample, mp 68.4–69.8°, was obtained by recrystallization from acetic acid-water.

Anal. Calcd for $C_{13}H_{14}O_4$: C, 66.65; H, 6.02. Found: C, 66.66; H, 5.94.

B. Resolution of Cyclopropylmethylcarbinyl Hydrogen Phthalate. To 800 ml of reagent grade acetone were added 81 g (0.345 mole) of racemic cyclopropylmethylcarbinyl phthalate and 136 g (0.345 mole) of anhydrous brucine. When the mixture was heated to reflux, the reactants dissolved, but a precipitate of crude brucine cyclopropylmethylcarbinyl hydrogen phthalate soon formed. The hot acetone solution was filtered and the filtrate, upon cooling, deposited 52 g of the brucine salt. The mother liquor was used to dissolve more of the initially formed crude brucine salt. Filtration and cooling of the solution gave 88 g of crystals. Repetition of the process dissolved the remaining crude salt and afforded another crop of 16 g.

The combined crystallized salt (156 g) was dissolved in the minimum amount (350 ml) of boiling reagent grade methanol and then cooled in a refrigerator, affording 81 g of salt, mp 166–170°. Seven additional recrystallizations gave 38 g of brucine (+)-cyclopropylmethylcarbinyl phthalate, mp 175.0–177.6°. From previous experiments, it was known that this melting point could not be raised by repeated recrystallizations from methanol.

Anal. Calcd for $C_{36}H_{40}N_2O_8$: C, 68.77; H, 6.41. Found: C, 68.18; H, 6.35.

The pure salt was decomposed by dissolving it in the minimum amount of boiling 95% ethanol and pouring the resulting solution into 240 ml of water and 16 ml of concentrated hydrochloric acid in a separatory funnel. An oil separated at the bottom of the funnel. It was known from preliminary experiments that the oil could not be induced to crystallize directly; consequently, it was dissolved in five volumes of glacial acetic acid; then, water was added to the cloud point. The solution was frozen solid in a Dry Ice-acetone bath and scratched as the solid warmed and melted. At about 15° a finely divided precipitate remained but turned to oil at room temperature. When the solution was cooled before it reached room temperature, oiling was prevented. The first crop (A) of optically pure phthalate was collected and dried in a vacuum desiccator over phosphorus pentoxide, 2.3 g, mp 57.8–59.8°, $[\alpha]_D^{25} + 33.1 \pm 0.2^\circ$ (c 10.2, carbon tetrachloride); the infrared spectrum of A was identical with that of the *d,l*-phthalate. Water was added to the mother liquor to the cloud point. Freezing, scratching while warming, and refrigeration of the solution gave a second crop (B) 1.6 g, mp 58.2–59.8°, $[\alpha]_D^{25} + 33.7 \pm 0.2^\circ$ (c 10.2). A third crop (C) was obtained in a similar manner, 1.0 g, mp 57.4–59.0°, $[\alpha]_D^{25} + 32.9 \pm 0.2^\circ$ (c 10.1).

Crop B was recrystallized from acetic acid-water by the above procedure and gave three fractions: B-1, 0.15 g, mp 57.8–59.6°; B-2, 0.50 g, mp 57.8–59.2°, $[\alpha]_D^{25} + 33.1 \pm 0.2^\circ$ (c 9.7); B-3, 0.3 g, mp 57.6–59.2°.

C. Reduction of (+)-Cyclopropylmethylcarbinyl Hydrogen Phthalate. The combined crops A, B-1–3, and C of the *d*-phthalate

(4.0 g, 0.017 mole, including all the samples used for measuring optical rotations, which had been evaporated to dryness under an air stream and dried) were dissolved in 75 ml of dry ether. The solution was added over a 0.5-hr period to 2.3 g (0.060 mole) of lithium aluminum hydride suspended in 75 ml of ether in a 500-ml, three-necked flask equipped with a mechanical stirrer, a reflux condenser, a pressure-equalizing addition funnel, and a nitrogen inlet. A nitrogen atmosphere and stirring were maintained throughout the reaction. The mixture was held at reflux for 1 hr and then 7.7 ml of ethyl acetate was added to decompose excess hydride. The mixture was stirred for an additional 15 min, the condenser was replaced by a Dry Ice condenser, and 10 ml of water was added. The mixture was then stirred and heated under reflux for 1 hr, stirred at room temperature for 4 hr, and then allowed to stand for 3 hr at which point all the gray salts had disappeared, leaving only a white precipitate. The ether was decanted and the precipitate was washed twice with 50-ml portions of ether. The combined ethereal solutions were dried over potassium carbonate. The ether was removed and the residue distilled. After 0.26 g of forerun, 1.17 g of a mixture, containing 82.6% of cyclopropylmethylcarbinol and 17.4% of ethanol and water (vpc) was obtained with bp 70–72° (96 mm), $\alpha_D^{30} + 18.25^\circ$ (neat). The main fraction was redistilled through the same column giving 0.19 g of forerun and 0.68 g of a mixture, containing 93.7% of carbinol and 6.3% of ethanol and water with bp 70° (90 mm), $\alpha_D^{25} + 19.45^\circ$ (neat). Linear extrapolation of the two observed rotations to 100% carbinol gave $\alpha_D^{25} + 20.1^\circ$.

(+)-Cyclopropylmethylcarbinyl Benzoate. In a 100-ml, round-bottomed flask, equipped with a magnetic stirrer, a reflux condenser, and a calcium chloride drying tube were placed 50 ml of dry ether, 0.30 g (0.012 mole) of sodium hydride, and 0.54 g (0.006 mole, $\alpha_D^{25} + 19.45^\circ$) of (+)-cyclopropylmethylcarbinol. The mixture was stirred under reflux for 4 hr. The white sodium alcoholate precipitated. The mixture was cooled to room temperature and 1.0 ml (0.009 mole) of benzoyl chloride was added. The mixture was stirred at reflux for 1.5 hr and at room temperature for 12 hr. After 24 more hr, 5 ml of water was added to decompose the remaining hydride and to dissolve the sodium salt. The ethereal phase was separated, extracted twice with 2-ml portions of water, and dried over magnesium sulfate. After removal of the solvent, the residue was distilled and gave 0.52 g (44%) of benzoate; bp 47–49° (1 mm), $\alpha_D^{25} + 33.82^\circ$ (neat), $n_D^{25} 1.5064$. The infrared spectrum of the product was identical with that of an analytically pure sample obtained from the decomposition of *N*-nitroso-*N*-(cyclopropylmethylcarbinyl)benzamide as described below.

Preparation and Decomposition of Optically Active *N*-Nitroso-*N*-(cyclopropylmethylcarbinyl)benzamide. For each of the two experiments, the nitrosamide was prepared from a mixture of 100 ml of a 0.5 *M* solution of nitrogen tetroxide (Matheson) in reagent grade carbon tetrachloride, 8.3 g (0.10 mole) of sodium acetate, and 4.7 g (0.025 mole) of the above (+)-*N*-(cyclopropylmethylcarbinyl)-benzamide, stirred magnetically for 30 min at 5°. The mixture was poured onto 100 g of ice, and the organic layer was removed and extracted with water and with 5% aqueous sodium bicarbonate and then dried over sodium sulfate; all operations were carried out at 0–5°. The solution was decanted and evaporated to dryness under vacuum at 0°, leaving the crude nitrosamide as a yellow oil. The per cent retention of optical activity in the product (cyclopropylmethylcarbinyl benzoate) of the decomposition of the nitrosamide was calculated on the basis that the starting benzamide was optically pure and the rotation of optically pure product is $\alpha_D^{25} + 33.82^\circ$.

A. Decomposition in Pentane. The crude nitrosamide was stirred overnight in 125 ml of reagent grade pentane at room temperature. The solution was then stirred with sodium hydroxide pellets to precipitate the benzoic acid formed during the decomposition. After filtration and distillation of the solvent, the residue was distilled and yielded 2.00 g (50%) of cyclopropylmethylcarbinyl benzoate, bp 55–58° (1 mm), $\alpha_D^{30} + 5.25^\circ$ (neat). A broad absorption band at 3200 cm^{-1} in the infrared spectrum of the product suggested the presence of benzoic acid as an impurity. Consequently, the product was dissolved in 50 ml of ether, and the ethereal solution was extracted with 50% aqueous potassium carbonate and dried over sodium sulfate. Removal of the solvent and distillation of the residue gave 1.25 g of benzoate, bp 56–58° (1 mm), $\alpha_D^{25} + 5.68^\circ$ (neat, 17% retention of optical activity), $n_D^{25} 1.5066$; the 3200 cm^{-1} band had disappeared. The nuclear magnetic resonance (nmr) spectrum and the infrared spectrum were consistent with the assigned structure.

Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 76.11; H, 7.39.

(36) R. V. Volkenburgh, K. W. Greenlee, J. M. Derfer, and C. E. Boord, *J. Am. Chem. Soc.*, 71, 3595 (1949).

B. Decomposition in Dioxane. The crude nitrosamide was stirred magnetically in 100 ml of purified dioxane at room temperature for 18 hr. The solution was then stirred with a sodium hydroxide pellet and decanted. The solvent was stripped and the residue was distilled and yielded 1.40 g (35%) of liquid, bp 67–72° (1 mm). Because of the presence of an infrared absorption band at 3200 cm^{-1} , the product was purified by dissolving it in 40 ml of ether and treating the solution as above; the yield was 0.71 g, bp 65° (1 mm), $\alpha_D^{25} + 7.18^\circ$ (neat, 21% retention of optical activity), $n_D^{25} 1.5065$; the infrared spectrum was identical with that of the analytically pure sample of the preceding preparation.

Deamination of Optically Active Cyclopropylmethylcarbinylamine with Nitrous Acid. For all but the last experiment, the reaction vessel was a 100-ml, round-bottomed flask, equipped with a magnetic stirrer, a reflux condenser, and a gas exit tube. The evolved gases were collected by displacing water from an inverted graduate cylinder. The pH measurements were made with a Beckman glass-electrode pH meter, Model H, on the entire reaction mixture cooled to room temperature. The pH of the reaction mixture was deliberately kept high to avoid acid-catalyzed racemization of the product, cyclopropylmethylcarbinol. The deaminations were conducted at reflux but were still very slow, as indicated by the rate of gas evolution, and virtually ceased as the reaction proceeded and the solution became more basic. Consequently, the reaction was periodically interrupted and more acid was added to lower the pH and speed up the reaction. The pH of the solution was measured before and after the reaction and before and after each addition of acid but only the extremes of the pH readings are reported. The total period of time under reflux and the total amount of acid used are given for each experiment. The products were isolated by continuous extraction of the reaction mixture (saturated with sodium chloride) with ether. The ethereal solution was dried over sodium sulfate and decanted. The ether was removed and the residue was distilled. All optical rotations were measured with neat samples.

A. The reactants were 50 ml of water, 8.7 g (0.052 mole) of 60% aqueous perchloric acid, 4.3 g (0.050 mole, $\alpha_D^{24} + 9.18^\circ$) of amine, and 10 g (0.14 mole) of sodium nitrite; 870 ml of gas was evolved after 9.5 hr of heating. The pH range was 8.2–9.2. The isolation procedure gave 0.25 g of forerun which was mostly methyl cyclopropyl ketone as determined by infrared and vpc analysis. The main fraction, 0.78 g, bp 69–72° (99 mm), $\alpha_D^{24} + 0.04^\circ$, had an infrared spectrum identical with that of cyclopropylmethylcarbinol with the exception of additional bands at 1600, 1660, and 1695 cm^{-1} . The 1695- cm^{-1} band corresponded to the carbonyl absorption band of methyl cyclopropyl ketone and the 1600- and 1600- cm^{-1} bands were attributed to the N–H deformation mode of cyclopropylmethylcarbinylamine. No satisfactory method of analyzing for small amounts (1–2%) of the amine (or the ketone) in the presence of the carbinol by vpc was found. However, the concentration of the amine in the product was estimated as 2% by comparing the infrared spectrum of the product with those of mixtures of amine and alcohol of known concentrations.

B. The reactants were 8.6 g (0.052 mole) of perchloric acid, 4.3 g (0.050 mole, $\alpha_D^{25} + 9.18^\circ$) of amine, and 5 g (0.07 mole) of sodium nitrite in 40 ml of water, and 980 ml of gas was collected over 11 hr of heating. The pH range was 8.3–8.9. The products isolated were 0.19 g of forerun, mostly alcohol with some ketone (vpc) and 0.67 g of alcohol containing 1% of amine (infrared), bp 70–72° (98 mm), $\alpha_D^{25} - 0.04^\circ$.

C. The reactants were 50 ml of water, 8.9 g (0.053 mole) of perchloric acid, 4.3 g (0.050 mole, $\alpha_D^{20} - 9.67^\circ$) of amine, and 10 g (0.14 mole) of sodium nitrite; 1050 ml of gas was evolved over 21.5 hr of heating. The pH range was 7.6–9.4. The usual isolation procedure (with the exception that the ether was removed through a 50-cm Helipak-packed column) gave 0.24 g of forerun, mostly ketone (vpc), and 1.39 g, bp 70° (95.5 mm). The main fraction was redistilled from 0.5 g of adipic acid (to remove amine) and gave 0.19 g of forerun and 1.01 g of alcohol containing 1% of amine (infrared), bp 70° (95 mm), $\alpha_D^{25} + 0.27^\circ$.

D. The apparatus was a 100-ml, three-necked flask equipped with pH electrodes, magnetic stirrer, a reflux condenser, a thermometer, and a gas-collecting system. To the flask were added 40 ml of water, 8.0 g (0.048 mole) of acid, 4.3 g (0.050 mole, $\alpha_D^{25} + 9.18^\circ$) of amine, and 5 g (0.07 mole) of sodium nitrite. The electrodes and the thermometer were adjusted so that they were well below the surface of the solution but did not interfere with the magnetic stirring bar. Stirring was maintained throughout the reaction. At 26°, the pH was 8.0. The solution was heated to 80° with an oil bath over a 10-min period, during which

time 45 ml of gas was collected. The pH meter now read 7.8 without adjusting the temperature compensating control. The solution was held at 80° and additional acid was added periodically, through the condenser, closing the system as soon as possible thereafter. By this method, the reading of the pH meter was maintained between 6.0 and 7.8. After 10 hr, 1200 ml of gas had been collected and the meter read 6.4 (5.5 after cooling the solution to room temperature). Isolation of the products gave 0.50 g of forerun, 1.61 g, bp 72–101° (98–81 mm), and 0.28 g, bp 56° (11 mm). The main fraction contained 14% of cyclopropylmethylcarbinol and 75% of an unknown compound (A) while the last fraction contained 3% of the alcohol and 91% of the unknown compound. The infrared spectrum of the unknown showed no prominent absorption in the region of 1500–5000 cm^{-1} except for bands in the C–H stretching region (2800–3100 cm^{-1}). On the basis of its nmr and infrared spectra it was assigned the structure bis-(cyclopropylmethylcarbinyl) ether.

Racemization of Cyclopropylmethylcarbinol under the Conditions of the Amine–Nitrous Acid Reaction. To 50 ml of water were added 6.4 g (0.038 mole) of 60% perchloric acid, 5.0 ml (0.039 mole) of 1-phenylethylamine, 7 g (0.11 mole) of sodium nitrite, and 1.21 g of cyclopropylmethylcarbinol, $\alpha_D^{25} - 1.36^\circ$ (neat). The initial pH was 7.0. The solution was heated under reflux for 5 hr and evolved 965 ml of gas. The cooled solution was now pH 8.9. The usual isolation procedure gave 0.08 g of forerun and then 0.75 g of cyclopropylmethylcarbinol, bp 70–71° (101 mm), $\alpha_D^{25} - 1.14^\circ$ (neat), corresponding to 84% retention of optical activity. The still residue contained 4.6 g of a red liquid.

4-Pyridylpyridinium dichloride was prepared by the method of Bowden and Green.³⁷ From 1000 g of technical grade thionyl chloride and 340 ml of pyridine was obtained 293 g of a golden brown powder, mp 160–166° (lit³⁷ mp 158–160°).

4-Hydroxypyridine was prepared in 69% yield by the method of Koenigs and Greiner³⁸ from 4-pyridylpyridinium dichloride.

4-Chloropyridine was prepared by the method of Leis and Curran.³⁹ From 38 g of phosphorus pentachloride, 38 g of phosphorus oxychloride, and 33 g of 4-hydroxypyridine was obtained 24 g (61%) of product, $n_D^{25} 1.5290$ (lit³⁹ $n_D^{25} 1.5280$), which was stored at –5° to prevent polymerization.

4-Benzyloxy pyridine was prepared after the method of Shaw⁴⁰ and had mp 51.6–54.8° (lit⁴⁰ mp 55–56°).

N-Methyl-4-benzyloxy pyridinium Iodide. On a steam bath were heated 0.50 g of 4-benzyloxy pyridine and 0.50 g of methyl iodide. The solution solidified after a few minutes. The solid was crystallized from ethanol–ethyl acetate giving 0.70 g (79%), mp 146.8–149.8°. Two recrystallizations from absolute ethanol gave 0.6 g of light tan crystals, mp 149.4–150.8° after vacuum drying.

Anal. Calcd for $\text{C}_{13}\text{H}_{14}\text{INO}$: C, 47.72; H, 4.31; I, 38.79. Found: C, 47.34; H, 4.49; I, 39.09.

N-Methyl-4-benzyloxy pyridinium perchlorate was prepared from 88 mg of N-methyl-4-benzyloxy pyridinium iodide dissolved in 6 ml of 80% ethanol to which was added a solution of silver perchlorate in ethanol until no more yellow precipitate would form. The solution was filtered from the precipitate and evaporated to dryness under vacuum. The residue was dissolved in 10 ml of methylene chloride and filtered, and ether was added to the cloud point. Cooling gave 41 mg (51%) of white crystals, mp 141.4–142.2° after drying over phosphorus pentoxide.

Anal. Calcd for $\text{C}_{13}\text{H}_{14}\text{ClNO}_3$: C, 52.09; H, 4.71; Cl, 11.83; N, 4.67. Found: C, 51.66; H, 4.69; Cl, 11.96; N, 4.89.

4-(Cyclopropylmethylcarbinyl)pyridine. In a 50-ml, round-bottomed flask, protected by a calcium chloride drying tube, were placed 2.4 g (0.032 mole) of cyclopropylcarbinol, 0.76 g (0.032 mole) of sodium hydride, and 10 ml of purified dimethyl sulfoxide. The mixture was stirred magnetically for 1 hr, when 3.2 g (0.028 mole) of 4-chloropyridine was added, and stirring was continued for 8 hr. The red solution was filtered and the precipitate was washed with hot benzene. The dimethyl sulfoxide solution and benzene washings were combined, the benzene was removed under vacuum, and the residue was distilled at 1 mm. After removal of the dimethyl sulfoxide (bp 31°) there was obtained 3.73 g (89%) of a colorless liquid, bp 57° (1 mm), which on redistillation gave three fractions, bp 85° (3 mm), $n_D^{25} 1.5124$ – 1.5260 . The third fraction, $n_D^{25} 1.5258$, was analyzed.

(37) K. Bowden and P. N. Green, *J. Chem. Soc.*, 1795 (1954).

(38) E. Koenigs and H. Greiner, *Ber.*, **64**, 1049 (1931).

(39) D. G. Leis and B. C. Curran, *J. Am. Chem. Soc.*, **67**, 79 (1945).

(40) E. Shaw, *ibid.*, **71**, 67 (1949).

Anal. Calcd for $C_9H_{11}NO$: C, 72.45; H, 7.43; N, 9.39. Found: C, 72.83; H, 7.82; N, 9.29.

The nmr spectrum of the third fraction was consistent with the assigned structure.

N-Methyl-4-(cyclopropylcarbinyloxy)pyridinium iodide was prepared from 1.5 g of 4-(cyclopropylcarbinyloxy)pyridine and 2 ml of methyl iodide in a tightly stoppered test tube. The exothermic reaction was moderated by periodically cooling the tube in ice-water. The mixture became thick and then crystallized. Recrystallization from methylene chloride-ether gave 2.00 g (68%) of yellow crystals, mp 110.4–111.1° after vacuum drying. The nmr spectrum was consistent with the assigned structure.

Anal. Calcd for $C_{10}H_{14}INO$: C, 41.25; H, 4.85; I, 43.59; N, 4.81. Found: C, 41.40; H, 4.85; I, 44.79; N, 5.04.

N-Methyl-4-(cyclopropylcarbinyloxy)pyridinium perchlorate was prepared from 0.40 g of N-methyl-4-(cyclopropylcarbinyloxy)pyridinium iodide dissolved in 10 ml of absolute ethanol to which a solution of silver perchlorate in ethanol was added until no more yellow precipitate would form. The mixture was boiled and filtered, and the precipitate was washed with 10 ml of hot ethanol. The combined ethanolic filtrates were evaporated to 10 ml under vacuum whereupon a white precipitate separated. Subsequent boiling and cooling gave 0.28 g of white crystals, which, after vacuum drying, had mp 87.0–87.6° (cloudy). The product was taken up in 2 ml of methylene chloride and filtered from a small amount of gray, insoluble material. Addition of ether to the filtrate and cooling gave 0.26 g (72%) of material having mp 87.6–88.0° after vacuum drying.

Anal. Calcd for $C_{10}H_{14}ClNO_3$: C, 45.55; H, 5.35; Cl, 13.45; N, 5.31. Found: C, 45.80; H, 5.52; Cl, 13.50; N, 5.80.

4-(Cyclopropylmethylcarbinyloxy)pyridine was prepared in a similar manner to 4-(cyclopropylcarbinyloxy)pyridine. From 5.6 g (0.065 mole) of cyclopropylmethylcarbinol, 1.56 g (0.065 mole) of sodium hydride, 20 ml of purified dimethyl sulfoxide, and 7.4 g (0.065 mole) of 4-chloropyridine was obtained 9.1 g (86%) of a colorless liquid, bp 72° (1 mm). Redistillation gave three fractions, bp 77° (2 mm), n_D^{25} 1.5130–1.5160. The third fraction, n_D^{25} 1.5160, was redistilled from barium oxide and analyzed.

Anal. Calcd for $C_{10}H_{13}NO$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.91; H, 8.02; N, 9.03.

The nmr spectrum of the product was consistent with the assigned structure.

N-Methyl-4-(cyclopropylmethylcarbinyloxy)pyridinium Iodide. In a stoppered flask were placed 2.94 g of 4-(cyclopropylmethylcarbinyloxy)pyridine and 3 ml of methyl iodide. The exothermic reaction was moderated by cooling the flask under a stream of water. The excess methyl iodide was removed under vacuum leaving 5.74 g (104%) of a viscous, orange oil. It was known from preliminary experiments that this oil could not be induced to crystallize from methylene chloride-ether; however, its nmr spectrum was consistent with the assigned structure. The oil was dissolved in 15 ml of reagent grade acetone and filtered. Crystallization was induced by cooling the solution in a Dry Ice-acetone bath with vigorous scratching. Just after the first crystal appeared, the solution was cooled at 0°, and the crystallization slowly continued. The white crystals were collected in a 2-ml, sintered-glass Büchner funnel. The funnel was quickly transferred to a stoppered, 15-ml centrifuge tube and was centrifuged for 5 min in a centrifuge cooled by placing Dry Ice in the guard bowl. The centrifuged crystals (1.8 g) were quickly placed in a vacuum desiccator where they began to melt. Before melting was complete, the product was cooled and 1.2 g of acetone was added. The mixture was stirred until solution was almost complete and cooled again. The precipitate that formed was collected as before and was placed in a vacuum desiccator where it melted to a slightly yellow oil weighing 0.90 g. Two more crystallizations from acetone gave 0.40 g of a nearly colorless oil which was dissolved in methylene chloride and filtered to remove a few particles of foreign material. The methylene chloride solution was placed in a vacuum desiccator over phosphorus pentoxide for 4 days, leaving 0.41 g of oil which was analyzed.

Anal. Calcd for $C_{11}H_{15}INO$: C, 43.29; H, 5.29; I, 41.59; N, 4.59. Found: C, 43.49; H, 5.53; I, 41.23; N, 4.52.

Metathesis of samples of the methiodide with silver perchlorate and with silver trifluoroacetate produced colorless oils which could not be induced to crystallize.

4-(1-Phenylethoxy)pyridine was prepared in a similar manner to 4-(cyclopropylcarbinyloxy)pyridine. From 5.1 g (0.042 mole) of 1-phenylethanol, 1.0 g (0.042 mole) of sodium hydride, 10 ml of purified dimethyl sulfoxide, and 5.1 g (0.045 mole) of 4-chloro-

pyridine was obtained 7.2 g (86%) of a viscous yellow liquid, bp 120° (1 mm). The product was refracted and a nearly colorless central cut, 5.0 g, had bp 94° (1 mm), n_D^{25} 1.5644.

Anal. Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.57; N, 7.03. Found: C, 78.02; H, 6.79; N, 7.04.

The analytical sample darkened upon standing unless sealed under nitrogen. The nmr spectrum of the product was consistent with the assigned structure.

The reaction of the alkoxy pyridine with methyl iodide produced a viscous orange oil which could not be induced to crystallize although its nmr spectrum was consistent with the structure N-methyl-4-(1-phenylethoxy)pyridinium iodide. From 1.00 g of the alkoxy pyridine was obtained 1.73 g (101%) of an orange oil after removing the excess methyl iodide under vacuum. The oil was dissolved in 1.90 g of glacial acetic acid and heated on a steam bath for 4 hr, at which time two phases formed. The lower phase solidified upon cooling the system to room temperature. The precipitate was collected and washed with ether and had mp 129–137°. Recrystallization from acetone gave 0.14 g of yellow crystals, mp 125–137°. The liquid phase of the reaction mixture was distilled through a simple head at 1 mm, the receiver being cooled in Dry Ice-acetone. Examination of the distillate by vpc showed acetic acid and one other peak. The unknown peak was collected on a preparative scale giving 182 mg of a yellow liquid. Repurification by preparative vpc failed to remove the yellow color. The unknown material was assigned the structure 1-phenylethyl acetate on the basis of its nmr spectrum.

Optically active 4-(cyclopropylmethylcarbinyloxy)pyridine was prepared in a similar fashion to the racemic compound. From 3.0 g (0.035 mole, α_D^{25} -3.39°) of cyclopropylmethylcarbinol, 0.84 g (0.035 mole) of sodium hydride, 15 ml of purified dimethyl sulfoxide, and 4.0 g (0.035 mole) of 4-chloropyridine was obtained 4.1 g (72%) of product, bp 65–66° (1 mm). Redistillation of the product gave 0.57 g of forerun and 3.40 g, bp 106–107° (6.5 mm), n_D^{25} 1.5156, α_D^{25} -0.87° (neat).

Preparation and Hydrolysis of Optically Active N-Methyl-4-(cyclopropylmethylcarbinyloxy)pyridine. The reaction of 2.37 g of the above optically active 4-(cyclopropylmethylcarbinyloxy)pyridine with excess methyl iodide gave 4.36 g (98%) of a viscous orange oil, $[\alpha]_D^{25} +0.3^\circ$ (c 6.8, chloroform), after removal of the excess methyl iodide in a vacuum desiccator over phosphorus pentoxide for 5 days. The infrared spectrum (neat) of the oil was similar to but not superimposable with that of the racemic methiodide. The variations were minor except for a broad band at 3440 cm^{-1} which was much stronger in the spectrum of the racemic methiodide.

The optically active methiodide (3.85 g) was dissolved in 50 ml of triply distilled water and 2 g of reagent grade lithium carbonate was added to buffer the solution. The mixture was stirred magnetically at room temperature for 36 hr and then continuously extracted with ether. The ethereal extracts (75 ml) were dried over sodium sulfate and then magnesium sulfate, the solvent was removed, and the residue was distilled, giving 0.57 g (53%) of product, bp 70° (89 mm), n_D^{25} 1.4373, $\alpha_D^{25} +0.15 \pm 0.05^\circ$ (neat). The infrared spectrum of the product was identical with that of an authentic sample of cyclopropylmethylcarbinol except for the presence of additional (weak) absorption bands at 965, 1170, 1240, 1645, and 1715 cm^{-1} . The latter two bands were broad and highly suggestive of an amine.

Solvolysis of N-Methyl-4-(cyclopropylcarbinyloxy)pyridine in 80% Ethanol. A mixture of 51.8 mg of the methiodide, 0.73 ml of absolute ethanol, and 0.15 ml of water was sealed in a glass tube and heated at 120° (bath temperature); the solid dissolved. After the solution was heated for 18 hr, it was analyzed by vpc under the conditions for the analysis of the products from the solvolysis of cyclopropylcarbinyloxy chloride.¹¹ Three major peaks appeared in the chromatogram, corresponding in retention times to the ethyl ethers of cyclopropylcarbinol, cyclobutanol, and allylcarbinol. The cyclobutyl and cyclopropylcarbinyloxy ethers were poorly resolved, but could be separated under different operating conditions. The ratio of the three ethers was cyclopropylcarbinyloxy/cyclobutyl/allylcarbinol = 3.6:1.5:1.0. Peaks with retention times equal to those of cyclobutanol, cyclopropylcarbinol, and allylcarbinol were also detectable but were too small to measure.

Solvolysis of N-Methyl-4-benzoyloxy pyridinium Iodide and Perchlorate in Glacial Acetic Acid. In 0.98 g of glacial acetic acid was dissolved 96 mg of the methiodide by warming the mixture on a steam bath. Approximately 30- μ l samples were sealed in capillary tubes and the tubes were heated in an oil bath at 109°. Capillaries were periodically withdrawn and their contents analyzed with a F and M programmed-temperature gas chromatograph, Model

202, using a silicone rubber column. The appearance of benzyl acetate was measured by comparing the chromatographs to that of a solution of benzyl acetate in acetic acid of known concentration. By this method the half-life of the reaction was estimated as 2–3 hr.

A 34-mg sample of the perchlorate was treated in the same way. Little or no benzyl acetate could be detected after 36 hr of heating.

For comparison, benzyl chloride was found to be unreactive under the same conditions.

Solvolysis of N-Methyl-4-(cyclopropylmethylcarbinyloxy)pyridinium Iodide in Ethanol. The methiodide (0.69 g) was a sample of unknown purity that had been recrystallized from acetone and dried under vacuum. A solution of the methiodide in 0.69 g of absolute ethanol was sealed in a glass tube and heated for 80 min at 98.4°. The resulting orange solution deposited a yellow precipitate when cooled to room temperature. The volatiles were removed under vacuum and collected in a Dry Ice–acetone trap. The residue was crystallized from ethanol giving 0.18 g of yellow crystals, mp 141.5–149.5°. Recrystallization from ethanol gave 0.10 g, mp 145–149°, which was triturated with boiling acetone in which it was insoluble. The vacuum-dried yellow crystals, mp 148.0–149.7°, were soluble in ethanol and the ethanolic solution gave an immediate yellow precipitate with alcoholic silver perchlorate. A solution of the solid in water, in which it was very soluble, had pH 2.

The volatiles from the original reaction (0.73 g) were examined by vpc and were found to contain one product besides ethanol. The product was separated by preparative vpc, giving 66 mg of a colorless liquid which was assigned the structure cyclopropylmethylcarbinyloxy ethyl ether on the basis of its nmr spectrum.⁴¹

Solvolysis of N-Methyl-4-(cyclopropylmethylcarbinyloxy)pyridinium Iodide in Glacial Acetic Acid. A sample of the methiodide of unknown purity was dissolved in glacial acid and heated at 125° for 8 hr. The solution became dark red. The volatiles were distilled into a Dry Ice trap under reduced pressure. The dark orange, crystalline residue was crystallized from ethanol giving yellow crystals, mp 147.4–149.8°. A mixture melting point with the crystalline product from the reaction of the methiodide with ethanol (above) was 147.8–149.7°.

The volatiles were examined by vpc and were found to contain, besides acetic acid, four major products, none of which corresponded in retention time to cyclopropylmethylcarbinyloxy acetate.

The reaction was repeated with 0.28 g of methiodide and 0.32 g of glacial acetic acid at 87° for 12 hr. The nonvolatile portion of the product was 0.15 g of a dark red, partially crystalline oil. The volatiles (0.32 g) were examined by vpc. Three of the four peaks of the chromatograph from the reaction at 125° were present but in different ratios. A new peak appeared which had the same retention time as cyclopropylmethylcarbinyloxy acetate.

Hydrolysis of N-Methyl-4-(cyclopropylcarbinyloxy)pyridinium Iodide. A solution of 25.0 mg of the iodide in 83.2 mg of triply distilled water was sealed in a glass tube and heated in an oil bath at 98.6° for 2 days. The reaction mixture was examined by vpc and found to contain, besides water, allylcarbinol, cyclobutanol, and cyclopropylcarbinol, although the peaks of the latter two alcohols were poorly resolved. The peaks indicated a ratio of cyclobutanol and cyclopropylcarbinol to allylcarbinol of 3.8:1. The ratio of cyclobutanol to cyclopropylcarbinol was judged, visually, to be about 10:1. That this ratio of alcohols resulted from rearrangement of the initially produced alcohols was indicated by adding 1 μ l of cyclopropylcarbinol to about one-third of the spent reaction mixture, sealing in glass, and heating or 2 days at 98.6°. The ratio of alcohols was essentially unchanged.

Consequently, a mixture of 12.2 mg of iodide, 7.3 mg of lithium carbonate, and 48.0 mg of water was sealed in glass and heated for 2 days at 98.6°. The concentrations of the alcoholic products were estimated by vpc, and a solution of the alcohols in water of the estimated concentrations was made. Comparison of the ratios of peak areas of the chromatograms of the reaction products and of the solution of known concentrations gave a more refined estimate. The total yield of alcohols was 99%; the ratio of cyclobutanol and cyclopropylcarbinol to allylcarbinol was 12.0:1; the ratio of cyclopropylcarbinol to cyclobutanol was 1.2–1.5 to 1. These ratios are very similar to those obtained in other hydrolytic reactions of cyclopropylcarbinyloxy derivatives where there is kinetic

rather than thermodynamic control of the product compositions.^{4,11}

N-Methyl- γ -pyridone was prepared by the method of Toomey and Riegel.⁴² The extremely hygroscopic solid had mp 96.2–98.4° (sealed capillary) (lit⁴² mp 92–94°).

In an attempt to prepare the hydroiodide, 0.10 g of the pyridine and 0.69 g of 48% aqueous hydrogen iodide were mixed and the water and excess hydrogen iodide were removed in a vacuum desiccator over phosphorus pentoxide. The yellow crystalline residue had mp 131–140°.

Kinetics of the Solvolyses of the N-Methyl-4-alkoxypyridinium Salts. A stock solution of 80% ethanol was made up from 400 ml of purified absolute ethanol and 100 ml of freshly boiled distilled water. For solvolyses in purely aqueous solvent, triply distilled water was used. The reactions were followed titrimetrically with 0.026 *M* aqueous sodium hydroxide standardized against potassium acid phthalate. The titrations were performed in a rubber-stoppered beaker protected from atmospheric carbon dioxide by an Ascarite tube and fitted with pH electrodes, a magnetic stirrer, and a 1-ml Koch buret with a capillary tip extending below the surface of the solution being titrated; a Leeds and Northrup pH indicator was used.

For the experiments at 71 and 96°, a weighed sample of salt was transferred to a volumetric flask and diluted to the mark with the appropriate solvent. Approximately 5.5-ml samples were sealed in freshly cleaned and dried glass ampoules. After the ampoules were placed in the bath, a "zero-time" sample was withdrawn when the bath reattained equilibrium (about 5 min). Ampoules were periodically withdrawn, quenched in ice-water, and brought to room temperature, and a 5-ml aliquot of the contents was added to 20 ml of carbon dioxide free distilled water. The end point of the titrations was taken as the pH corresponding to the point of maximum slope in a plot of pH vs. volume of base, determined for a few of the points in each run. Although the end point ranged from pH 7.0 to 7.4 during the various runs, the variation during a single run was no more than 0.2 pH units. Solvent "blanks" were treated in the same manner as the kinetic samples; the blank corrections were negligible in all cases. Solutions of the iodide salts turned noticeably brown during the kinetic runs; the perchlorate salt solutions remained colorless. The solvolysis at 30° was performed in a volumetric flask. At intervals, aliquots were quenched by pipetting them into ice-cold 95% ethanol and the titration was carried out immediately.

For all the experiments, the data were treated by calculating a first-order rate constant for each sample relative to the "zero time" sample. The "constants" determined in this fashion fell off

Table II. Solvolysis of 2.95×10^{-3} *M* N-Methyl-4-(cyclopropylmethylcarbinyloxy)pyridinium Iodide in Water at 30.0°

Time, hr	Unreacted, %	k_i , sec ⁻¹ $\times 10^{-5}$ ^a
0.00	89.9	
1.03	77.0	4.20
1.30	74.2	4.11
2.08	64.4	4.48
2.50	60.0	4.53
3.20	54.0	4.42
3.67	49.2	4.59
4.24	46.0	4.39
9.52	24.7	3.78
10.61	23.9	3.47
11.53	23.3	3.25

^a $k_i = 4.4 \times 10^{-5}$ sec⁻¹.

seriously after the first or second half-life. Consequently, the samples where this decrease was noticeable were ignored, and the remaining constants were averaged to give the final rate constant. Data for a typical run are given in Table II.

(41) P. R. Shafer, D. R. Davis, M. Vogel, K. Nagarajan, and J. D. Roberts, *Proc. Natl. Acad. Sci. U. S. A.*, **47**, 49 (1961); G. M. Whitesides, F. Kaplan, K. Nagarajan, and J. D. Roberts, *ibid.*, **48**, 1112 (1962).

(42) R. F. Toomey and E. R. Riegel, *J. Org. Chem.*, **17**, 1492 (1952).