mental accuracy. Since the C-2 and C-4 hydroxyl groups were methylated (hence, free), the C-3 hydroxyl must have been bound in the glycoside linkage and the C-5 hydroxyl in a pyranose ring, as shown in I and II.[12] This result does not however, establish definitely the ring form of ribose in intact neomycin B; this point and others dealing with the stereochemistry of neosamine B and the glycosidic link in neobiosamine B will be the subjects of future reports.

Acknowledgment.—This investigation was supported in part by a research grant, No. E-1278, from the National Institute of Allergy and Infectious Diseases, Public Health Service. We wish to express our thanks to the Upjohn Company for a gift of neomycin and also for assistance with paper electrophoreses.

(12) A structure similar to I recently has been assigned to paramobiosamine, a degradation product of the antibiotic paramomycin [T. H. Haskell, J. C. French and Q. R. Bartz, THIS JOURNAL, **81**, 3481 (1959)].

KENNETH L. RINEHART, JR.
DEPARTMENT OF CHEMISTRY ALEXANDER D. ARGOUDELIS
AND CHEMICAL ENGINEERING TOWNLEY P. CULBERTSON
UNIVERSITY OF ILLINOIS W. SCOTT CHILTON
URBANA, ILLINOIS KLAUS STREIGLER

RECEIVED APRIL 8, 1960

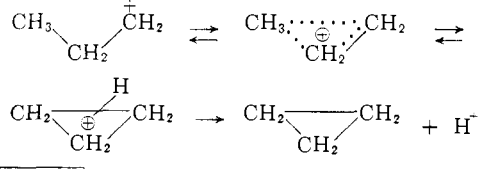
CYCLIZATION OF CARBONIUM TO CYCLOPROPANES[1]

Sir:

A primitive mechanistic explanation of rearrangements invoked cyclic intermediates such as cyclopropanes, epoxides, etc. Although these intermediates were discarded in the early part of this century, they have returned to the current literature in various forms as bridged ions. Experiments cited below emphasize the importance of some bridged intermediates.

It was noted in the de-oxidation of *n*-propyl alcohol[2] *n*-propyl carbonium ion being the postulated intermediate, that cyclopropane and propylene were reaction products. The resulting C_3H_6 is 90% propylene and 10% cyclopropane. Nitrous acid deamination of *n*-propylamine in aqueous solution also yields C_3H_6 which is 90% propylene and 10% cyclopropane. Also, cyclopropanes have been detected in other systems involving carbonium ion.[3,4]

These results can be rationalized by assuming that a protonated cyclopropane is a short-lived intermediate in this reaction.



(1) We wish to express our appreciation to Dr. M. S. Silver of Amherst College for communicating his results and for delaying publication of his work to permit simultaneous publication of these complementary results.

(2) P. S. Skell and I. Starer, THIS JOURNAL, **81**, 4117 (1959).

(3) M. S. Silver, *ibid.*, **82**, 2971 (1960).

(4) Probably related are the cationoid type reactions of diazo compounds in proton-donating solvents: L. Friedman and H. Shechter, *ibid.*, **81**, 5512 (1959).

CYCLOPROPANE FORMATION FROM DE-OXIDATION AND DIAZOTIZATION REACTIONS

Alcohol[a]	Cyclopropane in C_nH_{2n} products, %
i-Propyl	None
n-Propyl	10
n-Butyl	2
i-Butyl	4
s-Butyl	<0.5
t-Butyl	None
Neopentyl	None
t-Amyl	None
Amine[b]	
n-Propyl	10
Neopentyl	None
4,4-Dimethyl-1-pentyl	No cyclopropane

[a] At reflux, $HCBr_3$ and RO^- in ROH. [b] Aqueous solution at 100°.

It is attractive to think of the possibility that protonated cyclopropanes are not only intermediates in the route to cyclopropanes, but may also be the intermediates in the major pathways leading to rearranged carbonium ions. Thus, the opening of the three-membered ring may be the preferred route for alkyl substituted derivatives which can proceed to the more stable secondary and tertiary carbonium ions.[5] Labeling experiments suggested by these considerations are being examined. These suggestions, if valid, differ from the earlier ones in proposing that reaction of the protonated cyclopropane to yield cyclopropane and rearranged carbonium ions is rapid compared to protonation of the cyclopropane.

(5) The interconversion of *s*-butyl and *i*-butyl benzenes, etc., studied by R. M. Roberts, *et al.*, may involve a protonated cyclopropane lying perpendicular to the plane of the benzene ring, one edge of the cyclopropane closely associated with the aromatic π-electron system: THIS JOURNAL, **81**, 640 (1959), and earlier papers.

(6) Acknowledgment is made to the donors of The Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research and to the Office of Ordnance Research, Contract No. DA-36-061-ODR-607.

THE DEPARTMENT OF CHEMISTRY P. S. SKELL[6]
THE PENNSYLVANIA STATE UNIVERSITY
UNIVERSITY PARK, PENNSYLVANIA I. STARER

RECEIVED APRIL 2, 1960

FORMATION OF 1,2-DIMETHYLCYCLOPROPANE IN THE DEAMINATION OF SATURATED ALIPHATIC AMINES[1]

Sir:

The hydrocarbon fraction from the deamination of 3-methyl-2-aminobutane[2] at 56° in acetic acid has been found to contain the expected[3] 3-methyl-1-butene, 2-methyl-1-butene and 2-methyl-2-butene and two additional compounds. These compounds have been identified as *cis*- and *trans*-1,2-dimethylcyclopropane on the basis of gas chromatographic retention times, resistance to permanganate oxi-

(1) This research was supported in part by a grant from the Petroleum Research Fund, administered by the American Chemical Society, and grateful acknowledgment is hereby made to the donors.

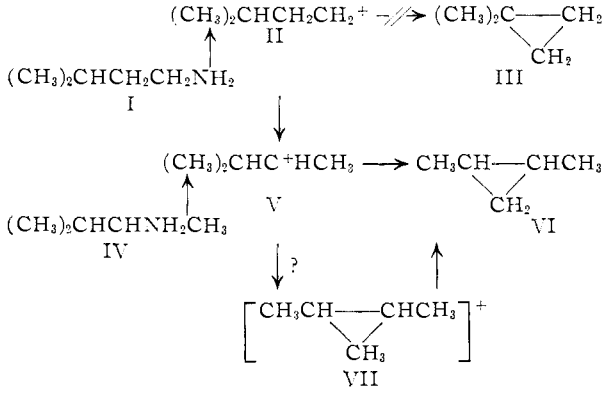
(2) Prepared according to J. S. Buck and A. M. Hjort, THIS JOURNAL, **59**, 2567 (1937), the amine had b.p. 85–87°. D. Trasciatti, *Gazz. chim. ital.*, **29**, II, 92 (1899) [*Chem. Zentr.*, **70**, II, 801 (1899)] gives b.p. 84–87°.

(3) S. Winstein and J. Takahashi, *Tetrahedron*, **2**, 316 (1958), have studied the acetolysis of 3-methyl-2-butyl *p*-toluenesulfonate.

dation and infrared spectra.[4] In the original hydrocarbon fraction, the *cis* isomer is present to the extent of 5.6%, and the *trans*, to the extent of 10.1%. This is the first time that the formation of a cyclopropane from the deamination of a saturated amine (IV → VI) has been reported.

It seemed possible that similar cyclizations might be observable in other systems. For instance, the 3-methyl-2-butyl cation (V) could be formed by hydrogen migration in the isoamyl cation (II), which in turn could be generated by the deamination of isoamylamine (thus, I → II → V). If the 3-methyl-2-butyl cation were implicated in the formation of 1,2-dimethylcyclopropane from the deamination of IV, then the 3-methyl-2-butyl cation formed by this alternative path from isoamylamine might also yield 1,2-dimethylcyclopropane (I → VI). On the other hand, the deamination of isoamylamine might produce 1,1-dimethylcyclopropane (I → III).

Experimentally, the deamination of isoamylamine gave a hydrocarbon fraction which contained 0.5% *cis*-1,2-dimethylcyclopropane and 1% *trans*-isomer, as determined by the procedures outlined above for the deamination of 3-methyl-2-aminobutane.[5] No 1,1-dimethylcyclopropane was detected in the deamination of isoamylamine and no cyclopropanes at all were detected in either the deamination of neopentylamine or in the acetolysis of 3-methyl-2-butyl *p*-toluenesulfonate.[3,6]



It is interesting to speculate on the mode of formation of these cyclopropanes. At least two possible explanations come to mind. First, a carbene-type mechanism may be involved, related to the "intramolecular insertion" reaction of diazoalkanes, recently described by Friedman and Shechter.[7] However, the conditions of the deamination reaction (acetic acid) do not appear favorable to the formation of a diazoalkane from an alkyldiazonium ion. The present observations on the behavior of isoamylamine and neopentylamine are also not readily accommodated in such a mechanism.[8]

A second explanation is that a discrete bridged methylcarbonium ion (VII) is produced and that this ion then loses a proton to yield the cyclopropanes.[9] Attempts at interpreting the results with isoamylamine and neopentylamine in terms of this mechanism also lead to difficulties, but they do not appear insurmountable. In any event, the present results and future experiments suggested by them should prove illuminating in the study of the nature of the intermediates in the amine–nitrous acid reaction.

The author thanks Dr. A. Kropf for helpful discussions.

(4) Infrared spectra were run at the University of Massachusetts, by kind permission of Dr. L. Carpino.

(5) The *cis*/*trans* ratio is about 1:2 for both isoamylamine and 3-methyl-2-aminobutane.

(6) It is estimated that 0.1% would have been detected in the present experiments.

(7) L. Friedman and H. Shechter, THIS JOURNAL, **81**, 5512 (1959).

(8) Decomposition of 2,2-dimethylpropanal tosylhydrazone (analogous to neopentylamine) gives a hydrocarbon fraction that is mainly 1,1-dimethylcyclopropane (ref. 7).

(9) D. J. Cram and J. E. McCarty, THIS JOURNAL, **79**, 2866 (1957), recently have discussed the question of bridged methylcarbonium ions.

MOORE LABORATORY OF CHEMISTRY
AMHERST COLLEGE MARC S. SILVER
AMHERST, MASSACHUSETTS

RECEIVED FEBRUARY 26, 1960

THE SYNTHESIS OF MALONYL-C^{14} COENZYME A

Sir:

Malonyl CoA has been established as one of the key intermediates in the biosynthesis of fatty acids.[1,2] In order to discover the detailed mechanism of the condensation of malonyl CoA with acyl CoA acceptors, it was essential to obtain isotopically labeled malonyl CoA of high purity in good yield. In a recent communication, Vagelos[3] has described a method for the synthesis of malonyl-coenzyme A, based on the preparation of a mixed anhydride of malonic acid. For the preparation of isotopically labeled malonyl CoA, the method of Vagelos seemed uneconomical since the over-all reported yield was of the order of 3.1 to 5.5% in respect to malonic acid. In our laboratory, a synthesis based on the observations of Khorana and co-workers[4] employing dicyclohexylcarbodiimide (DCC) as a condensing agent was used to synthesize the monothiophenyl ester of malonic acid. The latter compound was transesterified with coenzyme A according to the method of Wieland and Rueff.[5]

Experimental.—1 mM. of malonic acid (1-C^{14} or 2-C^{14}) and 1 mM. of thiophenol were dissolved in 5.0 ml. of N,N′-dimethylformamide at 0°. To the mixture was added with stirring over a period of 1 hour 500 mg. of DCC in 5 ml. of N,N′-dimethylformamide. The mixture was stirred for three hours at 0°. After the addition of 10 ml. of water, the stirring was continued for 15 minutes. The mixture was filtered with suction and the precipitate washed with water. The filtrate was made slightly acidic and extracted with several volumes of ether. The ether phase was washed with 0.01 *M* hydrochloric acid and with water. After drying over anhydrous sodium sulfate, the solution was shaken out with activated charcoal and filtered. The yield varied from 400 to 600 micromoles of monothiophenylmalonic ester as

(1) R. O. Brady, *Proc. U. S. Nat. Acad. Sci.*, **44**, 993 (1958).

(2) S. J. Wakil, THIS JOURNAL, **80**, 6465 (1958).

(3) P. R. Vagelos, *J. Biol. Chem.*, **235**, 346 (1960).

(4) H. G. Khorana, W. E. Razzell, P. T. Gilham, G. M. Tener and E. H. Pol, THIS JOURNAL, **79**, 1002 (1957).

(5) T. Wieland and L. Rueff, *Angew. Chem.*, **65**, 186 (1953).