sponds to a parallel alignment between the magnetic field and the z axis of the molecule (defined as that Cartesian coordinate perpendicular to the plane of the molecule). In this orientation all the hydrogens are equivalent to one another with respect to the magnetic field, and each of the two major lines is split into seven, *and only seven*, hyperfine lines. One of the two identical septets is shown in Figure 1. The relative intensities of the peaks of the septets are expected to fall in the binomial ratio 1:6:15:20:15:6:1. The measured ratio of the spectrum shown in Figure 1 is 1.5:5.4:14.4:20:14.7:6:1.1. The splitting between the peaks is 8.9 G. This is the value predicted on the basis of valence-bond theory.[9] As a result of the neglect of negative spin density on the central carbon atom, Hückel molecular orbital theory predicts the lower value of 7.1 G.

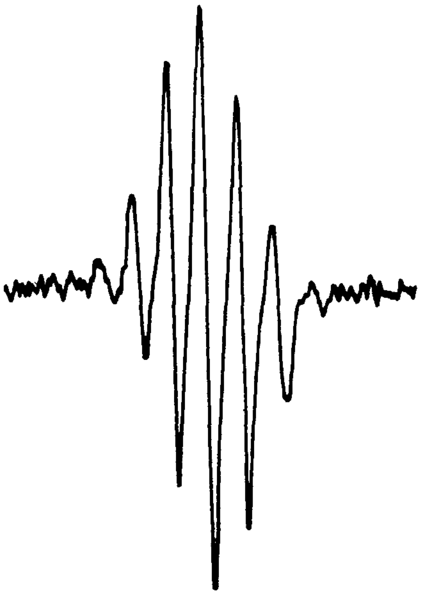

Figure 1. Single-crystal esr spectrum of trimethylenemethane (I). The septet shown, one of two, is the low-field peak. It is centered at 2940 G (klystron frequency 9150 Mc). Much more intense spectra show that *only* seven peaks are present. In the latter case, however, the use of higher power distorts the spectrum enough so that the expected binomial ratio of intensities is not reproduced as well as it is in the spectrum shown above.

The magnitude of the splitting between the two major lines shows the expected S-shaped angular dependence with respect to rotation of the magnetic field. At points below the maximum splitting the protons are no longer magnetically equivalent, and more complex unsymmetric splitting patterns are observed. The $\Delta m = 2$ transition[10] has also been observed in the present study. The latter transition shows rotationally dependent hyperfine structure, but this has not yet been studied in detail.

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useful here in that one knew what maximum splitting to expect and that this splitting corresponded to the desired one in which the z axis of the molecule was parallel to the magnetic field.[8]

[8] E. Wasserman, L. C. Snyder, and W. A. Yager, *J. Chem. Phys.*, **41**, 1763 (1964).

[9] H. M. McConnell, *ibid.*, **35**, 1520 (1961).

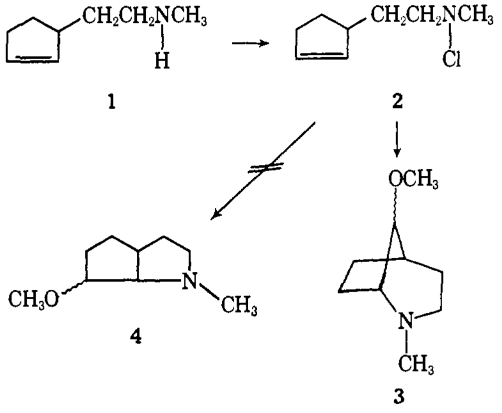
[10] J. H. van der Waals and M. S. deGroot, *Mol. Phys.*, **2**, 333 (1959); **3**, 190 (1960).

Solvolytic π Route to Azabicyclics

Sir:

Recent studies of alkyl migration to divalent, electron-deficient nitrogen[1] prompted us to explore the role of nitrenium ions in reactions analogous to other carbonium-ion-type processes. In view of the many well-established examples of the intramolecular addition of carbonium ions to double bonds,[2] we felt that the cyclization of nitrenium ions merited investigation,[3,4] especially in consideration of the biological importance of the azabicyclics. We now wish to report the conversion of a monocyclic olefinic N-chloramine into a bicyclic amino ether under solvolytic conditions.

When the amine **1** was treated with aqueous sodium hypochlorite, the N-chloramine **2** was obtained. Extraction of **2** with pentane followed by dilution of the pentane solution with methanol and evaporation of the pentane gave a methanolic solution of **2**. Refluxing this methanolic solution for 7 hr in the absence of silver ion or for 3 hr in the presence of silver nitrate (1.5 equiv) gave a single amino ether,[5] bp 92–94° (30 mm), in 55–65% yield. *Anal.* Calcd for $C_9H_{17}NO$: C, 69.63; H, 11.04; N, 9.02. Found: C, 69.54; H, 10.82; N, 9.09. In principle, cyclization could have occurred at either end of the double bond to yield either 8-methoxy-2-methyl-2-azabicyclo[3.2.1]octane (**3**) or 8-methoxy-2-methyl-2-azabicyclo[3.3.0]octane (**4**). Aside from es-



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[1] P. G. Gassman and B. L. Fox, *J. Am. Chem. Soc.*, **89**, 338 (1967); P. G. Gassman and R. L. Cryberg, *ibid.*, **90**, 1355 (1968).

[2] P. D. Bartlett, S. Banks, R. J. Crawford, and G. H. Schmid, *ibid.*, **87**, 1288 (1965), and references contained therein.

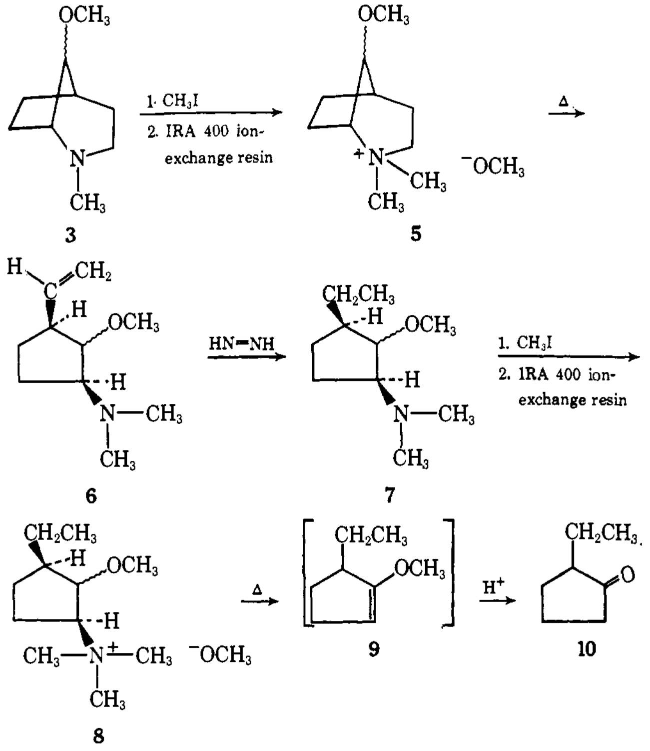
[3] The free-radical addition of nitrogen cation radicals and radicals to olefins has recently been reported: R. S. Neale, *ibid.*, **86**, 5340 (1964); R. S. Neale and N. L. Marcus, *J. Org. Chem.*, **32**, 3273 (1967); F. Minisoi, R. Galli, and M. Cecere, *Tetrahedron Letters*, 3163 (1966); K. Schrage, *ibid.*, 5795 (1966); and T. A. Foglia and D. Swern, *J. Org. Chem.*, **31**, 3625 (1966).

[4] Numerous examples of the addition of nitrenes to olefins have appeared. For leading references, see L. Horner and A. Christmann, *Angew. Chem.*, **75**, 707 (1963); R. A. Abramovitch and B. A. Davis, *Chem. Rev.*, **64**, 149 (1964); J. S. McConaghy, Jr., and W. Lwowski, *J. Am. Chem. Soc.*, **89**, 2357, 4450 (1967); see also W. Nagata, S. Hirai, Kawata, and T. Aoki, *ibid.*, **89**, 5045 (1967).

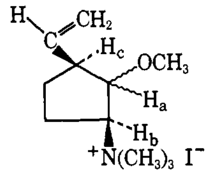
[5] In addition to the amino ether, small amounts of **1** were recovered.

tablishing the presence of an N-methyl and a secondary O-methyl group, nuclear magnetic resonance spectroscopy provided little evidence for the skeletal structure of the intramolecular cyclization product.

Since spectroscopic studies failed to provide sufficient data for distinguishing between **3** and **4**, a classical degradation procedure was utilized as outlined below.[6] This degradation gave the known 2-ethylcyclopentanone (**10**), identical in all respects with an authentic sample.[7] The presence of the ethyl group on the carbon adjacent to the carbonyl function requires that the ethyl group be next to the ether linkage in **7**. This would be the case if the cyclization product was **3**. Hence cyclization must have occurred exclusively at the 1 position of **2**.



The only feature of the cyclization which remains to be established is the stereochemistry at C-8. Mechanistically ionic additions to olefins generally yield *trans* products. In the special case of carbocyclics prepared *via* intramolecular cationic cyclization, only *trans* addition to the double bond was found.[2] Thus, on purely mechanistic analogy it would be predicted that the 8-methoxyl group should be *anti* to the nitrogen (*trans* to the nitrogen-containing bridge). Attempts to unequivocally establish the mechanistic prediction were unsuccessful. Very tentative evidence for the suspected stereochemistry was obtained from a comparison of the nmr spectra[8] of **11**, **12**, and **13**. In **11**, H_a, which appeared as a quartet centered at τ 6.73, showed a coupling constant of 9 cps with H_c and 6 cps with H_b In the model compound **12**, J_{ab} was 6 cps, while in the *cis* isomer **13**, J_{ab} was 4 cps. Unfortunately, even though the H_a–H_b coupling constants of **11** and **12** were identical, the proximity of J_{ab} for **13** does not allow an unequivocal assignment of the stereochemistry of the methoxy function of **3**.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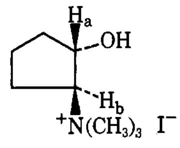
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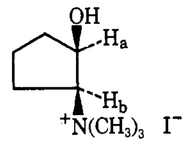
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The solvolytic π route offers an attractive synthetic method for the preparation of a large variety of elusive azabicyclics. We are presently investigating the scope, limitations, and mechanistic details[9] of the addition of divalent electron-deficient nitrogen to olefins.

Acknowledgment. We wish to thank the National Cancer Institute of the Public Health Service for Grant CA-07110 which supported this research.

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(6) Satisfactory elemental analyses were obtained for **6** and for the picrates of **3**, **6**, and **7**. The quaternary methoxides, **5** and **8**, were not analyzed because of their extremely hygroscopic nature. The crude vinyl ether **9** was hydrolyzed without purification.

(7) E. Zbiral, F. Wessely, and E. Lahrmann, *Monatsh. Chem.*, **91**, 92 (1960).

(8) Nmr measurements were made using a Varian HA-100 nuclear magnetic resonance spectrometer. Coupling constants were measured utilizing double and triple resonance techniques. We wish to acknowledge the assistance of Mr. Richard Cryberg in obtaining these spectra.

(9) As with analogous carbocyclic examples,[2] it is probable that π-electron participation is involved in the ionization of the N–Cl bond. It should be noted that such participation requires the intermediacy of a partially electron-deficient nitrogen species along the reaction pathway but forgoes the presence of a divalent nitrogen intermediate with a unit positive charge on nitrogen.

(10) Alfred P. Sloan Research Fellow, 1967–1969.

(11) National Science Foundation Undergraduate Research Participant, 1966–1967.

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Macromolecule–Small Molecule Interactions. A Synthetic Macromolecule with High Esterolytic Activity

Sir:

The pathway of action of an enzyme (E) involves[1] combination with a substrate (S) followed by one or more transfer or cleavage steps to yield products (P) (eq 1). Many efforts have been directed toward re-

$$E + S \rightleftharpoons ES \longrightarrow \longrightarrow E + P \qquad (1)$$

producing this phenomenon with synthetic macromolecules. Interactions, polar or apolar, which increase the concentration of the complex (ES) should increase the reactivity of E. For esterolytic reactions the steps following ES formation are facilitated by nucleophilic acid–base groups, and hence insertion of these in a synthetic macromolecule should favor esterolytic activity.

Many water-soluble synthetic polymers have been found to bind small molecules.[2–6] In our experience these linear polymers do not have an avidity comparable to the protein serum albumin.[7] We have now found, however, that a derivative of highly branched water-soluble poly(ethylenimine) (PEI-6)[8] with a small

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(1) L. Michaelis and M. L. Menten, *Biochem. Z.*, **49**, 333 (1913).

(2) U. P. Strauss and E. G. Jackson, *J. Polymer Sci.*, **6**, 649 (1951).

(3) W. Scholtan, *Makrmol. Chem.*, **11**, 131 (1953).

(4) S. Sato, *Kolloid Z.*, **154**, 19 (1957).

(5) I. M. Klotz and V. H. Stryker, *J. Am. Chem. Soc.*, **82**, 5169 (1960).

(6) P. Molyneux and H. P. Frank, *ibid.*, **83**, 3169 (1961).

(7) I. M. Klotz, F. M. Walker, and R. B. Pivan, *ibid.*, **68**, 1486 (1946).

(8) Dow Chemical Co. Bulletin "Montrek® Polyethyleneimine." PEI-6 has an average degree of polymerization of 15.