fore prefer the nonclassical intermediate, which predicts the observations.

The 3-methyl-2-norbornyl (12) rearrangements provide the first examples of established 3,2-shift stereochemistry in which the migration terminus is secondary. A tertiary benzyl terminus, as in 13, apparently produces behavior similar to that of 12.[11] In contrast, a simple tertiary terminus, as in 14, is reported[12] to result in only feeble selectivity. The series shown in Table I clearly does not fall into a readily explicable pattern, and further investigation seems necessary.

Table I

Cation	Migrating group	Selectivity, exo/endo	Ref.
12	H	≥100	Present work
13	H	High (?)	11
14	Me	2.6–5.7	12

(11) B. M. Benjamin, C. J. Collins, Z. K. Cheema, and R. Werth, International Symposium on Organic Reaction Mechanisms, Cork, Ireland, July 20–25, 1964, Abstracts, p. 38; C. J. Collins, Z. K. Cheema, R. G. Werth, and B. M. Benjamin, *J. Am. Chem. Soc.*, 86, 4913 (1964). These workers show convincingly that the formation of 3-*endo*-phenyl-2-norbornanone from 3-*endo*-phenyl-2,3-*exo*-norbornanediol involves a circuitous mechanism analogous to path B. Since, however, they do not estimate how little of the *exo*-phenyl isomer can be detected in the product mixture, the selectivity is not clear, although they imply it is high.

(12) W. R. Vaughan, C. T. Goetschel, M. H. Goodrow, and C. L. Warren, *ibid.*, 85, 2283 (1963).

(13) To whom inquiries should be directed at Madison.

(14) National Institutes of Health Predoctoral Fellow, 1964–1965.

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Halide Ion Catalyzed Equilibration of
1,1,2,3-Tetraalkylaziridinium Ions[1]

Sir:

When *trans*-1,2-dimethyl-3-isopropylaziridine (1) was quaternized with deuteriomethyl iodide (2) in benzene, equal amounts of the diastereomeric aziridinium ions 3a and 3b (as iodides) were isolated.[2] Although reasons were given as to why the observed products were likely to be those of a rate-controlled process, we felt uneasy about this conclusion because the observed product composition was identical with the expected equilibrium composition of 3a and 3b. We therefore decided to examine the quaternization of 1 with 2 under conditions that would allow direct determination of the stereochemistry of the reaction.

A methanol solution 0.67 M in 1 and 0.67 M in 2

(1) (a) Structure–Activity Relationships of Ethylenimines. VI. Supported by Grant No. CA-05528 from the National Cancer Institute of the Public Health Service. (b) Part V: A. T. Bottini and R. L. VanEtten, *J. Org. Chem.*, 30, in press.

(2) A. T. Bottini and R. L. VanEtten, *Ibid.*, 30, 575 (1965).
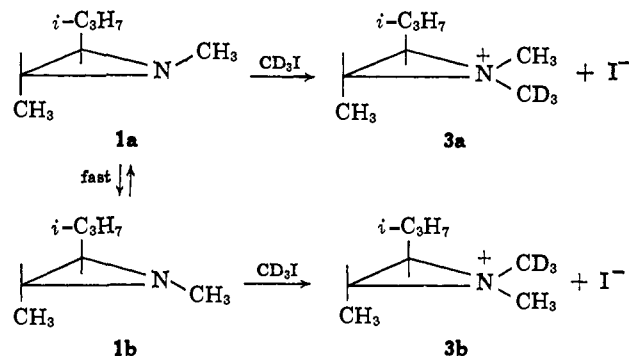
was prepared and the changing 60-Mc. n.m.r. spectrum of the solution was observed. As the reaction proceeded, the per cent reaction was determined by comparison of the intensities of the N-methyl bands due to 1 and 3, and the ratio of the concentrations of 3b and 3a was determined by comparison of the intensities of their N-methyl bands.[2,3]

The results obtained showed that the aziridinium ions 3a and 3b were equilibrated under the reaction conditions. Thus, after 45 min. at 27°, when the reaction was about 50% complete, the 3b:3a ratio was 2.4; but as the reaction proceeded to >97% completion (>1400 min.), the 3b:3a ratio decreased to unity. That the equilibration of 3a and 3b is in fact catalyzed by iodide ion was shown subsequently by the observation that addition of aqueous sodium iodide or potassium iodide to a 2.9:1 mixture of 3b and 3a in methanol caused equilibration of the aziridinium ions by a reaction that was first order in iodide ion.

The most reasonable mechanism for iodide ion catalysis of the interconversion of 3a and 3b is pictured below.
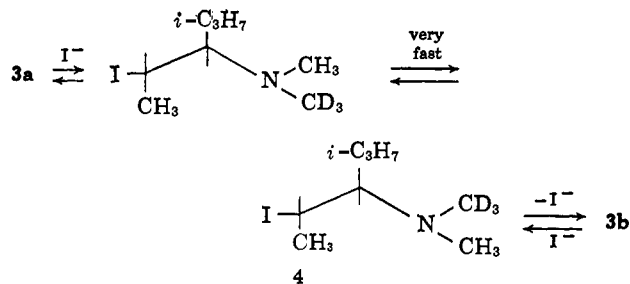
Reactions of iodide ion with 3a and 3b by SN2 attack at C-2 of the aziridinium ring result initially in formation of different rotamers of the same 2-iodoalkylamine 4. If one accepts the premise that rotation about the C-1–N bond *and* inversion of nitrogen in 4 occur more rapidly than ring closure to an aziridinium ion, the rotamers of 4 formed from 3a and 3b become equivalent in that ring closure to either 3a or 3b can occur with equal probability. As the principle of microscopic reversibility must be obeyed, interconversion of 3a and 3b *via* 4 must occur without disturbance of the steric relationship of the alkyl groups at C-2 and C-3 in the aziridinium ions.

Convincing support for the proposed mechanism has been obtained. The relative rates of iodide ion catalyzed equilibration of several pairs of diastereomeric 1-deuteriomethyl-1,2-dimethyl-3-alkylaziridinium

(3) (a) Results described in the accompanying communication[3b] allow assignment of the high-field N-methyl band of the aziridinium ions to 3b. (b) A. T. Bottini, B. F. Dowden, and R. L. VanEtten, *J. Am. Chem. Soc.*, 87, 3250 (1965).
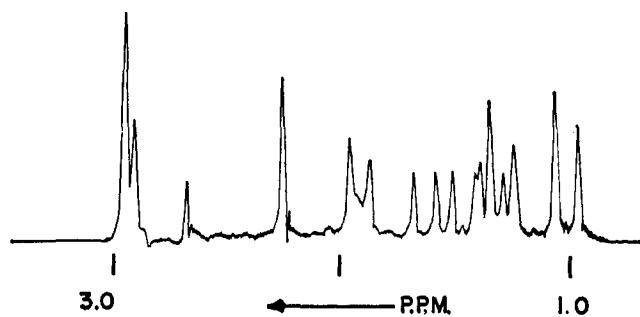
Figure 1. High-field portion of the 60-Mc. n.m.r. spectrum of the equilibrium mixture of 5a and 6a in methanol. The band at 2.68 p.p.m. (downfield relative to the tetramethylsilane resonance) is due to an impurity in the methanol; the band at 2.24 p.p.m. is the high-field C-13 satellite of the methanol resonance.

benzenesulfonates are related linearly to the relative rates of reaction with thiosulfate of the corresponding unlabeled aziridinium iodides.[4] As the irreversible reactions with thiosulfate follow second-order kinetics, the observed linear relationship indicates that the slow step in the iodide ion catalyzed equilibrations is an S_N2 reaction. Also, halide ion catalyzed equilibration of aziridinium ions occurs considerably more rapidly in methanol than in more polar water,[5,6] which further indicates that the slow step involves attack of halide ion on the positively charged aziridinium ring.
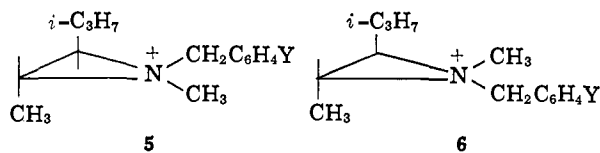
a, Y = H; b, Y = p-CH₃; c, Y = m-Cl; d, Y = p-NO₂

We have also examined the equilibria of several pairs of diastereomeric aziridinium ions (5a–d and 6a–d) prepared from 1 and benzyl bromides.[7] Because of the different steric requirements of the methyl and benzyl groups, the equilibrium constants of these diastereomers differ from unity. Examination of the n.m.r. spectrum of the equilibrium mixture of 5a and 6a (as the bromide salt) in methanol, the upfield portion of which is shown in Figure 1, confirms what had been anticipated, namely, that the more stable diastereomer is the one in which the C-2 methyl group is cis to the N-benzyl group, i.e., 6a, and reveals that the equilibrium constant 6/5 is 1.70.[8] Most significantly,

(4) cis-3-Methyl-, cis-3-ethyl-, trans-3-isopropyl-, and trans-3-t-butyl-1,1,2-trimethylaziridinium iodide. The unlabeled salts were characterized by means of n.m.r. spectroscopy, near quantitative (>96%) reaction with thiosulfate, and elemental analysis. The theoretical and experimental C and H analyses agreed in all cases to within 0.3%.
(5) See J. S. Gleave, E. D. Hughes, and C. K. Ingold, J. Chem. Soc., 236 (1935).
(6) For example, 5a and 6a are equilibrated by bromide ion about 200 times more rapidly in methanol than in water.
(7) A nonequilibrium mixture of 5a and 6a obtained from 1 and benzyl bromide in benzene gave a satisfactory elemental analysis. Anal. Calcd. for C₁₄H₂₂NBr: C, 59.16; H, 7.80. Found: C, 59.32; H, 7.82. The other diastereomeric aziridinium salts were not isolated but were characterized by means of n.m.r. spectroscopy. The upfield portions of their n.m.r. spectra are strikingly similar to that of the mixture of 5a and 6a.
(8) The proximity of the aromatic ring and the C-2 methyl group of 6a can be expected to result in an upfield shift of the C-2 methyl resonance relative to the resonance of the C-2 methyl group of 5a.[9] Consequently, the doublet centered at 1.94 p.p.m. is assigned to the C-2 methyl group of 6a, and the less intense doublet centered at 1.67 p.p.m. is assigned to the C-2 methyl group of 5a. Similarly, the less intense pair of doublets centered at 1.48 and 1.38 p.p.m. is assigned to the methyls of the isopropyl group of 5a, and the pair of doublets centered

the equilibrium constants (6/5) of the four pairs of diastereomeric aziridinium ions were the same to within experimental error (1.69 ± 0.03). This finding was particularly gratifying in that it appears to confirm the suppositions that the dipole moments of the diastereomeric aziridinium ions are nearly identical and that the difference in free energy can be ascribed solely to the difference in nonbonded interactions present in the diastereomers.

Because of the well-defined geometry of diastereomeric aziridinium ions such as 5 and 6 together with the absence of any significant contribution of electronic factors to the difference in their free energies, study of the thermodynamics of equilibria of diastereomeric trans-1,1,2,3-tetrasubstituted aziridinium ions appears to be ideally suited for assessing quantitatively the role of nonbonded interactions.

at 1.33 and 1.02 p.p.m. is assigned to the methyls of the isopropyl group of 6a.
(9) J. S. Waugh and R. W. Fessenden, J. Am. Chem. Soc., 79, 846 (1957).

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On the Stereochemistry of Quaternization of Amines[1]

Sir:

Knowledge of the confirmational equilibrium of trans-1,2-dimethyl-3-isopropylaziridine (1)[2] coupled with the fact that 1 can be quaternized to give reasonably tractable aziridinium salts[3] has made it possible to obtain an accurate answer to the question: knowing the stereochemistry of an ammonium salt formed by quaternization of a given tertiary amine, what inference can be made concerning the conformational equilibrium of the free base?[4] We report here the stereochemistry of quaternization of 1 under conditions that give rate-controlled products.

In order to examine the stereochemistry of quaternization of aziridines under conditions wherein equilibration of the products did not occur at a rate competitive with the quaternization reaction (see ref. 1b), we chose to study directly quaternization of aziridines with alkyl benzenesulfonates. Our choice was based on the fact that the benzenesulfonate anion is a much poorer nucleophile than iodide or bromide,[5] and thus would be far less likely to catalyze equilibration of the resulting aziridinium ions through the intermediacy of a 2-aminoalkylbenzenesulfonate.

We studied first the stereochemistry of quaternization of 1 with deuteriomethyl benzenesulfonate[6] in meth-

(1) (a) Structure–Activity Relationships of Ethylenimines. VII. Supported by Grant No. CA-05528 from the National Cancer Institute of the Public Health Service. (b) Part VI: A. T. Bottini, B. F. Dowden, and L. Sousa, J. Am. Chem. Soc., 87, 3249 (1965).
(2) A. T. Bottini, R. L. VanEtten, and A. J. Davidson, ibid., 87, 755 (1965).
(3) (a) A. T. Bottini and R. L. VanEtten, J. Org. Chem., 30, 575 (1965); (b) G. K. Helmkamp, R. D. Clark, and J. R. Koskinen, ibid., 30, 666 (1965).
(4) Leading references to the problem are: G. Closs, J. Am. Chem. Soc., 81, 5456 (1959); J. McKenna, J. White, and A. Tully, Tetrahedron Letters, No. 24, 1097 (1962). See also W. L. Meyers and N. Sapianchiay, J. Am. Chem. Soc., 86, 3343 (1964); J. McKenna, et al., J. Chem. Soc., 1711, 1726, 1729, 1733 (1965).
(5) J. Hine, "Physical Organic Chemistry," 2nd Ed., McGraw-Hill Book Co., Inc., New York, N. Y., 1962, Chapter 7.