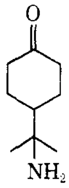
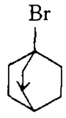
azabicyclo[2.2.2]octane (**2**) in 10% yield. **2**,[3] mp 55–56°, exhibited ir bands at 3280, 2850, 1370, 1350, 1090, 1050, and 775 cm^{-1}, and nmr bands at 1.25 s, (6 H), 1.4 (m, 2 H), 1.7 (s, 1 H), *ca.* 1.7 (m, 1 H), and 2.1 (m, 6 H) ppm. Chemical characterization was accomplished by hydrolysis to the amino ketone (**6**): mp 37–38°; ir bands at 2850, 1700, 1580, 1380, 1360, and 1040 cm^{-1}; nmr bands at 1.12 (s, 6 H), 1.25 (s, 2 H), 1.6 (m, 2 H), and 2.4 (m, 8 H) ppm. Wolff–Kishner reduction of **6** afforded dimethylcyclohexylcarbinamine[4] which was synthesized from α,α-dimethyl-α-cyclohexylacetamide[5] by Hofmann degradation.



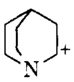
6

Analogous α-chloroamines have been isolated or proposed as intermediates in prior studies entailing *N*-haloamines and either aluminum chloride[1,6] or silver salts.[7] However, **2** appears to be unique in that the chlorine atom is at a bridgehead position of a bicyclic system. Open-chain compounds of the type $[RCH{=}NR_2]^+X^-$ exist as immonium salts.[8] The stability and covalent nature of **2** are most likely associated with the strain involved in introducing a carbon–nitrogen double bond at a bridgehead position.[9] The solvolysis of **2** is of particular interest in regard to bridgehead reactivity. Preliminary data for solvolysis in water or 80% ethanol indicate that **2** reacts appreciably faster than **7**.[10]



7

Another indication of the enhanced reactivity of the bridgehead chloride **2** is the immediate formation of precipitate on contact with aqueous silver nitrate at room temperature. In comparison, 4 hr were employed to effect reaction with **7**.[11] A more detailed kinetic study of the solvolysis of this unusual compound is underway. A related situation was reported[12] by Grob and Sieber in which the positions of the nitrogen and electron-deficient carbon were reversed. On the basis of the observation that the 2-quinuclidinyl cation **8** is somewhat more stable than its carbon counterpart (the bicyclo[2.2.2]-2-octyl cation), they proposed delocalization involving the bridgehead nitrogen.



8

The major nonbasic products, **3**, **4**, and **5**, from rearrangement of **1**, result from β scission of the carbon–carbon bond present in the shortest bridge. These known compounds were identified by comparison of their ir and nmr spectra to those of authentic materials.[13] This type of reaction has been previously encountered[14] with *N*-haloamines. Experiments were carried out to differentiate between polar and radical pathways. Since little or no inhibition was noted in the presence of oxygen, an ionic type fission appears more likely.

Acknowledgment. We are grateful to the National Science Foundation, Eli Lilly and Co., and the Graduate School of the University of Wisconsin—Milwaukee for support of this work.

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[3] Microanalyses were satisfactory.

[4] G. Drefahl, K. Ponsold, and G. Köllner, *J. Prakt. Chem.*, **23**, 136 (1964).

[5] H. Koch and W. Haaf, *Justus Liebigs Ann. Chem.*, **618**, 251 (1958).

[6] T. Sasaki, S. Eguchi, T. Kiriyama, and H. Suzuki, *Syn. Commun.*, **1**, 267 (1971).

[7] P. G. Gassman, *Accounts Chem. Res.*, **3**, 26 (1970).

[8] K. Harada, "The Chemistry of the Carbon–Nitrogen Double Bond," S. Patai, Ed., Interscience, New York, N. Y., 1970, p 259.

[9] For another example, see ref 7.

[10] R. C. Fort, Jr., and P. v. R. Schleyer, *Advan. Alicycl. Chem.*, **1**, 283 (1966).

[11] W. v. E. Doering, M. Levitz, A. Sayigh, M. Sprecher, and W. P. Whelan, Jr., *J. Amer. Chem. Soc.*, **75**, 1008 (1953).

[12] C. A. Grob and A. Sieber, *Helv. Chim. Acta*, **50**, 2531 (1967).

[13] We thank Drs. H. J. Wobben, R. Ter Heide, and R. Timmer for kindly furnishing spectral data on *dl*-cryptone (**4**).

[14] P. Kovacic, M. K. Lowery, and K. W. Field, *Chem. Rev.*, **70**, 639 (1970); D. C. Horwell and C. W. Rees, *Chem. Commun.*, 1428 (1969); J. M. Biehler and J.-P. Fleury, *Tetrahedron*, **27**, 3171 (1971).

[15] Postdoctoral, 1971–1972.

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Neighboring Group Participation by Bridgehead Nitrogen in Bridged Polycyclic Systems[1]

Sir:

The synthesis of molecules which would appear to extend the limits of Bredt's rule[2] has been the topic of several recent reports.[3] In addition, molecules with double bonds to bridgeheads have been postulated as intermediates in a variety of reactions[4] involving relatively strained bicyclic systems. In view of the experimental results referenced above, we questioned whether the seemingly anomalous stability of the cation **1** might not be due to stabilization of the positive charge by the nonbonding electrons of the bridgehead nitrogen.[5,6]

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[1] Paper XXVI in a series on the Chemistry of Nitrenium Ions. For the previous papers in this series see P. G. Gassman, A. J. Battisti, and K. Shudo, *Tetrahedron Lett.*, in press; P. G. Gassman and G. Hartman, *Chem. Commun.*, 853 (1972).

[2] J. Bredt, H. Thouet, and J. Schmitz, *Ann.*, **437**, 1 (1924); J. Wiseman, *J. Amer. Chem. Soc.*, **89**, 5966 (1967), and references contained therein.

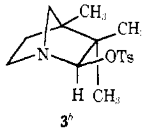
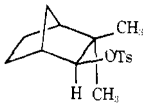
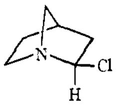
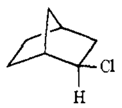
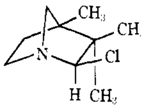
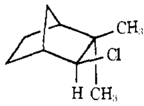
[3] For specific examples see (a) J. A. Marshall and H. Faubl, *ibid.*, **89**, 5965 (1967); (b) N. M. Weinshenker and F. D. Greene, *ibid.*, **90**, 505 (1968); (c) J. R. Wiseman, H.-F. Chan, and C. Ahola, *ibid.*, **91**, 2812 (1969); (d) W. Carruthers and M. I. Qureshi, *Chem. Commun.*, 832 (1969); (e) J. R. Wiseman and J. A. Chong, *J. Amer. Chem. Soc.*, **91**, 7777 (1969); (f) J. R. Wiseman and W. A. Pletcher, *ibid.*, **92**, 956 (1970); and (g) J. A. Marshall and H. Faubl, *ibid.*, **92**, 948 (1970).

[4] For discussions and leading references see ref 3e and 3f. See also R. Keese and E.-P. Krebs, *Angew. Chem., Int. Ed. Engl.*, **10**, 262 (1971).

[5] P. G. Gassman and R. L. Cryberg, *J. Amer. Chem. Soc.*, **91**, 2047 (1969); see also J. O. Reed and W. Lwowski, *J. Org. Chem.*, **36**, 2864 (1971).

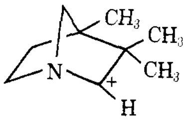
[6] When 4,7,7-trimethyl-2-chloro-2-azabicyclo[2.2.1]heptane was solvolyzed in methanol, a significant amount of 2-methoxy-3,3,4-trimethyl-1-azabicyclo[2.2.1]heptane was obtained. It was suggested that the methyl ether was formed from nucleophilic attack of methanol on **1**, which represents the Wagner–Meerwein rearrangement product of the initially formed nitrenium ion. However, a perplexing problem was associated with this hypothesis in that **1** should have been destablized

Table I. Rates of Solvolysis in Anhydrous Methanol

Compound	Temp, ±0.03°C	Rate, sec^{-1}	$k_{rel,25°}$ for tosylates	$k_{rel,25°}$ for chlorides
 3[b]	70.0	$(4.05 \pm 0.02) \times 10^{-4}$		
	60.0	$(1.14 \pm 0.03) \times 10^{-4}$		
	50.0	$(3.05 \pm 0.03) \times 10^{-5}$		
	25.0[a]	9.18×10^{-7}	1	
 4[b]	60.0	$(6.48 \pm 0.08) \times 10^{-4}$		
	50.0	$(2.08 \pm 0.01) \times 10^{-4}$		
	40.0	$(6.40 \pm 0.05) \times 10^{-5}$		
	25.0[a]	9.24×10^{-6}	10	
 5	190.0	$(1.60 \pm 0.02) \times 10^{-3}$		
	180.0	$(8.87 \pm 0.12) \times 10^{-4}$		
	170.0	$(4.50 \pm 0.02) \times 10^{-4}$		
	25.0[a]	2.70×10^{-10}		1
 6[c]	140.0	$(8.44 \pm 0.28) \times 10^{-4}$		
	120.0	$(1.89 \pm 0.04) \times 10^{-4}$		
	100.0	$(2.87 \pm 0.02) \times 10^{-5}$		
	25.0[a]	5.49×10^{-9}		20
 7[c]	150.0	$(1.19 \pm 0.02) \times 10^{-3}$		
	140.0	$(5.37 \pm 0.20) \times 10^{-4}$		
	130.0	$(2.20 \pm 0.04) \times 10^{-4}$		
	25.0[a]	7.72×10^{-10}		3
 8	25.0[d]	1.57×10^{-9}		6

[a] Extrapolated from higher temperatures. [b] Run in the presence of added triethylamine. [c] Run in the presence of added sodium acetate. [d] Calculated at 25° *via* the formula $k_4k_6/k_9 \cong k_8$ where k_9 equals the rate of solvolysis of *exo*-norbornyl tosylate (9) in methanol: W. Hückel and O. Vogt, *Justus Liebigs Ann. Chem.*, **695**, 16 (1966).

In order to test this hypothesis we have investigated the effect of the bridgehead nitrogen on the rates of solvolysis of molecules having the skeleton **2**. We now



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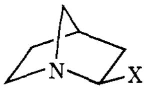

2

wish to report that the bridgehead nitrogen in the 1-azabicyclo[2.2.1]heptane system provides a significant driving force for the solvolytic loss of X⁻. We wish to suggest that this driving force is provided by the nonbonding electrons on nitrogen which act as a neighboring group in stabilizing the incipient carbenium ion *via* partial overlap with the developing p orbital. To the extent that this overlap occurs, with the resultant formation of a π bond, these results provide an intriguing insight into the limitations of Bredt's rule.

Table I lists the rates of methanolysis of a series of bicyclo[2.2.1]heptane derivatives. As can be seen, the relative rates vary from a factor of 20 for the comparison of **5** and **6**, through a factor of 10 for **3** and **4**, down to a factor of 2 for **7** and **8**. Since the value for **8** is calculated, the comparison of **7** and **8** might be considered to be the least dependable. The approximation which has been made here does not take into consideration the change in neighboring group participation which might accompany the change in leaving groups. However, in view of the close relationship of the models used for comparison, we feel that the **7** to **8** ratio calculated from the approximated rate for **8** should be reasonably reliable.

As Table I illustrates, the presence of the bridgehead nitrogen atoms in **3**, **5**, and **7** appears to have relatively little effect on the rates of solvolysis of the tosylates and chlorides studied. Qualitatively, if the nitrogen were only interacting with the incipient cationic center in an inductive manner, we would have anticipated a much larger rate difference due to the attachment of the relatively electronegative nitrogen *directly* to the atom bearing the positive charge.

In order to obtain a more quantitative (but still approximate) feeling for the inductive effect of a bridgehead nitrogen, we studied the base-catalyzed hydrolysis of **10**[7] and **11** and the acid-catalyzed hydrolysis of **11**[8]

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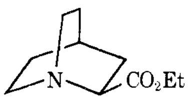
due to the electron-withdrawing inductive effect of nitrogen. In addition, it would appear that a relatively stable tertiary cation would result if a 1,2-methyl shift of the Nametkin type were to occur. However, no evidence for a methyl shift could be found. Thus, **1** appeared to derive some form of stabilization from the bridgehead nitrogen.

(7) 2-Carboethoxy-1-azabicyclo[2.2.2]octane (**11**) was chosen as a model system instead of 2-carboethoxy-1-azabicyclo[2.2.1]heptane because of its more accessible nature.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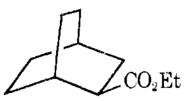
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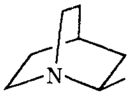
in 30:70 water–acetone. Extrapolation of these measurements to 25° gave values of $k_{B_{10}} = 2.03 \times 10^{-2}$ l./(mol sec), $k_{B_{11}} = 4.85 \times 10^{-4}$ l./(mol sec), and $k_{A_{11}} = 1.11 \times 10^{-5}$ l./(mol sec). Utilizing these values and the approximation specified[8] in the Taft relationship[9] allowed us to calculate $\Delta\sigma^* = \sigma^*_{12} - \sigma^*_{13} = 0.66$. If we assume that the difference in the inductive effects of the moieties **14** and **15** will be similar to that of **12** and **13**, we can use the ρ of -3.49 determined for secondary tosylates,[10] or the ρ of -2.33 calculated for *exo*-norbornyl tosylates,[11] to calculate the expected difference in the rates of solvolysis of **3** and **4** based on inductive effects alone.[12] Using the ρ value for acyclic secondary tosylates,[10] we obtain a predicted rate difference of 2.8×10^6, while the ρ for *exo*-norbornyl tosylates[11] led to a predicted difference of 2.0×10^4. Since these values are based on inductive effects alone, an increase in these differences by as much as 10^3 could be added if neighboring group participation were involved in the solvolysis of **4**, **6**, and **8**. As a result of the various approximations and uncertainties involved, the best quantitative picture we can present indicates that the bridgehead nitrogen atoms of **3**, **5**, and **7** are providing a rate acceleration of at least 10^3 and possibly of as much as 10^8 to the leaving of a suitable group from the 2 position. We presume that this accelerating effect is due to overlap of the nonbonding electrons on nitrogen with the developing p orbital at the 2 position. It should be noted that the methanolysis of **3** and **7** gave *exo*-2-methoxy-3,3,4-trimethyl-1-azabicyclo[2.2.1]heptane as the only product (99% yield).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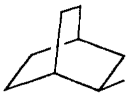
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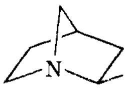
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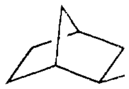
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Acknowledgment. We are indebted to the National Cancer Institute of the Public Health Service for support of this investigation and to Drs. J. Hine and G. R. Meyer for helpful discussions.

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(8) Since the base-catalyzed hydrolysis rates reflect primarily inductive influences while acid-catalyzed hydrolysis rates reflect primarily steric factors, the acid-catalyzed hydrolysis rates for **11** were used as approximate acid-catalyzed hydrolysis rates for **10** (which could not be measured directly for obvious reasons) in the calculation of a Taft σ^* value for **10**.

(9) For a detailed discussion see R. W. Taft, Jr., in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., Wiley, New York, N. Y., 1956, Chapter 13; see also R. W. Taft, Jr., *J. Amer. Chem. Soc.*, **75**, 4231 (1953).

(10) A. Streitwieser, Jr., *ibid.*, **78**, 4935 (1956).

(11) P. G. Gassman, J. L. Marshall, J. G. Macmillan, and J. Hornback, *ibid.*, **91**, 4282 (1969).

(12) In order to calculate this rate difference, the difference in the measured σ^* values of 0.66 was multiplied by 2.8 in order to compensate for moving the reactive center one carbon closer to the nitrogen atom. The usefulness of this approach has been questioned in cases where alkyl groups are involved [C. D. Ritchie, *J. Phys. Chem.*, **65**, 2091 (1961), has suggested that "σ^* values for alkyl groups are not consistent with the generality of the Taft equation"].

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The 4-Psinortricyclyl Cation System

Sir:

It was indicated previously that the same carbonium ion species are formed from the epimers of the 3-psinortricyclyl system under hydrolytic conditions.[1] In contrast, we now find that the solvolytic chemistries of the 4-psinortricyclyl epimers are strikingly dissimilar.

exo-4-Psinortricyclanol[1,2] (**1**-OH) was converted to the corresponding ketone with CrO_3–pyridine. Reduction with $LiAlH_4$ or Vitride gave a 3:97 mixture of **1**-OH and **2**-OH, respectively, separable by glpc.[3] Hydrogenation of **1**-OH and **2**-OH (10% Pd/C, 95% EtOH) produced *exo*- and *endo*-2-norborneol, respectively. Sulfonate esters of **2**-OH may be prepared routinely (tosylate mp ~28°; brosylate mp 47.0–48.5°), but attempts to prepare **1**-OTs with tosyl chloride–pyridine resulted in the isolation of nortricyclyl tosylate (**3**-OTs). However, oxidation of the epimeric mixture of sulfinate esters derived from **1**-OH with RuO_4 in CCl_4[4] in a 5° cold room produced a solution which contained 74% **1**-OTs and 26% **3**-OTs, as judged from the relative areas of their α H signals at τ 5.54 and 5.70, respectively. Since **1**-OTs proved to be much more reactive than **3**-OTs, this mixture was used for kinetic determinations.

Preliminary titrimetry indicated that only a small fraction of 1 equiv of tosylic acid is liberated from **1**-OTs in buffered acetic acid medium. Consequently, the rate of ionization (solvolysis plus ion pair return, *vide infra*) was measured by following the disappearance of the α H absorption in a temperature regulated nmr probe (0.02 *M* NaOAc buffer). The acetolysis rate for **2**-OTs was measured by routine titrimetry of *ca.* 0.01 *M* solutions containing a slight excess of NaOAc. Nmr examination of recovered sulfonate ester after *ca.* 1 acetolysis half-life failed to reveal any contamination by rearranged tosylate. Table I contains a summary of the rate data. The 2-norbornyl systems are included for comparison. Product data are given in Table II.

Table I. Acetolysis Rates for the 4-Psinortricyclyl and 2-Norbornyl Tosylates at 25°

Compound	k, sec^{-1}
exo-2-Norbornyl	2.33×10^{-5} [a]
endo-2-Norbornyl	8.28×10^{-8} [a]
1	$(6.3 \pm 0.6) \times 10^{-4}$ [b]
2	(1.06×10^{-6})[c]

[a] P. v. R. Schleyer, M. M. Donaldson, and W. E. Watts, *J. Amer. Chem. Soc.*, **87**, 375 (1965). [b] Measured directly by nmr monitoring; probe temperature was 24.5 ± 0.5°. [c] Extrapolated from data acquired at higher temperatures; $\Delta H^{\ddagger} = 24.8 \pm 0.2$ kcal/mol, $\Delta S^{\ddagger} = -2.5 \pm 0.6$ eu.

The rate acceleration of **1**-OTs relative to *exo*-2-norbornyl[5] is presumably due to relief of strain in **1**-OTs

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(1) R. K. Lustgarten, *J. Amer. Chem. Soc.*, **93**, 1275 (1971).

(2) Satisfactory spectral and analytical data were obtained for all new compounds except that **1**-OTs was prepared without isolation of intermediates and was not purified.

(3) The equilibrium between **1**-OH and **2**-OH (aluminum isopropoxide–isopropyl alcohol–acetone (trace), 99.6°) is *ca.* 81:19, respectively, established from either side.

(4) J. C. Martin and B. R. Ree, *J. Amer. Chem. Soc.*, **92**, 1660 (1970).

(5) Since the measurement for **1**-OTs includes ion pair return, it might better be compared with k_α for *exo*-2-norbornyl. Assuming k_α/k_t for the tosylate to be the same as for the brosylate,[6] the value in Table I for *exo*-2-norbornyl is increased by a factor of 4.6.