ted with a graded seal incorporating a 10-ml Pyrex reservoir in which the solution was frozen in liquid nitrogen, evacuated to about 13 μ, and thawed; this freeze-pump-thaw cycle was repeated five or more times; the cuvette was then flame-sealed. Kinetics of the thermal decyclization of **16** was monitored after an initial prolonged irradiation of a degassed solution of **14**.

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Probing the Endo Cavity of Bicyclo[2.2.1]heptane Systems. NH Proton Exchange, Nitrogen Inversion, and Amine Quaternization of *exo*- and *endo*-2-Dimethylaminonorbornane

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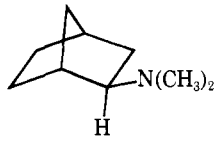
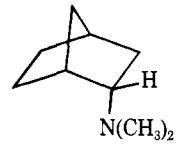
Abstract: We compare the rates of NH proton exchange, nitrogen inversion, and amine quaternization of *exo*- and *endo*-2-dimethylaminonorbornane. The exo and endo compounds do not display substantial differences as would be expected if the *endo*-dimethylamino group were subjected to unusual steric or solvation effects within the endo cavity.

Few observations have roused greater controversy among physical organic chemists than the rapid solvolysis of *exo*-2-norbornyl derivatives relative to their endo isomers. One school believes that the transition state for the exo compounds is *stabilized* by σ participation.[2] The other school maintains that the transition state for the endo derivatives is *destabilized* by steric hindrance to ionization.[3] Our entry into the debate begins here with the proposition that if departure of an endo leaving group is indeed inhibited by special steric or solvation effects, then other functionalities within the endo cavity should display modified behavior as well. In the following article the rates of NH-proton exchange, nitrogen inversion, and amine quaternization of *endo*-2-dimethylaminonorbornane are compared with the corresponding rates of the exo isomer.

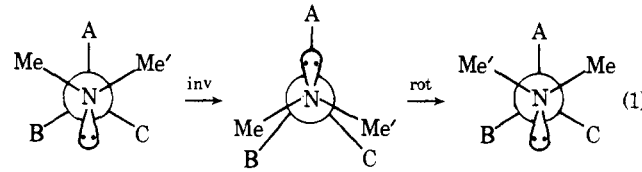


exo-I



endo-I

When *exo*-2-dimethylaminonorbornane (*exo*-I) is dissolved in an aqueous buffer of pH 2.70, the N-CH_3 groups of the protonated amine show a pair of doublets in the NMR (Figure 1A). The methyl groups (which are chemically shift nonequivalent because of the neighboring chiral center) have individual signals, both of which are split by the N proton. At pH 5.77, rapid exchange of the N proton with retention of configuration obliterates the spin-spin splitting, leaving a pair of singlets (Figure 1C). At pH values above 8.5 one observes only a sharp singlet (Figure 1G) because inversion of unprotonated amine destroys the diastereotopic nature of the N-CH_3 groups. As is evident from eq 1, inversion and rotation in either order (but not rotation alone) renders the N-CH_3 groups equivalent.



(1)

NH proton exchange of amines is *inhibited* by hydronium ion.[4] Clearly a *reverse* step in the exchange mechanism must be acid catalyzed (yielding an overall rate expression with H_3O^+ in the denominator). Such a mechanism, first formulated by Grunwald,[5] is given in eq 2; it describes all known proton-exchange reactions of ammonium salts. In ideal cases, each of the three component rate constants can be evaluated from observed rate constants and the pK_a of the amine. Since the rate constants in the mechanism, especially k_H, are sensi-

$$R_3NH^+ \cdots OH_2 + H_2O \underset{k_{-a}}{\overset{k_a}{\rightleftharpoons}} R_3N \cdots HOH + H_3O^+$$

$$R_3N \cdots HOH \xrightarrow{k_H} R_3N + HOH \qquad (2)$$

$$R_3N + H_3O^+ \xrightarrow{\text{fast}} R_3NH^+$$

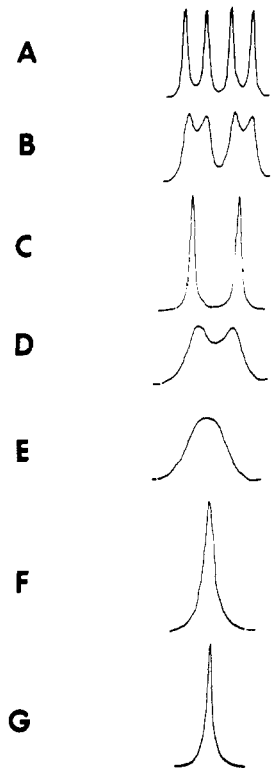
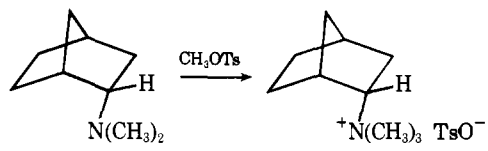


Figure 1. NMR spectra of the N-CH_3 protons of *exo*-2-dimethylaminonorbornane at pH values of (A) 2.70, (B) 3.46, (C) 5.77, (D) 7.17, (E) 7.46, (F) 8.23, (G) 8.48.

tive to subtle solvent-solute interactions,[5,6] we were anxious to apply the construct to *exo*-I and *endo*-I. Observed rate constants for NH proton exchange were secured from the NMR line shapes near pH 4.

Steric effects in amines can either accelerate or impede N-inversion rates depending on whether the tetrahedral ground state or the planar transition state is more destabilized by nonbonding repulsion. Thus, ground-state interactions in 1-*tert*-butylaziridine causes this amine to invert much faster than 1-methylaziridine.[7,8] On the other hand, steric effects inhibit the inversion of trigonal nitrogen in certain benzquinolone systems.[9,10] We determined the inversion rate of *exo*-I at pH 7–8 where the pair of singlets converges into a single peak. The method was essentially that of Saunders and Yamada.[11] Although a small chemical shift difference between the two N-CH_3 groups prevented us from determining an inversion rate for *endo*-I by ^{1}H NMR, we could obtain the inversion rate by ^{13}C NMR.

Finally, we compared the alkylation rates of *exo*-I and *endo*-I (eq 3). It would seem that if the endo cavity is so crowded that an endo chloride has difficulty leaving, then the endo dimethylamino group should resist conversion into a bulky and ionic quaternary nitrogen.



(3)

Experimental Section

***exo*-2-Dimethylaminonorbornane (*exo*-I).** *exo*-2-Aminonorbornane (Aldrich) was reductively methylated with 37% aqueous formaldehyde and sodium cyanoborohydride (Alfa-Ventron) in acetonitrile.[12] The crude product, obtained in 55% yield, was distilled twice under reduced pressure, bp 56–57 °C (10 mm) [lit.[13] bp 71 °C (20 mm)]. GLC analysis (40-ft column, i.d. = 0.093 in., packed with 6% Carbowax coated on Chromosorb W, 80/100 mesh) showed that the *exo*-2-dimethylaminonorbornane was contaminated by less than 1% of the endo isomer.

Anal. Calcd for $C_9H_{17}N$: C, 77.70; H, 12.23; N, 10.07. Found: C, 77.59; H, 12.22; N, 10.12.

***endo*-2-Dimethylaminonorbornane (*endo*-I).** Aldrich *endo*-2-aminonorbornane hydrochloride was treated with aqueous base to liberate the free amine which was then dimethylated in 46% yield by the procedure used for the exo compound, bp 48–49 °C (5 mm) [lit.[13] bp 68–69 °C (19 mm)]. GLC analysis showed that the amine was greater than 97% pure.

Anal. Calcd for $C_9H_{17}N$: C, 77.70; H, 12.23; N, 10.07. Found: C, 77.51; H, 12.29; N, 10.17.

***N,N*-Dimethyl-α-methylbenzylamine.** Aldrich α-methylbenzylamine (12.0 g) was dimethylated with 36 g of 91% formic acid and 38 g of 37% aqueous formaldehyde.[14,15] The solution was heated at 80 °C for 9 h after which the product was isolated and distilled under reduced pressure, bp 88–89 °C (16 mm), in the presence of *p*-nitrobenzoyl chloride. GLC analysis indicated a greater than 99% purity.

Anal. Calcd for $C_{10}H_{15}N$: C, 80.48; H, 10.13; N, 9.39. Found: C, 79.49; H, 9.97; N, 8.78.

pK_a Determinations. pK_a values, determined by potentiometric titration, are: *exo*-I, 10.36; *endo*-I, 10.11; and *N,N*-dimethyl-α-methylbenzylamine, 9.09.

Kinetics of NH Proton Exchange. Rates of NH proton exchange of *exo*-I and *endo*-I in aqueous formate buffers at 25 °C were deduced from the slow-passage NMR signal of the *N*-methyl protons. Both N-CH_3 doublets of *exo*-I coalesced into singlets near pH 3.8. Since the N-CH_3 groups of *endo*-I have nearly identical chemical shifts, the N-CH_3 region showed only a doublet in strong acid; the doublet merged into a broad singlet at pH 3.9. Observed rate constants were calculated with the aid of an RCA Spectra 70/55 computer which adjusted τ (the reciprocal of k_{obsd}) so as to minimize deviations between experimental and theoretical line widths of singlets or peak-to-valley ratios of doublets.[16] Each N-CH_3 signal of *exo*-I yielded a k_{obsd}, and agreement between the two values was always good. NMR spectra were recorded with a Jeol-JNM-MH-100 spectrometer equipped with a variable-temperature probe. Temperatures, checked frequently during a series of runs,[17] are believed to be accurate to ±0.7 °C. Five to six spectra were traced in both directions for each sample, and the resulting rate constants were averaged. An optimum constant homogeneity was achieved by adjusting the resolution control prior to each run while observing the methyl signal from a drop of CH_3CN added to the NMR tube. The CH_3CN was shown not to affect the kinetics. Natural line widths were measured under conditions of fast exchange (pH 5.8 for *exo*-I; pH 7.0 for *endo*-I). Coupling constants were obtained at pH values below 2 where exchange is slow (J_{exo} = 5.10 Hz and J_{endo} = 5.13 Hz). Spectra were recorded using amine concentrations of 0.15 M or greater, rf field of 0.1 mG, sweep width of 54 or 108 Hz, sweep time of 250 s, and filter bandwidth of 10 Hz. The error in k_{obsd}, estimated to be ±15%, arises from the assumption of a Lorentzian line shape, from the uncertainty in the effective relaxation time T_2 (derived from the natural line width), and from the uncertainty in the probe temperature.

Kinetics of N Inversion by ^{1}H and ^{13}C NMR Spectroscopy. The nitrogen inversion kinetics for *exo*-I were obtained in much the same manner as described for the NH proton exchange except that we monitored the collapse of the two N-CH_3 singlets into one peak in phosphate buffers of pH 7–8. The maximum separation of the two methyl singlets, $\Delta\nu_{AB}$, equals 11.05 Hz at 100 MHz. Since the N-CH_3 groups of *endo*-I possess such a small chemical shift difference ($\Delta\nu_{AB}$ < 1 Hz), it was impossible to measure N-inversion rates of this compound by ^{1}H NMR. These rates could, however, be secured by ^{13}C NMR line-shape analysis.[18] N-Inversion transforms the magnetically nonequivalent methyl carbons ($\Delta\nu_{AB}$ = 23.6 Hz at 20 MHz) into equivalent atoms (Figure 2). Temperature control of our Varian CFT-20 was a serious experimental problem. Attempts to maintain the probe temperature at 25 °C with the temperature control unit led to fluctuations of several degrees. Satisfactory temperature stability was achieved only at ambient probe temperature (33 ± 0.7 °C) with the control unit turned off. We are confident that our ^{13}C-based kinetics are reliable because the *exo*-I inversion rate at 33 °C (derived from ^{13}C NMR) exceeds the *exo*-I inversion rate at 25 °C (derived by ^{1}H NMR) by a reasonable factor of 2.2. This number takes into account a small pK_a difference at 33 and 25 °C. All ^{13}C experiments

Table I. Observed Rate Constants for NH Proton Exchange of *exo*- and *endo*-2-Dimethylaminonorbornane in Aqueous Buffers at 25 °C

Amine	[Amine], M	pH	[Buffer], M	k_{obsd}, s^{-1}
exo-I	0.15	3.10	0.066	2.55
	0.15	3.10	0.033	1.92
	0.15	3.10	0.007	1.31
	0.15	3.27	0.066	3.40
	0.15	3.27	0.033	2.69
	0.15	3.27	0.007	1.60
	0.15	3.43	0.066	4.37
	0.15	3.43	0.046	3.96
	0.15	3.43	0.026	3.21
	0.15	3.43	0.007	2.60
	0.45	3.46	0.019	5.20
	0.34	3.46	0.019	4.73
	0.23	3.46	0.019	3.55
	0.11	3.46	0.019	3.11
	0.15	3.61	0.066	6.02
	0.15	3.61	0.046	5.27
	0.15	3.61	0.026	4.59
	0.15	3.61	0.007	3.57
	0.15	3.75	0.066	7.02
	0.15	3.75	0.046	6.30
	0.15	3.75	0.026	5.57
	0.15	3.75	0.007	4.50
	0.15	3.97	0.066	11.1
	0.15	3.97	0.046	9.09
	0.15	3.97	0.026	7.76
	0.15	3.97	0.007	6.76
endo-I	0.15	3.58	0.060	4.26
	0.15	3.58	0.042	3.35
	0.15	3.58	0.024	2.46
	0.15	3.58	0.006	1.92
	0.47	3.77	0.048	6.74
	0.35	3.77	0.048	6.14
	0.24	3.77	0.048	5.55
	0.12	3.77	0.048	4.91
	0.15	3.81	0.060	5.30
	0.15	3.81	0.042	4.81
	0.15	3.81	0.024	3.50
	0.15	3.81	0.006	2.07
	0.15	3.95	0.060	6.92
	0.15	3.95	0.042	6.01
	0.15	3.95	0.024	5.08
	0.15	3.95	0.006	3.06
	0.15	4.19	0.060	13.6
	0.15	4.19	0.042	12.1
	0.15	4.19	0.024	10.9
	0.15	4.45	0.060	18.6
	0.15	4.45	0.042	16.8
	0.15	4.45	0.024	15.2
	0.15	4.45	0.006	14.0

utilized solutions 0.50 M in amine which required 10 000 transients. Concentrations greater than 0.50 M were avoided because of a small and unexplained concentration dependence of the inversion rate.

Kinetics of *endo*-I and *exo*-I Quaternization. A stoppered cuvette containing 3.00 ml of 0.20 M *exo*-I or *endo*-I in acetonitrile was equilibrated at 25.0 °C for 20 min within the thermostated cell compartment of a Cary 14 spectrophotometer. A small amount (50 μl) of 0.061 M methyl toluenesulfonate in acetonitrile was added with the aid of a small stirring rod flattened at one end. The decrease in absorbance at 273 nm was then traced as a function of time until the reaction was complete.[19] Pseudo-first-order plots were linear to greater than 2 half-lives.

Results and Discussion

Equation 2 and its rate constants k_a, k_{-a}, and k_H describe proton exchange of amine salts with water. Three species in addition to water were found to accept protons from the conjugate acids of *exo*-I and *endo*-I. These are buffer (k_f), hydroxide (k_x), and unprotonated amine (k_2):

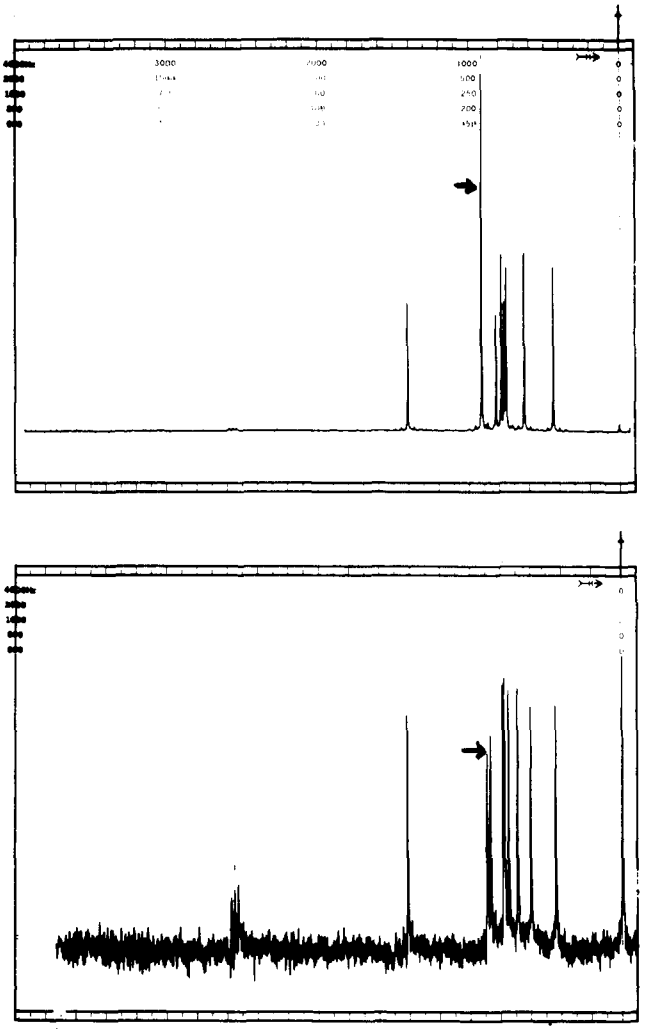
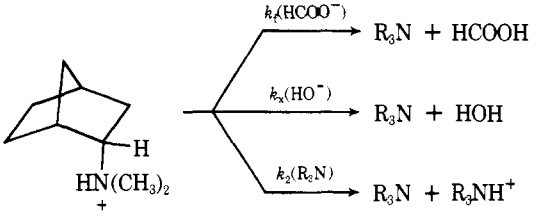


Figure 2. ^{13}C NMR spectra of *endo*-2-dimethylaminonorbornane neat (top) and in 2 N HCl (bottom) with Me_4Si as an external reference. Arrows point to N-CH_3 signals.



Free amine produced in these transfers is reprotonated by H_3O^+ (a diffusion-controlled reaction[20]). The overall result is NH proton exchange. We evaluated k_f from the raw data in Table I by plotting k_{obsd} vs. [HCO_2^-] at each pH value. The slopes of the plots for *endo*-I give an average k_f of 111 M^{-1} s^{-1}. A nearly identical value for k_f was obtained for *exo*-I (Table II). Similarly, k_2 was determined by plotting k_{obsd} vs. [free amine] at pH 3.46 for *exo*-I and at pH 3.77 for *endo*-I. The k_2 values for the two amines (Table II) differ by a factor of only 4.6. Moreover, the k_2 values are not very different from the $k_2 = 7.3 \times 10^7$ M^{-1} s^{-1} characteristic of a "normal" acyclic amine, *N,N*-dimethylhexylamine.[21]

By subtracting the k_f and k_2 reactions from the total exchange rate, we arrived at a rate parameter, k'_{obsd}, which encompasses only the water reaction (eq 2) and the k_x reaction. Equation 4 expresses k'_{obsd} in terms of the individual rate constants in these mechanisms (K_w = the autoprotolysis con-

Table II. Rate Constants for Proton Transfer from *exo*-I and *endo*-I to Water (k_a), Another Amine (k_2), Hydroxide (k_x), and Formate (k_f) in Aqueous Solutions at 25 °C

Amine	pK_a	k_a, s^{-1}	k_2, $M^{-1}\ s^{-1}$	k_x, $M^{-1}\ s^{-1}$	k_f, $M^{-1}\ s^{-1}$
exo-I	10.36	0.62 ± 0.30	$5.2 \pm 1.0 \times 10^7$	$2.6 \pm 0.6 \times 10^{10}$	106 ± 20
endo-I	10.11	<0.5	$1.2 \pm 0.2 \times 10^7$	$3.6 \pm 0.9 \times 10^{10}$	111 ± 15
$C_6H_{13}N(CH_3)_2$[a]	10.10	1.3	7.3×10^7	3.4×10^{10}	

[a] Reference 21.

Table III. pK_a Values of Several Sets of Aliphatic Amines

Amine	pK_a[a]	Ref
Cyclohexylamine	9.82	*b*
Cyclooctylamine	10.01	*b*
Hexamethylenimine	10.00	*b*
Octamethylenimine	9.39	*b*
Decamethylenimine	9.04	*b*
Di-*n*-propylamine	11.00	*c*
Di-*n*-butylamine	11.25	*c*
N-Methylpiperidine	10.08	*c*
N-Methylpyrrolidine	10.46	*c*

[a] pK_a values within each set of amines were determined by the same investigators. [b] H. C. Brown, D. H. McDaniel, and O. Hafliger in "Determination of Organic Structure by Physical Methods", E. A. Braude and F. C. Nachod, Ed., Academic Press, New York, N.Y., 1955, p 567. [c] H. K. Hall, Jr., *J. Am. Chem. Soc.*, **79**, 5441 (1957).

stant of water). Since k_H is much greater than $k_{-a}[H^+]$ at pH 3–4, eq 4 simplifies

$$k'_{obsd} = \frac{k_a k_H}{k_H + k_{-a}[H^+]} + \frac{k_x K_w}{[H^+]} \quad (4)$$

to eq 5. Equation 5 predicts that a plot of k'_{obsd} vs. $1/[H^+]$ should be linear with an intercept of k_a and a slope of $k_x K_w$. Values of k_a and k_x obtained from such plots are given in Table II.

$$k'_{obsd} = k_a + (k_x K_w/[H^+]) \quad (5)$$

Considerable error is associated with these rate constants because k'_{obsd} is merely a remnant of k_{obsd}. In fact, the error is sufficiently large that we could only set an upper limit to the k_a of *endo*-I.

The rate constants in Table II indicate that *exo*-I and *endo*-I have reactivities which are similar to each other and similar to those of an ordinary acyclic amine, *N,N*-dimethylhexylamine. Only a small variation in k_x was expected; diffusion-controlled reactions should not differ greatly in solutions of constant viscosity. But proton transfer to formate and amine are not diffusion controlled, and yet *exo*-I and *endo*-I have comparable k_f and k_2 values. Apparently, the *endo*-I dimethylammonium group has no problem exposing its N proton to a large acceptor molecule[22] outside the endo cavity despite the fact that at least one *N*-methyl group is thereby forced toward an endo ring proton. The data suggest, therefore, that severe steric interactions in the endo cavity are not present. A more definitive statement will be possible when comparisons with other systems become available. However, even at this time it is clear that either steric interactions in *endo*-I are unimportant or else steric interactions do not perturb the kinetic parameters in Table II. We describe below additional experiments which support the former alternative.

Table II also lists pK_a values for *exo*-I and *endo*-I. The pK_a of *endo*-I is identical with that of *N,N*-dimethylhexylamine and only 0.25 units less than that of *exo*-I. Fluctuations in pK_a among structurally related amines often exceed 0.25 (see Table III). Therefore the pK_a of *endo*-I is normal, and steric interactions are too small to impair the solvation of the *endo*-dimethylammonium ion.

At this point we must affirm that all "models", *endo*-I included, are necessarily imperfect. *endo*-I differs from the transition state for solvolysis of *endo*-2-norbornyl derivatives in the hybridization at C(2). The carbon bearing our "reporter group" in *endo*-I is tetrahedral, whereas the corresponding carbon in the solvolysis transition state is a partially formed carbonium ion. Flattening of the carbon in the latter case could enhance nonbonded interactions between the C(6) endo proton and the leaving group.[23] Nonetheless, the large size of the dimethylammonium group (A value = 2.4)[24] relative to halide (A = 0.4) or tosylate (A = 0.7) should more than compensate for hybridization differences. Since a dimethylammonium group seems to experience no serious steric problems in the endo cavity, neither should a leaving group, hybridization differences notwithstanding.

The pH-dependent NMR spectra of *exo*-I and *endo*-I yielded another useful parameter, the rate of nitrogen inversion.[25] Only unprotonated amine can undergo inversion.[11] By varying the acidity of the aqueous amine solutions we could control the fraction of protonated amine and hence the k_{obsd} for inversion. Equation 6 expresses this statement algebraically:[26]

$$k_{obsd} = k_{inv}\left(\frac{[B]}{[BH^+] + [B]}\right) \quad (6)$$

Observed inversion rates for *exo*-I fall within the "NMR window" at pH 7–8. In this pH range $[BH^+] \gg [B]$, so that eq 6 transforms into

$$k_{obsd} = k_{inv}(K_a/[H^+]) \quad (7)$$

in which K_a is the dissociation constant for BH^+. A plot of k_{obsd} vs. $1/[H^+]$ for *exo*-I is shown in Figure 3; the slope divided by K_a provides a $k_{inv} = 9.3 \times 10^3\ s^{-1}$. Inversion rates for *exo*-I, *endo*-I, and two benzylamines are tabulated in Table IV. As explained in the Experimental Section, we found it necessary to obtain the inversion rate for *endo*-I by ^{13}C spectroscopy.

In order to achieve magnetically equivalent $N\text{-}CH_3$ groups, the amine nitrogen must either invert and rotate (eq 1), rotate and invert, or do both simultaneously.[27,28] The dimethylamino group thereby sweeps out a volume equivalent to that occupied by a *tert*-butyl group ($A > 4.4$).[24] Despite the substantial spatial requirements for inversion and despite the known sensitivity of inversion to steric effects,[7-10] *exo*-I and *endo*-I have nearly identical inversion rates. Therefore, according to the inversion criterion, the exo and endo positions resemble each other sterically.

Our third line of experiments dealt with the kinetics of the Menschutkin reaction (a favorite for the study of steric effects[29]). We alkylated *exo*-I and *endo*-I with methyl *p*-toluenesulfonate in acetonitrile to produce the trimethylammonium derivatives. A trimethylammonium group demands even more room than a *tert*-butyl group because the positive charge on the nitrogen requires stabilization by solvent molecules or a counterion. Although the extent of bond formation in the transition state for the Menschutkin reaction is relatively small (i.e., there is an "early" transition state[30,31]), at least one

Table IV. Rate Constants for Nitrogen Inversion of Amines in Water

Amine	pK_a	NMR[a]	Temp, °C	k_{inv},[b] s^{-1}
exo-I	10.36	^1H	25	9×10^3
exo-I		^{13}C	33	2×10^4
endo-I	10.11	^{13}C	33	1×10^4
N,N-Dimethyl-α-methylbenzylamine	9.09	^1H	25	1×10^5
Dibenzylmethylamine[c]	7.5	^1H	25	2×10^5

[a] Amine concentrations were 0.15 and 0.50 M in the ^1H and ^{13}C runs, respectively. [b] k_{inv} for the ^{13}C runs were calculated using pK_a values at 33 °C. [c] Data are taken from ref 11.

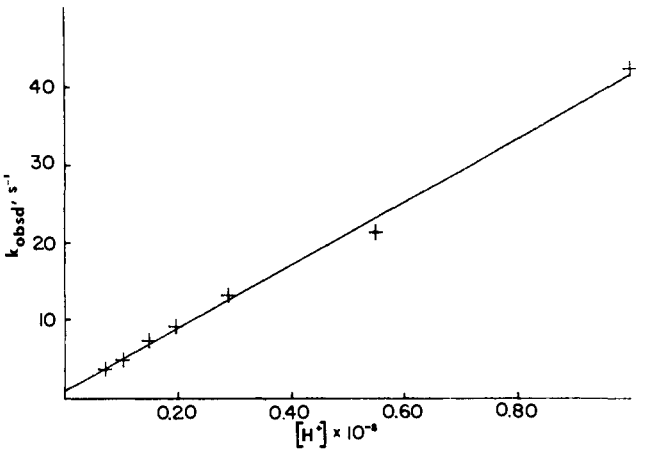
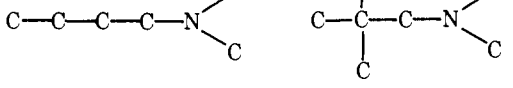


Figure 3. Plot of k_{obsd} for nitrogen inversion of *exo*-2-dimethylaminonorbornane at 25 °C vs. the reciprocal of the hydrogen ion concentration.

nitrogen substituent must be directed into the endo cavity when *endo*-I is alkylated. If, for example, methyl *p*-toluenesulfonate approaches the endo dimethylamino group from a position outside the endo cavity, then one of the methyl groups already fully bonded to the nitrogen is forced to point toward the endo ring protons. Nevertheless, *endo*-I alkylates at a rate only 20 times slower than *exo*-I. (If one adjusted the rate constants for the lesser basicity of *endo*-I, then the exo:endo alkylation rate ratio would be closer to 10.) Consider the significance of this result. We have measured the propensity of norbornyl systems to bear a substituent which *exceeds* the size of a *tert*-butyl group (with an *A* value six times that of tosylate). Peters and Brown[32] state, "Steric effects in norbornyl derivatives can be huge compared with the effects we are accustomed to dealing with in the more flexible aliphatic and alicyclic derivatives". Brown and Bonner[33] have shown that alkylation of *N,N*-dimethyl-*n*-butylamine with methyl iodide proceeds more than 100-fold faster than does the corresponding reaction of *N,N*-dimethylneopentylamine. Yet we find an exo:endo ratio



of less than 20. We can hardly support the contention that the exo:endo rate ratio of 1600 for the solvolysis of norbornyl brosylates[34] stems solely from the steric inhibition of ionization. Note that we do not deny the presence of special steric factors in the endo position; we simply believe that steric effects are insufficient to explain fully a solvolysis rate ratio of 1600. Admitedly, our pK_a values and rates of proton exchange, N inversion, and N alkylation may not be convincing when considered individually. Taken collectively, the data paint a picture of an unimpaired endo dimethylamino group.

Steric effects in the endo cavity can reasonably account for the frequently cited exo:endo ratios of nonsolvolytic reactions.[35] Many of these reactions, however, involve bulky reagents or reagents which form molecular aggregates. $LiAlH_4$ and CH_3MgX are typical examples; they react with norcamphor to give modest exo:endo ratios of 8.1 and 200, respectively. It goes without saying that one can construct substituted norbornyl systems in which the endo position is indeed severely hindered relative to an exo position[36] (and vice versa for that matter). Very likely we could have forced large rate differences between our exo and endo amines by, for example, placing two isopropyl groups on the nitrogens. But the significance of such a result in relation to the departure of an oxygen during the solvolysis of an *unsubstituted* norbornyl brosylate would be doubtful. *If* a dimethylamino group and its protonated and methylated derivatives have spatial requirements equivalent or greater than a departing chloride and or brosylate, hybridization differences at C(2) notwithstanding, then steric factors in the parent norbornyl system are inadequate to explain exo:endo solvolysis rate ratios.

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Homoallyl Interaction between the Nitrogen Lone Pair and the Nonadjacent π-Bond in Cyclic and Bicyclic Amines. V.[1] The Stereospecific Orientation of the Lone Pair Electrons in 7-Azanorbornene Derivatives

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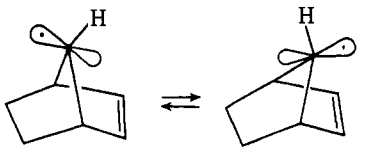
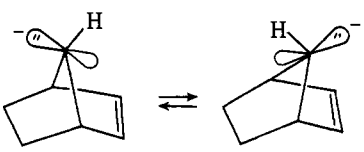
Abstract: In order to gain insight into the effect of n,π bishomoallyl interaction on the orientation of the lone pair electrons, we have carried out ^{1}H and ^{13}C NMR spectroscopic studies of 7-azanorbornene and 7-azanorbornadiene derivatives. Based on the stereospecific shifts and the line broadening effects of ^{1}H NMR signals induced by Eu^{3+} and Gd^{3+}, it was concluded that the lone pair electrons preferentially occupy an anti position with respect to the electron rich π-bond in *N*-methyl-7-azanorbornadiene-2,3-dicarboxylic acid. This preferential orientation of the nitrogen lone pair in 7-azanorbornene derivatives was also confirmed by the stereospecific ^{13}C chemical shift changes induced by *N*-methyl substitution and by the Eu(fod)$_3$-induced ^{1}H shifts. A similar trend of the specific lone pair orientation is also encountered for N-H 7-azanorbornene derivatives. From these experimental results it is concluded that n and π electrons are "repulsive" in bishomoallyl and bishomobenzyl interacting systems involved in the five- and six-membered cyclic and bicyclic amines and that the nitrogen lone pair electrons prefer an anti position with respect to the π bond or π electron rich group so as to avoid the "repulsive" interaction.

The 7-norbornenyl system offers a structural framework from which long-range nonbonded interactions may be examined. The 7-norbornenyl cation has been shown to exhibit such bonding to an unusual degree.[4] This has been attributed to the nonclassical nature of the 7-norbornenyl cation resulting from the overlapping of the unoccupied and the nonadjacent orbitals. Similarly, the nonclassical nature of the 7-norbornenyl radical has been proposed by Kochi et al.[5] based on its electron spin resonance spectrum. They claimed that I is more stable than II and that the interaction between the π orbital on C-2,3



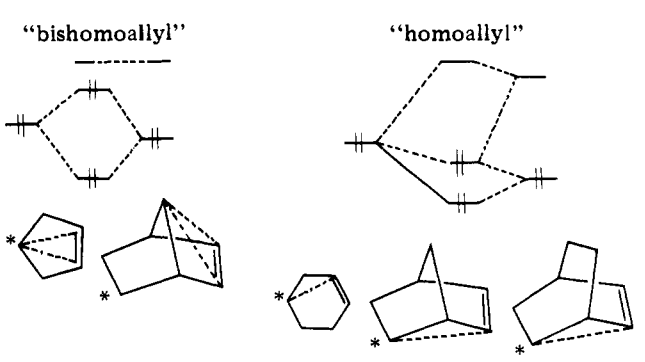
I II

and the half-occupied orbital on C-7 has a destabilizing effect. However, the studies on the nonbonded interaction between the doubly occupied n orbital (anion center) and the nonadjacent π group have been quite limited. Recently, the specific orientation of the lone pair electrons on C-7 in 7-norbornenyl anion has been studied[6] by stereospecific deuteron capture of anti and syn anion intermediates. The preference for *anti*-7-norbornenyl anion has been suggested and interpreted as resulting from possible bishomoantiaromatic character of this anion. Quantum chemical studies of 7-norbornenyl anion have also been performed.[7,8] The semiempirical molecular orbital calculations, however, failed to predict definitely the orientation of the lone pair electrons. It may be, therefore, readily seen from these examples that the problem on the transannular effect between the lone pair electrons and the neighboring π bond in bicyclic molecules is still open to further experimental and theoretical studies.



anti syn

In our recent photoelectron spectroscopic studies[1,9,10] on the nonbonded n,π interaction involved in several cyclic and bicyclic amines containing a nonadjacent π bond, it has been shown that the feature of the nonbonded n,π interaction is quite different between homoallyl and bishomoallyl n,π interacting systems. In the homoallyl interacting system, both n,π and n,π* interactions contribute competitively to the relative stability of the interacting system and, therefore, the system is elec-



* = N-H, N-CH$_3$