Nitrogen inversion rates in bicyclo[2.2.2]octyl hydrazines and amines by 13C NMR

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Gas-Liquid Chromatographic Analysis. All analyses were carried out on a Perkin-Elmer Model 226 fractometer equipped with a 150-ft length, 0.01-in. i.d. open tubular (Golay) column, coated with *m*-bis(*m*-phenoxyphenoxy)benzene modified with 20% Apiezon. A hydrogen flame-ionization detector with helium carrier gas of 30 psi was used, columns being operated at 145 °C, with detector temperature of 185–190 °C and injector block temperature of 310–320 °C. Peak areas were directly determined by use of a high-speed Infotronics electronic integrator. Characteristic retention times of the isomeric alkylnaphthalenes follow: 1-methylnaphthalene, 17.2 min; 2-methylnaphthalene, 15.5 min; 1-ethylnaphthalene, 22.9 min; 2-ethylnaphthalene, 21.9 min; 1-isopropylnaphthalene, 29.8 min; 2-isopropylnaphthalene, 28.8 min; 1-*tert*-butylnaphthalene, 37.7 min; 2-*tert*-butylnaphthalene, 34.1 min.

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Nitrogen Inversion Rates in Bicyclo[2.2.2]octyl Hydrazines and Amines by ^{13}C NMR

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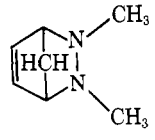
Abstract: Activation parameters for conformational change were determined by carbon NMR for 2,3-dimethyl-2,3-diazabicyclo[2.2.2]oct-5-ene, 2,3-dimethyl-2,3-diazabicyclo[2.2.2]octane, the 2,3-diethyl analogue, the 1,2,3,4-tetramethyl analogue, 2-methyl-1,2-diazabicyclo[2.2.2]octane, 2-methyl-2-azabicyclo[2.2.2]octane, 1,2-dimethyl-2-azabicyclo[2.2.2]octane, and 4,4-diethyl-2,6-diazatricyclo[5.2.2.$0^{2,6}$]undecane, and the results are discussed in terms of the shape of the potential barrier for such compounds.

Introduction

Hydrazine conformations have aroused considerable interest in recent years, largely because of the interesting interplay of steric and electronic effects upon N–N bond rotation and N inversion barriers.[1] Although acyclic hydrazines are known from several lines of evidence to have lone pair–lone pair dihedral angles near 90°,[2] cyclic hydrazines with dihedral angles of various sizes are known.[3] Dynamic NMR spectroscopy has been particularly frequently applied to cyclic hydrazines, and many studies of the barriers to conformational interconversion have appeared.[4-15] Anderson and Lehn[4c] discussed the form of the potential curve for methyl equilibration of 2,3-dimethyl-2,3-diazabicyclo[2.2.1]hept-5-ene (**1**) in detail, pointing out that the mirror image anti



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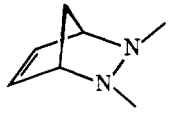
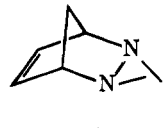
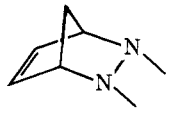


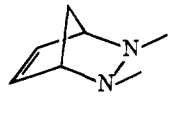
1a



1a′

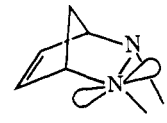


1s$_1$

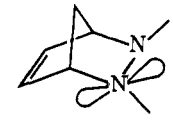


1s$_2$

forms **1a** and **1a′** are the only ones stable enough to be directly observed by NMR spectroscopy, that consecutive N inversion is obviously more favorable energetically than simultaneous double nitrogen inversion, and that the syn methyl forms **1s$_1$** and/or **1s$_2$** should be unstable intermediates, with the half-planar forms **1p$_1$** and/or **1p$_2$** being the



1p$_1$

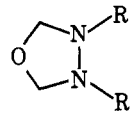


1p$_2$

transition states. They estimated that the half-planar forms should lie about 10 kcal/mol above the stablest form (**1a**/**1a′**) and that the syn forms **1s$_1$** and **1s$_2$** would be destabilized by the methyl–methyl interaction, which they expected to be 5 kcal/mol, producing the potential curve redrawn as Figure 1A. The same sort of curve was stated to be present for saturated and unsaturated bicyclic hydrazines.[4c]

The double barrier potential curve A will not be correct for all cyclic hydrazines since the activation energy for nitrogen inversion will decrease with increasing ring size,[1] and alkyl–alkyl strain for an eclipsed syn form will increase as the alkyl groups get larger. Jones, Katritzky, and coworkers[7a-d] have asserted that alkyl–alkyl repulsion, not flattening at nitrogen, is the highest barrier to be surmounted in several cyclic hydrazines. The large increase in the $\Delta G^{\ddagger}$ required for "double nitrogen inversion" in 3,4-dialkyl oxadiazolidines **2**(R) as R is changed from methyl to *tert*-butyl[15] indicates that alkyl–alkyl repulsion in the eclipsed form **2**-ecl is the highest barrier to be overcome, at least for **2**(iPr).

An important difference in the conformations of **1** and **2**



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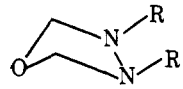
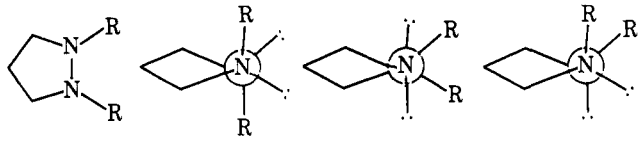


2-ecl

is that ring torsion in the bicycloheptanyl system is expected to be small, but a five-membered ring has substantial ring torsion. In the pyrazolidine (**3**) series, photoelectron spectroscopy studies have shown that **3**(Et) and **3**(iPr) exist in anti conformation $\mathbf{3a}_1$, while **3**(Me) exists in both $\mathbf{3a}_1$ and $\mathbf{3a}_2$ conformations with $\mathbf{3a}_2$ predominating. When ring torsion is present as in **3**, a single nitrogen inversion will interconvert $\mathbf{3a}_1$ to **3s** without forcing the R groups to pass each other, although these groups must pass to convert $\mathbf{3a}_1$ to its mirror image.

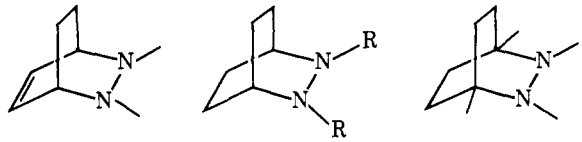


3 $\mathbf{3a}_1$ $\mathbf{3a}_2$ **3s**

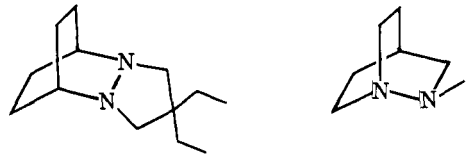
In hopes of more fully elucidating the energy relationships involved in conformational changes of cyclic hydrazines, we have investigated some hydrazines and amines in the bicyclo[2.2.2]octane series, using variable-temperature ^{13}C NMR. Because of the larger chemical shift differences and simplicity of the ^1H-decoupled spectra, ^{13}C NMR is superior to the frequently used ^1H NMR for hydrazines, especially since conformational assignments may frequently be made on the basis of chemical shifts.[16a]

Results

The structures of the compounds investigated by variable-temperature ^{13}C NMR here appear as **4–11.** All were prepared by published routes except **11.** After failure of the route analogous to that used to prepare **10,** we followed Scheme I in preparation of **11.** A Ritter reaction with acetonitrile on the easily available isoprene–methyl acrylate Diels–Alder adduct **12** gave a mixture of lactone **14,** its hydrolysis product, and the desired product **13,** which was separated by extraction. After esterification, heating with sodium methoxide in refluxing diglyme isomerized the ester (which presumably was the wrong diastereomer for cyclization), catalyzed the ring closure, and cleaved the acetyl group to give **15,** which was easily reduced and methylated to give **11.**



4 **5**, R = Me; **6**, R = Et **7**



8 **9**

10 **11**

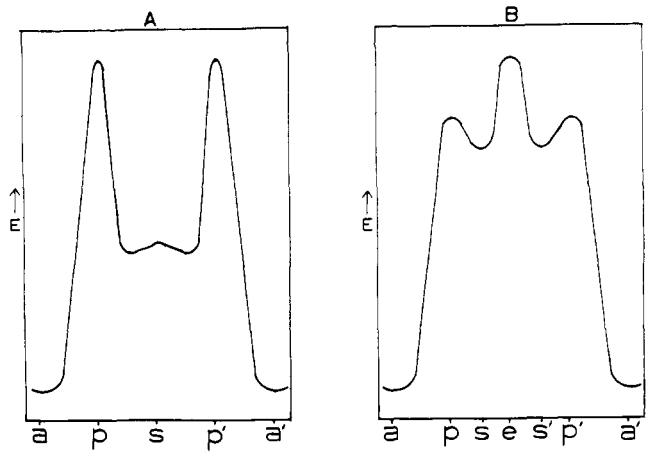
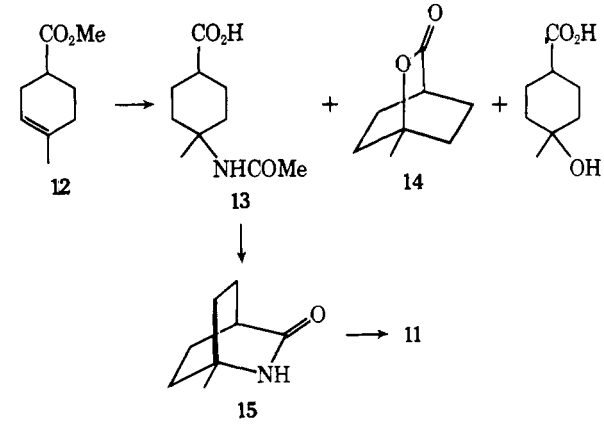


Figure 1 A. "Twofold barrier" potential curve for "double nitrogen inversion" of a bicyclic hydrazine, interconverting the mirror image anti forms *a* and *a'*, assuming no torsion of the bicyclic ring system (redrawn from ref 4b). B. "Central barrier" potential curve for "double nitrogen inversion" converting *a* to *a'*, assuming a large enough torsional barrier so the syn forms *s* and *s'* occur as minima separated from the eclipsed form *e*.

Scheme I



Anderson and Lehn[4b] have already measured the activation parameters for "double nitrogen inversion" of **4** by collapse of the methyl doublet in the ^1H NMR, but we redetermined them by ^{13}C NMR, both as a check upon how well our data would compare with literature values and because the ^{13}C NMR of **4** allows four independent measurements of these parameters. The room temperature NCH_3, C(1,4), C(5,6), and C(7,8) singlets separate into doublets of different $\Delta\nu$ values and, hence, different coalescence temperatures, all caused by the same process.[16b] The NMR spectra recorded were fit by line shape analysis, giving the activation parameters listed in Table I; an Eyring plot of the data for **4** is shown in Figure 2. It will be noted that the 95% confidence limits for the combined data are smaller than those for the individual sets, as should occur if all the variances are part of the same normal distribution. Thus, it appears that most of the deviations between the activation parameters determined from the four separate peaks can be accounted for statistically and that systematic error is small. This comparison does not include systematic error in temperature measurement, since all the data were obtained at one series of temperatures. See the Experimental Section for our temperature measurements. Also included in Table I are $\Delta G^{\ddagger}$ (T_c) values estimated by the coalescence temperature method. Agreement is quite good, as expected for ^{13}C work where uncoupled doublets are collapsing. Based on the data for **4**, reasonable maximum total error estimates for the activation parameters obtained for compounds **5–7,** where only a single collapse was occurring, are ±0.15 kcal/

Table I. Activation Parameters and Confidence Limits for 4 by Line Shape Analysis and Comparison with Coalescence Temperature Method

	Resonance analyzed				
	C(7–8)	NCH_3	C(1–4)	C(5–6)	All
			Line Shape Analysis		
No. of points	9	8	7	8	32
Temp range	57.3	57.7	42.6	42.6	57.3
Correlation coeff	0.9993	0.9997	0.9989	0.9986	0.9985
$\Delta H^{\ddagger}$, kcal/mol	11.81 ± 0.39[a]	12.09 ± 0.31	11.16 ± 0.62	11.52 ± 0.61	11.70 ± 0.24
$\Delta S^{\ddagger}$, eu	−1.79 ± 1.58	−0.49 ± 1.25	−4.34 ± 2.55	−2.81 ± 2.46	−2.11 ± 0.96
$\Delta G^{\ddagger}_{298}$, kcal/mol	12.35 ± 0.09	12.23 ± 0.06	12.46 ± 0.15	12.36 ± 0.14	12.33 ± 0.05
			Coalescence Temperature Analysis		
T_c, °C	−7	−24	−31	−16	
$\Delta\nu$ (T_c)	224.1	62.7	33.0	136.6	
$\Delta G^{\ddagger}$ (T_c)	12.22	12.03	11.99	12.04	
$\Delta G^{\ddagger}$ (T_c) from line shape analysis	12.29 ± 0.04	12.21 ± 0.02	12.21 ± 0.04	12.24 ± 0.05	

[a] All confidence limits at 95%.

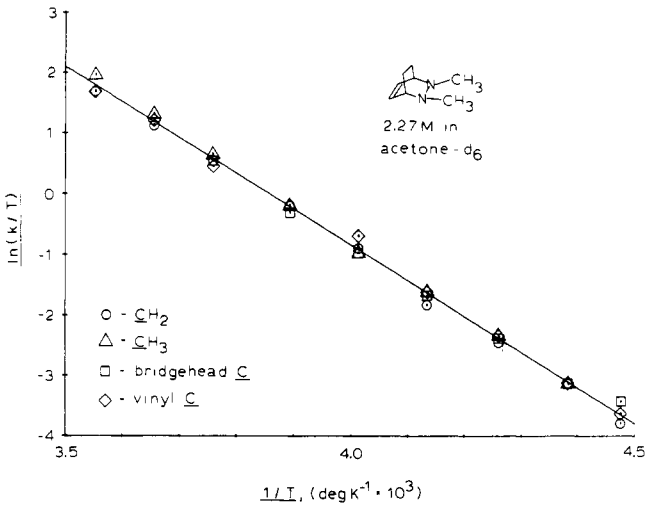
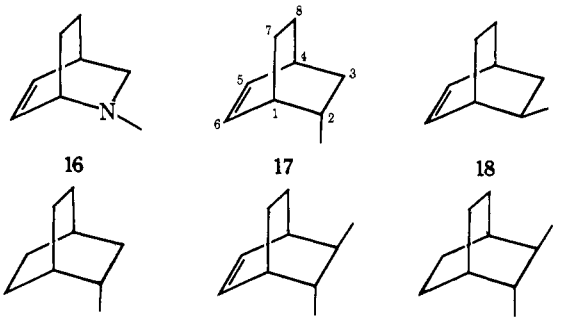


Figure 2. Eyring plot of ^{13}C data for 4.

mol in $\Delta G^{\ddagger}$, ±0.6 kcal/mol in $\Delta H^{\ddagger}$, and ±2.5 eu in $\Delta S^{\ddagger}$. Binsch[17a] has recently pointed out that the usual error analysis technique of propogating error into the activation parameters by using fit to the least-squares straight line of an Eyring plot is incorrect and gives errors that are unrealistically small. We found this to be the case, calculating $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ errors only half the size of those given above for the data of **5**. The numbers obtained for the other compounds run are collected in Table II. All line shape analyses in Table II are corrected for the temperature dependence of T_2*, the effective T_2 with no exchange, by the method of Yamamoto et al.[17b] This could not be done for **4** since all its signals have exchange processes at low temperature, but the lack of broadening in the Me_4Si peak and the fact that the corrections were so small for **5** as not to affect the activation parameters calculated make it unlikely that this affected the accuracy for **4**. As expected, the T_2* correction becomes significant for **9–11** and for **8**, a considerably larger molecule than the others. We also determined the ^{13}C spectrum of **16**, but it showed only one conformation at low temperature, and the lack of temperature sensitivity of the chemical shifts indicates that this conformation dominates even at higher temperatures. The spectra of several hydrocarbons (**17–21**) were run as chemical shift models and are summarized in Table IV. The assignment of the methylene carbons of **19** to the syn and anti bridges was assured by reduction of **17** and **18** with D_2, which differentiates these carbons in pairs. The bridgehead C(2,3) assignments in **21** used the fact that saturation of the double bond in *trans*-2,3-dimethylnorbornene move the bridgehead shifts upfield, but the C(2), C(3) shifts downfield.[18]



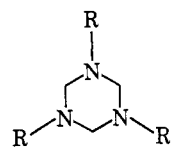
16 17 18

19 20 21

Discussion

Activation Parameters for 4–7. The complexity of the methylene region of compounds **5–8** precluded the analysis of such hydrazines by ^1H NMR;[4b] ^{13}C NMR does the job. The $\Delta G^{\ddagger}$ values for **4** and **5** are experimentally identical, and even $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are within our error limits of being the same. Thus, saturation of the 5,6 double bond of **4** does not change the rate of double nitrogen inversion. The bicyclic ring torsion in **5** was estimated to be 20° by photoelectron spectroscopy[3a] and is presumably near zero for **4**.

The diethyl compound **6** has a significantly (1.4 kcal/mol) higher $\Delta G^{\ddagger}$ than **5**, and it appears that a substantial portion of this increase is caused by an increase in $\Delta H^{\ddagger}$ (although our error of up to ±0.6 kcal/mol must be remembered), and there was a less certain decrease in $\Delta S^{\ddagger}$. We suggest that this result is more consistent with a potential curve like Figure 1B than one like Figure 1A, since the alkyl-alkyl interaction would be distinctly greater in the eclipsed conformation, which is the energy maximum in Figure 1B, than for the half-planar form maximum of Figure 1A. In fact, going from R = methyl to ethyl actually decreases the $\Delta G^{\ddagger}$ for conformational interconversion in **22**,[19]



22

although recent conformational work has shown that the triequatorial conformation assumed in the earlier work is incorrect.[20]

We ran **7**, the bridgehead dimethyl analogue of **5**, in the expectation that Figure 1A barrier would show a larger ac-

Table II. Activation Parameters for Nitrogen Inversion in Bicyclo[2.2.2]octylhydrazines and Amines

a. Coalescence Temperature Method

Compd	Resonance analyzed	T_c, °C	$\Delta\nu$ (T_c), Hz	$\Delta G^{\ddagger}_{T_c}$, kcal/mol	Solvent[a] (concn, M)
4	All four	−7−−31	224−233	12.07 av	A (2.3)
5	C_{5678}	−7	273.8	12.11	A (2.7)
6	C_{5678}	+25	253.2	13.68	A (1.4)
7	C_{5678}		ca. 233		A (1.2)
8	Bridge CH_2	−25	235.0	11.33	A (0.47)
	Ethyl CH_3	−45	22.7	11.44	A (0.47)
9	C_{67}	−101	234.3	7.74	B (1.6)
	C_{58}	−113	37.9	7.76	B (1.6)
10	C_{67}	−127	182.0	6.60	B (1.5)
11	C_{67}	−121	222−247	6.79−6.82	C (0.9)

b. Total Line Shape Analysis Method

Compd	Resonance analyzed	Temp range	No. of points	Cor coeff	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu	$\Delta G^{\ddagger}_{298\,°C}$, kcal/mol	$\Delta G^{\ddagger}_{T_X}$, kcal/mol	T_X, °C
4	All four	57.3	32	−0.9985	11.70 ± 0.24[b]	−2.11 ± 0.96[b]	12.33 ± 0.05[b]	12.26 ± 0.03[b]	−7
								12.25 ± 0.02	−16
								12.23 ± 0.02	−24
								12.21 ± 0.02	−31
5	C_{5678}	106.4	12	−0.9992	11.08 ± 0.32	−4.15 ± 1.20	12.32 ± 0.06	12.18 ± 0.04	−7
6	C_{5678}	80.3	8	−0.9994	12.13 ± 0.42	−5.39 ± 1.49	13.73 ± 0.05		
7	C_{5678}	94.8	7	−0.9991	10.41 ± 0.51	−8.85 ± 1.97	13.05 ± 0.10		
9	C_{67}	45.4	9	−0.9983	8.72 ± 0.45	5.37 ± 2.56	7.12 ± 0.32	7.86 ± 0.06	−113
								7.94 ± 0.09	−127
10	C_{67}	27.6	5	−0.9971	7.33 ± 1.03	5.63 ± 6.82	5.65 ± 1.01	6.51 ± 0.07	−127
11	C_{67}	37.9	6	−0.9968	7.69 ± 0.85	6.94 ± 5.49	5.62 ± 0.79	6.63 ± 0.07	−121
								6.68 ± 0.08	−127

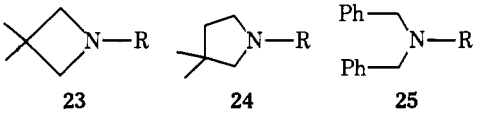
[a] Solvent A is acetone-d_6; solvent B is 35% by volume acetone-d_6 in CF_2Cl_2, which was necessary to keep **9**−**10** in solution at low temperatures; solvent C is 18% acetone-d_6 in CF_2Cl_2. [b] 95% confidence limits in the slope and intercept propagated into the activation parameters.

tivation barrier due to methyl-methyl interaction in the transition state for nitrogen inversion (the importance of such interactions in hydrazine conformational interconversions has been emphasized by Jones, Katritzky, and coworkers[7,21]), whereas a Figure 1B barrier would presumably be little affected. The experimental result of a 0.7 kcal/mol increase in $\Delta G^{\ddagger}$ apparently caused largely by a substantial decrease in $\Delta S^{\ddagger}$ (which was observed to decrease by 4.7 eu while $\Delta H^{\ddagger}$ probably decreased somewhat) is, in fact, probably consistent with either barrier type, since addition of the C methyls would interfere with free rotation of the N methyls in either type of transition state.

Conformation of 8. Our interest in the tricyclic compound **8** was principally to determine whether the lone pairs at nitrogen were cis or trans since we had invoked the cis-fused structure to account for its low oxidation potential,[22] in spite of the fact that we were unable to observe two types of ethyl groups in the low-temperature ^{1}H NMR. Although we interpreted the PES in terms of a zero degree dihedral angle cis conformation,[3a] we failed to point out that the trans-fused conformation would be expected to show the same splitting. The increased chemical shift range of ^{13}C NMR allows assignment to the cis-fused conformation without ambiguity since there is only one type of ethyl group in the trans-fused conformation. The lower $\Delta G^{\ddagger}$ observed than for the trans-substituted compounds seems experimentally significant, although accurate line shape analysis was precluded by the complexity of the spectra.

Activation Barriers for 9–11. Hydrazine **9** is of interest in the context of this work because the measured barrier is certainly for nitrogen inversion of a hydrazine nitrogen quite similar structurally to that of **5**. The PES spectrum of **9** indicated a bicyclic torsion of about 6°, somewhat less than the 20° estimated for **5**. There is one significant difference in the nitrogen inversion barriers for **5** and **9**: the transition state for **9** inversion has the N(1) lone pair held essentially orthogonal to the *p*-hybridized N(2) lone pair in the planar transition state, whereas in **5**, significant lone pair–lone pair repulsion must be present. Although **9** has a $\Delta G^{\ddagger}_{298}$ value 5.2 kcal/mol below that of **5**, the difference in $\Delta H^{\ddagger}$ is considerably smaller (2.4 kcal/mol observed) since $\Delta S^{\ddagger}$ was positive for **9**, like the amine **10**, and negative for **5**, like the other 2,3-diazabicyclo[2.2.2]octyl systems.[23] The statistical error for the activation parameters of 9 is somewhat larger than for **5**, but we believe the change in size of $\Delta S^{\ddagger}$ is significant. It is worth noting that a positive $\Delta S^{\ddagger}$ might be expected for a transition state which is planar at nitrogen, as those of **9**–**10** almost surely are, because of significantly decreased *N*-methyl methylene interaction.

Although Lehn and Wagner reported a $\Delta G^{\ddagger}$ (−175 ± 3 K) of 8.4 ± 0.3 kcal/mol for deuteriomethyl **10** in $CHFCl_2$,[24] we believe this value to be considerably too high. The value we observed of 5.65 (298 K) is 1.4$_7$ kcal/mol lower than that of hydrazine **9**, which is about the expected amount. The effect of α-heteroatom substitution has been discussed in detail by Lehn in terms of lone pair–lone pair repulsion, electronegativity effects, and electric dipole effects. As discussed above, the lone pair–lone pair repulsion effect is not present in the **10**–**9** comparison. Dewar and Jennings[2f] have pointed out that the transition states for nitrogen inversion of **23**–**25** doubtless assume the perpendicular geometry which cancels out the lone pair–lone pair repulsion, and comparison of R = NH_2 to CH_3 (or CD_3) gave differences of $\Delta\Delta H^{\ddagger}$ = 2.2 for **23**,[24b] $\Delta\Delta H^{\ddagger}$ = 1.2 for **24**,[25] and $\Delta\Delta G^{\ddagger}$ = 1.0 for **25**.[2f] Our result for the **10**–**9** comparison is in good agreement.



23 **24** **25**

The activation parameters for **11** are somewhat less certain than for **10**, because the upfield part of the C(6), C(7) doublet happens to overlap with the broadening C(5), C(8) peak and the C(7) Me peak at low temperature (see Table

Table III. ^{13}C Chemical Shifts for Bicyclo[2.2.2]octylhydrazines and Amines

Compound	Temp	Bridgehead	Methylene	*N*-Methyl	Other
4	Amb	54.57	19.92 (br)	43.65	132.88 (br), vinyl
	−83.5	53.14, 54.45	15.18, 23.93	42.25, 44.74	130.25, 135.47
5	Amb	52.16	22.83 (br)	43.53	
	−71.4	51.44	17.14, 27.84	43.55	
6	Amb	48.71	22.81 (br)		52.44, NCH_2; 13.83, Me
	−67.1	48.29	17.87, 27.64		52.37, NCH_2; 13.77 Me
7	Amb	51.88	30.46 (br)	39.83	26.19, CMe
	−83.2	51.84	25.56, 34.82	39.87	26.11
8	Amb	50.21	23.15 (br)		58.97, NCH_2; 46.17, quat; 27.35 QCH_2; 9.26, CH_3
	−69.4	49.63	17.91, 27.52		58.80, NCH_2; 45.81, quat.; 25.19, 27.77 QCH_2; 8.98, 9.84, CH_3.
9	Amb	24.05	26.23, 45.79	42.53	57.91, C(3)
	−127.3	23.42	24.73, 40.55 26.21, 49.83	42.13	57.08
10	Amb	26.98, 51.52	24.57, 25.56	43.15	58.23, C(3)
	−135.6	26.15, 51.17	19.94, 25.10 27.17, (br)	42.72	57.22
11	Amb	27.15, 49.86	26.40, 31.33	38.31	59.57, C(3); 25.76, CMe
	−136.1	26.44, 50.24	ca. 25.6[a] 35.22	37.75	58.61, C(3); ca. 25.6[a] CMe
16	Amb	31.77, 54.51	22.19, 27.70	45.31	132.20, 133.46, vinyls; 57.14, NCH_2
	−127.5	31.13, 53.92	21.44, 27.56	45.51	131.96, 133.60; 56.48

[a] The CMe peaks the broadening C(5)–C(8) peaks and upfield portion of the frozen C(6)–C(7) doublet all appear as a lump at 25.60 (−136.1), 25.53 (−143.7). The uncertainty in $\Delta\nu$ was put into the activation parameters (Table II).

Table IV. ^{13}C Chemical Shifts from Some Hydrocarbons

	C(1)[a]	C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	C(8)	Other
17	37.33	31.10[d]	36.47	32.79[d]	134.84[b]	132.67[b]	24.75[c]	27.07[c]	23.32 (Me)
18	36.26	31.21[d]	35.30	30.95[d]	136.82[b]	133.29[b]	19.17	26.69	20.60 (Me)
19	31.07[b]	31.20[b]	36.35	25.88	26.76	20.89	28.10[c]	25.68[c]	21.35 (Me)
20	41.42[b]	37.14[c]	38.02[c]	42.13[b]	136.86	131.97	27.38	18.13	18.79 (exo Me) 22.46 (endo Me)
21	32.00	40.60	40.60	32.00	27.85	20.50	27.85	20.50	19.36 (Me)

[a] Numbering is as shown on structure **17**, making the right front carbon in **17–21** C(2) in all cases, to facilitate comparison of the effect of structural changes. On each line, positions with ambiguities in assignment are indicated by superscripts.

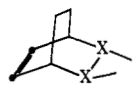
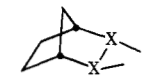
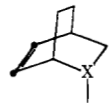
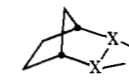
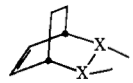
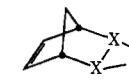
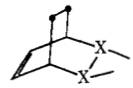
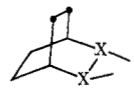
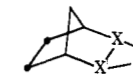
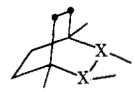
III), so simulations could only be performed on the downfield half of this doublet. Nevertheless, using the maximum and minimum possible $\Delta\nu$ values did not affect $\Delta G^{\ddagger}$ calculated by the T_c approximation (see Table II), and we do not feel the accuracy of $\Delta G^{\ddagger}$ calculated by simulation was affected appreciably. Because of the rather large statistical error in $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$, we think it is wise to compare $\Delta G^{\ddagger}$ for **10** and **11** in the temperature range where the experiment was done, to minimize the effect of $\Delta S^{\ddagger}$. At −127 °C (T_c for **10**), $\Delta G^{\ddagger}$ for **10** was 6.51 kcal/mol and that for **11** 6.68. This conclusion of virtually no effect of C(1)-methyl substitution upon $\Delta G^{\ddagger}$ is also that arrived at by looking at $\Delta G^{\ddagger}_{298}$ or the $\Delta G^{\ddagger}$ (T_c) values by the T_c method. This result shows that the **5–7** comparison is not a valid one to distinguish bicyclic torsion from nitrogen inversion since there is experimentally no increase in $\Delta G^{\ddagger}$ when an α-methyl group is added. This result shows that Jones and Katritzky's concept of methyl-methyl repulsions limiting ring and nitrogen inversion in hydrazines[7] is incorrect.[21] Although it is certainly true that the C–N bond is longer than the N–N bond, it is inconceivable to us that this bond length change could increase the steric interaction by an order of magnitude. It is lone pair–lone pair interaction, not methyl-methyl interaction, which dominates the conformational barriers in hydrazines with *N*-methyl substituents, although this is clearly not the case with *N*-isopropyl substituents.[15]

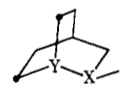
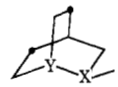
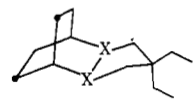
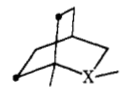
A final point which can be noted from Table II is that the $\Delta S^{\ddagger}$ values for **5–7** are all negative (−4–−9), whereas those for **9–11**, where nitrogen inversion is the only possible highest barrier to conformational interconversion, are all positive (5–7). Although $\Delta S^{\ddagger}$ is notoriously hard to measure accurately, we believe that we have established that $\Delta S^{\ddagger}$ is higher for **9–11** than for **4–7** and suggest that the difference in $\Delta S^{\ddagger}$ would be most consistent with a torsional eclipsing highest barrier for **5–7**.

Chemical Shifts. The temperature variations of the ^{13}C chemical shifts for these systems were nonlinear over the temperature range studied and varied in size for different carbons. All carbons showed higher δ at higher temperature. As an example of the temperature variations found, we list those for the nonbroadening carbons of **7**. The NCH_3 shift varied from ca. 0.83 mδ/deg in the 30–50 °C temperature range to ca. 0.20 mδ/deg at the low-temperature limit, while the CCH_3 carbon showed the oppositive curvature, 0.27 (30–50 °C), 4.35 (−83–−57 °C), and the bridgehead carbon 3.72 (30–50 °C), and 1.13 (−83–−57 °C). The total ranges of the δ changes observed may be obtained from Table III.

Work by Roberts and co-workers[26] on alcohols and that of Egger† and Djerassi[27] on amine chemical shift correlations have clearly indicated the direction to take for empirical prediction of δ values (deriving shift parameters for replacement of CH by N), but our data set is too small for such parameters to be derived. These data do show, however, that there will be stereochemical problems in deriving such empirical parameters for hydrazines. In Table V, we compare the amines and hydrazines run with their hydrocarbon analogues. The comparison must utilize the low-

Table V. $\Delta\delta$ Values for the Carbons Indicated

Entry	Structure	X = CH	X = N	Structure	X = CH[18]	X = N[14]
1		4.89	5.22		5.0	4.2
2		2.17	1.26 (amb) 1.64 (−127.5 °C)		1.9	1.5
3		0.71	1.31		0.9	0.8
4		9.25	8.75			
5		7.35 (Me)	10.70 (Me) 9.77 (Et)		9.2	9.2
6			9.26			
7		2.32	5.51 (amb) 6.12 (−127.5 °C)			

		X = Y = CH	X = N, Y = CH	X = Y = N
8		7.21	7.23	9.28
9		1.08 or 1.34	not frozen	1.48
10			9.61	
11		8.8–9.9 (−127)		

temperature spectra of the hydrazines since the nitrogen-containing systems are inverting slowly on the NMR time scale. The entries for **6** (entries 2 and 7) indicate changes in $\Delta\delta$ of the magnitude one might expect to see with temperature. Also included are $\Delta\delta$ values for bicyclo[2.2.1]heptyl systems taken from the literature.[14,18] The $\Delta\delta$ values for hydrocarbon and hydrazine systems roughly parallel each other, but there are significant quantitative differences. Although **4** has a $\Delta\delta$ value for the saturated bridge carbon 0.5 ppm less than that of the corresponding hydrocarbon (entry 4), the saturated hydrazine **5** has a 3.35 ppm greater $\Delta\delta$ value than its corresponding hydrocarbon, yet the $\Delta\delta$ difference is zero in the bicyclo[2.2.1]heptyl analogue. We suggest that the most likely candidate for this difference is the different lone pair–lone pair dihedral angle for **5**, which has significant bicyclic ring torsion, in contrast to the other two compounds. Since the energy levels of the lone pair MO's and dipole effects should be sensitive to dihedral angle, some effect of this angle is not surprising. This seems to indicate that it would be necessary to include the lone pair–lone pair dihedral angle in an empirically useful set of shift parameters. The surprising difference in $\Delta\delta$ for amine **16** and its hydrocarbon analogue (entry 7) of 3.19 ppm is another indication that lone pair effects are large enough to require inclusion in shift correlations. Entry 8 shows a substantial difference in hydrazine and amine lone pair effects since $\Delta\delta$ is zero comparing amine **10** with hydrocarbon **19**, but 2.07 for hydrazine **9** vs. **19**.

The hydrazine nitrogen lone pair effects cannot be considered separately, since in this case the bridgehead nitrogen lone pair is nearly equivalently disposed relative to the two carbons (PES indicates a ring torsion of about 6°[3a]), yet the effect on $\Delta\delta$ is substantial. There are, of course, bond length shortenings when C–N and N–N bonds are introduced, which may prove not to be ignorable either. Although this work has not given numbers to allow quantitative prediction of the ^{13}C NMR of other hydrazines from the NMR of the hydrocarbon, it has shown that there are likely to be difficulties in obtaining this goal.

Conclusion

A diagram showing the conformations of **5–7** is given as Figure 3. The ^{13}C NMR spectrum is consistent only with a single type *a* conformation, and the PES showed that the conformation occupied is a_1. In the diagram, nitrogen inversions are the diagonal equilibria and bicyclic ring tor-

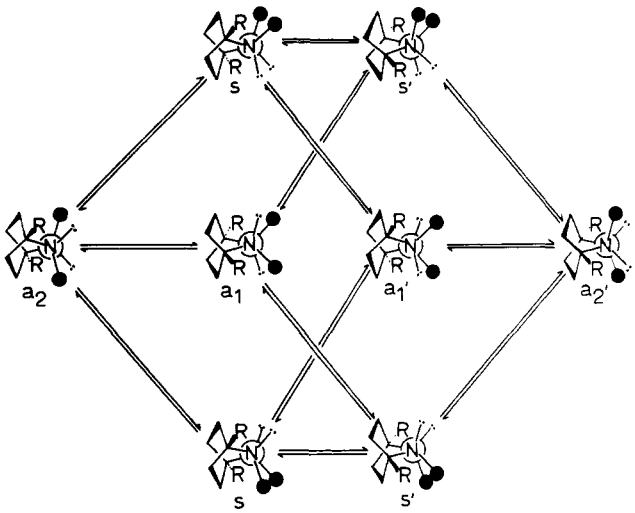


Figure 3. Diagram for conformational interconversions of **5–7** assuming N inversions and bicyclic torsions are not coupled.

sions the horizontal ones. The process observed by NMR is $a_1 \rightleftharpoons a'_1$. If a Figure 1A type of barrier occurred, the lowest energy pathway would be $a_1 \rightleftharpoons s' \rightleftharpoons a_2' \rightleftharpoons a_1$, with the $a_1 \rightleftharpoons s'$ half-planar transition state as the highest energy barrier. We argue that the $a_2 \rightleftharpoons s$ nitrogen inversion transition state is almost certainly lower in energy than the $a_1 \rightleftharpoons s'$ transition state, because there is less lone pair–lone pair interaction in the half-planar form. Since the bicyclic ring torsion $a_1 \rightleftharpoons a_2$ is surely far lower in energy than either nitrogen inversion, $a_1 \rightleftharpoons a_2 \rightleftharpoons s \rightleftharpoons s' \rightleftharpoons a_2' \rightleftharpoons a_1'$ (or $a_1 \rightleftharpoons a_2 \rightleftharpoons s \rightleftharpoons a_1$) is a pathway which could well be lower in energy. These pathways might well have the eclipsed conformation (the $s \rightleftharpoons s'$ transition state) or the $s \rightleftharpoons a_1'$ transition state, which is almost eclipsed, as the highest energy point in the pathway.

Although our activation parameter measurements do not prove which type of pathway is followed, as is argued in the discussion, they seemed more consistent with a nearly eclipsed type of highest barrier, which would correspond to a Figure 1B potential energy curve. If the Figure 1A potential barrier were correct for **5**, almost all of the 4.8 kcal/mol increase in $\Delta G^{\ddagger}$ for **5** compared with **9** would be attributable to lone pair–lone pair interaction, since the methyl–methyl interaction would be little larger for the half-planar transition state than in the a_1 conformation. If on the other hand, the potential barrier is of the Figure 1B type, the transition state would be the fully eclipsed syn molecule, approximately sp^3 hybridized at both nitrogens, and both lone pair and alkyl eclipsing interactions would contribute to the barrier.

Experimental Section

All compounds were purified by VPC (Varian-Aerograph A-90P) before ^{13}C NMR. For amines and hydrazines, a 15% XF-1150 column (⅜ in. × 10 ft, on 60–80 Chromosorb W) was employed and for hydrocarbons, 20% Apiezon J (⅜ in. × 10 ft, on 60–80 mesh Chromosorb W). Compounds **4–9** were prepared as previously described.[3a]

4-Acetoamido-4-methylcyclohexane-1-carboxylic Acid (13). 4-Methylcyclohex-3-ene-1-carboxylic acid[28] (35.98 g, 0.257 mol) and acetonitrile (32.47 g, 0.792 mol) were simultaneously added over a 20-min period to 130 ml of concentrated sulfuric acid, which was stirred and cooled in an ice bath. The mixture was allowed to warm to room temperature as it was stirred an additional 45 min and poured into 400 ml of an ice–water mixture, and after standing 15 min, the mixture was cooled, carefully basicified by addition of sodium hydroxide pellets, and extracted twice with 250 ml of ether each, which removes bicyclic lactone **14.** If the neutralization is carried out with sodium carbonate, over a 20% yield of **14** may be obtained from the ether extract, but little is obtained under these conditions. The aqueous phase is reacidified with concentrated HCl and continuously extracted (three portions, 8 h each) with ether, giving 7.36 g of a white solid consisting of a single diastereomer of **13** (mp 202–205 °C). Removal of ether gave 39.32 g of a sticky white solid containing mostly **13** and the hydroxy acid derived by hydrolysis of **14.** Much of the hydroxy acid could be removed by crystallization of this mixture from acetone, and washing the residues with hot ether removed more. An additional 5.53 g of **13** was obtained pure in this way, giving an isolated yield of 12.89 g (25%): NMR (Me_2SO-d_6, 60 MHz) δ 1.23 (s, 3 H), 1.81 (s, 3 H), 0.9–2.4 (m, 9 H), 7.08 (br s, 1 H), ca. 13 (very broad and concentration dependent, 1 H); ir (Nujol mull) 3365 (sharp), 3400–2300 (v broad), 1714 (strong); mass spectrum (calcd for $C_{10}H_{17}NO_3$, 199.120 84, *m/e* 199.120 65 (error 1.0 ppm).

1-Methyl-2-azabicyclo[2.2.2]octan-3-one (15). Acid **14** was esterified by refluxing 6.71 g with 150 ml of 0.27 M anhydrous hydrochloric acid–methanol solution in a flask fitted with a Soxhlet extractor filled with Linde 3A molecular sieves, giving 7.05 g (98.2%) of the methyl ester, mp 138–140 °C. A mixture of 5.77 g (27.1 mmol) of this methyl ester, 8.96 g (16.0 mmol) of commercial sodium methoxide, and 250 ml of digylme (distilled from lithium aluminum hydride) was refluxed under nitrogen for 8 h and distilled to dryness under vacuum-pump pressure with the aid of a heat gun. The residue was dissolved in 50 ml of water and extracted with 3 × 50 ml of chloroform. After drying and removal of chloroform, the last traces of diglyme were removed with a vacuum pump, and the sticky residue was sublimed to give 1.35 g (36%) of pure **15,** mp 134–130 °C (from ether), and a later crop of impure material (0.17 g): NMR ($CDCl_3$, 100 MHz) δ 1.29 (s, 3 H), 1.4–2.1 (m, 8 H), 2.5 (m, 1 H), 6.6 (br s, 1 H); ir (CCl_4) 3184, 2075, 2985, 2905, 2872, 1681 cm^{-1}; mass spectrum (calcd for $C_8H_{13}NO$, 139.099 71) *m/e* 139.099 76 (error 0.4 ppm).

1-Methyl-2-azabicyclo[2.2.2]octane. A solution of 1.356 g (9.75 mmol) of amide **15** in 150 ml of warm ether was added to a slurry of 2.21 g (58.3 mmol) of lithium aluminum hydride in 25 ml of ether, and the mixture was stirred magnetically and refluxed 13 h. After addition of 2.2 ml of H_2O, 2.2 ml of 15% sodium hydroxide, and 6.6 ml of H_2O, filtration, and distillation of the solvent, the residue was distilled: bp (94 mm) 120–103 °C; single peak by VPC, 833 mg (68%); NMR ($CDCl_3$, 100 MHz) 0.96 (s, 3 H), 1.21 (br s, 1 H), 1.4–1.84 (m, 9 H), 3.04 (br s, 2 H); ir (neat film) 2370, 2935, 2860, 1451, 1417 cm^{-1}; mass spectral peak match (calcd for $C_8H_{15}N$, 125.120 45) *m/e* 125.120 46 (error, 0.1 ppm).

1,2-Dimethyl-2-azabicyclo[2.2.2]octane (11). A solution of 0.5 g (4.0 mmol) of **15** in 25 ml of acetonitrile was treated with 3.5 g (43.2 mm) of 37% formalin and 1.57 g (25.0 mm) of sodium cyanoborohydride, and five drops of glacial acetic acid was added every 15 min for 1.5 h. Addition of NaOH pellets, extraction with 3 × 60 ml of pentane, drying over magnesium sulfate, and collection of the residue by VPC gave 243.4 mg (43.8%) of pure **11:** NMR ($CDCl_3$, 100 MHz) 0.94 (s, 3 H), 1.2–1.9 (m, 9 HO), 2.26 (s, 3 H), 2.74 (m, 2 H); ir (neat film) 2930, 2860, 2778 cm^{-1}; mass spectrum (calcd for $C_9H_{17}N$, 139.136 10) *m/e* 139.135 65 (error, 3.3 ppm).

2-Methyl-2-azabicyclo[2.2.2]oct-5-ene (16). A solution of 6.0 g (33.1 mmol) of 2-carboethoxy-2-azabicyclo[2.2.2]oct-5-ene[29] in 50 ml of ether was dropped into 2.5 g (66 mmol) of lithium aluminum hydride in 100 ml of ether, and the mixture was refluxed for 7 h. Work-up as for the reduction of **15** gave 2.46 g (60%) of colorless oil, bp (40 mm) 69 °C: NMR ($CDCl_3$) δ 1–2.1 (complex, 5 H), 2.23 (s, 3 H), 2.47 (br m, 1 H), 3.05 (dd, 9.4, 2.2 Hz, 1 H), 6.34 (complex, 2 H); ir no NH; mass spectrum (calcd for $C_8H_{13}N$, 123.104 80) *m/e* 123.104 97 (1.4 ppm error).

2-Methyl-2-azabicyclo[2.2.2]octane[30] (10). **16** was hydrogenated at atmospheric pressure over prereduced PtO_2 in pentane, and at 76% of **10** was isolated by preparative VPC from a mixture containing about 80% of the desired material. Spectral data: NMR ($CDCl_3$, 100 MHz) δ 1.3–2.2 (m, 9 H), 2.36 (s, 3 H), 2.46 (m, 1 H), 2.72 (m, 2 H); ir ($CDCl_4$) no NH, 2940, 2883, 2790 cm^{-1}; mass spectrum (calcd for $C_8H_{15}N$, 125.120 45) *m/e* 125.120 58 (1.1 ppm error).

5-*exo*-Methylbicyclo[2.2.2]oct-2-ene (18) was prepared from the exo ester by the method of Smith and Agosta,[31] and 5-*endo*-methylbicyclo[2.2.2]oct-2-ene (**17**) was obtained by the same series of

reactions in the endo ester. Both were oils[31] and purified by VPC. 2-Methylbicyclo[2.22]octane (**19**) was prepared by atmospheric pressure hydrogenation of **17** over 10% Pd/C in ether, and both **17** and **18** were reduced under the same conditions using deuterium gas to enable assignment of the ^{13}C NMR spectrum of **19;** all were purified by VPC and showed the expected spectral data.

***trans*-5,6-Bis(hydroxymethyl)bicyclo[2.2.2]oct-2-ene.** *trans*-5,6-Dicarboethoxybicyclo[2.2.2]oct-2-ene[32] [our bp (1.4–2 mm) 95–100 °C, in contrast to the reported[32] bp (0.5 mm) 122–124 °C] was reduced with lithium alumim hydride in refluxing tetrahydrofuran, giving a 78% yield of the diol: mp 72–73 °C (from ether); NMR ($CDCl_3$, 100 MHz), 0.8–1.8 (m, 6 H), 2.46 (m, 2 H), 3.09 (br t, 9 Hz, 1 H), 3.44 (m, 1 H), 3.56 (br d, 8 Hz, 2 H), 4.35 (br s, 2 H), 6.12 (br overlapping dd, 7, 7, 1 H), 6.37 (br overlapping dd, 7, 7, 1 H); ir ($CHCl_3$) 3626, 3346 (br), 2934, 2866, 1469 cm^{-1}; mass spectrum (calcd for $C_{10}H_{16}O_2$, 168.115 03) *m/e* 168.115 72 (4.1 ppm error).

***trans*-5,6-Dimethylbicyclo[2.2.2]oct-2-ene (20).[32]** The above diol (10.98 g, 65.3 mm) in 25 ml of pyridine was added dropwise over 2 h to a stirred, cooled solution of tosyl chloride (75.0 g, 0.394 mol) in 150 ml of pyridine and allowed to warm slowly to room temperature over 24-h period. The mixture was poured over 500.ml of ice and 50 ml of concentrated hydrochloric acid, and the mixture was extracted with 2 × 500 ml of chloroform. After removal of solvent and residual pyridine, crystallization from chloroform–ether (do not heat) gave 28.11 g (90%) of the bis(tosylate) (mp 126–130°). A mixture of 15.0 g (31.5 mmol) of the bis(tosylate) in 170 ml of tetrahydrofuran was added dropwise to a slurry of 5.0 g (132 mmol) of lithium aluminum hydride in 100 ml of THF, and the mixture was refluxed an additional 31 h. The usual basic work-up proved impossible due to foaming, so the LAH was quenched by addition of 20 ml of ethyl acetate, 5 ml of 15% aqueous sodium hydroxide, and 15 ml of H_2O. The gelatinous mixture proved infilterable, and 50 ml of concentrated HCl were added, and the organic phase was separated and combined with a 100 ml of ether wash of the aqueous phase. After drying over magnesium sulfate, distillation gave 1.03 g [bp (66 mm) 69–90 °C, 95% **20** by VPC] and 0.93 g [bp (66 mm) 90 °C, 70% **20** by VPC], total yield 38%. The substantial residue appeared to be largely half-reduced material. Purification was by VPC. Spectral data: NMR ($CDCl_3$, 100 MHz) δ 0.79 (3 H, d, J = 6 Hz), 0.99 (s, 3 H), 0.7–1.8 (m, 6 H), 2.15 (m, 2 H), 6.07 (br dd, 7, 7, 1 H), 6.34 (br dd, 7, 7, 1 H) (the previously reported[32] NMR describes the methyls as a doublet centered at δ 0.9; the spectrum at 60 MHz in benzene-d_6 looks somewhat closer to a doublet); ir (CCl_4) 3034, 2945, 2916, 2859, 1612; mass spectrum (calcd for $C_{10}H_{16}$, 136.125 20) *m/e* 136.125 32 (error 0.9 ppm).

***trans*-2,3-Dimethylbicyclo[2.2.2]octane[32c] (21)** was prepared by atmospheric pressure hydrogenation of 0.456 g of **20** in 25 ml of ether over 117 mg of 10% Pd/C. Filtration and removal of ether gave 0.44 g of a residue consisting of 78% **21** (by VPC peak ratios): NMR ($CDCl_3$, 100 MHz) δ 1.6–3.5 (m); ir ($CDCl_4$) 2950, 2930, 2895, 2865, 1470, 1377; mass spectrum (calcd for $C_{10}H_{18}$, 138.140 85) *m/e* 138.140 76 (0.7 ppm error).

^{13}C NMR Studies. Spectra were obtained on a Varian XL-100 spectrometer at 25.16 MHz and on a Bruker WH-270 at 67.92 MHz. All of the variable-temperature work was done in 5-mm tubes on the XL-100, using a variable-temperature assembly designed by Professor Paul Bender and a Varian 4540 controller. Temperatures were measured with a Doric DS-350 instrument (Cu-constantan thermocouple, digital read-out to 0.1 °C). The thermocouple was encased in a double-walled, solvent-filled 5-mm NMR tube, and the assembly was placed in the probe and equilibrated for 10 min before recording the temperature. The probe was allowed to equilibrate for at least 15 min at each temperature, the data were acquired, and the temperature was measured immediately afterward. We believe the quoted temperatures are accurate to ±1 °C.

To be practical in terms of instrument time, large substrate concentrations were necessary, and most experiments were run near 2 M (see Table II). At such high concentrations, viscosity broadening is rather pronounced at low temperatures. To test for the concentration effect on ^{13}C chemical shifts, we ran 1,1-dimethyl-2,2-dipropylhydrazine at 2.84 and 0.284 M concentration (deuterioacetone) and found less than 0.1 ppm shift for all four peaks. The spectral resolution was not less than 1.0 Hz per point in this work, and the accuracy of the chemical shifts is bounded by 1.0/25.16 = δ 0.04. Spectral simulations were carried out using a program utilizing the theory of Gutowsky and Holm[35b] written for the Wang 7208 by Professor H. W. Whitlock, plotted on a Wang 712, and compared with the experimental spectra visually. A transmission coefficient (κ)[33] of 1 was used for all compounds.[23]

Confidence limits in the slope and intercept were calculated equations of Bennett and Franklin[34] and propogated into the activation parameters. It is apparent that systematic errors in activation parameters can be present in DNMR results even where statistical error is low and that $\Delta S^{\ddagger}$ is affected the most, $\Delta H^{\ddagger}$ somewhat, and $\Delta G^{\ddagger}$ much less.[35a] Whenever possible, we used Yamamoto et al.'s[17] correction for T_2* and estimated the temperature dependence of $\Delta\nu$.[33]

Carbon NMR assignments were made using undecoupled spectra to count the attached protons and in some cases off-resonance decoupling. Some ambiguities are still present as indicated in Table IV.

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References and Notes

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Conformations of Saturated Phosphorus Heterocycles. IV. ^{1}H, ^{13}C, and ^{31}P Nuclear Magnetic Resonance Studies of Geometrical Isomers of 2-Z-4-Methyl- and 4-*tert*-Butyl-1,3,2-dioxaphospholanes

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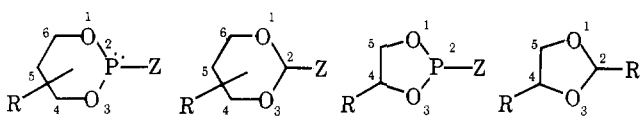
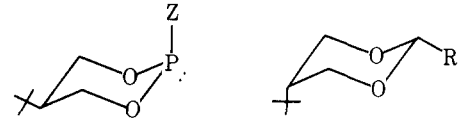
Abstract: The cis–trans stereoisomerism and conformations of a series of 2-Z-4-Me- and 2-Z-4-*tert*-butyl-1,3,2-dioxaphospholanes were studied by ^{1}H, ^{13}C, and ^{31}P NMR methods. For the 4-Me compounds (Z = Me_2N MeO, *t*-BuO, *t*-Bu, $PhCH_2$, and Ph), the trans/cis ratio regardless of Z was (65 ± 2)/(35 ± 2) at ambient temperatures corresponding to ΔG° = 0.4 kcal/mol. The trans/cis ratio was increased for the 4-*t*-Bu compounds (Z = MeO, Me_2N, *t*-Bu) with ΔG° = 0.8–1.0 kcal/mol. The greater thermodynamic stability of the trans isomer in these systems is directly opposite to the case for 2-Z-4-R-1,3-dioxanes in which the cis isomer is favored. This emphasizes the importance of the presence of the phosphorus heteroatom as found previously with the 2-Z-5-*tert*-butyl-1,3,2-dioxaphosphorinanes which have cis–trans thermodynamic stabilities opposite to those found for the analogous 1,3-dioxanes. The results of this work are reasonably well interpreted for each isomer in terms of two rapidly equilibrating half-chair conformers with 4-alkyl pseudoaxial or pseudoequatorial, although possible alternative explanations cannot be excluded. The cis isomers appear to be conformationally biased toward the form with 4-alkyl pseudoequatorial. The cis or trans geometry of a given isomer is easily assigned from ^{13}C or ^{31}P NMR spectroscopy alone. The ^{31}P resonance of the cis isomer appears in each case 2.4 to 7.4 ppm *downfield* from the trans isomer absorption, presumably as a result of the δ interaction of the 2-Z and 4-alkyl substituents. The cis and trans isomer assignments for the 4-Me compounds are made from ^{13}C spectra on the basis of the chemical shifts of the C-4, C-5, and C-4′ as influenced by the δ effect. The similarities of the 2-Z-4-R-1,3,2-dioxaphospholanes to other 1,3-dioxa and 1,3-dithia five-membered ring systems with P, As, or S at the 2 position are noted.

Over the past several years, there has been an increasing amount of interest in saturated heterocycles containing phosphorus and oxygen in five- and six-membered rings. The trivalent 1,3,2-dioxaphosphorinanes (**1**) and 1,3,2-dioxaphospholanes (**3**) are clearly analogous to the 1,3-dioxanes (**2**) and 1,3-dioxolanes (**4**). Differences in bond distances and angles imposed on such rings by substitution of phosphorus for carbon, however, might well be expected to affect the relative energies of cis or trans isomers and of their various conformers in important ways. Furthermore, in **1** and **3**, the presence of an electron lone pair on phosphorus will change the steric competition between the substituents at the 2 position and also result in vicinal interactions (between the oxygens and the substituents on the atom at the 2 position) different from those present in **2** and **4**. An example of the consequence of such effects is seen in the 2-Z-5-*tert*-butyl-1,3,2-dioxaphosphorinane series[1,2] (**1**, R = 5-*t*-Bu). For Z equal Cl, MeO, Ph, Me, and *i*-Pr, the cis isomer is the more stable form and populates almost entirely the conformer **5**. By contrast, the most stable conformer of the *less stable* isomer in the comparable 1,3-dioxane is **6**.[3] We have suggested[1,4] that the strong axial preference of Z in the 1,3,2-dioxaphosphorinanes is probably a result of more favorable vicinal interactions between the lone pairs on oxy-



1 **2** **3** **4**



5 **6**