be explained by altered local environments in the different reaction centers, because we have shown that solvent changes can modify the hyperfine splittings of bacteriochlorophyll and bacteriochlorins.[19] The agreement between calculated and observed values of ΔH for $P870^{\cdot+}$ alone does not distinguish between the slightly different dimeric models proposed by Norris et al.,[14,31] Boxer and Closs,[32] and Fong[28] for P870.

In the initial photoact of bacterial photosynthesis it is postulated that P870, donates, in less than 10 ps,[29] an electron to a nearby BPh to yield its anion radical[30] and $P870^{\cdot+}$. The latter is eventually reduced (in microseconds) by electron transfer from cytochrome c_2 which, in turn, may also function via a porphyrin radical.[21,33] The spin density profiles provided by ESR and ENDOR have, therefore, now allowed the electron distribution of the free radical species involved in the very first and last stages of cyclic electron transport in bacterial photosynthesis to be described in some detail. Because these radicals must be fixed in close proximity, the extent of overlap (or lack of it) between their electronic configurations must influence the rates of electron transfer between them.

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^{13}C NMR Studies of 9-Methyl-9-azabicyclo[3.3.1]nonane and Related Compounds

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Received March 19, 1976

Abstract: The ^{13}C NMR spectra for 9-methyl-9-azabicyclo[3.3.1]nonane (**1**) and 2-methyl-2-azaadamantane (**2**) were studied at low temperature. Comparison with the related hydrocarbons (N replaced by CH) reveals that the β carbons anti to the nitrogen lone pair are shifted upfield 1-2 ppm more than the syn carbons. Inversion barriers for **1** and **2** were determined by line shape analysis to be about 8.1 kcal/mol at −90 °C. 9-Dimethylamino-9-azabicyclo[3.3.1]nonane (**3**) showed no evidence for preferential line broadening to −132 °C, and must have a considerably lower barrier for nitrogen inversion.

Although considerable progress is being made in the interpretation of ^{13}C NMR chemical shifts, the sorting out of the various effects involved in molecules containing heteroatoms is a complex problem.[1] Reasonably consistent correlations were observed by Eggert and Djerassi[2] for a series of aliphatic amines when the observed chemical shifts were compared to those of the related hydrocarbons (N replaced by CH), and shift parameters were devised. Shift parameters which work for acyclic systems are known not to transfer successfully to cyclic ones, because of important conformational effects upon ^{13}C shifts. Several studies of carbon shifts of the most widespread class of cyclic amines, the piperidines, have appeared,[3-7] but these studies have not allowed answering a key question in the whole area of ^{13}C NMR of heteroatomic molecules, the size of the effect of lone pair configuration upon ^{13}C chemical shifts. We report here variable temperature studies on bi- and tricyclic piperidines in which nitrogen inversion is slow at low temperature, and in which both axial and equatorial lone pairs are present, allowing measurement of both the chemical shift changes with lone pair configuration and the activation parameters for nitrogen inversion in these systems.

Results

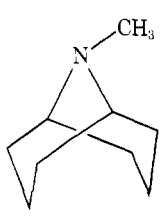
The NMR spectra for 9-azabicyclo[3.3.1]nonane derivatives

Table I. ^{13}C NMR Chemical Shifts of Some Bicyclo[3.3.1]nonyl Systems

Compd	Concn, M	Temp, °C	Chemical shifts, ppm from internal TMS					
			α^a	β^a	γ^a	Other		
1[e]	4.0[b]	+35	53.24	27.20	21.49	41.42 (Me)		
	0.4[c]	−78	53.02	27.08[d]	21.62	41.42		
				21.33 (2, 4)	21.33			
	0.4[c]	−118	52.74			41.32		
				32.24 (6, 8)	21.71			
2	1.6[b]	+35	53.83	33.41	28.94	41.88 (Me)	38.01 (10)	
				28.19	27.15			
	0.4[c]	−117	53.72			41.77	37.56	
				37.41	28.47			
3	2.9[b]	+34	49.89	29.04	21.12	45.43 (Me)		
	2.9[b]	−60	49.24	28.32	21.05	44.97		
	0.3[c]	−132	49.00	27.62	20.47	44.12		
				25.42 (2, 4)	22.56			
4	3.0[b]	+32	34.24			18.84 (Me)	26.79 (9)	
				34.56 (6, 8)	23.03			
				31.81 (2, 4)	28.83			
5	0.2[b]	+34	34.52			19.11 (Me)	39.10 (9)	39.65 (10)
				39.98 (6, 8)	29.16			
				31.99 (2, 4)	28.10			
6	0.8[b]	+36	30.65			43.24 (Me)	70.83 (9)	38.56 (10)
				37.95 (6, 8)	28.46			

[a] Positions listed are relative to position 9, a nitrogen atom for **1–3.** [b] In acetone-d_6. [c] Acetone-d_6 sample diluted with CF_2Cl_2. [d] Conformational broadening evident. [e] The room temperature ^{13}C NMR spectrum of **1** was reported by J. R. Wiseman and H. O. Krabbenhoft, *J. Org. Chem.*, **40,** 3222 (1975).

1–3 and analogues with the 9-aza atom replaced by a CH group (**4–6**) are reported in Table I. Nitrogen inversion be-



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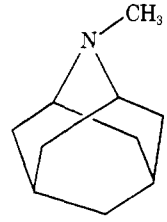

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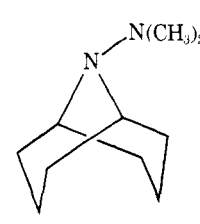

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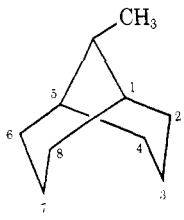

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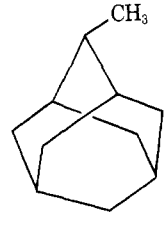

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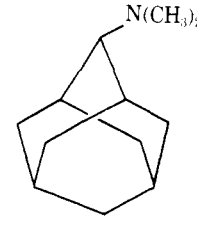

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comes slow on the NMR time scale at low temperatures for **1** and **2,** but not even broadening for slowing down of nitrogen inversion was observed for **3** down to −132 °C. Activation parameters for nitrogen inversion of **1** and **2** were calculated by line shape simulation of the β-carbon signals and are given in Table II.

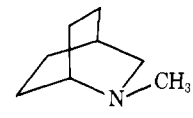
Table II. Activation Parameters for *N*-Methyl Inversion of **1** and **2**

	1	**2**
Temp range, °C	50	40
$\Delta G^{\ddagger}$ (temp, T_c)[a,b]	8.11 ± 0.04 (−90)	8.2 ± 0.13 (−90)
$\Delta G^{\ddagger}$ (25 °C)[a,b]	7.1 ± 0.3	7.8 ± 0.7
$\Delta H^{\ddagger}$[a,b]	9.7 ± 0.5	9.0 ± 1.3
$\Delta S^{\ddagger}$[a,c]	8.5 ± 2.5	4.0 ± 6.5

[a] Statistical error at 95% confidence level; transmission coefficient 1.0. [b] In kcal/mol. [c] In eu.

Discussion

(A) Chemical Shifts. Assignment of β carbons of **1** and **2** to the pairs with axial and equatorial lone pairs is easy, because of the large upfield shift known to occur when an axial methyl group is present. Comparison of the shifts for these carbons with the analogous ones of the hydrocarbon analogues **4** and **5** allows examination of the importance of lone pair configuration upon chemical shift. The shifts observed upon N for CH substitution appear in Figure 1, where it may be seen that both sets of β carbons are shifted upfield, and that a 1.8 ppm larger upfield shift is observed at the carbons with an equatorial lone pair (C_α–C_β bond antiparallel to the lone pair orbital) than at the ones with an axial lone pair (gauche bond orbital relationship) for **1,** while this difference is +1.0 ppm for **2.** Similar data for 2-methyl-2-azabicyclo[2.2.2]octane (**7**)[8] are included



7

to show how sensitive such differences are to structure. There is (probably; there remains an ambiguity in assignment of C_7 and C_8 of **7**) no such anti/gauche upfield shift difference for **7.** Bicyclic torsion of the bicyclic system of **7** undoubtably distorts the C_α–C_β lone pair alignments somewhat from the idealized values of 180 and 60° shown in Figure 1. Either the lone pair shift effect is extremely sensitive to the C_α–C_β lone pair dihedral angle, or (more likely in our opinion) the ^{13}C chemical shifts are sensitive enough to the small geometry changes which accompany N for CH substitution to significantly alter the configurational effect, even comparing the chair piperidine rings of **1** and **2** to the boat rings of **7.**

Small downfield shifts are observed at the β carbons in acyclic amines,[2] where conformations enforcing C_α-C_β lone pair overlap are not required, and also were observed at C_4 of **7**, where the conformation requires a nearly perpendicular $C_{c\alpha}$-C_β lone pair dihedral angle (actually, about 120° minus the torsional angle in the bicyclic system). Upfield shifts are observed when the N-C torsional angle is restricted to enforce C_α-C_β lone pair interaction. A slightly larger upfield shift (1–2 ppm) for piperidine carbons β to an equatorial lone pair compared to those β to an axial lone pair was observed. The magnitude of this effect is smaller than the axial *N*-alkyl upfield shift and in the same direction.

The 0.3 ppm γ carbon chemical shift difference in adamantane **5** is increased to 1.3 ppm in its amine analogue **2.** The rigid structure of **5** requires that the nitrogen lone pair C_α-C_β and C_γ-H bonds are nearly parallel and thus well situated for an interaction analogous to that suggested by Elliel, Grant, Wenkert, and co-workers[7] as being responsible for the antiperiplanar heteroatom upfield γ-shift effect. In contrast, the γ carbon chemical shift differences for **4** and **1** are only 0.5 and 0.4 ppm. The piperidine rings of bicyclo[3.3.1]nonane derivatives are well known to be rather flattened,[9] which would distort this orbital alignment.

The $C_{6,8}$ carbons of **3** appear 2.0 ppm upfield of those of the hydrocarbon **5,** an excellent example of the γ antiperiplanar heteroatom effect.[7] Even the δ carbon of **2** appears 1.6 ppm upfield of the corresponding carbon in **5,** showing that even longer-range heteroatom effects are easily detectable in some geometries.

(B) Nitrogen Inversion Barriers in 1 and 2. The nitrogen inversion barrier in *N*-methylpiperidine has not been measured[10] because the equatorial methyl conformation dominates (the axial conformation has recently been estimated to lie 1.35 to 1.77 kcal/mol higher in energy,[6b] although estimates based on rapid reactions give considerably larger estimates[6c,d]), and slowing of the ring reversal, a higher energy process,[11] is therefore the only conformational change which can be directly observed by NMR. Kessler and Leibfritz[12] and Riddell and Labaziewicz[13] have estimated nitrogen inversion barriers for *N*-methylpiperidine of 7.8–8.0 and 9.63 kcal/mol, respectively, but both groups appear to us to rather oversimplify the effects of α-heteroatom substitution on nitrogen inversion rates in arriving at these estimates.

The activation parameters observed for **1** and **2** agree within experimental error (see Table II), so the piperidine ring flattening which must be present in **1** cannot be a very important factor in determining the nitrogen inversion barrier. The previously "unpublished" ^{1}H NMR data for **1**,[14] $\Delta G^{\ddagger}(-80 \pm 10$ °C) = 9.5 ± 1.0 kcal/mol, do not agree with the barrier we determined, but the difficulties with obtaining quantitatively significant data for this compound by ^{1}H NMR are substantial. Comparison of the inversion barrier for the chair piperidine ring nitrogen of **1** and **2** with that of the boat piperidine ring nitrogen of **7**[8,15] is instructive. The $\Delta G^{\ddagger}(-90$ °C) for **7** is 1.8 kcal/mol below that of **1** and **2,** and $\Delta H^{\ddagger}$ is an even larger 2.4 kcal/mol less, in spite of the fact that **1** and **2** have an additional 1,3-diaxial CH, NMe interaction compared to **7,** so ground state strain considerations might lead one to expect a lower barrier. Presumably, the reason for the high barrier observed for **1** and **2** is the difficulty in expanding the C_1NC_5 angle in the transition state for nitrogen inversion because of the bi- or tricyclic ring system. The activation parameters observed for **1** and **2** are almost identical with those reported for *N*-methylpyrrolidine,[16] which is restricted to a smaller ring CNC angle at the transition state than is *N*-methylpiperidine.

(C) Hydrazine 3. Because of the rather high inversion barrier observed for **1** and **2,** and the increase in nitrogen inversion barrier caused by having an attached nitrogen,[8] we expected

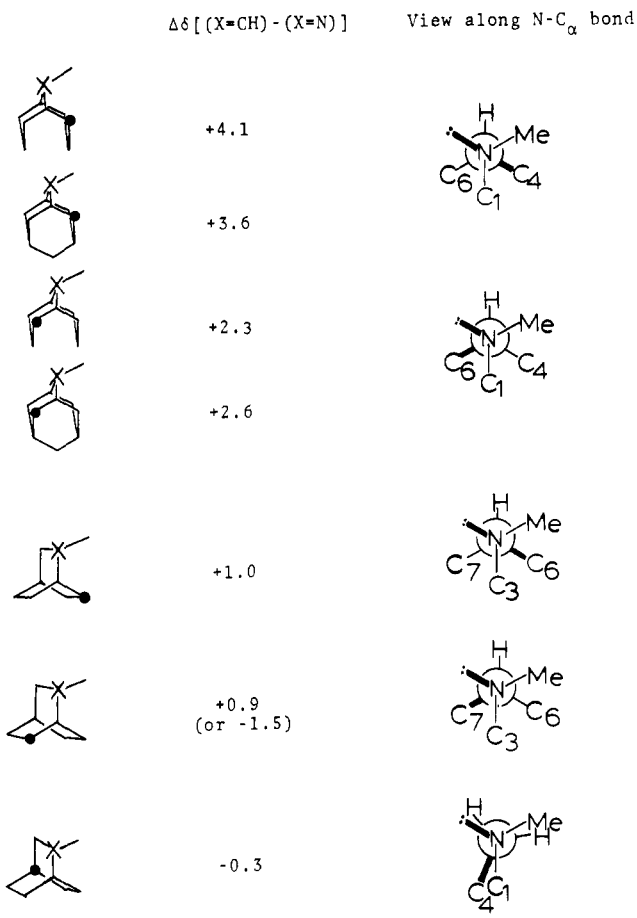
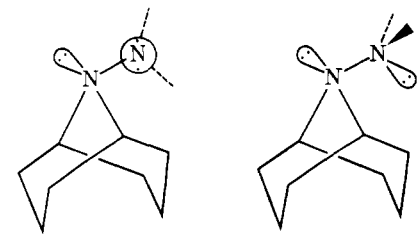


Figure 1. Chemical shift differences at the β carbons for substitution of N for CH in **1, 2,** and **7.** (A positive entry indicates an upfield shift for the nifrogen-containing compound.) Low temperature X=N spectra have been compared with room temperature X=CH spectra, which will cause positive increments of about 0.4 ppm independent of other factors.

little trouble in observing the β carbon signal of **3** separate into $C_{2,4}$ and $C_{6,8}$ peaks at low temperature, just as for **1** and **2.** To our surprise, we could not even detect preferential broadening of the β-carbon signal all the way down to −132 °C, the lowest temperature at which we were able to keep **3** in solution. Our inability to observe slowing of N_9 inversion is not caused by an inherently small $\Delta\delta(C_{2,4}$-$C_{6,8})$, because of the substantial (6 ppm) shift difference at these positions in **6;** an axial dimethylamino group causes substantial upfield shifts. We therefore conclude that we seriously underestimated the inversion barrier for **3** in the above considerations.

1-Dimethylaminopiperidine, like other 1,1-cycloalkyl and acyclic hydrazines, exists in a conformation with gauche lone pairs, as is shown by the low lone pair–lone pair splitting in its photoelectron spectrum[17] of 0.05 eV. If **3** were in this N-N bond rotamer, there would be serious *N*-methyl-β-methylene interactions (see **3a**), which could be relieved by N-N rotation to conformer **3b,** with a lone pair–lone pair dihedral angle of



3a **3b**

about 180°, and an expected PE splitting of 2.3 eV.[17] The consequent increase in lone pair–lone pair interaction should

destabilize **3b** relative to **3a**, and it was by no means obvious to us whether the steric destabilization of **3a** or the electronic destabilization of **3b** would be more important.

The PE spectrum of **3** shows peaks at 7.53, 8.42, and ca. 9.5–9.6 eV (the latter overlapping seriously with the onset of the σ ionization band). The relative sizes of the 7.53 and 8.42 eV peaks are about 2:1. We interpret these data as indicating that both conformations **3a** (the lone pair–lone pair splitting of 0.9 eV is larger than for dimethylaminopiperidine, but the flattening at N_9 expected to result from the serious steric interaction in **3a** would raise this separation even if the lone pair–lone pair dihedral angle was the same;[17] the angle might also be different) and **3b** (splitting of about 2 eV) are comparably populated. This requires that the IP_1 peaks for both *conformations be unresolved, as is frequently the case.*[17] Apparently the steric destabilization of **3a** and the electronic destabilization of **3b** are of comparable importance, and the nitrogen inversion barrier is lowered substantially by these factors.[25]

Experimental Section

9-Methyl-9-azabicyclo[3.3.1]nonane (1) was prepared by Wolf-Kishner reduction of the 3-keto compound, pseudo-pelletierine,[18] a reaction reported[19] without any details. A mixture of 60.34 g (0.914 mol) of 85% KOH pellets and 750 ml of diethylene glycol was heated and stirred in a 2 l. flask equipped with a reflux condenser and distillation head until solution was complete, and after cooling to 50 °C, 42.12 g (0.842 mol) of hydrazine hydrate and 36.13 g (2.36 mol) of pseudo-pelletierine were added. The mixture was heated for 2 h, while most of the excess water and hydrazine distilled off and was discarded; then the mixture was heated with a Wood's metal bath at 230 °C for 3 h. After cooling to room temperature, the distillate and residue were combined with 750 ml of H_2O, and extracted with 3 × 250 ml portions of ether. Extraction of the combined layers with 100 ml of water, drying over $MgSO_4$, and concentration gave an oil, which sublimed to give 28.09 g (85%) of **1**, mp 53–57 °C (lit.[20] mp 55–58 °C), in which no extraneous peaks were observed by ^{13}C NMR.

2-Methyl-2-azaadamantane (2) was prepared from the 2-tosylate[21] by hydrolysis[22] and reductive methylation. A mixture of 0.55 g of the tosylate, 0.37 g of phenol, and 3 ml of 48% HBr was heated 5 h at 100–115 °C, basified, and extracted with ether, and the organic layer was dried, concentrated, and sublimed, giving 0.18 g (1.29 mmol, 69%) of the free amine, which was mixed with 1 ml of formalin (12.5 mmol), 0.75 g of $NaBH_3CN$ (10 mmol of 83% pure Aldrich material), and five drops of acetic acid in 25 ml of ether and stirred for 18 h. Addition of 15% NaOH, separation of the ether layer, drying over $MgSO_4$, and concentration gave **2**,[21] which was isolated by preparative VPC.

2-Dimethylamino-2-azaadamantane (3) was prepared as previously described.[17b]

9-Methylenebicyclo[3.3.1]nonane. A solution of 6.3 ml of 1.16 M *n*-butyllithium in hexane was added dropwise by syringe through a septum cap to 2.59 g (7.24 mmol) of (methyl)triphenylphosphonium bromide in 30 ml of dry THF, and after stirring at ambient temperature for 90 min, a solution of 1.0 g (7.3 mmol) of 9-ketobicyclo-[3.3.1]nonane in 10 ml of dry THF was added dropwise to the red ylide solution. After 17 h of reflux, 25 ml of ether was added, the mixture was extracted with 100 ml of H_2O, the aqueous layer was reextracted with 50 ml of ether, and the combined organic layers were extracted twice with 100 ml each of water. Drying and distillation to 50 ml, removal of triphenylphosphine oxide by filtration, and concentration gave 0.45 g (45%) of a low-melting, foul-smelling solid. Spectral data: NMR ($CDCl_3$) δ 1.4–2.2 (m, 12 H), 2.44 (m, 2 H), 4.56 (s, 2 H); ir (CCl_4) no OH or CO, 1651, 883 cm^{-1}; empirical formula $C_{10}H_{16}$ established by ms.

9-Methylbicyclo[3.3.1]nonane (4) was prepared by catalytic reduction of the above olefin at atmospheric pressure, over prereduced PtO_2 in pentane in 96% yield, mp 90–91 °C (after sublimation, 1.0 mm, room temperature). Spectral data: NMR ($CDCl_3$) δ 1.03 (d, 3 H), 1.25–2.10 (m, 15 H); ir (CCl_4) no OH, Co, or C=C, 878 cm^{-1}; empirical formula $C_{10}H_{18}$, established by ms.

2-Methyladamantane (5), mp 146–148 °C (lit.[23] mp 144–146 °C), was prepared by catalytic hydrogenation of the olefin.

2-Dimethylaminoadamantane (6). A mixture of 750 mg (5 mmol) of 2-adamantanone, 4.5 g of 25% aqueous dimethylamine (25 mmol), and 630 mg (8.3 mmol) of sodium cyanoborohydride in 25 ml of acetic acid was stirred, and 10 drops of acetic acid were added, followed 30 min later by 20 more drops. After 19 h, 10 ml of 15% sodium hydroxide was added, and the two-phase mixture was extracted with pentane. After concentration, Kügelrohr distillation gave 0.46 g (47%) of **6**, which is an oil at room temperature. Final purification was by VPC. Spectral data: NMR ($CDCl_3$) δ 2.21 (s), 1.3–2.3 (complex m); ir, no NH or C=O; empirical formula $C_{12}H_{21}N$, established by ms.

^{13}C NMR measurements were performed and analyzed using the techniques previously described.[8]

Acknowledgments. We thank the National Science Foundation for financial support of this work, both through a research grant and the Major Instrument program. We thank Professor H. Stetter for generously supplying the precursor of **2**.

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(25) NOTE ADDED IN PROOF. As expected from the above discussion, 9-amino-9-azabicyclo[3.3.1]nonane, which lacks the *N*-methyl groups of **3**, has an N_9 inversion barrier easily measured by ^{13}C NMR. We obtained activation parameters: $\Delta G^{\ddagger}(-90\ °C) = 9.19 \pm 0.04$ kcal/mol, $\Delta G^{\ddagger}(25\ °C) = 9.9 \pm 0.3$ kcal/mol, $\Delta H^{\ddagger} = 8.6 \pm 0.5$ kcal/mol, $\Delta S^{\ddagger} = -3.2 \pm 2.5$ eu.