and 1,2 addition had all occurred to an appreciable extent. No evidence for the presence of vinylidene unsaturation was found.

Bis(2,2,6,6-tetramethyl-3,5-heptanediono)nickel(II)–Diisobutylaluminum Chloride Catalyzed Polymerization of Butadiene. Butadiene, 202 g (3.74 moles), was distilled into the reactor which contained a solution of 0.425 g (1.00 mmole) of bis(2,2,6,6-tetramethyl-3,5-heptanediono)nickel(II) in 1100 ml of dry deoxygenated perchloroethylene. The red-violet solution was then warmed to 75°, and ethylene was charged until the total pressure was 130 psig. Diisobutylaluminum chloride, 1.2 ml (6.0 mmoles), was then charged. The resulting mixture, orange in color, was then stirred for 30 min with no temperature rise or ethylene pressure drop noticeable. The temperature was then raised to 84° and maintained there for another 30 min before the reaction was terminated in the usual manner.

Distillation afforded 121 g of unreacted butadiene. No C$_6$ dienes were present in the product mixture. A major portion of the solvent was then removed *in vacuo* and the residual solution was treated with 1 l. of methanol, causing a polymer fraction to separate. The polymer was isolated and dried *in vacuo*, affording 68 g of a syrupy mass. The infrared spectrum of the material indicated that it was predominantly *trans*-1,4-polybutadiene.

Codimerization of Ethylene and Butadiene with a Catalyst Derived from Bis(2,2,6,6-tetramethyl-3,5-heptanediono)nickel(II), Triphenylphosphine, and Diisobutylaluminum Chloride. Butadiene, 97 g (1.80 moles), was distilled into the reactor, which contained a solution of 0.524 g (2.0 mmoles) of triphenylphosphine and 0.425 g (1.0 mmole) of bis(2,2,6,6-tetramethyl-3,5-heptanediono)nickel(II) in 1100 ml of dry deoxygenated perchloroethylene. The stirred mixture was then warmed to 63° and ethylene was charged until the total pressure was 97 psig. Diisobutylaluminum chloride, 1.2 ml (6.0 mmoles), was then added and the mixture was stirred at 63–68° for 1 hr before the reaction was terminated in the usual manner.

Distillation of the product mixture afforded 36 g of C$_4$ olefins consisting of butadiene (80%), 1-butene (17%), *trans*-2-butene (2%), and *cis*-2-butene (1%), as determined by vpc analysis.

The C$_6$ fraction consisted of a 72-g mixture of 3-methyl-1,4-pentadiene (12%), 1,4-hexadiene (71%, *trans*:*cis* = 3.7), and 2,4-hexadienes (17%).

Preparation of Bis(tri-*n*-butylphosphine)nickel(II) Chloride. The compound, prepared by the method of Jensen[38] in 80.5% yield from nickel chloride hexahydrate and tributylphosphine, exhibited mp 46–47° (lit.[38] mp 48–49°).

Preparation of Bis(2,2,6,6-tetramethyl-3,5-heptanediono)nickel(II). The compound was prepared by the method of Cotton and Fackler[39] by hydrolysis of the analogous copper(II) chelate and reaction of the thus purified dipivaloylmethane with nickel acetate. The yield of material, mp 219.5–222.6° (lit.[39] mp 217–221°, no yield given), was 15% based on the copper chelate.

Acknowledgment. We are indebted to Dr. R. C. Ferguson for his aid in the interpretation of some of the nmr and infrared spectra, and to the Analytical Division of the Elastomer Chemicals Department, Du Pont, for many of the analyses reported herein.

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(38) K. A. Jensen, *Z. Anorg. Chem.*, **229**, 265 (1936).

(39) F. A. Cotton and J. P. Fackler, Jr., *J. Am. Chem. Soc.*, **83**, 2818 (1961).

The Conformational Rivalry between the Nonbonding Electron Pair and the Proton on Nitrogen

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Abstract: Nuclear magnetic resonance and infrared evidence indicate that piperidine exists predominantly, but not completely, in the isomeric form with the lone pair equatorial. The nmr results are independent of any special effects of concentration or solvent.

The question of the steric requirements of a nonbonding electron pair relative to the requirements of a proton was perhaps considered first by Barton and Cookson[3] and subsequently in detail by numerous authors.[4] Although originally there was some controversy concerning the relative sizes of the lone pair and the methyl group,[5] little doubt remains that the latter is considerably larger.[6,7] A general consensus has developed in support of the contention that the proton is qualitatively larger than the lone pair.[7,8] By means of dipole-moment and thermodynamic calculations on piperidine, piperazine, and N-methylpiperazine, Allinger, *et al.*,[7] obtained an energy difference of 0.46 kcal/mole between the lone pair and the proton on nitrogen, with the proton being the larger. Since almost all previous work[8] has involved either highly substituted derivatives or polycyclic analogs of piperi-

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(1) (a) Supported in part by the Petroleum Research Fund, administered by the American Chemical Society (Grant 487-G1), and the National Science Foundation (Grant GP-6611), to whom the authors are indebted. (b) This work was communicated in part; see J. B. Lambert and R. G. Keske, *J. Am. Chem. Soc.*, **88**, 620 (1966).

(2) National Science Foundation Undergraduate Research Participant, 1965–1967.

(3) D. H. R. Barton and R. C. Cookson, *Quart. Rev.* (London), **10**, 44 (1956).

(4) For a review of the literature of this subject, see F. G. Riddell, *ibid.*, in press.

(5) M. Aroney and R. J. W. Le Fèvre, *J. Chem. Soc.*, 3002 (1958); M. J. Aroney, C.-Y. Chen, R. J. W. Le Fèvre, and J. D. Saxby, *ibid.*, 4269 (1964).

(6) The "larger" of two groups involved in a conformational rivalry by dent of attachment to a common atom in an otherwise unsubstituted, saturated six-membered ring is operationally defined as that group which preferentially assumes the equatorial position. Such an orientation may not directly reflect the relative sizes of the groups as measured, for example, by van der Waals radii. See E. L. Eliel, *Angew. Chem. Intern. Ed., Engl.*, **4**, 761 (1965), for a discussion of this point.

(7) N. L. Allinger, J. G. D. Carpenter, and F. M. Karkowski, *Tetrahedron Letters*, 3345 (1964); *J. Am. Chem. Soc.*, **87**, 1232 (1965).

(8) T. M. Moynehan, K. Schofield, R. A. Y. Jones, and A. R. Katritzky, *Proc. Chem. Soc.*, 218 (1961); *J. Chem. Soc.*, 2637 (1962); A. R. Katritzky, *Record Chem. Progr.*, **23**, 223 (1962); R. J. Bishop, L. E. Sutton, D. Dineen, R. A. Y. Jones, and A. R. Katritzky, *Proc. Chem. Soc.*, 257 (1964); N. W. J. Pumphrey and M. J. T. Robinson, *Chem. Ind.* (London), 1903 (1963); M. J. Aroney, C.-Y. Chen, R. J. W. Le Fèvre, and A. N. Singh, *J. Chem. Soc., Phys. Org.*, 98 (1966); P. J. Brignell, A. R. Katritzky, and P. L. Russell, *Chem. Commun.*, 723 (1966); E. L. Eliel and M. C. Knoeber, *J. Am. Chem. Soc.*, **88**, 5347 (1966).

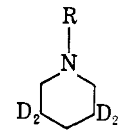
dine, the present study examines, with one exception, only unsubstituted piperidine and its N-alkyl derivatives. The spectroscopic methods used herein avoid the danger of obtaining misleading conclusions based on experimental variables that must be of the highest accuracy in order to be significant, but which are still quite sensitive to substrate purity. Furthermore, the spectroscopic methods permit the use of a wide range of experimental conditions, in particular that of solvent, thus assuring the generality of the conclusions.

Chemical-Shift Evidence

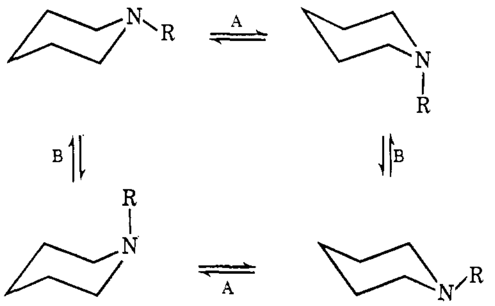
The chemical-shift difference between an axial and an equatorial proton attached to the same carbon atom on a six-membered ring is generally 25–30 Hz at 60 MHz, in the absence of substituent or heteroatom perturbations.[9] A small, isotropic substituent at the equatorial site of an adjacent atom will have little effect on δ_{ae}, since it is almost equivalently positioned with respect to both protons.[10] Most other types of substitution will have an affect on δ_{ae}, so our systems contain at most the single substituent. A heteroatom that is γ to a geminal proton pair rarely perturbs δ_{ae}.[11] For this reason, $\delta_{ae}(\gamma)$ serves as a control; it is independent of the heteroatom but is still sensitive to conformational effects. A β heteroatom appears to influence δ_{ae} somewhat,[12] but the present studies are not concerned with this particular effect. Finally, an α heteroatom influences δ_{ae} from at least three sources: (1) changes in the geometry of the ring with respect to that of cyclohexane; (2) substituents on the heteroatom; and (3) anisotropic magnetic properties of the heteroatom. For piperidine, the second and third sources are both important since the lone pair may be thought of either as a substituent or as an actual part of the nitrogen atom[7] that confers considerable anisotropy.

Hamlow[13] and Bohlmann[14] established that the chemical-shift difference between geminal protons adjacent (α) to nitrogen in ring-frozen systems is enhanced to 50–60 Hz when the lone pair is axial. This enhancement, the causes of which have been discussed elsewhere,[13] is associated with a pronounced upfield shift of the axial proton, which is *anti*-coplanar to the lone pair. Hence, an isomer with an equatorially oriented lone pair would not exhibit this enhancement. The assignment of the position of the lone pair in piperidine could thus in theory be made directly by examination of $\delta_{ae}(\alpha)$.

In order to avoid coupling between the α and the β protons, it was necessary to synthesize piperidine derivatives deuterated in the β positions (I–III). At room temperature, the ring protons of I–III give deuterium-broadened singlets, since ring inversion is nmr fast (Figure 1). The axial–equatorial differentiation occurs reversibly upon cooling. At −85°, both the α and the γ protons give AB spectra from which the respective δ_{ae} may be readily calculated. At these temperatures, ring inversion (process A) is nmr slow, but nitrogen inversion (process B) is still fast.



I, R = H
II, R = CH_3
III, R = t-C_4H_9



The values of δ_{ae} and J_{ae} are listed in Table I. $\delta_{ae}(\alpha)$ for N-methylpiperidine ranges from 56.5 to 66.1 Hz; that of N-*t*-butylpiperidine from 59.8 to 64.8 Hz. These enhanced values are consonant with a model in which the axial-lone-pair isomer predominates, as should be the case for all N-substituted piperidines.[15] $\delta_{ae}(\alpha)$ for piperidine itself, however, ranges from 26.1 to 32.4 Hz. This "normal" value indicates that the proton, rather than the lone pair, must occupy the axial position in the predominant isomer. The magnitude of $\delta_{ae}(\gamma)$ is "normal" for both the substituted and the unsubstituted cases. The variations with solvent are similar for all these systems, so they cannot have a conformational origin. Since protonation on nitrogen removes the lone pair, $\delta_{ae}(\alpha)$ should decrease substantially for II and III, with little effect in the case of I,

Table I. The Chemical-Shift Difference between Geminal Protons at the α and the γ Positions of Piperidines

R	Solvent	$\delta_{ae}(\alpha)$, Hz	$J_{ae}(\alpha)$, Hz	$\delta_{ae}(\gamma)$, Hz	$J_{ae}(\gamma)$, Hz
H	Methanol-d_4	26.1 ± 1.0	11.9 ± 0.4	24.8	13.1
	Cyclopropane	27.5	10.2	...	...
	CH_2Cl_2	29.0	12.3	26.9	13.4
	Toluene-d_8	32.4	11.2	29.4	12.4
CH_3	Methanol-d_4	56.5	11.4	31.1	12.9
	Cyclopropane	63.5	11.2	...	...
	CH_2Cl_2	61.4	11.2	34.4	13.1
	Toluene-d_8	66.1	11.0	39.4	12.9
t-C_4H_9	Methanol-d_4	59.8	10.7	31.7	12.6
	Cyclopropane	63.4	10.5	...	...
	CH_2Cl_2	64.8	11.4	...	...
	Toluene-d_8	63.8	10.2	33.3	11.3

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[9] F. A. L. Anet, M. Ahmad, and L. D. Hall, *Proc. Chem. Soc.*, 145 (1964); F. A. Bovey, F. P. Hood, III, E. W. Anderson, and R. L. Kornegay, *ibid.*, 146 (1964); *J. Chem. Phys.*, 41, 2041 (1964); F. A. L. Anet and M. Z. Haq, *J. Am. Chem. Soc.*, 87, 3147 (1965).

[10] L. M. Jackson, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, N. Y., 1959, pp 115–119.

[11] We have, however, observed substantial γ effects on δ_{ae} in protonated pentamethylene selenide and telluride.

[12] R. K. Harris and R. A. Spragg, *Chem. Commun.*, 314 (1966).

[13] H. P. Hamlow, S. Okuda, and N. Nakagawa, *Tetrahedron Letters*, 2553 (1964).

[14] F. Bohlmann, D. Schumann, and H. Schulz, *ibid.*, 173 (1965); F. Bohlmann, D. Schumann, and C. Arndt, *ibid.*, 2705 (1965).

[15] It is important to establish that the piperidine systems exist in nearly perfect (cyclohexane) chairs. The room-temperature spectrum of piperidine-4,4-d_2 was analyzed as an AA′BB′ system. The ratio of the average $^3J_{trans}$ to $^3J_{cis}$ was found to be 2.09. Such a value is diagnostic for the perfect chair. For the basis of this analysis, see J. B. Lambert, *J. Am. Chem. Soc.*, 89, 1836 (1967).

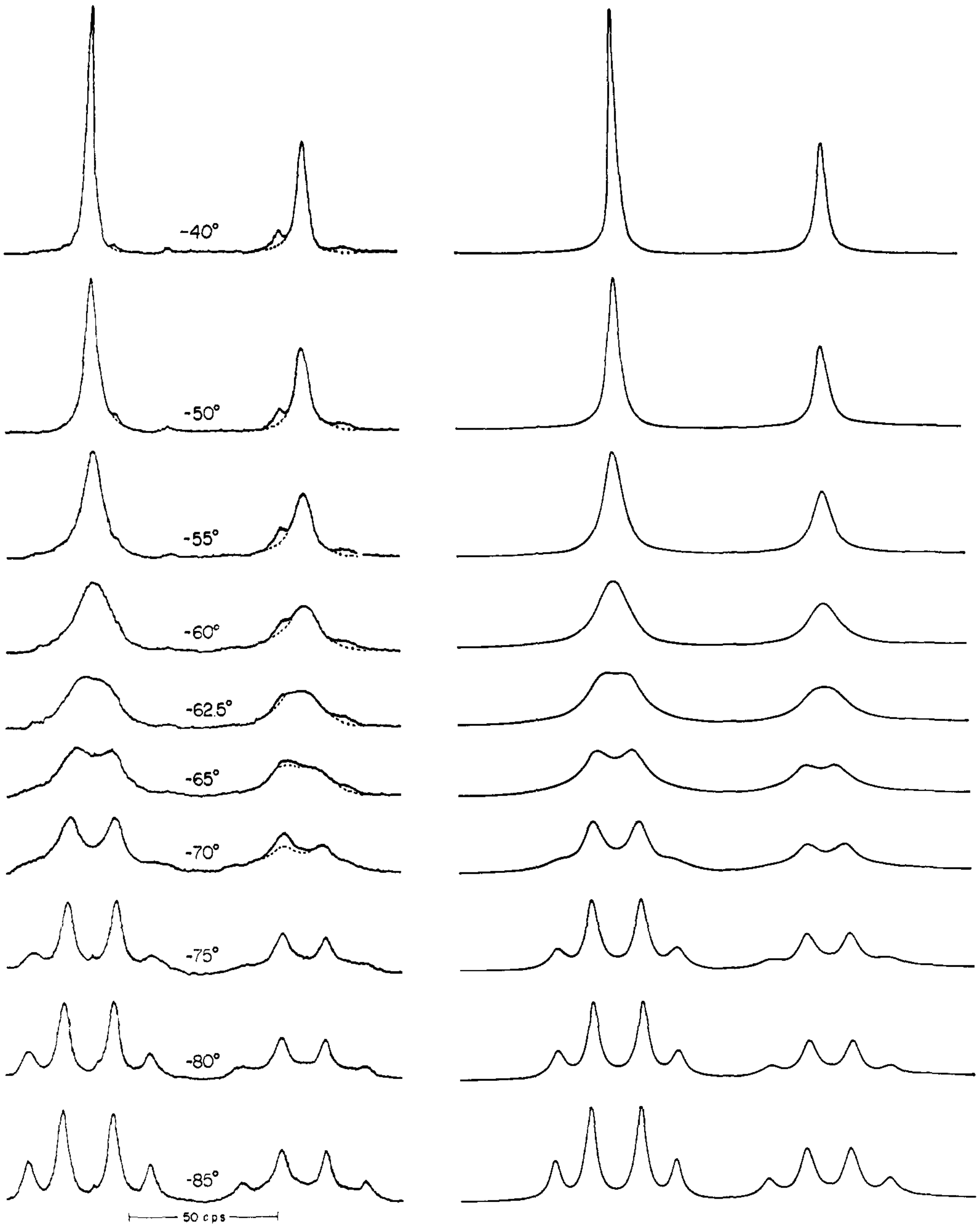


Figure 1. The 60-MHz spectrum of piperidine as a function of temperature. The experimental set of spectra is on the left. Since the field increases from left to right, the resonances of the α protons fall at the left of each spectrum. Apparent impurities near the resonances of the γ protons arise from incomplete deuteration at the β positions. Spectral data are given in Table IX.

Table II. The Effect of Protonation on Geminal Chemical-Shift Differences in Piperidines

	Gegenion	Solvent	$\delta_{ae}(\alpha)$, Hz	$J_{ae}(\alpha)$, Hz	$\delta_{ae}(\gamma)$, Hz	$J_{ae}(\gamma)$, Hz
$^{+}\mathrm{NH}_2$	Cl^-	$\mathrm{CD_3OD}$	>21.9[a]	13.1	16.1	13.3
	$\mathrm{FSO_3}^-$	$\mathrm{FSO_3H\text{-}SO_2}$	28.1	12.1	20.1	13.5
$^{+}\mathrm{NHCH}_3$	Cl^-	$\mathrm{CD_3OD}$	26.5	12.0	17.6	13.7
	$\mathrm{FSO_3}^-$	$\mathrm{FSO_3H\text{-}SO_2}$	35.8	12.4	22.6	14.2
$^{+}\mathrm{NH}\text{-}t\text{-}\mathrm{C_4H_9}$	Cl^-	$\mathrm{CD_3OD}$	38.5	12.0	16.7	13.3
	$\mathrm{FSO_3}^-$	$\mathrm{FSO_3H\text{-}SO_2}$	47.8	12.3	>25.1[a]	13.5
$^{+}\mathrm{NHC_6H_5}$	$\mathrm{FSO_3}^-$	$\mathrm{FSO_3H\text{-}SO_2}$	9.5	12.7	20.8	14.3

[a] Because of solvent overlap, only lower limits could be set in these cases.

in which the lone pair is equatorial. Indeed, $\delta_{ae}(\alpha)$ for II or III halves, but that of I remains essentially unchanged with protonation (Table II). Furthermore, $\delta_{ae}(\gamma)$, though lowered slightly, is approximately the same for all the protonated species. The decreased though still not "normal" value of 47.8 Hz for III-H$^+$ in sulfur dioxide may be due to incomplete protonation or, more likely, to a direct substituent effect. The anisotropic properties of the phenyl group serve to decrease $\delta_{ae}(\alpha)$ considerably; the normal value of $\delta_{ae}(\gamma)$

indicates that the effect must derive solely from the nature of the substituent, and not from a change in the ring conformation. Consideration of $\delta_{ae}(\alpha)$ and $\delta_{ae}(\gamma)$ for the protonated and unprotonated forms of I–III thus gives a qualitatively complete picture of both the location of the substituents on nitrogen and the conformation of the ring as a whole.[15,16]

Solvent Considerations

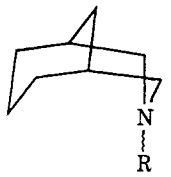
Since changes in medium are known to affect the conformational free energy of the hydroxyl and the amino groups,[17] it is important to determine the extent to which our experimental conclusions are dependent on solvent conditions. Low-temperature nmr experiments were performed with methanol-d_4, cyclopropane, methylene chloride, and toluene-d_8 (Table I). Although a modest effect is evident, there is a parallelism of behavior not only for all three cases (I–III), but also for both $\delta_{ae}(\alpha)$ and $\delta_{ae}(\gamma)$. For this reason, the effect probably does not derive from a conformational origin.

A wider range of solvents is not possible, because δ_{ae} must be measured at extremely low temperatures. Pertinent information, however, may also be obtained from the room-temperature spectra. The averaged position of the γ protons at room temperature is approximately the same for I and II. The upfield shift of the α-axial protons in II[18] generates an over-all upfield shift in the averaged position of the α protons with respect to that of I. Therefore, the distance between the α and the γ singlets ($\Delta\delta = \bar{\delta}_\gamma - \bar{\delta}_\alpha$) at room temperature (Figure 1) gives a direct measure of the extent to which the α-axial protons have been shifted upfield. The value of $\Delta\delta$ should be much smaller for II (axial lone pair) than for I (equatorial lone pair, no upfield shift of the α-axial protons). Any radical change in conformation should be detected by corresponding changes in $\Delta\delta$. As can be seen in Table III, $\Delta\delta$ remains close to 72 Hz for piperidine and 55 Hz for N-methylpiperidine over quite a wide variety of solvents. In particular, benzene (the dipole-moment solvent) and carbon tetrachloride offer no evidence for a change in conformation.

Table III. The Solvent Variation of $\Delta\delta = \bar{\delta}_\gamma - \bar{\delta}_\alpha$ for Piperidine and N-Methylpiperidine

Solvent	$\Delta\delta$(Piperidine), Hz	$\Delta\delta$(N-Methylpiperidine), Hz
Methanol-d_4	71.2 ± 0.6	55.9
Toluene-d_8	70.7	54.3
Methylene chloride	74.0	55.6
Cyclopropane	. . .	53.0
Carbon tetrachloride	73.5	52.9
Benzene	72.6	55.5
Dimethylformamide	. . .	53.7
Chloroform	74.9	56.2
20% Methanol–water	73.5	. . .

A different tack to avoid the limitations of low temperatures may be followed by examination of the 3-azabicyclo[3.3.1]nonane system (IV and V), in which the piperidine ring has been frozen into a single-chair conformation by the bicyclic constraint. The β,β'-diaxial substituents (β refers to the position with respect to the nitrogen atom, as though the ring were a substituted piperidine) will reduce the value of $\delta_{ae}(\alpha)$.[10] The coupling of the β,β'-diequatorial protons with the α protons is negligible. For the unsubstituted case IV, $\delta_{ae}(\alpha)$ is less than 5 Hz, a decrease, presumably caused by the β,β'-diaxial substituents, of about 20–25 Hz from I. For the methyl derivative V, $\delta_{ae}(\alpha)$ is about 40 Hz, a decrease also of about 20–25 Hz from II. Thus, since $\delta_{ae}(\alpha)$ is so much larger for V, there probably is a change in the position of the lone pair from equatorial to axial in going from IV to V. The ring-frozen system V permits a complete study of the effect of solvent on $\delta_{ae}(\alpha)$ (Table IV). Again, we find that $\delta_{ae}(\alpha)$ is only very modestly dependent on solvent, so that the conformational conclusions are not affected by the use of a particular solvent system. Protonation of the methyl derivative, with concomitant removal of the lone pair, expectedly reduces the value of $\delta_{ae}(\alpha)$ to 21.6 Hz (methanol-d_4) or 24.6 Hz (deuterium oxide).



IV, R = H
V, R = CH_3

Table IV. The Effect of Solvent on $\delta_{ae}(\alpha)$ in 3-Methyl-3-azabicyclo[3.3.1]nonane

Solvent	$\delta_{ae}(\alpha)$, Hz	Solvent	$\delta_{ae}(\alpha)$, Hz
Neat	38.6 ± 0.6[a]	Carbon disulfide	39.0
Cyclopentane	39.1	Diethyl ether	39.4
Toluene	39.7	Carbon tetrachloride	39.8
Benzene	40.1	Methanol	40.1
Chloroform	41.2	Methylene chloride	41.2
Tetrahydrofuran	41.2	Acetone	41.9

[a] The relatively large line width produces a substantial systematic error.

Concentration Considerations

Since dipole-moment measurements involve an extrapolation to infinite dilution,[7] it is necessary to determine the effect of concentration on $\delta_{ae}(\alpha)$ for piperidine. Furthermore, if the observed preference of the lone pair arises because in the equatorial position it is more effectively solvated or is associated with another molecule of piperidine, experiments at higher dilution may reveal a larger percentage of the axial-lone-pair isomer. Solvation, such as might be found in polar,

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(16) Harris and Spragg[12] have succeeded in freezing out the ring-inversion process for N-methylmorpholine and N,N′-dimethylpiperazine, but not for the corresponding unsubstituted compounds. Since the ring geometries are closely similar in all cases,[15] the failure to freeze out the latter set probably stems from a smaller δ_{ae}, which would depress T_c, rather than from a lower activation energy. The decrease in δ_{ae} in going from the substituted to the unsubstituted cases is consistent with a change in the location of the lone pair. The β effect apparently depresses δ_{ae} somewhat.

(17) E. L. Eliel, E. W. Della, and T. H. Williams, *Tetrahedron Letters*, 831 (1963); K. Brown, A. R. Katritzky, and A. J. Waring, *Proc. Chem. Soc.*, 257 (1964); E. L. Eliel and S. H. Schroeter, *J. Am. Chem. Soc.*, **87**, 5031 (1965).

(18) The α-axial protons in II are shifted upfield by the influence of the axial lone pair, but the α-equatorial protons are essentially unaffected. See Figure 1 in ref 1b.

hydroxylic media, must nonetheless have no influence on the position of the lone pair, since $\delta_{ae}(\alpha)$ and $\Delta\delta$ is quite independent of the choice of solvent (*vide supra*). There remains the possibility that solvation effects are simulated in nonpolar media by the solute itself through self-association. In this case, our experiments have determined the lone-pair preference in solvated or polymeric piperidine, but have said nothing about the free monomer. Therefore, the critical experiments are to be performed in nonpolar solvents at high dilution.

Information on $\delta_{ae}(\alpha)$ could be obtained directly at low temperatures with toluene-d_8 as the solvent (Table V). Data were assembled over a concentration range with a dilution factor up to 3.4. There is clearly no significant effect of concentration on $\delta_{ae}(\alpha)$ and hence on the position of the lone pair. If piperidine is present wholly as a dimer or as higher polymers even at these concentrations, the observed invariance of $\delta_{ae}(\alpha)$ is not significant. For this reason, the effective molecular weight of piperidine was determined by the depression of the freezing point of benzene (Table VI). The extent of association was found to be small at concentrations below 1 *m*; at a molality of 0.5, for example, the monomer represents about 90% of the species present. Thus, any physical measurement at concentrations below about 0.1 *m* must pertain to monomeric piperidine. Direct determination of $\delta_{ae}(\alpha)$ is not possible at these concentrations, but $\Delta\delta$ is readily available. As discussed in the previous section, a change in the location of the lone pair from the equatorial to the axial position would require a large decrease in $\Delta\delta$, because the α-axial resonances would be shifted in the direction of the γ resonances.[18] Since only two sharp peaks need be observed in this measurement, $\Delta\delta$ can be obtained at very low concentrations. The absence (Table VII) of any indication of a decrease in $\Delta\delta$, even at 0.017 *M*, for which there can be no self-association, demonstrates that monomeric piperidine must exist predominantly in the equatorial-lone-pair form.

Table V. Spectral Properties of Piperidine as a Function of Concentration in Toluene-d_8 at −85°

Molarity	$\delta_{ae}(\alpha)$, Hz	$J_{ae}(\alpha)$, Hz
2.01	31.7 ± 0.6	11.4
1.48	32.1	11.4
1.24	32.7	11.5
0.94	32.5	11.5
0.59	32.4	11.3

Table VI. The Molecular Weight of Piperidine as a Function of Concentration in Benzene

Molality	Mp depressn, °C[a]	Mol wt[b,c]	Mole % monomer
0.8772	3.80 ± 0.01	97.37	85.7
0.6764	3.10	95.13	88.3
0.6175	2.825	95.30	88.1
0.4629	2.17	92.99	90.8
0.4606	2.16	92.96	90.8
0.3344	1.585	91.97	92.0
0.2920	1.39	91.58	92.5
0.2248	1.09	89.92	94.4

[a] The melting point of benzene is 5.50°. [b] The cryoscopic constant of benzene was taken as 1.855°/mole. [c] The actual molecular weight of monomeric piperidine is 85.15.

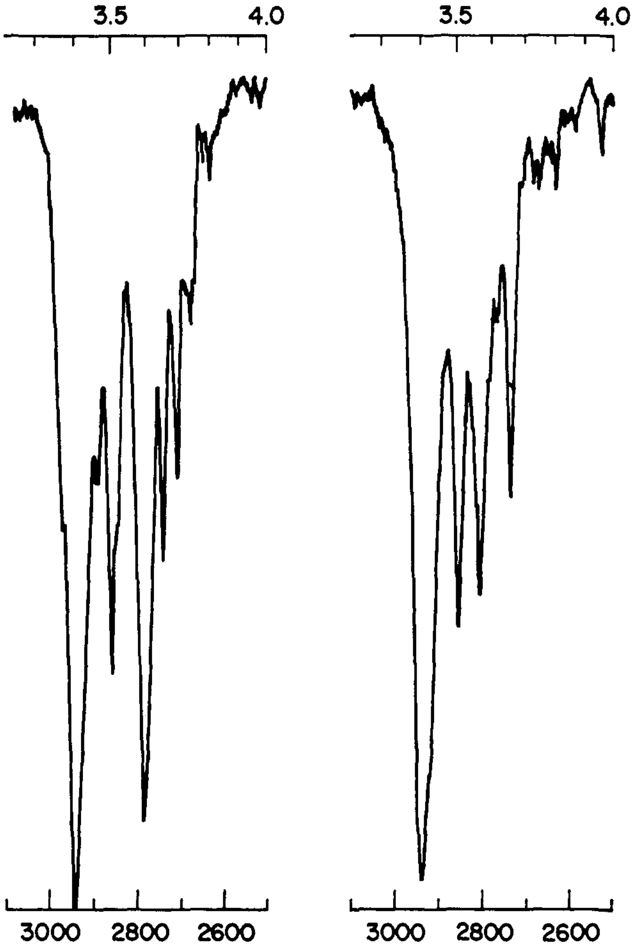

Figure 2. The infrared spectra of N-methylpiperidine (left) and piperidine, calibrated in microns (top) and reciprocal centimeters.

Table VII. The Variation of $\Delta\delta = \bar{\delta}_\gamma - \bar{\delta}_\alpha$ for Piperidine as a Function of Concentration in Benzene

Molarity	1.0	0.3	0.1	0.05	0.017
$\Delta\delta$, Hz[a]	72.6 ± 0.5	72.5	73.1	73.6	73.6

[a] Measured on the A-60-A at Loyola University, Chicago, Ill. We thank Dr. J. Wilt for making the instrument available to us.

Infrared Evidence

The correlation of infrared bands in the 2800–2650-cm^{-1} region with the stretching of carbon–hydrogen bonds that are *anti*-coplanar to a nitrogen lone pair[19] suggests an independent test of the lone-pair conformation. The bands should be present in piperidine systems only when the lone pair is axial, since this position provides an *anti*-coplanar relationship with the α-axial protons. The infrared spectra of piperidine (I) and its N-methyl derivative (II) were accordingly examined (Figure 2). Both spectra clearly show the in-plane and out-of-plane CH$_2$ vibrations near 2940 and 2850 ± 5 cm^{-1}. Small shoulders on the absorption from the

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(19) F. Bohlmann, *Ber.*, **91**, 2157 (1958).

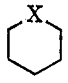
in-plane vibration of II arise from the asymmetric (2970 cm^{-1}) and symmetric (2870 cm^{-1}) stretching modes of the methyl group. Absorptions below about 2820 cm^{-1} probably may be considered "Bohlmann bands." Whereas N-methylpiperidine (II) has a very strong band at 2770 cm^{-1} and bands of medium intensity at 2730, 2690, and 2660 cm^{-1}, piperidine itself (I) has only medium-intensity bands at 2810 and 2730 cm^{-1}. The band at 2770 cm^{-1} in the spectrum of II clearly indicates the presence of an axial lone pair.[19] The pronounced decrease in the total intensity of bands below 2820 cm^{-1} in the spectrum of I with respect to that of II is indicative of a change in the location of the lone pair to the equatorial position. The peaks at 2810 and 2730 cm^{-1} either are "background" or are absorptions from some residual axial-lone-pair isomer. Examination of Sadtler spectra of cyclic nitrogen compounds in which an axial lone pair is impossible (pyrrolidine, azetidines, aziridine) reveals the presence of considerable tailing into the Bohlmann region. Until the question of 2800–2650-cm^{-1} background, *i.e.*, weak or tailing bands not associated with axial lone pairs, is settled, and because extinction coefficients for model systems are not available, the strongest conclusion we can reach from the infrared evidence alone is that the equatorial-lone-pair isomer is present predominantly, but not exclusively.

General Considerations

All the evidence presented thus far indicates that the lone pair of monomeric piperidine is predominantly equatorial. The present discussion has been concerned with a conformational determination, not with a consideration of the "steric requirements" or the "size" of the lone pair. Such considerations involve a number of presently indeterminant factors. The equatorial preference of the lone pair could result from (1) a true "size" effect; (2) hyperconjugative interactions; or (3) preferential solvation, including self-association. The experiments discussed in the previous sections eliminate (3) as a contributing factor. Any explanation in terms of size alone would require a more detailed knowledge of the potential functions for the hydrogen–lone-pair interactions. Consideration of hydrogen–hydrogen nonbonding interactions alone suggests[20] that the hydrogen atom on nitrogen has little positional preference, a condition not totally alien to the present results. If the piperidine ring is highly substituted, significant changes would be expected in the various interactions of the nitrogen lone pair and proton with other groups in the molecule, thereby possibly altering the lone-pair conformation.[8] For piperidine itself, the observed equatorial orientation of the lone pair may result from the hyperconjugative interaction suggested by Claxton.[21] The equatorial position is particularly suitable for delocalization of the lone pair into the various bonding situations of the saturated ring, whereas such an interaction is unlikely for an axial lone pair, the axis of which points away from the molecule.

Lone-Pair Positions in Heterocycles Analogous to Piperidine

The location of the lone pair has been determined for some other simple heterocycles. The oxygen function on sulfur in pentamethylene sulfoxide (VI) has a slight preference for the axial position.[22–24] The protonated heterocycles, VII–IX, exist wholly in the form with the proton axial.[25] Observation of the characteristically large axial–axial coupling between the acidic proton and two of the α protons precludes any other assignment.[26] Thus, in all cases in which a proton–lone-pair rivalry is possible, the proton always appears to prefer the axial position.



VI, X = SO
VII, X = $^{+}$SH
VIII, X = $^{+}$SeH
IX, X = $^{+}$TeH

Rate Studies

The nmr spectra of I–III were analyzed by computer simulation following the method of Alexander.[27] The observed and theoretical spectra for piperidine are given in Figure 1. The activation parameters are listed in Table VIII and the kinetic data appear in Table IX. A possible decrease in the energy of activation with increasing bulk of substitution is suggested. Riddell and Lehn[28] observed a more pronounced decrease in the same direction for the triply substituted hexahydrotriazines.

Table VIII. Activation Parameters for the Ring Inversion of Piperidine and Its Derivatives in Methanol-d_4

Compd	T_c, °C	E_a, kcal/mole	Log A
I	−63 ± 1	14.5 ± 0.5	16.9 ± 1.5
II	−28	14.4	14.8
III	−40	14.0	15.2

Experimental Section

The nmr spectra were taken on a Varian Model A-60 spectrometer equipped with a temperature probe. Computer calculations were carried out with the CDC-3400 and the Calcomp plotting accessory. Mass spectral analyses were performed by the Morgan-Schaffer Corp., Montreal, Quebec. Infrared spectra were measured on the Beckman IR-9.

Piperidine-3,3,5,5-d_4 (I). A mixture of 0.8 g of 1,5-dibromopentane-2,2,4,4-d_4[22] and 4 g of 20% ammonia in methanol was

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[20] E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience Publishers, Inc., New York, N. Y., 1965, pp 179–180.

[21] T. A. Claxton, *Chem. Ind.* (London), 1713 (1964).

[22] J. B. Lambert and R. G. Keske, *J. Org. Chem.*, **31**, 3429 (1966).

[23] C. R. Johnson and D. McCants, Jr., *J. Am. Chem. Soc.*, **86**, 2935 (1964).

[24] J. C. Martin and J. J. Uebel, *ibid.*, **86**, 2936 (1964).

[25] J. B. Lambert and R. G. Keske, in preparation.

[26] Considerable effort has been expended in attempts to perform such an experiment on piperidine, since the coupling pattern of the N-proton should indicate its location. As yet, either exchange or quadrupolar effects have prevented observation of any coupling, despite careful drying of the sample and irradiation at the nitrogen frequency (Professor E. W. Garbisch, University of Minnesota, kindly carried out the double irradiation experiments).

[27] S. Alexander, *J. Chem. Phys.*, **37**, 967, 974 (1962); **38**, 1787 (1963); **40**, 2741 (1964); G. M. Whitesides, Ph.D. Thesis, California Institute of Technology, 1964.

[28] F. G. Riddell and J. M. Lehn, *Chem. Commun.*, 375 (1966).

Table IX. Kinetic Parameters for Ring Inversion of Piperidine-3,3,5,5-d_4 (I) and Its N-Methyl (II) and N-*t*-Butyl (III) Derivatives in Methanol-d_4

I			II		III	
Temp, °C	$\tau(\alpha)$,[a] sec	$\tau(\gamma)$, sec	Temp, °C	$\tau(\gamma)$,[a,b] sec	Temp, °C	$\tau(\alpha)$,[a,c] sec
−50 ± 1[d]	0.0020	0.0015	−10.5	0.0015	−16.5	0.00040
−55	0.0045	0.0040	−17	0.0030	−22	0.00090
−60	0.0090	0.0085	−22	0.0070	−28	0.0018
−62.5	0.0150	0.013	−28	0.012	−34.5	0.0040
−65	0.022	...	−33	0.020	−39	0.0060
−70	0.045	0.035	−38.5	0.040	−44	0.012
−75	0.150	0.090	−44.5	0.090	−49	0.025
−80	0.30	...	...	...	−53.5	0.045
					−58	0.095

[a] Mean lifetime, *i.e.*, the reciprocal of the first-order rate constant; the error is generally about 10% of the value quoted. [b] The changes in the α-proton resonances could not be analyzed because of overlap of the methyl resonance. [c] The resonance of the *t*-butyl group obscures the γ resonances sufficiently to preclude an accurate kinetic analysis. [d] The temperature was determined at each point by measurement of the distance between the methanol peaks.

heated at 110° for 3 hr in a sealed ampoule. The tube was cooled and opened and the excess ammonia removed by forced effervescence. The methanol was removed by bulb-to-bulb distillation. The white solid was taken up in 3 ml of water and placed in a small test tube. Pellets of potassium hydroxide were added slowly until two layers separated. The upper layer was removed and purified by bulb-to-bulb distillation to give essentially pure piperidine-3,3,5,5-d_4 (140 mg).

N-Methylpiperidine-3,3,5,5-d_4 (II) and **N-*t*-butylpiperidine-3,3,5,5-d_4 (III)** were prepared from 1,5-dibromopentane-2,2,4,4-d_4 and methanol containing methylamine and *t*-butylamine, respectively, in the same manner as piperidine (I).

3-Azabicyclo[3.3.1]nonane (IV). Dimethyl isophthalate was converted to a mixture of *cis*- and *trans*-dimethyl 1,3-cyclohexanedicarboxylate by hydrogenation at room temperature over Adams catalyst.[29] Treatment of the corresponding diacid with ammonium hydroxide according to the method of Komppa[30] produced 1,3-cyclohexanedicarboximide which, upon reaction with lithium aluminum hydride, gave 3-azabicyclo[3.3.1]nonane.[31]

3-Methyl-3-azabicyclo[3.3.1]nonane (V). To a stirred solution of 3.0 g of 3-azabicyclo[3.3.1]nonane in 25 ml of methanol, refluxing gently,was added 5.2 g of methyl iodide in small portions through the condenser. Five minutes after completion of addition, the solution was cooled to room temperature, and 70 ml of dry ether was added. The resulting suspension was filtered, and the precipitate was washed with 100 ml of dry ether. The precipitate was dissolved in 100 ml of water and treated with 1 g of sodium hydroxide in 10 ml of water. The oily upper layer was removed and dried with potassium hydroxide pellets to give 3-methyl-3-azabicyclo[3.3.1]nonane, mol wt 139 by mass spectroscopy (calcd 139.24).

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(29) F. Ramirez and J. W. Sargent, *J. Am. Chem. Soc.*, **74**, 5785 (1952).

(30) G. Komppa, *Ber.*, **65**, 792 (1932).

(31) S. Rossi and C. Valero, *Farmaco* (Pavia) *Ed. Sci.*, **12**, 1008 (1957); *Chem. Abstr.*, **52**, 12861*a* (1958).

Acidity of Hydrocarbons. XXV. Secondary Isotope Effects in the Lithium Cyclohexylamide Catalyzed α-Deuterium Exchange of Ring-Deuterated Toluenes[1]

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Abstract: The protodedeuteration rates of toluene-α,4-d_2, -α,2,4,6-d_4, and -α,2,3,4,5,6-d_6 with lithium cyclohexylamide–cyclohexylamine at 50° are dissected to the following isotope effects per ring deuterium: *ortho*, −2.4%; *meta*, −0.4%; *para*, −1.8%. These rate retardations are in the direction and of the order of magnitude expected for deuterium as an electron-donating substituent but the variations with position are not explicable on any simple general basis.

Isotope effects are generally explicable by statistical mechanical treatments of the entire molecular systems involved. Since, in general, this is difficult or impossible, the total system is usually truncated to the region of isotopic change.[3] In some secondary deuterium isotope effects this type of simplication is not feasible because the effects are small, and there are no obvious simple changes in force constants. In such cases deuterium has been treated as a substituent of a subtle type, and its effects have been discussed with the language of substituent effects. For example, a number of previous studies have shown that deuterium exhibits a small but definite electron-donating "inductive effect"

(1) This research was supported in part by a grant from the National Science Foundation.

(2) National Science Foundation Postdoctoral Fellow, 1964–1965.

(3) M. J. Stern and M. Wolfsberg, *J. Chem. Phys.*, **45**, 4105 (1966).