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Infrared-spectral Studies on the Orientation of the Lone Pairs in Piperidine Derivatives[1]

Tadashi MASAMUNE, Mitsuo TAKASUGI and Minoru MATSUKI
Department of Chemistry, Faculty of Science, Hokkaido University, Sapporo

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The infrared spectra of stereoisomers of several piperidines and their *N*-methyl derivatives in carbon tetrachloride have been measured in the region of 3020 to 2500 cm^{-1}. The estimated intensities (A) of their Bohlmann bands have been analyzed, provided that Formula (1) concerning the intensity defined in the text holds for the compounds examined. The result indicates that piperidine exists mainly, but not exclusively, in the conformation with the lone pair axial.

For some years attention has been drawn to the steric requirement of a nitrogen lone pair.[2] In 1958 Aroney and LeFèvre[3] examined the Kerr constants of piperidine and *N*-methyl piperidine and concluded that the nitrogen lone pair is more bulky[4] than the hydrogen and approximately equivalent to the methyl group. Their conclusion has since been criticized by several groups,[5-11] especially by Allinger,[7] Katritzky,[5b] Lambert,[8a] and their co-workers,[12] and there remains now little doubt that the lone pair is axially oriented in *N*-substituted piperidines. However, no consistent conclusion is drawn regarding the relative orientation of the hydrogen and the lone pair in *N*-unsubstituted piperidines, although evidence has recently accumulated that the latter is smaller than the former.[13] In a preliminary communciation[11] we reported an attempt to determine a preference of the hydrogen for the equatorial position in *N*-unsubstituted piperidines on the basis of their Bohlmann bands, and the present paper describes the full details.

Bohlmann[14] reported an empirical relation between the configurations of quinolizidine derivatives and their infrared bands in the region of 2800 to 2700 cm^{-1} (general region, no exact limits) called the Bohlmann bands; namely, these bands have been correlated with the presence of at least two α-hydrogens oriented *anti*-coplanar to the lone pair. The property of this correlation has since been confirmed in the determination of configurations of related compounds[15]. Recently Hamlow and his co-workers[16] attempted to rationalize such "absorption bands" in the spectra and also "the large chemical shift difference[16,17] (0.80—0.93 ppm)" between the axial and equatorial α-protons, and proposed that these facts would be caused by the overlap of the lone pair and the anti-bonding σ^* C–H$_{\text{axial}}$ orbital on the adjacent carbon. Apart from this rationalization, although it seems to be most valid at least concerning the infrared

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[1] Part XVIII of "The Condensed Polynuclear Perhydro-compounds Containing Nitrogen"; Part XVII, Ref. 20.

[2] For a recent review, see F. G. Riddell, *Quart. Rev.*, **21**, 364 (1967); G. Yamamoto, *Kagaku no Ryoiki (J. Japan Chem.)*, **21**, 715, 817 (1967).

[3] a) M. J. Aroney and R. J. W. LeFèvre, *J. Chem. Soc.*, **1958**, 3002. b) M. J. Aroney, C. -Y. Chen, R. J. W. LeFèvre and J. D. Saxby, *ibid.*, **1964**, 4269.

[4] The "more bulky or larger" of the groups is defined in this context as that which preferentially assumes the equatorial position.

[5] a) T. M. Moynehan, K. Schofield, R. A. Y. Jones and A. R. Katritzky, *J. Chem. Soc.*, **1962**, 2637; K. Brown, A. R. Katritzky and A. J. Warning, *ibid.*, *(B)*, **1967**, 487. b) P. J. Brignell, A. R. Katritzky and P. L. Russel, *Chem. Commun.*, **1966**, 723. c) R. J. Bishop, L. E. Sutton, D. Dineen, R. A. Y. Jones, A. R. Katritzky and R. J. Wyatt, *J. Chem. Soc.*, *(B)*, **1967**, 493.

[6] N. W. J. Pumphrey and M. J. T. Robinson, *Chem. Ind.*, **1963**, 1903.

[7] N. L. Allinger, J. G. D. Carpenter and F. M. Karkowski, *J. Am. Chem. Soc.*, **87**, 1232 (1965).

[8] a) J. B. Lambert, R. G. Keske, R. E. Carhart and A. P. Jovanovich, *ibid.*, **89**, 3761 (1967). b) J. B. Lambert, R. G. Keske and D. K. Weary, *ibid.*, **89** 5921 (1967).

[9] E. L. Eliel and Sr. M. Carmeline Knoeber, *ibid.*, **88**, 5347 (1966).

[10] H. Booth and A. H. Bostock, *Chem. Commun.*, **1967**, 177.

[11] T. Masamune and M. Takasugi, *ibid.*, **1967**, 625.

[12] For the steric requirement of lone pairs on the atoms other than the nitrogen, see Refs. 2, 8b and 9.

[13] For the contrary conclusion, see Refs. 3b and 8a.

[14] F. Bohlmann, *Chem. Ber.*, **91**, 2157 (1958).

[15] For examples, see R. E. Brown, D. M. Lustgarten, R. J. Stanaback and R. I. Meltzer, *J. Org. Chem.*, **31**, 1489 (1966); H. O. House, B. A. Tefertiller and C. G. Pitt, *ibid.*, **31**, 1073 (1966); W. E. Rosen, *ibid.*, **30**, 2044 (1965); M. Hesse, W. v. Philipsborn, D. Schumann, G. Spiteller, M. Spiteller-Friedmann, W. I. Taylor, H. Schmid and P. Karrer, *Helv. Chim. Acta*, **99**, 878 (1964).

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

[17] F. Bohlmann, D. Schumann and H. Schulz, *ibid.*, **1965**, 173; F. Bohlmann, D. Schumann and C. Arndt, *ibid.*, **1965**, 2703.

bands, the Bohlmann bands are expected to appear in *N*-unsubstituted piperidines as well as in quinolizidines, as far as the above-mentioned spatial requirement is satisfied for the lone pair and the α-hydrogen. However, only little attention[6,18,19] has been paid to the bands of the piperidines and no quantitative estimation appears to have been reported. In the preceding paper[20] of this series, we described the preparation and configuration of stereoisomers of perhydroacridine and perhydrophenanthridine. Having utilized these and related piperidines, it was attempted to determine the orientation of the lone pair by measurement of their Bohlmann bands and subsequent analysis of the intensities on appropriate assumptions.

Experimental

The infrared absorption bands of the following piperidine derivatives have been measured in the region of 3020 to 2500 cm^{-1}: piperidine (I), *trans*- and *cis*-perhydroquinolines[21] (II and III), *trans, syn, trans*-, *trans, anti, cis*- and *trans, syn, cis*-perhydroacridines[20,22] (IV, V and VI), *trans, anti, trans*-, *trans, syn, cis*- and *cis, syn, cis*-perhydrophenanthridines[20,23] (VII, VIII and IX), *trans*- and *cis*-2,6-dimethylpiperidines[24] (X and XI), *N*-methyl derivatives (Ia to XIa) of I to XI, and quinolizidine[25] (XII). The configurations of these compounds have all been established. The spectra of the *N*-benzoyl derivatives (Ib to XIb) of I, II, V,[26] VII, and XI have also been measured.

Materials. Most of the compounds examined were prepared by procedures described in the literatures. Solid compounds were recrystallized to constant melting point and liquids were freshly distilled before use. Only *N*-benzoyl-α-perhydrophenanthridine (VIIb) and *N*-methyl-*trans*- and *cis*-2,6-dimethylpiperidines (Xa and XIa) were new.

Treatment of VII (200 mg) in ether (10 m*l*) with benzoyl chloride (0.6 m*l*) and 3 N aqueous potassium hydroxide solution (10 m*l*) at room temperature for 20 hr gave the crude *N*-benzoyl derivative, which on recrystallization from *n*-hexane afforded a pure sample (107 mg) of VIIb, mp 98—100°C.

Found: C, 80.55; H, 9.32; N, 4.44%. Calcd for $C_{20}H_{27}ON$: C, 80.76; H, 9.15; N, 4.71%.

A mixture of XI (350 mg), formic acid (1.0 m*l*) and 33% formalin (0.9 m*l*) was heated on a steam bath for 3 hr and then cooled. The mixture was diluted with conc potassium hydroxide solution, saturated with sodium chloride and extracted with ether. The ether extract, after being dried with anhydrous sodium sulfate, was distilled over solid potassium hydroxide. The distillate was redistilled over calcium oxide and a fraction (XIa, 78 mg) of bp 139—142°C was collected. In a similar way, the corresponding *trans* isomer (Xa) was obtained and had bp 140—143°C.

Found (XIa): C, 75.35; H, 13.61%. Calcd for $C_8H_{17}N$: C, 75.52; H, 13.47%.

Found (Xa): C, 75.23; H, 13.75%. Calcd for $C_8H_{17}N$: C, 75.52; H, 13.47%.

Measurements of the Infrared Spectra. The spectra were recorded at 23°C on a Nippon Bunko 402-G spectrophotometer with 0.2 and/or 0.5 mm cells, using carbon tetrachloride solutions containing about 0.03 M of the samples. The wave numbers quoted were believed to be accurate to ±3 cm^{-1}. The integrated intensities were expressed in this paper by $\int \varepsilon_\nu \delta\nu$, where ε_ν is the molecular extinction coefficient at the wave number ν.[27] The estimated uncertainty of the intensity was about 10%.

Results and Discussions

The spectra of several compounds are given in Figs. 1 to 4. As shown in the figures, each spectrum of *N*-unsubstituted- and *N*-methyl-piperidines and quinolizidine exhibited a sharp absorption minimum at 2820±3 cm^{-1}, but, to the contrary, that of *N*-benzoyl derivatives only a plain absorption curve near the region. This strongly suggests that the Bohlmann bands must be included in the bands below 2820 cm^{-1},[28] and also indicates that, in the amides, the overlap[16] in question of the lone pair is largely forbidden due to the overlap with the benzoyl group. Thus the bands below 2820 cm^{-1} of *N*-benzoyl derivatives would be reasonably regarded as the background in the region of the corresponding piperidines. Then we have defined the difference between the integrated intensity (I_A) of the band in the 2820 to 2500 cm^{-1} range and that (I_B) of its background at that (A) of the Bohlmann band.

Before considering the intensities, it is desirable to mention the conformations of piperidine rings. *trans*-Perhydroquinoline II, three perhydroacridines IV to IV, two perhydrophenanthridines VII and VIII, and their *N*-methyl derivatives all include at least one *trans*-fused linkage and exist in rigid

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[18] C.-Y. Chen and R. J. W. LeFèvre, *ibid.*, **1965**, 1611.

[19] R. Barchet and T. P. Forrest, *ibid.*, **1965**, 4229.

[20] T. Masamune, M. Ohno, K. Takemura and S. Ohuchi, This Bulletin, **41**, 2458 (1968).

[21] F. E. King, T. Henshall and R. L. St. D. Whitehead, *J. Chem. Soc.*, **1948**, 1373; M. Ehrenstein and W. Bunge, *Ber.*, **67**, 1715 (1934); C. F. Bailey and S. M. McElvain, *J. Am. Chem. Soc.*, **52**, 4015 (1930).

[22] T. Masamune and S. Wakamatsu, *Nippon Kagaku Zasshi (J. Chem. Soc. Japan, Pure Chem. Sect.)*, **77**, 1145 (1956).

[23] T. Masamune and Y. Kubota *ibid.*, **77**, 1467 (1956).

[24] a) R. K. Hill and T. H. Chan, *Tetrahedron*, **21**, 2015 (1965); R. K. Hill, T. H. Chan and J. A. Joule, *ibid.*, **21**, 147 (1965). b) A. Marcus and R. Wolffenstein, *Ber.*, **34**, 2426 (1901); *ibid.*, **32**, 2525 (1899).

[25] The authors are grateful to Dr. Ichiro Kawasaki, Osaka University, for providing them with quinolizidine.

[26] "Compound IVb" in a preliminary communication (Ref. 11) should be revised to "Vb."

[27] *Cf.* K. S. Seihardi and N. R. Jones, *Spectrochim. Acta*, **19**, 1013 (1963).

[28] The examination of each spectrum suggests that the tailing intensity in the region above 2820 cm^{-1} of the Bohlmann band would be negligibly small as compared with that in the region below 2820 cm^{-1} of the band produced by usual C–H vibrations.

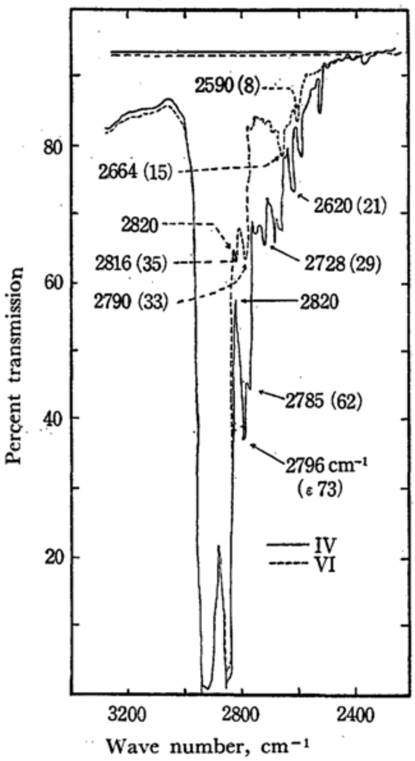


Fig. 1. Infrared spectra of α- and γ-perhydroacridines (IV and VI).
IV, 5.82 mg in 0.1 m*l* CCl_4, cell 0.2 mm
V, 4.93 mg in 0.1 m*l* CCl_4, cell 0.2 mm

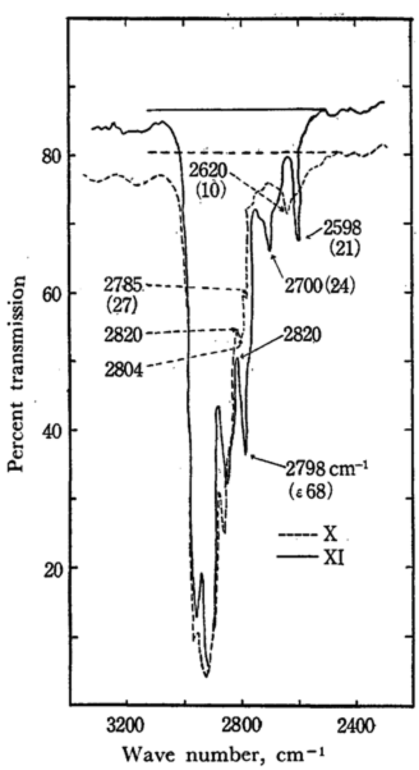
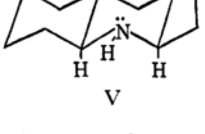


Fig. 2. Infrared spectra of *trans*- and *cis*-2,6-dimethylpiperidines (X and XI).
X, 8.0 mg in 0.2 m*l* CCl_4, cell 0.2 mm
XI, 8.0 mg in 0.2 m*l* CCl_4, cell 0.2 mm

conformations consisting of only chair-formed rings.[20] The other compounds except XII can take two conformations formed by ring inversion. In *trans*-2,6-dimethylpiperidine (X) and its *N*-methyl derivative Xa, the inversion leads to formation of the same conformer as the original, apart from the *N*-substituents, which has a conformation with one α-methyl group axial and with the other equatorial. To the contrary, the *cis* isomers XI and XIa, when flipped, are converted from a conformation with two equatorial α-methyl groups into a definitely unstable one with the two axial groups and are, therefore, essentially confined to the former. The same is the case in quinolizidine XII;[29] XII is practically fixed at one conformation with *trans*-fused rings, and only a negligible amount of the other conformer exists in the equilibrium mixture, which is formed by inversion of configuration at the nitrogen. Each of the remaining four compounds, *cis*-perhydroquinoline III, *cis, syn, cis*-perhydrophenanthridine IX, and their *N*-methyl compounds IIIa and IXa, would exist as an equilibrium mixture of conformers flipped with each other, one having two axial α-hydrogens and the other only one.[*1] At the present stage it might be impossible to discuss the ratio of the conformers, as it would very largely depending on the relative steric requirement of the lone pair and the *C*-hydrogen. In summary, all the compounds other than III, IIIa, IX and IXa have rigid or essentially fixed conformations. In most of those compounds two hydrogens are oriented axial on the α-carbons in the respective piperidine rings, while in VI, VIa, X and Xa only one hydrogen and in XII three hydrogens exist at the axial conformation.

Francis[30] measured the integrated intensities of



V

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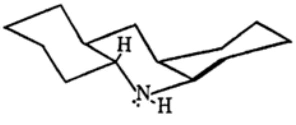
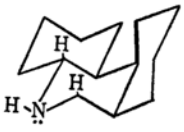
29) E. L. Eliel, N. L. Allinger, S. J. Angyal and G. A. Morrison, "Conformational Analysis," Interscience Publishers, New York, N. Y. (1965), p. 252.

[*1] The piperidine ring of the compound IX might adopt a twisted boat form owing to the presence of 1,3-diaxial methylene groups rather than a chair form. However, whatever the conformation is, the same conclusion will be drawn, because no discussion on the intensity of IX is involved in the section "Quantitative Consideration."

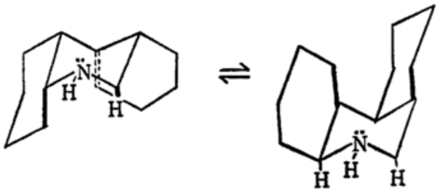
30) S. A. Francis, *J. Chem. Phys.*, **18**, 861 (1950).



VI



VIII



IX

the bands near 2900 cm^{-1}, produced by the in-plane and out of plane C–H vibrations, of a series of aliphatic hydrocarbons, and indicated the intensities to be interpretable well on the basis that the hydrocarbon molecule behaves like a non-interacting mixture of methyl, methylene and methine structural groups. Hence we first estimated the integrated intensities (I_t) of the bands in the 2820 to 3000 cm^{-1} range of the present compounds. Although the intensities varied largely depending on the number of the vibrations concerned (Table 1), the average (I_m) per one C–H vibration fell within $(1.6\pm0.1)\times10^3$ l/cm^2·mol, which was roughly equal to the corresponding, 1.3×10^3 l/cm^2·mol,[30] for a methylene group of aliphatic hydrocarbons.

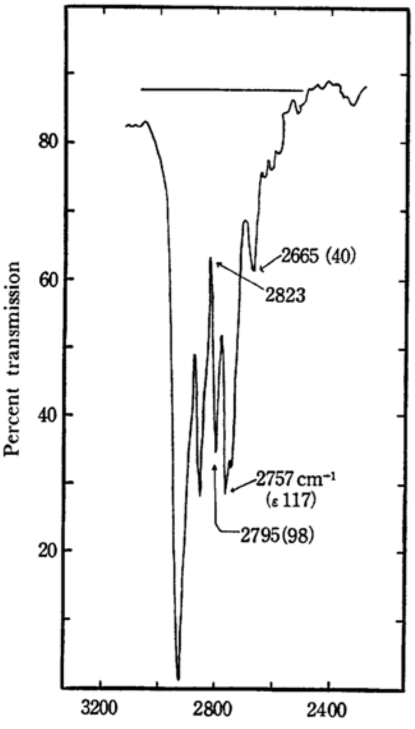


Fig. 3. Infrared spectrum of quinolizidine (XII).
XII, 5.7 mg in 0.2 ml CCl$_4$, cell 0.2 mm

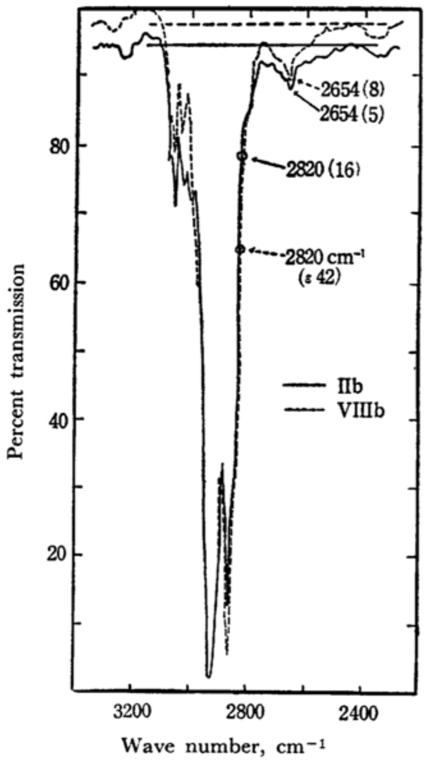


Fig. 4. Infrared spectra of *N*-benzoyl-*trans*-perhydroquinoline (IIb) and α-perhydrophenanthridine (VIIb).
IIb, 13.7 mg in 0.20 ml CCl$_4$, cell 0.2 mm
VIIb, 14.3 mg in 0.25 ml CCl$_4$, cell 0.2 mm

The integrated intensities (A) of the Bohlmann bands are summarized in Table 2. As shown in the table, the bands exhibited considerable intensity not only in *N*-unsubstituted piperidines having two axial α-hydrogens but also in those with only one. This observation, however, does not imply that the lone pair assumes exclusively the axial position in the piperidines.

Qualitative Consideration. The compounds examined are classified into two groups by the conformation of *N*-substituents. Compounds involved in the first class are *N*-methylpiperidines (Ia to XIa) and quinolizidine (XII). These compounds would be locked almost exclusively into a conformation with the lone pair axial. In compounds Ia, IIa, IVa Va, VIIa, VIIIa, XIa, and XII, which have two α-axial hydrogens and, accordingly, three hydrogens *anti*-coplanar to the axial lone

TABLE 1. INTEGRATED INTENSITIES OF THE BANDS IN THE REGION OF 3000 TO 2820 cm^{-1} OF PIPERIDINE DERIVATIVES

Compound	Intensities[a,b]		Compound	Intensities[a,b]		Compound	Intensities[a,b]	
	I_t	I_m		I_t	I_m		I_t	I_m
Ia	16.5	1.65	I	12.9	1.60	Ib	15.4	1.54
IIa	24.7	1.55	II	23.4	1.67	IIb	24.7	1.55
IIIa	25.6	1.60	III	22.4	1.60			
IVa	34.1	1.55	IV	31.8	1.59			
Va	34.1	1.55	V	30.8	1.54	Vb	34.3	1.55
VIa	36.4	1.58	VI	33.7	1.60			
VIIa	35.2	1.60	VII	32.9	1.65	VIIb	34.2	1.55
VIIIa	35.3	1.60	VIII	33.2	1.66			
IXa	37.7	1.70	IX	33.0	1.65			
Xa	23.0	1.53	X	21.2	1.63			
XIa	21.6	1.55	XI	18.5	1.54	XIb	21.8	1.55
XII	22.4	1.60						

a) The unit; $(l/\text{cm}^2\cdot\text{mol})\times 10^{-3}$.

b) The "I_t and I_m" refer to the total and average integrated intensities, respectively. The latter was obtained by division of I_t by the number of *C*-hydrogens which are not participating in the Bohlmann band.

TABLE 2. INTEGRATED INTENSITIES OF THE BOHLMANN BANDS OF PIPERIDINE DERIVATIVES

Compound	Intensities[a,b]			Compound	Intensities[a,b]		
	I_A	I_B	A		I_A	I_B	A
Ia	11.4	0.8[c]	10.6	I	5.6	0.6[h]	5.0
IIa	11.2	1.2[d]	10.0	II	5.6	1.0[i]	4.6
IIIa	11.6	1.2[d]	10.4	III	6.7	1.0[i]	5.7
IVa	11.8	1.8[e]	10.0	IV	6.0	1.6[j]	4.4
Va	12.5	1.8[e]	10.7	V	7.0	1.6[j]	5.4
VIa	6.5	1.8[e]	4.7	VI	3.6	1.6[j]	2.0
VIIa	12.2	1.7[f]	10.5	VII	6.1	1.5[k]	4.6
VIIIa	10.3	1.7[f]	8.6	VIII	4.7	1.5[k]	3.2
IXa	12.6	1.7[f]	10.9	IX	7.3	1.5[k]	5.8
Xa	5.7	1.0[g]	4.7	X	2.8	0.8[l]	2.0
XIa	10.5	1.0[g]	9.5	XI	5.4	0.8[l]	4.6
XII	11.5	1.0[i]	10.5				

a) The unit; $(l/\text{cm}^2\cdot\text{mol})\times 10^{-3}$.

b) The "I_A, I_B and A" refer to the integrated intensities of the band in the region below 2820 cm^{-1}, its background and the Bohlmann band, respectively.

c—g) These figures denote the intensities (I_B) in the 2820 to 2500 cm^{-1} range of Ib, IIb, Vb, VIIb and XIb, respectively.

h—l) These figures were obtained by multiplication of I_B of Ib, IIb, Vb, VIIb and XIb and the following fractions, 8/10, 14/16, 20/22, 20/22 and 12/14, respectively.[31]

pair and participating in the Bohlmann band, the intensities fell within (8.6 to 10.9)$\times 10^3$ $l/\text{cm}^2\cdot$mol (the unit will be omitted). On the other hand, compounds VIa and Xa, having only the two relevant hydrogens, showed the weak intensity of 4.7. Compounds of the second class are *N*-unsubstituted piperidines, in which the lone pair is located in an undetermined position. Of these piperidines, compounds except VI and X have two axial α-hydrogens and showed intensities of 3.2 to 5.8, which amounted to only 46% (55—36%) of those of the respective *N*-methyl derivatives. The two compounds have only one axial α-hydrogen and exhibited the weak intensity of 2.0, which accounted for only 43% of that of VIa and Xa.

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31) Both the numerator and denominator of the fraction refer to the number of hydrogens associated with the usual C–H vibrations in each compound. For example, both IIb and IIa would contain 16 relevant hydrogens, while II 14 hydrogens of such a kind. It should be mentioned that, without such a treatment which appears arbitrary, we arrive at almost the same value of N_H*.

If these decreases (46 and 43%) in intensity resulted from only a shift from axial to equatorial lone pair, it would be concluded that the lone pair assumes an equatorial conformation with a slight preference. However, the decreases are undoubtedly attributed to various factors, and one of those must be the number of the relevant hydrogens. As described above, the intensities of the compounds, when compared in the respective class, decreased to about half (55—43 and 62—35%) in passing from the three to two relevant hydrogens and from the two to one, respectively. These facts suggest that the number of α-axial hydrogens as well as the orientation of the lone pair would play a considerably great role for the decrease (46 and 43%) in question. Although it might be impossible to estimate these factors at the present stage, it would be inferred certainly that the lone pair adopts an equatorial conformation preferentially.

Quantitative Consideration. Bearing in mind the afore-mentioned qualitative consideration, we next attempted to analyze the observed intensities on the basis of the following assumptions: *the intensity (A) of the Bohlmann band in each compound is the sum of those due to individual C–H vibrations in question.* Apparently, this assumption might not strictly be correct, as bands due to overtone and/or combination would be included in the region in question. However, the perplexity due to these bands would be mostly eliminated, because the background would also include such bands. Moreover, the intensities of the bands, even if not completely eliminated, would not be great. In the previous section it has been shown that the intensity of absorption near 2900 cm^{-1} of usual C–H vibrations equals the sum of those due to individual vibrations concerned in both aliphatic hydrocarbons and the present compounds. The assumption described above was proposed on the analogy of this fact. In the present paper, we will proceed further with the analysis, leaving the detailed examination for the validity of this analogy till later on.

The intensity A of the Bohlmann band is concerned not only with the orientation of the lone pair and the number and kind of the relevant hydrogens (oriented on the α-carbon and *anti*-coplanar to the lone pair) as discussed already, but also with the extent of the overlap in question[16] and the ring distortion.[18] Hence, the above-mentioned assumption is expressed by the following formula:[32]

$$A = \sum N\times n\times I\times S\times R \qquad (1)$$

where N is N_{H} or N_{Me}, n is n_p, n_s or n_t, I is I_p, I_s or I_t, S is $S_{2\beta}$ or $S_{1\beta}$, and R is R_1 R_2 or R_3.

The "N_{H} and N_{Me}" refer to the mole fractions of conformers with an axially oriented lone pair on the nitrogen. The "n_p, n_s and n_t" are the number of relevant hydrogens in methyl, methylene and methine groups, respectively, and are given directly from the structure of the compound. The "I_p, I_s and I_t" represent the intensities for the C–H vibrations in question (whose hydrogen is present *solely* in a compound involving no distortions and located in methyl, methylene and methine groups, respectively) and are called the unit intensity. The "$S_{2\beta}$ and $S_{1\beta}$" are the ratios of the intensity produced by each vibration in question to the corresponding unit intensity, when an axial methylene or methyl substituent is present at the β-position to two α-carbons and one α-carbon bearing the relevant hydrogen(s), respectively.[18] The "$R_1(=1)$, R_2 and R_3" are the ratios of the intensity of each vibration to the corresponding unit intensity, when there are one, two and three relevant hydrogens in a compound, respectively.[16]

The second assumption follows as. *The mole fractions N_{H} and N_{Me} are approximately constant for all the N-unsubstituted- and N-methyl-piperidines having no methylene or methyl group syn-axial to the lone pair or the hydrogen on nitrogen, respectively;* namely, $N_{\mathrm{H}}=N_{\mathrm{H}}^*$ (N_{H} of piperidine) and $N_{\mathrm{Me}}=0.95$.[33] On the other hand, for compound V having the afore-mentioned axial group, the mole fraction N_{H} is expressed by $N_{\mathrm{H}}^*\times\beta_s$, where β_s is a parameter showing the effect of the group. *In compound Va, the N-methyl group is essentially fixed at the equatorial position;* namely, $N_{\mathrm{Me}}=1$. On the basis of these assumptions, the following equations are obtained for all the piperidines, having rigid or essentially fixed conformations, other than III, IIIa, IX and IXa.

For compounds with R_1;

VI and X　$N_{\mathrm{H}}^*\times I_t\times S_{1\beta}=2.0,\ 2.0=2.0$[34]　(2)

For compounds with R_2;

I　$N_{\mathrm{H}}^*\times 2I_s\times R_2=5.0$　(3)

II and VII　$N_{\mathrm{H}}^*\times (I_s+I_s)\times R_2=4.6,\ 4.6=4.6$　(4)

IV and XI　$N_{\mathrm{H}}^*\times 2I_t\times R_2=4.4,\ 4.6=4.6$　(5)

V　$N_{\mathrm{H}}^*\times 2I_t\times R_2\times\beta_s=5.4$　(6)

VIII　$N_{\mathrm{H}}^*\times (I_s+I_t)\times R_2\times S_{2\beta}=3.2$　(7)

VIa and Xa　$(I_p+I_t)\times R_2\times S_{2\beta}$
$=4.95,\ 4.95=4.95$　(8)

For compounds with R_3;

Ia　$(\mathrm{I}_p+2I_s)\times R_3=11.1$　(9)

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32) The intensity A might be affected by factors other than those described. If so, Formula (1) is not a mathematical expression of the first assumption but rather a new assumption. However, as far as we know, the intensity appears to depend only or mostly on these factors.

33) This value is cited from the report by Allinger *et al.*[7] The mole fraction N_{Me} of Ia has recently criticized by Katritzky *et al.*[5c]

34) The unit in Eqs. of (2) to (13); $10^{-3}\times l/\mathrm{cm}^2\cdot\mathrm{mol}$.

IIa and VIIa $(I_p+I_s+I_t)\times R_3$

$$=10.5,\ 10.5=10.5 \qquad (10)$$

IVa, Va and XIa $(I_p+2I_t)\times R_3$

$$=10.5,\ 10.7,\ 10.0=10.4 \qquad (11)$$

VIIIa $(I_s+I_t)\times R_3\times S_{2\beta}+I_p\times R_3=9.05$ (12)

XII $(2I_s+I_t)\times R_3=10.5$ (13)

From Eqs. (9), (10), (11) and (13), we obtain

$$I_s=0.94\times I_p \qquad (14)$$

and

$$I_t=0.84\times I_p \qquad (15)$$

From Eqs. (3) (4) and (5), we obtain $I_s=1.11\times I_t$, which is consistent with Eqs. (14) and (15). Inserting Eqs. (14) and (15) into Eqs. (9), (10), (11), (13) and Eqs. (3), (4) and (5) yields

$$I_p\times R_3=3.88\times 10^3\ l/\mathrm{cm}^2\cdot\mathrm{mol} \qquad (16)$$

and

$$N_H{}^*\times I_p\times R_2=2.64\times 10^3\ l/\mathrm{cm}^2\cdot\mathrm{mol} \qquad (17)$$

Inserting Eqs. (17) and (16) into Eqs. (7) and (12) respectively gives

$$S_{2\beta}=0.68,\ 0.74=0.71$$

From the value of $S_{2\beta}$, Eqs. (8) and (6), we obtain

$$N_H{}^*=0.70 \quad \text{and} \quad \beta_s=1.22^{35)}$$

For compounds III and IIIa of the four piperidines, in which two conformations are possible, the intensities were calculated, using the estimated values for the parameters and the above assumptions. For conformations of III and IIIa, having a methylene group *syn*-axial to the lone pair or the *N*-hydrogen and, accordingly, two axial α-hydrogens, the intensities of 5.7 and $10.8\times 10^3\ l/\mathrm{cm}^2\cdot\mathrm{mol}$ were calculated, respectively. On the other hand, for the other conformations which include only one axial α-hydrogen, the calculated intensities were 2.2 and $5.2\times 10^3\ l/\mathrm{cm}^2\cdot\mathrm{mol}$. These values, when compared with the corresponding observed intensities (Table 2), strongly suggest that these compounds assume the former conformation mainly.

The present result $N_H{}^*=0.70$ indicates that piperidine exists preferentially in the conformer with the lone pair axial, and is consistent with that obtained by Allinger ($N_H{}^*=0.68$),[7] Katritzky,[5a,5b] Booth,[10] and their co-workers, but not with those of other authors.[3,8a] We would emphasize that, while the value for $N_H{}^*$ is derived provided that the assumptions described hold for the compounds examined, this conclusion is considerably certain qualitatively. The above disagreement might be attributed to the difference in the experimental conditions or methods, or to the assumptions involved tacitly in the analysis of the results.

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[35] The following values are obtained for the other parameters on the assumption that $S_{2\beta}$ is equal to $S_{1\beta}$, although it appears improbable:

$$I_p,\ I_s \text{ and } I_s=4.79,\ 4.50 \text{ and } 4.02\times 10^3\ l/\mathrm{cm}^2\cdot\mathrm{mol}$$

$$R_2 \text{ and } R_3=0.79 \text{ and } 0.81.$$