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# INFRARED SPECTRAL STUDIES ON THE ORIENTATION OF THE ELECTRON LONE-PAIRS ON NITROGEN ATOMS

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In quinolizidine derivatives, infrared bands in the 2700-2800 $cm^{-1}$ region have been correlated with the presence of at least two _α_-hydrogen atoms oriented _trans_ to the lone pair (1, 2, 3). However a few exceptions [e.g., 3-epialloyohimbone and 3-epialloyohimbine (4)] have already been reported. Recently, Hamlow _et al_ (5) have attempted to rationalize such a "characteristic" absorption band in the infrared and also the "large" difference (0.93 p.p.m.) in proton magnetic resonance (p.m.r.) chemical shifts of the α-hydrogens in axial and equatorial dispositions by proposing that in saturated cyclic nitrogen compounds in which the direction of the nitrogen lone pair is fixed, partial participation of the lone pair in a $\sigma^*$ C-Hax orbital on the adjacent carbon takes place (see Fig. 1), and that this generates some double bond character between $C_\alpha$ and N with a simultaneous increase in electron density at the $C_\alpha$ axial proton.

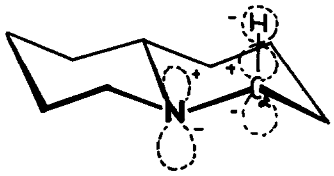
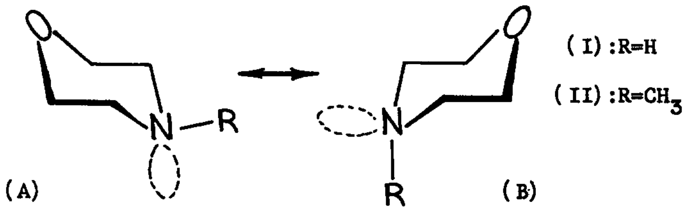
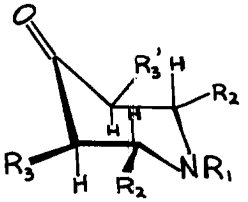


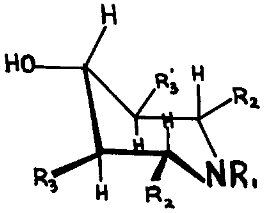
FIG. 1

In this preliminary communication, we wish to report that the infrared spectra of morpholine (I), N-methol-morpholine (II) and a number of substituted 4-piperidones (III), together with the corresponding α- and β-4-piperidinols, (IV) and (V), reveal that Bohlman's Correlation (I) must be applied with caution to systems other than quinolizidines or to quinolizidines whenever ring distortions may be involved.

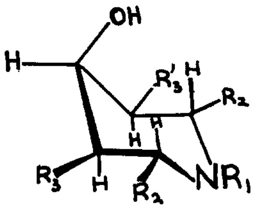




(III)



(IV)



(V)

Derivatives of (III), (IV) and (V) studied:

(a) $R_1=R_3=R_3'=H$,
$R_2=C_6H_5$.

(b) $R_1=CH_3$,
$R_2=C_6H_5$,
$R_3=R_3'=H$.

(c) $R_1=R_3'=H$,
$R_2=C_6H_5$,
$R_3=CH_3$.

(c) $R_1=R_3=CH_3$,
$R_2=C_6H_5$,
$R_3'=H$.

(e) $R_1=H$,
$R_2=C_6H_5$,
$R_3=R_3'=CH_3$.

(f) $R_1=R_3=R_3'=CH_3$,
$R_2=C_6H_5$.

The relevant observations are (solvent - $CCl_4$):

(i) Morpholine (1.6) and N-methyl-morpholine (6) both show distinct and relatively strong absorptions between 2700-2800 $cm^{-1}$,

(ii) All 2.6-diphenyl-4-piperidones (III) with $R_1=H$ show peaks only at 2725 $cm^{-1}$(w), 2790 $cm^{-1}$(s) and no obvious shoulders or absorptions in between.

(iii) All derivatives of (III) with $R_1=CH_3$ give a very strong N-Me absorption around 2780-2790 $cm^{-1}$ with no obvious shoulders in the 2700-2800 $cm^{-1}$ region.

(iv) All α-2.6-diphenyl-4-piperidinols (IV) with $R_1=H$ absorb at 2725 $cm^{-1}$(w), 2790 $cm^{-1}$(s), 2805 $cm^{-1}$(s) and show not very distinct shoulders around 2750-2760 $cm^{-1}$.

(v) All derivatives of (IV) with $R_1=CH_3$ show very strong N-Me absorptions around 2775-2780 $cm^{-1}$ which dominate the 2700-2800 $cm^{-1}$ region.

(vi) All β-2.6-diphenyl-4-piperidinols (V) with $R_1=H$ do not absorb in the 2700-2800 cm$^{-1}$ region; only tailings from strong absorptions in 2800-3100 cm$^{-1}$ are evident in the spectra. Weak absorptions are observable at 2725 cm$^{-1}$.

(vii) All derivatives of (V) with $R_1$=$CH_3$, again, exhibit a very prominent Ir-Me absorption between 2785-2790 cm$^{-1}$ and reveal no fine structures.

Since morpholine (I) and N-methyl-morpholine (II) have been shown (7) to exist in equilibria (A)$\leftrightarrow$(B), and for compound (I) the contribution from the conformer (B) is quite appreciable [see also ref.(8)], the presence of the absorption bands in the 2700-2800 cm$^{-1}$ does not, therefore, guarantee a unique disposition of the nitrogen lone-pair on a six-membered heterocyclic ring. [For a different attitude, see ref.(9)]. The absences of absorptions around 2760 cm$^{-1}$ - which seem to be the key points in Bohlman's Correlation (1, 2b) - in all the non-N-methylated and, very possibly, the N-methylated 4-piperidones and 4-piperidinols studied, can either be interpreted, in all cases, by the lone pairs on the nitrogen atoms of these conformationally rigid piperidine derivatives [the 2.6-disubstitution by phenyl groups requires that no inversion of the heterocyclic rings is possible, at least, at 1.2.6 positions (10)] being oriented equatorially and, thus, having no antiparallel C-H bonds in the α-positions or by concluding that Bohlman's correlation (1) does not hold for this series of compounds. Physical studies (8, 11) have shown that the first alternative is highly improbable. It seems to us that if the so-called "characteristic" band in the 2700-2800 $cm^{-1}$ region really has its origin in the orbital overlap of the lone pair and the neighboring $C\text{-}H_{axial}$ orbital, then such an overlap would be very sensitive to any distortions of the ring systems involved [e.g. compounds VIIIb, VIIIc, Xa and Xb in ref.(2a)]. Such a view receives further support from the similarities between the infrared spectra of compounds (III) and (IV) with R=H in the 2700-2800 $cm^{-1}$ region [these compounds, being known (11, 12) to exist essentially in relatively undistorted chair conformations], and the differences between their spectra and those of β-4-piperidinols (V) where the diaxial interactions (12) between the $C_2, C_6$ axial hydrogens and the axial $C_4$ hydroxyl group certainly can introduce some modification of the geometries of the six-membered rings compared with those in 4-piperidones (III) and α-4-piperidinols (IV).

The discrepancy between the i.r. spectral and optical rotational data for the stereochemistry at $C_3$ of some 3-substituted yohimbane derivatives reported recently (13) probably can also be explained if the distortion of the quinolizidine skeleton is taken into consideration.

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