

CONFORMATIONAL STUDY OF 3,5-DIMETHYL-2,6-DIPHENYL-4-PIPERIDINOLS\*

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The infrared spectrum of the  $\alpha$ -isomer of 1,3,5-trimethyl-2,6-diphenyl-4-piperidinol (Ia) was reported to show two distinct peaks in the region of 3500 to 3650  $\text{cm}^{-1}$  which were said to result from the unbonded and hydrogen-bonded OH (1). To rationalize the formation of an intramolecular hydrogen bond, it was necessary to propose that the non-bonded interactions of the equatorial methyl and phenyl groups were sufficient to cause a boat conformation of the 6-membered ring to be energetically favorable. The relative stability of this boat form has been questioned by Eliel (2) and Tichy (3). The lack of any obvious reason that there would be relief of non-bonded interactions by a conformational change from a distorted chair form to a boat form (2) caused us to reexamine the experimental data reported by the previous authors (1).

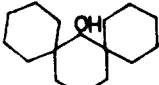
The infrared spectra of the  $\alpha$ -isomers of 1,3,5-trimethyl-2,6-diphenyl-4-piperidinol (Ia) and 3,5-dimethyl-2,6-diphenyl-4-piperidinol (Ib) were examined in carbon tetrachloride, and indeed two absorption bands which could be assigned to OH stretching vibrations were evident. A comparison of these absorption bands with the unbonded or  $\pi$ -bonded hydroxyls of comparable piperidinols showed, however, that the lower frequency band corresponded to the normal frequency of the hydroxyl and the second band at higher frequency was the unusual absorption (Figure 1). These findings suggested that the interpretation that hydrogen bonding to nitrogen had caused an absorption at lower energy was incorrect, and the presence of two absorption bands

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resulted from some structural feature which caused an increase in absorption frequency.\* Similar results have been noted with a number of hindered alcohols (4). It has been shown that the rotational conformers of the alcohols lead to absorption bands with different energies and, therefore, different frequencies. Thus, in a 6-membered ring the equatorial alcohols, with three rotational conformations, show an unsymmetrical OH absorption while the axial alcohol, capable of only two rotational conformers that are energetically favorable, gives a symmetrical absorption band (see Figure 2) (4a).

Table 1  
Hydroxyl Stretching Vibrations of Hindered Alcohols

Compounds	Infrared Bands cm <sup>-1</sup>		Ref.
$\alpha$ -1,3,5-Trimethyl-2,6-diphenyl-4-piperidinol (1a)	3647	3607	a
$\beta$ -1,3,5-Trimethyl-2,6-diphenyl-4-piperidinol (2a)	3650	----	a
$\alpha$ -3,5-Dimethyl-2,6-diphenyl-4-piperidinol (1b)	3652	3614	a
$\beta$ -3,5-Dimethyl-2,6-diphenyl-4-piperidinol (2b)	3654	----	a
1,3,5-Trimethyl-2,4,6-triphenyl-4-piperidinol (3)	3621		a
3,5-Dimethyl-2,4,6-triphenyl-4-piperidinol (4)	3624		a
1,1,3,3-Tetramethyl-2-indanol	3642	3628	b
2,6-Dimethylcyclohexan-1,4-diol	3643		c
2,6-Dimethylcyclohexanol	3650	3615	a
5 $\alpha$ -Cholestan-7 $\beta$ -ol	3650	3619	d
2,2,4,4-Tetramethylpentan-3-ol	3651	3626	d
5 $\alpha$ ,17 $\alpha$ -Pregnan-20 $\alpha$ -ol	3648	3622	e
1,5-Dimethylbicyclo [3,3,1] nonan-9-ol	3643	3625	f
	3652	3631	b

a. This work. b. The sample was kindly given to us by A. P. Krapcho, University of Vermont.  
c. Unpublished data of Robert Stolow, Tufts University. d. Reference 5. e. Reference 4d.  
f. References 4c and 4e.

\*During the course of this investigation Aaron, Ferguson and Rader also commented on these data (J. Am. Chem. Soc., 89, 1431 (1967) see footnote 37). Their comments, however, only offered an explanation for the small frequency shift as being due to a weak intramolecular hydrogen bond.

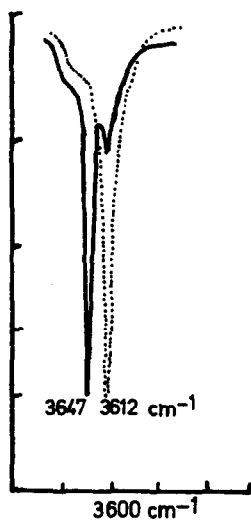


Figure 1. The infrared absorption due to the OH stretching vibration of 1a (————) and trans-1-methyl-4-phenyl-3-piperidinol (-----).

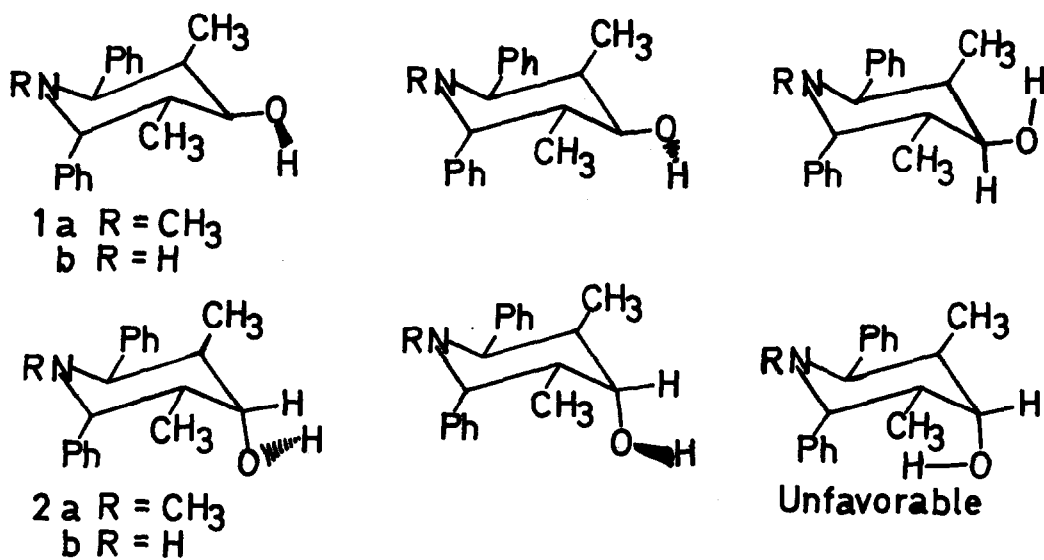


Figure 2. The possible rotational conformations of the hydroxyl groups in 1a and 2a.

The frequency of the absorption band due to the OH stretching vibration has been shown to increase with an increase in the degree of substitution of the  $\beta$  carbon atom trans and coplanar with the OH (5).  $\alpha$ -3,5-dimethyl-2,6,-diphenyl-4-piperidinols (Ia and b), with an equatorial hydroxyl, has two rotational conformers in which the OH bond is trans and coplanar to the substituted carbons at 3- or 5-positions and only one rotational conformer with the hydrogen trans and coplanar to the OH bond. Thus a large absorption at a frequency higher than that observed with secondary alcohols in which there is no highly substituted  $\beta$ -carbon would be expected. With the hydroxyl group in the axial conformation, as in 2, there are only two rotational conformers which are energetically favorable, and both of these have a substituted  $\beta$ -carbon trans and coplanar with the OH. Thus a single absorption band at the higher frequency was anticipated and was observed.

Thus, intramolecular hydrogen bonding need not be involved in the presence of the two absorption bands in the spectra of these piperidinols (1 and 2), and the earlier conformational assignments based on these data would then be in error. That a heterocyclic nitrogen was not necessary to show these two absorption bands in the  $3650\text{--}3500\text{ cm}^{-1}$  region of the spectrum was shown by the comparable spectra of several alkanols (Table 1). It is quite evident with these compounds that three rotational conformers are possible. The high frequency absorption resulted from the rotational conformers which had a highly substituted  $\beta$ -carbon trans and coplanar with the OH bond.

1,3,5-Trimethyl-2,4,6-triphenyl-4-piperidinol (3) and 3,5-dimethyl-2,4,6-triphenyl-4-piperidinol (4) were prepared. The steric strain in these heterocycles should emphasize the importance of any non-chair conformation and increase the strength of any intramolecular hydrogen bond. The absorption band due to the OH stretching vibration indicated only a weak  $\text{OH} \rightarrow \pi$  bond with the geminal phenyl substituent.

It is clear, therefore, that the presence of two maxima in the OH stretching region does not require the postulation of non-chair conformations for the 3,5-dimethyl-2,6-diphenyl-4-piperidinols (Ia and b). The remaining evidence for non-chair conformations of 1a and b was based on the coupling constants between the 4-proton and the adjacent hydrogens (6). It has recently been shown that the coupling constants obtained from models having no vicinal substituents cannot be used for the conformational analysis of compounds which do have vicinal substituents (7). There is, therefore, no evidence available which is not consistent with a slightly distorted chair as the conformation of the 6-membered ring of the 3,5-dimethyl-2,6-

diphenyl-4-piperidinols (1 and 2).

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