

INVESTIGATION OF THE SPATIAL ORIENTATION OF THE HYDROXY
GROUP AND THE INTRAMOLECULAR HYDROGEN BOND IN STEREO-
ISOMERIC 2,9-DIMETHYL- AND 1,2,9-TRIMETHYLDECAHYDRO-
4-QUINOLOLS AND THEIR 4-ETHYNYL-SUBSTITUTED DERIVATIVES
BY IR SPECTROSCOPY

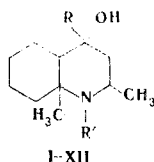
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The spatial orientation of the hydroxy group in stereoisomeric 2,9-dimethyl- and 1,2,9-trimethyldecahydro-4-quinolols and their 4-ethynyl-substituted derivatives was established by IR spectroscopy. The formation of an intramolecular hydrogen bond in the equatorial isomers of trans- and cis-2,9-dimethyl- and 1,2,9-trimethyldecahydro-4-quinolols and cis-2,9-dimethyl- and 1,2,9-trimethyl-4-ethynyldecahydro-4-quinolols, which leads to a small degree of distortion of the chair conformation of the heteroring, was demonstrated. The enthalpy of formation of the hydrogen bond was calculated.

The spatial orientation of the hydroxy group in stereoisomeric trans-fused 1,2,7-trimethyl- and 1,2-dimethyl-7-tert-butyldecahydro-4-quinolols is reliably established from the ν_{OH} frequency of the alcohols and the form of the band of the stretching vibrations of the C-O bonds of their acetates [1]. The ν_{OH} frequency is 3-7 cm^{-1} lower in the case of the equatorial isomers than in the case of the axial isomers, and the spectra of their acetates contain one ν_{C-O} band at 1200-1260 cm^{-1} , while the spectra of the acetates of the axial alcohols contain two absorption bands. A convenient characteristic for the identification of the equatorial isomers of 1,2,7-substituted decahydro-4-quinolols was also the presence, in addition to the principal ν_{OH} band, of a band or shoulder at 3600-3605 cm^{-1} due to the formation of an intramolecular hydrogen bond between the equatorial hydroxy group and an axial free electron pair of the nitrogen atom. It is apparent from an examination of Dreiding molecular models that the distance between the proton of the hydroxy group and the nitrogen atom in the decahydroquinoline alcohols in the chair conformation is 4.2-4.3 Å and is insufficient for the realization of an intramolecular hydrogen bond. It is assumed [2, 3] that hydrogen bonding is realized at distances that do not exceed the sum of the van der Waals radii of the interacting atoms. The observed intramolecular association in the equatorial isomers of the alcohols is thus associated with a small degree of distortion of the chair conformation of the heteroring, since the sum of the van der Waals radii of the nitrogen and hydrogen atoms is 3.7 Å.

In the present research we used IR spectroscopy to establish the spatial orientation of the hydroxy group and to study the intramolecular hydrogen bonding in trans- and cis-fused decahydroquinoline alcohols I-XII:



I-VIII R = H; IX-XII R = C≡CH;
I-IV, IX, X R' = H; V-VIII, XI, XII R = CH₃

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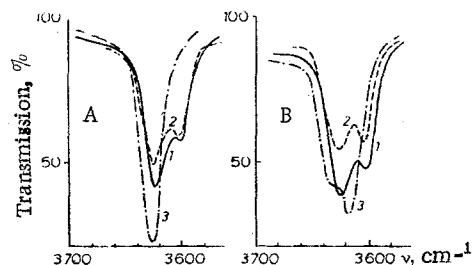


Fig. 1. Spectra of trans- (A) and cis-fused (B) equatorial isomers II and IV (1), VI and VIII (2), and axial isomers I and III (3).

TABLE 1. ν_{OH} Frequencies of the Stereoisomeric Alcohols and ν_{C-O} Frequencies of Their Acetates

Compound	Isomer	mp, °C	ν_{OH} , cm^{-1}	ν_{C-O} , cm^{-1}
trans-2,9-Dimethyldecahydro-4-quinolol	I	133	3626	—
	II	162	3626 and 3600	—
cis-2,9-Dimethyldecahydro-4-quinolol	III	150	3616 and 3630	—
	IV	150	3623 and 3600	—
trans-1,2,9-Trimethyldecahydro-4-quinolol	V	172	3628	1232 and 1255
	VI	122	3628 and 3600	1243
cis-1,2,9-Trimethyldecahydro-4-quinolol	VII	45	3620	1247
	VIII	72	3626 and 3602	1240 and 1248
trans-2,9-Dimethyl-4-ethynyldecahydro-4-quinolol	IX	143	3608	—
cis-2,9-Dimethyl-4-ethynyldecahydro-4-quinolol	X	102	3607—3598 broad maximum	—
trans-1,2,9-Trimethyl-4-ethynyldecahydro-4-quinolol	XI	147	3611	1232 and 1220
cis-1,2,9-Trimethyl-4-ethynyldecahydro-4-quinolol	XII	143	3603 and 3612	1234 and 1212

Secondary alcohols I-VI were synthesized by reduction of the individual cis- and trans-1,2,9-trimethyldecahydro-4-quinolones. Alcohols I and II, III and IV, and V and VI are epimeric pairs with respect to the 4 position, each of which was obtained from the corresponding decahydroquinolone isomer. Acetylenic alcohols IX-XI were obtained by ethynylation of the same ketones, during which only one alcohol isomer is formed from each ketone. Secondary alcohols VII and VIII and acetylenic alcohol XII were obtained by methylation of the nitrogen atom of alcohols V, VI, and XI. The synthesis and establishment of the structures of the investigated compounds by PMR spectroscopy and chemical methods were described in detail in [4].

It is apparent from Table 1 that the IR spectra of trans-alcohols I and V contain one ν_{OH} band at 3626 and 3668 cm^{-1} , respectively, while the spectra of their C_4 epimers II and VI, in addition to the principal band at the same frequencies, contain a band at 3600 cm^{-1} (Fig. 1, curve A). On the basis of this, an equatorial orientation of the hydroxy group should be assigned to alcohols I and V. The correctness of this assignment is also confirmed by the form of the ν_{C-O} band in the spectra of the acetates of the stereoisomeric trans-1,2,9-trimethyldecahydro-4-quinolols.

The spectra of cis-alcohols IV and VIII (Fig. 1, curve B) contain an additional band at 3600 cm^{-1} , and an equatorial orientation of the OH group should therefore be assigned to them. However, one band at 1248 cm^{-1} with a shoulder at 1240 cm^{-1} is observed in the spectrum of the acetate of isomer VIII in the region of the ν_{C-O} absorption. Epimer VII, which has a symmetrical ν_{OH} band at 3620 cm^{-1} , should have an axial orientation of the hydroxy group; however, a solitary band at 1247 cm^{-1} is observed in the spectrum of its acetate.

It is apparent that the correspondence between the form of the ν_{C-O} band, which reflects rotational isomerism of the ester group, and the orientation of the acetoxy group that was

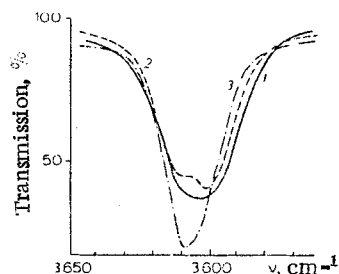


Fig. 2

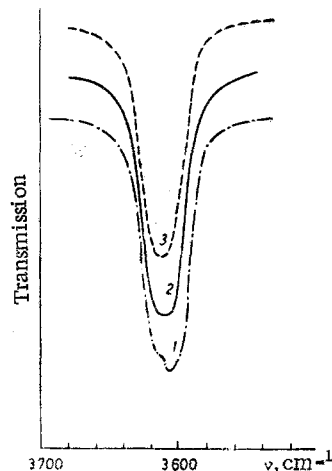


Fig. 3

Fig. 2. Spectra of equatorial isomers X (1) and XII (2) and axial isomer IX (3).

Fig. 3. Spectra of alcohol XII at 22 (1), 50 (2), and 70°C (3).

established in [1, 5] for the acetates of trans-fused alcohols of the decahydroquinoline series, is not satisfied in the case of alcohols with cis-fused rings. The differences in the manifestation of rotational isomerism of the ester group in the acetates of cis- and trans-decahydroquinolols are clearly apparent during an examination of molecular models.

In the case of the acetates of trans-decahydro-4-quinolols, when the equatorial acetoxy group rotates, it interacts with the equatorial 5-H proton, while the axial acetoxy group interacts with the axial 2-, 5-, and 9-H protons, which leads to the existence of one rotamer in the first case and three rotamers in the second case. It should be noted that three rather than two $\nu_{C=O}$ bands were more often observed in the spectra of the previously examined [1, 5] acetates of axial trans-fused decahydro-4-quinolols. This interesting fact requires special examination.

In acetates of cis-decahydro-4-quinolols with an equatorial acetoxy group the rotation of the latter is hindered as a consequence of interaction with the 5- and 6-H protons, and the existence of two rotameric forms is possible. In the case of an axial orientation of the acetoxy group complete rotation of the latter is impossible because of close approach to the carbocycle. For this acetate one might expect the existence of two rotational isomers, viz., one that is restricted by the 2- and 5-H protons and another that is restricted by the 2- and 8-H protons; the second rotamer is unlikely because of stronger steric interactions. Thus, the establishment of the spatial orientation of the ester group in acetates of cis-fused alcohols on the basis of the form of the $\nu_{C=O}$ band is ambiguous: A doublet absorption band may be observed in the spectrum both in the case of an axial orientation and in the case of an equatorial orientation of the acetoxy group. However, the solitary $\nu_{C=O}$ band is most likely a sign of an axial orientation of the acetoxy group. Taking into account the information set forth above, one should assign an equatorial orientation of the OH group to isomers IV and VIII and an axial orientation to isomer VII. Alcohol III, from which alcohol VIII was obtained, also has an axial OH group. However, a complex ν_{OH} band with a maximum at 3616 cm^{-1} and a shoulder at 3630 cm^{-1} , the origin of which could not be explained, is characteristic for the spectrum of this alcohol (Fig. 1, curve B). Our measurements of the band contour showed that no appreciable changes in the intensities of its components occur at 22–70°C.

One's attention is drawn to the fact that cis-2,9-dimethyl- and 1,2,9-trimethyldecahydro-4-quinolols are characterized by lower ν_{OH} values than the corresponding trans alcohols (Table 1). In contrast to the previously examined [1] trans-2,7-dimethyl- and 1,2,7-trimethyldecahydro-4-quinolols, the equatorial isomers have higher ν_{OH} frequencies than the axial isomers in series of epimeric pairs of cis-2,9-dimethyl- and 1,2,9-trimethyldecahydro-4-quinolols. The fact that the axial and equatorial epimers of trans-2,9- and 1,2,9-substituted secondary alcohols have identical ν_{OH} values is also curious.

TABLE 2. Frequency Shifts ($\Delta\nu_{OH}$) and Enthalpies of Formation of the Intramolecular Hydrogen Bonds in the Equatorial Isomers of the Alcohols

Isomer	$\Delta\nu_{OH}, \text{cm}^{-1}$	$\Delta H_1,$ kcal/mole	$\Delta H_2,$ kcal/mole
II	26	0,36	0,38
IV	23	0,35	0,40
VI	28	0,38	0,40
VIII	24	0,35	0,37
X	~10	—	—
XII	11	—	0,28

As we noted above, acetylenic alcohols IX-XII do not have epimers with respect to the C_4 center, and the establishment of the orientation of the hydroxy group for them is less reliable. However, the presence of a solitary band at 3611 cm^{-1} in the spectrum of trans-alcohol XI and of a band at 1232 cm^{-1} with a shoulder at 1220 cm^{-1} in the spectrum of its acetate makes it possible to assign an axial orientation for the OH group in this alcohol. trans-Alcohol IX is conformationally related to alcohol XI and also should have an axial orientation of the hydroxy group. cis-Alcohol X is characterized by a broad maximum band at $3595\text{-}3610 \text{ cm}^{-1}$ (Fig. 2, curve 1), which is the superimposition of two closely located bands of free and associated hydroxy groups. The maxima of the bands are separated appreciably in the spectrum of cis-alcohol XIII (Fig. 2, curve 2), which was obtained by methylation of alcohol X at the nitrogen atom. The changes in the intensity of the absorption of the free and associated hydroxy groups in the spectrum of alcohol XII at $22\text{-}70^\circ\text{C}$ are presented in Fig. 3. On the basis of the presence in the spectra of alcohols X and XII of two ν_{OH} bands and the doublet form of the $\nu_{C=O}$ band in the spectrum of the acetate of isomer XII, an equatorial orientation of the OH group should be assigned to these alcohols.

Thus, a distinctive feature of the equatorial isomers of cis- and trans-2,9-dimethyl- and 1,2,9-trimethyldecahydro-4-quinolols, as well as cis-2,9-dimethyl- and 1,2,9-trimethyl-4-ethynyldecahydro-4-quinolols, examined in this research is the formation of an intramolecular hydrogen bond. The ability of the hydroxy group and the unshared pair of electrons of the nitrogen atom to form an intramolecular hydrogen bond depends first and foremost on such factors as their proton-donor and proton-acceptor properties and the form of the energy function for inversion of the chair conformation of the heteroring [6, 7]. These factors will determine the distance at which the atoms that form the intramolecular hydrogen bond interact and upon which the magnitude of the $\Delta\nu_{OH}$ shift and the energy of this bond depend [2]. Low values of the $\Delta\nu_{OH}$ shift and the enthalpy of formation of the intramolecular hydrogen bond ($< 0.5 \text{ kcal/mole}$, Table 2) in the equatorial isomers of the alcohols indicate that the realization of intramolecular association leads to small distortions of the chair conformation of the heteroring, while the length of the intramolecular hydrogen bond differs only slightly from the sum of the van der Waals radii of the nitrogen and hydrogen atoms; the $\Delta\nu_{OH}$ and ΔH values for the cis alcohols are somewhat lower than for the trans alcohols, which can be explained by the small decrease in the conformational mobility of the chair conformation of the heteroring in the case of cis fusion. The intramolecular hydrogen bonds in acetylenic alcohols X and XII, in the spectra of which the $\Delta\nu_{OH}$ shifts are lower by a factor of 2.5 than in the spectra of the secondary alcohols, operate at a relatively large distance; this is evidently associated with compression of the heteroring when an ethynyl substituent is attached. One must also assume that the heteroring is compressed to a greater degree in the trans-fused alcohols than in the cis-fused alcohols, since the formation of intramolecular hydrogen bonds is not observed in the equatorial isomers of trans-fused 1-alkyl-4-ethynyl- and 1-alkyl-4-ethyldecahydro-4-quinolols [8].

The fact that the ratio of the intensities of the bands of associated and free OH groups is higher for the cis isomers of the alcohols than for the trans isomers (Fig. 1) should be noted. This can be explained by the large population of the axial orientation of the unshared electron pair of the nitrogen atom or by intensification of the proton-donor properties of the hydroxy groups in the cis alcohols. Methylation of the nitrogen atom (isomers IV, VIII, and XII) increases the proton-acceptor capacity of the unshared electron pair [9] and is accompanied by an increase in the intensities of the bands of the associated hydroxy

groups (Figs. 1 and 2). The latter is also explained by reorientation of the free electron pair from an equatorial to an axial orientation in the resulting tertiary base.

EXPERIMENTAL

The spectra of the investigated compounds were measured with a UR-20 spectrometer; the scanning rate was 25 cm⁻¹/min, and the spectral slit width was 4.9 cm⁻¹ at 3600 cm⁻¹ and 4.5 cm⁻¹ at 1250 cm⁻¹. The spectra of the alcohols were recorded from solutions in CCl₄ in a 2-cm thick fluorite cuvette at concentrations of 2-3.5·10⁻³ mole/liter, the spectra of the esters of the secondary alcohols were recorded from thin films between KBr windows, and the spectra of the esters of the acetylenic alcohols were recorded from solutions in CCl₄ and in KBr pellets. The accuracy in reproducing the wave numbers was ± 1 cm⁻¹. A thermostatted cell was used for the temperature measurements. The temperature of the cuvette was monitored by means of copper-constantan thermocouple with an accuracy of ± 1°C.

The enthalpies of formation of the intramolecular hydrogen bonds were determined by two methods, viz., from the temperature dependence of the integral intensities (for the ΔH₁ values in Table 2) and from the optical densities (for the ΔH₂ values in Table 2) of the bands of the free and associated hydroxy groups. The error in the determination of the energies by the two methods was ± 0.05 kcal/mole for the secondary alcohols. The van't Hoff equation in the following form was used in the calculations by the first method:

$$\Delta H = \frac{RT_1T_2}{T_2 - T_1} \ln \frac{K_{T_2}}{K_{T_1}},$$

where the K_{T₁} and K_{T₂} equilibrium constants were found from the ratio of the areas of the bands of the free and associated OH groups at arbitrarily selected temperatures T = 283 and 253 °K. The areas of the bands that were separated by a graphical method [10] were found by planimetry. The following expression of the van't Hoff equation was used in the calculations by the second method:

$$\Delta H = \frac{RT_1T_2}{T_2 - T_1} \ln \frac{D_1^{T_1} \cdot D_2^{T_2}}{D_1^{T_2} \cdot D_2^{T_1}},$$

where D₁^{T₁} and D₁^{T₂} are the optical densities at the maximum bands of the associated groups, D₂^{T₁} and D₂^{T₂} are the optical densities of the maximum bands of the free groups, and T₁ and T₂ are the arbitrarily selected temperatures of 296 and 343°K.

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