# AN INVESTIGATION OF THE CONFORMATION OF DECAHYDROQUINOLINE DERIVATIVES BY PROTON MAGNETIC RESONANCE*

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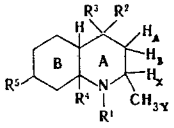
The configurations of a number of 1,2-, 1,2,7-, and 1,2,9-substituted decahydroquinolin-4-ones and decahydroquinolin-4-ols have been established by the PMR method. The values of the vicinal spin-spin coupling constants in the heterocyclic ring A of the compounds studied are characteristic and permit the conformation of a methyl group in position 2 to be determined. The nature of the PMR spectra in the series studied depends on the nature of the solvent, and in a number of cases this can be used for analytical purposes.

In order to study the relationship between structure and physiological activity in a number of decahydroquinoline derivatives (I) [2], it was necessary to determine the configurations of these compounds reliably. For this purpose, in addition to other methods such as mass spectrometry [3, 4], we have used the PMR method. It appeared likely that the analysis of the parameters of a multispin system, particularly for the angular protons and the $H_A$, $H_B$, and $H_X$ protons would permit the configurations of the individual centers and the conformation of the molecules of (I) as a whole to be judged. The present paper gives the results of an investigation of a large number of representatives of these substances by the PMR method.

A typical PMR spectrum for a compound (I) is shown in Fig. 1. The spectrum has the clearly resolved signals of all the protons of the heterocyclic part of the molecule, and also a poorly resolved multiplet from the protons of the carbocyclic ring B. The spectrum of the protons of the heterocyclic ring A consists of an $ABXY_3$ spin system. Irradiation with a strong radiofrequency field at the frequency of the protons of the 2-$CH_3$ group (Y) (double resonance) simplifies the spectrum to that of an ABX system. This is the way in which the parameters of the spectra for the 17 decahydroquinolines (I) given in the table were calculated.



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In some of the spectra, some of the lines of the $ABXY_3$ system overlap other lines of the spectrum, and for their isolation it was necessary to make use of the dependence of the chemical shifts on the properties of the solvent. In a number of cases a change of solvent did not lead to the desired changes in the spectral pattern, the majority of these relating to compounds (I) with an equatorial methyl group in position 2. The spectrum of the $H_X$ proton for such decahydroquinolines is located in a stronger field than for compounds with an axial methyl group and is superposed on the unresolved part of the spectrum of the protons of the carbocyclic ring B. The linkage of the rings in the molecules (I) was assigned on the basis

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*For a preliminary communication, see [1].

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TABLE 1. Chemical Shifts (δ) and Spin–Spin Coupling Constants (J) of the Decahydroquinoline Derivatives (I)

| Comp. | A/B linkage | Solvent | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | δ, ppm | | | | J, Hz | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | A | B | X | Y (*a*) | AB | AX | BX | XY |
| II | trans | $C_6H_6$ | $CH_3$ | C≡CH (*e*) | OH (*a*) | H | H | 2,43 | 1,86 | 2,97 | 1,14 | 14,0 | 6,2 | 1,8 | 7,0 |
| III | trans | $CDCl_3$ | $CH_3$ | $CH{=}CH_2$ (*e*) | OH (*a*) | H | H | 2,11 | 1,55 | 3,18 | 1,20 | 14,0 | 6,3 | 1,3 | 7,0 |
| | | $C_6H_6$ | | | | | | 1,96 | 1,34 | 2,92 | 1,16 | 14,0 | 6,1 | 1,9 | 7,0 |
| IV | trans | $CDCl_3$ | $CH_3$ | $C_2H_5$ (*e*) | OH (*a*) | H | H | 2,02 | 1,54 | 3,18 | 1,18 | 14,0 | 6,3 | 1,3 | 7,0 |
| | | $C_6H_6$ | | | | | | 1,72 | 1,43 | 2,98 | 1,17 | 14,0 | 6,3 | 1,3 | 7,0 |
| V | trans | $CDCl_3$ | $CH_3$ | $COCH_3$ (*e*) | OH (*a*) | H | H | 2,50 | 1,62 | 3,28 | 1,19 | 13,0 | 6.1 | 1,5 | 7,0 |
| | | $C_6H_6$ | | | | | | 1,78 | 1,13 | 2,97 | 1,19 | 12,5 | 6,3 | 1,3 | 7,0 |
| VI | trans | $C_6H_6$ | $CH_3$ | $CH{=}CH_2$ (*e*) | OH (*a*) | H | H | 1,48 | 1,28 | 2,43 | 0,97* | 14,0 | 11,6 | 3,0 | 6,5 |
| VII | trans | $C_6H_6$ | $CH_3$ | $COCH_3$ (*e*) | OH (*a*) | H | H | 1,53 | 1,09 | 2,56 | 0,93* | 12,5 | 11,5 | 2,5 | 6,0 |
| VIII | trans | $CDCl_3$ | $CH_3$ | O | | H | H | 2,86 | 2,13 | 3,43 | 0,93 | 13,0 | 6,6 | 2,0 | 6,5 |
| | | $C_6H_6$ | | | | | | 2,57 | 1,94 | 3,03 | 0,72 | 12,5 | 6,1 | 1,9 | 6,5 |
| | | $CS_2$ | | | | | | 2,71 | 1,96 | 3,32 | 0,90 | 12,0 | 6,0 | 2,0 | 6,5 |
| IX | trans | $CDCl_3$ | H | O | | H | H | 2,71 | 2,16 | 3,69 | 1,13 | 13,0 | 6,9 | 1,7 | 7,0 |
| | | $C_6H_6$ | | | | | | 2,26 | 1,96 | 3,26 | 0,88 | 13,0 | 6,5 | 2,1 | 7,0 |
| X | cis | $CDCl_3$ | H | O | | H | H | 2,69 | 2,13 | 3,73 | 1,13 | 13,0 | 6,8 | 1,8 | 6,5 |
| | | $C_6H_6$ | | | | | | 2,24 | 1,94 | 3,20 | 0,85 | 13,0 | 6,6 | 2,0 | 7,0 |
| XI | trans | $CDCl_3$ | $COC_6H_5$ | O | | H | H | 2,44 | 2,07 | 4,30 | 1,23 | 14,0 | 6,9 | 2,1 | 7,0 |
| | | $C_6H_6$ | | | | | | 2,03 | 1,68 | 3,92 | 0,73 | 14,0 | 7,4 | 2,0 | 7,0 |
| XII | cis | $CDCl_3$ | $COC_6H_5$ | O | | H | H | 2,85 | 2,37 | 4,53 | 1,20 | 17,5 | 6,9 | 1,7 | 7,0 |
| | | $C_6H_6$ | | | | | | 2,34 | 1,94 | 4,20 | 0,80 | 17,5 | 6,7 | 1,9 | 7,0 |
| XIII† | cis | $CDCl_3$ | $COC_6H_5$ | O | | H | H | 2,78 | 2,22 | — | 1,30* | 15,0 | 8,0 | 4,0 | 7,0 |
| XIV | trans | $CDCl_3$ | $CH_3$ | C≡CH | OH | H | $CH_3$ | 1,92 | 1,45 | 3,12 | 1,15 | 14,5 | 6,2 | 1,8 | 6,5 |
| XV | trans | $C_6H_6$ | $CH_3$ | $CH{=}CH_2$ | OH | H | $CH_3$ | 2,34 | 1,84 | 2,93 | 1,13 | 13,5 | 5,6 | 2,0 | 6,5 |
| XVI | trans | $C_6H_6$ | $CH_3$ | $C_2H_5$ | OH | H | $CH_3$ | 2,37 | 1,85 | 2,95 | 1,13 | 13,5 | 5,7 | 1,3 | 6,5 |
| XVII | trans | $C_6H_6$ | $CH_3$ | $COCH_3$ | OH | H | $CH_3$ | 1,99 | 1,09 | 2,97 | 1,18 | 12,5 | 6,0 | 1,4 | 6,5 |
| XVIII | trans | $CDCl_3$ | $CH_3$ | $COCH_3$ | OH | $CH_3$ | H | 1,71 | 1,30 | 2,90 | 1,09* | 12,0 | 11,0 | 2,6 | 6,5 |

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*2-$CH_3$ group equatorial.

† Values of J found from the $AMXY_3$ spectrum.

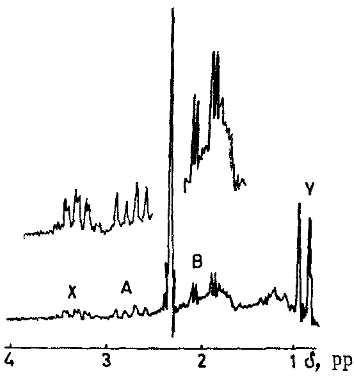

Fig. 1. PMR spectrum of 1,2-dimethyl-trans-decahydroquinolin-4-one in $CS_2$.

of the method of preparation [5] and also in accordance with Musher's rule [6, 7], which has previously been applied successfully to the analysis of complex nitrogen-containing heterocycles [8, 9]. Particular attention must be devoted to the fact that in the case of a cis-A/B linkage, regardless of the nature of the solvent, the $H_A$, $H_B$, and $H_X$ protons are deshielded more strongly than in the case of the trans-A/B linkage (compare the benzamides XI and XII). At the same time, there is practically no such difference for the pair of amino ketones (IX) and (X) (see Table 1).

It can be seen from the table that the conformation of the $C_2$ center can be judged from the $J_{AX}$ and $J_{BX}$ vicinal constants. In actual fact, with the axial arrangement of the $2\text{-}CH_3$ group the values of $J_{AX}$ are between 6.0 and 7.4 Hz and of $J_{BX}$ between 1.3 and 2.1 Hz. If, however, the $2\text{-}CH_3$ group is equatorial, the values of these constants rise considerably: $J_{AX} = 8.0\text{-}11.6$ Hz and $J_{BX} = 2.5\text{-}4.0$ Hz. The results obtained in this way agree with conclusions obtained from the chemical and mass-spectrometric investigation of compounds (I) (see, for example, [3,4] for substances II-VIII). Consequently, on the basis of the rules discussed above, the conformation of the $C_2$ center in a number of 1,2,7-trimethyldecahydroquinolin-4-ones (I) is ascribed as shown in Table 1 (XIV-XVII) from the characteristics of the PMR spectra.

When different solvents ($CDCl_3$, $C_6H_6$, $CS_2$, etc.) are used, a change is observed both in the values of the chemical shifts and in the spin–spin coupling constants, the greatest upfield shift of the signals of the $H_A$, $H_B$, and $H_X$ protons taking place in benzene solutions of the substances under study. The change in the values of the $J_{AX}$ and $J_{BX}$ constants does not exceed 0.6 Hz and cannot affect the validity of the concluclusions drawn on the conformation of the $C_2$ center. The observed change in the $J_{AB}$ geminal constant reaches somewhat greater values, amounting to 1.0 Hz for the amino ketone (VIII). As already mentioned, the dependence of the PMR spectra on the nature of the solvent was used to observe all the lines of the $ABXY_3$ spin system.

We may note that although for some others of the compounds studied all the lines of the type $ABXY_3$ spectra could not be isolated, nevertheless from the nature of the spectrum of the individual nuclei of this system and from the values of the $J_{AX}$ and $J_{BX}$ constants found from the spectrum in the AMX approximation it is possible to determine the conformation of the $2\text{-}CH_3$ group in a number of cases. This is the way in which the result given below for another five decahydroquinolines (I), not appearing in the table, were obtained: (XIX): $R^1 = CH_3$; $R^2$, $R^3 = O$; $R^4 = H$; $R^5 = CH_3$; $2\text{-}CH_3$ (a); (XX): $R^1 = CH_3$; $R^2 = CH = CH_2$; $R^3 = OH$; $R^4 = CH_3$; $R^5 = H$; $2\text{-}CH_3$ (e); (XXI): $R^1 = CH_3$; $R^2 = C_2H_5$; $R^3 = OH$; $R^4 = CH_3$; $R^5 = H$; $2\text{-}CH_3$ (e); (XXII): $R^1 = H$; $R^2$, $R^3 = O$; $R^4 = R^5 = H$; $2\text{-}CH_3$ (e); (XXIII): $R^1 = CH_3$; $R^2 = COCH_3$; $R^3 = OH$; $R^4 = H$; $R^5 = CH_3$; $2\text{-}CH_3$ (e).

In conclusion, it must be mentioned that the absence of a change in the values of the chemical shifts and the spin-spin coupling constants in a study of the temperature dependence of the spectra of solutions of N-methyl- and N-benzoyl-2-methyl-trans-decahydroquinolin-4-ones (VIII and IX, respectively) in $CS_2$ (down to −60°C) apparently shows that the conformations of these compounds are rigid.

## EXPERIMENTAL

The PMR spectra of the decahydroquinoline derivatives (I) were measured on a Varian DA-60 IL spectrometer using HMDS as internal standard. The chemical shifts are given in the δ scale relative to TMS.

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