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DIHYDROQUINOLONES—V*

HINDERED INVERSION IN DIHYDROQUINOLONES AND RELATED SYSTEMS

W. N. Speckamp, U. K. Pandit, P. K. Korver, P. J. van der Haak and H. O. Huisman
Laboratory for Organic Chemistry, University of Amsterdam, Nieuwe Achtergracht 129,
Amsterdam, The Netherlands

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Abstract—The NMR spectra of a number of benz[h]dihydroquinolones have been measured. The observed anomalies are explained in terms of a hindered nitrogen inversion.

The nature of the phenomenon was demonstrated by appropriate temperature scannings of the spectra and their comparison with the spectra of suitably chosen quinoline derivatives. In the spectrum of a β-disubstituted benz[h]dihydroquinolone the transition of an AB to an A_2 type system was shown to possess an activation energy of 23·0 ± 1·0 kcal/mol.

THE magnetic nonequivalence of stereochemically undistinguishable methylene protons in a variety of organic molecules has been the subject of several recent investigations. The factors responsible for such a nonequivalence are now recognized as, (a) restricted or prohibited internal rotation and conformational transformations[1] (b) presence of a centre of molecular asymmetry[2] (in the neighbourhood of the methylene group) and (c) restricted inversion of a nitrogen atom.[3] Nonequivalence can, and in many cases does, result from a combination of these factors.[4] It is important to note that whereas nonequivalence arising from conditions (a) and (c) may be averaged out by increasing the temperature, a similar averaging in case (b) cannot be achieved.

In the special case of a methylene group bonded to a nitrogen atom carrying two different substituents, blocking of the nitrogen inversion results in creation of an asymmetric environment in which the two methylene protons are unequally shielded. The consequential nonequivalence of geminal hydrogens in such a system is of the same type as that produced by proximity of an asymmetric carbon. A rapid inversion of the nitrogen bonds, however, would eliminate the cause of stereochemical asymmetry in such a molecule. In the NMR spectrum the latter transition will manifest itself in the collapse of the AB pattern for the methylene protons to a sharp singlet at the mean value of their individual chemical shifts. In view of the rapid inversion rates of tertiary amines[5] the asymmetric environment of a nitrogen atom is not commonly

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[*] Part IV: W. N. Speckamp and H. O. Huisman, *Rec. Trav. Chim.* (in press).

[1a] G. M. Whitesides, J. J. Grocki, D. Holtz, H. Steinberg and J. D. Roberts, *J. Amer. Chem. Soc.* **87**, 1058 (1965).

[1b] K. C. Dewhirst and C. A. Reilly, *J. Org. Chem.* **30**, 2870 (1965).

[2a] R. K. Hill and T. H. Chan, *Tetrahedron* **21**, 2015 (1965).

[2b] J. C. Randall, J. J. McLeskey, P. Smith and M. E. Hobbs, *J. Amer. Chem. Soc.* **86**, 3229 (1964).

[3a] A. T. Bottini and J. D. Roberts, *J. Amer. Chem. Soc.* **80**, 5203 (1958).

[3b] A. Loewenstein, J. F. Neumer and J. D. Roberts, *J. Amer. Chem. Soc.* **82**, 3599 (1960).

[4] R. Grashey, R. Huisgen, K. K. Sun and R. M. Moriarty, *J. Org. Chem.* **30**, 74 (1965).

[5] From calculations of Kincaid and Henriques[5a] a necessary condition for resolution of an amine at room temperature is $K_{inv} \ll 10^{-5}\ \text{sec}^{-1}$, corresponding to an inversion barrier of $E > 25$ kcal/mol.

[5a] J. F. Kincaid and F. C. Henriques Jr., *J. Amer. Chem. Soc.* **62**, 1474 (1940).

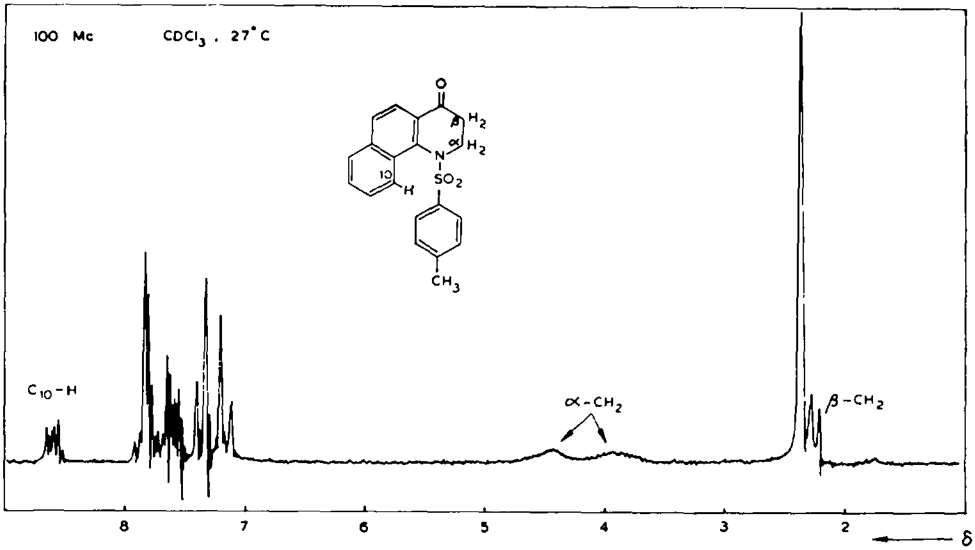

FIG. 1

detectable. However, in a few cases, measurable inversion rates have been successfully determined by NMR spectroscopy.

The inversion process of an amine, in which a nonplanar pyramidal nitrogen passes, through a planar transition state into its mirror image conformation, may be influenced by a variety of features inherent in the molecule. Reorganization of strained bonds, for example, appears to be energetically less feasible. Thus, while several aziridines[6] display a measurable extent of conformational stability, similar behaviour in larger nitrogen containing rings[7] has so far not been observed. On the other hand a lowering of the energy of the transition state for the inversion process, owing either to steric or electronic factors,[8] would be expected to cause an increase in the inversion rate. By the same reasoning, factors resulting in destabilization of the transition state for the inversion process could, in principle, cause the latter to slow down sufficiently so as to permit detection of the nitrogen in its pyramidal configuration. The first example of a slow amine inversion, caused by destabilization of the transition state owing to electronic factors, was described by Roberts.[8] More recently, a case of hindered nitrogen inversion, arising from a sterical destabilization of the transition state, was reported from this laboratory.[9] In the amine system I the unusually high energy barrier to inversion, observed in terms of the nonequivalence of α-methylene protons[10] (Fig. 1), was regarded as a consequence of steric interaction of the N—Ts group with the peri hydrogen at C_{10}.[11] The present investigation was aimed at a

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[6a] T. J. Bardos, C. Szantay and C. K. Navada, *J. Amer. Chem. Soc.* **87**, 5796 (1965).

[6b] A. B. Turner, H. W. Heine, J. Irving and J. B. Bush Jr., *J. Amer. Chem. Soc.* **87**, 1050 (1965).

[6c] A. L. Logothetis, *J. Org. Chem.* **29**, 3049 (1964).

[7] See Ref. 3*a*.

[8] D. L. Griffith and J. D. Roberts, *J. Amer. Chem. Soc.* **87**, 4089 (1965).

[9] W. N. Speckamp U. K. Pandit and H. O. Huisman, *Tetrahedron Letters*, 3279 (1964).

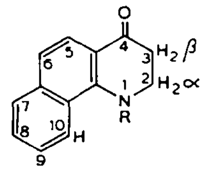
[10] The hydrogen atoms at C_2 are for reasons of convenience denoted as α-protons, similarly protons at C_3 are defined as β-protons.

[11] Decoupling experiments carried out by irradiating the β-protons did not change the shape of the α-proton signal.

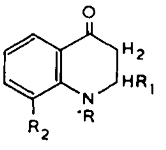
detailed examination of the factors affecting the inversion rate in substituted dihydroquinolone systems and at the scope and generality of the phenomenon.

In order to evaluate the influence of different structural features on the inversion process in systems such as I, we have examined the NMR spectra of substituted quinolines and benz[h]quinolines described in Table 1. The synthesis of compounds I–XIX has been reported elsewhere.[12] The choice of the latter quinoline derivatives was based upon several specific objectives. In the first place it was of considerable interest to investigate the generality of the phenomenon. Thus, several chemically different classes of compounds which possess the essential structural features are represented in the selection. As a simple model was chosen the N-benzenesulfonyl derivative II, in which the α- and β-methylene signals were not obscured by substituents carrying any interfering group. By a comparison of the T_c values[13] in the series of compounds XIV–XIX, which possess a substituent at the β-carbon, it was hoped to observe the influence of such substituents on the inversion process. Further, the relative simplicity of the expected spectra of these systems promised to afford a facile calculation of the energy parameters. Influence of the size of the substituent on the nitrogen atom was sought in a comparison of compounds II, III and IV; while the spectra of VII, VIII and X were expected to reveal the steric requirements necessary

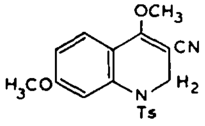
TABLE 1



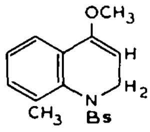
I R = Ts
II R = Bs
III R = Ms
IV R = H



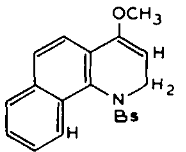
V R = Ts R_1 = H R_2 = H
VI R = Bs R_1 = CH_3 R_2 = H
VII R = Bs R_1 = H R_2 = CH_3
VIII R = Bs R_1 = CH_3 R_2 = CH_3



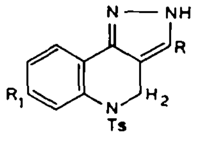
IX



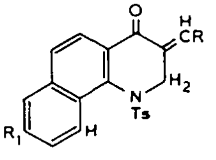
X

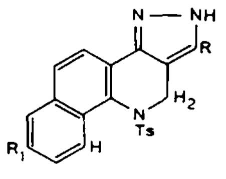


XI



XII R = H R_1 = H
XIII R = $COOCH_3$ R_1 = OCH_3





XIV R = OH R_1 = H
XV R = OH R_1 = OCH_3
XVI R = $COOCH_3$ R_1 = OCH_3

XVII R = H R_1 = H
XVIII R = H R_1 = OCH_3
XIX R = $COOCH_3$ R_1 = OCH_3

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[12] W. N. Speckamp and H. O. Huisman, Dihydroquinolones II and IV, *Rec. Trav. Chim.* (in press).
[13] T_c = coalescence temperature.

for hindering the inversion. In all classes of compounds studied the related two-ring systems, that is, compounds devoid of the angularly located aromatic ring, for example V, VI, IX, XII and XIII, were examined for purposes of comparison.

The NMR spectra of quinolines I–XIX are presented in a schematic form in Table 2. Spectra of quinoline derivatives V, IX, XII and XIII, where either the α-methylene group or the aromatic peri position is unsubstituted, show no unexpected features. Rapid inversion of the nitrogen results in magnetic equivalence of the α-methylene protons causing them to appear as a triplet in V and as singlets in IX, XII and XIII.

The spectrum of N-benzenesulfonyl derivative II, at room temperature, is of considerable interest. In contrast to the simplicity of the spectrum of V, the α-methylene protons appear as a broad hump in the region δ 3·8–4·4 suggesting their magnetic nonequivalence. That this nonequivalence is temperature dependent is clearly indicated in Figs. 2 and 3, which show the appropriate region of the spectrum at various temperatures, in deuterochloroform and diphenyl ether as solvents. Spectral changes upon lowering of temperature (below 40°C) manifested by transformation of

TABLE 2

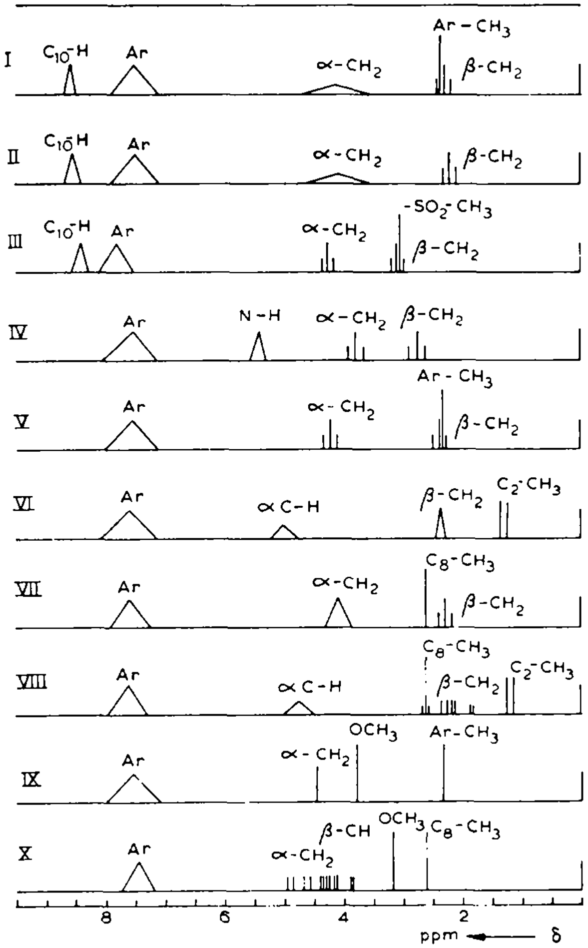
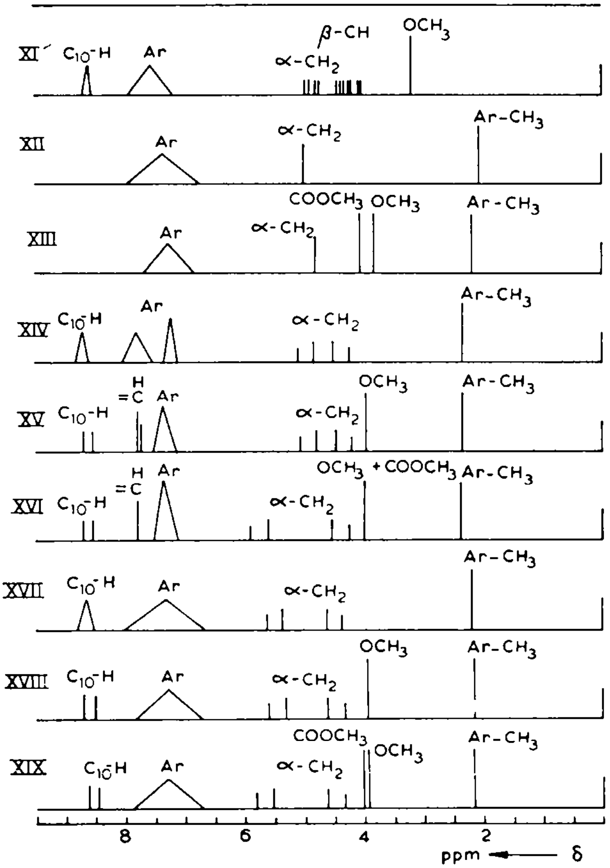


TABLE 2. (Contd.)



Graphical representation of the spectra of compounds I—XIX. All spectra have been recorded in deuterochloroform.

the hump due to α-methylene protons (Fig. 2a) to a multiplet (Figs. 2b and 2c) and those accompanying a rise in temperature, namely, development of a triplet at 70° (Fig. 3b) which is further sharpened at 100° (Fig. 3c), show the transition of the AB part of an ABXY system to the A_2 part of an A_2X_2 spectrum. Of interest is the relatively slower alteration in the X_2 part of the spectrum, which renders an explanation for the nonequivalence, in terms of a slow skeletal inversion, improbable. This is supported by measurements at temperatures below −30°, when, owing to slow inversion, both multiplets are observed to collapse into broad humps.[15] These changes can be seen in all compounds studied, including the ones which do not show hindered inversion in their spectra.

The generality of the phenomenon of nonequivalent methylene hydrogens is

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[14] Unless otherwise stated the spectra of compounds I-XIX presented in Table 2 have been measured as approximately 10% solution in $CDCl_3$.

[15] Field homogeneity was kept constant throughout the experiment. However, at temperatures below −40°, poor solubilities of the sulfonamides prevented further measurements.

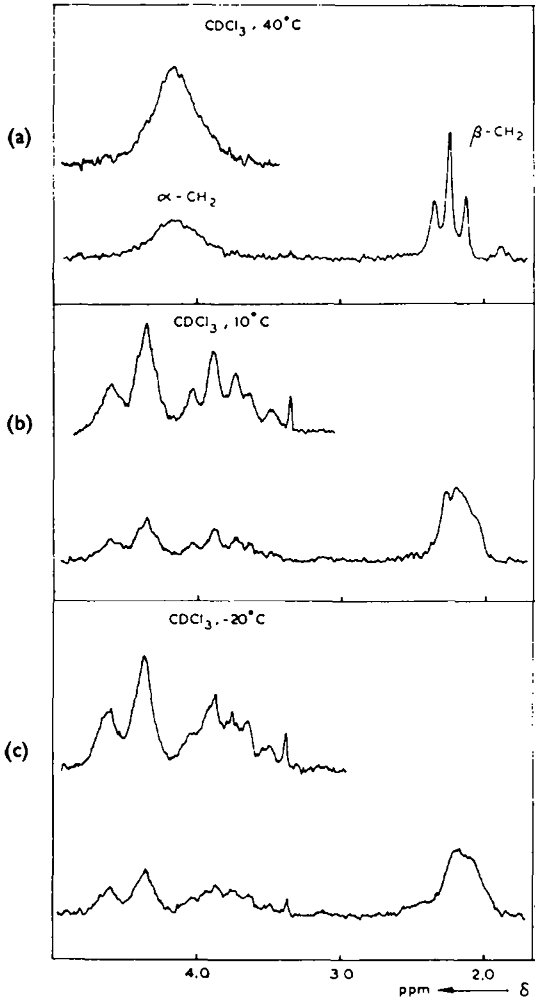

FIG. 2

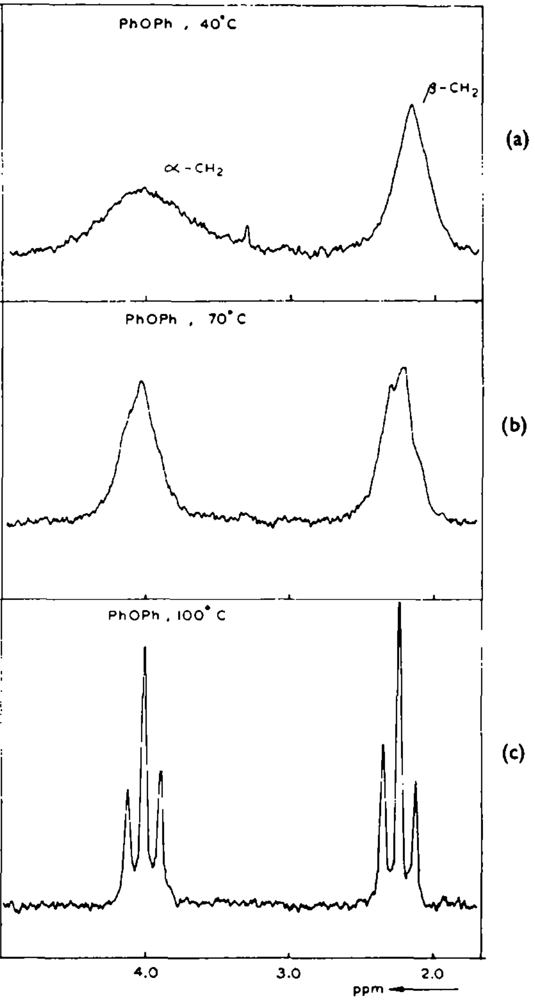

FIG. 3

apparent from the spectra described in the sequel, e.g. the twelve lines of an AMX system (J_{am} = 2·5 c/s; J_{ax} = 6·0 c/s; J_{mx} = 17·0 c/s and δ_{am} = 23 c/s), formed by coupling of the α-methylene protons with the olefinic β-hydrogen, in the spectrum of the enol ether XI (Fig. 4) and, the AB pattern with a typical spin–spin coupling (J = 16 c/s) for dissimilar geminal protons, in the spectrum of XV, are illustrative. Spectra of compounds XIV–XIX also follow the same pattern. Increase in temperature results in a disappearance of the inequality of protons in all the cases mentioned. Typical results for compound XV are shown in Fig. 5.

The unsymmetrical shielding of α-methylene protons in the aforementioned substituted benzquinoline systems can, in principle, arise from a variety of structural factors, We shall examine each one of these in turn. In the first instance, it is possible that the three bonds attached to the nitrogen atom are actually planar as in normal

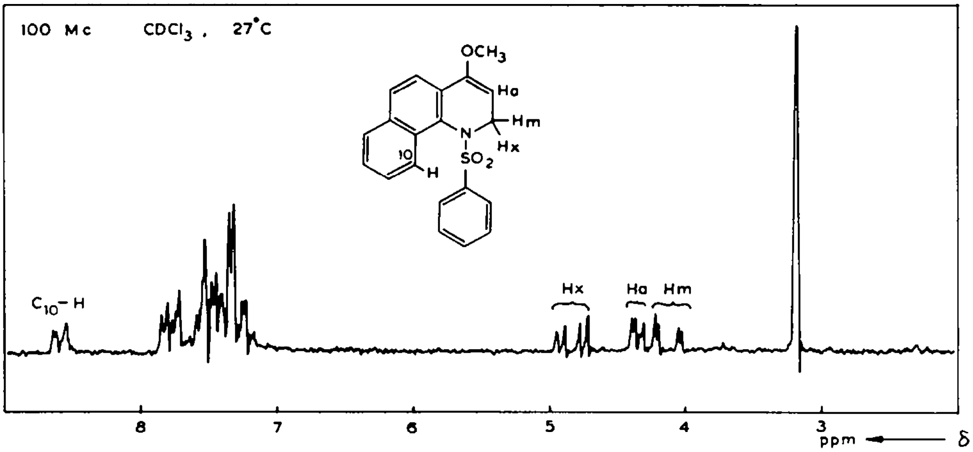
100 Mc
CDCl3 , 27°C
OCH3
Ha
Hm
Hx
N
SO2
10
H
C10- H
Hx
Ha
Hm
8
7
6
5
4
3
ppm ← δ

FIG. 4

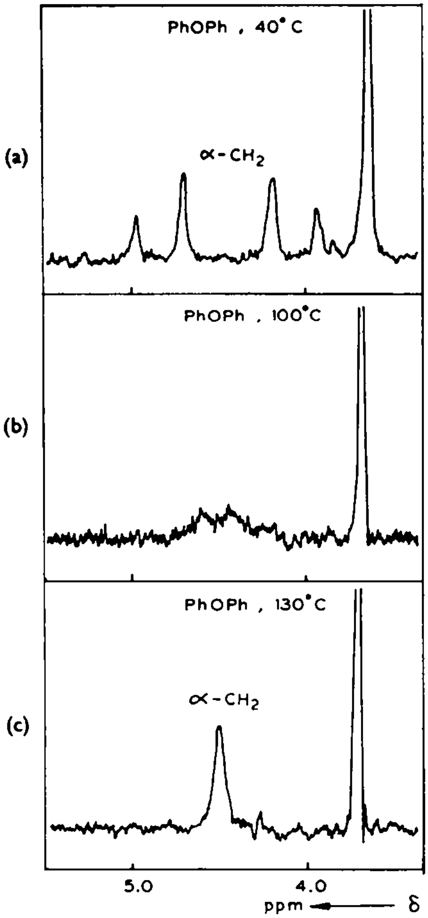
PhOPh , 40° C
(a)
α-CH2
PhOPh , 100°C
(b)
PhOPh , 130°C
(c)
α-CH2
5.0
4.0
ppm ← δ

FIG. 5

amides,[16] and that unsymmetrical shielding results from restriction of rotation of the arylsulfonyl group about the N—S bond.[17] There are, however, several lines of evidence which do not support this assumption. Firstly, a restriction of rotation about the N—S bond would predict an influence of the arylsulfonyl group on the peri hydrogen[18] (C_{10}—H in compounds I and II) which will be temperature dependent. The position of the peri-proton in these compounds, however, remains unchanged[19] with an increase in temperature to a value where the α-methylene protons become indistinguishable. Secondly, the spectrum of enol ether XI shows that the vinyl proton couples with the two adjacent methylene hydrogens with different coupling constants, thereby implying a nonplanar dihydropyridine ring structure in which the C_3—H makes different dihedral angles with the C_2-hydrogens. A lack of planarity for the heterocyclic ring in XI would appear to be insufficient to explain the large differences in the observed chemical shift of the α-protons. The unlikely possibility that dissimilar shielding of the α-methylene protons in various quinoline derivatives arises as a consequence of some hitherto unknown influence of the arylsulfonyl substituent was considered, but rejected on grounds that two-ring systems V, IX, XII and XIII, while possessing the same functional group, fail to exhibit any unexpected features in their spectra. A further series of measurements at a variety of temperatures confirmed this normal behaviour of the two-ring systems. As is seen from Fig. 6, the A_2X_2 pattern of quinolone V remains unchanged at temperatures as low as −30°. At still lower temperatures, collapse of both triplets occurs simultaneously, indicating thereby a *common origin*, which may be found in the slowing down of skeletal inversion. This observation also argues against any explanation for the nonequivalence of α-methylene protons which is based upon hindrance to the slow inversion of two pseudo-halfcrown conformations.

All of the observed facts can be conveniently explained by making only one assumption, namely, that the nitrogen atom in these benzquinolone amide systems possesses

[16] Although the normal amide conformation is a planar one in which the nitrogen atom is sp^2 hybridized,[16a] several cyclic[16b] and linear amides[16c] have been recognized in which the nitrogen lone pair has not a pure *p*-character, and in which the hybridization of the nitrogen atom is consequently between sp^2 and sp^3. This being the case, an inversion of the nitrogen bonds is always to be expected. Pertinent data, however, for sulfonamides have not been reported, except for the tetramethyl substituted sulfuramide[16d] in which the *p*-character of the nitrogen lone pair amounts to 89%.

[16a] R. L. Adelman, *J. Org. Chem.* **29**, 1837 (1964).

[16b] H. Pracejus, M. Kehlen, H. Kehlen and H. Matschiner, *Tetrahedron* **21**, 2257 (1965).

[16c] T. H. Sidall and C. A. Prohaska, *Nature* **208**, 582 (1965).

[16d] T. Jordan, W. Smith and W. N. Lipscomb, *Tetrahedron Letters* 37 (1965).

[17] A hindrance to the rotation due to $d\pi$–$p\pi$ interaction is not likely in view of the multiple degeneracy of the sulfur *d* orbitals.[17a]

[17a] R. M. Moriarty, *J. Org. Chem.* **30**, 600 (1965).

[18] Steric interactions of the peri type were also demonstrated by Tori[18a] and Martin.[18b]

[18a] W. Nagata, T. Terasawa and K. Tori, *J. Amer. Chem. Soc.* **86**, 3746 (1964).

[18b] R. H. Martin, N. Defay and F. Geerts-Evrard, *Tetrahedron* **20**, 1505 (1964).

[19] For steric reasons—interaction of the sulfonyl group with peri hydrogen—a deshielding of the C_{10}-proton is to be expected. However, possible paramagnetic contributions of the $S{=}O$ anisotropy[19a] and of the influence of the ring current of the tosyl-phenyl ring cannot be excluded. Provided the conformations at the nitrogen are the same in compounds II and III, an estimate of the latter type of deshielding could be obtained by a comparison of the C_{10}-proton resonances, which show a difference of 12 c/s at 60 Mc.

[19a] J. G. Pritchard and P. C. Lauterbur, *J. Amer. Chem. Soc.* **83**, 2105 (1961).

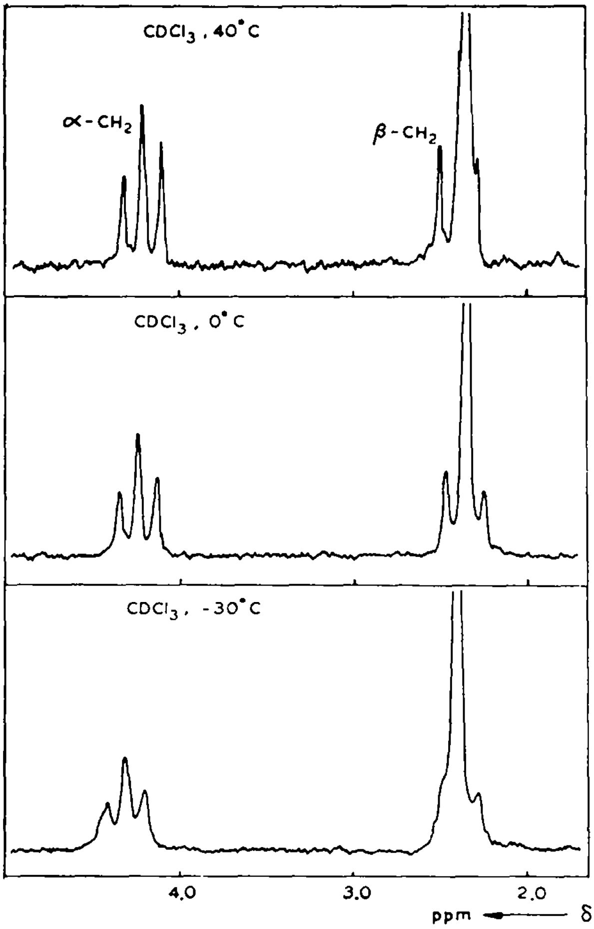

FIG. 6

some sp^3 character and that inversion of the pyramidal configuration about the nitrogen experiences an unusually large energy barrier. The principal cause of the latter appears to be steric in nature and presumably resides in the energy content of the transition state which involves interaction with adjacently located substituents. Possible contribution to a destabilization of the transition state, by a decrease of $p\pi$–$d\pi$ overlap of the nitrogen—sulphur bond, is not likely to significant, in view of earlier observations on N-toluenesulfonyl aziridines.[30]

The steric influence of a second phenyl ring (via the peri proton) is amply demonstrated by the NMR data. Thus, while compounds V, IX, XII and XIII do not exhibit the phenomenon of asymmetrical methylene hydrogens, the corresponding systems I, II, XI and XIV–XIX in which an additional angularly fused benzene ring provides strong steric interaction with the arylsulfonyl substituent, all show a measurable rate of nitrogen inversion. Similar behaviour has been well documented for ortho hydrogens

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[30] T. G. Traylor, *Chem. Ind.* 649 (1963).

of biphenyls,[21] peri hydrogens of 9,10-dihydrophenanthrenes,[22] and has been recently shown to be responsible for conformational isomerism in certain 9,10-dihydroanthracene[23] and dibenzo[a,d]cycloheptene derivatives.[24]

The size of a substituent on the nitrogen is, as could be expected, of prime significance. This is emphatically demonstrated by a comparison of the spectra of benzquinolones I and II with that of IV. The latter compound which lacks a bulky substituent, while possessing the extra aromatic ring, behaves analogously to the bicyclic quinolone V, and shows no significant changes in the spectrum on lowering the temperature of the sample. The absence of any measurable effect can be traced back to the relatively small energy effects involved in the mutual steric interaction of the peri hydrogens of 9,10-dihydrophenanthrenes.[22] An interesting case is provided by N-methylsulfonyl quinolone III which corresponds to a system with a substituent of intermediate size. At 40° the NMR spectrum of III reveals the α-methylene protons as a slightly diffused triplet (Fig. 7a) which acquires a neat appearance at 60° (Fig. 7b). At lower temperatures, on the other hand, the signal loses its structure and finally collapses to a broad hump (Figs. 7c and 7d). Another significant feature of the

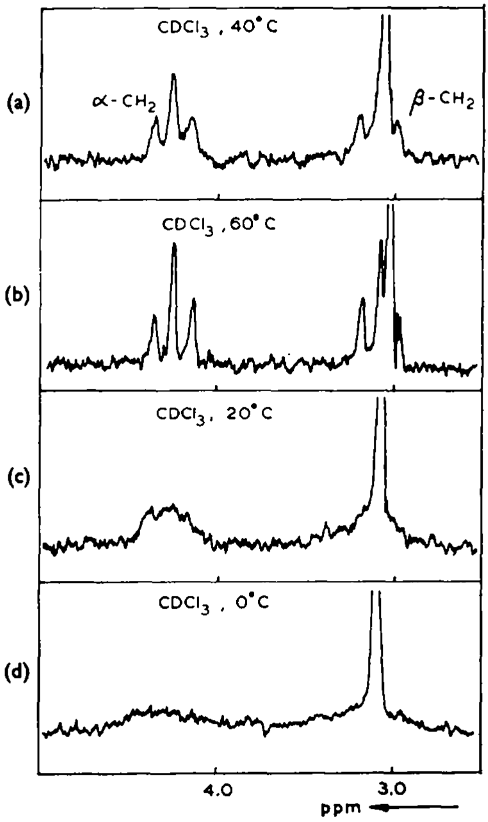

FIG. 7

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[21] K. Mislow, M. A. W. Glass, H. B. Hopps, E. Simon and G. H. Wahl Jr., *J. Amer. Chem. Soc.* **86**, 1710 (1964).

[22] M. Oki, H. Iwamura and N. Hayakawa, *Bull. Chem. Soc. Japan* **37**, 1865 (1964).

[23] D. Y. Curtin, C. G. Carlson and C. G. McCarty, *Can. J. Chem.* **42**, 565 (1964).

[24] A. Ebnöther, E. Jucker and A. Stoll, *Helv. Chim. Acta* **48**, 1237 (1965).

spectrum of III is the considerable displacement of the chemical shift of the β-methylene hydrogens in comparison to analogous protons in I, II, and V. Since the most likely origin for this effect lies in the diamagnetic shielding of β-hydrogens (in I, II and V) by aromatic rings of the nitrogen substituent, it follows that these rings must be in effective proximity to the C_3-carbon. Such a conformation is again consistent with the concept of a pyramidal hybridized nitrogen atom. It should be pointed out that the C_3-hydrogens of I and II also exhibit a sharp triplet at higher temperatures. While not collapsing as rapidly as the signal from the C_2-protons, it is considerably broadened at 40° and loses its structure altogether at lower temperatures (cf. Fig. 2).

TABLE 3

Compound[a]	Quartet collapsed at	Singlet observed at
XV	80°–90°	110°–120°
XVI	80°–90°	160°
XVIII	100°[b]	180°
XIX	100°[b]	—[c]

[a] All compounds measured in diphenylether.
[b] Exact determination difficult because of low-solubility.
[c] No singlet observed at 180°

Examination of Table 3 indicates that considerable variation exists between the changes in spectra of the different compounds upon alteration of temperature. Thus different classes of compounds, in which the structural variation resides at a site remote from the nitrogen atom, display inversion processes which are differently influenced by temperature. Comparison of XV and of XVI, XVIII and XIX indicates that progressively higher temperatures are required for attaining magnetic equivalence of the α-methylene protons. It would appear from this that the conformations of pyrazole-containing systems are exceptionally rigid in respect to nitrogen inversion. While the exact reason for this is not clear at the moment it would be expected that changes in conformation of the dihydropyridine ring cause an accompanying reorganization of bonds of the attached substituents. An inflexible substituent as the pyrazole ring, however, in view of its inability to accomodate such bond reorganization, may be anticipated to inhibit conformational changes in the ring and consequently offer a higher energy barrier to the inversion phenomenon.[25]

Using the method given by Alexander,[26] rate constants for the inversion process have been determined for compound XV. The method deals with the exchange narrowing of the absorption band for the α-methylene protons at temperatures above T_c. The height (A) of the absorption band at a certain temperature relative to the extrapolated height (A_0) at "infinite" temperature is related to the mean lifetime τ by the equation:

$$\frac{A}{A_0} = 1 - \frac{2T_2\delta\nu^2\tau + (T_2{}^2\delta\nu^4 + \delta\nu^2)\tau^2}{4 + 4\left(\frac{1}{T_2} + T_2\delta\nu^2\right)\tau + \left\{\left(\frac{1}{T_2} + T_2\delta\nu^2\right)^2 + J^2{}_{AB}\right\}\tau^2}$$

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[25] Similar raising of the inversion barrier in cycloheptatriene derivatives upon annelation of benzene rings has been observed.[25a]

[25a] W. Tochterman, U. Walter and A. Mannschreck, *Tetrahedron Letters* 2981 (1964).

[26] S. Alexander, *J. Chem. Phys.* 37, 967 (1962).

in which $\delta\nu$ is the difference in chemical shift when no inversion is observed. When $T_2\delta\nu^2 \gg 1$ and $T_2^2\delta\nu^4 \gg J_{AB}^2$, the equation is transformed to

$$k = 1/2\tau = T_2\delta\nu^2/4(A/A_0 - 1)$$

Results obtained are given in Table 4, where $\delta\nu = 44{\cdot}7$ c/s, $J_{AB} = 16{\cdot}4$ c/s and $T_2 = 2{\cdot}5$ sec.[27] The energy parameters were obtained from the equation $k = A_0^{-Ea/RT}$ which gives values of

$$E_a = 23 \pm 1{\cdot}0 \text{ kcal mol}^{-1}$$
$$\log A = 14{\cdot}1 \pm 0{\cdot}5$$

(On employing the equation, $k = RT/Nh \times e^{-\Delta G^+/RT}$ values for $\Delta H^+ = 22 \pm 1$ kcal mol^{-1} and $\Delta S^+ = 9{\cdot}6 \pm 2{\cdot}3$ cal deg^{-1} mol^{-1} were found.)

TABLE 4

T(°K)	A/A_0	k (sec^{-1})
427·1	0·818	$5{\cdot}62 \times 10^3$
419·0	0·693	$2{\cdot}82 \times 10^3$
410·8	0·527	$1{\cdot}38 \times 10^3$
401·0	0·356	$6{\cdot}91 \times 10^2$
392·2	0·247	$4{\cdot}10 \times 10^2$
383·0	0·144	$2{\cdot}11 \times 10^2$
373·7	0·082	$1{\cdot}12 \times 10^2$

Although no direct comparison of the calculated energy parameters with those obtained in related systems is possible, it may be pointed out that the results are consistent with the parameters obtained for the twisting of diphenylenes.[22] This may be traced back to the analogous transition states for both processes in which the energy barrier is mainly determined by the ortho–ortho repulsions.

Compounds VI, VII, VIII and X were examined with a view to study the influence of changes of substituents in the neighbourhood of the nitrogen atom and to obtain information concerning the conformation of the reduced heterocyclic ring. Replacement of the third aromatic ring by a methyl group at the C_8 position in VII and X give their spectra a remarkable similarity to those of II and XI, the patterns for the α-methylene protons being identical. Temperature studies fully confirm the identical behaviour of the C_8-methylated quinolones with their aromatic analogues. While the twelve line pattern in the spectrum of X changed into a diffused triplet at δ 3·79 and a doublet at δ 3·15 at 70°, the thermal stability of the enol ether was insufficient to allow high temperature experiments. The spectrum of VII showed a triplet for the α-methylene protons at higher temperatures (Fig. 8a), a hump at room temperature (Fig. 8b) and a multiplet at −20° (Fig. 8c). The chemical shift (singlet at δ 2·58) of the C_8-methyl hydrogens is appreciably displaced in comparison with the position of a similar methyl group in N-benzenesulfonyl-N-(*o*-tolyl)-3-aminopropionic acid (singlet at δ 2·29).[28] In view of the implicit buttressing of the methyl substituent by the

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[27] The error in k is mainly determined by the error in T_2. Since T_2 does not vary much over a limited temperature range, the influence on the error in E_a is small.

[28] In a number of other N-arylsulfonyl-N-(*o*-tolyl)amine derivatives the position of the aromatic methylgroup was about δ 2·30 ppm.

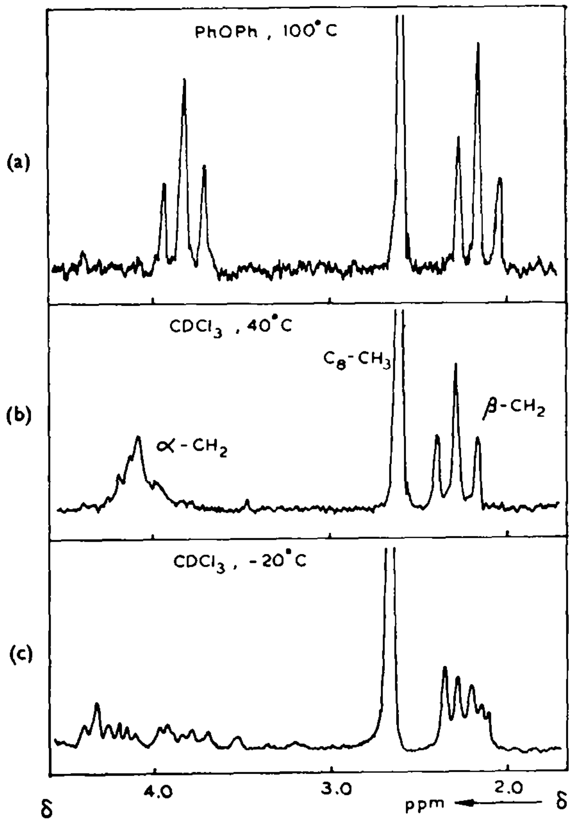

FIG. 8

arylsulfonyl group, one explanation for the latter displacement may be found in terms of a steric compression in which the aryl—CH_3 bond is bent from its normal position and brought into a configuration in which the methyl protons come under increased paramagnetic influence of the aromatic ring current. Down-field shifts of similar magnitude for the aromatic methyl groups have been observed in the spectra of *ortho–ortho* dimethylphenanthrene and related compounds.[29] It should, however, be pointed out that at this stage it is impossible to make an assessment of the contribution, if any, of the paramagnetic influence of the N-arylsulfonyl substituent to the shift of the aryl-CH_3.

Detailed examination of the NMR spectra of VI and VIII gave some significant information concerning the conformation of the reduced heterocyclic ring. Although the conformation of tetrahydroquinolines has been assumed to be a half-chair,[30] the

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[29] A. D. Cross and L. J. Durham, *J. Org. Chem.* **30**, 3200 (1965).

[30] It may be pointed out that while calculations made by Booth[30a] assume a half chair conformation, the results described do not exclude a pseudo-boat conformation of the type represented in Fig. 9 for the tetrahydroquinolines as well. The observed nonequivalence of the C_2-gem methyl groups in N-methyl-1,2,3,4-tetrahydro-2,2,4-trimethylquinoline could be explained on this basis by assuming a destabilization of two of the extreme conformations of the molecule as a result of NMe—C_4Me flagpole interactions.

[30a] H. Booth, *J. Chem. Soc.* 1841 (1964).

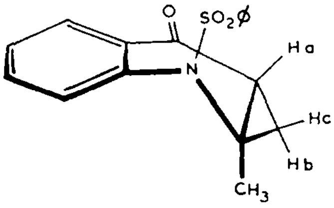

FIG. 9

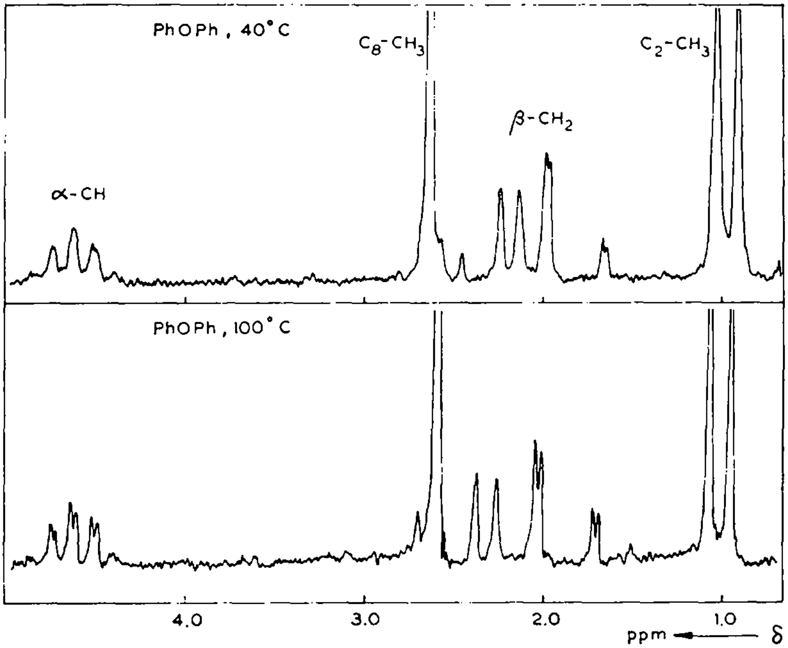

FIG. 10

data now obtained from the spectra of VI and VIII indicate that the stereochemistry of dihydroquinolones is decidedly not of the latter type. The coupling constants for the spin–spin interaction of C_α-H with the two C_β-protons in quinolones VI (J_{ac} = 6·5 c/s, J_{bc} = 1·5 c/s, J_{ab} = 19 c/s) and VIII (J_{ac} = 7·5 c/s, J_{bc} = 3·0 c/s, J_{ab} = 19 c/s)[31] suggest, assuming the reliability of Karplus equation in these systems, a conformation indicated by Fig. 9 for the latter compounds.[32] The room temperature spectrum of quinolone VIII, however, shows a distorted multiplet at δ 4·5–5 and the AB part of an ABX spectrum (δ 1·8–2·6), again indicative of a hindered inversion of nitrogen bonds owing to steric repulsions in going past the C_8-methyl. At higher temperature (Fig. 10b) the distorted multiplet becomes a quintuplet (J = 7 c/s) with an additional splitting of

[31] Measured in $CDCl_3$ as approximately 10% solution. In diphenylether the following J-values were obtained: at 40° J_{ac} = 7·0 c/s, J_{bc} = 2·5 c/s and J_{ab} = 19 c/s, while at 100° J_{ac} = 7·5 c/s, J_{bc} = 2·5 c/s and J_{ab} = 19·5 c/s. These results are completely in agreement with those obtained in $CDCl_3$ as a solvent.

[32] In addition, it is of interest to note the great similarity of the J value determined for dihydroquinolone VIII with the coupling constants in a rigid system such as norbornane (see: N. S. Bhacca and D. H. Williams, *Applications of NMR Spectroscopy in Organic Chemistry*, p. 52. Holden-Day, San Francisco, Amsterdam, London (1964).

1·5 c/s. It is interesting to note that the C_8-methyl resonance in compounds VII, VIII and X is at almost the same δ value.

EXPERIMENTAL

The spectra were obtained with a Varian A 60 spectrometer equipped with a Varian V 6440 variable temperature accessory. In addition, spectra of compounds I and XI were run on a Varian A-100 spectrometer. Temperatures of the kinetic runs are accurate within ±0·1° and were determined by direct measurement in the spinning sample tube with a copper-constantane thermocouple immediately before and after scanning a spectrum. Absorption peak heights (A) were measured relative to the height of the methyl band of the tosyl group as internal standard. The spectrometer was calibrated following the method of Jungnickel.[33] T_2 was determined by the method of Tiers.[34]

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[33] J. L. Jungnickel, *Anal. Chem.* 35, 1985 (1963).

[34] G. V. D. Tiers, *J. Phys. Chem.* 65, (1961).