239. N-*Substituted Heterocyclic Cations. Part V.* The Use of Proton Magnetic Resonance Spectroscopy in the Solution of Some Classical Structural Problems.*

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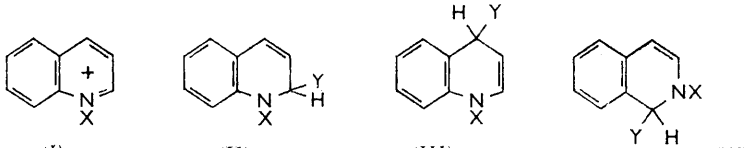
1,2- and 1,4-Dihydroquinolines may be distinguished by consideration of their proton magnetic resonance spectra. The same technique has been used to show where prototropic rearrangements and ring-opening reactions have occurred. The previous assignment of structure to the two 1,2-dicyano-1,2-dihydroquinolines is shown to be incorrect, and the product of reaction of quinoline with benzoyl chloride in aqueous alkali is shown to be a derivative of *trans*-cinnamaldehyde.

Three classical problems arise in the reaction of 1-substituted quinolinium ions with nucleophils. These are (i) the position of attachment of the nucleophil, (ii) whether prototropic shifts occur in the dihydroquinoline product under the (usually) basic conditions of the reaction, and (iii) whether, in those cases where the nucleophil is hydroxide ion, ring opening occurs following the formation of the dihydroquinoline. This Paper describes the solution of some of these problems with the aid of proton magnetic resonance spectrometry.

Position of Attack of the Nucleophil.—The addition of a nucleophil Y to 1-substituted quinolinium ion (I) can give rise to 1,2- or 1,4-dihydroquinolines (II or III, respectively). Many such dihydroquinolines have been described, but in only a few cases have the structures been reasonably substantiated. Structures based on chemical evidence are frequently suspect because of the ready reversibility of many of the additions, and the comparison of the ultraviolet spectra of the products with those of model compounds may give not only the wrong answer, but also the right answer for the wrong reasons, as is demonstrated below. The use of infrared evidence is limited, by the lack of relevant data for these compounds, to the identification of dihydroquinolines where a large number of other dihydroquinolines of known structure are available. The problem is aggravated by the fact that there are few suspected 1,4-dihydroquinolines; and for reasons which will become apparent, these lack sufficient structural characterisation. However, there are several 1,2-dihydroquinolines of certain structure; these include the products of reaction of alkoxide ions with the 1-cyanoquinolinium ion [1] (II; X = CN, Y = OMe or OEt) and the product of reaction of phenylmagnesium bromide with the 1-methylquinolinium ion (II; X = Me, Y = Ph).[2]



(I) (II) (III) (IV)

We have measured the proton magnetic resonance spectra of these known 1,2-dihydroquinolines together with those of other dihydroquinolines of less certain structure including two which are believed to be 1,4-dihydroquinolines. The results in Table 1 were obtained by the use of ABX analyses [3b] for the protons of the hetero-ring, both intensities and energies being calculated. The accuracy of the data did not justify the use of iterative

* Part IV, Huckings and Johnson, *J.*, 1964, 5371.

[1] Johnson, *J.*, 1962, 283.

[2] Schmid and Karrer, *Helv. Chim. Acta*, 1949, **32**, 960.

[3] Roberts, "An Introduction to the Analysis of Spin–Spin Splitting in High Resolution N.M.R. Spectra," W. A. Benjamin Inc., New York, 1962, (*a*) p. 63, (*b*) p. 71.

TABLE 1.

X	Y	Other groups	Structure	Solvent	J_{34} [b]	J_{23} [c]	J_{24} [b]	τ_2	τ_3	τ_4	Other	Ref. to prepn.	Notes
CN	OEt	—	II	CCl_4	9·8	4·6	−0·6	4·11	4·31	3·25	CH_2 6·32 CH_3 8·82	1	*d*
CN	OMe	—	II	CCl_4	9·8	4·6	−0·5	3·98	4·36	3·22	CH_3 6·64	1	*d*
Me	Ph	—	II	CCl_4	9·9	4·7	+0·5	4·94	4·45	3·76	C_6H_5 2·77 CH_3 7·39	2	*d*
Me	OEt	6,8-Dinitro	II	$CDCl_3$	9·7	4·7	−0·3	4·45	3·80	3·01		*a*	*de*
Me	OEt	6,8-Dinitro	II	$(CH_3)_2SO$	10·0	5·6	−0·6	4·33	3·70	2·74		*a*	*d*
Me	OMe	6,8-Dinitro	II	$CDCl_3$	10·5	5·1	−0·1	4·46	3·83	2·95	NCH_3 6·87 OCH_3 6·77	14	*df*
Me	CN	—	III	CCl_4	3·6 ±0·2	8·2 ±0·4	+0·9	3·92	5·17	5·36	CH_3 6·98	15	*de*
Me	PhC(CN)Me	—	III	$CDCl_3$	5·5 ±0·2	7·6 ±0·4	−0·1	3·75	5·33	5·97	NCH_3 7·04 CCH_3 8·42 C_6H_5 2·70	12	*d*

[a] Supplied by Dr. A. G. Davies. [b] ±0·4 c.sec.$^{-1}$ except where stated. [c] ±0·2 c.sec.$^{-1}$ except where stated. [d] *ABX* analysis. [e] *AMX* analysis by inspection. [f] NCH_3 and OCH_3 assignments may be reversed.

TABLE 2.

X	Y	Structure	Solvent	J_{34} (±0·2 c.sec.$^{-1}$)	J_{31} (±0·5 c.sec.$^{-1}$)	J_{41} (±0·5 c.sec.$^{-1}$)	τ_1	τ_3	τ_4	Ref. to prepn.	Note
COPh	CN	IV	$CDCl_3$	8·0	0	0	3·36	3·31	3·90	17	*g*
2,4-$C_6H_3(NO_2)_2$	OH	IV	$CDCl_3$	7·5	1·8	0·2	3·73	4·05	3·84	16	*g*
CN	O·O·CMe	IV	CCl_4	7·6	0	0	3·72	3·56	3·95	4	*g*
CN	OMe	IV	$CDCl_3$	7·4	0	0	4·01	3·53	4·02	4	*g*

[g] The reverse assignment of τ_3 and τ_4 is also possible.

TABLE 3.

X	Y	Structure	Solvent	J_{34} (c.sec.$^{-1}$)	J_{32} (c.sec.$^{-1}$)	J_{42} (c.sec.$^{-1}$)	τ_2	τ_3	τ_4	Ref. to prepn.
CN	CN	II	$CDCl_3$	10·0 ± 0·5	6·8 ± 0·5	−0·5 ± 0·5	4·47	4·10	3·25	7
CN	CN	VII	$CDCl_3$	4·5 ± 0·2	—	—	—	3·85	6·29	*h*

[h] See Experimental section.

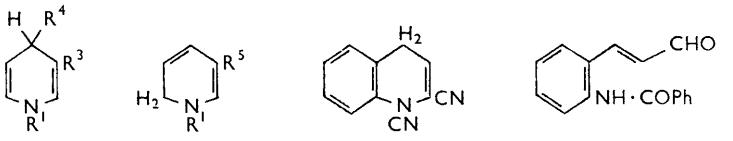
procedures. In two cases, it was possible to use the AMX approximation [3a] as a check. The results show quite clearly that there are two distinct sets of coupling constants for these compounds. For the majority of compounds, the largest coupling constant (J_{34}) has the value 10·1 ± 0·7, but in two cases the largest coupling constant (J_{23}) is only 7·6 and 8·2, both ±0·4 c./sec. The largest coupling constant in each case is believed to represent the coupling constant between the olefinic protons in the hetero-ring. The former group contains only the known and suspected 1,2-dihydroquinolines and the last two compounds are the suspected 1,4-dihydroquinolines. The following evidence supports the view that this difference in coupling constants is significant and is sufficient to characterise these compounds as 1,2- and 1,4-dihydroquinoline derivatives. (i) The value of J_{34} for the 1,2-dihydroquinolines is practically independent of the nature of substituents on the nitrogen or on the benzene ring, and is little affected by solvent changes. (ii) The coupling constant between the 3- and 4-protons in the AB + A or ABX spectra of 1,2-dihydroisoquinolines [4] (IV) (Table 2, $J_{34} = 7{\cdot}7 \pm 0{\cdot}5$ c./sec.) is not only independent of substituents but is very close to the coupling constants between the 3- and 4-protons of 1,4-dihydroquinolines. This is to be expected because the double bonds in 1,4-dihydroquinolines and in 1,2-dihydroisoquinolines are each α- to the ring nitrogen atom. (iii) It is known that the coupling constant between *cis*-protons of a *cis*-olefin decreases with increasing electronegativity of substituents [5] and it is therefore to be expected that the coupling constants J_{23} for 1,4-dihydroquinolines and J_{34} for 1,2-dihydroisoquinolines (each with the double bond α- to the ring nitrogen atom) would be less than J_{34} for 1,2-dihydroquinolines (with the double bond β- to the ring nitrogen atom). (iv) The value of J_{56} for several [6] 1,3-disubstituted and 1,3,4-trisubstituted 1,4-dihydropyridines (V) (each with the double bond α- to the ring nitrogen atom) is 8·1 ± 0·4 c./sec., and of J_{34} for several 1,5-disubstituted-1,2-dihydropyridines (VI) (with the double bond β- to the ring nitrogen atom) is 9·9 ± 0·4 c./sec. The structures of 4-cyano-1-methyl-1,4-dihydroquinoline and 4-(1-cyano-1-phenylethyl)-1,4-dihydro-1-methylquinoline are therefore confirmed and there is no reason to suppose that this method should not be applicable to the determination of the structure of other dihydroquinolines for which the appropriate double bond is not substituted.

Prototropic Rearrangements.—The reaction of the 1-cyanoquinolinium ion with anhydrous hydrogen cyanide gives rise to a dihydroquinoline of m. p. 100° which rearranges in the presence of basic catalysts to an isomer of m. p. 135°. It was originally believed that these were geometrical isomers about the ternary nitrogen,[7] but a later comparison [8] of their ultraviolet spectra with the spectra of phenyl cyanamide derivatives as models was taken as evidence that the isomer of higher m. p. had the structure (II; X = CN, Y = CN), and that the isomer of lower m. p. had the structure (VII). However, our measurements of the proton magnetic resonance spectra of both isomers show clearly that this assignment is incorrect. As shown in Table 3, the first formed isomer has the ABX spectrum of a 1,2-dihydroquinoline with $J_{34} = 10{\cdot}0$ c./sec. and the high m. p. isomer has the AX_2 spectrum corresponding to the compound (VII)

This easy prototropic rearrangement prompted us to investigate the possibility of similar rearrangements in the case of other dihydroquinolines, particularly where Y = CN, because Ingold [9] had previously suggested that rearrangement may occur in the case of 4-cyano-1,4-dihydro-1-methylquinoline. However, under conditions where the dicyano-dihydroquinoline rearranges instantaneously, no rearrangement of 4-cyano-1-methyl-1,4-dihydroquinoline was observed after several hours, nor was there any uptake of deuterium

[4] Johnson, *J.*, 1964, 200.
[5] Schaefer, *Canad. J. Chem.*, 1962, **40**, 200.
[6] Dieckmann, Englert and Wallenfels, *Tetrahedron*, 1964, **20**, 281.
[7] Mumm and Ludwig, *Annalen*, 1934, **514**, 34.
[8] Seeley, Yates, and Noller, *J. Amer. Chem. Soc.*, 1951, **73**, 772.
[9] Ingold, " Structure and Mechanism in Organic Chemistry," Bell and Sons Ltd., London, 1953, p. 577.

when this compound was prepared by the reaction of the 1-methylquinolinium ion with potassium cyanide in D_2O. A similar lack of deuterium uptake and rearrangement was observed in the formation and reaction of the dihydroquinoline derived from the 3-bromo-1-methylquinolinium ion and cyanide ion. (The proton magnetic resonance method of



(V) (VI) (VII) (VIII)

assignment fails with 3-substituted dihydroquinolines because the appropriate coupling constants do not exist in this case.)

Ring Opening.—Where the attacking nucleophil is hydroxide ion the product, if a 1,2-dihydroquinoline, can in principle undergo ring opening to a substituted cinnamaldehyde. The classic case is the product of reaction of quinoline with benzoyl chloride in aqueous alkali.[10] Structures (II; X = COPh, Y = OH) and (VIII) have been proposed, the latter having very recently been suggested on the basis of infrared evidence.[11] We have measured the proton magnetic resonance of this compound (Table 3), which shows clearly that it has the open chain structure (VIII). The aldehyde proton resonance doublet at very low field ($\tau = 0{\cdot}32$) is unmistakable, and the coupling constant between the two olefinic protons ($J = 16{\cdot}2$) is identical with that for *trans*-cinnamaldehyde ($J = 16{\cdot}2$).

Discussion.—The reasons for the formation of 1,2- and 1,4-dihydroquinolines can now be discussed with confidence. The results obtained here and in previous Papers of this series show that the more reactive cations, such as the 1-cyanoquinolinium ion give 1,2-dihydroquinolines, and as expected for a reaction in which a nucleophil approaches and then adds on to a cation, thermodynamic and kinetic control lead to the same result. However, the ready rearrangement of 1,2-dicyano-1,2-dihydroquinoline to 1,2-dicyano-1,4-dihydroquinoline indicates that a small effect, such as the increased conjugation with the 2-cyano-group, is sufficient to change the relative stability order. The tendency for 1,4-dihydroquinoline formation is greatest in the case of the least reactive 1-methylquinolinium ion, but as there are several examples in the literature of products formed by further reaction of both 1,2- and 1,4-dihydro-1-methylquinolines and as the introduction of nitro-groups into the benzene ring of the 1-methylquinolinium ion changes the orientation of addition of the nucleophil, the balance is delicate in this case also. It therefore seems that the difference between the reactive and less reactive 1-substituted quinolinium ions is due to the greater effect of the activating substituents on the nucleophilic localisation energy or electron density of the 2- rather than the 4-position, but that the energetic balance is such that quantum mechanical calculations are unlikely to provide the answer.

The compound 4-(1-cyano-1-phenylethyl)-1,4-dihydro-1-methylquinoline (III; Y = $PhC(CH_3)CN$, X = Me) deserves particular mention. Though the original chemical evidence [12] for the 1,4-assignment was reasonable, other evidence was suspect because it was based on a comparison of its ultraviolet spectrum with that of 1,2-dicyano-1,2-dihydroquinoline which at that time was believed to be 1,2-dicyano-1,4-dihydroquinoline, and on an invalid comparison with the ultraviolet spectrum of a compound having a more extended conjugated system and an additional band at long wavelengths. However, since this compound clearly is a 1,4-dihydroquinoline, it can be assumed that the corresponding α-cyanobenzyl compound (II; Y = PhCHCN, X = Me) is also a 1,4-dihydroquinoline. Iodination [12] of this compound with iodine and potassium acetate (probably

[10] Reissert, *Chem. Ber.*, 1905, **38**, 1603, 3415.
[11] Elliot, *J. Org. Chem.*, 1964, **29**, 305.
[12] Leonard and Foster, *J. Amer. Chem. Soc.*, 1952, **74**, 3671.

via the addition–elimination mechanism [13]) gives 4-(α-cyanobenzyl)-1,4-dihydroiodo-1-methylquinoline and subsequently 3-iodoquinoline. This accords with the previous suggestion [13] that the route to 3-halogenoquinolines *via* 1,2,3,4-tetrahydroquinolines can be accomplished through either 1,2- or 1,4-dihydroquinoline intermediates.

Experimental

Proton magnetic resonance measurements were carried out with a Perkin-Elmer 60 Mc./sec. spectrometer and in a few cases using a 40 Mc./sec. Varian spectrometer.

Preparation.—[$^2H_1$]Chloroform was supplied by Sass and Co. Carbon tetrachloride was B.D.H. spectroscopic grade. Dimethyl sulphoxide was purified by treatment with molecular sieves (B.D.H. grade 5A) followed by drying with barium oxide and distillation under reduced pressure. 1,2-Dicyano-1,4-dihydroquinoline was prepared by treatment of 1,2-dicyano-1,2-dihydroquinoline with triethylamine in chloroform. The solvent and excess of base were removed on evaporation and the residue was recrystallized from chloroform. 3-Bromo-2-(or 4-)cyano-1,2(or 1,4)-dihydro-1-methylquinoline was prepared by the reaction of potassium cyanide with an aqueous solution of 3-bromo-1-methylquinolinium iodide in a manner analogous to the preparation of 2-cyano-1-methyl-1,4-dihydroquinoline.[15] It was not isolated, but the proton magnetic resonance spectrum of a carbon tetrachloride extract of the reaction mixture was measured directly. Other materials were prepared by known methods, references to which are given in the Tables. 1,2-Dicyano-1,2-dihydroquinoline was also prepared by the reaction of 1-cyanoquinolinium fluoroborate with anhydrous hydrogen cyanide followed by working up as described in the literature.[7]

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[13] Johnson and Ridd, *J.*, 1962, 291.
[14] Rieche, Schmitz, and Dietrich, *Chem. Ber.*, 1959, **92**, 2239.
[15] Ainley and King, *Proc. Roy. Soc.*, 1938, *B*, **125**, 60.
[16] Beke and Szántay, *Annalen*, 1961, **640**, 127.
[17] Popp, *J.*, 1963, 1760.