The Conformation of 4-Acetylpyridine determined from Proton and Deuterium Nuclear Magnetic Resonance Spectra of a Nematic Phase

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Proton and proton–{deuterium} spectra of 4-[$^2H_3$]acetylpyridine have been recorded on nematic solutions and analysed to yield dipolar coupling constants, D_{ij}. The deuterium spectrum yields the quadrupole splitting, $\Delta\nu$, which together with the D_{ij} values was used to predict all the dipolar couplings in the spectrum of the fully protonated compound. This procedure enabled an analysis of the complex proton spectrum of 4-acetylpyridine in the same nematic solutions. It is demonstrated that the data from analysis of either the CD_3 labelled, or from the fully protonated compound can be used to investigate the structure of the pyridine ring and the conformational preference of the acetyl group.

PROTON n.m.r. spectra of molecules dissolved in liquid crystal solvents are a potential source of structural and conformational information, but they often present a formidable problem in spectral analysis.[1] It is possible to surmount this problem in some cases by first substituting some protons by deuterium and then to simplify the proton spectrum by decoupling.[2-4] However, this requires a decoupling power not available on most spectrometers and careful control of the temperature of the sample. We demonstrate the use of this technique here, but we show too that it is also possible to obtain proton spectra of high quality of the partially deuteriated molecules without decoupling. These can be analysed to yield a set of dipolar couplings, which together with a quadrupole splitting from the deuterium spectrum can be as useful as an analysis of the proton spectra of the parent compound in determining structure and conformation.

4-Acetylpyridine was chosen as a test case because it is representative of a class of molecules which can be easily synthesized containing a CD_3 group, whose proton spectrum is complex and which do have an unsolved conformational problem in the liquid state.

EXPERIMENTAL

The sample of 4-acetylpyridine was purchased from Aldrich and used after distillation. The deuteriated sample was made by treatment of 4-acetylpyridine (0.45 ml, 0.5 g) with K_2CO_3 in refluxing D_2O (2 ml) under nitrogen for 24 h. D_2O was then removed under vacuum and the product again exchanged with D_2O using K_2CO_3 as catalyst. The reaction mixture was worked up as above to yield after distillation (b.p. 100 °C) 4-[$^2H_3$]acetylpyridine ([$^2H_3$] 98.4, [$^2H_2$] 1.6; [$^2H_1$] 0% by mass spectra; total yield 85%).

Two liquid crystal solvents were used, Phase V, a mixture of alkoxyazoxybenzenes produced by E. Merck (Darmstadt) and E5, a mixture of alkylcyanobiphenyls manufactured by B.D.H. Chemicals Limited. Both are liquid crystalline at room temperature. Spectra were recorded on a Varian XL100-12 spectrometer in the pulse Fourier transform mode of operation, using an external fluorine field-frequency lock. The proton spectra of the non-deuteriated samples are shown in Figure 1 and were obtained with the following spectrometer settings: spectral width 12 kHz, 8 K of computer store and 4 K transients. Figure 2 shows a proton spectrum of 4-[$^2H_3$]acetylpyridine in Phase V, together with a proton–{deuterium} decoupled spectrum. Decoupling was achieved by irradiating at 15.35 MHz with a phase-modulated signal derived from the Varian Gyrocode system amplied to *ca.* 70 W by an ENI 3100 L amplifier and passed *via* a low pass filter to the decoupler coils. The matching circuit for the decoupling line was a replica of that normally used on the Varian spectrometer, but with moving-vane condensers in place of the low power moving disc variety. Signal acquisition was limited to 0.1 s, followed by a 4 s delay whose purpose is to allow the sample to remain at constant temperature. Both ^1H and ^1H–{^2H} spectra of 4-[$^2H_3$]acetylpyridine in E5 were also obtained with the XL 100 system, but we have also obtained a proton spectrum of this sample on our Bruker CXP 200 spectrometer which has the considerable advantage of being able to carry out the technique of convolution difference and hence improve the resolution and eliminate baseline distortions of the spectra, as illustrated in Figure 3. The free induction decay (f.i.d.) was the result of averaging the responses from 10 000 90° pulses and was accumulated into 8 K of computer store. This f.i.d. was then duplicated in a separate 8 K of store, multiplied with an exponential apodisation function corresponding to a linewidth of 10 Hz and 0.9 of this weighted f.i.d. subtracted from the original and Fourier-transformed to give the result shown in Figure 3.

Deuterium spectra were recorded on either the XL 100 at 15.35 MHz or on the CXP 200 instrument at 30.7 MHz on the same samples used for the proton spectra and at the same temperatures. In both cases the spectra were doublets broadened by unresolved dipolar interactions.

Analysis of Spectra.—The three kinds of spectra present a progression in the ease of analysis and were analysed in the following sequence. First, the ^1H–{^2H} spectrum was analysed to give the values of D_{12}, D_{13}, $D_{14} + D_{23}$, and the chemical shift difference δ_{12}. Secondly, the proton spectrum of the $^2H_3$ compound was analysed using a version of computer program LEQUOR [5] modified to include groups of equivalent deuterium nuclei. These spectra yield all the dipolar couplings independently, and the results for the two spectra analysed are given in Table 1. The deuterium spectra yield $\Delta\nu$ the quadrupole splittings given in Table 1, which can be used to predict D_{CH_3}, the dipolar coupling between protons in the methyl groups in the non-deuteriated compounds. This was done using the ratio of $\Delta\nu/D_{CH_3}$ found for anisoles.[6] At this stage it was possible to predict all the couplings in the proton spectra of the non-deuteriated compounds with sufficient precision to make

TABLE 1

N.m.r. parameters obtained by analysis of the proton and deuterium spectra of 4-acetyl- and 4-[$^2H_3$]acetyl-pyridine

	4-[$^2H_3$]Acetylpyridine		4-Acetylpyridine	
	Phase V	E5	Phase V	E5
D_{12}/Hz	−2 502.2 ± 0.1	−1 160.1 ± 0.4	−2 344.3 ± 0.1	−1041.0 ± 0.1
D_{13}/Hz	−14.6 ± 0.1	−108.6 ± 0.2	−16.5 ± 0.1	−102.7 ± 0.1
D_{14}/Hz	138.5 ± 0.9	−135.8 ± 1.0	124.2 ± 0.2	−131.2 ± 0.2
D_{1,CH_3}/Hz	−126.8 ± 0.4	−58.6 ± 0.8	−770.6 ± 0.1	−338.1 ± 0.1
D_{23}/Hz	158.0 ± 0.9	−156.8 ± 1.0	141.3 ± 0.3	−149.0 ± 0.2
D_{2,CH_3}/Hz	−27.7 ± 0.4	−14.2 ± 0.8	−172.2 ± 0.1	−88.1 ± 0.1
D_{CH_3}/Hz			634.3 ± 0.1	1 300.0 ± 0.1
δ_{12} (p.p.m.)	0.662 ± 0.01	0.975 ± 0.01	0.701 ± 0.01	0.987 ± 0.01
δ_{1,CH_3} (p.p.m.)			−4.609 ± 0.01	−4.630 ± 0.01
$\Delta\nu$/Hz	3 210 ± 20	10 475 ± 50		

iterative analysis possible and the results are given in Table 1.

RESULTS AND DISCUSSION

The dipolar couplings in Table 1 have been used to investigate two aspects of the structure of 4-acetylpyridine. The couplings between the protons in the pyridine ring were used to derive distance ratios r_{ij}/r_{23}, in which r_{23} is fixed at 4.112 Å, the value found for pyridine by microwave spectroscopy.[7] These ratios are affected by vibrational motions and to calculate this effect we have used the method of Lucas.[8] There has not been a vibrational analysis of 4-acetylpyridine and we have therefore used the vibrational wavefunctions calculated for pyridine [9] in order to calculate the effect of vibrational motion on the dipolar couplings within the pyridine ring of 4-acetylpyridine. This is of course an approximation, but a reasonable one which will suffice

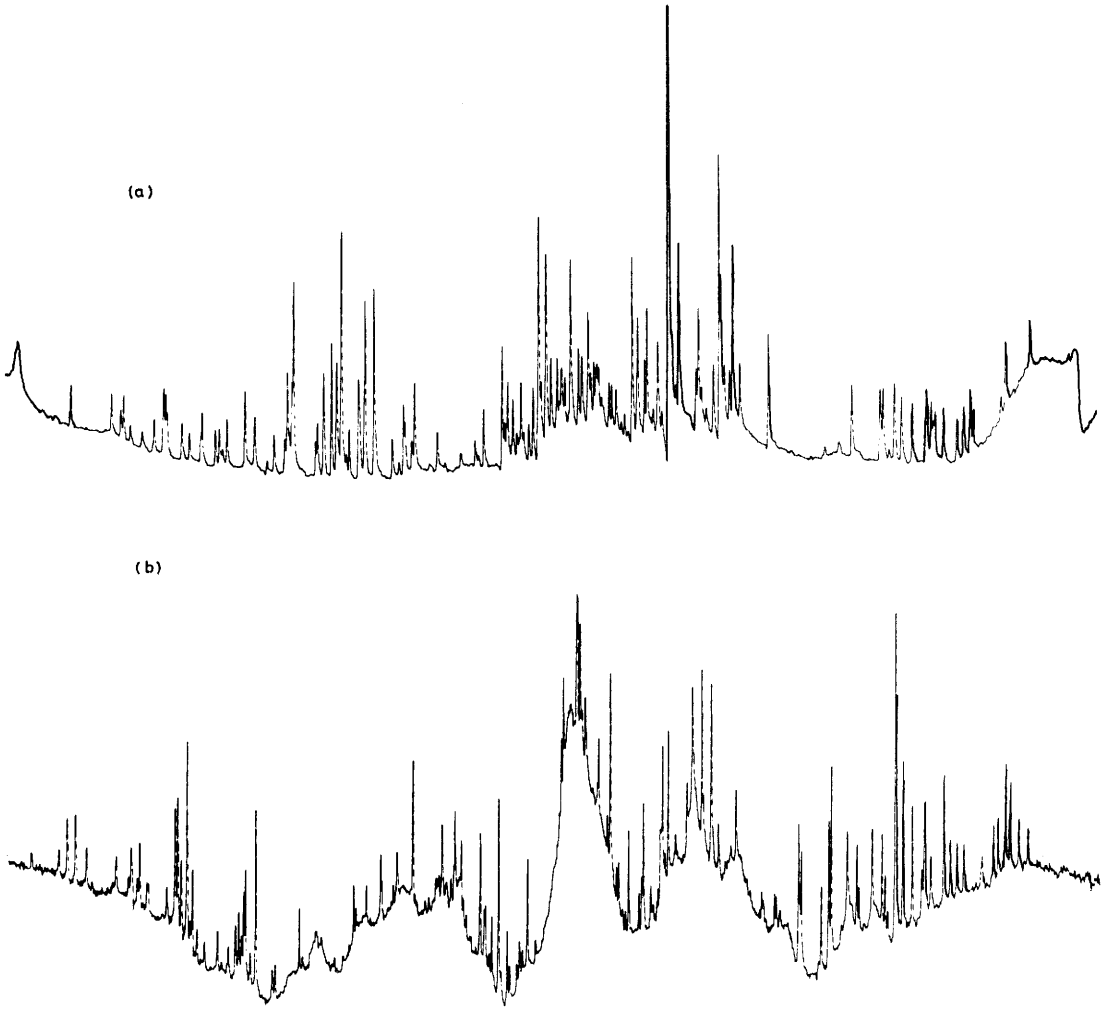

FIGURE 1 Proton n.m.r. spectra at 100 MHz of 4-acetylpyridine dissolved in (a) Phase V, (b) E5

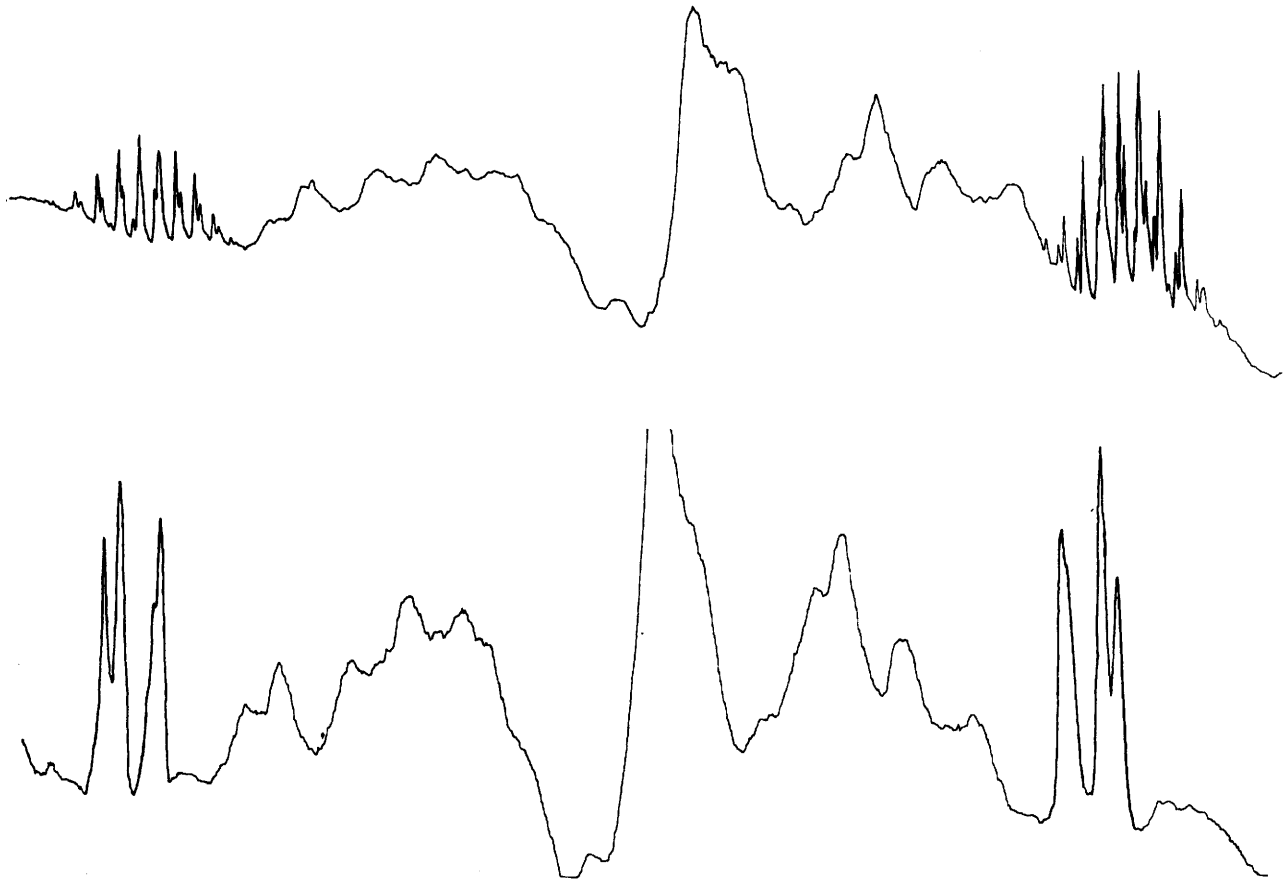

FIGURE 2 Proton and proton–{deuterium} spectrum of 4-[$^2H_3$]acetylpyridine dissolved in Phase V

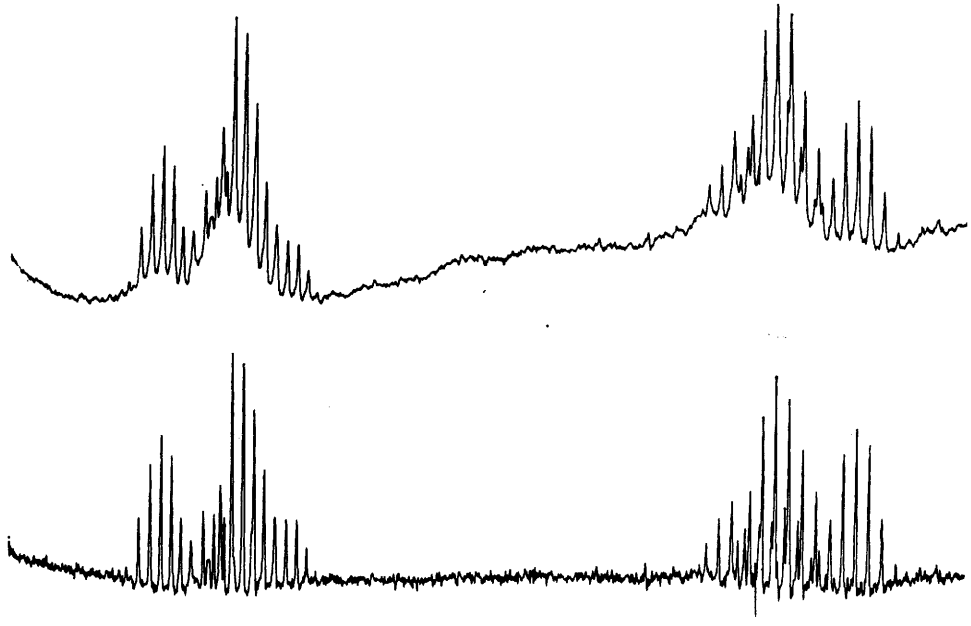

FIGURE 3 Proton spectrum at 200 MHz of 4-[$^2H_3$]acetylpyridine dissolved in E5 and showing the effect of convolution difference

to reveal any major effects. It was found that without vibrational averaging the ratios r_{12}/r_{23} varied between Phase V and E5 by 2.5%, which diminished to a maximum of 0.56% between the two phases for 4-acetylpyridine, as shown in Table 2. Vibrational averaging is

TABLE 2

Distance ratios, order parameters, and deuterium quadrupole coupling constants derived from n.m.r. data on 4-acetyl- and 4-[$^2H_3$]acetyl-pyridine *

	Phase V		E5		Microwave
	4-Acetyl	4-[$^2H_3$] Acetyl	4-Acetyl	4-[$^2H_3$] Acetyl	
r_{12}/r_{23}	0.602(3)	0.602(3)	0.606(3)	0.602(4)	0.604
r_{13}/r_{23}	1.188(3)	1.187(5)	1.189(1)	1.183(3)	1.188
r_{14}/r_{23}	1.044(2)	1.045(4)	1.046(1)	1.037(5)	1.047
θ(°)	120.29		120.02		
$S_{xx}-S_{yy}$	0.135		0.3070		
S_{zz}	0.299		0.132		
S_{xz}	0.110		0.027		
S_{33}		0.039(1)		0.139(2)	
q/kHz		165(5)		151(3)	

* The figures in parentheses are the uncertainties in the last significant figure.

therefore clearly important when attempting to compare structural information derived from spectra taken on samples dissolved in different phases. The results shown in Table 2 for the ratios lead us to conclude that the pyridine ring in 4-acetylpyridine is unchanged in structure between the two phases and is virtually identical with that in gaseous pyridine.

To investigate the structure and conformation of the methyl group it is necessary to use all the dipolar couplings for 4-acetylpyridine and, for the deuteriated samples, to use in addition the quadrupole splitting. For 4-acetylpyridine the number of structural parameters and order matrix elements required to describe the dipolar couplings exceeds the number of experimental quantities and hence we must resort to testing structural models. Our aim is necessarily restricted to seeking the simplest model which will fit the data. We will assume that vibrational corrections are unimportant when deciding between models, as found by studies on acetophenones [10-12] and anisoles.[6,10,12] This assumption is forced upon us by the lack of experimental data and the absence of a precise knowledge of the vibrational motions affecting the $COCH_3$ group. The study of a ^{13}C labelled anisole [6] found that attempting to use a purely theoretical vibrational wavefunction involved very large errors.

The simplest model which does fit the dipolar couplings has the following assumptions: (i) the methyl protons are moving rapidly between three positions related by a three-fold symmetry axis; (ii) the CH_3 has a tetrahedral arrangement with r_{CH} 1.09 Å and HCH 109.47°; (iii) the proton labelled 5 in Figure 4 lies in the plane of the pyridine ring; (iv) the methyl group as a whole moves rapidly between the two positions related by a mirror plane yz; and (v) the intermolecular potential $U_{ext.}$ which determines the orientational ordering of the molecule is sensitive to the different conformational states adopted by the molecule.[13]

With these assumptions there are the following unknown parameters which affect the dipolar couplings involving the CH_3 group: the angle θ and the order parameters S_{zz}, $S_{xx} - S_{yy}$, and S_{xz}.[13] The values of S_{zz} and $S_{xx} - S_{yy}$ are known from the ring dipolar couplings, hence the three dipolar couplings D_{1,CH_3}, D_{2,CH_3}, and D_{CH_3} can be used to determine θ and S_{xz}. The values

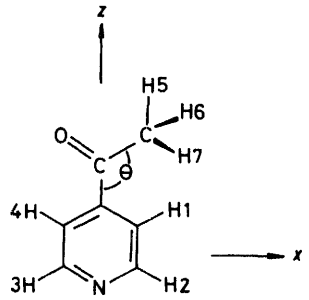

FIGURE 4 4-Acetylpyridine structure showing atom labelling and axes referred to in the text

obtained from the two sets of data are shown in Table 2 and are reasonable and hence the model is acceptable. The largest difference, ΔD_{ij}, between a calculated and observed coupling constant occurs for both sets of data for D_{2,CH_3} and is 2%. This residual can be reduced to zero by small adjustments to the methyl group structure, but could also be the result of neglecting vibrational averaging. A similar model, which has the CH(5) bond in a plane orthogonal to the pyridine ring, does not fit the data and can be neglected. We conclude, therefore, that the n.m.r. data on 4-acetylpyridine are in agreement with a model which also has been established for acetophenone [10,12] and which is most probably the correct kind of conformational model; we cannot be more precise because of the lack of experimental data.

The n.m.r. data obtained on the 4-[$^2H_3$]acetylpyridine samples can be used to investigate the conformational problem in a complementary way to that described for 4-acetylpyridine, except that the quadrupole splitting must be used in place of D_{CH_3}. Using data on the $^2H_3$ molecules has the considerable advantage that the spectra are much easier to analyse, but the dipolar couplings involving the protons and deuteriums are obtained with a lower relative precision. We have tested the model discussed earlier by using the six dipolar couplings to determine the value of S_{33} (see Figure 4), which can then be used to calculate the deuterium quadrupole coupling constant, q, which may then be compared with known values for CD_3 groups. The quadrupole splitting, $\Delta\nu$, is related to S_{33} and q by equation (1) where α is the DCD angle and we have

$$\Delta\nu = 3qS_{33}(3\cos^2\alpha - 1)/4 \qquad (1)$$

made the reasonable assumption that the asymmetry parameter of the quadrupole tensor for CD_3 nuclei is zero.[1] With α 109.47° equation (1) gives q as 164 ± 5 kHz from the Phase V data and 151 ± 3 kHz from E5 results. These values are in reasonable agreement with

each other, bearing in mind the neglect of vibrational averaging and are close to values found for other CD_3 groups, for example, 158.9 kHz for CDH_2OH,[14] 156.1 kHz for CDH_2CN,[14] and 160.7 kHz for CDH_2I.[15] We conclude, therefore, that the data obtained from analysing the proton spectra of 4-[$^2H_3$]acetylpyridine can be used to determine the conformation of the molecule and we are currently exploring the utility of this method for molecules containing CD_3 groups and whose proton spectra of the CH_3 compound are even more complex and hence more tedious to analyse than those for 4-acetylpyridine.

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