Conformations of the Formyl-, Acetyl-, and Benzoyl-pyridines

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Experimental dipole moments and molar Kerr constants for the 2-, 3-, and 4-formyl-, acetyl-, and -benzoylpyridines as solutes in cyclohexane at 25° are reported and analysed to provide information concerning the preferred conformations of these molecules.

MUCH valuable information concerning the preferred conformations of aromatic aldehydes and ketones has emerged from studies of molecular polarity and polarisability (see refs. 1—6 for some relevant examples). We have now examined the formyl-, acetyl-, and benzoylpyridines as solutes in cyclohexane at 25 °C. Experimental dipole moments and molar Kerr constants for these molecules are reported and analysed below.

EXPERIMENTAL

Materials.—Solutes were distilled or recrystallised (light petroleum) immediately before use to give: [b.p. (mmHg)] 2-formylpyridine, 54—56° (4·5); 3-formylpyridine, 62—64° (1·3); 4-formylpyridine, 53—55° (1·6); 2-acetylpyridine, 42—44° (1·5); 3-acetylpyridine, 72—74° (2·5); 4-acetylpyridine, 90—92° (10); 2-benzoylpyridine, 134—136° (1·5); 3-benzoylpyridine, 144—146° (*ca.* 2); and 4-benzoylpyridine, m.p. 72—73°.

Apparatus.—Dielectric constants were determined with equipment as in refs. 7 and 8; associated procedures giving polarisations are standard.[9a] Kerr effects at 589 nm were recorded photometrically.[10]

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[2] (*a*) J. Barassin and H. Lumbroso, *Bull. Soc. chim. France*, 1959, 1947; (*b*) J. Barassin, G. Queguiner, and H. Lumbroso, *ibid.*, 1967, 4707.

[3] P. H. Gore, P. A. Hopkins, R. J. W. Le Fèvre, L. Radom, and G. L. D. Ritchie, *J. Chem. Soc.* (*B*), 1971, 120.

[4] C. L. Cheng, R. J. W. Le Fèvre, G. L. D. Ritchie, P. A. Goodman, and P. H. Gore, *J. Chem. Soc.* (*B*), 1971, 1198.

[5] R. A. Y. Jones, A. R. Katritzky, and A. V. Ochkin, *J. Chem. Soc.* (*B*), 1971, 1795.

[6] C. T. Aw, H. H. Huang, and E. L. K. Tan, *J.C.S. Perkin II*, 1972, 1638.

[7] A. D. Buckingham, J. Y. H. Chau, H. C. Freeman, R. J. W. Le Fèvre, D. A. A. S. Narayana Rao, and J. Tardif, *J. Chem. Soc.*, 1956, 1405.

[8] R. J. W. Le Fèvre and D. J. Millar, *Chem. and Ind.*, 1971, 399.

[9] R. J. W. Le Fèvre, (*a*) ' Dipole Moments,' Methuen, London, 3rd edn., 1953, ch. 2; (*b*) *Adv. Phys. Org. Chem.*, 1965, **3**, 1; (*c*) *Rev. Pure Appl. Chem.*, 1970, **20**, 67.

[10] R. J. W. Le Fèvre and G. L. D. Ritchie, *J. Chem. Soc.*, 1963, 4933.

RESULTS

These are listed in the usual form in Table 1.* The symbols are those previously explained.[7,9,11]

Previous Measurements.—None of the solutes has previously been examined using cyclohexane as solvent. The dipole moments in Table 1 are in good agreement with literature data for benzene and carbon tetrachloride solutions.[1,2] Molar Kerr constants † are on record for some of the solutes (solvents as indicated): 2-formylpyridine[1] (benzene), +578; 2-acetylpyridine[1] (benzene), +396; 3-acetylpyridine[6] (carbon tetrachloride), +120; and 4-acetylpyridine[6] (carbon tetrachloride), +128.

DISCUSSION

Principle of Method.—Our approach is to use known bond and group dipole-moment and polarisability components, together with standard computational methods, to predict dipole moments and Kerr constants for possible stereostructures of each molecule. Comparison of the experimental data with the range of calculated values normally indicates the apparent molecular conformation. Anisotropic polarisabilities[9b] used in the calculations are given in Table 2. We have assumed valence angles of 120° around the carbonyl carbon atom. Exaltations of refraction and polarisability are shown in Table 3.

TABLE 1

Polarisations, refractions, dipole moments, and molar Kerr constants at 25 °C, from observations on solutions in cyclohexane

Molecule *	$\alpha\varepsilon_1$	β	$\gamma' n_1^2$	$_\infty P_2$/cm^3	R_D/cm^3	μ/D†	γ	δ	$10^{12}{}_\infty({}_{\mathrm{m}}K_2)$
2-FP	9·03 ± 0·07	0·26 ± 0·01		258 ± 2	29·8 ‡	3·33 ± 0·01	0·078 ‡	428 ± 8	+611 ± 12
3-FP	4·68 ± 0·02	0·275 ± 0·007		145·8 ± 0·6	29·9 ‡	2·37 ± 0·01	0·089 ‡	141 ± 4	+200 ± 6
4-FP	2·77 ± 0·03	0·268 ± 0·006		96·8 ± 0·6	29·8 ‡	1·79 ± 0·01	0·084 ‡	62 ± 2	+88 ± 3
2-AP	5·85 ± 0·04	0·236 ± 0·003		200 ± 1	34·1 ‡	2·84 ± 0·01	0·067 ‡	269 ± 2	+434 ± 3
3-AP	4·23 ± 0·06	0·256 ± 0·003		152 ± 2	33·8 ‡	2·39 ± 0·01	0·074 ‡	71 ± 1	+113 ± 2
4-AP	4·24 ± 0·02	0·254 ± 0·002		152·9 ± 0·6	33·9 ‡	2·39 ± 0·01	0·074 ‡	83 ± 1	+133 ± 1
2-BP	4·20 ± 0·10	0·322 ± 0·001	0·381 ± 0·007	227 ± 6	57·6 ± 0·3	2·86 ± 0·05	0·094 ± 0·002	99 ± 2	+239 ± 4
3-BP	4·48 ± 0·07	0·327 ± 0·002	0·361 ± 0·006	237 ± 3	56·4 ± 0·3	2·94 ± 0·03	0·088 ± 0·002	55 ± 1	+131 ± 2
4-BP	4·61 ± 0·03	0·323 ± 0·002	0·377 ± 0·009	243 ± 1	57·4 ± 0·4	2·99 ± 0·01	0·093 ± 0·002	241 ± 3	+589 ± 6

* FP = Formylpyridine, AP = acetylpyridine, BP = benzoylpyridine. † Calculated assuming $_DP = 1{\cdot}05\ R_D$. ‡ Calculated from data for pure liquids (ref. 2*a*).

TABLE 2

Anisotropic polarisabilities (Å^3) of bonds and groups

	b_L	b_T	b_V
C–H	0·65	0·65	0·65
C–C	0·97	0·26	0·26
C=O	2·30	1·40	0·46
C_5H_4N	10·05	9·75	5·80
C_6H_5	10·50	10·50	6·79

4-*Formylpyridine*.—Since benzaldehyde,[3] *p*-chlorobenzaldehyde,[4] and other *p*-substituted benzaldehydes[6] are known to be planar, it is reasonable to expect 4-formylpyridine also to exist in the resonance-stabilised planar form (Ia). To test this prediction we proceed to compare the observed molar Kerr constant with that calculated for (Ia).

The dipole moment, μ_r, of (Ia) can be considered as the vector resultant of components μ_1 (2·98 D, as in benzaldehyde[3]) inclined at an angle χ to the C=O bond and μ_2 (2·28 D, as in pyridine[12]) directed along the 1,4-molecular axis. From the expression $\mu_r^2 = \mu_1^2 + \mu_2^2 + 2\mu_1\mu_2 \cos(120 + \chi)$ the angle χ is calculable as 23°. It is noteworthy that for benzaldehyde[3] the corresponding angle is also *ca*. 20°.

With the exaltation of polarisability (Table 3) assigned along the *Y*-axis, the predicted molar Kerr constant for the planar form of (Ia) (+95) is in reasonable agreement with the experimental result (+88). We therefore infer that the 4-formylpyridine molecule is planar.

The dipole moments, polarisabilities, and treatment of exaltation found appropriate for 4-formylpyridine are now analogously applied to 3- and 2-formylpyridine, for each of which *two* planar forms must be considered.

TABLE 3

Exaltations of refraction (cm^3) and polarisability (Å^3)

Molecule *	R_D (obs)	R_D (calc.)	Δb
2-FP	29·8	28·7	0·9
3-FP	29·9	28·7	1·0
4-FP	29·8	28·7	0·8
2-AP	34·1	33·5	0·7
3-AP	33·8	33·5	0·3
4-AP	33·9	33·5	0·4
2-BP	57·6	53·0	4·9
3-BP	56·4	53·0	3·5
4-BP	57·4	53·0	4·6

* FP = Formylpyridine, AP = acetylpyridine, BP = benzoylpyridine.

3-*Formylpyridine*.—Dipole-moment studies by Lumbroso *et al*.[2] showed that, as a solute in benzene at 25°,

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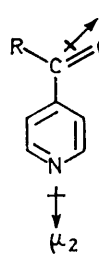
* Experimental data (incremental dielectric constants, *etc*.) are deposited as a Supplementary Publication SUP No. 20731 (5 pp.). For details of Supplementary Publications see *J.C.S. Dalton*, 1972, Index Issue. Items less than 10 pp. are supplied as full size copies.

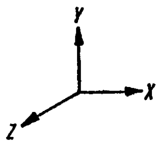
† Kerr constants are quoted throughout as $10^{12}{}_{\mathrm{m}}K$/e.s.u. mol^{-1}.

[11] C. G. Le Fèvre and R. J. W. Le Fèvre, *J. Chem. Soc.*, (*a*) 1953, 4041; (*b*) 1954, 1577; (*c*) *Rev. Pure Appl. Chem.*, 1955, **5**, 261; (*d*) 'Physical Methods of Organic Chemistry,' ed. Weissberger, Interscience, New York, 3rd edn., 1960, vol. 1, ch. 36, p. 2459.

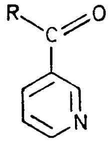
[12] A. L. McClellan, 'Tables of Experimental Dipole Moments,' Freeman, San Francisco, 1963.

3-formylpyridine exists as an equilibrium mixture of *ca.* 30% of the planar *cis*-form (IIa) and 70% of the corresponding *trans*-isomer (IIIa). Measurements of ^{1}H n.m.r. coupling constants by Karabatsos and Vane[13] confirmed this result.





(I)
a; R = H
b; R = Me



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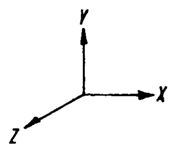
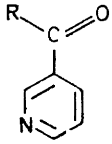


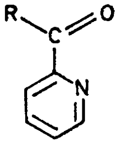


(III)

a; R=H
b; R=Me

Using the polarity and polarisability components found applicable in the case of 4-formylpyridine we have calculated dipole moments and Kerr constants for (IIa) and (IIIa). The results (which are to be compared with the experimental data in Table 1) are 3·97 D, +546 for (IIa) and 1·25 D, +86 for (IIIa). From the observed dipole moment (2·37 D) the relative abundances are (IIa) 30%, (IIIa) 70%, while the measured Kerr constant (+200) yields (IIa) 25%, (IIIa) 75%.

2-*Formylpyridine.*—Experimental evidence from dipole moments,[1,2] ^{1}H n.m.r. spectra,[13] and Kerr constants[1] has shown that the *trans*-conformation (Va) is strongly favoured over the *cis*-form (IVa). There is, however, some uncertainty concerning the precise isomer abundances, and estimates ranging from 100% *trans*[2] to 75—80% *trans*[1] have been given.



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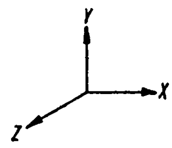

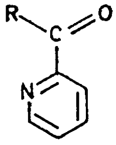

(V)

a; R=H
b; R = Me

The calculated dipole moment for (Va) is 3·53 D, and all other conformations have *larger* moments. Since the experimental result (3·33 D) is slightly *smaller* than this value we conclude that 2-formylpyridine (as a solute in cyclohexane at 25°) exists solely as (Va). The discrepancy between the observed and predicted dipole moments is almost certainly due to inductive interaction between the nitrogen atom and the C–H bond, arising from the proximity of these groups.

Analysis of the Kerr-effect data leads to a similar conclusion. The expected Kerr constants are (IVa) +1159 and (Va) +571, whereas the experimental results are +578 (in carbon tetrachloride) and +611 (in cyclohexane). Uncertainties in both the observed and predicted Kerr constants make it impossible definitely to exclude the presence of a small amount of the *cis*-form (IVa). However there is no doubt that 2-formylpyridine exists largely in the *trans*-conformation (Va).

We note also that the treatment of polarity and polarisability data for this molecule by Le Fèvre and Stiles[1] differs from ours in that these authors assumed the dipole moment of the formyl group to be directed along the axis of the C=O bond.

4-*Acetylpyridine.*—Although acetophenone[3] is known to be planar, *p*-chloroacetophenone[4] and other acetophenones with electron-withdrawing *para*-substituents[6] are undoubtedly non-coplanar, with dihedral angles, θ, of *ca.* 25°. In these molecules two competitive effects, which are rather finely balanced, operate to determine the effective value of θ: (i) a coplanarity-favouring mesomeric interaction, which tends to minimise θ, and (ii) various non-bonded repulsive interactions, due to crowding, which keep θ above a minimum. An electron-withdrawing *para*-substituent inhibits conjugation between the aromatic system and the acetyl group so that the latter acquires enhanced librational freedom.

Since Katritzky *et al.*[14] have adduced clear evidence from i.r. intensities that electron-acceptor groups (such as Ac) conjugate much less effectively with the 4-position of pyridine than with benzene, it is reasonable to expect the apparent conformation of 4-acetylpyridine to be similar to that of *p*-chloroacetophenone.

In order to analyse the Kerr constant of 4-acetylpyridine (Ib) it is necessary to establish the direction of action of the dipole moment of the acetyl group. Using a procedure analogous to that detailed for 4-formylpyridine (Ia) the corresponding angle for (Ib) emerges as 7°. This may be compared with the value of 10° assumed for *p*-chloroacetophenone.[4]

With the exaltation of polarisability assigned along the *Y*-axis, the calculated Kerr constant for the uniplanar structure (Ib) (which has $\theta = 0$) is +196, whereas the experimental value is only +133. Increasing the dihedral angle *lowers* the predicted Kerr constant, and agreement with the observed result occurs when $\theta = 25°$. There is, therefore, a close similarity between the effective conformations of 4-acetylpyridine and acetophenones with electron-withdrawing *para*-substituents.

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[13] G. J. Karabatsos and F. M. Vane, *J. Amer. Chem. Soc.*, 1963, **85**, 3886.

[14] A. R. Katritzky, C. R. Palmer, F. J. Swinbourne, T. T. Tidwell, and R. D. Topsom, *J. Amer. Chem. Soc.*, 1969, **91**, 636.

This conclusion supports the i.r. spectral evidence[14] concerning the nature of the aza-group as an aromatic 'substituent.'

3-*Acetylpyridine*.—The foregoing discussion of 4-acetylpyridine suggests that, contrary to previous assumptions,[2] the *cis* (IIb) and *trans* (IIIb) forms of 3-acetylpyridine may not be planar. In our analysis of data for this molecule we assume dihedral angles of 25° for (IIb) and (IIIb), together with the moment components and apportionment of exaltation found appropriate for 4-acetylpyridine.

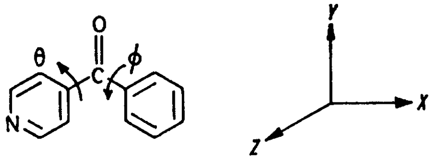
Calculated dipole moments and molar Kerr constants are (IIb), 4·28 D, +549, and (IIIb), 1·19 D, −22. Comparison with the experimental data (2·39 D, +113) indicates that for 3-acetylpyridine as a solute in cyclohexane at 25° the approximate isomer abundances are (IIb) 25% and (IIIb) 75%. Lumbroso *et al.*[2] reached a similar conclusion from their dipole-moment study of this molecule.

2-*Acetylpyridine*.—Polarity and polarisability considerations have previously been used to deduce the preferred conformation of 2-acetylpyridine. From dipole moments Lumbroso *et al.*[2] concluded that this molecule exists exclusively in the planar *trans*-conformation (Vb), rather than the *cis*-isomer (IVb), which is clearly disfavoured on electrostatic grounds. Analysis of the Kerr constant by Le Fèvre and Stiles[1] indicated that although (Vb) is strongly favoured, up to *ca.* 15% of (IVb) could also be present.

However the result for 4-acetylpyridine suggests, once again, that (IVb) and (Vb) may not be planar, and we assume initially dihedral angles of 25° in both conformers. The dipole moment of (Vb) (calculated without allowance for interaction between the nitrogen atom and the carbonyl group) is 3·09 D, and all other structures have higher moments. Since the experimental value is 2·84 D we conclude that only the *trans*-form (Vb) of 2-acetylpyridine occurs in cyclohexane at 25°. On the other hand the predicted Kerr constants for the two (non-planar) isomers are (IVb) +866 and (Vb) +291, so that the measured result is consistent with the presence of only 75% of (Vb). It therefore seems possible that for 2-acetylpyridine the interplanar angle is not as great as 25°. We note that if θ were taken as zero the calculated Kerr constants would be (IVb) +989, and (Vb) +358, in which case the relative abundance of (Vb) would be 88%.

4-*Benzoylpyridine*.—Conformations of this molecule are completely specified by two dihedral angles (θ,ϕ) defined in the following way. We imagine the C–CO–C group to be fixed in the XY-plane so that the orientations of the pyridyl and phenyl groups relative to this reference plane are θ and ϕ, respectively. The (0,0) structure is the sterically impossible uniplanar form shown (VI). Rotations θ,ϕ about the C_{ar}–C bonds are made in *anti-clockwise* directions if the rotation axis is viewed from the aromatic carbon atom to the carbonyl carbon atom.

Theoretical Kerr constants were computed with the exaltation of polarisability apportioned in the ratio $X : Y = 2 : 1$. Some representative results for conformations (θ,ϕ) are shown in Table 4. We note that the variation of $_{m}K$ with ϕ is much smaller than with θ. This is because the line of action of the molecular dipole moment is close to the rotation axis (the C_{ar}–C bond) for the phenyl group.



(VI)

We begin our analysis by considering only conformations having both θ and ϕ in the range 0—90° (*i.e.*, the top left quadrant of Table 4). It is easily deduced that combinations (θ,ϕ) for which there is agreement between observed and predicted Kerr constants range from (26,0) to (17,90). Once again, the actual molecular conformation is determined by competing steric and mesomeric effects. Since it has been shown[14] that conjugation of a carbonyl group is much stronger with a phenyl group than with a 4-pyridyl group, it seems reasonable to suggest that $\phi < \theta$, so that $\phi < 26°$. Examination of a scale model of 4-benzoylpyridine shows that if θ is *ca.* 25° then, on steric grounds, ϕ cannot be less than *ca.* 25°. Therefore the (25,25) structure appears to be the most likely within this region of Table 4.

TABLE 4

Calculated Kerr constants for conformations (θ,ϕ) of 4-benzoylpyridine

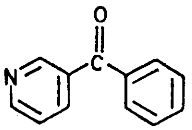
θ° ϕ°	0	30	60	90	120	150	180
0	+690	+554	+282	+146	+282	+554	+690
30	+676	+538	+270	+140	+278	+546	+676
60	+649	+514	+253	+126	+261	+522	+649
90	+635	+506	+248	+119	+248	+506	+635
120	+649	+522	+261	+126	+253	+514	+649
150	+676	+546	+278	+140	+270	+538	+676
180	+690	+554	+282	+146	+282	+554	+690

Application of similar reasoning to the complete set of data in Table 4 shows that there are in fact two equally favoured forms, (25,25) and (155,155), these being optical isomers. The structures (25,155) and (155,25) show severe steric interaction between *ortho*-hydrogen atoms and can therefore be eliminated.

The preferred conformation of 4-benzoylpyridine ($\theta = \phi = 25°$) is therefore consistent with the result for 4-acetylpyridine ($\theta = 25°$) and similar to that of benzophenone ($\theta = \phi = 42°$).

3-*Benzoylpyridine*.—Structures of 3-benzoylpyridine are also fixed by two dihedral angles (θ,ϕ), defined as for 4-benzoylpyridine, with (0,0) corresponding to the sterically disallowed planar *cis*-form (VII). However, for this molecule it proved impossible to find a single conformation for which both the predicted dipole moment and Kerr constant have the experimental values. Consequently it seems that 3-benzoylpyridine, like 3-formyl- and 3-acetyl-pyridine, exists as an equilibrium mixture of *cis* (VII) and *trans* (VIII) isomers. From the discussion of 4-benzoylpyridine it is reasonable to assume dihedral angles of 25° for both the pyridyl and the phenyl groups. The two forms are thus postulated to be the *cis* (25,25) and *trans* (155, 155) structures (which for 3-benzoylpyridine are *not* optical isomers).

Calculated dipole moments and Kerr constants for these conformations emerge as (VII), 4·62 D, +1082, and (VIII), 1·28 D, −9, respectively. From the observed dipole moment (2·94 D) the relative abundances are (VII) 35%, (VIII) 65%, while the Kerr constant (+131) gives (VII) 15%, (VIII) 85%. The conformational result for 3-benzoylpyridine (*ca.* 25% *cis*, 75% *trans*) therefore closely parallels the conclusions for both 3-formylpyridine and 3-acetylpyridine, with the *trans*-form being strongly favoured.



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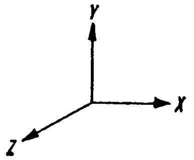
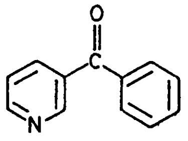
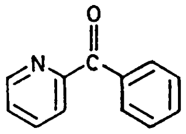




(VIII)

2-*Benzoylpyridine*.—As with 3-benzoylpyridine, an equilibrium mixture of non-planar *cis* (IX) and *trans* (X) isomers might be expected for this molecule. However the presence of a nitrogen atom instead of a C–H group in the *ortho*-position, suggests that *three* conformers (having dihedral angles of 25°) of 2-benzoylpyridine are sterically possible. These are a *cis*-form (25,25) and *two trans*-structures, (155,155) and (155,25), the latter being sterically impossible for 3-benzoylpyridine.

Predicted dipole moments emerge as: (25,25), 5·15 D; (155,155), and (155,25), 2·60 D. Comparison with the measured value (2·86 D) indicates relative abundances of *cis* 10% and *trans* 90%. The corresponding Kerr constants are (25,25) +1113, (155,155) +324, and (155,25) +164. From the observed Kerr constant (+239) it may also be concluded that 2-benzoylpyridine exists largely as a mixture of the two *trans*-conformations. The 2-benzoyl compound therefore exhibits the same strong preference for the *trans*-arrangement as the 2-formyl and 2-acetyl derivatives.



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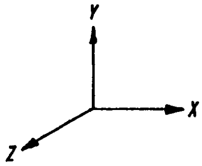

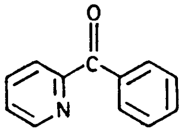

(X)

[3/575 *Received*, 19*th March*, 1973]