Conformations of 2-Formyl-, 2-Acetyl-, and 2 Benzoyl-pyrroles

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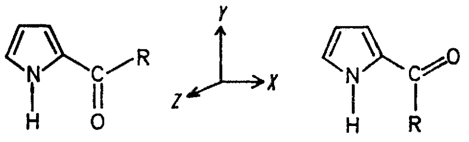
Experimental dipole moments ($10^{30}\mu$/C m) and molar Kerr constants [$10^{27}{}_{\infty}({}_{m}K_2)$/m^5 V^{-2} mol^{-1}] are reported for the following as solutes in cyclohexane at 25°: 2-formylpyrrole, 4·33, +76; 2-acetylpyrrole, 3·98, +50; and 2-benzoylpyrrole, 4·06, +42. The results are analysed to provide information concerning the preferred conformations of these molecules.

THE conformational preferences of heteroaromatic aldehydes and ketones are continuing to attract much attention. Various physical methods have been applied to the 2-substituted pyrroles (dipole moments,[1-3] i.r.[4-7] and n.m.r.[8-14] spectra, dielectric relaxation [2]) but some problems remain. It might reasonably be expected that 2-formylpyrrole would exist in the resonance-stabilised planar *cis*-form (Ia), in which the component dipoles are approximately antiparallel, rather than in the *trans*-form (IIa). Although this expectation was confirmed many years ago by measurements of dipole moments,[1] a recent n.m.r. spectral investigation [10] resulted in a contrary assertion, which has however since been refuted.[11-14] The corresponding acetyl and benzoyl compounds have been less studied, but it has been inferred that for these also the *cis*-arrangement is favoured.[1-3,6] In addition the apparent dipole moments of the 2-acylpyrroles are markedly solvent-dependent, a fact which has given rise to some unsatisfactory interpretations of experimental data.[2,3]



(I) (II)

a; R = H
b; R = Me
c; R = Ph

We here report and analyse dipole moments and molar Kerr constants at 25° for 2-formyl-, 2-acetyl-, and 2-benzoyl-pyrroles as solutes in cyclohexane.

EXPERIMENTAL

Solutes.—A commercial sample of 2-formylpyrrole (Aldrich) after recrystallisation from light petroleum had m.p. 45—46°. The acetyl and benzoyl compounds were prepared by a published procedure:[15] 2-acetylpyrrole (63%), purified by repeated recrystallisation after column (alumina) chromatography, m.p. 89° (lit.,[15] 89°); 2-benzoylpyrrole (60%), purified as above, m.p. 78° (lit.,[15] 77—78°).

Apparatus, Results, etc.—Dielectric constants were determined with apparatus as in ref. 16 and Kerr effects at 589 nm were recorded photometrically.[17] Details of

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procedures, symbols, solvent constants, *etc.*, have been given by Le Fèvre and Le Fèvre.[18] The results are summarised in Table 1. It should be noted that in this paper dipole moments (μ), molar Kerr constants ($_{m}K$), and molecular polarisabilities (b) are expressed in S.I., units rather than in the non-rationalised electrostatic (c.g.s., e.s.u.) system hitherto used. The conversion factors for these three physical quantities are, respectively: 1 C m = $0{\cdot}2998 \times 10^{30}$ D (dipole moment), 1 m^5 V^{-2} mol^{-1} = $0{\cdot}8988 \times 10^{15}$ e.s.u. mol^{-1} (molar Kerr constant), and 1 C m^2 V^{-1} = $0{\cdot}8988 \times 10^{16}$ cm^3 (polarisability). In the discussion which follows dipole moments are, for convenience, quoted as $10^{30}\mu$/C m and molar Kerr constants as $10^{27}{}_{m}K/m^5\ V^{-2}\ mol^{-1}$.

TABLE 1

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

Molecule ‡	$\alpha\varepsilon_1$	β	$\gamma'n_1^2$	$_\infty P_2/cm^3$	R_D/cm^3	$10^{30}\mu$/C m	γ	δ	$10^{27}(_{m}K_2)/m^5\ V^{-2}\ mol^{-1}$
2-FP	1·95 ± 0·02	0·269 ± 0·004	0·365 ± 0·017	67·2 ± 0·5	31·2 ± 0·5	4·33 ± 0·07	0·090 ± 0·004	54 ± 3	+76 ± 4
2-AP	1·48 ± 0·02	0·244 ± 0·005	0·299 ± 0·009	65·8 ± 0·6	35·0 ± 0·4	3·98 ± 0·07	0·074 ± 0·002	30·9 ± 0·9	+50 ± 1
2-BP	1·29 ± 0·01	0·317 ± 0·004	0·483 ± 0·015	91·4 ± 0·5	58·3 ± 0·8	4·06 ± 0·09	0·119 ± 0·004	17·0 ± 0·5	+42 ± 1

* Calculated assuming $_{D}P = 1{\cdot}05\ R_D$. † For each solute the incremental dielectric constants, Kerr effects, *etc.* were measured for five solutions within the concentration range 10^5w_2 = 378—1118. ‡ 2-FP = 2-Formylpyrrole, 2-AP = 2-acetylpyrrole, 2-BP = 2-benzoylpyrrole.

DISCUSSION

Analysis of Dipole Moments.—Table 2 summarises literature values for the dipole moments of the three molecules. A pronounced solvent dependence is apparent. At least three factors can be advanced as possible contributors to this effect: (i) solute–solute association, (ii) solute–solvent association, and (iii) a solvent-dependence of the free-energy difference between the *cis*- and *trans*-isomers, whose relative abundances would then vary from one medium to another.

TABLE 2

Solvent dependence of dipole moments (expressed as $10^{30}\mu$/C m) of 2-acylpyrroles

Solute \ Solvent [a]	C	CT	B	D
2-FP			6·27 [b]	8·07 [b]
			7·27 [c]	8·51 [c]
	4·34 [d]	5·30 [d]	7·34 [d]	8·57 [d]
	4·34 [e]			
2-AP			5·07 [b]	5·97 [b]
			6·07 [c]	6·61 [c]
			5·80 [d]	7·21 [d]
	3·97 [e]			
2-BP			6·04 [c]	6·37 [c]
	4·04 [e]			

[a] C = Cyclohexane, CT = carbon tetrachloride, B = benzene, D = 1,4-dioxan. [b] Ref. 1. [c] Ref. 2. [d] Ref. 3. [e] Present work.

Solute–solute association is known to occur for 2-acylpyrroles[19,20] but since the experimental dipole moments were obtained from observations on very dilute solutions (weight fractions <*ca.* 0·01) by procedures involving extrapolation to infinite dilution, interactions of this sort can be discounted. Stereospecific solute–solvent interactions also undoubtedly occur, specially in the donor solvents benzene and dioxan, but such effects are usually very much smaller than those encountered here.

Therefore we believe that (iii) is the predominant factor: reaction-field stabilisation of the more polar *trans*-form in polar or donor solvents reduces the free energy difference between the isomers, giving rise to a higher proportion of the *trans*-form and a correspondingly higher apparent dipole moment.[21] A quantitative treatment of this effect, developed by Abraham and Cooper,[22] was recently applied to the analogous molecule 2-formylfuran, for which the position of equilibrium between the two planar isomers is even more dependent on the nature of the medium.[23]

It may be noted that of the solvents listed in Table 2 cyclohexane is the least interactive and has the lowest dielectric constant so that isomer abundances in this medium will bear the closest resemblance to those in the vapour state at the same temperature.

To determine the preferred conformations of the three 2-acylpyrroles in cyclohexane at 25° we use known group moments to calculate expected dipole moments for the *cis*- and *trans*-isomers of each molecule. The moments of (I) and (II) can be considered to be approximately calculable as the vector resultants of components μ_1 acting along the H–N bond from H to N, and μ_2 directed along the axis of the C=O group. We take μ_1 as 5·80 (as found for pyrrole[3]) and μ_2 as 9·90 (from the moments of benzaldehyde,[24] acetophenone,[25] and benzophenone[26]). Bond angles for the heterocyclic ring were taken from the microwave structure of pyrrole.[27] In the absence of data for the appropriate pyrrole derivatives, bond angles for the substituent groups were assumed to be the same as found for

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2-formylfuran.[28] The inclinations of μ_1 to μ_2 then emerge as (I) 172 and (II) 55°, while the calculated dipole moments are (I) 4·23 and (II) 14·1. Agreement between the measured values and that predicted on this simple basis for the *cis*-conformation is in each case sufficiently good to exclude the presence of the *trans*-form, which has a much higher dipole moment.

Our conclusion is supported by the results of dielectric relaxation studies.[2] We note, however, that Cumper and Wood [2] attempted to explain their dipole moments for these molecules dissolved in *benzene* in terms of a single conformation. From the foregoing discussion of reaction-field stabilisation of the *trans*-form it seems more probable that in benzene 10—20% of this isomer is present, as suggested by Lumbroso *et al.*[3] The analysis of dipole moments by the latter workers nevertheless appears unsatisfactory in that their moment calculated for the *cis*-form of 2-formylpyrrole in cyclohexane (6·00) is significantly *greater* than the measured value (4·34). The reason for this discrepancy is that it was assumed that the line of action of the carbonyl group moment is inclined at 26° to the C=O axis, as in benzaldehyde. It seems, however, that the benzene and pyrrole molecules are sufficiently dissimilar to render this assumption invalid.

Analysis of Kerr Constants.—Here the procedure is to choose suitable molecule-fixed orthogonal axes and to transform the known bond and group moment and polarisability components into this axis system. Standard computational methods [18] are then used to predict Kerr constants for possible stereostructures of each molecule. Anisotropic polarisabilities [18,29] used in the calculations are shown in Table 3. Exaltations of refraction (ΔR_D/cm^3) and polarisability ($10^{40}\Delta b$/C m^2 V^{-1}), which are somewhat uncertain, are as follows: 2-formylpyrrole, 4·9, 5·6; 2-acetylpyrrole, 4·0, 4·6; 2-benzoylpyrrole, 7·9, 9·0. These exaltations are much larger than for the corresponding benzene derivatives. Therefore it may be inferred that the carbonyl group conjugates rather more effectively with a 2-pyrrolyl ring than with a phenyl group, as was proposed by Khan and Morgan [4] from i.r. spectral evidence. Such a suggestion is in accord with recent calculations [30,31] of the charge distribution in pyrrole: the π electron donating nitrogen atom in this molecule gives rise to an enhanced charge density at the 2-position, thereby facilitating mesomeric interaction with an electron-withdrawing group.

TABLE 3

Polarisability components (expressed as $10^{40}b$/C m^2 V^{-1}) for bonds and groups

	b_L	b_T	b_V
C–H	0·72	0·72	0·72
C–C	1·08	0·29	0·29
C=O	2·56	1·56	0·51
C_6H_5	11·69	11·69	7·56
C_4H_4N	8·95	9·66	5·72

2-Formyl- and 2-Acetyl-pyrrole.—For the planar *cis*- and *trans*-isomers of these molecules the exaltation was apportioned in the ratio $\Delta b_{xx} = \Delta b_{yy} = 2\Delta b_{zz}$. The calculated molar Kerr constants are: 2-formylpyrrole, +85 (I) and +658 (II); 2-acetylpyrrole, +80 (I) and +700 (II). In each case the experimental value is slightly *lower* than that predicted for the *cis*-conformer, which is therefore the only isomer present.

2-Benzoylpyrrole.—We here consider only structures having the coplanar *cis*-arrangement of the pyrrole ring and the carbonyl group, as required by the experimental dipole moment. It is obvious from steric considerations that for the pyrrole ring to be coplanar with the C–CO–C plane the phenyl ring must be significantly rotated from this plane. Particular conformations are defined by the dihedral angle ϕ between the planes of the aromatic ring and the carbonyl group. In calculating Kerr constants we distributed the exaltation isotropically, since the molecule cannot be uniplanar. Predicted Kerr constants for various values of ϕ are +131 (0°), +99 (30°), +34 (60°), and +1 (90°); the measured value (+42) corresponds to a dihedral angle of 55°. However because of the uncertainty associated with the assignment of the large exaltation this result may be in error by ±10°.

Conclusions.—From our measurements it is clear that in cyclohexane 2-formyl-, 2-acetyl-, and 2-benzoylpyrroles show a very strong preference for the *cis*-arrangement (I) in which the H–N and C=O dipoles are approximately antiparallel. The predominance of dipole–dipole interactions in determining the preferred conformations of 2-acylpyrroles is further evidenced by the *cis*-structures found even for molecules having bulky alkyl substituents on the nitrogen atom.[7] In 2-benzoylpyrrole the phenyl group is rotated by *ca.* 55° from the plane containing the pyrrole ring and the carbonyl group. The apparently anomalous result of Arlinger *et al.*[10] for 2-formylpyrrole may be due to their use of hexadeuterioacetone as solvent, in which significant reaction-field stabilisation of the more polar *trans*-isomer can be expected.

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