An Infrared Study of the Conformations and Association of Pyrrole-2-carbaldehydes and Pyrrole-2-carboxylates

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The NH and CO bands of solutions of pyrrole-2-carboxylates, pyrrole-2-carbaldehydes, and their *N*–Me analogues have been studied. Knowledge gained from the spectra of the aldehydes, which are known to adopt the *N,O-syn*-conformation, was applied in deducing the conformational preferences of the esters from their i.r. absorptions. The *N*-Me esters exist predominantly or exclusively in the *N*,carbonyl *O-syn*-arrangement. With the *N*–H esters both *syn*- and *anti*-rotamers are present, the former predominating, and in the case of t-butyl pyrrole-2-carboxylate the *syn*-form was shown to be thermochemically more stable than the *anti*-form by *ca.* 4.8 kJ mol^{-1}. The intermolecular associations of pyrrole-2-carbaldehyde and of t-butyl pyrrole-2-carboxylate give species containing more than two molecules of the substrates and involve similar enthalpy changes (*ca.* 22 kJ mol^{-1}).

THE formyl proton of furan-, thiophen-, and pyrrole-2-carbaldehydes provides a suitable probe for examining the conformational preferences of these aldehydes by ^{1}H n.m.r. spectrometry. The consensus of many studies [1] is that while furan-2-carbaldehyde exists as a mixture of two rotamers whose proportions are temperature and solvent dependent, the thiophen and pyrrole analogues (and 1-methylpyrrole-2-carbaldehyde) have a marked or even an exclusive preference for the *syn*-conformation [as (II) in the Scheme]; these conclusions are further strengthened by ^{13}C n.m.r. evidence.[2] Examination of the i.r. carbonyl absorptions of furan- and thiophen-carbaldehydes does not afford reliable information about the number of rotamers present; there may be little or no difference in position between the bands of the *syn*- and *anti*-forms, and doublet carbonyl absorption may arise from the incursion of Fermi resonance.[3] With the related alkyl furan- and thiophen-2-carboxylates the relative merits of the n.m.r. and i.r. methods for detecting rotational isomerism are reversed.[4] The ineffectiveness of ^{1}H n.m.r. spectrometry may stem from either or a combination of two factors, *viz.* insufficient difference between the rotamers' spectral characteristics, and a very low barrier to rotation between the forms. (^{13}C N.m.r. results indicate that the energy barrier is lower with the esters than with the aldehydes.[2])

In the present work the main object was to examine the conformational features of a series of pyrrole-2-carboxylates by i.r. spectrometry. However, since it was expected that the spectra of the esters lacking *N*-substituents would be complicated by the occurrence of association through hydrogen-bonding, the corresponding aldehydes were also to be studied in order to provide reference data on related compounds having a marked preference for the *syn*-conformation. There is little in the literature about the i.r. of either the esters or the aldehydes. Dilute solutions in carbon tetrachloride of *N*–H pyrrole esters show two NH stretching bands whose relative intensities are independent of concentration,[5] but no information about the carbonyl absorptions or the association of these compounds is available. Association of pyrrole-2-carbaldehydes was investigated by examining the intensities of the NH bands of the free (non-associated) forms in carbon tetrachloride as functions of concentration.[6] It was concluded that at very low concentrations (up to *ca.* 3×10^{-4} mol l^{-1}) the associated forms may be ' closed dimers ' [*e.g.* species (I) in the Scheme, from pyrrole-2-carbaldehyde] but that at higher concentrations a number of more highly associated forms predominate.

The NH and CO bands of pyrrole-2-carbaldehydes, alkyl pyrrole-2-carboxylates, and the *N*–Me analogues are recorded in Table 1; detailed examinations of one aldehyde and one ester are shown in Table 2. Central features of the interpretation (Scheme) of these results are that the *syn*-forms of all the pyrroles (*i.e.*, the aldehydes and esters of both the *N*–H and *N*–Me types) involve an electrostatic $N^{+} \cdots {}^{-}O$ attraction as in formula (II) and that those of the *N*–H aldehydes and esters may exhibit intramolecular hydrogen bonding as in formula (III).

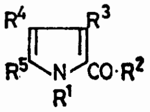
Since solutions of the *N*–Me aldehydes (14), (16), and (17) in carbon tetrachloride show only single carbonyl bands these must be attributed to the *N,O-syn*-forms (IV). In the more polar solvent, acetonitrile, the bands are broader. (This effect is general with the pyrrole esters and aldehydes. To obtain bands of similar heights in the two solvents the concentration of the acetonitrile solution must be increased by more than the factor corresponding to a ten-fold decrease in cell length.) The results with 4-bromo-1-methylpyrrole-2-carbaldehyde (15) indicate that the doublet absorption arises from Fermi resonance rather than rotational isomerism. Bromine substituents at the different nuclear positions cause shifts in the carbonyl bands similar to those observed with analogous furan- and thiophen-carbaldehydes.[3]

Solutions in carbon tetrachloride of the *N*–H aldehydes [compounds (10)—(13)] exhibit NH and CO doublets, the lower wavenumber components of which were shown by dilution experiments to arise from intermolecular association. For the parent aldehyde (10) the results in Table 2, which represent only the extremes and the middle of the range of concentrations used, exclude the possibility that the associated form is the dimer (I). (The concentration range of the present study is much higher than that of the Italian work.[6]) It was not possible to develop a satisfactory quantitative interpretation on the basis of a single associated form containing an integral number of aldehyde units, and, in agreement with the earlier work,[6] it must be concluded that there are several forms whose relative proportions depend on the concentration. The surprising feature is that the positions of the bands do not vary over a wide

TABLE 1

N–O and C=O bands of pyrrole esters and aldehydes

Solutions (concentration c, mg per g of solution) were examined at 303 K, as described previously [a] using cells of path lengths 1 cm or 5 mm (for CCl_4, NH region), 1 mm (for CCl_4, CO region), and 0.1 mm (for MeCN, CO region). Overlapping absorptions were resolved [a] to give symmetrical bands. The positions of bands (cm^{-1}) are followed, in parentheses, by their areas expressed as percentages of the total absorption in a particular region. The band intensities of compounds marked with an asterisk vary with concentration (CCl_4 solutions) as illustrated in Table 2; those of the other compounds are almost independent of concentration in the range c 5—0.05



Compound	R^1	R^2	R^3	R^4	R^5		Band 1	Band 2	Band 3	Band 4
(1)*	H	OMe	H	H	H	NH region	3 482(12)	3 566(63)	3 317(25)	
		CCl_4 (c 0.776)				CO region	1 730(11)	1 702(34)	1 678(9)	1 717(46)
		MeCN (c 16.6)				CO region	1 720(39)	1 701(55)		1 709(6)
(2)*	H	OEt	H	H	H	NH region	3 483(14)	3 466(56)	3 311(30)	
		CCl_4 (c 0.875)				CO region	1 724(18)	1 700(63)	1 686(19)	
		MeCN (c 16.8)				CO region	1 713(31)	1 699(69)		
(3)*	H	OBu^t	H	H	H	NH region	3 483(13)	3 465(59)	3 309(28)	
		CCl_4 (c 1.02)				CO region	1 717(18)	1 694(71)	1 677(11	
		MeCN (c 17.4)				CO region	1 701(42)	1 693(58)		
(4)	Me	OMe	H	H	H					
		CCl_4 (c 0.775)				CO region		1 710(100)		
		MeCN (c 16.4)				CO region		1 707(100)		
(5)	Me	OEt	H	H	H					
		CCl_4 (c 0.780)				CO region		1 706(100)		
		MeCN (c 17.0)				CO region		1 703(100)		
(6)	Me	OBu^t	H	H	H					
		CCl_4 (c 0.805)				CO region		1 701(100)		
		MeCN (c 17.3)				CO region		1 698(100)		
(7)	Me	OMe	H	Br	H					
		CCl_4 (c 0.899)				CO region		1 715(89)		1 704(11)
		MeCN (c 15.8)				CO region		1 713(76)		1 703(24)
(8)	Me	OMe	H	H	Br					
		CCl_4 (c 0.878)				CO region †		1 712(100)		
		MeCN (c 16.2)				CO region		1 709(100)		
(9)	Me	OMe	H	Br	Br					
		CCl_4 (c 0.097)				CO region		1 713(100)		
		MeCN (c 18.4)				CO region		1 712(100)		
(10)*	H	H	H	H	H	NH region		3 461(40)	3 274(60)	
		CCl_4 (c 0.302)				CO region †		1 667(55)	1 656(45)	
		MeCN (c 7.61)				CO region		1 663(100)		
(11)*	H	H	H	Br	H	NH region		3 448(41)	3 256(59)	
		CCl_4 (c 0.543)				CO region		1 672(56)	1 660(44)	
		MeCN (c 13.5)				CO region		1 668(100)		
(12)*	H	H	H	H	Br	NH region		3 442(50)	3 200(50)	
		CCl_4 (c 0.534)				CO region		1 677(60)	1 657(40)	
		MeCN (c 13.1)				CO region		1 663(100)		
(13)*	H	H	H	Br	Br	NH region †		3 430(39)	3 210(61)	
		CCl_4 (c 0.844)				CO region		1 672(53)	1 658(47)	
		MeCN (c 19.5)				CO region		1 669(100)		
(14)	Me	H	H	H	H					
		CCl_4 (c 0.672)				CO region		1 668(100) ‡		
		MeCN (c 17.2)				CO region		1 664(100)		
(15)	Me	H	H	Br	H					
		CCl_4 (c 0.724)				CO region §		1 679(92)		1 668(8)
		MeCN (c 18.2)				CO region		1 676(69)		1 668(31)
(16)	Me	H	Br	H	Br					
		CCl_4 (c 0.873)				CO region		1 670(100)		
		MeCN (c 18.5)				CO region		1 668(100)		
(17)	Me	H	H	Br	Br					
		CCl_4 (c 0.860)				CO region		1 676(100)		
		MeCN (c 18.8)				CO region		1 672(100)		

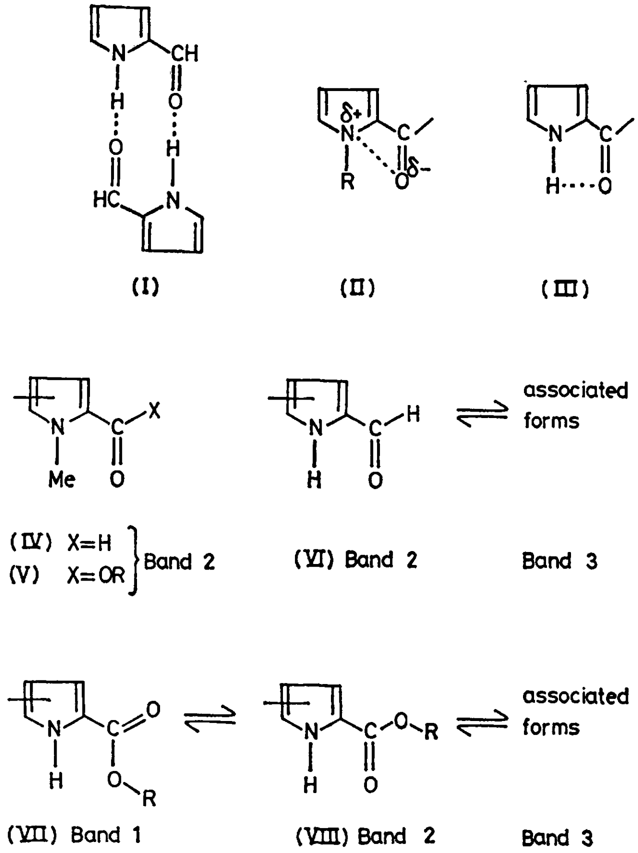
† The presence of an additional very weak band (or two such bands) was neglected during curve analysis. ‡ Broad, but apparently a single band. § Overtone region (1 cm cell), band at 3338 cm^{-1} (area 100%).

[a] D. J. Chadwick, J. Chambers, G. D. Meakins, and R. L. Snowden, *J.C.S. Perkin II*, 1972, 1959.

range of concentration; changes in the proportions of the forms might be expected to influence the maxima of the composite absorptions.

The higher wavenumber components of the NH and CO doublets of the aldehydes (10)—(13) are assigned to the *syn*-forms (VI). From the positions of the CO absorptions in the range of aldehydes it emerges that replacement of *N*-H by *N*-Me moves the bands to slightly higher wavenumber. This shift, in the direction opposite to that predicted from the inductive effect of the methyl group, is consistent with the removal of the weak intramolecular hydrogen bonding in the *N*-H compounds. [Although many factors may influence the positions of the NH bands, consideration of the esters (see later) suggests that the absorptions are at somewhat lower wavenumbers than they would be in the absence of intramolecular bonding.] Changing the solvent from carbon tetrachloride to the more polar acetonitrile causes a lowering of the wavenumbers of the CO bands with both *N*-H and *N*-Me aldehydes. The shifts are small, however, which suggests that the decrease in wavenumber by the standard dielectric effect is offset to some extent by an increase resulting from a weakening of the intramolecular electrostatic attraction. (That the *N*-H and *N*-Me aldehydes are similar in this respect indicates that intramolecular hydrogen bonding in the former is not the dominant feature in determining their CO bands' positions.)

SCHEME The bands assigned to the various forms are those listed under the appropriate headings in Table 1



Enthalpy differences * (KJ mol^{-1})

		$\Delta H°$, from	
		NH bands	CO bands
t-Butyl pyrrole-2-carboxylate (3)	*anti* ⟶ *syn*	−4.8	−4.9
	syn ⟶ associated forms	−21.2	21.6
Pyrrole-2-carbaldehyde (10)	*syn* ⟶ associated forms	−23.3	−23.2

* The regressions of ln (A_2/A_1) *versus* $1/T$ and ln (A_3/A_2) *versus* $1/T$ (Table 2) have correlation coefficients greater than 0.985.

The foregoing knowledge about the absorptions of the *syn*-forms of the aldehydes provides a firm basis for interpreting the i.r. characteristics of the esters. Solutions in carbon tetrachloride of the esters [(1)—(3)] containing *N*-H groups show three bands in the NH region and three or four in the CO region. Those under the heading band 3 in Table 1 are attributed to associated forms containing more than two molecules of the esters. The result that the relative intensities of the band 1 and band 2 absorptions are not dependent on concentration [as illustrated by t-butyl pyrrole-2-carboxylate (3) in Table 2] is in agreement with the assignment of these bands to rotational isomers. It may be assumed that the rotamers are the *syn-s-trans-* and the *anti-s-trans-*forms since it is known that esters adopt the *s-trans-*arrangement predominantly or exclusively unless the structural situation is unusual (as, for example, with esters of formic acid).[7] Correlation of the *N*,carbonyl *O-syn*-forms (VIII) with the band 2 absorptions and of the *anti*-rotamers (VII) with those listed under band 1 (Scheme) is clearly indicated by the positions of the NH bands, the somewhat lower wavenumbers of the *syn*-forms' absorptions being taken to signify weak intramolecular bonding in these rotamers. Fermi resonance appears to be responsible for the extra CO absorption (band 4) in the methyl ester (1). Replacement of carbon tetrachloride by acetonitrile as solvent causes a relative intensification of the *anti*-forms' absorptions and a marked shift of their CO bands to lower wavenumbers, but, as with the aldehydes, the positions of the *syn*-forms' absorptions are little affected.

With one exception [ester (7) in which Fermi resonance complicates the situation] the *N*-Me esters show single CO bands, and where direct comparisons can be made these absorptions are seen to be between those of the *N*-H esters' rotamers. However, in their positions and, more significantly, their solvent shifts the *N*-Me esters' CO bands resemble those of the *syn-* rather than the *anti*-forms of the *N*-H esters. The conclusion that the *N*-Me esters adopt the *syn*-conformation (V), which cannot be stabilised by hydrogen bonding, to a greater extent than do the *N*-H esters implies that the conformational preference of the *N*-Me esters stems from destabilisation of their *anti*-forms (as compared with those of the *N*-H esters). This raises the question of the relative steric requirements of the methoxy-group and the carbonyl oxygen atom in methyl esters. The assumption that the methoxy group is bigger would rationalise the present results, since the *anti*-forms would then involve the more severe repulsion between the ester and *N*-Me groups.

Variable temperature experiments (Table 2) establish that the *syn*-form of t-butyl pyrrole-2-carboxylate (3) is thermochemically more stable (by *ca.* 4.8 kJ mol^{-1}) than the *anti*-rotamer. The proportions of the forms, which may have different integrated absorption coefficients, cannot be determined reliably from the results but it seems likely that the *syn*-forms of esters (1)—(3) predominate at 30 °C, perhaps to the extent of *ca.* 80% in carbon tetrachloride and *ca.* 60% in acetonitrile. Similar enthalpies of association were found for the ester (3) and pyrrole-2-carbaldehyde (10).

TABLE 2

Detailed examination of t-butyl pyrrole-2-carboxylate (3) and pyrrole-2-carbaldehyde (10)

Solutions in CCl_4 (concentrations *c*, mg per g of solution) were examined in cells with path lengths ranging from 10 to 0.01 cm. The areas (A) of bands are percentages of the total absorption (A_T) in a particular region at a specified temperature. In the concentration dependence examinations A_T was taken as 100 at 303 K for each solution. In the temperature dependence studies A_T was taken as 100 at 258 K for each solution. A_T Values at higher temperatures (and individual A values) are percentages of A_T at 258 K. Bands are identified by subscripts, *e.g.*, A_1 denotes the area of an absorption listed under band 1 in Table 1

		NH region						CO region				
Compound	T/K	c	A_T	A_1	A_2	A_3	T/K	c	A_T	A_1	A_2	A_3
(3)	303	10.2	100	5	23	72	303	10.2	100	11	44	45
	303	1.02	100	13	59	28	303	1.02	100	18	71	11
	303	0.0968	100	18	82	0	303	0.0968	100	20	80	0
	258	1.04	100	5	31	64	258	0.998	100	12	66	22
	275		90	7	37	46	275		96	13	65	18
	303		76	10	44	22	303		87	16	62	9
	333		66	12	44	10	333		81	18	61	2
	348		58	13	45	0	348		77	19	58	0
(10)	303	3.27	100		10	90	303	3.27	100		18	82
	303	0.302	100		40	60	303	0.302	100		55	45
	303	0.163	100		50	50	303	0.163	100		64	36
	303	0.0312	100		88	12	303	0.0312	100		93	7
	258	0.163	100		18	82	258	0.147	100		30	70
	280		90		25	65	280		90		39	51
	288		81		27	54	288		87		43	44
	303		72		37	35	303		80		54	26
	318		64		37	27	318		75		55	20
	333		56		39	17	333		74		60	13
	348		52		39	12	348		72		62	10

EXPERIMENTAL

General directions were as described in *J. Chem. Soc.* (*C*), 1968, 2674 except that the ^1H n.m.r. spectra (in $CDCl_3$) were recorded at 100 MHz. Known compounds, numbered as in Table 1, were prepared by the literature methods in the following list: (1), M. K. A. Khan and K. J. Morgan, *Tetrahedron*, 1965, **21**, 2 197; (2), A. Treibs and A. Diett, *Annalen*, 1958, **619**, 80; (4), D. A. Shirley, B. A. Gross, and P. A. Roussel, *J. Org. Chem.*, 1955, **20**, 225; (5), R. Andrisano and G. Pappalardo, *Gazzetta*, 1955, **85**, 1 430; (7)—(9), P. Hodge and R. W. Rickards, *J. Chem. Soc.*, 1965, 459; (10) and (14), R. M. Silverstein, E. E. Ryshiewicz, C. Willard, and R. C. Koehler, *J. Org. Chem.*, 1955, **20**, 668; (11)—(13); H. J. Anderson and L-F. Lee, *Canad. J. Chem.*, 1965, **43**, 409.

Esters (3) *and* (6).—Treatment of pyrrole-2-carboxylic acid (1.5 g) with 2-methylpropene by the standard procedure,[8] and sublimation of the product at 0.5 mmHg gave *t-butyl pyrrole-2-carboxylate* (3) (0.65 g), m.p. 49—50 °C

(Found: C, 64.6; H, 7.8; N, 8.2. $C_9H_{13}NO_2$ requires C, 64.65; H, 7.8; N, 8.4%). Similarly 1-methylpyrrole-2-carboxylic acid (1.5 g) gave *t-butyl* 1-*methylpyrrole*-2-*carboxylate* (6) (0.71 g), b.p. 105—110 °C (bath temp.) at 15 mmHg (Found: C, 66.2; H, 8.4; N, 7.7. $C_{10}H_{15}NO_2$ requires C, 66.3; H, 8.3; N, 7.7%).

Aldehydes (15)—(17).*—Br_2 (0.94 ml) was added during 30 min to a stirred paste of 1-methylpyrrole-2-carbaldehyde (14) (2 g) and $AlCl_3$ (6 g) at 5 °C. After a further 10 min 2N-HCl (20 ml) was added, and the mixture was extracted with Et_2O. P.l.c. [4 × 1 m plates, 2 × light petroleum–Me_2CO (19 : 1)] of the material so obtained gave as the main product 4-*bromo*-1-*methylpyrrole*-2-*carbaldehyde* (15) (1.9 g), m.p. 93—95 °C [from light petroleum (b.p., 60—80 °C)] (Found: C, 38.2; H, 3.3; Br, 42.2. C_6H_6BrNO requires C, 38.3; H, 3.2; Br, 42.5%); τ 0.63 (CHO), 3.15 (2 H, m, 3- and 5-H), and 6.12 (s, 1-Me); *m/e* 189 [M^+ ($C_6H_6{}^{81}BrNO$), 100%].

The foregoing experiment was repeated, but with Br_2 (1.8 ml) being added at 20 °C. P.l.c. gave two products which were crystallised twice from light petroleum. The product with R_F 0.51 afforded 4,5-*dibromo*-1-*methylpyrrole*-2-*carbaldehyde* (17) (0.93 g), m.p. 118—120 °C (Found: C, 27.3; H, 1.9; Br, 59.8; N, 5.2. $C_6H_5Br_2NO$ requires C, 27.0; H, 1.9; Br, 59.9; N, 5.25%); τ 0.74 (CHO), 3.17 (s, 3-H), and 6.22 (s, 1-Me); *m/e* 269 [M^+ ($C_6H_5{}^{81}Br_2NO$), 100%]. The product with R_F 0.39 afforded 3,5-*dibromo*-1-*methylpyrrole*-2-*carbaldehyde* (16) (0.85 g), m.p. 114—115 °C (Found: C, 27.2; H, 1.9; Br, 59.8; N, 5.3%); τ 0.45 (CHO), 3.22 (s, 4-H), and 6.13 (s, 1-Me); *m/e* 269 (M^+, 100%).

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* The positions of the bromine substituents are based on a comparison between the ^1H n.m.r. spectra of these compounds and the spectra of the brominated *N*–H aldehydes of known structure.

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