Carbon-13 Nuclear Magnetic Resonance Spectra of Some Substituted Pyrroles

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The ^{13}C n.m.r. spectra of 55 pyrroles have been recorded and assigned. The pyrrole ring carbon chemical shifts can be predicted. to *ca.* 0·5 p.p.m., on the basis of additive substituent effects together with contributions due to adjacent substituents (steric compression shifts) and in the case of carbonyl functions in the α-positions. an additional ' conjugation effect '. The substituent chemical shift parameters obtained are analogous to those for substituted thiophens, and are compared with those obtained from ethylenes and benzene derivatives. The C(2) substituents affect mainly C(3) and C(5) (apart from the directly bonded carbon) and the C(3) substituents mainly C(2). and these directive effects may be rationalised by accepted resonance considerations. The steric compression effects parallel those found for other aromatic and olefinic systems; a buttressing effect of the next-but-one substituent was also identified. Novel conjugation effects were manifest for two α-carbonyl substituents at all the ring carbons.

SUBSTITUTED pyrroles form the synthetic and biosynthetic precursors of many molecules of biological importance, such as prodigiosin, the porphyrins, chlorophylls, vitamin B_{12}, and the bile pigments. In comparatively recent times, ^{13}C n.m.r. spectroscopy has been applied to studies of these biologically significant compounds,[1-4] as well as to investigations of the biosynthetic pathways to the production of some of them.[5-10] Specific assignment of ^{13}C resonances to particular carbon atoms in these compounds is often complex and time consuming, and especially in the case of pyrrole ring carbons, often impossible. We have therefore studied the ^{13}C n.m.r. spectra of simple substituted pyrroles as an aid to the study of the more complex macromolecules, in the hope of easing the problems of specifically assigning pyrrole ring ^{13}C resonances.

Few literature data are available on the effect of substituents on pyrrole ring ^{13}C resonances. Grant *et al.*[11,12] have studied five-membered heterocyclic compounds and their charged species, as well as the effect of methyl substitution on the ^{13}C resonances of such rings. Takahashi *et al.*[13] have studied the effect of monosubstitution on thiophen, although it is probable that the effects produced may not be exactly the same for sulphur as nitrogen analogues.

EXPERIMENTAL

The preparations of the pyrroles (1)—(55) can be found in previous publications from this department.† *N*-Methylated compounds were prepared using the thallium salt method.[14]

Individual compounds were dissolved in deuteriochloroform ($CDCl_3$) as 1·0M solutions whenever solubility allowed, or else as saturated solutions; 5% tetramethylsilane was added as an internal reference. The proton noise decoupled ^{13}C spectra were obtained using a Varian XL-100-15 FT spectrometer, with 8 K computer memory, and using 12 mm sample tubes. Spectra were routinely recorded on 5120 Hz sweep widths at 25·197 MHz using the fast Fourier transform technique. The accuracy of the ^{13}C chemical shifts with 2048 plot data points was ±2·5 Hz, *i.e.* 0·1 p.p.m. Proton off-resonance decoupled spectra, and smaller sweep widths were also used for assignment of resonances.

The INDO MO calculations were performed using

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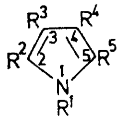

	R^1	R^2	R^3	R^4	R^5
(1)	H	H	H	H	H
(2)	H	CHO	H	H	H
(3)	H	Ac	H	H	H
(4)	H	CO_2Me	H	H	H
(5)	H	CO_2Et	H	H	Me
(6)	H	CO_2Et	Me	H	H
(7)	H	CO_2Et	Me	H	Me
(8)	H	CO_2Et	H	Me	Me
(9)	H	CO_2CH_2Ph	Me	H	Me
(10)	H	CO_2CH_2Ph	H	Me	Me
(11)	H	CO_2CH_2Ph	Me	Me	Me
(12)	H	CO_2Et	CH_2CO_2Et	H	Me
(13)	H	CO_2Et	$CH_2CH_2CO_2Et$	H	Me
(14)	H	CO_2CH_2Ph	$CH_2CH_2CO_2Me$	H	Me
(15)	H	CO_2Et	H	$CH_2CH_2CO_2Me$	Me
(16)	H	CO_2CH_2Ph	Me	CH_2CO_2Me	Me
(17)	H	CO_2CH_2Ph	Me	CH_2CO_2Et	Me
(18)	H	CO_2CH_2Ph	Me	$CH_2CH_2CO_2Me$	Me
(19)	H	CO_2Et	CH_2CO_2Et	$CH_2CH_2CO_2Et$	H
(20)	H	CO_2Et	CH_2CO_2Et	$CH_2CH_2CO_2Et$	Me
(21)	H	CO_2Et	$CH_2CH_2CO_2Me$	CH_2CO_2Me	Me
(22)	H	CO_2Et	$CH_2CH_2CO_2Et$	CH_2CO_2Et	Me
(23)	H	CO_2CH_2Ph	Me	Et	Me
(24)	H	CO_2Et	Et	Me	Me
(25)	H	CO_2Et	H	CHO	Me
(26)	H	CO_2Et	CH_2CO_2Et	CHO	Me
(27)	H	CO_2Et	Me	CHO	Me
(28)	H	CO_2Et	H	Ac	Me
(29)	H	CO_2Et	$CH_2CH_2CO_2Et$	Ac	Me
(30)	H	CO_2Et	Me	Ac	Me
(31)	H	CO_2CH_2Ph	Me	Ac	H
(32)	H	CO_2Et	Me	Et	CHO
(33)	H	CO_2CH_2Ph	Me	Et	CHO
(34)	H	CO_2CH_2Ph	Et	Me	CHO
(35)	H	CO_2CH_2Ph	Me	$CH_2CH_2CO_2Me$	CHO
(36)	H	CO_2Et	$CH_2CH_2CO_2Me$	CH_2CO_2Me	CHO
(37)	H	CO_2CH_2Ph	Me	H	Ac
(38)	H	CO_2CH_2Ph	Me	Me	Ac
(39)	H	H	Me	Ac	Me
(40)	H	Me	Me	Ac	H
(41)	H	Me	H	CO_2Et	Me
(42)	H	H	Me	CO_2Et	Me
(43)	H	Me	Me	CO_2Et	Me
(44)	H	Me	Me	H	CHO
(45)	H	Me	H	Me	CHO
(46)	H	Me	Et	Me	Ac
(47)	Me	CO_2Et	Me	CHO	Me
(48)	Me	CO_2Et	Me	Ac	Me
(49)	Et	CO_2Et	Me	Ac	Me
(50)	CH_2CO_2Et	CO_2Et	Me	CHO	Me
(51)	CH_2CO_2Et	CO_2Et	Me	Ac	Me
(52)	Me	CO_2CH_2Ph	Me	Me	Me
(53)	Me	CO_2CH_2Ph	Me	Et	Me
(54)	Me	CHO	H	H	H
(55)	Me	H	H	H	H

the CNINDO program[15] and standardised pyrrole ring geometry.

RESULTS

A. *Pyrrole Ring Carbons*.—The pyrrole ring ^{13}C resonances were observed in the range 105—145 p.p.m. downfield from tetramethylsilane (Table 2), *cf.* pyrrole, α-carbons 117·3 and β-carbons 107·6 p.p.m.[12]

The assignment of pyrrole ring carbons directly bonded to a hydrogen atom was straightforward but the quaternary ring carbon resonances presented a more difficult problem. This was carried out in the first instance by using substituent chemical shift (SCS) effects for thiophen derivatives,[13] assuming additivity.[16,17] Comparison of the observed shifts in groups of molecules then allowed refinement of the SCS parameters for the pyrrole series.

Additivity of SCS effects alone did not give good agreement between calculated and observed shifts, discrepancies of up to ±5 p.p.m. being observed. In compounds where there were adjacent methyl groups on the pyrrole ring, the chemical shifts of the methyl carbons (see section B) were

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TABLE 1

^{13}C Chemical shifts [a] of substituted pyrroles in chloroform solution

Compound [b]	Pyrrole ring carbons				Carbons of substituents at C(2)							Carbons of substituents at C(3)					Carbons of substituents at C(4)					Carbons of substituents at C(5)		Carbons of substituents at (N)			
	C(2)	C(3)	C(4)	C(5)	C=O	CH₂	Me	PhCatt	o-Ph	m-Ph	p-Ph	CH₂	CH₂	C=O	CH₂	Me	CH₂	CH₂	C=O	CH₂	Me	C=O	Me	CH₂	C=O	CH₂	Me
(1)	117·3	107·6	107·6	117·3																							
(2)	132·4	121·6	110·8	126·8	178·8																						
(3)	131·6	117·1	110·0	125·1	187·7		25·3																				
(4)	122·0	115·1	109·8	122·9	161·4		51·2																				
(5)	120·8	115·8	108·4	135·4	161·2	59·8	14·4																12·9				
(6)	119·0	127·4	112·1	121·2	161·2	59·6	14·4									12·7											
(7)	117·4	128·5	110·9	132·4	161·5	59·5	14·5									12·9							12·9				
(8)	119·9	116·4	119·1	130·6	161·1	59·6	14·5														(10·7)		(11·0)				
(9)	117·0	129·0	111·0	132·7	161·0	65·2		136·1	127·4	128·0	127·4					12·9							12·9				
(10)	118·6	116·9	118·6	131·2	160·8	65·3		136·1	127·4	128·0	127·4										(10·7)		(11·1)				
(11)	115·9	127·1	116·8	129·8	161·0	65·2		136·4	127·5	128·0	127·5					(10·8)					8·7		(11·3)				
(12)	118·0	124·0	110·7	132·1	160·5	(59·7)	(14·4)					32·9		171·2	(60·3)	(14·2)							13·0				
(13)	117·0	131·4	109·7	132·7	161·1	(59·6)	(14·4)					22·8	35·3	172·6	(59·9)	(14·2)							12·8				
(14)	117·6	128·7	110·4	135·2	160·9	65·3		136·1	127·5	128·1	127·5	22·7	33·6	172·7		51·6							13·0				
(15)	119·5	115·0	120·0	130·8	161·0	59·8	14·5										21·1	35·1	172·9		51·3		11·0				
(16)	116·4	127·5	114·1	131·4	161·1	65·3		136·1	127·5	128·0	127·5					(10·8)	29·8		171·5		51·6		(11·3)				
(17)	116·4	127·4	114·2	131·6	161·2	65·3		136·1	127·4	128·0	127·4					(10·9)	30·2		171·1	60·4	14·2		(11·3)				
(18)	116·2	126·9	119·7	130·4	161·1	65·2		136·1	127·4	128·0	127·4					(10·7)	19·5	34·8	172·8		51·3		(11·2)				
(19)	119·9	121·4	123·8	119·7	160·5	(59·9)	14·2					30·6		170·8	(60·1)	14·2	20·2	35·0	172·3	(60·4)	14·2						
(20)	117·4	122·3	119·9	130·2	160·9	(59·6)	(14·4)					31·0		171·1	(60·1)	(14·2)	19·4	35·2	172·4	(60·3)	(14·2)		11·3				
(21)	116·8	129·8	113·8	131·0	160·8	59·8	14·5					20·8	35·0	173·2		(51·8)	29·8		171·6		(51·3)		11·6				
(22)	116·6	129·8	113·7	131·3	160·9	(59·7)	14·2					20·8	35·2	172·6	(59·9)	14·2	30·0		171·2	(60·4)	14·2		11·3				
(23)	116·0	126·8	123·5	129·6	161·1	65·1		136·3	127·4	128·0	127·4					(10·6)				17·1	15·3		(11·2)				
(24)	115·6	133·4	115·5	129·7	161·4	59·3	14·4								18·5	15·1					8·4		11·2				
(25)	122·8	116·3	121·8	140·2	160·9	60·7	14·3												185·3				12·3				
(26)	119·9	124·3	120·9	141·3	160·6	60·7	14·2					30·6		171·1	60·7	14·2			185·0				11·5				
(27)	118·5	129·9	121·1	140·7	161·6	60·4	14·4									(10·5)			185·4				(12·2)				
(28)	119·9	117·2	122·0	139·6	161·0	60·5	14·4												194·1		28·1		13·8				
(29)	118·0	132·3	122·6	137·7	161·2	(60·5)	14·3					21·6	35·2	172·6	(60·0)	14·3			194·3		31·1		15·2				
(30)	117·7	128·9	123·0	138·2	161·4	60·1	14·4									12·7			194·7		31·1		14·9				
(31)	120·6	129·3	124·9	127·8	161·0	66·1		135·4	127·6	128·1	127·6					11·8			193·7		28·2						
(32)	124·3	125·7	136·0	129·3	160·5	60·6	14·4									9·6			16·9		16·3	178·8					
(33)	123·9	126·1	136·0	129·3	160·1	66·3		135·1	127·9	128·1	127·9					9·6			16·8		16·3	178·6					
(34)	123·3	133·4	128·8	130·0	160·0	66·4		135·0	127·9	128·1	127·9				17·5	14·9					8·2	178·7					
(35)	123·8	126·4	131·4	129·9	160·1	66·4		135·0	127·9	128·1	127·9					9·8	18·8	34·8	171·9		51·4	179·1					
(36)	124·0	129·8	124·6	130·4	159·8	61·1	14·2					19·8	34·4	172·7		(52·1)	29·2		170·5		(51·4)	179·4					
(37)	123·0	128·0	117·2	132·0	160·1	66·2		135·1	127·8	128·1	127·8					12·6						187·7	25·7				
(38)	121·6	124·9	127·3	130·4	160·1	66·1		135·2	127·8	128·1	127·8					(11·0)					(10·0)	187·8	28·5				
(39)	114·8	120·0	120·3	135·7												13·7			195·3		30·8		15·1				
(40)	126·1	114·9	123·7	123·4			(10·6)									(10·3)			194·3		27·5						
(41)	125·4	107·0	110·9	134·0			13·0												165·6	59·0	14·5		11·3				
(42)	114·2	120·8	110·0	135·7												12·6			166·2	58·9	14·5		(13·9)				
(43)	121·5	115·6	110·3	133·2			(10·9)									(10·4)			165·9	58·7	14·5		(13·8)				
(44)	136·9	118·6	123·5	129·9			(11·3)									(10·6)						176·7					
(45)	138·5	111·6	134·5	127·6			13·1														10·6	175·2					
(46)	131·6	124·0	127·5	125·6			(11·1)								17·1	15·3					(11·6)	185·5	27·7				
(47)	119·7	130·7	120·4	141·9	161·2	59·8	14·4									(10·7)			185·0				(10·9)				32·7
(48)	120·1	128·3	122·8	139·5	161·5	59·8	14·4									12·2			195·3		31·5		13·3				32·7
(49)	119·1	128·6	123·0	138·5	161·2	59·7	14·4									11·8			195·5		31·6		13·4			40·2	15·9
(50)	120·1	131·0	120·1	142·3	161·2	60·1	14·2									(10·4)			185·2				(11·0)	46·7	167·4	61·5	14·2
(51)	119·7	128·9	123·3	139·7	161·4	60·0	14·3									11·9			195·3		31·6		13·4	46·8	167·7	61·3	14·3
(52)	117·5	127·6	115·3	133·0	161·3	64·9		136·5	127·4	128·0	127·4					(10·2)					9·0		(11·8)				32·7
(53)	117·6	126·9	122·1	132·4	161·2	64·8		136·4	127·5	127·9	127·9					(10·0)				17·3	15·6		(11·6)				32·6
(54)	131·4	123·5	109·0	131·4	178·7																						36·2
(55)	121·1	107·8	107·8	121·1																							35·8

[a] In p.p.m. downfield from tetramethylsilane. [b] Ambiguous assignments are bracketed.

ca. 2 p.p.m. to high field in correspondence with steric compression shifts.[18-20] This work [18-20] showed that such sterically induced shifts are transmitted into aromatic rings, producing high field shifts of the point-of-attachment carbons. The observation of similar effects in the pyrrole derivatives is apparent on comparing the ^{13}C n.m.r. chemical shifts for the compounds studied, not only for methyl–methyl interactions, but also for methyl–methylene and methylene–methylene interactions.

Despite allowance for steric compression shifts, compounds possessing carbonyl groups attached to both α-ring positions did not give good agreement between calculated and observed shifts. Further effects due to interaction of carbonyl functions, and carbonyl functions with adjacent methyl and methylene groups were therefore considered. The nature of such effects is discussed later, and the actual effects finally utilised are listed in Tables 2 and 3.

TABLE 2

Substituent chemical shift effects [a] on pyrrole ring carbons

Substituent	C(2)	C(3)	C(4)	C(5)
2-Me	10·8	−1·2	1·1	−2·1
2-CHO	14·9	13·2	3·7	10·9
2-Ac	14·5	9·9	2·6	8·1
2-CO_2CH_2R (R = Me or Ph)	4·7	7·3	3·2	5·9
3-Me	−2·4	12·7	1·1	−0·9
3-Et	−3·7	18·3	−0·8	−0·6
3-CHO	10·8	11·6	−1·5	3·0
3-Ac	8·7	13·3	−0·7	1·6
3-CO_2Et	8·2	2·6	−0·6	−0·1
3-CH_2CO_2R (R = Me or Et)	−1·9	8·0	0·9	−0·7
3-$CH_2CH_2CO_2R$ (R = Me or Et)	−2·8	14·0	0·0	−0·6

[a] In p.p.m., positive denoting a downfield shift.

There remained some ambiguities, especially where chemical shifts were within 2 p.p.m. of each other. In the main, these ambiguities were ones of assigning two resonances, one to an α- and one to a β-carbon. To this end, some *N*-substituted pyrroles were studied. *N*-Methylation of pyrrole shifts the α-carbon resonances downfield by 3·8 p.p.m., and the β-carbon resonances by 0·2 p.p.m. In the tetrasubstituted pyrroles, the effects of *N*-methylation were observed to be 1—3 p.p.m. downfield shifts (α-carbons), and between 1 downfield and 0·5 p.p.m. upfield (β-carbons). The effects observed in any molecule were not symmetrical; however, the shifts thus produced were such as to clarify easily the ambiguities arising from the ^{13}C assignments. *N*-Methylpyrrole-2-carbaldehyde (54) had anomalous shifts relative to pyrrole-2-carbaldehyde (2), which may reflect the interaction between the *N*-methyl group and the formyl group, a process which has been studied previously by ^1H n.m.r. spectroscopy.[21,22]

TABLE 3

Additive chemical shift effects [a] on pyrrole ring carbons due to interacting substituents

Interacting groups	C(2)	C(3)	C(4)	C(5)
2-Me, 3-Me [b]	−0·7	−3·8	−0·1	0·2
2-Me, 3-CH_2 [b]	−0·2	−2·8	−0·1	0·1
3-Me, 4-Me [b]	−0·1	−2·8	−2·8	−0·1
3-Me, 4-CH_2 [b]	−0·7	−2·0	−2·1	0·4
3-CH_2, 4-CH_2 [b]	−0·1	−1·4	−1·4	−0·1
2-CO_2, 5-CO [c]	−5·1	−2·7	−5·2	−4·6
2-CO_2, 4-CO [c]	−1·1	2·0	−0·6	−3·4

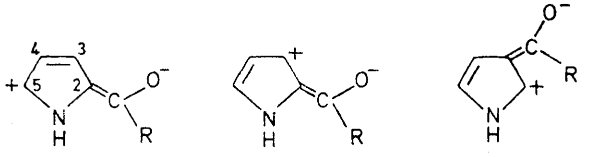
[a] In p.p.m., positive denoting a downfield shift. [b] Steric compression effects. [c] Group interaction effects.

Consideration of all SCS and interaction chemical shift effects and additivity principles led to the assignment of pyrrole ring carbons given in Table 1. The observed chemical shifts relative to those of pyrrole were then subjected to a computer analysis in order to solve for the best fit chemical shift effects. The root mean square error on the analysis was 0·5 p.p.m., compared with an initial error on the observed shifts (relative to pyrrole) of ±0·2 p.p.m. The results are given in Tables 2 and 3.

B. *Substituent Carbons.*—Assignment of the substituent carbons followed similar considerations. Methyl groups at the extremities of chain substituents were readily assigned by their relatively invariant chemical shifts (<0·4 p.p.m. range). In molecules where methyl groups at C(5) were not subject to steric effects of a neighbouring group, the chemical shift of the methyl carbon remained constant at δ 12·9. No similar 'free' β-methyl was present in the compounds studied. The rest of the substituent carbons were then assigned largely by consideration of the steric shift of neighbouring groups (see later) and these assignments are given in Table 1; there still remained some ambiguities, and these are indicated in this Table.

DISCUSSION

A. *Pyrrole Ring Carbons.*—The SCS parameters (Table 2) are comparable with those of monosubstituted thiophens,[13] except for those of the point-of-attachment carbons which are noticeably smaller. For C(2) substituents, C(4) is least affected, and for C(3) substituents, both C(4) and C(5) are not very sensitive. This is in accord with resonance effects and charge delocalisation expected between the substituent and the ring (*cf.* Scheme * and Table 4). The carbons least affected upon substitution will be C(4) [for C(2) substitution] and C(4) and C(5) [for C(3) substitution]. Furthermore, on this basis, less positive charge will be delocalised onto the ring in the case of C(3) substitution than for C(2) substitution, and therefore the SCS effects will be smaller in magnitude. These qualitative considerations are supported by the INDO calculations (Table 4).



(I) (II) (III)

SCHEME

Pyrrole SCS resemble those for ethylene rather than benzene (Table 5), especially for the C(2)–C(3) system bearing electron-withdrawing groups. As an extension

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* For the purposes of this discussion, those resonance contributors with a formal positive charge on nitrogen need not be considered.

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of the ethylene data, the conjugated system, butadiene,[23] may be considered. C(4)-Methylation [24] yields the methyl SCS shift parameters C(1) (−2·7), C(2) (+0·3), C(3) (−4·3), and C(4) (+12·4 p.p.m.), which although slightly larger, closely resemble the C(2) methyl substitution parameters for pyrrole, although the effects of methyl substitution are similar for all compounds considered.

The steric compression shifts [25] due to interaction of neighbouring methyl and methylene functions are all upfield (Table 3) on the ring point-of-attachment, as observed for *o*-xylene [19,20] and for substituted olefins.[24] The magnitudes are −0·7 and −3·8 [C(2)–C(3)] and −2·8 p.p.m. [symmetrical C(3)–C(4)] for methyl–methyl interactions, and −1·3 p.p.m. for C(3)–C(4) methylene–methylene interactions. The methyl–methylene interactions are intermediate in magnitude, as might reasonably be expected. The transmission to other carbons of the pyrrole ring, however, is small, as observed in the case of aromatic systems.[18-20] Although the steric compression shifts manifest on the methyl carbons due to a 2-methyl–3-methyl interaction are approximately the same, those on the point-of-attachment carbons C(2) and C(3) are not equal; the effect on C(2) is much smaller than on C(3) (the same inequity is observed for the 2-methyl–3-methylene interaction).

TABLE 4

π-Charge densities in pyrroles [a]

Compound	N	C(2)	C(3)	C(4)	C(5)	C=O
(1)	1·624	1·095	1·093	1·093	1·095	
(55)	1·591	1·102	1·090	1·090	1·102	
2-Methylpyrrole	1·633	1·076	1·109	1·089	1·096	
(2) [b]	1·611	1·119	1·044	1·096	1·057	C (0·822), O (1·252)
(3) [b]	1·608	1·117	1·054	1·097	1·060	C (0·825), O (1·269)
3-Methylpyrrole	1·623	1·112	1·076	1·104	1·086	
3-Formylpyrrole [c]	1·602	1·043	1·112	1·083	1·089	C (0·813), O (1·257)
3-Acetylpyrrole [c]	1·605	1·045	1·112	1·086	1·089	C (0·818), O (1·275)

[a] By the INDO approximation. [b] O *cis* to N. [c] O *cis* to α-C.

TABLE 5

Substituent chemical shift effects [a] for benzene [b] and ethylene [c] derivatives

	Benzene derivatives				Ethylene derivatives	
Substituent	C(*x*)	*o*	*m*	*p*	C(1)	C(2)
Me	9·4	0·7	−0·1	−3·0	10·3	−7·8
Et	15·8	−0·5	−0·1	−2·8	17·4	−10·0
CHO	8·1	1·3	0·6	5·9	13·6	13·2
Ac	8·7	0·1	−0·1	4·7	15·7	6·5
CO_2Et	2·3	1·2	−0·1	4·3	7·0	7·7
$CH_2CH_2CO_2Et$	12·2	0·1	−0·1	−2·2		

[a] In p.p.m. relative to parent compound, positive values denoting downfield shifts. [b] Compounds run as 1M solutions in $CDCl_3$. [c] *Cf.* ref. 16, pp. 70 and 184.

A further effect which must not be neglected is the mutual interaction of substituent groups (Table 3). The data demonstrate the considerable interaction shift occurring particularly with C(2) and C(5) carbonyl groups. This may be a saturation effect, and in agreement with this, the interacting effect is opposite to that of the SCS for these groups.

The much greater effect for C(2) and C(5) substituents, compared with those for C(2) and C(4) also suggests a resonance effect, but whether this is a result of changes in electron densities or ring geometry is uncertain. Similar effects have also been observed [26] for compounds such as terephthaldehyde, where the point-of-attachment carbons resonate at *ca.* 2·4 p.p.m. to higher field than expected from additivity effects.

The inclusion of similar interactions between alkyl and COR groups did not, however, significantly improve the fit of the data. Other interactions between neighbouring carbonyl and methyl or methylene groups have also been omitted from the final analysis.

B. *Substituent Carbons.*—The effect of gauche 1,4-interactions upon ^{13}C chemical shifts has been observed in a wide range of molecules.[18-20, 24, 25, 27-34] Comparison of the chemical shift of α-methyl carbons with methyl or methylene adjacent functions with that of an unhindered methyl group (12·9 p.p.m.) gives a high field steric shift of *ca.* −1·7 p.p.m. which is akin to that found [18-20] for aromatic compounds, but smaller than in olefins,[24] where the distance between the interacting groups is smaller. β-Methyl carbons also exhibit a similar upfield steric shift, with slightly more than double the effect for a β-methyl with two adjacent methyl or methylene groups.

Similar effects occur with neighbouring COMe and CHO functions. The size of these latter interactions is highly dependent upon the nature of the other substituent adjacent to them. For example, the chemical shift of a 5-methyl with a 4-COMe and a 3-CH_3 or -CH_2

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group is 14·9 p.p.m. [Table 1; compound (30)], but with a 3-hydrogen, the value is only 13·8 p.p.m. [Table 1; compound (28)]. Such effects are probably due to changes in the preferred orientation of the COR function, depending on the adjacent substituents.

Steric shifts are also manifest on the methylene carbons, where the effects are of the same order of magnitude, and in the same direction as for those acting upon methyl groups.

There are also longer range effects presumably related to the electron-withdrawing nature of COR functions. For example, in compound (35) the chemical shift of the 3-methyl carbon is 9·8 p.p.m., whereas that of the same carbon in compound (18) is 10·7 p.p.m.; the only difference between the two compounds is the replacement of a 5-formyl function by a methyl group.

Conclusions.—The ^{13}C n.m.r. spectra of substituted pyrroles show that the pyrrole ring ^{13}C chemical shifts follow additivity, depending upon the nature of the substituents and interactions between them. These latter effects are important because neglect of them can lead to erroneous assignment of resonances in the ^{13}C spectra.

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