Studies of Substituent Effects by Carbon-13 NMR Spectroscopy. Thiophene and Furan Chalcone Analogues

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¹³C NMR spectra of 39 thiophene and furan chalcone analogues in CDCl₃ solutions are reported. The effect of substituents on the ¹³C chemical shifts in the phenyl and in the 5-membered rings is discussed. ¹³C NMR shifts are correlated with Hammett parameters and with experimental shifts in the chalcone series.

INTRODUCTION

Side-chain reactivity and equilibria of 5-membered heterocycles have been widely investigated in our laboratory. Recent studies have included the nucleophilic reactivity of sulphonyl halides,¹ of furfuryl and thenyl chlorides² and of carbonyl compounds,³ as well as the acid dissociation of sulphonamides⁴ and the protonation equilibrium of carboxamides.⁵

Carbon-13 NMR spectroscopy is a useful tool to obtain information on the electronic environment of carbon atoms and has been used extensively for studying the electronic properties of a wide range of organic molecules. Substituent effects on the ¹³C NMR spectra of substituted chalcones have been studied in $CH_2Cl_2^6$ and $CHCl_3^7$ solutions and ¹³C chemical shifts correlated with electron densities and by the Hammett, DSP and Swain-Lupton equations.^{6,7} It was shown⁷ that the C-6 chemical shifts in series 1 depend on the substituents in the ethylene-linked aromatic ring while substituents in the carbonyl-linked ring influence the C-7 chemical shifts in series 2. (The numbering in series 3–8.)



We now report the ¹³C NMR spectra in CDCl₃ of 39 furan and thiophene chalcone analogues (series **3-8**) with the aim of studying the effect of the heteroatom Y and of other substituents (X, Z, W) on ¹³C chemical shifts.

These compounds should be suitable for the study of substituent effects in the 5-membered heterocycle since the C-6 chemical shifts should be mainly affected



by the electronic effects of Y and Z, steric effects being negligible. (A possible reason for the unsystematic behaviour of the sigma replacement constants of the heteroatoms in 5-membered heterocycles derived from different reactions, and/or equilibria,^{8,9} can be envisaged due to steric interaction of the heteroatom with the reaction site.^{8b,10}) Moreover, the characteristic splitting of C-6 and C-7 in the off-resonance decoupled (ORD) spectra, already reported for **3c** and **7c**, allows unambiguous assignment of the olefinic carbons.¹¹⁻¹³

RESULTS AND DISCUSSION

The ¹³C NMR chemical shifts of the thiophene and furan chalcone analogues are recorded in Tables 1 and 2, respectively, together with the substituent chemical shifts (SCS) in the phenyl and in the heterocyclic rings.

For carbons 1–4 the SCS is relative to the phenylunsubstituted compound in the same series (e.g. SCS for C-1 in **4f** is equal to δ_{C-1} **4f** – δ_{C-1} **4c**), while for carbons 8–11 the SCS is relative to the corresponding thiophene- or furan-unsubstituted derivative, **3** and **7**, respectively (e.g. the SCS for C-10 in **8f** is equal to δ_{C-10} **8f** – δ_{C-10} **7f**). The ¹³C spectra of **3c** and **7c** have been reported¹¹ and are in agreement with the chemical shifts in Tables 1 and 2. Carbon-fluorine coupling constants for the fluoro-derivatives are also listed in Tables 1 and 2.

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Table	1.	¹³ C	chemical	shifts	for	thiophene	chalcone	analogues,	series 3-	•6ª
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	·····	·····		Series 3			, · · · · · · · · · · · · · · · · · · ·	
	3 a	3b	3c ^b	30	I	3e	3f	3g
Contra 1	δ	δ	δ	δ		δ	δ	δ
Carbon	(505)	(SCS)	100 50	(SCS)	J	(SCS)	(SCS)	(SUS)
C-1	163.32 (20.70)d	143.55 (11.02)d	132.53	165.53	254.4	138.96 (6.42)d	117.83	149.94 (17.41)d
	112.67	120.26	120 42	115 59	22.1	129 69	122.25	(17.41)*
C-2	(-14 75) ^d	(0.84) ^d	128.42	(_12.84) ^d	22.1	128.00 (0.26) ^d	132.35 (3.93)d	123.79 (
	120 55	100.04/	100 10	120.04		120 56	(3.33)	(-4.03)
C-3	(2 37) ^d	(0.25) ^d	120.10	(2.66) ^d	0.0	(1 38)d	120.50 (0.40) ^d	129.20 /1.08\d
	130.85	135 /3	137.90	13/1 37	24	136.20	1/1 3/	1/2 96
C-4	(-7.05) ^d	(-2.47) ^d	137.30	(-3.53) ^d	2.4	(-1.70) ^d	(3.44) ^d	(5.06) ^d
C-5	187.97	189.26	189.56	188.02		188.15	188.34	188.26
C-6	120.43	120.67	120.58	120.08		119.88	119.72	119.79
C-7	136.20	136.67	136.96	137.26		137.43	138.60	138.96
C-8	140.43	140.38	140.16	140.14		140.01	139.76	139.85
C-9	131.55	131.79	131.82	132.14		132.15	132.77	133.08
C-10	128.32	128.43	128.60	128.85		128.92	128.58	128.55
C-11	128.14	128.26	128.18	128.26		128.21	129.68	129.85
Others	55.19	21.43					115.77	
	45	4-		Series 4				
	4+D δ	44C δ	40 δ		4e δ	4τ δ	4g δ	
Carbon	(SCS)		(SCS)	J°	(SCS)	(SCS)	(SCS)	
C-1	143.34	132.53	165.51	253.9	138.97	118.68	149.96	
0-1	(10.81) ^d		(32.98) ^d		(6.44) ^d	(-13.85) ^d	(17.43) ^d	
C-2	129.19	128.46	115.49	20.7	128.76	132.41	123.78	
02	(0.73) ^a		(–12.97) ^d		(0.30) ^d	(3.95) ^d	(-4.68) ^d	
C-3	128.40	128.28	130.80	8.4	129.61	128.64	129.25	
	(0.12)ª		(2.52) ^a		(1.33) ^d	(0.36) ^d	(0.97) ^d	
C-4	135.75	138.36	134.40	2.4	136.60	141.64	143.22	
0.5	(-2.61) ⁶	400 74	(-3.96)°		(-1.76)ª	(3.28) ^a	(4.86) ^a	
0-5	189.25	189.74	187.98		188.28	188.28	188.22	
C-0	119.90	119.78	119.23		119.11	118.68	118.87	
C-7	135.02	135.38	135.57		135.87	137.02	137.33	
C-8	134.59 (_5.79)e	134.53	134.53		134.41	134.18	134.23	(4.3) ^f
	(~0.79)	(-5.03)	(-5.01)-		(-5.60)-	(-5.58)°	(-5.62)°	
C-9	(10.52)e	142.01 (10.79)e	142.73 (10 59)e		142.92 (10.77)e	143.83 /11.06\e	144.01 (10 93)e	(10.9) ^f
	121 22	121 20	121 20		121 20	(11.00)	(10.00)	
C-10	(2.89)°	(2 78)e	(2 53)e		131.30 /2.46*	(3 04)e	131.68 /2.12\e	(2.8) ^f
	126 94	127 19	127.25		127 42	120 22	129.40	
C-11	(-1.32)°	(0.99)°	(-1.01)*		(-1.78) ^e	(-1.46) ^e	120.40 (1.45) ^e	(0.5) ^f
9-CH3	13.92	13.98	13.92		13.92	13.98	14 10	
Others	21.33					115.77		
				Series 5				
	5a	5b	5c	5	d	5e	5f	
	δ	δ	δ	δ		δ	δ	
Carbon	(SCS)	(SCS)		(SCS)	Je	(SCS)	(SCS)	
C-1	163.32	143.10	132.60 ⁹	165.51	253.9	138.85	117.89	
	(30.72) ^{a,n}	(10.50) ^{a,n}		(32.91) ^{a,n}		(6.25) ^{d,h}	(~14.71) ^{d,h}	
C-2	113.70	129.01	128.46	115.46	22.0	128.76	132.29	
	(-14.76) ^u	(0.55) ^a		(-13.00) ^a		(0.30) ^a	(3.83)ª	
C-3	130.47	128.28	128.22	130.77	9.7	129.61	128.52	
	(2.25) ^d	(0.06) ^d		(2.55) ^a	-	(1.39) ^o	(0.30) ^a	
C-4	131.19	135.63	138.44	134.72	2.3	136.60	141.58	
C F	(-7.25)-	(-2.81) ⁻	100.96	$(-3.72)^{\circ}$		(~1.84) ^a	(3.14) ^a	
C-5	100.04	189.19	189.80	188.10		188.40	188.28	
C-0	126.66	176.06	119.00	110.93		118.80	118.38	
0-7	130.00	120.30	137.45	137.09		137.93	130.97	
C-8	(-1.83) ^e	(-1.96) ^e	(-1 72) ^e	(-1.84)°		1 38.24 (_1 77) ^e	137.87 (1.89)e	(—1.9) ⁱ
_	132.29	132 35	122 /19	122.92		122.02	122.60	
C-9	(0.74) ^e	(0.56)°	(0.59) ^{e,h}	(0.69)°		(0.87) ^e	133.00 (0.91)♥	(0.2) ⁱ
	126 70	126 58	126 76	126.82		126.89	127.06	_
C-10	(-1.62)°	(-1.85)°	(-1.84)°	(-2.03)e		(-2.04)°	(-1.52)°	(-1.4) ⁱ
0.44	144.01	144.07	144.45	144.61		144 80	145 59	1
C-11	(15.87)°	(15.81)°	(16.27) ^e	(16.35)°		(16.59) ^e	(15.91)*	(14.2)'
11-CH₃	15.44	15.44	15.44	15.44		15.50	15.56	
Others	55.16	21.15					115.59	

Table 1. (Continued)

				Series 6				
	6a	6b	6c		6d	6e	6g	
Carbon	δ (SCS)	δ (SCS)	δ	δ (SCS)	J°	δ (SCS)	δ (SCS)	
C-1	163.49 (30.42) ^d	143.73 (10.66) ^d	133.07	165.58 (32.51) ^d	254.5	139.28 (6.21) ^d	151.20 (18.13) ^d	
C-2	113.79 (15.05) ^d	129.26 (0.42) ^d	128.84	115.64 (~13.20) ^d	22.0	128.85 (0.01) ^d	123.84 (-5.00) ^d	
C-3	130.61 (2.07) ^d	128.43 (0.11) ^d	128.54	130.86 (2.32) ^d	9.5	129.67 (1.13) ^d	129.26 (0.72) ^d	
C-4	130.61 (7.49) ^d	135.26 (2.84) ^d	138.10	134.14 (–3.96) ^d	2.4	136.08 (–2.02) ^a	142.67 (4.57) ^d	
C-5	187.61	188.91	189.69	187.73		188.02	187.97	
C-6	120.73	120.90	121.10	120.26		120.14	119.84	
C-7	135.26	135.67	136.37	136.26		136.55	137.90	
C-8	142.08 (1.65)°	142.02 (1.64) ^e	142.15 (1.99)°	141.79 (1.65) ^e		141.67 (1.66) ^e	141.32 (~1.47)°	(2.5) ⁱ
C-9	131.85 (0.30)°	132.02 (0.23) ^e	132.48 (0.66)°	132.37 (0.23)°		132.49 (0.34) ^e	133.37 (0.29)°	(1.2) ^j
C-10	131.14 (2.82) ^e	131.20 (2.77) ^e	131.51 (2.91)°	131.26 (2.41) ^e		131.32 (2.40)°	131.55 (3.00)°	(3.4) ⁱ
C-11	115.79 (12.35)°	116.02 (12.24)°	116.51 (11.67)°	116.43 (11.83)°		116.61 (11.60)°	117.61 (12.24)*	(-18.1) ^j
Others	55.25	21.43						

 $^{\rm a}$ Chemical shifts in ppm relative to TMS, calculated by adding 76.9 to the shift relative to the centre peak of ${\rm CDCl}_3.$

^b Chemical shifts are coincident, within experimental error, to those reported in Ref. 11.

^cCarbon-fluorine coupling constant, in Hz.

^d Substituent chemical shift with respect to the phenyl unsubstituted compound in the same series (X = H).

^e Substituent chemical shift with respect to the corresponding thiophene unsubstituted compound in series 3 (Z = W = H).

Phenyl ring carbons

The assignment of the phenyl ring carbon chemical shifts was mainly based on substituent chemical shift considerations, with the aid of the off-resonance de-coupled spectra.

Table 3 records the substituent chemical shifts in $CDCl_3$ for *para*-substituted acetophenones,¹⁴ chosen as model compounds, and for the substituted chalcones of series 2,⁷ whose structures are extremely close to those of the thiophene and furan analogues reported here. The excellent agreement of the substituent shifts for series **3–8** (Tables 1 and 2) with those in Table 3, and the relative intensities of the signals, allow complete assignment for the phenyl ring carbons. The assignment is supported by the characteristic carbon–fluorine coupling constants for the *para*-fluoro-derivatives.

The chemical shifts of the C-4 atoms depend on the Hammett σ constants for the X substituents, as already found for the corresponding carbons in series 2. The values of ρ are comparable with that found for series 2 (9.446),⁷ although the statistical parameters show a less satisfactory correlation (Table 4). Excellent correlations with slopes of unity are found between the C-4 chemical shifts in series 3-8 and the corresponding C-4 in series 2 (Table 5). The effect of

^f Chemical shifts for the corresponding carbons in 3-methylthiophene relative to the α and β carbons of thiophene in deuterioacetone, Ref 16b. ^a Alternative assignment.

h Add 0.19 for alternative assignment.

¹ Chemical shifts for the corresponding carbons of 2-methylthiophene relative to the α and β carbons of thiophene in deuterioacetone, Ref. 16b. ¹ Chemical shifts for the corresponding carbons of

2-bromothiophene relative to the α and β carbons of thiophene in deuterioacetone, Ref. 16b.

the X substituents on the C-4 chemical shifts, approximately predicted on the basis of Hammett sigma parameters, is thus constant in all series and can be accurately predicted from direct comparison of experimental shifts.

Heterocyclic ring carbons

Extensive systematic studies of the influence of the heteroatom and of other substituents on ¹H NMR¹⁵ and ¹³C NMR¹⁶ spectra of 5-membered heterocycles have been carried out by Gronowitz and co-workers. The chemical shifts of the ring carbons and protons caused by substituents were found to depend both on the substituents and on the heteroatom.^{16d} ¹³C Chemical shifts have been correlated^{16d} with ¹H shifts, with the electronegativity of the heteroatom and with reactivity parameters by the Swain-Lupton equation.¹⁷

¹³C substituent chemical shifts with respect to the α and β carbons of thiophene^{16b} and furan^{16d} have been measured for a wide variety of 2- and 3-substituted derivatives in deuterioacetone solutions. The values for 3-methylthiophene,^{16b} 2-methylthiophene,^{16b} 2bromothiophene^{16b} and 2-methylfuran^{16d} are reported in Tables 1 and 2 for comparison with the **4**, **5**, **6**, and

	7a	7b	7c ^b	Serie 7d	əs 7	7e	7f	79	
Carbon	δ (SCS)	δ (SCS)	δ	δ (SCS)	٦°	δ (SCS)	δ (SCS)	δ (SCS)	
C-1	163.38 (30.78) ^d	143.49 (10.89) ^d	132.60	165.46 (32.86) ^d	254.4	139.02 (6.42) ^d	117.96 (14.64) ^d	149.96 (17.36) ^a	
C-2	113.67 (14.79) ^d	129.20 (0.74) ^d	128.46	115.49 (12.97) ^d	20.6	129.73 (1.27) ^d	132.41 (3.95) ^d	123.67 (~4.79) ^d	
C-3	130.61 (2.27) ^d	128.43 (0.09) ^d	128.34	130.81 (2.47) ^d	10.3	128.79 (0.45) ^d	128.70 (0.36) ^d	129.20 (0.86) ^d	
C-4	130.96 (7.22) ^d	135.49 (2.69) ^d	138.18	134.32 (~3.86) ^d	2.9	136.38 (-1.80) ^d	141.46 (3.28) ^d	142.85 (4.67) ^d	
C-5	187.97	189.20	189.74	187.97		188.32	188.34	188.08	
C-6	119.08	119.26	119.41	118.55		118.55	118.32	118.14	
C-7	129.85	130.20	130.52	130.61		130.90	131.86	132.02	
C-8	151.73	151.67	151.72	151.44		151.44	151.36	151.14	
C-9	115.61	115.84	115.89	116.26		116.49	117.23	117.55	
C-10	1 12.43	112.49	112.49	112.55		112.67	112.85	112.90	
C-11	144.61	144.73	144.80	144.85		145.02	145.47	145.55	
Others	55.25	21.37					115.89		
	8a	8b	80	Serie 8d	əs 8	Re	Rf	80	
	δ	δ	δ	δ		δ	δ.	δ	
Carbon	(SCS)	(SCS)		(SCS)	Jc	(SCS)	(SCS)	(SCS)	
C-1	163.20 (30.72) ^d	143.26 (10.78) ^d	132.48	165.41 (32.93) ^d	254.4	138.85 _ (6.37) ^d	117.86 (14.62) ^d	149.90 (17.42) ^d	
C-2	113.61 (–14.85) ^a	129.14 (0.68) ^d	128.46	115.46 (13.00) ^d	22.0	129.68 (1.22) ^d	132.23 (3.77) ^d	123.61 (-4.85) ^d	
C-3	130.55 (2.24) ^d	128.43 (0.12) ^d	128.31	130.79 (2.48) ^d	8.8	128.70 (0.39) ^d	128.52 (0.21) ^d	129.14 (0.83) ^d	
C-4	131.14 (-7.18) ^a	135.67 (2.65) ^d	138.32	134.61 (3.71) ^d	2.9	136.72 (1.60) ^d	141.58 (3.26) ^d	143.14 (4.82) ^d	
C-5	188.14	189.32	189.72	188.02		188.34	188.10	188.02	
C-6	117.26	117.43	117.48	116.84		116.92	116.31	116.31	
C-7	130.02	130.32	130.72	130.79		131.01	131.80	132.08	
C-8	150.38 (1.35)*	150.38 (–1.29)°	150.27 (–1.45)°	150.20 (1.24)*		150.26 (–1.18)°	149.90 (−1.46)ª	149.90 (−1.24)°	(-1.9) ^f
C-9	1 17.67 (2.06)°	117.84 (2.00)°	118.18 (2.29)⁵	118.31 (2.05)°		118.38 (1.89)°	119.29 (2.06)*	119.73 (2.18)°	(0.7) ^f
C-10	109.14 (-3.29)°	109.20 (–3.29)°	109.32 (–3.17)°	109.31 (3.24)°		109.33 (–3.34)°	109.57 (3.28)*	109.73 (–3.17)°	(-4.1) ^f
C-11	155.55 (10.94)°	155.67 (10. 94)°	155.82 (11.02)°	155.96 (11.11)°		156.03 (11.01)°	156.64 (11.17)°	156.84 (11.29)°	(9.1) ^f
11-CH₃ Others	13.72 55.19	13.72 21.37	13.97	13.66		13.62	13.62 115.46	13.78	

Table 2. ¹³C chemical shifts for furan chalcone analogues, series 7 and 8^a

^{a-d} As in Table 1.

Substituent chemical shift with respect to the corresponding furan unsubstituted compound in series 7 (Z = W = H).

^f Chemical shifts for the corresponding carbons of 2methylfuran relative to the α and β carbons of furan in deuterioacetone, Ref. 16d.

Table 3. Substituent chemical shifts in 1-X,4-Y-disubstituted benzenes in CDCl₃

		Y = C(OMe ^a		Y ≕ COCHCHPh ^b			
x OMe	C-1 30.39	с-2 –14.61	с-з 2.04	C-4 6.80	с-1 30.67	с-2 - 16.64	с-з 0.32	с-4 7.48
Me	10.78	-0.91	-0.15	-2.43	10.71	-0.16	-1.13	2.60
F	32.67	-12.68	2.38	-3.64	32.86	14.73	0.98	-3.42
CI	6.41	0.49	1.12	-1.70	6.41	-0.57	0.16	-1.71
CN	-16.69	4.22	0.14	2.77	-14.70	2.11	0.73	3.24
NO2	17.38	-4.37	0.83	4.37	22.00	-6.49	0.81	4.86

^a From Ref. 14 ^b From Ref. 7.

Series	Carbon	ρ ^b	δο ⁶		 N ^e
	4	94(1.9)	135 3 (0.8)	0.912	7
•	ż	2.5 (0.1)	137.0 (0.0)	0.995	7
3	8	-0.60 (0.00)	140.2 (0.0)	0.960	7
	11	1.8 (0.3)	128.3 (0.1)	0.922	7
	4	8.0 (2.2)	136.2 (0.9)	0.881	6
	7	2.5 (0.1)	135.4 (0.0)	0.999	6
4	8	-0.44 (0.05)	120.2 (0.0)	0.977	6
	11	1.6 (0.06)	127.2 (0.0)	0.977	6
	4	8.9 (2.8)	135.6 (0.9)	0.845	6
5	7	2.4 (0.1)	137.4 (0.0)	0.995	6
	8	-0.74 (0.08)	138.4 (0.0)	0.978	6
	11	1.7 (0.1)	144.4 (0.0)	0.996	6
	4	9.4 (2.7)	135.2 (0.9)	0.871	6
e	7	2.4 (0.2)	136.1 (0.1)	0.985	6
0	8	-0.77 (0.16)	141.9 (0.1)	0.927	6
	11	1.7 (0.1)	116.3 (0.1)	0.987	6
	4	9.3 (2.0)	135.4 (0.8)	0.906	7
7	7	2.0 (0.0)	130.5 (0.0)	0.998	7
,	8	-0.50 (0.10)	151.6 (0.0)	0.916	7
	11	0.91 (0.04)	144.8 (0.0)	0.995	7
	4	9.3 (1.9)	135.6 (0.8)	0.910	7
0	7	1.9 (0.1)	130.6 (0.0)	0.996	7
ō	8	-0.49 (0.06)	150.3 (0.0)	0.969	7
	11	1.2 (0.1)	155.8 (0.0)	0.995	7
				-	

Table 4. Correlations of ¹³C chemical shifts with Hammett σ parameters^a for X Substituents

^a Hammett σ constants from J. Hine, Structural Effects on Equilibria in Organic Chemistry, p. 66. J. Wiley, New York (1975).

^b ρ = Slope, standard deviation of slope in parentheses.

[°] Intercept, standard deviation of intercept in parentheses.

^d Correlation coefficient.

* Number of substituents in the regression analysis.

8 series, respectively. Their agreement with the observed shifts is not as good as that found previously for the phenyl ring carbons; this is due to the inadequacy of the model compounds, which are mono substituted derivatives measured in a different solvent. (The most evident discrepancy is noted for the C-11 shifts in series 4, which are shielded with respect to that of 3c. The steric hindrance of the 9-methyl group in series 4 might, in fact, reduce the electron-withdrawing effect of the system attached to the 8-position.) However, we believe that the concordance of the observed shifts is sufficient to allow the assignment of thiophene and furan ring carbons.

The chemical shifts of C-8 and C-11 correlate with the Hammett parameters for the X substituents (Table 4). The ρ values for C-8 in series **3–8** are negative and comparable with that for C-8 in series **2** (-0.54), while those for C-11 are positive and considerably higher than that in series **2** (0.48).⁷

The occurrence of long-range substituent effects in extended π electron systems has been reported for the ¹³C shifts of other 'partially insulated' systems such as benzophenones¹⁸ and for 'fully insulated' systems such as N-benzylidenebenzylamines.¹⁹ However, the ρ values for C-11 in series **3–6** are higher than those recorded for more conjugated systems, such as Nbenzylideneanilines,²⁰ showing the high sensitivity of this position of the thiophene ring. This peculiarity is also highlighted by the ¹³C chemical shift 'responses'²¹ for these heterocyclic systems in the correlations of the C-11 chemical shifts for series **3–8** vs the reference C-11 shifts in series **2**, from analogously substituted benzenes. The least squares analyses are recorded in Table 5.

The unusually high sensitivity to substituent effects at C-5 in thiophene relative to C-para in benzene, already noted by Gronowitz *et al.*,^{16b} has been recently verified for arylcarbenium ions and discussed in relation to calculated charges and other experimental probes of charge distribution.²¹ It has been suggested that any theoretical treatment of the unusual sensitivity of the carbons adjacent to sulphur should explain this as a 'local effect'.²¹

Carbonyl carbons

The carbonyl carbon (C-5) shifts in series 3-8 are only slightly affected by the X substituents and no correlation with their Hammett substituent constants was observed. Satisfactory correlations with slopes of approximate unity were obtained with the corresponding C-5 shifts in series 2 when the nitro-derivatives (g) were omitted, and with those of the unsubstituted thiophene series 3, including all available terms in each series (Table 5).

Ethylenic carbons

The ethylenic carbons are easily assigned from their characteristic splittings in the ORD spectra. These splittings, due to higher order effects, were estimated, and the simulated and experimental spectra compared for **3c** and **7c**.¹³ The splittings observed for C-6 in the off-resonance decoupled spectra of **3a**, **3b** and **3e** are reported as examples in Fig. 1. The C-6 chemical shifts vary very little within each series ($\Delta \delta \sim 1$ ppm), being only slightly influenced by the inductive effect of the X substituents, as already noted by the Swain-Lupton treatment of data in series **2**.⁷

In series 1, the C-6 shifts were found to depend on the Hammett σ constants of the substituents in the ethylene-linked phenyl ring, according to the following equation: $\delta = 5.259\sigma + 121.29$. The C-6 shifts in series **3-8** are thus expected to be significantly influenced by the electronic effects of the Y, Z and W substituents.

Substituent effects in 5-membered heterocycles can be investigated by different approaches.

An approach implies the calculation of sigma replacement values for the heteroatoms, regarded as substituents, assuming ρ values for the 5-membered heterocyclic systems to be equivalent to those in benzenoid compounds.⁸ For substituted thiophene and furan derivatives, we can calculate sigma replacement values for the heteroatoms ($\sigma_{\alpha-Y}$) from the following equation:

$$\delta = \rho(\sigma_{\mathbf{W}} + \sigma_{\alpha - \mathbf{Y}}) + \delta_0$$

where ρ and δ_0 are the slope and the intercept of the Hammett plot, respectively, for the corresponding benzene derivatives (series 1) and σ_W is the Hammett sigma constant for the W substituent in the heterocyclic ring. In our case the sigma replacement values can

	Carbon	4	(5		 6	7	8	11
Series	series	2	2 ⁰	3	2 ⁰	3	2	2	2
_	Slope ^c	0.99 (0.02)	0.92 (0.09)	-	1.16 (0.08)		0.89 (0.01)	0.99 (0.15)	3.75 (0.72)
3	rd	0.999	0.981		0.992	_	1.000	0.950	0.918
	N°	7	6	_	6		7	7	7
	Slope ^c	1.04 (0.03)	1.00 (0.07)	1.08 (0.07)	1.38 (0.10)	1.17 (0.09)	0.89 (0.03)	0.71 (0.12)	3.23 (0.34)
4	rª	0.999	0.994	0.992	0.992	0.987	0.998	0.947	0.979
	N°	6	5	6	5	6	6	6	6
-	Slope ^c	0.98 (0.02)	0.98 (0.07)	1.04 (0.11)	1. 38 (0.01)	1.16 (0.14)	0.88 (0.04)	1.07 (0.16)	3.83 (0.43)
5	rd	0.999	0.990	0.978	0.992	0.973	0.996	0.955	0.975
	N°	6	6	6	6	6	6	6	6
•	Slope ^c	0.99 (0.02)	1.09 (0.04)	1.15 (0.11)	1.50 (0.15)	1.27 (0.16)	0.83 (0.08)	1.36 (0.15)	3.48 (0.27)
6	rd	0.999	0.998	0.981	0.985	0.971	0.982	0.975	0.988
	N٩	6	5	6	5	6	6	6	6
_	Slope ^c	0.99 (0.03)	0.98 (0.06)	1.06 (0.0 9)	1.31 (0.12)	1.20 (0.15)	0.72 (0.03)	0.85 (0.14)	1.96 (0.20)
/	r	0.999	0.993	0.984	0.984	0.964	0.996	0.935	0.970
	N°	7	6	7	6	7	7	7	7
•	Slope ^c	1.00 (0.00)	0.95 (0.14)	1.08 (0.13)	1.29 (0.15)	1.18 (0.19)	0.66 (0.03)	0.77 (0.16)	2.57 (0.22)
8	rd	1.000	0.959	0.966	0.975	0.943	0.996	0.903	0.982
	Ne	7	6	7	6	7	7	7	7

Table 5. Correlations of ¹³C chemical shifts of C-4, C-5, C-6, C-7, C-8 and C-11 in series 3–8 (Tables 1 and 2) with those of the corresponding shifts in series 2^a and 3

^a From Ref. 7

^b NO₂ derivatives (g) omitted

^c Standard deviation of the slope in parentheses

be derived from the above equation for the **c** derivatives (X = H) in all series, assuming the additivity of the effects of the Y and W substituents. $(\sigma_{para}$ -Methyl is used for **4c**, **5c** and **8c**; σ_{para} -bromo for **6c**.) $\sigma_{\alpha-S}$ Values calculated from **3c**, **4c**, **5c** and **6c** are

 $\sigma_{\alpha-S}$ Values calculated from **3c**, **4c**, **5c** and **6c** are equal to -0.14, -0.15, -0.15 and -0.27, respectively. The above values which are approximately constant apart from that for the bromo-derivative **6c**, provide an estimation of the electron donating effect of the sulphur atom. (The 'anomalous' effects of iodine and bromine on ¹³C chemical shifts are well known.²²) $\sigma_{\alpha-O}$ Values derived from **7c** and **8c** are -0.36 and -0.55, respectively, indicating the greater electrondonating character of the oxygen with respect to the sulphur atom in these systems. This is qualitatively in agreement with σ^+ constants for the heteroatoms in



Figure 1. Splittings observed for C-6 in the off-resonance decoupled spectra of 3a, 3b and 3e.

^d Correlation coefficient

Number of chemical shifts included in the analysis.

5-membered heterocycles, 23 which indicate oxygen to be a better electron donor.

A rather different approach is to apply the Hammett equation to 5-membered rings by considering the 4and 5-positions as *meta*- and *para*-like, respectively, using σ_m and σ_p values, and to consider the ρ values, compared with those for the corresponding benzenoid compounds, in terms of the intensity of transmission through the ring.^{8b} This approach, which cannot be applied here due to the insufficient number of substituents on the heterocyclic ring, has been criticized in a recent paper.²⁴ The alternative approach, proposed in the same paper,²⁴ implies direct comparison of the effects of substituents in a heterocyclic ring with those of the substituents in a benzene ring, acting on an identical reaction site.

A possible comparison allowed by the available experimental data on chalcones and their analogues involves the variation of the C-6 chemical shifts caused by the presence of a methyl group in the 11-position of benzene in series $1 (\Delta \delta_{C-6} = -0.90)$,⁷ of thiophene ($\Delta \delta_{C-6} = \delta_{C-6}$ $5c - \delta_{C-6}$ 3c = -0.98) and of furan ($\Delta \delta_{C-6} = \delta_{C-6}$ $8c - \delta_{C-6}$ 7c = -1.93). This suggests the following order for the transmission of the electronic effects of the methyl group through the rings: furan > thiophene > benzene. This trend is in agreement with the order of rho values for the ionization of carboxylic acids²⁵ and is in an inverse order with respect to the ground state aromaticities of the rings.²⁶

In conclusion, although the above approaches provide useful information on the effects exerted by Y, Z and W substituents and on their transmission through the rings, their use, dictated by the lack of better models, does not represent a rigorous quantitative treatment of general validity.

The C-7 ethylenic carbons show excellent correlations with the Hammett σ parameters for the X substituents in all series (Table 4), with ρ values lower than that reported for series 2 (2.86),⁷ those of the thiophene series 3-6 being higher than those of the furan series 7 and 8. Correlations with the corresponding C-7 shifts in series 2 (Table 5) are also excellent, with a slope obviously lower than unity.

C-7 Carbon signals for series 5, 3 and 6 are shifted to high field on increasing the inductive electronwithdrawing effect of the W substituents. The highfield shift of C-7 in series 4 with respect to those in series 5 can be ascribed to the steric effect of the adjacent methyl group at the 9-position.²⁷

CONCLUSIONS

The ¹³C chemical shifts for thiophene and furan chalcone analogues (series 3-8) can be conveniently used for the study of substituent effects in these systems, and the Hammett treatment of the data is often a suitable tool for elucidating the effect of the substituents. Dual parameter equations were not applied since the set of available data was estimated to be insufficient for such treatments.

Satisfactory correlations with experimental shifts in series 2 and 3 provide reliable ground for discussion when there is no correlation with substituent parameters, supporting the point of view of Exner,²⁸ Wold and Sjöström,²⁹ who recommend direct correlations between experimental quantities.

EXPERIMENTAL

Products

Thiophene and furan chalcone analogues were synthesized by Claisen-Schmidt condensation of 2thiophenealdehyde (series 3), 3-methyl-2-thiophenealdehyde (series 4), 5-methyl-2-thiophenealdehyde (series 5), 5-bromo-2-thiophenealdehyde (series 6), 2furanaldehyde (series 7) and 5-methyl-2-furanaldehyde (series 8) with substituted acetophenones³⁰ and the products were crystallized from ethanol.

All new chalcones gave correct analyses for C, H and N. Their melting points are recorded in Table 6. The ¹³C NMR spectra show the presence of only one isomer. The main IR bands include the band of *trans*-ethylenic double bonds³¹ at 990–955 cm⁻¹.

Table 6. Melting points of thiophene and furan chalcone analogues

	m.n.			mp	
Compound	(°C)	Ref.	Compound	(°C)	Ref.
3a	105	а	6a	137–138	а
3b	78	а	6b	8889	а
3c	58	а	6c	70–71	а
3d	90–91	а	6d	8990	а
3e	121	а	6e	125126	а
3f	141–142		6g	160-161	а
3g	166168	а			
4b	8182		7a	77–78	c
4c	67–68	_	7b	6263	d
4d	67–68		7c	35–36	e
4e	91–92	—	7d	6869	f
4f	137–138		7e	77	8
4g	162–163		7f	134135	_
			7g	141–142	9
5a	7172		8a	81-82	а
5b	74–75		8b	80-81	_
5c	53-54	ь	8c	63–64	b
5d	76–77	_	8d	6465	_
5e	80–81	—	8e	102–103	а
5f	120-122	—	8f	143–145	
			8g	154155	—

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Spectra

Spectra were measured at room temperature after dissolving 200 mg of sample in 1.5 ml of CDCl₃, which was also used as the internal standard. Those of the nitro-derivatives were recorded in more dilute solutions, owing to their low solubility.

¹³C NMR spectra of series **3**, **6**, **7** and **8** were recorded on a JEOL FX-100 spectrometer at 25.05 MHz. Typical conditions were: 5 KHz width; 8 K data points; pulse width 5 μ s (30°). The spectra of series **4** and **5** were recorded on a Bruker WP-80 spectrometer at 20.1 MHz. Typical conditions were: 5 KHz width; 8 K data points; pulse width 1 μ s (17°).

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