An Analysis of the Substituent Effects on ^{13}C and ^{17}O NMR Chemical Shifts of Some 5-Substituted 2-Acetylthiophenes by Linear Free Energy Relationships†

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The ^{13}C and ^{17}O NMR chemical shifts of the title compounds have been determined in $CDCl_3$. The analysis of the substituent induced chemical shift (SCS) values showed that ^{17}O data usefully complete ^{13}C data in the study of the transmission of substituent electronic effects through the heteroaromatic ring. A comparison with the corresponding data for acetophenones highlighted that the substituent–ring–probe interactions are larger in thiophene than in benzene derivatives. Concerning the controversial problem of the electronic interactions between –COX groups and π-systems the present data confirm the ability of the acetyl group to conjugate with aromatic or heteroaromatic rings.

Dedicated to Professor Salo Gronowitz on the occasion of his 65th birthday.

We have, for a long time, had an interest in the study of the transmission of substituent effects in the thiophene ring. Kinetic and equilibrium constant measurements of *ortho*-, *meta*- or *para*-like di- or poly-substituted thiophenes have been carried out and the data collected were analyzed by means of linear free energy relationships (LFERs).[1]

Recently[2] we utilized ^{13}C NMR spectroscopy in order to obtain information about the transmission of substituent effects on the carbon atoms of the side-chain and of the aromatic or the heteroaromatic ring in Ar–COX systems. The substituent chemical shifts (SCSs) induced at either the endocyclic and the exocyclic carbon atoms were treated by single (Hammett)[3] and/or dual substituent parameter (DSP) equations, this last treatment allowing the separation of polar and resonance components of the substituent effects. We used the *unconstrained* version (1) of the DSP equation developed by Ehrenson *et al.*[4a] where σ_I and σ_R are, respectively, the

$$SCS = \rho_I\sigma_I + \rho_R\sigma_R + i \quad (1)$$

inductive and the resonance substituent constants, ρ_I and ρ_R are the relevant susceptibility constants and i represents the intercept of the regression plane with the SCS axis ($\sigma_I = \sigma_R = 0$).

The DSP analysis of the recently examined (*meta*-like) 4-,[2a] (*para*-like) 5-[2a] and (*ortho*-like) 3-substituted[2b] thiophene-2-carboxylic acids and of the corresponding anions evidenced the occurrence of a reverse polar effect ($\rho_I < 0$) and a transmission of resonance effects where the conjugative interactions between the substituent and the carboxy group through the π-aromatic system are not important ($\rho_R \simeq 0$). In continuance of our research[2] and in particular of studies concerning the controversial problem of the electronic interactions between –COX groups and π-systems[2,4] we have now measured ^{13}C and ^{17}O NMR chemical shifts of a series of sixteen 5-substituted 2-acetylthiophenes **1** in $CDCl_3$ solutions, using a large set of substituents ranging from the strongly electron-withdrawing nitro and methylsulfonyl groups to the strongly electron-donating methoxy, piperidin-1-yl and *N*,*N*-dimethylamino groups.

The ^{13}C NMR spectrum of 2-acetylthiophene had already been examined in hexadeuterioacetone[5a,b] and in deuteriochloroform[6] solutions and compared with those of 3-acetylthiophene,[5b] acetophenone, 2-acetyl-furan, -selenole and -tellurole.[5a] In addition, the ^{17}O NMR spectrum of 2-acetylthiophene was examined and compared with those of 3-acetylthiophene, acetophenone, 2-acetyl-furan, -pyrrole and -*N*-methylpyrrole.[7]

As a matter of fact, the acetyl group is an excellent framework in which one can investigate substituent effects via NMR studies because it contains such probes as the carbon and the oxygen atoms of the carbonyl group. In addition, measurements of protonation equilibria[8] and of reactivity[9] as well as of other spectroscopic properties of the acetyl group can be easily collected.[10] It is convenient

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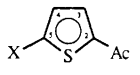

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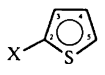

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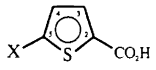
a : X = NO_2 **f** : X = Ac **j** : X = H **n** : X = SMe
b : X = CN **g** : X = I **k** : X = Ph **o** : X = OMe
c : X = SO_2Me **h** : X = Br **l** : X = Me **p** : X = $N(CH_2)_5$
d : X = CO_2Me **i** : X = Cl **m** : X = Et **q** : X = $N(Me)_2$
e : X = CHO



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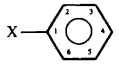

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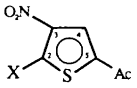

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to gather various chemical and physical data in order to check the occurrence of linear correlations between different series of data as well as to study the different energy variations as a function of the present substituent by comparing several chemical and physical properties.

Results and discussion

In Table 1 the ^{13}C and ^{17}O SCS values in deuteriochloroform solutions of compounds **1** are reported. Owing to the complexity of the effects which affect the ^{13}C SCS values,[11] the SCS values of endocyclic carbon atoms often gave only poor correlations with both single-parameter and DSP equations. In many aromatic and heteroaromatic systems good linear cross-correlations could be obtained between SCS values of *meta*- or *para*-disubstituted compounds (X–Ar–Y: X = variable substituent; Y = probe system) and SCS values of monosubstituted compounds (X–ArH).[4b,c] In view of this, we attempted some cross-correlations between SCS values of compounds **1** and those of monosubstituted thiophenes **2**.

^{13}C NMR data of monosubstituted thiophenes **2**. ^{13}C Chemical shifts in hexadeuterioacetone solutions of many monosubstituted thiophenes **2** have been reported by Gronowitz and coworkers[5b] and the results obtained discussed in terms of substituent effects, which were tentatively rationalised by using the two-parameter treatment proposed by Swain and Lupton.[12] Better statistical results have been achieved by Smith and Proulx[5c] by applying a three-parameter equation to the data of Gronowitz.[5b] Takahashi *et al.* studied some 2- and 3-substituted thiophenes[13] and showed the occurrence of some cross-correlations.

Since some of our substituents had not been tested in the previous studies[5b,13b] we determined the SCS values of all the monosubstituted thiophenes **2** in deuteriochloroform solution (Table 2). We observed that the solvent used had a very small effect: both ^{13}C chemical shifts and SCS values in the two solvents were very similar to each other.

Information about the electronic interactions between substituents and thiophene ring as compared with those observed in benzene compounds could be obtained either by comparing SCS values in monosubstituted thiophenes **2** and benzenes **4** or by using single-parameter and DSP eqns.

Both methods gave some interesting results: the good cross-correlations, e.g., of SCS values in deuteriochloro-

Table 1. SCS values of carbon and oxygen atoms of 5-substituted 2-acetylthiophenes **1** in $CDCl_3$.[a]

		^{13}C							^{17}O
Compound	X	C-2	C-3	C-4	C-5	CO	Me	Others	CO
1a	NO_2	3.80	−2.29	0.32	22.72	−0.19	−0.20		27.8
1b	CN	5.31	−1.25	9.65	−17.53	−0.87	0.22	113.22	24.4
1c	SO_2Me	6.07	−1.15	5.26	14.34	−0.30	0.19	45.73	17.2
1d	CO_2Me	4.40	−0.74	5.43	5.94	0.17	0.28	162.10, 52.63	29.8
1e	CHO	5.92	−0.50	7.41	14.37	0.22	0.30	183.43	25.9
1g	I	5.95	0.74	10.05	−48.26	−1.42	−0.25		1.9
1h	Br	1.58	0.09	3.20	−10.90	−1.05	−0.54		4.8
1i	Cl	−1.28	−0.49	−0.46	6.01	−0.86	−0.71		1.2
1j	H[b]	144.35	132.39	127.99	133.66	190.59	26.73		518.6
1k	Ph	−1.30	1.01	−4.14	19.07	−0.08	−0.22	133.29, 126.33, 129.07, 128.99	2.8
1l	Me	−2.06	0.63	−1.33	16.12	−0.26	−0.37	15.95	−9.1
1m	Et	−2.61	0.43	−3.20	23.63	−0.27	−0.43	23.91, 15.43	−8.5
1n	SMe	−1.13	0.62	−1.43	16.63	−1.18	−0.56	19.33	−7.9
1o	OMe	−13.61	0.53	−22.17	40.83	−0.63	−1.44	60.32	−22.9
1p	$N(CH_2)_5$	−17.02	3.06	−24.52	33.81	−2.01	−1.68	50.81, 24.84, 23.52	−44.2
1q	$N(Me)_2$	−17.16	3.47	−25.56	33.43	−2.17	−1.81	41.92	−51.1

[a] SCS values (ppm) relative to unsubstituted compound (**1j**). Downfield shifts are positive. [b] Chemical shifts (ppm) of ^{13}C relative to $CDCl_3$ (77.00 ppm) and of ^{17}O relative to external 1,4-dioxane (0.0 ppm).

Table 2. SCS values of carbon atoms of 2-substituted thiophenes **2** in $CDCl_3$.[a]

Compound	X	^{13}C C-2	C-3	C-4	C-5	Others
2a	NO_2	27.34	1.74	0.17	7.61	
2b	CN	−15.51	10.27	0.63	7.34	113.78
2c	SO_2Me	16.82	6.60	1.05	8.55	46.00
2d	CO_2Me	8.44	6.38	0.70	7.05	162.32, 51.75
2e	CHO	18.88	9.31	1.40	9.85	182.69
2f	Ac	19.35	5.62	1.21	8.66	190.59, 26.73
2g	I	−51.92	10.07	2.02	6.41	
2h	Br	−12.68	3.09	0.83	1.89	
2i	Cl	5.06	−0.76	−0.23	−1.01	
2j	H[b]	125.00	126.77	126.77	125.00	
2k	Ph	19.41	−3.73	1.19	−0.27	134.41, 125.94, 128.86, 127.42
2l	Me	14.43	−1.66	0.06	−2.02	14.90
2m	Et	22.21	−3.60	−0.20	−2.44	23.22, 16.01
2n	SMe	12.21	4.06	0.54	2.71	22.03
2o	OMe	41.64	−23.07	−2.15	−13.37	60.24

[a] SCS values (ppm) relative to the unsubstituted compound (**1j**). Downfield shifts are positive. [b] Chemical shifts (ppm) of ^{13}C relative to $CDCl_3$ (77.00 ppm).

Table 3. Statistical data[a] for the cross-correlations, for the single-parameter and DSP analysis of SCS values of carbon and oxygen atoms of 5-substituted-2-acetylthiophenes **1** and of 2-substituted thiophenes **2**

Line	Probe atom	Series	$\rho \pm s_\rho$ (or $\beta \pm s_\beta$)	SCS or $\Delta\nu_{C=O}$ of the probe atom, or substituent constant	Series	$i \pm s_i$	n	r(or R)	CL> (%)
1	C-2[b]	**2**	1.30 ± 0.12 1.40[d]	C_B-1[b,c]	**4**	2.39 ± 1.67	10	0.968 0.981	99.9
2	C-5[b]	**2**	1.47 ± 0.14 1.42[d]	C_B-4[b,c]	**4**	0.90 ± 0.63	10	0.967 0.935	99.9
3	C-3[b]	**2**	1.59 ± 0.28 1.62[d]	C_B-2[b,c]	**4**	2.49 ± 1.44	10	0.895 0.871	99.9
4	C-5[b]	**2**	ρ_I 7.13 ± 3.14 ρ_R^+ 15.9 ± 2.1	σ_I, σ_R^+		2.55 ± 1.34	12[e]	0.948	99.9
5	C_B-4[b]	**4**	ρ_I 5.56 ± 1.64 ρ_R^+ 10.5 ± 1.0	σ_I, σ_R^+		0.38 ± 0.68	9	0.980	99.9
6	C-2[b]	**1**	0.83 ± 0.05	C-5[b]	**2**	-1.13 ± 0.34	14	0.976	99.9
7	C-5[b]	**1**	0.95 ± 0.03	C-2[b]	**2**	0.16 ± 0.74	14	0.993	99.9
8	C-4[b]	**1**	0.92 ± 0.05	C-3[b]	**2**	-0.62 ± 0.41	14	0.983	99.9
9	C-5[b]	**1**	1.34 ± 0.10	C_B-4[b,c]	**5**	1.48 ± 1.39	10	0.980	99.9
10	C-4[b]	**1**	1.51 ± 0.15	C_B-3[b,c]	**5**	1.35 ± 1.14	10	0.963	99.9
11	C-2[b]	**1**	1.49 ± 0.14	C_B-1[b,c]	**5**	0.13 ± 0.69	10	0.967	99.9
12	C-α[b]	**1**	1.69 ± 0.24	C-α[f]	**6**	0.14 ± 0.20	8[g]	0.946	99.9
13	^{17}O (C=O)[b]	**1**	1.48 ± 0.10	$\Delta\nu_{C=O}$[h]	**1**	6.15 ± 1.59	16	0.969	99.9
14	^{17}O (C=O)[b]	**1**	31.2 ± 2.4	σ_P^+		3.11 ± 1.58	15	0.962	99.9
15	^{17}O (C=O)[b]	**1**	ρ_I 24.7 ± 7.4 ρ_R^+ 61.9 ± 5.7	σ_I, σ_R^+		3.45 ± 3.16	13	0.976	99.9
16	^{17}O(C=O)[b]	**1**	1.66 ± 0.09	^{17}O (C=O)[i]	**5**	2.05 ± 0.87	7	0.993	99.9

[a] ρ, susceptibility constant for the single-parameter or for the DSP analysis; β, slope of the cross-correlation; i, intercept, s_ρ, s_β and s_i, standard deviations; n, number of points; r (or R) correlation coefficient; CL, confidence level. [b] In deuteriochloroform. [c] Data from Ref. 4(b). [d] See Ref. 13(b). [e] If data for X = I are excluded from the correlation: ρ_I (6.32 ± 2.09), ρ_R^+ (16.5 ± 1.4), i (2.43 ± 0.89), n 11, r 0.979, CL > 99.9%. [f] In hexadeuteriodimethyl sulfoxide, data from Ref. 2(d). [g] If data for X = SMe are excluded from the correlation: β (1.84 ± 0.16), i (0.18 ± 0.13), n 7, r 0.981, CL > 99.9%. [h] In dimethyl sulfoxide, data from Ref. 10(b). $\nu_{C=O}$ for X = CO_2Me, NMe_2 and $N(CH_2)_5$: 1668.0, 1621.0 and 1622.0, respectively (this work). [i] In dioxane, data from Ref. 16.

form solutions for C-2 *vs.* C_B-1 (C_B indicates benzene carbon atom) and for C-5 *vs.* C_B-4, *inter alia*, showed that the electronic effects of substituents on the *ipso* as well as on the *para*-like carbon atoms are greater in thiophene than in the benzene system (Table 3, lines 1 and 2), as qualitatively pointed out by Gronowitz and coworkers.[5b] These authors, in fact, used the Swain and Lupton equation to analyze ^{13}C SCS data and calculated resonance susceptibility constants for thiophene compounds greater than for benzene compounds. On the other hand SCS values for carbon atoms *ortho*-like (C-3 vs. C_B-2) with respect to the variable substituent gave only a poor cross-correlation (Table 3, line 3), because a different combination of resonance, field and anisotropy effects is operative in the two systems (thiophene and benzene) which is also a function of the differences in geometry.

^{13}C SCS values for the *ipso*-carbon atom (C-2) as well as for the *ortho*-like carbon atom (C-3) did not give good DSP correlations [by using eqn. (1) or the Swain–Lupton equation] probably because of the different contributions of the anisotropy effects. In contrast ^{13}C SCS values for *para*-like (C-5) carbon atoms gave a good correlation by using the DSP eqn. (1) (Table 3, line 4). The resonance contribution for electron-donating substituents (ρ_R^+ 15.9) indicates the expected large prevalence of resonance on inductive effects (ρ_I 7.1). A similar treatment of ^{13}C SCS values for C_B-4 of monosubstituted benzenes (Table 3, line 5) allowed a comparison with the data for 2-substituted thiophenes and confirmed the conclusions reached by Gronowitz and coworkers[5b] using the Swain–Lupton equation.*

^{13}C and ^{17}O NMR data of 5-substituted 2-acetylthiophenes **1**. SCS values for endocyclic carbon atoms of **1** generally gave only poor correlations when treated with either a single-parameter or the DSP equation. Thus, we attempted a number of cross-correlations of SCS values for carbon atoms *ortho*- (C-4) or *para*-like (C-2) and *ipso* (C-5), with respect to the variable substituent, with SCS values for the corresponding carbon atoms of monosubstituted thiophenes **2** and 4-substituted acetophenones **5**.[2c] In all cases good cross-correlations were observed. Owing to the relatively small SCS values induced on *meta*-like (C-3) endocyclic carbon atoms, the statistical treatments gave poor results (not reported) for this site.

With electron-donating substituents at C-5 we observed SCS values at C-2 (*para*-like with respect to the variable substituent) in series **1** which were very similar to those for the corresponding *para*-like carbon atom (C-5) in series **2**; in contrast, with electron-withdrawing substituents we observed smaller SCS values in **1** than in **2**.

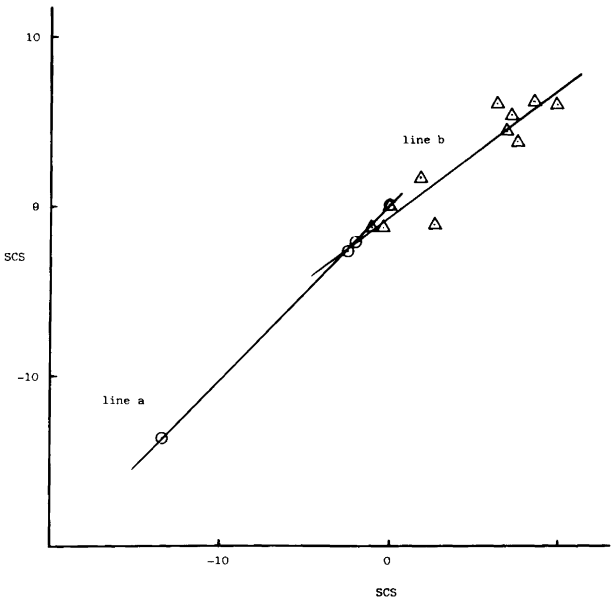


Fig. 1. SCS values at C-2 for **1** versus SCS values at C-5 for **2**: line a, X = OMe, Et, Me and H. $\beta = 1.02 \pm 0.01$, $i = -0.04 \pm 0.05$, $n = 4$, $r = 1.000$, CL > 99.9%; line b, X = H, SMe, Ph, Cl, Br, I, CHO, CO_2Me, SO_2Me, CN and NO_2. $\beta = 0.74 \pm 0.10$, $i = -0.69 \pm 0.57$, $n = 11$, $r = 0.930$, CL > 99.9%.

This dual behavior of the substituents studied reflects on the goodness of fit for the relevant regression (Table 3, line 6). For this reason we have attempted to group these data into two sets; the first including electron-donating substituents (in **1**, X = MeO, Et, Me) and hydrogen, and the second including the other substituents and hydrogen, again. The two cross-correlations obtained (see Fig. 1) gave a statistical confirmation of the different behavior of electron-donating and electron-withdrawing substituents (slopes 1.02 and 0.74, respectively) in 5-substituted 2-acetylthiophenes **1** and in 2-substituted thiophenes **2**.

Slopes near to unity (Table 3, lines 7 and 8) were observed when the SCS values for the carbon atom carrying the variable substituent (*ipso*-carbon, C-5) and for the carbon atom *ortho*-like with respect to the variable substituent (C-4) of **1** were plotted versus the SCS values for the corresponding carbon atoms (C-2 and C-3, respectively) of monosubstituted thiophenes **2**. For C-4 of **1** this behavior [different from that above mentioned (Table 3, line 6)] can be related to the non-conjugative relationship between the acetyl and C-4 (*meta*-like relationship) and in the case of C-5 (*ipso*-carbon atom) to the large range of the SCS values observed (ΔSCS ca. 94 ppm), which renders negligible the effect of the electronic interactions between the acetyl group and thiophene ring.

It must be remarked that excellent cross-correlations with slopes near to unity for SCS values of endocyclic carbon atoms of 5-substituted 2-thiophenecarboxylic acids **3** versus the corresponding SCS values of 2-substituted thiophenes **2** have been observed[2a] according to

* The analogous treatment of ^{13}C SCS values for C_B-2 of monosubstituted benzenes gave only poor results (not reported) with the DSP treatment [eqn. (1)], but the susceptibility constants calculated showed the expected trend.

the non-occurrence of conjugative interactions between the carboxy group and the aromatic rings.[2a,4]

Moreover the SCS values for the carbon atom carrying the variable substituent (*ipso*-carbon C-5), for the carbon atoms *ortho*- and *para*-like with respect to the variable substituent (C-4 and C-2, respectively) of **1** gave good cross-correlations with SCS values for the corresponding carbon atoms (C_B-4, C_B-3 and C_B-1, respectively) of 4-substituted acetophenones **5**. Slopes larger than unity (Table 3, lines 9–11), once again [9a,10] reflect the larger substituent–ring electronic interactions occurring in thiophene than in benzene compounds.

A further comment on the comparison between the effects induced by the substituents on the chemical shifts in thiophene and benzene compounds is worthwhile. In both the instances examined (comparison between monosubstituted thiophenes **2** and benzenes **4** or between 5-substituted 2-acetylthiophenes **1** and 4-substituted acetophenones **5**) the different susceptibilities of the SCS values to the substituent effects of thiophene compared with benzene derivatives cause the cross-correlation slopes to be higher for carbon atoms *ortho* and *para* to the substituents (average β value ca. 1.5) than for *ipso*-carbon atoms (average β value ca. 1.3). These differences can be related to the strength of the substituent–carbon atom interactions which cause a very large variation in SCS values and level any other effect (aromaticity or heteroaromaticity, different ability of aromatic and heteroaromatic rings to transmit substituent effects, etc.).

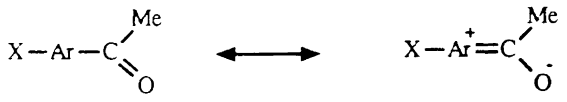
Concerning the effect of the substituents on the carbonyl carbon atom (C-α) the SCS values reported in Table 1 showed that all the substituents, except the methoxycarbonyl and the formyl groups, exerted a shielding effect on the ^{13}C chemical shifts whatever their polar effects were. The total range in SCS values was ca. 2.4 ppm and the small variations observed seemed random, so that it was not possible to observe acceptable correlations with any kind of substituent constant.* Therefore the long-range effect of the substituent present in the heterocyclic ring on the carbonyl carbon atom for compounds **1** was different from that observed for compounds **3**[2a] and also for 4-substituted acetophenones **5**.[2c,14] In fact, for both series of compounds **3** and **5** good correlations[2a,c] were obtained when SCS values for C – α were processed by the DSP analysis notwithstanding the well *known* different kinds of electronic effect operative in 5-substituted 2-thiophenecarboxylic acids **3**[2a] and in 4-substituted acetophenones **5**.[2c] This indicated that the failure of the correlation in the case of compounds **1** could not be ascribed either only to the acetyl group or only to the thiophene ring but it had to be related to the system acetyl group–thiophene ring–substituent as a whole. The lack of correlation could arise from a peculiarly large polarization of the π-system of thiophene or from some kind of transmission of the substituent effects through the endocyclic sulfur atom, which could appear relevant only when a group able to give strong conjugative interactions is linked to the thiophene ring.

However, the cross-correlation of SCS values of the carbonyl carbon atom in compounds **1** and in the previously studied 5-acetyl-3-nitro-2-X-thiophenes **6**[2d] was statistically significant (Table 3, line 12) in spite of the different solvent used. This result indicates that the variations of the chemical shifts observed are really systematic in nature. The value of the slope higher than unity is related to the levelling effect of the nitro group on the SCS values of carbonyl carbon atom in 5-acetyl-3-nitro-2-X-thiophenes **6**.[2d] Again the SCS values observed in series **1** can be rationalized on the grounds of effective conjugation between the thienyl ring and the acetyl group. Thus both electron-withdrawing and electron-donating substituents caused a small shielding of the probe C-α carbon by increasing the relative weights of resonance structures **7** and **8**, respectively.

In 5-substituted thiophene-2-carboxylic acids **3**, as we previously suggested,[2a] the conjugation between carboxylic group and thiophene ring is not very important. Therefore the comparison between C-α of the series **1** and **3** is not valid. On the other hand acetophenones **5** and 2-acetylthiophenes **1** represent systems which are different on account of the relative importance of the conjugative interaction between the acetyl group and the ring. The resonance structure **8** should play a less important role in acetophenones **5** than in 2-acetylthiophenes **1**. This viewpoint seems to be supported by the carbonyl stretching frequencies (ν_{CO} 1691.2[15] and 1674.3[10b] cm^{-1}, in carbon tetrachloride) and ^{17}O chemical shifts (539[16] and 518.6 ppm, in deuteriochloroform) of acetophenone and of 2-acetylthiophene, respectively. In fact, the above values indicate that the carbonyl group of acetophenone compared with 2-acetylthiophene has both a higher double-bond character and a lower electron density on the oxygen atom.

Both the physical measurements considered (ν_{CO} and ^{17}O chemical shift) depend on the double-bond character of the carbonyl bond and therefore on the relative importance of the resonance structures **7** and **8**. The observation of a good cross-correlation (Table 3, line 13) between ^{17}O SCS values measured for compounds **1** (data in Table 1) and ν_{CO} values shows, indeed, that the substituents present in the aromatic (or heteroaromatic) ring cause related variations of the experimental parameters.

The ^{17}O SCS data for the series **1** confirm that the oxygen atom is very sensitive to effects which modify the carbonyl electron distribution;[16–18] in particular, sub-



7 **8**

* As a matter of fact the best results were obtained by the DSP analysis (by using σ_I, σ_R^{BA}) which, however, gave only a poor correlation ($R \simeq 0.8$).

stituents in *para*-like positions which give rise to changes in the polarity of the carbon–oxygen bonds by means of their electronic (mesomeric and inductive) effects exert shielding or deshielding effects on the acyl oxygen, according to the chemical shift treatment already reported.[16,18] At variance with the ^{13}C values of C-α, the ^{17}O SCS values were satisfactorily correlated by means of a single-substituent parameter equation by using σ_p^+ values[19] as substituent constants (Table 3, line 14) or by means of the DSP equation (1) (Table 3, line 15). The different behavior shown by the two SCS data series is consistent with the resonance structures **7** and **8** which highlight the non-conjugative[4b] nature of the carbonyl carbon atom and, in contrast, the strong conjugation of the oxygen atom with the thienyl ring. Also, the large resonance susceptibility constants obtained (ρ^+ and ρ_R^+, respectively) can be interpreted on the grounds of the above conjugation. Moreover, the ρ^+ value calculated for ^{17}O SCS values for **1** (+31.2) is also higher than that obtained for acetophenones **5** (+22.5).[20] Accordingly, the ^{17}O SCS data for the series **1**, in contrast with the ^{13}C SCS data of C-α, give a good correlation with the corresponding values of acetophenones[16] (Table 3, line 16). The slope of the correlation, significantly higher than unity, once again indicates that the effects responsible for ^{17}O chemical shift variations operate more powerfully in the thiophene than in the benzene series.

Concluding remarks

In conclusion, the ^{17}O NMR chemical shifts, in contrast with the C-α ^{13}C NMR shifts, are suitable data to quantify the transmission of the substituent electronic effects in 2-acetylthiophenes. However, the data collected confirmed that the acetyl group bonded to an aromatic or heteroaromatic ring, unlike other COX groups,[2c,d,f] is able to conjugate with these rings and the extent of the conjugation is related to the particular nature of the aromatic or the heteroaromatic system.

A comparison of the substituent effects on the conjugated probe atoms (carbon atoms *ortho* and *para* with respect to the substituent in 5-substituted 2-acetylthiophenes **1** and in 2-substituted thiophenes **2**; the oxygen atom of the acetyl group in **1**) in thiophene and benzene derivatives always shows a larger effect in thiophene compounds (slopes of the cross-correlations ca. 1.5). In principle this fact can be related either to the participation of the transmission of the substituent effects via the heteroatom (on the assumption that this pathway is more efficient than the transmission via ring carbon atoms) or to the larger polarizability of the heteroaromatic π-system of the thiophene compared with the aromatic π-system of the benzene. The similar slope values for all the cross-correlations studied, including those relative to carbon *ortho*-like with respect to the substituent (Table 3, lines 3 and 10), for which it is not reasonable to assume transmission via the heteroatom, allows us to conclude that the transmission occurs via the heterocyclic π-system as a whole.

This statement agrees with our previous interpretation of the larger reactivity of thiophene with respect to benzene derivatives in both S_NAr and S_EAr reactions, which formerly had been attributed to the lower resonance energy[21] and to the larger polarization of π-system[22] of thiophene with respect to benzene and with recent statements concerning the transmission of substituent effects in five-membered heterocycles.[23]

Moreover the transmission of the substituent effects via the heteroatom can be discarded, if one remembers that in aromatic sulfides the sulfur bridge does not relay conjugation, but on the contrary shows a sharp tendency to behave as an isolator of conjugation,[24] and different behavior does not seem probable in thiophenes.

Experimental

Synthesis and purification of compounds. 5-Substituted 2-acetylthiophenes (X = OMe, SMe, Me, Et, Ph, H, Cl, Br, I, CHO, CO_2Me, CN, SO_2Me, NO_2) were prepared and purified as previously reported.[10b,25] 5-Piperidin-1-yl- and 5-dimethylamino-2-acetyl-thiophenes were synthesized from 5-bromo-2-acetylthiophene (1 g) and piperidine (2 ml) or dimethylamine (3.8 ml, water solution 32%) by heating at 150°C (in sealed tubes, 2 h) and at 80°C (2 days), respectively. The reaction mixtures were poured into water and the crude products purified by chromatography on a silica-gel column [eluants: toluene and toluene–ethyl acetate (1 : 1)]. *5-Piperidin-1-yl-* and *5-dimethylamino-2-acetylthiophenes* had m.p. 105–106°C (from methanol) and 54–55°C (from hexane), respectively, and gave satisfactory elemental analyses.

^{13}C and ^{17}O NMR measurements. ^{13}C NMR spectra were recorded on a Varian VXR-300 spectrometer in the Fourier transform mode for anhydrous $CDCl_3$ solutions at 25.0 ± 0.5°C: chemical shifts are given in ppm high frequency from Me_4Si as a secondary reference standard. Acquisition parameters were spectral width 16K, 16K data points, 30° pulse angle, quadrature phase detection and zero-filling to 32K before FT.[26a,b] The ^{17}O NMR spectra were recorded on the same instrument at 40.670 MHz; all spectra were acquired at natural abundance for anhydrous $CDCl_3$ solutions at 25.0 ± 0.5°C. Chemical shifts (δ) were referenced to external 1,4-dioxane.[27] Acquisition parameters were spectral width 30 kHz, 2K data points, 90° pulse angle (35 μs pulse width), quadrature phase detection, acquisition times $T_{acq} > 5\ T_2$, 50000–150000 scans. Processing parameters: exponential multiplication of the FIDs by a line-broadening (LB) factor of 10–25 Hz and zero-filling up to 16K[26] resulting in a digital resolution of 3.7 Hz per point after FT.

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