Substituent–Substituent Interactions in Carbon-13 Substituent Chemical Shifts of Phenols and Phenoxides

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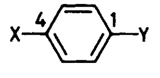
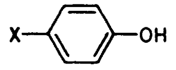
The non-additive behaviour of ^{13}C shifts observed for 4-X-substituted phenols or phenoxides are evidence for large substituent–substituent interactions (up to 5 p.p.m.; *i.e.*, 75% of the substituent shifts observed in monosubstituted benzenes). X-Induced *para*-substituent shifts on C(1) are analysed by non-linear Dual Substituent Parameter correlations or by proportionality relationships with the corresponding shifts in monosubstituted benzenes (provided that for phenoxides electron donor or acceptor groups are treated separately). Similar proportionality relationships are also established for *ipso* SCSs [on C(4)]. Extension of this data treatment to various families of *para*-substituted benzenes leads to a general approach to the effect of substituent interactions on SCS values. In the factorisation model proposed, deviations from additivity are expressed *via* the product of *ipso* and *para* SCS values, derived from the corresponding monosubstituted benzenes. The strict additivity of SCS values in *meta*-substituted derivatives is obeyed for phenols, whereas for phenoxides minute substituent–substituent interactions are observed.

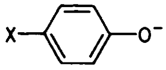
Recent interest has focused on the transmission of substituent effects in ^{13}C n.m.r. of benzenes derivatives, particularly regarding substituent-substituent interactions.[1–7] Empirical models based on the additivity of fixed increments have proved, in the past, to be very powerful in elucidating ^{13}C spectra for organic structural analysis.[8,9] However, various studies have shown unequivocal deviations from the additive schemes generally used in *para*-disubstituted benzenes. Extension of the range of structures investigated to charged structures (carbenium or hydroxycarbenium ions) allowed us to observe very large electronic interactions between the groups attached to the phenyl ring, reflected by important variations in substituent increments. Variations of up to 10 p.p.m. have been observed for *ipso* shifts of Me, I, or NO_2 groups, in contrast with the commonly accepted hypothesis of constant and additive group contributions.[1,3] Such interactions are of great interest for theoretical approaches to substituent influences and of major importance in empirical structural analysis.[1] However, up to now, attention has been paid exclusively to 1,4-substituted derivatives (**1**) and discussion mainly devoted to *para* influences, *i.e.*, to SCS induced on the *para* C(1) (linked to the fixed group Y) by variable substituent groups X.



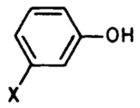
(**1**)



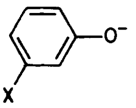
(**1a**)



(**1b**)



(**1c**)



(**1d**)

X = NO_2, CHO, COMe, CN, CF_3, Me, Et, Pr^i, F, Cl, I, Br, OMe, NH_2, NMe_2

In this work, we examine substituent shifts for four series of disubstituted benzenes where the fixed group is OH [phenols (**1a**), (**1c**)] or O^- [phenoxides (**1b**), (**1d**)].

The groups of compounds (phenols and phenoxides) studied herein have been selected on account of the important electronic effects of the functional groups, OH or O^-. Furthermore, recent work has pointed out the importance of ^{13}C parameters, and particularly of deprotonation shifts, in the study of related phenolic structures of chemical or biological interest.[10,11]

We have examined the non-additive behaviour in these systems no only on the carbon bearing the fixed OH or O^- groups but also, in a novel way, on the site of attachment of the variable X group, to obtain insight into substituent–substituent interactions. Despite the apparent symmetry of the X and Y groups when considering interaction problems in disubstituted benzenes, the search for suitable models for ^{13}C shift predictions is very useful for the discussion of SCS in the groups of compounds defined by a fixed Y group. It must be kept in mind, however, that the only observable data are the shifts for mono- (C_6H_5–X or C_6H_5–Y) and di-substituted (X–C_6H_4–Y) compounds and, unless the real mechanisms of substituent interactions are known, the unique significant parameter is the deviation from strict additivity of monosubstitution effects. Data treatment in terms of *ipso* or *para* shifts is therefore only an analytically convenient way of dissecting substituent shifts for the definition of heuristic models of correlation.

Experimental

^{13}C Shifts were measured at 35 °C on a Bruker WP 80 FT spectrometer, operating at 20.115 MHz with a ^2D lock (capillary inserted in the sample tube) and complete proton decoupling. Usual conditions correspond to a 4 000 Hz spectral width, sampled on an 8K memory block. Peak assignment was performed *via* examination of substituent shifts and occasionally undecoupled or 'off resonance' decoupled spectra. All phenols investigated are commercial products purified by crystallisation, sublimation, or distillation.

Table 1. ^{13}C SCS for *para*-substituted phenols and phenoxides [(**1a**) and (**1b**)] for Y = OH, O$^-$, and H. Positive values correspond to downfield shift variations (SCS) from the reference compounds (X = H) in each series. The chemical shifts (δ) of these reference compounds are indicated in the last row

	C(1)				C(2) and C(6)			C(3) and C(5)			C(4)		
X	OH	O$^-$	H^a	H^b	OH	O$^-$	H	OH	O$^-$	H	OH	O$^-$	H
O$^-$		-11.86		(-14.2)		-0.21	0.84		-11.18	-9.13		40.04	38.25
NH_2		-7.17	-10.15	(-12.39)		-0.26	0.87		-11.23	-13.50		18.95	18.55
Me	-6.03	-5.58	7.7	(-7.7)	0.79	-0.20	1.07	-14.75	-13.98	-14.42	33.36	34.04	31.51
OH	-6.57		-7.74		0.99		1.27	-13.39		-13.11	28.68		27.51
F	-3.33	-4.73	-4.39	(-4.1)	0.82	-0.60	1.13	-13.74	-14.65	-12.90	35.93	38.88	34.51
Cl	-1.87	-1.62	-1.73		1.43	0.89	1.52	-0.20	-0.81	0.26	4.81	3.34	5.91
Br	-1.32	-0.95	-1.36		1.98	1.75	1.80	2.79	2.18	3.20	-7.93	-9.64	-5.92
I	-1.87	0.2	-1.0		2.6	3.0	2.9	8.9	8.3	10.2	-38.0	-40.0	-34.1
Me	-1.32	-3.26	-3.03	(-3.2)	-0.20	-0.51	-0.10	0.44	0.11	0.68	9.45	9.19	9.73
Et	0.0	-3.14	-2.93		-0.27	-0.51	-0.19	-0.85	-1.18	-0.68	15.90	15.90	15.90
Pr^i	-2.28	-3.14	-2.75		-0.33	-0.51	-0.19	-2.25	-2.75	-2.08	20.60	20.59	20.54
CF_3	2.82	4.92	3.59	(3.27)	0.32	0.24	0.58	2.34	-3.30	-3.11	2.18	1.03	2.23
CN	4.08	5.85	4.35	(5.1)	1.09	0.71	0.70	4.67	4.67	3.60	-17.23	-21.35	-15.96
COMe	4.79	8.14	4.65	(5.3)	-0.09	-0.14	-0.12	1.19	2.24	0.25	10.04	7.85	9.06
CHO	5.39	10.27	5.88	(5.9)	0.22	0.77	0.54	2.33	4.19	1.09	9.77	7.85	7.76
NO_2	5.93	11.66	6.36	(6.8)	0.44	0.14	1.07	-3.45	-1.88	-4.90	20.99	19.18	20.29
δ for X = H	156.31	167.05	128.80	(129.19)	115.69	119.67	128.80	130.07	130.64	128.80	121.06	115.15	128.80

[a] SCS values in monosubstituted benzenes in CH_2Cl_2. [b] SCS values in monosubstituted benzenes in MeOH–H_2O–NaOH.

Table 2. ^{13}C SCS in *meta*-substituted phenols and phenoxides [(**1c**) and (**1d**)]. The value in the last row correspond to the chemical shifts of the reference compounds (X = H)

	C(1)		C(2)		C(3)		C(4)		C(5)		C(6)	
	OH	O$^-$	OH	O$^-$	OH	O$^-$	OH	O$^-$	OH	O$^-$	OH	=O$^-$
O$^-$		-1.21		-11.75		35.30		-7.97		0.19		-12.48
$N(Me)_2$	0.97	0.97	-15.72	-12.38	22.86	23.69	15.27	-11.56	0.26	0.14	-11.95	-.87
OMe	1.08	1.85	-13.74	-14.71	31.53	30.63	14.28	-14.18	0.55	0.24	-7.50	-6.51
OH	1.36		-12.57		27.69		12.95		0.80		-7.61	
Cl	0.77	1.75	0.65	-0.29	5.46	4.12	0.26	-0.45	0.98	0.73	-1.32	-1.36
Me	-0.07	0.0	0.68	0.48	10.31	10.10	0.83	0.72	-0.20	-0.19	-3.05	-3.16
CF_3	0.31	0.58	-2.89	-4.13	2.37	1.09	-3.28	-4.14	0.73	0.29	3.74	3.68
CN	0.56	0.49	3.51	2.81	-16.47	-18.74	3.88	3.44	1.05	0.63	5.28	5.92
NO_2	1.12	1.22	-4.76	-6.56	19.77	19.32	-4.92	-5.44	0.70	-0.19	6.74	7.52
δ for X = H	156.31	167.05	115.69	119.67	130.07	130.64	121.06	115.15	130.07	130.64	115.69	119.67

Phenoxide Ions.—The reported ^{13}C shifts were measured on 0.05 w/v solutions with respect to external C_6H_{12} and converted to the Me_4Si scale using the conversion factor $\delta_{C_6H_{12}}^{Me_4Si} = 27.0$ p.p.m. The effects of dilution and counter ions were checked by examination in various media. For solute concentrations of from 7×10^{-2} to 2.7M in 5M-NaOH, no sizeable variations occurred in the ^{13}C shifts of phenol. Similary, phenol and 4-methoxyphenol were studied in 5, 1, and 0.5M-NaOH and 0.5M-KOH (solute concentration 0.05M): the shifts remained almost constant (indicating the minor influence of the Na^+ and K^+ counter ions) and so appear to be representative of the phenoxide species. For comparison with benzenes, spectra were run in H_2O (0.5 cm^3) + 2.5M-NaOH in MeOH (2.5 cm^3). The SCS are almost identical with those observed in aqueous NaOH solutions.

Phenols.—^{13}C Shifts of phenol derivatives are known to be highly sensitive to solvent effects and association or autoassociation phenomena.[12,13] We have determined ^{13}C spectra in CH_2Cl_2 solutions of from 0.05 to 3M, at 35 °C. Dilution shifts are nearly linear if δ values are plotted against concentration, except for strongly autoassociated structures (for instance X = COMe). Detailed results will be published elsewhere.[14] It is sufficient here to point out that very varied behaviour was observed, even for the same ^{13}C site according to the nature of the X groups. The slopes of the δ *versus* concentration plots therefore vary considerably and may even change sign when hetero association involves the X group itself. For instance, for the C(4) atoms increasing the dilution induces upfield shifts for phenol, but deshielding shifts when X = NO_2 or CN. Owing to these differing behaviours, rather than quoting chemical shifts obtained at a fixed concentration or corrected with a constant correction term,[13] we prefer to determine infinite dilution shifts derived by a least-square treatment from the dilution curves. The corresponding values are reported in Tables 1 and 2.

Benzenes.—Substituent chemical shifts (SCS) for monosubstituted benzenes have been determined in CH_2Cl_2 solutions and agree well with literature values. For comparison with phenoxides, the SCS values have also been determined, for selected benzenes, in H_2O (0.5 cm^3) + 2.5M-NaOH in MeOH (2.5 cm^3), since Taft and co-workers.[7b] quoted that benzene SCS values are slightly solvent dependent (polar media induce increased downfield shifts for electronegative X groups; and H-bonding interactions may also alter the electron-releasing power of the groups). Changes appear for the *para* carbon only, but remain small. For instance, the SCS of X = NO_2, COMe, and CN decrease to 6.8, 5.3, and 5.1, respectively, from 6.4, 4.6, and 4.3 p.p.m. Similarly, for X = NH_2 the SCS varies from

Table 3. Proportionality relationships between phenols or phenoxides and benzenes. For equations (3) and (5) X = NH_2,OMe,F,Me (electron-releasing groups); and for equations (4) and (6) X = CF_3,CN.COMe,CHO,NO_2 (electron-withdrawing groups)

^{13}C site	Y	Equation	ρ[a]	f[b]
C(1)	OH	(1) $S_{p.X}^{OH} = 0.92\ S_{p.X}^{H} + 0.35$	0.99	0.15
	O^-	(2) $S_{p.X}^{O^-} = 1.06\ S_{p.X}^{H} + 1.52$	0.96	0.29
	OH (X donor)	(3) $S_{p,X}^{OH} = 0.79\ S_{p,X}^{H} - 0.18$	0.993	0.07
	OH (X acceptor)	(4) $S_{p,X}^{OH} = 0.94\ S_{p.X}^{H} - 0.14$	0.954	0.17
	O^- (donor)	(5) $S_{p,X}^{O^-} = 0.68\ S_{p,X}^{H} - 0.68$	0.95	0.21
	O^- (X acceptor)	(6) $S_{p,X}^{O^-} = 1.65\ S_{p.X}^{H} - 0.45$	0.97	0.16
C(3) or C(5)	OH	(7) $S_{o.X}^{OH} = 1.04\ S_{o.X}^{H} + 0.32$	0.994	0.10
	O^-	(8) $S_{o.X}^{O^-} = 1.02\ S_{o.X}^{H} + 0.33$	0.97	0.24
C(4)	OH	(9) $S_{i,X}^{OH} = 1.06\ S_{i,X}^{H} - 0.81$	0.998	0.04
	O^-	(10) $S_{i,X}^{O^-} = 1.14\ S_{i.X}^{H} - 2.2$	0.998	0.05

[a] Correlation coefficient. [b] Goodness of the fit.

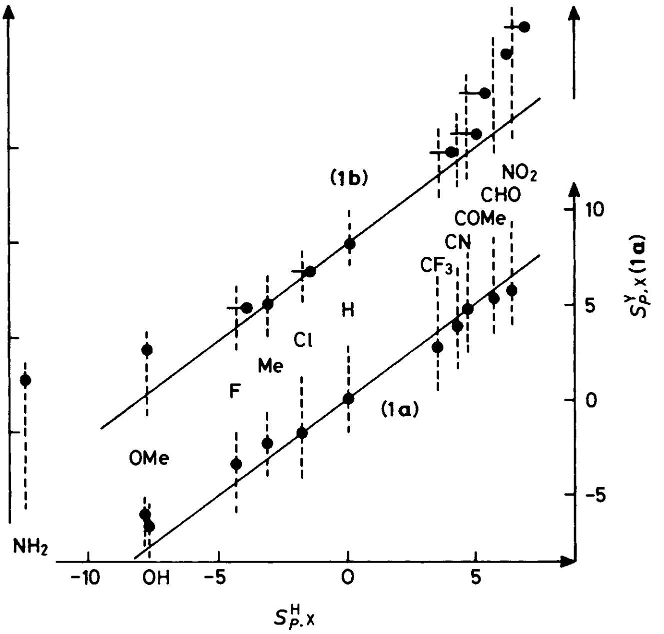


Figure 1. Plot of X induced *para*-substituent shifts $S_{p.X}^{Y}$ on C(1) for 4-substituted phenols (**1a**) and phenoxides (**1b**) *versus* the corresponding shifts in monosubstituted benzenes $S_{p.X}^{H}$. Benzene solvent shifts from CH_2Cl_2 to MeOH. HOH, NaOH solutions are indicated in plot (**1b**). The straight lines drawn of unit slope would correspond to strict additivity of SCS

−10.1 to −12.4 p.p.m. whereas no change is observed for X = OMe. It is worth noting that, for all groups investigated, these SCS values are close to the values quoted by Taft and co-workers in highly polar DMSO solutions.[7b]

Although unequivocal, these variations remain small and the important changes in the SCS values quoted here for compounds (**1a**—**d**) are not related to such minor medium effects, but actually reflect substituent–substituent interactions.

Discussion

SCS induced * on the various ^{13}C sites are collected in Tables 1 and 2. Examination of substituent–substituent interactions (leading to non-additive behaviour) will be performed largely *via* proportionality relationships between SCSs induced by variable X groups in phenols or phenoxides and the corresponding shifts in monosubstituted benzenes, as in Lynch's model.[2]

SCSs in para-*Substituted Compounds* (**1a**) *and* (**1b**).—The discussion is mainly devoted to the C(1) and C(4) sites (points of attachment of the substituent groups) since it may be expected that non-additive behaviour would be more important on these positions, whereas for C(2) and C(3) (in the *meta* position with respect to one of the substituent groups) substituent–substituent interactions would be minor. Indeed good linear correlations with close to unit slopes are obtained between shifts induced at C(3) [and C(5)] in phenols or phenoxides and in benzenes indicating that strict additivity of SCS nearly prevails on these carbons. SCSs induced by *meta* X groups remain small at C(2) [and C(6)] so that no statistical treatment was performed at this position.

C(1) *site*. The C(1) site is the point of attachment of OH or O^-. Large variations in the SCS values from the corresponding values in monosubstituted benzenes indicate important substituent–substituent interactions, especially for phenoxides: therefore, for X = COMe or NO_2, the SCS are, respectively, 8.1 and 11.7 compared with 5.3 and 6.8 p.p.m. in benzenes. This is illustrated in Figure 1 where the X induced SCS on C(1) $S_{p,X}^{Y}$ (Y being O^- or OH) are plotted against the corresponding values in benzenes ($S_{p,X}^{H}$). The plot clearly deviates from the unit slope correlations expected if strict additivity were to prevail. It is worth noting that these deviations represent (for X = NO_2 or COMe for instance) more than 75% of the 'usual' SCS values derived from monosubstituted benzenes. These results can be approximated by linear proportionality relationships with benzene SCS values. However, better results are obtained, especially for phenoxides, if electron-releasing and -withdrawing groups are separated in bilinear correlations [*cf.* equations (1)—(6) of Table 3].

C(4) *site*. This is the carbon where the variable X groups are attached. Proportionality relationships are similarly established for substituent induced shifts on the C(4) atom bearing these groups. The corresponding correlations (9) and (10) are indicated in Table 3. It is noticeable that, in contrast with the bilinear relations obtained for C(1), a unique linear correlation is valid for the *ipso* carbon C(4) with the whole set of X substituents investigated. Owing to the large variations of *ipso* SCS (*ca.* 50 p.p.m.), non-additive behaviour is better illustrated by plotting $S_{i.X}^{Y} - S_{i.X}^{H}$ *versus* $S_{i.X}^{H}$ (Figure 2).

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* Substituent induced chemical shifts (SCS) are quoted with respect to the corresponding unsubstituted or monosubstituted compounds, where *j* indicates the position (*ortho*, *meta*, *para*) of the carbon atom with respect to the varying group, X.

$$\delta_{jX}^{Y} = \delta_{X-C_6H_4-Y} - \delta_{H-C_6H_4-Y}$$

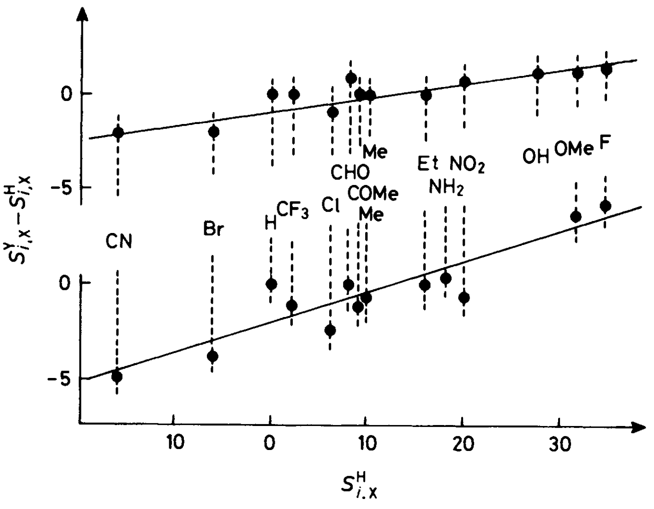


Figure 2. Plot of X induced *ipso* shift variations on C(4), $S_{i,X}{}^{Y} - S_{i,X}{}^{H}$, for 4-substituted phenols and phenoxides *versus ipso* shifts $S_{i,X}{}^{H}$ in monosubstituted benzenes

Substituent–Substituent Interactions.—Starting first with C(1) SCS, it may be noticed that the behaviour observed here with the strong electron-donating OH or O^- groups confirms and extends the recent results of Bromilow and co-workers,[7] in other *para*-substituted benzenes and may be interpreted similarly. The large π electron donation from OH or O^- releasing groups lessens mesomeric transfer from π donor X groups and conversely increases π interactions with withdrawing X groups. This is substantiated by the recent *ab initio* charge calculations of Reynolds *et al.* regarding π transfer from X to the phenyl ring.[15] It is noteworthy that for phenoxides, the slopes of these partial correlations are definitely greater and smaller than one (*i.e.*, 1.65 and 0.68, for X withdrawing or releasing groups respectively). This behaviour can be rationalised by using 'non-linear dual substituent parameter relationships,' according to the model recently proposed by Bromilow and co-workers.[7] In this treatment, resonance parameters of the variable X groups depend on the electronic power of the common Y group and are expressed *via* a hyperbolic law $(\sigma_R{}^{\circ})_X/1 - \varepsilon_Y(\sigma_R{}^{\circ})_X$, where ε_Y is related to the electron demand of Y. Furthermore, a sensitivity parameter (SCR or shift charge ratio) depending on the nature of the fixed Y group, is introduced to account for variations in the overall range of the observed SCS. This treatment, when applied to (**1a**) and (**1b**) leads to the following values for the electron demand (ε_Y) and SCR values: for phenols $\varepsilon_{OH} = 0.39$ and SCR = 165; and for phenoxides $\varepsilon_{O^-} = 1.41$ and $SCR_{O^-} = 224$. ε_{OH} is consistent with the values obtained for OMe and NH_2 (0.45 and 0.56) which are both strong π donor groups. It also agrees well with the relationship proposed between ε_Y and the σ_i, σ_R parameters of Y[16] [hence equation (5) of ref. 7 would lead to a calculated value for ε_{OH} of 0.45].

More unusual are the results obtained for phenoxides: SCR values seem to be among the highest observed. Similarly, $\varepsilon_{O^-} = 1.41$ is far larger than the values observed for Y = NH_2, OMe, or OH (0.5—0.4). This is consistent with the strong electronic influence of the O^- substituent. Indeed *ab initio* calculations indicate that O^- is a very powerful π donor and also a weak σ donor compared with OH, which acts as π donor but σ acceptor. It is therefore likely that the strong electron donation from O^- to the ring inhibits the action of X donor groups, and enhances the influence of X acceptor groups.

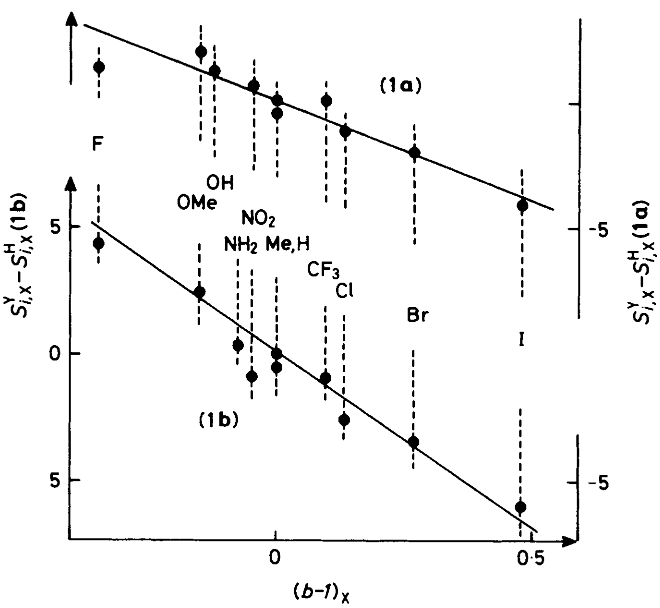


Figure 3. Plot of the interaction term, on C(4) ($I_{i,X}{}^{Y} = S_{i,X}{}^{Y} - S_{i,X}{}^{H}$) *versus* $(b - 1)_X$ values for phenols (**1a**) and phenoxides (**1b**). The straight lines drawn correspond to the theoretically expected slopes $S_{p,Y}{}^{H}$ (−7.7 and −14.2, respectively)

For C(4) (point of attachment of the variable X groups), important substituent–substituent interactions are also observed, as indicated by the slopes of equations (9) and (10) (Table 3) which differ from unity. The lack, to our knowledge, of substituent constants for O^- precludes the use of DSP relationships and prompted us to approach these interactions by generalising the linear model of *ipso* shifts we proposed previously. Our model expresses *ipso* shifts in 1,4-disubstituted benzenes ($X–C_6H_4–Y$) by proportionality relationships[1,3] [equation (11)], where the $(b - 1)_X$ coefficient characterises the

$$S_{i,X}{}^{Y} = S_{i,X}{}^{H} + (b - 1)_X S_{p,Y}{}^{H} \qquad (11)$$

susceptibility of the resonant site to X induced *ipso* shifts, depending on the nature of *para* Y groups.

This model implies that variations of *ipso* SCS, characterising the substituent–substituent interactions, $I_{i,X}{}^{X} = S_{i,X}{}^{Y} - S_{i,X}{}^{H}$ (Y = O^- or OH) would be linearly related to the $(b - 1)_X$ coefficients of the incoming X groups; the slope being the *para* increments of O^- or OH groups in monosubstituted benzenes. In Figure 3 these interaction terms $I_{i,X}{}^{OH}$ and $I_{i,X}{}^{O^-}$ are plotted *versus* the $(b - 1)_X$ values previously obtained. The good fit observed between experimental values and the straight lines 'theoretically expected' (*i.e.*, of slopes $S_{p,OH}{}^{H}$ and $S_{p,O^-}{}^{H}$) establish that our interaction model is also valid for the strong releasing OH and O^- groups.

Factorisation of Interactions.—A complete interpretation of $(b - 1)_X$ values for the variable X groups investigated is not yet available. However, it can be checked that these $(b - 1)_X$ values are roughly related to the corresponding *ipso* shifts of monosubstituted benzenes $S_{i,X}{}^{H}$ through a linear relationship of slope −0.011, as seen in Figure 4. So, the interaction term $I_{i,X}{}^{Y}$ can be written as the product of X *ipso* SCS and Y *para* SCS in monosubstituted benzenes, equation (12).

$$I_{i,X}{}^{Y} = -0.011\ S_{i,X}{}^{H}\ S_{p,Y}{}^{H} \qquad (12)$$

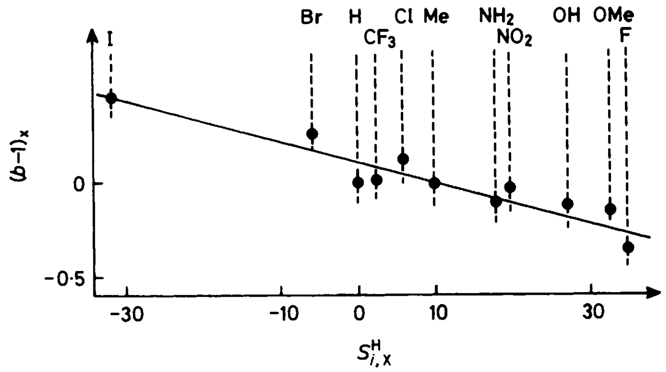
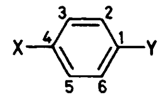
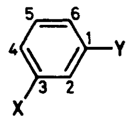


Figure 4. Plot of $(b - 1)_X$ values [from equation (11): $S_{i,X}^{\ Y} = S_{i,X}^{\ H} + (b - 1)_X S_{p,Y}^{\ H}$ *versus ipso* shifts in monosubstituted benzenes $S_{i,X}^{\ H}$]. $(b - 1)_X$ Values are O^-, −0.19; NMe_2, −0.42; NH_2, −0.09; OMe, − 0.15; OH, −0.12; F, −0.35; Cl, 0.13; Br, 0.27; I, 0.45; Me, 0; CF_3, 0.09; NO_2, −0.05. For substituent groups leading to bilinear relationships the $(b - 1)_X$ values correspond to the relationship obtained with only Y donor groups (this work and refs. 1 and 3).

$$(b - 1)_X = -0.0107\, S_{i,X}^{\ H} + 0.11\ (\rho = 0.89;\ 13\ \text{points})$$





The overall substituent shift on C(4) in X–C_6H_4–Y calculated by reference to benzene is therefore given by equation (13). This expression is very similar to the formalism

$$\Delta\delta_{i,X}^{\ Y} = S_{p,Y}^{\ H} + S_{i,X}^{\ H} - 0.011\, S_{p,Y}^{\ H}\, S_{i,X}^{\ H} \qquad (13)$$

used in the QFIT treatment (Quantitative Factorisation of Interaction Terms) that we have used largely for evaluating various physicochemical properties in polysubstituted aromatics.[17]

It should be noted that the general equation (12) can be derived by another parallel route. From literature data (and particularly ref. 7) a network of proportionality relationships [equation (14)] can be derived for *ipso* shifts of 1,4-

$$S_{i,X}^{\ Y} = a_Y\, S_{i,X}^{\ H} \qquad (14)$$

disubstituted benzenes. For electron releasing or withdrawing Y groups, slopes a_Y are large and smaller than unity, respectively (which would correspond to a strict additivity), and these values are related to the *para* SCS $S_{p,Y}^{\ H}$ by the linear relationship $a_Y = 0.997 - 0.0117 S_{p,Y}^{\ H}$ ($\rho = 0.97$ for 14 points). It may be easily checked that this equation will also lead, for the interaction term, to the value $I_{i,X}^{\ Y} = -0.0117 S_{i,X}^{\ H}\, S_{p,Y}^{\ H}$.

Equation (12) casts some light on the mechanisms involved in the observed non-additive behaviour. The term $S_{i,X}^{\ H}$ indicates the role of electronegativity effects that largely govern *ipso* shifts.[18] The influence of Y (in *para*) enters the $S_{p,Y}^{\ H}$ values. This term reflects π electron effects (mesomeric or π polarisation).

In previous studies on *para*-substituted benzenes, Lynch[2] indicated that the slopes b_X of proportionality relationships $(S_{p,X}^{\ H}/S_{p,X}^{\ Y})$ are linearly dependent on the inverse ionisation potential of the key atom of Y (atom bonded to the aromatic ^{13}C). Later, Inamoto[5] remarked that these slopes are related to the iota inductive parameter of the *ipso* groups. From DSP treatment and *ab initio* charge calculations, Taft and co-workers[4] suggested that the σ charge at ^{13}C, depending on the electron demand of the *ipso* groups, modulates the π electron transfer from the *para* groups.

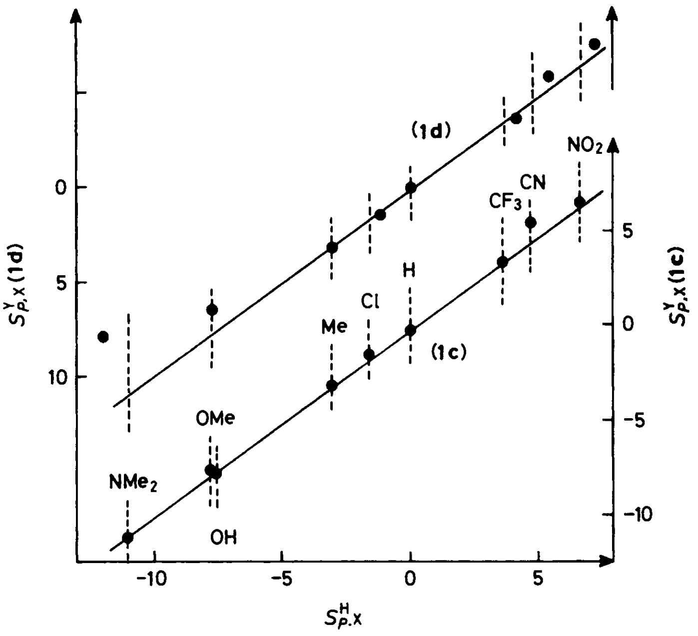


Figure 5. Plot of induced *para*-substituent shifts at C(6) for 3-substituted phenols (**1c**) and phenoxides (**1d**) *versus* corresponding shifts in monosubstituted benzenes $S_{p,X}^{\ H}$

The results obtained here are consistent with the above observations and provide a very simple and efficient model to evaluate SCSs and their deviations from additive schemes, using the well known and easily handled benzene SCS values. It is worth noting that, in spite of its very simple form, this model accounts for strong interactions created by groups with large electronic effects, such as OH and O^-.

Some limitations must, however, be kept in mind. The treatment proposed here for C(4) deals with linear correlations between the SCS values in mono- and di-substituted benzenes. However, in previous studies we pointed out varying behaviour in such relationships: monotonic plots (for halogens, OMe, *etc.*) but also bilinear correlations (alkyl groups, CF_3, *etc.*) with different slopes for Y group donors or acceptors. We only retain, for these groups, the b_X values corresponding to releasing Y groups. This complexity in behaviour indicates that the proposed analysis is only a first approximation and requires further study before a larger generalisation can be made.

Substituent–Substituent Interactions in meta-*Derivatives.*— Substituent–substituent interactions in benzene derivatives have been studied almost exclusively on C(1) and C(4) in *para*-substituted compounds. Indeed, for C(2) [and C(6)] or C(3) and [C(5)], one of the groups, X or Y, is in a *meta* position and exerts only weak electronic effects.

Additional outstanding information regarding group interactions can be gained with 1,3-disubstituted benzenes: here X and Y groups cannot be involved in direct resonance interaction (through conjugation) that would modify their own electronic power. So these systems are well suited for studying the additivity of perturbations arising from two groups on aromatic sites that have no direct mutual interactions.

From the results in Table 2, we have compared the SCS induced on each aromatic site in phenols and phenoxides (**1c** and **d**) with the corresponding values in monosubstituted benzenes. For phenols, a strict additivity of structural perturbations is observed leading to SCS values almost identical with those of benzenes [see for instance Figure 5 for C(6)]. In phenoxides, differing behaviour is observed. The SCSs remain quite small (<1.8 p.p.m.) at C(1) and C(5) sites, insensitive to the *meta* X groups; similarly O^- groups in *meta* positions do not affect C(3) (point of attachment of X) and the shifts remain equal to benzene SCSs. By contrast, for C(6), sizeable deviations appear between benzenes and phenoxides as evidenced by the non-linear plot observed in Figure 5. So the SCS values are -7.9 and 7.5 p.p.m. for X = NMe_2 and NO_2 in (**1d**) [compared with -12 and 6.7 p.p.m. for benzene or phenol, respectively, (**1c**)].

This non-linear plot indicates enhanced *para* effects of X withdrawing groups and reduced ones for X releasing. In line with the results obtained for *para*-substituted families (**1a** and **b**) these observations confirm that π interactions lead to *exaltation* of SCS values for donor–acceptor interactions or to *saturation* for groups of the same nature. However, the magnitude of these interactions are definitely smaller for *meta* derivatives (**1d**) (X and Y *ortho* or *para* to ^{13}C) than in (**1b**) (X and Y *ipso* or *para* to ^{13}C). The same is true for neutral compounds since additivity works well for (**1c**), but not for (**1a**). Less clear is the situation for C(2) and C(4) (*ortho* to variable X groups) since a plot of $\delta_{C(4)}$ and $\delta_{C(2)}$ *versus* benzene SCS values leads to a correlation with unit slope for C(4), whereas a curvature is observed for C(2). However, *ortho* effects correspond to the superposition of various mechanisms, including proximity effects, which may be differently modified in the case of variable X groups. So no detailed model has been proposed up to now.

Conclusions

In *para*-substituted phenols and phenoxides, non-additivity of substituent effects is shown for the carbon of attachment of the fixed groups OH or O^-, as it is for the carbon of attachment of the variable substituents. The fact that the interaction effect is studied on each carbon of attachment allows us to propose a general treatment for evaluation of the substituent chemical shift in *para*-substituted compounds using only the substituent chemical shift of monosubstituted benzenes. For the *meta*-substituted phenoxides, the non-additive effect is also shown but on the non-substituted carbons of the ring.

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