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Evidence of Substituent-Induced Electronic Interplay. Effect of the Remote Aromatic Ring Substituent of Phenyl Benzoates on the Sensitivity of the Carbonyl Unit to Electronic Effects of Phenyl or Benzoyl Ring Substituents

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Received October 15, 2003

Carbonyl carbon ^{13}C NMR chemical shifts δ_C(C=O) measured in this work for a wide set of substituted phenyl benzoates p-Y-$C_6H_4CO_2C_6H_4$-p-X (X = NO_2, CN, Cl, Br, H, Me, or MeO; Y = NO_2, Cl, H, Me, MeO, or NMe_2) have been used as a tool to study substituent effects on the carbonyl unit. The goal of the work was to study the cross-interaction between X and Y in that respect. Both the phenyl substituents X and the benzoyl substituents Y have a reverse effect on δ_C(C=O). Electron-withdrawing substituents cause shielding while electron-donating ones have an opposite influence, with both inductive and resonance effects being significant. The presence of cross-interaction between X and Y could be clearly verified. Electronic effects of the remote aromatic ring substituents systematically modify the sensitivity of the C=O group to the electronic effects of the phenyl or benzoyl ring substituents. Electron-withdrawing substituents in one ring decrease the sensitivity of δ_C(C=O) to the substitution of another ring, while electron-donating substituents inversely affect the sensitivity. It is suggested that the results can be explained by substituent-sensitive balance of the contributions of different resonance structures (electron delocalization, Scheme 1).

Introduction

Although the reactivity of an organic molecule is mainly determined by the functional group participating the reaction in question, it is also adjusted by other structural features of the molecule. Substituents attached to the molecule framework can enhance or diminish the reactivity. The mechanistic conclusions based on linear free energy relationships have been extremely fruitful. This concept relates changes in reactivity caused by changes in substitution in one reaction series to changes in equilibrium or reactivity in another series caused by the same changes in substitution. The most typical and the most useful linear free energy relationship is the Hammett equation which correlates rates and equilibria of side-chain reactions of para- and meta-substituted aromatic compounds. In its most conventional form, the Hammett equation is used as shown in eq 1

$$\frac{\log k}{\log k_o} = \rho\sigma \qquad (1)$$

where k is the rate coefficient for a para- or meta-substituted aromatic derivative, k_o that for the unsubstituted one, σ is the substituent constant for the substituent in question, and ρ is the reaction constant.[1] Usually, substitution in one site of the molecule is varied and conclusions are drawn on the basis of the magnitude of the reaction constant. A less studied aspect, however, is how much substitution in other parts of the molecule can adjust the sensitivity of the reaction in question to changes in the aforementioned substitution. In some reaction systems, very complicated data handling has been needed.[2]

The C=O functional group occurs in the most important organic molecular structures: in aldehydes, ketones, carboxylic acids, and their derivatives. The reactivity of these compounds is known to be significantly affected by the substitution in the groups joined the carbonyl carbon. In general, the electron-withdrawing substituents increase the reactivity while the electron-donating ones decrease it.[1] The main reason for this phenomenon is still under investigation. According to the transition-state theory, changes in reactivity are attributed to changes in the free energy of activation $\Delta G^{\ddagger} = G$(transition state) $- G$(ground state). So changes in both G(transition state) and in G(ground state) can contribute. Acyl-transfer reactions have an active role both in organic chemistry and in biological systems too. To get a deeper and more exact understanding about the substituent effects on the

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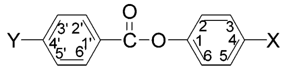
(1) Kirby, A. J. In *Comprehensive Chemical Kinetics*; Bamford, C. H., Tipper, C. F. H., Eds.; Elsevier Publishing Co.: Amsterdam, 1980; Vol. 10, Chapter 2, p 161. Connors, K. A. *Structure Reactivity Relationships: the Study of Reaction Rates in Solution*; VCH Publishers: New York, 1990; Chapter 7, p 311.

(2) Fujio, M.; Kim, H.-J.; Uddin, M. K.; Yoh, S.-D.; Rappoport, Z.; Tsuno, Y. *J. Phys. Org. Chem.* **2002**, *15*, 330.

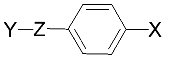
10.1021/jo035521u CCC: $27.50

CHART 1



Y = $\mathrm{NO_2}$ (**1**), Y = Cl (**2**) , H (**3**), Me (**4**) OMe (**5**), $\mathrm{NMe_2}$ (**6**)
X = $\mathrm{NO_2}$ (**a**), CN (**b**), Cl (**c**), Br (**d**), H (**e**), Me (**f**), OMe (**g**)

CHART 2



Z includes C=C, C=O, C=N and/or C≡C

electrophilic nature/reactivity of the carbonyl group, we have continued our work[3,4] with respect to the carboxylic acid derivatives.

The purpose of the present study was to investigate systematically the effect of a remote substituent on the sensitivity of the electronic character of the side-chain carbonyl group to aromatic substitution. Phenyl-substituted phenyl benzoates (Chart 1) were chosen as the model compounds, and ^{13}C NMR resonance of the carbonyl carbon was used as a tool to clarify (i) the effect of the substituent at the benzoyl moiety on the sensitivity of the carbonyl unit to the phenyl substitution and (ii) the effect of the substituent at the phenyl moiety on the sensitivity of the carbonyl unit to the benzoyl substitution, i.e., the cross-interaction between X and Y. ^{13}C NMR spectra were recorded for the compounds shown in Chart 1, and the effect of Y on the sensitivity of δ_C(C═O) to phenyl substitution X as well as the effect of X on the sensitivity of δ_C(C═O) to benzoyl substitution Y were analyzed.

Although the NMR shielding is not determined only by the electron density, linear correlations with positive slopes between the atomic charges and the ^{13}C NMR chemical shifts for probe nucleus in closely similar surroundings have been observed in several systems when the substitution was varied.[4−11] A carbon nucleus resonates at the higher field the higher the electron density at the carbon. A decrease in electron density of the carbonyl carbon, on then other hand, can be considered to facilitate nucleophilic attack on the carbon. NMR studies of transmission of substituent effects of aromatic ring substituents X in the organic molecules and especially the effect on the unsaturated side chain π-units have been widely performed.[3−5,9,12−18] However, there are only few systematic works concerning the influence of the component Y in such systems (Chart 2).[3−5,16,18]

CHART 3

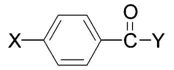
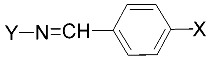


CHART 4



Dahn et al.[18] studied in the system shown in Chart 3, the effect of Y (Y = H, $\mathrm{CF_3}$, COOEt, Br, Cl, F, SEt, OCOPh, OH, $\mathrm{O^-Na^+}$, $\mathrm{NH_2}$) on the sensitivity of the ^{17}O NMR chemical shift of the carbonyl oxygen to the benzoyl substituent X. They suggested that the parameter ρ^+, obtained by correlating the δ_O(C═O) chemical shift values with σ^+(X) substituent parameters for every different Y, can be used as an empirical measure of the effect of Y on the electrophilicity of the carbonyl group. That was because it was realized that the parameter ρ^+ was the higher the higher was the δ_O(C═O) shift value for the unsubstituted derivative, i.e., X = H, for each Y. Dell'erba et al.[16] investigated a similar system by studying the effect of the electron-withdrawing nitro substituents in the phenyl ring of phenyl benzoates (mono-, di-, and trinitro substitutions) on the sensitivity of the carbonyl carbon ^{13}C NMR chemical shift to benzoyl substituent. The behavior of benzoyl-substituted phenyl benzoates was shown to be closely similar to that of benzoyl-substituted methyl benzoates, while 2,4,6-trinitrophenyl benzoates possessed characteristics similar to those of phenyl-substituted acetophenones. Our recent ^{13}C NMR and computational studies have shown for phenyl-substituted phenyl acetates that substituents in the aliphatic acyl group control the effect of the phenyl substituents on the polarization of the C═O unit.[3,4] Also, we have shown for imines, hydrazones, and related compounds that the sensitivity of the electronic structure of the azomethine group (Chart 4) to the phenyl substituents X is strongly affected by the group Y.[5]

Results

The ^{13}C NMR chemical shifts for the carbonyl carbon of the different phenyl-substituted phenyl benzoates **1**−**6** (cf. Chart 1) are collected in Table 1. In Tables 2 and 3 are shown the substituent-induced changes of the chemical shifts, SCS [δ_C(C═O)(substituted compound) − δ_C(C═O)(unsubstituted compound)], of the C═O carbon with respect of the substitutions X and Y, respectively.

Discussion

Our primary interest was to study if there is a systematic effect—as seen by the ^{13}C NMR chemical shift

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(3) Neuvonen, H.; Neuvonen, K. *J. Chem. Soc., Perkin Trans. 2* **1999**, 1497.

(4) Neuvonen, H.; Neuvonen, K.; Koch, A.; Kleinpeter, E.; Pasanen, P. *J. Org. Chem.* **2002**, *67*, 6995.

(5) Neuvonen, K.; Fülöp, F.; Neuvonen, H.; Koch, A.; Kleinpeter, E.; Pihlaja, K. *J. Org. Chem.* **2003**, *68*, 2151.

(6) Hehre, W. J.; Taft, R. W.; Topsom, R. D. *Prog. Phys. Org. Chem.* **1976**, *12*, 159.

(7) Krawczyk, H.; Szatylowicz, H.; Gryff-Keller, A. *Magn. Reson. Chem.* **1995**, *33*, 349.

(8) Lin, S.-T.; Lee, C.-C.; Liang, D. W. *Tetrahedron* **2000**, *56*, 9619.

(9) Neuvonen, K.; Fülöp, F.; Neuvonen, H.; Koch, A.; Kleinpeter, E.; Pihlaja, K. *J. Org. Chem.* **2001**, *66*, 4132.

(10) Matsumoto, K.; Katsura, H.; Uschida, T.; Aoyama, K.; Machiguchi, T. *Heterocycles* **1997**, *45*, 2443.

(11) Alvarez-Ibarra, C.; Quiroga-Feijóo, M. L.; Toledano, E. *J. Chem. Soc., Perkin Trans. 2* **1998**, 679.

(12) (a) Bromilow, J.; Brownlee, R. T. C.; Craik, D. J.; Fiske, P. R.; Rowe, J. E.; Sadek, M. *J. Chem. Soc., Perkin Trans. 2* **1981**, 753. (b) Dell'Erba, C.; Sancassan, F.; Novi, M.; Petrillo, G.; Mugnoli, A.; Spinelli, D.; Consiglio, G.; Gatti, P. *J. Org. Chem.* **1988**, *53*, 3564.

(13) Craik, D. J.; Brownlee, R. T. C. *Prog. Phys. Org. Chem.* **1983**, *14*, 1 and references therein.

(14) (a) Brownlee, R. T. C.; Craik, D. J. *Org. Magn. Reson.* **1981**, *15*, 248. (b) Brownlee, R. T. C.; Sadek, M.; Craik, D. J. *Org. Magn. Reson.* **1983**, *21*, 616. (c) Reynolds, W. F. *Prog. Phys. Org. Chem.* **1983**, *14*, 165.

(15) Hamer, G. K.; Peat, I. R.; Reynolds, W. F. *Can. J. Chem.* **1973**, *51*, 897, 915.

(16) Dell'Erba, C.; Sancassan, F.; Leandri, G.; Novi, M.; Petrillo, G.; Mele, A. *Gazz. Chim. Ital.* **1989**, *119*, 643.

(17) (a) Neuvonen, K.; Fülöp, F.; Neuvonen, H.; Pihlaja,K. *J. Org. Chem.* **1994**, *59*, 5895. (b) Neuvonen, K.; Fülöp, F.; Neuvonen, H.; Simeonov, M.; Pihlaja, K. *J. Phys. Org. Chem.* **1997**, *10*, 55.

(18) Dahn, H,; Péchy, P.; Van Toan, V. *Magn. Reson. Chem.* **1997**, *35*, 589.

TABLE 1. Carbonyl Carbon ^{13}C NMR Chemical Shifts δ_C(C=O) (in ppm) in CDCl$_3$ for Substituted Phenyl Benzoates p-Y-C$_6$H$_4$COO-C$_6$H$_4$-p-X

X/Y	NO$_2$	Cl	H	Me	OMe	NMe$_2$
NO$_2$	162.46	163.42	164.24	164.28	163.91	164.44
CN	162.53	163.50	164.33	164.37	164.01	164.55
Cl	163.10	164.11	164.95	165.01	164.66	165.24
Br	163.01	164.02	164.86	164.91	164.57	165.16
H	163.33	164.34	165.19	165.25	164.92	165.50
Me	163.51	164.54	165.38	165.44	165.11	165.71
OMe	163.68	164.70	165.55	165.60	165.28	165.87

TABLE 2. Substituent-Induced Changes of the Chemical Shift (SCS) for the Carbonyl Carbon (in ppm) in CDCl$_3$ When Varying X for Substituted Phenyl Benzoates p-Y-C$_6$H$_4$COO-C$_6$H$_4$-p-X [SCS = δ_C(C=O) for p-Y-C$_6$H$_4$COO-C$_6$H$_4$-p-X − δ_C(C=O) for p-Y-C$_6$H$_4$COO-C$_6$H$_5$]

	X/Y	NO$_2$	Cl	H	Me	OMe	NMe$_2$
σ(X)[a]/σ(Y)[a]		0.78	0.23	0	−0.17	−0.27	−0.83
0.78	NO$_2$	−0.87	−0.92	−0.95	−0.97	−1.01	−1.06
0.66	CN	−0.80	−0.84	−0.86	−0.88	−0.91	−0.95
0.23	Cl	−0.23	−0.23	−0.24	−0.24	−0.26	−0.26
0.23	Br	−0.32	−0.32	−0.33	−0.34	−0.35	−0.34
0	H	0	0	0	0	0	0
−0.17	Me	0.18	0.20	0.19	0.19	0.19	0.21
−0.27	OMe	0.35	0.36	0.36	0.35	0.36	0.37

[a] From ref 19.

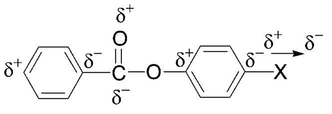
TABLE 3. Substituent-Induced Changes of the Chemical Shift (SCS) for the Carbonyl Carbon (in ppm) in CDCl$_3$ When Varying Y for Substituted Phenyl Benzoates p-Y-C$_6$H$_4$COO-C$_6$H$_4$-p-X [SCS = δ_C(C=O) for p-Y-C$_6$H$_4$COO-C$_6$H$_4$-p-X − δ_C(C=O) for C$_6$H$_5$COO-C$_6$H$_4$-p-X]

	X/Y	NO$_2$	Cl	H	Me	OMe	NMe$_2$
σ(X)[a]/σ(Y)[a]		0.78	0.23	0	−0.17	−0.27	−0.83
0.78	NO$_2$	−1.78	−0.82	0	0.04	−0.33	0.20
0.66	CN	−1.80	−0.83	0	0.04	−0.32	0.22
0.23	Cl	−1.85	−0.84	0	0.06	−0.29	0.29
0.23	Br	−1.85	−0.84	0	0.05	−0.29	0.30
0	H	−1.86	−0.85	0	0.06	−0.27	0.31
−0.17	Me	−1.87	−0.84	0	0.06	−0.27	0.33
−0.27	OMe	−1.87	−0.85	0	0.05	−0.27	0.32

[a] From ref 19.

of the carbonyl carbon—of the benzoyl substituent on the sensitivity of the electronic properties of the carbonyl unit to the phenyl substitution and also if there is a corresponding effect of the phenyl substituent on the sensitivity of the electronic effects of the carbonyl unit to the benzoyl substitution. Therefore, we will discuss separately the effect of phenyl and benzoyl substituents on δ_C(C=O).

Effect of Phenyl Substituent X on the C=O Carbon Resonance δ_C(C=O). With every different benzoyl substituent Y (**1**−**6**), when the phenyl substitution X (**a**−**g**) is varied the smallest shift value (the lowest frequency value) for the carbonyl carbon is observed with the most electron-withdrawing substitution X = NO$_2$ (σ = 0.78) and the largest shift value (the highest frequency value) with the most electron-donating substitution X = OMe (σ = −0.27) (Tables 1 and 2). In other words, electron-withdrawing substituents cause shielding while the electron-donating ones cause deshielding. This is opposite to the idea of the generalized electronic effect (a normal effect), a tendency of the substituent to release or withdraw electrons—usually quantified by Hammett or Hammett-type substituent constants. For every series **1**−**6**, a good linear correlation is observed between the ^{13}C NMR chemical shifts of the carbonyl carbons and the Hammett σ values[19] of the phenyl substituents X [cf. Table 4 and Figure 1; δ_C(C=O) = ρ(X)σ(X) + k]. The correlation coefficients from 0.9968 to 0.9983 indicate that the substituent effects are electronic in origin.The ρ(X) values are negative in all cases and the absolute value of ρ(X) is the higher the more electron-donating the benzoyl substituent Y is (Table 4). The latter fact is also seen by the slopes of the cross-correlations given in Table 5. The negativity of the ρ(X) values (Table 4) means that the more electron-withdrawing the phenyl substituent X is, the more shielded is the carbonyl carbon. This kind of *reverse substituent chemical shift effect* is in accordance with our previous observations for the carbonyl carbon of phenyl-substituted phenyl acetates, dichloroacetates, and trifluoroacetates.[3,4] Reverse effects have also been observed for some other unsaturated aromatic side-chain carbons.[5,9,12−18] The behavior has often been explained by the so-called π-polarization mechanism.[12a,13−15,17] The substituent dipole is then thought to polarize each π-unit as a localized system as shown in **7** for an electron-withdrawing substituent. In that case the process leads to increase in the electron density at the carbonyl carbon. This model, however, does not explain the fact that electron-withdrawing phenyl substituents are known to increase reaction rates of nucleophilic acyl substitutions of phenyl esters.[1,3,4] Both the reactivity and ^{13}C NMR chemical shift behavior described above can be better understood by considering the resonance structures of phenyl benzoates, i.e., the substituent-sensitive balance of electron delocalization. The electron-withdrawing phenyl substituents X inductively destabilize the resonance form **9** (Scheme 1) and therefore decrease the significance of its contribution destabilization of the phenyl benzoate structure as result. They obviously also diminish the importance of the resonance form **10**. Substituents capable to electron-withdrawing by resonance (NO$_2$, CN) allow the contribution of **11**, which also could mean increase in shielding of the carbonyl carbon. However, because the correlation of δ_C(C=O) with substituent parameter σ (not σ^-) was excellent, the contribution of **11** cannot be significant. Decreased resonance stabilization can contribute to the increase in reaction rates of the compounds while decreased contribution of **9** results in shielding of the carbonyl carbon, i.e., high-field (low-frequency) shift. This conclusion is in agreement with the ^{13}C NMR results of Dell'Erba et al.[16] for some nitrosubstituted phenyl benzoates. It is also supported by our previous findings concerning ^{13}C NMR chemical shifts of the carbonyl carbons, ν(C=O) frequency values, and C=O bond orders of substituted phenyl acetates. The reaction energies of the isodesmic reactions evaluating the substituent effects



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(19) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.

TABLE 4. Correlation Parameters ρ(X) or ρ_F(X) and ρ_R(X) Observed for Different Phenyl Substituted Phenyl Benzoates *p*-Y-C_6H_4COO-C_6H_4-*p*-X When Varying X and Correlating δ_C(C=O) Values with σ(X) or σ_F(X) and σ_R(X), Respectively[a,b]

Y	ρ(X) ± *s*	*r*	ρ_F(X) ± *s*	ρ_R(X) ± *s*	*r*	*f*	ρ_F(Y)/ρ_R(Y)
NO_2	−1.17 ± 0.04	0.9968	−1.05 ± 0.05	−1.39 ± 0.11	0.9944	0.11	0.76
Cl	−1.23 ± 0.04	0.9975	−1.10 ± 0.05	−1.47 ± 0.11	0.9946	0.11	0.75
H	−1.25 ± 0.04	0.9977	−1.13 ± 0.05	−1.49 ± 0.10	0.9959	0.10	0.76
Me	−1.27 ± 0.04	0.9975	−1.16 ± 0.05	−1.49 ± 0.10	0.9960	0.09	0.78
OMe	−1.31 ± 0.04	0.9980	−1.20 ± 0.04	−1.54 ± 0.09	0.9967	0.09	0.78
NMe_2	−1.38 ± 0.04	0.9983	−1.25 ± 0.04	−1.63 ± 0.09	0.9970	0.08	0.77

[a] *s*, standard deviation; *r*, correlation coefficient; *f* = sd/rms, where sd = standard deviation of the correlation and rms = root-mean-square of the data. [b] σ values from ref 19; σ_F and σ_R values from ref 20, except σ_F and σ_R for Br from ref 19; the values are given in the Supporting Information.

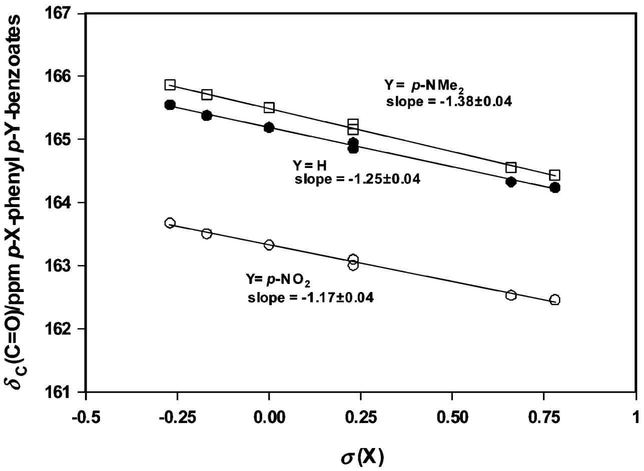
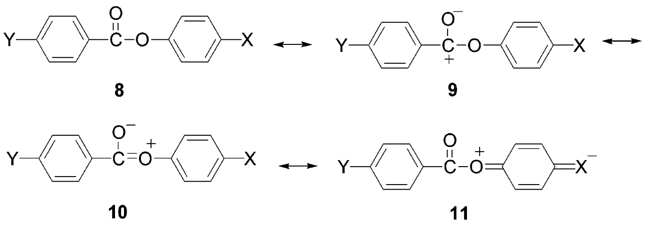


FIGURE 1. Plots of the ^{13}C NMR chemical shifts of the carbonyl carbon of phenyl-substituted phenyl benzoates *p*-Y-$C_6H_4CO_2C_6H_4$-*p*-X versus σ(X)[19] for series **1** (Y = NO_2) (○), series **3** (Y = H) (●), and series **6** (Y = NMe_2) (□).

TABLE 5. Statistical Data for the Cross-Correlations of the ^{13}C Chemical Shifts of the Carbonyl Carbon of Phenyl-Substituted Phenyl *p*-Y-Benzoates *p*-Y-C_6H_4COO-C_6H_4-*p*-X with Phenyl-Substituted Phenyl Benzoates C_6H_5COO-C_6H_4-*p*-X (i.e., Y = H)

Y	slope	*r*
NO_2	0.932 ± 0.009	0.9998
Cl	0.981 ± 0.004	0.99995
Me	1.014 ± 0.005	0.99993
OMe	1.048 ± 0.005	0.99994
NMe_2	1.097 ± 0.014	0.9996

SCHEME 1



on the stabilities of para- or meta-X-substituted phenyl acetates, dichloroacetates, and trifluoroacetates also agree with this interpretation. Electron-withdrawing substituents affect upfield C=O carbon chemical shift, increase the ν(C=O) frequency value and the C=O bond order while they systematically and clearly decrease the stability of the acetates.[3,4] In principle, an alternative possible reason for the reverse behavior of δ_C(C=O) could be the substituent sensitive variation in the conformational equilibrium between the *E* and *Z* conformations of the ester structure. However, in general, the *Z* conformations of carboxylic acid esters are much more stable than their *E* conformations and the contributions of the latter ones in general are insignifcant. In addition, the *E* conformations usually possess higher dipole moments than the *Z* conformations.[21] Therefore, a noticeable solvent effect on the substituent dependence of δ_C(C=O) should be observed if the substitution affects considerably the conformational equilibrium. We have previously shown for phenyl acetates that although the C=O carbon in DMSO-d_6 resonates on a slightly higher field than in $CDCl_3$ the reverse substituent dependence and the sensitivity to the substitution is quite similar in these two solvents.[4]

Some previous works with aromatic side-chain derivatives have shown that a better correlation of the ^{13}C NMR chemical shifts with substituent parameters is obtained with a dual substituent parameter approach than with a single parameter treatment.[5,12−17]

Therefore, we also fitted the δ_C(C=O) values observed when varying substituent X with eq 2 where SCS is the ^{13}C NMR shift for a substituted compound relative to that for the unsubstituted one. The correlations are good in all cases and both ρ_F(X) and ρ_R(X) turn to more negative when the electron-donating ability of Y increases but no improvement of the correlation is achieved when compared with the single parameter treatment (cf. Table 4). So the ratio of inductive and resonance contributions described by Hammett σ prevails for all of the series. This is also shown by the constancy of ρ_F(X)/ρ_R(X) when varying Y.

$$\mathrm{SCS} = \rho_F\sigma_F + \rho_R\sigma_R \qquad (2)$$

Effect of Benzoyl Substituent Y on ρ(X). The correlation parameter ρ(X) clearly varies when the benzoyl substitution is changed (Table 4). To quantitatively assess the effect of benzoyl substitution, the ρ(X)'s observed were correlated with the Hammett σ substituent constants of the benzoyl substituent Y. Again a good linear correlation with the slope of 0.13 ± 0.01 is obtained (Figure 2; *r* = 0.9877). The good correlation shows that the electronic effects of the benzoyl substituents systematically modify the sensitivity of the carbonyl carbon

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(20) Taft, R. W.; Topsom, R. D. *Prog. Phys. Org. Chem.* **1987**, *16*, 1.

(21) Jones, G. I. L.; Owen, N. L. *J. Mol. Struct.* **1973**, *18*, 1. Exner, O. In *The Chemistry of Double-Bonded Functional Groups*; Patai, S., Ed.; Interscience: London, 1977; p 1. Eliel, E. L.; Wilen, S. H. *Stereochemistry of Organic Compounds*; Wiley-Interscience: New York, 1994; pp 618−621. Larson, J. R.; Epiotis, N. D.; Bernardi, F. *J. Am. Chem. Soc.* **1978**, *100*, 5713.

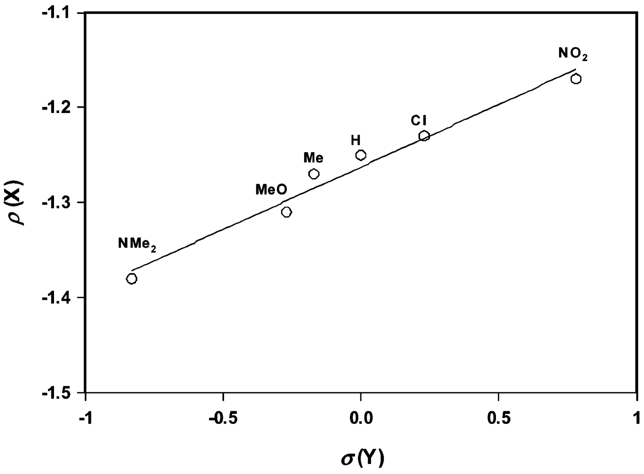


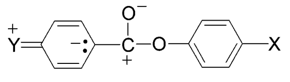
FIGURE 2. Plot for the ρ(X) values observed for phenyl benzoates p-Y-$C_6H_4CO_2C_6H_4$-p-X when varying X versus σ(Y).

resonance to the phenyl substitution. The positive value for the slope means that the more electron-withdrawing the benzoyl substitution is the less sensitive is the shielding of the carbonyl carbon to the phenyl substitution. This result is in line with the aliphatic acyl substitution effect observed recently by us for phenyl acetates. When the electron-withdrawing ability of acyl substituents in R in the series $RCOOC_6H_4$-p-X is increased the sensitivity of the ^{13}C NMR chemical shift of the carbonyl carbon to phenyl substitution X decreases.[3,4] In that case, a correlation of ρ with substituent parameters was not determined. The systematic decrease in the value of ρ(X) by electron-withdrawing benzoyl substituents can be interpreted by the diminished polarization of the carbonyl unit. The more electron-withdrawing the substituentY is the less significant is the contribution of **9** (Scheme 1). This means the decreased carbocation character of the carbonyl carbon. Consequently, when we consider that X also operates by adjusting the significance of **9** (cf. discussion above), the smaller is the total contribution of **9** for the molecule structure the less can the changes in its contribution alter the electronic character of the C=O carbon. In other words, the less significant is the carbocation character of the carbonyl carbon the less sensitive is its shielding to phenyl substitution.

To show the contribution of inductive and resonance effects of Y we also analyzed the effect of the benzoyl substitution Y on ρ(X) by eq 3. The $\rho(X)_{F,Y}$ and $\rho(X)_{R,Y}$ values then obtained are 0.089 ± 0.023 and 0.20 ± 0.02, respectively ($r = 0.9903$). The correlation is slightly better than that obtained by the single parameter correlation (slope = 0.13 ± 0.01; $r = 0.9877$). The ratio of inductive and conjugative effects of Y, $\rho(X)_{F,Y}/\rho(X)_{R,Y} = 0.44$.

$$\rho(X) = \rho(X)_H + \rho(X)_{F,Y}\sigma(Y)_F + \rho\,(X)_{R,Y}\sigma(Y)_R \quad (3)$$

Effect of Benzoyl Substituent Y on the C=O Carbon Resonance δ_C(C=O). With every different phenyl substituent X (**a**−**g**), electron-withdrawing benzoyl substituents Y cause upfield chemical shifts and the electron-donating ones have an opposite effect (Tables 1 and 3). In principle, this reverse behavior is in accordance with the observations for benzoyl-substituted methyl, phenyl, 4-nitrophenyl, 2,4-dinitrophenyl, and 2,4,6-trinitrophenyl benzoates.[12,16] For the latter esters it has been shown that Hammett parameter σ alone is not adequate to describe the effects of the benzoyl substituents on δ_C(C=O) but a dual substituent parameter approach is needed to separate the contributions of inductive and resonance effects. The same was also observed in this work. Correlations with σ show the trend but the correlations are only moderate (Table 6). Therefore, the data were analyzed by eq 2. The advantage of the dual substituent parameter approach is that it allows a characteristic balance between inductive and conjugative effects for every series. The correlation parameters are shown in Table 6. The good correlations indicate that the substituent effects are electronic in origin. Both ρ_F(Y) and ρ_R(Y) are negative and of the same general extent as those determined previously for other benzoic acid esters in $CDCl_3$.[12,16] The negativity of ρ_F(Y) and ρ_R(Y) means that both inductive and conjugative factors of the benzoyl substituents operate by a reverse way. Inductive effects are more significant than the resonance effects, the value of $\rho_F(Y)/\rho_R(Y)$ being around 3, but varying when X is varied. Electron-withdrawing substituents cause shielding of the carbonyl carbon while the electron-donating ones cause an inverse effect. These effects can be explained by a similar way than the effect of the phenyl substitution discussed above (cf. Scheme 1). Electron-donating substituents Y inductively stabilize the resonance form **9** and consequently increase its contribution, decrease in the electron density, i.e., deshielding, at the C=O carbon as a result. The negative ρ_R(Y) values can be explained by the influence of the resonance induced polar effect.[9,12a,14a,17] By that way the conjugative effects can operate reversely, i.e., for example deshielding as a result for an electron-donating Y due to the contribution of the resonance structure **12**. This explanation which is based on the substituent sensitive electron delocalization also agrees with the results of Dahn et al.[18] which have shown the high-field shift of the ^{17}O NMR resonance (i.e., shielding) of the carbonyl oxygen of several benzoyl derivatives by electron-donating benzoyl substituents.



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Effect of Phenyl Substituent X on ρ_F(Y) and ρ_R(Y). Although the variation of the values of ρ_F(Y) and ρ_R(Y) along the phenyl substitution X is smaller than the variation of ρ(X) along the benzoyl substitution Y, it is systematic (Table 6; cf. also the statistical data of the cross-correlations in Table 7). When the ρ_F(Y) and ρ_R(Y) values were correlated with σ values of the phenyl substituent X, slopes of 0.092 ± 0.013 ($r = 0.9540$) and 0.20 ± 0.06 ($r = 0.9635$), respectively, could be observed for $\rho_F(Y)_X$ and $\rho_R(Y)_X$. The electronic effects of the phenyl substituents affect the sensitivity of the carbonyl carbon ^{13}C NMR chemical shift to the benzoyl substitution. The more electron-withdrawing the phenyl substituent is the less sensitive is the shielding of the carbonyl carbon to the benzoyl substitution. The resonance parameter ρ_R(Y) is somewhat more sensitive to the phenyl substitution than the inductive parameter ρ_F(Y). This can also

TABLE 6. Correlation Parameters $\rho(Y)$ or $\rho_F(Y)$ and $\rho_R(Y)$ Observed for Different Phenyl-Substituted Phenyl Benzoates p-Y-C_6H_4COO-C_6H_4-p-X When Varying Y and Correlating δ_C(C=O) Values with $\sigma(Y)$ or $\sigma_F(Y)$ and $\sigma_R(Y)$, Respectively[a,b]

X	$\rho(Y) \pm s$	r	$\rho_F(Y) \pm s$	$\rho_R(Y) \pm s$	r	f	$\rho_F(Y)/\rho_R(Y)$
NO_2	−1.23 ± 0.32	0.8872	−2.41 ± 0.10	−0.74 ± 0.11	0.9949	0.10	3.26
CN	−1.26 ± 0.32	0.8915	−2.44 ± 0.10	−0.77 ± 0.10	0.9953	0.10	3.17
Cl	−1.33 ± 0.32	0.9030	−2.49 ± 0.10	−0.89 ± 0.10	0.9961	0.09	2.80
Br	−1.34 ± 0.31	0.9054	−2.49 ± 0.10	−0.89 ± 0.10	9.9962	0.09	2.80
H	−1.36 ± 0.31	0.9073	−2.50 ± 0.09	−0.92 ± 0.09	0.9968	0.08	2.72
Me	−1.37 ± 0.31	0.9100	−2.51 ± 0.10	−0.95 ± 0.10	0.9964	0.09	2.64
OMe	−1.37 ± 0.31	0.9094	−2.51 ± 0.10	−0.93 ± 0.09	0.9933	0.09	2.70

[a] *s*, standard deviation; *r*, correlation coefficient; f = sd/rms, where sd = standard deviation of the correlation and rms = root-mean-square of the data. [b] σ values from ref 19; σ_F and σ_R values from ref 20, except σ_F and σ_R for Br from ref 19; the values are given in the Supporting Information.

TABLE 7. Statistical Data for the Cross-Correlations of the ^{13}C Chemical Shifts of the Carbonyl Carbon of Benzoyl-Substituted p-X-Phenyl Benzoates p-Y-C_6H_4COO-C_6H_4-p-X with Benzoyl-Substituted Phenyl Benzoates p-Y-C_6H_4COO-C_6H_5 (i.e., X = H)

X	slope	r
NO_2	0.929 ± 0.022	0.99889
CN	0.944 ± 0.018	0.99931
Cl	0.989 ± 0.006	0.99992
Br	0.989 ± 0.005	0.99994
Me	1.008 ± 0.005	0.99995
OMe	1.005 ± 0.004	0.99997

been seen as the decrease of the ratio $\rho_F(Y)/\rho_R(Y)$ when the electron-donating ability of X increases (Table 6). The adjusting effect of X on the extent of $\rho_F(Y)$ and $\rho_R(Y)$ obviously is caused by the decrease of the contribution of the charge separated resonance form **9** when the electron-withdrawing ability of X increases.

Applicability of the Multiparameter Equations. To deal with the extensive data obtained we also used two different multiparameter equations: eq 4, which takes into account at the same time the variations of X and Y but assumes the parameters $\rho(X)$, $\rho_F(Y)$ and $\rho_R(Y)$ to be constant, and eq 5, which takes into account $\partial\rho(X)/\partial Y$, $\partial\rho_F(Y)/\partial X$ and $\partial\rho_R(Y)/\partial X$.

$$\delta_C(\mathrm{C{=}O}) = \rho(X)\sigma(X) + \rho_F(Y)\sigma_F(Y) + \rho_R(Y)\sigma_R(Y) + k \qquad (4)$$

$$\delta_C(\mathrm{C{=}O}) = \rho(X)_H\sigma(X) + \rho_F(Y)_H\sigma_F(Y) + \rho_R(Y)_H\sigma_R(Y) + \rho_F(X,Y)\sigma_F(Y)\sigma(X) + \rho_R(X,Y)\sigma_R(Y)\sigma(X) + k \qquad (5)$$

where

$$\rho_F(X,Y) = \rho(X)_{F,Y} + \rho_F(Y)_X \qquad (6)$$

$$\rho_R(X,Y) = \rho(X)_{R,Y} + \rho_R(Y)_X \qquad (7)$$

Eq 5 is derived from eq 4 by stating that

$$\rho(X) = \rho(X)_H + \rho(X)_{F,Y}\sigma_F(Y) + \rho(X)_{R,Y}\sigma_R(Y) \qquad (3)$$

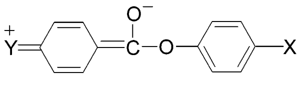
$$\rho_F(Y) = \rho_F(Y)_H + \rho_F(Y)_X\sigma(X) \qquad (8)$$

$$\rho_R(Y) = \rho_R(Y)_H + \rho_R(Y)_X\sigma(X) \qquad (9)$$

By eq 4 the following parameters were obtained: $\rho(X) = -1.27 \pm 0.03$, $\rho_F(Y) = -2.46 \pm 0.05$, $\rho_R(Y) = -0.89 \pm 0.05$, and $k = 165.18 \pm 0.02$ ($r = 0.9962$). Equation 5 gives: $\rho(X)_H = -1.25 \pm 0.06$, $\rho_F(Y)_H = -2.47 \pm 0.06$, $\rho_R(Y)_H = -0.93 \pm 0.05$, $\rho_F(X,Y) = 0.095 \pm 0.14$, $\rho_R(X,Y) = 0.20 \pm 0.13$, and $k = 165.18 \pm 0.02$ ($r = 0.9966$).

Comparison of the values of $\rho_F(X,Y) = 0.095 \pm 0.14$ and $\rho_R(X,Y) = 0.20 \pm 0.13$ with the sums $\rho(X)_{F,Y} + \rho_F(Y)_X = 0.18 \pm 0.04$ and $\rho(X)_{R,Y} + \rho_R(Y)_X = 0.40 \pm 0.08$, respectively (cf. eqs 6 and 7), shows that although the accuracy is not excellent the values agree satisfactorily [$\rho(X)_{F,Y} = 0.089 \pm 0.023$, $\rho(X)_{R,Y} = 0.20 \pm 0.02$, $\rho_F(Y)_X = 0.092 \pm 0.013$ and $\rho_R(Y)_X = 0.20 \pm 0.06$, cf. the preceding chapters]. In summary, the results show that (i) δ_C(C=O) values can be nicely correlated with the substituent parameters describing the ability of substituents to withdraw or release electrons in the molecule framework and (ii) the effect of both phenyl and benzoyl substituents on δ_C(C=O) of phenyl benzoates can be considered simultaneously. However, (iii) although the adjusting effect of the neighboring ring substituent could be clearly verified when considering the aromatic rings separately (cf. Tables 4 and 6), the accuracy of the cross-interaction parameters $\rho_F(X,Y)$ and $\rho_R(X,Y)$ obtained by eq 5 is not very good (large standard deviations). So eq 5 is not recommendable in this case but better results are obtained by studying the effect of Y on $\rho(X)$ and the effect of X on $\rho_F(Y)$ and $\rho_R(Y)$ separately. The reason for that obviously is the relatively small contribution of the cross-interaction terms. The latter explain ca. 10% or less of the change of δ_C(C=O). Therefore, testing of eq 5 in the future in some comparative systems possessing greater effects is challenging.

Comparison of the Effects of X and Y. Inspection of the effects of phenyl substituents X (Table 4) and benzoyl substituents Y (Table 6) shows that the inductive effect from the benzoyl side is ca. twice (2.1−2.3 times) as strong as that from the phenyl side. This is understandable due to the shorter distance between the substituent and the probe site in the former case (five bonds versus six bonds). Contrary, as regards the resonance contribution, the effect from the phenyl side is 1.6−1.9 times as strong as the effect from the benzoyl side. In principle, one would expect an opposite order, i.e., a similar order than that observed for the inductive effects. The situation can, however, be explained as follows. The benzoyl substituents possess two competitive resonance effects: due to the direct conjugation between the benzene ring and the carbonyl unit there is a normal resonance effect (**13**) ρ_R(Y, normal) which is >0, and in addition there is a resonance induced polar effect (**12**) ρ_R(Y, reverse) which is <0. The observed resonance effect $\rho_R(Y)_{observed}$ is the sum of these two effects. Therefore it can be that $|\rho_R(Y)_{observed}| < |\rho_R(X)_{observed}|$. If we consider that



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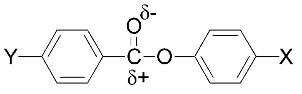
from the phenyl side only the resonance induced polar effect is in operation, i.e., $\rho_R(X)_{observed} = \rho_R(X,reverse)$, and that the effect of distance is the same than that observed for inductive effects, a ρ_R(Y, normal) value ca. 2 can be approximated for the normal resonance effect of substituents Y.

Conclusions

Both the benzoyl substituents Y and the phenyl substituents X have a reverse effect on the ^{13}C NMR chemical shift of the C=O carbon, δ_C(C=O), of phenyl benzoates, p-Y-$C_6H_4CO_2C_6H_4$-p-X, investigated. The electron-withdrawing substituents cause shielding while the electron-donating ones cause deshielding. The effects can be correlated with Hammett or Hammett-type substituent constants. These reverse effects can be understood by considering the effects of substituents X and Y on the contributions of different resonance structures of phenyl benzoates, i.e., on the electron delocalization. Substituents capable of electron-withdrawal by inductive effects destabilize resonance structures **9** and **10** (cf. Scheme 1) while those capable of electron donation stabilize them, reversing the substituent effect on δ_C(C=O) as a consequence ($\rho_F < 0$). The reverse resonance effect ($\rho_R < 0$) can be explained by the resonance induced polar effect (cf. **12**). Furthermore, the study of the effect of Y on the sensitivity of δ_C(C=O) to the phenyl substituents X, and for another the effect of X on the sensitivity of δ_C(C=O) to the benzoyl substituents Y, revealed an interesting interplay over the molecule. Because the substituent in one aromatic ring adjusts the significance of the contribution of the charged resonance structures it at the same time adjusts the sensitivity of δ_C(C=O) to the effect of the another ring substituents. This means a novel experimental verification of systematic changes in the polarization of the carbonyl unit (cf. **14**) by gradual changes in the electron-withdrawing/-donating power of the substituents in the molecule.



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This is an important aspect to be considered in the substitution versus reactivity considerations. From the reaction mechanistic point of view the present results mean that the ρ values observed for some nucleophilic acyl substitutions, for instance when substituent at phenyl moiety of phenyl benzoates is varied, must be considered paying attention also to the actual substitution at the benzoyl moiety. The present results are also interesting taking into account the goals of modern chemistry to develop molecular systems where weak intermolecular interactions, such as the electrostatic ones, occur. Related results with the above NMR works have recently been obtained by Liu et al., for instance in theoretical bond dissociation energy studies concerning para-substituted aromatic silanes[22] and para-substituted anilines.[23] There seems to prevail an interesting interaction over the aromatic and side-chain systems in that case too.

Experimental Section

Materials. Phenyl benzoates were prepared by standard procedures from substituted benzoyl chlorides and substituted phenols in dichloromethane in the presence of triethylamine, purified by recrystallization from benzene−petroleum ether (bp 40−60 °C) mixture, and characterized by the melting point determinations and ^{13}C NMR measurements. The melting point ranges and the spectral data are given in the Supporting Information.

Spectroscopic Measurements. The ^{13}C NMR spectra (125.78 MHz) were recorded in $CDCl_3$ at 25 °C at concentration of 0.1 mol L^{-1}. A low and constant sample concentration was used to avoid any disturbances from intermolecular associations. The deuterium of the solvent was used as a lock signal. The spectra were measured with a ^{1}H broad-band decoupling technique. The chemical shifts are expressed in ppm relative to TMS (0 ppm) used as an internal reference.

Supporting Information Available: Melting point and ^{13}C NMR data for the prepared substituted phenyl benzoates; σ, σ_F, and σ_R values used in the correlations. This material is available free of charge via the Internet at http://pubs.acs.org.

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[22] Cheng, Y.-H.; Zhao, X.; Song, K.-S.; Liu, L.; Guo, Q.-X. *J. Org. Chem.* **2002**, *67*, 6638.

[23] Song, K.-S.; Liu, L.; Guo, Q.-X. *J. Org. Chem.* **2003**, *68*, 262.