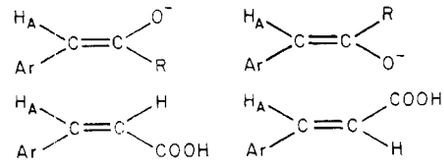
certainly predominant, while for aryl acetone anions (R = Me) the two isomers would be copresent as a rapidly equilibrating mixture.



That the *E* isomers show lower sensitivity is in line with results obtained for proton H_A in *Z* and *E* cinnamic acids.[3a]

Registry No. 1 (X = Y = H), 108-88-3; 1 (X = H; Y = SPh), 831-91-4; 1 (X = H; Y = Ph), 101-81-5; 1 (X = H; Y = CN), 140-29-4; 1 (X = H; Y = $CONMe_2$), 18925-69-4; 1 (X = H; Y = CO_2Me), 101-41-7; 1 (X = H; Y = COMe), 103-79-7; 1 (X = H; Y = COPh), 451-40-1; 1 (X = H; Y = SOPh), 833-82-9; 1 (X = H; Y = SOMe), 824-86-2; 1 (X = H; Y = SO_2Me), 3112-90-1; (*Z*)-1 (X = H; Y = NOH), 622-32-2; (*E*)-1 (X = H; Y = NOH), 622-31-1; **2** (X = H; Y = Ph), 18802-87-4; **2** (X = H; Y = CN), 18802-89-6; **2** (X = H; Y = $CONMe_2$), 61057-01-0; **2** (X = H; Y = CO_2Me), 61057-02-1; **2** (X = H; Y = COMe), 34438-76-1; **2** (X = H; Y = COPh), 54282-53-0; **2** (X = H; Y = SOPh), 71566-13-7; **2** (X = H; Y = SO_2Me), 32116-29-3.

Response to Polar-Inductive and Mesomeric Effects of Contiguous Substituents in Parent Oxygen Acids XOH and Nitroactivated Parent Carbon Acids XCH_2NO_2. The Phenylogy Principle[1]

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The universality of substituent constants derived from the benzenoid series is tested here for predicting properties of simple parent substrates XGMon, in which both the substituent functionality X and the monitor Mon are contiguous to the involved (reacting) functionality G. The approach considers the case of Mon = H in XGMon and

XGMon

1a, Mon = H; G = –O–
1b, Mon = H; G = $NO_2CH<$

uses acidities of the parent molecules XGH **1** for evaluating the effects of substituent X. Groups G = –O– and $NO_2CH<$ have been considered, and Table I reports acidities of parent oxygen acids XOH **1a**, of nitroactivated parent carbon acids XCH_2NO_2 **1b**, and of para-substituted phenols **2** together with our recently proposed set[2] of adjusted σ^-, σ_I, and σ_{R^-} constants. Polar-inductive σ_I constants are used when X exerts polar-inductive effects only (e.g., Me, Br, and OH), while enhanced σ^- constants are used when X is capable of conjugative delocalization with GH or G^-. The plots of Figure 1 show that acidities of at least 14 oxygen acids [from methanol (X = Me) to nitric acid (X = NO_2)] and of 8 nitroactivated carbon acids are linearly accounted for by such treatment: despite some scatter, the precision of the fit is impressive. The point for 4-hydroxypyridine (X = 4-py) is slightly deviant: it is dubious, however, whether it is the σ^- constant which is incorrect or whether it is the pK_a of 4-hydroxypyridine which is uncertain.[3] We noted previously[2a] that, in analogy with para-substituted anilines and phenols,[5] a number of substituents X presented a duality of σ^- constants depending on whether X were adjacent to nitrogen or oxygen functionalities. While the cyano group in XOH correctly requires the enhanced constant,[6] the goodness of the fit is not sensitive enough for preferring one of the two values of the benzoyl substituent. None of the available σ^- values accounts for acidities of parent oxygen acids XOH in which X is a functionality composed of second row atoms ($PhSO_2$, PhSO, $(EtO)_2P{=}O$), although at least for one of the functionalities ($PhSO_2$) no deviance is found for the line of XCH_2NO_2 vs. σ^-. The DSP treatment of oxygen and nitroactivated carbon acid acidities affords the excellent fitting parameters reported in Table II. The success of both treatments in accounting for the substituent effects finds its explanation in the way we have chosen the set of σ_I, σ^-, and σ_{R^-} constants: relative to the literature values, the present parameters were adjusted in consideration of systems in which the substituents were directly bonded to the reacting center and then tested. It is remarkable that sensitivities of oxygen acids in water and of nitroactivated carbon acids in Me_2SO are not so dissimilar as one would anticipate from the widely different stabilizing capacities of the two solvents toward negatively charged species and from the different abilities of Me_2SO and H_2O to hydrogen bond un-ionized oxygen acids. One is left to admit with Bordwell[10] that the electrostatic and mesomeric effects of substituents are submerged in a large sea of solvent effects (no matter how) operating at the reaction site. Inclusion in the DSP treatment (entry 2) of substituents (X = Me, OH, and Br) nonmesomerically interacting with the adjacent group –O– ($\sigma_R \rightarrow 0$) does not cause any statistically significant variation in the ρ_I and ρ_R values of entry 1. The simultaneous use of "mixed" substituents with different interacting properties (polar-inductive or polar-inductive mesomeric) is thus legitimated.

It is accepted that nonmesomeric interactions of substituents with adjacent groups respond linearly with σ^* constants of the substituents (see, e.g., the ionization constants of substituted alcohols[11] and of substituted

(1) Part 3 in Substituent Effect Treatment of Interactions between Contiguous Functionalities G–X.

(2) (a) S. Bradamante and G. A. Pagani, *J. Org. Chem.*, in press as Part 2; (b) *ibid.*, in press.

(3) The experimental pK_a values for 2- and 4-hydroxypyridine are 11.62 and 11.09, respectively:[4] these values are corrected into 9.09 and 7.74 to take into account the pyridone–hydroxypyridine tautomerism.[4] [$pK_{hydroxy} = pK_{exp} - \log (R + 1)$ where R = the ratio of pyridone–hydroxypyridine.] However, while in the case of the 2 isomer the ratio of tautomers can be accurately determined (2-pyridone:2-hydroxypyridine = 340), in the case of the 4 isomer the ratio is much higher (4-pyridone:4-hydroxypyridine = 2200): we believe that for this reason the above value might be considerably more approximate and thus constitute a source of imprecision.

(4) A. Albert, "Heterocyclic Chemistry", 2nd ed., The Athlone Press, London, 1968, pp 89–93.

(5) S. Ehrenson, R. T. C. Brownlee, and R. W. Taft, *Prog. Phys. Org. Chem.*, **10**, 50 (1973).

(6) The figure of 3.46 for the pK_a of cyanic acid in water may be approximate: Hine expects[7] a lower value to take into account for the anticipated cyanic–isocyanic acid equilibrium in water. The fact that a single tautomer (isocyanic acid) is present in the solid evidenced in old crystallographic[8] and spectroscopic studies[9] is of little significance for the position of the equilibrium in water. Because of all this, the point for X = CN is subject to some uncertainty: the pK_a value for the cyanic acid, interpolated from line A of Figure 1, is ca. 3.0, thus it is qualitatively in accord with Hine's prediction.

(7) J. Hine, "Structural Effects on Equilibria in Organic Chemistry", Wiley-Interscience, New York, 1975, p 185.

(8) W. C. v. Dohlen and G. B. Carpenter, *Acta Crystallogr.*, **8**, 646 (1955).

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Table I. Acidities of Parent Oxygen Acids, Para-Substituted Phenols, and α-Substituted Nitromethanes and Substituent Constants

entry[a] no.	X	σ	ref	σ_I	ref	σ_R	ref	XOH $pK_a(H_2O)$[b]	XOH ref	p-X-Ph-OH $pK_a(H_2O)$	p-X-Ph-OH ref	XCH_2NO_2 $pK_a(Me_2SO)$[b,c]
1	H	0	*d, e*	0	*f, g*	0	*e, h*	16.05	*i*	10.00	*j*	17.68
2	Ph	0.47	*e*	0.10	*f, g*	0.26	*e*	10.00	*j*	9.60	*j*	12.50
4	CO_2Me	0.74	*e, k, l*	0.26	*g*	0.39	*e*			8.47	*j*	9.5[m]
5	COMe	0.82	*e, k, l*	0.20	*g*	0.47	*e, h*	4.45	*j*	8.05	*j*	
6	COPh	0.94	*e*	0.21	*g*	0.52	*e*	3.90	*j*	7.95	*n*	8.0
		0.81	*e, o*									
7	CHO	0.98	*e, k, l*	0.26	*g, p*	0.49	*e*	3.45	*j*	7.62	*j*	
8	$COCF_3$	1.09	*e*	0.58	*g*	0.42	*e*	−0.07	*j*			
9	NO_2	1.27	*e, q, r*	0.80	*g*	0.46	*e, h*	−1.92	*j*	7.15	*j*	
10	CN	0.99	*e, k, l, o*	0.43	*g*	0.33	*e, h*	3.46	*j, s*	7.95	*j*	
12	SO_2Me	0.98	*e, t*	0.59	*f, g*	0.33	*e*	−1.68	*j*	7.83	*j*	
13	SOPh	0.76	*e*	0.46	*g*	0.26	*e*	1.20	*j*			
14	SO_2Ph	1.00	*e*	0.62	*g*	0.34	*e*					7.50
16	$PO(OEt)_2$	0.58	*e*	0.19	*g*	0.29	*e*	0.99	*j, u*			
		0.68	*e, o*	0.24	*v*	0.38	*e, o*					
		0.78	*o, w*									
		0.84	*w*									
19	2-py	0.55	*e*	0.12	*g*	0.31	*e*	9.09	*x*			
20	3-py	0.58	*e*	0.15	*g*	0.31	*e*	8.42	*x*			
21	4-py	0.81	*e*	0.18	*g*	0.45	*e*	7.74	*x*			
		0.73	*e, o*									
26	Me			0.04	*g*			15.50	*j*	10.26	*j*	17.02
								15.09	*y*			
29	OH			0.22	*g*			11.95	*j*	10.15	*j*	
34	Br			0.44	*f*							12.80
				0.56	*g*			8.68	*z*	9.36	*j*	
36	CH_2OH			0.10	*aa*							16.6
37	$B(OH)_2$	0.45	*t*					9.41	*j*			
38	Cl							7.54	*j*	9.38	*j*	

[a] Numbering of substituent entries as previously (ref 2). [b] Statistically corrected values for the number of ionizable protons and for the protonable oxygen sites. [c] Reference 21. [d] By definition. [e] Reference 2a. [f] Reference 5, p 4. [g] Reference 2b. [h] Reference 5, p 13. [i] Reference 22. [j] From the compilation of ref 23. [k] From Hine's compilation (ref 7, p 73). [l] From Wepster's compilation (ref 24). [m] pK_a of (ethoxycarbonyl)nitromethane. [n] Reference 25. [o] To be used only when in XGH_3, G = O. See ref 2a. [p] Reference 26. [q] Reference 27. [r] Reference 28. [s] Reference 6. [t] Reference 29. [u] pK_a of dimethyl phosphate. [v] Reference 30. [w] Reference 31. [x] Reference 4. [y] Reference 11. [z] Reference 32. [aa] Reference 33.

Table II. DSP Analysis of pK_a's for XOH and NO_2CH_2X

entry no.	system	ρ_I	ρ_R	*f*	SD	b^a	r^a	*n*	X
1	XOH	12.90436	−18.69899	0.04	0.54	0.992	0.990	9	Ph, COMe, COPh, CHO, $COCF_3$, NO_2, CN, 2-py, 3-py
2		−13.37338	−18.32273	0.05	0.58	1.03	0.994	12	as entry 1 + Me, OH, Br[b]
3	NO_2CH_2X	−9.90172	−14.36812	0.05	0.35	1.06	0.996	7	Ph, CO_2Et, COPh, SO_2Ph, Me, Br,[c] CH_2OH

[a] *b* is the slope of the line: $\Delta pK_{a(exptl)} - \Delta pK_{a(calcd)}$ + constant; *r* = correlation coefficient of the same (ref 2). [b] Using $\sigma_I = 0.56$. [c] Using $\sigma_I = 0.44$.

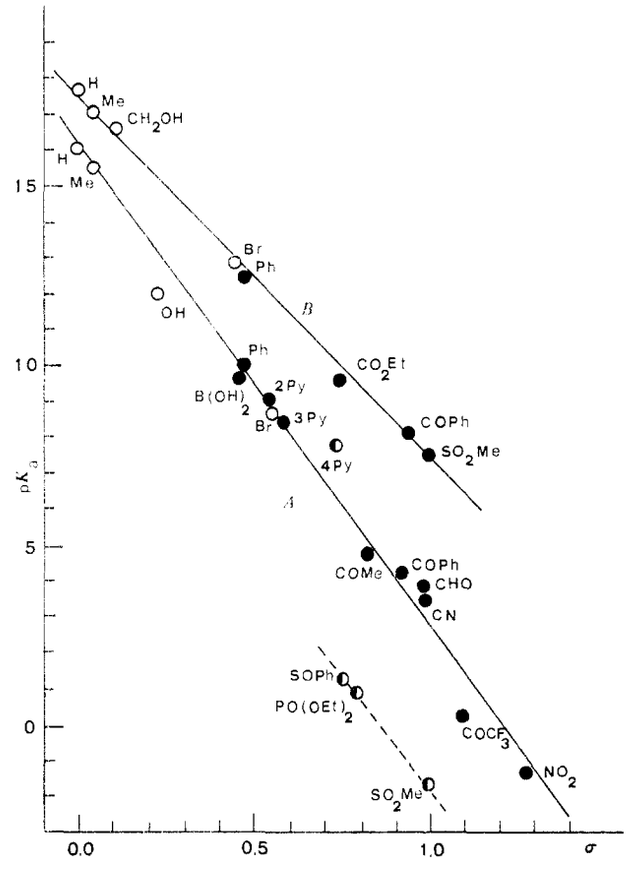


Figure 1. Linear free energy relationships for pK_a's of XOH-(H_2O), NO_2CH_2X (Me_2SO), and σ; open circles (O) are for those groups for which σ_I are used; closed circles (●) are for those groups for which σ^- are used; (◐) points excluded from correlations; line A, $pK_a = -13.98\sigma + 16.39$ for ● points only, $n = 11$, $r = 0.992$; $pK_a = -13.59\sigma + 16.31$ where $\sigma = \sigma^-$ for ● points and $\sigma = \sigma_I$ for O points, $n = 14$, $r = 0.992$; line B, $pK_a = -10.26\sigma + 17.48$ where $\sigma = \sigma^-$ for ● points and $\sigma = \sigma_I$ for O points, $n = 8$, $r = 0.998$.

1,1-dinitromethanes).[12] Our LFER treatment of substituted parent oxygen acids with the simultaneous use of polar-inductive (σ_I) and blended polar-inductive mesomeric (σ^-) constants of the contiguous functionality X is supported by the following facts.

(a) In O-substituted phenyl ethers **3**, the remote para ^1H monitor was shown[2] to precisely account for the *type* and *extent* of interaction between the two contiguous functionalities X and O, its variations responding either to σ_I or to σ^- constants of the substituent X, depending upon whether X interacts with the oxygen group by the polar-inductive only or also by the mesomeric delocalizative mechanism. (b) Whenever the substituent X is capable of "direct" delocalizative interactions with the group G = –O–, the ^1H_p response of **3** was shown[2] to be linearly related to that of the O–^1H monitor in para-substituted phenols **2**. (c) It is found now that for those substituents X which enter into direct conjugative interaction with the group G = –O–, acidities of parent oxygen acids XOH **1a** are linearly related to those of para-substituted phenols *p*-XPhOH (Figure 2): excluding some exceptions which will be discussed later on, the fitting is good and the slope of the plot indicates that the *p*-phenylene (C_6H_4) mediation in the transmission of effects causes a fall off of ca. 6.

It is generally accepted by common sense that delocalizative interactions between two functionalities mediated by a *p*-phenylene unit are somehow related to direct delocalizative unmediated interactions between the same functionalities. The occurrence of linear relationships between parent oxygen acids XOH **1a** and para-substituted phenols **2**, and between para-substituted phenols and *O*-substituted phenyl ethers **3**, is the experimental evidence for the *phenylogy principle*.[13] Thus, para-substituted phenols **2** and O-substituted phenyl ethers **3** should be regarded as phenyl homologues of parent oxygen acids XOH **1a**, deriving from formal *p*-phenylene (C_6H_4) insertion in between –O– and X and H and –O–, respectively.

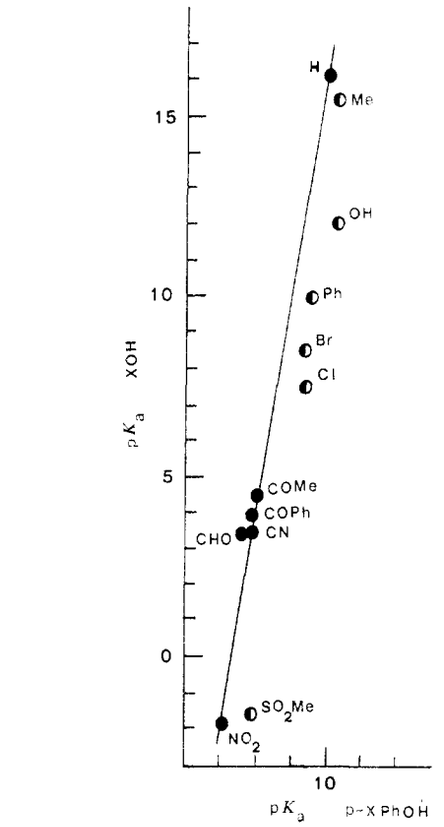
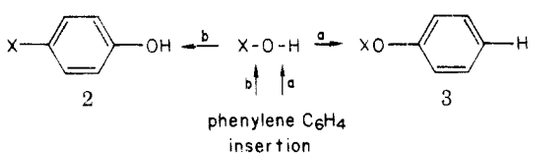


Figure 2. Linear free energy relationship for pK_a's of XOH and p-$XC_6H_4OH(H_2O)$. $pK_a(XOH) = 6.00pK_a(p\text{-}XC_6H_4OH) - 43.86$, $n = 6$, $r = 0.990$; closed circles (●) are for groups considered in the above relation; ◐ are for substituents excluded from the correlation.



The correlations found allow us to define the limits in which the phenylogy principle holds: the principle is not valid whenever the two functionalities do not interact by mesomeric delocalizative mechanism and when steric inhibition to full conjugation or other infringements to "direct" delocalizative mechanisms occur. The plot of Figure 2 indicates that points relative to X = Me, Br, Cl, and OH are deviant: this is the case of nonmesomeric delocalizative interactions. Other deviances are present. Steric inhibition to full conjugation has been[2a] and is here

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invoked for the deviance in the plot of Figure 2 for X = Ph in para-substituted diphenyl derivatives (e.g., in **2**, *p*-phenylphenol, or for *p*-phenylaniline[2a]). More interesting is the deviance presented by the sulfonyl functionality which indeed behaves differently depending upon the nature of the contiguous functionality.[14] The methylsulfonyl (and phenylsulfonyl) substituents show coherence in substrates **1b**, **2**, and **3**, and their effect is properly accounted for by $\sigma^- = 0.98$ (1.00), $\sigma_I = 0.59$ (0.62), and $\sigma_{R^-} = 0.34$, respectively. However, relative to these constants the sulfonyl functionality requires in oxygen acids **1a** enhanced constants and, inversely, in α-sulfonyl carbanions considerably weaker constants.[15] We believe this variable character is not at random but instead is indicative of different electron-withdrawing capacities associated with different bonding situations: the order of electron-withdrawing power is sulfonate anions $\gg$ *p*-sulfonyl phenoxides $\approx$ α-sulfonyl nitrocarbanions $\approx$ sulfonate esters $\approx$ sulfonamides > sulfonamidate anions[16] $\gg$ α-sulfonyl carbanions.[15] There is strong evidence[17] that in sulfonate anions (and in sulfate anions) delocalization is extensive all over the oxygen atoms, while it appears that in α-sulfonyl carbanions the sulfonyl functionality is rather poor in delocalizing the negative charge.[15,18] Whether variable resonance capacities of the sulfonyl group are accompanied also by variable polar inductive effects remains to be established.[19]

In conclusion, the phenylogy principle has its firm foundation on precise LFER. This principle allows the prediction of substituent effects of substituents adjacent and mesomerically interacting with the involved (reacting) center. Thus, enhanced constants derived from benzenoid substrates for remote functionalities still account for effects of contiguous, mesomerically-interacting functionalities. Furthermore, polar-inductive constants, derived from either benzenoid or aliphatic systems,[2b] account for polar-inductive effects of substituents adjacent to the involved (reacting) center. Provided that great care is exerted in the choice of the monitor property,[20] substituent effects of a functionality X contiguous to the involved (reacting) group G can be accounted for by appropriate substituent constants, which indeed deserve the title of universal.

Registry No. **1a** (X = H), 7732-18-5; **1a** (X = Ph), 108-95-2; **1a** (X = COMe), 64-19-7; **1a** (X = COPh), 65-85-0; **1a** (X = CHO), 64-18-6; **1a** (X = $COCF_3$), 76-05-1; **1a** (X = NO_2), 7697-37-2; **1a** (X = CN), 420-05-3; **1a** (X = SO_2Me), 75-75-2; **1a** (X = SOPh), 618-41-7; **1a** (X = $PO(OEt)_2$), 598-02-7; **1a** (X = 2-py), 598-02-7; **1a** (X = 3-py), 109-00-2; **1a** (X = 4-py) 626-64-2; **1a** (X = Me), 67-56-1; **1a** (X = OH), 7722-84-1; **1a** (X = Br), 13517-11-8; **1a** (X = $B(OH)_2$), 10043-35-3; **1a** (X = Cl), 7790-92-3; **1b** (X = H), 75-52-5; **1b** (X = Ph), 622-42-4; **1b** (X = CO_2Me), 2483-57-0; **1b** (X = COPh), 614-21-1; **1b** (X = SO_2Ph), 21272-85-5; **1b** (X = Me), 79-24-3; **1b** (X = Br), 563-70-2; **1b** (X = CH_2OH), 625-48-9; **2** (X = Ph), 92-69-3; **2** (X = CO_2Me), 99-76-3; **2** (X = COMe), 99-93-4; **2** (X = COPh), 1137-42-4; **2** (X = CHO), 123-08-0; **2** (X = NO_2), 100-02-7; **2** (X = CN), 767-00-0; **2** (X = SO_2Me), 14763-60-1; **2** (X = Me), 106-44-5; **2** (X = OH), 123-31-9; **2** (X = Br), 106-41-2; **2** (X = $B(OH)_2$), 71597-85-8; **2** (X = $B(OH)_2$), 71597-85-8.

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(20) The monitor or the detecting property, if properly chosen, should not be affected by the substituent X independently of the intervening group functionality G: e.g., SCS of a spin active monitor Mon in XGMon does not reflect polar-inductive and mesomeric capacities of the substituent X only, because the monitor itself is susceptible to magnetic anisotropy induced by the substituent independently of the intervening group G.
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