(m), 1420 (m), 1180 (s), 750 (m) cm^{-1}.

Anal. Calcd for $C_5H_{10}ClNO_2{\cdot}HCl$: C, 31.94; H, 5.90; N, 7.45; Cl, 37.71. Found: C, 31.60; H, 6.07; N, 7.30; Cl, 37.27.

(*S*)-(+)-4-Amino-5-bromopentanoic Acid Hydrobromide (1d·HBr). A solution of 330 mg (1.85 mmol) of **3d** in 10 mL of 1 N HBr was heated at reflux for 5 h. The reaction solution was cooled to room temperature and the solvent was removed in vacuo. The resulting dark oil was dissolved in 2 mL of H_2O and applied to a column (1 × 10 cm) of Dowex 50 (H^+ form). The column was washed with distilled water until the eluate was neutral, and the amino acid was eluted with 1 N HBr. The acidic fractions that gave a positive ninhydrin test were combined and concentrated in vacuo to a light yellow oil. Acetic acid was added and evaporated (2×). The oil was crystallized and recrystallized from acetic acid–ethyl acetate to give 230 mg of a white solid. Electrophoresis of this solid at 4.2 kV, pH 1.9, for 20 min showed one component at 18 cm toward the cathode as detected by ninhydrin: mp 137–138 °C; $[\alpha]^{20}_D$ +14.3° (*c* 10, 1 N HBr); NMR (D_2O) δ 1.9 (2 H, m), 2.4 (2 H, m), 3.6 (3 H, m), 4.6 (4 H, s, HDO); IR (KBr) 3120 (br), 1728 (s), 1605 (m), 1497 (s), 1175 (m), 620 (m) cm^{-1}.

Anal. Calcd for $C_5H_{10}BrNO_2{\cdot}HBr$: C, 21.68; H, 4.00; N, 5.06. Found: C, 22.01; H, 4.03; N, 4.70.

(*S*)-(+)-4-Amino-5-cyanopentanoic Acid Hydrochloride (1e·HCl). A solution of 124 mg (1.0 mmol) of **3e** in 5 mL of 1 N HCl was heated at reflux for 2 h. After the solution was cooled to room temperature, the solvent was removed in vacuo to give a gummy solid. Water (0.5 mL) was added and evaporated (2×). The residue was dissolved in 10 mL of absolute ethanol, cooled to 0 °C, and filtered through a sintered-glass funnel. The filtrate was concentrated and the residue was crystallized from ethanol–ethyl acetate to give 97 mg of fluffy white crystals. Electrophoresis for 20 min showed one spot at 17.5 cm toward the cathode as detected by ninhydrin: mp 147.5–149 °C; $[\alpha]^{20}_D$ +8° (*c* 2.5, 1 N HCl); NMR (D_2O) δ 0.9 (~1.5 H, t, *J* = 7 Hz), 1.9 (2 H, td, *J* = 7 Hz), 2.3 (2 H, m), 2.75 (2 H, d, *J* = 6 Hz), 3.5 (~1.5 H, m), 4.5 (~4.5 H, s, HDO); IR (KBr) 3100 (s, br), 2244 (w), 1723 (s), 1580 (m), 1496 (s), 1180 (s), 793 (m) cm^{-1}.

Anal. Calcd for $C_6H_{10}N_2O_2{\cdot}HCl{\cdot}{}^1/_2C_2H_5OH$: C, 41.81; H, 6.98; N, 13.87. Found: C, 42.09; H, 7.02; N, 14.25.

A sample of this solid that was recrystallized from ethanol–ethyl acetate (3×) was twice dissolved in 5 mL of distilled H_2O and was lyophilized. The resulting fluffy white solid was further dried under vacuum over P_2O_5, mp 149–151 °C.

Anal. Calcd for $C_6H_{10}N_2O_2{\cdot}HCl{\cdot}{}^1/_2H_2O$: C, 38.41; H, 6.45; N, 14.93. Found: C, 38.47; H, 6.14; N, 15.30.

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Registry No. 1a, 72478-99-0; **1b**·HCl, 72522-16-8; **1c**·HCl, 72479-00-6; **1d**·HBr, 72479-01-7; **1e**·HCl, 72479-02-8; **2c**, 7149-65-7; **3a**, 17342-08-4; **3b**, 72479-03-9; **3c**, 72479-04-0; **3d**, 72479-05-1; **3e**, 72479-06-2; L-glutamic acid, 56-86-0.

Theoretical Approach to Substituent Effects. Phenols and Phenoxide Ions

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Ab initio molecular orbital calculations on substituent interactions in substituted phenols and phenoxide ions have been performed. Theoretical gas-phase acidities are generally in satisfactory agreement with available gas-phase experimental data. The effects of substituents on acidity are largely determined by effects in the phenoxide anion and only to a slight extent by those in the corresponding neutral phenol. Substituents which interact favorably in the meta position of phenol generally act unfavorably at the para position and vice versa. Both σ and π charge transfer are found to be of importance in determining energies of interaction. The σ acceptance by a substituent stabilizes OH and O^- more effectively at the para position than at the meta position by a π-inductive mechanism. Direct π interactions are also more important for para substituents and result in stabilization by π acceptors and destabilization by π donors. The net results for the π-donating and σ-accepting groups (NH_2, OH, and F) are an increase in acidity at the meta position and a decrease in acidity (with the exception of the strongly σ-accepting F substituent) at the para position. For the σ- and π-accepting groups (NO_2, CN, CHO, and CF_3), both meta and para substitution lead to enhanced acidity, with a larger effect at the para position.

With the advent of both experimental and theoretical techniques for studying gas-phase chemical reactions, research on substituent effects has made significant recent progress. Specifically, the separation of intrinsic molecular effects from solution effects has become possible, enabling a clearer understanding of both to be obtained.[2]

The interaction of a large number of neutral substituents with an aromatic ring has recently been studied by using ab initio molecular orbital theory.[3] This paper extends that study first by the comparison of a neutral substituent (OH) with a charged one (O^-) and second by examining the interaction of each of these two groups with a series of additional substituents.[4] The results also provide theoretical estimates of the relative acidities of substituted phenols and enable the separation of the effect of the substituent on acidity into components due to the neutral phenol on the one hand and to the charged phenoxide ion on the other. Such a separation is at present not accessible

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(2) See, for example, R. W. Taft, *NATO Adv. Study Inst. Ser., Ser. B*, **40**, 271 (1979).

(3) W. J. Hehre, L. Radom, and J. A. Pople, *J. Am. Chem. Soc.*, **94**, 1496 (1972).

(4) A paper utilizing ab initio calculations to assess torsional barriers in para-substituted phenols has appeared: L. Radom, W. J. Hehre, J. A. Pople, G. L. Carlson, and W. G. Fateley, *J. Chem. Soc., Chem. Commun.*, 308 (1972).

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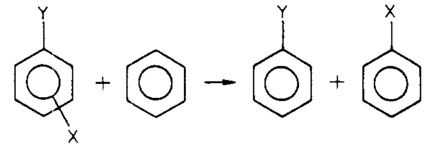
from available experimental data. A further aim is to study the interdependence of σ and π effects in aromatic systems. Often, only π effects are explicitly considered, and this paper attempts to assess the precise roles played by each in determining the stabilities of substituted phenols and phenoxides.

Methods

Ab initio molecular orbital calculations were carried out at the STO-3G level[5] by using a modified version of the Gaussian 70 system of programs.[6] Standard model geometries[7] were used for all substrates with the exception of the methoxy and amino substituents. For the methoxy group, the angle COC = 118.0° was used, this being the optimized value for anisole,[3] to minimize steric interactions between OCH_3 and the ring. For the amino group, the three bond angles about nitrogen were assumed equal and were optimized for each system examined. The C–O bond length was optimized in the phenoxide anion and the optimized value (1.28 Å) taken as "standard" for the substituted phenoxides. Calculations for each substrate were conducted on a number of possible conformations, and the energetically favored conformation was utilized in all subsequent analyses.

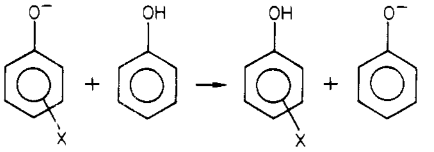
Results

Calculated total energies for the preferred conformations of substituted phenols and phenoxide ions are listed in Table I. Interaction energies between the substituents and the OH and O^- groups as well as the theoretical and experimental effects of the substituents on acidity are listed in Table II. Interaction energies are given by the energy of the reactions expressed in eq 1, where X is any



(1)

substituent and Y is either OH or O^-. The effect of the substituent on acidity is given by the energy change for reaction 2, which is just the difference in the interaction



(2)

energies (eq 1) for the OH and O^- groups. Tables III and IV list (for Y = OH and O^-, respectively) the σ and π charge displacements for all ring substituents as well as π-overlap populations for the C–X and C–Y bonds calculated by using Mulliken's method.[8] A positive value for a charge displacement indicates that the substituent is an electron acceptor from the ring.

Table I. Calculated Total Energies (hartrees) for Substituted Phenols and Phenoxide Ions[a]

substnt				
X	Y	isomer	conformation[b]	energy
OH	H		HOCC planar	−301.728 61
OH	CH_3	ortho	HOC· · ·CCH trans, trans	−340.312 21
		meta	HOC· · ·CCH trans, trans	−340.312 83
		para	HOCC trans	−340.311 75
OH	NH_2	ortho	HOC· · ·CN trans; $\alpha = 111.7°$[c]	−356.044 96
		meta	HOC· · ·CN trans; $\alpha =112.3°$[c]	−356.048 77
		para	HOC· · ·CN planar; $\alpha = 111.7°$[c]	−356.045 03
OH	OH	ortho	HOC· · ·COH cis, trans	−375.566 07
		meta	HOC· · ·COH cis, trans	−375.568 50
		para	HOC· · ·COH trans	−375.564 86
OH	OCH_3	meta	HOC· · ·COC trans, cis	−414.144 24
		para	HOC· · ·COC trans	−414.140 69
OH	F	ortho	HOC· · ·CF cis	−399.185 72
		meta	HOC· · ·CF cis	−399.188 57
		para	HOC· · ·CF planar	−399.186 49
OH	NO_2	ortho	HOC· · ·CN trans	−502.416 06
		meta	HOC· · ·CN cis	−502.421 03
		para	HOC· · ·CN planar	−502 423 83
OH	CN	ortho	HOC· · ·CN cis	−392.282 77
		meta	HOC· · ·CN cis	−392.281 28
		para	HOC· · ·CN planar	−392.283 17
OH	CHO	ortho	HOC· · ·CCO trans, trans	−412.954 69
		meta	HOC· · ·CCO cis, cis	−412.953 92
		para	HOC· · ·CCO cis	−412.955 07
OH	CF_3	ortho	HOC· · ·CCF trans, trans	−632.692 68
		meta	HOC· · ·CCF cis, trans	−632.692 83
		para	HOC· · ·CCF trans	−632.693 80
OH	Li	ortho	HOC· · ·CLi trans	−308.450 91
		meta	HOC· · ·CLi trans	−308.440 41
		para	HOC· · ·CLi planar	−308.439 45
O^-	H			−300.973 76
O^-	CH_3	ortho	OC· · ·CCH trans	−399.557 91
		meta	OC· · ·CCH cis	−399.557 37
		para	OC· · ·CCH planar	−399.555 27
O^-	NH_2	ortho	$\alpha = 108.8°$[c]	−355.290 11
		meta	$\alpha = 110.2°$[c]	−355.293 77
		para	$\alpha = 108.6°$[c]	−355.282 45
O^-	OH	ortho	OC· · ·COH cis	−374.819 94
		meta	OC· · ·COH trans	−374.818 42
		para	OC· · ·COH planar	−374.805 37
O^-	OCH_3	meta	OC· · ·COC cis	−413.392 74
		para	OC· · ·COC planar	−413.381 12
O^-	F	ortho		−398.434 70
		meta		−398.442 26
		para		−398.434 13
O^-	NO_2	ortho	OC· · ·CNO planar	−501.705 23
		meta	OC· · ·CNO planar	−501.695 04
		para	OC· · ·CNO planar	−501.715 45
O^-	CN	ortho		−391.560 92
		meta		−391.549 48
		para		−391.562 39
O^-	CHO	ortho	OC· · ·CCO trans	−412.222 52
		meta	OC· · ·CCO trans	−412.208 53
		para	OC· · ·CCO planar	−412.222 25
O^-	CF_3	ortho	OC· · ·CCF trans	−631.956 91
		meta	OC· · ·CCF cis	−631.951 32
		para	OC· · ·CCF planar	−631.957 18
O^-	Li	ortho		−307.684 92
		meta		−307.663 23
		para		−307.676 75

[a] Energies were calculated at the STO-3G level and are listed only for the most stable conformations (as specified) for each isomer. [b] The notation "HOC· · ·COC trans, cis", for example, means HOCC is trans and CCOC is cis. [c] α is the optimized value for the bond angles (assumed equal) about nitrogen.

Discussion

Charge Interactions. Comparison of the electronic properties of OH and O^- in the unsubstituted systems shows that both σ- and π-donating abilities increase considerably on deprotonation of the OH group. Whereas OH is a moderate π donor (q_π = −0.102) and a strong σ acceptor

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Table II. Effect of Substituents on Acidities of Phenols and on Stabilities of Phenols and Phenoxide Ions (kcal mol^{-1})

			relative acidity[c]		
				exptl	
substnt X	phenol[a]	phenoxide anion[b]	theor	ICR[d]	MS[e]
H	0.0	0.0	0.0	0.0	0.0
o-CH_3	−0.1	+0.2	+0.3	+0.3	+0.7
m-CH_3	+0.3	−0.1	−0.4	−0.5	−0.4
p-CH_3	−0.4	−1.4	−1.0	−1.2	−1.3
o-NH_2	−1.6	−1.6	0.0		+2.1
m-NH_2	+0.8	+0.7	−0.1	−1.3[g]	−0.9
p-NH_2	−1.5	−6.4	−4.9	−3.1[g]	−4.2
o-OH	−0.7	+4.8	+5.4		+9.7[f]
m-OH	+0.8	+3.8	+3.0		+4.2[f]
p-OH	−1.4	−4.4	−2.9		
m-OCH_3	+0.9	+3.0	+2.1	+1.0[g]	+1.5
p-OCH_3	−1.3	−4.3	−3.0	−1.1[g]	−0.8
o-F	−1.4	+1.0	+2.4	+3.8	+3.9
m-F	+0.4	+5.8	+5.4	+4.8	+5.8
p-F	−0.9	+0.7	+1.6	+2.1	+2.6
o-NO_2	−3.6	+24.0	+27.6		+13.9
m-NO_2	−0.5 (−0.4)[h]	+17.6 (+18.6)[h]	+18.1 (+19.0)[h]		+15.7
p-NO_2	+1.3 (+0.6)[h]	+30.4 (+22.6)[h]	+29.2 (+22.0)[h]		(+25.8)[i]
o-CN	+0.6	+21.3	+20.7		+16.2
m-CN	−0.4	+14.1	+14.5		+14.3
p-CN	+0.8	+22.2	+21.4		+17.7
o-CHO	+0.5	+14.7	+14.2		
m-CHO	0.0	+5.9	+5.9		+8.2[g]
p-CHO	+0.7	+14.5	+13.8		
o-CF_3	−0.3	+11.7	+12.0		
m-CF_3	−0.2	+8.2	+8.4		+9.3[g]
p-CF_3	+0.4	+11.9	+11.5		
o-Li	+7.1	+0.1	−7.0		
m-Li	+0.5	−13.5	−14.0		
p-Li	0.0	−5.0	−5.0		

[a] Values represent the energy of the reaction $XC_6H_4OH + C_6H_6 \rightarrow C_6H_5OH + C_6H_5X$. [b] Values represent the energy of the reaction $XC_6H_4O^- + C_6H_6 \rightarrow C_6H_5O^- + C_6H_5X$. [c] Values represent the energy of the reaction $XC_6H_4O^- + C_6H_5OH \rightarrow XC_6H_4OH + C_6H_5O^-$. [d] Data from ref 20. [e] Data from ref 21. [f] Statistical correction applied. [g] Unpublished results of M. Fujio, R. T. McIver, and R. W. Taft. [h] Corresponding values for NO_2 oriented orthogonally to the ring. [i] Estimated value; cf. ref 21.

(q_σ = +0.185), O^- is a very strong π donor (q_π = −0.506) but is only a mild σ acceptor (q_σ = −0.021) relative to H: q_σ = −0.063 and q_π = 0 for a hydrogen atom in benzene. This suggests that the negative charge on oxygen results in a decreased attractive electronic–nuclear interaction, raising the levels of the atomic orbitals on oxygen so that they all become substantially better electron donors. We term this a *shielding effect*; i.e., the orbitals are shielded by the additional electronic charge. It is observed for orbitals orthogonal to the orbital perturbed by deprotonation (e.g., the $2p_y$ orbital) as well as for those directly affected by the deprotonation (e.g., the 2s, $2p_x$, and $2p_z$ orbitals).

The interactions of substituents with OH and O^- through the aromatic ring are readily understood by using perturbation molecular orbital (PMO) theory[9] which offers a qualitative rationalization of the results obtained from the quantitative calculations. An important result of PMO theory is that two-electron interactions are stabilizing. Specifically, the interaction of a filled and an unfilled orbital (Figure 1) leads to a stabilization energy (SE) given by eq 3, where C_{rj} and C_{sk} represent the coefficients of the

$$SE = C_{rj}^2 C_{sk}^2 \beta_{rs}^2 / \Delta E \quad (3)$$

atomic orbitals on interacting atoms r and s in the molecular orbitals ψ_j and ψ_k, respectively, and β_{rs} represents the resonance integral associated with these atomic orbitals. ΔE represents the energy separation between the two interacting orbitals.

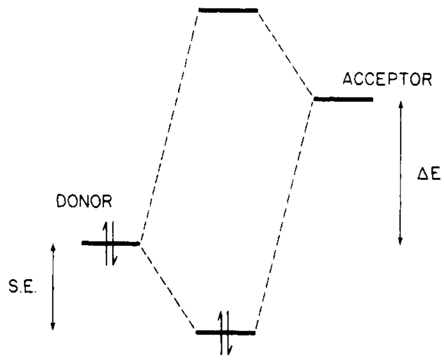

Figure 1. Generalized PMO diagram for interaction between donor and acceptor orbitals resulting in two-electron stabilization (SE).

Most of the substituent effects described here are understandable in terms of the PMO model. The question that requires analysis is how do the σ and π interactions between the OH (or O^-) group and the ring change as a result of introducing a substituent into the system.

Changes in the π charge transfer between OH (or O^-) and the ring appear to be brought about primarily by changes (resulting from the second substituent) in the energies of the ring π^* levels into which the OH (or O^-) group donates charge. Both σ- and π-donor substituents

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[9] For reviews on the PMO method, see: (a) I. Fleming, "Frontier Orbitals and Organic Chemical Reactions", Wiley-Interscience, New York, 1976; (b) N. D. Epiotis, W. R. Cherry, S. Shaik, R. Yates, and F. Bernardi, *Top. Curr. Chem.*, 70, 1 (1977); (c) G. Klopman, Ed., "Chemical Reactivity and Reactions Paths", Wiley-Interscience, New York, 1974; (d) R. F. Hudson, *Angew. Chem., Int. Ed. Engl.*, 12, 36 (1973); (e) M. J. S. Dewar and R. C. Dougherty, "The PMO Theory of Organic Chemistry", Plenum Press, New York, 1975.

Table III. Mulliken Charges and Overlap Populations for Substituted Phenols

substnt	isomer	$q_\sigma(Y)^a$	$q_\sigma(X)^a$	$q_\pi(Y)^a$	$q_\pi(X)^a$	$\pi(Ph-Y)^b$	$\pi(Ph-X)^b$	Δq^c
H		+0.185		-0.102		0.052		
CH_3	ortho	+0.187	-0.015	-0.101	-0.007	0.050	0.010	+0.008
	meta	+0.186	-0.011	-0.102	-0.009	0.053	0.010	+0.006
	para	+0.186	-0.003	-0.100	-0.007	0.050	0.009	-0.004
NH_2	ortho	+0.184	+0.130	-0.094	-0.091	0.042	0.042	-0.023
	meta	+0.184	+0.138	-0.104	-0.099	0.055	0.052	+0.003
	para	+0.186	+0.140	-0.095	-0.088	0.045	0.041	-0.013
OH	ortho[d]	+0.179	+0.179	-0.095	-0.095	0.043	0.043	-0.026
	meta[d]	+0.184	+0.184	-0.105	-0.105	0.055	0.055	+0.004
	para	+0.184	+0.184	-0.096	-0.096	0.046	0.046	-0.014
F	ortho	+0.175	+0.212	-0.099	-0.069	0.048	0.029	-0.027
	meta	+0.182	+0.213	-0.105	-0.080	0.055	0.041	-0.002
	para	+0.183	+0.212	-0.100	-0.074	0.049	0.034	-0.013
NO_2	ortho	+0.165	+0.219	-0.121	+0.038	0.064	0.036	-0.002
	meta	+0.172	+0.228	-0.105	+0.028	0.054	0.034	-0.008
	para	+0.177	+0.230	-0.115	+0.039	0.061	0.035	+0.017
orthogonal NO_2	meta	+0.172	+0.240	-0.106	-0.002	0.055	0.008	
	para	+0.176	+0.246	-0.111	0.000	0.059	0.007	
CN	ortho	+0.175	+0.105	-0.114	+0.036	0.060	0.046	+0.017
	meta	+0.177	+0.101	-0.105	+0.021	0.054	0.043	-0.009
	para	+0.179	+0.104	-0.111	+0.030	0.058	0.044	+0.011
CHO	ortho	+0.184	-0.011	-0.107	+0.039	0.055	0.049	+0.021
	meta	+0.181	-0.003	-0.103	+0.031	0.053	0.047	-0.002
	para	+0.183	0.000	-0.108	+0.041	0.056	0.049	+0.012
CF_3	ortho	+0.178	+0.013	-0.107	+0.013	0.056	0.018	-0.008
	meta	+0.180	+0.019	-0.104	+0.011	0.053	0.017	-0.005
	para	+0.182	+0.024	-0.107	+0.014	0.056	0.018	+0.008
Li	ortho	+0.190	-0.265	-0.092	+0.088	0.045	0.060	-0.001
	meta	+0.197	-0.275	-0.097	+0.087	0.049	0.056	+0.012
	para	+0.194	-0.261	-0.097	+0.103	0.048	0.065	+0.011

[a] $q_\sigma(Y)$, $q_\sigma(X)$, $q_\pi(Y)$, and $q_\pi(X)$ are the total σ and π charges, respectively, donated by the substituent, Y or X, to the ring. Y = OH (or O^- for Table IV), and X = additional substituent. [b] $\pi(Ph-Y)$ and $\pi(Ph-X)$ are Mulliken overlap populations of the adjacent π-type p orbitals in the bond joining Y and X, respectively, to the ring. Y = OH (or O^- for Table IV), and X = additional substituent. [c] Δq is the difference between the sum of the absolute magnitudes of the σ and π charges transferred from the substituents to the ring in the disubstituted benzene and the sum of the absolute magnitudes of the corresponding charges transferred in the monosubstituted benzene. A positive sign indicates the charge transfer sum is greater in the disubstituted ring. q_σ and q_π data for monosubstituted benzenes required to calculate Δq are taken from ref 3. [d] Values are averaged for the two OH groups which are not equivalent.

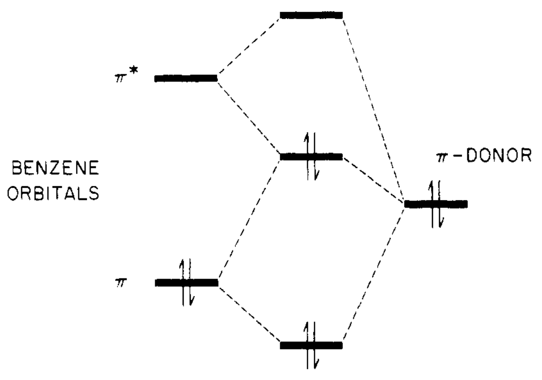


Figure 2. PMO diagram showing interaction of a π-donor substituent with π and π* orbitals of benzene, resulting in an increase in the ring LUMO energy.

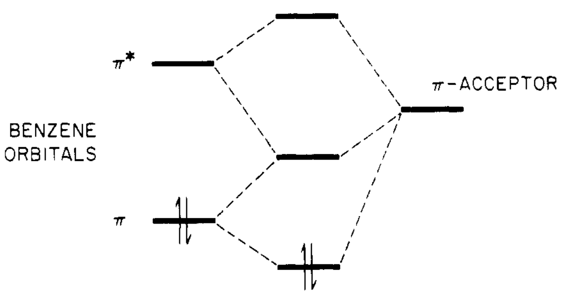


Figure 3. PMO diagram showing interaction of a π-acceptor substituent with π and π* orbitals of benzene, resulting in a decrease in the ring LUMO energy.

raise the ring π* energy levels while σ and π acceptors lower them. This affects the energy gap, ΔE (Figure 1), between the OH (or O^-) and ring orbitals and hence the extent of interaction. However, the means by which the σ and π interactions of the second substituent affect the ring π* levels appear to be different. π effects may be understood in terms of a simple PMO model. Thus a π-donor substituent interacts with benzene orbitals, as shown in Figure 2, to give an empty ring π* orbital of energy higher than before interaction. On the other hand, a π-acceptor substituent may interact with benzene orbitals to generate a new low-lying ring π* orbital (Figure 3) of energy lower than before interaction.

The effect of σ donors and acceptors appears to operate by a combination of inductive electron donation and withdrawal transmitted through the bond and some contribution from electrostatic-field interactions. The part transmitted through the bond appears to cause a change in the energies of the other molecular orbitals by the shielding and deshielding processes mentioned above. For example, an electron-withdrawing substituent on a given atom leads to a lowering of the energies of molecular orbitals associated with that atom by increasing the nuclear electronic attraction for the remaining electrons. Thus for substituted benzenes this results in a lowering of the π* levels by a σ-acceptor substituent (e.g., NO_2) and a raising of the π* levels by a σ-donor substituent (e.g., Li).

From eq 3 it may be seen that not only ΔE, the energy difference between the interacting orbitals, but also the coefficients of the atomic orbitals at the interacting centers are important in determining the magnitude of the interaction. Differences between meta and para interactions in disubstituted benzenes are best understood in terms of

Table IV. Mulliken Charges and Overlap Populations for Substituted Phenoxide Ions

substnt	isomer	$q_\sigma(Y)^a$	$q_\sigma(X)^a$	$q_\pi(Y)^a$	$q_\pi(X)^a$	$\pi(Ph\text{-}Y)^b$	$\pi(Ph\text{-}X)^b$	Δq^c	$\Delta q_t^{O^-\,d}$
H		−0.021		−0.506		0.221			0.000
CH_3	ortho	−0.022	+0.068	−0.507	+0.005	0.220	0.014	+0.060	+0.002
	meta	−0.020	+0.065	−0.508	−0.003	0.222	0.101	+0.054	+0.001
	para	−0.021	+0.085	−0.506	+0.005	0.221	0.001	+0.075	0.000
NH_2	ortho	−0.035	+0.186	−0.487	−0.058	0.212	0.016	+0.078	−0.006
	meta	−0.020	+0.191	−0.509	−0.071	0.224	0.033	+0.077	+0.002
	para	−0.028	+0.193	−0.491	−0.044	0.216	0.002	−0.006	−0.008
OH	ortho	−0.046	+0.227	−0.466	−0.077	0.206	0.025	+0.002	−0.016
	meta	−0.021	+0.233	−0.510	−0.086	0.224	0.044	+0.036	+0.003
	para	−0.029	+0.233	−0.490	−0.060	0.216	0.010	−0.002	−0.008
F	ortho	−0.032	+0.244	−0.503	−0.059	0.218	0.018	+0.016	+0.008
	meta	−0.022	+0.253	−0.513	−0.070	0.224	0.035	+0.036	+0.008
	para	−0.026	+0.250	−0.500	−0.049	0.219	0.009	−0.007	−0.001
planar NO_2	ortho	−0.011	+0.269	−0.597	+0.141	0.239	0.068	+0.233	+0.081
	meta	−0.027	+0.289	−0.524	+0.052	0.224	0.041	+0.107	+0.023
	para	+0.002	+0.278	−0.589	+0.150	0.238	0.069	+0.230	+0.059
orthogonal NO_2	meta	−0.026	+0.313	−0.526	+0.003	0.226	0.008		
	para	−0.013	+0.325	−0.548	+0.015	0.232	0.010		
CN	ortho	−0.016	+0.160	−0.553	+0.081	0.233	0.066	+0.157	+0.042
	meta	−0.025	+0.168	−0.521	+0.040	0.224	0.046	+0.101	+0.018
	para	−0.006	+0.167	−0.561	+0.095	0.233	0.069	+0.176	+0.040
CHO	ortho	−0.013	+0.048	−0.541	+0.120	0.229	0.080	+0.162	+0.026
	meta	−0.023	+0.060	−0.511	+0.057	0.222	0.054	+0.091	+0.007
	para	−0.005	+0.055	−0.557	+0.140	0.231	0.084	+0.197	+0.035
CF_3	ortho	−0.021	+0.097	−0.526	+0.029	0.228	0.030	+0.114	+0.020
	meta	−0.023	+0.094	−0.516	+0.017	0.223	0.020	+0.091	+0.012
	para	−0.014	+0.110	−0.534	+0.034	0.228	0.033	+0.133	+0.021
Li	ortho	−0.086	−0.051	−0.483	+0.219	0.215	0.112	−0.045	+0.042
	meta	−0.038	−0.055	−0.485	+0.128	0.215	0.074	−0.178	−0.004
	para	−0.001	−0.123	−0.559	+0.346	0.227	0.141	+0.145	+0.033

[a-c] See corresponding footnotes in Table III. [d] $\Delta q_t^{O^-}$ is the total charge density of the phenoxide oxygen in the substituted phenoxide relative to that (8.4727) for the parent phenoxide anion. The sign indicates increasing (−) or decreasing (+) negative charge.

the differences in the coefficients on the appropriate carbon atoms in the highest occupied molecular orbital (HOMO) of the appropriate monosubstituted benzene (i.e., of phenol or the phenoxide anion).

These general ideas may now be applied to our particular systems. We note initially that charge interactions within the σ framework are normally quite straightforward. Thus, the data in Table III show that σ acceptors (such as CN, CF_3, F, and NO_2) reduce the σ acceptance of the OH group while σ donors (such as Li) increase the σ acceptance. This is as would be expected. However, the π donation of the OH group appears to be affected by both σ and π effects of the additional substituent in a less predictable way. Whereas the π acceptors CN, CF_3, NO_2, and CHO enhance the π donation of the OH group through a lowering of the π^* orbitals of the ring (cf. Figure 2), Li, a π acceptor also, actually reduces the π donation of OH to the ring. This appears to be due to the powerful σ donation of Li which has the effect of raising the energies not only of σ-ring orbitals but also of the π and π^* orbitals as well, by the shielding effect. According to the PMO model described, a high-lying π^* orbital associated with the ring would then be less effective in interacting with the lone pair of oxygen resulting in a decrease in OH π donation. It would appear, therefore, that the energy-raising effect of σ donation by Li on the π^* orbitals more than compensates for the energy-lowering effect on the π^* orbitals of the formally vacant p orbital on Li.

One additional effect on the π donation of OH is observed for the substituents NH_2, OH, and F, which comprise a group of (decreasingly effective) π donors and (increasingly effective) σ acceptors. For these substituents, the π donation of OH is increased (compared with the effect of OH in phenol) when the substituent is meta but decreased when the substituent is para. This behavior may be understood by examination of the orbitals in the monosubstituted benzene with which the OH lone pair interacts (Figure 4).

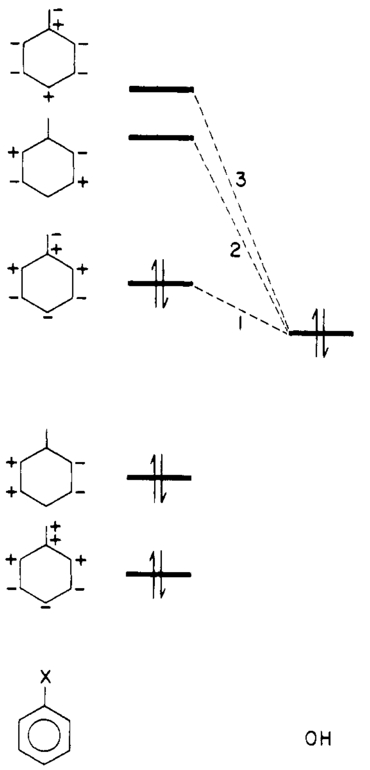
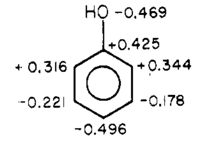


Figure 4. PMO diagram showing interaction of a monosubstituted benzene (X = NH_2, OH, or F) with the OH lone-pair orbital.

The orbital pattern for a monosubstituted benzene, where the substituent is a π donor and a σ acceptor, is schematically shown in Figure 4. The ability of the OH orbital to interact with the monosubstituted benzene is determined by several factors. (a) Introduction of an electronegative substituent into a benzene ring has the effect of lowering π and π^* orbitals by a deshielding process. (b) One of the degenerate π^* orbitals is higher in energy in the monosubstituted benzene than in benzene itself. (c) Interaction between the lone-pair OH orbital and the HOMO in the monosubstituted benzene (Figure 4, interaction 1) reduces the ability of the lone pair to interact with the π^* levels since it is now mixed in with the HOMO orbital.

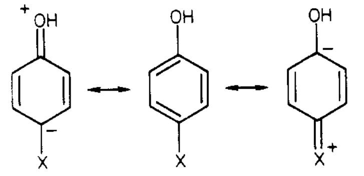
Enhanced π donation by OH at the meta position is dominated by factor a. Interaction of this type has previously been classified as a field-induced resonance effect.[10] We attribute it here to a π-inductive effect arising from the deshielding effect of an electronegative substituent. Reduced π donation at the para position is dominated by factor b, since the OH group cannot interact with the LUMO (Figure 4, interaction 2), due to symmetry constraints, but only with the orbital above the LUMO (interaction 3). The increased energy gap, consequently, brings about reduced π donation.

The reduced interaction of OH at the ortho position is brought about by factor c. The large coefficient at the ortho position in the HOMO means greater mixing of the HOMO and lone-pair orbitals (interaction 1), resulting in less effective π donation into the LUMO. For example, examination of the HOMO of phenol, **1**, indicates that coefficients of the $2p_y$ atomic orbitals on carbon are greater at the ortho (+0.316 and +0.344) positions than at the meta positions (−0.221 and −0.178).



1

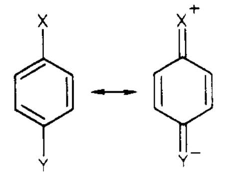
The reduced donation of π charge by OH groups into the ring when situated para (and ortho) to a second π donor has been noted previously and may be thought of as a repulsive π-saturation effect.[4,11] In resonance terms, this is equivalent to the two π donors competing with each other for conjugation with the ring and results in both contributions being reduced (eq 4). The enhanced donation by OH at the meta position is, however, not explicable in these terms (vide supra).



(4)

The interdependence of σ and π orbitals takes a different form in substituted phenoxides. Whereas a p-NO_2 group enhances π donation of O^- (from −0.506 to −0.589), it slightly increases the q_σ value of O^- (from −0.021 to +0.002) even though NO_2 is both a σ and π acceptor. This effect is contrary to what one might intuitively expect, i.e., that both σ and π donation of O^- would increase moderately with p-NO_2 substitution. The expected behavior is actually observed in m-nitrophenoxide, suggesting that the deviation of the p-NO_2 substituent stems from the particularly strong π donation of O^- when the NO_2 group is at the para position (up from −0.506 to −0.589). This strong π donation appears to lead to a comparatively electron-deficient oxygen which then compensates for the charge loss by becoming a less effective σ donor. What is significant is that it is the π charge of O^- that appears to respond to the substituent and that the σ effect then adjusts to accommodate the π effect rather than the other way around (where changes in the σ system would modify the π system).[12] This suggests that for this system π charge transfer (on a unit charge basis) is more effective in bringing about stabilization than σ charge transfer. As a result, minimum energy is obtained through enhanced π charge transfer at the expense of the less energetically effective σ charge transfer.

Useful information may be obtained by comparison of planar and orthogonal nitro groups in their interactions with phenol and the phenoxide ion. Rotation of the NO_2 from the planar to the orthogonal conformation has the effect of cutting off essentially all of the π effects associated with the group without affecting the conformationally independent σ component. The results indicate that the σ effect of the OH group is not dependent on the nitro-group conformation in either meta or para positions. Also, at the meta position, both planar and orthogonal NO_2 have similar effects on the π-donating properties of the OH group. At the para position, however, planar NO_2 enhances π donation of the OH compared with orthogonal NO_2. This merely illustrates the well-known phenomenon that a π-donor and a π-acceptor group on a para-disubstituted benzene may interact effectively through the π system and is generally expressed in terms of resonance structures (eq 5). In PMO terms the same picture may be more accurately represented by considering the interaction of the HOMO of a monosubstituted benzene (e.g., phenol, **1**) with a π acceptor (e.g., NO_2). Since the coefficient in the HOMO is substantially larger at the para position than at the meta positions, a π acceptor interacts most effectively at the para position. It is only the next phenol MO, **2**, below the HOMO that has coefficients which are large at the meta (and ortho) positions. However, due to the greater energy gap between this orbital and the vacant acceptor orbital, a weaker interaction takes place.



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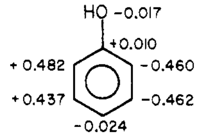

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Examination of the effect of NO_2 rotation in the nitrophenoxide ion also shows clearly that σ and π effects are closely intertwined. Thus planar NO_2 at the meta position enhances π donation by O^- from −0.506 in the unsubsti-

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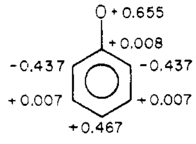
[10] T. J. Broxton, G. Butt, R. Liu, L. H. Teo, and R. D. Topsom, *J. Chem. Soc., Perkin Trans. 2*, 463 (1974).

[11] A. J. Hoefnagel, M. A. Hoefnagel, and B. M. Wepster, *J. Am. Chem. Soc.*, **98**, 6194 (1976).

[12] (a) This has been noted earlier for the meta and para carbons of monosubstituted benzenes generally, both in CNDO/2 calculations [R. T. C. Brownlee and R. W. Taft, *J. Am. Chem. Soc.*, **92**, 7007 (1970)] and in STO-3G calculations [W. J. Hehre, R. W. Taft, and R. D. Topsom, *Prog. Phys. Org. Chem.*, **12**, 159 (1976)]; (b) R. D. Topsom, *Prog. Phys. Org. Chem.*, **12**, 1 (1976); (c) R. T. C. Brownlee, G. Butt, M. P. Chan, and R. D. Topsom, *J. Chem. Soc., Perkin Trans. 2*, 1486 (1976).

tuted phenoxide to −0.524. This increase is due largely to the σ deshielding of all ring π and π^* orbitals, resulting in an enhanced donation of π charge from O^- to a ring π^* orbital, and is just the opposite of the behavior observed for the σ-shielding effect of lithium described earlier. This figure increases further to −0.589 in the para position due to the improved overlap (as reflected in larger coefficients) between the phenoxide HOMO (**3**) and the vacant NO_2 π^* orbitals. For orthogonal NO_2 at the meta position there is essentially no π charge transfer between the NO_2 substituent and the ring. Nevertheless, there is a significant enhancement of the π-charge donation of O^- because of the deshielding effect of the powerful σ-accepting NO_2 group. There is a further increase in π donation by O^- for orthogonal NO_2 at the para position. This may be attributed to greater overlap at the para position of the O^- donor orbital with the lowest unoccupied π molecular orbital of orthogonal nitrobenzene (**4**). In crude terms, this is equivalent to saying that the inductive effect of orthogonal *p*-NO_2 is relayed to O^- initially by the σ C–N bond to the ring carbon and from there through the π system (eq 6). Consistent with this, it has previously been found[3] that an orthogonal nitro substituent generates positive π charges at the ortho and para positions of the aromatic ring.



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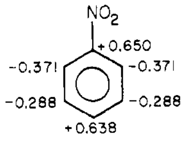

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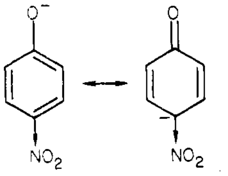
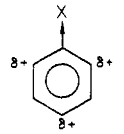


(6)

The overall conclusion is significant: namely, that a pure σ acceptor acts in much the same way as a π acceptor in that it induces significant π donation by a π donor when situated ortho and para to that donor. In the meta position this effect is less pronounced. This result appears to be a particularly good example of what has been termed the "π-inductive" effect. While the term has been applied to a number of related phenomena,[12-18] we use the expression here in the sense originally employed by Jaffé[17] and Dewar:[18] that is, changes in the π-electron density which are induced by attachment of a polar substituent onto the ring and which lead to an alternation of charge density around the ring, **5**. The effect has also been noted by Pollack and Hehre[19] for the pyridinium ion where carbon atoms ortho and para to nitrogen are calculated to have large positive charges associated with them.



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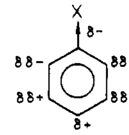

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This phenomenon is conceptually distinct from the more general effect of π polarization,[13-16] in which a charged or polar substituent on a π system polarizes that π system through its field effect, **6**. However, often the two effects are not readily distinguishable since in many cases they may be superimposed on one another.

Ortho effects have not been considered until this point. In general, ortho effects bear a close similarity to para effects. However, the possibility of direct charge interactions or H-bond chelation interactions also exists, leading to deviations from expected behavior. These will not be considered here.

Energy Interactions. The relative acidities for a number of substituted phenols are listed in Table II together with gas-phase experimental data obtained from both ion cyclotron resonance[20] and mass[21] spectrometry. As noted in a previous related study,[22] there is generally satisfactory agreement between the theoretical and experimental values. The effect of substituent on acidity depends both on π- and σ-electron properties. In gross terms, electron donation is acid weakening while electron acceptance is acid strengthening.

The theoretical results allow deeper insight into the nature of the effect of substituents on acidity through the separation of the effect of the substituent on the neutral phenol on the one hand and on the negatively charged phenoxide anion on the other. The energies of interaction between either the OH or the O^- groups and a second substituent on the ring are included in Table II. The values represent the energy changes for the reactions shown in eq 1, where Y is either OH or O^- and X is the additional substituent. The most obvious result that is observed is that energies of interaction of meta and para substituents with the charged O^- are considerably larger than those with OH. The former vary from −13.5 to +30.4 kcal mol^{-1} while the latter span a much narrower range from −1.5 to +1.3 kcal mol^{-1}. This, of course, merely supports the accepted view that the effects of substituents on phenol acidity are predominantly due to interactions in the anion.

Analysis of the σ and π charge transfer, q_σ and q_π, between the substituent and the ring is of value in understanding the interaction between substituents. In general, the greater the σ or π charge transfer between a substituent and the ring, the greater the substituent–ring stabilizing interaction. This is because charge transfers may be viewed as two-electron stabilizing interactions between two orbitals. If the effect of a second substituent is to decrease

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[13] W. F. Reynolds, I. R. Peat, M. H. Freedman, and J. R. Lyerla, Jr., *Can. J. Chem.*, **51**, 1857 (1973).

[14] A. R. Katritzky and R. D. Topsom, *J. Chem. Educ.*, **48**, 427 (1971).

[15] W. F. Reynolds, *Tetrahedron Lett.*, 675 (1977).

[16] (a) D. F. Ewing, S. Sotheeswaran, and K. J. Toyne, *Tetrahedron Lett.*, 2041 (1977); (b) W. Adcock and T. C. Khor, *J. Am. Chem. Soc.*, **100**, 7799 (1978).

[17] (a) H. H. Jaffé, *J. Chem. Phys.*, **20**, 279 (1952); (b) H. H. Jaffé, *J. Am. Chem. Soc.*, **77**, 274 (1955).

[18] (a) M. J. S. Dewar, *J. Am. Chem. Soc.*, **74**, 3340 (1952); (b) D. A. Brown and M. J. S. Dewar, *J. Chem. Soc.*, 2406 (1953); (c) M. J. S. Dewar and P. J. Grisdale, *J. Am. Chem. Soc.*, **84**, 3539 (1962).

[19] S. K. Pollack and W. J. Hehre, private communication.

[20] R. T. McIver and J. H. Silvers, *J. Am. Chem. Soc.*, **95**, 8462 (1973).

[21] T. B. McMahon and P. Kebarle, *J. Am. Chem. Soc.*, **99**, 2222 (1977).

[22] L. Radom, *J. Chem. Soc., Chem. Commun.*, 403 (1974).

the charge transfer between the original substituent and the ring, a decreased substituent–ring stabilizing interaction is brought about. Conversely, an increase in charge transfer corresponds to an increased stabilizing interaction. Since these changes in charge transfer between the substituent and the ring are induced by the second substituent, they may be viewed as either a destabilizing or a stabilizing interaction between the two substituents. In a similar manner, the effect of the first substituent on the interaction between the ring and the second substituent may also be analyzed. A convenient, albeit crude, measure of the changes in charge transfer from this point of view is provided by the difference between the sum of the absolute magnitudes of the σ and π charges transferred in the disubstituted benzene and the sum of the absolute magnitudes of the corresponding charges transferred in the two monosubstituted benzenes. The Δq values obtained in this manner are listed in Tables III and IV and are of particular value in the analysis of the interactions in the substituted phenols.

Examination of the interaction energies between OH and the substituents studied reveals that π donors (CH_3, F, OH, and NH_2) generally interact favorably with OH from the meta position but unfavorably from the para position (Table II). This behavior is just the energetic manifestation of the charge behavior discussed previously and is exemplified by the Δq values (Table III). At the para positions, there is a decrease in Δq (Table III) due to a reduction in the transfer of both σ charge (from the ring) and π charge (to the ring). The σ-charge reduction is due to the fact that the two groups are both attempting to withdraw charge from the σ-ring orbitals. The π donation of both substituents is also reduced due to the fact that both attempt to donate charge into the same π^* orbital. This reduces the effectiveness of both interactions, resulting in destabilization. At the meta position, however, there is an increase in π donation by both substituents since now each donates into different ring π^* orbitals, and, as a result of inductive withdrawal by the two substituents (or just OH in the case of CH_3), these π^* orbitals are now lower in energy. Thus while σ withdrawal at the meta position is reduced for both substituents for the same reason as for the para isomer, the π effect is energetically dominant (as was discussed earlier) and brings about a small overall stabilizing interaction.

For the substituents which are both σ and π acceptors (CN, NO_2, and CF_3), the situation is reversed. Here the para substituent interacts favorably with the OH, while the meta substituent interacts unfavorably. Examination of Table III shows that for meta substitution, Δq values are, in fact, negative, indicating a reduction in charge transfer. This reduction is due primarily to the decrease in the σ withdrawal of the OH group. There is actually an increase in the OH π donation (due to the lowering of the ring π^* orbitals by the substituent), but this is offset by the reduction in π acceptance by the substituent (due to the *deshielding* effect of OH). At the para position, however, Δq values are positive for the substituents CN, CHO, NO_2, and CF_3. This is brought about by greatly enhanced π interactions, only partially offset by reduced σ interactions.

While the stabilization energies are roughly related to Δq values, the two are not linked by general direct relationships. There are a number of possible reasons for this. First, as we have already noted, π charge transfers are energetically more effective than σ transfers. This appears to be the reason, for example, that Δq for *m*-fluorophenol is slightly negative even though the substituent interaction is stabilizing. Furthermore, there is no reason to think that all σ and π charge transfers are within themselves equally effective energetically. The phenolic hydrogen atom, which directly involves only σ charge effects of meta and para substituents, appears to be the atomic position for which there is the most direct relationship between corresponding effects on energy and charge.[23]

Table V. Approximate Inductive- (I) and Resonance- (R) Effect Contributions to the Acidities of Meta- and Para-Substituted Phenols (kcal mol^{-1})

substnt	I^a	$\sigma_I{}^c$	substnt	R^b	$\sigma_R{}^{-\,c}$
Li	−18.8	(−1.11)[d]	OH	−9.1	
CH_3	−0.2	−0.04	OCH_3	−7.8	−0.45
H	(0.0)	0.00	NH_2	−7.4	−0.45
NH_2	2.5	0.12	F	−5.8	−0.45
CHO	1.7	0.18[e]	CH_3	−0.9	−0.11
OCH_3	4.8	0.27	H	0.0	0.00
OH	6.2	0.29[f]	CF_3	4.8	0.17
CF_3	6.8	0.45	CN	10.6	0.33
F	7.4	0.50	CHO	12.2	
CN	10.8	0.56	Li	13.8	
NO_2	12.2	0.65	NO_2	17.1	0.46

[a] Obtained from eq 9 with $\alpha = 0.35$. [b] Obtained from eq 10 with $\alpha = 0.35$. [c] Parameters from ref 25 unless otherwise indicated. [d] Obtained as −18.8/17 (cf. text). [e] From J. Bromilow, R. T. C. Brownlee, D. J. Craik, M. Sadek, V. O. Lopez, and R. W. Taft, submitted for publication in *J. Org. Chem.* [f] From R. W. Taft, E. Price, I. R. Fox, I. C. Lewis, K. K. Andersen, and G. T. Davis, *J. Am. Chem. Soc.*, 85, 709 (1963).

This point is further illustrated by the effect of substituents on the total charge of the phenoxide oxygen, $\Delta q_t{}^{O^-}$, values of which are also recorded in Table IV. When these values are compared with either corresponding Δq values of Table IV or corresponding substituent stabilization energies of the phenoxide ions (Table II), only very crude parallel trends are found.

It is useful in understanding the effect of substituent on acidities to consider the approximate separation of inductive-field effects and π-electron-delocalization (resonance) effects. One means of analyzing the theoretically calculated relative acidities of meta- and para-substituted phenols in this manner is to use the empirical treatment of Taft and Lewis.[24] In the simplest form of this method, the inductive-field effect of a given substituent is assumed to be nearly equal at the meta and para positions, whereas its resonance effect is assumed to be reduced at the meta compared to the conjugated para position by a constant factor, α (typically equal to 0.3–0.5).

These assumptions are given in eq 7 and 8, in which I

$$\delta\Delta E_{(m)} = I + \alpha R \tag{7}$$

$$\delta\Delta E_{(p)} = I + R \tag{8}$$

and R are the inductive-field and resonance effects, respectively, and $\delta\Delta E_{(m)}$ and $\delta\Delta E_{(p)}$ are the theoretically calculated relative acidities for meta- and para-substituted phenols, respectively (from Table II). Eliminating R between eq 7 and 8 gives eq 9, and eliminating I between eq

$$\begin{gathered}\delta\Delta E_{(m)} - \delta\Delta E_{(p)}\alpha = I(1-\alpha)\\ \text{or } I = (\delta\Delta E_{(m)} - \delta\Delta E_{(p)}\alpha)/(1-\alpha)\end{gathered} \tag{9}$$

7 and 8 gives eq 10.

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(23) W. F. Reynolds, P. G. Mezey, W. J. Hehre, R. D. Topsom, and R. W. Taft, *J. Am. Chem. Soc.*, 99, 5821 (1977).

(24) R. W. Taft and I. C. Lewis, *J. Am. Chem. Soc.*, 80, 2436 (1958); 81, 5343 (1959).

$$\delta\Delta E_{(\mathrm{p})} - \delta\Delta E_{(\mathrm{m})} = R(1 - \alpha) \quad \text{or } R = (\delta\Delta E_{(\mathrm{p})} - \delta\Delta E_{(\mathrm{m})})/(1 - \alpha) \tag{10}$$

In Table V are given the I and R values obtained in this manner by using $\alpha = 0.35$. Values of I are given vertically according to increasing order, and this corresponds well to the classical inductive order (but not the order of the $q_\sigma(\mathrm{X})$ values of Tables III and IV). This is indicated by the values of the inductive parameter, σ_I, which are also given.[25] Theoretical calculations of the inductive order have recently been made on the basis of very different molecular systems but with similar results.[26,27] The present results are satisfactorily described by the correlation $I = 17\sigma_\mathrm{I}$. Values of R are also listed in increasing order. These results correspond *qualitatively* to the order of σ_R^- resonance effect parameters.[25] Both π-electron saturation effects (negative R values for NH_2, OH, OCH_3, and F) and direct-conjugation effects (enhanced R values for π-electron acceptors, e.g., CN and NO_2) are observed. A final point of interest is the fact that a single value of $\alpha = 0.35$ is applicable for all of the substituents in the theoretical calculations whereas for the acidities of phenols in water, enhanced resonance effects for para substituents which are strong π-electron acceptors require the use of $\alpha = 0.10$.[24] This result strongly suggests that aqueous solvent effects play an important role in exalted resonance effects at the para relative to the meta position.

As already noted, the major contributor to the values of $\delta\Delta E_{(\mathrm{m})}$ and $\delta\Delta E_{(\mathrm{p})}$, as well as to those of I and R, comes from the ionic state, i.e., the phenoxide ions. Table II discloses not only this but also the fact that the effects of substituents on the stabilities of phenols do not parallel the corresponding effects for the phenoxide ions. Thus, for example, although the para (or ortho) fluoro substituent destabilizes phenol, it stabilizes the phenoxide ion by the predominant interaction of the negative charge with the very strongly σ-accepting substituent. This I effect is more important than the R effect of the substituent. Similarly, the π acceptors m-CF_3, m-CN, and m-NO_2 also destabilize phenol but strongly stabilize the phenoxide ion.

The strongly electropositive Li substituent leads to unfavorable interactions in the phenoxide ion as expected, but a favorable π-acceptor interaction provides partial compensation at the para position. The I value of −18.8 kcal mol^{-1} for the Li substituent corresponds to $\sigma_\mathrm{I} \simeq -1.1$, much more negative (as expected) than that for any substituent for which relevant experimental information is available. The R value of 13.8 kcal mol^{-1} indicates a strong π-acceptor effect.

Conclusions

The foregoing study enables a number of points to be concluded regarding substituent effects in phenols and phenoxide ions.

(1) Both σ and π effects play significant roles in the interaction of substituents with the OH and O^- groups.

(2) π donors (e.g., OH, NH_2, F, and CH_3) interact favorably with the OH group in phenol at the meta position (due to the effect of σ withdrawal by one or both substituents on the π^* energy levels) but unfavorably at the para position (due to the effect of π donation into the same π^* orbitals).

(3) Substituents which are both σ and π acceptors (e.g., NO_2, CN, CF_3, and CHO) have a stabilizing interaction with the OH of phenol at the para position (due to the lowering by both σ and π effects of the π^* orbitals) and a destabilizing effect at the meta position (due to decreased σ withdrawal by the two substituents).

(4) A σ-accepting substituent in an aromatic ring acts in much the same way as a π acceptor by generating positive charges in the π system primarily at the ortho and para positions through a π-inductive mechanism. The mechanism produces enhanced stabilizing interactions of σ acceptors with π donors (e.g., O^- and OH) at the ortho and para positions.

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Registry No. Phenol, 108-95-2; *o*-methylphenol, 95-48-7; *m*-methylphenol, 108-39-4; *p*-methylphenol, 106-44-5; *o*-aminophenol, 95-55-6; *m*-aminophenol, 591-27-5; *p*-aminophenol, 123-30-8; *o*-hydroxyphenol, 120-80-9; *m*-hydroxyphenol, 108-46-3; *p*-hydroxyphenol, 123-31-9; *m*-methoxyphenol, 150-19-6; *p*-methoxyphenol, 150-76-5; *o*-fluorophenol, 367-12-4; *m*-fluorophenol, 372-20-3; *p*-fluorophenol, 371-41-5; *o*-nitrophenol, 88-75-5; *m*-nitrophenol, 554-84-7; *p*-nitrophenol, 100-02-7; *o*-cyanophenol, 611-20-1; *m*-cyanophenol, 873-62-1; *p*-cyanophenol, 767-00-0; *o*-formylphenol, 90-02-8; *m*-formylphenol, 100-83-4; *p*-formylphenol, 123-08-0; *o*-(trifluoromethyl)phenol, 444-30-4; *m*-(trifluoromethyl)phenol, 98-17-9; *p*-(trifluoromethyl)phenol, 402-45-9; *o*-lithiophenol, 72332-11-7; *m*-lithiophenol, 72332-12-8; *p*-lithiophenol, 72332-13-9; phenoxide, 3229-70-7; *o*-methylphenoxide, 20217-30-5; *m*-methylphenoxide, 20227-79-6; *p*-methylphenoxide, 22113-51-5; *o*-aminophenoxide, 63697-28-9; *m*-aminophenoxide, 68743-37-3; *p*-aminophenoxide, 19052-59-6; *o*-hydroxyphenoxide, 20217-29-2; *m*-hydroxyphenoxide, 20217-24-7; *p*-hydroxyphenoxide, 20217-26-9; *m*-methoxyphenoxide, 40529-20-2; *p*-methoxyphenoxide, 29368-59-0; *o*-fluorophenoxide, 32376-32-2; *m*-fluorophenoxide, 32376-33-3; *p*-fluorophenoxide, 32376-34-4; *o*-nitrophenoxide, 16554-53-3; *m*-nitrophenoxide, 16554-54-4; *p*-nitrophenoxide, 14609-74-6; *o*-cyanophenoxide, 72332-14-0; *m*-cyanophenoxide, 18938-12-0; *p*-cyanophenoxide, 14609-76-8; *o*-formylphenoxide, 38144-51-3; *m*-formylphenoxide, 38144-52-4; *p*-formylphenoxide, 18938-17-5; *o*-(trifluoromethyl)phenoxide, 72332-15-1; *m*-(trifluoromethyl)phenoxide, 72332-16-2; *p*-(trifluoromethyl)phenoxide, 72332-17-3; *o*-lithiophenoxide, 72332-18-4; *m*-lithiophenoxide, 72332-19-5; *p*-lithiophenoxide, 72332-20-8.

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(25) Values of σ_I and σ_R^- are taken from S. Ehrenson, R. T. C. Brownlee, and R. W. Taft, *Prog. Phys. Org. Chem.*, **10**, 1 (1973).

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