Determination of Hammett ρ Values for Substituted Phenylmercapto-, Phenylsulfinyl-, and Phenylsulfonylacetic Acids

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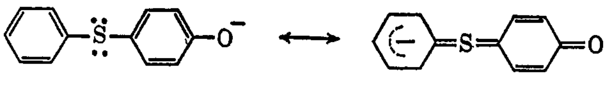
Hammett ρ values have been determined for a series of phenylmercapto-, phenylsulfinyl-, and phenylsulfonylacetic acids in water and 50% by volume dioxane–water. Comparison of these ρ values with ρ values reported previously for other similar systems indicates that the mercapto group is more effective in the transmission of inductive effects than is the methylene or oxy groups. In the present series the sulfinyl group is the least effective group for the transmission of inductive effects, with the sulfonyl group of intermediate effectiveness.

The resonance and inductive interaction of mercapto, sulfinyl, and sulfonyl groups with various systems has received a great deal of attention. Bordwell and Cooper[1] have evaluated the inductive and resonance effects of *m*- and *p*-methylmercapto and -methylsulfonyl groups on the ionization of phenols, anilinium ions, and benzoic acids. The difference in the σ constants for *p*-CH_3S– and *m*-CH_3S–, +0.14 and − 0.01, respectively, is significantly less than the difference between the σ_m and σ_p constants for methoxyl (0.39) but would still indicate the presence of a weak resonance interaction of the nonbonded electrons on sulfur with the aromatic ring. The σ_m for the CH_3SO_2– group is practically the same in the ionization of phenol, anilinium ions, and benzoic acid, whereas the σ_p constants for the CH_3SO_2– group in the ionization of phenol and anilinium ions are significantly greater, 0.26 and 0.42, respectively, than for benzoic acid. Bordwell and Cooper interpret this data as indicating the presence of appreciable resonance interaction between the phenol anion and the free aniline with the d-orbitals of sulfur.

Meyers[2] has noted similar effects in the ionization of hydroxydiphenyl sulfides, sulfoxides, and sulfones. The sulfoxide and sulfone groups increased the acidity of the phenols to a greater extent when in the *para* position indicating d-orbital resonance stabilization of the anion. From data on the hydroxydiphenylsulfides Meyers also proposed that the thio group is also capable of electron withdrawal by d-orbital interaction. This conclusion is based on the fact the *p*-phenylmercaptophenol is a stronger acid than the *meta* isomer by 0.28 p*K* units. It is interesting to note that *m*- and *p*-methylmercaptophenols have the same p*K*.[1] If d-orbital participation by sulfur is occurring in *p*-methylmercaptophenol, its effect is offset by transmission of the inductive effect of the methyl group by the sulfur atom to the aromatic ring. In *p*-phenylmercaptophenol the inductive electron-withdrawing effect of the phenyl is in the same direction as the proposed resonance effect of the sulfur atom. An additional factor in this case is the possible transmission of resonance effects through the sulfur atom as illustrated in the resonance contribution structure **1**. The sulfur atom is also capable of conjugatively transmitting π-electron spin densities in a similar fashion.[3]



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The ability of mercapto, sulfinyl, and sulfonyl groups to transmit resonance and/or inductive effects is difficult to evaluate from existing data. In an effort to assess the ability of these groups to transmit inductive effects the p*K* values of a series of substituted phenylmercapto-, phenylsulfinyl-, and phenylsulfonylacetic acids have been measured in water and 50% by volume dioxane–water.

Experimental

Substituted Thiophenols.—3-Methyl-, 4-nitro-, 4-*t*-butyl-, and 4-bromothiophenol were obtained from Aldrich Chemical Co., and 4-chlorothiophenol was obtained from Evans Chemetics Inc., New York, N. Y.

The remaining thiophenols were prepared following the procedure of Tarbell and Fukushima.[4] The corresponding substituted anilines were diazotized in aqueous hydrochloric acid with sodium nitrite and added to an aqueous solution of potassium ethyl xanthate at 50–60°. The reaction mixtures were heated on a steam bath for 0.5 hr., and the xanthates were recovered by extraction with ether. The xanthates were hydrolyzed with refluxing ethanolic potassium hydroxide for 8 hr. under a nitrogen atmosphere. The hydrolysis mixtures were poured into water, washed with ether, and acidified, and the free thiophenol was recovered by extraction with ether. The ether extract was dried over magnesium sulfate, and the solvent was then removed under reduced pressure. In many cases the crude thiophenol was used directly to prepare the substituted phenylmercaptoacetic acids.

Preparation of the Substituted Phenylmercaptoacetic Acids.—The substituted thiophenols were dissolved in aqueous base, a slight excess of chloroacetic acid was added, and the reaction mixture was heated on a steam bath 15 min. The basic solution was acidified, and the phenylmercaptoacetic acids were recovered by extraction with ether. The substituted phenylmercaptoacetic acids were repeatedly recrystallized from chloroform–petroleum ether mixtures until a sharp and constant melting point was obtained.[5] The physical properties and analytical data are contained in Table I.

Preparation of the Substituted Phenylsulfinylacetic Acids.—The substituted phenylsulfinylacetic acids were prepared by the method of Leonard and Johnson[6] by oxidation of the phenylmercaptoacetic acids with sodium metaperiodate in aqueous methanol. The phenylsulfinylacetic acids were recrystallized from chloroform–petroleum ether mixtures. The physical properties and analytical data are contained in Table I.

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[1] F. G. Bordwell and G. D. Cooper, *J. Am. Chem. Soc.*, **74**, 1058 (1952).

[2] C. Y. Meyers, *Gazz. chim. ital.*, **93**, 1206 (1963).

[3] R. E. Benson, D. R. Eaton, A. D. Josey, and W. D. Phillips, *J. Am. Chem. Soc.*, **83**, 3714 (1961); *J. Chem. Phys.*, **37**, 347 (1962).

[4] D. S. Tarbell and D. K. Fukushima, *J. Am. Chem. Soc.*, **68**, 1456 (1946).

[5] The thiophenols prepared *via* the xanthate were contaminated with the corresponding substituted phenols (indicated by infrared spectra of the crude thiophenols) which could not be effectively removed by vacuum distillation. The corresponding phenoxyacetic acids were difficult to remove from the phenylmercaptoacetic acids necessitating repeated recrystallization until satisfactory analyses were obtained.

[6] N. J. Leonard and C. R. Johnson, *J. Org. Chem.*, **27**, 282 (1962).

TABLE I

PHYSICAL CONSTANTS AND ANALYSIS OF ACIDS

Substituent	M.p., °C.	Lit. m.p., °C.	Calcd., % C	Calcd., % H	Calcd., % S	Found, % C	Found, % H	Found, % S
		Substituted Phenylmercaptoacetic Acids						
H	63.5–64.0	59–61[a]	...	...	...	...	...	...
p-CH_3	94.0–94.4	88.5–90[b]	...	...	...	...	...	...
m-CH_3	66.8–67.4	67–68[b]	...	...	...	...	...	...
p-$(CH_3)_3C$	59.8–60.2	58.5–59.0[b]	...	...	...	...	...	...
p-CH_3O	75.8–76.2	76–78[c]	...	...	...	...	...	...
m-CH_3O	62.3–63.5	62.5[d]	...	...	...	...	...	...
m-CH_3S	72.5–73.0	...	50.44	4.70	29.92	50.62	4.80	30.04
p-F	76.0–76.7	70,[e] 73[f]	...	...	...	...	...	...
p-Cl	107.0–108.0	105–107[c] 104–105[b]	...	...	...	...	...	...
p-Br	118.0–118.5	117–118[g]	...	...	...	...	...	...
m-F	73.5–74.2	71[f]	...	...	...	...	...	...
m-Cl	81.5–82.2	...	47.41	3.48	15.82	47.50	3.73	15.70
m-Br	86.8–87.6	87–89[h] 85–86[i]	...	...	...	...	...	...
p-NO_2	156.8–157.3	154[c] 149–151[b]	...	...	...	...	...	...
m-NO_2	136–137	...	45.07	3.31	15.04	45.09	3.56	14.97
		Substituted Phenylsulfinylacetic Acids						
H	116.0–117.6	116[j] 118–119.5[k]	...	...	...	...	...	...
p-CH_3	105.4–105.8	105–106[b]	...	...	...	...	...	...
m-CH_3	88.0–89.0	90–91[b]	...	...	...	...	...	...
p-$(CH_3)_3C$	129.4–130.2	125.6[b]	...	...	...	...	...	...
p-CH_3O	101.8–102.4	102–104[c]	...	...	...	...	...	...
p-F	126.0–126.8	...	47.52	3.49	15.86	47.64	3.79	16.04
p-Cl	131.5–132.5	129–131[c]	...	...	...	...	...	...
p-Br	149.0–149.5	...	36.52	2.68	12.19	36.55	2.81	12.39
m-F	103.5–104.3	...	47.52	3.49	15.86	47.75	3.84	15.86
m-Cl	109.4–109.8	...	43.94	3.23	14.66	44.10	3.27	14.52
m-Br	123.6–124.1	...	36.52	2.68	12.19	36.62	2.83	12.29
p-NO_2	182–183.5 dec.	177.0–177.5[b] 165.5–166 dec.[c]	...	...	...	...	...	...
m-NO_2	156.2–156.7	...	41.92	3.08	13.99	42.14	3.34	13.84
		Substituted Phenylsulfonylacetic Acids						
H	113–114	111.5–112.3[l]	...	...	...	...	...	...
p-CH_3	118.8–119.6	114–115[b]	...	...	...	...	...	...
m-CH_3	84.8–85.3	...	50.45	4.70	14.97	50.48	4.57	15.36
p-$(CH_3)_3C$	130.0–130.5	128–128.5[b]	...	...	...	...	...	...
p-CH_3O	114.2–115.0	...	46.95	4.38	13.93	47.14	4.51	13.80
m-CH_3O	116.5–117.0	...	46.95	4.38	13.93	46.90	4.29	13.97
p-F	106.6–107.7	...	44.04	3.23	14.69	44.10	3.48	14.77
p-Cl	124.0–124.8	120.5–121.5[b]	...	...	...	...	...	...
p-Br	148.5–149.2	...	34.43	2.53	11.49	34.41	2.57	11.86
m-F	115.0–116.0	...	44.04	3.23	14.69	44.06	3.50	14.59
m-Cl	141.0–142.0	...	40.95	3.01	13.66	41.19	3.26	13.85
m-Br	139–141	...	34.43	2.53	11.49	34.45	2.63	11.26
p-NO_2	169–172	171–172[b]	...	...	...	...	...	...
m-NO_2	122.5–123.5	...	39.19	2.88	13.08	39.31	3.06	12.95

[a] D. C. Gregg and C. A. Blood, Jr., *J. Org. Chem.*, **16**, 1255 (1961). [b] W. J. Kenney, J. A. Walsh, and D. A. Davenport, *J. Am. Chem. Soc.*, **83**, 4019 (1961). [c] G. Kresze, W. Schramm, and G. Cleve, *Chem. Ber.*, **94**, 2060 (1961). [d] G. W. Perold and P. F. A. van Lingen, *ibid.*, **92**, 293 (1959). [e] Y. E. Gerasimenko, S. M. Skein, G. G. Balsulina, A. P. Cherepivskaya, G. V. Semenyuk, and L. M. Yagupol'skii, *Zh. Obshch. Khim.*, **32**, 1870 (1962); *Chem. Abstr.*, **58**, 2524*f* (1963). [f] N. Sharghi and I. Lalezari, *J. Chem. Eng. Data*, **8**, 276 (1963). [g] D. Walker and J. Leib, *J. Org. Chem.*, **27**, 4455 (1962). [h] L. H. Werner, D. C. Schroeder, and S. Ricca, Jr., *J. Am. Chem. Soc.*, **79**, 1675 (1957). [i] C. W. Schimelpfenig, Jr., and J. J. Spurlock, *J. Org. Chem.*, **25**, 1251 (1960). [j] R. Pummer, *Ber.*, **42**, 2286 (1909). [k] See ref. 6. [l] A. C. Cope, D. E. Morrison, and L. Field, *J. Am. Chem. Soc.*, **72**, 59 (1950).

Preparation of the Substituted Phenylsulfonylacetic Acids.—The substituted phenylsulfonylacetic acids were prepared by oxidation of the phenylmercaptoacetic acids with an excess of 30% hydrogen peroxide in glacial acetic acid on a steam bath for 0.5 hr. The acetic acid solution was diluted with ice–water and extracted several times with chloroform or chloroform–ether mixtures. The extracts were dried over magnesium sulfate, and the solvent was removed under reduced pressure. The phenylsulfonylacetic acids were recrystallized from chloroform–ether and chloroform–methanol mixtures. The physical properties and analytical data are contained in Table I.

Determination of p*K* Values.—The experimental method and calculations used to determine the p*K* values have been described previously.[7] A Beckman Research Model pH meter was employed for pH measurements at 25 ± 0.3°. p*K* values were calculated incorporating the Debye–Hückel approximation for

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(7) D. J. Pasto and R. Kent, *J. Org. Chem.*, **30**, 2684 (1965).

ionic activities using a Univac 1107 high-speed computor. Table II lists the pK, root mean square deviation, and the number of points on the titration curve between 10-15 and 60–70% neutralization for the various acids in water and 50% by volume dioxane–water.

TABLE II

pK VALUES OF SUBSTITUTED ACIDS

Substituent	Water pK	Water R.m.s. dev.[a]	Water Points	50% dioxane–water pK	50% dioxane–water R.m.s. dev.	50% dioxane–water Points
			Phenylmercaptoacetic Acids			
H	3.566[b]	0.000_4	23	5.561	0.000_8	21
H	3.568[c]	0.001	15	...	...	..
p-CH_3	3.689[d]	0.001	17	5.673	0.000_4	19
m-CH_3	3.604[e]	0.000_4	17	5.630	0.000_4	21
p-$(CH_3)_3C$	3.758[f]	0.005	11	5.703	0.001	17
p-CH_3O	3.701[g]	0.000_7	21	5.723	0.001	18
m-CH_3O	3.546	0.000_0	20	5.562	0.000_3	17
m-CH_3S	3.468[f]	0.008	20	5.577	0.003	19
p-F	3.584	0.002	17	5.510	0.000_9	19
p-Cl	3.527[f,h]	0.003	15	5.422	0.000_5	22
p-Br	3.543[f]	0.003	10	5.414	0.000_8	19
m-F	3.513	0.001	22	5.410	0.000_0	21
m-Cl	3.597[f]	0.004	19	5.423	0.000_5	22
m-Br	3.530[f]	0.000_3	18	5.424	0.000_6	21
p-NO_2	3.375[f,i]	0.008	12	4.999	0.000_6	20
m-NO_2	3.400[f]	0.003	16	5.216	0.000_2	17
			Phenylsulfinylacetic Acids			
H	2.732[j]	0.004	19	4.363	0.001	24
p-CH_3	2.740	0.000_8	20	4.423	0.001	23
m-CH_3	2.756	0.000_8	16	4.424	0.002	21
p-$(CH_3)_3C$	2.773	0.002	17	4.476	0.006	20
p-CH_3O	2.754	0.001	19	4.473	0.003	18
p-F	2.653	0.005	18	4.280	0.002	19
p-Cl	2.664	0.002	17	4.259	0.004	17
p-Br	2.657	0.000_2	17	4.274	0.005	17
m-F	2.675	0.000_9	17	4.273	0.004	17
m-Cl	2.663	0.000_5	17	4.287	0.004	21
m-Br	2.674	0.001	18	4.294	0.003	21
p-NO_2	2.586	0.000_1	16	4.052	0.005	17
m-NO_2	2.624	0.002	19	4.145	0.002	17
			Phenylsulfonylacetic Acids			
H	2.513[k]	0.002	19	4.407	0.003	19
p-CH_3	2.542	0.000_7	18	4.480	0.002	22
m-CH_3	2.567	0.003	13	4.492	0.002	23
p-$(CH_3)_3C$	2.598	0.000_4	20	4.552	0.000_5	15
p-CH_3O	2.602	0.002	14	4.452	0.002	18
m-CH_3O	2.588	0.002	21	4.435	0.002	18
p-F	2.479	0.002	19	4.275	0.001	22
p-Cl	2.424	0.001	21	4.286	0.004	17
p-Br	2.519	0.002	13	4.289	0.007	14
m-F	2.432	0.002	22	4.259	0.003	18
m-Cl	2.454	0.003	22	4.300	0.003	18
m-Br	2.523	0.005	19	4.315	0.002	20
p-NO_2	2.330	0.002	16	4.014	0.005	16
m-NO_2	2.362	0.003	14	4.089	0.005	19

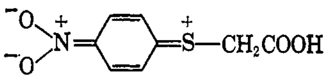
[a] Root mean square deviation. [b] Lit.[8] 3.53 and H. D. Crockford and T. B. Douglas [*J. Am. Chem. Soc.*, **56**, 1472 (1934)] reported 3.56. [c] Duplicate determination. [d] Lit.[8] 3.61. [e] Lit.[8] 3.56. [f] Procedure used for the slightly soluble acids (see Experimental). [g] Lit.[8] 3.75. [h] Lit.[8] 3.62 (±0.05). [i] Lit.[8] 3.15? [j] Crockford and Douglas (footnote *b*) reported 2.66. [k] Crockford and Douglas (footnote *b*) reported 2.64.

Sample sizes of 80–100 mg. in 75.00 ml. of water were employed except in cases of limited solubility in water. A 75-ml. aliquot of a saturated solution of the slightly soluble acid was diluted to 100.0 ml. and titrated to the end point with standardized base to determine the amount of acid in the solution. Acids for which such techniques were necessary are indicated in Table II, a few of these leading to a relatively large deviation in the Hammett plot (circled points in Figure 1 for water as solvent).

Discussion

The plots of the pK data obtained in the present studies[8] *vs.* the substituent constant σ are illustrated in Figures 1, 2, and 3. Several of the phenylmercaptoacetic acids, particularly the m-CH_3S–, m-chloro-, and p-t-butyl-, displayed limited solubility in water and may be the reason for the high degree of scattering for those three points (double circles in Figure 1).

It is of interest to note the excellent correlation of the p-nitro substituent in Figure 1 for $pK_A{}^{H_2O}$. This correspondence would indicate that a resonance contribution structure 2 is not overly important in the ground state. If 2 were an important contributing



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structure the p-nitro acid might be expected to show significant deviation from σ_p toward $\sigma_p{}^-$ (+1.27 for the nitro group). The deviations of the nitro substituents in 50% dioxane–water is probably due to changes in σ with change in solvent composition and not due to contribution by structure 2. Similarly electron donation by p-fluoro and p-methoxy to the d-orbitals of sulfur does not appear to be occurring to a significant extent. This also appears to be the case with these substituents in the phenylsulfinyl- and phenylsulfonylacetic acids series. In fact the p-fluoro group is consistently off the line in Figures 2 and 3 (double circles at σ = 0.062) and correlates much better with the σ constant for inductive interaction only[9] (only σ_I values for p-fluorine and p-methoxyl differ significantly from the normal σ values). Significant deviation of the p-methoxy group occurs only in p-methoxyphenylsulfonylacetic acid in 50% dioxane–water. The extent to which the effects of such resonance electron donation or withdrawal will be felt at the carboxyl group might be quite small and such effects might not be apparent beyond the normal scatter of experimental points. An additional factor which may be present is that a molecular conformation for favorable π-electron overlap with the d-orbitals on sulfur might not be favorable and hence the effects of such electron delocalization would not be noticeable.

The ρ values obtained from the plots in Figures 1, 2, and 3 are tabulated in Table III along with ρ values for other similar systems for comparison purposes. The ability of the mercapto group to transmit inductive effects is greater than for methylene or oxygen (see footnote *e* of Table III), probably owing to the greater polarizability of the electrons about the sulfur atom.

The ability of the sulfinyl group to transmit substituent inductive effects is significantly reduced and on going to the sulfonyl group is increased. In an independent study[7] it has been shown that phenylsulfinylacetic acid exists predominatly in the conforma-

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(8) Several of the pK values of acids encountered in this work had been measured previously [O. Behagel, *J. prakt. Chem.*, **114**, 287 (1926)] but could not be incorporated with the present data owing to the extreme scattering of points.

(9) R. W. Taft, *J. Phys. Chem.*, **64**, 1805 (1960).

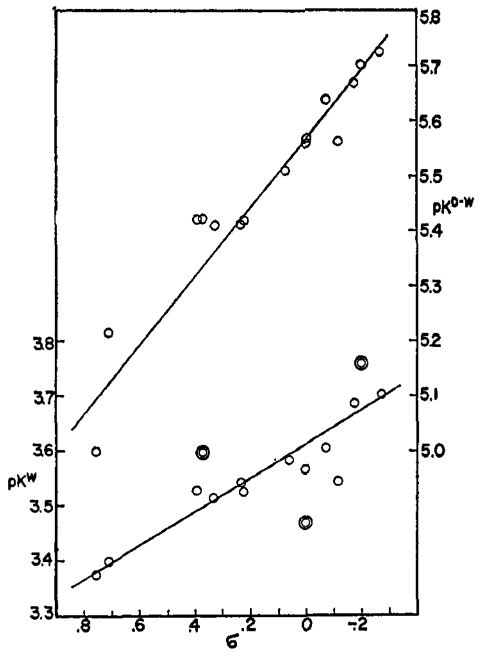


Figure 1.—Hammett plot of $pK_A^{H_2O}$ and $pK_A^{D-H_2O}$ for substituted phenylmercaptoacetic acids.

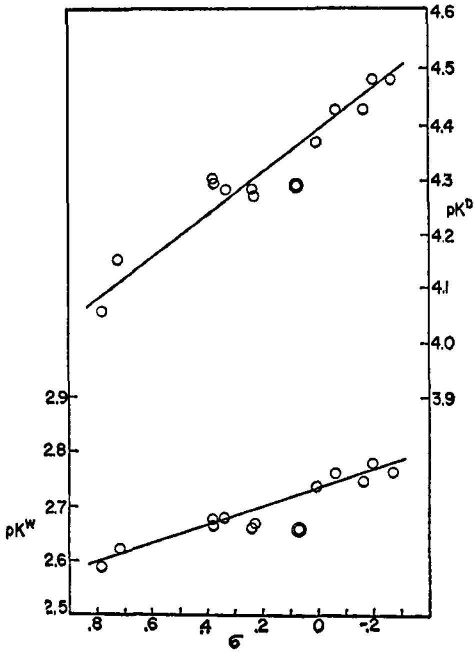


Figure 2.—Hammett plot of $pK_A^{H_2O}$ and $pK_A^{D-H_2O}$ for substituted phenylsulfinylacetic acids.

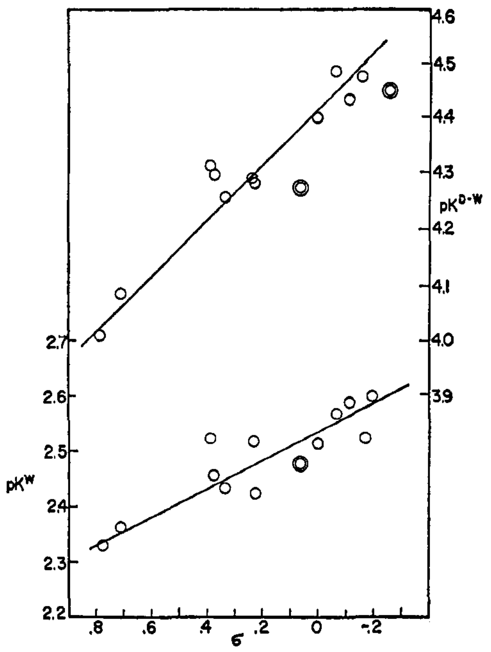


Figure 3.—Hammett plot of $pK_A^{H_2O}$ and $pK_A^{D-H_2O}$ for substituted phenylsulfonylacetic acids.

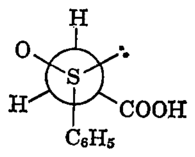
Table III

Hammett ρ Values

Acid series	Solvent	ρ value	s^a	r^b
Phenylmercaptoacetic	Water	0.300	0.053	1.000
Phenylmercaptoacetic	50% dioxane-water	0.622	0.153	0.991
Phenylsulfinylacetic	Water	0.166	0.042	0.996
Phenylsulfinylacetic	50% dioxane-water	0.380	0.106	1.000
Phenylsulfonylacetic	Water	0.253	0.061	0.994
Phenylsulfonylacetic	50% dioxane-water	0.507	0.136	0.999
Phenylacetic^c	Water	0.562	0.039	0.982
β-Phenylpropionic^c	Water	0.237	0.003	0.997
β-Phenylcinnamic^c	Water	0.418	0.019	0.995
Phenoxyacetic	Water	0.226^d	0.130	1.000
		0.342^e	0.221	0.999

[a] Standard deviation of the experimental measurements from the regression line. [b] Correlation coefficient. [c] Values taken from table in P. R. Wells, *Chem. Rev.*, **63**, 184 (1963). [d] Derived from data on *m*-chloro-, *m*-methoxy-, *m*-methyl-, *m*-nitro-, and phenoxyacetic acid in water in the authors' laboratories. [e] Calculated from data given by O. Behaghel [*J. prakt. Chem.*, **114**, 287 (1926)] for *p*-chloro-, *m*-methyl-, *p*-methyl-, *p*-nitro-, and phenoxyacetic acid. Comparison of p*K* values determined by Behagel for several substituted phenymercaptoacetic acids with those obtained in the present study is very poor, Behagel's results being high in some cases and low in others (see footnotes *d*, *e*, and *g*–*i* in Table II). The relatively large standard deviation for this ρ value would indicate that this ρ value may not be very reliable and that 0.226 may be the better value.

tion illustrated as **3** in which no intramolecular hydrogen bonding is possible. The transmission of the inductive effects by the sulfinyl group may be partially shunted into the highly polar sulfur–oxygen bond instead of being directed entirely through the methylene group to the carboxyl group, thus reducing the over-all effect. In phenylsulfonylacetic acid intramolecular hydrogen bonding is possible in all conformations and a portion of the substituent effect may be transmitted directly through the sulfur–oxygen bond, as well as through the methylene group, affecting the strength of the hydrogen bond interaction and hence the acidity of the acid. The reduction of the ρ value for the sulfonyl group relative to the mercapto group may be due to a partial loss of the substituent effect into the other sulfur–oxygen bond or due to a general decreased ability of the sulfonyl group to transmit inductive effects through the sulfur atom by a decrease in the polarizability of the electrons about the sulfur atom.



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