EFFECT OF INTRAMOLECULAR HYDROGEN BONDING ON IONIZATION CONSTANTS OF SUBSTITUTED SALICYLIC ACIDS

G. E. Dunn and Fei-lin Kung
Chemistry Department, University of Manitoba, Winnipeg, Manitoba
Received December 14, 1965

ABSTRACT

Ionization constants at 25 °C have been determined by a spectrophotometric method for 17 substituted salicylic acids. These have been fitted to the simple Hammett relationship and to the extended one proposed by Jaffe, which takes into account the transmission of substituent effects by the *o*-hydroxy group. The results with Jaffe's equation show that substituent effects on acidity are transmitted only slightly, if at all, through the intramolecular hydrogen bond of a chelate ring. Possible interpretations of the results are discussed.

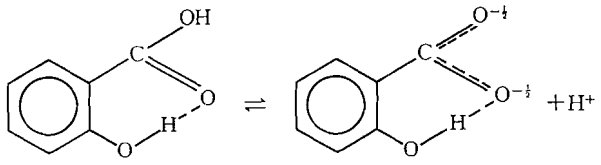
Salicylic acid is well known to be a decidedly stronger acid than benzoic or the other monohydroxybenzoic acids. The relevant ionization constants are shown in Table I, where it may be seen that the second *o*-hydroxy group in 2,6-dihydroxybenzoic acid has an even greater effect than the first. Since the hydroxy group normally has a strong resonance effect of electron release, a hydroxy group in the ortho position might have been expected

TABLE I

Ionization constants of hydroxybenzoic acids in water at 25 °C (1)

Substituent	$K \times 10^5$	$K/K_{benzoic}$
Benzoic	6.30	1.0
m-Hydroxy	8.33	1.32
p-Hydroxy	2.62	0.42
o-Hydroxy	105	16.7
2,6-Dihydroxy	6 000	952

to decrease the strength of a benzoic acid just as it does when in the para position. The anomalous increase in acid strength produced by an *o*-hydroxy group is commonly attributed to intramolecular hydrogen bonding between the phenolic hydroxyl and the carboxyl group (2–8). Among the hydroxybenzoic acids, chelation is possible only for the ortho isomer and, since it would be expected to be stronger in the anion than in the unionized acid, it should stabilize the anion more than it does the acid and so cause increased ionization.



If the above argument is correct, then a substituent in the 4- or 5-position of salicylic acid should influence the ionization constant by two paths. For example, an electron-withdrawing group, such as nitro, in the 5-position should exert its normal acid-strengthening influence on the carboxyl group by way of the usual combination of

inductive, field, and resonance effects, as in the corresponding nitrobenzoic acid. This effect would be represented in terms of the Hammett relationship (9) by

$$\log K/K_0 = \rho_1\sigma_1, \quad [1]$$

where K is the ionization constant of 5-nitrosalicylic acid, K_0 is that of salicylic acid, σ_1 is the Hammett substituent constant for the *m*-nitro group, and ρ_1 is Hammett's reaction constant for the ionization of salicylic acids under the conditions concerned. Second, the substituent should have a similar but larger effect on the acidity of the phenolic group, thus increasing the strength of the chelating hydrogen bond and so exerting a further acid-strengthening influence on the carboxyl group. This second effect would be represented by

$$\log K/K_0 = \rho_2\sigma_2^-, \quad [2]$$

where σ_2^- is the Hammett *p*-nitro substituent constant for use with phenols and amines (Hammett's σ^*), and ρ_2 is a Hammett reaction constant representing the susceptibility of the ionization of salicylic acids to subsequent influences by way of the chelate hydrogen bond. Jaffe (10) has shown that influences through the two paths should be additive, so that the overall effect of a substituent should be given by

$$\log K/K_0 = \rho_1\sigma_1 + \rho_2\sigma_2^-. \quad [3]$$

He found (10) that, in the case of the salicylic acids, eq. [3] was not an improvement over eq. [1]. Jaffe attributed this to the fact that the six substituents for which data were available (11) were such that σ_1 and σ_2 are linearly related, so that for these substituents eqs. [1] and [3] become indistinguishable. He proposed that eqs. [1] and [3] can be distinguished only when the correlation coefficient between σ_1 and σ_2 is less than 0.9.

Since there was available in our laboratory a collection of sixteen 4- and 5-substituted salicylic acids prepared in connection with a study of their decarboxylation (12), it appeared to be worthwhile to determine their ionization constants, both for comparison with their rates of decarboxylation and for a test of eq. [3]. The fact that the correlation constant between σ_1 and σ_2^- for the 16 acids is 0.723 makes them particularly suitable for the latter purpose. The present paper reports the results of these determinations.

EXPERIMENTAL

Materials

The 5-methyl-, 4-nitro-, 5-nitro-, 4-hydroxy, 5-hydroxy-, 5-bromo-, 4-ethoxy-, 5-chloro-, and 5-iodosalicylic acids, as well as salicylic acid itself, were commercial products. The 4-methoxy- and 5-methoxysalicylic acids were prepared by methylating the corresponding hydroxy acids (12). All the acids were purified to constant melting point by one or more recrystallizations from water or aqueous ethanol; the melting points reported are for the recrystallized acids. All melting points were determined with a Hershberg melting point apparatus (13) by using calibrated Anschütz thermometers, and are expressed in degrees Centigrade.

3-Methylsalicylic Acid

A product sold commercially under the name 2,4-cresotic acid (m.p. 166.8–168.0°) and consequently supposed to be 4-methylsalicylic acid (2-hydroxy-4-methylbenzoic acid) was found to have an ionization constant which, according to the Hammett parameters derived from the other salicylic acids, was inconsistent with its supposed structure. Decarboxylation of the acid with copper powder in hot quinoline gave a cresol which was converted into the dibromo derivative by the usual method (14). This derivative produced no depression in the melting point when mixed with the dibromo derivatives prepared from an authentic sample of *o*-cresol. The "2,4-cresotic acid" must therefore have its methyl and hydroxyl groups ortho to each other. Its large ionization constant (0.962×10^{-3}) shows that the carboxyl and hydroxyl groups are also ortho to each other, so that the acid must be 3-methylsalicylic acid (2-hydroxy-3-methylbenzoic acid). Melting points of the *p*-bromophenacyl, *p*-nitrobenzyl, acetyl, and dinitro derivatives confirm this structure. Its ionization constant is therefore reported in Table III under the heading 3-methylsalicylic acid.

4-Methylsalicylic Acid

This acid was prepared by treating 4-methylanthranilic acid with nitrous acid. A solution of 7.6 g of 4-methylanthranilic acid in 33 ml concentrated sulfuric acid and 45 ml water was cooled to 0–5° and stirred while 4 g sodium nitrite in 10 ml water was added dropwise over a period of 10 min. The mixture was stirred for another 15 min, and then poured into 200 ml boiling water. When this solution was cooled, 4-methylsalicylic acid precipitated out; after two recrystallizations from water 1.1 g (14.5%) melting at 177.0–177.8° (lit. (15) m.p. 172°) was recovered.

4-Cyanosalicylic Acid

This acid was prepared from 4-aminosalicylic acid by the Sandmeyer reaction. A solution of 10.0 g of 4-aminosalicylic acid in 30 ml of concentrated sulfuric acid and 60 ml water was cooled to 0–5° and stirred while 20 g sodium nitrite in 100 ml water was added slowly until the mixture gave a positive test with starch–iodide paper. The cold solution was poured into 200 ml water containing 14.5 g cuprous cyanide and enough potassium cyanide to keep the latter in solution. The mixture was warmed to 60° for half an hour, and then filtered. The residue was extracted with three 200 ml portions of ether, and 4-cyanosalicylic acid was recovered from the ether. After several recrystallizations from water the yield was 0.2 g (2%) melting at 228.0–229.0° (lit. (16) m.p. 227–229°).

5-Cyanosalicylic Acid

This compound has not previously been reported in the literature. The cyano group was introduced by the method of Friedman and Schechter (17). A solution of 11.9 g 5-iodosalicylic acid and 4.65 g cuprous cyanide in 50 ml dimethylformamide was refluxed for 2 days. The resulting brown mixture was cooled and poured into a solution of 10 g ferric chloride hexahydrate in 30 ml concentrated hydrochloric acid and 30 ml water. This mixture was heated on a steam bath for half an hour, and then extracted with three 200 ml portions of ether. The extract was washed with aqueous sodium bisulfite, dried, and evaporated. The residue, after several recrystallizations from water, yielded 3.1 g (43%) of 5-cyanosalicylic acid melting at 224.0–225.0°. The characteristic nitrile band in the infrared spectrum of the acid was present at 2 230 cm^{-1}.

Anal. Calcd. for $C_8H_5NO_3$: C, 58.90; H, 3.09; N, 8.59. Found: C, 58.90; H, 3.12; N, 8.77.

Method

A spectrophotometric method was chosen for the determination of the ionization constants because it had been used previously in this laboratory on anthranilic acids (18) and could be extended, if desired, to include the overlapping ionization constants of the zwitterionic aminosalicylic acids.

For the ionization of a monoprotic acid in water,

$$HB \rightleftarrows H^+ + B^-,$$

the ionization constant may be expressed by

$$K = \frac{[H^+][B^-]}{[HB]},$$

where the quantities in brackets represent molar concentrations or, at high ionic strengths, activities. If the total concentration of acid (ionized plus un-ionized) is C, then

$$K = \frac{[H^+][B^-]}{C - [B^-]} = \frac{[H^+](C - [HB])}{[HB]},$$

so that

$$[B^-] = \frac{KC}{[H^+] + K} \quad \text{and} \quad [HB] = \frac{C[H^+]}{[H^+] + K}.$$

Since hydronium ion does not absorb in the visible or ultraviolet regions, the total absorbance, A, of the equilibrium solution of HB is given by

$$A = A_{HB} + A_B,$$

where A_{HB} is the absorbance of the equilibrium concentration of un-ionized acid HB, and A_B is the absorbance of the equilibrium concentration of anion B^-. For a 1 cm cell the Beer–Lambert relationship converts the preceding equation into

$$A = \epsilon_{HB}[HB] + \epsilon_B[B^-],$$

where ϵ = molar absorptivity.

When the expressions for [HB] and $[B^-]$ derived above are introduced, this becomes

$$A = C \times \frac{\epsilon_{HB}[H^+] + \epsilon_B K}{[H^+] + K}. \qquad [4]$$

Since A, $[H^+]$, and C are observable quantities, eq. [4] contains only three unknowns: K, ϵ_{HB}, and ϵ_B.

In principle, ϵ_{HB} and ϵ_B can be determined experimentally by measurements made in strongly acidic and strongly basic solutions, respectively. However, these strongly acidic and basic solutions will have much larger ionic strengths than are necessary in the equilibrium region, and it is desirable to make all measurements at the same low ionic strength. Hence, in the present work the absorbances were measured at one wavelength for several (usually 16) different values of $[H^+]$ in the equilibrium region at an ionic strength of 0.01, and all three unknowns were obtained by fitting the data to eq. [4] by the least squares method (19). All measurements were made at the same total concentration of a substituted salicylic acid, so that the actual value of C is unimportant provided it is such as to give absorbances suitable for measurement. It varied from acid to acid, but averaged about 10^{-4} M.

The apparatus and procedure for choosing appropriate wavelengths, concentrations, and pH ranges, as well as for making the measurements of pH and absorbances, are the same as those previously described (18).

RESULTS

Figure 1 shows the ultraviolet absorption spectra of salicylic and 5-nitrosalicylic acids at pH values of about 0, 3, and 9. The spectra of all the other acids resembled that of salicylic

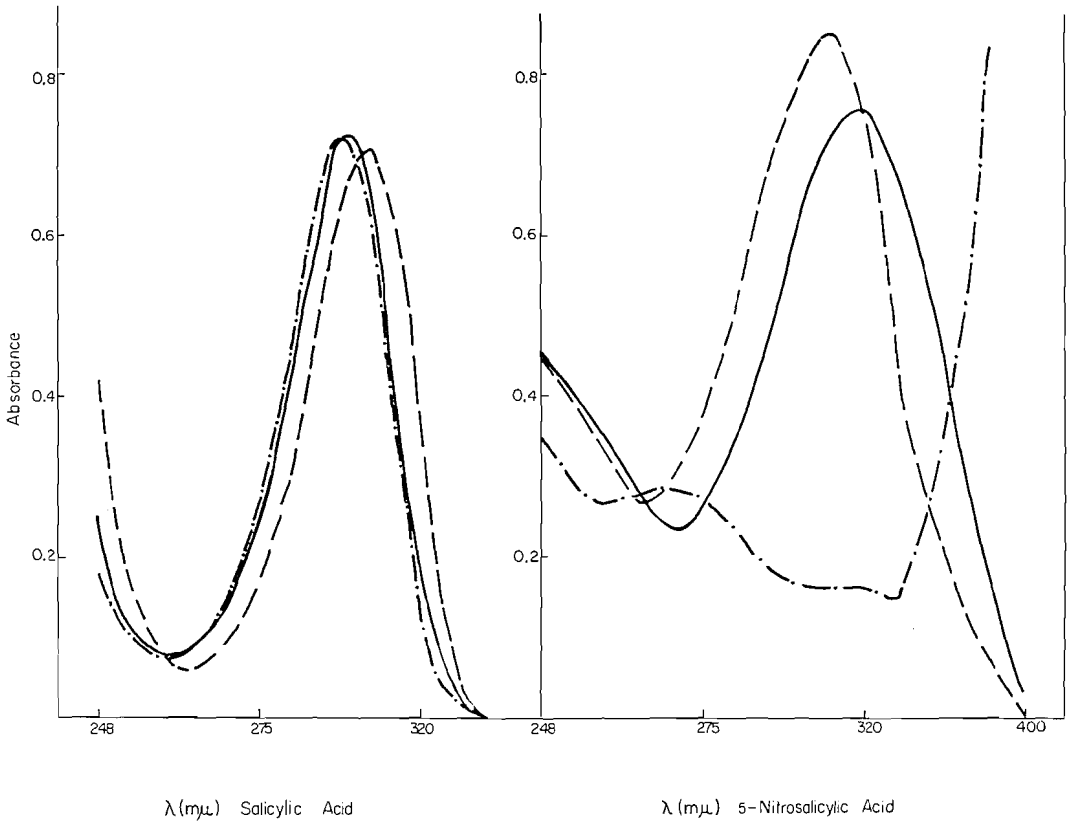


FIG. 1. Effect of pH on the ultraviolet spectra of salicylic acids. LEGEND: —, formate buffer (pH ~ 3); — —, 1 N hydrochloric acid; —·—, ammonia buffer (pH ~ 9).

acid, with small shifts in wavelength and absorptivity as the substituents varied. The 5-nitro acid is distinctly different from the others, no doubt because the p-nitro substituent activates the phenolic group to the point where it is significantly ionized at pH 9.

The absorbance and pH data obtained for salicylic and 5-nitrosalicylic acids are reported in Table II. In Fig. 2, the experimental points are compared with the curves calculated by using the data of Table II to solve eq. [4]. The measurements in 1 N hydrochloric acid and ammonia buffers (shown as the first and last items of Table II) were used to provide the

TABLE II

Variation of absorbance with pH for salicylic and 5-nitrosalicylic acids at 25 °C and $\mu = 0.010$

Salicylic acid, 2.5×10^{-4} M			5-Nitrosalicylic acid, 0.9×10^{-4} M		
Buffer*	pH	A (313 mμ)	Buffer*	pH	A (310 mμ)
1.0 N HCl	—	0.653	1.0 N HCl	—	0.946
HCl	0.649	0.652	HCl	0.652	0.938
HCl	1.115	0.648	HCl	1.145	0.933
HCl	1.538	0.639	HCl	1.562	0.924
HCl	2.065	0.617	HCl	2.082	0.902
HCl	2.291	0.593	HCl	2.285	0.890
HCl	2.489	0.570	HCl	2.474	0.880
ACl	2.702	0.533	ACl	2.691	0.869
ACl	2.897	0.500	ACl	2.884	0.858
ACl	3.075	0.470	ACl	3.060	0.854
ACl	3.276	0.432	ACl	3.276	0.850
ACl	3.482	0.405	ACl	3.497	0.846
F	3.628	0.387	F	3.658	0.845
F	3.817	0.369	F	3.860	0.844
F	3.999	0.357	F	4.130	0.843
A	4.970	0.328	A	4.995	0.840
A	5.832	0.328	A	5.815	0.840
NH_3	9	0.328	NH_3	9	0.194

*F = formate, A = acetate, ACl = chloroacetate.

preliminary estimates of $C\epsilon_{HB}$ and $C\epsilon_B$ required for fitting eq. [4]. They were not included among the points to be fitted because they were obtained at ionic strengths greater than 0.01, but they are reported for comparison with the values of $C\epsilon_{HB}$ and $C\epsilon_B$ obtained from eq. [4]. For salicylic acid they may be compared with the calculated values $C\epsilon_{HB} = 0.653$

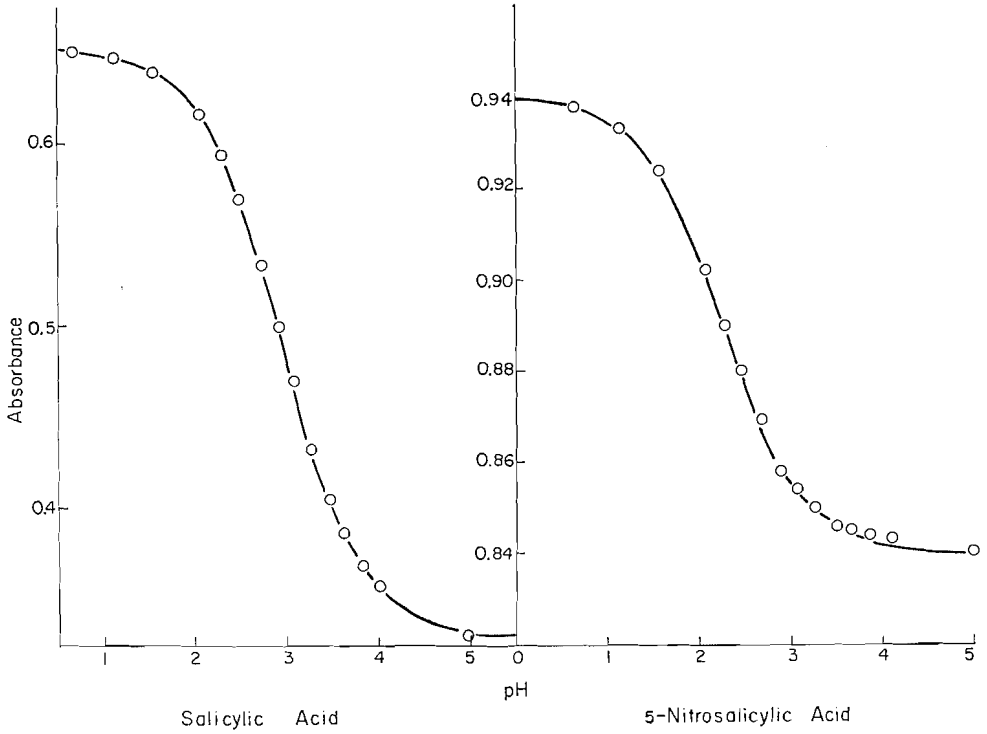


FIG. 2. Determination of ionization constants. LEGEND: O, experimental points; —, line calculated from eq. [4] by using the least squares values of K, $C\epsilon_{HB}$, and $C\epsilon_B$.

$\pm$ 0.005 and $C\epsilon_B = 0.328 \pm 0.003$; the agreement is equally good for all the other acids except the 5-nitro acid. For this acid eq. [4] gives $C\epsilon_{HB} = 0.940 \pm 0.008$ and $C\epsilon_B = 0.840 \pm 0.004$, which are in good agreement with the data of Table II at pH $\sim$ 0 and 6, respectively, but not with that in ammonia. This is further evidence that the phenolic group of 5-nitrosalicylic acid is significantly ionized at pH $\sim$ 9.

Table III shows the ionization constants of the various substituted salicylic acids and their standard deviations obtained from the least squares fit of the data to eq. [4]. Also

TABLE III

Ionization constants of substituted salicylic acids at 25 °C

Substituent	λ (mμ)	Concentration $\times 10^4$ M	$K \times 10^3$		
			μ = 0.010	Thermodynamic	Literature
4-OCH_3	305	1.4	0.532±0.018	0.494±0.017	
4-OH	255	0.4	0.635±0.009	0.591±0.008	0.505 (21); 0.605 (22)
4-OC_2H_5	305	1.6	0.679±0.021	0.630±0.020	
4-CH_3	308	1.8	0.830±0.037	0.770±0.034	0.72 (23)
5-CH_3	325	2.5	1.002±0.033	0.931±0.030	0.86 (23)
3-CH_3	318	2.4	1.033±0.031	0.962±0.029	1.018 (23); 1.00 (11)
None	313	2.5	1.107±0.031	1.02±0.03	1.05 (24); 1.06 (25)
5-OH	337	2.2	1.117±0.036	1.04±0.02	1.08 (21)
5-OCH_3	342	2.0	1.239±0.032	1.15±0.03	
4-Br	315	2.0	1.991±0.079	1.85±0.07	
5-Cl	325	3.0	2.148±0.111	1.99±0.10	1.97 (26); 2.35 (27); 2.23 (25)
5-I	325	3.0	2.153±0.094	2.00±0.09	
5-Br	328	3.0	2.618±0.086	2.43±0.08	2.44 (27); 2.40 (21); 2.20 (25)
5-CN	270	2.5	4.519±0.180	4.19±0.16	
4-CN	334	2.0	4.808±0.181	4.46±0.16	
5-NO_2	310	0.9	5.188±0.170	4.82±0.16	7.59 (27); 8.00 (28)
4-NO_2	288	0.8	5.309±0.406	4.93±0.36	5.88 (27)

shown are the wavelengths and concentrations at which the absorbance and pH measurements were made. The last column of Table III gives literature values for the ionization constants of those acids for which they are available. For comparison with these, thermodynamic ionization constants were estimated from our observed ionization constants by multiplying each by 0.929, the activity of the unsubstituted salicylate ion at an ionic strength of 0.010 reported by Kielland (20).

It is seen that our calculated thermodynamic ionization constants agree reasonably well with the literature values except for the nitro acids. Here the 4-nitro acid is stronger than the 5-nitro, where previous workers found the opposite order. The earlier results were obtained by a conductometric method, and it appears that they could be too high because of the phenolic ionization which our spectra show to be strongly activated in the 5-nitro acid by the *p*-nitro group. It may be noted that only one of the literature values was considered to be sufficiently reliable to be included in the I.U.P.A.C. tabulations of dissociation constants, although all but one were available when the compilation was made (1).

DISCUSSION

Jaffe has proposed (10) that eqs. [1] and [3] can be distinguished only when σ_1 and σ_2 have a correlation coefficient less than 0.9. For the 16 acids used in the present work, this correlation coefficient is 0.723. The σ values were taken from Hine's tables (8) by using σ^- for σ_2 when dealing with the 5-nitro and 5-cyano acids.

The data of Table III were fitted by the least squares method (19) to eq. [1] in the form

$$\log K = \rho_1\sigma_1 + \log K_0.$$

Since the standard deviations of log K were very similar for all substituents, the points were weighted equally. The calculated value of ρ_1 is 0.889 ± 0.061, and of log K_0 is -2.989 ± 0.025 (observed, -2.991 ± 0.013). The external estimate of error* (s_{ext}) is 0.0524. Figure 3 shows the data and the calculated line as a plot of log K against σ_1. The fit appears to be as good as that found in most other Hammett plots.

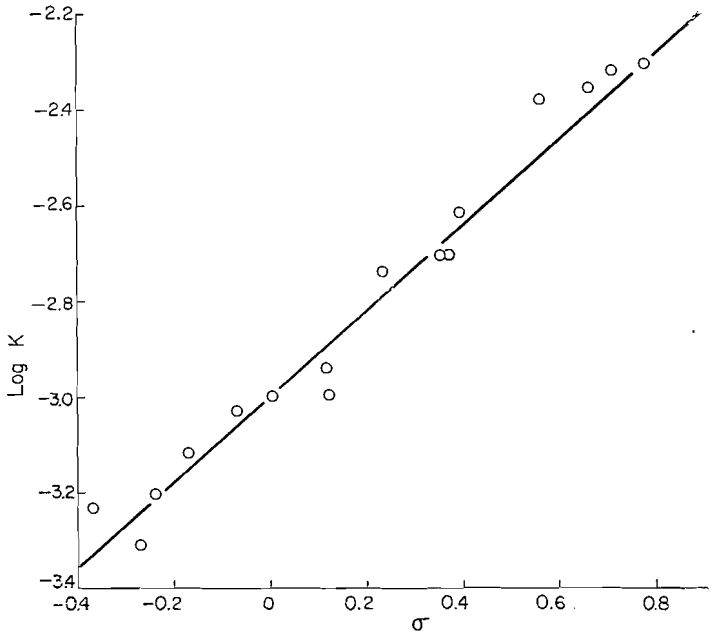


FIG. 3. Hammett plot of σ vs. the data from Table III.

The least squares fit (19) of the same data to eq. [3] in the form

$$\log K = \rho_1\sigma_1 + \rho_2\sigma_2 + \log K_0$$

gives $\rho_1 = 0.820 \pm 0.038$, $\rho_2 = 0.101 \pm 0.046$, log $K_0 = -2.997$, and $s_{ext} = 0.0454$. It is seen that ρ_2 is very small (only about double its standard deviation). The Student's t test (19) indicates that ρ_2 differs from zero only at the 95% confidence level (conditions under which Jaffe considers eq. [3] to be not significantly better than eq. [1] (10)). Consequently, we may conclude that the electronic effects of substituents upon the ionization constants of salicylic acids are transmitted only very slightly, if at all, through the phenolic hydroxyl group.

The reason for the failure of the chelate ring to transmit a substituent effect to the carboxyl group is not obvious. Comparison of the ionization constants reported in Table III with those in Table I shows that the range of ionization constants produced by changing substituents in salicylic acid is one-fourth as large as the difference in the ionization constants of salicylic and *p*-hydroxybenzoic acids. If the latter difference is produced entirely by chelation, it is surprising that the former one is independent of chelation. Several possible interpretations present themselves, but none is unequivocal.

For example, it might be argued that the variation in phenolic acidity produced by substituents is not large enough to affect the strength of the intramolecular hydrogen bond

The external estimate of error, s_{ext}, is given by $s_{ext}^2 = \sum (y - \bar{y})^2/n$, where y is log K observed, $\bar{y}$ is log K calculated from the equation, and n is the degrees of freedom ($n = 14$ for eq. [1] and 13 for eq. [3]).

significantly. Rubin and Panson (29), however, have shown that substituents in phenols do produce significant changes in the strength of intermolecular hydrogen bonds with pyridine. The ρ value for this complex formation in carbon tetrachloride is about +1. It would therefore seem probable that substituents should have a significant effect on the strength of chelation in salicylic acids.

An extension of the above argument suggests that an electronic effect which makes the phenolic group more acidic (strengthening chelation) will make the carboxylate group less basic (weakening chelation), so that the intramolecular hydrogen bond will be little affected by substituents. No doubt these opposing effects do exist, but they strengthen the expectation that the data should fit eq. [3] rather than eq. [1]. This can perhaps best be seen by considering them in an equation of the Hammett form. The total effect of a substituent on the ionization constant of a substituted salicylic acid would then involve three terms, which could be represented by

$$\log K/K_0 = \rho_1\sigma_1 + \rho_2\sigma_2 + \rho_3\sigma_3. \qquad [5]$$

The first term ($\rho_1\sigma_1$) corresponds to the usual substituent effect found in benzoic acids, the second term represents the substituent effect on the acidity of the phenolic group, and the third term represents the effect of the substituent on the basicity of the carboxylate ion. Since the first and third terms represent processes taking place at the carboxyl group, σ_1 applies to both; but since the second term represents the acidity of the phenolic group, σ_2 is different. For example, a 4-substituted acid has $\sigma_1 = \sigma_p$ and $\sigma_2 = \sigma_m$, whereas a 5-substituted acid will require $\sigma_1 = \sigma_m$ and $\sigma_2 = \sigma_p$. Hence, eq. [5] reduces to

$$\log K/K_0 = (\rho_1 + \rho_3)\sigma_1 + \rho_2\sigma_2,$$

which is equivalent to eq. [3]. Furthermore, since ρ_3 will be negative and ρ_1 positive, some cancellation will occur between ρ_1 and ρ_3, and this will tend to diminish the importance of the "direct" route for substituent influence in comparison with the "indirect" one via the intramolecular hydrogen bond.

Another obvious way to explain the absence of an "indirect" substituent effect is to suppose that in aqueous solution intramolecular hydrogen bonding is replaced by intermolecular hydrogen bonds between anion and solvent. The probability of the survival of chelate hydrogen bonds in aqueous solutions of carboxylic acids has been debated much (30, 32), but remains uncertain. Concerning salicylate ion, there is very little evidence, except that from ionization constants. Voroshin and Vlasov interpret the ultraviolet spectrum of sodium salicylate as indicating the presence of a chelate hydrogen bond in ethanol solution (31), and Chapman *et al.* reach similar conclusions from an infrared study of sodium salicylate in heavy water (32). Certainly, it is very difficult to account for the enhanced ionization of *o*-hydroxybenzoic acid over the para acid without recourse to chelation in the anion. It is true that other benzoic acids having bulky ortho substituents show a similarly enhanced ionization in aqueous solution, as shown in Table IV, and this is usually attributed to destabilization of the un-ionized acid by steric interference, with conjugation between the carboxylic group and the aromatic ring (4, 5, 8, 30, 33). However, the hydroxy group is much smaller than any of the other ortho groups which increase benzoic acid ionization, and its effect is larger. It is possible that in aqueous solution solvation of the phenolic group may increase its effective size, but whether this could be large enough to account for the enhanced acidity of salicylic acids is, at present, impossible to say. Further work on the transmission of substituent effects through chelation is in progress.

TABLE IV

Ionization constants of substituted benzoic acids in water at 25 °C (1)

	$K \times 10^5$	
Substituent	Ortho	Para
None	6.30	6.30
Methyl	12.35	4.24
Ethyl	16.1	4.44
Isopropyl	23.15	4.43
t-Butyl	29.1	3.98
Fluoro	54.1	7.22
Chloro	119.8	10.32
Bromo	140	9.95
Iodo	137	—

ACKNOWLEDGMENT

The authors are grateful to the National Research Council for a grant in aid of this project.

REFERENCES

1. G. KORTÜM, W. VOGEL, and K. ANDRUSSOW. Dissociation constants of organic acids in aqueous solution. Butterworths, London. 1961.
2. W. BAKER. J. Chem. Soc. 1687 (1934).
3. G. E. K. BRANCH and D. L. YABROFF. J. Am. Chem. Soc. **56**, 2568 (1934).
4. C. K. INGOLD. Structure and mechanism in organic chemistry. Cornell University Press, Ithaca, New York. 1953. pp. 744–749.
5. H. C. BROWN, D. H. MCDANIEL, and O. HÄFLIGER. *In* Determination of organic structures by physical methods. Vol. I. *Edited by* E. A. BRAUDE and F. C. NACHOD. Academic Press, Inc., New York. 1955. pp. 603–629.
6. E. S. GOULD. Mechanism and structure in organic chemistry. Henry Holt & Co., New York. 1959. p. 30.
7. G. C. PIMENTEL and A. L. MCLELLAN. The hydrogen bond. W. H. Freeman & Co., San Francisco. 1960. p. 182.
8. J. HINE. Physical organic chemistry. 2nd ed. McGraw-Hill Book Co., Inc., New York. 1962. p. 100.
9. L. P. HAMMETT. Physical organic chemistry. McGraw-Hill Book Co., Inc., New York. 1940.
10. H. H. JAFFE. J. Am. Chem. Soc. **76**, 4261 (1954).
11. J. SHORTER and F. J. STUBBS. J. Chem. Soc. 1180 (1949).
12. G. E. DUNN and E. G. JANZEN. Unpublished work.
13. E. B. HERSHBERG. Ind. Eng. Chem. Anal. Ed. **8**, 312 (1936).
14. R. L. SHRINER, R. C. FUSON, and D. Y. CURTIN. The systematic identification of organic compounds. 4th ed. John Wiley & Sons, Inc., New York. 1960.
15. T. MUKAI, M. KUNORI, H. KISHI, T. MUROI, and K. MATSUI. Proc. Japan Acad. **27**, 410 (1951).
16. H. BRETSCHNEIDER and W. KLOTZER. Monatsh. Chem. **82**, 13 (1951).
17. L. FRIEDMAN and H. SCHECHTER. J. Org. Chem. **26**, 2522 (1961).
18. P. LEGGATE and G. E. DUNN. Can. J. Chem. **43**, 1158 (1965).
19. W. E. DEMING. Statistical adjustment of data. John Wiley & Sons, Inc., New York. 1944.
20. J. KIELLAND. J. Am. Chem. Soc. **59**, 1677 (1937).
21. J. KENDALL. Medd. Kgl. Vetenskapakad. Nobelinst. **2**, 38 (1913); Chem. Abstr. **8**, 1044 (1914).
22. C. T. ABICHANDANI and K. K. F. JATKAR. J. Indian Chem. Soc. **16**, 385 (1939).
23. F. STOHMANN and H. LANGBEIN. J. Prakt. Chem. **50**, 399 (1894).
24. L. J. MINNICK and M. J. KILPATRICK. J. Phys. Chem. **43**, 259 (1939).
25. Z. L. ERNST and J. MENASHI. Trans. Faraday Soc. **59**, 230 (1963).
26. A. COPPADORO. Gazz. Chim. Ital. **32**, 542 (1902).
27. L. G. BRAY, J. F. J. DIPPY, R. C. HUGHES, and J. W. LAXTON. J. Chem. Soc. 2405 (1957).
28. G. MAGNANINI. Gazz. Chim. Ital. **21**, 215 (1891).
29. J. RUBIN and G. S. PANSON. J. Phys. Chem. **69**, 3089 (1965).
30. D. H. MCDANIEL and H. C. BROWN. Science, **118**, 370 (1953). R. E. DODD, R. E. MILLER, and W. F. K. WYNNE-JONES. J. Chem. Soc. 2790 (1961), and references therein.
31. E. M. VOROSHIN and V. G. VLASOV. Zh. Obsch. Khim. **30**, 3004 (1960).
32. D. CHAPMAN, D. R. LLOYD, and R. H. PRINCE. J. Chem. Soc. 550 (1964).
33. G. S. HAMMOND and D. H. HOGLE. J. Am. Chem. Soc. **77**, 338 (1954). G. FERGUSON and J. M. ROBERTSON. *In* Advances in physical organic chemistry. Vol. I. *Edited by* V. Gold. Academic Press, Inc., New York. 1963. pp. 241–242, and references therein.