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The Substituent Effect. I. Normal Substituent Constants from the Hydrolysis of Substituted-benzyl Benzoates

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The rates of the alkaline hydrolyses of 24 *m*- and *p*-substituted-benzyl benzoates were measured in 70% (v/v) aqueous acetone at 25°C. The given set of σ^0 constants was precisely identical with our standard set derived from *m*- and *p*-substituted ethyl phenylacetates. The general utility of σ^0 constants is demonstrated for unexalted and exalted resonance reactivities as the reference scale in our LArSR equation:

$$\log k/k_0 = \rho(\sigma^0 + r^+\Delta\bar{\sigma}_R^+ + r^-\Delta\bar{\sigma}_R^-)$$

The accommodation of extensive data makes it evident that the Hammett equation in its original form[1] fails to correlate the substituent effect of *para* electron-releasing groups on the electrophilic reactivity with the same line, such as *meta* substituents.[2-4] The resonance theory clearly anticipates that the conjugatively electron-releasing *para* substituents can interact strongly by resonance with the electron-deficient reaction center and that, in consequence, such *para* substituents deviate from the correlation line of the uninteracting substituents.[2-7] The effect of the resonance interaction can vary with reactions, depending on the degree of electron deficiency of the reaction site at the transition state relative to the ground state (or the final to initial state). The effect of *meta* substituents is approximately independent of such an interaction, so as to give generally satisfactory correlations with the Hammett σ_m values.[6,7] It is, therefore, necessary to introduce an additional term for *para* substituent effects taking this interaction into account in order to improve the Hammett relation for these reactions.

With this point in mind, we proposed Eq. (1) for correlating the effect of substituents on the electrophilic reaction of benzene derivatives;[8,9]

$$\log k/k_0 = \rho(\sigma^0 + r\Delta\bar{\sigma}_R^+) \qquad (1)$$

where r is the variable describing the degree of resonance, and where the parameter, $\Delta\bar{\sigma}_R^+$, which corresponds to $\sigma^+ - \sigma^0$ in Brown and Okamoto's scale,[3] is the substituent constant measuring the capacity of substituents to donate electrons by resonance.

σ^0 is the substituent constant defined originally by Taft[5,6] as the measure of the insulated substituted phenyl polar effect; we practically determined a set of reliable σ^0 values from the substituent effects on the alkaline hydrolysis of ethyl phenylacetates.[9]

The generality of this linear aromatic substituent reactivity (LArSR) relationship (1) was demonstrated by applying it to about 70 representative reactions with excellent precision.[9] Thereafter, our LArSR Eq. (1) has been utilized to describe the substituent effects on various electrophilic reactions and to elucidate the mechanism of reactions by a number of investigators.[9]

The same type of treatment has been shown to apply to the effects of conjugatively electron-attracting (+R) substituents on σ^--type nucleophilic reactions.[9] Eq. (1) can be thus modified as a generalized form to Eq. (2);

$$\log k/k_0 = \rho\sigma^0 + \phi^\pm \qquad (2)$$

$$\phi^+ = \rho r^+\Delta\bar{\sigma}_R^+ \text{ and } \phi^- = \rho r^-\Delta\bar{\sigma}_R^-$$

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[1] L. P. Hammett, *J. Amer. Chem. Soc.*, **59**, 96 (1937); "Physical Organic Chemistry", McGraw-Hill, New York (1940), Chapt. 7.

[2] Y. Tsuno, T. Ibata, and Y. Yukawa, This Bulletin, **32**, 960 (1959); Y. Yukawa and Y. Tsuno, *ibid.*, **32**, 965 (1959).

[3] H. C. Brown and Y. Okamoto, *J. Amer. Chem. Soc.*, **79**, 1914 (1957); *ibid.*, **80**, 4979 (1958); H. C. Brown, "Advances in Physical Organic Chemistry", Vol. 1, Academic Press, New York (1963), Chap. 2.

[4] P. R. Wells, *Chem. Rev.*, **63**, 171 (1963).

[5] R. W. Taft, Jr., *J. Phys. Chem.*, **64**, 1805 (1960).

[6] R. W. Taft, Jr., and I. C. Lewis, *J. Amer. Chem. Soc.*, **80**, 2436 (1958); *ibid.*, **81**, 5343 (1959); R. W. Taft, Jr., S. Ehrenson, I. C. Lewis, and R. E. Glick, *ibid.*, **81**, 5354 (1959).

[7] H. van Bekkum, P. E. Verkade, and B. M. Wepster, *Rec. Trav. Chim.*, **78**, 815 (1959).

[8] Y. Yukawa and Y. Tsuno, This Bulletin, **32**, 971 (1959).

[9] Y. Yukawa, Y. Tsuno, and M. Sawada, *ibid.*, **39**, 2274 (1966).

where $\Delta\bar{\sigma}_R^-$ is defined in the same way as $\Delta\bar{\sigma}_R^+$ by the quantities, $\sigma^- - \sigma^0$, for *para* +R substituents. Eq. (2) is essentially a separation of the general substituent effect on benzene reactivities into the insulated aryl polar effect, $\rho\sigma^0$, and additional pi-resonance exaltation effects, ϕ^+ and ϕ^-.

In view of the importance of the σ^0 constant as the standard of our LArSR relationship, and also of other relevant equations, it is necessary to examine more critically the generality of our set of σ^0 constants in practical reactivity correlations. In this connection, we have derived a set of σ^0-type substituent constants from the substituent effect on the alkaline hydrolysis of substituted benzyl esters of benzoic acid, where additional pi-electronic interaction of substituents with the reaction center is precluded structurally by an intervening methylene group.

The present paper will be mainly concerned with a comparison of this new set of substituent constants with our standard set of σ^0 constants, and also with a statistical examination of the applicability and limitation of these substituent constants.

Experimental

Materials. Almost all of the *meta-* and *para-*substituted-benzyl benzoates were successfully prepared by the esterification of benzoyl chloride with the corresponding carbinols in pyridine.[10] Carbinols were obtained from the appropriate ethyl or methyl benzoates by the $LiAlH_4$ reduction[11] except for nitro derivatives. *m-* and *p-*Nitrobenzyl alcohols were obtained by the Meerwein-Ponndorf reduction[12] of the corresponding aldehydes. Next, five benzyl esters were obtained as follows.

m- *or* p-*Methylsulfonylbenzyl Benzoate*: A mixture of *m-* or *p-*methylmercaptobenzyl benzoate (7 g), glacial acetic acid (40 m*l*), and 30% aq. hydrogen peroxide (11 m*l*), was heated under reflux for 4 hr. After the usual procedure, the crude methylsulfonylbenzyl benzoate (6 g) obtained was recrystallized from benzene - hexane or benzene - ligroin.

p-*Methylsulfinylbenzyl Benzoate*: *p-*Methylmercaptobenzyl benzoate (6 g) and 30% aq. hydrogen peroxide (11 m*l*) in acetone (200 m*l*) were allowed to stand at room temperature for 6 days. After the removal of the solvent, the residue was taken up in benzene and ether. The organic layer was washed with an aq. Na_2CO_3 solution and dried. A solid product (5.5 g) was recrystallized from aq. EtOH or benzene - ligroin to give colorless needles.

m- *or* p-*Cyanobenzyl Benzoate*: A solution of *m-* or *p-*bromobenzyl benzoate and cuprous cyanide in DMF was refluxed for 4 hr. The hot solution was then treated by Friedman's method.[13] Recrystallization from ligroin - benzene or 80% aq. EtOH gave pure esters.

All of the esters were purified by fractionation or recrystallization. The physical constants and the elemental analysis

Table 1. Physical constants and analytical data of arylcarbinyl benzoates

Substituent	Bp (mmHg) or Mp	Carbon		Hydrogen		Other	
		Found	Calcd	Found	Calcd	Found	Calcd
H	111.5 (0.3)[a]	79.40	79.23	5.82	5.70		
p-CH_3	169—171 (5)	79.98	79.62	6.60	6.24		
m-CH_3	143.5 (0.7)	79.97	79.62	6.61	6.24		
p-C_2H_5	156.5 (1)	79.77	79.97	6.80	6.71		
p-*i*-Pr	159.5—160.5 (0.6)	80.18	80.28	7.13	7.13		
p-*t*-Bu	170.5 (3), 46	80.71	80.56	7.55	7.51		
p-CH_3O	158 (1.3)[b]	74.68	74.36	5.55	5.83		
p-C_6H_5O	202—204 (1.5)	78.92	78.93	5.26	5.30		
p-CH_3S	203—203.5 (5)	70.41	69.74	5.46	5.46	12.56	12.41 (S)
m-CH_3S	203—205 (5)	69.90	69.74	5.42	5.46	12.47	12.41 (S)
p-F	127 (0.7)						
p-Cl	59[c]	67.90	68.16	4.68	4.49	14.15	14.37 (Cl)
m-Cl	153—154 (1.1)	68.40	68.16	4.78	4.49	14.37	14.37 (Cl)
p-Br	47—48[d]	58.02	57.76	4.10	3.81	27.20	27.45 (Br)
m-Br	154—155 (0.8)	57.97	57.76	3.38	3.81	27.73	27.45 (Br)
p-NO_2	88.5[e]	65.40	65.37	4.31	4.31	5.62	5.44 (N)
m-NO_2	71	65.18	65.37	4.16	4.31	5.45	5.44 (N)
p-CN	64.5—65.5	75.86	75.94	4.56	4.67	5.78	5.90 (N)
m-CN	44.5—45	76.02	75.94	4.57	4.67	6.10	5.90 (N)
p-$SOCH_3$	70.5—71	65.73	65.67	5.14	5.14	11.42	11.69 (S)
p-SO_2CH_3	96.0—96.5	61.87	62.05	4.79	4.86	11.13	11.04 (S)
m-SO_2CH_3	78.5—79	61.78	62.05	4.84	4.86	11.13	11.04 (S)

a) "Organic Syntheses", Coll. Vol. 1, p. 104. b) B. Gastambide and J. Blanc, *Bull. Chim. Soc. France*, **1962**, 2064; *C. A.*, **58**, 12455d (1963). c) T. Suehiro, S. Hibino, and T, Saito, This Bulletin, **41**, 1707 (1968). d) B. A. Fiekers and E. M. DiGeronimo, *J. Amer. Chem. Soc.*, **70**, 1654 (1948). e) E. J. Bourne, M. Stacey, J. C. Tatlow, and J. M. Tedder, *J. Chem. Soc.*, **1949**, 2976.

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[10] M. L. Bender, H. Matsui, R. J. Thomas, and S. W. Tobey, *J. Amer. Chem. Soc.*, **83**, 4193 (1961).

[11] W. G. Brown, "Organic Reactions", Vol. 6, John Wiley and Sons, New York, (1942), Chapt. 10.

[12] A. L. Wilds, "Organic Reactions", Vol. 2, Chapt. 5.

[13] L. Friedman and H. Shechter, *J. Org. Chem.*, **26**, 2522 (1961).

data of these esters are listed in Table 1.

Solvent. Acetone which had been treated with potassium permanganate was distilled, dried over potassium carbonate, and fractionated. The stock solution of 70% aqueous acetone was made up by mixing 70 parts (by volume) of acetone with 30 parts (by volume) of freshly-boiled, deionized water.

Kinetic Measurements. The rates of the alkaline hydrolyses of all the arylcarbinyl benzoates were determined in a 70% (v/v) aqueous acetone solution at 25.00°C±0.01 by means of the usual titration method. The procedure employed for those measurements was essentially the same as that described in the literature.[14] The aqueous acetone solution of sodium hydroxide was freshly prepared and standardized frequently. The reaction was started by mixing up solutions containing exactly equimolar amounts of the ester and alkali to give an initial concentration of about 0.02 mol/*l* in the final mixture. Ten m*l* samples were withdrawn from the reaction flask at appropriate intervals, quenched with 10 m*l* of a HCl solution of a known concentration (about 0.03—0.04 N) and about 10 m*l* of acetone, and back-titrated with a standardized NaOH solution of about 0.02 N, bromothymol blue being used as the indicator. The end point was obtained by comparison with the color standard of sodium benzoate in 70% aq. acetone containing the same amount of indicator as was used in the titration. For nitro, cyano, methylsulfinyl, and methylsulfonyl derivatives, a low initial concentration of about 0.01 mol/*l* was employed because of the higher reaction rate to be followed by titration, and a 15 m*l* aliquot was utilized in each titration.

The initial titer, C_0, was determined by the use of the alkaline solution alone. All runs which involved more than 11 measurements followed the second-order kinetic law, covering up to an 80% reaction. The bimolecular rate constant, k_2, was obtained from the plot of $(C_x-C_0)/t$ against C_x, where C_x was the titer at $t=X$. The experimental uncertainty of a run was estimated to be much better than 2%, and the rate constants from repeated runs agreed within ±2% or better.

TABLE 2. RATE CONSTANTS OF ALKALINE HYDROLYSIS OF ARYLCARBINYL BENZOATES IN 70% (v/v) AQ. ACETONE AT 25°C

Substituent	$10^3\times k_2$ [a]	Substituent	$10^3\times k_2$ [a]
H	6.74	*p*-F	10.7
p-Me	5.13	*p*-Cl	12.8
m-Me	5.77	*m*-Cl	15.8
p-Et	5.02	*p*-Br	13.2
p-*i*-Pr	4.88	*m*-Br	16.6
p-*t*-Bu	4.56	*p*-NO_2	43.2
p-MeO	4.79	*m*-NO_2	33.3
p-PhO	7.57	*p*-CN	33.9
p-MeS	7.57	*m*-CN	29.8
m-MeS	8.88	*p*-SOMe	24.7
p-Ph	7.35	*p*-SO_2Me	36.8
2-Naph[b]	7.74	*m*-SO_2Me	32.7

a) $l\cdot mol^{-1}\cdot sec^{-1}$. b) 2-Naphthyl group.

Results and Discussion

Table 2 lists the rate constants of the hydrolyses of 24 *m*- and *p*-substituted-benzyl benzoates in 70% (v/v) aqueous acetone at 25°. A precise Hammett relation was followed only by *meta* substituted and *para* +R substituted derivatives. The reaction constant, ρ_m, was obtained by fitting a regression line to log *k* against σ_m for *meta* substituents (including unsubstituted one); $\rho_m=0.981$, $(\log k_0)_{calc}=-2.169$; correlation coefficient, 0.999, and standard deviation, ±0.005.[15] From the structural features of the present system, it can be expected that the substituent effect can be described in terms of the σ^0 constants.

The plot of $\log k/k_0$ against σ^0 gives an excellent straight line for all *meta* and *para* substituents, as is shown in Fig. 1. The ρ value obtained by least-squares fitting was 0.978 with a satisfactorily high precision; correlation coefficient, 0.999, and standard deviation, ±0.010.[16] The correlational parameters are identical to the above ρ_m and intercept within the precision on the order of experimental uncertainty. These facts indicate that alkaline hydrolysis of arylcarbinyl benzoates is a typical σ^0 reactivity in which any additional resonance effect of the direct conjugation between aryl groups and the reaction center is completely absent.

As has been pointed out frequently, most of σ^0 reactivities available are comparatively less sensitive to the substituent change because of the attenuating effect by intervening methylene. Naturally, the uncertainty involved in the derived set of substituent constants is inevitably larger. The fact that the present reaction resulted in an excellent σ^0 plot with a relatively high ρ value is highly appreciated; thus, this reaction may be utilized as the secondary reference in the determination of σ^0 constants. Apparent

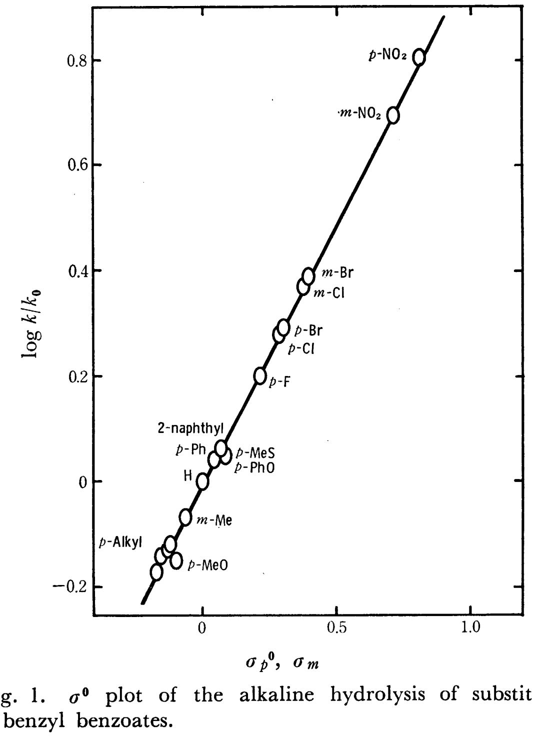

Fig. 1. σ^0 plot of the alkaline hydrolysis of substituted-benzyl benzoates.

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[14] D. P. Evans, J. J. Gordon, and H. B. Watson, *J. Chem. Soc.*, **1937**, 1430.

[15] *n*(numbers of substituents) = 5.

[16] *n* = 15.

TABLE 3. COMPARISON OF VARIOUS SETS OF σ^0 AND σ

Substituent	σ^0			σ[d]	Substituent	σ^0			σ[d]
	Previous[a]	Present[b]	Taft's[c]			Previous[a]	Present[b]	Taft's[c]	
p-Me	−0.124	−0.123	−0.15	−0.170	*m*-Me	−0.069	−0.070	−0.07	−0.069
p-Et	−0.131	−0.133		−0.151	*m*-F	0.337		0.35	0.337
p-i-Pr	−0.156	−0.145			*m*-Cl	0.373	0.375	0.37	0.373
p-t-Bu	−0.174	−0.175		−0.197	*m*-Br	0.391	0.397	0.38	0.391
p-MeO	−0.100	−0.152	−0.12	−0.268	*m*-MeS		0.120		
p-PhO	0.076	0.049		(−0.061)	*p*-CN		0.714	0.69	0.653 (0.720)
p-MeS	0.083	0.049		(−0.047)	*p*-SOMe		0.573		(0.564)
p-F	0.212	0.203	0.17	0.062	*p*-SO_2Me		0.749		(0.721)
p-Cl	0.281	0.282	0.27	0.227	*p*-NO_2	0.778	0.821	0.82	0.778
p-Br	0.30	0.296	0.26	0.232	*m*-CN		0.655	0.62	0.607 (0.671)
p-Ph	0.039	0.037			*m*-SO_2Me		0.697		(0.659)
2-Naph	0.062	0.059		0.042	*m*-NO_2	0.710	0.705	0.70	0.710

a) Previous set of σ^0 derived from hydrolysis of ethyl phenylacetates (Ref. 9). For *meta* substituents σ_m values are taken. b) Apparent σ^0 calculated by $\rho_m=0.981$. c) Ref. 5. d) Hammett σ constants. In parentheses the apparent σ calculated from hydrolysis rates of ethyl benzoates in 85% aq. ethanol (Ref. 17).

TABLE 4. SUMMARY OF CORRELATIONS OF σ^0 TYPE REACTIVITIES[a]

No.	Reaction	ρ	s[1]	R[2]	n[3]	Ref.[4]
1	Saponification, ethyl arylacetates, 60% acetone, 25°	0.978			21	5
2	Saponification, X-benzyl benzoates, 70% acetone, 25°	0.978	0.010	0.9992	15	6
3	pK_a, Phenylacetic acids, water, 25°	0.480	0.012	0.9966	11	7
4	Saponification, benzyl acetates, 60% acetone, 25°	0.796	0.017	0.9984	8	8
5	Phenylacetic acids with diphenyldiazomethane. EtOH, 36°	0.353	0.011	0.9975	6	9
6	Saponification, ethyl arylacetates, 88% EtOH, 30°	1.021	0.023	0.9984	7	10
7	Saponification, ethyl arylacetates, 85% EtOH, 25°	1.104	0.036	0.9965	10	11
8	Saponification, ethyl arylpropionates, 88% EtOH, 30°	0.638	0.012	0.9988	11	12
9	Saponification, ethyl arylpropionates, 88% EtOH, 30°	0.635	0.011	0.9989	6	13
10	pK_a, Benzylammonium ions, water, 25°	1.089	0.033	0.9958	11	14
11	Saponification, ethyl arylcyclopropylcarboxylates, 88% EtOH, 30°	0.882	0.020	0.9982	8	13
12	pK_a, *trans*-Arylcyclopropylcarboxylic acids, 50% EtOH, 25°	0.517	0.016	0.994	7	15
13	pK_a, *N*-(2,4-dinitrophenyl)-X-benzylammonium ions, water, 25°	1.703	0.055	0.9956	9	16
14	Benzylamines with 2,4-dinitrochlorobenzene, azeotropic EtOH, 45°	−0.761	0.027	0.994	12	17

a) The Hammett type correlation based on the standard set of $\sigma_p{}^0$ and σ_m. Reference numbers in the last column refer to those below the table rather than those in the text.

1) Standard deviation. 2) Correlation coefficient. 3) The number of substituents involved in the calculation. 4) Reference numbers refer to the following rather than those cited in the text. 5) Ref. 9 in the text. 6) Present study. 7) J. F. J. Dippy and J. E. Page, *J. Chem. Soc.*, **1938**, 357; J. F. J. Dippy, S. R. C. Hughes, and J. W. Laxton, *ibid.*, **1934**, 1470; *ibid.*, **1954**, 4102; J. F. J. Dippy and F. R. Williams, *ibid.*, **1934**, 161; J. F. J. Dippy and R. H. Lewis, *ibid.*, **1937**, 1426. 8) E. Tommila and C. N. Hinshelwood, *ibid.*, **1938**, 1801; E. Tommila, *Ann. Acad. Sci. Fennicae*, Ser. A 59, No. 4, 3 (1942); *Chem. Abstr.*, **38**, 6172^9 (1944). 9) R. M. O'Ferrall and S. I. Miller, *J. Amer. Chem. Soc.*, **85**, 2440 (1963). 10) K. Kindler, *Ann. Chem.*, **452**, 90 (1927); A. Fischer, J. Packer, J. Vaughan, A. F. Wilson, and E. Wong, *J. Org. Chem.*, **24**, 155 (1959). 11) J. G. Watkinson, W. Watson, and B. L. Yates, *J. Chem. Soc.*, **1963**, 5437. 12) R. Fuchs and J. A. Caputo, *J. Org. Chem.*, **31**, 1524 (1966). 13) R. Fuchs and J. J. Bloomfield, *ibid.*, **28**, 910 (1963). 14) L. F. Blackwell, A. Fischer, R. D. Topsom, and J. Vaughan, *J. Chem. Soc.*, **1964**, 3588. 15) R. Fuchs, C. A. Kaplan, J. J. Bloomfield, and L. F. Hatch, *ibid.*, **27**, 733 (1962). 16) A. Fischer, M. P. Hartshorn, O. M. Senanayake, and J. Vaughan, *J. Chem. Soc.*, *B*, **1967**, 833. 17) A. Fischer, R. S. H. Hickford, G. R. Scott, and J. Vaughan, *ibid.*, *B*, **1966**, 466.

σ^0 values calculated by using the ρ_m value of 0.981 are given in Table 3, together with our previous set of σ^0 values, which were determined by the alkaline hydrolysis of ethyl phenylacetates.[9] Taft's values[5] are also given for the sake of comparison. The present set agrees generally with our previous set of σ^0 values within ±0.01 in σ unit. Good agreement is also found between ours and Taft's set of σ^0 values within the usual limits of precision of substituent constants.

In the last column of the table, the standard set of σ values is also included for further comparison. The difference between σ^0 and σ is significant for conjugatively electron-releasing (−R) *para* substituents; the σ^0 values are less effectively electron-releasing than the σ values for all these *para* groups. This, of course, arises from the effective through-conjugation of these −R groups with the reaction center, COOH, in the σ-reference reaction, pK_a of benzoic acids. On the other hand, no significant difference between the two sets is observed in conjugatively electron-attract-

TABLE 5. COMPARISON OF APPARENT σ^0 VALUES[a]

X[b] / Y[c]	1[d]	2	3	4	5	6	7
p-Me	−0.124	−0.122	−0.112	−0.113		−0.113	−0.130
m-Me	−0.074	−0.069		−0.067			
p-MeO	−0.100	−0.151[e]	−0.093	−0.112	−0.14[e]	−0.117	−0.100
m-MeO					0.06		−0.005[e]
p-F	0.212	0.206	0.142[e]	0.209			0.193
m-F	0.352						
p-Cl	0.281	0.285	0.261	0.302	0.28	0.320	0.298
m-Cl	0.336	0.379	0.365		0.41		0.344
p-Br	0.30	0.299	0.267	0.284			0.327
m-Br	0.351	0.400					
p-I			0.288	0.286	0.33		0.315
m-I			0.325	0.266	0.45		0.328
p-NO_2	0.808	0.825		0.806	0.77	0.761	0.758
m-NO_2	0.713	0.710	0.728	0.679			0.753
p-CN		0.718					
m-CN		0.660					
p-NH_2					−0.33	−0.364	−0.323
p-Et	−0.131	−0.131	−0.118				
p-i-Pr	−0.156	−0.143	−0.158				
p-t-Bu	−0.174	−0.174	−0.212				

X[b] / Y[c]	8	9	10	11	12	13	14
p-Me	−0.127	−0.132	−0.123	−0.112		−0.086	−0.102
m-Me	−0.052		−0.040			−0.098	−0.091
p-MeO	−0.130	−0.092	−0.095	−0.139	−0.11		−0.152[e]
m-MeO	0.047		0.107			0.131	0.067
p-F	0.196		0.097[e]			0.084[e]	0.172
m-F	0.317		0.336			0.397	0.360
p-Cl	0.290	0.287	0.244	0.278	0.32	0.260	0.326
m-Cl	0.373	0.398	0.364	0.403	0.35		0.375
p-Br			0.253	0.301	0.31	0.254	0.296
m-Br			0.391		0.35	0.378	0.422
p-NO_2	0.790	0.763	0.832	0.768	0.89	0.812	0.732[e]
m-NO_2	0.719		0.694	0.702	0.73	0.707	0.711
p-CN						0.736	0.681
m-CN						0.654	0.635
p-NH_2	−0.332						

a) Evaluated from the correlational parameters in Table 4. b) Substituent. c) Reaction number in Table 4.

d) $\sigma^0_{p\text{-COMe}} = 0.491$, $\sigma^0_{m\text{-COMe}} = 0.389$.

e) Values which are not included in the derivation of averaged σ^0 (Table 8).

ing (+R) *para* substituents where no through-conjugation with the conjugatively electron-attracting reaction center, COOH, is effectively operative in σ-reactivities.

In *para* electron-attracting groups, the nitro group gives a slightly higher σ_p^0 value, 0.82, than the σ_p value, but for others the σ_p values appear to be generally applicable as substitute for the σ^0 values. The σ^0 values for $SOCH_3$ and SO_2CH_3 do not appear to have been well-examined, but the obtained values are practically in accord with the corresponding σ values. *Meta-* and *para*-cyano groups give slightly higher values than the corresponding σ values, but consistent behavior was observed for the cyano groups in the hydrolysis of ethyl benzoates in aqueous ethanol.[17]

The apparent σ^0 value for the *p*-methoxy group, −0.15, is obviously different from the standard σ^0 value, −0.10. Taft has statistically derived dual σ^0 constants for this group, −0.16 in non-aqueous solutions and −0.12 in aqueous solutions.[5] The substituent constant for the methoxy group is considerably sensitive to the solvent change; this variation may be due to the change in the degree of the hydrogen-bonding interaction of the solvent with the basic oxygen of the methoxy group. In the case of the *p*-phenoxy group, the solvent interaction with the substituent will be less effective because of the lower basicity of the oxygen and because of the highly-crowded circumstances around it.

The solvent effect on the substituent constants may be expected to operate more or less effectively for all

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[17] Y. Yukawa, Y. Tsuno, and M. Sawada, unpublished.

polar substituent groups, not only for electron-releasing groups but also for electron-attracting groups. Despite the minor variation due mostly to the solvent modification of the nature of the substituent groups, a set of finite substituent constants appears to be practically determined for most of the substituent groups.

Before we determine the most reliable set of σ^0 constants, it appears necessary to check more critically the applicability of these constants to general σ^0-type reactivities. As far as we are aware, not many more than a dozen sets of data on σ^0 reactivities in which the through-conjugation is precluded by the structure are available in the literature. Table 4 includes the correlational parameters for these sets of reactivities, obtained by the least-squares application with σ^0 constants, while Table 5 lists the sets of apparent σ_0 values obtained from the respective reactions using the correlation parameters shown in Table 4. In these calculations, we have employed the selected σ^0 values given in the first column of Table 3 as the primary standard. For well-behaving *para* substituents, $\sigma_p{}^0$ values taken in principle from our standard set were employed, but for *meta* substituents the standard σ_m values were employed instead of $\sigma_m{}^0$.

The correlations resulted are excellent, as measured by correlation coefficients higher than 0.99, in all cases. The uncertainty in the apparent σ^0 value is estimated to be within 0.02 σ-unit for most of the substituents in each series, although it depends largely upon the magnitude of ρ's.

If the σ^0 values were applicable only to precise correlations of the reactivities of the specified structure insulated by intervening methylene, their utility would be so limited as to be of little value. However, their exist a substantial number of reactivities which are practically correlated by σ^0 values within the limits of the usual precision of fit. Table 6 shows the results of σ^0 correlations for such a class of reactivities of interest. The results are of practical importance not only in examining the generality of σ^0, but also in estimating the σ^0 values for substituents other than those involved in the σ^0 resorting, since the substituents involved in the former specified class of reactivities are limited in fact to the substituents of the so-called

TABLE 6. SUMMARY OF CORRELATIONS OF APPARENT σ^0-TYPE REACTIVITIES[a)]

No.	Reaction	ρ	S	R	n	Ref.
15	Benzoic acids with diphenylguanidine, benzene, 25°	2.127	0.032	0.9988	13	18
16	pK_a, Ar-PO_3H^-, water, 25°	1.129	0.037	0.9966	10	19
17	Alkaline hydrolysis, phenoxytriethylsilanes, 51% aq. ethanol, 25°	1.977	0.016	0.9994	6	20
18	pK_a, phenoxyacetic acids, water, 25°	0.304	0.014	0.9900	8	21
19	1-Cl, 2-NO_2-Benzenes with sodium thiophenoxide, methanol, 35°	5.203	0.14	0.996	14	22
20	Alkaline hydrolysis, phenyl tosylates	1.845	0.036	0.9989	9	23
21	Alkaline hydrolysis, phenyldinitrophenyl ethers	1.009	0.024	0.9977	15	24
22	pK_a, thiophenols, 48% aq. ethanol, 25°	2.605	0.037	0.9990	10	25
23	pK_a, phenols, water, 25°	2.247		0.9983		26

a) The Hammett type correlation based on the standard set of $\sigma_p{}^0$ and σ_m. In entries 19—23, the correlation is based on *meta* and $-R$ *para* substituents. Reference numbers in the last column refer to those below the Table.

18) M. M. Davis and H. H. Hetzer, *J. Res. Nat. Bur. Stand. A*, **60**, 596 (1958). 19) H. H. Jaffé, L. D. Freedman, and G. O. Doack, *J. Amer. Chem. Soc.*, **75**, 2209 (1953). 20) E. Aekerman, *Acta, Chem. Scand.*, **11**, 373 (1957). 21) N. V. Hayes and G. E. K. Branch, *J. Amer. Chem. Soc.*, **65**, 1555 (1943). 22) A. M. Porto, L. Altieri, A. J. Castro, and J. A. Brieux, *J. Chem. Soc., B*, **1966**, 963. 23) V. M. Maremae and V. A. Palm, "Organic Reactivity", Vol. 1, **2**, 85 (1964). 24) A. V. Ivanov, A. J. Kaminski, S. S. Gitis, and Z. A. Kosina, *ibid.*, Vol. 4, 290 (1967); S. S. Gitis, A. V. Ivanov, A. J. Kaminski, and Z. A. Kosina, *ibid.*, Vol. 3, **3**, 142 (1966). 25) F. G. Bordwell and H. H. Andersen, *J. Amer. Chem. Soc.*, **75**, 6019 (1953); G. Schwarzenbach and H. A. Egli, *Helv. Chim. Acta*, **17**, 1176 (1934). 26) Y. Tsuno, M. Fujio, and Y. Yukawa, unpublished results.

TABLE 7. COMPARISON OF APPARENT σ^0 VALUES[a)]

X[b)] / Y[c)]	15	16	17	18	19	20	21	22	23
p-Me	−0.111	−0.126	−0.113	−0.099	−0.115	−0.116	−0.152	−0.106	−0.136
p-MeO	−0.160[d)]		−0.110	−0.093	−0.098	−0.105	−0.120	−0.110	−0.113
p-F	0.166[d)]			0.181			0.198		
p-Cl	0.262	0.308	0.280	0.270	0.269	0.267	0.302	0.281	0.257
p-Br	0.283	0.237			0.290		0.313	0.304	0.267
p-I	0.277								0.290
p-NO_2	0.719	0.769		0.961[d)]		0.895[d)]	0.856[d)]		
p-CN	0.597			0.833[d)]					
p-NH_2	−0.382	−0.382			−0.396	−0.371	−0.34		
p-NMe_2						−0.41	−0.388		
p-OH	−0.151	−0.134						−0.213	

a) Evaluated from the correlational parameters in Table 6. b) Substituent. c) Reaction number in Table 6.
d) Values which are not included in the derivation of averaged σ^0 (Table 8).

well-behaving category. The apparent substituent constants derived are given in Table 7.

The substituent constant, σ^0, is a measure of the substituent effect referred to the special case of Eq. (2), where both ϕ^+ and ϕ^- are diminished to zero (i.e., $r^+=r^-=0$). These reactivities may be classified as the apparent σ^0 class reactivity, regardless of the reaction mechanism or the interaction mechanism of substituents and the reaction center. Davis's data on the ion-pair formation of substituted benzoic acids with diphenylguanidine (Entry 15) are highly instructive. The course of the reaction may be compared with that of the acid dissociation of benzoic acids, where $-$R *para* substituents exhibit a substantial pi-resonance exaltation to give Hammett σ values ($r^+=0.27$). The excellent fit to the σ^0 of the $-$R *para* groups in the ion-pair formation may perhaps be due to the cancellation of the exalted resonance interactions of substituents and the reaction center between the initial and final states. In Entry 18 (the pK_a of phenoxyacetic acids), $-$R *para* groups such as cyano and nitro groups indicate the exalted contribution to a considerable extent (see Table 7). In this system, the through-conjugation with the reaction site is, of course, inhibited by the intervening methylene, while the insulated pi-system is extended to the phenoxy lone-pair orbital with which the direct resonance interaction of $+$R *para* groups is possible. Thus, the conjugative electron-withdrawal of $+$R groups can be relatively exalted as compared with that of the same groups attached to the insulated benzene pi-system.

In general reactivities, both ϕ^+ and ϕ^- terms, or, often, either one of them, are exalted to varying extents, as is evidenced by the wide applicability of Eq. (2). The extent of contributions from both terms varies continuously, depending upon reactions, but the relative importance of the two terms is independent of each other. As a general trend, however, a significant contribution of one of them is accompanied by an insignificant or, usually, a minimized contribution of the other. The effect of $-$R substituents in the σ^--type reactivities may be minimized to follow σ^0 constants, regardless of the exalted resonance contribution from $+$R *para* substituents, since no significant additional resonance interaction can be expected between $-$R *para* substituents and the electron-donative reaction center. The reactivities which correspond to the case of $r^->0$ and $r^+=0$ in Eq. (2) can thus be utilized to examine the significance of σ^0 values for $-$R *para* substituents.

Entry 22 is a typical example of such a case. In this reaction, $+$R *para* substituents give a high r^- value of 0.52 characteristic of σ^--type nucleophilic reactivities, which $-$R *para* substituents fit the ρ_m line with $\sigma_p{}^0$ values. The $-$R group in more strongly σ^--type reactivities, such as the pK_a of phenols, may be expected to give good correlations with the $\sigma_p{}^0$ values. This is actually true for weak $-$R *para* substituents in the reaction (Entry 23); however, the examination of the effect of strongly electron-releasing groups suffers from the levelling effect.

The entries of Table 6 thus consist of two classes of reactivities; one corresponds to the case of $r^+=r^-=0$ (Entries 15—18), and the other, to $r^+=0$ but $r^->0$ (Entries 19—23). The former class reactivities are correlated with the σ^0 values in closely the same way, otherwise noted, as for the specified class of reactivities given in Table 4. The latter class satisfies the partial σ^0 correlations, and the correlational data of this class are based upon all *meta* substituents and only $-$R *para* substituents.

It is clear that the σ^0 values for the respective substituents in the specified σ^0 reactivity class (in Table 5) are not different from those in the apparent σ^0 reactivity class, and that, furtheremore, there is no essential difference in the apparent σ^0 values for $-$R substituents between the class $r^+=0$ but $r^->0$ and the above two classes. The constancy of the apparent σ^0 values appears to be of a comparable order for *meta* and *para* substituents, or a little better for the former substituents. The respective values are all in good agreement with those of our sets given in Table 3. A set of averaged σ^0 values is given for the respective substituents in the first column of Table 8. The average deviation is less than ±0.02 for all the substituents. The values marked in Tables 5 and 7 were not included in the averaging. As has been mentioned before,

TABLE 8. COMPARISON OF AVERAGED AND RELIABLE σ^0

Substituent	Averaged σ^0	n	Reliable σ^0
p-NMe$_2$	-0.40	2	-0.48
p-NH$_2$	-0.358	9	-0.36
p-OH	-0.16	3	-0.16
p-MeO	-0.108	17	-0.100
	-0.15	5	-0.152
p-Me	-0.124	20	-0.124
p-Et	-0.127	3	-0.131
p-i-Pr	-0.153	3	-0.156
p-t-Bu	-0.187	3	-0.174
p-Ph	0.038	2	0.039
p-PhO	0.063	2	0.07
p-MeS	0.066	2	0.083
p-F	0.196	8	0.212
p-Cl	0.284	23	0.281
p-Br	0.287	16	0.296
p-I	0.298	6	
p-COMe	0.491	1	(0.502)
p-CN	0.682	4	0.653
p-SOMe	0.573	1	(0.573)
p-SO$_2$Me	0.749	1	
p-NO$_2$	0.800	14	0.808
m-Me	-0.070	7	-0.069
m-MeO	0.082	5	
m-MeS	0.120	1	(0.120)
m-F	0.352	5	0.337
m-Cl	0.372	11	0.373
m-Br	0.382	6	0.391
m-I	0.342	4	
m-COMe	0.389	1	0.376
m-CN	0.648	3	0.607
m-SO$_2$Me	0.697	1	
m-NO$_2$	0.713	11	0.709

the *p*-methoxy group appears to require also another special value, -0.15, for the reactivity in a non-aqueous solution or in a less aqueous one as well as the usual value of -0.100. For the *p*-fluoro group, a constant value, 0.20, is obtained from these entries except for the dissociations of benzylammonium ions, for which another σ^0 value, 0.09, appears to be required.

All the *meta* substituents gave values of σ^0 identical with the corresponding σ_m values. As is shown in Table 3, the present reaction results in considerably higher σ^0 values for both *meta* and *para* cyano groups. The average set gives the same value for *meta* cyano group, but for *p*-cyano group gives a value rather close to the σ_p value. However, the considerably large average deviation and the insufficient number of entries make this conclusion less significant.

As a summary of these results, the set in the last column of Table 8 can be proposed as the most reliable set of σ^0 constants. The values for representative *meta* substituents are taken from the standard σ_m values, which are derived by definition from the pK_a's of benzoic acids in water (25°C). For several substituents of which the standard σ values are unknown, σ^0 values from our studies are selected. The values for *para* substituents are generally taken from our previous set of $\sigma_p{}^0$ values derived from the alkaline hydrolysis of ethyl phenylacetates. Although the set of averaged values might also be taken as the standard, we prefer to define the standard set by a single set of data since the averaged value is subject to change depending on the number of data entries. This definition is reasonable since the agreement of the set with the averaged set is well within the practical limits of uncertainty of Hammett-type substituent constants.

This set of σ^0 values may, we believe, be reliable to the order of 0.01 σ-unit for most of the substituents. The σ^0 values for *p*-NMe$_2$ and *p*-OH are not, however, regarded as equally reliable as those for other groups because of the insufficient number of existing data. Further examination for these substituents is now in progress. The σ^0 constants selected for $+$R *para* substituents are not well-established except for the *p*-nitro group. For *p*-SO$_2$Me and *p*-SOMe, even their standard σ values have not yet been well-established; additional data must be obtained.

Our proposed set of σ^0 values is not intended for direct application to the limited class of σ^0 reactivities, but for general use as a reference substituent constant in our LArSR equation; the σ^0 constants are referred to the unexalted substituent effect (*i.e.*, $r^+=r^-=0$), and they give, by definition, the resonance substituent constants, $\Delta\bar{\sigma}_R^+$ or $\Delta\bar{\sigma}_R^-$, as the increments from σ^+ or σ^-.

In general applications of our LArSR equation as well as in the derivation of σ^0, σ^+, and σ^- constants, the determination of appropriate ρ values should be required. Since the effect of *para* substituents usually involves a certain extent of resonance exaltation, the ρ value must be practically determined by the correlation of the *meta*-reactivities with the σ_m values. That is, the ρ value and all these treatments are based primarily upon the assumption of the reaction independency of the *meta*-substituent effects, or on the assumption of the constancy of σ_m values. This is the reason why we have selected the standard σ_m values for the above set of σ^0 values for well-behaving *meta* substituents.

The set of $\sigma_p{}^0$ values is derived from the data in aqueous organic solvents. Since the standard σ values are given by the changes in the pK_a values of benzoic acids in pure water, we have to take into account the solvent change of substituent constants when we compare the present set with the corresponding σ values. However, the substituent constants obtained in aqueous organic solutions appear to be practically of a wider application in describing the substituent effects on general organic reactivities, because most of the data are obtained not in purely aqueous solutions, but in aqueous organic solutions.