Quantitative Separation of Hyperconjugation Effects from Steric Substituent Constants

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L.C.A.O.–M.O. calculations lead to the equation, $E_s{}^c = E_s + 0.306(n - 3)$, which is useful for the quantitative separation of hyperconjugation effects (α-hydrogen bonding effects) from Taft's steric substituent constants, E_s, to obtain corrected steric substituent constants, $E_s{}^c$. For several reaction series, it is shown that $E_s{}^c$-values are more applicable than are E_s-values.

Taft[1a] has defined the steric substituent constant, E_s, as log $(k/k_0)_A$, where k and k_0 are the rate constants for the acidic hydrolysis of a substituted ester and of a reference ester. He indicates[1b] that hyperconjugation effects[2] (as used in the present article, "hyperconjugation" has the meaning of "α-hydrogen bonding" as proposed by Kreevoy and Eyring[3]) are generally much smaller than steric effects. For RCO_2R' with α-hydrogens in R, hyperconjugation will stabilize the unsaturated reactant state relative to the saturated[4] transition state and, therefore, will increase the activation energy and decrease the rate constant. However, the replacement in the reference CH_3CO_2R' of α-hydrogens by alkyl groups increases the steric effect which decreases the rate constant and decreases the hyperconjugation effect which increases the rate constant. Therefore, Taft's steric substituent constants for R of RCO_2R' may be expressed as

$$E_s = E_s{}^c + h(n - 3) \tag{1}$$

where $E_s{}^c$ is a corrected steric substituent constant, h is the reaction constant for hyperconjugation and n is the number of α-hydrogens.

We have used the L.C.A.O.–M.O. method described by Kreevoy and Eyring[3] to obtain a value of 0.432 kcal./mole[5] per α-hydrogen for ester hydrolysis. This value is equivalent to an h-value at 35° of -0.306 log unit of change in log k per α-hydrogen. Substitution in the preceding equation and rearrangement gives

$$E_s{}^c = E_s + 0.306(n - 3) \tag{2}$$

$E_s{}^c$-Values calculated by eq. 2 and Taft's E_s- and E_s'-values for 8 substituents (the only ones for which both E_s- and E_s'-values are available) are given in Table I. As defined by Taft, E_s' is the steric substituent constant for R' of RCO_2R'.

For the saponification of esters, the effect of the interposition of the oxygen between the R' and the carbonyl carbon of RCO_2R' should make the steric substituent constant for R' appreciably larger (more positive) than that for R when R and R' are identical. This requirement is not met by Taft's E_s- and E_s'-values but is met by the calculated $E_s{}^c$-values and Taft's E_s'-values. Moreover, there should be a correlation between the steric constants for R and

(1) R. W. Taft, Jr., "Steric Effects in Organic Chemistry," M. S. Newman, ed., John Wiley and Sons, Inc., New York, N. Y., 1956: (a) p. 599, (b) p. 672, (c) p. 598, (d) p. 645, (e) p. 619, (f) p. 644.

(2) R. S. Mulliken, C. A. Rieke and W. G. Brown, J. Am. Chem. Soc., 63, 41 (1941).

(3) M. M. Kreevoy and H. Eyring, ibid., 79, 5121 (1957).

(4) M. L. Bender, ibid., 73, 1626 (1951).

(5) M. M. Kreevoy and R. W. Taft, Jr., ibid., 79, 4016 (1957), using their "10 to 1" rule, have estimated this value to be about 0.5 kcal./mole.

TABLE I
STERIC SUBSTITUENT CONSTANTS

Substituent	$E_s{}^c$ for R of RCO_2R'	$E_s{}^a$ for R of RCO_2R'	E_s' for R' of RCO_2R'
CH_3	0.00	0.00	0.00[b]
C_2H_5	− .38	− .07	− .09[b]
n-C_3H_7	− .67	− .36	− .30[c]
n-C_4H_9	− .70	− .39	− .34[c]
i-C_3H_7	−1.08	− .47	− .42[b]
i-C_4H_9	−1.24	− .93	− .22[b]
s-C_4H_9	−1.74	−1.13	−1.00[c]
t-C_4H_9	−2.46	−1.54	−1.60[c]

[a] Ref. 1c.　[b] Ref. 1d.　[c] R. W. Taft, Jr., private communication.

R' of RCO_2R'. Using the data from Table I, correlation coefficients of 0.895 for the relationship between Taft's E_s- and E_s'-values and of 0.937 for the relationship between the calculated $E_s{}^c$-values and Taft's E_s'-values are found. Further, as shown below for a variety of reaction series, the $E_s{}^c$-values are more applicable than are the E_s-values.

Applications of Corrected Steric Substituent Constants, $E_s{}^c$. 1. Saponification Rate Constants of Esters, RCO_2R', in 40% Aqueous Dioxane at 35°.[6]—In the alkaline hydrolysis of RCO_2R' esters, the rate-determining step is the coördination of the OH^- with the carbonyl carbon. If R(or R') is electron withdrawing (i.e., σ^{*1e} is positive), the electron density on the carbonyl carbon will be decreased, the coördination of that carbon with the OH^- will be facilitated, the activation energy will be decreased, and the rate constant will be increased. By analogous reasoning, if R is electron releasing (i.e., σ^* is negative), then the rate constant will be decreased. Also, the reaction site is trigonal in the reactant state but tetrahedral[4] in the transition state. Consequently, the steric effect of R will be greater in the transition state than in the less-crowded reactant state. This leads to an increase in the energy of activation and a decrease in the rate constant. Further, the reaction site is unsaturated in the reactant state but saturated in the transition state. Therefore, α-hydrogens in R will be involved in hyperconjugation with the carbonyl group in the reactant state. No such phenomenon exists in the transition state. Therefore, α-hydrogens in R stabilize the reactant state relative to the transition state, increase the activation energy and decrease the rate constant. However, Taft[1a,1e] has calculated E_s and σ^* for R relative to CH_3. Consequently, hyperconjugation effects of α-hydrogens in R are also being treated

(6) B. J. Yager, M.S. Thesis, The A. and M. College of Texas, August, 1960.

relative to CH_3; that is, $(n - 3)$ is being used, where n is the number of α-hydrogens in R. Because of the interposition of the O between the carbonyl C and the R' of RCO_2R', there are no hydrogens in R' which are α to the carbonyl group; consequently, there is no hyperconjugation involving R'. Summarizing, the factors which control the rate constant for the saponification of RCO_2R' are polar, steric and hyperconjugation effects of R and polar and steric effects only of R'.

In Table II, values of the second-order saponification rate constant (k), Taft's polar substituent

TABLE II

SECOND-ORDER SAPONIFICATION RATE CONSTANTS AT 35° AND SUBSTITUENT CONSTANTS FOR NINE METHYL ESTERS

R in RCO_2CH_3	k, M^{-1} min.$^{-1}$	σ^{*a}	$(n-3)^b$
CH_3	19.3	0.000	0
C_2H_5	14.7	$-.100$	-1
n-C_3H_7	7.44	$-.115$	-1
i-C_3H_7	5.23	$-.190$	-2
n-C_4H_9	5.96	$-.130$	-1
i-C_4H_9	2.12	$-.125$	-1
s-C_4H_9	1.49	$-.210$	-2
t-C_4H_9	0.676	$-.300$	-3
$C_6H_5CH_2$	26.1	$+.215$	-1

^{a} Ref. 1e. ^{b} n is the number of α-H's in R of RCO_2CH_3.

constant (σ^{*1e}), and the number of α-hydrogens in R relative to the number in the methyl group $(n - 3)$ are given for nine methyl esters, RCO_2CH_3. For the $C_6H_5CH_2$ group, $E_s = -0.38^{1c}$ and E_s^c, calculated by eq. 2, is -0.69. The E_s- and E_s^c- values for the other eight substituents in Table II are given in Table I. For the nine methyl esters, RCO_2CH_3, the following multiple regression analyses[7a] were carried out in order to demonstrate the validity of the above-discussed effects. The analysis of the multiple regression of log k on σ^* and E_s gives

$$\log k = 1.31 + 1.54\sigma^* + 0.709E_s \quad (3)$$
$$\quad\quad\quad (0.001) \quad\quad (0.001)$$

with a multiple correlation coefficient, R, of 0.992 and a standard deviation from regression, s, of 0.076. In eq. 3, 1.54 is the polar reaction constant, ρ^*, and 0.709 is the steric reaction constant, δ. The numbers in parentheses below these two parameters are the significance levels as determined by "Student's" t-tests.[7b,8] From these results, it can be seen that a good relationship is obtained by using Taft's σ^*- and hybrid E_s-values, the latter being combinations of steric and hyperconjugation effects.

Replacing the E_s-values, analysis of the multiple regression of log k on σ^* and E_s^c gives

$$\log k = 1.36 + 1.48\sigma^* + 0.471E_s^c \quad (4)$$
$$\quad\quad\quad (0.025) \quad\quad (0.005)$$

with $R = 0.970$ and $s = 0.149$. All of these data show that eq. 4 is a much poorer relation than is eq. 3. The reason for this is that no hyperconjugation

(7) G. W. Snedecor, "Statistical Methods," 5th ed., The Iowa State College Press, Ames, Iowa, 1956: (a) Chap. 14; (b) pp. 46, 418 and 441; (c) p. 428; (d) Chap. 6.

(8) To say that the "Student's" t-test shows that the parameter, 1.54, of eq. 3 is significant at the 0.001 level means that the probability of finding a more significant value for this parameter is less than 0.001.

effect was included in the analysis leading to eq. 4, while Taft's hybrid E_s-values were used in deriving eq. 3.

Finally, analysis of the multiple regression of log k on σ^*, E_s^c, and $(n - 3)$ gives the excellent relationship

$$\log k = 1.25 + 1.75\sigma^* + 0.848E_s^c - 0.383(n - 3) \quad (5)$$
$$\quad\quad\quad (0.001) \quad\quad (0.001) \quad\quad (0.001)$$

with $R = 0.998$ and $s = 0.043$. An F-test[7c] (analysis of variance) shows that eq. 5 provides a highly significant improvement in fit over eq. 3. In summary, eq. 4 shows that hyperconjugation effects must be considered, eq. 3 shows that these effects are considered fairly well by using Taft's hybrid E_s-values, while eq. 5 demonstrates that considerable improvement over eq. 3 results by using separated hyperconjugation effects and steric effects along with polar effects.

Under the same experimental conditions, the rate constants for nine acetate esters, CH_3CO_2R', were determined.[6] The results are, R' being given first and then the corresponding k-value in $1 M^{-1}$ min.$^{-1}$: CH_3, 19.3; C_2H_5, 8.90; n-C_3H_7, 6.75; i-C_3H_7, 1.84; n-C_4H_9, 5.38; i-C_4H_9, 3.95; s-C_4H_9, 0.954; t-C_4H_9, 0.103; and $C_6H_5CH_2$, 14.0. These nine substituents are the same as those in the methyl esters and, consequently, the substituent constants σ^*, E_s, and E_s^c are the same as given previously. For these nine acetate esters, analysis of the multiple regression of log k on σ^* and E_s gives

$$\log k = 1.27 + 1.80\sigma^* + 0.928E_s \quad (6)$$
$$\quad\quad\quad (0.10) \quad\quad (0.01)$$

with $R = 0.952$ and $s = 0.248$. In addition to the relatively small R-value and large s-value for eq. 6, it should also be noted that the values of $\rho^* = 1.80$ and $\delta = 0.928$ are anomalously larger than the corresponding parameters of eq. 3 and 5. Because of the interposition of the O between R' and the carbonyl carbon of CH_3CO_2R', these parameters in eq. 6 should be smaller than those in eq. 3 and 5.

Using E_s^c instead of E_s, the multiple regression analysis gives

$$\log k = 1.40 + 1.34\sigma^* + 0.730E_s^c \quad (7)$$
$$\quad\quad\quad (0.05) \quad\quad (0.001)$$

with $R = 0.980$ and $s = 0.161$. Comparing eq. 6 and 7, the R- and s-values and the significance levels of ρ^* and δ all show that eq. 7 provides a better correlation for the data. Moreover, as should be the case, the ρ^*- and δ-values for eq. 7 are smaller than those of eq. 3 and 5. Thus, it is shown that E_s^c-values are more applicable than E_s- values to this case in which hyperconjugation effects do not exist.

2. Acid-catalyzed Alcoholysis Rate Constants of β-Naphthyl Esters, RCO_2-β-$C_{10}H_7$, at 25°.—Harfenist and Baltzly have reported[9] the first-order rate constants at 25° for the methanolysis, n-propanolysis and isopropanolysis of six RCO_2-β-$C_{10}H_7$ esters where R = CH_3, C_2H_5, n-C_3H_7, n-C_5H_{11}, i-C_3H_7 and t-C_4H_9. For R = n-C_5H_{11}, $E_s = -0.40^{1c}$ and $E_s^c = -0.71$ (calculated by eq. 2); E_s- and E_s^c-values for the other five substituents are given in Table I.

(9) M. Harfenist and R. Baltzly, J. Am. Chem. Soc., 69, 362 (1947)

For the methanolyses, Taft[1f] has found

$$\log k = -2.24 + 1.38E_s; \quad r = 0.992, s = 0.106 \quad (8)$$

where 1.38 is the steric reaction constant, δ, and r is the linear correlation coefficient. Replacing E_s by E_s^c, linear regression analysis[7d] gives

$$\log k = -2.09 + 0.888E_s^c; \quad r = 0.997, s = 0.071 \quad (9)$$

Equations 8 and 9 are directly comparable since they both involve the same number of variables and degrees of freedom (d.f.).

For the n-propanolyses

$$\log k = -2.90 + 1.67E_s; \quad r = 0.988, s = 0.160 \quad (10)$$

Equation 10 differs slightly, but not significantly, from that reported previously[1f] due to the omission of the data for β-naphthyl n-caproate from the previous derivation. Replacing E_s by E_s^c, there results

$$\log k = -2.72 + 1.08E_s^c; \quad r = 0.997, s = 0.082 \quad (11)$$

For the isopropanolyses, Taft[1f] found

$$\log k = -4.11 + 1.88E_s; \quad r = 0.985, s = 0.203 \quad (12)$$

Replacing E_s by E_s^c, there results

$$\log k = -3.90 + 1.23E_s^c; \quad r = 0.996, s = 0.105 \quad (13)$$

Comparing the r- and s-values for the above three pairs of equations, it is evident that a better fit is provided by E_s^c-values.

The results of multiple regression analyses[7a] of $\log k$ on σ^* and/or $(n - 3)$ in addition to E_s or E_s^c show that there is no significant polar or hyperconjugation effect. Consequently, these alcoholyses are controlled by steric effects and E_s^c-values should be more applicable.

3. Enthalpies of Reaction of 2-Monoalkylpyridines with Boron Trifluoride in Nitrobenzene.— Brown and Horowitz have reported[10] the enthalpies of reaction of five 2-monoalkyl pyridines (where the 2-substituent is H, CH_3, C_2H_5, i-C_3H_7 and t-C_4H_9) with boron trifluoride in nitrobenzene.

Linear regression analysis[7d] of the data gives

$$-\Delta H = 22.1 + 3.63E_s; \quad r = 0.921, s = 1.77 \quad (14)$$

A significantly different relationship, due to omission of the data for unsubstituted pyridine, has been reported previously.[1f] Replacing E_s by E_s^c, there results

$$-\Delta H = 24.0 + 3.46E_s^c; \quad r = 0.975, s = 1.02 \quad (15)$$

It is evident that a better relationship is provided by eq. 15.

4. Saponification Rate Constants of Alkyl Esters of m- and p-Substituted Benzoic Acids in 60% Aqueous Dioxane at 35°.—A further striking example of the applicability of E_s^c-values is given in the following article.[11]

Experimental[6]

Materials.—The esters used in this study were obtained from commercial sources or prepared by well-known methods and were purified by fractionation through a 1.5-cm. × 25-cm. column filled with 0.3-cm. glass helices (17 theoretical plates) or through a 1.0-cm. × 25-cm. spinning band column (25 theoretical plates).

Dioxane was purified[12] and then distilled over sodium through a 12-bulb Snyder column. The constant-boiling (101°) middle fraction was collected and used. The solvent mixture used in this study was prepared in 1-liter quantities by measuring 400 ml. of the purified dioxane into a 1-liter volumetric flask and then diluting with deionized water (distilled water that had been passed through a research-grade mixed-bed ion exchange column). This required 612 ml. of water due to the imperfect solution formed. In this paper, this mixed solvent is referred to as 40% aqueous dioxane.

Standard 0.1 M sodium hydroxide solution was prepared by appropriate dilution with deionized water of a carbonate-free, saturated sodium hydroxide solution.

Determination of Saponification Rate Constants.—The following modification of the method described by Daniels, et al.,[13] was used. Approximately 0.002 mole of ester was weighed into a 100-ml. volumetric flask containing 10 ml. of 40% aqueous dioxane, the flask being kept stoppered as much as possible during the weighing. The mixture was diluted to 100 ml. with 40% aqueous dioxane. A 100-ml. portion of sodium hydroxide solution of exactly the same molarity as that of the ester was prepared by adding the required volume of standard 0.1 M aqueous sodium hydroxide solution to 40 ml. of dioxane in a 100-ml. volumetric flask and then diluting with deionized water. These two 100-ml. flasks, an empty 250-ml. flask, and a conductivity cell[14] (1.3 cm.$^{-1}$ cell constant) were placed in a water-bath set at 35.06 ± 0.015° by means of a platinum resistance thermometer (calibrated by the U. S. National Bureau of Standards). After reaching bath temperature, the ester solution was poured first into the 250-ml. flask, followed by the sodium hydroxide solution with mixing. An electric timer was started when one-half of the base had been added. The conductivity cell was rinsed with the reaction solution, then filled with that solution, stoppered, replaced in the bath, and sealed with paraffin. Conductance readings were taken after 5 minutes from time zero and at various intervals until 90% of the ester had been saponified. A Wheatstone bridge[15] in conjunction with a 1000-c.p.s. oscillator[16] was used to make the conductance readings, the null-point being obtained by means of a cathode-ray oscilloscope.

A plot of $1/R_t$ as abscissa versus $1/t$ $(1/R_0 - 1/R_t)$ as ordinate gives a straight line with slope $= ka$, where $1/R_t$ and $1/R_0$ are the conductance readings at time t and at time zero, k is the second-order rate constant and a is the initial molarity of ester. The slope of the line, obtained by linear regression,[7d] was divided by the initial ester molarity, a, to obtain the second-order rate constant. $1/R_0$ was obtained either by extrapolation to time zero of a plot of $1/R_t$ versus time or, for the faster reactions, by measuring the conductance of a solution of only sodium hydroxide in 40% aqueous dioxane of the same molarity as initially in the reaction mixture.

Rate constant determinations were made in triplicate on each ester. For the 17 esters, the average deviation from the mean of triplicate k-values exceeded 1.9% only in the case of 2.5% for methyl n-valerate and the maximum deviation from the mean exceeded 2.5% only in the cases of 2.9% for methyl isovalerate and of 2.6% for methyl α-methylbutyrate. The k-values found for the methyl esters, RCO_2CH_3, are given in Table II and those found for the acetate esters, CH_3CO_2R', are given in the paragraph preceding eq. 6.

(12) C. A. Kraus and R. A. Vingee, ibid., **56**, 511 (1934).

(13) F. Daniels, J. H. Mathews, J. W. Williams, P. Bender and R. A. Alberty, "Experimental Physical Chemistry," 5th ed., McGraw–Hill Book Co., Inc., New York, N. Y., 1956, p. 130.

(14) Fisher Scientific Co., New York, N. Y., Cat. No. 9-367. Similar to that of G. Jones and G. M. Bollinger, J. Am. Chem. Soc., **53**, 441, Type L, Fig. 14 (1931).

(15) Leeds and Northrup Co., Philadelphia, Penna., Cat. No. 4754.

(16) Central Scientific Co., Chicago, Ill., Cat. No. 70029.

(10) H. C. Brown and R. H. Horowitz, J. Am. Chem. Soc., **77**, 1733 (1955).

(11) C. K. Hancock and C. P. Falls, ibid., **83**, 4214 (1961).