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The Change in the Six Number as a Variable in Quantitative Structure-Reactivity Correlations of Esters<sup>1</sup>

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Newman's steric six-number effect is, by Taft's definition, included in the over-all steric substituent constant,  $E_s^c$ , for the R group of an ester,  $\text{RCO}_2\text{R}'$ . On the other hand, the steric six-number effect is not correctly included in  $E_s^c$  for many R' groups since these groups have six-numbers in the R' position which are different from the six-numbers of the same groups when in the R position. The change in the six number,  $\Delta 6$ , for a substituent is defined as the six number of that substituent when present as the R group minus the six number of the same substituent when present as the R' group. For the saponification and alcoholysis of esters, in which the R group is fixed while the R' group is varied, it is shown that  $\Delta 6$  is an additional significant independent variable in quantitative structure-reactivity correlations.

For the esterification of carboxylic acids and the saponification of esters, Newman<sup>2</sup> has shown that the six number of a substituent (*i.e.*, the number of atoms in the six position from the carbonyl oxygen atom as atom number one) makes a large contribution to the total steric effect of that substituent. Use of the change in the six number in quantitative structure-reactivity correlations of esters leads, as shown below, to very significant improvement in the correlations for cases where the substituent in the alkyl component of the esters is varied.

As summarized previously,<sup>3</sup> in the absence of  $\alpha,\beta$ -unsaturation in the R group, the factors which control the saponification rate constant of aliphatic esters,  $\text{RCO}_2\text{R}'$ , are polar, steric, and hyperconjugation effects of the R group and polar and steric effects of the R' group.

Taft has defined<sup>4a</sup> the steric substituent constant,  $E_s$ , of a substituent, R in  $\text{RCO}_2\text{R}'$ , as  $E_s \equiv \log(k/k_0)_A$ , where  $k$  and  $k_0$  are the rate constants for the acid-catalyzed hydrolysis of  $\text{RCO}_2\text{R}'$  and  $\text{CH}_3\text{CO}_2\text{R}'$ . Both rate constants are determined under the same experimental conditions and the R' groups in the two esters are identical. By this definition,  $E_s$  is the total steric effect of R and includes the steric six-number effect. However,  $E_s$  contains a hyperconjugation effect which can be separated quantitatively<sup>3</sup> to obtain the corrected total steric substituent constant,  $E_s^c$ , which still includes the steric six-number effect. The inclusion of the steric six-number effect in  $E_s^c$  by definition is further substantiated by the fact that the use of  $E_s^c$  in structure-reactivity correlations for variations of R in  $\text{RCO}_2\text{R}'$  is very successful as illustrated by eq. 2 below.

For a series of esters,  $\text{RCO}_2\text{R}'$ , where the R' group is fixed while the R group is varied, the saponification rate constants,  $k$ , agree quite closely with eq. 1 obtained by multiple regression analysis.<sup>5a</sup>

$$\log k = \log k_0 + \rho^* \sigma^* + E_s^c \delta + h(n-3) \quad (1)$$

In eq. 1,  $k_0$  is the regression value for the saponification rate constant of  $\text{CH}_3\text{CO}_2\text{R}'$ ,  $\rho^*$  is the polar reaction constant,  $\sigma^*$  is the polar substituent constant<sup>4b</sup> for the R group,  $\delta$  is the steric reaction constant,  $E_s^c$  is obtained by quantitative separation<sup>3</sup> of hyperconjugation effects from Taft's steric substituent constant<sup>4c</sup> for the R group,  $h$  is the reaction constant for hyperconjugation, and  $n$  is the number of  $\alpha$ -hydrogens in the R group.

As an example of eq. 1, using the saponification rate constants<sup>3</sup> in 40% aqueous dioxane at 35° given in the second column of Table I for nine methyl esters,  $\text{RCO}_2\text{CH}_3$ , and the corresponding substituent con-

TABLE I  
SECOND-ORDER SAPONIFICATION RATE CONSTANTS<sup>3</sup> IN 40% AQUEOUS DIOXANE AT 35° FOR NINE METHYL ESTERS,  $\text{RCO}_2\text{CH}_3$ , AND FOR NINE ACETATE ESTERS,  $\text{CH}_3\text{CO}_2\text{R}'$

Substituent, R or R'	$k, M^{-1} \text{ min.}^{-1}$		$\log \frac{k(\text{CH}_3\text{CO}_2\text{R}')}{k(\text{RCO}_2\text{CH}_3)}$	$\Delta 6$ for R' <sup>a</sup> in $\text{CH}_3\text{CO}_2\text{R}'$
	Methyl esters, R in $\text{RCO}_2\text{CH}_3$	Acetate esters, R' in $\text{CH}_3\text{CO}_2\text{R}'$		
<i>i</i> -C <sub>4</sub> H <sub>9</sub>	2.12	3.95	+0.270	+3
CH <sub>3</sub>	19.3	19.3	(.000)	(0)
<i>n</i> -C <sub>3</sub> H <sub>7</sub>	7.44	6.75	-.042	0
<i>n</i> -C <sub>4</sub> H <sub>9</sub>	5.96	5.38	-.044	0
<i>s</i> -C <sub>4</sub> H <sub>9</sub>	1.49	0.954	-.194	-3
C <sub>2</sub> H <sub>5</sub>	14.7	8.90	-.218	-3
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	26.1	14.0	-.271	(+2)
<i>i</i> -C <sub>3</sub> H <sub>7</sub>	5.23	1.84	-.454	-6
<i>t</i> -C <sub>4</sub> H <sub>9</sub>	0.676	0.103	-.818	-9

<sup>a</sup>  $\Delta 6$  is the six number of a substituent in the acyl portion of an ester minus the six number of that same substituent in the alkyl portion of an ester.

TABLE II

## SUBSTITUENT CONSTANTS

Substituent	$\sigma^{*a}$	$E_s^{cb}$	$(n-3)^c$	$\Delta 6^d$
CH <sub>3</sub>	0.000	0.00	0	0
C <sub>2</sub> H <sub>5</sub>	-.100	-.38	-1	-3
<i>n</i> -C <sub>3</sub> H <sub>7</sub>	-.115	-.67	-1	0
<i>i</i> -C <sub>3</sub> H <sub>7</sub>	-.190	-1.08	-2	-6
<i>n</i> -C <sub>4</sub> H <sub>9</sub>	-.130	-0.70	-1	0
<i>i</i> -C <sub>4</sub> H <sub>9</sub>	-.125	-1.24	-1	3
<i>s</i> -C <sub>4</sub> H <sub>9</sub>	-.210	-1.74	-2	-3
<i>t</i> -C <sub>4</sub> H <sub>9</sub>	-.300	-2.46	-3	-9
<i>n</i> -C <sub>5</sub> H <sub>11</sub>	-.162 <sup>e</sup>	-0.71	-1	0
<i>i</i> -C <sub>5</sub> H <sub>11</sub>	-.162 <sup>e</sup>	-0.66	-1	0
(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CH	-.225	-2.59	-2	0
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	.215	-0.69	-1	2
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CH <sub>2</sub>	.080	-0.69	-1	-1
CH <sub>3</sub> OCH <sub>2</sub> CH <sub>2</sub>	.232 <sup>f</sup>	-1.08	-1	-2
ClCH <sub>2</sub> CH <sub>2</sub>	.385	-1.21	-1	-3

<sup>a</sup> Ref. 4b. <sup>b</sup> Calcd. from Taft's steric substituent constant (ref. 4c) by the method in ref. 3. <sup>c</sup>  $n$  is the number of  $\alpha$ -hydrogens in R of  $\text{RCO}_2\text{R}'$ . <sup>d</sup>  $\Delta 6$  is the six number of a substituent in the acyl portion of an ester minus the six number of that same substituent in the alkyl portion of an ester. <sup>e</sup> A. B. Hoefelmeyer and C. K. Hancock, *J. Am. Chem. Soc.*, **77**, 4746 (1955). <sup>f</sup> Calcd. by dividing the  $\sigma^*$ -value of 0.65 for the  $\text{CH}_3\text{OCH}_2\text{CH}_2$  group [H. B. Charman, D. R. Vinard and M. M. Kreevoy, *ibid.*, **84**, 347 (1962)] by 2.8 (ref. 4d).

stants given in Table II, multiple regression analysis yields eq. 2

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

(<0.001) (<0.001) (<0.001)

$$R = 0.998, s = 0.043 \quad (2)$$

where  $R$  is the multiple correlation coefficient and  $s$  is the standard deviation from regression. The numbers in parentheses below the three coefficients of eq. 2 are the significance levels as determined by "Student's"

(1) Presented before the Organic Section at the 18th Southwest Regional A. C. S. Meeting, Dallas, Tex., December 7, 1962.

(2) M. S. Newman, *J. Am. Chem. Soc.*, **72**, 4783 (1950).

(3) C. K. Hancock, E. A. Meyers and B. J. Yager, *ibid.*, **83**, 4211 (1961).

(4) 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. 619, (c) p. 598, (d) p. 592, (e) p. 644.

*t*-tests.<sup>5b</sup> These results indicate that all three independent variables are highly significant and that the deviation of experimental  $\log k$  values from  $\log k$  values calculated by eq. 2 is of the same order of magnitude as the experimental error in measurement of  $\log k$ . Analysis of variance (*F*-test)<sup>6a</sup> confirms that a highly significant improvement is obtained by inclusion of  $(n - 3)$  as an additional variable in the multiple regression analysis. Also, the very close fit provided by eq. 2 serves to substantiate the proposal that the steric six-number effect of R in  $\text{RCO}_2\text{R}'$  is included in the total steric effect,  $E_s^c$ , of R.

In contrast to the above-mentioned excellent quantitative correlations, only fairly good correlations are obtained for series in which the R group of the ester,  $\text{RCO}_2\text{R}'$ , is fixed while the R' group is varied. For example, using the saponification rate constants<sup>3</sup> in 40% aqueous dioxane at 35° given in the third column of Table I for nine acetate esters,  $\text{CH}_3\text{CO}_2\text{R}'$ , and the corresponding substituent constants given in Table II, multiple regression analysis yields eq. 3.

$$\log k = 1.40 + 1.34\sigma^* + 0.730E_s^c, R = 0.980, s = 0.161 \quad (3)$$

(0.05)      (<0.001)

Although eq. 3 provides a fairly good fit for the data, it is apparent that the fit is not as good as that of eq. 2 for the nine methyl esters. A similar trend is indicated below in eq. 6, 7 and 9.

It appears that the effect of a substituent when present as R of  $\text{RCO}_2\text{R}'$  should be somewhat proportional to the effect of that same substituent when present as R' of  $\text{RCO}_2\text{R}'$ , the proportionality involving the direct transmission of the effect of R to the carbonyl carbon atom relative to the indirect transmission of the effect of R', through the interposed oxygen atom, to the carbonyl carbon atom. In other words, if R and R' are identical, it appears that  $\log [(k \text{ for } \text{CH}_3\text{CO}_2\text{R}')/(k \text{ for } \text{RCO}_2\text{CH}_3)]$  should be essentially constant. Inspection of these values in the fourth column of Table I shows that they vary over a range of 1.1 log units. It is believed that this wide variation in values of  $\log [(k \text{ for } \text{CH}_3\text{CO}_2\text{R}')/(k \text{ for } \text{RCO}_2\text{CH}_3)]$  is due to a hitherto unrecognized third independent variable as explained below.

The steric six-number effect of a particular substituent in the acyl component of an ester (R of  $\text{RCO}_2\text{R}'$ ) is included in the total steric substituent constant,  $E_s^c$ ; on the other hand, for that same particular substituent in the alkyl component of an ester (R' of  $\text{RCO}_2\text{R}'$ ) we now recognize that the steric six-number effect may or may not be correctly included in  $E_s^c$ . This arises from the fact that, upon moving a particular substituent from R to R' of  $\text{RCO}_2\text{R}'$ , the six number may, depending upon the structure of that substituent, increase, decrease or remain the same as a result of the interposition of the oxygen atom between the particular substituent and the carbonyl carbon atom. For example, if the particular substituent that is moved from R to R' of  $\text{RCO}_2\text{R}'$  is: (1)  $\text{C}_2\text{H}_5$ , then the six number increases by three; (2) *i*- $\text{C}_4\text{H}_9$ , then the six number decreases by three; (3) *n*- $\text{C}_3\text{H}_7$ , then the six-number remains the same (see Table II for other examples). In view of the above, it seems appropriate to consider the change in the six-number,  $\Delta 6$ , as a third independent variable in multiple regression analysis of saponification rate data involving variation of R' of  $\text{RCO}_2\text{R}'$ . As used herein,  $\Delta 6$  for a substituent

is the six number of that substituent in the acyl component of the ester minus the six number of the same substituent in the alkyl component of the ester. Values of  $\Delta 6$  calculated by this method are given in Table II.

Values of  $\log [(k \text{ for } \text{CH}_3\text{CO}_2\text{R}')/(k \text{ for } \text{RCO}_2\text{CH}_3)]$  and of  $\Delta 6$  for nine substituents are given in the fourth and fifth columns of Table I. The  $\log [(k \text{ for } \text{CH}_3\text{CO}_2\text{R}')/(k \text{ for } \text{RCO}_2\text{CH}_3)]$  value of zero for the methyl group is meaningless since in this case only the two esters,  $\text{CH}_3\text{CO}_2\text{R}'$  and  $\text{RCO}_2\text{CH}_3$ , are identical. Consequently, the  $\Delta 6$ -value of zero for the methyl group is disregarded in the linear regression analysis<sup>5c</sup> described below. Also, the questionable  $\Delta 6$ -value of plus two for the benzyl group is disregarded in the linear regression analysis. Comparison of pairs of values for the other seven groups shows that  $\Delta 6$  decreases regularly as  $\log [(k \text{ for } \text{CH}_3\text{CO}_2\text{R}')/(k \text{ for } \text{RCO}_2\text{CH}_3)]$  decreases. Linear regression analysis<sup>5c</sup> of the seven pairs of values gives  $\log [(k \text{ for } \text{CH}_3\text{CO}_2\text{R}')/(k \text{ for } \text{RCO}_2\text{CH}_3)] = 0.004 + 0.0847(\Delta 6)$ ,  $r = 0.990$ ,  $s = 0.054$ , where  $r$  is the linear correlation coefficient. This good correlation indicates that the surprising variation in the values of  $\log [(k \text{ for } \text{CH}_3\text{CO}_2\text{R}')/(k \text{ for } \text{RCO}_2\text{CH}_3)]$  is largely accounted for by the accompanying variation in the change in the six-number,  $\Delta 6$ .

If the value of  $\log [(k \text{ for } \text{CH}_3\text{CO}_2\text{R}')/(k \text{ for } \text{RCO}_2\text{CH}_3)]$  of  $-0.271$  for the benzyl group is substituted in the above equation, then a  $\Delta 6$ -value of  $-3$  is calculated for the benzyl group. This value differs markedly from the  $\Delta 6$ -value of  $+2$  obtained by straightforward application of Newman's method which leads to a six number of four for the  $\text{C}_6\text{H}_5\text{CH}_2$  group in  $\text{C}_6\text{H}_5\text{CH}_2\text{CO}_2\text{CH}_3$  and a six number of two for the  $\text{C}_6\text{H}_5\text{CH}_2$  group in  $\text{CH}_3\text{CO}_2\text{CH}_2\text{C}_6\text{H}_5$ . However, as shown below, this  $\Delta 6$ -value of  $+2$  for the benzyl group is highly questionable and the calculated  $\Delta 6$ -value of  $-3$  seems more appropriate. The four six-atoms for the  $\text{C}_6\text{H}_5\text{CH}_2$  group in  $\text{C}_6\text{H}_5\text{CH}_2\text{CO}_2\text{CH}_3$  consist of two *o*-hydrogen atoms and two *m*-carbon atoms. Inspection of the molecular model shows that the two *m*-carbon atoms exert no steric six-number effect and that the steric six-number effect of the two *o*-hydrogen atoms is relatively small. Consequently, it may be estimated that the "effective" six number of the  $\text{C}_6\text{H}_5\text{CH}_2$  group in  $\text{C}_6\text{H}_5\text{CH}_2\text{CO}_2\text{CH}_3$  is  $<2$ . The two six-atoms for the  $\text{C}_6\text{H}_5\text{CH}_2$  group in  $\text{CH}_3\text{CO}_2\text{CH}_2\text{C}_6\text{H}_5$  are the two *o*-carbon atoms. Inspection of the molecular model shows that these two *o*-carbon atoms exert a strong steric six-number effect and shows also that the two *o*-hydrogen atoms exert a steric seven-number effect which is greater than the steric six-number effect of the two *o*-carbon atoms. Consequently, it may be estimated that the "effective" six number of the  $\text{C}_6\text{H}_5\text{CH}_2$  group in  $\text{CH}_3\text{CO}_2\text{CH}_2\text{C}_6\text{H}_5$  is  $>4$ . These estimated six numbers of  $<2$  and  $>4$  for the  $\text{C}_6\text{H}_5\text{CH}_2$  group in the acyl and alkyl components of esters lead to an estimated or "effective"  $\Delta 6$  of about  $-3$  for this group which agrees with the value calculated from the linear regression equation above.

Including  $\Delta 6$ -values with the data used to obtain eq. 3, multiple regression analysis gives eq. 4.

$$\log k = 1.35 + 0.688\sigma^* + 0.664E_s^c + 0.0477(\Delta 6), R =$$

(0.045)      (<0.001)      (0.004)

0.997,  $s = 0.070$  (4)

Comparison of *R*- and *s*-values shows that eq. 4 is a significant improvement over eq. 3 and the probability level, 0.004, of the coefficient of  $\Delta 6$  in eq. 4 indicates that  $\Delta 6$  is a highly significant independent variable.<sup>6b</sup> Moreover, the positive sign of the coefficient of  $\Delta 6$  in eq. 4 is theoretically correct since this means that the saponification rate constant will tend to be decreased

(5) 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) Chap. 6.

(6) (a) H. H. Jaffé, *J. Org. Chem.*, **23**, 874 (1958). (b) Analysis of variance (*F*-test) confirms that a highly significant improvement is obtained by inclusion of  $\Delta 6$  as an additional variable in the multiple regression analysis.

by substituents with negative  $\Delta\delta$ -values. This follows from the fact that if  $\Delta\delta$  is negative for a substituent, then, by definition, the six number of that substituent in the alkyl portion of the ester is greater than the six number of the same substituent in the acyl portion of the ester; consequently, the rate-slowing steric effect of that substituent is underestimated by its  $E_s^c$ -value.

**Further Applications of the Change in the Six Number,  $\Delta\delta$ .** 1. **Acid-catalyzed Alcoholysis Rate Constants at 25° of  $\beta$ -Naphthyl Esters,  $\text{RCO}_2\text{-}\beta\text{-C}_{10}\text{H}_7$ .**—The first-order rate constants of Harfenist and Baltzly<sup>7</sup> for twenty-one acid-catalyzed alcoholyses are given in Table III. Taft showed<sup>4e</sup> that the rate constants for the six methanolyses or for the six 1-propanolyses or for the six 2-propanolyses are separately correlated fairly well with his steric substituent constant,  $E_s$ .<sup>4c</sup> More recently, it was shown<sup>3</sup> that Taft's correlations could be improved significantly by replacing  $E_s$  with the corrected steric substituent constant,  $E_s^c$ .

TABLE III  
ACID-CATALYZED ALCOHOLYSIS RATE CONSTANTS AT 25° OF  
 $\beta$ -NAPHTHYL ESTERS<sup>7</sup>

$$\text{RCO}_2\text{-}\beta\text{-C}_{10}\text{H}_7 + \text{R}'\text{OH} \xrightarrow{\text{N HCl}} \text{RCO}_2\text{R}' + \beta\text{-C}_{10}\text{H}_7\text{OH}$$

R	R'	Log $k$	R	R'	Log $k$
CH <sub>3</sub>	CH <sub>3</sub>	-2.201	<i>n</i> -C <sub>3</sub> H <sub>7</sub>	<i>n</i> -C <sub>3</sub> H <sub>7</sub>	-3.398
C <sub>2</sub> H <sub>5</sub>	CH <sub>3</sub>	-2.401	<i>n</i> -C <sub>5</sub> H <sub>11</sub>	<i>n</i> -C <sub>3</sub> H <sub>7</sub>	-3.411
<i>n</i> -C <sub>3</sub> H <sub>7</sub>	CH <sub>3</sub>	-2.633	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	<i>n</i> -C <sub>3</sub> H <sub>7</sub>	-3.914
<i>n</i> -C <sub>5</sub> H <sub>11</sub>	CH <sub>3</sub>	-2.714	<i>t</i> -C <sub>4</sub> H <sub>9</sub>	<i>n</i> -C <sub>3</sub> H <sub>7</sub>	-5.456
<i>i</i> -C <sub>3</sub> H <sub>7</sub>	CH <sub>3</sub>	-3.039	CH <sub>3</sub>	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	-4.043
<i>t</i> -C <sub>4</sub> H <sub>9</sub>	CH <sub>3</sub>	-4.345	C <sub>2</sub> H <sub>5</sub>	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	-4.360
CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	-2.818	<i>n</i> -C <sub>3</sub> H <sub>7</sub>	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	-4.644
C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	-3.073	<i>n</i> -C <sub>5</sub> H <sub>11</sub>	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	-4.684
<i>i</i> -C <sub>3</sub> H <sub>7</sub>	C <sub>2</sub> H <sub>5</sub>	-3.845	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	-5.301
CH <sub>3</sub>	<i>n</i> -C <sub>3</sub> H <sub>7</sub>	-2.836	<i>t</i> -C <sub>4</sub> H <sub>9</sub>	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	-7.004
C <sub>2</sub> H <sub>5</sub>	<i>n</i> -C <sub>3</sub> H <sub>7</sub>	-3.118			

It appears that the log  $k$ -values of Harfenist and Baltzly for all twenty-one of the alcoholyses should correlate collectively with the effects of the R group of the ester,  $\text{RCO}_2\text{-}\beta\text{-C}_{10}\text{H}_7$ , and with the effects of the R' group of the alcohol, R'OH. Consequently, the analysis of the multiple regression of log  $k$  on:  $\sigma^*$  for R,  $E_s^c$  for R, ( $n-3$ ) for R,  $\sigma^*$  for R',  $E_s^c$  for R', ( $n-3$ ) for R', and  $\Delta\delta$  for R' was carried out and "Student's"  $t$ -tests<sup>5b</sup> of significance were made on these seven independent variables. The least significant variable was rejected and the multiple regression analysis was repeated. Analysis of variance ( $F$ -test) confirms that no significant improvement is obtained by inclusion of any of the rejected variables as an additional variable in the multiple regression analysis. This procedure was continued until the remaining independent variables were all highly significant. By this means, the variables were rejected in the following order: (1)  $\sigma^*$  for R', (2) ( $n-3$ ) for R, (3) ( $n-3$ ) for R', and (4)  $\sigma^*$  for R. The remaining equation is eq. 5.

$$\log k = -1.91 + 1.07E_{sR}^c + 1.22E_{sR'}^c + 0.130\Delta\delta, \\ (\lt 0.001) \quad (\lt 0.001) \quad (\lt 0.001) \\ R = 0.994, s = 0.141 \quad (5)$$

If  $\Delta\delta$  is arbitrarily omitted, the analysis of the multiple regression of log  $k$  on  $E_{sR}^c$  and  $E_{sR'}^c$  gives eq. 6.

$$\log k = -1.86 + 1.05E_{sR}^c + 1.83E_{sR'}^c, R = 0.974, \\ (\lt 0.001) \quad (\lt 0.001) \\ s = 0.281 \quad (6)$$

It can be seen that eq. 5 provides a much better fit for the data than does eq. 6. Also, the "Student's"  $t$ -test shows that  $\Delta\delta$  of eq. 5 is an additional significant

variable.<sup>6b</sup> Compared to the  $s$ -value of 0.070 for eq. 4, the  $s$ -value of 0.141 for eq. 5 may appear to indicate a poorer fit for eq. 5. However, the former value, 0.070, is 3.1% of the range in log  $k$  values of 2.27 log units for the saponification of the nine acetate esters while the latter value, 0.141, is only 2.9% of the range of log  $k$  values of 4.80 log units for the twenty-one alcoholyses.

Equation 5 indicates that the rates of these acid-catalyzed alcoholyses are controlled by the steric effects of the R group of the ester,  $\text{RCO}_2\text{-}\beta\text{-C}_{10}\text{H}_7$ , and of the R' group of the alcohol, R'OH, and that the polar effect of either of these groups is relatively unimportant. These indications are consistent with the mechanism quoted by Harfenist and Baltzly<sup>7</sup> which involves, as the rate-determining step, the coordination of the oxygen atom of the alcohol with the carbonyl carbon atom of the protonated ester.

2. **Saponification Rate Constants of Alkyl Lactates,  $\text{CH}_3\text{CHOHCO}_2\text{R}'$ , in Water at 10°.**—Vogel and Warner have reported<sup>8</sup> the following saponification rate constants in water at 10° for nine alkyl lactates,  $\text{CH}_3\text{CHOHCO}_2\text{R}'$  (R' is given first and then the corresponding  $k$ -value in  $M^{-1} \text{min.}^{-1}$ ): CH<sub>3</sub>, 42.6<sup>9</sup>; C<sub>2</sub>H<sub>5</sub>, 17.5<sup>9</sup>; *n*-C<sub>3</sub>H<sub>7</sub>, 14.0<sup>9</sup>; *n*-C<sub>4</sub>H<sub>9</sub>, 13.6<sup>9</sup>; *i*-C<sub>4</sub>H<sub>9</sub>, 14.7; *s*-C<sub>4</sub>H<sub>9</sub>, 2.65; *t*-C<sub>4</sub>H<sub>9</sub>, 0.251; CH<sub>3</sub>OCH<sub>2</sub>CH<sub>2</sub>, 44.3; ClCH<sub>2</sub>CH<sub>2</sub>, 96.6. Using these data and appropriate substituent constants from Table II, multiple regression analysis gives eq. 7.

$$\log k = 1.79 + 2.28\sigma^* + 0.569E_s^c, R = 0.971, s = 0.212 \quad (7) \\ (0.001) \quad (0.001)$$

Equation 7 provides a fairly good fit for the data. However, the excellent correlation of eq. 8 results when  $\Delta\delta$  is included in the multiple regression analysis.<sup>6b</sup>

$$\log k = 1.71 + 2.31\sigma^* + 0.374E_s^c + 0.0675\Delta\delta, R = 0.996, \\ (\lt 0.001) \quad (0.001) \quad (0.002) \\ s = 0.084 \quad (8)$$

The  $s$ -value of 0.084 for eq. 8 is only 3.2% of the range of log  $k$  values of 2.59 log units for the nine saponifications.

3. **Saponification Rate Constants of Alkyl Benzoates,  $\text{C}_6\text{H}_5\text{CO}_2\text{R}'$ , in 60% Aqueous Dioxane at 35°.**—Hancock and Falls have reported<sup>10</sup> the following saponification rate constants in 60% aqueous dioxane at 35° for eleven alkyl benzoates,  $\text{C}_6\text{H}_5\text{CO}_2\text{R}'$  (R' is given first and then the corresponding  $k$ -value in  $M^{-1} \text{min.}^{-1}$ ): CH<sub>3</sub>, 1.74; C<sub>2</sub>H<sub>5</sub>, 0.553; *n*-C<sub>3</sub>H<sub>7</sub>, 0.379; *i*-C<sub>3</sub>H<sub>7</sub>, 0.0919; *n*-C<sub>4</sub>H<sub>9</sub>, 0.289; *i*-C<sub>4</sub>H<sub>9</sub>, 0.240; *s*-C<sub>4</sub>H<sub>9</sub>, 0.0468; *i*-C<sub>5</sub>H<sub>11</sub>, 0.234; C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>, 0.960; C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>CH<sub>2</sub>, 0.504; (C<sub>2</sub>H<sub>5</sub>)<sub>2</sub>CH, 0.0162. Equation 9 results from statistical treatment of these data and corresponding substituent constants from Table II.

$$\log k = 0.113 + 1.52\sigma^* + 0.620E_s^c, R = 0.981, s = 0.128 \quad (9) \\ (0.003) \quad (\lt 0.001)$$

A better fit for the data is provided by eq. 10 which results from inclusion of  $\Delta\delta$  as an additional independent variable.<sup>6b</sup>

$$\log k = 0.138 + 1.15\sigma^* + 0.652E_s^c + 0.0389\Delta\delta, \\ (0.004) \quad (\lt 0.001) \quad (0.018) \\ R = 0.992, s = 0.089 \quad (10)$$

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(9) Calculated by the Arrhenius equation from  $k$ -values at 0° and 15°.

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