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Kinetic study of hydrolysis of benzoates. Part XXIII—Influence of the substituent and temperature on the kinetics of the alkaline hydrolysis of alkyl benzoates in aqueous 2.25 M Bu_4NBr and 80% DMSO

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epoc ABSTRACT: The second-order rate constants k_2 ($M^{-1}\ s^{-1}$) for the alkaline hydrolysis of substituted alkyl benzoates, $C_6H_5CO(O)R$ (R = CH_3, CH_2Cl, CH_2CN, $CH_2C{\equiv}CH$, $CH_2C_6H_5$, CH_2CH_2Cl, $CH_2CH_2OCH_3$), were measured in aqueous 2.25 M *n*-Bu_4NBr and in 80% (v/v) DMSO solution at several temperatures. The log *k* values were analyzed using the equation $\log k = \log k_0 + \rho\sigma + \delta E_s^B$. The E_s^B scale has been proposed for the steric effect of alkyl substituents in the alkyl part of esters: $E_s^B = (\log k_R - \log k_{CH_3})_{H^+}$, where *k* is the rate constant for the acidic hydrolysis of substituted alkyl benzoates or acetates in water. As polar substituent parameters, both Taft σ^* and σ_I constants were used. The dual parameter treatments of the log *k* values with σ and E_s^B constants gave excellent correlations ($R = 0.997$). For 2.25 M *n*-Bu_4NBr, 80% (v/v) DMSO and pure water at 25 °C, calculated susceptibilities to the inductive effect of alkyl substituents ρ^* were found to be 2.07, 2.21 and 1.64, respectively. The corresponding ρ_I values were 4.64, 4.94 and 3.64. The dependence of ρ_I on solvent and temperature in the alkaline hydrolysis of substituted alkyl benzoates was similar to that observed earlier for *meta*- and *para*-substituents in the alkaline hydrolysis of substituted phenyl benzoates and tosylates. The substituent dependence of the activation energy, *E*, was found to be completely caused by the polar effect. Susceptibility to steric effect in the alkaline hydrolysis of alkyl benzoates ($\delta \approx 1$) appeared to be independent of the solvent and temperature. Copyright © 2002 John Wiley & Sons, Ltd.
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KEYWORDS: alkyl benzoates; alkaline hydrolysis; substituent effects

INTRODUCTION

In previous papers, the temperature dependence of substituent effects on the alkaline hydrolysis of *ortho*-, *meta*- and *para*-substituted phenyl benzoates, $C_6H_5CO_2C_6H_4X$,[1–7] and tosylates, $CH_3C_6H_4SO_2OC_6H_4X$,[8–13] in water, in aqueous 2.25 M Bu_4NBr and in 80% (v/v) DMSO, and also in the alkaline hydrolysis of substituted alkyl benzoates, $C_6H_5CO_2R$, in water[14,15] were studied.

As a further extension of our studies on substituent effects, the kinetic effect of alkyl substituents (R = CH_3, CH_2Cl, CH_2CN, $CH_2C{\equiv}CH$, $CH_2C_6H_5$, CH_2CH_2Cl, $CH_2CH_2OCH_3$) on the alkaline hydrolysis of substituted alkyl benzoates, $C_6H_5CO_2R$, in aqueous 2.25 M Bu_4NBr and in 80% (v/v) DMSO at various temperatures was studied. The aim of this work was to separate the influence of the polar and steric factors and to establish how these factors vary with the solvent and temperature when the electronegativity of the substituent in the alkyl component of ester is varied.

The kinetics of the alkaline hydrolysis of esters RCO_2R' involving a variable substituent in the alkyl part have been studied mainly in the case of saturated hydrocarbon substituents with a rather narrow range of σ^* variation. We could find only a few publications[14–22] providing data on the kinetics of the alkaline hydrolysis of esters with electronegative or electron-accepting substituents ($\sigma^* > 0$) in the alkyl part of esters. The kinetics of the alkaline hydrolysis of alkyl benzoates in DMSO–water mixtures has been studied only in the case of saturated hydrocarbon substituents.[23–27] To our knowledge, there are also no kinetic data in the literature on the alkaline hydrolysis of substituted alkyl benzoates in 2.25 M aqueous *n*-Bu_4NBr over a wide temperature range.

The structure–reactivity relationship in the alkaline hydrolysis of esters RCO_2R' involving a variable alkyl

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substituent R (α,β-saturated) in the acyl component, was introduced by Taft[28,29] as the sum of independent polar and steric factors:

$$\log k = \log k_0 + \rho^*\sigma^* + \delta E_s \quad (1)$$

Some authors[30,31] have maintained that the Taft steric E_s scale does not represent a complete separation of steric and polar effects. Therefore, several scales of steric constants as true measures of the steric effects have been proposed.

Hancock and co-workers[16,32,33] and Palm and co-workers[34,35] calculated 'corrected' steric parameters E_s^c and E_s^o, respectively, by removing the contribution of hyperconjugation from the steric substituent constants E_s. Charton[36–41] defined steric parameters ν_X based on the van der Waals radii r_x ($\nu_x = r_x - r_H$). The steric constants referenced to hydrogen, E_s^e, were calculated by Unger and Hansch[42] from the Taft E_s values by subtracting 1.24. MacPhee *et al.*[43,44] recalculated the Taft E_s scale based on a single defining reaction (the acid-catalyzed esterification of carboxylic acids in MeOH) and termed the scale E_s'. Kramer[45,46] proposed the calculated E_B constants for 96 alkyl C_nH_{2n+1}-substituents. For aliphatic substituents C_nH_{2n+1} it has been shown[46,47] that the Taft E_s values are linearly related to the σ^* constants. Some authors[22,48] have considered the E_s values for the β-substituted alkyl groups to be too negative and those groups have been excluded from the analysis as essentially deviating points.

In the present work, the steric E_s^B scale[49,50] defined as the Taft E_s values for aliphatic substituents in the alkyl part of esters was used in the data analysis. We preferred alkyl groups containing electronegative substituents —CH_2X and —CH_2CH_2X. Saturated hydrocarbon substituents were avoided to prevent complications in the data analysis. In order to compare the inductive effect of alkyl substituents ($R = XCH_2$) with the same effect of substituents in a benzene ring, the inductive scale σ_I[51] was used:

$$\sigma_{I(X)}/\sigma^*_{(XCH_2)} = 0.45 \quad (2)$$

Considering that the polar effect of aliphatic substituents depends on the solvent, two main problems arise. The susceptibility of the polar effects of aliphatic substituents, ρ^*, to the change of the solvent composition has been observed to be weak in comparison with the Hammett ρ values in the case of *meta*- and *para*-substituted phenyls.[52–54] The second problem is connected with the relationship between the Taft ρ^* values and the Hammett reaction constants ρ. Although the susceptibility to polar effects of aliphatic substituents, ρ^*, and *meta*- and *para*-substituted phenyls, ρ, has been equalized in case of the alkaline hydrolysis of ethyl and benzyl esters[28] in aqueous acetone, no universal proportionality between the ρ^* and ρ° values has been detected, i.e. $\rho^*/\rho^\circ \neq 1$ and $\rho^*/\rho^\circ \neq$ constant.[34] Equality of the ρ^* and ρ° values under conditions different from the standard values should be observed only in the case of a proportional change in both ρ^* and ρ° values with change in conditions.

EXPERIMENTAL

The preparation procedure and characteristics of substituted alkyl benzoates, $C_6H_5CO_2R$, and the technique for kinetic measurements have been described previously.[7] Cyanomethyl ($R = CH_2CN$) and propargyl ($R = CH_2C{\equiv}CH$) benzoates were provided by Bogatkov *et al.* (Moscow M. V. Lomonosov Institute of Fine Chemical Technology). As alkali, tetrabutylammonium hydroxide (n-Bu_4NOH) was used for the kinetic measurements in aqueous 2.25 M Bu_4NBr and in 80% (v/v) dimethyl sulfoxide (DMSO). The preparation of n-Bu_4NOH solution and the purification of n-Bu_4NBr have been described earlier.[1] In water, NaOH was used as alkali. NaOH was purified from carbonates by ion exchange by Albert and Serjeant as described.[55] DMSO (pure grade) was dried over BaO and distilled over CaH_2 under vacuum.[56] To avoid the influence of salt effects, the kinetic measurements in 2.25 M Bu_4NBr, were performed at a constant n-Bu_4NOH concentration: $c_{OH^-} = 0.0184$ M. The measurements in aqueous 80% DMSO and in water were performed in the alkali concentration range 0.002–0.06 M.

For kinetic measurements the spectrophotometric method was applied.[1] Wavelengths of $\lambda = 282$ nm in aqueous 2.25 M Bu_4NBr and $\lambda = 280$ nm in 80% DMSO were used for all the substituted alkyl benzoates. In water the following wavelengths were used: $\lambda = 275$ nm for $X = CH_2CN$, 274 nm for $X = CH_2C{\equiv}CH$, 240 nm for $X = CH_2Cl$ and 240 nm for $X = CH_2C_6H_5$. The kinetic measurements were carried out under pseudo-first-order conditions with excess alkali. The pseudo-first-order rate constants k_1 were determined using a least-squares computer program. In aqueous 2.25 M Bu_4NBr, the second-order rate constants were calculated by dividing the pseudo-first-order rate constants k_1 by the alkali concentration. The measurements were repeated and the arithmetic means of the corresponding second-order rate constants k_2 were calculated. In 80% DMSO and in water, the rate constants for each alkyl benzoate were determined at 3–5 hydroxide concentrations. At each hydroxide concentration 3–6 runs were performed and the arithmetic means of the corresponding pseudo-first-order rate constants k_1 were calculated. The second-order rate constants k_2 for 80% DMSO and water were calculated according to the equation

$$k_1 = k_2 c_{OH^-} + \text{constant} \quad (3)$$

The data analysis was carried out on a PC/XT 486

Table 1. Second-order rate constants k_2 for the alkaline hydrolysis of alkyl benzoates $C_6H_5CO_2$-R in aqueous 2.25 M Bu_4NBr, 80% (v/v) DMSO and water at 25 °C[a]

R	10^2k_2 (M^{-1} s^{-1})		
	2.25 M Bu_4NBr	80% DMSO	Water
CH_3	1.42 ± 0.12	32.0 ± 1.1	
CH_2CN	146 ± 7	–	213 ± 4
CH_2Cl	92.9 ± 4.3	3370 ± 180	167 ± 2
$CH_2C{\equiv}CH$	5.71 ± 0.42	194 ± 1	22.2 ± 1.8
$(CH_2)_2Cl$	3.72 ± 0.22	106 ± 5	–
$CH_2C_6H_5$	1.74 ± 0.10	51.0 ± 3.2	6.44 ± 0.41
$(CH_2)_2OCH_3$	1.51 ± 0.09	31.1 ± 1.3	–

[a] A table containing the second-order rate constants k_2 at several temperatures is available as supplementary material (Table S1) at the epoc website at http://www.wiley.com/epoc.

computer, using the multiple parameter linear least-squares (LLSQ) procedure.[57] In this paper the results of the data treatment are given mainly at a confidence level of 0.99.

DISCUSSION

Data analysis

The log k_2 values for the alkaline hydrolysis of substituted alkyl benzoates in aqueous 2.25 M Bu_4NBr, 80% DMSO and pure water at various temperatures (Tables 1 and S1) were analyzed with the following equations:

T = constant, X ≠ constant:

$$\log k_R = \log k_0 + \rho^*\sigma^* + \delta E_s^B \quad (4)$$

$$\log k_R = \log k_0 + \rho_I\sigma_I^X + \delta E_s^B \quad (5)$$

$T \neq$ constant, X = constant:

$$\log k = \log A - E/2.3RT \quad (6)$$

Steric constants for the variable substituent in the alcohol component of the ester, E_s^B, were calculated using the equation $E_s^B = (\log k_{H^+}^R - \log k_{H^+}^{CH_3})$, where $k_{H^+}^R$ and $k_{H^+}^{CH_3}$ are the rate constants for the acidic hydrolysis of R-substituted and CH_3-substitued alkyl benzoate or acetate, respectively, in water.[49,50] The steric substituent constant E_s^B for chloromethyl group, R = CH_2Cl, was calculated as the difference in the log k values for the acidic hydrolysis of chloromethyl formate and methyl formate in water at 25 °C. The substituent parameters σ^*, σ_I and E_s^B and the Taft E_s steric constants are listed in Table 2.

The cross-correlations among independent variables, characterized by values $R^2(\sigma^*E_s^B)$, $R^2(\sigma^*E_s)$ and $R^2(E_s^BE_s)$, appeared to be insignificant [$R^2(\sigma^*E_s^B) = 0.066$, $R^2(\sigma^*E_s) = 0.126$, $R^2(E_s^BE_s) = 0.364$].

The magnitudes of the steric constants E_s^B, determined for the alkyl component of the esters, were compared with the Taft steric scale E_s, proposed for the acyl component. No correlation ($R^2 = 0.364$, see Table 4) was observed between the Taft E_s values and the E_s^B constants when all alkyl substituents were taken into account, including those with electronegative groups at the β-position. At the same time, a fairly good correlation ($R = 0.986$) between the Taft E_s values and the E_s^B constants was obtained when substituents with electronegative groups at the α-position (R = CH_2CN, CH_2Cl, CH_2OCH_3, CH_2COCH_3, $CH_2C_6H_5$, CH_3) were included (see Fig. 1):

$$E_s = (0.038 \pm 0.032) + 1.52(\pm 0.11)E_s^B \quad (7)$$

$$R = 0.986, s = 0.059, n/n_0 = 6/6$$

For a chloromethyl substituent, CH_2Cl, two alternative values for E_s^B were used, $E_s^B = -0.17$ and -0.49, obtained from the data in water at 25 °C for the acidic hydrolysis of substituted alkyl formates and acetates, respectively. When $E_s^B = -0.49$ was used, the point for the chloromethyl substituent deviated significantly (Fig. 1). Therefore, in further data analysis $E_s^B = -0.17$ for the chloromethyl substituent was applied.

For comparison, the E_s values for R = $CH_2CH_2OCH_3$, CH_2CH_2OH and CH_2CH_2OEt were calculated according to the equation

$$\log k = (0.915 \pm 0.137) + (2.56 \pm 0.14)\sigma^* + (0.94 \pm 0.17)E_s \quad (8)$$

for the alkaline hydrolysis of substituted ethyl acetates, RCO_2Et, in water at 25 °C[50] when mainly alkyl substituents with electronegative groups at the α-position were included: $R = CH_2CN$, CH_2Cl, CH_2Br, CH_2OCH_3, $CH_2C_6H_5$, CH_2CH_3, CH_3. The magnitudes of E_s found according to Eqn. (8) for β-alkyl substituents appeared to be considerably smaller than the Taft E_s values, determined from the acidic hydrolysis: for R = $CH_2CH_2OCH_3$, CH_2CH_2OH and $CH_2CH_2OC_2H_5$, the

Table 2. Substituent parameters used in the correlations and values of log *A* and activation energy, *E* (kJ mol^{-1}), for the alkaline hydrolysis of alkyl benzoates $C_6H_5CO_2R$ in aqueous 2.25 M Bu_4NBr, 80% DMSO and water

R					2.25 M Bu_4NBr		80% DMSO		Water	
R = CH_2X	σ^*[a] for R	σ_I[b] for X	$-E_s^{Bc}$ for R	$-E_s$[d] for R	log *A*	*E*	log *A*	*E*	log *A*	*E*
CH_3	0	0	0	0	7.62 ± 0.31	53.20 ± 3.97	7.50 ± 0.14	45.78 ± 0.83	7.38 ± 0.07	48.98 ± 0.42
CH_2CN	1.30	0.58	0.55[e]	0.94	6.72 ± 0.36	37.64 ± 2.09	–	–	6.71 ± 0.50	39.16 ± 2.81
CH_2Cl	1.05	0.47	0.17[f]	0.24	7.00 ± 0.23	40.23 ± 1.47	6.91 ± 0.35	30.84 ± 1.56	7.27 ± 0.23	40.42 ± 1.36
$CH_2C{\equiv}CH$	0.61[g]	0.27[h]	0.41[i]	–	7.02 ± 0.20	48.28 ± 1.18	7.06 ± 0.44	38.32 ± 2.55	7.19 ± 0.19	44.87 ± 2.55
$(CH_2)_2Cl$	0.385	0.17	0.23	0.90	7.11 ± 0.30	47.53 ± 1.72	7.24 ± 0.37	41.09 ± 2.16	7.28 ± 0.33	46.86 ± 1.92
$CH_2C_6H_5$	0.215	0.11	0.24[j]	0.38	7.38 ± 0.50	52.66 ± 2.63	7.40 ± 0.50	44.20 ± 1.85	7.21 ± 0.48	48.18 ± 2.78
$(CH_2)_2OCH_3$	0.187	0.07	0.20	0.77	7.27 ± 0.45	51.80 ± 2.62	7.33 ± 0.12	44.70 ± 0.715	6.96 ± 0.34	46.55 ± 1.99
CH_2OCH_3	0.52	0.25	0.06[k]	0.19	–	–	–	–	–	–
CH_2COCH_3	0.60	0.28	0.51[l]	0.75	–	–	–	–	–	–

[a] Refs 28,51.
[b] Refs 51,58.
[c] Refs 49,50.
[d] The Taft E_s substituent constants, referenced to CH_3.[42]
[e] Calculated using data for acid-catalyzed hydrolysis (AH) of $CH_3CO_2CH_2CN$ in water at 25 °C. Log $k = -4.50$ and log $k_{CH_3} = -3.95$.[59]
[f] Calculated using data for AH of formates in water at 25 °C: for HCO_2CH_2Cl, log $k = -2.79$ and log $k_{CH_3} = -2.62$.[50]
[g] The $(\sigma^*)_{CH_2}X$ value was obtained as $1/2.8(\sigma^*_X)$.[60]
[h] The σ_I value was calculated as $\sigma_I = 0.45\sigma^*_{CH_2}X$.
[i] The E_s^B value was calculated from log $k = -0.14$[61] for the basic hydrolysis (BH) of $CH_3CO_2CH_2C{\equiv}CH$ in water at 25 °C by the relationship $E_s^B = (-0.14 - \log k_{CH_3}) - 1.71\sigma^*$.
[j] The E_s^B value was obtained from the data for AH of $CH_3CO_2CH_2C_6H_5$ in water at 25 °C; log $k = -4.19$ was used.[62]
[k] The E_s^B value was obtained from BH of $CH_3CO_2CH_2OCH_3$ in water at 25 °C; log $k = 0.05$ was used.[63]
[l] $^qE_s^B$ was obtained from AH of $CH_3CO_2CH_2COCH_3$ in water at 25 °C; log $k = -4.464$ used.[64]

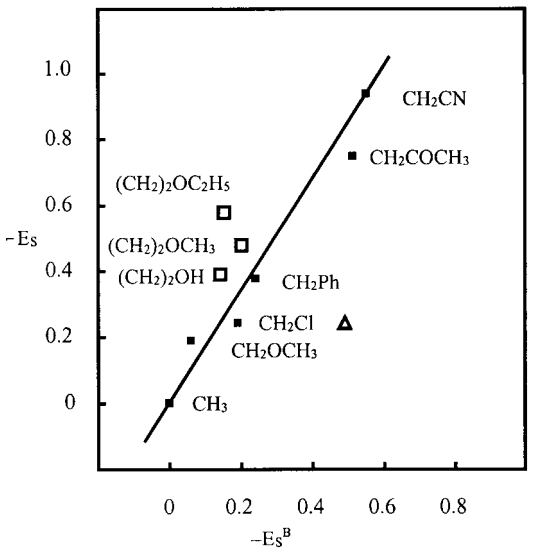

Figure 1. Dependence of the Taft steric substituent constants, E_s, on the E_s^B values. The E_s values for R = $(CH_2)_2OCH_3$, $(CH_2)_2OH$ and $(CH_2)_2OC_2H_5$ were calculated according to Eqn. (8). For R = CH_2Cl two alternative values for E_s^B were used: (■) − 0.17 and (Δ) − 0.49

$(E_s)_{calc}$ and E_s values were −0.48 and −0.77, −0.39 and −0.85, and −0.58 and −0.97, respectively.

In the data analysis according to Eqns ((4)–(6)), the second-order rate constants k_2 reported in Tables 1 and S1 and in Ref. 7 were used. The results of the statistical data treatment with Eqns ((4)–(6)) for the alkaline hydrolysis of substituted alkyl benzoates in aqueous 2.25 M Bu_4NBr, 80% DMSO and water are given in Tables 2 and 3. In Fig. 2, the relationships between the ($\log k - 1.2E_s^B$) values and the σ^* constants in the three investigated media at 25 °C are shown. Figure 3 illustrates the variation of the activation energies E with the substituent constants σ^*.

The experimental $\log k_{obs}$ values and the predicted $\log k_{calc}$ values for the alkaline hydrolysis of substituted alkyl benzoates were compared. The $\log k_{cal}$ values at 25 °C were calculated using Eqn. (4). For the relation $\log k_{calc} = a + b \log k_{obs}$ the following values were found: in 2.25 M Bu_4NBr, $a = 0.0051 \pm 0.0443$, $b = 1.002 \pm 0.031$, $s = 0.066$; in 80% DMSO, $a = -0.0029 \pm 0.034$, $b = 1.010 \pm 0.048$, $s = 0.082$; in water, $a = 0.019 \pm 0.022$, $b = 1.008 \pm 0.023$, $s = 0.048$. R was in range 0.995–0.998. The average deviation of ($\log k_{obs} - \log k_{calc}$) was 0.05 log k units.

Influence of solvent and substituents

The alkaline hydrolysis of substituted alkyl benzoates proceeds by a $B_{Ac}2$ mechanism[65,66] via a tetrahedral intermediate $[RCO(OH)OR']^-$, which involves the attack of a hydroxide ion on the carbonyl carbon as the rate-determining step. When the ester contains electron-withdrawing electronegative substituents the electron density on the carbonyl carbon decreases, the OH^- attack on that carbon is facilitated, the rate increases and the activation energy decreases. The reaction site could be considered as trigonal in the reactant state but tetrahedral in the transition state and the steric factor should lead to a decrease in the rate constant.

For all alkyl benzoates the rate constants decrease on going from water to 2.25 M aqueous Bu_4NBr and increase considerably on transfer from pure water to 80% aqueous DMSO. Although the rate for the unsubstituted derivative, i.e. methyl benzoate, changes in the opposite direction, the polar effect of substituents was found to increase by nearly the same magnitude in the considered media (see Table 3). It has been assumed[1] that in alkaline hydrolysis of benzoates in aqueous 2.25 M Bu_4NBr solution, hydrophobic solvation (with the organic part of quaternary ammonium ions) stabilizes ester molecules in the ground state and the tetrahedral intermediate is less solvated than in water. The decrease in the rate of the alkaline hydrolysis of methyl benzoate in aqueous 2.25 M

Table 3. Results of the analyses of log k values for the alkaline hydrolysis of alkyl benzoates $C_6H_5CO_2R$ in aqueous 2.25 M Bu_4NBr, 80% (v/v) DMSO and water in terms of Eqns (4)[a] and (5) at several temperatures[b]

		2.25 M Bu_4NBr		80% DMSO		Water	
t (°C)	Eqn	ρ_I	δ	ρ_I	δ	ρ_I	δ
15	5	4.74 ± 0.19	1.19 ± 0.22	5.04 ± 0.23	1.05 ± 0.19	3.68 ± 0.17	0.99 ± 0.21
25	5	4.64 ± 0.19	1.24 ± 0.24	4.94 ± 0.21	1.32 ± 0.18	3.64 ± 0.15	0.98 ± 0.19
35	5	4.37 ± 0.17	1.26 ± 0.21	–	–	–	–
40	5	–	–	4.57 ± 0.20	1.05 ± 0.26	3.50 ± 0.22	0.95 ± 0.27
45	5	4.26 ± 0.20	1.20 ± 0.24	–	–	–	–
50	5	4.15 ± 0.18[c]	1.09 ± 0.22	4.37 ± 0.22[d]	0.99 ± 0.27	3.26 ± 0.11	1.00 ± 0.14

[a] The ρ^* values calculated with Eqn. (4) for 2.25 M Bu_4NBr, 80% DMSO and water are as follows: at 15 °C, 2.12 ± 0.08, 2.26 ± 0.11, 1.65 ± 0.11; at 25 °C, 2.07 ± 0.08, 2.21 ± 0.11, 1.64 ± 0.07; at 35 °C, 1.95 ± 0.09; at 40 °C, 2.05 ± 0.11, 1.57 ± 0.09; at 45 °C, 1.90 ± 0.26; at 50 °C, 1.85 ± 0.07, 1.94 ± 0.11, 1.47 ± 0.08, respectively. The δ values were in the range 0.91–1.29.
[b] Correlation coefficient = 0.993–0.998. Number of data: $n = 7$ for 2.25 M Bu_4NBr, $n = 6$ for 80% DMSO and $n = 8$ for water.
[c] $\log k = 0.639$ for R = CH_2CN–benzoate at 50 °C calculated according to Eqn. (6) was included.
[d] $\log k = 1.923$ for R = CH_2Cl–benzoate at 50 °C calculated according to Eqn. (6) was included.

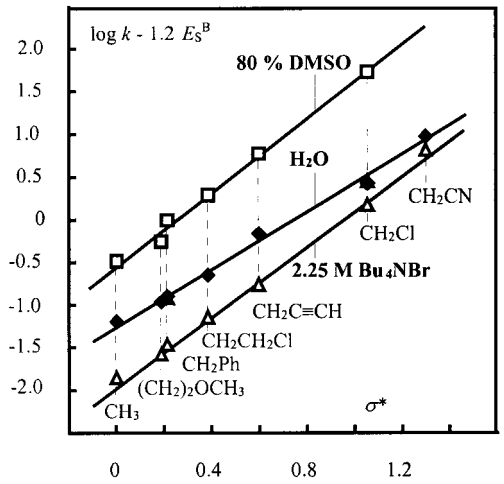

Figure 2. Relationship between the log $k - 1.2E_S^B$ values and the substituent constants σ^* for the alkaline hydrolysis of substituted alkyl benzoates $C_6H_5CO_2R$ in aqueous 2.25 M Bu_4NBr, 80% DMSO and pure water at 25 °C. $\delta = 1.2$ was used, as the average value of δ for 2.25 M Bu_4NBr, 80% DMSO and pure water

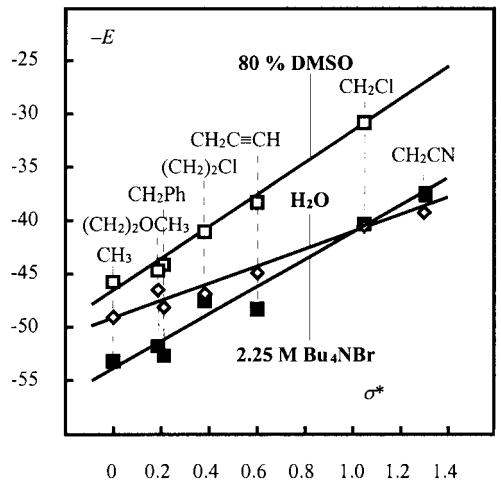

Figure 3. Dependence of the activation energies E (kJ mol^{-1}) on the substituent constants σ^* for the alkaline hydrolysis of substituted alkyl benzoates $C_6H_5CO_2R$ in aqueous 2.25 M Bu_4NBr, 80% DMSO and pure water

Bu_4NBr and the increase in the activation energy E compared with water are in accord with the enhanced stabilization of the ground state by the solvation.

The observed increase in the alkaline hydrolysis rates when pure water is replaced by 80% DMSO has been attributed to the cumulative effect of two factors:[67,68] the capacity of DMSO to solvate effectively the transition state and the presence of a highly desolvated and hence active OH^- ion in aprotic solvents.

The variation of the reaction rate with the substituent in the alkaline hydrolysis of alkyl benzoates appeared to be nicely described by a linear combination of polar and steric terms [see Eqns (4) and (5), Table 3 and Fig. 2] in the case of the three media considered: 2.25 M Bu_4NBr solution, 80% DMSO and pure water. Dual parameter analysis of the log k values with σ and E_s^B constants gave an excellent correlation with a correlation coefficient $R = 0.997$.

The magnitudes of ρ^* at various temperatures appeared to be in ranges 1.8–2.1, 1.9–2.26 and 1.47–1.65 for 2.25 M Bu_4NBr, 80% DMSO and pure water, respectively (Table 3). The corresponding magnitudes of ρ_I at 25 °C are 4.64, 4.94 and 3.64.

The susceptibility to the steric effect of the substituents δ, appeared to be independent of the solvent and temperature. The δ values in the range 0.9–1.3 (Table 3), approximately of the same magnitude as in 2.25 M Bu_4NBr, 80% DMSO and pure water, support the assumption made by Taft that the steric effect is the same in the corresponding basic and acidic ester hydrolyses ($\delta = 1.0$ for the acidic hydrolysis of substituted alkyl benzoates at 49.5 °C[49]).

On going from pure water to 2.25 M Bu_4NBr and to 80% DMSO, the polar effect of aliphatic substituents increases considerably. This is in accordance with the similar electrophilicitie's of these two media, which are considerably smaller than that of water.[69] The ρ^* value at 25 °C is increased by 0.43 units of ρ^* on going from pure water to 2.25 M Bu_4NBr and by 0.57 units of ρ^* from pure water to 80% DMSO (Table 3). The change in the ρ^* value with the solvent for the alkaline hydrolysis of alkyl benzoates proved to be nearly the same as that found for the acidic dissociation of substituted acetic acids in these solvents. The ρ^* values for the acidic dissociation of α-substituted acetic acids for water,[52,70] 80% (w/w) aqueous DMSO[70,71] and 7.75 M Bu_4NBr,[54,72,73] were found to be 1.71, 2.21 and 2.25, respectively. The change in the ρ^* value with the solvent appeared to be comparable to the variation of ρ_I with the solvent in the case of *ortho*-substituents in the alkaline hydrolysis of phenyl benzoates.

On going from pure water to aqueous 2.25 M Bu_4NBr and 80% DMSO, the changes in the ρ_I value for the alkaline hydrolysis of alkyl benzoates was about 1.0 and 1.3 units of ρ_I (Table 3). A similar change in the $(\rho^\circ)_{m,p}$ value on going from water to 2.25 M Bu_4NBr and 80% DMSO has been found for the alkaline hydrolysis of *meta*- and *para*-substituted phenyl benzoates[1] and phenyl tosylates and also for the acidic dissociation of *meta*- and *para*-substituted benzoic acids.[74] The change in the $(\rho_I)_{CH_2X}$ value with the solvent in the acidic dissociation of acetic acids appeared to be nearly the same as the change in the ρ° values for the acidic dissociation of benzoic acids on going from pure water to the gas phase:

$$(\rho_I)_{CH_2X} = 3.167(\pm 0.151) + 0.957(\pm 0.031)\rho^\circ \quad (9)$$

Equation (9) includes the $(\rho_I)_{CH_2X}$ values for α-substituted acetic acids and the ρ° values[74] for the *meta*- and *para*-substituted benzoic acids in H_2O, aqueous 80% DMSO, aqueous 7.75 M Bu_4NBr, DMSO[70] and in the gas

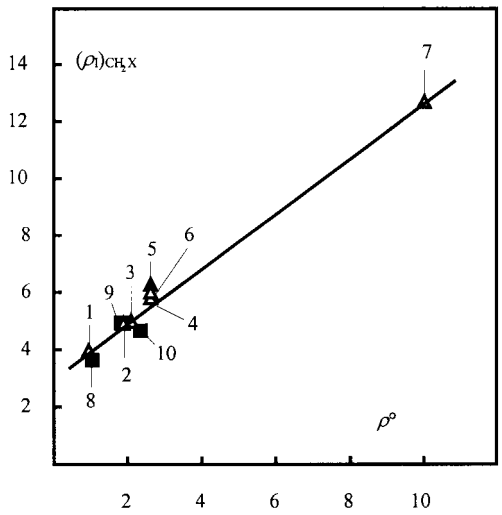

Figure 4. Relationship between the $(\rho_I)_{CH_2X}$ values for alkyl substituents CH_2X and the ρ° constants for *meta*- and *para*-substituted phenyls in various media. Acidic dissociation of carboxylic acids (points 1–7); alkaline hydrolysis of benzoates (points 8–10). Water (points 1 and 8), aqueous 80% DMSO (points 2 and 9), aqueous 7.75 M Bu_4NBr (point 3), pure DMSO (points 4–6), aqueous 2.25 M Bu_4NBr (point 10) and gas phase (point 7)

phase [for the gas phase $(\rho_I)_{CH_2X} = 12.7$, $\rho^\circ = 10.0$[75]] (Fig. 4). From pure water to the gas phase the change in the ρ_I value for α-substituted acetic acids was 8.7 units of ρ_I and the corresponding change in the ρ° value for benzoic acids was 9.1 units of ρ°.

In water at 25 °C, the log k values for the alkaline hydrolysis of substituted ethyl acetates,[50] $RCO_2C_2H_5$, were found to be related to the log k values of the alkaline hydrolysis of substituted alkyl benzoates $C_6H_5CO_2R$ as follows:

$$\log k_{RCOOEt} = 0.925(\pm 0.053) + 1.53(\pm 0.059)\ \log\ k_{PhCOOR} \quad (10)$$

$$R = 0.994, s = 0.12, n = 9$$

where R = CH_3, CH_2Cl, CH_2CN, $CH_2C_6H_5$, $CH_2CH_2OCH_3$, CH_2Br, CH_2OCH_3, CH_2CH_2OH, $CH_2CH_2OCH_2CH_3$. The log k values for the alkaline hydrolysis of alkyl benzoates, R = CH_2Br, CH_2OCH_3, CH_2CH_2OH, $CH_2CH_2OCH_2CH_3$, were calculated using the following relationship in water at 25 °C:

$$\log k_{CH_3COOR} = 0.559(\pm 0.034) + 1.045(\pm 0.033)\ \log\ k_{PhCOOR} \quad (11)$$

A linear relationship between the log k values for ethyl acetates and alkyl benzoates [Eqn. (10)] could be observed owing to the 1.5-fold stronger influence of both polar and steric effects of the acyl component of esters than of their alkyl component. Previously[76] for the polar effect a similar conclusion was proposed in the case of and *meta*- and *para*-substituted phenyls.

The magnitudes of $(E_s)_{calc}$ for β-substituents, like the E_s values for α-substituents in the acyl component of esters, turned out to be ~1.5 times larger than the corresponding E_s^B values for the alkyl part of the esters (Fig. 1). Probably, in the alkaline hydrolysis, β-substituents in the acyl component of esters exert a considerably less pronounced steric hindrance than in their acidic hydrolysis.

Dependence on temperature

The activation energies E for the alkaline hydrolysis of alkyl benzoates (Table 2, Fig. 3) appeared to increase in the case of most alkyl benzoates on going from water to 2.25 M Bu_4NBr solution, and to decrease in the case of all alkyl benzoates when the medium is changed from water to 80% DMSO. The dependence of E on substituent effects is completely caused by the polar effect of the alkyl substituents (see Fig. 3). The slope of the relationship between the activation energy E and σ^* constants is, like the ρ^* values, greater in 2.25 M Bu_4NBr and in 80% DMSO than in pure water. In the basic hydrolysis of esters, the electron-withdrawing substituents stabilize the translation state by charge delocalization and, therefore, decrease the activation energy E. In contrast, the electron-repelling substituents localize the negative charge of the activated complex and so increase E. The substituent effect on the activation energy is greater in 2.25 M Bu_4NBr and 80% DMSO than in water owing to the reduced electrophilic solvation of the reaction center in 2.25 M Bu_4NBr and 80% DMSO. In aqueous 2.25 M Bu_4NBr, the polar effect of electron-withdrawing substituents and the salting-in effect of the medium influence the activation energy in two opposite directions. For chloromethyl benzoate the salting-in effect of the solvent is compensated for by the increased polar effect of the substituent (see Fig. 3) and the activation energy for chloromethyl benzoate in 2.25 M Bu_4NBr equals that found for water (40.2 kJ mol^{-1}). In 80% DMSO solution a similar situation arises for electron-repelling substituents. In 80% DMSO, the increased electron-repelling effect of substituents (compared with water) destabilizes the activated complex as much as 80% DMSO destabilizes the ground state in comparison with water.

The steric factor, independent of temperature, appeared to influence only the log A value, the entropy of the reaction. The magnitudes of (log $A - 1.2\ E_s^B$) were found to be virtually independent of the σ^* constants in water and only very slightly dependent on σ^* in 2.25 M Bu_4NBr and 80% DMSO. Therefore, the alkaline hydrolysis of alkyl benzoates in water could be considered as an isoentropic reaction series whereas in 2.25 M Bu_4NBr and 80% DMSO the isoentropic and isokinetic relationships are indistinguishable. It is

Table 4. Values of $const_1$ and $\Delta \times 10^3 = (const_1 \times 10^3)_S - (const_1 \times 10^3)_{H_2O}$ calculated according to Eqns (12) and (13)

Compounds	Solvent S	$const_1 \times 10^3$	$\Delta \times 10^3$
Substituted alkyl benzoates	2.25 M Bu_4NBr	1.77	0.70
		0.79[a]	0.32[a]
	80% DMSO	1.86	0.79
		0.87[a]	0.40[a]
	Water	1.07	
		0.47[a]	
m- and *p*-substituted phenyl benzoates	2.25 M Bu_4NBr	1.34[b]	1.01[b]
	80% DMSO	0.93[c]	0.60[c]
	Water	0.33[c]	
o-Substituted phenyl benzoates	2.25 M Bu_4NBr	0.89[b]	0.29[b]
	80% DMSO	0.95[c]	0.35[c]
	Water	0.6[b]	

[a] ρ^* was used.
[b] Ref. 1.
[c] Ref. 4.

surprising that the log *A* value or the entropic factor remains nearly unchanged in the case of alkyl substituents on going from water to 2.25 M Bu_4NBr and 80% DMSO. In contrast, for phenyl benzoates a considerable change in the log *A* value (2.7 units) has been observed on going from water to 2.25 M Bu_4NBr.[1]

In Table 4 are listed the values characterizing the variation of the $(\rho_I)_{CH_2X}$, $(\rho^\circ)_{m,p}$ and $(\rho_I)_{ortho}$ values with temperature (Fig. 5) and with the solvent. The values in Table 4 were obtained from the following relationships:

$$\rho = \text{const} + \text{const}_1(1/T) \quad (12)$$

$$\Delta = (\text{const}_1)_S - (\text{const}_1)_{H_2O} \quad (13)$$

In water, the influence of the inductive effect of alkyl substituents, XCH_2, appeared to be nearly 3.5 times larger than that of *meta*- and *para*-substituents when the data at a single temperature were considered (Table 3). Similarly, in the case of alkyl substituents the dependence of the inductive term on temperature was observed to be nearly 3.2 times stronger than the same dependence for *meta*- and *para*-substituents (see $const_1$ values in Table 4). The variation of the ρ^* values with the solvent and temperature was found to be identical with the corresponding change in ρ_I values in the case of *ortho*-substituents. From the relationship[1] $(E^X - E^H)/4.1868\sigma = 2.3R\text{const}_1$, it follows that in the alkaline hydrolysis of alkyl benzoates, the substituent-dependent activation energy $(E^X - E^H)$ varies with the solvent in a similar manner to the variation in the case of *meta*- and *para*-substituted phenyl benzoates when the σ_I scales for alkyl benzoates and the σ° scale for substituted phenyl benzoates were used and in a similar manner to that of *ortho*-substituted phenyl benzoates when the dependence of the activation energy on the polar effect is described in terms of σ^* constants.

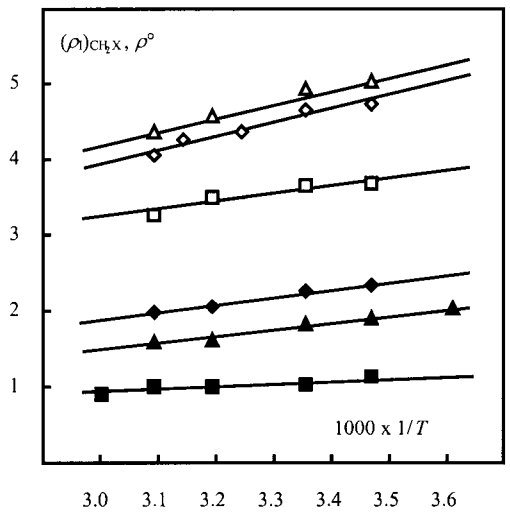

Figure 5. Dependence of the $(\rho_I)_{CH_2X}$ values for the alkaline hydrolysis of alkyl benzoates (open symbols) and ρ° constants for the alkaline hydrolysis of *meta*-and *para*-substituted phenyl benzoates (closed symbols) on $1/T$ in water (squares), 80% DMSO (triangles) and 2.25 M Bu_4NBr (diamonds)

Supplementary material

The second-order rate constants k_2 for the alkaline hydrolysis of substituted alkyl benzoates $C_6H_5CO_2R$ in aqueous 2.25 M Bu_4NBr, 80% (v/v) DMSO and water at various temperatures (Table S1) are available as supplementary material at the epoc website at http://www.wiley.com/epoc.

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