

SUBSTITUENT EFFECTS ON THE BASE-CATALYSED HYDROLYSIS OF PHENYL ESTERS OF *para*-SUBSTITUTED BENZOIC ACIDSIngrid BAUEROVÁ^{1,*} and Miroslav LUDWIG²

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Received August 4, 2000

Accepted October 26, 2000

Seventeen model phenyl esters of 4-substituted benzoic acids were synthesised by the reaction of substituted benzoyl chlorides with phenol in aqueous alkaline solutions (Schotten–Baumann reaction), in pyridine (Einhorn reaction), or by the reaction of substituted benzoic acids with phosphorus oxychloride. Structures and purity of the model compounds were confirmed by ¹H NMR and ¹³C NMR spectroscopy as well as by HPLC and elemental analysis. Phenyl 4-aminobenzoate was synthesised by reduction of phenyl 4-nitrobenzoate in methanol on palladium. Kinetics of base-catalysed hydrolysis of model phenyl esters occurring by the B_{Ac}2 mechanism were measured by UV spectrophotometry in 50% (v/v) aqueous dimethyl sulfoxide solutions at 25 °C under pseudo-first-order conditions, ($[NaOH] = 0.001\text{--}1.0 \text{ mol l}^{-1}$). The addition of OH⁻ to phenyl benzoates was used to establish the kinetic J_E⁻ acidity scale. Linear relation between J_E⁻ and log k_{obs} with the slope near unity was found for all the model compounds. The kinetic constants of hydrolysis of phenyl esters of 4-substituted benzoic acids precisely obey the Hammett relationship (σ_p) with $\rho = 2.44$. Quantitatively comparable results have been obtained by application of Alternative Interpretation of Substituent Effects theory (AISE) using the σ^+ set of substituent constants.

Key words: Esters; Phenyl benzoates; Base-catalysed hydrolysis; Kinetic acidity function; Substituent effects; AISE; Hammett equation; Kinetics; Chemometrics.

The organic chemistry term “substituent effects” generally means the difference between behaviour of a studied substituted molecule and that of the reference non-substituted, parent molecule, which is usually expressed as the difference in a measured quantity. The first description of substituent effects was given by Hammett^{1,2}, who found a linear relationship between logarithm of catalytic rate constants log k of base-catalysed hydrolysis of *meta*- and *para*-substituted ethyl benzoates and logarithm of dissociation constants log K_A of correspondingly substituted benzoic acids. A newer study in the field of quantitative description of substituent effects is the

method of Alternative Interpretation of Substituent Effects (AISE)³⁻⁵. The basic idea of this approach is the assumption that each substituent possesses only a single quality described by a single substituent constant σ^i . This quality, however, can be transmitted to the reaction centre by three different ways, according to which substituents are classified in three groups.

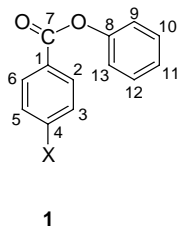
Group I is formed by the substituents that possess no π electrons at the atom linked to the basic skeleton (*i.e.*, substituents of the types of hydrogen or alkyl group), the group II includes substituents that have a free electron pair at the first atom linked to the basic skeleton (such as halogens, alkoxy groups, amino and (di)methylamino groups), and the group III includes substituents with a multiple bond between the first and the second atoms polarised in the direction away from the basic skeleton (substituents such as nitro, cyano, methylsulfonyl, or acetyl group). The AISE principle is expressed mathematically by a family of three intersecting straight lines according to Eq. (1):

$$\log k = \log k_0 + \rho_I \delta_I (\sigma^i - \sigma_0^i) + \rho_N \delta_N (\sigma^i - \sigma_0^i) + \rho_E \delta_E (\sigma^i - \sigma_0^i), \quad (1)$$

where σ^i is the substituent constant, ρ_I , ρ_N , and ρ_E are the reaction constants related to the substituent constants of groups I, II, III, δ_I , δ_N , and δ_E is Kronecker delta taking the value 1 or 0 depending on whether the substituent involves the given interaction or not. The iso-effect σ_0^i is given by the point of intersection of three straight lines of the $\log k$ vs σ^i dependence. As compared with the earlier methods, this method has an advantage in being independent of the skeleton type, reaction centre type, and position of substituent.

Esters of substituted carboxylic acids are substances that have become a basis for studies of substituent effects. In the past, these studies paid considerable attention to alkyl esters of carboxylic acids; they were used to extend the definition series of substituent constants to verify of validity of the Hammett-type relationships and for studies of a number of reactions involving neighbouring group participation, *e.g.*, hydroxy and alkyl(aryl)carbonyl groups⁶⁻¹⁰. These studies successfully adopted base-catalysed hydrolysis as the model reaction, because this hydrolysis – in comparison with the acid-catalysed hydrolysis – offers a number of experimental advantages owing to its irreversibility.

Base-catalysed hydrolysis of esters usually proceeds by the $B_{Ac}2$ mechanism. This reaction can be represented either as a one-step substitution process without formal participation of carbonyl group ($A_N D_N$ or concerted reaction) or an addition-elimination process with a tetrahedral intermediate ($A_N + D_N$ reaction)^{11,12}. The two-step addition-elimination mechanism is replaced by the one-step concerted mechanism in cases where the tetrahedral intermediate is so unstable that there is no barrier to its decomposition (the barrier does not exist for some of its vibrations), and this formation of intermediate becomes in fact the transition state. The presumption of the existence of tetrahedral intermediate started from the discovery of two competition reactions – hydrolysis and isotopic exchange of carbonyl oxygen atom with solvent during hydrolyses of some alkyl benzoates¹³. However, in the hydrolysis of phenyl benzoate, this exchange was unmeasurably slow¹⁴. Further attempts at differentiation between these two mechanistic types – the synchronous or stepwise process – used various aryl esters (the experiments being extended to various nucleophiles) and brought contradictory results^{15–21}.



1	X
a	H
b	CH ₃
c	C ₂ H ₅
d	CF ₃
e	CN
f	NO ₂
g	NH ₂
h	N(CH ₃) ₂
i	OCH ₃
j	OC ₂ H ₅
k	OC ₃ H ₇
l	OC ₄ H ₉
m	F
n	Cl
o	Br
p	I
r	SO ₂ CH ₃

An extension and completion of description of substituent effects in the region mentioned are the main objects of this communication. As suitable model compounds for this study, we selected phenyl esters of 4-substituted benzoic acids **1**, with a special aim to synthesise compounds with as broad a spectrum of substituents as possible. Some of the substrates synthesised have not been described in literature yet.

EXPERIMENTAL

Structure and purity of model compounds **1** were confirmed by using UV, ^1H NMR and ^{13}C NMR spectroscopy, and by HPLC. The substances not yet described in literature were also subjected to elemental analysis. Melting points of synthesised compounds **1** were measured by using of Kofler apparatus without correction. The ^1H and ^{13}C NMR spectra of model compounds **1** were measured in deuterated chloroform, scanned at 25 °C on an AMX 360 spectrometer (Bruker, 360.14 MHz, hexamethyldisiloxane, δ 0.05). Chemical shifts are given in ppm (δ -scale), coupling constants (J) in Hz.

Syntheses of Phenyl Esters of 4-Substituted Benzoic Acids. General Procedures

Method A (ref.²²)

Phenol (0.1 mol) was dissolved in pyridine (five- to ten-fold volume) and the equivalent amount of 4-substituted benzoyl chloride was slowly added dropwise with cooling. The reaction mixture often turned yellow and pyridine hydrochloride separated as a precipitate. The mixture was left to stand for at least 6 h, whereupon it was added dropwise to cold dilute sulfuric acid. The resulting mixture was extracted twice with ether, the extract was washed with water, dried with anhydrous sodium sulfate, ether was evaporated, and the residue was purified either by recrystallisation from ethanol or by vacuum distillation.

Phenyl benzoate (1a). Yield 48.3%, m.p. 65–67 °C (ref.²³ 65–67 °C). ^1H and ^{13}C NMR spectra were in accord with the published data (ref.²⁴).

Phenyl 4-methylbenzoate (1b). Yield 56.5%, m.p. 58–60 °C (ref.²⁵ 73 °C). ^1H NMR: 2.41 s, 3 H (CH_3); 8.07 d, 2 H (H-2, H-6); 7.26 d, 2 H (H-3, H-5); 7.18–7.22 m, 3 H (H-9, H-11, H-13); 7.39 t, 2 H, $J = 5.9$ (H-10, H-12). ^{13}C NMR: 21.66 (CH_3); 165.07 (C-7); 126.67 (C-1); 130.05 (C-2, C-6); 129.29 (C-3, C-5); 144.23 (C-4); 150.88 (C-8); 121.60 (C-9, C-13); 129.13 (C-10, C-12); 125.72 (C-11).

Phenyl 4-cyanobenzoate (1e). Yield 65.7%, m.p. 81–83 °C (ref.²⁶ 87 °C). ^1H NMR: 7.79 d, 2 H (H-2, H-6); 8.29 d, 2 H (H-3, H-5); 7.20 d, 2 H, $J = 5.8$ (H-9, H-13); 7.28 t, 1 H, $J = 6.1$ (H-11); 7.42 t, 2 H, $J = 6.0$ (H-10, H-12). ^{13}C NMR: 116.84 (CN); 163.43 (C-7); 133.27 (C-1); 130.48 (C-2, C-6); 132.25 (C-3, C-5); 117.71 (C-4); 150.38 (C-8); 121.28 (C-9, C-13); 129.51 (C-10, C-12); 126.21 (C-11).

Phenyl 4-ethoxybenzoate (1j). Yield 89.0%, m.p. 100–102 °C. ^1H NMR: 1.44 t, 3 H, $J = 5.4$ (CH_3); 4.11 q, 2 H, $J = 5.4$ (CH_2); 8.12 d, 2 H (H-2, H-6); 6.95 d, 2 H (H-3, H-5); 7.18 d, 2 H, $J = 5.9$ (H-9, H-13); 7.24 t, 1 H, $J = 5.8$ (H-11); 7.41 t, 2 H, $J = 6.0$ (H-10, H-12). ^{13}C NMR: 14.54 (CH_3); 63.66 (CH_2); 164.82 (C-7); 121.48 (C-1); 132.14 (C-2, C-6); 114.11 (C-3, C-5); 163.17 (C-4); 150.94 (C-8); 121.67 (C-9, C-13); 129.29 (C-10, C-12); 125.56 (C-11).

Phenyl 4-propoxybenzoate (1k). Yield 98.0%, m.p. 80–82 °C. ^1H NMR: 1.04 t, 3 H, $J = 5.7$ (CH_3); 1.81 m, 2 H (CH_2); 3.98 t, 2 H, $J = 5.1$ (CH_2); 8.12 d, 2 H (H-2, H-6); 6.96 d, 2 H (H-3, H-5); 7.16–7.25 m, 3 H (H-9, H-11, H-13); 7.39 t, 2 H, $J = 6.0$ (H-10, H-12). ^{13}C NMR: 13.71 (CH_3); 22.31 (CH_2); 69.62 (CH_2); 164.81 (C-7); 121.43 (C-1); 132.12 (C-2, C-6); 114.14 (C-3, C-5); 163.37 (C-4); 150.95 (C-8); 121.67 (C-9, C-13); 129.27 (C-10, C-12); 125.54 (C-11). For $\text{C}_{16}\text{H}_{16}\text{O}_3$ (256.3) calculated: 74.91% C, 6.24% H; found: 74.79% C, 6.39% H.

Method B (ref.²⁷)

A solution of phenol (0.22 mol) and sodium hydroxide (0.22 mol) in water (100 ml) was added to 4-substituted benzoyl chloride (0.1 mol), and the mixture was shaken for 0.5–5 h, whereupon it was extracted with ether. The subsequent work-up was the same as in the method A.

Phenyl 4-(trifluoromethyl)benzoate (1d). Yield 17.2%, m.p. 83–85 °C (ref.²⁸ 87–88 °C). ¹H NMR: 7.75 d, 2 H (H-2, H-6); 8.29 d, 2 H (H-3, H-5); 7.20 d, 2 H, *J* = 5.9 (H-9, H-13); 7.27 t, 1 H, *J* = 5.7 (H-11); 7.42 t, 2 H, *J* = 6.0 (H-10, H-12). ¹³C NMR: 123.73 q, ¹*J*(¹³C, ¹⁹F) = 273.52 (CF₃); 163.86 (C-7); 132.72 (C-1); 130.44 (C-2, C-6); 125.49 q, ³*J*(¹³C, ¹⁹F) = 3.62 (C-3, C-5); 134.90 q, ²*J*(¹³C, ¹⁹F) = 32.96 (C-4); 150.55 (C-8); 121.41 (C-9, C-13); 129.49 (C-10, C-12); 126.10 (C-11).

Phenyl 4-nitrobenzoate (1f). Yield 55.6%, m.p. 119–121 °C (ref.²⁹ 129 °C). ¹H NMR: 8.34 d, 2 H (H-2, H-6); 8.28 d, 2 H (H-3, H-5); 7.21 d, 2 H, *J* = 5.8 (H-9, H-13); 7.29 t, 1 H, *J* = 5.8 (H-11); 7.42 t, 2 H, *J* = 6.1 (H-10, H-12). ¹³C NMR: 163.06 (C-7); 132.54 (C-1); 131.02 (C-2, C-6); 123.45 (C-3, C-5); 134.69 (C-4); 150.29 (C-8); 121.18 (C-9, C-13); 129.43 (C-10, C-12); 126.15 (C-11).

Phenyl 4-methoxybenzoate (1i). Yield 45.5%, m.p. 61–64 °C (ref.³⁰ 58–59 °C). ¹H NMR: 3.86 s, 3 H (CH₃); 8.13 d, 2 H (H-2, H-6); 6.96 d, 2 H (H-3, H-5); 7.17–7.25 m, 3 H (H-9, H-11, H-13); 7.39 t, 2 H, *J* = 6.0 (H-10, H-12). ¹³C NMR: 55.36 (CH₃); 164.77 (C-7); 121.66 (C-1); 132.14 (C-2, C-6); 113.60 (C-3, C-5); 163.75 (C-4); 150.94 (C-8); 121.74 (C-9, C-13); 129.28 (C-10, C-12); 125.57 (C-11).

Phenyl 4-butoxybenzoate (1l). Yield 47.5%, m.p. 85 °C (ref.³¹ 90–92 °C). ¹H NMR: 0.98 t, 3 H, *J* = 5.7 (CH₃); 1.51 m, 2 H (CH₂); 1.79 m, 2 H (CH₂); 4.03 t, 2 H, *J* = 5.0 (CH₂); 8.12 d, 2 H (H-2, H-6); 6.95 d, 2 H (H-3, H-5); 7.18 d, 2 H, *J* = 5.8 (H-9, H-13); 7.23 t, 1 H, *J* = 5.7 (H-11); 7.39 t, 2 H, *J* = 6.1 (H-10, H-12). ¹³C NMR: 10.33 (CH₃); 19.072 (CH₂); 31.01 (CH₂); 67.87 (CH₂); 164.84 (C-7); 121.43 (C-1); 132.14 (C-2, C-6); 114.15 (C-3, C-5); 163.40 (C-4); 150.96 (C-8); 121.69 (C-9, C-13); 129.30 (C-10, C-12); 125.57 (C-11).

Phenyl 4-chlorobenzoate (1n). Yield 49.6%, m.p. 95–97 °C (ref.³² 100.5 °C). ¹H NMR: 8.12 d, 2 H (H-2, H-6); 7.39–7.74 m, 4 H (H-10, H-12, H-3, H-5); 7.19 d, 2 H, *J* = 6.2 (H-9, H-13); 7.26 t, 1 H, *J* = 5.8 (H-11). ¹³C NMR: 164.21 (C-7); 127.90 (C-1); 131.42 (C-2, C-6); 129.42 (C-3, C-5); 140.00 (C-4); 150.64 (C-8); 121.49 (C-9, C-13); 128.82 (C-10, C-12); 125.92 (C-11).

Phenyl 4-bromobenzoate (1o). Yield 41.2%, m.p. 112–113 °C (ref.³³ 116–117 °C). ¹H NMR: 8.05 d, 2 H (H-2, H-6); 7.63 d, 2 H (H-3, H-5); 7.19 d, 2 H, *J* = 5.8 (H-9, H-13); 7.26 t, 1 H, *J* = 5.9 (H-11); 7.42 t, 2 H, *J* = 6.1 (H-10, H-12). ¹³C NMR: 164.37 (C-7); 128.70 (C-1); 131.83 (C-2, C-6); 131.53 (C-3, C-5); 128.36 (C-4); 150.63 (C-8); 121.48 (C-9, C-13); 129.42 (C-10, C-12); 125.93 (C-11).

Phenyl 4-iodobenzoate (1p). Yield 72.0%, m.p. 124–126 °C (ref.³⁴ 130–131 °C). ¹H NMR: 7.84–7.90 m, 4 H (H-2, H-3, H-5, H-6); 7.19 d, 2 H, *J* = 5.9 (H-9, H-13); 7.26 t, 1 H, *J* = 6.2 (H-11); 7.42 t, 2 H, *J* = 6.0 (H-10, H-12). ¹³C NMR: 164.62 (C-7); 128.94 (C-1); 131.41 (C-2, C-6); 137.85 (C-3, C-5); 101.47 (C-4); 150.64 (C-8); 121.48 (C-9, C-13); 129.43 (C-10, C-12); 125.93 (C-11).

Method C (ref.³⁵)

A mixture of 4-substituted benzoyl chloride (0.05 mol) and phenol (0.05 mol) was treated with POCl₃ (0.05 mol), the mixture was heated with flame until a melt was formed and

then on a water bath for another 3 h. After cooling, the reaction mixture was treated with sodium hydroxide solution (200 ml; 10%), and the phenyl benzoate formed was collected by filtration, washed with water, and purified by two recrystallisations from ethanol.

Phenyl 4-ethylbenzoate (1c). Yield 57.5%, m.p. 54–55 °C. ^1H NMR: 1.26 t, 3 H, $J = 5.9$ (CH_3); 2.71 q, 2 H, $J = 5.9$ (CH_2); 8.10 d, 2 H (H-2, H-6); 7.28 d, 2 H (H-3, H-5); 7.17–7.26 m, 3 H (H-9, H-11, H-13); 7.41 t, 2 H, $J = 6.2$ (H-10, H-12). ^{13}C NMR: 15.12 (CH_3); 28.90 (CH_2); 165.10 (C-7); 126.87 (C-1); 130.19 (C-2, C-6); 127.97 (C-3, C-5); 150.44 (C-4); 150.89 (C-8); 121.63 (C-9, C-13); 129.31 (C-10, C-12); 125.64 (C-11). For $\text{C}_{15}\text{H}_{14}\text{O}_2$ (226.3) calculated: 79.55% C, 6.19% H; found: 79.42% C, 6.20% H.

Phenyl 4-(dimethylamino)benzoate (1h). Yield 94.0%, m.p. 175–176 °C (ref.³⁶ 180–181 °C). ^1H NMR: 3.07 s, 6 H (CH_3); 8.06 d, 2 H (H-2, H-6); 6.72 d, 2 H (H-3, H-5); 7.17–7.25 m, 3 H (H-9, H-11, H-13); 7.41 t, 2 H, $J = 6.0$ (H-10, H-12). ^{13}C NMR: 39.99 (CH_3); 165.35 (C-7); 116.05 (C-1); 131.85 (C-2, C-6); 110.76 (C-3, C-5); 153.51 (C-4); 151.25 (C-8); 121.84 (C-9, C-13); 129.19 (C-10, C-12); 125.25 (C-11).

Phenyl 4-fluorobenzoate (1m). Yield 31.5%, m.p. 51–53 °C (ref.³⁷ 63.5–64.5 °C). ^1H NMR: 8.20 d, 2 H (H-2, H-6); 7.13–7.20 m, 4 H (H-9, H-13, H-3, H-5); 7.23 t, 1 H, $J = 6.1$ (H-11); 7.41 t, 2 H, $J = 5.9$ (H-10, H-12). ^{13}C NMR: 164.63 (C-7); 126.69 (C-1); 132.67 d, $^3J(^{13}\text{C}, ^{19}\text{F}) = 9.42$ (C-2, C-6); 115.67 d, $^2J(^{13}\text{C}, ^{19}\text{F}) = 22.01$ (C-3, C-5); 164.37 d, $^1J(^{13}\text{C}, ^{19}\text{F}) = 302.59$ (C-4); 150.71 (C-8); 121.54 (C-9, C-13); 129.41 (C-10, C-12); 125.87 (C-11).

Phenyl 4-(methylsulfonyl)benzoate (1r). Yield 90.5%, m.p. 138–141 °C. ^1H NMR: 3.07 s, 3 H (CH_3); 8.08 d, 2 H (H-2, H-6); 8.39 d, 2 H (H-3, H-5); 7.21 d, 2 H, $J = 5.9$ (H-9, H-13); 7.28 t, 1 H, $J = 5.9$ (H-11); 7.43 t, 2 H, $J = 6.0$ (H-10, H-12). ^{13}C NMR: 44.20 (CH_3); 163.58 (C-7); 134.24 (C-1); 130.98 (C-2, C-6); 127.57 (C-3, C-5); 144.70 (C-4); 150.40 (C-8); 121.31 (C-9, C-13); 129.53 (C-10, C-12); 126.21 (C-11). For $\text{C}_{14}\text{H}_{12}\text{O}_4\text{S}$ (276.3) calculated: 60.80% C, 4.34% H, 11.58% S; found: 60.63% C, 4.50% H, 11.47% S.

Phenyl 4-Aminobenzoate (1g)

A solution of phenyl 4-nitrobenzoate (**1f**; 0.0034 mol) in 180 ml methanol and Pd catalyst was shaken in an autoclave under the hydrogen pressure of 300 kPa for 3 days, whereupon methanol was evaporated and the residue was recrystallised twice from ethanol. Yield: 0.2 g (28.7%) phenyl 4-aminobenzoate **1g** with m.p. 159–160 °C (ref.³⁸ 175 °C). ^1H NMR: 4.13 s, 2 H (NH_2); 7.99 d, 2 H (H-2, H-6); 6.66 d, 2 H (H-3, H-5); 7.18 d, 2 H, $J = 5.9$ (H-9, H-13); 7.24 t, 1 H, $J = 5.8$ (H-11); 7.39 t, 2 H, $J = 6.2$ (H-10, H-12). ^{13}C NMR: 165.10 (C-7); 118.62 (C-1); 132.21 (C-2, C-6); 113.72 (C-3, C-5); 151.09 (C-4); 151.33 (C-8); 121.77 (C-9, C-13); 129.24 (C-10, C-12); 125.40 (C-11).

Kinetic Measurements

The solutions were prepared from NaOH p.a., commercial dimethyl sulfoxide (p.a., Fluka AG) and redistilled water freed from carbon dioxide by short boiling. The stock aqueous solutions of NaOH (1 and 2 mol l^{-1}) were standardised by titration with oxalic acid (phenolphthalein). The solutions for kinetic measurements were prepared by mixing the respective amounts of NaOH stock solution and dimethyl sulfoxide and filling up the volume of calibrated flask by addition of 50% (v/v) aqueous dimethyl sulfoxide. pH of the least concentrated NaOH solution (0.001 mol l^{-1}) was measured on a Titralab 3 (Radiometer) apparatus with an automatic burette ABU 93.

Kinetic measurements were performed on a Hewlett-Packard HP 8452A instrument. Prior to the measurement, the solution of NaOH in aqueous dimethyl sulfoxide (approximately 2 ml) in a quartz cell was kept in a thermostat at 25 ± 0.1 °C, and a solution of model compounds **1** in 1,4-dioxane (approximately 4 μ l) was added with a Hamilton (701 N) syringe. The content of cell was thoroughly mixed and then the absorbance changes were monitored at 296 nm (306 nm for **1g**, 274 nm for **1l**, and 280 nm for **1p**). The results of measurement were evaluated by non-linear regression using an optimisation program. The observed rate constants are given in Table I.

RESULTS AND DISCUSSION

Evaluation and Interpretation of Kinetic Acidity Function

A part of the kinetic measurements were carried out in non-ideal media, thus it was necessary, for obtaining the values of logarithm of catalytic rate constants $\log k_{\text{cat}}$, to plot the values of logarithm of the observed rate constants $\log k_{\text{obs}}$ against the values of acidity function values instead of pH. Literature³⁹ gives an acidity function J_- constructed from values of the equilibrium constants of the addition reaction of hydroxide ion to substituted benzaldehydes in 50% (v/v) aqueous dimethyl sulfoxide in the interval of sodium hydroxide concentration range from 0.01 to 1.5 mol l⁻¹. Hence, the scale does not cover the whole range of concentrations of solution used in hydrolysis of the model compounds. For two model compounds (**1f** with NO₂ substituent and **1r** with SO₂CH₃), it was not at all possible to construct the dependence of $\log k_{\text{obs}}$ vs J_- . These substrates reacted very rapidly even at low concentrations of sodium hydroxide (0.001–0.005 mol l⁻¹); hence, the kinetic measurements at higher concentrations were impossible.

By plotting logarithm of the observed rate constant $\log k_{\text{obs}}$ against the values of acidity function J_- we obtained a series of straight lines whose slopes were not equal to unity but varied from 0.49 (**1d** with CF₃ substituent) or 0.56 (**1e** with CN substituent) up to 1.05 (**1l** with OC₄H₉ substituent). The other slope values varied around 0.98 in average. Therefore, it was necessary to construct an original acidity function from the data measured.

The acidity function was referenced to the pH value measured for the sodium hydroxide solution of the lowest concentration, *i.e.* 0.001 mol l⁻¹ (pH 11.81). For constructing the acidity function, we used a data matrix containing the individual sodium hydroxide concentrations associated with the corresponding logarithms of the observed rate constant, $\log k_{\text{obs}}$. Using an iterative way of calculation and the "ACID" program (ref.⁴⁰), we obtained a new acidity function J_-^E (the exponent E symbolising the substrate,

TABLE I
Observed rate constant $k_{\text{obs}} \cdot 10^4$ (s^{-1}) for base-catalysed hydrolysis of model phenyl esters **1** at various concentrations of sodium hydroxide (mol l^{-1}) in 50% (v/v) aqueous dimethyl sulfoxide at 25 °C

Com- pound	c[NaOH]																			
	0.001	0.002	0.003	0.005	0.01	0.02	0.03	0.05	0.06	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1	
1a	3.75	8.51	13.7	27.0	41.6	83.9	137	241	283	533	968	1370	1450	1520						
1b		3.67	5.44	11.2	20.3	44.6	72.1	114	135	224	475	570	773	929	1000					
1c			4.43	9.16	17.0	37.5	54.4	92.4	95.3	197	419	507	623	700	932					
1d	42.4	85.5	137	291	489	866	1250													
1e	145	356	521	837	1450	2960														
1f							4.22	4.73	7.57	12.7	25.1	37.1	47.2	57.2	67.4	70.9	79.9	90.0	97.1	
1g										7.16	15.6	23.1	30.4	35.2	42.4	48.1	52.0	60.9	68.1	
1h	198	429	587	1090																
1i				5.38	10.3	24.4	36.0	56.8	71.8	123	234	332	443	571	650	723	761	788	863	
1j				4.27	7.86	17.3	28.6	51.7	56.8	97.9	181	261	299	444	417	426	429	596		
1k					7.17	16.3	24.9	45.0	55.2	97.7	171	216	260	249	364	333	414	525		
1l					5.91	15.3	24.7	46.5	47.4	86.7	183	251	257	473	486	571	663	733		
1m	6.38	12.4	17.3	39.6	74.4	162	235	427	464	1340										
1n	13.4	20.9	39.4	82.1	163	309	488	802												
1o	12.8	17.1	28.9	81.7	146	298	464	730												
1p	7.33	19.8	43.4	60.8	166	413	555	746												
1r	239	474	653	1220																

benzoic acid esters). Their values for selected concentrations of sodium hydroxide are presented in Table II.

The extremely low slope values (0.49 or 0.56) in the dependence of logarithm of the observed rate constant ($\log k_{\text{obs}}$) on values of acidity function J_- (Table III) in the cases of model compounds **1d** and **1e** were most probably due to the small number of points serving for construction of the linear dependence (three points for compound **1d** and only two points for compound **1e**) and to the fact that the acidity function J_- exhibits more distinct deviations from the assumed smooth course in the concentration range of 0.01–0.1 mol l⁻¹.

Evaluation of Calculation Method of Catalytic Rate Constants

By plotting the logarithm of the observed rate constants, $\log k_{\text{obs}}$, against the kinetic acidity function J_-^E , we obtained linear dependences whose slopes are close to unity for all the substrates studied. The intercepts of this dependence should correspond to the $\log(k_{\text{cat}}K_{\text{W}})$ values. As this value for 50% (v/v) aqueous dimethyl sulfoxide is not available in literature, the whole construction was referenced to the unsubstituted substrate, for which the intercept value was adjusted as equal to zero by definition. This

TABLE II
Acidity function J_-^E in 50% (v/v) aqueous dimethyl sulfoxide at 25 °C in dependence on sodium hydroxide concentration

c[NaOH], mol l ⁻¹	J_-^E	c[NaOH], mol l ⁻¹	J_-^E
0.001	11.81	0.1	13.90
0.002	12.11	0.2	14.20
0.003	12.31	0.3	14.42
0.005	12.57	0.4	14.49
0.01	12.86	0.5	14.59
0.02	13.18	0.6	14.66
0.03	13.39	0.7	14.73
0.05	13.62	0.8	14.77
0.06	13.70	0.9	14.83
		1	14.90

procedure resulted in the intercept values of the $\log k_{\text{obs}}$ vs J_-^E dependence corresponding to differences in logarithms of catalytic rate constants $\Delta \log k_{\text{cat}} = (\log k_{\text{cat}}^X - \log k_{\text{cat}}^H)$.

Evaluation of Substituent Effects

Description of Substituent Effects by Hammett-Type Relationships

In order to describe the substituent effects at *para* position, we correlated the differences in logarithms of catalytic rate constants $\Delta \log k_{\text{cat}}^{\text{para}}$ with the Hammett σ_p constants⁴¹ (Eq. (2)):

TABLE III

Intercepts (a_0) the dependence of $\log k_{\text{obs}}$ on acidity function J_-^E relative to unsubstituted substrate (N , number of measurements; r , correlation coefficient; s , residual standard deviation)

Compound	Substituent	N	a_0	r	s
1a	H	14	0.000	0.9981	0.056
1b	CH ₃	14	-0.332	0.9992	0.035
1c	C ₂ H ₅	13	-0.419	0.9982	0.047
1d	CF ₃	7	1.046	0.9962	0.051
1e	CN	6	1.596	0.9956	0.048
1f	NO ₂	4	1.723	0.9966	0.031
1g	NH ₂	13	-1.597	0.9984	0.029
1h	N(CH ₃) ₂	10	-1.799	0.9981	0.020
1i	OCH ₃	16	-0.619	0.9988	0.036
1j	OCH ₂ H ₅	15	-0.744	0.9969	0.056
1k	OCH ₃ H ₇	14	-0.798	0.9964	0.052
1l	OC ₄ H ₉	14	-0.755	0.9979	0.046
1m	F	10	0.254	0.9957	0.075
1n	Cl	8	0.538	0.9978	0.046
1o	Br	8	0.491	0.9942	0.077
1p	I	8	0.512	0.9920	0.099
1r	SO ₂ CH ₃	4	1.778	0.9981	0.022

$$\Delta \log k_{\text{cat}}^{\text{para}} = -(0.082 \pm 0.030) + (2.437 \pm 0.070)\sigma_{\text{p}} \quad (2)$$

$$N = 17, r = 0.9939, s = 0.124.$$

The explained variability is 98.78%.

The reaction constant ρ has a value of about 2.4, which indicates that, as expected, the rate-limiting step involves a nucleophilic attack at the reaction centre. The absolute value of the reaction constant confirms the presumption that the hydroxide ion attacks the atom next to the benzene ring, *i.e.* the carbonyl carbon atom, which agrees with the presumed $B_{\text{Ac}2}$ mechanism.

The obtained value of the reaction constant could not be compared with analogous ρ values from literature determined on structurally similar substrates in the same medium. However, it is obvious that the value of the reaction constant increases on going from aqueous medium to mixed solvent dimethyl sulfoxide–water^{42,43}, and it does not much change with varying substituent in the alcohol residue³⁷. For base-catalysed hydrolysis of 4-substituted phenyl benzoates in 80% (v/v) dimethyl sulfoxide–water medium, the ρ constant is 1.81 (ref.⁴⁴). Hence the reaction constant of base-catalysed hydrolysis of our model substances is substantially higher. This fact supports the hypothesis that there appears a formal negative charge at carbonyl oxygen in the attack by hydroxide ion, which indicates a complete change of hybridisation from sp^2 to sp^3 (ref.⁴⁵).

The close correlation and low residual standard deviation in the dependence of differences between logarithms of catalytic rate constants ($\Delta \log k_{\text{cat}}^{\text{para}}$) on σ_{p} constants does not confirm the hypothesis^{36,46} that in the hydrolysis of *para*-substituted model phenyl esters with an electron-donor substituent, the value of rate constant $k_{\text{cat}}^{\text{para}}$ is distinctly lower than it should be considering to the σ_{p} constants of the respective substituent. Hence the model phenyl esters obviously do not exhibit any marked resonance stabilisation in the ground states.

The kinetic data obtained for the *para*-substituted derivatives were also treated by the PCA method⁴⁷, which uses the latent variables. The obtained values of logarithm of the observed rate constant $\log k_{\text{obs}}$ were arranged into a matrix of dimensions 17×19 , where the rows of matrix corresponded to the individual substituents and the columns to individual concentrations of sodium hydroxide. The matrix was filled to 54.8%. The number of necessary latent variables was determined by the *F*-test (test of hypothesis about

significance of increment of explained variability) to be three, the second and the third variables being at the limit of statistical significance.

The score vector t_1 obtained by the PCA method has no physical meaning with respect to definition of the method but it can be assigned one if it is possible to find a vector of substituent constants that correlates well with the given score vector. The close correlation relationship between differences of logarithm of the catalytic rate constants ($\Delta \log k_{\text{cat}}^{\text{para}}$) and the Hammett σ_p constants indicates that the score vector t_1 probably describes the electron effects of substituents at *para* position. The linear relationship between the score vector t_1 and the vector of substituent constants σ_p is mathematically expressed by Eq. (3):

$$t_1 = (0.486 \pm 0.009) + (0.678 \pm 0.021)\sigma_p \quad (3)$$

$$N = 17, r = 0.9926, s = 0.037 .$$

Description of Substituent Effects by AISE Theory

In order to verify the relationship describing the substituent effects from *para* position by means of the AISE theory, we used the kinetic data obtained for the model substances representing all three groups of substituents – the class I formed by substituents H, CH₃, C₂H₅ and CF₃, the class II involving F, Cl, Br, I, NH₂, N(CH₃)₂, OCH₃, and the class III containing CN, NO₂ and SO₂CH₃ substituents. Substituent constants σ^i are given in ref.⁴⁸.

The optimisation of five parameters ($\log k_0$, ρ_I , ρ_N , ρ_E , and σ_0^i) by means of Eq. (1) gave a correlation equation (4):

$$\begin{aligned} \Delta \log k_{\text{cat}}^{\text{para}} = & (1.619 \pm 0.097) + (3.457 \pm 0.171)[\sigma^i - (0.515 \pm 0.018)] + \\ & + (7.747 \pm 0.339)[\sigma^i - (0.515 \pm 0.018)] + \\ & + (1.518 \pm 1.529)[\sigma^i - (0.515 \pm 0.018)] \end{aligned} \quad (4)$$

$$N = 14, R = 0.9965, s = 0.112 .$$

A comparison of residual standard deviation and explained variability in the Hammett-type correlation ($r^2 = 0.9878$) with that in the AISE theory ($R^2 = 0.9931$) shows that both approaches are quantitatively comparable.

This work was supported by the Grant Agency of the Czech Republic (grant No. 203-98-0602).

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