

**FURTHER STUDIES ON THE EXTENDED HAMMETT EQUATION  
COMPRISING THE HYDROPHOBIC CONSTANT: REACTIVITY DATA  
FOR BENZOIC ACIDS, ARYLACETIC ACIDS,  $\beta$ -ARYLPROPIONIC  
ACIDS, *trans*- AND *cis*-CINNAMIC ACIDS, METHYL BENZOATES;  
DISSOCIATION CONSTANTS, DDM REACTION AND ALKALINE  
HYDROLYSIS IN VARIOUS WATER-ORGANIC SOLVENT MIXTURES\***

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*Dedicated to Professor Otto Exner on the occasion of his 65th birthday.*

The extended Hammett equation  $\Delta = \rho\sigma + h\pi$  comprising the hydrophobic constant  $\pi$  is found to be effective in the title compounds and reactivities in various solvent mixtures. In 32 vol. % tert-butanol-water  $h_m$  decreases in the order  $\text{ArCOOMe}$  ( $-0.25$ ), *cis*- $\text{ArCH}=\text{CHCOOH}$  ( $-0.18$ ),  $\text{ArCOOH}$  and  $\text{ArCH}_2\text{COOH}$  ( $-0.16$ ),  $\text{ArCH}_2\text{CH}_2\text{COOH}$  and *trans*- $\text{ArCH}=\text{CHCOOH}$  ( $-0.07$ ). For  $\text{ArCOOH}$ , mixtures like 40–60% methanol, 50% ethanol, 50% acetone and 50% dioxane give similar  $h_m$  values of circa  $-0.05$ . For  $\text{ArCH}_2\text{COOH}$  the effects of 3-iodo and 4-iodo substituents are acid-weakening in 32% tert-butanol. The consequences of the  $h\pi$  term for  $\rho$ ,  $\sigma$ , and the averaging of  $\sigma$  values, are discussed.

Recently<sup>1</sup>, we have drawn attention to the lack of precision of the Hammett equation (1) in several water-organic solvent mixtures for several systems; the main body of evidence

$$\log K - \log K^0 \equiv \Delta = \rho\sigma \quad (1)$$

consisted of  $\text{p}K$  values of benzoic acids in aqueous tert-butanol (TB/ $\text{H}_2\text{O}$ ) and aqueous ethanol (E/ $\text{H}_2\text{O}$ ). Convincingly better statistical data were obtained with the extended Hammett equations (2)–(4), comprising Hansch's<sup>2</sup> hydrophobic,

$$\Delta = \rho\sigma + h\pi \quad (2)$$

$$\Delta_m = \rho_m\sigma_m + h_m\pi \quad (3)$$

$$\Delta_p = \rho_p\sigma_p + h_p\pi \quad (4)$$

\* Part XII in the series Substituent Effects; Part XI: *J. Chem. Soc., Perkin Trans. 2*, 1989, 977.

constant  $\pi$ . In our most marked example, relating to a set of 24 compounds of the (*meta*-)ArCOOH series in 32TB (32 vol. % TB, 8 mole %), Eq. (1) and (3) give, respectively, standard deviations  $s$  0.170 and 0.037, correlation coefficients  $R$  0.961 and 0.998, with  $h$  in Eq. (3)  $-0.161 \pm 0.008$ . In 50E (22 mole %) the same set gives, respectively,  $s$  0.059 and 0.028,  $R$  0.995 and 0.999, with  $h$   $-0.051 \pm 0.006$ . Maximum values of  $h$  occur at about 32TB and 40E; in 85E Eq. (1) is followed closely with  $s$  0.047 and  $R$  0.997, and Eq. (3) does not give any improvement. Furthermore, if the substituents in the set are limited to those having  $\pi$  values within a narrow range (0.27 to  $-0.73$ , the "inside" set<sup>1</sup>,  $n$  10) Eq. (1) performs well even in 32TB with  $s$  0.057,  $R$  0.996, although Eq. (3) is better, with  $s$  0.034,  $R$  0.999, but imprecise  $h$   $-0.181 \pm 0.045$ . Apparently, one of the criteria for a substituent to be "well behaved" is that it has a small  $\pi$  value.

## RESULTS AND DISCUSSION

In the present paper we give  $pK$  values of ArCOOH in E/H<sub>2</sub>O and TB/H<sub>2</sub>O in addition to those given earlier<sup>1,3,4,5</sup>, and data in methanol-water (M/H<sub>2</sub>O), acetone-water (A/H<sub>2</sub>O) and dioxane-water (D/H<sub>2</sub>O). Additional data are also given of  $pK$  values of ArCH<sub>2</sub>COOH<sup>4,6</sup>, ArCH<sub>2</sub>CH<sub>2</sub>COOH<sup>4,7</sup> and *cis*- and *trans*-ArCH=CHCOOH<sup>4</sup>. Included are data on the reaction of ArCOOH with diazodiphenylmethane (DDM), and on the alkaline hydrolysis of ArCOOMe.

These data have been collected in Tables I–IV. Table V lists the regression data for Eq. (1) and Eq. (3), arranged in pairs to facilitate comparison. As in our previous paper<sup>1</sup> the conclusion is that Eq. (3) performs well and also when Eq. (1) fails.

The attentive reader will note that in most of the series the number of data points,  $n$ , is too small to comply with the requirements of proper statistics<sup>8,9</sup>. Nevertheless, we give the complete set of statistical data because this provides the simplest way of showing the quality of Eq. (1) and Eq. (3). Again, as far as possible, the sets include substituents with high and low  $\sigma_m$  (H 0, I 0.352, NO<sub>2</sub> 0.710) and high and low  $\pi$  (H 0, NO<sub>2</sub>  $-0.28$ , I 1.12, *t*-Bu 1.98). An experimental ratio  $\Delta$ -3-I/ $\Delta$ -3-NO<sub>2</sub> different from 0.5 and a ratio  $\Delta$ -3-*t*-Bu/ $\Delta$ -3-NO<sub>2</sub> different from  $-0.1$  guarantees that Eq. (1) is not satisfactory. A good fit with Eq. (3) then gives at least a provisional confirmation that the  $h\pi$  term is a valuable extension.

With this in mind we first list the various sets in order of decreasing  $h_m$  in 32TB (Table VI).

The near-equality of  $h$  for ArCOOH and ArCH<sub>2</sub>COOH is well-founded; near-equality also holds for ester hydrolysis in 56 wt. % A (ArCOOMe,  $h$   $-0.11$ ; ArCH<sub>2</sub>COOEt,  $h$   $-0.10$ , ref.<sup>1</sup>). The position of ArCOOMe above ArCOOH is supported by data in 50–60A (ArCOOMe,  $h$   $-0.11$ ; ArCOOH,  $h$   $-0.06$ ). The high value for *cis*-ArCH=CHCOOH certainly needs confirmation;  $\Delta$ -3,5-di-*t*-Bu  $-0.76$  versus  $\Delta$ -3-NO<sub>2</sub> 0.37 in 32TB is rather conspicuous, though, and indicates that only

TABLE I

Benzoic acids: Thermodynamic  $pK$  values of the parent, and substituent effects expressed as  $100(pK^o - pK)$  in various solvents, at  $25^\circ C^a$

40M (4.96)					
3-NO <sub>2</sub> 90	3-I	40	3,5-di-t-Bu	-34	3-CEt <sub>3</sub> -28
60M (5.49)					
3-NO <sub>2</sub> 99	3-I	41	3,5-di-t-Bu	-35	3-CEt <sub>3</sub> -27
80M (6.22)					
3-NO <sub>2</sub> 103	3-I	45	3,5-di-t-Bu	-28	3-CEt <sub>3</sub> -21
10E (4.37)					
3-NHCONH <sub>2</sub> <sup>b</sup>		11	4-COOMe	47	4-OH -39
3,5-diOMe		22	4-NHAc	-3	4-SO <sub>2</sub> Me 75
50E (5.48)					
3-neoPent	-30	3,5-diBr	102	4-COOMe	63
3-t-Pent	-30	4-neoPent	-24	4-NEt <sub>2</sub>	-107 <sup>d</sup>
3-MeC=CMe <sub>2</sub>	-22	4-t-Pent	-25	4-Pyrrolidin-1-yl	-104 <sup>d</sup>
3-CH <sub>2</sub> SiMe <sub>3</sub>	-33	4-Hept	-23	4-Piperidin-1-yl	-62 <sup>d</sup>
3-CO-t-Bu	38	4-cycloHex	-21	4-NHFO	-2
3-NH <sub>2</sub>	-8 <sup>c</sup>	4-bicyclo[2.2.2]		4-NHAc	-7
3-NMe <sub>2</sub>	-14 <sup>c</sup>	Octan-1-yl	-20	4-N=NPh	39
3-NHCONH <sub>2</sub> <sup>b</sup>	14	4-CH <sub>2</sub> Ph	-14	4-OH	-53
3-O-Octyl	-4	4-CH=CH <sub>2</sub>	-3	4-OEt	-34
3,5-diEt	-35	4-MeC=CMe <sub>2</sub>	-18	4-OPh	-2
3,5-di-iPr	-41	4-Ph	3	4-SO <sub>2</sub> Me	109
3,5-diOMe	22	4-CH <sub>2</sub> SiMe <sub>3</sub>	-37		
3,5-diSiMe <sub>3</sub>	-40	4-CO-t-Bu	51		
75E (6.29)					
3-neoPent	-20	3,5-diBr	122	4-Piperidin-1-yl	-69 <sup>e</sup>
3-t-Pent	-15	4-neoPent	-15	4-NHNH <sub>2</sub>	-75
3-CH <sub>2</sub> SiMe <sub>3</sub>	-27	4-t-Pent	-16	4-NHFO	-2
3-CO-t-Bu	50	4-Hept	-19	4-NHAc	-11
3-NH <sub>2</sub>	-12 <sup>e</sup>	4-cycloHex	-17	4-N=NPh	49
3-NMe <sub>2</sub>	-19 <sup>e</sup>	4-CH <sub>2</sub> Ph	-8	4-OH	-60
3-O-Octyl	7	4-Ph	8	4-OEt	-34
3,5-diEt	-28	4-CH <sub>2</sub> SiMe <sub>3</sub>	-31	4-OPh	-2
3,5-di-iPr	-30	4-CO-t-Bu	62	4-SO <sub>2</sub> Me	116
3,5-diOMe	24	4-COOMe	73	3,5-diMe-4-NO <sub>2</sub>	91

TABLE I  
 (Continued)

85E (6·77)					
3-neoPent	—16	3-NH <sub>2</sub>	—20	4-neoPent	—16
3-t-Pent	—19	3-NMe <sub>2</sub>	—24	4-CH <sub>2</sub> SiMe <sub>3</sub>	—34
3-CH <sub>2</sub> SiMe <sub>3</sub>	—26	3-NHCONH <sub>2</sub> <sup>b</sup>	9	4-CO-t-Bu	62
3-CO-t-Bu	53	3-OH	—6	4-Piperidin-1-yl	—72 <sup>c</sup>
		3-O-Octyl	0		
22TB (4·78)					
3-neoPent	—47	3-NHCONH <sub>2</sub> <sup>b</sup>	13	4-Ph	—13
3-CH <sub>2</sub> SiMe <sub>3</sub>	—62	3,5-diEt	—51	4-CO-t-Bu	38
3-CO-t-Bu	25	3,5-di-iPr	—60	4-OH	—43
32TB (5·28)					
3-neoPent	—54	3,5-diSiMe <sub>3</sub>	—85	4-CH <sub>2</sub> SiMe <sub>3</sub>	—63
3-t-Pent	—61	4-neoPent	—43	4-CO-t-Bu	43
3-CH <sub>2</sub> SiMe <sub>3</sub>	—67	4-t-Pent	—46	4-Piperidin-1-yl	—74 <sup>f</sup>
3-CO-t-Bu	27	4-Hept	—48	4-OH	—46
3-NHCONH <sub>2</sub> <sup>b</sup>	21	4-cycloHex	—45	4-OPh	—27
3-O-Octyl	—33	4-bicyclo[2.2.2]		3,5-diMe-4-NO <sub>2</sub>	68
3,5-diEt	—61	Octan-1-yl	—51	3,5-di-t-Bu-4-NO <sub>2</sub>	21
3,5-di-iPr	—71	4-CH <sub>2</sub> Ph	—29	4-t-Bu-3-NO <sub>2</sub>	69
3,5-diOMe	15	4-Ph	—14		
10A (4·46)					
3-Me	—6	3-Br	44	4-Me	—16
3-COMe	41	3-I	39	4-COMe	53
3-NO <sub>2</sub>	80	3,5-diMe	—13	4-NO <sub>2</sub>	84
3-OMe	13	3,5-diNO <sub>2</sub>	155	4-OH	—37
3-F	37	3-OH	6	4-OMe	—30
3-Cl	41	3-OMe	13	4-F	11
				4-Cl	26
50A (5·82)					
3-Me	—16	3,5-diNO <sub>2</sub>	202	4-CH <sub>2</sub> SiMe <sub>3</sub>	—46
3-COMe	56	3-neoPent	—27	4-COMe	67
3-NO <sub>2</sub>	107	3-CEt <sub>3</sub>	—40	4-NH <sub>2</sub>	—88 <sup>f</sup>
3-OMe	14	3-CH <sub>2</sub> SiMe <sub>3</sub>	—40	4-NMe <sub>2</sub>	—98 <sup>f</sup>
3-F	49	3-OH	1	4-NO <sub>2</sub>	117
3-Cl	53	3-SiMe <sub>3</sub>	—17	4-OH	—48
3-Br	55	4-Me	—20	4-OMe	—32
3-I	47	4-neoPent	—27	4-F	26
3,5-diMe	—25	4-t-Bu	—23	4-Cl	43
3,5-di-t-Bu	—47	4-CEt <sub>3</sub>	—30	4-SiMe <sub>3</sub>	—72

TABLE I  
(Continued)

50D (6·32)					
3-Me	-15	3-F	48	3-I	43
3-t-Bu	-25	3-Cl	49	3-OH	-1
3-NO <sub>2</sub>	105	3-Br	49		

<sup>a</sup> 40M (4·96), etc.: solvent 40 ml absolute methanol in 100 ml final solution, and (in parentheses) pK of benzoic acid, E ethanol, TB t-butanol, A acetone, D dioxane; <sup>b</sup> additional data for 3-NHCONH<sub>2</sub> (solvent, 100A): 10TB 8, 40TB 21, 50TB 22, 60TB 22, 75TB 20, 90TB 16, 80Methyl Cellosolve 6; <sup>c</sup> correction for tautomeric equilibrium estimated (cf. ref.<sup>5</sup>), measured pK<sub>2</sub>: 3-NH<sub>2</sub> 5·59, 3-NMe<sub>2</sub> 5·66; <sup>d</sup> ref.<sup>5</sup>; <sup>e</sup> no correction needed for tautomerism (see ref.<sup>5</sup>); <sup>f</sup> correction for tautomerism (probably less than 0·03, cf. ref.<sup>5</sup>) not applied.

10% of the effect of 3,5-di-t-Bu is covered by  $\rho\sigma$ . Comparison with ArCOOH and *trans*-ArCH=CHCOOH gives the stronger indications that distance is one of the factors determining  $h$ ; the  $h$  value for ArCH<sub>2</sub>CH<sub>2</sub>COOH then is in harmony with preponderance of the extended form. The value of  $h$  for the DDM reaction possibly reflects a considerable ionic character of the transition state.

As to other solvent mixtures our data tend to show that in 40–60M, 50E, 50A and 50D the  $h$  values are similar, around -0·05, for ArCOOH, ArCH<sub>2</sub>COOH and *cis*-ArCH=CHCOOH; it should be born in mind that they do not necessarily represent the maximum values in the several mixtures. In mixtures like 10E, 10A, 85E (and usually 75E) Eq. (1) is followed closely and  $h$  is indistinguishable from zero. In this connection we note that with  $h$  -0·03 and  $\pi$  1·98 (t-Bu) the  $h\pi$  term, 0·06 log units, may be close to or even within the sum of experimental error and the intrinsic deviations of Eq. (1). The (small) values of  $h$  for ArCH<sub>2</sub>COOH in 80MCS and 30DMSO are somewhat surprising in that we found no deviations from Eq. (1) for ArCOOH in these mixtures<sup>1</sup>. The available data in water do not disclose irregularities, except *cis*-ArCH=CHCOOH, but here, as in the other solvents, the data are remarkably scarce and the substituents are not suitable for the purpose of testing Eq. (3).

Our new data for ArCOOH give extensive confirmation for the failure of Eq. (1) in several solvents. We select from 32TB the  $\Delta$  values\*: 3-O-Octyl -0·33; 3,5-diSiMe<sub>3</sub> -0·85 (50E -0·40); 4-Alkyl, increasing approximately linearly with

\*  $\pi$ -Values used in the regressions are given in Table V. We quote here some further values<sup>2</sup> of groups appearing in this paper: n-Hept 3·8 (by extrapolation of C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>), neoPent 2·6 (est.), t-Pent 2·6 (est.), cycloHex 2·51, CH<sub>2</sub>Ph 2·01, CH=CH<sub>2</sub> 0·82, Ph 1·96, CH<sub>2</sub>SiMe<sub>3</sub> 2·00, SiMe<sub>3</sub> 2·59, NEt<sub>2</sub> 1·18, NHNH<sub>2</sub> -0·88, NHFo -0·98, NHAc -0·97, NHCONH<sub>2</sub> -1·30, N=NPh 1·69, O-Octyl 3·6 (est. OC<sub>1</sub>-OC<sub>4</sub>), OPh 2·08, *meta*-diCl 1·25, *meta*-diBr 1·62.

TABLE II  
Arylacetic acids: Thermodynamic  $pK$  values of the parent and substituent effects expressed as  $100(pK^o - pK)$  in various solvents, at 25°C<sup>a</sup>

H <sub>2</sub> O (4·31)							
3-t-Bu	-7 <sup>b</sup>	3-CF <sub>3</sub>	15	3-OH	2	4-t-Bu	-6 <sup>b</sup>
4-CN	34	4-NHAc	4	4-OH	-9		
40M (5·06)							
3-NO <sub>2</sub>	39	3-I		14		3,5-di-t-Bu	-22
5E (4·42)							
3-t-Bu	-8	4-t-Bu		-7			
10E (4·50)							
3-t-Bu	-9	3-CH <sub>2</sub> OH		3		3-I	14
3,5-diNO <sub>2</sub>	69 <sup>c</sup>	3-CF <sub>3</sub>		19		4-t-Bu	-8
50E (5·47)							
3-CH <sub>2</sub> OH	9	3,5-diNO <sub>2</sub>		97 <sup>c</sup>		3-CF <sub>3</sub>	24
75E (6·20)							
3-CH <sub>2</sub> OH	5	3,5-diNO <sub>2</sub>		113 <sup>c</sup>		3-CF <sub>3</sub>	34
85E (6·72)							
3-t-Bu	-9	3-NO <sub>2</sub>		62		3,5-di-t-Bu	-17
3,5-diNO <sub>2</sub>	122	4-Me		-7		4-t-Bu	-6
22TB (4·76)							
3-t-Bu	-26						
32TB (5·21)							
3-Me	-19	3-t-Bu		-44		3-CH <sub>2</sub> OH	14
3-NO <sub>2</sub>	42	3-F		10		3-Cl	4
3-Br	1	3-I		-4		3,5-diMe	-36
3,5-di-t-Bu	-74	3,5-diNO <sub>2</sub>		90		3-OH	7
3-OMe	1	4-Me		-18		4-t-Bu	-40
4-NHAc	6	4-NO <sub>2</sub>		54		4-OH	-7
4-OMe	-9	4-F		5		4-I	-1
80MCS (7·25)							
3-t-Bu	-11	3-NO <sub>2</sub>		59		3,5-di-t-Bu	-21
4-Me	-9	4-t-Bu		-7		4-F	18
4-I	28						

TABLE II  
(Continued)

10A (4·60)					
3-NO <sub>2</sub>	37	4-NO <sub>2</sub>	47		
30DMSO (4·88)					
3-t-Bu	-12	3-NO <sub>2</sub>	41	3,5-di-t-Bu	-23
4-Me	-8	4-t-Bu	-10		

<sup>a</sup> H<sub>2</sub>O (4·31), etc.: solvent and p*K* parent. MCS methyl cellosolve, DMSO dimethyl sulfoxide (see also Table I, note<sup>a</sup>); <sup>b</sup> extrapolated from data in 10E and 5E; <sup>c</sup> ref.<sup>4</sup>.

increasing number of carbon atoms (but almost constant in 75E), of which 4-*n*-heptyl -0·48, 4-bicyclo[2.2.2]octan-1-yl -0·51, 4-CEt<sub>3</sub> -0·57; 4-Ph -0·14; 4-CH<sub>2</sub>SiMe<sub>3</sub> -0·63 (50E -0·37); 3-CH<sub>2</sub>SiMe<sub>3</sub> -0·67 (50E -0·33). The data for CH<sub>2</sub>SiMe<sub>3</sub> call for a reinterpretation on the present basis of the work, in 50% E, by Eaborn and Parker<sup>10</sup>. We confirm Bowden and Shaw's<sup>11</sup> observation (in H<sub>2</sub>O and 80% MCS) that Δ-4-CO-t-Bu is relatively small; however, their interpretation on the basis of steric inhibition of resonance is put in doubt by our finding the same for Δ-3-CO-t-Bu.

TABLE III

β-Arylpropionic acids, *trans*- and *cis*-cinnamic acids ArXXCOOH: Thermodynamic p*K* values of the parent and substituent effects expressed as 100(p*K*<sup>o</sup> - p*K*) in various solvent mixtures, at 25°C

Substituent	XX			
	CH <sub>2</sub> -CH <sub>2</sub> <sup>a</sup>	CH=CH <sup>a</sup> <i>trans</i>	CH=CH <sup>a</sup> <i>cis</i>	CH=CH <sup>b</sup> <i>cis</i>
H	5·58	5·40	4·94	4·67
3-Me	-11	-11		
3-NO <sub>2</sub>	21	50	37	38
3-Cl	3	21	6	
3,5-diMe	-19	-23		
3,5-di-t-Bu	-35	-40	-76	-29
4-NO <sub>2</sub>	34			

<sup>a</sup> 32TB; <sup>b</sup> 40M.

The  $\text{ArCH}_2\text{COOH}$  series is worthy of special comment. Due to the lower  $\rho$  and equal  $h$  the deviations from Eq. (1) are much more pronounced than for  $\text{ArCOOH}$ . Thus, in 32TB, with  $n$  12, Eq. (1) has  $R$  0.90; with the 8 "outside" substituents ( $0.27 < \pi < -0.73$ )  $R$  is as low as 0.74 (Eq. (3),  $R$  0.997). Again, with  $\Delta$ -3- $\text{NO}_2$  0.42,  $\Delta$ -3-*t*-Bu is  $-0.44$ . The behaviour of the *meta* halogens is quite striking: F, Cl, Br, I have  $\Delta$  0.10, 0.04, 0.01 and  $-0.04$ , respectively.

In the  $\text{ArCOOH}$  series we found  $h_p = 0.76h_m$  by applying Eq. (5) to data points for 15 substituents in *meta*

$$\Delta(32\text{TB}) = \rho \Delta(50\text{E}) + h_m\pi + h_p\pi \quad (5)$$

position, the same 15 substituents in *para* position, and the parent ( $n$  31). The corresponding procedure for  $\text{ArCH}_2\text{COOH}$  ( $n$  13) gives the (relative) values  $h_m -0.133 \pm 0.007$  and  $h_p -0.138 \pm 0.007^*$ , so that we have no reason to distinguish between  $h_m$  and  $h_p$  in this series.

### $\rho$ Values

The  $\rho$  values obtained here and in the literature through Eq. (1) are usually close to the "true"  $\rho$  values of Eq. (3). This can be largely traced back to: (a) most of the commonly used substituents have  $\pi$  in a small range; (b) 3- $\text{NO}_2$  (or 4- $\text{NO}_2$ ) is included; (c) many common substituents have  $\sigma$  about half that of  $\text{NO}_2^{**}$ . Factor (a) can be illustrated by listing the 10 "inside" groups ( $0.27 > \pi > -0.73$ ) out of the 24 groups of ref.<sup>1</sup>: H,  $\text{CMe}_2\text{OH}$ , CHO, COMe, COOMe, CN,  $\text{NO}_2$ , OMe, OEt, F. Factor (c) can be illustrated by noting that in the  $\sigma_m$  range 0.33–0.44 are found: CHO, COMe, COOMe,  $\text{CF}_3$ , F, Cl, Br, I. If H and 3- $\text{NO}_2$  are present in the set, the last series contributes little to  $\rho$  whatever the size of the  $h\pi$  term; the least-square slope is dominated by the points for H and  $\text{NO}_2$ , and, since  $\pi$  for  $\text{NO}_2$ ,  $-0.28$ , is small, this slope is also close to that of Eq. (3). Thus, for  $\text{ArCH}_2\text{COOH}$  in 32TB the set H, F, Cl, Br, I,  $\text{NO}_2$ , gives  $R$  as low as 0.76 but  $\rho$  0.57 is close to  $\Delta$ -3- $\text{NO}_2$ / $\sigma$ -3- $\text{NO}_2$  0.59, and to  $\rho$  0.62 from Eq. (3) with  $n$  12.

Strongly different slopes can be conjured up by a provocative choice of substituents. In the same  $\text{ArCH}_2\text{COOH}$  series the set H,  $\text{CH}_2\text{OH}$ , *t*-Bu and di-*t*-Bu gives  $\rho$  4.4 in 32TB ( $R$  0.98) and 2.0 in 50E ( $R$  0.99); the pair H/I gives  $\rho -0.1$ . By way of counterpoint we note that  $h$  is approximated here by  $\Delta$ -3-*t*-Bu/ $\pi$ -3-*t*-Bu, yielding  $-0.22$ , or by  $\Delta$ -3,5-di-*t*-Bu/ $\pi$ -3,5-di-*t*-Bu, yielding  $-0.19$ .

\* The correlation has (relative)  $\rho$   $0.848 \pm 0.020$ ,  $s$  0.014,  $R$  0.9991, int.  $-0.027$ ,  $F$  1 641. The equation  $\Delta(32\text{TB}) = \rho \Delta(50\text{E})$  gives  $s$  0.094,  $R$  0.945.

\*\*  $\sigma_m$  Values between 0.17–0.33 and 0.44–0.70 are rare.



$\sigma$  Values

Mixed solvents have often been introduced in order to avoid solubility problems with water as the solvent, even if this were the solvent of choice. The availability of pure ethanol, its likeness to water, and the practical and numerical attraction of the 1 : 1 ratio, then led to "50% ethanol"\* approaching the status of (secondary) standard solvent and  $\sigma$  values derived from data in this mixture as (secondary) standard  $\sigma$  values. Ironically, the choice of 50% ethanol has been about the worst possible in the E/H<sub>2</sub>O range. For 3-t-Bu the  $h\pi$  term represents 0.07  $\sigma$ -units in the ArCOOH series and 0.16  $\sigma$ -units in the ArCH<sub>2</sub>COOH series.

The above touches on the question of obtaining "best  $\sigma$  values" by any of the averaging procedures. It is clear that the indiscriminate use of data from mixed solvents has to be discouraged. This holds the more if systems with positive  $h$  are included<sup>1</sup> (ArNH<sub>3</sub><sup>+</sup>, ArCH<sub>2</sub>NH<sub>3</sub><sup>+</sup>), since the deviations in opposite direction enlarge the total ranges of  $\sigma$  values and the standard deviations of the averages.

TABLE IV

Rates of benzoic acids reactions with DDM, and methyl benzoates alkaline hydrolyses in various solvent mixtures, at 25°C, expressed as 100 (log  $k$  - log  $k^\circ$ )

Substituent	ArCOOH + DDM <sup>a</sup>			ArCOOMe + OH <sup>-b</sup>		
	75E	32TB	50TB	56% A <sup>c</sup> w/w	56% A <sup>d</sup> w/w	32TB
H	5.25	20.1	3.81	9.01	10.4	10.0
3-Me				-25	-21	
3-t-Bu					-38	-73
3-NO <sub>2</sub>	64	69	73	159	159	143
3-Cl	29	28			79	47
3-Br				72		
3-I				65		
3,5-diMe					-44	
3,5-di-t-Bu	-20	-51	-39			-127
4-NO <sub>2</sub>	68			184	184	

<sup>a</sup> 10<sup>5</sup>  $k_2$  (1 mol<sup>-1</sup> min<sup>-1</sup>); <sup>b</sup> 10<sup>3</sup>  $k_2$  (1 mol<sup>-1</sup> s<sup>-1</sup>); <sup>c</sup> see ref.<sup>45</sup>; <sup>d</sup> ref.<sup>46</sup>.

\* Many different 50% ethanol mixtures can be distinguished: 50 ml + 50 ml, 50 g + 50 g (w/w), 50 ml ethanol → 100 ml (with absolute ethanol our 50E), 50 ml water → 100 ml, each of these with 100% ethanol or "96%" ethanol. Our impression is that all or most of these have been actually used.

TABLE V

Regression data pertaining to Eqs (1) and (3): dissociation constants, DDM reaction, alkaline ester hydrolysis<sup>a</sup>

Solvent	<i>n</i>	$q \pm s_q$	<i>s</i>	<i>R</i>	int.	<i>F</i>	$h_m \pm s_h$
ArCOOH							
40M	4	1.393 ± 0.111 1.254 ± 0.010	0.074 0.005	0.9937 1.0000	-0.081 -0.001	156 15 620	-0.041 ± 0.002
60M	4	1.504 ± 0.115 1.365 ± 0.052	0.076 0.026	0.9942 0.9997	-0.084 -0.003	172 736	-0.041 ± 0.010
80M	4	1.499 ± 0.066 1.427 ± 0.061	0.044 0.030	0.9980 0.9995	-0.046 -0.003	508 545	-0.022 ± 0.012
50E	24 <sup>b</sup>	1.571 ± 0.035 1.484 ± 0.019	0.059 0.028	0.9946 0.9989	-0.069 -0.030	2 017 4 675	-0.051 ± 0.006
50E	22 <sup>c</sup>	1.582 ± 0.037 1.506 ± 0.026	0.045 0.027	0.9944 0.9980	-0.060 -0.034	1 779 2 375	-0.044 ± 0.008
32TB	24 <sup>b</sup>	1.652 ± 0.101 1.375 ± 0.026	0.170 0.037	0.9612 0.9983	-0.194 -0.071	267 3 034	-0.161 ± 0.008
32TB	22 <sup>c</sup>	1.630 ± 0.113 1.356 ± 0.037	0.134 0.038	0.9555 0.9967	-0.161 -0.067	210 1 418	-0.159 ± 0.010
10A	11	1.093 ± 0.006 1.097 ± 0.008	0.009 0.009	0.9998 0.9999	0.007 0.004	28 650 13 870	0.004 ± 0.005
50A	12	1.558 ± 0.052 1.467 ± 0.033	0.073 0.039	0.9946 0.9986	-0.063 -0.001	916 1 601	-0.058 ± 0.011
26.5D	7 <sup>d</sup>	1.259 ± 0.046 1.243 ± 0.016	0.030 0.010	0.9966 0.9997	-0.031 -0.003	740 3 108	-0.052 ± 0.008
43.5D	7 <sup>d</sup>	1.378 ± 0.055 1.361 ± 0.032	0.035 0.021	0.9961 0.9989	-0.042 -0.012	631 933	-0.055 ± 0.017
73.5D	7 <sup>d</sup>	1.503 ± 0.046 1.488 ± 0.018	0.030 0.012	0.9976 0.9997	-0.033 -0.005	1 051 3 512	-0.051 ± 0.009
50D	8	1.540 ± 0.071 1.453 ± 0.010	0.052 0.007	0.9936 0.9999	-0.072 -0.003	467 14 820	-0.075 ± 0.004
ArCH <sub>2</sub> COOH							
H <sub>2</sub> O	5 <sup>e</sup>	0.494 ± 0.016 0.489 ± 0.009	0.010 0.005	0.9984 0.9997	-0.012 -0.004	925 1 752	-0.015 ± 0.005
40M	4	0.656 ± 0.100 0.532 ± 0.012	0.066 0.006	0.9776 0.9999	-0.074 -0.001	43 2 688	-0.037 ± 0.002
10E	11 <sup>f</sup>	0.525 ± 0.013 0.507 ± 0.007	0.018 0.009	0.9974 0.9994	-0.027 -0.014	1 728 3 227	-0.019 ± 0.004
50E	12 <sup>g</sup>	0.766 ± 0.046 0.683 ± 0.010	0.067 0.013	0.9826 0.9994	-0.078 -0.017	280 3 823	-0.055 ± 0.003

TABLE V  
(Continued)

Solvent	<i>n</i>	$\rho \pm s_\rho$	<i>s</i>	<i>R</i>	int.	<i>F</i>	$h_m \pm s_h$
75E	12 <sup>g</sup>	0.862 ± 0.029	0.042	0.9944	-0.046	884	
		0.813 ± 0.015	0.019	0.9990	-0.010	2 231	-0.032 ± 0.005
85E	5	0.904 ± 0.014	0.018	0.9997	-0.024	4 349	
		0.880 ± 0.005	0.005	1.0000	-0.003	29 360	-0.011 ± 0.002
32TB	12	0.856 ± 0.130	0.190	0.9010	-0.242	43	
		0.617 ± 0.026	0.033	0.9974	-0.067	864	-0.157 ± 0.009
32TB	8 <sup>h</sup>	0.925 ± 0.347	0.217	0.7367	-0.287	7	
		0.599 ± 0.045	0.026	0.9972	-0.081	445	-0.152 ± 0.008
32TB	4 <sup>i</sup>	0.679 ± 0.065	0.067	0.9922	-0.057	126	
		0.469 ± 0.049	0.020	0.9997	-0.006	720	-0.392 ± 0.084
80MCS	4	0.906 ± 0.062	0.042	0.9954	-0.046	216	
		0.824 ± 0.008	0.004	1.0000	-0.002	11 360	-0.024 ± 0.002
30DMSO	4	0.696 ± 0.098	0.067	0.9806	-0.072	50	
		0.565 ± 0.008	0.004	1.0000	-0.002	6 944	-0.038 ± 0.002
ArCH <sub>2</sub> CH <sub>2</sub> COOH							
H <sub>2</sub> O	5 <sup>j</sup>	0.209 ± 0.008	0.006	0.9978	-0.006	686	
		0.204 ± 0.011	0.006	0.9983	-0.003	298	-0.005 ± 0.007
50E	6 <sup>k</sup>	0.407 ± 0.063	0.049	0.9547	-0.047	41	
		0.327 ± 0.010	0.007	0.9994	-0.003	1 231	-0.034 ± 0.002
75E	6 <sup>k</sup>	0.451 ± 0.013	0.010	0.9983	-0.006	1 178	
		0.438 ± 0.011	0.007	0.9993	0.001	1 095	-0.005 ± 0.003
32TB	6	0.494 ± 0.135	0.104	0.8771	-0.130	13	
		0.327 ± 0.048	0.031	0.9923	-0.039	96	-0.070 ± 0.011
<i>trans</i> -ArCH=CHCOOH							
H <sub>2</sub> O	4 <sup>l</sup>	0.417 ± 0.034	0.021	0.9935	0.008	153	
		0.408 ± 0.049	0.027	0.9945	0.015	45	-0.016 ± 0.038
50E	6 <sup>k</sup>	0.734 ± 0.032	0.025	0.9962	0.002	518	
		0.701 ± 0.025	0.016	0.9987	0.021	593	-0.014 ± 0.006
75E	6 <sup>k</sup>	0.726 ± 0.024	0.018	0.9979	-0.008	951	
		0.700 ± 0.014	0.009	0.9996	0.006	1 843	-0.011 ± 0.003
32TB	6	0.896 ± 0.136	0.104	0.9570	-0.116	44	
		0.727 ± 0.042	0.027	0.9979	-0.024	349	-0.071 ± 0.009
<i>cis</i> -ArCH=CHCOOH							
H <sub>2</sub> O	4 <sup>l</sup>	0.397 ± 0.037	0.023	0.9914	0.019	115	
		0.422 ± 0.006	0.003	0.9999	0.002	3 012	-0.045 ± 0.004

TABLE V  
 (Continued)

Solvent	<i>n</i>	$\rho \pm s_\rho$	<i>s</i>	<i>R</i>	int.	<i>F</i>	$h_m \pm s_h$
40M	3	0.706 ± 0.212 0.513	0.137	0.9577	-0.104	11	-0.055
50E	4 <sup>k</sup>	0.895 ± 0.158 0.691 ± 0.048	0.105 0.024	0.9702 0.9993	-0.108 0.004	32 335	-0.059 ± 0.010
75E	4 <sup>k</sup>	0.811 ± 0.136 0.636 ± 0.038	0.090 0.019	0.9731 0.9994	-0.094 0.003	36 444	-0.051 ± 0.007
32TB	4	1.065 ± 0.466 0.458 ± 0.028	0.309 0.014	0.8506 0.9999	-0.334 0.002	5 1 811	-0.176 ± 0.006
ArCOOH + DDM							
75E	4	0.950 ± 0.058 0.883 ± 0.052	0.038 0.025	0.9963 0.9992	-0.041 -0.004	270 314	-0.019 ± 0.010
32TB	4	1.265 ± 0.254 0.934 ± 0.001	0.168 0.000	0.9621 1.0000	-0.183 0.000	25	-0.096 ± 0.000
50TB	3	1.224 ± 0.242 1.003	0.156	0.9809	-0.119	25	-0.063
ArCOOMe + OH <sup>-</sup>							
56%A (w/w)	5	2.251 ± 0.135 2.210 ± 0.045	0.086 0.028	0.9946 0.9996	-0.081 -0.014	277 1 316	-0.125 ± 0.024
56%A (w/w)	6	2.393 ± 0.109 2.242 ± 0.052	0.082 0.031	0.9959 0.9996	-0.100 -0.008	481 1 673	-0.106 ± 0.021
32TB	5	2.789 ± 0.509 1.939 ± 0.123	0.365 0.063	0.9535 0.9991	-0.506 -0.037	30 551	-0.252 ± 0.025

<sup>a</sup> Sets of data are in pairs, the upper gives results with Eq. (1), the lower results with the same data points with Eq. (3) and thus includes a value of *h* and its standard deviation, *s<sub>h</sub>* standard deviation of  $\rho$ , *s* standard deviation of the experimental points, int. intercept, *FF* test, if not noted otherwise the data used can be identified as the first *n* data (including H) in Tables I–IV; values of  $\sigma_m$  and  $\pi$ , respectively, used in the regressions: Me -0.069, 0.56, t-Bu -0.07, 1.98, CH<sub>2</sub>OH 0.07, -1.03, COMe 0.376, -0.55, NO<sub>2</sub> 0.710, -0.28, OMe 0.12, -0.02, F 0.337, 0.14, Cl 0.373, 0.71, Br 0.391, 0.86, I 0.352, 1.12, diMe -0.13, 1.07, di-t-Bu -0.14, 3.96, diNO<sub>2</sub> 1.379, -0.64, ( $\sigma$  as in ref.<sup>1</sup>,  $\pi$  from ref.<sup>2</sup>); <sup>b</sup> ref.<sup>1</sup>; <sup>c</sup> as for *n* = 24, but 3,5-di-t-Bu and 3,5-diNO<sub>2</sub> omitted, showing that extreme values of  $\pi$  and  $\sigma$  do not unduly dominate the results; <sup>d</sup> 3-OH omitted, (ref.<sup>47</sup>); <sup>e</sup> H, Me, NO<sub>2</sub>, Cl, I (ref.<sup>48</sup>); <sup>f</sup> H, Me, diMe, NO<sub>2</sub>, F, Cl, Br (ref.<sup>6</sup>), t-Bu, CH<sub>2</sub>OH, I, diNO<sub>2</sub> (present work); <sup>g</sup> as for 10E, 3,5-di-t-Bu added; <sup>h</sup> „outside” (cf. ref.<sup>1</sup>), 0.27 <  $\pi$  < -0.73; <sup>i</sup> „inside” (cf. ref.<sup>1</sup>), 0.27 >  $\pi$  > -0.73; <sup>j</sup> ref.<sup>49</sup>, 3-NO<sub>2</sub> Δ 0.14 (ref.<sup>7</sup>), 3,5-diMe Δ -0.04 (present work); <sup>k</sup> as for 32TB, Table III; <sup>l</sup> ref.<sup>4</sup>.

Two approaches can be considered to accommodate these problems. The first is to derive new (secondary)  $\sigma$  values only from systems that follow Eq. (1) very closely. This amounts to accepting a further practical restriction of the Hammett equation (1) in addition to those imposed by charged groups, through-resonance, etc., and implies ignoring an enormous amount of data from mixed solvents.

The second approach is to use the data from Eq. (3) – which are based on substituent effects in water – to calculate new pseudo-aqueous secondary  $\sigma$  values,  $\sigma^s$ , by working backwards, i.e., by using Eq. (6). As a numerical

$$\sigma^s = (\Delta - h\pi)/\rho \quad (6)$$

example may serve  $\sigma^s$ -4-t-Bu as derived from the  $\text{ArCH}_2\text{COOH}$  series ( $\sigma^n$  or  $\sigma^0$ ); the averages for all seven solvents are  $\Delta/\rho -0.21 \pm 0.12$  and  $\sigma^s -0.06 \pm 0.03$ : deleting the data in 32TB the averages are  $\Delta/\rho -0.14 \pm 0.04$  and  $\sigma^s -0.05 \pm 0.02$ . Not surprisingly, these  $\sigma^s$  values are less negative than the normal  $\sigma$  values listed by Wold<sup>9</sup>,  $-0.15$ , by Exner<sup>12</sup>,  $-0.17$ , and by ourselves<sup>6</sup>,  $-0.14$ . For 4-Me the averages of the seven values,  $-0.15 \pm 0.04$  and  $-0.11 \pm 0.02$ , respectively, are much closer together, as expected on the basis of its small  $\pi$  value (0.56).

### CONCLUDING REMARKS

It is clear from this and the previous paper<sup>1</sup> that Eq. (3) gives a great improvement over Eq. (1). In a sense the Hammett structure/effect proportionalities hold better than the results with the Hammett equation (1) suggest: the deviations described by  $h\pi$  terms stem primarily from the peculiarities of the solvent mixtures<sup>1</sup>.

TABLE VI

Reaction constants  $h_m$  for reactivities of substituted benzoic, phenylacetic, phenylpropionic and cinnamic acids in 32 TB, at 25°C

Reaction	$h_m$
$\text{ArCOOMe} + \text{OH}^-$	$-0.25$
$\text{ArCH}=\text{CHCOOH}$ ( <i>cis</i> )	$-0.18$
$\text{ArCOOH}$	$-0.16$
$\text{ArCH}_2\text{COOH}$	$-0.16$
$\text{ArCOOH} + \text{DDM}$	$-0.10$
$\text{ArCH}_2\text{CH}_2\text{COOH}$	$-0.07$
$\text{ArCH}=\text{CHCOOH}$ ( <i>trans</i> )	$-0.07$

It should not go unnoticed, however, that the data also show irregularities which are not covered by Eq. (3). We restrict ourselves to a few examples of various character concerning OR groups.

In our previous paper<sup>1</sup> we noted already that in the ArCOOH series 3-OH did not behave well. We here give some of these and related data:

$\Delta$ -3-OH:	H <sub>2</sub> O 0.07, 50E 0.03, 85E -0.06, 32TB 0.06
$\Delta$ -3-OMe:	H <sub>2</sub> O 0.12, 50E 0.11, 85E 0.08, 32TB 0.10
$\Delta$ -3-OEt:	H <sub>2</sub> O 0.10, 50E 0.07, 85E 0.05, 32TB 0.00
$\Delta$ -3-OPh:	H <sub>2</sub> O 0.25, 50E 0.16, 85E 0.22, 32TB -0.13

The irregularity in these examples is that  $\Delta$  does not follow the increase of  $\rho$  from H<sub>2</sub>O-85E. On the other hand the change in  $\Delta$  from 50E to 32TB follows  $h\pi$ , increasing for OH ( $\pi -0.67$ ), decreasing for OEt ( $\pi +0.38$ ), and decreasing strongly for OPh ( $\pi 2.08$ ). This possibly means that the anomaly in question increases or decreases from water to 50E and then remains constant. Accordingly, Dippy's<sup>13</sup> value for 3-OPh in water, 0.25, is not incompatible with our data which give  $\sigma^s 0.15 \pm 0.01$  ( $n 4$ ).

For 4-OPh in the ArCH<sub>2</sub>COOH series the situation is not clear. The values of  $\Delta$  in 10E, 50E and 75E, 0.00, 0.03 and 0.04, respectively, do not reflect the  $h\pi$  term of 0.11 pK units to be expected in 50E, and the corresponding  $\sigma^s$  values 0.08, 0.20 and 0.14 are too far apart. Of course, these calculated values are rather uncertain because  $\pi$  is high and  $\rho$  values are low.

More conclusive are the results with ArCOOH;  $\Delta$ -4-OPh in 50E, 75E and 32TB: -0.02, -0.02 and -0.27, respectively, yield  $\sigma^s 0.06, 0.01$  and 0.04, average  $0.04 \pm 0.02$ . This average is rather different from the  $\sigma$  value listed by Exner<sup>12</sup>, 0.14, and the value in water obtained by Dippy and Lewis<sup>13</sup>, -0.320. The difference with Exner's value, which was based on "the values of Wepster"<sup>14</sup>, can be accounted for with unusual certainty as based on a misunderstanding; the pK of 4-OPh-benzoic acid (and of the 3-OPh isomer) in "50E" is quoted correctly and appears in the present paper, but, due to incomplete information on our part, it was not made clear that it is a thermodynamic value which should not be compared with an apparent pK of benzoic acid (5.72 instead of our 5.48). As to Dippy's -0.320, this was footnoted by Exner<sup>15</sup> as "unaccountable". We agree with this mild judgement.

## EXPERIMENTAL

### Materials

Most of the compounds and procedures have been characterized or described in references<sup>1,3,4,6,7,16</sup>; we give some further data here (substituent, m.p. or b.p., solvent of crystallization).

*Benzoic Acids*

3-MeC=CMe<sub>2</sub>, 101.5–102.5°C (see ref.<sup>17</sup>); 3-CH<sub>2</sub>SiMe<sub>3</sub>, 96.5–97°C, petroleum ether 60 to 80°C (see ref.<sup>18</sup>); 3-CO-t-Bu, 110.5–111.5°C, aq. methanol (see ref.<sup>3</sup>); 3-NH<sub>2</sub>, 173–174.5°C, water; 3-NMe<sub>2</sub>, 151.5–153°C, ethanol; 3-NHCONH<sub>2</sub>, 270–272°C (dec.), ethanol (ref.<sup>19</sup>), 3-O-octyl, 74–75°C, aq. ethanol; from 3-hydroxybenzoic acid and octyl bromide (cf. ref.<sup>20</sup>); 4-t-pent, 107–108.5°C, aq. ethanol (ref.<sup>21</sup>); 4-heptyl, 101–102°C, methanol (Kon. Shell, Amsterdam); 4-cyclohexyl, 198–199.5°C, ethanol (ref.<sup>22</sup>); 4-bicyclo[2.2.2]octan-1-yl, 258–260°C, ethanol (ref.<sup>23</sup>); 4-benzyl, 159–160°C, aq. ethanol (ref.<sup>24</sup>); 4-vinyl, 140°C (Kofler Heizbank), 30% ethanol (E. S. Waight, London); 4-MeC=CMe<sub>2</sub>, 101.5–102.5°C (see ref.<sup>17</sup>); 4-Ph, 227 to 228°C, ethanol; by oxidation of 4-acetobiphenyl with potassium permanganate in aqueous pyridine (see refs<sup>25,26</sup>); 4-CH<sub>2</sub>SiMe<sub>3</sub>, 179–180°C, petroleum ether 60–80°C (see ref.<sup>18</sup>); 4-CO-t-Bu, 164 to 165°C, aq. ethanol; by oxidation of 4-methyl pivalophenone (cf. ref.<sup>26</sup>); 4-COOMe, 221.5 to 223°C, acetone (cf. ref.<sup>27</sup>); 4-NHNH<sub>2</sub>·HCl, 239–240°C, 2M-HCl (ref.<sup>28</sup>); 4-NHFO, 259–260°C, ethanol; 4-NHAc, 257–259°C, methanol; 4-NEt<sub>2</sub>, 193.5–195°C (ref.<sup>29</sup>); 4-pyrrolidin-1-yl, 285–288°C, ethanol (see ref.<sup>29</sup>); 4-piperidin-1-yl, 225–226.5°C, ethanol (see ref.<sup>29</sup>); 4-N=NPh, 248–249.5°C, ethanol (ref.<sup>30</sup>); 4-OH, 216–217.5°C, water; 4-OEt, 199.5–201°C, ethanol; 4-OPh, 159–160°C, ethanol; by bromination of diphenyl ether, followed by a Grignard reaction in the presence of ethyl bromide (cf. ref.<sup>31</sup>); 4-SO<sub>2</sub>Me, 274–275.5°C, water; 3,5-diEt, 129–130°C, petroleum ether; from 3,5-diethyl-4-bromobenzene<sup>32</sup> by a Grignard reaction; 3,5-di-iPr, 100 to 100.5°C, aq. methanol; by oxidation of 1,3,5-tri-isopropylbenzene (cf. ref.<sup>33</sup>); 3,5-diOMe, 184 to 185°C, ethanol; 3,5-diBr, 220–221°C, aq. ethanol (ref.<sup>34</sup>); 3,5-diSiMe<sub>3</sub>, 171.5–172°C (ref.<sup>35</sup>).

*Arylacetic Acids*

3-Hydroxymethylphenylacetic acid, 95–96°C, ether–petroleum ether; by bromination of 3-methylphenylacetic acid with bromosuccinimide<sup>36</sup> followed by alkaline hydrolysis.

*Methyl Benzoates*

3-Me, 114–115°C/26 mm; 3-t-Bu, 121–123°C/12 mm; 3,5-diMe, 32–33°C, petroleum ether 40–60°C. Further data in refs<sup>4,26</sup>.

## Solvents

Methanol, dry, Baker Analyzed; acetone, Baker Analyzed, distilled; dioxane: CR Merck (Chromatography), dried over K<sub>2</sub>CO<sub>3</sub>, refluxed for 2 h with SnCl<sub>2</sub>·2 H<sub>2</sub>O to remove peroxides, and distilled under N<sub>2</sub>.

Properties of the mixtures with water are as follows (mole %, wt. %,  $d_4^{25}$ ,  $D_s$ ,  $\delta R^1$ ): 40M: 22.1, 33.5, 0.940, 63.9, 0.01; 60M: 38.0, 52.1, 0.906, 55.2, 0.04; 80M: 60.7, 73.3, 0.858, 45.5, –0.09; 10A: 2.62, 7.98, 0.984, 74.1, –0.02; 50A: 18.5, 42.3, 0.928, 53.2, –0.13; 56% A w/w: 28.3, 56.0, –, 44.4, –, 26.5% D w/w: 6.87, 26.5, –, 56.2, –, 43.5% D w/w: 13.6, 43.5, –, 43.1, –, 73.5% D w/w: 36.2, 73.5, –, 16.8, –, 50D: 16.9, 49.9, 1.030, 36.0, –0.08.

Dielectric constants,  $D_s$ , at 25°C: M/H<sub>2</sub>O, see ref.<sup>37</sup>; A/H<sub>2</sub>O, see ref.<sup>38</sup>; D/H<sub>2</sub>O, see ref.<sup>39</sup>.

Values of  $pK_w$ , in 10A 14.23, 50A 15.46, and 50D 15.53, from data in ref.<sup>40</sup>.

## Methods

$pK$  Values: the thermodynamic dissociation constants have been determined as described and exemplified previously<sup>1,7,16</sup>.

*Reaction with diazodiphenylmethane (DDM).* The general procedures of Roberts et al.<sup>42</sup> were adopted: 0.003M-DDM, prepared according to ref.<sup>41</sup>, ratio acid/DDM circa 10, cell length 5 or 10 cm, wavelength 525 nm. Stock solutions were brought at such a temperature that after mixing the temperature was 25°C. First-order kinetics were strictly obeyed. Small corrections were applied, where necessary, for oxonium ion-catalysis (the magnitude of which was determined with solutions of hydrochloric acid). In order to keep these corrections small (of the order of 1%) some acid solutions were partly neutralized<sup>42</sup>. The percentage of ester formation in 75E was determined for ArCOOH (and ArCH<sub>2</sub>CH<sub>2</sub>COOH) as 37 ± 2% for several substituents<sup>43</sup>; our *k* values are not corrected for this figure<sup>43</sup>.

*Alkaline ester hydrolysis.* In 56% acetone-water (w/w) the procedure of Tommila and Hinshelwood<sup>44</sup> was used (ester and sodium hydroxide 0.01M). In 32TB the reaction was followed spectrophotometrically at suitable wavelengths between 225 and 240 nm (c. 10<sup>-4</sup>M ester, 0.01M sodium hydroxide). Stock solutions were brought at such a temperature that after mixing the temperature was 25°C.

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## REFERENCES

1. Hoefnagel A. J., Wepster B. M.: *J. Chem. Soc., Perkin Trans. 2*, 1989, 977.
2. Hansch C., Leo A.: *Substituent Constants for Correlation Analysis in Chemistry and Biology*. Wiley-Interscience, New York 1979; Hansch C., Leo A., Unger S. H., Kim K. H., Nikaitani D., Lien E. J.: *J. Med. Chem.* 16, 1207 (1973); Leo A.: *J. Chem. Soc., Perkin Trans. 2*, 1983, 825.
3. Reuvers A. J. M., van Bekkum H., Wepster B. M.: *Tetrahedron* 26, 2683 (1970).
4. Hoefnagel A. J., Hoefnagel M. A., Wepster B. M.: *J. Org. Chem.* 43, 4720 (1978).
5. van de Graaf B., Hoefnagel A. J., Wepster B. M.: *J. Org. Chem.* 46, 653 (1981).
6. Hoefnagel A. J., Wepster B. M.: *J. Am. Chem. Soc.* 95, 5357 (1973).
7. Hoefnagel A. J., Monshouwer J. C., Snorn E. C. G., Wepster B. M.: *J. Am. Chem. Soc.* 95, 5350 (1973).
8. Exner O. in: *Advances in Linear Free Energy Relationships* (N. B. Chapman and J. Shorter, Eds), p. 1. Plenum Press, London 1972.
9. Wold S., Sjöström M. in: *Correlation Analysis in Chemistry* (N. B. Chapman and J. Shorter, Eds), p. 1. Plenum Press, New York 1978; Sjöström M., Wold S.: *Chem. Scr.* 9, 200 (1976).
10. Eaborn C., Parker S. H.: *J. Chem. Soc.* 1954, 939.
11. Bowden K., Shaw M. J.: *J. Chem. Soc.*, B 1971, 161.
12. Exner O. in: *Correlation Analysis in Chemistry* (N. B. Chapman and J. Shorter, Eds), p. 439. Plenum Press, New York 1978.
13. Dippy J. F. J., Lewis R. H.: *J. Chem. Soc.* 1937, 1426.
14. Exner O., Lakomý J.: *Collect. Czech. Chem. Commun.* 35, 1371 (1970).
15. Exner O.: *Collect. Czech. Chem. Commun.* 31, 65 (1966).
16. van Veen A., Hoefnagel A. J., Wepster B. M.: *Rec. Trav. Chim. Pays-Bas* 90, 289 (1971).
17. Kieboom A. P. G., van Bekhum H.: *J. Catal.* 25, 342 (1972).
18. Eaborn C., Parker S. H.: *J. Chem. Soc.* 1954, 939.
19. Menshuskin N.: *Justus Liebigs Ann. Chem.* 153, 83 (1870).
20. Herbert A. J.: *Trans. Faraday Soc.* 63, 555 (1967).



21. Cagniant P., Buu-Hoi: *Bull. Soc. Chim. Fr.* [5] 9, 841 (1942).
22. Bodroux D., Thomassin R.: *Bull. Soc. Chim. Fr.* [5] 6, 1411 (1939).
23. Broxton T. J., Capper G., Deady L. W., Lenko A., Topsom R. D.: *J. Chem. Soc., Perkin Trans. 2*, 1972, 1237.
24. Mitter P.: *Ber. Dtsch. Chem. Ges.* 45, 1207 (1912).
25. Hammond G. S., Reeder C. E.: *J. Am. Chem. Soc.* 80, 573 (1958).
26. van Hartingsveldt W., Verkade P. E., Wepster B. M.: *Rec. Trav. Chim. Pays-Bas* 75, 349 (1956).
27. Wohl A., Nagelschmidt E.: *Ber. Dtsch. Chem. Ges.* 43, 3474, 3477 (1910).
28. Fischer E.: *Justus Liebigs Ann. Chem.* 212, 316, 337 (1882).
29. Weringa W. D., Janssen M. J.: *Rec. Trav. Chim. Pays-Bas* 87, 1372 (1968).
30. Ansporn H. D.: *Org. Synth., Coll. Vol. III*, p. 711. Wiley, New York 1955.
31. Bowen D. M.: *Org. Synth., Coll. Vol. III*, p. 553. Wiley, New York 1955.
32. Benkeser R. A., Hickner R. A., Hoke D. I., Thomas O. H.: *J. Am. Chem. Soc.* 80, 5289 (1958).
33. van Helden R., Bickel A. F., Kooyman E. C.: *Rec. Trav. Chim. Pays-Bas* 80, 1257 (1961).
34. Elion L.: *Rec. Trav. Chim. Pays-Bas* 42, 145 (1923).
35. van der Meulen Bosma F. O. J.: Unpublished results.
36. Kalir A.: *Org. Synth., Coll. Vol. V*, p. 825. Wiley, New York 1973.
37. Albright P. S., Gosting L. J.: *J. Am. Chem. Soc.* 68, 1061 (1946).
38. Åkerlöf G.: *J. Am. Chem. Soc.* 54, 4125 (1932).
39. Critchfield F. E., Gibson, Jr. J. A., Hall J. L.: *J. Am. Chem. Soc.* 75, 1991 (1953).
40. Woolley E. M., Hurkot D. G., Hepler L. G.: *J. Phys. Chem.* 74, 3908 (1970).
41. Smith L. I., Howard K. L.: *Org. Synth., Coll. Vol. III*, p. 351. Wiley, New York 1955.
42. Roberts J. D., McElhill E. A., Armstrong R.: *J. Am. Chem. Soc.* 71, 2923 (1949); Roberts J. D., Watanabe W., McMahon R. E.: *J. Am. Chem. Soc.* 73, 760 (1951).
43. Buckley A., Chapman N. B., Shorter J.: *J. Chem. Soc.* 1963, 178; *J. Chem. Soc., B* 1969, 195; and papers cited therein.
44. Tommila E., Hinshelwood C. N.: *J. Chem. Soc.* 1938, 1801; Tommila E.: *Ann. Acad. Sci. Fenn. Ser. A*, No. 13, 1 (1941).
45. Tommila E., Brehmer L., Elo H.: *Ann. Acad. Sci. Fenn., Ser. A*, LIX (No. 9), 1 (1942); AII, 16, 1 (1945).
46. Hoefnagel M. A.: Unpublished results.
47. Elliott J. H., Kilpatrick M.: *J. Phys. Chem.* 45, 485 (1941).
48. Dippy J. F. J.: *Chem. Rev.* 25, 151 (1939); Dippy J. F. J., Hughes S. R. C., Kitchiner B. C.: *J. Chem. Soc.* 1964, 1275.
49. Dippy J. F. J., Page J. E.: *J. Chem. Soc.* 1938, 357.