

DISSOCIATION CONSTANTS OF SUBSTITUTED BENZOIC ACIDS IN WATER AND IN ORGANIC SOLVENTS*

Miroslav LUDWIG, Václav BARON, Karel KALFUS, Oldřich PYTELA
and Miroslav VEČEŘA

*Department of Organic Chemistry,
Institute of Chemical Technology, 532 10 Pardubice*

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Potentiometric titration has been used to measure dissociation constants of 38 monosubstituted benzoic acids in water and in 6 organic solvents (methanol, ethanol, dimethylformamide, acetonitrile, sulfolane, acetone). The results have been analyzed and interpreted from the point of view of substituent and solvent effects on the dissociation of the title substrates. It has been proved that solvents affect not only the reaction constant but also the substituent constant of the Hammett equation.

Substituted benzoic acids represent the basic substrates chosen by Hammett¹ for quantitative interpretation of substituent effects in benzenic derivatives. Highly important in this respect — according to the Hammett usage — are the dissociation constants of substituted benzoic acids in water at 25°C. But the dissociation constants in other solvents cannot be neglected either (estimation of secondary σ values, investigation of effects of medium on the dissociation, the so-called “problematic” substituents as, *e.g.*, hydroxyl or carboxyl groups, *etc.*). Literature presents extensive sets of dissociation constants of benzoic acids²⁻⁴ in a number of solvents, however, they do not quite completely fulfil the requirement of experimental homogeneity of data. This fact introduces problems into interpretation of substituent effects in this highly important series of benzoic acids, and it makes the correct adjustment of σ constants more difficult.

The aim of this work was to estimate the dissociation constants of an extensive set of monosubstituted benzoic acids (38 derivatives) in a selected set of solvents involving amphiprotic (water, methanol, ethanol) as well as dipolar aprotic-protophilic (dimethylformamide) and protophobic ones (acetonitrile, acetone, tetramethylene sulfone).

The experiments were chosen in such way that the dissociation constants obtained were applicable as a basis for construction of a new scale of the σ substituent constants of the Hammett equation.

* Part IV in the series on Solvent Effects on Dissociation of Weak Acids. Part III: This Journal 51, 1948 (1986).

TABLE I
Melting temperatures of monosubstituted benzoic acids $\text{XC}_6\text{H}_4\text{CO}_2\text{H}$ in comparison with those of ref.⁵

X	T_{exp} , °C	T_{ref} , °C	X	T_{exp} , °C	T_{ref} , °C	X	T_{exp} , °C	T_{ref} , °C
H	122–123	122.5	4-NHCOCH ₃	256–257	256–258 ^f	3-SO ₂ NH ₂	245–246	244.5–245 ⁱ
3-CH ₃	112–114	111–113	3-OH	200–201	200–201.5	4-SO ₂ NH ₂	289–290	290–290.5 ^j
4-CH ₃	179–180	179–180	4-OH	215–216	214.5–215.5	3-SO ₃ H	141–142	141
4-t-C ₄ H ₉	160–162	160–161 ^a	3-OCH ₃	109–111	110	3-F	124–125	124
3-CF ₃	102–103	103–104.5 ^b	4-OCH ₃	184–185	184.2	4-F	182–183	182.6
3-CN	218–218.5	217	3-OC ₆ H ₅	145–146	145	3-Cl	157–159	158
4-CN	213–214	214	4-OC ₆ H ₅	159–160	159.5	4-Cl	240–242	241.5
3-COCH ₃	171–172	172	3-SH	145–146	146–147	3-Br	155–156	155
4-COCH ₃	209–210	210	4-SH	219–220	219	4-Br	253–254.5	254.5
3-COOH	346–347	345–347	4-SCH ₃	191–192	192	3-I	186–187	186.7
4-COOH	305	300 Subl. ^c	3-SO ₂ CH ₃	236–237	236–238 ^g	4-I	270–271	270
4-NH ₂	187–188	187	4-SO ₂ CH ₃	276–277	275 ^g	3-NO ₂	140–141	140–141
3-NHCOCH ₃	249–250	252 ^d			267–268 ^h	4-NO ₂	241.5–242	242
		248–249 ^e						

a, b, c, d, e, f, g, h, i, j Refs^{6–15}.

EXPERIMENTAL

The monosubstituted benzoic acids used were characterized by their melting points (Table I).

Purification of solvents. Water was distilled twice, potassium permanganate being added in the first distillation, whereupon it was boiled under a closure filled with soda lime for 15 min. Methanol and ethanol were purified by the Lund-Bjerrum method^{16,17}. The purification of dimethylformamide (Reachim, *p.a.*) was described in a previous communication¹⁸. Acetone (Lachema, *p.a.*) was dried^{5,6} by two days standing with anhydrous calcium chloride (150 g per 1 l acetone), decanted and distilled, and absolutized by 15 min standing with anhydrous calcium sulphate (800 g per 1 l acetone), whereupon the drying agent was removed, and the solvent was redistilled with exclusion of air humidity. Acetone (Apolda, *p.a.*) was purified according to Kolthoff^{19,20}. Sulfolane (Merck, *p.a.*) was absolutized¹⁶ by shaking with activated alumina at 35°C for 2 h. Then the drying agent was filtered off, and sulfolane was distilled in vacuum.

The potentiometric measurement of dissociation constants was described in a previous communication¹⁸. The following calibration standards were used in the individual solvents: 2,4-dinitrophenol, 2,6-dinitrophenol, picric acid (HPi), and benzoic acid (BA). The pK_{HA} values used for the calibration are listed in Table II. Each titration was repeated four times, the pK_{HA} value was determined from the half-equivalence point.

RESULTS AND DISCUSSION

Table III presents the values of dissociation constants of 38 monosubstituted benzoic acids in the form of pK_{HA} along with their standard deviations for all the 7 solvents used. The pK_{HA} data presented without the standard deviations were obtained from a single measurement each.

The regression dependence of all the experimental pK_{HA} values on the Hammett substituent σ constants³² gave the results listed in Table IV. Comparison of the pK_{HA}^0 values in the individual solvents shows that the dissociation is the most extensive in water where the charged particles formed are best solvated. The other amphiprotic solvents — methanol and ethanol — behave similarly. The effect of dimethylform-

TABLE II
 pK_{HA} Values of the acids used for the calibration (HPi — picric acid, BA — benzoic acid)

Solvent	2,4-Dinitrophenol	2,6-Dinitrophenol	HPi	BA	Ref.
Water	3.96	3.70	0.71	4.20	21
Methanol	7.85	7.63	3.67	9.41	22, 23
Ethanol	—	—	4.10	10.25	24, 25
Dimethylformamide	6.34	6.18	3.65	12.27	26–28
Acetonitrile	16.00	16.45	11.00	20.7	26, 29
Sulfolane	—	—	17.4	26.3	30
Acetone	—	—	9.2	18.2	31

TABLE III

The \overline{pK}_{HA} and s_{pK} values for dissociation of substituted benzoic acids ($X-C_6H_4-COOH$) in water, methanol, ethanol, sulfone, dimethylformamide, acetonitrile, sulfolane, and acetone at 25°C

X	Water		Methanol		Ethanol		Dimethyl- formamide		Acetonitrile		Sulfolane		Acetone	
	\overline{pK}_{HA}	s_{pK}	\overline{pK}_{HA}	s_{pK}	\overline{pK}_{HA}	s_{pK}	\overline{pK}_{HA}	s_{pK}	\overline{pK}_{HA}	s_{pK}	\overline{pK}_{HA}	s_{pK}	\overline{pK}_{HA}	s_{pK}
H	4.21	0.00	9.41	0.00	10.25	0.00	12.27	0.00	20.70	0.00	26.29	0.00	18.20	0.00
3-CH ₃	4.27	0.01	9.47	0.02	10.35	0.03	12.38	0.05	20.76	0.08	27.08	0.07	18.40	0.20
4-CH ₃	4.35	0.00	9.61	0.01	10.43	0.04	12.58	0.06	20.86	0.07	27.35	0.02	18.33	0.11
4-t-C ₄ H ₉	4.36	0.00	9.61	0.03	10.41	0.03	12.56	0.07	20.94	0.03	27.42	0.04	18.57	0.18
3-CF ₃	3.75	0.00	8.69	0.02	9.39	0.05	11.04	0.02	19.67	—	25.88	0.05	—	—
3-CN	3.59	0.02	8.46	0.04	9.08	0.02	10.73	0.02	19.33	0.06	25.57	0.08	16.69	0.21
4-CN	3.50	0.00	8.36	0.02	9.06	0.03	10.77	0.05	19.23	0.09	25.56	0.08	16.74	0.12
3-COCH ₃	3.86	0.03	8.88	0.01	9.57	0.03	11.52	0.04	19.89	0.08	26.28	0.03	17.43	0.23
4-COCH ₃	3.74	0.01	8.75	0.02	9.52	0.04	11.40	0.03	19.69	0.07	26.15	0.01	17.28	0.22
3-COOH ^a	—	—	8.85	0.03	9.56	0.03	11.34	0.06	—	—	—	—	17.24	0.30
4-COOH ^a	—	—	8.25	—	9.38	—	11.21	0.08	—	—	25.85	0.08	—	—
4-NH ₂	4.78	0.00	10.31	0.02	11.29	0.02	13.96	0.03	22.03	0.06	28.44	0.05	19.78	0.11
3-NHCOCH ₃	4.06	0.04	9.25	0.07	10.12	0.02	12.24	0.01	20.67	—	—	—	18.05	0.10
4-NHCOCH ₃	4.30	0.01	9.57	—	10.32	—	12.45	0.09	—	—	—	—	—	—
3-OH	4.09	0.01	9.37	0.03	10.39	0.02	12.50	0.05	20.60	0.07	27.04	0.03	18.41	0.11
4-OH	4.59	0.00	9.93	0.05	10.89	0.02	13.25	0.04	21.16	0.04	27.71	0.05	19.04	0.18

3-OCH ₃	4-12	0-03	9-30	0-06	10-13	0-03	12-10	0-06	20-53	0-06	26-79	0-02	18-18	0-12
4-OCH ₃	4-49	0-01	9-75	0-02	10-61	0-06	12-78	0-05	21-21	0-00			18-77	0-21
3-OC ₆ H ₅	3-95	0-02	9-00	0-04	9-70	0-03	11-49	0-08	20-00	0-05	26-22	0-02	17-39	0-26
4-OC ₆ H ₅							11-14	0-08	19-80	0-05	25-91	0-04		
3-SH	3-96	0-03	8-90	0-05	9-53	0-03	11-47	0-08	20-00	0-07	26-25	0-04	17-51	0-27
4-SH			9-29	0-04	10-23	0-04	12-02	0-11			26-68	0-04	17-92	0-25
4-SCH ₃	4-20	0-01	9-43	0-03	10-20	0-06	12-19	0-09			27-00	0-04	18-22	0-23
3-SO ₂ CH ₃	3-53	0-00	8-43	0-03	9-11	0-05	10-82	0-05	19-24	0-04	25-55	0-05	16-75	0-10
4-SO ₂ CH ₃	3-48	0-01	8-36	0-05	9-13	0-06	10-84	0-06	19-24	0-05	25-65	0-02	16-82	0-06
3-SO ₂ NH ₂	3-68	0-01	8-65	0-05	9-40	0-02	11-19	0-07	19-28	0-05	25-76	0-05	17-00	0-29
4-SO ₂ NH ₂	3-63	0-02	8-55	0-02	9-39	0-01	11-28	0-07	19-56	0-08	25-80	0-03	16-90	0-14
3-SO ₃ H ^a			9-45	0-06	10-21	0-02	12-34	0-10						
3-F	3-88	0-02	8-87	0-03	9-64	0-07	11-36	0-01	19-92	0-10	26-08	0-06	17-40	0-23
4-F	4-16	0-04	9-26	0-04	9-93	0-04	11-84	0-01	20-35	0-04	26-62	0-07	17-89	0-20
3-Cl	3-84	0-05	8-85	0-01	9-56	0-05	11-19	0-08	19-72	0-09	26-05	0-04	16-88	0-23
4-Cl	4-00	0-04	9-01	0-02	9-76	0-05	11-54	0-03	20-12	0-04	26-35	0-05	17-47	0-15
3-Br	3-86	0-05	8-78	0-02	9-54	0-04	11-16	0-03	19-75	0-04	25-95	0-09	17-03	0-14
4-Br	3-99	0-08	9-06	0-03	9-71	0-06	11-57	0-02	20-00	0-03	26-22	0-04	17-47	0-29
3-I	3-88	0-04	8-83	0-03	9-59	0-05	11-31	0-02	19-75	0-05	25-98	0-06	17-27	0-21
4-I	4-00	0-04	9-03	0-03	9-70	0-04	11-60	0-02	20-02	0-03	26-27	0-10	17-56	0-20
3-NO ₂	3-50	0-00	8-31	0-06	8-98	0-05	10-51	0-08	18-99	0-09	25-34	0-05	16-52	0-15
4-NO ₂	3-40	0-01	8-23	0-01	8-91	0-03	10-58	0-06	18-95	0-07	25-40	0-03	16-43	0-20

^a Present as anions.

amide (a representative of protophilic dipolar aprotic solvents) approaches that of amphiprotic solvents, which is obviously due to its ability to stabilize the proton in the solution. On the contrary, protophobic dipolar aprotic solvents (acetonitrile, acetone, sulfolane) lack this property, which is reflected in the small dissociation constant value.

With regard to magnitude of the reaction constant ρ of the Hammett relation, the solvents used fall into two groups. In amphiprotic solvents, where both the proton and the conjugated base are well solvated, the sensitivity of the process studied to substituents is generally lower. Dipolar aprotic solvents also exhibit poor solvation of the conjugated base, whereby the sensitivity of dissociation to stabilization of the conjugated base is increased. No difference can be observed between dipolar aprotic solvents protophilic and protophobic.

From Table IV it follows that the σ substituent constants used³² agree best with the pK_{HA} values determined in water, which stands in accordance with the conditions of validity of the Hammett equation. The correlation is worsened on going to non-aqueous solvents, the worsening being not explainable by more increased experimental error: first of all it is explained by different solvation of the large set of substituents. A marked example is, *e.g.*, 4-NH₂ group for which the differences between the pK_{HA} values measured and those calculated from the regression dependence have the following values in the individual solvents: water 0.00, methanol 0.08, ethanol 0.13, dimethylformamide 0.34, acetone 0.30, acetonitrile 0.29, and sulfolane 0.39. The amphiprotic solvents, which can form hydrogen bonds with dissociable substituents or with substituents carrying free electron pairs, distinctly affect not only the sensitivity of chemical processes (as a whole) to substituents but also relative contributions of the individual substituents to stabilization of the reaction centre.

TABLE IV

Parameters of the Hammett relation for dissociation of benzoic acids in water and in organic solvents

Solvent	$-\log K^0$	$s_{\log K^0}$	ρ	s_ρ	r	s	n
Water	4.21	0.05	1.00	0.01	0.998	0.06	132
Methanol	9.39	0.08	1.47	0.02	0.990	0.08	145
Ethanol	10.21	0.10	1.66	0.01	0.979	0.12	146
Dimethylformamide	12.33	0.12	2.27	0.01	0.956	0.17	155
Acetonitrile	20.57	0.19	2.05	0.01	0.975	0.20	126
Sulfolane	26.87	0.34	2.07	0.01	0.946	0.38	134
Acetone	18.17	0.16	2.29	0.07	0.951	0.24	136

Comparison of the reaction ρ constants found (Table IV) with literature data shows a good agreement in water (our measurements give the definition value $\rho = 1$), ρ : 1.01 ± 0.06 (number of substituents 30), ref.³³; 0.944 ± 0.017 (16), ref.³⁴. In principle, the agreement is found with methanol ρ : 1.41 ± 0.07 (19), ref.³³; 1.39 ± 0.05 (16), ref.³⁴; 1.54 (5), ref.³⁵; 1.38 (13), ref.³⁶; 1.34 (13), ref.³⁷; 1.40 (7), ref.³⁸. The literature data for ethanol exhibit a large scattering ρ : 1.32 ± 0.05 (18), ref.³³; 1.60 ± 0.06 (16), ref.³⁴; 1.96 (9), ref.³⁵; 1.69 (13), ref.³⁹; 1.53 (16), ref.⁴⁰, our own results exhibiting reasonable agreement with at least three of them. A good agreement is found with dimethylformamide, ρ : 2.35 ± 0.08 (9), ref.³³; 2.32 ± 0.09 (16), ref.³⁴; 2.36 (20), ref.⁴¹. Our value of the reaction constant for acetonitrile is the lowest out of the literature data, ρ : 2.57 ± 0.17 (9), ref.³³; 2.49 ± 0.11 (16), ref.³⁴; 2.65 (4), ref.⁴²; 2.27 (10), ref.⁴³, whereas with acetone the situation is opposite, ρ : 1.80 ± 0.08 (16), ref.³⁴; 1.96 (5), ref.⁴². The reason can be in the selection of substituents and their σ values adjusted for aqueous medium (the interactions in the sense of the above discussion).

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