ANALYSIS OF SUBSTITUENT EFFECTS IN NAPHTHALENE SKELETON

Patrik PAŘÍK[1,*] and Miroslav LUDWIG[2]

Department of Organic Chemistry, Faculty of Chemical Technology, University of Pardubice, nám. Čs. legií 565, 532 10 Pardubice, Czech Republic; e-mail: [1] patrik.parik@upce.cz, [2] miroslav.ludwig@upce.cz

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Dedicated to Professor Otto Exner on the occasion of his 80th birthday in recognition of his contributions to physical organic chemistry and chemometrics. We are proud to have had the opportunity to collaborate with him for a long time.

The dissociation constants of 45 substituted 1- and 2-naphthoic acids in six organic solvents (methanol, ethanol, acetonitrile, dimethylformamide, dimethyl sulfoxide, pyridine) have been used to evaluate the substituent effects in the naphthalene skeleton. The dissociation constants data have been treated traditionally by using Dewar–Grisdale equation and the Taft DSP equation, and the alternative interpretation of substituent effects (AISE) method. Quantitative comparison of substituent effects and their transmission from different positions, combination of inductive and resonance effects from various positions, and effects of solvents are discussed. Best results are predominantly provided by the AISE. Substituent effects are stronger in the case of substituents affecting from ring of the naphthalene skeleton bearing carboxylic group than from ring not bearing carboxylic group, and there are no substantial differences between the individual positions of this ring. The contribution of resonance effects at 4α and 8β positions distinctly changes with the medium. Special quality of substituent H was found in comparison with other substituents presumably due their bulkier character. The principal component analysis (PCA) has been also applied to treat the mean dissociation constants using the single substituent property approach. The dissociation together with reactivity data for other naphthalene derivatives have been tested for comprehensive evaluation using PCA. There was found a large similarity of naphthalene reactivity data tested from the point of view of substituent effects.

Keywords: Naphthoic acids; Dissociation constants; Substituent effects; Solvent effects; Chemometrics; Naphthalenes; Carboxylic acids; Acidity; AISE.

In physical organic chemistry considerable attention has been paid to studies of substituent effects, the main object being the benzene derivatives, while the models containing more extensive aromatic skeletons have been neglected. A survey of papers dealing with study of acid-base properties of substituted naphthoic acids in mixed aqueous-organic solvents is presented

in our previous communication[1]. From the survey it can be seen that this topic was systematically tested only by Dewar and Grisdale[2], and Wells and Adcock[3], who used the dissociation data of substituted 1- and 2-naphthoic acids for description of substituent effects in the naphthalene system. Other comprehensive reports dealing with substituent effects in naphthalene derivatives involve the dissociation of naphthylamines[4] and naphthols[5], hydrolysis of naphthoate esters[6], solvolysis of naphthylethyl chlorides[7–9], detritiation of tritionaphthalenes[10], and ^{19}F NMR studies of fluoronaphthalenes[11]. The last extensive study analysing the substituent effects in naphthalene-type compounds is the report by Wells, Ehrenson and Taft[12]. Our previous paper[1] gave dissociation constants of 38 substituted naphthoic acids in four organic solvents, and the data obtained were used to examine the substituent effects on dissociation of model compounds in non-aqueous media by means of the Hammett equation mainly by using substituent parameters adjusted for benzene derivatives. The next communication[13] extends this work to other substrates and media used, and provides a comparison of benzene and naphthalene skeletons.

The present paper is focused on new treatment of the previously measured and published[1,13] dissociation constants of naphthoic acids in non-aqueous media. The examination of substituent effects observed is based on application of the Dewar–Grisdale FM equation[2] and the Taft dual substituent parameters (DSP) equation[12]. Furthermore, a relatively new approach, i.e. alternative interpretation of substituent effects[14] (AISE), is used for the first time for analysis of substituent effects in naphthalene-type derivatives. The AISE is based on the presumption of a single substituent property regardless of the type of molecule skeleton or reaction center. The variability of data matrix has also been evaluated by the methods working with latent variables. Both of the AISE and the latent variables methods represent new approach in treatment of naphthoic acids data.

EXPERIMENTAL

The dissociation constants of 45 substituted naphthoic acids, i.e. 3-, 4-, and 5-substituted 1-naphthoic acids (series 3α, 4α, and 5α, respectively) and 4-, 5-, 6-, 7-, and 8-substituted 2-naphthoic acids (series 4β, 5β, 6β, 7β, and 8β, respectively) have been measured at 25 °C in six organic solvents: methanol (MeOH), ethanol (EtOH), acetonitrile (AN), dimethylformamide (DMF), dimethyl sulfoxide (DMSO), and pyridine[13] (Py) (every experiment was repeated three times). The experimental results in the form of pK_{HA} values were treated with regression analysis. The linear regression was used in correlation with the Hammett equation with the Δ_{calc} parameters adjusted by Wells and Adcock[3] for naphthalene derivatives without direct conjugation between the substituent and reaction center. The correlation ac-

cording to Taft DSP equation made use of the σ_I and σ_R^0 parameters[12], which were also designed for the naphthalene-type compounds. Recently, an alternative theory was devised for interpretation of substituent effects, AISE [14], using σ^i substituent parameters, which extends the dimensions of understanding substituent effects, but so far it has only been tested on benzene derivatives. Therefore, the dissociation data for naphthoic acids were also used to test AISE. The correlations of pK_{HA} vs σ^i were carried out; their solution requires the methods of non-linear regression. The mean dissociation constants $p\overline{K}_{HA}$ were analyzed by latent variable methods, the principal component analysis (PCA).

RESULTS AND DISCUSSION

Derivatives carrying substituents at positions exhibiting no distinct steric interference between the reaction center and substituent or distinct *peri* interference were chosen for this study; therefore, we did not involve 2-substituted 1-naphthoic acids, and 1-, 3-, and 8-substituted 2-naphthoic acids. Nevertheless, two of the derivatives studied (8-chloro-1-naphthoic and 8-nitro-1-naphthoic acids) contain substituents in *peri* position. Both the derivatives were weaker acids than 1-naphthoic acid in all the media used. This finding agrees with the previous ones, viz. that substituents in the 8 position of 1-naphthyl systems behave in such way as if there were no electronic effect present[15]. This is probably due to the mutual orientation of the substituent dipole and carboxylic group dipole[16]. Therefore, these two derivatives were excluded from further discussion.

1-Naphthoic Acids

The dissociation constants pK_{HA} of 3-, 4-, and 5-substituted 1-naphthoic acids were treated together by making use of multiple regression. The correlation of pK_{HA} vs Δ_{calc} with the Hammett type equation led to triple linear regression, the correlation of pK_{HA} vs σ_I, σ_R^0 with the DSP equation was solved by six-fold linear regression, and the correlation of pK_{HA} vs σ^i with AISE was solved by non-linear regression with initial optimization of eleven parameters. The results of these correlation procedures for the individual solvents are presented in Tables I–III.

On the basis of evaluation of values of correlation coefficients *R* of individual regressions in all the solvents it can be stated that the best results are predominantly provided by the AISE. This result contributes to extension of the validity and applicability of the theory. The interpretation capacity of the substituent parameters used decreases in the series: σ^i, Δ_{calc}, σ_I and σ_R^0, hence the one-parameter correlations provide better results. The comparison of reaction constants ρ of the individual correlation procedures gives

TABLE I

The regression coeficients with their standard deviations *s*, overall standard deviations *s*, correlation coeficients *R*, and number of experimental data *n* in multiple linear regressions of pK_{HA} vs Δ_{calc} [a] for 3-, 4-, and 5-substituted 1-naphthoic acids in various solvents

Solvent	pK^0 (*s*)	$\rho_{3\alpha}$ (*s*)	$\rho_{4\alpha}$ (*s*)	$\rho_{5\alpha}$ (*s*)	*s* (*R*)	*n*
MeOH	8.97 (0.01)	0.85 (0.03)	0.96 (0.02)	0.92 (0.03)	0.051 (0.995)	54
DMF	11.83 (0.02)	1.42 (0.05)	1.31 (0.03)	1.35 (0.06)	0.093 (0.992)	54
Py	9.42 (0.02)	1.22 (0.04)	1.23 (0.03)	1.03 (0.05)	0.087 (0.991)	54
AN	20.24 (0.02)	1.02 (0.05)	1.04 (0.03)	1.31 (0.06)	0.098 (0.985)	54
EtOH	9.81 (0.01)	0.97 (0.03)	1.10 (0.02)	1.04 (0.03)	0.053 (0.996)	54
DMSO	10.52 (0.02)	1.21 (0.04)	1.25 (0.03)	1.18 (0.05)	0.086 (0.992)	54

[a] Δ_{calc} value for substituent 5-OCH_3 (0.12) was replaced by Δ_{obs} value (-0.09)[3].

TABLE II

The regression coeficients with their standard deviations *s*, overall standard deviations *s*, correlation coeficients *R*, and number of experimental data *n* in multiple linear regressions of pK_{HA} vs σ_I, σ_R^0 for 3-, 4-, and 5-substituted 1-naphthoic acids in various solvents

Solvent	pK^0 (*s*)	ρ_I (*s*), ρ_R (*s*)			*s* (*R*)	*n*
		3α	4α	5α		
MeOH	8.96 (0.04)	1.27 (0.10)	1.38 (0.10)	0.95 (0.10)	0.109 (0.986)	54
		0.62 (0.13)	2.61 (0.11)	0.59 (0.10)		
DMF	12.01 (0.08)	2.49 (0.20)	2.35 (0.19)	1.76 (0.20)	0.214 (0.977)	54
		1.16 (0.25)	3.25 (0.21)	1.17 (0.20)		
Py	9.54 (0.06)	2.06 (0.14)	2.10 (0.13)	1.31 (0.13)	0.144 (0.985)	54
		0.82 (0.17)	2.77 (0.14)	0.91 (0.14)		
AN	20.23 (0.04)	1.51 (0.10)	1.46 (0.10)	1.39 (0.10)	0.110 (0.989)	54
		0.97 (0.13)	2.83 (0.11)	0.66 (0.11)		
EtOH	9.85 (0.05)	1.53 (0.13)	1.70 (0.12)	1.15 (0.13)	0.137 (0.983)	54
		0.76 (0.16)	2.80 (0.14)	0.75 (0.13)		
DMSO	10.71 (0.07)	2.17 (0.16)	2.29 (0.15)	1.59 (0.16)	0.171 (0.982)	54
		1.35 (0.20)	2.71 (0.17)	1.13 (0.16)		

information about the solvating ability of individual solvents for the charged particles in an acid-base process. The reaction constants have the lowest values in MeOH, and their magnitude increases in the series: MeOH, EtOH, AN, Py, DMSO, DMF. Hence the dissociation products, particularly the conjugate bases of individual acids, are well solvated by amphiprotic solvents MeOH and EtOH, as well as by AN, whereas in dipolar aprotic protophilic solvents, particularly DMSO and DMF, is the degree of stabilization of the conjugate base lower due to a worse solvation.

TABLE III

The regression coeficients with their standard deviations *s*, overall standard deviations *s*, correlation coeficients *R*, and number of experimental data *n* in correlations of pK_{HA} vs σ^i (AISE) for 3-, 4-, and 5-substituted 1-naphthoic acids in various solvents

Solvent	x_{iso} (*s*)[a]	y_{iso} (*s*)[a]	ρ_I (*s*), ρ_N (*s*), ρ_E (*s*)			*s* (*R*)	*n*
			3α	4α	5α		
MeOH	0.42	8.43	–0.15 (0.07)	1.62 (0.12)	–0.15 (0.07)	0.075 (0.994)	54
	(0.01)	(0.04)	2.17 (0.15)	5.74 (0.18)	2.35 (0.14)		
			1.98 (0.27)	4.05 (0.24)	0.72 (0.31)		
DMF	0.42	10.90	–0.07 (0.08)[b]	2.74 (0.14)	–0.07 (0.08)[b]	0.088 (0.996)	54
	(0.01)	(0.07)	4.58 (0.18)	8.58 (0.20)	5.29 (0.16)		
			3.01 (0.36)	4.44 (0.31)	0.03 (0.52)[b]		
Py	0.40	8.78	–0.24 (0.12)	2.26 (0.19)	–0.24 (0.12)	0.119 (0.990)	54
	(0.02)	(0.08)	3.28 (0.26)	7.10 (0.28)	4.10 (0.23)		
			3.03 (0.38)	4.64 (0.32)	0.54 (0.51)[b]		
AN	0.45	19.50	–0.43 (0.07)	2.26 (0.11)	–0.43 (0.07)	0.074 (0.995)	54
	(0.01)	(0.06)	3.04 (0.14)	6.07 (0.17)	2.56 (0.14)		
			2.14 (0.03)	4.13 (0.30)	1.81 (0.37)		
EtOH	0.40	9.25	–0.14 (0.08)[b]	1.83 (0.13)	–0.14 (0.08)[b]	0.080 (0.995)	54
	(0.01)	(0.05)	2.70 (0.17)	6.74 (0.19)	3.06 (0.16)		
			2.36 (0.26)	4.28 (0.22)	0.91 (0.30)		
DMSO	0.42	9.75	–0.25 (0.08)	2.64 (0.16)	–0.25 (0.08)	0.087 (0.996)	54
	(0.02)	(0.09)	4.69 (0.18)	7.16 (0.19)	4.90 (0.16)		
			2.78 (0.36)	4.51 (0.28)	–0.38 (0.57)[b]		

[a] Coordinates of isoeffect point. [b] Insignificant regression coeficients.

Comparison of reaction constants ρ at the particular positions of naphthalene skeleton can enable the evaluation of the extent of transmission of substituent effects from particular positions. (This discussion cannot be based on the correlation results of pK_{HA} vs Δ_{calc}, since the parameters Δ_{calc} were adjusted on the basis of a constant slope for all the positions of the naphthalene ring.) A good picture is presented by the correlation procedures with σ_I and σ_R^0. As it can be seen, the substituents show the strongest effects in the combinations 4α and the weakest ones most likely in the combination 5α. The resulting mixture of inductive and resonance effects can be characterized by the blending factors $\lambda = \rho_R/\rho_I$ given in Table IV. The overall substituent effects at 3α and 5α positions are predominantly caused by inductive contributions, while the resonance effects (which, in addition, substantially change with the medium) predominate at 4α position. Similar results were also obtained from the data describing the dissociation of substituted 1-naphthoic acids in 50% aqueous ethanol[2], where the λ values 0.47, 1.51, and 0.62 were found for the positions 3α, 4α, and 5α, respectively[12]. The comparison of partial effects at the individual positions is apparent in the ratios $\rho_{I,X\alpha}/\rho_{I,3\alpha}$ and $\rho_{R,X\alpha}/\rho_{R,3\alpha}$ (X = 4 or 5) given in Table IV. The inductive effects at positions 3α and 4α manifest themselves to a comparable extent, being about one quarter lower at 5α position. The resonance effects at 5α position are comparable to or slightly lower than those at 3α position, being on the other hand several times higher at 4α position. A change in medium causes distinct changes in the ratios $\rho_{R,4\alpha}/\rho_{R,3\alpha}$, which

TABLE IV
Blending factors λ in positions 3, 4, and 5 of 1-naphthoic acids and comparison of inductive and resonance effects in these positions

Solvent	$\lambda = \rho_R/\rho_I$			$\rho_{I,X\alpha}/\rho_{I,3\alpha}$		$\rho_{R,X\alpha}/\rho_{R,3\alpha}$	
	3α	4α	5α	4α	5α	4α	5α
MeOH	0.49	1.89	0.62	1.09	0.75	4.23	0.95
DMF	0.47	1.38	0.67	0.95	0.71	2.80	1.01
Py	0.40	1.32	0.69	1.02	0.64	3.37	1.10
AN	0.64	1.93	0.48	0.97	0.92	2.93	0.69
EtOH	0.50	1.65	0.66	1.11	0.75	3.69	0.99
DMSO	0.62	1.18	0.71	1.05	0.73	2.01	0.84

decrease in the order MeOH, EtOH, Py, AN, DMF, and DMSO. This again reflects the fact that the resonance contributions of substituents at 4α position substantially change with changing medium.

Using the essential presumption of AISE that a substituent has only a single property which is transmitted to the reaction center in various ways depending on the arrangement of the substituent–basic skeleton–reaction center system, we arranged the $p\bar{K}_{HA}$ values of 1-naphthoic acids in matrix ***A*** containing 8 rows (substituents) and 18 columns (one for each position-solvent combination). The position dependence of substituent effects is thus projected, on the basis of the PCA calculation, into the loading of individual columns (i.e. into the values of loading vectors) and not into score vectors, which characterize the individual rows. The calculation by the PCA method on the full filled non-standardized ***A*** matrix found two latent variables as statistically significant, viz. $t1_A$ and $t2_A$ (Table V), which described 97.96 and 1.51%, respectively, of the variability of the source data set. The values of the first score vector $t1_A$ characterize the properties of substituents attached to 1-naphthyl system irrespective of their position. Values of the second score vector $t2_A$ show a special quality of H substituent, which is well documented in the $t2_A$ vs $t1_A$ plot (Fig. 1). It was found that this character of H substituent manifests itself only at 4α position using follow-up PCA calculations. This is caused by the fact that all the other substituents (being somewhat bulkier than H) are probably exposed

TABLE V
Values of the first and second score vector $t1_A$ and $t2_A$, and the first score vector $t1_B$ calculated by the PCA method on matrix ***A*** and ***B***, respectively

Substituent	Matrix **A**		Matrix **B**
	$t1_A$	$t2_A$	$t1_B$
NH_2	1.000	0.000	–
OCH_3	0.729	0.170	1.000
CH_3	0.603	0.308	0.901
H	0.580	1.000	0.816
Cl	0.331	0.050	0.480
Br	0.319	0.029	0.460
CN	0.071	0.274	0.070
NO_2	0.000	0.250	0.000

to a higher steric tension at this position caused by the presence of the adjacent *peri* hydrogen substituent. Such a character of H substituent should also manifest itself at the 5α position. However, the transmission of substituent effects from this position is much weaker than from the 4α position, and therefore we probably do not observe this property here. The values of the first loading vector $\boldsymbol{p1}_A$ have the meaning of the reaction constants, and, at the individual positions, they predominantly increase in the series: MeOH, EtOH, AN, Py, DMSO, DMF. This order is the same as that of

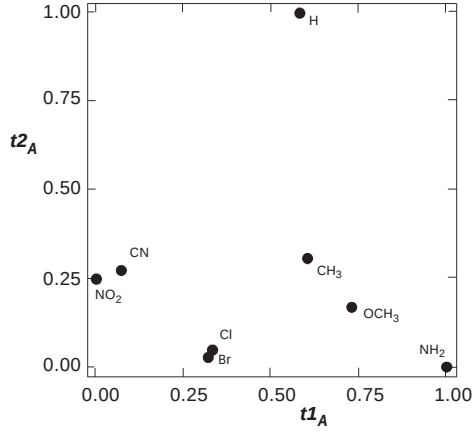

FIG. 1
Dependence of the second on the first latent variable, $\boldsymbol{t2}_A$ vs $\boldsymbol{t1}_A$

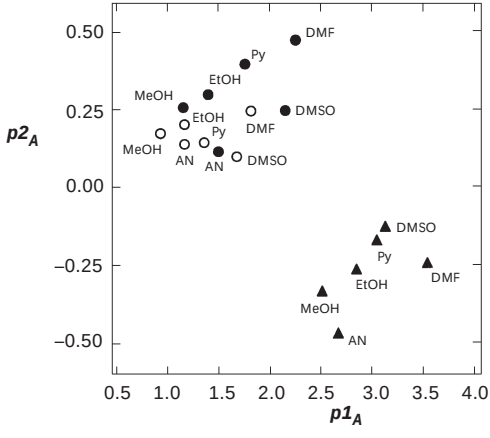

FIG. 2
Dependence of the second on the first loadings vector, $\boldsymbol{p2}_A$ vs $\boldsymbol{p1}_A$. ● 3α, ▲ 4α, ○ 5α

the reaction constants found on the basis of regression analysis. Besides, the $\boldsymbol{p1_A}$ values increase in the order 5α, 3α, 4α, which is why the transmission of substituent effects is the weakest from 5α position and the strongest from 4α position. This finding again agrees with the results of regression analysis. The given properties of loading vectors are illustrated in Fig. 2 showing the dependence of $\boldsymbol{p2_A}$ vs $\boldsymbol{p1_A}$. A special character of substituent H in the 4α position hypothesis can be further documented and supported by distinct separation of this position from positions 3α and 5α when comparing values of the $\boldsymbol{p2_A}$ loading vector (see Fig. 2).

2-Naphthoic Acids

The dissociation constants pK_{HA} of 4-, 5-, 6-, 7-, and 8-substituted 2-naphthoic acids for each particular solvent were also treated together with multiple regression. The correlation of pK_{HA} vs Δ_{calc} was solved by application of five-fold linear regression; that of pK_{HA} vs σ_I, σ_R^0 led to a ten-fold linear regression, and the correlation of pK_{HA} vs σ^i with AISE was solved by nonlinear regression with initial optimization of seventeen parameters. The results of all the correlation procedures are presented in Tables VI–VIII.

TABLE VI
The regression coeficients with their standard deviations *s*, overall standard deviations *s*, correlation coeficients *R*, and number of experimental data *n* in multiple linear regressions of pK_{HA} vs Δ_{calc} for 4-, 5-, 6-, 7-, and 8-substituted 2-naphthoic acids in various solvents

Solvent	pK^0 (*s*)	$\rho_{4\beta}$ (*s*)	$\rho_{5\beta}$ (*s*)	$\rho_{6\beta}$ (*s*)	$\rho_{7\beta}$ (*s*)	$\rho_{8\beta}$ (*s*)	*s* (*R*)	*n*
MeOH	9.36 (0.01)	0.83 (0.04)	0.92 (0.05)	1.05 (0.04)	0.98 (0.04)	0.68 (0.03)	0.054 (0.979)	75
DMF	12.19 (0.02)	1.62 (0.07)	1.37 (0.08)	1.31 (0.07)	1.30 (0.07)	1.13 (0.05)	0.092 (0.975)	75
Py	9.71 (0.01)	1.23 (0.06)	1.21 (0.08)	1.37 (0.06)	1.26 (0.07)	0.98 (0.05)	0.087 (0.972)	75
AN	20.51 (0.02)	1.28 (0.09)	0.93 (0.12)	1.05 (0.09)	1.65 (0.10)	0.60 (0.07)	0.130 (0.932)	75
EtOH	10.20 (0.01)	1.04 (0.05)	1.25 (0.06)	1.29 (0.05)	1.43 (0.05)	0.76 (0.04)	0.069 (0.980)	75
DMSO	10.87 (0.02)	1.43 (0.07)	1.12 (0.08)	1.21 (0.08)	1.15 (0.07)	1.10 (0.05)	0.094 (0.968)	75

On the basis of all the correlation procedures in the most of media we can see that the success of application of substituent constants to interpretation of observed substituent effects decreases in the order: σ^i, σ_I and σ_R^0, Δ_{calc}, this order being somewhat different from that found with 1-naphthoic acids. The best explaining capacity is seen with the σ^i parameters. The observed substituent effects in the naphthalene skeleton, both in the 2-naphthyl and 1-naphthyl systems, are predominantly best described by the AISE theory. The explaining capacity of dual substituent parameters σ_I and σ_R^0 is comparable in both the series. On the other hand, the Δ_{calc} parameters give significantly worse results in the series of 2-naphthoic acids than with 1-naphthoic acids, hence the Dewar and Grisdale's FM equation can better adjust the naphthalene substituent constants for the substituted 1-naphthyl derivatives.

TABLE VII

The regression coeficients with their standard deviations *s*, overall standard deviations *s*, correlation coeficients *R*, and number of experimental data *n* in multiple linear regressions of pK_{HA} vs σ_I, σ_R^0 for 4-, 5-, 6-, 7-, and 8-substituted 2-naphthoic acids in various solvents

Solvent	pK^0 (*s*)	ρ_I (*s*), ρ_R (*s*)					*s* (*R*)	*n*
		4β	5β	6β	7β	8β		
MeOH	9.31	0.99 (0.05)	0.73 (0.04)	0.71 (0.04)	0.68 (0.04)	0.63 (0.04)	0.050	75
	(0.01)	–[a]	–[a]	0.93 (0.06)	0.64 (0.04)	0.63 (0.06)	(0.984)	
DMF	12.12	1.96 (0.09)	1.09 (0.08)	0.85 (0.06)	0.86 (0.06)	1.06 (0.06)	0.089	75
	(0.02)	–[a]	–[a]	1.28 (0.10)	1.17 (0.08)	1.05 (0.10)	(0.982)	
Py	9.66	2.01 (0.20)	0.98 (0.08)	0.96 (0.07)	0.89 (0.07)	0.99 (0.07)	0.094	75
	(0.03)	1.37 (0.05)	–[a]	1.20 (0.11)	1.13 (0.09)	0.59 (0.11)	(0.975)	
AN	20.41	1.46 (0.11)	0.65 (0.09)	0.57 (0.08)	1.11 (0.08)	0.48 (0.08)	0.105	75
	(0.03)	–[a]	–[a]	1.36 (0.12)	0.78 (0.09)	0.52 (0.12)	(0.959)	
EtOH	10.11	1.45 (0.11)	0.96 (0.05)	0.84 (0.04)	0.94 (0.04)	0.61 (0.04)	0.054	75
	(0.02)	0.76 (0.23)	–[a]	1.12 (0.06)	0.96 (0.05)	0.93 (0.06)	(0.989)	
DMSO	10.86	1.84 (0.07)	0.98 (0.06)	0.88 (0.05)	0.87 (0.05)	1.20 (0.05)	0.073	75
	(0.02)	–[a]	–[a]	1.16 (0.08)	1.01 (0.06)	0.51 (0.08)	(0.985)	

[a] Insignificant regression coeficients.

The reaction constants ρ of the individual correlation procedures increase in the overall average order: MeOH, AN, EtOH, DMSO, Py, DMF. The solvent effects on dissociation of 2-naphthoic acids are thus slightly different from those on dissociation of the 1-isomers; in spite of that, it is interesting that amphiprotic solvents and AN solvate the dissociation products of naphthoic acids better than the dipolar aprotic protophilic solvents do.

TABLE VIII

The regression coeficients with their standard deviations *s*, overall standard deviations *s*, correlation coeficients *R*, and number of experimental data *n* in correlations of pK_{HA} vs σ^i (AISE) for 4-, 5-, 6-, 7-, and 8-substituted 2-naphthoic acids in various solvents

Solvent	x_{iso} (*s*) y_{iso} (*s*)[a]	ρ_I (*s*), ρ_N (*s*), ρ_E (*s*)					*s* (*R*)	*n*
		4β	5β	6β	7β	8β		
MeOH	0.24	–0.02 (0.08)[b]	–0.02 (0.08)[b]	0.16 (0.11)[b]	0.08 (0.11)[b]	–0.27 (0.12)	0.053	75
	(0.01)	3.83 (0.29)	2.50 (0.25)	1.91 (0.18)	1.79 (0.12)	2.17 (0.18)	(0.984)	
	9.38 (0.02)	–	1.57 (0.25)	1.93 (0.08)	1.70 (0.12)	1.61 (0.07)		
DMF	0.24	–0.11 (0.10)[b]	–0.11 (0.10)[b]	0.05 (0.14)[b]	–0.08 (0.14)[b]	–0.51 (0.15)	0.067	75
	(0.01)	7.91 (0.45)	4.50 (0.03)	2.79 (0.22)	3.14 (0.16)	4.08 (0.24)	(0.990)	
	12.29 (0.03)	–	2.64 (0.11)	2.66 (0.09)	2.49 (0.09)	2.87 (0.09)		
Py	0.22	0.26 (0.13)	0.26 (0.13)	0.14 (0.18)[b]	–0.38 (0.19)	–0.78 (0.20)	0.078	75
	(0.01)	5.36 (0.03)	3.33 (0.30)	2.80 (0.23)	3.08 (0.18)	3.52 (0.24)	(0.984)	
	9.84 (0.03)	–	2.23 (0.12)	2.63 (0.10)	2.36 (0.10)	2.44 (0.10)		
AN	0.28	–3.99 (1.94)	–3.99 (1.94)	–0.16 (0.13)[b]	–4.30 (1.88)	–4.94 (1.98)	0.097	75
	(0.01)	2.98 (0.17)	1.64 (0.21)	0.93 (0.21)	1.94 (0.20)	1.38 (0.20)	(0.968)	
	20.79 (0.06)	–	1.47 (0.13)	1.73 (0.12)	2.21 (0.12)	1.41 (0.12)		
EtOH	0.21	–0.06 (0.10)[b]	–0.06 (0.10)[b]	–0.04 (0.15)[b]	–0.16 (0.15)[b]	–0.42 (0.16)	0.063	75
	(0.01)	4.31 (0.25)	3.36 (0.25)	2.34 (0.18)	2.72 (0.15)	2.14 (0.18)	(0.987)	
	10.29 (0.03)	–	2.08 (0.10)	2.37 (0.08)	2.43 (0.08)	1.87 (0.08)		
DMSO	0.19	–0.13 (0.13)[b]	–0.13 (0.13)[b]	–0.10 (0.18)[b]	–0.28 (0.19)[b]	–0.55 (0.20)	0.072	75
	(0.01)	5.59 (0.03)	3.35 (0.25)	2.09 (0.18)	2.76 (0.16)	3.86 (0.23)	(0.987)	
	11.05 (0.03)	–	2.00 (0.11)	2.41 (0.09)	2.17 (0.09)	2.56 (0.09)		

[a] Coordinates of isoeffect point. [b] Insignificant regression coeficients.

On the basis of the results of ten-fold linear regressions of pK_{HA} vs σ_I, σ_R^0, it is possible to evaluate the inductive and resonance contributions to substituent effects from the individual positions of 2-naphthoic acids. The results of blending factors $\lambda = \rho_R/\rho_I$ and the comparison of inductive and resonance effects at particular positions of the 2-naphthyl system are presented in Table IX. The values of blending factors λ in "pseudometa" position 4β are close to the λ value (0.61) found for the dissociation of 2-naphthoic acids in 50% aqueous ethanol[12] and also to the λ values found at the other "pseudometa" position of the naphthalene skeleton, i.e. 3α position. From the λ values at 6β, 7β, and 8β positions it is roughly seen that the proportion of resonance effects gradually decreases at these positions, which contradicts the idea of 6β and 8β positions being formally alternating and the 7β position formally non-alternating. At the 8β position, the resonance contributions are probably lowered by the steric effect of *peri* hydrogen substituent in the adjacent position 1, which tends to lower the coplanarity between the substituent and naphthalene skeleton; also the λ values at 8β position markedly change with medium.

The comparison of inductive effect at individual positions can be evaluated on the basis of ratios $\rho_{I,X\beta}/\rho_{I,4\beta}$ (X = 5, 6, 7, or 8) given in Table IX. It can be stated that the actions of inductive effects from the positions in ring B of the naphthalene skeleton are mutually comparable and these effects are approximately half of those from 4β position. Similarly, it is possible to compare the resonance effects by means of $\rho_{R,X\beta}/\rho_{R,6\beta}$ ratios (see Table IX). As already stated, the resonance effects at 6β, 7β, and 8β posi-

TABLE IX
Blending factors λ in positions 4, 5, 6, 7, and 8 of 2-naphthoic acids and comparison of inductive and resonance effects in these positions

Solvent	$\lambda = \rho_R/\rho_I$				$\rho_{I,X\beta}/\rho_{I,4\beta}$				$\rho_{R,X\beta}/\rho_{R,6\beta}$	
	4β	6β	7β	8β	5β	6β	7β	8β	7β	8β
MeOH	–	1.30	0.95	1.00	0.74	0.72	0.68	0.64	0.69	0.68
DMF	–	1.51	1.36	1.00	0.56	0.43	0.44	0.54	0.91	0.82
Py	0.68	1.25	1.27	0.59	0.49	0.48	0.44	0.49	0.94	0.49
AN	–	2.38	0.71	1.08	0.45	0.39	0.76	0.33	0.58	0.38
EtOH	0.52	1.33	1.01	1.53	0.66	0.58	0.65	0.42	0.86	0.84
DMSO	–	1.32	1.16	0.43	0.53	0.48	0.47	0.65	0.87	0.44

tions gradually decrease, and the solvent effects also become apparent. The lowering of resonance effects at the 8β position as compared with the 6β position is the largest in AN, DMSO, and Py, and, on the other hand, the lowest in EtOH and DMF. Hence at 8β position, the resonance effects decrease particularly in dipolar aprotic protophilic solvents, which again can be explained by steric hindrance to resonance by solvation and the presence of adjacent *peri* hydrogen substituent, as it was the case for the 4α position.

For a comprehensive treatment of average dissociation constants $p\bar{K}_{HA}$ of 4-, 5-, 6-, 7-, and 8-substituted naphthoic acids we adopted the method of principal component analysis (PCA). Like in the case of 1-naphthoic acids, the average dissociation constants $p\bar{K}_{HA}$ of 2-naphthoic acids were arranged in a matrix of 8 rows (substituents) and 30 columns (position–solvent combinations) in order to find the extent of operation of substituent effects from the individual position of 2-naphthyl system. The low informative value of the first latent variable (only 78.25%) found on the basis of the PCA calculation carried out on this matrix and the structure of this first score vector (1.000 for NH_2 and 0.000 for all other substituents) reflect the fact that the NH_2 substituent is only contained in series 7β. This first latent variable only explains the absence of amino derivatives from the other series. Therefore, for further analysis we left out the row corresponding to the NH_2 substituent from the source matrix, which led to matrix ***B*** filled to 80% and having 7 rows and 30 columns. The PCA calculation on the nonstandardized matrix ***B*** found one latent variable $\boldsymbol{t1_B}$ to be statistically significant (see Table V), this variable describing 96.80% of variability of the source set and expressing the substituent effect of substituents attached to the 2-naphthyl system irrespective of the point of attachment. The second latent variable proved to be insignificant, describing only 0.78% of variability. The first loading vector $\boldsymbol{p1_B}$ expresses the loading of columns of matrix ***B*** and the individual values have the meaning of the reaction constants; values of $\boldsymbol{p1_B}$ reflect solvent effects on acid-base equilibria and position dependence of substituent effects. From the dependence of the second on the first loading vector, $\boldsymbol{p2_B}$ vs $\boldsymbol{p1_B}$ in Fig. 3, it is seen that the extent of transmission of substituent effects from the individual positions of ring B (not bearing carboxylic group) of the naphthalene skeleton is less than half of that from position 4β in ring A (bearing carboxylic group), and, at the same time, that there are no substantial differences between the individual positions in ring B. The lowest values of score vector $\boldsymbol{p1_B}$ are predominantly those in MeOH; then they increase in an average order of: AN, EtOH, DMSO, Py, DMF. This order, expressing the solvation effects of the individ-

ual solvents on dissociation of 2-naphthoic acids, is identical with that found on the basis of regression analysis.

Comparison of Substituent Effects on Various Naphthalene Derivatives

Using the PCA method, the measured values and some earlier selected data series have been summarily analyzed in order to compare the substituent effects observed in dissociation of naphthoic acids in non-aqueous media with those observed in reactions of other naphthalene derivatives. These literature series have been chosen due to their relatively complete and integrated form. The wider analysis using other literary data sets was not valid because of small number of substrates and low fulfilling of data matrices.

For the analysis of 1-naphthyl derivatives, we assembled data matrix ***C*** with the following dimensions: 46 rows (substituents at 3α, 4α, 5α, 6α, and 7α positions) and 11 columns (the properties studied). The matrix was filled up to 46% and contained the following data: the dissociation constants pK_{HA} of 1-naphthoic acids measured by us in six organic solvents (6 columns, one column for each), the pK_{HA} values of 1-naphthoic acids measured in 50% aqueous ethanol[2], IR wavenumbers of carbonyl group in methyl 1-naphthoates[2], dissociation constants of 1-aminonaphthalenes in water[4], rate constants of detritiation of 1-tritionaphthalenes in trifluoroacetic acid[17], and relative rate constants of solvolyses of 1-(1-naphthyl)-ethyl chlorides in 80% aqueous acetone[7,8]. Assembling of this matrix is rather different from matrix ***A*** where position is combined with solvent

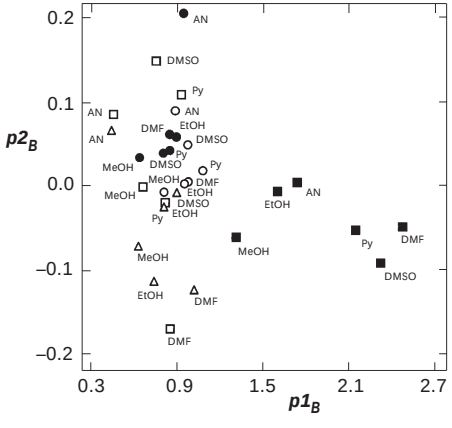

FIG. 3

Dependence of the second on the first loadings vector, $p2_B$ vs $p1_B$. ■ 4β, □ 5β, ○ 6β, ● 7β, △ 8β

then individual columns represent this joint quality. Position is combined with substituent in the case of matrix ***C*** where this joint quality is represented by individual rows. The PCA calculation carried out on this source matrix ***C*** found the first latent variable $t1_C$ (Table X) explaining 97.10% of variability of the data source. The second latent variable was statistically significant and explained another 1.56% of variability; its physical meaning is not clear. The presumably different character of individual reaction series could be interpreted by different distance and arrangement of the reaction center with substituent, but this behavior was not proved here.

In order to examine the 2-naphthyl derivatives, their physico-chemical properties were arranged in matrix ***D*** containing 6 columns with the pK_{HA} values of 2-naphthoic acids measured by us in six non-aqueous media and 5 further columns (one for each data set) for pK_{HA} of 2-naphthoic acids in 50% aqueous ethanol[3], rate constants of hydrolyses of methyl 2-naphthoates in 70% aqueous dioxane[6], dissociation constants of 2-aminonaphthalenes in water[4], rate constants of detritiation of 2-tritionaph-

TABLE X
Values of the first score vector $t1_C$ calculated by the PCA method on matrix ***C*** (1-naphthyl derivatives)

3α	$t1_C$	4α	$t1_C$	5α	$t1_C$	6α	$t1_C$	7α	$t1_C$
3-NH_2	0.640	4-NH_2	1.000	5-NH_2	0.619	–	–	–	–
3-OCH_3	0.389	4-OCH_3	0.756	5-OCH_3	0.517	6-OCH_3	0.513	7-OCH_3	0.554
3-CH_3	0.512	4-CH_3	0.608	5-CH_3	0.470	6-CH_3	0.488	7-CH_3	0.502
–	–	4-C_2H_5	0.590	5-C_2H_5	0.473	–	–	–	–
3-CO_2Me	0.340	–	–	–	–	–	–	–	–
3-OH	0.475	4-OH	0.831	5-OH	0.539	6-OH	0.547	7-OH	0.582
H	0.496	H	0.496	H	0.496	H	0.496	H	0.496
3-I	0.272	4-I	0.411	–	–	–	–	–	–
–	–	4-F	0.517	5-F	0.363	–	–	–	–
3-Cl	0.267	4-Cl	0.384	5-Cl	0.359	6-Cl	0.387	7-Cl	0.405
3-Br	0.285	4-Br	0.375	5-Br	0.348	6-Br	0.394	7-Br	0.420
3-CN	0.143	4-CN	0.095	5-CN	0.251	6-CN	0.342	7-CN	0.330
3-NO_2	0.096	4-NO_2	0.000	5-NO_2	0.209	6-NO_2	0.267	7-NO_2	0.263

thalenes in trifluoroacetic acid[17], and relative rate constants of solvolyses of 1-(2-naphthyl)ethyl chlorides in 80% aqueous acetone[9]. The resulting matrix ***D*** with 48 rows and 11 columns was filled up to 47%. This matrix was assembled in the same way as matrix ***C***. Its PCA analysis revealed the first score vector $t1_D$ (Table XI) explaining 94.23% of variability of the source set. The second latent variable describing 2.41% of the variability was at the limit of statistical significance, and therefore its physical meaning was not examined.

The high extent of variability explained by the first latent variable in the case of both the 1-naphthyl and 2-naphthyl derivatives (97.10 and 94.23%, respectively) documents a large similarity between the behavior of naphthoic acids and other naphthalene derivatives from the point of view of substituent effects. The found latent variables $t1_C$ and $t1_D$ have the meaning of substituent constants and can be used to quantify the substituents effects in the 1- and 2-naphthyl systems, respectively.

TABLE XI
Values of the first score vector $t1_D$ calculated by the PCA method on matrix ***D*** (2-naphthyl derivatives)

4β	$t1_D$	5β	$t1_D$	6β	$t1_D$	7β	$t1_D$	8β	$t1_D$
H	0.659	H	0.659	H	0.659	H	0.659	H	0.659
4-NH_2	0.785	–	–	–	–	7-NH_2	0.914	8-NH_2	0.693
–	–	–	–	6-NMe_2	1.000	7-NMe_2	0.822	–	–
4-OCH_3	0.676	5-OCH_3	0.633	6-OCH_3	0.852	7-OCH_3	0.702	8-OCH_3	0.760
4-CH_3	0.738	5-CH_3	0.679	6-CH_3	0.780	7-CH_3	0.707	8-CH_3	0.690
4-CO_2Me	0.390	–	–	–	–	–	–	–	–
4-OH	0.693	5-OH	0.674	–	–	7-OH	0.765	8-OH	0.853
4-I	0.416	–	–	6-I	0.480	7-I	0.449	8-I	0.632
4-F	0.398	–	–	6-F	0.588	7-F	0.523	8-F	0.594
4-Cl	0.304	–	–	6-Cl	0.541	7-Cl	0.495	8-Cl	0.491
4-Br	0.302	5-Br	0.447	6-Br	0.541	7-Br	0.472	8-Br	0.481
4-CN	0.047	5-CN	0.228	6-CN	0.283	7-CN	0.310	8-CN	0.328
4-NO_2	0.000	5-NO_2	0.283	6-NO_2	0.222	7-NO_2	0.248	8-NO_2	0.302

CONCLUSIONS

The substituent effects in 3-, 4-, and 5-substituted 1-naphthoic acids are very well explained by σ^i constants of the AISE theory and by Δ_{calc} parameters. From the values of dissociation constants and from results of regression analysis it follows that the substituent effects operate more weakly from ring B of the naphthalene skeleton than from ring A. A rough approximation of 3α and 4α positions can be seen in *meta* and *para* positions of benzene system. The resulting substituent effects from 5α position, in spite of the fact that this position is considered alternating, are predominantly due to the inductive effect. A blend of inductive and resonance effects at this position is approximately similar to that at 3α position, and both the effects act more weakly at 5α position. The contribution of resonance effects at 4α position distinctly changes with the medium, due probably to the steric hindrance to resonance by solvation.

The substituent effects in 4-, 5-, 6-, 7-, and 8-substituted 2-naphthoic acids are very well explained by the σ^i constants of the AISE theory. From the results of regression analysis it follows that the substituent effects operate more weakly from ring B of the naphthalene skeleton than they do from ring A, and there are no substantial differences between the individual positions in ring B. The 4β position can roughly be compared with 3α and *meta* positions. The contribution of resonance effect at 8β position is significantly changed with changing medium.

On the basis of results obtained, the AISE method can be unambiguously recommend for description and evaluation of substituent effects in the naphthalene skeleton. The presented results contribute to support the validity and to extend the applicability of this alternative interpretation of substituent effects. Furthermore, it is the first communication applying AISE to naphthalene-type derivatives. Comparing with other two regression methods, some disadvantage of AISE method flows from determination of large number of regression parameters therefore necessity of more extensive data set.

PCA analysis found that there is a large similarity in chemical behavior of various naphthalene-type derivatives from the point of view of substituent effects.

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