Amidines. Part 32.[1] Influence of Substitution at the Amino Nitrogen Atom on the Sensitivity to Substitution at the Imino Nitrogen Atom. pK_a Values of N^1-Methyl-N^1-phenylformamidines in Water–Ethanol Solutions

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A series of new N^1-methyl-N^1-phenylformamidines ($RN{=}CH{-}NMeC_6H_5$, 13 compounds) containing variable substituents at the imino nitrogen atom has been synthesized. The pK_a values of the compounds have been measured in four binary ethanol–water solvents and correlated with Hammett-type substituent constants, and with pK_a values of the corresponding primary amines determined in the same solvents. It is shown that substitution at the amino nitrogen atom has considerable influence on the sensitivity of the amidino group to the polar effects of substituents at the imino nitrogen atom. The parameters for both types of regression depend on the solvent.

The equation for prediction of the pK_a values for trisubstituted amidines, enabling explanation of changes in the ρ values for substitution at one site caused by substitution at the other two sites, is derived.

It is already known[2] that the basicity of compounds containing the amidino $-N{=}\overset{|}{C}-N<$ group depends on the substituents at the three sites (both nitrogen atoms and the amidino carbon atom) and that the imino nitrogen atom is the protonation site. It has been shown[2-12] that in the cases of series of amidines containing a substituent at any of the three sites, their pK_a values obey the Hammett eqn. (1).

$$pK_a = pK_a^\circ - \rho\sigma \qquad (1)$$

It has been found that the pK_a values of amidines containing, at the imino nitrogen atom, substituents of any kind correlate with the pK_a values of the corresponding primary amines,[1,9,11,13-15] and that such correlations may serve for prediction of the pK_a values of trisubstituted amidines. Correlations are in the form of eqn. (2), where the term pK_a° has the same meaning as in the Hammett equation.

$$pK_a(\text{amidine}) = pK_a^\circ + \alpha[pK_a(\text{amine}) - pK_a(\text{aniline})] \qquad (2)$$

It has also been shown[15-17] that both the ρ values, as well as the α values for substitution at the imino nitrogen atom depend on polar effects of the substituent at the functional carbon atom. The pK_a values of amidines containing two substituted phenyl rings, one at the imino nitrogen atom and the second at the amidino carbon atom, do not obey dual parameters eqn. (3), where σ_{Im} and σ_{F} are Hammett-type constants of substituents at the imino nitrogen atom and functional carbon atom, respectively, but obey eqn. (4), with the term μ representing the mutual interaction of substituents.

$$pK_a = pK_a^\circ - \rho_{\text{Im}}\sigma_{\text{Im}} - \rho_{\text{F}}\sigma_{\text{F}} \qquad (3)$$

$$pK_a = pK_a^\circ - \rho_{\text{Im}}\sigma_{\text{Im}} - \rho_{\text{F}}\sigma_{\text{F}} - \mu\sigma_{\text{Im}}\sigma_{\text{F}} \qquad (4)$$

Eqn. (4) ensures that, if the substituent at one of these sites is not varied in the series, *e.g.* at the functional carbon atom (σ_{F} constant), a linear correlation [eqn. (1)] will be obtained, where the observed ρ value is equal to the value of ($\rho_{\text{Im}} + \mu\sigma_{\text{F}}$).

Recently, as a result of *ab initio* calculations for model fluoroformamidines, it was shown[18,19] that the ρ value for substitution at any site of the amidino group depends not only on the site of substituent but also on substitution at the other two sites, and that the μ values for each pair of substitution sites are different.

Table 1 Compounds investigated

$RN{=}CH{-}N(CH_3)Ph$

Compound	R
1	p-$C_6H_4NO_2$
2	m-C_6H_4Cl
3	p-C_6H_4Cl
4	m-C_6H_4OMe
5	C_6H_5
6	m-C_6H_4Me
7	p-C_6H_4Me
8	p-C_6H_4OMe
9	Benzyl
10	Allyl
11	Hexyl
12	Butyl
13	Isopropyl

Thus, the questions arose as to what extent the ρ and α values [eqns. (1) and (2)] for substitution at the imino nitrogen atom depend on polar effects of substituent at the amino nitrogen atom, and as to whether the changes of these values with solvent are similar for various series and are thus predictable.

For this reason, we have synthesized a series of N^1-methyl-N^1-phenylformamidines containing various substituents R at the imino nitrogen atom and have measured their pK_a values in four binary ethanol–water mixtures to compare them and their regression parameters with those obtained for other series.

Experimental

Synthesis of Formamidines.—The N^1-methyl-N^1-phenylformamidines under study (see Table 1) were obtained in our laboratory by reacting equimolar amounts of (N-methyl-N-phenyl)chloromethaniminium chloride with the corresponding primary amine according to the following procedures.

(N-*Methyl*-N-*phenyl*)*chloromethaniminium chloride.* To a solution of N-methyl-N-phenylformamide (0.06 mol) in dry chloroform (30 cm^3), a solution of oxalyl chloride (0.06 mol)

Table 2 Characterization of N^1-methyl-N^1-phenylformamidines

(a) N^2-Phenyl derivatives

Compound	Retention	^{1}H NMR chemical shifts (δ)[a]		Phenyl ring at N^1			Phenyl ring at N^2				
R	index[b]	N=CH–N	NCH_3	2,6-H	4-H	3,5-H	2,6-H	4-H	3,5-H	CH_3	CH_2
1 p-$C_6H_4NO_2$	2363 ± 5	8.22	3.54	7.37	7.12	7.08	8.11		7.25		
2 m-C_6H_4Cl	2145 ± 2	9.08	3.52	7.30	7.16	7.07	7.21	7.16	7.07		
3 p-C_6H_4Cl	2217 ± 5	8.05	3.49	7.30	6.99	7.05	7.23		6.97		
4 m-C_6H_4OMe	2174 ± 8	8.09	3.48	7.30	7.17	7.09	7.30	7.15	6.60	3.78	
5 C_6H_5	1980 ± 6	8.10	3.57		7.02–7.33			7.02–7.33			
6 m-C_6H_4Me	2017 ± 2	8.08	3.48	7.31	7.17	7.15		6.85–7.43		2.32	
7 p-C_6H_4Me	2074 ± 12	8.09	3.50	7.33	7.17	7.13	7.11		6.95	2.32	
8 p-C_6H_4OMe	2125 ± 8	8.12	3.53	7.35	6.99	7.15	7.25		6.96	3.83	
9 Benzyl	1992 ± 0	8.03	3.38		7.02–7.48			7.02–7.48			4.60

(b) N^2-Alkyl derivatives

Compound	Retention	^{1}H NMR chemical shifts (δ)[a]		Phenyl ring at N^1			Alkyl group at N^2			
R	index[b]	N=CH–N	NCH_3	2,6-H	4-H	3,5-H	NCH	CH_2	CH_3	=CH
10 Allyl	1559 ± 1	7.89	3.32	7.26	7.07	7.00	4.00	5.12		5.94
11 Hexyl	1770 ± 11	7.92	3.32	7.28	7.09	7.06	3.34	~1.12	0.88	
12 Butyl	1579 ± 2	7.89	3.29	7.25	7.05	7.02	3.28	~1.41	0.88	
13 Isopropyl	1397 ± 0	7.99	3.32	7.28	7.08	7.06	3.26		1.19	

[a] For $CDCl_3$ solutions. [b] On GE SE-30 column at 280 °C.

Table 3 ^{13}C NMR spectra ($CDCl_3$ solutions) of N^1-methyl-N^1-phenylformamidines

(a) N^2-Phenyl derivatives

Compound		Phenyl ring at N^1					Phenyl ring at N^2					
R	N=C–N	C-1	C-2,6	C-4	C-3,5	NCH_3	C-1	C-2	C-3	C-4	C-5	C-6
1 p-$C_6H_4NO_2$	144.4	151.9	120.7	125.1	129.6	34.6	157.7	121.4	125.3	129.6	125.3	121.4
2 m-C_6H_4Cl	144.8	151.3	120.1	123.1	129.5	34.1	152.9	121.2	134.5	124.4	129.9	119.7
3 p-C_6H_4Cl	144.9	151.1	120.1	124.3	129.5	34.1	150.1	122.4	129.0	129.5	129.0	122.4
4 m-C_6H_4OMe[a]	145.0	152.9	119.8	124.0	129.6	34.0	151.0	119.8	160.4	109.2	129.4	113.4
5 C_6H_5	145.1	151.4	119.8	123.3	129.4	34.0	150.9	124.0	129.0	121.2	129.0	124.0
6 m-C_6H_4Me[b]	145.2	150.7	119.8	123.9	129.4	33.9	150.7	122.0	138.7	124.0	128.8	118.2
7 p-C_6H_4Me[c]	145.2	150.7	119.7	123.9	129.6	33.9	148.9	121.0	129.4	132.6	129.4	121.0
8 p-C_6H_4OMe[d]	144.8	150.4	119.7	123.8	129.4	33.9	150.4	121.8	114.4	155.0	114.4	121.8
9 $CH_2C_6H_5$[e]	145.5	152.8	119.1	123.0	129.2	33.8	141.5	127.5	128.3	126.5	128.3	127.5

(b) N^2-Alkyl derivatives

Compound		Phenyl ring at N^1					Phenyl ring at N^2					
R	N=C–N	C-1	C-2,6	C-4	C-3,5	NCH_3	C-1	C-2	C-3	C-4	C-5	C-6
10 Allyl	145.6	152.8	119.1	123.0	129.3	33.7	58.4	138.1	114.6			
11 Hexyl	145.7	151.6	118.8	122.7	129.3	33.6	56.6	32.4	31.8	27.0	22.7	14.1
12 Butyl	145.7	151.6	118.8	122.7	129.3	33.5	56.3	34.6	20.4	14.0		
13 Isopropyl	145.8	149.8	118.7	122.5	129.2	33.5	56.5	25.5				

[a] OMe, 55.1. [b] Me, 21.3. [c] Me, 20.7. [d] OMe, 55.5. [e] CH_2, 59.8.

in chloroform (20 cm^3) was added dropwise, at room temperature, with stirring. The reaction mixture was stirred until evolution of gaseous by-products (CO and CO_2) ceased.

N^1-*Methyl*-N^1-*phenylformamidines*. To a solution of primary amine (0.06 mol) in dry chloroform (20 cm^3) was added dropwise the solution of (N-methyl-N-phenyl)chloromethaniminium chloride freshly obtained in the preceding step, followed by triethylamine (0.1 mol) in chloroform (10 cm^3). After two days, the chloroform was evaporated off, the thick residue was dissolved in hydrochloric acid (1 mol dm^{-3}, 15 cm^3) and the acidic solution was washed twice with ethyl acetate (30 cm^3). The aqueous solution was basified at 0 °C with aqueous NaOH solution (3 mol dm^{-3}; 20 cm^3) and immediately extracted with diethyl ether (3 × 50 cm^3). Combined extracts were dried over 4 Å molecular sieves and evaporated to yield the crude amidine. Solid amidines were recrystallized from methanol, the others were dissolved in an equimolar amount of hydrochloric acid (36%), diluted with water (20 cm^3) and washed with diethyl ether (2 × 10 cm^3). After immediate basification with 3 mol dm^{-3} NaOH solution (20 cm^3), amidines were extracted with diethyl ether (3 × 10 cm^3), dried over 4 Å molecular sieves and, after evaporation of the ether, the

Table 4 pK_a values of N^2-substituted N^1-methyl-N^1-phenylformamidines in various binary ethanol–water solvents at 25 ± 0.1 °C[a]

Compound	Ethanol % (w/w)			
R	95.6	80	70	50
1 p-$C_6H_4NO_2$	3.54 ± 0.03	3.19 ± 0.02	3.45 ± 0.03	3.33 ± 0.04
2 m-C_6H_4Cl	4.36 ± 0.01	4.12 ± 0.02	4.10 ± 0.01	3.98 ± 0.03
3 p-C_6H_4Cl	4.68 ± 0.01	4.39 ± 0.02	4.35 ± 0.03	4.24 ± 0.02
4 m-C_6H_4OMe	5.14 ± 0.03	4.87 ± 0.03	4.76 ± 0.03	4.62 ± 0.04
5 C_6H_5	5.16 ± 0.04	4.99 ± 0.02	4.93 ± 0.04	4.67 ± 0.05
6 m-C_6H_4Me	5.51 ± 0.03	5.11 ± 0.03	5.10 ± 0.02	4.90 ± 0.03
7 p-C_6H_4Me	5.60 ± 0.03	5.31 ± 0.04	5.20 ± 0.02	5.06 ± 0.03
8 p-C_6H_4OMe	5.72 ± 0.03	5.29 ± 0.02	5.36 ± 0.01	4.98 ± 0.05
9 Benzyl	8.20 ± 0.04	7.90 ± 0.04	7.79 ± 0.03	7.66 ± 0.03
10 Allyl	8.41 ± 0.03	7.96 ± 0.03	8.05 ± 0.02	8.12 ± 0.02
11 Hexyl	8.72 ± 0.02	8.41 ± 0.02	8.55 ± 0.02	8.58 ± 0.04
12 Butyl	8.88 ± 0.02	8.63 ± 0.01	8.52 ± 0.02	8.64 ± 0.02
13 Isopropyl	8.98 ± 0.02	8.73 ± 0.01	8.67 ± 0.02	8.80 ± 0.02

[a] At ionic strength $\mu = 0.01$, using imidazole pK_a as the standard.

compounds obtained (yields 25–45%) were pure enough for pK_a determinations.

Structure and Purity of Formamidines.—The structures of the amidines obtained were confirmed by their room temp. ^1H (100 MHz) and ^{13}C NMR spectra (see Tables 2 and 3). Chemical shifts in the ^1H NMR spectra are in good agreement with additivity parameters derived earlier for amidines,[20,21] and the numbers of protons in each group are consistent with the structures assigned.

The purity of the amidines obtained was checked by GLC on a 1 m column packed with 15% silicone gum rubber GE SE-30 on Chromosorb WAW 60–80 mesh. Analyses were carried out at 280 °C using nitrogen at a flow rate of 25 cm^3 min^{-1} and a flame ionization detector. Retention indices of amidines are given in Table 2. The amidines were more than 99% pure, except for the m-chlorophenyl derivative **2**, which contained about 5% of m-chloroaniline. However, as there is considerable difference in the pK_a values between each amidine and the corresponding amine, this has no influence on the accuracy of pK_a determination by a potentiometric method. Additional evidence of purity was provided by the titration volumes and the shapes of the titration curves.

pK_a Measurements.—The pK_a values were determined by potentiometric titration in 95.6% ethanol at 25.0 ± 0.2 °C using a Mera ELWRO model N517 pH-meter and combined glass electrode type ERH-11. Samples of 0.15 mmol of investigated amidine dissolved in 15 cm^3 of 0.01 mol dm^{-3} tetramethylammonium chloride in the corresponding binary solvent were titrated with a solution of HCl (0.15 mol dm^{-3}) in the same solvent, while the sample was mixed by means of dry and acidic-impurity-free (such as CO_2) flow of nitrogen bubbles. The titrant was added in 40 mm^3 portions by means of the dispenser (UNIPAN, model 344A) at a rate of about 5–6 injections min^{-1}. The titrant was prepared by saturation of the corresponding binary solvent with dry, gaseous HCl until the required concentration (0.15 mol dm^{-3}) was reached, and standardized by potentiometric titration of Na_2CO_3 samples. The whole titration procedure (addition of the titrant, data collection, calculations and corrections) was controlled by means of microcomputer, connected on-line to the pH-meter and dispenser, and operated by a program designed in our laboratory for the purpose.

Obtained pK_a values were corrected according to the known relation[22] given in eqn. (5) where the pH value is measured at

$$pK_{a_i} = pH_i - pH_s + pK_{a_s} \qquad (5)$$

the 1/2 neutralization point, pK_{a_i} and pK_{a_s} are the pK_a values of the compound investigated (i) and the standard (s). Imidazole was used as the standard for pK_a determination.

The pK_a values were determined for two identical samples of each compound. Prior to and after every two measurements, the standard solution of imidazole was titrated to check accuracy. Experimental details and precautions taken to obtain reliable results were the same as in previous papers.[11,16] As the standard for pK_a determination, imidazole was used because its pK_a values in water–ethanol mixtures are known.[23] Obtained pK_a values, with confidence intervals calculated at a significance level of 0.05, are summarized in Table 4.

Discussion of Errors.—The error of potentiometric titration using this procedure, as estimated, should not exceed 0.05 pK_a units. Errors caused by the ionic strength changes from μ = 0.01 to 0.018, occurring during titration, are much smaller and can be neglected. Determined pK_a values may include a systematic error contributed by the pK_a values of the standard (imidazole) in water–ethanol mixtures but, on account of its constancy, this has no influence on the regression coefficients.

Results and Discussion

The experimental points seldom lie on the regression line and it is usually only a line of best fit. The correlation parameters depend to a certain degree on the set of substituents in the series. Addition or subtraction of one of the experimental points may sometimes significantly alter the slope of a correlation line. Therefore, to obtain reliable results, only series containing compounds with the same set of substituents are compared, so the ρ-values of the series studied previously are recalculated in this paper.

Linear Correlations with σ Constants.—It has already been shown[1,11,14,15] that when considering series of amidines containing various substituents at the phenyl ring on either nitrogen atom, the most suitable are σ^0 values,[24,25] while ordinary σ values[26] are suitable only for substituents on the phenyl ring at the amidino carbon atom. In the literature, however, ordinary σ values have been applied for substitution at the imino nitrogen atom.[27,28] For pK_a values obtained in each solvent, we have compared correlations with both, σ^0 and σ values.

The parameters of the regressions (Table 5) indicate that, as with other series of amidines with a variable substituent at one of the two nitrogen atoms, correlations with σ^0 values are of higher quality. However, as indicated by both estimators (the correlation coefficient r and Exner's ψ function),[29] correlations with σ values are still satisfactory. This is the reason why this pattern was not found earlier.

Table 5 Parameters of regressions[a] with substituent constants [eqn. (1)]

% EtOH	σ	pK_a^o	ρ	r	ψ
95.6	σ	5.23	2.18 ± 0.28	0.992	0.148
	σ^o	5.27	2.19 ± 0.26	0.993	0.136
80	σ	4.92	2.13 ± 0.34	0.987	0.183
	σ^o	4.96	2.16 ± 0.25	0.993	0.134
70	σ	4.89	1.91 ± 0.22	0.993	0.130
	σ^o	4.92	1.92 ± 0.22	0.993	0.134
50	σ	4.69	1.73 ± 0.29	0.986	0.193
	σ^o	4.71	1.75 ± 0.26	0.989	0.174

[a] At a confidence level of 0.95.

Table 6 The ρ values recalculated for series of formamidines[a] containing the same set[b] of substituents

	Series			
% EtOH	FMePh	FDM	FPM	FOPM
95.6	2.19	2.61[c]	2.40[d]	1.52[d]
80	2.16	2.64[d]	2.68[d]	2.32[d]
50	1.75	2.34[d]	2.71[d]	2.23[d]

[a] N^1-Methyl-N^1-phenylformamidines (FMePh), N^1,N'-dimethylformamidines (FDM), N^1,N^1-pentamethyleneformamidines (FPM), N^1,N^1-(3-oxapentamethylene)formamidines (FOPM). [b] Aryl substituents as in this paper. [c] Based on data from ref. 31. [d] Based on data from ref. 1.

Table 7 Parameters of regressions[a] with pK_a values of corresponding primary amines [eqn. (2)]

% EtOH	pK_a^o	α	r	ψ	n
95.6	2.58	0.64 ± 0.02	0.998	0.060	13
80	2.82	0.61 ± 0.04	0.997	0.084	11
50	2.83	0.49 ± 0.12	0.973	0.264	8

[a] At a confidence level of 0.95.

Influence of Substitution at the Amino Nitrogen on the Polar Effect of Substituent at Imino Nitrogen Atom.—Regressions of both type obtained for N^1-methyl-N^1,N^2-diphenylformamidines can be compared with those obtained previously for other series of amidines. The data in Table 6 indicate that exchanging the phenyl ring at the amino nitrogen atom for a more electron-donating substituent such as a methyl group (FMePh *vs.* FDM) causes not only considerable increase in the basicity of each amidine (about 2.2 pK units) but also a discernible increase in the ρ value *i.e.* an increase of sensitivity of amidino group to substitution at the imino nitrogen atom.

Thus, for prediction of the pK_a values of amidines containing two substituents, one at imino and the second at the amino nitrogen atom, eqn. (6) [analogous to eqn. (4)] should be used.

$$pK_a = pK_a^o - \rho_{Im}\sigma_{Im} - \rho_{Am}\sigma_{Am} - \mu_{ImAm}\sigma_{Im}\sigma_{Am} \quad (6)$$

Because the μ value for interaction between substituents at imino and amino nitrogen atoms is not the same for nitrogen and functional carbon, for the sake of clarity, the subscript indicates the sites of both substituents.

Obtained results, combined with previous findings that the ρ values for substitution at both nitrogen atoms depend on the substituent at the amidino carbom atom, provide further evidence for the conclusion based on *ab initio* calculations[19] that the effect of substitution at either site of the amidino group depends on the substituents at the other two sites. Moreover, they indicate that the more electron-donating the substituent at one site, the higher the sensitivity of the amidino group to the polar effects of substituent at the other site.

The aforesaid leads to the conclusion that general eqn. (7) for prediction of the pK_a values of amidines containing various substituents at the three sites of the amidino group should contain additional cross-terms representing mutual interaction between substituents for all three combinations of pairs of substitution sites. These terms are in the form $\mu_{k,l}\sigma_k\sigma_l$, where σ_k and σ_l are the σ values of substituents at each pair of the sites (k and l) of the amidino group and the term $\mu_{k,l}$ represents mutual interaction between substituents at these two sites.

$$pK_a = pK_a^o - \rho_1\sigma_1 - \rho_2\sigma_2 - \rho_3\sigma_3 - \mu_{1,2}\sigma_1\sigma_2 - \mu_{1,3}\sigma_1\sigma_3 - \mu_{2,3}\sigma_2\sigma_3 \quad (7)$$

Eqn. (7) ensures that in the case of a series where two substituents are invariant (*e.g.* σ_2 and σ_3 are constant), linear eqn. (1) will be obtained. In such case, the observed ρ value will be equal to the expression $(\rho_1 + \mu_{1,2}\sigma_2 + \mu_{1,3}\sigma_3)$ and the observed pK_a^o given by $(pK_a^o - \rho_2\sigma_2 - \rho_3\sigma_3 - \mu_{2,3}\sigma_2\sigma_3)$. In the case where only one substituent is invariant (*e.g.* σ_3 is constant), the observed ρ_1 value will be equal to the expression $(\rho_1 + \mu_{1,3}\sigma_3)$ and ρ_2 equal to $(\rho_2 + \mu_{2,3}\sigma_3)$.

The three sites of amidino group are the imino (Im) and amino (Am) nitrogen atoms and functional (F) carbon atom. On the basis of five series of amidines (25 compounds in each series), the μ value for interaction between imino nitrogen and functional carbon atom (μ_{ImF}) was found to be 0.76 ± 0.08. For determination of the values of the terms μ_{AmF} and μ_{ImAm}, representing interactions between amino nitrogen and functional carbon atom, and between both nitrogen atoms, respectively, investigations of several appropriate series of amidines are necessary.

Influence of the Solvent on Correlations with Hammett-type Constants and with p*K*$_a$ *Values of Amines.*—ρ-Values for the studied N^1-methyl-N^1-phenylformamidines decrease with increasing concentration of water in ethanol–water solutions. In mixtures containing less than 50% of ethanol, solubility of phenyl derivatives (**1**–**8**) is too small for potentiometric pK_a determination, thus it is impossible to determine the relationship between these two values. However, it can be concluded that it is not linear.

In the case of N^1,N^1-pentamethylenebenzamidines,[30] the α value [eqn. (2)] for solutions in 90% ethanol was the same as for 50% ethanol, suggesting that it might be the same for other solutions, and thus may facilitate prediction of pK_a values of amidines in various solvents. However the results obtained for the series of N^1,N^1-dialkyl-N^2-phenylformamidines,[1] where it was found that both, the ρ and α values depend on the solvent, called this assumption into question.

To check out how far this assumption is true, we have correlated the pK_a values of studied amidines with the pK_a values of corresponding primary amines [eqn. (2)] measured in the same solvents (Table 7). For 95.6 and 80% ethanol, the obtained correlations are of very good quality. For 50% ethanol, the correlation is only satisfactory, but this is most probably due to the smaller number of experimental points accessible. For 80% ethanol, the α value is very close to that of 95.6% ethanol. However, the test of parallelism disclosed that for 95.6 and 80% ethanol, the slopes of regression lines are undoubtedly different. For 50% ethanol, the α value is considerably smaller (about 20%). This indicates that the α value depends on the solvent. The similarity of α values observed for the series of benzamidines in 80 and 50% ethanol is, like their proximity in 95.6 and 80% ethanol for the N^1-methyl-N^1-phenylformamidines studied here, just a matter of coincidence. It has to be pointed out that the relationship between α values and the composition of ethanol–water binary solvent is not the same for various series of amidines.

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