The Influence of the Size and Position of the Alkyl Groups in Alkylimidazole Molecules on Their Acid-Base Properties

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Dissociation constants of HL^+ acids, where L stands for 1-alkylimidazole, 1-alkyl-2-methylimidazole, 1-alkyl-2-ethylimidazole, 1-alkyl-2-propylimidazole, 1-alkyl-4-methylimidazole and 1-alkyl-2-ethyl-4-methylimidazole, were determined potentiometrically. For each of the homologous series of these bases, a relationship has been derived between the pK_a value and the number of carbon atoms in the hydrocarbon group for $(CH_2)_n \leq 13$. The basicity of the alkylimidazoles has been found to increase linearly with increasing carbon chain length. The slopes of straight plots of $pK_a = f(n_{CH2})$ have been found to increase with increasing basicity of homologous series of the alkylimidazoles.

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Alkylimidazoles are stable aromatic bases, which are characterized by high boiling points and good stability to oxidizing and reducing agents. There are many methods of synthesis of alkylimidazoles [1-3]. Sparingly water-soluble hydroxyalkylimidazoles are useful in the extraction of heavy metal cations, having an atomic number greater than 26 including copper, cobalt, zinc and lead [4].

To describe the quantitatively processes in extraction systems, knowledge of protonation constants of the ligands, K_a, stability constants of their metal complexes, β_n, and partition coefficients, P_n, of the compounds between immiscible aqueous and organic solvent phases are needed [5-10].

Alkyl-1,3-diazoles containing more than four carbon atoms in the hydrocarbon chain are sparingly soluble in water. For this reason, almost all published papers to date with acid-base and complex-forming properties of alkylimidazoles have dealt with the first four alkyl derivatives of this series. Only one work mentions 1-pentylimidazole [11] and another one 1-butyl-2-methylimidazole [12]. The pK_a values for investigated alkylimidazoles are listed in Table 1.

The purpose of this work was to evaluate the influence of the position, number and size of the alkyl groups on the pK_a values of sparingly soluble mono-, di- and tri-alkylimidazoles.

Table 1

The pK_a Values of Selected Alkylimidazoles in Aqueous Solutions at 25 °C and Fixed Ionic Strength, I = 0.5 (KNO_3)

Base	pKa	Ref.
Imidazole	6.95	[13]
	6.97	[14]
1-alkylimidazoles		
1-Methylimidazole	7.21	[15]
	7.19	[16]
1-Ethylimidazole	7.26	[17]
	7.30	[18]
1-Propylimidazole	7.22	[17]
1-Butylimidazole	7.21	[19]
1-Isobutylimidazole	7.23	[20]
1-Pentylimidazole	7.23	[11]
2-alkylimidazoles		
2-Methylimidazole	7.85	[18]
	8.10	[21][22]
2-Ethylimidazole	7.99	[23]
	8.00	[18]
2-Propylimidazole	8.02	[14][24]
2-Isopropylimidazole	7.97	[14][24]
2-Butylimidazole	8.00	[14][6]
2-Isobutylimidazole	7.97	[14]
	7.98	[6]
1,2-alkylimidazoles		
1,2-Dimethylimidazole	8.21	[25]
	8.22	[15]
1-Methyl-2-ethylimidazole	8.13	[22]
1-Ethyl-2-methylimidazole	8.21	[26]
1-Propyl-2-methylimidazole	8.20	[27]
1-Butyl-2-methylimidazole	8.18	[12]
1,4-alkylimidazoles		
1,4-Dimethylimidazole	7.75	[30]
2,4-alkylimidazoles		
2,4-Dimethylimidazole	8.50	[18]
2-Ethyl-4-methylimidazole	8.68	[23]
1,2,4-alkylimidazoles		
1,2,4-Trimethylimidazole	8.64	[22]
1,2,4,5-alkylimidazoles		
1,2,4,5-Tetramethylimidazole	9.20	[28][29]
4,5-alkylimidazoles		
4,5-Dimethylimidazole	8.19	[31]
4,5-Diethylimidazole	8.19	[23]
2,4,5-alkylimidazoles		
2,4,5-Trimethylimidazole	8.92	[18]
4(5)-alkylimidazoles		
4(5)-Methylimidazole	7.69	[32]
	7.80	[33]

Table 2

The pK_a Values ± 0.02 at 25 °C and Fixed Ionic Strength I = 0.5 (KNO_3) and Boiling Points at Definite Pressure of the Sparingly Soluble Alkylimidazoles

base	boiling point/ °C	pressure/ mmHg	pK_a
1-alkylimidazoles			
1-Hexylimidazole	134-136	12	7.30
1-Heptylimidazole	107-110	3	7.32
1-Octylimidazole	115-117	2	7.36
1-Nonylimidazole	112-123	3	7.43
1,2-alkylimidazoles			
1-Ethyl-2-methylimidazole	110-112	11	8.18
1-Butyl-2-methylimidazole	140-141	10	8.26
1-Pentyl-2-methylimidazole	130-131	14	8.30
1-Pentyl-2-ethylimidazole	133-135	12	8.37
1-Hexyl-2-ethylimidazole	131-140	2	8.38
1-Octyl-2-ethylimidazole	143-145	8	8.45
1-Octyl-2-propylimidazole	155-158	12	8.55
1,4-alkylimidazoles			
1,4-dimethylimidazole	120-122	24	7.86
1-Ethyl-4-methylimidazole	110-114	4	7.87
1-Propyl-4-methylimidazole	118-119	8	7.88
1-Isobutyl-4-methylimidazole	125-128	4	7.93
1-Pentyl-4-methylimidazole	130-133	14	7.97
1-Hexyl-4-methylimidazole	132-134	28	8.01
1-Heptyl-4-methylimidazole	128-131	10	8.05
1-Octyl-4-methylimidazole	144-146	10	8.10
1-Nonyl-4-methylimidazole	150-152	8	8.11
1-Decyl-4-methylimidazole	158-161	12	8.15
1,2,4-alkylimidazoles			
1-Ethyl-2-ethyl-4-methylimidazole	120-122	10	8.69
1-Propyl-2-ethyl-4-methylimidazole	134-137	15	8.74
1-Butyl-2-ethyl-4-methylimidazole	140-142	10	8.78
1-Pentyl-2-ethyl-4-methylimidazole	147-150	8	8.84
1-Hexyl-2-ethyl-4-methylimidazole	150-153	6	8.92
1-Heptyl-2-ethyl-4-methylimidazole	155-158	12	8.95
1-Octyl-2-ethyl-4-methylimidazole	162-165	10	9.03
1-Nonyl-2-ethyl-4-methylimidazole	166-167	8	9.01
1-Decyl-2-ethyl-4-methylimidazole	174-177	3	9.15

EXPERIMENTAL

Reagents.

The alkylimidazoles used in this work were synthesized by A. Skrzypczak, Technical University, Poznan-Poland. Purity of the obtained liquids was checked by HLPC method by means of apparatus of Liquochrom firm-type 307. The method of internal pattern was used, which gave an evaluated purity level for bases of 98.4%.

Structure of these compounds was verified by ^1H and ^{13}C NMR spectra by means of spectrometer – type Varian 300 VT.

The boiling points at definite pressure for studied alkylimidazoles are presented in Table 2.

Potassium nitrate (p.a., POCh, Gliwice) was purified by double crystallization and determined gravimetrically.

Nitric acid solutions were prepared from ready-to-use standarized samples (POCh, Gliwice). Their concentrations were established against sodium carbonate (p.a.) and sodium tetraborate decahydrate (p.a.). Potassium hydroxide (POCh, Gliwice) was purified from carbonates and after dilution determined with nitric acid.

Equipment.

Potentiometric measurements were run on PHM 250 pH-meter (Radiometer,Copenhagen) equipped with a combination electrode (glass-calomel) C 2401-8 (Radiometer,Copenhagen). The pH-meter was calibrated with buffer solutions of pH = 4.005 ± 0.010 and 7.000 ± 0.010 supplied by Radiometer.

Procedure.

All measurements were run at 25 ± 0.l °C at an ionic strength of 0.5 maintained by aqueous HNO_3 or KNO_3 solutions.

The method of potentiometric titration was used for determination of the acid dissociation constants.

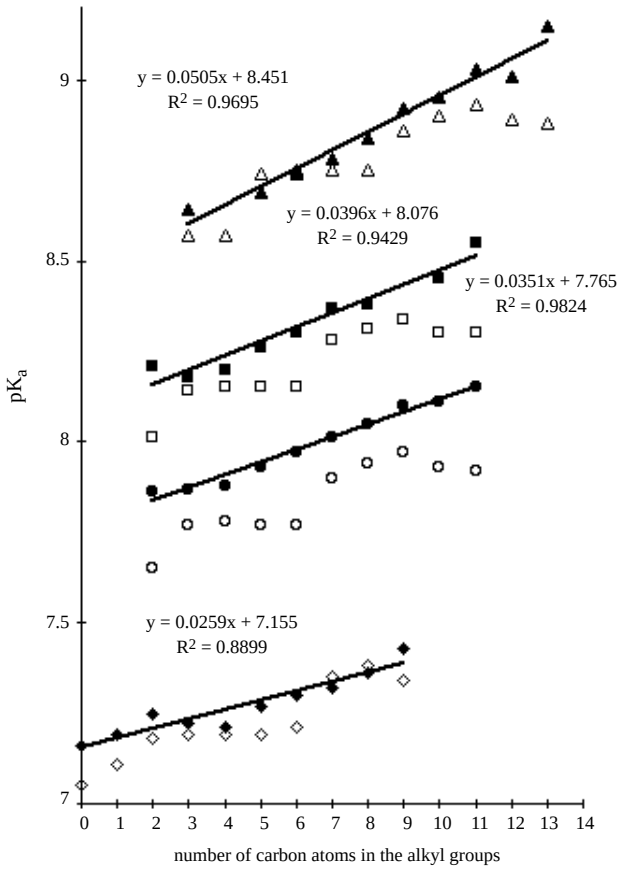

Figure 1. Relation between pK_a and the number of carbon atoms in the alkyl groups for 1-alkylimidazoles (◆ ◇), 1,4-dialkylimidazoles (●❍), 1,2-dialkylimidazoles(■□), and 1,2,4-trialkylimidazoles (▲△); black mark-experimental results and white-results of program ACD/pK_a DB

The weighed sample of the heterocyclic base was dissolved in a solution containing nitric acid (I = 0.5) in excess. Next, this solution was titrated with standarized KOH solution corrected for I = 0.5 with KNO_3.

Calculations.

The acid dissociation constants of the protonated 1,3-diazoles were calculated from the equation:

$$K_a = \frac{[H_3O^+][L]}{[HL^+]} = \frac{[H_3O^+](C_L + [H_3O^+])}{((C_{HNO_3} - C_{KOH}) - [H_3O^+])}$$

where $[H_3O^+]$, [L] and $[HL^+]$ are, respectively, equilibrium concentrations of the hydronium ion, the free azole and its protonated form, where as C_L, C_{HNO_3}, and C_{KOH} are analytical concentrations of the ligand, HNO_3 and KOH, respectively, in aqueous solution.

Simultaneously with experimental methods the pK_a values were calculated by means of computer program ACD/pK_a DB (Advanced Chemistry Development Inc.-Canada). The accuracy of calculations for simple structures is usually better than ± 0.2 pK_a units and for more complex structures the error increases to ± 0.5 pK_a units.

Results and Discussion.

Protonation constants of the sparingly soluble 1,3-diazoles determined in this work are summarized in Table 2. Their values show that the position of the alkyl groups in the imidazole ring, as in the case of the soluble alkylimidazoles, has a distinct influence on its acid-base properties. The enhanced basicity of the imidazole ring is an outcome of the inductive effect, which contributes to increased electron density around the pyridine nitrogen atom.

The influence of the position and size of the alkyl groups on the basicity of the 1,3-diazoles is presented in Figure 1 (pK_a as a function of the number of carbon atoms in the alkyl chain). The graphical data are supplemented with earlier ones for soluble alkylimidazoles.

The error range of pK_a values calculated by ACD/pK_a DB program for examined alkylimidazoles are as follows:

1-Alkylimidazoles ± (0. 10 - 0. 12)

1,4-Alkylimidazoles ± (0. 10 - 0. 17)

1,2-Alkylimidazoles ± (0. 25 - 0. 33)

1,2,4-Alkylimidazoles ± (0. 27 - 0. 38)

It can be understood from the data above that the pKa values calculated by this method gave only initial information about acid-base properties of alkylimidazoles.

Values calculated by the program with regard to the upper limit of errors are shown in the graph alongside the experimental results. Scattering of experimental results is considerably smaller than data computed by means the program.

As seen, in all the homologous series of the imidazoles, the basicity increases linearly with increasing length of the hydrocarbon chain. Linear equations of the function $K_a = f(n_{CH2})$ for particular classes of the 1,3-diazoles are as follows:

$pK_a = an + b$

$pK_a = 0.0259n + 7.155$ $R^2 = 0.8899$ for 1-alkylimidazoles

$pK_a = 0.0351n + 7.765$ $R^2 = 0.9824$ for 1,4-dialkylimidazoles

$pK_a = 0.0396n + 8.076$ $R^2 = 0.9429$ for 1,2-dialkylimidazoles

$pK_a = 0.0505n + 8.451$ $R^2 = 0.9695$ for 1,2,4-trialkylimidazoles

where : R^2 – square of correlation coefficient.

The independent variable *n* in these equations stands for the sum of carbon atoms in alkyl substituents attached to the imidazole ring. The intercept value "b" in the equations can be utilized for comparison of basicities of the homologous series of the compounds. Accordingly, the basicity increases in the following series:

1-alkylimidazoles < 1,4-dialkylimidazoles < 1,2-dialkylimidazoles < 1,2,4-trialkylimidazoles

As seen, the inductive effect of the alkyl substituents is more pronounced when the substituents are in α position in relation to each other. Hence, 1,2-dialkylimidazoles are stronger bases than 1,4-dialkylimidazoles.

Another conclusion can be derived from slopes "a" in the equations. Namely, the slope increases with increasing basicity of the homologous series of the l,3-diazoles. Thus, it can be speculated that the more basic imidazoles are more prone to the inductive effect than 1-alkylimidazoles.

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