

NOTE

Protonation site for anilines in aqueous media

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By means of the PM3 method it has been shown that the protonation of 2-, 3-, 4-methoxyanilines, 4-methylthioaniline, 2-, 3-, 4-aminobenzoic acids, 2-, 3-, 4-nitroanilines in the gaseous phase proceeds *via* the amine nitrogen atom. The same result, attributed to the aqueous medium, was obtained for 4-methoxyaniline, 4-aminobenzoic acid and 4-nitroaniline.

Keywords: anilines, protonation, quantum chemical computation.

Earlier,¹ we computed the enthalpies and free energies of gaseous-phase proton affinity for aniline and 62 of its derivatives with different kinds of electron-donor and electron-acceptor substitution in the aromatic ring and at the nitrogen atom. Linear correlations of the type pK_a vs. PA were found. Deviations of the data for *ortho* substituted anilines from the above relationships were discussed in view of possible hydrophobic hydration of the molecular fragments adjacent to the protonation centre.

To establish the relationships pK_a vs. PA and to evaluate the medium contribution to the basicity of anilines, one has to be sure that protonation of all the surveyed molecules occurs *via* the amine nitrogen. The latter is usually assumed, often by default.^{2–6}

Using the PM3 method (the computational details have been described previously¹), we have computed proton affinities for the protonation of a few typical arylamines at alternative basic centers (Table I). As can be seen, even in the gas phase protonation at the amino group is preferential. Although, for 4-aminobenzoic acid and 4-nitroaniline the differences in enthalpies and free energies of the proton affinity for protonation *via* the nitrogen and oxygen atoms are comparatively small.

The greater the number n of water molecules built into a cluster, up to 729 in a cubic cell with 28.00 Å sides, which corresponds to the density of liquid water,⁷ the more adequately is hydration considered. The results presented in Table I show (as found previously^{1,8,9}) that when the value of n is sufficiently large (107), the density of the distribution of water molecules in the cell approaches the value for the liquid state, even a partial occupation of the cell volume by the species I–III is not considered.

TABLE I. Enthalpies ($\Delta\Delta H_f$) and free energies ($\Delta\Delta G_f$) of the gaseous-phase proton affinity of some anilines for protonation at alternative reaction centers (PM3 data)

Compound	$\Delta\Delta H_f/(4.184 \text{ kJ/mol})$		$\Delta\Delta G_f/(4.184 \text{ kJ/mol})$	
	N	O (S)	N	O (S)
2-Methoxyaniline	220.16	176.87	211.09	166.88
3-Methoxyaniline	214.26	170.18	205.03	161.64
4-Methoxyaniline (I)	216.92	173.23	207.68	164.58
4-Methylthioaniline	213.79	207.67	205.31	198.96
2-Aminobenzoic acid	215.30	193.76*	207.51	185.05
3-Aminobenzoic acid	209.36	197.54*	200.34	188.24
4-Aminobenzoic acid (II)	207.05	205.40*	198.26	196.33
4-Nitroaniline (III)	198.78	196.07	190.16	187.01

*Protonation at the carbonyl oxygen atom

Quantum chemical PM3 results for supermolecules containing protonated molecular systems **I–III** along with 107 water molecules. Computation routine characteristics

Cluster*	HyperChem cubic cell side/Å	Quantity of water molecules per unit of the volume of a cubic cell/Å ⁻³	Gradient norm (kJ/mol Å)
IN + 107 H ₂ O	15.18	0.0306	10.21
IO + 107 H ₂ O	15.18	0.0306	11.95
IIN + 107 H ₂ O	15.19	0.0305	9.39
IIO + 107 H ₂ O	15.18	0.0306	9.66
IIIN + 107 H ₂ O	15.19	0.0305	9.73
IIIO + 107 H ₂ O	15.18	0.0306	10.22
729 H ₂ O	28.00	0.0332	–

*N, O – Forms protonated at the nitrogen and oxygen atoms, respectively

Enthalpy differences $\Delta\Delta H_f = \Delta H_f(N \text{ } 107 \text{ H}_2\text{O}) - \Delta H_f(O \text{ } 107 \text{ H}_2\text{O})$ for clusters containing anilines protonated at the nitrogen and oxygen atoms

Protonated molecule	$\Delta\Delta H_f/(4.184 \text{ kJ/mol})$
I	–85.89
II	–23.25
III	–6.96

For the cations of 4-methoxyaniline (**I**), 4-aminobenzoic acid (**II**) and 4-nitroaniline (**III**) conjugate acids, we computed clusters including the aforesaid molecular systems along with 107 water molecules, using the PM3 method.

As Table I shows, for aqueous solutions, the conclusion concerning the preferential protonation of anilines at the nitrogen atom remains valid. Moreover, the medium

increases the difference between the heats of formation of the conjugate acids of the anilines I–III (or, which is just the same, between enthalpies of the proton affinities of the compounds I–III) as compared to the gaseous phase.

Thus, the protonation of anilines proceeds *via* the amine nitrogen atom, even if other possible centers of electrophilic attack do exist in the molecule, and the data discussed previously¹ was interpreted correctly.

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ИЗВОД

МЕСТА ПРОТОНАЦИЈЕ КОД АНИЛИНА У ВОДЕНОЈ СРЕДИНИ

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Користећи РМЗ методу показано је да се протонација 2-, 3-, 4-метоксианилина, 4-метилтиоанилина, 2-, 3-, 4-нитроанилина у гасовитој фази одиграва преко атома азота у аминок групи. Исти резултати су добијени и за 4-метоксианилин, 4-аминобензојву киселину и 4-нитроанилин у воденој средини.

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REFERENCES

1. A. N. Pankratov, I. M. Uchaeva, S. Yu. Doronin, R. K. Chernova, *J. Serb. Chem. Soc.* **66** (2001) 161
2. A. Albert, E. P. Serjeant, *Ionization Constants of Acids and Bases*, Chapman and Hall, London, 1971, p. 179
3. A. J. Gordon, R. A. Ford, *The Chemist's Companion, A Handbook of Practical Data, Techniques, and References*, A Wiley-Interscience Publication, Wiley, New York, London, Sydney, Toronto 1972, Russian Edition: Mir, Moscow, 1976, p. 543
4. P. Sykes, *A Guidebook to Mechanism in Organic Chemistry*, Longman Scientific & Technical, London, Wiley, New York, 1986. Russian Edition: *Reaction Mechanisms in Organic Chemistry* (in Russian), Mir, Moscow, 1991, p. 448
5. A. S. Dneprovskii, T. I. Temnikova, *Theoretical Bases of Organic Chemistry* (in Russian), Khimiya, Leningrad, 1991, p. 560
6. R. Graglia, E. Pramauro, E. Pelizzetti, *Annali di Chimica* **74** (1984) 41
7. Yu. I. Naberukhin, V. A. Luchnikov, G. G. Malenkov, E. A. Zheligovskaya, *Zh. Strukt. Khim.* **38** (1997) 713
8. A. N. Pankratov, O. A. Bilenko, S. P. Mushtakova, *Afinidad* **57** (2000) 201
9. A. N. Pankratov, S. P. Mushtakova, *Zh. Anal. Khim.* **55** (2000) 799.