Eclética Química

Print version ISSN **0100-4670***On-line version* ISSN **1678-4618**

Eclet. Quím. vol.23 São Paulo 1998

http://dx.doi.org/10.1590/S0100-46701998000100006

Basicities of primary arylamines and calculated amine nitrogen electronic charges

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ABSTRACT: Mülliken charges on nitrogen atoms were calculated for several arylamines, utilizing the AM1 Quantum Chemistry method, relating their values to experimental amine pKa . Direct relation between pKa and nitrogen charges was found. The amines energies of protonation, calculated by the same method, also correlate directly with these charges.
KEYWORDS: Arylamines; basicity ; N Mülliken charge; AM1.

Introduction

The primary amines are organic bases with general formula RNH_2 , that react with the proton according to the equation:

$RNH_2 + H^+ RNH^+_3$

If R is an aryl group, then the amine is an aromatic amine or arylamine, represented by $ArNH_2$.

The logarithm of the dissociation constant of the protonated arylamine, pK_a , is defined as

$$ArNH_3^+ \longrightarrow ArNH_2 + H^+$$

$$K_a = \frac{[ArNH_2][H^+]}{[ArNH_3^+]} \text{ and } pK_a = -\log K_a$$

It increases with the amine basicity as the acidity of the protonated amine decreases. On the other hand, it is reasonable to suppose that the greater the electronic charge on the amine nitrogen the stronger will be its basicity.

Quantum Chemistry methods offer the possibility of calculating atomic charges. There are several ways to define them, and the Mlliken atomic charges are the most commonly used in molecular orbital theory. These quantities are not "observables" in the Quantum Mechanics sense, and have only an approximate relation to experiment. Their values are sensitive to the semi-empirical calculation method or to the basis set of an *ab initio* procedure. But, values obtained by the same method for similar chemical groups in related molecules, can be of significance for comparative purposes.

Calculations have been performed for atomic charges on nitrogen for several arylamines, utilizing the AM1 semi-empirical Quantum Chemistry method. These results are compared with the trend of experimental pK_a values and of calculated protonation energies.

We have chosen an ensemble of arylamines chemically very similar in order to test the sensitivity of the method . All of them, except aniline, have fused benzene rings. Different quantum model chemistry methods have also been tested for the same purpose. The method which resulted in the best correlation between nitrogen charge and pK_a, was utilized for further investigation on this matter.

Methods

The amine structures were initially optimized by Molecular Mechanics calculation with a modified MM2 force field.[1,2,4] A trial of the electronic calculation method more suitable to our purpose was carried out by single point calculation for the resulting structures using the following Quantum Chemistry methods: a) Semi-empirical: Extended Hückel, EH,[10] and the SCF techniques CNDO/2,[12,13] INDO,[13] MINDO/3,[3] MNDO[6] and AM1,[7] ; b) *Ab initio* procedure with a minimal STO-3G basis set.[5,9,14]

After this initial search, the structures were reoptimized by the AM1 Quantum Chemistry method and the Mülliken charges of the amine nitrogens and the protonation energies were calculated by the same method. These charges and energies were correlated one with other and both with the experimental pK_a values. The protonation energy was expressed as:

$$\mathbf{D}E = E_{AH}^{\ +} - (E_A + E_H^{\ +})$$

Where AH^+ protonated amine
A amine in the base form
H^+ proton

Since $E_H^{\ +} = 0$, $\mathbf{D}E = E_{AH}^{\ +} - E_A = f (pK_a)$ (Figure 2)

The amines pK_a were obtained from the literature.[8]

Results and discussion

Table 1 shows the net charges on amine nitrogens, as obtained by various calculation methods, and the amines pK_a. First, we observe that the charges vary according to the method, confirming the lack of significance of their absolute values. On the other hand, the results obtained by a given method may be compared among themselves and vary slightly from one compound to another. The sensibility to differentiate the nitrogen charge among compounds of different amine pK_a varies according to the method, and this was one important criterion to the method choice.

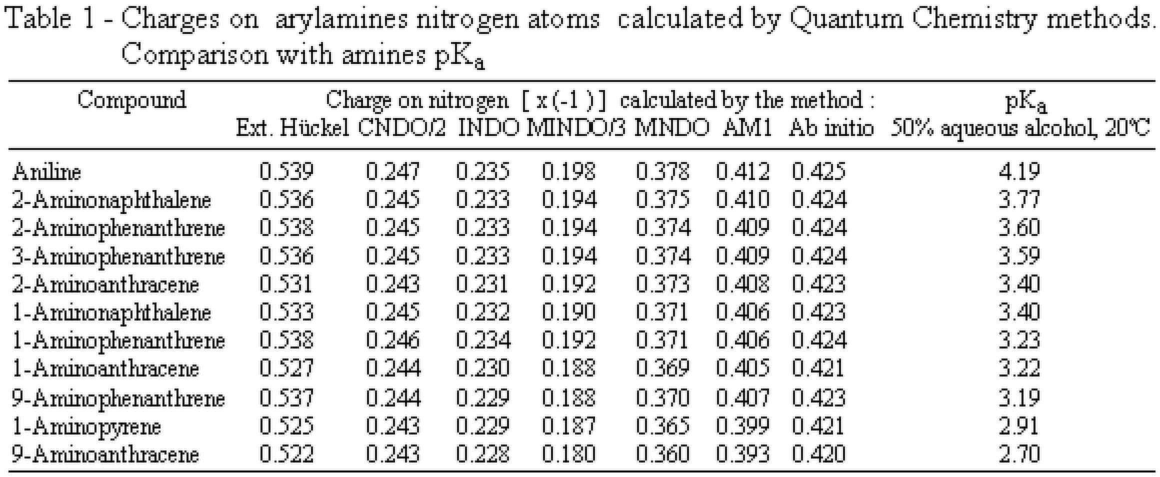

Table 1 - Charges on arylamines nitrogen atoms calculated by Quantum Chemistry methods. Comparison with amines pK_a

Compound	Charge on nitrogen [x (-1)] calculated by the method :							pK_a
	Ext. Hückel	CNDO/2	INDO	MINDO/3	MNDO	AM1	Ab initio	50% aqueous alcohol, 20°C
Aniline	0.539	0.247	0.235	0.198	0.378	0.412	0.425	4.19
2-Aminonaphthalene	0.536	0.245	0.233	0.194	0.375	0.410	0.424	3.77
2-Aminophenanthrene	0.538	0.245	0.233	0.194	0.374	0.409	0.424	3.60
3-Aminophenanthrene	0.536	0.245	0.233	0.194	0.374	0.409	0.424	3.59
2-Aminoanthracene	0.531	0.243	0.231	0.192	0.373	0.408	0.423	3.40
1-Aminonaphthalene	0.533	0.245	0.232	0.190	0.371	0.406	0.423	3.40
1-Aminophenanthrene	0.538	0.246	0.234	0.192	0.371	0.406	0.424	3.23
1-Aminoanthracene	0.527	0.244	0.230	0.188	0.369	0.405	0.421	3.22
9-Aminophenanthrene	0.537	0.244	0.229	0.188	0.370	0.407	0.423	3.19
1-Aminopyrene	0.525	0.243	0.229	0.187	0.365	0.399	0.421	2.91
9-Aminoanthracene	0.522	0.243	0.228	0.180	0.360	0.393	0.420	2.70

The difference expressed in percentages between the extreme N charge values calculated by each method are as follows: EH 3.8% , CNDO/2 1.6% , INDO 3.1% , MINDO/3 10.0% , MNDO 5.0% , AM1 4.8% and *ab initio* (minimal basis set) 1.4% . The *ab initio* and CNDO/2 methods show little sensibility to detect amine nitrogen charge variation in function of aryl group. By this point of view, the *ab initio* calculation with the minimal basis set STO-3G gave the poorest result, showing very little charge variation and several identical N charge values for different arylamines. Even the semi-empirical single-electron potential Extended Hückel method shows a better result. This points for the necessity of more sofisticated basis sets utilization for having more reliable *ab initio* calculations results. More sensible methods are MINDO/3, AM1 and MNDO. On the other hand, the AM1 method gave a better correlation coefficient (R) for the individual data points in relation to the line fitted to this plot, under linear regression calculation of pK_a= f (N charge) (Table 2). This result, summed to the fact that the AM1 method is the more precise semi-empirical Quantum Chemical method available, have suggested its choice for the present work.

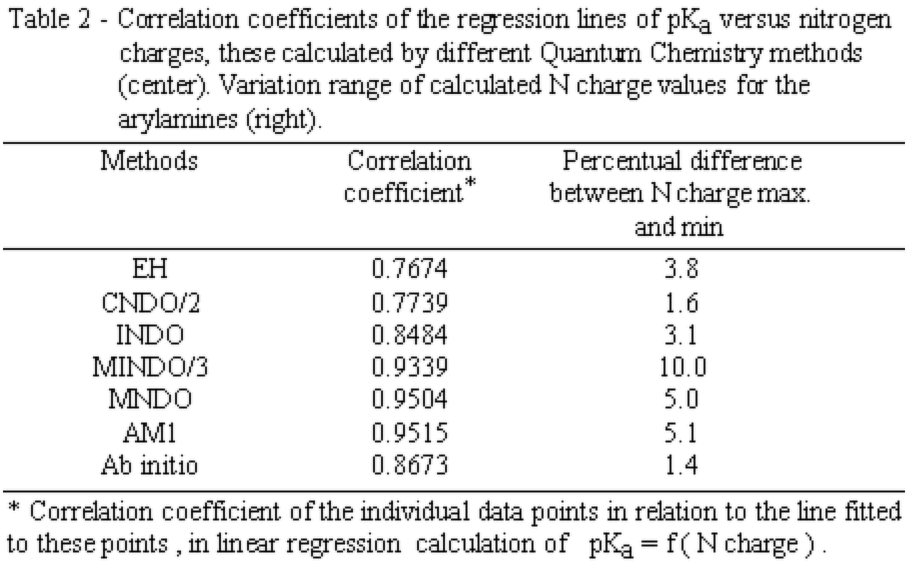

Table 2 - Correlation coefficients of the regression lines of pK_a versus nitrogen charges, these calculated by different Quantum Chemistry methods (center). Variation range of calculated N charge values for the arylamines (right).

Methods	Correlation coefficient*	Percentual difference between N charge max. and min
EH	0.7674	3.8
CNDO/2	0.7739	1.6
INDO	0.8484	3.1
MINDO/3	0.9339	10.0
MNDO	0.9504	5.0
AM1	0.9515	5.1
Ab initio	0.8673	1.4

* Correlation coefficient of the individual data points in relation to the line fitted to these points , in linear regression calculation of $pK_a = f(\text{N charge})$.

Figure 1 shows the amines pK_a in function of their AM1 calculated N Mülliken charges. The points were fitted to a linear function (top) , with $R = 0.9515$, and to a second order polynomial function (bottom), with $R = 0.9770$, which is better. The pK_a increases with N charge, as was expected. So, the Mülliken negative charge value on every atom of the molecule can be related with electron density distribution, and a high electron density site or an intense local negative charge is a protonic affinity place. In other words, it is a high basicity center, manifested by a high pK_a value.

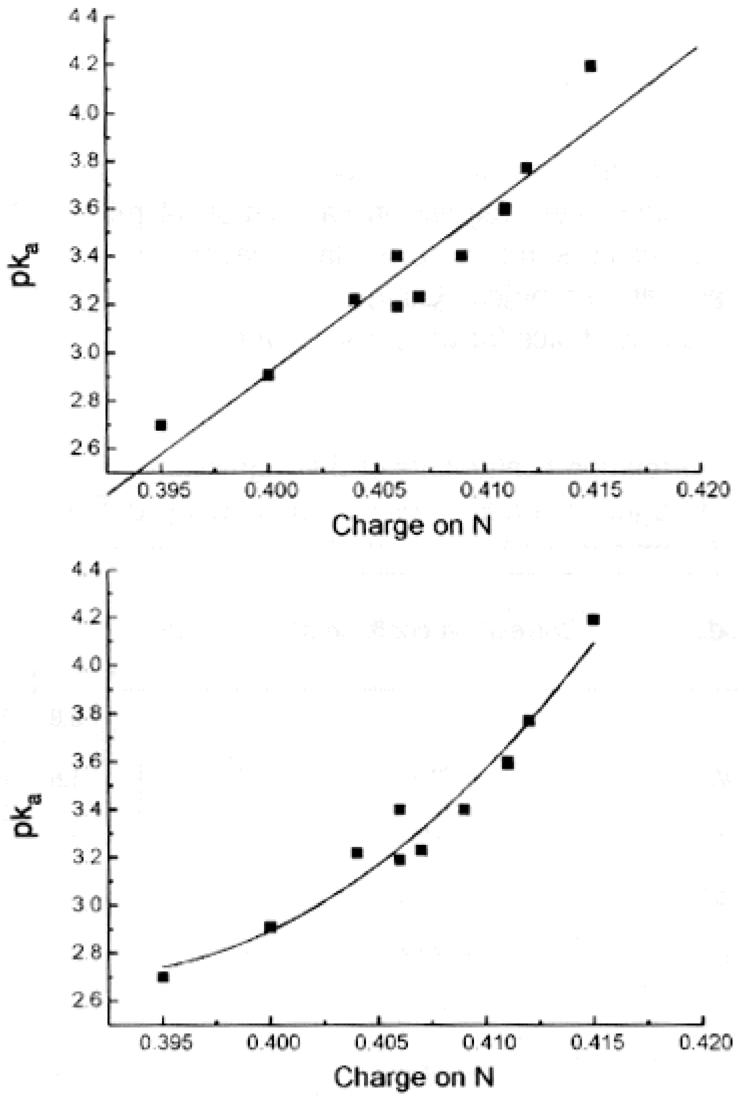

FIGURE 1 - Arylamines pK_a versus nitrogen charges (x -1) calculated by AM1 method. Linear fit curve (top) and 2nd order polynomial fit curve (bottom).

The calculated *in vacuum* energies of protonation absolute values grow with the amine pK_a or, which has the same meaning, with the amine basicities. Figure 2 shows the linearity between both, and Figure 3 the analogous (like the pK_a) behavior of calculated protonation energies against the amines nitrogen charges. This coherent result confirms the utility of the AM1 method for the comparison among electronic amine properties calculated in vacuum and their experimental pK_a values in solution.

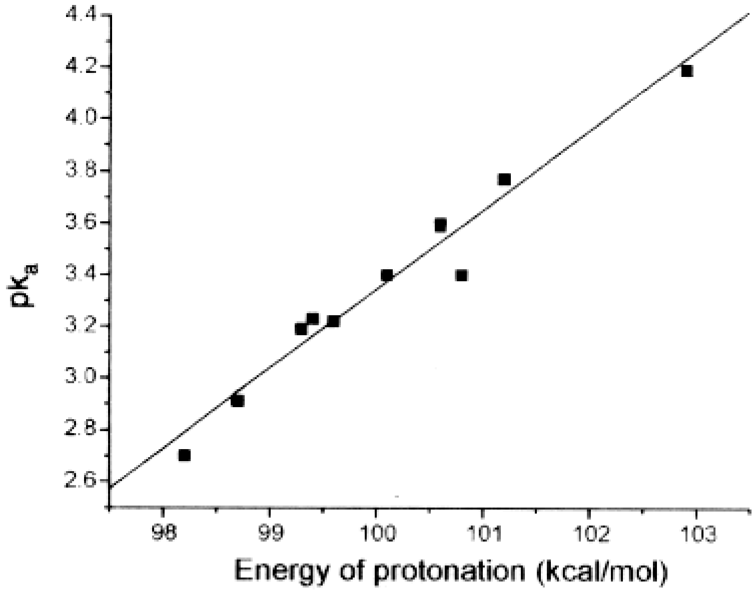

FIGURE 2 - Arylamines pK_a versus energy of protonation calculated by AM1 method.

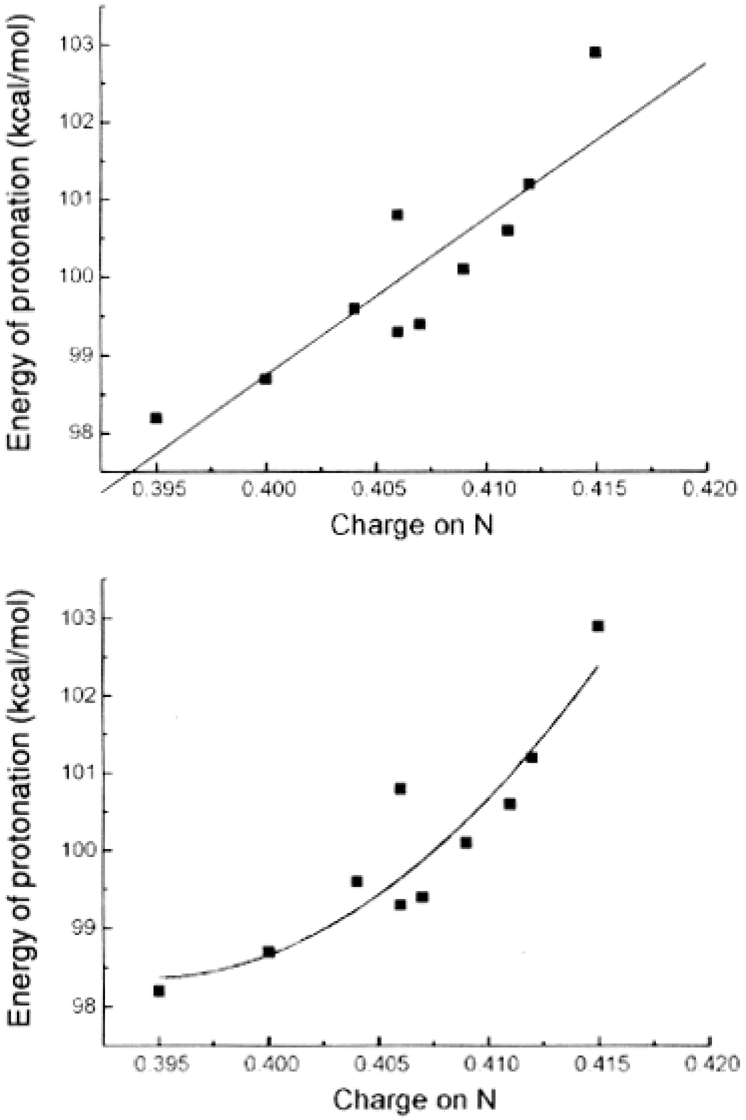

FIGURE 3 - Arylamines energy of protonation versus nitrogens charges [x(-1)], both calculated by AM1 method. Linear fit curve (top) and 2nd order polynomial fit curve (bottom).

A doubt may arise as to the correctness of the comparison between the pK_a value, measured in solution, and a figure calculated for the molecule in vacuum. The protonation equilibrium constant in vacuum and in solution may vary depending on the difference between the solvatation energy of the protonated and non-protonated species. We have performed an AM1 calculation of the arylamines for a simulated water medium , in which each amine would be surrounded by 43 TIP3P water molecules models.[11] Hydration energy was calculated as the difference between the total energy of the amine and water together and separately for each other. The hydration energy has changed 43% in average with protonation. Otherwise, the energy of protonation, calculated also by AM1 method, and directly related with the basicity, has grown only 7.1% in average with hydration, showing that in this case it is less sensible to the medium parameters. Protonation energy relates directly to the equilibrium constant of the protonation reaction, namely, to its basicity constant. The analogous behavior of the protonation energy calculated in vacuum and the experimental pK_a value in solution, when compared mutually and both with N charges, indicates the validity of predictions made.

In conclusion, it is possible to correlate the calculated electronic charge on amine nitrogen with the amine basicity. For the studied arylamines, whose pK_a varie little from one to the other, the nitrogen charges also do not show major changes. Hence, although sensibility of the method is not very good, it may be considered as useful for semi-quantitative predictions.

Acknowledgments

We are grateful to Fapesp (Brazilian Agency) for the financial support.

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RESUMO: Foram calculadas as cargas de Mülliken sobre os átomos de nitrogênio para diversas arilaminas, empregando-se para tal o método AM1 da Química Quântica. Tais cargas foram relacionadas com os valores experimentais dos pK_a das aminas. Foi obtida uma relação direta entre pK_a e carga dos átomos de nitrogênio. As energias de protonação das aminas, calculadas pelo mesmo método, também se correlacionam diretamente com aquelas cargas.

PALAVRAS-CHAVE: Arilaminas; basicidade; cargas de Mülliken; AM1.

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Recebido em 21.11.1997.

Aceito em 24.11.1997.

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