Predicting Protonation Constants in Polyazaalkanes

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An easy model which allows to calculate protonation constants in polyamines containing *n* equivalent or near equivalent protonation sites from simple molecular analysis is reported.

Polyazaalkanes are well known molecules which have been revealed to be good receptors for metal ions and anions.[1] In anion coordination chemistry, especially, protonation processes play an important role in these molecules due to the formation of highly charged water soluble polyammonium species.[1] We develop here an easy model which allows theoretical prediction of overall protonation constants in systems containing *n* equivalent or near equivalent protonation sites, providing that the first protonation constant is known or has been predicted by other methods.[3]

In the model, we propose that the decrease in the successive protonation constants is a consequence of the difference in electrostatic energy between the successive protonated states. In systems containing near equivalent protonation sites ΔG_{bond} and ΔG_{solv} would be nearly the same and therefore the difference between the logarithms of the first and the *i*th protonation constant can be related with the Coulombic interaction between the already protonated groups and the new protonated site as eqn. (3)

$$\log K_i = \log K_1 - \frac{e^2 N_A}{2.3RT4\pi\varepsilon_0\varepsilon}\sum_{j=1}^{i-1}\frac{1}{r_{ji}} \qquad (3)$$

where r_{ij} are the distances between the *i*th protonated atom and the *j*th already protonated groups. eqn. (3) can be rewritten to calculate the stepwise overall protonation constants (β_i) as

$$\log\beta_i = i\log K_1 - \frac{e^2 N_A}{2.3RT4\pi\varepsilon_0\varepsilon}\sum_{k=1}^{i}\sum_{l=1}^{k-1}\frac{1}{r_{kl}} \qquad (4)$$

and the last overall constant β_n (involving all protonation processes) is related with the first protonation constant and the r_{kl} distances between all ammonium groups as:

$$\log\beta_n = n\log K_1 - \frac{e^2 N_A}{2.3RT4\pi\varepsilon_0\varepsilon}\sum_{k=1}^{n}\sum_{l=1}^{k-1}\frac{1}{r_{kl}} \qquad (5)$$

It is known that bulk relative permittivity of water (≈78) is reduced near organic molecules and that in general ε is a function with the distance $\varepsilon(r)$. We have found that a good agreement is found between the predicted and experimental constants (see below) assuming that $\varepsilon(r) = \varepsilon/(1 + b/r)$ (where b is an experimental parameter and ε the macroscopic relative permittivity of the medium). We can therefore rewrite eqn. (5) as:

$$\log\beta_n = n\log K_1 - \left[\frac{e^2 N_A}{2.3RT4\pi\varepsilon_0\varepsilon}\sum_{k=1}^{n}\sum_{l=1}^{k-1}\frac{1}{r_{kl}} + B\sum_{k=1}^{n}\sum_{l=1}^{k-1}\frac{1}{{r_{kl}}^2}\right] \qquad (6)$$

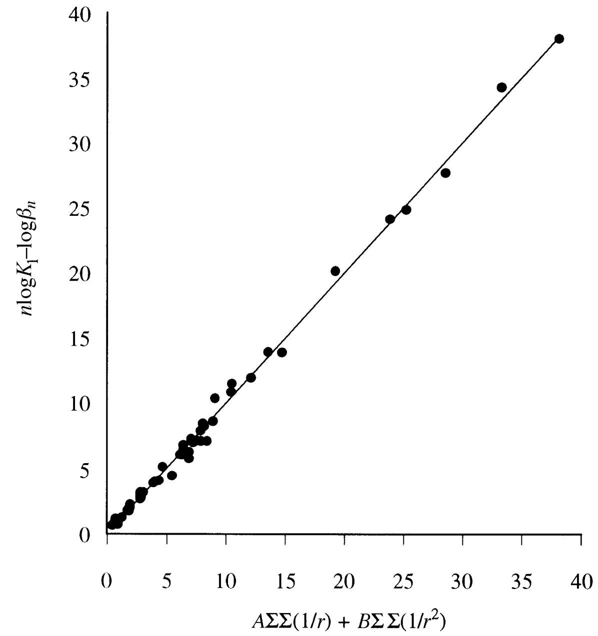

Fig. 1 $n\log K_1 - \log\beta_n$ *vs.* $3.144\Sigma\Sigma(1/r_{kl}) + B\Sigma\Sigma(1/{r_{kl}}^2)$ for 60 polyamines containing from two to ten protonation sites

In the full-text version there is a list of near 60 different polyazaalkanes, containing from two to ten protonation processes, whose stepwise protonation constants have been determined experimentally. The totally protonated molecules were studied using molecular modeling programs such as PCMODEL[6] to calculate the distances between ammonium groups. With all those data a regression fit using eqn. (6) allowed us to calculate B ($B = 30.6 \pm 0.4$ Å^2, r in Å for a fixed value of $e^2N_A/(2.3RT4\pi\varepsilon_0\varepsilon) = 3.144$ Å. Similar results have been obtained by fitting the more general equation $\log\beta_n = n\log K_1 - [A\Sigma\Sigma(1/r) + B\Sigma\Sigma(1/r^2)]$; $A = 3.2 \pm 0.5$ Å; $B = 30 \pm 3$ Å^2). Fig. 1 shows the good agreement found.

Once the B value is known, eqn. (6) allows prediction of the successive overall protonation constant providing that the first one is known and the r_{kl} distances are calculated on the basis of simple molecular analysis. Although to obtain precise information of the actual protonation path is not easy, eqn. (6) allows one to evaluate theoretically the different possible protonation processes, suggest a protonation sequence and compare the data with those obtained experimentally. We have found that amongst all the possible protonation paths the one showing generally the best agreement with the experimental data is that which gives a larger beta (β_i) value, suggesting that for each new protonation step the proton is placed as far as possible from already charged groups as it was observed experimentally for some polyamines using NMR techniques.[2,8] Additionally if a theoretical approach is found for predicting B values the method would be adequately applied to evaluate constants in other solvents than water. The protonation

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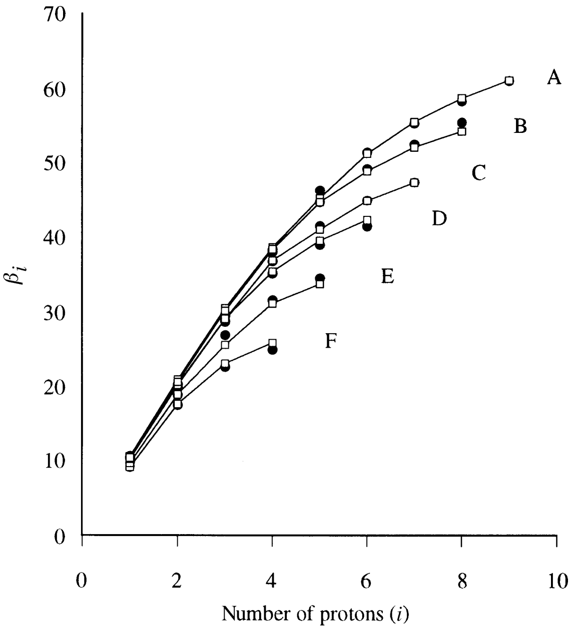

Fig. 2 Experimental (●) and calculated (□) β_i overall protonation constants for some selected polyamines.
(A) $CH_3NH[CH_2CH_2NH]_7CH_2CH_2NHCH_3$,
(B) $CH_3NH[CH_2CH_2NH]_6CH_2CH_2NHCH_3$,
(C) $CH_3NH[CH_2CH_2NH]_5CH_2CH_2NHCH_3$,
(D) $CH_3NH[CH_2CH_2NH]_4CH_2CH_2NHCH_3$,
(E) $H_2N[CH_2CH_2NH]_3CH_2CH_2NH_2$,
(F) $(CH_3)_2N[CH_2CH_2NH]_2CH_2CH_2N(CH_3)_2$

constants were theoretically calculated for about 60 polyazaalkanes, and when compared with the experimental values in general a good agreement was found for open-chain polyazaalkanes and large cyclic polyamines. Fig. 2 shows graphically the good agreement found between the experimental and calculated β_i constants for some selected polyamines.

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Techniques used: computer modelling

References: 10

Table 1: Experimental and predicted overall protonation constants (β)

Table 2: Protonation path for $CH_3(NHCH_2CH_2)_6NHCH_3$ and the agreement between the calculated and experimental log β_i values

Schemes: 1

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3 See for example: J. Clark and D. D. Perrin, *Quart. Rev.*, 1964, **18**, 295.

6 PCMODEL, *Molecular Modelling for Personal Computers and Workstations*, Serene Software, 1988.

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