# Influence of Different Dielectric Continuum Solvent Models on the Accuracy of pK_a Values

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The most common computational approach for calculation of pK_a values is based on the thermodynamical cycle shown in Figure 1. Within this approach, solvation energies (ΔG_{sol}) can be calculated by various methods, of which dielectric continuum solvent models (DCSM) are particularly interesting because of their low demands for computer resources. However, in a series of papers Klamt and coworkers[1] pointed to a systematic discrepancy between calculated and experimental pK_a's, where parameters a and b (eq. 2) significantly differ from the ideal values of 1 and $[G^{\circ}_{sol}(H^+) + \Delta G^{\circ \rightarrow}*]$, respectively. To overcome this problem, we have employed linear correlation between experimental pK_a's and the „*reduced basicities*" ($\Delta G'_{a,sol}$) in acetonitrile (eq. 2).[2,3] In continuation of this work, quest for the simplest, but yet the most adequate, DCSM for the calculation of pK_a values of different nitrogen bases was conducted.
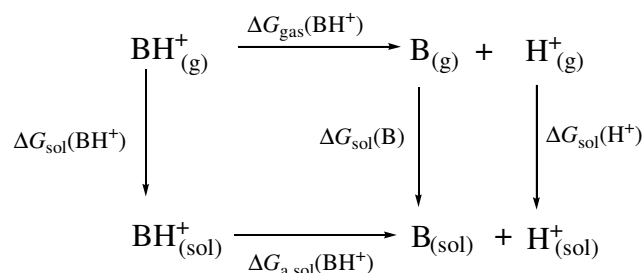
$$2.303RT \times pK_a(BH^+) = \Delta G^{\circ}_{gas}(BH^+) + \Delta G^{\circ}_{sol}(B) - \Delta G^{\circ}_{sol}(BH^+) + G^{\circ}_{sol}(H^+) + \Delta G^{\circ \rightarrow}* \qquad (1)$$

$$2.303RT \times pK_a(BH^+) = \qquad a \times \Delta G'_{a,sol} \qquad + \qquad b \qquad (2)$$

Figure 1. Thermodynamic cycle used for the calculation of pK_a

Herein detailed analysis of quality of different DCS models applied will be presented. For this purpose, performance of several variants of PCM solvation models will be compared with that of COSMO, SMX and SS(V)PE approaches. Quality of each method will be discussed in terms of deviation of the regression parameters a and b (slope and intercept, respectively) from the ideal values. In addition, possibility of $G^{\circ}_{sol}(H^+)$ calculations from the intercept b will be presented. The latter is particularly important for the solvents for which no experimental data for $G^{\circ}_{sol}(H^+)$ is available in literature.

[1] A. Klamt, F. Eckert, M. Diedenhofen, *J. Phys. Chem. A* **2003**; *107*, 9380.

[2] Z. Glasovac, M. Eckert-Maksić, Z.B. Maksić, *New J. Chem.* **2009**; *33*, 588.

[3] B. Kovačević, Z. B. Maksić, *Org. Lett*. **2001**; *3*, 1523.