The Development of Accurate pK_a Calculations

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To determine the most accurate computational method for calculating acid dissociation constants, we explored the dissociation of the ammonium cation using various energy, solvation and thermodynamic methods.

The pK_a was determined using two thermodynamic cycles. Method 1:

$pK_a = \Delta Gaq/2.303RT$, where $\Delta Gaq = \Delta Ggas + \Delta\Delta Gsol$[1]

$$\begin{array}{ccccc} & & \Delta Ggas & & \\ NH_{4(g)}^{+} & \rightarrow & NH_{3(g)} & + & H^{+}_{(g)} \\ \uparrow -\Delta Gs(NH4^{+}) & & \downarrow \Delta Gs(NH_3) & & \downarrow \Delta Gs(H^{+}) \\ NH_4^{+}{}_{(aq)} & \rightarrow & NH_{3(aq)} & + & H^{+}_{(aq)} \\ & & \Delta Gaq & & \end{array}$$

Our $\Delta Ggas$ value was calculated using the G3[2] and G3B3[3] model chemistries, and the value of -6.28 kcal/mol[1] for $G(H^+)$. To obtain $\Delta Gsol$ we used two different continuum solvation methods, CPCM (at the G3, G3B3, HF/6-31G*, HF/6-31+G* levels of theory) and SM6 (using B3LYP/6-31G*), with calculations on either the gas phase optimized structure in solution or the optimizing the structure.

Method 2 used the CPCM G3[2] and G3B3[3] methods to directly obtain ΔGaq, through frequency calculations in solution. This calculation is based on the following equation:

$$\Delta G_{aq}rxn = Gaq(NH_3) - Gaq(NH_4^+) + Gaq\ H^+$$

Both methods were used to calculate the pK_a of the ammonium ion for the following four reactions with varying implicit and explicit waters[4].

$$NH_4^+ \rightarrow NH_3 + H^+$$
$$NH_4^+ \bullet H_2O \rightarrow NH_3 \bullet H_2O + H^+$$
$$NH_4^+ \bullet H_2O \rightarrow NH_3 + H_3O^+$$
$$NH_4^+ \bullet H_2O \rightarrow NH_3 + H^+ + H_2O$$

This comparison of various solvation, energy, and thermodynamic methods allowed us to observe the most efficient way to determine an accurate value of acid dissociation constants. Results are presented in the poster. For future research, we hope to expand our test set and determine the best method that is consistent for generating reliable pK_a values.

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