

## Chemistry 478 — Molecular Modeling

### Laboratory #3 — Computing Acidity and Basicity in the Gas Phase and in Water

Quantum methods can be used to determine the absolute and relative acidity and basicity of molecules in the “gas phase”. Through the combination of implicit solvation models with the QM calculations, the same values can be estimated in solution. In the first part of this lab you will compute the thermodynamics of the acid-base reaction between acetic acid and ammonia in both the gas and aqueous phase. The second part will look at the relative basicity of a series of simple alkyl amines. Experimental data for the amine series is shown in the table below:

Amine	Gas Phase Basicity (kcal/mol; NH <sub>3</sub> =0)	Aqueous Phase pKa of Conjugate Acid
NH <sub>3</sub>	- 0 -	9.24
MeNH <sub>2</sub>	9	10.65
Me <sub>2</sub> NH	16	10.78
Me <sub>3</sub> N	19	9.80

Finally, in a third set of calculations, we investigate the acidity of some phenols to further examine the effect of substituents on overall electronic structure as well as acidity/basicity.

#### Protocol

- (1)** Using Spartan Student, use MP2/6-311+G\*\* calculations to find the equilibrium geometry for acetic acid, acetate anion, ammonia and ammonium cation. To build ammonium, you can start with the tetravalent nitrogen atom available in the Inorganic section of the Build panel. The results will contain both the gas phase QM energy, and the energy in an implicit aqueous environment (see the Properties tab under the Display menu).
- (2)** Use these values to estimate the energetics for the reaction (acetic acid + ammonia -> acetate + ammonium) in both the gas and aqueous phase.
- (3)** Perform a series of calculations on each of the amines in the above table. For each of these amines, find the gas phase QM energy and solvation energy using the HF/STO-3G, MP2/6-311+G\*\* and PM3 semi-empirical models. How do your results compare with the experimental data?
- (4)** Repeat for the corresponding protonated cation of each amine. Use the Surfaces tab on the Setup menu to compute the electrostatic potential around each of the four cations.
- (5)** Use PM3 calculations to estimate the relative acidities of the common aromatic alcohols phenol (C<sub>6</sub>H<sub>5</sub>-OH), *p*-nitrophenol, and *p*-methoxyphenol.

**(6)** As in (4) compute the electrostatic potential around each of the phenolate anions. Save images of the electrostatic potentials, and include them in your lab report.

## Questions

**(1)** What kind of energies are you computing in step (1) ? Are they enthalpies, free energies, or something else? What is the experimental equilibrium constant for the acetic acid + ammonia system in water? How do your calculations compare?

**(2)** Consult the Spartan Student manual (and the internet) to determine the type of “implicit solvent” model being used in your calculations? Note that the underlying QM calculations in Spartan are performed by a QM software package called Q-Chem. Thus, you may also wish to look at the Q-Chem manual, which can be found in the Software section of the Chem 478 web site.

**(3)** Which level of calculation appears to give the best results for the relative basicities and pKa values of the four amines? Do the methods handle gas aqueous phase equally well?

**(4)** Display all four of the electrostatic potential surfaces from step (4) at the same time, and make sure they are at the same contour level (“IsoValue”). Include an image of the surfaces in your report. Regions of maximum positive potential will be those stabilized most effectively by solvent. Where are the charged regions localized in each cation? What effect does methyl substitution appear to have on these regions? On the basis of electrostatic potentials, what would you conclude to be the ordering of the solvation energies in these systems? Is your visual estimate in accord with your calculated solvation energies?

**(5)** Find the experimental pKa values for the three phenols in the literature. How do the relative pKa values from your calculations agree with the experimental data?

**(6)** In order to estimate the absolute aqueous acidity (i.e., the actual aqueous pKa) for these phenols, you would need an estimate of the “solvation energy” of the proton. Explain. Can you compute the proton solvation using Spartan Student? Try it and see what happens. The value of the proton solvation energy has been a subject of some controversy. Do a literature search to find a “best estimate” for this values, and combine it with your calculation results for phenol to model the absolute pKa for this molecule. Is your final value reasonable?