Determination of the Choice of Theoretical Method for a Pyridine / Protonated Pyridine System

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Abstract: The choice of a theoretical method in computational chemistry is a critical consideration for the computational chemistry practitioner. The choice of a theoretical method is evaluated as applied to the protonation of the pyridine molecule, a benzene-like cyclic organic compound containing a single nitrogen atom in the ring. Geometry optimizations are performed on both a neutral pyridine molecule and a positively charged pyridinium cation, where a proton is attached to the nitrogen atom. The optimizations are performed using two semi-empirical methods, AM1 and PM3, using the MOPAC software. Geometry optimizations are also performed using a density functional theory (DFT) hybrid functional (B3LYP/6-31G(p,d) on both of the organics. Single point energy calculations are performed on the proton using AM1 and PM3. A comparison of the heats of formation for the reaction, calculated using Hess’ Law, shows that the DFT theoretical method is significantly better (1.6% error as compared to the experimental value) than that of the PM3 method (5% error) or the AM1 method (10% error).

Key words: theoretical method, model chemistry, pyridine, pyridinium, protonation, heats of formation

Introduction

One of the most critical decisions to be made by the practitioner of computational chemistry is that of choosing the most appropriate theoretical method. The chemist must make a decision as to which theoretical method is best suited for both the problem to be solved, the accuracy of the data needed to address the research question, and the computational resources (software and computational time) available to perform the calculations.

Most computational chemists have the knowledge and resources to choose from one of four methods: 1) molecular mechanics/molecular dynamics; 2) semi-empirical methods; 3) ab initio methods; and 4) density functional theory (DFT) methods. These four areas represent, in the broadest terms, the four levels of theory, or theoretical methods that can be applied to any computational chemistry research problem. The choice of a theoretical method is often predicated on logistical considerations such as the amount of time one has to perform the calculations, the amount of computing resources available, the need to share resources with other researchers, and the size of the molecule. As an example of the last item, it is conventional wisdom that ab initio quantum chemical techniques are generally limited to molecules that are under 100 atoms in size. The practical number for ab initio calculations tends to be closer to 50 atoms or less.

The choice of a theoretical method is also referred to as the model chemistry. In choosing a model chemistry, one describes both the specific form of the broad-level theoretical method. For example, under the category of ab initio quantum methods, one can choose a variety of methods, such as Hartree-Fock, Moller Plessett, or one of the Configuration Interaction (CI) methods. These are typically referred to in describing the model chemistry by the commonly accepted acronyms, such as HF, MP2, or CIS, respectively.

The model chemistry description, particularly for the quantum methods (ab initio and DFT), also includes a notation of the basis set used in the calculation. The basis set represents that set of
numbers that is used to begin the determination of the wavefunction, which in term determines the atomic orbitals (AOs) and, using the linear combination of atomic orbitals (LCAO) approximation, the molecular orbitals (MOs). As a general rule, the larger the basis set, the more accurate the results of the calculation (and also the more computing time needed to perform those calculations!).

In describing the model chemistry, a standard format is used. The level of theory and the basis set used to ensure that the molecule has been optimized geometrically is first reported, and then the level of theory used to perform the calculations (separated by a double //) is reported. For example, supposing that a molecule has been optimized geometrically using a Hartree-Fock level of theory with a STO-3G basis set, then the calculations performed with a Hartree-Fock level of the theory and a 6-31G(p,d) basis set, one would describe the calculation as follows:

\[ \text{HF/STO-3G//HF/6-31(p,d)} \]

The choice of a theoretical method, or model chemistry, is of considerable interest to the computational practitioner. As more methods are developed and more experience are gained in the use of a variety of theoretical methods, so too will our abilities to choose the right method for the right problem. Our interest here is to evaluate the optimal model chemistry for studying the protonation of organic ring structures. As a model organic structure, we have chosen pyridine, a benzene-like ring structure that has a substituted nitrogen atom, replacing one of the carbons in the ring. Like benzene, pyridine has an alternating double bond structure reflecting the resonance of the molecule. In this research, we are modeling the protonation of the nitrogen, with the goal of determining the change in the heat of formation \( (\Delta H_f) \). The reaction heat of formation will be calculated using Hess’ Law:

\[
\Delta H_f^{\text{rxn}} = \Sigma \Delta H_f^{\text{products}} - \Sigma \Delta H_f^{\text{reactants}}
\]  

\( (1) \)

Computational Approach

Using the molecular editor builder of WebMO on the North Carolina High School Computational Chemistry Server, the molecules pyridine, protonated pyridine, and a proton (H+) were built. The structure of the pyridine molecule is shown below:

![Pyridine](image)

The protonated version of this molecule, known as a pyridinium cation, adds a hydrogen to the nitrogen atom, with a subsequent increase in the charge of the molecule to a cation (positively-charged ion):

![Protonated Pyridine](image)

Following building, each molecule was optimized using the “comprehensive cleanup” molecular mechanics package found in the WebMO molecular editor. Following this rough optimization, pyridine and protonated pyridine were optimized with MOPAC, a semi-empirical software package. Each of two molecules was optimized three times from an initial build followed by a comprehensive cleanup. The first optimization was performed using MOPAC with the AM1 basis set. The second was performed with MOPAC using the PM3 basis set. Finally, the third optimization was performed using Gaussian 03 using a hybrid density functional theory (DFT) model chemistry, specifically the B3LYP/6-31G(p,d) model chemistry. In addition, a proton (H+) was built. Using MOPAC, single point energies (molecular energies) were calculated using both the AM1 and PM3 basis sets.

Results and Discussion

For MOPAC calculations, all energies are reported as heats of formation with units of kilocalories per mole (kcal/mol). DFT calculations resulted in energies reported in units of hartrees (Eh). These energy values were converted to kcal/mol energy units using the conversion factor 1 Eh = 627.51 kcal/mol.

The data results are shown in Table 1.1.
Table 1.1 Computational Results

<table>
<thead>
<tr>
<th>Molecule</th>
<th>AM1 (kcal/mol)</th>
<th>PM3 (kcal/mol)</th>
<th>BSLYP/6-31G(d) (kcal/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyridine</td>
<td>32.03655</td>
<td>30.3684</td>
<td>-248.264973</td>
</tr>
<tr>
<td>Protonated Pyr</td>
<td>184.16286</td>
<td>187.20335</td>
<td>-248.6599778</td>
</tr>
<tr>
<td>Proton</td>
<td>314.915</td>
<td>353.50566</td>
<td>1.481</td>
</tr>
<tr>
<td>∆Hf</td>
<td>-162.79073</td>
<td>-196.69071</td>
<td>-231.9557007</td>
</tr>
<tr>
<td>Percent error</td>
<td>25.73%</td>
<td>10.27%</td>
<td>5.82%</td>
</tr>
</tbody>
</table>

The value for the proton for the DFT calculation was obtained from literature. The overall ∆Hf for the reactions were calculated using Hess’ Law (Equation 1), based on the reaction:

Protonated pyridine → Pyridine + H⁺

Figure 1.1 shows a comparison of the ∆Hf for the three theoretical methods.

Figure 1.1. ∆Hf for methods

Percent error determinations for the three methods were calculated using the experimental value of -219.2 kcal/mol for the heat of formation for the reaction. The percent error calculations are reported in Table 1.1.

Conclusions

Based on the data and data analysis, the results suggest that the more powerful quantum chemical theoretical method – specifically, the choice of the DFT hybrid functional – provides a significant improvement in the accuracy of the ∆Hf for the protonation of pyridine. Both semi-empirical methods using the AM1 and PM3 basis sets resulted in a percent error determination greater than 10% (25.73% and 10.27%, respectively). It can be stated, therefore, that the choice of the DFT hybrid theoretical method is the most superior choice for organic protonation methods. Further studies on other organic moieties to substantiate this finding are currently underway.

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