

Comparative studies of density functionals in modelling hydrogen bonding energetics of acrylamide dimers

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Abstract. Intermolecular interaction energies and conformer geometries of the hydrogen bonded acrylamide dimers have been studied by using the second-order Møller-Plesset (MP2) perturbation theory and the density functional theory (DFT) with 17 density functionals. Dunning's correlation consistent basis sets (up to aug-cc-pVTZ) have been used to study the basis set effects. The DFT calculated interaction energies are compared to the reference energy data calculated by the MP2 method and the coupled cluster method at the complete basis set (CCSD(T)/CBS) limit in order to determine the relative performance of the studied density functionals. Overall, dispersion-energy-corrected density functionals outperform uncorrected ones. The ω B97XD density functional is particularly effective in terms of both accuracy and computational cost in estimating the reference energy values using small basis sets and is highly recommended for similar calculations for larger systems.

Keywords: acrylamide dimer; ab initio calculation; density functional theory; hydrogen bonded complexes

1. Introduction

Hydrogen bonds are non-covalently binding interactions which play a crucial role in supramolecular physics, chemistry, and biology (Jeffrey and Saenger 1991, Boutis 1992, Grabowski 2006). Hydrogen bonded clusters or segments containing conjugated bonding patterns such as N-H---O, O-H---N and C-H---O are the building blocks of biologically important macromolecules such as proteins and DNA/RNA. The stability of a hydrogen bonded complex is ultimately determined by the intermolecular interaction potentials among separate subsystems. Fundamental studies of intermolecular interactions often start with dimeric systems, with gradually increasing complexity from many-body effects. In particular, molecular dimers containing amide functional groups have recently attracted intense attention due to their concurrent double hydrogen bonding characteristics (Grabowski *et al.* 2006, Frey and Leutwyler 2006, Mardyukov *et al.* 2007, Kemnitz and Loewen 2007, Nagaraju and Sastry 2011, Riley *et al.* 2010, Adhikari and Scheiner 2013, Cato *et al.* 2013, Eckert-Maksic *et al.* 2014). A great deal of efforts has been focused on aliphatic primary amides while relatively less attention has been paid on conjugated amides. In this

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Table 1 Geometrical parameters of the optimized syn- and skew-acrylamide monomer structures. The calculations are performed at the MP2 theory with the aug-cc-pVDZ (aDZ) and the aug-cc-pVTZ (aTZ) basis sets. Here bond lengths are in angstroms (0.1 nanometers) and bond angles and dihedral angles are in degrees

| Geometry | syn-acrylamide | | skew-acrylamide | | |
|--------------------|---------------------|-------------------|-----------------|------|------|
| | aDZ | aTZ | aDZ | aTZ | |
| Bond Lengths | C6=O7 | 1.23 | 1.22 | 1.24 | 1.23 |
| | C6-N8 | 1.37 | 1.36 | 1.38 | 1.37 |
| | C1=C4 | 1.35 | 1.33 | 1.35 | 1.34 |
| | C4-C6 | 1.50 | 1.49 | 1.50 | 1.49 |
| | C1-H2 | 1.09 | 1.08 | 1.09 | 1.08 |
| | C1-H3 | 1.09 | 1.08 | 1.09 | 1.08 |
| | C4-H5 | 1.10 | 1.08 | 1.09 | 1.08 |
| | N8-H9 | 1.01 | 1.00 | 1.01 | 1.00 |
| | N8-H10 | 1.01 | 1.01 | 1.01 | 1.01 |
| | Bond Angles | \angle O7-C6-N8 | 122 | 122 | 122 |
| \angle O7-C6-C4 | | 123 | 123 | 121 | 121 |
| \angle N8-C6-C4 | | 114 | 114 | 116 | 116 |
| \angle C1-C4-H5 | | 121 | 121 | 121 | 121 |
| \angle C4-C1-H2 | | 120 | 119 | 122 | 122 |
| \angle C4-C1-H3 | | 121 | 121 | 121 | 121 |
| \angle C6-C4-C1 | | 120 | 120 | 125 | 125 |
| \angle C6-C4-H5 | | 119 | 119 | 114 | 114 |
| \angle C6-N8-H9 | | 122 | 122 | 119 | 120 |
| \angle C6-N8-H10 | | 118 | 118 | 116 | 116 |
| \angle H2-C1-H3 | | 119 | 119 | 117 | 117 |
| \angle H9-N8-H10 | | 119 | 119 | 117 | 117 |
| Dihedral Angles | \angle C1C4-C6N8 | -180 | -180 | 24 | 23 |
| | \angle C1C4-C6O7 | -0 | -0 | -153 | -155 |
| | \angle C4C6-N8H9 | -0 | -0 | 25 | 23 |
| | \angle C4C6-N8H10 | -180 | -180 | 173 | 173 |
| | \angle O7C6-N8H9 | -180 | -180 | -158 | -159 |
| | \angle O7C6-N8H10 | -0 | -0 | -10 | -9 |
| | \angle O7C6-C4H5 | 180 | 180 | 23 | 22 |
| | \angle H2C1-C4H5 | -180 | -180 | -176 | -176 |
| | \angle H3C1-C4H5 | 0 | 0 | 2 | 2 |
| | \angle H2C1-C4H6 | 0 | 0 | -1 | -1 |
| | \angle H3C1-C4H6 | -180 | -180 | 177 | 177 |
| | \angle N8C6-C4H5 | -0 | -0 | -160 | -161 |

work we study the simplest α , β -unsaturated amide, acrylamide (Duarte *et al.* 2005, Girma *et al.*

2005, Guo and Wu 2008, Sharma *et al.* 2013, Ayvaz *et al.* 2013, Jiang *et al.* 2014, Singh *et al.* 2014).

In this paper we carry out geometry optimization calculations for the acrylamide monomers and dimers using the second-order Møller-Plesset (MP2) perturbation theory and the density functional theory (DFT). We consider in this work 17 modern density functionals, including B3LYP, CAM-B3LYP, X3LYP, mPW1PBE, mPW3PBE, LC-PBE, HSEH1PBE, B2PLYP, B2PLYPD, M05, M05-2X, M06, M06-2X, M06L, B97D, B97X, and B97XD (Frisch *et al.* (2009)). Dunning's correlation consistent basis sets (up to aug-cc-pVTZ) (Dunning (1989)) are employed. To calibrate the DFT calculated dimer structures and energetics, we perform a benchmark study on 12 stable conformers of the acrylamide dimer using the MP2 method. For the most stable conformer we also perform the coupled cluster CCSD(T) single point calculations, which are the current state of the art standards for intermolecular interactions. The minimum-energy structure corresponds to the double hydrogen bonded complex. Both the geometries and energetics are analyzed for this complex.

2. Methods and calculations

We carried out the Berny geometry optimization and vibrational normal mode analysis by using the Gaussian 09 suite of program package (Frisch *et al.* 2009). The structures of the stable complexes were obtained by extensive geometry optimization calculations under tight convergence criteria. For the DFT calculations, we consider 17 density functionals in comparison with the MP2 or CCSD(T) calculations. Dunning's correlation consistent basis sets (cc-pVXZ and aug-cc-pVXZ, X=D, T) were employed in the calculations. No symmetry or rigid molecule constraints were imposed in the geometry optimization calculations. The normal mode frequency analysis has been carefully checked to assure that there are no imaginary frequencies and all obtained configurations are true minima but not saddle points. The transition state and the reaction pathway were searched using the intrinsic reaction coordinate (IRC) utility program implemented in Gaussian 09 (Frisch *et al.* 2009). The dimer interaction energy was calculated as the difference between the total energy of the complex and the sum of the energies of isolated monomers (the supermolecule approach). The basis set superposition errors (BSSE) were calibrated by the counterpoise correction procedure proposed by Boys and Bernardi (Boys and Bernardi 1970). For the optimized structures we performed single-point CCSD(T) calculations (Bartlett 1989) with the basis sets up to aug-cc-pVDZ. The CCSD(T) binding energies at the complete basis set (CBS) limits were obtained using the numerical extrapolation method of Helgaker *et al.* (1997).

3. Results and discussion

The isolated acrylamide molecule was first optimized at the MP2 level of theory with the aug-cc-pVDZ (aDZ) and the aug-cc-pVTZ (aTZ) basis sets. The O=C-N-H linkage has been known to exhibit zwitterionic resonance structures so the initial conformations for the isolated acrylamide are chosen to start from non-planar geometries and the subsequent geometry optimization calculations determine the stable conformations. We found two isomers denoted as syn and skew, as shown in Fig. 1. The calculated geometrical parameters (bond lengths, bond angles and dihedral angles) for the two isomeric structures are listed in Table 1. As we can see from Fig. 1 and Table 1, the syn structure is planar while the skew structure is slightly nonplanar (off by about 20 degrees

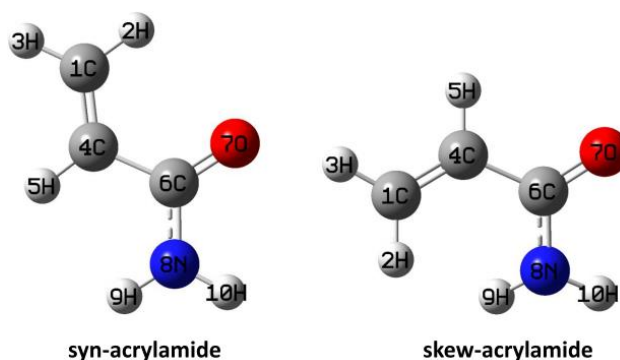


Fig. 1 The two optimized structures of the acrylamide monomer denoted as the syn and the skew acrylamides

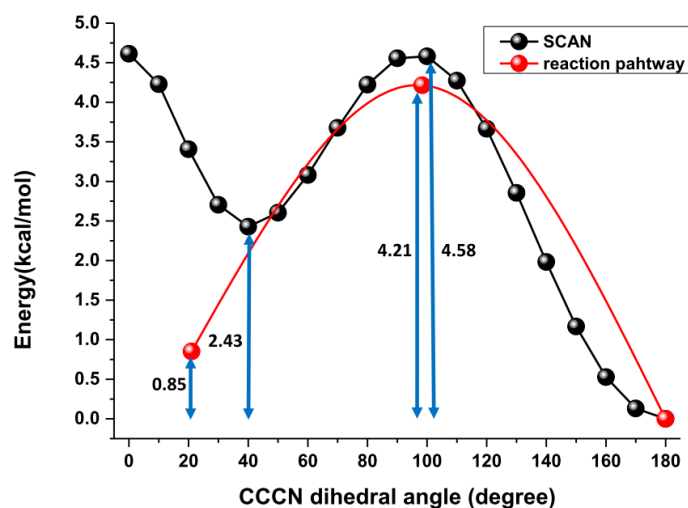


Fig. 2 The isomerization reaction profiles from the syn to the skew structures of the acrylamide monomer. Here the reaction pathway is searched by the IRC utility and the scanned (SCAN) path is along the CCCN dihedral angle as defined in Fig. 1 and Table 1

for the CCCN dihedral angle). We have calculated the syn-skew isomerization reaction pathway and searched for the transition state. The potential energy profile along the reaction coordinate is shown in Fig. 2. Energetically, the syn structure is more stable than the skew structure by an energy difference of 0.85 kcal/mol, and the syn to skew isomerization barrier height is 4.21 kcal/mol along the IRC. Notice that the IRC does not correspond exactly to the CCCN dihedral angle.

By using the MP2/aug-cc-pVDZ level of theory, we found 12 stable conformers, as shown in Fig. 3. In Table 2 we list the geometrical parameters of the dimers. According to their binding patterns, these conformers can be categorized into 4 types, as forming (1) double N-H---O bonds, (2) single N-H---O bond, (3) single N-H---O bond with single C-H---O bond, and (4) double C-H---O bonds. The complexes with the double N-H---O bond patterns are energetically favored over other stable complexes. In fact the N-H---O type double hydrogen bond is also dominant in trimer formation and additional water molecules would diminish the bond strength per bond (Singh *et al.*

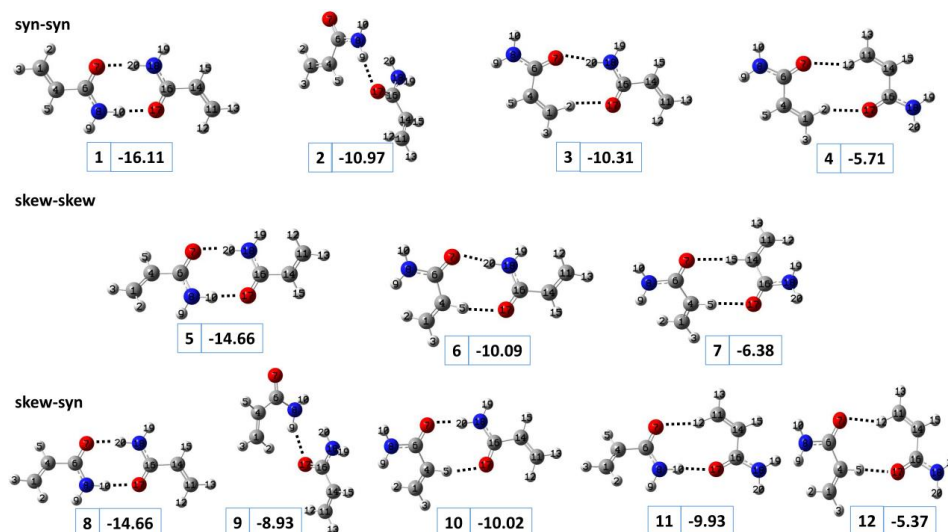


Fig. 3 The searched stable acrylamide dimers, denoted as conformer 1-12. The binding energies in kcal/mol are shown in the corresponding boxes

Table 2 The calculated dimeric geometry parameters by using MP2/aug-cc-pVDZ. The bond length is in unit of angstroms. The bond angles and dihedral angles are in degrees

| | 6C=7O | 6C-8N | 8N-10H | 4C-6C | 1C=4C | 16C=17O | 16C-18N | 18N-20H | 14C-16C | 11C=14C | \angle 7-8-17-18 |
|---------|-------|-------|--------|-------|-------|---------|---------|---------|---------|---------|--------------------|
| Dimer1 | 1.234 | 1.346 | 1.022 | 1.490 | 1.333 | 1.234 | 1.346 | 1.022 | 1.490 | 1.333 | 0.10 |
| Dimer2 | 1.235 | 1.380 | 1.022 | 1.501 | 1.351 | 1.243 | 1.366 | 1.016 | 1.496 | 1.350 | 82.60 |
| Dimer3 | 1.240 | 1.364 | 1.021 | 1.502 | 1.350 | 1.240 | 1.370 | 1.012 | 1.494 | 1.351 | 0.10 |
| Dimer4 | 1.236 | 1.375 | 1.012 | 1.497 | 1.351 | 1.236 | 1.375 | 1.012 | 1.497 | 1.351 | 1.02 |
| Dimer5 | 1.249 | 1.356 | 1.028 | 1.497 | 1.352 | 1.249 | 1.356 | 1.028 | 1.497 | 1.352 | 0.17 |
| Dimer6 | 1.243 | 1.371 | 1.013 | 1.493 | 1.354 | 1.243 | 1.363 | 1.024 | 1.499 | 1.353 | 0.68 |
| Dimer7 | 1.239 | 1.378 | 1.013 | 1.495 | 1.354 | 1.239 | 1.378 | 1.013 | 1.495 | 1.354 | 13.43 |
| Dimer8 | 1.249 | 1.356 | 1.029 | 1.497 | 1.352 | 1.247 | 1.357 | 1.029 | 1.498 | 1.350 | 0.08 |
| Dimer9 | 1.237 | 1.383 | 1.015 | 1.496 | 1.353 | 1.243 | 1.365 | 1.010 | 1.497 | 1.350 | 89.12 |
| Dimer10 | 1.243 | 1.371 | 1.013 | 1.493 | 1.354 | 1.241 | 1.364 | 1.024 | 1.501 | 1.350 | 1.44 |
| Dimer11 | 1.242 | 1.364 | 1.022 | 1.499 | 1.353 | 1.239 | 1.370 | 1.012 | 1.494 | 1.351 | 117.00 |
| Dimer12 | 1.238 | 1.380 | 1.014 | 1.495 | 1.354 | 1.236 | 1.374 | 1.012 | 1.496 | 1.351 | 14.38 |

2014). The BSSE corrected interaction energies of these complexes are in the order of 1 (16.11) > 8 (14.66) = 5 (14.66) > 2 (10.97) > 3 (10.31) > 6 (10.09) > 10 (10.02) > 11 (9.93) > 9 (8.93) > 6 (6.38) > 4 (5.71) > 12 (5.37) in magnitude (positive energy values in kcal/mol shown in the parentheses). We will focus on the minimum-energy conformer 1 (the syn-syn dimer) in the following DFT calculations.

For conformer 1, the binding energies were calculated by using the density functional theory with 17 modern density functionals, including B3LYP, CAM-B3LYP, X3LYP, mPW1PBE, mPW3PBE, LC-PBE, HSEH1PBE, B2PLYP, B2PLYPD, M05, M05-2X, M06, M06-2X, M06L, B97D, B97X, and B97XD. Dunning's correlation consistent basis sets (cc-pVXZ and aug-cc-

Table 3 The DFT calculated binding energies of the syn-syn dimeric structure by using the methods of MP2, CCSD(T) and DFT with the 17 density functionals. The complete basis set (CBS) limits are obtained by using the numerical extrapolation method of Helgaker et al. using the cc-pVDZ (DZ) and cc-pVTZ (TZ) basis sets and denoted as CBS(DZ-TZ). The CPU time for each is recorded from using the aug-cc-pVDZ (aDZ) basis set in the energy calculation

| | DZ | TZ | aDZ | CBS(DZ-TZ) | CPU time (aDZ) |
|------------------|--------|--------|--------|------------|-----------------|
| M05 | -15.23 | -15.41 | -15.62 | -15.49 | 6hr 37min |
| M052X | -15.43 | -16.35 | -15.88 | -16.74 | 6hr 28min |
| M06 | -15.79 | -16.30 | -16.90 | -16.51 | 7hr 26min |
| M062X | -15.68 | -16.14 | -16.04 | -16.33 | 6hr 33min |
| M06L | -15.55 | -16.24 | -15.90 | -16.53 | 6hr 44min |
| B97D | -16.89 | -15.83 | -17.07 | -15.38 | 4hr 11min |
| ω B97X | -16.65 | -17.00 | -17.16 | -17.15 | 10hr 03min |
| ω B97XD | -16.51 | -16.74 | -16.85 | -16.84 | 11hr 12min |
| X3LYP | -15.12 | -15.15 | -15.52 | -15.16 | 4hr 52min |
| B3LYP | -14.41 | -14.36 | -14.79 | -14.34 | 2hr 25min |
| CAM-B3LYP | -15.75 | -16.17 | -16.12 | -16.35 | 10hr 52min |
| B2PLYP | -14.29 | -14.75 | -15.40 | -14.94 | 8hr 12min |
| B2PLYPD | -15.85 | -16.30 | -16.95 | -16.49 | 14hr 08min |
| mPW1PBE | -14.77 | -14.84 | -14.94 | -14.87 | 4hr 59min |
| mPW3PBE | -15.05 | -14.95 | -15.25 | -14.91 | 4hr 54min |
| LC- ω PBE | -14.31 | -14.55 | -14.48 | -14.65 | 10hr 00min |
| HSEH1PBE | -16.00 | -16.02 | -16.26 | -16.03 | 9hr 57min |
| MP2 | -13.71 | -14.73 | -16.11 | -15.16 | 2d 23hr 07min |
| CCSD(T) | -13.03 | -15.22 | -15.12 | -16.15 | 106d 11hr 09min |

pVXZ, X=D, T) were employed in the calculations. In Table 3 we show a comparison of the DFT calculated energies with the reference MP2 and CCSD(T) data using the cc-pVDZ (DZ), cc-pVTZ (TZ), and aug-cc-pVDZ (aDZ) basis sets. We see that most of these modern density functionals perform very well in reproducing the reference values within 1 kcal/mol, which is usually taken as a suitable chemical accuracy. In general, dispersion-corrected density functionals have better performance than those uncorrected. However, if taking into account the computational cost as listed in Table 3 as the CPU calculation time, we find that B3LYP, ω B97XD, X3LYP and M05 density functionals outperform others in balancing the accuracy and computational cost. Among these, the ω B97XD density functional using the DZ basis set contains the most dispersion energy components and thus outperforms others.

Because the calculated intermolecular interaction energies are not direct observables, we compare the spectral frequencies using the ω B97XD/aDZ level of theory and the experimental data (Jonathan 1961). The calculated vibrational frequencies in wavenumbers for the C=C, C=O, symmetric NH₂, and asymmetric NH₂ are 1650 (1645), 1703 (1681), 3205 (3175), and 3569 (3331), respectively, with the experimental data shown in the parentheses. These values are also consistent with our previous spectral analysis using the MP2/aDZ level of theory (Wang *et al.* 2016).

4. Conclusions

A theoretical study on the acrylamide dimer has been performed at the MP2 and DFT levels of theory. Among the 17 modern density functionals used to test their utilities, the ω B97XD density functional outperforms others in determining the binding energies of hydrogen bonded complexes. It is found that the syn monomer and the double hydrogen bonded syn-syn dimer are the most stable structures with no significant possibility for tautomer structures to be formed. The study provides a systematic geometric and energetic data for experimental identification of formation of acrylamide dimers, being particularly important in food chemistry studies.

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