

Assessment of the Performance of B2PLYP-D for Describing Intramolecular π - π and σ - π Interactions

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Intramolecular π - π and σ - π interactions are omnipresent for numerous energetic and structural phenomena in nature, and the exact description of these nonbonding interactions plays an important role in the accurate prediction of the three-dimensional structures for numerous interesting molecular systems such as protein folding and polymer shaping. We have selected two prototype molecular systems for benchmarking calculations of intramolecular π - π and σ - π interactions. Accurately describing conformational energy of such systems requires highly elaborate but very expensive *ab initio* methods such as coupled cluster singles, doubles, and (triples) (CCSD(T)). Our calculations reveal a double hybrid density functional incorporating dispersion correction (B2PLYP-D) that agrees excellently with the CCSD(T) results, indicating that B2PLYP-D can serve as a practical method of choice.

Key Words : Conformation analysis, Density functional theory, Dispersion interaction, π - π interaction, σ - π interaction

Introduction

Electronic structure calculations in organic, biomolecular, and nano-based material systems have widely used traditional density-functional theory (DFT).¹⁻³ However, the dispersion interaction lacks a correct description with the common correlation and exchange functionals.⁴⁻⁶ Over the last decade, the DFT approach has developed to account accurately for dispersion interactions.⁷⁻¹⁸ A simple approach directly adds empirical potential without modifying exchange-correlation functional forms. The representative two methods include the atom pair-wise additive treatment of dispersion energy (DFT-D)¹¹⁻¹³ and dispersion correcting atom-centered one-electron potentials (DCACP).¹⁴⁻¹⁶ A nonempirical means modifies the density functional by adding nonlocal vdW density functional⁷⁻¹⁰ or by applying a double hybrid density functional.^{17,18} These usually perform well because they account for dispersion by perturbative second-order correction terms (PT2).¹⁹ Since Grimme initially proposed the B2PLYP functional¹⁷ describing the mixture of Hartree-Fock (HF) and generalized gradient approximations (GGA) exchange and of PT2 and GGA

correlation, a combination method using DFT-D (B2PLYP-D) and the original method (B2PLYP) has been applied to numerous organic, bio-related, and rare-gas systems.²⁰⁻²⁷

This work selects two practical molecular systems, 3-(4-hydroxyphenyl)-*N*-benzyl-propionamide (HNBPA)²⁸ and 3-(2-aminoethyl)indole, tryptamine (TRA)²⁹ for benchmarking calculations for dispersive π - π interactions between two intramolecular aromatic rings and σ - π interactions between indole ring and the ethylamine side chain, respectively. Figure 1 shows the chemical structures of both molecules and indicates three (φ , θ , and τ) and two (β and π) flexible coordinates in the HNBPA and TRA structures, respectively. These intramolecular π - π and σ - π interactions closely related to the prediction of the molecular shapes and separations of the macromolecules³⁰⁻³⁷ such as base stacking of DNA,^{30,31} the stability of proteins,^{32,33} and the dispersion separation of the single wall carbon nanotube (SWNT).³⁴⁻³⁶ The authors applied the B2PLYP and B2PLYP-D methods to the conformers of HNBPA and TRA and compared them to the most popular B3LYP and second order Møller-Plesset (MP2) levels of theory¹⁹ as well as the coupled cluster singles doubles with the perturbative triples (CCSD(T)) method,^{38,39} which is used as reference data in the present work.

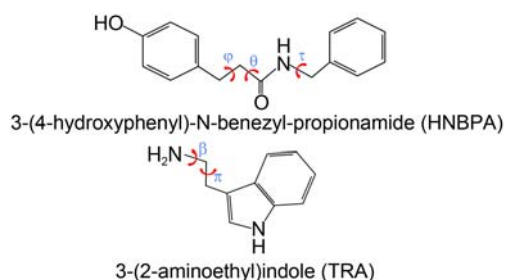


Figure 1. Chemical structures of HNBPA and TRA.

Computational Details

The hybrid density functional with perturbative second-order correction consists of a mixture of DFT components and the MP2 correlation energy calculated with the DFT orbitals and their energies. The exchange-correlation energy E_{xc} is expressed by

$$E_{xc} = (1 - a_x)E_x^{GGA} + a_x E_x^{HF} + bE_c^{GGA} + cE_c^{PT2}, \quad (1)$$

where the two parameters (a_x and c) are obtained in a least-squares-fit procedure to the G2/97 set of heat of formations.⁴⁰ The optimum a_x and c are founded as 0.53 and 0.27, respectively.¹⁷

Dispersion-corrected DFT approaches (DFT-D) are augmented with an empirical correction for long-range dispersion effects. The total energy is described by a sum of damped interatomic potentials of the form C_6R^{-6} added to the usual DFT energy. A detailed description of these methods and a determination of the parameters appears in Refs. [12] and [17].

The present work uses the correlation consistent aug-cc-pVDZ basis sets. For practicality, the CCSD(T)/aug-cc-pVDZ results were evaluated by $E[\text{CCSD(T)/6-31+G(d)}] - E[\text{RIMP2/6-31+G(d)}] + E[\text{RIMP2/aug-cc-pVDZ}]$.^{41,42} The B3LYP and RIMP2 calculations were carried out using the GAUSSIAN 09⁴³ and TURBOMOLE program package,⁴⁴ respectively. The B2PLYP-D calculations were done using the ORCA program,⁴⁵ and the CCSD(T) energies were calculated using the MOLPRO program package.⁴⁶

Results and Discussion

3-(4-Hydroxyphenyl)-*N*-benzyl-propionamide (HNBPA).

Bichromophoric systems are useful for examining the effects of electronic coupling. A biologically relevant single chain bichromophore molecule, 3-(4-hydroxyphenyl)-*N*-benzyl-propionamide (HNBPA) contains two spectroscopically distinguishable ultraviolet chromophores. A chain six bonds long containing an amide group connects the phenyl and phenol chromophores.

Our previous study analyzed several conformers of HNBPA with various electron structure calculations²⁸ and showed

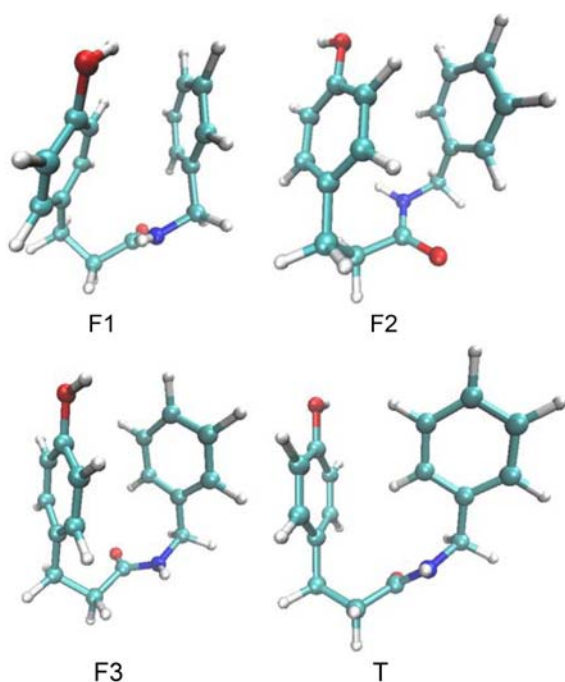


Figure 2. Optimized structures for four folded conformational minima of HNBPA calculated at RIMP2 level of theory.

Table 1. Relative energies (in kcal/mol) of four folded structures of HNBPA calculated by CCSD(T), RIMP2, B3LYP, B2PLYP and B2PLYP-D levels of theory

Conformers	CCSD(T)	RIMP2	B3LYP	B2PLYP	B2PLYP-D
F1	0.00	0.00	0.00	0.00	0.00
F2	0.89	1.29	0.06	0.70	1.26
F3	1.64	2.14	0.76	1.53	2.19
T	0.86	2.63	-2.56	-1.33	0.69
RMS ^a	0.00	0.94	1.81	1.10	0.34

^aRoot mean square deviation given relative to the CCSD(T) energies.

that dispersion interactions play a major role in determining the relative stability of the folded and extended structures. This study examines the four folded structures of HNBPA to evaluate relative conformational stability according to different orientations of two chromophoric rings. Figure 2 depicts the four folded structures of the conformers of HNBPA optimized using the RIMP2 electronic structure method. Three of them have face-to-face chromophoric rings (F1, F2, and F3), and one conformer takes a more perpendicular T-shaped (T) structure.

We performed the energy calculations with various electronic structure methods in these optimized geometries at the RIMP2 level of theory. Table 1 shows the energies of four folded HNBPA conformers relative to that of conformer F1 by calculations using the CCSD(T), RIMP2, B3LYP, B2PLYP, and B2PLYP-D methods. It also presents the root mean square (RMS) deviation relative to the CCSD(T) energies. The performance of the RIMP2 and B2PLYP methods are similar, having RMS deviations of 0.94 and 1.10 kcal/mol, respectively, while the RIMP2 and B2PLYP tend to over- and underestimate the relative energies, respectively. The RIMP2 and B2PLYP-D methods correctly predict the lowest energy isomer (F1), but the B3LYP and B2PLYP methods indicate that the T isomer has the lowest energy.

The energy of the T conformer, calculated using the B2PLYP-D method, comes very close to that using the CCSD(T) calculations (energy difference is only 0.17 kcal/mol). Overall, the B2PLYP-D method shows the best energy description for four conformers, followed by RIMP2, B2PLYP, and B3LYP.

3-(2-Aminoethyl)indole (TRA). Based on the indole ring structure, 3-(2-aminoethyl)indole (TRA) relates chemically to the amino acid tryptophan. Some have challenged the theoretically conformational analysis of TRA because of the significant differences in relative energies obtained from the B3LYP and RIMP2 calculations.²⁹ In this regard, this present system offers an effective benchmark system for investigating conformational stability using the dispersion-corrected density functional method. The present work selected and optimized ten different isomers caused by β and π rotational angle (see Fig. 1) with the RIMP2 level of theory. Figure 3 shows these optimized geometries.

Table 2 reports the relative energies of ten conformers of TRA calculated using the CCSD(T), RIMP2, B3LYP,

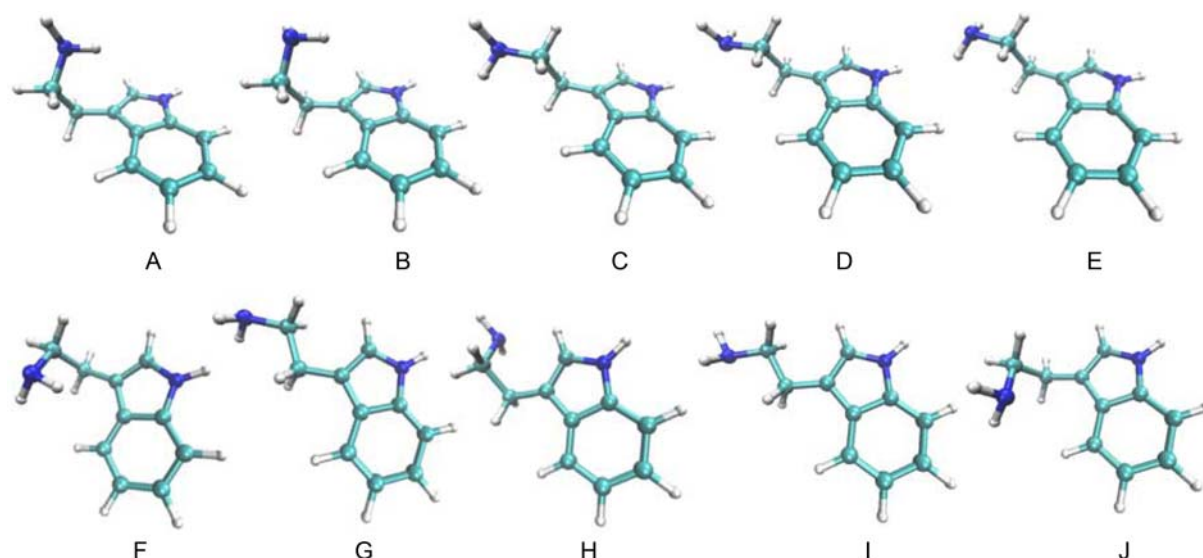


Figure 3. Ten local minima of TRA optimized at the RIMP2 level of theory.

Table 2. Relative energy (in kcal/mol) of ten structures of TRA calculated by CCSD(T), RIMP2, B3LYP, B2PLYP and B2PLYP-D levels of theory

Conformers	CCSD(T) ^a	RIMP2 ^a	B3LYP	B2PLYP	B2PLYP-D
A	0.00	0.00	0.00	0.00	0.00
B	0.50	0.65	0.28	0.41	0.40
C	1.42	1.83	0.30	0.81	1.31
D	1.43	1.84	0.32	0.84	1.32
E	1.46	1.91	0.31	0.86	1.33
F	0.82	0.95	0.98	0.95	0.74
G	2.06	2.75	0.57	1.28	1.79
H	1.77	2.24	0.82	1.28	1.57
I	2.21	2.85	0.63	1.37	1.92
J	3.02	3.35	2.50	2.75	3.03
RMS ^b	0.00	0.42	0.99	0.52	0.16

^aThe results of the CCSD(T) and RIMP2 methods from Ref. [29]. ^bRoot mean square deviation given relative to the CCSD(T) energies.

B2PLYP, and B2PLYP-D methods. Conformer A is chosen as zero energy because the energy of A is the lowest in the CCSD(T) calculations. All relative energies of ten isomers calculated with RIMP2 method are overestimated compared to those of the CCSD(T) level of theory whereas the energies evaluated with the B2PLYP methods are underestimated, excepting the F isomer. When we add long-range dispersion interaction to the B2PLYP method (B2PLYP-D), the relative energies of all isomers almost perfectly match the result of the CCSD(T) level of theory. The RMS deviation of ten conformers calculated with this method is only 0.16 kcal/mol: B2PLYP-D > RIMP2 > B2PLYP > B3LYP.

Conclusions

This work applied double hybrid density functional combined with long-range dispersion correction to the two benchmarking systems, HNBPA and TRA molecules. Re-

markably, the B2PLYP-D method outperforms the B3LYP and MP2 electronic structure method for describing the intramolecular π - π and σ - π interactions of moderate-size systems. Thus, the authors affirm its successful, accurate, and practical use for the prediction of three-dimensional molecular shapes of systems with less scaling $O(N^5)$ with system size than the scaling $O(N^7)$ of the CCSD(T) level of theory. We propose that the B2PLYP-D method offers a benchmark for the future development of dispersion-corrected DFTs.

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