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Acetamide planarity revisited : Density functional and second order Møeller-Plesset perturbation studies†

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Density functional theory (DFT) with nonlocal functionals, BLYP, BP86, B3LYP and ACM, with split-valence basis sets has been applied to the prediction of molecular structure and torsional barrier of acetamide, a peptide mimic. Møeller-Plesset calculations truncated to the second order (MP2) have been performed on acetamide for comparison with DFT results. The conformation of the methyl group observed in MP2 calculations is different from that in DFT calculations. DFT promises to be a powerful method for molecular structure determination and conformational analysis of peptides in future at the same level of accuracy as NMR, X-ray crystallography, and neutron diffraction.

Acetamide contains a peptide moiety, sandwiched between a methyl group and a hydrogen atom, and has served as a simple model for the peptide unit. Because of this reason, it has been the subject of numerous Quantum Chemical and experimental studies. Most of the recent Quantum Chemical studies of acetamide reported in the literature[1-12] have utilized Hartree Fock and some post-Hartree Fock methods and structures predicted by these studies are not always in complete agreement with the experimental studies. Neutron diffraction studies of acetamide reported in the literature by Jeffrey *et al.*[13] are probably the most accurate data on its structure. As a part of our effort in developing fast and dependable force fields for classical molecular mechanics and dynamics studiesl[4,15] we have relied on gradient corrected density functional theory for the prediction of acetamide structure. Density functional theory, DFT[16-20] is a first principle Quantum Mechanical method originally developed for problems in solid state physics and recently it is gaining acceptance as a powerful method for molecular structure calculations. DFT includes electron correlation effects[21-23] whose true impact on conformational energetics is yet to be ascertained at a quantitative level. The basic notion in the density functional theory is that the energy of a multi-electron system can be expressed in terms of its density. Till recently DFT calculations were performed[18] with local density functionals (LDF). However, in the recent past DFT calculations are being performed with gradient corrected density (nonlocal) functionals (NLF)[18] which are considered to be more accurate than LDF for predicting geometeries and conformational energetics. NLDFT is computationally efficient and has been demonstrated by previously reported studies in the literature to be of comparable accuracy and in many cases much superior to conventional post-Hartree Fock methods.[18,19]

Methods

The Fock matrix,F, in Kohn-Sham self-consistent procedure is expressed as:

$$F = H + J + K^{XC} \quad \ldots (1)$$

where H is the one-electron Hamiltonian matrix, J is the Couolmb matrix, and K^{XC} is the DFT exchange-

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Refs. 42, 43 are previous DFT studies from our laboratories.

correlation matrix. The calculation of H and J proceed in the same way as in HF calculations. DFT exchange-correlation matrix, K^{xc}, are calculated by numerical integration using atom-centered grids.[24] The DFT calculations on acetamide were performed using two different exchange-correlational functionals: (a) A combination of the local functional of Vosko, Wilk, and Nusair (VWN)[25] with the nonlocal exchange functional of Becke[26] and the nonlocal correlational functional of Lee, Yang, and Parr (BLYP),[22,23] the semilocal (generalized gradient corrected) exchange-correlation energy functional used was taken from Becke[26] and the correlation energy functional of Perdew (BP),[27] incorporating the semilocal corrections selfconsistently. B3LYP hybrid functional defines the the exchange functional as a linar combination of Hartree-Fock, local, and gradient-corrected exchange terms[28-30]. The exchange functional is combined with a local and gradient-corrected correlation functional. The correlation functional used is actually $C*E_C^{LYP} + (1 - C)*E_C^{VWN}$, where LYP is the correlation functional of Lee, Yang, and Parr[22,23] which includes both local and nonlocal terms, and VWN is the Vosko, Wilk and Nusair 1980 correlation functional fitting the RPA solution to the uniform gas, often referred to as Local Spin Density (LSD) correlation.[25] (b) The adiabatic connection method(ACM) of Becke[30] where the exchange-correlational energy ($E_{\chi c}$) is expressed as :

$$E_{\chi c}=E_{\chi c}^{LDA} + a_0 (E^{\chi\ exact}-E^{\chi\ LDA}) + a_1 E_{\chi}^{B} + a_2 Ec^{P91} \quad ...(2)$$

where $E_{\chi c}^{LDA}$ is the Vosko-Wilk-Nusair local exchange correlation energy,[25] $E^{\chi\ exact}$ is the HF exact exchange energy, $E^{\chi\ LDA}$ is the local exchange energy, E_{χ}^{B} is the Becke nonlocal exchange energy, and Ec^{P91} is the Perdew and Wang nonlocal correlation energy. The coefficients a_0, a_1, and a_2 are determined by least square fit to the experimental atomisation energies, ionisation energies, and proton affinities from Pople's Gl database.[31] The DFT calculations were implemented using an in-house computer program[32] on a workstation without resorting to the use of CRAY supercomputer. The program is configured to handle a molecular system

Table I — Comparison of calculated and experimental geometries of acetamide from DFT/BLYP and DFT/ACM with DZVP basis set

Bond Length (Å)/ Bond Angle (°)	BLYP/ DZVP	ACM/ DZVP	MP2/ 6-31+G**[a]	HF/6-31G*	EXPT.[b]
C'=O	1.241	1 .225	1.232	1.197	1.220
C'–N	1.385	1.377	1.371	1.359	1.380
C'–C	1.535	1.515	1.511	1.514	1.519
N–H	1.015	1.005	1.007	0.995	1.022
N–H	1.018	1.008	1.005	0.993	1.022
C–H	1.100	1.091	1.085	1.080	1.124
C–H	1.100	1.091	1.088	1.086	1.124
C–H	1.100	1.091	1.089	1.085	1.124
N–C'=O	121.99	122.07	121.9	122.2	121.9
N–C'–C	115.73	115.87	–	–	–
O=C'-C	122.28	122.07	122.7	122.8	122.8
H–N–H	119.23	119.35	–	–	–
C'–N–H1	122.64	122.53	121.9	117.7	121.9
C'–N–H2	118.12	118.13	117.1	121.9	117.7
C'–C–H1	113.90	113.90	112.3	111.6	111.6
C'–C–H2	108.51	108.41	108.6	108.9	108.9
C'–C–H3	108.51	108.41	109.0	109.6	109.6
H–C–H	109.14	109.22	–	–	–

[a] Wong M W & Wiberg K B, *J Phys Chem*, 96, **1992**, 668.

[b] Kitano M & Kuchitsu K, *Bull Chem Soc Japan*, 46, **1973**, 3081.

Table II — Data predicting a slightly non-polar peptide moiety in acetamide

BLYP/6-31G**

	–209.14896	–209.22266	–209.22322	–208.61117
	BLYP/ 6-31G**	BP86/ 6-31G**	B3LYP/ 6-31G**	MP2/ 6-31G**
Energy (au)				
C–N	1.382	1.377	1.368	1.373
C–O	1.234	1.233	1.222	1.228
C–C	1.536	1.529	1.523	1.515
C–Ha	1.100	1.102	1.093	1.085
C–Hg	1.100	1.102	1.092	1.089
C–H-g	1.100	1.101	1.094	1.089
N–Ha	1.015	1.015	1.006	1.004
N–Hc	1.017	1.017	1.009	1.006
N–C–O	122.20	122.26	122.3	122.1
N–C–C	115.32	115.27	115.5	114.5
O–C–C	122.47	122.47	122.2	123.4
H–N–H	118.47	118.91	119.1	117.6
C–N–Ha	122.65	122.99	122.9	120.8
C–N–Hc	117.58	117.85	118.0	116.4
C–C–Ha	114.17	114.32	114.0	108.6
C–C–Hg	108.78	108.72	108.5	110.9
C–C–H-g	108.58	108.54	108.7	110.3
Hg–C–Ha	108.90	108.83	109.2	109.8
H-g–C–Ha	108.96	109.01	108.9	109.2
O–C–N–Ha	172.44	176.78	179.0	165.0
O–C–N–Hc	5.69	2.58	1.0	11.3
C–C–N–Ha	8.28	3.25	179.0	16.4
C–C–N–Hc	175.03	177.45	178.6	170.2
C–O–N–C	0.5	0.0	0.3	1.0
N–C–Hc–Ha	7.0	3.1	1.0	14.0

with more than 100 atoms. BLYP, BP86, B3LYP, and MP2 with 6-31G(*d*, *p*) calculations were performed with Gaussian 92 program.[33]

MP2 calculations require a Hartree-Fock calculation followed by a Møeller-Plesset correlation energy correction truncated to the second order. This method for elec-tronic structure calculation has been widely discussed.[34-37]

Results and Discussion

Acetamide was found to assume two isoenergetic structures from HF/6-31G* calculations (unpublished). Of these two structures, one was found to contain a planar peptide moiety whereas the second one was found to contain a slightly non-planar peptide moiety. These two structures of acetamide obtained from previous HF/6-31G* studies (unpublished) were optimised using DFT with gradient corrected functionals,

BLYP, BP86, B3LYP, and ACM. Møeller Plesset MP2 method was also used in the calculations of acetamide, all of them with double zeta (ξ) VP and 6-31G (*d*, *p*) basis sets. These two structures (Cs and C1) differ in energy by a few micro Hartrees based on BLYP/DZVP calculations whereas DZVP calculations predict them to be isoenergetic. The geometries of these two structures are comparable with the structure derived from electron diffraction study of acetamide in the gas-phase by Kitano and Kuchitsu,[38] and neutron diffraction studies by Jeffrey *et al.*[13] (see **Table I**).

Acetamide structure has been the center of intense controversy in the literature since 1972.[1-12] Most of the studies have reported a planar structure for the peptide moiety in acetamide. Electron diffraction studies by Kitano and Kuchitsu[38] has provided little information, if any, on the planarity of the peptide moiety in acetamide. Neutron diffraction studies on the rhombohedral form of acetamide[13] have shown that the peptide moiety in acetamide is slightly nonplanar and that one C–H bond is normal to the plane of nonhydrogen atoms, for infrared studies by Hansen *et al.*[39] and Kydd and Dunham[40] have shown that the peptide moiety is nearly planar. Recently Wong and Wiberg[41] have reported a high level *ab initio* study of acetamide using basis sets upto 6-31+G** with electron correlation included in the Møeller-Plesset perturbation (MP2) and configuration interaction with single and double (CSID) levels and found that the lowest energy conformer of acetamide was nonplanar with one C-H bond of the methyl group almost perpendicular to the plane of non-hydrogen atoms and a slightly pyramidal N atom. Our studies reported here using DFT BLYP, BP86, B3LYP, MP2 with 6-31G (*d*, *p*) basis sets predict a slightly non-planar peptide moiety in acetamide (**Table II**) based on dihedral angles, τ , H_a–C–C=O. In addition, there are two isoenergetic structures predicted for acetamide on the basis of DFT BLYP with DZVP basis set and one of them contains a slightly nonplanar peptide moiety. For the lowest energy conformer of the two isoenergetic conformers of acetamide, DFT BLYP, BP86, B3LYP, MP2 with 6-31G (*d*, *p*) basis sets calculations predict C=O, C–N and C–C bond lengths of 1.241 Å, 1.385 Å, and 1.535 Å which are longer by 0.02 Å in comparison with similar values from DFT ACM DZVP calculations, which are suggestive of a functional dependence.

Seven transition states that interconnect the minima described in **Table III** for acetamide were selected from previous HF/6-31 G* calculations(unpublished). These seven transition states differ by their torsion angle, τ, described about the peptide bond, C–N. Conformer **3** has a conformational energy difference of 17.24 kcal $mole^{-1}$ which is extremely close to the experimental

TABLE III — Geometry of transition states of acetamide from DFT/BLYP and DFTIACM with DZVP basis set

	Transition State 1		Transition State 2		Transition State 3		Transition State 4		Transition State 5		Transition State 6		Transition State 7	
	BLYP	ACM	BLYP	ACM	BLYP	ACM	BLYP	ACM	BLYP	ACM	BLYP	ACM	BLYP	ACM
C'=O	1.229	1.214	1.229	1.214	1.224	1.209	1.224	1.209	1.228	1.213	1.224	1.209	1.223	1.209
C'–N	1.481	1.453	1.481	1.453	1.475	1.448	1.473	1.446	1.447	1.453	1.474	1.446	1.476	1.446
C'–C	1.519	1.501	1.528	1.509	1.534	1.515	1.542	1.522	1.529	1.501	1.541	1.521	1.534	1.521
N–C'=O	123.25	123.08	122.91	122.8	120.19	120.45	120.13	120.36	122.03	123.12	120.11	120.49	120.22	120.45
N–C'–C	112.97	113.28	114.78	115.2	117.36	117.81	118.82	18.84	115.69	113.24	118.85	118.59	117.30	118.58
O=C'–C	123.78	123.64	122.31	122.0	122.46	122.24	121.05	120.80	122.28	123.65	121.04	120.93	122.48	120.97
C_b	–54.77	+55.55	+54.39	+55.17	–123.86	–122.75	+124.05	–123.02	–93.46	–55.55	–124.03	–123.25	+123.83	+123.1
	+54.74	–55.55	–54.39	–55.17	+123.86	+122.75	–124.05	+123.02	+93.46	+55.55	+124.03	+123.25	–123.83	–123.12

[a] Bond lengths are in Å, bond and torsion angles are in degrees.

value of 16.7 to 17.3 kcal mole^{-1}. In striking contrast to DFT results on formamide,[42,43] barrier heights for acetamide varies from 15.34 kcal mole^{-1} to 23.07 kcal mole^{-1} depending on the basis set used in the calculation.

DFT calculations of molecular structure and conformations promises to emerge as a potentially powerful probe in conformational analysis of biological molecules.

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