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CHEMICAL THERMODYNAMICS AND THERMOCHEMISTRY

Thermochemistry and NBO Analysis of Peptide Bond: Investigation of Basis Sets and Binding Energy[1]

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Abstract—Ab initio methods were used to analyze the structure, energetic and binding energy of the five began dipeptides with methionine, Met-Gly, Met-Ala, Met-Ser, Met-Cys, and Met-Thr dipeptides, in gas phase. The structures of the dipetides and involved amino acids in them were optimized by using Hartree–Fock and DFT methods and 3-21G(*d*), 6-31G(*d*), 6-311G, 6-311G(*d*), and 6-311+G(*d*) basis sets. The effect of basis sets and electron correlations were analyzed with special emphasis on the calculated binding energies and thermodynamic functions. All used methods revealed that Met-Thr has the highest binding energy among all of the five dipeptide molecules. These numerical results suggest that Thr donates the proton easier than other four amino acids and it has the most tendency to join with methionine and it forms the most strong bond with methionine. This fact may be the reason behind the obtained high binding energies for Met-Thr at all levels. From comparison of the values of binding energy for dipeptides in different levels of theory, we could identify that the order of tendency for joint with methionine is Thr > Gly > Ala > Cys > Ser. Also, these data represented that the highest binding energy provide in HF/6-311G level for all of the dipeptides (14.4202, 11.2387, 8.3267, 9.8853, 17.3362 kcal mol^{-1} for dipeptides 1–5, respectively). Moreover, natural bond orbital (NBO) analysis demonstrated that the effect of basis sets and electron correlations on σ_{N1-C2} bonding orbital occupancy is the same as the basis set and electron correlation effects on binding energy of dipeptides in all cases. The obtained results from studying the effect of basis sets and electron correlations on binding energy, NMR and NBO properties showed that the effect of basis sets is almost independent of molecular structure and computational method, while electron correlation effects are relatively dependent to molecular structure and basis set type. In investigating the effect of basis sets and electron correlations on binding properties, the NBO results are in good agreement with the energetic and thermochemistry data at all levels of calculations.

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INTRODUCTION

The formation of peptide bonds is the basic requirement for the structure of all proteins and consequently for the development and continuation of life. Therefore, the peptide bonds are always a matter of intense investigation in biology, physics and chemistry. The formation of a peptide bond between two amino acids is an instance of a condensation reaction. The two molecules of amino acids join covalently to form the bond together and to eliminate a molecule of water.

Since glycine and alanine are the two most simple amino acids, the peptide bonds containing them are the most extensively studied by the theoreticians using ab initio quantum mechanical calculations [1–5 and the references therein]. Furthermore, solvent effects have been also studied on dipeptide structures [6–8 and the references therein].

But also, there is experimental and theoretical published data about began dipeptides with methionine. Methionine is one of only two amino acids encoded by a single codon (AUG) in the standard genetic code. The codon AUG is also significant in protein synthesis. It carries the start message for a Ribosome to begin protein translation from mRNA. As a consequence, methionine is incorporated into the N-terminal position of all proteins in eukaryotes and archaea during translation, although it is usually removed by post-translational modification. Methionine can also occur at other positions in the protein.

Ivanova has carried out the part of systematic studies on Met-His and His-Met dipeptides and also Met-Gly-Gly and Gly-Gly-Met tripeptides in point of view of structural and IR-spectral characterizations [9, 10]. In addition, Reedjik has investigated Au (III) and Pt (II) complexes with methionine containing peptides and proteins arises from their potential antitumor effect [11, 12].

For above mentioned reasons, in this work, we investigated the structure and energetic of the dipeptides which begin with methionine in gas phase and neutral form:

[1] The article is published in the original.

(1) methionyl–glycine (Met-Gly)

NH_2–CH ($CH_2CH_2SCH_3$)–CO–NH–CH_2COOH,

(2) methionyl–alanine (Met-Ala)

NH_2–CH ($CH_2CH_2SCH_3$)–CO–NH–CH (CH_3)–COOH,

(3) methionyl–serine (Met-Ser)

NH_2–CH ($CH_2CH_2SCH_3$)–CO–NH–CH (CH_2OH)–COOH,

(4) methionyl–cysteine (Met-Cys)

NH_2–CH ($CH_2CH_2SCH_3$)–CO–NH–CH (CH_2SH)–COOH,

(5) methionyl–threonine (Met-Thr)

NH_2–CH ($CH_2CH_2SCH_3$)–CO–NH–CH (CH (CH_3) OH)–COOH.

When methionine combines with other amino acids to form a dipeptide, donates a hydroxyl group and other amino acids remove a proton and the releasing water molecule. In this paper, we used Hartree–Fock and DFT methods with different basis sets to calculate the structure and energy of dipeptide molecules. The basic interest of the present study is to analyze the effect of basis sets and electron correlations in DFT level on the structure, binding energy and thermodynamic functions, NBO and NMR properties. In addition, we compared the energetic and thermochemistry results with NBO (natural bond orbital) data and the agreement between them. Unfortunately, because of limitation of computational resources, we could not study the effect of basis sets and electron correlations using of high level ab initio quantum mechanical methods.

COMPUTATIONAL DETAILS

Geometry optimizations were performed by using Hartree–Fock (HF) and Beck's three parameter hybrid with the Lee–Yang–Parr correlation functional, B3LYP [13, 14], methods with the 3-21G(*d*), 6-31G(*d*), 6-311G, 6-311G(*d*) and 6-311+ G(*d*) basis sets on Met-Gly, Met-Ala, Met-Ser, Met-Cys, Met-Thr, Gly, Ala, Cys, Ser, Thr, Met, and water. Energy minimum molecular geometries were located by minimizing energy with respect to all geometrical coordinates without imposing any constraints. The nature of the stationary points for compounds has been fixed by the imaginary frequencies. For minimum state structures, only real frequency values were accepted. The vibrational frequencies of optimized molecules were calculated in temperature of 298.150 K and pressure of 1.0 atm by using same method and basis set for optimization. The binding energies for all of the five dipeptides were calculated at all of the above theoretical methods, with and without the *ZPE*. The thermodynamic functions (all corrected for the zero point energy), i.e., E_0, enthalpy H (sum of electronic and thermal enthalpy), Gibbs free energy G (sum of electronic and thermal free energy) and entropy S, were calculated according to the following relations:

$$E = E_0 + E_{vib} + E_{rot} + E_{trans},$$

$$H = E + RT, \quad G = H - TS,$$

as defined in the output of the frequency calculation in GAUSSIAN manual. Finally, using the corresponding calculated thermodynamic data for initial and final states, ΔH, ΔS, ΔG were also determined.

In [15, 16] nuclear magnetic shielding calculations were carried out on optimized structures using same method and basis set for optimization and the values of symmetric shielding ($\Delta\sigma$) and asymmetry shielding (η) were calculated by below formulas:

$$\sigma_{iso} = \frac{1}{3}(\sigma_{11} + \sigma_{22} + \sigma_{33}), \quad (1)$$

$$\Delta\sigma = \sigma_{33} - \frac{1}{2}(\sigma_{11} + \sigma_{22}), \quad (2)$$

and

$$\eta = |\sigma_{22} - \sigma_{11}|/|\sigma_{33} - \sigma_{iso}|. \quad (3)$$

NBO analysis was then performed on optimized structures by using the same method and basis set for optimization by the NBO 3.1 program [17, 18]. The natural charges of N1, C2, O4 atoms, the bonding and antibonding orbital occupancies in the optimized structures of compounds 1–5, the stabilization energies associated with $\sigma_{N1-C2} \longrightarrow \sigma^*_{C2-O4}$, $\sigma_{N1-C2} \longrightarrow \sigma^*_{N1-C3}$, $\pi_{C2-O4} \longrightarrow \pi^*_{C2-O4}$ delocalizations and also σ_{N1-C2} and σ_{C2-O4} bonds deviation were calculated by using NBO analysis. In the NBO analysis, the electronic wave functions are interpreted, in terms of a set of occupied Lewis and a set of unoccupied non-Lewis localized orbitals. The delocalization effects (or donor–acceptor charge transfers) can be estimated from the presence of off-diagonal elements of the Fock matrix in the NBO basis. The NBO program searches for an optimal natural Lewis structure, which has the maximum occupancy of its occupied NBOs, and in general agrees with the pattern of bonds and lone pairs of the standard structural Lewis formula. Therefore, the new orbitals are more stable than pure Lewis orbitals, stabilizing the wave function and giving a set of molecular orbital equivalent to canonical molecular orbital. All calculations in present work were performed by using the GAUSSIN 98 program [19].

RESULTS AND DISCUSSION

Hartree–Fock and Beck's three parameter hybrid with the Lee–Yang–Parr correlation functional, B3LYP, methods with the 3-21G(*d*), 6-31G(*d*), 6-311G, 6-311G(*d*) and 6-311+G(*d*) basis sets were used for geometry optimizations of dipeptides 1–5 and involved amino acids in them. Binding energies for dipeptides were calculated as the difference between the sum of the equilibrium energies from the two individual amino acids in the initial state and that from the final state (dipeptide molecule + water).

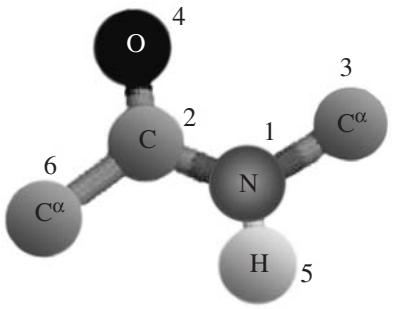

Fig. 1. The structure of the peptide bond taken from considered dipeptides in present work.

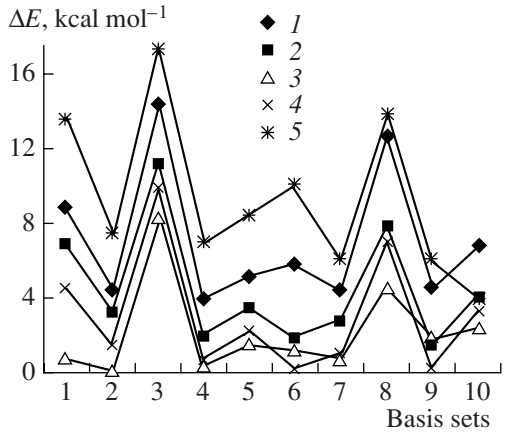

Fig. 2. Graphical representation of the binding energies of the five depiptide molecules calculated at HF and DFT levels with different basis sets; *1*—Met-Gly, *2*—Met-Ala, *3*—Met-Ser, *4*—Met-Cys, *5*—Met-Thr.

The obtained results demonstrated that Met-Thr has the highest binding energy and enthalpy among all of the considered dipeptide molecules at all levels of calculations, (see Table 1, Figs. 1 and 2). These numerical results suggest that Thr donates the proton easier than other four amino acids and has the most tendency to join with methionine and it forms the most strong bond with methionine. This fact may be the reason behind the obtained high binding energies for Met-Thr at all levels. From comparison of the values of binding energy and enthalpy for dipeptides in different levels of theory, we could identify that the order of tendency for joint with methionine is Thr > Gly > Ala > Cys > Ser. In addition, the thermochemistry calculations showed that Met-Thr has also the highest Gibbs free energy among these compounds. Hence; the formation of peptide bond in Met-Thr is the most spontaneity process among these five processes.

These results also revealed that Met-Ser has the highest ZPE^c of binding and the lowest binding Gibbs free energy among five considered dipeptide molecules at all levels of calculations. These results may be explained based on this fact that there is a hydroxyl functional group in the structure of serine amino acid.

Furthermore, the energetic and thermochemistry data represented that the highest binding energy, enthalpy and Gibbs free energy provide in HF/6-311G level for all of the compounds 1–5.

The total of the obtained results indicated that the split valance basis set of 6-311G makes the highest binding energy, enthalpy, Gibbs free energy and dipole moment for considered dipeptides in both HF and DFT level of theory. Now, we investigate the effect of basis sets and electron correlations on properties of dipeptides 1–5.

Corrected zero-point energy. The energy of the zero-point vibrational frequency is different in the initial and final states. This difference is termed here as ZPE^c. As it can be seen, Table 1 demonstrated the basis set and electron correlation effects on ZPE^c of binding of dipeptides. These data reveal that both split valance (6-311G(*d*) vs. 6-31G(*d*) results) and polarized (6-311G(*d*) vs. 6-31G results) basis sets increase ZPE^c of binding in all cases. While the effect of grown basis set (6-31G(*d*) vs. 3-21G(*d*) results) and diffuse functions (6-311G(*d*) vs. 6-311+G(*d*) results) is negligible on ZPE^c of binding. These results recall that electron correlations in DFT level decrease evidently ZPE^c in these compounds. It is interesting to note that the electron correlation effect on ZPE^c is dependent to dipeptide structure in some extent.

Binding energy. Table 1 also allows an analysis of the influence of basis set at the different levels of theory on binding energy. As it is observed, the grown basis set decrease binding energy extremely in these molecules. This deduction is the more evident in Hartree–Fock level. For example, binding energy of Met-Thr decreases from 13.6660 to 7.3164 kcal mol^{-1}. The split valance of basis set decrease slowly binding energy in most occasions. Adding polarized functions also decrease severely binding energy in both HF and DFT level. On the other hand, additions of diffuse functions to heavy atoms increase obviously binding energy in most cases. Furthermore, these results recall that electron correlations often decrease binding energy. But, they are almost dependent to dipeptide structure. For instance, electron correlations cause to sever deduction of binding energy of Met-Thr in all cases. Contrary, they cause to increase binding energy of Met-Ser in most occasions. We point out that the effect of basis sets and electron correlations on binding E_0 is the same as binding energy.

Binding enthalpy. The obtained results reveal that the grown basis set decrease relatively intense binding enthalpy in most cases and the most deduction is seen in Met-Thr. Also, the split valance of basis set decrease binding enthalpy in these molecules. Moreover, adding polarized functions decrease strongly binding enthalpy, while additions of diffuse functions to heavy atoms increase binding enthalpy in all occasions. At last, the electron correlations decrease binding enthalpy. How-

Table 1. Calculated binding energies (kcal mol^{-1}), calculated thermodynamic functions (enthalpies, Gibbs free energies (kcal mol^{-1}) and entropies (in kcal mol^{-1} K^{-1})), the dipole moment values (μ, D), symmetric (Δσ), and asymmetric (η) chemical shielding (ppm), for dipeptides 1–5 in different levels of theory

Method	ΔZPE^c	ΔE	ΔE_0	ΔH	ΔS	ΔG	μ	Δσ			η		
								N1	C2	O4	N1	C2	O4
Met-Gly													
HF/3-21G*	1.283	8.866	10.149	9.384	0.00485	7.939	6.080	−40.197	52.427	40.234	−0.589	4.117	10.877
HF/6-31G*	1.568	4.510	6.078	5.375	0.00588	3.623	6.399	−11.197	78.271	282.950	−5.584	2.033	0.512
HF/6-311G	1.125	14.420	15.545	14.213	−0.00077	14.458	7.448	−35.812	56.687	78.687	15.267	4.323	5.960
HF/6-311G*	1.679	3.997	5.676	4.792	0.00679	2.742	6.376	−22.633	78.693	249.813	3.141	2.347	0.839
HF/6-311 + G*	1.704	5.156	6.860	5.958	0.00469	0.559	6.551	−26.521	69.813	187.436	−2.256	1.691	1.381
B3LYP/3-21G*	1.438	5.777	7.215	6.467	0.00306	0.555	5.636	25.657	81.983	377.976	−3.503	1.806	0.087
B3LYP/6-31G*	1.535	4.383	5.918	5.117	0.00416	3.878	5.458	−4.472	61.738	129.152	−14.030	2.699	2.112
B3LYP/6-311G	0.990	12.600	13.589	12.361	−0.00047	12.233	6.302	−124.128	2.609	−453.6	0.488	104.064	2.023
B3LYP/6-311G*	1.549	4.527	6.076	5.211	0.00374	4.093	5.631	−66.280	42.767	−88.678	0.295	4.968	5.953
B3LYP/6-311+G*	1.536	6.861	8.397	7.576	0.00445	6.248	5.802	−77.708	31.407	−172.371	0.061	7.100	3.380
Met-Ala													
HF/3-21G*	1.643	6.971	8.614	7.668	0.00574	5.969	7.516	−2.570	36.091	28.033	19.891	2.850	10.016
HF/6-31G*	1.803	3.142	4.944	4.0424	0.00418	2.797	6.743	−20.385	−13.062	−171.203	0.849	−11.394	2.710
HF/6-311G	1.623	11.239	12.861	11.890	0.00564	10.206	8.307	−30.996	−24.160	−224.501	1.018	10.354	2.674
HF/6-311G*	1.986	2.021	4.007	2.864	0.00409	1.625	6.794	−25.506	−8.889	−190.436	0.368	18.568	2.636
HF/6-311 + G*	1.941	3.393	5.334	4.223	0.00452	2.875	6.906	−32.123	−17.040	−212.990	0.276	10.108	2.429
B3LYP/3-21G*	1.884	1.886	3.770	2.743	0.00416	1.502	6.999	−14.130	25.274	−29.222	2.528	3.838	9.384
B3LYP/6-31G*	1.804	2.728	4.532	3.515	0.00515	1.980	6.437	−33.642	−13.672	−209.435	0.206	10.560	2.216
B3LYP/6-311G	1.561	7.852	9.413	8.485	0.00627	6.349	7.789	−46.048	−22.120	−269.932	0.359	8.541	2.111
B3LYP/6-311G*	–	1.512	–	–	–	–	6.515	−38.260	−9.915	−228.186	−0.056	16.525	2.299
B3LYP/6-311+G*	1.806	4.044	5.850	4.810	0.00452	3.256	6.747	−46.582	−21.274	−262.350	−9.026	8.225	2.049
Met-Ser													
HF/3-21G*	2.119	0.769	2.888	1.599	0.00203	0.996	2.379	−91.604	22.204	−163.82	0.334	1.578	0.342
HF/6-31G*	1.920	0.154	2.074	1.173	0.00125	0.801	2.289	−99.017	−0.961	−299.46	0.228	95.379	0.918
HF/6-311G	1.874	8.327	10.200	8.939	0.00138	8.526	2.677	−124.960	−42.341	−377.845	0.207	16.546	1.074
HF/6-311G*	2.329	−0.424	1.905	0.521	0.00102	0.216	2.395	−111.389	4.700	−322.879	0.309	21.798	0.949
HF/6-311+G*	2.329	1.452	3.781	2.404	0.00128	2.022	2.344	86.584	−15.526	−323.47	−0.161	48.229	0.933

Table 1. (Contd.)

Method	ΔZPE^c	ΔE	ΔE_0	ΔH	ΔS	ΔG	μ	Δσ			η		
								N1	C2	O4	N1	C2	O4
B3LYP/3-21G*	1.692	1.259	2.952	2.017	0.00509	0.500	4.960	−80.598	27.240	−198.15	0.669	1.289	0.581
B3LYP/6-31G*	1.795	0.650	2.445	1.392	0.00412	0.166	4.943	−230.741	15.894	−101.29	0.708	4.135	0.215
B3LYP/6-311G	1.843	4.528	6.371	5.147	0.00246	4.146	2.796	−125.592	16.292	−326.051	0.101	0.064	0.620
B3LYP/6-311G*	2.243	1.822	4.064	0.947	0.00146	−1.382	2.621	−116.816	24.801	−277.506	0.028	0.469	0.628
B3LYP/6-311+G*	1.955	2.406	4.361	3.202	0.00089	2.941	5.174	−127.602	14.640	−375.150	−0.029	6.704	0.837
						Met-Cys							
HF/3-21G*	1.904	4.545	6.449	5.282	0.00189	4.720	5.112	−39.166	9.006	−242.190	0.401	20.004	2.293
HF/6-31G*	1.708	1.485	3.192	2.374	0.00140	1.958	5.489	−54.946	−14.990	−369.960	0.593	14.015	1.905
HF/6-311G	1.558	9.885	11.443	10.367	0.00248	9.626	6.263	−69.269	−27.299	−439.614	−0.270	10.140	1.966
HF/6-311G*	2.105	0.642	2.748	1.485	0.00124	1.116	5.484	−63.738	−8.718	−389.900	0.491	25.807	1.916
HF/6-311 + G*	2.108	2.156	4.263	3.006	0.00138	2.594	5.616	−12.103	123.490	−388.618	18.647	−0.457	1.888
B3LYP/3-21G*	2.049	0.2496	2.298	1.133	0.00192	0.658	4.262	−35.793	30.587	−83.897	0.503	4.235	3.993
B3LYP/6-31G*	1.882	1.0387	2.9205	1.774	0.00048	1.631	4.738	−61.803	−1.848	−397.725	−0.366	−96.868	1.662
B3LYP/6-311G	1.549	7.060	8.609	7.553	0.00169	6.782	5.256	−0.285	−6.510	470.300	−78.850	35.119	1.659
B3LYP/6-311G*	1.923	0.358	2.280	1.065	0.00053	0.910	4.750	−77.089	−53.204	−414.776	−0.544	31.249	1.710
B3LYP/6-311+G*	1.977	3.293	5.270	4.431	0.00054	3.882	4.940	−80.788	1.673	−410.345	−0.372	119.092	1.691
						Met-Thr							
HF/3-21G*	1.067	13.666	14.733	13.928	0.00806	11.526	2.463	−95.364	3.627	−305.790	0.4593	4.241	0.135
HF/6-31G*	1.635	7.316	8.951	8.188	0.00347	7.1549	2.633	−96.338	−11.330	−347.860	0.191	6.197	0.640
HF/6-311G	1.1496	17.336	18.486	17.599	0.00614	15.769	6.093	−119.314	−392.560	−19.543	0.256	0.527	3.497
HF/6-311G*	1.962	7.004	8.965	7.793	0.00362	6.714	5.158	−108.679	−5.629	−362.795	0.173	13.216	0.641
HF/6-311 + G*	3.106	8.511	11.617	9.292	0.00702	11.634	4.991	−110.108	−9.145	−357.779	0.177	7.927	0.626
B3LYP/3-21G*	1.039	9.980	11.020	10.319	0.00995	7.352	5.866	−99.624	15.886	−215.574	0.473	0.026	−0.023
B3LYP/6-31G*	1.822	6.207	8.029	6.925	0.00324	5.958	4.985	−101.290	15.894	−302.741	0.215	4.135	0.708
B3LYP/6-311G	1.069	13.728	14.797	13.994	0.00702	11.634	5.869	−124.485	4.428	−376.111	0.484	4.777	0.164
B3LYP/6-311G*	1.823	6.094	7.917	6.765	0.00299	5.874	5.127	−118.688	11.643	−346.337	0.445	2.833	0.283
B3LYP/6-311+G*	1.720	8.810	10.529	9.438	0.00448	8.103	4.674	31.948	−1.936	−341.022	0.390	4.419	0.298

Note: Values ΔZPE^c corrected by multiplying by scaling factors 0.8929 and 0.9804 in HF/6-31G(*d*) and B3LYP/6-31G(*d*) levels of theory, respectively.

ever, this deduction is comparatively dependent to dipeptide structure and basis set type. For example, the electron correlations with 3-21G(*d*) basis set decrease binding enthalpy in most occasions, while they with 6-311+G(*d*) basis set increase binding enthalpy in all cases (see Table 1).

Binding entropy. As it is observed in Table 1, the grown basis set often decrease binding entropy in these molecules. The split valance of basis set hasn't specific effect on binding entropy in most cases. Adding polarized functions also decrease binding entropy in both HF and DFT level. On the other hand, additions of diffuse functions to heavy atoms increase binding entropy in most occasions. Contrary, the electron correlations decrease binding entropy. But, they are almost dependent to dipeptide structure.

Binding Gibbs energy. The table data reveal that the grown basis set decrease binding Gibbs free energy in most cases. Also, the split valance of basis set often decrease binding free energy in these molecules. Moreover, adding polarized functions decrease strongly binding free energy in all cases. But, additions of diffuse functions to heavy atoms increase binding free energy in dipeptides. At last, the electron correlations decrease binding free energy. However, this deduction is relatively dependent to dipeptide structure. For instance, the electron correlations decrease binding free energy in Met-Thr in all cases; while they increase binding free energy in Met-Gly in most cases (see Table 1).

Dipole moment. We were reported dipole moment of dipeptide molecules in Table 1 at different levels of theory. The results of all methods reveal that Met-Ala and Met-Ser have the highest and lowest dipole moment, respectively, among these compounds. The greatest dipole moment also is perceived in HF/6-311G level of theory for mentioned dipeptides (the values of 7.4480, 8.3067, 2.6769, 6.2632 and 6.0928 D, respectively, for compounds 1–5). The table data demonstrate that the grown basis set hasn't main effect on dipole moment of dipeptides. But, split valance of basis set often increase dipole moment, while adding polarized functions to heavy atoms decrease dipole moment in all cases. In addition, the addition of diffuse functions increases dipole moment in these dipeptides. Here, it is pointed out that the electron correlation effects in DFT level on dipole moment is almost dependent to dipeptide structure. For example, the electron correlations decrease dipole moment in Met-Gly, Met-Ala, and Met-Cys. However, they increase dipole moment in Met-Ser.

The peptide bond length. Table 2 shows the effect of basis sets and electron correlations on peptide bond length. The table data demonstrate that grown basis set and adding polarized functions increase peptide bond length, while diffuse functions decrease peptide bond length in most occasions. But, split valance of basis set hasn't important effect on peptide bond length. Electron correlations also increase evidently peptide bond length in most cases. So, it can be concluded that the results of basis set and electron correlation effects on peptide bond length are in reasonable agreement with energetic and thermochemistry results. In addition, the results of X-ray crystallographic studies on similar molecules represent that peptide bond length (N1–C2) is in range of 1.32–1.33 Å [20]. Therefore, the data deviation of experimental values is in range of 0.01–0.04 Å. These results also indicate that B3LYP method overestimates the bond distances and HF/6-311 level makes the most correlation with experimental values. The above deviations in the geometrical parameters between the experimental and theoretical values can be accounted for from the fact that the structure determined for the solid state involves the intermolecular interactions whereas the results of the calculations are applicable to the gas phase.

Atomic charges. Based on calculated charges by using NBO, can be revealed that the grown basis set increase positive and negative charges on involved atoms in peptide bond (N1, C2, O4), while split valance of basis set decrease negative charge on N1 atom and increase positive and negative charges on atoms of carbonyl group (C, O). It is an interesting point which split valance of basis set makes differences between atomic species, on the other hand, adding polarized functions to heavy atoms increase positive and negative charges on N1, C2, O4 atoms of peptide bond. But, addition of diffuse functions increase negative charge on N atom and decrease atomic charges on atoms of carbonyl group (C2, O4) in most occasions. So, diffuse basis sets also make differences between atomic types. Electron correlations decrease severely positive and negative charges on involved atoms in peptide bond in all cases (see Table 2).

Resonance energy. From data of Table 2, we can conclude that the resonance energy for $\sigma_{N1-C2} \longrightarrow \sigma^*_{C2-O4}$, $\sigma_{N1-C2} \longrightarrow \sigma^*_{N1-C3}$, $\pi_{C2-O4} \longrightarrow \pi^*_{C2-O4}$ delocalizations often decrease with grown basis set. Contrary, resonance energy of these elocalizations increase by increasing of split valance in most cases. Also, adding polarized functions increase resonance energy for $\sigma_{N1-C2} \longrightarrow \sigma^*_{C2-O4}$, $\sigma_{N1-C2} \longrightarrow \sigma^*_{N1-C3}$ delocalizations and decrease resonance energy for $\pi_{C2-O4} \longrightarrow \pi^*_{C2-O4}$ delocalization. So, it can be revealed that polarized functions make differences in influence on delocalization. But, addition of diffuse functions to heavy atoms decrease all of the considered delocalizations in most occasions.

Moreover, electron correlations result the deduction of resonance energy for $\sigma_{N1-C2} \longrightarrow \sigma^*_{C2-O4}$, $\sigma_{N1-C2} \longrightarrow \sigma^*_{N1-C3}$ delocalizations while they result the increase of resonance energy for $\pi_{C2-O4} \longrightarrow \pi^*_{C2-O4}$ delocalization. Consequently, electron correlations also make differences in influence of resonance energy delocalizations.

Table 2. Calculated bond length, natural charges, resonance energies (E_2), bonding and antibonding orbital occupancies, σ bonds deviation (Dev) for involved atoms and bonds in peptide bond of dipeptides 1–5 using NBO analysis based on the optimized structures in different levels of theory

Method	Bond length N1–C2	Natural charges			E_2 (kcal mol^{-1})			Occupancies						Dev σ_{N1-C2}	Dev σ_{C2-O4}
		N1	C2	O4	$\sigma_{N1-C2} \rightarrow \sigma^*_{C2-O4}$	$\sigma_{N1-C2} \rightarrow \sigma^*_{N1-C3}$	$\pi_{C2-O4} \rightarrow \pi^*_{C2-O4}$	σ_{N1-C2}	σ_{C2-O4}	π_{C2-O4}	σ^*_{N1-C2}	σ^*_{C2-O4}	π^*_{C2-O4}		
Met-Gly															
HF/3-21G*	1.347	–0.76680	0.8022	–0.67222	–	2.34	1.14	1.99144	1.99604	1.99238	0.06073	0.03607	0.20279	N – C 4.5	C 20.3 O 25.5
HF/6-31G*	1.349	–0.74217	0.84447	–0.73042	0.84	1.53	1.13	1.98965	1.99395	1.99131	0.05912	0.03573	0.18820	N – C 3.2	C 21.3 O 25.3
HF/6-311G	1.344	–0.68391	0.79998	–0.73540	1.05	1.51	1.90	1.98979	1.99116	1.98900	0.05287	0.04697	0.20242	N – C 3.2	C 24.5 O 27.4
HF/6-311G*	1.349	–0.70424	0.84688	–0.73020	1.60	1.60	1.12	1.98931	1.99303	1.99045	0.05924	0.03188	0.19046	N 1.0 C 3.4	C 20.0 O 23.4
HF/6-311+G*	1.348	–0.71300	0.83415	–0.72981	1.19	1.39	1.38	1.99015	1.99221	1.98971	0.05861	0.03890	0.18927	N – C 3.5	C 27.9 O 27.0
B3LYP/3-21G*	1.359	–0.65875	0.62577	–0.56107	–	1.57	1.12	1.99115	1.99640	1.99186	0.07707	0.06537	0.26820	N 1.4 C 5.6	C 25.2 O 30.4
B3LYP/6-31G*	1.362	–0.66013	0.69105	–0.63382	0.61	1.28	1.21	1.98961	1.99485	1.99173	0.07371	0.04480	0.26109	N – C 4.4	C 21.6 O 25.2
B3LYP/6-311G	1.358	–0.61073	0.65886	–0.64854	0.68	1.21	1.66	1.98898	1.99311	1.99036	0.06750	0.06370	0.26841	N – C 4.7	C 26.2 O 28.8
B3LYP/6-311G*	1.359	–0.63111	0.70185	–0.64659	1.11	1.32	1.22	1.98841	1.99375	1.99081	0.07313	0.03831	0.26604	N – C 4.5	C 19.6 O 22.4
B3LYP/6-311+G*	1.359	–0.63791	0.68546	–0.64769	0.85	1.10	1.37	1.98954	1.99292	1.99035	0.07303	0.05086	0.25721	N 1.6 C 4.0	C 27.9 O 26.9
Met-Ala															
HF/3-21G*	1.342	–0.75076	0.81205	–0.70679	–	2.26	1.22	1.99249	1.99550	1.98403	0.05421	0.01555	0.24899	N 1.2 C 3.1	C 4.8 O 6.0
HF/6-31G*	1.344	–0.73520	0.84924	–0.77282	0.71	1.78	0.77	1.99066	1.99449	1.99025	0.05457	0.01402	0.22849	N – C 2.4	C 4.8 O 5.8
HF/6-311G	1.345	–0.69313	0.81283	–0.77602	0.86	1.58	1.97	1.98967	1.98998	1.98749	0.04904	0.04001	0.22149	N 1.6 C 2.1	C 19.1 O 21.5
HF/6-311G*	1.345	–0.70343	0.85387	–0.77687	1.33	1.83	1.29	1.98913	1.99168	1.98967	0.05471	0.02930	0.21161	N 1.6 C 2.5	C 15.8 O 18.6
HF/6-311+G*	1.345	–0.70652	0.83857	–0.77269	1.04	1.48	1.22	1.99034	1.99171	1.98996	0.05500	0.02703	0.21522	N – C 3.1	C 17.8 O 17.5
B3LYP/3-21G*	1.348	–0.62603	0.64274	–0.58640	–	1.41	2.16	1.99308	1.99450	1.97717	0.06251	0.02195	0.35361	N 1.2 C 3.1	C 6.3 O 7.5

Table 2. (Contd.)

Method	Bond length N1–C2	Natural charges			E_2 (kcal mol^{-1})			Occupancies						Dev σ_{N1-C2}	Dev σ_{C2-O4}
		N1	C2	O4	$\sigma_{N1-C2} \rightarrow \sigma^*_{C2-O4}$	$\sigma_{N1-C2} \rightarrow \sigma^*_{N1-C3}$	$\pi_{C2-O4} \rightarrow \pi^*_{C2-O4}$	σ_{N1-C2}	σ_{C2-O4}	π_{C2-O4}	σ^*_{N1-C2}	σ^*_{C2-O4}	π^*_{C2-O4}		
B3LYP/6-31G*	1.352	–0.64013	0.69419	–0.67415	–	1.28	1.39	1.99131	1.99397	1.98477	0.06329	0.01854	0.32036	N – C 2.6	C 5.8 O 6.8
B3LYP/6-311G	1.355	–0.60428	0.67157	–0.68793	0.53	1.17	2.17	1.99014	1.99138	1.98393	0.05884	0.04373	0.31352	N 1.6 C 2.4	C 17.0 O 18.8
B3LYP/6-311G*	1.352	–0.61816	0.70709	–0.69121	0.88	1.36	1.57	1.98941	1.99216	1.98570	0.06350	0.03158	0.30232	N 1.6 C 2.6	C 13.4 O 15.5
B3LYP/6-311+G*	1.353	–0.61971	0.68793	–0.68944	0.72	1.06	1.57	1.99052	1.99179	1.98621	0.06461	0.03212	0.30208	N – C 3.2	C 16.0 O 15.6
Met-Ser															
HF/3-21G*	1.348	–0.76709	0.80322	–0.67675	–	2.62	1.07	1.99199	1.99558	1.99249	0.05992	0.01796	0.22009	N 1.8 C 3.3	C 9.4 O 12.0
HF/6-31G*	1.349	–0.74076	0.84666	–0.73973	0.91	2.01	0.68	1.99000	1.99445	1.99338	0.05947	0.01427	0.21023	N – C 2.8	C 6.9 O 8.3
HF/6-311G	1.349	–0.69633	0.80466	–0.73581	1.08	1.81	1.04	1.98874	1.99254	1.99216	0.05343	0.01695	0.22164	N 1.7 C 2.6	C 10.2 O 11.7
HF/6-311G*	1.350	–0.70578	0.85014	–0.73984	1.66	2.00	0.64	1.98847	1.99341	1.99358	0.05972	0.01173	0.20932	N 1.7 C 3.0	C 3.7 O 4.0
HF/6-311+G*	1.350	–0.71222	0.84074	–0.73615	1.28	1.64	0.62	1.98999	1.99337	1.99299	0.05948	0.01287	0.20904	N 1.7 C 3.0	C 4.6 O 4.2
B3LYP/3-21G*	1.371	–0.65075	0.64701	–0.54855	–	1.75	1.53	1.99147	1.99502	1.99211	0.07949	0.01683	0.28753	N 1.8 C 3.5	C 7.6 O 8.9
B3LYP/6-31G*	1.368	–0.65461	0.69970	–0.62727	0.58	1.54	1.06	1.98988	1.99425	1.99247	0.07667	0.01348	0.27562	N 1.0 C 3.1	C 4.0 O 4.5
B3LYP/6-311G	1.363	–0.61798	0.66340	–0.64581	0.71	1.36	1.47	1.98883	1.99259	1.99099	0.06799	0.01516	0.29982	N 1.9 C 3.0	C 3.5 O 3.6
B3LYP/6-311G*	1.360	–0.63076	0.70360	–0.65086	1.09	1.55	1.10	1.98832	1.99294	1.99159	0.07285	0.01589	0.28112	N 1.9 C 3.2	C 5.8 O 6.6
B3LYP/6-311+G*	1.366	–0.62751	0.69509	–0.63875	0.81	1.28	0.99	1.98945	1.99283	1.99169	0.07730	0.01541	0.27368	N – C 3.7	C 5.4 O 5.2
Met-Cys															
HF/3-21G*	1.353	–0.76766	0.81086	–0.66670	–	2.43	0.89	1.99182	1.99584	1.99287	0.06033	0.01056	0.21858	N 1.6 C 3.6	C 3.2 O 3.5
HF/6-31G*	1.353	–0.74380	0.85753	–0.73414	0.90	1.92	0.58	1.99024	1.99466	1.99390	0.06048	0.01058	0.20680	N – C 2.7	C 1.2 O –
HF/6-311G	1.352	–0.69897	0.81760	–0.73036	1.14	1.75	0.94	1.98878	1.99260	1.99253	0.05413	0.01418	0.21704	N 1.8 C 2.5	C 7.9 O 8.7

Table 2. (Contd.)

Method	Bond length N1–C2	Natural charges			E_2 (kcal mol^{-1})			Occupancies						Dev σ_{N1-C2}	Dev σ_{C2-O4}
		N1	C2	O4	$\sigma_{N1-C2} \rightarrow \sigma^*_{C2-O4}$	$\sigma_{N1-C2} \rightarrow \sigma^*_{N1-C3}$	$\pi_{C2-O4} \rightarrow \pi^*_{C2-O4}$	σ_{N1-C2}	σ_{C2-O4}	π_{C2-O4}	σ^*_{N1-C2}	σ^*_{C2-O4}	π^*_{C2-O4}		
HF/6-311G*	1.354	–0.70999	0.86272	–0.73365	1.66	1.95	0.60	1.98846	1.99333	1.99354	0.06073	0.01044	0.20367	N 1.8 C 2.9	C 2.6 O 2.4
HF/6-311+G*	1.354	–0.71481	0.84894	–0.73074	1.27	1.59	0.60	1.98994	1.99335	1.99318	0.06078	0.01220	0.20381	N – C 3.4	C 4.3 O 4.3
B3LYP/3-21G*	1.363	–0.65327	0.64274	–0.55632	–	1.55	1.54	1.99187	1.99492	1.98938	0.07305	0.01230	0.30129	N 2.0 C 3.5	C 1.2 O –
B3LYP/6-31G*	1.366	–0.65766	0.70252	–0.63112	0.59	1.40	1.03	1.99015	1.99425	1.99124	0.07359	0.01311	0.27826	N 1.1 C 3.1	C 4.1 O 4.5
B3LYP/6-311G	1.367	–0.61897	0.67672	–0.63879	0.69	1.29	1.43	1.98867	1.99258	1.99043	0.06864	0.01849	0.28865	N 1.8 C 3.0	C 9.1 O 9.9
B3LYP/6-311G*	1.366	–0.63323	0.71725	–0.64191	1.05	1.46	1.05	1.98799	1.99294	1.99105	0.07449	0.01644	0.27124	N 1.7 C 3.3	C 8.4 O 9.4
B3LYP/6-311+G*	1.366	–0.63551	0.69879	–0.64139	0.85	1.16	0.99	1.98943	1.99280	1.99102	0.07480	0.01494	0.27467	N – C 3.6	C 5.2 O 4.8
Met-Thr															
HF/3-21G*	1.352	–0.76436	0.81187	–0.67781	–	2.83	0.99	1.99130	1.99583	1.99393	0.06149	0.01242	0.21952	N 1.6 C 3.5	C 5.4 O 6.5
HF/6-31G*	1.351	–0.73324	0.85605	–0.74260	0.77	2.15	1.21	1.98952	1.99313	1.99216	0.05966	0.03574	0.18626	N 1.1 C 2.7	C 21.1 O 25.4
HF/6-311G	1.348	–0.68959	0.81591	–0.74394	1.08	2.05	1.19	1.98797	1.99201	1.99245	0.05360	0.02166	0.21665	N 1.9 C 2.5	C 12.8 O 14.7
HF/6-311G*	1.351	–0.70120	0.86057	–0.74400	1.36	2.21	1.44	1.98757	1.99138	1.99116	0.05982	0.04433	0.17717	N 2.9 C 1.9	C 24.9 O 29.3
HF/6-311+G*	1.350	–0.70340	0.84854	–0.74244	0.91	1.86	1.94	1.98948	1.98969	1.98918	0.05958	0.06653	0.16210	N – C 3.8	C 37.8 O 37.9
B3LYP/3-21G*	1.366	–0.65761	0.64457	–0.55962	–	1.80	1.52	1.99146	1.99519	1.99176	0.07700	0.02203	0.28693	N 1.9 C 3.7	C 10.5 O 12.7
B3LYP/6-31G*	1.365	–0.65302	0.70140	–0.63881	0.60	1.63	1.07	1.98961	1.99434	1.99242	0.07322	0.01291	0.27989	N 1.2 C 3.0	C 2.4 O 2.5
B3LYP/6-311G	1.363	–0.61602	0.67371	–0.64988	0.66	1.54	1.56	1.98785	1.99243	1.99117	0.06777	0.02770	0.28509	N 2.9 C 2.0	C 13.6 O 15.1
B3LYP/6-311G*	1.363	–0.62991	0.71417	–0.65266	1.06	1.72	1.07	1.98721	1.99299	1.99227	0.07324	0.01276	0.27883	N 2.0 C 3.1	C 1.5 O –
B3LYP/6-311+G*	1.362	–0.62703	0.69619	–0.65402	0.87	1.40	1.07	1.98919	1.99274	1.99228	0.07341	0.01634	0.28113	N – C 3.9	C 6.4 O 6.0

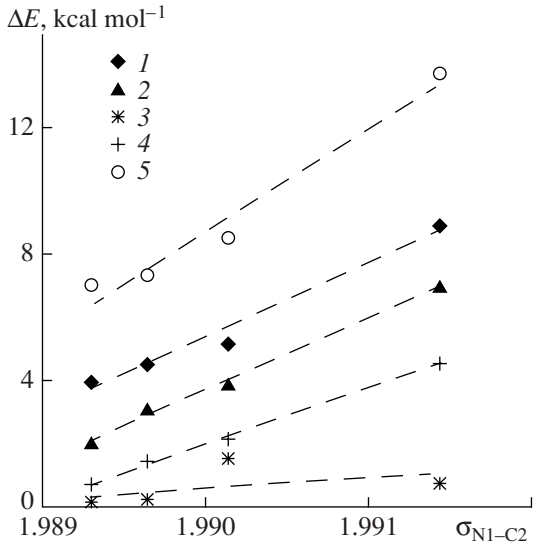

Fig. 3. Calculated binding energies for dipeptides 1–5, plotted as a function of $\sigma_{Nl–C2}$ occupancies in HF level with different basis sets.

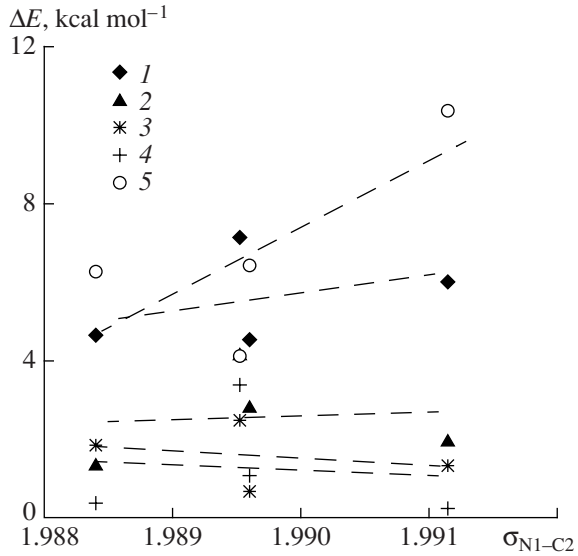

Fig. 4. Calculated binding energies for dipeptides 1–5, plotted as a function of $\sigma_{Nl–C2}$ occupancies in B3LYP level with different basis sets.

So, it is seen that the effect of electron correlations on resonance energy for $\sigma \longrightarrow \alpha^*$ delocalizations is in good agreement with energetic results.

Bonding and antibonding orbital occupancies. Table 2 shows the effect of basis sets and electron correlations on $\sigma_{N1–C2}$, $\sigma_{C2–O4}$, and $\pi_{C2–O4}$ bonding and $\sigma^*_{N1–C2}$, $\sigma^*_{C2–O4}$, and $\pi^*_{C2–O4}$ antibonding orbital occupancies of considered molecules. The results reveal that the considered σ and σ* bonding and antibonding orbital occupancies decrease with grown basis set. But, the $\pi_{C2–O4}$ bonding orbital occupancy increases in most cases. So, these data recall the effect of grown basis set is specified and make differences between molecular orbital types. Furthermore, split valance of basis set often decrease σ and π bonding orbital occupancies. But, they haven't the important effect on antibonding orbital occupancies. As it can be seen, adding polarized functions decrease $\sigma_{N1–C2}$, $\sigma^*_{C2–O4}$, and $\pi^*_{C2–O4}$ bonding and antibonding orbital occupancies and increase $\sigma_{C2–O4}$, $\pi_{C2–O4}$, and $\sigma^*_{N1–C2}$ bonding and antibonding orbital occupancies in most occasions. But, the addition of diffuse functions increase $\sigma_{N–C}$ bonding orbital occupancies and decrease $\sigma_{C2–O4}$, $\pi_{C2–O4}$ bonding orbital occupancies, while these functions haven't often the special effect on antibonding orbital occupancies.

Also, the electron correlations decrease $\sigma_{N1–C2}$, $\sigma_{C2–O4}$, and $\pi_{C2–O4}$ considered bonding orbital occupancies and increase $\sigma^*_{N1–C2}$, $\sigma^*_{C2–O4}$, and $\pi^*_{C2–O4}$ antibonding orbital occupancies. However, this effect is mostly dependent to dipeptide structure. For instance, electron correlations decrease σ and π bonding orbital occupancies in Met-Cys, while they increase σ and π bonding orbital occupancies in Met-Gly in most cases. So, based on the obtained results it can be revealed that the effect of basis sets and electron correlations on $\sigma_{N1–C2}$ bonding orbital occupancy is the same as the basis set and electron correlation effects on binding energy of dipeptides in all cases (see Figs. 3 and 4). As it is seen, linear relation between binding energy and $\sigma_{N1–C2}$ bonding orbital occupancy in HF level is more obvious.

Bonds deviation. Data of Table 2 reveal that the grown basis set decrease $\sigma_{N1–C2}$ bond deviation and increase $\sigma_{C2–O4}$ bond deviation. But, split valance and polarized basis sets increase $\sigma_{N1–C2}$ bond deviation in most cases. The addition of diffuse functions often increase $\sigma_{N1–C2}$ and $\sigma_{C2–O4}$ bonds deviation. Also, the electron correlations increase $\sigma_{N1–C2}$ bond deviation in most occasions. While they haven't mainly important effect on $\sigma_{C2–O4}$ bond deviation. So, it can be again concluded that the results of basis set and electron correlation effects on a bonds deviation of $\sigma_{C2–O4}$ peptide are in good agreement with energetic results in most cases.

Δσ and η values. From data of Table 1 be deduced that grown basis set often decrease Δσ and η. But, split valance of basis set decrease Δσ and increase η in most occasions. Then, split valance of basis set makes differences between shielding tensors. Polarized basis sets also increase considerably Δσ, while they haven't main effect on η in most cases. The addition of diffuse functions often decreases Δσ and η. Moreover, the electron correlations decrease Δσ and η in most occasions. But, these effects are dependent to dipeptide structure in some extent. For example, the electron correlations with 3-21G(*d*) basis set increase Δσ and decrease η in Met-Gly in all cases, while they decrease Δσ and η in Met-Ala in most occasions.

CONCLUSIONS

The above reported ab initio MO, DFT calculations and NBO and NMR analysis provide a reasonable picture from structural and energetic for the began dipeptides with methionine effectively, the results show that:

—Met-Thr has the highest binding energy and enthalpy among the considered dipeptide molecules at all levels of calculations;

—numerical results for binding energy suggest that Thr donates the proton easier than other four amino acids and it has the most tendency to join with methionine and it forms the most strong bond with methionine (This fact may be the reason behind the high binding energies of Met-Thr obtained at all levels);

—from comparison of the values of binding energy for dipeptides in different levels of theory was identified that Thr, Gly, Ala, Cys, Ser respectively have the most tendency to join with methionine;

—these data represented that the highest binding energy provide in HF/6-311G level for all of the dipeptides;

—the effect of basis set on binding energy and other properties of dipeptides is independent of computational methods and molecular structures;

—electron correlations effects are dependent to molecular structure of dipeptides and basis set type in most cases;

—the total of the obtained results indicated that the split valance basis set of 6-311G makes the highest binding energy, enthalpy, Gibbs free energy and dipole moment for considered dipeptides in both HF and B3LYP levels of theory.

In addition, NBO results revealed also that:

—based on the obtained results, it can be revealed that the effect of basis sets and electron correlations on σ_{N1-C2} bonding orbital occupancy is the same as the basis set and electron correlation effects on binding energy of dipeptides in all cases;

—in investigation the effect of basis sets and electron correlations on binding energy, the NBO results are in good agreement with the energetic and thermochemistry results for compounds 1–5 at all levels of calculations.

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REFERENCES

1. P. Chaudhuri and S. Canuto, THEOCHEM **577**, 267 (2002).
2. I. R. Gould, W. D. Cornell, and I. H. Hillier, J. Am. Chem. Soc. **116**, 9250 (1994).
3. T. Head-Gordon, M. Head-Gordon, M. J. Frisch, et al., J. Am. Chem. Soc. **113**, 5989 (1991).
4. H. Bohm and S. Brode, J. Am. Chem. Soc. **113**, 7129 (1991).
5. C. D. Keefe and J. K. Pearson, THEOCHEM **679**, 65 (2004).
6. Y. K. Kang and H. S. Park, THEOCHEM **593**, 55 (2002).
7. C. Benzi, R. Improta, G. Scalmani, and V. Barone, J. Comput. Chem. **23**, 341 (2002).
8. E. Langella, N. Rega, R. Improta, et al., J. Comput. Chem. **22**, 650 (2001).
9. B. B. Ivanova, THEOCHEM **782**, 122 (2006).
10. B. B. Ivanova and M. G. Arnaudov, Spectrochim. Acta, Part A **65**, 56 (2006).
11. J. Reedjic, Inorg. Chim. Acta **198**, 837 (1994).
12. J. Reedjic, Chem. Commun., p. 801 (1996).
13. D. Becke, J. Chem. Phys. **98**, 5648 (1993).
14. Lee, W. Yang and R. G. Parr, Phys. Rev. B: Condens. Matter **37**, 785 (1988).
15. R. Cammi, J. Chem. Phys. **109**, 3185 (1998).
16. R. Cammi and B. Mennucci, J. Chem. Phys. **110**, 7627 (1999).
17. E. D. Glendening, A. E. Reed, J. E. Carpenter, and F. Reinhold, *NBO Version 3.1*.
18. R. Reed, L. A. Curtiss and F. Weinhold, Chem. Rev. **88**, 899 (1988).
19. M. J. Frisch, G. W. Trucks, H. B. Schlegel, et al., *Gaussian 98* (Gaussian Inc., Pittsburgh PA, London, 1998).
20. L. Padmaja, C. Ravikumar, C. James, et al., Spectrochim. Acta, Part A (in press).