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Vibrational Frequencies of Amides and Amide Dimers: The Assessment of PW91$_{XC}$ Functional

George V. Papamokos and Ioannis N. Demetropoulos*

Department of Chemistry, Sector of Physical Chemistry, University of Ioannina, Panepistemioupoli Dourouti, 45110 Ioannina, Greece

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PW91$_{XC}$ functional has recently been assessed for the interaction energies of selected dimers in which the nonbonded interactions play a critical role. In this study, we assess the PW91$_{XC}$ functional with the 6-31+G* basis set for the vibrational spectra of amide and amide dimers. The set of molecules chosen consists of (a) the monomeric amides: formamide, acetamide, *cis*-NMF, *trans*-NMF, *N*,*N*-DMF, *cis*-NMA, *trans*-NMA, (b) the covalent dipeptides *N*-acetyl−glycine-*N*′-methylamide in C_7^{eq} and C_5 conformations and the C_7^{ax}, C_7^{eq}, C_5^{ext}, β_2, α_p conformers of *N*-acetyl-L-alanine-*N*′-methylamide, (c) the dimers *cis*-NMA cyclic dimer, two conformations of *trans*-NMA dimer and four conformations of formamide dimer. This set has been also used for the assessment of the EDF1 functional for the prediction of vibrational spectra. Comparison of PW91$_{XC}$/6-31+G* results with EDF1, B3LYP, and MP2 values with the same basis set accentuate PW91$_{XC}$ as the best performing functional for amide I and II modes while for amide III mode EDF1 performs better. Overall, PW91$_{XC}$ has the better performance with EDF1 following close. We propose that PW91 may be used for the study of proteins and polypeptidic chains.

1. Introduction

Density-functional theory has become a widely used tool for the calculation of the electronic structure and the properties of atoms, molecules, and solids.[1−4] It is an alternative solution for systems that demand electron correlation corrections but the computational cost that they entail under Møller−Plesset perturbation theory, configuration interaction, multiconfigurational self-consistent field, or coupled cluster techniques, makes molecular systems of polymer, material and biology science unapproachable. The accuracy of the method, employing one of the current functionals based on generalized gradient approximations (GGA), is in many cases of similar quality to MP2 results and some times, it surpasses it, while the computational cost is comparable to that of an RHF calculation.

In DFT, the ground-state molecular energy E_0 together with other ground-state molecular properties is calculated based on the ground-state electron density p_0, since in DF theory E_0 is a functional of p_0.[2,4] However, the density functionals are approximately described because the E_{xc} factor, the exchange and correlation functional, is not exactly known. Various approximate functionals have been developed but the main drawback of the theory remains: There is not a systematic procedure to improve such a functional.[2,4] Thus, the study of the accuracy of an E_{xc} dictates DF calculations employing the examined functional in a series of model molecules and comparison of the results with experimental data available in order to assess the accuracy of the method.

The emergence of new functionals in the scientific literature increases rapidly. A systematic study of the comparisons and assessments of the available functionals can drive anyone to the conclusion that the accuracy of results achieved is critically depended on the system that these functionals are applied to.[5−30]

Handy and Cohen[6] introduced another point of view related to the increasing number of new arising functionals stating that "...New DFT functionals are being presented at an increasing rate, at the risk of the subject being swamped and possibly the quality of such functionals not being reliably assessed and compared."

An answer to the comment above, could be the description of the future of DFT development, which has been pictured as "Jacob's ladder".[31,32] It applies mainly to the nonempirical approach, a classic strategy of physicists, although in a wider sense it can include the semiempirical approach, the refinement of hybrid functionals, a favorite strategy of chemists. The main goal of the development is the "divine" functional where exchange and correlation are treated exactly. Inevitably, critical questions are raised. Is the "divine" functional possible to reach? Is there a need for a third approach substantially different from the two main strategies?[31]

Nevertheless, many new emerging functionals have produced remarkably accurate results either for energetic and geometrical calculations or for a variety of properties of molecular systems of interest. One of the interesting fields of physical chemistry, in which DFT performs extremely well, with relatively low computational cost, is frequency calculations. Several studies[33−39] have shown that vibrational frequencies calculated employing DFT methods, agree well with experiment and are much superior to the Hartree−Fock (HF) theory. In many cases, the performance surpasses MP2 results.[40−42]

Why the computation of the frequencies is so important? New approaches in qualitative analysis brought forth new techniques such as Fourier self-deconvolution and second-derivative resolution enhancement.[43,44] Moreover, advances in Raman instrumentation such as Raman microscopy and 2D imaging entailed significant enrichment in the amount of data obtained from spectral observation. However, profound elucidation of spectroscopic information derived from experiment, demands ac-

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* To whom correspondence should be addressed. E-mail: idimitr@cc.uoi.gr. Fax: ++30-651-98798.

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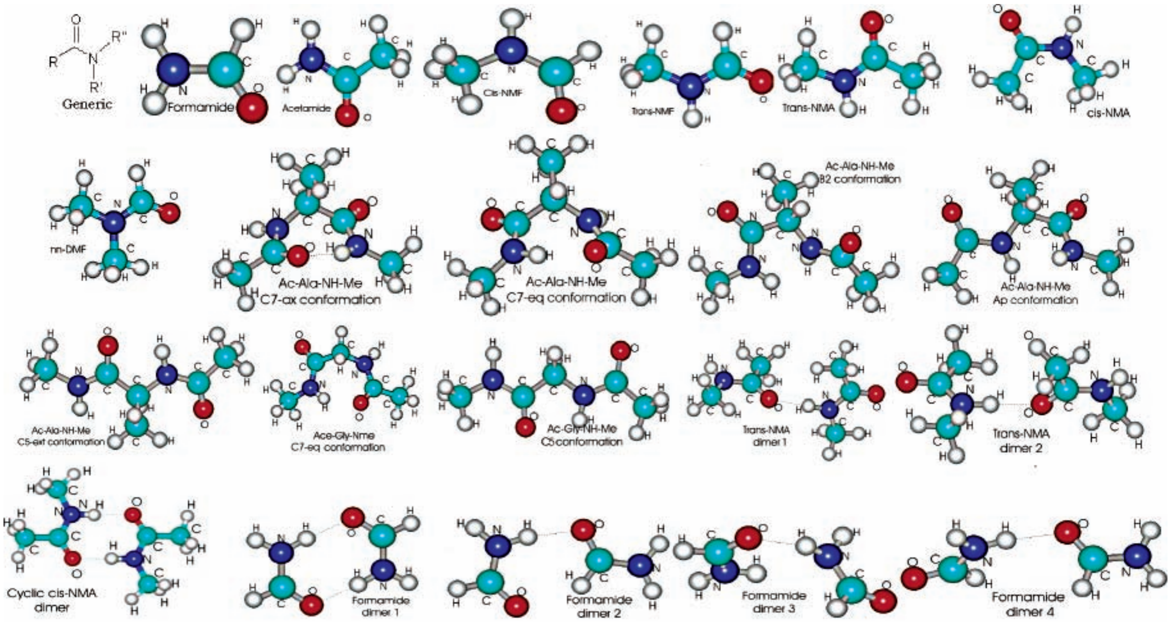

Figure 1. Group of monomers and dimers studied for the assessment of the PW91 model.

curate normal-mode analysis.[45−48] Thereupon, the normal mode calculation of vibrations of molecular systems of interest is somehow a plain procedure.

Polypeptides and proteins are molecules of special interest because of their close conjunction with life sciences. Their infrared spectroscopy is widely studied because valuable pieces of information can be derived about their primary and secondary structure. The most widely used modes for the assignment of protein structure are amide I−III modes.[42] (Amide I mode: CO stretch mainly, combined with an out of phase CN stretch, Amide II mode: out of phase combination of NH in plane bend with CN stretch, Amide III mode: in-phase combination of NH in-plane bend and CN stretch.)

A respectable number of studies have been published for proteins and polypeptides concerning conformational behavior employing correlated ab initio theory or DFT.[49−56]

To our knowledge, vibrational frequencies produced by correlated ab initio theory or DFT are available mainly for amides and amide dimers. For polypeptides, such studies have recently emerged in the literature.[57]

Hirst and Watson in their recent work,[42] assessed the EDF1[58] functional for the calculation of frequencies of amide and amide dimers. They demonstrated that their results are in better agreement with experiment, compared to MP2 and B3LYP results.[59] (Basis set: 6-31+G*.) Mirkin and Krimm showed that the amide III mode of alanine dipeptide varies its frequency, as a function of ϕ and ψ values.[45] Their observations resulted from B3LYP calculations.

There is a wide variety of currently available density functional in the literature, among them PBE, EDF1, B3LYP, and $\mathrm{PW91_{XC}}$. PBE[15] model provides relatively high accuracy for a variety of systems including hydrogen bonds.[56] On the other hand, a recent assessment does not recommend the nonmodified version of PBE for chemical use.[6]

Tsusuki and Luthi[9] demonstrated that the PW91[60] model performs better than B3LYP[61] when hydrogen bonds or dispersion interactions are present and suggested that it could be a very good choice for systems containing these kinds of interaction; it is suggested for calculations of protein molecules. Dispersion interaction and hydrogen bonds play a critical role in many polypeptide and protein chains.

In the present work, we assess $\mathrm{PW91_{XC}}$ functional for the calculation of frequencies of amide and amide dimers and we compare our results with those of MP2, B3LYP, and EDF1. The accuracy of the results of frequency calculations combined with the previous energetic assessment of $\mathrm{PW91_{XC}}$[9] will allow us to suggest $\mathrm{PW91_{XC}}$ as a valuable functional for computations of protein and polypeptidic molecules.

2. Computational Methods

The group of monomers and dimers studied for EDF1 functional[42] were also used for the evaluation of the PW91 model (Figure 1). (For a detailed literature survey of experimental and computational results on the IR spectrum of the group of monomers and dimers, study ref 42 and references there in.) The monoamides and covalent dipeptides are formamide, acetamide, *cis*-NMF, *trans*-NMF, *N*,*N*-DMF, *cis*-NMA, *trans*-NMA, *N*-acetyl−glycine-*N*′-methylamide, and *N*-acetyl-L-alanine-*N*′-methylamide. The covalent dipeptides were treated in various conformations: for glycine dipeptide the C_7^{eq} and C_5 conformations were studied while for alanine dipeptide the C_7^{ax}, C_7^{eq}, C_5^{ext}, β_2, and α_p conformations were treated. C_7^{eq} conformation of glycine and alanine dipeptide is calculated in other works as the energetically lowest conformation of both dipeptides.[42,45,52,55,56] The dimers are the *cis*-NMA cyclic dimer, two conformations of *trans*-NMA dimer, and four conformations of formamide dimers.

The important role of high-level theoretical calculations on small molecules is well documented in the referred work of Watson and Hirst.

The initial geometries of simple amide monomers and covalent dipeptides were built in Hyperchem 6.0.[62] The initial geometries of the dimers were (a) for formamide dimers the optimized geometries of the MP2/aug-cc-pVTZ level of theory,[63] (b) for cyclic *cis*-NMA dimer the optimized geometry of the MP2/aug-cc-pVDZ level of theory,[63] and (c) for *trans*-NMA dimer 1 and 2 the optimized geometry of EDF1 level of theory.[42] After proper transformation of the hyperchem and Cartesian coordinate files to Gaussian Z-matrix, done by babel,[64] all calculations proceeded using the G98 A7[65] program. The geometries met full unconstrained minimization using very tight optimization criteria (opt = verytight scf = tight) employing the 6-31+G* basis set. Successful frequency calculations took place then, employing obviously the $PW91_{XC}$/6-31+G* model. (Where necessary, the basis set was expanded for the better understanding of the behavior of the functional.)

This basis was chosen because (a) it is a relatively small basis set that permits its use for large molecules such oligopeptides, which are the subject of our future study. Testing a small basis set on such model systems, will allow us to approach larger molecules without the need to employ cc-pV(X)Z basis sets. (b) The results are comparable with those obtained by the EDF1 functional under the same basis set.

The design of the present work comprises the treatment of the group of dimers with the BSSE[66] procedure employing the CP correction.[67]

All calculations are made under the default grid, which is a pruned (75 302) grid, having 75 radial shells and 302 angular points per shell, resulting in about 7000 points per atom.

The calculations took place on a 16 Origin 2000 processors machine.

3. Results and Discussion

PW91 is a general functional that is not oriented to the description of a specific interaction. To our knowledge, this is the first time the PW91 exchange and correlation functionals are applied for the calculation of amide, amide dimers, and covalent dipeptides frequency calculations.

The choice of the set of molecules, made previously by Hirst and his co-worker and adopted by us, is particularly significant: This set of molecules includes interactions that play a critical role in protein and polypeptide chemistry. Amidic bonds are the backbone bonds of proteins and polypeptide chains while hydrogen bonding characterizes their secondary structure. It is well-known (e.g., ref 68) that the MP2/6-31G* level of theory is able to structurally approach monomeric bond lengths and bond angles with less than 1% deviation from experiment. For dimers however, dispersion forces demand further expansion of orbitals. In the discussion concerning structural data below, we emphasize on dimers and covalent dipeptides presenting results of MP2/aug-cc-pV(D,T)Z, whereas for monomers, comparison is done with MP2/6-31G* values.

For the evaluation of the accuracy of our reported results, we employ the absolute deviation (AD) and the average absolute deviation (AAD). Where experimental results are present, we compare our theoretical results with them defining AD as $|\Delta(\exp - \mathrm{calc})|$; the absolute difference between experimental and theoretical value is considered. In any other case, we compare our values with those of the higher theoretical level available, defining AD as $|(\text{highest level of theory} - PW91_{XC}/6\text{-}31{+}G^*)|$. AAD is the sum of absolute deviations for a given molecule or mode, divided by the number of the counted deviations.

We discuss separately, values of AAD for the three categories of molecules: monomeric amides, dimers and covalent dipeptides. For each molecular category we report in the text structural AD and AAD values that are not present in the tables. AD and AAD frequency values for each method are reported in tables.

3.1. Geometrical and Energetic Aspects of $PW91_{XC}$ Results.

Before we proceed to the study and comparison of the produced frequencies, we will commend on the geometrical and energetic results.

Tables 1−3 present selected structural parameters of the minimized molecules on which PW91 exchange and correlation functionals were employed. We compared them with MP2, B3LYP and EDF1 results of previous works. Minimized geometries of all molecules studied employing $PW91_{XC}$ functional, along with their energies, is presented in Supporting Information.

3.1.1. Simple Monomeric Amides. For the monomers studied (see Table 1S), we can conclude that for their structural parameters, $PW91_{XC}$ behaves excellently in comparison with MP2 results. The largest AD for bond distance r_{CO} in Table 1S reaches 0.003 Å, whereas for formamide, *cis*-NMA, and *trans*-NMA, it becomes zero. Similar results are produced for r_{CN}, $r_{NR'}$, and $r_{NR''}$ with the AD of $PW91_{XC}$ from MP2 results fluctuating between zero and 0.01 angstrom. The average absolute deviation (AAD) of all bond distances reported in Table 1S is 0.005 Å for PW91. The AAD of all bond distances for EDF1 is 0.005 Å, whereas for B3LYP, it is 0.004 Å.

The AD of $PW91_{XC}$ results from MP2 for bending angles is in most cases inconsiderable (under 1°) and the largest difference does not surpass 6.0° (CNR″ bending angle of *cis*-NMA). The AAD from MP2 of all bond angles is for $PW91_{XC}$, EDF1 and B3LYP 1.2, 0.8, and 0.5°, respectively.

Examining the absolute deviation of the results concerning the dihedral angles from MP2, we see that they converge to values comparable with those of MP2 although in few cases the deviation raises. This deviation is not dramatic however, while the AAD for $PW91_{XC}$, EDF1, and B3LYP, always in comparison with MP2, is 5.1, 5.3, and 5.0, respectively. In a previous work,[68] geometries of simple amides were optimized at the MP2/6-31+G* level of theory. Their agreement with experimental results for bond lengths was 0.012 Å in AAD with a maximum of 0.021 Å. For valence angles, the AAD was 0.6° with a maximum 1.2°. Considering the deviations of MP2 from experimental values, we can conclude that for the structural parameters studied, the three functionals produce quite reliable results.

3.1.2. Dimers. One of the dimers, *trans*-NMA, in its two initial coplanar conformations,[42] was not located. Both conformations 1 and 2 failed to result to a coplanar minimum.[69] Additionally, at the MP2/aug-cc-pVDZ level of theory,[63] after examination of possible structures, a *trans*-NMA dimer in coplanar conformation was not also reported. Reasonably, values of *trans*-NMA dimer 1 and 2 are not present in the tables. The minimized nonplanar structure that we located is available in Supporting Information.

$PW91_{XC}$ is the best performing functional for every selected value in comparison with MP2/aug-cc-pVTZ level of theory for formamide dimers or with MP2/aug-cc-pVDZ for cyclic-*cis*-NMA dimer.

The AD (Table 1) does not surpass 0.024 Å for r_{HO}, whereas maximum B3LYP and EDF1 having 0.07 and 0.172 Å AD values, respectively. The AAD for $PW91_{XC}$, B3LYP, and EDF1 is 0.015, 0.067, and 0.131 Å, respectively.

For r_{NO}, the maximum AD value for $PW91_{XC}$, B3LYP, and EDF1 is 0.057, 0.1, and 0.213 Å, respectively, whereas the AAD is 0.034, 0.054, and 0.171 Å.

For the NHO angle, the maximum/average AD values for each functional are $PW91_{XC}$ = 7.2°/2.2°, B3LYP = 10.9°/3.6°, EDF1 = 16.8°/6.8°, whereas for the COH angle, these values become $PW91_{XC}$ = 11.7°/3.3°, B3LYP = 22.3°/7.0°, EDF1 = 31.5°/13.1°.

The values of CH···O═C part of structure for formamide dimer 2, reported in Table 1, depict the same performance for every functional with the exception of the <COH value.

In general, $PW91_{XC}$ confirmed its very good performance for dimers,[9] where van der Waals forces are critical, and proved

TABLE 1: Selected Structural Parameters of the Dimers Studied, Employing PW91$_{\mathrm{XC}}$/6-31+G* Model and from Previous Theoretical Work

		formamide				*cis*-NMA	*trans*-NMA	
theoretical level	str. prm.	dimer 1	dimer 2	dimer 3	dimer 4	cyclic dimer	dimer 1	dimer 2
				NH- - -O═C				
PW91$_{\mathrm{XC}}$/6-31+G* [a]	r_{HO}(Å)	1.832	1.864	1.959	1.927	1.814	not located[b]	
MP2/6-31+G* [c]		1.907	1.935	2.030	1.969	1.871	1.952	1.956
MP2/aug-cc-pVDZ[d]		1.836	1.876	1.976	1.940	1.799	not reported	
MP2/aug-cc-pVTZ [d]		1.825	1.857	1.935	1.904			
B3LYP/6-31+G* [c]		1.886	1.911	2.004	1.976	1.876	2.021	1.995
EDF1/6-31+G* [c]		1.922	1.968	2.098	2.076	1.909	2.201	2.183
PW91$_{\mathrm{XC}}$/6-31+G* [a]	r_{NO} (Å)	2.869	2.888	2.937	2.951	2.856	not located[b]	
MP2/6-31+G* [c]		2.928	2.945	2.979	2.982	2.901	2.965	2.952
MP2/aug-cc-pVDZ[d]		2.863	2.891	2.939	2.929	2.832	not reported	
MP2/aug-cc-pVTZ [d]		2.842	2.863	2.902	2.894			
B3LYP/6-31+G* [c]		2.909	2.922	2.973	2.994	2.905	3.004	3.010
EDF1/6-31+G* (c)		2.949	2.988	3.115	3.096	2.942	3.200	3.195
PW91$_{\mathrm{XC}}$/6-31+G* [a]	$<_{\mathrm{NHO(deg)}}$	173.7	168.0	156.7	173.0	178.5	not located[b]	
MP2/6-31+G* [c]		172.4	167.6	153.6	172.8	179.3	172.7	179.6
MP2/aug-cc-pVDZ[d]		174.2	168.8	156.0	162.7	177.7	not reported	
MP2/aug-cc-pVTZ[d]		174.2	168.9	158.4	165.8			
B3LYP/6-31+G* [c]		172.2	167.0	157.4	176.7	179.9	162.4	175.0
EDF1/6-31+G* [c]		172.8	171.1	175.2	178.1	179.1	166.9	172.3
PW91$_{\mathrm{XC}}$/6-31+G* [a]	$<_{\mathrm{COH(deg)}}$	120.4	107.8	111.5	120.6	120.1	not located[d]	
MP2/6-31+G* [c]		122.2	107.4	111.3	124.1	120.7	141.9	133.6
MP2/aug-cc-pVDZ[d]						118.6	not reported	
MP2/aug-cc-pVTZ[d]		120.2	105.7	110.3	108.9			
B3LYP/6-31+G* [c]		122.2	109.6	114.0	131.2	121.9	178.4	147.5
EDF1/6-31+G* [c]		121.1	110.6	141.8	134.2	121.7	164.8	148.9

CH···O═C
Formamide Dimer 2

	r_{HO}(Å)	r_{CO} (Å)	$<_{\mathrm{CHO(deg)}}$	$<_{\mathrm{COH(deg)}}$
PW91$_{\mathrm{XC}}$/6-31+G* [a]	2.277	3.228	142.3	114.6
MP2/6-31+G* [c]	2.304	3.249	143.0	115.2
MP2/aug-cc-pVDZ[d]	2.274	3.231	143.6	113.8
MP2/aug-cc-pVTZ[d]	2.234	3.190	144.9	113.1
B3LYP/6-31+G* [c]	2.336	3.262	140.5	115.8
EDF1/6-31+G* [c]	2.616	3.500	136.4	113.8

[a] Values taken from present work. [b] Both structures were not located applying very tight optimization criteria. [c] Values taken from ref 42. [d] Values taken from ref 63.

TABLE 2: CP Corrected Interaction Energies (kcal/mol) of the Dimers Studied Compared with High Levels of Theory

	PW91$_{\mathrm{XC}}$						
	6-31+G(d)	6-311+G(d)	6-311+G(d,p)	6311++G(d,p)	6-311++G(2d,2p)	6-311++G(df,p)	estim. CBS value[63]
formamide dimer 1	−16.23	−15.48	−15.96	−15.92	−16.31	−15.74	−14.35
formamide dimer 2	−10.29	−9.98	−10.04	−10.08	−10.05	−9.92	−9.70
formamide dimer 3	−7.77	−7.82	−7.70	−7.70	−7.60	−7.59	−7.34
formamide dimer 4	−7.15	−7.21	−6.93	−7.04	−6.98	−6.98	−6.76
cis-NMA cyc dimer	−17.5	−16.7	−17.17	−17.21	−17.39	−17.06	−17.18[a]

[a] The level of theory is not the CBS limit for *cis*-NMA dimer but it is BSSE corrected at MP2/(aug-cc-pVTZ).[63]

to be the best functional for such calculations. It is important to mention that these results were achieved with a relatively small basis set. The results validate the use of PW91$_{\mathrm{XC}}$/6-31+G* model for the structural description of such molecules with a tolerant percentage of error. However, some properties demand expansion of basis set for their accurate validation. Polarizabilities may be a good example.

We make this comment because we want to distinguish the performance of the method employing this basis set from the incompleteness of the basis set itself. The success of the method for these results should not become misleading for properties that demand, in any case, expansion of the basis set. Conclusively, if for instance, employing PW91$_{\mathrm{XC}}$/6-31+G* for the calculation of polarizabilities leads to inaccurate results we should not ascribe it to PW91$_{\mathrm{XC}}$ model at once, despite its approximate nature, but, first of all, to the incompleteness of the basis set.

The interaction energies were calculated and the BSSE error was corrected for all calculations of the dimers. For better evaluation of the results of the interaction energy and the BSSE error behavior employing the PW91$_{\mathrm{XC}}$ model, we expanded the basis set: 6-31+G*, 6-311+G*, 6-311+G**, 6-311++G**, 6-311++G(df,p), and 6-311++G(2d, 2p) were implemented for all dimers (see Table 2).

The PW91$_{\mathrm{XC}}$ model produced CP corrected interaction energies of the four formamide dimers in excellent agreement with CBS values[63] (Table 2). The same result is observed for the cyclic *cis*-NMA dimer.

Tsuzuki and Luthi[9] have also reported that the PW91$_{\mathrm{XC}}$/cc-pVDZ interaction energies of hydrogen bonded dimers are very close to the CCSD(T) limit (the error fluctuates between 17% and 5%).

We also studied selected structural parameters of the dimers for their behavior related to the increase of the basis set and

TABLE 3: Variance of r_{H-O} (Å) with the Basis Set for the Dimers Studied

	6-31+G(d)	6-311+G(d)	6-311+G(d,p)	6-311++G(d,p)	6-311++G(2d,2p)	6-311++G(df,p)
formamide dimer 1	1.832	1.854	1.82	1.82	1.802	1.824
formamide dimer 2	1.864	1.884	1.863	1.862	1.848	1.866
formamide dimer 3	1.959	1.982	1.961	1.961	1.951	1.963
formamide dimer 4	1.927	1.943	1.933	1.933	1.927	1.937
cis-NMA cyc. dimer	1.814	1.826	1.797	1.797	1.786	1.799

TABLE 4: ϕ, ψ Dihedral Angles and Energies of the Covalent Dipeptides Studied in Various Conformations under Several Theoretical Levels

	Ac−Ala-NHMe			
	$PW91_{XC}$/6-31+G* [a]	EDF1/6-31+G* [b]	B3LYP/6-31+G* [b]	MP2/aug-cc-pVDZ[c]
C_7^{eq} ϕ	−82.5	−83.9	−83.0	−82.6
C_7^{eq} ψ	72.8	76.6	74.6	75.8
En.(au) C_7^{eq}	−495.695740944	−495.9340205	−495.8784168	−494.5635029
C_5^{ext} ϕ	−155.9	−146.1	−154.9	−161.1
C_5^{ext} ψ	161.4	151.4	159.2	155.5
En.(au) C_5^{ext}	−495.6932827	−495.9329274	−495.8766823	−494.56046
β_2 ϕ	−116.9	−116.0	−113.7	−82.3
β_2 ψ	15.8	12.9	12.4	−9.5
En.(au) β_2	−495.691277959	−495.9307948	−495.8740482	−494.55854
C_7^{ax} ϕ	72.2	72.3	73.1	73.7
C_7^{ax} ψ	−54.6	−54.9	−55.2	−53.7
En.(au) C_7^{ax}	−495.691803458	−495.9298560	−495.8744567	−494.55987
α_p ϕ	−166.0	−159.8	−164.7	−164.7
α_p ψ	−43.2	−49.9	−44.1	−38.3
En.(au) α_p	−495.684584029	−495.9240066	−495.8679065	−494.55312

	Ac-Gly-NHMe		
C_7 ϕ	−81.6	−83.1	−82.1
C_7 ψ	67.6	71.3	69.1
En.(au) C_7	−456.397914981	−456.6180044	−456.5608526
C_5 ϕ	180.0	180.0	−159.8
C_5 ψ	180.0	180.0	−49.9
En.(au) C_5	−456.39632268	−456.5600361	−456.6178082

[a] Present work. [b] Values taken from ref 42. [c] Values taken from ref 52.

the interesting addition of diffuse and polarization functions in hydrogens. Detailed structural data for all dimers studied are presented in Table 4s. In Table 3, we present the behavior of r_{H-O} for the dimers of formamide and cyclic *cis*-NMA.

Increasing the flexibility in the valence region (from 6-31+G* to 6-311+G*) resulted to the lengthening of the hydrogen bond. The difference reached the maximum of the 0.023 Å in formamide dimer 3, whereas the lowest lengthening was met in *trans*-NMA dimer (0.011 Å, see Table 4s). For formamide 2 dimer, the CH···O═C bond was shortened by 0.047 Å (Table 4s).

The addition of diffuse and polarization functions (6-311++G**) shortens the hydrogen bonds, whereas the addition of 2 sets of polarization functions on every atom (6-311++G-(2d, 2p)) reaches for all cases the minimum bond length with the exception of *trans*-NMA dimer (Tables 3 and 4s). For formamide 2 dimer, in the CH···O═C bond, we observe the opposite results. The hydrogen bond is lengthening as diffuse and polarization functions are added. For an exhaustive study on the strength of these hydrogen bonds in formamide and *N*-methylacetamide dimers employing MP2/aug-cc-pV(DT)Z level of theory, see ref 63.

3.1.3. Covalent Dipeptides. PW91 calculations of covalent dipeptides Ac-Ala-NH-Me and Ac-Gly-NH-Me have produced the C_7^{eq} and C_7 conformations as those with the lowest values of energies among all others (Table 4). This comes in agreement with previous theoretical treatments. The characteristic ϕ and ψ angles of the alanine dipeptide are calculated successively and the AD for every functional, compared with MP/2aug-cc-pZDV, is under 7° for every value with two exceptions: every ϕ value of β_2 conformation and EDF1 ϕ value of C^5_{ext} conformation. For glycine dipeptide, to our knowledge, values of MP2/aug-cc-pDZV calculations are not available. The β_2 conformation is located in a very flat part of the PES that permit ϕ, ψ angles a broad fluctuation with very small energy changes.[52]

TABLE 5: Selected Structural Parameters of Alanine Dipeptide Studied, Employing $PW91_{XC}$/6-31+G* Model Compared with MP2/aug-cc-pVDZ Level of Theory

theoretical level	structural parameter	C_7^{eq}	C_5	α_p	C_7^{ax}
	NH···O═C				
$PW91_{XC}$/6-31+G* [a]	r_{HO}(Å)	2.01	2.17	NP	1.88
MP2/aug-cc-pVDZ[b]		2.02	2.23	NP	1.88
$PW91_{XC}$/6-31+G* [a]	r_{NO} (Å)	2.92	2.67	NP	2.83
MP2/aug-cc-pVDZ[b]		2.91	2.68	NP	2.82
$PW91_{XC}$/6-31+G* [a]	$<_{NHO(deg)}$	146.1	107.6	NP	151.5
MP2/aug-cc-pVDZ[b]		144.8	105.0	NP	151.7
$PW91_{XC}$/6-31+G* [a]	$<_{COH(deg)}$	105.0	85.8	NP	105.0
MP2/aug-cc-pVDZ[b]		104.8	84.7	NP	103.2
	NH···N				
$PW91_{XC}$/6-31+G* [a]	r_{HN}(Å)	NP	NP	2.52	2.74
MP2/aug-cc-pVDZ[b]		NP	NP	2.48	2.70
$PW91_{XC}$/6-31+G* [a]	r_{NN} (Å)	NP	NP	2.81	3.01
MP2/aug-cc-pVDZ[b]		NP	NP	2.76	2.97
$PW91_{XC}$/6-31+G* [a]	$<_{NHN(deg)}$	NP	NP	95.3	95.5
MP2/aug-cc-pVDZ[b]		NP	NP	95.0	95.1
$PW91_{XC}$/6-31+G* [a]	$<_{CNH(deg)}$	NP	NP	74.3	66.1
MP2/aug-cc-pVDZ[b]		NP	NP	76.0	65.9

[a] Present work. [b] Values taken from ref 52. NP: not present

In Table 5, we present structural parameters of alanine dipeptide in $PW91_{XC}$/6-31+G* and MP2/aug-cc-pVDZ[52] levels of theory. $PW91_{XC}$ produces results that are very close to those

TABLE 6: Calculated Amide I Frequencies Compared with Experimental Data

		Δ(expt − calc)					
species	expt (cm^{-1})	MP2/ 6-31+G*[l]	B3LYP/ 6-31+G*[l]	B3LYP/ 6-311++G(2d,2p)[l]	B-LYP/ 6-31+G*[l]	EDF1/ 6-31+G*[l]	PW91$_{XC}$/ 6-31+G*[m]
formamide[a,b]	1755	−40	−45	−26	−16	−9	1
acetamide[c−f]	1733	−47	−38	−19	−7	1	10
trans-NMF[g]	1721	−49	−60	−42	−26	−27	−21
N,*N*-DMF[h]	1677	−83	−87	−68	−53	−52	−42
cis-NMA[g,i]	1707	−56	−51	−32	−21	−10	−2
trans-NMA[g,i]	1707	−46	−44	−32	−8	−10	1
Ac-Gly-NHMe[j] C$_7$	1707		−46			−14	−3
	1683		−40			−3	12
Ac-Gly-NHMe[j] C$_5$	1707		−48			−15	−3
	1693		−40			−4	12
Ac−Ala-NHMe[j] C$_7^{eq}$	1705		−39			−16	−3
	1680		−40			−1	−15
Ac−Ala-NHMe[j] C$_5^{ext}$	1705		−43			−10	3
	1688		−42			−8	6
cis-NMA cyclic dimer[k]	1695	−68	−48	−27		−10	1
		−33	−16	4		19	34
trans-NMA dimer 1[k]	1686	−67	−57	−38		−24	−6[n]
		−55	−49	−30		−16	6[n]
tans-NMA dimer 2[k]	1686	−64	−56	−36		−22	
		−55	−47	−27		−15	
average absolute dev.		55	47	32	22	14	10
average dev.		−55	−47	−31	−22	−12	−1

[a,b] see ref 72a and 72b; value compared with 72b. [c−f] See ref 72c, 72d, 72e, 72f; value compared with 72f. [g] See ref 72g. [h] See ref 72h. [i] See ref 72i. [j] See ref 72j. [k] See ref 72k. [l] Theoretical values: see ref 42. [m] Theoretical values: present work. [n] Values refer to one nonplanar *trans*-NMA dimer as found from our calculations. Experimental values:

TABLE 7: Calculated Amide II Frequencies Compared with Experimental Data

		Δ(expt − calc)					
species	expt (cm^{-1})	MP2/ 6-31+G*[k]	B3LYP/ 6-31+G*[k]	B3LYP/ 6-311++G(2d,2p)[k]	B-LYP/ 6-31+G*[k]	EDF1/ 6-31+G*[k]	PW91$_{XC}$/ 6-31+G*[l]
formamide[a,b]	1580	−71	−60	−44	−7	−27	−10
acetamide[c−f]	1600	−63	−46	−25	12	−15	3
trans-NMF[g]	1528	−52	−43	−31	−41	−9	23
N,*N*-DMF[h]	1507	−76	−49	−37	−57	−18	−5
cis-NMA[g,i]	1485	−86	−57	−42	−67	−27	11
trans-NMA[g,i]	1511	−79	−50	−16	−49	−30	−17
Ac-Gly-NHMe[j]C$_7$	1553		−41			−9	−7
	1516		−42			−5	5
Ac-Gly-NHMe[j] C$_5$	1516		−60			−40	−29
	1496		−47			−9	1
Ac−Ala-NHMe[j] C$_7^{\mathrm{eq}}$	1550		−54			−9	−5
	1513		−51			1	14
Ac−Ala-NHMe[j] C$_5^{\mathrm{ext}}$	1513		−61			−38	−29
	1496		−48			−13	1
average absolute dev.		71	51	33	39	18	11
average dev.		−71	−51	−32	−35	−18	−3

[a,b] Experimental values: see ref 72a and 72b; value compared with 72b. [c−f] Experimental values: see ref 72c, 72d, 72e, 72f; value compared with 72f. [g] Experimental values: see ref 72g. [h] Experimental values: see ref 72h. [i] Experimental values: see ref 72i. [j] Experimental values: see ref 72j. [k] Theoretical values: see ref 42. [l] Theoretical values: present work.

of MP2/aug-cc-pVDZ for the C═O···NH hydrogen bond. The AD in hydrogen bond distances is not greater than 0.01 Å with the exception of C$_5$ conformation that reaches 0.05 Å. The NH···N part shows a larger deviation with an average of 0.04 Å. For every conformation, the critical selected angles are less than 2°.

We do not report values of β_2 conformation since PW91 ϕ, ψ angles are quite away from those of MP2/aug-cc-pVDZ due to the flat PES at this region. The internal hydrogen bonds are presented in a stability order: N−H···O and N−H···N.[63,70] The third kind of internal hydrogen bonding is C−H···O. It is not reported though, because the correlation results do report structural data for more than two such bonds, the connectivity of which is not clear. Some of these values are quite close. For this reason, we will not risk a comparison for which the two sets of values may refer to two different sets of atoms. There is also an energetic reason: the energy influence is about −0.5 kcal/mol but a chemist can overcome this problem making the hydrogen donor more acidic adding electron withdrawing groups entailing an increase in strength up to −3 kcal/mol.[71]

The addition of diffuse and polarization functions in hydrogens does not have any dramatic changes in hydrogen bonding as concluded from alanine dipeptide calculations. For alanine dipeptide we only studied 6-31+G(d,p) and 6-31++G(d,p) basis sets (see Table 4s). The differences in the distance of the stronger hydrogen bond are impalpable. For an exhaustive conformational study of the alanine dipeptide at the MP2 and DFT levels study ref 52 and references there in.

In general, the PW91$_{XC}$ functional is a dependable functional for covalent dipeptides. Taking under consideration that (a)

TABLE 8: Calculated Amide III Frequencies Compared with Experimental Data

		Δ(expt − calc)					
species	expt (cm^{-1})	MP2/6-31+G*[k]	B3LYP/6-31+G*[k]	B3LYP/6-311++G(2d,2p)[k]	B-LYP/6-31+G*[k]	EDF1/6-31+G*[k]	PW91$_{XC}$/6-31+G*[l]
formamide[a,b]	1255	−48	−23	−12	−7	−1	7
acetamide[c−f]	1319	−66	−37	−23	−16	−7	−2
trans-NMF[g]	1207	−62	−24	−11	1	0	−72
N,*N*-DMF[h]	1388	−83	−55	−44	−51	−18	8
cis-NMA[g,i]	1325	−66	−35	−23	−14	−6	3
trans-NMA[g,i]	1266	−57	−26	−82	−10	−14	22
Ac-Gly-NHMe[j]C_7	1288		−38			−4	7
	1271		−35			0	4
Ac-Gly-NHMe[j] C_5	1271		−11			23	33
	1246		−14			19	31
Ac−Ala-NHMe[j] C_7^{eq}	1281		−40			25	34
	1257		−41			22	26
Ac−Ala-NHMe[j] C_5^{ext}	1257		−21			13	23
	1240		−9			27	36
average absolute dev.		64	29	33	17	13	22
average dev.		−64	−29	−32	−16	6	11
AAD for modes I−III		61	43	32	26	15	14
AD for modes I−III		−61	−43	−32	−24	−9	2

[a,b] Experimental values: see ref 72a and 72b; value compared with 72b. [c−f] Experimental values: see ref 72c, 72d, 72e, 72f; value compared with 72f. [g] Experimental values: see ref 72g. [h] Experimental values: see ref 72h. [i] Experimental values: see ref 72i. [j] Experimental values: see ref 72j. [k] Theoretical values: see ref 42. [l] Theoretical values: present work.

TABLE 9: Variance of the Characteristic Amide Frequencies of the Formamide in Respect with the Basis Set Used Employing PW91$_{XC}$

		Δ(expt − calc)				
mode	expt (cm^{-1})	6-31+G(d)	6-31+G(d,p)	6-311+G(d)	6-311+G(df,p)	6-311+G(2d,2p)
amide I	1755	1	5	20	12	19
amide II	1580	−10	10	−17	17	11
amide III	1255	7	15	14	22	19

TABLE 10: Variance of the Characteristic Amide Frequencies of the Acetamide in Respect with the Basis Set Used Employing PW91$_{XC}$

		Δ (expt − calc)				
mode	expt (cm^{-1})	6-31+G(d)	6-31+G(d,p)	6-311+G(d)	6-311+G(df,p)	6-311+G(2d,2p)
amide I	1733	10	12	15	16	29
amide II	1600	3	25	−3	34	30
amide III	1319	−2	9	7	15	13

MP2/aug-cc-pVDZ is a computationally “expensive” method and (b) the small differences of the two methods between their structural values, one can carefully employ PW91$_{XC}$ for reliable conformational search. The word “carefully” is added because we assume that PW91$_{XC}$ is going to meet difficulty in describing very weak dispersion forces with high accuracy.

3.2. Vibrational Analysis. Tables 6−8 depict the difference between calculated and experimental[72] values of characteristic amide I, II, and III frequencies concerning molecules under study for which experimental data are available.

3.2.1. Amide I Mode. Simple Monomeric Amides. Studying Table 6, one can conclude that PW91$_{XC}$ is the best performing functional. The Average Absolute Deviation value from experimental data of MP2/6-31+G*, B3LYP/6-31+G*, B3LYP/6-311++G(2d, 2p), B-LYP/6-31+G*, EDF1/6-31+G* and PW91$_{XC}$/6-31+G* is 54, 54, 37, 22, 18 and 13 cm^{-1}; the average deviation values are −54, −54, −37, −22, −18, and −9 cm^{-1}. The deviation reaches its maximum value at *N*,*N*-DMF (−42 cm^{-1}). However, for the same molecule all other functionals perform worse than PW91$_{XC}$. With the exclusions of *trans*-NMF and *N*,*N*-DMF, the deviation of PW91$_{XC}$ does not surpass 10 cm^{-1}. EDF1 performs as second best and B-LYP as third. B3LYP with a small basis set produces deviations that reach −87 cm^{-1}. These deviations fall as the basis set increases, however it does not reach the accuracy of EDF1 and PW91$_{XC}$.

Covalent Dipeptides. Again, the best performing functional between B3LYP, EDF1, and PW91$_{XC}$ is the last one, with EDF1 following closely. AADs employing 6-31+G* basis for B3LYP, EDF1, and PW91$_{XC}$ are 42, 9, and 7 cm^{-1}. An important observation is that the unscaled harmonic frequencies of EDF and PW91$_{XC}$ for this mode do not deviate more than 16 cm^{-1}. B3LYP deviates always more than −39 cm^{-1}. Probably, difficulties encountered by this functional arise from the fact that B3LYP is not a suggested functional for the treatment of Wan der Waals forces, forces that are present in these conformations of glycine and alanine dipeptide. The basis set is also small for this functional.

trans-NMA Dimer. As mentioned in structural analyses, we have not located *trans*-NMA dimer in a coplanar conformation. However, Torri et al.[72(k)] reported experimental values of amide I mode for cyclic *cis*-NMA dimer and *trans*-NMA dimer 1 and 2. What did they really do in their elegant work? They calculated the structures, among others, of the dimers above at the HF/6-31++G**. They also observed IR spectra in Ar and N_2 matrixes. They then assigned the observed and calculated values taking for granted that trans-NMA dimer 1 and 2 are present in their matrixes. Studying section D and Table 8 of their published work,[72k] we tried to reassign their experimental data with our calculated values. Consequently, the values of PW91$_{XC}$ functional for the dimers of NMA refer to one cis-NMA cyclic dimer and one nonplanar trans NMA dimer the geometry of which is given in Supporting Information (Table 2S). Following the cogitation of the scientists in ref 72k, we assigned the higher value of spectrum (1695 cm^{-1}) to cis dimer and the lower value to trans dimer. The AAD values for MP2/6-31+G*, B3LYP/6-31+G*, B3LYP/6-311++G(2d,2p), EDF1/6-31+G*, and PW91$_{XC}$/6-31+G* are 57, 46, 27, 18, and 12 cm^{-1}. The PW91$_{XC}$ method is still the best performing method, with EDF1 following. B3LYP improves as the basis set increases. Excluding the second value of amide I mode of cyclic NMA, for which experimental data is not available, all values deviate less than or equal to 6 cm^{-1}! For all reported values of amide I mode, the AAD (reported in Table 6) accentuate PW91$_{XC}$ as the

TABLE 11: Variance of the Characteristic Amide Frequencies of the trans-NMF in Respect with the Basis Set Used Employing PW91$_{XC}$

		Δ (expt − calc)										
mode	expt (cm^{-1})	6-31+G(d)	6-31+G(d,p)	6-311+G(d)	6-311+G(df,p)	6311++G(2d,2p)	cc-VDZ	cc-VTZ	cc-VQZ	aug-cc-VDZ	aug-cc-VTZ	aug-cc-VQZ
amide I	1721	−21	−17	−17	−16	−3	−54	−26	17	−3	6	8
amide II	1528	23	38	26	45	40	59	42	43	59	44	42
amide III	1207	−72	−62	−67	−59	−60	−53	−58	−59	−55	−55	−59

functional that produces results closest to the experimental values. EDF1 is also very close as the work in ref 42 proved.

3.2.2. Amide II Mode. Simple Monomeric Amides. Amide II mode results (Table 7) are similar to those of amide I. The AAD value for MP2/6-31+G*, B3LYP/6-31+G*, B3LYP/6-311++G-(2d, 2p), B-LYP/6-31+G*, EDF1/6-31+G*, and PW91$_{XC}$/6-31+G* is 71, 51, 33, 39, 21, and 12 cm^{-1}, respectively. The maximum deviation of PW91$_{XC}$ is observed for *trans*-NMF (23 cm^{-1}) and *trans*-NMA (−17 cm^{-1}). Two values are equal or very close to 10 cm^{-1} (formamide and *cis*-NMA), whereas for acetamide and *N*,*N*-DMF, the deviation is the smaller observed (3 and −5 cm^{-1}).

Covalent Dipeptides. The AAD values for this part of the molecular set studied are 42, 9, and 7 cm^{-1}. PW91$_{XC}$ systematically produces better values in every case; EDF1 is quite close as well. Three values deviate close to 15 cm^{-1}, whereas all others are close to 3 cm^{-1}. EDF1 shows almost the same performance. Only conformations, for which experimental values exist, are present.

We can observe the effect of hydrogen bonding in frequency values in amide II mode in Table 7 as well as in amide I mode in Table 6. A decrease of the predicted values is evident in molecules containing hydrogen bonds. The influence of hydrogen bonding over the vibrational frequencies is a strong point for those who prefer anharmonic treatment for the correction of the frequencies instead of the use of a scaling factor.

The AAD for all reported values of amide II mode of MP2/6-31+G*, B3LYP/6-31+G*, B3LYP/6-311++G(2d, 2p), B-LYP/6-31+G*, EDF1/6-31+G*, and PW91$_{XC}$/6-31+G* are 55, 47, 32, 22, 14, and 10 cm^{-1}. Observations made for amide I mode stand for amide II mode as well.

There is not experimental data of the amidic mode II for the dimers, which makes us to proceed with amide III mode discussion. All values of molecules and conformations that experimental data are not available are reported as Supporting Information.

3.2.3. Amide III Mode. Simple Monomeric Amides. The AAD values of amide III mode for simple monomeric amides of MP2/6-31+G*, B3LYP/6-31+G*, B3LYP/6-311++G(2d, 2p), B-LYP/6-31+G*, EDF1/6-31+G*, and PW91$_{XC}$/6-31+G* levels of theory are 64, 33, 33, 17, 8, and 19 cm^{-1} respectively. For this mode, EDF1 and BLYP perform better than PW91$_{XC}$. The maximum AAD is met at trans-NMF with the extraordinary value of −72 cm^{-1} (Table 8). It is important to mention that if this value is excluded then the AAD value drops to 8 cm^{-1} and makes PW91$_{XC}$ equivalent to EDF1.This value is the worst value among all functionals. *trans*-NMA has a relatively high value also for PW91$_{XC}$: 22 cm^{-1}. The remaining molecules produce a deviation under 10 cm^{-1}. *Trans*-NMA does not improve as the basis set increases for B3LYP: For the small basis the deviation is −26 cm^{-1} while for the large basis set the deviation reaches −82 cm^{-1}.

Covalent Dipeptides. The AAD values for B3LYP/6-31+G*, EDF1/6-31+G*, and PW91$_{XC}$/6-31+G* levels are 26, 17, and 24 cm^{-1}. EDF1 again performs better for this set of molecules for the amide III mode. Excluding Ac-Gly-NHMe at its C_7 conformation, of which the deviation does not reach even 10 cm^{-1}, all other values of PW91$_{XC}$ lay about 20−30 cm^{-1} away from the experimental values. EDF1 shows a similar but better behavior: for the same dipetide and the same conformation the AAD is −4 and 0 cm^{-1}, whereas all other values of AAD are between 10 and 20 cm^{-1}. PW91$_{XC}$ is though, the second best performing functional. As in amide II mode section, experimental data for dimers are not available.

Table 8 provides also the overall performance for every comparable value with experimental results available, and for all amide modes studied: The AAD for MP2/6-31+G*, B3LYP/6-31+G*, B3LYP/6-311++G(2d, 2p), B-LYP/6-31+G*, EDF1/6-31+G*, and PW91$_{XC}$/6-31+G* is respectively 61, 43, 32, 26, 15, and 14 cm^{-1}. PW91 is, overall, the best performing functional differing by 1 cm^{-1} (quite suspenseful result!). The difference though with EDF1 is very small.

Table 5S, in the Supporting Information, presents all of the calculated normal modes of EDF1,[42] PW91, and every experimental frequency, available to us through literature, for the molecules formamide, acetamide, *trans*-NMF, *N*,*N*-DMF, *cis*-NMA, and *trans*-NMA. This table is another piece of evidence that corroborates the use of PW91$_{XC}$/6-31+G* model for accurate unscaled calculations of frequencies of such molecules. After a statistical elaboration, we observed that PW91 model is in most cases the best performing functional. It has the smallest AAD for all molecules with the exception of *trans*-NMF. Deviations however are expected to increase, and they do, for low-frequency modes because of the anharmonicity factor.

As concluded from the data presented, PW91 exchange and correlation functionals, along with EDF1 employing 6-31+G* basis set, are the best choices for computing frequencies of amides. Computed amide I and II modes come in closer agreement with experiment under PW91 model while EDF1 performs better for the amide III mode. The distinctions are not made with the scope this to become a rule since the Δ(exp-calc) values under both functionals and for all modes are small (the exception of amide III of trans-NMF is mentioned above). It aims to the suggestion below: A combination of computations employing these two functionals with the 6-31+G* basis set, for molecules containing amide bonds with no experimental data, would probably produce reliable and comparable values for their frequencies. The usage of more than one functionals is quite common in recent works.[73,74]

All molecules were treated in gas phase, whereas the experimental data were collected for instance in argon, krypton, xenon, or nitrogen matrixes. However, even rare gases matrixes affect the vibrational properties of the trapped amides although in helium clusters the expected effects are smaller.[75,76] In the case of acetamide, where gas phase results are available, PW91 model performs extremely well.

It is also known that electron correlation methods perform exceptionally well for vibrational frequencies when a large basis set is implemented, something that leads to computationally expensive results. This must be one of the reasons that MP2/6-31+G* results are not as close to experimental as DFT

TABLE 12: Variance of the Characteristic Amide Frequencies of the trans-NMA in Respect with the Basis Set Used Employing PW91$_{XC}$

		Δ(expt − calc)				
mode	expt (cm^{-1})	6-31+G(d)	6-31+G(d,p)	6-311+G(d)	6-311+G(df,p)	6311++G(2d,2p)
amide I	1707	1	4	7	7	20
amide II	1511	17	−5	−15	5	0
amide III	1266	−22	33	30	38	37

TABLE 13: Variance of the Characteristic Amide Frequencies of the nn-DMF in Respect with the Basis Set Used Employing PW91$_{XC}$

		Δ(expt − calc)				
mode	expt (cm^{-1})	6-31+G(d)	6-31+G(d,p)	6-311+G(d)	6-311+G(df,p)	6311++G(2d,2p)
amide I	1677	−42	−28	−37	−36	23
amide II	1388	−5	18	15	25	24
amide III	1266	8	19	17	23	23

methods the success of which, is partially based on their approximate nature.

Another interesting point for discussion is that of anharmonicity and scaling factors. It is now well established that the harmonic approximation gives unsatisfactory results in floppy biological molecules and structures containing intramolecular hydrogen bonds. The technique of employing an empirical scaling factor also fails to treat specific modes of molecules where hydrogen bonds are present[75,76] (difference reaches 84 cm^{-1} in conformer II of glycine for the stretching mode of OH[75]). However, the PW91$_{XC}$ functional performed very well in amide I mode (C=O stretch) for the dipeptides of glycine and alanine. These dipeptides contain a hydrogen bond (C$_7$ conformation) that the characteristic oxygen is participating in, without anharmonic treatment. This fact does not lessen the merit of anharmonic treatment. It propels an investigation on the PW91 anharmonic treatment of several molecules, which is also beyond the aim of this work.

Scaling factors show many discrepancies in the whole range of frequency calculations especially in cases where hydrogen bonds are present.[75,76] Where usage of scaling factors arise inevitably, we propose different scaling factors for different regions of the spectrum with proper assessment for each region and functional.

The range of basis set used for the EDF1 was also employed for PW91 model [6-31+G(d,p) to 6311++(2d,2p)]. Especially for *trans*-NMF, where the differences found are the biggest of every other molecule, the basis set range was expanded up to aug-cc-VQZ.

In general, the difference Δ(exp − calc) employing large basis set, fluctuates close to the 6-31+G(d) differences. The peak of $\Delta(\mathrm{exp} - \mathrm{calc})_{6-31+G(d)}$- $\Delta(\mathrm{exp} - \mathrm{calc})_{\mathrm{large-basis}}$ is at 37 cm^{-1} and is located at the trans-NMF spectrum with cc-VDZ basis. Tables 9−13 depict the PW91$_{XC}$ performance over the series of basis sets described above. As reported in the literature,[9] an improvement of the basis set does not lead to a definite improvement of the results. In this case, the opposite trend is often observed contrary to the wave function methods.

For space reasons, intensities are not presented in the tables. We have to report however that all intensities follow the trend of EDF1 and B3LYP; consequently, they have the same magnitude, and in cases where the calculated EDF1 intensity touches zero, PW91$_{XC}$ behaves identically. This of course does not mean identical numbers of intensities but a number very close to that of EDF1. (Values can be obtained via communication with the authors.)

4. Conclusions

PW91$_{XC}$ functional is previously proposed as a good performing functional for systems that include hydrogen bonds and $\pi-\pi$ interactions. In the present work, for the first time, it is assessed for frequency calculations of amide and amide dimers. Reasonably, a representative molecular set is necessary for its assessment. This set was chosen to be the set for which EDF1 was assessed. The presented results allow us to propose it as one of the best performing functionals for frequency calculations of systems containing amidic bonds.

The unscaled calculated frequencies for amidic modes I and II are closer to experimental results than every other functional or method studied, and in some cases the difference reaches zero. For amidic mode III it is the second best functional. For all normal modes, it is the best performing functional wherever experimental values are available. The average absolute deviation of experimental and calculated values is the smallest for PW91$_{XC}$ in comparison with EDF1 results. However, the difference is quite small.

PW91$_{XC}$ seems to perform very well for the calculation of frequencies of amidic bond containing systems. It is certainly better than B3LYP and BLYP not only for frequency calculations but also for the evaluation of intermolecular energy interaction of the hydrogen bonded dimers. Along with the EDF1 model, it can give reliable results close to the experimental values for monomers and dimers although dimers should be treated with care because of the known problems of DFT in the field of the estimation of dispersion forces. It is well-known that DFT encounters great difficulty in treating Van der Waals systems.[8,16,77]

Although quite an old enough functional, to our knowledge, it is the first time that it is assessed for frequency calculations of systems containing amidic bonds. From this point of view, the criticism that was earlier reported in the Introduction section, declaring that functionals are not reliably assessed because of their increasing number, takes a credit. Probably, before the emergence of a functional in the literature, it should first be applied to a bigger number of benchmark sets, representative of critical chemical phenomena.

On the other hand, we do not propose the deceleration of research concerning the future of DFT. Now, that either functionals of the third rung[32] of the "Jacobs scale", or corrected ones by a dispersion factor, [8,78] or functionals containing coefficients of the long-range dispersion (see ref 31, 68−72 of our ref 5) emerge in the literature, a discussion for the representative expansion of benchmark sets may drive to more reliable assessment of the new functionals proposed.

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Supporting Information Available: Selected structural parameters of the monomers studied, employing various theoretical levels, optimized geometries in Cartesian format and energies of all molecules studied employing PW91$_{XC}$. Corrected energies for the dimers. Variance of selected structural parameters of the dimers and covalent dipeptides with the basis set. Harmonic unscaled vibrational frequencies computed employing EDF1 and PW91 model compared with experimental data for amide monomers. Normal modes of the dimers and covalent dipeptides in various conformations calculated employing PW91$_{XC}$/6-31+G* model. Amide I, II, and III modes for conformations of covalent dipeptides and amide I and II modes for dimers employing PW91$_{XC}$/6-31+G* model of theory. Their experimental data are not available. This material is available free of charge via the Internet at http://pubs.acs.org.

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(69) One reason may be the different convergence criteria between the present and the referred (ref 42) work: The referred work employed default convergence criteria of the program used for its calculations: (max. grad.: $3.0 \times 10^{-4} E_h a_0^{-1}$, max. at. disp.: $1.2 \times 10^{-3} a_0$, max. energy change: $1.0 \text{ x } 10^{-6} E_h$). We also minimized trans- NMA dimer 1 and 2 in B3LYP/6-31+G* level of theory (same level as in ref 42) with very tight optimization criteria (scf = tight/opt = verytight, GDIIS) and we did not locate either of the coplanar conformations.

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