Journal of Chemistry and Chemical Sciences, *Vol.9(10), 285-295, October, 2019* *ISSN 2229-760X (Print)*
(An International Research Journal), *www.chemistry-journal.org* *ISSN 2319-7625 (Online)*

Evaluation of Exchange-Correlation Functionals for Calculating ^{1}H and ^{13}C NMR Chemical Shifts of a Series of Lactones and Lactams in Solution

Nadia FASKA* and Fatima EL BAZ

Faculty of Applied Sciences Ait Melloul,
University Ibn Zohr Agadir, MOROCCO.
LCAPE, Department of Chemistry,
Faculty of Sciences, University Ibn Zohr Agadir, MOROCCO.
email: n.faska@uiz.ac.ma.

(Received on: October 14, 2019)

ABSTRACT

Experimental and theoretical ^{1}H and ^{13}C NMR chemical shifts for a set of lactones and lactams were determined and analyzed. The theoretical NMR chemical shifts were calculated using density functional theory (DFT) and gauge independent atomic orbital (GIAO) approach in fourteen exchange-correlation functionals. The experimental versus computed chemical shift values for proton and carbon were compared and evaluated using linear correlation (R^2), mean absolute error (MAE), mean squared error (MSE), and root mean squared error (RMSE) with respect to the relative ability of each functional to predicting ^{1}H and ^{13}C nuclear magnetic resonance spectra. For ^{13}C NMR chemical shifts, statistical evaluation of data indicates that the most accurate prediction of ^{13}C chemical shifts is achieved at B3PW91, wB97XD, and CAM-B3LYP functionals, although B3PW91 proved marginally superior to the others. For ^{1}H shift data, the best results were obtained using the B3LYP, B3PW91, and MPW1PW91 functionals. The calculated results of ^{1}H and ^{13}C NMR chemical shifts for all the nuclei studied in the series of lactones and lactams are in good agreement with the experimental data.

Keywords: Chemical shifts, density functional theory, lactones, lactams, GIAO.

INTRODUCTION

Methods of density-functional theory DFT become an essential tool in modern molecular quantum chemistry. The best DFT functionals generally give results comparable in

quality with those of more elaborate ab initio methods at a fraction of the computational cost.[1, 2] DFT calculation of NMR shielding at very accurate levels of approximation are available at literature.[3-7] The most common method of performing this calculation is the gauge-including atomic orbital (GIAO) method[8,9], but other methods include individual gauge origins for different localized molecular orbitals (IGLO)[10, 11] and individual gauges for atoms in molecules (IGAIM)[12, 13]. The GIAO-DFT approach is thought to provide satisfactory chemical shifts for various nuclei[14-16] with larger molecules.

A large number of studies report the experimental NMR spectra and comparison with theoretical predictions. Guzzo *et al*. evaluated the exactitude of DFT for the calculation of ^{1}H and ^{13}C chemical shifts in calix[4]arenes. They reported that the B3LYP, B3PW91, and PBE1PBE for ^{1}H NMR chemical shifts and M06-2X, ωB97X-D, and LC-WPBE for ^{13}C NMR chemical shifts using the 6-31+G(d,p) method provides highly accurate qualitative and quantitative data.[17] Costa et al. found that the ωB97X-D/6-31G(d,p) is an accurate method for calculating the NMR spectra of aromatic compounds.[18, 19] Kart et al. have confirmed the suitability for ^{1}H NMR prediction with the B3LYP6-311G(d,p) functional within azocalix[4]arenes in $CDCl_3$ solvent.[20] A similar study was carried out by Hill et al. with the B3LYP/6-31++G(d, p) in drug molecules[21] and Lampert et al. who used three levels of theory (HF, B3LYP and BLYP) and four basis sets from (6-31G(d,p), to 6-311++G(2df,2dp) in phenol and 2-hydroxybenzoyl compounds.[22]

In this work we report DFT ^{1}H and ^{13}C NMR calculations using the GIAO method and TMS as reference, for a series of lactones: β-propiolactone, γ-butyrolactone, δ-valerolactone and ε-caprolactone, and lactams: azetidin-2-one, pyrrolidin-2-one, δ-valerolactam, and ε-caprolactam (see Fig. 1) in dichloromethane solution to assess the ability of different exchange-correlation functionals to reproduce experimental ^{1}H and ^{13}C NMR spectra measured in CD_2Cl_2 solution. Lactones and lactams are chosen because of their biological interests. The lactone group is present in a large series of pharmaceutical medication[23,24]. Lactamic group is the base of many antibiotics.[25]

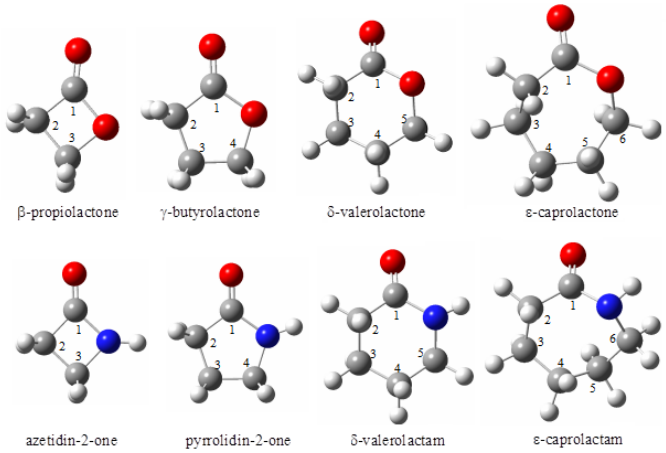


Fig 1. Molecular structures of the lactones and lactams studied

MATERIAL AND METHODOLOGY

1. NMR spectra acquisition

The ^{1}H and ^{13}C NMR spectra were obtained at ambient temperature in deuterated dichloromethane CD_2Cl_2 in a dedicated 5 mm probe. NMR spectra were acquired with a Bruker 300 spectrometer at 300.13 MHz for ^{1}H (65 k data points, 30° excitation pulse duration of 8.7 μs, spectral width of 5 kHz, acquisition time of 7.81 s and relaxation delay of 2 s) and at 75.47 MHz for ^{13}C (65 k data points, 45° excitation pulse duration of 6.7 μs, spectral width of 18 kHz, acquisition time of 1.82 s and relaxation delay of 2 s). The chemical shifts were related to Tetramethylsilane TMS as an internal standard (δ = 0.00). The general reproducibility of chemical shift data was estimated to be better than ± 0.01 ppm. All compounds were available commercially and were dried and purified before use. Their purities were checked from their ^{1}H and ^{13}C spectra. The samples were prepared by weight and volumetrically.

2. Computational Details

All of the DFT computations have been carried out with the Gaussian 09 computational chemistry software[26], using 14 exchange-correlation XC functionals in the DFT benchmarking, including: B3LYP[27, 28], B3PW91[29], BP86[30], BPV86[31], CAM-B3LYP[32], LSDA[33], LC-wPBE[34], M06-2X[35], MPW1PW91[36], PBEPBE[37, 38], HSEH1PBE[39], HCTH[40], TPSSTPSS[41] and wB97X-D.[42] The origins, nomenclature and characteristics of the exchange-correlation XC functionals studied have been described elsewhere.[43] After geometry optimization using the 6-311G+(2d, p) basis set, the harmonic frequencies were calculated at the same level. The absence of imaginary frequencies verified that all structures were true minima at their respective levels of calculation.

For the ^{1}H and ^{13}C chemical shifts, we employed the Gauge-Independent Atomic Orbital (GIAO) method.[8, 9] In all cases absolute isotropic magnetic shieldings (σ) were transformed into chemical shifts (δ/ppm) by reference to the shieldings of a standard compound Tetramethylsilane (TMS) calculated at the same level. (Equation. 1)

$$\delta_{cal} = \sigma_{TMS} - \sigma \quad (1)$$

We computed the effects of solvation using Barone and Cossi's implementation of the polarizable conductor model (CPCM)[44] at 6-311+G(2d,p) level, which is based on the Polarized Continuum Model (PCM) of Tomasi and co-workers. In this model, the solute cavities are modeled on the optimized molecular shape and include both electrostatic and nonelectrostatic contributions to the energies. The CPCM calculations were performed with tesserae of 0.3 $Å^2$ average size.

3. Statistical analyses

The quality between the calculated and experimental NMR spectra was analyzed by using a variety of statistical methods. The mean absolute error (MAE / ppm, Eq.3); the mean squared error (MSE / ppm^2, Eq. 4); the root mean squared error (RMSE / ppm, Eq.5) and Chi-squared (χ^2 / ppm, Eq. 6). Statistical analyses were carried out to determine which method produced the best results. Statistical analyses were performed using Microsoft Excel 2013.

$$MAE = \frac{\sum_{i=1}^{n}|\delta_i^{cal}-\delta_i^{exp}|}{n} \quad (2)$$

$$MSE = \frac{\sum_{i=1}^{n}(\delta_i^{cal}-\delta_i^{exp})^2}{n} \quad (3)$$

$$RMSE = \sqrt{MSE} = \sqrt{\frac{1}{n}\sum_{i=1}^{n}(\delta_i^{cal} - \delta_i^{exp})^2} \quad (4)$$

$$\chi^2 = \sum_{i=1}^{n}\frac{(\delta_i^{cal}-\delta_i^{exp})^2}{\delta_i^{cal}} \quad (5)$$

Where *n* is the total number of chemical shifts under consideration. In addition to the MAE, MSE, RMSE and χ^2 analyses, least-squares linear regression analysis was used to compare the calculated *versus* experimental ^{13}C chemical shifts.

RESULTS AND DISCUSSION

The ^{1}H and ^{13}C NMR chemical shifts were computed using Fourteen different exchange-correlation functionals described previously using the GIAO method and 6-311+G(2d,p) basis set in dichloromethane solvent. TMS was used as a reference in calculating and measuring the ^{1}H and ^{13}C chemical shifts. We have grouped our experimental and calculated results by compounds rang: lactones and lactams.

Overall, the calculated ^{1}H and ^{13}C NMR spectra are in excellent quantitative and qualitative agreement with the experimental spectrum. After calculations of the ^{1}H and ^{13}C NMR chemical shifts of lactones and lactams, $\Delta\delta$ was calculated according to Equation 6.

$$\Delta\delta = \delta_{exp} - \delta_{cal} \quad (6)$$

None of the fourteen exchange–correlation functionals tested presents large deviations ($\Delta\delta$), but some show better results than others. Comparing the differences between the experimental

and theoretical values ($\Delta\delta$), the most discrepant result for ^{13}C values was obtained for the carbon C_1 of δ-Valerolactame and C_4 of ε-Caprolactone with a maximum $\Delta\delta = 13.150$ ppm and $\Delta\delta = 12.198$ ppm respectively for HCTH exchange–correlation functionals.

For the ^{1}H chemical shifts, the best results were obtained for the hydrogen atoms in α position to the carbonyl group, in all compounds, and for the hydrogen of N-H group for lactams, which are acid hydrogens, with a minimum $\Delta\delta(C - \underline{H_\alpha}) = 0.003$ and 0.011 ppm for δ-Valerolactone and 2-Pyrrolidinone respectively at B3LYP, and $\Delta\delta(N - H) = 0.015$ ppm at MPW1PW91 for δ-Valerolactame.

To quantify the performance of each functionals, the statistical analysis using mean absolute error (MAE), the mean squared error (MSE), root mean squared error (RMSE) and Chi-squared (χ^2) was performed, and the results are also summarized in Tables 1–4 and figure 2. The MAE, MSE, and RMSE parameters are measures of the fitting error. These are used to estimate which functional gives a more accurate prediction, as smaller values indicate a smaller error. Pearson's chi-squared χ^2 is also mean to express how good a model can fit the experimental data, taking into account the sum of differences of observed and expected outcome frequencies.

As the data presented in Tables 2 and 4 indicate, for all carbon in selected compounds, the B3PW91 method for lactones and CAM-B3LYP for lactams (with dichloromethane solvation effects included) were able convincingly to predict ^{13}C NMR chemical shifts. The CAM-B3LYP exchange-correlation functionals give the smallest errors for lactams with 1.438 ppm for the mean absolute error (MAE) and 1.837 ppm for the root mean squared error (RMSE), ahead of B3PW91 and wB97XD (MAE values of 2.033 – 2.109 ppm, RMSE values 2.429 – 2.340 ppm respectively). The B3PW91 method for lactones gives the best results with MAE of 0,085 ppm. These values indicate that the XC functionals used in this work, perform satisfactorily when compared to the values presented in the literature from other studies.[17, 21] The HCTH exchange-correlation functionals, enormously overestimate the ^{13}C NMR chemical shifts with MAEs of 4.714 and 5.050 ppm, RMS errors of 5.409 and 6.102 ppm (for lactones and lactams respectively).

For ^{1}H NMR chemical shifts, the functionals with the best performance were B3LYP, B3PW91 and MPW1PW91, exchange-correlation functionals showed the lowest values of RMSE and MAE and χ^2, while PBEPBE and HCTH have the worst results for lactones and lactams respectively.

Table 1. The ^{1}H NMR chemical shifts of lactones calculated using 14 exchange-correlation functionals and 6-311G+(2d,p) basis set in CD_2Cl_2 solvent and experimental values (in ppm relative to TMS), and statistical parameters defined in equations. 2-5. MAE = mean absolute error; MSE = mean squared error; RMSE = the root mean squared error; χ^2 = Chi-squared.

Compounds	H_i	B3LYP	B3PW91	BPV86	CAM-B3LYP	LSDA	MPW1PW91	PBEPBE	HSEH1PBE	HCTH	TPSSTPSS	wB97X-D	LC-wPBE	M06-2X	BP86	δ_{exp}
β-Propiolactone	H_2	2,624	3,017	3,112	3,140	3,011	3,137	4,332	3,151	3,182	3,043	3,114	3,127	2,513	3,325	2,839
	H_3	4,471	4,508	4,078	4,616	4,074	4,556	4,989	3,789	3,887	3,772	4,822	4,610	4,471	4,875	4,667
γ-Butyrolactone	H_2	2,347	2,253	2,029	2,535	2,119	2,299	3,250	2,251	2,276	2,149	2,727	2,256	2,253	2,527	2,449
	H_3	2,124	2,036	1,871	2,224	1,963	2,076	3,101	1,975	2,115	1,948	2,319	1,999	2,040	2,211	2,168
	H_4	4,245	4,194	4,606	4,530	4,178	4,281	5,286	4,194	4,413	4,138	4,218	4,221	4,221	4,342	4,320
δ-Valerolactone	H_2	2,426	2,384	2,205	3,025	2,290	2,427	3,397	2,387	2,448	2,315	2,537	2,328	2,365	2,546	2,423
	H_3	1,801	1,746	1,614	1,824	1,676	1,803	2,844	1,767	1,879	1,707	1,873	1,675	1,739	1,855	1,76
	H_4	1,577	1,654	1,466	1,748	1,542	1,652	2,695	1,658	1,730	1,620	1,765	1,626	1,639	1,770	1,671
	H_5	4,254	4,276	4,870	4,534	4,310	4,303	5,041	4,127	4,496	4,470	4,227	4,217	4,127	4,431	4,377
ε-Caprolactone	H_2	2,451	2,482	2,336	2,539	2,433	2,515	3,116	2,779	2,547	2,422	2,645	2,407	2,471	2,577	2,502
	H_3	1,797	1,764	1,948	1,843	1,542	1,768	2,701	1,964	1,973	1,576	1,908	1,766	1,598	1,886	1,817
	H_4	1,671	1,671	1,753	1,730	1,595	1,765	2,176	1,768	1,798	1,624	1,763	1,568	1,658	1,774	1,601
	H_5	1,765	1,727	1,857	1,802	1,640	1,767	2,328	1,897	1,822	1,662	1,782	1,664	1,722	1,781	1,669
	H_6	4,354	4,457	4,953	4,544	4,077	4,315	5,172	4,265	4,855	5,022	4,459	4,320	4,277	4,520	4,477
^{1}H NMR statistical analysis parameters																
MAE		0,090	0,085	0,289	0,143	0,188	0,094	0,835	0,217	0,192	0,214	0,140	0,109	0,133	0,120	
MSE		0,011	0,011	0,104	0,042	0,060	0,015	0,771	0,089	0,074	0,100	0,024	0,017	0,027	0,027	
RMSE		0,107	0,104	0,322	0,204	0,245	0,121	0,878	0,299	0,271	0,316	0,155	0,132	0,163	0,165	
χ^2		0,056	0,056	0,473	0,195	0,288	0,076	3,201	0,383	0,300	0,410	0,126	0,088	0,139	0,129	
R^2		0,996	0,993	0,937	0,982	0,977	0,990	0,942	0,948	0,944	0,931	0,992	0,990	0,992	0,990	

Table 2. The ^{13}C NMR chemical shifts of lactones calculated using 14 exchange-correlation functionals and 6-311G+(2d,p) basis set in CD_2Cl_2 solvent and experimental values (in ppm relative to TMS), and statistical parameters defined in equations. 2-5. MAE = mean absolute error; MSE = mean squared error; RMSE = the root mean squared error; χ^2 = Chi-squared.

Compounds	C_i	B3LYP	B3PW91	BPV86	CAM-B3LYP	LSDA	MPW1PW91	PBEPBE	HSEH1PBE	HCTH	TPSSTPSS	wB97X-D	LC-wPBE	M06-2X	BP86	δ_{exp}
β-Propiolactone	C_1	171,267	166,911	165,662	168,917	169,796	166,186	165,570	165,249	162,685	163,568	170,986	164,858	177,813	165,651	167,600
	C_2	41,117	37,850	40,628	37,858	41,005	36,649	40,253	35,955	40,804	40,484	41,628	41,051	38,576	40,662	38,100
	C_3	60,088	56,326	59,394	56,817	59,860	54,890	58,996	53,754	59,480	58,418	59,215	59,712	55,106	59,357	57,700
γ-Butyrolactone	C_1	180,058	175,660	174,980	174,694	180,981	174,859	174,981	180,113	172,505	173,379	174,720	173,581	187,097	174,990	177,451
	C_2	29,642	26,277	28,898	26,402	29,702	25,054	28,782	29,857	30,292	29,404	24,438	29,966	26,206	28,903	26,725
	C_3	25,590	21,832	25,261	21,582	25,007	20,557	25,152	25,441	27,093	25,992	19,455	24,000	20,435	25,283	21,354
	C_4	70,267	66,248	70,358	67,493	72,342	64,728	70,255	69,776	70,897	69,590	69,699	68,661	65,933	70,378	67,981
δ-Valerolactone	C_1	171,209	170,806	165,549	171,146	170,934	171,403	165,468	171,269	163,493	164,508	172,217	175,343	178,381	165,543	170,377
	C_2	33,364	33,321	32,687	31,795	33,707	33,408	32,665	33,140	34,014	32,860	33,281	32,174	29,505	32,712	32,674
	C_3	24,828	24,554	24,540	20,427	24,183	24,614	24,609	24,387	26,895	25,189	18,095	21,880	18,728	24,575	18,231
	C_4	26,410	25,927	25,511	22,476	25,649	26,108	25,625	25,911	27,700	26,004	19,756	23,984	20,791	25,549	21,271
	C_5	72,565	72,326	72,748	68,747	74,069	72,153	72,736	72,026	73,215	71,696	65,824	70,420	68,232	72,777	68,454
ε-Caprolactone	C_1	178,167	173,694	172,879	175,900	176,993	178,215	172,957	178,196	170,590	171,376	178,821	181,670	190,319	174,449	174,802
	C_2	37,363	33,367	36,784	35,903	35,079	37,340	36,683	37,111	37,641	36,654	37,327	36,325	38,887	38,372	33,124
	C_3	33,040	28,434	32,682	28,603	26,615	32,578	32,252	32,482	34,074	32,290	25,865	23,765	26,323	27,814	27,989
	C_4	26,901	26,350	26,220	23,580	24,076	26,444	26,390	26,276	28,760	26,890	31,881	26,354	32,602	34,289	22,515
	C_5	33,083	28,541	32,073	29,150	30,289	32,597	32,858	32,507	34,704	32,798	32,294	30,293	33,169	31,678	28,936
	C_6	70,083	67,829	71,102	68,349	70,554	70,617	71,079	70,532	71,500	70,005	70,323	69,078	71,678	70,691	68,115
^{13}C NMR statistical analysis parameters																
MAE		3,545	1,805	3,356	2,229	3,328	3,115	3,313	3,383	4,714	3,595	2,726	2,910	4,423	3,323	
MSE		17,644	7,052	15,925	5,696	14,156	14,716	15,990	15,796	29,260	18,450	11,147	10,858	38,521	18,121	
RMSE		4,201	2,656	3,991	2,387	3,763	3,836	3,999	3,974	5,409	4,295	3,339	3,295	6,207	4,257	
χ^2		9,029	4,203	7,987	2,823	7,201	7,561	7,970	8,241	13,097	8,670	5,050	4,106	8,115	8,967	
R^2		0,9995	0,9987	0,9994	0,9996	0,9991	0,9975	0,9993	0,9981	0,9992	0,9994	0,9972	0,9976	0,9963	0,9979	

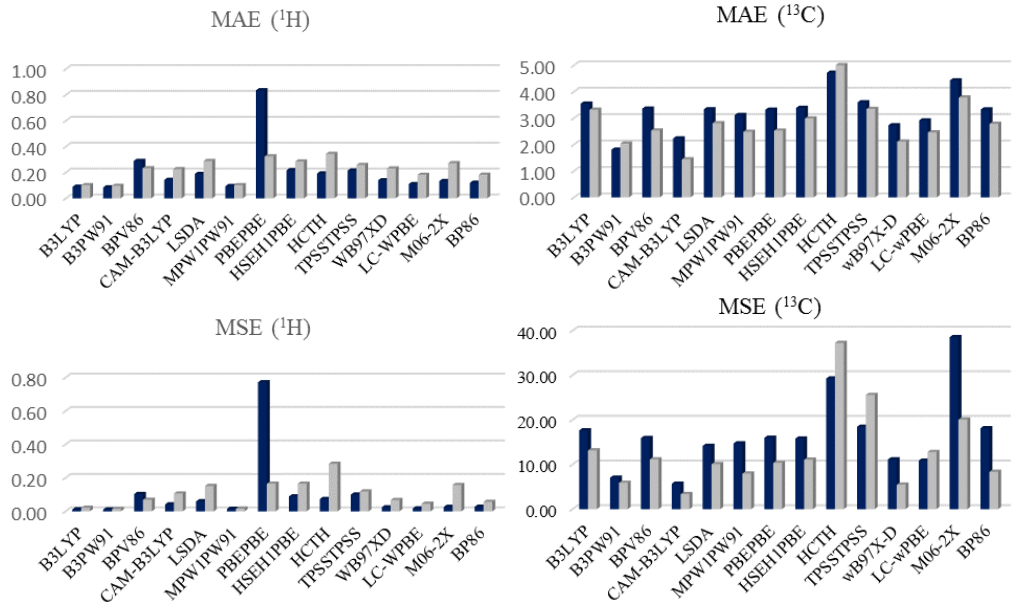
Table 3. The ^{1}H NMR chemical shifts of lactams calculated using 14 exchange-correlation functionals and 6-311G+(2d,p) basis set in CD_2Cl_2 solvent and experimental values (in ppm relative to TMS), and statistical parameters defined in equations. 5. MAE = mean absolute error; MSE = mean squared error; RMSE = the root mean squared error; χ^2 = Chi-squared.

Compounds	H_i	B3LYP	B3PW91	BPV86	CAM-B3LYP	LSDA	MPW1PW91	PBEPBE	HSEH1PBE	HCTH	TPSSTPSS	WB97XD	LC-WPBE	M06-2X	BP86	δ_{exp}
2-Azetidinone	N-H	5,786	6,100	5,646	5,672	5,742	5,875	5,786	5,713	4,877	5,655	6,469	5,754	5,907	5,899	6,131
	H_2	2,872	2,826	2,730	2,948	2,701	2,907	2,847	2,860	2,862	2,730	3,166	2,832	2,917	2,972	2,999
	H_3	3,284	3,293	3,072	3,242	2,976	3,191	3,015	3,214	3,181	3,064	3,601	3,110	3,206	3,272	3,305
2-Pyrrolidinone	N-H	6,949	6,877	6,947	6,318	6,053	6,899	5,997	5,825	5,978	6,295	6,929	6,679	5,959	6,642	7,092
	H_2	1,927	1,906	1,836	2,017	1,922	2,011	1,820	2,068	2,077	1,950	2,162	2,075	2,076	2,069	1,938
	H_3	1,792	1,826	1,784	1,908	1,893	1,978	1,802	2,005	1,909	1,883	1,998	1,938	2,011	1,987	1,850
	H_4	2,518	2,629	3,117	3,136	2,826	2,905	2,140	3,130	3,408	3,243	3,252	3,136	3,321	3,241	2,893
δ-Valerolactame	N-H	6,187	6,213	6,237	5,681	5,614	6,269	5,869	5,653	5,297	5,741	6,380	6,154	5,489	5,968	6,284
	H_2	2,435	2,442	1,988	2,295	2,103	2,252	2,173	2,213	2,283	2,601	2,996	2,144	2,182	2,277	2,550
	H_3	1,755	1,714	1,519	1,771	1,645	1,753	1,615	1,720	1,839	1,858	1,825	1,624	1,682	1,818	1,779
	H_4	1,560	1,661	1,321	1,675	1,561	1,671	1,502	1,669	1,753	1,767	1,749	1,562	1,558	1,724	1,588
	H_5	2,998	3,028	2,781	3,310	3,128	3,131	2,742	3,280	3,144	3,137	3,297	3,085	3,240	3,144	3,033
ε-Caprolactame	N-H	6,376	6,394	6,764	5,871	5,961	6,499	6,118	5,957	5,639	5,833	6,642	6,481	5,955	5,997	6,562
	H_2	2,350	2,307	2,163	2,388	2,252	2,359	2,182	2,323	2,382	2,254	2,523	2,286	2,336	2,405	2,409
	H_3	0,003	0,007	0,003	0,095	0,178	0,005	0,200	0,276	0,208	0,101	0,004	0,026	0,215	0,030	1,805
	H_4	0,000	0,001	0,006	0,003	0,000	0,003	0,008	0,008	0,009	0,000	0,023	0,009	0,009	0,008	1,801
	H_5	0,002	0,000	0,002	0,002	0,001	0,008	0,001	0,012	0,002	0,001	0,011	0,004	0,013	0,009	1,730
	H_6	0,056	0,027	0,016	0,019	0,002	0,000	0,265	0,018	0,078	0,038	0,040	0,019	0,055	0,037	3,156
^{1}H NMR statistical analysis parameters																
MAE		0,101	0,097	0,232	0,225	0,288	0,102	0,324	0,285	0,343	0,258	0,231	0,181	0,272	0,183	
MSE		0,021	0,014	0,069	0,107	0,152	0,016	0,165	0,165	0,284	0,119	0,068	0,045	0,158	0,057	
RMSE		0,144	0,120	0,263	0,327	0,389	0,128	0,407	0,407	0,533	0,344	0,260	0,213	0,397	0,238	
χ^2		0,108	0,090	0,523	0,385	0,690	0,105	0,921	0,635	1,036	0,475	0,492	0,269	0,606	0,263	
R^2		0,997	0,998	0,990	0,990	0,991	0,997	0,987	0,982	0,978	0,991	0,995	0,992	0,987	0,992	

Table 4. The ^{13}C NMR chemical shifts of lactams calculated using 14 exchange-correlation functionals and 6-311G+(2d,p) basis set in CD_2Cl_2 solvent and experimental values (in ppm relative to TMS), and statistical parameters defined in equations. 2-5. MAE = mean absolute error; MSE = mean squared error; RMSE = the root mean squared error; χ^2 = Chi-squared.

Compounds	C_i	B3LYP	B3PW91	BPV86	CAM-B3L-YP	LSDA	MPW1PW91	PBEPBE	HSEH1PBE	HCTH	TPSSTPSS	wB97X-D	LC-wPBE	M06-2X	BP86	δ_{exp}
2-Azetidinone	C_1	174,633	166,922	160,533	173,227	165,697	167,838	160,263	167,585	158,357	159,446	169,350	170,282	176,018	167,094	169,600
	C_2	42,781	42,194	41,117	42,866	42,073	42,333	40,851	41,794	41,736	41,221	42,122	41,088	39,036	40,686	38,300
	C_3	38,098	37,834	36,689	37,560	36,002	37,794	36,189	37,201	38,094	37,756	37,491	35,895	32,021	37,245	35,300
2-Pyrrolidinone	C_1	179,466	178,762	173,069	180,560	179,379	179,591	174,807	174,479	170,066	171,132	181,107	178,375	189,126	176,507	179,400
	C_2	31,384	31,726	30,503	28,290	31,568	31,868	30,365	31,477	31,818	30,667	31,980	31,743	32,996	31,970	30,500
	C_3	24,352	24,449	23,905	20,213	23,480	24,514	23,815	24,176	25,987	24,706	24,096	22,472	24,168	24,478	21,000
	C_4	44,205	44,430	44,194	39,969	44,654	44,374	44,008	44,062	45,436	44,469	43,864	42,175	44,423	44,723	42,600
δ-Valerolactame	C_1	179,289	167,659	168,798	173,623	170,976	167,218	173,669	167,223	159,650	161,620	169,144	167,803	181,785	170,165	172,800
	C_2	34,568	30,413	27,281	30,885	34,905	29,188	33,702	29,226	32,348	31,611	28,252	23,278	30,016	33,846	31,600
	C_3	25,355	21,050	19,463	20,986	24,791	19,804	24,765	19,843	24,311	23,182	19,570	18,496	20,248	25,025	22,500
	C_4	26,145	21,675	20,493	22,013	25,229	20,508	24,111	20,568	24,577	23,492	19,429	17,520	19,058	24,308	21,400
	C_5	45,756	41,771	42,956	41,350	46,433	40,386	45,454	40,426	44,130	43,624	40,121	32,959	40,594	45,852	42,200
ε -Caprolactame	C_1	182,376	178,592	178,664	180,431	179,128	179,438	179,600	173,331	169,964	168,680	179,854	178,972	182,845	176,241	179,600
	C_2	39,807	39,569	38,253	36,320	40,800	39,589	39,264	39,408	40,155	36,529	39,552	38,516	41,245	40,850	36,900
	C_3	27,136	26,537	25,442	22,825	26,368	26,626	26,616	26,477	28,983	24,644	26,083	23,963	26,544	25,038	23,400
	C_4	34,672	32,028	31,267	30,181	35,039	34,105	31,457	34,070	36,202	31,896	31,362	30,809	34,475	33,877	29,900
	C_5	34,298	33,453	32,147	31,389	35,642	33,677	33,337	34,590	35,197	30,966	32,474	31,235	35,671	34,753	30,700
	C_6	45,611	42,431	41,357	41,423	46,186	45,410	45,328	45,239	46,748	43,067	43,950	43,893	45,894	44,940	42,600
^{13}C NMR statistical analysis parameters																
MAE		3,313	2,033	2,529	1,438	2,805	2,478	2,524	2,984	5,010	3,344	2,109	2,457	3,777	2,782	
MSE		13,163	5,902	11,15(	3,376	10,083	7,968	10,360	11,081	37,22(	25,575	5,474	12,797	20,080	8,351	
RMSE		3,628	2,429	3,340	1,837	3,175	2,823	3,219	3,329	6,102	5,057	2,340	3,577	4,481	2,890	
χ^2		5,315	2,421	3,085	1,325	4,773	3,603	3,085	3,740	8,643	3,980	2,877	7,955	5,465	3,687	
R^2		0,9994	0,9991	0,998(	0,9992	0,9994	0,9984	0,9987	0,9986	0,9991	0,9995	0,998(	0,9968	0,9981	0,9998	

In Figure 2, we present the performance of the selected exchange-correlation functionals for the calculation of ^{13}C chemical shifts of selected lactones and lactams based on the statistical analysis.



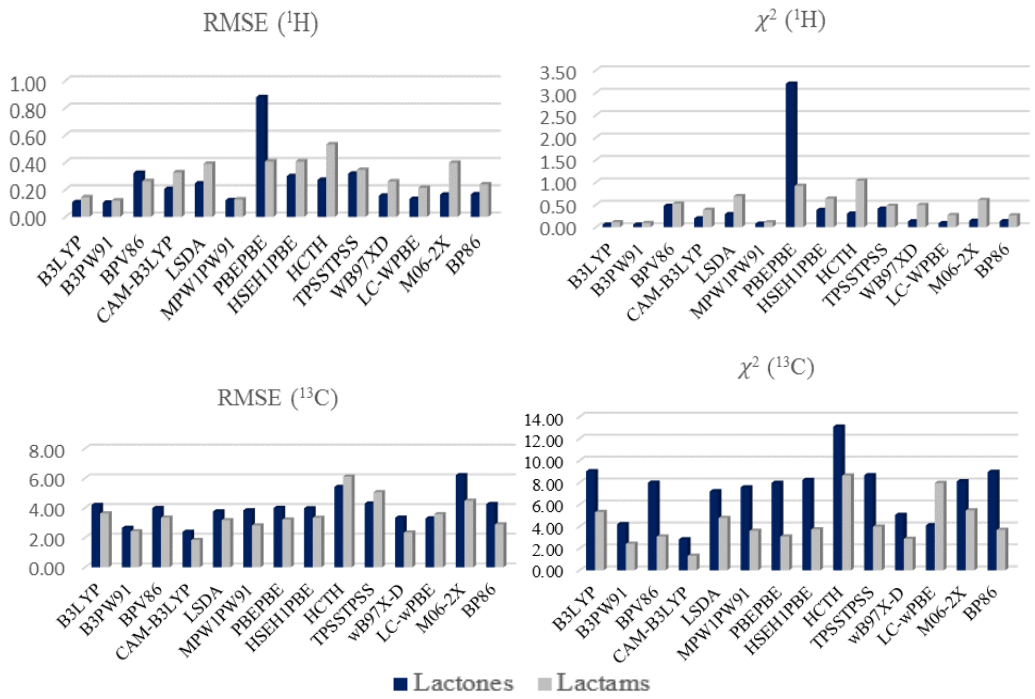


Fig 2. Results from the statistical treatment MAE, MSE, RMSE, and χ^2 of the theoretical calculations ^{1}H and ^{13}C NMR chemical shifts in the studied lactones and lactams.

In addition to the MAE, MSE, RMSE and χ^2 analyses, least-squares linear regression analysis was used to compare the calculated versus experimental ^{1}H and ^{13}C chemical shifts. The regression coefficients, R^2, in Tables 1-4 indicate that calculated values are strongly correlated to the experimental shifts: all R^2 values are reveals than 0.980 for ^{1}H chemical shifts and 0.996 for ^{13}C NMR data. The agreement between theory and experiment is quite impressive; indicating that for this level of calculation, there is no need for any ad hoc scaling of the calculated results.

CONCLUSION

As a result, DFT methods have become the dominant approach for modeling chemical shieldings. In this study, the results of experimental and DFT level of theory with the combination of GIAO NMR method and 6-311G+(2d, p) basis set are reported. We have tested the performances of several exchange–correlation DFT functionals in describing ^{1}H and ^{13}C chemical shifts for some lactones and lactams and compared them with experimental data. The statistical comparison between deferent functionals reveals that B3PW91, wB97XD, and CAM-B3LYP are more accurate in the calculation of ^{13}C chemical shifts. For ^{1}H shift data, the best performance was obtained using the B3LYP, B3PW91, and MPW1PW91 functionals.

REFERENCES

1. J. K. Labanowski, J. W. Anzelm, Density Functional Methods in Chemistry; *Springer-Verlag*: New York, (1991).
2. G. E. Scuseria, *J.Chem.Phys*, 97, 7528–7530 (1992).
3. M. B. Ferraro, *J.Mol. Struc: THEOCHEM*, 528, 199–209 (2000).
4. I. Alakorta, J. Elguero, *Structural Chemistry*, 4, 377-389 (2003).
5. P. Chomoch, L. Stefaniak, E. Melzer, S. Baloniak, G.A. Webb, *Magnetic Resonance in Chemistry*, 37, 493–497 (1999).
6. G. Berionni, B. Pegot, G. Régis, *Magnetic Resonance in Chemistry*, 48, 101-110 (2009).
7. J.A. Dabado, N. Benkadour, S. Melchor, D. Portal, *J.Mol.Struc: THEOCHEM*, 672, 127–132 (2004).
8. K. Wolinski, J. F. Hilton, P. Pulay, *J.Am.Chem.Soc*, 112, 8251-60 (1990).
9. J. R. Cheeseman, G. W. Trucks, T. A. Keith, M. J. Frisch, *J.Chem.Phys*, 104, 5497-509 (1996).
10. M. Schindler, *Magn.Reson.Chem*, 26, 394–407 (1988).
11. W. Kutzelnigg, U. Fleischer, M. Schindler, NMR Basic Principles and Progress, 165-262 (1990).
12. T. A. Keith, R. F. W. Bader, *Chem.Phys.Lett*, 194, 1–8 (1992).
13. N. H. Werstiuk, J. Ma, *Canadian Journal of Chemistry*, 74, 875–884 (1996).
14. M. Barfield, P. Fagerness, *J.Am.Chem.Soc*, 119, 8699–8711 (1997).
15. B. Osmialowski, E. Kolehmainen, R. Gawinecki, *Magn.Reson.Chem*, 39, 334–340 (2001).
16. K.Dybiec, A. Gryff-Keller, *Magn.Reson.Chem*, 47, 63–66 (2009).
17. R. N. Guzzo, M. J. C. Rezende, V. Kartnaller, J. W. de M. Carneiro, S. R. Stoyanov, *L. M. da. Costa*, 1157, 97–105 (2018).
18. L. M. Da Costa, S. Hayaki, S. R. Stoyanov *Phys Chem Chem Phys* 14, 3922 (2012).
19. L. M. Da Costa, S. R. Stoyanov, S. Gusarov, X. Tan, M. R. Gray, J. M.Stryker, A. Kovalenko, *Energy & Fuels*, 26, 2727–2735 (2012).
20. H. H. Kart, A. Bayrakdar, S. Elcin, H. Deligoz, M. Karabacak, *Spectrochim Acta - Part A Mol Biomol Spectrosc* 146, 151–162 (2015).
21. D. E. Hill, N. Vasdev, J. P. Holland, *Comp.Theo.Chem*, 105, 161–172. H (2015).
22. Lampert, W. Mikenda, A. Karpfen, H. Kählig, *J.Phys.Chem A*, 101, 9610–9617 (1997).
23. F. M. Dean, Naturally Occurring Oxygen Ring Compounds; Butterworth: London., (1963).
24. G. Rousseau, *Tetrahedron*, 51, 2777–2849 (1995).
25. M. S. Wilke, A. L. Lovering, N. C. Strynadka, *Curr.Opin. Microbiol* 8, 525–533 (2005).
26. M. J. Frisch, G. W. Trucks, H. B. Schlegel & all, Gaussian, Inc., Wallingford CT, (2009).
27. A.D. Becke, *Journal of Chemical Physics*, 98, 5648-5652 (1993).
28. K. Burke, J.P. Perdew, Y. Wang, Electron density functional theory: Recent Progress and New Directions, Ed. J. F. Dobson, G. Vignale, and M. P. Das (Plenum, 1998).
29. A.D. Becke, *Physical Review A*, 38, 3098–3100 (1988).
30. J.P. Perdew, *Physical Review, B* 33, 8822-8824 (1986).
31. T. Yanai, D. P. Tew, N. C. Handy, *Chem.Phys.Lett*, 393, 51–57 (2004).
32. S.H. Vosko, L. Wilk, M. Nusair, *Canadian Journal of Physics*, 58, 1200-1211 (1980).
33. C. Adamo, V. Barone, *J.Chem.Phys*, 110, 6158 (1999).

34. Y. Zhao and D. G. Truhlar, *Journal of Physical Chemistry*, 110, 5121-29 (2006).
35. C. Adamo, V. Barone, *J.Chem.Phys*, 108, 664–675 (1998).
36. J.P. Perdew, K. Burke, M. *Physical Review Letters*, 77, 3865-3868 (1996).
37. J.P. Perdew, K. Burke, M. Ernzerhof, *Physical Review Letters*, 78, 1396 (1997).
38. T. M. Henderson, A. F.Izmaylov, G. Scalmani, G. E. Scuseria, *Journal of Chemical Physics*, 131, 044108 (2009).
39. A. D. Boese, N. C. Handy, *J.Chem.Phys*, 114, 5497–5503 (2001).
40. J. Tao, J. P. Perdew, V. N. Staroverov, G. E. Scuseria, *Physical Review Letters*, 91, 1-4 (2003).
41. M. M. Quintal, A. Karton, M. A. Iron, A. D. Boese, J. M. L. Martin, *J. Phys. Chem A*, 110, 709–716 (2006).
42. V. Barone, M. Cossi, *J. Phys. Chem A*, 102, 1995–2001 (1998).
43. E. Cancès, B. Mennucci, J. Tomasi, *J.Chem.Phys*, 107, 3032–3041 (1997).
44. M. Cossi, V. Barone, R. Cammi, J. Tomasi, *Chem.Phys.Lett*, 255, 327–335 (1996).