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Density functional theory: ^{1}H- and ^{13}C-NMR spectra of some coumarin derivatives

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Abstract: For some synthesized coumarin derivatives, ^{1}H- and ^{13}C-NMR isotropic chemical shifts and some other molecular properties were calculated using the density functional theory. The calculations yielded reliable results that were in good correlation with experimental data. This is a good basis for collaboration between experimentalists and quantum chemists.

Keywords: NMR spectra; Spartan 10 software; quantum chemistry; chemical shifts.

INTRODUCTION

NMR spectroscopy is one of the key analytical methods in modern organic and synthetic chemistry. It is widely used for structure elucidation and in investigations of the reactivity and reaction mechanisms involving organic molecules. In addition, the irreplaceable role of NMR spectroscopy is commonly recognized in biochemistry, biology and pharmacy for structure determination and in studies of biomolecular dynamics.[1]

After preliminary NMR measurements have been realized, it is then decided whether a direct structure determination using other methods should be performed.[2]

Experimentalists expect additional information from quantum chemical calculations; this is obtained by the calculation of NMR chemical shifts for some structure and comparing them to existing NMR data. If the two sets of NMR data

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correlate well, all the molecular properties that were obtained by the calculations can be assigned to the new compound and accordingly, the experimentalist obtains a detailed description. In this way, the calculation of NMR chemical shifts provides an ideal basis for collaboration between experimentalists and quantum chemists.[2]

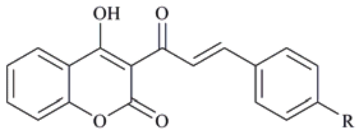
In recent years, density functional theory (DFT) calculations have been used extensively for the calculation of a wide variety of molecular properties, such as equilibrium structure, charge distribution, NMR spectra, and to provide reliable results that are in good correlation with experimental data.[3,4]

A series of 3-cinnamoyl-4-hydroxycoumarin derivatives were prepared, as reported in a previous paper.[5] In the present research, ^{13}C-NMR spectra and ^{1}H-NMR spectra of these derivatives were recorded. The Beck three-parameter exchange functional[6] with the Lee, Yang and Parr[7] correlation functional (B3LYP), developed by Truhlar *et al*.[8] were used to perform theoretical calculations on the structure, the ^{1}H- and ^{13}C-NMR spectra and some additional properties of the investigated compounds. Correlation coefficients were used to compare the experimentally observed and theoretically computed shifts for each synthesized compound.

MATERIALS AND METHODS

Investigated compounds

The experimental and theoretical properties of three 3-substituted derivatives of 4-hydroxycoumarin were studied. The structures of the investigated compounds are presented in Fig. 1.



R= Br, OCH_3, Cl

Fig. 1. Structure of the synthesized compounds.

NMR measurements

The one- and two-dimensional homo- and heteronuclear ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker AV-600 spectrometer, operating at 600.133 MHz for the ^{1}H nucleus and 150.917 MHz for the ^{13}C nucleus. The samples were measured in DMSO-d_6 solutions at 298 and 373 K in 5 mm NMR tubes. The chemical shifts, ppm, are referred to TMS as an internal standard. The following measurement techniques were used: standard ^{1}H-, attached proton test (APT), correlation spectroscopy (COSY), and heteronuclear multiple quantum correlation (HMQC) and heteronuclear multiple bond correlation (HMBC) spectroscopy. The 2D NMR spectra were measured in the pulsed field gradient mode (*z*-gradient).

Theoretical calculations

All the calculations were realized using Spartan 10 software.

The geometries were optimized at the B3LYP level of theory along with standard 1, 2 and 3 G (d) basis set as shown in Fig. 2.

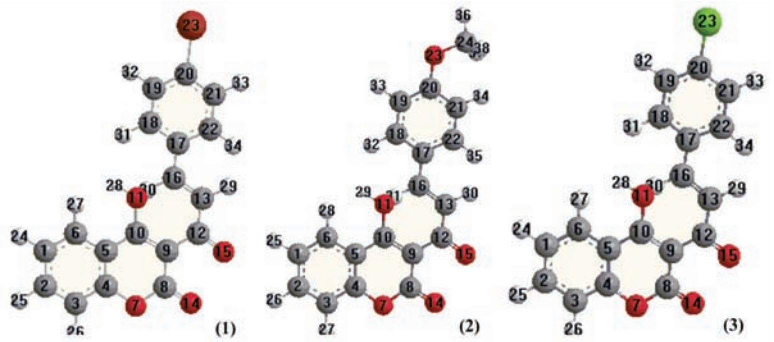


Fig. 2. The optimized geometry of the compounds.

The harmonic vibration frequencies were calculated by this method and the results were compared with the experimental spectra. This method was used for calculating ^{1}H- and ^{13}C- NMR chemical shifts at the B3LYP/6-31*G (d) level for the three synthesized coumarin derivatives.

RESULTS AND DISCUSSION

Spectral data of the prepared compounds are given in the Supplementary material to this paper.

Bond lengths and bond angles

The optimized structural parameters, bond lengths and bond angles for the thermodynamically preferred geometry of compounds **1**–**3** determined at the B3LYP/6-31*G level are presented in Table I in accordance with the atom numbering scheme of the molecules shown in Fig. 2.

From the structural data, it was observed that the various C–C bond distances calculated between the carbon atoms and the C–H and C–O bond length are found to be nearly the same for all three structures. The influence of the substituent on the molecular parameters, particularly on the C–C bond distance of ring carbon atoms, seems to be negligibly small.

The calculated bond angles are very similar to each other in these molecules. An investigation of bond angles $O_7–C_8–O_{14}$, $O_7–C_8–C_9$, $C_9–C_{12}–C_{15}$ and $C_9–C_{12}–C_{13}$ showed that these atoms were sp^2 hybridized and that they were completely planar. This data clearly indicates that there is a pronounced tautomer structure between the OH and the C=O group, which is shown in Fig. 3.

Comparison of the experimentally measured and theoretically computed shifts

Chemical shifts calculated using the B3LYP level with the 6-31*G (d) basis sets can be utilized to eliminate the uncertainties in the fundamental assignments of

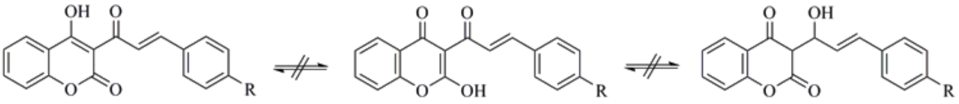


Fig. 3. Tautomerization of the coumarin derivatives.

the spectra. The ^{1}H- and ^{13}C- theoretical and experimental chemical shifts, isotropic shielding tensors and assignments of **1**–**3** are presented in Tables II and III, respectively.

TABLE I. Selected structural parameters calculated for compounds **1**–**3** by the DFT B3LYP method with 6-31*G basis sets

Bond length, nm				Bond angles, °			
Bond	Compound			Bond	Compound		
	1	**2**	**3**		**1**	**2**	**3**
O_7–C_4	0.138	0.136	0.136	O_7–C_4–C_5	121.80	121.86	121.40
C_4–C_5	0.141	0.141	0.140	C_4–O_7–C_8	122.13	122.64	123.48
C_3–C_4	0.139	0.140	0.140	C_4–C_3–H_{26}	118.88	118.56	119.02
C_5–C_6	0.141	0.141	0.141	C_5–C_6–H_{27}	120.96	120.57	118.64
O_7–C_8	0.140	0.141	0.140	O_7–C_8–O_{14}	116.87	116.88	114.96
C_8–O_{14}	0.122	0.121	0.121	O_7–C_8–C_9	117.00	116.70	117.18
C_8–C_9	0.144	0.145	0.146	C_9–C_{10}–C_5	120.84	120.89	120.92
C_9–C_{12}	0.152	0.152	0.148	C_9–C_{12}–C_{15}	119.48	119.79	118.00
C_{10}–O_{11}	0.136	0.135	0.131	C_{10}–O_{11}–H_{28}	110.19	110.40	104.72
C_{12}–C_{13}	0.146	0.147	0.147	C_9–C_{12}–C_{13}	119.27	119.79	120.20
C_{13}–C_{16}	0.135	0.135	0.135	C_{13}–C_{16}–H_{29}	117.63	117.63	118.18
C_{16}–C_{17}	0.146	0.146	0.146	C_{17}–C_{16}–H_{30}	114.94	114.75	114.90
C_{17}–C_{18}	0.141	0.140	0.141	C_{17}–C_{18}–H_{31}	119.43	119.03	120.10
C_{17}–C_{22}	0.141	0.141	0.141	C_{17}–C_{22}–H_{34}	120.18	119.88	119.16
C_{22}–C_{21}	0.139	0.138	0.139	C_{20}–C_{19}–H_{32}	120.33	121.11	120.26
C_{20}–C_{19}	0.140	0.140	0.140	C_{21}–C_{20}–C_{19}	121.36	119.56	121.01

TABLE II. The experimental and calculated ^{1}H-isotropic chemical shifts, ppm, with respect to DMSO-d_6 for compounds **1**–**3**

Assignment	**1**		**2**		**3**	
	Calcd.	Exp.	Calcd.	Exp.	Calcd.	Exp.
H_{24}	7.36	7.40	–	–	7.12	7.40
H_{25}	7.99	7.79	7.07	7.38	7.50	7.78
H_{26}	7.07	7.36	7.40	7.76	7.00	7.35
H_{27}	8.32	8.02	7.10	7.33	8.00	8.01
H_{28}	–	–	7.80	8.00	–	–
H_{29}	8.41	8.22	–	–	8.05	8.21
H_{30}	7.93	7.92	8.30	8.14	7.98	7.93
$H_{31,34}$ for compound **2** H_{31}	7.67	7.65	7.68	7.98	7.46	7.71
$H_{32,33}$ for compound **2** $H_{32,35}$	7.56	7.65	7.70	7.68	7.11	7.49
$H_{33.34}$	–	–	6.80	7.03	–	–
$H_{36,37,38}$	–	–	3.7	3.84	–	–

TABLE III. The experimental and calculated ^{13}C-isotropic chemical shifts, ppm, with respect to DMSO-d_6 for compounds **1**–**3**

Assignment	**1**		**2**		**3**	
	Calcd.	Exp.	Calcd.	Exp.	Calcd.	Exp.
C_1	129.20	124.00	121.7	123.9	122.68	124.00
C_2	134.21	135.90	131.3	135.7	134.43	135.00
C_3	119.53	116.20	118.0	116.1	116.34	116.20
C_4	158.60	153.80	156.4	153.7	157.17	153.80
C_5	115.70	115.40	115.7	115.7	116.80	115.30
C_6	130.60	124.80	118.4	124.7	127.20	124.80
C_8	167.60	158.90	160.9	159.0	161.80	158.90
C_9	107.60	100.50	112.1	100.0	104.90	100.50
C_{10}	177.20	179.60	179.8	180.1	178.00	179.60
C_{12}	199.30	190.80	192.2	190.4	199.00	190.80
C_{13}	127.40	123.20	125.3	119.3	126.40	123.00
C_{16}	146.00	144.00	146.4	146.2	146.56	143.90
C_{17}	139.10	132.00	127.6	126.7	133.30	132.80
C_{18}, C_{22}	130.20	130.00	130.5	130.5	130.40	129.80
C_{19}, C_{21}	132.00	131.60	114.0	114.4	129.00	128.60
C_{20}	126.50	124.20	160.7	162.0	137.60	135.50
C_{24}	–	–	54.3	55.0	–	–

The aromatic ring carbons gave resonances in the region from 100–150 ppm in the ^{13}C-NMR spectra and from 6.0–8.5 ppm in the ^{1}H-NMR spectra of **1**–**3**.

At the higher temperature, the hydrogen of the hydroxy group on the coumarin moiety (OH at C_4 for compounds **1**–**3**) was not visible in the ^{1}H-NMR spectra (Table II), because of fast hydrogen/deuterium exchange.

It is also interesting to note that this hydrogen was also not visible on the theoretical spectra obtained from the software. The software does not estimate shifts for hydrogen atoms attached to heteroatoms because it also takes into consideration the effects of the solvent.

Due to the influence of the electronegative atom, the values of the chemical shift of C_2, C_{17}, C_{18} and C_{22} in compounds differed significantly in the shift positions in range 126.7–135.9 ppm and the corresponding values of chemical shifts related to C_2, C_{17}, C_{18} and C_{22} were 134.21, 139.10 and 130.20 ppm for compound **1**, 131.30, 127.60 and 130.50 ppm for compound **2** and 134.43, 133.30 and 130.40 ppm for compound **3**, respectively. The higher chemical shift of C_{20} is due to the attachment of the electron withdrawing substituent (Br, OCH_3 or Cl) at C_{20}. The downfield signals at 7.67 and 7.56 ppm for compound **1**, 7.68 and 7.70 ppm for compound **2** and 7.46 and 7.11 ppm for compound **3** are assigned to protons $H_{31,34}$ and $H_{32,33}$ for **1** and **3**, and H_{31} and $H_{32,35}$ for **2**, respectively. This strongly indicates the electron withdrawing nature of Br, methoxy and Cl in their neighborhood. The electron withdrawing methoxy group increased the deshielding of the olefinic proton H_{31} and aromatic protons H_{32}–H_{35} more than Br and Cl.

A downfield shift was observed for C_9 compared with C_8, C_{10} and C_{12} for all three compounds, as given in Table III. This was due to the tautomerization between C_8–C_9–C_{10}–C_{12}.

The calculated and experimental chemical shift values given in Tables II and III show good correspondence. The correlation factors of the linear regression used to compare the experimentally measured and theoretically computed NMR shifts for each compound (**1**–**3**) are presented in Table IV.

TABLE IV. The correlation factors of compared chemical shifts for compounds **1–3**

Compound	R^2 for ^{1}H-NMR	R^2 for ^{13}C-NMR
1	0.939	0.979
2	0.984	0.983
3	0.942	0.990

CONCLUSIONS

Selected structural parameters of the optimized geometries of the coumarin compounds were obtained by DFT calculations. The vibration frequencies of the fundamental modes of the compounds was precisely assigned and analyzed, and the theoretical results were compared with the experimental vibrations. The ^{1}H- and ^{13}C-NMR chemical shifts were calculated and the assignments were compared with the experimental values. The conducted research provided complete vibration assignments, structural information and NMR chemical shifts of these compounds.

SUPPLEMENTARY MATERIAL

Spectral data of the prepared compounds are available electronically from http:// //www.shd.org.rs/JSCS/, or from the corresponding author on request.

ИЗВОД

ТЕОРИЈА ФУНКЦИОНАЛА ГУСТИНЕ: ^{1}H- И ^{13}C-NMR СПЕКТРИ ДЕРИВАТА КУМАРИНА

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За неке синтетизоване деривате кумарина, ^{1}H- и ^{13}C-NMR изотропна хемијска померања и нека друга молекулска својства израчуната су помоћу теорије функционала густине. Нађено је да су резултати поуздани и у доброј сагласности са експерименталним подацима. Ово представља добру основу за сарадњу између експериментатора и квантних хемичара.

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