

NMR and vibrational spectra of 2-methoxycarbonyl-7-methyl-1,3-thiazino[3,2-b][1,2,4]triazine-4,8-dione: a joint of experimental and DFT

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ABSTRACT

The IR and NMR spectra were coupled with quantum chemical calculations in DFT approach using the hybrid B3LYP exchange-correlation functional to confirm the structure of 2-methoxycarbonyl-7-methyl-1,3-thiazino[3,2-b][1,2,4]triazine-4,8-dione **2d**.

Keywords: Density functional theory; Infrared spectra; NMR

INTRODUCTION

Thiazol derivatives have been known for more than seven decades [1]. These compounds are effective not only in preventing, but also curing, established arthritic disorders in rats [2]. These classes of compounds can be used for controlling Alzheimer by inhibiting the acetyl cholinesterase, which promotes memory function and delays the cognitive decline without altering the underlying pathology [3-5]. For these facts, we decided to study molecular and electronic structures of compound **2d** as a special compound.

COMPUTATIONAL DETAILS

Theoretical density functional theory (DFT) calculations were applied for **2d**. The geometrical structure of the synthesized compound was optimized and its NMR and vibrational spectra were calculated by using the density functional theory with the hybrid B3LYP exchange-correlation functional [6-7] with 6-31+G (d,p) basis sets [8-9]. The

polarization functions have been added for better treatment of amine group and sulfur. NMR shielding tensors were computed with the Gauge-Independent Atomic Orbital (GIAO) method [10-11]. The theoretical results enabled us to assign experimental IR and NMR spectra of the molecule. All the calculations are performed by Gaussian 03 program [12].

EXPERIMENTAL

The ¹H NMR and ¹³C NMR spectra were recorded at room temperature by Bruker Avance NMR spectrometer operating at 400.13 MHz and tetramethylsilane (TMS) as internal standard. The NMR measurements of compound **2d** were recorded on liquid state samples, using DMSO-d₆.

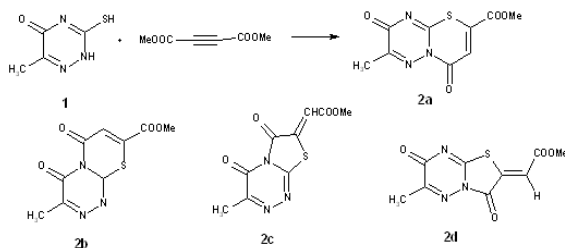
The IR spectra were recorded on a Bruker IFS-88 instrument (the samples were used as KBr disks in the range 4000–400 cm⁻¹).

RESULTS AND DISCUSSION

Compound **2d** was synthesized according to Scheme 1, with the reaction of DMAD

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(dimethyl acetylene dicarboxylate) and 6-methyl-1,2,4-triazine-3(2H)-thione-5(4H)-one **1** in acetonitrile. Using of asymmetric triazine, four cyclic structures **2a-d** are possible [13]. The IR and NMR spectra of these compounds were coupled with quantum chemical calculations in DFT approach of hybrid B3LYP exchange-correlation functional to confirm the structure of the synthesized compound. Previously it was shown that DFT methods perform NMR spectra calculations very well and give accurate results [14-21].



Scheme 1. Process of the synthesis.

The optimized structure of **2d**, is given in Fig. 1 with atom numbers. Shielding tensors of Compound **2d** were evaluated using of GIAO. In order to express the chemical shifts in ppm, the geometry of the TMS molecule had been optimized and then its NMR spectrum was calculated by using the

same method and basis set as in the case of the calculations on the compound **2d**. The calculated isotropic shielding constants were then transformed to chemical shifts relative to TMS. The calculated spectra are compared with the experimental data.

Theoretical and experimental chemical shifts of ^1H and ^{13}C of **2d** are given in Table 1. Theoretical ^1H and ^{13}C chemical shifts for this compound in solvent are very close to experimental data. As in Figure 1 compound **2d** has nine carbon atoms and shows nine different carbon peaks in ^{13}C NMR spectrum. C1, C5, C6, C10, C12, C14, C16, C18, and C21 are in agreement with the structure regarding molecular symmetry.

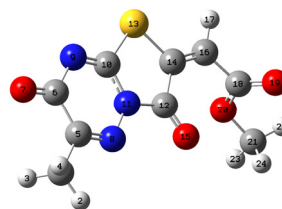


Fig. 1. Optimized structure of **2d** at DFT/B3LYP/6-31+G(d,p) level.

Table 1. Experimental and calculated ^{13}C , ^1H and ^{15}N NMR chemical shifts (ppm) of **2d**

Nucleus	Experimental	B3LYP/6-31+G(d,p)	Difference
H2, H3, H4	2.3	1.7	0.6
H17	7.3	6.1	1.2
H22, H23, H24	3.8	3.3	0.5
C1	11.3	29.9	18.6
C5	154.6	171.4	16.8
C6	154.1	171.0	16.9
C10	163.9	179.5	15.6
C12	144.4	170.2	25.8
C14	129.0	147.3	18.3
C16	121.3	147.2	25.9
C18	164.5	179.8	15.3
C21	54.3	64.4	10.1

The methyl protons of H2, H3, and H4 (see Fig. 1) are expected to give a singlet in 2.2 ppm. Methoxy and methylene protons indicate a singlet at 3.8 and 7.3 ppm, respectively.

A least squares fit of all data, as shown in Figure 2, shows a strong linear relationship with an R-square value of 0.996 at B3LYP/6-31+G (d, p).

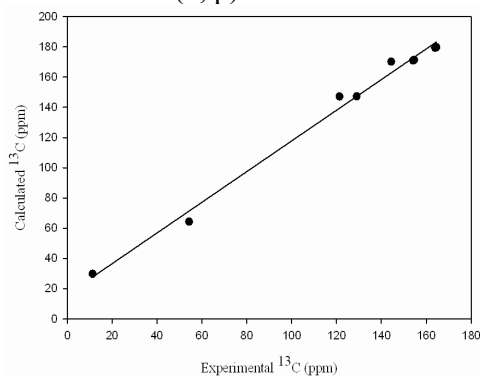


Fig. 2. Plot of calculated vs. experimental chemical shifts of ^{13}C -data.

The estimated standard error is 5.30. Linear regression for empirical scaling of theoretical data based on Forsyth and Sebag's approach [22], $\delta_{\text{calc}} = a + b\delta_{\text{exp}}$, was made, and 16.292 and 1.015 values were obtained for a and b, respectively.

The IR spectrum of compound **2d** showed two carbonyl absorptions in 1701 and 1759 cm^{-1} . Moreover, the absorptions of C=N and C=C were observed in 1595 and 1560 cm^{-1} , respectively. It will worth mentioning that there was no absorption for NH bonds. DFT calculations of the vibrational properties of

2d showed three main peaks in 1604.2, 1281.2, and 1802.1 cm^{-1} , assigned to asymmetric stretch of the rings, bending of hydrogen and symmetric stretch of the part of the ring connected to ester and symmetric vibrations of carbonyl of ester, respectively and a more complex spectrum for **2d** (see Fig. 3).

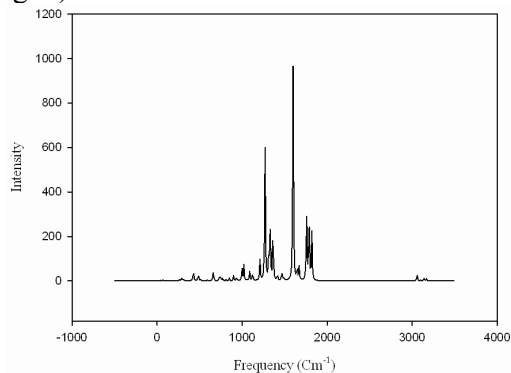


Fig. 3. Calculated IR absorption spectra of **2d** performed at DFT/ B3LYP/6-31+G(d,p) level.

CONCLUSION

Application of DFT calculation method yields ^1H , ^{13}C NMR chemical shifts and $^1\text{-}^3\text{J}(\text{C},\text{H})$ coupling constants which are in reasonable agreement with the experimental results. Thus, the DFT/6-31+G(d,p) level of theory is more consistent with NMR spectra of **2d**. Comparing the experimental and calculated results, indicates that there was a good agreement between theory and experiment and joint of experiment with theoretical calculation gives a strong confidence for synthesized compound.

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