Solid state structural and theoretical investigations of a biologically active chalcone

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ABSTRACT

The computational methods are presently emerging as an efficient and reliable tool for predicting structural properties of biologically important compounds. In the present manuscript, the solid state structural and theoretical investigations of a biologically active chalcone i-e (E)-3-(4-(hexyloxy)phenyl)-1-phenylprop-2-en-1-one (**6c**) have been reported. The solid state structure of **6c** was measured by X-ray crystallographic technique whereas the optimized molecular geometry, vibrational frequencies, the simulated UV–vis spectra (in gas and in methanol solvent), ^{1}H and ^{13}C NMR chemical shift (in gas and in chloroform solvent) values, HOMO-LUMO analysis, the molecular electrostatic potential (MEP) surface and thermodynamic parameters were calculated by using DFT/B3LYP method with 6-311++G(d,p) basis set in ground state. The results of the theoretical investigations were found to be in good agreement with experimental data.

1. Introduction

Chalcones (benzylideneacetophenones) are the biologically important molecules which represent one of the largest classes of plant metabolites and are important precursors in the biosynthesis of flavonoids and related compounds that play major role in the plant defense mechanism [1–8]. Due to their immense importance, a number of chalcone derivatives have been synthesized in recent years with diverse applications in medicinal chemistry. These are usually accessed by the Claisen–Schmidt condensation reaction of acetophenones and benzaldehydes. The opportunity of installing different substituents on the two aryl rings and their ability to undergo Michael reaction are the two important features that make this class of compounds extremely attractive drug scaffold. They are known to have anti-fungal, anti-bacterial, anti-cancer, anti-glycation, anti-inflammatory, analgesic, anti-oxidant, anti-plasmo-dial, immunosuppressive, anti-leishmanial and anti-pyretic properties [9–16]. In addition to their applications in medicinal

chemistry, they have recently been explored as molecules with nonlinear optical and luminescent properties [17–20].

Recently, the computational methods have become an efficient and reliable tool for predicting structural properties and solving chemical reactivity related problems [21–26]. Keeping the importance of various computational methods in view, and our recent interest in the solid state structural [27–31] and spectral properties [32–35] of biologically active molecules, we started a program [36,37] on theoretical calculations of solid state and spectral properties of biologically important molecules in comparison to experimental data. Herein, as continuation of this program, we report the solid state structure, measured through X-ray diffraction technique and the quatum chemical computations, calculated at B3LYP/6-311++G(d,p) level of the theory of (E)-3-(4-(hexyloxy) phenyl)-1-phenylprop-2-en-1-one (**6c**), which we previously [15] reported as antiglycating agent. The results of the theoretical calculations including molecular geometry, vibrational frequencies (IR and Raman spectra), ^{1}H and ^{13}C NMR chemical shift values, electronic absorption spectrum, HOMO-LUMO analysis, and molecular electrostatic potential (MEP) of **6c** are described in comparison to experimental results.

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2. Experimental

2.1. General

The FT-IR (Fourier Transform InfraRed) and the Raman spectra of compound **6c** were recorded at Bruker Tensor-37 spectrophotometer and Horiba Jobin-Yvon LabRAM HR High Resolution Raman Spectrometer (Laser Power 14.7 mW at 632.8 nm laser wavelength, Grating 1800), respectively. The UV−vis (ultraviolet−visible) spectrum of **6c** was measured at Shimadzu UV-1800 UV−vis Spectrophotometer. The ^1H and ^{13}C NMR spectra were obtained from Bruker 300 MHz NMR spectrophotometer using $CDCl_3$ solvent containing TMS as internal reference.

2.2. Crystallographic studies

Single crystal of **6c** was mounted in random orientation on a glass fiber on a Stoe IPDS-II two circle diffractometer [38] equipped with graphite monochromated Mo Kα radiation ($\lambda = 0.71073$ Å). The structure was solved by direct methods using SHELXS97 and refined with full-matrix least-squares on F2 with SHELXL-97 [39]. All non-hydrogen atoms were refined anisotropically. The crystal data and refinement details of **6c** are summarized in Table 1. Further information can be seen in Table S1−S4, supplementary material.

2.3. Computational details

All calculations in this study were carried out with the GaussView 05 molecular visualization program and Gaussian 09 package program [40,41]. The optimized molecular structure, vibrational frequencies, HOMO-LUMO analyses, molecular electrostatic potential (MEP) surface and thermodynamic parameters and atomic charges of **6c** have been calculated using DFT/B3LYP method with 6-311++G(d,p) basis set. In DFT method, since the high frequency region for the vibrational modes usually includes the stretching vibrational modes related to functional groups of a molecule and the lower frequency region can cover the overlapped bands of the compounds, the characteristic properties of high and low frequency

regions require different scaling factors [42,43]. Therefore, the calculated vibrational wavenumbers were scaled as 0.958 for frequencies higher than 1700 cm^{-1} and as 0.983 for frequencies less than 1700 cm^{-1} for the B3LYP/6-311++G(d,p) level [44]. The assignments of fundamental vibrational modes of **6c** were performed on the basis of potential energy distribution (PED) analysis by using VEDA 4 program [45,46].

The UV−vis. calculations or the electronic absorption maximum wavelengths (λ_{max}) of **6c** in both gas phase and methanol solvent were performed using the time dependent DFT (TD-DFT) method with integral equation formalism polarizable continuum model (IEFPCM) at the B3LYP/6-311++G(d,p) level [47,48]. The HOMOs and LUMOs energy values and their 3D plots were calculated and simulated at the B3LYP/6-311++G(d,p) level.

For the NMR analysis, the optimized molecular geometry of **6c** was first obtained at the B3LYP/6-311++G(d,p) level in the framework of IEFPCM and then, the ^1H and ^{13}C NMR chemical shifts were calculated using the gauge-invariant atomic orbital (GIAO) method after the molecular geometry was optimized at the B3LYP/6-311++G(d,p) level in gas phase and in chloroform solvent ($\varepsilon = 4.71$) [49,50]. The computed ^1H and ^{13}C NMR chemical shifts were compared with the experimental analogs recorded with respect to TMS as the reference for chemical shielding.

In Gaussian package program, the quantum chemical computations have been performed for gas phase of isolated molecule, while the experimental data was recorded in both solid and solution state of molecule.

3. Results and discussion

3.1. Molecular geometry

The optimized molecular structure of **6c** is given in Fig. 1, whereas the optimized molecular geometry parameters using DFT/B3LYP method with 6-311++G(d,p) basis set are presented in Table 2 in comparison to experimental values.

As shown in Fig. 1, two aromatic rings are connected through α,β-unsaturated carbonyl which is the main chalcone moiety [37]. Therefore, by considering Table 1 and Fig. 1, C1−C2 single bond and

Table 1
Crystal data and structure refinement parameters of **6c**.

Crystal data	6c
CCDC	1409316
Chemical formula	$C_{21}H_{24}O_2$
M_r	308.40
Crystal system, space group	Triclinic, $P1$
Temperature (K)	173
a, b, c (Å)	5.8269 (4), 15.4577 (13), 19.3483 (15)
β (°)	91.588 (6), 90.411 (6), 94.827 (6)
V (Å³)	1735.8 (2)
Z	4
Radiation type	Mo Kα
μ (mm^{-1})	0.07
Crystal size (mm)	$0.35 \times 0.31 \times 0.27$
Data collection	
Diffractometer	STOE *IPDS* II two-circle-diffractometer
Absorption correction	−
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	16299, 6455, 4020
R_{int}	0.050
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.608
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.043, 0.107, 0.86
No. of reflections	6455
No. of parameters	416
H-atom treatment	H-atom parameters constrained
$\Delta\rangle_{max}$, $\Delta\rangle_{min}$ (e Å^{-3})	0.19, −0.17