Experimental (X-ray Diffraction and FT-IR) and Quantum Chemical Studies (HF and DFT) of Ethyl 3-hydroxy-7-methyl-3-(3-methyl-3-phenylcyclobutyl)-5-phenyl-3,5-dihydro-5H-thiazolo [3,2-a]pyrimidine-6-carboxylate

Etil 3-hidroksi-7-metil-3-(3-metil-3-fenilsiklobütil)-5-fenil-3,5dihidro-5H-tiyazolo [3,2-a] pirimidin-6-karboksilat'ın Deneysel (X-ışını kırınımı ve FT-IR) ve Kuantum Kimyasal (HF ve DFT) Çalışmaları

Research Article

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ABSTRACT

The title compound, ethyl 3-hydroxy-7-methyl-3-(3-methyl-3-phenylcyclobutyl)-5-phenyl-3,5-dihydro-5H-thiazolo[3,2-α]pyrimidine-6-carboxylate, was synthesized and characterized by experimental and quantum chemical methods. The crystal structure of compound was brought to light by single crystal X-ray diffraction method and its vibrational spectrum (FT-IR) in solid state was observed in the region 4000-400 cm^{-1}. The molecular geometry was those obtained from the X-ray structure determination was optimized using Hartree-Fock and Density Functional Theory (DFT/B3LYP) method with the 6-31G(d) basis set in ground state. From the optimized geometry of the molecule, geometric parameters (bond lengths, bond angles, torsion angles) and vibrational assignments of the compound have been theoretically calculated and compared with the experimental data. The obtained structural and vibrational results are well in agreement with the experimental measurement. The frontier molecular orbital (FMO) and Mulliken population analysis of the optimized geometries were investigated by theoretical calculation results.

Key Words
Thiazolo[3,2-α]-pyrimidine, X-ray diffraction, IR spectroscopy, Density Functional Theory, HOMO and LUMO, Mulliken Charge.

ÖZ

Etil 3-hidroksi-7-metil-3-(3-metil-3-fenilsiklobütil)-5-fenil-3,5-dihidro-5H-tiyazolo [3,2-a] pirimidin-6-karboksilat başlıklı bileşik sentezlenmiştir ve deneysel ve kuantum kimyasal yöntemlerle karakterize edilmiştir. Bileşiğin kristal yapısı tek-kristal X-ışını kırınımı yöntemi ile aydınlatılmış ve katı halde titreşimsel spektrumu (FT-IR) 400-4000 cm^{-1} aralığında gözlenmiştir. X-ışını kırınımından elde edilen moleküler geometri temel halde Yoğunluk Fonksiyoneli Teorisi (YFT) yöntemi 6-31G(d) baz seti ile optimize edilmiştir. Optimize geometriden elde edilen bağ uzunlukları, bağ açıları, torsion açıları ve titreşimsel işaretlemeleri deneysel dataları ile karşılaştırılmıştır. Yapısal ve titreşimsel işaretlemeler deneysel ölçümlerle iyi bir uyum içindedir. Optimize geometriye ait sınır moleküler orbital ve Mulliken yük analizi teorik hesaplama sonuçları kullanılarak incelenmiştir.

Anahtar Kelimeler
Tiazol[3,2-α]-pirimidin, X-ışını kırınımı, IR spektroskopisi, Yoğunluk Fonksiyoneli Teorisi, HOMO ve LUMO, Mulliken yükü.

INTRODUCTION

Cyclobutane is an organic compound formed by the four carbon atoms. Although itself is of no commercial or biological significance, it is known that the more complex derivatives are important in biology and biotechnology [1]. Also, 3-substituted cyclobutane carboxylic acid derivatives exhibit significant pharmacological activities such as anti-inflammatory and anti-depressant activity [2]. Thiazole, or 1,3-thiazole, is a heterocyclic compound that contains both sulfur and nitrogen atoms. Thiazole derivatives show a diverse range of biological activities such as antimicrobial [3-5], anti-inflammatory [6,7], antitumor [8,9], anticonvulsant [10] and antifungal [11,12], etc. It is known that the thiazolo[3,2-a]pyrimidine derivatives possess a variety of biological and [13,14], antinociceptive [15], antibacterial [16-18], antiviral [19,20], antihypertensive [21], antibiofilm [22,23], antitubercular [17,18], antivirulence [24], antioxidant [25], etc. In the light of the effects given above, the compounds containing cyclobutane, thiazole and thiazolo[3,2-a] pyrimidine functionalities in one molecule have seen to be important.

Determination of the structural and spectroscopic properties of compounds using both experimental techniques and theoretical methods has been attracted interest for many years. To the best of our knowledge, the title compound is a novel compound firstly synthesized in our laboratories by us and there is no any information present in literature about its molecular and vibrational spectroscopic properties. The aim of the present work was to describe and characterize the molecular structure and vibrational frequencies of the compound, both experimentally and theoretically. In the experimental study, the molecule was prepared and characterized by single-crystal X-ray diffraction and FT-IR methods. In theoretical study, the molecular structure of the title compound in the ground state have been calculated using the Hartree-Fock (HF) and Density Functional Theory (DFT) (B3LYP) with 6-31G(d) basis set. The calculated geometric parameters (bond lengths, bond angles, torsion angles), and vibrational assignments compared with their experimental data.

MATERIALS AND METHODS

### Synthesis and Characterization

To a solution of 4-phenyl-2-thioxo-1,2,3,4-tetrahydro-pyrimidine-5-carboxylic acid ethyl ester (2.6233 g, 10 mmol) in 50 mL of ethanol, a solution of 1-methyl-1-phenyl-3-(2-chloro-1-oxoethyl) cyclobutane (2.2271 g, 10 mmol) in 20 mL of absolute ethanol was added, stirred 3 h (TLC), made alkaline with an aqueous solution of NH_3 (5%), brilliant yellow precipitate separated by suction and crystallized from EtOH (Scheme 1). Yield: 63%, melting point: 427 K.

General Remarks

All chemicals were of reagent grade and used as commercially purchased without further purification. The melting point was determined by Gallenkamp melting point apparatus. The FT-IR spectrum of the tittle compound was recorded in the range 4000-400 cm^{-1} using a Mattson 1000 FT-IR spectrometer with KBr pellets.

Crystal Structures Determination and Refinement

The single-crystal X-ray data were collected on a STOE IPDS II image plate diffractometer at 296 K. Graphite-monochromated Mo Kα radiation (λ = 0.71073 Å) and the w-scan technique were used. The structure of title compound was solved by
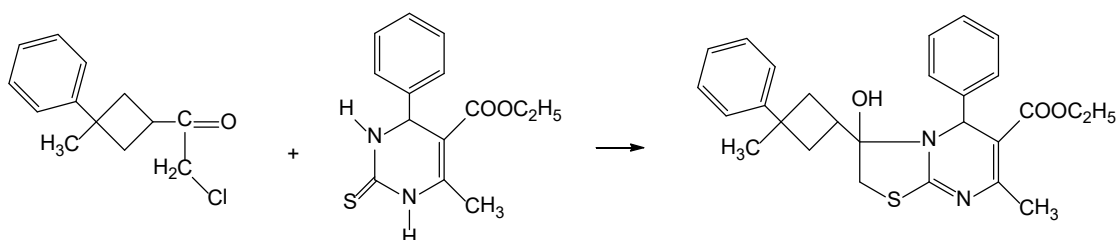
Scheme 1. Synthetic pathway for the synthesis of the target compound.

direct methods using SHELXS-97 [26] and refined through the full-matrix least-squares method using SHELXL-97 [27], implemented in the WinGX [28] program suite. Non-hydrogen atoms were refined with anisotropic displacement parameters. All H atoms were located in a difference Fourier map and were refined isotropically. Data collection: Stoe X-AREA [29], cell refinement: Stoe X-AREA [29], data reduction: Stoe X-RED [29]. The general-purpose crystallographic tool PLATON [30] was used for the structure analysis and presentation of the results. The structure was refined to R_{int}= 0.053 with 3810 observed reflections using I > 2σ(I) threshold. The ORTEP-3 program for Windows was used for preparation of figures. Details of the data collection conditions and the parameters of the refinement process are given in Table 1.

Details of the Theoretical Calculation

All the calculations were carried out by using Gaussian 03 package [31] and Gauss-View molecular visualization software [32] on the personal computer without restricting any

Table 1. Crystal data collection and structure refinement parameters for the title compound.

Data collection	
Diffractometer	STOE IPDS-2
Wavelength (Å)	0.71073 Mo Kα
θ range for data collection (º)	1.5 ≤ θ ≤ 27.3
Index ranges	
h_{min}, h_{max}	-7, 8
k_{min}, k_{max}	-24, 24
l_{min}, l_{max}	-24, 24
Measurement method	**ω taraması**
Reflections collected	12583
Independent reflections	4964
Observed reflections [I > 2σ(I)]	3810
Absorption correction	Integrasyon (X–RED32)
T_{min}, T_{max}	0.905, 0.954
R_{int}	0.053
Refinement	
Refinement method	SHELXL-97
Parameters	298
$R[F^2 > 2\sigma(F^2)]$	0.046
$wR(F^2)$	0.129
$GooF = S$	1.06
$\Delta\rho_{min}$, $\Delta\rho_{max}$ (e/ Å³)	-0.28, 0.20

symmetry for the title compound. For modeling, the initial guess of the compound was first obtained from the X-ray coordinates and this structure was optimized by Hartree-Fock (HF) and Density Functional Theory (DFT)/B3LYP methods with and 6-31G(d) as basis set. From the optimized geometry of the molecule, geometric parameters (bond lengths, bond angles, torsion angles) and theoretical harmonic frequencies of the title compound have been calculated and compared with the experimental data. Besides, frontier molecular orbitals (FMOs) and Mulliken population analysis of the title compound were investigated by theoretical calculations.

RESULTS AND DISCUSSION

Structural Description

The title compound, methyl 5-(4-hydroxy-3-methoxyphenyl)-2-(4-methoxybenzylidene)-7-methyl-3-oxo-2,3-dihydro-5H-thiazolo[3,2-a]-pyrimidine-6-carboxylate, with the crystal data shown in Figure 1. X-ray diffraction analysis has revealed that the title compound crystallizes in monoclinic system with space group P 2_1/c. The unit cell dimensions are a= 6.5335 (3) Å, b= 19.7921 (7) Å, c= 19.3274 (8) Å and V= 2437.50 (17) Å³.

The molecular structure of compound has "C1" symmetry. It is composed of the cyclobutane, phenyl rings, and an ester group in addition to the heterocycles such as a thiazole, and a pyrimidine rings. The dihedral angles between the cyclobutane plane **A** (C7-C10), the thiazole plane **B** (S1/N1/C12-C14), and the pyrimidine plane **C** (N1/N2/C14-C16) are 86.10° (**A/B**), 13.32° (**B/C**) and 82.48° (**A/C**).

The cyclobutane ring was adopted butterfly conformation. The bond lengths between the carbon atoms are average 1.546 Å and bond angles formed by the three carbons are average 89.27° for the cyclobutane ring in the compound. When these values are compared with the previously reported cyclobutane derivatives [33,34], it is seen that there are no significant differences.

In the thiazole ring, the S1−C13 and S1−C14 bond

lengths are 1.790 (2) and 1.7361 (18) Å, respectively. These values are close to the standard value for an S−Csp^2 single bond (1.76 Å) [35]. The thiazole ring is planar with a maximum deviation of 0.0794 Å. Thiazole ring are not coplanar with the pyrimidine ring. The average angle between the plane of the thiazole ring and the plane of the pyrimidine ring is 13.32°. Structural parameters of the pyrimidine are as follows: average C N distance is 1.310 (2) Å, the C-N distance is 1.331 (2) Å. These parameters are comparable with the related pyrimidine derivatives reported in the literature [36-38].

It does not observed π–π stacking (face-to-face) interactions in the crystal structure. There are, however, two D–H···A and two D–H···Cg(π-ring) (edge-to-face) interactions, details of which are given in Table 2 The hydroxyl atom O1 in the molecule at (x, y, z) acts as hydrogen-bond donor, via atom H1O, to pyrimidine ring atom N2 in the molecule at (x+1, y, z). The thiazole ring atom C13 in the molecule at (x, y, z) acts as hydrogen-bond donor, via atom H13B, to carboxyl atom O3 in the molecule at (x, −y+1/2, z–1/2). The cyclobutane atom C8 at (x,y,z) forms an intramolecular C−H···Cg(π-ring) contact, this time via atom H8B, with the centroid of the C22-C27 ring. Atom C14 at (x, y, z) forms an intermolecular C−H···Cg(π-ring) contact, via atom H11C, with the centroid of the C1-C6 ring of the molecule at (1-x,1-y, -z) (Figure 2).

The molecular structure of the title compound was also studied theoretically. The starting coordinates were those obtained from the X-ray structure determination. The molecular geometry

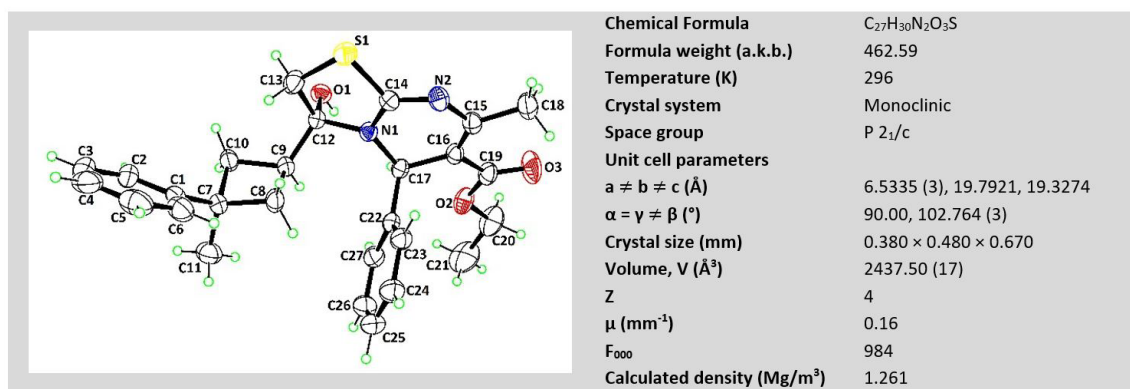**Table 2.** Hydrogen-bond geometry (Å, °) for the title compound.

D−H···A	D−H	H···A	D···A	D−H···A
O1−H1O···N2i	0.82	2.14	2.747 (2)	131
C13−H13B···O3i	0.97	2.59	3.176 (2)	119
C8−H8B···Cg1	0.97	2.61	3.430(2)	143
C11−H11C···Cg2iii	0.96	2.89	3.540(3)	126

Symmetry codes: (i) x+1, y, z; (ii) x, −y+1/2, z–1/2; (iii) 1–x,1–y, −z.
Cg1: the centroid of the C22-C27 ring, Cg2: the centroid of the C1-C6 ring

(X-ray coordinates) was optimized using Hartre-Fock (HF) and Density Functional Theory (DFT/B3LYP) method with the 6-31G(d) basis set in ground state. The total energy, zero-point vibrational energy, entropy and dipole moment values obtained for optimized geometries are presented in Figure 3.

Conventionally, two methods were used in comparison the molecular structures. The first method is to calculate the correlation value (R^2) between X-ray and theoretical structure. The optimized some geometrical parameters (bond lengths, bond angles and torsion angles) calculated by HF/6-31G(d) and DFT/B3LYP/6-31G(d) methods with corresponding to experimental values are listed in Table 3. We have calculated correlation value (R^2) between these parameters. R^2 values are 0.9962 and 0.9939 for bond lengths, 0.9985 and 0.9979 for bond angles, 0.9682 and 0.9658 for torsion angles at HF/6-31G(d) and DFT/B3LYP/6-31G(d) levels, respectively. According to correlations values, the HF/6-31G(d) method gave accurate results for the bond lengths, bond

Chemical Formula	$C_{27}H_{30}N_2O_3S$
Formula weight (a.k.b.)	462.59
Temperature (K)	296
Crystal system	Monoclinic
Space group	P 2$_1$/c
Unit cell parameters	
a ≠ b ≠ c (Å)	6.5335 (3), 19.7921, 19.3274
α = γ ≠ β (°)	90.00, 102.764 (3)
Crystal size (mm)	0.380 × 0.480 × 0.670
Volume, V (Å³)	2437.50 (17)
Z	4
μ (mm⁻¹)	0.16
F$_{000}$	984
Calculated density (Mg/m³)	1.261

Figure 1 : A view of the title compound showing the atom-numbering scheme with the crystal data. Displacement ellipsoids are drawn at the 30% probability level.
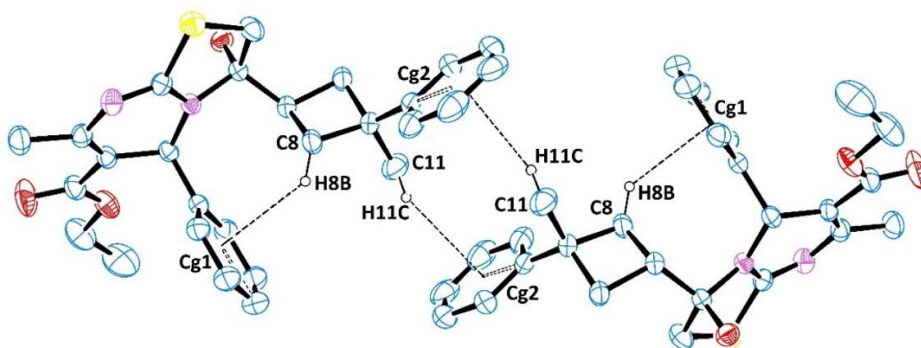
Figure 2: The intra- and inter-molecular hydrogen bondings in the crystal structure

Parameters	HF/6-31G(d)	DFT/B3LYP/6-31G(d)
Total energy (a.u.)	-1770.89492876	-1780.28388058
Zero-point vibrational energy (kcal/mol)	351.99413	327.56454
Entropy (cal/mol-K)	194.011	204.357
Heat capacity at const. volume (CV, cal/mol-K)	110.396	119.511
Rotational constants (GHz)		
A	0.20284	0.20044
B	0.07902	0.07854
C	0.07015	0.06969
Dipole Moment (Debye)		
μ_x	-4.0403	-4.1924
μ_y	-4.3433	-4.0713
μ_z	-1.7700	-1.6057
$\mu_{top.}$	6.1904	6.0605

Figure 3. Optimized geometries and their theoretically calculated some parameters.

angles, and torsion angles compared with the DFT/B3LYP/6-31G(d) method. Second method for globally comparing the structures obtained with the theoretical calculations is by overlapping the molecular skeleton with that obtained from X-ray diffraction, giving a RMSE of 0.497 Å for HF6-31G(d) and 0.483 Å for DFT/B3LYP/6-31G(d) calculations (Figure 4). According to these results, it may be concluded that the HF/6-31G(d) calculation well reproduce the geometry of the title compound. It was noted here that the experimental results belong to solid phase and theoretical calculations belong to gaseous phase. In the solid state, the existence of the crystal field along with the intermolecular interactions has connected the molecules together, which result in the differences of bond parameters between the calculated and experimental values [39].

Vibrational Spectra

The Fourier Transform Infrared Spectrum (FT-IR) of the title compound was recorded employing a "Mattson 1000 FT-IR spectrometer" using KBr pellet technique in the range of 4000-400 cm^{-1}. The theoretical IR spectra have been calculated with HF and DFT/B3LYP methods with the 6-31G(d) basis set in ground state. In order to compare the theoretical results with experimental values of those, scaling factor which are 0.8929 and 0.9626 for HF/6-31G(d) and DFT/B3LYP/6-31G(d) is applied to all of the calculated frequencies, respectively. The overlapped experimental and scaled theoretical FT-IR spectra of the title compound are given in Figure 5.

The title compound belongs to C1 point group symmetry and consists of 63 atoms. It has seen 183 normal modes of vibration using the formula 3N-6. The fundamental vibrational wavenumbers of compound calculated by HF/6-31G(d) and DFT/B3LYP/6-31G(d) methods. The vibrational bands assignments have been made by using Gauss View molecular visualization program [32]. Some observed and calculated frequencies in the infrared spectra of the title compound and their

Table 3. Some selected geometric parameters (Å, °).

Geometric Parameters	Experimental [X-ray diffraction]	Calculated	
		HF/6-31G(d)	DFT/B3LYP/6-31G(d)
Bond lengths (Å)			
C6−C7	1.506 (3)	1.518	1.517
C7−C11	1.528 (3)	1.535	1.539
C7−C8	1.545 (2)	1.555	1.566
C9−C12	1.525 (2)	1.531	1.536
C12−O1	1.401 (2)	1.403	1.427
C13−S1	1.790 (2)	1.810	1.832
S1−C14	1.7361 (18)	1.751	1.765
C14−N1	1.331 (2)	1.347	1.360
C14−N2	1.310 (2)	1.275	1.298
C16−C19	1.463 (3)	1.470	1.464
C19−O3	1.202 (2)	1.194	1.220
C19−O2	1.337 (3)	1.335	1.371
	R^2	0.9962	0.9939
Bond Angles (°)			
C7−C8−C9	89.66 (13)	89.08	89.08
C12−N1−C14	116.80 (13)	115.46	115.08
C13−S1−C14	92.18 (8)	91.87	91.58
N1−C14−N2	126.95 (16)	127.61	127.40
C16−C17−C22	111.74 (13)	111.50	111.78
O2−C19−O3	121.47 (19)	121.44	121.30
	R^2	0.9985	0.9979
Torsion Angles (°)			
C1−C6−C7−C10	48.2 (2)	39.74	38.77
C16−C17−C22−C27	61.2 (2)	70.83	70.85
C19−C16−C17−C22	75.35 (19)	76.39	78.10
N1−C17−C22−C23	119.91 (17)	129.59	129.33
	R^2	0.9682	0.9658
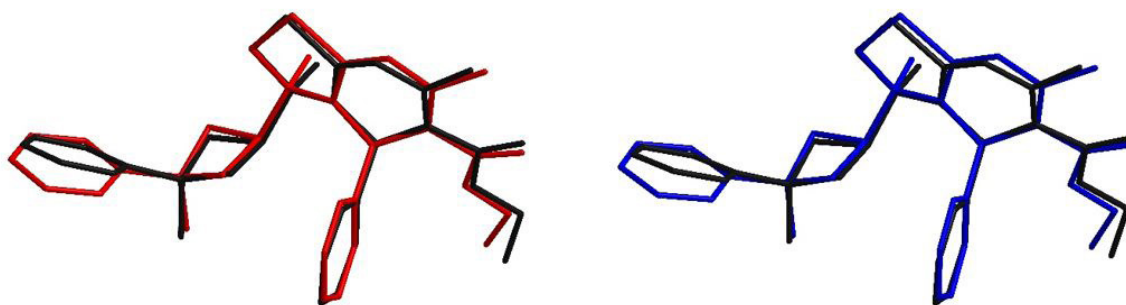
Figure 4. Atom-by-atom superimposing of the structures calculated [HF/6-31G(d) = red, DFT/B3LYP/6-31G(d) = blue] over the X-ray structure (black) for the title compound. Hydrogen atoms omitted for clarity.
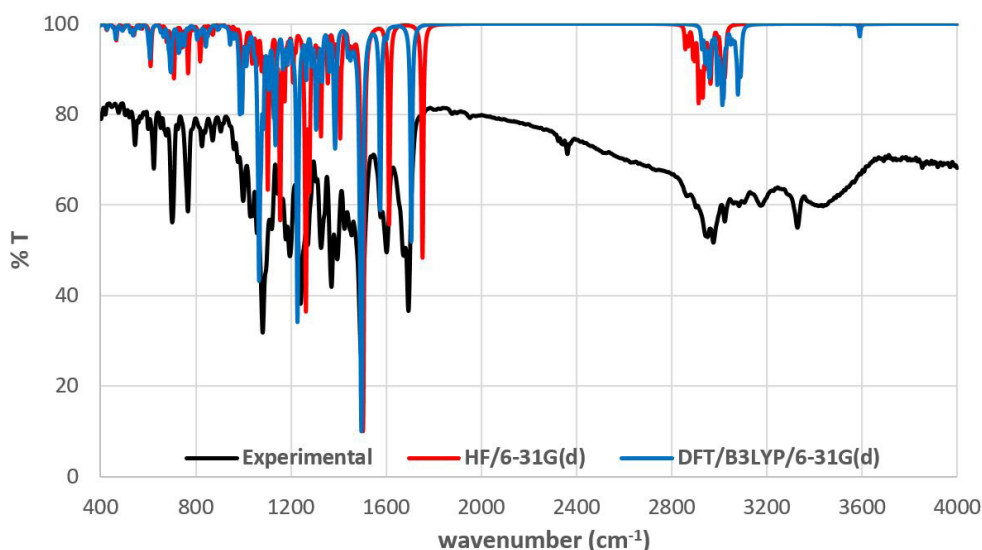
Figure 5. Theoretical [at HF/6-31G(d) and DFT/B3LYP/6-31G(d) levels] and experimental FT-IR spectra of the title compound.

probable assignments are given in Table 4.

As can be seen from the Table 4, an acceptable agreement exists between the experimental and theoretical vibrational frequencies. The correlation coefficients are 0.9908 and 0.9937 for HF/6-31G(d) and DFT/B3LYP/6-31G(d), respectively. According to these correlation values, DFT/B3LYP/6-31G(d) method gave accurate results compared with the HF/6-31G(d) method in determining vibrational spectra. Some experimentally obtained vibrational frequencies were supported by literature values.

O-H Vibrations

It is well known that the high frequency region above 3000 cm^{-1} is the characteristic region for the ready identification of C−H, O−H and N−H stretching vibrations. These vibrations are sensitive to hydrogen bondings. The non-hydrogen bonded or free hydroxyl group absorb strongly in 3550-3700 cm^{-1} region [40]. In the IR spectra of the compound, the absorption at 3327 cm^{-1} is assigned to the stretching vibrations of O−H bond that has been calculated at 3658 and 3587 cm^{-1} for HF/6-31G(d) and DFT/B3LYP/6-31G(d) levels, respectively. The difference between the experimental and theoretical values take its source from the O1−H1O···N2 intermolecular hydrogen bondings.

Vibrational modes: ν, stretching; α, scissoring; γ, rocking; , wagging; , twisting; θ, ring; breathing. Abbreviations: s, symmetric; as, asymmetric.

Phenyl Ring Vibrations

It is known that the C−H and C C stretching vibrations of the aromatic compounds usually appear in 2900-3150 and 1100-1500 cm^{-1} frequency ranges, respectively [41]. The C−H aromatic stretching modes were recorded at 3082 cm^{-1} experimentally and computed at 3014, 2995 and 2991 cm^{-1}, respectively. The C C stretching vibrations predicted at 1617, 1616, 1595 and 1590 cm^{-1} in the theoretical spectra show good agreement with the experimental FT-IR bands at 1600 cm^{-1}.

Cyclobutane Vibrations

The cyclobutane ring of symmetric and asymmetric C−H$_2$ vibration mode is known to monitor the 3100-3000 cm^{-1}. The asymmetric stretching C−H$_2$ observed at 2950 cm^{-1} in FT-IR spectrum. This value is not significantly different from those in the literature; 2960 [33], 2975 [34], 2929 and 2855 [42]. The symmetric stretching C−H$_2$ observed at 2950 cm^{-1} in FT-IR spectrum and also these vibrations calculated at 2914, 2895 and 2974, 2961 cm^{-1} for HF/6-31G(d) and DFT/B3LYP/6-31G(d) levels, respectively. The, scissoring C−H$_2$, wagging C−H$_2$, twisting C−H$_2$ and

Table 4. Comparison of the observed and calculated vibrational spectra of the compound (cm⁻¹).

Assignment	Experimental (Kbr)	Calculated [6-31G(d)]	
		HF	DFT/B3LYP
νO−H	3327	3658	3587
ν_sC−H$_{aromatic}$	-	3027	3092
ν_sC−H$_{aromatic}$	-	3023	3089
ν_{as}C−H$_{aromatic}$	3082	3014	3085
ν_{as}C−H$_{2thiazole}$	-	3006	3063
ν_{as}C−H$_{aromatic}$	3082	2995	3062
ν_{as}C−H$_{aromatic}$	3082	2991	3057
ν_{as}C−H$_{2cyclobutane}$	3023	2965	3029
ν_{as}C−H$_{2cyclobutane}$	3023	-	3012
ν_sC−H$_{2thiazole}$	-	2953	3005
ν_{as}C−H$_{2cyclobutane}$	3023	2939	-
νC−H	2975	2921	2952
ν_sC−H$_{2cyclobutane}$	2950	2914	2974
ν_sC−H$_{2cyclobutane}$	2950	2895	2961
νC−H$_{cyclobutane}$	2912	2889	2940
ν_sC−H$_3$	-	2869	2943
ν_sC−H$_{3cyclobutane}$	2864	2857	2927
νC O$_{carboxyl}$	1694	1752	1705
νC C$_{aromatic}$	1600	1617	1602
νC C$_{aromatic}$	1600	1616	1599
νC N$_{pyrimidine}$ + νC C$_{pyrimidine}$	1674	1612	1574
νC C$_{aromatic}$	1600	1595	1486
νC C$_{aromatic}$	1600	1590	1490
νC N$_{pyrimidine}$ + νC C$_{pyrimidine}$	1495	1502	1495
αC−H$_{2cyclobutane}$	1423	1482	1475
αC−H$_{2cyclobutane}$	1423	1468	1443
αC−H$_{2thiazole}$	-	1462	1455
C−H	-	1406	1385
ν_sC−H$_{3cyclobutane}$	1370	1395	1382
C−H	-	1381	1360
C−H$_{cyclobutane}$	1270	1265	1359
ωC−H$_{2cyclobutane}$	1239	1235	1212
δC−H$_{2thiazole}$	-	1207	1185
C−H$_{pyrimidine}$	-	1172	1165
δC−H$_{2cyclobutane}$	1029	1035	1044
$\theta_{cyclobutane}$	998	946	943
νS−CH$_2$	766	805	794
	R^2	0.9908	0.9937
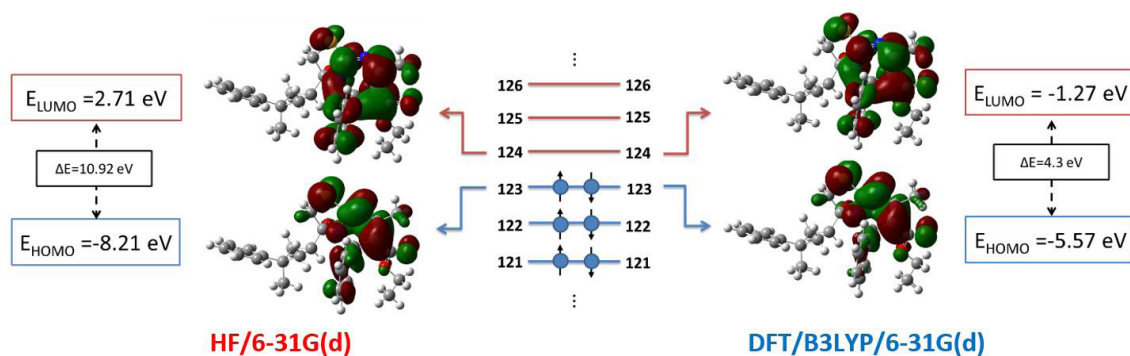
Figure 6. The molecular orbital diagrams, energies and energy gaps for the optimized geometries.
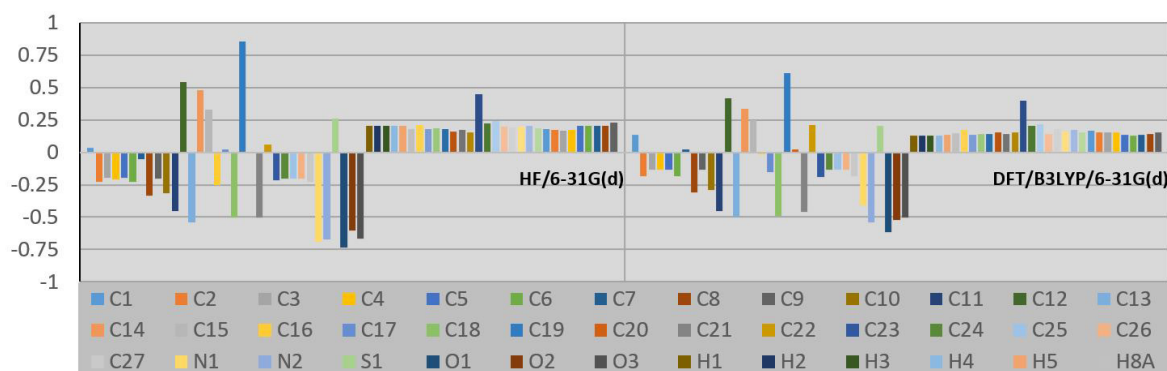
Figure 7. The Mulliken charges of diagram for the title compound.

breathing vibrations observed at 1423, 1239 and 1029 cm^{-1} in FT-IR spectrum for cyclobutane ring.

HOMO and LUMO Analysis

The distributions of the HOMO and LUMO orbitals computed at the HF/6-31(d) and DFT/B3LYP/6-31G(d) levels for the title compound are shown in Figure 6. The calculations indicate that the title compound has 123 occupied molecular orbitals. HOMO and LUMO energies are -8.21 and 2.71 eV for HF/6-31G(d) level, -5.57 and -1.27 eV for DFT/B3LYP/6-31G(d) level, respectively.

By using HOMO and LUMO energy values for a molecule, electronegativity, chemical hardness and chemical softness can be calculated as follows:

$$\chi=(I+A)/2 \text{(electronegativity)}$$
$$\eta=(I-A)/2 \text{ (chemical hardness)}$$
$$S=1/2\eta \text{ (chemical softness)}$$

where I and A are ionization potential and electron affinity;

$$I=-E_{HOMO}$$
$$A=-E_{LUMO}$$

respectively [43]. The ionization potential (I), the electron affinity (A), the absolute electronegativity (χ), the absolute hardness (η) and softness (S) for molecule have been calculated at the same levels and the results are given in Table 5.

The value of the energy separation between the HOMO and LUMO is 10.92 eV for HF/6-31G(d) level and 4.30 eV for DFT/B3LYP/6-31G(d) level. These energy gaps indicate that the title structure is quite stable.

Mulliken Population Analysis

The Mulliken charge distributions of the title compound were calculated using HF/6-31G(d)

Table 5. The parameters related to frontier molecular orbitals.

Parameters	HF/6-31G(d)	DFT/B3LYP/6-31G(d)
I (eV)	8.21	5.57
A (eV)	-2.71	1.27
χ (eV)	2.75	3.42
η (eV)	5.46	2.15
S (eV^{-1})	0.092	0.233

Table 6. Mulliken charges of the atoms in hydrogen bondings for the title compound.

D−H•••A	HF/6-31G(d)			DFT/B3LYP/6-31G(d)		
	D	H	A	D	H	A
O1−H1O⋯N2	-0.739	0.449	-0.674	-0.614	0.399	-0.538
C13−H13B⋯O3	-0.543	0.224	-0.665	-0.496	0.215	-0.519
C8−H8B⋯Cg1	-0.332	0.179	-1.111	-0.308	0.146	-0.983
C11−H11C⋯Cg2	-0.453	0.172	-1.054	-0.451	0.139	-0.895

and DFT/B3LYP/6-31G(d) levels. The calculated charge for all atoms has been given in Figure 7.

It is well-known that the Mulliken charges confirm the hydrogen bondings in the molecular structure of compound. For the title compound, the Mulliken charges corresponding to the atoms in hydrogen bondings are shown in Table 6. As can be seen in Table 6, these charges confirmed that the intra- and intermolecular hydrogen bondings.

CONCLUSIONS

The title compound, ethyl 3-hydroxy-7-methyl-3-(3-methyl-3-phenylcyclobutyl)-5-phenyl-3,5-dihydro-5H-thiazolo[3,2-α]pyrimidine-6-carboxylate ($C_{27}H_{30}N_2O_3S$), was both experimentally and theoretically investigated. The important conclusions to be obtained from this study are the following:

i. The compound was synthesized and brought to light its molecular structure by single-crystal X-ray diffraction method in our laboratory. The crystal structure and geometric parameters of the compound were obtained.

ii. The initial guess of the compound was first obtained from the X-ray coordinates was optimized by Hartree-Fock (HF) and Density Functional Theory (DFT)/B3LYP method with 6-31G(d) as basis set. The HF/6-31G(d) method gave accurate results compared with the DFT/B3LYP/6-31G(d) method in determining molecular structure of the title compound.

iii. By using optimized geometries of molecule, theoretical IR spectra was calculated and compared with experimental FT-IR spectrum. The DFT/B3LYP/6-31G(d) method is better than HF/6-31G(d) method for assigning vibrational modes of the title compound.

iv. The frontier molecular orbitals (HOMO and LUMO) and related to parameters were generated by theoretical results.

v. The calculated Mulliken charges confirm the hydrogen bonding in the crystal structure.

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