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Investigation of 9-(2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one: Crystal structure, AIM and NBO analysis

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ABSTRACT

Single crystal X-ray analysis reveals that the 9-(2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one, crystallizes in the centrosymmetric space group $P2_1/c$. In the crystal, molecules form as a dimer through a *keto-enol* type hydrogen-bonding pattern along with intermolecular C—H···O interactions. The crystal structure of the title compound is further stabilized by intermolecular H···H interactions. Various intermolecular interactions present in the crystal structure are quantified by Hirshfeld surface analysis, PIXEL energy, NBO, AIM and DFT calculations. The energetics of the title compound is also compared with that of the two closely related analogs. Further, the vibrational modes of the interacting groups are characterized using both the experimental and simulated FT-IR and FT-Raman spectra. The experimental and calculated UV—visible spectra are compared and agree well. The time-dependent DFT spectra suggest that the ligand-to-ligand charge transfer within the molecule is responsible for the intense absorbance.

1. Introduction

Xanthene derivatives show important biological activities such as anti-viral, anti-bacterial, anti-inflammatory and anti-nociceptive due to the presence of pyran ring and incorporate into a wide variety of these therapeutic agents [1–4]. Specifically, xanthene-1,8-dione derivatives are a part of the structural unit in several natural products [5]. These heterocycles have also been used as dyes and as fluorescent materials [6]. In view of these, we synthesized the title compound by the one-pot condensation reaction of two equivalents of dimedone and one equivalent of 2-hydroxybenzaldehyde and zinc chloride is used as a catalyst. This reaction was conducted at room temperature and it leads to the formation of the tetraketone intermediate (see Scheme 1). Several derivatives have been structurally characterized in their tetraketone intermediate forms [7–11]. In all of these derivatives, two intramolecular *keto-enol* type hydrogen-bonding patterns are observed. The title compound was obtained at room temperature from the tetraketone intermediate form by the intramolecular nucleophilic addition of phenolic hydroxyl group with dimedone carbonyl group.

In this work, we present the crystal and molecular structure of the tetrahydro-1*H*-xanthen-1-one derivative, namely 9-(2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one. The crystal structure analysis reveals that the title compound exists in the enol form. The crystal structures of the two closely related analogs of the title compound have already been reported [12,13]. We also report a comparative study in the context of molecular conformation, lattice energy and Hirshfeld surface analysis for the title compound along

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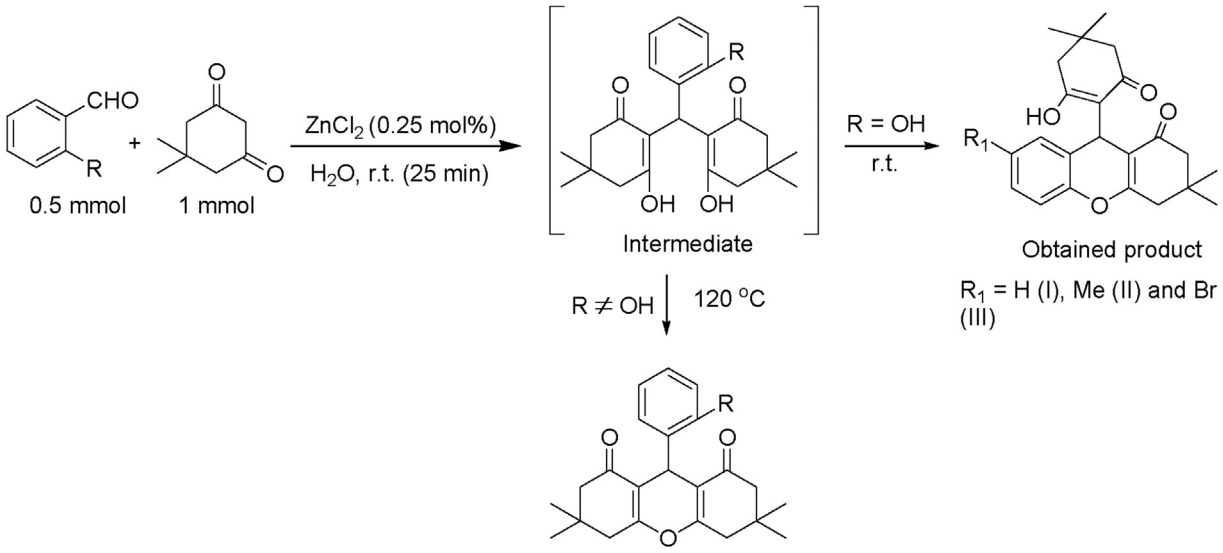

Scheme 1. Synthetic route for (I).

with two of its analogs. The structure of the title compound was optimized in the gas phase using the M05-2X functional with the 6-31+G(d) basis set. The harmonic vibrational frequencies are computed at the same level of theory to confirm the global minima. To get a better understanding of how various intermolecular interactions contribute toward crystal packing, we quantified the energetics of these interactions using PIXEL method. Moreover, the intermolecular interactions in the crystal structure are visualized using Hirshfeld surface analysis and the relative contributions of various interactions were estimated using 2D fingerprint plots. Furthermore, the existence of various intra-and intermolecular interactions was confirmed through the atoms-in-molecules (AIM) analysis and the natural bond orbital (NBO) study.

2. Experimental

In order to prepare the title compound (**I**), a reaction mixture of dimedone (140 mg, 1 mmol), aromatic aldehyde (0.5 mmol), ammonium acetate (231 mg, 3 mmol) and $ZnCl_2$ (17 mg, 0.125 mmol) were successively added and stirred at room temperature for 30 min. After completion, cold water (5 mL) was added and the mixture was stirred for 10 min. The solid product of (**I**) were isolated by simple filtration, washed with hexane and a portion of the sample was recrystallized from absolute ethanol for spectral analysis. Single crystals of (**I**) were obtained from ethanol by the slow evaporation method. A plausible mechanism for the formation of the product is shown in Scheme 1 and the details were given in the supplementary information section.

The FT-IR spectrum of the title compound was measured in the frequency region of 4000–400 cm^{-1} on a Perkin Elmer FT–IR spectrophotometer using the KBr pellet technique. The Raman spectrum was recorded using the 1064 nm line of Nd:YAG laser as excitation wavelength in the region of 4000–50 cm^{-1} on a Bruker RFS-27 FT-Raman spectrometer. The UV–Vis absorption spectrum was recorded (200–700 nm) on an Eppendorf Bio-spectrophotometer in DMSO solvent.

2.1. Single crystal X-ray diffraction

The X–ray intensity data for the title compound was collected on a Rigaku AFC12 Saturn724 + diffractometer. The crystal structure of the title compound was solved by the SIR92 program [14] and all the non-hydrogen atoms were refined anisotropically using the SHELXL2014 program [15]. The hydrogen atoms were placed in idealized geometrical positions (C–H = 0.93–0.98 Å) and constrained to ride on their parent atoms. The hydrogen atoms bonded to the methyl carbons were allowed to rotate freely about the C–C bonds. The ORTEP and packing figures were produced using the program MERCURY [16]. **Crystal data:** $C_{23}H_{26}O_4$, M = 366.46, 0.40 × 0.25 × 0.25 mm^3, monoclinic, space group $P2_1/c$, a = 7.060(3), b = 20.290(10), c = 13.680(7) Å, α = 90°, β = 93.379(7)°, γ = 90°, V = 1956.2(16) $Å^3$, Z = 4, D_c = 1.244 Mg m^{-3}, F_{000} = 784, *MoKα* radiation, λ = 0.71075 Å, 2θmax = 50°, 18418 reflections collected, 3439 unique (R_{int} = 0.0432), Final GooF = 1.188, R_1 = 0.0615, wR_2 = 0.1153, R indices based on 2956 reflections with I > 2σ(I) (refinement on F^2), 248 parameters, μ = 0.084 mm^{-1}. CCDC-1499266 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/data_request/cif or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email:deposit@ccdc.cam.ac.uk.

2.2. Hirshfeld surface analysis and pixel energy calculation

The Hirshfeld surface (HS) and 2D fingerprint plots were generated for the title structure using the program CrystalExplorer 3.1 [17] as mentioned in our earlier work [18–20]. A comparative analysis of Hirshfeld surfaces mapped with different properties such as d_i, d_e, d_{norm}, electrostatic potential, shape index and curvedness of the title compound and two of its analogs were performed. In order to quantify the energies associated with the various intermolecular interactions exist in the crystal structure, PIXEL calculation was carried out as reported earlier [18–20]. Briefly, the distances involving hydrogen atoms are moved to their neutron values (C–H = 1.083 Å and O–H = 0.986 Å) before the calculation. The electron density of the molecule has been obtained at the MP2/6-31G** level of theory using Gaussian 09 [21]. The total energy is partitioned into the corresponding Coulombic, polarization, dispersion and repulsion energies.