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Synthesis and Crystal Structure of 1-(4-fluorophenyl)-3-(3,4,5-trimethoxyphenyl)-2-propen-1-one

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The title compound $C_{18}H_{17}FO_4$ was synthesized and recrystallized from an organic solution. The crystal structure of 1-(4-fluorophenyl)-3-(3,4,5-trimethoxyphenyl)-2-propen-1-one was determined by X-ray diffraction analysis. The title compound crystallizes in the monoclinic crystal class in the space group $P2_1/c$ with cell parameters $a = 7.6930(6)$Å, $b = 15.2320(11)$Å, $c = 14.1280(12)$Å, $\beta = 106.596(3)°$, $Z = 4$, and $V = 1586.6(2)$Å³. The unsaturated keto group is not strictly planar and is in a s-cis conformation.

Keywords: chalcone derivative; crystal growth; 1-(4-fluorophenyl)-3-(3,4,5-trimethoxyphenyl)-2-propen-1-one; X-ray diffraction

INTRODUCTION

Chalcones represent one of the most abundant and ubiquitous groups of natural products [1]. In the past few years, they have been shown to possess interesting biological properties including anti-invasive [2], anticancer [3], inhibitory activation [4], antimalarial [5], antimicrobial [6], antimutagenic [7], radioprotective [8], and anti-inflammatory

effects [9] and synthetic intermediates in the presence of other compounds [10]. Further, a series of dimethoxy and trimethoxy chalcone derivatives, with various patterns of fluorination, are important compounds because of their influence on nitric oxide production in lipopolysaccharide-stimulated murine RAW 264.7 cells [11]. The trimethoxychalcone derivative with a fluoro substituent at position C-4′ was found to be a better inhibitor of nitric oxide production than with trifluoromethyl substituent at the same position.

Recently, it has been noted that, among many organic compounds reported for their second harmonic generation, chalcone derivatives are known for their excellent blue light transmittance and good crystallizability [12–15]. In view of their outstanding behavior, chalcones have been the subject of several experimental and theoretical studies, mainly aimed at determining their crystal structure [16–18]. We, herein, report the synthesis and crystal structure of 1-(4-fluorophenyl)-3-(3,4,5-trimethoxyphenyl)-2-propen-1-one.

EXPERIMENTAL

Synthesis and Crystal Growth

Chalcone derivatives can be synthesized by the Claisen–Schmidt condensation method [19]. This is the reaction of substituted acetophenone with substituted benzaldehyde in the presence of an alkali. To synthesize 4′-fluoro-3,4,5-trimethoxychalcone, we used commercially available Analytical Reagent (AR)-grade chemicals. 4′-Fluoroacetophenone (0.01 mol) and 3,4,5-trimethoxybenzaldehyde (0.01 mol) were dissolved in ethanol (60 ml). Sodium hydroxide (5 ml, 30%) was then added dropwise to the solution, and it stirred for 2 h. The content of the flask were poured into ice-cold water, and the resulting crude solid was collected by filtration. The compound was dried and recrystallized twice with acetone. The schematic diagram of the title compound is shown.
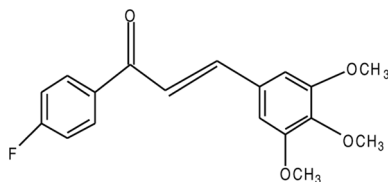
It is well known that chalcone derivatives are soluble in organic solvents such as ethyl alcohol, methanol, benzene, chloroform, Dimethylformamide (DMF), and acetone. Acetone is a suitable solvent for crystal growth. Good-quality single crystals of 4′-fluoro-3,4,5-trimethoxychalcone were grown from acetone in 10 days by the slow evaporation technique [20].

Structure Determination

A single crystal of the title compound with dimensions $0.3 \times 0.27 \times 0.25$ mm was chosen for X-ray diffraction study. The measurements were made on a DIPLabo imaging plate system at room temperature equipped with a normal focus 3-kW sealed X-ray source with graphite monochromated MoKα radiation. The crystal-to-detector distance is fixed at 120 mm with a detector area of 441×240 mm^2. Thirty-six frames of data were collected by the oscillation method. Each exposure of the image plate was set to a period of 400 s. Successive frames were scanned in steps of $5°$ per minute with an oscillation range of $5°$. Image processing and data reduction were done using Denzo [21]. The reflections were merged with Scalepack [22]. All the frames could be indexed using a primitive monoclinic lattice. The structure was solved by direct methods using SHELXS-97 [23]. All the nonhydrogen atoms were revealed in the first Fourier map. Full-matrix least squares refinement with isotropic

TABLE 1 Crystal Data and Structure Refinement Table

Parameter	Value
Empirical formula	$C_{18} H_{17} O_4 F$
Formula weight	316.32
Temperature	293(2) K
Wavelength	0.71073Å
Crystal system	Monoclinic
Space group	$P2_1/c$
Cell dimensions	$a = 7.6930(6)$ Å
	$b = 15.2320(11)$ Å
	$c = 14.1280(12)$ Å
	$\beta = 106.596(3)$
Volume	1586.6(2) Å^3
Z	4
Density (calculated)	1.324 Mg/m^3
F_{000}	664
Crystal size	$0.3 \times 0.27 \times 0.25$
Crystal color	Pale Yellow
Theta range for data collection	$2.76°$ to $32.52°$
Index ranges	$-11 \leq h \leq 11, -22 \leq k \leq 22,$ $-21 \leq l \leq 21$
Reflections collected	9828
Independent reflections	5525 [R (int) = 0.0321]
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	5525/0/212
Goodness-of-fit on F^2	1.037
Final R indices [I > 2σ (I)]	$R1 = 0.0682, \omega R2 = 0.1880$
R indices (all data)	$R1 = 0.1517\ \omega R2 = 0.2350$
Extinction coefficient	0.039(5)
Largest diff. peak and hole	0.351 and -0.220 e.A^{-3}

temperature factors for all the atoms was carried out using SHELXL-97 [24]. Refinement of nonhydrogen atoms with anisotropic parameters was started at this stage. The hydrogen atoms were placed at chemically acceptable positions and were allowed to ride on their parent atoms. Refinement was carried out using 5525 reflections and 212 parameters using SHELXL-97. The residuals saturated at $R_I = 0.0682$. The details of the crystal data and refinement are given in Table 1.

RESULTS AND DISCUSSION

Table 2 gives the atomic coordinates and equivalent thermal parameters of the nonhydrogen atoms. Tables 3 and 4 gives the list of bond lengths and bond angles respectively, which are in good agreement with the standard values. The ORTEP of the molecule with thermal ellipsoids drawn at 50% probability is shown in Fig. 1. Figures 2–4 represent the packing of the molecules when viewed along the *a, b,* and *c* axes, respectively. The molecular structure consists of two

TABLE 2 Atomic Coordinates and Equivalent Thermal Parameters of the Nonhydrogen Atoms

Atom	x	y	z	Ueq
C(1)	3680(3)	1560(1)	1988(1)	59(1)
C(2)	4780(3)	2044(1)	2760(1)	63(1)
C(3)	6363(3)	2428(1)	2673(1)	65(1)
C(4)	6827(3)	2329(1)	1794(1)	64(1)
C(5)	5708(3)	1870(1)	1005(1)	61(1)
C(6)	4132(2)	1468(1)	1104(1)	56(1)
O(7)	4433(2)	2176(1)	3662(1)	84(1)
C(8)	2981(5)	1855(2)	3779(2)	96(1)
O(9)	7454(3)	2823(1)	3498(1)	98(1)
C(10)	8145(4)	3662(2)	3446(2)	99(1)
O(11)	8457(2)	2677(1)	1792(1)	85(1)
C(12)	8967(4)	2630(2)	914(2)	94(1)
C(13)	2986(3)	924(1)	318(1)	59(1)
C(14)	3224(3)	759(1)	−556(2)	62(1)
C(15)	2021(3)	177(1)	−1284(2)	58(1)
O(16)	880(2)	−275(1)	−1068(1)	74(1)
C(17)	2215(3)	135(1)	−2306(1)	59(1)
C(18)	3274(4)	707(2)	−2656(2)	88(1)
C(19)	3469(4)	622(2)	−3589(2)	102(1)
C(20)	2589(4)	−47(2)	−4168(2)	82(1)
C(21)	1494(4)	−607(2)	−3871(2)	80(1)
C(22)	1314(3)	−519(2)	−2931(2)	70(1)
F(23)	2803(3)	−152(1)	−5086(1)	116(1)

Note: $U_{eq} = (1/3)\sum_i\sum_j U_{ij}(a_i^*.a_j^*)(\mathbf{a_i.a_j})$.

TABLE 3 Bond Lengths (Å)

Atoms	Length	Atoms	Length
C(1)–C(2)	1.386(3)	O(11)–C(12)	1.406(3)
C(1)–C(6)	1.396(3)	C(13)–C(14)	1.323(3)
C(2)–C(3)	1.388(3)	C(14)–C(15)	1.468(3)
C(2)–O(7)	1.390(2)	C(15)–O(16)	1.221(2)
C(3)–O(9)	1.367(2)	C(15)–C(17)	1.496(3)
C(3)–C(4)	1.394(3)	C(17)–C(18)	1.377(3)
C(4)–O(11)	1.362(2)	C(17)–C(22)	1.380(3)
C(4)–C(5)	1.388(3)	C(18)–C(19)	1.375(3)
C(5)–C(6)	1.400(3)	C(19)–C(20)	1.361(4)
C(6)–C(13)	1.462(3)	C(20)–C(21)	1.346(3)
O(7)–C(8)	1.273(3)	C(20)–F(23)	1.363(3)
O(9)–C(10)	1.394(3)	C(21)–C(22)	1.381(3)

benzene rings attached to a propenone chain at the 1,3-position. The molecule is nonplanar with a dihedral angle between the two benzene rings of $20.86(11)°$, which is larger than the reported value of $11.0(1)°$ for 1-(2-hydroxy-4-methoxyphenyl)-3-(2,3,4-trimethoxyphenyl)prop-2-en-1-one [25]. The unsaturated keto group is not strictly planar. It is in the s-*cis* conformation as indicated by the C13–C14–C15–O16 torsion angle value of $-9.9(3)°$ with respect to the olefinic double bond, which is comparable with the similar conformation reported for 1-(4-chlorophenyl)-3-(4-hydroxyphenyl)-prop-2-en-1-one   where   the

TABLE 4 Bond Angles (^{0})

| Atoms	Angle	Atoms	Angle
C(2)–C(1)–C(6)	120.33(18)	C(4)–O(11)–C(12)	118.15(17)
C(1)–C(2)–C(3)	20.55(18)	C(14)–C(13)–C(6)	127.06(18)
C(1)–C(2)–O(7)	124.41(18)	C(13)–C(14)–C(15)	122.74(18)
C(3)–C(2)–O(7)	115.04(17)	O(16)–C(15)–C(14)	121.34(19)
O(9)–C(3)–C(2)	116.80(18)	O(16)–C(15)–C(17)	119.63(17)
O(9)–C(3)–C(4)	123.75(19)	C(14)–C(15)–C(17)	119.03(17)
C(2)–C(3)–C(4)	119.22(17)	C(18)–C(17)–C(22)	117.9(2)
O(11)–C(4)–C(5)	123.64(18)	C(18)–C(17)–C(15)	123.48(18)
O(11)–C(4)–C(3)	115.52(17)	C(22)–C(17)–C(15)	118.57(18)
C(5)–C(4)–C(3)	120.79(18)	C(19)–C(18)–C(17)	121.5(2)
C(4)–C(5)–C(6)	119.73(18)	C(20)–C(19)–C(18)	118.4(2)
C(1)–C(6)–C(5)	119.33(17)	C(21)–C(20)–C(19)	122.3(2)
C(1)–C(6)–C(13)	119.08(17)	C(21)–C(20)–F(23)	118.6(2)
C(5)–C(6)–C(13)	121.54(17)	C(19)–C(20)–F(23)	119.0(2)
C(8)–O(7)–C(2)	117.93(17)	C(20)–C(21)–C(22)	118.8(2)
C(3)–O(9)–C(10)	120.63(19)	C(17)–C(22)–C(21)	121.0(2)
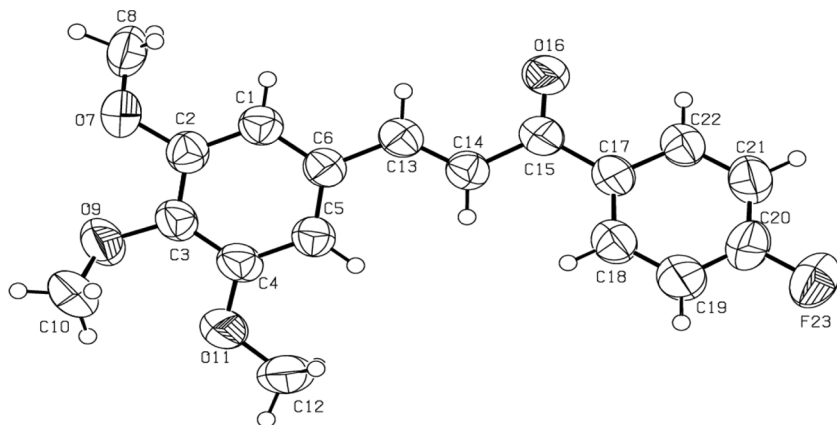
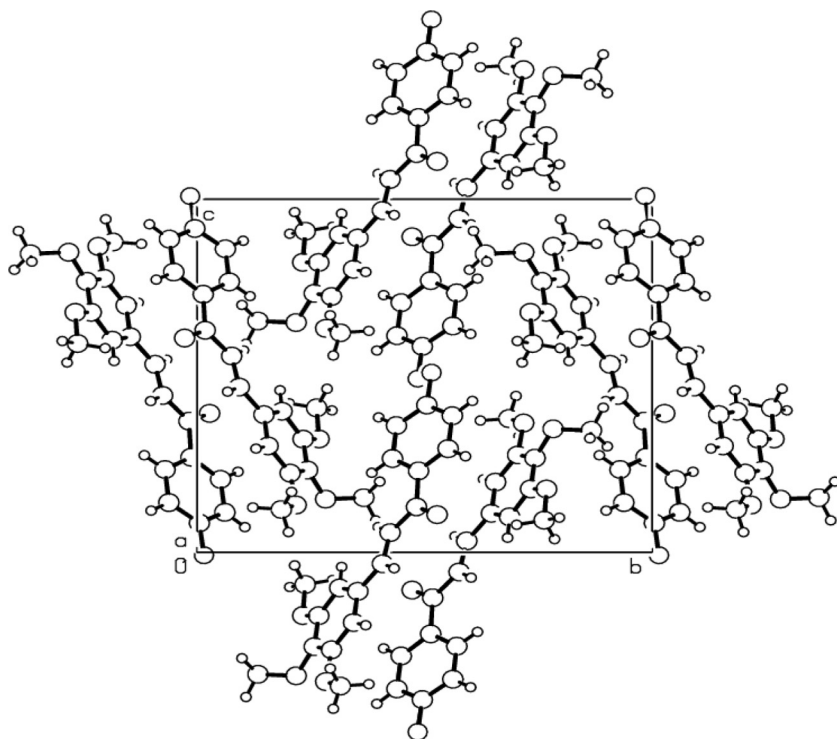**FIGURE 1** ORTEP of the molecule with 50% probability.

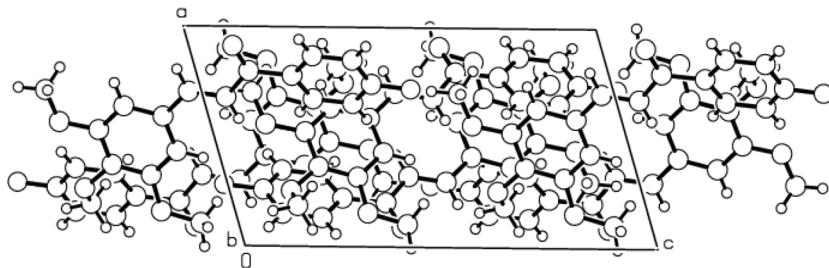**FIGURE 2** Packing of the molecules when viewed down the *a* axis.

FIGURE 3 Packing of the molecules when viewed down the *b* axis.

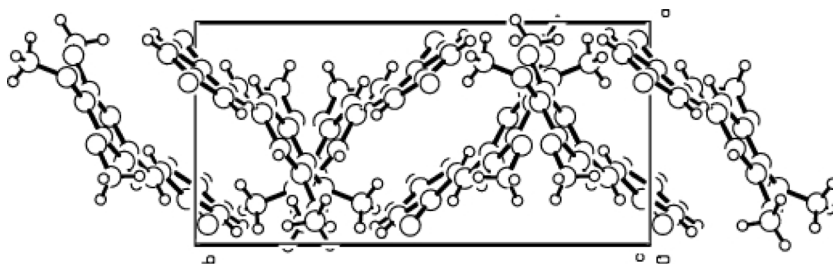**FIGURE 4** Packing of the molecules when viewed down the *c* axis.

torsion angle value is $8.6(4)°$ [26]. The bond lengths O7–C8, O9–C10, and O11–C12 are comparable to the corresponding values in a similar structure [25]. The torsion angle values of C8–O7–C2–C1 $= -2.2(30)°$ and C12–O11–C4–C5 $= 5.3(3)°$ indicate that the O7 and O11 methoxy groups are coplanar with the attached benzene ring. The other methoxy group at O9 is in a $+synclinal$ conformation as indicated by the torsion angle value of $53.0(3)°$ for C10–O9–C3–C4. The molecules appears to be stacked when viewed down the *a* axis.

ACKNOWLEDGMENTS

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