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Crystal structure of 6-(4-fluorophenyl)-4-methoxy-2H-pyran-2-one, C₁₂H₉FO₃

Table 1: Data collection and handling.

Crystal:	Colourless Rod
Size:	0.50 × 0.19 × 0.16 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	0.12 mm ⁻¹
Diffractometer, scan mode:	Bruker APEX-II, φ and ω
$\theta_{\max}$, completeness:	27.4°, 98%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	8040, 2142, 0.018
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 1942
$N(\text{param})_{\text{refined}}$:	146
Programs:	Bruker [1], SHELX [2, 3], Mercury [4]

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Abstract

C₁₂H₉FO₃, triclinic, $P\bar{1}$ (no. 2), $a = 7.1983(6)$ Å, $b = 7.3732(6)$ Å, $c = 9.6439(8)$ Å, $\alpha = 81.489(5)^\circ$, $\beta = 88.634(4)^\circ$, $\gamma = 71.065(4)^\circ$, $V = 478.66(7)$ Å³, $Z = 2$, $R_{\text{gt}}(F^2) = 0.0362$, $wR_{\text{ref}}(F^2) = 0.1015$, $T = 100(2)$ K.

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The molecular structure is shown in the figure. Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

Source of material

The dianion of ethyl acetoacetate (1.83 g, 14.04 mmol) was formed by the sequential treatment of the parent compound in THF (60 mL) with NaH (60% dispersion in mineral oil, 1.12 g, 28.0 mmol) and *n*-butyllithium (2.5 M in hexane, 9.2 mL, 23.20 mmol). Addition of ethyl 4-fluorobenzoate (2.36 g, 14.04 mmol) to the reaction mixture yielded ethyl (Z)-5-(4-fluorophenyl)-5-hydroxy-3-oxopent-4-enoate. Refluxing

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²).

Atom	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
F1	0.34170(12)	0.79159(12)	0.91465(8)	0.0224(2)
O1	0.31232(14)	0.06558(13)	0.28267(9)	0.0165(2)
O2	0.12032(13)	0.63559(12)	0.33314(9)	0.0147(2)
O3	−0.02087(15)	0.73199(13)	0.12224(10)	0.0207(2)
C1	0.2746(2)	0.00563(18)	0.15319(13)	0.0180(3)
H1A	0.132569	0.047985	0.134322	0.027*
H1B	0.328030	−0.135939	0.161302	0.027*
H1C	0.337513	0.064182	0.076082	0.027*
C2	0.24409(18)	0.25668(17)	0.28849(13)	0.0130(2)
C3	0.28477(18)	0.30711(17)	0.41944(12)	0.0134(3)
H3	0.354591	0.209469	0.492774	0.016*
C4	0.22279(18)	0.49457(17)	0.43721(12)	0.0123(2)
C5	0.25280(17)	0.57338(17)	0.56325(12)	0.0125(2)
C6	0.19936(18)	0.77347(18)	0.56231(13)	0.0145(3)
H6	0.143243	0.859198	0.479371	0.017*
C7	0.22719(19)	0.84865(18)	0.68094(13)	0.0161(3)
H7	0.189996	0.984671	0.680682	0.019*
C8	0.31034(19)	0.72021(19)	0.79907(13)	0.0155(3)
C9	0.33530(19)	0.44896(18)	0.68597(13)	0.0150(3)
H9	0.371753	0.312707	0.687739	0.018*
C10	0.36460(19)	0.52178(19)	0.80508(13)	0.0165(3)
H10	0.420531	0.437336	0.888573	0.020*
C11	0.07485(19)	0.59398(18)	0.20336(12)	0.0147(3)
C12	0.14505(18)	0.39537(18)	0.18272(12)	0.0144(3)
H12	0.122569	0.360313	0.095264	0.017*

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of ethyl (Z)-5-(4-fluorophenyl)-5-hydroxy-3-oxopent-4-enoate (0.23 g, 0.9 mmol) and 1,8-diazobicyclo[5.4.0]undecan-7-ene (DBU, 0.16 g, 1.0 mmol) in benzene (5 mL) overnight, according to the method described by Cervello *et al.* [5],

led to base-mediated cyclization to yield 6-(4-fluorophenyl)-4-hydroxy-2H-pyran-2-one. Methylation of the product (0.41 g, 2.0 mmol) with dimethyl sulfate (0.38 g, 3.0 mmol) in the presence of potassium carbonate (0.8 g, 6.0 mmol) afforded the product 6-(4-fluorophenyl)-4-methoxy-2H-pyran-2-one. Crystals were obtained by hot recrystallization using methanol. **Yield** = 97%, **m.p.** 202–206 °C. **¹H NMR** (400 MHz, CDCl₃) δ [ppm] = 7.80 (ddd, 2H, *J* = 7.1, 5.2, 2.1 Hz), 7.13 (t, 2H, *J* = 8.7), 6.35 (d, 1H, *J* = 2.1 Hz), 5.53 (d, 1H, *J* = 2.1 Hz), 3.85 (s, 3H, OCH₃). **¹³C NMR** (400 MHz, CDCl₃) δ [ppm] = 171.4, 164.5 (d, *J* = 252.4 Hz), 164.1, 159.4, 128.0 (d, *J* = 8.7 Hz), 127.5 (d, *J* = 3.5 Hz), 116.2 (d, *J* = 22.1 Hz), 97.9 (d, *J* = 1.1 Hz), 88.5, 56.2 (OCH₃). **¹⁹F NMR** (400 MHz, CDCl₃) δ [ppm] = −108.50 (m). **HRMS-ESI(+)** calcd. for C₁₂H₉FO₃Na [M+Na]⁺ 243.0433, found 243.0433. **IR** (neat) (cm^{−1}) = 1727, 1265, 1217, 1165, 1069, 1008, 839, 797.

Experimental details

The visual crystal structure information was performed using Mercury [4] system software. All C—H_{aromatic}, C—H_{methyl} and C—H_{methylene} bond distances were restrained to 0.95 Å, 0.98 Å and 0.99 Å with $U_{\text{iso}}(\text{H}_{\text{aromatic}} \text{ and } \text{H}_{\text{methylene}}) = 1.2U_{\text{eq}}$ and $U_{\text{iso}}(\text{H}_{\text{methyl}}) = 1.5U_{\text{eq}}$ of parent atom, respectively.

Comment

Many biologically active compounds containing a 2-pyrone moiety are known [6]. These compounds and synthetic analogues are associated with a diverse range of biological activities such as antiviral [7], anti-malarial, and anti-tuberculosis activities [8], hence there is an ongoing interest in the synthesis of these compounds. Several studies have shown that the incorporation of fluorine in molecules are likely to enhance the biological activities [9], which stimulated our interest in the synthesis of fluorinated 2-pyrones [10].

The crystal structure of the title compound has one molecular unit consisting of 4-fluorophenyl and pyrone moieties. Compared to the non-fluorinated molecule, the presence of the fluorine atom decreased the dihedral angle between the 4-fluorophenyl and pyrone rings from 8.8° to 7.2° [11]. Furthermore, the methoxy group was found to be more co-planar with the pyrone ring given a C1—O1—C2—C12 torsion angle of −0.5° compared to that observed in

the non-fluorinated derivative [11]. Non-classical intermolecular C12—H12···O3 (symmetry code: $-x, 1-y, -z$) and C10—H10···F1 (symmetry code: $1-x, 1-y, 2-z$) hydrogen bonds form alternating eight-membered rings with two donor atoms and an acceptor. These hydrogen bonding patterns link neighbouring molecules to form a one-dimensional supramolecular structure.

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