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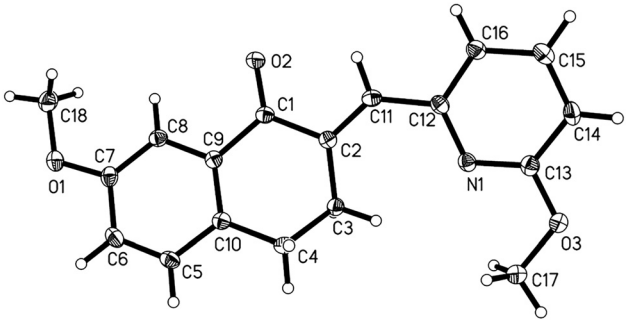
Crystal structure of (*E*)-7-methoxy-2-((6-methoxypyridin-2-yl)methylene)-tetralone, $C_{18}H_{17}NO_3$



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Abstract

$C_{18}H_{17}NO_3$, triclinic, $P\bar{1}$ (no. 2), a = 4.0929(4) Å, b = 12.9527(11) Å, c = 14.4228(12) Å, α = 70.171(8)°, β = 87.229(8)°, γ = 87.567(8)°, V = 718.16(12) Å^3, Z = 2, $R_{gt}(F)$ = 0.0549, $wR_{ref}(F^2)$ = 0.1526, T = 99.9(3) K.

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

Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.15 × 0.12 × 0.11 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.09 mm^{-1}
Diffractometer, scan mode:	SuperNova,
θ_{max}, completeness:	25.5°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	4714, 2660, 0.042
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\sigma(I_{obs})$, 2124
$N(param)_{refined}$:	201
Programs:	CrysAlis^{PRO} [1], Shelx [2, 3]

Source of material

The title compound {systematic name: (*E*)-7-methoxy-2-((6-methoxypyridin-2-yl)methylene)-3,4-dihydronaphthalen-1(2*H*)-one} was prepared according to a literature protocol [4]. 7-Methoxy-1-tetralone (0.53 g, 3.0 mmol) and 6-methoxy-2-pyridinecarbaldehyde (0.41 g, 3.0 mmol) were dissolved in methanol (10 mL). Aqueous NaOH (0.60 g, 15.0 mmol) solution (3 mL) was added to the above solution. The reaction mixture was stirred until completion of the reaction (monitored by TLC). Then, it was cooled in an ice bath for 20 min. The solids were filtered off and the residues were purified on a silica gel by column chromatography using petroleum ether/ethyl acetate (2:1, *v/v*) as the eluent to produce light yellow powders. Crystals suitable for X-ray diffraction were obtained by slow evaporation from methanol at room temperature.

Experimental details

The H atoms were placed in idealized positions and treated as riding on their parent atoms, with d (C–H) = 0.93 Å (aromatic) and 0.97 Å (methylene), U_{iso}(H) = 1.2U_{eq}(C), and d(C–H) = 0.96 Å (methyl), U_{iso}(H) = 1.5U_{eq}(C). Displacement ellipsoids are drawn at the 35% probability level.

Comment

1-Tetralones, also known as 3,4-dihydronaphthalen-1(2*H*)-ones, have attracted the attention of chemists and pharmacists because of their potential applications for novel modulators of allergic and inflammatory phenomena and inhibitors of retinoic acid (RA)-metabollizing enzymes [5, 6]. In order to obtain novel pharmaceutical agents,

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C1	0.8932 (5)	0.65626 (14)	0.16741 (13)	0.0215 (4)
C2	0.7312 (5)	0.72771 (14)	0.21974 (13)	0.0203 (4)
C3	0.7835 (5)	0.69310 (13)	0.32835 (13)	0.0224 (4)
H3A	0.639175	0.736137	0.357335	0.027*
H3B	1.007410	0.706690	0.339160	0.027*
C4	0.7151 (5)	0.57074 (14)	0.37833 (13)	0.0226 (4)
H4A	0.771521	0.548179	0.447041	0.027*
H4B	0.483280	0.559332	0.376104	0.027*
C5	0.9975 (5)	0.39189 (15)	0.38072 (14)	0.0248 (5)
H5	0.935214	0.361534	0.447066	0.030*
C6	1.1765 (5)	0.32829 (15)	0.33572 (14)	0.0273 (5)
H6	1.232012	0.255789	0.371612	0.033*
C7	1.2744 (5)	0.37250 (15)	0.23654 (14)	0.0249 (5)
C8	1.1857 (5)	0.47998 (14)	0.18311 (14)	0.0226 (4)
H8	1.248110	0.509892	0.116740	0.027*
C9	1.0022 (5)	0.54312 (14)	0.22931 (13)	0.0204 (4)
C10	0.9074 (5)	0.50092 (14)	0.32894 (13)	0.0210 (4)
C11	0.5586 (5)	0.81598 (14)	0.16365 (13)	0.0225 (4)
H11	0.551297	0.821417	0.097805	0.027*
C12	0.3809 (5)	0.90467 (14)	0.18738 (13)	0.0223 (4)
C13	0.2055 (5)	0.98777 (14)	0.29846 (14)	0.0244 (5)
C14	0.0570 (5)	1.07664 (15)	0.22600 (15)	0.0288 (5)
H14	−0.049705	1.133695	0.241718	0.035*
C15	0.0759 (5)	1.07572 (15)	0.13119 (14)	0.0295 (5)
H15	−0.017966	1.132873	0.080569	0.035*
C16	0.2371 (5)	0.98832 (15)	0.11154 (14)	0.0249 (5)
H16	0.248408	0.986000	0.047716	0.030*
C17	0.3289(6)	0.89823 (15)	0.46620 (14)	0.0325 (5)
H17A	0.238639	0.831305	0.465483	0.049*
H17B	0.286711	0.905347	0.529839	0.049*
H17C	0.560790	0.896779	0.452808	0.049*
C18	1.5485 (6)	0.34415 (17)	0.09731 (15)	0.0344 (5)
H18A	1.355831	0.363651	0.059011	0.052*
H18B	1.673117	0.288442	0.080016	0.052*
H18C	1.679046	0.407776	0.084055	0.052*
N1	0.3651 (4)	0.90504 (11)	0.28168 (11)	0.0225 (4)
O1	1.4560 (4)	0.30353 (10)	0.19940 (10)	0.0328 (4)
O2	0.9342 (4)	0.68720 (10)	0.07762 (9)	0.0310 (4)
O3	0.1806 (4)	0.98961 (10)	0.39229 (10)	0.0302 (4)

3,4-dihydronaphthalen-1(2*H*)-one and its derivatives were designed and synthesized to innovative 1-tetralone derivatives with judicious functional groups and different substituents. (*E*)-2-(3,4-dimethoxybenzylidene)-7-methoxy-tetralone exhibits obvious inhibition activity against Bcl-2 (B cell lymphoma 2) protein [7]. 2-(2-Bromo-3,4,5-trimethoxybenzylidene)-6-methoxy-tetralone possesses potent inhibitory activity against monoamine oxidase and acetylcholinesterase, which can be a promising agent for the treatment of Alzheimer's disease [8]. Some 2-arylidene-1-tetralones with methoxy groups showed the antioxidant activity against radical scavenging [9]. These results demonstrate that active 1-tetralone derivatives all contain the fraction of α,β-unsaturated keto and methoxy group. The pharmacophore of α,β-unsaturated keto can establish the primary binding interaction with bio-thiols from susceptible neoplasms with lower toxicity [10]. The methoxy group can improve molecular lipophilicity and increase the ability of the membrane permeability. Based on these consideration, 2-arylidene-1-tetralones with methoxy groups were designed and synthesized in our laboratory, which show evident anti-neuroinflammatory property with relatively low toxicity [11]. Additionally, 1-tetralone derivatives that contain pyridinyl groups demonstrated antiproliferative activity against a variety of cancer cell lines [12]. As a part of the search for new anti-inflammatory and antitumor agents, a new 1-tetralone derivative with methoxy group and pyridine ring was synthesized by the aldol condensation reaction.

There is one independent molecule in the asymmetric unit (cf. the Figure). The bond length of C2–C11 is 1.349(2) Å, which represents a typical C=C double bond, and the ethylene moiety in the enone linkage adopts an *E* configuration [13]. Other bond lengths and bond angles are all in the normal ranges [14–17]. In the title molecule, the cyclohexanone ring displays an envelope conformation with the flap atom C4 deviating by 0.493(3) Å from the least-squares plane of the ring. The dihedral angle between the benzene and pyridine rings is 24.28(7)°. In the crystal, molecules are connected through weak C–H–O hydrogen bonds. It is noteworthy that the peripheric heteroatoms with free electron pairs (such as O and N) can be considered as the potential hydrogen bonding acceptors and such weak interactions will play a crucial role in the biological activity [18].

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