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Crystal structure of 2-methoxyphenyl 2-(6-methoxynaphthalen-2-yl)propanoate, $C_{21}H_{20}O_4$

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Abstract

$C_{21}H_{20}O_4$, monoclinic, $P2_1$ (no. 4), $a = 5.7726(10)$ Å, $b = 12.662(2)$ Å, $c = 12.068(3)$ Å, $\beta = 92.377(11)^\circ$, $V = 881.3(3)$ Å³, $Z = 2$, $R_{gt}(F) = 0.0342$, $wR_{ref}(F^2) = 0.0887$, $T = 296(2)$ 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

Naproxen acylchloride was synthesized according to the literature method [5]. The 2-methoxyphenol (Guaiacol, 0.01 mol, 1.24 g) and 4-(dimethylamino)-pyridin (DMAP, 0.0015 mol, 0.18 g) were dissolved in dry tetrahydrofuran (20 mL) and triethylamine (0.015 mol, 2 mL). The solution of naproxen acylchloride in dry tetrahydrofuran was dropwise

Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	$0.18 \times 0.16 \times 0.14$ mm
Wavelength:	Cu $K\alpha$ radiation (1.54178 Å)
μ :	0.71 mm^{-1}
Diffractometer, scan mode:	Bruker D8 VENTURE, φ and ω
θ_{max} , completeness:	68.4° , 99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	14,272, 3185, 0.037
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2\sigma(I_{\text{obs}})$, 2892
$N(\text{param})_{\text{refined}}$:	229
Programs:	Bruker [1], Olex2 [2], SHELX [3, 4]

added at 0 °C. The reaction mixture was stirred for 2 h at room temperature. The reaction mixture was filtrated and the filtrate was concentrated under vacuum. The residue was dissolved in dichloromethane, successively washed with 5% NaOH solution and water to pH = 7, and dried with anhydrous Na_2SO_4 . The solution was filtrated, and concentrated under vacuum to obtain the crude product. The crude product was purified by recrystallization in ethyl acetate. The single crystals were obtained from tetrahydrofuran solution.

Experimental details

A suitable crystal was selected and tested on a Bruker D8 VENTURE diffractometer. Using OLEX2 [2], the structure was solved with the SHELXT [3] structure solution program using Intrinsic Phasing and refined with the SHELXL [4].

Comment

Naproxen is a nonsteroidal anti-inflammatory drug. It is often used for treating rheumatic, rheumatoid arthritis and osteoarthritis. However, it often brings gastrointestinal side effects such as ulcers, gastric perforation and bleeding in long-term administration because of its carboxylic acid group. As early as 1980, a study has shown that Ibuprofen–Guaiacol ester is less toxic than the Ibuprofen and is a better prodrug [6]. So, we synthesized a Naproxen–Guaiacol ester and hope to reduce the side effects.

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

Atom	x	y	z	<i>U</i> _{iso} */ <i>U</i> _{eq}
O1	0.0001 (3)	0.48664 (17)	0.07878 (14)	0.0639 (5)
C1	−0.1982 (6)	0.5269 (3)	0.0203 (2)	0.0730 (9)
H1A	−0.195822	0.505636	−0.055967	0.110*
H1B	−0.197992	0.602634	0.024719	0.110*
H1C	−0.335396	0.499860	0.052572	0.110*
O2	0.4818 (4)	0.59612 (17)	0.80009 (18)	0.0720 (6)
C2	0.0325 (4)	0.51042 (19)	0.18883 (18)	0.0452 (5)
O3	0.2220 (3)	0.46677 (13)	0.76704 (14)	0.0510 (4)
C3	0.2401 (4)	0.4696 (2)	0.23713 (19)	0.0495 (6)
H3	0.339764	0.431046	0.194016	0.059*
C5	0.1473 (4)	0.54476 (16)	0.41404 (18)	0.0392 (5)
O4	0.5835 (3)	0.39689 (15)	0.65217 (15)	0.0626 (5)
C4	0.2957 (4)	0.48620 (19)	0.34612 (19)	0.0464 (5)
H4	0.433355	0.458729	0.376798	0.056*
C6	−0.0605 (4)	0.58568 (17)	0.36475 (18)	0.0391 (5)
C7	−0.1153 (4)	0.56775 (18)	0.25022 (19)	0.0447 (5)
H7	−0.251261	0.594988	0.217498	0.054*
C8	−0.2081 (4)	0.6435 (2)	0.4333 (2)	0.0476 (5)
H8	−0.344838	0.672010	0.402767	0.057*
C9	−0.1536 (4)	0.6581 (2)	0.5429 (2)	0.0495 (6)
H9	−0.255025	0.695429	0.586207	0.059*
C10	0.0548 (4)	0.61755 (18)	0.59245 (19)	0.0429 (5)
C11	0.2012 (4)	0.56301 (18)	0.52739 (18)	0.0421 (5)
H11	0.340004	0.537274	0.558625	0.050*
C12	0.1087 (5)	0.6407 (2)	0.7145 (2)	0.0552 (6)
H12	−0.033611	0.629073	0.754314	0.066*
C13	0.2942 (5)	0.56876 (19)	0.76509 (19)	0.0485 (5)
C14	0.1813 (8)	0.7567 (3)	0.7322 (3)	0.0950 (14)
H14A	0.321552	0.770118	0.694502	0.142*
H14B	0.206976	0.769990	0.810031	0.142*
H14C	0.060645	0.802275	0.703026	0.142*
C15	0.3769 (4)	0.39165 (19)	0.81506 (19)	0.0466 (5)
C16	0.3353 (5)	0.3539 (2)	0.9182 (2)	0.0559 (6)
H16	0.210167	0.379146	0.956557	0.067*
C17	0.4812 (6)	0.2774 (2)	0.9658 (2)	0.0639 (7)
H17	0.455511	0.251625	1.036417	0.077*
C18	0.6626 (6)	0.2407 (2)	0.9078 (2)	0.0674 (8)
H18	0.760571	0.189666	0.939375	0.081*
C19	0.7029 (5)	0.2781 (2)	0.8029 (2)	0.0617 (7)
H19	0.826514	0.251724	0.764402	0.074*
C20	0.5603 (4)	0.3546 (2)	0.7548 (2)	0.0492 (6)
C21	0.7683 (5)	0.3596 (2)	0.5888 (2)	0.0612 (7)
H21A	0.768467	0.396838	0.519533	0.092*
H21B	0.748635	0.285399	0.574946	0.092*
H21C	0.912962	0.371263	0.629109	0.092*

A view on the structure of the title molecule is shown in the Figure. The molecule structure of the title compound is similar to the 2-acetyl-5-methoxyphenyl 2-(6-methoxynaphthalen-2-yl) propanoate [7]. One carbon-oxygen double bond exists in the compound, the C–O double bond distance (C13–O2) is 1.197(3) Å. The torsion angles of C10–C12–C13–O3, C13–O3–C15–C16, C13–O3–C15–C20 and C14–C12–C13–O2 are −65.2(3)°, 104.5(3)°, −78.3(3)° and −9.3(4)° respectively. All the bond lengths and angles are in the expected ranges [8].

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