Crystal structure of 2-acetyl-5-methoxyphenyl 2-(6-methoxynaphthalen-2-yl) propanoate, $C_{23}H_{22}O_5$

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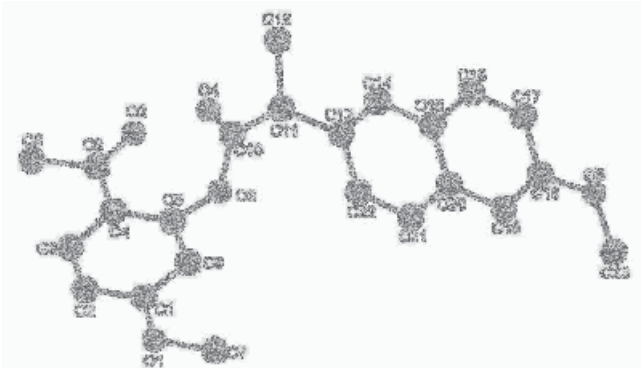

Abstract

$C_{23}H_{22}O_5$, monoclinic, $P2_1$ (no. 4), a = 8.225(2) Å, b = 8.276(2) Å, c = 14.640(3) Å, β = 95.66(3)°, V = 991.7(3) Å^3, Z = 2, $R_{gt}(F)$ = 0.0417, $wR_{ref}(F^2)$ = 0.1035, T = 290 K.

Table 1. Data collection and handling.

Crystal:	colourless prisms, size 0.24×0.25×0.40 mm
Wavelength:	Mo K_α radiation (0.71073 Å)
μ:	0.89 cm^{-1}
Diffractometer, scan mode:	Rigaku R-AXIS RAPID, ω
$2\theta_{max}$:	54.96°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	9366, 3998
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 2985
$N(param)_{refined}$:	257
Programs:	SHELX [3]

Source of material

Naproxen (0.015 mol, 3.45 g) was dissolved in anhydrous methylene chloride (12 mL), and then oxalyl chloride (0.018 mol, 1.7 mL) and two drops of *N*, *N*-dimethylformamide was dropwise added at 0 °C. The solution was stirred overnight at room temperature. After the solvent and excess oxalyl chloride was removed by vacuum distillation, the residue was washed three times with dry toluene to obtain a yellow solid, naproxen acylchloride. Paeonol, 1-(2-hydroxy-4-methoxyphenyl)- ethanone (0.01 mol, 1.66 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). To the solution a solution of naproxen acylchloride in dry tetrahydrofuran was dropwise added at 0 °C. The reaction mixture was stirred for 5 h at room temperature. The reaction mixture was filtrated to remove the solid and the filtrate was concentrated under vacuum to remove the solvent. The residue was dissolved in methylene chloride, successively washed with 5% $NaHCO_3$ solution and water to pH = 7, and dried with anhydrous Na_2SO_4. The solution was filtrated, and concentrated under vacuum to obtain crude product. The crude product was purified by recrystallization in ethyl acetate. The single crystals were obtained from methanol solution.

Experimental details

All the carbon-bounded H atoms were positioned geometrically with d(C–H) = 0.93-0.98 Å and U_{iso}(H) = 1.2 or 1.5 U_{eq}(C).

Discussion

Naproxen, a typical non-steroidal anti-inflammatory drug with aryl propionic acid group, was used for treating rheumatic, rheumatoid arthritis and osteroarthritis. However, it always brings about serious gastrointestinal side effects such as ulcers, bleeding, and gastric perforation in long-term administration [1]. Carboxylic acid group on the propionic acid molecules is the main reason causing gastrointestinal adverse reaction [2]. In order to reduce side effects of naproxen, we have synthesized a Naproxen-Paeonol ester as a prodrug. In the title crystal structure, the benzene ring and naphthalene ring are not coplanar with a dihedral angle of 67.72(6)°. There is no π-π stacking interactions between the arene rings. All the bond distances and angles are within normal ranges.

Table 2. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	x	y	z	U_{iso}
H(2)	2*a*	–0.0533	0.2463	0.4957	0.082
H(3)	2*a*	0.1986	0.1294	0.4965	0.075
H(6)	2*a*	–0.0480	0.1633	0.7654	0.060
H(7A)	2*a*	–0.3216	0.1920	0.7288	0.120
H(7B)	2*a*	–0.4154	0.3451	0.6887	0.120
H(7C)	2*a*	–0.2476	0.3645	0.7484	0.120
H(9A)	2*a*	0.5831	–0.0489	0.5528	0.138
H(9B)	2*a*	0.4694	0.0915	0.5130	0.138
H(9C)	2*a*	0.4115	–0.0884	0.5012	0.138
H(11)	2*a*	0.4004	–0.1201	0.9047	0.052
H(12A)	2*a*	0.5780	0.1548	0.9710	0.089
H(12B)	2*a*	0.6451	0.0138	0.9138	0.089
H(12C)	2*a*	0.6071	–0.0167	1.0152	0.089
H(14)	2*a*	0.3935	0.1684	1.0781	0.050
H(16)	2*a*	0.2981	0.2872	1.2203	0.062
H(17)	2*a*	0.1088	0.3005	1.3232	0.067
H(19)	2*a*	–0.1747	–0.0221	1.1788	0.054
H(21)	2*a*	–0.0767	–0.1425	1.0371	0.057
H(22)	2*a*	0.1163	–0.1597	0.9359	0.056
H(23A)	2*a*	–0.3643	0.0922	1.2625	0.123
H(23B)	2*a*	–0.3626	0.0909	1.3697	0.123
H(23C)	2*a*	–0.2736	–0.0463	1.3201	0.123

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Table 3. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	2*a*	–0.0764(2)	0.2166(3)	0.6303(2)	0.054(1)	0.060(1)	0.054(1)	0.006(1)	–0.0103(9)	–0.000(1)
C(2)	2*a*	–0.0014(3)	0.2059(3)	0.5502(2)	0.075(1)	0.082(2)	0.045(1)	0.013(1)	–0.011(1)	0.008(1)
C(3)	2*a*	0.1499(3)	0.1357(3)	0.5511(2)	0.070(1)	0.075(2)	0.042(1)	0.006(1)	0.003(1)	–0.000(1)
C(4)	2*a*	0.2331(2)	0.0732(2)	0.6311(2)	0.0526(9)	0.049(1)	0.049(1)	–0.0022(9)	–0.0039(8)	0.0005(9)
C(5)	2*a*	0.1526(2)	0.0861(2)	0.7097(1)	0.0511(9)	0.046(1)	0.045(1)	–0.0069(8)	–0.0118(8)	0.0065(9)
C(6)	2*a*	0.0012(2)	0.1565(3)	0.7110(2)	0.053(1)	0.054(1)	0.042(1)	–0.0049(9)	–0.0009(8)	0.0009(9)
C(7)	2*a*	–0.3095(3)	0.2980(4)	0.7039(2)	0.053(1)	0.099(2)	0.087(2)	0.007(1)	–0.001(1)	–0.031(2)
C(8)	2*a*	0.3963(2)	–0.0033(3)	0.6306(2)	0.058(1)	0.049(1)	0.073(2)	–0.003(1)	–0.003(1)	–0.012(1)
C(9)	2*a*	0.4719(3)	–0.0132(4)	0.5413(2)	0.068(1)	0.115(3)	0.094(2)	0.007(2)	0.012(1)	–0.036(2)
C(10)	2*a*	0.3366(2)	0.0951(2)	0.8438(1)	0.0377(8)	0.045(1)	0.045(1)	0.0037(8)	0.0005(7)	–0.0015(9)
C(11)	2*a*	0.3986(2)	–0.0075(2)	0.9253(1)	0.0427(8)	0.042(1)	0.044(1)	0.0055(8)	–0.0037(7)	–0.0011(8)
C(12)	2*a*	0.5734(2)	0.0406(3)	0.9595(2)	0.0429(9)	0.077(2)	0.056(1)	0.0071(9)	–0.0046(8)	–0.003(1)
C(13)	2*a*	0.2760(2)	0.0052(2)	0.9964(1)	0.0415(8)	0.0390(9)	0.040(1)	0.0032(7)	–0.0081(7)	0.0027(8)
C(14)	2*a*	0.2985(2)	0.1069(2)	1.0700(1)	0.0428(8)	0.039(1)	0.043(1)	–0.0067(7)	–0.0054(7)	0.0030(8)
C(15)	2*a*	0.1820(2)	0.1215(2)	1.1341(1)	0.0477(8)	0.036(1)	0.039(1)	–0.0038(7)	–0.0042(7)	0.0023(8)
C(16)	2*a*	0.2043(2)	0.2242(3)	1.2114(2)	0.061(1)	0.047(1)	0.046(1)	–0.0148(9)	–0.0025(9)	–0.0056(9)
C(17)	2*a*	0.0916(2)	0.2326(3)	1.2726(2)	0.076(1)	0.049(1)	0.041(1)	–0.009(1)	–0.000(1)	–0.0062(9)
C(18)	2*a*	–0.0511(2)	0.1391(2)	1.2599(1)	0.060(1)	0.045(1)	0.042(1)	–0.0013(9)	0.0053(9)	0.0032(9)
C(19)	2*a*	–0.0792(2)	0.0387(2)	1.1865(1)	0.0467(9)	0.043(1)	0.045(1)	–0.0053(8)	0.0003(8)	0.0032(9)
C(20)	2*a*	0.0372(2)	0.0271(2)	1.1220(1)	0.0421(8)	0.0356(9)	0.041(1)	–0.0002(7)	–0.0051(7)	0.0012(8)
C(21)	2*a*	0.0168(2)	–0.0789(2)	1.0459(1)	0.0439(8)	0.047(1)	0.049(1)	–0.0097(8)	–0.0052(8)	–0.0062(9)
C(22)	2*a*	0.1324(2)	–0.0891(2)	0.9854(1)	0.0467(9)	0.049(1)	0.043(1)	–0.0029(8)	–0.0041(8)	–0.0097(9)
C(23)	2*a*	–0.3006(3)	0.0665(3)	1.3192(2)	0.084(2)	0.075(2)	0.095(2)	–0.016(1)	0.045(2)	–0.013(2)
O(1)	2*a*	–0.2262(2)	0.2870(2)	0.6231(1)	0.0582(8)	0.092(1)	0.071(1)	0.0201(8)	–0.0066(7)	0.001(1)
O(2)	2*a*	0.4723(2)	–0.0532(2)	0.6998(2)	0.0708(9)	0.088(2)	0.097(2)	0.0265(9)	–0.0122(9)	0.009(1)
O(3)	2*a*	0.2169(2)	0.0152(2)	0.7918(1)	0.0589(7)	0.0547(8)	0.0490(9)	–0.0128(6)	–0.0153(6)	0.0139(7)
O(4)	2*a*	0.3768(2)	0.2295(2)	0.8275(1)	0.0649(8)	0.0440(8)	0.063(1)	–0.0041(7)	–0.0062(7)	0.0058(7)
O(5)	2*a*	–0.1548(2)	0.1595(2)	1.3269(1)	0.0823(9)	0.069(1)	0.052(1)	–0.0116(8)	0.0205(8)	–0.0077(8)

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