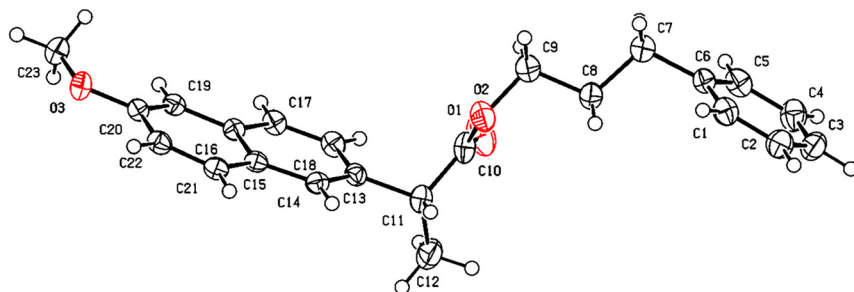


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Crystal structure of 3-phenylpropyl 2-(6-methoxynaphthalen-2-yl)propanoate, $C_{23}H_{24}O_3$



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Abstract

$C_{23}H_{24}O_3$, orthorhombic, $P2_12_12_1$ (no 19), $a = 5.7576(2)$ Å, $b = 7.7223(4)$ Å, $c = 41.6710(16)$ Å, $V = 1852.77(14)$ Å³, $Z = 4$, $R_{gt}(F) = 0.0442$, $wR_{ref}(F^2) = 0.1068$, $T = 170$ K.

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The crystal 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 materials

Naproxen (0.02 mol, 4.60 g) was dissolved in dichloromethane (20 mL), and oxalyl chloride (0.024 mol, 2.2 mL) and two drops of DMF were dropwise added at 0 °C. The solution was stirred for 3 h at room temperature. After the solvent and excess oxalyl chloride was removed by vacuum distillation, a yellow solid was obtained. Phenylpropanol (0.02 mol, 2.72 g) and DMAP (0.0015 mol, 0.18 g) were dissolved in dry dichloromethane (40 mL) and

Table 1: Data collection and handling.

Crystal:	Colorless block
Size:	0.13 × 0.07 × 0.05 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	0.08 mm ⁻¹
Diffraction, scan mode:	BRUKER D8 VENTURE, φ and ω -scans
θ_{max} , completeness:	26.4°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int} :	14,331, 3782, 0.055
Criterion for I_{obs} , $N(hkl)_{gt}$:	$I_{obs} > 2\sigma(I_{obs})$, 2873
$N(param)_{refined}$:	237
Programs:	Bruker programs [1], OLEX2 [2], SHELX [2]

triethylamine (0.03 mol, 4 mL). The naproxen acylchloride in dry dichloromethane was dropwise added at 0 °C. The mixture was stirred for 1 h at room temperature. The reaction mixture was filtrated and the filtrate was concentrated under vacuum to remove the solvent. The residue was dissolved in dichloromethane, successively washed with 5% NaOH solution and water to pH = 7, and finally dried with anhydrous Na₂SO₄. The solution was filtrated, and concentrated under vacuum to obtain the crude product. The crude product was purified by recrystallization in ethanol. The crystals were obtained from tetrahydrofuran.

Experimental details

The hydrogen atoms were positioned geometrically ($C-H = 0.95-0.99$ Å). The U_{iso} values of the hydrogen atoms of methyl groups were set to 1.5 $U_{eq}(C)$ and the U_{iso} values of all other hydrogen atoms were set to 1.2 $U_{eq}(C)$.

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

	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} */ <i>U</i> _{eq}
O1	0.8267 (4)	0.1851 (3)	0.64640 (6)	0.0525 (7)
O2	0.6521 (4)	0.4189 (3)	0.62498 (5)	0.0395 (5)
O3	0.5870 (3)	−0.0573 (3)	0.43290 (4)	0.0320 (5)
C1	0.6373 (5)	0.8505 (4)	0.72672 (7)	0.0354 (7)
H1	0.549873	0.895201	0.709247	0.042*
C2	0.5594 (6)	0.8757 (4)	0.75768 (7)	0.0390 (8)
H2	0.419027	0.937194	0.761390	0.047*
C3	0.6851 (6)	0.8118 (4)	0.78328 (7)	0.0400 (8)
H3	0.630820	0.828616	0.804586	0.048*
C4	0.8891 (6)	0.7238 (4)	0.77790 (7)	0.0407 (8)
H4	0.976486	0.680570	0.795499	0.049*
C5	0.9678 (6)	0.6981 (4)	0.74661 (7)	0.0362 (7)
H5	1.108853	0.637307	0.742999	0.043*
C6	0.8418 (5)	0.7606 (4)	0.72073 (7)	0.0311 (7)
C7	0.9173 (6)	0.7235 (4)	0.68659 (7)	0.0376 (8)
H7A	1.081980	0.686533	0.686409	0.045*
H7B	0.903641	0.830073	0.673521	0.045*
C8	0.7654 (6)	0.5807 (4)	0.67213 (6)	0.0359 (7)
H8A	0.776871	0.476281	0.685815	0.043*
H8B	0.601493	0.619542	0.672428	0.043*
C9	0.8299 (6)	0.5325 (4)	0.63827 (7)	0.0426 (8)
H9A	0.843145	0.638331	0.624988	0.051*
H9B	0.982028	0.472783	0.638137	0.051*
C10	0.6681 (6)	0.2490 (4)	0.63178 (7)	0.0355 (8)
C11	0.4624 (5)	0.1507 (4)	0.61812 (6)	0.0315 (7)
H11	0.327333	0.231743	0.616827	0.038*
C12	0.3952 (6)	−0.0004 (4)	0.63965 (7)	0.0450 (9)
H12A	0.257425	−0.057967	0.630865	0.067*
H12B	0.360845	0.042539	0.661259	0.067*
H12C	0.524010	−0.083208	0.640677	0.067*
C13	0.5213 (5)	0.0904 (4)	0.58420 (6)	0.0248 (6)
C14	0.3731 (5)	0.1241 (4)	0.55921 (6)	0.0251 (6)
H14	0.234282	0.187066	0.563185	0.030*
C15	0.4221 (5)	0.0673 (4)	0.52763 (6)	0.0231 (6)
C16	0.6320 (5)	−0.0241 (3)	0.52141 (6)	0.0230 (6)
C17	0.7800 (5)	−0.0595 (4)	0.54780 (6)	0.0273 (6)
H17	0.919045	−0.123103	0.544395	0.033*
C18	0.7265 (5)	−0.0038 (4)	0.57807 (6)	0.0289 (7)
H18	0.829369	−0.028956	0.595275	0.035*
C19	0.6897 (5)	−0.0718 (4)	0.48950 (6)	0.0244 (6)
H19	0.827519	−0.135674	0.485361	0.029*
C20	0.5468 (5)	−0.0258 (4)	0.46469 (6)	0.0253 (6)
C21	0.2737 (5)	0.1053 (4)	0.50138 (6)	0.0263 (6)
H21	0.129344	0.161362	0.505146	0.032*
C22	0.3357 (5)	0.0624 (4)	0.47085 (6)	0.0271 (6)
H22	0.236268	0.092024	0.453499	0.033*
C23	0.7995 (5)	−0.1417 (4)	0.42487 (7)	0.0362 (7)
H23A	0.811449	−0.152717	0.401501	0.054*
H23B	0.802635	−0.257014	0.434664	0.054*
H23C	0.930414	−0.073214	0.432927	0.054*

Discussion

Phenylpropanol is a phenyl-alcohol choleretic (proprietary name, livonal) with a superactive cholcretic effect. It exerts its powerful effect as a high performance choleretic secretion promoter and a mild spasmolytic. In clinical practice, the indications for livonal include the treatment of cholecystitis, cholelithiasis, biliary tract infection, and biliary tract postoperative syndrome [4]. The clinical formulation of phenylpropanol is soft capsule. But the orally taking of this preparation has a great thrill with discomfort of stomach, easily brought some adverse reaction such as nausea, disgorge and so on. Naproxen is a kind of nonsteroidal anti-inflammatory drugs, has obvious inhibition of prostaglandin synthesis, clinically as a treatment for diseases such as rheumatism, rheumatoid arthritis, osteoarthritis [5, 6]. Now studies have also shown that naproxen also has antiviral [7] and anti-cancer [8] effects. However, such drugs also have many disadvantages, such as poor water solubility, low bioavailability and great irritation to gastrointestinal mucosa. In this paper, phenylpropanol and naproxen were esterified by prodrug principle, in an attempt to find drugs with better clinical effect and fewer side effects.

The title compound contained one phenyl and one naphthyl moiety. The C–O bond distances are 1.367(3) Å (O3–C20), 1.426(3) Å (O3–C23), 1.345(4) Å (O2–C10), 1.458(4) Å (O2–C9), 1.204(4) Å (O1–C10), respectively. In the molecule of the title compound bond lengths and angles are very similar to those given in the literature [9–11].

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References

1. BRUKER. *APEX2, SAINT-Plus, XPREP*; Bruker AXS Inc.: Madison, Wisconsin, USA, 2008.
2. Dolomanov O. V., Bourhis L. J., Gildea R. J., Howard J. A. K., Puschmann H. Olex2: a complete structure solution, refinement and analysis program. *J. Appl. Crystallogr.* 2009, 42, 339–341.
3. Sheldrick G. M. Crystal structure refinement with *Shelxl*. *Acta Crystallogr.* 2015, C71, 3–8.

4. Shi J. S., Ren B., Ma Q. J. Experimental study of artmisiae capillaris and radix curcumae in preventing gallstone formation in guinea pigs. *World Chin. J. Dig.* 1998, 7, 564–566.
5. Brooks P. M., Cleland L. G., Haski A. L. Evaluation of a single daily dose naproxen in osteoarthritis. *Rheumatology* 1982, 21, 242–246.
6. Liyanage S. P., Macauley D. I., English J. R. Naproxen and sulindac in the treatment of osteoarthritis of the hip and knee. *Rheumatology* 1981, 20, 184–187.
7. Dilly S., Fotso A. F., Lejal N. From naproxen repurposing to naproxen analogues and their antiviral activity against influenza a virus. *J. Med. Chem.* 2018, 61, 7202–7217.
8. Cao Y., Khan A., Slotani A. Spectroscopic, density functional theory, cytotoxicity and antioxidant activities of sulfasalazine and naproxen drugs combination. *Arab. J. Chem.* 2021, 14, 103190.
9. Kriegner H., Weil M., Jones M. J. The methanol sesquisolvate of sodium naproxen. *Acta Crystallogr.* 2018, E74, 1624–1627.
10. Yang Z., Wei S., Wang W. (S)-2-(1*H*-imidazol-1-yl)-3-phenylpropanol. *Acta Crystallogr.* 2008, E64, o631.
11. Tang G.-M., Wang J.-H., Zhao C., Wang Y.-T., Cui Y.-Z., Cheng F.-Y., Weng S. Ng: Multi odd–even effects on cell parameters, melting points, and optical properties of chiral crystal solids based on S-naproxen. *CrystEngComm* 2015, 17, 7258.