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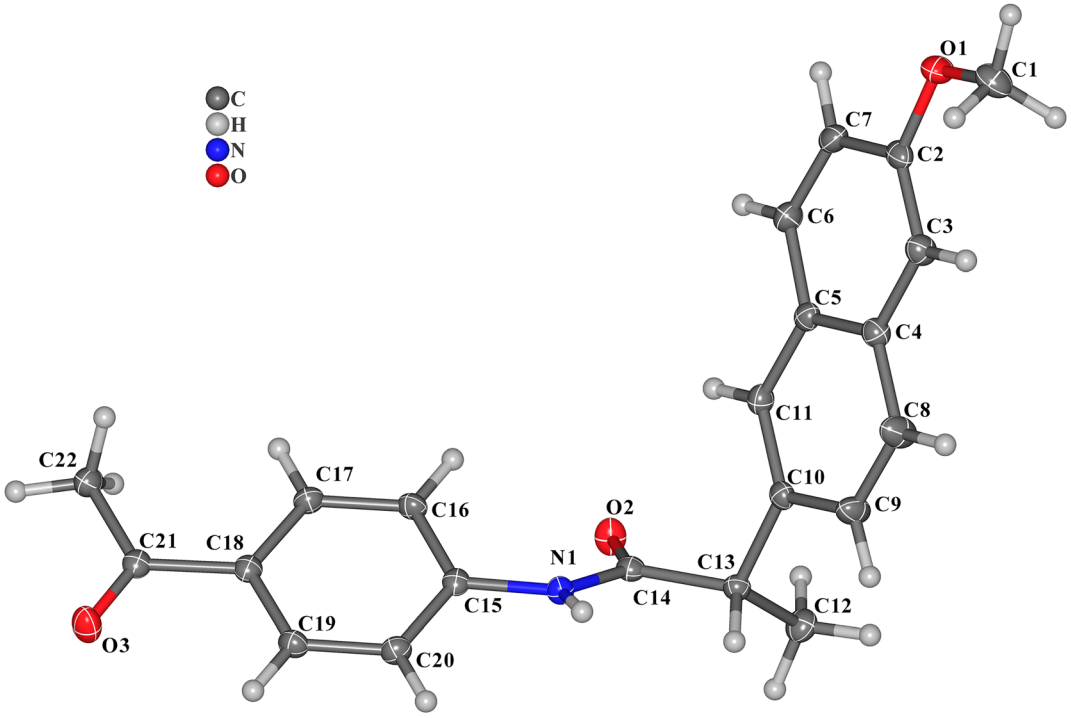
Crystal structure of N-(4-acetylphenyl)-2-(6-methoxynaphthalen-2-yl)propanamide, $C_{22}H_{21}NO_3$



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Abstract

$C_{22}H_{21}NO_3$, orthorhombic, $P2_12_12_1$ (no. 19), a = 5.1909(2) Å, b = 15.8945(8) Å, c = 20.9637(11) Å, V = 1729.65(14) Å^3, Z = 4, $R_{gt}(F)$ = 0.0266, $wR_{ref}(F^2)$ = 0.0683, T = 100(2) K.

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The molecular structure is shown in the figure. Table 1 contains the crystallographic data and the list of the atoms including atomic coordinates and displacement parameters can be found in the cif-file attached to this article.

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Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.12 × 0.11 × 0.10 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.09 mm^{-1}
Diffractometer, scan mode:	Bruker APEX-II, φ and ω scans
θ_{max}, completeness:	27.5°, 100 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	75157, 3968, 0.029
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 3,877
$N(param)_{refined}$:	238
Programs:	Bruker,[1] Olex2,[2] SHELX[3]

1 Source of materials

Naproxen acylchloride was synthesized according to the literature method.[4] 4–Aminoacetophenone (0.01 mol, 1.35 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 added at 0 °C. The

reaction mixture was stirred for 2 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 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 crude product. The crude product was purified by recrystallization in ethanol. The single crystals were obtained from tetrahydrofuran solution.

2 Experimental details

Coordinates of hydrogen atoms were refined with constraints or restraints. The U_{iso} values were set to be $1.5U_{eq}$ of the carrier atom for methyl H atoms and $1.2U_{eq}$ for the remaining H atoms.

3 Comment

Naproxen is one of the most widely prescribed drugs for the treatment and management of inflammatory diseases. Long term use of naproxen can cause serious adverse reactions, such as erosion, narrowing, bleeding, and perforation in the gastrointestinal tract. The pharmacological effects of naproxen are related to the inhibition of COX-1 and COX-2 enzymes. However, due to poor selectivity, naproxen is associated with severe gastrointestinal toxicity. COX-1 inhibition leads to depletion of the gastrointestinal mucosa, which is related to gastrointestinal toxicity. In addition, naproxen contains a free carboxyl group, which, when ionized, leads to an increase in acidity, a decrease in gastric pH, and complicates the problem.[5,6] Research has shown that using naproxen as a prodrug can reduce the gastrointestinal side effects of naproxen and improve its bioavailability.[7] In this study, we prepared a new prodrug of naproxen that masked the free carboxylic acid groups of naproxen, thereby reducing related side effects.

The title compound contained one benzene ring and one naphthalene ring. The C=O double bond lengths in the molecule are 1.2297(17) Å (C14=O2) and 1.2197(18) Å (C21=O3), respectively, exhibiting the double bond character (see the Figure). The C–N bond lengths are 1.3628(18) Å (C14–N1) and 1.4117(17) Å (C15–N1), respectively. The dihedral angles of ring 1 (C2–C3–C4–C5–C6–C7) and ring 2 (C5–C4–C8–C9–C10–C11), ring 1 (C2–C3–C4–C5–C6–C7) and ring 3 (C15–C16–C17–C18–C19–C20), ring 2 (C5–C4–C8–C9–C10–C11) and ring 3 (C15–C16–C17–C18–C19–C20) are 1.920°, 56.277°, 55.668°, respectively. The other bond distances and angles are in their normal ranges according to the previously reported compounds.[8–10]

Author contribution: All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Conflict of interest: The authors declare no conflicts of interest regarding this article.

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