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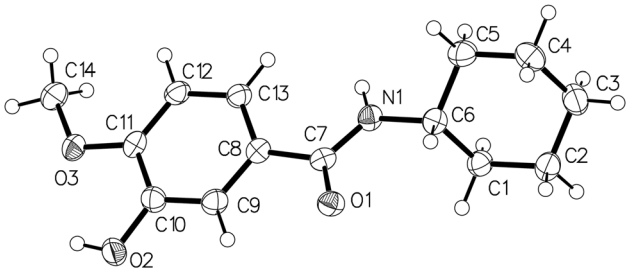
The crystal structure of *N*-cyclohexyl-3-hydroxy-4-methoxybenzamide, $C_{14}H_{19}NO_3$



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Abstract

$C_{14}H_{19}NO_3$, monoclinic, *Cc* (no. 9), a = 11.1235(5) Å, b = 15.3724(5) Å, c = 8.1110(3) Å, β = 109.3980(10)°, V = 1308.21(9) Å^3, Z = 4, $R_{gt}(F)$ = 0.0300, $wR_{ref}(F^2)$ = 0.0703, T = 170 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.

Table 1: Data collection and handling.

Crystal:	Colorless block
Size:	0.19 × 0.12 × 0.08 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.09 mm^{-1}
Diffractometer, scan mode:	D8 VENTURE, φ and ω
θ_{max}, completeness:	26.4°, 98%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	5397, 2183, 0.030
Criterion for I_{obs}, $N(hkl)_{gt}$:	I_{obs} > 2 σ(I_{obs}), 2059
$N(param)_{refined}$:	166
Programs:	Bruker [1], Olex2 [2], SHELX [3,4]

Source of material

The 3-hydroxy-4-methoxybenzoic acid (10 mmol), cyclohexylamine (10.4 mmol), and *N*,*N*-diisopropylethylamine (20 mmol) were dissolved in DMF (20 mL) initially, and 2-(7-azabenzotriazol-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate (HATU, 10.4 mmol) was added to the solution with stirring. After the mixture was stirred for 5 h, the reaction was completed (monitored by TLC). A saturated NaCl solution (100 mL) was added, and the product was extracted with ethyl acetate (50 mL) three times. The combined organics were washed with 5% citric acid, 5% $NaHCO_3$, and H_2O. Subsequently, the mixture was dried over $MgSO_4$, filtered, and concentrated under vacuum to give the title product. Suitable crystals of the title compound were obtained by recrystallization in ethyl acetate and dried at ambient temperature for one week.

Experimental details

Hydrogen atoms were added in their geometrically idealized positions and treated as riding models on their parent atoms with U_{iso}(H) = 1.2 U_{eq}(C).

Comment

Amides are common functional groups in many biologically active molecules, natural products, and polymer materials and have attracted significant interest from medicinal chemists and chemical biologists [5–7]. The arylamides have been developed for various applications due to the ease of functionalization *via* substitution of the aromatic rings and the termini of the scaffold [8]. Arylamide derivatives have been widely used to inhibit treatment-related protein–protein interactions, such as Bcl-x$_L$/Bak [9], p53/HDM2 [10], and c-Myc-Max [11]. They also effectively inhibit the aggregation of human proteins such as islet amyloid polypeptide [12] and amyloid-β [13]. Here, we report the crystal structure of a new methoxybenzamide derivative. Similar systems have been widely studied so far [14–22].

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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	0.8289 (2)	0.54322 (15)	0.8073 (3)	0.0300 (5)
H1A	0.829744	0.563750	0.691953	0.036*
H1B	0.836374	0.479027	0.809599	0.036*
C2	0.9426 (2)	0.58201 (15)	0.9510 (3)	0.0342 (5)
H2A	0.947738	0.556171	1.064961	0.041*
H2B	1.022184	0.567471	0.927759	0.041*
C3	0.9306 (2)	0.67980 (16)	0.9600 (3)	0.0406 (6)
H3A	0.936580	0.706160	0.851639	0.049*
H3B	1.001976	0.702560	1.059705	0.049*
C4	0.8050 (3)	0.70588 (16)	0.9818 (3)	0.0446 (7)
H4A	0.797911	0.770094	0.979177	0.054*
H4B	0.803547	0.685583	1.096951	0.054*
C5	0.6912 (2)	0.66731 (16)	0.8376 (3)	0.0363 (5)
H5A	0.611450	0.682380	0.860001	0.044*
H5B	0.686784	0.692608	0.723536	0.044*
C6	0.7030 (2)	0.56904 (14)	0.8306 (2)	0.0264 (5)
H6	0.702083	0.544733	0.944565	0.032*
C7	0.5438 (2)	0.45542 (14)	0.7058 (2)	0.0244 (4)
C8	0.4313 (2)	0.42465 (14)	0.5572 (2)	0.0250 (5)
C9	0.3970 (2)	0.33760 (15)	0.5611 (3)	0.0297 (5)
H9	0.445840	0.301741	0.654755	0.036*
C10	0.2946 (2)	0.30240 (14)	0.4333 (3)	0.0292 (5)
C11	0.2232 (2)	0.35452 (15)	0.2931 (2)	0.0268 (5)
C12	0.2550 (2)	0.44134 (14)	0.2892 (2)	0.0289 (5)
H12	0.205877	0.477203	0.195750	0.035*
C13	0.3583 (2)	0.47678 (14)	0.4209 (2)	0.0273 (5)
H13	0.378812	0.536592	0.417306	0.033*
C14	0.0574 (2)	0.35981 (16)	0.0171 (3)	0.0389 (6)
H14A	−0.002209	0.320728	−0.066351	0.058*
H14B	0.117680	0.383832	−0.035700	0.058*
H14C	0.009878	0.407350	0.047473	0.058*
N1	0.59438 (17)	0.53236 (12)	0.6914 (2)	0.0275 (4)
H1	0.561283	0.562353	0.594380	0.033*
O1	0.58582 (15)	0.40977 (10)	0.83943 (17)	0.0294 (4)
O2	0.26862 (16)	0.21647 (11)	0.4463 (2)	0.0422 (5)
H2	0.200688	0.203312	0.366500	0.063*
O3	0.12553 (14)	0.31251 (10)	0.17128 (18)	0.0322 (4)

The figure shows the molecular configuration of the title compound. In the amide functional group, the bond lengths of C7–O1, C7–N1, and N1–C6 are 1.245(3) Å, 1.331(3) Å, and 1.465(3) Å, and the angles of O1–C7–N1 and C7–N1–C6 are 121.99(16)° and 122.59(16)°, respectively. The molecule's structure is similar to the stereo-configurations of the compounds reported in references [18–22]. Methoxy and hydroxyl groups replace hydrogen atoms on the benzene ring, and the lengths of the C–O bonds are both 1.364(3) Å. The dihedral angle between the ring C8···C13 and the mean plane of the cyclohexane group (C1···C6) is 51.76°. The bond lengths and angles are all in the expected ranges.

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