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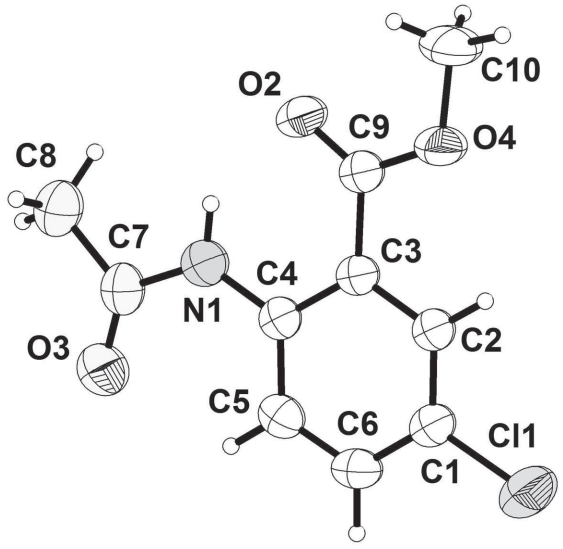
Crystal structure of methyl 2-acetamido-5-chlorbenzoate, $C_{10}H_{10}ClNO_3$



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Abstract

$C_{10}H_{10}ClNO_3$, orthorhombic, *Ibam* (no. 72), $a = 16.124(5)$ Å, $b = 19.588(5)$ Å, $c = 6.8155(18)$ Å, $V = 2152.6(10)$ Å^3, $Z = 8$, $R_{gt}(F) = 0.0424$, $wR_{ref}(F^2) = 0.1186$, $T = 296(2)$ K.

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The title crystal structure is shown in the figure. Tables 1 and 2 contain details on crystal structure and measurement conditions and a list of the atoms including atomic coordinates and displacement parameters.

Source of material

All chemicals, reagents and solvents are of analytical grade and are commercially available. Preparation of methyl 2-amino-5-chlorobenzoate: A mixture of methyl 5-chloro-2-nitrobenzoate (5.34 g, 0.029 mol) and concentrated hydrochloric acid (22.5 mL) was added to ethyl acetate (15 mL).

Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.22 × 0.20 × 0.18 mm
Wavelength:	Mo $K\alpha$ radiation (0.71073 Å)
μ:	3.4 cm^{-1}
Diffractometer, scan mode:	Bruker APEXII, φ and ω
$2\theta_{max}$, completeness:	50.2°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	6767, 1062, 0.046
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\,\sigma(I_{obs})$, 807
$N(param)_{refined}$:	93
Programs:	Bruker [1], SHELX [2]

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

Atom	x	y	z	U_{iso}*/U_{eq}
C1	1.08454(17)	0.12754(15)	0.0000	0.0490(7)
C2	0.99954(17)	0.12583(13)	0.0000	0.0452(7)
H2	0.9720	0.0841	0.0000	0.054*
C3	0.95419(15)	0.18665(13)	0.0000	0.0420(6)
C4	0.99611(18)	0.24971(13)	0.0000	0.0424(6)
C5	1.08301(18)	0.24924(15)	0.0000	0.0508(7)
H5	1.1118	0.2904	0.0000	0.061*
C6	1.12626(17)	0.18874(16)	0.0000	0.0523(8)
H6	1.1839	0.1892	0.0000	0.063*
C7	0.9769(2)	0.37648(14)	0.0000	0.0545(8)
C8	0.9078(2)	0.42768(17)	0.0000	0.0726(10)
H8A[a]	0.9251	0.4679	0.0694	0.109*
H8B[a]	0.8601	0.4084	0.0633	0.109*
H8C[a]	0.8941	0.4395	−0.1328	0.109*
C9	0.86205(16)	0.18266(15)	0.0000	0.0472(7)
C10	0.74602(18)	0.1100(2)	0.0000	0.1026(17)
H10A[a]	0.7244	0.1212	0.1272	0.154*
H10B[a]	0.7329	0.0634	−0.0305	0.154*
H10C[a]	0.7217	0.1395	−0.0967	0.154*
Cl1	1.13951(5)	0.05102(5)	0.0000	0.0782(4)
N1	0.95027(14)	0.31016(12)	0.0000	0.0526(7)
H1	0.8973	0.3049	0.0000	0.063*
O2	0.81563(12)	0.23088(11)	0.0000	0.0640(7)
O3	1.04934(14)	0.39303(11)	0.0000	0.0766(8)
O4	0.83563(12)	0.11894(11)	0.0000	0.0736(8)

[a]Occupancy: 0.50.

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To the reaction mixture was added a solution of tin chloride (16.8 g, 0.089 mol) in ethyl acetate (25 mL). The reaction mass was stirred for 16 h at room temperature and then poured to the ice water. The pH of the reaction mass was adjusted to 8.0 to 9.0 with aqueous sodium hydroxide solution. The separated aqueous layer was extracted with ethyl acetate and the solid (4.29 g, 96%) which was used in the next reaction without purification was got by removing ethyl acetate with a rotary evaporator. Preparation of methyl 2-acetamido-5-chlorobenzoate: To a solution of methyl 2-amino-5-chlorobenzoate (4.3 g, 0.027 mol) and K_2CO_3 (19.2 g, 0.139 mol) in acetone (90 mL), acetyl chloride (10.9 g, 0.139 mol) was added dropwise and the reaction mixture was stirred at 0 °C for 0.25 h then left to warm to ambient temperature (approx. 30 °C). The progress of the reaction was monitored by TLC. On completion, the reaction mixture was filtered and the filtrate was evaporated with vacuum distillation to afford the crude product (4.1 g; 66.9%), which was dispersed in a mixture of petroleum ether and Et_2O to afford the pure product. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 10.97 (s, 1H), 8.70 (d, J = 9.1 Hz, 1H), 8.00 (d, J = 2.6 Hz, 1H), 7.49 (dd, J = 10.8, 4.3 Hz, 1H), 3.94 (s, 3H), 2.24 (s, 3H). Crystals were obtained in hexane/chloroform at room temperature.

Experimental details

All hydrogen atoms were placed in geometrically calculated positions. The U_{iso} values of the hydrogen atoms of methyl groups were set to $1.5U_{eq}(C_{methyl})$ and the U_{iso} values of all other hydrogen atoms were set to $1.2U_{eq}(C)$. Both methyl groups show a disorder of its hydrogen atoms.

Discussion

Methyl 2-amino-5-hydroxybenzoate has a very broad application prospects as an important intermediate in pharmaceutical synthesis, such as benzyloxyphenyl methylaminophenol derivatives as STAT3 signaling pathway inhibitors, kainate receptors of new oxazole[4,5-*c*]quinolin-4-one derivatives, potassium channel modulators and plasminogen activator inhibitor-1 inhibitor [3–6].

The structure of the title compound was elucidated by spectroscopic methods and X-ray diffraction. All non-hydrogen atoms are located on a mirror plane of the orthorhombic space group. All geometric parameters are in the expected ranges (*cf*. the figure, Table 2). The molecules packing in the crystal structure is stabilized by intermolecular hydrogen bonds (N1—H1$\cdots$O2).

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