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Crystal structure of 7-chloro-*N*-(4-iodobenzyl)-1,2,3,4-tetrahydroacridin-9-amine, C₂₀H₁₈ClIN₂

Table 1: Data collection and handling.

Crystal:	Colorless block
Size:	0.12 × 0.12 × 0.10 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	1.86 mm ⁻¹
Diffractometer, scan mode:	Bruker APEX-II, ω
$\theta_{\max}$, completeness:	25.5°, >99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	12,027, 3478, 0.024
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2\sigma(I_{\text{obs}})$, 3124
$N(\text{param})_{\text{refined}}$:	218
Programs:	Bruker [1], SHELX [2, 3], Diamond [4]

Source of material

Zinc chloride (3.47 g, 25.4 mmol) was added to a mixture of 5-chloro-2-aminobenzonitrile (3.88 g, 25.4 mmol) and cyclohexanone (30.5 mL, 294.6 mmol). The reaction was kept at 120 °C for 16 h, then cooled to room temperature and the solvent was filtered. To the residue, 50 mL ether was added and the resulting solid was collected after filtration. To the solid, 50 mL of a 30% solution of NaOH in water was poured and kept under stirring overnight. The reaction mixture were extracted with DCM (3 × 50 mL), the organic layers were combined and dried over anhydrous Na₂SO₄. The solvent was evaporated under reduced pressure to produce the desired product as a yellowish solid with 89% yield. A part of the aforementioned product 7-chloro-1,2,3,4-tetrahydroacridin-9-amine (0.47 g, 2 mmol) was dissolved in dichloromethane (16 mL), 50% NaOH (10 mL), and tetrabutyl hydrogen sulfate tetrabutylammonium hydrogen sulfate (TBAHS, 1.6 mmol), and finally stirred at room temperature for 30 min. To this mixture was added 1-(bromo-methyl)-4-iodobenzene (0.45 g, 2.2 mmol) and stirred at room temperature for 4 h. Liquid separation: the organic phase was washed with water, dried with anhydrous sodium sulfate, and silica gel column chromatography was used to obtain the target compound, yield 50%. 7-27-chloro-*N*-(4-iodobenzyl)-1,2,3,4-tetrahydroacridin-9-amine. Light yellow powder, yield 50%. m.p. 118–121 °C; **Anal. Calcd.** for C₂₀H₁₈ClI, 53.53; H, 4.04; N, 6.24. Found: C, 53.40; H, 4.23; N, 6.47. **MS** (EI) m/z : 356.08 (M)⁺.

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Abstract

C₂₀H₁₈ClIN₂, monoclinic, $P2_1/n$ (no. 14), $a = 9.5271(19)$ Å, $b = 16.936(3)$ Å, $c = 12.012(2)$ Å, $\beta = 105.06(3)^\circ$, $V = 1871.5(7)$ Å³, $Z = 4$, $R_{\text{gt}}(F) = 0.0436$, $wR_{\text{ref}}(F^2) = 0.1396$, $T = 296(2)$ K.

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The molecular structure is shown in Figure. Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

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

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} */ <i>U</i> _{eq}
C1	0.2010 (4)	0.7274 (2)	0.5189 (3)	0.0342 (7)
C2	0.2434 (4)	0.6690 (2)	0.4492 (3)	0.0422 (8)
H2	0.1853	0.6595	0.3753	0.051*
C3	0.3676 (4)	0.6268 (2)	0.4890 (3)	0.0449 (9)
H3	0.3931	0.5877	0.4435	0.054*
C4	0.4564 (4)	0.6426 (2)	0.5983 (4)	0.0459 (9)
C5	0.4217 (4)	0.6981 (2)	0.6692 (3)	0.0403 (8)
H5	0.4838	0.7074	0.7417	0.048*
C6	0.2902 (4)	0.7416 (2)	0.6317 (3)	0.0322 (7)
C7	0.2413 (4)	0.7988 (2)	0.7017 (3)	0.0333 (7)
C8	0.1082 (4)	0.8361 (2)	0.6546 (3)	0.0371 (8)
C9	0.0353 (4)	0.8217 (2)	0.5376 (3)	0.0408 (8)
C10	−0.1040 (5)	0.8644 (3)	0.4796 (4)	0.0589 (12)
H10A	−0.1821	0.8261	0.4588	0.071*
H10B	−0.0930	0.8882	0.4089	0.071*
C11	−0.1475 (5)	0.9283 (3)	0.5529 (4)	0.0671 (14)
H11A	−0.0885	0.9751	0.5534	0.081*
H11B	−0.2486	0.9426	0.5209	0.081*
C12	−0.1260 (5)	0.8980 (3)	0.6743 (4)	0.0622 (12)
H12A	−0.1772	0.8484	0.6732	0.075*
H12B	−0.1650	0.9356	0.7194	0.075*
C13	0.0357 (4)	0.8860 (3)	0.7288 (3)	0.0480 (9)
H13A	0.0831	0.9371	0.7416	0.058*
H13B	0.0486	0.8606	0.8032	0.058*
C14	0.3485 (4)	0.8862 (2)	0.8738 (3)	0.0383 (8)
H14A	0.4209	0.8786	0.9464	0.046*
H14B	0.2587	0.9019	0.8913	0.046*
C15	0.3980 (4)	0.9527 (2)	0.8089 (3)	0.0354 (7)
C16	0.4659 (4)	0.9399 (2)	0.7218 (3)	0.0398 (8)
H16	0.4798	0.8884	0.6998	0.048*
C17	0.5135 (4)	1.0022 (3)	0.6669 (3)	0.0459 (9)
H17	0.5588	0.9925	0.6084	0.055*
C18	0.4937 (4)	1.0781 (2)	0.6989 (4)	0.0481 (9)
C19	0.4282 (5)	1.0927 (3)	0.7861 (4)	0.0580 (11)
H19	0.4157	1.1443	0.8082	0.070*
C20	0.3808 (5)	1.0301 (3)	0.8408 (4)	0.0516 (10)
H20	0.3367	1.0401	0.8999	0.062*
N1	0.0774 (3)	0.7690 (2)	0.4724 (2)	0.0403 (7)
N2	0.3247 (3)	0.81085 (18)	0.8124 (2)	0.0381 (7)
H2A	0.3669	0.7701	0.8491	0.046*
Cl1	0.61939 (16)	0.59038 (9)	0.64411 (13)	0.0837 (5)
I1	0.55785 (4)	1.17295 (2)	0.61211 (4)	0.0826 (2)

Experimental details

All H atoms were included in calculated positions and refined as riding atoms, with C–H = 0.93 Å with *U*_{iso}(H) = 1.5 *U*_{eq}(C) for methyl H atoms and 1.2 *U*_{eq}(C) for all other H atoms.

Comment

Alzheimer's disease (Alzheimer's disease, AD) is a central neurodegenerative disease that is common in the elderly and caused by a variety of factors [5]. The clinical symptoms of AD are mainly manifested as long-term memory loss, confusion, language disorders, low mood, irritability and aggressiveness, which seriously threaten the health and social development of humans around the world [6]. In recent years, with the increasingly serious global aging, the prevalence of AD has been increasing year by year. According to a report by the World Alzheimer Organization in 2015, it is estimated that there will be more than 130 million AD patients worldwide in 2050 [7]. Due to its complex etiology and multifactorial development, the disease cannot be cured. The current clinical treatment is mainly to relieve symptoms, but the effect of reducing or preventing disease progression is not significant [8–10]. Therefore, looking for more effective AD treatment drugs has great practical and social significance. Tacrine is the first reversible and non-selective inhibitor of acetylcholinesterase, which approved by the FDA in 1993 for the treatment of AD [11]. Clinical trials have proved that the drug can improve senile dementia, but its bioavailability and therapeutic index are low, and it has greater liver toxicity [12], which greatly limits its application and has been withdrawn from clinical use. However, tacrine still has some beneficial effects in the treatment of AD. Researcher try to develop derivatives of tacrine to reduce the toxicity of other treatment methods in AD [13].

There is one independent molecule in the asymmetric unit (shown in Figure). In the molecule of the title compound bond lengths are very similar to those given in the literature for 9-benzylamino-1-hydroxy-1,2,3,4-tetrahydroacridine hydrogen maleate [14]. In the title structure, the part of quinoline is approximately planar. The dihedral angles formed by the quinoline plane and the C15–C20 plane was 80°. The molecular conformation is characterized by the C7–N2–C14–C15, C7–C8–C13–C12, C8–C13–C12–C11, C13–C12–C11–C10, and C12–C11–C10–C9 torsion angles of −51.5(5)°, −160.6(4)°, −52.0(5)°, 66.8(5)°, and −43.2(5)°.

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