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NOTE

Crystal and Molecular Structure of (*S*)-*N*-(2-Hydroxyphenyl)pyrrolidine-2-carboxamide

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Abstract (*S*)-*N*-(2-Hydroxyphenyl)pyrrolidine-2-carboxamide was synthesized from Cbz-L-proline through two steps and characterized by NMR and MS. The crystal structure was determined from single-crystal X-ray diffraction data. It crystallizes in the monoclinic space group, $P2_1$, with unit cell dimensions $a = 7.284(6)$ Å, $b = 10.262(9)$ Å, and $c = 7.975(7)$ Å, $\alpha = 90.00°$, $\beta = 114.451(14)°$, $\gamma = 90.00°$ and $Z = 2$. The absolute configuration of the chiral center is determined as *S*. In the crystal structure, intermolecular and intramolecular hydrogen bonds are responsible for the formation of a 1-dimensional network.

Keywords L-Proline · (*S*)-*N*-(2-Hydroxyphenyl) pyrrolidine-2-carboxamide · X-ray structure

Introduction

Proline, as well as its derivatives, has been widely used in asymmetric aldol condensation and related reactions as a bifunctional catalyst since it was first used by List [1–3]. Several theoretical studies have highlighted the importance of the carboxylic acid functionality of proline in this reaction: it orients the incoming aldehyde through a hydrogen bond, which ensures that the reaction proceeds on only one face of the pyrrolidine ring; it lowers the activation barrier of the reaction by charge stabilization along the C–C bond formation by means of the intramolecular hydrogen bond [1–5]. Based on this mechanism, many proline derivatives have been designed, synthesized and used in the asymmetric aldol condensations [6–8]. The tile compound, (*S*)-*N*-(2-hydroxyphenyl)pyrrolidine-2-carboxamide, has been synthesized and used in the catalysis synthesis of asymmetric Aldol condensation and Michael addition [9, 10]. In this article, we synthesized (*S*)-*N*-(2-hydroxyphenyl)pyrrolidine-2-carboxamide (shown as Scheme 1) and determined the crystal structure by single-crystal X-ray diffraction.

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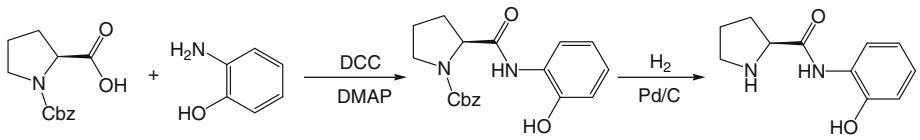
Experimental

All starting materials and solvents (A.R. grade) were commercially available and were used without further purification. NMR spectra were recorded in the stated solutions, on a Bruker Drx-400 spectrometer, operating at 500 MHz for ^{1}H and 125 MHz for ^{13}C; δ values are reported in ppm and *J* values in hertz. Mass spectra were recorded on a Micromass Platform II spectrometer, using the direct-inlet system operating in the electron impact (ESI) mode at 75 eV.

Synthesis of (*S*)-*N*-(2-Hydroxyphenyl)pyrrolidine-2-carboxamide

0.249 g Cbz-L-proline (1 mmol), 0.019 g *o*-aminophenol, and 0.206 g DCC and 0.012 g DMAP was dissolved in 15 mL anhydrous THF. The mixture was stirred under room temperature. Completion of the reaction was

Scheme 1 Synthesis of (*S*)-*N*-(2-hydroxyphenyl)pyrrolidine-2-carboxamide



monitored by TLC check, the solvent was distilled off under reduced pressure and the residue was separated by column chromatography (silica gel, petroleum ether/ethyl acetate = 10:1–4:1) to give the target products. Colorless crystals of the title compound were obtained in ethanol by recrystallization. Overall yield 67%; m.p. 170–172 °C (170 °C [10]); $[\alpha]_D^{20} = -47.0$ ($c = 1.0$, CH_3OH) ($[\alpha]_D^{20} = -45.6$ ($c = 1.0$, CH_2Cl_2H) [10]); ^{1}H-NMR (D_6-Acetone, 500 MHz), δ: 7.16 (1H, d, $J = 1.0$ Hz), 7.05 (1H, dd, $J = 8.0$, 1.5 Hz), 6.94 (1H, dd, $J = 8.0$, 1.0 Hz), 6.85 (1H, d, $J = 1.5$ Hz), 3.98 (1H, dd, $J = 9.5$, 4.5 Hz), 2.95 (1H, m), 2.82 (1H, m), 2.08 (1H, m), 1.96 (1H, m), 1.84 (1H, m), 1.73 (1H, m), 1.43 (1H, m), 1.30 (1H, m); ^{13}C-NMR (D_6-Acetone, 125 MHz), δ: 206.2, 176.3, 155.4, 131.4, 129.8, 125.0, 120.5, 117.9, 64.0, 49.1, 26.5, 25.9; MS (ESI) *m/z*: 207 (M + 1).

Table 1 Experimental data

Empirical formula	$C_{11}H_{14}N_2O_2$
Formula weight	206.24
Temperature	296(2)
Wavelength (Mo K_α)	0.71073
Crystal system	Monoclinic
Space group	$P2_1$
Crystal data	
a (Å)	7.284(6)
b (Å)	10.262(9)
c (Å)	7.975(7)
α (°)	90.00
β (°)	114.451(14)
γ (°)	90.00
Volume	542.7(8)
Z	2
Density (calculated)	1.263 mg/m^3
Absorption coefficient	0.123
F(000)	242
Crystal size	0.47 × 0.40 × 0.28 mm^3
Theta range for data collection (°)	1.5–25.0
Index ranges	$-9 \le h \le 6$; $-13 \le k \le 13$; $-9 \le l \le 10$
Reflections collected	3376
Independent reflections	2402
Reflections theta (°)	2.8–28.3
Absorption correction transmission	0.7661–0.8346
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	2402/1/137
Goodness-of-fit on F^2	1.099
Final R indices [$I > 2\sigma(I)$]	$R1 = 0.0574$; $wR2 = 0.1499$
R indices (all data)	$R1 = 0.0514$; $wR2 = 0.1570$
Refine different density	−0.261 to 0.045

X-ray Data Collection and Structure Refinement

All H atoms were positioned geometrically, with C–H = 0.93–0.98 Å, and refined with a riding model, with

Table 2 Selected bond lengths (Å) and angles (°)

Bond	Dist. (Å)	Bond	Dist. (Å)
C6–C7	1.398(3)	C8–C9	1.370(4)
C6–C11	1.386(3)	C8–C7	1.394(3)
C6–N2	1.409(3)	C1–N1	1.465(3)
C10–C9	1.388(4)	C1–C5	1.513(3)
C10–C11	1.390(4)	C1–C2	1.545(4)
O1–C5	1.239(3)	N1–C4	1.459(4)
N2–C5	1.333(3)	C3–C2	1.513(5)
O2–C7	1.355(3)	C3–C4	1.527(5)
Angle	(°)	Angle	(°)
C7–C6–C11	119.4(2)	O1–C5–C1	121.19(19)
C7–C6–N2	116.11(18)	N2–C5–C1	115.35(18)
C11–C6–N2	124.46(19)	C8–C9–C10	120.6(2)
C5–N2–C6	127.83(18)	O2–C7–C6	116.43(19)
C9–C8–C7	120.3(2)	O2–C7–C8	123.93(19)
C10–C11–C6	120.5(2)	C6–C7–C8	119.6(2)
N1–C1–C5	112.32(18)	C3–C2–C1	104.5(2)
N1–C1–C2	106.4(2)	N1–C4–C3	106.0(2)
C5–C1–C2	111.2(2)	O1–C5–N2	123.5(2)
C1–N1–C4	108.2(2)	C2–C3–C4	101.9(2)

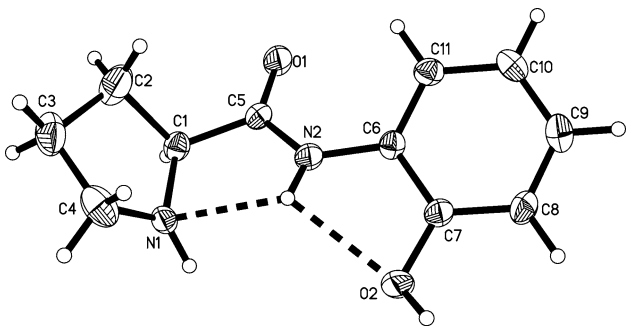


Fig. 1 The molecular structure of the title molecule

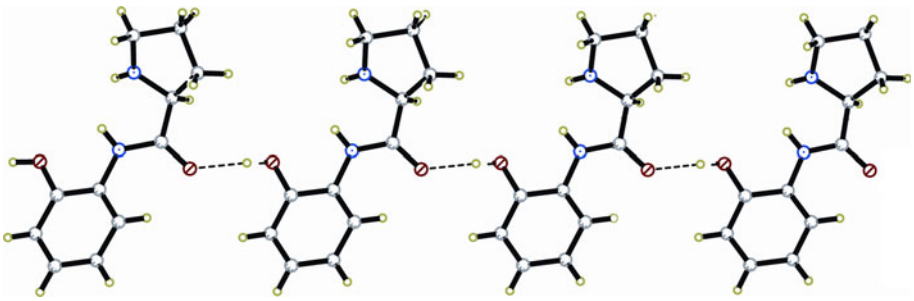


Fig. 2 The intermolecular hydrogen bonds in the crystal

$U_{iso}(H) = 1.2\ U_{eq}$(carrier). Data collection: SMART [11]; cell refinement: SAINT [11]; data reduction: SAINT [11]; program (s) used to solve structure: SHELXS97 [12]; program (s) used to refine structure: SHELXL97 [13]; molecular graphics: Ortep-3 for Windows [14]; software used to prepare material for publication: WinGX [15].

Results and Discussion

The main experimental data is displayed in Table 1; selected bond lengths and bond angles for the title compound are listed in Table 2. The molecular structure is shown in Fig. 1, and the intermolecular hydrogen bonds are depicted in Fig. 2. The X-ray structural determination of the title compound confirmed the assignment of its structure from NMR and MS spectra data.

Geometric parameters of the title compound are in the usual ranges. It crystallizes in the monoclinic space group, $P2_1$, with unit cell dimensions $a = 7.284(6)$ Å, $b = 10.262(9)$ Å, and $c = 7.975(7)$ Å. In the molecule, there are two rings, pyrrolidine and phenyl connected by a carboxamide group. The pyrrolidine displays a typical envelope conformation, C1, C2, C4 and N1 compose a plane with the C2–C1–N1–C4 torsion angle of −4.007(275)°, and C3 projects out of this plane, C2–C3 and C4–C3 formed the flap of the envelope. The bond angles of the pyrrolidine part are in the range of 101.929(296)° (C2–C3–C4) to 108.146(213)° (C4–N1–C1). The absolute configuration could not be determined by anomalous dispersion effects, but was assigned with reference to an unchanging chiral center in the parent molecule. The plane of the carboxamide group contents the atoms of C1, C5, O1 and N2 with the dihedral angle of 23.719(184)° between phenyl plane. N2, C6, C7 and O2 compose a plane with the N2–C6–C7–O2 torsion angle of −1.066(308)°.

There are intramolecular hydrogen bonds in the title molecule: N(2)–H(2A)···O(2) [N(2)···O(2) = 2.622(3) Å, ∠N(2)H(2A)O(2) = 103°] and N(2)–H(2A)···N(1) [N(2)···N(1) = 2.622(3) Å, ∠N(2)H(2A)N(1) = 114°] (Fig. 1). The intramolecular hydrogen bonds form two pseudo-five-membered rings, thus locking the molecular conformation and eliminating conformational flexibility. Intermolecular hydrogen bonds of the type O–H···O are found in the crystal structure, O(2)–H(2B)···O(1) [O(2)···O(1) = 2.643(3) Å, ∠O(2)H(2B)O(1) = 174° (Fig. 2), and generate 1-D supra-molecular structures. In the crystal, the phenyl moieties pack together layer by layer staggeredly, the distance of the planes is 5.884(5) Å, and no π–π stacking interactions are observed.

Supplementary Material

Crystallographic data for the structure reported in this paper have been deposited at the Cambridge Crystallographic Data Center. Copies of the data (CCDC 768004) can be obtained free of charge upon application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (E-mail: deposit@ccdc.cam.ac.uk).

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