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The crystal structure of methyl ((4-aminobenzyl) sulfonyl)-D-prolinate, $C_{13}H_{18}N_2O_4S$

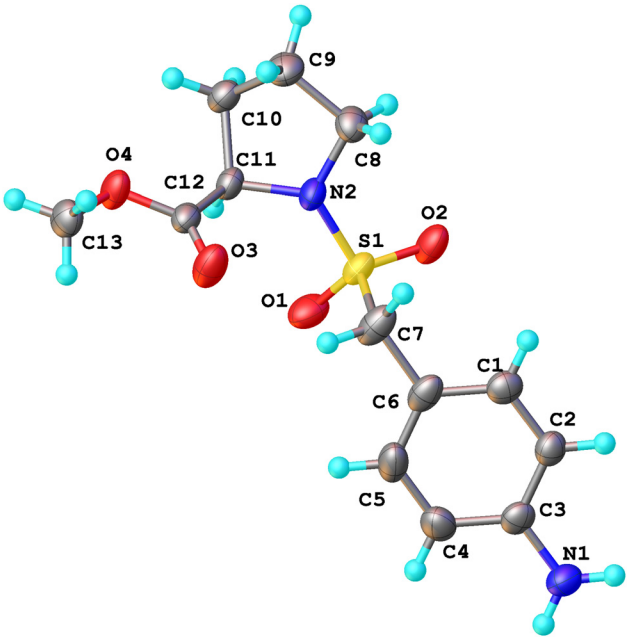

Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.16 × 0.13 × 0.11 mm
Wavelength:	Cu *K*α radiation (1.54178 Å)
μ:	2.23 mm^{-1}
Diffractometer, scan mode:	Bruker APEX-II, φ and ω
θ_{max}, completeness:	78.9°, 98 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	19,530, 2917, 0.041
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\sigma(I_{obs})$, 2868
$N(param)_{refined}$:	182
Programs:	CrysAlis^{PRO},[1] SHELX[2,3]

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Abstract

$C_{13}H_{18}N_2O_4S$, orthorhombic, $P2_12_12_1$ (no. 19), a = 6.8690(1) Å, b = 12.0694(2) Å, c = 16.6748(3) Å, V = 1382.42(4) Å^3, Z = 4, $R_{gt}(F)$ = 0.0278, $wR_{ref}(F^2)$ = 0.0729, T = 150 K.

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1 Source of material

(4–Nitrophenyl)methanesulfonyl chloride (2.81 g, 12.0 mmol), methyl pyrrolidine-2-carboxylate hydrochloride (2.39 g, 14.4 mmol) and 4-dimethylaminopyridine (3.52 g, 28.8 mmol) were dissolved in dichloromethane (50 mL) and reacted for 3 h at room temperature. At the end of the reaction, an appropriate amount of ethyl acetate was added to the reaction system, stirred and left to stand for 10 min, then the precipitate was filtered and the resulting filtrate was concentrated under vacuum. The crude product was purified by silica gel column chromatography (petroleum ether: ethyl acetate = 3:1, *v*: *v*). The purified white solid (1.62 g, 4.94 mmol) was dissolved in 20 mL of ultra-dry methanol, stannous chloride (5.57 g, 24.7 mmol) was added and the reaction was carried out at reflux at a temperature of 343 K for 2 h. The end point of the reaction was detected by thin layer chromatography (TLC). At the end of the reaction, the pH was adjusted to 7–8 with saturated Na_2CO_3 solution, followed by addition of an appropriate amount of ethyl acetate and stirring for 1 h. The filtrate was washed sequentially with deionized water and brine and dried over night with anhydrous sodium sulfate. The crude product was purified by silica gel column chromatography (petroleum ether: ethyl acetate = 2:1, *v*:*v*). The final product was obtained as desirable crystals by recrystallization in a system of dichloromethane and methanol (1:1, *v*:*v*).

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C1	0.5926 (3)	0.51717 (17)	0.61473 (12)	0.0234 (4)
H1	0.458057	0.521565	0.601854	0.028*
C2	0.6716 (3)	0.41633 (17)	0.63707 (12)	0.0221 (4)
H2	0.591224	0.352324	0.639136	0.027*
C3	0.8695 (3)	0.40807 (17)	0.65665 (12)	0.0219 (4)
C4	0.9838 (3)	0.50363 (18)	0.65337 (13)	0.0276 (4)
H4	1.117909	0.499797	0.666996	0.033*
C5	0.9033 (3)	0.60398 (18)	0.63041 (14)	0.0287 (5)
H5	0.983410	0.668062	0.628014	0.034*
C6	0.7069 (3)	0.61237 (17)	0.61082 (12)	0.0251 (4)
C7	0.6160 (4)	0.72196 (18)	0.58898 (13)	0.0286 (5)
H7A	0.507790	0.709578	0.550789	0.034*
H7B	0.714146	0.769438	0.562363	0.034*
C8	0.2088 (3)	0.90125 (18)	0.62294 (13)	0.0248 (4)
H8A	0.125549	0.873557	0.667061	0.030*
H8B	0.186292	0.855597	0.574493	0.030*
C9	0.1702 (3)	1.02402 (18)	0.60616 (14)	0.0275 (5)
H9A	0.192387	1.041644	0.548901	0.033*
H9B	0.034996	1.044305	0.620549	0.033*
C10	0.3155 (3)	1.08416 (17)	0.65917 (12)	0.0224 (4)
H10A	0.269985	1.087156	0.715454	0.027*
H10B	0.338972	1.160520	0.639745	0.027*
C11	0.4990 (3)	1.01284 (15)	0.65133 (11)	0.0193 (4)
H11	0.580221	1.019724	0.700842	0.023*
C12	0.6220 (3)	1.03891 (16)	0.57721 (12)	0.0200 (4)
C13	0.7667 (3)	1.18426 (17)	0.50264 (13)	0.0260 (4)
H13A	0.696581	1.169595	0.452566	0.039*
H13B	0.890358	1.143779	0.502464	0.039*
H13C	0.792317	1.263873	0.507328	0.039*
N1	0.9499 (3)	0.30564 (14)	0.67581 (11)	0.0262 (4)
H1A	1.075163	0.300155	0.686151	0.031*
H1B	0.875510	0.246334	0.677575	0.031*
N2	0.4162 (2)	0.90094 (14)	0.64607 (10)	0.0208 (3)
O1	0.6899 (2)	0.82534 (13)	0.72326 (10)	0.0299 (4)
O2	0.3827 (2)	0.71849 (12)	0.71203 (9)	0.0284 (3)
O3	0.6911 (3)	0.97101 (13)	0.53279 (10)	0.0325 (4)
O4	0.6494 (2)	1.14802 (12)	0.57013 (9)	0.0263 (3)
S1	0.52546 (7)	0.79070 (4)	0.67657 (3)	0.02036 (13)

2 Experimental details

The H atoms were placed in idealized positions and treated as riding on their parent atoms, with *d*(C–H) = 0.98 Å (methyl), U_{iso}(H) = 1.5U_{eq}(C), and *d*(C–H) = 0.99 Å (methylene), U_{iso}(H) = 1.2U_{eq}(C), and *d*(C–H) = 1.00 Å (methyne), U_{iso}(H) = 1.2U_{eq}(C), and *d*(C–H) = 0.95 Å (aromatic), U_{iso}(H) = 1.2U_{eq}(C). The H atoms at N1 were placed in difference maps and treated as riding.

3 Comment

Sulfonamides are important compounds with a wide range of applications,[4] and can also serve as important intermediates in certain chemical reactions. Several structures of this class of compounds are known.[5,6] Building on previous research in our laboratory,[7,8] we synthesized methyl((4-aminobenzyl) sulfonyl)-D-prolinate. The whole molecule is composed of two parts, *p*-aminobenzenesulfonyl and D-proline methyl ester. According to the method previously reported in the literature,[9] we used sulfonyl chloride (4-nitrobenzyl)methanesulfonyl chloride as the raw material, and coupled it with an amine-based compound (pyrrolidine-2-carboxylic acid methyl ester hydrochloride), and then stannous chloride was used as a reducing agent.

The ORTEP diagram is shown in the figure. Bond lengths and angles are all in the expected ranges.[5–7] The *p*-aminobenzenesulfonyl and D-proline methyl esters are connected by N(2)–S(1). The bond length of N(2)–S(1) is 1.6100(17) Å. The bond angle of N(2)–S(1)–C(7) is 106.67(10)°. The torsion angle of N(2)–S(1)–C(7)–C(6) is −175.35(16)°. The bond angle of the sulfonyl group O(2)=S(1)=O(1) is 119.36(10)°. The bond length of S(1)=O(1) is 1.4342(17) Å, and the bond length of S(1)=O(2) is 1.4390(16) Å. The benzene ring of *p*-aminobenzenesulfonyl, defined as C1–C2–C3–C4–C5–C6, and the pyrrolidine ring of D-proline methyl ester, defined as N2–C8–C9–C10–C11, are nearly coplanar, and the dihedral angle between them is about 17.5°. C(11) is a chiral C, and the molecule adopts a D stereoselective conformation. The carboxymethyl ester structure attached to it enhances the lipid solubility of the molecule,[10] which has a torsion angle of 1.7(3)° for O(3) =C(12)–O(4)–C(13). The amino group at the C(3) position is obtained by reduction of the nitro group by stannous chloride as a reductant, and can act as a proton donor or form hydrogen bonds with other atoms.[11,12] This conformation may increase the possibility of interaction with bioactive molecules or produce enhanced biological activity.[13,14]

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