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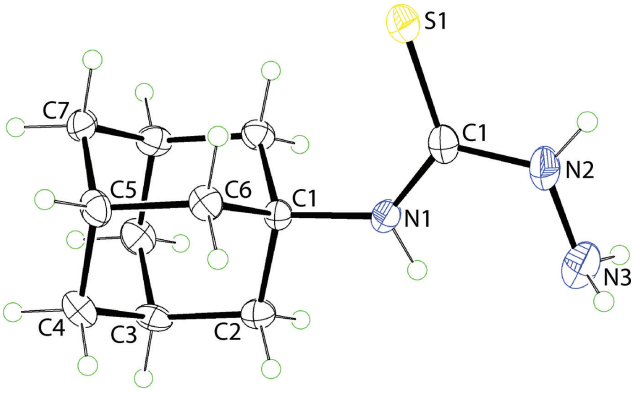
Crystal structure of 1-(adamantan-1-yl)-3-aminothiourea, $C_{11}H_{19}N_3S$



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Abstract

$C_{11}H_{19}N_3S$, monoclinic, $C2/m$ (no. 12), $a = 10.789(3)$ Å, $b = 6.959(3)$ Å, $c = 15.196(4)$ Å, $\beta = 96.843(13)°$, $V = 1132.7(6)$ Å^3, $Z = 4$, $R_{gt}(F) = 0.0568$, $wR_{ref}(F^2) = 0.1414$, $T = 293(2)$ 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.

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Table 1: Data collection and handling.

Crystal:	Colourless plate
Size:	0.48 × 0.42 × 0.05 mm
Wavelength:	Mo $K\alpha$ radiation (0.71073 Å)
μ:	0.26 mm^{-1}
Diffractometer, scan mode:	Bruker APEX-II, φ and ω
θ_{max}, completeness:	25.0°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	7771, 1093, 0.135
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\,\sigma(I_{obs})$, 762
$N(param)_{refined}$:	89
Programs:	Bruker [1], SHELX [2, 3], WinGX/ORTEP [4]

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

Atom	x	y	z	U_{iso}*/U_{eq}
S1	0.53346(10)	0.500000	0.36464(7)	0.0370(4)
N1	0.7848(3)	0.500000	0.3712(2)	0.0301(8)
H1N	0.854(2)	0.500000	0.405(2)	0.036*
N2	0.7036(3)	0.500000	0.5022(2)	0.0435(10)
H2N	0.640(3)	0.500000	0.531(3)	0.052*
N3	0.8264(4)	0.500000	0.5461(2)	0.0456(10)
H3N	0.839(3)	0.393(3)	0.574(2)	0.055*
C1	0.7962(3)	0.500000	0.2747(2)	0.0232(9)
C2	0.9361(3)	0.500000	0.2662(3)	0.0302(10)
H2A[a]	0.974727	0.612885	0.295235	0.036*
H2B[a]	0.974727	0.387115	0.295235	0.036*
C3	0.9571(3)	0.500000	0.1685(3)	0.0309(10)
H3	1.046913	0.500002	0.163813	0.037*
C4	0.8977(2)	0.3206(4)	0.1231(2)	0.0366(8)
H4A	0.911152	0.319594	0.061148	0.044*
H4B	0.935789	0.206168	0.151022	0.044*
C5	0.7583(2)	0.3213(4)	0.13097(18)	0.0318(7)
H5	0.719989	0.206382	0.102037	0.038*
C6	0.7381(2)	0.3201(4)	0.22922(17)	0.0292(7)
H6A	0.649435	0.316663	0.234550	0.035*
H6B	0.776195	0.206288	0.257743	0.035*
C7	0.6976(4)	0.500000	0.0865(3)	0.0322(10)
H7A	0.608904	0.499999	0.091880	0.039*
H7B	0.708112	0.500000	0.024033	0.039*
C8	0.6833(4)	0.500000	0.4131(2)	0.0290(10)

[a]Occupancy: 0.5.

Source of material

Hydrazine hydrate (98%, 5 mL) was added to a hot solution of 1-adamantyl isothiocyanate (1.93 g, 0.01 mol) in ethanol (10 mL) and the mixture was heated under reflux with stirring for 1 h. On cooling, the precipitated crude product was filtered, washed with cold ethanol, dried and crystallised from ethanol to yield 2.12 g (94%) of the title compound as transparent plates. **M.pt**: 468–470 K. **^{1}H NMR** (DMSO-d_6, 700.17 MHz): δ 8.40 (s, 1H, NH), 7.43 (t, 1H, NH, $J = 10.5$ Hz), 4.50 (d, 2H, NH_2, $J = 10.5$ Hz), 2.51 (s, 6H, Adamantane-H), 2.05 (s, 3H, Adamantane-H), 1.63 (s, 6H, Adamantane-H). **^{13}C NMR** (DMSO-d_6, 176.08 MHz): δ 179.55 (C=S), 29.47, 36.43, 41.85, 50.37 (Adamantane-C). **ESI-MS**: m/z 224.0 $[M-H]^-$, 226.0 $[M+H]^+$.

Experimental details

The C-bound H atoms were geometrically placed (C—H = 0.97–0.98 Å) and refined as riding with $U_{iso}(H) = 1.2U_{eq}(C)$. The N-bound H atoms were located from a difference Fourier map and refined with N—H = 0.88 ± 0.01 Å, and with $U_{iso}(H)$ set to $1.2U_{eq}(N)$.

Comment

The diverse pharmacological activities of adamantane-based drugs are well known. Early examples include amantadine, which was approved as a potent drug against Influenza A viral infections, and tromantadine, which is currently used against herpes simplex skin viral infections [5]. More recently, 3-(4-chlorophenyl)-*N*-(pyridin-4-ylmethyl) adamantane-1-carboxamide (ABC294640) was approved as an anti-cancer drug for the treatment of patients with advanced solid tumours in response to its ability to act as a sphingosuine kinase inhibitor [6]. In connection with the present study, describing the investigation of a hybrid adamantane-thiosemicarbazide species, thiosemicarbazide and thiosemicarbazone derivatives have also been reported to possess marked chemotherapeutic properties [7, 8]. The title compound, 4-(1-adamantyl)-3-thiosemicarbazide was previously isolated as a minor by-product during the reaction of *N*-(adamantan-1-yl)-4-ethoxycarbonylpiperidine-1-carbothioamide with excess hydrazine hydrate, in ethanol, at reflux temperature [9]. In connection of on-going biological [10, 11] and crystallographic [12, 13] studies of related species, the present investigation describes the synthesis and single-crystal X-ray structural analysis of the title structure (I).

The molecular structure (I) is shown in the Figure (35% probability ellipsoids with unlabelled atoms related by the symmetry operation x, $1-y$, z). The molecule has crystallographically imposed mirror symmetry, with the mirror plane bisecting the adamantyl residue and contains the N(H)C(=S)N(H)N atoms of the thiosemicarbazide residue. The C-bound amine-hydrogen atom is *anti* with respect to the thione bond and the N-amide is *syn*, so the terminal amine group is *anti* to the thione bond. The C8—N1 [1.330(5) Å], C8—S1 [1.695(4) Å], C8—N2 [1.345(5) Å] and N2—N3 [1.411(5) Å] bond lengths follow our expectations. Simiarly, the bond angles about the C8 atom generally follow the forecast, with those involving the doubly-bonded S1 atom, i.e. N1—C8—S1 [126.1(3)°] and N2—C8—S1 [118.0(3)°], being wider than that subtended by the N atoms, i.e. N1—C8—N2 is 116.0(3)°. It is likely that the relatively narrow N2—C8—S1 angle is the result of the steric demand of the proximate adamantyl residue as seen in the C1—N1—C8 angle of 130.0(3)°.

The most closely related structure in the literature is that where the N1-substituted adamantyl group is replaced by a methyl group [14]. Alternatively, when the adamantyl remains intact, the closest structure resembling (I) is one where the terminal NH_2 residue is substituted by a phenyl group [15]. In both instances, there is no change of conformation, i.e. the *anti*/*syn* relationships, about the NC(=S)N chromophore.

Despite their being four acidic H atoms in the molecule of (I), besides an intramolecular N1—H1n···N3 hydrogen bond [N1—H1n···N3: H1···N3 = 2.20(3) Å, N1···N3 = 2.642(4) Å with angle at H1n = 112(2)°], the only intermolecular contact involving these potential donors is a N2—H2n···S1 hydrogen bond. These hydrogen bonds occur between molecules related by 2-fold symmetry [N2—H2n···S1^i: H2n···S1^i = 2.59(4) Å, N2···S1^i = 3.445(4) Å with angle at H2n = 173(4)° for symmetry operation (i): $1-x$, y, $1-z$]. The resultant dimeric aggregates assemble without directional interactions between them. Globally, the dimers are arranged into layer in the ac-plane and stack along the *b*-axis in an ···ABA··· fashion.

In order to gain greater insight into the molecular packing of (I), especially in the absence of significant directional interactions between dimeric aggregates, the Hirshfeld surfaces were calculated along with the full and decomposed two-dimensional fingerprint plots. This was accomplished with Crystal Explorer 17 [16] following literature protocols [17]. There are significant contributions to the Hirshfeld surface by S···H/H···H [16.0%], C···H/H···C [3.9%] and N···H/H···N [3.3%]. However, reflecting the lack of directional interactions in the molecular packing, the most dominant contrbutions to the surface contacts are from H···H contacts, at 76.8%.

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