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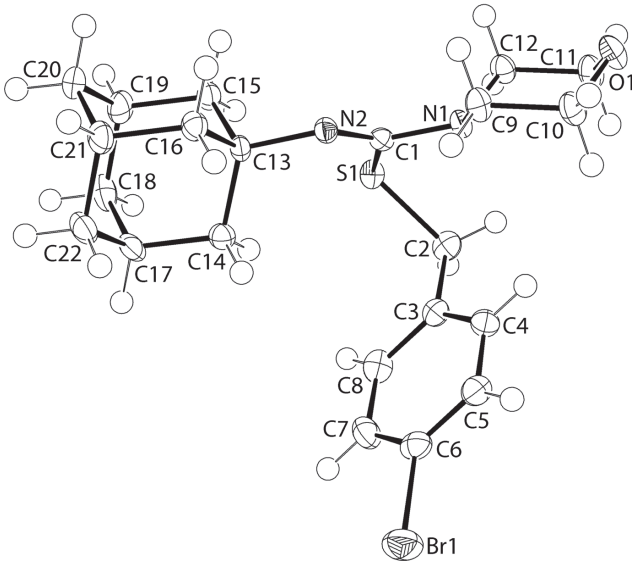
Crystal structure of 4-bromobenzyl (*Z*)-*N*-(adamantan-1-yl)morpholine-4-carbothioimidate, $C_{22}H_{29}BrN_2OS$



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Abstract

$C_{22}H_{29}BrN_2OS$, triclinic, $P\bar{1}$ (no. 2), $a = 7.1722(3)$ Å, $b = 10.2350(4)$ Å, $c = 14.8756(6)$ Å, $\alpha = 73.607(2)°$, $\beta = 84.7020(10)°$, $\gamma = 88.7210(10)°$, $V = 1043.11(7)$ Å^3, $Z = 2$, $R_{gt}(F) = 0.0467$, $wR_{ref}(F^2) = 0.0870$, $T = 296(2)$ 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.

Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.44 × 0.15 × 0.11 mm
Wavelength:	Mo $K\alpha$ radiation (0.71073 Å)
μ:	2.09 mm^{-1}
Diffractometer, scan mode:	Bruker APEX-II, φ and ω
θ_{max}, completeness:	33.8°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	29518, 8337, 0.066
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\,\sigma(I_{obs})$, 5322
$N(param)_{refined}$:	244
Programs:	Bruker [1], SHELX [2, 3], WinGX/ORTEP [4]

Source of material

4-Bromobenzyl bromide (500 mg, 2.0 mmol) and anhydrous potassium carbonate (276 mg, 2 mmol) were added to an anhydrous acetone (15 mL) solution of *N*-(adamantan-1-yl)morpholine-4-carbothioamide (560 mg, 2 mmol) and the mixture was heated under reflux for 4 h. The solvent was then distilled off *in vacuo* and the residue was washed with water (20 mL), dried and crystallized from ethanol to yield 380 mg (85%) of the title compound as colourless crystals. M. pt.: 371–373 K. Single crystals suitable for X-ray analysis were obtained by the slow evaporation of a $CHCl_3$/EtOH (*v:v*) solution of the compound held at room temperature. ^{1}H NMR ($CDCl_3$, 700.17 MHz): δ [p.p.m.] 1.63–1.69 (m, 6H, adamantane-H), 1.84 (m, 6H, adamantane-H), 2.01 (s, 3H, adamantane-H), 3.25–3.30 (m, 4H, morpholine-H), 3.69–3.74 (m, 4H, morpholine-H), 3.91 (s, 2H, benzylic-CH_2), 7.17 (d, 2H, Ar—H, $J = 7.5$ Hz), 7.45 (d, 2H, Ar—H, $J = 7.5$ Hz). ^{13}C{^{1}H} NMR ($CDCl_3$, 176.08 MHz): δ [p.p.m.] 29.59, 29.94, 36.57, 54.69 (adamantane-C), 37.76 (benzylic-CH_2), 49.70, 66.85 (morpholine-C), 121.00, 130.51, 137.26, 146.91 (Ar—C), 156.46 (C=N). ESI-MS, *m/z* (Rel. Int.): 449.4 [$M + 2 + H$, 100]$^+$, 451.4 [$M + 2 + H$, 98]$^+$.

Experimental details

The C-bound H atoms were geometrically placed (C—H = 0.93–0.98 Å) and refined as riding with $U_{iso}(H) = 1.2U_{eq}(C)$.

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
Br1	1.20216(3)	0.36045(2)	0.54756(2)	0.02552(6)
S1	0.55468(6)	0.14208(4)	0.28378(3)	0.01351(9)
O1	1.14454(17)	0.01989(12)	0.07956(9)	0.0182(3)
N1	0.87498(18)	0.15584(14)	0.17322(9)	0.0113(3)
N2	0.73859(18)	0.36611(14)	0.16104(9)	0.0118(3)
C1	0.7319(2)	0.23870(16)	0.19672(11)	0.0108(3)
C2	0.7038(2)	0.03562(17)	0.36897(12)	0.0163(3)
H2A	0.6252	−0.0259	0.4189	0.020*
H2B	0.7840	−0.0192	0.3380	0.020*
C3	0.8239(2)	0.11681(16)	0.41139(11)	0.0140(3)
C4	1.0159(2)	0.12684(18)	0.38708(12)	0.0161(3)
H4	1.0697	0.0843	0.3435	0.019*
C5	1.1287(2)	0.19982(18)	0.42722(12)	0.0166(3)
H5	1.2571	0.2063	0.4107	0.020*
C6	1.0475(2)	0.26246(17)	0.49185(12)	0.0168(4)
C7	0.8560(3)	0.25542(18)	0.51715(12)	0.0196(4)
H7	0.8027	0.2982	0.5607	0.023*
C8	0.7465(2)	0.18307(18)	0.47583(12)	0.0181(4)
H8	0.6177	0.1786	0.4915	0.022*
C9	1.0376(2)	0.22895(17)	0.11485(12)	0.0146(3)
H9A	1.0759	0.3009	0.1400	0.018*
H9B	1.0053	0.2698	0.0511	0.018*
C10	1.1958(2)	0.12835(18)	0.11499(13)	0.0163(3)
H10A	1.3042	0.1755	0.0767	0.020*
H10B	1.2305	0.0911	0.1787	0.020*
C11	0.9860(2)	−0.05104(17)	0.13587(13)	0.0175(4)
H11A	1.0193	−0.0918	0.1995	0.021*
H11B	0.9510	−0.1238	0.1108	0.021*
C12	0.8209(2)	0.04254(17)	0.13826(12)	0.0142(3)
H12A	0.7803	0.0779	0.0756	0.017*
H12B	0.7175	−0.0077	0.1791	0.017*
C13	0.6064(2)	0.46803(16)	0.18183(11)	0.0111(3)
C14	0.5903(2)	0.47399(17)	0.28468(11)	0.0137(3)
H14A	0.5425	0.3879	0.3261	0.016*
H14B	0.7129	0.4895	0.3023	0.016*
C15	0.4107(2)	0.44547(17)	0.15427(12)	0.0139(3)
H15A	0.4202	0.4413	0.0897	0.017*
H15B	0.3600	0.3594	0.1943	0.017*
C16	0.6827(2)	0.60650(16)	0.11913(12)	0.0140(3)
H16A	0.8054	0.6223	0.1367	0.017*
H16B	0.6966	0.6048	0.0540	0.017*
C17	0.4575(2)	0.58975(17)	0.29518(12)	0.0166(4)
H17	0.4466	0.5923	0.3608	0.020*
C18	0.2631(2)	0.56547(18)	0.26744(13)	0.0192(4)
H18A	0.1790	0.6379	0.2751	0.023*
H18B	0.2121	0.4798	0.3080	0.023*
C19	0.2790(2)	0.56173(18)	0.16454(13)	0.0177(4)
H19	0.1549	0.5461	0.1468	0.021*
C20	0.3584(3)	0.69740(18)	0.10043(13)	0.0196(4)
H20A	0.2746	0.7710	0.1059	0.024*
H20B	0.3693	0.6949	0.0355	0.024*
C21	0.5518(2)	0.72245(17)	0.12900(12)	0.0164(4)
H21	0.6027	0.8092	0.0881	0.020*
C22	0.5343(3)	0.72672(17)	0.23178(12)	0.0178(4)
H22A	0.6560	0.7442	0.2497	0.021*
H22B	0.4506	0.7995	0.2390	0.021*

Comment

The highly lipophilic adamantane cage constitutes a core pharmacophore of several drugs [5]. After the development of amantadine as efficient anti-viral drug against influenza A viruses [6] and as anti-parkinsonian drug [7], adamantane derivatives attracted the attention of several drug manufacturers for the development of more potent and safer bioactive agents. As a result of this intensive search, several adamantane derivatives were developed and are currently used as effective therapeutic agents. Among the major biological activities displayed by adamantane based derivatives, the anti-viral [8], anti-cancer [9], anti-bacterial and anti-fungal [10], anti-malarial [11] and anti-diabetic [12] activities are the most important ones. It is also well known that isothiourea derivatives are of particular value in medicinal chemistry, exhibiting significant anti-viral [13], anti-cancer [14] and anti-bacterial [15] activities. The title compound was very recently prepared among a series of adamantane-isothiourea hybrid derivatives, which displayed marked, broad spectrum anti-bacterial activity [16].

The molecule [systematic name: 4-bromophenyl] methyl-*N*-(tricyclo[3.3.1.1^{3,7}]decan-1-yl)morpholine-4-carboximidothioate] is shown in the figure (70% displacement ellipsoids) and is constructed about a planar CN_2S chromophore with the r.m.s. deviation of the C1, N1, N2 and S1 atoms being 0.008 Å. The configuration about the C1=N2 bond [1.262(2) Å] is *Z*, and the conformation of the morpholinyl ring is that of a chair. The bromobenzyl group is orientated to lie over the remaining part of the molecule but is slightly inclined towards the morpholinyl group with the C2—S1—C1—N1 torsion angle being 46.80(13)° compared with the C2—S1—C1—N2 torsion angle of −130.63(15)°.

With the exception of weak π—π stacking between centrosymmetrically related molecules [inter-centroid *Cg*(C3—C8)···*Cg*(C3—C8)^{i} distance = 3.8802(11) Å for symmetry operation ^{i}: 2 − *x*, − *y*, 1 − *z*], the molecular packing is devoid of directional interactions. This observation is highlighted by the high contribution to the calculated Hirshfeld surface by H···H contacts, that is 68.5% [17, 18]. The next highest contribution to surface of 14.0% is due to Br···H/H···Br contacts but, none of these occur within the sum of the respective van der Waals radii.

The structure of the present compound has two literature precedents, that is with 4-nitrobenzyl [16] and 3,5-trifluorobenzyl [19] groups. The superimposition of the three molecules reveals a very high degree of concordance in the molecular structures with any minor variations in conformation being associated only with the relative orientations of the substituted benzyl groups. Bond lengths and other geometric parameters are in the expected ranges for such a compound [20].

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