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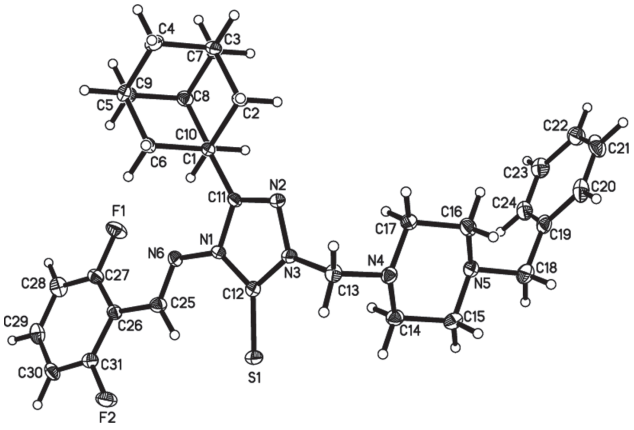
Crystal structure of 3-(adamantan-1-yl)-1-[(4-benzylpiperazin-1-yl)methyl]-4-[(*E*)-(2,6-difluorobenzylidene)amino]-1*H*-1,2,4-triazole-5(4*H*)-thione, $C_{31}H_{36}F_2N_6S$



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Abstract

$C_{31}H_{36}F_2N_6S$, monoclinic, $P2_1/c$ (no. 14), $a = 14.7561(8)$ Å, $b = 24.6766(13)$ Å, $c = 7.7811(4)$ Å, $\beta = 95.888(2)°$, $V = 2818.4(3)$ Å^3, $Z = 4$, $R_{gt}(F) = 0.0624$, $wR_{ref}(F^2) = 0.1445$, $T = 100$ K.

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Tables 1 and 2 contain details of the measurement method and a list of the atoms including atomic coordinates and displacement parameters.

Table 1: Data collection and handling.

Crystal:	Yellow needles Size 0.49 × 0.21 × 0.16
Wavelength:	Mo K_α radiation (0.71073 Å)
μ:	1.61 cm^{-1}
Diffractometer, scan mode:	Bruker Apex II, φ and ω
$2\theta_{max}$, completeness:	55.0°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	9934, 6468
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 4817
$N(param)_{refined}$:	365
Programs:	Bruker programs [25], SHELX [26]

Source of material

1-Benzylpiperazine (353 mg, 1 mmol) and a 37% formaldehyde solution (1.0 mL) were added to a stirred hot solution of 5-(adamantan-1-yl)-4-(2,6-difluorobenzylideneamino)-4*H*-1,2,4-triazole- 3-thiol (747 mg, 2 mmol), in ethanol (10 mL), and the mixture was heated under reflux for 15 min. Stirring was continued for 12 h at room temperature and the mixture was allowed to stand overnight. Cold water (5 mL) was gradually added and the mixture was stirred for 20 min. The precipitated crude product was filtered, washed with water, dried, and crystallized from ethanol to yield 900 mg (80%) of the title compound ($C_{31}H_{36}F_2N_6S$) as colourless needle crystals. M.P.: 421–423 K [17]. Single crystals suitable for X-ray analysis were obtained by slow evaporation of a $CHCl_3$:EtOH (1:1; 5 mL) solution at room temperature. **^{1}H NMR** ($CDCl_3$, 500.13 MHz): δ 1.80 (s, 6H, adamantane-H), 2.09 (s, 3H, adamantane-H), 2.18 (s, 6H, adamantane-H), 2.41–2.52 (m, 4H, piperazine-H), 2.95 (s, 4H, piperazine-H), 3.52 (s, 2H, PhCH_2), 5.17 (s, 2H, CH_2), 7.03 (t, 2H, Ar—H, $J = 8.5$ Hz), 7.25–7.32 (m, 5H, Ar—H), 7.45–7.49 (m, 1H, Ar—H), 10.65 (s, 1H, CH = N). **^{13}C NMR** ($CDCl_3$, 125.76 MHz): δ 28.0, 35.52,

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
S1	0.97668(5)	0.46948(2)	0.23439(8)	0.02047(16)
F1	0.74649(10)	0.30124(6)	0.5218(2)	0.0266(4)
F2	1.04001(10)	0.30416(6)	0.3347(2)	0.0273(4)
N1	0.84177(14)	0.45159(8)	0.4548(2)	0.0147(4)
N2	0.79924(14)	0.53516(8)	0.5099(2)	0.0155(4)
N3	0.86593(14)	0.53501(8)	0.3977(3)	0.0156(4)
N4	0.86437(14)	0.61665(8)	0.2129(3)	0.0160(4)
N5	0.73701(15)	0.64156(8)	−0.0791(3)	0.0185(5)
N6	0.83721(14)	0.39557(8)	0.4738(3)	0.0164(4)
C1	0.71672(16)	0.46542(9)	0.6608(3)	0.0147(5)
C2	0.66778(17)	0.51537(9)	0.7275(3)	0.0168(5)
H2A	0.7131	0.5400	0.7892	0.020*
H2B	0.6362	0.5354	0.6286	0.020*
C3	0.59822(18)	0.49750(10)	0.8503(3)	0.0191(5)
H3A	0.5672	0.5302	0.8927	0.023*
C4	0.64749(18)	0.46709(10)	1.0051(3)	0.0205(5)
H4A	0.6931	0.4911	1.0684	0.025*
H4B	0.6031	0.4559	1.0853	0.025*
C5	0.69487(18)	0.41699(10)	0.9387(3)	0.0189(5)
H5A	0.7264	0.3968	1.0391	0.023*
C6	0.76539(17)	0.43475(9)	0.8181(3)	0.0165(5)
H6A	0.7973	0.4026	0.7779	0.020*
H6B	0.8112	0.4587	0.8813	0.020*
C7	0.52722(17)	0.46040(10)	0.7538(3)	0.0211(5)
H7A	0.4945	0.4802	0.6555	0.025*
H7B	0.4821	0.4489	0.8323	0.025*
C8	0.57500(17)	0.41062(10)	0.6874(3)	0.0180(5)
H8A	0.5286	0.3863	0.6245	0.022*
C9	0.62426(18)	0.37990(10)	0.8408(3)	0.0200(5)
H9A	0.5796	0.3677	0.9192	0.024*
H9B	0.6548	0.3475	0.7988	0.024*
C10	0.64429(17)	0.42812(9)	0.5644(3)	0.0166(5)
H10A	0.6127	0.4477	0.4644	0.020*
H10B	0.6742	0.3957	0.5205	0.020*
C11	0.78471(16)	0.48445(9)	0.5424(3)	0.0141(5)
C12	0.89530(17)	0.48463(9)	0.3621(3)	0.0160(5)
C13	0.90839(17)	0.58716(9)	0.3568(3)	0.0172(5)
H13A	0.9106	0.6106	0.4603	0.021*
H13B	0.9721	0.5800	0.3340	0.021*
C14	0.86854(18)	0.58909(10)	0.0466(3)	0.0187(5)
H14A	0.8324	0.5552	0.0441	0.022*
H14B	0.9325	0.5794	0.0323	0.022*
C15	0.83131(17)	0.62573(10)	−0.0992(3)	0.0201(5)
H15A	0.8698	0.6586	−0.1006	0.024*
H15B	0.8333	0.6067	−0.2108	0.024*
C16	0.73477(19)	0.66966(10)	0.0861(3)	0.0207(5)
H16A	0.6715	0.6806	0.1007	0.025*
H16B	0.7725	0.7028	0.0872	0.025*
C17	0.77057(18)	0.63294(10)	0.2335(3)	0.0189(5)
H17A	0.7688	0.6522	0.3447	0.023*
H17B	0.7315	0.6004	0.2350	0.023*
C18	0.70184(19)	0.67613(11)	−0.2241(3)	0.0270(6)
H18A	0.7074	0.6566	−0.3337	0.032*
H18B	0.7396	0.7093	−0.2241	0.032*
C19	0.60367(19)	0.69217(10)	−0.2166(3)	0.0212(6)
C20	0.5806(2)	0.74361(10)	−0.1626(3)	0.0264(6)
H20A	0.6273	0.7693	−0.1311	0.032*
C21	0.4907(2)	0.75797(11)	−0.1542(3)	0.0298(7)
H21A	0.4761	0.7933	−0.1174	0.036*
C22	0.4222(2)	0.72115(11)	−0.1990(3)	0.0272(6)
H22A	0.3603	0.7313	−0.1953	0.033*
C23	0.4439(2)	0.66922(11)	−0.2498(3)	0.0253(6)
H23A	0.3970	0.6435	−0.2786	0.030*
C24	0.53408(19)	0.65506(10)	−0.2583(3)	0.0235(6)
H24A	0.5486	0.6195	−0.2933	0.028*
C25	0.89500(17)	0.36578(9)	0.4068(3)	0.0171(5)
H25A	0.9396	0.3820	0.3436	0.021*
C26	0.89317(16)	0.30654(9)	0.4265(3)	0.0155(5)
C27	0.82227(17)	0.27572(10)	0.4794(3)	0.0178(5)
C28	0.82366(18)	0.21974(10)	0.4874(3)	0.0227(6)
H28A	0.7731	0.2002	0.5223	0.027*
C29	0.90022(18)	0.19275(10)	0.4437(3)	0.0214(6)
H29A	0.9025	0.1543	0.4505	0.026*
C30	0.97328(18)	0.22065(10)	0.3903(3)	0.0205(6)
H30A	1.0255	0.2021	0.3587	0.025*
C31	0.96806(17)	0.27621(10)	0.3845(3)	0.0180(5)

36.47, 38.36 (adamantane-C), 50.51, 53.12 (piperazine-C), 63.18 (Ph*C*H$_2$), 68.96 (CH$_2$), 110.89, 112.17, 127.04, 128.18, 129.29, 133.11, 137.96, 152.11 (Ar—C), 155.47, 161.05 (triazole C-5 & CH = N), 163.19 (C = S). **ESI-MS**, *m/z*: 563 [M+H]$^+$.

Discussion

Derivatives of adamantane have long been known for their antiviral activity against the influenza A [1–4], herpes simplex [5] and HIV [6–8] viruses. Several adamantane-based drugs are currently used as efficient therapies for the control central nervous disorders [9–12]. In addition, potent antimicrobial [13–18], anti-inflammatory [16–18] and anticancer [19, 20] activities were reported for adamantane-based derivatives. 1,2,4-Triazole derivatives were also recognized as a structural motif of particular value in medicinal chemistry possessing diverse biological activities [21–23]. In the present study, we report the crystal structure together with the synthesis of the title 1,2,4-triazole-*N*-Mannich base which was reported to exhibit marked antifungal activity [17]. This contribution is part of study on admantyl-based drugs [24]

There is one complete molecule in the asymmetric unit of the title structure. All bond lengths and angels are in the expected ranges.

The molecules packing in the crystal structure is stabilized *via* two intermolecular hydrogen bonds, of which S1 and F2 work as hydrogen bond acceptors and C14 and C15 work as hydrogen bond donors. The distance of the interactions between C14—H14B···S1^{i} and C15—H15A···F2^{i} are 2.85 and 2.54 Å, respectively and the angles are 135 and 130°, respectively. Symmetry codes: (i) −*x*+2, −*y*+1, −*z*.

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