Crystal Structure of 1-(4-Benzylpiperazino)methyl-3-phenyl-1,2,4-triazole-5-thione

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The title compound, 1-(4-benzylpiperazino)methyl-3-phenyl-1,2,4-triazole-5-thione, $C_{20}H_{23}N_5S$, crystallizes in the monoclinic space group $P2_1/c$ with the following unit cell parameters: $a = 18.6157(9)\text{\AA}$, $b = 11.0013(5)\text{\AA}$, $c = 21.6202(14)\text{\AA}$, $\beta = 120.561(4)^\circ$ and $V = 3812.7(4)\text{\AA}^3$. The crystal structure was solved with a final $R = 0.1045$ using 4996 independent reflections and contains two independent molecules in the asymmetric unit. Each independent molecule exists as part of an N-H...N hydrogen-bonded centrosymmetric $R_2^2(18)$ dimer. An extensive three-dimensional network of N-H...N, C-H...N and C-H...S hydrogen bonds, with π - π and π -ring interactions are responsible for crystal stabilization. Intermolecular hydrogen bonds and C-H... π interactions produce $R_2^2(10)$, $R_3^3(19)$, $R_4^4(26)$, $R_6^6(37)$ and $R_8^8(54)$ rings.

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Since the development of new analgesic/antiinflammatory compounds that are safer and as effective as opioids for the treatment of pain and inflammation continues to be a challenging problem in medicinal chemistry, our recent interest has focused on the synthesis and chemistry of this type of compound. We have synthesized various potential analgesic-antiinflammatory substances derived from 1,2,4-triazole-5-thiones.¹ The title compound is one of the mannich derivatives of 1,2,4-triazole-5-thiones having analgesic antiinflammatory activity. The details of the concerned compound were published elsewhere.² Here, we report on its crystal structure.

To a solution of 3-phenyl-1,2,4-triazole-5-thione (1.5 mmol)

Table 1 Crystal and experimental data

Formula: $C_{20}H_{23}N_5S$
Formula weight: 365.49
Crystal system: monoclinic
Space group: $P 2_1/c$ $Z = 8$
 $a = 18.6157(9)\text{\AA}$
 $b = 11.0013(5)\text{\AA}$ $\beta = 120.561(4)^\circ$
 $c = 21.6202(14)\text{\AA}$
 $V = 3812.7(4)\text{\AA}^3$
Density = 1.273 g cm^{-3}
No. of reflections used = 38736
 $2\theta_{\text{max}} = 59.36^\circ$ Mo K_α
 $R = 0.1045$
 $(\Delta/\sigma)_{\text{max}} = 0.000$
 $(\Delta\rho)_{\text{max}} = 0.69\text{ e \AA}^{-3}$
 $(\Delta\rho)_{\text{min}} = -0.35\text{ e \AA}^{-3}$
Measurement: STOE IPDS II
Program system: STOE X-RED
Structure determination: Direct methods
Refinement: full matrix
CCDC number: CCDC 648387

Table 2 Atomic coordinates and temperature factors

Atom	x	y	z	U_{eq}
C1A	0.3475(3)	-0.2571(5)	0.2101(3)	0.0450(11)
C2A	0.3967(4)	-0.3605(5)	0.2353(3)	0.0539(13)
C3A	0.3706(5)	-0.4688(5)	0.1981(4)	0.0645(17)
C4A	0.2953(5)	-0.4758(6)	0.1346(4)	0.0671(17)
C5A	0.2458(4)	-0.3735(6)	0.1089(4)	0.0661(17)
C6A	0.2710(4)	-0.2664(5)	0.1460(3)	0.0572(14)
C7A	0.3741(3)	-0.1409(5)	0.2487(3)	0.0436(11)
C8A	0.3790(3)	0.0508(5)	0.2700(3)	0.0463(11)
C9A	0.4856(4)	0.0375(6)	0.4038(3)	0.0530(13)
C10A	0.5792(4)	0.1541(6)	0.3796(3)	0.0561(14)
C11A	0.6706(4)	0.1869(5)	0.4114(4)	0.0574(14)
C12A	0.6194(4)	-0.0474(5)	0.4295(3)	0.0530(13)
C13A	0.7109(4)	-0.0166(6)	0.4612(3)	0.0567(14)
C14A	0.8101(4)	0.1113(6)	0.4451(4)	0.0630(16)
C15A	0.8591(3)	0.0163(5)	0.4332(3)	0.0511(13)
C16A	0.9043(4)	-0.0710(6)	0.4845(3)	0.0617(16)
C17A	0.9507(4)	-0.1556(6)	0.4744(4)	0.0703(19)
C18A	0.9544(4)	-0.1553(7)	0.4130(4)	0.0715(19)
C19A	0.9095(4)	-0.0699(7)	0.3598(3)	0.0687(18)
C20A	0.8614(4)	0.0172(6)	0.3695(3)	0.0571(14)
N1A	0.4317(3)	-0.0118(4)	0.3309(2)	0.0480(10)
N2A	0.4289(3)	-0.1335(4)	0.3177(2)	0.0479(10)
N3A	0.3427(3)	-0.0320(4)	0.2174(2)	0.0453(10)
N4A	0.5715(3)	0.0614(5)	0.4253(3)	0.0534(11)
N5A	0.7199(3)	0.0774(4)	0.4156(3)	0.0507(11)
S2	0.36063(11)	0.20316(13)	0.26394(9)	0.0626(5)
C1B	0.1396(3)	0.1817(5)	0.3597(3)	0.0458(11)
C2B	0.0909(4)	0.0778(5)	0.3393(3)	0.0567(14)
C3B	0.1217(5)	-0.0296(6)	0.3304(4)	0.0693(18)
C4B	0.2004(5)	-0.0361(6)	0.3402(4)	0.0720(19)
C5B	0.2476(5)	0.0673(6)	0.3587(4)	0.0671(17)
C6B	0.2194(4)	0.1748(5)	0.3700(4)	0.0562(14)
C7B	0.1091(3)	0.2977(5)	0.3726(3)	0.0446(11)
C8B	0.1071(3)	0.4842(5)	0.3998(3)	0.0489(12)
C9B	-0.0282(4)	0.4718(6)	0.4000(3)	0.0537(13)
C10B	-0.0883(4)	0.5784(5)	0.2849(3)	0.0555(14)
C11B	-0.1703(4)	0.6248(5)	0.2249(3)	0.0603(16)
C12B	-0.1514(3)	0.3937(5)	0.2905(3)	0.0506(13)
C13B	-0.2357(4)	0.4367(6)	0.2302(3)	0.0527(13)
C14B	-0.3080(4)	0.5726(6)	0.1245(3)	0.0621(16)
C15B	-0.3606(4)	0.4803(5)	0.0706(3)	0.0502(13)
C16B	-0.3531(4)	0.4577(6)	0.0106(3)	0.0592(15)
C17B	-0.4068(5)	0.3771(7)	-0.0424(4)	0.0697(18)
C18B	-0.4654(4)	0.3170(6)	-0.0349(4)	0.0680(18)
C19B	-0.4743(4)	0.3371(6)	0.0238(3)	0.0612(16)
C20B	-0.4220(4)	0.4172(6)	0.0764(3)	0.0568(14)
N1B	0.0415(3)	0.4236(4)	0.3960(2)	0.0505(11)
N2B	0.0420(3)	0.3026(4)	0.3782(2)	0.0504(11)
N3B	0.1491(3)	0.4048(4)	0.3839(2)	0.0480(10)
N4B	-0.1029(3)	0.4981(4)	0.3314(2)	0.0487(10)
N5B	-0.2253(3)	0.5236(4)	0.1821(2)	0.0465(10)
S1	0.13098(11)	0.63352(15)	0.42328(11)	0.0699(5)

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Fig. 1 The schematic diagram of the title compound.

Fig. 2 The molecular structure of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 40% probability.

Table 3 Selected geometric parameters (Å)

C7A N2A 1.313(7)	C8A N3A 1.341(7)	C8A S2 1.702(6)
N1A N2A 1.364(6)	C7B N2B 1.318(7)	C8B N3B 1.329(7)
C8B S1 1.710(6)	N1B N2B 1.387(6)	

in EtOH (20 mL) was added an equimolar quantity of benzylpiperazine, and then 35% aqueous formaldehyde (0.3 mL). The reaction mixture was refluxed over a water-bath for 2 h and cooled to room temperature. The resulting precipitate was filtered and recrystallized from ethanol.

The structure was solved by direct methods with SHELXS-97³ and refined by full-matrix least-squares procedures on F^2 , using the program SHELXL-97.³ All non-hydrogen atoms were refined anisotropically. All hydrogen atom positions were refined using a riding model. Since the quality of the examined crystal was poor, the index values of R (0.1045) and wR (0.3612) are not good enough for a crystallographic solution.

The molecular structure of (Fig. 1) has two crystallographically independent molecules in the asymmetric unit (Fig. 2); selected bond lengths are given in Table 3. The compound crystallizes in the space group $P2_1/c$ with $Z' = 2$, and the hydrogen bonding was analyzed with the aid of PLATON.⁴ The N2A–C7A and N2B–C7B bond lengths are indicative of a significant double-bond character, respectively (Table 3).

Atom N3A in the reference molecule at (x, y, z) acts as a hydrogen-bond donor *via* H3AA, respectively, to atom N5Aⁱ, and thus forms a centrosymmetric $R_2^2(18)$ [A].⁵ Similarly, atom N3B acts as hydrogen-bond donor *via* H3BB to N5Bⁱⁱ, so as to form a second centrosymmetric ring motif, this time of the $R_2^2(18)$ [B] type. The propagation of C–H...S hydrogen-bonds thus forms a chain of edge-fused $R_2^2(18)$ [A] and $R_2^2(18)$ [B] rings running parallel to [100], generated by translation. The interlinked $C_3^3(12)$ antiparallel chains along the a -axis are formed through C13B–H133...S2ⁱⁱ, N3B–H3BB...N5Bⁱⁱ and C13Bⁱⁱ–H133ⁱⁱⁱ...S2 interactions [symmetry codes in Table 4]. Similarly, interlinked $C_3^3(22)$ antiparallel chains along the c -axis are formed through C18B–H18B...N2Aⁱⁱⁱ, N3B–H3BB...N5Bⁱⁱ and C18Bⁱⁱ–H18Bⁱⁱⁱ...N2A^{vii} [symmetry code: (vii) = $1-x, -y, 1-z$] interactions. Hence, the combination of the $C_3^3(12)$, $C_3^3(22)$ and $R_2^2(18)$ motifs generates a sheet containing $R_2^2(18)$, $R_4^4(26)$ and $R_8^8(54)$ rings, alternating in a checker-board fashion (Fig. 3).

In the extended structure, there are also π - π and π -ring

Fig. 3 A stereo view of part of the crystal structure of (I), showing the formation of a hydrogen-bonded sheet built from $R_2^2(18)$, $R_4^4(26)$ and $R_8^8(54)$ rings. H atoms not involved in these interactions and phenyl rings have been omitted for clarity.

Table 4 Hydrogen-bond geometry (Å)

D–H...A	D–H	H...A	D...A	D–H...A
N3A–H3AA...N5A ⁱ	0.86	2.01	2.769(6)	146
N3B–H3BB...N5B ⁱⁱ	0.86	2.10	2.794(7)	138
C13B–H133...S2 ⁱⁱ	0.97	2.83	3.511(6)	128
C18B–H18B...N2A ⁱⁱⁱ	0.93	2.53	3.425(8)	163
C6A–H6A...Cg3 ⁱ	0.93	2.71	3.581(8)	156
C13A–H131...Cg2 ^{iv}	0.97	2.80	3.576(6)	138
C6B–H6B...Cg4 ^v	0.93	3.14	4.009(7)	157
C13B–H134...Cg1 ⁱ	0.97	2.93	3.880(7)	166
C17B–H17B...Cg1 ^{vi}	0.93	3.00	3.870(9)	157

Cg1=C1A–C6A; Cg2=C1B–C6B; Cg3=C15A–C20A; Cg4=C15B–C20B (i) = $-x+1, y, -z+1/2$, (ii) = $-x, y, -z+1/2$, (iii) = $x-1, -y, z-1/2$, (iv) = $-x, -y+1, -z$, (v) = $-x, y, -z+1/2$, (vi) = $-x+1, -y+1, -z+1$

interactions. An intermolecular π - π contact occurs between the two symmetry-related phenyl rings (Cg3) of neighboring molecules. Ring Cg3 is oriented in such a way that the perpendicular distance from Cg3 to Cg3^{viii} is 3.347 Å [symmetry code: (viii) = $-x, 2-y, -z$]. The distance between the ring centroids is 3.721(4) Å. Similarly, the other two symmetry-related phenyl rings, Cg4 and Cg4^{vi}, also form an intermolecular π - π contact. Rings Cg4 and Cg4^{vi} are oriented in such a way that the perpendicular distance from Cg4 to Cg4^{vi} is 3.295 Å. The distance between the ring centroids is 3.674(4) Å. The compound also contains five intermolecular C–H... π interactions between rings Cg1, Cg2, Cg3 and Cg4. The details of these interactions are given in Table 4. Intermolecular hydrogen bonds and C–H... π interactions produce $R_2^2(10)$, $R_3^3(19)$ and $R_6^6(37)$ rings.

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