Three 1,2,4-triazole derivatives containing subtituted benzyl and benzylamino groups

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The title compounds, 4-benzylamino-3-(4-methylbenzyl)-1H-1,2,4-triazol-5(4H)-one, $C_{17}H_{18}N_4O$, (I), 3-(4-methylbenzyl)-4-(4-methylbenzylamino)-1H-1,2,4-triazol-5(4H)-one, $C_{18}H_{20}N_4O$, (II), and 3-(4-chlorobenzyl)-4-(4-methylbenzylamino)-1H-1,2,4-triazol-5(4H)-one, $C_{17}H_{17}ClN_4O$, (III), were obtained from the corresponding Schiff base in the presence of diglyme and NaBH$_4$. Each compound contains a 1,2,4-triazole ring and two benzene rings, which are essentially planar. The molecules are linked by a combination of intermolecular N—H⋯O and N—H⋯N hydrogen bonds. Additionally, there is a weak π–π stacking interaction in (I), involving the benzene ring of the aminobenzyl group and the partially aromatic 1,2,4-triazole moiety, with a centroid–centroid distance of 3.7397 (10) Å.

Comment

1,2,4-Triazole and its derivatives have been used as starting materials for the synthesis of many heterocycles (Desenko, 1995). Substituted 1,2,4-triazoles have also been used as ligands to obtain metal complexes with specific properties (Kaszuwara *et al.*, 1992; Prins *et al.*, 1996; Drabent *et al.*, 2004). Studies indicate that the 1,2,4-triazole moiety is associated with anticorrosion (Al-Kharafi *et al.*, 1986) and anti-inflammatory action (Gupta & Bhargava, 1978), and also with pharmacological activities, such as antiviral, analgesic, anti-microbial, antidepressant and antifungal effects (Jones *et al.*, 1965; Sughen & Yoloye, 1978; Cansiz *et al.*, 2001; Kane *et al.*, 1988; Massa *et al.*, 1992). As a contination of our studies of the structural analysis of Schiff-base-containing substituted 1,2,4-triazole derivatives (Arslan *et al.*, 2004; Yilmaz *et al.*, 2004), we report here the crystal and molecular structures of three sub-stituted 1,2,4-triazole compounds, namely 3-(4-methylbenzyl)-4-benzylamino-1H-1,2,4-triazol-5(4H)-one, (I), 3-(4-methyl-benzyl)-4-(4-methylbenzylamino)-1H-1,2,4-triazol-5(4H)-one, (II), and 3-(4-chlorobenzyl)-4-(4-methylbenzylamino)-1H-1,2,4-triazol-5(4H)-one, (III), which are expected to exhibit pharmacological properties and act as suitable ligands in coordination chemistry. The title compounds were obtained from the corresponding Schiff base in the presence of diglyme and NaBH$_4$.
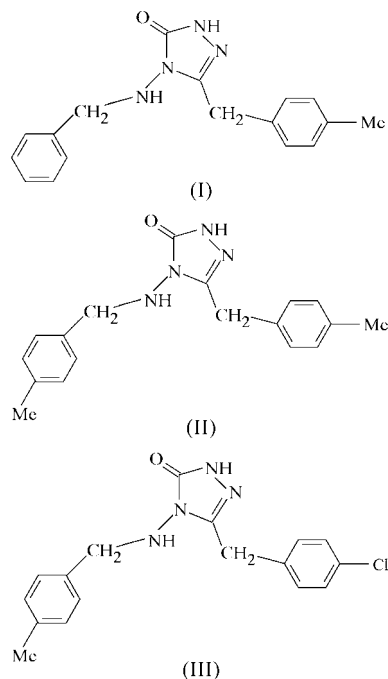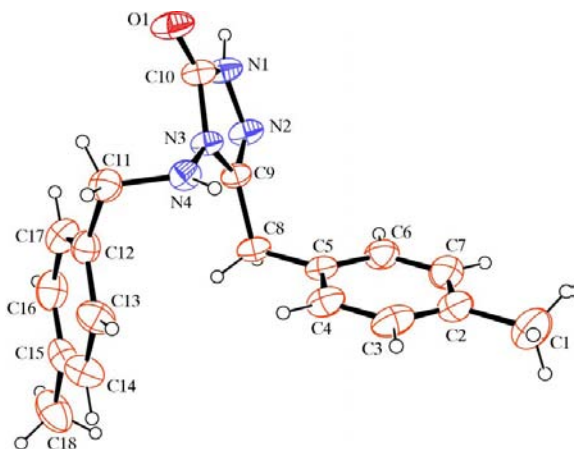

Views of the molecules of compounds (I)–(III), including the atom-numbering schemes, are shown in Figs. 1–3. Compounds (I)–(III) consist mainly of three bonded planar rings, namely a triazole ring (A), a benzyl benzene ring (B) and a benzylamino benzene ring (C). The r.m.s. deviations for rings A, B and C are 0.007, 0.004 and 0.001 Å, respectively, in
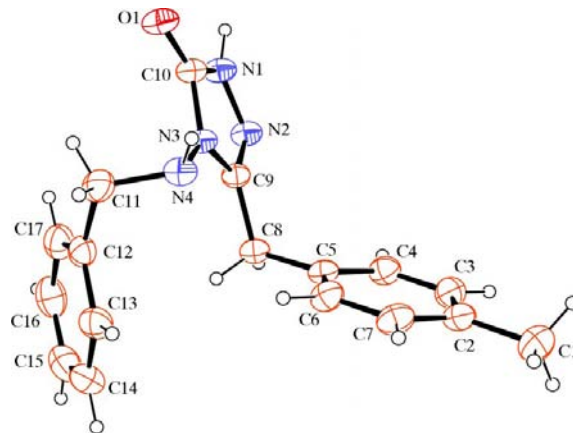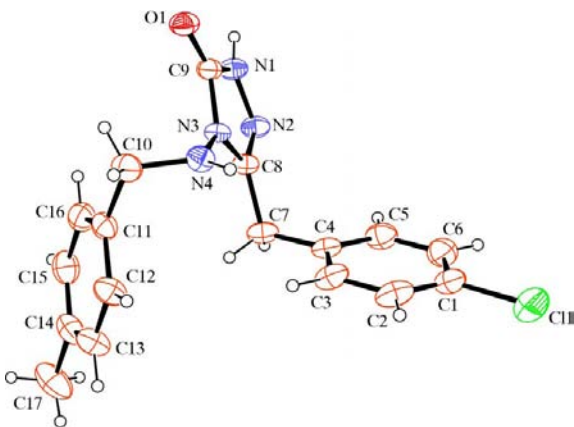

Figure 1
The molecule of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 40% probability level and H atoms are shown as small spheres of arbitrary radii.

organic compounds

(I), 0.002, 0.002 and 0.007 Å in (II), and 0.001, 0.005 and 0.002 Å in (III). The molecules of (I)–(III) adopt similar conformations (Figs. 1–3). The dihedral angles between rings *A*/*B* and *A*/*C* are 62.05 (5) and 46.44 (5)°, respectively, in (I), 69.99 (10) and 44.89 (10)° in (II), and 67.58 (12) and 49.48 (10)° in (III). A non-planar disposition of the three rings has been observed in similar 1,2,4-triazole derivatives (Zhu *et al.*, 2000; Bruno *et al.*, 2003; Arslan *et al.*, 2004; Yilmaz *et al.*, 2004). The slightly different rotations of these rings may be due to stacking interactions of the 1,2,4-triazole moiety. The orientation of the rings obviously leaves atom N2 available as a possible metal coordination site, together with the adjacent atoms N1, N3 and N4. The coordinating and pharmacologically active fragments are connected to an aromatic spacer (the benzyl group), controlling the distance between the sites and also allowing a possible electronic coupling. However, the C8—C9 bonds in (I) and (II) [C7—C8 in (III)] are almost the same length, thus confirming the absence of important conjugation effects.

The five-membered triazole rings in (I)–(III) have the same planar geometry as all similar fragments reported in the Cambridge Structural Database (*ConQuest*, Version 3.6; Allen, 2002). The interatomic distances within the triazole rings of (I)–(III) are not equal, ranging from 1.287 (4) to 1.394 (3) Å, but similar bonds display comparable bond lengths and angles, as listed in Tables 1–3. The C9—N2 bonds in (I) and (II) [C8—N2 in (III)] is the only double bond, being much shorter than the other C—N bonds in the triazole ring. On the other hand, the C11—N4 bond in (I) and (II) [C10—N4 in (III)] has single-bond character and is significantly longer than the C—N bonds in the ring. The remaining bond lengths in (I)–(III) show no unusual values. The N3—N4—C11—C12 methylamine system in (I) and (II) [N3—N4—C10—C11 in (III)] is not planar, as evidenced by the torsion angles, which have a mean value of 75 (1)°. However, the same fragment with a C═N double bond in a 1,2,4-triazole derivative was reported to be planar (Bruno *et al.*, 2003).
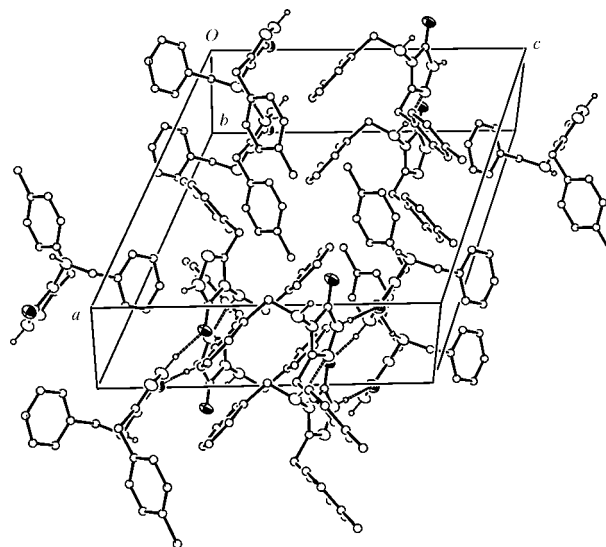

Figure 2
The molecule of (II), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 40% probability level and H atoms are shown as small spheres of arbitrary radii.
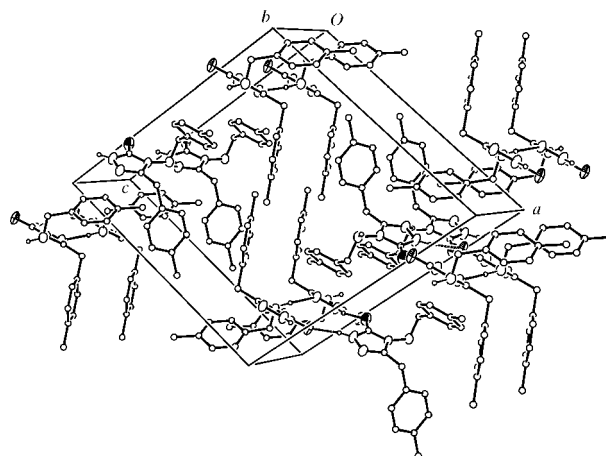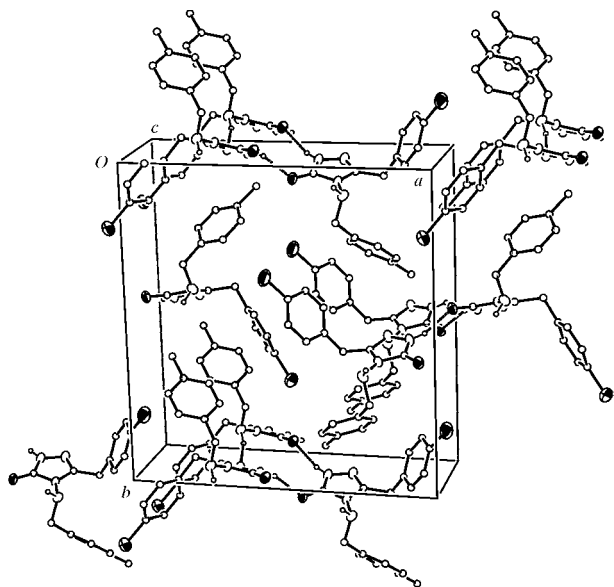

Figure 3
The molecule of (III), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 40% probability level and H atoms are shown as small spheres of arbitrary radii.

Figure 4
A packing diagram for (I). H atoms bound to C atoms have been omitted for clarity.

Figure 5
A packing diagram for (II). H atoms bound to C atoms have been omitted for clarity.

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0697P)^2]$
$R[F^2 > 2\sigma(F^2)] = 0.039$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.106$	$(\Delta/\sigma)_{max} = 0.008$
$S = 0.93$	$\Delta\rho_{max} = 0.15$ e Å^{-3}
3008 reflections	$\Delta\rho_{min} = -0.20$ e Å^{-3}
209 parameters	Extinction correction: *SHELXL97*
H atoms treated by a mixture of	(Sheldrick, 1997)
independent and constrained	Extinction coefficient: 0.020 (2)
refinement	

Table 1
Selected geometric parameters (Å, °) for (I).

C8—C9	1.4875 (18)	C11—N4	1.476 (2)
C9—N2	1.3004 (17)	C11—C12	1.497 (2)
C9—N3	1.3625 (17)	N1—N2	1.3911 (17)
C10—N1	1.3390 (19)	N3—N4	1.4069 (16)
C10—N3	1.3825 (16)		
N2—C9—N3	110.59 (11)	C10—N1—N2	112.41 (11)
N1—C10—N3	103.36 (11)	C9—N3—C10	108.87 (11)
N4—C11—C12	110.77 (12)	N3—N4—C11	111.08 (12)
C12—C11—N4—N3	75.04 (15)		

Table 2
Hydrogen-bond geometry (Å, °) for (I).

D—H⋯A	D—H	H⋯A	D⋯A	D—H⋯A
N1—H1⋯O1^i	0.97 (2)	1.81 (2)	2.7676 (15)	169.9 (18)
N4—H4A⋯N2^{ii}	0.888 (18)	2.236 (19)	3.0933 (18)	162.2 (15)

Symmetry codes: (i) $-x, y + \frac{1}{2}, -z + \frac{3}{2}$; (ii) $x, y - 1, z$.

Figure 6
A packing diagram for (III). H atoms bound to C atoms have been omitted for clarity.

The packing of the molecules in (I)–(III) are shown in Figs. 4–6. Analysis of the crystal packing of the title compounds reveals that the molecules are linked by means of similar intermolecular N—H⋯O and N—H⋯N hydrogen bonds (Tables 4–6). It seems that the N—H⋯O hydrogen bonds are stronger than the N—H⋯N interactions. In contrast with (II) and (III), in (I), a weak π–π stacking interaction between the benzene ring of the aminobenzyl group and the partially aromatic 1,2,4-triazole ring is observed [Cg⋯$Cg(x, \frac{3}{2} - y, \frac{1}{2} + z) = 3.7397$ (10) Å]. Similar interactions in (II) and (III) are longer than 4.5 Å.

Experimental

The syntheses and characterizations of the title compounds have been reported elsewhere by Kahveci & Ikizler (2000). Single crystals suitable for X-ray measurements were obtained by crystallization from ethyl acetate in each case.

Compound (I)

Crystal data

$C_{17}H_{18}N_4O$	Mo $K\alpha$ radiation
$M_r = 294.35$	Cell parameters from 12 405
Monoclinic, $P2_1/c$	reflections
$a = 17.0906$ (13) Å	$\theta = 1.3$–26.0°
$b = 5.9866$ (3) Å	$\mu = 0.08$ mm^{-1}
$c = 15.6784$ (15) Å	$T = 293$ (2) K
$\beta = 108.496$ (7)°	Prismatic, colourless
$V = 1521.3$ (2) Å^3	$0.49 \times 0.43 \times 0.19$ mm
$Z = 4$	
$D_x = 1.285$ Mg m^{-3}	

Data collection

Stoe IPDS-2 diffractometer	$R_{int} = 0.053$
Rotation scans	$\theta_{max} = 26.1°$
20 832 measured reflections	$h = -21 \rightarrow 21$
3008 independent reflections	$k = -7 \rightarrow 7$
2054 reflections with $I > 2\sigma(I)$	$l = -19 \rightarrow 19$

Compound (II)

Crystal data

$C_{18}H_{20}N_4O$	Mo $K\alpha$ radiation
$M_r = 308.38$	Cell parameters from 9419
Monoclinic, $P2_1/c$	reflections
$a = 16.8511$ (19) Å	$\theta = 1.2$–25.0°
$b = 5.996$ (5) Å	$\mu = 0.08$ mm^{-1}
$c = 17.650$ (2) Å	$T = 293$ (2) K
$\beta = 109.403$ (9)°	Prismatic, colourless
$V = 1682.0$ (14) Å^3	$0.50 \times 0.44 \times 0.40$ mm
$Z = 4$	
$D_x = 1.218$ Mg m^{-3}	

Data collection

Stoe IPDS-2 diffractometer	1482 reflections with $I > 2\sigma(I)$
Rotation scans	$R_{int} = 0.092$
Absorption correction: integration	$\theta_{max} = 26.0°$
(*X-RED32*; Stoe & Cie, 2002)	$h = -20 \rightarrow 20$
$T_{min} = 0.962$, $T_{max} = 0.987$	$k = -7 \rightarrow 7$
22 631 measured reflections	$l = -21 \rightarrow 21$
3284 independent reflections	

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.021P)^2]$
$R[F^2 > 2\sigma(F^2)] = 0.041$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.078$	$(\Delta/\sigma)_{max} < 0.001$
$S = 0.97$	$\Delta\rho_{max} = 0.12$ e Å^{-3}
3284 reflections	$\Delta\rho_{min} = -0.14$ e Å^{-3}
214 parameters	Extinction correction: *SHELXL97*
H atoms treated by a mixture of	(Sheldrick, 1997)
independent and constrained	Extinction coefficient: 0.0090 (7)
refinement	

Table 3
Selected geometric parameters (Å, °) for (II).

C8—C9	1.486 (2)	C11—N4	1.476 (2)
C9—N2	1.298 (2)	C11—C12	1.506 (3)
C9—N3	1.369 (2)	N1—N2	1.3858 (18)
C10—N1	1.342 (2)	N3—N4	1.407 (2)
C10—N3	1.382 (2)		
N2—C9—N3	110.23 (16)	C9—N2—N1	105.11 (15)
N1—C10—N3	103.13 (16)	C9—N3—C10	108.97 (15)
N4—C11—C12	110.60 (16)	N3—N4—C11	110.56 (15)
C10—N1—N2	112.55 (15)		
C12—C11—N4—N3	77.5 (2)		

Table 4
Hydrogen-bond geometry (Å, °) for (II).

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
N1—H1$\cdots$O1^i	0.86	1.91	2.740 (2)	163
N4—H4$A\cdots$N2^{ii}	0.95 (2)	2.12 (2)	3.011 (3)	154.3 (17)

Symmetry codes: (i) $-x, y + \frac{1}{2}, -z + \frac{3}{2}$; (ii) $x, y - 1, z$.

Compound (III)

Crystal data

$C_{17}H_{17}ClN_4O$	Mo $K\alpha$ radiation
$M_r = 328.80$	Cell parameters from 18 401
Orthorhombic, $Pna2_1$	reflections
$a = 16.5043$ (10) Å	$\theta = 1.2$–25.9°
$b = 17.4355$ (13) Å	$\mu = 0.23$ mm^{-1}
$c = 5.919$ (3) Å	$T = 293$ (2) K
$V = 1703.1$ (9) Å^3	Prism, colourless
$Z = 4$	$0.50 \times 0.38 \times 0.17$ mm
$D_x = 1.282$ Mg m^{-3}	

Data collection

Stoe IPDS-2 diffractometer	$R_{int} = 0.117$
Rotation scans	$\theta_{max} = 25.9°$
22 931 measured reflections	$h = -20 \rightarrow 20$
3228 independent reflections	$k = -21 \rightarrow 21$
1815 reflections with $I > 2\sigma(I)$	$l = -6 \rightarrow 7$

Table 5
Selected geometric parameters (Å, °) for (III).

C7—C8	1.489 (2)	C10—N4	1.473 (3)
C8—N2	1.288 (2)	C10—C11	1.498 (3)
C8—N3	1.365 (2)	N1—N2	1.389 (2)
C9—N1	1.332 (2)	N3—N4	1.400 (2)
C9—N3	1.387 (2)		
N2—C8—N3	111.39 (15)	C9—N1—N2	112.95 (16)
N1—C9—N3	103.22 (18)	C8—N3—C9	108.10 (17)
N4—C10—C11	111.12 (16)	N3—N4—C10	111.39 (16)
C11—C10—N4—N3	−76.2 (2)		

Table 6
Hydrogen-bond geometry (Å, °) for (III).

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
N1—H1$\cdots$O1^i	0.86	1.93	2.7349 (19)	156
N4—H4$\cdots$N2^{ii}	0.92 (2)	2.13 (2)	2.990 (3)	156.2 (19)

Symmetry codes: (i) $-x, -y + 1, z + \frac{1}{2}$; (ii) $x, y, z - 1$.

Refinement

Refinement on F^2	$(\Delta/\sigma)_{max} = 0.005$
$R[F^2 > 2\sigma(F^2)] = 0.031$	$\Delta\rho_{max} = 0.14$ e Å^{-3}
$wR(F^2) = 0.053$	$\Delta\rho_{min} = -0.13$ e Å^{-3}
$S = 0.74$	Extinction correction: SHELXL97
3228 reflections	Extinction coefficient: 0.0251 (10)
213 parameters	Absolute structure: Flack (1983),
H atoms: see below	with 1395 Friedel pairs
$w = 1/[\sigma^2(F_o^2) + (0.0002P)^2]$	Flack parameter: 0.12 (7)
where $P = (F_o^2 + 2F_c^2)/3$	

The amine H atoms in (I) were refined freely, whereas in (II) and (III), the H atom on N1 was placed in a calculated position, while the H atom on N4 was refined freely. Other H atoms were placed in calculated positions, with C—H distances in the range 0.93–0.97 Å and with U_{iso}(H) = $1.2U_{eq}$(C). The methyl H atoms were not well resolved and no great reliance should be placed on their reported coordinates.

For all compounds, data collection: X-AREA (Stoe & Cie, 2002); cell refinement: X-AREA; data reduction: X-RED32 (Stoe & Cie, 2002); structure solution: SHELXS97 (Sheldrick, 1997); structure refinement: SHELXL97 (Sheldrick, 1997); molecular graphics: ORTEP-3 (Farrugia, 1997); publication software: SHELXL97.

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