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N—H···N and C—H···π interactions in 4-amino-3-methyl-5-(*p*-tolyl)-4*H*-1,2,4-triazole and 4-amino-3-methyl-5-phenyl-4*H*-1,2,4-triazole

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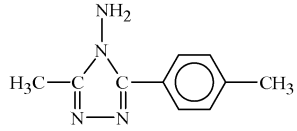
The title compounds, $C_{10}H_{12}N_4$, (I), and $C_9H_{10}N_4$, (II), have been synthesized and characterized both spectroscopically and structurally. The dihedral angles between the triazole and benzene ring planes are 26.59 (9) and 42.34 (2)°, respectively. In (I), molecules are linked principally by N—H···N hydrogen bonds involving the amino NH_2 group and a triazole N atom, forming $R_4^4(20)$ and $R_2^4(10)$ rings which link to give a three-dimensional network of molecules. The hydrogen bonding is supported by two different C—H···π interactions from the tolyl ring to either a triazole ring or a tolyl ring in neighboring molecules. In (II), intermolecular hydrogen bonds and C—H···π interactions produce $R_3^4(15)$ and $R_4^4(21)$ rings.

Comment

1,2,4-Triazole and its derivatives belong to a class of exceptionally active compounds possessing a wide spectrum of biological properties, including anti-inflammatory, antifungal, antiviral (Mahomed *et al.*, 1993; Massa *et al.*, 1992; Mullican *et al.*, 1993), analgesic, anticonvulsant and antidepressant activities (Bradbury & Rivett, 1991; Sughen & Yoloye, 1978; Kane *et al.*, 1988). Some of these compounds are also known to exhibit anticancer activity, *e.g.* anastrozole, or 2,2′-[5-(1*H*-1,2,4-triazol-1-ylmethyl)-1,3-phenylene]bis(2-methylpropionitrile), and letrozole, or 1-[bis(4-cyanophenyl)methyl]-1,2,4-triazole (Bonte, 2000; Lønning, 1996, 2001). These completely selective and well tolerated modern, orally active, non-steroidal aromatase inhibitors are being used increasingly in the treatment of advanced breast cancer in postmenopausal women. Apart from their pharmacological significance, 1,2,4-triazole derivatives exhibit interesting chemical properties. The ability of triazoles to form a bridge between metal ions makes such ligands very important for magnetochemical applications. Some complexes containing substituted 1,2,4-triazole ligands have potential uses as optical sensors or molecular-based memory devices (Kahn & Martinez, 1998; Garcia *et al.*, 1997). In spite of the chemical and medicinal importance of this class of compounds, relatively few crystal structure determinations of 1,2,4-triazole derivatives have been reported (Cambridge Structural Database, Version 5.27 of November 2005; Allen, 2002). In addition to the X-ray structure determination reported here, the title compound, (I), has also been characterized by IR, ^{1}H NMR and ^{13}C NMR spectroscopies and by elemental analysis.



Compound (I) consists of a 1,2,4-triazole ring with methyl, amino and *p*-tolyl substituents at the 3-, 4- and 5-positions, respectively (Fig. 1). Least-squares mean-plane calculations for the triazole (N1/N2/C3/N4/C5) and benzene (C1*P*–C6*P*) rings show that these are approximately planar, with respective maximum deviations of 0.0027 (10) Å for atom C5 and 0.0066 (11) Å for atom C1*P*, the two atoms forming the external bond linking the two rings. The dihedral angle between the triazole and benzene ring planes is 26.59 (9)°.

The N4—N4*A* bond length (Table 1) is similar to the corresponding distance in 4-amino-3,5-bis(4-pyridyl)-1,2,4-triazole [1.411 (4) Å; Guo & Du, 2002]. The C3═N2 and C5═N1 distances are in good agreement with those found for structures containing the 1,2,4-triazole ring [see, for example, Özbey *et al.* (2000) and Zhu *et al.* (2000)]. The N1—N2 bond length is elongated to 1.3859 (19) Å; this value is comparable

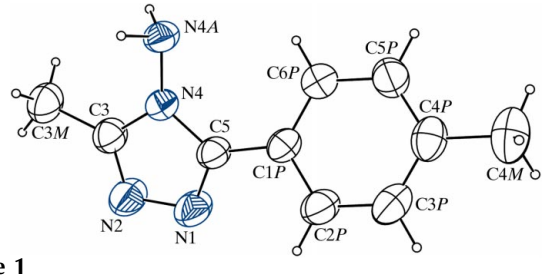


Figure 1
A view of (I), showing the atom-numbering scheme and 40% probability displacement ellipsoids.

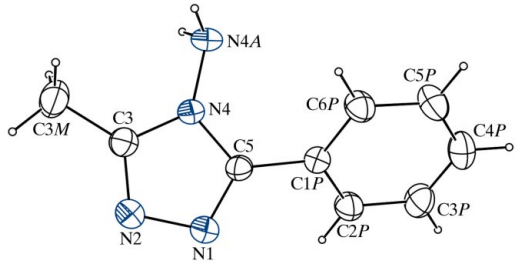


Figure 2
A view of (II), showing the atom-numbering scheme and 40% probability displacement ellipsoids.

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to those observed in 1-methyl-3,5-diphenyl-1*H*-1,2,4-triazole (Yazıcı *et al.*, 2004).

Compound (II) consists of a 1,2,4-triazole ring with methyl, amino and phenyl substituents at the 3-, 4- and 5-positions, respectively (Fig. 2). The 1,2,4-triazole (N1/N2/C3/N4/C5) and phenyl (C1*P*–C6*P*) rings are approximately planar, the respective maximum deviations from the least-squares planes being 0.0028 (10) Å for atom C5 and 0.0056 (15) Å for atom C3*P*. The dihedral angle between these planes 42.34 (2)°. The N1—N2 bond length (Table 3) agrees with the corresponding distance in 3,6-bis(2-chlorophenyl)-1,4-dihydro-1,2,4,5-tetrazine [1.395 (3) Å; Zachara *et al.*, 2004].

Molecules are linked by intermolecular hydrogen bonding, and we employ graph-set notation (Bernstein *et al.*, 1995) to describe the patterns of hydrogen bonding. In (I), the arrangement of the interactions (Fig. 3 and Table 2) can be described by the graph-set notation $R_4^4(20)$. The interlinking interactions are described by the notation $R_2^4(10)$. The combined effect of the linked $R_4^4(20)$ and $R_2^4(10)$ motifs is to generate a three-dimensional network of molecules.

In (II), the one-dimensional assemblies formed by hydrogen bonding are enforced by weaker intermolecular interactions. N—H···N contacts are observed along the main chains, between the 4-amino-1,2,4-triazole rings of adjacent molecules. Amino atom N4*A* in the molecule at (*x*, *y*, *z*) acts as a hydrogen-bond donor, *via* H4*AB*, to atom N1 in the molecule at (*x* − 1, *y*, *z*), while atom N4*A* at (*x* − 1, *y*, *z*), in turn, acts as

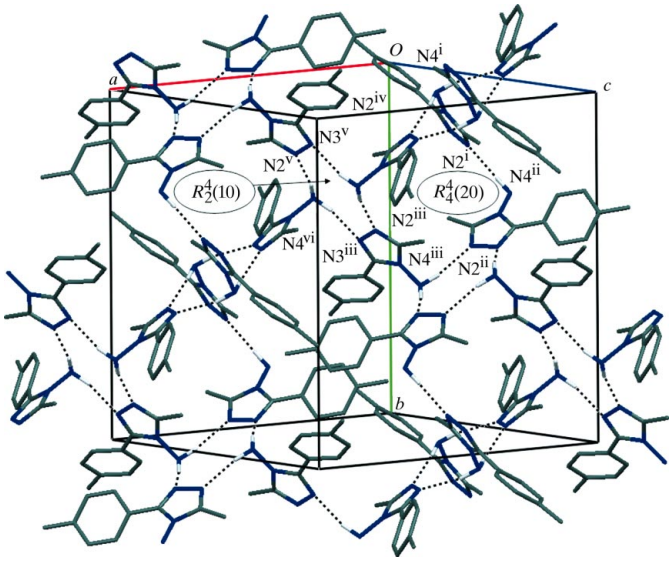

Figure 3
A view, parallel to (101), of the three-dimensional hydrogen-bonding network in (I). Dashed lines indicate N—H···N hydrogen bonds. H atoms not involved in these interactions have been omitted for clarity. [Symmetry codes: (i) *x*, *y* − 1, *z*; (ii) $y-\frac{3}{4}, -x+\frac{3}{4}, -z+\frac{7}{4}$; (iii) $-x+1, -y+\frac{3}{2}, z$; (iv) $-y+\frac{7}{4}, x-\frac{1}{4}, -z+\frac{7}{4}$; (v) $x+\frac{1}{2}, y-1, -z+\frac{3}{2}$; (vi) $y-\frac{1}{4}, -x+\frac{3}{4}, z-\frac{1}{4}$.]

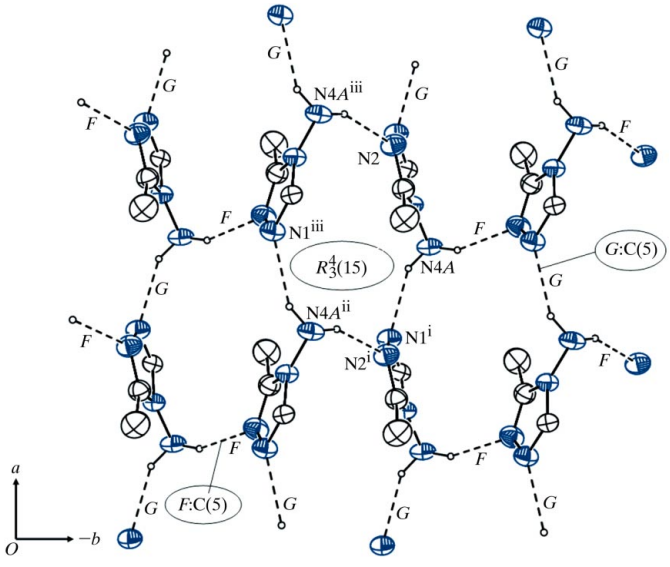

Figure 4
The packing of (II), showing the $R_3^4(15)$ ring pattern. Dashed lines indicate hydrogen bonds. H atoms not involved in these interactions and phenyl rings have been omitted for clarity. [Symmetry codes: (i) *x* − 1, *y*, *z*; (ii) $-x, y+\frac{1}{2}, -z+\frac{3}{2}$; (iii) $-x+1, y+\frac{1}{2}, -z+\frac{3}{2}$.]

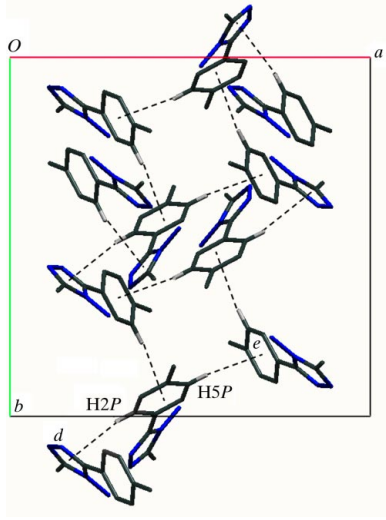

Figure 5
A view of (I), parallel to (110), showing the C—H···π interactions, between (*d*) triazole and tolyl groups, and (*e*) tolyl and tolyl groups as dashed lines. H atoms not involved in these interactions have been omitted for clarity.

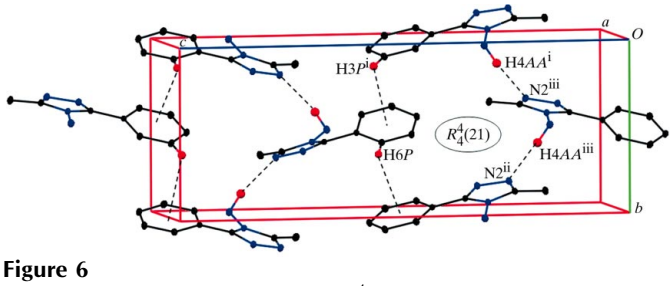

Figure 6
The packing of (II), showing the $R_4^4(21)$ ring pattern. Dashed lines indicate hydrogen bonds and C—H···π interactions. H atoms not involved in these interactions have been omitted for clarity. [Symmetry codes: (i) $x-\frac{1}{2}, -y+\frac{1}{2}, -z+1$; (ii) $x-\frac{1}{2}, -y+\frac{3}{2}, -z+1$; (iii) $-x+\frac{1}{2}, -y+1, z-\frac{1}{2}$.]

a donor to N1 at $(x-2, y, z)$. In this manner, a $C(5)$ (motif G) chain is formed, running along the a axis. The arrangement of N4A—H4AB···N1^{i}, N4A^{ii}—H4AA^{ii}···N2^{i}, N4A^{ii}—H4AB^{ii}···N1^{iii} and N4A^{iii}—H4AA^{iii}···N2 interactions [symmetry codes: (i) $x-1, y, z$; (ii) $-x, y+\frac{1}{2}, -z+\frac{3}{2}$; (iii) $-x+1, y+\frac{1}{2}, -z+\frac{3}{2}$] can be described by the graph-set notation $R_3^4(15)$. Amino atom N4A in the molecule at $(1-x, \frac{1}{2}+y, \frac{3}{2}-z)$ acts as a hydrogen-bond donor, *via* H4AA, to N2 in the molecule at (x, y, z), while N4A at (x, y, z), in turn, acts as a donor to N2 at $(1-x, y-\frac{1}{2}, \frac{3}{2}-z)$. In this manner, a $C(5)$ (motif F) chain is formed, running along the b axis (Fig. 4). The geometry of the hydrogen bonding is given in Table 4.

Compound (I) also contains two intermolecular C—H···π contacts from the 1,2,4-triazole ring to two different symmetry-related molecules (Fig. 5). The first is from atom C2P in the tolyl ring of the reference molecule to the centroid (d) of the triazole ring related by the symmetry operation $(\frac{5}{4}-y, \frac{3}{4}+x, -\frac{1}{4}+z)$ [C2P···d = 3.8088 (19) Å, H2P···d = 2.96 Å and C2P—H2P···d = 152°]. The second C—H···π contact is between C5P in the tolyl ring and the centroid (e) of the symmetry-related tolyl ring at $(-\frac{1}{4}+y, \frac{5}{4}-x, \frac{5}{4}-z)$ [C5P···e = 3.7366 (19) Å, H5P···e = 2.89 Å and C5P—H5P···e = 153°].

In (II), interlinked C3P^{i}—H3P^{i}···Ph [C3P^{i}···Ph = 3.659 (2) Å, H3P^{i}···Ph = 2.97 Å and C3P^{i}—H3P^{i}···Ph = 132°; symmetry code: (i) $x-\frac{1}{2}, -y+\frac{1}{2}, 1-z$; Ph is the centroid of the phenyl ring], C6P—H6P···Ph^{ii} [C6P···Ph^{ii} = 3.574 (2) Å, H6P···Ph^{ii} = 2.88 Å and C6P—H6P···Ph^{ii} = 133°; symmetry code: (ii) $x-\frac{1}{2}, -y+\frac{3}{2}, 1-z$], N4$A^{iii}$—H4$AA^{iii}$···N2^{ii} [symmetry code: (iii) $-x+\frac{1}{2}, -y+1, z-\frac{1}{2}$] and N4$A^{i}$—H4$AA^{i}$···N2^{iii} interactions define an $R_4^4(21)$ ring pattern (Fig. 6).

Experimental

For the preparation of (I), acyl hydrazone (0.005 mol) was added to a solution of hydrazine hydrate (0.01 mol) in 1-propanol (50 ml) and the mixture was refluxed for 24 h. On cooling, a precipitate was formed, and this product was filtered off and dried. The dry product was washed with benzene (20 ml). The insoluble part in benzene was recrystallized from 1-propanol to afford the pure compound. Recrystallization from ethyl acetate gave a white product (yield 87%). Single crystals of (I) were obtained from ethyl acetate at room temperature by slow evaporation (m.p. 488–489 K). IR (KBr, cm^{-1}): 3245–3142 (ν_{NH_2}), 1652 ($\nu_{C=N}$); ^{1}H NMR (DMSO-d_6): δ 2.38 (6H, CH_3), 6.05 (*s*, 2H, NH_2) [ar-H: 7.30 (*d*, 2H, J = 7.80 Hz), 7.92 (*d*, 2H, J = 7.80 Hz)]; ^{13}C NMR (DMSO-d_6): δ 153.06 (triazole C_3), 152.10 (triazole C5) [ar-C: 138.67, 128.81 (2C), 127.57 (2C), 124.71], 20.83 (ar-CH_3), 9.80 (CH_3). Elemental analysis calculated for $C_{10}H_{12}N_4$: C 63.81, H 6.43, N 29.76%; found: C 63.80, H 6.41, N 29.73%. For the preparation of compound (II), acyl hydrazone (0.005 mol) was added to a solution of hydrazine hydrate (0.01 mol) in 1-propanol (50 ml) and the mixture was refluxed for 24 h. On cooling, a precipitate was formed, and this product was filtered off and dried. The dry product was washed with benzene (20 ml). The insoluble part in benzene was recrystallized from 1-propanol to afford the pure compound. Recrystallization from ethyl acetate gave a white product (yield 75%). Single crystals of (II) were obtained from ethyl acetate at room temperature by slow evaporation (m.p. 467–468 K). IR (KBr, cm^{-1}): 3255–3150 (ν_{NH_2}), 1645 ($\nu_{C=N}$); ^{1}H NMR (DMSO-d_6): δ 2.40 (*s*, 3H, CH_3), 6.06 (*s*, 2H, NH_2) [ar-H: 7.40–7.70 (*m*, 3H), 8.00–8.20 (*m*, 2H)]; ^{13}C NMR (DMSO-d_6): δ 53.86 (triazole C_3), 152.33 (triazole C_5) [ar-C: 129.00, 128.22 (2C), 127.65 (2C), 127.38], 9.73 (CH_3). Elemental analysis calculated for $C_9H_{10}N_4$: C 62.05, H 5.79, N 32.16%; found: C 62.04, H 5.77, N 32.76%.

Compound (I)

Crystal data

$C_{10}H_{12}N_4$
M_r = 188.24
Tetragonal, $I4_1/a$
a = 16.4033 (11) Å
c = 15.7192 (12) Å
V = 4229.5 (5) Å^3
Z = 16
D_x = 1.182 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.08 mm^{-1}
T = 296 K
Square prism, colorless
0.66 × 0.57 × 0.51 mm

Data collection

Stoe IPDS-II diffractometer
ω scan
7427 measured reflections
2082 independent reflections
1511 reflections with $I > 2\sigma(I)$
R_{int} = 0.061
θ_{max} = 26.0°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.041
$wR(F^2)$ = 0.115
S = 1.01
2082 reflections
138 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0594P)^2 + 0.2861P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.11 e Å^{-3}
$\Delta\rho_{min}$ = −0.11 e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.0019 (6)

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

N1—N2	1.3859 (19)	N4—N4A	1.4090 (16)
N1—C5	1.3091 (19)	C1P—C5	1.4629 (19)
N2—C3	1.301 (2)		
C5—N4—N4A	125.74 (11)	C5—N1—N2	108.12 (12)
N4A—N4—C5—C1P	−5.6 (2)	C6P—C1P—C5—N4	−28.0 (2)
C6P—C1P—C5—N1	151.09 (17)		

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

D—H···A	D—H	H···A	D···A	D—H···A
N4A—H4AB···N1^{vii}	0.975 (19)	2.072 (19)	3.0269 (19)	166.2 (14)
N4A—H4AA···N2^{viii}	0.932 (19)	2.12 (2)	3.033 (2)	166.2 (15)

Symmetry codes: (vii) $y-\frac{3}{4}, -x+\frac{5}{4}, z+\frac{1}{4}$; (viii) $-y+\frac{7}{4}, x+\frac{3}{4}, -z+\frac{7}{4}$.

Compound (II)

Crystal data

$C_9H_{10}N_4$
M_r = 174.21
Orthorhombic, $P2_12_12_1$
a = 6.1062 (8) Å
b = 7.3981 (11) Å
c = 19.653 (4) Å
V = 887.8 (3) Å^3
Z = 4
D_x = 1.303 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.09 mm^{-1}
T = 296 K
Prism, colorless
0.62 × 0.52 × 0.40 mm

Data collection

Stoe IPDS-II diffractometer	1556 reflections with $I > 2\sigma(I)$
ω scan	$R_{int} = 0.080$
4368 measured reflections	$\theta_{max} = 26.0°$
1692 independent reflections	

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0683P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.040$	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2) = 0.107$	$\Delta\rho_{max} = 0.19$ e Å^{-3}
$S = 1.04$	$\Delta\rho_{min} = -0.22$ e Å^{-3}
1692 reflections	Extinction correction: *SHELXL97*
128 parameters	Extinction coefficient: 0.056 (11)
H atoms treated by a mixture of independent and constrained refinement	Absolute structure: Flack (1983), 660 Friedel pairs
	Flack parameter: 0 (2)

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

N4—N4*A*	1.4081 (18)	N1—C5	1.306 (2)
N2—C3	1.310 (2)	C1*P*—C5	1.474 (2)
N2—N1	1.396 (2)		
C5—N4—N4*A*	125.43 (13)	C5—N1—N2	107.71 (12)
C6*P*—C1*P*—C5—N1	−136.80 (19)		

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N4*A*—H4*AA*···N2^{iv}	0.95 (3)	2.19 (3)	3.078 (2)	156 (2)
N4*A*—H4*AB*···N1^{i}	0.92 (2)	2.20 (2)	3.0411 (19)	151.4 (18)

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

For both compounds, methyl H atoms were located in a difference Fourier synthesis and then refined as rigid rotating groups [C—H = 0.96 Å and U_{iso}(H) = 1.5U_{eq}(C)]. Aromatic H atoms were placed geometrically and refined using a riding model [C—H = 0.93 Å and U_{iso}(H) = 1.2U_{eq}(C)]. Atoms H4*AA* and H4*AB* bound to N4*A* were refined freely.

For both compounds, data collection: *X-AREA* (Stoe & Cie, 2002); cell refinement: *X-AREA*; data reduction: *X-RED* (Stoe & Cie, 2002); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997) and *MERCURY* (Macrae *et al.*, 2006); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: MY3010). Services for accessing these data are described at the back of the journal.

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