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7,7-Dimethyl-2-phenyl-6,7-dihydro-1,2,4-triazolo[1,5-*a*][1,3,5]triazin-5-amine

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7,7-Dimethyl-2-phenyl-6,7-dihydro-1,2,4-triazolo[1,5-*a*][1,3,5]triazin-5-amine[1]

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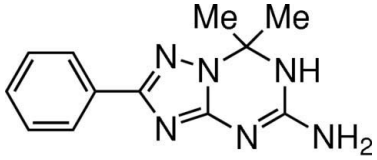
Key indicators: single-crystal X-ray study; T = 223 K; mean σ(C–C) = 0.002 Å; R factor = 0.051; wR factor = 0.126; data-to-parameter ratio = 16.2.

The title compound, $C_{12}H_{14}N_6$, was synthesized *via* cyclocondensation of 5-guanidino-3-phenyl-1,2,4-triazole with acetone. Only one tautomeric form with the NH H atom vicinal to the methyl groups was observed in the crystal structure. The triazine ring adopts a flattened half-boat conformation. The dihedral angle between the triazole and phenyl rings is 9.99 (5)°. The crystal packing is stabilized by intermolecular N—H···N hydrogen bonds which link the molecules into a chain along the *a* axis.

Related literature

The 1,2,4-triazolo[1,5-*a*][1,3,5]triazine (5-azapurine) heterocyclic system has been reviewed by Dolzhenko *et al.* (2006). For related literature, see also: Dolzhenko *et al.* (2005); Dolzhenko & Chui (2006); Dolzhenko *et al.* (2007).



Experimental

Crystal data

$C_{12}H_{14}N_6$
M_r = 242.29
Orthorhombic, *Pbca*
a = 9.9667 (6) Å
b = 12.6544 (8) Å
c = 18.9142 (12) Å
V = 2385.5 (3) Å^3
Z = 8
Mo $K\alpha$ radiation
μ = 0.09 mm^{-1}
T = 223 (2) K
0.38 × 0.38 × 0.22 mm

Data collection

Bruker SMART APEX CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2001)
T_{min} = 0.923, T_{max} = 0.981
15692 measured reflections
2732 independent reflections
2345 reflections with $I > 2\sigma(I)$
R_{int} = 0.032

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.051
$wR(F^2)$ = 0.126
S = 1.11
2732 reflections
169 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.24 e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N4—H4N···N5^{i}	0.88 (2)	2.10 (2)	2.9768 (17)	176 (2)
N6—H6B···N1^{i}	0.87	2.07	2.9113 (18)	163

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

Data collection: *SMART* (Bruker, 2003); cell refinement: *SAINT* (Bruker, 2003); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 2003); software used to prepare material for publication: *SHELXTL*.

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: CI2379).

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supplementary materials

Acta Cryst. (2007). E**63**, o2796 [**doi:10.1107/S1600536807021009**]

7,7-Dimethyl-2-phenyl-6,7-dihydro-1,2,4-triazolo[1,5-*a*][1,3,5]triazin-5-amine

A. V. Dolzhenko, G. K. Tan, L. L. Koh, A. V. Dolzhenko and W. K. Chui

Comment

4,6-Diamino-1,2-dihydro-1,3,5-triazines, such as antimalarial drug cycloguanil and WR 99210 (Fig. 1) are known to be potent inhibitors of dihydrofolate reductase (DHFR). Our laboratory has been working on the fused *s*-triazines as DHFR inhibitors in the search for potential antibacterial, antiparasitic and anticancer agents (Dolzhenko *et al.*, 2005, Dolzhenko & Chui, 2006). The 5-aza-analogues of purine heterocyclic system, *viz.* 1,2,4-triazolo[1,5-*a*][1,3,5]triazines has been shown to possess a wide range of biological activities (Dolzhenko, Dolzhenko & Chui, 2006), therefore we became interested in using this nucleus as a skeleton for the construction of potential DHFR inhibitors (Dolzhenko *et al.*, 2007).

5-Amino-6,7-dihydro[1,2,4]triazolo[1,5-*a*][1,3,5]triazine (I) which shares some structural similarity with the *gem*-dimethyl substituted antifolate triazines (Fig. 1) was synthesized and its structural investigation was carried out in order to facilitate further molecular modeling and docking studies. Theoretically, four tautomeric forms are possible for the synthesized compound due to annular tautomerism (Fig. 2). However, only one form namely 5-amino-7,7-dimethyl-2-phenyl-6,7-dihydro[1,2,4]triazolo[1,5-*a*][1,3,5]\ triazine (Fig. 3) was observed in the crystal.

The triazine ring of the fused heterocyclic core adopts a half-boat conformation, with atoms C9 and N5 at the bow and stern. The angle between the flagpole and bowsprit methyl groups is 111.33 (13)°. The mean planes of the triazole (N1/C7/N2—N3/C8) and phenyl (C1—C6) rings make a dihedral angle of 9.99 (5)°. The N4—C10, N5—C10 and N6—C10 bond distances are similar that suggests guanidine-like electron delocalization in the N4—N6/C10 fragment of the molecule. The crystal packing is stabilized by intermolecular N—H···N hydrogen-bonds (Table 1) which link the molecules into a chain along the *a* axis.

Experimental

5-Guanidino-3-phenyl-1,2,4-triazole (0.50 g, 2.5 mmol) was heated under reflux in acetone (8 ml) containing piperidine (0.05 ml, 0.5 mmol) for 18 h. After cooling, the precipitated solid was filtered, washed with acetone and recrystallized from ethanol (m.p. 567 K).

Refinement

Atom H4N was located in a difference map and refined isotropically. The remaining H atoms were placed in calculated positions (N—H = 0.87 Å and C—H = 0.94 or 0.97 Å), and included in the final cycles of refinement using a riding model, with U_{iso}(H) = 1.2U_{eq}(C, N) or 1.5U_{eq}(methyl C). A rotating group model was used for the methyl groups.

Figures

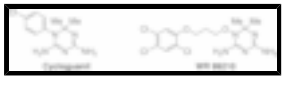


Fig. 1. The structures of the antifolate 1,3,5-triazines.

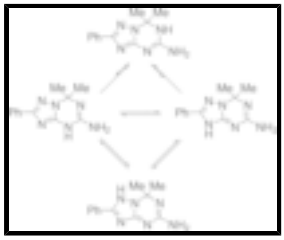


Fig. 2. The annular tautomerism in (I).

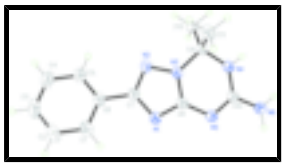


Fig. 3. The molecular structure of (I), showing the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

7,7-Dimethyl-2-phenyl-6,7-dihydro-1,2,4-triazolo[1,5-*a*][1,3,5]triazin- 5-amine

Crystal data

$C_{12}H_{14}N_6$	D_x = 1.349 Mg m^{-3}
M_r = 242.29	Melting point: 567 K
Orthorhombic, *Pbca*	Mo *K*α radiation λ = 0.71073 Å
Hall symbol: -P 2ac 2ab	Cell parameters from 3419 reflections
a = 9.9667 (6) Å	θ = 2.8–24.6º
b = 12.6544 (8) Å	μ = 0.09 mm^{-1}
c = 18.9142 (12) Å	*T* = 223 (2) K
V = 2385.5 (3) Å^3	Block, colourless
Z = 8	0.38 × 0.38 × 0.22 mm
F_{000} = 1024	

Data collection

Bruker SMART APEX CCD area-detector diffractometer	2345 reflections with $I > 2\sigma(I)$
Monochromator: graphite	R_{int} = 0.032
T = 223(2) K	θ_{max} = 27.5º
φ and ω scans	θ_{min} = 2.2º
Absorption correction: multi-scan (SADABS; Sheldrick, 2001)	*h* = −12→12
T_{min} = 0.923, T_{max} = 0.981	*k* = −16→16
15692 measured reflections	*l* = −24→20
2732 independent reflections	

Refinement

Refinement on F^2	H atoms treated by a mixture of independent and constrained refinement
Least-squares matrix: full	$w = 1/[\sigma^2(F_o^2) + (0.0592P)^2 + 0.7044P]$ where $P = (F_o^2 + 2F_c^2)/3$

$R[F^2 > 2\sigma(F^2)] = 0.051$

$wR(F^2) = 0.126$

$S = 1.11$

2732 reflections

169 parameters

Primary atom site location: structure-invariant direct methods

Secondary atom site location: difference Fourier map

Hydrogen site location: inferred from neighbouring sites

$(\Delta/\sigma)_{max} = 0.001$

$\Delta\rho_{max} = 0.25$ e Å^{-3}

$\Delta\rho_{min} = -0.23$ e Å^{-3}

Extinction correction: none

Special details

Geometry. All s.u.'s (except the s.u. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell s.u.'s are taken into account individually in the estimation of s.u.'s in distances, angles and torsion angles; correlations between s.u.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell s.u.'s is used for estimating s.u.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted R-factor wR and goodness of fit S are based on F^2, conventional R-factors R are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R- factors based on ALL data will be even larger.

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

	x	*y*	*z*	U_{iso}*/U_{eq}
N1	0.37457 (12)	0.65120 (10)	0.10869 (6)	0.0291 (3)
N2	0.19963 (12)	0.58806 (10)	0.04415 (6)	0.0296 (3)
N3	0.16605 (12)	0.59905 (10)	0.11387 (6)	0.0279 (3)
N4	0.03331 (12)	0.62047 (11)	0.21265 (7)	0.0311 (3)
H4N	−0.047 (2)	0.6331 (15)	0.2304 (10)	0.045 (5)*
N5	0.26523 (12)	0.65592 (11)	0.22214 (6)	0.0319 (3)
N6	0.12227 (13)	0.69071 (11)	0.31414 (6)	0.0367 (3)
H6A	0.1895	0.7154	0.3384	0.044*
H6B	0.0422	0.6900	0.3325	0.044*
C1	0.54355 (16)	0.64131 (12)	−0.01825 (9)	0.0359 (4)
H1	0.5857	0.6534	0.0255	0.043*
C2	0.61893 (18)	0.64144 (13)	−0.07971 (10)	0.0424 (4)
H2	0.7118	0.6538	−0.0776	0.051*
C3	0.5583 (2)	0.62357 (14)	−0.14375 (10)	0.0486 (5)
H3	0.6097	0.6230	−0.1854	0.058*
C4	0.4215 (2)	0.60640 (15)	−0.14692 (9)	0.0517 (5)
H4	0.3799	0.5945	−0.1908	0.062*
C5	0.34574 (18)	0.60667 (14)	−0.08594 (9)	0.0402 (4)
H5	0.2526	0.5954	−0.0885	0.048*
C6	0.40643 (15)	0.62352 (11)	−0.02072 (8)	0.0293 (3)
C7	0.32580 (14)	0.62084 (11)	0.04426 (7)	0.0270 (3)
C8	0.27040 (14)	0.63578 (11)	0.15129 (7)	0.0269 (3)

C9	0.03860 (13)	0.56495 (12)	0.14464 (7)	0.0278 (3)
C10	0.14201 (14)	0.65383 (11)	0.24861 (8)	0.0277 (3)
C11	0.03960 (17)	0.44561 (13)	0.15463 (9)	0.0384 (4)
H14A	0.1180	0.4254	0.1818	0.058*
H14B	0.0423	0.4113	0.1088	0.058*
H14C	−0.0409	0.4241	0.1796	0.058*
C12	−0.07755 (15)	0.59963 (13)	0.09832 (8)	0.0338 (3)
H13A	−0.1616	0.5817	0.1213	0.051*
H13B	−0.0722	0.5639	0.0530	0.051*
H13C	−0.0731	0.6754	0.0911	0.051*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
N1	0.0221 (6)	0.0391 (7)	0.0261 (6)	−0.0008 (5)	0.0012 (5)	0.0018 (5)
N2	0.0286 (6)	0.0368 (6)	0.0234 (6)	−0.0032 (5)	0.0038 (5)	−0.0005 (5)
N3	0.0223 (6)	0.0387 (7)	0.0227 (6)	−0.0031 (5)	0.0019 (4)	−0.0001 (5)
N4	0.0202 (6)	0.0463 (7)	0.0267 (6)	−0.0017 (5)	0.0031 (5)	−0.0044 (5)
N5	0.0208 (6)	0.0506 (7)	0.0242 (6)	−0.0010 (5)	0.0000 (5)	−0.0002 (5)
N6	0.0234 (6)	0.0573 (8)	0.0295 (7)	−0.0030 (6)	0.0016 (5)	−0.0084 (6)
C1	0.0319 (8)	0.0398 (8)	0.0360 (8)	0.0029 (6)	0.0052 (6)	0.0031 (7)
C2	0.0379 (9)	0.0404 (9)	0.0489 (10)	0.0031 (7)	0.0167 (7)	0.0055 (7)
C3	0.0620 (12)	0.0447 (10)	0.0392 (10)	0.0003 (8)	0.0254 (9)	0.0001 (7)
C4	0.0702 (13)	0.0566 (11)	0.0282 (8)	−0.0132 (10)	0.0088 (8)	−0.0067 (8)
C5	0.0436 (10)	0.0454 (9)	0.0314 (8)	−0.0115 (7)	0.0043 (7)	−0.0031 (7)
C6	0.0319 (8)	0.0276 (7)	0.0284 (7)	−0.0007 (6)	0.0058 (6)	0.0014 (5)
C7	0.0258 (7)	0.0295 (7)	0.0256 (7)	−0.0001 (5)	0.0021 (5)	0.0026 (5)
C8	0.0209 (6)	0.0337 (7)	0.0260 (7)	−0.0002 (5)	−0.0011 (5)	0.0024 (5)
C9	0.0213 (7)	0.0360 (7)	0.0260 (7)	−0.0041 (5)	0.0016 (5)	−0.0002 (6)
C10	0.0229 (7)	0.0343 (7)	0.0260 (7)	0.0011 (5)	−0.0001 (5)	0.0013 (6)
C11	0.0389 (9)	0.0362 (8)	0.0400 (9)	−0.0038 (6)	0.0052 (7)	0.0035 (7)
C12	0.0254 (7)	0.0423 (8)	0.0337 (8)	−0.0028 (6)	−0.0033 (6)	−0.0008 (6)

Geometric parameters (Å, °)

N1—C8	1.3286 (18)	C2—C3	1.373 (3)
N1—C7	1.3670 (18)	C2—H2	0.94
N2—C7	1.3241 (19)	C3—C4	1.382 (3)
N2—N3	1.3675 (16)	C3—H3	0.94
N3—C8	1.3410 (18)	C4—C5	1.379 (2)
N3—C9	1.4624 (17)	C4—H4	0.94
N4—C10	1.3470 (18)	C5—C6	1.390 (2)
N4—C9	1.4666 (18)	C5—H5	0.94
N4—H4N	0.88 (2)	C6—C7	1.4690 (19)
N5—C10	1.3266 (18)	C9—C12	1.517 (2)
N5—C8	1.3652 (19)	C9—C11	1.522 (2)
N6—C10	1.3389 (19)	C11—H14A	0.97
N6—H6A	0.87	C11—H14B	0.97
N6—H6B	0.87	C11—H14C	0.97

C1—C2	1.384 (2)	C12—H13A	0.97
C1—C6	1.386 (2)	C12—H13B	0.97
C1—H1	0.94	C12—H13C	0.97
C8—N1—C7	102.79 (12)	C5—C6—C7	120.05 (14)
C7—N2—N3	101.48 (11)	N2—C7—N1	115.29 (12)
C8—N3—N2	110.75 (11)	N2—C7—C6	121.70 (13)
C8—N3—C9	124.46 (12)	N1—C7—C6	123.01 (13)
N2—N3—C9	124.49 (11)	N1—C8—N3	109.69 (13)
C10—N4—C9	124.34 (12)	N1—C8—N5	126.68 (13)
C10—N4—H4N	118.6 (12)	N3—C8—N5	123.61 (13)
C9—N4—H4N	117.1 (12)	N3—C9—N4	103.82 (11)
C10—N5—C8	113.69 (12)	N3—C9—C12	110.36 (12)
C10—N6—H6A	120.0	N4—C9—C12	109.91 (12)
C10—N6—H6B	120.0	N3—C9—C11	109.67 (12)
H6A—N6—H6B	120.0	N4—C9—C11	111.51 (12)
C2—C1—C6	120.48 (16)	C12—C9—C11	111.33 (13)
C2—C1—H1	119.8	N5—C10—N6	118.58 (13)
C6—C1—H1	119.8	N5—C10—N4	124.07 (13)
C3—C2—C1	120.14 (17)	N6—C10—N4	117.30 (13)
C3—C2—H2	119.9	C9—C11—H14A	109.5
C1—C2—H2	119.9	C9—C11—H14B	109.5
C2—C3—C4	119.90 (16)	H14A—C11—H14B	109.5
C2—C3—H3	120.0	C9—C11—H14C	109.5
C4—C3—H3	120.0	H14A—C11—H14C	109.5
C5—C4—C3	120.24 (18)	H14B—C11—H14C	109.5
C5—C4—H4	119.9	C9—C12—H13A	109.5
C3—C4—H4	119.9	C9—C12—H13B	109.5
C4—C5—C6	120.30 (17)	H13A—C12—H13B	109.5
C4—C5—H5	119.9	C9—C12—H13C	109.5
C6—C5—H5	119.9	H13A—C12—H13C	109.5
C1—C6—C5	118.94 (14)	H13B—C12—H13C	109.5
C1—C6—C7	121.00 (14)		
C7—N2—N3—C8	−0.51 (15)	N2—N3—C8—N1	0.58 (16)
C7—N2—N3—C9	−174.53 (13)	C9—N3—C8—N1	174.60 (13)
C6—C1—C2—C3	−0.2 (2)	N2—N3—C8—N5	179.00 (13)
C1—C2—C3—C4	0.6 (3)	C9—N3—C8—N5	−7.0 (2)
C2—C3—C4—C5	−0.3 (3)	C10—N5—C8—N1	166.91 (14)
C3—C4—C5—C6	−0.4 (3)	C10—N5—C8—N3	−11.2 (2)
C2—C1—C6—C5	−0.5 (2)	C8—N3—C9—N4	23.14 (18)
C2—C1—C6—C7	178.63 (14)	N2—N3—C9—N4	−163.64 (13)
C4—C5—C6—C1	0.8 (2)	C8—N3—C9—C12	140.88 (14)
C4—C5—C6—C7	−178.32 (16)	N2—N3—C9—C12	−45.91 (18)
N3—N2—C7—N1	0.28 (16)	C8—N3—C9—C11	−96.12 (16)
N3—N2—C7—C6	−179.93 (13)	N2—N3—C9—C11	77.09 (17)
C8—N1—C7—N2	0.05 (16)	C10—N4—C9—N3	−25.30 (18)
C8—N1—C7—C6	−179.74 (13)	C10—N4—C9—C12	−143.35 (14)
C1—C6—C7—N2	−169.39 (14)	C10—N4—C9—C11	92.70 (17)
C5—C6—C7—N2	9.7 (2)	C8—N5—C10—N6	−168.20 (13)

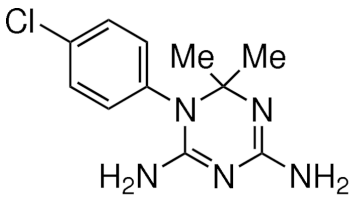
C1—C6—C7—N1	10.4 (2)	C8—N5—C10—N4	9.1 (2)
C5—C6—C7—N1	−170.48 (14)	C9—N4—C10—N5	11.3 (2)
C7—N1—C8—N3	−0.37 (15)	C9—N4—C10—N6	−171.38 (14)
C7—N1—C8—N5	−178.73 (14)		

Hydrogen-bond geometry (Å, °)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N4—H4N···N5^{i}	0.88 (2)	2.10 (2)	2.9768 (17)	176 (2)
N6—H6B···N1^{i}	0.87	2.07	2.9113 (18)	163

Symmetry codes: (i) *x*−1/2, *y*, −*z*+1/2.

Fig. 1



Cycloguanil

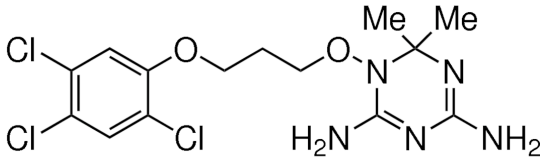


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Fig. 2

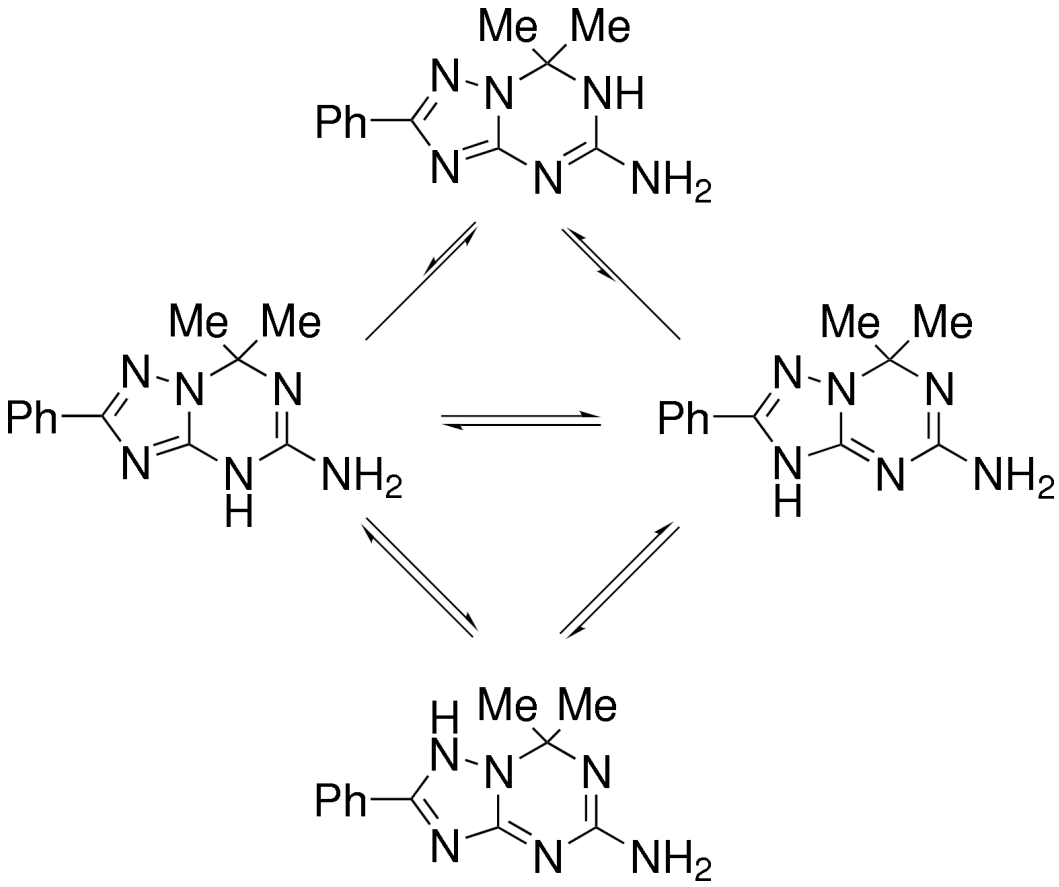

Fig. 3