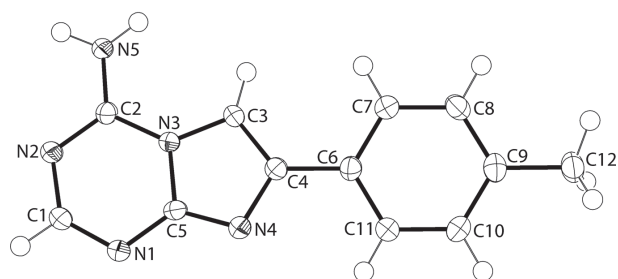


Felicia Phei Lin Lim, Anton V. Dolzhenko, Nathan R. Halcovitch and Edward R.T. Tiekink\*

# Crystal structure of 7-(4-methylphenyl)imidazo[1,2-a][1,3,5]triazin-4-amine, C<sub>12</sub>H<sub>11</sub>N<sub>5</sub>



<https://doi.org/10.1515/ncrs-2017-0371>

Received November 27, 2017; accepted February 24, 2018; available online March 15, 2018

## Abstract

C<sub>12</sub>H<sub>11</sub>N<sub>5</sub>, monoclinic, *P*<sub>2</sub><sub>1</sub>/*n* (no. 14), *a* = 7.3455(1) Å, *b* = 12.2470(1) Å, *c* = 12.1689(1) Å, β = 103.505(1)°, *V* = 1064.45(2) Å<sup>3</sup>, *Z* = 4, *R*<sub>gt</sub>(*F*) = 0.0365, *wR*<sub>ref</sub>(*F*<sup>2</sup>) = 0.0987, *T* = 100 K.

CCDC no.: 1825596

The asymmetric unit of the title crystal structure is shown in the figure. Tables 1 and 2 contain details on crystal structure and measurement conditions and a list of the atoms including atomic coordinates and displacement parameters.

## Source of material

The compound was prepared and characterised as described in the literature [5]. Crystals for the crystallographic study were obtained from the slow evaporation of a very dilute methanol solution.

## Experimental details

The C-bound H atoms were geometrically placed (C–H = 0.98–0.99 Å) and refined as riding with *U*<sub>iso</sub>(H) = 1.2–1.5*U*<sub>eq</sub>(C). The N-bound hydrogen atoms were located in difference Fourier maps, but were refined with a distance

\*Corresponding author: Edward R.T. Tiekink, Research Centre for Crystalline Materials, School of Science and Technology, Sunway University, 47500 Bandar Sunway, Selangor Darul Ehsan, Malaysia, e-mail: edwardt@sunway.edu.my

Felicia Phei Lin Lim and Anton V. Dolzhenko: School of Pharmacy, Monash University Malaysia, Jalan Lagoon Selatan, Bandar Sunway, Selangor Darul Ehsan 47500, Malaysia

Nathan R. Halcovitch: Department of Chemistry, Lancaster University, Lancaster LA1 4YB, UK

Table 1: Data collection and handling.

Crystal:	Block, colourless
Size:	0.44 × 0.16 × 0.09 mm
Wavelength:	Cu Kα radiation (1.54184 Å)
μ:	0.73 mm <sup>-1</sup>
Diffractometer, scan mode:	SuperNova, φ and ω-scans
θ <sub>max</sub> , completeness:	76.5°, >99%
<i>N</i> ( <i>hkl</i> ) <sub>measured</sub> , <i>N</i> ( <i>hkl</i> ) <sub>unique</sub> , <i>R</i> <sub>int</sub> :	18249, 2225, 0.026
Criterion for <i>I</i> <sub>obs</sub> , <i>N</i> ( <i>hkl</i> ) <sub>gt</sub> :	<i>I</i> <sub>obs</sub> > 2 σ( <i>I</i> <sub>obs</sub> ), 2132
<i>N</i> ( <i>param</i> ) <sub>refined</sub> :	163
Programs:	CrysAlis <sup>PRO</sup> [1], SHELX [2, 3], WinGX and ORTEP [4]

restraint of N–H = 0.88 ± 0.01 Å, and with unconstrained *U*<sub>iso</sub>(H).

## Discussion

The 5-aza-7-deaza-isostere (imidazo[1,2-a][1,3,5]triazine) of the purine system is an important scaffold for the construction of various drugs. Such compounds have been developed as inhibitors for enzymes, e.g. focal adhesion kinase [6]. Further, these compounds display anti-viral activity [7], are agonists of opioid m-receptors [8] and function as ligands for adenosine receptors [9]. A hindrance to the embellishment of this class of compound has been the difficulty in their synthesis. Very recently, a new procedure for the synthesis of 5-aza-7-deaza-isosteres was developed, i.e. through the reaction of 2-aminoimidazoles, triethylorthoformate and cyanamide under microwave irradiation [5]. The title compound was one of the new compounds synthesised in the course of that study.

The title molecule is shown in the figure (70% displacement ellipsoids) and comprises a six- and five-membered fused ring system connected to the 4-methylphenyl group at C4. The r.m.s. deviation of the nine atoms of the imidazo-triazine group is 0.0218 Å with the maximum deviations being 0.0399(7) Å for the C2 atom and to the other side of the least-squares plane, 0.0273(7) Å for the C3 atom. The amino-N5 atom lies 0.1258(13) Å out of the plane in the direction of the C2 atom. There is a twist between this plane and that through the appended 4-methylphenyl group as seen in the dihedral angle of 12.39(4)° formed between them. The overall molecular geometry resembles that reported for the 4-methoxyphenyl derivative [5].

**Table 2:** Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å<sup>2</sup>).

Atom	x	y	z	U <sub>iso</sub> <sup>*</sup> /U <sub>eq</sub>
N1	0.65755(12)	0.76747(7)	0.76013(7)	0.0160(2)
N2	0.56271(12)	0.90789(7)	0.62085(7)	0.0152(2)
N3	0.43165(12)	0.73441(7)	0.58693(7)	0.0135(2)
N4	0.51177(12)	0.59379(7)	0.70583(7)	0.0153(2)
N5	0.35748(13)	0.86947(7)	0.44944(7)	0.0167(2)
H1N	0.2954(19)	0.8213(10)	0.4000(11)	0.027(4)*
H2N	0.382(2)	0.9366(8)	0.4286(12)	0.026(4)*
C1	0.65857(14)	0.86774(8)	0.72106(8)	0.0158(2)
H1	0.7367	0.9183	0.7696	0.019*
C2	0.45045(14)	0.83930(8)	0.55095(8)	0.0137(2)
C3	0.32629(14)	0.64623(8)	0.53665(8)	0.0145(2)
H3	0.2379	0.6448	0.4659	0.017*
C4	0.37712(14)	0.56166(8)	0.61100(8)	0.0143(2)
C5	0.54085(14)	0.69780(8)	0.68995(8)	0.0139(2)
C6	0.30889(14)	0.44836(8)	0.59856(8)	0.0147(2)
C7	0.20768(15)	0.40938(9)	0.49422(9)	0.0175(2)
H7	0.1760	0.4576	0.4315	0.021*
C8	0.15305(15)	0.30053(9)	0.48163(9)	0.0184(2)
H8	0.0847	0.2754	0.4100	0.022*
C9	0.19638(14)	0.22754(8)	0.57174(9)	0.0172(2)
C10	0.29339(15)	0.26757(8)	0.67647(9)	0.0186(2)
H10	0.3222	0.2196	0.7395	0.022*
C11	0.34874(15)	0.37631(8)	0.69031(9)	0.0172(2)
H11	0.4140	0.4018	0.7625	0.021*
C12	0.14124(16)	0.10914(9)	0.55662(9)	0.0212(2)
H12A	0.0357	0.0951	0.5912	0.032*
H12B	0.2476	0.0633	0.5930	0.032*
H12C	0.1045	0.0919	0.4758	0.032*

As anticipated, the molecular packing features a number of conventional hydrogen-bonding interactions. Thus, centrosymmetrically related molecules associate *via* amine-N—H...N(triazine) hydrogen bonds and eight-membered {...HNCN}<sub>2</sub> synthons [N5—H2n...N2: 2.066(11) Å and 179.6(17)° for symmetry operation 1−x, 2−y, 1−z]. The dimeric aggregates are connected into twisted, one-dimensional supramolecular chains, parallel to [1 0 1], *via* amine-H...amine-N—H...N(triazine) hydrogen bonds, involving the other amine-H and triazine-N atoms [N5—H1n...N1:

2.074(13) Å and 168.2(12)° for symmetry operation −1/2 + x, 3/2−y, −1/2 + z].

**Acknowledgements:** This work is supported by the Ministry of Higher Education, Malaysia under the Fundamental Research Grant Scheme (FRGS).

## References

1. Rigaku/Oxford Diffraction: CrysAlisPro. Rigaku Corporation, The Woodlands, TX, USA (2015).
2. Sheldrick, G. M.: A short history of SHELX. *Acta Crystallogr.* **A64** (2008) 112–122.
3. Sheldrick, G. M.: Crystal structure refinement with SHELXL. *Acta Crystallogr.* **C71** (2015) 3–8.
4. Farrugia, L. J.: WinGX and ORTEP for Windows: an update. *J. Appl. Cryst.* **45** (2012) 849–854.
5. Lim, F. P. L.; Low, S. T.; Ho, E. L. K.; Halcovitch, N. R.; Tiekink, E. R. T.; Dolzhenko, A. V.: A multicomponent reaction of 2-aminoimidazoles: microwave-assisted synthesis of novel 5-aza-7-deaza-adenines. *RSC Adv.* **7** (2017) 51062–51068.
6. Dao, P.; Smith, N.; Tomkiewicz-Raulet, C.; Yen-Pon, E.; Camacho-Artacho, M.; Lietha, D.; Herbeuval, J.-P.; Coumoul, X.; Garbay, C.; Chen, H.: Design, synthesis, and evaluation of novel imidazo[1,2-a][1, 3, 5]triazines and their derivatives as focal adhesion kinase inhibitors with antitumor activity. *J. Med. Chem.* **58** (2015) 237–251.
7. Dukhan, D.; Leroy, F.; Peyronnet, J.; Bosc, E.; Chaves, D.; Durka, M.; Storer, R.; La Colla, P.; Seela, F.; Gosselin, G.: Synthesis of 5-aza-7-deazaguanine nucleoside derivatives as potential anti-flavivirus agents. *Nucleosides Nucleotides Nucleic Acids* **24** (2005) 671–674.
8. Matosiuk, D.; Fidecka, S.; Antkiewicz-Michaluk, L.; Lipkowski, J.; Dybala, I.; Koziol, A. E.: Synthesis and pharmacological activity of new carbonyl derivatives of 1-aryl-2-iminoimidazolidine: Part 2. Synthesis and pharmacological activity of 1,6-diaryl-5,7(1H)dioxo-2,3-dihydroimidazo[1,2-a][1, 3, 5]triazines. *Eur. J. Med. Chem.* **37** (2002) 761–772.
9. Da Settimo, F.; Primofiore, G.; Taliani, S.; La Motta, C.; Novellino, E.; Greco, G.; Lavecchia, A.; Cosimelli, B.; Iadanza, M.; Klotz, K.-N.; Tuscano, D.; Trincavelli, M. L.; Martini, C.: A1 adenosine receptor antagonists, 3-aryl[1, 2, 4]triazino[4,3-a]benzimidazol-4-(10H)-ones (ATBIs) and *N*-alkyl and *N*-acyl-(7-substituted-2-phenylimidazo[1,2-a][1, 3, 5]triazin-4-yl)amines (ITAs): different recognition of bovine and human binding sites. *Drug Dev. Res.* **63** (2004) 1–7.