

https://dspace.org/

The crystal structure of N1N3bis15dimethyl3oxo2phenyl23dihydro1Hpyrazol4yl propanediamide hydrate C25H26N6O4 2H2O

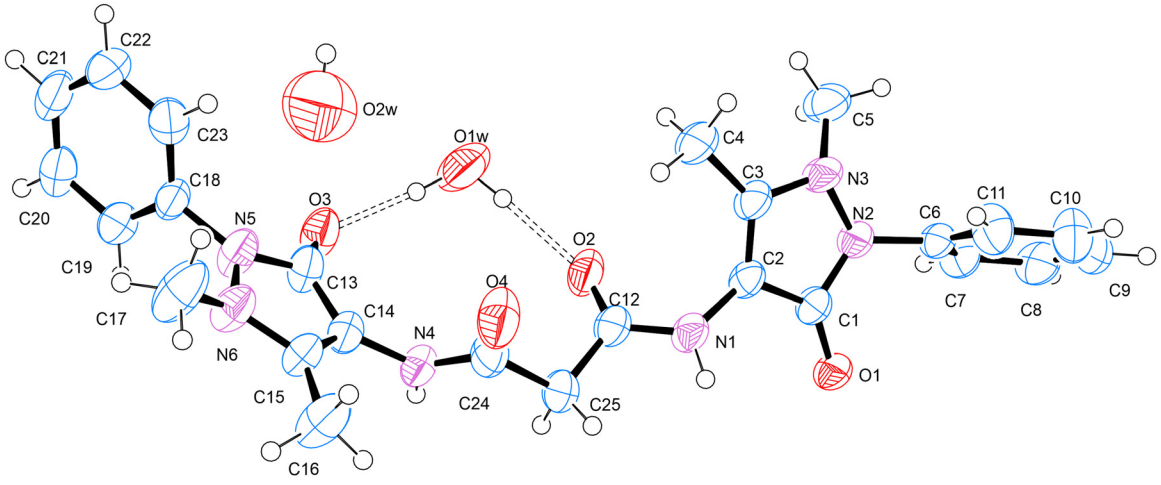
M Smith; Andreas Lemmerer

https://hdl.handle.net/10539/42531
DOAJ

Downloaded from a DSpace repository. https://dspace.org/

Mark G. Smith* and Andreas Lemmerer

The crystal structure of *N1,N3*-bis(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)\ propanediamide hydrate, $C_{25}H_{26}N_6O_4$, $2(H_2O)$



https://doi.org/10.1515/ncrs-2023-0507
Received November 20, 2023; accepted December 31, 2023;
published online January 24, 2024

Abstract

$C_{25}H_{26}N_6O_4$, $2(H_2O)$, triclinic, $P\bar{1}$ (no. 2), a = 9.8423(6) Å, b = 11.2923(7) Å, c = 13.3810(8) Å, α = 69.053(3)°, β = 73.926(4)°, γ = 68.979(3)°, V = 1277.49(14) Å^3, Z = 2, $R_{gt}(F)$ = 0.0757, $wR_{ref}(F^2)$ = 0.2364, T = 173 K.

CCDC no.: 1873551

Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.29 × 0.20 × 0.14 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.10 mm^{-1}
Diffractometer, scan mode:	Bruker D8 Venture Photon CCD, ω
θ_{max}, completeness:	28.0°, >99 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	22,991, 6140, 0.063
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\sigma(I_{obs})$, 3310
$N(param)_{refined}$:	348
Programs:	Bruker (*1*), SHELX (*2*, *3*), WinGX/ORTEP-3 (*4*), PLATON (*5*)

1 Source of materials

All reagents used were commercially available and used without further purification. An amount of 0.074 g of 4-aminoantipyrine (0.365 mmol) and 0.039 g of malonic acid (0.376 mmol) were added into a sample vial. The solids were dissolved in 3 mL of a 1:1 mixture of 1,2-dichloroethane:methanol, stirred for 30 min at room temperature, and were left to stand very slightly opened to the atmosphere. The resultant solid was re-dissolved in chloroform and again left to stand very slightly opened to the atmosphere. Colourless blocks were afforded after three days (Tables 1 and 2).

2 Experimental details

C-bound hydrogen atoms were located in the difference map then positioned geometrically and were allowed to ride on their respective parent atoms with thermal displacement parameters 1.2 times of the parent C atom. The coordinates and isotropic displacement parameters of all N-bound and

***Corresponding author: Mark G. Smith**, Chemistry Department, University of South Africa, Unisa Science Campus 28, Pioneer Avenue Florida, Roodepoort, Gauteng, South Africa, E-mail: smithm2@unisa.ac.za. https://orcid.org/0000-0003-2553-2540
Andreas Lemmerer, School of Chemistry, Molecular Sciences Institute, University of the Witwatersrand, Johannesburg, Gauteng, South Africa

Open Access. © 2023 the author(s), published by De Gruyter. This work is licensed under the Creative Commons Attribution 4.0 International License.

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C1	0.6786 (3)	0.8612 (3)	0.0977 (2)	0.0414 (7)
C2	0.5624 (3)	0.8049 (3)	0.1647 (2)	0.0420 (7)
C3	0.6230 (3)	0.6766 (3)	0.2158 (2)	0.0474 (7)
C4	0.5496 (4)	0.5765 (3)	0.2956 (3)	0.0651 (10)
H4A	0.558727	0.567145	0.369294	0.098*
H4B	0.597096	0.490897	0.280079	0.098*
H4C	0.444858	0.605704	0.289645	0.098*
C5	0.8775 (4)	0.5583 (4)	0.2582 (3)	0.0667 (10)
H5A	0.884783	0.60918	0.301475	0.1*
H5B	0.975068	0.525856	0.216878	0.1*
H5C	0.841992	0.482882	0.306602	0.1*
C6	0.9409 (3)	0.7538 (3)	0.0372 (2)	0.0428 (7)
C7	1.0329 (4)	0.8229 (3)	0.0335 (3)	0.0525 (8)
H7	1.012101	0.869197	0.085456	0.063*
C8	1.1572 (4)	0.8239 (3)	−0.0476 (3)	0.0616 (10)
H8	1.220165	0.873064	−0.051666	0.074*
C9	1.1899 (4)	0.7558 (3)	−0.1208 (3)	0.0622 (10)
H9	1.276178	0.75576	−0.174718	0.075*
C10	1.0966 (4)	0.6866 (4)	−0.1161 (3)	0.0702 (11)
H10	1.117933	0.639908	−0.167841	0.084*
C11	0.9720 (4)	0.6849 (4)	−0.0363 (3)	0.0622 (9)
H11	0.908576	0.636355	−0.032658	0.075*
C12	0.3135 (3)	0.8914 (3)	0.2536 (3)	0.0503 (8)
C13	−0.1345 (4)	0.8295 (3)	0.5725 (3)	0.0530 (8)
C14	−0.1459 (3)	0.8915 (3)	0.4621 (2)	0.0473 (7)
C15	−0.2694 (4)	0.8813 (3)	0.4435 (2)	0.0505 (8)
C16	−0.3248 (5)	0.9282 (5)	0.3396 (3)	0.0764 (12)
H16A	−0.297669	0.853862	0.309515	0.115*
H16B	−0.280774	0.997086	0.288141	0.115*
H16C	−0.432541	0.96473	0.352554	0.115*
C17	−0.4481 (5)	0.7503 (5)	0.5507 (3)	0.0824 (14)
H17A	−0.500776	0.791958	0.488768	0.124*
H17B	−0.518859	0.755633	0.617904	0.124*
H17C	−0.396535	0.657149	0.554231	0.124*
C18	−0.3041 (3)	0.7218 (3)	0.7287 (2)	0.0478 (8)
C19	−0.3756 (4)	0.7997 (3)	0.7966 (3)	0.0531 (8)
H19	−0.397697	0.893311	0.768403	0.064*
C20	−0.4161 (4)	0.7421 (4)	0.9071 (3)	0.0599 (9)
H20	−0.466745	0.795948	0.954429	0.072*
C21	−0.3824 (4)	0.6075 (4)	0.9467 (3)	0.0643 (10)
H21	−0.407897	0.567692	1.022257	0.077*
C22	−0.3118 (4)	0.5283 (4)	0.8783 (3)	0.0674 (10)
H22	−0.290186	0.434731	0.906954	0.081*
C23	−0.2720 (4)	0.5847 (4)	0.7678 (3)	0.0597 (9)
H23	−0.22411	0.530873	0.720141	0.072*
C24	0.0495 (4)	0.8999 (3)	0.3074 (3)	0.0521 (8)
C25	0.1585 (3)	0.9734 (3)	0.2339 (3)	0.0554 (9)
H25A	0.134587	1.059287	0.248471	0.066*
H25B	0.1518	0.99138	0.157149	0.066*
N1	0.4117 (3)	0.8761 (3)	0.1641 (2)	0.0466 (6)
N2	0.8071 (3)	0.7606 (2)	0.1156 (2)	0.0452 (6)
N3	0.7740 (3)	0.6434 (2)	0.1831 (2)	0.0499 (7)
N4	−0.0416 (3)	0.9523 (3)	0.3850 (2)	0.0475 (6)
N5	−0.2559 (3)	0.7810 (3)	0.6160 (2)	0.0584 (8)
N6	−0.3422 (3)	0.8181 (3)	0.5375 (2)	0.0565 (7)
O1	0.6732 (2)	0.97313 (19)	0.03454 (16)	0.0473 (5)
O2	0.3462 (3)	0.8437 (3)	0.34494 (18)	0.0646 (7)
O3	−0.0431 (3)	0.8175 (3)	0.62809 (18)	0.0643 (7)
O4	0.0457 (3)	0.8000 (3)	0.2921 (2)	0.0774 (8)
H1	0.380 (4)	0.927 (3)	0.101 (3)	0.049 (9)*
H4	−0.033 (5)	1.033 (4)	0.394 (3)	0.093 (14)*
O1W	0.2422 (4)	0.7038 (4)	0.5518 (3)	0.162 (2)
H1W	0.269598	0.73732	0.480884	0.242*
H2W	0.150396	0.749045	0.578267	0.242*
O2W	−0.1295 (6)	0.4583 (5)	0.5498 (3)	0.1467 (18)
H3W	−0.077112	0.388863	0.589105	0.17 (3)*

O-bound H atoms were allowed to refine freely. Diagrams and publication material were generated using ORTEP-3 (*4*), WinGX (*6*) and PLATON (*5*).

3 Discussion

4–Aminoantipyrine (4AAP) was historically used as an antipyretic pharmaceutical drug (Acheson (*7*)), and as a prophylactic against oxidative stress (Teng et al. (*8*)). The crystal structure of 4AAP has been reported by Li et al. (*9*) and by Mnguni and Lemmerer (*10*) and a co-crystal of 4AAP has been reported by Smith and Lemmerer (*11*). Derivatives of 4AAP account for at least two pharmaceutical drugs, aminoantipyrine and 4-(N,N-dimethyl)-aminoantipyrine, both which have been used as analgesics for over 100 years. This paper presents the crystal structure a new derivative of 4AAP.

As shown in the figure, the asymmetric unit contains one molecule of *N1,N3*-bis(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl) propanediamide and two molecules of water. Although the stoichiometry of the reactants was 1:1, both carboxylic acid groups of the malonic acid reacted with the amine groups of two separate 4AAP molecules. One of the water molecules forms a bridge via hydrogen bonding through its two H-atoms to the carbonyl oxygen atoms of O2 and O3 respectively. This bridge creates an *R*(11) hydrogen bonded ring. There is a second water molecule in the asymmetric unit, but it was not possible to determine the position of the second hydrogen atom, and hence it is shown in the diagram as having only one hydrogen atom, resulting in a larger ellipsoid. In the packing, two *N1,N3*-bis(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl) propanediamide molecules are joined to each other via two N–H···O heterosynthons, formed between the amine hydrogen atoms and the antipyrine carbonyl oxygen atoms. This reults in an *R*(10) hydrogen bonded ring between the two molecules. The extensive hydrogen bonding results in a 3D packing network.

Author contributions: The author has accepted responsibility for the entire content of this submitted manuscript and approved submission.

Research funding: The University of the Witwatersrand and the Molecular Sciences Institute are thanked for providing the infrastructure and financial support to do this work. Mark G. Smith thanks the Chemistry Department of the University of South Africa for their financial support and Andreas Lemmerer thanks the Wits Friedel Sellschop award for funding.

Conflict of interest statement: The author declares no conflict of interest regarding this article.

References

1. Bruker. *APEX2 (Version 2012.10–0), SAINT (Version 27B), SADABS (Version 2012/1)*; BrukerAXS Inc.: Madison, Wisconsin, USA, **2012**.
2. Sheldrick G. M. *SHELXTL* – Integrated Space-Group and Crystal-Structure Determination. *Acta Crystallogr.* **2015**, *A71*, 3–8.
3. Sheldrick G. M. Crystal Structure Refinement with SHELXL. *Acta Crystallogr.* **2015**, *C71*, 3–8.
4. Farrugia L. J. WinGX and ORTEP for Windows: An Update. *J. Appl. Crystallogr.* **2012**, *45*, 849–854.
5. Spek A. L. Structure Validation in Chemical Crystallography. *Acta Crystallogr.* **2009**, *D65*, 148–155.
6. Farrugia L. J. WinGX Suite for Small-Molecule Single-Crystal Crystallography. *J. Appl. Crystallogr.* **1999**, *32*, 837–838.
7. Acheson R. M. An Introduction to the Chemistry of Heterocyclic Compounds. *J. Pharm. Sci.* **1960**, *49*, 739.
8. Teng Y., Liu R., Li C., Zhang H. Effect of 4-Aminoantipyrine on Oxidative Stress Induced by Glutathione Depletion in Single Human Erythrocytes Using a Microfluidic Device Together with Fluorescence Imaging. *J. Hazard. Mater.* **2011**, *192*, 1766–1771.
9. Li Y., Liu Y., Wang H., Xiong X., Wei P., Li F. Synthesis, Crystal Structure, Vibration Spectral, and DFT Studies of 4-Aminoantipyrine and Its Derivatives. *Molecules* **2013**, *18*, 877.
10. Mnguni M. J., Lemmerer A. A Structural Study of 4-Aminoantipyrine and Six of Its Schiff Base Derivatives. *Acta Crystallogr*. **2015**, *C71*, 103–109.
11. Smith M. G., Lemmerer A. Novel Crystal Forms of 4-Aminoantipyrine and Its Derivatives: Co-Crystallizing a Reluctant Molecule. *J. Mol. Struct.* **2019**, *1175*, 307–313.