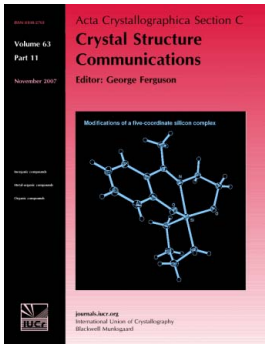
Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701
Editor: **Anthony Linden**

Arcyriaflavin A monohydrate

José A. Fernandes, Filipe A. Almeida Paz, Joana Marques, Maria P. M. Marques and Susana S. Braga

Acta Cryst. (2011). C**67**, o57–o59



Acta Crystallographica Section C: Crystal Structure Communications specializes in the rapid dissemination of high-quality studies of crystal and molecular structures of interest in fields such as chemistry, biochemistry, mineralogy, pharmacology, physics and materials science. The numerical and text descriptions of each structure are submitted to the journal electronically as a Crystallographic Information File (CIF) and are checked and typeset automatically prior to peer review. The journal is well known for its high standards of structural reliability and presentation. *Section C* publishes approximately 1000 structures per year; readers have access to an archive that includes high-quality structural data for over 10000 compounds.

Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

Arcyriaflavin A monohydrate

José A. Fernandes,[a] Filipe A. Almeida Paz,[a]* Joana Marques,[a] Maria P. M. Marques[b] and Susana S. Braga[a]

[a]Department of Chemistry, University of Aveiro, CICECO, 3810-193 Aveiro, Portugal, and [b]Departamento de BioquíDepartamento de Bioquímica, Faculdade de Ciências e Tecnologia, Universidade de Coimbra, Apartado 3126, 3001-401 Coimbra, Portugal
Correspondence e-mail: filipe.paz@ua.pt

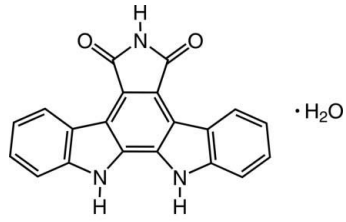
Received 23 October 2010
Accepted 15 December 2010
Online 7 January 2011

The asymmetric unit of the title compound comprises the monohydrated form of the natural product arcyriaflavin A [systematic name: 12,13-dihydro-5*H*-indolo[2,3-*a*]pyrrolo[3,4-*c*]-carbazole-5,7(6*H*)-dione monohydrate], $C_{20}H_{11}N_3O_2\cdot H_2O$. Individual molecular units are engaged in hydrogen-bonding interactions, forming two-dimensional zigzag supramolecular layers parallel to the ($\bar{1}$02) plane. The close packing of the layers is mediated by strong co-operative π–π stacking interactions, in tandem with interlayer hydrogen bonds involving the solvent water molecule.

Comment

Arcyriaflavin A is a natural product belonging to the family of indolocarbazole alkaloids. This family has potential therapeutic application in the treatment of cancer (Sánchez *et al.*, 2006) because of its ability to inhibit protein kinases. The most widely known indolocarbazole alkaloid is staurosporine, a potent inhibitor of phospholipid/Ca^{2+}-dependent protein kinase (protein kinase C) from rat brain (Tamaoki *et al.*, 1986). Several of its derivatives have already entered clinical trials as anticancer agents (Sánchez *et al.*, 2006), and it was also the model drug for the study of Meggers and co-workers on the design of metal complexes as protein kinase inhibitors (Bregman *et al.*, 2006). The title compound, (I), is an attractive aglycone staurosporine derivative, first isolated from the myxomycete *Arcyria denudata* (Steglich, 1989). It has a wide span of cytotoxic and antiproliferative action, ranging from moderate antibiotic activity against fungi and bacteria (Keller & Everhart, 2010) to *in vitro* antiviral properties towards the human cytomegalovirus (Slater *et al.*, 1999) and cytotoxicity towards the K562 human chronic myelogenous leukaemia cell line (Liu *et al.*, 2007). In addition, it also works *via* kinase inhibition, namely of the cyclin-dependent kinase 4 (CDK4) (Zhu *et al.*, 2003).

The asymmetric unit of (I) comprises an arcyriaflavin A molecule and a solvent water molecule (Fig. 1). The organic molecules arrange themselves in a zigzag fashion, forming layers parallel to the ($\bar{1}$02) plane (Fig. 2*a*). Within these layers, the molecules are interconnected by strong directional hydrogen bonds [$D\cdots A$ distances in the range 2.811 (2)–3.066 (2) Å and D—H$\cdots A$ angles greater than *ca* 156°; see Table 1 for specific details (dashed lines in Fig. 2)]. On the other hand, the dominant supramolecular contacts between adjacent layers are π–π stacking forces (Fig. 2*b*), with a distance between aromatic rings of *ca* 3.38 Å.



(I)

Within each layer, the arcyriaflavin A molecules are arranged into dimers *via* two N$\cdots$O hydrogen bonds related by a centre of inversion, forming a hydrogen-bonding pattern that can be described by an $R_2^2(8)$ graph-set motif (Grell *et al.*, 1999). It is noteworthy that the two molecular units are not coplanar, with the mean planes being *ca* 0.65 Å from each other. The β-diamine group (atoms N1 and N2) acts as a two-proton donor to the neighbouring solvent water molecule, forming a ring of graph set $R_2^1(7)$. The water molecule bridges adjacent arcyriaflavin A molecules from two distinct supramolecular layers *via* O—H$\cdots$O hydrogen-bonding interactions with the carbonyl groups (atoms O1 and O2). One of these interactions (O1*W*$\cdots$O1), together with the aforementioned $R_2^1(7)$ and $R_2^2(8)$ rings, promotes the formation of the two-dimensional supramolecular layers. The remaining interaction of the water molecule [O1*W*$\cdots$O2^{iii}; symmetry code: (iii) $-x+1, -y+1, -z+1$] connects different layers, as shown in Fig. 2(*b*).

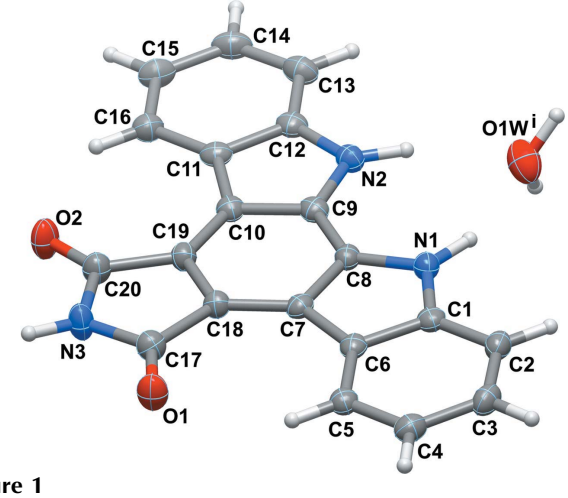


Figure 1
The asymmetric unit of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level. [Symmetry code: (i) $-x+1, y+\frac{1}{2}, -z+\frac{1}{2}$.]

 doi:10.1107/S0108270110052741

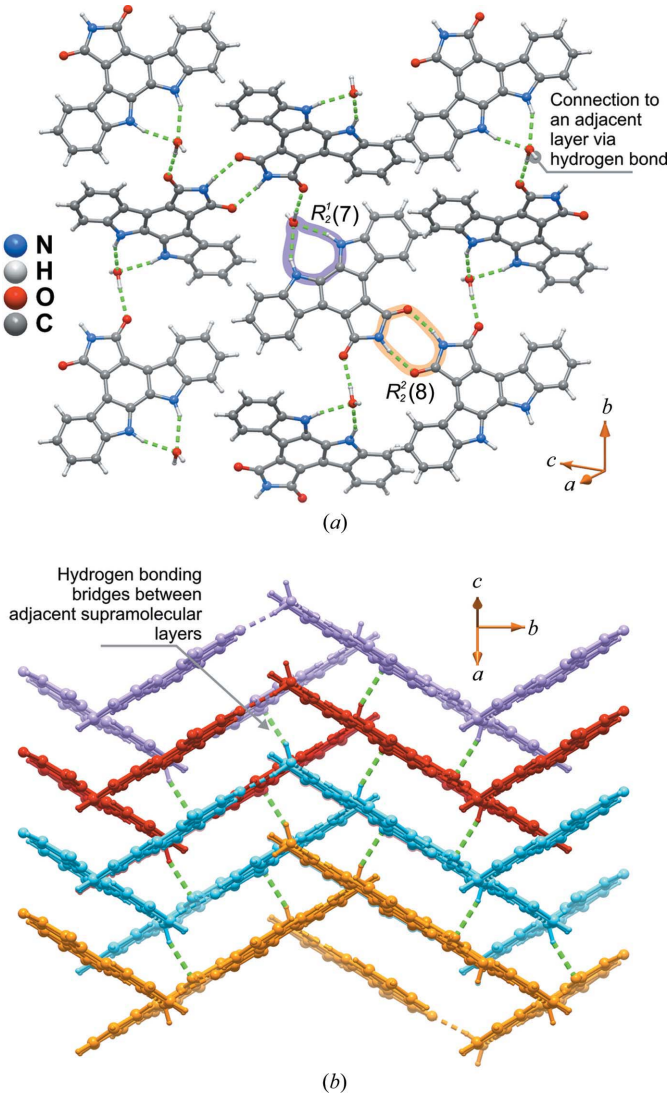


Figure 2
(*a*) Schematic representation of the two-dimensional supramolecular layer formed by the hydrogen-bonding interactions between arcyriaflavin A and water molecules. (*b*) A simplified view of the crystal packing, showing the hydrogen-bonding connections between adjacent layers *via* the solvent water molecule. Hydrogen bonds are represented as dashed lines. See Table 1 for geometric details of these interactions.

Experimental

Arcyriaflavin A was purchased from Tocris Bioscience (>98% purity) and used as received without further purification. Orange needle-shaped crystals suitable for the crystallographic studies reported here were isolated over a period of one week by slow evaporation from an ethanolic solution.

Crystal data

$C_{20}H_{11}N_3O_2\cdot H_2O$
M_r = 343.33
Monoclinic, $P2_1/c$
a = 4.7347 (1) Å
b = 18.1877 (7) Å
c = 18.1068 (6) Å
β = 93.594 (2)°
V = 1556.17 (9) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.10 mm^{-1}
T = 150 K
0.11 × 0.04 × 0.03 mm

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O1W^{i}	0.96 (2)	2.16 (2)	3.065 (2)	155.6 (17)
N2—H2···O1W^{i}	0.94 (2)	2.03 (2)	2.939 (2)	161.8 (19)
N3—H3···O2^{ii}	0.93 (2)	1.95 (2)	2.858 (2)	163.1 (19)
O1W—H1X···O2^{iii}	0.90 (3)	2.19 (3)	3.062 (2)	164 (2)
O1W—H1Y···O1	0.96 (3)	1.86 (3)	2.810 (2)	171 (2)

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

Data collection

Bruker X8 APEXII KappaCCD diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1998)
T_{min} = 0.989, T_{max} = 0.997
13901 measured reflections
4172 independent reflections
2477 reflections with $I > 2\sigma(I)$
R_{int} = 0.057

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.053
$wR(F^2)$ = 0.141
S = 1.00
4172 reflections
250 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.26 e Å^{-3}
$\Delta\rho_{min}$ = −0.24 e Å^{-3}

H atoms bound to aromatic C atoms were placed in idealized positions and included in the final structural model in a riding-motion approximation, with C—H = 0.95 Å and U_{iso}(H) = 1.2U_{eq}(C). H atoms associated with the solvent water molecule and the N—H groups were located directly from a difference Fourier map. The positions of these atoms were refined, with U_{iso}(H) = 1.5U_{eq}(N,O).

Data collection: *APEX2* (Bruker, 2006); cell refinement: *APEX2*; data reduction: *SAINT-Plus* (Bruker, 2005); program(s) used to solve structure: *SHELXTL* (Sheldrick, 2008); program(s) used to refine structure: *SHELXTL*; molecular graphics: *DIAMOND* (Brandenburg, 2009); software used to prepare material for publication: *SHELXTL*.

The authors are grateful to the Fundação para a Ciência e a Tecnologia (FCT, Portugal) for general financial support, for a postdoctoral research grant (No. SFRH/BPD/63736/2009, to JAF), for a doctoral research grant (No. SFRH/BD/44791/2008, to JM) and for specific funding toward the purchase of the single-crystal diffractometer.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GT3028). Services for accessing these data are described at the back of the journal.

References

Brandenburg, K. (2009). *DIAMOND*. Version 3.2. Crystal Impact GbR, Bonn, Germany.
Bregman, H., Carroll, P. J. & Meggers, E. (2006). *J. Am. Chem. Soc.* **128**, 877–884.
Bruker (2005). *SAINT-Plus*. Version 7.23a. Bruker AXS Inc., Madison, Wisconsin, USA.
Bruker (2006). *APEX2*. Version 2.1-RC13. Bruker AXS Inc., Madison, Wisconsin, USA.

Grell, J., Bernstein, J. & Tinhofer, G. (1999). *Acta Cryst.* B**55**, 1030–1043.
Keller, H. W. & Everhart, S. E. (2010). *Fungi*, **3**, 13–27.
Liu, R., Zhu, T., Li, D., Gu, J., Xia, W., Fang, Y., Liu, H., Zhu, W. & Gu, Q. (2007). *Arch. Pharm. Res.* **30**, 270–272.
Sánchez, C., Méndez, C. & Salas, J. A. (2006). *Nat. Prod. Rep.* **23**, 1007–1045.
Sheldrick, G. M. (1998). *SADABS*. Version 2.01. Bruker AXS Inc., Madison, Wisconsin, USA.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Slater, M. J., Cockerill, S., Baxter, R., Bonser, R. W., Gohil, K., Gowrie, C., Robinson, J. E., Littler, E., Parry, N., Randall, R. & Snowden, W. (1999). *Bioorg. Med. Chem.* **7**, 1067–1074.
Steglich, W. (1989). *Pure Appl. Chem.* **61**, 281–288.
Tamaoki, T., Nomoto, H., Takahashi, I., Kato, Y., Morimoto, M. & Tomita, F. (1986). *Biochem. Biophys. Res. Commun.* **135**, 397–402.
Zhu, G., Conner, S., Zhou, X., Shih, C., Brooks, H. B., Considine, E., Dempsey, J. A., Ogg, C., Patel, B., Schultz, R. M., Spencer, C. D., Teicher, B. & Watkins, S. A. (2003). *Bioorg. Med. Chem. Lett.* **13**, 1231–1235.