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Arcyriaflavin A monohydrate

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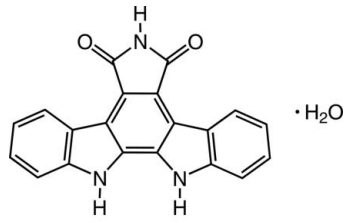
The asymmetric unit of the title compound comprises the monohydrated form of the natural product arcyriaflavin A [systematic name: 12,13-dihydro-5*H*-indolo[2,3-*a*]pyrrolo[3,4-*c*]-carbazole-5,7(6*H*)-dione monohydrate], $C_{20}H_{11}N_3O_2\cdot H_2O$. Individual molecular units are engaged in hydrogen-bonding 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*).

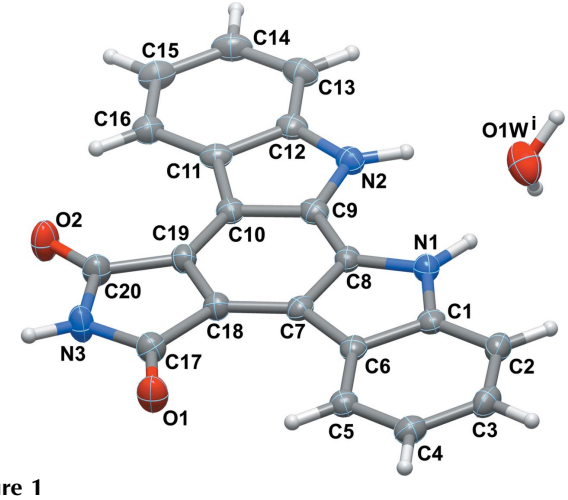


Figure 1
The asymmetric unit of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level. [Symmetry code: (i) $-x+1, y+\frac{1}{2}, -z+\frac{1}{2}$.]

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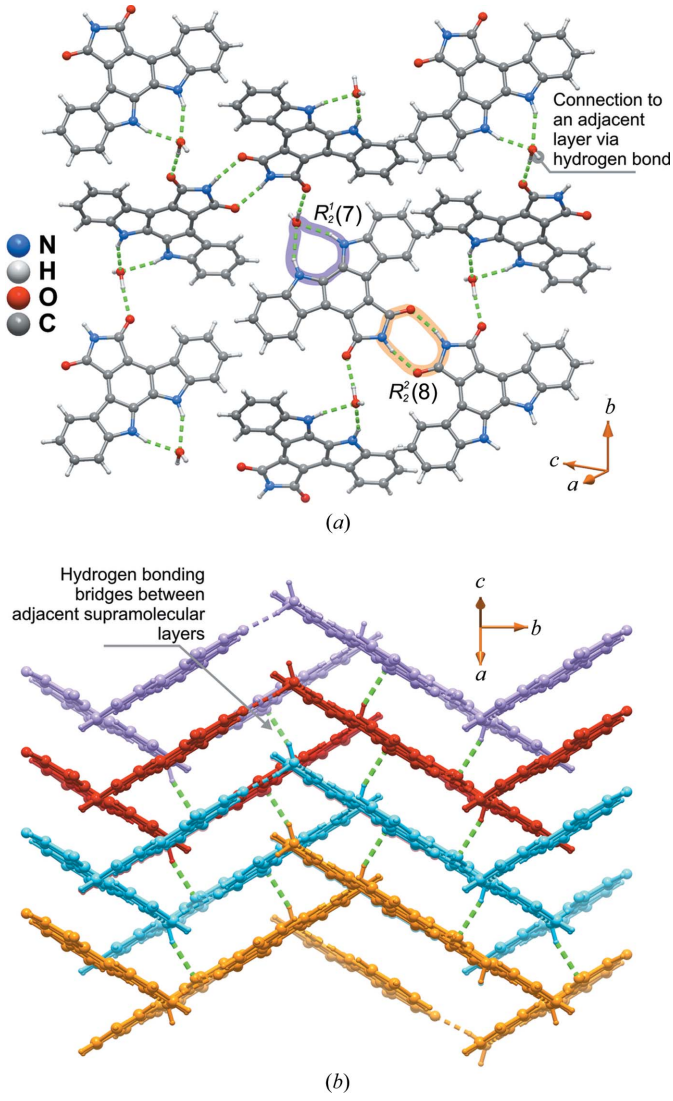

Figure 2
(*a*) Schematic representation of the two-dimensional supramolecular layer formed by the hydrogen-bonding interactions between arcyriaflavin A and water molecules. (*b*) A simplified view of the crystal packing, showing the hydrogen-bonding connections between adjacent layers *via* the solvent 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*.

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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.

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