Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

3,3,6,6-Tetramethyl-9-(4-pyridyl)-3,4,6,7,9,10-hexahydro-1,8(2*H*,5*H*)-acridinedione monohydrate

P. G. Aravindan,[a] M. Yogavel,[a] D. Velmurugan,[a]* P. Murugan,[b] S. Shanmuga Sundara Raj[c] and H.-K. Fun[d]

[a]Department of Crystallography and Biophysics, University of Madras, Guindy Campus, Chennai 600 025, India, [b]Department of Organic Chemistry, University of Madras, Guindy Campus, Chennai 600 025, India, [c]B3121 Medical Centre North, Department of Medicine-Nephrology, Nashville, USA, and [d]X-ray Crystallography Unit, School of Physics, Universiti Sains Malaysia, 11800 USM, Penang, Malaysia

Correspondence e-mail: d_velu@yahoo.com

Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.002 Å
R factor = 0.051
wR factor = 0.146
Data-to-parameter ratio = 18.5

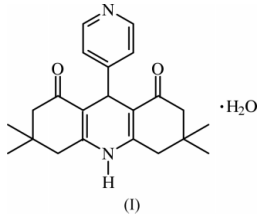
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 31 March 2003
Accepted 8 April 2003
Online 23 April 2003

In the acridine moiety of the title compound, $C_{22}H_{26}N_2O_2\cdot H_2O$, the central dihydropyridine ring adopts a flattened boat conformation, while the outer cyclohexene rings adopt sofa conformations. In the crystal structure, N—H···O and O—H···O hydrogen bonds involving the water molecule and C—H···O hydrogen bonds link the inversion-related molecules to form layers parallel to the (011) plane. Adjacent layers are linked by O—H···N hydrogen bonds involving the water molecule.

Comment

Acridine derivatives exhibit a wide range of biological activities, especially mutagenic, antitumour (Talacki *et al.*, 1974) and anti-amoebic activities (Prasad Krishna *et al.*, 1984). Acridine-containing drugs have been found to posses anti-protozoal activity (Karolak-Wojciechowska *et al.*, 1996) and are used for the treatment of Alzheimer's disease (Bandoli *et al.*, 1994). The ability of acridine to intercalate between the base pairs of DNA is well known (Neidle, 1979; Fan *et al.*, 1997). Substituted hexahydroacridine-1,8-dione, which resembles K-channel openers, relaxes KCl-preconcentrated urinary-bladder smooth muscle *in vitro* (Li *et al.*, 1996; Trivedi *et al.*, 1995). Acridine-1,8-diones exhibit fluorescence and laser activities (Selladurai *et al.*, 1990). Acridinediones were found to lase around 475–495 nm (Murugan *et al.*, 1998). The present study of the title compound, (I), is part of a series of investigations on the crystal structures of acridinedione derivatives.



(I)

In the acridine moiety, the central pyridine ring (*B*) adopts a flattened boat conformation, while the outer rings (*A* and *C*) adopt sofa conformations as confirmed by the total puckering amplitudes (Cremer & Pople, 1975) [Q_T = 0.470 (2), 0.144 (2) and 0.469 (2) Å for rings *A*, *B* and *C*, respectively] and the asymmetry parameters (Nardelli, 1983) [Δ_S(C1*A*) = 0.032 (1), Δ_S(C9) = 0.007 (1) and Δ_S(C1*A*—C4*A*) = 0.021 (1), Δ_S(C6) = 0.001 (1) for rings *A*, *B* and *C*, respectively]. The puckering of ring *B* is quite small, owing to the π conjugation in the C1*A*—C4*A*—N10—C5*A*—C8*A* system, as indicated by the bond distances: C1*A*—C4*A* = 1.360 (2), C4*A*—N10 = 1.366 (2), N10—C5*A* = 1.377 (2) and C5*A*—C8*A* = 1.357 (2) Å. Similar features have also been observed in other acridinedione

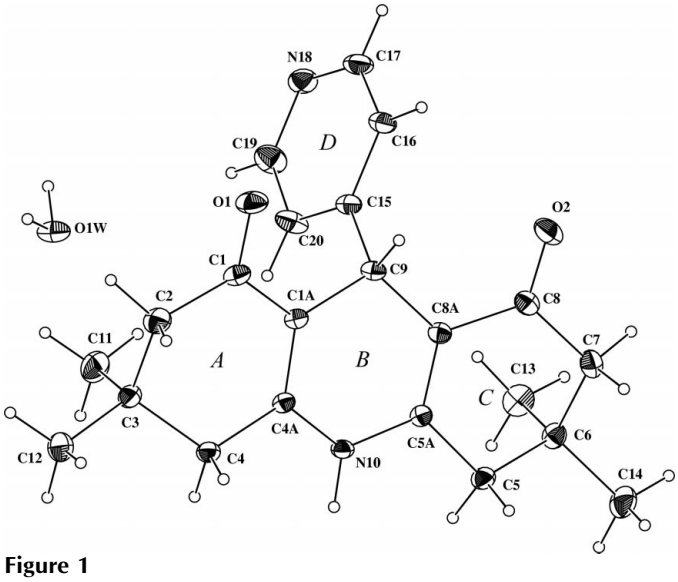


Figure 1
The molecular structure of title compound, showing 35% probability displacement ellipsoids.

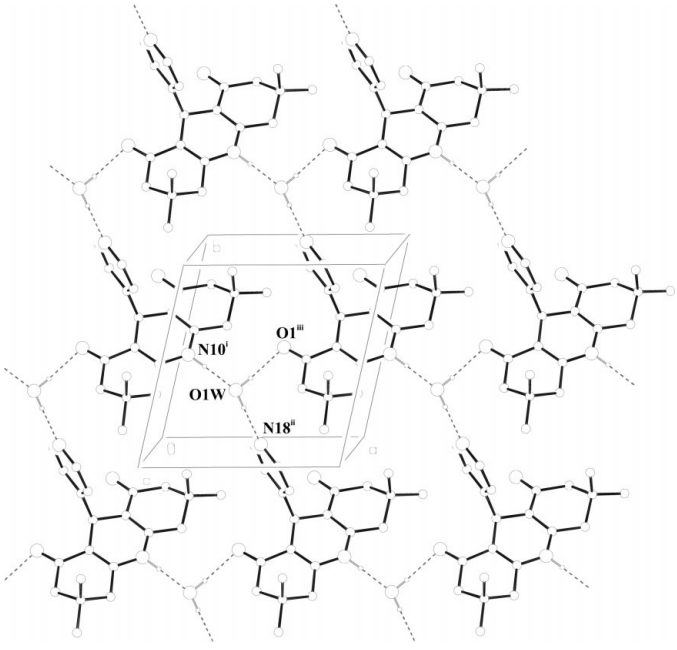


Figure 2
A view of the hydrogen-bonding network involving the water molecules [symmetry codes: (i) $1-x, 1-y, 1-z$; (ii) $1-x, -y, 1-z$; (iii) $-x, 1-y, 1-z$]. For clarity, H atoms not involved in hydrogen bonding have been omitted.

analogues (Gunasekaran *et al.*, 1997; Ganesh, Banumathi *et al.*, 1998; Ganesh *et al.*, 1999; Sankaranarayanan *et al.*, 1998). The C4*A*—C1*A*—C9—C15 torsion angle of 111.8 (2)° shows that the pyridyl ring (*D*) is axial to the acridine moiety. The acridine moiety is folded about the line passing through atoms C9 and N10, as seen from the dihedral angle of 14.38 (3)° between the C1/C2/C4/C4*A*/N10/C9/C1*A* and C5/C7/C8/C8*A*/C9/N10/C5*A* planes. The folding of the acridine moiety about the C9···N10 line is well documented (Ganesh, Velmurugan *et al.*, 1998; Ganesh, Banumathi *et al.*, 1998; Ganesh *et al.*, 1999; Sankaranarayanan *et al.*, 1998, 1999; Jeyakanthan *et al.*, 2000, 2002). The sum of the bond angles around N10 [359.3 (1)°] indicates sp^2 hybridization. In ring *B*, the C—N bond lengths (Table 1) are in agreement with the mean Csp^2—Nsp^2 bond length of 1.355 (14) Å reported by Allen *et al.* (1987).

The hydrogen-bonding network involving the water molecules is shown in Fig. 2. The water molecules take part in O—H···O, N—H···O and O—H···N hydrogen bonds. The N10—H10···O1*W*^{i}, O1*W*—H2*W*···O1^{iii}, C11—H11*B*···O1^{iii} and C17—H17···O2^{iv} (symmetry codes as in Table 2) hydrogen bonds link the inversion-related molecules to form layers parallel to the (011) plane. Adjacent layers are linked by O1*W*—H1*W*···N18^{ii} hydrogen bonds.

Experimental

To dimedone (0.75 g, 5.3 mmol) and pyridine-4-carboxaldehyde (0.28 g, 2.6 mmol) in ethanol was added ammonia (excess) and the mixture was refluxed for 8 h to afford the title compound. Single crystals were grown by slow evaporation from a solution in chloroform–methanol (1:1).

Crystal data

$C_{22}H_{26}N_2O_2\cdot H_2O$
$M_r = 368.46$
Triclinic, $P\overline{1}$
$a = 9.1333$ (5) Å
$b = 9.8999$ (5) Å
$c = 12.0435$ (7) Å
$\alpha = 74.876$ (1)°
$\beta = 81.705$ (1)°
$\gamma = 73.137$ (1)°
$V = 1003.26$ (9) Å^3
$Z = 2$
$D_x = 1.220$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3984 reflections
$\theta = 1.8$–28.3°
$\mu = 0.08$ mm^{-1}
$T = 293$ (2) K
Plate, yellow
0.48 × 0.26 × 0.12 mm

Data collection

Siemens SMART CCD area-detector diffractometer
ω scans
7019 measured reflections
4804 independent reflections
3516 reflections with $I > 2\sigma(I)$
$R_{int} = 0.022$
$\theta_{max} = 28.3°$
$h = -12 \rightarrow 12$
$k = -13 \rightarrow 12$
$l = -13 \rightarrow 16$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.051$
$wR(F^2) = 0.146$
$S = 1.03$
4804 reflections
260 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0728P)^2 + 0.1035P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.23$ e Å^{-3}
$\Delta\rho_{min} = -0.19$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O1—C1	1.2352 (18)	C9—C15	1.531 (2)
O2—C8	1.2255 (19)	C17—N18	1.333 (2)
C4*A*—N10	1.3660 (17)	N18—C19	1.328 (2)
C5*A*—N10	1.3774 (18)		
C4*A*—N10—C5*A*	121.49 (12)	C19—N18—C17	116.01 (15)
C1*A*—C9—C15—C20	−43.72 (19)	C8*A*—C9—C15—C16	−100.75 (16)
C1*A*—C9—C15—C16	135.57 (14)		

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N10—H10···O1W^{i}	0.93 (2)	1.87 (2)	2.799 (2)	174 (2)
O1W—H1W···N18^{ii}	0.91 (3)	1.96 (3)	2.869 (2)	179 (2)
O1W—H2W···O1^{iii}	0.85 (3)	2.06 (3)	2.902 (2)	175 (2)
C11—H11B···O1^{iii}	0.96	2.47	3.326 (2)	149
C17—H17···O2^{iv}	0.93	2.44	3.366 (2)	172

Symmetry codes: (i) $-x, 1-y, 1-z$; (ii) $1-x, -y, 1-z$; (iii) $1-x, 1-y, 1-z$; (iv) $1-x, -y, 2-z$.

Atoms H10, H1W and H2W were located from a difference Fourier map and refined isotropically; the remaining H atoms were fixed geometrically and allowed to ride on their attached atoms. For the refined H atoms, the O—H distances are 0.85 (3) and 0.91 (3) Å, and the N—H distance is 0.93 (2) Å. Rotating-group refinement was used for the methyl groups.

Data collection: *SMART* (Siemens, 1996); cell refinement: *SAINT* (Siemens, 1996); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ZORTEP* (Zsolnai, 1997) and *PLATON* (Spek, 1990); software used to prepare material for publication: *SHELXL*97 and *PARST* (Nardelli, 1995).

Financial support from the Department of Science and Technology (DST) and the University Grants Commission (UGC), Government of India, are gratefully acknowledged.

References

Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, A. G. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans.* 2, pp. S1–19.
Bandoli, G., Dolmella, A., Gatto, S. & Nicolini, M. (1994). *J. Chem. Crystallogr.* **24**, 301–310.
Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
Fan, J.-Y., Tercel, M. & Denny, W. A. (1997). *Anti-Cancer Drug Res.* **12**, 277–293.
Ganesh, V. K., Banumathi, S., Velmurugan, D., Ramasubbu, N. & Ramakrishnan, V. T. (1998). *Acta Cryst.* C**54**, 633–635.
Ganesh, V. K., Banumathi, S., Velmurugan, D. & Ravikumar, K. (1999). *Cryst. Res. Technol.* **34**, 929–934.
Ganesh, V. K., Velmurugan, D., Bidya Sagar, M. & Murugan, P. (1998). *Acta Cryst.* C**54**, 557–559.
Gunasekaran, K., Velmurugan, D. & Murugan, P. (1997). *Acta Cryst.* C**53**, 1512–1514.
Jeyakanthan, J., Shanmuga Sundara Raj, S., Velmurugan, D., Fun, H.-K., Joseph Rajan, T. & Ramakrishnan, V. T. (2000). *Acta Cryst.* C**56**, 1109–1112.
Jeyakanthan, J., Yogavel, M., Joseph Rajan, T., Velmurugan, D. & Sekar, K. (2002). *Cryst. Res. Technol.* **37**, 1029–1037.
Karolak-Wojciechowska, J., Morzek, A., Amiel, P., Brouant, P. & Barbe, J. (1996). *Acta Cryst.* C**52**, 2939–2941.
Li, J. H., Yasay, G. D., Kan, S. T., Ohnmacht, C. J., Trainor, D. A., Boney, A. D., Heppner, T. J. & Nelson, M. T. (1996). *Drug Res.* **46**, 523–530.
Murugan, P., Shanmugasundaram, P., Ramakrishnan, V. T., Venkatachalapathy, B., Srividya, N., Ramamurthy, P., Gunasekaran, K. & Velmurugan, D. (1998). *J. Chem. Soc. Perkin Trans.* 2, pp. 999–1003.
Nardelli, M. (1983). *Comput. Chem.* **7**, 95–98.
Nardelli, M. (1995). *J. Appl. Cryst.* **28**, 659.
Neidle, S. (1979). *Prog. Med. Chem.* **16**, 151–221.
Prasad Krishna, B. N., Bansal, I., Das, P. & Srivatsava, R. (1984). *Curr. Sci.* **53**, 778–780.
Sankaranarayanan, R., Shanmuga Sundara Raj, S., Velmurugan, D. & Fun, H.-K. (1999). *Acta Cryst.* C**55**, 1513–1514.
Sankaranarayanan, R., Velmurugan, D., Murugan, P. & Ramasubbu, N. (1998). *Acta Cryst.* C**54**, 1534–1535.
Selladurai, S., Subramaninan, K. & Ramakrishnan, V. T. (1990). *J. Crystallogr. Spectrosc. Res.* **20**, 227–232.
Sheldrick, G. M. (1997). *SHELXS*97 and *SHELXL*97. University of Göttingen, Germany.
Siemens (1996). *SMART* and *SAINT*. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Spek, A. L. (1990). *Acta Cryst.* A**46**, C-34.
Talacki, R., Carrel, H. L. & Glusker, J. P. (1974). *Acta Cryst.* B**30**, 1044–1047.
Trivedi, S., Potterlee, L., McConvill, M. W., Li, J. H., Ohnmacht, C. J., Trainor, D. A. & Kau, S. T. (1995). *Mol. Path. Pharmacol.* **88**, 137–151.
Zsolnai, L. (1997). *ZORTEP*. University of Heidelberg, Germany.