Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

11-Methylpyrido[2,3-*b*]acridine-5,12-dione

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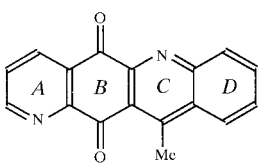
Received 13 July 1999
Accepted 22 October 1999

The title molecule, $C_{17}H_{10}N_2O_2$, is a synthetic precursor to the cytotoxic marine alkaloid ascididemin and is also structurally related to cleistopholine, a plant-derived antifungal agent. The molecule was found to be essentially planar with the only significant deviations from planarity being for the quinone O atoms.

Comment

The search for new human anticancer agents from the marine environment has resulted in the isolation of a large range of polycyclic alkaloids based upon the pyridoacridine framework (Molinski, 1993). Two such examples are the cytotoxic pentacyclic alkaloids ascididemin and its analogue 2-bromoleptoclinidinone (Kobayashi *et al.*, 1988; Bloor & Schmitz, 1987; deGuzman & Schmitz, 1989; Bracher, 1997; Lindsay *et al.*, 1998). Both molecules associate with DNA, probably *via* base-pair intercalation. In direct contrast to this, previous studies have noted that the tetracyclic synthetic precursor to ascididemin, 11-methylpyrido[2,3-*b*]acridine-5,12-dione, (I) (NSC 659780), exhibits only modest cytotoxicity (Bracher, 1997), and moderate antibacterial and antifungal properties (Lindsay *et al.*, 1995). As part of our studies directed towards understanding the chemistry (Lindsay *et al.*, 1997, 1998; Copp *et al.*, 1999) and biological activities (Lindsay *et al.*, 1995; Copp *et al.*, 1999) of ascididemin and related marine alkaloids, we now report on the crystal structure of (I).



(I)

The title molecule (see Fig. 1) was found to be highly planar, with the greatest deviations from the mean molecular plane being for the quinone atoms O1 [0.125 (4) Å] and O2 [0.195 (4) Å], thus making it a good DNA intercalating chromophore. There are few reported X-ray studies of the quinoline–quinone substructure present in rings *AB* of (I) although this fragment is present in many biologically active agents, including the antibiotic streptonigrin (Chiu & Lipscomb, 1975) and aza-analogues of the antitumour agent mitoxantrone (Krapcho *et al.*, 1994). Bond lengths observed for rings *A* and *B* of (I) are comparable with those reported for other quinoline–quinone-bearing compounds (Chiu & Lipscomb, 1975; Kita *et al.*, 1991; Gieren & Schanda, 1977). However, steric congestion between the quinone O1 and methyl C1′ atoms is apparent in (I), as evidenced by bond angles of 118.8 (3) (O1—C12—C12a) and 122.6 (3)° (O1—C12—C11a). This interaction is presumably also responsible for the quinone O atoms bending out of the plane of the rings. Extensive π–π stacking was evident in the crystal of (I), with rings *BCD* of one molecule overlapping rings *ABC* of an adjacent molecule (Fig. 2). The perpendicular separation between individual chromophores is 3.4 Å.

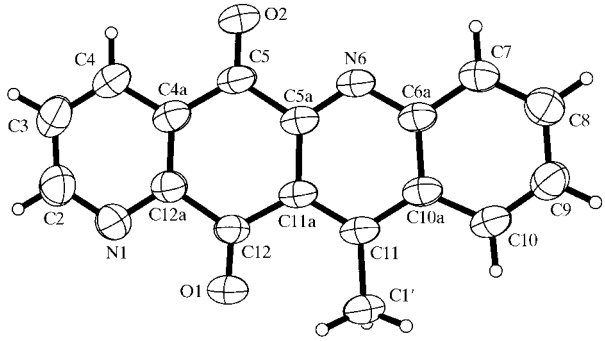


Figure 1
The structure of (I) showing 50% probability displacement ellipsoids.

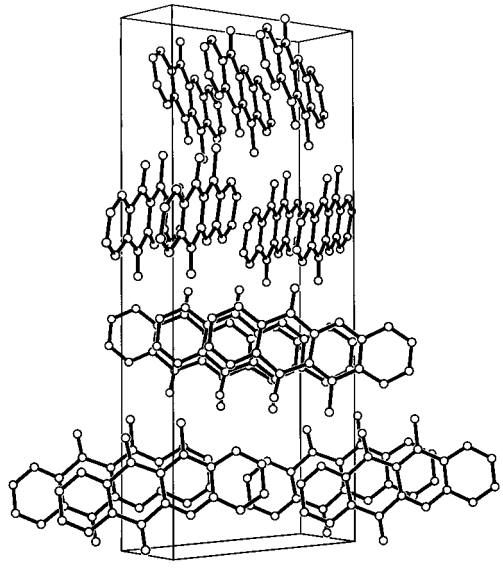


Figure 2
The unit cell contents showing the π–π stacking.

Experimental

11-Methylpyrido[2,3-*b*]acridine-5,12-dione was prepared by a published route and yielded spectroscopic data identical in all respects with those reported previously (Bracher, 1989). Recrystallization from a methanol–dichloromethane solution yielded yellow–brown needles [m.p. 520–525 K, literature 513–521 K (Bracher, 1989)] suitable for X-ray analysis. Full assignment of ^{1}H and ^{13}C NMR data was made by use of standard two-dimensional NMR techniques. ^{1}H NMR (200 MHz, $CDCl_3$): δ 9.16 (1H, *dd*, J = 4.6, 1.8 Hz, H-2), 8.73 (1H, *dd*, J = 8.0, 1.8 Hz, H-4), 8.45 (1H, *dd*, J = 8.5, 0.9 Hz, H-10), 8.38 (*dd*, J = 8.5, 0.9 Hz, H-7), 7.93 (1H, *ddd*, J = 8.3, 6.9, 1.4 Hz, H-8), 7.79 (1H, *ddd*, J = 8.3, 6.9, 1.4 Hz, H-9), 7.77 (1H, *dd*, J = 7.9, 4.6 Hz, H-3), 3.32 (3H, *s*, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.3 (*s*, C-12), 181.8 (*d*, J = 4 Hz, C-5), 155.6 (*ddd*, J = 183, 8, 4 Hz, C-2), 152.7 (*dd*, J = 6, 3 Hz, C-11), 150.2 (*t*, J = 5 Hz, C-12a), 148.6 (*t*, J = 8 Hz, C-6a), 147.5 (*s*, C-5a), 135.7 (*dd*, J = 170, 6 Hz, C-4), 132.7 (*dd*, J = 163, 9 Hz, C-8), 132.3 (*dd*, J = 165, 7 Hz, C-7), 130.0 (*d*, J = 7 Hz, C-4a), 125.5 (*dd*, J = 161, 8 Hz, C-10), 129.8 (*dd*, J = 163, 9 Hz, C-9), 129.8 (*m*, C-10a), 127.9 (*dd*, J = 167, 9 Hz, C-3), 125.5 (*m*, C-11a), 16.7 (*q*, J = 130 Hz, CH_3).

Crystal data

$C_{17}H_{10}N_2O_2$
M_r = 274.27
Orthorhombic, $Pca2_1$
a = 25.7526 (17) Å
b = 4.2348 (3) Å
c = 11.2966 (7) Å
V = 1231.97 (14) Å^3
Z = 4
D_x = 1.479 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 5243 reflections
θ = 1.5–25.0°
μ = 0.099 mm^{-1}
T = 293 (2) K
Needle, brown
0.94 × 0.18 × 0.18 mm

Data collection

Siemens SMART CCD diffractometer
Area-detector ω scans
Absorption correction: multi-scan (Blessing, 1995; Sheldrick, 1998)
T_{min} = 0.912, T_{max} = 0.982
6391 measured reflections
2040 independent reflections
1845 reflections with $I > 2\sigma(I)$
R_{int} = 0.057
θ_{max} = 25°
$h = -25 \rightarrow 30$
$k = -5 \rightarrow 5$
$l = -14 \rightarrow 12$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.054
$wR(F^2)$ = 0.141
S = 1.016
2040 reflections
190 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0608P)^2 + 0.3024P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.032
$\Delta\rho_{max}$ = 0.16 e Å^{-3}
$\Delta\rho_{min}$ = −0.18 e Å^{-3}

Data collection: *SMART* (Siemens, 1994); cell refinement: *SAINT* (Siemens, 1994); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997*a*); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997*b*); molecular graphics: *SHELXTL* (Siemens, 1994); software used to prepare material for publication: *SHELXL*97.

Table 1
Selected geometric parameters (Å, °).

O1—C12	1.195 (4)	C4a—C12a	1.385 (4)
O2—C5	1.205 (4)	C4a—C5	1.483 (5)
N1—C12a	1.335 (4)	C5a—C11a	1.430 (4)
N1—C2	1.338 (5)	C5a—C5	1.496 (4)
N6—C5a	1.313 (4)	C11a—C12	1.489 (4)
N6—C6a	1.358 (4)	C12a—C12	1.509 (4)
C1′—C11	1.510 (4)		
O2—C5—C4a	120.6 (3)	C10a—C11—C1′	119.0 (3)
O2—C5—C5a	121.6 (3)	O1—C12—C11a	122.6 (3)
C4a—C5—C5a	117.9 (2)	O1—C12—C12a	118.8 (3)
C11a—C11—C10a	117.6 (2)	C11a—C12—C12a	118.6 (2)
C11a—C11—C1′	123.4 (3)		

Supplementary data for this paper are available from the IUCr electronic archives (Reference: JA1007). Services for accessing these data are described at the back of the journal.

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