Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

(1*R*,2*R*)-Ethyl 1-azido-2-hydroxy-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole-9-carboxylate

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.003 Å
R factor = 0.032
wR factor = 0.083
Data-to-parameter ratio = 10.0

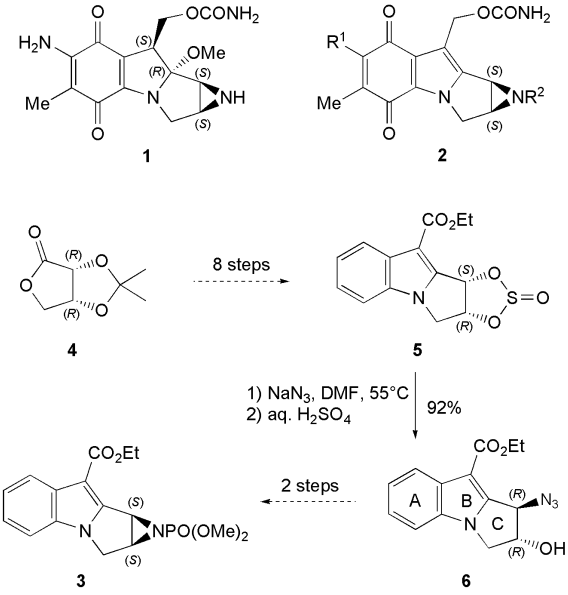
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

The crystal structure of the title compound, $C_{14}H_{14}N_4O_3$, confirms both the sites of attachment and the *trans* arrangement of the hydroxy and azide substituents, and reveals intermolecular hydrogen bonding between OH and C=O units, resulting in a chain of molecules along the *b* axis.

Received 6 December 2004
Accepted 4 January 2005
Online 8 January 2005

Comment

Mitomycin C, (1), a widely prescribed drug for the treatment of solid tumours, is the best known representative of the mitomycins, a small group of *Streptomyces* metabolites having potent antibacterial and antitumour activity (Franck, 1978; Remers & Dorr, 1988; Kasai & Kono, 1992; Danishefsky & Schkeryantz, 1995). Considerable effort has been devoted to the synthesis of these structurally intriguing compounds and analogues such as the aziridinomitosenes, which have the general structure (2). We have recently published an asymmetric synthesis of (3), a tetracyclic model for aziridinomitosenes, from the chiral lactone precursor (4) (Michael *et al.*, 2001). A key step in the late-stage construction of the aziridine ring was the nucleophilic ring opening of the cyclic sulfite (5) with an azide ion. Although the reaction produced an azido alcohol in an excellent yield of 92%, spectroscopy alone did not provide conclusive evidence for either the regiochemistry or the stereochemistry of ring opening. Since crystals of the product (6) could readily be grown from ethyl acetate/hexane, the structure of this important late intermediate was therefore investigated by X-ray crystallography.



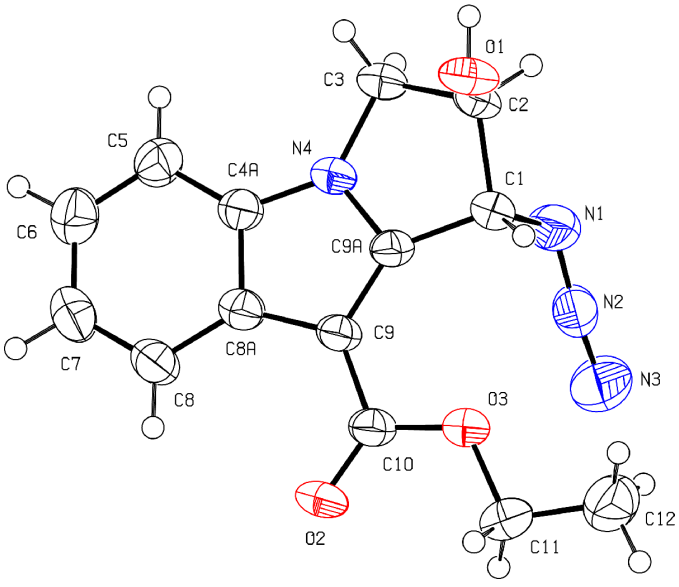


Figure 1
A view of (6) with the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

The molecular structure of the product was revealed as (6) (Fig. 1). The labile sulfite system is thus attacked by azide ion at atom C1 (effectively a reactive benzylic position), with the expected inversion of configuration at the C atom. The *trans* disposition of the azide and alcohol substituents at atoms C1 and C2, respectively, is clearly demonstrated by the N1—C1—C2—O1 torsion angle of −149.18 (16)°. The azide substituent itself is not perfectly linear, as shown by the N1—N2—N3 bond angle of 172.0 (2)°. There is also a substantial difference in the N—N bond lengths; the N1—N2 distance between the central N atom and that closest to the heterocyclic core is 1.220 (2) Å, while the N2—N3 bond length is shorter at 1.129 (2) Å. A search of the Cambridge Structural Database (CSD; Version 5.25, update 3 of July 2004; Allen, 2002) showed that these are quite typical features for organic azides, many examples of which have been reported. The indole moiety (rings *A* and *B*) is essentially planar as expected, but in ring *C*, atom C2 lies out of the C1/C9*A*/N4/C3 plane [C1—C9*A*—N4—C3 = −3.9 (2)°] by 0.417 (2) Å. The absolute configuration of (6), inferred from the known absolute configuration of the chiral precursor (4), could not be confirmed crystallographically. A notable feature of the crystal packing (Fig. 2) is the presence of hydrogen-bonded chains of molecules along the *b* axis, the effect arising from interaction between the H atom of the hydroxy group and the ester carbonyl group of an adjacent molecule (Table 1).

Experimental

A solution of the sulfite (5) (109 mg, 0.35 mmol) and sodium azide (44 mg, 0.67 mmol, 1.9 equivalents) in DMF (2.2 ml) was heated at 328 K (internal temperature) under an atmosphere of N_2 for 4 h. The solvent was removed *in vacuo* to give an orange oil (212 mg), which was dissolved in THF (2.2 ml). Addition of concentrated H_2SO_4 (0.02 ml) caused brief effervescence. After addition of water (0.01 ml), the resulting solution was stirred under N_2 for 1 h at room temperature. Neutralization with saturated aqueous $NaHCO_3$ resulted in the separation of a viscous milky oil. The reaction mixture was diluted with water (10 ml) and separated. The aqueous phase was extracted with EtOAc (3 × 15 ml). The combined organic phases were dried (Na_2SO_4) and concentrated *in vacuo* to afford a crude brown solid (98 mg). Purification by column chromatography on silica gel with 10–30% EtOAc–hexane mixtures gave azido alcohol (6) (94 mg, 92%); yellow powder, m.p. 402.5 K (from EtOAc–hexane); $[\alpha]_D^{23}$ −2.2 (c 0.92, abs. EtOH). Analysis found: C 58.77, H 4.70, N 19.07%; $C_{14}H_{14}N_4O_3$ requires: C 58.74, H 4.93, N 19.57%. Crystals suitable for X-ray crystallography were obtained as yellow–brown plates by slow growth from a solution of (6) in EtOAc/hexane.

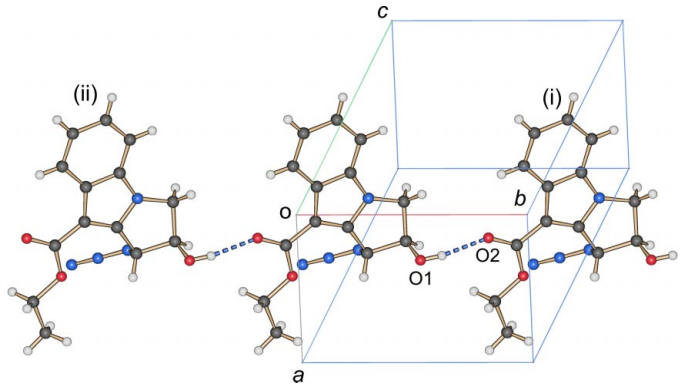


Figure 2
Part of the crystal structure of (6), showing the intermolecular hydrogen bonding along the *b* axis. [Symmetry codes: (i) *x*, *y* + 1, *z*; (ii) *x*, *y* − 1, *z*.]

Crystal data

$C_{14}H_{14}N_4O_3$
M_r = 286.29
Orthorhombic, $P2_12_12_1$
a = 5.8464 (9) Å
b = 8.8422 (14) Å
c = 26.927 (4) Å
V = 1392.0 (4) Å^3
Z = 4
D_x = 1.366 Mg m^{-3}
Mo *Kα* radiation
Cell parameters from 809 reflections
θ = 2.8–24.4°
μ = 0.10 mm^{-1}
T = 293 (2) K
Plate, yellow–brown
0.40 × 0.24 × 0.10 mm

Data collection

Bruker SMART CCD area-detector diffractometer
φ and ω scans
9551 measured reflections
1968 independent reflections
1439 reflections with $I > 2\sigma(I)$
R_{int} = 0.030
θ_{max} = 28.0°
h = −7 → 7
k = −11 → 9
l = −35 → 33

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.032
$wR(F^2)$ = 0.083
S = 1.09
1968 reflections
196 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0435P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.005
$\Delta\rho_{max}$ = 0.15 e Å^{-3}
$\Delta\rho_{min}$ = −0.11 e Å^{-3}
Extinction correction: *SHELXTL*
Extinction coefficient: 0.0084 (19)

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

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1A···O2^{i}	0.83 (2)	1.94 (2)	2.7553 (19)	166 (2)

Symmetry code: (i) $x, y+1, z$.

In the absence of significant anomalous dispersion effects, Friedel pairs were merged and the $\Delta f''$ term was set to zero; the absolute configuration was assumed from that known for the precursor (4). With the exception of H1*A*, all H atoms were first located in a difference map, and then positioned geometrically and allowed to ride on their respective parent atoms, with C—H bond lengths of 0.93 (aromatic), 0.96 (CH_3), 0.97 (CH_2) or 0.98 Å (other CH), and isotropic displacement parameters equal to 1.2 (CH and CH_2) or 1.5 (CH_3) times U_{eq} of the parent atom. Atom H1*A* was located in the difference map, then refined freely.

Data collection: *SMART-NT* (Bruker, 1998); cell refinement: *SAINT-Plus* (Bruker, 1999); data reduction: *SAINT-Plus*; program(s) used to solve structure: *SHELXTL* (Bruker, 1999); program(s) used to refine structure: *SHELXTL*; molecular graphics: *PLATON* (Spek, 2003) and *SCHAKAL97* (Keller, 1997); software used to prepare material for publication: *SHELXTL*.

This work was supported by grants from the National Research Foundation, Pretoria (NRF, GUN 2053652), the University of the Witwatersrand and the Mellon Postgraduate Mentoring Programme (sponsored by the Andrew W. Mellon Foundation).

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