Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

(1*S*,4*R*,5*R*,6*R*)-6-Methoxycarbonyl-4-pivaloyloxy-2-(pivaloyloxymethyl)-bicyclo[3.1.0]hex-2-ene-1-carboxylic acid

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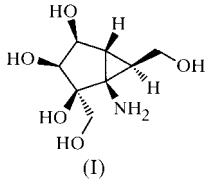
Received 16 September 1999
Accepted 25 November 1999

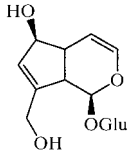
The stereochemistry of the title compound, $C_{20}H_{28}O_8$, a key step in the preparation of analogues of mannostatins, potent inhibitors of α-mannosidase, has been established. The carboxylic acid group at C1 unexpectedly eclipses the C1—C2 bond. The cyclopropane ring makes a dihedral angle of 109.4 (2)° with the cyclopentene ring.

Comment

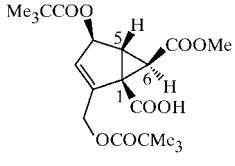
Polyhydroxylated aminocyclopentanes, exemplified by mannostatins *A* and *B*, isolated from the culture broth of *Streptoverticillium verticillus*, exhibit potent inhibiting activity towards α-mannosidase (Aoyagi, Hamada *et al.*, 1989; Aoyagi, Elbein *et al.*, 1990). Consequently, they display interesting biological activities, such as antiviral, antimetastasic and immunomodulator (Jacob, 1995, and references cited therein; Breton *et al.*, 1991). To contribute to the investigation of



(I)



(II)



(III)

structure–activity relationships, we prepared the conformationally restricted bicyclo[3.1.0]hexane analogue, (I) (Cachet *et al.*, 2000). A novel synthetic approach was developed, starting from the natural iridoid aucubin, (II), as the source of chiral cyclopentane. The key step was the reaction of iodolactones derived from (II) with sodium triethylsilanolate (TMSONa) to create the cyclopropane ring. In the course of the synthesis, compound (III) was obtained. The stereochemistry at C1, C5, C6 and consequently, the mechanism of the TMSONa rearrangement were established by this X-ray diffraction analysis.

The carboxylic acid at C1 eclipses unexpectedly the C1—C2 bond [torsional angle C2—C1—C7—O9 0.9 (3)°]. This is probably to be ascribed to the hydrogen bond which links the carboxylic acid O8—H to the O13 carbonyl of a symmetry-related molecule ($-x$, $-\frac{1}{2}+y$, $1-z$) [O8···O13 2.702 (2), H···O13 1.93 Å and O8—H···O13 156.5°]. The cyclopentene ring is practically planar: C4 being 0.067 (3) Å from the mean plane of the four other atoms. The cyclopropane ring makes a dihedral angle of 109.4 (2)° with the mean plane of the cyclopentene ring (Fig. 1).

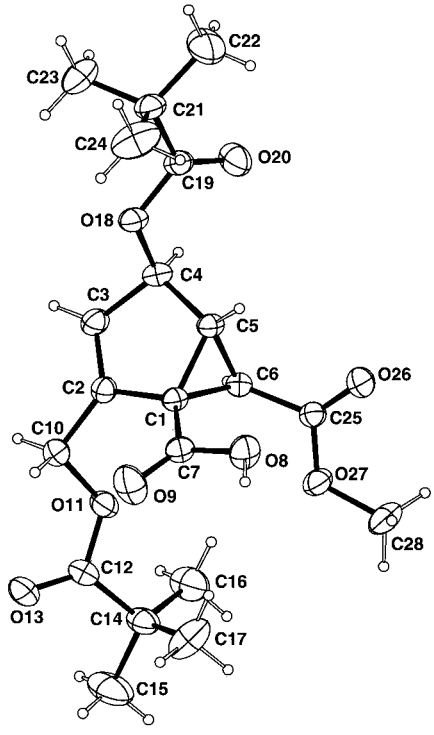


Figure 1
ORTEP (Johnson, 1965) plot of (III) with the atomic numbering. Ellipsoids are drawn at the 30% probability level.

Experimental

Crystal data

$C_{20}H_{28}O_8$
M_r = 396.42
Monoclinic, $P2_1$
a = 8.869 (2) Å
b = 9.836 (2) Å
c = 12.225 (6) Å
β = 91.40 (3)°
V = 1066.1 (6) Å^3
Z = 2
D_x = 1.235 Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 12.9–18.7°
μ = 0.797 mm^{-1}
T = 293 (2) K
Prism, colourless
0.50 × 0.30 × 0.30 mm
Crystal source: chemical synthesis

Data collection

Nonius CAD-4 diffractometer
$\theta/2\theta$ scans
4755 measured reflections
3601 independent reflections
3430 reflections with $I > 2\sigma(I)$
$R_{int} = 0.050$
$\theta_{max} = 66.90^\circ$
$h = -10 \rightarrow 10$
$k = -11 \rightarrow 11$
$l = -10 \rightarrow 14$
3 standard reflections
frequency: 120 min
intensity decay: 2%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.040$
$wR(F^2) = 0.108$
$S = 1.055$
3601 reflections
255 parameters
H atoms constrained
$w = 1/[\sigma^2(F_o^2) + (0.0707P)^2 + 0.0992P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.018$
$\Delta\rho_{max} = 0.20$ e Å^{-3}
$\Delta\rho_{min} = -0.20$ e Å^{-3}
Extinction correction: *SHELXL*93 (Sheldrick, 1993)
Extinction coefficient: 0.0211 (15)

A total of 1626 Friedel pairs were measured. The absolute configuration was not established by anomalous dispersion effects. The enantiomer has been assigned by reference to an unchanging chiral centre in the synthetic procedure.

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1987); cell refinement: *CAD*-4 *Software*; data reduction: *NONIUS* (Riche, 1989); program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*93; molecular graphics: *R3M* (Riche, 1983) and *ORTEP* (Johnson, 1965).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GS1062). Services for accessing these data are described at the back of the journal.

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