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Key indicators

Single-crystal X-ray study

$T = 294\text{ K}$

Mean $\sigma(\text{C}-\text{C}) = 0.007\text{ \AA}$

R factor = 0.027

wR factor = 0.063

Data-to-parameter ratio = 13.3

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

(2*R*,3*S*,4*S*,5*R*)-4-Hydroxy-3-iodo-5-methyltetrahydro- 2-furylmethyl benzoate

The crystal structure determination of the title compound, $\text{C}_{13}\text{H}_{15}\text{IO}_4$, has allowed the relative stereochemistry between the tetrasubstituted C atoms on the tetrahydrofuran moiety to be confirmed. The title compound is a precursor of the ionophoric antibiotic Aplasmomycin. The compound is involved in both intra- and intermolecular hydrogen bonding, the latter link the molecules into chains running along the b axis.

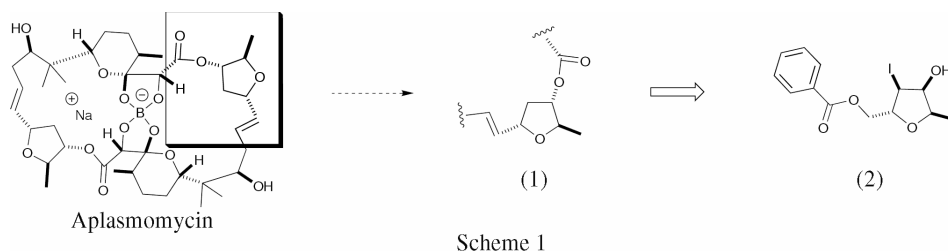
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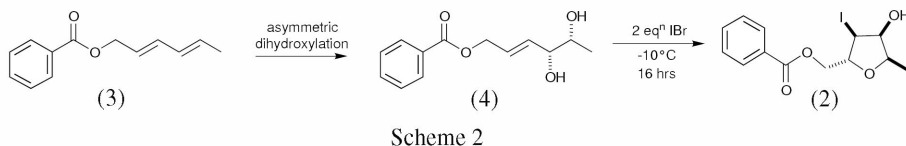
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Comment

The title compound, (2), was synthesized as part of an ongoing synthetic project towards the synthesis of the C_2 -symmetric boron-containing antibiotic Aplasmomycin (Scheme 1; Knight *et al.*, 2000). Aplasmomycin and its congeners are metabolites of *Streptomyces griseus* and are a unique family of boron-containing ionophoric antibiotics which show activity against Gram-positive bacteria. To date, two total and two formal syntheses of Aplasmomycin have been reported (Corey *et al.*, 1982; White *et al.*, 1986; Nakata *et al.*, 1986; Matsuda *et al.*, 1990).



Tetrahydrofuran (1) differentially appended at the 2-, 4- and 5-positions is a crucial component of Aplasmomycin. The precursor to (1) in our prospective synthesis of the natural product required tetrahydrofuran (2). 3-Iodotetrahydrofuran,



(2) was readily synthesized in three steps using commercially available hexa-2,4-dien-1-ol as the starting material. Esterification of this with benzoyl chloride yielded quantitatively the ester (2) (Scheme 2), reaction of which under Sharpless asymmetric dihydroxylation conditions (273 K, aqueous 'BuOH; 1:1, 0.004 eqⁿ K_2OsO_4 , 0.01 eqⁿ DHQD-PHAL, 3 eqⁿ $\text{K}_3\text{Fe}(\text{CN})_6$, 3 eqⁿ K_2CO_3 , 1 eqⁿ MeSO_2NH_2) yielded diol (4)

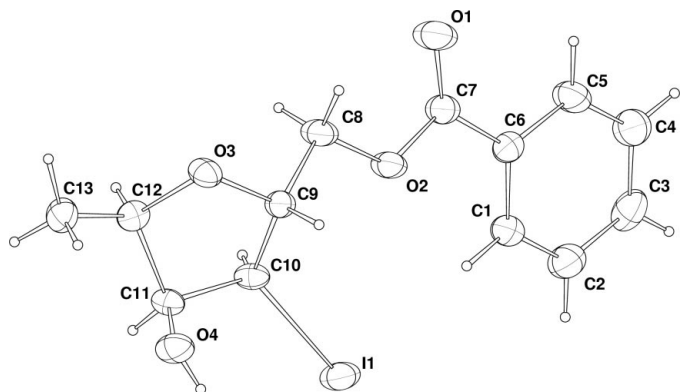


Figure 1
View of (1) (50% probability displacement ellipsoids)

(55%). Finally, treatment of diol (4) under anhydrous conditions with 2 eqⁿ of iodine monobromide (263 K) gave (2) via a 5-endo-trig iodocyclization (Knight *et al.*, 1999, 2000). Subsequent diiodination (Bu₃SnH, AIBN) and Mitsunobu mediated alcohol inversion (DIAD, PPh₃, *p*-nitrobenzoic acid) yielded precursor the tetrahydrofuran (1) (Scheme 2).

To our knowledge, this is the first reported crystal structure determination of a 2,3,4,5-tetrahydrofuran appended with a hydroxymethyl group (esterified), an I atom, a hydroxyl and a methyl group. The X-ray determination was necessary to confirm the stereochemistry as NMR coupling constant data was ambiguous and NOE data only was considered insufficient upon which to base the subsequent synthetic plans.

The title molecule is involved in both intra- and intermolecular hydrogen bonding. An interaction between the hydroxyl H atom of O4 and the O atom of the tetrahydrofuran links the molecules into chains running along the *b* axis. The large deviation from linearity of this bond [132 (5)^o] is a direct result of an additional competitive interaction between the same hydrogen and I1.

The tetrahydrofuran ring is puckered in an envelope form with C11 deviating by −0.640 (6) Å from the plane of the remaining four atoms. The conformation around the *sp*³ atoms C8 and C9 is almost perfectly staggered [O3—C9—C8—O2 = 173.2 (4)^o] such that O3 and O2 adopt a *trans* configuration.

There are four chiral centres in the molecule all within the tetrahydrofuran ring; C9 = *R*, C10 = *S*, C11 = *S* and C12 = *R*.

Experimental

To a 50 ml flame-dried round-bottomed flask equipped with a stirrer-bead and a suba-seal was added 500 mg (2.11 mmol) of (4). Diol (4) was dissolved in 25 ml of dry acetonitrile (Perrin & Armarego, 1988; acetonitrile refluxed and distilled from calcium hydride under argon, according to the procedure stated in the reference). To the cold (263 K) stirred solution, under argon, was added solid iodine monobromide in one portion (873 mg, 4.22 mmol, 2 equivalents). The resulting solution was stirred at 263 K in the dark under argon (flask wrapped in aluminium foil). After 16 h, TLC analysis indicated that all of the starting material had been consumed (eluent; ether: petrol, 1:1). The crude reaction mixture was stripped of the acetonitrile *in vacuo* (bath temperature no higher than 308 K) and replaced with

50 ml of dichloromethane. The dichloromethane solution was washed with water (3 × 50 ml), then with 2.5 *M* aqueous sodium thiosulfate (2 × 75 ml) and finally with saturated brine solution (50 ml) before being dried (MgSO₄), filtered and the solvent removed *in vacuo*. The crude product was purified *via* flash column chromatography (silica gel) using 1:1 pentane/ether as eluent. The title compound was obtained as a white solid (595 mg, 78%). Suitable crystals were grown by dissolving the purified product in a small amount of pure solvent and allowing the solvent to evaporate slowly.

Crystal data

C₁₃H₁₅IO₄
M_r = 362.15
 Orthorhombic, *P*2₁2₁2₁
a = 4.7970 (10) Å
b = 11.886 (2) Å
c = 23.775 (5) Å
V = 1355.6 (5) Å³
Z = 4
D_x = 1.774 Mg m^{−3}

Mo *K*α radiation
 Cell parameters from 4354 reflections
 θ = 3.09–25.03^o
 μ = 2.37 mm^{−1}
T = 293 (2) K
 Block, colourless
 0.5 × 0.3 × 0.3 mm

Data collection

Nonius KappaCCD area-detector diffractometer
 φ and ω scans to fill Ewald sphere
 Absorption correction: empirical (SORTAV; Blessing, 1997)
T_{min} = 0.352, *T_{max}* = 0.492
 4354 measured reflections

2233 independent reflections
 2051 reflections with *I* > 2σ(*I*)
R_{int} = 0.025
 θ_{max} = 25.0^o
h = −4 → 4
k = −14 → 13
l = −28 → 28

Refinement

Refinement on *F*²
R(*F*) = 0.027
wR(*F*²) = 0.063
S = 1.05
 2233 reflections
 168 parameters
 H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0282P)^2 + 0.4539P]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\text{max}} = 0.001$
 $\Delta\rho_{\text{max}} = 0.72 \text{ e } \text{Å}^{-3}$
 $\Delta\rho_{\text{min}} = -0.55 \text{ e } \text{Å}^{-3}$
 Absolute structure: Flack (1983),
 888 Friedel pairs
 Flack parameter = −0.03 (3)

Table 1

Selected geometric parameters (Å, °).

I1—C10	2.137 (4)	C5—C6	1.388 (6)
O2—C8	1.447 (5)	C7—O1	1.205 (5)
O3—C9	1.445 (5)	C7—O2	1.335 (5)
O3—C12	1.453 (5)	C7—C6	1.482 (7)
O4—C11	1.408 (5)	C9—C8	1.514 (6)
C1—C2	1.371 (7)	C9—C10	1.528 (6)
C1—C6	1.387 (6)	C10—C11	1.526 (6)
C2—C3	1.381 (7)	C12—C13	1.495 (6)
C3—C4	1.382 (8)	C12—C11	1.534 (6)
C5—C4	1.362 (7)		
O1—C7—O2	122.2 (4)	C2—C1—C6	120.1 (5)
O1—C7—C6	124.6 (4)	C2—C3—C4	119.5 (5)
O2—C7—C6	113.1 (4)	C4—C5—C6	121.5 (5)
O2—C8—C9	108.2 (3)	C5—C6—C7	119.0 (4)
O3—C9—C8	107.2 (3)	C5—C4—C3	119.7 (5)
O3—C9—C10	105.8 (3)	C7—O2—C8	116.7 (3)
O3—C12—C13	110.9 (4)	C8—C9—C10	114.0 (4)
O3—C12—C11	103.4 (3)	C9—O3—C12	109.1 (3)
O4—C11—C10	113.9 (4)	C9—C10—I1	114.0 (3)
O4—C11—C12	107.6 (3)	C10—C11—C12	99.8 (3)
C1—C6—C5	118.5 (5)	C11—C10—C9	103.7 (3)
C1—C6—C7	122.5 (4)	C11—C10—I1	113.7 (3)
C1—C2—C3	120.8 (5)	C13—C12—C11	115.9 (4)
O3—C9—C8—O2	−173.2 (4)		

Table 2

Hydrogen-bonding geometry (Å, °).

$D-H \cdots A$	$D-H$	$H \cdots A$	$D \cdots A$	$D-H \cdots A$
$O4-HO4 \cdots O3^i$	0.78 (5)	2.51 (5)	3.090 (4)	132 (5)
$O4-HO4 \cdots I1$	0.78 (5)	2.88 (5)	3.294 (3)	115 (4)

Symmetry code: (i) $-x, y - \frac{1}{2}, \frac{3}{2} - z$.

Data collection: *DENZO* (Otwinoski & Minor, 1997) and *COLLECT* (Hooft, 1998); cell refinement: *DENZO* and *COLLECT*; data reduction: *DENZO* (Otwinoski & Minor, 1997), *COLLECT* (Hooft, 1998) and *maXus* (Mackay *et al.*, 1998); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *CAMERON* (Watkin *et al.*, 1993); software used to prepare material for publication: *WinGX* (Farrugia, 1998).

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References

- Blessing, R. H. (1997). *J. Appl. Cryst.* **30**, 421–426.
 Corey, E. J., Pan, B.-C., Hug, D. H. & Deardorff, D. R. (1982). *J. Am. Chem. Soc.* **104**, 6816.
 Farrugia, L. J. (1998). *WinGX*. University of Glasgow, Scotland.
 Flack, H. D. (1983). *Acta Cryst.* **A39**, 876–881.
 Hooft, R. (1998). *COLLECT*. Nonius BV, Delft, The Netherlands.
 Knight, D. W., Bedford, S. B., Bell, K. E., Bennet, F., Hayes, C. J. & Shaw, D. E. (1999). *J. Chem. Soc. Perkin Trans. 1*, pp. p. 2143.
 Knight, D. W., Bew, S. P. & Middleton, R. J. (2000). *Tetrahedron Lett.* **41**, 4447 and *ibid.*, **41**, 4451.
 Mackay, S., Gilmore, C. J., Edwards, C., Tremayne, M., Stewart, N. & Shankland, K. (1998). *maXus*. University of Glasgow, Scotland.
 Matsuda, F., Tomiyoshi, N., Yanagiya & Matsumoto, T. (1990). *Tetrahedron*, **46**, 3469.
 Nakata, T., Saito, K. & Oishi, T. (1986). *Tetrahedron Lett.* **27**, 6345.
 Otwinoski, Z. & Minor, W. (1997). *Methods Enzymol.* **276**, 307–767.
 Perrin, D. D. & Armarego, W. L. F. (1988). *Purification of Laboratory Chemicals*, 3rd ed. Pergamon Press.
 Sheldrick, G. M. (1990). *Acta Cryst.* **A46**, 467–473.
 Sheldrick, G. M. (1997). *SHELXL97*. University of Göttingen, Germany.
 Watkin, D. M., Pearce, L. & Prout, C. K. (1993). *CAMERON*. Chemical Crystallography Laboratory, University of Oxford, England.
 White, J. D., Vedananda, T. R., Kang, M.-C. & Choudhry, S. C. (1986). *J. Am. Chem. Soc.* **108**, 8105.