Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

(2a*RS*,3*RS*,4a*SR*,6a*RS*,6b*SR*)-3-Hydroxy-2a,3,4a,6,6a,6b-hexahydro-1,4-dioxacyclopenta[cd]pentalen-2(5*H*)-one

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Received 13 March 2007
Accepted 27 March 2007

The molecular structure of the title compound [enantiomers (VIII) and (VIII*a*)], $C_8H_{10}O_4$, was determined in the course of our studies on the synthesis of cyclopenta[1,2-*b*]furan-4-one derivatives. Tricyclic (VIII*a*) consists of a planar bridged lactone unit and the two other ring systems in the envelope conformation. It contains five chiral C atoms and was obtained as a racemic mixture. The X-ray analysis showed the compound to possess a half-acetal unit with an *endo* orientation of the half-acetal ether bridge with respect to the lactone unit.

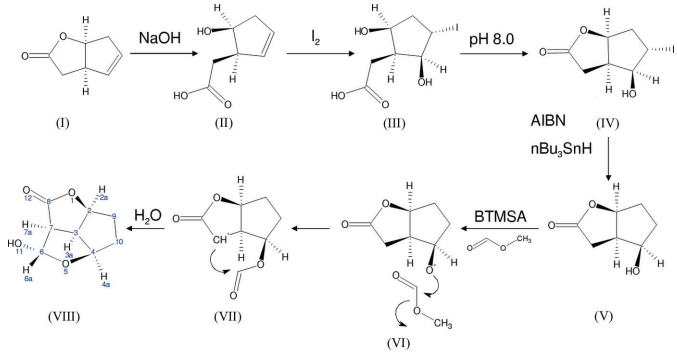
Key indicators

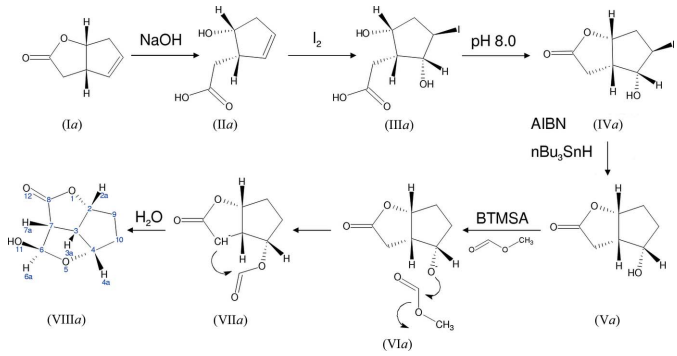
Single-crystal X-ray study
T = 193 K
Mean σ(C–C) = 0.002 Å
R factor = 0.043
wR factor = 0.112
Data-to-parameter ratio = 12.7

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

Comment

In the synthesis of prostaglandin derivatives the compound 3,3a,6,6a-tetrahydro-2*H*-cyclopenta[*b*]furan-2-one [(I) and (I*a*); Pirkle *et al.*, 1977] was reported as a suitable starting material (Corey & Mann, 1973; Collington *et al.*, 1983). In this study, we used alkaline iodolactonization of racemic (I) to generate (IV*a*) as enantiomers with defined stereochemistry (see schemes). For clarity of mechanistic considerations, in the reaction schemes the stereochemistry of the two enantiomers is shown independently.





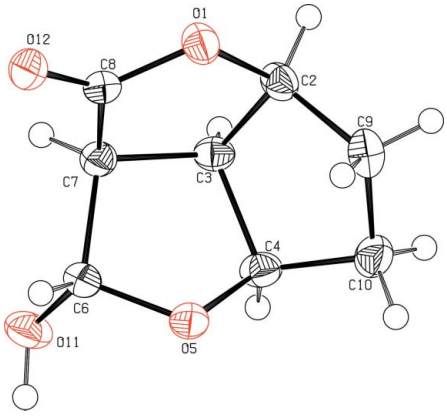


Figure 1
The molecular structure of (VIII). Displacement ellipsoids are drawn at the 50% probability level. H atoms are depicted as circles of arbitrary size.

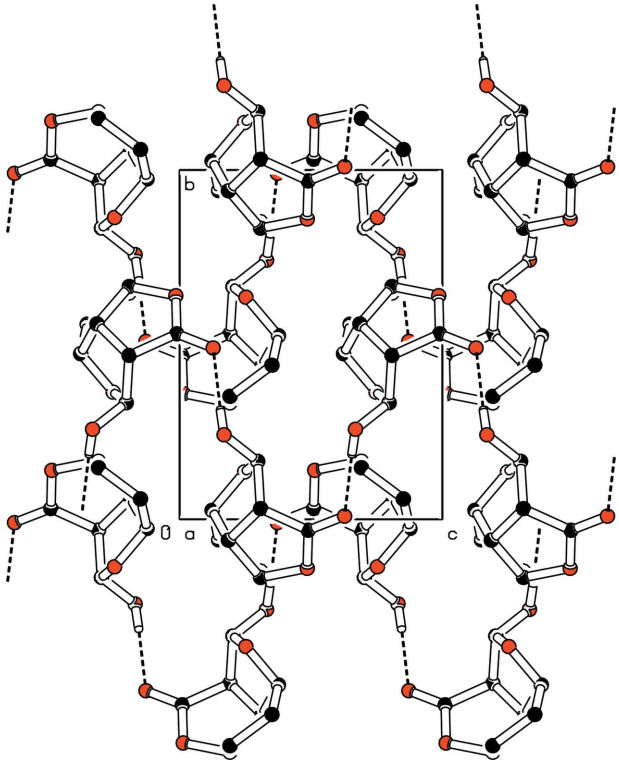


Figure 2
Crystal packing of racemic (VIII)/(VIII*a*) viewed along the *a* axis. O—H···O hydrogen bonds are shown as dashed lines.

The progress of the iodolactonization of (I*a*) is pH-dependent and proceeds *via* ring opening (II*a*) and iodinization to (III*a*), possessing the same chiral centers as the starting material. After the electrophilic attack on the double bond by iodine from the unhindered site of the cyclopentene ring compound (III*a*) was obtained. Ring closure at pH 8 (conditions controlled by addition of solid CO_2) resulted in (3a*R*,4*S*,5*S*,6a*S*)-4-hydroxy-5-iodohexahydro-2*H*-cyclopenta-[*b*]furan-2-one, (IV), and (3a*S*,4*R*,5*R*,6a*R*)-4-hydroxy-5-iodohexahydro-2*H*-cyclopenta[*b*]furan-2-one, (IV*a*) (Tömösközi, *et al.*, 1985). In the subsequent step, the iodine was removed by a radical reaction using tri-*n*-butyltin hydride (Grieco, *et al.*, 1975) to generate compound (V*a*). In the next step, (V*a*) was conveniently deprotonated by the sterically hindered base sodium bis(trimethylsilyl)amide (BTMSA) and the resulting alcoholate (VI*a*) formylated by methyl formate. Apparently, *via* deprotonated (VII*a*) a half-acetal was formed by electrophilic attack of the carbanion at C7 to generate the title compound, (VIII*a*), as a racemic mixture. Interestingly, the defined stereochemistry of (VIII*a*), in particular at C7 and C4, indicates a mechanism discussed as follows: the formylation takes place first at the alcoholate which is attached to chiral C4. In the second step forming the half-acetal, the attack of the carbanion C7 is now possible only from the *endo* position, leaving the final tricyclic molecule with defined stereochemistry at C4, C6 and C7.

The lactone ring (O1/C2/C3/C7/C8) is planar while the half-acetal ring system (C3/C4/O5/C6/C7) and the carbocycle (C2–C4/C10/C9) are in the envelope conformation. Since the starting material was employed as a racemic mixture, (2a*S*,3*S*,4a*R*,6a*S*,6b*R*)-3-hydroxyhexahydro-2*H*,3*H*-1,4-dioxacyclopenta[*cd*]pentalen-2-one, (VIII), and (2a*R*,3*R*,4a*S*,6a*R*,-6b*S*)-3-hydroxyhexahydro-2*H*,3*H*-1,4-dioxacyclopenta[cd]-pentalen-2-one, (VIII*a*), are generated. The crystal packing is characterized by intermolecular hydrogen bonds (Table 1). Every molecule is connected to two neighbours across the *c*-glide plane, resulting in a zigzag chain along the *c* axis.

Experimental

In a three-necked round-bottomed flask, racemic 3,3a,6,6a-tetrahydro-2*H*-cyclopenta[*b*]furan-2-one, (Ia) (1 g), and NaOH (880 mg) were dissolved in water (40 ml) and stirred for 15 min, then cooled to 273 K. At this temperature dry ice was added slowly over a period of 20 min to reach pH 8. A solution of KI (12 g) and I_2 (6 g) in water (20 ml) was added and the reaction mixture was stirred overnight in an ice bath. The completeness of the reaction was monitored by TLC (ethyl acetate/hexanes 1:1). After again cooling to 273 K, Na_2SO_3 was added until the reaction mixture became colourless followed by addition of KNa-tartrate (2 g). The mixture was extracted twice with 100 ml of dichloromethane and the organic phase separated, dried over Na_2SO_4 and evaporated to give a slightly yellow oil. The residue was purified by column chromatography using ethyl acetate/hexanes (1:1) to yield 1.42 g (66%) of (IV) as a clear oil which was dissolved in dry benzene. After addition of tri-*n*-butyltin hydride (2.56 g) and azobisisobutyronitrile (AIBN, 65 mg) the reaction was heated to 323 K for 1 h and then the solvent evaporated almost to dryness. The residue was extracted with benzene (100 ml) over a short silica gel column to remove impurities while the product remained on the silica gel. A new extraction with ethyl acetate (200 ml) yielded 600 mg of (V) which was dried in vacuum. The compound and 0.6 ml of formic acid methyl ester were dissolved in 10 ml of dry THF and added dropwise at 273 K to 1.76 ml of a 2*M* THF solution of sodium bis(trimethylsilyl)amide (BTMSA) in a dry three-necked round-bottomed flask under an argon flow. The progress of the reaction was monitored by TLC (ethyl acetate/hexanes 5:1). After stirring for 2 h all starting material had disappeared, 10% HCl (10 ml) was added and the mixture extracted twice with 100 ml of ethyl acetate. The organic phase was separated, dried over Na_2SO_4 and evaporated almost to dryness. The residue was purified by flash chromatography

(ethyl acetate/hexanes 5:1) to yield 70% of the title compound as a racemic mixture (VIII)/(VIII*a*). Crystals of the title compound for X-ray analysis precipitated as colourless blocks from ethylacetate solution.

Crystal data

$C_8H_{10}O_4$
M_r = 170.16
Monoclinic, $P2_1/c$
a = 9.7712 (6) Å
b = 10.0443 (3) Å
c = 8.1779 (5) Å
β = 112.568 (3)°
V = 741.16 (7) Å^3
Z = 4
Cu $K\alpha$ radiation
μ = 1.05 mm^{-1}
T = 193 (2) K
0.35 × 0.26 × 0.26 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
Absorption correction: none
1483 measured reflections
1400 independent reflections
1302 reflections with $I > 2\sigma(I)$
R_{int} = 0.034
3 standard reflections
frequency: 60 min
intensity decay: 5%

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.043
$wR(F^2)$ = 0.112
S = 1.08
1400 reflections
110 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.34 e Å^{-3}
$\Delta\rho_{min}$ = −0.23 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
O11—H11A···O12^{i}	0.84	1.96	2.7888 (16)	173

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

H atoms attached to carbon atoms were positioned geometrically (C—H = 0.99–1.00 Å); the H atom bonded to O11 was located in a difference Fourier map. All H atoms were treated as riding atoms with U_{iso}(H) values set at 1.2U_{eq} of the parent atom (1.5U_{eq} for hydroxyl).

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989); cell refinement: *CAD-4 Software*; data reduction: *CORINC* (Dräger & Gattow, 1971); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97*.

We are grateful to Dr W. Zimmermann, Institute of Pharmacy, Tübingen, for helpful discussions.

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