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(3a*S**,10*R**,10a*S**,10b*S**,13*R**,13a*R**)-8-Formyl-6-hydroxy-13-methoxy-1,1,7-trimethyl-5-oxo-1,2,3,3a,5,9,10,10a,13,13a-decahydrocyclohepta[*c*]furo[3,4-*e*]chromen-10-yl acetate

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Key indicators

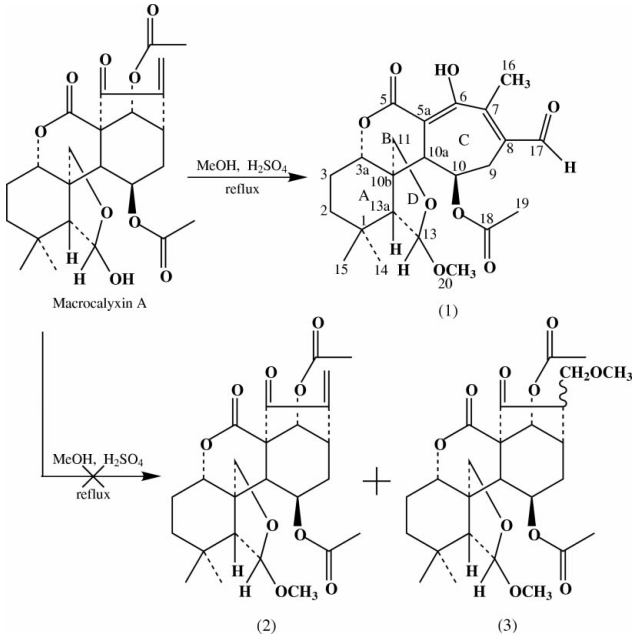
Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.005 Å
R factor = 0.048
wR factor = 0.119
Data-to-parameter ratio = 8.8

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

The title compound, $C_{23}H_{30}O_8$, was prepared from macrocalyxin A and its structure was established from the ESI–MS, ^{1}H NMR, ^{13}C NMR and X-ray crystallographic data. Two unique molecules are present in the asymmetric unit.

Comment

The title compound, (1), was obtained as an unexpected product when macrocalyxin A in methanol was refluxed in the presence of concentrated sulfuric acid. This reaction was expected to produce a monomethyl acetal, (2), and its methoxy derivative, (3). However, the sole product was the new compound (1). This was a surprising result, as macrocalyxin A has the same framework (Chen *et al.*, 1986, 1987) as enmein (1*S*,4*S*,6*S*,8*R*,9*R*,12*S*,13*S*,16*R*)-6,9-dihydroxy-7,7-dimethyl-17-methylene-3,10-dioxapentacyclo[14.2.1.0^{1,13}.0^{4,12}.0^{8,12}]nonadecane-2,18-dione), which transforms directly to give two ether products (Fujita *et al.*, 1972). The asymmetric unit of (1) consists of two molecules (Figs. 1 and 2); small differences between the two may be attributed to crystal-packing effects. Data relating to molecule 1 of the asymmetric unit will be used in the discussion that follows.



The crystal packing is shown in Fig. 3. A key difference between macrocalyxin A and enmein is the acetoxy group, which is linked to the conjugated α-methylenecyclopentanone of macrocalyxin A. A possible mechanism for the formation of (1) would be acid-catalysed methanolysis of the acetate group followed by a retroaldol condensation and subsequent

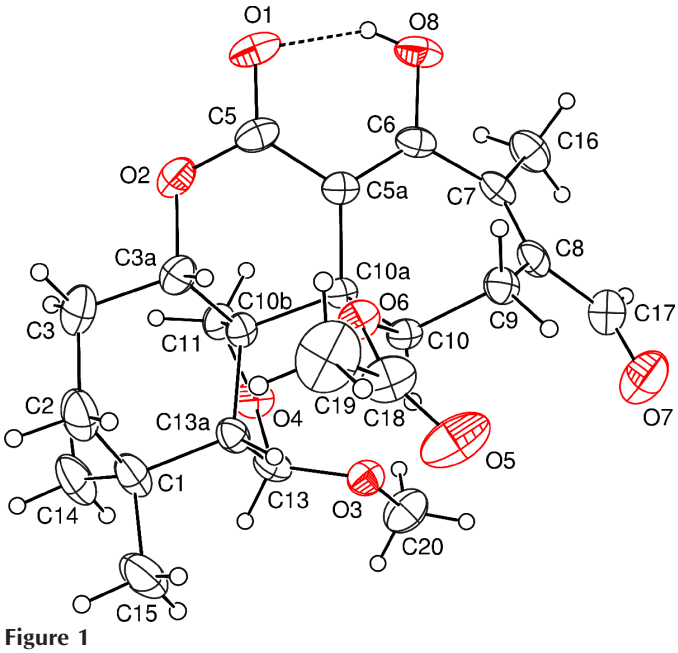


Figure 1
Perspective view of molecule 1 of the title compound, shown with 30% probability displacement ellipsoids. H atoms are drawn as spheres of arbitrary radius. The dashed line indicates an intramolecular hydrogen bond.

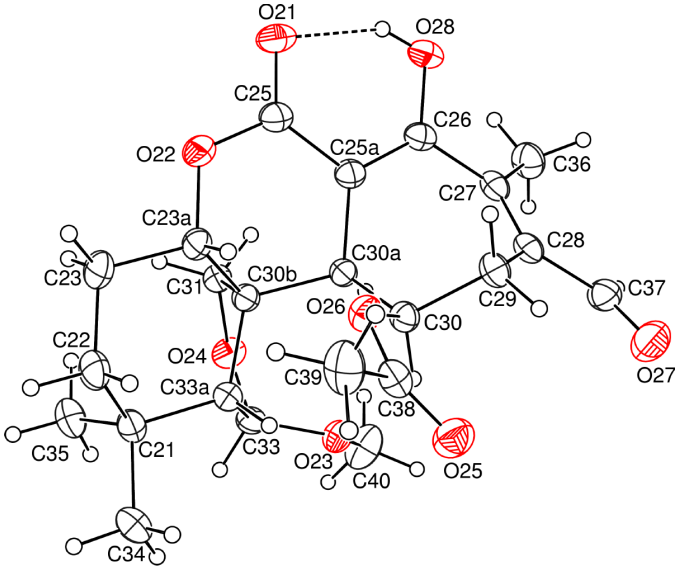


Figure 2
Perspective view of molecule 2 of the title compound, shown with 30% probability displacement ellipsoids. H atoms are drawn as spheres of arbitrary radius. The dashed line indicates an intramolecular hydrogen bond.

isomerization, both of which again require acid catalysis. Compound (1) contains a five-membered ring, two six-membered rings and one seven-membered ring and some geometrical features of the rings were investigated using *PLATON* (Spek, 2003). Cyclohexane ring *A* (C1–C3/C3a/C10b/C13a) adopts a chair conformation with puckering parameters (Cremer & Pople, 1975) $Q = 0.521$ Å, $\theta = 164.2$ and $\varphi = 274.1°$; ring *B* (O2/C3a/C10b/C10a/C5a/C5) exists in a half-chair conformation ($Q = 0.499$ Å, $\theta = 48.8$ and $\varphi = 90.8°$); seven-membered ring *C* (C5a/C6–C10/C10a) has $Q = 1.026$ Å; five-membered ring *D* (O4/C13/13a/C10b/C11) adopts a twist conformation with C13a *exo* and C10b *endo* from the mean plane of the remaining three atoms. The stereochemistry at the *A*/*B* and *A*/*D* ring junctions is *trans* and *cis*, respectively. Following the rearrangement, the C6 O atom is in the enol form, a tautomer that is stabilized by an intramolecular hydrogen-bonding interaction [O8—H8O···O1 = 2.495 (4) Å, Table 2]. The formation of a double bond at C5a=C6 generates an extensive conjugated chain for the atoms O1/C5/C5a/C6/C7/C8/C17/O7.

Experimental

A solution of macrocalyxin A (240 mg) in MeOH (20 ml) was refluxed for 6 h after the addition of concentrated H_2SO_4 (0.8 ml). The reaction mixture was concentrated to 10 ml and poured into a solution of Na_2CO_3 (3.7 g) in ice water; the MeOH was removed under reduced pressure. Extraction with 3 × 10 ml $CHCl_3$, washing with 3 × 10 ml H_2O, drying with anhydrous Na_2SO_4, and evaporation of the solvent left 327 mg of an oily residue. Thin-layer chromatography on silica gel, eluting with $CHCl_3$, gave the title compound as colorless crystals (54.7 mg). Crystals suitable for X-ray structure analysis were obtained by slow evaporation, at room temperature, of a solution in $CHCl_3$ and MeOH in a 1:1 ratio. ESI–MS *m*/*z* 435 $[M + H]^+$, 433 $[M - H]^-$. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.94 (6H, *s*, 2 × Me), 1.86 (1H, *s*, H13*a*), 2.06 (3H, *s*, OAc), 2.34 (3H, *d*, $J = 1$ Hz, Me), 2.73 (1H, *d*, $J = 4$ Hz, H10*a*), 3.18 (3H, *s*, OMe), 3.62, 3.99 (2 × 1H, *d*, *AB*, $J = 9$ Hz, H11*a*, H11*b*), 4.71 (1H, *s*, H13), 4.98 (1H, *dd*, $J = 5.5$, 12.5 Hz, H3*c*), 5.55 (1H, *m*, H10). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.0 (CH_3, C-16), 21.4 (CH_3, C-19), 23.2 (CH_2, C-3), 23.4 (CH_3, C-14), 29.4 (CH_2, C-9), 31.1 (C, C-1), 33.1 (CH_3, C-15), 38.0 (CH_2, C-2), 44.5 (CH, C-10a), 46.0 (C, C-10b), 53.4 (CH, C-13a), 54.5 (CH_3, C-20), 74.3 (CH_2, C-11), 78.1 (CH, C-3a), 81.1 (CH, C-10), 98.4 (C, C-5a), 108.5 (CH, C-13), 137.3 (C, C-7), 148.4 (C, C-8), 168.8 (C, C-6), 172.7 (C, C-18), 176.1 (C, C-5), 188.8 (CH, C-17).

Crystal data

$C_{23}H_{30}O_8$
$M_r = 434.47$
Monoclinic, $P2_1$
$a = 11.6288$ (9) Å
$b = 14.0386$ (11) Å
$c = 13.7457$ (10) Å
$\beta = 98.3490$ (10)°
$V = 2220.2$ (3) Å^3
$Z = 4$
$D_x = 1.300$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 4360 reflections
$\theta = 4.3$–46.5°
$\mu = 0.10$ mm^{-1}
$T = 293$ (2) K
Block, colorless
0.48 × 0.35 × 0.22 mm

Data collection

Bruker SMART CCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Bruker, 1999)
$T_{min} = 0.724$, $T_{max} = 0.980$
13086 measured reflections
4997 independent reflections
4028 reflections with $I > 2\sigma(I)$
$R_{int} = 0.088$
$\theta_{max} = 27.0°$
$h = -14 \rightarrow 14$
$k = -17 \rightarrow 17$
$l = -17 \rightarrow 11$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.048$
$wR(F^2) = 0.119$
$S = 0.84$
4997 reflections
571 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0814P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.26$ e Å^{-3}
$\Delta\rho_{min} = -0.24$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O1—C5	1.239 (4)	O21—C25	1.223 (4)
C5—C5a	1.446 (5)	C25—C25a	1.456 (4)
C5a—C6	1.365 (5)	C25a—C26	1.366 (4)
C6—C7	1.479 (5)	C26—C27	1.480 (4)
O7—C17	1.206 (5)	O27—C37	1.180 (4)
C7—C8	1.344 (5)	C27—C28	1.351 (4)
C8—C17	1.468 (5)	C28—C37	1.470 (4)
O1—C5—O2	116.7 (3)	O21—C25—O22	115.8 (3)
O1—C5—C5a	122.4 (4)	O21—C25—C25a	123.9 (3)
O2—C5—C5a	120.7 (3)	O22—C25—C25a	120.2 (3)
C6—C5a—C5	117.7 (3)	C26—C25a—C25	117.2 (3)
C6—C5a—C10a	120.2 (3)	C26—C25a—C30a	120.4 (3)
C5—C5a—C10a	121.8 (3)	C25—C25a—C30a	121.7 (2)
O8—C6—C5a	123.6 (3)	O28—C26—C25a	124.0 (3)
O8—C6—C7	113.3 (3)	O28—C26—C27	113.3 (3)
C5a—C6—C7	122.8 (3)	C25a—C26—C27	122.7 (3)
C8—C7—C6	119.2 (3)	C28—C27—C26	119.3 (3)
C8—C7—C16	127.2 (3)	C28—C27—C36	125.0 (3)
C6—C7—C16	113.6 (3)	C26—C27—C36	115.6 (3)
C7—C8—C17	121.6 (3)	C27—C28—C37	120.6 (3)
C7—C8—C9	121.6 (3)	C27—C28—C29	122.5 (3)
C17—C8—C9	116.8 (3)	C37—C28—C29	116.7 (3)
O1—C5—C5a—C6	−4.2 (5)	O21—C25—C25a—C26	−2.8 (5)
C5a—C6—C7—C8	−45.4 (4)	C25a—C26—C27—C28	−42.9 (4)
C6—C7—C8—C9	−9.2 (4)	C26—C27—C28—C29	−2.6 (4)
C7—C8—C17—O7	179.1 (4)	C27—C28—C37—O27	165.4 (4)

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O8—H8O···O1	0.82	1.78	2.495 (4)	146
O28—H28O···O21	0.82	1.80	2.526 (3)	146
O28—H28O···O23^{i}	0.82	2.56	3.125 (3)	127

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

H atoms were placed in geometrically calculated positions (C—H = 0.93–0.98 Å), and the methyl and hydroxy H atoms were refined in the riding-model approximation, with $U_{iso} = 1.5U_{eq}$ of the corresponding carrier atom. The remaining H atoms were refined with $U_{iso} = 1.2U_{eq}$ of the corresponding carrier atom. Both independent molecules have the same absolute configuration, although this could not be determined reliably from the X-ray data and Friedel reflections were merged. The relative stereochemistry is shown in the scheme and figures.

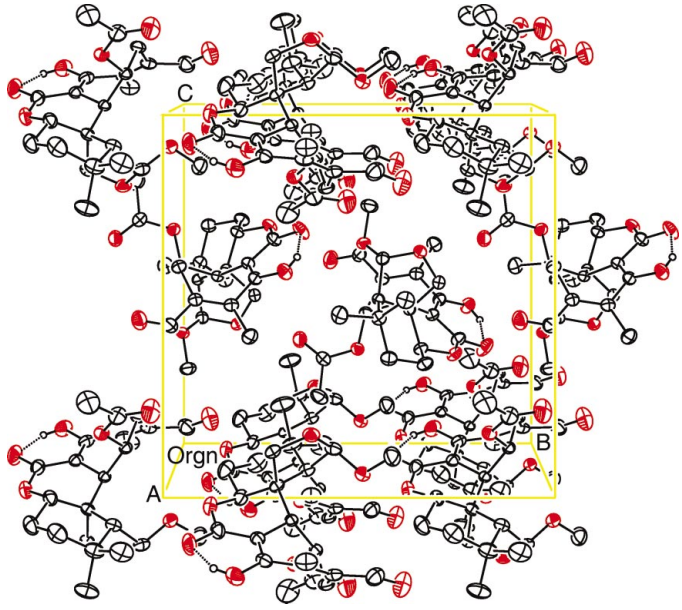


Figure 3
Crystal packing diagram for the title compound viewed normal to the (100) plane. H atoms have been omitted for clarity, except for these involved in hydrogen bonds.

Data collection: *SMART* (Bruker, 1999); cell refinement: *SAINT* (Bruker, 1999); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 (Farrugia, 1997); software used to prepare material for publication: *SHELXL*97.

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