Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

Two isomeric cucurbitane derivatives

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Received 29 January 2009
Accepted 18 April 2009
Online 25 April 2009

Two isomeric cucurbitane derivatives, 3β,7α,11β-triacetoxycucurbit-5(10)-ene, (I), and 3β,7α,11β-triacetoxy-5α-cucurbit-1(10)-ene, (II), both $C_{36}H_{58}O_6$, have their single endocyclic C=C double bonds in different positions. This results in differences in the conformation of the four-ring system, which is close to a half-chair/half-chair/chair/half-chair arrangement in (I) and to a half-chair/twist-boat/boat/half-chair arrangement in (II). The orientation of some of the substituents is also different; the 3β-acetoxy group is in an equatorial position in (I) but in an axial position in (II), while the 11β-acetoxy group occupies an axial position in (I) and an equatorial position in (II). The asymmetric unit of (I) contains two symmetry-independent molecules which do not differ significantly, being related by a pseudo-twofold axis of symmetry. In both structures, the aliphatic chain fragments are disordered and the disorder persists at lower temperatures.

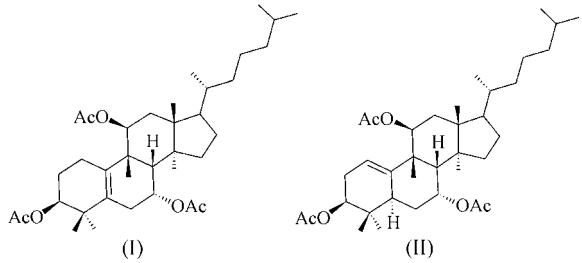
Comment

Cucurbitacins, a large group of tetracyclic triterpenes, have the 19(10→9b)*abeo*-lanostane (cucurbitane) carbon skeleton. These natural products have been isolated from various plants (Lavie & Glotter, 1971; Chen *et al.*, 2005, and references therein; Miró, 1995) and attract considerable attention owing to their unique structural features, multi-functionality and diverse biological activities (Chen *et al.*, 2005; Miró, 1995).

The cucurbitacins are biogenetically derived from 2,3-oxidosqualene *via* 10α-cucurbita-5,24-dien-3β-ol (cucurbitadienol) as the crucial intermediate (Shibuya *et al.*, 2004). In chemical synthesis, the cucurbitane derivatives are available from the reaction of 9-substituted lanostane derivatives *via* C-9 carbocationic intermediates (Paryzek, 1976, 1979; Edwards & Paryzek, 1983; Edwards & Kolt, 1987).

Several crystallographic analyses of cucurbitacins have aimed to establish unambiguously the structure of compounds isolated from natural sources. Besides other characteristic features, most natural cucurbitacins are characterized by the presence of the 5,6-double bond in the carbon skeleton. Accordingly, X-ray data for a number of cucurbit-5-ene derivatives have been accumulated, namely 10α-cucurbitadienol C-3 acetate (Nes *et al.*, 1991), cucurbit-5-ene-3,22,23,24,25-pentaol (Okabe *et al.*, 1980), (20*R*)-16-α-acetoxy-20-hydroxy-24,25,26,27-tetranor-2β-(β-D-tetraacetylglucopyranosyloxy)-10α-cucurbit-5-ene-3,11,22-trione trihydrate (Weinges *et al.*, 1989), cucurbitacin E (Wu *et al.*, 2004), 3β-hydroxy-7β,25-dimethoxycucurbita-5,23(*E*)-diene (Harinantenaina *et al.*, 2006), datiscoside bis(*p*-iodobenzoate) dihydrate (Restivo *et al.*, 1973), datiscoside dibenzene solvate (Sasamori *et al.*, 1983) and 3β,16β-dihydroxy-7β-ethoxycucurbita-5,24-diene (Fujimoto *et al.*, 1986).

In our investigation of the Lewis acid-catalysed reaction of 9β,11β-epoxy-5α-lanostane derivatives, a series of compounds having the rearranged lanostane skeleton have been isolated and characterized. Spectroscopic methods (mostly ^{1}H and ^{13}C NMR) identified two compounds as the cucurbit-5(10)-ene and 5α-cucurbit-1(10)-ene derivatives, indicating the presence of the double bond in a rather unusual position in ring *A* (Figs. 1 and 2 show the nomenclature of the rings). There are only a few structurally characterized compounds with the 5(10)-ene steroid skeleton and even fewer with the 1(10)-ene analogue. A search of the Cambridge Structural Database (Version 5.30 of November 2008; Allen, 2002), using a search fragment that excluded additional fused rings, gave 11 hits for the former and only two for the latter. We report here the crystal structures of the isomeric 5(10)-ene and 1(10)-ene cucurbitane derivatives 3β,7α,11β-triacetoxycucurbit-5(10)-ene, (I), and 3β,7α,11β-triacetoxy-5α-cucurbit-1(10)-ene, (II).



Crystals of both (I) and (II) proved very difficult to grow, resulting in samples of limited diffraction quality. We related this to the presence in both structures of disorder, which persisted despite the data collection temperature being lowered to 100 (1) K for (I) and to 190 (1) K for (II). The higher temperature employed for (II) was dictated by a decline in diffraction quality upon further cooling. The disorder affects the chain fragments; the alternative positions were resolved for five terminal atoms in molecule *A* of (I), denoted (I*A*), with site-occupancy factors of 0.7/0.3, for four atoms in molecule *B* of (I) [denoted (I*B*), 0.5/0.5] and for three atoms in (II) [0.631 (13)/0.369 (13)].

In (I), there are two symmetry-independent molecules in the asymmetric part of the unit cell. A normal probability plot (*International Tables for X-ray Crystallography*, 1974, Vol. IV, pp. 293–309; Abrahams & Keve, 1971) shows that the differences between the independent molecules in this case are statistical only and not systematic in nature. For the bond lengths in the ordered part of the molecule, the correlation

 doi:10.1107/S0108270109014528

factor R^2 between the experimental and theoretical values is 0.96, the deviation of the *a* parameter (or slope in $y = ax + b$, in this case $y = 1.64x - 0.05$) from unity points to the typical underestimation of the s.u. values, while the small value of the *b* parameter indicates the lack of systematic errors. There is, in fact, quite good pseudo-twofold symmetry along the *c*-axis direction, which connects the main parts of the otherwise independent molecules. For the ordered part of the molecules, the mean values of the combination of the coordinates ($x_A + x_B$, $y_A + y_B$, $z_A - z_B$) are 1.122 (7), 2.001 (3) and −0.001 (4), consistent with an approximate twofold axis along *z* at (0.561, 1.000, *z*).

The bond lengths and angles are close to typical values; the mean value of the Csp^3-Csp^3 bonds is 1.54 (2) Å in both structures. The relevant parameters that establish the location of the endocyclic C═C double bonds are C5*A*═C10*A* [1.352 (5) Å] and C5*B*═C10*B* [1.334 (5) Å] in (I), and C1═C10 [1.333 (4) Å] in (II).

The different placement of the double bond heavily influences the conformations of the four-ring skeletons, and it is notable that the two symmetry-independent molecules in (I) have very similar conformations. In (I), rings *A* and *B* are close to the half-chair conformation (*B* less so than *A*), with an almost planar ring junction. In (II), ring *A* is again close to half-chair, of course with a different location for the approximate local twofold axis, but ring *B* is closer to a distorted twist-boat conformation, and the ring junction is *cisoid*. The most unexpected differences are observed in the conformations of ring *C*, apparently unaffected by the differences in ring *A*. The former is close to a standard chair conformation in (I), while in (II) this conformation can be described as a distorted boat. This latter conformation has not been observed previously in any of the steroids having a similar ring structure with a double bond in either the C1═C10 or the C5═C10 positions. The *B*/*C* junction is *cis* in (I), but in (II) it is significantly flattened; the torsion angles around the junction bond C8—C9 are −18.4 (4) and 2.3 (4)°. Finally, rings *D* are quite regular half-chairs in both structures. The symmetry of the rings can be described by referring to the ideal symmetry, using so-called asymmetry parameters (Duax & Norton, 1975; see Table 1). The orientations of some of the acetoxy groups also differ in the two isomers. The 3β-acetoxy group is in the equatorial position in (I), while it is in the axial position in (II), and the 11β substituent is closer to an axial position in (I) but almost in an equatorial position in (II). The 7α-acetoxy group is in the equatorial position in both compounds, and the C18, C19 and C30 methyl groups are all axial.

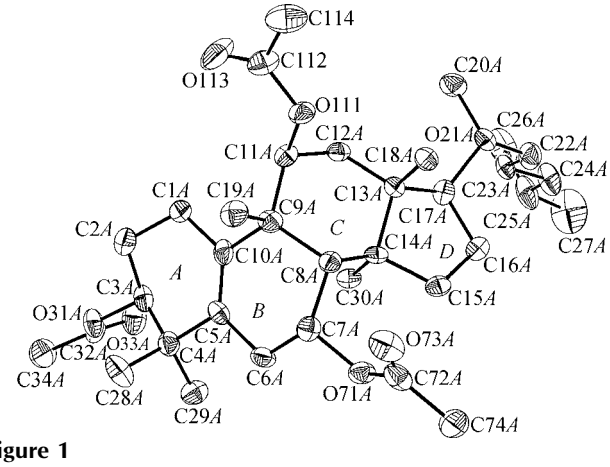


Figure 1
Displacement ellipsoid representation of molecule (I*A*), showing the atom-labelling scheme. Ellipsoids are drawn at the 50% probability level and H atoms are depicted as spheres of arbitrary radii. Only one of the alternative positions of the aliphatic chain is shown.

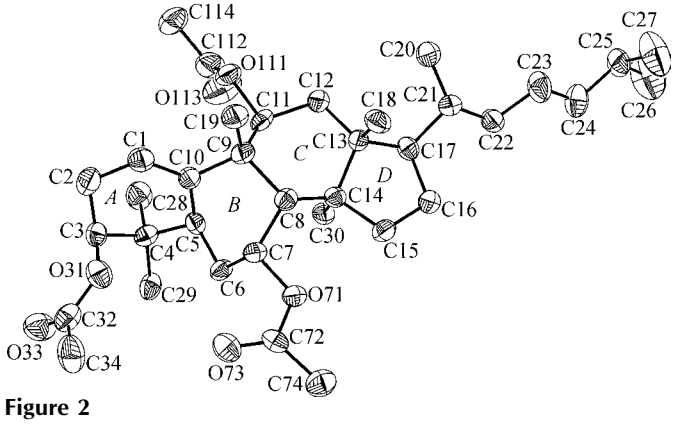


Figure 2
Displacement ellipsoid representation of (II), showing the atom-labelling scheme. Ellipsoids are drawn at the 50% probability level and H atoms are depicted as spheres of arbitrary radii. Only one of the alternative positions of the aliphatic chain is shown.

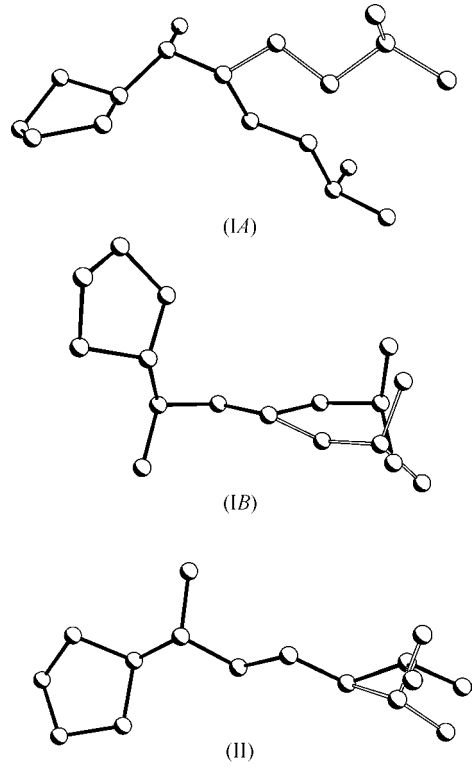


Figure 3
The different modes of disorder in the three reported molecules. The site-occupancy factors are 0.7/0.3 in (I*A*), 0.5/0.5 in (I*B*) and 0.631 (13)/0.369 (13) in (II). The solid and open bonds designate disorder components of higher and lower occupancy, respectively.

The alkyl chain disorder illustrated in Fig. 3 is observed at both room and lower temperature, suggesting that it is static rather than dynamic in nature. The conformation along the chain (C20···C26 and C20···C27) can be described as g^-ttg^+ and g^-ttt (g^+ttg^+ and g^+ttt) in (I*A*), g^-ttg^- and g^-ttg^+ (g^-ttt and g^-ttg^-) in (I*B*), and g^+ttg^+ and g^+ttt (g^+ttg^- and g^+ttg^+) in (II); the symbols in parentheses refer to the second alternative position of the chain.

The crystal structure of (I) features a number of relatively weak but directional C—H···O contacts (Table 2), which are generally symmetrical with respect to both symmetry-independent molecules (*cf.* C2, C21 and C29), and they connect both types of molecules (*i.e.* there are $A\cdots B$ contacts as well as $A\cdots A$ and $B\cdots B$ contacts). The structure of (II) lacks such contacts.

Experimental

Details of the synthesis and the spectroscopic data for the title compounds will be published in a separate paper (Koenig *et al.*, 2009). Crystals appropriate for an X-ray diffraction experiment were obtained by slow evaporation from heptane solutions.

Compound (I)

Crystal data

$C_{36}H_{58}O_6$
M_r = 586.82
Orthorhombic, $P2_12_12_1$
a = 14.0270 (8) Å
b = 19.6354 (10) Å
c = 26.2445 (12) Å
V = 7228.4 (6) Å^3
Z = 8
Mo $K\alpha$ radiation
μ = 0.07 mm^{-1}
T = 100 K
0.5 × 0.2 × 0.2 mm

Data collection

Kuma KM-4-CCD four-circle diffractometer
33755 measured reflections
7355 independent reflections
4921 reflections with $I > 2\sigma(I)$
R_{int} = 0.045

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.052
$wR(F^2)$ = 0.147
S = 0.94
7355 reflections
838 parameters
164 restraints
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.34 e Å^{-3}
$\Delta\rho_{min}$ = −0.21 e Å^{-3}

Table 1
Asymmetry parameters.

	(I*A*)	(I*B*)	(II)
A	ΔC_2(2–3): 6.8	ΔC_2(2–3):5.4	ΔC_2(1–10): 0.76
B	ΔC_s(5–8): 4.8 ΔC_2(5–10): 17.2	ΔC_s(5–8): 7.8 ΔC_2(5–10): 13.8	ΔC_2(6): 14.6 ΔC_2(5–10): 16.9
C[a]	ΔC_s(9): 10.2 ΔC_2(9–11): 1.4 ΔC_s(8): 20.7 ΔC_2(11–12): 22.0	ΔC_s(9): 7.8 ΔC_2(9–11): 4.1 ΔC_s(8): 20.9 ΔC_2(11–12): 24.1	ΔC_2(8–9): 18.7 ΔC_s(11): 15.8
D	ΔC_2(13–14): 1.50	ΔC_2(13–14): 0.61	ΔC_2(13–14): 1.53

Note: (*a*) for ring *C* in (I), the smallest and largest values of the asymmetry parameters are given.

Table 2
Intermolecular contact geometry (Å, °) for (I).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C2*A*—H2*A*2···O117^{i}	0.99	2.58	3.512 (6)	156
C21*A*—H21*A*···O73*A*^{ii}	1.00	2.55	3.298 (5)	132
C29*A*—H292···O73*B*	0.96	2.49	3.437 (5)	171
C2*B*—H2*B*2···O113^{iii}	0.99	2.66	3.482 (6)	140
C34*B*—H34*F*···O117^{iv}	0.96	2.40	3.354 (5)	175
C74*B*—H74*F*···O33*A*^{v}	0.96	2.62	3.577 (6)	172
C21*B*—H21*B*···O73*B*^{v}	1.00	2.54	3.308 (5)	133
C29*B*—H295···O73*A*	0.96	2.53	3.469 (5)	167

Symmetry codes: (i) $x-1, y, z$; (ii) $x-\frac{1}{2}, -y+\frac{3}{2}, -z+2$; (iii) $x+1, y, z$; (iv) $-x+2, y-\frac{1}{2}, -z+\frac{3}{2}$; (v) $x+\frac{1}{2}, -y+\frac{5}{2}, -z+2$.

Compound (II)

Crystal data

$C_{36}H_{58}O_6$
M_r = 586.82
Orthorhombic, $P2_12_12_1$
a = 9.0958 (9) Å
b = 14.8510 (16) Å
c = 25.526 (2) Å
V = 3448.1 (6) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.08 mm^{-1}
T = 190 K
0.35 × 0.3 × 0.1 mm

Data collection

Kuma KM-4-CCD four-circle diffractometer
16585 measured reflections
4159 independent reflections
2124 reflections with $I > 2\sigma(I)$
R_{int} = 0.081

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.055
$wR(F^2)$ = 0.078
S = 0.99
4159 reflections
412 parameters
8 restraints
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.19 e Å^{-3}
$\Delta\rho_{min}$ = −0.18 e Å^{-3}

H atoms were located geometrically and refined as riding, with $U_{iso}(H) = xU_{eq}(C)$, where x = 1.3 in (I) and 1.5 in (II) for methyl H atoms and x = 1.2 for all others. The representation of the disorder in the alkyl chains by two sets of atomic positions is probably modelling a larger number of chain orientations; the disorder components were subjected to weak geometrical restraints [the C—C bonds were restrained to a target value of 1.54 (2) Å]. In (I), restraints for approximate isotropic behaviour and rigid-bond restraints were also applied to the displacement parameters. Site-occupation factors were set, on the basis of equivalent displacement parameters, at 0.7/0.3 and 0.5/0.5 in the two molecules of (I), while in the case of (II) the occupancies refined to 0.631 (13)/0.369 (13). Our attempts to refine these factors in the structure of (I) were abandoned owing to high correlations with the U^{ij} parameters of the disordered fragment. Details of the ambient-temperature structure determinations of (I) and (II) have been deposited as supplementary data in CIF format.

For both compounds, data collection: *CrysAlis Pro* (Oxford Diffraction, 2009); cell refinement: *CrysAlis Pro*; data reduction: *CrysAlis Pro*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *XP* in *Stereochemical Workstation Operation Manual* (Siemens, 1989) and *Mercury* (Macrae *et al.*, 2006) for (I) and *XP* for (II); software used to prepare material for publication: *SHELXL97*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: BM3076). Services for accessing these data are described at the back of the journal.

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