Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

Bis[14β-hydroxy-3β-*O*-(L-thevetosyl)-5β-card-20(22)-enolide] methanol solvate monohydrate and 3β-*O*-(L-2′-*o*-acetylthevetosyl)-14β-hydroxy-5β-card-20(22)-enolide

Suchada Chantrapromma,[a] Anwar Usman,[b] Hoong-Kun Fun,[b]* Surat Laphookhieo,[a] Chatchanok Karalai,[a] Yanisa Rat-a-pa[a] and Kan Chantrapromma[c]

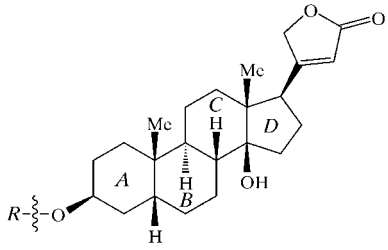
[a]Department of Chemistry, Faculty of Science, Prince of Songkla University, Hat-Yai, Songkhla 90112, Thailand, [b]X-ray Crystallography Unit, School of Physics, Universiti Sains Malaysia, 11800 USM, Penang, Malaysia, and [c]Institute of Science, Walailak University, Thasala, Nakhon Si Thammarat 80160, Thailand
Correspondence e-mail: hkfun@usm.my

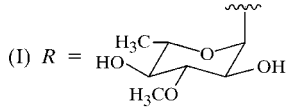
Received 29 October 2002
Accepted 16 December 2002
Online 18 January 2003

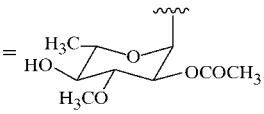
The title compounds, $2C_{30}H_{46}O_8\cdot CH_3OH\cdot H_2O$, (I), and $C_{32}H_{48}O_9$, (II), respectively, are cardenolide glycosides which were isolated from the seeds of *Cerbera odollam*. There are two crystallographically independent cardenolide molecules in (I), together with one methanol and one water solvate molecule. In both (I) and (II), the steroid nuclei are in *cis*/*trans*/*cis* configurations, with the cyclopentane rings showing conformational flexibility, *viz*. an envelope conformation in (I) and a twisted conformation in (II). In both compounds, the lactone ring is nearly orthogonal to the cyclopentane ring. The packing of (I) is composed of molecular layers stabilized by five O—H···O hydrogen bonds. In the packing of (II), the molecules are packed into columns by one O—H···O hydrogen bond, and are further interconnected into a three-dimensional network by one O—H···O and three C—H···O interactions.

Comment

Cerbera odollam Gearnth (Apocynaceae) are widely distributed in the South-East Asian and Indian Ocean regions. It has been reported that the leaves and fruits of this plant possess cardiotonic properties and have effects on the central nervous system (Chen & Steldt, 1942; Hien *et al.*, 1991; Lasserre *et al.*, 1992). We have isolated cerbinal from the bark of this plant and it exhibited moderate bioactivity against mycobacterium tuberculosis and breast-cancer cells in preliminary testing (Laphookhieo *et al.*, 2001). The compounds of the present study, (I) and (II), were isolated from the seeds of *cerbera odollam* and showed the characteristics of cardenolide glycosides. Preliminary testing of these compounds showed that both have strong activities against human breast-cancer cells, human small-cell lung cancer and human oral epidermoid carcinoma. As part of these studies, we have undertaken the X-ray crystal structure analyses of compounds (I) and (II) in order to establish their molecular structures and relative stereochemistries.



(I) R = 

(II) R = 

$\cdot 0.5CH_3OH\cdot 0.5H_2O$

The bond lengths and angles in (I) and (II) show normal values (Allen *et al.*, 1987). In both compounds, the steroid nucleus has a *cis*/*trans*/*cis* configuration for the *A*–*B*/*B*–*C*/*C*–*D* rings. In all cases, the cyclohexane *A*, *B* and *C* rings have a standard chair conformation, whereas the cyclopentane *D* ring shows some conformational flexibility. Attempted refinement of the Flack (1983) parameters was unsuccessful and thus the absolute configurations could not be determined. The structures reported and the *Scheme* above assume the L-form.

In the crystal structure of (I) (Fig. 1), the asymmetric unit contains two crystallographically independent molecules, (I*A*) and (I*B*), having similar chiralities, bond lengths and angles. The molecules are related by a local rotation axis.

In molecules (I*A*) and (I*B*), the cyclopentane *D* ring (C13–C17) adopts an envelope conformation, with atom C14 displaced from the C13/C15/C16/C17 plane by 0.586 (8) and 0.605 (4) Å in (I*A*) and (I*B*), respectively. The lactone ring (O1/C20–C23) attached at atom C17 is essentially planar, which is due mainly to the conjugation of the C=C and C=O bonds; this ring is approximately orthogonal to the mean plane of the *D* ring, with a dihedral angle of 83.2 (3)° in molecule (I*A*) and 88.3 (4)° in molecule (I*B*). The orientation of the lactone ring is also determined by the C13—C17—C20—C22 torsion angle, which is −101.7 (7)° in molecule (I*A*) and −107.8 (7)° in molecule (I*B*).

The relative orientations of the glycosidic linkages (O3/C24–C28) are determined by the C2—C3—O2—C24 (φ_1) and C3—O2—C24—C25 (φ_2) torsion angles; φ_1 and φ_2 are 159.6 (4) and 173.1 (4)°, respectively, in molecule (I*A*), and 156.6 (4) and 173.2 (4)° in molecule (I*B*).

In the crystal of (I), there is one methanol and one water solvate molecule, which were incorporated during recrystallization. Within the asymmetric unit, both solvate molecules are linked to molecule (I*A*) through O5*A*—H5*AA*···O1*W* and O9—H9*AA*···O4*A* hydrogen bonds, while molecules (I*A*) and (I*B*) are interconnected almost symmetrically by O8*A*—H8*AA*···O7*B* and O8*B*—H8*BB*···O7*A* hydrogen

  DOI: 10.1107/S0108270102023065

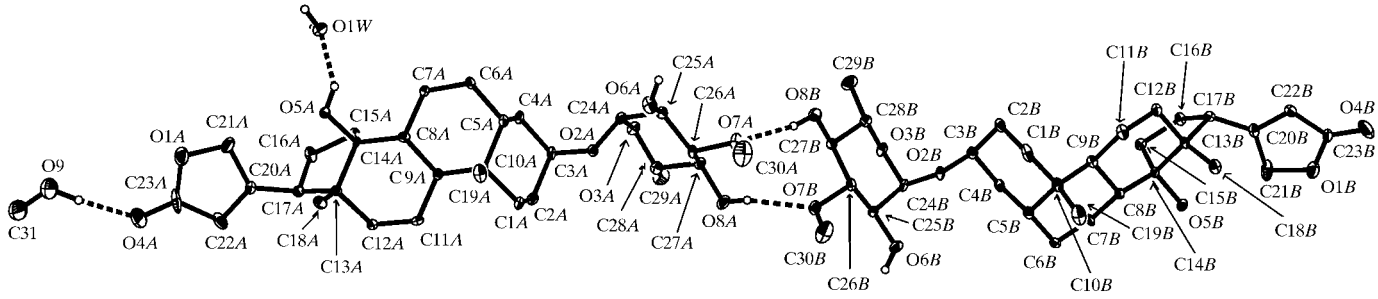


Figure 1
The structure of compound (I), showing 30% probability displacement ellipsoids and the atom-numbering scheme. H atoms have been omitted for clarity.

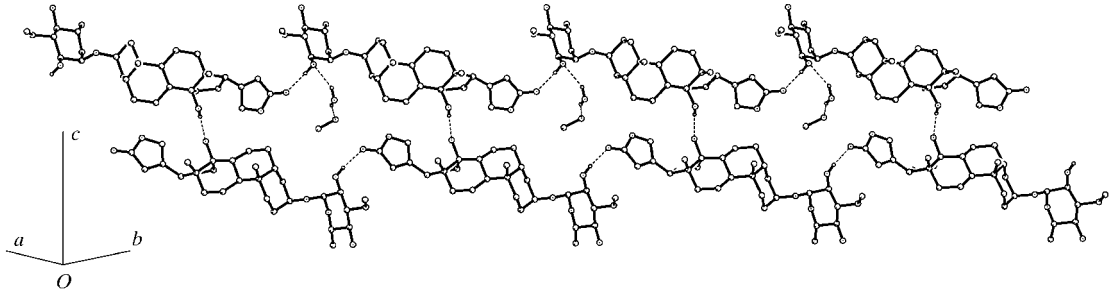


Figure 2
Packing diagram for compound (I), showing the molecular ribbons. H atoms have been omitted, except for those involved in hydrogen-bond interactions (dashed lines).

bonds. In the packing, there are five O—H···O hydrogen bonds [O6*A*—H6*AA*···O4*A*^{i}, O5*B*—H5*BB*···O5*A*^{ii}, O6*B*—H6*BB*···O4*B*^{iii}, O1*W*—H1*W*1···O9^{iv} and O1*W*—H2*W*1···O6*B*^{v}; see Table 1 for symmetry codes] interconnecting the molecules into molecular ribbons perpendicular to the *c* direction (Fig. 2).

In compound (II) (Fig. 3), the cyclopentane *D* ring adopts a twisted conformation, with atoms C13 and C14 displaced on opposite sides of the C15/C16/C17 plane by 0.294 (2) and 0.339 (2) Å, respectively. The planar lactone ring is also nearly orthogonal to the *D* ring, with a dihedral angle of 85.2 (1)°. The C13—C17—C20—C22 torsion angle is −96.6 (3)°, and the φ_1 and φ_2 values are 96.7 (2) and 158.4 (2)°, respectively, which are much smaller than those in compound (I).

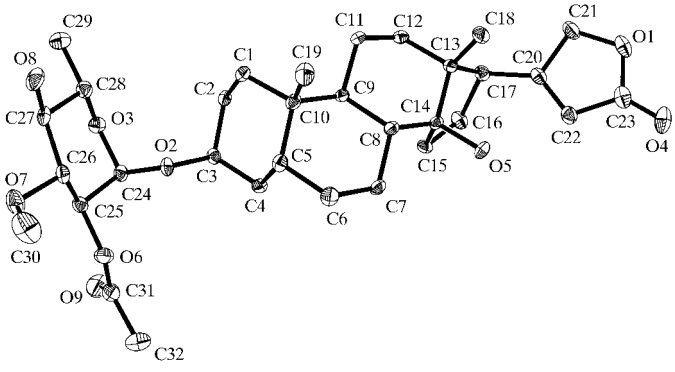


Figure 3
The structure of compound (II), showing 50% probability displacement ellipsoids and the atom-numbering scheme. H atoms have been omitted for clarity.

In the packing of compound (II), the molecules are linked by O8—H8*A*···O9^{vii} hydrogen bonds into columns parallel to the *a* direction (see Table 2 for symmetry codes). Two adjacent molecular columns are interconnected by O5—H5*A*···O8^{vi}, C25—H25···O5^{ix} and C32—H32*B*···O4^{ix} hydrogen bonds (Fig. 4), and are further interconnected by C3—H3···O4^{viii} into a three-dimensional network.

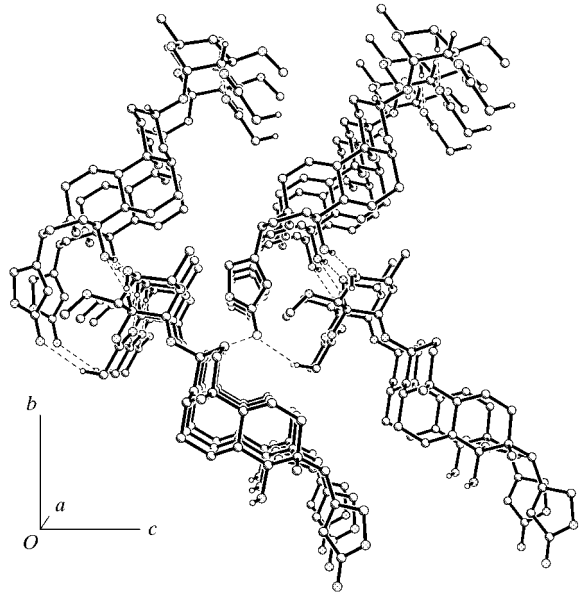


Figure 4
Packing diagram for compound (II), showing the interconnections of two adjacent molecular columns. H atoms have been omitted, except for those involved in hydrogen-bond interactions (dashed lines).

Experimental

Fresh seeds (940 g) of *Cerbera odollam* were extracted twice with methylene chloride (2.5 l) over periods of 5 d at room temperature. The mixture was filtered and concentrated under reduced pressure. Some white solids (0.3085 g) precipitated and were purified by preparative TLC (eluant: 2% methanol in ether), yielding (I) (R_F = 0.19, 30% acetone–hexane) and (II) (R_F = 0.38, 30% acetone–hexane). Both compounds were recrystallized from chloroform/methanol [m.p.: 475–479 and 493–497 K for (I) and (II), respectively].

Compound (I)

Crystal data

$2C_{30}H_{46}O_8{\cdot}CH_4O{\cdot}H_2O$	Z = 1
M_r = 1119.39	D_x = 1.250 Mg m^{-3}
Triclinic, $P\overline{1}$	Mo $K\alpha$ radiation
a = 10.4353 (5) Å	Cell parameters from 7201 reflections
b = 10.4491 (5) Å	θ = 1.4–29.5°
c = 14.8760 (7) Å	μ = 0.09 mm^{-1}
α = 92.412 (1)°	T = 213 (2) K
β = 101.471 (1)°	Slab, colorless
γ = 109.599 (1)°	0.44 × 0.32 × 0.10 mm
V = 1487.1 (1) Å^3	

Data collection

Siemens SMART CCD area-detector	6292 independent reflections
	4368 reflections with $I > 2\sigma(I)$
ω scans	R_{int} = 0.072
Absorption correction: empirical (*SADABS*; Sheldrick, 1996)	θ_{max} = 27.0°
	$h = -12 \rightarrow 13$
T_{min} = 0.961, T_{max} = 0.991	$k = -10 \rightarrow 13$
9863 measured reflections	$l = -18 \rightarrow 12$

Refinement

Refinement on F^2	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)]$ = 0.066	$w = 1/[\sigma^2(F_o^2) + (0.0841P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2)$ = 0.182	$(\Delta/\sigma)_{max} < 0.001$
S = 0.97	$\Delta\rho_{max}$ = 0.68 e Å^{-3}
6292 reflections	$\Delta\rho_{min}$ = −0.70 e Å^{-3}
715 parameters	

Table 1
Hydrogen-bonding geometry (Å, °) for (I).

D—H···A	D—H	H···A	D···A	D—H···A
O5*A*—H5*AA*···O1*W*	0.82	2.11	2.770 (5)	137
O5*B*—H5*BB*···O5*A*^{ii}	0.82	2.34	3.161 (4)	174
O6*A*—H6*AA*···O4*A*^{i}	0.82	1.95	2.756 (8)	170
O6*B*—H6*BB*···O4*B*^{iii}	0.82	1.84	2.659 (8)	173
O8*A*—H8*AA*···O7*B*	0.82	2.15	2.941 (6)	163
O8*B*—H8*BB*···O7*A*	0.82	2.16	2.961 (6)	167
O9—H9*AA*···O4*A*	0.90	1.92	2.792 (9)	165
O1*W*—H1*W*1···O9^{iv}	0.85	1.95	2.762 (7)	159
O1*W*—H2*W*1···O6*B*^{v}	0.85	2.16	2.926 (6)	150

Symmetry codes: (i) $x-1, 1+y, z$; (ii) $x-2, 1+y, z-1$; (iii) $1+x, y-1, z$; (iv) $x-1, y, z$; (v) $1+x, y-1, 1+z$.

Compound (II)

Crystal data

$C_{32}H_{48}O_9$	D_x = 1.237 Mg m^{-3}
M_r = 576.70	Mo $K\alpha$ radiation
Monoclinic, $P2_1$	Cell parameters from 8192 reflections
a = 7.3351 (3) Å	θ = 1.9–29.5°
b = 21.4770 (9) Å	μ = 0.09 mm^{-1}
c = 9.9056 (4) Å	T = 293 (2) K
β = 97.007 (1)°	Slab, colourless
V = 1548.8 (1) Å^3	0.50 × 0.48 × 0.26 mm
Z = 2	

Data collection

Siemens SMART CCD area-detector	3461 independent reflections
	3057 reflections with $I > 2\sigma(I)$
ω scans	R_{int} = 0.104
Absorption correction: empirical (*SADABS*; Sheldrick, 1996)	θ_{max} = 27.0°
	$h = -9 \rightarrow 9$
T_{min} = 0.957, T_{max} = 0.977	$k = -27 \rightarrow 16$
10 311 measured reflections	$l = -12 \rightarrow 12$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0277P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)]$ = 0.045	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2)$ = 0.106	$\Delta\rho_{max}$ = 0.46 e Å^{-3}
S = 1.01	$\Delta\rho_{min}$ = −0.42 e Å^{-3}
3461 reflections	Extinction correction: *SHELXL*97
376 parameters	Extinction coefficient: 0.059 (4)
H-atom parameters constrained	

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

D—H···A	D—H	H···A	D···A	D—H···A
O5—H5*A*···O8^{vi}	0.82	1.98	2.777 (3)	163
O8—H8*A*···O9^{vii}	0.82	2.01	2.828 (3)	175
C3—H3···O4^{viii}	0.98	2.55	3.295 (3)	132
C25—H25···O5^{ix}	0.98	2.36	3.311 (3)	164
C32—H32*B*···O4^{ix}	0.96	2.45	3.345 (4)	154

Symmetry codes: (vi) $2-x, y-\frac{1}{2}, 2-z$; (vii) $1+x, y, z$; (viii) $1-x, \frac{1}{2}+y, 1-z$; (ix) $1-x, \frac{1}{2}+y, 2-z$.

For both compounds, data collection: *SMART* (Siemens, 1996); cell refinement: *SAINT* (Siemens, 1996); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 1997); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL, PARST* (Nardelli, 1995) and *PLATON* (Spek, 1990).

This work has received financial support from the Higher Education Development Project: Postgraduate Education and Research Program in Chemistry, Royal Thai Government, Taiyo Group (Japan), and the Biodiversity Research and Training Program (BRT). The Bioassay Research Facility of BIOTEC is also gratefully acknowledged for bioactivity tests. The authors would like to thank the Malaysian Government and Universiti Sains Malaysia for research grant R&D No. 305/PFIZIK/610961.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: TA1401). Services for accessing these data are described at the back of the journal.

References

Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, A. G. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans.* 2, pp. S1–19.
Chen, K. K. & Steldt, F. A. (1942). *J. Pharmacol.* **76**, 167–174.
Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.
Hien, T. T. M., Navarro-Delmasure, C. H. & Tran, V. Y. (1991). *J. Ethnopharmacol.* **34**, 201–206.
Laphookhieo, S., Karalai, C., Chantrapromma, S., Fun, H.-K., Usman, A., Rat-a-pa, Y. & Chantrapromma, K. (2001). *Acta Cryst.* C**57**, 1352–1353.
Lasserre, B., Trans, M. H. & Pham, H. A. (1992). *Med. Sci. Res.* **18**, 667–669.
Nardelli, M. (1995). *J. Appl. Cryst.* **28**, 659.
Sheldrick, G. M. (1996). *SADABS*. University of Göttingen, Germany.
Sheldrick, G. M. (1997). *SHELXTL*. Version 5.1. Bruker AXS Inc., Madison, Wisconsin, USA.
Siemens (1996). *SMART* and *SAINT*. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Spek, A. L. (1990). *Acta Cryst.* A**46**, C-34.