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Study of Cerleaside A, a Glycoside from *Cerbera odollam*

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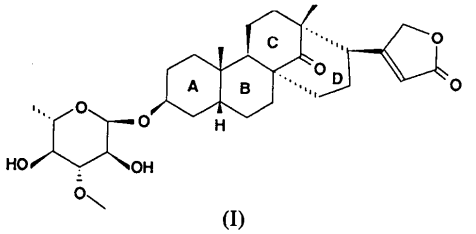
Abstract

Cerleaside A is a glycoside isolated in small amounts from the leaves of *Cerbera odollam* Gaertn. The aglycone part is a rearranged steroid substitued at C17 by a γ-lactone and at C3 by a sugar, L-thevetose. One water molecule, which is distributed on two sites with an occupancy factor of 0.5, is in a cavity delimited by the sugar and lactone groups to which it is hydrogen bonded.

Comment

From the leaves of *Cerbera odollam* Gaertn., a plant from the south of Vietnam possessing cardiotonic properties (Pételot, 1953), we isolated three known glycosides: cerberin (Frèrejacque, 1949; Lasserre *et al.*, 1992), tanghinin and deacetyltanghinin (Helfenberger & Reichstein, 1952; Abe & Yamaguchi, 1977). A fourth compound (I) has been isolated in small amounts. It has m.p. 481–483 K (MeOH) and $[\alpha]_D$ = −22.3 (MeOH, c = 0.13); its molecular formula is $C_{30}H_{44}O_8$ giving a peak at m/z 533 (M+1) in its chemical ionization mass spectrum.



(I)

The spectroscopic data clearly indicate the presence of thevetose: ^{1}H NMR ($CDCl_3$), 200 MHz, δ: 1.33 (3H, d, J = 6, $CH_3$6′), 3.23 (1H, t, J = 9, H4′), 3.33 (1H, t, J = 9, H3′), 3.66 (1H, dd, J = 9, J' = 4, H2′), 3.76 (3H, s, OCH_3), 3.80 (1H, m, H5′), 4.75 (1H, d, J = 4, H1′); ^{13}C NMR ($CDCl_3$) δ: 17.5 ($CH_3$6′), 60.6 (OCH_3), 67.6 (C5′), 73.4 (C2′), 74.8 (C4′), 84.7 (C3′), 97.5 (C1′). ^{1}H-^{1}H and ^{1}H-^{13}C COSY experiments allowed us to assign accurately the signals of the sugar moiety in the ^{1}H and ^{13}C NMR spectra. A signal at δ 5.75 in the ^{1}H NMR ($CDCl_3$) spectrum is in agreement with the presence of an unsaturated γ-lactone, but the spectroscopic data gave no indication of the aglycone moiety. This compound shows spectroscopic analogies with cerleaside A, a glycoside previously isolated by Yamaguchi, Abe & Wan (1987) from *Cerbera odollam* leaves from Singapore. So to identify with certainty the product we had isolated, an X-ray crystallographic study was carried out.

The molecule of cerleaside A is shown in Fig. 1 with the atom numbering. The absolute configuration of the molecule has been deduced from that of the rearranged steroid moiety. All the six-membered rings are chair-shaped with a *cis* junction between the *A*/*B* and *B*/*C* rings. An L-thevetose appears fixed on C3, with all its substituents in equatorial positions except for O1 which is axial. In the crystal, strong hydrogen bonds hold together the molecules, as seen in Fig. 2. The hydroxyl group O4′—H is linked to the carbonyl O atom O25 of the neighbouring lactone [O4′—H···O25($2-x$, $-\frac{1}{2}+y$, $1-z$) 2.813 (5) Å, 155.4°] and to the hydroxyl group O2′—H of another molecule [O4′···H—O2′($1-x$, $-\frac{1}{2}+y$, $-z$) 2.787 (5) Å, 177.2°].

Two solvent molecules were found in difference maps. As their vicinity excluded the simultaneous presence of both, they were treated as statistical water molecules with occupancy factors of 0.5. These molecules are in a cavity delimited by the sugar and lactone groups to

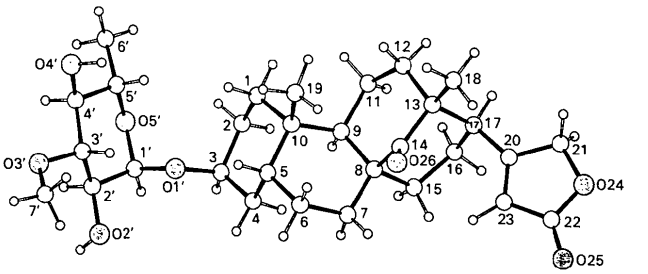


Fig. 1. Perspective view of the molecule showing the atom labelling.

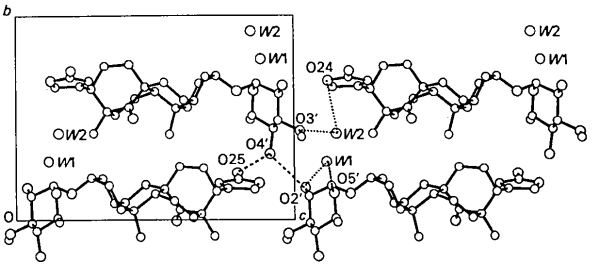


Fig. 2. Projection along the *a* axis showing the hydrogen-bond network. The water molecules *W*1 and *W*2 are statistical (occupancy 0.5).

which they are hydrogen bonded. Each water molecule bridges two molecules of cerleaside A through atoms O2′(x, y, z) and O5′($1 + x, y, z$) for *W*1 [*W*1···O2′ 2.74 (1) and *W*1···O5′ 3.11 (1) Å] and through atoms O3′($1 - x$, $\frac{1}{2} + y$, $-z$) and O24($2 - x$, $\frac{1}{2} + y$, $1 - z$) for *W*2 [*W*2···O3′ 2.95 (1), *W*2···O24 3.08 (2) Å]

Experimental

Crystal data

$C_{30}H_{44}O_8.H_2O$
M_r = 550.69
Monoclinic
$P2_1$
a = 7.687 (3) Å
b = 11.553 (5) Å
c = 16.003 (8) Å
β = 91.26 (3)°
V = 1420.8 (10) Å^3
Z = 2
D_x = 1.29 Mg m^{-3}
Cu $K\alpha$ radiation
λ = 1.5418 Å

Cell parameters from 25 reflections
θ = 10.7–16.8°
μ = 0.73 mm^{-1}
T = 293 K
Prism
0.50 × 0.35 × 0.25 mm
Colourless
Crystal source: from the leaves of *Cerbera odollam* Gaertn.

Data collection

Nonius CAD-4 diffractometer
$\theta/2\theta$ scans
Absorption correction: none
4447 measured reflections
2542 independent reflections
2205 observed reflections [$I > 3.0\sigma(I)$]

R_{int} = 0.067
θ_{max} = 64.93°
$h = -9 \rightarrow 9$
$k = -13 \rightarrow 13$
$l = 0 \rightarrow 18$
3 standard reflections
frequency: 60 min
intensity variation: none

Refinement

Refinement on F
Final R = 0.048
wR = 0.066
S = 1.45
2200 reflections
360 parameters
H-atom parameters not refined
Calculated weights $w = 1/[\sigma^2(F) + 0.00220F^2]$

$(\Delta/\sigma)_{max}$ = 0.16
$\Delta\rho_{max}$ = 0.23 e Å^{-3}
$\Delta\rho_{min}$ = −0.25 e Å^{-3}
Extinction correction: none
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV, Table 2.2B)

The H atoms HO2′ and HO4′ were located in difference maps and readjusted, as for the others, in theoretical positions (O—H = 1.00 Å). The isotropic temperature factors of the H atoms were set equal to 1.10 × U_{eq} of the bonded atoms. Data collection: *CAD-4 Software* (Enraf–Nonius, 1989). Data reduction: *NONIUS* (Riche, 1989). Program(s) used to solve structure: *SHELXS86* (Sheldrick, 1986). Program(s) used to refine structure: *SHELX76* (Sheldrick, 1976). Molecular graphics: *R3M* (Riche, 1983); *ORTEP* (Johnson, 1965). Software used to prepare material for publication: *ACTACIF* (Riche, 1992).

Table 1. *Fractional atomic coordinates and equivalent isotropic thermal parameters* (Å^2)

$U_{eq} = \frac{1}{3}\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	U_{eq}
C1	0.4702 (4)	0.0509†	0.3789 (2)	0.030 (3)
C2	0.4258 (5)	0.1667 (4)	0.3374 (3)	0.037 (4)
C3	0.5598 (5)	0.2037 (4)	0.2749 (3)	0.034 (3)
C4	0.7406 (5)	0.1994 (4)	0.3145 (2)	0.032 (3)
C5	0.7844 (4)	0.0828 (4)	0.3552 (2)	0.029 (3)
C6	0.9699 (5)	0.0858 (5)	0.3929 (3)	0.037 (4)
C7	0.9837 (4)	0.1713 (4)	0.4654 (2)	0.032 (3)
C8	0.8551 (4)	0.1498 (4)	0.5353 (2)	0.026 (3)
C9	0.6648 (4)	0.1269 (4)	0.4997 (2)	0.025 (3)
C10	0.6528 (4)	0.0457 (4)	0.4221 (2)	0.025 (3)
C11	0.5409 (5)	0.0931 (4)	0.5710 (3)	0.035 (4)
C12	0.6172 (5)	0.0121 (4)	0.6395 (3)	0.037 (4)
C13	0.8092 (5)	0.0300 (4)	0.6683 (3)	0.032 (3)
C14	0.9176 (4)	0.0507 (4)	0.5913 (2)	0.028 (3)
C15	0.8585 (5)	0.2602 (4)	0.5912 (3)	0.035 (4)
C16	0.7777 (5)	0.2521 (4)	0.6778 (3)	0.035 (4)
C17	0.8276 (5)	0.1402 (4)	0.7252 (2)	0.033 (3)
C18	0.8690 (6)	−0.0776 (5)	0.7169 (3)	0.045 (4)
C19	0.6806 (5)	−0.0821 (4)	0.4455 (3)	0.036 (4)
C20	1.0053 (5)	0.1535 (4)	0.7659 (3)	0.034 (3)
C21	1.0282 (6)	0.1497 (6)	0.8584 (3)	0.051 (5)
C22	1.2858 (6)	0.1972 (5)	0.8021 (3)	0.048 (4)
C23	1.1604 (5)	0.1788 (5)	0.7335 (3)	0.045 (4)
O24	1.2059 (4)	0.1801 (5)	0.8752 (2)	0.061 (4)
O25	1.4349 (4)	0.2287 (5)	0.7995 (3)	0.071 (4)
O26	1.0481 (4)	−0.0046 (4)	0.5777 (2)	0.043 (3)
C1′	0.4547 (5)	0.1666 (4)	0.1338 (3)	0.042 (4)
C2′	0.5228 (6)	0.1174 (5)	0.0536 (3)	0.041 (4)
C3′	0.5156 (6)	−0.0144 (5)	0.0565 (3)	0.038 (4)
C4′	0.3304 (6)	−0.0528 (5)	0.0734 (3)	0.036 (4)
C5′	0.2550 (5)	0.0082 (4)	0.1488 (3)	0.036 (4)
C6′	0.0623 (6)	−0.0102 (5)	0.1551 (3)	0.050 (5)
C7′	0.7414 (8)	−0.0937 (6)	−0.0277 (4)	0.068 (6)
O1′	0.5620 (3)	0.1301 (4)	0.2018 (2)	0.034 (2)
O2′	0.6937 (4)	0.1576 (4)	0.0399 (2)	0.059 (3)
O3′	0.5625 (4)	−0.0647 (5)	−0.0222 (2)	0.059 (4)
O4′	0.3222 (4)	−0.1758 (4)	0.0860 (2)	0.042 (3)
O5′	0.2768 (4)	0.1320 (4)	0.1436 (2)	0.042 (3)
*W*1	0.9489 (12)	0.2866 (9)	0.1174 (8)	0.096 (12)
*W*2	0.7134 (20)	0.4220 (13)	0.1526 (8)	0.163 (19)
HO2′	0.69019	0.21575	−0.00638	0.064
HO4′	0.39008	−0.19619	0.13792	0.046

† The y coordinate of atom C1 was fixed to define the origin of the non-centrosymmetric space group.

Table 2. *Geometric parameters* (Å, °)

C1—C2	1.529 (5)	C15—C16	1.534 (6)
C1—C10	1.552 (5)	C16—C17	1.544 (7)
C2—C3	1.514 (6)	C17—C20	1.508 (5)
C3—C4	1.516 (5)	C20—C21	1.486 (6)
C3—O1′	1.445 (5)	C20—C23	1.343 (6)
C4—C5	1.531 (6)	C21—O24	1.430 (6)
C5—C6	1.537 (5)	C22—C23	1.460 (6)
C5—C10	1.549 (5)	C22—O24	1.349 (6)
C6—C7	1.525 (7)	C22—O25	1.205 (6)
C7—C8	1.529 (5)	C1′—C2′	1.508 (7)
C8—C9	1.580 (5)	C1′—O1′	1.415 (5)
C8—C14	1.525 (6)	C1′—O5′	1.437 (5)
C8—C15	1.558 (6)	C2′—C3′	1.525 (8)
C9—C10	1.558 (6)	C2′—O2′	1.415 (6)
C9—C11	1.552 (5)	C3′—C4′	1.521 (6)
C10—C19	1.537 (6)	C3′—O3′	1.440 (6)
C11—C12	1.547 (6)	C4′—C5′	1.523 (6)
C12—C13	1.550 (5)	C4′—O4′	1.437 (7)
C13—C14	1.522 (5)	C5′—C6′	1.502 (6)
C13—C17	1.570 (7)	C5′—O5′	1.442 (7)
C13—C18	1.532 (7)	C7′—O3′	1.420 (7)
C14—O26	1.213 (5)		

C2—C1—C10	114.7 (3)	C8—C14—O26	122.8 (4)
C1—C2—C3	112.7 (3)	C13—C14—O26	122.1 (4)
C2—C3—C4	110.2 (3)	C8—C15—C16	117.8 (4)
C2—C3—O1′	112.9 (3)	C15—C16—C17	113.2 (4)
C4—C3—O1′	107.0 (3)	C13—C17—C16	112.1 (3)
C3—C4—C5	113.4 (3)	C13—C17—C20	113.7 (3)
C4—C5—C6	109.9 (3)	C16—C17—C20	109.9 (3)
C4—C5—C10	113.4 (3)	C17—C20—C21	120.9 (4)
C6—C5—C10	110.5 (3)	C17—C20—C23	131.2 (4)
C5—C6—C7	111.2 (4)	C21—C20—C23	107.7 (4)
C6—C7—C8	114.6 (3)	C20—C21—O24	105.8 (4)
C7—C8—C9	111.8 (3)	C23—C22—O24	109.0 (4)
C7—C8—C14	110.6 (3)	C23—C22—O25	129.2 (5)
C7—C8—C15	106.5 (3)	O24—C22—O25	121.7 (5)
C9—C8—C14	111.3 (3)	C20—C23—C22	108.6 (4)
C9—C8—C15	110.3 (3)	C21—O24—C22	108.9 (4)
C14—C8—C15	106.1 (3)	C2′—C1′—O1′	109.6 (4)
C8—C9—C10	115.2 (3)	C2′—C1′—O5′	109.7 (4)
C8—C9—C11	110.8 (3)	O1′—C1′—O5′	111.9 (4)
C10—C9—C11	114.1 (3)	C1′—C2′—C3′	109.7 (4)
C1—C10—C5	106.3 (3)	C1′—C2′—O2′	110.5 (4)
C1—C10—C9	111.6 (3)	C3′—C2′—O2′	111.5 (4)
C1—C10—C19	105.4 (3)	C2′—C3′—C4′	109.3 (4)
C5—C10—C9	110.9 (3)	C2′—C3′—O3′	111.5 (4)
C5—C10—C19	110.2 (3)	C4′—C3′—O3′	106.9 (4)
C9—C10—C19	112.2 (3)	C3′—C4′—C5′	112.3 (4)
C9—C11—C12	116.3 (3)	C3′—C4′—O4′	110.9 (4)
C11—C12—C13	118.3 (4)	C5′—C4′—O4′	109.2 (4)
C12—C13—C14	108.4 (3)	C4′—C5′—C6′	112.4 (4)
C12—C13—C17	110.7 (3)	C4′—C5′—O5′	111.5 (4)
C12—C13—C18	108.4 (4)	C6′—C5′—O5′	105.1 (4)
C14—C13—C17	107.4 (3)	C3—O1′—C1′	115.4 (3)
C14—C13—C18	112.0 (4)	C3′—O3′—C7′	114.3 (4)
C17—C13—C18	110.0 (4)	C1′—O5′—C5′	113.2 (3)
C8—C14—C13	115.0 (3)		

C10—C1—C2—C3	55.2 (3)	C15—C16—C17—C13	−46.2 (4)
C1—C2—C3—C4	−51.6 (4)	C16—C17—C13—C14	55.0 (4)
C2—C3—C4—C5	52.8 (4)	C17—C13—C14—C8	−64.6 (4)
C3—C4—C5—C10	−56.3 (4)	C13—C14—C8—C15	58.8 (4)
C4—C5—C10—C1	53.6 (3)	C16—C17—C20—C21	116.7 (5)
C5—C10—C1—C2	−53.7 (3)	C16—C17—C20—C23	−57.2 (4)
C10—C5—C6—C7	−59.9 (4)	C4—C3—O1′—C1′	−146.4 (5)
C5—C6—C7—C8	55.8 (4)	C3—O1′—C1′—C2′	155.8 (5)
C6—C7—C8—C9	−46.1 (4)	O1′—C1′—C2′—C3′	62.2 (4)
C7—C8—C9—C10	42.8 (3)	C1′—C2′—C3′—C4′	56.0 (4)
C8—C9—C10—C5	−48.3 (3)	C2′—C3′—C4′—C5′	−51.0 (4)
C9—C10—C5—C6	56.0 (4)	C3′—C4′—C5′—O5′	50.4 (4)
C8—C9—C11—C12	−39.6 (3)	C4′—C5′—O5′—C1′	−55.7 (4)
C9—C11—C12—C13	38.2 (4)	C5′—O5′—C1′—C2′	61.4 (4)
C11—C12—C13—C14	−43.0 (4)	O5′—C1′—C2′—C3′	−61.0 (4)
C12—C13—C14—C8	55.1 (4)	O2′—C2′—C3′—O3′	−63.3 (4)
C13—C14—C8—C9	−61.2 (4)	C2′—C3′—O3′—C7′	93.2 (5)
C14—C8—C9—C11	50.1 (3)	O3′—C3′—C4′—O4′	65.7 (4)
C14—C8—C15—C16	−47.3 (4)	O4′—C4′—C5′—C6′	−68.4 (4)
C8—C15—C16—C17	43.8 (4)		

Lists of structure factors, anisotropic thermal parameters and H-atom coordinates have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 71312 (12 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: PA1053]

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Structural Studies of the Regioselectivity of Bishydroxylation of Polycyclic Methylenecyclobutanol Derivatives

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Abstract

With tricyclic methylenecyclobutanols as starting materials, the following compounds were prepared and their crystal structures determined: *cis-transoid-cis*-7,8-dihydroxytricyclo[7.5.0.0^{2,8}]tetradec-1-yl acetate (2) and *cis-cisoid-cis*-8,9-dihydroxytricyclo[6.5.0.0^{2,7}]tridec-2-yl acetate (4). The stereochemistry at the ring junctions is retained during the reaction. The conformations of