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Structure of Cueunicin Acetate

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Abstract. $C_{22}H_{32}O_5$, $M_r = 376{\cdot}5$, orthorhombic, $P2_12_12_1$, $a = 16{\cdot}964\ (4)$, $b = 19{\cdot}288\ (8)$, $c = 6{\cdot}219\ (2)$ Å, $V = 2034{\cdot}9$ Å^3 at 138 (2) K; $a = 17{\cdot}17\ (2)$, $b = 19{\cdot}42\ (2)$, $c = 6{\cdot}275\ (1)$ Å, $V = 2092{\cdot}3$ Å^3, $Z = 4$, $D_m = 1{\cdot}201$, $D_x = 1{\cdot}195$ g cm^{-3} at 295 K; Cu $K\bar{\alpha}$, $\lambda = 1{\cdot}5418$ Å, $\mu = 7{\cdot}0$ cm^{-1}, $F(000) = 816$, $R = 0{\cdot}033$ for all 2423 unique reflections taken at 138 K. The diterpene is a cembranolide in which a 14-membered ring is *cis*-fused with a methylene-substituted γ-lactone ring, while an ether linkage across the macrocyclic ring forms a six-membered ring. This structure determination confirms the one proposed by Gross [PhD thesis (1974), Univ. of Oklahoma]. The lactone ring is approximately perpendicular to the plane of the cembrane ring and the ring is more planar than those observed in other cembranolides.

Introduction. The cembranolides cueunicin and cueunicin acetate were isolated from the hexane extract of the Caribbean gorgonian, *Eunicea mammosa Lamouroux*, collected near Curacao, Netherlands Antilles (Gross, 1974). Cueunicin itself could not be induced to crystallize, but the acetate of cueunicin produced crystalline material, which was recrystallized from benzene/hexane mixtures. Cueunicin can easily be converted into the acetate and Gross (1974) proposed the structures of cueunicin and cueunicin acetate from an analysis of the NMR spectral data and this structure is confirmed in the present communication.

Experimental. Prismatic colorless crystal, 0·48 × 0·20 × 0·13 mm; Enraf–Nonius CAD-4 diffractometer with liquid-N_2 low-temperature device; 48 reflections with $14 < \theta < 28°$, Cu $K\alpha_1$ ($\lambda = 1{\cdot}54051$ Å), throughout all octants of reciprocal space, to refine cell constants; systematic absences: $h00$, $k =$ odd, $0k0$, $k =$ odd, $00l$, $l =$ odd; no absorption correction; $2\theta_{max} = 150°$; $0 \le h \le 21$, $0 \le k \le 24$, $0 \le l \le 7$; three standard reflections measured after every 7200 s of X-ray exposure showed no deterioration; 2423 unique reflections, 2285 observed [$I > 2\sigma(I)$]; scan width $(1{\cdot}0 + 0{\cdot}15 \tan\theta)°$, aperture width $(3{\cdot}0 + 0{\cdot}86 \tan\theta)$ mm, height 6 mm; scan time ≤ 60 s; structure solved by direct methods using tangent refinement (Karle & Karle, 1966) and *MULTAN* (Germain, Main & Woolfson, 1971); refinement: block-diagonal least squares (Ahmed, 1966); function minimized $w(|F_o| - |F_c|)^2$ with $w = \sigma(F_o)^{-2}$; H atoms from difference Fourier synthesis and refined isotropically; non-H atoms anisotropic; R (for all unique reflections) = 0·033, R(obs) = 0·031, $S = 1{\cdot}52$; Δ/σ(max) = 20%. Atomic scattering factors and anomalous-dispersion corrections from *International Tables for X-ray Crystallography* (1974); H-atom scattering factors (Stewart, Davidson & Simpson, 1965).

It has been proposed that the cembranolides from the Pacific belong to the α series, while those from the Caribbean assume the β configuration (Weinheimer, Matson, Hossain & van der Helm, 1977). Alternatively, the suggestion was made that all cembrane diterpenes from the order Alcyonacea belong to the α series and those isolated from species in the order Gorgonacea belong to the β series (Tursch, Braekman, Daloze & Kaisin, 1978). Either way this would suggest cueunicin acetate to belong to the β series, which assigns the absolute configuration at C(1), which is the configuration shown in all figures.

Discussion. The atomic coordinates are given in Table 1.* A stereoscopic view of cueunicin acetate is shown in Fig. 1. The bond distances are given in Fig. 2 together with the atom numbering, consistent with that proposed earlier (Weinheimer *et al.*, 1977). The bond angles and torsion angles are listed in Table 2.

The molecular structure of cueunicin acetate has the following features: (*a*) a 14-membered carbocyclic ring, with a *trans* (178°) double bond at C(7)=C(8); (*b*) a γ-lactone ring that is *cis* fused at C(1) and C(14) and

* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 42621 (15 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Table 1. *Atomic coordinates* (x, $y \times 10^5$, $z \times 10^4$) *and* U_{eq} ($Å^2 \times 10^4$) *values*

Standard deviations for the last digit are in parentheses.

	x	y	z	U_{eq}*
O(1)	33019 (6)	91578 (6)	4316 (2)	231 (3)
O(2)	29133 (7)	95743 (6)	1149 (2)	314 (3)
O(3)	49484 (6)	89634 (5)	5522 (2)	237 (3)
O(4)	63682 (6)	103342 (6)	4175 (2)	214 (3)
O(5)	57469 (7)	104482 (6)	975 (2)	300 (4)
C(1)	39198 (9)	101676 (7)	5898 (3)	182 (4)
C(2)	48256 (9)	102215 (6)	5947 (3)	196 (4)
C(3)	51803 (7)	96226 (6)	4675 (3)	183 (4)
C(4)	60933 (9)	96127 (7)	4565 (3)	184 (4)
C(5)	64154 (9)	91414 (7)	2750 (3)	225 (4)
C(6)	67034 (10)	84053 (7)	3335 (3)	247 (5)
C(7)	60639 (9)	79009 (7)	3928 (3)	235 (4)
C(8)	60689 (10)	74198 (7)	5466 (3)	235 (5)
C(9)	53410 (10)	69794 (7)	5832 (4)	277 (5)
C(10)	49559 (10)	70803 (7)	8049 (3)	271 (5)
C(11)	47861 (9)	78391 (7)	8591 (3)	229 (4)
C(12)	41187 (9)	81752 (7)	7277 (3)	201 (4)
C(13)	43067 (9)	89482 (7)	7027 (3)	188 (4)
C(14)	36368 (7)	94155 (7)	6326 (3)	174 (4)
C(15)	35822 (9)	103164 (7)	3704 (3)	193 (4)
C(16)	32263 (9)	96699 (7)	2866 (3)	212 (4)
C(17)	35671 (10)	108978 (9)	2592 (3)	186 (5)
C(18)	64588 (10)	94562 (9)	6742 (3)	238 (4)
C(19)	67485 (10)	72853 (9)	6963 (3)	312 (5)
C(20)	33167 (10)	80399 (9)	8318 (4)	301 (5)
C(21)	61500 (9)	106775 (7)	2388 (3)	226 (4)
C(22)	64689 (10)	114074 (9)	2438 (3)	299 (5)

* $U_{eq} = \frac{1}{3}\sum_{i,j} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j$.

Table 2. *Bond angles* (°) (*e.s.d.'s:* 0·1–0·2°) *and conformational angles* (°) (*e.s.d.'s:* 0·3°)

C(14)	C(1)	C(2)	111·6	C(11)	C(12)	C(13)	108·1
C(15)	C(1)	C(2)	112·6	C(11)	C(12)	C(20)	111·0
C(14)	C(1)	C(15)	102·5	C(13)	C(12)	C(20)	113·2
C(1)	C(2)	C(3)	109·4	C(12)	C(13)	C(14)	116·9
C(2)	C(3)	C(4)	115·3	C(12)	C(13)	O(3)	104·1
C(2)	C(3)	O(3)	112·0	C(14)	C(13)	O(3)	111·7
O(3)	C(3)	C(4)	106·3	C(13)	C(14)	C(1)	111·9
C(3)	C(4)	C(5)	113·1	C(13)	C(14)	O(1)	109·6
C(3)	C(4)	O(4)	108·0	C(1)	C(14)	O(1)	107·0
C(3)	C(4)	C(18)	111·7	C(1)	C(15)	C(16)	108·3
C(5)	C(4)	O(4)	108·7	C(1)	C(15)	C(17)	130·1
C(5)	C(4)	C(18)	112·9	C(16)	C(15)	C(17)	121·6
O(4)	C(4)	C(18)	101·7	C(15)	C(16)	O(1)	110·1
C(4)	C(5)	C(6)	118·6	C(15)	C(16)	O(2)	128·3
C(5)	C(6)	C(7)	115·1	O(1)	C(16)	O(2)	121·6
C(6)	C(7)	C(8)	128·5	C(14)	O(1)	C(16)	111·2
C(7)	C(8)	C(9)	119·5	C(4)	O(4)	C(21)	120·6
C(7)	C(8)	C(19)	124·7	O(4)	C(12)	O(5)	125·5
C(9)	C(8)	C(19)	115·8	O(4)	C(21)	C(22)	110·1
C(8)	C(9)	C(10)	114·2	O(5)	C(21)	C(22)	124·4
C(9)	C(10)	C(11)	113·5	C(3)	O(3)	C(13)	117·8
C(10)	C(11)	C(12)	115·1				

C(14)	C(1)	C(2)	C(3)	45	C(10)	C(11)	C(12)	C(13)	−149
C(1)	C(2)	C(3)	C(4)	179	C(11)	C(12)	C(13)	C(14)	−164
C(2)	C(3)	C(4)	C(5)	−163	C(12)	C(13)	C(14)	C(1)	−174
C(3)	C(4)	C(5)	C(6)	−99	C(13)	C(14)	C(1)	C(2)	9
C(4)	C(5)	C(6)	C(7)	71	O(1)	C(14)	C(1)	C(15)	10
C(5)	C(6)	C(7)	C(8)	−141	C(14)	C(1)	C(15)	C(16)	−7
C(6)	C(7)	C(8)	C(9)	178	C(1)	C(15)	C(16)	O(1)	1
C(7)	C(8)	C(9)	C(10)	−116	C(15)	C(16)	O(1)	C(14)	6
C(8)	C(9)	C(10)	C(11)	52	C(16)	O(1)	C(14)	C(1)	−10
C(9)	C(10)	C(11)	C(12)	70					

methylene substituted [C(15)]; (*c*) an ether linkage between C(3) and C(13), forming a six-membered ring in a boat conformation (Fig. 1); (*d*) an acetate group at C(4), which is a hydroxyl group in cueunicin; and (*e*) methyl substitution at C(4), C(8) and C(12). This confirms the structure proposed by Gross (1974). The molecular structure of cueunicin is very similar to jeunicin (van der Helm, Enwall, Weinheimer, Karns & Ciereszko, 1976), with the difference being that in the latter compound the ether linkage is between C(4) and C(13), forming a seven-membered ring, while the hydroxyl function is at C(3) rather than at C(4).

The bond distances are normal, but the endocyclic bond angles in the 14-membered ring are larger than the expected values. This, however, has been observed in other 14-membered rings of the diterpene lactones, and indicates the strain in the carbocyclic ring. The cembrane ring is quite flat. The r.m.s. deviation of the atoms in the ring is 0·434 Å.

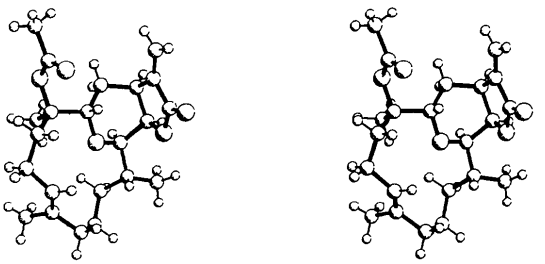

Fig. 1. A stereoview of the molecule of cueunicin acetate.

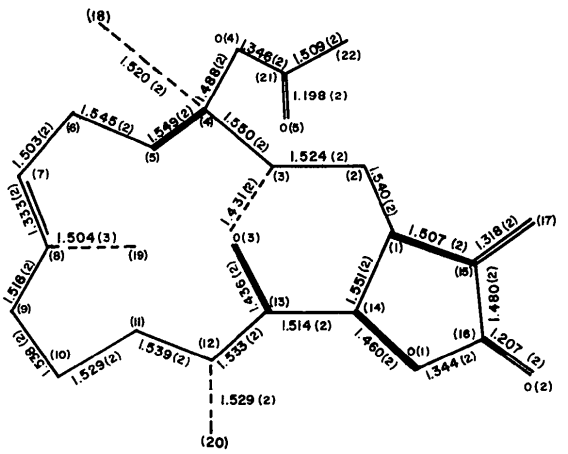

Fig. 2. Atom numbering and bond distances in cueunicin acetate.

Table 3. *Deviations* (Å) *of atoms from the least-squares planes through the five atoms of the γ-lactone rings*

	Eupalmerin acetate[a]	Lobophytolide[b]	Jeunicin iodobenzoate[c]	Peunicin[d]	Cueunicin acetate[e]
O(1)	0·104	0·030	0·127	0·097	0·047
C(1)	0·159	0·074	0·181	0·127	0·051
C(14)	−0·161	−0·064	−0·188	−0·137	−0·059
C(15)	−0·105	−0·061	−0·115	−0·080	−0·028
C(16)	0·004	0·021	0·004	−0·007	−0·011
C(17)	−0·388	−0·271	−0·459	−0·285	−0·122
O(2)	0·027	−0·044	0·015	0·009	−0·029
Mean e.s.d.'s (Å)	0·002	0·01	0·01	0·002	0·002

References: (*a*) Ealick *et al.* (1975); (*b*) Karlsson (1977); (*c*) van der Helm *et al.* (1976); (*d*) Chang *et al.* (1980); (*e*) present communication.

The γ-lactone ring deviates from the ideal envelope conformation. However, the sum of endocyclic torsion angles ($\sum|\gamma|$) of 34 (3)° is significantly smaller than that found in other cembranolides [*i.e.* 76° in peunicin (Chang, Ciereszko, Hossain & van der Helm, 1980), 106° in jeunicin (van der Helm *et al.*, 1976)]. The lactone ring is *cis*-fused with the cembrane ring and its plane lies nearly perpendicular to the plane of the cembrane ring (dihedral angle is 86·2°). The bond distances and angles of the γ-lactone are nearly identical with those observed in other cembranolides, eupalmerin acetate (Ealick, van der Helm & Weinheimer, 1975), eunicin (Hossain, Nicholas & van der Helm, 1968), jeunicin, peunicin and lobophytolide (Karlsson, 1977). But unlike in other cembranolides, the five-membered lactone ring is nearly flat in the present structure (Table 3). The r.m.s. deviation of the atoms is 0·043 Å in cueunicin and this value is about 1/3 of the r.m.s. deviation in the other molecules. The only exception is lobophytolide, where the lactone ring is *trans*-fused with the cembrane ring. Cueunicin is the only example where a *cis*-fused γ-lactone assumes such a planar geometry. Even the deviation of the *exo* methylene group [atom C(17)] in the present structure is quite small, 0·122 Å, as compared to 0·459 Å in jeunicin, 0·388 Å in eupalmerin acetate and 0·285 Å in peunicin.

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Structure of Methyl 2,3′-*O*-Anhydro-1-β-D-fructofuranosylorotate

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Abstract. $C_{12}H_{14}N_2O_8$, $M_r = 314{\cdot}25$, orthorhombic, $P2_12_12_1$, $a = 13{\cdot}601$ (1), $b = 20{\cdot}533$ (1), $c = 9{\cdot}497$ (1) Å, $V = 2652{\cdot}3$ (2) Å^3, $Z = 8$, $D_m = 1{\cdot}579$, $D_x = 1{\cdot}574$ g cm^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, $\mu = 11{\cdot}1$ cm^{-1}, $F(000) = 1312$, room temperature, final $R = 0{\cdot}040$ for 2391 independent observed reflections.

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