

Dihydroglaucolide-C, C₂₁H₂₈O₈

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Abstract

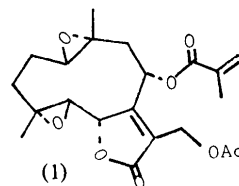
Glaucolide-C is a germacradiene-type sesquiterpene lactone isolated from *Vernonia steetzii*. The highly oxygenated glaucolide series of α,β -unsaturated γ -lactones differs from most other members of this class by having an endocyclic double bond. Glaucolide-C is unstable upon standing, but hydrogenation of the side-chain double bond imparts long-term stability. The dihydro compound crystallizes in the orthorhombic space group $P2_12_12_1$ with $a = 10.367$ (3), $b = 25.121$ (9) and $c = 7.986$ (2) Å. The structure was refined by full-matrix least-squares techniques to a final R factor of 0.048. The ten-membered ring adopts a chair-chair conformation with the C(4) and C(10) methyl groups lying *syn* on the β face. The two double bonds of the germacradiene ring have been replaced by epoxide functions.

Introduction

Vernonia species (Compositae) have yielded many highly oxygenated sesquiterpene lactones which belong to the chemically interesting glaucolide series. In addition to being useful in chemosystematic investigations, one member of the series, glaucolide-A, was shown to be a potent insect-feeding deterrent and growth inhibitor for several species of lepidoptera larvae, probably accounting for the role of the compounds in these plants (Burnett, Mabry & Jones, 1978; Mabry & Gill, 1979). The glaucolide series of sesquiterpene lactones differs from most other members of this class of natural products in having the double bond of the α,β -unsaturated γ -lactone endocyclic rather than exocyclic.

Experimental

Glaucolide-C (1) was isolated from *Vernonia steetzii* Sch.-Bip., collected 12th November, 1970, in the state of Jalisco, Mexico, just north of Guadalajara, by Dr Sam Jones Jr (collection No. 20581), Department of Botany, University of Georgia. Silica-gel column chromatography of the 4.7 g of syrup obtained from 250 g of dried leaves afforded glaucolide-C as fine needles: m.p. 421–423 K, UV(EtOH), $\lambda_{\max 1} = 210$ nm (ϵ , 25 000), $\lambda_{\max 2} = 280$ nm (ϵ , 120); IR 1767, 1718, 1631 and 1222 cm^{-1} ; PMR(CDC₁₃): δ , 1.50, 1.55(*s*, 2CH₃), 1.95(*brs*, vinyl methyl), 2.09(*s*, acetate), 2.62 (*d*, $J = 8$ Hz, H5), 4.85(*AB*, H13a, H13b), 4.99(*d*, $J = 8$ Hz, H6), 5.14(*d*, $J = 9$ Hz, H8), 5.65(*brs*, 1H), 6.12(*brs*, 1H). Glaucolide-C is unstable upon standing, but hydrogenation of the side-chain double bond imparts long-term stability and crystals suitable for an X-ray diffraction investigation were obtained.



A crystal of dimensions 0.50 × 0.15 × 0.65 mm was used to collect intensity data on a Syntex $P2_1$ diffractometer system by the θ - 2θ scanning technique using a variable scan speed and a graphite monochromator (Cu $K\alpha$, $\lambda = 1.54178$ Å). Room-temperature lattice parameters were refined by a least-squares procedure utilizing 15 reflexions whose intensities were measured by a centering routine associated with the Syntex diffractometer. Systematic absences were consistent with space group $P2_12_12_1$.

Crystal data

C₂₁H₂₈O₈, $M_r = 408.45$, orthorhombic, $P2_12_12_1$, $a = 10.367$ (3), $b = 25.121$ (9), $c = 7.986$ (2) Å, $V = 2080$ (1) Å³, $Z = 4$, $d_c = 1.304$ Mg m⁻³.

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Table 1. Atomic positional parameters ($\times 10^4$, $\times 10^3$ for H atoms) and thermal parameters ($\times 10^2$) for dihydroglaucolide-C
$$U_{\text{eq}} = (U_1 U_2 U_3)^{1/3}.$$

	x	y	z	U_{eq} (\AA^2)		x	y	z	U (\AA^2)
C(1)	5451 (2)	5460 (1)	8896 (3)	4.9	H(1a)	457 (3)	532 (1)	913 (4)	5.1
C(2)	6287 (3)	5090 (1)	7919 (4)	5.7	H(2a)	706 (3)	530 (1)	757 (4)	6.0
C(3)	5512 (3)	4801 (1)	6568 (4)	5.2	H(2b)	668 (3)	477 (1)	876 (4)	6.2
C(4)	4692 (2)	5169 (1)	5503 (3)	4.6	H(3a)	488 (3)	456 (1)	703 (3)	4.1
C(5)	3373 (2)	5277 (1)	6106 (3)	4.1	H(3b)	605 (3)	460 (1)	601 (4)	5.1
C(6)	2587 (2)	5763 (1)	5685 (3)	4.3	H(5)	301 (3)	510 (1)	711 (4)	5.3
C(7)	2457 (2)	6161 (1)	7091 (3)	3.8	H(6)	281 (3)	596 (1)	476 (5)	7.5
C(8)	3555 (2)	6516 (1)	7607 (3)	3.9	H(8)	417 (3)	655 (1)	666 (3)	4.5
C(9)	4285 (2)	6359 (1)	9201 (3)	4.7	H(9a)	455 (2)	667 (1)	966 (3)	4.5
C(10)	5509 (2)	6046 (1)	8840 (3)	4.5	H(9b)	370 (3)	617 (1)	987 (3)	4.6
C(11)	1239 (2)	6153 (1)	7618 (3)	4.3	H(13a)	31 (4)	680 (2)	839 (5)	8.0
C(12)	497 (2)	5782 (1)	6574 (4)	5.1	H(13b)	-34 (5)	630 (2)	946 (7)	12.7
C(13)	546 (2)	6451 (1)	8952 (4)	5.7	H(14a)	606 (4)	570 (2)	508 (5)	8.4
C(14)	5400 (3)	5534 (1)	4347 (4)	6.5	H(14b)	583 (5)	540 (2)	346 (6)	10.3
C(15)	6541 (2)	6343 (1)	7918 (4)	5.6	H(14c)	480 (3)	578 (1)	384 (4)	6.9
O(16)	1289 (2)	5572 (1)	5398 (2)	5.6	H(15a)	684 (5)	665 (2)	884 (6)	10.7
O(17)	-628 (2)	5666 (1)	6651 (3)	6.6	H(15b)	729 (4)	609 (1)	759 (5)	7.8
O(18)	3010 (2)	7043 (1)	7910 (2)	4.7	H(15c)	626 (3)	642 (1)	706 (4)	7.3
O(19)	1370 (2)	6539 (1)	10349 (2)	5.9	H(24a)	294 (7)	726 (3)	1212 (11)	14.9
O(20)	6011 (2)	5760 (1)	10265 (2)	6.5	H(24b)	284 (17)	684 (6)	1333 (32)	21.3
O(21)	3574 (2)	4912 (1)	4747 (2)	5.9	H(24c)	169 (7)	721 (3)	1310 (12)	16.3
C(22)	1299 (3)	7018 (1)	11092 (4)	6.3	H(27)	303 (4)	800 (1)	864 (6)	8.0
O(23)	557 (3)	7357 (1)	10654 (3)	7.9	H(28a)	86 (4)	827 (2)	711 (5)	7.6
C(24)	2224 (6)	7066 (2)	12470 (6)	10.8	H(28b)	87 (4)	767 (2)	750 (6)	8.7
C(25)	3345 (2)	7438 (1)	6885 (3)	5.0	H(28c)	129 (4)	797 (2)	570 (6)	8.3
O(26)	4041 (4)	7376 (1)	5723 (3)	9.1	H(29a)	326 (14)	829 (5)	525 (19)	22.8
C(27)	2749 (3)	7960 (1)	7411 (4)	6.0	H(29b)	433 (5)	842 (2)	662 (6)	8.3
C(28)	1332 (4)	7961 (2)	6956 (6)	7.9	H(29c)	322 (5)	876 (2)	665 (7)	11.3
C(29)	3437 (5)	8431 (1)	6667 (8)	9.1					

A periodically monitored reflexion showed no significant crystal deterioration. Of the 2168 independent reflexions measured, 126 had intensities less than $2\sigma(I)$ and were excluded from the refinement. Lorentz and polarization corrections were applied, but no absorption corrections were made.

The direct-methods program *MULTAN* (Germain, Main & Woolfson, 1971) was used to calculate phases for the 400 $|E|$ values greater than 1.28. The phase set with the largest combined figure of merit was selected, and the E map calculated with these phases revealed the positions of 20 nonhydrogen atoms. Alternate least-squares refinements and difference Fourier calculations yielded the coordinates of the nine missing heavy atoms and all H atoms. Least-squares refinement with 2040 reflexions was terminated at $R = 0.048$, where $R = \sum ||F_o| - |F_c|| / \sum |F_o|$, and $R_w = 0.064$. The function minimized in the refinement was $\sum w(|F_o| - |F_c|)^2$ where $w = 1/\sigma(I)$ was determined from counting statistics. H atom thermal parameters were refined isotropically.

A final difference map showed no peak larger than 0.3 e \AA^{-3} and during the final cycle of refinement no shift was greater than 0.2σ . Atomic scattering factors were taken from *International Tables for X-ray*

Crystallography (1974). Atomic positional parameters are given in Table I while interatomic distances, valence angles and torsion angles are presented in Table 2.*

Discussion

Fig. 1 is an *ORTEP* drawing (Johnson, 1965) of dihydroglaucolide-C. It has been assumed that the absolute configuration at C(6) is the same for all germacranolides (Neidle & Rogers, 1972), and the S configuration at C(6) was confirmed for glaucolide-D (Taylor, Watson, Betkouski, Padolina & Mabry, 1976). The chair-chair conformation of the ten-membered ring is the same as that found in glaucolides-D (3) and -E (2) (Gopalakrishna, Adams, Watson, Betkouski & Mabry, 1977) with dihydroglaucolide-C exhibiting a maximum torsion-angle deviation of 12° from the values found in -D and -E. The bond lengths around the

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35572 (18 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. Interatomic distances (Å), valence angles (°) and torsion angles (°) for dihydroglaucolide-C

C(1)–C(2)	1.492 (4)	C(9)–C(10)	1.521 (3)
C(1)–C(10)	1.474 (3)	C(10)–C(15)	1.498 (3)
C(1)–O(20)	1.450 (3)	C(10)–O(20)	1.442 (3)
C(2)–C(3)	1.529 (4)	C(11)–C(12)	1.469 (3)
C(3)–C(4)	1.518 (3)	C(11)–C(13)	1.487 (4)
C(4)–C(5)	1.474 (3)	C(12)–O(16)	1.355 (3)
C(4)–C(14)	1.494 (4)	C(12)–O(17)	1.204 (3)
C(4)–O(21)	1.458 (3)	C(13)–O(19)	1.422 (4)
C(5)–C(6)	1.506 (3)	O(19)–C(22)	1.344 (3)
C(5)–O(21)	1.436 (3)	C(22)–O(23)	1.200 (4)
C(6)–C(7)	1.510 (3)	C(22)–C(24)	1.465 (6)
C(6)–O(16)	1.446 (3)	O(18)–C(25)	1.333 (3)
C(7)–C(8)	1.504 (3)	C(25)–O(26)	1.186 (4)
C(7)–C(11)	1.331 (3)	C(25)–C(27)	1.510 (4)
C(8)–C(9)	1.532 (3)	C(27)–C(28)	1.514 (5)
C(8)–O(18)	1.460 (2)	C(27)–C(29)	1.504 (5)
C(1)–H(1)	1.00 (3)	C(14)–H(14c)	0.96 (3)
C(2)–H(2a)	1.00 (3)	C(15)–H(15a)	1.10 (5)
C(2)–H(2b)	1.12 (3)	C(15)–H(15b)	1.04 (4)
C(3)–H(3a)	0.97 (3)	C(15)–H(15c)	0.76 (3)
C(3)–H(3b)	0.87 (3)	C(24)–H(24a)	0.93 (8)
C(5)–H(5)	0.99 (3)	C(24)–H(24b)	1.10 (21)
C(6)–H(6)	0.92 (4)	C(24)–H(24c)	0.83 (8)
C(8)–H(8)	0.99 (3)	C(27)–H(27)	1.02 (5)
C(9)–H(9a)	0.90 (3)	C(28)–H(28a)	0.92 (4)
C(9)–H(9b)	0.94 (3)	C(28)–H(28b)	0.98 (5)
C(13)–H(13a)	1.02 (4)	C(28)–H(28c)	1.00 (5)
C(13)–H(13b)	1.07 (5)	C(29)–H(29a)	1.20 (14)
C(14)–H(14a)	0.99 (4)	C(29)–H(29b)	0.93 (5)
C(14)–H(14b)	0.90 (5)	C(29)–H(29c)	0.86 (6)
C(1)C(2)C(3)	111.1 (2)	C(1)C(10)O(20)	59.6 (1)
C(2)C(3)C(4)	113.6 (2)	C(1)O(20)C(10)	61.3 (1)
C(3)C(4)C(5)	116.7 (2)	C(10)C(1)O(20)	59.1 (1)
C(3)C(4)C(14)	116.4 (2)	C(10)C(1)C(2)	125.6 (2)
C(3)C(4)O(21)	114.0 (2)	C(2)C(1)O(20)	119.1 (2)
C(5)C(4)C(14)	123.0 (2)	C(15)C(10)O(20)	112.2 (2)
C(5)C(4)O(21)	58.6 (1)	C(7)C(11)C(12)	109.0 (2)
C(14)C(4)O(21)	114.0 (2)	C(7)C(11)C(13)	132.7 (2)
C(6)C(5)O(21)	115.3 (2)	C(12)C(11)C(13)	118.2 (2)
C(4)C(5)C(6)	125.3 (2)	C(11)C(12)O(16)	108.9 (2)
C(4)C(5)O(21)	60.1 (1)	C(11)C(12)O(17)	129.2 (2)
C(5)O(21)C(4)	61.3 (1)	O(16)C(12)O(17)	121.9 (2)
C(5)C(6)C(7)	114.8 (2)	C(12)O(16)C(6)	108.9 (2)
C(5)C(6)O(16)	105.7 (2)	C(11)C(13)O(19)	110.4 (2)
C(7)C(6)O(16)	104.8 (2)	C(13)O(19)C(22)	116.8 (2)
C(6)C(7)C(8)	121.9 (2)	O(19)C(22)O(23)	122.8 (2)
C(6)C(7)C(11)	108.1 (2)	O(19)C(22)C(24)	111.7 (3)
C(8)C(7)C(11)	129.8 (2)	O(23)C(22)C(24)	125.5 (3)
C(7)C(8)C(9)	116.7 (2)	C(8)O(18)C(25)	118.2 (2)
C(7)C(8)O(18)	106.8 (2)	O(18)C(25)O(26)	122.9 (2)
C(9)C(8)O(18)	106.6 (2)	O(18)C(25)C(27)	111.7 (2)
C(8)C(9)C(10)	112.8 (2)	C(27)C(25)O(26)	125.4 (2)
C(9)C(10)C(1)	118.5 (2)	C(25)C(27)C(28)	109.4 (2)
C(9)C(10)C(15)	115.5 (2)	C(25)C(27)C(29)	112.3 (3)
C(9)C(10)O(20)	114.1 (2)	C(28)C(27)C(29)	111.4 (3)
C(1)C(10)C(15)	122.9 (2)		
10–1–2–3	–110.4 (3)	5–6–7–8	74.0 (2)
1–2–3–4	49.4 (3)	6–7–8–9	–102.6 (2)
2–3–4–5	–89.3 (3)	7–8–9–10	96.9 (2)
3–4–5–6	155.5 (2)	8–9–10–1	–95.5 (2)
4–5–6–7	–106.0 (2)	9–10–1–2	151.7 (2)
7–11–12–O(16)	–0.7 (3)	O(16)–6–7–11	5.0 (2)
11–12–O(16)–6	4.0 (2)	6–7–11–12	–2.7 (2)
12–O(16)–6–7	–5.4 (2)		

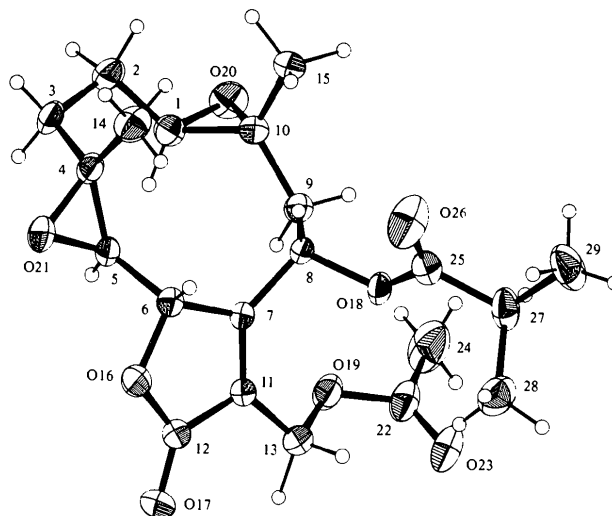
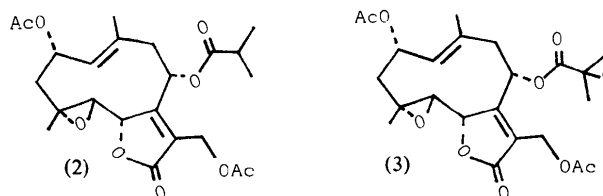


Fig. 1. ORTEP drawing of dihydroglaucolide-C. Thermal ellipsoids are drawn at the 35% probability level. H atoms are represented by spheres of arbitrary size.

ring agree within 3σ with those in the reference compounds except for the C(10)–C(1) bond. The three C=O bonds average 1.196 (9) Å, the three C(sp^2)–O(sp^3) distances average 1.344 (11) Å, the four C–O epoxide distances average 1.447 (10) Å, the two C(sp^3)–C(sp^3) bonds of the epoxide ring average 1.474 (3) Å and the four C(sp^3)–CH₃ distances average 1.503 (9) Å.



The endocyclic double bond at C(7)–C(11) is typical of the glaucolide series of germacranolides and the five-membered γ -lactone ring exhibits a flattened envelope conformation with C(6) being the flap. The shift of the C(11)–C(13) double bond found in most germacranolides to the C(7)–C(11) position in the glaucolide series is responsible for the lack of significant cytotoxic activity of these molecules (Watson, Reinecke & Hitt, 1975 and references therein).

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The Structure of Cholesteryl Laurate at 198 K

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Abstract

Cholesteryl laurate ($C_{39}H_{68}O_2$) at 198 K is monoclinic, space group $P2_1$ with $a = 12.983(3)$, $b = 8.838(1)$, $c = 31.803(4)$ Å, $\beta = 90.41(2)^\circ$ and $Z = 4$. Integrated intensities for 3825 reflections with $I > 2\sigma(I)$ were measured at 198 K, using an automatic diffractometer and graphite-monochromated $Cu K\alpha$ radiation. Atomic coordinates for the 82 non-hydrogen atoms from the cholesteryl laurate room-temperature structure were used as a starting model. Refinement by block-diagonal least-squares methods gave a final R factor of 0.062. In contrast to the room-temperature structure, all atoms are clearly resolved and 127 of the 136 H atoms were experimentally located. The molecules are packed in an antiparallel array in the crystal structure forming monolayers of thickness $d_{(001)} = 31.8$ Å. The central regions of the monolayers are characterized by efficient molecular packing and are separated by interface regions which are more loosely packed. The major differences between the room-temperature and low-temperature structures occur in this interface region. At 298 K the laurate chain of molecule (B) has an almost extended conformation with possible disordering, but at 198 K the (B) chain is distally bent and is well ordered.

Introduction

A series of X-ray crystal structure determinations of cholesteryl esters has been undertaken. These structures are of interest as they may provide models for molecular associations in less ordered lipid systems. At room temperature, the crystal structures of cholesteryl nonanoate (Guerina & Craven, 1979), decanoate (Pattabhi & Craven, 1979), undecanoate (Sawzik & Craven, 1980), and laurate (Dahlén, 1979; Sawzik & Craven, 1979a) are isostructural and have been designated type I monolayers in order to distinguish them from other structure types in the cholesteryl ester series (Guerina & Craven, 1979). A notable feature of type I monolayer structures is the contrast between the molecular close packing within the layer, and the loose packing of the interface region between layers. In the cholesteryl laurate structure at 298 K, large apparent thermal vibrational averaging and possibly conformational disordering obscure atomic details in the interface region. The room-temperature study represents a desirable compromise in that the crystal structure is near a phase transition, yet the number of available X-ray intensity data is adequate for structure determination. We report here the low-temperature (198 K) crystal structure of cholesteryl laurate. This