

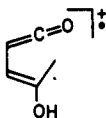
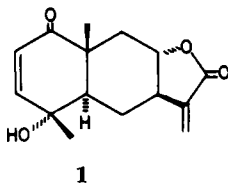
THE MOLECULAR STRUCTURE OF A NEW EUDESMANOLIDE,
SUBCORDATOLIDE B, FROM *CALEA SUBCORDATA*

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ABSTRACT.—The isolation and structure determination of a new eudesmanolide, subcordatolide B (**1**), from *Calea subcordata* is reported. The structure was inferred from nmr and mass spectral data, and the molecular structure of subcordatolide B was determined by single-crystal X-ray diffraction.

In a chemical study of the genus *Calea*, subtribe Galinsoginae of the tribe Heliantheae (Compositae) (1), we have isolated and determined the structure of a new 12,8 α -lactonized eudesmanolide type sesquiterpene lactone from *Calea subcordata* S.F. Blake from the state of Tachira, Venezuela.

A, m/z 98 (100)

RESULTS AND DISCUSSION

SPECTROSCOPIC CHARACTERIZATION.—Column and thin layer chromatographic procedures applied to the crude terpenoid extract of *C. subcordata* provided a colorless, crystalline compound that we named subcordatolide B (**1**), $C_{15}H_{18}O_4$, mp 188.5–189°. The presence of an α -methylene- γ -lactone moiety was indicated by an ir band at 1770 cm^{-1} and further corroborated by three one-proton signals in the pmr spectrum at 6.13 (H-13a), 5.49 (H-13b), and 2.46 (H-7). Pmr signals at 6.66 (H-3) and 5.90 (H-2), together with a strong ir band at 1680 cm^{-1} , suggested the presence of a conjugated cyclohexanone moiety in subcordatolide B (**1**), and the presence of hydroxyl(s) was clearly shown by ir bands at 3595 and 1115 cm^{-1} . Further assignments of the basic skeleton of **1** were deduced from extensive double irradiation experiments, the results being summarized in Table 1. The mass spectrum of **1** gave a parent peak at m/z 262, a base peak at m/z 98, and other intense peaks at m/z 149, 55, and 43. The base peak at m/z 98 was assigned to ion A derived from **1** by a retro-Diels-Alder process.

Structural data obtained by single-crystal X-ray diffraction corroborated the conclusions obtained by spectroscopic analysis.

CRYSTAL STRUCTURE ANALYSIS.—The molecular structure of subcordatolide B, determined by X-ray diffraction, is illustrated in Figure 1. The α -methylene- γ -lactone ring is *trans*-fused to the eudesmane skeleton at C7-C8. The overall conformation of the molecule is given by the torsion angles in Table 2 and may be described in terms of the

TABLE 1. Pmr Parameters^a of Subcordatolide B (1)

H-2	5.90 d(10.0)
H-3	6.66 d(10.0)
H-5	2.23 dd(12.0; 3.0)
H-6a	2.50 ddd(13.0; 3.0; 3.0)
H-6b	1.58 m
H-7	2.46 m
H-8	3.94 ddd(12.0; 12.0; 3.6)
H-9a	2.51 dd(12.0; 3.6)
H-9b	1.77 dd(12.0; 12.0)
H-13a	6.13 d(3.2)
H-13b	5.49 d(3.0)
H-14	1.22 s
H-15	1.40 s

^aSpectrum was obtained at 200 MHz in CDCl₃. TMS was used as internal standard and chemical shifts are recorded in ppm relative to TMS. Signals are designated as follows: s=singlet, d=doublet, m=multiplet. Figures in parentheses are coupling constants on line separation in Hertz.

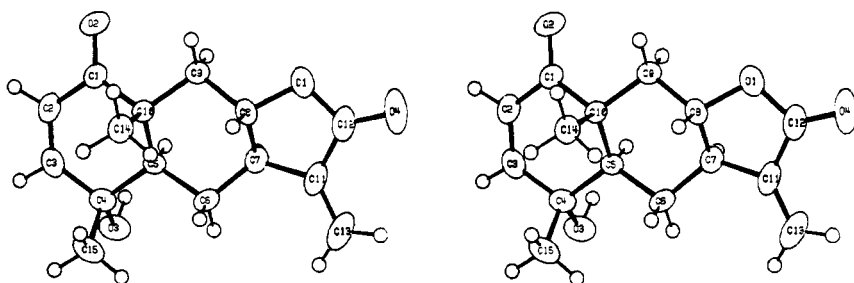


FIGURE 1. Stereoscopic representation of the subcordatolide B molecule.

TABLE 2. Coordinates for Subcordatolide B

Atom	x	y	z
O1	-0.1586(2)	0.3775(2)	0.5701(2)
O2	0.0391(3)	0.8201(2)	0.6173(2)
O3	0.4531(2)	0.5551(2)	0.7860(2)
O4	-0.2391(3)	0.1848(2)	0.5879(2)
C1	0.1502(3)	0.7551(3)	0.6273(2)
C2	0.2934(4)	0.8045(3)	0.6655(2)
C3	0.4072(4)	0.7334(3)	0.6932(2)
C4	0.4070(4)	0.5970(3)	0.6928(2)
C5	0.2447(3)	0.5473(2)	0.6730(2)
C6	0.2398(4)	0.4078(3)	0.6555(2)
C7	0.0730(4)	0.3706(3)	0.6526(2)
C8	-0.0088(3)	0.4380(3)	0.5743(2)
C9	-0.0158(3)	0.5735(3)	0.5929(2)
C10	0.1506(3)	0.6212(2)	0.5971(2)
C11	0.0205(4)	0.2429(3)	0.6328(2)
C12	-0.1369(4)	0.2598(3)	0.5956(2)
C13	0.0914(6)	0.1375(3)	0.6370(3)
C14	0.2219(4)	0.6195(3)	0.4959(2)
C15	0.5318(4)	0.5484(4)	0.6266(3)

conformations of the three fused rings. The six-membered ring containing the unsaturation exhibits torsion angles with approximate local symmetry C_2 . The angle about the double bond is near zero (C1-C2-C3-C4, -1.8°), and the approximate twofold axis bisects the double bond and C5-C10. The saturated six-membered ring has very nearly the chair conformation, with torsion angle magnitudes deviating from 60° by an average of only 3.7° . The lactone ring is distinctly nonplanar (sum of torsion angle magnitudes = 129°) and has nearly the half chair conformation, with the local twofold axis passing through C12 and bisecting C7-C8.

Bond distances are normal, with individual standard deviations 0.003-0.005 Å. Average values for important bond types are 1.316 Å for C=C, 1.215 Å for C=OO, 1.503 Å for C(sp²)-C(sp³), and 1.535 Å for C(sp³)-C(sp³). The only significant intermolecular interaction is a hydrogen bond O3-H . . . O4, with O . . . O distance 2.940(3) Å, H . . . O distance 1.95 Å, and O-H . . . O angle 164° .

Determination of the absolute configuration of subcordatolide B by application of Beecham's rule (2) was attempted. This is based on the correlation of the sign of the Cotton effect (CE) of the $n-\pi^*$ methylene lactone transition near 250 nm and the exocyclic C13=C11-C12=O torsion angle derived from the X-ray data of a methylene lactone (3). In the case of subcordatolide B, the intense negative CE at 230 nm, most likely due to the K-band of the cyclohexenone portion of **1**, washed out the weaker $n-\pi^*$ lactone band not allowing the assignment of its absolute configuration. Therefore, the representation given in Figure 1 remains tentative but was chosen to conform to that found in all sesquiterpene lactones from higher plants (4).

EXPERIMENTAL

C. subcordata was collected on September 12, 1979, in the state of Tachira, Venezuela, 13.3 km from Delicias along the road toward Villa Paez (L. Urbatsch, No. 3427, voucher deposited at Louisiana State University). The air-dried plant material (456 g) was extracted and worked up as previously described (5), providing 16.4 g of crude syrup. The crude terpenoid extract was chromatographed on a silica-gel column with petrol-Me₂CO mixtures of increasing polarity providing 64 fractions of 200 ml each.

Fractions 21-24 gave 40 mg of crude subcordatolide B (**1**). Preparative tlc on silica gel with Me₂CO-CHCl₃ (10:90) as eluent yielded 30 mg of a white powder, which, after recrystallization from CHCl₃, gave 17 mg of pure subcordatolide B (**1**), C₁₅H₁₈O₄, mp 188.5-189°; uv λ max (EtOH) 216 nm (ϵ 8.75 × 10³), 224 nm (ϵ 7.98 × 10³); cd (C, 1.67 × 10⁻⁴, MeOH) [θ]₃₃₀ - 1.73 × 10³, [θ]₂₃₂ - 2.12 × 10⁴, [θ]₂₀₄ + 1.03 × 10⁵; ir ν max (film) 3595 (OH), 1770 (γ-lactone), 1680 (conjugated CO), 1150 cm⁻¹ (tertiary OH); ms 70 eV, *m/z* (rel. int.) 262 (11.5, M⁺), 247 (11.0, M⁺-Me), 244 (2.7, M⁺-H₂O), 234 (11.7, M⁺-CO), 229 (3.4, M⁺-Me-H₂O), 219 (5.3, M⁺-Me-CO), 149 (29.8, C₉H₉O₂), 98 (100.0, A, C₅H₆O₂), 55 (30.5, C₃H₃O), 43 (23.9, CH₃CO).

X-RAY DATA.—A crystal of dimensions 0.24 × 0.29 × 0.52 mm was used for data collection on an Enraf-Nonius CAD4 diffractometer equipped with MoKα radiation (λ = 0.71073 Å) and a graphite monochromator. Crystal data: C₁₅H₁₈O₄, MW = 262.3, orthorhombic space group P2₁2₁2₁, *a* = 8.756(2), *b* = 10.926(3), *c* = 14.020(2) Å, *Z* = 4, *d*_c = 1.299 g/cm³, μ(MoKα) = 0.87 cm⁻¹. Data were collected by ω-2θ scans of variable speed, designed to yield I ≈ 25σ(I) for all significant reflections. One octant of data having 1° < θ < 25° was measured, yielding 1377 unique reflections, of which 1026 had I > 3σ(I), and were used in the refinement. Data reduction included corrections for background, Lorentz, and polarization effects; absorption was negligible.

The structure was solved by direct methods (MULTAN 78) (6) and refined by full matrix, weighted least squares methods. The absolute configuration was chosen to conform to that found in all sesquiterpene lactones from higher plants (4). Nonhydrogen atoms were refined anisotropically, while hydrogen atoms were located in difference maps and included as fixed contributions with isotropic B = 5.0 Å². Convergence was achieved with R = 0.040, R_w = 0.051 based on observed reflections, and residual electron density was less than 0.18e Å⁻³. Coordinates are given in Table 3; anisotropic thermal parameters, bond distances, bond angles, and structure factors are available as supplementary material.

TABLE 3. Selected Torsion Angles of Subcordatolide B

Atom 1	Atom 2	Atom 3	Atom 4	Angle (degree)
C1	C2	C3	C4	-1.8
C2	C3	C4	C5	-10.4
C3	C4	C5	C6	170.8
C4	C5	C6	C7	171.4
C5	C6	C7	C8	59.4
C6	C7	C8	C9	-65.6
C7	C8	C9	C10	61.4
C8	C9	C10	C1	-173.4
C9	C10	C1	C2	160.3
C10	C1	C2	C3	-14.9
C4	C5	C10	C1	-53.3
C3	C4	C5	C10	38.7
C2	C1	C10	C5	40.4
C8	C9	C10	C5	-54.9
C9	C10	C5	C6	54.9
C10	C5	C6	C7	-55.5
C7	C8	O1	C12	-31.1
C8	O1	C12	C11	9.4
O1	C12	C11	C7	16.0
C12	C11	C7	C8	-33.2
C11	C7	C8	O1	39.1
O4	C12	C11	C13	22.0
O2	C1	C2	C3	167.7

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