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SONDERIANIN, A FURANOID DITERPENE FROM *CROTON SONDERIANUS*

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Key Word Index—*Croton sonderianus*; Euphorbiaceae; diterpene; clerodane; sonderianin.

Abstract—From the heartwood of *Croton sonderianus* was isolated a new furanoid diterpene, sonderianin. The structure was elucidated by spectral analysis, X-ray studies and chemical evidence.

INTRODUCTION

The benzene extract of the heartwood of *Croton sonderianus* Muell. Arg. has been shown to have specific activity against *Mycobacterium smegmatis* and *Staphylococcus aureus* (J. D. McChesney and L. A. Mitscher, unpublished results). From this extract was isolated a novel diterpene, sonderianin (**1**), bearing the backbone-rearranged clerodane-type carbon skeleton.

RESULTS AND DISCUSSION

The molecular formula of sonderianin (**1**), $C_{21}H_{26}O_5$, was determined by high resolution MS [$M^{+\cdot}$ obs. 358.1756 (12%), calc. 358.1773]. The IR spectrum revealed the presence of carbonyl groups (γ-lactone, 1760 cm^{-1} and α,β-unsaturated ester, 1710 cm^{-1}), one double bond (1645 cm^{-1}) and one β-substituted furan system (1515 and 880 cm^{-1}) [1,2]. The ^1H NMR spectrum in $CDCl_3$ (270 MHz) showed signals for three furan protons (δ 7.45, H-15; 7.43, H-16; 6.40, H-14), one olefinic proton (δ 6.53, H-3), one tertiary methyl (δ 1.46, Me-18), one secondary methyl (δ 1.02, Me-17), one methoxy group (δ 3.70, MeOCO-19) and one $-CH_2CHOCO$ system (δ 2.40, CH_2-11 and 5.40, H-12). The other assignments for the additional proton signals and their correlations were determined by extensive decoupling experiments (Table 1). The ^{13}C NMR spectrum (Table 1) allowed the assignments of two quaternary carbons, three CH, five CH_2, and confirmed the presence of two methyl groups.

The occurrence of a mono-β-substituted furan moiety, an α,β-unsaturated ester, a γ-lactone and a secondary methyl and analysis of analogous diterpene structures in the literature [1,3–6] made it possible to propose a clerodane-type diterpene structure (**1**).

The multiplet at δ 1.48 (H-8) (^1H NMR spectrum) changed to a pair of doublets (J = 4, 10 Hz) on irradiation of the methyl at 1.02 (Me-17). These J values indicated that the H-8 is axial. The signal at 1.59 appeared as a pair of doublets (J = 4, 10 Hz) and revealed that the H-10 is axial.

The structure proposed for sonderianin (**1**) was confirmed by ^{13}C NMR analysis. Table 1 lists the carbon shifts, assigned by comparative analysis of the proton-noise decoupled and single-frequency off-resonance decoupled spectra, by standard chemical shift theory and comparison with the data reported for other furanoid diterpenes with the clerodane skeleton [1, 3–6].

Catalytic hydrogenation of **1** gave a neutral crystalline hexahydro derivative (mp 169–171°) and an acid octahydrosonderianin, the latter formed by catalytic hydrogenolysis of a γ-lactone allylically situated to a furan ring, a reaction well documented in the literature [7, 8]. In both derivatives, the ^1H NMR spectrum showed the disappearance of the bands at δ 7.45, 7.43, 6.40, 6.53 and 5.40, assigned to the furan, oxymethine and olefinic protons respectively. In their place appeared a four-proton multiplet centred at 3.80. In addition the ^1H NMR of the octahydro derivative presented a broad signal at 10.80 interchangeable by addition of D_2O.

Unequivocal proof of the structure and relative configuration of sonderianin (**1**) was achieved by X-ray crystallographic analysis. The colourless crystals of **1** have the space group $P2_12_12_1$ with a = 7.314, b = 10.481 and c = 24.276Å. Independent data were obtained for 2098 planes of which 975 had $F > 3\sigma(F)$ and were used in the refinement. Intensities were measured using graphite monochromatic CuKα radiation. The structure was solved by the MULTAN method. Table 2 shows angles and interatomic distances (standard deviation in parentheses) related to Fig. 1.

EXPERIMENTAL

Mps are uncorr. ^1H and ^{13}C NMR spectra were recorded at 270 and 25.2 MHz respectively, and chemical shifts (δ ppm) were measured from TMS as internal standard.

Isolation of sonderianin (**1**). Chromatography of the C_6H_6 extract (25 g) on Si gel (125 g) of heartwood of *Croton sonderianus*, collected on Taperoaba-Sobral, Ceará, Brazil, yielded colourless needles of sonderianin (**1**, 800 mg).

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Table 1. NMR spectral data of sonderianin (1) (δ values in ppm, $CDCl_3$, TMS as internal standard)

Carbon	^{1}H NMR (270 MHz) and decoupling experiments	^{13}C NMR (25.2 MHz)
1	1.70–1.90 (Hβ, *m*)	19.7 (*t*)
	2.20–2.49 (Hα, *m*)	
2	2.20–2.49 (2H, *m*)	26.8*(*t*)
3	6.53 (1H, *t*, *J* = 3.0 Hz)	135.3 (*d*)
4	—	142.3 (*s*)
5	—	37.6 (*s*)
6	1.70–1.90 (Hα, *m*)	
	2.46 (Hβ, *m*)	
7	1.18 (Hβ, *m*)	26.5*(*t*)
	2.06 (Hα, *m*)	
8	1.48 (Hα, *m*)	40.4 (*d*)
9	—	51.6 (*s*)
10	1.59 (Hα, *dd*, *J* = 4.0, 10.0 Hz)	52.4 (*d*)
11	2.40 (2H, *d*, *J* = 8.5 Hz)	44.7 (*t*)
12	5.40 (1H, *t*, *J* = 8.5 Hz)	71.6 (*d*)
13	—	125.6 (*s*)
14	6.40 (1H, *m*)	108.0 (*d*)
15	7.45 (1H, *m*)	143.8 (*d*)
16	7.43 (1H, *m*)	139.3 (*d*)
17	1.02 (3H, *d*, *J* = 7.0 Hz)	16.8 (*q*)
18	1.46 (3H, *s*)	19.7 (*q*)
19	—	164.5 (*s*)
20	—	173.0 (*s*)
OMe	3.70 (3H, *s*)	51.2 (*q*)

* Assignments may be interchanged.

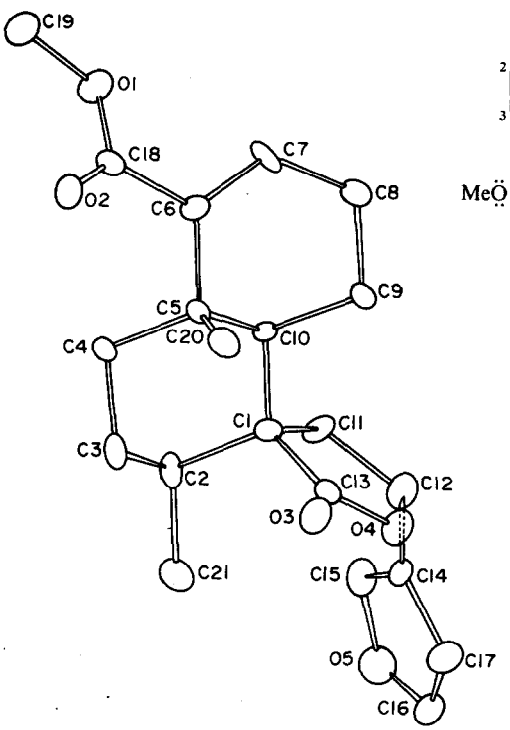
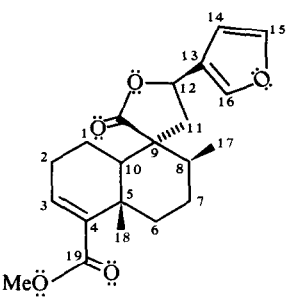
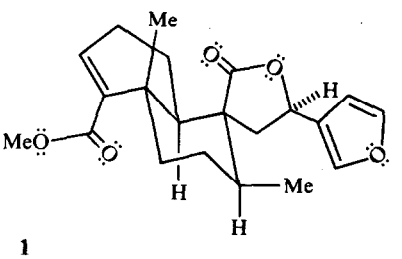


Fig. 1. Stereoscopic view of sonderianin (1).





1

Sonderianin (1) Mp 134–137°; $[\alpha]_D^{25}$ −55.2° (*c* 5.0, $CHCl_3$); ν_{max}^{KBr} cm^{-1}: 3170, 3050, 1760, 1710, 1645, 1515, 1465, 1445, 1285, 1260, 1240, 1180, 1160, 1085, 1035, 1000, 880, and 820; λ_{max}^{MeOH} nm (log ε): 215 (3.87) and 242 sh (2.80). MS *m/e* (rel. int.): 358 (12.2), 327 (17.0), 326 (44.0), 232 (28.2), 204 (20.5), 202 (100.0), 201 (39.2), 200 (77.8), 199 (53.2), 101 (25.6), 95 (16.0, $C_5H_3O_2^{+\cdot}$ and $C_6H_7O^{+}$), 94 (9.1, $C_6H_6O^{+\cdot}$), 81 (14.3, $C_5H_5O^{+}$). Catalytic hydrogenation of sonderianin with Pd/C (10%) in MeOH yielded a white solid, mp 169–171°, $M^{+\cdot}$ = 364 ($C_{21}H_{32}O_5$) and one acid residue $M^{+\cdot}$ = 366 ($C_{21}H_{34}O_5$).

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Table 2. Interatomic distances and angles related to Fig. 1 (standard deviation in parentheses)

At 1	At 2	At 3	d_{12}(Å)	d_{23}(Å)	Angle 1–2–3 (degrees)
C2	C1	C10	1.55(1)	1.57(1)	108.9(7)
C2	C1	C11	1.55(1)	1.55(1)	108.3(7)
C2	C1	C13	1.55(1)	1.48(1)	112.3(7)
C10	C1	C11	1.57(1)	1.55(1)	108.6(6)
C10	C1	C13	1.57(1)	1.48(1)	114.0(6)
C11	C1	C13	1.55(1)	1.48(1)	104.4(6)
C1	C2	C3	1.55(1)	1.52(1)	112.6(7)
C1	C2	C21	1.55(1)	1.58(1)	111.2(7)
C3	C2	C21	1.52(1)	1.58(1)	109.7(7)
C2	C3	C4	1.52(1)	1.55(1)	110.9(7)
C3	C4	C5	1.55(1)	1.58(1)	109.3(7)
C4	C5	C6	1.58(1)	1.52(1)	110.1(7)
C4	C5	C10	1.58(1)	1.55(1)	107.0(6)
C4	C5	C20	1.58(1)	1.54(1)	109.3(7)
C6	C5	C10	1.52(1)	1.55(1)	104.6(6)
C6	C5	C20	1.52(1)	1.54(1)	108.3(7)
C10	C5	C20	1.55(1)	1.54(1)	117.3(7)
C5	C6	C7	1.52(1)	1.31(1)	123.2(9)
C5	C6	C18	1.52(1)	1.51(1)	118.9(8)
C7	C6	C18	1.31(1)	1.51(1)	117.6(8)
C6	C7	C8	1.34(1)	1.50(1)	124.1(8)
C7	C8	C9	1.50(1)	1.57(1)	115.3(8)
C8	C9	C10	1.57(1)	1.58(1)	107.2(7)
C1	C10	C5	1.57(1)	1.55(1)	119.5(7)
C1	C10	C9	1.57(1)	1.58(1)	110.4(6)
C5	C10	C9	1.55(1)	1.58(1)	109.3(6)
C1	C11	C12	1.55(1)	1.59(1)	105.1(7)
C11	C12	C14	1.59(1)	1.49(1)	112.9(8)
C11	C12	C4	1.59(1)	1.44(1)	104.5(7)
C14	C12	C4	1.49(1)	1.44(1)	108.7(7)
C1	C13	O3	1.48(1)	1.22(1)	128.9(8)
C1	C13	O4	1.48(1)	1.22(1)	112.5(7)
O3	C13	O4	1.22(1)	1.35(1)	118.6(8)
C12	C14	C15	1.49(1)	1.38(1)	128.5(9)
C12	C14	C17	1.49(1)	1.44(1)	125.6(9)
C15	C14	C17	1.38(1)	1.44(1)	105.8(8)
C14	C15	O5	1.38(1)	1.37(1)	109.6(9)
C17	C16	O5	1.33(1)	1.39(1)	110.3(1.0)
C14	C17	C16	1.44(1)	1.33(1)	107.3(1.1)
C6	C18	O1	1.51(1)	1.31(1)	111.9(8)
C6	C18	O2	1.51(1)	1.19(1)	124.4(9)
O1	C18	O2	1.31(1)	1.19(1)	123.7(9)
C18	O1	C19	1.31(1)	1.47(1)	117.1(9)
C12	O4	C13	1.44(1)	1.35(1)	113.4(7)
C15	O5	C16	1.37(1)	1.39(1)	106.9(9)

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