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12-HYDROXYHARDWICKIC ACID AND SONDERIANIAL, *NEO*-CLERODANES FROM *CROTON SONDERIANUS*

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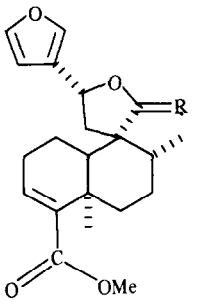
Key Word Index—*Croton sonderianus*; Euphorbiaceae; 'marmeleiro preto'; diterpenes; *neo*-clerodane.

Abstract—Two new *neo*-clerodane diterpenes, 12-hydroxyhardwickic acid and sonderianial have been characterized from the hexane extract of the roots of *Croton sonderianus*. Their structures were established by a combination of spectroscopic analysis and chemical interconversions. They are likely biogenetic precursors of the known sonderianin, a major constituent of *Croton sonderianus* heartwood.

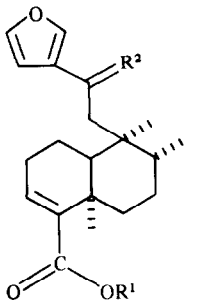
INTRODUCTION

Croton sonderianus Muell. Arg. (Euphorbiaceae), marmeleiro preto, is the most abundant and widespread shrub in the northeast of Brazil. Field observations document that it occurs at a density of four to six million plants per hectare. It is a shrub, rarely more than 12 feet tall, and possesses a characteristic essential oil with a turpentine-like odour. The oil is present in all parts of the plant from the roots to the leaves and is in an average concentration of 1.0% of the dry weight.

Preliminary phytochemical studies of the heartwood of *C. sonderianus* revealed the presence of a new clerodane [1], sonderianin (**1**) and two new cleisthantane diterpenes in addition to the known coumarin, scopoletin [2].



	R
1	O
4	αH,βOH



	R^1	R^2
2	H	H
2a	Me	H
3	H	H,OH
3a	Me	H,OH
3b	Me	H,OAc
3c	Me	O

GCMS analysis of the essential oil allowed the characterization of 19 mono-and sesquiterpenes, and six fatty acids as principal components of the glycerides of the fatty oil from the seeds [3].

We prepared a hexane extract of the roots of the plant and found it to possess antimicrobial activity when tested *in vitro* [4]. Fractionation of the extract gave sonderianin [**1**] and hardwickic acid (**2**) [5], and two new *neo*-clerodanes 12-hydroxyhardwickic acid (**3**) and sonderianial (**4**).

RESULTS AND DISCUSSION

Fractionation of the antimicrobial hexane extract of the roots of the Brazilian shrub, *Croton sonderianus* Muell. Arg. has led to the characterization of the known *neo*-clerodanes sonderianin (**1**) hardwickic acid (**2**), and two new substances whose structures suggest they may be biogenetic links between hardwickic acid and sonderianin.

The hexane extract was partitioned into neutral and acidic portions by treatment with aqueous base. The acidic portion was coarsely fractionated by rapid chromatography on silica. An intermediately polar fraction was again chromatographed on silica and finally on Florisil to yield pure hardwickic acid. A somewhat more polar fraction from the initial chromatography of the acid fraction of the extract could not be effectively separated by a similar sequence of chromatography. Instead, formation of the esters of the fraction with excess diazomethane in ether gave a mixture of esters. Dissolution of the mixture in ethanol and treatment with 20% aqueous potassium hydrogen at room temperature yielded, upon extraction of the alkali solution with hexane, a homogenous diterpene ester, **3a**, in the hexane phase. The ester present in the hexane phase showed $[M]^+$ (*m/z*) 346 ($C_{21}H_{30}O_4$), and IR absorptions of 3480 (O-H), 1710 (C=O), 1630 (C=C), 1500 and 875 (furan ring), 1250 (O-Me), and 1050 (C-OH) cm^{-1}. Its ^1H NMR spectrum showed clearly a multiplet at δ7.50 for 2H, a triplet at δ6.73 (1H), a multiplet at 6.47 (1H), a double doublet centred at δ4.87

(1H, $J=4.5$ and 9.0 Hz), an ester methyl at δ3.70, two quaternary methyls at δ1.30 and 0.75, and a tertiary methyl at δ0.78 (3H, *d*, $J=6.0$ Hz). These results suggested an ester-alcohol structure with a M_r only 16 mass units higher than that of methylhardwickiate (**2a**). This is suggestive of an extra oxygen on the hardwickiate skeleton with no extra unsaturation. The presence of only one absorption at δ7.50 for both 'α' protons in the furan ring (H-15 and H-16), as in sonderianin (**1**) is suggestive for the placement of hydroxyl group at the carbon adjacent to the furan ring, C-12, which was in agreement with the observed doublet of doublets at δ4.87 for H-12 as it is an asymmetric carbon adjacent to a methylene.

Comparison of the ^{13}C NMR spectrum of the alcohol-ester, **3a**, with the one of methylhardwickiate (**2a**) offered strong evidence for that structural proposition. The ester alcohol showed all 21 signals in its PND spectrum. The major differences between the two spectra were the presence of the peak at δ63.0 (doublet in the SFORD spectrum) assigned to C-12 in the new material that was not observed for methylhardwickiate (**2a**) and the disappearance of one CH_2 absorption at *ca* δ18.3 in **2a** which was not present in **3a**. This is consistent with the deshielding α-effect of a hydroxyl group to C-12. Additionally, the deshielding β-effect at C-11 can be observed by comparing the chemical shift of C-11 in methylhardwickiate (either δ39.0 or 36.1) and that of **3a** which falls at δ46.0. All the other absorptions are in similar positions in both spectra.

Acetylation of **3a** in acetic anhydride–pyridine yielded an acetate derivative, **3b**, $[M]^+$ (*m/z*) 388 ($C_{23}H_{32}O_5$), showing no hydroxy absorption in its IR but two carbonyl absorptions at 1735 and 1710 cm^{-1} besides the expected absorptions for the carbon–carbon double bond (1635 cm^{-1}), and furan ring (1500 and 875 cm^{-1}). The ^{1}H NMR of the acetate showed in addition to the expected absorptions for the furan and carbon–carbon double bond hydrogens, a triplet like absorption at δ5.90 (1H, $J=7.0$ Hz) very similar to the one present in the ^{1}H NMR of (**1**) and in agreement with the expected deshielding effect of acetylation on H-12.

Final structural proof for the placement of the hydroxyl group at C-12 in the methylhardwickiate structure came from the facile oxidation of **3a** by manganese dioxide. The oxidation product, **3c**, showed no hydroxyl but rather an extra carbonyl absorption at 1665 cm^{-1} for the conjugated ketone adjacent to the furan ring. Its ^{1}H NMR was in agreement with the structural change. No double doublet a δ4.87 was observed and the furan proton absorptions changed to δ8.03 (1H, *br s*, H-16), 7.45 (1H, *m* H-15) and 6.80 (1H, *br s*, H-14). Besides the large deshielding effect on H-16, bonded to the carbon in conjugation with the carbonyl and H-14 near to the carbonyl, the ^{1}H NMR of the ketone showed an additional singlet at δ2.70 with integration for two protons which is assigned to H-11. The ^{13}C NMR spectrum of the ketone showed an extra absorption at δ193.8 compatible with a conjugated carbonyl and the disappearance of the carbinolic carbon at δ63.0 present in **3a**.

Analysis of the fragmentation pattern of the alcohol-ester, **3a**, in the mass spectrometer, was also in agreement with the structural proposition. The fragmentation peaks of *m/z* (rel. int.) 219 (78), 234 (20), particularly the base peak at 97 (100) must originate from the 12-hydroxyfuran structural moiety. The peak with *m/z* 97, when present, is not an intense peak for most clerodane diterpenes such as **2**, except for those bearing an oxygen at C-12 and becomes the base peak or nearly the base peak in compounds like **3a**, with an hydroxy at C-12. In agreement with this assignment was the presence of the base peak with *m/z* 139 (100) for the acetate derivative whose structure can be proposed as the corresponding acetate form of ion showing *m/z* 97.

Coarse fractionation of the neutral portion of the extract yielded 11 fractions. Fraction nine was carefully chromatographed on a column of silica for TLC to yield a white solid showing mp 130–133°, $[M]^+$ (*m/z*) 360 ($C_{21}H_{28}O_5$), $[\alpha]_D^{23}$ −85.8° ($CHCl_3$; *c* 7.3), Ir ν_{max}^{KBr} 3400 (O-H), 1705 (C=O), 1500 and 880 cm^{-1}. Its ^{1}H NMR spectrum showed only one absorption at δ7.50 for both α-hydrogens characteristic of a β-substituted furan ring attached to a carbon bearing an oxygenated function similar to **1** or **3** or their derivatives. Additionally, it showed a vinyl hydrogen in a double bond conjugated to a carboxymethyl at δ6.82, the β-furan hydrogen at δ6.57, a singlet at δ5.40 (1H, H-20) close to a double doublet centred at δ5.25 (1H, $J=7.0$ and 11.0 Hz), a methoxy absorption at δ3.70 (–OMe), an absorption at δ2.65, exchangeable with D_2O, a quaternary methyl at δ1.30 and a tertiary methyl at δ0.96. Comparison of the ^{1}H NMR spectra of **4** and sonderianin (**1**) suggested by the appearance of the extra singlet at δ5.40 and the exchangeable absorption at δ2.65 that **4**, was the cyclic hemiacetal form of sonderianin (**1**). This was in accord with the presence of only the conjugated carboxymethyl absorption in the IR at 1705 cm^{-1} and the disappearance of δ-lactone absorption at 1740 cm^{-1} for sonderianin. Comparison of the ^{13}C NMR spectrum of **4**, to the one obtained from sonderianin **1** was indeed in agreement with that structural proposition. The disappearance of the δ-lactone carbonyl absorption at δ173.0 for sonderianin and the appearance of the absorption at δ100.2 (doublet in the SFORD spectrum) for the cyclic hemiacetal carbon agreed with the structural change.

Final proof for the structure of **4**, came through its facile oxidation by manganese dioxide. Recrystallization of the oxidation product gave a substance which was identical to sonderianin by mixture melting point determination. TLC behaviour and spectral comparison.

A close inspection of the ^{13}C NMR spectra of the two compounds shows that besides the two major absorption differences between **4** and **1** discussed above, a doublet in the SFORD spectrum appearing at δ40.4 for **1**, and at δ44.6 for **4**, assigned to C-8 was also different. As all the other absorptions are in similar positions in both spectra, perhaps one can gain some information about the stereochemistry of the hemiacetal hydroxyl. Since C-8 and not C-10 (the latter appearing in both spectra at δ52.4) had its absorption position modified, the hydroxyl group should be directed toward C-8 where the stereochemical interaction of the hydroxyl at C-20 with C-8 is similar to the 1,3-axial hydroxy interaction of cyclohexanols. Thus the new diterpene, named sonderianial, may be represented by the structure **4**.

EXPERIMENTAL

Extraction and isolation. The entire roots of *Croton sonderianus* Muell. Arg. were used in this study. The whole plant was collected in Sobral, Ceara, Brazil and was identified by Dr. Afranio G. Fernandes. The voucher specimens representing the

collection are deposited at herbarium of the Departmento de Botanica, Universidade Federal do Ceara', Fortaleza-CE, 60.021 Brazil.

The roots of 'marmeleiro preto' were air-dried at room temp. and ground. The ground material (1.6 kg dry weight) was then extracted by percolation with hexane. The hexane solution upon evapn under red. pres. at 40° yielded 85.0 g of a yellowish resinous extract which showed antimicrobial activity [4].

Sonderianin (**1**). Upon standing at room temp. for a short time, a crystalline ppt. began to form in the hexane extract. A first crop of sonderianin was obtained by filtration of the pptd material and recrystallization from hexane to yield 2.75 g mp 133–135° (lit. mp 134–137°, $[\alpha]_D^{23}$ −45.5° ($CHCl_3$; *c* 5.0). IR ν_{max}^{KBr} cm^{-1}: 1755, 1705, 1635, 1500, 870; EIMS (probe) 70 eV; 358 $[M]^+$ (11), 325 $[M-MeOH]^+$ (77), 311 $[M-MeOH-Me]^+$ (15), 232 (82), 187 (46), 159 (68), 105 (100), 95 (91), 94 (75); ^1H NMR (90 MHz, $CDCl_3$): δ7.48 (2H, *m*, H-15, H-16), 6.50 (1H, *t*, *J* = 3.0 Hz, H-3), 6.40 (1H, *m*, H-14), 5.40 (1H, *t*, *J* = 8.5 Hz, H-12), 3.68 (3H, *s*, OMe), 1.40 (3H, *s*, H-19), 1.00 (3H, *d*, *J* = 7.0 Hz, H-17); ^{13}C NMR (15 MHz, $CDCl_3$): δ173.0 (*s*, C-20), 164.5 (*s*, C-18), 143.8 (*d*, C-15), 142.3 (*s*, C-4), 139.3 (*d*, C-16), 135.3 (*d*, C-3), 125.6 (*s*, C-13), 108.0 (*d*, C-14), 71.6 (*d*, C-12), 52.4 (*d*, C-10), 51.6 (*s*, C-9), 51.2 (*q*, OMe), 4.4.7 (*t*, C-11), 40.4 (*d*, C-8), 37.6 (*s*, C-5), 35.2 (*t*, C-6), 26.8 (*t*, C-2), 26.5 (*t*, C-7), 19.7 (*q*, C-19), 19.7 (*t*, C-1), 16.8 (*q*, C-17). Compared to an authentic sample [1].

Partitioning of hexane extract: acid and neutral fractions. The resinous extract remaining after the recovery of sonderianin was solubilized in 200 ml of C_6H_6 and stirred for 30 min with 150 ml of 20% NaOH–H_2O soln. The aq. basic phase was recovered and the treatment repeated twice more with fresh base soln. The remaining C_6H_6 phase was washed with dist. H_2O, dried over Na_2SO_4 and evapd under red. pres. to yield 25.0 g of a clear yellowish oily fraction designated the neutral fraction. This was sealed under dry N_2 and stored at 5°. The combined aq alkali solns were neutralized in the cold with conc. HCl by dropwise addition. The neutralized soln was extracted ×3 with 150 ml portions of C_6H_6. The C_6H_6 extracts were combined, dried over Na_2SO_4 and evapd under red. pres. to yield 47.8 g of a clear, brownish resinous fraction designated the acid fraction. Both fractions showed antimicrobial activity *in vitro*. The crude acid fraction was coarsely fractionated in the following manner: 30 g of the acidic portion was absorbed onto 30 g of silica gel (70–230 mesh) and that packed onto the top of a silica gel (150 g) layer in a large diameter column. Elution of the column with a mixture of hexane – EtOAc – HOAc (35:5:4:10) gave 20 fractions of 100 ml. Four additional 150 ml fractions were obtained by elution with a mixture of hexane–EtOAc–MeOH (4:3:3). Comparison of the collected fractions by TLC and ^1H NMR allowed us to combine them into 8 pooled fractions, F1/1 through F1/8.

Hardwickic acid (**2**). Fraction F1/3 (5.7 g) was absorbed onto 10 g of silica gel and chromatographed over 100 g of silica gel for TLC (column diameter 5.5 cm). The column was eluted with hexane–$CHCl_3$ (1:1) and 35, 20 ml, fractions collected and then the column was washed with $CHCl_3$–MeOH 5%. The fractions were combined after TLC and ^1H NMR comparison to give seven fractions, F2/1 through F2/7. The fraction F2/5 (670 mg) was absorbed onto 6.7 g of Florisil for TLC and chromatographed over 50 g of Florisil for TLC (column diameter 2.5 cm). elution with $CHCl_3$ gave 34, 20 ml, fractions. From fractions 16 to 20, 152 mg of homogeneous hardwickic acid was obtained in solid form, mp 88–89° which upon attempted recrystallization could never be recovered crystalline. $[\alpha]_D^{23}$ −85.5° ($CHCl_3$; *c* 0.9); IR ν_{max}^{film} cm^{-1}: 3500–3100 (sh), 2650–2500 (sh), 1685, 1500, 1260, 1030, 880; UV λ_{max}^{MeOH} nm (log ε): 213 (3.83); EIMS (probe) 70 eV, *m/z* (rel. int.); 316 $[M]^+$ (5.3), 301 $[M-Me]^+$ (1.1), 283 $[M-Me-H_2O]^+$ (5.1), 221 (26), 203 (22), 175 (20), 125 (90), 95 (100), 81 (70); ^1H NMR (90 MHz, $CDCl_3$): δ12.1 (1H, *br s*, acid H), 7.37 (1H, *m*, H-15), 7.23 (1H, *br s*, H-16), 6.90 (1H, *t*, *J* = 3.0 Hz, H-3), 6.25 (1H, *m*, H-14), 127 (3H, *s*, H-19), 0.85 (3H, *d*, *J* = 6.0 Hz, H-17), 0.80 (3H, *s*, H-20); ^{13}C NMR (15 MHz, $CDCl_3$): δ173.1 (*s*, C-18), 143.5 (*d*, C-16), 142.8 (*s*, C-4), 139.4 (*d*, C-15), 138.1 (*d*, C-3), 126.5 (*s*, C-13), 111.8 (*d*, C-14), 47.6 (*d*, C-10), 39.7 (*s*, C-9), 39.5 (*t*, C-11), 38.3 (*s*, C-5), 37.0 (*t*, C-6), 36.6 (*d*, C-8), 28.0 (*t*, C-2), 27.1 (*t*, C-7), 20.9 (*q*, C-19), 18.6 (*t*, C-1, C-2), 18.2 (*q*, C-20), 16.2 (*q*, C-17).

The same Florisil column was 'washed' with 250 ml of $CHCl_3$–MeOH 10% followed by 250 ml of $CHCl_3$ and then used to recycle the combined fractions 21 to 34. Elution with $CHCl_3$–MeOH 1% yielded 391 mg more of hardwickic acid.

Hardwickic acid methyl ester (**2a**). Hardwickic acid (**2**). 120 mg, was diluted in 15 ml of Et_2O and methylated with excess CH_2N_2. Filtration of the reaction residue dissolved in Et_2O over a small column of silica gel yielded 110 mg of **2a**, as an oil $[\alpha]_D^{23}$ −104° ($CHCl_3$:*c* 1.1), UV λ_{max}^{MeOH} nm (log ε): 214 (3.38): $CD\Delta\varepsilon_{239}$ −4.43; (MeOH; *c* 14.0); IR ν_{max}^{neat} cm^{-1}: 1710, 1630, 1500, 1250, 1230, 875; EIMS (probe) 70 eV *m/z* (rel. int.): 330 $[M]^+$ (2.5), 315 $[M-Me]^+$ (2.5), 315 $[M-Me]^+$ (0.4), 299 $[M-OMe]^+$ (2.3) 283 $[M-Me-MeOH]^+$ (8.6), 235 $[M-95]^+$ (24), 203 (38), 139 (100), 96 (55), ^1H NMR (90 MHz, $CDCl_3$): δ7.37 (1H, *m*, H-15), 7.21 (1H, *br s*, H-16), 6.50 (1H, *t*, *J* = 3.5 Hz, H-3), 6.26 (1H, *m*, H-14), 3.65 (3H, *s*, OMe), 1.25 (3H, *s*, H-19), 0.85 (3H, *d*, *J* = 6.0 Hz, H-17), 0.78 (3H, *s*, H-20); ^{13}C NMR ($CDCl_3$): δ167.8 (*s*, C-18), 142.7 (*d*, C-16), 142.7 (*s*, C-4), 138.5 (*d*, C-15), 136.7 (*d*, C-3), 125.7 (*s*, C-13), 111.0 (*d*, C-14), 51.1 (*q*, OMe), 46.8 (*d*, C-10), 39.0 (*s*, C-9), 38.9 (*t*, C-11), 37.7 (*s*, C-5), 36.5 (*d*, C-8), 36.1 (*t*, C-6), 27.5 (*t*, C-2), 27.1 (*t*, C-7), 20.5 (*q*, C-19), 18.3 (*q*, C-20), 18.3 (*t*, C-1), 17.1 (*t*, C-12), 16.0 (*q*, C-17). Comparison made with authentic (−)-methylhardwickiate, kindly provided by Dr Suk Dev [5]. Compound **2a** and (−)-methylhardwickiate were identical in all respects.

12-*Hydroxyhardwickic acid methyl ester* (**3a**). A portion of fraction F1/6, 2 g, was dissolved in 256 ml of Et_2O and methylated with excess CH_2N_2. The methylation product was chromatographed over silica gel with elution with 10% EtOAc in hexane. Similar fractions (TLC comparison) were combined to produce two major fractions: F3/3 (two components by TLC), 360 mg, and F3/4, 1.01 g. Attempted chromatographic separation of fraction F3/3 (310 mg) over Florisil was without success. All fractions were recombined (300 mg), dissolved in 15 ml of EtOH and mixed with 4 ml of 20% aq. KOH. To this mixture H_2O was added until the soln became slightly turbid (3.5 ml) and then the mixture stirred overnight at room temp. The basic reaction mixture was then extracted with 10 ml of hexane and twice with 10 ml of CCl_4. As the hexane and CCl_4 phases were similar by TLC, they were combined, dried over Na_2SO_4, and evapd under red. pres. to yield 122 mg of 12-hydroxyhardwickic acid methyl ester (**3a**) as an oil, homogeneous by TLC and GC, $[\alpha]_D^{23}$ −80.9° ($CHCl_3$; *c* 7.3), IR ν_{max}^{neat} cm^{-1}: 3480, 3070, 1710, 1640, 1500, 1430, 1250, 1020, 875; EIMS (probe) 70 eV *m/z* (rel. int.): 346 $[M]^+$ (1.7), 328 $[M-H_2O]^+$ (3.1), 313 $[M-H_2O-Me]^+$ (5.2), 299 $[M-MeOH-Me]^+$ 281 (5), 234 (20), 219 (78), 175 (44), 139 (64), 97 (100); ^1H NMR (90 MHz, $CDCl_3$): δ7.50 (2H, *m*, H-15), (H-16), 6.73 (1H, *t*, *J* = 3.0 Hz, H-3), 6.47 (1H, *m*, H-14), 4.87 (1H, *dd*, *J* = 4.5, 9.0 Hz, H-12), 3.70 (3H, *s*, OMe), 1.30 (3H, *s*, H-19), 0.78 (3H, *d*, *J* = 6.0 Hz, H-17), 0.75 (3H, *s*, H-20); ^{13}C NMR (15 MHz, $CDCl_3$): δ167.9 (*s*, C-18), 143.4 (*d*, C-16), 142.2 (*s*, C-4), 138.3 (*d*, C-15), 137.7 (*d*, C-3), 131.6 (*s*, C-13), 108.5 (*d*, C-14), 63.0 (*d*, C-12), 51.0 (*q*, OMe), 47.2 (*d*, C-10), 46.0 (*t*, C-11), 39.5 (*s*, C-9) 37.8 (*s*, C-5), 36.8 (*d*, C-8), 35.8 (*t*, C-6), 27.4 (*t*, C-7), 27.1 (*t*, C-2), 20.9 (*q*, C-19), 18.4 (*t*, C-1), 17.9 (*q*, C-20), 16.0 (*q*, C-17).

12-*Acetoxyhardwickic acid methyl ester* (**3b**). 12-hydroxyhardwickic acid methyl ester, 20 mg, was dissolved in pyridine

(1 ml). To the stirred soln was added Ac_2O (0.5 ml) and the reaction stirred overnight at room temp. The reaction mixture was diluted with 10 ml of cold H_2O, stirred for 1 hr at room temp., and extracted (3 × 10 ml) with CCl_4. The combined organic layers were washed with cold 6 M HCl (2 × 10 ml) satd brine and dried over Na_2SO_4. Evapn of the solvent at red. pres. and filtration of the residue through a small column of silica (1 g) with hexane–$CHCl_3$ (1:1) as solvent gave 18 mg of an oil, acetate (**3b**); IR ν_{max}^{neat} cm^{-1}: 1735, 1710, 1630, 1500, 1435, 1370, 1240, 1025, 880; EIMS (probe) 70 eV *m/z* (rel. int.): 388 $[M]^+$ (0.1), 357 $[M-OMe]^+$ (0.05), 328 $[M-HOAc]^+$, 313 $[M-HOAc-Me]^+$ 234 (46), 219 (50), 203 (43), 139 (100); ^1H NMR (90 MHz, $CDCl_3$): δ7.45 (2H, *m*, H-15, H-16), 6.68 (1H, *t*, J = 3.0 Hz, H-3), 6.43 (1H, *m*, H-14), 5.90 (1H, *t*, J = 7.0 Hz, H-12), 3.67 (3H, *s*, OMe), 1.95 (3H, *s*, MeCO), 1.25 (3H, *s*, H-19), 0.77 (3H, *s*, H-20), 0.76 (3H, *d*, J = 6.0 Hz, H-17).

12-Oxo-hardwickic acid methyl ester (**3c**). 12-Hydroxyhardwickic acid methyl ester, 70 mg, was dissolved in 10 ml of hexane and stirred overnight with 700 mg of activated MnO_2. The MnO_2 was filtered and the filtrate passed over a small silica gel column to yield 30 mg of homogeneous ketone, **3c**, as an oil; IR ν_{max}^{neat} cm^{-1}: 3070, 1710, 1665, 1450, 1435, 1250, 1230, 1160, 875; EIMS (probe) 70 eV *m/z* (rel. int.): 334 $[M]^+$ (1.3), 313 $[M-OMe]^+$ (2.4), 284 $[M-HCO_2Me]^+$ (1.8), 234 $[M-CH_2$=C-furyl$]^+$ (19.4), 219 $[234-Me]^+$ (100), 187 (30.0), 175 (12.0), 105 (25.0), 95 (30); ^1H NMR (90 MHz, CCl_4): δ8.03 (1H, *br s*, H-16), 7.45 (1H, *m*, H-15), 6.80 (1H, *br s*, H-14), 6.55 (1H, *t*, J = 3.0 Hz, H-3), 3.65 (3H, *s*, OMe), 2.70 (2H, *br s*, H-11), 1.25 (3H, *s*, H-19), 0.90 (3H, *d*, J = 7.0 Hz, H-17), 0.85 (3H, *s*, H-20); ^{13}C NMR (15 MHz, C_6D_6: δ193.8 (*s*, C-12), 166.7 (*s*, C-18), 146.8 (*d*, C-16), 144.2 (*d*, C-15), 142.3 (*s*, C-4), 137.5 (*d*, C-3), 130.4 (*s*, C-13), 109.2 (*d*, C-14), 50.7 (*q*, OMe), 47.6 (*d*, C-10), 47.6 (*t*, C-11), 42.4 (*s*, C-9), 38.4 (*c*, D-8), 37.6 (*s*, C-5), 35.8 (*t*, C-6), 27.7 (*t*, C-7), 27.2 (*t*, C-2), 20.9 (*q*, C-19), 19.3 (*t*, C-1), 17.7 (*q*, C-20), 16.7 (*q*, C-17).

Isolation of sonderianial (**4**). A portion of the neutral fraction, 25 g, was dissolved in 150 ml of hexane and refrigerated for 12 hr. Filtration and recrystallization of the solid material from hexane gave 1.2 g of sonderianin (**1**). The mother liquors were concd and a 20 g portion was absorbed onto 20 g of silica gel, and chromatographed over 100 g of silica gel (230–400 mesh) using initially hexane and later hexane–MeOH 5% as eluents. Similar fractions (TLC) were combined and designated F4/1–F4/11.

Chromatography of F4/9, 2.27 g, on a column of silica gel for TLC (150 g) and elution with hexane–$CHCl_3$ (1:1) yielded a solid material which was recrystallized from hexane to yield 130 mg of sonderianial (**4**) as colourless plates, mp. 130–133°, $[\alpha]_D^{23}$ −85.8° ($CHCl_3$; *c* 7.3): IR ν_{max}^{KBr} cm^{-1}: 3390, 1705, 1625, 1500, 1430, 1250, 1230, 1025, 800; EIMS (probe) 70 eV *m/z* (rel. int.): 360 $[M]^+$ (0.1), 343 $[M-OH]^+$ (0.2), 329 $[M-OMe]^+$ (2), 314 $[M-MeOH-Me]^+$ (10) 239 (1); ^1H NMR (90 MHz, $CDCl_3$): δ7.60 (2H, *m*, H-15, H-16), 6.82 (1H, *m*, H-e), 6.57 (1H, *m*, H-14), 5.40 (1H, *s*, H-20), 5.25 (1H, *dd*, J = 7.0, 11.0 MHz, H-12), 3.76 (3H, *s*, OMe), 2.70 (1H, *br s*, OH), 1.30 (3H, *s*, H-19), 0.96 (3H, *d*, J = 7.0 Hz, H-17); ^{13}C NMR (15 MHz, $CDCl_3$: δ167.8 (*s*, C-18), 143.2 (*d*, C-15), 141.4 (*s*, C-4), 139.1 (*d*, C-16), 138.0 (*d*, C-3), 125.6 (*s*, C-13), 109.0 (*d*, C-14), 100.2 (*d*, C-20), 70.0 (*d*, C-12), 53.5 (*s*, C-9), 52.4 (*d*, C-10), 51.1 (*q*, OMe), 44.6 (*d*, C-8), 44.1 (*t*, C-11), 38.6 (*s*, C-5), 36.5 (*t*, C-6), 29.0 (*t*, C-7, C-2), 21.4 (*t*, C-1), 20.8 (*q*, C-19), 18.1 (*q*, C-17).

Oxidation of sonderianial; formation of sonderianin (**1**). Sonderianial (**4**), 15 mg, was dissolved in 4 ml of hexane and stirred with 200 mg of activated MnO_2 for 48 hr at room temp. The reaction mixture was filtered through a small layer of silica (1 g) to separate the MnO_2 and the column washed with $CHCl_3$. Evapn of $CHCl_3$ gave a white solid, 9 mg, identical to authentic sonderianin (**1**).

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