Phytochemistry, Vol. 21, No. 10, pp. 2571–2574, 1982.
Printed in Great Britain.

0031-9422/82/102571-04$03.00/0

TWO CLEISTANTHANE TYPE DITERPENES FROM *CROTON SONDERIANUS*

AFRÂNIO A. CRAVEIRO and EDILBERTO R. SILVEIRA

Universidade Federal do Ceará, Departamento de Química Orgânica e Inorgânica, Centro de Ciências, Caixa Postal, 935, 60.000 Fortaleza, Ceará, Brazil

(*Received* 16 *December* 1981)

Key Word Index—*Croton sonderianus*; Euphorbiaceae; diterpene; clerodane; scopoletin; cleistanthane; 3,4-seco-cleistanthane; ^{13}C NMR.

Abstract—Sonderianol (12-hydroxy-3-oxo-cleistanth-8, 11, 13, 15-tetraene) and 3, 4-seco-sonderianol (methyl 12-hydroxy-3, 4-seco-cleistanth-8, 11, 13, 15, 18(4)-penten-3-oate), two new diterpenes with cleistanthane skeletons, were isolated from heartwood of *Croton sonderianus*.

INTRODUCTION

A benzene extract of *Croton sonderianus* Muell. Arg. was shown to have antibiotic activity against *Micobacterium smegmatis* (ATCC no. 14468) and *Staphylococcus aureus* (ATCC no. 6538).* Previous work on this extract had yielded a new furan diterpene, sonderianin (**1**), having a rearranged clerodane type carbon skeleton [1].

This paper reports on the isolation from the benzene extract of a coumarin, scopoletin (**2**), and two new diterpenes with the cleistanthane type carbon skeleton, sonderianol (**3**) and 3,4-seco-sonderianol (**4**).

RESULTS AND DISCUSSION

Additional chromatographic work on the benzene extract of heartwood afforded scopoletin (**2**), sonderianol (**3**) and 3, 4-seco-sonderianol (**4**).

The first of the above compounds was obtained as a crystalline yellow substance (mp 202–205°) which fluoresced in UV. Comparison of its physical and spectroscopic data with analogous data in the literature [2, 3] indicated it to be 6-methoxy-7-hydroxycoumarin (**2**) i.e. scopoletin (lit. mp 204°).

Sonderianol (**3**) was a crystalline yellow substance (mp 169–172°) showing 20 spectral lines in the uncoupled ^{13}C NMR spectrum (Table 1); its single frequency off resonance decoupled spectrum (SFORD) allowed the assignment of eight quaternary carbons (C), three methynic carbons (CH), five methylenic carbons (CH_2) and four methyl groups, suggesting the partial formula $C_{20}H_{25}$. The mass spectrum had, $[M]^+$ at *m/z* 298 giving strong support for a diterpene of molecular formula $C_{20}H_{26}O_2$; furthermore the base peak at *m/z* 125 was indicative of a tricyclic diterpene skeleton with an aromatic phenolic system in ring C and a carbonyl at C-3 [4].

Further analysis of the ^{13}C NMR spectrum allowed the assignment of the carbonyl located in the six-membered ring (δ219.7, C-3). This assignment was confirmed by strong absorption at ν_{max} 1695 cm^{-1} in the IR spectrum. The ^1H NMR spectrum (Table 1) was in agreement with the above observations and contained a singlet at δ6.68 (1H, H-11) assigned to one aromatic proton located *ortho* to an oxygenated function. The presence of a penta-substituted aromatic ring in sonderianol was confirmed by absorption at ν_{max} 870 cm^{-1} in the IR spectrum. Furthermore, the ^1H NMR spectrum contained a broad band at δ5.14 (1H, –OH) shifted by addition of D_2O which was assigned to a phenolic hydroxyl group. This was confirmed by intense absorption at ν_{max} 3400 cm^{-1} in the IR. Three sets of peaks centred at δ6.60 (1H, *dd*, $J = 10$ and 17 Hz, H-15), 5.55 (1H, *dd*, $J = 2$ and 10 Hz, H-16), and 5.23 (1H, *dd*, $J = 2$ and 17 Hz, H-16) were characteristic of an AMX terminal vinyl system. Four sharp singlets each of which integrated for three protons, were assigned to four methyl groups; one located in the aromatic ring (δ2.20, Me-17), one located at a quaternary carbon (δ1.29, Me-20) and two gem-methyls (δ1.12, Me-19 and δ1.15, Me-18).

Comparison with the spectral data of analogous substances [5–7] as well as matching of ^{13}C NMR experimental data with theoretical values calculated using the additivity rule [9] (Table 2), suggested structure **3**. Confirmation of this structure and assignment of the stereochemistry of the chiral centres [C-5 and C-10 $[\alpha]_D$-72° (EtOH; *c* 0.25)], was possible by hydrogenation of the vinyl function and formation of the methyl ether. The final product was identical by TLC, mixed mp and spectral data with an authentic sample of 12-methoxy-3-oxo-cleistanth-8, 11, 13-triene (**5**) [5–7].

3, 4-Seco-sonderianol (**4**) was a methyl ester, showing 21 spectral lines in the ^{13}C NMR spectrum (Table 1). SFORD analysis revealed the presence of eight carbons without hydrogen substitution (C), three CH, six CH_2 and four methyl carbons. From these data it was possible to infer a partial formula of $C_{21}H_{27}$. Mass spectral analysis gave $[M]^+$ at *m/z* 328 suggesting an empirical formula $C_{21}H_{28}O_3$. The ^1H NMR spectrum (Table 1) displayed signals at δ6.74

*Antibiotic experiments carried out by Dr. J. D. McChesney, Department of Pharmacognosy, University of Mississippi.

Table 1. ^{13}C NMR and ^{1}H NMR spectral data for compounds **3** and **4**

Carbon no.	^{13}C NMR ($CDCl_3$, 25.2 MHz)		^{1}H NMR ($CDCl_3$, 60 MHz)	
	3	**4**	**3**	**4**
1	38.2 *t*	34.8 *t*	1.66–1.94 *m*	1.79–2.06 *m*
2	34.9 *t*	28.6 *t*	2.36–2.82 *m*	2.29–2.84 *m*
3	219.7 *s*	175.3 *s*	—	—
4	47.6 *s*	141.3* *s*	—	—
5	50.5 *d*	46.6 *d*	2.36–2.82 *m*	2.06–2.27 *m*
6	20.5 *t*	24.9 *t*	1.66–1.94 *m*	1.79–2.06 *m*
7	29.4 *t*	29.6 *t*	2.36–2.82 *m*	2.29–2.84 *m*
8	125.7 *s*	127.0 *s*	—	—
9	140.1 *s*	139.1* *s*	—	—
10	37.6 *s*	41.2 *s*	—	—
11	111.2 *d*	111.6 *d*	6.68 *s*	6.74 *s*
12	153.4 *s*	152.6 *s*	—	—
13	120.8 *s*	120.0 *s*	—	—
14	146.6 *s*	146.9 *s*	—	—
15	136.2 *d*	135.5 *d*	6.60 *dd*(10, 17)†	6.61 *dd*(11, 18)
16	120.5 *t*	119.6 *t*	5.55 *dd*(2, 10)	5.52 *dd*(2, 11)
			5.23 *dd*(2, 17)	5.17 *dd*(2, 18)
17	13.1 *q*	12.9 *q*	2.20 *s*	2.20 *s*
18	24.7 *q*	114.3 *t*	1.15 *s*	4.94 *m*
				4.70 *m*
19	26.9 *q*	22.8 *q*	1.12 *s*	1.78 *s*
20	21.2 *q*	27.9 *q*	1.29 *s*	1.22 *s*
21	—	51.7 *q*	—	3.64 *s*
			5.14 *s*‡	6.50 *s*‡

*The assignments can be interchanged.
†*J* (Hz).
‡Change with D_2O.

Table 2. Theoretical δ values calculated for the ^{13}C NMR absorptions of the aromatic carbons in structure **3** and comparison with observed δ values. ($\Delta = \delta$ theoretical $- \delta$ observed)

Carbon no.	Basic value	Contribution of the substituents located on position: C-1	*Ortho*	*Meta*	*Para*	δ Calculated value	δ Observed value[5–7]	Δ
C-8	128.5	+8.9	(−1.1) + (0.7)	−0.1	−7.3	129.6	125.7	+3.8
C-9	128.5	+8.9	+0.7	(+0.4) + (+1.4)	−2.9	137.0	140.1	−3.1
C-11	128.5	—	(−12.7) + (+0.7)	2(−0.1)	−1.2	115.1	111.2	+3.9
C-12	128.5	+26.9	+0.7	(−0.1) + (+0.4)	−2.9	153.5	153.4	+0.1
C-13	128.5	+8.9	(−1.1) + (−12.7)	−0.1	−2.9	120.6	120.8	−0.2
C-14	128.5	+13.1	2(+0.7)	(+1.4) + (−0.1)	—	144.3	146.6	−2.3

(1H, *s*, H-11), 6.61 (1H, *dd*, $J = 11$, 18 Hz), 6.50 (1H, *br*, shifted in D_2O, –OH), 5.52 (1H, *dd*, $J = 2$, 11 Hz, H-16), 5.17 (1H, *dd*, $J = 2$, 18 Hz, H-16), 2.20 (3H, *s*, Me-17) and 1.22 (3H, *s*, H-20) analogous to sonderianol (see Table 1). An additional signal at δ 3.64 (3H, s, –OMe) was assigned to a methoxy function, and signals at δ4.94 (1H, *br s*, H-18), 4.70 (1H, *br s*, H-18) and 1.78 (3H, *s*, Me-19) were related to an ABX_3 system in an isopropenyl group. ^{13}C NMR lines at δ152.6, 146.9, 141.3 or 139.1, 127.0, 120.0, 135.5, 111.6, 129.9, 29.6, 27.9 and 12.9 were very similar to the penta-substituted aromatic ring in sonderianol (see Table 1). The remaining signals at δ51.7, 141.3 or 139.1, 114.3 and 22.8 were in agreement with A ring opening in the cleistanthane skeleton of sonderianol and suggested for 3, 4-seco-sonderianol the structure of a 3,4-seco-cleistanthanic methyl ester (**4**). This hypothesis was strongly supported by the known photochemical opening of the A ring in diterpenes with a 3-oxo function [10, 11] (Fig. 1). Further evidence for this structure was obtained by hydrogenation, methylation and hydrolysis of 3, 4-seco-sonderianol and spectrometric analysis of the derivatives thus obtained.

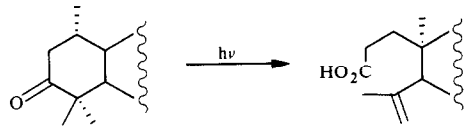
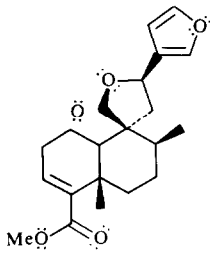
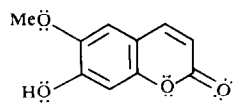


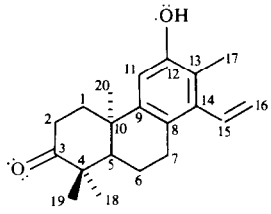
Fig. 1.



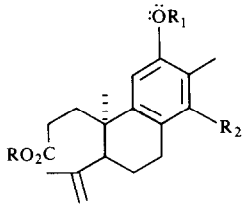
1

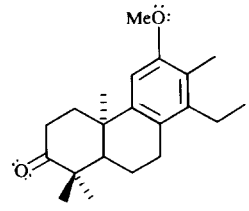


2



3





5

	R	R_1	R_2
4	-Me	-H	$-CH=CH_2$
6	-Me	-Me	$-CH=CH_2$
7	-H	H	$-CH=CH_2$

EXPERIMENTAL

Mps are uncorr. ^1H and ^{13}C NMR spectra were recorded at 60 and 25.2 MHz respectively, with TMS as int. standard.

Isolation of scopoletin (**2**), *sonderianol* (**3**) *and* 3, 4-*seco-sonderianol* (**4**). Chromatography of the C_6H_6 extract (25 g) of 1.15 kg of heartwood of *Croton sonderianus*, on Si gel (125 g) yielded in the fraction eluted with hexane, sonderianin (**1**)[1], and pale-yellow needles of scopoletin (**2**) (30 mg), mp 202–205°, lit. 204° [2, 3].

Chromatography of the fraction eluted with $CHCl_3$ yielded yellow needles of senderianol (**3**) (60 mg), and 3, 4-seco-sonderianol (**4**) (300 mg) as a green wax.

Sonderianol (**3**). Mp 169–172°; ν_{max}^{KBr} cm^{-1}: 3400, 3150, 3030, 3000, 2980, 2940, 1695, 1640, 1600, 1480, 1430, 1420, 1400, 1350, 1310, 1290, 1245, 1180, 1160, 1130, 1120, 1110, 1040, 1025, 950, 930, and 870; MS *m/z* (rel. int.): 298 $[M]^+$ (93), 283(7), 255(8), 241(50), 197(79), 185(60), 173(46), 147(39), 145(31), 125(69), 115(40), 91(36), 83(33), 55(60) and 43(100).

O-*Methyl dihydrosonderianol.* Sonderianol was treated with Me_2SO_4, in the usual manner followed by posterior hydrogenation in Pd–C 10%MeOH, under pressure, to give a white solid identical by mmp (112–113°), TLC, ^1H NMR and IR spectral data to an authentic sample of 12-hydroxy-33-oxo-cleistanth-8-11, 13-triene (**5**) [7], IR ν_{max}^{KBr} cm^{-1}: 3010, 2890, 1695, 1600, 1460, 1375, 1290, 1270, 1200, 1160, 1110, 1085, 1075 and 840; MS *m/z* (rel. int.): 314 $[M]^+$ (54), 299(39), 285(4), 271(3), 257(49), 243(17), 229(21), 213(50), 189(45), 187(37), 163(62), 159(22), 141(30), 125(100), 115(37), 91(37), 83(53), 69(39) and 55(41); ^1H NMR(60 MHz, $CDCl_3$): δ6.60 (1H, *s*, H-11), 3.78 (3H, *s*, –OMe), 2.83–2.47 (7H, *m*), 2.19(3H, *s*, H-17), 1.90–1.62(4H, *m*), 1.30(3H, *s*, H-20), and 1.13(9H, *m*, H-16, H-18, and H-19).

3, 4-*Seco-sonderianol* (**4**). Green wax; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3450, 3110, 3050, 2875, 1715, 1640, 1600, 1445, 1405, 1400, 1385, 1310, 1270, 1200, 1120, 1035, 1000, 935, 905, 890, and 765; MS *m/z* (rel. int.): 328$[M]^+$, (31), 313(5), 297(7), 285(80), 259(11), 253(31), 241(82), 227(16), 213(93), 199(100), 185(85), 171(52), 157(30), 141(34), 128(42), 115(57), 91(32), 77(23), 69(30), 55(59), and 41(75).

O-Methyl-3, 4-*seco-sonderianol.* Compound **4** was treated with Me_2SO_4, by the usual method, yielding 12-*O*-methyl-3, 4-seco-sonderianol (**6**), colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3130, 3050, 2870, 1740, 1640, 1595, 1460, 1440, 1330, 1305, 1280, 1260, 1195, 1170, 1120, and 1060; MS *m/z* (rel. int.): 342$[M]^+$ (32), 327(3), 311(4), 299(5), 273(25), 267(20), 255(90), 241(19), 227(100), 213(86), 199(72), 185(43), 165(30), 153(33), 141(39), 128(42), 115(59), 91(39), 77(22), 73(12), 59(21), and 42(24); ^1H NMR (60 MHz, CCl_4): δ6.55(1H, *s*, H-11), 6.50 (1H, *dd*, J = 10, 17 Hz, H-15), 5.40(1H, *dd*, J = 2,10 Hz, H-16), 5.01(1H, *dd*, J = 2, 17 Hz, H-16), 4.85(1H, *br s*, ABX_3 system, H-18), 4.61 (1H, *br s*, ABX_3 system, H-18), 3.72(3H, *s*, ϕ-OMe), 3.43(3H, *s*, O=C-OMe), 2.07(3H, *s*, H-17), 1.77(3H, *s*, H-19), and 1.20(3H, *s*, H-20); ^{13}C NMR (25.2 MHz, $CDCl_3$, SFORD): δ 34.8 (*t*, C-1), 28.5(*t*, C-2), 174.1(*s*, C-3), 140.7(*s*, C-4 C-9), 46.7(*d*, C-5), 24.8(*t*, C-6), 29.5(*t*, C-7), 126.9 (*s*, C-8), 138.7(*s*, C-9, or C-4), 41.4(*s*, C-10), 107.0(*d*, C-11), 156.2(*s*, C-12), 122.1(*s*, C-13), 146.6(*s*, C-14), 135.4 (*d*, C-15), 119.3 (*t*, C-16), 13.0(*q*, C-17), 114.2(*t*, C-18), 23.4(*q*, C-19), 27.9(*q*, C-20), 51.1(*q*, O=C-OMe), and 55.4(*q*, ϕ-OMe).

3, 4-*Seco-sonderianic acid.* Compound **4** was refluxed in EtOH–KOH yielding 3,4-seco-sonderianic acid as a colourless gum (**6**); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3450, 3110, 3000, 2900, 2650, 1700, 1630, 1585, 1420, 1190, 1100, 1020, 920, 890, and 745; ^1H NMR (60 MHz, CCl_4): δ7.88(1H, *br s*, disappeared with D_2O, O=C-OH), 6.70(1H, *s*, H-11), 6.60(1H, *dd* J = 12, 17Hz, H-15), 5.53(1H, *dd*, J = 2, 12 Hz, H-16), 5.15(1H, *dd*, J = 2, 17Hz, H-16), 4.97(1H, *br s*, ABX_3 system, H-18), 4.72(1H, *br s* ABX_3 system H-18), 2.20(3H, *s*, H-17), 1.77(3H, *s*, H-19), 1.22(3H, *s*, H-20); MS *m/z* (rel. int.): 314$[M]^+$ (87), 299(65), 285(8), 271(6), 257(80) 243(30), 228(36), 213(86), 187(49), 163(77), 149(100), 141(30), 125(91) 115(31), 91(20), 83(23), 69(10) and 57(19).

Tetrahydro-3, 4-*seco-sonderianol.* Compound **4** was hydrogenated in Pd–C 10% MeOH, under pressure to give the respective tetrahydro derivative; ^1H NMR (60 MHz, CCl_4): δ6.68(1H, *s*, H-11), 3.62(3H, *s*, O=C-OMe), 2.40–2.90(7H, *m*), 2.20(3H, *s*, H-17), 1.75–2.10(5H, *m*), 1.22(3H, *s*, H-20), and 0.85–1.00(9H, *m*, H-16, H-18, and H-19); MS *m/z*(rel. int.): 332$[M]^+$ (06), 301(04), 287(03), 255(10), 245(50), 215(35), 203(45), 188(100), 175(100), 159(60), 147(40), 128(38), 119(100), 107(50), 91(70), and 81(52).

Acknowledgements—This work was supported by Conselho Nacional de Desenvolvimento Científico e Technológico (CNPq), Financiadora de Estudos e Projetos (FINEP), and Coordenadoria do Aperfeiçoamento de Pessoal de Nível Superior (CAPES). We are indebted to Dr. K. H. Pegel (Chemistry Department, Natal University, Durban, South Africa) for an authentic sample of **5**, and to Dr. H. E. Gottlieb (The Weizmann Institute of Science, Israel) for recording the ^{13}C NMR spectrum.

REFERENCES

1. Craveiro, A. A., Silveira, E. R., Braz Filho, R. and Mascarenhas, Y. P. (1981) *Phytochemistry* **20**, 852.
2. Pouchert, C. J. and Campbell, J. R. (1974) in *The Aldrich Library of NMR Spectra.*
3. Pouchert, C. J. (1975) in *The Aldrich Library of Infrared Spectra*, 2nd edn.
4. Enzell, C. R. and Ryhage, R. (1967) *Ark. Kemi* **27**, 213.
5. McGarry, E. J., Pegel, K. H., Phillips, L. and Waight, E. S. (1969) *J. Chem. Soc. Chem. Commun.* **17**, 1074.
6. Candy, H. A., Pakshong, J. M. and Pegel, K. H. (1970) *J. Chem. Soc. C* 2536.
7. McGarry, E. J., Pegel, K. H., Phillips. L. and Waight, E. S. (1971) *J. Chem. Soc. C* 904.
8. Gunasekera, S. P., Cordell, G. A. and Farnsworth, N. R. (1979) *J. Nat. Prod.* **42**, 658.
9. Levy, G. C., Lichter, R. L. and Nelson, G. L. (1980) *Carbon-13 Nuclear Magnetic Resonance Spectroscopy* 2nd edn, p. 111. John Wiley, New York.
10. Arigoni, D., Barton, D. H. R., Bernasconi, R., Djerassi, C., Mills, J. S. and Wolff, R. E. (1960) *J. Chem. Soc.* 1900.
11. Whitham, G. H. (1960) *J. Chem. Soc.* 2016.