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ALKALOIDS AND AN ACETYLENIC LACTONE FROM THE STEM BARK OF *SAPRANTHUS PALANGA**

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Key Word Index—*Sapranthus palanga*; Annonaceae; acetylenic lactone; sapranthin; alkaloids; liriodenine; 9*S*-sebiferine.

Abstract—In addition to the known alkaloids 9*S*-sebiferine and liriodenine the stem bark of *Sapranthus palanga* has yielded the novel acetylenic lactone sapranthin. Primarily on the basis of spectral data sapranthin has been identified as 3-(hexadeca-11,15-diena-7,9-diynyl)-4-hydroxy-5-methyltetrahydrofuran-2-one.

INTRODUCTION

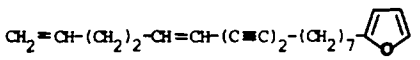
The genus *Sapranthus* Seem. occurs in Mexico and Central America and is characterized by species with large dark-coloured flowers emitting a carrion-like odour [2–4]. *Sapranthus palanga* R. E. Freis is a medium sized tree found in the deciduous forests of Costa Rica. In the only previous study reported [5] the leaves were found to be devoid of condensed tannin but contained traces of alkaloids. As far as we can ascertain there have been no serious phytochemical analyses of this or any other species of the genus to date.

RESULTS AND DISCUSSION

On standing a petrol extract of the stem bark yielded a colourless crystalline solid more of which was obtained by CC of the supernatant over silica gel. This compound, to which we assign the trivial name sapranthin, was obtained in a total yield of 0.06%. It was optically active and analysed for $C_{21}H_{28}O_3$ by high resolution mass spectrometry. The UV spectrum was characterized by a series of five maxima between 227 and 281 nm, typical of an acetylenic chromophore [6, 7]. The presence of an acetylenic moiety was also suggested by the compound's sensitivity to daylight, which resulted in the formation of a violet insoluble material [8].

The IR spectrum revealed bands at 3450 and 1740 cm^{-1} indicative of hydroxy and lactone carbonyl functions. Acetylation yielded a monoacetate (1780 and 1740 cm^{-1}) suggesting the presence of a single hydroxyl moiety. In the high resolution mass spectra a major ion at m/z 128 $[C_6H_8O_3]^+$ was found to contain all three oxygen atoms, requiring that the compound contained a terminal oxygenated section linked to an unsaturated hydrocarbon chain.

The only previous report of acetylenes in the Annonaceae was for 16 related compounds, typified by 1, from the roots of *Alphonsea ventricosa* [7]. A close examination of the high-field ^1H NMR spectrum of sapranthin and its monoacetate (Table 1) revealed the presence of the same terminal $CH_2{=}CH{-}(CH_2)_2{-}CH{=}CH{-}(C{\equiv}C)_2$ moiety, with the internal double bond *trans*-substituted, as had been found in 1 and three of the other *Alphonsea* acetylenes. The other major feature of the ^1H NMR spectrum was a series of four signals which were linked by decoupling experiments. These consisted of a secondary methyl group, two oxy-



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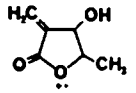

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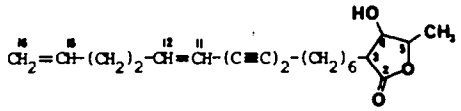

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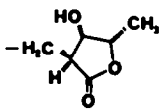

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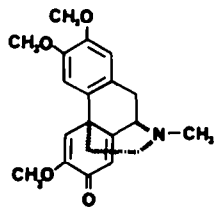

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*Part 21 in the series "Chemistry of the Annonaceae". For Part 20 see ref. [1].

Table 1. ^{1}H NMR chemical shifts for 3 and its acetate (coupling constants given in brackets) and ^{13}C NMR chemical shifts for 3

Carbon number	^{1}H 3	^{1}H 3-Ac	^{13}C 3
2	—	—	176.4
3	2.54 *dt* (7.3, 1.5)	2.65 *dt* (8.0, 5.7)	48.4
4	3.86 *dd* (7.1, 1.5)	4.92 *dd* (5.7, 4.4)	80.1*
5	4.20 *dq* (7.1, 6.3)	4.40 *dq* (6.6, 4.4)	78.7*
5-Me	1.46 *d* (6.3)	1.46 *d* (6.6)	18.1
1′	1.81–1.87 *m*	1.80–2.10 *m*	†
2′–5′	1.40–1.50 *m*	1.40–1.50 *m*	†
6′	2.10–2.31 *m*	2.10–2.31 *m*	†
7′–10′	—	—	‡
11′	5.51 *d* (15.9)	5.51 *d* (15.9)	115.2
12′	6.27 *dt* (15.9, 6.9)	6.27 *dt* (15.9, 6.8)	137.3
13′–14′	2.10–2.31 *m*	2.10–2.31 *m*	†
15′	5.77 *m*	5.77 *m*	146.9
16′	5.00 *dd* (17.0, 1.5)	5.00 *m*	108.9
	5.07 *dd* (10.8, 1.5)	5.07 *m*	
Ac		2.11 *s*	

^{1}H NMR spectra run at 360 MHz.
*Interchangeable.
†Eight triplets at δ32.5, 32.3, 28.8, 28.4, 28.2, 27.9, 26.3, 19.3.
‡Four singlets at δ83.5, 73.8, 72.9, 62.2.

methine protons and a further deshielded proton (δ2.54) which showed coupling to one of the oxymethine protons and to the equivalent protons of a methylene group. The resonance position of this proton further suggested the presence of an α-carbonyl moiety and thus the occurrence of these functions in a substituted tetrahydrofuran-2-one system, which would also account for the *m/z* 128 fragment (**2**) in the mass spectrum.

Linkage of the acetylenic moiety to **2** through a methylene chain gives the final structure **3** for sapranthin. An analysis of the ^{13}C NMR spectrum (Table 1) and the mass spectrum fully support the proposed structure. To date it has not been possible to unambiguously assign the relative stereochemistry of the substituents on the tetrahydrofuran nucleus. The relatively large coupling constant between H-5 and H-4 suggests that they are eclipsed and that the methyl and hydroxyl substituents are therefore *cis*. By contrast the coupling constant between H-4 and H-3 is small, suggesting a dihedral angle of *ca* 120°, as would be found if the two protons were *trans*. The relationship between H-5 and H-4 is supported by a nuclear Overhauser experiment which revealed no enhancement of H-4 on irradiation of the methyl signal, indicating their *trans* relationship. Using these arguments the relative stereochemistry of the substituents on the tetrahydrofuran can tentatively be depicted as in **4**.

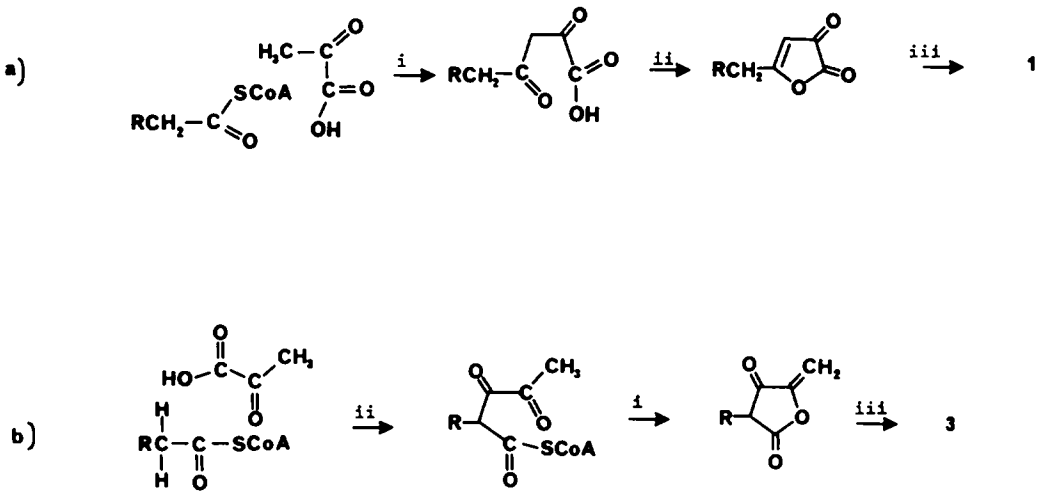
Gopinath *et al.* [7] suggest that the *Alphonsea* acetylenes are formed from combination of a C_{18} unit with a C_3 pyruvate group through a single linkage involving terminal carbons of both compounds (Scheme 1a). The same pathway is probably valid for sapranthin, but in this case coupling of the C_{18} and pyruvate precursors has taken a different course, involving two linkages (Scheme 1b).

Two alkaloids were obtained from the basic fraction of a methanol extract. The oxoaporphine liriodenine, the commonest alkaloid in the Annonaceae [9], was readily identified by direct comparison with authentic material. The second proved to be the unusual morphinandienone 9*S*-sebiferine (**5**), previously reported in the Annonaceae only from *Duguetia obovata* [10] and *Polyalthia cauliflora* var. *beccarii* [11]. Identity was again confirmed by comparison with authentic material.

EXPERIMENTAL

Mps uncorr. UV: EtOH. IR: KCl discs. ^{1}H NMR: run in $CDCl_3$ (field strength in text); ^{13}C NMR run in $CDCl_3$ at 90.56 MHz, TMS as int. standard. EIMS run at 70 eV at elevated temp. Petrol refers to bp 40–60° fraction.

Plant material. Stem bark and leaves were collected from



Scheme 1. Possible biosynthetic routes to the acetylenic compounds of the Annonaceae. (i) CoASH; (ii) $-H_2O$; (iii) reduction.

vouchered trees found in the Santa Rosa National Park, Costa Rica [4].

Isolation of compounds. Powdered stem bark (500 g) was extracted by Soxhlet successively with petrol, $CHCl_3$ and MeOH. On standing the petrol extract yielded a ppt of **3** (250 mg). The supernatant was concd and subjected to CC over silica gel. Elution with toluene–EtOAc (17:3) gave sitosterol (80 mg); further elution with 20% EtOAc gave more **3** (50 mg). The MeOH extract was concd, ppted with HCl, filtered, the filtrate adjusted to pH 9 with NH_3 soln and then extracted into $CHCl_3$. The $CHCl_3$ fraction was concd and subjected to CC over silica gel. Elution with 6% MeOH in $CHCl_3$ gave liriodenine (20 mg). Elution with 10% MeOH gave impure **5** which was then purified by centrifugal prep. TLC (silica gel; $CHCl_3$–MeOH, 23:2) to give **5** (100 mg).

Sapranthin (**3**). Needles from petrol, mp 88–90°, $[\alpha]_D^{20}$ −30° (*c* 0.01; $CHCl_3$). Found: $[M]^+$ 328.2068; $C_{21}H_{28}O_3$ requires 328.2038. UV λ_{max} nm (log ε): 227 (3.59), 238 (3.82), 250 (4.10), 264 (4.21), 281 (4.14). IR ν_{max} cm^{-1}: 3450 (OH), 3080 ($CH=CH_2$), 2230 (C≡C), 1740 (C=O), 1640 ($C=CH_2$), 1060. ^1H NMR and ^{13}C NMR: see Table 1. EIMS *m/z* (rel. int.): 328 $[M]^+$ (5), 185 $[C_{14}H_{17}]$ (11), 171 $[C_{13}H_{15}]^+$ (34), 157 $[C_{12}H_{13}]^+$ (45), 145 $[C_{11}H_{13}]^+$ (58), 144 $[C_{11}H_{12}]^+$ (73), 143 $[C_{11}H_{11}]^+$ (71), 129 $[C_{10}H_9]^+$ (100), 128 $[C_6H_8O_3]^+$ (1), 111 $[C_6H_7O_2]^+$ (7), 99 $[C_5H_7O_2]^+$ (12). *Sapranthin acetate.* Compound **3** (40 mg) dissolved in pyridine (5 ml) was treated with Ac_2O (1 ml) at room temp. for 24 hr. After normal work-up and purification by centrifugal prep. TLC (silica gel, toluene–EtOAc–HOAc, 8:2:1) the acetate (35 mg) was obtained as a brown oil. Found: $[M]^+$ 370.2131; $C_{22}H_{30}O_4$ requires 370.2144. IR ν_{max} cm^{-1}: 1780, 1740. ^1H NMR: see Table 1.

Liriodenine. Yellow needles from $CHCl_3$, mp 275–277° (lit. [12] 275–276°). Found: $[M]^+$ 275.0562; $C_{17}H_9NO_3$ requires 275.0582. Identical with an authentic sample [13] by UV, IR, NMR, EIMS.

9*S*-*Sebiferine* (**5**). Brown amorphous solid, $[\alpha]_D^{20}$ + 13° (*c* 0.3; $CHCl_3$) (lit. [10] + 13°). Found: $[M]^+$ 341.1606; $C_{20}H_{23}NO_4$ requires 341.1541. UV λ_{max} nm: 243, 287. IR ν_{max} cm^{-1}: 3400, 1660, 1640, 1620, 1500. ^1H NMR (250 MHz): δ 1.90 (2H, *m*, H-15), 2.47 (3H, *s*, NMe), 2.60 (1H, *dd*, *J* = 6.4, 2.9 Hz, H-16), 3.06 (1H, *dd*, *J* = 17.7, 6.6 Hz, H-10α), 3.40 (1H, *dd*, *J* = 17.7 Hz, H-10β), 3.70 (1H, *d*, *J* = 6.6 Hz, H-9), 3.81 (3H, *s*, 6-OMe), 3.86, 3.89 (2 × 3H, 2 × *s*, 3-OMe and 8-OMe), 6.33, 6.37 (2 × 1H, 2 × *s*, H-1 and H-8), 6.64 (1H, *s*, H-4), 6.82 (1H, *s*, H-5). EIMS *m/z* (rel. int.): 341 $[M]^+$ (100), 340 (17), 326 $[M-Me]^+$ (21), 313 $[M-CO]^+$ (18), 312 (11), 298 (33), 282 (16).

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REFERENCES

1. Muhammad, I., Waterman, P. G. and Thomas, D. W. (1986) *Fitoterapia* **57**, 58.
2. Fries, R. E. (1959) in *Die Naturlichen Pflanzenfamilien* (Engler, A. and Prantl, K., eds) 2nd edn, Vol. 17aII. Dunker & Humblot, Berlin.
3. Hutchinson, J. (1964) *The Genera of Flowering Plants*, Vol. 1. University Press, Oxford.
4. Janzen, D. H. and Leisner, R. (1980) *Brenesia* **18**, 15.
5. Janzen, D. H. and Waterman, P. G. (1984) *Biol. J. Linn. Soc.* **21**, 439.
6. Bohlmann, F., Arndt, C., Bornowski, H., Jastrow, H. and Kleine, K. M. (1962) *Chem. Ber.* **95**, 1320.
7. Gopinath, K. W., Mahanta, P. K., Bohlmann, F. and Zdero, C. (1976) *Tetrahedron* **32**, 737.
8. Bohlmann, F., Burkhardt, T. and Zdero, C. (1973) *Naturally Occurring Acetylenes*. Academic Press, New York.
9. Leboeuf, M., Cavé, A., Bhaumik, P. K., Mukherjee, B. and Mukherjee, R. (1982) *Phytochemistry* **21**, 2783.
10. Roblot, F., Hocquemiller, R., Cavé, A. and Moretti, C. (1983) *J. Nat. Prod.* **46**, 862.
11. Jossang, A., Leboeuf, M., Cavé, A., Sevenet, T. and Padmawinata, K. (1984) *J. Nat. Prod.* **47**, 504.
12. Bick, I. R. C. and Douglas, G. K. (1964) *Tetrahedron Letters* 1629.
13. Waterman, P. G. and Muhammad, I. (1985) *Phytochemistry* **24**, 523.