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PRENYLATED BIANTHRONES AND VISMIONE F FROM *PSOROSPERMUM FEBRIFUGUM**

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Key Word Index—*Psorospermum febrifugum*; Guttiferae; geranyloxyemodin; 2-geranylemodin; vismiones D and F; bianthrones.

Abstract—The roots of *Psorospermum febrifugum* collected in Malawi contained together with the known vismione D and geranyloxyemodin four new compounds: vismione F and the three bianthrones A_1, A_{3a} and A_{3b}. All the isolated compounds contained C- or O-geranyl substituents and showed a close biogenetic relationship.

INTRODUCTION

In the chemosystematic investigation on the secondary metabolites of the tribe Vismieae (subfam. Hypericoideae) [1], we isolated three new vismiones and 3-geranyloxyemodin (1), from the fruits of *Psorospermum febrifugum* Spach. collected in Nigeria [2]. Previously, Kupchan *et al.* [3] had isolated from the roots of the same plant, collected in Tanzania, psorospermin (40 mg/kg), a xanthone with significant antitumor activity in the P388 *in vivo* system as well as cytotoxicity against the KB *in vitro* system. By contrast, Cassady *et al.* [4] found that roots, collected in Nigeria, contained 3-geranyloxyemodin anthrone (2) also active on P388, but less potent than psorospermin [4, 5]. More recent works of the same group [6] were not available in details. This paper deals with our examination of the roots of *Psorospermum febrifugum*, collected in Malawi.

RESULTS AND DISCUSSION

The extracts of the bark and the woody parts of the roots revealed a different composition on TLC and were separately processed. From the root bark extract, six compounds were isolated by CC (see Experimental) and two of them were identified as 3-geranyloxyemodin (1) and vismione D (3) [2]. The first new pigment, $C_{50}H_{54}O_4$, namely bianthrone A_1, showed UV data for an anthrone without a free hydroxy group on C-3 (or C-6) and signals in the ^1H NMR spectrum for two O-geranyl groups. The presence of these substituents was supported by two successive losses of 136 a.m.u. in the mass spectrum. Other signals in the ^1H NMR spectrum (Table 1) were due to four *meta*-coupled aromatic protons, two aromatic methyls and four H-bonded phenolic hydroxyls. From the above data the bianthrone A_1 was assigned the structure 4 and was considered to be a mixture of the *meso* and (±)-forms. In fact, acid treatment of 4 gave emodin bianthrone (5), as a mixture of *meso* and (±)-forms, which was coincident with a synthetic sample prepared from emodin according to the literature [7–9]. The only difference was in the *ratio* between the *meso* and (±) forms (1:1 and 2:3, respectively) calculated from the signals due to the H-bonded hydroxyls in the ^1H NMR spectra.

Two other compounds, $C_{50}H_{54}O_4$, namely bianthrones A_{3a} (mp 157–159°) and A_{3b} (mp 148–150°) were obtained from the root bark extract. They showed identical UV and mass data and slight differences in the ^1H NMR spectra (Table 1). Notably, in the mass spectra two successive losses of 136 and 123 a.m.u. suggested that both O- and C-geranyl groups were present. This assumption was in accordance with the shift of the UV maxima with sodium acetate (free 3-OH) and the presence of two different methylene signals (δ4.50 and 3.35, respectively) in the ^1H NMR spectra. From these data both compounds A_{3b} and A_{3b} were assigned the structure of the unsymmetrical bianthrone 6 in its two racemic forms, but it was impossible to say which was which. As confirmation of the gross structure 6, ferric chloride oxidation of A_{3a} and A_{3b} gave emodin and 2-geranylemodin (7), a compound also present in the fruits [B. Botta and F. Delle Monache, unpublished results].

The last compound obtained from the extract, $C_{25}H_{30}O_5$, showed the characteristic features (UV visible and ^1H NMR) of the vismiones [2] and was named vismione F. On the basis of the spectral evidence and of its transformation to 7 under alkaline conditions, it was assigned the structure 8.

In the wood extract only (−)epi-catechin and procyanidin B_2, previously found in the fruits [12], were detected, but not psorospermin, probably because of the lack of material.

Most of the product isolated from the fruits [2] and the roots of *P. febrifugum* are chemically related in the manner shown in Scheme 1. These transformations may occur during the isolation procedure [2, 12] and the question arises as to whether or not the anthrones, anthraquinones and bianthrones are genuine natural products. In practice, the compounds 1, 4 and 6 were certainly detected (TLC)

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*Part 2 in the series "Chemistry of *Psorospermum* genus". For Part 1 see ref. [2].

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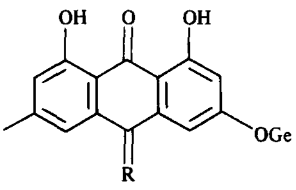
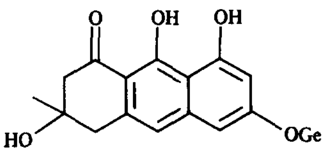


1 R=O
2 R=H_2



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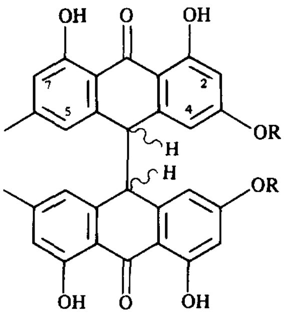
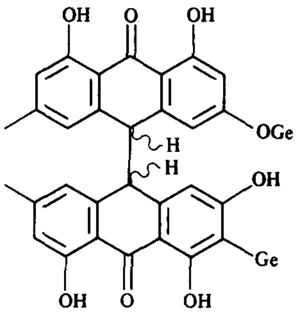


4 R=Ge
5 R=H



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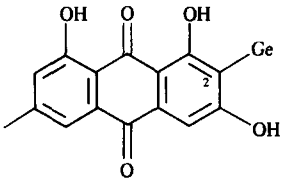

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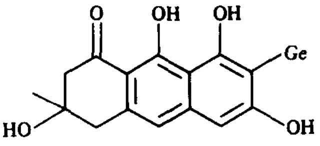


8

Ge =

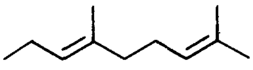
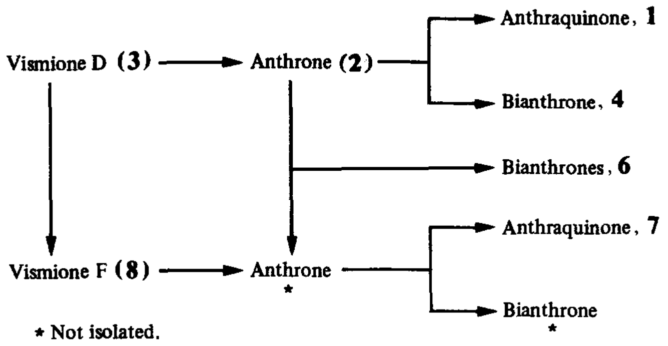


Table 1. ^{1}H NMR data of bianthrones ($CDCl_3$, δ)

H	A_1* (4)	5 [9] (meso)	5 [9] (±)	A_{3a}† (6)	A_{3b}† (6)
2,2′	5.70	6.03	6.03	6.03 (1H)	6.03 (1H)
4,4′	6.20	6.18	6.23	6.30	6.26
5,5′	6.50	6.67	6.63	6.52	6.60
7,7′	5.85	6.21	6.23	5.80	5.80
10,10′	3.97	4.47	4.47	4.13	4.15
OH-1,1′, 8,8′	11.90, 11.80, 11.60, 11.50	11.86 (2H), 11.78 (2H)	11.92 (2H), 11.68 (2H)	12.40, 12.03, 11.66 (2H)	12.36, 12.0, 11.80 (2H)
Me	2.37	2.23	2.18	2.25	2.25

*5.43 (2H, *br*, *t*, *J* = 7 Hz, 5.08 (2H, *br*, *m*), 4.45 (4H, *br d*, *J* = 7 Hz), 2.15–2.0 (8H, *m*), 1.72, 1.65 and 1.58 (6H each, *br s*).

†5.40–4.90 (4H, *m*), 4.50 (2H, *br d*, *J* = 7 Hz), 3.35 (2H, *br d*, *J* = 7 Hz), 2.15–2.0 (8H, *m*), 1.85–1.55 (18H).



Scheme 1. Biogenetic relationships among the metabolities of *P. febrifugum*.

in the crude extract of the roots, with the bianthrone **4** as the main component.

EXPERIMENTAL

Plant material. The roots of *P. febrifugum* were collected and identified in the University of Malawi in March 1983 (Voucher specimen PSF 1983, Herbarium of Centro Chimica dei Recettori).

Extraction and fractionation. Air dried finely ground bark of roots (35 g) was extracted with cold Me_2CO (× 2). The pooled extracts gave a residue (5.1 g) which on silica gel afforded six fractions with the indicated eluants: RB_1 (1.2 g, CH_2Cl_2), RB_2 (810 mg, $CHCl_3$), RB_3 (400 mg, $CHCl_3$–MeOH, 19:1), RB_4 (1.5 g, $CHCl_3$–MeOH, 9:1), RB_5 (170 mg, $CHCl_3$–MeOH, 4:1) and RB_6 (870 mg, MeOH). Further purification yielded: geranyloxyemodin (200 mg), bianthrone A_1 (850 mg) and an unidentified pigment (40 mg) from RB_1 (silica gel; hexane–EtOAc, 9:1); bianthrones A_{3_a} (145 mg) and A_{3_b} (85 mg) from RB_2 (silica gel; hexane–EtOAc, 4:1); vismione D (190 mg) from RB_3 (crystallization from $CHCl_3$–hexane); vismione F (145 mg) from RB_5 (crystallization from $CHCl_3$–hexane). Fractions RB_4 (mixture of vismiones D and F) and RB_6 were not further processed. Vismione D (**3**) and geranyloxyemodin (**2**) were identified by comparison (mp, TLC and ^1H NMR) with authentic samples [2].

Finely ground wood of the roots (100 g) was extracted with cold Me_2CO and the residue (1.6 g) partitioned between $CHCl_3$ and H_2O. The $CHCl_3$ phase contained bianthrones A_1, A_{3_a} and A_{3_b}. The H_2O phase was saturated with NaCl and extracted with EtOAc. The residue (180 mg) from the organic layer gave a positive vanillin–HCl test. Elution with EtOAc on silica gel containing 5% H_2O afforded procyanidin B_2 and (−)-epicatechin which were identified by comparison ([α], mp, ^1H NMR) with authentic samples.

Bianthrone A_1 (**4**). Mp 134–136° (yellow solid, Et_2O–hexane), $[\alpha]_D$ 0° ($CHCl_3$, *c* 0.3). UV λ_{max}^{EtOH} and λ_{max}^{AcONa} nm: 279, 363; ^1H NMR: Table 1; EIMS (probe) 70 eV, *m/z* (rel. int.): 782 $[M]^+$ (17), 646 $[M-C_{10}H_{16}]^+$ (3), 510 $[646-C_{10}H_{16}]^+$ (9), 492 (8), 392 (15), 390 (15), 371 (45), 306 (57), 256 (100). Bianthrone A_1 (150 mg) was refluxed for 1 hr in 3 N HCl. Standard work-up and purification on silica gel ($CHCl_3$–MeOH, 49:1) gave 10,10′-emodin bianthrone (**5**, 60 mg) as a mixture of *meso* and (±)-diastereomers [9], identified by comparison (co-TLC and ^1H NMR) with a sample prepared from emodin by reduction to emodin anthrone [7] followed by dimerization with 1% $FeCl_3$ in EtOH [8].

Bianthrone A_{3_a} (**6**). Mp 157–159° (yellow needles, Et_2O–hexane), $[\alpha]_D$ 0° ($CHCl_3$, *c* 0.2). {Found C, 83.45; H, 7.68; $C_{50}H_{54}O_4$ requires C, 83.52; H, 7.57%.] UV λ_{max}^{EtOH} nm: 278, 363; λ_{max}^{AcONa}: 278, 370; EIMS (probe) 70 eV, *m/z* (rel. int.): 782 $[M]^+$ (3), 646 $[M-C_{10}H_{16}]^+$ (6), 524 $[646-C_9H_{14}]^+$ (6), 522 $[646-C_9H_{16}]^+$ (9), 509 (10), 392 (15), 390 (26), 371 (28), 323 (21), 306 (70), 269 (71), 256 (100).

Bianthrone A_{3_b} (**6**). Mp 148–150° (yellow needles, Et_2O–hexane), $[\alpha]_D$ 0°. UV and EIMS coincident with those of anthrone A_{3_a}. A mixture (100 mg) of the bianthrones A_{3_a} and A_{3_b} was refluxed for 1 hr with 6% $FeCl_3 \cdot 6H_2O$ in 2.5 M H_2SO_4 [10]. Standard work-up and purification gave emodin and 2-geranylemodin identified by direct comparison with authentic samples.

2-*Geranylemodin* (**7**). Mp 208–210° (red–orange solid, EtOH). UV λ_{max}^{EtOH} nm: 254, 284, 442; λ_{max}^{AcONa}: 258, 324, 438, 520; $\lambda_{max}^{AlCl_3}$ after 30′ [11]: 252, 279, 464; ^1H NMR (60 MHz, DMSO-d_6): δ12.30 (1H, *s*, OH), 11.90 (1H, *s*, OH), 7.40 (1H, *d*, *J* = 2 Hz, H-5), 7.20 (1H, *s*, H-4), 7.06 (1H, *d*, *J* = 2 Hz, H-7), 5.30–4.9 (2H, *m*), 3.40 (2H, *d* (*br*), *J* = 7 Hz), 2.35 (3H, *s*), 2.10–1.95 (4H, *m*), 1.76, 1.57 and 1.50 (3H each, *s*, *br*). (C_5D_5N): δ7.50 (*s*, H-4), 3.75 (2H, *d*); EIMS (probe) 70 eV, *m/z* (rel. int.): 406 $[M]^+$ (4), 338 (50), 323 (16), 309 (12), 305 (7), 295 (100), 283 (75).

Vismione F (**8**). Mp 144–146° (brown–red solid, CH_2Cl_2–hexane): UV $\lambda_{max}^{CHCl_3}$ nm (log ε): 281, 320 sh, 410 (4.70, 3.98, 4.11); ^1H NMR (60 MHz, Me_2CO-d_6): δ16.53 (1H, *s*, OH-9), 10.0 (1H, *s*, OH-1), 6.60 (1H, *s*, H-10), 6.50 (1H, *s*, H-4), 5.30 (1H, *t*, *J* = 7 Hz), 5.0 (1H, *t*, *br*), 3.40 (2H, *d*, *J* = 7 Hz), 2.90 and 2.73 (2H each, *s* (*br*); CH_2-5, CH_2-7), 2.05–1.90 (4H, *m*), 1.75 (3H, *s*, *br*), 1.60 (6H, *s*, *br*), 1.32 (3H, *s*, Me-6). EIMS (probe) 70 eV, *m/z* (rel. int.): 410 $[M]^+$ (46), 395 (4), 392 $[M-H_2O]^+$ (6), 367 (5), 341 (17), 325 (32), 323 (7), 299 (12), 287 $[M-C_9H_{15}]^+$ (100), 274 (51), 269 $[M-H_2O-C_9H_{15}]^+$ (28), 256 (17), 245 (19). Vismione F by prolonged contact with silica gel or under alkaline conditions (C_5H_5N and air [2]) gave 2-geranylemodin (**7**) as the main product.

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