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3-GERANYLOXY-6-METHYL-1,8-DIHYDROXYANTHRAQUINONE AND VISMIONES C, D AND E FROM *PSOROSPERMUM FEBRIFUGUM*

B. BOTTA, F. DELLE MONACHE†, G. DELLE MONACHE, G. B. MARINI BETTOLO and J. U. OGUAKWA*

Centro Chimica dei Recettori del C. N. R., Università Cattolica, Via della Pineta Sacchetti 644, 00168 Rome, Italy; *Department of Chemistry, University of Nigeria, Nsukka, Nigeria

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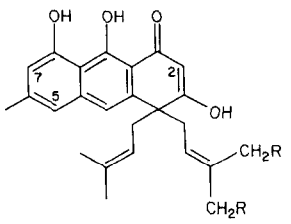
Key Word Index—*Psorospermum febrifugum*; Guttiferae; Vismieae; prenylated anthracenes; 3-geranyloxy-6-methyl-1,8-dihydroxyanthraquinone; vismiones C, D and E.

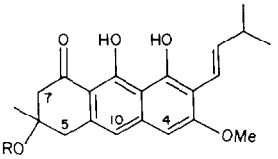
Abstract—Three new vismiones and 3-geranyloxy-6-methyl-1,8-dihydroxyanthraquinone were isolated from the berries of *Psorospermum febrifugum* together with the known chrysophanic acid, 2-isoprenylemodin and ferruginin B. Their structures were established through chemical and spectral means. The occurrence of prenylated anthracenes only in Vismieae suggests their use as systematic markers for the tribe.

INTRODUCTION

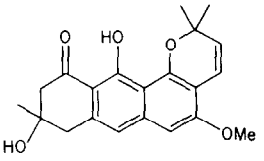
From the berries of plants of the genus *Vismia*, we have isolated [1–4] six ferruginins (**1**, with one additional isoprenyl chain on C-7, C-5 or C-2) and three vismiones (**2**–**4**). The two types of compounds are biogenetically closely correlated [5] and only one, namely harunganin (**1**, R = H and isoprenyl chain on C-5) was previously reported to occur in *Harungana madagascariensis* [6].



1 R=H, OH



2 R = Ac
3 R = H



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According to Engler [7], the tribe Vismieae (Guttiferae, Hypericoideae) contains three genera, i.e. *Vismia*, *Harungana* and *Psorospermum*. This paper deals with the examination of the berries of *Psorospermum febrifugum*, a shrub growing in tropical Africa [8] and largely used in folk medicine [9–12]. From the roots Kupchan *et al.* [13] recently isolated a new antileukemic xanthone.

†To whom correspondence should be addressed.

RESULTS AND DISCUSSION

The acetone extract of the berries contains α- and β-selinene, chrysophanic acid, 2-isoprenylemodin (**5**), ferruginin B (**1**, R = H and isoprenyl chain on C-2) and four new pigments, whose separation is described in the Experimental. 2-Isoprenylemodin and ferruginin B have been previously isolated only from the bark of *Vismia guaramirangae* [14] and from the berries of *V. baccifera* var. *ferruginea* [2], respectively.

The first new pigment, $C_{25}H_{26}O_5$ (M^+ 406) showed UV absorption and ^1H NMR signals in the aromatic region very similar to those of emodin and physcion. Like the latter, it did not show a bathochromic shift of the UV maxima after addition of sodium acetate, therefore, a substituent on OH-3 must be present. In agreement, in the mass spectrum, the pigment after the loss of 136 amu from the molecular ion, exhibited the same fragmentation as emodin; the latter was also formed on hydrolysis of the pigment.

The nature of the substituent was shown to be a geranyl chain by the ^1H NMR spectrum (see Experimental) and structure **6** was assigned to the pigment.

The other three pigments, $C_{22}H_{24}O_6$, $C_{25}H_{30}O_5$ and $C_{21}H_{24}O_5$ showed UV visible (Table 1) and ^1H NMR spectra (Table 2) which closely resembled those of the previously known vismiones and were named vismione C, D and E, respectively. Characteristic features in the ^1H NMR spectra of vismiones (Table 2) are the signals due to two phenolic hydroxy groups, one of which is highly chelated (*ca* δ 10 and 16.2, respectively), and to the C-5 and C-7 methylenes in the range δ 2.70–3.40. In vismiones B, D, E and deacetylvismione A, where the C-6 hydroxyl is free, the methylene protons are equivalent and appear as broad singlets; conversely, in vismiones A and C, where the C-6 hydroxyl is acetylated, they are no longer equivalent and show up as doublet of doublets with geminal coupling. In the latter case the C-6 methyl signal is shifted from *ca* δ 1.35 to 1.75, as expected.

With these features in mind, structure **7** can be assigned to vismione C (M^+ 384). The C-2 isoprenyl chain was

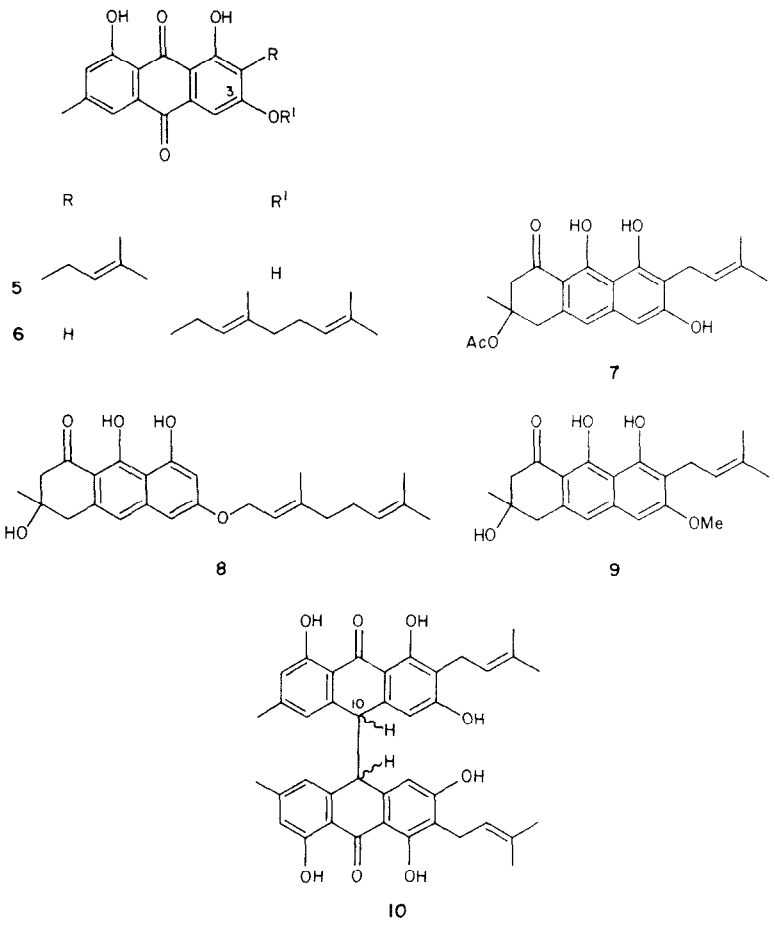

Table 1. UV visible spectra in ethanol of vismiones (λ_{max} nm)

Vismione A (**2**)	243, 291, 335 sh, 410
Deacetylvismione A (**3**)	244, 292, 414
Vismione B (**4**)	241, 302, 411
Vismione C (**7**)	234, 280, 325, 340, 400
Vismione D (**8**)	230, 275, 318, 398
Vismione E (**9**)	228, 274, 321, 404

deduced from the ^{1}H NMR data (Table 2) and the C-6 acetyl was substantiated by IR absorption (ν_{max} 1720 cm^{-1}) and by the loss of 60 amu from the molecular ion in the mass spectrum. Confirmation of the structure was provided by the transformation of vismione C to 2-isoprenylemodin (**5**) (see below). This pigment is the first example of a vismione with a free OH-3.

Vismione D (M^+ 410) exhibited in the ^{1}H NMR spectrum (Table 2) signals due to three aromatic protons (two of which were *meta* coupled) and to an *O*-geranyl chain; consequently structure **8** was assigned to the pigment. Successive losses of water and of the C_{10} chain in the mass spectrum, as well as its transformation to **6**, confirmed the structure. Vismione D is the first member of the class without *C*-prenylation. Finally, to vismione E, an isomer of deacetylvismione A (**3**), structure **9** was assigned from the presence in the ^{1}H NMR spectrum of additional signals due to an isoprenyl chain, two isolated aromatic protons and one methoxy group.

As previously mentioned [1], vismiones, mainly those with a C-6 acetoxyl group, are quite unstable. Under alkaline conditions vismione A (**2**) loses a molecule of acetic acid and rearranges to an anthrone, which is oxidized in air to an anthraquinone and a mixture of two bianthrones [meso- and (±)-form]. The two isomers can be separated by prep. TLC, but soon yield the original mixture on keeping in solution. This behaviour was attributed to conjugation between the double bond of the chain and the aromatic ring. Now vismione C (**7**), where the conjugation is absent, kept in pyridine in a stream of air gave the anthraquinone **5** and only one bianthrone (**10**). This is in agreement with the above assumption. Vismiones are also sensitive to prolonged contact with SiO_2 and considerable losses occur during chromatographic purification. For this reason, the anthraquinones **5** and **6** may not be true natural products; while the latter can be definitely identified in crude extracts by TLC, the former was obscured by other pigments.

The finding of prenylated anthracenes, i.e. vismiones and ferruginins only in Vismieae suggests their use as markers for this tribe.

EXPERIMENTAL

Plant material. The berries of *Psorospermum febrifugum* Spach were collected in July 1980 in Nigeria and identified by Dr. A. Ozioko (University of Nigeria, Nsukka). A voucher sample is in

Table 2. ^{1}H NMR data of vismiones

	OH-1	H-2	OR-3	H-4	H-5	H-6	H-7	OH-9	H-10
Vismione A (**2**)	10.30	*	3.93	6.70	3.58 and 3.03	1.77	3.22 and 2.83	16.30	6.80
					(*d*, J = 16 Hz)	1.68	(*d*, J = 16 Hz)		
Deacetylvismione A (**3**)	10.30	*	3.86	6.60	2.90	1.33	2.70	16.15	6.65
Vismione B (**4**)		*	3.93	6.73	3.0	1.37	2.80	14.70	6.83
Vismione C (**7**)	9.85	†	9.1 *br*	6.52	3.55 and 3.15	1.73	3.20 and 2.90	16.30	6.63
					(*d*, J = 14 Hz)	1.63	(*d*, J = 12 Hz)		
Vismione D (**8**)	9.63	6.30	§	6.50	2.93	1.32	2.75	16.27	6.72
		(*d*, J = 2 Hz)		*d*, J = 2 Hz					
Vismione E (**9**)	9.93	‡	3.90	6.67	3.03	1.30	2.83	16.43	6.85

Solvent acetone-d_6 ($CDCl_3$ for **3**); δ-value; J in Hz; H-10 and H_2-5 singlets are broadened by long-range couplings.
*Not reported from the original work [1] for simplicity.
†5.20 (1H, *t*, J = 7 Hz), 3.37 (2H, *d*, J = 7 Hz), 1.73 (3H, *s*), 1.63 (3H, *s*).
‡5.20 (1H, *t*, J = 7 Hz), 3.40 (2H, *d*, J = 7 Hz), 1.75 (3H, *s*), 1.63 (3H, *s*).
§5.40 (1H, *t*, J = 7 Hz), 5.05 (1 H, *br t*), 4.57 (2H, *d*, J = 7 Hz), 2.05 (4H, *br*), 1.73, 1.60, 1.56 (3H each, *s*).

the Herbarium of Centro Chimica dei Recettori del C.N.R. under the cipher PSF 1980.

Extraction and fractionation. The ground berries (1.2 kg) were extracted in a Soxhlet (24 hr) with Me_2CO to give a dark orange oil (A, 48 g). A portion (20 g) was chromatographed on Si gel to give the following fractions with the indicated solvent: A_1, A_2, A_3, A_4 (CH_2Cl_2); A_5 ($CHCl_3$); A_6, A_7 ($CHCl_3$–Me_2CO, 19:1); A_8 ($CHCl_3$–Me_2CO, 9:1), A_9 (Me_2CO). A portion (400 mg) of A_1 (1.3 g) was purified on $AgNO_3$–Si gel (1:4) with C_6H_6–heptane (1:1) to give α-selinene (150 mg) and β-selinene (75 mg). A_2 (1.7 g) was partitioned between hexane and MeOH–H_2O (9:1) to eliminate triglycerides; crystallization of the MeOH–H_2O soluble portion yielded 3-geranyloxy-6-methyl-1,8-dihydroxyanthraquinone (300 mg) and prep. TLC (C_6H_6–hexane, 4:1) of the mother liquor the same pigment (70 mg) and chrysophanic acid (50 mg). A_3 (2.2 g) containing mainly triglycerides, was not further processed. Crystallization of A_4 (710 mg) gave ferruginin B (590 mg). A_5 (3.2 g) containing fatty acids and a pigment in small quantity was not examined. A_6 (600 mg) was washed with cold CH_2Cl_2 giving the insoluble 2-isoprenylemodin (50 mg). Si gel chromatography ($CHCl_3$–Me_2CO, 19:1) followed by prep. TLC (C_6H_6–EtOAc, 19:1, two runs) of the soluble portion yeilded vismione C (total 180 mg). Si gel CC ($CHCl_3$–Me_2CO, 93:7) of A_7 (2.3 g) gave: vismione D (200 mg) and a mixture of vismione A and E, which were separated by prep. TLC (C_6H_6–EtOAc, 4:1); vismione D (75 mg); and vismione E (125 mg). A_8 and A_9 were not further processed.

α-Selinene and β-selinene. Their identification was based on optical rotations, IR and ^{1}H NMR spectra as well as on comparison with authentic specimens previously obtained in this laboratory [1].

2-Isoprenylemodin (**5**), *chrysophanic acid and ferruginin B.* These pigments were identified by spectral data (UV, IR, ^{1}H NMR) and comparison with authentic specimens from this laboratory [2, 14]. For 2-isoprenylemodin a ^{1}H NMR (60 MHz DMSO-d_6) spectrum was obtained: δ12.40 (1H, *s*), 12.0 (1H, *s*), 7.46 (*br d*, J = 2 Hz, H-5), 7.23 (*s*, H-4), 7.13 (*br d*, J = 7 Hz, H-7), 5.34 (1H, *t*, J = 7 Hz), 3.34 (2H, *d*, J = 7 Hz), 2.43 (3H, *s*), 1.82 (3H, *s*), 1.72 (3H, *s*). The identification was confirmed by cyclization of the isoprenyl chain with TFA [14].

3-Geranyloxy-6 methyl-1,8-dihydroxyanthraquinone (**6**). Mp 119–121° (dec.) (orange crystals, CH_2Cl_2–heptane). Found: C, 73.97; H, 6.40. $C_{25}H_{26}O_5$ requires: C, 73.86; H, 6.45%. UV λ_{max}^{EtOH} nm: 225, 263, 281 sh, 440. ^{1}H NMR (60 MHz $CDCl_3$): δ 12.23 (1 H, *s*), 12.08 (1 H, *s*), 7.50 (*br d*, J = 1.8 Hz, H-5), 7.27 (*d*, J = 2.5 Hz, H-4), 7.0 (*br d*, J = 1.8 Hz, H-7), 6.60 (*d*, J = 2.5 Hz, H-2), 5.43 (1H, *t*, J = 7 Hz), 5.05 (1H, *br*), 4.60 (2H, *d*, J = 7 Hz), 2.40 (3H, *s*), 2.10 (4H, *m*), 1.77 (3H, *s*), 1.67 (3H, *s*), 1.60 (3H, *s*). EIMS (probe) 70 eV, *m/z* (rel. int.): 406 $[M]^+$ (38), 270 $[M-136]^+$ (100), 254 (11), 242 (17), 241 (12), 214 (6), 213 (8), 197 (6), 196 (4), 185 (7), 157 (5), 139 (9). Compound **6** (50 mg) in methanolic 2 N H_2SO_4 was refluxed (5 hr). Standard work-up and crystallization (EtOH) gave emodin (20 mg) identified by spectral data (UV, ^{1}H NMR) and direct comparison (mmp and TLC).

Vismione C (**7**). Mp 100–105° (dec.) (orange-brown crystals, CH_2Cl_2–heptane). Found: C, 68.90; H, 6.25. $C_{23}H_{24}O_6$ requires: C, 68.73; H, 6.29%. UV $\lambda_{max}^{CHCl_3}$ nm (log ε): 245 sh (4.16), 278 (4.33), 398 (3.95). EIMS (probe) 70 eV, *m/z* (rel. int.): 384 $[M]^+$ (18), 324 $[M-MeCOOH]^+$ (80), 309 $[324-Me]^+$ (25), 295 $[324-CHO]^+$ (25), 281 $[324-C_3H_7]^+$ (47), 269 $[324-C_4H_7]^+$ (100), 268 (34); metastable peaks at 273.3 (384 → 324), 243.7 (324 → 281) and 223.3 (324 → 269).

Vismione D (**8**). Mp 142–145° (dec.) (red-brown crystals, MeOH). Found: C, 73.02; H, 7.45. $C_{25}H_{30}O_5$ requires: C, 73.14; H, 7.37%. UV $\lambda_{max}^{CHCl_3}$ nm (log ε): 279 (4.79), 322 (4.0), 402 (4.24). EIMS (probe) 70 eV, *m/z* (rel. int.): 410 $[M]^+$ (13), 392 $[M-H_2O]^+$ (10), 274 $[M-136]^+$ (100), 256 $[274-H_2O]^+$ (95), 241 (17), 232 (12), 228 (10), 227 (12), 216 (22), 213 (16), 212 (16); metastable peak at 239.2 (274 → 256).

Vismione E (**9**). Mp 161–164 (dec.) (red-brown crystals, CH_2Cl_2–heptane). Found: C, 70.89; H, 6.64. $C_{21}H_{24}O_5$ requires: C, 70.76; H, 6.79%. UV $\lambda_{max}^{CHCl_3}$ nm log ε): 245 sh (4.40), 278 (4.71), 326 (4.11), 406 (4.19). EIMS (probe) 70 eV, *m/z* (rel. int.): 356 $[M]^+$ (100), 341 $[M-Me]^+$ (75), 339 (38), 338 (33), 323 $[341-H_2O]^+$ (32), 313 (29), 301 $[M-C_4H_7]^+$ (98), 299 (33), 295 (63), 288 (35), 283 (82), 271 (26), 270 (20), 259 (45), 255 (14), 254 (18), 253 (16), 242 (19), 213 (19); metastable peaks at 326.6 (356 → 341), 306 (341 → 323) and 254.5 (356 → 301).

Transformation of vismiones in alkaline conditions. The vismione in C_5H_5N was kept under a stream of air at room temp. (2–3 hr). In these conditions vismione D (10 mg) gave **6** and emodin, identified by TLC. Vismione C (100 mg) gave **5** (35 mg) and **10** (18 mg) after Si gel chromatography (C_6H_6–EtOAc, 9:1). Bianthrone, **10**; mp 212–213°. UV λ_{max}^{EtOH} nm: 280 sh, 366. ^{1}H NMR (60 MHz; $CDCl_3$–CD_3OD, 19:1: δ 12.35 (*s*), 11.90 (*s*), 6.50 (*br d*, H-7, H-7'), 6.23 (*s*, H-4, H-4'), 5.60 (*br d* H-5, H-5'), 5.20 (2H, *t*, J = 7 Hz), 4.15 (*s*, H-10, H-10'), 3.35 (4H, *d*, J = 7 Hz), 2.15 (6H, *s*), 1.83 (6H, *br s*), 1.73 (6H, *br s*). EIMS (probe) 70 eV, *m/z* (rel. int.): 646 $[M]^+$ (not observed), 324 (69), 323 (32), 309 (25), 307 (41), 281 (77), 269 (100), 246 (10), 231 (10).

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