Phytochemistry, Vol. 21, No. 2, pp. 417–419, 1982.
Printed in Great Britain.

0031-9422/82/020417-03$03.00/0

2-ISOPRENYLEMODIN AND 5,5'-DIMETHOXYSESAMIN FROM VISMIA GUARAMIRANGAE*

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(*Revised received* 12 *June* 1981)

Key Word Index—*Vismia guaramirangae*; Guttiferae; bark; exudate; anthranoids; 2-isoprenylemodin; sesquiterpenes; dammaradienol; lignans; sesamin; 5,5'-dimethoxysesamin.

Abstract—The secondary metabolites γ-hydroxyferruginin A, madagascin, chrysophanic acid, physcion, β-caryophyllene, humulene, sitosterol, sesamin and a rare triterpene, dammaradienol were isolated from the bark and exudate of *Vismia guaramirangae*. The structures of a new anthraquinone, 2-isoprenylemodin, and of a new lignan, 5,5'-dimethoxysesamin, were established on the basis of chemical and spectroscopic evidence.

INTRODUCTION

The isolation of interesting products, mainly prenylated anthranoids and benzophenones, from the berries [1] and the leaves [2] of plants of the *Vismia* genus prompted us to investigate the extracts of the barks and the exudates in order to have a complete picture of the secondary metabolism of this genus. We now report the results of the analyses of bark and exudates of *Vismia guaramirangae*, the berries of which have been shown to contain three new triprenylated anthranoids [3].

RESULTS AND DISCUSSION

From the NaOH-soluble fraction of the benzene extract of the barks, five pigments were isolated besides betulinic acid. Four of them were identified as γ-hydroxyferruginin A(**1**) [3], madagascin (**2**), chrysophanic acid (**3**) and physcion (**4**), respectively. This is the first time that madagascin, previously reported only in *Harungana madagascariensis* [4], has been found in the *Vismia* genus.

The fifth pigment (**5**), $C_{20}H_{18}O_5$, MW 338, was an isomer of madagascin which did not contain an *O*-isoprenyl group, as indicated by the absence in the mass spectrum of the characteristic loss of 68–69 mu [5]. The UV spectrum was very similar to that of physcion and madagascin, but the bathochromic shift on addition of NaOAc indicated a free β-hydroxy group. Owing to the low solubility of **5**, the NMR spectrum was unsatisfactory for the determination of the substitution pattern, but the presence of a *C*-isoprenyl group was suggested (see Experimental). These data led us to consider the product as a new *C*-isoprenylemodin. The delay in the appearance of the bathochromic shift in the UV spectrum after the addition of $AlCl_3$[6] restricted the position of the C_5-chain to C-2 or C-7. The cyclization of the C_5-chain in acid medium confirmed that the new pigment was 2-isoprenylemodin, **5**. The reaction led to a more soluble product, **6**, whose NMR spectrum exhibited signals for two chelated hydroxyls and an aromatic ring pattern similar to that of madagascin and physcion, except for the absence of the H-2 signal ($\delta \sim$ 6.60 in the spectra of madagascin and physcion).

2-Isoprenylemodin is a rare example of a prenylated anthraquinone and may be biogenetically correlated to madagascin through a Claisen rearrangement.

From the neutral fraction of the benzene extracts of the barks three sesquiterpenes, two triterpenes and two lignans were isolated. The sesquiterpenes were identified as β-caryophyllene, isocaryophyllene and humulene, all previously isolated from other *Vismia* species [7]. The two triterpenes were shown to be β-sitosterol and dammaradienol(**7**), the latter a quite rare triterpene previously reported only from Dammar resin obtained from the exudate of plants of the Dipterocarpaceae [8], from *Inula helenium* (Compositae) [9] and from *Antidesmia bunius* (Euphorbiaceae) [10]. The identification of **7** was performed by comparison of its physical data (as well as of those of its acetyl derivative), mainly the broad singlet (5H) at δ 2.03, due to the allylic protons, in the NMR spectrum and the MS fragmentation pattern [10], with the published data.

One lignan was identified as (±)-sesamin, **8**, on the

*Part 8 in the series "Chemistry of the *Vismia* Genus". For Part 7, see Gonzalez, J., Delle Monache, F., Delle Monache, G. and Marini Bettolo, G. B. (1980) *Planta Med.* **40**, 347.

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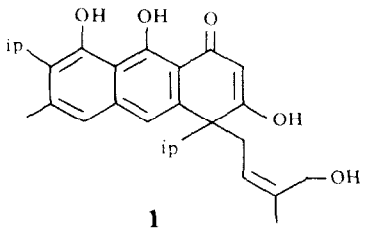

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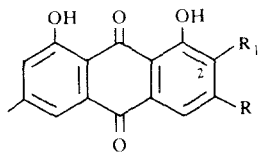
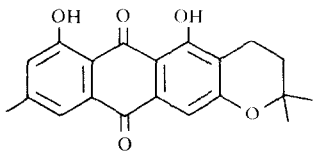
ip = isoprenyl



	R	R_1
2	Oip	H
3	H	H
4	OMe	H
5	OH	ip



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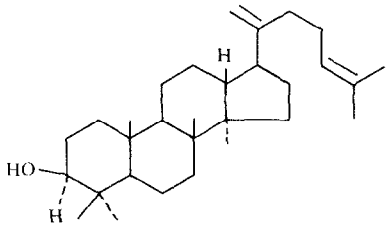

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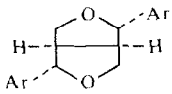

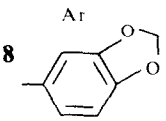

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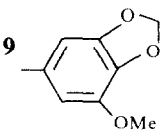

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basis of the physical data, while the other was a new symmetrical and diequatorial lignan (**9**) containing a methoxyl in each aromatic ring in addition to a methylendioxy group as indicated by NMR (δ 3.87, *s*) and MS (M^+414), where a 30 mu shift of the typical fragment ions was observed with respect to sesamin. The position of the methoxyls on C-5 and C-5′ was established by the study of lanthanide-induced shift (LIS) in the NMR spectrum. At a molar ratio 1:3 [Eu(fod)$_3$ vs substrate] the aromatic protons, which were equivalent in the normal NMR spectrum (δ 6.40, *s*), were shifted differently and showed *meta* coupling.

To the best of our knowledge lignans of the 2,6-diaryl-3,7-dioxobicyclo(3,3,0)octane skeleton have not been reported in Guttiferae.

In the exudate physcion, chrysophanic acid, 2-isoprenylemodin, betulinic acid, sesamin and 5–5′-dimethylsesamin were found.

EXPERIMENTAL

Plant material. The bark and the exudate of *Vismia guaramirangae* Huber [syn. *Vismia reichardtiana* (Kuntse) Ewan, comb. nov., syn. *Vismia guttifera* Salzm., syn. *Vismia baccifera* var. *angustifolia* Reich., syn. *Vismia cearensis* Huber] [12] were collected in Jan. 1978 in Brazil (Serra de Pacatuba, near Fortaleza, Ceará) from the plant used as the source of berries in the previous study [3].

Extraction and fractionation. Air-dried finely ground bark (3 kg) was extracted with cold C_6H_6 (×2) and the extracts evaporated (residue A, 42 g). A portion (26 g) of the extract was dissolved in Et_2O and washed with aq. 10% K_2CO_3 and 1 N NaOH successively. The Et_2O was evaporated (residue B, 6.3 g) and the K_2CO_3 and NaOH solns were separately acidified (2 N HCl) and extracted with Et_2O. Evaporation of the solvents gave residues C (5.5 g) and D (13.5 g), respectively. Residue C was mainly fatty acids and was not further examined.

Residue B (5.2 g) was roughly separated on Si gel into three subfractions: B_1 (hexane), B_2 (C_6H_{14}–EtOAc, 9:1), B_3 (C_6H_{14}–EtOAc, 4:1). Extended purification gave the following compounds (approx. amount): β-caryophyllene (300 mg), isocaryophyllene (500 mg) and humulene (100 mg) from B_1 ($AgNO_3$–Si gel, 1:9; C_6H_6); dammaradienol (500 mg) and sitosterol (150 mg) from B_2 (Al_2O_3, C_6H_6–Me_2CO, 19:1); sesamin (120 mg), betulinic acid (370 mg) and 5,5′-dimethoxysesamin (50 mg) from B_3 (SiO_2 gel, C_6H_6–EtOAc, 9:1).

Residue D (3.4 g) was roughly separated on Si gel into two useful subfractions, D_1 (C_6H_6) and D_2 (C_6H_6–EtOAc, 4:1). Extended purification gave madagascin (20 mg), chrysophanic acid (100 mg) and physcion (50 mg) from D_1 (Si gel, C_6H_6); 2-isoprenylmodin (90 mg), γ-hydroxyferruginin A (200 mg) and betulinic acid (150 mg) from D_2 (Si gel; C_6H_6–EtOAc, 9:1 and 8:2). γ-Hydroxyferruginin A, chrysophanic acid, physcion, sitosterol, betulinic acid, β-caryophyllene, isocaryophyllene and humulene were identified by comparison (IR, ^{1}H NMR, TLC, mmp) with authentic specimens previously isolated in this laboratory.

Madagascin (2). Mp 154–156° (lit. [4] mp 156–157°. UV λ_{max}^{EtOH} nm: 255, 265, 287, 480; ^{1}H NMR (60 MHz, $CDCl_3$): δ 12.03 (1H, *s*), 11.90 (1H, *s*), 7.43 (1H, *d* (*br*), $J = 2$ Hz, H-5), 7.17 (1H, *d*, $J = 2$ Hz, H-4), 6.95 (1H, *d* (*br*), $J = 2$ Hz, H-7), 6.50 (1H, *d*, $J = 2$ Hz, H-2), 5.40 (1H, *t* (*br*), $J = 7$ Hz), 4.58 (2H, *d* (*br*), $J = 7$ Hz), 2.38 (3H, *s*), 1.75 (6H, *s* (*br*)); EIMS (probe) 70 eV, *m/z* (rel. int.): 338 $[M]^+$ (20), 270 $[M-68]^+$ (100).

2-*Isoprenylemodin* (**5**). Mp 242–245° (orange crystals, C_6H_6). UV λ_{max}^{EtOH} nm: 254, 282, 345 (sh), 438; λ_{max}^{AcONa} 530 nm; λ_{max}^{MeONa} 535 nm; $\lambda_{max}^{AlCl_3}$ 535 nm after 25 min. IR ν_{max}^{KBr} cm^{-1}; 1620, 1580, 1480, 1430, 1380, 1335, 1300, 1260, 1230, 1190, 1080, 1040, 880; ^{1}H NMR (60 MHz, C_5D_5N): δ 7.5–7.0 (3H, *m* (*br*)), 5.40 (1H), 3.73 (2H), 2.20 (3H, *s*), 1.78 (6H); EIMS (probe) 70 eV, *m/z* (rel. int.): 338 $[M]^+$ (55), 323 (19), 309 (11), 305 (7), 295 (92), 283 (100), 255 (6).

5 (50 mg) was dissolved in TFA and left to stand overnight. Evaporation of the solvent and purification (Si gel, C_6H_6–EtOAc, 4:1) gave the cyclo compound, **6** (25 mg), mp 183–186° (CH_2Cl_2–C_6H_{14}). ^{1}H NMR (60 MHz, $CDCl_3$): δ 12.58 (1H, *s*), 12.08 (1H, *s*), 7.57 (1H, *d* (*br*), $J = 2$ Hz, H-5), 7.22 (1H, *s*, H-4), 7.0 (1H, *d* (*br*), $J = 2$ Hz, H-7), 2.73 (2H, *t*, $J = 7$ Hz), 2.40 (3H, *s*), 1.83 (2H, *t*, $J = 7$ Hz), 1.37 (6H, *s*).

Dammaradienol (**7**). Mp 132–135° (MeOH), $[\alpha]_D + 43°$ ($CHCl_3$, *c* 0.6) (lit. [8] mp 136–138° $[\alpha]_D + 47$; lit. [10] mp 136°). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610, 2920, 2850, 1630, 1440, 1370, 1200, 1020, 980, 880; ^{1}H NMR (60 MHz, $CDCl_3$): δ 5.17 (1H, *t* (*br*)), 4.73 (2H, *s* (*br*)), 3.23 (1H, X part of ABX), 2.03 (5H, *s* (*br*)), 1.70 (3H, *s*), 1.63 (3H, *s*), 1.0 (6H, *s*), 0.87 (6H, *s*), 0.78 (3H, *s*); EIMS (probe) 70 eV *m/z* (rel. int.): 426 $[M]^+$ (88), 411 (7), 408 (5), 399 (5), 393 (5), 339 (3), 317 (7), 315 (13), 300 (6), 299 (12), 218 (37), 208 (25), 207 (100), 190 (35), 189 (68), 175 (28). Acetylation gave dammaradienyl acetate, mp 148–150° (EtOH) (lit. [10] mp 151°; lit. [8] mp 151–153°). ^{1}H NMR (60 MHz, $CDCl_3$): δ 5.17 (1H, *t* (*br*)), 4.73 (2H, *s* (*br*)), 4.48 (1H, X part of ABX), 2.05 (8H, *s*, OAc + 5 allylic H), 1.71 (3H, *s*), 1.63 (3H, *s*), 0.95 (3H, *s*), 0.87 (12H, *s*).

(±) *Sesamin* (**8**). Mp 126–128° (lit. [13] mp 129–130°), $[\alpha]_D$ 0 ± 5° ($CHCl_3$, *c* 0.5). ^{1}H NMR (60 Mz, $CDCl_3$) identical to the figure in ref. [14]; EIMS (probe) 70 eV *m/z* (rel. int.): 354 $[M]^+$ (64), 336 (1), 323 (7), 219 (5), 203 (31), 189 (10), 178 (18), 161 (58), 149 (100), 135 (71), 131 (47), 122 (40).

(±) 5,5'-*Dimethoxysesamin* (**9**). Amorphous solid, $[\alpha]_D$ 0 ± 5° ($CHCl_3$, *c* 0.4). ^{1}H NMR (60 MHz, CCl_4): δ 6.40 (4H, *s*), 5.87 (4H, *s*, –O–CH_2–O), 4.65 (2H, *d*, $J = 4$ Hz, H-1, H-1'), 4.33–3.68 (4H, *dq*, $J = 9.2$, $J = 7.2$, $J = 3.8$ Hz; H-3, H-3', H-4, H-4'), 3.0 (2H, *m*, H-2, H-2'), 3.87 (6H, *s*). Addition of Eu(fod)$_3$ to a soln of **9** (24 mg) in CCl_4 (0.6 ml) gave the following chemical shifts for the aromatic protons (δ 6.40, *s*, 4H): 10 mg Eu(fod)$_3$, δ 6.63 (*s*); 20 mg Eu(fod)$_3$, δ 7.16 (*d*, $J = 2$ Hz) and δ 7.06 (*d*, $J = 2$ Hz); 27 mg Eu(fod)$_3$, δ 7.63 (*d*, $J = 2$ Hz) and δ 7.48 (*d*, $J = 2$ Hz); EIMS (probe) 70 eV *m/z* (rel. int.): 414 $[M]^+$ (42), 396 (2), 383 (3), 249 (6), 234 (7), 233 (9), 219 (9), 217 (5), 191 (60), 179 (100), 165 (76), 161 (42), 152 (37).

Acknowledgement—Two of us (G.D.M. and R.A.L.) thank the Conselho Nacional de Pesquisas (Brazil) for financial support.

REFERENCES

1. Delle Monache, G., Gonzalez Gonzalez, J., Delle Monache, F. and Marini Bettolo, G. B. (1980) *Phytochemistry* **19**, 2025.
2. Gonzalez Gonzalez, J., Delle Monache, F., Delle Monache, G. and Marini Bettolo, G. B. (1980) *Planta Med.* **40**, 347.
3. Delle Monache, F., Faini Torres, F., Marini Bettolo, G. B. and Alves De Lima, R. (1980) *Lloydia* **43**, 487.
4. Ritchie, E. and Taylor, W. C. (1964) *Tetrahedron Letters* 1431.
5. Ritchie, E., Taylor, W. C. and Shannon, J. S. (1964) *Tetrahedron Letters* 1437.
6. Alves De Lima, R. and Delle Monache, G. (1977–1978) *R. Acad. Naz.* XL (*Rome*) **3**, 181.
7. Ferrari, F., Delle Monache, F., Marini Bettolo, G. B. and Maxfield, P. (1977) *Atti Acad. Naz. Lincei* (*Rome*) **43**, 413.
8. Mills, J. S. (1956) *J. Chem. Soc.* 2196.
9. Yoshioka, I. and Yamada, I. (1963) *Yakugaku Zasshi* **83**, 801.
10. Hui, W. H. and Sung, M. L. (1968) *Aust. J. Chem.* **21**, 2137.
11. Talapatra, S. K., Bhar, D. S. and Talapatra, B. (1974) *Aust. J. Chem.* **27** 1137.
12. Ewan, J. (1962) *U.S. Natl. Mus. Contrib. Natl Herbarium* **35**, 293.
13. Grimshaw, J. (1976) in *Rodd's Chemistry of Carbon Compounds* (Coffey, S., ed) 2nd edn, Vol. 3, Part D, p. 263. Elsevier, Amsterdam.
14. Takahashi, K. and Nokagawa, T. (1966) *Chem. Pharm. Bull.* **14**, 641.