7. Lenherr, A., Fang, N. and Mabry, T. J. (1986) *J. Nat. Prod.* 49, 185.
8. Fang, N., Yu, S. and Mabry, T. J. (1986) *J. Nat. Prod.* (in press).
9. Yu, S., Fang, N. and Mabry, T. J. (1987) *Phytochemistry.* submitted.
10. Mabry, T. J., Markham, K. R. and Thomas, M. B. (1970) *The Systematic Identification of Flavonoids.* Springer, New York.

Phytochemistry, Vol. 26, No. 7, pp. 2133–2135, 1987.
Printed in Great Britain.

0031-9422/87 $3.00 + 0.00

SESQUITERPENE ALKALOIDS FROM THE CELASTRACEAE

ANTONIO G. GONZÁLEZ, CARMEN M. GONZÁLEZ, ISABEL L. BAZZOCCHI, ANGEL G. RAVELO, JAVIER G. LUIS and XORGE A. DOMÍNGUEZ*

Instituto Universitario de Química Orgánica, Universidad de La Laguna, Tenerife, Canary Islands, Spain; * Instituto Tecnológico y de Estudios Superiores de Monterrey, Monterrey, México

(*Received* 17 *October* 1986)

Key Word Index—*Orthosphenia mexicana*; *Rzedowskia tolantonguensis*; Celastraceae; sesquiterpene alkaloids; dihydro-β-agarofuran derivative.

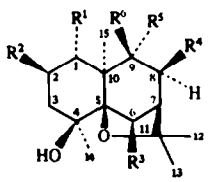
Abstract—The new sesquiterpene alkaloids 1α-benzoyloxy-6β-nicotinoyloxy-9β-acetoxy-4β-hydroxydihydro-β-agarofuran, 1α-cinnamoyloxy-6β-nicotinoyloxy-9β-acetoxy-2β,4β-dihydroxydihydro-β-agarofuran, 1α-benzoyloxy-6β-nicotinoyloxy-8β,9α-diacetoxy-4β-hydroxydihydro-β-agarofuran and 1α-benzoyloxy-6β-nicotinoyloxy-9α-acetoxy-8β,4β-dihydroxydihydro-β-agarofuran were isolated from the aerial part of *Orthosphenia mexicana* and from the root bark of *Rzedowskia tolantonguensis* and their structures determined by spectroscopic and chemical studies.

INTRODUCTION

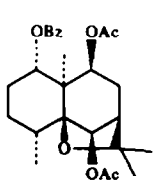
The Celastraceae frequently yield polyester dihydro-β-agarofuran sesquiterpenes [1] and when the ester formation is due to nicotinic acid or its derivatives, these sesquiterpenes are termed Celastraceae alkaloids [2]. From the American Celastraceae, sesquiterpenes [3], diterpenes [3], triterpenes [4] and triterpene quinone methides [5] have been isolated. The alkaloid-containing fractions of *Orthosphenia mexicana* [6] and *Rzedowskia tolantonguensis* [7], plants endemic to north-eastern Mexico, have now been analysed.

RESULTS

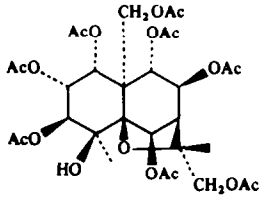
Compound 1 was assigned the structure 1α-benzoyloxy-6β-nicotinoyloxy-9β-acetoxy-4β-hydroxydihydro-β-agarofuran based on the following data. It was isolated as a crystalline solid, mp 139–141°, molecular formula $C_{30}H_{35}O_8N$. The IR spectrum showed hydroxyl and ester group bands; the alcohol grouping was tertiary since it could not be acetylated under normal conditions. The mass spectrum suggested the presence of a nicotinate with fragments at *m/z* 124 and 106, a benzoate fragment at *m/z* 105 and an acetate fragment at *m/z* 42 [8]. The ^{1}H NMR spectrum showed signals corresponding to the protons of a nicotinate with the geminal proton at δ 5.66 as a singlet, a benzoate with the geminal proton centred at 5.35 as a double doublet (J = 4.0, 12.0 Hz) an acetate methyl at 1.62 with the geminal proton at 5.08 as a doublet (J = 6.5 Hz) and four angular methyls as singlets at 1.34, 1.41, 1.50 and 1.51. Analysis of the above data character-



	R¹	R²	R³	R⁴	R⁵	R⁶
1	OBz	H	ONic	H	H	OAc
2	OCinn	OH	ONic	H	H	OAc
3	OCinn	OAc	ONic	H	H	OAc
4	OBz	H	ONic	OAc	OAc	H
5	OBz	H	ONic	OH	OAc	H
6	OBz	H	OH	OH	OAc	H
7	OH	H	OH	OH	OH	H
8	OAc	H	OH	OAc	OH	H
10	OCinn	OH	OAc	H	H	OAc



9



11

ized a polyester dihydro-β-agarofuran sesquiterpene. Comparison of the ^{1}H NMR data of **1** with those of celorbicol ester A (**9**) [9], the structure of which was established by X-ray analysis, located a benzoate at C-1α, an acetate at C-9β and the remaining nicotinate at C-6β (Table 1). These assignments were later confirmed by double resonance experiments.

Product **2** was obtained as an amorphous solid. The IR spectrum showed alcohol and ester bands. Its mass spectrum showed fragments indicative of cinnamate at *m/z* 148, acetate and nicotinate. This was confirmed by ^{1}H NMR spectral studies where the acetate methyl appeared as a singlet at δ1.94 with the geminal proton as a doublet at 4.88 (J = 6.6 Hz). The aromatic protons of the nicotinate grouping were observed as were the vinyl protons; the geminal proton appeared as a broad singlet at 5.63. A proton geminal to a secondary alcohol group appeared at 3.68 (*m*) which was coupled with the cinnamate group geminal proton. We have previously identified sesquiterpene **10** [10], which is similar to **2** but differing in the group to be found at C-6 which is an acetate in the case of **10** and a nicotinate in **2**. The comparison of the two compounds allowed the identification of **2**. When **2** was treated with acetic anhydride in pyridine at room temperature the ester **3** was produced (Table 1).

Product **4** was isolated as a solid which crystallized in needles, mp 114–116°. The mass spectrum had the highest fragment at *m/z* 580, corresponding to the loss of a methyl from the molecular ion and other fragments suggesting the presence of two acetates, a benzoate and a nicotinate. The ^{1}H NMR spectrum showed signals for two acetate groups at δ1.46 and 1.87 and four methyls at 1.32, 1.48, 1.50 and 1.68. From the ^{1}H NMR data (Table 1) it could be deduced that a benzoate group should be found at C-1α and a nicotinate at C-6β. From double resonance experiments the two acetate groups were assigned to C-8β and C-9α, since the coupling constants J_{8-9} indicated the same configuration for these groups as in isoeuonyminol octa-acetate (**11**) [11, 12]. Therefore, the structure of **4** was defined as 1α-benzoyloxy-6β-nicotinoyloxy-8β,9α-diacetoxy-4β-hydroxydihydro-β-agarofuran.

Product **5** was identified as 1α-benzoyloxy-6β-nicotinoyloxy-9α-acetoxy-8β,4β-dihydroxydihydro-β-agarofuran from its spectroscopic data and chemical correlation with **4**. Acetylation of **5** yielded **4**.

The partial hydrolysis of **5** with triethylamine at 5° led to the denicotinoyl derivative **6**. In its ^{1}H NMR spectrum there was no singlet at δ5.88, as was present in the spectrum of **5**, while a new doublet appeared centred at 4.85 (J = 5.2 Hz) corresponding to the proton geminal to the hydroxyl group at C-6 which was coupled with the hydroxyl proton. The structure of **6** was thus determined as 1α-benzoyloxy-9α-acetoxy-4β,6β,8β-trihydroxydihydro-β-agarofuran. Total hydrolysis of **5** gave the product **7** which, when acetylated, yielded the diacetate **8**, with ester formation only at C-1α and C-8β (Table 1).

EXPERIMENTAL

Mps are uncorr. ^{1}H NMR spectra were obtained using $CDCl_3$ as solvent, unless otherwise stated. IR spectra were taken in $CHCl_3$. Dry chromatography was carried out on silica gel 0.05–0.2 mm. Voucher specimens of *Orthosphenia mexicana* and *Rzedowskia tolantonguensis* have been lodged with the Biology Department of the Instituto Tecnológico y de Estudios Superiores de Monterrey, Mexico, nos 7723 and 7853, respectively. The aerial part of *Orthosphenia mexicana* was extracted with MeOH and after filtering and solvent evapn, yielded 26 g of extract. The root bark of *Rzedowskia tolantonguensis* was extracted with *n*-hexane and 3.2 g obtained. Both extracts were subjected to repeated chromatography with mixtures of petrol–EtOAc as eluent. From *O. mexicana* the following products were isolated: 1α-benzoyloxy-6β-nicotinoyloxy-9β-acetoxy-4β-hydroxydihydro-β-agarofuran (**1**) (5 mg); 1α-cinnamoyloxy-6β-nicotinoyloxy-9β-acetoxy-2β,4β-dihydroxydihydro-β-agarofuran (**2**) (20 mg); 1α-benzoyloxy-6β-nicotinoyloxy-9α-acetoxy-4β,8β-dihydroxydihydro-β-agarofuran(**5**) (25 mg). From *R. tolantonguensis* were isolated: (**1**) (20 mg) and 1α-benzoyloxy-6β-nicotinoyloxy-8β,9α-diacetoxy-4β-hydroxydihydro-β-agarofuran (**4**) (20 mg).

1α-Benzoyloxy-6β-nicotinoyloxy-9β-acetoxy-4β-hydroxydihydro-β-agarofuran (**1**). Mp 139–148°. $[M]^+$ at *m/z* 537.2383 (calc. for $C_{30}H_{35}O_8N$ 537.2359). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3540, 3000, 2948, 2920, 2845, 1720, 1590, 1450, 1384, 1365, 1278, 1258, 1235, 1135, 1108, 1090, 1023, 965. ^{1}H NMR (200 MHz): δ1.34 (3H, *s*), 1.41 (3H, *s*), 1.50 (3H, *s*), 1.51 (3H, *s*), 1.62 (3H, *s*), 2.34 (1H, *d*, J = 3.0 Hz), 3.01 (1H, *s*), 5.08 (1H, *d*, J = 6.5 Hz), 5.32 and 5.35 (1H, *dd*, J = 4.0, 12.0 Hz), 5.66 (1H, *s*), 7.46 (4H, *m*), 8.05 (2H, *m*), 8.48 (1H, *m*), 8.78 (1H, *d*, J = 4.0 Hz), 9.35 (1H, *br s*). EIMS *m/z* (rel. int.): 537 $[M]^+$ (1), 452 (4), 451 (14), 400 (4), 354 (2), 232 (4), 228 (4), 175 (4), 149 (18), 135 (5), 124 (25), 119 (4), 106 (74), 105 (100), 95 (7), 81 (7), 77 (27).

1α-Cinnamoyloxy-6β-nicotinoyloxy-9β-acetoxy-2β,4β-dihydroxydihydro-β-agarofuran (**2**). Amorphous solid. $[M - CH_3COOH]^+$ at *m/z* 519.2184 (calc. for $C_{30}H_{33}O_7N$ 519.2255). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3540, 3000, 2945, 2920, 2840, 1720, 1630, 1445, 1365, 1280, 1245, 1160, 1135, 1020. ^{1}H NMR (200 MHz): δ1.39 (3H, *s*), 1.42 (3H, *s*), 1.53 (6H, *s*), 1.94 (3H, *s*), 3.68 (1H, *m*), 4.88 (1H, *d*, J = 6.6 Hz), 5.41 (1H, *d*, J = 10.6 Hz), 5.63 (1H, *br s*), 6.41 (1H, *d*, J = 16.0 Hz), 7.40 (4H, *m*), 7.57 (2H, *m*), 7.71 (1H, *d*, J = 16.0 Hz), 8.49 (1H, *d*, J = 8.4 Hz), 8.80 (1H, *m*), 9.35 (1H, *m*). EIMS *m/z* (rel. int.): 579 $[M]^+$ (0.3), 564 (0.2), 546 (2), 504 (1), 493 (3), 450 (3), 438 (3), 416 (7), 371 (5), 328 (7), 290 (9), 248 (9), 230 (6), 182 (7), 167 (5), 151 (13), 124 (70), 103 (43).

1α-Cinnamoyloxy-6β-nicotinoyloxy-2β,9β-diacetoxy-4β-hydroxydihydro-β-agarofuran (**3**). Compound **2** (15 mg, 0.026 mmol) was treated with Ac_2O in pyridine and extracted with EtOH in the usual way, yielding **3** (10 mg, 0.016 mmol, yield 62%) as an amorphous solid. ^{1}H NMR (200 MHz): δ1.42 (3H, *s*), 1.45 (3H, *s*), 1.50 (6H, *s*), 1.84 (3H, *s*), 1.96 (3H, *s*), 3.13 (1H, *br s*), 4.84 (1H, *d*, J = 6.0 Hz), 4.93 (1H, *m*), 5.62 (1H, *br s*), 5.64 (1H, *d*, J = 10.0 Hz), 6.43 (1H, *d*, J = 16.0 Hz), 7.35 (4H, *m*), 7.56 (2H, *m*), 7.67 (1H, *d*, J = 16.0 Hz), 8.48 (1H, *br s*). EIMS *m/z* (rel. int.): 621 $[M]^+$ (1), 606 (1), 563 (1), 535 (5), 488 (2), 458 (5), 426 (2), 290 (3), 273 (3), 226 (1), 149 (29), 124 (23), 106 (44), 105 (65), 103 (26), 95 (22), 81 (23), 77 (24).

1α-Benzoyloxy-6β-nicotinoyloxy-8β,9α-diacetoxy-4β-hydroxydihydro-β-agarofuran (**4**). Mp 114–116°. $[M-15]^+$ at *m/z* 580.2233 (calc. for $C_{31}H_{34}O_{10}N$ 580.2179). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3660, 3550, 2950, 2860, 1725, 1585, 1445, 1365, 1330, 1275, 1175, 1105, 1065, 1045, 1025. ^{1}H NMR (200 MHz): δ1.32 (3H, *s*), 1.46 (3H, *s*), 1.48 (3H, *s*), 1.50 (3H, *s*), 1.68 (3H, *s*), 1.87 (3H, *s*), 2.64 (1H, *d*, J = 3.0 Hz), 2.85 (1H, *s*), 5.11 and 5.17 (1H, *dd*, J = 4.0, 12.0 Hz), 5.37 and 5.42 (1H, *dd*, J = 3.3 and 10.0 Hz), 5.79 (1H, *s*), 5.97 (1H, *d*, J = 10.0 Hz), 7.46 (4H, *m*), 8.01 (2H, *m*), 8.46 (1H, *m*), 8.78 (1H, *m*), 9.34 (1H, *d*, J = 1.6 Hz). EIMS *m/z* (rel. int.): 595 $[M]^+$ (1), 581 (2), 536 (2), 535 (3), 510 (5), 509 (15), 474 (2), 271 (14), 228 (5), 148 (10), 124 (43), 106 (74), 105 (100), 95 (7), 77 (27).

1α-Benzoyloxy-6β-nicotinoyloxy-9α-acetoxy-8β,4β-dihydroxydihydro-β-agarofuran (**5**). Mp 184–186°. $[M]^+$ at *m/z*

Table 1. ^{1}H NMR spectral data*

Compound	H-1	H-2	H-6	H-7	H-8	H-9	Ac-1	Ac-2	Ac-8	Ac-9
1	5.35		5.66			5.08				1.62
	(*dd*, 4.0, 12.0)		(*s*)			(*d*, 6.5)				(*s*)
2	5.41	3.68	5.63			4.88				1.94
	(*d*, 10.6)	(*m*)	(*br s*)			(*d*, 6.6)				(*s*)
3	5.64	4.93	5.62			4.84		1.84		1.96
	(*d*, 10.0)	(*m*)	(*br s*)			(*d*, 6.0)		(*s*)		(*s*)
4	5.14		5.79	2.64	5.40	5.97			1.87	1.46
	(*dd*, 4.0, 12.0)		(*s*)	(*d*, 3.0)	(*dd*, 3.3, 10.0)	(*d*, 10.0)			(*s*)	(*s*)
5	5.27		5.88	2.79	4.47	6.06				1.87
	(*dd*, 4.0, 12.0)		(*s*)	(*d*, 2.6)	(*dd*, 2.6, 9.0)	(*d*, 9.0)				(*s*)
6	5.10		4.85	2.47	3.93	5.77				1.68
	(*dd*, 4.0, 10.0)		(*d*, 5.2)	(*d*, 3.0)	(*m*)	(*d*, 9.0)				(*s*)
8	5.20		5.14	2.44	4.76	4.33	2.07		2.01	
	(AB, *d*, 4.0 Hz)		(*d*, 5.0)	(*d*, 3.0)	(*dd*, 3.0, 10.0)	(*d*, 8.0)	(*s*)		(*s*)	

*Run in $CDCl_3$ at 200 MHz. Values are in δ. Multiplicities and coupling constants (Hz) are given in parentheses.

553.2311 (calc. for $C_{30}H_{35}O_9N$ 553.2386). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 3540, 3000, 2945, 1720, 1588, 1445, 1365, 1275, 1110, 1023, 1003. ^{1}H NMR (200 MHz, C_2D_6O): δ1.50 (3H, *s*), 1.60 (3H, *s*), 1.64 (3H, *s*), 1.70 (3H, *s*), 1.87 (3H, *s*), 2.79 (1H, *d*, J = 2.6 Hz), 2.84 (1H, *s*), 4.45 and 4.49 (1H, *dd*, J = 2.6, 9.0 Hz), 5.24 and 5.30 (1H, *dd*, J = 4.0, 12.0 Hz), 5.88 (1H, *s*), 6.06 (1H, *d*, J = 9.0 Hz), 7.46 (4H, *m*), 8.01 (2H, *m*), 8.46 (1H, *m*), 8.78 (1H, *br s*), 9.34 (1H, *br s*). EIMS *m/z* (rel. int): 553 [M]$^+$ (1), 539 (1), 538 (2), 535 (1), 520 (2), 467 (9), 305 (10), 271 (12), 259 (9), 148 (9), 124 (39), 121 (8), 105 (100), 95 (10), 77 (23).

Acetate of compound 5. Compound 5 (25 mg, 0.045 mmol) was treated with Ac_2O in pyridine and after usual extraction, yielded 4 (12 mg, 0.020 mmol, yield 45%).

Hydrolysis of compound 5. Compound 5 (78 mg, 0.141 mmol) was dissolved in MeOH (3 ml) and treated with 0.2 ml of triethylamine at 5° for 16 hr, taken to dryness and chromatographed, yielding 5 (30 mg) and 6 (30 mg, 0.067 mmol, yield 48%).

1α-Benzoyloxy-9α-acetoxy-6β,8β,4β-trihydroxydihydro-β-agarofuran (6). ^{1}H NMR (200 MHz): δ1.35 (3H, *s*), 1.40 (3H, *s*), 1.54 (3H, *s*), 1.57 (3H, *s*), 1.68 (3H, *s*), 2.47 (1H, *d*, J = 3.0 Hz), 3.14 (1H, *br s*), 3.93 (1H, *m*), 4.40 and 5.29 (2H, *d*, J = 5.2 Hz), 5.07 and 5.12 (1H, *dd*, J = 4.0, 10.0 Hz), 5.77 (1H, *d*, J = 9.0 Hz). EIMS *m/z* (rel. int.): 433 [M − 15]$^+$ (17), 415 (2), 388 (1), 370 (2), 355 (6), 293 (5), 202 (19), 166 (28), 149 (56), 105 (100).

Hydrolysis of compound 6. Compound 6 (19 mg) dissolved in MeOH (12 ml) and C_6H_6 (5 ml), was heated under reflux for 2 days, the volume was reduced under lowered pressure, the substance was poured into H_2O and extracted with EtOAc in the usual manner and after purification yielded 10 mg of 7.

Acetate of compound 7. Compound 7 (10 mg) was treated with Ac_2O in pyridine and extracted with EtOAc in the usual manner, yielding 8 (2 mg).

1α,8β-Diacetoxy-6β,9α,4β-trihydroxydihydro-β-agarofuran (8). ^{1}H NMR (200 MHz): δ1.15 (3H, *s*), 1.49 (3H, *s*), 1.51 (3H, *s*), 1.56 (3H, *s*), 2.01 (3H, *s*), 2.07 (3H, *s*), 2.44 (1H, *d*, J = 3.0 MHz), 4.33 (1H, *d*, J = 8.0 Hz), 4.39 and 5.14 (2H, *d*, J = 5.0 Hz), 4.74 and 4.79 (1H, *dd*, J = 3.0, 10.0 Hz), 5.19 and 5.22 (1H, *dd*, J_{AB} = 4.0 Hz). EIMS *m/z* (rel. int.): 371 [M − 15]$^+$ (2), 368 (1), 353 (1), 326 (2), 311 (2), 308 (3), 251 (4), 248 (4), 233 (5), 205 (8), 191 (9), 149 (10), 109 (25), 98 (53), 83 (26).

Acknowledgements—To CAICYT grant no. 0694-84 and AIETI Foundation for partial financial support.

REFERENCES

1. Brüning, R. and Wagner, H. (1978) *Phytochemistry* **17**, 1821.
2. Manske, R. H. F. (1977) *The Alkaloids*, Vol. 16, p. 215. Academic Press, New York.
3. Bazzocchi, I. L. (1986) Ph.D. thesis, Universidad de La Laguna.
4. González, A. G., González, C. M., Ravelo, A. G., Domínguez, X. A. and Fraga, B. M. (1986) *J. Nat. Prod.* **49**, 148.
5. González, A. G., Fraga, B. M., González, C. M., Ravelo, A. G., Ferro, A., Domínguez, X. A., Martínez, M. A., Fayos, J., Perales, A. and Rodríguez, M. L. (1983) *Tetrahedron Letters* **24**, 3033.
6. Rzedowsky, J. (1975) *Ciencia (México)* **16**, 139.
7. González-Medrano, F. (1981) *Bol. Soc. Botánica México* 41.
8. Baudoin, G., Tillequin, F., Koch, M., Tran Hun Dan, M., Guilben, J. and Jacquemin, H. (1984) *Heterocycles* **22**, 2221.
9. Smith, C. R., Jr., Hiller, R. W., Weisleder, D., Rohwedder, W. K., Eickman, N. and Clardy, J. (1976) *J. Org. Chem.* **41**, 3264.
10. González, A. G., González, C. M., Ravelo, A. G., Fraga, B. M. and Domínguez, X. A. *Heterocycles* (in press).
11. Shizury, Y., Wada, H., Sugiura, K., Yurada, K. and Hirata, Y. (1973) *Tetrahedron* **29**, 1773.
12. González, A. G., Bazzocchi, I. L., Ravelo, A. G., Luis, A. G., Domínguez, X. A. *Heterocycles* (in press).