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A SESQUITERPENE EVONINOATE ALKALOID FROM *MAYTENUS GUIANENSIS*

JOSÉ R. DE SOUSA, JOSÉ A. PINHEIRO, ELAINE F. RIBEIRO, EDWARD DE SOUZA and J. GUILHERME S. MAIA*

Departamento de Química da Universidade Federal de Minas Gerais, 30.000-Belo Horizonte, MG, Brazil; *Instituto Nacional de Pesquisas da Amazônia, CNPq, 69.000-Manaus, Am, Brazil

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Key Word Index—*Maytenus guianensis*; Celastraceae; chichuá; root; alkaloid; mayteine.

Abstract—The trunk wood and root of *Maytenus guianensis* contain 4'-*O*-methyl-(−)-epigallocatechin, proanthocyanidin A, dulcitol, sitosterol, β-sitostenone and friedelan-3,7-dione. The trunk wood also furnished *N*,*N*-dimethylserine. A new sesquiterpene alkaloid, named mayteine, was isolated from the root.

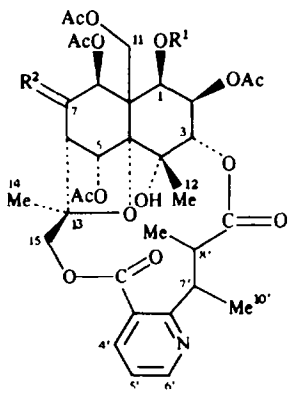
INTRODUCTION

Various sesquiterpene alkaloids have been isolated from members of Celastraceae. Thus euonymine (**1**), evonine (**4**) and wilfordine (**2**) were isolated from the fruits of *Euonymus alatus* [1]. Compounds **1** and **4** are sesquiterpene polyesters of the evoninic acid, and compound **2** is a polyester of the wilfordic acid.

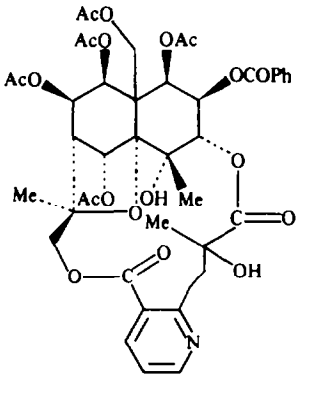
In the present study we describe the isolation and structural determination of mayteine, a new sesquiterpene alkaloid from the root of *Maytenus guianensis*, a celastraceous tree from the Manaus region of Amazonas State, Brazil, known as 'chichuá'. Mayteine (**3**) was recognized to be a benzoyleuonymine by comparison of its ^{1}H NMR data with those of euonymine (**1**) [2], evonine (**4**) [3] and wilfordine (**2**) [1].

RESULTS AND DISCUSSION

The structural proposal for mayteine (**3**) with a characteristic evoninoate moiety is consistent with the spectroscopic properties of this alkaloid. The IR, UV and ^{1}H NMR spectra indicated an aromatic partial structure. The IR spectrum contained bands assignable to a monosubstituted benzene ring (710 cm^{-1}), hydroxyl (3490 cm^{-1}) and an ester carbonyl (1750–1730 cm^{-1}, br). The UV absorption spectra of **3** in ethanol [λ_{max} 269 (log ε 3.79) and 233 nm (log ε 4.30)] as well as in 1% hydrochloric acid [λ_{max} 269 (log ε 3.92) and 235 nm (log ε 4.20)] are almost identical with those of wilfordine (**2**) [4] in the two respective solvents from 220 to 300 nm, thereby demonstrating the similarity of the chemical structure of these two compounds.



	R^1	R^2	
1	Ac	β-OAc, α-H	(euonymine)
3	COPh	β-OAc, α-H	(mayteine)
4	Ac	O	(evonine)



2 (wilfordine)

The mass spectral fragmentation pathways of **3** and evonine (**4**) [5] correspond well with each other. However, in addition to the fragments at *m/z* 206 (54%) and 107 (93%) from the evoninoate moiety, the spectrum of **3** exhibited further peaks at *m/z* 105 (benzoyl, 100%), 866 $[M-H]^+$ (14%) and 867 $[M]^+$ (6%).

The ^{1}H NMR spectrum of **3** showed the presence of five acetate groups (3H each, *s*, δ1.72, 2.12, 2.16, 2.22, 2.35), one benzoate (δ7.85 *dd*, J = 8.0 and 1.5 Hz, 7.56 *m*, and 7.43 *t*, J = 8.0 Hz) and one hydroxyl group (δ4.54, disappeared on addition of D_2O). ^{1}H NMR spectral data of **3**, **1**, **2** and **4** are listed in Table 1, which shows that these four compounds are closely related. The ^{1}H NMR spectra of **3** and **4** clearly showed that **3** was an evoninic acid derivative (cf. signals of H-4′–H-11′, Table 1).

The substitution pattern of the sesquiterpene part of **3** was identified through ^{1}H NMR spectral comparison ($CDCl_3$) with **1** and **2** (Table 1). The signals of H-1, H-2, H-8 and H-11 in **3** were observed in a field region significantly lower than that of the corresponding protons in **1**, indicating that the benzoate group was located on one of the possible four positions, C-1, C-2, C-8 and C-11.

The following result from the ^{1}H NMR spectra is consistent with the position of the benzoate group at C-1. The signal due to H-1 appeared at δ5.90 in **3**, whereas the signal of H-1 in **2** was observed with a significant shift to a higher field (δ5.75). Furthermore it was observed that the signals due to H-2 and H-3 in **3** appeared in a field region higher (δ5.36 and 4.80, respectively) than those on wilfordine (**2**) (δ5.49 and 5.08, respectively). This inference is consistent with the chemical shift values of methynes of three monobenzoates synthesized from **4** in which the acetyl group at C-1, C-2 and C-11 was substituted by a benzoyl group [δ6.07 (H-1), 5.57 (H-2) and 4.99 *s* (H-11), respectively] [6].

Couplings were confirmed by double resonance experiments at 400 MHz with spectrum expansion of the following protons: H-1, δ5.90 (H-2, *d*, $J_{2,3}$ = 2.5 Hz);

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

H	1	2	3†	4
1	5.55 (*d*, 4.0)	5.75 (*d*, 3.0)	5.90 (*d*, 4.0)	
2	5.23 (*dd*, 4.0, 2.5)	5.49 (*dd*, 3.0, 3.0)	5.36 (*dd*, 4.0, 2.5)	
3	4.72 (*d*, 2.5)	5.08 (*d*, 3.0)	4.80 (*d*, 2.5)	
5	7.02 (*d*, 1.0)	6.84 (*s*)	7.09 (*br s*)	
6	2.33 (*dd*, 3.8, 1.0)	2.39 (*d*, 4.0)	2.37 (*br d*, 4.0)	
7	5.51 (*dd*, 6.2, 3.8)	5.58 (*dd*, 6.0, 4.0)	5.53 (*dd*, 6.0, 4.0)	
8	5.34 (*d*, 6.2)	5.39 (*d*, 6.0)	5.43 (*d*, 6.0)	
11	4.50–5.13 (ABq, 13.5)	4.40–5.58 (ABq, 14.0)	4.70–5.34 (ABq, 13.5)	
15	3.72 (*d*, 12.0)	3.75 } (ABq, 12.0)	3.72 (*d*, 12.0)	
15	5.94 (*br d*, 12.0)	5.81 }	5.95 (*br d*, 12.0)	
4′			8.10 (*dd*, 8.0, 2.0)	8.07 (*dd*, 8.0, 2.0)
5′			7.28 (*dd*, 8.0, 2.0)	7.25 (*dd*, 8.0, 2.0)
6′			8.73 (*dd*, 4.5, 2.0)	8.69 (*dd*, 4.5, 2.0)
7′			4.54 (*br*)	~4.69 ($J_{7',8'} \neq 0$)
8′			2.60 (*q*, 7.0)	2.58 (*q*, 7.0)
10′			1.41 (*d*, 7.0)	1.41 (*d*, 7.0)
11′			1.22 (*d*, 7.0)	1.22 (*d*, 7.0)

*Chemical shifts (in δ values) relative to internal TMS. Multiplicities and coupling constants (Hz) are given in parentheses. Spectra were taken in $CDCl_3$ at 100 MHz (1), 60 MHz (2) and 400 MHz (3).

†The signals due to H-12 and H-14 appeared at 1.60 (*d*, 1.0) and 1.43 (*s*).

H-3, 4.80 (H-2, *d*, $J_{1,2} = 4.0$ Hz; H-7, 5.53 (H-8, *br s*); H-15, 3.72 (H-15 at δ5.95 *s*); H-11, 4.70 (H-11 at δ5.34 *s*) and H-8′, 2.60 (H-11's and H-7′ perturbed).

It should be noted that the optical rotations of **3** $[\alpha]_D^{25}$ −9.36° ($CHCl_3$; *c* 0.47), **1** $[\alpha]_D^{20}$ −20° ($CHCl_3$; *c* 0.32) [2] and neoeuonymine $[\alpha]_D^{20}$ −11° ($CHCl_3$; *c* 0.49) [2] are closely related.

Therefore, we accept the structure **3** as the most probable for mayteine.

EXPERIMENTAL

All mps are uncorr. IR spectra were taken in KBr discs. ^{1}H NMR spectra were determined at 100 MHz, and at 400 MHz in the Institut d'Electronique Université Paris XI-Centre d'Orsay.

Root wood of *M. gulanensis* Klotzch was reduced to powder (2 kg), exhaustively extracted with EtOH at room temp. and then extracted with the same solvent in a Soxhlet. The concd hot EtOH extract was filtered, affording dulcitol (3.2 g) (*Schaefferia cuneifolia* A. Gray, Celastraceae) [7], identified by direct comparison with authentic specimen.

The EtOH extract (248 g) obtained at room temp. was chromatographed on a silica gel column. The $CHCl_3$–MeOH (9:1) fraction was evapd and the residue, which gave a positive reaction with Dragendorff's reagent, was purified over a neutral alumina column with $CHCl_3$ to give mayteine (**3**) (0.81 g), a white amorphous solid, mp 172–175°. (Found: C, 59.38; H, 5.59; N, 1.40. $C_{43}H_{49}NO_{18}$ requires: C, 59.51; H, 5.69; N, 1.61%.) $CHCl_3$–MeOH (8:3) eluted 4′-*O*-methyl-(−)-epigallocatechin (0.93 g) and $CHCl_3$–MeOH (4:1) eluted proanthocyanidin A (0.20 g) (*Maytenus rigida*, Celastraceae) [8]; their identities were ascertained by IR, ^{1}H NMR, MS, mp and were also characterized as Me and acetyl derivatives.

Root bark was reduced to powder (1.76 kg) and extracted successively with *n*-hexane, which removed a mixture of sitosterol and β-sitostenone (0.24 g), and with EtOAc. The EtOAc extract (240 g) was chromatographed on a silica gel column. The *n*-hexane–C_6H_6 (2:3) fraction afforded 1.2 g of friedelan-3,7-dione (putranjivadione, *Putranjiva roxburghii*, Euphorbiaceae), which was identified by a combination of chemical and physical methods. White needles, mp 282–284° (C_6H_6–$CHCl_3$), lit. [9] mp 284–289° ($CHCl_3$–Me_2CO); IR ν_{max} cm^{-1}: 1720 (sh), 1710. MS *m/z* (rel. int.): 440 $[M]^+$ (100), 425 (21), 288 (7), 207 (17), 205 (54). ^{1}H NMR (60 MHz, $CDCl_3$): δ0.78, 0.87, 0.90, 0.97, 1.00, 1.05, 1.20, 1.30 (Me), 1.40–2.85 (CH_2, CH). Putranjivadione was converted to putranjivadiol ($LiAlH_4$), friedelan-3-ol-7-one ($NaBH_4$), friedelan-7-one (Huang–Minlon) and friedelan-7-ol, spectral data as required by lit. [9].

Trunk wood was reduced to powder (11 kg) and extracted with EtOH. The concd EtOH extract was filtered and the residue furnished *N,N*-dimethylserine (2.3 g) by exhaustive extraction with hot MeOH. Amorphous solid, mp > 300°; MS *m/z* (rel. int.): 133 $[M]^+$ (40) ($C_5H_{11}NO_3$ by HRMS); ^{1}H NMR (60 MHz, TFA–D_2O): δ3.00 (*s*, 3H), 3.10 (*s*, 3H), 3.85–4.20 (3H, *m*) and dulcitol (30 g). The mother liquor from the EtOH extract was evapd and the residue chromatographed on a silica gel column to afford sitosterol (0.24 g), 4′-*O*-methyl-(−)-epigallocatechin (12.0 g) and proanthocyanidin A (7.23 g). The EtOH bark wood extract (6.5 g) was also chromatographed on a silica gel column and afforded friedelan-3,7-dione (0.025 g).

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