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FUNEBRADIOL, A NEW PYRROLE LACTONE ALKALOID FROM *QUARARIBEA FUNEBRIS* FLOWERS

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ABSTRACT.—The flowers of *Quararibea funebris* have yielded another new pyrrole lactone alkaloid, named funebradiol [**1**]. This compound was elucidated by the use of nmr, ir, and mass spectral interpretation. A potentially new biosynthetic pathway is postulated.

The Zapotec Indians of Oaxaca, Mexico use the fragrant flowers of *Quararibea funebris* (Llave) Visher (Bombacaceae) to flavor various chocolate beverages. It is known locally as ponzonque and elsewhere as tejate (1). Medicinally the flowers are utilized by the indigenous people as an antipyretic, as a cough remedy, to control "psychopathic fears," and to regulate menstruation (2). The genus as a whole has received very little attention from a phytochemical standpoint. Previous investigations uncovered a new structural class of pyrrole alkaloids (3–5). Substitution on the pyrrole occurs at the 1, 2, and 5 positions with the unique substitution at position 1 of a γ-butyrolactone moiety. Funebral [**2**] is representative (5). In a continuing investigation of the species, an additional new pyrrole lactone alkaloid, named funebradiol [**1**], has been isolated and characterized.

The amorphous solid was isolated from the basic fraction of a 95% EtOH extract of the flowers using Si gel chromatography. The low resolution ei mass spectrum produced a weak molecular ion at *m/z* 237 and a strong ion at *m/z* 219 $[M-H_2O]^+$. Glycerol fabms gave *m/z* 260 $[M+Na]^+$, and fdms showed *m/z* 237. Hreims gave *m/z* 219.0887, which requires 219.0896 for $C_{12}H_{13}NO_3$ $[M-H_2O]^+$. Eims and fabms both produced *m/z* 111, which is a diagnostic fragment for the lactone portion of the molecule. Also an additional fragment at *m/z* 174 $[219-CO_2H]^+$ was found in the eims, typical for γ-lactones (4). The uv spectrum (MeOH) gave absorptions for two separate chromophores: $\lambda = 219$ nm indicating the α, β unsaturated γ-lactone and $\lambda = 266$ nm for the pyrrole moiety. The ir spectrum exhibited absorptions at 3370 cm^{-1} and 1745 cm^{-1}, indicating the presence of a hydrogen-bonded hydroxyl group and a conjugated γ-lactone carbonyl, respectively. The 470 MHz ^1H nmr (Table 1) gave a relatively simple first-order spectrum showing the pyrrole protons H-3 and H-4 at 6.13 ppm (d, $J = 3.1$ Hz) and 6.21 ppm (d, $J = 3.1$ Hz) respectively. The two nonequivalent hydroxymethyl protons occur at 4.56 ppm and 4.36 ppm. The lactone portion of the structure gave ^1H- and ^{13}C-nmr values very similar to the co-occurring quabalactone III (Table 1, Figure 1). The carbon spectrum gave rise to four pyrrole carbons with the α carbons at 153.9 and 152.4 ppm and the β carbons at 107.5 and 108.1 ppm. The hydroxymethyl carbons appear at two significantly different areas of the spectrum (56.6 ppm and 41.7 ppm). This observation may be explained by the shielding effect caused by intramolecular hydrogen bonding: when one of the hydroxyl groups hydrogen bonds to the carbonyl in the lactone, the other hydroxymethyl group is positioned in very close proximity to the olefinic methyl group. This

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TABLE 1. ^{1}H- and ^{13}C-nmr Shifts[a] of Funebradiol [**1**], Funebral [**2**] and Quabalactone III [**3**].

Atom	Compound					
	1[b]		**2**		**3**	
	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C
1	—	—	—	—	—	170.8
2	—	152.4	—	132.1	3.45 (NH_2)	129.0
3	6.13 (d, 3.1)	107.5	6.29 (d, 3.6)	111.0	—	128.1
4	6.21 (d, 3.1)	108.1	7.02 (d, 3.6)	126.1	4.75 (q, 6.0)	78.6
5	—	153.9	—	142.6	1.35 (d, 6.0)	18.6
6a	4.56 (s)	56.6	4.66 (d, 13.6)[c]	56.5	1.80 (d, 1.0)	9.8
6b	4.56 (s)	56.6	4.73 (d, 13.6)[c]	56.5		
7	4.36 (s)	41.7	9.44 (s)	178.9		
8	—	171.4	—	172.2		
9	—	130.2	5.05 (d, 11.3)	62.7		
10	—	128.6	2.76 (d,d,q, 11.3, 9.4, 6.6)	43.5		
11	4.73 (q,q, 6.6, 1.2)	79.0	4.27 (d,q, 9.4, 6.1)	80.7		
12	1.35 (d, 6.6)	18.5	1.61 (d, 6.1)	18.4		
13	1.92 (d, 1.2)	10.5	1.15 (d, 6.6)	14.7		

[a]All chemical shifts are in ppm using $CDCl_3$ solvent except as noted with TMS as the internal reference. Multiplicities and coupling constants (Hz) of proton resonances are in parentheses. Compounds **1** and **2** were run at 470 MHz for ^{1}H nmr and 50 MHz for ^{13}C nmr. Compound **3** was run at 60 MHz for ^{1}H nmr and 15 MHz for ^{13}C nmr.

[b]^{13}C and ^{1}H assignments for atoms 3 and 4, as well as the ^{13}C assignments for atoms 2 and 5 and 9 and 10 in funebradiol, may be interchanged.

[c]These values may be interchanged.

steric hindrance produces a dramatic shielding effect of the non-hydrogen-bonded carbon (41.7 ppm) relative to the hydrogen-bonded group (56.6 ppm).

Funebradiol [**1**] exhibits optical activity $[\alpha]^{25}D$ 8.6°. The chiral center at position 11 is depicted in the *R* configuration based on the previously determined absolute configuration of the presumed biosynthetic precursor quabalactone III (Figure 1) (3–5).

Pyrrole compounds in higher plants (with the exception of chlorophylls) are rare. It is interesting that from this species to date, three separate distinct pyrroles have been isolated and identified. The biosynthesis of the chlorophylls has been extensively explored and determined; however, the substitution pattern on the pyrrole moieties isolated from *Q. funebris* suggests a different orgin because of the co-occurrence of a number of α-amino γ-lactones. The α-amino group could serve as a nucleophile around which a pyrrole moiety could be formed from a suitable electrophile. If this is correct, then a unique biogenetic pathway can be postulated. This is depicted in Figure 1. The primary nitrogen of the co-occurring quabalactone III [**3**] apparently bonds to a six-carbon sugar derivative such as diketogluconic acid (6) (Figure 1), then through a series of nucleophilic additions, dehydrations, reductions and subsequent aromatization, the pyrrole moiety of **1** is formed. This is analogous to the formation of funebral [**2**] and funebrine (3–5). This novel biosynthetic pathway has yet to be proven. Recently a new *N*-substituted γ-butyrolactone pyrrole **4** similar in structure to **2** was isolated from 10-day-old roots of *Pisum sativum* (7) and was found to alter stages in the cell cycle of root cortex cells. Lynn *et al.* (7) theorized

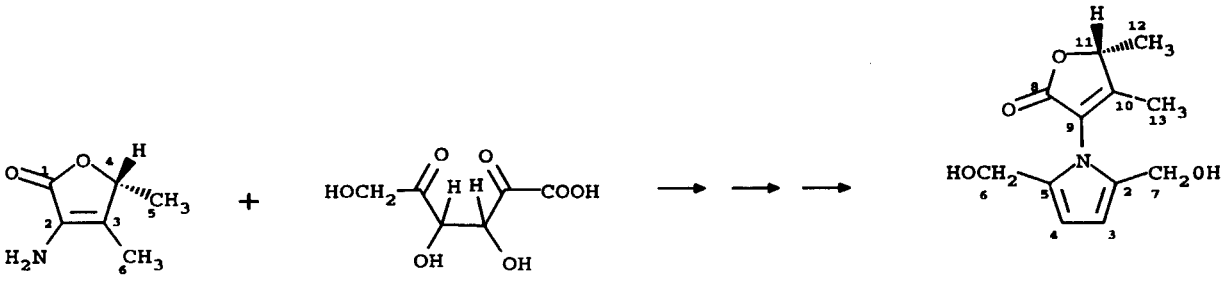

FIGURE 1. Structures and proposed biogenetic scheme for funebradiol [1].

that compound **4** is formed by a pathway similar to that which is seen in the formation of opines (8).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—The ^{1}H-nmr spectra were obtained on a Nicolet NTC-470 in $CDCl_3$, and the ^{13}C-nmr spectrum was determined on a Nicolet NT-200. Ir spectra were measured on a Beckman IR-33, and uv spectra were recorded on a Beckman DU-7. Optical rotations were obtained on a Perkin-Elmer 241 polarimeter. Low resolution ei and ci mass spectra were obtained on a Finnigan 4023 quadrupole mass spectrometer. High resolution and fab mass spectra were measured on a Kratos MS 50.

MATERIALS AND METHODS.—Details of the acquisition of the plant material, the extraction procedure, and the fractionation have been described previously (4).

ISOLATION OF FUNEBRADIOL.—The basic fraction (1454 mg) obtained from the 95% EtOH extract of ground flowers (450 g) was subjected to flash cc and preparative Si gel tlc (1.0 mm. thickness, F-254 indicator) with 5% MeOH in $CHCl_3$ as the mobile phase, R_f 0.34; the yield of funebradiol was 35.1 mg as an amorphous gum.

FUNEBRADIOL [**1**].—Hreims ($C_{12}H_{13}NO_4$) $[M-H_2O]^+$ calcd 219.0896, found 219.0887; fabms (glycerol) *m/z* 260, 111; fdms *m/z* 237; eims *m/z* (rel. int.) 237 (<1%), 236 (<1), 220 (4.5), 219 (16.7), 191 (3.1), 174 (3.9), 149 (5.5), 119 (3.1), 112 (7.2), 111 (58.8), 97 (12.9), 95 (11.3), 94 (14.2), 85 (39.8), 84 (11.8), 83 (100) base peak; ir (neat on NaCl plates) 3370, 3120, 2970, 2910, 2860, 1745, 1665, 1505, 1330, 1170, 1065, 1010, 780 cm^{-1}; uv (MeOH) λ max 219 nm (log ε = 3.34), λ max = 266 nm (log ε = 2.97); $[\alpha]^{25}D$ 8.6° (*c* = 0.3, MeOH).

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