*Journal of Natural Products*
*Vol. 49, No. 4, pp. 695-698, Jul-Aug 1986*



# FUNEBRAL, A NEW PYRROLE LACTONE ALKALOID FROM *QUARARIBEA FUNEBRIS*

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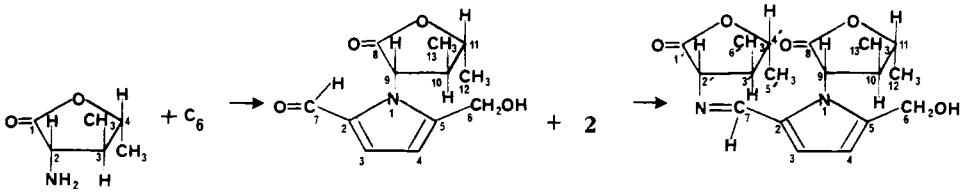
The odorous flowers of *Quararibea funebris* (Llave) Visher (Bombacaceae) are used by the Indians of Oacaxa, Mexico, to flavor various local chocolate drinks. Medicinally the plant is used for several ailments including the control of "psychopathic fears" (1,2), and there is some evidence that the flowers may be hallucinogenic.[1]

In previous papers (3,4), we reported the identification of a novel pyrrole lactone alkaloid, funebrine (**1**), and a group of new substituted butyro-lactones (quabalactones) from *Q. funebris* flowers. It was postulated that funebrine (**1**) is formed by the condensation of two molecules of the lactone **2** and a six carbon sugar derivative (see Figure 1). Apparently one molecule of **2** is initially combined with the sugar derivative with subsequent dehydration and ring closure. A second molecule of **2** then condenses with this aldehyde intermediate to give an alkaloid containing the imine linkage (Schiff base). In this paper, we report the isolation and identification of the presumed penultimate precusor to funebrine, a new aldehydic lactone pyrrole, which we are naming funebral (**3**).



**2** **3** Funebral **1** Funebrine

FIGURE 1. Proposed biosynthetic formation of funebral (**3**) and funebrine (**1**).

## RESULTS AND DISCUSSION

The aldehyde **3** was isolated by preparative tlc from the phenolic fraction of a 95% EtOH extract of the dried flowers. The compound gave a green Ehrlich test indicative of pyrroles. The hrms established the molecular formula $C_{12}H_{15}NO_4$ (mw 237.1001). The uv absorption spectrum [λ max 291.5 nm (log ε=4.13), 257 nm (log ε=3.88)] indicated a carbonyl conjugated with an aromatic system. The ir spectrum showed the presence of two carbonyls at 1780 $cm^{-1}$ and 1665 $cm^{-1}$. The former absorption was assigned to the lactone carbonyl, and the second suggested an aldehyde conjugated with an aromatic ring. The aromatic aldehyde function was also revealed by the presence of the fragment *m/z* 208 (M-29) in the mass spectrum. A primary alcohol is evidenced by absorbances at 3400 $cm^{-1}$ and 1043 $cm^{-1}$ in the ir spectrum and the fragment *m/z* 219 (M-18) in the mass spectrum. The 470 MHz $^1H$ nmr of **3** in DMSO gave a spectrum similar to that of funebrine (**1**) in DMSO-$d_6$ (see Table 1).

[1]R.G. Wasson, personal communication, 1982.

TABLE 1. $^1$H-nmr Values (ppm) [a]for Funerbal (**3**) and Funebrine (**1**)

| Carbon No.[b] | Compound | | |
|---|---|---|---|
| | **3** | | **1** |
| | $CDCl_3$ | DMSO-$d_6$ | DMSO-$d_6$ |
| 2 | — | — | — |
| 3 | 7.02(d;3.6) | 7.22(d;4.0) | 6.67(d;3.8) |
| 4 | 6.29(d;3.6) | 6.28(d;4.0) | 6.18(d;3.8) |
| 6a | 4.66(d;13.6)[c] | 4.94(d;5.7) | 4.48(d,5.6) |
| 6b | 4.73(d;13.6)[c] | 4.94(d;5.7) | 4.48(d,5.6) |
| 6-OH[d] | 2.40(bs) | 5.42(t;5.7) | 5.28(t;5.6) |
| 7 | 9.44(s) | 9.30(s) | 8.0(s) |
| 9 | 5.05(d;11.3) | 5.19(d;11.3) | 5.16(d;11.4) |
| 10 | 2.76(d,d,q;11.3,9.4,6.6) | 2.47(m) | 2.93(d,d,q;11.4,9.7,6.6) |
| 11 | 4.27(d,q;9.4,6.1) | 4.28(d,q;9.4,6.2) | 4.23(d,q;9.7,6.1) |
| 12 | 1.61(d:6.11) | 1.42(d;6.2) | 1.37(d;6.1) |
| 13 | 1.15(d;6.6) | 1.02(d;6.6) | 1.01(d;6.6) |
| 2′ | — | — | 3.83(d;10.9) |
| 3′ | | | 2.26(d,d,q;10.9,9.3,6.5) |
| 4′ | | | 4.21(d,q;9.3,6.2) |
| 5′ | | | 1.31(d;6.2) |
| 6′ | | | 0.98(d;6.5) |

[a]Spectra run at 470 MHz with TMS as internal standard. Resonance multiplicity and $J$ values (Hz) in parenthesis.

[b]Note: numbering scheme is different than that given in Raffauf *et al.* (3).

[c]Values may be reversed.

[d]Confirmed by $D_20$ addition.

The presence of signals at 7.22 ppm (d, $J$=4.0 Hz) and 6.28 ppm (d, $J$=4.0 Hz) was typical of the protons at positions 3 and 4 on the pyrrole ring, respectively. A non-exchangeable signal at 9.44 ppm (s) was assigned to the aldehyde. The signal at 4.94 ppm (d, $J$=5.7 Hz) was assigned to the hydroxymethyl protons which were coupled to the hydroxy proton, occurring at 5.42 ppm (t, $J$=5.7 Hz). The OH triplet disappeared from the spectrum upon the addition of $D_2O$ and resulted in a singlet for the hydroxymethyl protons. This same coupling observation was also seen in funebrine (**1**) for the analogous protons. $^1$H-nmr chemical shifts and spin coupling values of protons at positions 9,10, and 11 coupled with the mass spectrum (*m/z* 124, M-lactone) (3,5,6) indicated the presence of a lactone moiety identical to the lactone which is attached to position 1 in funebrine (**1**). Although the resonance multiplicity of proton 9 in **3** was obscured by the DMSO peak in the $^1$H-nmr spectrum, the expected spin coupling pattern was observed when the spectrum was run in $CDCl_3$ (see Table 1). Homonuclear decoupling experiments further supported the structure of **3**. The 50 MHz $^{13}$C-nmr spectra of **3** were obtained including an APT (attached proton test) spectrum (7); the chemical shifts are reported in Table 2. The decoupled and APT spectra fully supported the proposed structure.

Several significant differences in the $CDCl_3$ and DMSO-$d_6$ $^1$H-nmr spectra of **3** were apparent. The two diastereotopic hydroxymethyl protons (6a and 6b) in the $CDCl_3$ spectrum were no longer observed as being magnetically equilvalent (4.66 ppm; d, $J$=13.6 Hz and 4.73 ppm; d, $J$=13.6 Hz) as in the DMSO spectrum (4.94 ppm). A second difference in the $CDCl_3$ spectrum was the absence of coupling to the hydroxymethyl protons with the hydroxy proton. A ten-

TABLE 2. 50 MHz $^{13}$C-nmr APT Values for Funebral (**3**)[a]

| Carbon | Chemical shift (ppm) |
|---|---|
| 2 | −142.6 |
| 3 | 126.1 |
| 4 | 111.0 |
| 5 | −132.1 |
| 6 | −56.5 |
| 7 | 178.9 |
| 8 | −172.2 |
| 9 | 62.7 |
| 10 | 43.5 |
| 11 | 80.7 |
| 12 | 18.4 |
| 13 | 14.7 |

[a]Spectrum run in $CDCl_3$ with TMS as internal standard.

tative explanation for these two differences would be the presence of intramolecular hydrogen bonding between the hydroxy proton and the lactone carbonyl at position 8 in $CDCl_2$ solution, inhibiting free rotation. This would result in "fixed" positions for protons 6a and 6b in relation to the chiral centers in the lactone portion of funebral.

Funebral (**3**) contains three adjacent chiral centers and is optically active $[\alpha]^{32}D = -19.0°$. A positive Cotton effect is observed in cd spectra for α-amino acids (3,8,9). We presume that the lactone portion of funebral is formed from the congeneric α-aminobutyrolactone (**2**) which is derived from the co-occurring α-amino acid 2*S*,3*S*,4*R*-γ-hydroxyisoleucine (3,4). A positive Cotton effect ($[\theta] = +1.35 \times 10^4$) was found in the cd spectrum of **3** thus indicating an *S* configuration for position 9. The absolute configuration of **3** was designated as 9*S*,10*S*,11*R*.

Since the structure of alkaloid **1** was determined mainly from X-ray studies and the initial $^1$H-nmr spectrum was produced on a low field instrument (60 MHz), a re-evaluation of the previous $^1$H-nmr assignments of funebrine was undertaken. Analogous protons 9 and 2′ were observed to occur in two significantly different regions of the spectrum (5.16 ppm and 3.83 ppm, respectively, see Table 1), while the other analogous protons on the lactones we found in somewhat similar environments. It was previously assumed (3) the proton 9 produced the resonance most downfield because of the deshielding effect of the pyrrole ring current. Using **3** as a model, proton 9 in funebral (**3**) has a similar chemical shift (5.19 ppm) when compared to proton 9 of funebrine (**1**); this reinforces the previous $^1$H-nmr assignment for this proton. In a similar fashion, all $^1$H-nmr signals for the pyrrole-attached lactone appear downfield compared to the imine-attached lactone protons. These assignments were supported by homonuclear decoupling experiments.

## 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 Cary 17. Optical rotations were obtained on a Perkin-Elmer 241 polarimeter. Cd spectra were determined on a Cary 60 spectropolarimeter with a Model 6001 cd attachment. Low resolution mass spectra were obtained on a Finnigan 4023 quadrupole mass spectrometer. High resolution mass spectrum were measured on a Kratos MS 50.

MATERIALS AND METHODS.—Details of the acquistion of the plant material, the extraction procedure and the fractionation have been described previously (3).

ISOLATION OF FUNEBRAL (**3**).—The phenolic fraction (8 mg) obtained from the 95% EtOH extract of ground flowers (10 g) was subjected to preparatory silica-gel tlc (0.25 mm thickness, F-254 indicator) with 2% MeOH in $CHCl_3$ as the mobile phase, Rf 0.34; yield of funebral, 0.53 mg (0.0053%). For comparison purposes, funebrine (**1**) was previously isolated in 0.00083% yield (3).

FUNEBRAL (**3**).—High resolution eims $C_{12}H_{15}NO_4$, theoretical 237.1001, found 237.1023; eims *m/z* (rel. int.) 237.1 ($M^+$, 59.4%), 219 (11.4), 208 (27.0), 190 (20.0), 180 (74.3), 136 (37.3)., 124 (43.2; ir (NaCl plates) 3400 $cm^{-1}$, 3120, 2922, 1780, 1665, 1590, 1455, 1190, 1043, 775; uv (MeOH) λ max=291.5 nm (log ε: 4.13), 257 nm (log ε: 3.88); $[\alpha]^{32}D = -19.0°$ (*c*=0.05, MeOH); cd

$[\theta]=+1.35\times10^4$ (210.5 nm), $\Delta\epsilon=+4.1$ (MeOH).

## ACKNOWLEDGMENTS

We acknowledge Mr. Eric Kolodziej for his assistance in obtaining the mass spectra. High-resolution (470 MHz) $^1$H-nmr spectra were recorded at the Purdue University Biological Magnetic Resonance Laboratory (NIH Grant RR1077). We are grateful to Xinje Wu and Kent Rupprecht for help in running some of the $^1$H-nmr spectra. We also wish to thank Matt McDonough for the cd spectra. This investigation was partially supported by Public Health Service, National Cancer Institute Grant #CA38151.

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*Received 13 December 1985*