

TWO NEW ACRIDONE ALKALOIDS FROM THE ROOTS OF MARSH GRAPEFRUIT¹

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Abstracts — Two new acridone alkaloids, margrapine-A and -B were isolated from the roots of Marsh grapefruit (*Citrus paradisi* Macf.). Their structures were characterized on the basis of spectroscopic evidence.

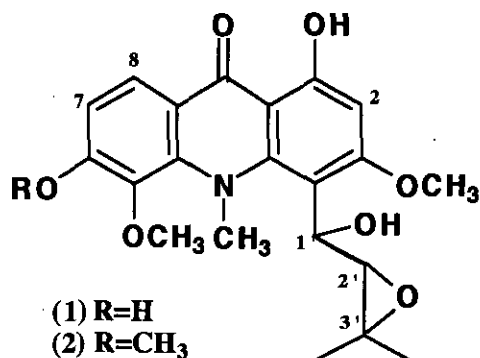
In the course of our research on the phytochemical aspects of *Citrus* plants, we have demonstrated the isolation and structure elucidation of many new acridone alkaloids and coumarins.² Previous investigation of the constituents of the roots of Marsh grapefruit (*C. paradisi* Macf.) furnished to isolate new acridone alkaloids, azacridone-A,³ citbismine-A, -B, -C,⁴ -D, -E,⁵ fuoparadine, *trans*-dihydrocitracridone-I,⁶ marshdine and marshmine.⁷ Further investigation resulted in the isolation of two new acridone alkaloids, named margrapine-A (1) and -B (2). In this paper, we wish to report the structural elucidation of these new alkaloids.

Margrapine-A (1) was isolated as a yellow oil, $[\alpha]_D -16.7^\circ$ (CHCl₃). The molecular formula C₂₁H₂₃NO₇ was defined by molecular ion peak in the HR ms (*m/z* 401.1510). The ir (1625, 1590 cm⁻¹) and uv spectra [225 (sh), 264, 295 (sh), 331, 381 nm] suggested the presence of 9-acridone skeleton.⁸ The ¹H-nmr spectrum showed signals due to chelated hydroxyl (δ 14.48), *ortho*-coupled [δ 8.05, 6.98 (each 1H, d, *J*= 8.5 Hz)], and a lone (δ 6.42) aromatic protons. Because the lowest aromatic proton signal at δ 8.05 was characteristic to H-8 deshielded by 9-carbonyl

Table 1 $^1\text{H-Nmr}$ data of **1** and **2**

	1	2
H-1	14.48	14.45
H-2	6.42	6.39
3-MeO	3.98	3.93
5-MeO	3.87	3.89
6-MeO		3.71
H-7	6.98(8.5)	6.98(8.6)
H-8	8.05(8.5)	8.03(8.6)
N-Me	3.78	3.74
H-1'	4.86(4.9)	4.31(4.9)
1'-OH	6.34	6.32
H-2'	3.44(4.9)	3.70(4.9)
3'-Me	0.97	0.88
	1.21	1.11

J values in parentheses are expressed in Hz.



group, the location of *ortho*-coupled protons could be assigned to H-8 and H-7 and chelated hydroxyl group was assignable to locate at C-1. Three signals at δ 3.78, 3.87 and 3.98 in $^1\text{H-nmr}$ and δ 49.3, 60.4 and 56.1 in $^{13}\text{C-nmr}$ showed the presence of an *N*-methyl and two *O*-methoxy groups. Irradiation of the *N*-methyl signal at δ 3.78 showed a 14% increment of the signal at δ 4.86 (H-1'), thus the alkyl substituent was assigned to locate at C-4. When the methoxy signal at δ 3.98 was irradiated, a 15% increment was observed in the signal at δ 6.42 (H-2), suggesting the location of the methoxyl group to C-3. No increments were observed on irradiation of the methoxy signal at δ 3.87, thus this group was determined to locate at C-5. The presence of 1-hydroxy-3-methyl-2,3-epoxybutyl group was suggested by the signals at δ 1.21, 0.97 (each 3H, s, 3'-Me), 3.44, 4.86 (each 1H, d, $J=4.9$ Hz) in the $^1\text{H-nmr}$ spectrum and the signals at δ 77.5 (d), 67.9 (d), 58.4 (s), 19.1 (q), 24.6 (q) in the $^{13}\text{C-nmr}$ spectrum. The fragment ions at m/z 300 [$\text{M}^+ - (\text{C}_5\text{H}_9\text{O}_2)$] and 330 [$\text{M}^+ - (\text{C}_4\text{H}_7\text{O})$] in the mass spectrum also supported the existence of this group. From the above mentioned results, the structure of margrapine-A was assigned as **1**, except for the stereochemistry of the C-4 alkyl group.

Margrapine-B (**2**) was obtained as yellow oil, $[\alpha]_{\text{D}} -37.5^\circ$ (CHCl_3). The molecular formula $\text{C}_{22}\text{H}_{25}\text{NO}_7$ was established by HR ms (m/z 415.1667). The ir and uv spectra showed the characteristic absorptions of 9-acridone skeleton.⁸ As shown in Table 1, comparison of the $^1\text{H-nmr}$ signals of **2** with those of margrapine-A (**1**) showed very similar patterns except for the presence of an additional methoxy signal on aromatic ring. The presence of the same alkyl group at C-4 as **1** was supported by characteristic fragment ions at m/z 314 [$\text{M}^+ - (\text{C}_5\text{H}_9\text{O}_2)$] and

344 [$M^+ - (C_4H_7O)$] in the ms spectrum. Thus, we assigned the structure **2** to margrapine-**B** except for the stereochemistry of the alkyl group.

EXPERIMENTAL

Isolation The repeated preparative thin layer chromatography of the CH_2Cl_2 eluate obtained through the separation process of the acetone extract of Marsh grapefruit (*C. paradisi* Macf.)⁷ [solvent: acetone:hexane(1:1), $CHCl_3$:MeOH(9:1), benzene:MeOH (8:2), $CHCl_3$:MeOH (19:1)] gave margrapine-**A**(1)(1.5 mg) and margrapine-**B**(2)(0.7 mg).

Margrapine-A(1): Yellow oil; $[\alpha]_D -16.7^\circ$ ($c=0.036$, $CHCl_3$); high ms m/z: 401.1510 (M^+ , found), 401.1475 (calcd for $C_{21}H_{23}NO_7$); eims m/z: 401, 383, 331, 330 (base peak), 329, 315, 314, 312, 311, 302, 301, 300, 296, 299, 298, 297; ir ν_{max} ($CHCl_3$, cm^{-1}): 3500, 1625, 1590; uv λ_{max} (EtOH, nm): 225 (sh), 264, 295 (sh), 331, 381; 1H -nmr ($CDCl_3$, δ): Table 1. ^{13}C -nmr ($CDCl_3$, δ): 182.1 (C-9), 165.4 (C-3), 165.3 (C-1), 154.9 (C-6), 150.5 (C-10a), 142.4 (C-4a), 136.3 (C-5), 123.6 (C-8), 118.2 (C-8a), 112.2 (C-7), 106.8 (C-9a and C-4), 95.0 (C-2), 77.5 (C-1'), 67.9 (C-2'), 60.4 (5-MeO), 58.4 (C-3'), 56.1 (3-MeO), 49.3 (N-Me), 24.6 (3'-Me), 19.1 (3'-Me).

Margrapine-B (2): Yellow oil; $[\alpha]_D -37.5^\circ$ ($c=0.008$, $CHCl_3$); high ms m/z: 415.1667 (M^+ , found), 415.1631 (calcd for $C_{22}H_{25}NO_7$); eims m/z: 415, 383, 344 (base peak), 330, 315, 314, 312, 311, 301, 300, 298; ir ν_{max} ($CHCl_3$, cm^{-1}): 3300, 1630, 1600; uv λ_{max} (EtOH, nm): 226 (sh), 264, 331, 375; 1H -nmr ($CDCl_3$, δ): Table 1.

ACKNOWLEDGEMENT

The authors are grateful to Misses K. Suwa and S. Takeyama, Mukogawa Women's University, for measurements of ms and nmr spectra and to Mr. S. Katsuno, Meijo University, for measurements of high-resolution ms.

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Received, 8th July, 1996