TWO NEW ACRIDONE ALKALOIDS FROM THE ROOTS OF MARSH GRAPEFRUIT [1]

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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.

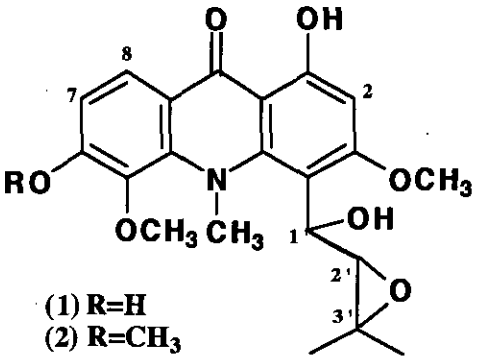
In the course of our research on the phytochemical aspects of *Citrus* plants, we have demonstrated the isolation and structure elucidation of many new acridone alkaloids and coumarins.[2] Previous investigation of the constituents of the roots of Marsh grapefruit (*C. paradisi* Macf.) furnished to isolate new acridone alkaloids, azacridone-A,[3] citbismine-A, -B, -C,[4] -D, -E,[5] furoparadine, *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° ($CHCl_3$). The molecular formula $C_{21}H_{23}NO_7$ 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 ^{1}H-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}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.



(1) R=H
(2) R=CH_3

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}H-nmr and δ 49.3, 60.4 and 56.1 in ^{13}C-nmr showed the presence of an *N*-methyl and two *O*-methyl 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}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}C-nmr spectrum. The fragment ions at m/z 300 [M^+ - ($C_5H_9O_2$)] and 330 [M^+ - (C_4H_7O)] 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, $[\alpha]_D$ -37.5° ($CHCl_3$). The molecular formula $C_{22}H_{25}NO_7$ 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}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 [M^+ - ($C_5H_9O_2$)] 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° (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 νmax ($CHCl_3$, cm^{-1}): 3500, 1625, 1590; uv λmax (EtOH, nm): 225 (sh), 264, 295 (sh), 331, 381; ^{1}H-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° (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 νmax ($CHCl_3$, cm^{-1}) 3300, 1630, 1600; uv λmax (EtOH, nm): 226 (sh), 264, 331, 375; ^{1}H-nmr ($CDCl_3$, δ): Table 1.

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