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CITBISMINE-A, A NEW BISACRIDONE ALKALOID FROM *CITRUS PARADISI*

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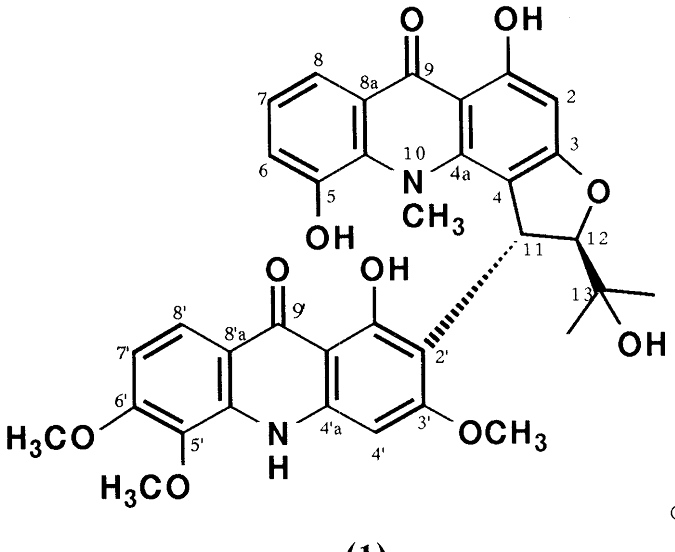
A novel type bisacridone alkaloid, named citbismine-A, was isolated from the roots of Marsh grapefruit; its structure was elucidated by spectroscopic method and unequivocally by X-ray crystal analysis as **1**.

KEYWORDS bisacridone; citbismine-A; *Citrus paradisi*; Rutaceae; crystal structure

Recently, we have reported the isolation and structure elucidations of many new bicoumarins[1)] and acridone-coumarin dimers[2)] from genus *Citrus* plants (Rutaceae). On continuing our investigations on the constituents of these species, we investigated the constituents of Marsh grapefruit (*C. paradisi* Macf.)[3)] and isolated a novel type dimeric acridone alkaloid having dihydrofuran ring. Though many acridone alkaloids have been isolated from genus *Citrus*, this is the first example of a dimeric acridone alkaloid. The acetone extract of roots of Marsh grapefruit was subjected to column, centrifugal, and preparative thin-layer chromatographies using silica gel, resulting in the isolation of citbismine-A in $8.5 \times 10^{-4}\%$ yield.

Citbismine-A (**1**) was obtained as yellow cubes, mp 335-336°C (from DMSO), $[\alpha]_D \pm 0^\circ$ (DMSO). The molecular formula $C_{35}H_{32}N_2O_{10}$ was assigned from HR-MS (m/z 640.2068 [M^+]). The UV[λ_{max}(EtOH) 228 (sh), 265, 272, 298 (sh), 330, 384 nm] and IR [ν_{max}($CHCl_3$) 3400, 1720, 1625, 1600, 1560 cm $^{-1}$] spectra indicated the presence of 1-hydroxy-9-acridone skeleton.[4)] The ^{1}H-NMR spectrum showed signals due to two chelated hydroxy groups [δ 15.28, 14.85 (each 1H, s, disappearing with addition of D_2O)], ABC type [δ 7.58 (1H, d, J= 7.9 Hz), 7.19 (1H, d, J= 7.9 Hz), 7.04 (1H, t, J= 7.9 Hz)], AB type [δ 8.00, 6.95 (each 1H, d, J= 9.2 Hz)], and two lone [δ 6.75, 6.16 (each 1H, s)] aromatic protons. Two lowest signals of ABC and AB type signals at δ 8.00 and 7.58 were considered to be deshielded by 9- and 9'-carbonyl groups and were assignable to H-8 and H-8'. The signals of two hydrogen-bonded hydroxyl groups also suggested the presence of two 1-hydroxy-9-acridone nuclei in this compound. Thus, the new compound was concluded to have dimeric 1-hydroxy-9-acridone structure. The three-proton singlets at δ 3.98, 3.86, 3.79, 3.42 in ^{1}H- and δ 60.65, 56.33, 55.52, 44.29 in ^{13}C-NMR spectra showed the existence of an N-methyl and three methoxy groups. The presence of 2-hydroxyisopropyl substituted dihydrofuran ring was also indicated by the signals at δ 5.57, 4.38 (each 1H, d, J= 4.9 Hz), 4.69 (1H, s, disappeared with D_2O), and 1.29, 1.25 (each 3H, s). From the above mentioned results, the structure of citbismine-A was assumed to have dimeric structure



(1)

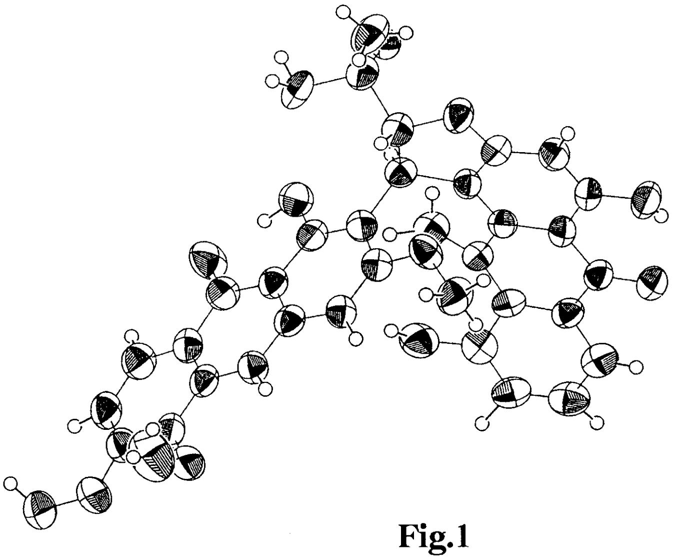


Fig.1

composed of 1,3,5-trioxygenated-9-acridone and 1,3,5,6-tetraoxygenated-9-acridone. Because determinations of the location of N-methyl and methoxy groups by NOE experiment were unfruitful, the orientation of dihydrofuran ring, the linking position of two acridone nuclei, and the relative stereochemistry were unequivocally established by X-ray analysis5) as shown in Fig. **1**.

The bisacridone alkaloids so far isolated from plant sources fall into the following two categories: (i) the two acridone units are linked by an ether bridge as in atalanine and ataline6); (ii) the two acridone units are attached through a carbon-carbon bond as in glycobismine-A, -B, and -C.7) Though glycobismines are linked by a C-C bond between dihydropyran and aromatic rings, citbismine-A is the first example of bisacridone alkaloid, which could be classified as the third category, attached by a C-C bond between dihydrofuran and aromatic rings.

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5) Crystal data for **1**. $C_{35}H_{32}N_2O_{10}$, M= 640.00, triclinic, a=9.837 (3), b= 11.466 (3), c= 17.277 (3)Å^3, α= 75.01 (2), β= 86.46 (2), γ= 84.58 (2)$^{\circ}$, V= 1872.6 (9)Å^3, Z=2, space group P-1 (# 2), Dc= 1.49 g/cm^3. Data were collected on Mac Science MXC18 diffractometer with Cu Kα radiation. Final R value was 0.1438 for 6938 reflections.
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