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 and acridone-coumarin dimers 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.) 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% yield.

Citbismine-A (I) was obtained as yellow cubes, mp 335-336°C (from DMSO), [α]D ±0° (DMSO). The molecular formula C35H32N2O10 was assigned from HR-MS (m/z 640.2068 [M+]). The UVλmax (EtOH) 228 (sh), 265, 272, 298 (sh), 330, 384 nm and IR νmax (CHCl3) 3400, 1720, 1625, 1600, 1560 cm⁻¹ spectra indicated the presence of 1-hydroxy-9-acridone skeleton. The 1H-NMR spectrum showed signals due to two chelated hydroxy groups [δ 15.28, 14.85 (each 1H, s, disappearing with addition of D2O)], 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 1H- and δ 60.65, 56.33, 55.52, 44.29 in 13C-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 D2O), and 1.29, 1.25 (each 3H, s). From the above mentioned results, the structure of citbismine-A was assumed to have dimeric structure.
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 dhydrofuran ring, the linking position of two acridone nuclei, and the relative stereochemistry were unequivocally established by X-ray analysis\(^5\) 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 ataline\(^6\); (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 dhydrofuran and aromatic rings.

REFERENCES AND NOTES

3) The plant was cultivated and collected at the orchard of Okitsu Branch, Fruit Tree Research Station, Shizuoka.
5) Crystal data for 1. C\textsubscript{35}H\textsubscript{32}N\textsubscript{2}O\textsubscript{10}, M= 640.00, triclinic, a=9.837 (3), b= 11.466 (3), c= 17.277 (3)\textsubscript{\AA}\textsuperscript{3}, α= 75.01 (2), β= 86.46 (2), γ= 84.58 (2)°, V= 1872.6 (9)\textsubscript{\AA}\textsuperscript{3}, Z=2, space group P-1 (# 2), D= 1.49 g/cm\textsuperscript{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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