HONYUMINE, A NEW LINEAR PYRANOACRIDONE ALKALOID FROM CITRUS GRANDIS OSBECK

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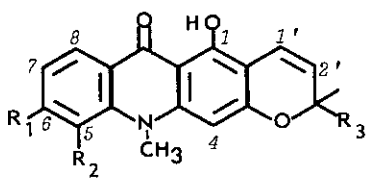
Abstract —— A linear pyranoacridone alkaloid, honyumine, was isolated from the root bark of Citrus grandis Osbeck, and the structure was assigned as formula 1.

CITRUS grandis Osb. (Chines name: Honyu) is a fruiter belonging to Rutaceae. The peel of this plant has been used as a folk medicine in the treatment of stomachache in Taiwan. In continuing our investigations on the chemical constituents of the genus Citrus, [1-6] we now wish to report the isolation and the structure elucidation of a new linear pyranoacridone alkaloid named honyumine from the root bark of C. grandis Osb. collected in Taiwan.

Honyumine (1) was isolated as yellow granules, mp 175-176°C (acetone), from the acetone extract of the root bark of the plant by repeated chromatograhpic separation on silica gel with benzene-acetone (9:1) as an eluant (yield: 0.00062% from the dried root bark). The molecular formula $C_{20}H_{19}NO_5$ of this alkaloid was established by high resolution mass spectrometry (Calcd. for $C_{20}H_{19}NO_5$ 353.1262. Found 353.1264). The UV spectrum [λ_{max}(EtOH) (log ε): 224 (3.98), 262 (4.15), 290sh (4.64), 301 (4.75), 327 (4.05), 350sh (3.55), and 393 (3.59) nm] showed a close resemblance to those of glycofoline (2) and pyranofoline (3) which we isolated from Glycosmis citrifolia (Rutaceae), thus suggesting a linear pyranoacridone nucleus for honyumine.[7] The presence of phenolic hydroxyl groups was

clear from the IR band at 3480 cm^{-1} and ^{1}H-NMR (100 MHz, acetone-d_6) signals at δ 15.20 and 9.03 (exchangeable with D_2O). The lower field signal at δ 15.20 together with an IR band at 1640 cm^{-1} is characteristic to an intramolecular hydrogen-bonded C-1 hydroxyl group in a 9-acridone.[8-10] The ^{1}H-NMR spectrum showed the presence of a methoxyl (δ 3.79), an N-methyl (δ 4.04), and two tertiary methyl groups [δ 1.47 (6H, s)]. The six-proton singlet at δ 1.47 and an AB type quartets at δ 5.67 (d, J=10 Hz) and 6.71 (dd, J=0.5 & 10 Hz) having a long range coupling with a signal at δ 6.36 (1H, d, J=0.5 Hz, H-2 or H-4) were assigned to a dimethylpyran ring system attached to ring C. The linear orientation of the pyran ring was established by a nuclear Overhauser effect (n.O.e.) experiment.[11] Irradiation of the N-methyl signal produced a 23 % enhancement of only the signal at δ 6.28 (H-4). In ^{13}C-NMR spectrum (100 MHz, $CDCl_3$),[12] appearances of the N-methyl carbon and the olefinic C-1' of the dimethylpyran ring at δ 39.1 and 116.0, respectively also supported the linear orientation.[13] An additional AB type signal (J=9 Hz) at δ 6.95 and 8.04 in the ^{1}H-NMR spectrum was attributed to mutually ortho-located protons (H-7 & H-8), the lower field signal (H-8) being deshielded by C-9 carbonyl moiety. The observation of C-7 at δ 111.4 in the ^{13}C-NMR spectrum coupled with the absence of n. O. e. enhancement between H-7 and the methoxyl signal, suggested the locations of a methoxyl and a hydroxyl group at C-5 and C-6, respectively.[13] On the basis of these results, honyumine should be represented by formula 1.



(1): R_1= OH, R_2= OCH_3, R_3= CH_3

(2): R_1= H, R_2= OH, R_3= CH_3

(3): R_1= H, R_2= OH, R_3= CH_2-CH_2-CH=C(-CH_3)-CH_3

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11 The n. O. e. experiments were carrided out by using 400 MHz NMR spectrometer in $CDCl_3$ solution, and slightly different chemical shifts were observed as follow: δ 1.49 (6H, s, $2CH_3$), 3.75 (3H, s, OCH_3), 3.98 (3H, s, NCH_3), 5.57 (1H, d, J=10 Hz, H-2'), 6.28 (1H, d, J=0.5 Hz, H-4), 6.75 (1H, dd, J=0.5 & 10 Hz, H-1'), 6.95 (1H, d, J=9 Hz, H-7), and 8.15 (1H, d, J=9 Hz, H-8).

12 ^{13}C-NMR spectrum of honyumine (1): δ 28.5 (q, 2 CH_3), 39.1 (q, OCH_3), 61.8 (q, NCH_3), 78.0 (s, C-3'), 92.3 (d, C-4), 103.1 (s), 105.0 (s), 111.4 (d, C-7), 116.0 (d, C-1'), 117.5 (s), 124.0 (d, C-8), 126.8 (d, C-2'), 134.4 (s), 137.8 (s), 146.7 (s), 154.7 (s), 159.6 (s), 159.9 (s), and 180.4 (s, C-9)

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