HONYUMINE, A NEW LINEAR PYRANOACRIDONE ALKALOID FROM CITRUS GRANDIS OSBECK

Tian-Shung Wu, * Shiow-Chyn Huang, Ting-Ting Jong, and Jeng-Shiow Lai
Department of Applied Chemistry, Providence College of Arts and Science, Taichung 400, Taiwan, R. O. C.

Hiroshi Furukawa *
Faculty of Pharmacy, Meijo University, Tempaku, Nagoya 468, Japan

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. (Chinese 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 chromatographic separation on silica gel with benzene-acetone (9:1) as an eluant (yield: 0.00062% from the dried root bark). The molecular formula C\textsubscript{20}H\textsubscript{19}NO\textsubscript{5} of this alkaloid was established by high resolution mass spectrometry (Calcd. for C\textsubscript{20}H\textsubscript{19}NO\textsubscript{5} 353.1262, Found 353.1264). The UV spectrum (\(\lambda_{\text{max}}\) (EtOH) (log \(\varepsilon\)): 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 8 15.20 and 9.03 (exchangeable with D\(_2\)O). The lower field signal at 8 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 (8 3.79), an N-methyl (8 4.04), and two tertiary methyl groups (8 1.47 (6H, s)). The six-proton singlet at 8 1.47 and an AB type quartets at 8 5.67 (d, \(J=10\) Hz) and 6.71 (dd, \(J=0.5 \& 10\) Hz) having a long range coupling with a signal at 8 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 8 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\(^{1}\) of the dimethylpyran ring at 8 39.1 and 116.0, respectively also supported the linear orientation.\(^13\) An additional AB type signal (\(J=9\) Hz) at 8 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 8 111.4 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 \(1\).

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(1): R_1 = \text{OH}, \; R_2 = \text{OCH}_3, \; R_3 = \text{CH}_3 \\
(2): R_1 = \text{H}, \; R_2 = \text{OH}, \; R_3 = \text{CH}_3 \\
(3): R_1 = \text{H}, \; R_2 = \text{OH}, \; R_3 = \text{CH}_2\text{-CH}_2\text{-CH=CH}_3 \\
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REFERENCES AND NOTES
11 The n. o. e. experiments were carried out by using 400 MHz NMR spectrometer in CDCl$_3$ solution, and slightly different chemical shifts were observed as follow: $\delta$ 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 homyumine (1): $\delta$ 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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