HETEROCYCLES, Vol 19, No 5, 1982

ACRIDONE ALKALOID. III[1] STRUCTURE OF GLYCOFOLINE, A NEW MONOTERPENOID ACRIDONE ALKALOID FROM GLYCOSMIS CITRIFOLIA (WILLD.) LINDL.

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Abstract ——— A new monoterpenoid acridone alkaloid glycofoline(1) was isolated from the root- and stem-bark of Glycosmis citrifolia (Willd.) Lindl., and the structure was elucidated on the basis of the spectral data and a chemical transformation.

Glycosmis citrifolia (Willd.) Lindl.[2] (G. cochinchinensis Pierre) (Rutaceae) is a wild shrub which has been claimed as a folk medicine in the treatment of skin itchy, scabies, boil and ulcer[3]. T.-H. Yang et al.[4] have isolated a phenylalkylamine candicine from the bark of this plant. This paper describes the isolation and the structural elucidation of a new acridone alkaloid named glycofoline (1) from the stem- and root-bark of G. citrifolia collected in Heng Chun Tropical Botanical Garden (Kehg-Ting Botanical Garden), Taiwan.

Glycofoline (1), an orange syrup (content:0.006%), $C_{24}H_{25}NO_4$, $[\alpha]_D$ -15.1° ($CHCl_3$, c=1.0). The UV spectrum [λmax(MeOH)(log ε): 225(4.13), 268(sh, 4.32), 280(sh, 4.39), 297(4.59), 308(4.65), 335(sh, 3.92), and 415(3.53) nm] showed the characteristic absorption of the 9-acridone nucleus[5]. The presence of the phenolic hydroxyl group in glycofoline was clear from the deep green ferric reaction, the IR band at 3200 cm^{-1}, and ^{1}H-n.m.r. peaks at δ 14.82 and 8.00 (exchangeable with D_2O). The lower signal at δ 14.82 and IR bands at 3200/1625 cm^{-1} indicated the presence of strong intramolecular hydrogen bonded hydroxyl and carbonyl groups. Furthermore, the ^{1}H-n.m.r. of glycofoline showed a sharp three-protons singlet at δ 4.00 due to an N-methyl group, and ABX pattern signals at δ 7.85 (1H, dd, J=8 & 2Hz), 6.96 (1H, t, J=8Hz), and 7.13 (1H, dd, J=8 & 2Hz) attributed to H-8, being deshielded by the carbonyl group, H-7, and H-6, respectively. A sharp one-proton singlet at δ 6.23 could be assigned to a lone aromatic proton at H-4 (or H-2). The ^{1}H- and ^{13}C-n.m.r. spectra of glycofoline further revealed the presence of the partial structure in Fig 1.

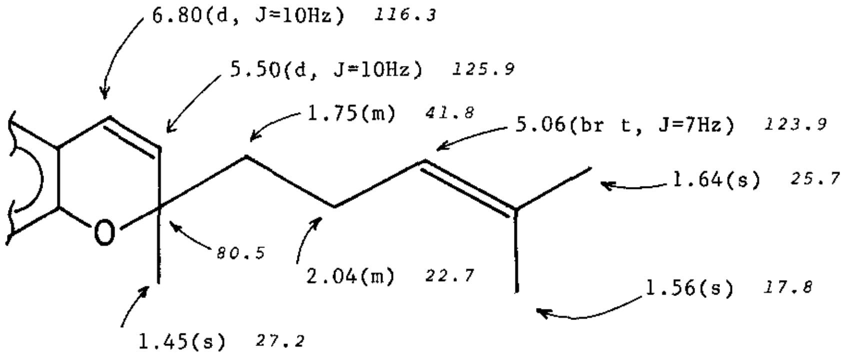
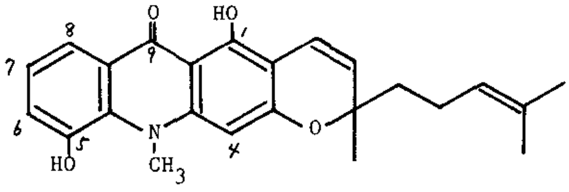


Fig 1. ^1H- and ^{13}C-n.m.r. spectra of glycofoline in $CDCl_3$.
(^{13}C-n.m.r. spectral data are in italics[6])

This feature was supported by the characteristic MS fragmentation pattern[7] of glycofoline : m/z 391 (M^+, 25%), 376 ($M-CH_3$, 8%), 322 ($M-[-CH_2CH=C(CH_3)_2]$, 5%), 308 ($M-[-CH_2CH_2CH=C(CH_3)_2]$, 100%), and 265 ($M-[-CH_3COCH_2CH_2CH=C(CH_3)_2]$, 5%). The linear orientation of the pyran ring could be established by the NOE experiment : Irradiation of the N-methyl signal at δ 4.00 produced 20% enhancement of the signal at δ 6.23 (H-4).

The above data were in excellent accord with the structure 1 for glycofoline[8].



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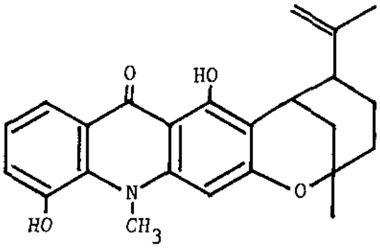

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In agreement with this proposition, treatment of 1 with HCl in $CHCl_3$ furnished a cyclization product (2)[9]. $C_{24}H_{25}NO_4$, m.p. 238-240° . IR νmax(KBr): 3320, 1620, 1585, and 1550 cm^{-1}. UV λmax(MeOH)(log ε): 232(3.83), 260(sh, 3.95), 267(4.04), 280(sh, 3.96), 289(4.04), 308(sh, 3.26), and 413(2.37) nm. ^{1}H-n.m.r. ($CDCl_3$ + acetone-d_6):δ 1.20(3H, s, CH_3), 1.42(3H, s, CH_3), 3.70(1H, m, benzylic-CH), 4.08(3H, s, N-CH_3), 4.46(2H, br s, C=CH_2), 6.36(1H, s, H-4), 7.07(1H, t, J=8Hz, H-7), 7.25(1H, dd, J=8 & 2Hz, H-6), 7.91(1H, dd, J=8 & 2Hz, H-8), 9.09(1H, br s, C_5-OH), and 16.35(1H, s, C_1-OH). The similar cyclization reaction have been reported in the monoterpenoid carbazoles, mahanimbine[7], cyclomahanimbine[10], and isomahanimbine[11] isolated from Murraya koenigii Spreng.

On the biogenetic view points, occurrence of glycofoline(1) in optically active form indicated the enzymatic cyclization of the corresponding geranyl acridone. This is the first example of the isolation of the monoterpenoid acridone alkaloid from natural sources[12].

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Received, 11th January, 1982