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TWO NEW ACRIDONE ALKALOIDS FROM *GLYCOSMIS* SPECIES

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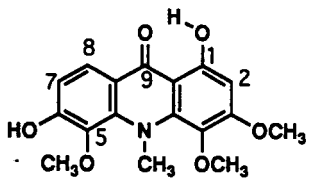
ABSTRACT.—Two new acridone alkaloids, named glycofolinine [**1**] and acrifoline [**2**], were isolated from the root bark and stem bark of *Glycosmis citrifolia* collected in Taiwan. Their structures were elucidated by spectroscopic methods.

A number of acridone alkaloids have been isolated and characterized from *Glycosmis citrifolia* (Willd.) Lindl. (Rutaceae) grown in Taiwan (1). In a further investigation of this plant, we describe herein the isolation and structural elucidation by spectroscopic methods of two new acridone alkaloids, named glycofolinine [**1**] and acrifoline [**2**].

Glycofolinine [**1**] was isolated as yellow prisms, mp 161–163°, and the molecular formula of $C_{17}H_{17}NO_6$ was determined by hrms. The presence of the 1-hydroxy-9-acridone skeleton in **1** was suggested by the uv and ir bands (see Experimental) (2) together with a strongly hydrogen-bonded proton signal at δ_H 14.20 in the ^{1}H-nmr spectrum. The ^{1}H- and ^{13}C-nmr spectra of **1** showed signals assignable to three MeO groups, one N-Me (δ_C 47.11), ortho-located H-7 (δ_H 6.92, d, J=8.8 Hz) and H-8 (δ_H 7.91, d, J=8.8 Hz) (3) signals, and a lone aromatic H [δ_H 6.37, s] attached to C-2 (or C-4). The signal (δ_C 95.28) of the carbon bearing the lone aromatic H, in the single-pulse ^{13}C-nmr spectrum obtained without decoupling, appeared as a double doublet coupled with a directly bonded H at δ_H 6.37 and the hydrogen-bonded OH-1, indicating that this carbon was affixed to C-2. The chemical shift value of the N-Me carbon signal (δ_C 47.11) in the ^{13}C-nmr spectrum suggested the presence of substituents at C-4 and C-5 (4). In nOe experiments, irradiation of the MeO signal at δ_H 3.97 produced a 12% enhancement of the signal at δ_H 6.37 (H-2). Irradiation of the OH signal at δ_H 10.52 (DMSO-d_6) produced a 9% enhancement of the signal at δ_H 6.92 (H-7). However, no increment of any signal was observed on irradiation of the N-Me and other MeO signals. These data indicated the location of a OH group at C-6 in the acridone nucleus. The results of an HMBC experiment of glycofolinine, as shown by arrows in Figure 1, also supported the



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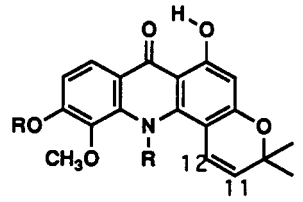

2 R=H
3 R=Me

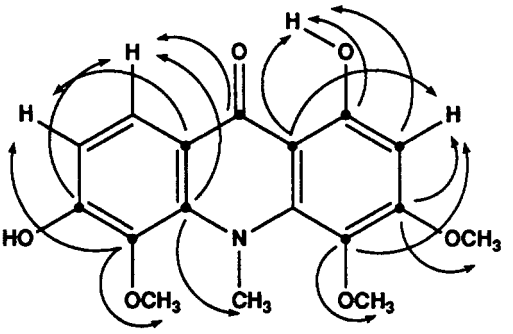

FIGURE 1. Long-range correlations (C-H) in the HMBC spectrum of glycofolinine [**1**].

assignment of structure **1** for this isolate.

Acrifoline [**2**] was obtained as a yellow amorphous powder. The molecular formula was proposed as $C_{19}H_{17}NO_5$ by hrms. The uv spectrum showed bands characteristic of a 9-acridone chromophore (2). The ^{1}H-nmr spectrum showed signals due to a strongly hydrogen-bonded OH, an NH, a MeO, a 2,2-dimethylpyran unit, the ortho-located H-7 and H-8 (3), and a lone aromatic H (see Experimental). Treatment of **2** with MeI in Me_2CO in the presence of anhydrous K_2CO_3 gave the *N,O*-dimethyl derivative **3**, which was shown to be identical, by spectral comparison, with citracridone-II [**3**] previously isolated from *Citrus depressa* (5). In an nOe experiment on **2**, irradiation of the MeO signal at δ_H 4.05 showed no enhancement of any proton signal, locating the MeO and OH groups at C-5 and C-6, respectively. On the basis of these data, structure **2** was assigned for acrifoline, corresponding to the des-*N*-methyl derivative of citracridone-I which was previously obtained from *C. depressa* (5).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Mps were taken on a micro-melting point hot-stage apparatus (Yanagimoto). ^{1}H- and ^{13}C-nmr spectra were recorded on JEOL GX-270 or GX-400 spectrometers in Me_2CO-d_6. Chemical shifts are shown as δ values with TMS as internal standard. Eims were taken using Hitachi M-80 or a JEOL JMS-HX-110 spectrometer having a direct inlet system. Uv spectra were recorded on a Jasco Uvidec-610C double-beam spectrophotometer in MeOH, and ir spectra on a Jasco IR-810 spectrometer in $CHCl_3$.

PLANT MATERIAL.—*Glycosmis citrifolia* (Willd.) Lindl. (Rutaceae) was collected in Heñg Chun Tropical Graden, Kehg-Ting Botanical Garden, Taiwan. A herbarium specimen is deposited in the Herbarium of the Chia-Nan Junior College of Pharmacy, Tainan, Taiwan.

EXTRACTION AND ISOLATION.—The mother liquor from a C_6H_6-Me_2CO (19:1) fraction, obtained from the EtOH extract of the dried root and stem bark (7 kg) of the plant as reported previously (1), was treated by Si gel cc ($CHCl_3$-MeOH, 50:1) and prep. tlc [hexane-Me_2CO (2:1), hexane-EtOAc (2:1), *i*-Pr_2O, and/or $CHCl_3$-MeOH (50:1)] to afford **1** (110 mg) and **2** (26 mg).

Glycofolinine [**1**].—Yellow prisms, mp 161–163°; ir ν max 3510 (br), 1630, 1590, 1580 cm^{-1}; uv λ max 204, 220, 260, 268, 332, 395 nm; ^{1}H nmr δ 14.20 (1H, s, OH-1), 7.91 (1H, d, J=8.8 Hz, H-8), 6.92 (1H, d, J=8.8 Hz, H-7), 6.37 (1H, s, H-2), 3.97 (3H, s, OMe-3), 3.86 (3H, s), 3.77 (9H, s), 2×OMe and NMe; ^{1}H nmr (DMSO-d_6) δ 14.20 (1H, s, OH-1), 10.52 (1H, br, OH-6), 7.79 (1H, d, J=8.8 Hz, H-8), 6.90 (1H, d, J=8.8 Hz, H-7), 6.43 (1H, s, H-2), 3.89 (3H, s, OMe-3), 3.76 (3H, s, OMe-5), 3.68 (3H, s, OMe-4), 3.66 (3H, s, NMe); ^{13}C nmr δ 182.76 (s, C=O), 161.63 (s), 161.12 (s), 157.43 (s), 143.95 (s), 143.06 (s), 137.63 (s), 131.59 (s), 123.67 (d), 118.62 (s), 117.03 (s), 113.67 (d), 95.28 (dd; irradiation of OH-1—collapsed to doublet, C-2), 61.34 (q, OMe), 61.11 (q, OMe), 56.98 (q, OMe), 47.11 (q, NMe); ^{13}C nmr (DMSO-d_6) δ 180.80 (s, C=O), 159.41 (s, C-1), 159.31 (s, C-3), 156.49 (s, C-6), 142.62 (s, C-10a), 141.31 (s, C-4a), 136.28 (s, C-5), 129.75 (s, C-4), 121.77 (d, C-8), 116.24 (s, C-8a), 113.07 (s, C-7), 104.74 (s, C-9a), 94.04 (d, C-2), 60.21 (q, OMe-4), 59.89 (q, OMe-5), 56.20 (q, OMe-3), 46.42 (q, NMe); nOe irradiation of OMe (δ_H 3.97), 12% enhancement of H-2 (δ_H 6.37);

irradiation of OH (δ_H 10.52, DMSO-d_6), 9% enhancement of H-7 (δ_H 6.90, DMSO-d_6); irradiation of 3H singlet (δ_H 3.86) and 6H singlet (δ_H 3.77), no enhancement of any signal; eims *m/z* [M^+] 331 (75), 316 (100), 301 (73), 300 (32), 165 (10); hreims *m/z* 331.1029 (calcd for $C_{17}H_{17}NO_6$, 331.1054); R_f 0.27 ($CHCl_3$-MeOH, 50:1).

Acrifoline [**2**].—Yellow amorphous powder; ir ν max 3460 (br), 1640, 1610, 1570 cm^{-1}; uv λ max 203, 267, 293 (sh), 336 (sh), 396 nm; ^1H nmr δ 14.65 (1H, s, OH-1), 9.09 (1H, s, NH), 7.87 (1H, d, J=8.8 Hz, H-8), 6.93 (1H, d, J=8.8 Hz, H-7), 6.89 (1H, d, J=10.8 Hz, H-12), 6.03 (1H, s, H-2), 5.68 (1H, d, J=10.8 Hz, H-11), 4.05 (3H, s, OMe), 1.45 (6H, s, Me_2-10); ^{13}C nmr δ 182.12 (C=O), 166.18, 160.88, 154.67, 138.58, 137.24, 134.55, 127.33, 122.76, 116.60, 115.27, 114.18, 105.03, 99.47, 98.04, 78.30, 61.56, 55.92; nOe irradiation of OMe (δ_H 4.05), no enhancement of any signals; eims *m/z* $[M]^+$ 339 (43), 324 (90), 309 (53), 154 (13), 110 (36), 101 (42); hreims *m/z* 339.1101 (calcd for $C_{19}H_{17}NO_5$, 339.1105); R_f 0.27 ($CHCl_3$-MeOH, 50:1).

METHYLATION OF **2**.—A mixture of Me_2CO solution (2 ml) of **2** (3.6 mg), anhydrous K_2CO_3 (3.0 mg), and MeI (3.1 mg) was refluxed for 2.5 h. The solution was filtered and the filtrate concentrated. The residue was subjected to prep. Si gel tlc (hexane-Me_2CO, 3:1) to yield **3** (3.7 mg) as yellow needles, mp 157–159° from Et_2O. This product was found to be identical with the authentic sample of citracridone-II [**3**] by ir, uv, ^1H-nmr, and ms comparison(s).

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