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# THE STRUCTURE OF GLYCOBISMINE-A, THE FIRST NATURALLY OCCURRING "BINARY" ACRIDONE ALKALOID CONTAINING A CARBON-CARBON LINKAGE[1)]

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The structure of glycobismine-A (1), the first naturally occurring a C-C linked bisacridone alkaloid isolated from Glycosmis citrifolia (Willd.) Lindl. (Rutaceae) has been determined by spectral and chemical experiments.

KEYWORDS—— glycobismine-A; Glycosmis citrifolia; Rutaceae; acridone alkaloid; bisacridone; $^{13}$C-NMR; $^{1}$H-NMR

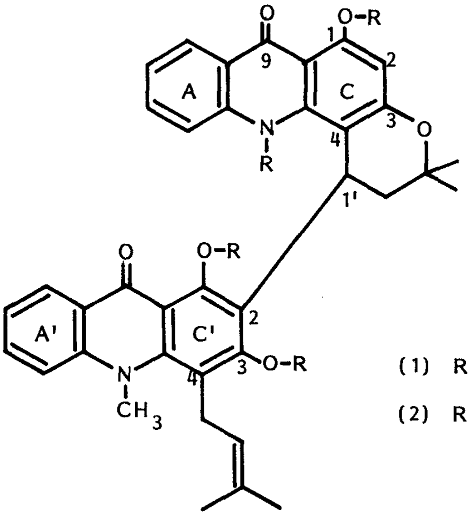
In a preceding paper,[2)] we reported the isolation of sixteen acridone alkaloids from Glycosmis citrifolia (Willd.) Lindl. (Rutaceae) collected in Taiwan. Seven of them were novel and were reported for the first time and could be divided into five groups: the linear pyranoacridone, the monoterpenoid acridone, the furanoacridone, the hexa-oxygenated acridone, and the prenylated acridone. In continuing our investigation of the acridone alkaloids of this plant, we now describe the first isolation and the structural elucidation of a "binary" acridone alkaloid glycobismine-A, containing a carbon-carbon linkage between two acridone nuclei.

Glycobismine-A (1) was isolated as yellow needles, mp 256-258°C, $[\alpha]_D$ ± 0° ($CHCl_3$),[3)] (yield: 0.002% from the dried bark), from the methanolic mother liquor from which atalaphyllidine, a mono-acridone alkaloid, was obtained.[2)] The molecular formula, $C_{37}H_{34}N_2O_6$, was established by elemental analysis and observation of the molecular ion at m/z 602 in the mass spectrum. The presence of two 1-hydroxy-9-acridone nuclei in this alkaloid was suggested by the UV (in MeOH) absorptions [$\lambda_{max}$ nm (log $\varepsilon$): 219 (sh., 4.64), 235 (sh., 4.72), 246 (4.75), 282 (4.73), 300 (sh., 4.62), 336 (sh., 4.13), 372 (4.20), and 423 (4.02)], IR (in $CHCl_3$) bands [$\nu_{max}$ cm$^{-1}$: 3360, 1630, 1600, and 1580], and $^{1}$H-NMR (400MHz, in $CDCl_3$) signals [$\delta$ 16.51 and 14.12] due to two strongly hydrogen-bonded hydroxy protons besides two deuterium exchangeable proton signals at $\delta$ 9.14 and 6.00. Further, the $^{1}$H-NMR (400MHz, $\delta_H$) and $^{13}$C-NMR (25MHz, $\delta_C$, in $CDCl_3$) spectra of glycobismine-A (1) coupled with the results of proton decoupling experiments revealed the presence of a prenyl group [$\delta_H$ 1.68 (3H, s), 1.72 (3H, s), 3.29 (2H, br t),[4)] and 5.25 (1H, br s); $\delta_C$ 18.2 (q), 25.6 (q), and 27.3 (t)], two 1,2-disubstituted aromatic rings assigned to ring-A and -A' having no substituent [$\delta_H$ 7.07 (1H, d, J=8.3Hz), 7.16 (1H, t, J=8.3Hz), 7.50 (1H, t, J=8.3Hz), 8.26 (1H, d, J=8.3Hz), and $\delta_H$ 7.35 (1H, t, J=8.8Hz), 7.43 (1H, d, J=8.8Hz), 7.76 (1H, t, J=8.8Hz), 8.45 (1H, d, J=8.8Hz)], a 4-substituted 2,2-dimethyl-3,4-dihydropyran ring fused with an acridone nucleus [$\delta_H$ 1.37 (3H, s), 1.56 (3H, s), 2.24 (1H, dd, J=8.5, 13.7Hz), 2.47 (1H, dd, J=10.7, 13.7Hz), 4.99 (1H, dd, J=8.5, 10.7Hz), and $\delta_C$ 23.2 (q), 29.7 (q), 38.3 (t), 23.6 (d), 76.9 (s)], an N-methyl moiety [$\delta_H$ 3.81 (3H, s), and $\delta_C$ 43.9 (q)], and a lone aromatic proton [$\delta_H$ 6.26 (1H, s), and $\delta_C$ 98.3 (d)] due to H-2 (or H-4) on ring-C (or -C').

Treatment of glycobismine-A (1) with $CH_3I$-$K_2CO_3$ in acetone gave N,O,O,O-tetramethyl derivative (2): $M^+$ m/z 658; $\delta_H$ (100MHz, in $CDCl_3$) 2.80, 3.38, 3.46, 3.96, and 4.06 (each 3H, s); $\delta_C$ 43.2, 43.9, 56.2, 61.4, and 62.9 (each q).

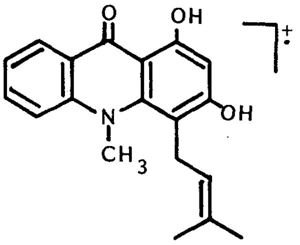
In the mass spectrum of glycobismine-A (1), principal fragment ions were shown at m/z 602 (25%), 309 (77%), 294 (100%), 293 (26%), 278 (82%), and 241 (74%). The molecular ion at m/z 602 was considered to give rise to two ions from the halves of the molecule at m/z 309 (3) and m/z 293 (4). The base peak in the spectrum at m/z 294 included an ion 5 and/or the ion derived from 3 by the elimination of $\cdot CH_3$, and an ion of m/z 241 also from the same ion 3 by that of $\cdot CH_2CH=C(CH_3)_2$, followed by transfer of a hydrogen atom. An ion of m/z 278 was considered to have the structure 6.

On the other hand, in the lower half of glycobismine-A (1), the location of the prenyl moiety at C-4 was adduced from the appearances of an N-methyl carbon at δ 43.9, and a methylene carbon of the prenyl moiety at δ 27.3 in the $^{13}$C-NMR spectrum of 1,$^{5)}$ and the remaining hydroxy group was placed on biogenetic grounds$^{6)}$ at C-3 rather than at C-2. The angular orientation of the dimethyl-dihydropyran ring in the upper half was indicated by the following $^{13}$C-NMR spectral data: 1) a new N-methyl carbon signal appearing in the spectrum of 2 was observed at δ 43.2.$^{5)}$ 2) a doublet carbon signal coupled with a proton at δ 6.26 in the $^{1}$H-NMR spectrum of 1 appeared at δ 98.3.$^{7)}$



(1) R = H

(2) R = $CH_3$



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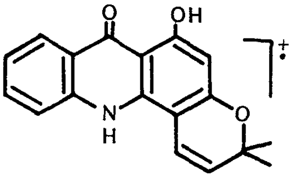

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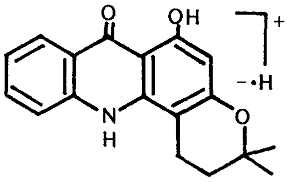

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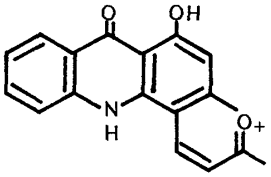


(6)

All this taken together, the linkage of the two acridone nuclei was concluded to be between C-1' and C-2 in the upper and lower halves of the molecule, respectively, and the structure of glycobismine-A was proposed as **1**.

Two bisacridone alkaloids having an ether linkage have been isolated from Rutaceous plant.[8) ] Glycobismine-A (**1**) is the first example of a C-C linked bisacridone alkaloid isolated from natural sources.[9)]

## REFERENCES AND NOTES

1) Part XII in the series "H. Furukawa: Acridone Alkaloids." For Part XI see T.-S. Wu, *Yakugaku Zasshi*, **103**, 1103 (1983).

2) T.-S. Wu, H. Furukawa, C.-S. Kuoh, and K.-S. Hsu, *J. Chem. Soc., Perkin Trans. 1*, **1983**, 1681.

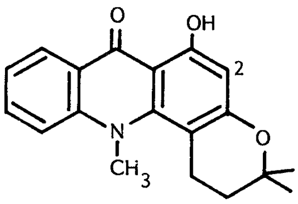
3) Also no absorption was observed in the CD (200-400 nm, in EtOH) spectrum.

4) Irradiation of the proton at δ 5.26 caused this overlapped triplet-like signal to collapse to a quartet with J=13.6Hz.

5) H. Furukawa, M. Yogo, and T.-S. Wu, *Chem. Pharm. Bull.*, **31**, 3084 (1983).

6) S. Johne and D. Groger, *Die Pharmazie*, **27**, 195 (1972).

7) The carbon signals of C-2 in **7**, and C-4 in **8** were observed at δ 98.7, and 91.4, respectively, in $^{13}$C-NMR (in $CDCl_3$) spectra.



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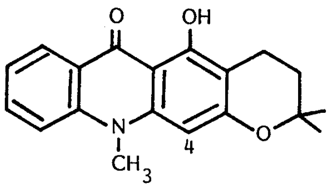

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8) A. W. Fraser and J. R. Lewis, *J. Chem. Soc., Chem. Commun.*, **1973**, 615.

9) The C-C linked dimeric and trimeric acridones have been reported to be prepared by treatment of the corresponding monomer with 10N HCl in MeOH.[10, 11)]

10) S. Funayama and G. A. Cordell, *Planta Medica*, **48**, 263 (1983).

11) S. Funayame and G. A. Cordell, *Heterocycles*, **20**, 2379 (1983).

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