Acridone Alkaloids. Part 9.[1] Chemical Constituents of *Glycosmis citrifolia* (Willd.) Lindl. Structures of Novel Linear Pyranoacridones, Furoacridones, and Other New Acridone Alkaloids

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Sixteen acridone alkaloids were isolated from *Glycosmis citrifolia* (Willd.) Lindl. (Rutaceae) collected in Taiwan. Seven of them are novel and are reported for the first time, and can be divided into four groups: the linear pyranoacridones glycofoline (1a) and pyranofoline (2a), the furoacridone furofoline-II (3b), the hexa-oxygenated acridone (4a), and the prenylated acridones glycocitrine-I (5a), -II (5c), and 3-*O*-methylglycocitrine-II (5d).

The structures were elucidated from spectral data and chemical transformations. N.O.e. experiments on the methoxymethyl derivatives of phenolic acridones were successfully applied to the determination of the position of the hydroxy group on the acridone nucleus. The location of the prenyl group of (5c) was established by correlation with compound (8), employing cyclization of (5c) with benzeneselenenyl chloride. Formic acid-catalysed cyclization of (5c) induced undesirable rearrangement of the prenyl group to form the products (9) and (10).

Glycosmis citrifolia (Willd.) Lindl.[2] (*G. cochinchinensis* Pierre) (Rutaceae) is a wild shrub and has been used as a folk medicine in the treatment of skin itch, scabies, boils, and ulcers.[3] In spite of such a useful medicinal source, the chemical constituents of the plant have not been disclosed. Only Yang *et al.*[4] have reported the isolation of a phenylalkylamine (candicine) from the bark.

In the present paper we report that systematic fractionation of the alkaloidal constituents of the stem and root barks of *G. citrifolia* yielded seven new acridone alkaloids which we have named glycofoline (1a), pyranofoline (2a), furofoline-II (3b), glyfoline (4a), glycocitrine-I (5a), glycocitrine-II (5c), and 3-*O*-methylglycocitrine-II (5d) as well as nine known acridones.

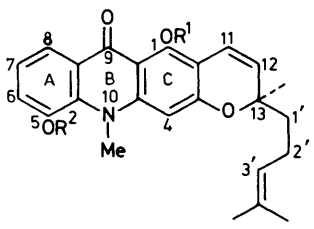
The ethanolic extract was partitioned between chloroform and water, and the chloroform-soluble components were treated by column chromatography on silica gel to afford nineteen compounds.

Structure of Glycofoline (1a).—Glycofoline was isolated as orange needles, m.p. 216—218 °C, $[\alpha]_D$ −15.1° in chloroform, and its molecular formula was determined as $C_{24}H_{25}NO_4$ by high-resolution mass spectrometry. The u.v. absorption bands at $\lambda_{max.}$ 225, 268sh, 280sh, 297, 308, 335sh, and 415 nm (Figure 1) were similar to those of the usual pyranoacridone alkaloids,[5,6] taking into account the bathochromic shift (*ca.* 30 nm), and suggested that there was an olefinic bond conjugated linearly to the 9-acridone nucleus. The i.r. band at 3 200 cm^{-1}, and ^1H n.m.r. peaks in deuteriochloroform at δ 14.82 and 8.00 (both exchangeable on deuteriation), indicated the presence of two phenolic hydroxy groups; their presence was confirmed by a deep green colour on reaction with iron(III) chloride. The lower signal at δ 14.82 and i.r. band at 1 625 cm^{-1} also indicated that one hydroxy group was strongly intramolecularly hydrogen-bonded and located perhaps at C-1 of the 9-acridone nucleus. The ^1H n.m.r. spectrum of glycofoline showed a sharp three-proton singlet at δ 4.00 due to an *N*-methyl group, and ABX pattern signals at δ 6.96 (t, *J* 8 Hz), 7.13 (dd, *J* 8, 2 Hz), and 7.85 (dd, *J* 8, 2 Hz) attributed to 7-H, 6-H, and 8-H, respectively, this last proton being deshielded by 9-carbonyl group.† A sharp one-proton singlet at δ 6.23 could be assigned to a lone aromatic proton 4-H (or 2-H). Further analyses of the ^1H and ^{13}C n.m.r. spectra of glycofoline revealed the presence of the partial structure shown in Figure 2. This feature was supported by the characteristic mass-fragmentation pattern[7] of glycofoline: *m/z* 376 ($M^+ - CH_3$), 322 {$M^+ - [CH_2CH{=}C(CH_3)_2]$}, 308 {$M^+ - [CH_2CH_2CH{=}C(CH_3)_2]$, 100%}, and 265 {$M^+ - [CH_3COCH_2CH_2CH{=}C(CH_3)_2]$}.

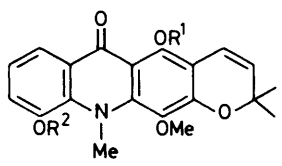
The orientation of the pyran ring was established by a nuclear Overhauser effect (n.O.e.) experiment. Irradiation of the *N*-methyl signal at δ 4.00 produced a 20% enhancement of only the signal at δ 6.23 (4-H). This result, coupled with the observation[8] of a marked diamagnetic shift (Δδ +0.3) of the 11-H (*peri* to 1-OH) signal by acetylation of the C-1 hydroxy group in glycofoline, showed the presence of a linear orientation of the pyran ring with respect to the acridone nucleus, which is different from that of the known pyranoacridone alkaloids previously isolated from natural sources. The bathochromic shift (*ca.* 30 nm) of the most intense u.v. band of glycofoline compared with that of the usual angular acridones is well explained as the result of the linear orientation of the pyran ring. In addition, the ^{13}C n.m.r. chemical-shift value of the *N*-methyl carbon (δ_C 41.0 p.p.m.) also indicated the lack of a substituent at C-4.[9] Treatment of glycofoline with hydrogen chloride in chloroform furnished a cyclization product, m.p. 238—240 °C, the ^1H n.m.r., i.r., and u.v. spectra of which were consistent with structure (7) (see Experimental section). Similar acid-catalysed cyclizations of the C_6 side-chain have been reported in the monoterpenoid carbazoles mahanimbine,[7] cyclomahanimbine,[10] and isomahanimbine [11] isolated from *Murraya koenigii* Spreng.

Next, we investigated the c.d. spectrum of glycofoline to determine the absolute configuration at C-13. The c.d. curve of glycofoline displayed a negative Cotton effect in the 265—276 nm region due to the styrene chromophore, as shown in Figure 3. According to the proposal by Crabbé,[12] this indicates that the pyranoacridone ring system should have positive chirality. The bulky C_6 side-chain of glycofoline preferenti-

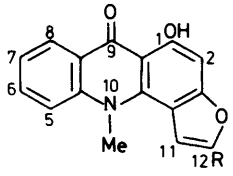
† The semi-systematic numbering schemes used for compounds (1)—(12) are based on that of acridine.



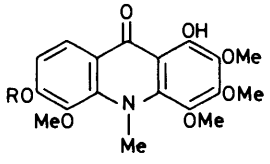
(1) a; $R^1 = R^2 = H$
b; $R^1 = H, R^2 = Ac$
c; $R^1 = R^2 = Ac$



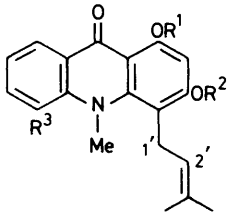
(2) a; $R^1 = R^2 = H$
b; $R^1 = H, R^2 = CH_2OMe$
c; $R^1 = Ac, R^2 = CH_2OMe$



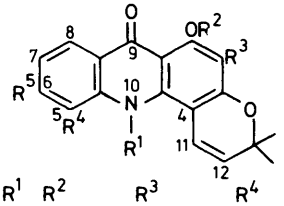
(3) a; R = H
b; $R = C(OH)Me_2$



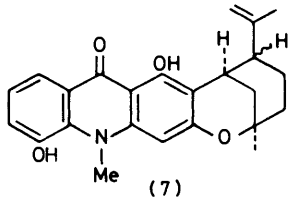
(4) a; R = H
b; $R = CH_2OMe$



	R^1	R^2	R^3
(5) a;	H	Me	OH
b;	H	Me	OCH_2OMe
c;	H	H	H
d;	H	Me	H
e;	Ac	Me	OAc



	R^1	R^2	R^3	R^4	R^5
(6) a;	Me	H	$CH_2CH{=}CMe_2$	H	H
b;	Me	H	$CH_2CH{=}CMe_2$	OH	H
c;	Me	H	H	OMe	OH
d;	Me	H	H	OH	H
e;	Me	H	H	H	H
f;	H	Me	H	H	H
g;	H	H	H	OH	H
h;	H	H	H	H	H



(7)

ally adopts the pseudoequatorial conformation and so the absolute configuration at C-13 was determined as *R*.

On the basis of the chemical and spectral results stated above, we assigned structure (1a) to glycofoline.

From the biogenetic viewpoint, the occurrence of glycofoline (1a) in the optically active form indicated possible enzymatic cyclization of the corresponding geranyl acridone. This is the first example of the isolation of a monoterpenoid acridone alkaloid from natural sources.*

Structure of Pyranofoline (2a).—Pyranofoline was crystallized from acetone as orange needles, m.p. 212—214 °C. The

* A synthesis of the compound which lacks the C-5 hydroxy group of glycofoline (1a) has been reported (W. M. Bandaranayake, M. J. Begley, B. O. Brown, D. G. Clarke, L. Crombie, and D. A. Whiting, *J. Chem. Soc., Perkin Trans. 1*, 1974, 998).

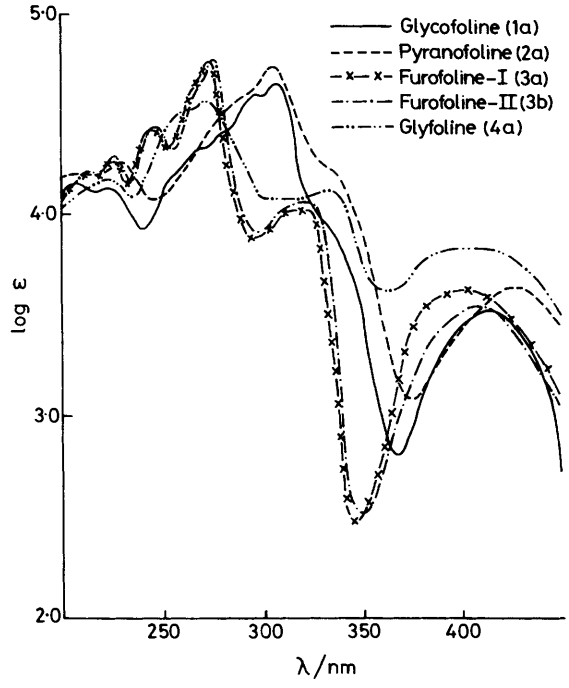


Figure 1. U.v. spectra of acridone alkaloids isolated from *Glycosmis citrifolia*

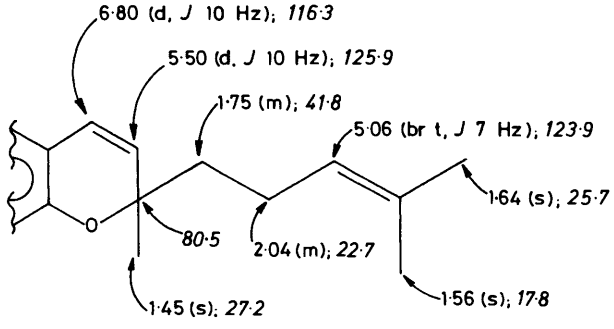


Figure 2. ^1H and ^{13}C N.m.r. spectral data of the partial structure of glycofoline (1a) in $CDCl_3$. [^{13}C N.m.r. δ-values (p.p.m.) are in italics.]

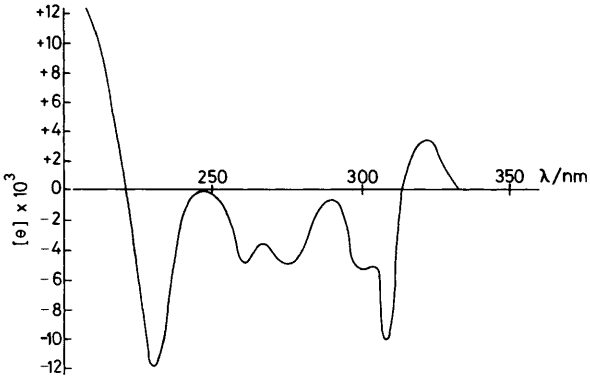


Figure 3. C.d. spectrum of 4.09×10^{-4}M glycofoline (1a) in methanol

mass spectrum (M^+, 353) and microanalysis established the molecular formula as $C_{20}H_{19}NO_5$. The u.v. spectrum (Figure 1) showed a close resemblance to that of (1a), thus suggesting a linear pyranoacridone structure for the compound.[6]

The presence of an intramolecular hydrogen-bonded phenolic hydroxy group was suggested by a deep green colour on reaction with iron(III) chloride, an i.r. band at 1 630 cm^{-1}, and a ^1H n.m.r. signal at δ 14.26 as well as that of another phenolic hydroxy group (δ 6.76); both n.m.r. signals disappeared on deuteriation.

The ^1H n.m.r. spectrum differs from that of (1a) only by the presence of signals from a methoxy (δ 3.79) and a methyl group (δ 1.64) on a quaternary carbon instead of the signals assigned to an aromatic proton (δ 6.23) and a C_6 side-chain of (1a). The AB-type signals at δ 5.58 and 6.77 (each 1 H, d, *J* 10 Hz) together with a six-proton singlet at δ 1.64 suggested a dimethylpyran system. The linear orientation of the dimethylpyran ring was established by the following evidence: (i) the similarity of the chemical shift of 11-H at δ 6.77 with that of 11-H of (1a) at δ 6.78, both of which were shifted to lower field by 0.1—0.2 p.p.m. compared with the signals from the corresponding proton in the usual *N*-methylacridone alkaloids carrying an angular pyran ring. (ii) The observation of a diamagnetic shift (Δδ +0.23 p.p.m.) of the 11-H signal at δ 6.70 in the derivative (2b) on acetylation of the C-1 hydroxy group.[8] (iii) The appearance of the C-11 signal at δ_C 116.0 p.p.m. which is similar to the case of (1a) (δ_C 116.1 p.p.m.) and is higher by 4 p.p.m. than in the case of *N*-methylacridone with an angularly orientated dimethylpyran ring.[9]

Moreover, the *N*-methyl carbon signal at δ_C 46.4 p.p.m. indicated that C-4 and C-5, both *peri* to the *N*-methyl group, would be substituted with a hydroxy and a methoxy group.[9] In order to determine the location of the hydroxy group (either C-4 or C-5), an n.O.e. experiment was carried out on the methoxymethyl ether [(2b)], m.p. 112—114 °C, prepared by treatment of pyranofoline with chloromethyl methyl ether and sodium hydroxide in the presence of a phase-transfer catalyst. The ^1H n.m.r. spectrum of (2b) showed methoxymethyl proton signals at δ 3.51 (3 H, s) and 5.25 (2 H, s), together with the signal of the hydrogen-bonded 1-hydroxy proton (δ 14.13). In the n.O.e. experiment, an 11.2% enhancement of the signal at δ 7.35 (dd, *J* 2 and 8 Hz, 6-H) appeared on irradiation of the methylene proton (δ 5.25), whereas no n.O.e. enhancement was observed at any proton signal on irradiation at δ 3.76, the signal assigned to the *N*-methyl and *O*-methyl groups. Therefore, the methoxymethyl group was unambiguously placed at C-5, and thence the methoxy group at C-4.

On the basis of these results, pyranofoline was assigned structure (2a).

Whereas all of the pyranoacridone alkaloids isolated to date from natural sources have an angular ring system, glycofoline (1a) and pyranofoline (2a) are the only linear pyranoacridone alkaloids so far found in Nature.

Structure of Furofoline-I (3a) *and -II* (3b).—Furofoline-I, m.p. 245—246 °C, and -II, m.p. 213—215 °C, were both isolated from acetone as yellow needles, and determined to have the molecular formulae $C_{16}H_{11}NO_3$ and $C_{19}H_{17}NO_4$, respectively, by mass spectrometry and elemental analysis. The striking similarity of the u.v. absorptions (Figure 1) between furofoline-I and -II suggested they possessed the same basic 9-acridone structure.[5,6]

† Furofoline-I (3d) is also known as furacridone. However, furacridone was identified only as a mixture with (11) but not fully characterized (J. Reisch, Zs. Rózsa, K. Szendrei, I. Novák, and E. Minker, *Phytochemistry*, 1977, **16**, 151).

The ^1H n.m.r. features of these two alkaloids were also similar and indicated an isolated four-spin system [δ 7.74 (dd, *J* 2 and 8 Hz), 7.56 (t, *J* 8 Hz), 7.33 (t, *J* 8 Hz), and 8.45 (dd, *J* 2 and 8 Hz) for furofoline-I and δ 7.70 (dd, *J* 2 and 8 Hz), 7.40 (dd, *J* 2 and 8 Hz), 7.34 (dt, *J* 2 and 8 Hz), and 8.43 (1 H, dd, *J* 2 and 8 Hz) for furofoline-II] assignable to 5- to 8-H,[13] indicating that ring A was unsubstituted. The presence of a signal due to a strongly chelated hydroxy group [δ 14.76 for furofoline-I and 14.84 for furofoline-II] suggested it was situated at C-1, *peri* to the C-9 carbonyl group.

The major differences were the spectral features derived from the furan moiety. In furofoline-I, 11-H at δ 7.15 and 12-H at δ 7.60 were coupled to each other and 11-H also showed a zig-zag-type long-range coupling to 2-H (δ 6.78, *J* 1 Hz), the isolated aromatic proton on ring C, akin to the situation of the 4,5,6-trisubstituted benzofuran system.[14]

On the other hand, in furofoline-II, the appearance of a six-proton singlet at δ 1.67 accompanying an alcoholic hydroxy signal at δ 4.50 instead of the 12-H signal (δ 7.60) in furofoline-I, and the mass fragmentation pattern of furofoline-II {*m/z* 308 ($M^+ - CH_3$, 100%), 305 ($M^+ - H_2O$), 290 ($M^+ - H_2O - CH_3$), and 264 [$M^+ - C(OH)(CH_3)_2$]} suggested the presence of an isopropyl alcohol moiety attached to C-12 in furofoline-II; the location of the isopropyl alcohol group at C-12 was confirmed by the observation of long-range coupling between the signals at δ 6.71 (2-H) and 7.14 (11-H). The orientation of the furan ring of both alkaloids was established by an n.O.e. experiment. Irradiation of the *N*-methyl signal of both furofoline-I (δ 4.20) and -II (δ 4.31) produced an 18.4 and a 15.2% enhancement of the signal at δ 7.15 and 7.14, respectively, both assignable to 11-H of furofoline-I and -II, respectively.

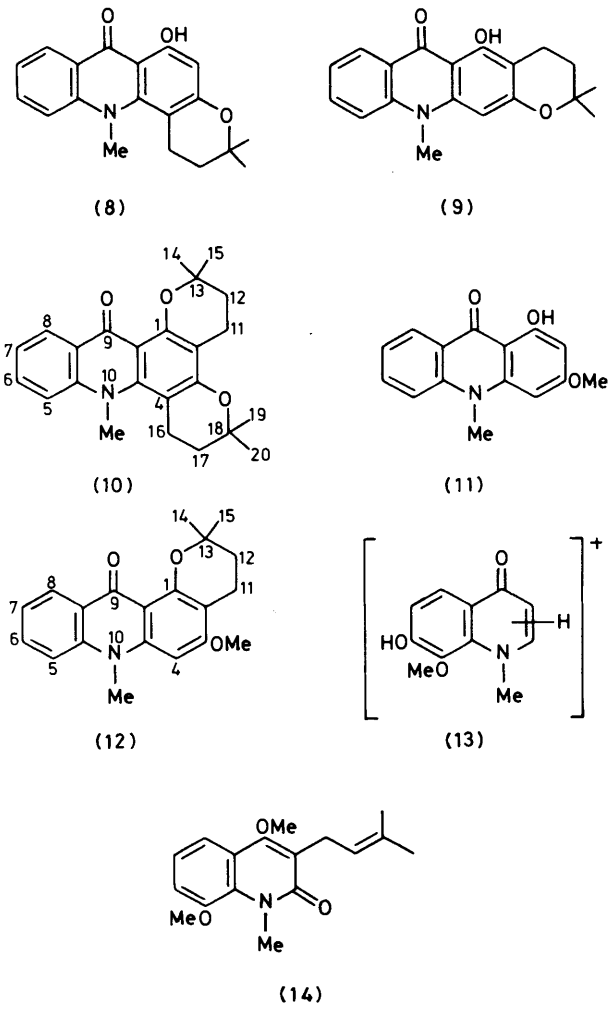
These results led us to assign structures (3a) and (3b) to furofoline-I and -II, respectively.

Several dihydro derivatives of furoacridones have been isolated from Rutaceous plants, and the first member of this series was rutacridone.[15,16] Our paper describes the first isolation of furoacridone itself from natural sources.†

Structure of Glyfoline (4a).—Glyfoline was obtained as orange plates from acetone, m.p. 215—217 °C. The molecular formula $C_{18}H_{19}NO_7$ was fixed on the basis of mass spectral (M^+, 361) and elemental analysis. The u.v. spectrum showed a typical absorption associated with a 9-acridone nucleus [5,6] (Figure 1). A bathochromic shift of the most intense u.v. band with sodium methoxide or aluminium chloride, the i.r. bands at 3 400 and 1 610 cm^{-1}, and the ^1H n.m.r. signals at δ 14.10 and 8.76 (both disappeared on deuteriation) all indicated the presence of two phenolic hydroxy groups, one of which chelated with the 9-carbonyl moiety. In the aromatic-proton region of the ^1H n.m.r. spectrum, only two one-proton signals, *ortho*-coupled to each other, at δ 6.90 and 7.93 (each 1 H, d, *J* 10 Hz) were observed. The lower signal (δ 7.93) was well known as being characteristic of 8-H of 9-acridones. The remaining signals, which appeared at δ 3.78, 3.81, 3.84, 3.89, and 4.09 (each 3 H, s), were assigned to four methoxy and one *N*-methyl group. These data, coupled with the empirical formula of glyfoline, indicated its structure to be a hexaoxygenated *N*-methyl-9-acridone.

The mass spectrum of glyfoline showed a fragment peak at *m/z* 204 (75%) assigned to the ion (13), diagnostic of 1,2,3,4-tetra-*O*-substituted acridone alkaloids.[17]

The location of a hydroxy group at C-6 (and not at C-5) was confirmed by an n.O.e. experiment on the methoxymethyl ether [(4b)]. On irradiation of the methylene protons of the methoxymethyl ether moiety (δ 5.36), a 12% enhancement of the signal at δ 6.90 (7-H) was observed. Consequently, glyfoline may be represented by structure (4a).



Glyfoline (4a) is the first hexa-*O*-substituted *N*-methyl-9-acridone to be isolated from Nature.

Structure of Glycocitrine-I (5a).—Glycocitrine-I, m.p. 210—212 °C, $C_{20}H_{21}NO_4$, was isolated as orange-yellow needles from chloroform solution. The u.v. and i.r. spectra exhibited bands characteristic of the 1-hydroxy-9-acridone system (see Experimental section). The ^{1}H n.m.r. spectrum ([$^2H_6$]acetone) showed singlets at δ 14.23 and 9.25, assignable to a strongly hydrogen-bonded phenolic proton at C-1 and another hydroxy group, respectively, ABX-pattern signals at δ 7.72 (dd, *J* 2 and 8 Hz), 7.12 (t, *J* 8 Hz), and 7.28 (dd, *J* 2 and 8 Hz), and a sharp, one-proton singlet at δ 6.37. The double doublet at δ 7.72, the X-part of the ABX-type signal, was attributed to 8-H.

The presence of a prenyl * moiety in glycocitrine-I was suggested by ^{1}H n.m.r. signals at δ 1.68, 1.77 (each 3 H, s), 3.47 (2 H, d, *J* 7 Hz), and 5.30 (1 H, m), and mass fragments at *m/z* 284 ($M^+ - C_4H_7$) and 271 ($M^+ - C_5H_8$), together with ^{13}C n.m.r. ($CDCl_3$ + [$^2H_6$]DMSO) † signals at δ_C 25.7 (q), 18.0 (q), 26.3 (t), and 123.8 p.p.m. (d). As in the case of furofoline (3a), the lower chemical shift of the *N*-methyl carbon (δ_C 48.09 p.p.m.) is characteristic of the *N*-methyl-9-acridone nucleus having substituents at both *peri*-positions (C-4 and C-5).[9] The appearance of the methylene carbon signal at δ_C 26.27 p.p.m. was suggestive of the location of a prenyl moiety at C-4.[9] The observations of a paramagnetic shift (Δδ −0.33 p.p.m.) of the lone aromatic-proton signal at δ_H 6.37 in (5a) by acetylation of the C-1 hydroxy group,[18] and a 24% n.O.e. enhancement between the signals at δ_H 3.93 and 6.37, established that a methoxy group and a lone aromatic proton were located at C-3 and C-2, respectively. Therefore, the remaining hydroxy group must be located at C-5, and this was confirmed by an n.O.e. experiment on the methoxymethyl ether (5b), m.p. 118—121 °C. The n.O.e. experiment caused a 7% selective increase in the double doublet at δ_H 7.38 (*J* 2 and 8 Hz, 6-H) on irradiation of the methylene signal at δ_H 5.29.

On the basis of these spectral data, the structure of glycocitrine-I was confirmed as (5a).

Structure of Glycocitrine-II (5c) *and* 3-*O*-*Methylglycocitrine-II* (5d).—Glycocitrine-II, orange needles from acetone, m.p. 168—169 °C, $C_{19}H_{19}NO_3$, showed a deep green colour on reaction with iron(III) chloride, and u.v., i.r., and ^{1}H n.m.r. spectra typical of a 1-hydroxy-9-acridone. The presence of a prenyl moiety in glycocitrine-II as in (5a) was also suggested by the ^{1}H n.m.r. and mass spectra (see Experimental section). The ^{1}H n.m.r. spectrum showed four aromatic-proton signals assignable to protons in the non-substituted A ring, and a one-proton singlet assigned to 2-H, whose location was established definitely by chemical conversion of glycocitrine-II into (6e) (see below).

On the other hand, treatment of glycocitrine-II with diazomethane or CH_3I–K_2CO_3 in acetone afforded a monomethyl ether [(5d)] as orange needles, m.p. 134—135 °C, $C_{20}H_{21}NO_3$. This compound was also isolated from the same plant and the two samples were shown to be identical by ^{1}H n.m.r., mass, and i.r. spectral comparison and mixed m.p. determination. The ^{13}C n.m.r. spectrum of (5d) showed signals, at δ_C 43.8 and 27.1 p.p.m., due to an *N*-methyl and a methylene carbon of the prenyl moiety, respectively. The chemical-shift values of these carbons suggested the location of the prenyl moiety to be at C-4,[9] the same as in (5a).

The structure of glycocitrine-II and 3-*O*-methylglycocitrine were thus proposed to be (5c) and (5d), respectively.

Furthermore, in order to confirm the location of the prenyl moiety of (5c) chemically, cyclization with formic acid was attempted. This reaction has usually been applied for the purpose of determination of the location of a prenyl moiety in phenolic acridone alkaloids. In our present study, the unexpected formation of four compounds was shown by t.l.c. to have occurred on treatment of (5c) with formic acid. Three of them (products A, B, and C) could be isolated and characterized.

Products A, m.p. 218—219 °C and B, m.p. 182—184 °C had the same molecular weight and were considered to be isomeric products of cyclization. The ^{1}H n.m.r. spectra of both A and B revealed a lower-field one-proton singlet due to a hydrogen-bonded hydroxy group at C-1 and an A_2B_2-type signal accompanying two *C*-methyl resonances as a singlet assignable to a dimethyldihydropyran ring (see Experimental section). Product A was shown to be identical, by i.r. and ^{1}H n.m.r. spectral comparison and mixed m.p. determination, with dihydronoracronycine (8) obtained by catalytic hydrogenation of noracronycine. Accordingly, the structure of product B could be represented by formula (9). Another product, C, was obtained as a pale yellow syrup. The i.r. and ^{1}H n.m.r. spectra of this compound indicated the absence of an hydroxy group at C-1. In the ^{1}H n.m.r. spectrum, the appearance of two pairs of A_2B_2-type signals at δ_H 1.74 (t, *J* 7 Hz), 1.81 (t, *J* 7 Hz), 2.63 (t, *J* 7 Hz), and 2.85 (t, *J* 7 Hz), and four *C*-

* Prenyl is 3-methylbut-2-enyl.
† DMSO is dimethyl sulphoxide.

methyls as a twelve-proton singlet at δ_H 1.43 revealed the presence of two dimethyldihydropyran rings in the molecule. These spectral data suggested structure (10) for product C.

The formation of the unexpected products (9) and (10) by formic acid-catalysed cyclization of (5c), together with the normal cyclization product (8), is considered to indicate that this reaction occurred through not only an intramolecular, but also an intermolecular process, and this was substantiated by the following experiment. Treatment of (5d) with formic acid gave two products, one of which was obtained as orange-yellow needles, m.p. 171—172 °C. The ^{1}H n.m.r. spectrum showed a hydrogen-bonded C-1 hydroxy-proton signal at δ_H 14.67 and a two-proton singlet at δ_H 6.16, together with signals from aromatic protons on ring A, and *N*- and *O*-methyl groups. However, no signal assignable to a prenyl or dimethyldihydropyran moiety was observed. The structure of this product was thus assigned as (11), corresponding to the deprenylated derivative of (5d), and was confirmed by identification with an authentic sample by comparison of ^{1}H n.m.r., i.r., and mass spectra and mixed m.p. The other product, pale yellow needles, m.p. 160—162 °C, showed a ^{1}H n.m.r. spectrum ($CDCl_3$ + [$^2H_6$]acetone) where the signal corresponding to the chelated C-1 hydroxy proton had disappeared and the signals due to the dimethyldihydropyran system [δ 1.46 (6 H, s), 1.83 (2 H, t, *J* 7 Hz), and 2.63 (2 H, t, *J* 7 Hz)] and a singlet at δ 6.38 (4-H) had appeared, along with aromatic- (ring A), *N*-methyl-, and *O*-methyl-proton signals. These data were consistent with structure (12) for this product. Formation of (11) and (12) from (5d) showed that this reaction proceeded in an intermolecular manner.

On the basis of the results stated above, we emphasize that conclusions from formic acid-catalysed cyclization reactions to determine the location of a prenyl group should only be derived with care.

As another method for cyclization of a prenyl moiety with a phenolic hydroxy group, we attempted the reaction with benzeneselenenyl chloride.[19] Treatment of (5c) with benzeneselenenyl chloride in dry ethyl acetate at −50 to −75 °C, followed by hydrogen peroxide and anhydrous magnesium sulphate, afforded yellow needles, m.p. 204—205 °C as the sole product. This compound was shown to be identical with noracronycine (6e) by i.r., ^{1}H n.m.r. and mass spectral comparison and mixed m.p. determination.

On the basis of the results mentioned above, the cyclization of prenylacridone alkaloids with formic acid for the determination of the location of a prenyl group proved to be disadvantageous since the intermolecular transfer of a prenyl group and then cyclization, and/or dealkylation, also occurred. The use of benzeneselenenyl chloride was found to be more useful for this purpose.

Other compounds isolated from the same plant material were characterized as *N*-methylseverifoline (6a),[20] 5-hydroxy-*N*-methylseverifoline (6b),[20] citracridone-I (6c),[21,22] 5-hydroxynoracronycine (6d),[21,22] noracronycine (6e),[23] de-*N*-methylacronycine (6f),[23] de-*N*-methylnoracronycine (6h),[23] *p*-hydroquinone, and β-sitosterol by comparison of the ^{1}H n.m.r., i.r., and mass spectra, and/or mixed m.p. The physical constants and spectroscopic data (u.v., i.r., and ^{1}H n.m.r.) of (6g) and (14) were in agreement with those described in the literature for atalaphyllidine [24] and 4,8-dimethoxy-1-methyl-3-(3-methylbut-2-enyl)-2-quinolone.[25]

Experimental

All m.p.s were measured on a micromelting point hot-stage apparatus (Yanagimoto). ^{1}H and ^{13}C N.m.r. spectra were recorded on PS-100 (JEOL) and FX-100 (JEOL) spectrometers, respectively, in $CDCl_3$ except where stated otherwise. Chemical shifts were shown in δ-values with tetramethylsilane as internal reference. Mass spectra were taken with an M-52 (Hitachi) spectrometer with a direct inlet system, and the high-resolution mass spectrum was measured with a JMS D-300 double-focusing mass spectrometer (JEOL). U.v. spectra were determined in MeOH, and i.r. spectra recorded in KBr discs except where stated otherwise. Silica gel GF_{254} (Merck) and silica gel 60 (70—230 mesh ASTM) (Merck) were used for t.l.c. and column chromatography, respectively. Organic solutions were dried over $MgSO_4$.

Extraction and Separation.—The dried root and stem bark (7 kg) of *Glycosmis citrifolia* (Willd.) Lindl. was collected in Heng Chun Tropical Botanical Garden (Kehg-Ting Botanical Garden), Taiwan, and extracted with ethanol under reflux. The ethanolic extract was partitioned between chloroform and water. The chloroform layer was separated, dried, and concentrated to give a brown syrup which was treated with diethyl ether. The ether-soluble fraction was subjected to silica-gel column chromatography with successive elution with benzene, di-isopropyl ether, diethyl ether, and acetone. The benzene eluant was rechromatographed on silica gel and eluted with n-hexane–EtOAc (5 : 1) to afford (14) (2.5 g), (6a) (0.25 g), (5d) (0.43 g), and (6e) (3.1 g), successively. The di-isopropyl ether fraction was also subjected to silica-gel column chromatography and elution with benzene–acetone (19 : 1) gave, successively, β-sitosterol (2.5 g), (6c) (0.3 g), (6d) (0.1 g), (6b) (0.08 g), (1a) (0.42 g), (4a) (0.1 g), (3b) (0.04 g), (5c) (2.1 g), (5a) (0.05 g), (6h) (2.1 g), (6g) (1.5 g), (3a) (0.01 g), (2a) (0.15 g), and *p*-hydroquinone (0.3 g). The diethyl ether eluant was rechromatographed on silica gel and eluted with benzene–acetone (2 : 1) to obtain (6f) (1.3 g).

Glycofoline (1a). Orange needles, m.p. 216—218 °C (from diethyl ether), $[\alpha]_D$ −15.1° (c 1.0, $CHCl_3$) (Found: M^+, 391.1958. $C_{24}H_{25}NO_4$ requires *M*, 391.1936); $\lambda_{max.}$ 225 (log ε 4.13), 268sh (4.32), 280sh (4.39), 297 (4.59), 308 (4.65), 335sh (3.92), and 415 nm (3.53); $\nu_{max.}$ 3 200, 1 625, 1 585, and 1 555 cm^{-1}; *m/z* 391 (M^+, 25%), 376 (8), 322 (5), 308 (100), and 265 (5); δ_H 1.45, 1.56, and 1.64 (each 3 H, s, CCH_3), 1.75 (2 H, t, *J* 7 Hz, 1′-H), 1.92—2.25 (2 H, m, 2′-H), 4.00 (3 H, s, NCH_3), 5.06 (1 H, m, 3′-H), 5.50 (1 H, d, *J* 10 Hz, 12-H), 6.23 (1 H, s, 4-H), 6.78 (1 H, d, *J* 10 Hz, 11-H), 6.96 (1 H, t, *J* 8 Hz, 7-H), 7.13 (1 H, dd, *J* 2 and 8 Hz, 6-H), 7.85 (1 H, dd, *J* 2 and 8 Hz, 8-H), 8.00 (1 H, s, 5-OH), and 14.82 (1 H, s, 1-OH); δ_C 180.1 (s), 160.8 (s), 158.5 (s), 146.7 (s), 146.4 (s), 133.7 (s), 131.8 (s), 125.9 (d), 123.9 (d), 123.3 (s), 122.6 (d), 120.6 (d), 117.4 (d), 116.3 (d), 105.2 (s), 102.5 (s), 92.0 (d), 80.5 (s), 41.8 (t), 41.0 (q), 27.2 (q), 25.7 (q), 22.7 (t), and 17.7 p.p.m. (q); c.d. (4.09 × 10^{-4}M-MeOH) $[\theta]_{210}$ +11 241, $[\theta]_{221}$ 0, $[\theta]_{231}$ −11 975, $[\theta]_{247}$ 0, $[\theta]_{261}$ −4 888, $[\theta]_{267}$ −3 421, $[\theta]_{275}$ −4 888, $[\theta]_{290}$ −489, $[\theta]_{300}$ −5 132, $[\theta]_{305}$ −4 985, $[\theta]_{308}$ −10 020, $[\theta]_{313}$ 0, and $[\theta]_{320}$ +3 421.

Pyranofoline (2a). Orange needles from acetone, m.p. 212—214 °C (Found: C, 67.4; H, 5.3; N, 3.9. $C_{20}H_{19}NO_5$ requires C, 68.0; H, 5.4; N, 4.0%); $\lambda_{max.}$ 230 (log ε 4.26), 284sh (4.53), 306 (4.74), 332sh (4.23), and 427 nm (3.64); $\nu_{max.}$ ($CHCl_3$) 3 240, 1 630, 1 610, and 1 585 cm^{-1}; *m/z* 353 (M^+), 338 (100%), 323, 320, 308, and 292; δ_H 1.64 (6 H, s, 2 × CCH_3), 3.79 (3 H, s, OCH_3), 3.84 (3 H, s, NCH_3), 5.58 (1 H, d, *J* 10 Hz, 12-H), 6.77 (1 H, d, *J* 10 Hz, 11-H), 6.76 (1 H, br s, 5-OH), 7.00—7.20 (2 H, m, 6- and 7-H), 7.87 (1 H, dd, *J* 3 and 7 Hz, 8-H), and 14.26 (1 H, s, 1-OH); δ_H ($CDCl_3$ + [$^2H_6$]DMSO) 1.53 (6 H, s, 2 × CCH_3), 3.81 (3 H, s, OCH_3), 3.87 (3 H, s, NCH_3), 5.58 (1 H, d, *J* 10 Hz, 12-H), 6.75 (1 H, d, *J* 10 Hz, 11-H), 7.08 (1 H, t, *J* 8 Hz, 7-H), 7.22 (1 H, dd, *J* 2 and 8 Hz, 6-H), 7.76 (1 H, dd, *J* 2 and 8 Hz, 8-H), and 9.57 (1 H, s, 5-OH); δ_C ($CDCl_3$ + [$^2H_6$]DMSO) 182.1 (s), 154.4 (s), 153.2 (s), 148.1 (s), 142.3 (s), 137.0 (s), 129.5 (s), 126.8 (d),

124.4 (s), 122.7 (d), 119.9 (d), 116.1 (d), 116.0 (d), 106.1 (s), 103.4 (s), 77.9 (s), 60.6 (q), 46.4 (q), and 28.3 p.p.m. (q).

Furofoline-I (3a). Yellow plates from acetone, m.p. 245—246 °C (Found: C, 72.6; H, 4.05; N, 5.3. $C_{16}H_{11}NO_3$ requires C, 72.4; H, 4.2; N, 5.3%); $\lambda_{max.}$ 226 (log ε 4.27), 245 (4.43), 266sh (4.62), 274 (4.76), 312infl (4.01), 323 (4.02), and 405 nm (3.62); $\nu_{max.}$ ($CHCl_3$) 1 620, 1 590, and 1 570 cm^{-1}; *m/z* 265 (M^+, 100%), 250, 236, 223, 222, and 205; δ_H ($CDCl_3$ + [$^2H_6$]acetone) 4.20 (3 H, s, NCH_3), 6.78 (1 H, d, *J* 1 Hz, 2-H), 7.15 (1 H, dd, *J* 1 and 2 Hz, 11-H), 7.33 (1 H, t, *J* 8 Hz, 7-H), 7.56 (1 H, t, *J* 8 Hz, 6-H), 7.60 (1 H, d, *J* 2 Hz, 12-H), 7.74 (1 H, dd, *J* 2 and 8 Hz, 5-H), 8.45 (1 H, dd, *J* 2 and 8 Hz, 8-H), 14.76 (1 H, s, 1-OH).

Furofoline-II (3b). Yellow needles from acetone, m.p. 213—215 °C. The $FeCl_3$ test gave a positive reaction (Found: C, 71.2; H, 5.5; N, 4.2. $C_{19}H_{17}NO_4$ requires C, 70.6; H, 5.3; N, 4.3%); $\lambda_{max.}$ 226 (log ε 4.29), 247 (4.43), 268sh (4.61), 276 (4.77), 312infl (4.03), 323 (4.07), and 409 nm (3.55); $\nu_{max.}$ 3 390, 1 620, 1 590, and 1 535 cm^{-1}; *m/z* 323 (M^+), 308, 305, 290 (100%), 264, 262, 204, and 152; δ_H($CDCl_3$ + [H_6]acetone) 1.67 (6 H, s, 2 × CCH_3), 4.31 (3 H, s, NCH_3), 4.50 (1 H, s, OH), 6.71 (1 H, d, *J* 1 Hz, 2-H), 7.14 (1 H, d, *J* 1 Hz, 11-H), 7.34 (1 H, dt, *J* 2 and 8 Hz, 7-H), 7.40 (1 H, dd, *J* 2 and 8 Hz, 6-H), 7.70 (1 H, dd, *J* 2 and 8 Hz, 5-H), 8.43 (1 H, dd, *J* 2 and 8 Hz, 8-H), and 14.84 (1 H, s, 1-OH).

Glyfoline (4a). Orange plates from acetone, m.p. 215—217 °C (Found: C, 60.2; H, 5.3; N, 3.9. $C_{18}H_{19}NO_7$ requires C, 59.8; H, 5.3; N, 3.9%); $\lambda_{max.}$ 223sh (log ε 4.17), 261sh (4.50), 272 (4.56), 333 (4.12), and 409 nm (3.83); $\nu_{max.}$ ($CHCl_3$) 3 400, 1 610, 1 580, and 1 560 cm^{-1}; *m/z* 361 (M^+, 13%), 346 (73), 316 (100), and 204 (75); δ_H($CDCl_3$ + [$^2H_6$]acetone) 3.78, 3.81, 3.84, 3.89, and 4.09 (each 3 H, s, together 4 × OCH_3 and NCH_3), 6.90 (1 H, d, *J* 10 Hz, 7-H), 7.93 (1 H, d, *J* 10 Hz, 8-H), 8.76 (1 H, s, 6-OH), and 14.10 (1 H, s, 1-OH).

Glycocitrine-I (5a). Orange needles from chloroform, m.p. 210—212 °C (Found: C, 71.0; H, 6.3; N, 4.1. $C_{20}H_{21}NO_4$ requires C, 70.8; H, 6.2; N, 4.1%); $\lambda_{max.}$ 228 (log ε 4.17), 268 (4.57), 322sh (4.01), 337 (4.07), and 415 nm (3.58); $\nu_{max.}$ 3 240, 1 620, 1 585, and 1 565 cm^{-1}; *m/z* 339 (M^+, 50%), 324 (51), 308 (16), 294 (25), 284 (37), 282 (50), and 271 (100); δ_H([$^2H_6$]acetone) 1.68 and 1.77 (each 3 H, s, CCH_3), 3.47 (2 H, d, *J* 7 Hz, 1′-H_2), 3.65 (3 H, s, NCH_3), 3.93 (3 H, s, OCH_3), 5.30 (1 H, m, 2′-H), 6.37 (1 H, s, 2-H), 7.12 (1 H, t, *J* 8 Hz, 7-H), 7.28 (1 H, dd, *J* 2 and 8 Hz, 6-H), 7.72 (1 H, dd, *J* 2 and 8 Hz, 8-H), 9.25 (1 H, s, 5-OH), and 14.23 (1 H, s, 1-OH); δ_C($CDCl_3$ + [$^2H_6$]DMSO) 182.9 (s), 165.0 (s), 163.1 (s), 150.3 (s), 148.6 (s), 138.4 (s), 131.3 (s), 124.8 (s), 123.8 (d), 122.7 (d), 119.9 (d), 116.1 (d), 108.9 (s), 107.2 (s), 93.4 (d), 55.9 (q), 48.1 (q), 26.3 (t), 25.7 (q), and 18.0 p.p.m. (q).

Glycocitrine-II (5c). Orange needles from acetone, m.p. 168—169 °C, which gave a deep green colour on reaction with $FeCl_3$ (Found: C, 73.8; H, 6.2; N, 4.5. $C_{19}H_{19}NO_3$ requires C, 73.8; H, 6.2; N, 4.5%); $\lambda_{max.}$ 226 (log ε 4.27), 251 (4.48), 268sh (4.54), 275 (4.74), 304 (4.12), 334 (3.95), and 405 nm (3.77); $\nu_{max.}$ 3 400, 1 610, 1 585, and 1 560 cm^{-1}; *m/z* 309 (M^+, 51%), 294 (37), 264 (10), 254 (25), 252 (46), and 241 (100); δ_H($CDCl_3$ + [$^2H_6$]acetone) 1.70 and 1.76 (each 3 H, s, CCH_3), 3.47 (2 H, d, *J* 7 Hz, 1′-H_2), 3.88 (3 H, s, NCH_3), 5.26 (1 H, m, 2′-H), 6.24 (1 H, s, 2-H), 7.20 (1 H, t, *J* 8 Hz, 7-H), 7.54 (1 H, d, *J* 8 Hz, 5-H), 7.70 (1 H, t, *J* 8 Hz, 6-H), 8.18 (1 H, dd, *J* 2 and 8 Hz, 8-H), 9.46 (1 H, br s, 3-OH), and 14.63 (1 H, s, 1-OH); δ_C($CDCl_3$ + [$^2H_6$]DMSO) 180.8 (s), 164.3 (s), 162.7 (s), 147.1 (s), 145.6 (s), 133.6 (d), 131.1 (s), 125.4 (d), 124.6 (d), 121.0 (d, s), 116.4 (d), 106.4 (s), 105.2 (s), 97.1 (d), 43.4 (q), 26.9 (t), 25.5 (q), and 18.0 (q).

3-O-*Methylglycocitrine-II* (5d). Orange needles from acetone, m.p. 134—135 °C (Found: C, 74.3; H, 6.5; N, 4.3. $C_{20}H_{21}NO_3$ requires C, 74.3; H, 6.55; N, 4.3%); $\lambda_{max.}$ 226, 252, 274, 304, 333, and 409 nm; $\nu_{max.}$ 1 620, 1 575, and 1 550 cm^{-1}; *m/z* 323 (M^+), 308, 292, 280, 279, 278, 268, 266, 255 (100%), and 236; δ_H([$^2H_6$]acetone) 1.72 (3 H, s, CCH_3), 1.76 (3 H, s, CCH_3), 3.42 (2 H, d, *J* 7 Hz, 1′-H_2), 3.86 (3 H, s, NCH_3), 3.93 (3 H, s, OCH_3), 5.30 (1 H, m, 2′-H), 6.34 (1 H, s, 2-H), 7.21 (1 H, t, *J* 8 Hz, 7-H), 7.52 (1 H, d, *J* 8 Hz, 5-H), 7.70 (1 H, t, *J* 8 Hz, 6-H), 8.18 (1 H, dd, *J* 2 and 8 Hz, 8-H), and 14.70 (1 H, s, 1-OH); δ_C 181.7 (s), 165.3 (s), 163.7 (s), 146.7 (s), 146.1 (s), 133.8 (d), 131.6 (s), 125.9 (d), 124.5 (d), 121.2 (d, s), 116.3 (d), 106.9 (s), 106.5 (s), 93.3 (d), 55.9 (q), 43.8 (q), 27.1 (t), 25.6 (q), and 18.1 p.p.m. (q). This compound was shown to be identical with an authentic sample prepared from (5c) with diazomethane (i.r. and ^1H n.m.r. spectral comparison).

Methylation of glycocitrine-II (5c). (a) Compound (5c) (30 mg) was dissolved in acetone (5 ml) and the solution was refluxed with methyl iodide (2 ml) and anhydrous potassium carbonate (2 g) for 1 h. The solution was filtered and the filtrate was concentrated. The residue was recrystallized from acetone to yield (5d) (28 mg), m.p. 134—135 °C.

(b) Compound (5c) (30 mg) was dissolved in diethyl ether (20 ml) and a few drops of methanol were added. A solution of diazomethane in diethyl ether (5 ml) was then added and the mixture was left overnight. The solvent was evaporated to give a crystalline residue which was recrystallized from acetone to give (5d) as orange needles, m.p. 134—135 °C. The ^1H n.m.r., i.r., u.v., and mass spectra of the 3-*O*-methyl ether obtained by both methods were consistent with structure (5d).

General Procedure of Methoxymethylation.—A solution of a phenolic acridone (30 mg) in dichloromethane (5 ml), 1% aqueous sodium hydroxide (10 ml), and a phase-transfer catalyst (Adogen 464 from Aldrich) (2 mg) were stirred together at room temperature for 30 min, and then excess of chloromethyl methyl ether was added until reaction was complete (monitored by t.l.c.). The reaction mixture was extracted with dichloromethane. The organic layer was dried and concentrated. The residue was chromatographed on silica gel and eluted with benzene–acetone (9 : 1) to afford the methoxymethyl ether.

5-O-*Methoxymethylpyranofoline* (2b). Orange needles from diethyl ether, m.p. 112—114 °C; $\lambda_{max.}$ 230, 280, 306, and 425 nm; $\nu_{max.}$ ($CHCl_3$) 1 630, 1 610, 1 585, and 1 555 cm^{-1}; *m/z* 397 (M^+), 382 (100%), 367, 352, 338, 332, and 322; δ_H 1.52 (6 H, s, 2 × CCH_3), 3.51 (3 H, s, CH_2OCH_3), 3.76 (6 H, s, NCH_3 and 4-OCH_3), 5.25 (2 H, s, CH_2), 5.53 (1 H, d, *J* 10 Hz, 12-H), 6.70 (1 H, d, *J* 10 Hz, 11-H), 7.10 (1 H, t, *J* 8 Hz, 7-H), 7.35 (1 H, dd, *J* 2 and 8 Hz, 6-H), 7.88 (1 H, dd, *J* 2 and 8 Hz, 8-H), and 14.13 (1 H, s, 1-OH).

6-O-*Methoxymethylglyfoline* (4b). Orange needles from diethyl ether, m.p. 105—109 °C; $\lambda_{max.}$ 225, 260sh, 275, 333, and 418 nm; $\nu_{max.}$ ($CHCl_3$) 1 610, 1 580, and 1 550 cm^{-1}; *m/z* 405 (M^+), 390 (100%), 375, 360, 346, 330, 316, 302, and 300; δ_H 3.57, 3.80, 3.82, 3.91, and 3.96 (each 3 H, s, OCH_3), 4.15 (3 H, s, NCH_3), 5.36 (2 H, s, CH_2), 7.14 (1 H, d, *J* 10 Hz, 7-H), 8.04 (1 H, d, *J* 10 Hz, 8-H), and 13.89 (1 H, s, 1-OH).

5-O-*Methoxymethylglycocitrine-I* (5b). Yellow needles from chloroform, m.p. 118—121 °C; $\lambda_{max.}$ 227, 268, 336, and 410 nm; $\nu_{max.}$ ($CHCl_3$) 1 610, 1 590, and 1 555 cm^{-1}; *m/z* 383 (M^+), 368 (100%), 352, 336, 328, 324, 315, 308, 300, 294, 282, and 270; δ_H 1.70 (3 H, s, CCH_3), 1.77 (3 H, s, CCH_3), 3.46 (2 H, d, *J* 7 Hz, 1′-H_2), 3.55 (3 H, s, CH_2OCH_3), 3.59 (3 H, s, NCH_3), 3.89 (3 H, s, 3-OCH_3), 5.29 (2 H, s, CH_2), 6.34 (1 H, s, 2-H), 7.16 (1 H, t, *J* 8 Hz, 7-H), 7.38 (1 H, dd, *J* 2 and 8 Hz, 6-H), 7.92 (1 H, dd, *J* 2 and 8 Hz, 8-H), and 14.02 (1 H, s, 1-OH).

Acetylation of Glycofoline (1a).—Treatment of (1a) (20 mg) with acetic anhydride and anhydrous sodium acetate at 100 °C for 8 h and work-up in the usual way afforded a yellow residue which showed two spots on t.l.c. [silica gel; benzene–acetone (9 : 1)]. Separation by preparative layer chromatography (p.l.c.) gave the monoacetate (1b) and the diacetate (1c). *Monoacetate* (1b). Yellow syrup, $\lambda_{max.}$ 207, 226, 258, 270sh, 283sh, 296sh, 306, 332sh, and 413 nm; $\nu_{max.}$ ($CHCl_3$) 1 760, 1 630, 1 580, and 1 555 cm^{-1}; *m/z* 433 (M^+), 418, 390, 350 (100%), 308, and 293; δ_H 1.42 (3 H, s, CCH_3), 1.55 (3 H, s, CCH_3), 1.63 (3 H, s, CCH_3), 1.71 (2 H, t, *J* 7 Hz, 1′-H_2), 1.90—2.25 (2 H, m, 2′-H_2), 2.34 (3 H, s, OAc), 3.74 (3 H, s, NCH_3), 5.02 (1 H, m, 3′-H), 5.44 (1 H, d, *J* 10 Hz, 12-H), 6.10 (1 H, s, 4-H), 6.71 (1 H, d, *J* 10 Hz, 11-H), 7.11 (1 H, t, *J* 8 Hz, 7-H), 7.23 (1 H, dd, *J* 2 and 8 Hz, 6-H), 8.20 (1 H, dd, *J* 2 and 8 Hz, 8-H), and 14.42 (1 H, s, 1-OH).

Diacetate (1c). Yellow syrup, $\lambda_{max.}$ 206, 223, 267sh, 290, 304, 323sh, 350, and 400 nm; $\nu_{max.}$ ($CHCl_3$) 1 760, 1 610, 1 595, and 1 550 cm^{-1}; *m/z* 475 (M^+), 433, 418, 390, 350 (100%), 308, and 293; δ_H 1.44 (3 H, s, CCH_3), 1.56 (3 H, s, CCH_3), 1.64 (3 H, s, CCH_3), 1.74 (2 H, t, *J* 7 Hz, 1′-H_2), 1.94—2.25 (2 H, m, 2′-H_2), 2.35 (3 H, s, OAc), 2.49 (3 H, s, OAc), 3.73 (3 H, s, NCH_3), 5.04 (1 H, m, 3′-H), 5.61 (1 H, d, *J* 10 Hz, 12-H), 6.48 (1 H, d, *J* 10 Hz, 11-H), 6.57 (1 H, s, 4-H), 7.11 (1 H, t, *J* 7 Hz, 7-H), 7.22 (1 H, dd, *J* 2 and 7 Hz, 6-H), and 8.17 (1 H, dd, *J* 2 and 7 Hz, 8-H).

Acetylation of 5-O-*Methoxymethylpyranofoline* (2b).—Treatment of (2b) with acetic anhydride and sodium acetate at 100 °C for 8 h gave the acetate (2c) as a yellow syrup, $\lambda_{max.}$ 208, 225, 295, 330sh, and 403 nm; $\nu_{max.}$ ($CHCl_3$) 1 755, 1 630, 1 595, 1 580, and 1 550 cm^{-1}; *m/z* 439 (M^+), 397 (100%), 382, 332, 223, and 205; δ_H 1.54 (6 H, s, 2 × CCH_3), 2.48 (3 H, s, OAc), 3.53 (3 H, s, OCH_3), 3.71 (3 H, s, NCH_3), 3.86 (3 H, s, OCH_3), 5.28 (2 H, s, CH_2), 5.70 (1 H, d, *J* 10 Hz, 12-H), 6.47 (1 H, d, *J* 10 Hz, 11-H), 7.09 (1 H, t, *J* 7 Hz, 7-H), 7.33 (1 H, dd, *J* 2 and 7 Hz, 6-H), and 7.84 (1 H, dd, *J* 2 and 7 Hz, 8-H).

Acetylation of Glycocitrine-I (5a).—Glycocitrine-I (5a) (20 mg) was treated in the same manner as (1a) to afford the diacetate (5e) (19 mg) as a pale yellow syrup, $\lambda_{max.}$ 207, 225, 262, 292sh, 314, and 384 nm; $\nu_{max.}$ ($CHCl_3$) 1 755, 1 630, 1 590, and 1 550 cm^{-1}; *m/z* 423 (M^+), 381, 366 (100%), 339, 324, and 282; δ_H([$^2H_6$]acetone) 1.68 (3 H, s, CCH_3), 1,78 (3 H, s, CCH_3), 2.32 (3 H, s, OAc), 2.41 (3 H, s, OAc), 3.47 (3 H, s, NCH_3), 3.51 (2 H, d, *J* 7 Hz, 1′-H_2), 3.93 (3 H, s, OCH_3), 5.28 (1 H, m, 2′-H), 6.70 (1 H, s, 2-H), 7.21 (1 H, t, *J* 7 Hz, 7-H), 7.40 (1 H, dd, *J* 2 and 7 Hz, 6-H), and 7.92 (1 H, dd, *J* 2 and 7 Hz, 8-H).

Cyclization of Glycocitrine-II (5c) *with Formic Acid.*—Compound (5c) (50 mg) was heated at 90—100 °C for 4 h with formic acid (85%; 3 ml) and the mixture was then left at room temperature overnight. Water was added and the solution extracted with chloroform. The extract was washed in turn with dilute aqueous sodium hydrogen carbonate and water, dried, and concentrated. The residue showed four spots on t.l.c. [silica gel; benzene–acetone (9 : 1)]: A (R_F 0.52), B (0.64), C (0.26), and D (0.45). The proportions of these four products, determined by ^1H n.m.r. spectroscopy, were 2 : 8 : 1 : 0.5. Separation by p.l.c. gave the products A, B, and C in pure form. Attempts to purify product D were unsuccessful.

Product A (8). Yellow needles from diethyl ether, m.p. 218—219 °C; $\lambda_{max.}$ 228, 253, 277, 303, 334, and 399 nm; $\nu_{max.}$ ($CHCl_3$) 1 635, 1 590, and 1 560 cm^{-1}; *m/z* 309 (M^+, 100%), 294, 254, 241, and 225; δ_H 1.42 (6 H, s, 2 × CCH_3), 1.72 (2 H, t, *J* 7 Hz, 12-H_2), 2.84 (2 H, t, *J* 7 Hz, 11-H_2), 3.80 (3 H, s, NCH_3), 6.14 (1 H, s, 2-H), 7.18 (1 H, dt, *J* 2 and 8 Hz, 7-H), 7.33 (1 H, dd, *J* 2 and 8 Hz, 5-H), 7.60 (1 H, dt, *J* 2 and 8 Hz, 6-H), 8.22 (1 H, dd, *J* 2 and 8 Hz, 8-H), and 14.18 (1 H, s, exchangeable with D_2O, 1-OH). This compound was shown to be identical (i.r., ^1H n.m.r., t.l.c., and mixed m.p.) with dihydronoracronycine (8).

Product B (9). Yellow needles from diethyl ether, m.p. 182—184 °C; $\lambda_{max.}$ 227, 250, 266sh, 275, 295sh, 332, and 404 nm; $\nu_{max.}$ ($CHCl_3$) 1 635, 1 600, 1 590, and 1 560 cm^{-1}; *m/z* 309 (M^+), 294, 266, 254 (100%), 253, 241, 225, 197, 196, and 182; δ_H 1.40 (6 H, s, 2 × CCH_3), 1.85 (2 H, t, *J* 7 Hz, 12-H_2), 2.73 (2 H, t, *J* 7 Hz, 11-H_2), 3.68 (3 H, s, NCH_3), 6.20 (1 H, s, 4-H), 7.20 (1 H, dt, *J* 2 and 8 Hz, 7-H), 7.36 (1 H, dd, *J* 2 and 8 Hz, 5-H), 7.60 (1 H, dt, *J* 2 and 8 Hz, 6-H), 8.36 (1 H, d, *J* 2 and 8 Hz, 8-H), and 15.05 (1 H, s, exchangeable with D_2O, 1-OH).

Product C (10). Pale yellow syrup, $\lambda_{max.}$ 229, 254, 276, 304, 323, and 393 nm; $\nu_{max.}$ ($CHCl_3$) 1 620, 1 590, 1 585, and 1 555 cm^{-1}; *m/z* 377 (M^+, 100%), 362, 334, 322, 306, 278, and 266; δ_H 1.43 (12 H, s, 4 × CCH_3), 1.74 (2 H, t, *J* 7 Hz, 17-H_2), 1.81 (2 H, t, *J* 7 Hz, 12-H_2), 2.63 (2 H, t, *J* 7 Hz, 11-H_2), 2.85 (2 H, t, *J* 7 Hz, 16-H_2), 3.72 (3 H, s, NCH_3), 7.14 (1 H, dt, *J* 2 and 8 Hz, 7-H), 7.28 (1 H, dd, *J* 2 and 8 Hz, 5-H), 7.54 (1 H, dt, *J* 2 and 8 Hz, 6-H), and 8.31 (1 H, dd, *J* 2 and 8 Hz, 8-H).

Treatment of 3-O-*Methylglycocitrine-II* (5d) *with Formic Acid.*—A solution of compound (5d) (50 mg) in formic acid 85%; 3 ml) was heated at 90—100 °C for 4 h and then left overnight, diluted with water, and extracted with chloroform. The extract was washed in turn with aqueous sodium hydrogen carbonate and water, dried, and concentrated. The residue showed two spots on t.l.c. [benzene–acetone (9 : 1)] which were separated by p.l.c. on silica gel to afford compound (11) (18 mg) as orange needles, m.p. 171—172 °C; $\lambda_{max.}$ 223, 248sh, 263, 271, 294, 325sh, and 395 nm; $\nu_{max.}$ ($CHCl_3$) 1 625, 1 590, and 1 555 cm^{-1}; *m/z* 255 (M^+, 100%), 225, 212, 197, 184, and 182; δ_H 3.67 (3 H, s, NCH_3), 3.82 (3 H, s, OCH_3), 6.16 (2 H, s, 2- and 4-H), 7.16 (1 H, dt, *J* 2 and 8 Hz, 7-H), 7.34 (1 H, dd, *J* 2 and 8 Hz, 5-H), 7.59 (1 H, dt, *J* 2 and 8 Hz, 6-H), 8.30 (1 H, dd, *J* 2 and 8 Hz, 8-H), and 14.67 (1 H, s, 1-OH), and compound (12), pale yellow needles from acetone (20 mg), m.p. 160—162 °C; $\lambda_{max.}$ 225, 250sh, 265sh, 272, 295, 320sh, and 387 nm; $\nu_{max.}$ ($CHCl_3$) 1 625, 1 595, and 1 555 cm^{-1}; *m/z* 323 (M^+), 308, 281, 269 (100%), 239, 226, and 211; δ_H ([$^2H_6$]acetone + $CDCl_3$) 1.46 (6 H, s, 2 × CCH_3), 1.83 (2 H, t, *J* 7 Hz, 12-H_2), 2.63 (2 H, t, *J* 7 Hz, 11-H_2), 3.78 (3 H, s, NCH_3), 3.95 (3 H, s, OCH_3), 6.38 (1 H, s, 4-H), 7.12 (1 H, dt, *J* 2 and 8 Hz, 7-H), 7.39 (1 H, dd, *J* 2 and 8 Hz, 5-H), 7.55 (1 H, dt, *J* 2 and 8 Hz, 6-H), and 8.38 (1 H, dd, *J* 2 and 8 Hz, 8-H).

Cyclization of Glycocitrine-II (5c) *with Benzeneselenenyl Chloride.*—A dry ethyl acetate solution of benzeneselenenyl chloride (0.1 mmol) was added slowly to a stirred ethyl acetate solution of compound (5c) (0.1 mmol) at −75 to −50 °C. After 1 h the reaction mixture was washed with water, dried, and evaporated. The residue was dissolved in tetrahydrofuran, and 30% hydrogen peroxide (1 ml) and then anhydrous magnesium sulphate (2 g) were added. The mixture was stirred for 1 h, washed with water, dried, and concentrated. The residue showed two spots on t.l.c. [benzene–acetone (9 : 1)]. Separation by p.l.c. gave yellow needles (18 mg), m.p. 204—205 °C, and orange needles, m.p. 168—169 °C (8 mg), which were shown to be identical with (6e) and starting material (5c), respectively, by i.r., ^1H n.m.r., and mass spectral comparisons, and mixed m.p. determinations.

Cyclisation of Glycofoline (1a).—Compound (1a) (30 mg) was treated with concentrated HCl (0.5 ml) in chloroform (10 ml) for 30 min. The mixture was then diluted with water and extracted with chloroform. The extract was washed in turn with aqueous sodium hydrogen carbonate and water, dried, and concentrated to yield a yellow residue. T.l.c. revealed two spots. The residue was purified by p.l.c. to afford yellow needles of compound (7), m.p. 238—240 °C; $\lambda_{max.}$ 232, 260sh, 280, 289, 308, and 413 nm; $\nu_{max.}$ 3 320, 1 620, 1 585, and 1 550 cm^{-1}; *m/z* 391 (M^+), 376, 351, 337, 322, 320, 308, 293, 283, 282, 270, and 256; δ_H ($CDCl_3$ + [$^2H_6$]acetone) 1.20 (3 H, s, CCH_3), 1.42 (3 H, s, CCH_3), 3.70 (1 H, m, benzylic H), 4.08 (3 H, s, NCH_3), 4.46 (2 H, br s, $C{=}CH_2$), 6.36 (1 H, s, 4-H), 7.07 (1 H, t, *J* 8 Hz, 7-H), 7.25 (1 H, dd, *J* 2 and 8 Hz, 6-H), 7.91 (1 H, dd, *J* 2 and 8 Hz, 8-H), 9.09 (1 H, br s, 5-OH), and 16.35 (1 H, s, 1-OH).

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