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# Carbazole alkaloids from roots of *Glycosmis arborea*

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**Abstract**

A new carbazole alkaloid, designated as glycoborinine, was isolated from the roots of *Glycosmis arborea*, along with two other known carbazole alkaloids, viz. glycozoline and glycozolidine, and two known quinoline alkaloids, viz. skimianine and 3-(3′,3′-dimethylallyl)-4,8-dimethoxy-*N*-methylquinolin-2-one. Its structure was elucidated mainly on the basis of its 2D NMR spectral analyses. 

*Keywords: Glycosmis arborea*; Rutaceae; Carbazole alkaloids; Glycoborinine; 2D NMR

## 1. Introduction

*Glycosmis arborea*, an indigenous plant popularly known as *Ashshoura*, *Bon-nimbu*, etc., is used locally against fever, liver complaints and certain other diseases (Sastri, 1956). The isolation of furoquinoline, quinazoline and acridine alkaloids was earlier reported (Chakravarti, Chakravarti, & Chakravarti, 1953; Chatherjee & Gbosh Majumdar, 1954; Chakraborty & Barman, 1961; Pakrashi & Bhattacharyya, 1962) from this species. During our present investigation on the roots of *G. arborea*, we isolated three carbazole alkaloids (**1--3**) and two quinoline alkaloids (**4**–**5**), of which one carbazole alkaloid (**1**) was new and designated as glycoborinine. The other two carbazole alkaloids were proven to be the known glycozoline (**2**) (Chakraborty, 1961, 1969) and glycozolidine (**3**) (Chakraborty & Das, 1966; Islam, Bhattacharyya, & Chakraborty, 1972) and the two quinoline alkaloids were identified as skimmianine (**4**) (Pakrashi & Bhattacharyya, 1963) and 3-(3′,3′-dimethylallyl)-4,8-dimethoxy-*N*-methyl quinolin-2-one (**5**) (Rastogi, Kapil, & Popli, 1980). During elucidation of the structures of the compounds by 2D NMR, the $^{1}H$ and $^{13}C$ chemical shifts of all the compounds were assigned unambiguously and it was observed that the assignment of $^{13}C$ chemical shifts reported (Bhattacharyya & Chakraborty, 1987) for some alkaloids, viz. **2**, were erroneous. We report herein the structural elucidation of **1**, as well as the unambiguously assigned $^{1}H$ and $^{13}C$ chemical shifts for **1**–**3**.

## 2. Results and discussion

The petrol extract of the roots of *G. arborea* on chromatographic resolution over neutral alumina yielded **2**, **3** and **5**, whilst the chloroform-soluble part of the methanol extract furnished pure **1**, **2** and **4**. The structures of the five compounds were elucidated mainly on the basis of 1D and 2D NMR, viz. PND, DEPT, $^{1}H$–$^{1}H$ COSY, HSQC, HMBC and NOESY spectral analyses.

Glycoborinine (**1**) had the molecular formula $C_{18}H_{17}NO_2$ from its high resolution mass spectrum. The $^{13}C$ NMR spectrum (Table 1) displayed signals for 18 carbons, of which three were $CH_3$, six aromatic CH, eight aromatic quaternary carbons and one oxygenated non-aromatic quaternary carbon ($\delta$ 75.54 s). The $^{1}H$ NMR spectrum (Table 2) exhibited signals for six aromatic methine protons, of which two were singlets and the remaining four appeared as two pairs of mutually coupled doublets ($^{1}H$–$^{1}H$ COSY). This spectrum also showed singlets for one aromatic methyl and two aliphatic tertiary methyl groups. The HMBC spectrum (Table 3) of **1** gave valuable information about its structure. Thus, while the two- and three-bond correlations of the methine proton singlets at $\delta$ 6.82 (H-1) and 7.79 (H-4), as well as the aromatic methyl proton signal at $\delta$ 2.37 with those of the neighbouring carbons, clearly suggested the presence of the part structure A (Fig. 1) in the molecule; the correlations of the mutually coupled methine proton signals at $\delta$ 6.78 (H-7) and 7.11 (H-8) indicated the existence of a second part structure **B** in the molecule. Moreover, the correlations of the aliphatic methyl proton ($\delta$ 1.47) signal and the mutually coupled pair of methine

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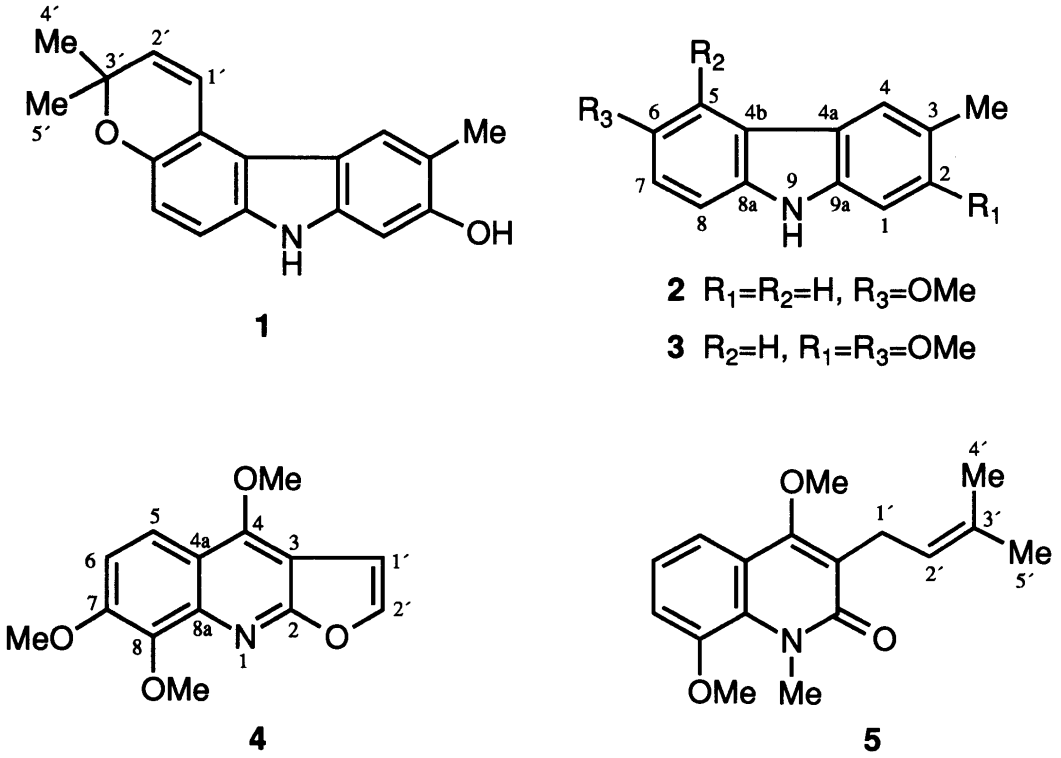


Structure 1.

Table 1
$^{13}$C Chemical shifts[a] ($\delta$, $CDCl_3$, 125 MHz) of alkaloids **1**–**3**

| Carbon | **1**[b] | **2**[c] | **3** |
|---|---|---|---|
| C-1 | 96.5 | 110.4 | 92.5 |
| C-2 | 154.5 | 127.2 (119.8) | 157.5 |
| C-3 | 117.4 | 128.3 | 119.0 |
| C-4 | 123.8 | 120.1 (126.6) | 121.4 |
| C-4a | 116.6 | 123.6[d] | 116.3 |
| C-4b | 119.3 | 123.5[d] | 124.0 |
| C-5 | 115.0 | 103.0 (114.5) | 102.6 |
| C-6 | 146.1 | 153.7 | 153.9 |
| C-7 | 113.5 | 114.9 (102.1) | 113.0 |
| C-8 | 110.4 | 111.3 | 110.9 |
| C-8a | 135.8 | 134.7 | 134.2 |
| C-9a | 141.6 | 138.5 | 140.1 |
| C-10 | 16.7 | 21.4 | 16.7 |
| C-1′ | 120.9 | – | – |
| C-2′ | 131.2 | – | – |
| C-3′ | 75.5 | – | – |
| C-4′ | 27.2 | – | – |
| C-5′ | 27.2 | – | – |
| $CH_3O$-2 | – | – | 55.5 |
| $CH_3O$-6 | – | 56.0 | 56.1 |

[a] Chemical shifts assigned on the basis of 2D NMR spectral analyses.
[b] Spectrum recorded in $CDCl_3$–$CD_3OD$.
[c] Figsures in parentheses are assignments reported in Bhattacharyya and Chakraborty (1987).
[d] Values may be interchanged.

proton signals at $\delta$ 5.81 and 7.25, demonstrated the presence of a third part structure **C** in the molecule. The joining of the three partial structures resulted in the formation of the total structure **1** for glycoborinine. The structure **1** was finally confirmed by the NOE interactions observed in its NOESY spectrum as depicted in Fig. 2.

Table 2
$^1$H Chemical shifts[a] ($\delta$, $CDCl_3$, 500 MHz) of alkaloids **1**–**3**

| $^1$H | **1**[b] | **2** | **3** |
|---|---|---|---|
| H-1 | 6.82 s | 7.275 d (8.2) | 6.79 s |
| H-2 | – | 7.21 br d (8.2) | – |
| H-4 | 7.79 br s | 7.82 br s | 7.74 br s |
| H-5 | – | 7.52 d (2.5) | 7.44 d (2.5) |
| H-7 | 6.78 dd (8.6, 0.6) | 7.03 dd (8.9, 2.5) | 6.95 dd (8.8, 2.5) |
| H-8 | 7.11 d (8.6) | 7.23 d (8.9) | 7.23 d (8.8) |
| H-9 | – | 7.78 br s | 7.69 br s |
| $H_3$-10 | 2.37 s | 2.54 s | 2.35 s |
| H-1′ | 7.25 d (9.8) | – | – |
| H-2′ | 5.81 d (9.8) | – | – |
| $H_3$-4′ | 1.47 s | – | – |
| $H_3$-5′ | 1.47 s | – | – |
| $CH_3O$-2 | – | – | 3.88 s |
| $CH_3O$-6 | – | 3.91 s | 3.91 s |

[a] Coupling constant $J$ (Hz) in parentheses.
[b] Spectrum recorded in $CDCl_3$–$CD_3OD$.

Table 3
One-bond ($^1H$–$^{13}C$ COSY) and multiple-bond (HMBC) $^1H$–$^{13}C$ correlation data of alkaloid **1**

| | One-bond correlation | Multiple-bond correlations ($\delta_C$, ppm) | | | |
|---|---|---|---|---|---|
| $\delta_H$ (ppm) | $\delta_C$ (ppm) | $\delta_C$ (ppm) | | | |
| 6.82 (H-1) | 96.5 (C-1) | 116.6 (C-4a) | 117.4 (C-3) | 141.6 (C-9a) | 154.5 (C-2) |
| 7.79 (H-4) | 123.8 (C-4) | 16.7 (C-10) | 96.5 (C-1) | 116.6 (C-4a) | 119.3 (C-4b) |
| | | 141.6 (C-9a) | 154.5 (C-2) | | |
| 6.78 (H-7) | 113.5 (C-7) | 115.0 (C-5) | 135.8 (C-8a) | 146.1 (C-6) | – |
| 7.11 (H-8) | 110.4 (C-8) | 115.0 (C-5) | 119.3 (C-4b) | 146.1 (C-6) | – |
| 2.37 ($H_3$-10) | 16.7 (C-10) | 117.4 (C-3) | 123.8 (C-4) | 154.5 (C-2) | – |
| 7.25 (H-1′) | 120.9 (C-1′) | 27.2 (C-4′, -5′) | 115.0 (C-5) | 119.3 (C-4b) | 146.1 (C-6) |
| | | 75.5 (C-3′) | | | |
| 5.81 (H-2′) | 131.2 (C-2′) | 27.2 (C-4′, -5′) | 75.5 (C-3′) | 115.04 (C-5) | – |
| 1.47 ($H_3$-4′, -5′) | 27.2 (C-4′, -5′) | 27.2 (C-4′, -5′) | 75.5 (C-3′) | 131.2 (C-2′) | – |

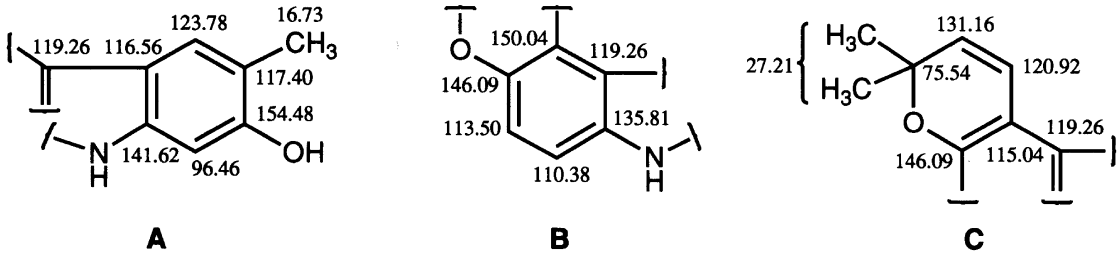


Fig. 1. Part structures of compound **1** derived from HMBC data and [13] chemical shifts of their carbons.

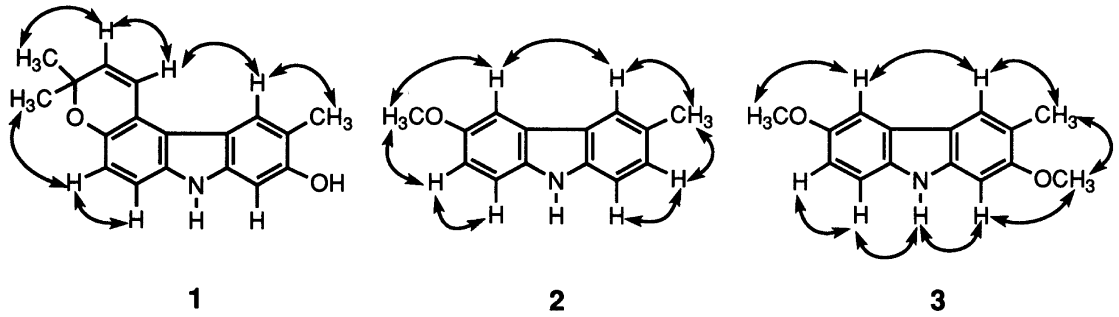


Fig. 2. NOE interactions observed in the NOESY spectra of compounds **1**–**3**.

The remaining four compounds were identified as glycozoline (**2**), glycozolidine (**3**), skimmianine (**4**) and 3-(3′,3′-dimethylallyl)-4,8-dimethoxy-*N*-methylquinolin-2-one (**5**) by detailed analyses of their 2D NMR spectra. In the process of identification, $^{13}C$ and $^1H$ chemical shifts of all the compounds were assigned unambiguously and those of the carbazole alkaloids (**2**–**3**) are summarised in the Tabs. 1–2, respectively. The assignments of $^1H$ chemical shifts were confirmed by the NOE interactions observed in their NOESY spectra Fig. 2. Having thus assigned the $^1H$ chemical shifts of the compounds, the corresponding $^{13}C$ chemical shifts could easily be assigned from their $^1H$–$^{13}C$ COSY or HSQC spectra. The quaternary carbons of the compounds were assigned on the basis of HMBC data.

It was observed that the $^{13}C$ chemical shift assignments of glycozoline (**2**) reported in the literature (Bhattacharyya & Chakraborty, 1987) did not correspond to those of ours and were found to be erroneous. So far, as substitution-induced chemical shift additivity rules are concerned, the reported assignments of C-2, C-4, C-5 and C-7 of **2** (shown in parentheses in Table 1) seem to be logical. However, on the basis of 2D NMR spectral analyses, the reported chemical shifts of C-2 and C-4, as well as C-5 and C-7, must be interchanged as shown in Table 1. It is, therefore, clear that in a mul-

tisubstituted aromatic system, the chemical shifts of the carbons cannot always be assigned with certainty by the application of additivity rules.

## 3. Experimental

### 3.1. General

M.p.'s: uncorr. NMR: recorded on a 500 MHz instrument, with TMS as int. standard. EIMS: 30 eV.

### 3.2. Plant material

Roots of *Glycosmis arborea* (Roxb.) DC were collected from M/s United Chemical and Allied Products, 10 Clive Row, Calcutta 700 001, India, and a voucher specimen is available in the herbarium of the Company.

### 3.3. Isolation

Air-dried and milled roots (5.5 kg) were successively extracted with petrol (60–80°C) and MeOH at room temp. The extracts were evaporated to dryness under red. pres. to obtain the petrol extract (28 g) and the MeOH extract (50 g). While the petrol extract on repeated chromatography over neutral alumina yielded **2** (124 mg), **3** (68 mg) and **5** (1.5 g), the $CHCl_3$-sol. part (8 g) of the MeOH extract on chromatographic purification over the same adsorbent furnished pure glycoborinine (**1**, 32 mg), **2** (60 mg) and **4** (147 mg).

### 3.4. Glycoborinine (*1*)

Recrystallised from benzene–MeOH, m.p. 220–221°C. UV $\lambda_{max}$ nm: 262, 269, 293, 335. EI-MS *m/z* (rel. int.): 279.1269 ($[M]^+$, 32), 264 (100). $^{13}C$ NMR: Table 1. $^1H$ NMR: Table 2.

### 3.5. Glycozoline (*2*)

Recrystallised from petrol–$CHCl_3$, m.p. 177–178°C (lit. (Chakraborty, 1961, 1969) m.p. 181–182°C). UV $\lambda_{max}$ nm: 252, 264, 304, 343. EI-MS *m/z* (rel. int.): 211.0978 ($[M^+]$, 100), 196 (97), 168 (30), 167 (19). $^{13}C$ NMR: Table 1. $^1H$ MMR: Table 2.

### 3.6. Glycozolidine (*3*)

Recrystallised from benzene–MeOH, m.p. 166–167°C (lit. (Chakraborty & Das, 1966) m.p. 161–162°C). UV $\lambda_{max}$ nm: 234, 260, 310, 371, 375. EI-MS *m/z* (rel. int.): 241.1108 ($[M]^+$, 100), 226 (68), 198 (14), 183 (14). $^{13}C$ NMR: Table 1. $^1H$ NMR: Table 2.

### 3.7. Skimmianine (*4*)

Recrystallised from benzene–MeOH, m.p. 177–178°C (lit. (Pakrashi & Bhattacharyya, 1963) m.p. 176°C). UV $\lambda_{max}$ nm: 249, 320, 331. EI-MS *m/z* (rel. int.): 259.0834 ($[M]^+$, 86), 244 (100), 230 (46), 216 (24), 201 (17). $^{13}C$ NMR: $\delta$ 164.4 (C-2), 102.0 (C-3), 157.2 (C-4), 114.9 (C-4a), 118.2 (C-5), 112.0 (C-6), 152.1 (C-7), 142.0 (C-8), 141.5 (C-8a), 104.7 (C-1′), 143.0 (C-2′), 59.0 ($CH_3O$-4), 56.8 ($CH_3O$-7), 61.7 ($CH_3O$-8). $^1H$ NMR: $\delta$ 7.98 d ($J=9.4$ Hz, H-5), 7.21 d ($J=9.4$ Hz, H-6), 7.00 d ($J=3.0$ Hz, H-1′), 7.55 d ($J=3.0$ Hz, H-2′), 4.40 s ($CH_3O$-4), 4.02 s ($CH_3O$-7), 4.12 s ($CH_3O$-8).

### 3.8. 3-(3′,3′-Dimethylallyl)-4,8-dimethoxy-N-methylquinolin-2-one (*5*)

Oil. UV $\lambda_{max}$ nm: 239, 255, 285, 293, 322. EI-MS *m/z* (rel. int.): 287.1513 ($[M]^+$, 61), 272 (98), 257 (17), 244 (100), 218 (26), 148 (25). $^{13}C$ NMR: $\delta$ 164.8 (C-2), 122.5 (C-3), 159.8 (C-4), 119.9 (C-4a), 115.7 (C-5), 122.3 (C-6), 113.3 (C-7), 148.5 (C-8), 130.3 (C-8a), 24.2 (C-1′), 121.4 (C-2′), 132.2 (C-3′), 17.8 (C-4′), 25.5 (C-5′), 56.5 ($CH_3O$-4), 61.4 ($CH_3O$-8), 35.3 ($CH_3$-N). $^1H$ NMR: $\delta$ 7.43 dd ($J=7.9$, 1.5 Hz, H-5), 7.15 dd ($J=7.9$, 7.9 Hz, H-6), 7.03 dd ($J=7.9$, 1.5 Hz, H-7), 3.39 d ($J=6.7$ Hz, H-1′), 5.26 m (H-2′), 1.81 s ($H_3$-4′), 1.69 d ($J=0.9$ Hz, $H_3$-5′), 3.87 s ($CH_3O$-4), 3.88 s ($CH_3O$-8), 3.94 s ($CH_3$-N).

## References


Bhattacharyya, P. & Chakraborty, D. P. (1987). In W. Herz, H. Grisebach, G. W. Kirby, & C. Tamm (Eds.), *Fortschritte Der Chem. Org. Naturst.* (Vol. 52, p. 159). New York: Springer-Verlag.

Chakraborty, D. P. (1961). *Tetrahedron Lett.*, *0*, 661.

Chakraborty, D. P. (1969). *Phytochemistry*, *8*, 769.

Chakraborty, D. P., & Barman, B. K. (1961). *Trans. Bose Res. Inst.*, *24*, 121.

Chakraborty, D. P., & Das, B. P. (1966). *Sci. Cult.*, *32*, 181.

Chakravarti, D., Chakravarti, R. N., & Chakravarti, S. C. (1953). *J. Chem. Soc.*, 3337.

Chatherjee, A., & Gbosh Majumdar, S. (1954). *J. Am. Chem. Soc.*, *76*, 2459.

Islam, A., Bhattacharyya, P., & Chakraborty, D. P. (1972). *J. Chem. Soc. Chem. Commun.*, 537.

Pakrashi, S. C., & Bhattacharyya, J. (1962). *J. Sci. Ind. Res.*, *21B*, 49.

Pakrashi, S. C., & Bhattacharyya, J. (1963). *Anal. Biochem. Exp. Med.*, *23*, 123.

Rastogi, K., Kapil, R. S., & Popli, S. P. (1980). *Phytochemistry*, *19*, 945.

Sastri, B. N. (1956). *The wealth of India* (Vol. 4, p. 150). New Delhi: Council of Scientific and Industrial Research.