

ALKALOIDS OF *KOLOBOPETALUM AURICULATUM**

D. DWUMA-BADU,† J. S. K. AYIM,† O. REXFORD,† A. M. ATEYA,‡ D. J. SLATKIN,‡
J. E. KNAPP‡ and P. L. SCHIFF, JR.‡§

†Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Science and Technology, Kumasi, Ghana;

‡Department of Pharmacognosy, School of Pharmacy, University of Pittsburgh, Pittsburgh, PA 15261, U.S.A.

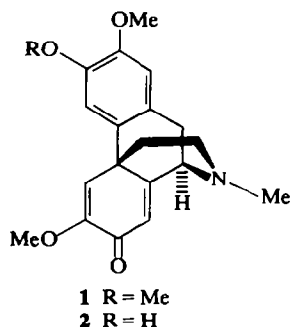
(Received 2 July 1979)

Key Word Index—*Kolobopetalum auriculatum*; Menispermaceae; morphinandienone alkaloids; O-methylflavinantine; aporphine alkaloids; N-methylcorydine; magnoflorine.

Kolobopetalum auriculatum Engl. (Menispermaceae) is a lofty climber indigenous to Ghana, the Ivory Coast and other parts of West Africa [1]. The reputed medicinal uses of numerous West African Menispermaceous species [1] and the absence of any literature reference on the absence of this genus prompted us to undertake a phytochemical investigation of this plant.

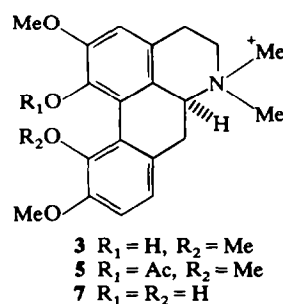
The dried leaves and twigs of *Kolobopetalum auriculatum* (0.9 kg) were moistened with dil. NH_4OH and extracted by percolation with EtOH. The resulting extract was concentrated to a viscous mass, treated with dil. HOAc and filtered. The filtrate was alkalized with NH_4OH and repeatedly extracted with CHCl_3 . The combined CHCl_3 extracts (4 g) were evaporated and chromatographed over alumina with dry Et_2O to afford O-methylflavinantine (1) (0.05 g), mp 159° , $[\alpha]_D^{26} - 10^\circ$ (MeOH, $c = 0.29$), identical to an authentic sample [2] by a direct comparison (UV, IR, $^1\text{H NMR}$, MS, mp, mmp). To our knowledge, this is only the second report of this alkaloid from nature. O-Methylflavinantine was first described as a methylation product of flavinantine (2) [3], an alkaloid of *Croton flavens* L. (Euphorbiaceae) [3], and later first isolated as a natural alkaloid from *Rhigiocarya racemifera* Miels (Menispermaceae) [2].

The ammoniacal layer remaining after extraction of the nonquaternary alkaloids was acidified (pH 2) with

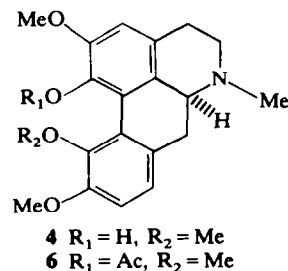


* Part 26 in the series "Constituents of West African Medicinal Plants". For Part 25, see Tackie, A. N., Reighard, J., Slatkin, D. J., Schiff, P. L., Jr. and Knapp, J. E. (1979) *J. Natl. Prod.* **42**, submitted for publication.

§ To whom correspondence should be addressed



HCl and the quaternary alkaloids precipitated with Mayer's reagent [4]. The precipitate was filtered, washed with H_2O , dissolved in MeOH and passed over an ion-exchange column (IRA-401 [I⁻] in MeOH). Evaporation of the eluate afforded a brown mass (20 g) of crude quaternary iodide salts, which was chromatographed over silica gel (100 g). Elution with 2% MeOH in CHCl_3 afforded N-methylcorydine iodide (3) (0.15 g), mp $218-221^\circ$, $[\alpha]_D^{20} + 155^\circ$ (MeOH, $c = 1.09$), which was identified by direct comparison (UV, IR, $^1\text{H NMR}$, MS, mp, mmp) with an authentic reference sample (prepared by treating corydine (4) [5] in Me_2CO with MeI) and by dequaternization of O-acetyl-N-methylcorydine iodide (5) to O-acetylcorydine (6) according to the procedure of Wilson and Joule [6]. Hydrolysis of O-acetylcorydine in methanolic K_2CO_3 gave corydine (4) (UV, IR, $^1\text{H NMR}$, MS, mp, mmp). N-Methylcorydine has been previously isolated from *Fagara nigrescens* (Rutaceae) [7], *Polyalthia oliveri* (Annonaceae) [8] and *Zanthoxylum punctatum* (Rutaceae) [9]. This appears to be the first isolation of N-methylcorydine from a member of the Menispermaceae.



Continued elution of the column with the same solvent gave magnoflorine iodide (7) (0.30 g) identical to an authentic reference sample [10] by direct comparison (UV, IR, ¹H NMR, MS, mp, mmp). Magnoflorine was first isolated in 1954 from *Magnolia grandiflora* (Magnoliaceae) [11] and has since been isolated from numerous genera of the Aristolochiaceae, Berberidaceae, Euphorbiaceae, Magnoliaceae, Menispermaceae, Papaveraceae, Ranunculaceae and Rutaceae [11].

Biological significance

Extracts of this species as well as the alkaloid O-methylflavine have been shown to possess analgesic and antitussive properties [12]. Magnoflorine has been found to possess a curare-like action with resultant relaxation of skeletal muscle and death due to respiratory paralysis [13–15].

Acknowledgements—The authors are grateful to Mr. K. Obeng-Darko (F.L.S.) of the Faculty of Agriculture, University of Science and Technology, Kumasi, Ghana for identification and collection of the plant material. A voucher specimen is on deposit at the Faculty of Pharmacy, University of Science and Technology, Kumasi, Ghana. The authors are also grateful to Mr. John Naworal, Graduate School of Public Health, University of Pittsburgh for determining the mass spectra. The investigation was supported in part by grants from the International Foundation of Science, Stockholm, Sweden; the Health Research Services Foundation (R-15), Pittsburgh, PA and the National Institutes of Health (5S01RR05455-10). The mass spectrometry facility was supported by Research Grant RR-00273 from the National Institutes of Health.

REFERENCES

1. Irvine, F. R. (1961) *Woody Plants of Ghana*, p. 32. Oxford University Press, London.
2. Tackie, A. N., Dwuma-Badu, D., Knapp, J. E., Slatkin, D. J. and Schiff, P. L., Jr. (1974) *Phytochemistry* **13**, 2884.
3. Stuart, K. L., Chambers, C. and Byfield, D. (1969) *J. Chem. Soc. C* 1681.
4. Hodgman, C. D., Weast, R. C. and Selby, S. M. (1958) *Handbook of Chemistry and Physics*, 39th edn. p. 1552. Chemical Rubber Publishing Company, Cleveland.
5. Tackie, A. N., Dwuma-Badu, D., Lartey, P. A., Schiff, P. L., Jr., Knapp, J. E. and Slatkin, D. J. (1974) *Lloydia* **37**, 6.
6. Wilson, N. D. V. and Joule, J. A. (1968) *Tetrahedron* **24**, 5493.
7. Kuck, A. M. (1966) *Chem. Ind.* 118.
8. Hamonnière, M., Leboeuf, M. and Cavé, A. (1977) *Phytochemistry* **16**, 1029.
9. Stermitz, F. R. and Sharifi, I. A. (1977) *Phytochemistry* **16**, 2003.
10. Flor, S. C., Doorenbos, N. J., Svoboda, G. H., Knapp, J. E. and Schiff, P. L., Jr. (1974) *J. Pharm. Sci.* **63**, 618.
11. Guinaudeau, H., Leboeuf, M. and Cavé, A. (1975) *Lloydia* **38**, 275.
12. Gyang, E. A., Dwuma-Badu, D., Ayim, J. S. K., Noamesi, B. K. and Ansa-Asamoah, R. (1975) *Ghana Pharm. J.* **3**, 130.
13. Inoue, K. (1957) *Nippon J. Pharmacol.* **53**, 797; (1958) *Chem. Abstr.* **52**, 18870.
14. Ogui, K. (1958) *Jpn. J. Pharmacol.* **7**, 137; (1958) *Chem. Abstr.* **52**, 18896.
15. Fakhritidonov, S. F. and Kamilov, I. K. (1967) *Farmkol. Alkaloidov Glikozidov*, 149; *Chem. Abstr.* (1969) **70**, 2221.