Phytochemistry, 1980, Vol. 19, pp. 161–162. © Pergamon Press Ltd. Printed in England. 0031-9422/80/0101-0161 $02.00/0

HERNAGINE, A NEW APORPHINE ALKALOID, AND 3-CYANO-4-METHOXYPYRIDINE FROM *HERNANDIA NYMPHAEFOLIA*

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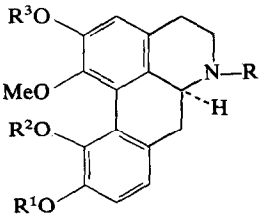
(*Received* 20 *April* 1979)

Key Word Index—*Hernandia nymphaefolia*; Hernandiaceae; aporphine alkaloids; hernagine; pyridine alkaloid; 3-cyano-4-methoxypyridine.

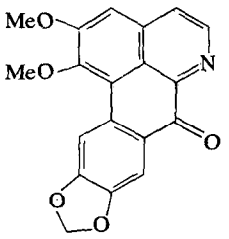
Several alkaloids from the bark of the plant of *Hernandia* species have been isolated previously [1–3]. We here report on the isolation and characterization of a new aporphine alkaloid and a pyridine alkaloid from the leaves of *Hernandia nymphaefolia* (Presl) Kubitzki (Japanese name, Hasunoha-giri) collected on Iriomote Island.

Hernagine, a new alkaloid, was separated as an oil by careful Si gel column chromatography from the phenolic fraction. The ^{1}H NMR (100 MHz, $CDCl_3$, δ) spectrum of hernagine† showed 3 methoxyls at 3.49, 3.55 and 3.86, 3 aromatic protons at 6.68 (1H, *s*) and 6.85 (2H, *s*), but no methylimino protons. Treatment of hernagine with formaldehyde and $NaBH_4$ afforded *N*-methylhernagine as a yellow oil, $[\alpha]_D^{25}+144°$ ($CHCl_3$). The MS exhibited a M^+ at *m/e* 341 and the base peak at *m/e* 310. The UV spectrum (λ_{max}^{EtOH} nm (log ε): 221 (4.39), 269 (4.04), and 307 (3.73)) of *N*-methylhernagine was characteristic of a 1, 2, 10, 11-substituted aporphine [4]. The ^{1}H NMR spectrum also supported this substitution pattern [4] (NMe: δ 2.71; 3×OMe: δ 3.49, 3.53 and 3.87; C-3 H: δ 6.64 (1H, *s*); C-8,9 H: δ 6.85 (2H, *s*)). Two of 3 methoxyls gave signals markedly upfield from that of the other methoxy group, and accordingly, C-1 and C-11 positions must be substituted with methoxyl groups. This leaves only two possible structures, **2** and **3** [5], for *N*-methylhernagine. A comparison of the ^{1}H NMR spectra of *N*-methylhernagine in DMSO-d_6, with and without added KOH, showed an upfield shift of 0.45 and 0.59 ppm in two aryl protons at δ 6.91 (1H, *d*, J = 8 Hz) and 6.78 (1H, *d*, J = 8 Hz), respectively, and 0.25 ppm in another aryl proton at δ 6.85 (1H, *s*) [4]. Since these observations indicated that the hydroxyl group must be present at C-10, structure **1** was proposed for hernagine, and **2** for its *N*-methyl derivative.

We also isolated and characterized **3** aporphine alkaloids, nornantenine (**8**) [6], laurotetanine (**9**) [7] and *N*-methyllaurotetanine (**10**) [7], and an oxoaporphine alkaloid, oxonantenine (**4**) [6], in addition to the known aporphine alkaloids, ovigerine (**5**) [1–3], nandigerine (**6**) [2, 3] and isocorydine (**7**) [2] from the bark of the plant of the same species.



1 R = R^1 = H; R^2 = R^3 = Me
2 R = R^2 = R^3 = Me; R^1 = H
3 R = R^1 = R^2 = Me; R^3 = H
7 R = R^1 = R^3 = Me, R^2 = H



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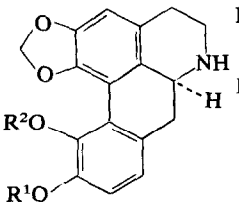
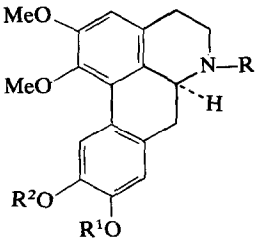
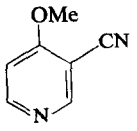


5 R^1R^2 = CH_2
6 R^1 = H; R^2 = Me



8 R = H; R^1R^2 = CH_2
9 R = R^1 = H; R^2 = Me
10 R = R^2 = Me; R^1 = H



11

3-Cyano-4-methoxypyridine (**11**), obtained from both the phenolic and non-phenolic base fractions, was crystallized from ether solution as colorless needles, mp 124°. The IR ($CHCl_3$) spectrum showed a nitrile group at 2230 cm^{-1} and the UV spectrum showed

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† Contamination with a small amount of nandigerine (**6**) was recognized. An efficient procedure for its separation was not devised and hernagine (**1**) could only be separated as its N-methyl derivative (**2**).

absorptions at λ_{max}^{EtOH} 231 and 272 nm. Its ^{1}H NMR ($CDCl_3$, δ) spectrum revealed the presence of 3 aromatic protons at 6.82 (1H, *d*, $J = 6$ Hz), 8.53 (1H, *d*, $J = 6$ Hz) and 8.56 (1H, *s*), and a methoxyl group at 3.94. The MS exhibited a M^+ at *m/e* 134 as the base peak. Finally, the structure of this alkaloid was established by direct comparison (mmp, IR and ^{1}H NMR) with synthetic 3-cyano-4-methoxypyridine (**11**) prepared by the method of Wieland *et al.* [8].

3-Cyano-4-methoxypyridine (**11**) has not been previously obtained from natural sources and we are investigating the biological role of this simple pyridine alkaloid.

REFERENCES

1. Tomita, M., Lu, S. -T. and Chen, Y. -Y. (1969) *J. Pharm. Soc. Jpn* **86,** 763.
2. Cava, M. P., Bessho, K., Douglas, B., Markey, S., Raffauf, R. F. and Weisbach, J. A. (1966) *Tetrahedron Letters* 1577.
3. Furukawa, H., Ueda, F., Ito, M., Ito, K. Ishii, H. and Haginiwa, J. (1972) *J. Pharm. Soc. Jpn* **92,** 150.
4. Shamma, M. (1972) in *The Isoquinoline Alkaloids, Chemistry and Pharmacology*, p. 195.
5. Kametani, T., Koizumi, M., Shishido, K. and Fukumoto, K. (1971) *J. Chem. Soc. C* 1923.
6. Johns, S. R., Lamberton, J. A. and Sioumis, A. A. (1967) *Aust. J. Chem.* **20,** 1457.
7. Tewari, S., Bhakuni, D. S. and Dhar, M. M. (1972) *Phytochemistry* **11,** 1149.
8. Wieland, T., Fest, C. and Pfleiderer, G. (1961) *Ann.* **642,** 163.

Phytochemistry, 1980, Vol. 19, pp. 162–163. 0031-9422/80/0101-0162 $02.00/0

MAYFOLINE, A NOVEL ALKALOID FROM *MAYTENUS BUXIFOLIA*

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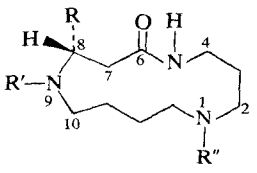
(*Received* 8 *May* 1979)

Key Word Index—*Maytenus buxifolia*; Celastraceae; spermidine alkaloid; mayfoline.

Compounds reacting with the Dragendorff reagent were detected in *Maytenus buxifolia* (A. Rich.) Griseb. (Celastraceae) [1]. Mayfoline has now been isolated from the aerial parts of the plant. Structure **1** with a characteristic hydroxylamine moiety is consistent with the spectroscopic and chemical properties of this alkaloid. Similar macrocyclic spermidine alkaloids occur in other *Maytenus* species and further Celastraceae [2, 3].



1 R = Ph, R′ = H, R″ = OH
2 R = Ph, R′ = Ac, R″ = OAc
3 R = C_6H_{11}, R′ = R″ = H

The IR, UV and ^{1}H NMR spectra indicated an aromatic partial structure; absorption at 707 cm^{-1} corresponds to a monosubstituted benzene ring. Absorption maxima at 1663 and 1547 cm^{-1} are in accordance with a secondary amide linkage. The empirical formula was shown to be $C_{16}H_{25}N_3O_2$ by high resolution MS. The base peak at *m/e* 274 is formed by loss of OH. The peaks at *m/e* 146 and 131 arise by elimination to yield a cinnamoyl derivative and subsequent cleavage of the C(4)–N(5) and N(5)–C(6) bond, respectively (see Fig. 1) [2]. The fragment at *m/e* 160 reveals four unsubstituted CH_2 groups between N-1 and N-9 [2]. By acetylation with Ac_2O–Py, mayfoline was converted into the *N,O*-diacetate (**2**) with absorption at 1747, 1663, 1645 and 1204 cm^{-1} as well as ^{1}H NMR singlets at δ 2.06 and 2.29 ppm. Like *N*-acetylcelacinnine [2], *N*-acetylcyclocelabenzene, and *N*-acetylisocyclocelabenzene [3], **2** shows a double doublet at δ 5.67 in the ^{1}H NMR spectrum for 8-H, thus indicating the partial structure N(Ac)–CH(Ph)–CH_2. The ^{1}H NMR spectrum of **2** lacks CHOAc