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2-*O*-ACETYL CHLIDANTHINE; AN ALKALOID FROM *HAEMANTHUS MULTIFLORUS*

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Key Word Index—*Haemanthus multiflorus*; Amaryllidaceae; bulbs; alkaloids; 2-*O*-acetylchlidanthine; lycorine; galanthamine; haemultine; hippadine.

Abstract—The bulbs of *Haemanthus multiflorus* afforded, in addition to four known alkaloids, a new Amaryllidaceae alkaloid, 2-*O*-acetylchlidanthine. Its structure was elucidated by spectroscopic methods as well as by chemical transformations

INTRODUCTION

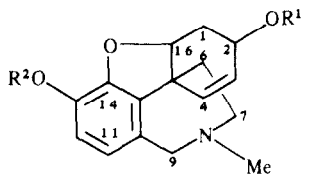
Haemanthus multiflorus Martyn is cultivated in Egypt as a garden flower. The extracts of *Haemanthus* species are used in popular medicine in the treatment of several diseases [1, 2].

A number of alkaloids were earlier reported from *H. multiflorus* Martyn of European and Indian origin [1, 3–6]. We now wish to report the isolation and characterization from this plant of a new alkaloid, 2-*O*-acetyl chlidanthine (**1**), and the known alkaloids galanthamine (**2**) [7], lycorine [8], haemultine [5] and the phenanthridone alkaloid hippadine [9]. This is the first report of a phytochemical investigation of the species cultivated in Egypt.

RESULTS AND DISCUSSION

The powdered, air-dried bulbs of *H. multiflorus* were first extracted with *n*-hexane and then with methanol and the alkaloids subsequently isolated by treating the crude extracts with 5% hydrochloric acid, followed by basification and extraction with chloroform.

From the basic fraction galanthamine (**2**), lycorine, haemultine and the new alkaloid 2-*O*-acetylchlidanthine (**1**) were isolated. From the non-basic fraction only the indole derivatives hippadine was obtained.



1 R^1 = COMe, R^2 = H
2 R^1 = H, R^2 = Me

Compound **1**, $C_{18}H_{21}NO_4$ (HRMS) is an optically active base which crystallizes from methanol as colourless needles (mp 215–217°) and gives a positive ferric chloride test for phenols.

Its UV maxima are similar to those of galanthamine type alkaloids [7] and its IR spectrum exhibits bands characteristic for hydroxyl (3385 cm^{-1}) and carbonyl (1730 cm^{-1}) groups.

The 400 MHz ^1H NMR spectrum of **1** in $CDCl_3$ establishes the presence of an acetyl group (δ2.01) and an *N*-methyl group (δ2.40). It also shows an AB-pattern centred at δ3.67 and 4.13 indicative of an unsubstituted C-9 position. This finding and the +ve test with ferric chloride, establish that acetylation has occurred in position 2. The spectrum also showed the presence of two olefinic protons (δ5.87 and 6.26) in addition to two vicinal aromatic protons (δ6.52 and 6.63).

Comparison of the ^{13}C NMR data of compound **1** with those of galanthamine [10] confirm the proposed structure (Table 1).

EXPERIMENTAL

General. Mps: uncorr; ^1H NMR: 90 or 400 MHz, TMS as int. standard. MS: 70 eV. TLC: silica gel using EtOAc—petrol (1:1) (S-I) and $CHCl_3$–MeOH (9:1) (S-II). Spots were visualized by their fluorescence at 254 nm or by spraying with Dragendorff's reagent.

Plant material. The bulbs of *H. multiflorus* Martyn were collected in May 1987 from the plants propagated near the Chiraton Hotel, Cairo, Egypt. The plant was identified and authenticated by Prof. Dr N-El-Hadidi (Faculty of Science, Cairo University, Cairo) and a voucher sample has been deposited at the Herbarium of the Pharmacognosy Department, Faculty of Pharmacy, Assiut University.

Extraction and isolation of alkaloids. Powdered plant material (1 kg) was subjected to continuous Soxhlet extraction using hexane, and the marc was then further exhaustively extracted with MeOH. The residue (20 g) was acidified with 5% aq. HCl and then extracted with $CHCl_3$ (5 × 500 ml). The combined $CHCl_3$ extracts yielded, after evapn of the solvent, fraction I (9 g).

Table 1. ^{13}C NMR* data of 2-acetylchlidanthine (1) and galanthamine (2)

C	1	2
1	27.9 (*t*)	30.0 (*t*)
2	63.3 (*d*)	62.2 (*d*)
3	122.8[a] (*d*)	126.8[a] (*d*)
4	122.0[a] (*d*)	126.0[a] (*d*)
5	48.1 (*s*)	48.2 (*s*)
6	33.9 (*t*)	34.0 (*t*)
7	53.5 (*t*)	54.3 (*t*)
9	60.1 (*t*)	60.5 (*t*)
10	127.7[b] (*s*)	129.5[b] (*s*)
11	130.6 (*d*)	121.6 (*d*)
12	115.5 (*d*)	110.5 (*d*)
13	145.3[c] (*s*)	145.5[c] (*s*)
14	140.4[c] (*s*)	144.0[c] (*s*)
15	131.3[b] (*s*)	132.7[b] (*s*)
16	86.2 (*d*)	88.1 (*d*)
N-Me	41.3 (*q*)	42.2 (*q*)
Ac	170.9/21.3 (*s*/*q*)	—
OMe	—	55.5 (*q*)(*t*)

*$CDCl_3$
[a]Values may be interchanged.

The aq. phase was basified with conc. NH_3 and extracted with $CHCl_3$ (4 × 500 ml), evapn of the solvent gave fraction II (4 g).

Chromatographic fractionation. Fraction I was separated on a silica gel column (150 × 3 cm) by elution with hexane, followed by hexane–EtOAc (1:1). Fractions (100 ml) were monitored by TLC (S-I). Fractions 30–48 afforded colourless flakes of hippadine (100 mg) after crystallization from MeOH.

Fraction II was triturated in MeOH (50 ml) to give lycorine (500 mg) as a creamy powder. The filtrate was concd and passed through a Sephadex LH-20 column (60 × 3 cm). Elution was carried out with MeOH–$CHCl_3$ (1:9) and 200 fractions (each *ca* 20 ml) were collected over a 24 hr period. From fractions 20–30 and 52–60, **2** (40 mg) and haemultine (10 mg) were isolated while fraction 40–46 contained impure **1** which was purified by prep. TLC to yield the new alkaloid **1** (20 mg) with R_f 0.36 (S-II).

2-O-Acetylchlidanthine (**1**). Colourless needles (MeOH), mp 215–217°, $[\alpha]_D^{20} = -45.8$ ($CHCl_3$; c 0.5) UV λ_{max} nm 205, 234, 290; IR λ_{max}^{KBr} cm^{-1}: 3385, 2980, 1730 (Ac), 1620 and 1040; ^1H NMR (400 MHz, $CDCl_3$): δ6.63 (*d*, *J* = 8.6 Hz, H-12), 6.52 (*d*, *J* = 8.6 Hz, H-11), 6.26 (*d*, *J* = 10 Hz, H-4), 5.87 (*ddd*, *J* = 10, 4.5, 0.5 Hz, H-3), 5.32 (*m*, H-2), 4.54 (*m*, H-16), 4.13 (*d*, *J* = 15.5, H-9 B), 3.30 (*m*, H-7), 3.67 (*d*, *J* = 15.5, H-9α), 3.08 (*m*, H-7), 2.59 (*m*, H-1), 2.40 (*s*, N–CH_3), 2.15 (*m*, H-6), 2.06 (*m*, H-1), 2.01 (*m*, Ac), 1.58 (*m*, H-6); ^{13}C NMR: see Table 1. MS *m/z* (rel. int.): 215.1461 (63) ($C_{18}H_{21}NO_4$ requires 215, 1470), 214 [M^+–H]* (20), 287 [M −H−CO]* (8), 256 ($C_{16}H_{18}NO_2$(100), 255 ($C_{16}H_{17}NO_2$) (69) 254 ($C_{16}H_{16}NO_2$) (34).

Galanthamine (**2**). Colourless cubes, mp 126–128 (MeOH), $[\alpha]_D^{20} = -115$ (EtOH; *c* 0.5). IR λ_{max}^{KBr} cm^{-1}: 3350, 1620. The base was shown to be identical with an authentic sample (TLC, mmp and ^1H NMR). ^{13}C NMR: Table 1.

Lycorine. Colourless needles (EtOH), mp 252–254°, mp undepressed on admixture with an authentic sample [9].

Haemultine. Colourless needles, mp 170–172; its spectral data are similar with those reported [5].

Hippadine. Colourless needles (MeOH), mp 207–210°. The mp was undepressed on admixture with an authentic sample [9].

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