

NARCISSUS ALKALOIDS, VIII. MESEMBRENONE: AN UNEXPECTED ALKALOID FROM *NARCISSUS PALLIDULUS*¹JAUME BASTIDA, FRANCESC VILADOMAT, JOSE MANUEL LLABRES,
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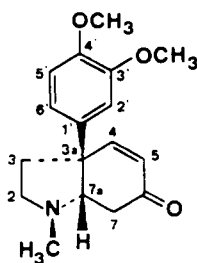
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ABSTRACT.—The extract of the aerial parts of *Narcissus pallidulus* afforded an unforeseen alkaloid, mesembrenone [1]. The structure was elucidated by spectroscopic and chemical methods. This is the third report of a mesembrine-type alkaloid from the plant family Amaryllidaceae.

Continuing our systematic investigation on the Iberian *Narcissus* plants, we have analyzed *Narcissus pallidulus* Graells (Amaryllidaceae). Even though there have been some efforts aimed to regard this species in a separate genus, at present it is included in the section Ganymedes, a primitive group in the *Narcissus* L. genus (2). No phytochemical analysis has been reported on this plant. In the present communication we report the isolation and structure elucidation of mesembrenone [1], an alkaloid belonging to the mesembrine group. Although both amaryllidaceous and mesembrine-type alkaloids have common biogenetic precursors, further studies have demonstrated that the biosyntheses of these two classes of alkaloids are fundamentally different (3). The presence of mesembrenone in *N. pallidulus* is of chemotaxonomic interest because mesembrines seem to be restricted to Aizoaceae-Mesembryanthemoideae (Dicotyledones) (4). Only twice before has the occurrence of mesembrane-type alkaloids in this plant family, namely amisine from *Hymenocallis arenicola* (5) and mesembrenol from *Crinum oliganthum* (6), been reported. Some doubts were cast on this finding because of its unexpectedness (7). However, our present communication gives support to the sporadic presence in the Amaryllidaceae of such alkaloids as those found in some *Sceletium* (Aizoaceae) species (8).

Further investigations may prove if this type of alkaloid, rare in this plant family, is more widespread in the genus *Narcissus*.

Mesembrenone [1] was identified by means of its spectroscopic properties (ir, ms,



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¹For Part VII in this series see Bastida *et al.* (1).

^{13}C , and ^1H nmr) as well as by its chemico-physical properties that were identical with those reported in the literature.

RESULTS AND DISCUSSION

The mixture obtained from the EtOH extract of the whole plants of *N. pallidulus* was purified and fractionated by Si gel cc to yield the alkaloid mesembrenone [1]. The molecular formula $\text{C}_{17}\text{H}_{21}\text{NO}_3$ was obtained by elemental analysis and the mol wt deduced from the mass spectrum. The structure elucidation was established on the basis of its physical and spectroscopic data. Thus, the mass spectrum shows the parent peak at m/z 287 and characteristic fragmentations at m/z 219, 70, and 42 for 3-dimethoxyphenyl-1-methylpyrrolinium cation, $\text{CH}_2=\text{N}^+(\text{CH}_3)\text{CH}=\text{CH}_2$ and $\text{CH}_2=\text{N}^+=\text{CH}_2$, respectively, which constitutes a general process for these systems (8).

The most important signals of the ^1H -nmr spectrum are: (a) singlets at δ 2.32 for the *N*-methyl group and δ 3.89 and 3.90 for two methoxy groups; (b) two doublets of doublets at δ 6.74 and 6.11 for olefinic protons H-4 and H-5, having coupling constants of 2.0 and 0.8 Hz for the long-range coupling with H-7a and H-7 α , respectively (9); (c) a singlet at δ 6.88 and two doublets at δ 6.82 and 6.89 for the aromatic protons 2', 6', and 5', respectively; and (d) the presence of a multiplet at δ 3.34 identified as H-2 α due to its deshielding by the *cis* lone pair of the nitrogen atom. Thus, the mesembrenone hydrochloride exhibits H-2 α at δ 4.67 ($\Delta\delta = 1.33$). Decoupling experiments confirmed this assignment, as well as those of H-2 β , H-3 α , and H-3 β (see Experimental). These data provide a full assignment of the ^1H -nmr spectrum of mesembrenone.

The ^{13}C -nmr spectrum is in agreement with the literature (10). Nonetheless, the signal corresponding to the methylene at C-2 is not observed in this spectrum for it is masked by those of the methoxy groups at δ 55.6. The overlapping was proved by obtaining the spectrum of the mesembrenone hydrochloride form, where C-2 appears at δ 54.2 ($\Delta\delta = -1.4$) and the methoxy groups at δ 55.7 and 56.7. The shielding effect caused by the protonation of the *N* atom (11) is also observed in the carbons C-7a ($\Delta\delta = -5.7$) and C-7 ($\Delta\delta = -1.7$).

EXPERIMENTAL

PLANT MATERIAL.—The whole plants of *N. pallidulus* Graells [= *N. triandrus* L. ssp. *pallidulus* (Graells) Rivas Goday] (Amaryllidaceae) were collected by us during the flowering period in April 1985, from the Guarda region, Portugal, and identified by Dr. Javier Fernández Casas, Botanic Institute of Madrid. A voucher specimen (No. 32937) has been deposited at the Herbarium of the Faculty of Pharmacy, University of Barcelona, Spain.

GENERAL.—Mp's are uncorrected. Ir spectra were measured in CHCl_3 on a Perkin-Elmer 1430 spectrophotometer. Mass spectra were obtained with a Hewlett Packard 59865 A spectrometer operating at 70 eV. Nmr spectra were recorded in CDCl_3 on a Varian XL-200 instrument working at 200 MHz and 50.3 MHz for ^1H and ^{13}C , respectively. Chemical shifts are reported in δ (ppm) values and coupling constants (*J*) in Hz. TMS was used as internal standard.

ALKALOID ISOLATION.—The fresh plants (2.35 kg) were exhaustively extracted with EtOH at room temperature. The EtOH extract was filtered, concentrated under reduced pressure, and then acidified with HOAc up to a 5% solution. The filtered acidic solution was washed with Et_2O to remove neutral material and extracted with CHCl_3 . The alkaloids detected in the CHCl_3 phase were present in so little amount that they could not be chemically characterized. The aqueous acidic solution was alkalized with Na_2CO_3 to pH 8–9 and the alkaloids extracted with CHCl_3 . The CHCl_3 phase was then washed with a Na_2CO_3 solution, and the solvent was removed to give an alkaloid residue (2485 mg). The crude alkaloid extract was then chromatographed on a Si gel column (170 g). Elution with an increasing polarity solution of EtOAc-EtOH (10:2) afforded an amorphous alkaloid, which was further purified by means of preparative tlc. After solubilization with EtOH, this residue was treated with picric acid and was crystallized in MeOH/ Me_2CO , yielding 73.7 mg of crystals.

Mesembrenone [1].— $\text{C}_{17}\text{H}_{21}\text{NO}_3$; found C 53.60, H 4.62, N 10.82; $\text{C}_{23}\text{H}_{24}\text{N}_4\text{O}_{10}$ requires C

53.48, H 4.65, N 10.85; mp of picrate 177–180°; ν max (CHCl₃) cm⁻¹ 1680, 1605, 1590, 1510, 1460, 1410; ms *m/z* (rel. int.) [M]⁺ 287 (12), 258 (2), 219 (4), 149 (2), 128 (7), 115 (16), 91 (6), 70 (100), 42 (54); ¹H nmr (CDCl₃) δ 2.21 (1H, ddd, *J* = 12.6 Hz, 8.4 Hz, 4.2 Hz, H-3 β), 2.32 (3H, s, NMe), 2.43 (1H, dd, *J* = 8.4 Hz, 2.4 Hz, H-3 α), 2.50 (1H, dd, *J* = 8.4 Hz, 4.8 Hz, H-7 β), 2.50–2.55 [masked by H-7, H-2 β (assigned by decoupling experiments)], 2.55 (1H, brd, *J* = 8.4 Hz, H-7 α), 2.65 (1H, m, H-7a), 3.34 (1H, m, H-2 α), 3.89 (3H, s, OMe), 3.90 (3H, s, OMe), 6.11 (1H, dd, *J* = 10.1 Hz, 0.8 Hz, H-5), 6.74 (1H, dd, *J* = 10.1 Hz, 2 Hz, H-4), 6.82 (1H, d, *J* = 8 Hz, H-6'), 6.88 (1H, s, H-2'), 6.89 (1H, d, *J* = 8 Hz, H-5'); ¹³C nmr (CDCl₃) in agreement with Jeffs *et al.* (10).

Mesembrenone hydrochloride.—Mp 190–192° [lit. (7) 192–193°, lit. (8) 204–207°]; ν max (CHCl₃) cm⁻¹ 2960, 1690, 1605, 1510, 1460, 1410; ¹H nmr (CDCl₃) δ 2.0–2.2 (1H, m, H-3 β), 2.73 (3H, d, *J* = 5 Hz, NMe), 2.75 (1H, dd, *J* = 8.4 Hz, 4.8 Hz, H-7 β), 2.9–3.0 (1H, m, H-7 α), 3.0–3.2 (3H, m, H-2 β , H-3 α , H-7a), 3.88 (3H, s, OMe), 3.96 (3H, s, OMe), 4.67 (1H, br, *W*_{1/2} = 16 Hz, H-2 α), 6.48 (1H, d, *J* = 10.4 Hz, H-5), 6.84 (1H, d, *J* = 8 Hz, H-6'), 6.92 (1H, d, *J* = 8 Hz, H-5'), 6.97 (1H, dd, *J* = 10.4 Hz, 2 Hz, H-4), 7.23 (1H, d, *J* = 2 Hz, H-2'); ¹³C nmr (CDCl₃) δ 33.1 (C-3), 36.9 (C-7), 41.4 (NMe), 50.3 (C-3a), 54.2 (C-2), 56.0 (OMe), 56.7 (OMe), 67.8 (C-7a), 110.2 (C-5'), 111.5 (C-2'), 119.2 (C-6'), 130.1 (C-1'), 131.6 (C-5), 148.8 (C-4), 149.2 (C-4'), 149.8 (C-3'), 193.4 (C-6).

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