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NARCISSUS ALKALOIDS, XVII¹. OBESINE, A NOVEL ALKALOID
FROM *NARCISSUS OBESUS*

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ABSTRACT.—Phytochemical studies on *Narcissus obesus* resulted in the isolation of seven Amaryllidaceae alkaloids. Six of them, bicolorine, 5,6-dihydrobicolorine, epimacronine, galanthamine, pretazettine, and haemanthamine, are common in this genus, whereas obesine [1] is reported here for the first time. The stereochemistry and structural determination of this new alkaloid have been carried out by spectroscopic analyses and by application of 2D nmr techniques.

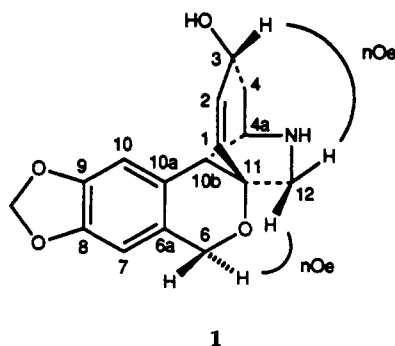
As part of a continuing study on the alkaloidal constituents of the genus *Narcissus* L., we describe here the isolation and characterization of obesine [1] from *Narcissus obesus* Salisb. (Amaryllidaceae).

The MeOH extract of *N. obesus* was fractionated as described in the Experimental section. Each alkaloid-containing fraction was separated by conventional chromatographic methods. Compound 1 showed in its eims a molecular ion peak at m/z 287 and characteristic fragments at m/z 203 and 188, which originated from a cleavage of the pyrrolidinic ring, together with a base peak at m/z 176.

The ¹H-nmr spectrum, recorded in MeOH-*d*₄ (Table 1) exhibited two singlets at δ 6.70 and 6.66, for the aromatic protons H-10 and H-7, respectively. The assignment was made according to the benzylic couplings with H-10b and H-6, observed in the COSY experiment. Two doublets at δ 6.13 and 5.86 were assigned to the olefinic protons H-2 and H-1, respectively. A broad singlet, corresponding to the proton of the C-4a position, was masked by the

TABLE 1. ¹H-nmr Chemical Shift Values and Coupling Constants for Compound 1.

Proton			
H-1	5.86	d	8.3
H-2	6.13	d	8.3
H-3	4.30-4.40	m	
H-4 α	2.39	brd	13.0
H-4 β	1.68	ddd	13.0, 11.5, 4.2
H-4a	3.15	brs	
H-6 α	4.02	d	16.3
H-6 β	4.38	d	16.3
H-7	6.66	s	
H-10	6.70	s	
H-10b	2.81	brd	<1
H-12 _{exo}	3.01	d	11.5
H-12 _{endo}	3.10	d	11.5
OCH ₂ O	5.99	s	

¹For part XVI in this series, see Codina *et al.* (1).

doublet at δ 3.10 assigned to the H-12 endo. The H-4a showed correlation with the protons of the C-4 position and with H-10b (δ 2.81), thus allowing its unambiguous assignment. Comparatively, the chemical shift of H-11 in the related alkaloid 3-*epi*-macronine (δ 4.43) (2) is more deshielded than H-10b of **1** (δ 2.81) by effect of oxygen in the α position. Furthermore, the small coupling constant between H-4a and H-10b ($J < 1$) is in accordance with an angle of about 90° (see Dreiding models). Two doublets at δ 4.38 and 4.02 were assigned to the protons β and α of the methylene of the C-6 position. The signal of the proton of the C-3 position is masked by the H-6 β proton. The H-6 α proton is assigned at higher fields as consequence of the nOe effect with H-12 endo (δ 3.10) observed in the 2D nOe experiment. On the other hand, the α disposition of H-3 is confirmed also by the nOe effect between H-3 and H-12 exo (δ 3.01).

The most characteristic signals of the ^{13}C nmr (Table 2) were as follows. A singlet at 82.7 ppm corresponded to the carbon of the C-11 position. The DEPT experiment revealed the quaternary nature of this carbon; furthermore, this

chemical shift value indicated the presence of oxygen in a neighboring position, thus confirming its assignment. Two methine carbons at δ 50.3 and 68.5 were unambiguously assigned as C-10b and C-4a by XCOR experiment; in the same way, the signals corresponding to the aromatic carbons C-7 and C-10 were assigned at 107.3 and 110.0 ppm, respectively. The assignment of the C-2 and the quaternary carbons C-9 and C-8 was made by means of the COLOC technique, which shows long range couplings. Therefore, the correlation between the singlet at δ 6.66 (H-7) and the signal at 143.7 ppm permitted its assignment at C-9. Similarly, the correlation between the singlet at δ 6.70 (H-10) and the signal at 148.8 ppm confirmed the assignment of C-8. On the other hand, the assignment of the olefinic carbon C-2 was made on the basis of the correlation observed with H-4 α . The chemical shift of the methine carbon C-11 in 3-*epi*-macronine (δ 80.1) (3) (DEPT experiment), was deshielded in the quaternary C-11 of **1** (δ 82.7). The values of the chemical shifts of both compounds are in agreement with the α disposition of the oxygen atom, thus corroborating the assignments of C-10b and C-11.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.— ^1H - (250 MHz) and ^{13}C - (62.5 MHz) nmr spectra were recorded on a Bruker AC250 spectrometer using TMS as internal standard. Chemical shifts are reported in δ (ppm) values and coupling constants (J) in Hz. Eims were obtained with a Hewlett-Packard 59865 A instrument operating at 70 eV. $[\alpha]_D$ was recorded in a Perkin-Elmer 241 polarimeter. Analytical and preparative tlc were carried out on Si gel 60 F₂₅₄ plates (Merck). Si gel 60 Merck (70–230 mesh) and Si gel SDS Chromagel 60 A CC (230–400 mesh) were used for cc and flash cc, respectively. Spots on chromatograms were detected by Dragendorff's reagent and under uv light (254 nm).

PLANT MATERIAL.—The whole plants of *N. obesus* were collected in March 1990, during the flowering period, in Setubal, Portugal. The plants were identified by Prof. Javier Fernández Casas, Real Jardín Botánico de Madrid, and a

TABLE 2. ^{13}C -nmr Chemical Shift Values for Compound **1**.

Carbon	
C-1	132.4 d
C-2	136.5 d
C-3	63.6 d
C-4	34.4 t
C-4a	68.5 d
C-6	62.2 t
C-6a	131.0 s
C-7	107.3 d
C-8	148.4 s
C-9	147.3 s
C-10	111.0 d
C-10a	125.0 s
C-10b	50.3 d
C-11	82.7 s
C-12	55.7 t
OCH ₂ O	101.9 t

voucher specimen has been deposited at the Herbarium of the Faculty of Pharmacy, University of Barcelona, Spain.

EXTRACTION AND ISOLATION.—The freshly collected aerial parts and bulbs of *N. obesus* (4 kg) were crushed and extracted with MeOH in a Soxhlet apparatus for 10 h. The extract obtained by evaporation of the MeOH was dissolved in 2% HCl, and the mixture was filtered. After removal of the neutral material with Et₂O, the acidic solution was made basic (pH 8–9) with Na₂CO₃ and extracted with CHCl₃ and CHCl₃-MeOH (3:2). A brown gum (2.6 g) was thus obtained. This crude alkaloid extract was fractionated by flash chromatography, eluting with CHCl₃-MeOH (9.5:0.5). Further purification through preparative tlc afforded bicolorine (18 mg), 5,6-dihydrobicolorine (39 mg), epimacronine (10 mg), galanthamine (38 mg), pretazettine (30 mg), haemanthamine (54 mg), and obesine (39 mg).

Obesine [1].—Exact mass *m/z* 287.1161, calcd for C₁₆H₁₇O₄N, *m/z* 287.1158. [α]_D²⁰ -5.6 (MeOH, *c* = 0.69); ms *m/z* (rel. int.) [M]⁺ 287 (47), 203 (47), 188 (55), 176 (100), 174 (80), 161 (41), 148 (51), 131 (39), 103 (39), 89 (32), 77 (34), 55 (45).

Bicolorine, 5,6-dihydrobicolorine, epimacronine,

galanthamine, pretazettine, and haemanthamine.—These alkaloids were chromatographically and spectrally (ir, nmr, eims) identical with authentic compounds previously isolated by us (3,4).

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