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3-HYDROXYTALATISAMINE FROM *ACONITUM NASUTUM**

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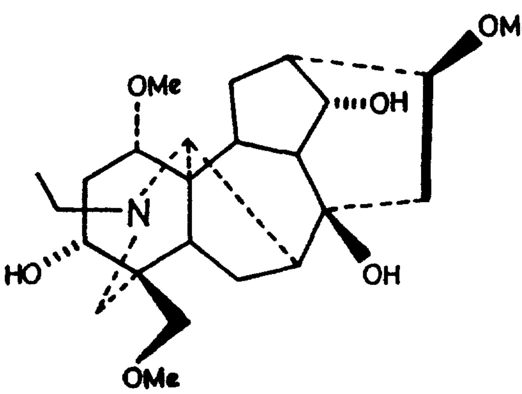
Key Word Index—*Aconitum nasutum*; Ranunculaceae; norditerpenoid alkaloids; 3-hydroxytalatisamine.

Abstract—Together with five known alkaloids, a new norditerpenoid alkaloid was isolated from the above-ground parts of *Aconitum nasutum*. The new compound was identified as 3-hydroxytalatisamine on the basis of 1D and 2D NMR techniques.

INTRODUCTION

Aconitum species are used in traditional medicine, especially in China [1–3], while in Turkey, due to their high toxicity, they are not included in folk medicine, but used only as pain relievers under a physician's control [4]. Of the four *Aconitum* species found in Turkey, we have recently studied *A. orientale* [5]. In the present paper, we have investigated the alkaloids of *A. nasutum*, which was collected from eastern Turkey, near the Russian border. There is only one previous investigation of this species by a Russian group [6], but aconosine was not obtained from the Turkish collection. We have isolated five known diterpenoid alkaloids, talatisamine [7], lycoctonine [8], columbidine [9], 14-acetyltalatisamine [10] and anthranoyllycoctonine [11], and one new alkaloid 3-hydroxytalatisamine (**1**). In this report, we describe the isolation and structural identification of **1**.



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RESULTS AND DISCUSSION

The molecular formula of **1**, $C_{24}H_{39}NO_6$ (*m/z* 437.2770, calc. 437.2777), was derived from its HREI mass spectrum and ^{13}C NMR (DEPT) spectrum, which showed four methyl quartets, seven methylene triplets, nine methine doublets (for 10 methine groups) and three quaternary carbon singlets. There were six oxygen-bearing C atoms represented by five signals (δ 72.0 *d*, 72.8 *s*, 75.6 *d*, 78.5 *t* and 82.3 *d*), three of them carrying three methoxyl groups; the other three, therefore, should have hydroxyl groups. The ^1H NMR spectrum together with the ^{13}C NMR spectrum provided the most information for **1**. The signals [δ_H 1.10 (3H, *t*, $J = 7$ Hz, NCH_2CH_3); δ_C 13.5] showed the presence of an *N*-ethyl group, together with three methoxyl groups at [δ_H 3.28 (3H, *s*, C-18′); δ_C 59.5 and 3.35 (6H, *s*, C-1′ and C-16′); δ_C 56.3 and 56.5] indicating that **1** is a norditerpenoid alkaloid. Other important signals were at [δ_H 2.9 (1H, *br d*, $J = 10$ Hz, H-18a) and 3.1 (1H, *br d*, $J = 10$ Hz, H-18b); δ_C 78.5 C-18], indicating that one of the methoxyl groups was at C-18 [δ_H 3.4 (2H, *m*, H-1 and H-16); δ_C 82.3 (C-1) and (C-16), the two other methoxyl groups being at C-1 and C-16 (δ 82.3). The signal at [δ_H 4.1 (1H, *dd*, $J = 2$ and 4.5 Hz, H-14β; δ_C 75.6] on D_2O-exchange collapsed the double of doublets at δ 4.1 to a triplet ($J = 4.5$ Hz), thus indicating that one of the hydroxyl groups must be placed at C-14. The second hydroxyl was placed at C-8 following from the singlet signal

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*This paper is dedicated to Prof. Dr Rudolf Hansel (Münich, Germany) on the occasion of his 75th birthday.

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observed at δ 72.8. There was another doublet signal at δ 72.0, which should correspond to the carbon atom carrying the third hydroxyl group. This group could be placed at one of the following places, C-2, C-3, C-6, C-12 or C-15; the signal for C-15 with a β-OH appears at δ 69.0 and at 78–82 in the case of α-OH [13]. Although an hydroxyl group at C-12 is rather rare in norditerpenoid alkaloids, nevertheless it appears at δ 76–77 [12, 13]; if the hydroxyl group is at C-6 and β it is observed at δ 77–80 with α being δ 70–71. In norditerpenoid alkaloids, there is no example known with a C-2 carrying a hydroxyl group. When the hydroxyl group is at C-3 the chemical shift would be *ca* δ 71–72 and it would induce an upfield shift on the chemical shift of C-1 and a downfield shift on the chemical shift of C-2 and C-4. In the present case, a signal at [δ_H 3.72 (1H, *t*, $J = 4$ Hz); δ_C 72.0] was attributed to a C-3α hydroxyl group; however, the chemical shift of C-1 (δ 82.3) was lower than expected and the chemical shifts of C-2 (δ 37.7) and C-4 (δ 45.8) were higher than those with no hydroxyl group at C-3. Similar compounds with a 3α-hydroxyl group induced the same chemical shifts [14–16]. A HETCOR experiment revealed the correlations between carbons and protons (Table 1). A selective INEPT experiment showed long-range correlations through three bonds and, in some cases, two and four bonds. Irradiation of the proton at δ 4.1 (H-14) enhanced C-8 and C-10, irradiation of H-12 (δ 1.3) enhanced C-9, C-11 and C-14, and that of H-3 (δ 3.72) enhanced C-1, C-4 and C-5, while irradiation of H-9 (H-10) δ 2.28 (2.30) enhanced C-1 and C-13 and irradiation of H-19 (δ 2.47) enhanced C-3, C-5 and C-18. A NOESY experiment showed that the stereochemistry of the compounds was similar to that of talatisamine (**2**), and H-3β showed NOE with H-6β (δ 1.8) and H-7β (δ 2.2). All ^{13}C NMR signals of **1** were similar to those of (**2**) except for C-1 to C-5, indicating the presence of a hydroxyl group at C-3. Spectral data are in agreement with the proposed structure for **1**.

EXPERIMENTAL

General. IR spectra were recorded in $CHCl_3$. ^{1}H and ^{13}C NMR were measured using a Bruker AM 400, 2D experiments on a 500-MHz Bruker ORX.

Plant material. Above-ground parts of *A. nasutum* Fisch. et Reicht. were collected from Ardahan (Ardanuc Pass) near the Russian border in August 1984 and identified by Dr R. Ilarslan. A voucher is deposited in the Herbarium of the Faculty of Sciences, University of Ankara, No. Ilarslan 1675.

Extraction and separation. Powdered plant material (0.5 kg) was extracted with EtOH by percolation and the extract obtained evapd to dryness at 35° *in vacuo*. The residue was treated with 0.5 N H_2SO_4 and ex-

Table 1. ^{1}H and ^{13}C NMR data for compound **1** and ^{13}C NMR data for compound **2**

	1		**2**
C	^{1}H NMR	^{13}C NMR	(^{13}C NMR)
1	3.40 *m*	82.3 *d*	86.1
2	2.37 *dd*	37.7 *t*	25.7
	2.42 *dd*		
3	3.72 *t*	72.0 *d*	32.6
4	—	45.8 *s*	38.6
5	2.30 *br d*	48.5 *d*	37.7
6	1.80 *dd*	24.6 *t*	24.8
7	2.20 *d*	46.0 *d*	45.7
8	—	72.8 *s*	72.7
9	2.28 *m*	47.0 *d*	46.9
10	2.30 *m*	45.2 *d*	45.7
11	—	48.8 *s*	48.6
12	1.30 *dd*	28.7 *t*	28.6
13	2.00 *m*	45.3 *d*	45.7
14	4.10 *dd*	75.6 *d*	75.7
15	1.80 *dd*	39.1 *t*	39.2
16	3.40 *m*	82.3 *d*	82.2
17	3.30 *s*	62.8 *d*	62.8
18	3.10 *br d*	78.5 *t*	79.4
	2.90 *br d*		
19	2.47 *d*	53.2 *t*	53.1
	2.37 *d*		
NCH_2	2.80 *q*	49.5 *t*	49.4
CH_3	1.10 *t*	13.5 *q*	13.6
C-1 OMe	3.35 *s*	56.3 *q*	56.1
C-16 OMe	33.5 *s*	56.5 *q*	56.3
C-18 OMe	3.28 *s*	59.6 *q*	59.3

tracted with $CHCl_3$. NaOH (5%) was then added to the acidic soln (pH 10) and the soln extracted with $CHCl_3$. The $CHCl_3$ extract was evapd to dryness, yielding 1.5 g of a crude alkaloidal mixt. which was chromatographed over basic alumina (column 3 × 50 cm). The alkaloidal mixts obtained were further sepd and/or purified by prep. silica gel and alumina TLC (Merck). The following compounds were obtained: **2** (90 mg), 14-acetyltalatisamine (8 mg), columbidine (12 mg), lycoctonine (14 mg), anthranoyllycoctonine (7 mg) and **1** (10 mg).

3-Hydroxytalatisamine (**1**). Amorphous. $[\alpha]_D$ $-14.3°$ (c 0.3, $CHCl_3$). IR$\nu_{max}^{CHCl_3}$ cm^{-1}: 3404, 2928, 2823, 2361, 1634, 1455, 1381, 1295, 1226, 1160, 1090, 990, 944, 905, 753. ^1H and ^{13}C NMR ($CDCl_3$): Table 1. HREIMS m/z (rel. int. %): 437.2770 $[M]^+$ ($C_{24}H_{39}NO_6$) (6), 406 $[M-OMe]^+$ (96), 376 $[M-2\times OMe+H]^+$ (100), 69 (3), 58 (4), 55 (2).

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