Notes

Norditerpenoid and Diterpenoid Alkaloids from Turkish *Consolida orientalis*

Filiz Meriçli,[†] Ali H. Meriçli,[†] Ayhan Ulubelen,[†] Haridutt K. Desai,[‡] and S. William Pelletier*[,‡]

Faculty of Pharmacy, University of Istanbul, 34452 Istanbul, Turkey, and Institute for Natural Products Research and Department of Chemistry, The University of Georgia, Athens, Georgia 30602-2556

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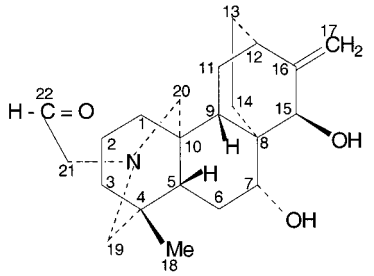
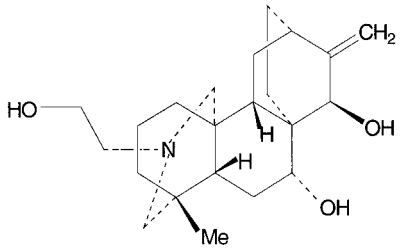
From the aerial parts of *Consolida orientalis* collected in Turkey, a new diterpenoid alkaloid designated as consorientaline has been isolated along with the known norditerpenoid alkaloids delsoline, delcosine, gigactonine, and takaosamine. The structure of consorientaline (**1**) was established by spectroscopic studies and chemical correlation with dihydroajaconine (**2**).

Turkish *Delphinium* and *Consolida* (Ranunculaceae) species are used externally in the treatment of rheumatic pain and sciatica and also against body lice.[1] In continuation of our investigations of Turkish *Aconitum*, *Delphinium*, and *Consolida* species[2−4] for diterpenoid alkaloids, we have now studied *Consolida orientalis* (Gay) Schrod., which occurs throughout Turkey. In a previous investigation of the diterpenoid alkaloids of this plant collected in Spain,[5,7] the occurrence of delcosine, delsoline, gigactonine, 18-methoxygadesine, and 18-hydroxy-14-*O*-methylgadesine was reported. There are also some reports of aromatic acids, benzoxazolines, and anthocyanins in the flowers of *C. orientalis*.[7−9] In the present investigation, we report the isolation and identification of four norditerpenoid alkaloids, one of which (takaosamine) has not been found in this species before, and a new diterpenoid alkaloid consorientaline (**1**). Structure elucidation of the new compound through its physical and detailed NMR spectroscopic studies, along with chemical correlation with dihydroajaconine (**2**), is reported here.

From the aerial parts of *C. orientalis* collected at an altitude of 900 m in Ankara, Turkey, we have isolated a novel diterpenoid alkaloid designated as consorientaline. The molecular formula, $C_{22}H_{34}NO_3$ (ESIMS, MW, $[M + 1]^+$, *m*/*z* 360.2), was derived for the new alkaloid by HRFABMS $[M + 1]^+$, *m*/*z* 360.2589, calcd 360.2538). The ^{1}H NMR spectrum did not show signals for methoxyl or acetoxyl groups, which are characteristic of norditerpenoid alkaloids, suggesting that **1** is a diterpenoid alkaloid. The characteristic signals in the ^{1}H NMR spectrum were at δ 0.84 (3H, s t-Me), 5.10, 5.02 (each 1H, br s, C=CH_2), and 8.74 (1H, s, CHO). The ^{13}C NMR spectrum showed 22 signals for the 22 carbon atoms in the molecule, of which four are nonprotonated carbons at δ 33.0, 42.4, 45.7, 153.8, six methines at δ 35.2, 39.2, 43.2, 67.5, 69.4, 182.6, 11 methylenes at δ 18.4, 18.7, 24.1, 27.9, 29.5, 34.1, 40.7, 57.2, 59.2, 63.8, 109.6, and one methyl group at δ 24.5. The characteristic carbon resonances of an exocyclic methylene group were readily located at δ 153.8 and 109.6 for C-16 and C-17, respectively. A methine signal at δ 182.6 clearly indicated an aldehydic carbonyl resonance, and the signals at δ 69.4 (d) and 67.5 (d) belong to two oxygenated carbons. In the ^{1}H NMR spectrum, the aldehydic proton attached to the methylene group appeared as a singlet and not as the expected triplet and was thus similar to that in chellespontine[10] for an *N*-CH_2C*H*O group. The first of the two hydroxyl groups of **1** should be located next to the exocylic methylene group to account for the downfield shift of C-16 as in chellespontine[10] (δ 156.4 and 109.5), sadosine[11] (δ 155.4 and 110.1), and atisine[12] (δ 157.5 and 108.9) and should have a β configuration. When there is no hydroxyl group at C-1, C-2, and C-3 in ring A, the signal for C-2 appears at ca. δ 20 as in the case of atisine[12] (δ 22.7) and brunonine[13] (δ 19.5). Since the most upfield ^{13}C NMR signal was at δ 18.4 (t), **1** does not bear an OH in ring A. The remaining methylenes on which a second hydroxyl group may be located are C-6, C-7, C-11, C-13, C-14, C-19, and C-20. Two of the low-field methylene



1 Consorientaline



2 Dihydroajaconine

* To whom correspondence should be addressed. Tel: (706) 542 5800. Fax: (706) 542 5804. E-mail: pelletier@sunchem.chem.uga.edu.
[†] University of Istanbul.
[‡] University of Georgia.

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Table 1. NMR Data of Consorientaline (**1**) in $CDCl_3$

position	δ_C		δ_H (J, Hz)	COSY	NOESY
1	34.1 t	1_α	2.88 m	1_β,2_α,2_β	
		1_β	1.90 m	1_α,2_α,2_β	
2	18.4 t	2_α	1.86 br d	1_α,1_β,2_β,	
		2_β	1.03 m	1_α,1_β,2_α	
3	40.7 t	3_α	1.63 m	2_α,2_β,3_β-	
		3_β	1.40 br d	2_α,2_β,3_α	
4	33.0 s				
5	43.2 d	5	1.64 br, s($W_{1/2}$=5.2)	6_α,6	
6	18.7 t	6_α	1.60 m	5_β,6_β,7_β	6_β, 9_β
		6_β	1.21 dd(2.1,12.3)	6_α,7_β	5_β,7_β,15_α
7	67.5 d	7	3.84 br d	6α,6β	5_β,7_β,15_β
8	42.4 s				
9	39.2 d	9_β	2.14 d(3.7)	11_α,11_β	5_β,7_β,15_β
10	45.7 s				
11	29.5 t	11_α	1.91 dd(3.1,12.3)	9_β,11_β	
		11_β	1.50 m	11α	
12	35.2 d	12_β	2.37 br s	11_α,11_β	11_β,13_α,13_β
13	24.1 t	13_α	1.80 m	13β,14α,14β	
		13_β	1.91 m	13_α,14_α,14_β	
14	27.9 t	14_α	1.90 m	13_α,13_β	
		14_β	1.82 m	13_α,13_β	
15	69.4 d	15_α	4.26 d(3.8)	17_a,17_b	7_β(w),9_β(wk)
16	153.8 s				
17	109.6 t	17_a	5.02 br s	17_b,15_β	
		17_b	5.10 br s	17_a,15_β	
18	24.5q	18	0.84 s		
19	59.2 t	19_a	3.75 d(10.9)	19_b	6_α
		19_b	3.40 d(10.9)	19_a	20
20	57.2t		4.10 br s		
21	63.8t	21_α	3.60 m	21_β	
		21_β	3.85 m	21_α	
22	182.6 d		8.74 s		

triplets at δ 59.2 and 57.2 should belong to C-19 and C-20 as in chellespontine,[10] and the examples cited in ref 10 and the former signal can be assigned to C-19 (δ 3.75 and 3.40, AB, J = 10.9 Hz) based on the observed NOE correlation between one of the protons on C-19 (δ 3.40) and C-20 (δ 4.10, br s), which belongs to the second signal at δ 57.2. These results rule out the possibility of C-19 and C-20 as the position of the second hydroxyl group. The remaining methylene groups are C-6, C-7, C-13, and C-14. Among them C-13 and C-14 were observed at δ 24.1 (t) and 27.9 (t), respectively, similar to ajaconine[14] and uncinatine.[15] From the two remaining positions, the hydroxyl group was assigned to C-7. The proton-bearing carbons were assigned unambiguously by a HETCOR experiment (Table 1). The COSY spectrum showed the sequences from H-6 to H-7 (δ 3.84), as well as between H-5 and H-6. COSY experiments showed the correlations H-1−H-3, H-5−H-7, and H-12−H-14. The stereochemistry of the hydroxyl group at C-7 was determined to be α by NOE correlations between H-19 and H-6_α (δ 1.60) and between H-6_β (δ 1.21) and H-7_β (δ 3.84) (Table 1); so consorientaline (**1**) contains a *N*-CH_2CHO group as in the case of chellespontine[10] and has an atisane skeleton with an α-OH group at C-7 and a β-OH group at C-15 as in the cases of dihydroajaconine (δ 71.9)[16] and brunonine (δ 70.6).[13] Structure **1** was finally confirmed when reduction of **1** with $NaBH_4$ furnished dihydroajaconine (**2**), identical in all respects (IR, ^{1}H NMR, and TLC behavior) with those of an authentic sample.

Experimental Section

General Experimental Procedures. Melting points are corrected and were determined on a Thomas-Kofler hot stage equipped with a microscope. IR spectra were recorded on a Perkin-Elmer Model 1420 spectrophotometer. NMR spectra were recorded on a Bruker AC-300 spectrometer using standard Bruker software. ESIMS were recorded on a Perkin-Elmer SCIEX API-1 mass spectrometer. HRFABMS were determined on a Fisons AutoSpek ETOFFPD FAB^+ mass spectrometer. Chromatographic separations on a Chromatotron[17] were carried out on rotors coated with a 1 mm thick layer of Al_2O_3 60 PF-254, 365 (EM 1104), or SiO_2 60 HF (EM 7749); vacuum liquid chromatography (VLC)[18] was carried out on columns of basic Al_2O_3 (EM 1085) or SiO_2 60 (EM 7736). Thin-layer chromatograms were run using the solvent system toluene−acetone−MeOH−NH_4OH (49.5:41.5:8:5) and toluene−EtOAc−diethylamine (7:2:1 or 7:3.5:1).

Plant Material. Aerial parts (1250 g, dry wt) of *Consolida orientalis* (Gay.) Schrod. were collected and identified by two of us (A.H.M. and F.M.) near Ankara, Turkey, at an elevation of 900 m, in June 1996. A voucher specimen has been deposited in the Herbarium of the Faculty of Pharmacy, Ankara University (No. AEF 19589), Ankara, Turkey.

Extraction of Crude Alkaloids. Dried and powdered aerial parts of *C. orientalis* (1250 g) were extracted exhaustively, by percolation at room temperature, with 80% EtOH and the extract evaporated in vacuo to give a gummy residue (97.52 g). This was dissolved in CH_2Cl_2 (500 mL) and extracted with 2% H_2SO_4 (v/v) (200 mL × 10). The acidic fraction was washed with CH_2Cl_2 (200 mL × 3). The combined acid fraction was basified with aqueous NH_4OH. Extraction with CH_2Cl_2 (at pH 10−12) (300 mL × 10) and evaporation of the combined extracts in vacuo gave a crude mixture of alkaloids (1.802 g).

Isolation of Alkaloids. The crude alkaoidal mixture was first separated by VLC[18] on a basic Al_2O_3 column (5 × 55 cm) and eluted with hexane in a step gradient (100 mL each) of first $CHCl_3$ and then $CHCl_3$ and MeOH. Twenty-five fractions (100 mL each) were collected and pooled according to their TLC pattern to give three main fractions.

Combined VLC fractions 10−15 (eluted with $CHCl_3$−MeOH, 100:0 to 97:3, 183 mg) were chromatographed on a SiO_2 rotor with hexane−$CHCl_3$−MeOH mixtures, and delsoline (mp 213-215 °C, 67.3 mg, lit.[19] mp 215−216 °C) was obtained.

Combined VLC fractions 16 and 17 (eluted with $CHCl_3$−MeOH, 96:4 to 95:5, 711 mg) were chromatographed on a SiO_2

rotor with hexane−$CHCl_3$−MeOH mixtures to give delcosine (mp 201−203 °C, 88.1 mg, lit.[19] mp 203−205 °C), gigactonine (mp 165−167 °C, 130.2 mg, lit.[19] mp 168−169 °C), and takaosamine (mp 173−175 °C, 41.3 mg, lit.[19] mp 174−175 °C).

Combined VLC fractions 18−21 (eluted with $CHCl_3$−MeOH, 80:20 to 70:30, 208.5 mg) were chromatographed on a basic alumina rotor with hexane−$CHCl_3$−MeOH mixtures, and amorphous consorientaline (**1**, 10.3 mg) was obtained.

Consorientaline (1): amorphous; $[\alpha]^{25}_D$ −22.72° (*c* 0.33, $CHCl_3$); IR ν_{max} (KBr) 2910, 1730 (CHO), 990, 892 (C=CH_2) cm^{-1}, ^1H and ^{13}C NMR assignments, see Table 1; HRFABMS *m*/*z* 360.2589 $[M + 1]^+$ (calcd for $C_{22}H_{34}NO_3$, 360.2538).

All the known compounds were identified by comparison of their mp, IR, ^1H and ^{13}C NMR data, and co-TLC behavior with those of authentic samples.

Reduction of Consorientaline (1) with $NaBH_4$. Consorientaline (**1**, 4.2 mg) was dissolved in MeOH (3 mL), $NaBH_4$ (17.1 mg) was added to the solution in small portions for 15 min, and the mixture was left at room temperature overnight. Solvent was evaporated in vacuo and to the residue water (5 mL) was added. Extraction with CH_2Cl_2 (15 mL × 5) and evaporation of the dried (anhydrous Na_2SO_4) extract gave a gummy residue (3.1 mg). The residue was purified on a small Al_2O_3 column to give a gum (2.1 mg). Comparison by TLC, co-TLC, and the ^1H NMR spectra of the product with those of an authentic sample of dihydroajconine (**2**) showed them to be identical.

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