

NEW ALKALOIDS FROM CONSOLIDA HELLESPONTICA

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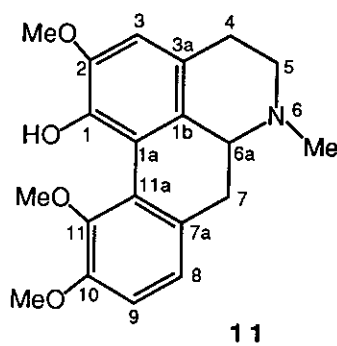
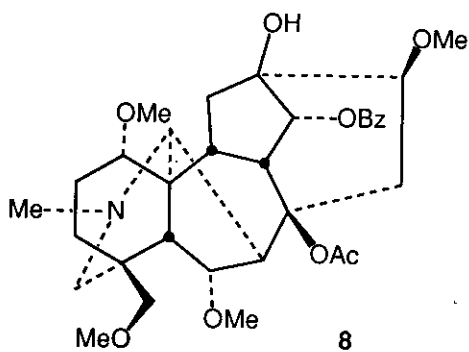
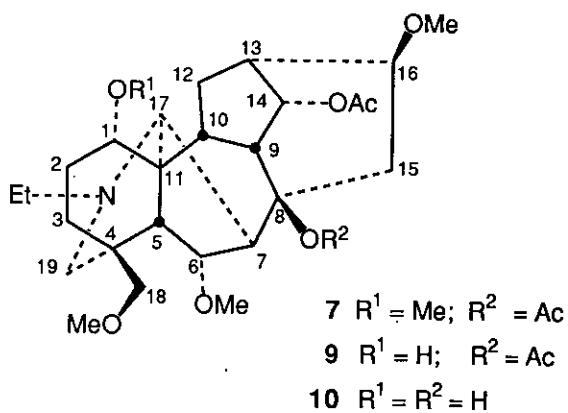
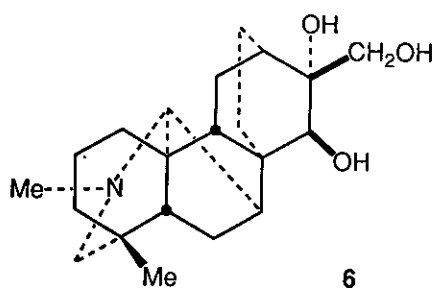
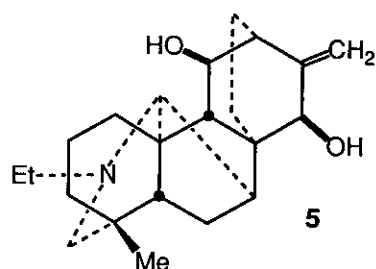
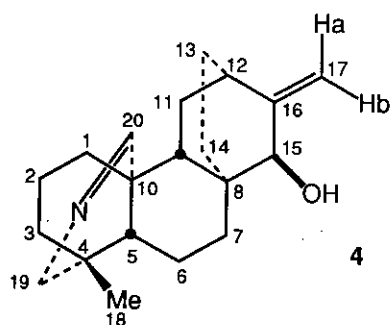
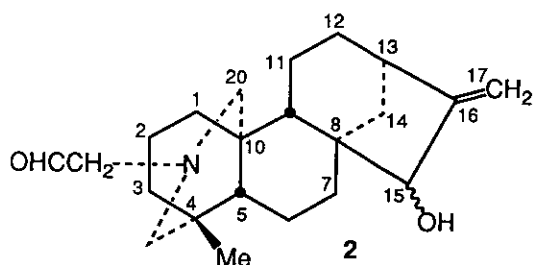
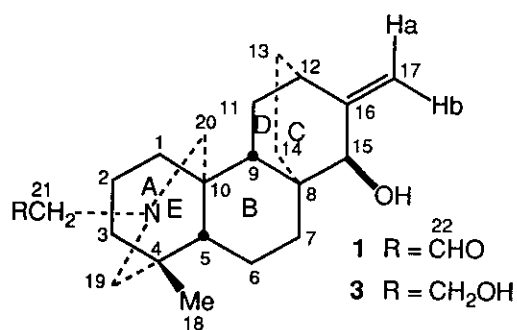
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Abstract – From the aerial parts of Consolida hellespontica (Boiss.) Chater we have isolated the new diterpenoid alkaloids chellespontine (**1**) and azitine (**4**). The norditerpenoid alkaloid 1-*O*-methyldelphisine (**7**) has not been reported earlier as occurring in nature, and the aporphine alkaloid (+)-corydine (**11**) has been isolated for the first time in the Ranunculaceae family. Besides these, the known alkaloids delphinine (**8**), delphisine (**9**) and bullatine C (14-acetylneoline) (**10**) have been isolated from this plant. The structures of these alkaloids were established by chemical correlation and spectroscopic studies.

Consolida hellespontica (Boiss.) Chater [Syn. Delphinium hellespontica (Boiss.), D. tomentosum (Boiss.)] grows in the Zonguldak and Kastamonu regions in Turkey at an altitude of 640 m and no chemical work has been reported for this plant. We have investigated the alkaloids of C. hellespontica and isolated by conventional chromatographic procedures such as vlc¹ and centrifugal chromatography (Chromatotron)² seven alkaloids (A-G). The new diterpenoid alkaloid (A), designated as chellespontine (**1**), crystallized as colorless plates, mp 227–230°C, and showed in the ir spectrum: $\nu_{\max}$ (KBr) 2910, 1730 (CHO), 1655, (C=CH₂) cm⁻¹. The ¹H nmr spectrum of chellespontine showed signals at δ 0.84 (3H, s, *tert*-Me), 3.93 (1H, br s, CH-OH), 5.10, 5.37 (each 1H, br s, C=CH₂), 9.43 (1H, s, CHO). The eims of chellespontine gave a molecular ion peak at *m/z* 343 indicating the molecular formula C₂₂H₃₃NO₂ for the alkaloid. The ¹³C nmr spectrum of chellespontine (Table 1) exhibited 21 lines for 22 carbon atoms of the molecule (the signal at δ 25.9 accounts for two carbons) and a DEPT spectrum revealed four non-protonated carbons at δ 156.4, 46.4, 38.1 33.4, five methines at δ 183.5, 75.0, 44.9, 40.1, 36.3, twelve methylenes at δ 109.5, 64.5, 59.5, 58.3, 41.0, 35.0, 31.0, 28.1, 25.9, 25.9, 19.8 19.4, and one methyl group at δ 24.7.



The diterpenoid alkaloids from the genus *Consolida* and *Delphinium* usually conform to two main groups: the norditerpenoid alkaloids (C₁₉) of aconitine and/or lycoctonine-type and the diterpenoid alkaloids (C₂₀) having an atisane or veatchine-type ring skeleton.³ The former class of compounds are usually methoxylated but not the latter. The 22 carbon atoms of chellesspontine confirmed by its ¹³C nmr spectrum together with the absence of methoxyl groups, excluded the norditerpenoid skeleton. We therefore considered the diterpenoid alkaloid (C₂₀) skeleta for chellesspontine. The molecular formula of chellesspontine indicated seven degrees of unsaturation, of which two are accounted for by the exocyclic methylene and the aldehydic functions. The characteristic carbon resonances of an atisane- or veatchine-type exocyclic methylene group were readily located at δ 156.4 (s) and δ 109.5 (t) for C-16 and C-17 and the protons at δ 5.10 and 5.37 for the exocyclic methylene group. Of the only two methine doublets downfield of δ 44.9, the signal at δ 183.5 (d) clearly indicated an aldehydic carbon resonance and the signal at δ 75.0 (d) is an oxygenated carbon. The remaining three methines are attached to carbons which are not attached to oxygen or nitrogen atoms. Chellesspontine contains an exocyclic methylene, an *N*-CH₂CHO and a secondary hydroxyl group. We noticed that in the ¹H nmr spectrum, the aldehydic proton attached to the methylene group appeared as a singlet and not as the expected triplet at δ 9.43. A literature search showed that in all the cases, the aldehydic proton of *N*-CH₂CHO has been reported to be a singlet or a broad singlet.⁴ The hydroxyl group of chellesspontine should be located next to the exocyclic methylene group to account for the downfield shift of C-16 (δ 156.4 and 109.5) as in the case of sadosine⁵ (δ 155.4 and 110.1), ryosenamine⁶ (δ 155.2 and 109.6), and atisine⁷ (δ 157.5 and 108.9). On the basis of these data, we arrived at two alternative structures (1) and (2) for chellesspontine. A comparison of the ¹³C nmr values of 1 with dihydroatisine (3), dihydroveatchine⁷ and dihydrogarryfoline⁸ indicated that the values of the rings B, C and D of 1 are very similar to those of 3 having an atisane skeleton. The chemical shifts of C-8, C-9, C-11, C-14, C-15, C-16 and C-17 in 1 widely differ from the values in dihydrogarryfoline and dihydroveatchine. The ¹³C nmr spectra of 3 in CDCl₃ and C₅D₅N are very similar in their chemical shifts (Table 1). The ¹³C nmr chemical shift assignments of dihydroatisine (3), atisine azomethine (azitine) (4) and other diterpenoid alkaloids were essentially made with the help of proton decoupling techniques, additivity relationships and effects owing to specific structural changes in a number of closely related alkaloids.^{7,8} Denudatine (5) and dictyzine (6) are closely similar in their structures to 1, 3 and 4 except for a bond between C-7 and C-20. Unambiguous ¹³C chemical shift assignments have been made for denudatine (5)⁹ and dictyzine (6)¹⁰ as a result of detailed nmr studies. Although we have not carried out detailed nmr work on 1, 3 and 4, we have assigned the ¹³C nmr chemical shifts for these alkaloids, by comparison of the values assigned to 5 and 6. This has necessitated the change of some literature values shown by an asterisk in Table 1.

In selective INEPT experiments,¹¹ saturation of the H-18 methyl singlet led to an enhancement of the quaternary carbon at δ 33.4 which was assigned to C-4, two bonds removed from H-18. In addition, a

methylene at δ 59.5 assigned to C-19, also showed enhancement three bonds removed from H-18, and an unexpected polarization transfer to C-6 (δ 19.4), four bonds removed. Some other ^{13}C chemical shift assignments of cheloespontine (1) have been confirmed by selective INEPT studies (Table 2). The structure of cheloespontine was confirmed by reduction with NaBH_4 to afford a compound identical in all respects (tlc, mp, mixture mp, ir, ^1H and ^{13}C nmr) with dihydroatisine (3). The alkaloid (3) has been isolated from *Aconitum heterophyllum*¹² and it has been prepared by the NaBH_4 reduction of atisine.¹³

Table 1. ^{13}C Nmr Chemical Shifts and Assignments for Cheloespontine (1), Dihydroatisine (3), Denudatine (5), Dictyzine (6) and Azitine (4).

Carbon	1 ^a	3 ^a	3 ^{b,8}	5 ^{c,9}	6 ^{d,10}	4 ^a	4 ^{b,7}
C-1	25.9	28.4	26.4*	26.1	27.6	25.9	26.1
C-2	19.8	23.1	23.2	20.3	21.8	19.5	19.6*
C-3	41.0	40.8	40.2*	39.8	41.2	34.2	34.1
C-4	33.4	33.7	33.6	33.5	35.3	32.9	32.8
C-5	44.9	50.1	49.6	51.7	54.0	46.9	46.9
C-6	19.4	17.9	17.4	22.5	24.0	20.1	20.0*
C-7	35.0	42.0	41.4*	46.6	44.0	42.3	42.4*
C-8	38.1	38.0	37.4	43.1	43.0	37.3	37.4
C-9	40.1	39.9	39.5	52.2	42.5	38.1	38.1
C-10	46.4	38.3	38.0	45.0	46.9	42.5	42.5
C-11	31.0	32.1	31.5*	71.6	24.7	30.9	31.0*
C-12	36.3	37.1	36.4	41.8	36.5	35.9	36.0
C-13	25.9	26.9	26.4*	24.0	23.0	25.1	25.5*
C-14	28.1	28.4	27.7*	27.7	29.0	28.1	28.1*
C-15	75.0	77.0	76.8	76.7	87.1	75.8	75.2
C-16	156.4	157.5	156.3	154.2	81.1	156.6	156.2
C-17	109.5	109.4	109.6	108.5	67.9	109.2	108.9
C-18	24.7	26.7	26.4	26.5	27.0	25.9	25.8
C-19	59.5	59.8	60.2	57.1	60.8	60.4	60.2
C-20	58.3	61.0	58.0*	71.0	74.7	166.2	166.4
C-21	64.5	54.7	54.0*	50.1	44.5	—	—
C-22	183.5	62.4	60.7	13.5	—	—	—

^a $\text{C}_5\text{D}_5\text{N}$; ^b CDCl_3 ; ^c CD_3SOCD_3 ; ^d CD_3OD .

The alkaloid (B) $\text{C}_{20}\text{H}_{29}\text{NO}$, mp 178-179°C, ms m/z 299 (M^+), designated as azitine (4), was isolated during the chromatographic separation of the pH 10 alkaloidal fraction. The ^{13}C nmr spectrum

showed 20 signals for 20 carbon atoms (Table 1). The resonances at 156.6 (s) and 109.2 (t) ppm suggested that the alkaloid is of the atisine-type and these could be assigned to C-16 and C-17, respectively, of the exocyclic methylene group. The two broad signals at δ 5.04 and 5.10 in the ^1H nmr spectrum supported the presence of the exocyclic methylene group. The signal at δ 3.69 (δ C 75.8 d)

Table 2. Nmr Data from Selective INEPT Experiments

Table 2. NMR Data from Selective INEPT Experiments				
Irradiation of proton assigned to	δ (ppm)	Enhancement of the carbon signals assigned to*		
Alkaloid 1		Strong	Medium	Weak
CH ₃ -18	0.84	33.4 (C-4)	59.5 (C-19)	19.4 (C-6)
H-12 (H-9)	2.38	75.0 (C-15) 156.4 (C-16)	40.0 (C-9)	109.5 (C-17)
H-15	3.93	156.4 (C-16)		
H-17 _a	5.09	36.3 (C-12)		
H-17 _b	5.40	75.0 (C-15)	156.4 (C-16)	
Alkaloid 4				
H-5	1.02	19.5 (C-6) 42.5 (C-10)	38.1 (C-9)	
H-12	2.40	156.6 (C-16) 75.8 (C-15)	38.1 (C-9) 25.1 (C-14)	109.2(C-17)
H-19	3.41	42.3 (C-3) 166.2 (C-20)	32.9 (C-4)	
H-15	3.70	156.6 (C-16) 38.1 (C-9)	109.2 (C-17)	35.9 (C-12)
H-17 _a	5.05	35.9 (C-12)	156.6 (C-16)	75.8 (C-15)
H-17 _b	5.10	156.6 (C-16) 75.8 (C-15)		
H-20	7.90	60.4 (C-19) 46.9 (C-5)	42.5 (C-10)	

*Strong 61-100%, Medium 40-60%, Weak < 40%

is clearly due to the proton attached to a hydroxyl group and the two proton signals at δ 3.41 and 3.42 (δ C 60.4, t) can be assigned to the $N\text{-CH}_2$ group. The methine proton far downfield at δ 7.87 indicated the presence of an azomethine function $N=\text{CH}$, which is supported by the ^{13}C signal at

166.2 (d) ppm. Structure **4** for azitine is supported by its nmr spectral data. The azomethine group is located on $N=C(20)$ and not $N=C(19)$ as is clear from the selective INEPT experiments (Table 2). Azitine was shown to be identical with the azomethine (**4**) prepared by $KMnO_4$ oxidation of atisine¹⁴ and its occurrence in nature has not been reported earlier. That the alkaloids (**1**) and (**4**) are not artefacts of atisine generated during the isolation procedure, was shown by the recovery of atisine and partial isomerization to isoatisine after treatment under conditions identical to those used for the isolation of chellespontine (**1**).

Compound (C) was identified as 1-*O*-methyldephisine (**7**); this is the first report of the natural occurrence of this alkaloid. The compound was prepared earlier by methylation of dephisine with trimethyloxonium tetrafluoroborate and bis-1,8-dimethylaminonaphthalene (proton sponge).¹⁵ The compounds (D), (E) and (F) were identified as the known norditerpenoid alkaloids delphinine¹⁶ (**8**), dephisine¹⁷ (**9**), and bullatine C¹⁸ (**10**), respectively. These alkaloids were found to be identical in their physical and spectral properties when compared with authentic samples. The alkaloid (G) was obtained as a crystalline compound, mp 146-148°C, and its molecular formula $C_{20}H_{23}NO_4$ was derived by its mass spectrum (M^+ , m/z 341). The 1H and ^{13}C nmr spectral data indicated this to be a hydroxy-*N*-methyltrimethoxyaporphine. A comparison of the tlc, mixture mp, proton¹⁹ and ^{13}C nmr spectral data showed it to be identical with (+)-corydine (**11**). The ^{13}C nmr chemical shift assignments were based on the δ values recorded for isocorydine²⁰ and corydine methochlorate.²¹ This is the first example of the isolation of an aporphine alkaloid from the Ranunculaceae family.

EXPERIMENTAL

Melting points are corrected and were determined on a Thomas-Kofler hot stage equipped with a microscope and polarizer. Infrared spectra were obtained on a Perkin-Elmer model 1420 spectrophotometer. 1H (300.13 MHz) and ^{13}C (75.5 MHz) and SINEPT nmr spectra were recorded on a Bruker AC-300 spectrometer. The ^{13}C nmr chemical shift multiplicities were determined from DEPT spectra. Mass spectra were determined on a Finnigan Quadrupole 4023 instrument. Optical rotations were measured on a Perkin-Elmer model 141 polarimeter. Chromatographic separations on a Chromatotron were carried out on rotors coated with 1 mm thick layer of Al_2O_3 (EM 1104-3) or SiO_2 (EM-7749); vlc was carried out with Merck Al_2O_3 (EM 1085).

Plant material: – The aerial parts of *Consolida hellespontica* were collected by one of the authors (B.S.) from the fields between Zonguldak and Kastamonu, at an altitude of 640 m. A voucher specimen (GUH-1810) is deposited in the herbarium of the Department of Pharmacognosy, Gazi University, Ankara, Turkey.

Isolation of alkaloids: – Dried and powdered aerial parts of *C. hellespontica* (3.0 kg) were extracted by percolation at room temperature with EtOH and evaporation of the extract *in vacuo* gave a gum (280 g). Part of this (76.1 g) was extracted with hexane (2 l) to give a residue (4.67 g). The defatted material was dissolved in CHCl₃ (300 ml) and extracted with 2% (v/v) H₂SO₄ (200 ml x 10). The acidic fraction was washed with CHCl₃ (300 ml x 3) and the CHCl₃ fractions were combined to give the neutral fraction. The acidic fraction was basified with Na₂CO₃ (pH 10) and extracted with CHCl₃ (700 ml x 7) to give the crude alkaloid (2.46 g). This was chromatographed on Al₂O₃ by vlc¹ and eluted with a gradient of hexane, Et₂O and MeOH. Twelve fractions (F₁–F₁₂) (each 150 ml) were collected and combined as per their tlc pattern.

Isolation of 1-O-methyldelphisine (C)(7) and delphinine (D)(8) from fractions F₁–F₃: – The combined fraction F₁–F₃ (520 mg; eluted with hexane: 10, 20 and 30% Et₂O) was chromatographed on an Al₂O₃ rotor and eluted with a gradient of hexane, Et₂O and MeOH and visualized under uv (λ 254 and 365 nm). Fractions 5 and 6 (hexane: 7 and 8% Et₂O, 50 ml each), gave 1-O-methyldelphisine (7; 111.2 mg), mp 138–139°C. Tlc, ir spectra and mixture mp of the alkaloid were identical with those of an authentic sample.¹⁵ Fractions 9–11 (hexane: 15, 20 and 30% Et₂O, 50 ml each) gave delphinine (8; 103.3 mg), mp 192–193°C, identical in its tlc, ir spectrum and mixture mp with those of an authentic sample.¹⁶

Isolation of delphisine (E)(9), bullatine C (F)(10) and (+)-corydine (G)(11): – The fraction F₄ (207 mg, hexane: 40% Et₂O, 450 ml) and fractions 12–15 from the chromatography of F₁–F₃ (42.3 mg) were combined on the basis of their tlc similarity, chromatographed on an Al₂O₃ rotor and eluted with a gradient of hexane, Et₂O and MeOH. Fractions 9–16 (hexane: 20 and 25% Et₂O) gave bullatine C (10; 58.9 mg), identical in all respects with an authentic sample.¹⁸

Fractions 1–5 were rechromatographed on a silica gel rotor and eluted with a gradient of hexane, CHCl₃ and MeOH. The first three fractions (hexane: 10, 50 and 100% CHCl₃, 100 ml each) afforded delphisine (9; 31.3 mg), mp 122–123°C, identical in its properties with those of an authentic sample.¹⁷ Fraction 4 (CHCl₃; 100 ml) gave (+)-corydine (11; 4.65 mg), mp 146–148°C. ¹H nmr (CDCl₃): δ 6.69 (1H, s, H-3), 2.56 (3H, s, N-CH₃), 6.92 (1H, d J=9 Hz, H-8), 7.09 (1H, d J=9 Hz, H-9), 3.74 (3H, s, 11-OCH₃), 3.91, 3.92 (each 3H, s, 2,10-OCH₃), 8.71 (1H, br s, 1-OH); ¹³C nmr (CDCl₃): δ 143.9 (C-1), 123.6 (C-1_a), 123.6 (C-1_b), 149.1 (C-2), 110.8 (C-3), 126.6 (C-3_a), 28.6 (C-4), 52.6 (C-5), 43.5 (N-CH₃), 62.6 (C-6_a), 35.2 (C-7), 130.5 (C-7_a), 124.3 (C-8), 111.2 (C-9), 151.7 (C-10), 142.3 (C-11), 130.5 (C-11_a). The alkaloid (G) was identical with an authentic sample¹⁹ of (+)-corydine, in its tlc, mixture mp, ir, ¹H and ¹³C nmr spectral comparison.

Isolation of cheloespontine (A)(1) and azitine (B)(4): – The highly colored fractions F₁₀–F₁₁ (297 mg) obtained by elution with Et₂O and Et₂O:50% MeOH were submitted to acid-base extraction and the

crude alkaloid (210 mg) was chromatographed on a silica gel rotor. Elution with CHCl_3 and 10% MeOH gave a mixture (83.5 mg) and further elution with MeOH and MeOH: Et_3N did not elute the blue fluorescent (λ 254 nm) band. The fluorescent band was scraped out and extracted with 2% H_2SO_4 (35 ml). Basification with 20% NaOH (pH 14) and extraction with CHCl_3 (100 ml x 3) gave a gum (57.5 mg). This was purified on an Al_2O_3 rotor (1mm; neutral EM 1092) and eluted with CHCl_3 and MeOH. Fractions 1-6 (CHCl_3 and 1-5% MeOH) gave a residue (17.1 mg). This material was again separated on an Al_2O_3 rotor and eluted with hexane: 40% Et_2O to give azitine (**4**; 9.1 mg), mp 177-179°C, identical in its tlc, mixture mp, ^1H and ^{13}C nmr spectrum with those of an authentic synthetic sample.⁷ Fractions 11-23 were obtained by elution with CHCl_3 and 5-20% MeOH to afford chellespontine (**1**; 33.2 mg), mp 227-230°C; $[\alpha]_D + 14.6^\circ$ (MeOH, c, 0.56); ms: m/z 343 (M^+ , 12%), 342 ($\text{M}^+ - 1$, 23.4), 328 ($\text{M}^+ - \text{CH}_3$, 2.9), 314 ($\text{M}^+ - \text{CHO}$, 5.6), 300 ($\text{M}^+ - \text{COCH}_3$, 2.9), 257 (3.4), 241 (0.6), 186 (13.2), 159 (11.4), 105 (6.4), 91 (29), 55 (55.2), 41 (100). For the ^{13}C nmr data see Table 1.

Reduction of chellespontine (**1**) with NaBH_4 to dihydroatisine (**3**): – Chellespontine (**1**, 5.1 mg) was dissolved in MeOH (2 ml) and to the solution was added NaBH_4 (15 mg) in four portions and the mixture kept overnight. Usual work up gave dihydroatisine (**3**, 3.5 mg), mp 157-159°C, identical in its tlc, mixture mp, ir and ^1H nmr spectrum with those of an authentic sample.⁸

Effect of the isolation procedure of (**1**) on atisine: – Atisine (99 mg) was adsorbed on a silica gel rotor and eluted with a gradient of hexane, CHCl_3 , MeOH and Et_3N as reported for the isolation of **1**. The silica gel was scraped, extracted with 2% H_2SO_4 and the alkaloidal fraction was isolated after basification with NaOH. This mixture on purification on an Al_2O_3 rotor gave atisine and isoatisine²² as identified by comparison of their ^1H and ^{13}C nmr spectra.

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REFERENCES

1. S. W. Pelletier, H. P. Chokshi, and H. K. Desai, *J. Nat. Prod.*, 1986, **49**, 892.
2. H. K. Desai, B. S. Joshi, A. M. Panu, and S. W. Pelletier, *J. Chromatogr.*, 1985, **322**, 223.
3. S. W. Pelletier and L.H. Keith, *The Alkaloids*, Vol. 12, Chapter 1, p. 2; Vol. 12, Chapter 2, p. 136, ed. by R. H. F. Manske, Academic Press, New York, 1970.
4. R. J. Sundberg and K. G. Gadamasetti, *Tetrahedron*, 1991, **47**, 5673; M. Rubiralta, A. Diez, A. Balet, and J. Bosch, *Tetrahedron*, 1987, **43**, 3021; P. Magnus, N. L. Sear, C. S. Kim, and N. Vicker, *J. Org. Chem.*, 1992, **57**, 70.

5. T. Okamoto, H. Sanjoh, K. Yamaguchi, Y. Iitaka, and S. Sakai, *Chem. Pharm. Bull.*, 1983, **31**, 360; H. Sanjoh, T. Okamoto, and S. Sakai, *J. Pharm. Soc. Japan*, 1985, **104**, 738.
6. S. Sakai, T. Okazaki, K. Yamaguchi, H. Takayama, and N. Aimi, *Chem. Pharm. Bull.*, 1987, **35**, 2615.
7. N. V. Mody and S. W. Pelletier, *Tetrahedron*, 1978, **34**, 2421.
8. S. W. Pelletier, N. V. Mody, and H. K. Desai, *J. Org. Chem.*, 1981, **46**, 1840.
9. D. Uhrin, B. Proksa, and J. Zhamiansan, *Planta Medica*, 1991, **57**, 390.
10. B. S. Joshi, S. W. Pelletier, X. Zhang, and J. K. Snyder, *Tetrahedron*, 1991, **47**, 4299.
11. A. Bax, *J. Magn. Reson.*, 1984, **57**, 314; A. Bax, J. A. Ferretti, N. Nashed, and D. M. Jarina, *J. Org. Chem.*, 1985, **50**, 3029.
12. S. W. Pelletier, R. Aneja, and K. W. Gopinath, *Phytochemistry*, 1968, **7**, 625.
13. O. E. Edwards and T. Singh, *Can. J. Chem.*, 1954, **32**, 465.
14. S. W. Pelletier and W. A. Jacobs, *J. Am. Chem. Soc.*, 1956, **78**, 4139.
15. S. W. Pelletier and J. T. Etse, *J. Nat. Prod.*, 1989, **52**, 145.
16. K. B. Birnbaum, K. Wiesner, E. W. K. Jay, and L. Jay, *Tetrahedron Letters*, 1971, 867; S. W. Pelletier and Z. Djarmati, *J. Am. Chem. Soc.*, 1976, **98**, 2626.
17. S. W. Pelletier, W. H. De Camp, S. Lajsic, Z. Djarmati, and A. H. Kapadi, *J. Am. Chem. Soc.*, 1974, **96**, 7815; S. W. Pelletier, Z. Djarmati, S. Lajsic, and W. H. DeCamp, *J. Am. Chem. Soc.*, 1976, **98**, 2617; S. W. Pelletier and Z. Djarmati, *J. Am. Chem. Soc.*, 1976, **98**, 2626.
18. H. C. Wang, D. Z. Zhu, Z. Y. Zhao, and R. H. Zhu, *Acta Chimica Sinica*, 1980, **38**, 475; H. Takayama, A. Tokita, M. Ito, S. Sakai, F. Kurosaki, and T. Okamoto, *J. Pharm. Soc. Japan*, 1982, **102**, 245; G. de la Fuente, R. D. Acosta, and T. Orribo, *Heterocycles*, 1989, **29**, 205.
19. A. H. Jackson and J. A. Martin, *J. Chem. Soc. (C)*, 1966, 2222.
20. A. J. Marsaioli, F. A. M. Reis, A. F. Magalhaes, E. A. Ruveda, and A. M. Kuck, *Phytochemistry*, 1979, **18**, 165.
21. E. Wenkert, B. L. Buckwalter, I. R. Burfitt, M. J. Gasic, H. E. Gottlieb, E. W. Hagaman, F. M. Schell, and P. M. Wovkulich, "Topics in Carbon-13 NMR Spectroscopy" ed. by G. C. Levy, Vol. 2, Wiley-Interscience, New York, 1976.
22. W. A. Jacobs and L. C. Craig, *J. Biol. Chem.*, 1943, **147**, 567; K. Wiesner, R. Armstrong, M. F. Bartlett, and J. A. Edwards, *Chem. and Ind.*, 1954, 132; S. W. Pelletier and N. V. Mody, *J. Am. Chem. Soc.*, 1977, **99**, 284.

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