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# Willipelletierine, a new diterpenoid alkaloid from *Consolida scleroclada* (Boiss.) Schrod.

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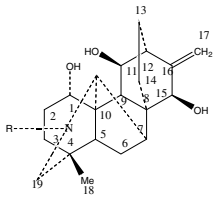
***Dedicated to Prof. Dr. S. William Pelletier, Athens, USA[4]***

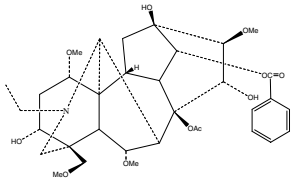
From the aerial parts of *Consolida scleroclada* (Boiss.) Schrod. collected in Turkey, a new diterpenoid alkaloid named willipelletierine has been isolated along with the known diterpenoid alkaloids aconitine, lapaconidine, and delcosine. The structure for willipelletierine was established on the basis $^1$H, $^{13}$C, DEPT, homonuclear $^1$H COSY, HETCOR and NOESY NMR studies.

## 1. Introduction

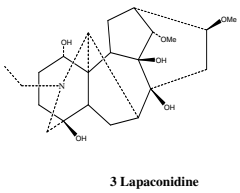
*Consolida* species are toxic plants like *Aconitum* and *Delphinium* species of the same plant family Ranunculaceae. In continuation of our investigations of Turkish *Consolida* species [1–3] we have now chemically studied *Consolida scleroclada* (Boiss.) Schrod. No previous work had been done on this species for its diterpenoid alkaloid constituents. The chemical investigation of the aerial parts of *C. scleroclada* led to the isolation of a new diterpenoid alkaloid, willipelletierine (**1**) together with the known alkaloids aconitine (**2**), lapaconidine (**3**), and delcosine (**4**) [4–6].



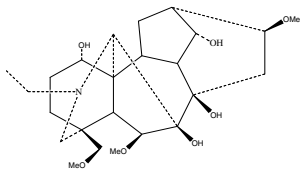
**1 Willipelletierine R = Me**
**5 Lepenine R = Ethyl-**



**2 Aconitine**



**3 Lapaconidine**



**4 Delcosine**

## 2. Investigations, results and discussion

From the aerial parts of *C. scleroclada* collected at an altitude of 1200 m in Isparta-Gönen, Turkey, we have isolated a novel diterpenoid alkaloid designated as willipelletierine, $[\alpha]_D^{25} + 1.20^0$ (0.1, $CHCl_3$). The molecular formula, $C_{21}H_{31}NO_3$ (ESI, MW, [M + 1] m/z 346), was derived for the alkaloid by HRFABMS $[M + 1]^+$ m/z 346.23590; calc. 346.23821) and confirmed from the $^{13}$C NMR spectral and DEPT data. The IR spectrum showed hydroxyl absorption at 3440 $cm^{-1}$, but no carbonyl or aromatic absorptions were observed. A completely decoupled $^{13}$C NMR spectrum confirmed 21 carbon atoms of the molecule. The DEPT spectra showed four signals for quaternary carbons at δ 154.0, 50.8, 43.5, and 33.9; eight signals for methines at δ 77.6, 72.6, 69.9, 68.9, 53.9, 51.2, 46.6 and 41.6; seven signals for methylenes at δ 109.4, 59.0, 38.2, 30.5, 27.3, 24.4 and 22.8; and two signals for methyls at δ 43.8 and 25.7. The $^1$H NMR spectrum proved the absence of methoxyl groups and the presence

**Table: NMR data of willipelletierine (1) and $^{13}$C NMR data of lepenine (5)**

| Position | | $^1$H (J, Hz) | COSY $^1$H-$^1$H | $^{13}$C (**1**) | $^{13}$C (**5**) |
|---|---|---|---|---|---|
| 1 | 1β | 4.10 dd (7,10) | H-2α, H-2β | 69.9 d | 70.7 d |
| 2 | 2α | 2.30 m | H-1, H-2β, H-3α, H-3β | 30.5 t | 31.1 t |
| | 2β | 1.80 m | H-1, H-2α, H-3α, H-3β | | |
| 3 | 3α | 1.56 m | H-2α, H-2β, H-3β | 38.2 t | 38.6 t |
| | 3β | 1.30 d (13) | H-2α, H-2β, H-3α | | |
| 4 | – | | – | 33.9 s | 33.7 s |
| 5 | 5 | 1.32 d (9) | H-6a | 51.2 d | 52.3 d |
| 6 | 6a | 1.23 m | H-5, H-6b | 22.8 t | 23.1 t |
| | 6b | 2.80 dd (7,14) | H-6a, H-7 | | |
| 7 | 7 | 2.17 br s | H-20 | 41.6 d | 42.2 d |
| 8 | – | | – | 43.5 s | 43.6 s |
| 9 | 9 | 1.31 dd (8,9) | H-11 | 53.9 d | 53.8 d |
| 10 | – | | – | 50.8 s | 50.9 s |
| 11 | 11 | 4.44 dd (4,10) | H-9, H-12 | 72.6 d | 72.9 d |
| 12 | 12 | 2.17 m | H-11, H-13a, H-13b | 46.6 d | 46.2 d |
| 13 | 13a | 1.45 m | H-12, H-13b, H-14a, H-14b | 24.4 t | 24.5 t |
| | 13b | 1.70 m | H-12, H-13a, H-14a, H-14b | | |
| 14 | 14a | 1.09 m | H-13a, H-13b, H-14b | 27.3 t | 27.4 t |
| | 14b | 1.91 m | H-13a, H-13b, H-14a | | |
| 15 | 15 | 4.26 br s | H-17a, H-17b | 77.6 d | 77.9 d |
| 16 | – | | – | 154.0 s | 154.3 s |
| 17 | 17a | 5.01 s | H-15, H-17b | 109.4 t | 109.5 t |
| | 17b | 5.21 s | H-15, H-17a | | |
| 18 | $CH_3$-18 | 0.69 s | – | 25.7 q | 26.0 q |
| 19 | 19a | 2.53 d (11) | H-19b | 59.0 t | 57.0 t |
| | 19b | 2.21 d (11) | H-19a | | |
| 20 | 20 | 3.64 s | H-5, H-6a, H-7 | 68.9 d | 67.8 d |
| 21 | $CH_3$-21 | 2.33 s | – | 43.8 q | 50.8 t |
| 22 | – | – | – | – | 13.6 t |

of an exocyclic methylene group ($\delta_H$ 5.21, 5.01 each s and ($\delta_C$ 154.0 and 109.4) along with a methyl group ($\delta_H$ 0.72, 3H s) and ($\delta_C$ 25.7 q). On the biogenetic considerations, it is a diterpenoid ($C_{20}$) alkaloid. There are three hydroxyls attached to carbons, which were observed at $\delta_C$ 77.6, 72.6 and 69.2. One of the $\delta_H$ 4.26 (1H, br s), $\delta_C$ 77.6 (d), should be located at C-15; next to the exocyclic methylene group to account for the downfield shift of C-16 ($\delta_C$ 154.0 and 109.4). From the NMR signals ($\delta_C$ 69.9 d, $\delta_H$ 4.10 1 H, dd J = 7.10 Hz), the second hydroxyl should be placed at C-1, the correlation of H-1 with the protons at C-2 ($\delta_C$ 30.5 t, $\delta_H$ 2.30, H-2 α, 1.80 H-2β) was observed in the COSY spectrum. According to the NMR signals again (α 72.6 d, $\delta_H$ 4.41 1 H, dd, J = 4.10 Hz) the third hydroxyl should be placed at C-11, the correlation of H-11 with the protons at C-9 ($\delta_C$ 53.9 d, $\delta_H$ 1.31, 1 H, dd, J = 7.9 Hz) was observed in the COSY spectrum. All the $^1$H and $^{13}$C NMR data are very close to those of lepenine (**5**) [7]. The only difference is the absence of the peaks for an ethyl group and the presence of a N-methylgroup ($\delta_C$ 43.8 q, $\delta_H$ 2.33, 3 H, s); this methyl group also shows NOE with H-20 and H-7. The NMR data of willipelletierine (**1**) and the $^{13}$C NMR data of lepenine (**5**) are given in the Table.

## 3. Experimental

### *3.1. Equipment*

Optical rotations were measured on Perkin-Elmer Model 141 polarimeter in $CDC1_3$. ESI MS were recorded on a Perkin-Elmer SCIEX API-1 mass spectrometer. HR FAB MS were determined on a Fisons Auto Spek. ETOFFPD FAB$^+$ MASS SPECTROMETER. NMR spectra were recorded on a Bruker AC-300 spectrometer. VLC [8] was carried out with Merck $Al_2O_3$ (EM 1085) and $SiO_2$ 60 (EM 7736). Chromatographic separations on a Chromatotron [9] were carried out on rotors coated with 1 mm thick layer of $Al_2O_3$ 60 PF-254, 365 (EM 1.104) or $SiO_2$ 60 HF (EM 7749). Thin layer chromatograms were run using the solvent system toluene : acetone : MeOH : $NH_4OH$ (49.5 : 41.5 : 8:5) and toluene : EtOAc : DEA (72 : 2 : 1 or 7 : 3.5 : 1).

### *3.2. Plant material*

Aerial parts (600 g) of *Consolida scleroclada* (Boiss.) Schrod. were collected and identified by one of us (H.O.) in Isparta-Gönen, Turkey at an elevation of 1200 m, in July 1999. A voucher specimen has been deposited in the Herbarium of Faculty of Science and Literature, Süleyman Demirel University (No. Ozcelik 7953) Isparta, Turkey.

### *3.3. Extraction and isolation*

The crude alkaloidal extract (600 mg) obtained from 600 g of aerial parts was first separated by VLC on a basic $Al_2O_3$ column (EM 1085) with hexane-$CHCl_3$- MeOH mixtures. VLC fraction 6 (hexane-$CHCl_3$ 50 : 50) (142 mg) was chromatographed on a $SiO_2$ rotor with hexane-$CHCl_3$-MeOH mixtures and aconitine (**2**, 14 mg) and lapaconidine (**3**, 8 mg) were isolated. VLC fractions 7–9 (hexane-$CHCl_3$ 40 : 60 to 20 : 80) (56 mg) were combined and chromatographed on a $SiO_2$ rotor with hexane-$CHCl_3$-MeOH mixtures to give delcosine (**4**, 5 mg). VLC fraction 10–12 (hexane-$CHCl_3$ 10 : 90 to 100% $CHCl_3$) (221 mg) were combined and chromatographed on a basic alumina rotor with hexane-$CHCl_3$-MeOH mixtures to give willipelletierine (**1,** 12 mg). All the known compounds were identified by comparison of their $^1$H and $^{13}$C NMR data and co-TLC behavior with those of authentic samples.

[4] This compound and paper are dedicated to Prof. Dr. S. William Pelletier, Head and the founder of the Institute for Natural Products Research (The University of Georgia, Athens, Georgia, USA), for his remarkable works including being the editor of "Alkaloids: Chemical and Biological Perspectives" (Vol. 1–13) and unforgettable contributions and self-dedication to the diterpenoid alkaloids.

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**References**

1 Ulubelen, A.; Desai, H. K.; Srivastava, S. K.; Hart, B. P.; Prak, J. C.; Joshi, B. S.; Pelletier, S. W.; Meriçli, A. H.; Meriçli, F.; Özen, H. C.: J. Nat. Prod. **59**, 770 (1996)
2 Meriçli, A. H.; Meriçli, F.; Seyhan, V.; Ulubelen, A.; Desai, H. K.; Joshi, B. S.; Teng, Q.; Pelletier, S. W.: Heterocycles **45**, 1955 (1997)
3 Meriçli, A. H.; Meriçli, F.; Ulubelen, A.; Desai, H. K.; Joshi, B. S.; Pelletier, S. W.; Özden, S.; Küçükislamoğlu, M.: Heterocycles **47**, 329 (1998)
4 Pelletier, S. W.; Djarmati, Z.: J. Am. Chem. Soc. **98**, 2626 (1976)
5 Pelletier, S. W.; Mody, N. V.; Sawhney, R. S.: Can. J. Chem. **57**, 1652 (1979)
6 Pelletier, S. W.; Glinsky, J. A.; Joshi, B. S.; Chen, S. Y.: Heterocycles **20**, 1347 (1983)
7 Batsuren, D.; Tunsag, J.; Batbayar, N.; Meriçli, A. H.; Meriçli, F.; Teng, Q.; Desai, H. K.; Joshi, B. S.; Pelletier, S. W.: Heterocycles **49**, 327 (1998)
8 Pelletier, S. W.; Chokshi, H. P.; Desai, H. K.: J. Nat. Prod. **49**, 892 (1986)
9 Desai, H. K.; Trumbull, E. R.; Pelletier, S. W.: J. Chromatogr. **366**, 439 (1986)

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