Ternatine, a new diterpene alkaloid from *Delphinium ternatum*

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A new alkaloid, ternatine ($C_{24}H_{33}NO_5$), was isolated from aerial parts of the *Delphinium ternatum* plant. According to the ^1H, ^{13}C NMR, IR, and mass spectra of the base and its triacetate, ternatine was assumed to have the structure of 4β-methyl-7α-isobutyryloxy-11α,15β,19β-trihydroxyhetisane.

Key words: *Delphinium ternatum*, aerial parts; diterpene alkaloids.

Earlier we reported the isolation of a B[1] base of $C_{24}H_{33}NO_5$ structure (high resolution MS 415.2364) from *Delphinium ternatum* plant.[1] Further investigations showed that this compound is new; it was named ternatine (**1**). The ^1H NMR spectrum of base **1** contains a tertiary methyl group singlet (3 H) at δ 0.99 and two isopropyl group doublets (both 3 H) at 1.23 and 1.22 (^3J = 7.0 Hz).

Deuteration showed that ternatine contains three active hydrogen atoms. Alkaline hydrolysis of base **1** results in an amino alcohol, *i.e.*, ternatidine $C_{20}H_{27}NO_4$ (**2**).

Along with a molecular ion peak (*m/z* 415) with 37% intensity, peaks of ions with *m/z* (I_{rel} (%)) 397 (25), 387 (75), 327 (44), 309 (100), 300 (47), 291 (31), 280 (44), and 264 (25) are also present in the mass spectrum of the base isolated. Intense absorption bands at 1100, 1710, and 3500 cm^{-1} are observed in the IR spectrum of compound **1**.

The composition, analysis of the spectral data, and the results of alkaline hydrolysis of base **1** indicate that ternatine belongs to diterpene alkaloids of the hetisine type and that one of its secondary hydroxyl groups is esterified with isobutyric acid.

The existence of three free secondary hydroxyl groups in the alkaloid is confirmed by acetylation of **1** with acetic anhydride in the presence of *p*-toluenesulfonic acid that yields ternatine triacetate $C_{30}H_{39}NO_8$ (**3**).

The proton-decoupled ^{13}C NMR spectrum of ternatine contains signals of 24 C atoms. The ^{13}C signals were assigned by a comparative analysis of the spectral parameters of compound **1** and Guan-Fu base Z (**4**)[2], acorine (**5**)[3], hypognavine (**6**)[4], and septenetriosine (**7**)[5] (Table 1).

The assignment of the proton signals in the ^1H NMR spectra of ternatine and its triacetate was carried out using selective double resonance and by comparative analysis of its characteristics. The data summarized in Table 2 indicate that the acyloxy group in ternatine is located at the C(7) atom, and the three secondary hydroxy groups are located at the C(11), C(15), and C(19) atoms.

The most complete picture of the coupling interaction was obtained for ternatine triacetate **3**. Based on the three coupling constants, $^3J_{11,9}$ = 8.7 Hz, $^3J_{11,12}$ < 1 Hz, and $^4J_{11,13}$ = 2.2 Hz, an α-equatorial orientation was found for the hydroxy group at the C(11) atom. Based on the coupling constants and the mode of variation of chemical shifts of the *gem*-hydroxyl protons due to acylation, as well as on the basis of the ^{13}C NMR spectroscopic data,[2–9] a β-orientation was proposed for the hydroxy groups at the C(15) and C(19) atoms, and an α-orientation was proposed for the isobutyryloxy group at the C(7) atom.

Table 1. Chemical shifts (δ) in the ^{13}C NMR spectra of ternatine **1** (in CD_3OD), Guan-Fu base Z (**4**), acorine (**5**), hypognavine (**6**), and septenetriosine (**7**) (in $CDCl_3$)

Atom	1	4	5	6	7
C(1)	30.1	31.4	31.2	68.1	69.0
C(2)	29.7	69.6	70.1	73.2	70.4
C(3)	20.6	36.7	36.6	33.0	39.1
C(4)	53.2	37.6	37.5	35.8	39.7
C(5)	61.5	59.9	60.1	50.6	58.8
C(6)	66.6	63.0	63.1	64.1	60.5
C(7)	65.2	31.9	32.0	29.0	31.1
C(8)	43.8	44.3	44.2	44.3	42.1
C(9)	50.0	53.5	53.6	80.3	79.8
C(10)	52.0	46.3	46.4	54.0	53.0
C(11)	74.0	76.0	76.2	39.2	33.5
C(12)	40.2	52.7	52.7	34.8	36.1
C(13)	34.5	79.9	80.0	33.5	33.1
C(14)	44.4	80.2	80.3	42.4	43.3
C(15)	70.2	31.1	31.2	72.4	30.7
C(16)	153.6	144.7	144.8	154.6	150.3
C(17)	110.2	108.2	108.2	110.0	104.8
C(18)	23.5	29.7	29.7	29.3	28.4
C(19)	91.9	63.0	63.1	63.5	95.2
C(20)	70.4	69.1	69.2	71.8	60.5
C(1′)	177.2	176.5	171.2	—	—
C(2′)	35.3	34.4	21.6	—	—
C(3′)	19.8, 19.2	20.0	—	—	—

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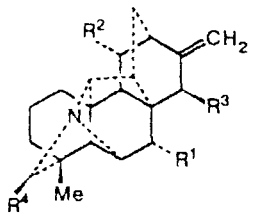
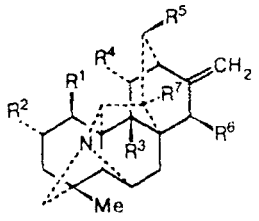
Table 2. Chemical shifts (δ) and coupling constants (J/Hz) in the ^{1}H NMR spectra of ternatine (**1**) and ternatine triacetate (**3**) (in $CDCl_3$)

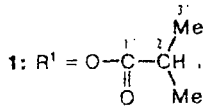
Assignment	1	3
$H_3C(18)$	0.99 (s)	0.87 (s)
$HC(C\underline{H}_3)_2$	1.22, 1.23 (both d, ^3J = 7.0)	1.19, 1.23 (both d, ^3J = 7.0)
$\underline{H}C(CH_3)_2$	2.69 (m)	2.66 (m)
H(6)	3.52 (br.m)	3.42 (br.m, $^3J_{6,7}$ = 2.9, $^3J_{6,5}$ < 0.5, $^4J_{6,20}$ ≈ 1.1)
H(7)	5.16 (d, ^3J = 2.9)	5.01 (d, $^3J_{7,6}$ = 2.9)
H(9)	2.12 (d, ^3J = 8.8)	2.35 (dd, $^3J_{9,11}$ = 8.7, $^4J_{9,14}$ = 2.2)
H(11)	4.46 (br.d, ^3J = 8.4)	5.20 ($^3J_{11,9}$ = 8.7, $^3J_{11,12}$ < 1, $^4J_{11,13}$ = 2.2)
H(12)	2.20 (br.t, $W_{1/2}$ = 6 Hz)	2.28 (br.t, $^3J_{12,11}$ < 1, $^3J_{12,13}$ + $^3J_{12,13'}$ = 6.1)
H(15)	3.86 (s)	5.14 (s)
H(17)	5.05 (s, 2 H)	5.21, 5.06 (both br.s)
H(19)	4.21 (s)	5.53 (s)
H(20)	2.77 (br.m)	2.84 ($^3J_{20,14}$ < 1, $^4J_{20,6}$ ≈ 1.1)
CH_3COO	—	2.04 (s, 6 H); 2.07 (s, 3 H)



1—3



4—6



1: R^1 = O—C(=O)—CH(Me)—Me, $R^2 = R^3 = R^4$ = OH

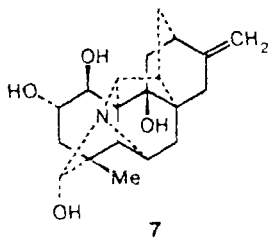
2: $R^1 = R^2 = R^3 = R^4$ = OH

3: R^1 = OCOCHMe$_2$, $R^2 = R^3 = R^4$ = OAc

4: $R^1 = R^3 = R^6$ = H, R^2 = OCOCHMe$_2$, $R^4 = R^5 = R^7$ = OH

5: $R^1 = R^3 = R^6$ = H, R^2 = OCOMe, $R^4 = R^5 = R^7$ = OH

6: $R^1 = R^3 = R^6$ = OH, R^2 = OCOPh, $R^4 = R^5 = R^7$ = H



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Experimental

IR spectra were recorded on a UR-20 spectrophotometer. Mass spectra were obtained on an MX-1310 spectrometer equipped with a system for direct introduction into the ion source. ^{1}H NMR spectra were recorded on a Bruker WM-500 spectrometer in $CDCl_3$ with $SiMe_4$ as the internal standard; ^{13}C NMR spectra were recorded on Tesla BS-567A and Varian CFT-20 spectrometers in CD_3OD.

Extraction of *Delphinium ternatum*. Aerial parts of the plant (3.8 kg) were extracted with chloroform at room temperature (7 times). The extracts were treated with 56% H_2SO_4. The acid solutions were combined, washed with ether, cooled, alkalized with sodium carbonate, and extracted with ether and chloroform to give washing fraction *A* (1.91 g), alkaline ether fraction *B* (11 g), and alkaline chloroform fraction *C* (1.92 g).

Ternatine (1). The ether fraction *B* was dissolved in ethanol and acidified with 10% perchloric acid, and the resulting precipitate of methyllycaconitine perchlorate (4.38 g) was separated. The mother liquor was alkalized with sodium carbonate and extracted successively with petroleum ether, benzene, ether, and chloroform. The benzene fraction (5.76 g) was extracted with chloroform to give 0.58 g of ternatine, m.p. 236—238 °C (from acetone).

Ternatidine (2). Compound **1** (0.07 g) was mixed with 10% methanol alkali (20 mL) and heated for 1 h. The solvent was evaporated, and the residue was dissolved in 5% H_2SO_4, washed with ether, alkalized with sodium carbonate, and extracted with chloroform. The alkaline chloroform solution was concentrated to yield 0.04 g of a chromatographically homogeneous residue. IR, ν/cm^{-1}: 3500 (OH); 1100 (C—O). MS, m/z: $[M]^+$ 345.

Ternatine triacetate (3). A mixture of ternatine (0.03 g) and *p*-toluenesulfonic acid (0.03 g) in acetic anhydride (4 mL) was kept for 5 days at room temperature. After that, the mixture was concentrated, and the residue was dissolved in water, alkalized with sodium carbonate, and extracted with chloroform. The solvent was evaporated, and the residue was chromatographed on an Al_2O_3 column. The reaction products were eluted with hexane—ether mixtures (5 : 1 → 3 : 1 → 2 : 1 → 1 : 1). The fraction eluted with the 2 : 1 mixture yielded 0.02 g of a chromatographically homogeneous residue, ternatine triacetate. MS, m/z (I_{rel} (%)): 541 $[M]^+$ (45), $[M-42]^+$ (25), $[M-102]^+$ (100).

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