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NORDITERPENOID ALKALOIDS FROM *ACONITUM TRANSSECTUM*

SHANGZHEN ZHENG, LIMING GAO,* XIAOJIANG HAO,† XIAOXIONG WANG and XUWEI SHEN

Department of Chemistry, Northwest Normal University, Lanzhou, 730070, People's Republic of China;
† Kunming Institute of Botany, Academia Sinica, Kunming, 650204, People's Republic of China

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Key Word Index—*Aconitum transsectum*; Ranunculaceae; diterpenoid alkaloids; transconitines A, B and C; yunaconitine; crassicauline A; foresaconitine; talatisamine; 8-deacetylyunaconitine; geniconitine; indaconitine; forestine; 14-acetyltalatisamine and chasmanine.

Abstract—Three new norditerpenoid alkaloids, transconitine A, B and C, together with the known alkaloids yunaconitine, crassicauline A, foresaconitine, talatisamine, 8-deacetylyunaconitine, geniconitine, indaconitine, forestine, 14-acetyltalatisamine and chasmanine were isolated from *Aconitum transsectum* Diels. The structures of the three new alkaloids were determined by NMR spectroscopy and that of transconitine A partial synthesis.

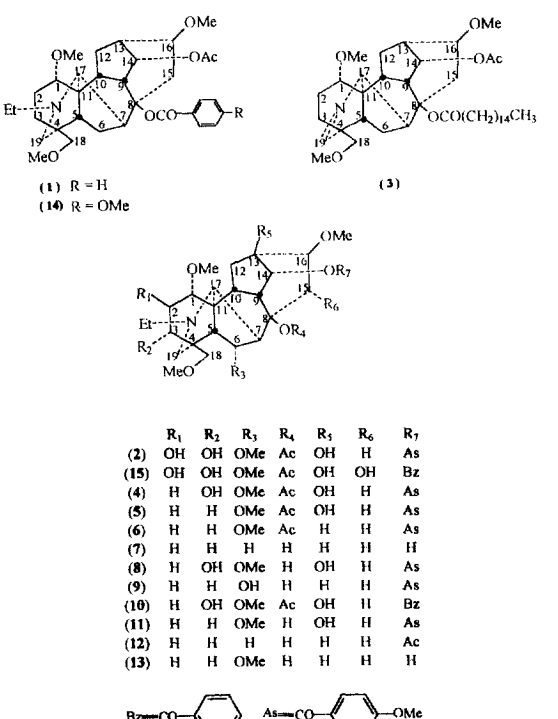
INTRODUCTION

The analysis of the main nor-diterpene alkaloids of the roots of *Aconitum transsectum* has been reported previously [1]. Further investigation of the diterpene alkaloids of this plant has resulted in the identification of three new minor compounds transconitine A (**1**), B (**2**) and C (**3**), together with 10 known alkaloids yunacoitine (**4**), crassicualine A (**5**), foresaconitine C (**6**), talatisamine (**7**), 8-deacetylyunaconitine (**8**), geniconitine (**9**), indaconitine (**10**), forestine (**11**), 14-acetyltalatisamine (**12**) and chasmanine (**13**).

RESULTS AND DISCUSSION

The new bases, whose elementary composition was determined by HR mass spectrometry, showed characteristic signals of norditerpenoid alkaloids in their ^{13}C NMR spectra [2, 3] and characteristic fragmentation of such compounds in their mass spectra [4].

The NMR spectra of transconitine A (**1**) $C_{33}H_{45}NO_7$ gave signals at δ_H 1.09 (3H, *t*, $J = 7$ Hz), δ_C 49.3 *t* and 13.3 *q* for an *N*-ethyl group, δ_H 3.21, 3.24 and 3.29 (3H each, *s*), δ_C 56.0 *q*, 56.4 *q* and 59.4 *q* for three methoxy groups, δ_H 1.76 (3H, *s*), δ_C 21.3 *q* and 171.3 *s* of an acetate group. (IR ν_{max} 1725 and 1240 cm^{-1}), and δ_H 7.93 (2H, *d*, $J = 8$ Hz), 7.49 (1H, *t*, $J = 8$ Hz), 7.36 (2H, *t*, $J = 8$ Hz) indicated one benzoic acid ester group. The ^{13}C NMR spectrum (Table 1) contained only three singlets at δ_C 38.4 (C-4), 48.9 (C-11) and 86.7 (C-8), indicating that the compound was an aconitine-type norditerpenoid alkaloid possessing a tertiary benzoic acid ester group or an acetate group at C-8 [2, 3]. The ^1H NMR spectrum exhibited a signal

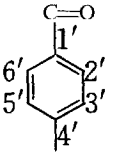


	R_1	R_2	R_3	R_4	R_5	R_6	R_7
(2)	OH	OH	OMe	Ac	OH	H	As
(15)	OH	OH	OMe	Ac	OH	OH	Bz
(4)	H	OH	OMe	Ac	OH	H	As
(5)	H	H	OMe	Ac	OH	H	As
(6)	H	H	OMe	Ac	H	H	As
(7)	H	H	H	H	H	H	H
(8)	H	OH	OMe	H	OH	H	As
(9)	H	H	OH	H	H	H	As
(10)	H	OH	OMe	Ac	OH	H	Bz
(11)	H	H	OMe	H	OH	H	As
(12)	H	H	H	H	H	H	Ac
(13)	H	H	OMe	H	H	H	H

Fig. 1. The chemical structure of compounds **1–15**.

* Author to whom correspondence should be addressed.

Table 1. ^{13}C NMR spectral data of compounds **1**, **2**, **3**, **14** and **15** (in $CDCl_3$, 400 MHz, TMS)

C	**1**	**14** [5]	**2**	**15** [6]	**3**
1	85.2	85.1	83.5	83.6	82.5
2	26.3	26.1	65.4	65.2	26.5
3	32.4	32.2	67.9	67.7	35.6
4	38.4	38.1	43.9	43.8	48.0
5	41.6	41.4	49.9	45.6	37.1
6	24.6	24.6	82.6	82.4	24.5
7	45.9	45.6	45.7	44.9	41.3
8	86.7	85.9	85.2	91.5	84.7
9	42.5	42.1	46.0	45.3	44.3
10	38.7	38.6	40.7	40.5	40.9
11	48.9	48.5	52.7	52.4	49.3
12	28.8	28.4	37.4	38.1	28.7
13	45.0	44.8	74.7	73.8	48.1
14	75.5	75.3	78.4	78.6	75.3
15	37.7	37.5	39.5	78.6	37.6
16	82.9	82.7	83.8	90.1	82.4
17	61.6	61.6	60.1	59.3	61.7
18	79.4	79.1	71.9	71.6	75.7
19	53.2	52.7	48.5	48.6	164.0
N—CH_2	49.3	49.0	45.5	43.8	—
CH_3	13.3	13.1	12.1	12.0	—
1-OCH_3	56.0	55.1	55.9	56.0	56.0
6-OCH_3	—	—	58.8	58.4	—
16-OCH_3	56.4	55.8	58.4	60.9	56.4
18-OCH_3	59.4	59.1	58.8	58.7	59.4
4′-OCH_3	—	56.2	55.4	—	—
C=O	171.3	171.1	169.7	172.2	170.7
|					
CH_3	21.3	21.1	21.5	21.2	21.2
C=O	164.8	164.3	166.1	166.0	—
	131.6	123.8	122.7	129.7	—
	129.4	131.1	131.7	129.5	—
	128.3	113.2	113.8	128.5	—
	132.9	162.9	163.6	133.2	—
	128.3	113.2	113.8	128.5	—
OMe	129.4	131.1	131.7	129.5	—
C=O					171.8
|					
CH_2					34.7
|					
$(CH_2)_{13}$					23.6–32.0
|					
CH_3					14.0

Carbon multiplicities were determined by DEPT pulse sequence.

at δ 4.81 (1H, *t*, $J = 5$ Hz), attributable to a proton attached to C-14. Because transconitine A (**1**) revealed a 3H singlet at δ 1.76 and a 1H triplet at δ 4.81, it is probably due to an acetate group at C-14. The key point for structural elucidation of **1** was determination of the location of two ester groups. Comparison of the ^1H NMR data of **1** with those of dolichotine (**14**) [5], showed the same chemical shifts of the C-14 proton and methyl protons of the acetyl group suggesting that **1** was 8-benzoyl-14-acetyltalatisamine. Treatment of **7** with acetic anhydride in pyridine gave 14-acetyltalatisamine (**12**) in 90% yield, which on treatment with benzoyl chloride at 30–35° gave transconitine A (**1**).

The ^1H NMR spectrum of transconitine B (**2**), $C_{35}H_{49}NO_{12}$, showed the presence of an ethyl group (3H, *t*, $J = 7$ Hz) at δ 1.15, four aliphatic methoxyls (each 3H, *s*, 3.19, 3.27, 3.30 and 3.50) and an aromatic methoxyl at δ 3.84. The signal at δ 1.34 (3H, *s*) was due to an acetate group. The spectrum also showed a signal at δ 4.85 (1H, *d*, $J = 5$ Hz) attributable to a proton attached to C-14 carrying an aromatic ester group. The NMR spectrum of **2** (^{13}C NMR data see Table 1) showed that its structure was very similar to

that of yunaconitine (**4**). The NMR and mass spectral data of **2** indicated that it had an additional hydroxyl group when compared with **4**. The absence of the peak of M^+-49 ion (M^+-31-18) in the mass spectrum of **2** showed that **2** and **4** differed in the substitution of ring-A [6]. Comparison of the ^{13}C NMR data of ring-A between transconitine B and altaconitine (**15**) [6] indicated that the additional hydroxyl group was located at the C-2β position. Thus, the structure of **2** was elucidated as 2-hydroxyyunaconitine.

The ^1H and ^{13}C NMR spectra of transconitine C (**3**), $C_{40}H_{65}NO_7$, showed that it lacked an *N*-ethyl group but had a long-chain fatty ester group, δ_H 0.83 (3H, *t*, J = 7 Hz), 1.14–1.42 (26H, *br s*) and δ_C 14.0 *q*, 34.7 *t*, 23.6–32.0 *t*, 171.8 *s*, three methoxy groups, δ_H 3.15, 3.30 and 3.32 (3H each, *s*) and δ_C 56.0, 56.4 and 59.4 *q*, and an acetate group, δ_H 2.00 (3H, *s*), δ_C 21.2 *q* and 170.7 *s* (IR ν_{max} 1720 and 1240 cm^{-1}). The ^1H NMR spectrum showed a signal at 4.77 (1H, *t*, J = 5 Hz) attributable to a proton attached to a C-14 and a signal at 7.12 (1H, *d*, J = 1 Hz) attributable to 19-H. The ^{13}C NMR (Table 1) spectrum contained only three singlets at δ_C 48.0 (C-4), 49.3 (C-11) and 84.7 (C-8), suggesting that transconitine C was an aconitine-type norditerpenoid alkaloid possessing a tertiary long-chain fatty acid ester group or an acetate group at C-8 [2, 3]. The absence of N-Et and the presence of a N=CH moiety in **3** indicated that it was an imine alkaloid, like bulleyanitine A [7]. The mass spectrum exhibited a fragment at *m/z* 256 corresponding to palmitic acid. According to mass spectral fragmentation pattern of norditerpenoid alkaloids substituted with an ester group, the loss of the C-8 ester takes precedence over loss of a C-1 methoxyl group when a large ester group is attached at C-8. However, regardless of whether the C-8 ester or the C-1 OMe group is lost first, the intense characteristic peak always corresponds to a fragment ion which has lost the C-1 OMe [5]. The mass spectrum of transconitine C exhibited an intense peak at *m/z* 384 [M-$C_{15}H_{31}COOH$-OMe]$^+$ (45%) showing an α-methoxyl group at C-1, and another ion at *m/z* 416 [M-$C_{15}H_{31}COO$]$^+$ (40%), indicating that the alkaloid possessed a palmityl group at C-8. The structure of transconitine C was thus shown to be **3**.

EXPERIMENTAL

General. Mps: uncorr. IR: $CHCl_3$ and KBr. EIMS 70 ev. NMR spectra were measured with a Bruker AM400 in $CDCl_3$, using TMS as int. standard. DEPT expts were carried out with standard pulse sequences. Silica gel H (100–200, mesh) was used for CC and silica gel G was employed for TLC. Visualization was made using Dragendorff's reagent.

Plant material. Aconitum transsectum Diels was collected in the mountain of Yulong of Lijang district in Yunnan. It was authenticated by Prof. Qin-er Yang (Beijing Institute of Botany, Academia Sinica, Beijing, China) and a voucher specimen is deposited in the Kunming Institute of Botany.

Extraction and isolation. Air-dried ground roots (5 kg) were extracted with 90% EtOH at room temp. during 5 days. The EtOH extract was treated with 5% HCl and filtered. The acid soln was basified with NH_4OH to pH 11 and extracted with $CHCl_3$ to give crude alkaloid (100 g). CC of this fr. on silica using gradient elution with the petrol–Me_2CO–diethylamine (::to::), followed by further CC when necessary, allowed the isolation, in order of increasing polarity, of transconitine A (**1**) (15 mg, 0.0150%), transconitine B (**2**) (16 mg, 0.0160%), transconitine C (**3**) (21 mg, 0.0210%), yunaconitine (**4**) [8] mp 142–144° (4.2 g, 4.2%), crassicauline A (**5**) [9, 10] mp 166–168° (4.5 g, 4.5%), foresaconitine (**6**) [12] mp 158–160° (60 mg, 0.0600%), talatisamine (**7**) [13, 14] mp 141–143° (1.2 g, 1.2%), 8-deacetylyunaconitine (**8**) [15] mp 101–105° (45 mg, 0.0450%), geniconitine (**9**) [16] mp 235–237° (17 mg, 0.0170%), indaconitine (**10**) [18] mp 166–168° (52 mg, 0.0520%), forestine (**11**) [14] (45 mg, 0.0450%), 14-acetyltalatisamine (**12**) [19, 20] (63 mg, 0.0630%) and chasmanine (**13**) [10, 21] mp 82–84° (78 mg, 0.0780%). Known alkaloids were identified by comparison with authentic samples (TLC, mp, IR, MS, ^1H and ^{13}C NMR).

Transconitine A (**1**). Amorphous, $[\alpha]_D^{20}$ +16.9° ($CHCl_3$; *c* 0.016). $[M]^+$ *m/z* 567.3144 for $C_{33}H_{45}NO_7$ (calc. 567.3196). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1725, 1700, 1620, 1240. ^1H NMR (400 MHz): δ 1.09 (3H, *t*, J = 7 Hz, N-CH_2CH_3), 1.76 (3H, *s*, $OCOCH_3$), 3.21, 3.24 and 3.29 (3H each, *s*, 3 × OMe), 4.81 (1H, *t*, J = 5 Hz, H-14β), 7.36 (2H, *t*, J = 8 Hz, Ar-2H), 7.49 (1H, *t*, J = 8 Hz, Ar-H) and 7.93 (2H, *d*, J = 8 Hz, Ar-2H). EIMS *m/z* (rel. int.): 567 (9) $[M]^+$, 552 (50), 536 (100), 522 (5), 462 (15), 445 (51), 414 (67), 386 (43), 354 (21), 252 (12), 122 (45), 105 (69), 77 (56). For ^{13}C NMR see Table 1.

Transconitine B (**2**). Amorphous $[\alpha]_D^{20}$ +12.3° ($CHCl_3$; *c* 0.021). $[M]^+$ *m/z* 675.3258 for $C_{35}H_{49}NO_{12}$ (calc. 675.3255). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500, 1715, 1700, 1640, 1600, 1250. ^1H NMR (400 MHz): δ 1.15 (3H, *t*, J = 7 Hz, N-CH_2CH_3), 1.34 (3H, *s*, $OCOCH_3$), 3.19, 3.27, 3.30, 3.50 and 3.84 (3H each, *s*, 5 × OMe), 4.85 (1H, *d*, J = 5 Hz, H-14β), 4.08 (1H, *d*, J = 5 Hz, H-6β), 6.88, 7.93 (2H each, *dd*, $J_1 = J_2$ = 9 Hz, 4 × Ar-H). EIMS *m/z* (rel. int.): 675 (61) $[M]^+$, 660 (39), 644 (54), 616 (70), 584 (32), 421 (30), 284 (20), 152 (33), 135 (100), 77 (30). For ^{13}C NMR see Table 1.

Transconitine C (**3**). Amorphous $[\alpha]_D^{20}$ +40.0° ($CHCl_3$; *c* 0.018). $[M]^+$ *m/z* 671.4767 for $C_{40}H_{65}NO_7$ (calc. 671.4761). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2910, 1720, 1625, 1240. ^1H NMR (400 MHz): δ 0.83 (3H, *t*, J = 7 Hz, $CO(CH_2)_{14}CH_3$), 1.14–1.42 (26H, *br s*, $CO(CH_2)_{13}CH_3$), 2.00 (3H, *s*, $OCOCH_3$), 3.15, 3.30 and 3.32 (3H each, *s*, 3 × OMe), 4.77 (1H, *t*, J = 5 Hz, H-14β), 7.12 (1H, *d*, J = 1 Hz, H-19). EIMS *m/z* (rel. int.): 671 (66) $[M]^+$, 656 (13), 640 (24), 432 (5), 416 (40), 384 (45), 256 (20). For ^{13}C NMR see Table 1.

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