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# NORDITERPENOID ALKALOIDS FROM *ACONITUM TRANSSECTUM*

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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.
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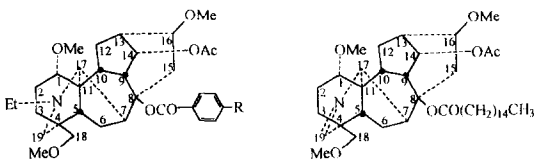
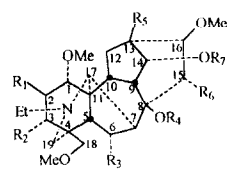
## INTRODUCTION

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**).




| | $R_1$ | $R_2$ | $R_3$ | $R_4$ | $R_5$ | $R_6$ | $R_7$ |
|---|---|---|---|---|---|---|---|
| (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 |

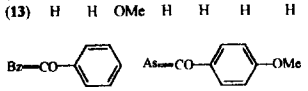



Fig. 1. The chemical structure of compounds **1–15**.

## 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 $\delta_H$ 1.09 (3H, *t*, $J$ = 7 Hz), $\delta_C$ 49.3 *t* and 13.3 *q* for an *N*-ethyl group, $\delta_H$ 3.21, 3.24 and 3.29 (3H each, *s*), $\delta_C$ 56.0 *q*, 56.4 *q* and 59.4 *q* for three methoxy groups, $\delta_H$ 1.76 (3H, *s*), $\delta_C$ 21.3 *q* and 171.3 *s* of an acetate group. (IR $\nu_{max}$ 1725 and 1240 $cm^{-1}$), and $\delta_H$ 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 $\delta_C$ 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

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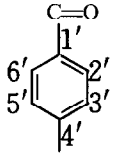
Table 1. $^{13}C$ NMR spectral data of compounds **1**, **2**, **3**, **14** and **15** (in $CDCl_3$, 400 MHz, TMS)

| 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 $\delta$ 4.81 (1H, *t*, $J = 5$ Hz), attributable to a proton attached to C-14. Because transconitine A (**1**) revealed a 3H singlet at $\delta$ 1.76 and a 1H triplet at $\delta$ 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 $\delta$ 1.15, four aliphatic methoxyls (each 3H, *s*, 3.19, 3.27, 3.30 and 3.50) and an aromatic methoxyl at $\delta$ 3.84. The signal at $\delta$ 1.34 (3H, *s*) was due to an acetate group. The spectrum also showed a signal at $\delta$ 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-2$\beta$ 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, $\delta_H$ 0.83 (3H, *t*, $J$ = 7 Hz), 1.14–1.42 (26H, *br s*) and $\delta_C$ 14.0 *q*, 34.7 *t*, 23.6–32.0 *t*, 171.8 *s*, three methoxy groups, $\delta_H$ 3.15, 3.30 and 3.32 (3H each, *s*) and $\delta_C$ 56.0, 56.4 and 59.4 *q*, and an acetate group, $\delta_H$ 2.00 (3H, *s*), $\delta_C$ 21.2 *q* and 170.7 *s* (IR $\nu_{max}$ 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 $\delta_C$ 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 $\alpha$-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): $\delta$ 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-14$\beta$), 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): $\delta$ 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-14$\beta$), 4.08 (1H, *d*, $J$ = 5 Hz, H-6$\beta$), 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): $\delta$ 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-14$\beta$), 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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