# Four New Nor-Diterpenoid Alkaloids from Aconitum brachypodum 

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#### Abstract

Four new $\mathrm{C}_{19}$-nor-diterpenoid alkaloids, named brachyaconitines $\mathrm{A}-\mathrm{D}(\mathbf{1}-\mathbf{4})$, were isolated from the roots of Aconitum brachypodum Diels. Their structures were elucidated as 3-O-acetyl-20-deethyl-20-formylaconitine (1), 3-O-acetyl-19,20-didehydro-20-deethylaconitine (2), 3-O-acetyl-8-de(acety-loxy)-7,8,17,20-tetradehydro-20-deethyl-7,17-secoaconitine (3), and 1-O-methylflavaconitine (4) by means of MS, IR, 1D- and 2D-NMR analyses. The structure of compound $\mathbf{1}$ was confirmed by an Xray diffraction experiment.


Introduction. - Aconitum brachypodum Diels., a commonly used folk-medicinal herb, is mainly distributed in Yunnan and Sichuan Provinces of China [1]. Its dried roots, 'Xue-Shang-Yi-Zhi-Hao' in the Chinese Pharmacopoeia [2], is widely used in traditional Chinese medicine for the treatment of rheumatism and pains [3]. As part of our ongoing phytochemical investigation on A. brachypodum, four new diterpenoid alkaloids, named brachyaconitines A-D (1-4; Fig. 1), were isolated from the


1


3



4

Fig. 1. Compounds $\mathbf{1 - 4}$, isolated from Aconitum brachypodum Diels.
$95 \% \mathrm{EtOH}$ extract of its roots, together with the five known compounds bullatine A [4], aconitine $=(1 \alpha, 3 \alpha, 6 \alpha, 14 \alpha, 15 \alpha, 16 \beta)$-20-ethyl-1,6,16-trimethoxy-4-(methoxymethyl)-aconitane-3,8,13,14,15-pentol 8-acetate 14-benzoate [5], neoline [6], hypaconitine [7], and songorine [8]. All of the isolated compounds showed a positive reaction with Dragendorff's reagent. This article describes the isolation and structural elucidation of the four new compounds.

Results and Discussion. - Compound 1 was obtained as colorless prisms from pyridine. Its HR-ESI-MS exhibited a quasi-molecular-ion peak at $m / z 710.2771$ ( $[M+$ $\mathrm{Na}]^{+}$), corresponding to the molecular formula $\mathrm{C}_{35} \mathrm{H}_{45} \mathrm{NO}_{13}$ with 14 degrees of unsaturation. The IR spectrum showed the absorption bands for $\mathrm{OH}\left(3500 \mathrm{~cm}^{-1}\right)$, conjugated-ester $\mathrm{C}=\mathrm{O}\left(1721 \mathrm{~cm}^{-1}\right)$, amide $\mathrm{C}=\mathrm{O}\left(1664 \mathrm{~cm}^{-1}\right)$, and aromatic-ring functions (1602 and $1451 \mathrm{~cm}^{-1}$ ). In the ${ }^{1} \mathrm{H}$-NMR spectrum (Table 1), four MeO groups

Table 1. ${ }^{1} H$-NMR Data $\left(\mathrm{CDCl}_{3}\right)$ of Compounds 1-4. $\delta$ in $\mathrm{ppm}, J$ in Hz .

|  | 1 ${ }^{\text {a }}$ ) | $2^{\text {a }}$ ) | $3^{\text {a }}$ ) | 4 ${ }^{\text {b }}$ ) |
| :---: | :---: | :---: | :---: | :---: |
| CH(1) | 3.14-3.18 ${ }^{\text {c }}$ ) | $3.20-3.25^{\text {c }}$ ) | $3.22-3.27^{\text {c }}$ ) | $4.01(d, J=6.2)$ |
| $\mathrm{CH}_{2}(2)$ | $\begin{aligned} & 1.37(d d, J=12.7,10.4), \\ & 2.47-2.52(m) \end{aligned}$ | $\begin{aligned} & 1.73-1.79(\mathrm{~m}) \\ & 2.00-2.06(\mathrm{~m}) \end{aligned}$ | $\begin{aligned} & 1.14(d d, J=12.1,12.1) \\ & 2.29-2.32(m) \end{aligned}$ | $\begin{aligned} & \left.1.36-1.43^{\mathrm{c}}\right), \\ & 1.91-1.94(\mathrm{~m}) \end{aligned}$ |
| $\begin{aligned} & \mathrm{CH}(3) \text { or } \\ & \mathrm{CH}_{2}(3) \end{aligned}$ | $4.41(d d, J=13.0,5.4)$ | $5.12(d, J=6.3)$ | $4.92(d d, J=15.3,8.7)$ | $\begin{aligned} & \left.1.36-1.43^{\mathrm{c}}\right), \\ & 1.77-1.80(\mathrm{~m}) \end{aligned}$ |
| $\mathrm{CH}(5)$ | $2.51(d, J=6.8)$ | $2.31(d, J=6.9)$ | 2.21-2.28 ${ }^{\text {c }}$ ) | $2.55(d, J=6.5)$ |
| CH(6) | 4.16 ( $d, J=7.0$ ) | 3.99 ( $d, J=7.1$ ) | $4.52(d d, J=10.6,7.7)$ | 4.52 ( $d, J=5.2$ ) |
| CH(7) | 2.68 (br. s) | 2.90 (br. $s$ ) | 5.66 ( $d, J=5.6$ ) | 2.80 (br. s) |
| CH(9) | 2.85 ( dd, $J=6.7,5.8)$ | $2.72(t, J=4.8)$ | 2.31-2.35 ${ }^{\text {c }}$ ) | 2.75 ( $d, J=5.0$ ) |
| CH(10) | 2.17 ( $d d, J=6.9,5.9$ ) | 2.15-2.19 ${ }^{\text {c }}$ ) | 2.45-2.52 ${ }^{\text {c }}$ ) | - |
| $\mathrm{CH}_{2}(12)$ | $\begin{aligned} & 2.05-2.31(\mathrm{~m}), \\ & 2.94(d d, J=11.6,5.2) \end{aligned}$ | $\begin{aligned} & 2.15-2.19(\mathrm{~m}), \\ & 2.35-2.39(\mathrm{~m}) \end{aligned}$ | $2.45-2.52^{\text {c }}$ ) | $\begin{aligned} & 2.17 \text { (br. } s \text { ), } \\ & 2.51 \text { (br. } s \text { ) } \end{aligned}$ |
| CH(14) | $4.87(d, J=5.0)$ | $4.89(t, J=4.7)$ | $5.10(t, J=4.1)$ | $5.39(d, J=5.1)$ |
| CH(15) | 4.47 ( $d, J=5.1)$ | 4.48 ( $d, J=4.3$ ) | 4.86 ( $d, J=4.3$ ) | 3.70 (br. s) |
| CH(16) | $3.32(d, J=5.1)$ | $3.40-3.46{ }^{\text {c }}$ ) | $3.27-3.33{ }^{\text {c }}$ ) | 3.37 ( $d, J=5.2$ ) |
| CH(17) | 4.03 (br. s) | 4.17 (br. s) | 7.85 (br.s) | 2.88 (br. s) |
| $\mathrm{CH}_{2}(18)$ | $\begin{aligned} & 3.08(d, J=8.9), \\ & 3.94(d, J=8.9) \end{aligned}$ | $\begin{aligned} & \left.3.40-3.46^{c}\right) \\ & 4.05(d, J=8.5) \end{aligned}$ | $\begin{aligned} & 2.98(d, J=8.8) \\ & 4.02(d, J=8.8) \end{aligned}$ | $\begin{aligned} & 3.01(d, J=8.3), \\ & 3.58(d, J=8.4) \end{aligned}$ |
| $\mathrm{CH}_{2}$ (19) or CH(19) | $\begin{aligned} & 2.94(d d, J=13.9,5.4), \\ & 4.02(d, J=13.2) \end{aligned}$ | 7.37 (br. $s$ ) | $\begin{aligned} & \left.2.31-2.35^{\mathrm{c}}\right) \\ & \left.2.77-2.83^{\mathrm{c}}\right) \end{aligned}$ | $\begin{aligned} & \left.2.16-2.20^{c}\right), \\ & \left.3.22-3.27^{c}\right) \end{aligned}$ |
| $\mathrm{N}-\mathrm{CHO}$ | 8.10 (br. s) | - | - | - |
| $\mathrm{MeO}-\mathrm{C}(1)$ | 3.14 (s) | 3.06 (s) | 3.21 (s) | 3.14 (s) |
| $\mathrm{MeO}-\mathrm{C}(6)$ | 3.19 (s) | 3.18 (s) | 3.22 (s) | 3.26 (s) |
| $\mathrm{MeO}-\mathrm{C}(16)$ | 3.20 (s) | 3.25 (s) | 3.24 (s) | 3.29 (s) |
| $\mathrm{MeO}-\mathrm{C}(18)$ | 3.75 (s) | 3.75 (s) | 3.76 (s) | 3.76 (s) |
| $\mathrm{AcO}-\mathrm{C}(3)$ | 2.03 (s) | 2.06 (s) | 2.07 (s) | - |
| $\mathrm{AcO}-\mathrm{C}(8)$ | 1.32 (s) | 1.33 (s) | - | 1.39 (s) |
| $\mathrm{CH}\left(2^{\prime}, 6^{\prime}\right)$ | $8.01(d, J=7.6)$ | 8.01 ( $d, J=7.6$ ) | $8.05(d, J=7.2)$ | 8.01 ( $d, J=7.2$ ) |
| CH( $3^{\prime}, 5^{\prime}$ ) | 7.45 ( $d d, J=7.6$ ) | 7.44 ( $d d, J=7.5$ ) | 7.45 ( $d d, J=7.2$ ) | 7.45 ( $d d, J=7.3$ ) |
| CH(4') | $7.57(t, J=7.6)$ | $7.57(t, J=7.5)$ | $7.57(t, J=7.3)$ | $7.57(t, J=7.3)$ |

$\left.{ }^{\text {a }}\right) 500 \mathrm{MHz} .{ }^{\mathrm{b}}$ ) $400 \mathrm{MHz} .{ }^{\text {c }}$ ) Overlapped.
$(\delta(\mathrm{H}) 3.14,3.19,3.20$, and $3.75(4 s))$ were observed together with two AcO groups $(\delta(\mathrm{H}) 1.32$ and $2.03(2 s))$, and a Bz unit $(\delta(\mathrm{H}) 7.45(d d, J=7.6,2 \mathrm{H}), 7.57(t, J=7.6$, 1 H ), and $8.01(d, J=7.6,2 \mathrm{H})$ ). Its ${ }^{13} \mathrm{C}$-NMR (DEPT) spectrum (Table 2) displayed 35 C -atom signals including $6 \mathrm{Me}, 4 \mathrm{CH}_{2}$, and 17 CH groups, and 8 quaternary C -atoms, suggesting that compound $\mathbf{1}$ might be an aconitine-type $\mathrm{C}_{19}$-nor-diterpenoid alkaloid, bearing the following groups: one $\mathrm{C}_{19} \mathrm{H}_{19}$, two OH , four MeO , two AcO , one BzO , and one NCHO. Careful analyses of the ${ }^{1} \mathrm{H}$ - and ${ }^{13} \mathrm{C}$-NMR data suggested that the structure of compound $\mathbf{1}$ was similar to that of 3-O-acetylaconitine [9]. The main difference between the two compounds is that compound $\mathbf{1}$ contains an $N$-formyl unit instead of a N -ethyl group in 3-O-acetylaconitine. The long-range HMBCs (Fig. 2) between the formyl H-atom $(\delta(\mathrm{H}) 8.10$ (br. $s)$ ) and $\mathrm{C}(17)$ and $\mathrm{C}(19)$ confirmed the location of the additional formyl group. Compound $\mathbf{1}$ was presumed to possess a similar relative

Table 2. ${ }^{13} \mathrm{C}$-NMR Data $\left(\mathrm{CDCl}_{3}\right)$ of Compounds $\mathbf{1}-\mathbf{4}$. $\delta$ in ppm .

|  | $1^{\text {a }}$ ) | 2 ${ }^{\text {a }}$ ) | $3^{\text {a }}$ ) | $4^{\text {b }}$ ) |
| :---: | :---: | :---: | :---: | :---: |
| C(1) | 78.9 (d) | 80.3 (d) | 79.7 (d) | 82.9 (d) |
| C(2) | 30.8 (t) | 30.0 (t) | 29.9 (t) | 23.9 (t) |
| C(3) | 70.5 (d) | 72.9 (d) | 71.7 (d) | 28.9 (t) |
| C(4) | 41.1 (s) | 49.7 (s) | 47.3 (s) | 38.7 (s) |
| C(5) | 46.5 (d) | 44.3 (d) | 42.6 (d) | 39.6 (d) |
| C(6) | 82.9 (d) | 83.8 (d) | 86.4 (d) | 79.8 (d) |
| C(7) | 51.0 (d) | 50.2 (d) | 131.2 (d) | 48.5 (d) |
| C(8) | 90.1 (s) | 90.1 (s) | 137.1 (s) | 89.5 (s) |
| C(9) | 43.0 (d) | 42.4 (d) | 41.3 (d) | 52.7 (d) |
| C(10) | 40.3 (d) | 40.4 (d) | 41.5 (d) | 78.9 (s) |
| C(11) | 48.5 (s) | 49.5 (s) | 42.2 (s) | 55.0 (s) |
| C(12) | 34.0 ( $t$ ) | 35.5 ( $t$ ) | 38.5 ( $t$ ) | 46.1 ( $t$ ) |
| C(13) | 74.1 (s) | 74.0 (s) | 75.3 (s) | 74.7 ( $s$ ) |
| C(14) | 78.3 (d) | 78.8 (d) | 79.2 (d) | 78.3 (d) |
| C(15) | 78.7 (d) | 78.5 (d) | 73.8 (d) | 78.8 (d) |
| C(16) | 89.9 (d) | 89.6 (d) | 92.2 (d) | 88.9 (d) |
| C(17) | 57.7 (d) | 60.7 (d) | 165.0 (d) | 57.3 (d) |
| C(18) | 71.2 (t) | 72.4 (t) | 71.9 ( $t$ ) | 80.0 ( $t$ ) |
| C(19) | 39.2 (t) | 163.0 (d) | 52.1 (t) | 49.7 ( $t$ ) |
| $\mathrm{N}-\mathrm{CHO}$ | 163.1 (d) | - | - | - |
| $\mathrm{MeO}-\mathrm{C}(1)$ | 55.7 (q) | 55.8 (q) | 57.0 (q) | 55.4 (q) |
| $\mathrm{MeO}-\mathrm{C}(6)$ | 57.8 (q) | 57.4 (q) | 58.2 (q) | 58.0 (q) |
| $\mathrm{Me} \mathrm{O}-\mathrm{C}(16)$ | 61.0 (q) | 61.0 (q) | 61.6 (q) | 61.2 (q) |
| $\mathrm{MeO}-\mathrm{C}(18)$ | 58.9 (q) | 58.9 (q) | 58.7 (q) | 59.1 (q) |
| $A c \mathrm{O}-\mathrm{C}(3)$ | 170.1 (s), 21.0 (q) | 170.4 (s), 21.0 (q) | 170.1 (s), 21.2 (q) | - |
| $A c \mathrm{O}-\mathrm{C}(8)$ | 172.2 (s), 21.2 (q) | 172.0 (s), 21.2 (q) | - | 172.0 (s), 21.2 (q) |
| COO-C(14) | 165.9 (s) | 165.9 (s) | 166.1 (s) | 166.1 ( $s$ ) |
| $\mathrm{C}\left(1^{\prime}\right)$ | 129.6 (s) | 129.5 (s) | 129.7 (s) | 129.5 (s) |
| $\mathrm{C}\left(2^{\prime}, 6^{\prime}\right)$ | 129.6 (d) | 129.5 (d) | 129.9 (d) | 129.6 (d) |
| $\mathrm{C}\left(3^{\prime}, 5^{\prime}\right)$ | 128.7 (d) | 128.6 (d) | 128.5 (d) | 128.7 (d) |
| $\mathrm{C}\left(4^{\prime}\right)$ | 133.4 (d) | 133.3 (d) | 133.3 (d) | 133.4 (d) |

$\left.\left.{ }^{\text {a }}\right) 125 \mathrm{MHz} .{ }^{\text {b }}\right) 100 \mathrm{MHz}$.


1


3


2


4

Fig. 2. Selected ${ }^{1} \mathrm{H},{ }^{1} \mathrm{H}$-COSYs $(-)$ and $\mathrm{HMBCs}(\mathrm{H} \rightarrow \mathrm{C})$ of compounds $\mathbf{1}-\mathbf{4}$
configuration as 3-O-acetylaconitine, based on their almost identical ${ }^{1} \mathrm{H}$ - and ${ }^{13} \mathrm{C}-\mathrm{NMR}$ data (Tables 1 and 2) and the ROESY correlations (Fig. 3). The structure and relative configuration of $\mathbf{1}$ was confirmed by an X-ray crystallographic analysis (Fig. 4), and thus compound $\mathbf{1}$ was characterized as 3 - $O$-acetyl-20-deethyl-20-formylaconitine (1).


Fig. 3. Selected ROESY correlations of compound $\mathbf{1}$

Compound 2 was isolated as colorless prisms and assigned the molecular formula $\mathrm{C}_{34} \mathrm{H}_{43} \mathrm{NO}_{12}$ by analyses of the ESI-MS $\left(\mathrm{m} / \mathrm{z} 658\left([M+\mathrm{H}]^{+}\right)\right)$and HR-ESI-MS $(\mathrm{m} / \mathrm{z}$ $\left.658.2846\left([M+\mathrm{H}]^{+}\right)\right)$. The NMR data of $2($ Tables 1 and 2$)$ were essentially identical with those of compound $\mathbf{1}$, suggesting that 2 was also an aconitine-type $\mathrm{C}_{19}$-norditerpenoid alkaloid. Compound $\mathbf{2}$ differed from $\mathbf{1}$ mainly at $\mathrm{C}(19)$ where a $\mathrm{N}=\mathrm{CH}(19)$ moiety was deduced by comparing the NMR data with those of 20-demethyl-19,20didehydrodelphinine [10]. The presence of a double bond between the N -atom and


Fig. 4. X-Ray crystal structure of compound 1. Arbitrary atom numbering.
$\mathrm{C}(19)$ was verified by the HMBCs (Fig. 2) between the olefinic H-C(19) ( $\delta(\mathrm{H}) 7.37$ (br.s)) and $\mathrm{C}(3), \mathrm{C}(4), \mathrm{C}(5), \mathrm{C}(17)$, and $\mathrm{C}(18)$. Consequently, brachyaconitine B (2) was defined as 3 - $O$-acetyl-19,29-didehydro-20-deethylaconitine (2).

Compound $\mathbf{3}$ was obtained as a white powder. The molecular formula $\mathrm{C}_{32} \mathrm{H}_{41} \mathrm{NO}_{10}$ was deduced by ESI-MS $\left(\mathrm{m} / \mathrm{z} 600\left([M+\mathrm{H}]^{+}\right)\right)$and HR-ESI-MS $(\mathrm{m} / \mathrm{z} 600.2786([M+$ $\left.\mathrm{H}]^{+}\right)$). Comparison of its 1D-NMR spectra (Tables 1 and 2) with those of secokaraconitine [11] showed high similarity (karaconitine $=(1 \alpha, 2 \alpha, 6 \alpha, 14 \alpha, 15 \alpha, 16 \beta)$-20-ethyl-1,6,16-trimethoxy-4-(methoxymethyl)aconitane-2,8,13,14,15-pentol 8-acetate 14-benzoate), except that there was an additional AcO group in compound $3(\delta(H) 2.07(s$, $3 \mathrm{H}) ; \delta(\mathrm{C}) 170.1(s)$ and $21.2(q))$. The AcO group was determined to be linked at $\mathrm{C}(3)$ by the HMBCs between $\delta(\mathrm{H}) 4.92(d d, J=15.3,8.7, \mathrm{H}-\mathrm{C}(3))$ and $\delta(\mathrm{C}) 170.1(\mathrm{AcO}$, $\mathrm{C}=\mathrm{O})$ ), $\mathrm{C}(2), \mathrm{C}(4), \mathrm{C}(5)$, and $\mathrm{C}(19)$. The full NMR data assignments of compound $\mathbf{3}$ were performed with the aid of the ${ }^{1} \mathrm{H},{ }^{1} \mathrm{H}$-COSY, HSQC, and HMBC data. Consequently, the structure of compound 3, named 3-O-acetyl-8-de(acetyloxy)-7,8,17,20-tetradehydro-20-deethyl-7,17-secoaconitine (3), was elucidated as shown in Fig. 1.

Compound 4 had the molecular formula $\mathrm{C}_{32} \mathrm{H}_{43} \mathrm{NO}_{11}$ as derived from ESI-MS $(\mathrm{m} / \mathrm{z}$ $\left.618\left([M+\mathrm{H}]^{+}\right)\right)$, HR-ESI-MS $\left(m / z 618.2912\left([M+\mathrm{H}]^{+}\right)\right)$, and the ${ }^{13} \mathrm{C}$-NMR data (Table 2). Compound 4 had a MeO rather than a OH group at $\mathrm{C}(1)$ as deduced from the comparison of its 1D-NMR (Tables 1 and 2) and MS data with those of flavaconitine $\quad(=(1 \alpha, 6 \alpha, 14 \alpha, 15 \alpha, 16 \beta)-6,16$-dimethoxy-4-(methoxymethyl)aconitane-$1,8,10,13,14,15$-hexol 8 -acetate 14-benzoate) [6]. The position of this MeO group was established by the correlation of $\mathrm{MeO}-\mathrm{C}(1)$ to $\mathrm{C}(1)$ in the HMBC spectrum (Fig. 2). Hence, compound 4 was defined as 1- $O$-methylflavaconitine (4).

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## Experimental Part

General. Column chromatography (CC): silica gel $\left(\mathrm{SiO}_{2} ; 200-300\right.$ mesh, Qingdao Meigao Chemical Ltd., Qingdao, P. R. China); $\mathrm{Al}_{2} \mathrm{O}_{3}$ (Shanghai Wusi Chemical Reagents Company, Ltd.); Sephadex LH-20 (Pharmacia Fine Chemical Co., Ltd., Germany). M.p.: XRC-1 micro melting-point apparatus; uncorrected. Optical rotations: Horiba-SEPA-300 polarimeter. UV Spectra: Shimadzu-UV-2401A spectrophotometer; $\lambda_{\max }(\log \varepsilon)$ in nm . IR Spectra: Bio-Rad-FTS-135 spectrometer; $\tilde{v}$ in $\mathrm{cm}^{-1}$. 1D- and 2D-NMR Spectra: Bruker-AM-400 and -DRX-500 spectrometers; chemical shifts $\delta$ in ppm with reference to the solvent signals, $J$ in Hz. EI- and ESI-MS: VG-Autospec-3000 spectrometer at 70 eV ; in $m / z$ (rel. \%). HR-ESI-MS: API-Qstar-Pulsar-1 spectrometer; in $m / z$ (rel. \%).

Plant Material. The roots of Aconitum brachypodum Diels. were collected in Dongchuan of Yunnan Province, P. R. China, in November 2006, and authenticated by Prof. Dr. Li-Gong Lei from Kunming Institute of Botany. A voucher specimen (No. KIB 2006-11-03) had been deposited with the Group of Anti-virus and Natural Medicinal Chemistry, Kunming Institute of Botany, Chinese Academy of Sciences.

Extraction and Isolation. The roots of $A$. brachypodum ( 50 kg ) were powdered and extracted three times with $90 \% \mathrm{EtOH}$ under reflux for 2 h . After evaporation of the solvent, the crude extract was dissolved in $2 \%$ aq. HCl soln. (201) and then filtrated. The acidic soln. was basified to pH 9.0 with $25 \%$ $\mathrm{NH}_{3}$ soln. and extracted with $\mathrm{CHCl}_{3}$ and the org. phase concentrated to furnish a crude alkaloid extract $(520 \mathrm{~g})$. The extract was purified by $\mathrm{CC}\left(\mathrm{SiO}_{2}(5.2 \mathrm{~kg} ; 200-300\right.$ mesh $)$, petroleum ether/acetone $/ \mathrm{Et}_{2} \mathrm{NH}$ $15: 1: 1 \rightarrow 3: 1: 1)$ : Fractions $A-E . F r . B(45.1 \mathrm{~g})$ was subjected to $\mathrm{CC}\left(\mathrm{SiO}_{2}\right.$, petroleum ether/acetone/ $\left.\mathrm{Et}_{2} \mathrm{NH} 15: 1: 1\right)$, followed by $\mathrm{CC}\left(\mathrm{Al}_{2} \mathrm{O}_{3}\right.$, petroleum ether/acetone $\left.7: 1\right)$ and finally CC (Sephadex LH-20, $\left.\mathrm{CHCl}_{3} / \mathrm{MeOH} 1: 1\right)$ : bullatine $\mathrm{A}(15.3 \mathrm{~g})$, neoline $(1.2 \mathrm{~g})$, and songorine $(18.5 \mathrm{~g})$. Fr. C $(50.9 \mathrm{~g})$ was purified by $\mathrm{CC}\left(\mathrm{SiO}_{2}\right.$, petroleum ether/acetone/ $\left.\mathrm{Et}_{2} \mathrm{NH} 15: 3: 1\right)$ and further by $\mathrm{CC}\left(\mathrm{Al}_{2} \mathrm{O}_{3}\right.$, petroleum ether/acetone $5: 1): \mathbf{1}(80 \mathrm{mg}), \mathbf{2}(23 \mathrm{mg}), \mathbf{3}(33 \mathrm{mg}), \mathbf{4}(15 \mathrm{mg})$, aconitine $(0.5 \mathrm{~g})$, and hypaconitine ( 0.6 g ).

Brachyaconitine $A(=$ rel-( $1 \alpha, 3 \alpha, 6 \alpha, 14 \alpha, 15 \alpha, 16 \beta)-3,8$-Bis(acetyloxy)-14-(benzoyloxy)-13,15-dihy-droxy-1,6,16-trimethoxy-4-(methoxymethyl)aconitane-2D-carboxaldehyde; 1): Colorless prisms (pyridine). M.p. $232-233^{\circ} .[\alpha]_{\mathrm{D}}^{23.0}=-44.35(c=3.74, \mathrm{MeOH})$. UV (MeOH): $230(4.17)$. IR ( KBr ): 3500, 2937, 2825, 1721, 1664, 1602, 1451, 1440, 1279, 713. NMR: Tables 1 and 2. ESI-MS (pos.): 710 ([ $M+$ $\mathrm{Na}]^{+}$). HR-ESI-MS (pos.): $710.2771\left([M+\mathrm{Na}]^{+}, \mathrm{C}_{35} \mathrm{H}_{45} \mathrm{NNaO}_{13}^{+}\right.$; calc. 710.2789).

Brachyaconitine $B(=$ rel- $(1 \alpha, 3 \alpha, 6 \alpha, 14 \alpha, 15 \alpha, 16 \beta)-19,20$-Didehydro-1,6,16-trimethoxy-4-( methoxy-methyl)aconitane-3,8,13,14,15-pentol 3,8-Diacetate 14-Benzoate; 2): Colorless prisms (pyridine). M.p. $150-151^{\circ} .[\alpha]_{\mathrm{D}}^{23.7}=+69.50(c=0.94, \mathrm{MeOH}) . \mathrm{UV}(\mathrm{MeOH}): 230(4.15) . \mathrm{IR}(\mathrm{KBr}): 3500,2935,1723$, 1640, 1603, 1563, 1452, 1371, 1279, 1106, 712. NMR: Tables 1 and 2. ESI-MS (pos.): $658\left([M+H]^{+}\right)$. HR-ESI-MS (pos.): $658.2846\left([M+\mathrm{H}]^{+}, \mathrm{C}_{34} \mathrm{H}_{44} \mathrm{NO}_{12}^{+}\right.$; calc. 658.2864$)$.

Brachyaconitine $C$ (= rel- $(1 \alpha, 3 \alpha, 6 \alpha, 14 \alpha, 15 \alpha, 16 \beta)-7,8,17,20$-Tetradehydro-1,6,16-trimethoxy-4-(me-thoxymethyl)-7,17-secoaconitane-3,13,14,15-tetrol 3-Acetate 14-Benzoate; 3): White powder. M.p. 216$217^{\circ} .[\alpha]_{\mathrm{D}}^{23.7}=+11.49(c=0.24, \mathrm{MeOH}) . \mathrm{UV}(\mathrm{MeOH}): 230(4.19)$. IR (KBr): 3422, 2933, 1730, 1639, 1602, 1450, 1234, 1101, 719. NMR: Tables 1 and 2. EI-MS: $599\left(2, M^{+}\right), 568\left(21,[M-\mathrm{MeO}]^{+}\right), 540(37)$, 105 (100). HR-ESI-MS (pos.): $600.2786\left([M+\mathrm{H}]^{+}, \mathrm{C}_{32} \mathrm{H}_{42} \mathrm{NO}_{10}^{+}\right.$; calc. 600.2809).

Brachyaconitine $D$ (=rel-(1 $\alpha, 6 \alpha, 14 \alpha, 15 \alpha, 16 \beta)-1,6,16$-Trimethoxy-4-(methoxymethyl)aconitane-8,10,13,14,15-pentol 8-Acetate 14-Benzoate; 4): Colorless prisms (MeOH). M.p. $165-166^{\circ} \cdot[\alpha]_{D}^{22.1}=$ $+23.81(c=0.80, \mathrm{MeOH}) . \mathrm{UV}(\mathrm{MeOH}): 230(4.15)$. IR (KBr): 3497, 2936, 1723, 1603, 1453, 1280, 1098, 716. NMR: Tables 1 and 2. ESI-MS (pos.): $618\left([M+H]^{+}\right)$. HR-ESI-MS (pos.): $618.2912([M+$ $\mathrm{H}]^{+}, \mathrm{C}_{32} \mathrm{H}_{44} \mathrm{NO}_{11}^{+}$; calc. 618.2914).

X-Ray Crystal Structure Data of Compound 1. A colorless prismatic crystal was obtained from pyridine. Crystal data: $\mathrm{C}_{35} \mathrm{H}_{45} \mathrm{NO}_{13}, M_{\mathrm{r}} 687.84$; triclinic, space group $P 1$; crystal dimensions: $0.20 \times 0.20 \times$
0.30 mm ; unit-cell dimensions: $a=8.854(18) \AA, b=11.159(2) \AA, c=11.544(2) \AA, \alpha=106.89(3)^{\circ}, \beta=$ $105.27(3)^{\circ}, \gamma=103.63(3)^{\circ}, V=990.8(3) \AA^{3} ; Z=1 ; D_{\mathrm{x}}=1.315 \mathrm{~g} / \mathrm{cm}^{3}$. Data were collected with a $M A C$ $D I P-2030 K$ diffractometer, a graphite monochromator ( $\omega$ scan, $2 \theta_{\max }=24.0^{\circ}$ ), and $\operatorname{Mo} K_{\alpha}$ radiation. The total number of independent reflections was 3847 , of which 3456 were observed $|F|^{2} \geq 2 \sigma|F|^{2}$. The structure was solved by a direct method, with SHELXS-97, expanded with difference Fourier techniques, and refined with NOMCSDP and full-matrix least-squares calculations. Final indices: $R_{1}=0.056$, $w R_{2}=0.145, S=1.327$. CCDC-741409 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/data_request/cif.

## REFERENCES

[1] 'Zhongyao Da Cidian (The Dictionary of Chinese Crude Drugs)', Ed. Jiangsu New Medical College, Shanghai Science and Technology Press, Shanghai, China, 1977, pp. 2089-2090.
[2] China Pharmacopoeia Committee, 'Pharmacopoeia of China', People’s Medical Publishing House, Beijing, China, 1977, p. 580.
[3] G. N. Li, 'Yunnan Zhiwu Zhi (Chinese Medicine Record of Yunnan)', Yunnan Science and Technology Press, Yunnan, China, 1990, pp. 472-473.
[4] L. S. Ding, E. F. Wu, Y. Z. Chen, Nat. Prod. Res. Dev. 1994, 6, 50.
[5] S. W. Pelletier, Z. Djarmati, J. Am. Chem. Soc. 1976, 98, 2626.
[6] S. Y. Chen, S. H. Li, X. J. Hao, Acta Bot. Sin. 1986, 28, 86.
[7] Y. G. Wang, Y. L. Zhu, R. H. Zhu, Acta Pharm. Sin. 1980, 15, 526.
[8] H. Hikino, Y. Kuroiwa, C. Konno, J. Nat. Prod. 1983, 46, 178.
[9] L. M. Liu, H. C. Wang, Y. L. Zhu, Acta Pharm. Sin. 1983, 18, 39.
[10] Y. Bai, H. K. Desai, S. W. Pelletier, J. Nat. Prod. 1994, 57, 963.
[11] M. N. Sultankhodzhaev, Atia-tul-Wahab, M. I. Choudhary, Atta-ur-Rahman, Chem. Nat. Compd. 2003, 39, 512.

