Novel Products from Oxidation of the Norditerpenoid Alkaloid Pseudaconine with HIO_4

Feng-Peng WANG,*[a] Qiao-Hong CHEN,[a] Zheng-Bang LI,[a] and Bo-Gang LI[b]

Department of Chemistry of Medicinal Natural Products, School of Pharmacy, West China University of Medical Sciences,[a] Chengdu 610041, People's Republic of China and Chengdu Institute of Biology, Chinese Academy of Sciences,[b] Chengdu 610041, People's Republic of China. Received October 20, 2000; accepted January 16, 2001

Oxidation of pseudaconine 8, a norditerpenoid alkaloid, with HIO_4 led to a series of novel interesting products, depending greatly on reaction medium and work-up conditions. Treatment of 8 in MeOH–H_2O (1 : 1) with $NaIO_4$ gave compounds 10 and 11, but compound 12 was obtained quantitatively when the final reaction solution was alkalized with conc. NH_4OH. The imine 12 was also obtained in 100% yield by treating 8 in 5% HCl solution with $NaIO_4$ followed by alkalizing the reaction products to pH>9 with conc. NH_4OH. When the work up pH was 7—8, only *N*,*O*-mixed acetal-ketal 13 was formed in 96% yield, which was converted quantitatively to 12 by further alkalizing. When the reaction mixture was alkalized to pH 7—8 with Na_2CO_3, a hemiacetalketal 14 was afforded quantitatively, which was converted to 15 in 87% yield by further treatment with Na_2CO_3 or 5% NaOH methanol. Compound 15 could be converted back to 14 by treatment with 10% HCl solution. Acetylation of the imine 12 gave the compounds 16 and 17 in 15% and 19% yields, respectively. All of the new compounds were isolated and fully characterized.

Key words norditerpenoid alkaloid; pseudaconine; 1,2-glycol oxidation

The important pharmacological activities and structural complexity of the norditerpenoid alkaloids have stimulated increased interest in phytochemistry and medicinal chemistry.[1)] Many efforts have been made to search for more active analogues.[1b,2—4)] In the course of these works, it has been observed that these diterpenoid alkaloids have a propensity to undergo complex reactions in the skeletal core.[1c—e)] We wish to report herein the novel products from oxidation of the norditerpenoid alkaloid pseudaconine with HIO_4 when we tried to modify the D-ring in its molecule.

Reference 1*c* summarized HIO_4 oxidations of the glycol system in the lycoctonine-type norditerpenoid alkaloids bearing the 7,8-dihydroxyl groups, but that of the 13,14-glycol system in the aconitine-type norditerpenoid alkaloids has been reported only by Wiesner *et al*.[5)] in their chemical elucidation of the structure of aconitine (Chart 1). Here, it is worthy of note that oxidation of **1** with HIO_4 only gave compound **3** instead of **2**, whereas under similar conditions an aldehyde-ketone **5** was obtained from compound **4**. Recently, we reported a novel rearrangement product **7** from oxidation of 8,9-glycol-containing lappaconitine **6** with HIO_4 (Chart 2).[6)]

Results and Discussion

To functionalize the C-12 position of the norditerpenoid alkaloids, pseudaconine **8** was chosen as starting material. Like the oxidation realized by Wiesner *et al*.,[5)] compound **8** in MeOH–H_2O was oxidazed by $NaIO_4$ at room temperature for 4 h. After direct extraction with $CHCl_3$ followed by a Chromatodron separadion (Si gel H, $CHCl_3$–MeOH system), two major products **10** (26% yield) and **11** (22% yield) appeared on the scene as methanolic adducts of the desired compound **9**. Both compounds **10** and **11** have the same molecular formula $C_{26}H_{43}NO_9$ (HR-FAB-MS). The ^{1}H- and ^{13}C-NMR spectra of **10** showed five aliphatic methoxyl groups (δ_H 3.25, 3.29, 3.30, 3.44, 3.49, each 3H, s; δ_C 55.2 q, 56.4 q, 57.4 q, 57.7 q, 59.1 q), a hemiketal (δ_C 97.3 s) and an acetal (δ_H 4.92, 1H, d, J=2.4 Hz; δ_C102.1 d). Its structure was de-

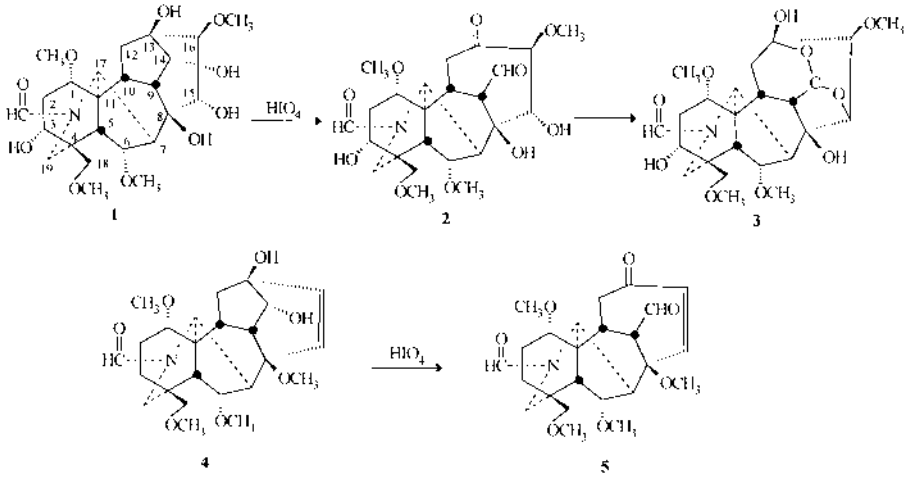

Chart 1

* To whom correspondence should be addressed. e-mail: wfp@wcums.edu.cn

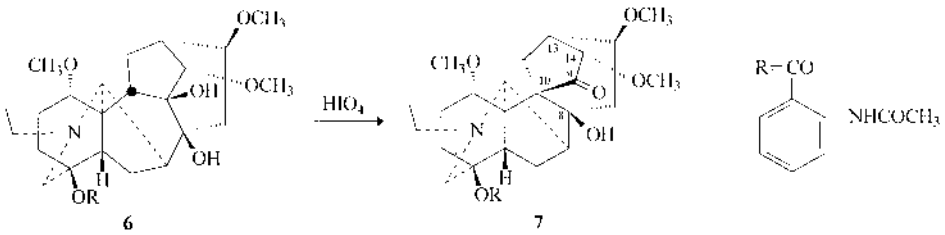

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Chart 2

Table 1. ^{13}C-NMR Data for **10**, **11**, **13** and **14**

Carbon	**10**	**11**	**13**	**14**
1	81.9 d	81.7 d	82.0 (81.9) d	82.1 (82.0) d
2	32.8 t	32.6 t	33.0 (32.8) t	33.1 (33.1) t
3	71.6 d	71.8 d	71.8 (71.7) d	71.8 (71.7) d
4	43.4 s	43.3 s	43.3 (43.3) s	43.4 (43.4) s
5	46.6 d	46.5 d	46.8 (46.6) d	46.9 (46.8) d
6	83.2 d	83.2 d	83.2 (83.0) d	83.2 (83.3) d
7	52.2 d	53.9 d	52.4 (53.6) d	53.1 (52.6) d
8	75.4 s	74.0 s	75.7 (73.8) s	73.7 (75.7) s
9	43.6 d	43.8 d	43.5 (44.0) d	44.1 (43.5) d
10	40.6 d	37.4 d	40.6 (36.9) d	40.7 (37.0) d
11	52.1 s	51.4 s	52.0 (51.3) s	51.4 (52.0) s
12	31.3 t	30.6 t	31.0 (30.8) t	31.1 (30.8) t
13	97.3 s	95.5 s	97.3 (95.8) s	97.3 (95.8) s
14	102.1 d	98.2 d	95.3 (91.5) d	95.3 (91.5) d
15	40.7 t	41.1 t	40.7 (40.8) t	40.9 (40.8) t
16	83.5 d	83.5 d	83.6 (83.5) d	83.7 (83.5) d
17	60.4 d	61.0 d	60.4 (60.7) d	60.4 (60.8) d
18	77.5 t	77.6 t	77.5 (77.5) t	77.5 (77.5) t
19	48.2 t	48.2 t	48.0 (48.0) t	48.5 (48.4) t
21	48.5 t	48.6 t	48.5 (48.4) t	48.8 (48.8) t
22	13.2 q	13.2 q	13.4 (13.4) q	13.3 (13.3) q
1′	56.4 q	57.7 q	57.6 (57.4) q	57.5 (57.3) q
6′	57.7 q	57.8 q	57.9 (57.6) q	57.9 (57.6) q
14′	55.2 q	54.9 q	—	—
16′	57.4 q	55.1 q	55.2 (55.1) q	55.1 (55.1) q
18′	59.1 q	59.1 q	59.1 (59.1) q	59.1 (59.1) q

termined on the basis of spectral data (Table 1). Likewise, the ^{1}H- and ^{13}C-NMR spectra of **11** displayed five aliphatic methoxyl groups (δ_H 3.24, 3.28, 3.29, 3.39, 3.43, each 3H, s; δ_C 54.9 q, 55.1 q, 57.7 q, 57.8 q, 59.1 q), a hemiketal (δ_C 95.5 s) and an acetal (δ_H 4.97, 1H, d, J=1.6 Hz; δ_C 98.2 d) moiety. These observations led us to deduce that these two compounds (**10**, **11**) are a pair of epimers at C-14. As shown in Fig. 1, because of the presence of the γ-gauche effect between the 14α-H and the 8-hydroxyl group, the δ value of C-14 in **11** shifted upfield as compared with **10**.

We have observed that HIO_4 oxidation products of pseudaconine **8** depended greately on reaction medium and conditions of work up. After treatment of **8** in MeOH–H_2O with $NaIO_4$, a novel product **12** was obtained quantitatively when the reaction mixture was alkalized to pH>9 with conc. NH_4OH. The HR-EI-MS spectra showed a molecular ion peak at m/z 480.2834 corresponding to that of the expected compound **12** ($C_{25}H_{40}N_2O_7$). In comparison to the ^{1}H- and ^{13}C-NMR spectra of compounds **10** or **11**, those of compound **12** did not show the methoxyl signal attributed to C-14, but did show signals at δ_H 8.13 (d, J=4.2 Hz), δ_C 166.8 (s) and an additional nitrogen atom. These observations suggested the presence of an imine moiety, and the structure of

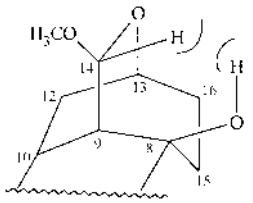


Fig. 1. Partial Structure of **11**

12 was confirmed unambiguously on the basis of (2D)-NMR (Table 2).

Treatment of **8** in 5% HCl with $NaIO_4$ at room temperature for 4 h gave quantitatively the imine **12** after being alkalized to pH>9 with conc. NH_4OH but working up at pH 7—8 led to compound **13** instead of **12**. Compound **13** $C_{25}H_{42}N_2O_8$ (HR-EI-MS) was obtained as an amorphous powder and a mixture of a pair of epimers. The ^{1}H- and ^{13}C-NMR spectra of **13** showed a hemiketal (δ_C 97.3/95.8, s) and an *N*,*O*-mixed acetal (δ_H 5.53 (5.38), d, J=1.6 Hz; δ_C 95.3/91.5, d), and as well as an NH_2 group (δ_H 4.99/4.90, each br s, exchangeable), and its structure was deduced on the basis of the spectral data (Table 1 and Experimental section). Treatment with 5% NaOH in MeOH **13** can be converted to **12** quantitatively.

The formation of compound **12** can be explained by the mechanism depicted in Chart 4: HIO_4 oxidation of pseudaconine **8** first produces an intermediate **18** (Chart 5), and then, the intermediate **19** so formed attacks the C-13 carbonyl leading to an intermediate **20** followed by dehydration to give the final product **12**. As shown in Chart 3, if alkalization to pH 7—8 was done with Na_2CO_3 instead of conc. NH_4OH, none of either compound **12** or **13** was observed on TLC, and, in fact, compound **14** $C_{25}H_{41}NO_9$ (HR-EI-MS) was obtained quantitatively as a mixture of a pair of epimers. Its MS spectrum showed the characteristic fragment ion peaks at m/z 481 (M−H_2O) and 468 (M−OCH_3). The ^{1}H- and ^{13}C-NMR spectra of **14** also indicated the presence of the hemiacetal and ketal moieties (δ_H 5.56/5.40, d, J=1.6 Hz; δ_C 95.3/91.5, d; δ_C 97.3/95.8, s). The structure and assignment of the ^{13}C-NMR signals (Table 1) for **14** were carried out by comparison with the analogues such as **10**, **11** and **13**.

Interestingly, we found that treatment of **14** with saturated Na_2CO_3 overnight or 5% NaOH methanol at room temperature for 1 h gave a first novel C/D-nor-rearranged product **15** in 87% yield by the hydrolysis and aldol condensation, which could be returned to the starting material **14** *via* a retroaldol and acetal-ketalization process by treatment with 10% HCl. The MS spectra of compound **15** $C_{25}H_{39}NO_8$ (HR-EI-MS) displayed the characteristic fragment ion peaks at m/z 466

Table 2. NMR Data for **12** (400 MHz for ^{1}H, 100 MHz for ^{13}C)

No	δ_C	δ_H (J=Hz)	^{1}H–^{1}H COSY	HMBC (H→C)
1	82.1 d	3.28 t (5.2)	H-2 (1.78), H-2 (2.20)	C-10, C-11, C-17, C-1′
2	31.9 t	1.78 m (hidden) (α)	H-1, H-2 (2.20)	C-3, C-4, C-11
		2.20 m (hidden) (β)	H-1, H-2 (1.78)	C-3, C-4, C-11
3	71.4 d	3.92 dd (6.4, 4.4)	H-2 (1.78), H-2 (2.20)	C-1, C-18
4	43.4 s	—	—	—
5	45.0 d	2.20 d (6.4)	H-6	C-3, C-4, C-6, C-7, C-10, C-11, C-17, C-19
6	83.2 d	4.26 d (6.4)	H-5	C-4, C-7, C-8, C-17, C-6′
7	52.9 d	2.0 br s (W1/2=5.2)	—	C-8, C-11, C-17
8	73.2 s	—	—	—
9	43.8 d	2.79 t (6.0)	H-14, H-10	C-8, C-10, C-12, C-14, C-15
10	39.0 d	1.79 m (hidden)	H-9, H-12	C-1, C-8, C-9, C-11, C-13, C-17
11	51.6 s	—	—	—
12	31.9 t	2.21 m (hidden) (α)	H-12 (2.62), H-10	C-9, C-10, C-11, C-13, C-16
		2.62 d (10.8) (β)	H-12 (2.21)	
13	86.8 s	—	—	—
14	166.4 d	8.14 d (4.8)	H-9	C-9, C-10, C-13
15	41.7 t	1.53 dd (14, 9.6) (α)	H-15α, H-16	C-7, C-8, C-16
		2.25 dd (14, 6) (β)	H-15β, H-16	C-7, C-8, C-9, C-13, C-16
16	81.7 d	3.35 m (hidden)	H-15	C-16′
17	61.3 d	3.09 br s (W1/2=3.0)	—	C-5, C-10, C-11, C-19
18	77.6 t	3.46 (8.8)	H-18 (3.72)	C-4, C-5, C-19, C-18′
		3.72	H-18 (3.46)	C-4, C-5, C-19, C-18′
19	48.7 t	2.68 (11)	H-19 (2.90)	
		2.90	H-19 (2.68)	
21	48.7 t	2.48 q (6.8)	H-22	C-22
22	12.7 q	1.17 t (6.8)	H-21	C-21
1′	55.3 q	3.31 s	—	C-1
6′	58.0 q	3.38 s	—	C-6
16′	58.3 q	3.45 s	—	C-16
18′	59.1 q	3.32 s	—	C-18

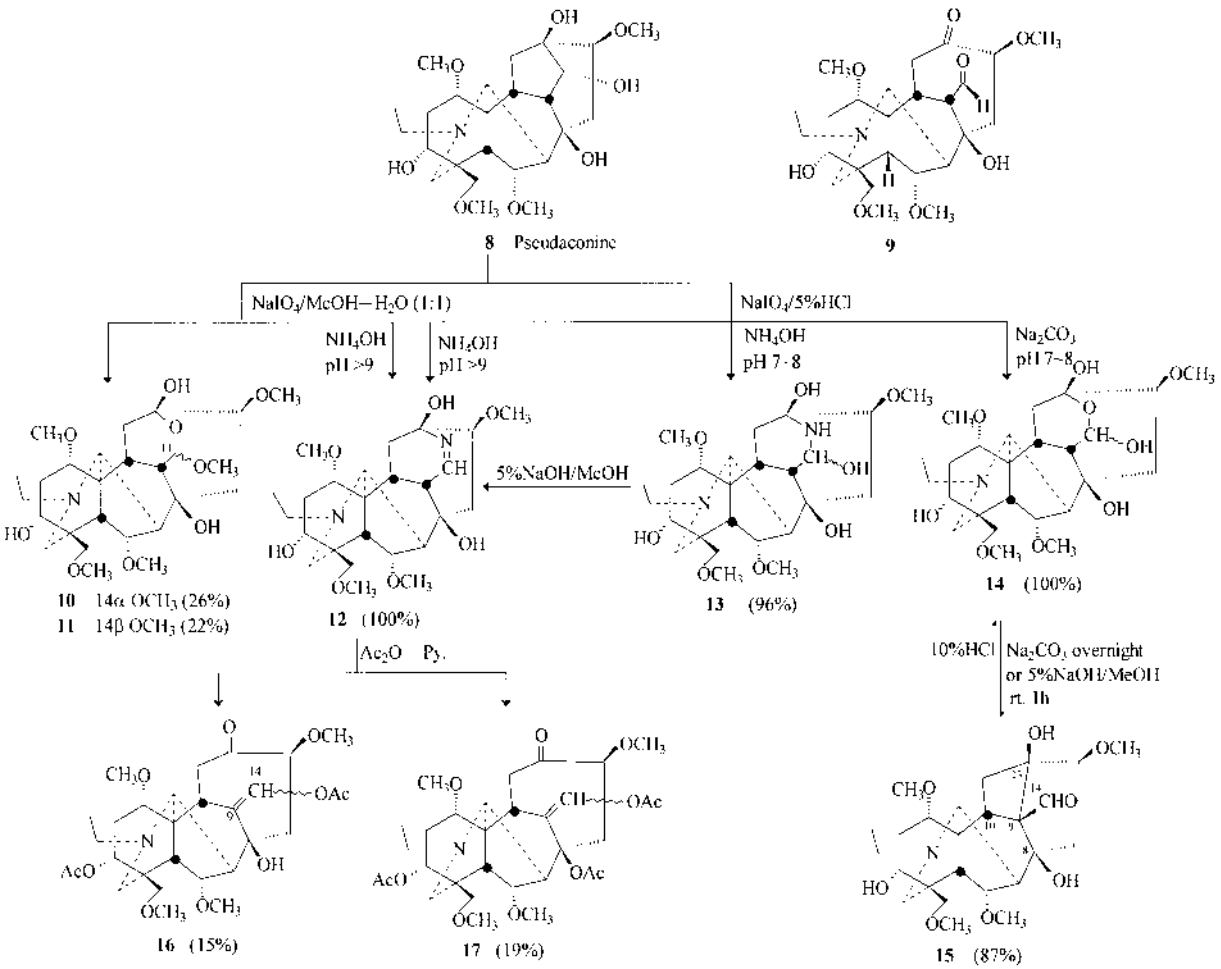


Chart 3

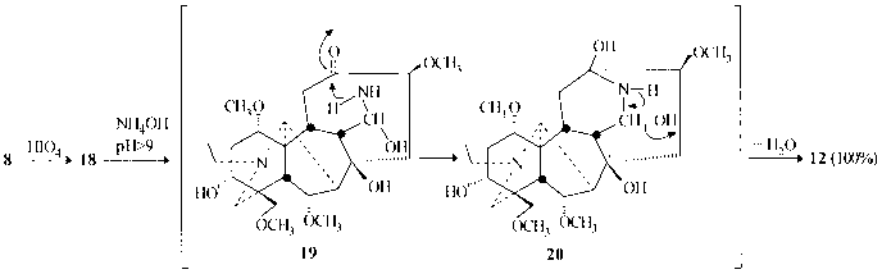
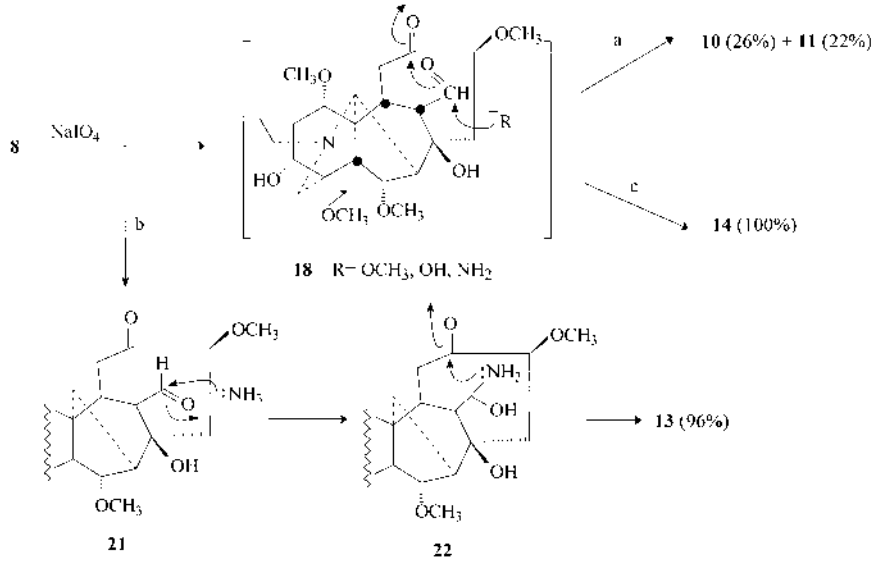


Chart 4



a). MeOH-H_2O; b). (1) 5%HCl, (2) NH_4OH; c). (1) 5%HCl, (2) Na_2CO_3

Chart 5

($M-CH_3$), and 450 ($M-OCH_3$, base peak), and its IR, ^{1}H- and ^{13}C-NMR spectra (Experimental section and Table 3) exhibited the presence of an aldehyde group (1698 cm^{-1}; δ_H 9.70, 1H, s; δ_C 202.5, d), which can only occur on the β face of the C-ring according to the molecular model and the structure of **15** can thus be determined on the basis of its 2D-NMR spectra (Table 3).

It is worthy of note that chemical shifts for many carbons in the ^{13}C-NMR spectra of **15** were changed greatly as compared with that of **14**. A process of formation of the compounds **10**, **11**, **13** and **14** shown in Chart 5 was postulated.

Finally, an unsuccessful attempt to prepare only the 3-acetyl derivative of compound **12** led to obtained poor yield of both ketone enolates **16** and **17**. Compounds **16** $C_{29}H_{43}NO_{10}$ (HR-EI-MS) and **17** $C_{31}H_{45}NO_{11}$ (HR-EI-MS) were afforded as an amorphous powder. Their ^{1}H- and ^{13}C-NMR spectra showed the presence of the ketone groups (δ_C 209.0 s), the trisubstituted double bonds (δ_H 7.17, 1H, s; δ_C 127.4 s, 130.8 d for **16**; δ_H 7.09, 1H, s; δ_C 124.6 s, 131.5 d for **17**) and the acetyl groups (δ_H 2.05, 2.18, each 3H, s; δ_C 167.4 s, 170.1 s, 20.8 q, 21.1 q, for, **16**; δ_H 2.05, 2.08, 2.20, each 3H, s; δ_C 167.2 s, 169.4 s, 170.1 s, 20.8 q, 21.1 q, 22.3 q, for **17**). Two acetyl groups in **16** could be located at C-3 and C-14 based on their reaction conditions (Ac_2O/pyridine, room temperature) and the δ value of C-8 (δ 76.1s, Table 2) as in the 8-hydroxyl norditerpenoid alkaloids.[7] An additional acetyl group in **17**, in contract, can be assigned to C-8 as compared with the ^{13}C-NMR spectra of **16**, suggesting that compound **17** might be derived from **16** *via* the 1,3-acetyl migration followed by further acetylation. The structures of **16** and **17** were deduced based mainly on the spectral data (Table 4 and Experimental section).

In summary, all the novel compounds show here involve a great degree of change at the C-ring, the cleavage of the C-13, C-14 bond followed by the formation of a cyclic hemiketal or *O*,*N*-mixed hemiketals (**10**—**14**) but not the expected aldehyde ketone **9**. It is interesting that the formation of compounds **10**, **11**, **12**, **13** and **14** depended greatly on the reaction medium and conditions in work up, and it is worth noting that compound **15** was the first C/D-nor-rearranged norditerpenoid alkaloid. Though these highly functionalized norditerpenoid alkaloids have been extensively studied for at least the past fifty years, new or unexpected reactions are still being discovered and can lead to new and interesting compounds.

Experimental

General Experimental Procedures Optical rotations were measured in a 1.0 dm tube with a PE-341 polarimeter at 20±1 °C. ^{1}H- and ^{13}C-NMR spectra were acquired on a Bruker AC-E 200 or a Varian INOVA-400/54 spectrometer, in $CDCl_3$ with tetramethylsilane (TMS) as internal standard; IR spectra were recorded on a Perkin–Elmer 983 spectrometer; EI-MS and FAB-MS were obtained with a CG Auto-spec 3000 and a VG 70A mass spectrometer, respectively; TLC was performed on Silica gel GF_{254} pre-

Table 3. NMR Data for **15** (400 MHz for ^{1}H, 100 MHz for ^{13}C)

No	δ_C	δ_H mult (J=Hz)	^{1}H–^{1}H COSY	HMBC (H→C)
1	82.1 d	3.21 m (hidden)	H-2	C-5, C-10, C-11, C-17, C-1′
2	33.9 t	2.22 t (6.0) (α)	H-1, H-3	C-1, C-3, C-4, C-11
		2.56 m (hidden) (β)	H-1, H-3	C-1, C-3, C-11
3	72.4 d	3.72 dd (12.8, 4.0)	H-2	C-18, C-19
4	42.6 s	—	—	—
5	47.8 d	1.94 d (6.4)	H-6	C-4, C-7, C-10, C-11, C-17, C-18, C-19
6	85.8 d	3.34 d (6.4)	H-5	C-4, C-8, C-17, C-6′
7	48.8 d	2.14 br s (W1/2=6.0)	—	C-6, C-8, C-9, C-11, C-15, C-17
8	88.2 s	—	—	—
9	65.1 s	—	—	—
10	39.0 d	2.98 dd (9.8, 9.2)	H-12	C-8, C-9, C-11, C-12, C-14, C-17
11	48.8 s	—	—	—
12	31.5 t	2.17 m (hidden) (α)	H-10	C-11, C-13, C-16
		2.58 m (hidden) (β)	H-10	C-10, C-11, C-13, C-16
13	85.2 s	—	—	—
14	202.5 d	9.68 s	—	C-9, C-10
15	40.0 t	2.18 m (hidden) (α)		C-8, C-9, C-13, C-16
		2.48 m (hidden) (β)	H-16	C-7, C-8
16	87.7 d	3.48 d (5.2)	H-15 (2.48)	C-8, C-9, C-16′
17	62.6 d	3.46 br s (W1/2=3.0)	—	C-5, C-6, C-7, C-8, C-10, C-11, C-19, C-21
18	77.4 t	3.58	H-18 (3.86)	C-3, C-4, C-19, C-18′
		3.86 ABq (9.2)	H-18 (3.58)	C-3, C-4, C-5, C-18′
19	47.0 t	2.34	H-19 (2.04)	C-3, C-4, C-18′, C-21
		3.04 ABq (11.2)	H-19 (2.34)	C-3, C-4, C-5, C-17
21	49.0 t	2.50 m (hidden)	H-22	C-22
22	13.2 q	1.10 t (7.2)	H-21	C-21
1′	56.3 q	3.24 s	—	C-1
6′	56.8 q	3.22 s	—	C-6
16′	57.6 q	3.44 s	—	C-16
18′	59.2 q	3.29 s	—	C-18

Table 4. ^{13}C-NMR Data for Compounds **16** and **17**

Carbon	**16**	**17**	Carbon	**16**	**17**
1	85.0 d	85.1 d	14	130.8 d	131.5 d
2	31.4 t	31.6 t	15	43.3 t	41.9 t
3	71.4 d	71.3 d	16	84.6 d	86.3 d
4	42.1 s	41.9 s	17	62.0 d	61.7 d
5	46.8 d	46.8 d	18	71.9 t	71.7 t
6	79.6 d	78.6 d	19	48.7 t	48.6 t
7	51.5 d	46.4 d	21	47.4 t	47.1 t
8	76.1 s	85.6 s	22	13.4 q	13.2 q
9	127.4 s	124.6 s	1′	55.0 q	54.7 q
10	41.4 d	41.2 d	6′	57.2 q	57.1 q
11	51.7 s	51.4 s	16′	57.7 q	57.7 q
12	42.7 t	40.8 t	18′	58.8 q	58.8 q
13	209.0 s	209.0 s	OAc	167.4 s, 170.1 s	167.2 s, 169.4 s, 170.1 s
				20.8 q, 21.1 q	20.8 q, 21.1 q, 22.3 q

coated plates, sprayed with a modified Dragendoff's reagent for detection; column chromatography was performed using Silica gel H; chromatographic separation on a Chromatodron was carried out on rotors coated with 1mm thick layers of Silica gel H and 0.5% CMC. All of Silica gel GF_{254} and Silica gel H used in the experiments were purchased from the Qindao Sea Chemical Factory, People's Republic of China.

Compounds 10 and 11 To a solution of $NaIO_4$ (1350 mg, 6.31 mmol) in H_2O (17.5 ml), pseudaconine **8** (520 mg, 1.08 mmol) in MeOH (17.5 ml) was added and the solution was kept at room temperature for 7 h. After this, the reaction solution was extracted with $CHCl_3$ (20 ml×4), and the combined chloroform solutions were dried over anhydrous Na_2SO_4. After removal of $CHCl_3$ *in vacuo* the residue (485 mg) was purified by a Chromatotron (Si gel, $CHCl_3$/MeOH/95/5) affording compounds **10** (134 mg, 26% yield) and **11** (114 mg, 22% yield). **10** was obtained as a white amorphous powder. $[\alpha]_D$ +30.7° (c=0.81, $CHCl_3$); ^{1}H-NMR (400 MHz) δ 1.08 (3H, t, J=7.2 Hz, $\underline{NCH_2CH_3}$), 3.25, 3.29, 3.30, 3.44, 3.49 (each 3H, s, OCH_3×5), 3.90 (1H, s, exchangeable in D_2O, OH), 4.17 (1H, d, J=6.4 Hz, H-6β), 4.92 (1H, d, J=2.4 Hz, H=14β), 4.96 (1H, s, exchangeable in D_2O, OH); ^{13}C-NMR (50 MHz) see in Table 1; FAB-MS m/z (%) 514 (M^++1, 100); HR-FAB-MS m/z 514.2997 (M^++1) (Calcd for $C_{26}H_{43}NO_9$, 514.3016). **11** also was obtained as a white amorphous powder. $[\alpha]_D$ +11.1° (c=1.01, $CHCl_3$); ^{1}H-NMR (400 MHz) δ 1.05 (3H, t, J=7.0 Hz, $NCH_2\underline{CH_3}$), 3.24, 3.28, 3.29, 3.42 (each 3H, s, OCH_3×4), 3.53, 3.65 (each 1H, ABq, J=8.8 Hz, H_2-18), 4.16 (1H, d, J=6.8 Hz, H-6β), 4.79 (1H, s, exchangeable in D_2O, OH), 4.97 (1H, d, J=1.6 Hz, H-14α); ^{13}C-NMR (50 MHz) see Table 1; FAB-MS m/z (%) 514 (M^++1, 100); HR-FAB-MS m/z 514.2991 (M^++1) (Calcd for $C_{26}H_{43}NO_9$, 514.3016).

Compound 12 Method 1: To a solution of pseudaconine **8** (200 mg, 0.41 mmol) in 5% HCl (5 ml), $NaIO_4$ (600 mg, 2.8 mmol) was added and the solution was kept at room temperature for 4 h. After being this reaction solution was alkalized with conc. NH_4OH to PH>9, the solution was extracted with $CHCl_3$ (10 ml×4). The combined chloroform solutions were dried over anhydrous Na_2SO_4 and evaporated *in vacuo* to give a white amorphous powder **12** (200 mg, 100% yield).

Method 2: To a solution of $NaIO_4$ (1000 mg, 4.67 mmol) in H_2O (13 ml), pseudaconine **8** (350 mg, 0.73 mmol) in MeOH (13 ml) was added and the solution was kept at room temperature for 7 h. After removal of methanol *in vacuo* the residue was diluted with conc. NH_4OH (5 ml) and the solution was stirred overnight. Work up using the usual method and purification gave compound **12** (324 mg, 92% yield). **12**: $[\alpha]_D$ +16.6° (c, 1.04, $CHCl_3$); ^{1}H (400 MHz)- and ^{13}C (100 MHz)-NMR see in Table 2; IR (KBr) cm^{-1} 3410 (OH), 1640 (C=N); EI-MS m/z (%) 480 (M^+, 4), 465 (7), 450 (57), 449 (M−31, 43); FAB-MS m/z (%) 481 (M^++1, 100), HR-EIMS m/z 480.2834 (Calcd for $C_{25}H_{40}N_2O_7$, 480.2835).

Compound 13 To a solution of pseudaconine **8** (300 mg, 0.62 mmol) in 5% HCl (10 ml), $NaIO_4$ (900 mg, 4.2 mmol) was added and the solution was kept at room temperature for 4 h. After being alkalized to pH 7—8 with conc. NH_4OH the solution was extracted with $CHCl_3$ (10 ml×4). The combined chloroform solutions were dried over anhydrous Na_2SO_4 and evaporated *in vacuo* to give a white amorphous powder **13** (290 mg, 96% yield). $[\alpha]_D$ +17.1° (c=0.69, $CHCl_3$); ^{1}H-NMR (200 MHz) δ 1.14 (3H, t, J=7.0 Hz, $\underline{NCH_2CH_3}$), 3.24, 3.29, 3.29, 3.43 (each 3H, s, OCH_3×4), 4.99

(4.90) (each 1H, br s, exchangeable in D_2O, NH_2), 5.53 (5.38) (1H, d, J=1.6 Hz, H-14); ^{13}C-NMR (100 MHz) see Table 1; EI-MS m/z (%) 498 (M^+, 2), 481 (31), 468 (36), 450 (100); HR-FAB-MS m/z 498.2885 (Calcd for $C_{25}H_{42}N_2O_8$, 498.2941).

Conversion of 13 to 12 To 5% NaOH methanol solution (5 ml), compound **13** (300 mg, 0.60 mmol) was added and kept the solution at room temperature for 4 h. After removal of methanol *in vacuo* the residue was diluted with $CHCl_3$ (20 ml), and the solution was washed with H_2O (50 ml×2) and worked up by the general method to give **12** (300 mg, 100% yield).

Compound 14 To a solution of pseudaconine **8** (145 mg, 0.30 mmol) in 5% HCl (5 ml), $NaIO_4$ (450 mg, 2.10 mmol) was added and the solution was kept at room temperature for 4 h. Thereafter, the reaction solution was alkalized to pH 7—8 with saturated Na_2CO_3 solution and extracted with $CHCl_3$ (10 ml×5). After removal of chloroform *in vacuo* compound **14** (145 mg, 100% yield) was obtained. $[\alpha]_D$ +26.2° (c=1.21, $CHCl_3$); ^{1}H-NMR (400 MHz) δ 1.10 (3H, t, J=6.8 Hz, $\underline{N}CH_2\underline{CH_3}$), 3.24, 3.32, 3.32, 3.44 (each 3H, s, OCH_3×4), 5.02 (4.98) (each 1H, br s, exchangeable D_2O, OH), 5.56 (5.40) (1H, d, J=1.6 Hz, H-14); ^{13}C-NMR (100 MHz) see Table 1; EI-MS m/z (%) 499 (M^+, 3), 481 (M−8, 33), 468 (M−31, 32), 466 (38), 450 (100); HR-EI-MS m/z 499.2768 (Calcd for $C_{25}H_{41}NO_9$, 499.2781).

Conversion of 14 to 15 Method 1: To a saturated Na_2CO_3 solution (5 ml), compound **14** (200 mg, 0.41 mmol) in $CHCl_3$ (5 ml) was added and the solution was kept at room temperature overnight. The separated aqueous layer was extracted with $CHCl_3$ (15 ml×3). After evaporation of the combined chloroform solutions *in vacuo* the residue was purified by column chromatography (Si gel, 6 g) eluting with. cyclohexane–acetone (5 : 1) to give compound **15** (120 mg, 60% yield).

Method 2: To 5% NaOH methanol (5 ml), compound **14** (150 mg, 0.31 mmol) was added and the solution was kept at room temperature for 5 h. After removal of methanol *in vacuo* the residue was diluted with $CHCl_3$ (20 ml) and then washed with H_2O (5 ml×2). Evaporation of chloroform layer under reduced pressure gave a residue that was purified by a column chromatography (Si gel, 5 g) eluting with cyclohexane–acetone (5 : 1) to give compound **15** (130 mg, 87% yield). $[\alpha]_D$ +16.7° (c, 0.90, $CHCl_3$); ^{1}H (400 MHz)- and ^{13}C (100 MHz)-NMR see Table 3; IR (KBr) cm^{-1} 3333 (OH), 1698 (CHO); EI-MS m/z (%) 481 (M^+, 8), 466 (19), 450 (M−31, 100); HR-EI-MS m/z 481.2678 (Calcd for $C_{25}H_{39}NO_8$, 481.2675).

Compounds 16 and 17 To a mixed solution of acetic anhydride (0.5 ml, 5.3 mmol) and pyridine (2 ml), compound **12** (300 mg, 0.625 mmol) was added and the solution was kept at room temperature overnight. Evaporation of the reaction solution *in vacuo* gave a residue that was chromatographed on Si gel (10 g) column eluting with $CHCl_3$–MeOH (96.5 : 3.5) to give compounds **16** (50 mg, 15% yield) and **17** (70 mg, 19% yield). Compound **16**: ^{1}H-NMR (200 MHz) δ 1.08 (3H, t, J=7.2 Hz, $\underline{N}CH_2\underline{CH_3}$), 2.05, 2.18 (each 3H, s, OAc×2), 3.19, 3.19, 3.26, 3.33 (each 3H, s, OCH_3×4), 4.83 (1H, dd, J=10.4, 5.4 Hz, H-3β), 7.17 (1H, s, H-14); ^{13}C-NMR (50 MHz) see Table 4; IR (KBr) cm^{-1} 3640 (OH), 1740 (C=O); EI-MS m/z (%) 565 (M^+, 8), 547 (20), 534 (12), 548 (M−OAc, 85); HR-EI-MS m/z 565.2882 (Calcd for $C_{29}H_{43}NO_{10}$, 565.2886). Compound **17**: ^{1}H-NMR (200 MHz) δ 1.05 (3H, t, J=7.0 Hz, $\underline{N}CH_2\underline{CH_3}$), 2.05, 2.08, 2.20 (each 3H, s, OAc×3), 3.18, 3.19, 3.19, 3.27, (each 3H, s, OCH_3×4), 4.86 (1H, dd, J=11.0, 5.20 Hz, H-3β), 7.29 (1H, s, H-14); ^{13}C-NMR (50 MHz) see Table 4; IR (KBr) cm^{-1} 3032 (C=H), 1746 (C=O); EI-MS m/z (%) 607 (M^+, 3), 576 (M−31, 12), 548 (M−OAc, 85); HR-EI-MS m/z 607.3013 (Calcd for $C_{31}H_{45}NO_{11}$, 607.2992).

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References and Notes

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