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A novel conversion of norditerpenoid alkaloids into aconane-type diterpenes

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Abstract—Two methods for the synthesis of *N*,19-*seco* norditerpenoid alkaloids were developed. One method prepared new *N*,19-*seco* norditerpenoid alkaloids possessing an oxaziridine group from yunaconitine in five steps involving acetylation, imination, quaternization, formation of *N*,*O*-mixed ketal, and oxidation in 50% overall yield. Another method provided a series of novel *N*,19-*seco* norditerpenoid alkaloids bearing the oximino or nitro groups through oxidation of the imine *N*-oxides with HIO_4 in moderate yields. Two novel aconane-type diterpenes were synthesized from an *N*,19-*seco* nitro compound and an imine *N*-oxide through Nef reaction and HIO_4 oxidation, respectively, in moderate yields.

1. Introduction

The norditerpenoid alkaloids are a group of highly oxygenated complex natural products displaying interesting chemical reactions[1] and important biological activities, such as analgesic, local anesthetic, anti-inflammatory and anti-arrhythmia.[2] They were isolated mainly from both *Aconitum* and *Delphinium* plants (*Ranunculaceae*).[3] In order to search for high activity, low-toxicity compounds, we have carried out a series of the structure modifications of the norditerpenoid alkaloids for evaluation of their biological activities.[4] We reported the synthesis of 12,13-*seco* norditerpenoid alkaloids.[4j] No chemical studies on the *N*,17-*seco* norditerpenoid alkaloid have been reported so far. Herein, we report in detail a novel conversion of the norditerpenoid alkaloids into the aconane-type diterpenes.

2. Results and discussion

It is known that hydrolysis of imminium salts generally gives an aldehyde or a ketone. This led us to try the cleavage of the *N*,C(19) bonds of the immonium salts starting from the imines via quaternization (Scheme 1). Reaction of compound **3** obtained from yunaconitine **1**[5] via **2** (Scheme 2)[4b] with CH_3I at room temperature afforded the immonium salt **4** quantitatively. Its ^1H (^{13}C) NMR spectra displayed distinct signals (δ_H 9.62, 1H, brs; δ_C 179.3 d) for an immonium moiety. Treatment of **4** with either 5% HCl at room temperature for 24 h or conc. NH_4OH for 10 min, gave the *N*,*O*-mixed acetal **5** (100% yield) instead of the expected *N*,19-*seco* compound **6**, but further treatment of **5** with CH_3I led to return **4**. The MS (FAB and HRFAB) of compound **5** showed the pseudo molecular ion (M^++1) at *m*/*z* 704 corresponding to the formula $C_{36}H_{49}NO_{13}$, In comparison with the NMR spectra of **4**, those of compound **5** showed the absence of an immonium group and the appearance of one *N*,*O*-mixed ketal group at C-19 (δ_H 4.32, s; δ_C 84.0, d), in addition to the upfield shift of *N*–CH_3 from δ_H 4.20 (δ_C 47.6) to δ_H 2.57 (δ_C 37.7). The stereochemistry of C-19 of **5** was '*R*', based on the nOe relationship between H-19 (δ_H 4.32, s) and 3α-OAc (δ_H 2.03, s).

However, when **4** was treated with 5% NaOH at 40°C for 30 min the unexpected rearrangement product **8** was obtained.[6] As mentioned before, in our case, hydrolysis of the N^+=C(19) group in **4** is highly unreactive toward acids or bases possibly due to other competitive reactions such as addition or elimination. As previously pointed out,[4b] a plausible mechanism for formation of imine **3** from **2** is shown in Scheme 3.

It appears that the introduction of an electron withdrawing group *N*→*O* greatly activated the *N*–C(19) bond, thus resulting in the easy cleavage of this bond. Oxidation of **5** with *m*-CPBA resulted in the formation of the desired *N*,19-*seco* product **10** via the intermediate **9** in 73% yield besides the by-product **11** (8%) (Scheme 4). The NMR spectra of **10** showed the presence of an aldehyde group (δ_H 10.19, 1H, s; δ_C 202.0, d), indicating the formation of the *N*,19-*seco* norditerpenoid alkaloid. The molecular formula ($C_{36}H_{47}NO_{14}$) of compound **10** was inferred from its HRFAB and ^{13}C NMR spectra. As compared with **5**, the

Keywords: norditerpenoid alkaloid; *N*,19-*seco* norditerpenoid alkaloid; *N*,17-*seco* noriterpenoid alkaloid; diterpene; aconane-type diterpene.

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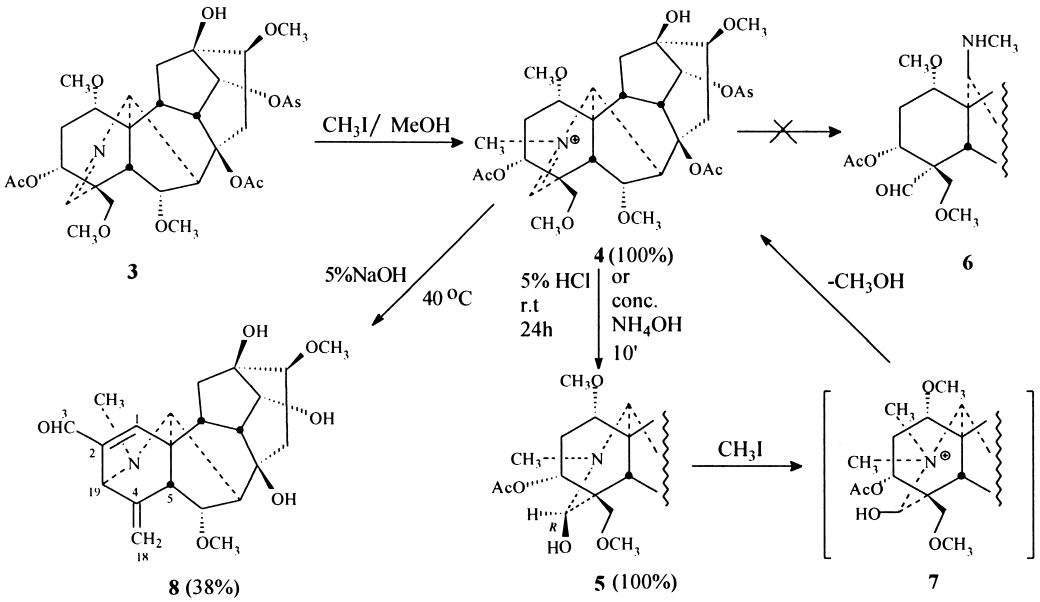
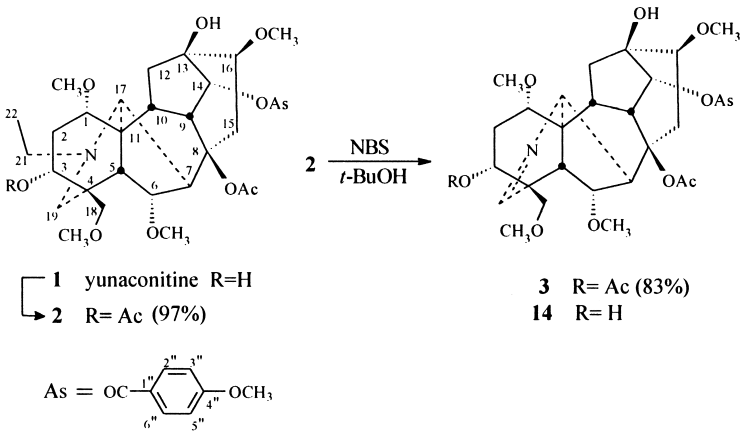
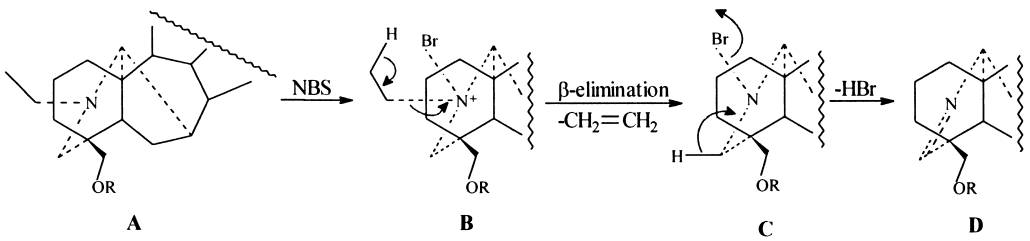


Scheme 1.



Scheme 2.

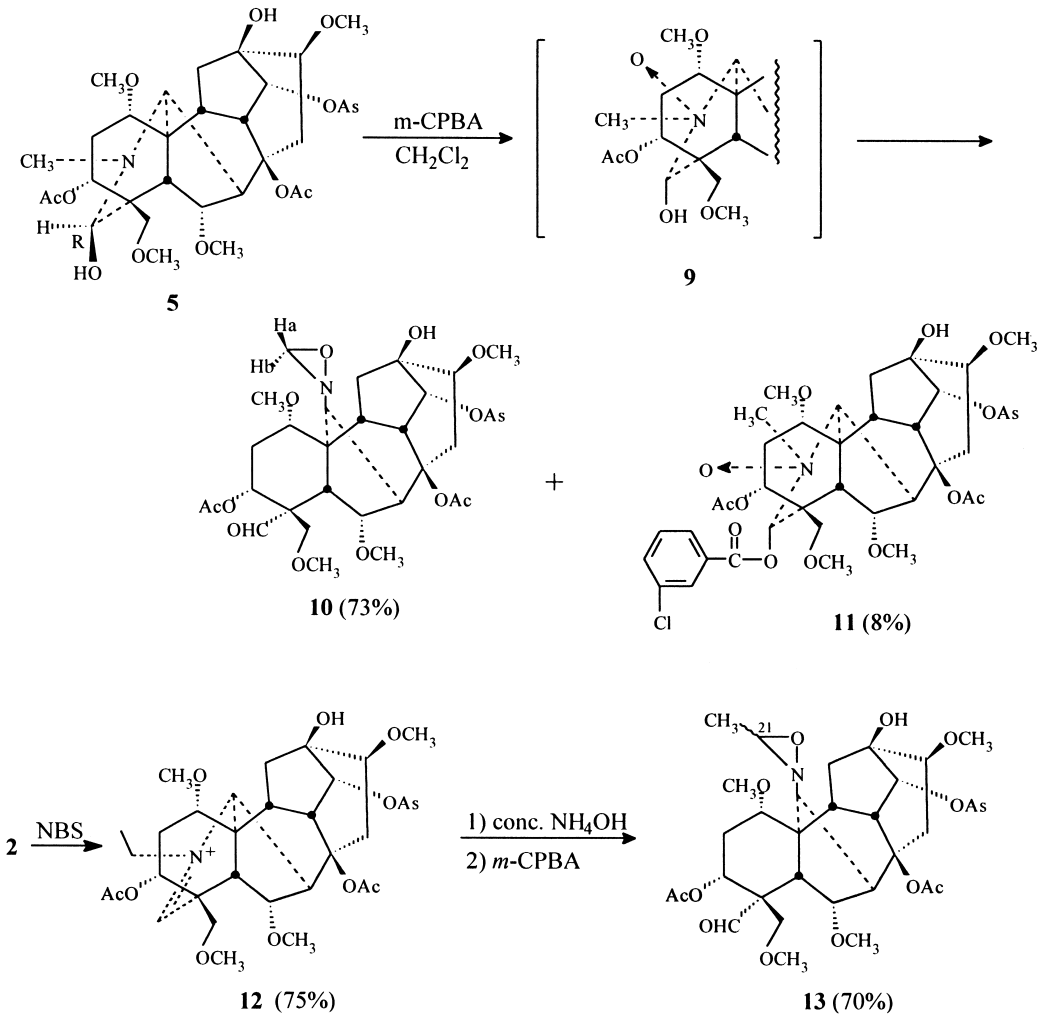


Scheme 3.

NMR spectra of compound **10** displayed the absence of an *N*-methyl group and the presence of an oxaziridine moiety [δ_H 3.98, 3.87 (each 1H, ABq, J=10.0 Hz); δ_C 76.2]. Finally, the structure of **10** has been proved by its 2D NMR spectra (Table 1). Similarly, treatment of **12** obtained from **2** with conc. NH_4OH followed by reaction with *m*-CPBA afforded the *N*,19-*seco* product **13** in 70% yield, as a pair of epimers at C-21 (Scheme 4).

The formation of **13** can be explained by the mechanism depicted in Scheme 5. Peracid oxidation of the imminium salt **12** (**A**) through a Baeyer–Villiger type process[7,8] to form **B**, and then, ring closure in **B** with loss of MCBA to give **C** that follows in the second peracid oxidation to form the intermediate **D** followed by attack of $^{-}$OH to afford the oxaziridine **E** (**13**).

The *N*,19-*seco* compounds **10** or **13** showed some characteristic reactions due to the presence of the aldehyde and oxaziridine groups. To further investigate the nature of the reaction for preparation of the *N*,17-*seco* products, we accomplished the following. Earlier, Polonski reported that



Scheme 4.

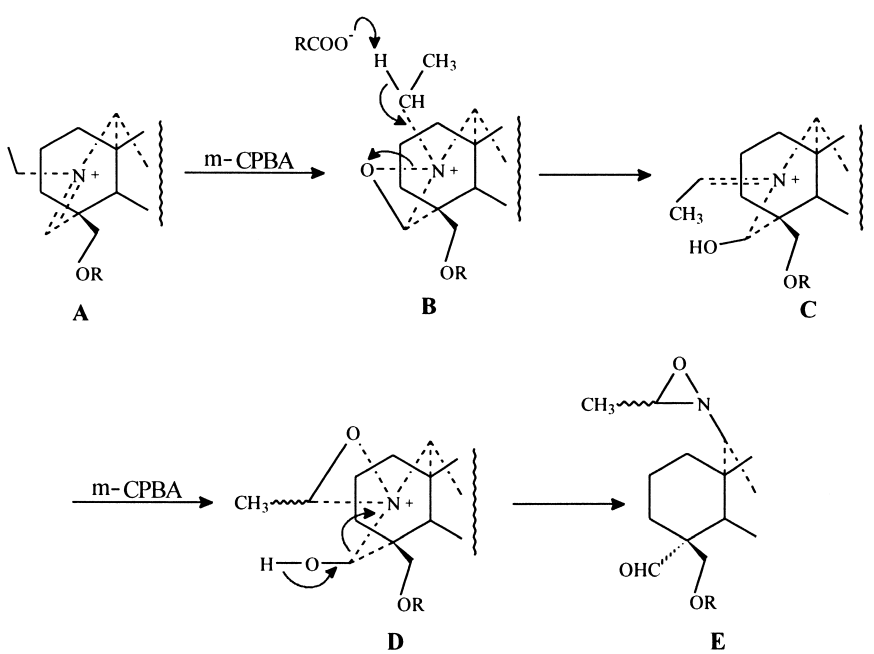
the oxaziridine-containing compound may be converted into the aldehyde and hydroxylamine via an acid-catalyzed hydrolysis.[9] But, reaction of **10** with 15% HCl to afford the hydroxylamine failed, resulting in the reconstruction of the *N*=C(19) bond (**14**). The formation of compound **14** from **10** can be explained by the mechanism depicted in Scheme 6. The nitrogen atom of oxaziridine moiety in **10** first undergoes a protonation under acid condition (**A→B**), followed by a like-β-elimination (**B→C**) and hydrolysis (**C→D**) to give a salt **D**, which liberated the free base **E** during a work-up using NH_4OH. Finally, compound **E** with an aldehyde group newly formed is further accompanied by an addition (**E→F**) and the elimination of a molecule of water, leading to **G**.

An attempt to oxidize the aldehyde group in **10** with $KMnO_4$ to prevent the reformation of the *N*–C(19) bond gave **15** in 64% yield. The molecular formula ($C_{36}H_{47}NO_{15}$) of compound **15** could be established by its HRFAB. The IR and NMR spectra of **15** showed the presence of a carboxyl group (3425, 3277, 1723 cm^{-1}; δ_C 177.5), and a formamide group [1673 cm^{-1}; δ_H 8.23 (8.28), 1H, d, J=1.6 (2.0) Hz, *H*CONH–; δ_H 9.98, 1H, dd, J=8.4, 1.6 Hz, exchangeable with D_2O, HCON*H*; δ_C 162.5, HMQC]. The ^1H NMR spectrum of **15** showed clearly that it is a mixture of a pair of the conformers (about 8:1 based on the integration of the CHO signals) due to the presence of formamide group. Treatment of acid **15** with CH_3I led to the methyl ester **16** (64% yield) that was followed by hydrolysis with 15% HCl to give the products **17** and **18** in 50 and 26% yield, respectively (Scheme 7).

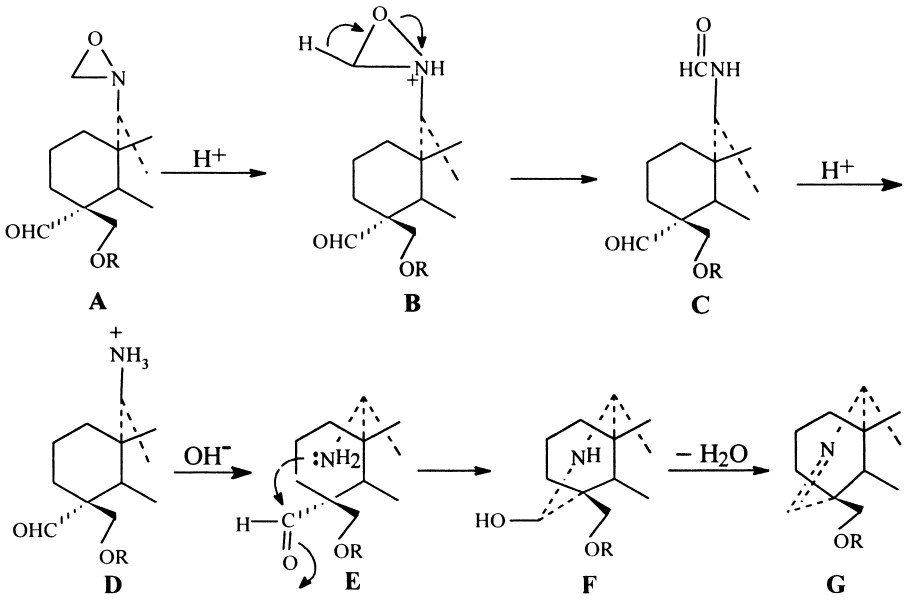
After our first attempted cleavage of the *N*,C(19) bond of the norditerpenoid alkaloids mentioned above, we now turned to an alternative method for this purpose. In 1960, Büchi et al.[10] reported that the norditerpenoid alkaloids bearing an imine *N*-oxide reacted with HIO_4 to afford the *N*,19-*seco* norditerpenoid alkaloids. Thus we have used a similar method for cleavage of the *N*–C(19) bonds of the norditerpenoid alkaloids. First, treatment of **14** with *m*-CPBA at room temperature using Pelletier's method[11] furnished compound **19** in 80% yield. In comparison to the ^{13}C NMR spectrum of **14**, those of compound **19** showed an upfield shift of C-19 from 164.6 to 136.5 and the downfield shift of C-17 from 61.5 to 73.1. This was attributed to N-oxidation.[10] HIO_4 was added to a methanolic solution of **19** and then this solution was allowed to stand at 0°C overnight. This resulted in formation of both compounds **20** and **21** in 55 and 21% yield, respectively (Scheme 8). The MS (FAB and HRFAB) of both compounds showed their

Table 1. NMR data of compounds **10** and **13**

No.	10				13
	δ_H	Mult (J=Hz)	δ_C	HMBC (H→C)	δ_C
1	3.29	dd (5.2, 11.6)	82.6 d	C-10, C-1′	82.7 (82.3) d
2	1.69	dd(11.6, 22.6)	30.4 t	C-1, C-3, C-4	30.6 (30.2) t
	2.14	m (hidden)		C-1, C-11, C-17	
3	4.84	dd (2.8, 12.0)	68.9 d	C-1, C-4	69.2 (69.1) d
4	–	–	52.8 s	–	53.1 (52.9) s
5	2.78	d (8.8)	51.0 d	C-4, C-6, C-10, C-11 C-17, C-18	51.1 (51.1) d
6	3.74	d (8.8)	81.7 d	C-8, C-11, C-17, C-6′	81.9 (81.8) d
7	3.33	S	53.4 d	C-6, C-8, C-9, C-11, C-17	61.8 (53.0) d
8	–	–	82.6 s	–	83.0 (82.8) s
9	2.54	dd (5.2, 6.4)	42.7 d	C-8, C-10, C-12, C-13, C14, C-15	42.8 (42.8) d
10	2.11	m (hidden)	45.5 d	C-8, C-9, C-12, C-17	45.7 (45.7) d
11	–	–	51.8 s	–	52.7 (52.0) s
12	1.98	m	33.5 t	C-16, C-11, C-13, C-14, C-10	33.9 (33.6) t
	1.96	m			
13	–	–	75.6 s	–	75.8 (75.8) s
14	4.74	d (4.8)	78.3 d	C-8, C-9, C-13	78.1 (78.0) d
15	2.31	dd (6.0, 16.0)	39.6 t	C-7, C-8, C-16	40.0 (39.8) t
	2.27	dd (hidden)			
16	3.16	dd (hidden)	83.3 d	C-7, C-8, C-9, C-17	83.5 (83.4) d
17	1.92	S	74.0 d	C-5, C-6, C-10, C-20	77.2 (73.0) d
18	3.56	ABq (10.0)	70.0 t	C-4, C-11, C-18′	70.2 (70.1) t
	3.08	ABq (10.0)			
19	10.19	S	202.0 d	C-4, C-18	203.0 (202.5) d
21	3.98	ABq (10.0)	76.2 t	C-17	84.2 (80.1) d
	3.87	ABq (10.0)		C-17	
22	–	–	–	–	17.9 (14.3) q
1′	3.22	S	56.4 q	C-1	56.4 (56.2) q
6′	2.93	S	57.0 q	C-6	57.2 (57.0) q
16′	3.43	S	58.6 q	C-16	58.8 (58.8) q
18′	3.23	S	59.1 q	C-18	59.3 (59.3) q
3-Oac	–	–	169.9 s	–	170.0 (170.0) s
	1.92	S	20.7 q	C-3′	21.0 (21.0) q
8-Oac	–	–	169.2 s	–	169.4 (169.3) s
	1.25	S	21.2 q	C-8′	21.3 (21.3) q
14-Oas	–	–		–	
CO			165.9 s		165.9 (165.9) s
1″	– –	–	122.2 s	–	122.2 (122.2) s
2″,6″	7.89	m	131.5 d	C-14′, C-4″, C-6″,	131.6 (131.6) d
3″,5″	6.82	m	113.6 d	C-1″, C-4″, C-5″	113.8 (113.8) d
4″	–	–	163.4 s	–	163.6 (163.6) s
4″-OCH_3	3.75	S	55.4 q	C-4″	55.4 (55.4) q

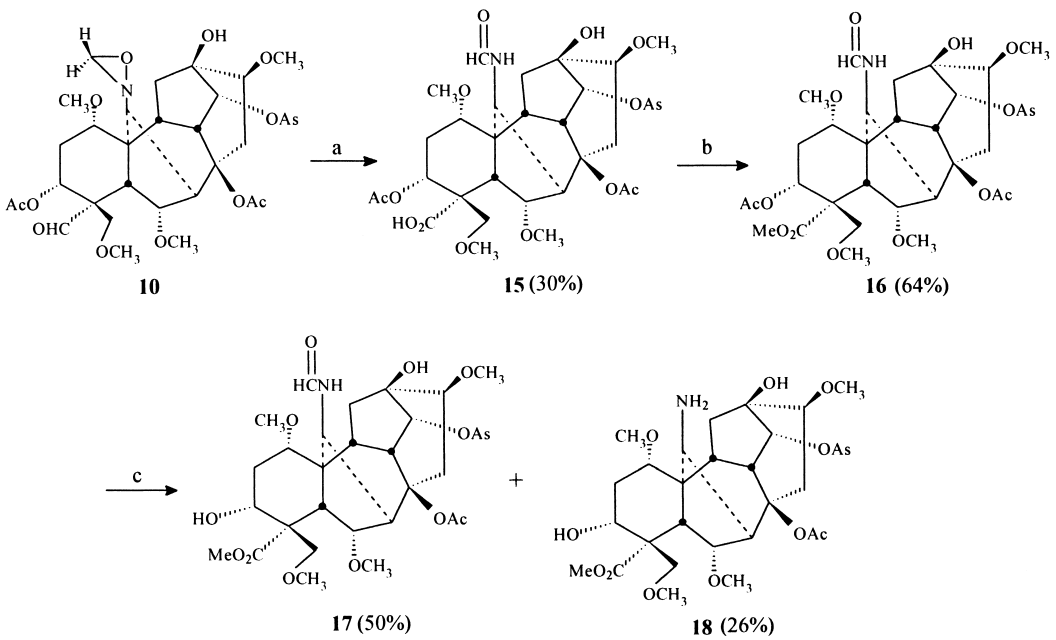


Scheme 5.

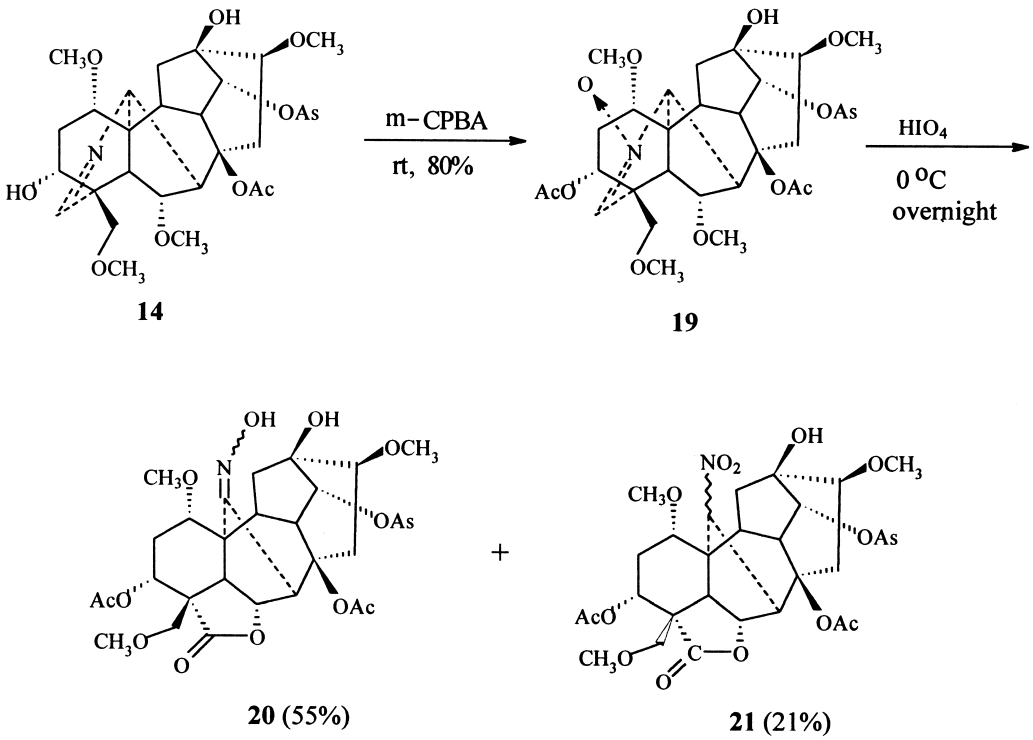


Scheme 6. A plausible mechanism for formation from **10** to **14**.

molecular ions (M^++1) at *m/z* 688 and 704 corresponding to the formula $C_{34}H_{41}NO_{14}$ and $C_{34}H_{41}NO_{15}$, respectively. The IR and NMR spectra of compounds **20** and **21** displayed the five-membered lactone moiety (1779 cm^{-1} and δ_C 172.5 for **20**; 1784 cm^{-1} and δ_C 172.9 for **21**), and characteristic signals at 3381, 1104 cm^{-1}, δ_H 9.55 (1H, brs, exchangeable), and δ_C 154.7, indicating the presence of the oximino group for **20**. As compared with compound **20**, the ^{13}C NMR spectrum of compound **21** showed a significant upfield shift of C-17 from 154.7 to 89.9 due to conversion from the nitro group. However, attempted treatment of compound **20** under Beckmann rearrangement conditions to give **23** via **22** resulted in the formation of a chloro-containing oxime **25**, which was produced possibly via an intermediate **24** (Scheme 9). The MS (FAB) of **25**, $C_{34}H_{40}NO_3Cl$ (HRFAB), showed one chloro-containing molecular ion at *m/z* 706 (43, M_I^++1) and 708 (16, M_I^++1). The IR and ^{13}C NMR spectra of compound **25** exhibited distinct signals at 1780 cm^{-1}, δ_C 173.5 for the γ-lactone moiety, and δ_C 154.9 for the oxime group. The NMR spectra of **25** also exhibited four methoxyl groups at δ_H 3.26, 3.45, 3.78 and 3.79, the first three of which were attributed to C-18, C-16 and C-4″, respectively, based on the HMBC spectrum (Table 3). This led to the location of the remaining methoxyl group (δ_H 3.79) at the oxime group. A one-proton signal at δ 5.34 (m) in the ^1H NMR spectrum of **25** can be assigned to H-1 due to the presence of the multi-bond $^1H-^{13}C$ correlations with C-2, C-3 and C-11 (HMBC, Table 3) and the absence of an oxygenated methine carbon, as compared with **20**, indicating location of the additional chloro atom at C-1. Finally, our hypothetical structure of **25** was established by its 2D NMR (Table 3) and single crystal



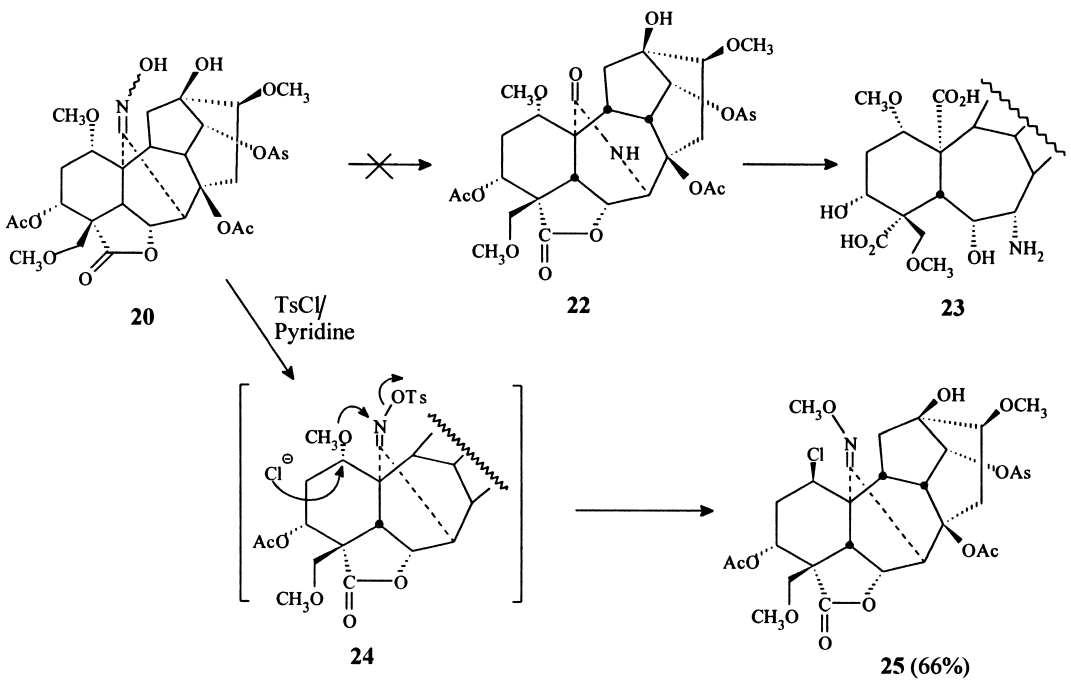
Scheme 7. (a) $KMnO_4$/acetone/10% H_2SO_4; (b) CH_3I/CH_3OH, Na_2CO_3; (c) 15% HCl, THF.



Scheme 8.

X-ray analysis (Fig. 1). In order to prevent participation of the 1-OCH_3 group, we have studied the nature of the reaction by synthesizing the new *N*,19-*seco* oxime **30** (35% yield), which was obtained from **26** using a four step sequence including acetylation, and subsequent oxidations with NBS, *m*-CPBA and HIO_4. Treatment of the *N*-oxide **29** from **28** with 2.5 equiv. HIO_4 in MeOH at 0–2°C overnight afforded the *N*,19-*seco* oxime **30** (65%), while **29** was reacted with an excess of HIO_4 in MeOH at room temperature overnight to give the nitro-containing *N*,19-*seco* compound **31** quantitatively (Scheme 10). The structures of both the desired compounds **30** and **31** could be assigned by comparison of the NMR spectra with the analogues **20** and **21**.

In contrast to the preparation of the *N*,19-*seco* norditerpenoid alkaloids, the cleavage of the *N*,C(17) bond has not been reported. Stephen et al.[12] reported that treatment of the oxaziridine possessing an α-hydrogen, as **32**,[12] with bases afforded α-hydroxylimines followed by hydrolysis to give



Scheme 9.

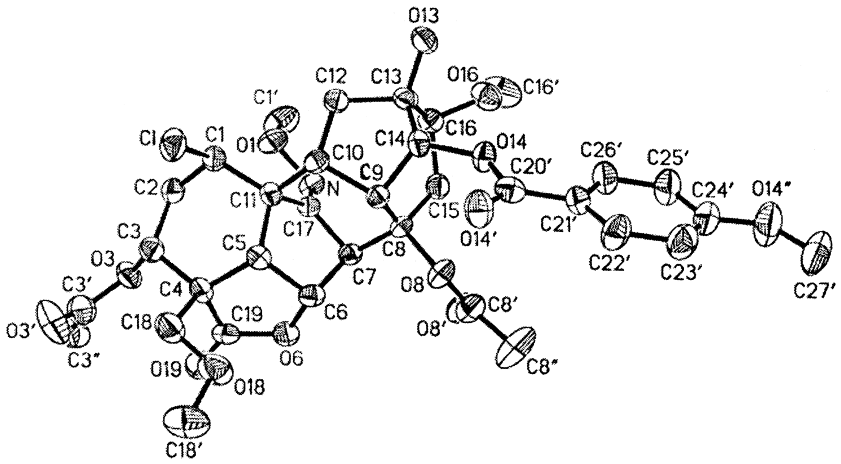


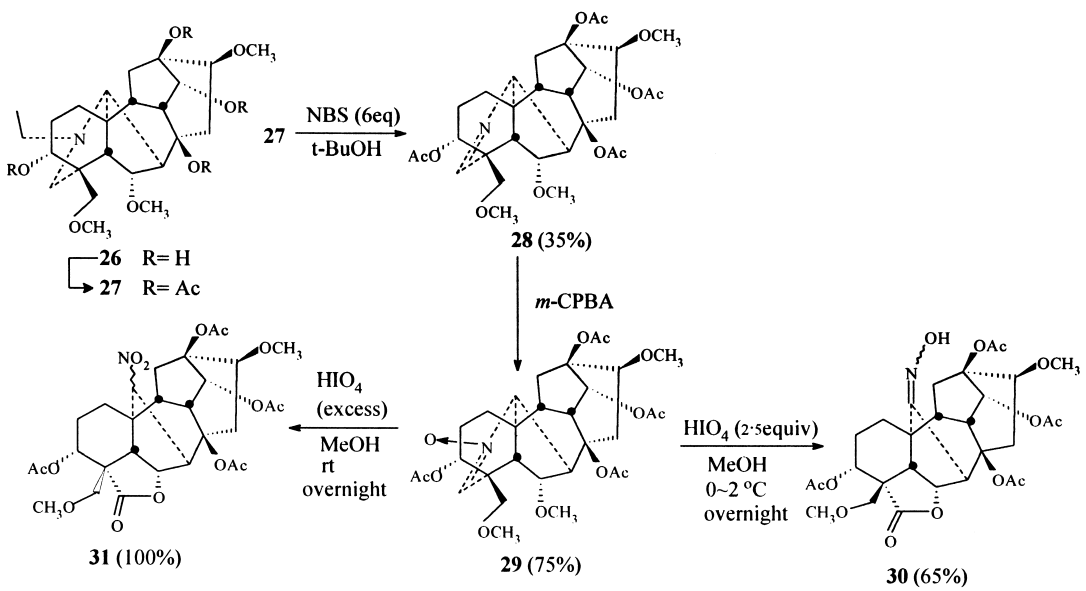
Figure 1. ORTEP drawing of **25**.

an aldehyde/ketone. However, when similar reaction conditions were applied to compound **10**, no desired compound **33** was detected.

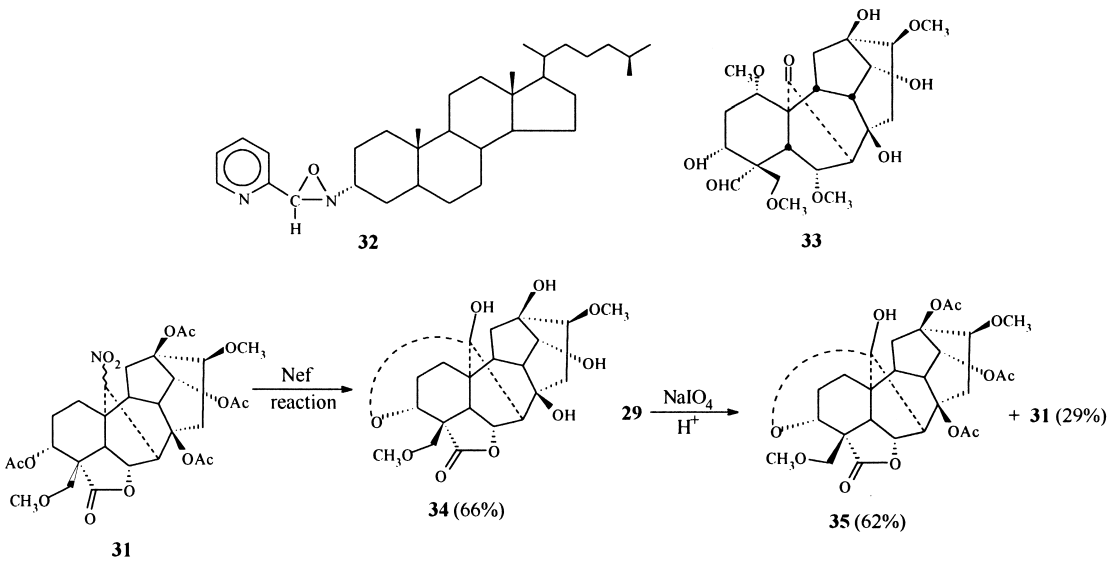
On the other hand, the fact that attempts to prepare the *N*,17-*seco* compound **22** from oxime **20** via Beckmann rearrangement (Scheme 9) failed led to search another method for this purpose. It is known that aliphatic nitro compounds may be converted through a Nef reaction into the corresponding ketones.[13] According to this method, the *N*,19-*seco* compound **31** was reacted with NaOH in MeOH at room temperature overnight, to which conc. HCl was then added. This solution was allowed to stand first at 0°C for 1 h, then at room temperature for 12 h to give the *N*,17-*seco* compound **34** in 66% yield (Scheme 11) with no response to Dragendorff's reagent. Its ^{1}H (^{13}C) NMR spectra showed the presence of two methoxyl groups (δ_H 3.21, 3.26, each 3H, s; δ_C 58.7, q, 59.4, q), one γ-lactone moiety (1765 cm^{-1}; δ_C 178.5, s) and a ketal group (δ_C 113.3, s). The structure of **34** has been established by unambiguous assignments of all of its ^{1}H (^{13}C) signals on the basis of 2D NMR spectra (Table 5). This is the first novel aconane-type diterpene produced from norditerpenoid alkaloids.

Interestingly, oxidative cleavage of the imine *N*-oxide **29** with only $NaIO_4/H^+$ instead of HIO_4 also afforded the aconane-type diterpene **35** in 62% yield (Scheme 11). The structure of **35** was determined based on spectral techniques and comparison with **34**.

In conclusion, a highly effective method for the synthesis of *N*,*O*-mixed acetals has been developed, which may provide a good basis for the cleavage of the *N*–C(19) bond through oxidation of the *N*,*O*-mixed ketals. Some new *N*,19-*seco* norditerpenoid alkaloids possessing an oxaziridine group (**10**, **13**) have been synthesized from yunaconitine **1** in five steps including acetylation, imination, quaternization, formation of *N*,*O*-mixed ketals and oxidation in 50% overall yields. This is a novel method for the synthesis of *N*,19-*seco* norditerpenoid alkaloids. When the cleavage of the *N*–C(19) bonds of the norditerpenoid alkaloids according to Büchi et al.[10] through oxidation of the imine *N*-oxides with HIO_4 has been studied, a series of novel *N*,19-*seco*



Scheme 10.



Scheme 11.

norditerpenoid alkaloids bearing the oximino or nitro groups (**20**, **30** or **21**, **31**) were prepared in moderate yield. Thus, we now have two methods for the synthesis of the *N*,19-*seco* norditerpenoid alkaloids.

Despite the fact that the attempt to synthesize the *N*,17-*seco* norditerpenoid alkaloids through hydrolysis of the oxaziridine according to the literature[9] failed for the *N*,19-*seco* oxaziridines (**10**), this method is still worth further investigation. Two novel aconane-type diterpenes (**34**, **35**) were synthesized from the *N*,19-*seco* nitro compound (**30**) through Nef reaction and the imine *N*-oxide (**29**) in moderate yield. It is worthy of note that the formation of **30**, **31** or **35** greatly depended on the reaction conditions (HIO_4 or $NaIO_4$–HCl). Thus, we have developed a new conversion method from the norditerpenoid alkaloids to the aconane-type diterpenes.

3. Experimental

3.1. General

Melting points are uncorrected. IR spectra were recorded on a Nicolet 200 SXV spectrometer; MS spectra were obtained with a Auto-Spec-3000 instrument; ^1H and ^{13}C NMR spectra were acquired on a Bruker Ac-E 200 or a Varian INOVA-400/54 spectrometer, with TMS as internal standard; Silica gel GF_{254} and H (10–40 μm, Qingdao Sea Chemical Factory, China) were used for TLC and CC. Only key signals in the ^1H NMR spectra, except for **10**, **25** and **34**, are reported.

3.1.1. 3-Acetylyunaconitine (2). To a solution of yunaconitine **1**, which was purchased from Yunnan Institute of Botany (200 mg, 0.30 mmol) in pyridine (5 mL), Ac_2O (5 mL) was added and the solution was allowed to stand at room temperature overnight. After basifying to pH 10 with 10% Na_2CO_3, the solution was extracted with $CHCl_3$ (15 mL×3) and the combined chloroform solutions were dried over anhydrous Na_2SO_4. Evaporation in vacuum afforded a residue (white amorphous powder, 198 mg, 97%), which was identified by comparison with the authentic sample [TLC: cyclohexane–acetone/2:1; $CHCl_3$–MeOH/95:5].

3.1.2. Compound 3. To a solution of 3-acetylyunaconitine **2** (700 mg, 1.00 mmol) in *t*-BuOH (40 mL), NBS (1.06 g, 6.00 mmol) was added and the solution was heated at 40°C overnight. Evaporation in vacuum to dryness afforded a residue, which was diluted with water. After basifying to pH 11 with NH_4OH, the solution was extracted with $CHCl_3$ (20 mL×3). Drying (Na_2SO_4), removal of solvent, and column chromatography (silica gel H, 30 g, $CHCl_3$–CH_3OH/99:1 to 98:1.5) afforded the pure product as a white amorphous powder, 556 mg (83%). Mp 125–127°C; R_f (95% $CHCl_3$–CH_3OH) 0.45; $[\alpha]_D^{20}$=+63.3 (*c* 0.30, $CHCl_3$); ν_{max} (KBr) 3441 (OH), 2934, 1713 (COO), 1640 (C=N), 1605, 1510, 1256, 1104 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.99, 6.92 (each 2H, AA′BB′, *J*=8.8 Hz, Ar-H), 7.37 (1H, brs, 19-H), 5.14 (1H, d, *J*=6.6 Hz, H-3β), 4.90 (1H, d, *J*=4.8 Hz, H-14β), 3.85 (3H, s, Ar-OCH_3), 3.55, 3.27, 3.18, 3.10 (each 3H, s, OCH_3×4), 2.07 (3H, s, 3-OAc); 1.31 (3H, s, 8-OAc), δ_C (50 MHz, $CDCl_3$) 170.3 (*CO*CH_3), 169.5 (*CO*CH_3) 165.9 (Ar*CO*), 163.4 (C-4″), 163.2 (C-19), 131.1 (C-2″,C-6″), 122.4 (C-1″), 113.7 (C-3″,C-5″), 84.0 (C-8), 83.5 (C-6), 83.0 (C-16), 80.3 (C-1), 78.3 (C-14), 74.6 (C-13), 72.9 (C-3), 72.4 (C-18), 61.5 (C-17), 58.9 (C-18′), 58.7 (C-16′), 57.3 (C-6′), 55.7 (C-1′), 55.3 (4″-OCH_3), 54.0 (C-7), 50.7 (C-4), 49.7 (C-11), 44.5 (C-5), 42.9 (C-9), 40.2 (C-10), 38.4 (C-15), 35.1 (C-12), 29.9 (C-2), 21.9 (CO*C*H_3), 21.4 (CO*C*H_3); *m/z* (EI) 671 (5, M^+), 612 (45, M−AcO); HRMS (FAB): M^++1, found 672.3059, $C_{35}H_{46}NO_{12}$ requires 672.3020.

3.1.3. Compound 4. To a solution of compound **3** (300 mg, 0.45 mmol) in methanol (5 mL), CH_3I (0.5 mL) was added and the solution was allowed to stand at room temperature overnight. Evaporation in vacuum afforded the product as a white amorphous powder, 363 mg (100%); mp 185–186°C; R_f (90% $CHCl_3$–MeOH) 0.55; ν_{max} (KBr) 3451 (OH), 2940, 2830, 1724 (COO), 1616 (C=N), 1284, 1233,

1105 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 9.62 (1H, brs, H-19), 7.98, 6.94 (each 2H, AA′BB′, J=8.6 Hz, Ar-H), 5.57 (1H, d, J=6.0 Hz, H-3β), 4.88 (1H, d, J=4.8 Hz, H-14β), 4.20 (3H, s, NCH_3), 3.88, 3.65, 3.33, 3.24, 3.12 (each 3H, s, OCH_3×5), 2.31 (3H, s, 3-OAc), 1.36 (3H, s, 8-OAc); δ_C (100 MHz, $CDCl_3$) 179.3 (C-19), 170.6 ($CO$$CH_3$), 169.6 ($CO$$CH_3$), 165.7 (Ar$CO$), 163.7 (C-4″), 131.6 (C-2″,C-6″), 121.8 (C-1″), 113.9 (C-3″,C-5″), 82.1 (C-8), 81.5 (C-1), 81.5 (C-16), 78.0 (C-6), 77.7 (C-14), 74.5 (C-13), 74.4 (C-3), 72.7 (C-18), 69.3 (C-17), 59.1 (C-16′), 59.1 (C-18′), 57.9 (C-6′), 56.9 (C-1′), 55.4 (4″-OCH_3), 54.3 (C-7), 54.3 (C-4), 53.0 (C-11), 47.6 (C-21), 41.8 (C-9), 41.8 (C-5), 38.6 (C-15), 37.7 (C-10), 35.4 (C-12), 26.4 (C-2), 21.9 (COCH_3), 21.2 (COCH_3); m/z (FAB) 687 (100, M^++1); HRMS (FAB): M^++1, found 687.3174, $C_{36}H_{48}NO_{12}$ requires 687.3176.

3.1.4. Compound 5. To a solution of compound **4** (100 mg, 0.12 mmol) in CH_2Cl_2 (5 mL), conc. NH_4OH (5 mL) was added, and stirred for 10 min. The water layer was extracted with $CHCl_3$ (5 mL×3). Drying (Na_2SO_4) and evaporation afforded the product as white amorphous powder; 85 mg (100%); mp 160–162°C; R_f (90% $CHCl_3$–MeOH) 0.40; $[\alpha]_D^{20}$=+42.0 (c 0.50, $CHCl_3$); ν_{max} (KBr) 3427 (OH), 2932, 1724 (COO), 1606, 1513, 1256, 1100 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.99, 6.90 (each 2H, AA′BB′, J=8.8 Hz, Ar-H), 4.90 (1H, t, J=5.0 Hz, H-3β), 4.84 (1H, d, J=4.6 Hz, H-14β), 4.32 (1H, s, H-19), 3.85, 3.52, 3.28, 3.21, 3.20 (each 3H, s, OCH_3×5), 2.57 (3H, s, NCH_3), 2.03 (3H, s, 3-OAc), 1.30 (3H, s, 8-OAc); δ_C (50 MHz, $CDCl_3$) 169.9 (COCH_3), 169.6 (COCH_3), 165.9 (ArCO), 163.3 (C-4″), 131.6 (C-2″,C-6″), 122.4 (C-1″), 113.6 (C-3″,C-5″), 84.4 (C-8), 84.0 (C-19), 83.2 (C-16), 80.5 (C-1), 80.5 (C-6), 78.1 (C-14), 74.6 (C-13), 70.5 (C-3), 70.2 (C-18), 60.7 (C-17), 58.8 (C-16′), 58.8 (C-18′), 58.0 (C-6′), 56.1 (C-1′), 55.4 (4″-OCH_3), 52.1 (C-7), 49.8 (C-11), 47.4 (C-4), 45.6 (C-5), 44.5 (C-9), 40.0 (C-10), 38.8 (C-15), 37.7 (C-21), 34.6 (C-12), 31.1 (C-2), 21.5 (COCH_3), 21.0 (COCH_3); m/z (FAB) 704 (100, M^++1); HRMS (FAB): M^++1, found 704.3300, $C_{36}H_{50}NO_{13}$ requires 704.3282.

3.1.5. Compounds 10 and 11. To a solution of compound **5** (412 mg, 0.58 mmol) in CH_2Cl_2 (10 mL), m-CPBA (400 mg, 2.32 mmol) was added. The solution was allowed to stand at room temperature for 20 min, then 10% Na_2CO_3 solution (10 mL) was added. Extraction (CH_2Cl_2, 8 mL×3), drying (Na_2SO_4), evaporation and column chromatography (silica gel H, cyclohexane–acetone/3:1) afforded the pure product **10** (white amorphous powder, 300 mg, 73%) and a by-product **11** (white amorphous powder, 40 mg, 8%).

Compound **10**. Mp 170–172°C; R_f (67% cyclohexane–acetone) 0.50; $[\alpha]_D^{20}$=+20.0 (c 0.30, $CHCl_3$); ν_{max} (KBr) 3461 (OH), 2931, 1724 (COO), 1604, 1511, 1236, 1100 cm^{-1}; δ_H (400 MHz, $CDCl_3$) and δ_C (100 MHz, $CDCl_3$) see Table 1; m/z (EI) 717 (5, M^+), 687 (15), 672 (16); HRMS (FAB): M^++1, found 718.3095, $C_{36}H_{48}NO_{14}$ requires 718.3074.

Compound **11**. Mp 249–251°C; R_f (67% cyclohexane–acetone) 0.54; $[\alpha]_D^{20}$=+71.4 (c 0.50, $CHCl_3$); ν_{max} (KBr) 3455 (OH), 2893, 2820, 1733 (COO), 1605, 1576, 1513, 1463, 1430, 1369, 1256, 1168, 1100, 1022, 976, 750 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.94, 7.85, 7.52, 7.36 [each 1H, m, C_6H_4–Cl (m)], 8.00, 6.90 (each 2H, AA′BB′, J=8.8 Hz, H-2″/6″, H-3″/5″), 6.55 (1H, s, H-19), 4.95 (1H, dd, J=10.0, 7.8 Hz, H-3β), 4.84 (1H, d, J=4.8 Hz, H-14β), 3.85, 3.53, 3.28, 3.27, 3.27 (each 3H, s, OCH_3×5), 2.47 (3H, s, N–CH_3), 1.91 (3H, s, 3-OAc), 1.29 (3H, s, 8-OAc); δ_C (100 MHz, $CDCl_3$) 169.9 (COCH_3), 169.3 (COCH_3), 166.0 (ArCO), 163.4 (C-4″), 162.9 (ArCO), 134.5 (C-3‴), 133.2 (C-6‴), 131.6 (C-1‴), 131.6 (C-2″,C-6″), 129.9 (C-2‴), 129.7 (C-3‴), 127.8 (C-5‴), 122.5 (C-1″), 113.7 (C-3″,C-5″), 95.6 (C-19), 85.1 (C-8), 84.1 (C-16), 83.5 (C-1), 80.8 (C-6), 78.2 (C-14), 75.0 (C-13), 70.7 (C-17), 69.7 (C-18), 68.9 (C-3), 59.0 (C-18′), 58.7 (C-16′), 58.3 (C-6′), 56.2 (C-1′), 55.4 (4″-OCH_3), 50.7 (C-4), 50.2 (C-7), 49.9 (C-11), 46.5 (C-5), 44.7 (C-21), 43.7 (C-9), 43.0 (C-10), 39.8 (C-15), 33.7 (C-12), 30.3 (C-2), 21.5 (COCH_3), 20.9 (COCH_3); m/z (EI) 859 (9, M_1^+), 857 (25, M_2^+), 787 (9), 718 (5); HRMS (FAB): M^++1, found 858.3046, $C_{43}H_{53}NO_{15}Cl$ requires 858.3103.

3.1.6. Compound 12. To a solution of 3-acetylyunaconitine **2** (200 mg, 0.29 mmol) in t-BuOH–H_2O–HOAc (5:1:0.5, v/v) (20 mL), NBS (305 mg, 1.74 mmol) was added and the solution was heated at 40°C for 6 h. Removal of solvent, basifying (NH_4OH), extraction ($CHCl_3$), drying (Na_2SO_4) and column chromatography afforded the pure product (white amorphous powder, 150 mg, 75%). Mp 159–161°C; R_f (90% $CHCl_3$–MeOH) 0.50; $[\alpha]_D^{20}$=+42.0 (c 0.50, $CHCl_3$); ν_{max} (KBr) 3430 (OH), 2925, 2851, 1725 (COO), 1605, 1511, 1459, 1371, 1257, 1171, 1106, 1024 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 9.59 (1H, brs, H-19), 7.93, 6.89 (each 2H, AA′BB′, J=8.8 Hz, Ar-H), 5.53 (1H, d, J=5.6 Hz, H-3β), 4.86 (1H, d, J=4.6 Hz, H-14β), 3.83, 3.58, 3.28, 3.14, 3.06 (each 3H, s, OCH_3×5), 2.22 (3H, s, 3-OAc), 1.55 (3H, s, N–CH_2CH_3), 1.32 (3H, s, 8-OAc); δ_C (50 MHz, $CDCl_3$), 179.9 (C-19), 170.5 ($CO$$CH_3$), 169.6 ($CO$$CH_3$), 165.7 (Ar$CO$), 163.7 (C-4″), 131.6 (C-2″,C-6″), 121.7 (C-1″), 113.8 (C-3″,C-5″), 82.2 (C-8), 82.0 (C-16), 81.5 (C-1), 78.7 (C-6), 77.7 (C-14), 74.4 (C-13), 74.1 (C-3), 72.9 (C-18), 66.9 (C-17), 59.1 (C-18′), 59.1 (C-16′), 57.7 (C-6′), 56.0 (C-21), 55.9 (C-1′), 55.4 (4″-OCH_3), 54.8 (C-7), 52.7 (C-4), 48.8 (C-11), 42.1 (C-5), 41.8 (C-9), 38.6 (C-15), 38.0 (C-10), 35.6 (C-12), 31.7 (C-2), 21.4 (COCH_3), 21.2 (COCH_3), 14.3 (C-22); m/z (EI) 700 (2, M^+), 685 (9, M–CH_3), 670 (7 M–OCH_3+1); HRMS (FAB): M^++1, found 701.3414, $C_{37}H_{51}NO_{12}$ requires 701.3411.

3.1.7. Compound 13. To a solution of compound **12** (100 mg, 0.12 mmol) in CH_2Cl_2 (5 mL), conc. NH_4OH (5 mL) was added, then stirring vigorously at room temperature for 10 min. After a general work-up, the pure amorphous powder (85 mg) was obtained. To a solution of this residue in CH_2Cl_2 (5 mL), m-CPBA (83 mg 0.48 mmol) was added and the solution was allowed to stand at room temperature for 20 min. Basifying (10% Na_2CO_3), extraction ($CHCl_3$, 8 mL×3), drying (Na_2SO_4), removal of solvent and column chromatography (silica gel H, cyclohexane–acetone/3.5:1) afforded the pure product (white amorphous powder, 61 mg, 70%). Mp 159–161°C; R_f (97% $CHCl_3$–MeOH) 0.50; $[\alpha]_D^{20}$=−56.4 (c 0.55, $CHCl_3$); ν_{max} (KBr) 3458 (OH), 2930, 1725 (COO), 1605, 1513, 1257, 1100 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 10.32 (10.23) (1H, s, H-19), 7.96 (7.96), 6.88 (6.88) (each 2H, AA′BB′, J=8.6 Hz, Ar-H), 4.90 (4.90) (1H, dd, J=13.0, 2.4 Hz,

Table 2. ^{13}C NMR data of compounds **15**, **16**, **17**, **18**, **20** and **21**

No.	**15**	**16**	**17**	**18**	**20**	**21**
1	81.8 d	81.8 d	83.2 d	82.1 d	81.8 d	81.0 d
2	28.4 t	28.5 t	32.6 t	32.1 t	29.7 t	28.8 t
3	69.8 d	69.8 d	66.2 d	65.9 d	68.5 d	67.3 d
4	50.4 s	50.8 s	52.0 s	51.4 s	51.8 s	51.5 s
5	50.6 d	49.8 d	49.9 d	50.8 d	51.3 d	52.1 d
6	81.0 d	81.0 d	79.5 d	78.3 d	77.1 d	79.9 d
7	50.6 d	50.9 d	51.0 d	52.3 d	49.4 d	55.3 d
8	83.6 s	83.7 s	83.6 s	82.5 s	83.6 s	82.3 s
9	49.2 d	47.4 d	48.0 d	46.8 d	44.8 d	47.1 d
10	42.5 d	42.4 d	42.7 d	42.3 d	43.6 d	43.1 d
11	50.2 s	50.2 s	49.9 s	49.5 s	50.6 s	50.5 s
12	33.3 t	33.3 q	34.2 t	33.2 t	35.1 t	33.8 t
13	75.8 s	75.6 s	75.9 s	75.6 s	75.2 s	75.6 s
14	78.2 d	78.2 d	78.3 d	78.0 d	78.2 d	77.5 d
15	39.5 t	39.5 t	40.0 t	39.5 t	38.0 t	40.6 t
16	82.9 d	82.7 d	82.9 d	82.8 d	83.1 d	82.8 d
17	55.7 d	55.8 d	55.2 d	55.9 d	154.7 s	89.9 d
18	71.1 t	70.6 t	–	–	75.4 t	75.1 t
19	177.5 s	175.2 s	175.1 s	175.2 s	172.5 s	172.9 s
21	162.5 d	160.2 d	160.3 d	–	–	–
22	–	–	–	–	–	–
1′	56.2 q	56.4 q	56.6 q	56.3 q	57.2 q	56.4 q
6′	57.8 q	57.8 q	57.4 q	57.9 q	–	–
16′	58.8 q	58.8 q	58.9 q	59.0 q	58.6 q	59.2 q
18′	59.1 q	59.1 q	59.5 q	59.3 q	59.4 q	59.4 q
19′	–	51.8 q	52.0 q	52.3 q	–	–
OAc	170.0 s	169.5 s	169.3 s	168.8 s	170.6 s	170.7 s
	169.4 s	169.2 s	–	–	20.8 q	20.9 q
	20.9 q	20.7 q	21.3 q	21.0 q	168.9 s	169.0 s
	21.3 q	21.2 q	–	–	21.1 q	21.0 q
14-Oa s						
CO	166.0 s	166.0 s	166.2 s	166.6 s	166.1 s	165.8 s
1″	122.3 s	122.3 s	122.3 s	121.9 s	122.0 s	121.7 s
2″,6″	131.6 d	131.6 d	131.7 d	131.6 d	131.6 d	131.8 d
3″,5″	113.7 d	113.7 d	113.8 d	113.8 d	113.8 d	113.9 d
4″	163.4 s	163.4 s	163.6 s	163.3 s	163.6 s	163.7 s
4″-OMe	55.3 q	55.3 q	55.4 q	55.3 q	55.3 q	55.4 q

H-3β), 4.80 (4.82) (1H, d, *J*=4.2 Hz, H-14β), 4.04 (4.36) (1H, q, *J*=5.0 Hz, N*CH*CH$_3$), 3.82 (3.82), 3.50 (3.50), 3.30 (3.30), 3.30 (3.00), 3.00 (3.00) (each 3H, s, OCH$_3$×5), 1.98 (2.00) (3H, s, 3-OAc), 1.37 (1.57) (3H, d, *J*=5.0 Hz, –NCH*CH*$_3$), 1.31 (1.32) (3H, s, 8-OAc); δ_C (50 MHz, CDCl$_3$) see Table 1; *m/z* (EI) 731 (2, M$^+$), 716 (3, M−CH$_3$), 672 (12), 644 (50); HRMS (FAB): M$^+$+1, found 732.3222, $C_{37}H_{50}NO_{14}$ requires 732.3231.

3.1.8. Compound 14. A solution of compound **10** (80 mg, 0.11 mmol) in 15% HCl (10 mL) was allowed to stand at room temperature for 5 h. Basifying (NH$_4$OH, pH 11), extraction (CHCl$_3$, 8 mL×3), drying (Na$_2$SO$_4$), and column chromatography (silica gel H, CHCl$_3$–CH$_3$OH/98:2) afforded the pure product (**14**) (white amorphous powder, 20 mg, 30%) besides the other product (**3**) (30 mg, 46%). *Compound* **14**. Mp 135–137°C; R_f (95% CHCl$_3$–MeOH) 0.40; δ_H (200 MHz, CDCl$_3$) 8.00, 6.87 (each 2H, AA′BB′, Ar-H), 7.49 (1H, brs, H-19), 4.88 (1H, d, *J*=4.8 Hz, H-14β), 3.84, 3.54, 3.33, 3.26, 3.05 (each 3H, s, OCH$_3$×5), 1.03 (3H, s, 8-OAc); δ_C (50 MHz, CDCl$_3$) 169.5 (*CO*CH$_3$), 165.9 (Ar*CO*), 164.6 (C-19), 163.5 (C-4″), 131.7 (C-2″,C-6″) 122.3 (C-1″), 113.8 (C-3″,C-5″), 84.1 (C-8), 83.1 (C-16), 83.1 (C-6), 82.1 (C-1), 78.5 (C-14), 76.2 (C-13), 74.6 (C-18), 73.3 (C-3), 61.5 (C-17), 59.1 (C-18′), 58.8 (C-16′), 57.1 (C-6′), 56.5 (C-1′), 55.4 (4″-OCH$_3$), 53.9 (C-7), 52.0 (C-11), 51.2 (C-4), 45.5 (C-5), 40.7 (C-10), 39.7 (C-15), 36.1 (C-12), 31.0 (C-2), 21.4 (CO*CH*$_3$); *m/z* (EI) 629 (5, M$^+$) 597 (15), 566 (30). The structure of **14** was identified by comparison of NMR and TLC (CHCl$_3$–MeOH/95:5; ether–acetone/7:3) with the authentic sample.

3.1.9. Compound 15. To a solution of compound **10** (340 mg, 0.47 mmol) in a mixture of acetone (8 mL) and 10% H$_2$SO$_4$ (4 mL), KMnO$_4$ (600 mg, 3.79 mmol) was added and the solution was stirred at room temperature for 3.5 h. To the reaction solution was added NaHSO$_3$ (500 mg) and the solution was stirred vigorously. Filtering, washing with acetone, removal of solvent, diluting (H$_2$O, 10 mL), extraction (CHCl$_3$, 10 mL×3), drying (Na$_2$SO$_4$), evaporation and column chromatography (silica gel H, CHCl$_3$–CH$_3$OH/98:2) afforded the product as white amorphous powder, 100 mg (30%). Mp 249–251°C; R_f (90% CHCl$_3$–MeOH/9:1) 0.46; $[\alpha]_D^{20}$=+34.1 (*c* 0.44, CHCl$_3$); ν_{max} (KBr) 3425 (OH), 3277 (COOH), 2935, 1723 (COO), 1673 (CONH), 1606, 1512, 1257, 1099 cm^{-1}; δ_H (400 MHz, CDCl$_3$) 9.98 (1H, d, *J*=8.4 Hz, HCO*NH*, exchangeable with D$_2$O), 8.23 (8.28) (1H, dd, *J*=1.6 (2.0) Hz, *HCO*NH), 8.00, 6.89 (each 2H, AA′BB′, *J*=8.6 Hz, Ar-H), 5.05 (1H, dd, *J*=12.8, 4.4 Hz, H-3β), 4.83 (1H, d, *J*=4.4 Hz, H-14β), 3.84, 3.58, 3.37, 3.20, 3.06 (each 3H, s, OCH$_3$×5), 2.05 (3H, s, 3-OAc), 1.31 (3H, s, 8-OAc); δ_C (100 MHz, CDCl$_3$) see Table 2; HMQC: correlation between *H*CON and H*C*ON; *m/z* (FAB) 734 (65, M$^+$+1), 674 (10); HRMS (FAB): M$^+$+1, found 734.3057, $C_{36}H_{48}NO_{15}$ requires 734.3023.

3.1.10. Compound 16. To a solution of compound **15** (100 mg, 0.14 mmol) in CH$_3$OH (3 mL), a mixture of CH$_3$I (0.5 mL) and anhydrous Na$_2$CO$_3$ (7 mg) was added and the solution was stirred at room temperature overnight. Filtration, removal of solvent and column chromatography (silica gel H, CHCl$_3$–CH$_3$OH/99:1) afforded the pure product as white amorphous powder, 65 mg (64%). Mp 159–161°C; R_f (97% CHCl$_3$–MeOH) 0.45; $[\alpha]_D^{20}$=+18.4 (*c* 0.38, CHCl$_3$); ν_{max} (KBr) 3453 (OH), 3305 (NH), 2944, 2835, 1720 (COO), 1675 (CONH), 1605, 1549, 1512, 1438, 1369, 1257, 1171, 1096, 1029, 981, 772 cm^{-1}; δ_H (200 MHz, CDCl$_3$) 8.92 (1H, dd, *J*=8.4, 1.6 Hz, *NH*CHO), 8.09 (8.21) (1H, d, *J*=1.6 (1.6) Hz, *H*CONH) 7.98, 6.85 (each 2H, AA′BB′, *J*=8.6 Hz, Ar-H), 5.01 (1H, dd, *J*=3.6, 1.3 Hz, H-3β), 4.78 (1H, d, *J*=5.0 Hz, H-14β), 3.62 (3H, s, C(19)OOCH$_3$), 3.81, 3.55, 3.35, 3.20, 2.96 (each 3H, s, OCH$_3$×5), 1.97 (3H, s, 3-OAc), 1.27 (3H, s, 8-OAc); δ_C (50 MHz, CDCl$_3$) see Table 2; *m/z* (EI) 747 (1, M$^+$), 717 (3), 687 (20); HRMS (FAB): M$^+$+1, found 748.3138, $C_{37}H_{50}NO_{15}$ requires 748.3180.

3.1.11. Compounds 17 and 18. To a solution of compound **16** (165 mg, 0.22 mmol) in THF (3 mL), 15% HCl (4 mL) was added and the solution was stirred first at room temperature for 2 h, then at 50°C for 3 h. Removal of solvent, basifying (NH$_4$OH, pH 8) extraction (CHCl$_3$, 5 mL×4), drying (Na$_2$SO$_4$) and column chromatography (silica gel H, CHCl$_3$–CH$_3$OH/99:1) afforded the pure product as white amorphous powder (**17**: 77 mg, 50%; **18**: 40 mg, 26%).

Compound **17**. Mp 204–205°C; R_f (95% CHCl$_3$–MeOH) 0.40; $[\alpha]_D^{20}$=−5.6 (*c* 0.71, CHCl$_3$); ν_{max} (KBr) 3450 (OH), 3302 (NH), 2929, 1715 (COO), 1668 (CONH), 1606, 1552, 1512, 1461, 1370, 1282, 1258, 1170, 1100, 1024 cm^{-1}; δ_H

Table 3. NMR data of compound **25**

No.	δ_H	Mult (J=Hz)	δ_C	HMBC (H→C)
1	5.34	m	58.3 d	C-2, C-3, C-11
2	1.96	ddd (2.0, 11.2, 16.0)	34.2 t	C-1, C-3, C-4, C-11
	2.15	m		
3	5.43	dd (4.8, 11.2)	65.8 d	C-2, C-4, C-18, C-19, C-3′
4	–	–	50.2 s	–
5	2.97	d (7.2)	50.8 d	C-4, C-10, C-11, C-17, C-18, C-19
6	4.61	d (7.2)	77.1 d	C-8, C-11, C-17, C-19, C-7′
7	3.70	s	55.7 d	C-3, C-5, C-6, C-8, C-11, C-15, C-17
8	–	–	83.5 s	–
9	2.79	dd (4.4, 6.4)	42.9 d	C-8, C-10, C-12, C-13, C-14
10	2.85	m	41.7 d	C-8, C-9, C-11, C-17
11	–	–	55.7 s	–
12	1.39	dd (6.0, 14.8)	33.6 t	C-10, C-11, C-13, C-14, C-16
	2.10	dd (hidden)		C-10, C-13, C-16
13	–	–	75.4 s	–
14	4.82	d (4.4)	78.1 d	C-8, C-13, C-16, C-14′
15	2.25	dd (5.6, 14.8)	39.2 t	C-7, C-8
	3.20	dd (8.8, 14.8)		C-7, C-8, C-9, C-13
16	3.12	dd (5.6, 8.8)	83.1 d	C-14, C-16′
17	–	–	154.9 s	–
18	3.39	ABq (8.4)	77.8 t	C-3, C-4, C-5, C-19
	3.57	ABq (8.4)		C-4, C-5, C-19
19	–	–	173.5 s	–
16′	3.45	s	58.9 q	C-16
18′	3.26	s	59.4 q	C-18
N–OCH_3	3.79	s	62.7 q	–
3-OAc	–	–	170.4 s	–
	2.05	s	20.9 q	C-3′
8-OAc	–	–	169.0 s	–
	1.31	s	21.1 q	C-8′
14-OAs				
CO	–	–	165.9 s	–
1″	–	–	122.0 s	–
2″,6″	7.92	AA′BB′ (8.8)	131.6 d	C-14′, C-4″, C-6″
3″,5″	6.86	AA′BB′ (8.8)	113.8 d	C-1″, C-4″, C-5″
4″	–	–	163.6 s	–
4″-OCH_3	3.78	s	55.4 q	C-4″

(200 MHz, $CDCl_3$) 9.38 (1H, dd, J=8.8, 1.6 Hz, HCO*NH*), 8.07 (8.20) (1H, d, J=1.6 (1.6) Hz *H*CONH–), 8.02, 6.93 (each 2H, AA′BB′, J=8.8 Hz, Ar-H), 4.81 (1H, d, J=4.8 Hz, H-14β), 4.37 (1H, brs, 3-OH), 4.24 (1H, A of AB, J=9.2 Hz, H-18), 3.72 (3H, s, C(19)OO*CH*$_3$), 3.87, 3.60, 3.36, 3.25, 2.99 (3H, s, OCH_3×5), 1.33 (3H, s, 8-OAc); δ_C (50 MHz, $CDCl_3$) see Table 2; m/z (EI) 705 (1, M^+), 675 (2, M−30), 645 (17), 630 (18); HRMS (FAB): M^++1, found 706.3013, $C_{35}H_{48}NO_{14}$ requires 706.3074.

Compound **18**. Mp 161–163°C; R_f (95% $CHCl_3$–MeOH) 0.46; $[\alpha]_D^{20}$=+27.8 (c 0.79, $CHCl_3$); ν_{max} (KBr) 3426 (OH, NH), 2927, 2851, 1716 (COO), 1606, 1513, 1460, 1370, 1258, 1172, 1109 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.95, 6.90 (each 2H, AA′BB′, J=8.8 Hz, Ar-H), 4.77 (1H, d, J=4.6 Hz, H-14*β*), 3.67 (3H, s, C(19)OO*CH*$_3$), 3.82, 3.57, 3.31, 3.31, 3.05 (each 3H, s, OCH_3×5), 1.32 (3H, s, 8-OAc); δ_C (50 MHz, $CDCl_3$) see Table 2; m/z (EI) 677 (2, M^+), 662 (17, M−CH_3), 646 (57); HRMS (FAB): M^++1, found 678.3141, $C_{34}H_{48}NO_{13}$ requires 678.3125.

3.1.12. Compound 19. To a solution of compound **14** (100 mg, 0.15 mmol) in CH_2Cl_2 (5 mL), *m*-CPBA (77 mg, 0.45 mmol) was added and the solution was reacted at room temperature for 2 h. General work-up and column chromatography (silica gel H, $CHCl_3$–CH_3OH/98:2) afforded the pure product (white amorphous powder, 86 mg, 48%). Mp 118–120°C; R_f (95% $CHCl_3$–MeOH) 0.50; $[\alpha]_D^{20}$=+19.4 (c 0.98, $CHCl_3$); ν_{max} (KBr) 3440 (OH), 2934, 1721 (COO), 1642 (C=N), 1605, 1513, 1257, 1103 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.99, 6.91 (each 2H, AA′BB′, J=8.8 Hz, Ar-H), 6.75 (1H, d, J=1.3 Hz, H-19), 5.24 (1H, dd, J=6.0, 4.2 Hz, H-3β), 4.89 (1H, d, J=4.8 Hz, H-14β), 3.86, 3.56, 3.27, 3.19, 3.11 (each 3H, s, OCH_3×5), 2.06 (3H, s, 3-OAc), 1.32 (3H, s, 8-OAc); δ_C (50 MHz, $CDCl_3$) 170.4 (*CO*CH_3), 169.2 (*CO*CH_3), 165.8 (Ar*CO*), 163.6 (C-4″), 136.5 (C-19), 131.7 (C-2″,C-6″), 122.1 (C-1″), 113.8 (C-3″,C-5″), 82.9 (C-8), 82.3 (C-16), 82.1 (C-1), 78.9 (C-6), 78.0 (C-14), 74.5 (C-13), 74.0 (C-3), 73.1 (C-17), 73.0 (C-18), 58.9 (C-16′), 58.9 (C-18′), 57.3 (C-6′), 56.0 (C-1′), 55.4 (4″-OCH_3), 54.4 (C-7), 51.6 (C-11), 45.5 (C-4), 43.4 (C-5), 42.5 (C-9), 38.6 (C-10), 38.3 (C-15), 35.4 (C-12), 28.3 (C-2), 21.3 (CO*CH*$_3$), 20.9 (CO*CH*$_3$); m/z (EI) 687 (18, M^+), 671 (4), 612 (25); HRMS (FAB): M^++1, found 688.2913, $C_{35}H_{45}NO_{13}$ requires 688.2969.

3.1.13. Compounds 20 and 21. To a solution of 3-acetylyunaconitine *N*-oxide (**19**) (200 mg, 0.29 mmol) in MeOH (5 mL), HIO_4 (334 g, 1.74 mmol) was added and the solution was allowed to stand at 0–2°C overnight. Work-up and chromatography over Chromatodron (silica gel H, 1 mm, cyclohexane–acetone/3:1) afforded the pure products **20** (110 mg, 55%) and **21** (colorless needles, 43 mg, 21%).

Compound **20**. Mp 189–191°C; R_f (67% cyclohexane–acetone) 0.52; $[\alpha]_D^{20}$=−24.0 (c 0.50, $CHCl_3$); ν_{max} (KBr)

Table 4. ^{13}C NMR data of compounds **26**, **27**, **28**, **29**, **30** and **31**

No.	26	27	28	29	30	31
1	28.9 t	25.9 t	25.0 t	25.3 t	24.3 t	20.2 t
2	29.1 t	28.6 t	28.3 t	27.3 t	24.6 t	24.6 t
3	74.9 d	73.9 d	73.4 d	73.7 d	70.6 d	66.1 d
4	43.0 s	42.1 s	45.6 s	46.1 s	51.3 s	51.2 s
5	49.3 d	46.7 d	55.3 d	56.0 d	45.4 d	52.7 d
6	82.5 d	80.1 d	79.6 d	79.1 d	79.3 d	79.3 d
7	52.0 d	42.7 d	41.6 d	40.4 d	48.2 d	47.2 d
8	73.9 s	85.6 s	84.0 s	82.9 s	83.7 s	82.7 s
9	49.1 d	48.3 d	45.7 d	44.9 d	50.6 d	50.2 d
10	41.4 d	40.9 d	41.4 d	41.4 d	41.2 d	40.7 d
11	45.7 s	46.0 s	50.4 s	46.1 s	45.5 s	49.9 s
12	37.2 t	37.1 t	36.8 t	36.6 t	33.9 t	35.3 t
13	76.5 s	81.1 s	81.0 s	80.6 s	81.5 s	81.2 s
14	79.1 d	77.0 d	76.9 d	76.7 d	77.0 d	76.1 d
15	43.0 t	39.7 t	38.5 t	38.3 t	38.1 t	39.9 t
16	83.1 d	83.7 d	83.8 d	82.3 d	78.2 d	81.2 d
17	64.5 d	63.2 d	63.0 d	73.7 d	155.8 s	89.5 d
18	77.6 t	71.7 t	70.8 t	70.8 t	76.1 t	77.4 t
19	48.8 t	48.8 t	165.0 d	135.4 d	173.6 s	174.3 s
21	47.1 t	47.5 t	–	–	–	–
22	13.5 q	13.3 q	–	–	–	–
6′	57.4 q	57.7 q	57.6 q	57.2 q	–	–
16′	57.9 q	57.7 q	58.0 q	58.2 q	58.2 q	58.4 q
18′	59.1 q	58.1 q	58.9 q	58.9 q	59.4 q	59.4 q
	–	169.4 s	169.1 s	168.7 s	168.7 s	168.7 s
OAc	–	170.3 s	169.9 s	169.7 s	170.4 s	170.2 s
	–	170.5 s	170.4 s	170.3 s	170.7 s	170.3 s
	–	170.5 s	170.5 s	170.3 s	170.7 s	170.3 s
	–	21.0 q	20.9 q	20.9 q	20.9 q	20.5 q,
	–	21.1 q	21.0 q	21.0 q	20.9 q	20.9 q
	–	21.1 q	21.1 q	22.0 q	21.0 q	21.0 q
		22.1 q	22.2 q	22.1 q	21.8 q	21.8 q

3381 (OH), 2932, 1779 (γ-lactone), 1732, 1605, 1511, 1257, 1104 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 9.55 (1H, brs, –C=N*OH*), 7.98, 6.89 (each 2H, AA′BB′, J=8.8 Hz, Ar-H), 4.98 (1H, dd, J=3.2, 12.0 Hz, H-3), 4.84 (1H, d, J=5.2 Hz, H-14β), 4.72 (1H, d, J=6.4 Hz, H-6β), 3.85, 3.47, 3.34, 3.31 (each 3H, s, OCH_3×4), 1.37 (3H, s, 8-OAc), (1H, d, J=6.4 Hz, H-5); δ_C (50 MHz, $CDCl_3$) see Table 2; *m/z* (FAB) 688 (90, M^++1) HRMS (FAB):M^++1, found 688.2642, $C_{34}H_{42}NO_{14}$ requires 688.2605.

Compound **21**. Mp 248–250°C; R_f (67% cyclohexane–acetone) 0.44; $[\alpha]_D^{20}$=+27.3 (*c* 0.22, $CHCl_3$); ν_{max} (KBr) 3435 (OH), 2940, 1784 (γ-lactone), 1733 (COO), 1643, 1605, 1510, 1254, 1101, 1029 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 8.00, 6.93 (each 2H, AA′BB′, J=8.8 Hz, Ar-H), 5.13 (1H, dd, J=11.8, 4.2 Hz, H-3β), 4.85 (1H, d, J=6.2 Hz, H-6β), 4.83 (1H, d, J=4.8 Hz, H-14β), 4.43 (1H, s, H-17), 3.87, 3.62, 3.55, 3.27 (each 3H, s, OCH_3×4), 2.18 (3H, s, 3-OAc), 1.37 (3H, s, 8-OAc); δ_C (50 MHz, $CDCl_3$) see Table 2; *m/z* (FAB) 704 (100, M^++1); HRMS (FAB): M^++1, found 704.2519, $C_{34}H_{42}NO_{15}$ requires 704.2554.

3.1.14. Compound 25. To a solution of compound **20** (90 mg, 0.13 mmol) in pyridine (5 mL), TsCl (126 mg, 0.65 mmol) was added and the mixture was stirred at room temperature for 48 h. Removal of solvent, deluting with water, basifying (10% Na_2CO_3, pH 10), extraction ($CHCl_3$, 10 mL×3), drying (Na_2SO_4), evaporation of the combined chloroform layers and purification by column chromatography (silica gel H, cyclohexane–acetone/15:4) afforded the product as colorless needles, 65 mg (66%); mp 241–243°C; R_f (75% cyclohexane–acetone) 0.50; $[\alpha]_D^{20}$=+4.7 (*c* 0.85, $CHCl_3$); ν_{max} (KBr) 3454 (OH), 2934, 1780 (γ-lactone), 1739 (COO), 1643, 1605, 1510, 1254, 1101, 1029 cm^{-1}; δ_H (400 MHz, $CDCl_3$) and δ_C (100 MHz, $CDCl_3$) see Table 3; *m/z* (FAB) 706 (43, M_1^++1), 708 (16, M_2^++1); HRMS (FAB): M^++1, found 706.2224, $C_{34}H_{41}NO_3Cl$ requires 706.2266. *Crystal structure for* **25**. A colorless orthorhombic crystal from cydohexane–acetone was mounted on a P_4 four circle diffractometer and exposed to graphite-monochromated Mo Kα irradiation. The unit cell parameters are a=9.490 (2) Å, b=14.269 (3) Å, c=29.806 (5) Å, in space group $P2_12_12_1$, of the 5261 measured with $1.58 \leq \theta \leq 25.00°$ scan, 4799 were independently observed at the level of $F_0 > 4\sigma(F_0)$. The structure was solved by the directed method using the program SHELXTL and the atomic parameters were refined by the full-matrix least squares on F^2 method. The final R indices [$I > 2\sigma(I)$] was $R1$=0.0484, $WR2$=0.1108.

3.1.15. Compound 26. To a solution of yunaconitine **1** (1066 mg, 1.62 mmol) in acetone (20 mL), Jones reagent (1.75 mL, 4.8 mmol) was added dropwise under ice-water bath and the solution was stirred at 0°C for 20 min. Deluting (H_2O, 20 mL), basifying (conc. NH_4OH, pH 11), extraction ($CHCl_3$, 20 mL×5), drying (Na_2SO_4), and evaporation afforded the white amorphous powder, which was dissolved in 5% methanolic NaOH (25 mL) and heated at 55°C for 30 min. Removal of solvent, deluting (H_2O, 10 mL), extraction ($CHCl_3$, 10 mL×5), drying (Na_2SO_4), and evaporation afforded the white amorphous powder (726 mg). This residue (700 mg) was dissolved in 95% EtOH (35 mL). To this solution, 10% Pd–C (120 mg, 70 mL) was added and the mixture was stirred under hydrogen steam at room temperature for 5.5 h. Filtration was evaporated under reduced pressure to give the white amorphous powder (710 mg) that was subdivided into two parts A (100 mg) and B (610 mg).

To a solution of part A (100 mg, 0.22 mmol) in MeOH (3 mL), $NaBH_4$ (110 mg) was added and the mixture was stirred at room temperature for 30 min. Work-up using a general method afforded the product **26** as white amorphous powder, 104 mg (100%); mp 86.5–87.5°C; R_f (90% $CHCl_3$–MeOH) 0.38; $[\alpha]_D^{20}$=+15.1 (*c* 1.06, $CHCl_3$); ν_{max} (KBr) 3436 (OH), 2966, 2892, 2822, 1452, 1389, 1353, 1277, 1233, 1199, 1106, 1038, 978 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 3.42, 3.32, 3.32, (each 3H, s, OCH_3×3), 1.09 (3H, t, J=7.2 Hz, NCH_2CH_3); δ_C (50 MHz, $CDCl_3$) see Table 4; *m/z* (EI) 453 (100, M^+), 438 (91, M−15), 422 (28, M−31), 404 (29), 390 (52); HRMS (EI): M^+, found 453.2743, $C_{24}H_{39}NO_7$ requires 453.2726.

3.1.16. Compound 27. To a solution of compound **26** (104 mg, 0.23 mmol) in Ac_2O (4 mL), *p*-TsOH (110 mg) was added and the solution was heated at 60°C for 3 h. After pouring into ice water, the solution was basified with conc. NH_4OH to pH 11. Extraction ($CHCl_3$, 10 mL×3), drying (Na_2SO_4), removal of solvent afforded the pure product as colorless needle crystals, 150 mg (100%); mp 179–180°C; R_f (90% $CHCl_3$–MeOH) 0.75; $[\alpha]_D^{20}$=+11.9 (*c* 1.01, $CHCl_3$); ν_{max} (KBr) 2936, 1736 (COO), 1447, 1368, 1107, 1252, 1037 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.95 (1H, d, J=5.4 Hz, H-3β), 4.88 (1H, d, J=5.2 Hz, H-14β), 3.32, 3.25, 3.20 (each 3H, s, OCH_3×3), 2.06, 2.01, 1.97 (each 3H,

Table 5. NMR data of compounds **34** and **35**

No	**34**				**35**
	δ_H	Mult (J=Hz)	δ_C	HMBC (H→C)	δ_C
1	1.50	m (hidden)	17.7 t	C-10, C-11	18.2 t
	2.10	m (hidden)		C-5, C-11	
2	1.88	m (hidden)	21.2 t	–	21.3 t
3	4.06	d (2.0)	72.5 d	C-1, C-17, C-19	72.3 d
4	–	–	54.0 s	–	52.9 s
5	2.95	d (8.4)	47.8 d	C-3, C-4, C-7, C-10, C-17, C-18	48.5 d
6	5.15	d (8.4)	77.6 d	C-8, C-17, C-19	76.3 d
7	2.42	s	58.9 d	C-5, C-6, C-8, C-9, C-11, C-15, C-17	52.9 d
8	–	–	70.9 s	–	81.1 s
9	2.11	m (hidden)	45.8 d	C-8, C-10, C-12, C-13, C-14, C-15	40.6 d
10	2.22	m (hidden)	36.5 d	C-5, C-8, C-9, C-11, C-12, C-17	37.2 d
11	–	–	41.9 s	–	41.9 s
12	1.52	m (hidden)	35.0 t	C-10, C-11, C-13, C-14, C-16	33.5 t
	1.71	t (14)		C-9, C-10, C-11, C-13, C-16	
13	–	–	76.5 s	–	80.9 s
14	3.72	d (4.5)	77.8 d	C-8, C-13, C-16	76.3 d
15	2.20	m (hidden)	40.4 t	C-7, C-8, C-9, C-16	37.5 t
	2.40	m (hidden)		C-7, C-8, C-9, C-13, C-16	
16	2.57	t (8.4)	82.2 d	C-12, C-13, C-14, C-15, C-16′	78.3 d
17	–	–	113.3 s	–	111.9 s
18	3.43	ABq (9.6)	70.5 t	C-4, C-5, C-18′	70.4 t
	3.55	ABq (9.6)		C-4, C-5, C-18′	
19	–	–	178.5 s	–	177.4 s
16′	3.21	s	58.7 q	C-16	58.4 q
18′	3.26	s	59.4 q	C-18	59.2 q
OAc	–	–	–	–	168.4 s
	–	–	–	–	169.9 s
	–	–	–	–	170.3 s
	–	–	–	–	21.0 q
	–	–	–	–	21.0 q
	–	–	–	–	21.8 q

s, OAc×4), 1.10 (3H, t, J=7.0 Hz, NCH_2CH_3); δ_C (50 MHz, $CDCl_3$) see Table 4; m/z (EI) 621 (13, M^+), 606 (6, M−15), 590 (2, M−31), 578 (7, M−43), 562 (100, M−59); HRMS (EI): M^+, found 621.3112, $C_{32}H_{47}NO_{11}$ requires 621.3149.

3.1.17. Compound 28. To a solution of compound **27** (300 mg, 0.48 mmol) in *t*-BuOH (10 mL), NBS (516 mg, 2.88 mmol) was added and the mixture was heated at 50–55°C for 3.5 h. Removal of solvent, deluting ($CHCl_3$: 10 mL; 10% NH_4OH: 20 mL), extraction ($CHCl_3$, 10 mL×2), drying (Na_2SO_4) and column chromatography (silica gel H, cyclohexane–acetone/3:1→$CHCl_3$–MeOH/99:1) afforded the product as a white amorphous powder, 100 mg (35%). Mp 105–106°C; R_f (50% cyclohexane–acetone) 0.48; $[\alpha]_D^{20}$=+43.4 (c 1.06, $CHCl_3$); ν_{max} (KBr) 2941, 2821, 1735 (COO), 1643 (C=N), 1437, 1369, 1236, 1189, 1105, 1037 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.39 (1H, brs, H-19), 4.92 (1H, dd, J=10.3, 4.8 Hz, H-3β), 4.85 (1H, d, J=5.0 Hz, H-14β), 4.07, 3.47 (each 1H, ABq, J=8.8 Hz, H_2-18), 3.28, 3.22, 3.14, (each 3H, s, OCH_3×3), 2.05, 2.01, 2.01, 1.91 (each 3H, s, OAc×4); δ_C (50 MHz, $CDCl_3$) see Table 4; m/z (EI) 591 (13, M^+), 560 (16, M−31), 532 (100, M−59), 500 (40), 472 (59); HRMS (EI): M^+, found 591.2651, $C_{30}H_{41}NO_{11}$ requires 591.2679.

3.1.18. Compound 29. To a solution of compound **28** (146 mg, 0.25 mmol) in $CHCl_3$ (6 mL), *m*-CPBA (113 mg, 0.65 mmol) was added and the solution was stirred at room temperature for 50 min, then eluted with 10% Na_2CO_3 (6 mL). The separated aqueous layer was extracted with $CHCl_3$ (10 mL×3). Drying (Na_2SO_4), removal of solvent afforded the product as white amorphous powder, 112 mg (75%). Mp 153–154.5°C; R_f (50% cyclohexane–acetone) 0.23; $[\alpha]_D^{20}$=+75.5 (c 1.06, $CHCl_3$); ν_{max} (KBr) 2939, 1736 (COO), 1643 (C=N), 1593, 1440, 1370, 1235, 1105, 1039 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 6.78 (1H, brs, H-19), 5.01 (1H, dd, J=9.4, 4.8 Hz, H-3β), 4.89 (1H, d, J=5.2 Hz, H-14β), 3.32, 3.26, 3.21 (each 3H, s, OCH_3×3), 2.10, 2.06, 2.01, 1.98 (each 3H, s, OAc×4); δ_C (50 MHz, $CDCl_3$) see Table 4; m/z (EI) 607 (100, M^+), 548 (50, M−59), 532 (77, M−75), 488 (46), 472 (37), 456 (47); HRMS (EI): M^+, found 607.2622, $C_{30}H_{41}NO_{12}$ requires 607.2628.

3.1.19. Compound 30. To a solution of compound **29** (200 mg, 0.33 mmol) in MeOH (8 mL), HIO_4 (160 mg, 0.83 mmol) was added and the mixture was stirred at 0–2°C overnight. Basifying (10% Na_2CO_3, pH>9), extraction ($CHCl_3$, 10 mL×3), drying (Na_2SO_4), removal of solvent and column chromatography (silica gel H, $CHCl_3$–MeOH/100:2) afforded the pure product as white amorphous powder, 129 mg (65%). Mp 185–186°C; R_f (95% $CHCl_3$–MeOH) 0.56; $[\alpha]_D^{20}$=−9.4 (c 0.85, $CHCl_3$); ν_{max} (KBr) 3417 (OH), 2925, 2853, 1737 (COO), 1643 (C=N), 1444, 1371, 1234, 1112, 1042 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 9.15 (1H, brs, =N–OH), 4.89 (2H, m, H-3β, H-6β), 4.76 (1H, d, J=4.6 Hz, H-14β), 3.36, 3.27 (each 3H, s, OCH_3×2), 2.12, 2.12, 2.06, 2.02 (each 3H, s, OAc×4); δ_C (50 MHz, $CDCl_3$) see Table 4; m/z (EI) 607 (6, M^+), 576 (5, M−31), 547 (100, M−60), 532 (32), 487 (77); HRMS (EI): M^+, found 607.2276, $C_{29}H_{37}NO_{13}$ requires 607.2264.

3.1.20. Compound 31. To a solution of compound **29** (58 mg, 0.096 mmol) in MeOH (3 mL), HIO_4 (130 mg, 0.67 mmol) was added and the solution was stirred at room temperature overnight. Basifying (10% Na_2CO_3, pH>9), extraction ($CHCl_3$, 5 mL×3), drying (Na_2SO_4), and removal of solvent afforded the pure product as white amorphous powder, 60 mg (100%). Mp 155–156°C; R_f (95% $CHCl_3$–MeOH) 0.60; $[\alpha]_D^{20}$=+17.5 (*c* 1.03, $CHCl_3$); ν_{max} (KBr) 2925, 2853, 1776 (COO), 1739 (COO), 1636, 1561, 1443, 1370, 1236, 1115, 1039 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 5.01 (1H, d, *J*=4.8 Hz, H-3β), 4.88 (2H, d, *J*=5.6 Hz, H-14β, H-6β), 4.26 (1H, brs, H-17), 3.91 (1H, t, *J*=7.6 Hz, H-16α), 3.36, 3.34 (each 3H, s, OCH_3×2), 2.12, 2.10, 2.05, 2.05, (each 3H, s, OAc×4); δ_C (50 MHz, $CDCl_3$) see Table 4; *m/z* (EI) 623 (16, M^+), 607 (33, M−16), 563 (33, M−60), 532 (40), 517 (60), 503 (75); HRMS (EI): M^+, found 623.2234, $C_{29}H_{37}NO_{14}$ requires 623.2214.

3.1.21. Compound 34. To a solution of compound **31** (100 mg, 0.16 mmol) in ethanolic 5% KOH (3 mL) was added dropwise a solution of water (2.5 mL), ethanol (2.5 mL) and conc. HCl (3 mL) under ice-bath, first stirred under this condition for 3 h, then continued to react at room temperature for 12 h. Extraction ($CHCl_3$, 10 mL×3), drying (Na_2SO_4), removal of solvent and column chromatography (silica gel H, $CHCl_3$–MeOH/93:7) afforded the pure product as white amorphous powder, 45 mg (66%). Mp 215–215.5°C; R_f (90% $CHCl_3$–MeOH) 0.30; $[\alpha]_D^{20}$=−300.0 (*c* 0.22, CH_3OH); ν_{max} (KBr) 3530 (OH), 2935, 1765 (γ-lactone), 1548, 1449, 1349, 1243, 1173, 1094, 1047, 980 cm^{-1}; δ_H (400 MHz, DMSO-d_6) and δ_C (100 MHz, DMSO-d_6) see Table 5; *m/z* (EI) 424 (8, M^+), 407 (12, M−17), 405 (16, M−19), 389 (31, M−35), 374 (75), 358 (19), 345 (24), 325 (100); HRMS (EI): M^+, found 424.1741, $C_{21}H_{28}O_9$ requires 424.1733.

3.1.22. Compound 35. To a solution of compound **29** (100 mg, 0.16 mmol) in MeOH (3 mL) was added $NaIO_4$ (300 mg, 1.40 mmol) in 5% HCl (10 mL) and the solution was stirred at room temperature for 7 h. Basifying (saturated Na_2CO_3, pH>9), extraction ($CHCl_3$, 10 mL×3), drying (Na_2SO_4), removal of solvent and column chromatography (silica gel H, cyclohexane–acetone/3:1) afforded the products as white amorphous powder, **35** (69 mg, 62%) and **31** (30 mg, 29%). Compound **35**. Mp 164–165°C; R_f (50% cyclohexane–acetone) 0.80; $[\alpha]_D^{20}$=−39.2 (*c* 1.07, $CHCl_3$); ν_{max} (KBr) 3434 (OH), 2927, 2853, 1780 (γ-lactone), 1740 (COO), 1554, 1444, 1369, 1234, 1117, 1039 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 5.01 (1H, d, *J*=8.4 Hz, H-6β), 4.85 (1H, d, *J*=5.0 Hz, H-14β), 4.13 (1H, t, *J*=3.0 Hz, H-3β), 3.34, 3.26 (each 3H, s, OCH_3×2), 3.01 (1H, d, *J*=8.4 Hz, H-5), 2.12, 2.04, 2.00 (each 3H, s, OAc×3); δ_C (50 MHz, $CDCl_3$) see Table 5; *m/z* (EI) 550 (7, M^+), 533 (M−17), 517 (33), 490 (35), 473 (100); HRMS (EI): M^+, found 550.2016, $C_{27}H_{34}O_{12}$ requires 550.2050.

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