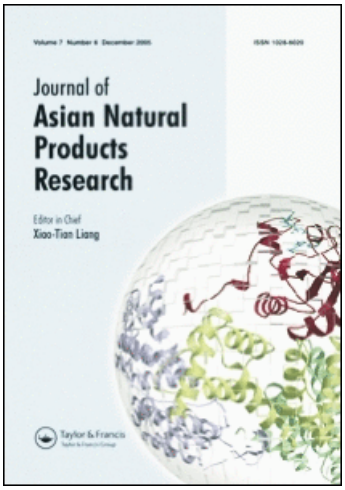

Journal of Asian Natural Products Research
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713454007

Further studies on CAB approach toward chemical conversion of C_{19}-diterpenoid alkaloids to taxoids: synthesis of the vital intermediate C-nor-aconanone

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To cite this Article Shen, Xiang-Li , Chen, Qiao-Hong and Wang, Feng-Peng(2009) 'Further studies on CAB approach toward chemical conversion of C_{19}-diterpenoid alkaloids to taxoids: synthesis of the vital intermediate C-nor-aconanone', Journal of Asian Natural Products Research, 11: 2, 97 — 109
To link to this Article: DOI: 10.1080/10286020801967128
URL: http://dx.doi.org/10.1080/10286020801967128

Journal of Asian Natural Products Research
Vol. 11, No. 2, February 2009, 97–109

Further studies on CAB approach toward chemical conversion of C_{19}-diterpenoid alkaloids to taxoids: synthesis of the vital intermediate C-nor-aconanone

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(*Received 4 December 2006; final version received 23 June 2007*)

In the title study, the synthesis of the vital intermediate C-nor-aconanone (**3**) from **4** was completed through 11 steps, mainly including semipinacol rearrangement, formation of the imines by the treatment of **10** or **20** with NBS, the cleavage of N—C(19) bonds in **11** or **21** by treatment with *m*-CPBA and subsequently with LTA, as well as the rupture of the N—C(17) bonds in **22** by a modified Nef reaction (NaH/*t*-BuOH → $KMnO_4/H_2O$). One-pot procedure was successfully developed starting from **11** or **21** to afford the *N*,19-*seco*-C-nor product **15** or **22**, respectively, in reasonably good yields.

Keywords: *N*,19-*seco*-C_{19}-diterpenoid alkaloid; *N*,17-*seco*-C_{19}-diterpenoid alkaloid; Aconane-type diterpene; semipinacol rearrangement; imine; *m*-CPBA–LTA oxidation

1. Introduction

Since 1996, we have carried out a series of research [1], especially on the key modifications of the rings A, B, and C of the C_{19}-diterpenoid alkaloids, toward chemical conversion of the C_{19}-diterpenoid alkaloids. After these, in the previous paper [1,2], we found that the CAB approach, e.g., modification in the ring C → A → B (CAB) sequence [2], was advisable based on the observation that the semipinacol rearrangement for the C-ring modification of the C_{19}-diterpenoid alkaloids cannot occur when following the breakage of either the N—C(19) or C(7)—C(17) bond, and synthesized the key intermediate **1**. The Nef reaction was applied with the expectation of the rupture of N—C(17) bond in **1** to give the ketone **2**; however, the products were very complex, probably due to the exposition of the hydroxyl group at C-8 in **1**.

In a continuation of research on the CAB approach toward the chemical conversion of C_{19}-diterpenoid alkaloids to taxoids, we have synthesized the key intermediate C-nor-aconanone (**3**) similar to **2** through the CAB route reported in the literature [2]. Herein, we reported the synthesis of the intermediate **3** from 3,13-diacetylyunaconitine (**4**) through 14 steps, together with the characterization of about 19 new or novel complex products and their derivatives.

2. Results and discussion

After the preparation of the key intermediate **2** from **1** having the hydroxyl group at C-8 in very low yield due to the presence of hydroxyl group at C-8, we turned our attention to substrates without the hydroxyl group at C-8 on the influence of cleavage of the N—C(19) bond in C-nor-norditerpenoid alkaloids.

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ISSN 1028-6020 print/ISSN 1477-2213 online

DOI: 10.1080/10286020801967128
http://www.informaworld.com

First, the synthesis began with the starting material 3,15-diacetylyunaconitine (**4**) [1j] affording compound **11** in 40.6% overall yield in 12 steps including the key semipinacol rearrangement (**8 → 9a/9b**) [1e] and the imine formation (**10 → 11**) developed in this laboratory [1b,h,i,2]. It is observed that **9a** was converted easily to **9b** only when carried out under the alkaline conditions as shown in the literature [1g]. The structure of **11** was determined easily by comparison of the NMR spectral data with those of **12** [2]. However, the treatment of **11** with *m*-CPBA/$CHCl_3$ or *m*-CPBA/EtOH—H_2O gave the oxazolidine compound **13** in 7.5 or 72% yield, respectively, rather than the expected nitrone **14**, an important finding of an obvious enhancement of the yield of oxazolidine only using *m*-CPBA/EtOH—H_2O system due to the influence of the polarized solvent [3]. Compound **11**, then, was exposed to *m*-CPBA (rt, 30 min) followed by the addition of LTA (rt, 24 h); for example, the so-called one-pot method fortunately afforded the desired compound **15** as a white amorphous powder in 51% yield. In the ^1H and ^{13}C NMR spectra of **15** (see Section 4), the presence of γ-lactone (δ_H 4.78, d, $J = 7.0$ Hz, H-6β; δ_C 174.5, s, C-19) was confirmed. Its IR spectrum also showed an absorption of the nitro group (1556–1375 cm^{-1}).

Encouraged by the successful obtainment of compound **15**, we are forced to try the cleavage of the N—C(17) bond in **15** by the Nef reaction. According to the literature [4], keeping the solution of **15** in 5% KOH methanol overnight followed by a long treatment with HCl resulted in the obtainment of compound **16**, as blue amorphous powder, in 51% yield. When compared with **15**, the lack of a tertiary carbon signal at δ_C 90.7 (C-17 for **15**) and the presence of an extra quaternary carbon signal at δ_C 130.8 (C-17) were displayed in the ^{13}C NMR spectrum of **16**, implying that it had a distinct structural moiety of the *N*,*O*-mixed ketal instead of the usual hemiketal. This deduction was supported by the following facts: the odd molecular weight (*m*/*z* 447), the blue color due to the nitroso group, and mechanistical consideration [3]. The structure of **16** was further confirmed by the treatment with Ac_2O–pyridine or Ac_2O—TsOH, which gave only the monoacetyl derivative **17**, $C_{23}H_{29}NO_8$ (HR-ESI-MS), as blue powder, which was treated with CH_3COOOH to give quantitatively a colorless compound **18**. The presence of a nitro group rather than the nitroso group in **18** was confirmed based on the key points as below: the 16 more mass units and the obvious up-field shifts of the δ values for C-7 (δ_C 51.2), C-11 (δ_C 41.8), and C-17 (δ_C 111.7) (Table 1) of **18** when compared with those of **17** (Scheme 1). Finally, the structure of **18** was determined by its 2D-NMR (^1H—^1H COSY, HMQC, HMBC) (Figure 1). In addition, the α-orientation of H-13 in compounds **10**–**18** was deduced from the coupling constants ($J_{13,16} = 9.6$–11.2 Hz for **10**, **11**, **13**, **15**, **17**, and **18**), especially according to the literature [2]. We also found it interesting that **17** was very unstable in solution for the cultivation of single crystals, resulting in a change of color from first blue (**17**), to bright green, and eventually to yellow. Conversion of **15** to **16** could be explained easily according to the mechanism of the Nef reaction [5] (Scheme 2). The first step being the formation of the salt (A) from **15** by KOH treatment, then acidation to give B followed by a nucleophilic attack of OH at C-3 on C-17 in nitronic acid (B) to give C and subsequent dehydration to form **16**.

Owing to the unsuccessful results mentioned above, we decided to prepare compound **3**, in which the hydroxyl groups at C-3 and C-13 were protected by TBSOTf from **10** prior to the Nef reaction.

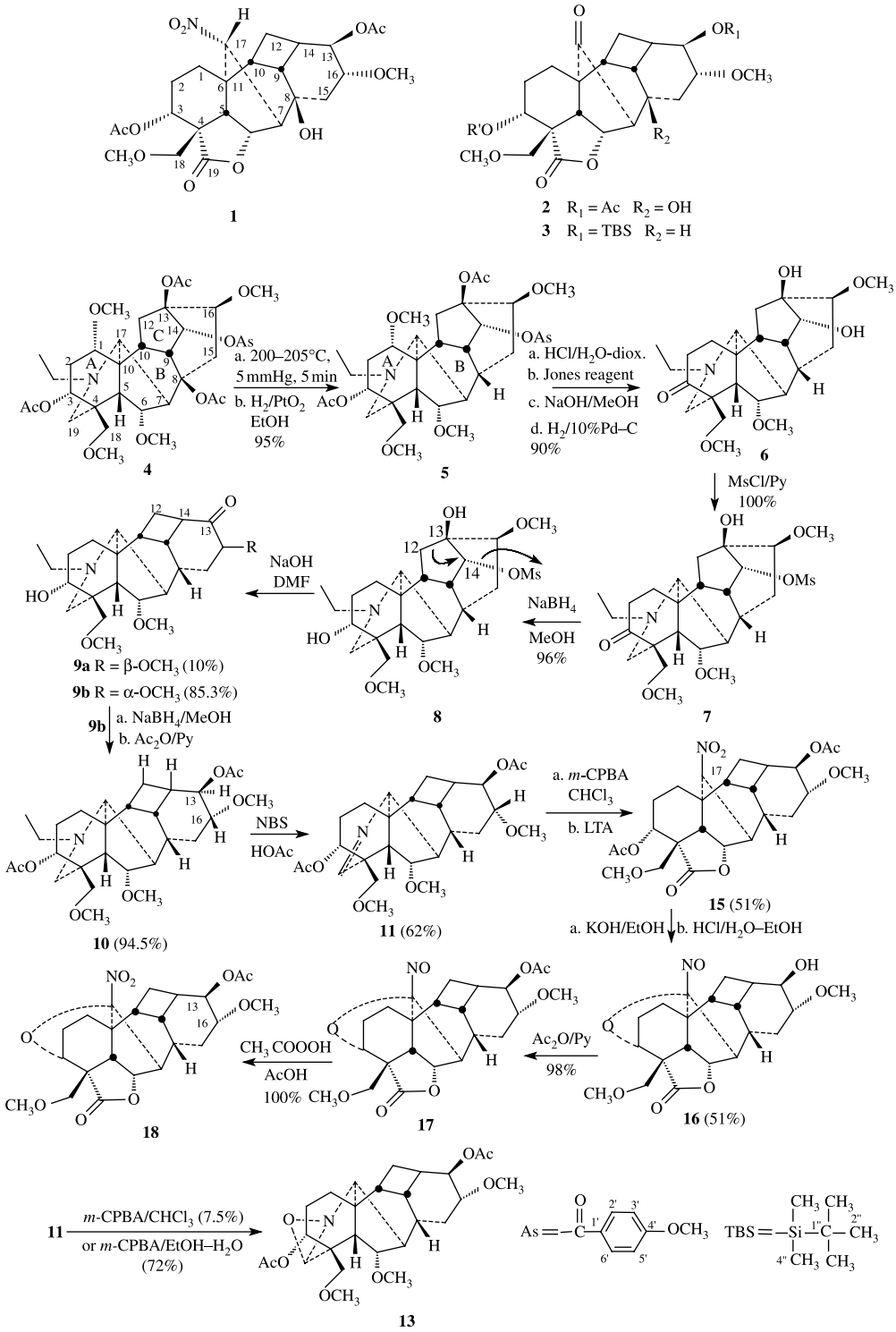
Hydrolysis of **10** with NaOH/MeOH, followed by protection with TBSOTf to avoid a negative participation of the hydroxyl groups at C-3 and C-13, the preparation of imine (**21**), and subsequent formation of the nitro compound using the afore-mentioned one-pot method developed by us, afforded successfully a colorless compound **22** in 27.7% overall yield in four steps from **10** to **22** (Scheme 3). In the ^1H and ^{13}C NMR

Table 1. ^{1}H and ^{13}C NMR spectral data of compounds **18** and **3**.

	18		**3**	
Carbon	δ_C	δ_H	δ_C	δ_H
1	17.1 t	1.37–1.45 m (β), 2.31–2.33 m (α)	18.0 t	0.90–0.93 m (β), 2.26–2.27 m (α)
2	21.9 t	1.79–1.83 m (α), 2.16–2.18 m (β)	26.8 t	1.39–1.42 m (α), 1.58–1.62 m (β)
3	72.2 t	4.09 t (2.8)	68.6 t	3.78 dd (6.6, 1.2)
4	53.8 s	–	53.8 s	–
5	47.7 d	2.83 d (8.0)	45.5 d	2.89 d (7.8)
6	80.7 d	4.67 d (8.4)	79.6 d	4.71 d (7.2)
7	51.2 d	2.87 d (3.2)	55.4 d	2.35 d (2.4)
8	37.9 s	2.50–2.58 m	45.3 d	2.62–2.67 m
9	28.3 d	2.41–2.48 m	28.2 d	2.36–2.38 m
10	38.5 d	2.36–2.40 m	53.6 d	2.53–2.55 m
11	41.8 s	–	48.9 s	–
12	25.4 t	1.86–1.94 m (β), 2.11–2.14 m (α)	24.3 t	1.71–1.72 m (β), 1.94–1.96 m (α)
13	66.0 d	5.04 dd (9.6, 4.4)	64.7 d	3.99 dd (9.6, 4.2)
14	30.2 d	2.90–3.00 m	32.1 d	2.57–2.58 m
15	27.0 t	1.66–1.76 m	26.1 t	1.55–1.58 m (β), 1.87–1.91 m (α)
16	79.2 d	3.02 ddd (10.8, 4.4, 2.8)	80.5 d	2.82 ddd (12.0, 3.0, 1.8)
17	111.7 s	–	214.7 d	–
18	70.8 t	3.31 d (hidden), 3.62 d (9.2)	76.3 t	3.36 d (hidden), 3.62 d (9.2)
19	177.7 s	–	176.2 s	–
16-OCH_3	56.5 q	3.30 s	56.1 q	3.28 s
18-OCH_3	59.5 q	3.35 s	59.4 q	3.34 s
8—OC(=O)—CH_3	170.7 s	–	–	–
	20.6 q	2.07 s	–	–
3-OTBS 1″			18.3 s	–
2″			25.8 q	0.84 s
3″			−5.2 q	−0.03
4″			−4.6 q	0.02
13-OTBS 1″			18.5 s	–
2″			25.9 q	0.86 s
3″			−5.0 q	0.00
4″			−4.2 q	0.05

TBS = $-Si(CH_3)_2-C(CH_3)_3$ (3″, 4″, 1″, 2″)

spectra of **22** (see Section 4), the presence of γ-lactone (δ_H 4.71, d, $J = 6.8$ Hz, H-6β; δ_C 85.8, d, C-6; 174.0, s, C-19) was confirmed. Its IR spectrum also showed absorption of the nitro group (1554–1387 cm^{-1}). In addition, the δ values of both H-17 (δ_H 5.30 br s) and C-17 (δ_C 90.4 d) moved toward downfield when compared with those of **21**. Finally, an attempt to prepare **3** by the successive treatment of **22** with NaOH first and then with acid, e.g., a typical Nef reaction, failed. But when the reaction of **22** with DBN in the presence of $(CH_3)_3SiBr$ at room temperature for 12 h and then oxidation by *m*-CPBA under mild conditions (no strong bases or acids), according to the literature [5], led to the unexpected compound **23** in 86% yield, rather than **3**, probably due to the non-formation of silicyl ether of the nitronic acid [5] under weak basic condition. The presence of the hydroxyl group (3428 cm^{-1}) and the lack of the signal for H-17 in the IR and ^{1}H NMR spectra of **23** when compared with those of **22** were evident. Finally, compound **22** was exposed



Scheme 1. The synthesis of compounds **18** and **13**.

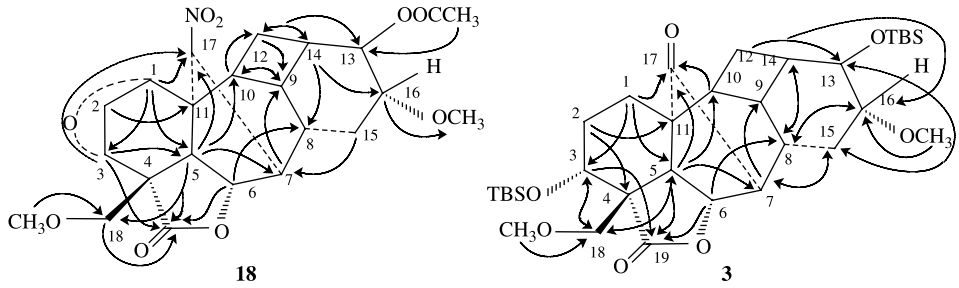
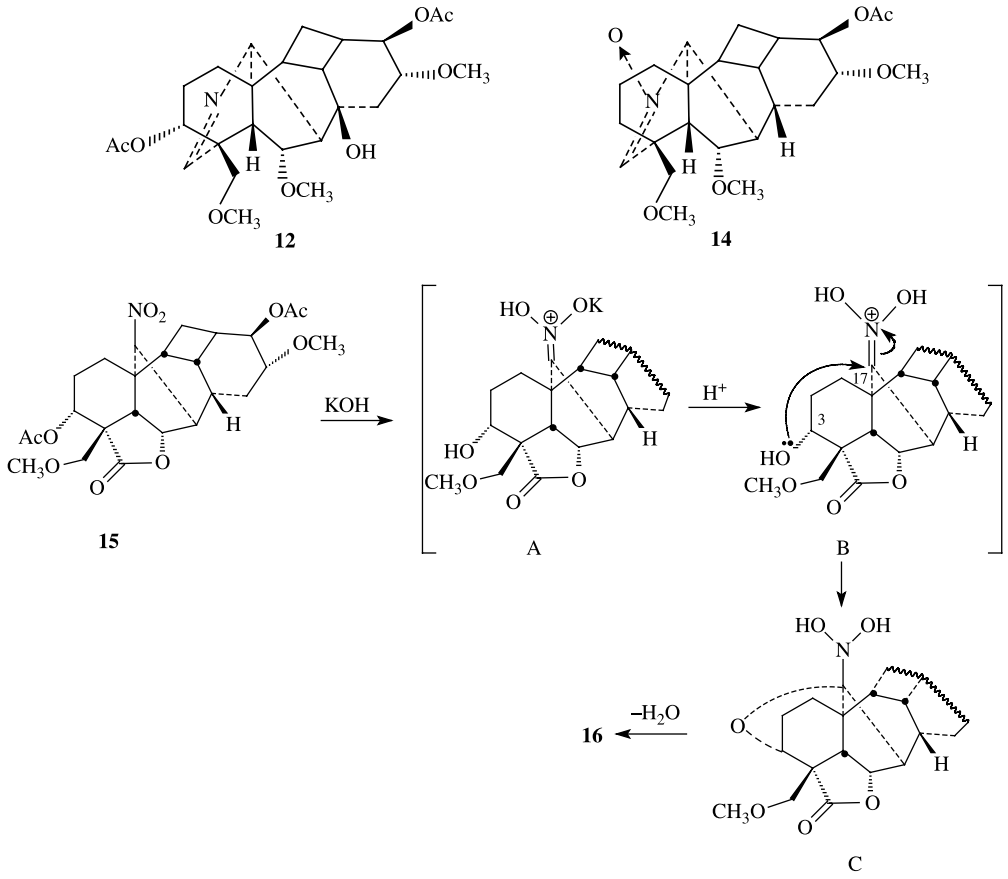
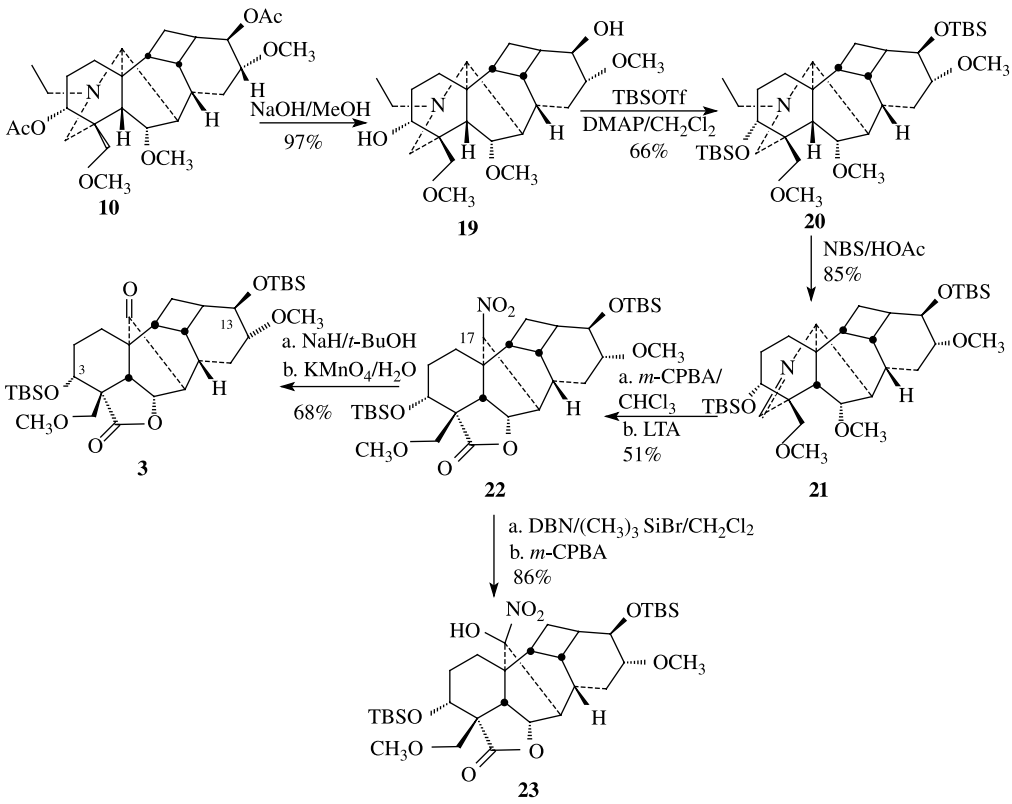


Figure 1. Selective HMBC (H → C) correlations of **18** and **3**.



Scheme 2. A plausible mechanism for the formation of **16** from **15**.

successively to NaH/*t*-BuOH and $KMnO_4/H_2O$ using another modified Nef reaction [5] to give the desired C-nor-aconanone **3** in 68% yield (Scheme 3). The IR and ^{13}C NMR spectra of **3**, $C_{33}H_{55}NO_7Si_2$ (HR-ESI-MS), showed both the characteristic signals at 1776 cm^{-1} and δ_C 214.7 for the ketone group at C-17. The structure of **3** was



Scheme 3. The synthesis of compounds **3** and **23**.

confirmed by an extensive spectral analysis including 2D-NMR (HMQC, $^1H—^1H$ COSY, HMBC) (Table 1; Figure 1).

3. Conclusion

The presence of rigidly fused polycyclic system, chemical complexity caused by the structures including the nitrogen atom, and strong dependence upon the substrates derived from the C_{19}-diterpenoid alkaloids often led to much more difficulties for the modifications and conversions of the C_{19}-diterpenoid alkaloids.

The cleavage of the N—C(19) bond in the modifications of ring A strongly depended upon the substrates. The treatment of only the substrates having no hydroxyl group at C-8 and the OAc-(OTBS) at C-13, such as **11** and **21**, using a modified one-pot (*m*-CPBA–LTA) method gave the desired *N*,*C*(19)-*seco*-nitro products **15** and **22** in good yields (51%). This result is consistent with our previous observation [2].

We have developed a easy cleavage of the N—C(19) bond in the imines (**11**, **21**) in moderate yield, which is so good work-up that can be carried out in one-pot fashion (*m*-CPBA–LTA) rather than two-step which at first involved in treatment with *m*-CPBA, and then with HIO_4, reported by us [1h,2]. The *m*-CPBA–LTA protocol provides a new route to cleavage of the N—C bonds, which should be broadly applicable in organic synthesis.

The vital intermediate C-nor-aconanone (**3**) from **4** was obtained in 11 steps, mainly including the key semipinacol rearrangement, NBS oxidation of tertiary amine, cleavage of the N—C(19) bond using a one-pot step (*m*-CPBA–LTA), and a modified Nef reaction [4], in 12.4% overall yield.

In a further study mentioned above, 19 C_{19}-diterpenoid alkaloids were obtained,

which were new compounds as determined by the spectral data (^{1}H and ^{13}C NMR, 2D-NMR, HR-MS).

4. Experimental

4.1 General experimental procedures

Melting points were determined on a Kofler block (uncorrected); optical rotations were measured in a 1.0 dm cell with a PE-314 polarimeter at 20 ± 1°C; IR spectra were recorded on a Nicolet 200 SXV spectrometer; MS spectra were obtained with a Auto-Spec-3000 instrument; the ^{1}H and ^{13}C NMR spectra were acquired on a Bruker ACE 200 or a Varian INOVA-400/54 spectrometer, with TMS as an internal standard; silica gel GF_{254} and H (10–40 μm, Qingdao Sea Chemical Factory, Qingdao, China) were used for TLC and CC. Only key signals except for compounds **3** and **18** in the ^{1}H NMR spectra are reported.

4.2 Compound 5

Compound **4** (1.25 g, 1.687 mmol) was pyrolyzed under vacuum at 200–205°C for 15 min in a 500 ml round-bottomed flask. To a solution of the residue in 95% EtOH (50 ml), PtO_2 (36 mg) was added and the solution was stirred under hydrogen steam at room temperature for 48 h. The filtrate was evaporated under reduced pressure to give compound **5** (white amorphous powder, 1.1 g, 95.4%). The structure of **5** was identified by comparison of TLC [petroleum ether–acetone (2:1), $CHCl_3$—CH_3OH (98:2), $CHCl_3$–acetone (9:1)] with the authentic sample.

4.3 Compound 6

To a solution of compound **5** (252 mg, 0.368 mmol) in dioxane–H_2O (4:1, 15 ml), conc. hydrochloric acid (0.8 ml) was added and the solution was refluxed for 12 h. Basifying (conc. NH_4OH, pH 12), extraction ($CHCl_3$, 25 ml × 3), drying (Na_2SO_4), and evaporation afforded the pure product (white amorphous powder, 209 mg, 95%). To a solution of the residue (180 mg, 0.3 mmol) in acetone (3 ml), Jones reagent (0.3 ml, 0.822 mmol) was added dropwise under ice water bath and the solution was stirred at room temperature for 30 min. Ten percent methanolic NaOH (10 ml) was added and the solution was heated at 50°C for 1 h. Filtration, removal of solvent, diluting (H_2O, 15 ml), extraction ($CHCl_3$, 15 ml × 3), drying (Na_2SO_4), and evaporation afforded the white amorphous powder (118 mg, 90.8%). To a solution of the residue (90 mg, 0.208 mmol) in 95% EtOH (5 ml), 10% Pd–C (16 mg) was added and the solution was stirred under hydrogen steam at room temperature for 12 h. Then the filtrate was evaporated under reduced pressure to give compound **6** (white amorphous powder, 94 mg, 90%).

Compound ***6***. Mp 128–129°C; R_f (95% $CHCl_3$—CH_3OH) 0.46; $[\alpha]_D^{20} = -33.1$ (*c* 1.04, $CHCl_3$); ν_{max} ($CHCl_3$) 3385 (OH), 2932, 2824, 1729 (COO), 1458, 1216, 1102 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.07 (3H, br s, NCH_2CH_3); 3.20, 3.31, 3.42 (each 3H, s, 3 × OCH_3); 3.90 (1H, d, $J = 5.2$ Hz, H-14β); 4.08 (1H, d, $J = 6.4$ Hz, H-6β); δ_C (50 MHz, $CDCl_3$) 85.1 (C-6), 84.2 (C-16), 78.7 (C-14), 76.1 (C-13), 75.4 (C-18), 64.3 (C-17), 59.0 (C-18′), 58.0 (C-6′), 58.0 (C-16′), 52.9 (C-4), 52.7 (C-21), 48.6 (C-19), 46.0 (C-11), 45.4 (C-7), 44.1 (C-5), 41.0 (C-9), 39.5 (C-8), 38.3 (C-2), 37.3 (C-15), 34.5 (C-10), 30.8 (C-12), 25.8 (C-1), 12.7 (C-22); ESI-MS: *m/z* 436 ($[M + H]^+$, 100).

4.4 Compound 7

To a solution of compound **6** (90 mg, 0.207 mmol) in pyridine (1.5 ml), MsCl (0.03 ml, 0.387 mmol) was added and the solution was stirred at room temperature for 45 min. Removal of solvent, diluting (H_2O, 5 ml), basifying (conc. NH_4OH, pH 12), extraction ($CHCl_3$, 10 ml × 3), drying (Na_2SO_4), and evaporation afforded the pure product (white amorphous powder, 103 mg, 100%).

Compound ***7***. Mp 99–100°C; R_f (50% petroleum ether–acetone) 0.84; $[\alpha]_D^{20} = -33.4$ (*c* 1.58, $CHCl_3$); ν_{max} (KBr) 3448

(OH), 2930, 2821, 1716 (COO), 1637, 1458, 1352, 1175, 1099, 969 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.02 (3H, t, $J = 7.2$ Hz, NCH_2CH_3); 3.11 (3H, s, OMs); 3.21, 3.34, 3.42 (each 3H, s, 3× OCH_3); 4.01 (1H, d, $J = 6.4$ Hz, H-6β); 4.63 (1H, d, $J = 4.8$ Hz, H-14β); δ_C (50 MHz, $CDCl_3$) 217.5 (C-3), 86.3 (C-16), 84.6 (C-6), 84.3 (C-14), 75.4 (C-18), 74.9 (C-13), 64.0 (C-17), 58.9 (C-18′), 58.1 (C-16′), 58.0 (C-6′), 53.0 (C-4), 52.9 (C-21), 48.2 (C-19), 46.0 (C-11), 45.3 (C-7), 44.1 (C-5), 40.1 (C-9), 38.5 (C-2), 38.1 (C-8), 38.1 (OMs), 37.1 (C-15), 35.2 (C-10), 30.7 (C-12), 25.8 (C-1), 13.2 (C-22); ESI-MS: *m/z* 536 ($[M + Na]^+$, 100).

4.5 Compound 8

To a solution of compound **7** (93 mg, 0.181 mmol) in MeOH (3 ml), $NaBH_4$ (43 mg, 1.16 mmol) was added and the solution was stirred at room temperature for 12 h. Removal of solvent, diluting (H_2O, 10 ml), extraction ($CHCl_3$, 15 ml × 3), drying (Na_2SO_4), and evaporation afforded the pure product (white amorphous powder, 90 mg, 96%).

Compound ***8***. Mp 125–126°C; R_f (95% $CHCl_3$–CH_3OH) 0.52; $[\alpha]_D^{20} = +3.1$ (*c* 1.51, acetone); ν_{max} (KBr) 3442 (OH), 2932, 1637, 1452, 1351, 1175, 1100, 968 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.09 (3H, t, $J = 7.2$ Hz, NCH_2CH_3); 3.08 (3H, s, OMs); 3.29, 3.31, 3.40 (each 3H, s, 3 × OCH_3); 4.60 (1H, d, $J = 5.2$ Hz, H-14β); δ_C (100 MHz, $CDCl_3$) 86.5 (C-16), 84.9 (C-6), 84.8 (C-14), 77.4 (C-18), 75.0 (C-13), 74.7 (C-3), 63.0 (C-17), 59.1 (C-18′), 57.9 (C-16′), 57.8 (C-6′), 48.8 (C-21), 48.7 (C-7), 47.2 (C-19), 46.2 (C-11), 45.2 (C-5), 43.4 (C-4), 40.5 (C-9), 38.5 (C-8), 38.1 (OMs), 37.0 (C-15), 34.3 (C-10), 30.4 (C-12), 29.6 (C-2), 29.2 (C-1), 13.5 (C-22); ESI-MS: *m/z* 516 ($[M + H]^+$, 100); HR-ESI-MS: *m/z* 516.2610 $[M + H]^+$ (calcd for $C_{25}H_{42}NO_8S$, 516.2626).

4.6 Compounds 9a and 9b

To a solution of compound **8** (85 mg, 0.165 mmol) in DMF (6 ml), NaOH (120 mg) was added and the solution was refluxed at 180°C for 30 min. Removal of solvent, diluting (H_2O, 10 ml), extraction ($CHCl_3$, 10 ml × 3), drying (Na_2SO_4), evaporation, and column chromatography [silica gel H, petroleum ether–acetone (6:1)] afforded the pure products as white amorphous powder (**99**: 7 mg, 10.1%; **9b**: 59 mg, 85.3%).

Compound ***9a***. Mp 100–101°C; R_f (50% petroleum ether–acetone) 0.81; $[\alpha]_D^{20} = +39.6$ (*c* 1.64, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 1.03 (3H, t, $J = 7.2$ Hz, NCH_2CH_3); 3.27, 3.27, 3.29 (each 3H, s, 3 × OCH_3); 3.47, 3.97 (each 1H, ABq, $J = 8.4$ Hz, H_2-18); δ_C (100 MHz, $CDCl_3$) 213.9 (C-13), 87.7 (C-6), 81.5 (C-16), 77.4 (C-18), 74.8 (C-3), 62.7 (C-17), 59.1 (C-18′), 57.9 (C-16′), 57.5 (C-6′), 48.6 (C-7), 48.6 (C-19), 47.1 (C-21), 44.3 (C-4), 44.3 (C-5), 42.4 (C-8), 42.3 (C-11), 36.4 (C-14), 35.3 (C-10), 33.4 (C-15), 32.9 (C-9), 29.3 (C-2), 29.3 (C-12), 26.7 (C-1), 13.4 (C-22); ESI-MS: *m/z* 744 ($[M + H]^+$, 100); HR-ESI-MS: *m/z* 420.2760 $[M + H]^+$ (calcd for $C_{24}H_{38}NO_5$, 420.2744).

Compound ***9b***. Mp 71–72°C; R_f (50% petroleum ether–acetone) 0.64; $[\alpha]_D^{20} = +57.2$ (*c* 3.75, acetone); ν_{max} (KBr) 3457 (OH), 2926, 2825, 1716 (COO), 1652, 1454, 1387, 1375, 1297, 1200, 1107 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.05 (3H, t, $J = 7.2$ Hz, NCH_2CH_3); 3.31, 3.34, 3.46 (each 3H, s, 3 × OCH_3); 3.50, 3.82 (each 1H, ABq, $J = 9.2$ Hz, H_2-18); δ_C (100 MHz, $CDCl_3$) 212.3 (C-13), 87.3 (C-6), 82.2 (C-16), 77.2 (C-18), 74.6 (C-3), 62.5 (C-17), 59.1 (C-18′), 58.0 (C-16′), 57.9 (C-6′), 48.6 (C-7), 48.5 (C-19), 47.1 (C-21), 44.5 (C-4), 44.0 (C-5), 42.5 (C-8), 42.3 (C-11), 38.7 (C-9), 38.1 (C-14), 34.3 (C-10), 33.6 (C-15), 29.3 (C-2), 28.5 (C-12), 26.7 (C-1), 13.4 (C-22); ESI-MS: *m/z* 420 ($[M + H]^+$, 100); HR-ESI-MS: *m/z* 420.2758 $[M + H]^+$ (calcd for $C_{24}H_{38}NO_5$, 420.2744).

4.7 Compound 10

To a solution of compound **9b** (102 mg, 0.243 mmol) in MeOH (5 ml), $NaBH_4$ (43 mg, 1.16 mmol) was added and the solution was

stirred at room temperature for 12 h. Removal of solvent, diluting (H_2O, 10 ml), extraction ($CHCl_3$, 15 ml × 3), drying (Na_2SO_4), and evaporation afforded the pure product as white amorphous powder, which was dissolved in pyridine (3 ml); Ac_2O (0.3 ml) was added and the solution was stirred at room temperature for 12 h. Removal of solvent, basifying (conc. NH_4OH, pH 12), extraction ($CHCl_3$, 15 ml × 3), drying (Na_2SO_4), and evaporation afforded the pure product (white amorphous powder, 116 mg, 94.5%).

Compound ***10***. Mp 72–73°C; R_f (75% petroleum ether–acetone) 0.55; $[\alpha]_D^{20} = +43.9$ (*c* 1.24, $CHCl_3$); ν_{max} (KBr) 3445 (OH), 2935, 1736 (COO), 1653, 1458, 1375, 1243, 1107, 1031 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.07 (3H, t, $J = 7.2$ Hz, NCH_2CH_3); 2.02, 2.10 (each 3H, s, 2 × OAc); 3.18, 3.30, 3.30 (each 3H, s, 3 × OCH_3); 4.92 (1H, dd, $J = 12.0$, 5.6 Hz, H-3β); 5.11 (1H, dd, $J = 9.6$, 3.4 Hz, H-13); δ_C (50 MHz, $CDCl_3$) 170.6, 170.2 ($COCH_3$), 87.8 (C-6), 78.5 (C-16), 74.3 (C-3), 72.1 (C-18), 66.5 (C-13), 62.1 (C-17), 58.7 (C-18′), 58.1 (C-6′), 56.3 (C-16′), 48.3 (C-21), 48.1 (C-19), 46.5 (C-7), 44.5 (C-11), 43.2 (C-5), 42.3 (C-8), 41.4 (C-4), 39.4 (C-9), 29.8 (C-10), 29.2 (C-14), 27.6 (C-15), 26.5 (C-2), 26.3 (C-12), 23.6 (C-1), 21.7, 20.8 ($COCH_3$), 13.4 (C-22); ESI-MS: *m/z* 506 ($[M + H]^+$, 100); HR-ESI-MS: *m/z* 506.3095 $[M + H]^+$ (calcd for $C_{28}H_{44}NO_7$, 506.3112).

4.8 Compound 11

To a solution of compound **10** (290 mg, 0.574 mmol) in HOAc (10 ml), NBS (604 mg, 3.412 mmol) was added and the solution was stirred at room temperature for 2 h. After pouring into ice water (20 ml), the solution was basified with conc. NH_4OH to pH 12. Extraction ($CHCl_3$, 15 ml × 3), drying (Na_2SO_4), evaporation, and column chromatography [silica gel H, petroleum ether–acetone (3:1)] afforded the pure product (white amorphous powder, 169 mg, 62%).

Compound ***11***. Mp 74–75°C; R_f (67% petroleum ether–acetone) 0.58; $[\alpha]_D^{20} = +88.4$ (*c* 0.91, $CHCl_3$); ν_{max} (KBr) 3446 (OH), 2932, 1735, 1647, 1458, 1375, 1243, 1105 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.06, 2.11 (each 3H, s, 2 × OAc); 3.27, 3.28, 3.33 (each 3H, s, 3 × OCH_3); 3.51, 4.15 (each 1H, ABq, $J = 8.8$ Hz, H_2-18); 3.79 (1H, d, $J = 7.0$ Hz, H-6β); 4.03 (1H, br s, H-17); 4.96 (1H, dd, $J = 11.2$, 4.6 Hz, H-3β); 5.11 (1H, dd, $J = 9.6$, 3.4 Hz, H-13); 7.39 (1H, d, $J = 2.4$ Hz, H-19); δ_C (100 MHz, $CDCl_3$) 170.8, 169.9 ($COCH_3$), 163.6 (C-19), 88.5 (C-6), 78.6 (C-16), 73.4 (C-3), 70.2 (C-18), 66.4 (C-13), 63.1 (C-17), 58.9 (C-18′), 58.0 (C-6′), 56.5 (C-16′), 52.2 (C-7), 49.9 (C-4), 45.0 (C-5), 44.2 (C-11), 42.4 (C-8), 39.3 (C-9), 29.5 (C-10), 29.1 (C-14), 27.6 (C-15), 27.3 (C-12), 26.4 (C-2), 24.4 (C-1), 20.9, 20.8 ($COCH_3$); ESI-MS: *m/z* 476 ($[M + H]^+$, 100); HR-ESI-MS: *m/z* 476.2657 $[M + H]^+$ (calcd for $C_{26}H_{38}NO_7$, 476.2643).

4.9 Compound 13

To a solution of compound **11** (11.3 mg, 0.024 mmol) in EtOH—H_2O (2:1, 5 ml), *m*-CPBA (17.1 mg, 0.0745 mmol) was added and the solution was stirred at room temperature for 12 h. Removal of solvent, basifying (conc. NH_4OH, pH 12), extraction ($CHCl_3$, 10 ml × 3), drying (Na_2SO_4), evaporation, and column chromatography [silica gel H, petroleum ether–acetone (4:1)] afforded the pure product (white amorphous powder, 8.5 mg, 72%).

Compound ***13***. Mp 81–82°C; R_f (67% petroleum ether–acetone) 0.78; $[\alpha]_D^{20} = +45.4$ (*c* 0.39, $CHCl_3$); ν_{max} ($CHCl_3$) 3349 (OH), 3019, 2945, 1738 (COO), 1559, 1461, 1374, 1318, 1237, 1110, 1045 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.09, 2.12 (each 3H, s, 2 × OAc); 3.26, 3.33, 3.34 (each 3H, s, 3 × OCH_3); 3.49, 4.21 (each 1H, ABq, $J = 8.6$ Hz, H_2-18); 3.70 (1H, d, $J = 4.8$ Hz, H-6β); 4.15 (1H, s, H-19); 4.98 (1H, dd, $J = 11.6$, 4.8 Hz, H-3β); 5.09 (1H, dd, $J = 9.6$, 3.4 Hz, H-13); ESI-MS: *m/z* 492 ($[M + H]^+$, 25); HR-ESI-MS: *m/z* 514.2389 $[M + Na]^+$ (calcd for $C_{26}H_{37}NNaO_8$, 514.2411).

4.10 Compound 15

To a solution of compound **11** (88 mg, 0.185 mmol) in $CHCl_3$ (2 ml), *m*-CPBA (60 mg, 0.261 mmol) was added and the solution was stirred at room temperature for 30 min. LTA (130 mg, 0.281 mmol) was added and the solution was stirred at room temperature for 12 h. Removal of solvent, diluting (acetone, 10 ml), basifying (conc. NH_4OH, pH 10), centrifuging, and the supernatant was evaporated under reduced pressure. Extraction ($CHCl_3$, 10 ml × 3), drying (Na_2SO_4), evaporation, and column chromatography [silica gel H, petroleum ether–acetone (4:1)] afforded the pure product (white amorphous powder, 48 mg, 51%).

Compound ***15***. Mp 88–89°C; R_f (67% petroleum ether–acetone) 0.40; $[\alpha]_D^{20} = +19.0$ (*c* 1.22, $CHCl_3$); ν_{max} (KBr) 3446 (OH), 2939, 1774, 1737, 1654, 1556, 1458, 1375, 1241, 1104, 1030 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.02, 2.13 (each 3H, s, 2 × OAc); 3.31, 3.33 (each 3H, s, 2 × OCH_3); 4.78 (1H, d, $J = 7.0$ Hz, H-6β); 4.96 (1H, dd, $J = 9.6$, 2.8 Hz, H-13); 5.03 (1H, dd, $J = 8.8$, 3.6 Hz, H-3β); 5.25 (1H, s, H-17); δ_C (50 MHz, $CDCl_3$) 174.5 (C-19), 90.7 (C-17), 86.4 (C-16), 77.2 (C-18), 76.9 (C-6), 67.2 (C-13), 66.8 (C-3), 59.4 (C-18′), 56.7 (C-16′), 51.4 (C-4), 51.0 (C-7), 50.1 (C-5), 49.6 (C-8), 49.1 (C-11), 37.1 (C-9), 29.3 (C-15), 28.2 (C-10), 27.0 (C-14), 24.8 (C-12), 23.2 (C-2), 20.6 (C-1); ESI-MS: *m/z* 530 ($[M + Na]^+$, 78); 476 (M-OCH_3, 100); HR-ESI-MS: *m/z* 530.2015 $[M + Na]^+$ (calcd for $C_{25}H_{33}NNaO_{10}$, 530.1997).

4.11 Compound 16

Compound **15** (140 mg, 0.276 mmol) was dissolved in 5% methanolic KOH (3 ml) and the solution was stirred at room temperature for 12 h. This solution was added dropwise to a mixture of EtOH (2.5 ml), H_2O (2.5 ml), and conc. hydrochloric acid (3 ml) under ice water bath and the solution was stirred at room temperature for 15 h. Diluting (H_2O, 10 ml), extraction ($CHCl_3$, 15 ml × 3), drying (Na_2SO_4), evaporation, and column chromatography [silica gel H, petroleum ether–acetone (4:1)] afforded the pure product (blue amorphous powder, 57 mg, 51%).

Compound ***16***. Mp 102–103°C; R_f (67% petroleum ether–acetone) 0.48; $[\alpha]_D^{20} = -3.8$ (*c* 0.60, $CHCl_3$); ν_{max} (KBr) 3462 (OH), 2938, 2886, 2831, 1773, 1638, 1547, 1459, 1383, 1303, 1222, 1198, 1098, 1057 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 3.28, 3.33 (each 3H, s, 2× OCH_3); 3.17, 3.46 (each 1H, ABq, $J = 9.2$ Hz, H_2-18); 4.14 (1H, dd, $J = 9.4$, 3.8 Hz, H-3β); 5.06 (1H, d, $J = 7.2$ Hz, H-6β); δ_C (50 MHz, $CDCl_3$) 178.3 (C-19), 130.8 (C-17), 84.3 (C-6), 80.2 (C-16), 70.8 (C-18), 70.5 (C-3), 63.1 (C-13), 59.4 (C-18′), 57.6 (C-7), 56.1 (C-16′), 53.7 (C-4), 50.8 (C-11), 47.7 (C-5), 40.1 (C-8), 39.2 (C-9), 31.1 (C-10), 29.3 (C-14), 28.0 (C-15), 27.3 (C-12), 20.9 (C-2), 15.6 (C-1); ESI-MS: *m/z* 406 ($[M + H]^+$, 100); HR-ESI-MS: *m/z* 406.1854 $[M + H]^+$ (calcd for $C_{21}H_{28}NO_7$, 406.1860).

4.12 Compound 17

To a solution of compound **16** (68 mg, 0.168 mmol) in pyridine (2 ml), Ac_2O (1.0 ml) was added and the solution was stirred at 40°C for 12 h. Removal of solvent, extraction ($CHCl_3$, 10 ml × 3), washing (10% HCl, 10 ml; H_2O, 10 ml), drying (Na_2SO_4), and evaporation afforded the pure product (blue amorphous powder, 1.42 g, 98%).

Compound ***17***. Mp 201–202°C; R_f (67% petroleum ether–acetone) 0.55; $[\alpha]_D^{20} = +67.3$ (*c* 0.67, $CHCl_3$); ν_{max} (KBr) 3438 (OH), 2949, 1781, 1728 (COO), 1647, 1550, 1459, 1374, 1250, 1100, 1031 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.93 (3H, s, OAc); 3.26, 3.28 (each 3H, s, 2 × OCH_3); 3.15, 3.45 (each 1H, ABq, $J = 9.2$ Hz, H_2-18); 5.06 (1H, d, $J = 7.4$ Hz, H-6β); 5.12 (1H, dd, $J = 9.8$, 3.4 Hz, H-13); δ_C (100 MHz, $CDCl_3$) 178.3 (C-19), 170.9 (*CO*CH_3), 130.9 (C-17), 84.4 (C-6), 78.6 (C-16), 70.7 (C-18), 70.5 (C-3), 66.4 (C-13), 59.3 (C-18′), 57.4 (C-7), 56.4 (C-16′), 53.7 (C-4), 50.8 (C-11), 47.6 (C-5), 39.4 (C-8), 39.3 (C-9), 30.4 (C-10), 29.4

(C-15), 28.8 (C-14), 27.7 (C-12), 20.8 (C-2), 20.6 ($CO\mathit{CH_3}$), 15.5 (C-1); ESI-MS: *m/z* 470 ($[M + Na]^+$, 85); 448 ($[M + H]^+$, 100); HR-ESI-MS: *m/z* 470.1773 $[M + Na]^+$ (calcd for $C_{23}H_{29}NNaO_8$, 470.1785).

4.13 Compound 18

To a solution of compound **17** (33 mg, 0.074 mmol) in HOAc (1 ml), 10% CH_3COOOH (3.0 ml) was added and the solution was stirred at 70°C for 50 min. Diluting (H_2O, 5 ml), extraction ($CHCl_3$, 10 ml × 3), drying (Na_2SO_4), and evaporation afforded the pure product (white amorphous powder, 39 mg, 100%).

Compound ***18***. Mp 114–115°C; R_f (67% petroleum ether–acetone) 0.52; $[\alpha]_D^{20} = +1.72$ (*c* 0.87, $CHCl_3$); ν_{max} (KBr) 3735, 3446 (OH), 2931, 1779, 1733, 1653, 1546, 1457, 1374, 1247, 1089, 1054, 1034 cm^{-1}; δ_H (400 MHz, $CDCl_3$): see Table 1; δ_C (100 MHz, $CDCl_3$): see Table 1; HR-ESI-MS: *m/z* 486.1731 $[M + Na]^+$ (calcd for $C_{23}H_{29}NNaO_9$, 486.1735).

4.14 Compound 19

Compound **10** (2.0 g, 3.960 mmol) was dissolved in 5% methanolic NaOH (40 ml) and stirred at 50°C for 45 min. Removal of solvent, diluting (H_2O, 100 ml), extraction ($CHCl_3$, 80 ml × 3), drying (Na_2SO_4), and evaporation afforded the pure product (white amorphous powder, 1.62 g, 97%).

Compound ***19***. Mp 63–64°C; R_f (67% petroleum ether–acetone) 0.48; $[\alpha]_D^{20} = +25.5$ (*c* 3.62, acetone); ν_{max} (KBr) 3432 (OH), 2925, 1717, 1647, 1454, 1377, 1200, 1105 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.04 (3H, t, $J = 7.0$ Hz, $NCH_2\mathit{CH_3}$); 3.26, 3.34, 3.36 (each 3H, s, 3 × OCH_3); δ_C (50 MHz, $CDCl_3$) 87.3 (C-6), 80.3 (C-16), 77.6 (C-18), 75.1 (C-3), 63.3 (C-13), 62.5 (C-17), 59.0 (C-18′), 57.8 (C-6′), 56.1 (C-16′), 49.1 (C-14), 48.5 (C-7), 48.5 (C-21), 47.2 (C-19), 44.7 (C-11), 43.1 (C-5), 42.9 (C-8), 42.3 (C-4), 39.3 (C-9), 30.4 (C-10), 29.4 (C-15), 26.8 (C-12), 25.8 (C-2), 23.0 (C-1), 13.4 (C-22); ESI-MS: *m/z* 422 ($[M + H]^+$, 100).

4.15 Compound 20

To a solution of compound **19** (1.42 g, 3.37 mmol) and DMAP (150 mg) in CH_2Cl_2 (6 ml), TBSOTf (2.0 ml, 8.215 mmol) was added and the solution was stirred at room temperature for 2 h. Basifying (conc. NH_4OH, pH 12), extraction ($CHCl_3$, 80 ml × 3), drying (Na_2SO_4), evaporation, and column chromatography [silica gel H, cyclohexane–acetone (30:1)] afforded the pure products as white amorphous powder (1.45 g, 66%).

Compound ***20***. Mp 35–37°C; R_f (92% cyclohexane–acetoacetate) 0.72; $[\alpha]_D^{20} = +12.6$ (*c* 2.95, $CHCl_3$); ν_{max} (KBr) 2927, 1733, 1471, 1386, 1360, 1251, 1199, 1112 cm^{-1}; δ_H (400 MHz, $CDCl_3$) −0.01, 0.00, 0.03, 0.03 [each 3H, s, $(\mathit{CH_3})_2SiC(CH_3)_3$]; 0.87, 0.91 [each 9H, s, $(CH_3)_2SiC(\mathit{CH_3})_3$]; 1.03 (3H, t, $J = 7.2$ Hz, $NCH_2\mathit{CH_3}$); 3.20, 3.28, 3.31 (each 3H, s, 3 × OCH_3); 3.61 (1H, dd, $J = 6.0$, 2.4 Hz, H-6β); 3.74 (1H, dd, $J = 11.6$, 6.0 Hz, H-3β); 3.94 (1H, dd, $J = 8.8$, 1.2 Hz, H-13); δ_C (100 MHz, $CDCl_3$) 88.7 (C-6), 81.1 (C-16), 72.2 (C-18), 71.4 (C-3), 65.8 (C-13), 62.9 (C-17), 58.2 (C-18′), 58.1 (C-6′), 56.1 (C-16′), 48.7 (C-21), 46.8 (C-7), 46.8 (C-19), 44.7 (C-11), 44.0 (C-5), 42.8 (C-4), 42.7 (C-8), 39.6 (C-9), 31.9 (C-14), 30.8 (C-2), 29.6 (C-10), 26.7 (C-1), 26.0, 25.9 [$(CH_3)_2SiC(\mathit{CH_3})_3$], 25.5 (C-15), 22.7 (C-12), 18.5, 18.1 [$(CH_3)_2Si\mathit{C}(CH_3)_3$], 13.4 (C-22), −3.7, −4.5, −5.0, −5.0 [$(\mathit{CH_3})_2SiC(CH_3)_3$]; ESI-MS: *m/z* 650 ($[M + H]^+$, 100); HR-ESI-MS: *m/z* 650.4642 $[M + H]^+$ (calcd for $C_{36}H_{68}NO_5Si_2$, 650.4631).

4.16 Compound 21

To a solution of compound **20** (1.2 g, 1.849 mmol) in HOAc (30 ml), NBS (2.15 g, 12.14 mmol) was added and the solution was stirred at room temperature for 1 h. After pouring into ice water (80 ml), the solution was basified with conc. NH_4OH to pH 12. Extraction ($CHCl_3$, 80 ml × 3), drying

(Na_2SO_4), evaporation, and column chromatography [silica gel H, cyclohexane–acetone (16:1)] afforded the pure product (white amorphous powder, 968 mg, 85%).

Compound ***21***. Mp 63–65°C; R_f (86% cyclohexane–acetone) 0.65; $[\alpha]_D^{20} = +25.5$ (*c* 0.85, $CHCl_3$); ν_{max} (KBr) 3422 (OH), 2929, 2888, 2856, 1720, 1694, 1462, 1387, 1253, 1107, 1034 cm^{-1}; δ_H (400 MHz, $CDCl_3$) −0.01, 0.01, 0.03, 0.04 [each 3H, s, $(CH_3)_2SiC(CH_3)_3$]; 0.86, 0.89 [each 9H, s, $(CH_3)_2SiC(CH_3)_3$]; 3.27, 3.29, 3.30 (each 3H, s, 3 × OCH_3); 3.89, 3.91 (each 1H, ABq, $J = 8.0$ Hz, H_2-18); 7.28 (1H, br s, H-19); δ_C (100 MHz, $CDCl_3$) 164.8 (C-19), 89.2 (C-6), 81.2 (C-16), 71.8 (C-3), 69.8 (C-18), 65.4 (C-13), 62.9 (C-17), 58.3 (C-18′), 58.0 (C-6′), 56.0 (C-16′), 53.4 (C-7), 51.6 (C-4), 45.1 (C-5), 44.3 (C-11), 42.8 (C-8), 39.8 (C-9), 31.6 (C-14), 30.6 (C-2), 29.5 (C-10), 27.4 (C-1), 25.9, 25.7 $[(CH_3)_2SiC(CH_3)_3]$, 25.4 (C-15), 23.9 (C-12), 18.4, 17.9 $[(CH_3)_2SiC(CH_3)_3]$, −4.1, −4.6, −5.0, −5.3 $[(CH_3)_2SiC(CH_3)_3]$; ESI-MS: *m/z* 620 ($[M + H]^+$, 100); HR-ESI-MS: *m/z* 620.4156 $[M + H]^+$(calcd for $C_{34}H_{62}NO_5Si_2$, 620.4161).

4.17 Compound 22

To a solution of compound **21** (288 mg, 0.465 mmol) in $CHCl_3$ (20 ml), *m*-CPBA (120 mg, 0.522 mmol) was added and the solution was stirred at room temperature for 30 min. LTA (552 mg, 1.193 mmol) was added and the solution was stirred at room temperature for 36 h. Removal of solvent, diluting (acetone, 30 ml), basifying (10% Na_2CO_3, pH 9), centrifuging, and the supernatant was evaporated under reduced pressure. Extraction ($CHCl_3$, 20 ml × 3), drying (Na_2SO_4), evaporation, and column chromatography [silica gel H, cyclohexane–acetone (12:1)] afforded the pure product (white amorphous powder, 156 mg, 51%).

Compound ***22***. Mp 70–71°C; R_f (86% cyclohexane–acetone) 0.58; $[\alpha]_D^{20} = -5.1$ (*c* 2.14, acetone); ν_{max} (KBr) 3446 (OH), 2929, 2855, 1777 (COO), 1554, 1471, 1387, 1253, 1189, 1103, 1028 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.03, 0.04, 0.05, 0.06 [each 3H, s, $(CH_3)_2SiC(CH_3)_3$]; 0.89, 0.91 [each 9H, s, $(CH_3)_2SiC(CH_3)_3$]; 3.32, 3.35 (each 3H, s, 2 × OCH_3); 4.71 (1H, d, $J = 6.8$ Hz, H-6β); 5.30 (1H, s, H-17); δ_C (50 MHz, $CDCl_3$) 174.0 (C-19), 90.4 (C-17), 85.8 (C-6), 79.4 (C-16), 76.3 (C-18), 68.6 (C-3), 66.2 (C-13), 59.2 (C-18′), 58.6 (C-16′), 52.8 (C-4), 51.1 (C-7), 51.0 (C-5), 50.3 (C-8), 49.4 (C-11), 36.8 (C-9), 31.4 (C-14), 28.4 (C-2), 27.7 (C-15), 26.4 (C-10), 25.9, 25.8 $[(CH_3)_2SiC(CH_3)_3]$, 23.2 (C-1), 22.0 (C-12), 18.4, 18.1 $[(CH_3)_2SiC(CH_3)_3]$, −4.4, −4.7, −4.8, −5.0 $[(CH_3)_2SiC(CH_3)_3]$; ESI-MS: *m/z* 652 ($[M + H]^+$, 100); HR-ESI-MS: *m/z* 652.3700 $[M + H]^+$ (calcd for $C_{33}H_{58}NO_8Si_2$, 652.3695).

4.18 Compound 23

To a solution of compound **22** (68 mg, 0.104 mmol) in CH_2Cl_2 (5 ml), DBN (0.06 ml) and $(CH_3)_3SiBr$ (0.09 ml) were added under ice water bath and the solution was stirred at room temperature for 12 h. A solution of *m*-CPBA (180 mg) in CH_2Cl_2 (3 ml) was added dropwise to the mixture under ice water bath and the solution was stirred at room temperature for 12 h. Washing (10% Na_2CO_3, 10 ml; dilute hydrochloric acid, 10 ml; $NaHCO_3$ saturation solution, 10 ml; H_2O, 10 ml), drying (Na_2SO_4), evaporation, and column chromatography [silica gel H, cyclohexane–acetone (12:1)] afforded the pure product (white amorphous powder, 60 mg, 86%).

Compound ***23***. Mp 187–188°C; R_f (67% petroleum ether–acetone) 0.77; $[\alpha]_D^{20} = -19.1$ (*c* 2.83, acetone); ν_{max} (KBr) 3428 (OH), 2930, 2893, 2856, 1779, 1638, 1553, 1462, 1385, 1252, 1206, 1105, 1054, 1024 cm^{-1}; δ_H (200 MHz, $CDCl_3$) −0.07, −0.01, 0.07, 0.09 [each 3H, s, $(CH_3)_2SiC(CH_3)_3$]; 0.83 [9H, s, $(CH_3)_2SiC(CH_3)_3$]; 3.26, 3.29 (each 3H, s, 2× OCH_3); 3.13, 3.48 (each 1H, ABq, $J = 8.4$ Hz, H_2-18); 4.60 (1H, d, $J = 7.8$ Hz, H-6β); δ_C (50 MHz, $CDCl_3$) 175.8 (C-19), 101.8 (C-17), 82.9 (C-6), 81.7 (C-16), 80.0 (C-18), 66.2 (C-13), 64.2 (C-3),

59.4 (C-18′), 56.0 (C-16′), 53.6 (C-7), 52.3 (C-4), 50.0 (C-8), 48.7 (C-11), 46.2 (C-5), 42.2 (C-9), 32.3 (C-14), 29.4 (C-2), 29.4 (C-10), 26.0 (C-15), 25.8, 25.7 [$(CH_3)_2$-SiC(CH_3)$_3$], 25.7 (C-1), 23.0 (C-12), 18.3, 18.1 [$(CH_3)_2$SiC(CH_3)$_3$], −4.6, −4.9, −5.0, −5.3 [(CH_3)$_2$SiC(CH_3)$_3$]; ESI-MS: *m/z* 636 (M—OCH_3, 25); 620 (M-HNO_2, 100).

4.19 Compound 3

To a suspension of NaH (287 mg, 11.86 mmol) in *t*-BuOH (10 ml) stirred at 45°C for 30 min, a solution of compound **23** (120 mg, 0.184 mmol) in *t*-BuOH (1 ml) was added and the mixture was stirred at room temperature for 30 min. A solution of $KMnO_4$ (124 mg) in H_2O (2 ml) was added dropwise to the mixture under ice water bath and the solution was stirred violently for 30 min. Treating with 10% $Na_2S_2O_3$ (1.5 ml), centrifuging, and the supernatant was extracted by $CHCl_3$ (20 ml × 3), drying (Na_2SO_4), evaporation, and column chromatography [silica gel H, cyclohexane–acetone (12:1)] afforded the pure product (white amorphous powder, 78 mg, 68%).

*Compound **3***. Mp 78–79°C; R_f (67% petroleum ether–acetone) 0.84; $[\alpha]_D^{20} = -25.7$ (*c* 1.26, $CHCl_3$); ν_{max} (KBr) 3432 (OH), 2939, 2847, 1776 (CO), 1715 (COO), 1464, 1258, 1102, 1020 cm^{-1}; δ_H (400 MHz, $CDCl_3$): see Table 2; δ_C (100 MHz, $CDCl_3$): see Table 2; ESI-MS: *m/z* 621 ($[M + H]^+$, 100); HR-ESI-MS: *m/z* 621.3658 $[M + H]^+$ (calcd for $C_{33}H_{56}O_7Si_2$, 621.3642).

Acknowledgements

Financial support for this research was provided from the National Natural Science Foundation of China (no. 30472075) and the Excellent Ph.D. Dissertation Foundation of China (no. 200367). We graciously acknowledge Prof. Xiao-Tian Liang of Institute of Materia Medica, Chinese Academy of Medical Sciences, China, for helpful discussion on the subject and inspection of this manuscript.

References

[1] (a) F.P. Wang, J.Z. Wang, and R. Zhang, *Heterocycles* **45**, 659 (1997). (b) F.P. Wang, Z.B. Li, J.S. Yang, and B.G. Li, *Chin. Chem. Lett.* **10**, 453 (1999). (c) F.P. Wang, J.S. Yang, Q.H. Chen, L. Yu, and B.G. Li, *Chem. Pharm. Bull*. **48**, 1912 (2000). (d) F.P. Wang, Q.H. Chen, and B.G. Li, *Chem. Pharm. Bull*. **49**, 689 (2001). (e) F.P. Wang, Q.H. Chen, and B.G. Li, *Tetrahedron* **42**, 4705 (2001). (f) L. Xu, Q.H. Chen, and F.P. Wang, *Tetrahedron* **58**, 4267 (2002). (g) Q.H. Chen and F.P. Wang, *Chem. Pharm. Bull*. **50**, 1310 (2002). (h) Q.H. Chen, L. Xu, and F.P. Wang, *Tetrahedron* **58**, 9431 (2002). (i) Q.H. Chen, L. Xu, and F.P. Wang, *Heterocycles* **57**, 2357 (2002). (j) Q.H. Chen and F.P. Wang, *J. Asian Nat. Prod. Res.* **5**, 43 (2003). (k) X.L. Sheng and F.P. Wang, *Chem. Pharm. Bull.* **52**, 1095 (2004). (l) X.L. Sheng and F.P. Wang, *Chem. Pharm. Bull.* **53**, 267 (2005).
[2] F.P. Wang and L. Xu, *Tetrahedron* **61**, 2149 (2005).
[3] Y. Ogata and Y. Sawaki, *J. Am. Chem. Soc.* **95**, 4687 (1976).
[4] W.E. Noland, *Chem. Rev.* **55**, 137 (1955).
[5] N. Kornblum, A.S. Erickson, W.J. Kelley, and B. Henggeler, *J. Org. Chem.* **47**, 4534 (1982).