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To seek an approach toward the chemical conversion of C_{19}-diterpenoid alkaloids to taxoids

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Abstract—This study, as a part of conversion of the C_{19}-diterpenoid alkaloids to the taxoids, described the search of a suitable route to the key intermediate B with four approaches (ABC, ACB, BCA, and CAB) designed and examined. In these cases, a new and efficient approach (CAB) toward the synthesis of the vital intermediates **51** or **52** has been developed. The key steps include the use of a semipinacol rearrangement treatment of **41** with NaOH/DMF under refluxing conditions for **30** min to afford **42**, and the rupture of the *N*-C-19 bond found in **45** or **48** to give **51** or **52**, respectively, through NBS imination followed by the creation of the oxaziridine **47** or the nitrone **50** and finally HIO_4 oxidation cleavages.

1. Introduction

Since Taxol® (paclitaxel, **1**)[1] and Taxotere® (docetaxel, **2**)[2] are currently two of the most exciting drugs in cancer chemotherapy,[3–4] efforts to synthesize taxol (**1**) have produced a wide variety of strategies for construction of the core structures[5] and to-date six total syntheses have been reported.[6–11] The diterpenoid alkaloids are a group of highly oxygenated complex natural products displaying a lot of interesting chemical reactions.[12] They were isolated mainly from both *Aconitum* and *Delphinium* plants (Ranunculaceae) as a rich source.[13] With careful skeletal analysis we have designed a strategy toward conversion of the C_{19}-diterpenoid alkaloids to the taxoids via a series of the degradational steps (Scheme 1). As showed in Scheme 1, the key steps for conversion from A (C_{19}-diterpenoid alkaloids) include mainly modifications of the A ring (de-amination, e.g. cleavage of the *N*-C-19 and *N*-C-17 bonds), the B ring (cleavage of the C-17–C-7 and C-10–C-11 bonds), and the C ring (C-10 or C-12 functionality and cleavage of the C-10–C-12 and C-12–C-13 bonds). After these cleavages to give the key intermediate D which was converted to the taxoids E via a cyclization by pinacol-like coupling developed by Swindell.[14]

On the basis of these considerations, our search for the starting materials has focused on the C_{19}-diterpenoid alkaloids from *Aconitum* species, which are widely distributed in southwest area of China.[15] Among the numerous naturally occurring this type alkaloids, only several compounds such as yunaconitine (**3**), indaconitine (**4**), and crassicauline A (**5**), etc. isolated from many plants are considered to be very useful.

In the course of studies on the chemistry of C_{19}-diterpenoid alkaloids,[16] we have broken through the key cleavages of rings A, B, and C in these alkaloids (Scheme 1, F). Although the results already have provided an important base for conversion into the taxoids, it takes still great effort to afford the vital intermediate **C** (Scheme 1). This is due to the most rigidly complex fused polycyclic system, chemical complexity derived from the *N*-atom, and strong dependence up on the substrates of the C_{19}-diterpenoid alkaloids. In an effort to seek an effective sequence allowed us to convert **A** obtained from the starting material yunaconitine (**3**) into the key intermediate C (Scheme 1) we describe in this paper a number of chemical transformation and other new findings for the purpose. To this end, four different lines of attack (approaches ABC, ACB, BCA, and CAB) designed according to modified sequence of the ring systems have been undertaken.

2. Results and discussion

2.1. Approach ABC

We reported that HIO_4 oxidation of the *N*,*O*-mixed acetal **6**

Keywords: C_{19}-diterpenoid alkaloid; Yunaconitine; N,19-*seco* C19-diterpenoid alkaloid; Semipinacol rearrangement; Imine; Oxaziridine; Nitrone; Taxoid.
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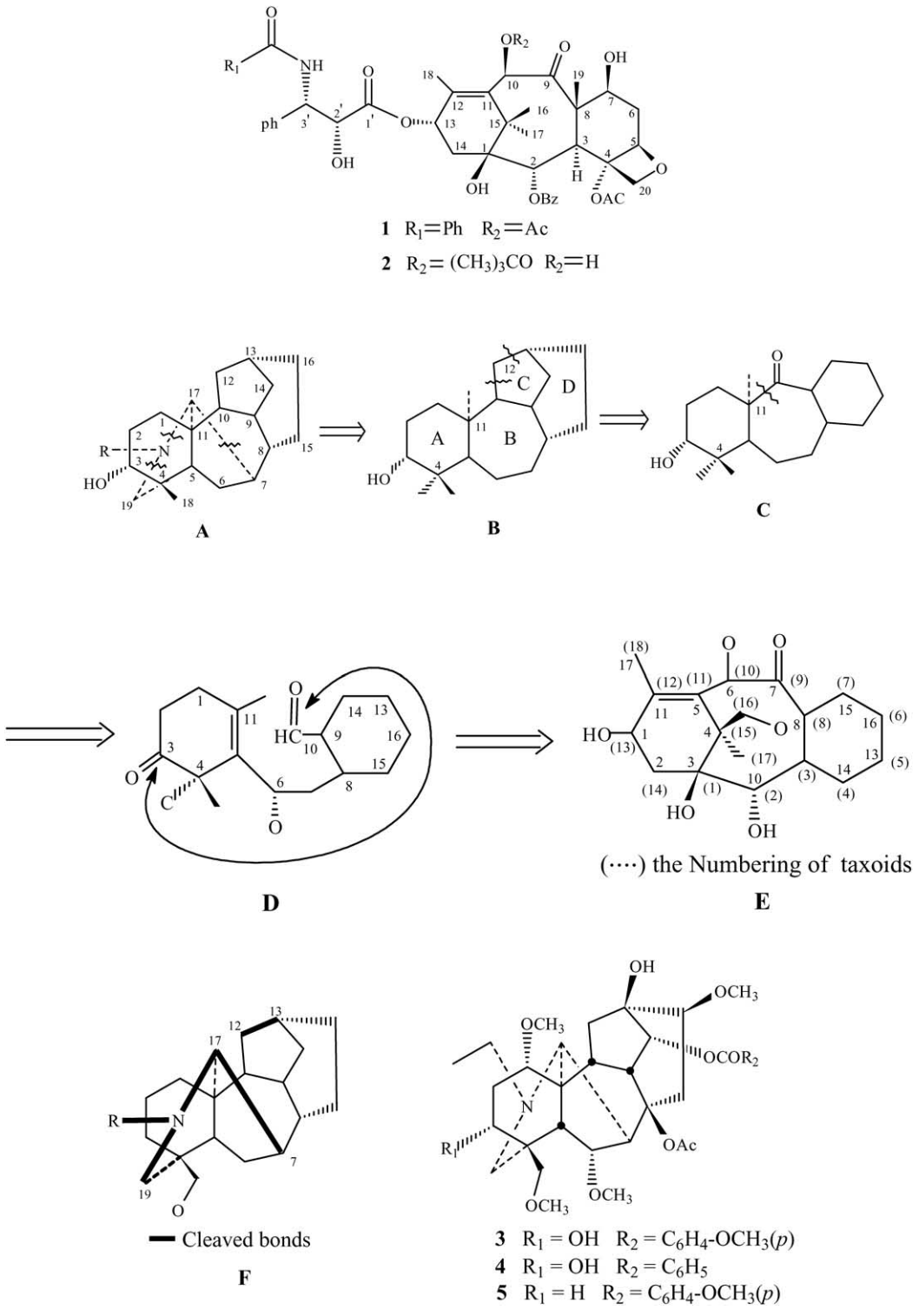
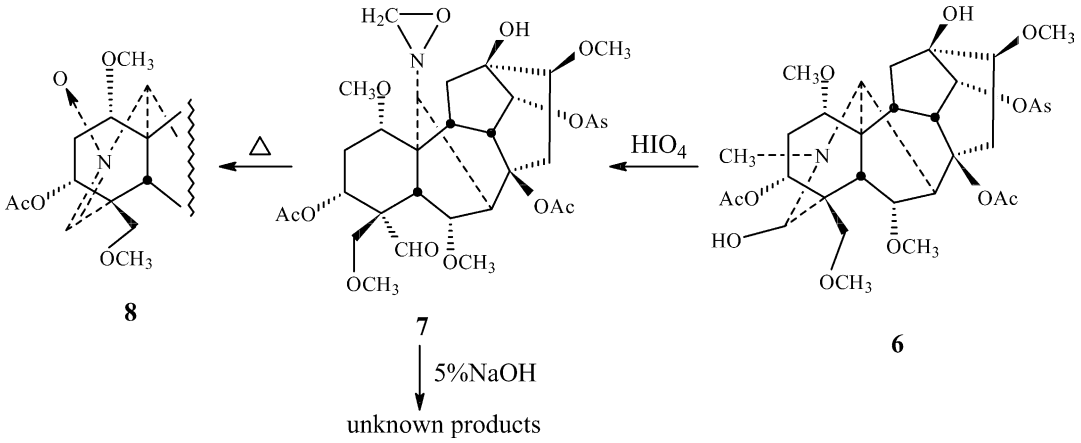


Scheme 1.

gave oxaziridine (**7**)[16t,17] which is unstable to acids, bases, and heating due to decomposition or formation of nitrone **8**[16t] probably because of participation of the hydroxyl at C-8 and the aldehyde group (Scheme 2). But an attempt to reduce the aldehyde group with $NaBH_4$–CH_3OH, or KBH_4–AcOH, which should permit avoiding reformation of the *N*-C-19 bond in **7** or **9**, gave only compounds **10** (49%) or **11** (73%), respectively. Treatment of **7** with K_2CO_3 in CH_3OH–H_2O afforded compounds **9** and **12** (ca.3:1) in 98% total yield (Scheme 3). The presence of *N*-CH_3 group in **10** and **11** was supported by the ^1H and ^{13}C NMR spectra (δ_H 2.60, s; δ_C 42.2, q for **10**; δ_H 2.64, s; δ_C 42.5, q for **11**). The ^{13}C NMR spectrum of **12** exhibited a distinctic lactam signal at δ_C 174.4 s. The afore-mentioned results might prove the aldehyde group in **7** to be recalcitrant mainly due to the bulkiness of hydroxyl or acetyl group at C-3 which was found in our subsequent research.[18]

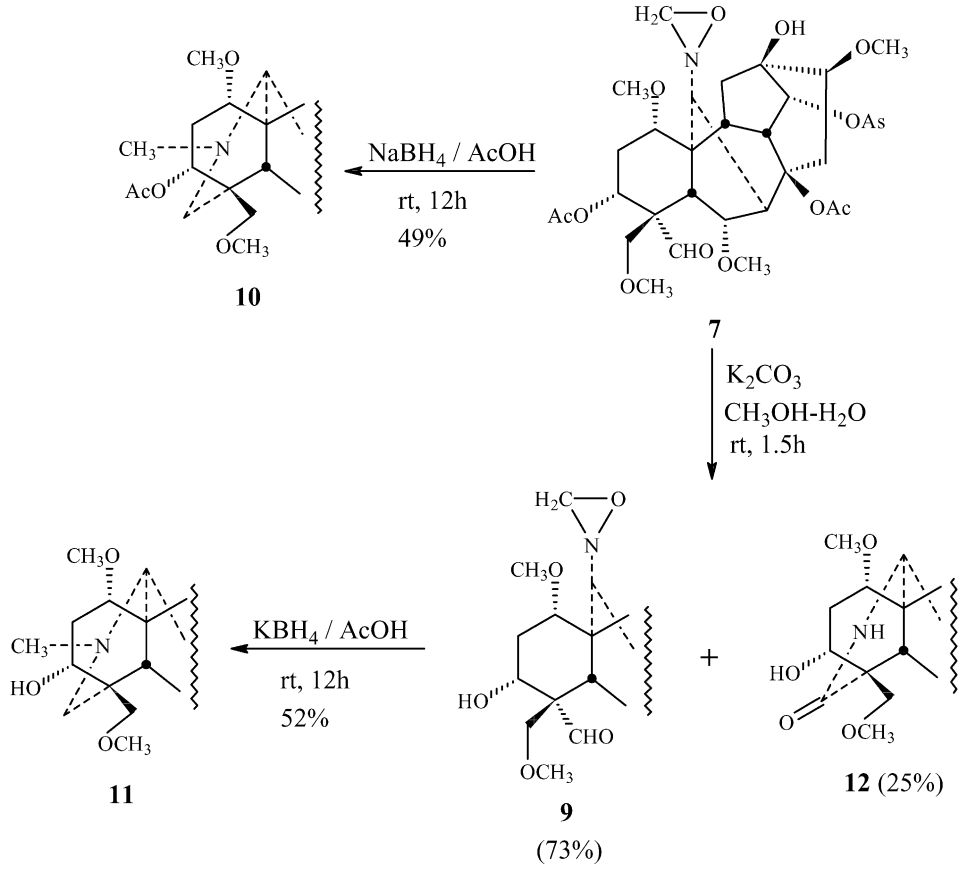


Scheme 2.

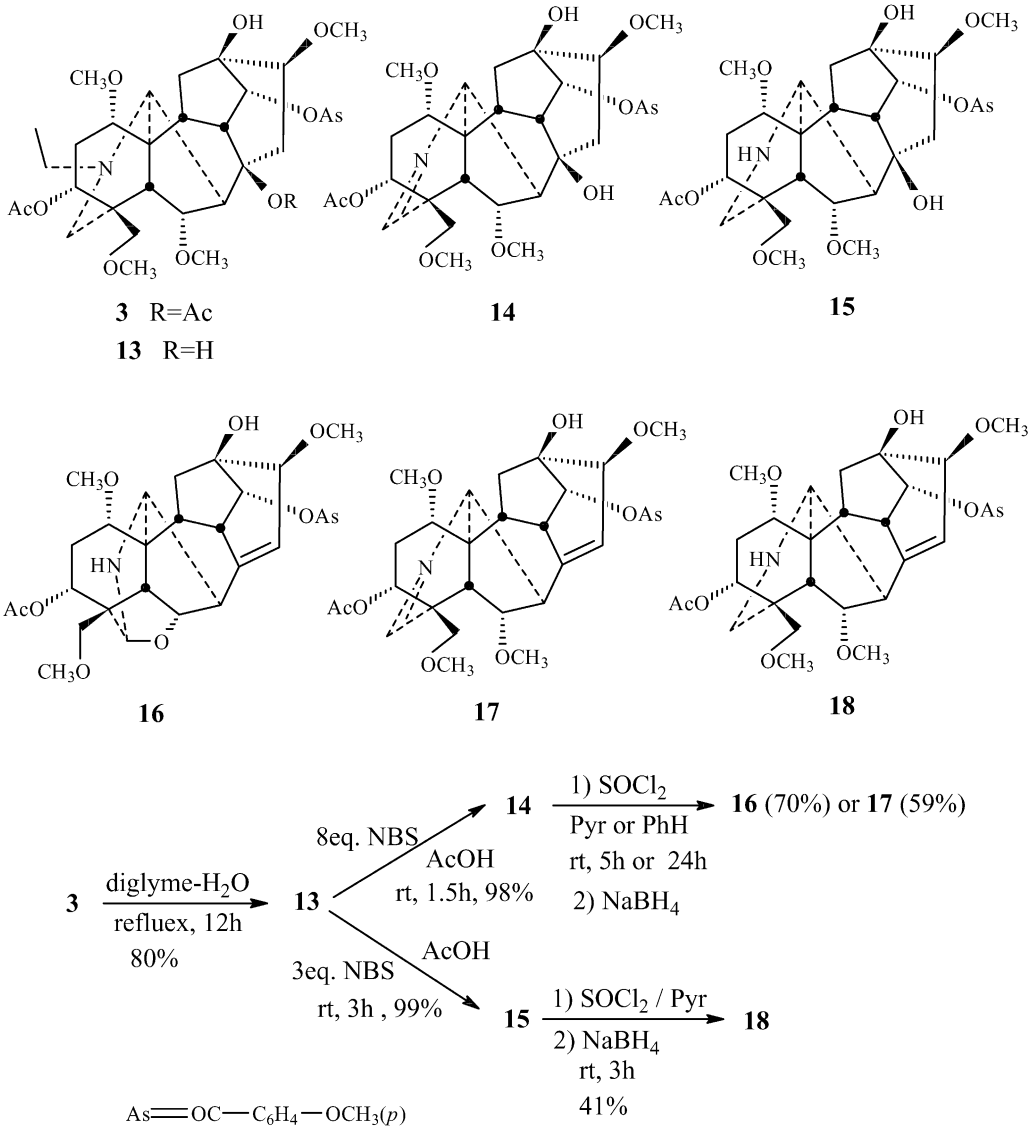
Our studies also showed that after the first fragmentation of C-7–C-17 bond in the molecule it is very difficult to prepare the *N*,19-*seco* compounds with the lower yield of the intermediate imines which are neccessary. Taking the findings into account, we decided prepare, at first, the imines such as **14** based on our developing protocol,[16i,t,v] followed by deamination and cleavaging the C-7–C-17 bond to give **B** (Scheme 1).

Selective hydrolysis of the starting material yunaconitine (**3**) in diglyme-H_2O (4:1) under refluxing conditions gave compound **13** which reacted with a mixture of glacial acetic acid and 8 equiv of NBS to give imine **14** in nearly quantitative yield, along with an important finds to be obviously enhancing the yield of imines using NBS/AcOH rather than NBS/*t*-BuOH previously reported by us,[16t] and the quantitative obtainment of *N*-deethyl product **15** with a three-fold amount of NBS (Scheme 4).

Attempted treatment of imine **14** with $SOCl_2$-pyridine or $SOCl_2$–C_6H_6 followed by $NaBH_4$ to fragment the C-7–C-17 bond via an intermediate 8-chlorro derivative, as previously reported by us,[16n,w] gave compounds **16** (70%) or **17** (59%) respectively. In the ^1H and ^{13}C NMR spectra of **16**, the signals at δ_H 5.66, d, $J=6.2$ Hz (H-15); δ_C 144.2 s (C-8), 116.7 d (C-15) for a trisubstituted double bond and at δ_H



Scheme 3.



Scheme 4.

4.83, dd, J=4.4, 2.0 Hz (H-6); δ_H 4.66, s (H-19); δ_C 87.6 d (C-19) for an *N*,*O*-mixed acetal moiety which also was supported by showing the correlation between H-6 and C-19 in the HMBC spectrum of **16**. The structure of **16** was established based on 2D NMR spectrum (Table 1). The ^{1}H NMR spectrum of **17** showed an imine signal at δ_H 7.47 (br s, H-19) and a trisubstituted double bond at δ_H 5.82 (d, J= 6.2 Hz, H-15). Interestingly, the *N*-deethyl compound **15** was exposed to $SOCl_2$ followed by $NaBH_4$ in similar procedure[16n,w] also produced the pyro product **18** (41%) instead of the desired 7,17-*seco* compound. This seems to show that the obtainment of 7,17-*seco* compounds, in our cases, required to meet simultaneously an anti-periplanar relationship between the lone pair of nitrogen atom and the C-8-Cl bond, and the tertiary amine patterns of the nitrogen atom.

2.2. Approach ACB

This approach was fashioned after the unsuccesseful ABC sequence. Attempt to strong alkaline rearrangement of the nitro compounds to the C-nor compounds by a reported method from this laboratory[16q,s] resulted in the complex products, which led us to try again reduction of the nitro group followed by protecting the amino group using TsCl. The 3,13-diacetylyunaconitine (**19**)[17] was exposed to NBS (8 equiv)-AcOH to give nearly quantitatively the imine **20** which was reacted with *m*-CPBA at room temperature to afford nitrone **21** (100%). An imine group (δ_H 6.72, d, J= 1.2 Hz, H-19; δ_C 135.4 d, C-19) was observed in the ^{1}H and ^{13}C NMR spectra of **21**. Treatment of **21** with molar excess of HIO_4 at room temperature gave the nitroso compound **22** as a blue amorphous powder. In the ^{1}H and ^{13}C NMR spectra of **22**, a γ-lactone moiety (δ_H 4.92, d, J=7.2 Hz (H-6β); δ_C 173.2 s (C-19)) was showed, and a methine carbon signal at δ_C 105.8 (d) can be assigned to C-17 bearing a nitroso group by comparison with those of the analogues.[16t] Reduction of **22** with Zn–conc. HCl gave the amine **23** (69%) together with the other two by-products **24** (18%) and **25** (8%) (Scheme 5). The carbon signals at δ_C 55.5 d (C-17) and 54.3 d (C-7) in **23** compared with those of **22** were obviously upfield-shifted (C-17: $\Delta\delta$-50.3; C-7: $\Delta\delta$-2.7). The MS spectrum of **24**, $C_{36}H_{45}O_{15}$ (HRMS), gave

Table 1. ^{1}H and ^{13}C NMR data for compound **16** (^{1}H: 400 MHz; ^{13}C: 100 MHz, $CDCl_3$)

No.	δ_C	δ_H Mult (J=Hz)	^{1}H–^{1}HCOSY	HMBC (H→C)
1	83.5 d	3.40 dd (6.0, 12.8)	H-2α, H-2β	C-17, C-1′, C-11, C-2, C-10
2	30.2 t	2.54 m (hidden)	H-2, H-1, H-3	C-1, C-3, C-4, C-11
		2.39 m	H-2, H-1, H-3	C-1, C-3, C-4, C-11
3	70.7 d	5.44 dd (6.8, 12.0)	H-2α, H-2β	C-19, C-18, C-4, C-5, C-2, 3-O*C*OCH$_3$
4	50.6 s	—	—	—
5	50.5 d	2.55 dd (hidden)	H-6, H-19 (w)	C-19, C-1, C-6, C-18, C-3, C-7, C-4, C-11, C-10
6	80.1 d	4.83 dd (2.0, 4.4)	H-5, H-17 (w)	C-19, C-17, C-4, C-5, C-11
7	56.4 d	3.10 br s	H-17	C-6, C-17, C-5, C-11, C-9
8	144.2 s	—	—	—
9	45.1 d	2.64 t (3.0)	H-10, H-14	C-8, C-15, C-13, C-14, C-11, C-12
10	48.2 d	2.23 m	H-12α, H-12β, H-9	C-8, C-1, C-17, C-11, C-9
11	49.0 s	—	—	—
12	37.9 t	1.99 dd (6.4, 14.8)	H-10, H-12	C-16, C-13, C-14, C-11, C-10
		1.92 dd (7.2, 14.8)	H-10, H-12	C-16, C-13, C-14, C-10, C-9
13	78.2 s	—	—	—
14	78.0 d	4.91 dd (0.8, 3.6)	H-9, H-16 (w)	C-16, C-13, C-9, C-1″, C-8
15	116.7 d	5.66 d (6.2)	H-16	C-16, C-14, C-7, C-9
16	83.4 d	3.40 (hidden)	H-15, H-14	C-8, C-15, C-13, C-14, -16′, C-12
17	68.3 d	3.27 br s (hidden)	H-7, H-6	C-19, C-1, C-6, C-5, C-11
18	74.5 t	3.23 ABq (9.2)	H-18 (δ 3.15)	C-19, C-3, C-18′, C-4, C-5
		3.15 ABq (9.2)	H-18 (δ 3.23)	C-19, C-3, C-18′, C-4, C-5
19	87.6 d	4.66 br s	—	C-6, C-18, C-17, C-4, C-5
1′	56.8 q	3.29 s	—	C-1′
16′	57.4 q	3.35 s	—	C-16′
18′	59.1 q	3.25 s	—	C-18′
O=C	170.3 s	2.05 s	—	-
CH$_3$	21.0 q	2.05 s	—	CO
O=C 1″	168.0 s	—	—	—
2″	122.5 s	—	—	—
7″ 3″	131.9 d	7.98 AA′BB′ (8.8)	H-4″	C-1″, C-5″, C-7″, C-2″, C-4″
6″ 4″	113.4 d	6.90 AA′BB′ (8.8)	H-3″	C-5″, C-6″, C-3″, C-2″
5″	163.3 s	—	—	—
OCH$_3$	55.3 q	3.85 s	—	C-5″

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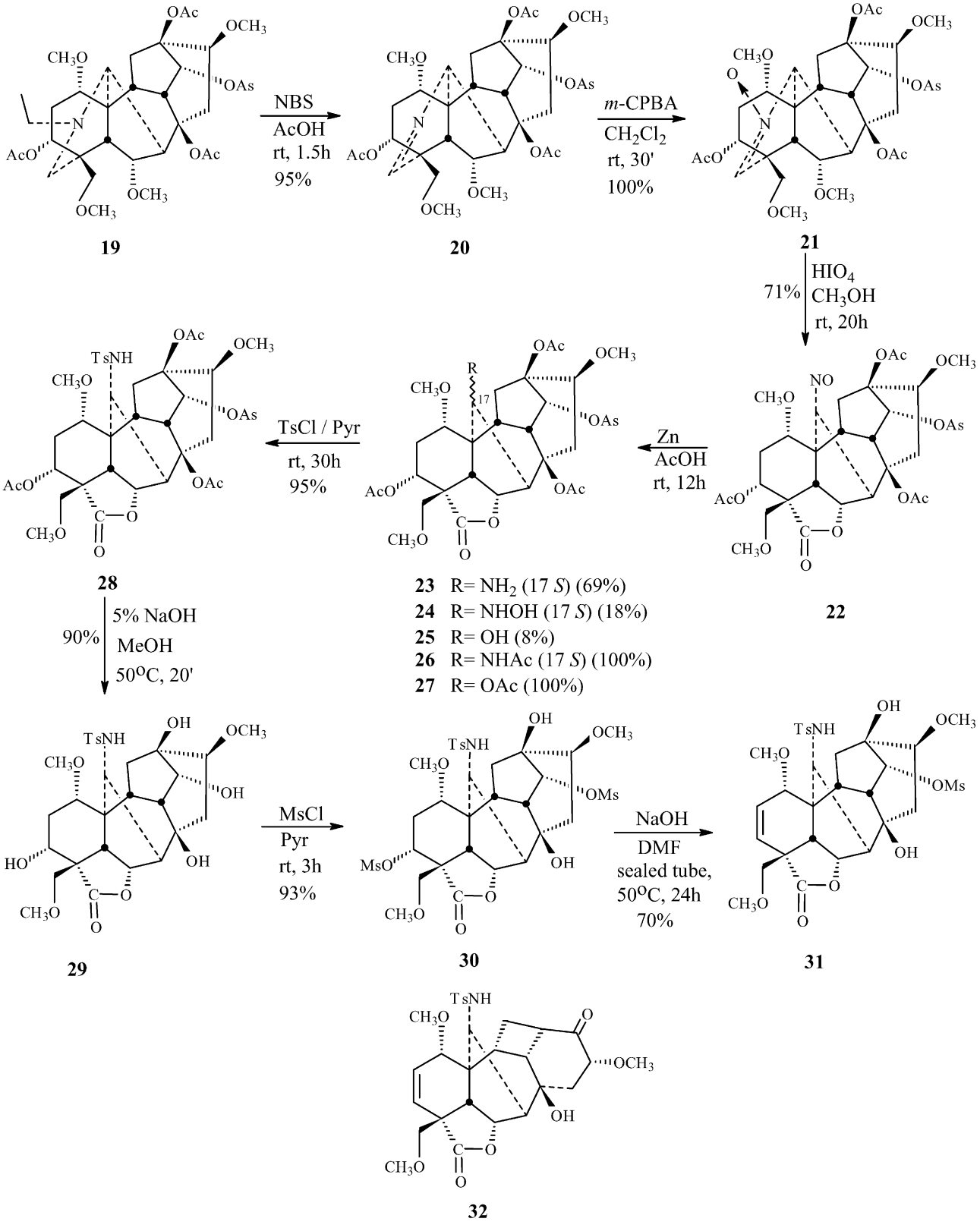
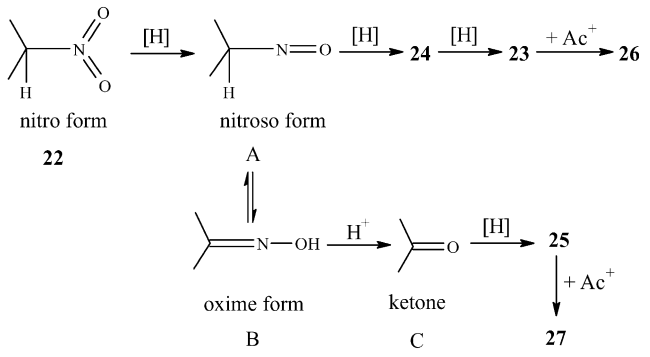
the molecular ion peak at m/z 731 which is 16 more unit than those of **23**. The ^{1}H and ^{13}C NMR spectra of **24** are very similar to those of **23**, except for C-17 (δ_C 64.5 d) being downfield-shifted by 9 ppm compared with those of **23**. From these facts mentioned above, the structure of **24** can be determined. The structure of **25** was established on the basis of the following key points: the odd molecular weight (m/z 716); a methine carbon signal at δ_C 74.7 (d) bearing to C-17; and a negative result to Dragendorff's reagent, which resulted from deamination. Acetylation of **23** and **25** with Ac_2O gave compounds **26** and **27**, respectively. In the ^{1}H NMR spectrum of **27**, an additional acetyl group was assigned at C-17 by the presence of the townfield signal at δ_H 5.03 (H-17) as compared with those of **25**. Apparently, configurations of C-17 in compounds **23**, **24**, and **26**, except for **25** and **27**, as the parent compound **22**, are deduced to be *S*. A plausible origin of these compounds **23**∼**27** can be rationalized mechanistically as shown in Scheme 6. Reduction of the nitro compound **22**, at first, gave the nitroso form A which was reduced again successively to give compounds **24** and **23**. In addition, there is an equilibration of the nitroso (A)-oxime (B) tautomerism.[19] Hydrolysis of B led to the ketone C, further reduction of C afforded **25**. Acetylation of **23** and **25** with AcOH resulted in obtainment of **26** and **27**, respectively. It is worth of note that the tautomerism between the nitroso and the oxime under alkaline condition was found by TLC detection (neutral silica gel GF_{254}: $CHCl_3$–MeOH=7:3, one spot; alkalized silica gel GF_{254}: $CHCl_3$–MeOH=95:5, two spots) and the NMR trial. When measuring the sample containing a few saturated Na_2CO_3 the ^{1}H and ^{13}C NMR spectra of **22** showed a distinctic signal at δ 155.7 (s) for the oxime group[16t], with ratio of about 3:1 based on the peak area of the H-14β signals at δ_H 4.99 for **22** and δ_H 4.84 for the oxime. Compound **23** was subjected to protection of the amino group, hydrolysis using 5% NaOH followed by sulfonation to give successively compounds **28** (95%), **29** (90%) and **30** (93%). The proton signal of H-17 (δ_H 5.66, d J=2.4 Hz) in the ^{1}H NMR spectrum of **28** compared with those of **23** was downfield-shifted due to the substitution of the OTs group. The ^{1}H and ^{13}C NMR spectra of **30** showed two OMs groups (δ_H 2.94, 2.97, each 3H, s; δ_C 38.1 q, 38.4 q), and the downfield-shift signals at δ_H 4.76 (1H, d, J=5.0 Hz, H-3β) and δ_H 4.43 (1H, d, J=4.2 Hz, H-14β) as compared with those of **29**. However, semipinacol rearrangement of **30** under various conditions (NaOH/DMF, reflux, 20 h[16q]; DBN/*o*-xylene, sealed tube, 180 °C, 12 h; NaOAc/HOAc, sealed tube, 150 °C, 24 h) resulted in formation of **31** (70%) rather than the desired product **32** (Scheme 5). This is incomprehensibly different from the results described in the literature.[16q]



Scheme 5.

2.3. Approach BCA

Owing to the unsuccesseve efforts described herein, we are forced to propose another approach BCA aiming at cleaving the C-7–C-17 bond using our developing protocol[16n,w] prior to modification of the ring C or A. According to the literature,[16w] the 7,17-*seco* compound **34** from **19** via **33** was prepared smoothly in 74% yield (Scheme 7). Its structure was established by spectral data and comparison with the authentic sample. Alkaline hydrolysis of **34**



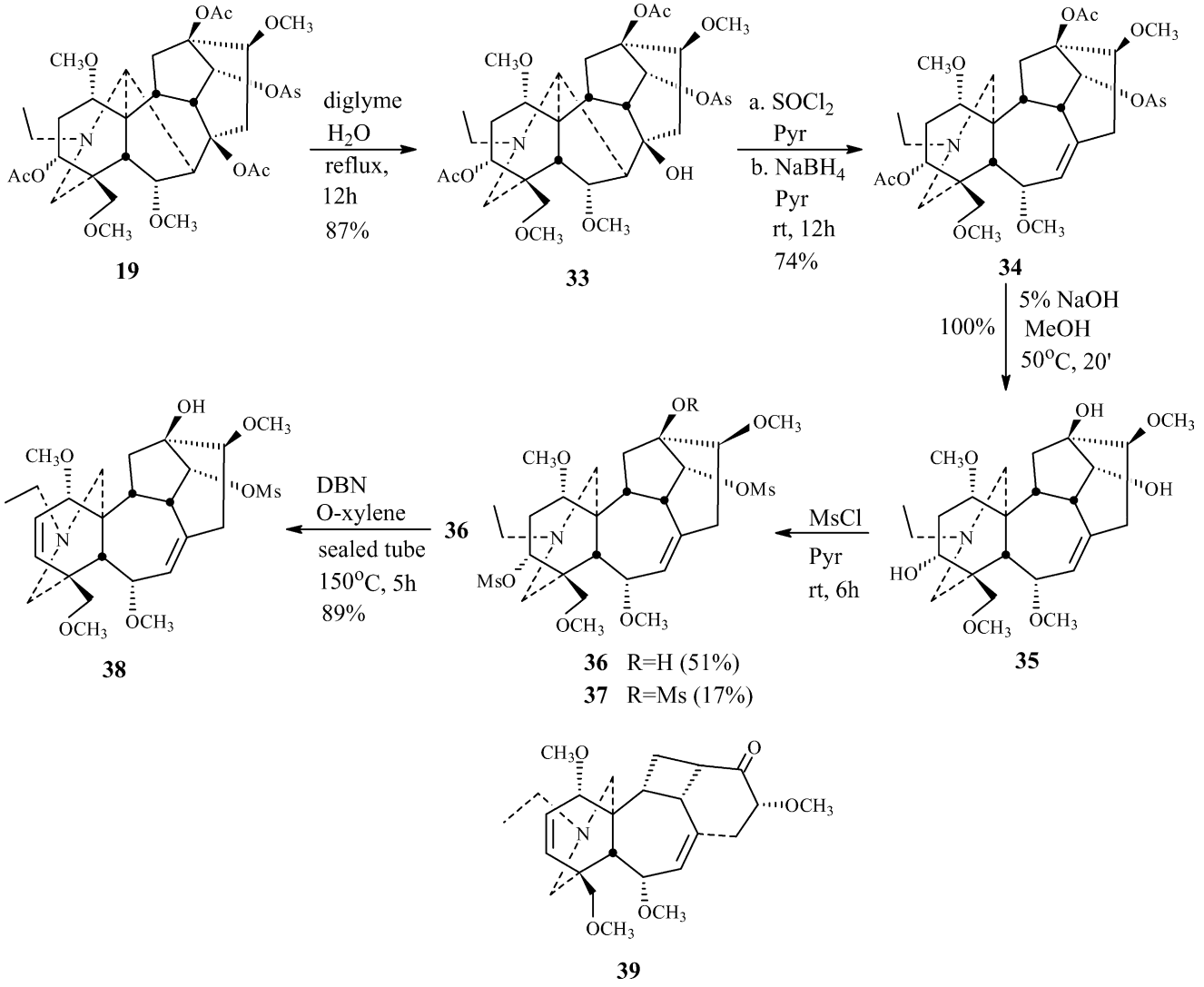
Scheme 6.

followed by sulfonation using MsCl/pyridine gave the desired product **36** (51%) along with the by-product **37** (17%) (Scheme 7). But, treatment of **36** under different conditions (DBN/ *o*-xylene, sealed tube, 180 °C; NaOH/ DMF, reflux, 12 h[16q]) gave compound **38** instead of the expected C-nor product **39** (Scheme 7). The ^{1}H and ^{13}C NMR spectra of **38** exhibited the presence of a disubstituted double bond (δ_H 5.92, dd, $J=9.8$, 2.0 Hz for H-3; 5.59, hidden for H-2; δ_C 136.8 d for C-2, 129.0 d for C-3), and a trisubstituted double bond (δ_H 5.61, hidden, H-7; δ_C 131.5 s, C-8; 125.7 d, C-7). Apparently the *N*,19-*seco* compound **30** in the approach ACB or the 7,17-*seco* compound **38** in the approach BCA approach was not an adequate form of semipinacol rearrangement probably due to harsh requirement on the substrates.

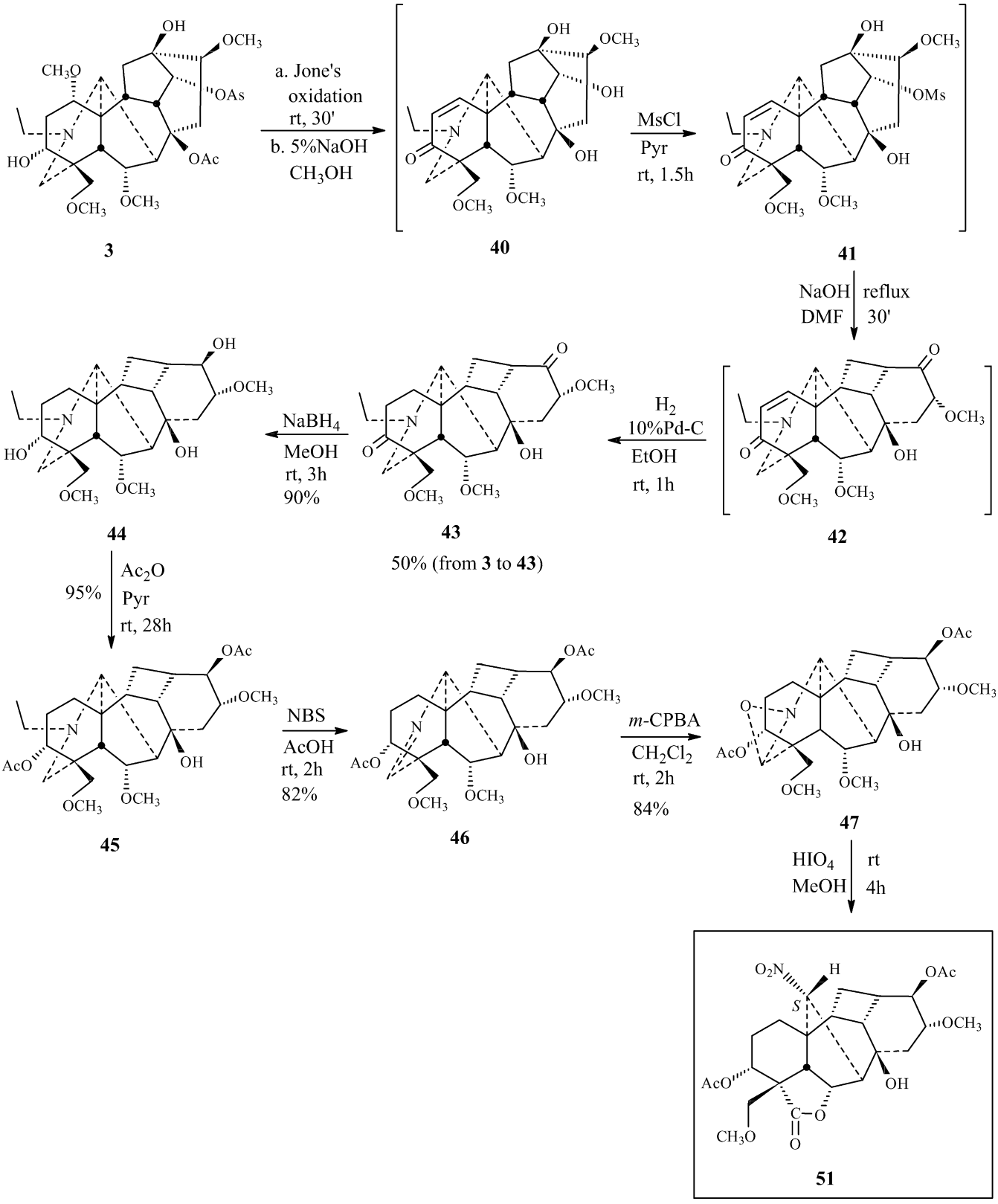
As mentioned above, all three approaches turned out to be ineffective and the last-mentioned method gave rise to the expected key intermediates **51** and **52**.

2.4. Approach CAB

The synthesis began with the starting material yunaconitine (**3**) afforded compound **43** in 50% overall yield through one-pot four step method[16s] including a key semipinacol rearrangement (Scheme 8). Its structure was determined by TLC comparison (silica gel GF_{254}, $CHCl_3$–MeOH=9:1) with the authentic sample. Reduction of **43** with $NaBH_4$ to avoid a negative participation of the keton group at C-3 followed by acetylation and subsequent formation of the imine afforded successively compounds **44**, **45**, and **46** in 70% overall yield in three steps from **43** to **46** (Scheme 8).



Scheme 7.



Scheme 8.

In the ^{1}H and ^{13}C NMR spectra of **46**, the signals at δ_H 7.39 (d, $J=1.2$ Hz, H-19) and δ_C 164.2 (d) (C-19) can be assigned to the imine group. The α-configuration of the hydroxyl group at C-3 in **44**, **45**, and **46** was supported from their larger $^{3}J_{2a,3a}$ coupling constant (9–13 Hz). In slight surprise, *m*-CPBA oxidation of **46** in an apotic media, e.g. CH_2Cl_2, resulted in formation of oxaziridine **47** in highly 84% yield where the addition to C=N is not favored presumably by participation of the more electron-donating hydroxyl group than the acetyl group as **49** at C-8.[20] The ^{1}H

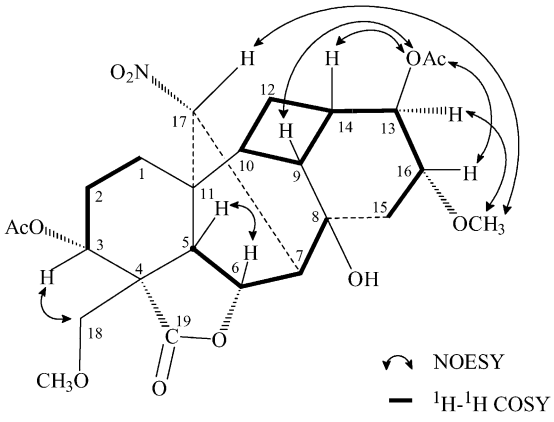


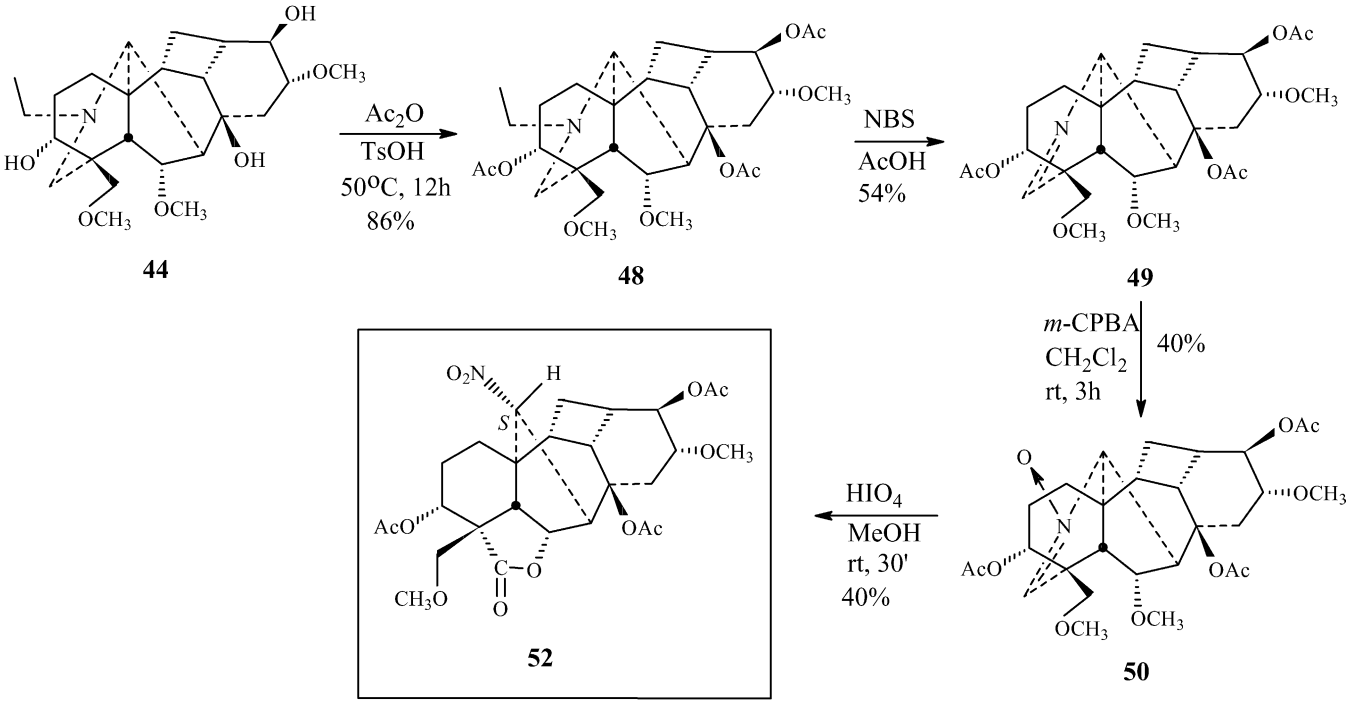
Figure 1. Key NOESY and ^{1}H–^{1}H COSY correlations of **51**.

and ^{13}C NMR spectra of **47** showed the absence of the imine or the nitrone group and the apparance of a methine carbon signal at δ_C 76.0 bearing an additional oxygen atom, together with consideration of the more 16 mass unit as compared with the molecular ion peak (*m*/*z* 491) of **46**, indicating that **47** had an oxaziridine moiety (δ_H 4.17, s, H-19; δ_C 76.0 d, C-19). In constract with **46**, treatment of triacetyl derivative **49** from **44** via **48** with *m*-CPBA under similar conditions afforded the desired nitrone **50** in modest yield of 40% which was oxidized using HIO_4 to the key intermediate **52** in only 40% yield. Wheres compound **47** was exposed to HIO_4 rather than bases or acids, where the decomposition was observed by bases, to give the analogue **51** in poor 26% yield differing from the report in the literature,[16t] indicating that obviously effect of the rearranged C-nor compounds such as **49** on formation of the nitrone. However, this is a new useful method for the ring opening of oxaziridines. In the ^{1}H and ^{13}C NMR spectra of **51** (Table 3) and **52** (see Section 4), the presence of γ-lactones [**51**: δ_H 5.63 (d, J=7.2 Hz, H-6β); δ_C 83.6 d (C-6), 177.7 s (C-19); **52**: δ_H 5.11 (d, J=7.2 Hz, H-6β); δ_C 81.9 d (C-6), 174.1 s (C-19)] was confirmed. Their IR spectra also showed absorption of the nitro groups (**51**: 1558–1378 cm^{-1}; **52**: 1550–1380 cm^{-1}). The α-orientation of H-13 in compounds **44**–**52** was deduced from the coupling constants ($J_{13,16}$=6.4–12 Hz) (see Section 4), especially including NOESY of **51** (Fig. 1), in which the correlations of OAc-13 (δ_H 2.18, 3H, s) with H-9β, H-14β, and H-16β as well as OCH_3-16α with H-13α and H-17 were observed. Similarly, α-configuration of the OAc group at C-3 in **51** also was confirmed due to the NOESY correlations between H-3β and H_2-18 (Fig. 1) as well as a larger $^3J_{2a,3a}$ coupling constant (9.2 Hz). The NOESY correlation of H-5β with H-6β in the NOESY spectrum of **51** suggested that the γ-lactone was located under the rings A and B, showing mechanically that the γ-lactone was formed prior to the *O*-demethylation of 6-OCH_3 group. The 2D NMR experiments (HMQC, ^{1}H–^{1}H COSY, HMBC, NOESY) of **51** further gave the assignments of all the ^{1}H and ^{13}C signals (Table 3). Comparison of the ^{13}C NMR spectra of **51** and **52** showed that there, as expected, are only minor differences mainly restricted to the vicinity of the C-8 function (Scheme 9).

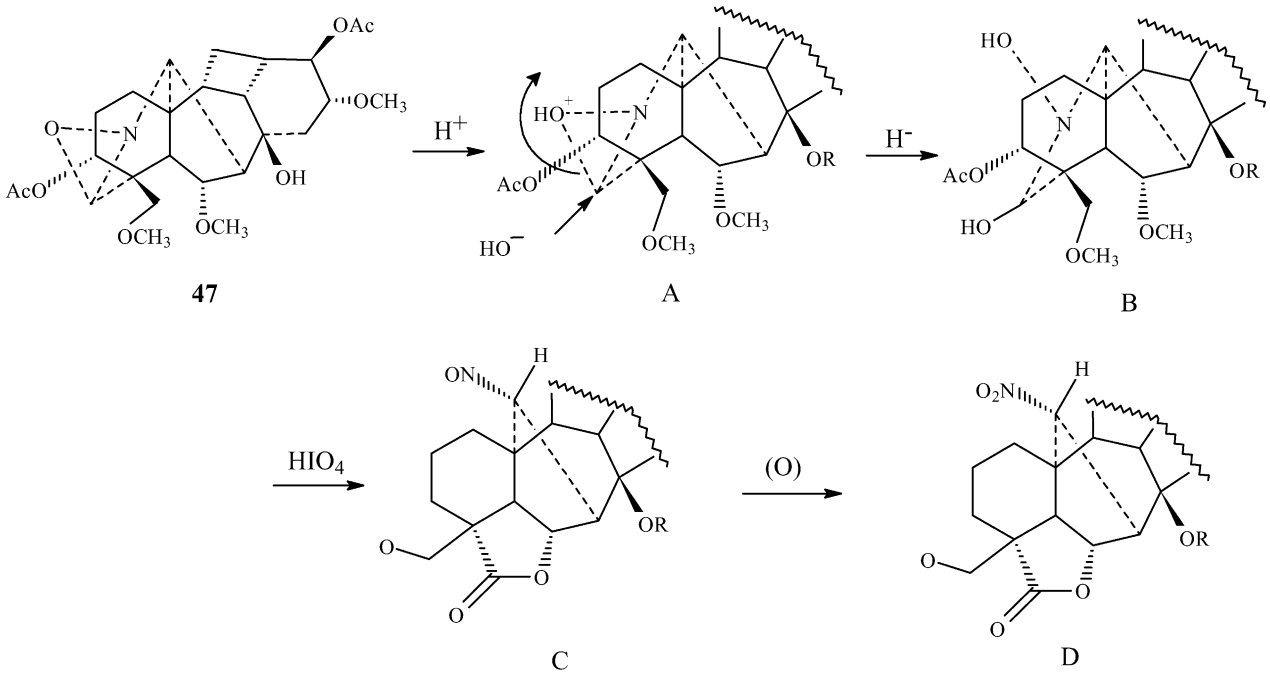
Compound **47** was converted into **51** presumably via a several step mechanism, the first step being protonation of H^+ to the oxygen atom (A), followed by an nucleophilic attack of OH^- to A and a subsequent glycol-like cleavage in company with formation of the γ-lacton moiety[16t] to afford C and its oxidized form D (Scheme 10).

3. Conclusion

This study, as a part of conversion of the C_{19}-diterpenoid



Scheme 9.



Scheme 10.

alkaloids to the taxoids, made us to drop the idea to seek a suitable route toward the key intermediate C (Scheme 1) with four approaches designed and examined based on our previous break-through results.

In the approach ABC (route 1), an attempt to reduce the aldehyde group in **7** using various regents failed mainly due to the bulkiness of hydroxyl or acetyl group at C-3. Formation of the key imines followed by cleaving the C-7–C-17 bond or preparation of the 7,17-*seco* compound using the secondary amine with respect of a protocol developed by this laboratory[16j,t,n,u,w] was then attempted.

Consequently, these were proved to be unsuccessful along with the obtainment of **16** having the new *N*,*O*-mixed acetal moiety. This seems to show that when preparing the 7,17-*seco* compounds it is necessary to meet both an anti-periplanar relationship between the lone pair of nitrogen atom and the C-8–Cl bond, as well as the tertiary pattern of the nitrogen atom in the substrates. In addition, an optimazed procedure was found to be very useful for imination or *N*-deethylation using 8 or 3 equiv of NBS, respectively with good application scope in the C_{19}-diterpenoid alkaloids.

The second approach (ACB) involves treatment of the nitroso **22** with Zn/AcOH–HCl to afford the desired compound **23** in high yield along with two interesting by-products **24** and **25**. After pretection of the amino group followed by hydrolysis and sulfonation the key compound **30** from **23** was obtained. However, to attempt conversion of **30** or **36** in the approach BCA (route 3) to the corresponding C-nor compoumd **32** or **39**, respectively, under various conditions via semipinacol rearrangement failed. This led to conclude that the *N*,19-*seco* compound **30** in the approach ACB or the 7,17-*seco* compound **36** in the approach BCA was not an adequate form of semipinacol rearrangement probably due to harsh requirement on the substrates.

Taking three unsuccessful approaches mentioned above into accunt, we offer the fourth approach CAB which at first involved in treatment of yunaconitine (**3**) using our method[16q] via semipinacol rearrangement to give the C-nor compound, and then, in cleaving the *N*-C-19 bond through three steps mainly including imination, formation of the oxaziridine or the nitrone, and HIO_4 oxidation fragmentation. Interestingly, an expected preparations of nitrone from **46** by *m*-CPBA oxidation resulted in the obtainment of oxaziridine **47** (84%) in constrast to those where *m*-CPBA oxidation of **49** led to produce nitrone **50** in moderate yield being much lower than those of *N*-oxidation of the imines from the substrates without the ring C rearrangment. Thus effect of the 8-OR (R=H, Ac) on formation of the nitrones or the oxaziridines was observed, which is worth to further research. Finally, we have found that treatment of oxaziridine **47** or nitrone **50** with HIO_4 afforded successively the key intermediate **51** or **52** in modest to moderate yield, which provided an important base for synthesis toward the vital intermediate C in Scheme 1. Further optimization of the reaction and application for synthesis of the key intermediates **51** and **52** are currently in progress.

In the course of our afore-mentioned studies, 43 C_{19}-diterpenoid alkaloids were obtained, of which 33 are structurely the new or novel compounds which were determined by spectral data (^1H and ^{13}C NMR, 2D NMR, HRMS).

4. Experimental

4.1. General

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; ^{1}H 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 except for **16** and **51** in the ^{1}H NMR spectra are reported.

4.2. Approach ABC

4.2.1. Compounds 9 and 12. To a solution of compound **7** (100 mg, 0.14 mmol) in MeOH (5 mL), 10% K_2CO_3 (1 mL) was added the solution was stirred at room temperature for 1.5 h, then saturated NH_4Cl solution (80 mL) was added. Diluting (H_2O, 10 mL), extraction (CH_3Cl, 50 mL×3), drying (Na_2SO_4), evaporation and column chromatography (silica gel H, $CHCl_3$–CH_3OH/98:2 to 95:5) afforded the pure products **9** (white amorphous powder, 69 mg, 73%) and **12** (white amorphous powder, 23 mg, 25%).

4.2.2. Compound 9. Mp 173–174 °C; R_f (95% $CHCl_3$–CH_3OH) 0.52; $[\alpha]_D^{20}=+28.5$ (*c* 0.6, $CHCl_3$); ν_{max} (KBr) 3469 (OH), 2939, 2828, 1718 (COO), 1649, 1608, 1514, 1460, 1260, 1102 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.36 (3H, s, 8-OAc), 3.00, 3.33, 3.42, 3.55, 3.87 (each 3H, s, OCH_3×5), 4.83 (1H, d, $J=4.4$ Hz, H-14β), 6.93, 8.00 (each 2H, AA′BB′, $J=8.4$ Hz, Ar-H), 10.3 (1H, s, H-19); δ_C (50 MHz, $CDCl_3$) 209.8 (C-19), 169.3 (*CO*CH_3), 165.3 (*CO*Ar), 163.5 (C-4″), 131.6 (C-2″, C-6″), 122.1 (C-1″), 113.7 (C-3″, C-5″), 83.3 (C-16), 83.1 (C-1), 82.7 (C-8), 81.8 (C-6), 78.0 (C-14), 76.2 (C-20), 75.7 (C-13), 74.1 (C-17), 71.5 (C-18), 67.9 (C-3), 59.3 (C-18′), 58.7 (C-16′), 57.1 (C-6′), 56.2 (C-1′), 55.3 (4′-OCH_3), 55.2 (C-4), 53.3 (C-7), 51.9 (C-11), 51.3 (C-5), 45.8 (C-10), 42.8 (C-9), 39.7 (C-15), 33.9 (C-2), 33.5 (C-12), 21.2 (CO*CH*$_3$); *m*/*z* (EI) 675 (3, M^+); HRMS (FAB): M^++H, found 676.2950, $C_{34}H_{46}NO_{13}$ requires 676.2969.

4.2.3. Compound 12. Mp 163–164 °C; R_f (95% $CHCl_3$–CH_3OH) 0.50; $[\alpha]_D^{20}=+50.8$ (*c* 0.50, $CHCl_3$); ν_{max} (KBr) 3452 (OH), 2930, 1718 (COO), 1650, 1607, 1514, 1461, 1371, 1259, 1102 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.33 (3H, s, 8-OAc), 3.07, 3.29, 3.44, 3.50, 3.87 (each 3H, s, OCH_3×5), 4.00, 4.15 (each 1H, $J=9.2$ Hz, H_2-18), 4.84 (1H, d, $J=4.8$ Hz, H-4β), 6.93, 8.00 (each 2H, AA′BB′, $J=8.4$ Hz, Ar-H); δ_C (50 MHz, $CDCl_3$) 174.4 (C-19), 169.9 (*CO*CH_3), 166.0 (*CO*Ar), 163.5 (C-4″), 131.6 (C-2″, C-6″), 122.3 (C-1″), 113.6 (C-3″, C-5″), 82.8 (C-16), 82.7 (C-8), 82.6 (C-1), 80.5 (C-6), 78.9 (C-14), 76.3 (C-18), 75.0 (C-13), 68.5 (C-3), 58.9 (C-18′), 58.6 (C-16′), 57.9 (C-17), 57.1 (C-6′), 55.7 (C-1′), 55.3 (4″-OCH_3), 52.3 (C-11), 48.5 (C-4, C-7), 45.3 (C-9), 43.1 (C-5), 40.3 (C-10), 36.8 (C-15), 34.9 (C-12), 33.9 (C-2), 21.4 (CO*CH*$_3$); *m*/*z* (EI) 645 (4, M^+); HRMS (FAB): M^++H, found 646.2859, $C_{33}H_{44}NO_{12}$ requires 646.2864.

4.2.4. Compound 10. To a solution of compound **7** (200 mg, 0.28 mmol) in HOAc (12 mL), $NaBH_4$ (200 mg, 5.26 mmol) was added and the solution was stirred at room temperature for 12 h. After pouring into ice water (10 mL), the solution was basified with NH_4OH to pH 9. Extraction (CH_3Cl, 10 mL×3), drying (Na_2SO_4), evaporation and column chromatography (silica gel H, $CHCl_3$–CH_3OH/98.5:1.5) afforded the pure product (white amorphous powder, 94 mg, 49%). **10**: mp 135–136 °C; R_f (95% $CHCl_3$–CH_3OH) 0.54; $[\alpha]_D^{20}=+26.2$ (*c* 0.8, $CHCl_3$); ν_{max} (KBr) 3507 (OH), 2935, 1732 (COO), 1608, 1514, 1460, 1370, 1257, 1096 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.33 (3H, s, 8-OAc), 2.04 (3H, s, 3-OAc), 2.60 (3H, s, *N*-CH_3), 3.17, 3.18, 3.24, 3.50, 3.84 (each 3H, s, OCH_3×5), 4.06 (1H, d, $J=6.8$ Hz, H-6β), 4.85 (1H, d, $J=5.0$ Hz, H-14β), 4.90 (1H, t, $J=5.8$ Hz, H-3β), 6.90, 7.99 (each 2H, AA′BB′, $J=8.8$ Hz, Ar-H); δ_C (50 MHz, $CDCl_3$) 170.0 (*CO*CH_3), 169.7 (*CO*CH_3), 165.9 (*CO*Ar), 163.3 (C-4″), 131.6 (C-2″, C-6″), 122.5 (C-1″), 113.6 (C-3″, C-5″), 85.1 (C-8), 83.5 (C-16), 83.0 (C-1), 81.7 (C-6), 78.2 (C-14), 74.7 (C-13), 71.5 (C-18), 71.3 (C-3), 62.9 (C-17), 58.6 (C-16′, C-18′), 58.0 (C-6′), 56.4 (C-1′), 55.3 (4″-OCH_3), 49.9 (C-11, C-19), 48.2 (C-7), 45.5 (C-5), 45.0 (C-9), 42.4 (C-4), 42.2 (C-21), 40.4 (C-10), 39.1 (C-15), 35.3 (C-12), 31.8 (C-2), 21.5 (CO*CH*$_3$), 21.0 (CO*CH*$_3$); *m*/*z* (EI) 687 (10, M^+), 656 (65, M−OCH_3), 628 (55, M−OAc); HRMS (FAB): M^++H, found 688.3336, $C_{36}H_{50}NO_{12}$ requires 688.3333.

4.2.5. Compound 11. To a solution of compound **9** (100 mg, 0.15 mmol) in HOAc (8 mL), KBH_4 (100 mg, 1.85 mmol) was added and the solution was stirred at room temperature for 12 h. After pouring into ice water (10 mL), the solution was basified with conc. NH_4OH to pH 9. Extraction (CH_3Cl, 10 mL×3), drying (Na_2SO_4), evaporation and column chromatography (silica gel H, $CHCl_3$–CH_3OH/95:5) afforded the pure product (white amorphous powder, 50 mg, 52%). **11**: mp 157–158 °C; R_f (90% $CHCl_3$–CH_3OH) 0.50; $[\alpha]_D^{20}=+30.5$ (*c* 0.4, $CHCl_3$); ν_{max} (KBr) 3450 (OH), 2928, 1728 (COO), 1652, 1605, 1510, 1458, 1250, 1108 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.35 (3H, s, 8-OAc), 2.64 (3H, s, *N*-CH_3), 3.13, 3.29, 3.35, 3.56, 3.86 (each 3H, s, OCH_3×5), 4.87 (1H, d, $J=5.0$ Hz, H-14β), 6.93, 8.00 (each 2H, AA′BB′, $J=8.8$ Hz, Ar-H); δ_C (50 MHz, $CDCl_3$) 169.9 (*CO*CH_3), 166.1 (*CO*Ar), 163.5 (C-4″), 131.7 (C-2″, C-6″), 122.4 (C-1″), 113.8 (C-3″, C-5″), 84.8 (C-8), 83.2 (C-16), 82.7 (C-1), 81.4 (C-6), 78.2 (C-14), 74.6 (C-13), 71.0 (C-18), 70.7 (C-3), 64.4 (C-17), 59.0 (C-18′), 58.9 (C-16′), 57.9 (C-6′), 56.2 (C-1′), 55.3 (4″-OCH_3), 50.5 (C-11), 50.2 (C-19), 48.2 (C-7), 45.3 (C-9), 44.2 (C-5), 43.6 (C-4), 42.5 (C-21), 40.7 (C-10), 39.4 (C-15), 35.7 (C-12), 32.6 (C-2), 21.3 (CO*CH*$_3$); *m*/*z* (EI) 645 (6, M^+), 627 (11, M−H_2O), 614 (2, M−OMe); HRMS (FAB): M^++H, found 646.3232, $C_{34}H_{48}NO_{11}$ requires 646.3227.

4.2.6. Compound 13. To a solution of compound **3** (1.05 g, 1.50 mmol) in diglyme (80 mL), H_2O (20 mL) was added and the solution was heated at reflux for 13 h. Removal of solvent and column chromatography afforded the pure product (white amorphous powder, 785 mg, 80%), which was taken to next step directly.

4.2.7. Compound 14. To a solution of compound **13** (500 mg, 0.76 mmol) in HOAc (15 mL), NBS (1.08 g, 6.08 mmol) was added and the solution was stirred at room temperature for 1.5 h. After pouring into ice water (20 mL), the solution was basified with conc. NH_4OH to pH 10. Extraction ($CHCl_3$, 15 mL×3), drying (Na_2SO_4), and evaporation afforded the pure product (white amorphous

powder, 467 mg, 98%). **14**: mp 135–136 °C; R_f (90% $CHCl_3$–CH_3OH) 0.45; $[\alpha]_D^{20}=+87.5$ (*c* 0.7, $CHCl_3$); ν_{max} (KBr) 3468 (OH), 2936, 1715 (COO), 1608, 1514, 1459, 1257, 1106 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 2.08 (3H, s, 3-OAc), 3.19, 3.24, 3.28, 3.40, 3.86 (each 3H, s, $OCH_3\times4$), 3.46, 4.16 (each 1H, ABq, $J=8.8$ Hz, H_2-18), 5.12 (1H, dd, $J=5.6$, 8.0 Hz, H-3β), 5.14 (1H, d, $J=4.8$ Hz, H-14β), 6.93, 8.00 (each 2H, AA′BB′, $J=8.4$ Hz, Ar-H), 7.45 (1H, d, $J=1.2$ Hz, 19-H); δ_C (100 MHz, $CDCl_3$) 170.2 (*CO*CH_3), 166.5 (*CO*Ar), 164.1 (C-19), 163.5 (C-4″), 131.7 (C-2″, C-6″), 122.1 (C-1″), 113.7 (C-3″, C-5″), 83.0 (C-16), 82.6 (C-6), 80.9 (C-1), 79.8 (C-14), 76.1 (C-13), 72.6 (C-3), 72.4 (C-18), 72.3 (C-8), 61.6 (C-17), 59.0 (C-7, C-18′), 58.3 (C-16′), 57.2 (C-6′), 55.9 (C-1′), 55.3 (4″-OCH_3), 50.4 (C-4), 49.9 (C-11), 46.4 (C-5), 44.7 (C-9), 41.9 (C-10), 40.8 (C-15), 35.7 (C-12), 30.4 (C-2), 21.9 (CO*CH*$_3$); *m/z* (EI) 629 (12, M^+), 570 (13, M−OAc); HRMS (FAB): M^++H, found 630.2911, $C_{33}H_{44}NO_{11}$ requires 630.2914.

4.2.8. Compound 15. To a solution of compound **13** (200 mg, 0.30 mmol) in HOAc (10 mL), NBS (162 mg, 0.91 mmol) was added and the solution was stirred at room temperature for 3 h. After pouring into ice water (20 mL), the solution was basified with conc. NH_4OH to pH 10. Extraction ($CHCl_3$, 15 mL×3), drying (Na_2SO_4), and evaporation afforded the pure product (white amorphous powder, 190 mg, 99%).

4.2.9. Compound 16. A solution of compound **14** (300 mg, 0.48 mmol) in pyridine (30 mL) was treated with $SOCl_2$ (2 mL) and stirred at room temperature for 5 h. Removal of solvent gave the residue, which was dissolved in MeOH (30 mL). To the solution $NaBH_4$ (300 mg) was added and this solution was stirred at room temperature for 3 h. Removal of solvent, basifying (NH_4OH, pH 9), extraction ($CHCl_3$, 10 mL×3), drying (Na_2SO_4), evaporation and column chromatography (silica gel H, cyclohexane–acetone/3:1) afforded the pure product (white amorphous powder, 200 mg, 70%). **16**: mp 132–133 °C; R_f (50% cyclohexane–acetone) 0.44; $[\alpha]_D^{20}=+17.6$ (*c* 0.6, $CHCl_3$); ν_{max} (KBr) 3465 (OH, NH), 2938, 2825, 1734 (COO), 1608, 1513, 1459, 1255, 1105 cm^{-1}; δ_H (400 MHz, $CDCl_3$) and δ_C (100 MHz, $CDCl_3$) see Table 1; *m/z* (ESI) 620 (100, M^+); HRMS (FAB): M^++H, found 598.2660, $C_{32}H_{40}NO_{10}$ requires 598.2652.

4.2.10. Compound 17. To a solution of compound **14** (35 mg, 0.056 mmol) in benzene (2 mL), $SOCl_2$ (0.3 mmol) was added and the solution was allowed to stand at room temperature for 24 h. After removal of solvent, the solution was neutralized with $NaHCO_3$ (5 mL). Extraction ($CHCl_3$, 3 mL×3), drying (Na_2SO_4), evaporation and column chromatography (silica gel H, cyclohexane–acetone/2:1) afforded the pure product (white amorphous powder, 20 mg, 59%). **17**: δ_H (200 MHz, $CDCl_3$) 2.06 (3H, s, 3-OAc), 3.21, 3.26, 3.29, 3.40, 3.85 (each 3H, s, $OCH_3\times5$), 4.94 (1H, d, $J=4.4$ Hz, H-14β), 5.00 (1H, dd, $J=4.6$, 8.8 Hz, H-3β), 5.82 (1H, d, $J=6.0$ Hz, 15-H), 6.90, 8.00 (each 2H, AA′BB′, $J=8.8$ Hz, Ar-H), 7.47 (1H, br s, H-19).

4.2.11. Compound 18. To a solution of compound **15** (50 mg, 0.08 mmol) in pyridine (3 mL), $SOCl_2$ (0.2 mL) was added and the solution was stirred at room temperature for 3 h. Evaporation in vacuum to dryness afforded a residue, which was dissolved in MeOH (10 mL). To the solution $NaBH_4$ (100 mg) was added and this solution was stirred at room temperature for 2 h. Removal of solvent gave the residue which was basified with 10% Na_2CO_3. Extraction ($CHCl_3$, 5 mL×3), drying (Na_2SO_4), evaporation and column chromatography (silica gel H, $CHCl_3$–CH_3OH/98:2) afforded the pure product (white amorphous powder, 20 mg, 41%).**18**: mp 137–138 °C; R_f (95% $CHCl_3$–CH_3OH) 0.46; $[\alpha]_D^{20}=+122.5$ (*c* 0.5, $CHCl_3$); ν_{max} (KBr) 3466 (OH, NH), 2928, 1712 (COO), 1608, 1513, 1460, 1317, 1256, 1100 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.04 (3H, s, 3-OAc), 3.22, 3.25, 3.34, 3.38, 3.85 (each 3H, s, $OCH_3\times5$), 4.90 (1H, dd, $J=5.0$, 12.2 Hz, H-3β), 4.94 (1H, d, hidden, H-14β), 5.70 (1H, d, $J=6.2$ Hz, 15-H), 6.90, 8.00 (each 2H, AA′BB′, $J=8.8$ Hz, Ar-H); *m/z* (FAB) 614 (35, M^++H), 135 (100); HRMS (FAB): M^++H, found 614.2971, $C_{33}H_{44}NO_{10}$ requires 614.2965.

4.3. Approach ACB

4.3.1. Compound 20. To a solution of compound **19**[20] (2.20 g, 2.96 mmol) in HOAc (40 mL), NBS (4.22 g, 23.7 mmol) was added and the solution was allowed to stand at room temperature for 1.5 h. After pouring into ice water (50 mL), the solution was basified with conc. NH_4OH to pH 9. Extraction ($CHCl_3$, 20 mL×3), drying (Na_2SO_4), and evaporation afforded the pure product (white amorphous powder, 2.1 g, 95%). **20**: δ_H (200 MHz, $CDCl_3$) 1.29 (3H, s, 8-OAc), 2.05, 2.07 (each 3H, 3-OAc and 13-OAc), 3.09, 3.19, 3.24, 3.40, 3.86 (each 3H, s, $OCH_3\times5$), 5.12 (1H, d, $J=5.6$ Hz, 14β-H), 5.13 (1H, t, $J=7.0$ Hz, 3β-H), 6.90, 8.00 (each 2H, AA′BB′, $J=8.8$ Hz, Ar-H), 7.37 (1H, d, $J=1.0$ Hz, 19-H).The structure of **20** was identified by comparison of ^1H NMR and TLC (cyclohexane–acetone/1:1; $CHCl_3$–CH_3OH/9:1) with the authentic sample.

4.3.2. Compound 21. To a solution of compound **20** (2.00 g, 2.81 mmol) in CH_2Cl_2 (30 mL), *m*-CPBA (970 mg, 5.82 mmol) was added and the solution was stirred at room temperature for 30 min. To the reaction solution was added 10% Na_2CO_3 solution and the mixture was stirred vigorously. The organic layer was separated and the water layer was extracted with $CHCl_3$ (15 mL×2). Drying (Na_2SO_4), and evaporation afforded the pure product (white amorphous powder, 2.02 g, 100%). **21**: mp 175–176 °C; R_f (90% $CHCl_3$–CH_3OH) 0.42; $[\alpha]_D^{20}=+113.0$ (*c* 0.5, $CHCl_3$); ν_{max} (KBr) 2937, 2828, 1736 (COO), 1608, 1514, 1461, 1257, 1104 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.31 (3H, s, 8-OAc), 2.06, 2.07 (each 3H, s, 3- and 13-OAc), 3.11, 3.22, 3.27, 3.42, 3.68 (each 3H, s, $OCH_3\times5$), 5.11 (1H, d, $J=5.2$ Hz, H-14β), 5.24 (1H, dd, $J=4.0$, 6.4 Hz, H-3β), 6.72 (1H, d, $J=1.2$ Hz, 19-H), 6.94, 8.03 (each 2H, AA′BB′, $J=8.8$ Hz, Ar-H); δ_C (100 MHz, $CDCl_3$) 170.4 (*CO*CH_3), 170.4 (*CO*CH_3), 169.1 (*CO*CH_3), 165.7 (*CO*Ar), 163.6 (C-4″), 135.4 (C-19), 131.8 (C-2″, C-6″), 122.0 (C-1″), 113.8 (C-3″, C-5″), 82.8 (C-8), 82.2 (C-16), 81.2 (C-1), 78.9 (C-6, C-14), 78.7 (C-13), 74.0 (C-3), 73.1 (C-17), 73.0 (C-18), 58.8 (C-18′), 58.3 (C-16′), 57.2 (C-6′), 56.1 (C-1′), 55.3 (4″-OCH_3), 54.2 (C-7), 51.5 (C-11), 45.3 (C-4), 43.3 (C-5), 41.2 (C-9), 39.3 (C-10), 38.4 (C-15), 35.3 (C-12), 28.4 (C-2), 21.2 (CO*CH*$_3$), 21.0 (CO*CH*$_3$), 20.9 (CO*CH*$_3$); *m/z* (EI) 729 (5, M^+), 697 (3), 654 (40); HRMS

(FAB): $M^+ + H$, found 730.3073, $C_{37}H_{48}NO_{14}$ requires 730.3075.

4.3.3. Compound 22. To a solution of compound **21** (550 mg, 1.33 mmol) in MeOH (25 mL), $HIO_4 \cdot 2H_2O$ (906 mg, 3.98 mmol) was added and the mixture was stirred at room temperature for 20 h. Removal of solvent, basifying (10% Na_2CO_3, 20 mL), extraction ($CHCl_3$, 10 mL×3), drying (Na_2SO_4), evaporation and column chromatography (silica gel H, $CHCl_3$–CH_3OH/70:1) afforded the pure product (blue crystal powder, 390 mg, 71%). **22**: mp 185–186 °C; R_f (97% $CHCl_3$–CH_3OH) 0.50; $[\alpha]_D^{20} = +59.2$ (*c* 1.1, $CHCl_3$); ν_{max} (KBr) 2940, 2843, 1783 (γ-lactone), 1738 (COO), 1608, 1514, 1460, 1257, 1102 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.25 (3H, s, 8-OAc), 1.94, 2.07 (each 3H, s, 3 and 13-OAc), 3.07, 3.25, 3.33, 3.76 (each 3H, s, OCH_3×4), 4.92 (1H, d, J=7.2 Hz, H-6β), 4.99 (1H, d, J=4.6 Hz, H-14β), 5.21 (1H, dd, J=3.2, 12.8 Hz, H-3β), 6.84, 7.92 (each 2H, AA′BB′, J=8.4 Hz, Ar-H); δ_C (50 MHz, $CDCl_3$) 173.2 (C-19), 170.5 (*CO*CH_3), 170.1 (*CO*CH_3), 168.9 (*CO*CH_3), 165.8 (*CO*Ar), 163.6 (C-4″), 131.8 (C-2″, C-6″), 121.7 (C-1″), 113.7 (C-3″, C-5″), 105.8 (C-17), 82.1 (C-8, C-13), 81.6 (C-1, C-16), 79.3 (C-6), 78.2 (C-14), 75.1 (C-18), 68.3 (C-3), 59.5 (C-18′), 58.2 (C-16′), 57.2 (C-6′), 57.0 (C-7), 56.2 (C-1′), 55.4 (4″-OCH_3), 53.2 (C-5), 51.8 (C-11), 51.7 (C-4), 44.8 (C-9), 42.1 (C-10), 40.3 (C-15), 33.9 (C-12), 31.2 (C-2), 21.0 (CO*CH₃*), 21.0 (CO*CH₃*), 20.9 (CO*CH₃*); *m/z* (EI) 730 (25, $M^+ + H$), 699 (4, $M - OCH_3$), 670 (15); HRMS (FAB): $M^+ + H$, found 730.2714, $C_{36}H_{44}NO_{15}$ requires 730.2711.

4.3.4. Compounds 23, 24 and 25. To a solution of compound **22** (450 mg, 0.62 mmol) in HOAc (8 mL) and excess Zn dust (1.0 g), conc. HCl (1 mL) was added dropwise with stirring vigorously. The mixture was stirred at room temperature for 12 h. After filtration, the filtrate was poured into ice water (10 mL). Basifying (conc. NH_4OH, pH 9), extraction ($CHCl_3$, 10 mL×3), drying (Na_2SO_4), evaporation and column chromatography (silica gel H, $CHCl_3$–CH_3OH/200:1.5) afforded the pure product **23** (colorless crystal needle, 304 mg, 69%), **24** (white amorphous powder, 80 mg, 18%) and **25** (white amorphous powder, 35 mg, 8%).

4.3.5. Compound 23. Mp 244–245 °C; R_f (99% $CHCl_3$–CH_3OH) 0.58; $[\alpha]_D^{20} = +26.8$ (*c* 0.4, $CHCl_3$); ν_{max} (KBr) 3461 (OH), 2929, 2856, 1780 (γ-lactone), 1736 (COO), 1608, 1514, 1403, 1257, 1100 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.31 (3H, s, 8-OAc), 2.03, 2.08 (each 3H, s, 3 and 13-OAc), 3.30, 3.32, 3.37, 3.84 (each 3H, s, OCH_3×4), 3.94 (1H, s, H-17), 4.77 (1H, d, J=6.2 Hz, H-6β), 5.02 (1H, d, J=5.0 Hz, H-14β), 5.04 (1H, dd, J=4.2, 9.6 Hz, H-3β), 6.90, 8.00 (each 2H, AA′BB′, J=8.8 Hz, Ar-H); δ_C (50 MHz, $CDCl_3$) 174.1 (C-19), 170.7 (*CO*CH_3), 170.4 (*CO*CH_3), 169.3 (*CO*CH_3), 165.9 (*CO*Ar), 163.6 (C-4″), 131.8 (C-2″, C-6″), 122.0 (C-1″), 113.8 (C-3″, C-5″), 82.6 (C-1, C-8, C-13), 81.1 (C-16), 79.7 (C-6), 76.6 (C-14), 74.6 (C-18), 67.9 (C-3), 59.4 (C-18′), 58.2 (C-16′), 56.5 (C-1′), 55.5 (C-17), 55.3 (4″-OCH_3), 54.3 (C-7), 51.8 (C-4), 51.3 (C-5), 50.6 (C-11), 44.5 (C-9), 41.8 (C-10), 40.9 (C-15), 34.2 (C-12), 30.2 (C-2), 21.2 (CO*CH₃*), 21.1 (CO*CH₃*), 21.0 (CO*CH₃*); *m/z* (FAB) 716 (100, $M^+ + H$), 656 (7, $M - OAc + H$); HRMS (FAB): $M^+ + H$, found 716.2918, $C_{36}H_{46}NO_{14}$ requires 716.2918.

4.3.6. Compound 24. Mp 191–192 °C; R_f (99% $CHCl_3$–CH_3OH) 0.52; $[\alpha]_D^{20} = +15.0$ (*c* 1.4, $CHCl_3$); ν_{max} (KBr) 3470 (OH), 2929, 2856, 1782 (γ-lactone), 1737 (COO), 1608, 1514, 1461, 1258, 1100 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.31 (3H, s, 8-OAc), 2.03, 2.12 (each 3H, s, 3 and 13-OAc), 3.25, 3.29, 3.34, 3.84 (each 3H, s, OCH_3×4), 4.77 (1H, d, J=6.2 Hz, H-6β), 4.99 (1H, dd, J=3.8, 10.2 Hz, H-3β), 5.01 (1H, d, J=4.8 Hz, H-14β), 5.48 (1H, br s, NH-*OH*), 6.91, 8.00 (each 2H, AA′BB′, J=8.6 Hz, Ar-H); δ_C (50 MHz, $CDCl_3$) 174.1 (C-19), 170.6 (*CO*CH_3), 170.4 (*CO*CH_3), 169.2 (*CO*CH_3), 166.0 (*CO*Ar), 163.6 (C-4″), 131.8 (C-2″, C-6″), 122.0 (C-1″), 113.8 (C-3″, C-5″), 82.5 (C-8), 82.3 (C-13), 81.9 (C-1), 81.7 (C-16), 79.6 (C-6), 76.6 (C-14), 74.2 (C-18), 67.4 (C-3), 64.5 (C-17), 59.4 (C-18′), 58.3 (C-16′), 56.6 (C-1′), 55.4 (4″-OCH_3), 51.8 (C-4), 51.4 (C-7), 49.9 (C-11), 49.5 (C-5), 44.9 (C-9), 42.2 (C-10), 40.7 (C-15), 34.2 (C-12), 30.7 (C-2), 21.3 (CO*CH₃*), 21.1 (CO*CH₃*), 21.0 (CO*CH₃*); *m/z* (FAB) 732 (100, $M^+ + H$), 672 (15, $M - OAc + H$); HRMS (FAB): $M^+ + H$, found 732.2870, $C_{36}H_{46}NO_{15}$ requires 732.2867.

4.3.7. Compound 25. Mp 188–190 °C; R_f (99% $CHCl_3$–CH_3OH) 0.48; $[\alpha]_D^{20} = +45.8$ (*c* 0.6, $CHCl_3$); ν_{max} (KBr) 3461 (OH), 2928, 2856, 1778 (γ-lactone), 1733 (COO), 1608, 1514, 1461, 1259, 1099 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.30 (3H, s, 8-OAc), 2.02, 2.09 (each 3H, s, 3 and 13-OAc), 3.31×2, 3.35, 3.83 (each 3H, s, OCH_3×4), 4.06 (1H, s, H-17), 4.77 (1H, d, J=6.2 Hz, H-6β), 5.00 (1H, d, J=4.6 Hz, H-14β), 5.04 (1H, d, J=4.6, 12.0 Hz, H-3β), 6.90, 7.98 (each 2H, AA′BB′, J=8.6 Hz, Ar-H); δ_C (50 MHz, $CDCl_3$) 173.7 (C-19), 170.5 (*CO*CH_3), 170.3 (*CO*CH_3), 169.2 (*CO*CH_3), 165.9 (*CO*Ar), 163.6 (C-4″), 131.8 (C-2″, C-6″), 121.9 (C-1″), 113.8 (C-3″, C-5″), 82.3 (C-8), 82.2 (C-13), 81.8 (C-1), 81.6 (C-16), 79.6 (C-6), 76.5 (C-14), 75.4 (C-18), 74.7 (C-17), 67.3 (C-3), 59.4 (C-18′), 58.2 (C-16′), 56.6 (C-1′), 55.4 (4″-OCH_3), 54.9 (C-7), 51.8 (C-4), 51.1 (C-11), 50.6 (C-5), 43.6 (C-9), 41.4 (C-10), 40.6 (C-15), 34.1 (C-12), 31.8 (C-2), 21.2 (CO*CH₃*), 21.0 (CO*CH₃*), 21.0 (CO*CH₃*); *m/z* (FAB) 717 (20, $M^+ + H$), 657 (18, $M - OAc + H$); HRMS (FAB): $M^+ + H$, found 717.2753, $C_{36}H_{45}O_{15}$ requires 717.2758.

4.3.8. Compound 26. To a solution of compound **23** (30 mg, 0.04 mmol) in Ac_2O (2 mL), *p*-TsOH (20 mg) was added and the mixture was stirred at room temperature for 20 h. After pouring into ice water (5 mL), the solution was basified with conc. NH_4OH to pH 9. Extraction ($CHCl_3$, 5 mL×3), drying (Na_2SO_4) and evaporation afforded the pure product (white amorphous powder, 32 mg, 100%). **26**: mp 162–163 °C; R_f (75% cyclohexane–acetone) 0.55; $[\alpha]_D^{20} = +46.0$ (*c* 0.5, $CHCl_3$); ν_{max} (KBr) 3410 (*N*H), 2929, 1776 (γ-lactone), 1738 (COO), 1674 (CONH), 1608, 1514, 1461, 1259, 1099 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.33 (3H, s, 8-OAc), 2.01, 2.07, 2.16 (each 3H, s, OAc×3), 3.25, 3.37, 3.42, 3.86 (each 3H, s, OCH_3×4), 4.46 (1H, d, J=8.8 Hz, H-17), 4.84 (1H, d, J=6.4 Hz, H-6β), 5.02 (1H, dd, J=3.0, 8.0 Hz, H-3β), 5.06 (1H, d, J=5.2 Hz, H-14β), 5.72 (1H, brd, J=8.8 Hz, 17-*NH*Ac), 6.94, 8.03 (each 2H, AA′BB′, J=8.8 Hz, Ar-H); δ_C (100 MHz, $CDCl_3$) 174.0 (C-19), 170.2 (*CO*CH_3), 170.0 (*CO*CH_3), 169.1 (*CO*CH_3),

169.0 (*CO*CH_3), 166.0 (*CO*Ar), 163.7 (C-4″), 131.9 (C-2″, C-6″), 122.0 (C-1″), 113.9 (C-3″, C-5″), 83.3 (C-1), 82.4 (C-8, C-13), 81.2 (C-16), 79.8 (C-6), 76.5 (C-14), 75.3 (C-18), 67.7 (C-3), 59.5 (C-18′), 58.5 (C-16′), 56.8 (C-1′), 55.4 (4″-OCH_3), 54.9 (C-17), 52.6 (C-7), 52.0 (C-4), 51.9 (C-5), 50.8 (C-11), 46.4 (C-9), 41.6 (C-10), 40.6 (C-15), 34.5 (C-12), 30.0 (C-2), 22.5 (CO*CH₃*), 21.2 (CO*CH₃*), 21.1 (CO*CH₃*), 21.0 (CO*CH₃*); *m/z* (EI) 758 (100, M^++H), 698 (33, M−OAc+H); HRMS (FAB): M^++H, found 758.3035, $C_{38}H_{48}NO_{15}$ requires 758.3024.

4.3.9. Compound 27. To a solution of compound **25** (20 mg, 0.03 mmol) in Ac_2O (2 mL), *p*-TsOH (10 mg) was added and the mixture was stirred at room temperature for 12 h. General work-up afforded the pure product (white amorphous powder, 21 mg, 100%). **27**: mp 157–158 °C; R_f (75% cyclohexane–acetone) 0.50; $[\alpha]_D^{20}=-82.0$ (*c* 0.7, $CHCl_3$); ν_{max} (KBr) 2929, 1775 (γ-lactone), 1741 (COO), 1608, 1514, 1461, 1371, 1241, 1101 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.31 (3H, s, 8-OAc), 2.06, 2.07, 2.17 (each 3H, s, OAc×3), 3.28, 3.36, 3.42, 3.86 (each 3H, s, OCH_3×4), 4.79 (1H, d, *J*=6.4 Hz, H-6β), 5.03 (1H, hidden, H-17), 5.04 (1H, d, *J*=4.8 Hz, H-14β), 5.05 (1H, dd, *J*=4.0, 12.0 Hz, H-3β), 6.93, 8.03 (each 2H, AA′BB′, *J*=8.8 Hz, Ar-H); δ_C (100 MHz, $CDCl_3$) 173.2 (C-19), 170.7 (*CO*CH_3), 170.2 (*CO*CH_3), 169.4 (*CO*CH_3), 168.8 (*CO*CH_3), 166.0 (*CO*Ar), 163.7 (C-4″), 131.9 (C-2″, C-6″), 122.0 (C-1″), 113.9 (C-3″, C-5″), 82.4 (C-8), 82.0 (C-13), 81.4 (C-1), 81.0 (C-16), 79.6 (C-6), 76.3 (C-14), 75.8 (C-17), 74.4 (C-18), 67.6 (C-3), 59.4 (C-18′), 58.4 (C-16′), 56.7 (C-1′), 55.4 (4″-OCH_3), 53.6 (C-7), 51.7 (C-5), 51.6 (C-4), 49.5 (C-11), 44.5 (C-9), 41.8 (C-10), 39.9 (C-15), 34.2 (C-12), 30.0 (C-2), 21.2 (CO*CH₃*), 21.2 (CO*CH₃*), 21.1 (CO*CH₃*), 21.0 (CO*CH₃*); *m/z* (ESI) 759 (40, M^++H); HRMS (FAB): M^++H, found 759.2870, $C_{38}H_{46}O_{16}$ requires 759.2864.

4.3.10. Compound 28. To a solution of compound **23** (300 mg, 0.42 mmol) in pyridine (15 mL), TsCl (240 mg, 1.26 mmol) was added and the solution was allowed to stand at room temperature for 30 h. Removal of solvent, basifying (10% Na_2CO_3, 20 mL), extraction ($CHCl_3$, 10 mL×3), drying (Na_2SO_4), evaporation and column chromatography (silica gel H, $CHCl_3$–CH_3OH/100:1) afforded the pure product as a white amorphous powder, 345 mg, (95%). **28**: mp 178–179 °C; R_f (98% $CHCl_3$–CH_3OH) 0.42; $[\alpha]_D^{20}=+5.5$ (*c* 1.7, $CHCl_3$); ν_{max} (KBr) 3466 (OH), 2939, 1778 (γ-lactone), 1740 (COO), 1607, 1514, 1460, 1371, 1258, 1101 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.27 (3H, s, 8-OAc), 1.96, 2.20 (each 3H, s, OAc×2), 2.41 (3H, s, Ar-CH_3), 3.17, 3.31, 3.45, 3.86 (each 3H, s, OCH_3×4), 4.84 (1H, d, *J*=6.4 Hz, H-6β), 5.00 (1H, d, *J*=5.0 Hz, H-14β), 5.09 (1H, dd, *J*=2.8, 7.8 Hz, H-3β), 5.66 (1H, d, *J*=2.4 Hz, H-17), 6.93, 8.00 (each 2H, AA′BB′, *J*=8.8 Hz, OAs), 7.32, 7.80 (each 2H, AA′BB′, *J*=8.4 Hz, Ts); δ_C (50 MHz, $CDCl_3$) see Table 2; *m/z* (FAB) 870 (20, M^++H), 810 (7, M−OAc+H); HRMS (FAB): M^++H, found 870.3013, $C_{43}H_{52}NO_{16}S$ requires 870.3007.

4.3.11. Compound 29. A solution of compound **28** (380 mg, 0.44 mmol) in 5% methanolic NaOH (15 mL) was heated at 50 °C for 20 min. Removal of solvent, diluting (H_2O, 30 mL), extraction (EtOAc, 20 mL×4), drying (Na_2SO_4) and evaporation afforded the pure product (colorless crystal needle, 240 mg, 90%). **29**: mp 234–235 °C; R_f (90% $CHCl_3$–CH_3OH) 0.50; $[\alpha]_D^{20}=+56.4$ (*c* 0.5, CH_3OH); ν_{max} (KBr) 3427 (OH), 3108 (NH), 2928, 1768 (γ-lactone), 1601, 1460, 1377, 1330, 1096 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.40 (3H, s, Ar-CH_3), 2.97, 3.33, 3.43 (each 3H, s, OCH_3×3), 5.14 (1H, d, *J*=5.4 Hz, H-6β), 7.28, 7.73 (each 2H, AA′BB′, *J*=8.0 Hz, Ts); δ_C (50 MHz, CD_3COCD_3) see Table 2; *m/z* (FAB) 610 (100, M^++H); HRMS (FAB): M^++H, found 610.2327, $C_{29}H_{40}NO_{11}S$ requires 610.2322.

4.3.12. Compound 30. To a solution of compound **29** (300 mg, 0.49 mmol) in pyridine (10 mL), MsCl (0.20 mL, 2.57 mmol) was added and the solution was allowed to stand at room temperature for 3 h. Removal of solvent, diluting (H_2O), basifying (10% Na_2CO_3, pH 11), extraction ($CHCl_3$, 10 mL×3), drying (Na_2SO_4) and evaporation afforded the pure product as a white amorphous powder, 350 mg, (93%). **30**: mp 152–153 °C; R_f (95% $CHCl_3$–CH_3OH) 0.48; $[\alpha]_D^{20}=+19.4$ (*c* 0.6, $CHCl_3$); ν_{max} (KBr) 3507 (OH), 3320 (NH), 2935, 1771 (γ-lactone), 1639, 1460, 1350, 1176, 1094 cm^{-1}; δ_H (200 MHz, $CDCl_3$+CD_3OD) 2.28 (3H, s, Ar-CH_3), 2.94, 2.97 (each 3H, s, OMs×2), 3.05, 3.20, 3.26 (each 3H, s, OCH_3×3), 4.43 (1H, d, *J*=4.2 Hz, H-14β), 4.76 (1H, d, *J*=5.0 Hz, H-3β), 5.03 (1H, d, *J*=6.4 Hz, H-6β), 7.19, 7.58 (each 1H, AA′BB′, *J*=8.0 Hz, Ts); δ_C (50 MHz, $CDCl_3$+CD_3OD) see Table 2; *m/z* (FAB) 766 (100, M^++H); HRMS (FAB): M^++H, found 766.1869, $C_{31}H_{44}NO_{15}S_3$ requires 766.1873.

4.3.13. Compound 31. To a mixture of compound **30** (100 mg, 0.13 mmol) and anhydrous NaOAc (200 mg, 2.43 mmol) in sealed tube (20 mL), HOAc (3 mL) was added and the solution was stirred at 150 °C for 24 h. Diluting (ice water), basifying (NH_4OH, pH 10), extraction ($CHCl_3$, 5 mL×3), drying (Na_2SO_4), evaporation and column chromatography (silica gel H, $CHCl_3$–CH_3OH/25:1) afforded the pure product as a white amorphous powder, 80 mg, (70%). **31**: mp 232–233 °C; R_f (90% $CHCl_3$–CH_3OH) 0.51; $[\alpha]_D^{20}=-13.0$ (*c* 0.7, $CHCl_3$); ν_{max} (KBr) 3487 (OH), 3324 (NH), 2934, 1758 (γ-lactone), 1638, 1460, 1353, 1167, 1091 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.44 (3H, s, Ar-CH_3), 3.12, 3.25, 3.31, 3.41 (each 3H, s, OCH_3×3), 4.68 (1H, d, *J*=4.8 Hz, H-14β), 4.80 (1H, s, H-17), 5.12 (1H, d, *J*=7.2 Hz, H-6β), 5.92 (1H, dd, *J*=2.0, 10.4 Hz, H-2), 6.04 (1H, dd, *J*=1.6, 10.4 Hz, H-3), 7.31, 7.73 (each 1H, AA′BB′, *J*=8.8 Hz, Ts); δ_C (50 MHz, $CDCl_3$) see Table 2; *m/z* (FAB) 670 (85, M^++H); HRMS (FAB): M^++H, found 670.1988, $C_{30}H_{40}NO_{12}S_2$ requires 670.1992.

4.4. Approach BCA

4.4.1. Compound 33. To a solution of compound **19** (1.10 g, 1.48 mmol) in diglyme (40 mL), H_2O (10 mL) was added and the solution was heated at reflux for 12 h. Diluting (H_2O, 40 mL), basifying (NH_4OH, pH 10), extraction ($CHCl_3$, 20 mL×3), drying (Na_2SO_4), evaporation and column chromatography (silica gel H, $CHCl_3$–CH_3OH/50:1) afforded the pure product as a white amorphous powder, 900 mg, (87%), which was identified

Table 2. ^{13}C NMR data of compounds **28**, **29**, **30**, and **31**

Carbon	**28**	**29**	**30**	**31**
1	82.1 d	83.9 d	83.2 d	82.4 d
2	28.9 t	32.2 t	30.0 t	128.1 d
3	66.5 d	67.1 d	73.3 d	127.9 d
4	51.6 s	52.8 s	52.0 s	50.7 s
5	50.4 d	51.5 d	48.8 d	48.9 d
6	79.6 d	81.3 d	79.3 d	78.6 d
7	52.1 d	52.0 d	57.2 d	57.0 d
8	82.0 s	78.0 s	75.1 s	75.4 s
9	45.5 d	48.3 d	44.5 d	45.6 d
10	40.9 d	46.1 d	44.0 d	43.7 d
11	50.4 s	51.0 s	50.4 s	50.1 s
12	34.4 t	36.2 t	33.8 t	33.6 t
13	82.0 s	72.4 s	70.8 s	70.3 s
14	76.5 d	78.8 d	83.9 d	84.2 d
15	39.8 t	43.9 t	42.0 t	42.3 t
16	80.3 d	85.3 d	81.6 d	81.6 d
17	57.7 d	58.1 d	58.1 d	57.1 d
18	76.6 t	78.6 t	75.8 t	78.2 t
19	173.5 s	178.5 s	174.0 s	175.7 d
1′	56.6 q	56.3 q	56.1 q	56.6 q
16′	58.4 q	58.7 q	58.2 q	58.3 q
18′	59.4 q	59.4 q	59.0 q	59.4 q
O=C	170.2 s	—	—	—
|	170.2 s	—	—	—
CH_3	168.7 s	—	—	—
	21.1 q	—	—	—
	21.1 q	—	—	—
	21.0 q	—	—	—
SO_2	137.2 s	138.0 s	135.8 s	136.1 s
	129.3 d	130.3 d	129.4 d	129.5 d
	127.9 d	128.5 d	127.3 d	127.7 d
	143.4 s	144.0 s	143.7 s	143.6 s
CH_3	21.5 q	21.3 q	21.1 q	21.4 q
O=C	165.9 s	—	—	—
	121.8 s	—	—	—
	131.8 d	—	—	—
	113.8 d	—	—	—
	163.6 s	—	—	—
OCH_3	55.4 q	—	—	—
OMs	—	—	38.4 q	38.7 q
	—	—	38.1 q	—

by comparison with the authentic sample [TLC: cyclohexane–acetone/2:1; $CHCl_3$–CH_3OH/98:2].

4.4.2. Compound 34. To a solution of compound **33** (900 mg, 1.28 mmol) in pyridine (20 mL), $SOCl_2$ (1.0 mL) was added and the solution was stirred at room temperature for 12 h. To the reaction solution was added excess $NaBH_4$ and the reaction solution continued to stand at room temperature for 3 h. Removal of solvent, diluting (H_2O, 40 mL), basifying (conc. NH_4OH, pH 10), extraction ($CHCl_3$, 20 mL×3), drying (Na_2SO_4), evaporation and column chromatography (silica gel H, cyclohexane–acetone/4:1) afforded the pure product as a white amorphous powder, 650 mg, (74%), which was identified by comparison with the authentic sample [TLC: cyclohexane–acetone/2:1; $CHCl_3$–CH_3OH/96:4].

4.4.3. Compound 35. A solution of compound **34** (400 mg, 0.59 mmol) in 5% methanolic NaOH (15 mL) was heated at 50 °C for 20 min. Removal of solvent, diluting (H_2O, 50 mL), extraction ($CHCl_3$, 10 mL×3), drying (Na_2SO_4) and evaporation afforded the pure product (white amorphous powder, 274 mg, 100%). **35**: mp 92–93 °C; R_f (90% $CHCl_3$–CH_3OH) 0.42; $[\alpha]_D^{20} = +40.4$ (*c* 0.5, $CHCl_3$); ν_{max} (KBr) 3427 (OH), 2930, 1639, 1451, 1376, 1180, 1100 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.98 (3H, t, $J=7.2$ Hz, *N*-CH_2CH_3), 3.33, 3.33, 3.34, 3.45 (each 3H, s, OCH_3×4), 4.15 (1H, d, $J=2.8$ Hz, H-14β), 5.58 (1H, br s, H-7); δ_C (100 MHz, $CDCl_3$) 133.5 (C-8), 126.8 (C-7), 85.4 (C-1, C-16), 82.6 (C-6), 79.8 (C-14), 77.8 (C-13), 74.3 (C-18), 70.5 (C-3), 59.1 (C-18′), 57.7 (C-16′), 57.6 (C-6′), 56.1 (C-1′), 52.1 (C-19), 51.6 (C-17), 49.5 (NCH_2CH_3), 43.9 (C-5), 43.7 (C-11), 42.2 (C-4), 41.6 (C-9), 40.9 (C-10), 38.9 (C-15), 38.5 (C-12), 35.3 (C-2), 12.0 (NCH_2CH_3); *m/z* (EI) 467 (15, M^+), 452 (100, $M-CH_3$), 436 (75, $M-OCH_3$), 378 (85); HRMS (FAB): $M^+ + H$, found 468.2959, $C_{25}H_{42}NO_7$ requires 468.2961.

4.4.4. Compounds 36 and 37. To a solution of compound

35 (220 mg, 0.47 mmol) in pyridine (15 mL), MsCl (0.14 mL, 1.80 mmol) was added and the solution was stirred at room temperature for 6 h. Removal of solvent, diluting (H_2O, 50 mL), basifying (10% Na_2CO_3, 20 mL), extraction ($CHCl_3$, 10 mL×3), drying (Na_2SO_4), evaporation and column chromatography (silica gel H, $CHCl_3$–CH_3OH/100:0.7) afforded the pure products as white amorphous powder (**36**: 150 mg, 51%; **37**: 55 mg, 17%).

4.4.5. Compound 36. Mp 113–114 °C; R_f (99% $CHCl_3$–CH_3OH) 0.56; $[\alpha]_D^{20}=+18.4$ (*c* 0.5, $CHCl_3$); ν_{max} (KBr) 3477 (OH), 2934, 1638, 1458, 1352, 1176, 1102 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.97 (3H, t, $J=7.2$ Hz, *N*-CH_2CH_3), 3.03, 3.07 (each 3H, s, OMs×2), 3.29, 3.37, 3.37, 3.34 (each 3H, s, OCH_3×4), 4.66 (1H, d, $J=2.0$ Hz, 14β-H), 4.83 (1H, dd, $J=6.4$, 11.6 Hz, H-3β), 5.56 (1H, br s, H-7); δ_C (100 MHz, $CDCl_3$) 131.8 (C-8), 127.0 (C-7), 88.8 (C-14), 85.1 (C-16), 84.3 (C-1), 81.1 (C-6), 79.5 (C-3), 76.8 (C-13), 71.2 (C-18), 58.5 (C-18′), 57.8 (C-6′, C-16′), 56.1 (C-1′), 51.6 (C-19), 50.8 (C-17), 49.4 (NCH_2CH$_3$), 43.3 (C-11), 42.9 (C-5), 42.2 (C-4), 40.8 (C-9), 40.5 (C-10), 38.7 (C-15), 38.6 (C-12), 38.2 (OMs), 38.2 (OMs), 33.2 (C-2), 11.8 (NCH_2CH_3); *m*/*z* (EI) 623 (1, M^+), 608 (3, M−CH_3), 432 (100, M−OMs×2-H); HRMS (FAB): M^++H, found 624.2520, $C_{27}H_{46}NO_{11}S_2$ requires 624.2512.

4.4.6. Compound 37. Mp 110–111 °C; R_f (99% $CHCl_3$–CH_3OH) 0.5; $[\alpha]_D^{20}=+8.8$ (*c* 0.5, $CHCl_3$); ν_{max} (KBr) 2938, 1639, 1459, 1355, 1170, 1105 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.96 (1H, t, $J=7.2$ Hz, *N*-CH_2CH_3), 3.03, 3.10, 1.13 (each 3H, s, OMs×3), 3.29, 3.35, 3.37, 3.41 (each 3H, s, OCH_3×4), 4.83 (1H, dd, $J=5.2$, 11.6 Hz, H-3β), 4.90 (1H, br s, H-14β), 5.69 (1H, br s, H-7); δ_C (100 MHz, $CDCl_3$) 130.5 (C-8), 127.4 (C-7), 90.8 (C-13), 86.8 (C-14), 83.8 (C-1), 83.3 (C-16), 80.8 (C-6), 79.1 (C-3), 71.2 (C-18), 58.5 (C-18′), 57.7 (C-16′), 56.7 (C-6′), 56.0 (C-1′), 51.4 (C-19), 50.5 (C-17), 49.4 (NCH_2CH$_3$), 43.2 (C-11), 42.2 (C-4), 42.1 (C-5), 40.5 (C-9), 40.4 (C-10), 40.2 (OMs), 39.2 (C-15), 39.1 (C-12), 38.9 (OMs), 38.4 (OMs), 33.2 (C-2), 11.8 (NCH_2CH_3); *m*/*z* (EI) 701 (1, M^+), 605 (14, M−OMs-1), 510 (75, M−OMs×2-1), 414 (25, M−OMs×3-H-H); HRMS (FAB): M^++H, found 702.2287, $C_{28}H_{48}NO_{13}S_3$ requires 702.2288.

4.4.7. Compound 38. To a mixture of compound **36** (100 mg, 0.13 mmol) and *o*-xylene (2.5 mL) in sealed tube (20 mL), DBN (0.5 mL) was added and the solution was heated at 150 °C for 5 h. Removal of *o*-xylene and column chromatography (silica gel H, $CHCl_3$–CH_3OH/9:1) afforded the pure product (oil, 30 mg, 89%). **38**: mp 240–241 °C; R_f (80% $CHCl_3$–CH_3OH) 0.50; $[\alpha]_D^{20}=-13.4$ (*c* 0.5, $CHCl_3$); ν_{max} (KBr) 3468 (OH), 3324, 2930, 1612, 1459, 1353, 1276, 1170, 1106 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.93 (3H, t, $J=$ 7.2 Hz, *N*-CH_2CH_3), 3.03 (3H, s, OMs), 3.30, 3.31, 3.36, 3.40 (each 3H, s, OCH_3×4), 4.65 (1H, d, $J=3.0$ Hz, H-14β), 5.59 (1H, dd, hidden, H-2), 5.61 (1H, br s, H-7), 5.92 (1H, dd, $J=2.0$, 9.8 Hz, H-3); δ_C (100 MHz, $CDCl_3$) 136.8 (C-2), 131.5 (C-8), 129.0 (C-3), 125.7 (C-7), 88.3 (C-14), 87.4 (C-1), 84.8 (C-16), 79.3 (C-6), 78.1 (C-18), 77.3 (C-12), 59.2 (C-18′), 58.1 (C-16′), 57.9 (C-6′), 56.4 (C-1′), 53.2 (C-19), 51.6 (C-17), 50.8 (NCH_2CH$_3$), 43.8 (C-5), 43.3 (C-4), 43.2 (C-11), 41.9 (C-9, C-10), 38.8 (C-12), 38.6 (C-15), 38.3 (OMs), 10.9 (NCH_2CH_3); *m*/*z* (EI) 527 (7, M^+), 521 (13, M−CH_3), 432 (100, M−OMs); HRMS (FAB): M^++H, found 528.2640, $C_{26}H_{42}NO_8S$ requires 528.2631.

4.5. Approach CAB

4.5.1. Compound 43. To a solution of yunaconitine (**3**) (1.55 g, 2.35 mmol) in acetone (10 mL), Jones reagent (3 mL, 8.22 mmol) was added dropwise under ice-water bath and the solution was stirred at room temperature for 30 min. Diluting (H_2O, 30 mL), basifying (conc. NH_4OH, pH 11), extraction ($CHCl_3$, 15 mL×4), drying (Na_2SO_4) and evaporation afforded the white amorphous powder, which was dissolved in 5% methanolic NaOH (15 mL) and heated at 50 °C for 30 min. Removal of solvent, diluting (H_2O, 30 mL), extraction ($CHCl_3$, 15 mL×3), drying (Na_2SO_4) and evaporation afforded the white amorphous powder (1.06 g, 100%). This residue (1.06 g, 2.35 mmol) was dissolved in pyridine (30 mL), MsCl (0.35 mL, 4.70 mmol) was added and the solution was stirred at room temperature for 1.5 h. Removal of solvent, diluting (H_2O, 30 mL), extraction ($CHCl_3$, 15 mL×3), drying (Na_2SO_4), and evaporation afforded the pure product (white amorphous powder, 1.17 g, 95%), which was dissolved in DMF (50 mL), NaOH (200 mg) was added and the solution was refluxed for 30 min. General work-up afforded the white amorphous powder (912 mg, 90%).

To a solution of the residue (912 mg, 2.12 mmol) in 95% EtOH (30 mL), 10% Pd–C (90 mg) was added and the solution was stirred under hydrogen steam at room temperature for 1 h. Filtration was evaporated under reduced pressure to give the pure product **43** (white amorphous powder, 915 mg, 100%), which was identified by comparison with the authentic sample [TLC: silica gel GF_{254}, cyclohexane–acetone/3:1; $CHCl_3$–CH_3OH/95:5].

4.5.2. Compound 44. To a solution of compound **43** (800 mg, 1.85 mmol) in MeOH (30 mL), $NaBH_4$ (500 mg, 13.15 mmol) was added and the solution was stirred at room temperature for 3 h. Removal of solvent, diluting (H_2O, 40 mL), extraction ($CHCl_3$, 15 mL×3), drying (Na_2SO_4), and evaporation afforded the pure product (white amorphous powder, 726 mg, 90%). **44**: mp 160–161 °C; R_f (90% $CHCl_3$–CH_3OH) 0.44; $[\alpha]_D^{20}=+12.5$ (*c* 0.2, $CHCl_3$); ν_{max} (KBr) 3426 (OH), 2930, 1649, 1459, 1379, 1203, 1175, 1101 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.08 (3H, t, $J=7.2$ Hz, *N*-CH_2CH_3), 3.32, 3.33, 3.39 (each 3H, s, OCH_3×3), 3.87 (1H, dd, $J=2.8$, 6.0 Hz, H-13), 4.08 (1H, dd, $J=2.4$, 9.6 Hz, H-3β); δ_C (100 MHz, $CDCl_3$) 84.3 (C-6), 77.7 (C-8), 77.0 (C-16), 76.7 (C-18), 74.4 (C-3), 64.6 (C-13), 62.8 (C-17), 59.0 (C-18′), 57.8 (C-16′), 56.0 (C-6′), 52.0 (C-7), 48.6 (NCH_2CH$_3$), 48.0 (C-5), 47.1 (C-19), 43.9 (C-11), 42.9 (C-9), 42.3 (C-4), 40.3 (C-10), 34.5 (C-15), 29.6 (C-14), 29.1 (C-12), 25.9 (C-2), 21.8 (C-1), 13.4 (NCH_2CH_3); *m*/*z* (EI) 437 (25, M^+), 422 (100, M−CH_3); HRMS (FAB): M^++H, found 438.2854, $C_{24}H_{40}NO_6$ requires 438.2856.

4.5.3. Compound 45. To a solution of compound **44** (700 mg, 1.60 mmol) in pyridine (30 mL), Ac_2O (3 mL) was added and the solution was heated at room temperature for 28 h. Removal of solvent, basifying (10% Na_2CO_3, 20 mL), extraction ($CHCl_3$, 10 mL×3), drying (Na_2SO_4), and evaporation afforded the pure product (white

amorphous powder, 791 mg, 95%). **45**: mp 72–73 °C; R_f (95% $CHCl_3$–CH_3OH) 0.46; $[\alpha]_D^{20}=+56.5$ (*c* 0.5, $CHCl_3$); ν_{max} (KBr) 3452 (OH), 2932, 1738 (COO), 1639, 1459, 1378, 1247, 1112, 1100 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.91 (3H, t, $J=6.8$ Hz, *N*-CH_2CH_3), 2.05, 2.13 (each 3H, s, OAc×2), 3.22, 3.34, 3.36 (each 3H, s, OCH_3×3), 4.97 (1H, dd, $J=5.2$, 12.4 Hz, H-3β), 5.22 (1H, dd, $J=6.4$, 7.2 Hz, H-13); δ_C (50 MHz, $CDCl_3$) 170.5 ($CO$$CH_3$), 170.2 ($CO$$CH_3$), 84.4 (C-6), 77.7 (C-8), 75.1 (C-3), 74.0 (C-16), 71.7 (C-18), 66.2 (C-13), 64.1 (C-17), 58.7 (C-18′), 57.9 (C-16′) 56.3 (C-6′), 51.8 (C-7), 48.4 (NCH_2CH_3), 48.0 (C-19), 46.2 (C-5), 43.7 (C-11), 42.3 (C-9), 41.4 (C-4), 40.0 (C-10), 36.5 (C-15), 29.6 (C-12), 29.4 (C-14), 25.9 (C-2), 22.8 (C-1), 21.1 ($CO$$CH_3$), 20.8 ($CO$$CH_3$), 13.3 ($NCH_2CH_3$); *m/z* (ESI) 522 (100, M^++H); HRMS (FAB): M^++H, found 522.3061, $C_{28}H_{44}NO_8$ requires 522.3067.

4.5.4. Compound 46. To a solution of compound **45** (760 mg, 1.45 mmol) in HOAc (40 mL), NBS (2.08 g, 11.77 mmol) was added and the solution was stirred at room temperature for 2 h. After pouring into ice water (50 mL), the solution was basified with conc. NH_4OH to pH 10. Extraction ($CHCl_3$, 10 mL×3), drying (Na_2SO_4), evaporation and column chromatography (silica gel H, $CHCl_3$–CH_3OH/25:1) afforded the pure product (white amorphous powder, 585 mg, 82%). **46**: mp 110–111 °C; R_f (90% $CHCl_3$–CH_3OH) 0.41; $[\alpha]_D^{20}=+111.0$ (*c* 0.7, $CHCl_3$); ν_{max} (KBr) 3452 (OH), 2937, 1736 (COO), 1650 (C=N), 1461, 1378, 1246, 1210, 1108 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 2.06, 2.12 (each 2H, s, OAc×2), 3.28, 3.32, 3.34 (each 3H, s, OCH_3×3), 4.11 (each 1H, ABq, $J=8.8$ Hz, H_2-18), 4.04 (1H, dd, $J=1.2$, 6.8 Hz, H-6β), 3.59 (1H, s, H-17), 4.97 (1H, dd, $J=4.4$, 11.2 Hz, H-3β), 5.18 (1H, dd, $J=3.6$, 10.0 Hz, H-13), 7.39 (1H, d, $J=1.2$ Hz, H-19); δ_C (100 MHz, $CDCl_3$) 170.7 ($CO$$CH_3$), 169.8 ($CO$$CH_3$), 164.2 (C-19), 84.9 (C-6), 75.4 (C-8), 74.7 (C-16), 73.3 (C-3), 69.9 (C-18), 66.0 (C-13), 64.8 (C-17), 60.8 (C-7), 58.9 (C-18′), 57.9 (C-16′), 56.3 (C-6′), 49.8 (C-11), 45.2 (C-5), 43.5 (C-4), 42.9 (C-9), 39.2 (C-10), 36.0 (C-15), 29.3 (C-14), 26.4 (C-12), 26.3 (C-2), 23.5 (C-1), 20.9 ($CO$$CH_3$), 20.7 ($CO$$CH_3$); *m/z* (EI) 491 (15, M^+), 432 (100, M−OAc); HRMS (FAB): M^++H, found 492.2601, $C_{26}H_{38}NO_8$ requires 492.2597.

4.5.5. Compound 47. To a solution of compound **46** (520 mg, 1.06 mmol) in CH_2Cl_2 (35 mL), *m*-CPBA (367 mg, 2.12 mmol) was added and the solution was stirred at room temperature for 2 h. To the reaction mixture was added 10% Na_2CO_3 (20 mL) with stirring vigorously. The organic layer was separated and the aqueous layer was extracted with $CHCl_3$ (10 mL×3). Drying (Na_2SO_4) and evaporation afforded the pure product (white amorphous powder, 450 mg, 84%). **47**: mp 117–118 °C; R_f (95% $CHCl_3$–CH_3OH) 0.45; $[\alpha]_D^{20}=+52.8$ (*c* 0.5, $CHCl_3$); ν_{max} (KBr) 3452 (OH), 2931, 1739 (COO), 1460, 1378, 1245, 1210, 1108 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 2.10, 2.13 (each 3H, s, OAc×2), 3.28, 3.34, 3.38 (each 3H, s, OCH_3×3), 3.50, 4.18 (each 1H, ABq, $J=10.0$ Hz, H_2-18), 3.86 (1H, s, H-17), 3.88 (1H, dd, $J=2.4$, 8.8 Hz, H-6β), 4.17 (1H, s, H-19), 4.99 (1H, dd, $J=4.8$, 12.0 Hz, H-3β), 5.17 (1H, dd, $J=3.6$, 10.0 Hz, H-13); δ_C (100 MHz, $CDCl_3$) 170.6 ($CO$$CH_3$), 169.6 ($CO$$CH_3$), 83.7 (C-6), 77.0 (C-8), 76.0 (C-19), 74.8 (C-16), 73.1 (C-3), 68.7 (C-18), 66.1 (C-13), 65.0 (C-17), 58.8 (C-18′), 58.0 (C-7), 58.2 (C-16′), 56.3 (C-6′), 44.9 (C-11), 44.4 (C-4), 43.9 (C-5), 42.6 (C-9), 39.5 (C-10), 36.1 (C-15), 29.1 (C-14), 25.8 (C-12), 25.1 (C-2), 23.1 (C-1), 20.9 ($CO$$CH_3$), 20.8 ($CO$$CH_3$); *m/z* (EI) 507 (13, M^+), 492 (85, M−CH_3), 432 (100, M−CH_3–HOAc); HRMS (EI): M^+, found 507.2455, $C_{26}H_{37}NO_9$ requires 507.2468.

4.5.6. Compound 48. To a solution of compound **44** (45 mg, 0.10 mmol) in Ac_2O (2 mL), *p*-TsOH (50 mg) was added and the solution was heated at 50 °C for 12 h. Diluting (ice water), basifying (conc. NH_4OH, pH 10), extraction ($CHCl_3$, 5 mL×3), drying (Na_2SO_4) and evaporation afforded the pure product (white amorphous powder, 50 mg, 86%). **48**: mp 70–71 °C; R_f (95% $CHCl_3$–CH_3OH) 0.44; $[\alpha]_D^{20}=+48.1$ (*c* 0.7, $CHCl_3$); ν_{max} (KBr) 3451 (OH), 2934, 1738 (COO), 1459, 1375, 1244, 1112 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.12 (3H, t, $J=7.2$ Hz, *N*-CH_2CH_3), 2.02, 2.05, 2.14 (each 3H, s, OAc×3), 3.21, 3.32, 3.33 (each 3H, s, OCH_3×3), 4.97 (1H, dd, $J=6.4$, 11.6 Hz, H-3β), 5.26 (1H, dd, $J=3.2$, 8.8 Hz, H-13); δ_C (100 MHz, $CDCl_3$) 170.3 ($CO$$CH_3$), 170.2 ($CO$$CH_3$), 160.1 ($CO$$CH_3$), 89.4 (C-8), 85.0 (C-6), 75.3 (C-16), 73.9 (C-3), 71.6 (C-18), 66.9 (C-13), 63.0 (C-17), 58.6 (C-18′), 58.1 (C-16′), 56.7 (C-6′), 48.2 (C-7), 48.1 (NCH_2CH_3), 47.4 (C-19), 46.6 (C-5), 43.8 (C-11), 43.0 (C-9), 41.3 (C-4), 39.4 (C-10), 31.8 (C-15), 30.6 (C-14), 25.8 (C-2), 25.5 (C-12), 22.2 (C-1), 21.4 ($CO$$CH_3$), 21.1 ($CO$$CH_3$), 20.9 ($CO$$CH_3$), 13.2 ($NCH_2CH_3$); *m/z* (EI) 562 (10, M^+-H), 548 (10, M−CH_3), 503 (12, M−HOAc), 472 (40, M−OCH_3–HOAc), 444 (100, M−OAc×2-H); HRMS (EI): M^+, found 563.3081, $C_{30}H_{45}NO_9$ requires 563.3094.

4.5.7. Compound 49. To a solution of compound **48** (55 mg, 0.10 mmol) in HOAc (2 mL), NBS (139 mg, 0.78 mmol) was added and the solution was stirred at room temperature for 3 h. General work-up and column chromatography (silica gel H, $CHCl_3$–CH_3OH/98:2) afforded the pure product as a white amorphous powder, 28 mg, (54%). **49**: mp 80–81 °C; R_f (95% $CHCl_3$–CH_3OH) 0.46; $[\alpha]_D^{20}=+98.0$ (*c* 0.7, $CHCl_3$); ν_{max} (KBr) 2943, 1775 (COO), 1717 (COO), 1648 (C=N), 1432, 1375, 1241, 1108 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 2.00, 2.07, 2.13 (each 3H, s, OAc×3), 3.28, 3.31, 3.35 (each 3H, s, OCH_3×3), 4.97 (1H, dd, $J=4.8$, 12.0 Hz, H-3β), 5.22 (1H, dd, $J=4.0$, 8.0 Hz, H-13), 7.41 (1H, br s, H-19); δ_C (100 MHz, $CDCl_3$) 170.2 ($CO$$CH_3$), 169.8 ($CO$$CH_3$), 169.8 ($CO$$CH_3$), 164.0 (C-19), 86.5 (C-8), 85.5 (C-6), 75.3 (C-16), 73.1 (C-3), 69.6 (C-18), 67.4 (C-13), 63.1 (C-17), 58.8 (C-18′), 58.2 (C-16′), 57.8 (C-7), 57.0 (C-6′), 49.9 (C-11), 45.7 (C-5), 43.6 (C-4), 41.4 (C-9), 39.3 (C-10), 32.5 (C-15), 26.3 (C-2), 26.2 (C-12), 23.2 (C-1), 22.3 (C-14), 20.9 ($CO$$CH_3$), 20.9 ($CO$$CH_3$), 20.9 ($CO$$CH_3$); *m/z* (ESI) 533 (100, M^+); HRMS (FAB): M^++H, found 534.2707, $C_{28}H_{40}NO_9$ requires 534.2703.

4.5.8. Compound 50. To a solution of compound **49** (28 mg, 0.053 mmol) in CH_2Cl_2 (2 mL), *m*-CPBA (18 mg, 0.105 mmol) was added and the solution was stirred at room temperature for 30 min. General work-up and column chromatography (silica gel H, $CHCl_3$–CH_3OH/99:1) afforded the pure product as a white amorphous powder, 12 mg, (40%). **50**: mp 105–106 °C; R_f (96% $CHCl_3$–CH_3OH) 0.50; $[\alpha]_D^{20}=+16.7$ (*c* 0.3, $CHCl_3$); ν_{max} (KBr)

Table 3. ^{1}H and ^{13}C NMR data of **51** (^{1}H: 400 MHz, ^{13}C: 100 MHz; $CDCl_3$)

No.	δ_H Mult (J=Hz)	δ_C	HMBC (H→C)
1	~1.80 m	22.6 t	C-2, C-10, C-11
2	1.50 m (α)	18.0 t	C-11
	1.80 m (β)		C-1, C-11
3	5.22 dd (9.2, 5.6)	66.4 d	C-1, C-2, C-4, C-5, C-18, C-19
4	—	52.2 s	—
5	2.54 m	48.0 d	C-7, C-17, C-18, C-19
6	5.63 d (7.2)	83.6 d	C-5, C-11, C-19
7	3.80 s	55.8 d	C-6, C-8, C-17
8	—	76.2 s	—
9	2.50 m	49.9 d	C-8
10	~2.30 m	37.4 d	C-5, C-8, C-9, C-14
11	—	49.7 s	—
12	1.40 m	24.9 t	C-9, C-11
13	5.05 dd (12.8, 3.2)	66.2 d	C-16, OO*C*CH$_3$ (δ_C 169.1)
14	3.02 m	29.1 d	C-8, C-10, C-12, C-16
15	~2.00 m	37.7 t	C-8, C-13, C-16
	~2.30 m		C-8, C-13, C-16
16	3.57 m	74.2 d	C-8
17	4.90 s	91.8 d	C-6, C-7, C-8
18	3.33 ABq (hidden)	77.1 t	C-19
	3.51 ABq (hidden)		C-19
19	—	177.7 s	—
16-OCH$_3$	3.33 s	56.4 q	C-16
18-OCH$_3$	3.33 s	59.4 q	C-18
3-OAc	2.02 s	170.2 s	OO*C*CH$_3$ (δ_C 170.2)
		20.9 q	
13-OAc	2.18 s	169.1 s	OO*C*CH$_3$ (δ_C 169.1)
		20.5 q	

2936, 1736 (COO), 1656, 1432, 1375, 1241, 1108 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 2.00, 2.08, 2.11 (each 3H, s, OAc×3), 3.28, 3.32, 3.39 (each 3H, s, OCH$_3$×3), 5.01 (1H, dd, J=6.4, 13.2 Hz, H-3β), 5.27 (1H, dd, J=3.6, 8.4 Hz, H-13), 6.17 (1H, br s, H-19); *m/z* (ESI) 572 (58, M$^+$+Na); HRMS (FAB): M$^+$+H, found 550.2656, $C_{28}H_{40}NO_{10}$ requires 550.2652.

4.5.9. Compound 51. To a solution of compound **47** (300 mg, 0.59 mmol) in MeOH (15 mL), excess $HIO_4 \cdot 2H_2O$ (800 mg, 3.76 mmol) was added and the mixture was stirred at room temperature for 4 h. Removal of solvent, basifying (10% Na_2CO_3, 30 mL), extraction ($CHCl_3$, 15 mL×4), drying (Na_2SO_4), evaporation and column chromatography (silica gel H, petroleum ether–acetone/3:1) afforded the pure product **51** (white amorphous powder, 80 mg, 26%) and a by-product **47** (white amorphous powder, 120 mg, 40%). **51**: mp 114–115 °C; R_f (50% petroleum ether–acetone) 0.48; $[\alpha]_D^{20}=-1.70$ (*c* 0.5, $CHCl_3$); ν_{max} (KBr) 3450 (OH), 2941, 1780 (γ-lactone), 1740 (COO), 1558, 1461, 1378, 1243, 1107 cm^{-1}; δ_H (400 MHz, $CDCl_3$) and δ_C (100 MHz, $CDCl_3$) see Table 3; *m/z* (EI) 523 (4, M$^+$), 507 (3, M−CH$_3$), 463 (40, M−CH$_3$-*N*O$_2$), 419 (100); HRMS (EI): M$^+$, found 523.2057, $C_{25}H_{33}NO_{11}$ requires 523.2054.

4.5.10. Compound 52. To a solution of compound **50** (12 mg, 0.022 mmol) in MeOH (2 mL), excess $HIO_4 \cdot 2H_2O$ (50 mg, 0.23 mmol) was added and the mixture was stirred at room temperature for 12 h. A general work-up and column chromatography (silica gel H, $CHCl_3$–CH_3OH/100:1) afforded the pure product (white amorphous powder, 5 mg, 40%). **52**: mp 96–97 °C; R_f (98% $CHCl_3$–CH_3OH) 0.46; $[\alpha]_D^{20}=-28.4$ (*c* 0.5, $CHCl_3$); ν_{max} (KBr) 2938, 1776 (γ-lactone), 1738 (COO), 1550, 1458, 1380, 1243, 1108 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 2.06, 2.07, 2.13 (each 3H, s, OAc×3), 3.33 (6H, s, OCH$_3$×2), 5.00 (1H, dd, J=4.0, 7.6 Hz, H-13), 5.24 (1H, dd, J=5.6, 9.2 Hz, H-3β), 5.11 (1H, d, J=7.2 Hz, H-6β), 5.49 (1H, s, H-17); δ_C (100 MHz, $CDCl_3$) 174.1 (C-19), 170.3 (*CO*CH$_3$), 170.1 (*CO*CH$_3$), 169.3 (*CO*CH$_3$), 89.0 (C-17), 84.1 (C-8), 81.9 (C-6), 76.7 (C-18), 75.1 (C-16), 67.1 (C-13), 66.7 (C-3), 59.3 (C-18′), 57.0 (C-16′), 56.1 (C-7), 51.5 (C-4), 51.1 (C-5), 49.5 (C-9), 49.4 (C-11), 37.0 (C-15), 36.9 (C-10), 29.2 (C-14), 24.7 (C-12), 21.9 (C-1, CO*CH$_3$*), 20.9 (CO*CH$_3$*), 20.5 (CO*CH$_3$*), 19.7 (C-2); *m/z* (ESI) 588 (58, M$^+$+Na); HRMS (EI): M$^+$, found 565.2160, $C_{27}H_{35}NO_{12}$ requires 565.2159.

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