

## *m*CPBA Oxidation of Acetyllycoctonine and Its New Products

Xiang-Li SHEN and Feng-Peng WANG\*

Department of Chemistry of Medicinal Natural Products, West China College of Pharmacy, Sichuan University; No. 17, Duan 3, Renmin Nan Road, Chengdu 610041, P. R. China. Received June 25, 2004; accepted September 30, 2004

**Treatment of a lycoctonine-type alkaloid acetyllycoctonine (4) with *m*CPBA at room temperature led to acetyllycoctonine *N*-oxide (5) as the major product together with other interesting compounds 6–12 as the minor products, which were derived from oxidation involving the nitrogen atom<sup>1)</sup> and Cope elimination as well as Polonovski-like fragmentation. All of those new compounds (5–12) were fully characterized.**

**Key words** C<sub>19</sub>-diterpenoid alkaloid; acetyllycoctonine; oxidation involving nitrogen atom; *N*-oxidation

The diterpenoid alkaloids are a synthetic or structurally modified target for a long time due to their complex and diversities displaying a lot of interesting chemical reactions<sup>1,2)</sup> and several biological activities.<sup>3,4)</sup> Some papers<sup>5–9)</sup> reported that treatment of the aconitine-type alkaloids and their derivatives with *m*CPBA lead to the main products the *N*-oxides together with the by-products, the amides or the *N,O*-mixed ketal. In contrast, oxidation of the lycoctonine-type alkaloids with *m*CPBA has been reported rarely yet besides deltaline (1) containing 7,8-methoxylene and ajacine (2) having the 7,8-glycol group. The former gave the *N*-oxide in high yield of 95.8%, but the latter only in lower yield of 20%.<sup>6)</sup> In conjunction with our ongoing research program, we have found that treatment of a lycoctonine-type alkaloid acetyllycoctonine (4) with *m*CPBA afforded not only the major compound acetyllycoctonine *N*-oxide (5) but also the interesting by-products (6–12). This paper deals with the isolation and structural elucidation of these new compounds (5–12).

### Results and Discussion

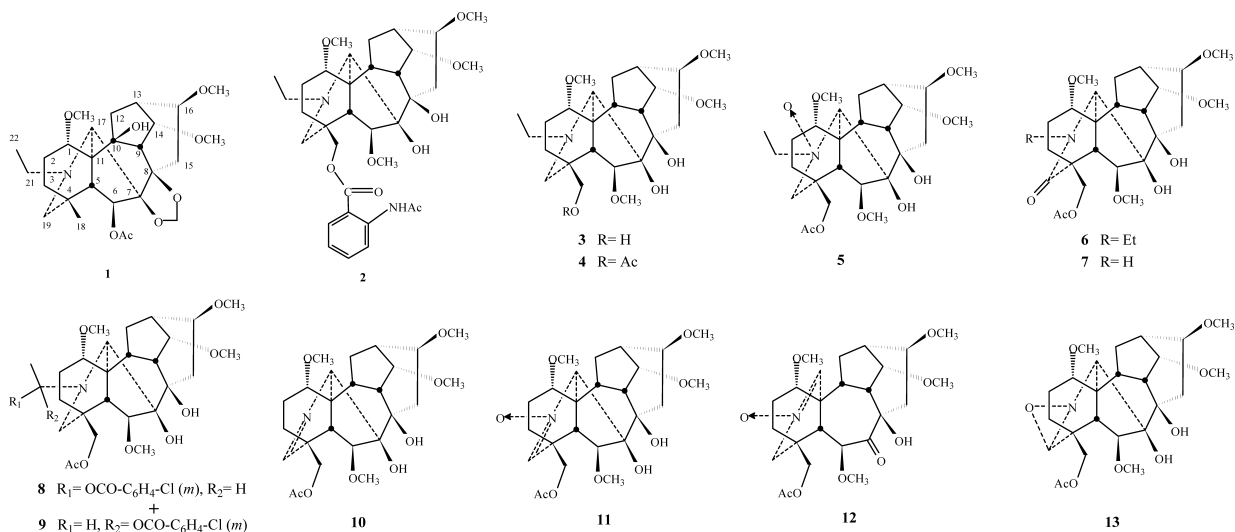
When acetyllycoctonine (4) derived from lycoctonine (3) reacted with *m*CPBA at room temperature for 30 min, followed by a column chromatography (silica gel H, CHCl<sub>3</sub>–MeOH system), the major product acetyllycoctonine *N*-oxide (5) (31%) was obtained together with the other new interesting minor compounds 6 (0.9%), 7 (2.8%), 8 (8.5%), 9 (7.2%), 10 (1.3%), 11 (1.5%), and 12 (1.5%).

Compound 5 has the molecular formula, C<sub>27</sub>H<sub>43</sub>NO<sub>9</sub>,

based on its HR-MS. The <sup>1</sup>H- and <sup>13</sup>C-NMR spectra of 5 showed the characteristic signals at δ<sub>H</sub> 1.41 (3H, t, *J*=6.6 Hz) and δ<sub>C</sub> 8.8 (q) for an *N*-ethyl group.<sup>5,6)</sup> This led to determine readily the structure of 5. <sup>13</sup>C-NMR comparison of 4 and 5 (Table 1) showed the differences of the δ values of many carbons, *e.g.* C-1, C-2, C-4, C-6, C-7, C-10, C-12, C-13, C-18, especially in C-17, C-19, C-21, and C-22, due to the *N*-oxidation effect.<sup>5,6)</sup>

The molecular formulae of compounds 6 (C<sub>27</sub>H<sub>41</sub>NO<sub>9</sub>) and 7 (C<sub>25</sub>H<sub>37</sub>NO<sub>9</sub>) were derived from their HR-MS. As compared with 7, the <sup>1</sup>H- (<sup>13</sup>C-) NMR and MS spectra of 6 showed the appearance of an additional *N*-ethyl group (δ<sub>H</sub> 1.10 t, *J*=7.2 Hz; δ<sub>C</sub> 43.6 t, 11.9 q) and more 28 mass units corresponding to the CH<sub>2</sub>CH<sub>2</sub> moiety of the *N*-ethyl group in 6. The <sup>13</sup>C-NMR data of both the compounds 6 and 7 also exhibited the distinctive lactam group at δ<sub>C</sub> 169.9 s and 173.3 s, respectively. The structures of these two compounds, thus, were assigned to be 6 and 7. As showed in Table 1, apparently, because of the presence of the electron-donating *N*-ethyl group, the d value of C-19 in 6 shifted upfield as compared with 7.

Compounds 8 and 9 have the same formula, C<sub>34</sub>H<sub>46</sub>NO<sub>11</sub>Cl, which was assigned by HR-ESI-MS *m/z* 680.2823 (*M*+*H*, Calcd 680.2831) for 8 and *m/z* 702.2662 (*M*+*Na*, Calcd 702.2651) for 9. Their <sup>1</sup>H- and <sup>13</sup>C-NMR spectra are very similar except for C-17, C-19 and C-21 (Table 1). In the <sup>1</sup>H- (<sup>13</sup>C-) NMR spectra of 8 and 9, a 1H-quartet signal at *ca.* δ<sub>H</sub> 6.3 (*J*=5.4 Hz) and a 3H-doublet sig-



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

Table 1.  $^{13}\text{C}$ -NMR Data of Compounds **4**–**11**

| Carbon              | <b>4</b> <sup>(10)</sup> | <b>5</b> | <b>6</b> | <b>7</b> | <b>8</b> | <b>9</b> | <b>10</b> | <b>11</b> |
|---------------------|--------------------------|----------|----------|----------|----------|----------|-----------|-----------|
| 1                   | 84.0                     | 87.4     | 83.5     | 83.6     | 83.6     | 83.7     | 81.9      | 81.7      |
| 2                   | 26.1                     | 23.7     | 25.0     | 25.1     | 26.2     | 26.4     | 20.0      | 20.6      |
| 3                   | 31.9                     | 30.2     | 28.3     | 28.5     | 30.8     | 30.7     | 24.5      | 26.6      |
| 4                   | 37.2                     | 39.4     | 47.2     | 47.1     | 39.1     | 39.2     | 46.1      | 42.1      |
| 5                   | 43.3                     | 49.0     | 49.1     | 49.2     | 49.9     | 49.7     | 42.9      | 42.9      |
| 6                   | 90.9                     | 88.8     | 91.9     | 91.7     | 90.4     | 90.4     | 90.6      | 90.7      |
| 7                   | 88.5                     | 83.9     | 85.9     | 85.3     | 87.4     | 87.1     | 86.5      | 84.8      |
| 8                   | 77.5                     | 78.3     | 76.4     | 76.2     | 77.1     | 77.1     | 77.0      | 76.4      |
| 9                   | 50.4                     | 43.0     | 42.7     | 42.8     | 43.4     | 43.4     | 42.9      | 42.8      |
| 10                  | 38.1                     | 47.8     | 45.2     | 44.6     | 45.7     | 45.8     | 45.3      | 46.1      |
| 11                  | 49.0                     | 50.0     | 48.7     | 48.5     | 49.0     | 49.6     | 50.5      | 50.6      |
| 12                  | 28.7                     | 30.6     | 29.3     | 28.6     | 28.4     | 28.3     | 30.4      | 30.3      |
| 13                  | 46.1                     | 36.1     | 37.5     | 37.7     | 37.7     | 37.7     | 38.0      | 38.0      |
| 14                  | 84.0                     | 83.0     | 81.9     | 81.7     | 83.0     | 82.3     | 83.9      | 83.9      |
| 15                  | 33.7                     | 33.5     | 33.2     | 33.1     | 34.1     | 34.0     | 33.1      | 33.3      |
| 16                  | 82.6                     | 81.5     | 81.3     | 81.4     | 82.4     | 82.1     | 80.7      | 80.0      |
| 17                  | 64.6                     | 76.9     | 63.2     | 59.2     | 68.5     | 67.5     | 64.2      | 77.7      |
| 18                  | 69.1                     | 71.2     | 66.2     | 65.6     | 68.4     | 68.3     | 65.7      | 66.2      |
| 19                  | 52.4                     | 69.4     | 169.9    | 173.3    | 55.3     | 57.1     | 167.5     | 136.2     |
| 21                  | 51.0                     | 68.6     | 43.6     | —        | 97.6     | 98.5     | —         | —         |
| 22                  | 14.1                     | 8.8      | 11.9     | —        | 19.0     | 18.9     | —         | —         |
| 1-OCH <sub>3</sub>  | 55.7                     | 56.1     | 55.1     | 55.7     | 55.1     | 55.4     | 56.3      | 56.3      |
| 6-OCH <sub>3</sub>  | 57.8                     | 57.5     | 57.8     | 57.8     | 57.7     | 57.7     | 57.7      | 57.8      |
| 14-OCH <sub>3</sub> | 58.0                     | 58.2     | 58.5     | 58.5     | 58.2     | 58.2     | 58.6      | 58.7      |
| 16-OCH <sub>3</sub> | 56.3                     | 56.8     | 56.3     | 56.4     | 56.3     | 55.9     | 56.4      | 56.5      |
| 18-OCO              | 170.9                    | 170.3    | 170.3    | 170.2    | 170.5    | 170.6    | 170.4     | 170.3     |
| CH <sub>3</sub>     | 20.8                     | 20.5     | 20.7     | 20.7     | 20.6     | 20.6     | 20.6      | 20.6      |
| 21-OCO              | —                        | —        | —        | —        | 164.1    | 163.8    | —         | —         |
| 1'                  | —                        | —        | —        | —        | 132.4    | 132.0    | —         | —         |
| 2'                  | —                        | —        | —        | —        | 129.6    | 129.7    | —         | —         |
| 3'                  | —                        | —        | —        | —        | 134.2    | 134.5    | —         | —         |
| 4'                  | —                        | —        | —        | —        | 129.3    | 129.5    | —         | —         |
| 5'                  | —                        | —        | —        | —        | 127.7    | 127.8    | —         | —         |
| 6'                  | —                        | —        | —        | —        | 132.7    | 133.0    | —         | —         |

Table 2. 2D-NMR Data of Compound **12**

| Carbon              | $\delta_{\text{H}}$                                         | $\delta_{\text{C}}$ | HMBC (H→C)                                                                                     |
|---------------------|-------------------------------------------------------------|---------------------|------------------------------------------------------------------------------------------------|
| 1                   | 3.09 dd (15.2, 4.4)                                         | 91.7 d              | C-10, C-11, C-17                                                                               |
| 2                   | 1.19—1.29 m ( $\alpha$ )<br>2.03—2.05 m ( $\beta$ )         | 23.5 t              | C-1<br>—                                                                                       |
| 3                   | 1.60—1.64 m ( $\beta$ )<br>1.87—1.90 m ( $\alpha$ )         | 33.1 t              | C-2, C-4, C-19<br>C-1, C-2, C-5                                                                |
| 4                   | —                                                           | 39.2 s              | —                                                                                              |
| 5                   | 2.13 s                                                      | 49.5 d              | C-1, C-4, C-6, C-7, C-11, C-17, C-18, C-19                                                     |
| 6                   | 3.77 d (1.6)                                                | 88.6 d              | C-4, C-5, C-7, C-8, C-11                                                                       |
| 7                   | —                                                           | 207.7 s             | —                                                                                              |
| 8                   | —                                                           | 74.8 s              | —                                                                                              |
| 9                   | 3.78—3.80 m                                                 | 40.6 d              | C-8, C-11, C-12, C-14, C-15                                                                    |
| 10                  | 2.47—2.53 m                                                 | 45.2 d              | C-1, C-8, C-9, C-11, C-12, C-13, C-14, C-17                                                    |
| 11                  | —                                                           | 46.0 s              | —                                                                                              |
| 12                  | 1.48 dd (15.6, 7.6) ( $\beta$ )<br>2.11—2.18 m ( $\alpha$ ) | 28.1 t              | C-10, C-13, C-14, C-16<br>C-13, C-14                                                           |
| 13                  | 2.63—2.65 m                                                 | 36.2 d              | C-14, C-15                                                                                     |
| 14                  | 3.35—3.36 m                                                 | 80.3 d              | C-8, C-13                                                                                      |
| 15                  | 1.58 dd (17.2, 6.4) ( $\alpha$ )<br>2.47—2.53 m ( $\beta$ ) | 33.5 t              | C-8, C-14<br>C-8, C-9, C-13                                                                    |
| 16                  | 3.78—3.80 m                                                 | 84.2 d              | C-8, C-12, C-14, C-15                                                                          |
| 17                  | 7.06 s                                                      | 136.6 d             | C-5, C-10, C-19                                                                                |
| 18                  | 3.88 ABq (12.0)<br>4.24 ABq (11.6)                          | 67.7 t              | C-3, C-4, C-5, C-19, <u>OCOCH<sub>3</sub></u><br>C-3, C-4, C-5, C-19, <u>OCOCH<sub>3</sub></u> |
| 19                  | 3.56 ABq (16.8)<br>3.79—3.82 hidden                         | 62.8 t              | C-3, C-4, C-5, C-17<br>C-3, C-4, C-5, C-17, C-18                                               |
| 1-OCH <sub>3</sub>  | 3.25 s                                                      | 56.3 q              | C-1                                                                                            |
| 6-OCH <sub>3</sub>  | 3.38 s                                                      | 58.4 q              | C-6                                                                                            |
| 14-OCH <sub>3</sub> | 3.31 s                                                      | 57.0 q              | C-14                                                                                           |
| 16-OCH <sub>3</sub> | 3.45 s                                                      | 58.1 q              | C-16                                                                                           |
| 18-OCO              | —                                                           | 170.2 s             | —                                                                                              |
| CH <sub>3</sub>     | 2.09 s                                                      | 20.6 q              | <u>OCOCH<sub>3</sub></u>                                                                       |

nal at around  $\delta_{\text{H}}$  1.5 ( $J=5.4$  Hz) were attributed to H-21 and H<sub>3</sub>-22, respectively, implying the presence of a oxygenated substitution at the C-21 position and also that compounds **8** and **9** are a pair of epimers.

Compounds **10** and **11** have the molecular formulae  $\text{C}_{25}\text{H}_{37}\text{NO}_8$  (HR-EI-MS  $m/z$  479.2500 Calcd 479.2519) and  $\text{C}_{25}\text{H}_{37}\text{NO}_9$  (HR-EI-MS  $m/z$  495.2456 Calcd 495.2468), respectively. They also possess the same unsaturated degree ( $n=8$ ) but the presence of difference of 16 mass units between **10** and **11** in the MS spectra, indicating that **11** is possibly derived from the *N*-oxidation of **10**. The  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectra of **10** and **11** exhibited the distinctive imine signals (**10**:  $\delta_{\text{H}}$  7.72 brs,  $\delta_{\text{C}}$  167.5 d; **11**:  $\delta_{\text{H}}$  6.77 d,  $J=1.2$  Hz,  $\delta_{\text{C}}$  136.2 d). In addition, their  $^{13}\text{C}$ -NMR spectra (Table 1) are similar except for C-4, C-7, C-17 and C-19. It is worthy to note that changes of the  $\delta$  values caused by the *N*-oxidation from **10** to **11** corresponding to **4**→**5** are less together with a great upfield-shift of the  $\delta$  value of C-19 in the  $^{13}\text{C}$ -NMR spectra of **11** as compared with those of **10**.

Compound **12**,  $\text{C}_{25}\text{H}_{37}\text{NO}_9$  (HR-EI-MS  $m/z$  495.2473 Calcd 495.2468), was obtained as a white amorphous powder

with smaller *R<sub>f</sub>* value (0.43) on TLC (petroleum ether–acetone 1 : 1). The  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectra of **12** showed the presence of four methoxyl groups ( $\delta_{\text{H}}$  3.25 s, 3.31 s, 3.38 s, 3.45 s), an acetyl group ( $\delta_{\text{H}}$  2.09 s,  $\delta_{\text{C}}$  170.2 s, 20.6 q), an imine group ( $\delta_{\text{H}}$  7.06 s,  $\delta_{\text{C}}$  136.6 d), and a ketone group ( $\delta_{\text{C}}$  207.7s). Its structure was confirmed by 2D-NMR spectra. It is also a novel artifact 17,7-seco  $\text{C}_{19}$ -diterpenoid alkaloid.

Finally, our results together with the data on the oxidation involved the nitrogen atom of diterpenoid alkaloids<sup>1)</sup> led us to propose a plausible process from **4** to compounds **5**–**12** depicted in Chart 1: *m*-CPBA oxidation of acetyllycoctonine (**4**) first produces the *N*-oxide **5**, and then, **5** was subjected to a Cope elimination to give the intermediate **A** in company with loss of a molecular ethylene. Cleavage of the C<sub>17</sub>–C<sub>7</sub> bond in **A** via a Polonovski-like process formed the imine ketone **B** followed by treating with *m*-CPBA to afford **12**. The salt **D** formed from **A** under acid condition gave **10a** through an  $\alpha$ -elimination of water, *m*-CPBA oxidation of **10** afforded competitively the nitron **11** instead of the oxaziridine **13**.<sup>9,11)</sup> Another pathway of formation of **10** involved possibly in a Cope elimination of the intermediate **G**, and continued the

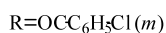
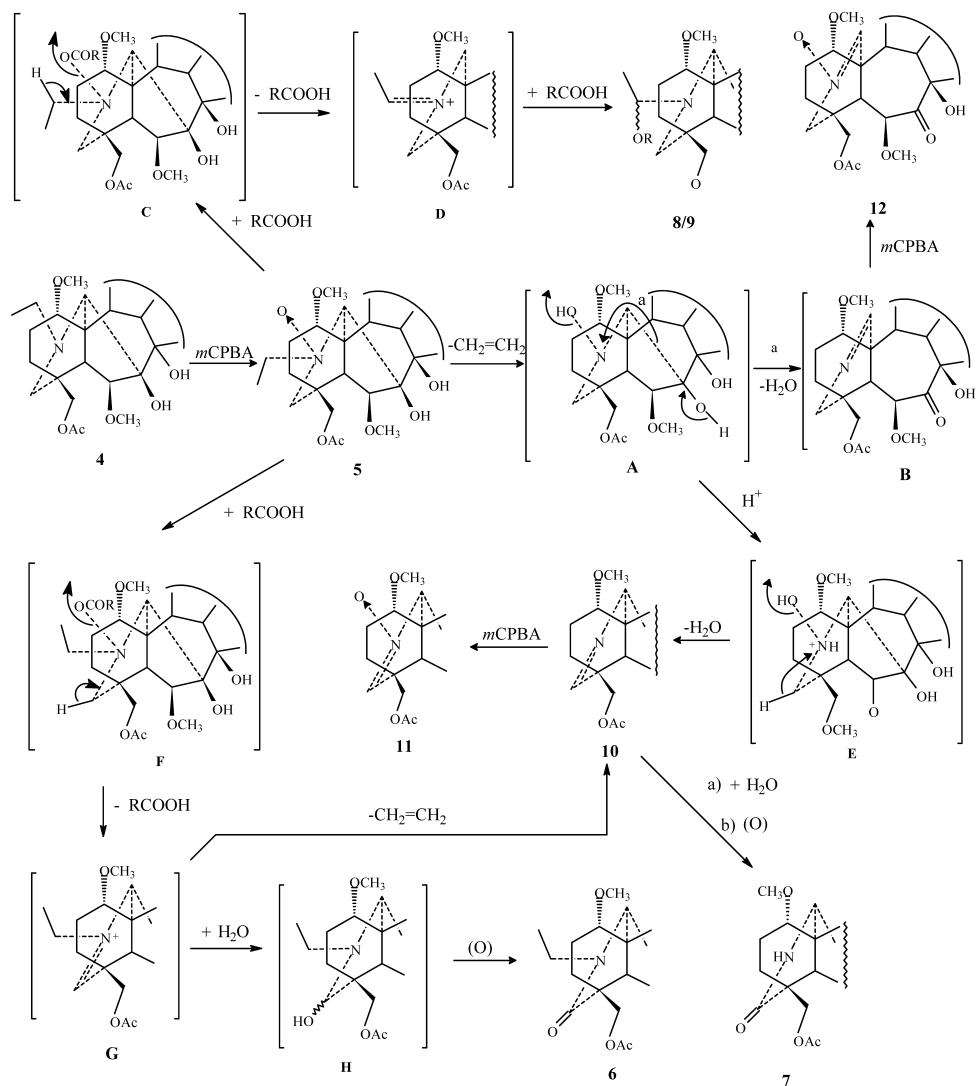


Chart 1

reaction of **10** with H<sub>2</sub>O followed by oxidation led to form **7**. On the other hand, esterification of **5** with (*m*)Cl–C<sub>5</sub>H<sub>6</sub>COOH gave the intermediates **C** and **F**, leading to produce a pair of regioisomeric immonium salts **D** and **G**. The former reacted with (*m*)Cl–C<sub>5</sub>H<sub>6</sub>COOH to form a pair of epimer **8** and **9**, the latter in the presence of H<sub>2</sub>O gave the intermediate **H** followed by oxidation into **6**.

## Experimental

**General Experimental Procedure** Melting points were uncorrected. IR spectra were recorded on a Nicolet FT-IR 200SXV spectrometer. Optical rotations were measured with a JASCO DIP-370 polarimeter. <sup>1</sup>H- and <sup>13</sup>C-NMR spectra were acquired on a Varian INOVA 400/54 or a Bruker AC-E 200 spectrometer in CDCl<sub>3</sub> with TMS as internal standard. MS spectra were obtained on Finnigan LCQ and Micromass Auto Spec Ultima-Tof spectrometer.

**Preparation of Compounds (5)–(12)** To acetyllycoctonine (**4**) (1.28 g, 2.52 mmol) prepared from lycotoniine (**3**) with acetic anhydride in CHCl<sub>3</sub> (30 ml) *m*CPBA (2.15 g, 12.6 mmol) was added, and this solution was stirred at room temperature for 30 min. Evaporation in vacuum to give a residue, which was subjected to column chromatography on silica gel H (total amount of 200 g) using CHCl<sub>3</sub>–MeOH (98:2→9:1)→petroleum–acetone–H<sub>2</sub>O (50:50:1) as eluents yield the major compound (**5**) (399 mg, 31%), and the minor ones (**6**) (37 mg, 2.8%), (**7**) (12 mg, 0.9%), (**8**) (146 mg, 8.5%), (**9**) (123 mg, 7.2%), (**10**) (15 mg, 1.3%), (**11**) (20 mg, 1.5%), and (**12**) (20 mg, 1.5%).

**Compound 5:** White amorphous powder, C<sub>27</sub>H<sub>43</sub>NO<sub>9</sub>, HR-ESI-MS *m/z* 526.3021 (M+H, Calcd 526.3010), mp 128–129 °C, [α]<sub>D</sub><sup>20</sup> +23.3° (*c*=1.965, CHCl<sub>3</sub>); IR (cm<sup>-1</sup>): 3460 (OH), 1741 (COO). <sup>1</sup>H-NMR (200 MHz, CDCl<sub>3</sub>) δ: 1.41 (3H, t, *J*=6.6 Hz, N-CH<sub>2</sub>CH<sub>3</sub>); 2.04 (3H, s, OAc); 3.24, 3.27, 3.36, 3.37 (each 3H, s, 4×OCH<sub>3</sub>); 3.58 (1H, t, *J*=4.4 Hz, H-14β); <sup>13</sup>C-NMR (50 MHz, CDCl<sub>3</sub>): see Table 1; ESI-MS: *m/z* 526 (M+1, 100).

**Compound 6:** White amorphous powder, C<sub>27</sub>H<sub>41</sub>NO<sub>9</sub>, HR-EI-MS *m/z* 523.2774 (M<sup>+</sup>, Calcd 523.2781), mp 80–81 °C, [α]<sub>D</sub><sup>20</sup> +26.6° (*c*=1.330, CHCl<sub>3</sub>); IR (cm<sup>-1</sup>): 3479 (OH), 1746 (COO), 1633 (CONR). <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ: 1.10 (3H, t, *J*=7.2 Hz, N-CH<sub>2</sub>CH<sub>3</sub>); 2.06 (3H, s, OAc), 3.20, 3.35, 3.36, 3.41 (each 3H, s, 4×OCH<sub>3</sub>), 3.64 (1H, t, *J*=4.4 Hz, H-14β), 3.76 (1H, s), 3.93 (1H, s), 4.06 (1H, m), 4.27, 4.59 (2H, ABq, *J*=12.0 Hz, H<sub>2</sub>-18); <sup>13</sup>C-NMR (50 MHz, CDCl<sub>3</sub>): see Table 1; EI-MS: *m/z* 523 (M<sup>+</sup>, 20), 505 (M–18, 90), 490 (45), 432 (50).

**Compound 7:** White amorphous powder, C<sub>25</sub>H<sub>37</sub>NO<sub>9</sub>, HR-EI-MS *m/z* 495.2470 (M<sup>+</sup>, Calcd 495.2468), mp 97–98.5 °C, [α]<sub>D</sub><sup>20</sup> +64.9° (*c*=0.535, CHCl<sub>3</sub>); IR (cm<sup>-1</sup>): 3465 (OH), 1741 (COO), 1661 (CONH). <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ: 2.08 (3H, s, OAc), 3.26, 3.34, 3.40, 3.43 (each 3H, s, 4×OCH<sub>3</sub>); 3.65 (1H, t, *J*=4.4 Hz, H-14β); 4.29, 4.58 (each 1H, ABq, *J*=12.0 Hz, H<sub>2</sub>-18); 6.25 (1H, d, *J*=4.4 Hz, NH); <sup>13</sup>C-NMR (50 MHz, CDCl<sub>3</sub>): see Table 1; EI-MS: *m/z* 495 (M<sup>+</sup>, 15), 480 (M–15, 85), 464 (M–31, 20).

**Compound 8:** White amorphous powder, C<sub>34</sub>H<sub>46</sub>NO<sub>11</sub>Cl, HR-ESI-MS *m/z* 680.2823 (M+H, Calcd 680.2831), mp 78–79 °C, [α]<sub>D</sub><sup>20</sup> +18.8° (*c*=0.595, CHCl<sub>3</sub>); IR (cm<sup>-1</sup>): 3467 (OH), 3067 (Ar), 1740 (COO), 1640, 1573 (Ar). <sup>1</sup>H-NMR (200 MHz, CDCl<sub>3</sub>) δ: 1.51 (3H, d, *J*=5.4 Hz, N-CHCH<sub>3</sub>); 2.06 (3H, s, OAc); 3.40, 3.41 (each 6H, s, 4×OCH<sub>3</sub>); 3.56 (1H, t, *J*=4.4 Hz, H-14β); 6.39 (1H, q, *J*=5.4 Hz, N-CHCH<sub>3</sub>); 7.35–8.06 (4H, m, H-Ar); <sup>13</sup>C-

NMR (50 MHz, CDCl<sub>3</sub>): see Table 1; ESI-MS: *m/z* 702 (M+Na, 100).

**Compound 9:** White amorphous powder, C<sub>34</sub>H<sub>46</sub>NO<sub>11</sub>Cl, HR-ESI-MS *m/z* 702.2662 (M+Na, Calcd 702.2651), mp 80–81 °C, [α]<sub>D</sub><sup>20</sup> +22.7° (*c*=2.140, CHCl<sub>3</sub>); IR (cm<sup>-1</sup>): 3459 (OH), 3094 (Ar), 1742 (COO), 1663, 1571 (Ar). <sup>1</sup>H-NMR (200 MHz, CDCl<sub>3</sub>) δ: 1.56 (3H, d, *J*=5.6 Hz, N-CHCH<sub>3</sub>); 2.06 (3H, s, OAc); 3.31, 3.26, 3.42, 3.42 (each 3H, s, 4×OCH<sub>3</sub>); 6.38 (1H, q, *J*=5.4 Hz, N-CHCH<sub>3</sub>); 7.37–8.12 (4H, m, H-Ar); <sup>13</sup>C-NMR (50 MHz, CDCl<sub>3</sub>): see Table 1; ESI-MS: *m/z* 702 (M+Na, 100).

**Compound 10:** White amorphous powder, C<sub>25</sub>H<sub>37</sub>NO<sub>8</sub>, HR-EI-MS *m/z* 479.2500 (M<sup>+</sup>, Calcd 479.2519), mp 136–137 °C, [α]<sub>D</sub><sup>20</sup> +103.8° (*c*=0.530, CHCl<sub>3</sub>); IR (cm<sup>-1</sup>): 3466 (OH), 1743 (COO), 1635 (C=N). <sup>1</sup>H-NMR (200 MHz, CDCl<sub>3</sub>) δ: 2.09 (3H, s, OAc), 3.13, 3.33, 3.34, 3.39 (each 3H, s, 4×OCH<sub>3</sub>); 3.64 (1H, t, *J*=4.4 Hz, H-14β); 4.21, 4.31 (each 1H, ABq, *J*=11.4 Hz, H<sub>2</sub>-18); 7.72 (1H, br s, H-19); <sup>13</sup>C-NMR (50 MHz, CDCl<sub>3</sub>): see Table 1; EI-MS: *m/z* 479 (M<sup>+</sup>, 100), 464 (M–15, 95), 448 (M–31, 90).

**Compound 11:** White amorphous powder, C<sub>25</sub>H<sub>37</sub>NO<sub>9</sub>, HR-EI-MS *m/z* 495.2456 (M<sup>+</sup>, Calcd 495.2468), mp 127–128 °C, [α]<sub>D</sub><sup>20</sup> +21.9° (*c*=0.740, CHCl<sub>3</sub>); IR (cm<sup>-1</sup>): 3449 (OH), 1742 (COO), 1599 (C=N). <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ: 2.10 (3H, s, OAc); 3.22, 3.34, 3.40, 3.42 (each 3H, s, 4×OCH<sub>3</sub>); 3.67 (1H, t, *J*=4.4 Hz, H-14β), 3.98 (1H, d, *J*=0.8 Hz, H-6β), 4.15, 4.19 (2H, ABq, *J*=11.2 Hz, H<sub>2</sub>-18), 6.77 (1H, d, *J*=1.2 Hz, H-19); <sup>13</sup>C-NMR (50 MHz, CDCl<sub>3</sub>): see Table 1; EI-MS: *m/z* 495 (M<sup>+</sup>, 30), 480 (M–15, 72), 464 (M–31, 60).

**Compound 12:** White amorphous powder, C<sub>25</sub>H<sub>37</sub>NO<sub>9</sub>, HR-EI-MS *m/z* 495.2473 (M<sup>+</sup>, Calcd 495.2468), mp 131–132 °C, [α]<sub>D</sub><sup>20</sup> –3.4° (*c*=0.670, CHCl<sub>3</sub>); IR (cm<sup>-1</sup>): 3429 (OH), 1739 (COO), 1708 (CO), 1578 (C=N). <sup>1</sup>H- (400 MHz) and <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) see Table 2; EI-MS: *m/z* 495 (M<sup>+</sup>, 40), 479 (M–16, 35), 464 (M–31, 60).

**Acknowledgments** This work was supported by the National Natural science Foundation of China (No. 30472075).

## References

- Wang F. P., Liang X. T., "The Alkaloids: Chemistry and Biology," Vol. 42, ed. by Cordell G. A., Academic Press, New York, 1992, pp. 151–247.
- Wang F. P., Liang X. T., "The Alkaloids: Chemistry and Biology," Vol. 59, ed. by Cordell G. A., Elsevier Science, New York, 2002, pp. 1–280.
- Benn M. H., Jacyno J. M., "The Alkaloids: Chemistry and Biological Perspectives," Vol. 1, ed. by Pelletier S. W., Wiley & Sons, New York, 1983, pp. 120–153.
- Dzhakhgirov F. N., Sultankhodzhaev M. N., Tashkhodzhaev B., Silmov B. T., *Khim. Priro. Soedin.*, **33**, 254–270 (1997).
- Wang F. P., Pelletier S. W., *West China J. Pharm. Sci.*, **4**, 193–200 (1989).
- Bai Y. L., Desai H. K., Pelletier S. W., *J. Nat. Prod.*, **58**, 929–933 (1995).
- Wang F. P., Pelletier S. W., *Chin. Chem. Lett.*, **2**, 103–106 (1991).
- Wang F. P., Fan J. Z., Li Z. B., Yang J. S., Li B. G., *Chin. Chem. Lett.*, **10**, 375–378 (1999).
- Chen Q. H., Xu L., Wang F. P., *Tetrahedron*, **58**, 9431–9444 (2002).
- Pelletier S. W., Mody N. V., Sawhney R. S., Bhattacharyya J., *Heterocycles*, **7**, 327–339 (1977).
- Ogata Y., Sawaki Y., *J. Am. Chem. Soc.*, **95**, 4687–4692, 4692–4698 (1973).