Scutebarbatines W—Z, New *neo*-Clerodane Diterpenoids from *Scutellaria barbata* and Structure Revision of a Series of 13-Spiro *neo*-Clerodanes

Fei WANG,*[a,b] Fu-Cai REN,[b] Ya-Ju LI,[b] and Ji-Kai LIU*[,a]

[a] *State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences; Kunming 650204, China: and* [b] *BioBioPha Co., Ltd.; Kunming 650204, China.*

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Four new *neo*-clerodane diterpenoids, scutebarbatines W—Z (1—4), were isolated from the ethanol extract of *Scutellaria barbata* (Labiatae), and their structures were elucidated on the basis of extensive spectroscopic studies. In addition, the proposed structures of at least seven 13-spiro subtype *neo*-clerodanes: scutehenanine B (5), scutebarbatine G (6), 6-*O*-nicotinoylscutebarbatine G (7), barbatin A (8), 6,7-di-*O*-nicotinoylscutebarbatine G (9), 6-*O*-nicotinoyl-7-*O*-acetylscutebarbatine G (10), and scutebarbatine F (11), reported by Dai and co-workers from the same species, were incorrectly assigned and have been revised by reanalysis of the published NMR data.

Key words *Scutellaria barbata*; *neo*-clerodane diterpenoid; structure revision

Species of the genus *Scutellaria* (family Labiatae) are deemed as the source of the most potent *neo*-clerodane insect antifeedants known so far, and over 150 *neo*-clerodane diterpenoids have been isolated from this genus, which makes them potentially useful as ecologically acceptable agents for pest control.[1)] Recently, a series of cytotoxic *neo*-clerodanes were reported from *Scutellaria barbata*—a traditional Chinese herbal medicine named "Ban Zhi Lian."[2—14)] As part of BioBioPha to assemble a large-scale natural compound library which is very valuable in the discovery of new lead compounds from nature,[15—19)] further chemical investigation on *S. barbata* afforded four new *neo*-clerodane derivatives, scutebarbatines W—Z (**1**—**4**) (Fig. 1), along with nine known *neo*-clerodanes, scutebatas A—C,[13)] scutebatas E—G,[11,13)] scutebarbatines A and B,[2,4)] and 6-*O*-nicotinoylbarbatin C.[6)] Furthermore, the structures of at least following seven 13-spiro *neo*-clerodanes: scutehenanine B (**5**),[10)] scutebarbatine G (**6**),[5)] 6-*O*-nicotinoylscutebarbatine G (**7**),[9)] barbatin A (**8**),[4)] 6,7-di-*O*-nicotinoylscutebarbatine G (**9**),[5)] 6-*O*-nicotinoyl-7-*O*-acetylscutebarbatine G (**10**),[5)] and scutebarbatine F (**11**),[3)] continuously reported by Dai and co-workers from the same plant, were incorrectly assigned and have been revised. Herein, we report the structure elucidation of new compounds as well as structure revision of some analogues.

Results and Discussion

Compound **1**, obtained as amorphous powder, had a molecular formula of $C_{33}H_{37}NO_8$ based on the positive high resolution-electrospray ionization (HR-ESI)-MS, showing a quasi-molecular ion peak at *m*/*z* 598.2426 (Calcd for $C_{33}H_{37}NO_8Na$, 598.2416). The ^{1}H-NMR spectrum (Table 1) showed the following legible signals: one olefinic proton at δ_H 5.34 (br s), three oxygenated methine protons at δ_H 5.77 (ddd, J=9.1, 6.4, 5.4 Hz), 5.43 (d, J=10.0 Hz) and 3.69 (dd, J=12.0, 10.0 Hz), two AB doublet protons at δ_H 4.34 and 4.24 (each d, J=9.1 Hz) assignable to an oxygenated methylene, and four methyl singlets at δ_H 1.67, 1.44, 1.40, and 1.10, together with nine characteristic aromatic protons due to one benzoyloxy and one nicotinoyloxy groups. The ^{13}C-NMR spectrum (Table 1) revealed 20 carbon resonances except for the signals of the forenamed aromatic substitutes, including one ester carbonyl carbon at δ_C 174.5 (s), one trisubstituted double bond at δ_C 143.4 (s) and 120.4 (d), and six oxygen-bearing carbons at δ_C 82.1 (s), 79.6 (t), 77.2 (d), 76.2 (s), 74.6 (d) and 71.1 (d). Considering the above NMR character and its biological source,[11,13)] this compound should be a *neo*-clerodane diterpenoid with a 3-en-13-spiro-15,16-γ-lactone moiety. The heteronuclear multiple bond coherence (HMBC) correlations (Fig. 2) allowed us to position the benzoyloxy and nicotinoyloxy groups at C-1 and C-6, respectively. On account of almost overlapping (δ_C 165.66, 165.62) of two aromatic ester carbonyl carbon signals in $CDCl_3$, it is very necessary to change the deuterated solvent (δ_C 167.2, 166.1 in CD_3OD) for unambiguous assignment of the two aromatic substitutes by HMBC spectrum.

The relative configuration of **1** was deduced from its rotating frame Overhauser effect spectroscopy (ROESY) spectrum (Fig. 2). The observable correlations of H-7↔Me-17, Me-19 and Me-20; H-1↔Me-19 and Me-20, indicated that these protons were cofacial and α-oriented, whereas the correlation of H-6↔H-10 was indicative of their β-orientation. The configuration of C-13 was determined to be *R** by the ROESY correlation of Me-17↔H-14a, and the more detailed ROESY information was summarized in Fig. 2. Accordingly, the structure of **1** was elucidated as (13*R**)-1β-benzoyloxy-6α-nicotinoyloxy-7β-hydroxy-8β,13-epoxy-3-*neo*-cleroden-15,16-olide, named scutebarbatine W.

Generally, when no substitution happens in the rings C and D, there is a reliable and more convenient method to determine the configuration at C-13, which can be achieved just by observation of the diagnostic ^{1}H- and ^{13}C-NMR signals in

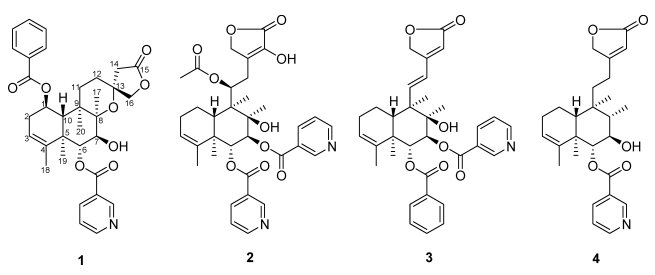

Fig. 1. Structures of Scutebarbatines W—Z (**1**—**4**)

∗ To whom correspondence should be addressed. e-mail: wangfei@mail.kib.ac.cn; jkliu@mail.kib.ac.cn

Table 1. NMR Data of Carbon-Skeleton Parts of Scutebarbatines W—Z (**1**—**4**)

No.	**1**[a]		**2**[b]		**3**[a]		**4**[a]	
	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H
1	71.1 (d)	5.77 (ddd, 9.1, 6.4, 5.4)	19.9 (t)	1.81, 2.27 (m)	19.3 (t)	1.36, 1.66 (m)	17.9 (t)	1.58, 1.69 (m)
2	32.7 (t)	2.19, 2.72 (m)	26.2 (t)	2.00, 2.17 (m)	26.1 (t)	1.96—2.12 (m)	26.3 (t)	2.00, 2.13 (m)
3	120.4 (d)	5.34 (br s)	124.0 (d)	5.24 (br s)	123.1 (d)	5.23 (br s)	123.2 (d)	5.25 (br s)
4	143.4 (s)	—	141.5 (s)	—	140.9 (s)	—	141.5 (s)	—
5	43.8 (s)	—	43.6 (s)	—	43.4 (s)	—	43.4 (s)	—
6	77.2 (d)	5.43 (d, 10.0)	76.9 (d)	6.32 (d, 10.1)	75.4 (d)	5.92 (d, 10.0)	82.5 (d)	5.03 (d, 9.6)
7	74.6 (d)	3.69 (dd, 12.0, 10.0)	77.5 (d)	6.06 (d, 10.1)	76.7 (d)	5.73 (d, 10.0)	73.6 (d)	3.65 (dd, 9.6, 9.3)
8	82.1 (s)	—	77.9 (s)	—	76.8 (s)	—	42.7 (d)	1.61 (m)
9	38.3 (s)	—	48.2 (s)	—	48.4 (s)	—	39.1 (s)	—
10	43.5 (d)	2.68 (d, 9.1)	41.1 (d)	2.71 (br d, 11.9)	42.7 (d)	2.40 (br d, 12.3)	45.3 (d)	1.57 (m)
11	28.3 (t)	1.59, 2.05 (m)	76.3 (d)	5.99 (br d, 11.0)	147.0 (d)	6.42 (d, 16.9)	35.7 (t)	1.63, 1.73 (m)
12	29.4 (t)	1.56, 2.15 (m)	29.6 (t)	3.07 (dd, 14.0, 11.0) 3.71 (br d, 14.0)	121.9 (d)	6.46 (d, 16.9)	22.0 (t)	2.21, 2.31 (m)
13	76.2 (s)	—	129.7 (s)	—	162.2 (s)	—	170.0 (s)	—
14	42.2 (t)	2.57, 2.76 (each d, 17.0)	140.6 (s)	—	114.9 (d)	5.94 (br s)	115.4 (d)	5.87 (br s)
15	174.5 (s)	—	171.1 (s)	—	174.1 (s)	—	173.8 (s)	—
16	79.6 (t)	4.24, 4.34 (each d, 9.1)	69.6 (t)	4.72, 5.02 (each d, 15.9)	70.7 (t)	5.00 (br s)	73.0 (t)	4.76 (br s)
17	20.4 (q)[c]	1.40 (s)	21.6 (q)	1.67 (s)	22.4 (q)	1.07 (s)	11.0 (q)	1.03 (d, 6.6)
18	20.3 (q)[c]	1.67 (br s)	20.7 (q)	1.75 (br s)	20.1 (q)	1.59 (br s)	20.6 (q)	1.57 (br s)
19	16.3 (q)	1.44 (s)	17.5 (q)	1.50 (s)	17.4 (q)	1.45 (s)	17.6 (q)	1.34 (s)
20	21.4 (q)	1.10 (s)	16.5 (q)	1.10 (s)	15.4 (q)	1.28 (s)	18.9 (q)	0.89 (s)
7-OH		2.07 (d, 12.0)						1.78 (br s)
8-OH				7.34 (br s)		2.79 (br s)		
14-OH				12.82 (br s)				

a, *b*) Measured in $CDCl_3$ (δ_H 7.26, δ_C 77.0 ppm) and pyridine-d_5 (δ_H 8.71, δ_C 149.9 ppm), respectively. *c*) Interchangeable.

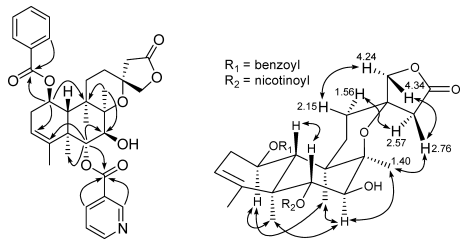

Fig. 2. Significant HMBC and ROESY Correlations of **1**

$CDCl_3$. Presence of the signals around at δ_H 2.57, 2.76 (each d, H-14, $\Delta \approx 0.20$ ppm) and at δ_C 42.2 (t, C-14), 79.6 (t, C-16) is indicative of a 13*R** form, while a 13*S** analogue will display a set of signals at 2.60, 3.15 (each d, H-14, $\Delta \approx 0.55$ ppm) and at δ_C 44.3 (t, C-14), 76.4 (t, C-16). The rule can efficaciously assign the configuration at C-13 of this subtype of *neo*-clerodanes. By chance, scutebarbatine W (**1**) was found to be contaminated by a trace amount of the C-13 epimer (13*S** form) in our current study, in addition, more minor C-13 epimers can be also detectable in the NMR spectra (see supporting information in ref. 13) of scutebatas D, E and F.

Recently, Dai and co-workers uninterruptedly reported many new *neo*-clerodanes from the same plant.[3—10,14] However, the authors proposed a series of wrong structures because of failure to comprehend NMR information, especially the application of HMBC correlations and the calculation of coupling constants. Now scutehenanine B (**5**)[10] is chosen to discuss its structure revision. Compound **5** is found to be identical with **1**, and the conclusion is based on the following forceful evidence or reasons: 1) the NMR data (see supporting information in ref. 10) are in complete accord with those of **1**; 2) the authors did not accurately handle the HMBC and ROESY correlations, and did not know how to calculate coupling constants of complex signals, for example, the proton signal at δ_H 5.77 is a legible ddd coupling and not so-called double doublet with $J = 12.2$, 3.5 Hz; 3) because of almost overlapping of two aromatic ester carbonyl carbons in $CDCl_3$, the ester carbonyl signal of the benzoyloxy group can not be observed at δ_C 165.9 and was imaginary. According to the above discussion and combining the reported NMR data, the nicotinoyloxy group at C-11 and the spirocarbon configuration of scutebarbatine G (**6**)[5] and 6-*O*-nicotinoylscutebarbatine G (**7**)[9] should be adjusted to at C-1 and as 13*R** form, respectively. Similarly, the substitute at C-11 in barbatin A (**8**),[4] 6,7-di-*O*-nicotinoylscutebarbatine G (**9**)[5] and 6-*O*-nicotinoyl-7-*O*-acetylscutebarbatine G (**10**)[5] should be all repositioned at C-1, and the original assignment of scutebarbatine F (**11**)[3] is more unimaginable and should be revised as shown in Fig. 3. Among them, 6-*O*-nicotinoyl-7-*O*-acetylscutebarbatine G (**10**) and scutebarbatine F (**11**) are actually identical with subsequently reported barbatine D[11] and barbatine C[11] (=scutebata F),[13] respectively. The structural revision of **5**—**11** has been summarized in Fig. 3.

Scutebarbatine X (**2**), obtained as amorphous powder, had the molecular formula $C_{34}H_{38}N_2O_{10}$ according to its positive HR-ESI-MS at *m*/*z* 657.2425 (Calcd for $C_{34}H_{38}N_2O_{10}Na$, 657.2424). The ^1H- and ^{13}C-NMR spectra (Table 1) bearing two nicotinoyloxy and one acetoxy groups were very similar to those of scutebatas A and B,[13] which suggested that **2** was a 6,7,8,11,14-pentaoxygenated 3,13-*neo*-clerodadien-15,16-olide derivative. The HMBC correlations allowed us to position the two nicotinoyloxy and one acetoxy groups at C-6, C-7 and C-11, respectively. By comparing the ROESY spectrum with reported, the relative configuration of C-6, C-7 and

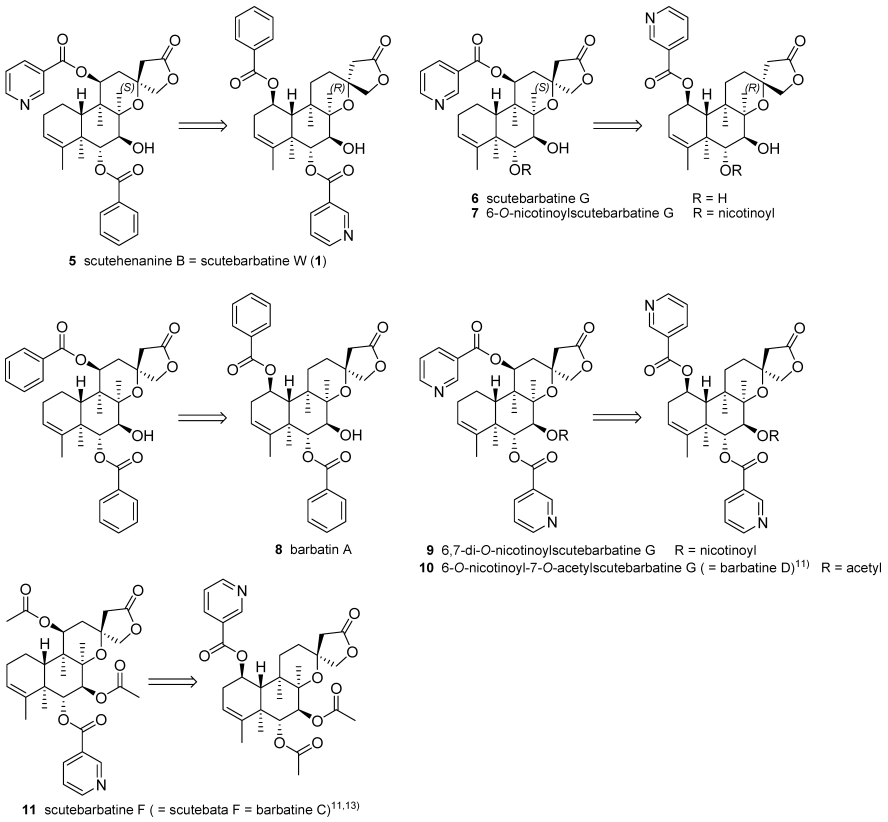

Fig. 3. Structure Revision of **5**—**11**

C-11 was found to be the same as those of scutebatas A and B. Therefore, the structure of **2** was determined as (11*S**)-6α,7β-dinicotinoyloxy-8β,14-dihydroxy-11-acetoxy-3,13-*neo*-clerodadien-15,16-olide.

Scutebarbatine Y (**3**) was also obtained as amorphous powder. Its molecular formula was determined to be $C_{33}H_{35}NO_7$ on the basis of the positive HR-ESI-MS at *m*/*z* 580.2298 (Calcd for $C_{33}H_{35}NO_7Na$, 580.2311). The ^{1}H-NMR spectrum (Table 1) showed the following clear signals: four olefinic protons at δ_H 6.46, 6.42 (each d, J=16.9 Hz), 5.94 (br s) and 5.23 (br s), a pair of intercoupling protons at δ_H 5.92 (d, J=10.0 Hz) and 5.73 (d, J=10.0 Hz), two protons at δ_H 5.00 (2H, s) assignable to an oxygenated methylene, as well as four methyl singlets at δ_H 1.59 (br s), 1.45, 1.28 and 1.07. The ^{1}H- and ^{13}C-NMR data (Table 1) were very similar to those of scutebarbatine A,[2,11] nevertheless a set of newly arisen benzoyloxy signals displaced the resonances of a nicotinoyloxy group in scutebarbatine A. The HMBC correlations from the proton at δ_H 5.92 (1H, d, J=10.0 Hz, H-6) to the carbons at δ_C 140.9 (s, C-4), 17.4 (q, C-19) and 166.0 (s), and from the protons at δ_H 7.78 (2H, d, J=8.2 Hz) to the carbon at δ_C 166.0 (s), were observed, therefore the newly arisen benzoyloxy group was assigned to C-6. The relative configuration of **3** was deduced to be the same as those of scutebarbatines A and B based on their accordant NMR data (including coupling constants) and similar optical rotation behavior.[2,4,11] Thus the structure of **3** was established as 6α-benzoyloxy-7β-nicotinoyloxy-8β-hydroxy-3,11(*E*),13-*neo*-clerodatrien-15,16-olide.

Scutebarbatine Z (**4**), amorphous powder, possessed the molecular formula $C_{26}H_{33}NO_5$, determined by the positive HR-ESI-MS at *m*/*z* 462.2263 (Calcd for $C_{26}H_{33}NO_5Na$, 462.2256). The ^{1}H-NMR spectrum (Table 1) displayed two olefinic protons at δ_H 5.87 (br s) and 5.25 (br s), two oxygenated methine protons at δ_H 5.03 (d, J=9.6 Hz) and 3.65 (dd, J=9.6, 9.3 Hz), two protons at δ_H 4.76 (2H, s) assignable to an oxygenated methylene, four methyl signals at δ_H 1.57 (br s), 1.34 (s), 1.03 (d, J=6.6 Hz) and 0.89 (s), as well as a set of characteristic nicotinoyloxy protons. The ^{13}C-NMR spectrum (Table 1) revealed 20 carbon resonances except for a set of nicotinoyloxy signals, including one ester carbonyl carbon at δ_C 173.8 (s), four olefinic carbons at δ_C 170.0 (s), 141.5 (s), 123.2 (d) and 115.4 (d), and three oxygen-bearing carbons at δ_C 82.5 (d), 73.6 (d) and 73.0 (t). The above NMR character allowed us to make a conclusion that this compound was a 6,7-dioxygenated 3,13-*neo*-clerodadien-15,16-olide derivative. The strong HMBC correlations from the proton at δ_H 5.03 (1H, d, J=9.6 Hz, H-6) to the carbons at δ_C 141.5 (s, C-4), 17.6 (q, C-19) and 166.3 (s) indicated that the nicotinoyloxy group was located at C-6. The relative configuration of C-6 and C-7 was in accordance with those of **1**—**3** based on the similarity of their H-6/H-7 coupling constants. As a result, the structure of **4** was determined as 6α-nicotinoyloxy-7β-hydroxy-3,13-*neo*-clerodadien-15,16-olide.

Experimental

General Experimental Procedures Optical rotations were measured on a Jasco P-1020 (Jasco International Co., Ltd., Tokyo, Japan) automatic digital polarimeter. IR spectra were recorded using a Bruker Tensor 27 FT-IR (Bruker Optics GmbH, Ettlingen, Germany) spectrometer with KBr pellets. UV data were obtained from online HPLC analysis. NMR spectra were carried out on either a Bruker DRX-500 or AV-400 (Bruker BioSpin GmbH,

Rheinstetten, Germany) spectrometer with the deuterated solvent as an internal standard. ESI-MS (including HR-ESI-MS) were measured on an API QSTAR Pulsar i (MDS Sciex, Concord, Ontario, Canada) mass spectrometer. Silica gel 200—300 mesh (Qingdao Marine Chemical Inc., Qingdao, China), Sephadex LH-20 (Amersham Biosciences, Uppsala, Sweden), Chromatorex MB C18 (40—75 μm, Fuji Silysia Chemical Ltd., Kasugai, Aichi, Japan) and MCI gel CHP 20P (75—150 μm, Mitsubishi Chemical Corp., Tokyo, Japan) were used for normal pressure column chromatography. Fractions were monitored and analyzed by TLC (Qingdao Marine Chemical Inc., China), in combination with Agilent 1200 series HPLC system (Eclipse XDB-C18 column, 5 μm, 4.6×150 mm).

Plant Material The whole plants of *S. barbata* were collected in Xinping County of Yunnan Province, China, in March 2008, and identified by Mr. Yu Chen of Kunming Institute of Botany, CAS. A voucher specimen (No. BBP2010010SB) was deposited at BioBioPha.

Extraction and Isolation Dried and powdered whole plants (9.5 kg) of *S. barbata* were extracted with 95% ethanol at room temperature. The alcohol extract was concentrated to give a residue (*ca.* 1.0 kg), which was fractionalized by silica gel column chromatography eluted with a solvent system of petroleum ether (PE)/acetone (20 : 1, 10 : 1, 6 : 1, 3 : 1, 1 : 1, 0 : 1) and then pure methanol to yield fractions A—G, respectively. Fraction D eluted by 25% acetone was separated on silica gel using a solvent system of $CHCl_3$/MeOH (50 : 1, 20 : 1) to obtain subfractions I and II, respectively. Subfraction I was further isolated and purified by silica gel, Sephadex LH-20 ($CHCl_3$/MeOH, 1 : 1), C18 (40→75% MeOH in water), MCI (60→100% MeOH in water) columns and recrystallization to afford **4** (3.0 mg) and **3** (10 mg), and compound **1** (47 mg) was obtained from subfraction II in the same way. Fraction E eluted by 50% acetone was repeatedly isolated and purified by silica gel, MCI (60→100% MeOH in water) and Sephadex LH-20 ($CHCl_3$/MeOH, 1 : 1) columns to afford **2** (142 mg). The retention times (t_R) of **1**—**4** from analysis-type HPLC (50→100% MeOH in H_2O over 6 min followed by 100% MeOH to 10 min, 1 ml/min, 20 °C) were 7.3, 6.6, 7.7 and 6.7 min, respectively.

Scutebarbatine W (**1**): Colorless powder, $[\alpha]_D^{19}$ −55.9° (c=0.24, MeOH). UV λ_{max} (MeOH): 226, 263 nm. IR (KBr): 3431, 1782, 1712, 1637, 1279, 1109, 1037 cm^{-1}. NMR data of the carbon-skeleton part: see Table 1. NMR data ($CDCl_3$) of the substitute groups: 1-benzoyloxy, δ_H 7.97 (2H, d, J=7.8 Hz), 7.60 (1H, t, J=7.8 Hz), 7.47 (2H, t, J=7.8 Hz), δ_C 165.66 or 165.62 (s) [167.2 ppm in CD_3OD], 133.4 (d), 130.0 (s), 129.4 (2×d), 128.6 (2×d); 6-nicotinoyloxy, δ_H 9.26 (1H, br d, J=1.8 Hz), 8.79 (1H, dd, J=4.9, 1.8 Hz), 8.32 (1H, ddd, J=7.8, 1.8, 1.8 Hz), 7.42 (1H, br dd, J=7.8, 4.9 Hz), δ_C 165.62 or 165.66 (s) [166.1 ppm in CD_3OD], 153.5 (d), 150.9 (d), 137.2 (d), 126.4 (s), 123.4 (d). ESI-MS (pos.): 598 $[M+Na]^+$. HR-ESI-MS (pos.): 598.2426 (Calcd for $C_{33}H_{37}NO_8Na$, 598.2416).

Scutebarbatine X (**2**): Colorless powder, $[\alpha]_D^{23}$ −50.8° (c=0.18, MeOH). UV λ_{max} (MeOH): 223, 264 (sh), 272 (sh) nm. IR (KBr): 3484, 1763, 1730, 1590, 1289, 1112, 1020 cm^{-1}. NMR data of the carbon-skeleton part: see Table 1. NMR data (C_5D_5N) of the substitute groups: 6-nicotinoyloxy, δ_H 9.36 (1H, br d, J=1.8 Hz), 8.70 (1H, dd, J=4.9, 1.8 Hz), 8.22 (1H, ddd, J=7.9, 1.8, 1.8 Hz), 7.19 (1H, br dd, J=7.9, 4.9 Hz), δ_C 165.5 (s), 154.0 (d), 151.0 (d), 137.0 (d), 126.5 (s), 123.8 (d); 7-nicotinoyloxy, δ_H 9.26 (1H, br d, J=1.8 Hz), 8.64 (1H, dd, J=4.9, 1.8 Hz), 8.09 (1H, ddd, J=7.9, 1.8, 1.8 Hz), 7.04 (1H, br dd, J=7.9, 4.9 Hz), δ_C 165.7 (s), 154.2 (d), 151.3 (d), 137.2 (d), 125.6 (s), 123.4 (d); 11-acetoxy, δ_H 2.15 (3H, s), δ_C 171.4 (s), 21.0 (q). ESI-MS (pos.): 657 $[M+Na]^+$. HR-ESI-MS (pos.): 657.2425 (Calcd for $C_{34}H_{38}N_2O_{10}Na$, 657.2424).

Scutebarbatine Y (**3**): Colorless powder, $[\alpha]_D^{25}$ −104.7° (c=0.10, MeOH). UV λ_{max} (MeOH): 223 (sh), 259 nm. IR (KBr): 3426, 1781, 1745, 1726, 1643, 1594, 1451, 1285, 1113, 1028 cm^{-1}. NMR data of the carbon-skeleton part: see Table 1. NMR data ($CDCl_3$) of the substitute groups: 6-benzoyloxy, δ_H 7.78 (2H, d, J=8.2 Hz), 7.41 (1H, t, J=7.3 Hz), 7.26 (2H, dd, J=8.2, 7.3 Hz), δ_C 166.0 (s), 133.1 (d), 129.8 (s), 129.3 (2×d), 128.3 (2×d); 7-nicotinoyloxy, δ_H 9.00 (1H, br d, J=1.8 Hz), 8.63 (1H, dd, J=4.9, 1.8 Hz), 8.08 (1H, ddd, J=7.8, 1.8, 1.8 Hz), 7.21 (1H, br dd, J=7.8, 4.9 Hz), δ_C 164.8 (s), 153.4 (d), 150.9 (d), 137.2 (d), 124.9 (s), 123.0 (d). ESI-MS (pos.): 580 $[M+Na]^+$. HR-ESI-MS (pos.): 580.2298 (Calcd for $C_{33}H_{35}NO_7Na$, 580.2311).

Scutebarbatine Z (**4**): Colorless powder, $[\alpha]_D^{25}$ −26.5° (c=0.10, MeOH). UV λ_{max} (MeOH): 214, 257 (sh), 263, 272 (sh) nm. IR (KBr): 3426, 1784, 1753, 1717, 1636, 1597, 1282, 1112, 1029 cm^{-1}. NMR data of the carbon-skeleton part: see Table 1. NMR data ($CDCl_3$) of the substitute group: 6-nicotinoyloxy, δ_H 9.28 (1H, br s), 8.79 (1H, br d, J=4.9 Hz), 8.34 (1H, br d, J=7.8 Hz), 7.42 (1H, br dd, J=7.8, 4.9 Hz), δ_C 166.3 (s), 153.6 (d), 151.0 (d), 137.3 (d), 126.5 (s), 123.4 (d). ESI-MS (pos.): 462 $[M+Na]^+$. HR-ESI-MS (pos.): 462.2263 (Calcd for $C_{26}H_{33}NO_5Na$, 462.2256).

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