Rearranged Taxanes from the Bark of *Taxus yunnanensis*

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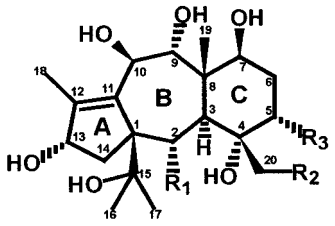
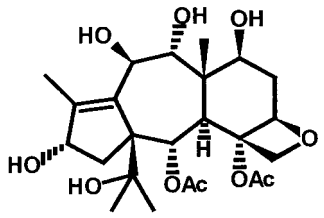
Five new 11(15→1)-*abeo*-taxane diterpenoids, taxuyunnanines K−O (**1**−**5**), were isolated from an ethanol extract of the bark of *Taxus yunnanensis*, and their structures were determined using MS and NMR techniques. Compounds **1**/**2** and **4**/**5** are rearranged taxane diterpenoids possessing an opened oxetane ring moiety at C4(20). Compounds **4**/**5** are rearranged taxoids lacking an oxygenated functionality at C-4.

Taxoids or taxane diterpenoids are a class of well-known secondary metabolites which have been found only in plants of the genus *Taxus* or in associated endophytic fungi.[1] Due to the discovery and development of taxol (paclitaxel) as an effective chemotherapeutic anticancer agent,[2,3] and due partly to its unique structure, reports on the phytochemistry, semisynthesis, and biosynthesis of this molecule and related taxoids proliferated, including a number of review articles.[4−6]

Taxus yunnanensis, Cheng, et L. K. Fu (Taxaceae), is an evergreen tree mainly distributed in the Northern and Northwestern areas of Yunnan province, People's Republic of China. It is rich in paclitaxel and paclitaxel-like compounds.[7,8] Our investigations on the root of this plant have resulted in the isolation of a number of new and known taxoids including paclitaxel.[9−12] Two new baccatin III type taxoids were discovered in our previous study on the bark,[13] and the present paper describes the isolation of five new rearranged taxoids, viz., taxuyunnanines K−O (**1**−**5**) from this material.



1 R_1=OH, R_2=OBz, R_3=OAc
2 R_1=OBz, R_2=OAc, R_3=OH



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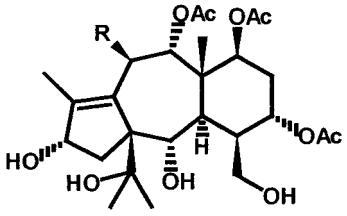

4 R=OH
5 R=OAc

Results and Discussion

Compounds **1**−**5** were isolated from the $CHC1_3$-soluble fraction of an EtOH extract of the dried bark of *T. yunnanensis*. The structures of these compounds were determined by spectroscopic analysis, including ^{1}H, ^{13}C, DEPT-90, DEPT-135, ^{1}H−^{1}H COSY, HMQC, and HMBC NMR spectroscopy.

Taxuyunnanine K (**1**) had a molecular formula of $C_{29}H_{40}O_{11}$ by HRMS. The ^{1}H and ^{13}C NMR spectra showed that **1** had four characteristic taxane tertiary methyl groups [δ_H 2.20, 1.76, 1.68, and 1.43 (singlets); δ_C 29.6 (q), 27.2 (q), 15.8 (q), and 11.8 (q)]. They also showed the presence of an acetoxy group [δ_H 2.30 (3H, s); δ_C 170.9 (s) and 21.4 (q)] and a benzoxy group [δ_H 8.26 (2H, dd, J = 8.3, 1.2 Hz), 7.33 (2H, t, J = 7.9 Hz), 7.44 (1H, t, J = 7.4 Hz); δ_C 166.9 (s), 131.0 (s), 130.2 (2C, d), 128.7 (2C, d), and 133.2 (d)]. In addition, the spectra also indicated an oxymethylene, a methine, and six oxymethine groups. Furthermore, two quaternary, two oxyquaternary, and two olefinic quaternary carbons were identified. A taxane skeleton was thus apparent. However, in the NMR spectral data of **1**, the downfield resonance of C-1 [δ_C 70.0 (s)] suggested a rearranged A-ring carbon skeleton. The 11-(15→1)-*abeo*-taxane skeleton of **1** was also supported by the correlation between C-l and H-10 [δ_H 5.19 (1H, d, J = 9.4 Hz)] in the HMBC spectrum.

The molecular formula of **1**, corresponding to 10 double-bond equivalents, implied an opened oxetane ring moiety. In the HMBC spectrum, a pair of H_2-20 AB doublets at δ_H 5.74 (1H, ABd, J = 11.8 Hz) and 4.99 (1H, ABd, J = 11.8 Hz) showed ^{1}H−^{13}C long-range correlations with the carbonyl carbon signal at δ_C 166.9 (s), which, in turn, gave a further correlation with the aromatic proton signal at δ_H 8.26 (2H, dd, J = 8.3, 1.2 Hz). These data showed unequivocally the connection of a benzoxy group to C-20, which clearly results from cleavage of the oxetane ring. The acetoxy substituent at C-5 could be readily assigned in view of the long-range ^{1}H−^{13}C correlations of the H-5 [δ_H 6.00 (1H, t, J = 3.1 Hz)] and the acetyl CH_3 signals with the carbonyl carbon of δ_C 170.9 (s).

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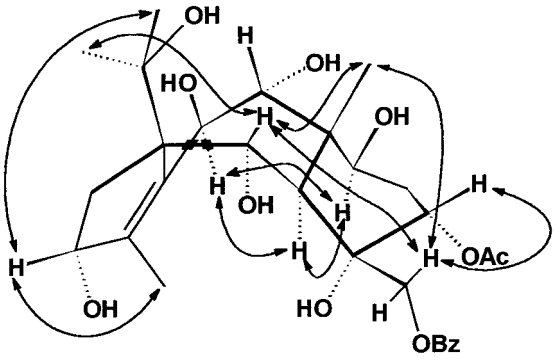

Figure 1. Selected ROESY correlation of taxuyunnanine K (**1**).

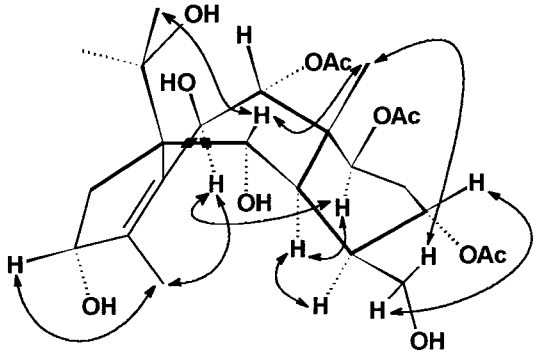

Figure 2. Selected ROESY correlation of taxuyunnanine N (**4**).

To define the configurations of the secondary alcohols in **1**, a ROESY experiment was performed. The observation of ROESY correlations (Figure 1) between H-2 and CH_3-16 and CH_3-19 established the α-orientation of the hydroxyl group at C-2. Correlations of H-7 with H-3, H-9 with H-2, H-10 with H-3 and H-7, and H-13 with CH_3-17 provided the clues to the configurations of the hydroxyl groups at C-7, C-9, C-10, and C-13 as *β*, α, *β*, and α, respectively. Since H-5 exhibited ROE with one of the protons of H_2-20 at δ_H 4.99 (1H, ABd, J = 11.8 Hz), the acetoxy group at C-5 and the benzoxymethylene group at C-4 should have *E*-configurations. Moreover, correlations of the above-mentioned proton of H_2-20 at δ_H 4.99 with H-2 and CH_3-19 were also observed, leading to assignments of the *β*-configuration to the benzoxymethylene group at C-4 and the α-configuration of the acetoxy group at C-5. The structure of taxuyunnanine K was therefore deduced as **1**.

Taxuyunnanine L (**2**) had the same molecular formula ($C_{29}H_{40}O_{11}$) as **1**, as determined by a combination of negative FABMS (*m*/*z* 563 $[M - H]^+$) and ^1H and ^{13}C NMR spectra, including DEPT. This was confirmed by HR-FABMS. The similarity of the NMR spectra of **2** to those of **1** indicated that **2** is an isomer of **1**, with **2** differing only by the positions of its benzoxy and acetoxy groups. The downfield resonance of H-2 [δ_H 6.02 (1H, d, J = 7.0 Hz)] and the upfield resonance of H-5 [δ_H 3.73 (1H, t, br d, J = 2.8 Hz)], coupled with the slight upfield resonance of H_2-20 [δ_H 4.25 (1H, ABd, J = 12.2 Hz) and 3.96 (1H, ABd, J = 12.2 Hz)], suggested that the two ester groups were attached at C-2 and C-20, respectively, rather than at C-20 and C-5 as in **1**. This observation was confirmed by the HMBC spectrum of **2**, in which the H-2 and the aromatic proton signals at δ_H 8.07 (2H, dd, J = 8.6, 1.5 Hz) correlated with the same carbonyl carbon resonance at δ_C 167.6 (s). Likewise, the H_2-20 and acetyl methyl signals at δ_H 1.57 (3H, s) gave correlations with the same carbonyl carbon at δ_C 170.5 (s). Thus, the benzoxy and acetoxy groups were unequivocally located at C-2 and C-20, respectively. The very similar coupling patterns of **2** and **1** also suggested similar stereochemistry. Consequently, the structure of **2** was established as 5-deacetoxy-20-debenzoxy-2-benzoxy-20-acetoxytaxuyunnanine K and was named taxuyunnanine L.

Taxuyunnanine M (**3**) gave a molecular ion peak at *m*/*z* 484 by FABMS, consistent with a molecular formula of $C_{24}H_{36}O_{10}$ (confirmed by HRFABMS). The ^1H NMR spectrum of **3** was similar to that of **1** except for the absense of the benzoxy signal. However, differences observed in the respective ^{13}C NMR spectra, especially in the medium-field area, indicated an intact oxetane in **3**. The oxymethylene carbon signal of δ_C 74.8 (t, C-20) was in agreement with that of common taxanes, which appear at *ca.* δ_C 75. In view of the C-1 signal at δ_C 68.1 (s) and the seven double-bond equivalents, it appeared that **3** was an *abeo*-taxane with an oxetane ring moiety. The lower field shift of H-2 [δ_H 6.46 (1H, d, J = 7.4 Hz)], due to the deshielding effect of the neighboring carbonyl group, implied an acetoxy group attached to C-2. This was confirmed by the long-range $^1H-^{13}C$ correlation between the H-2 signal and an acetyl carbonyl carbon signal at δ_C 171.4 (s) in the HMBC spectrum. The relative high-field proton chemical shifts at C-7 [δ_H 4.85 (1H, t, J = 8.7 Hz)], C-9 [δ_H 4.99 (1H, br d, J = 7.9 Hz), C-10 [δ_H 5.12 (1H, br d, J = 7.9 Hz)], and C-13 [δ_H 4.96 (1H, br t, J = 6.6 Hz)] revealed that one of the two acetoxy groups in **3** could not be attached to any of these carbons. The only available position for attachment was at C-4, in accordance with the absence of any coupling between the skeletal proton signal and the carbonyl carbon resonance at δ_C 170.2 (s). On comparing the coupling constants and the 2D ROESY data with those of **1** and the known 7,13-dideacetyl-9,10-debenzoyltaxchinin C,[14] the structure and the stereochemistry of taxuyunnanine M were deduced to be **3**.

Taxuyunnanine N (**4**) showed a $[M]^+$ ion at *m*/*z* 528 in the FABMS spectrum, corresponding to a molecular formula of $C_{26}H_{40}O_{11}$, as confirmed by HRFABMS. Besides the three acetyl methyl singlets [δ_H 2.31, 2.14, and 2.04] and the four characteristic taxane tertiary methyl singlets [δ_H 2.25, 1.87, 1.50, and 1.40] in the ^1H NMR spectrum, the C-1 quaternary carbon signal at δ_C 69.6 (s) and the C-20 oxymethylene carbon signal at δ_C 62.1 (t) in the ^{13}C NMR spectrum suggested that **4** could be another 11-(15→11)-*abeo*-taxane with an opened oxetane ring moiety. This assumption was supported by the correlation of H-10 [δ_H 5.28 (1H, d, J = 9.5 Hz)] with C-1 in the HMBC spectrum and the seven double-bond equivalents in the molecular formula. However, it was obvious that the characteristic H-3 doublet of **1** [δ_H 3.46 (1H, d, J = 7.1 Hz)] or **2** [δ_H 3.07 (1H, d, J = 7.0 Hz)] was replaced by a doublet of doublets at δ_H 3.26 (1H, dd, J = 7.8, 4.2 Hz) in the ^1H NMR spectrum and that the oxyquaternary carbon of **1** or **2** at *ca.* δ_C 76 was substituted by a methine carbon signal at δ_C 43.8 (d) in the ^{13}C NMR spectra. These data indicated that the C-4 position in **4** was not oxygenated. The relationship of H-2/H-3/H-4/H-20 was established using a $^1H-^1H$ COSY experiment, in which the H-4 mutiplet at δ_H 3.11 (1H, m) was simultaneously coupled with H-3, H_2-20, and H-5. Deshielding of H-5 [δ_H 5.37 (1H, br s)], H-7 [δ_H 5.93 (1H, dd, J = 11.5, 5.0 Hz)], and H-9 [δ_H 6.39 (1H, br d, J = 9.8 Hz)] indicated that the three acetoxy groups were located at C-5, C-7, and C-9, respectively. Further evidence was obtained from the HMBC spectrum, in which H-5, H-7, and H-9 correlated with the three acetyl carbonyl carbon resonances at δ_C 170.7 (s), 170.1(s), and 171.1(s), respectively. In the ROESY spectrum (Figure 2), the H_2-20 protons exhibited correlations with CH_3-19, which

suggested that the hydroxymethylene at C-4 was β-oriented. The other secondary oxy-groups at C-2, C-5, C-7, C-9, C-10, and C-13 were elucidated as α, α, β, α, β, and α, respectively, on the basis of the comparison of their coupling constants and the ROESY data with those of the known taxuyuntin G.[15] The structure of taxuyunnanine N was assigned as **4**.

Taxuyunnanine O (**5**) had a molecular formula of $C_{28}H_{42}O_{12}$, as deduced from a negative FABMS (*m/z* 569 $[M - H]^+$) and its ^1H and ^{13}C NMR spectra. Confirmation was provided by HRFABMS. The NMR spectra closely resembled those of **4**, with the only difference being the presence of an additional acetyl group. A HMBC experiment, as described for **4**, led to the location of the additional acetyl group at C-10, with the other three acetyl groups remaining at C-5, C-7, and C-9, respectively. The spectral evidence led to the structure of taxuyunnanine O as **5**.

Although nearly 400 taxoids have been found in different *Taxus* species, *abeo*-taxoids with an opened oxetane ring system are rare, with only six such compounds being reported to date. Three of them were previously isolated from *T. yunnanensis*.[15−17] The current report adds to the phytochemical data of yew trees, and it may be of chemotaxonomic significance to this taxonomically troublesome genus.

Experimental Section

General Experimental Procedures. 1D and 2D NMR experiments were performed either on a Bruker AM-400 or a DRX-500 spectrometer. Chemical shifts (δ) were expressed in ppm with reference to the solvent signals. FABMS and HRFABMS were taken on a VG Auto Spec-3000 or on a Finnigan MAT 90 instrument. IR spectra were recorded on a Bio-Rad FTS-135 spectrometer with KBr pellets. UV spectral data were obtained on a UV 210A spectrometer. Optical rotations were carried out on a HORIBA SEPA-300 High Sensitive polarimeter or a Perkin-Elmer model 241 polarimeter. Column chromatography was performed either on silica gel (200−300 mesh, Qingdao Marine Chemical, China), silica gel H (10−40 μm, Qingdao Marine Chemical, China), or Lichroprep RP18 gel (40−63 μm, Merck, Darmstadt, Germany). Fractions were monitored by TLC, and spots were visualized by heating silica gel plates sprayed with 10% H_2SO_4 in EtOH.

Plant Material. The bark of *T. yunnanensis* Cheng et L. K. Fu (Taxaceae) was collected in the Lijiang Prefecture of Yunnan Province, People's Republic of China. A voucher specimen has been deposited at the Yunnan Academy of Forestry, Kunming, Yunnan, People's Republic of China.

Extraction and Isolation. Dried bark (50 kg) was milled and extracted by maceration in EtOH for one week, and the extract was concentrated, in vacuo, to a syrup, diluted with H_2O, and partitioned with $CHCl_3$. The $CHCl_3$ layer was evaporated, in vacuo, to afford a residue (500 g), which was absorbed on 800 g of silica gel and chromatographed on a prepacked (2 kg) silica gel column. Gradient elution was accomplished with $CHCl_3$−Me_2CO. The Me_2CO fractions were combined and filtered, and the solvent was evaporated to afford 38 g of a residue, which was subjected to further silica gel column (No. 2) chromatography using $CHCl_3$−MeOH as the eluting solvent in ascending order of polarity to provide 70 fractions. Fractions 14−29 were combined (4.9 g) and sequentially chromatographed on silica gel, eluted with $CHCl_3$−*i*-PrOH (9:1); on silica gel eluted with petroleum ether−*i*-PrOH (8:2); and on RP_{18} silica gel eluted with MeOH−H_2O (1:1) and acetonitrile−H_2O (2:8), to yield compounds **1** (9 mg), **2** (16 mg), **3** (3 mg), and **5** (101 mg). Compound **4** (20 mg) was isolated from silica gel column chromatographic fractions 57−58 (0.35 g) by sequential column chromatography on silica gel (elution with petroleum ether−EtOAc, l:2) and on RP_{18} gel (stepwise elution with MeOH−H_2O, 2:1, and acetonitrile−H_2O, 4:6).

Taxuyunnanine K (1): white powder (9 mg); $[\alpha]_D^{20}$ −3.86 (*c* 0.10, MeOH); ^1H NMR (pyridine-d_5, 500 MHz, *J* in Hz) δ 5.25 (1H, br t, *J* = 7.9, H-2), 3.46 (1H, d, *J* = 7.1, H-3), 6.00 (1H, t, *J* = 3.1, H-5), 2.44 (2H, m, H-6), 4.70 (1H, dd, *J* = 11.3, 5.4, H-7), 4.80 (1H, br d, *J* = 8.8, H-9), 5.19 (1H, d, *J* = 9.4, H-10), 5.04 (1H, br t, *J* = 7.2, H-13), 2.76 (1H, dd, *J* = 13.9, 7.0, H-14a), 2.40 (1H, dd, *J* = 13.9, 7.0, H-14b), 1.76 (3H, s, CH_3-16), 1.43 (3H, s, CH_3-17), 2.20 (3H, s, CH_3-18), 1.68 (3H, s, CH_3-19), 5.74 (1H, ABd, *J* = 11.8, H-20a), 4.99 (1H, ABd, *J* = 11.8, H-20b), 8.26 (2H, dd, *J* = 8.3, 1.2, Bz), 7.33 (2H, t, *J* = 7.9, Bz), 7.44 (1H, t, *J* = 7.4, Bz), 2.30 (3H, s, 5-OAc), 6.67 (1H, d, *J* = 8.3, 2-OH); ^{13}C NMR (pyridine-d_5, 125 MHz) δ 70.0 (s, C-1), 69.3 (d, C-2), 44.9 (d, C-3), 76.7 (s, C-4), 71.5 (d, C-5), 33.8 (t, C-6), 70.2 (d, C-7), 44.0 (s, C-8), 81.6 (d, C-9), 69.9 (d, C-10), 139.9 (s, C-11), 144.8 (s, C-12), 77.1 (d, C-13), 39.5 (t, C− 14), 76.5 (s, C-15), 27.2 (q, C-16), 29.6 (q, C-17), 11.8 (q, C-18), 15.8 (q, C-19), 66.8 (t, C-20), 166.9 (s, Bz), 131.0 (s, Bz), 130.2 (d, Bz), 128.7 (d, Bz), 133.2 (d, Bz), 170.9 (s, OAc−C═O), 21.4 (q, OAc−CH_3); negative FABMS *m/z* 563 $[M - H]^+$ (5), 545 (2), 503 (4), 459 (5), 441 (3), 381 (3), 121 (100); HRFABMS *m/z* 563.2486 (calcd for $C_{29}H_{39}O_{11}$: 563.2492).

Taxuyunnanine L (2): white powder (16 mg); $[\alpha]_D^{15}$ −48.82° (*c* 0.85, MeOH); UV (MeOH) λ_{max} (log ϵ) 201 (4.3), 232 (4.1), 273 (2.8) nm; IR (KBr) ν_{max} 3404, 2979, 2926, 1719, 1603, 1452, 1385, 1280, 1178, 1110, 1070, 1044, 989, 937, 716 cm^{-1}; ^1H NMR (400 MHz, Me_2CO-d_6, *J* in Hz) δ 6.02 (1H, d, *J* = 7.0, H-2), 3.07 (1H, d, *J* = 7.0, H-3), 3.73 (1H, br d, *J* = 2.8, H-5), 1.84 (1H, m, H-6a), 1.71 (1H, m, H− 6b), 4.18 (1H, dd, *J* = 11.1, 4.8, H-7), 4.29 (1H, d, *J* = 10.4, H-9), 4.58 (1H, d, *J* = 9.8, H-10), 4.58 (1H, overlap, H-13), 2.58 (1H, dd, *J* = 13.4, 7.2, H-14a), 2.26 (1H, dd, *J* = 14.0, 7.2, H-14b), 1.04 (3H, s, CH_3-16), 1.06 (3H, s, CH_3-17), 1.89 (3H, s, CH_3-18), 1.39 (3H, s, CH_3-19), 4.25 (1H, ABd, *J* = 12.2, H-20a), 3.96 (1H, ABd, *J* = 12.2, H-20b), 8.07 (2H, dd, *J* = 8.6, 1.5, Bz), 7.50 (2H, dd, *J* = 7.4, 1.6, Bz), 7.62 (1H, dd, *J* = 7.4, 5.6, Bz), 1.57 (3H, s, 20-OAc), 4.78 (IH, br s, 7-OH), 4.37 (1H, br s, 15-OH); ^{13}C NMR (100 MHz, Me_2CO-d_6) δ 69.2 (s, C-1), 72.1 (d, C-2), 45.4 (d, C-3), 75.3 (s, C-4), 70.9 (d, C-5), 34.4 (t, C-6), 69.1 (d, C-7), 44.5 (s, C-8), 81.5 (d, C-9), 69.9 (d, C-10), 138.8 (s, C-11), 146.9 (s, C-12), 78.3 (d, C-13), 40.3 (t, C-14), 76.6 (s, C-15), 25.7 (q, CH_3-16), 28.7 (q, CH_3-17), 11.5 (q, CH_3-18), 14.7 (q, CH_3-19), 65.1 (t, C-20), 167.6 (s, Bz), 132.0 (s, Bz), 130.6 (d, Bz), 129.4 (d, Bz), 133.9 (d, Bz), 170.5 (s, OAc−C═O), 20.1 (q, OAC−CH_3); negative FABMS *m/z* 563 $[M - H]^+$ (18), 503 (3), 399 (7), 355 (21), 325 (3), 121 (100), 99 (6), 77 (9); HRFABMS *m/z* 563.2423 (calcd for $C_{29}H_{39}O_{11}$: 563.2492).

Taxuyunnanine M (3): white powder (3 mg); $[\alpha]_D^{20}$ −35.56 (*c* 0.05, MeOH); ^1H NMR (pyridine-d_5, 500 MHz, *J* in Hz) δ 6.46 (1H, d, *J* = 7.4, H-2), 3.47 (1H, d, *J* = 7.3, H-3), 5.34 (1H, d, *J* = 8.7, H-5), 2.95 9 (1H, dt, *J* = 15.8, 8.4, H-6a), 2.34 (H, overlap, H-6b), 4.85 (1H, t, *J* = 8.7, H-7), 4.99 (IH, br d, *J* = 7.9, H-9), 5.12 (1H, br d, *J* = 7.9, H-10), 4.96 (1H, br t, *J* = 6.6, H-13), 2.34 (1H, dd, *J* = 14.5, 7.0, H-14a), 2.20 (1H, dd, *J* = 14.5, 7.4, H-14b), 1.39 (3H, s, CH_3-16), 1.31 (3H, s, CH_3-17), 2.10 (3H, s, CH_3-18), 2.30 (3H, s, CH_3-19), 4.80 (1H, ABd, *J* = 7.3, H-20a), 4.67 (1H, ABd, *J* = 7.4, H-20b), 2.06 (3H, s, 2-OAc), 2.38 (3H, s, 4-OAc), 5.72 (1H, br s, 15-OH); ^{13}C NMR (pyridine-d_5, 125 MHz) δ 68.1 (s, C-1), 69.7 (d, C-2), 45.4 (d, C-3), 80.1 (s, C-4), 85.7 (d, C-5), 38.6 (t, C-6), 73.2 (d, C-7), 43.2 (s, C-8), 81.5 (d, C-9), 69.4 (d, C-10), 138.5 (s, C-11), 146.2 (s, C-12), 76.9 (d, C-13), 40.1 (t, C-14), 75.9 (s, C-15), 25.1 (q, CH_3-16), 28.5 (q, CH_3-17), 11.8 (q, CH_3-18), 13.1 (q, CH_3-19), 74.8 (t, C-20), 171.4 (s, 2-OAc−C═O), 21.8 (q, 2-OAc−CH_3), 170.2.(s, 4-OAc−C═O), 22.4 (q, 4-OAc−CH_3); positive FABMS *m/z* 507 $[M + Na]^+$ (24), 485 $[M + H]^+$ (8), 449 (11), 309 (6), 329 (5), 271 (15), 207 (19), 121 (33), 115 (100), 105 (40); HRFABMS *m/z* 485.2393 (calcd for $C_{24}H_{37}O_{10}$: 485.2387).

Taxuyunnanine N (4): white powder (20 mg); $[\alpha]_D^{20}$ −32.10 (*c* 0.40, MeOH); ^1H NMR (pyridine-d_5, 500 MHz, *J* in Hz) δ 5.26 (1H, t, *J* = 9.1, H-2), 3.26 (1H, dd, *J* = 7.8, 4.2, H-3), 3.11 (1H, m, H-4), 5.37 (1H, br s, H-5), 2.18 (1H, m, H-6a), 2.07 (1H, m, H-6b), 5.93 (1H, dd, *J* = 11.5, 5.0, H-7), 6.39 (1H, br d, *J* = 9.8, H-9), 5.28 (1H, d, *J* = 9.5, H-10), 5.00 (1H, br t, *J* = 7.2, H-13), 2.53 (1H, dd, *J* = 14.3, 7.1, H-14a), 2.43 (1H, dd, *J* = 14.2, 7.4, H-14b), 1.87 (3H, s, CH_3-16), 1.40 (3H, s,

CH_3-17), 2.25 (3H, s, CH_3-18), 1.50 (3H, s, CH_3-19), 4.29 (1H, t, J = 9.6, H-20a), 4.01 (1H, dd, J = 10.0, 7.9, H-20b), 2.31 (3H, s, 5-OAc), 2.14 (3H, s, 7-OAc), 2.04 (3H, s, 9-OAc), 5.96 (1H, br d, J = 3.0, 2-OH), 6.78 (1H, br s, 15-OH); ^{13}C NMR (pyridine-d_5, 125 MHz) δ 69.6 (s, C-1), 66.2 (d, C-2), 42.1 (d, C-3), 43.8 (d, C-4), 71.1 (d, C-5), 30.8 (t, C-6), 70.8 (d, C-7), 44.4 (s, C-8), 81.1(d, C-9), 67.7 (d, C-10), 139.7 (s, C-11), 144.9 (s, C-12), 76.8 (d, C-13), 40.8 (t, C-14), 76.2 (s, C-15), 27.9 (q, CH_3-16), 28.6 (q, CH_3-17), 11.7 (q, CH_3-18), 14.5 (q, CH_3-19), 62.1 (t, C-20), 170.7 (s, 5-OAc−C═O), 21.4 (q, 5-OAc−CH3), 170.1 (s, 7-OAc-C═O), 21.7 (q, 7-OAc−CH_3), 171.1 (s, 9-OAc−C═O), 21.5 (q, 9-OAc−CH_3); positive FABMS m/z 551 $[M + Na]^+$ (7), 493 (7), 433 (17), 375 (12), 331 (7), 313 (14), 133 (62), 121 (80), 105 (100); HRFABMS m/z 551.2473 (calcd for $C_{26}H_{40}O_{11}Na$: 551.2468).

Taxuyunnanine O (5): white powder (101 mg); $[\alpha]_D^{15}$ −42.44° (*c* 0.86, MeOH); UV (MeOH) λ_{max} (log ϵ) 210 (3.6), 249 (2.6) nm; IR (KBr) ν_{max} 3437, 2977, 2943, 2488, 1734, 1650, 1439, 1376, 1253, 1144, 1066, 1030, 995, 943, 907, 604 cm^{-1}; ^{1}H NMR (400 MHz, Me_2CO, J in Hz) δ 4.60 (1H, d, J = 8.0, H-2), 2.55 (1H, dd, J = 7.9, 4.2, H-3), 2.33 (1H, m, H-4), 4.90 (1H, br s, H-5), 1.93 (1H, m, H-6a), 1.76 (1H, m, H-6b), 5.32 (1H, dd, J = 11.4, 5.0, H-7), 5.62 (1H, d, J = 10.5, H-9), 6.15 (1H, d, J = 10.6, H-10), 4.57 (1H, t, J = 7.2, H-13), 2.27 (1H, m, H-14a), 1.72 (1H, dd, J = 13.0, 5.6, H-14b), 1.25 (3H, s, CH_3-16), 1.24 (3H, s, CH_3-17), 1.89 (3H, s, CH_3-18), 1.10 (3H, s, CH_3-19), 3.87 (1H, dd, J = 10.4, 7.9, H-20a), 3.64 (1H, dd, J = 10.1, 8.2, H-20b), 1.97 (3H, s, 5-OAc), 2.00 (3H, s, 7-OAc), 2.05 (3H, s, 9-OAc), 1.89 (3H, s, 10-OAc); ^{13}C NMR (100 MHz, Me_2CO) δ 69.0 (s, C-1), 66.7 (d, C-2), 41.2 (d, C-3), 43.6 (d, C-4), 70.8 (d, C-5), 30.5 (t, C-6), 70.3 (d, C-7), 44.4 (s, C-8), 77.5 (d, C-9), 69.9 (d, C-10), 134.8 (s, C-11), 151.1 (s, C-12), 76.4 (d, C-13), 40.4 (t, C-14), 76.8 (s, C-15), 27.4 (q, CH_3-16), 28.0 (q, CH-17), 11.9 (q, CH_3-18), 14.1 (q, CH_3-19), 62.3 (t, C-20), 170.4 (s, 5-OAc−C═O), 21.1 (q, 5-OAc−CH_3), 169.7 (s, 7-OAc−C═O), 20.8 (q, 7-OAc−CH_3), 170.5 (s, 9-OAc−C═O), 21.3 (q, 9-OAc-CH_3), 168.6 (s, 10-OAc−C═O), 20.7 (q, 10-OAc−CH_3); negative FABMS m/z 569 $[M - H]^+$ (46), 509 (3), 491 (4), 463 (5), 447 (9), 433 (2), 405 (11), 387 (9), 373 (5), 339 (3), 311 (3), 283 (1), 173 (1), 123 (1), 59 (100); HRFABMS m/z 569.2678 (calcd for $C_{28}H_{41}O_{12}$: 569.2598).

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References and Notes

(1) Stierle, A.; Strobel, G.; Stierle, D. *Science* **1993**, *260*, 214−217.
(2) Wani, M. C.; Taylor, H. L.; Wall, M. E.; Coggon, P.; McPhail, A. T. *J. Am. Chem. Soc.* **1971**, *93*, 2325−2327.
(3) Horwitz, S. B. *Trends Pharmacol. Sci.* **1992**, *13*, 134−136.
(4) Kingston, D. G. I.; Molinero, A. A.; Rimoldi, J. M. *Prog. Chem. Org. Nat. Prod.* **1993**, *61*, 1−206.
(5) Baloglu, E.; Kingston, D. G. I. *J. Nat. Prod.* **1999**, *62*, 1448−1472.
(6) Pharmar, V. S.; Jha, A.; Bisht, K. S.; Taneja, P.; Singh, S. K.; Kumar, A.; Jain, R.; Lsen, C. E. *Phytochemistry* **1999**, *50*, 1267−1304.
(7) Zhang, Z. P.; Jia, Z. J. *Phytochemistry* **1990**, *29*, 3673−3675.
(8) Chen, W. M.; Chang, P. L.; Wu, B.; Zheng, Q. T. *Acta Pharm. Sin.* **1991**, *26*, 747−754.
(9) Zhang, H. J.; Takeda, Y.; Minami, Y.; Yoshida, K.; Unemi, N.; Mu, Q.; Xiang, W.; Sun, H. D. *Acta Bot. Yunnanica* **1993**, *15*, 424−426.
(10) Zhang, H. J.; Sun, H. D.; Takeda, Y. *J. Nat. Prod* **1995**, *58*, 1153−1159.
(11) Zhang, H. J.; Mu, Q.; Xiang, W.; Yao, P.; Sun, H. D.; Takeda, Y. *Phytochemistry* **1997**, *44*, 911−915.
(12) Zhang, H. J.; Takeda, Y.; Sun, H. D. *Phytochemistry* **1995**, *39*, 1147−1151.
(13) Li, S. H.; Zhang, H. J.; Yao, P.; Sun, H. D. *Chin. Chem. Lett.* **1998**, *9*, 1017−1020.
(14) Chen, R.; Kingston, D. G. I. *J. Nat. Prod.* **1994**, *57*, 1017−1021.
(15) Yue, Q.; Fang Q. C.; Liang, X. T. *Chin. Chem. Lett.* **1995**, *6*, 225−228.
(16) Zhou, J. Y.; Zhang, P. L.; Chen, W.. M.;- Fang, Q. C. *Phytochemistry* **1998**, *48*, 1387−1389.
(17) Zhang, S.; Lee, C. T. L.; Kashiwada, Y.; Chen, K. J. *J. Nat. Prod.* **1994**, *57*, 1580−1583.

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