Taxezopidines B−H, New Taxoids from Japanese Yew *Taxus cuspidata*

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Seven new taxoids, taxezopidines B−H (**1**−**7**), have been isolated from seeds and stems of Japanese yew *Taxus cuspidata* Sieb. et Zucc. and the structures elucidated on the basis of spectroscopic data. Taxezopidine B (**1**) is the first taxoid with a double bond at C-3 and C-4.

Chemical studies on constituents of different yew trees have resulted in the isolation of a large number of taxoids.[1] In our continuing search for bioactive taxoids, we previously isolated a series of new taxoids, taxuspines A−H and J−Z[2−9] and taxezopidine A,[10] from stems, leaves, and seeds of the Japanese yew *Taxus cuspidata* Sieb. et Zucc. (Taxaceae). Further invenstigation on extracts of seeds and stems of *T. cuspidata* have led to isolation of seven new taxoids, taxezopidines B−H (**1**−**7**) (Chart 1). In this paper, the isolation and structure elucidation of **1**−**7** are described.

Results and Discussion

The methanolic extract of seeds of *T. cuspidata* collected at Sapporo was partitioned between toluene and water, and then the aqueous layer was extracted with chloroform. The chloroform-soluble portion was purified by successive chromatographies on a silica gel column followed by a reversed-phase column to afford taxezopidines B (**1**, 0.000 25%), C (**2**, 0.000 52%), and D (**3**, 0.000 63%). Alternatively, the methanolic extract of yew stems was partitioned between toluene and water, and the toluene-soluble portions were again subjected to successive chromatographies on a silica gel column followed by reversed-phase column to afford taxezopidines E (**4**, 0.000 36%), F (**5**, 0.000 28%), G (**6**, 0.000 15%), and H (**7**, 0.000 14%) together with known taxoids, baccatin III,[11] *N*-methylpaclitaxel C,[12] and 10-(β-hydroxybutyryl)-10-deacetylpaclitaxel.[13]

Taxezopidine B (**1**) was obtained as a colorless amorphous solid, and the molecular formula was established to be $C_{26}H_{38}O_{10}$ by HRFABMS [*m/z* 511.2529 $(M + H)^+$, Δ −1.4 mmu]. IR absorptions implied that **1** possessed hydroxy (3446 cm^{-1}) and ester (1718 cm^{-1}) groups. Analyses of the ^1H and ^{13}C NMR data and HMQC spectrum provided evidence that **1** possesses three acetyl groups, one tetrasubstituted olefin, one ketone carbon, four oxymethines, two methines, one oxymethylene, three methylenes, two quaternary carbons, one oxygenated quaternary carbon, and four methyl groups. The $^1H-^1H$ COSY spectrum revealed the connectivities of C-1 to C-2, C-5 to C-7, C-9 to C-10, C-12 to C-18, and C-14 to C-1. In the HMBC spectrum, long-range $^1H-^{13}C$ correlations of H_2-14 and H_3-18 to C-13 (δ 209.5), H-1 to C-11, H_2-14 to C-15, H_3-18 to C-11, and H_2-14 to C-12 indicated that **1** possessed a cyclohexanone moiety (ring A), while the correlations of H_3-16 and H_3-17 to C-1, C-11, and C-15 revealed that Me-16 and Me-17 were attached at C-15. HMBC cross-peaks of H-2 to C-3, C-8, and C-15 and H-10 to C-11 and C-15 revealed the presence of an eight-membered ring (ring B), while the presence of a cyclohexene moiety with an olefin at C-3 (ring C) was deduced from HMBC correlations of H-5 to C-20, H-2 and H-20b to C-3 and C-4, and H_3-19 to C-3 and C-8. Three acetoxy groups were attached at C-2, C-9, and C-10 based on HMBC correlations, while two hydroxy groups were connected to C-5 (δ_c 66.13) and C-11 (δ_c 79.8) by the correlation of a hydroxy proton (δ_H 2.86) to C-5 and the other hydroxy proton (δ_H 3.01) to C-11. The remaining hydroxy group was attached at C-20 judging from the chemical shift of C-20 (δ_C 64.46). Thus, the structure of taxezopidine B was assigned to be **1**. Relative stereochemistry of **1** was deduced from NOESY data and $^1H-^1H$ coupling constants (Figure 1). A boatlike conformation of ring B was elucidated from the coupling constant (7.1 Hz) between H-9 and H-10 and NOESY correlations of H-2 to H-9, H-16, and H-19, while a chairlike conformation of ring C was deduced from NOESY correlations of H-7a to H-10, H_2-12, and H-18.

The HREIMS spectra [*m/z* 392.2217 (M^+), Δ +1.8 mmu; *m/z* 392.2183 (M^+), Δ −1.6 mmu] of taxezopidines C (**2**) and D (**3**) gave the same molecular formula, $C_{22}H_{32}O_6$. The ^1H, ^{13}C, and 2D NMR spectra implied that the structures of **2** and **3** were very similar to each other, having a 6/8/6-membered ring system with an acetoxy, an *exo*-methylene, and four methyl groups. The HMBC correlations revealed that **2** and **3** possessed the same cyclohexanone ring (ring A) and cyclohexane ring (ring C) with an *exo*-methylene at C-4, one acetoxy group at C-9 (for **2**) or C-10 (for **3**) in ring B, and two of three hydroxy groups at C-2 and C-5 by $^1H-^1H$ COSY connectivities of H-2/OH-2 and H-5/OH-5 for **2** or **3**. The other hydroxy group was connected to C-10 (in **2**) and C-9 (in **3**), judging from the chemical shifts of H-9 and H-10 and HMBC correlations. Thus, the structures of taxezopidines C and D were assigned to be **2** and **3**, respectively. Relative stereochemistries of **2** and **3** were deduced from NOESY data and $^1H-^1H$ coupling constants.

Taxezopidine E (**4**) was obtained as a colorless amorphous solid and showed the pseudomolecular ion peak at *m/z* 539 $(M + H)^+$ in the FABMS spectrum. HRFABMS analysis revealed the molecular formula to be $C_{31}H_{38}O_8$ [*m/z* 539.2680 $(M + H)^+$, Δ +3.5 mmu]. IR

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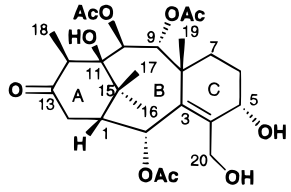
Chart 1



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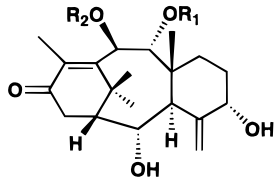
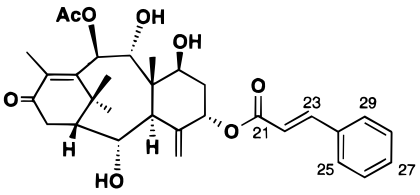


2 R_1=Ac, R_2=H
3 R_1=H, R_2=Ac



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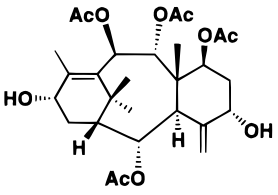

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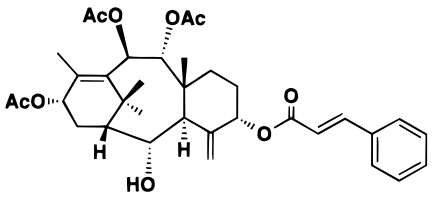

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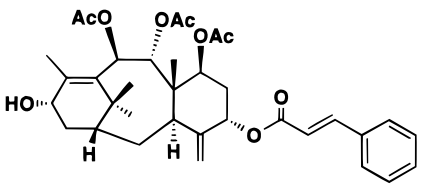

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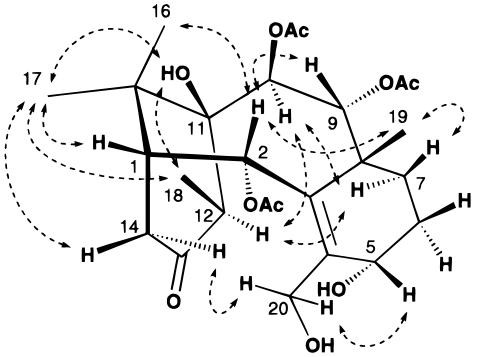

Figure 1. Relative stereochemistry of taxezopidine B (1). Dotted arrows denote NOESY correlation.

absorptions indicated the presence of hydroxy (3400 cm^{-1}), ester (1715 cm^{-1}), and α,β-unsaturated carbonyl (1670 cm^{-1}) groups. Proton signals due to a cinnamoyl group appeared at δ_H 7.75 (2H, d, J = 7.1 Hz), 7.44 (2H, d, J = 7.1 Hz), 7.43 (1H, m), 7.67 (1H, d, J = 15.9 Hz; *trans*-oriented), and 6.38 (1H, d, J = 15.9 Hz). UV absorption at 279 nm also supported the presence of the cinnamoyl group. Since 10 out of 13 unsaturations deduced from the molecular formula were thus accounted for, **4** was inferred to contain three rings. HMBC correlations of H-14a to C-13 (δ_C 199.29), H_3-16 and H_3-17 to C-1, C-11, and C-15, and H_3-18 to C-11, C-12, and C-13 suggested the presence of a cyclohexenone ring (ring A), while the presence of rings B and C was indicated by HMBC correlations of H-3 to C-4, H-20a to C-3 and C-5, H_3-19 to C-3, C-7, C-8, and C-9, and H-10 to C-11. One acetoxy group was attached at C-10 on the basis of an HMBC correlation between an oxymethine proton (δ_H 6.08, H-10) and the acetyl carbonyl carbon (δ_C 170.01). A hydroxy group was attached at C-2, C-7, and C-9, judging from the respective chemical shifts of H-2 (δ_H 4.23), H-7 (δ_H 4.24), and H-9 (δ_H 4.32). Thus, the structure of taxezopidine E was assigned to be **4**. The relative stereochemistry of **4** was elucidated by the NOESY data and $^1H-^1H$ coupling constants.

The molecular formula of taxezopidine F (**5**) was determined to be $C_{28}H_{40}O_{10}$ by HREIMS [*m*/*z* 536.2634 $(M)^+$, Δ +1.3 mmu]. The ^1H NMR spectrum of **5** in $CDCl_3$ showed proton signals due to an *exo*-methylene (δ_H 4.87 and 5.30), four methyls (δ_H 0.95, 0.97, 1.68, and 2.34), four acetyl methyls (δ_H 1.99, 2.04, 2.04, and 2.07), and five oxymethines (δ_H 4.32, 4.36, 5.60, 5.84, and 6.16). The ^1H, ^{13}C, and 2D NMR data of **5** showed the presence of a 6/8/6-membered ring system. Detailed analysis of the $^1H-^1H$ COSY spectrum of **5** implied connectivities of C-1 to C-3, C-5 to C-7, C-9 to C-10, and C-13 to C-1. HMBC correlations of H_3-16 and H_3-17 to C-15, H_3-18 to C-12 and C-13, H_3-19 to C-3, C-7, C-8, and C-9, and H-20a to C-3 and C-5 indicated that Me-16 and Me-17, Me-18, and Me-19 were attached at C-15, C-12, and C-8, respectively, while an *exo*-methylene was attached at C-4. From HMBC correlations of H-2, H-7, H-9, and H-10 to acetyl carbonyl carbons (δ_C 168.94, 168.94, 169.32, and 169.32, respectively), four acetoxy groups were connected to C-2, C-7, C-9, and C-10. The chemical shifts of H-5 (δ_H 4.32, m) and H-13 (δ_H 4.36, m) indicated that two hydroxyl groups were attached at C-5 and C-13. Thus, the structure of taxezopidine F was assigned to be **5**. Relative stereochemistry of **5** was elucidated from the NOESY data and $^1H-^1H$ coupling constants.

Taxezopidine G (**6**) showed the molecular ion peak at *m*/*z* 608 in the EIMS spectrum, and the molecular formula, $C_{35}H_{44}O_9$, was established by the HREIMS [*m*/*z* 548.2770 $(M - AcOH)^+$, Δ −0.4 mmu] and ^{13}C NMR spectrum. The ^1H, ^{13}C, and 2D NMR data of **6** showed the presence of a 6/8/6-membered ring system, while the

^{1}H and ^{13}C NMR data of **6** resembled those of taxinine E.[14] The olefin proton signals of a cinnamoyl group at C-5 appeared at δ_H 7.78 (1H, d, J = 16.0 Hz), 7.49 (2H, m), 7.41 (2H, m), 7.41 (1H, m), and 6.65 (1H, d, J = 16.0 Hz), and the cinnamoyl carbonyl carbon (δ_C 166.33) showed an HMBC correlation for H-5. Three acetoxy groups were attached at C-9, C-10, and C-13 on the basis of the HMBC correlations and oxymethine proton resonances (δ_H 5.88, H-9; δ_H 6.05, H-10; δ_H 5.84, H-13), while a hydroxy group was attached at C-2 by the oxymethine resonance at δ_H 4.22. HMBC correlations of H-20a to C-3 and H-20b to C-5 indicated the presence of an *exo*-methylene at C-4. Thus, the structure of taxezopidine G was assigned to be **6**. The relative stereochemistry of **6** was elucidated by the NOESY spectrum.

The molecular formula, $C_{35}H_{44}O_9$, of taxezopidine H (**7**), which is the same as that of **6**, was established by the HREIMS [*m/z* 548.2772 $(M - AcOH)^+$, Δ −0.2 mmu] and ^{13}C NMR spectrum. Detailed analyses of ^{1}H, ^{13}C, and 2D NMR spectra of **7** revealed that the structure of **7** was similar to that of **6**, except for functional groups at C-2, C-7, and C-13. Three acetoxy and one cinnamate groups were attached at C-7, C-9, C-10, and C-5, respectively, on the basis of the HMBC correlations, while a hydroxy group was connected to C-10 judging from the ^{1}H NMR chemical shift of H-13 (δ_H 4.54). Thus, the structure of taxezopidine H was assigned to be **7**. The relative stereochemistry of **7** was elucidated by the NOESY spectrum.

Taxezopidines B−H (**1**−**7**) are new taxoids isolated from seeds and stems of the Japanese yew *T. cuspidata* Sieb. et Zucc. Taxezopidine B (**1**) is the first example of a taxoid containing a 6/8/6-membered ring system with a double bond at C-3.

Experimental Section

General Methods. Optical rotations were determined on a JASCO DIP-370 polarimeter. UV and IR spectra were obtained on JASCO Ubest-35 and JASCO IR report-100 and FT/IR-230 spectrometers, respectively. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker ARX-500 spectrometer. The 7.26 ppm resonance of residual $CHCl_3$ and 77.0 ppm of $CDCl_3$ were used as internal references. EIMS was obtained on a JEOL DX-303 spectrometer operating at 70 eV. FABMS was measured on a JEOL HX-110 spectrometer by using glycerol matrix.

Collection, Extraction, and Separation. The Japanese yew *T. cuspidata* Sieb. et Zucc. was collected at Sapporo, Hokkaido. The MeOH extract (87.7 g) of the seeds (401 g) of the yew was partitioned between $CHCl_3$ (500 mL × 4) and H_2O (500 mL). The $CHCl_3$-soluble portion was evaporated under reduced pressure to give a residue (7.82 g), which was subjected to a silica gel column (4 × 32 cm) eluted with hexane/acetone (4:1 → 1:1) to give fractions **a** (140 mg) and **b** (984 mg). Fraction **a** was applied to a reversed-phase column (YMC-GEL ODS 60, 350/250 mesh, 0.5 × 6 cm; MeOH/H_2O, 7:3) and gave a viable fraction (90.8 mg), which was further purified by successive C_{18} HPLC (YMC-Pack ODS AM-323, 5 μm, 10 × 250 mm; flow rate 2.5 mL/min; UV detection at 227 nm; MeOH/H_2O, 1:1) and then by SiO_2 HPLC column (Develosil 60−5, 5 μm, 10 × 250 mm; flow rate 2.5 mL/min; UV detection at 254 nm; hexane/EtOAc, 2:1) chromatographies to give taxezopidines C (**2**, 2.1 mg, t_R 23.2 min) and D (**3**, 2.5 mg, t_R 23.6 min). Fraction **b** was subjected to the same ODS column isolation conditions as fraction **a** to give taxezopidine B (**1**, 1.0 mg, t_R 10.4 min). The stems (1.2 kg) of the yew were extracted with MeOH (15 L × 4), and the extract was partitioned between toluene (1 L × 4) and H_2O (750 mL). The toluene-soluble portions were evaporated under reduced pressure to give a residue (24.5 g), part of which (15.9 g) was subjected to a silica gel column (hexane/acetone, 8:1) to give a crude fraction (3.22 g), and the other part (1.82 g) was subjected to a silica gel column using a different solvent system ($CHCl_3$/acetone, 20:1) to afford crude fractions **c** (122 mg) and **d** (195 mg). Fraction **d** was applied to a reversed-phase column (YMC-GEL ODS 60, CH_3CN/H_2O, 1:1) to give a viable fraction (55 mg), which was purified by reversed-phase HPLC (YMC-Pack ODS AL-323, 10 × 250 mm; flow rate, 2.5 mL/min; UV detection at 227 nm; CH_3CN/H_2O, 1:1) to give taxezopidine F (**5**, 1.3 mg, t_R 16.8 min). Fraction **c** was chromatographed by the same conditions as those for fraction **d** to give *N*-methylpaclitaxel C (0.8 mg, t_R 12.8 min). Toluene extract (115 g) obtained from the stems (11 kg) of the yew was subjected to a silica gel column (hexane/acetone, 8:1) to give a fraction (29.2 g), which was separated by a reversed-phase column (YMC GEL ODS 60, CH_3CN/H_2O, 4:1) followed by a silica gel column ($CHCl_3$/acetone, 5:1) to give crude fractions **e** (0.9 g) and **f** (2.67 g). Fraction **e** was separated by a silical gel column ($CHCl_3$/acetone, 40:1) and a reversed-phase column (YMC GEL ODS 60, MeOH/H_2O, 4:1) to give a crude fraction (374 mg) containing **6** and **7**. Part of this mixture (101 mg) was subjected to reversed-phase HPLC (YMC-Pack, ODS-AM-323, S-5 μm 120A, 10 × 250 mm; flow rate, 2.5 mL/min; UV detection at 227 nm; MeOH/H_2O, 70:30) to give taxezopidines G (**6**, 4.4 mg, t_R 53.6 min) and H (**7**, 4.1 mg, t_R 48.8 min). Fraction **f** was subjected to a reversed-phase column (YMC-GEL ODS 60, CH_3CN/H_2O, 1:1) to give fractions **g** (400 mg) and **h** (276 mg). Fraction **h** was further subjected to successive chromatographies on a silica gel column ($CHCl_3$/acetone, 4:1) and a reversed-phase HPLC column (Develosil ODS-HG-5, 10 × 250 mm; flow rate, 2.5 mL/min; UV detection at 227 nm; MeOH/H_2O, 60:40) to give taxezopidine E (**4**, 1.8 mg, t_R 31.2 min) and 10-(β-hydroxybutyryl)-10-deacetylpaclitaxel (3.6 mg, t_R 14.0 min). Fraction **g** was subjected to a Sephadex LH-20 column ($CHCl_3$/MeOH, 1:1) and the same reversed-phase HPLC as described above for the purification of fraction **h** to give baccatin III (2.2 mg, t_R 5.6 min).

Taxezopidine B (1): colorless amorphous solid; $[\alpha]^{26}_D$ +10.4° (*c* 0.10, $CHCl_3$); IR (film) ν_{max} 3446, 2925, 2365, 1718, 1370, 1027 cm^{-1}; ^{1}H and ^{13}C NMR (Table 1); FABMS *m/z* 511 $(M + H)^+$; HRFABMS *m/z* 511.2529 $(M + H)^+$, calcd for $C_{26}H_{39}O_{10}$, 511.2543; ^{1}H−^{1}H COSY correlations (C_6D_6, H/H) 1/2, 5/6a, 5/6b, 6a/6b, 7a/7b, 6/7, 9/10, 13/18, 14a/14b, 14a/1, 20a/20b; HMBC correlations (Table 1); NOESY correlations (C_6D_6, H/H) 1/17, 1/16, 2/1, 2/9, 2/16, 2/19, 5/6a, 5/6b, 6a/6b, 6b/19, 7a/7b, 7b/19, 9/16, 9/19, 10/7a, 10/12, 10/18, 11-OH/18, 11-OH/16, 12/7a, 12/18, 14b/1, 14b/17, 16/17, 20/5-OH, 20a/20b.

Taxezopidine C (2): colorless amorphous solid; $[\alpha]^{28}_D$

Table 1. ^{1}H and ^{13}C NMR Data of Taxezopidine B (**1**) in C_6D_6

position	^{1}H[a]		*J* (Hz)	^{13}C[a]		H coupled with C[b]
1	2.06	br s		50.10	d	H-2, H-16, H-17
2	6.30	br s		72.02	d	H-1, H-14
3				137.08	s	H-2, H-19, H-20b
4				141.91	s	H-2, H-20b
5	4.10	br s		66.13	d	5-OH
6(a)	1.75	m		20.22	t	
(b)	1.50	m				
7(a)	1.96	m		23.79	t	H-9, H-19
(b)	1.48	m				
8				43.87	s	H-2, H-7a, H-19
9	6.11	d	7.1	75.82	d	H-10, H-19
10	5.40	d	7.1	76.01	d	H-9
11				79.80	s	H-1, H-10, H-16, H-17, H-18 11-OH
12	2.91	q	6.8	50.79	d	H-14, H-18
13				209.54	s	H-14, H-18
14	2.86[c]	m		38.03	t	H-2
15				44.50	s	H-2, H-10, H-14, H-16, H-17
16	1.71	s		23.81	q	H-1, H-17
17	1.00	s		30.90	q	H-16
18	1.52	d	6.8	9.83	q	
19	1.21	s		26.00	q	H-9
20(a)	4.60	d	12.0	64.46	t	H-5
(b)	3.98	d	12.0			
5-OH	2.86	br s				
11-OH	3.01	br s				
20-OH	1.75	br s				
2-AcO	1.66	s		20.81	q	
				168.00	s	H-2
9-AcO	1.65	s		20.83	q	
				170.47	s	H-9
10-AcO	1.60	s		20.20	q	
				171.48	s	H-10

[a] δ in ppm. [b] HMBC correlations. [c] 2H.

+17.3°(*c* 0.10, $CHCl_3$); IR (film) ν_{max} 3421, 2924, 1718, 1654, 1260 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.65 (1H, d, J = 10.1 Hz, H-9), 5.26 (1H, s, H-20a), 5.22 (1H, s, H-20b), 5.02 (1H, dd, J = 10.1, 3.8 Hz, H-10), 4.27 (1H, dd, J = 6.8, 5.9 Hz, H-2), 4.21(1H, 1H, m, H-5), 3.45 (1H, d, J = 5.9 Hz, H-3), 2.80 (1H, dd, J = 7.2, 19.7 Hz, H-14a), 2.32 (1H, d, J = 6.8 Hz, H-1), 2.21 (1H, d, J = 19.7 Hz, H-14b), 2.15 (3H, s, C*H*$_3$CO-9), 2.06 (3H, s, H$_3$−18), 2.05 (1H, d, J = 3.8 Hz, OH-10), 1.86 (1H, d, J = 6.5 Hz, OH-2), 1.77 (1H, m, H-6a), 1.73 (3H, s, H$_3$-16), 1.71 (1H, m, 7a), 1.65 (1H, m, 6b), 1.65 (1H, m, 7b), 1.55 (1H, brd, OH-5), 1.24 (3H, s, H$_3$-17), 1.12 (3H, s, H$_3$-19); ^{13}C NMR ($CDCl_3$) δ 200.34 (s, C-13), 172.5 (s, 9-CH$_3$*C*O), 153.67 (s, C-11), 148.97 (s, C-4), 135.80 (s, C-12), 114.68 (t, C-20), 79.19 (d, C-9), 71.86 (d, C-10), 75.94 (d, C-5), 68.41(d, C-2), 51.61 (d, C-1), 44.97 (s, C-8), 42.83 (d, C-3), 37.65 (s, C-15), 37.65 (q, C-17), 35.83 (t, C-14), 31.15(t, C-7), 25.75(t, C-6), 25.53 (q, C-16), 21.00 (q, 9-*C*H$_3$CO), 17.56(q, C-19), 13.95 (q, C-18); EIMS *m*/*z* 392 (M$^+$); HREIMS *m*/*z* 392.2217 (M$^+$), calcd for $C_{22}H_{32}O_6$ 392.2199; ^{1}H−^{1}H COSY correlations ($CDCl_3$, H/H) 1/2, 2/3, 2/2-OH, 5/6, 5/5-OH, 6a/6b, 7a/7b, 6/7, 9/10, 14a/14b, 14a/1, 20a/20b; HMBC correlations ($CDCl_3$, H/C) 1/11, 1/13, 3/8, 5/3, 5/7, 7/9, 9/9-CH$_3$*C*O, 9/10, 10/15, 14a/2, 14a/13, 14a/15, 16/1, 16/11, 16/15, 16/17, 17/1, 17/11, 17/15, 17/16, 18/11, 18/12, 18/13, 19/3, 19/9, 20a/3, 20b/5; NOESY correlations ($CDCl_3$, H/H) 1/16, 1/17, 2/1, 2/16, 2/19, 3/7a, 3/18, 7a/18, 7b/19, 9/16, 9/19, 10/7a, 10/18, 14a/18, 16/17, 20a/2-OH.

Taxezopidine D (3): colorless amorphous solid; $[\alpha]^{29}_D$ +8.4° (*c* 0.10, $CHCl_3$); IR (film) ν_{max} 3445, 2923, 1717, 1654, 1260 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.90 (1H, d, J = 9.8 Hz, H-10), 5.22 (1H, s, H-20a), 5.21(1H, s, H-20b), 4.21 (1H, m, H-5), 4.18 (1H, dd, J = 9.8, 4.7 Hz, H-9), 4.17 (1H, dd, J = 6.8, 5.6 Hz, H-2), 3.46 (1H, d, J = 5.6 Hz, H-3), 2.77(1H, dd, J = 6.9, 19.8 Hz, H-14a), 2.31(1H, d, J = 6.9 Hz, H-1), 2.21 (1H, d, J = 19.8 Hz, H-14b), 2.20 (3H, s, H$_3$-18) 2.20 (1H, d, J = 4.7 Hz, OH-9), 2.12 (3H, s, C*H*$_3$CO-10), 1.98 (1H, d, J = 6.5 Hz, OH-2), 1.77 (1H, m, H-6a), 1.71 (1H, m, H-7a), 1.65 (1H, m, H-6b), 1.65 (1H, m, 7b), 1.56 (3H, s, H$_3$-16), 1.43 (1H, brd, OH-5), 1.11 (3H, s, H$_3$-17), 0.90 (3H, s, H$_3$-19); ^{13}C NMR ($CDCl_3$) δ 200.11 (s, C-13), 170.17 (s, 10-CH$_3$*C*O), 150.33 (s, C-11), 149.37 (s, C-4), 137.77 (s, C-12), 114.10 (t, C-20), 76.76 (d, C-10), 75.85 (d, C-9), 75.85 (d, C-5), 68.31 (d, C-2), 51.29 (d, C-1), 45.52 (s, C-8), 43.10 (d, C-3), 38.00 (s, C-15), 37.65 (q, C-17), 35.76 (t, C-14), 31.56 (t, C-7), 26.77 (t, C-6), 25.53 (q, C-16), 21.18 (q, 10-*C*H$_3$CO), 17.56 (q, C-19), 13.95 (q, C-18); EIMS *m*/*z* 392 (M$^+$); HREIMS *m*/*z* 392.2183 (M$^+$), calcd for $C_{22}H_{32}O_6$ 392.2199; ^{1}H−^{1}H COSY correlations ($CDCl_3$, H/H) 1/2, 2/3, 2/2-OH, 5/6, 5/5-OH, 6a/6b, 7a/7b, 6/7, 9/10, 14a/1, 14a/14b, and 20a/20b; HMBC correlations ($CDCl_3$, H/C) 1/11, 1/13, 3/8, 5/3, 5/7, 7/9, 9/10, 10/15, 10/10-CH$_3$*C*O, 14a/2, 14a/13, 14a/15, 16/1, 16/11, 16/15, 16/17, 17/1, 17/11, 17/15, 17/16, 18/11, 18/12, 18/13, 19/3, 19/9, 20a/3, 20b/5; NOESY correlations ($CDCl_3$, H/H) 1/16, 1/17, 2/1, 2/16, 2/19, 3/7a, 3/18, 7a/10, 7a/18, 7b/19, 9/16, 9/19, 10/18, 14a/18, 16/17, 20a/2-OH.

Taxezopidine E (4): colorless amorphous solid; $[\alpha]^{22}_D$ +24° (*c* 0.2, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 219 (4.15), 279 (4.18) nm; IR (film) ν_{max} 3400, 1715, 1670, 1170, 1370, 1240 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.75 (2H, d, J = 7.1 Hz, H-25 and H-29), 7.67 (1H, d, J = 15.9 Hz, H-23), 7.44 (2H, d, J = 7.1 Hz, H-26 and H-28), 7.43 (1H, m, H-27), 6.38 (1H, d, J = 15.9 Hz, H-22), 6.08 (1H, d, J = 10.1 Hz, H-10), 5.52 (1H, s, 20b), 5.47 (1H, s, H-20a), 5.35 (1H, m, H-5), 4.32 (1H, d, J = 10.1 Hz, H-9), 4.24 (1H, q, J = 14.6, 4.1 Hz, H-7), 4.23 (1H, m, H-2), 3.06 (1H, d, J = 6.1 Hz, H-3), 2.85 (1H, q, J = 9.8, 6.2 Hz, H-14a), 2.37 (1H, d, J = 9.8 Hz, H-1), 2.25 (3H, s, H$_3$-18), 2.21 (1H, m, H-6a), 2.17 (3H, s, AcO), 2.19 (1H, m, H-14b), 1.78 (1H, m, H-6b), 1.60 (3H, s, H$_3$-16), 1.24 (3H, s, H$_3$-19), 1.17 (3H, s, H$_3$-17); ^{13}C NMR ($CDCl_3$) δ 199.29 (s, C-13), 170.01 (s, *C*OCH$_3$), 166.43 (s, C-21), 151.43 (s, C-11), 146.07 (d, C-23), 142.50 (s, C-4), 137.43 (s, C-12), 134.28 (s, C-24), 130.70 (d, C-27), 128.96 (d, C-25 and C-29), 128.56 (d, C-26 and C-28), 119.29 (t, C-20), 117.50 (d, C-22), 77.57 (d, C-9), 76.75 (d, C-10), 75.86 (d, C-5), 71.35 (d, C-7), 66.42 (d, C-2), 51.43 (d, C-1), 47.50 (s, C-8), 43.57 (d, C-3), 37.86 (t, C-6), 37.85 (s, C-15), 37.82 (q, C-17), 35.71 (t, C-14), 27.14 (q, C-16), 21.07 (q, CO*C*H$_3$), 14.28 (q, C-18), 13.02 (q, C-19); FABMS *m*/*z* 539 (M + H)$^+$; HRFABMS *m*/*z* 539.2680 (M + H)$^+$, calcd for $C_{31}H_{39}O_8$ 539.2645; ^{1}H−^{1}H COSY correlations ($CDCl_3$, H/H) 1/2, 1/14a, 2/3, 5/6a, 5/6b, 6a/7, 9/10, 22/23, 25/26, 26/27, 27/28, 28/29; HMBC correlations ($CDCl_3$, H/C) 1/2, 1/3, 1/11, 1/13, 3/4, 3/20, 5/7, 5/20, 6a/5, 9/7, 9/8, 9/10, 10/9, 10/11, 10/12, 10/15, 14a/2, 14a/13, 16/1, 16/11, 16/15, 16/17, 17/1, 17/11, 17/15, 17/16, 18/11, 18/12, 18/13, 19/3, 19/7, 19/8, 19/9, 20a/3, 20a/5, 22/24, 23/21, 23/25, 27/25, 25/27; NOESY correlations ($CDCl_3$, H/H) 1/2, 1/16, 1/17, 2/16, 2/19, 3/7, 3/10, 3/14a, 3/20a, 3/22, 5/6a, 5/6b, 5/20a, 6b/7, 7/10, 9/16, 9/19, 10/18, 14b/17, 16/17, 18/22, 19/20b, 25/26, 26/27.

Taxezopidine F (5): colorless amorphous solid; $[\alpha]^{25}_D$ −13.4° (*c* 0.17, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 206 (4.03), 218 (4.01) nm; IR (film) ν_{max} 3420, 1720, 1360, 1240, 1020 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.16 (1H, d, J = 10.9 Hz, H-10), 5.84 (1H, d, J = 10.9 Hz, H-9), 5.60 (1H, dd, J = 5.3, 11.6 Hz, H-7), 5.50 (1H, dd, J = 5.7, 6.0 Hz, H-2), 5.30 (1H, s, H-20b), 4.87 (1H, s, H-20a), 4.36 (1H, m, H-13), 4.32 (1H, m, H-5), 3.38 (1H, d, J = 5.7 Hz, H-3), 2.70 (1H, m, H-14b), 2.34 (3H, s, H-18), 2.07 (3H, s, 7-OAc), 2.04 (3H, s, 2-OAc), 2.04 (3H, s, 9-OAc), 1.99 (3H, s, 10-OAc), 1.96 (1H, m, H-6b), 1.78 (1H, d, J = 6.0 Hz, H-1), 1.69 (1H, m, H-6a), 1.68 (1H, s, H_3-16), 1.52 (1H, m, H-14a), 0.97 (3H, s, H_3-19), 0.95 (3H, s, H_3-17); ^{13}C NMR ($CDCl_3$) δ 169.32 (s, 7-CH_3CO), 169.32 (s, 9-CH_3CO), 168.94 (s, 2-CH_3CO), 168.94 (s, 10-CH_3CO), 145.21 (s, C-4), 145.01 (s, C-12), 133.10 (s, C-11), 116.91 (t, C-20), 76.01 (d, C-5), 75.95 (d, C-9), 72.41 (d, C-10), 70.03 (d, C-2), 69.87 (d, C-7), 67.54 (d, C-13), 47.55 (d, C-1), 47.47 (s, C-8), 40.84 (s, C-3), 38.33 (s, C-15), 37.51 (t, C-6), 32.23 (t, C-14), 32.23 (q, C-17), 25.84 (q, C-19), 21.47(q, 7-CH_3CO), 21.35 (q, 9-CH_3CO), 21.04 (q, 2-CH_3CO), 20.75 (q, 10-CH_3CO), 16.71 (q, C-18), 12.90 (q, C-16); EIMS *m/z* 536 $(M)^+$; HREIMS *m/z* 536.2634 $(M)^+$, calcd for $C_{28}H_{40}O_{10}$ 536.2621; $^1H-^1H$ COSY correlations ($CDCl_3$, H/H) 1/2, 1/14a, 2/3, 5/6a, 5/6b, 6a/6b, 6b/7, 9/10, 13/14, 14a/14b, 20a/20b; HMBC correlations ($CDCl_3$, H/C) 1/2, 1/3, 1/11, 1/13, 1/15, 2/8, 2/CH_3CO, 3/1, 5/7, 9/7, 9/8, 9/10, 9/CH_3CO, 10/9, 10/15, 10/CH_3CO, 14b/2, 14b/12, 16/1, 16/11, 16/15, 17/1, 17/11, 17/15, 18/12, 18/13, 19/3, 19/7, 19/9, 20a/3, 20a/5; NOESY correlations ($CDCl_3$, H/H) 1/2, 1/14b, 1/17, 2/9, 2/16, 2/19, 3/7, 3/14a, 5/6a, 5/6b, 7/6b, 7/10, 7/18, 9/10, 9/16, 9/19, 10/18, 13/14b, 13/17.

Taxezopidine G (6): colorless amorphous solid; $[\alpha]^{25}_D$ +25.2° (*c* 0.2, $CHCl_3$); IR (film) ν_{max} 3460, 2930, 2340, 1735, 1637, 1240 cm^{-1}; UV (MeOH) λ_{max} (log ϵ) 218 (4.31), 223 (sh), 278 (4.26) nm; ^1H NMR ($CDCl_3$) δ 7.78 (1H, d, J = 16.0 Hz, H-23), 7.49 (2H, m, H-25 and H-29), 7.41 (2H, m, H-26 and H-28), 7.41 (1H, m, H-27), 6.65 (1H, d, J = 16.0 Hz, H-22), 6.05 (1H, d, J = 10.5 Hz, H-10), 5.88 (1H, d, J = 10.5 Hz, H-9), 5.84 (1H, dd, J = 12.5, 12.5 Hz, H-13), 5.56 (1H, s, H-20a), 5.50 (1H, s, H-20b), 5.45 (1H, s, H-5), 4.22 (1H, d, J = 6.4 Hz, H-2), 3.21 (1H, d, J = 6.4 Hz, H-3), 2.65 (1H, m, H-14a), 2.28 (3H, s, H_3-18), 2.09 (1H, d, J = 11.0 Hz, H-1), 2.06 (3H, s, 10-AcO), 2.01 (3H, s, 9-AcO), 1.91 (1H, dd, J = 13.2, 1.0 Hz, H-6a), 1.81 (1H, dd, J = 9.9, 1.0 Hz, H-6b), 1.68−1.80 (2H, m, H-7a and H-7b), 1.77 (3H, s, 13-AcO), 1.70 (3H, s, H_3-16), 1.63 (1H, br, 2-OH), 1.31 (1H, dd, J = 15.0, 8.1 Hz, H-14b), 1.14 (3H, s, H_3-17), 0.96 (3H, s, H_3-19); ^{13}C NMR ($CDCl_3$) δ 170.69 (s, 13-CH_3CO), 170.26 (s, 9-CH_3CO), 169.81 (s, 10-CH_3CO), 166.33 (s, C-21), 145.53 (d, C-23), 143.59 (s, C-4), 136.62 (s, C-12), 134.32 (s, C-24), 133.61 (s, C-11), 130.56 (d, C-27), 129.04 (d, C-25 and C-29), 128.05 (d, C-26 and C-28), 119.42 (d, C-20), 118.74 (d, C-22), 78.56 (d, C-5), 77.10 (d, C-9), 72.40 (s, C-10), 70.53 (d, C-13), 70.35 (d, C-2), 51.26 (s, C-1), 45.67 (d, C-3), 44.45 (s, C-8), 37.35 (s, C-15), 31.73 (q, C-17), 29.19 (t, C-14), 28.35 (t, C-6), 27.57 (q, C-16), 26.91 (t, C-7), 21.00 (q, 9-CH_3CO), 21.00 (q, 13-CH_3CO), 20.80 (q, 10-CH_3CO), 17.93 (q, C-19), 15.31 (q, C-18); EIMS *m/z* 608 (M^+), 548 $(M - HOAc)^+$; HREIMS *m/z* 548.2770 $(M - AcOH)^+$, calcd for $C_{33}H_{40}O_7$ 548.2774; $^1H-^1H$ COSY correlations ($CDCl_3$, H/H) 2/1, 2/2-OH, 2/3, 5/6a, 5/6b, 6a/6b, 7a/7b, 9/10, 13/14a, 13/14b, 14a/14b, 14a/1, 22/23, 25/26, 26/27; NOESY correlations ($CDCl_3$, H/H) 2/1, 2/16, 2/19, 3/7b, 3/14b, 3/18, 5/6a, 5/6b, 9/2, 9/16, 9/19, 10/7b, 10/18, 13/14a, 13/17, 14a/1, 14b/17, 19/16, 20/2-OH, 22/7, 22/18, 25/22, 23/25, 25/26, 26/27; HMBC correlations ($CDCl_3$, H/C), 1/3, 1/11, 1/13, 1/15, 3/1, 3/2, 3/4, 3/5, 3/8, 3/19, 3/20, 5/3, 5/7, 5/20, 5/21, 6a/4, 6a/5, 6a/8, 6b/7, 9/7, 9/8, 9/10, 9/11, 9/12, 9/9-CH_3CO, 10/9, 10/11, 10/12, 10/15, 10/10-CH_3CO, 13/13-CH_3CO, 14a/2, 14a/12, 14a/13, 16/1, 16/11, 16/15, 16/17, 17/1, 17/15, 17/16, 19/3, 19/7, 19/8, 19/9, 20/3, 20/5, 22/21, 22/24, 23/21, 23/22, 23/25, 25/26, 25/27, 26/24, 27/25.

Taxezopidine H (7): colorless amorphous solid; $[\alpha]^{26}_D$ +5.6° (*c* 0.12, $CHCl_3$); IR (film) ν_{max} 3450, 2980, 1720, 1640, 1240 cm^{-1}; UV (MeOH) λ_{max} (log ϵ) 206 (4.02), 218 (4.05), 279 (3.98) nm; ^1H NMR ($CDCl_3$) δ 7.72 (1H, d, J = 15.9 Hz, H-23), 7.54 (2H, m, H-25 and H-29), 7.39 (2H, m, H-26 and H-28), 7.39 (1H, m, H-27), 6.69 (1H, d, J = 15.9 Hz, H-22), 6.26 (1H, d, J = 11.0 Hz, H-10), 5.86 (1H, d, J = 11.0 Hz, H-9), 5.64 (1H, dd, J = 11.6, and 5.1 Hz, H-7), 5.52 (1H, dd, J = 2.5, 3.3 Hz, H-5), 5.35 (1H, s, H-20a), 5.01 (1H, s, H-20b), 4.54 (1H, brs, H-13), 3.05 (1H, d, J = 5.4 Hz, H-3), 2.82 (1H, m, H-14a), 2.40 (3H, s, H_3-18), 2.05 (1H, m, H-6a), 2.06 (3H, s, 7-OAc), 2.03 (3H, s, 9-AcO), 1.99 (3H, s, 10-AcO), 1.90 (1H, dd, J = 11.4, 5.8 Hz, H-2a), 1.84 (1H, dd, J = 11.6, 4.6 Hz, H-6b), 1.80 (1H, m, H-2b), 1.79 (1H, m, H-1), 1.56 (3H, s, H_3-17), 1.10 (1H, dd, J = 13.1, 5.5 Hz, H-14b), 0.95 (3H, s, H_3-16), 0.85 (3H, s, H_3-19); ^{13}C NMR ($CDCl_3$) δ 170.26 (s, 9-CH_3CO), 169.73 (s, 7-CH_3CO), 169.33 (s, 10-CH_3CO), 166.23 (s, C-21), 146.59 (d, C-23), 145.88 (s, C-4), 141.63 (s, C-12), 134.47(s, C-24), 134.24 (d, C-11), 130.36 (d, C-27), 128.92 (d, C-25 and C-29), 128.21 (d, C-26 and C-28), 117.78 (d, C-22), 115.74 (t, C-20), 76.88 (d, C-9), 75.18 (d, C-5), 72.41 (d, C-10), 70.04 (d, C-7), 68.16 (d, C-13), 46.41(s, C-8), 40.03 (d, C-1), 38.96 (s, C-15), 37.92(d, C-3), 36.34 (t, C-14), 34.13 (t, C-6), 31.80 (q, C-17), 27.22 (t, C-2), 26.56 (q, C-16), 21.39 (q, 7-CH_3CO), 21.05 (q, 10-CH_3CO), 20.84 (q, 9-CH_3CO), 16.12(q, C-18), 12.99 (q, C-19); EIMS *m/z* 608 (M^+), 548; HREIMS *m/z* 548.2772 $(M - AcOH)^+$, calcd for $C_{33}H_{40}O_7$ 548.2774; $^1H-^1H$ COSY correlations ($CDCl_3$, H/H) 2/1, 2/3, 5/6a, 5/6b, 6a/6b, 7a/7b, 9/10,13/14a, 13/14b, 13/13-OH, 14a/14b, 14a/1, 22/23, 25/26, 26/27; NOESY correlations ($CDCl_3$, H/H): 2/1, 2/16, 2/19, 3/7b, 3/14b, 3/18, 5/6a, 5/6b, 6a/6b, 9/2, 9/16, 9/19, 10/7b, 10/18, 13/14a, 13/17, 14a/1, 14a/14b, 14b/17, 19/16, 20/2-OH, 22/7, 22/18, 25/22, 23/25, 25/26, 26/27; HMBC correlations ($CDCl_3$, H/C) 1/11, 1/13, 3/4, 3/8, 3/19, 3/20, 5/3, 5/7, 5/20, 5/21, 6b/4, 7/19, 7/7-CH_3CO, 9/7, 9/8, 9/10, 9/19, 9/9-CH_3CO, 10/9, 10/11, 10/12, 10/15, 10/10-CH_3CO,14a/2, 14a/12,14a/13, 14b/13, 16/1, 16/11, 16/15, 16/17, 17/1, 17/11, 17/16, 19/3, 19/7, 19/8, 19/9, 20/3, 20/5, 22/21, 22/24, 23/21, 23/22, 23/25, 25/26, 25/27, 26/24, 27/25.

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