Pergamon

Tetrahedron, Vol. 52, No. 37, pp. 12159-12164, 1996
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0040-4020/96 $15.00 + 0.00

PII: S0040-4020(96)00706-5

Taxuspines Q, R, S, and T, New Taxoids from Japanese Yew *Taxus cuspidata*

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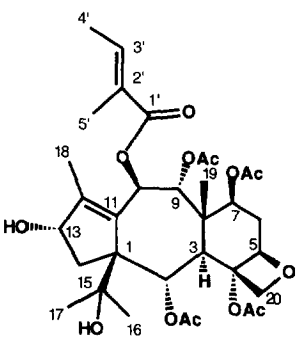
Abstract: Four new taxoids, taxuspines Q ~ T (**1** ~ **4**), have been isolated from stems of the Japanese yew *Taxus cuspidata* Sieb. et Zucc. and the structures elucidated on the basis of spectroscopic data. Taxuspine Q (**1**) is the first example of taxoid containing 5/7/6-membered ring system with a tiglic acid moiety. Copyright © 1996 Elsevier Science Ltd

Numerous taxoids have been isolated from various yew trees, but only a few basic structural types exist, and variation is mostly found in acylation pattern.[1] In our continuing search for bioactive taxoids, we isolated previously new taxoids containing rearranged taxane diterpenoids, taxuspines A ~ H and J ~ P[2~6] from stems and leaves of the Japanese yew *Taxus cuspidata* Sieb. et Zucc. Further invenstigation on extracts of stems of this yew led to isolation of four new taxoids, named taxuspines Q ~ T (**1** ~ **4**). In this paper we describe the isolation and structure elucidation of **1** ~ **4**.



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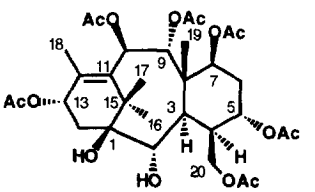

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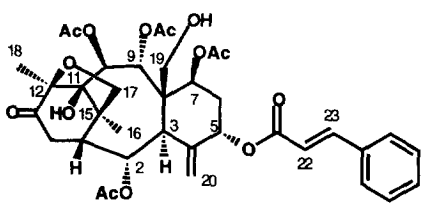

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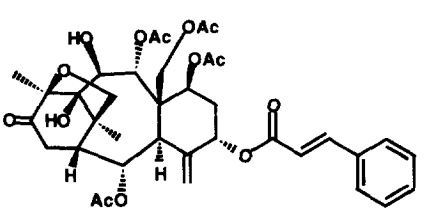

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Table 1. ^{1}H and ^{13}C NMR Data of Taxuspine Q (**1**) in $CDCl_3$

position	$^{1}H^{a}$		*J*(Hz)	$^{13}C^{a}$		H coupled with C^{b}
1				67.50	s	H-2, H-16, H-17
2	6.05	d	8.1	68.10	d	H-3
3	3.12	d	8.1	44.51	d	H-5, H-7, H-19
4				80.90	s	H-3, H-5, H-20a, H-20b
5	4.91	d	7.2	85.10	d	H-20a, H-20b, H-7
6 (a)	1.86	m		34.99	t	
(b)	2.51	m				
7	5.47	t	8.0	70.01	d	H-5, H-9
8				46.50	s	H-2, H-9, H-19
9	6.01	d	10.3	77.51	d	H-10, H-19
10	6.35	d	10.3	68.50	d	H-9
11				135.11	s	H-9, H-14a, H-14b, H-18
12				151.05	s	H-13, H-14a, H-14b, H-18
13	4.45	m		78.00	d	H-18
14 (a)	1.60	d	11.8	39.51	t	
(b)	2.25	m				
15				76.01	s	H-16, H-17
15-OH	2.76	s				
16	1.12	s		25.01	q	H-17
17	1.05	s		27.52	q	H-16
18	2.01	s		12.20	q	
19	1.75	s		13.11	q	
20 (a)	4.39	d	7.6	75.10	t	
(b)	4.52	d	7.6			
1'				165.57	s	H-5', H-3'
2'				126.12	s	H-5', H-4'
3'	6.71	q	7.0	138.91	d	H-5', H-4'
4'	1.76	d	7.0	12.24	q	H-3'
5'	1.73	s		14.55	q	H-3'
2-AcO	2.10	s		21.40	q	
				172.50	s	H-2
4-OAc	2.18	s		22.41	q	
				169.95	s	
7-AcO	1.91	s		20.73	q	
				171.01	s	H-7
9-AcO	2.01	s		20.73	q	
				171.02	s	H-9

a) in ppm b) in HMBC spectrum

The methanolic extract of stems of the yew collected at Sapporo was partitioned between toluene and water. The toluene soluble portions were subjected to a silica gel column followed by reversed-phase column chromatographies to afford taxuspines Q (**1**, 0.00029%), R (**2**, 0.00026%), S (**3**, 0.00021%), and T (**4**, 0.00019 %).

Taxuspine Q (**1**) showed the pseudomolecular ion peak at *m/z* 651 $(M+H)^{+}$ in the FDMS spectrum. HRFDMS analysis revealed the molecular formula to be $C_{33}H_{46}O_{13}$ [*m/z* 651.3000 $(M+H)^{+}$, Δ -1.6 mmu]. IR absorptions at 3450 and 1720 cm^{-1} implied that **1** possessed hydroxy and ester groups. Analyses of the ^{1}H and ^{13}C NMR data (Table 1) and HMQC spectrum of **1** provided four acetyls, one tetrasubstituted olefin, one trisubstituted olefin, six oxymethines, one methine, three methylenes, two oxygenated quaternary carbons, and six methyl groups. Detailed analysis of the ^{1}H-^{1}H COSY spectrum revealed connectivities of C-2 to C-3, C-5 to C-7, C-9 to C-10, C-13 to C-14, and C-3' to C-4'. In the HMBC spectrum, long-range ^{1}H-^{13}C correlations of H-13 and H_2-14 to C-11 and C-12 indicated the

presence of a cyclopentene moiety (ring A). HMBC correlations of H_3-18 to C-11, C-12, and C-13 revealed that Me-18 was attached at C-12. Two methyl proton (δ_H 1.05 and 1.12), a deuterium-exchangeable proton (δ_H 2.76), and an oxygenated quaternary carbon (δ_C 76.01, C-15) signals indicated the presence of a hydroxyisopropyl group, which was attached at C-1 from HMBC correlations of H_3-16 and H_3-17 to C-1. HMBC cross-peaks of H-2 to C-1 and C-8, H-9 to C-8, C-10, and C-11 revealed the presence of a seven-membered ring (ring B), while the correlations of H-3 and H-5 to C-4 and H-7 to C-3 implied the presence of a cyclohexane moiety (ring C). These results suggest that **1** consisted of 5/7/6-membred ring system.[7] Three out of four acetoxy groups were attached at C-2, C-7, and C-9, based on HMBC correlations, while a hydroxyl group was connected to C-13 (δ_H 4.45). The remaining acetoxy group (δ_C 169.95) was connected to C-4, judging from the ^{13}C NMR chemical shift of C-4 (δ_C 80.90) and the NOESY correlation of H-20a to the acetyl methyl protons (δ_H 2.18). The signals at δ_H 4.39 and 4.52 (each 1H, d, J = 7.6 Hz) and δ_C 75.10 and HMBC correlations of H-20a and H-20b to C-4 and C-5 indicated the presence of an oxetane ring fused to ring C. HMBC correlations of H_3-5' to C-1' and C-2', H-3' to C-1', and H_3-4' to C-2' and a NOESY correlation of H_3-5' to H-4' revealed the presence of a tiglic acid moiety. The tiglic acid was attached at C-10, judging from NOESY correlations of H-3' to H_3-16 and 15-OH. Thus the structure of taxuspine Q was assigned to be **1**. Relative stereochemistry of **1** was elucidated by the NOESY spectrum (Fig. 1).

Taxuspine R (**2**) showed the pseudomolecular ion peak at *m/z* 655 $(M+H)^+$ in the FABMS spectrum, and the molecular formula, $C_{32}H_{47}O_{14}$, was determined by HRFABMS [*m/z* 655.2596 $(M+H)^+$, Δ +3.0 mmu]. The ^1H and ^{13}C NMR and 2D NMR spectra of **2** showed the presence of 6/8/6-membered ring system without any oxygen functionality or exomethylene at C-4.[5,8] Detailed analysis of the ^1H-^1H COSY spectrum of **2** implied connectivities of C-2 to C-7, C-9 to C-10, C-13 to C-14, and C-4 to C-20. From HMBC correlations, Me-18 was attached at C-12 and six acetoxy groups were attached at C-5, C-7, C-9, C-10, C-13, and C-20. The chemical shifts of C-1 (δ_C 79.56) and H-2 (δ_H 3.97, d, J = 7.8 Hz) indicated that two hydroxyl groups were connected to C-1 and C-2. Thus the structure of taxuspine R was assigned to be **2**. Relative stereochemistry of **2** was elucidated by the NOESY spectrum and comparison with spectral data of known related compounds.[5,8]

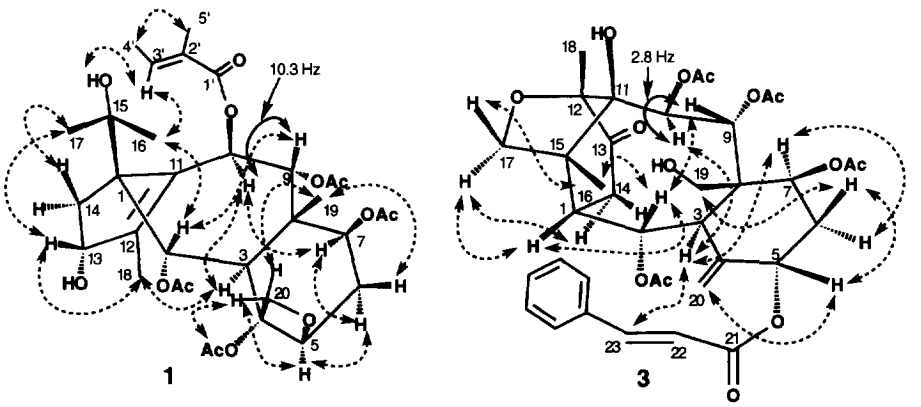

Figure 1. Relative Stereochemistries of Taxuspines Q (1) and S (3). Dotted arrows denote NOESY correlations.

The molecular formula, $C_{37}H_{44}O_{14}$, of taxuspine S (**3**) was elucidated by HRFABMS [*m/z* 713.2846 $(M+H)^+$, Δ +3.7 mmu]. The ^1H and ^{13}C NMR spectra of **3** resembled those of taxacin.[9] HMBC correlations of H-17a to C-11, C-12, and C-15 and proton signals (δ_H 3.67 and 4.16, d, J = 8.1 Hz; H-17a and H-17b) revealed the presence of a tetrahydrofuran ring fused to ring A. The olefin proton signals of a cinnamoyl group at C-5 appeared at δ_H 6.72 (1H, d, J = 16.1 Hz) and 7.91 (1H, d, J = 16.1 Hz; trans-oriented) and the cinnamoyl carbonyl carbon (δ_C 165.96) showed an HMBC correlation for H-5. Four acetoxy groups were attached at C-2, C-7, C-9, and C-10 based on the HMBC correlations and oxymethine proton resonances (δ_H 6.30, H-2; δ_H 5.47, H-7; δ_H 5.74, H-9; δ_H 5.48, H-10). The presence of a ketone (δ_C 204.5) at C-13 was elucidated by HMBC correlations of H_3-18, H-14a, and H-14b to C-13. HMBC correlations of H-20a to C-3 and H-20b to C-5 indicated the presence of an exomethylene at C-4. A hydroxyl group was attached at C-19 by the methylene resonances at δ_H 3.78 (dd, J = 11.5 and 3.2 Hz, H-19a) and δ_H 4.13 (dd, J = 11.5 and 3.2 Hz, H-19b), and δ_C 64.01 (C-19). Thus the structure of taxuspine S was assigned to be **3**. The relative stereochemistry was elucidated by the NOESY spectrum (Fig. 1).

The molecular formula, $C_{37}H_{44}O_{14}$, of taxuspine T (**4**), which was the same as that of **3**, was elucidated by HRFABMS [*m/z* 713.2777 $(M+H)^+$, Δ -3.2 mmu]. Detailed analyses of ^1H and ^{13}C NMR and 2D NMR spectra of **4** revealed that the structure of **4** was quite similar to that of **3**, except for functional groups at C-10 and C-19. Four acetoxy groups were attached at C-2, C-7, C-9, and C-19 based on the HMBC correlations, while a hydroxyl group was connected to C-10 from HMBC correlations of the hydroxy proton (δ_H 4.45) to C-10. Thus the structure of taxuspine T was assigned to be **4**. The relative stereochemistry was elucidated by the NOESY spectrum.

Taxuspines Q ~ T (**1** ~ **4**) are new taxoids from stems of the Japanese yew *Taxus cuspidata* Sieb. et Zucc. Taxuspine Q (**1**) is the first example of taxoid containing 5/7/6-membered ring system with a tiglic acid moiety. Pharmacological activities of **1** ~ **4** are currently investigated.

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 spectrometers, respectively. ^1H and ^{13}C NMR spectra were recorded on Bruker ARX-500 and AMX-600 spectrometers. The 7.26 and 7.20 ppm resonance of residual $CHCl_3$ and C_6H_6 and 77.0 and 123.5 ppm of $CDCl_3$ and C_6D_6 were used as internal references, respectively. FDMS was obtained on a JEOL JMS-SX102A spectrometer. FABMS was measured on a JEOL HX-110 spectrometer by using glycerol matrix.

Collection, Extraction, and Separation. The Japanese yew *Taxus cuspidata* Sieb. et Zucc. was collected at Sapporo, Hokkaido. The stems (1.2 kg) of the yew was extracted with MeOH (15 L x 4). The MeOH extract was partitioned between toluene (1 L x 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 (15.9g) was subjected to a silica gel column (4.2 x 35 cm) eluted with hexane/acetone (8:1) to give a fraction (3.22 g), part of which (1.11 g) was subjected to a silica gel column (2.5 x 35 cm) eluted with $CHCl_3$/acetone [20:1 (1000 mL) → 10:1 (300 mL) → 5:1 (360 mL)] to afford two fractions **I** (38.6 mg) and **II** (122.2 mg). Fraction **I** was applied to a reversed-phase column (YMC-GEL ODS 60, 350/250 mesh, 1.5 x 18 cm; CH_3CN/H_2O, 1:1) to give fraction **a** (17.7 mg), which was subjected to C_{18} HPLC column (YMC-Pack ODS AL-323, 5 μm, 10 x 250 mm; flow rate 2.5 mL/min; UV detection at 227 nm; eluent CH_3CN/H_2O, 1:1) to give taxuspine R (**2**, 0.8 mg, t_R 11.2 min). Fraction **II** was separated by a reversed-phase column (YMC GEL ODS 60, 350/250 mesh, 2.5 x 15 cm; CH_3CN/H_2O, 1:1) to give a fraction (55.0 mg), which was purified under the same separation condition as fraction **a** to give taxuspine Q (**1**, 1.2mg, t_R 18.4 min) and a fraction (3.2 mg, t_R 28.1 min), the latter of which was subjected to a silica gel column (0.6 x 5.0 cm)

with CH_2Cl_2/CH_3CN (5:1) to give taxuspine S (**3**, 1.0 mg). On the other hand, the stems (11 kg) of the yew was subjected to the same extraction and partition steps as described above to give toluene extract (115 g), which was subjected to a silica gel column to give a fraction (3.83g). The fraction was separated by a reversed-phase column (YMC GEL ODS 60, 350/250 mesh, 2.5 x 15 cm; CH_3CN/H_2O, 4:1) followed by a Sephadex LH-20 column (3.5 x 100 cm, $CHCl_3$/MeOH, 1:1), a silica gel column (1.5 x 37 cm, $CHCl_3$/acetone, 4:1), a reversed-phase HPLC (YMC-Pack ODS AL-323, 5 μm, 10 x 250 mm; CH_3CN/H_2O, 1:1), and a silical gel column (0.6 x 4 cm, $CHCl_3$/acetone 1:1) to give taxuspine T (**4**, 1.2 mg).

Taxuspine Q (1): A colorless amorphous solid; $[\alpha]^{21}_D$ -8.2° (*c* 0.12, $CHCl_3$); UV (MeOH) λ_{max} 275.0 (ε 2900) and 208.0 (12000) nm; IR (film) ν_{max} 3450, 1720, 1360, and 1240 cm^{-1}; ^1H and ^{13}C NMR (see Table 1); FDMS *m/z* 651 $(M+H)^+$; HRFDMS *m/z* 651.3000 $(M+H)^+$, calcd for $C_{33}H_{47}O_{13}$, 651.3016; HMBC correlations (see Table 1); NOESY correlations ($CDCl_3$ H/H): 2/9, 2/16, 2/19, 3/7, 3/10, 3/14a, 3/18, 5/6a, 5/6b, 5/20a, 6a/19, 6b/7, 7/10, 9/19, 10/18, 13/14b, 13/17, 13/18, 14b/16, 14b/17, 14b/15-OH, 19/20b, 20a/4-CH_3CO, 16/3', 3'/4', 3'/15-OH, and 4'/5'.

Taxuspine R (2): A colorless amorphous solid; $[\alpha]^{21}_D$ +68° (*c* 0.15, $CHCl_3$); IR (film) ν_{max} 3450, 1730, 1360, and 1230 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.17 (1H, d, *J* = 11.2 Hz, H-10), 6.11 (1H, t, *J* = 6.2 Hz, H-13), 5.79 (1H, d, *J* = 11.2 Hz, H-9), 3.97 (1H, d, *J* = 7.8 Hz, H-2), 5.38 (1H, dd, *J* = 10.0 and 3.8 Hz, H-7), 4.99 (1H, d, *J* = 2.3 Hz, H-5), 4.54 (1H, d, *J* = 10.2 Hz, H-20b), 3.97 (1H, t, *J* = 10.2 Hz, H-20a), 2.76 (1H, t, *J* = 7.8 Hz, H-3), 2.33 (1H, m, H-4), 2.30 (1H, m, H-14a), 2.22 (3H, s, 13-CH_3CO), 2.21 (3H, s, H_3-18), 2.12 (3H, s, 9-CH_3CO), 2.07 (3H, s, 20-CH_3CO), 2.06 (3H, s, 7-CH_3CO), 2.05 (3H, s, 5-CH_3CO), 2.01 (3H, s, 10-CH_3CO), 2.01 (1H, m, H-14b), 1.92 (1H, m, H-6b), 1.81 (1H, m, H-6a), 1.65 (3H, s, H_3-16), 1.28 (3H, s, H_3-17), and 0.99 (3H, s, H_3-19); ^{13}C NMR ($CDCl_3$) δ 170.20 (s, 20-$CH_3\underline{C}O$), 170.28 (s, 9-$CH_3\underline{C}O$), 170.24 (s, 7-$CH_3\underline{C}O$), 170.24 (s, 13-$CH_3\underline{C}O$), 169.89 (s, 5-$CH_3\underline{C}O$), 169.85 (s, 10-$CH_3\underline{C}O$), 134.70 (s, C-12), 128.50 (s, C-11), 78.70 (s, C-1), 75.15 (d, C-9), 71.75 (d, C-2), 71.75 (d, C-10), 71.74 (d, C-13), 70.95 (d, C-5), 69.56 (d, C-7), 66.65 (t, C-20), 46.10 (s, C-8), 42.50 (d, C-3), 42.01(d, C-4), 35.85 (s, C-15), 29.95 (t, C-6), 28.43 (q, C-17), 22.50 (q, C-16), 22.10 (q, 13-$\underline{C}H_3CO$), 21.05 (q, 7-$\underline{C}H_3CO$), 22.01 (t, C-14), 21.05 (q, 5-$\underline{C}H_3CO$), 20.04 (q, 10-$\underline{C}H_3CO$), 21.03 (q, 20-$\underline{C}H_3CO$), 20.76 (q, 9-$\underline{C}H_3CO$), 15.02 (q, C-18), and 14.13 (q, C-19); FABMS *m/z* 655 $(M+H)^+$, 595 $(M+H\text{-}AcOH)^+$, 577 $(M+H\text{-}AcOH\text{-}H_2O)^+$, and 517 $(M+H\text{-}2AcOH\text{-}H_2O)$; HRFABMS *m/z* 655.2996 $(M+H)^+$, calcd for $C_{32}H_{47}O_{14}$, 655.2966; HMBC correlations ($CDCl_3$, C/H): 1/14a, 1/14b, 1/16, 1/2, 3/2-OH, 3/19, 4/3, 4/20a, 4/20b, 5/20a, 5/20b, 7/5, 8/2, 8/9, 8/19, 9/10, 9/19, 10/9, 11/16, 11/17, 11/18, 12/13, 12/14a, 12/14b, 12/18, 13/18, 15/10, 15/16, 15/17, 16/17, 17/16, 20/3, 5-$CH_3\underline{C}O$/5, 7-$CH_3\underline{C}O$/7, 9-$CH_3\underline{C}O$/9, 10-$CH_3\underline{C}O$/10, 13-$CH_3\underline{C}O$/13, 20-$CH_3\underline{C}O$/20a, and 20-$CH_3\underline{C}O$/20b; NOESY correlations ($CDCl_3$, H/H): 2/2-OH, 2/9, 2/16, 2/19, 3/4, 3/7, 3/10, 3/14a, 3/18, 3/20a, 4/5, 4/20a, 4/20b, 5/6a, 5/6b, 5/20a, 6a/19, 6a/20a, 6b/7, 7/10, 7/18, 9/16, 9/19, 10/18, 13/14b, and 13/17.

Taxuspine S (3): A colorless amorphous solid; $[\alpha]^{25}_D$ -4.4° (*c* 0.13, $CHCl_3$); UV (MeOH) λ_{max} 280 (ε13200), 218 (11200), and 206 (12300) nm; IR (film) ν_{max} 3400, 1710, 1620, 1360, 1240, and 1050 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.91 (1H, d, *J* = 16.1 Hz, H-23), 7.80 (2H, m, H-25 and H-29), 7.40 (2H, m, H-26 and H-28), 7.40 (1H, m, H-27), 6.72 (1H, d, *J* = 16.0 Hz, H-22), 6.30 (1H, dd, *J* = 9.0 and 2.5 Hz, H-2), 5.74 (1H, d, *J* = 2.8 Hz, H-9), 5.50 (1H, m, H-5), 5.48 (1H, d, *J* = 2.8 Hz, H-10), 5.47 (1H, dd, *J* = 10.6 and 5.4 Hz, H-7), 5.01 (1H, s, H-20a), 4.80 (1H, s, H-20b), 4.16 (1H, d, *J* = 8.1 Hz, H-17b), 4.13 (1H, dd, *J* = 11.5 and 3.2 Hz, H-19a), 3.87 (1H, brs, 11-OH), 3.78 (1H, dd, *J* = 11.5 and 3.2 Hz, H-19b), 3.67 (1H, d, *J* = 8.1 Hz, H-17a), 3.40 (1H, d, *J* = 9.0 Hz, H-3), 2.91 (1H, dd, *J* = 18.0 and 11.7 Hz, H-14b), 2.57 (1H, d, *J* = 18.0 Hz, H-14a), 2.46 (1H, dd, *J* = 11.7 and 2.5 Hz, H-1), 2.23 (1H, m, H-6b), 2.14 (3H, s, 10-CH_3CO), 2.12 (3H, s, 9-CH_3CO), 2.01 (1H, brs, 19-OH), 1.94 (6H, s, 2-CH_3CO and 7-CH_3CO), 1.70 (1H, m, H-6a), 1.54 (3H, s, H_3-16), and 1.21 (3H, s, H_3-18); ^{13}C NMR ($CDCl_3$) δ 204.5 (s, C-13), 172.61 (s, 9-$CH_3\underline{C}O$), 172.51 (s, 2-$CH_3\underline{C}O$), 170.48 (s, 10-$CH_3\underline{C}O$), 169.74 (s, 7-$CH_3\underline{C}O$), 165.96 (s, C-21), 146.06 (d, C-23), 141.94 (s, C-4), 135.01 (s, C-24), 130.20 (d, C-27), 128.77 (d, C-26 and C-28), 128.73 (d, C-25 and C-29), 117.82 (d, C-22), 115.06 (t, C-20), 91.28 (s, C-12), 82.17 (t, C-17), 80.67 (s, C-11), 74.09 (d, C-5), 70.28 (d, C-2), 70.28 (d, C-10), 68.61 (d, C-7), 64.01 (d, C-9), 59.40 (t, C-19), 50.03 (s, C-8), 49.57 (d, C-1), 48.15 (s, C-15), 40.05 (d, C-3), 36.82 (t, C-6), 21.30 (q, 2-$\underline{C}H_3CO$), 34.02 (t, C-14), 21.30 (q, 10-$\underline{C}H_3CO$), 20.85 (q, 7-$\underline{C}H_3CO$), 20.85 (q, 9-$\underline{C}H_3CO$), 14.96 (q, C-16), and 12.40 (q, C-18); FABMS *m/z* 713 $(M+H)^+$; HRFABMS *m/z* 713.2846 $(M+H)^+$, calcd for $C_{37}H_{45}O_{14}$, 713.2809; HMBC correlations (C/H, C_6D_6); 1/2, 1/14b, 1/17, 2/3, 2/14b, 3/20a, 3/2, 5/20b, 5/7, 7/9, 8/3, 9/10, 11/9, 11/18, 11/16, 11/17a, 12/17a, 12/18, 13/18, 13/14a, 13/14b, 15/16, 15/17a, 16/17a, 16/17b, 9-$CH_3\underline{C}O$/9, 10-$CH_3\underline{C}O$/10, 2-$CH_3\underline{C}O$/2, 21/5, 21/23, and 24/22; NOESY correlations ($CDCl_3$, H/H) 1/2, 1/14b, 1/17a, 2/9, 2/17a, 2/19a, 2/20a, 3/7, 3/10, 3/14a, 5/6b, 5/20b, 6a/7, 6b/9, 6b/19b, 9/16, 14b/17a, 25/26, and 26/27.

Taxuspine T (4): A colorless amorphous solid; $[\alpha]^{25}_{D}$ -13.4° (*c* 0.17, $CHCl_3$); UV (MeOH) λ_{max} 280 (ε 12700), 218 (10200), and 205.5 (10700) nm ; IR (film) ν_{max} 3420, 1720, 1630, 1360, 1240, and 1020 cm^{-1}; ^1H NMR (C_6D_6) δ 8.08 (1H, d, *J* = 16.1 Hz, H-23), 7.80 (2H, m, H-25 and H-29), 7.40 (2H, m, H-26 and H-28), 7.40 (1H, m, H-27), 7.42 (1H, d, *J* = 16.1 Hz, H-22), 6.42 (1H, dd, *J* = 9.4 and 1.1 Hz, H-2), 5.82 (1H, d, *J* = 3.8 Hz, H-9), 5.72 (1H, dd, *J* = 3.3 and 5.9 Hz, H-7), 5.23 (1H, s, H-20b), 5.02 (1H, m, H-5), 4.62 (1H, s, H-20a), 4.55 (1H, d, *J* = 11.8 Hz, H-19a), 4.45 (1H, brs, 10-OH), 4.40 (1H, d, *J* = 7.9 Hz, H-17b), 4.30 (1H, d, *J* = 11.8 Hz, H-19b), 4.19 (1H, m, H-10), 3.87 (1H, brs, 11-OH), 3.41 (1H, d, *J* = 9.4 Hz, H-3), 3.35 (1H, d, *J* = 7.9 Hz, H-17a), 2.95 (1H, dd, *J* = 17.5 and 11.6 Hz, H-14b), 2.51 (1H, d, *J* = 17.5 Hz, H-14a), 2.21 (1H, dd, *J* = 11.6 and 1.1 Hz, H-1), 2.15 (3H, s, 19-CH_3CO), 1.87 (1H, m, H-6b), 1.85 (3H, s, H_3-18), 1.81 (3H, s, H_3-16), 1.61 (3H, s, 2-CH_3CO), 1.58 (3H, s, 9-CH_3CO), 1.51 (1H, m, H-6a), and 1.49 (3H, s, 7-CH_3CO); ^{13}C NMR (C_6D_6) δ 210.02 (s, C-13), 173.20 (s, 7-$CH_3\underline{C}O$), 171.10 (s, 19-$CH_3\underline{C}O$),170.01 (s, 2-$CH_3\underline{C}O$), 170.01 (s, 9-$CH_3\underline{C}O$), 165.05 (s, C-21), 146.79 (d, C-23), 140.04 (s, C-4), 135.02 (s, C-24), 130.92 (d, C-27), 129.53 (d, C-26 and C-28), 129.35 (d, C-25 and C-29), 119.02 (d, C-22), 117.01 (t, C-20), 94.05 (s, C-12), 83.35 (t, C-17), 81.62 (s, C-11), 74.88 (d, C-5), 69.64 (d, C-2), 69.32 (d, C-9), 68.60 (d, C-7), 64.91 (d, C-10), 61.18 (t, C-19), 51.12 (s, C-15), 49.58 (d, C-1), 49.14 (s, C-8), 40.03 (d, C-3), 36.95 (t, C-6), 36.49 (t, C-14), 21.39 (q, 7-$\underline{C}H_3CO$), 21.29 (q, 2-$\underline{C}H_3CO$), 20.97 (q, 9-$\underline{C}H_3CO$), 20.50 (q, 19-$\underline{C}H_3CO$), 15.51 (q, C-16), and 13.93 (q, C-18); FABMS *m/z* 713 $(M+H)^+$; HRFABMS *m/z* 713.2772 $(M+H)^+$, calcd for $C_{37}H_{45}O_{14}$, 713.2804; HMBC correlations (C_6D_6, C/H); 1/3, 1/14b, 1/16, 2/1, 2/3, 3/1, 3/19a, 3/19b, 3/20a, 4/3, 5/20b, 6/7, 7/3, 7/5, 7/6a, 7/9, 8/3, 9/3, 11/1, 11/16, 11/17a, 11/17b, 11/18, 11/10-OH, 12/17a, 12/18, 13/1, 13/14b, 13/18, 15/16, 15/17a, 15/17b, 19/3, 20/3, 21/23, 24/22, 25/23, 25/26, 27/25, 2-$CH_3\underline{C}O$/2, 7-$CH_3\underline{C}O$/7, 9-$CH_3\underline{C}O$/9, 19-$CH_3\underline{C}O$/19a, and 19-$CH_3\underline{C}O$/19b; NOESY correlations (C_6D_6, H/H): 1/2, 1/17a, 2/9, 2/16, 2/19a, 3/7, 3/10, 3/14a, 5/6a, 5/20b, 6a/7, 7/10, 9/16, 10/18, 20b/22, and 23/25.

Acknowledgements: Authors thank N. Yoshida (Hokkaido University) for his help with collection of the yew and K. Watanabe (Hokkaido University) for measurement of FDMS. This work was partly supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports, and Culture of Japan.

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(*Received in Japan* 24 *June* 1996; *accepted* 25 *July* 1996)