Pergamon

Tetrahedron, Vol. 52, No. 41, pp. 13145-13150, 1996

0040-4020/96 $15.00 + 0.00

PII: S0040-4020(96)00777-6

Taxuspines U, V, and W, New Taxane and Related Diterpenoids from the Japanese Yew *Taxus cuspidata*

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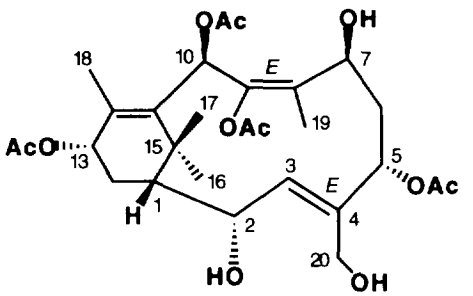
Abstract: Three new taxane and related diterpenoids, taxuspines U, V, and W (**1** ~ **3**), have been isolated from stems of the Japanese yew *Taxus cuspidata* Sieb. et Zucc. and the structures elucidated on the basis of spectroscopic data. Taxuspine U (**1**) is a very rare bicyclic taxane related diterpenoid from yew trees of genus *Taxus*, while taxuspine W (**3**) is a rare taxoid having a 2(3→20)-abeotaxane skeleton.

Many taxane-type diterpenoids have been found in yew trees of various *Taxus* species and some of them exhibit interesting biological activities.[1,2] In our continuing search for bioactive natural products, we previously isolated some new taxoids, taxuspines A ~ H and J ~ T, from the Japanese yew *Taxus cuspidata* Sieb. et Zucc.[3~8] Further investigation on extracts of stems of this yew led to isolation of three new taxane and related diterpenoids, taxuspines U, V, and W (**1** ~ **3**). In this paper we describe the isolation and structure elucidation of **1** ~ **3**.

The methanolic extract of stems of *T. cuspidata* collected at Sapporo was partitioned between toluene



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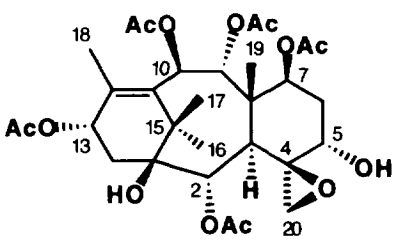

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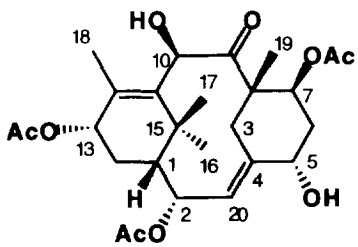

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Table 1. ^{1}H and ^{13}C NMR Data of Taxuspine U (**1**) in $CDCl_3$

position	$^{1}H^{a}$		*J*(Hz)	$^{13}C^{a}$		H coupled with C^{b}
1	1.78	dd	7.8, 4.2	48.0	d	H-16, H-17
2	4.68	dd	10.2, 4.2	66.7	d	H-14a
3	5.59	d	10.2	127.5	d	H-1
4				135.4	s	H-6b
5	5.54	brs		71.0	d	H-3, H-20a, H-20b
6(a)	2.43	ddd	15.7, 8.4, 3.0	36.3	t	
6(b)	2.06	m				
7	4.40	d	7.7	63.7	d	H-19
8				128.8	s	H-6a, H-19
9				139.9	s	H-7, H-10, H-19
10	6.83	s		68.3	d	
11				136.5	s	H-10, H-13, H-16, H-17, H-18
12				136.0	s	H-10, H-13, H-14a, H-18
13	5.42	d	10.1	69.8	d	H-1
14(a)	2.56	ddd	16.4, 10.1, 8.4	25.1	t	H-2
14(b)	2.11	m				
15				36.2	s	H-16, H-17
16	1.10	s		32.5	q	H-17
17	1.23	s		29.7	q	H-16
18	2.02	s		15.9	q	H-10
19	1.52	s		11.3	q	H-7
20(a)	4.31	d	12.3	58.8	t	H-3
20(b)	3.78	d	12.3			
5-AcO	2.21	s		20.8	q	
				169.8	s	H-5
9-AcO	2.21	s		21.5	q	
				169.8	s	
10-AcO	1.98	s		20.4	q	
				169.4	s	H-10
13-AcO	2.12	s		21.5	q	
				170.2	s	H-13

a) δ in ppm b) HMBC correlations

and water, and the water layer was extracted with chloroform. The toluene and chloroform soluble portions were subjected to a silica gel column followed by reversed-phase and silica gel column chromatographies, and centrifuged partition chromatography (CPC) to afford taxuspines U (**1**, 0.000017%), V (**2**, 0.00092 %), and W (**3**, 0.00027 %).

Taxuspine U (**1**) was shown to have the molecular formula, $C_{28}H_{40}O_{11}$, by HREIMS [*m/z* 492.2357 $(M\text{-}AcOH)^{+}$, Δ -0.2 mmu] and ^{13}C NMR data (Table 1). IR absorptions at 3400 and 1730 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, five oxymethines, one oxymethylene, one trisubstituted olefin, two tetrasubstituted olefins, and four methyl groups. Since seven out of nine unsaturations were thus accounted for, **1** was inferred to contain two rings. Detailed analysis of the ^{1}H-^{1}H COSY spectrum revealed connectivities of C-1 to C-3, C-5 to C-7, and C-13 to C-1. In the HMBC spectrum cross-peaks of H-13 to C-11 and C-12, H_3-16 and H_3-17 to C-1, C-11, and C-15, and H_3-18 to C-11 and C-12 indicated the presence of a cyclohexene moiety (ring A), Me-18 at C-12, and Me-16 and Me-17 at C-15. HMBC cross-peaks of H-3 to C-5, H-6b to C-4, H-7 to C-9 and C-19, H-10 to C-9 and C-11, and H_3-19 to C-8

Table 2. Molecular Mechanics Calculations for Diastereomers **1a-d**

diastereomer	H-7/H-10 (Å)	distance[a] H-7/H_3-18 (Å)	H-5/H-20b (Å)
1a (5*S** 7*S**)	2.42	2.98	2.23
1b (5*S** 7*R**)	3.61	3.70	2.43
1c (5*R** 7*S**)	2.45	2.66	3.61
1d (5*R** 7*R**)	3.70	3.97	3.42

a) Distances for the lowest energy conformers.

suggested the presence of a cyclododecadiene moiety (ring B) and Me-19 at C-8. The presence of a hydroxymethyl (C-20) at C-4 was deduced from the NMR data (δ_H 3.78 and 4.31, H-20; δ_C 58.8, C-20) and the HMBC cross-peaks of H-3 to C-20 and H_2-20 to C-5. The NMR data (δ_H 4.68 and δ_C 66.7, C-2; δ_H 4.40 and δ_C 63.7, C-7) revealed that two hydroxy groups were attached at C-2 and C-7. NOESY cross-peaks of H-7/H-10 and H-2/H-20a implied that both geometries of the double bonds at C-3 and C-8 were *E*-configuration. Three acetyl carbonyl carbons (δ_C 169.4, 169.8, and 170.2) showed HMBC correlations from H-10, H-5, and H-13, respectively, indicating that three acetoxy groups were attached at C-10, C-5, and C-13. The olefin carbon resonance at C-9 (δ_C 139.9) implied that the remaining acetoxy group was attached at C-9.[9,10] Thus the structure of taxuspine U was assigned to be **1**. NOESY correlations of H-1/H-14a, H-1/H_3-17, H-13/H-14a, and H-13/H_3-17 indicated boat conformation of ring A (Fig. 1), while those of H-1/H-2 and H-2/H-16 implied that a hydroxy group at C-2 was α-oriented. The α-orientation of H-10 was deduced from a NOESY correlation of H-10/H_3-18. The relative stereochemistries at C-5 and C-7 were investigated by combination of the NOESY data and molecular mechanics calculations, in which four diastereomers (**1a**, 5*S**7*S**; **1b**, 5*S**7*R**; **1c**, 5*R**7*S**; **1d**, 5*R**7*R**) were considered, and systematic conformational searching[11] for each diastereomer was carried out by using Macromodel program[12]. The calculation of the distances between H-7/H-10, H-7/H_3-18, and H-5/H-20b of conformational isomers within 3 kcal/mol molecular energy for each stereoisomer (**1a** ~ **1d**) was summarized in Table 2. The distances of H-7/H-10, H-7/H_3-18, and H-5/H-20b for **1a** were within 3.0 Å, while those of **1b** ~ **1d** were over 3.0 Å. These results suggested that relative stereochemistry of

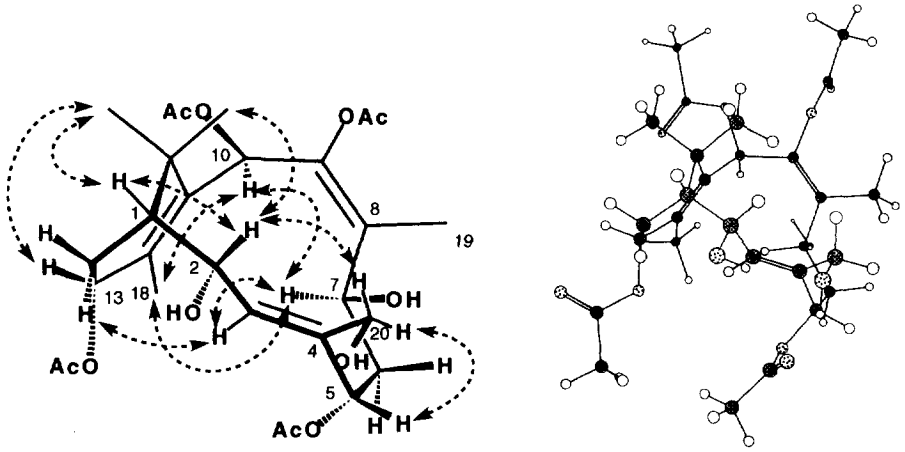

Figure 1. Three-dimensional Structures (left: NOESY correlations; right: MM2 calculation) of Taxuspine U (**1**)

ring B in taxuspine U (**1**) was 2*R**, 5*S**, 7*S**, and 10*R**.

The molecular formula, $C_{30}H_{42}O_{13}$, of taxuspine V (**2**) was established by HRFABMS [*m/z* 716.3522 $(M+DEA+H)^+$, Δ +1.8 mmu]. The presence of five acetyls, six oxymethines, one oxymethylene, one tetrasubstituted olefin, and four methyl groups was indicated by analyses of the ^1H and ^{13}C NMR data and HMQC spectrum of **2**. Connectivities of C-13 to C-14, C-2 to C-3, C-5 to C-7, and C-9 to C-10 were deduced from the ^1H-^1H COSY spectrum. HMBC correlations of H_3-18 to C-11 and C-12 revealed that Me-18 was attached at C-12, while cross-peaks of H_3-16 and H_3-17 to C-1, C-11, and C-15 indicated that Me-16 and Me-17 were connected to C-15. In the HMBC spectrum of **2** H-14a showed long-range ^1H-^{13}C correlations with C-1, C-12, and C-15, indicating the presence of a cyclohexene moiety (ring A). HMBC correlations of H-3 to C-1 and C-8, H-9 to C-8, and H-10 to C-11 revealed the presence of an eight-membered ring (ring B), while the presence of a cyclohexane ring (ring C) was deduced from HMBC correlations of H-5 to C-3 and C-4 and H-6b to C-8. The signals of geminal protons (δ_H 2.25 and 3.63, d, J = 5.4 Hz) and a methylene carbon (δ_C 50.0) indicated that **2** had an epoxide, which was attached at C-4 by NOESY correlations of H-3/H-20a and H-5/H-20b. ^1H-^{13}C long-range couplings of H_3-19 to C-7 and C-8 were indicative of the presence of Me-19 at C-8. According to the HMBC correlations, three acetoxy groups were located at C-2, C-9, and C-10, while the remaining acetoxy groups were attached at C-7 and C-13 from comparison of oxymethine proton signals (δ_H 5.61, H-7; δ_H 5.97, H-13) with those of usual taxoids.[1] Two hydroxy groups were attached at C-1 (δ_C 75.5) and C-5 (δ_C 76.3). Thus the structure of taxuspine V was assigned to be **2**. Relative stereochemistry of **2** was elucidated on the basis of NOESY data. The NOESY correlation of H-14a/H-20a indicated that the epoxide was β-oriented, while the small ^1H-^1H coupling constant (J = 2.9 Hz) between H-5 and H_2-6 suggested pseudo-equatrial orientation of H-5.

Taxuspine W (**3**) was shown to have the molecular formula, $C_{26}H_{36}O_9$, by HRFABMS [*m/z* 491.2257 $(M-H)^-$, Δ +2.4 mmu]. Analyses of the ^1H and ^{13}C NMR data and HMQC spectrum of **3** provided three acetyls, one tetrasubstituted olefin, one trisubstituted olefin, five oxymethines, one methine, one ketone, and four methyl groups. In the HMBC spectrum of **3** cross-peaks of H_3-16 and H_3-17 to C-1, C-11, and C-15 revealed the presence of Me-16 and Me-17 at C-15, while HMBC correlations of H_3-18 to C-11, C-12, and C-13 revealed that Me-18 was attached at C-12. Cross-peaks of H-2 to C-4, H-20 to C-3, H-3a to C-8 and C-9 (δ_C 213.1), and H-10 to C-10 and C-11 in the HMBC spectrum indicated the presence of a ten-membered ring (ring B), while ^1H-^{13}C long-range correlations of H-3a to C-5 and C-7 revealed the presence of a cyclohexane moiety (ring C). HMBC correlations of H_3-19 to C-7, C-8, and C-9 implied that Me-19 was attached at C-8. Two deuterium-exchangeable protons (δ_H 2.61 and 4.20) were assigned to ones of hydroxy groups at C-5 and C-10 from HMBC correlations. Three acetoxy groups were attached at C-2, C-7, and C-13 by comparison of oxymethine proton signals (δ_H 5.71, H-2; δ_H 5.07, H-7; δ_H 5.35, H-13) with those of taxoids involving 6/10/6-membered ring system.[1] Thus the structure of taxuspine W was assigned to be **3**. Relative stereochemistry of **3** was elucidated by the NOESY spectrum and ^1H-^1H coupling constants, indicating boat conformation for rings A and C.

Taxuspines U ~ W (**1** ~ **3**) are new taxane and related diterpenoids from the Japanese yew *Taxus cuspidata* Sieb. et Zucc. Taxuspine U (**1**) is a very rare bicyclic taxane related diterpenoid from yew trees of genus *Taxus*[9,10], while taxuspine W (**3**) is a rare taxoid having a 2(3→20)-abeotaxane skeleton. Pharmacological activities of **1** ~ **3** 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 a JEOL EX-400, Bruker ARX-500 and AMX-600 spectrometers. The 7.26 ppm resonance of residual $CHCl_3$ and 77.1 ppm of $CDCl_3$ were used as internal references, respectively. EIMS was obtained on a JEOL DX-303 spectrometer operating at 70 eV. FABMS was measured on an HX-110 spectrometer. Computer modeling was carried out with the Macromodel program (version 5.0) using a Silicon Graphics Personal IRIS workstation.

Collection, Extraction, and Separation. The Japanese yew *Taxus cuspidata* Sieb. et Zucc. was collected at Sapporo, Hokkaido. The stems (4.6 kg) of the yew was extracted with MeOH (15 L x 4). The MeOH extract was partitioned between toluene (900 mL x 4) and H_2O (900 mL). The aqueous layer was extracted with $CHCl_3$ (1000 mL x 3). The $CHCl_3$ soluble portions were evaporated under reduced pressure to give a residue (5.2 g), which was subjected to a silica gel column (4.5 x 39 cm) eluted with $CHCl_3$/MeOH [95:5 (600 mL)] to afford a fraction (440 ~ 560 mL). This fraction was applied to a Sephadex LH-20 column (2 x 95 cm) eluted with MeOH/$CHCl_3$ (1:1) to yield a fraction (330 ~ 450 mL), which was subjected to a silica gel column (2.5 x 35 cm) eluted with $CHCl_3$/EtOH [49:1 (450 mL) → 19:1 (500 mL)] to afford one fraction (800 ~ 950 mL). This fraction was applied to CPC (Sanki Engineering Co. Ltd., Model LLB-M) with $CHCl_3$/MeOH/H_2O/*i*-PrOH (65:65:40:2). A fraction (descending mode, 100 ~ 140 mL) was purified by reversed-phase HPLC [ASAHIPAK ODP-50, 1.0 x 25 cm, Asahi Chemical Industry Co.Ltd., MeCN/H_2O (60:40), flow rate 0.75 mL/min] to give taxuspine U (**1**, t_R 24.0 min, 0.8 mg). The stems (11.0 kg) of the same yew was extracted with MeOH (50 L x 5), a part (250 g) of which was partitioned between toluene (800 mL x 4) and H_2O (900 mL). The aqueous layer was extracted with $CHCl_3$ (800 mL x 4). The $CHCl_3$ soluble portions were evaporated under reduced pressure to give a residue (23 g), which was subjected to a silica gel column (4.0 x 36 cm) eluted with $CHCl_3$/MeOH [98:2 (800 mL) → 97:3 (500 mL)] to afford a fraction (660 ~ 810 mL, 1210 mg). The fraction was applied to a Sephadex LH-20 column (3.5 x 97 cm) eluted with MeOH/$CHCl_3$ (1:1) to give a fraction (340 ~ 370 mL), which was subjected to CPC with *n*-hexane/EtOAc/MeOH/H_2O (9:4:2:5). A fraction (ascending mode, 70 ~ 170 mL) was subjected to a reversed-phase HPLC [YMC pack AM-323, YMC Co. Ltd., 1.0 x 25 cm, MeOH/H_2O (60:40), flow rate 2.5 mL/min] to afford taxuspine W (**3**, t_R 18.4 min, 3.0 mg). The toluene soluble portions were evaporated under reduced pressure to give a residue (24.6 g), a part (8.0 g) of which was subjected to a silica gel column (4.0 x 34 cm) eluted with *n*-hexane/acetone [8:1 (500 mL) → 4:1 (500 mL) → 2:1 (500 mL)] to afford a fraction (1010 ~ 1340 mL). The fraction was applied to an ODS column (2.5 x 10 cm) eluted with MeCN/H_2O (8:2) to yield one fraction (520 ~ 620 mL), which was subjected to a reversed-phase HPLC (YMC pack AM-323, 1.0 x 25 cm, MeOH/H_2O (80:20), flow rate 2.5 mL/min] to afford one fraction (t_R 8.8 min), which was purified by the same HPLC [MeCN/H_2O (50:50), flow rate 2.5 mL/min] to give taxuspine V (**2**, t_R 10.4 min, 3.5 mg).

Taxuspine U (1): A colorless amorphous solid; $[\alpha]^{22}_D$ +18.0° (*c* 0.07, MeOH); IR (film) ν_{max} 3400, 1730, and 1240 cm^{-1}; UV (MeOH) λ_{max} 207 nm (ε 9000); ^1H and ^{13}C NMR (Table 1); EIMS *m/z* (%) 492 (M^+-AcOH, 0.26), 474 (0.41), 432 (2.1), 414 (1.0), 390 (0.94), 372 (3.3), 355 (1.6), and 312 (6.3); HREIMS *m/z* 492.2357 (M-AcOH)$^+$ calcd for $C_{26}H_{36}O_9$, 492.2359; HMBC correlations (Table 1); NOESY correlations ($CDCl_3$, H/H): 1/2, 1/14a, 1/16, 1/17, 2/16, 2/20a, 3/7, 3/14b, 5/6a, 5/6b, 5/20b, 7/10, 7/18, 10/18, 13/14a, 13/17, and 13/18.

Taxuspine V (2): A colorless plate (crystallized from *n*-hexane/acetone); mp 230-232 °C; $[\alpha]^{20}_D$ +56° (*c* 0.58, $CHCl_3$); IR (film) ν_{max} 3470, 1740, and 1240 cm^{-1}; UV (MeOH) λ_{max} 220 nm (ε 6200); ^1H NMR ($CDCl_3$) δ 6.23 (1H, d, *J* = 11.0 Hz, H-10), 5.97 (1H, d, *J* = 11.0 Hz, H-9), 5.97 (1H, m, H-13), 5.61 (1H, m, H-7), 5.50 (1H, d, *J* = 3.4 Hz, H-2), 3.63 (1H, d, *J* = 5.4 Hz, H-20a), 3.41 (1H, d, *J* = 3.4 Hz, H-3), 3.02 (1H, t, *J* = 2.9 Hz, H-5), 2.55 (1H, dd, *J* = 15.3, 10.3 Hz, H-14a), 2.25 (1H, d, *J* = 5.4 Hz, H-20b), 2.20 (3H, s, CH_3-18), 2.10 (3H,s, CH_3CO), 2.08 (3H, s, CH_3CO), 2.06 (3H, s, CH_3CO), 2.05 (3H, s, CH_3CO), 2.02 (1H, m, H-6a), 1.99 (3H, s, CH_3CO), 1.93 (1H, dd, *J* = 15.3, 4.8 Hz, H-14b), 1.81 (1H, ddd, *J* = 13.8, 4.3, 2.8 Hz, H-6b), 1.60 (3H, s, CH_3-16), 1.20 (3H, s, CH_3-19), and 1.12 (3H, s, CH_3-17); ^{13}C NMR ($CDCl_3$) δ 169.8 (s, $CH_3\underline{C}O$), 169.8 (s, $CH_3\underline{C}O$), 169.7 (s, $CH_3\underline{C}O$), 169.5 (s, $CH_3\underline{C}O$), 169.2 (s, $CH_3\underline{C}O$), 140.8 (s, C-12), 136.6 (s, C-11), 76.3 (d, C-5), 75.5 (s, C-1), 75.3 (d, C-9), 71.8 (d, C-2), 71.3 (d, C-10), 71.1 (d, C-13), 68.5 (d, C-7), 60.5 (s, C-4), 50.0 (t, C-20), 47.0 (s, C-8), 42.9 (s, C-15), 39.5 (d, C-3), 38.6 (t, C-14), 32.7 (t, C-6), 28.9 (q, C-17), 21.5 (q, $\underline{C}H_3CO$), 21.0 (q, $\underline{C}H_3CO$), 21.0 (q, $\underline{C}H_3CO$), 20.9 (q, $\underline{C}H_3CO$), 20.7 (s, $\underline{C}H_3CO$), 20.5 (q, C-16), 16.0 (q, C-18), and 13.2 (q, C-19); FABMS (positive ion, diethanolamine matrix) *m/z* 716 (M+DEA+H)$^+$; HRFABMS *m/z* 716.3522 (M+DEA+H)$^+$, calcd for $C_{34}H_{54}NO_{15}$, 716.3504; HMBC correlations

($CDCl_3$, H/C): 2/3, 2/8, 2/15, 2/$CH_3\underline{C}O$, 3/1, 3/2, 3/4, 3/7, 3/8, 3/19, 5/3, 5/4, 5/7, 6b/4, 6b/5, 6b/7, 6b/8, 7/19, 9/7, 9/8, 9/10, 9/$CH_3\underline{C}O$, 10/9, 10/11, 10/12, 10/15, 10/$CH_3\underline{C}O$, 14a/1, 14a/2, 14a/12, 14a/13, 14b/15, 16/1, 16/11, 16/15, 16/17, 17/1, 17/11, 17/15, 17/16, 18/11, 18/12, 19/7, and 19/8; NOESY correlations ($CDCl_3$, H/H): 2/9, 2/16, 2/19, 3/7, 3/14b, 3/20a, 5/6a, 5/6b, 5/20b, 6a/7, 7/10, 7/18, 9/16, 10/18, 13/14a, 13/18, 14a/17, 14b/20a, and 16/17.

Taxuspine W (3): A colorless amorphous solid; $[\alpha]^{30}_D$ -94.7° (*c* 0.32, MeOH); IR (film) ν_{max} 3440, 1730, 1680, and 1240 cm^{-1}; UV (MeOH) λ_{max} 206 nm (ε 7500); ^1H NMR ($CDCl_3$) δ 5.71 (1H, dd, *J* = 9.6, 1.6 Hz, H-2), 5.65 (1H, d, *J* = 9.6 Hz, H-20), 5.45 (1H, d, *J* = 2.5 Hz, H-10), 5.35 (1H, d, *J* = 10.0 Hz, H-13), 5.07 (1H, dd, *J* = 12.0, 3.8 Hz, H-7), 4.49 (1H, brt, *J* = 7.1 Hz, H-5), 4.20 (1H, d, *J* = 2.5 Hz, OH-10), 2.70 (1H, d, *J* = 15.8 Hz, H-3a), 2.70 (1H, m, H-14a), 2.61 (1H, d, *J* = 7.1 Hz, OH-5), 2.19 (3H, s, CH_3CO), 2.09 (2H, m, H-6), 2.04 (3H, s, CH_3CO), 2.04 (3H, s, CH_3CO), 2.00 (1H, d, *J* = 15.8 Hz, H-3b), 1.95 (1H, d, *J* = 16.6 Hz, H-14b), 1.94 (3H, s, CH_3-18), 1.65 (1H, dd, *J* = 6.3, 1.6 Hz, H-1), 1.31 (3H, s, CH_3-19), 1.21 (3H, s, CH_3-16), and 1.19 (3H, s, CH_3-17); ^{13}C NMR ($CDCl_3$) δ 213.1 (s, C-9), 170.1 (s, $CH_3\underline{C}O$), 170.1 (s, $CH_3\underline{C}O$), 170.0 (s, $CH_3\underline{C}O$), 138.4 (s, C-4), 135.5 (s, C-11), 134.1 (s, C-12), 125.0 (d, C-20), 77.4 (d, C-10), 70.7 (d, C-2), 70.7 (d, C-7), 69.9 (d, C-13), 68.4 (d, C-5), 52.7 (s, C-8), 47.0 (d, C-1), 37.4 (s, C-15), 35.7 (t, C-3), 35.4 (q, C-17), 26.7 (t, C-14), 24.1 (q, C-16), 21.4 (t, C-6), 21.4 (q, C-19), and 18.4 (q, C-18); EIMS *m/z* (%) 432 (M^+- AcOH, 0.3), 372 (0.7), 312 (0.9), and 43 (100); FABMS (negative ion, glycerol matrix) *m/z* 491 $(M-H)^-$; HRFABMS *m/z* 491.2257 $(M-H)^-$, calcd for $C_{26}H_{35}O_9$, 491.2233; HMBC correlations ($CDCl_3$, H/C): 1/2, 1/11, 1/13, 1/14, 1/20, 2/4, 2/14, 2/20, 3a/4, 3a/5, 3a/7, 3a/8, 3a/9, 3b/19, 5-OH/4, 5-OH/5, 6/8, 7/9, 7/19, 10/9, 10/11, 10/12, 10/15, 10-OH/9, 13/11, 13/12, 14a/1, 14a/15, 14b/2, 16/1, 16/15, 16/17, 17/1, 17/15, 17/16, 18/11, 18/12, 18/13, 19/3, 19/7, 19/8, 19/9, 20/3, and 20/5; NOESY correlations ($CDCl_3$, H/H): 1/2, 1/14a, 1/16, 2/3a, 2/16, 3a/16, 3b/19, 5/5-OH, 5/6, 5-OH/7, 5-OH/18, 5-OH/20, 7/10, 7/18, 10/18, 10/10-OH, 10-OH/16, 13/14a, 13/14b, 13/17, and 14b/20.

Acknowledgements: Authors thank N. Yoshida (Hokkaido University) for his help with collection of the yew. This work was partly supported by a Grant-in-Aid for Research Fellowships of the Japan Society for the Promotion of Science for Young Scientists and 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* 8 *August* 1996; *accepted* 26 *August* 1996)