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Taxuspines K, L, and M, New Taxoids from Japanese Yew *Taxus Cuspidata*

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Abstract: Three new taxoids, taxuspines K ~ M (**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 K (**1**) is the first example of a taxane diterpene containing a 6/8/6-membered ring system with a tetrahydrofuran ring at C-2, C-3, C-4, and C-20 from yew trees.

Since excellent antitumor activity and unique mechanism of action of taxol were discovered, more attention has been paid for isolation of new taxane diterpenoids from various species of yews.[1] In our continuing search for bioactive natural products, we have isolated previously new taxane diterpenoids, taxuspines A ~ C[2], D[3], and E ~ H and J[4] from stems and leaves of the Japanese yew *Taxus cuspidata* Sieb. et Zucc. Further investigation on extracts of stems of this yew led to isolation of three new taxane diterpenoids, named taxuspines K ~ M (**1** ~ **3**). In this paper the isolation and structure elucidation of taxuspines K ~ M (**1** ~ **3**) are described.

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 K (**1**, 0.00017%), L (**2**, 0.00014%), and M (**3**, 0.00016%).

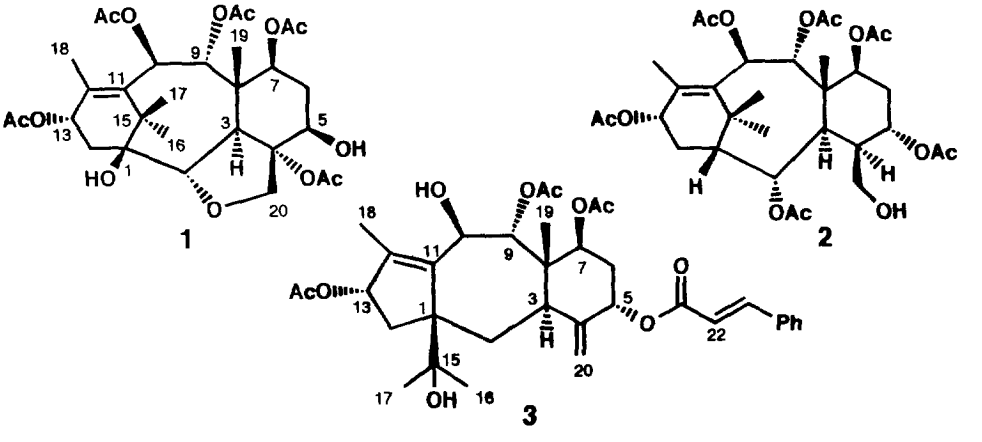

Table 1. ^{1}H and ^{13}C NMR Data of Taxuspine K (1) in $CDCl_3$

position	$^{1}H^{a}$		*J*(Hz)	$^{13}C^{a}$		H coupled with C^{b}
1				76.27	s	H-2, H-3, H-14a, H-14b, H-16, H-17
2	4.26	d	7.0	85.04	d	H-20b
3	2.81	d	7.0	50.33	d	H-19, H-20a, H-20b
4				96.40	s	H-3, H-5, H-20a, H-20b
5	4.36	m		70.01	d	H-6a
6 (a)	2.05	m		21.21	t	H-7
(b)	1.76	m				
7	5.11	dd	11.0, 4.0	70.65	d	H-6a, H-19
8				43.77	s	H-2, H-3, H-7, H-10, H-19
9	5.18	d	4.5	77.57	d	H-3, H-10, H-19
10	6.05	d	4.5	73.40	d	H-9
11				134.44	s	H-9, H-10, H-13, H-16, H-17, H-18
12				136.67	s	H-13, H-14a, H-14b, H-18
13	6.02	t	8.0	71.43	d	H-18
14 (a)	2.40	m		35.97	t	
(b)	2.32	m				
15				42.60	s	H-10, H-14a, H-16, H-17
16	1.51	s		22.97	q	H-17
17	1.18	s		27.58	q	H-16
18	1.80	s		17.60	q	
19	1.45	s		15.61	q	H-3
20 (a)	3.71	d	11.7	69.97	t	H-5
(b)	4.34	d	11.7			
4-AcO	2.14	s		169.25	s	
				22.69	q	
7-AcO	2.11	s		168.99	s	H-7
				22.43	q	
9-AcO	2.06	s		168.60	s	H-9
				21.11	q	
10-AcO	2.03	s		168.47	s	H-10
				21.00	q	
13-AcO	2.10	s		168.86	s	H-13
				21.17	q	

a) in ppm b) in HMBC spectrum

Taxuspine K (1) was obtained as a colorless amorphous solid and showed the molecular ion peak at *m/z* 610 (M^+) in the EIMS spectrum. HREIMS analysis revealed the molecular formula to be $C_{30}H_{42}O_{13}$ [*m/z* 610.2595 (M^+), Δ -3.0 mmu]. IR absorptions at 3440 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 five acetyls, one tetrasubstituted olefin, six oxymethines, one methine, three methylenes, two oxygenated quaternary carbons, and four methyl groups. Detailed analysis of the ^{1}H-^{1}H COSY spectrum implied connectivities of C-2 to C-3, C-5 to C-7, C-9 to C-10, and C-13 to C-14. In the HMBC spectrum of 1 H_2-14 showed long-range ^{1}H-^{13}C correlations with C-1, C-12, and C-15, and H-13 showed cross-peaks with C-11 and C-12, indicating the presence of a cyclohexene moiety (ring A). HMBC correlations of H_3-18 to C-11 and C-12 revealed that Me-18 was attached at C-12. HMBC correlations of H_3-16 and H_3-17 to C-1, C-11, and C-15 indicated that Me-16 and Me-17 were attached at C-15. Cross-peaks of H-2 to C-1, H-3 to C-8, H-10 to C-8, and H-10 to C-11 in the HMBC spectrum revealed the presence of an eight-membered ring (ring B). HMBC correlations of H-3 to C-4 and H-7 to C-8 implied the presence of a cyclohexane moiety (ring C). Four acetoxy groups were attached at C-10, C-9, C-13, and C-7 by the HMBC correlations for acetoxy carbonyl carbons at δ_C 168.47, 168.60, 168.86, and 168.99 to H-10, H-9, H-13, and H-7, respectively. The remaining acetoxy group (δ_C 169.25) was connected to C-4, judging

from ^{13}C NMR chemical shift (δ_C 96.40) at C-4. The ^1H and ^{13}C NMR data of C-1 and C-5 (δ_C 76.27, C-1; δ_H 4.36 and δ_C 70.01, C-5) indicated that a hydroxy group was attached to each carbon. HMBC correlations of H-20b to C-2, C-3, and C-4 indicated that a tetrahydrofuran ring was formed by C-2, C-3, C-4, and C-20. This was supported by the geminal coupling constant of H-20 (11.7 Hz) in ^1H NMR spectrum and the ^{13}C NMR chemical shift of C-2 (δ_C 85.04). The ^1H and ^{13}C NMR data of taxuspine K (**1**) were similar to those of derivative[6,7] of baccatin III. Thus the structure of taxuspine K was assigned to be **1**. Relative stereochemistry of **1** (Fig. 1) was elucidated by the NOESY spectrum. NOESY correlations of H-13/H-14b, H-13/H-17, and H-14b/H-17 in **1** revealed that the H-13 was β-oriented on ring A. A chair-like conformation of ring B was deduced from the coupling constant (4.5 Hz) between H-9 and H-10, and NOESY correlations of H-16/H-19, H-3/H-14a, while a chair-like conformation of ring C was assigned from NOESY correlations of H-3/H-7, H-5/H-6a, and H-6b/H-19. The NOESY spectrum showed cross-peaks of H-2/H-19, H-3/H-7, and H-9/H-19, indicating *trans* junction between rings B and C. The β-orientation of H-2 and H-9 was assigned by NOESY correlations of H-2/H-16, H-2/H-19, and H-9/H-19. The β-orientation of a hydroxyl group at C-5 was deduced from NOESY correlations of H-5/H-7 and H-5/H-6a. The α-orientation of H-7 and H-10 was assigned on the basis of those of H-7/H-3 and H-10/H-18, while the β-orientation of C-20 was deduced from NOESY correlations of H-20b/H-19 and H-20b/H-6b. Thus the relative stereochemistry of **1** was concluded as shown in Fig. 1.

Taxuspine L (**2**), a colorless amorphous solid, showed a fragment ion peak at *m/z* 578 in the EIMS spectrum, and the molecular formula, $C_{32}H_{46}O_{13}$, was determined by HREIMS [*m/z* 578.2757 (M^+-AcOH), Δ +3.0 mmu]. The ^{13}C NMR spectrum of **2** showed signals due to ten primary, three secondary, nine tertiary, and ten quaternary carbons. IR absorptions at 3440 and 1720 cm^{-1} indicated the presence of hydroxy and ester groups, respectively. The ^1H NMR spectrum of **2** in $CDCl_3$ showed proton signals due to four methyls (δ_H 0.85, 1.14, 1.74, and 2.23), six acetyl methyls (δ_H 1.97, 2.02, 2.04, 2.09, 2.11, and 2.24), and an oxygenated methylene group (δ_H 3.41 and 3.48). Detailed analysis of the ^1H-^1H COSY spectrum of **2** implied connectivities of C-1 to C-7, C-9 to C-10, C-13 to C-1, and C-4 to C-20. HMBC correlations of H_3-18 to C-11 and C-12 revealed that Me-18 was attached at C-12. In the HMBC spectrum

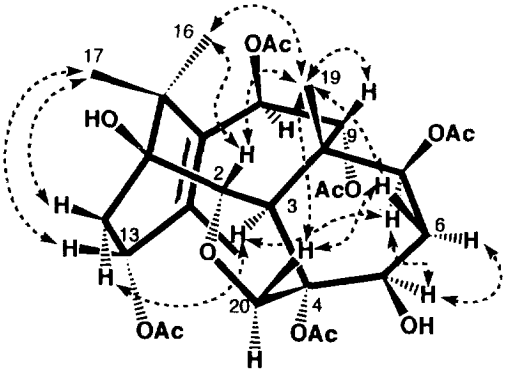

Figure 1. Relative Stereochemistry of Taxuspine K (**1**)
Dotted arrows denote NOESY correlations.

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 attached at C-15. An HMBC correlation between H-9 and C-11 implied the connectivity of rings A and B. Long-range couplings of H_3-19 to C-3, C-7, C-8, and C-9 indicated that Me-19 was attached at C-8 and ring B was connected to ring C. According to the HMBC correlations, six acetoxy groups were attached at C-2, C-5, C-7, C-9, C-10, and C-13. Thus the structure of taxuspine L was assigned to be **2**. Relative stereochemistry of **2** was elucidated by the NOESY spectrum and by comparison with the related compounds.[8] The NOESY correlations of H-19/H-20a and H-19/H-20b in **2** revealed that the hydroxymethyl group at C-4 was β-oriented on ring C. A boat-like conformation of ring B was elucidated from the coupling constant (11.0 Hz) between H-9 and H-10, and NOESY correlations of H-2/H-9 and H-3/H-14a, while a chair conformation of ring C was assigned from NOESY correlations of H-3/H-7, H-5/H-6a, and H-6b/H-19. The NOESY spectrum showed cross-peaks of H-2/H-9, H-2/H-19, H-3/H-7, and H-9/H-19, indicating *trans* junction between rings B and C. The β-orientation of H-2 and H-9 was assigned by NOESY correlations of H-2/H-9, H-2/H-16, H-9/H-16, and H-9/H-19, while α-orientation of H-4, H-7 and H-10 was assigned on the basis of those of H-4/H-3, H-4/H-14a, H-7/H-3, H-7/H-10, H-7/H-18, and H-10/H-18.

The molecular formula, $C_{35}H_{44}O_{10}$, of taxuspine M (**3**) was established by HREIMS [*m/z* 564.2323 [(M - *i*-PrOH)$^+$, Δ -3.6 mmu]. The ^1H and ^{13}C NMR spectra of **3** resembled those of taxuspine A having an unusual 5/7/6-membered ring system. The olefin proton signals of the cinnamoyl group at C-5 appeared at δ_H 6.40 (1H, d, J = 16.0 Hz) and 7.68 (1H, d, J = 16.0 Hz; *trans*-oriented). Three acetoxy groups were attached at C-7, C-9, and C-13 based on the HMBC correlations and oxymethine proton signals (δ_H 5.56, H-7; 5.65, H-9; 5.45, H-13). Two methyl proton (δ_H 1.16 and 1.38), a deuterium-exchangeable proton (δ_H 2.50), and an oxygenated quaternary carbon (δ_C 76.51, C-15) signals indicated the presence of a hydroxyisopropyl group at C-1 like taxuspine A.[2] The hydroxyisopropyl group was inferred to be β-oriented on ring A, since NOESY correlations of H-16/H-13, H-16/H-14b, and H-17/H-2b were revealed. The proton signal due to a hydroxyl group at C-10 in **3** was observed in place of a benzoyloxy group in taxuspine A[2]. Thus the structure of taxuspine M was assigned as **3**. The relative stereochemistry was elucidated by the NOESY spectrum. The coupling constant between H-9 and H-10 (J = 9.6 Hz) suggested that the B/C ring in **3** adopted a boat/chair conformation in solution.[9]

Taxuspines K ~ M (**1** ~ **3**) are new taxane diterpenoids isolated from stems of the Japanese yew *Taxus cuspidata* Sieb. et Zucc. Taxuspine K (**1**) is the first example of a taxane diterpene containing a 6/8/6-membred ring system with a tetrahydrofuran ring at C-2, C-3, C-4, and C-20 from yew trees, although a taxoid containing a 5/7/6 membered-ring system with a tetrahydrofuran ring at the same position as that of **1** has been more recently isolated.[10] Taxuspine L (**2**) is a rare example[8,11] of taxoids involving a hydroxymethyl group at C-4. Taxuspine M (**3**) is a taxoid having a rearranged 11(15→1)*abeo*-taxane skeleton. Taxuspines K ~ M (**1** ~ **3**) exhibited cytotoxicity against murine lymphoma L1210 cells with IC_{50} values of 4.5, 10.0, and 1.2 μg/mL, respectively, and human epidermoid carcinoma KB cells with IC_{50} values of 8.8, 4.5, and 5.8 μg/mL, respectively.

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 77.0 ppm of $CDCl_3$ were used as internal references, respectively. EIMS was obtained on a JEOL DX-303 spectrometer operating at 70 eV. Wako C-300 silica gel (Wako Pure Chemical) was used for glass column chromatography. TLC was carried out on Merck silica gel GF_{254}.

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 (4 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 (400 mL) → 4:1 (300 mL) → 2:1 (300 mL) → 1:1 (250 mL) → 3:7 (350 mL)] to give a fraction (3.22 g, 1300 ~ 1600 mL), part of which (1.11 g) was subjected to a silica gel column (2.5 x 35 cm) eluted with chloroform/acetone [20:1 (1000 mL) → 10:1 (300 mL) → 5:1 (360 mL) → 1:1 (200 mL)] to afford two fractions **I** (112 mg, 1430 ~ 1820 mL) and **II** (115 mg, 1820 ~ 2130 mL). Fraction **I** was applied to a reversed-phase column [YMC-GEL ODS 60, 350/250 mesh, 1.5 x 29 cm; eluent: CH_3CN/H_2O, 5:6 (110 mL) → 6:5 (110 mL) → 3:1 (200 mL)] to give taxuspine M (**3**, 1.2 mg, 300 ~ 320 mL) and fraction **a** (14.2 mg, 40 ~ 70 mL), which was continued to separate by a reversed-phase HPLC column (YMC-Pack ODS AL-323, 5 μm, 1 x 25 cm; flow rate 2.5 mL/min; UV detection at 227 nm; eluent: CH_3CN/H_2O, 1:1) to give taxuspine L (**2**, 1.1 mg, t_R 13.6 min). Fraction **II** was separated by the reversed-phase column (YMC-GEL ODS 60, 350/250 mesh, 2.5 x 15 cm; eluent CH_3CN/H_2O 1:1) to give fraction **b** (36.0 mg), which was purified by the same procedure used for the fraction **a** to give taxuspine K (**1**, 1.3 mg, t_R 9.6 min).

Taxuspine K (1): A colorless amorphous solid; $[\alpha]^{29}_D$ +14° (*c* 0.10, $CHCl_3$); IR (film) ν_{max} 3440, 1730, and 1230 cm^{-1}; ^1H and ^{13}C NMR (Table 1); EIMS *m/z* (%) 610 (M^+, 1.5), 550 (1.5), 490 (1.1), 388 (2.4), 328 (1.4), and 43 (100), ; HREIMS *m/z* 610.2595 (M^+) calcd for $C_{30}H_{42}O_{13}$, 610.2625; ^1H-^1H COSY correlations ($CDCl_3$, H/H): 2/3, 5/6a, 5/6b, 6a/7, 6b/7, 9/10, and 13/14; NOESY correlations ($CDCl_3$, H/H): 2/16, 2/19, 3/7, 3/14a, 5/6a, 5/7, 6a/6b, 6a/7, 6b/19, 6b/20b, 9/10, 9/19, 10/18, 13/14b, 13/17, 14a/14b, 14b/17, 16/17, 16/19, 19/20b, and 20a/20b.

Taxuspine L (2): A colorless amorphous solid; $[\alpha]^{28}_D$ +108° (*c* 0.18, $CHCl_3$); IR (film) ν_{max} 3440, 1720, and 1230 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.17 (1H, d, *J* = 11.0 Hz, H-10), 5.93 (1H, t, *J* = 8.3 Hz, H-13), 5.86 (1H, d, *J* = 11.0 Hz, H-9), 5.44 (1H, dd, *J* = 5.4, 2.1 Hz, H-2), 5.40 (1H, dd, *J* = 5.0, 5.8 Hz, H-7), 5.11 (1H, d, *J* = 2.4 Hz, H-5), 3.48 (1H, d, *J* = 11.4 Hz, H-20a), 3.41 (1H, dd, *J* = 11.4, 7.4 Hz, H-20b), 2.75 (1H, t, *J* = 5.4 Hz, H-3), 2.66 (1H, m, H-6b), 2.61 (1H, m, H-14a), 2.24 (3H, s, CH_3CO), 2.23 (3H, s, H_3-18), 2.11 (3H, s, CH_3CO), 2.09 (3H, s, CH_3CO), 2.06 (1H, m, H-4), 2.04 (3H, s, CH_3CO), 2.02 (3H, s, CH_3CO), 1.98 (1H, m, H-1), 1.97 (3H, s, CH_3CO), 1.85 (1H, dd, *J* = 5.0, 2.4 Hz, H-6a), 1.74 (3H, s, H_3-16), 1.46 (1H, m, H-14b), 1.14 (3H, s, H_3-17), 0.85 (3H, s, H_3-19); ^{13}C NMR ($CDCl_3$) δ 170.36 (s, $CH_3\underline{C}O$), 170.12 (s, $CH_3\underline{C}O$), 169.86 (s, $CH_3\underline{C}O$), 169.83 (s, $CH_3\underline{C}O$), 169.70 (s, $CH_3\underline{C}O$), 169.16 (s, $CH_3\underline{C}O$), 137.74 (s, C-12), 134.58 (s, C-11), 75.62 (d, C-9), 71.74 (d, C-10), 71.00 (d, C-5), 70.71 (d, C-13), 70.40 (d, C-2), 69.59 (d, C-7), 64.36 (t, C-20), 47.83 (d, C-1), 46.47 (d, C-4), 45.57 (s, C-8), 39.73 (d, C-3), 37.73 (s, C-15), 31.55 (q, C-16), 29.91 (t, C-6), 27.85 (t, C-14), 26.95 (q, C-17), 21.73 (q, $\underline{C}H_3CO$), 21.51 (q, $\underline{C}H_3CO$), 21.39 (q, $\underline{C}H_3CO$), 20.97 (q, $\underline{C}H_3CO$), 20.92 (q, $\underline{C}H_3CO$), 20.75 (q, $\underline{C}H_3CO$), 14.92 (q, C-18), 14.03 (q, C-19); EIMS *m/z* (%) 578 (M^+-AcOH, 0.3), 536 (0.3), 518 (3), 476 (4), 458 (3), 417 (8), 398 (2), 357 (4), 338 (2), 314 (3), 255 (18), 195 (8), 151 (12), and 43 (100); HREIMS *m/z* 578.2757 (M - AcOH)$^+$, calcd for $C_{30}H_{42}O_{11}$, 578.2727; ^1H-^1H COSY correlations ($CDCl_3$, H/H): 1/2, 1/14a, 1/14b, 2/3, 3/4, 4/5, 4/20a, 4/20b, 5/6a, 5/6b, 6a/7, 6b/7, 9/10, and 13/14; NOESY correlations ($CDCl_3$, H/H): 1/2, 1/14b, 1/16, 1/17, 2/9, 2/16, 3/4, 3/7, 3/14a, 4/14a, 5/6b, 5/20b, 6a/6b, 6a/7, 6b/19, 6b/20a, 7/10, 9/16, 9/19, 10/18, 13/14b, 13/17, 14a/14b, 14b/17, 16/17, 19/20a, 19/20b, and 20a/20b; HMBC correlations ($CDCl_3$, C/H): 1/14b, 1/16, 1/17, 2/14a, 3/2, 3/19, 4/20b, 4/6, 5/3, 5/20a, 5/20b, 7/5, 7/9, 7/19, 8/9, 8/19, 9/10, 9/19, 10/9, 11/10, 11/13, 11/14a, 11/16, 11/17, 11/18, 12/10, 12/13, 12/14a, 12/18, 13/18, 15/14b, 15/16, 15/17, 19/7, 19/9, 6 x $CH_3\underline{C}O$/2, 5, 7, 9, 10, and 13.

Taxuspine M (3): A colorless amorphous solid; $[\alpha]^{28}_D$ +35° (*c* 0.07, $CHCl_3$); IR (film) ν_{max} 3400, 1720, and 1240 cm^{-1}; UV (MeOH) λ_{max} 217 (ε 17500), 223 (sh), and 277 nm (15400); ^1H NMR ($CDCl_3$) δ 7.68 (1H, d, *J* = 16.0 Hz, H-23), 7.52 (2H, m, H-25 and H-29), 7.40 (2H, m, H-26 and H-

28), 7.40 (1H, m, H-27), 6.40 (1H, d, J = 16.0 Hz, H-22), 5.65 (1H, d, J = 9.6 Hz, H-9), 5.56 (1H, dd, J = 5.3, 5.4 Hz, H-7), 5.52 (1H, m, H-5), 5.45 (1H, m, H-13), 5.35 (1H, s, H-20b), 4.90 (1H, s, H-20a), 4.80 (1H, d, J = 9.6 Hz, H-10), 2.72 (1H, d, J = 8.6 Hz, H-3), 2.50 (1H, s, 15-OH), 2.38 (1H, m, H-14b), 2.19 (1H, m, H-2a), 2.10 (3H, s, 7-AcO), 2.08 (3H, s, 9-AcO), 2.04 (1H, m, H-6b), 1.90 (1H, m, H-6a), 1.90 (3H, s, H-18), 1.56 (3H, s, 13-AcO), 1.46 (1H, m, H-2b), 1.38 (3H, s, H_3-16), 1.16 (3H, s, H_3-17), 1.15 (1H, m, H-14a), 0.96 (3H, s, H_3-19); ^{13}C NMR ($CDCl_3$) δ 170.14 (s, 7-$CH_3\underline{C}O$), 170.90 (s, 13-$CH_3\underline{C}O$), 170.0 (s, 9-$CH_3\underline{C}O$), 165.63 (s, C-21), 145.09 (d, C-23), 145.09 (s, C-4), 141.81 (s, C-12), 134.34 (s, C-11), 130.87 (s, C-24), 130.49 (d, C-27), 128.94 (d, C-25 and C-29), 128.07 (d, C-26 and C-28), 118.22 (d, C-22), 114.00 (t, C-20), 80.01 (d, C-13), 77.27 (d, C-9), 76.51 (s, C-15), 73.50 (d, C-5), 69.98 (d, C-7), 68.16 (s, C-1), 64.41 (d, C-10), 44.70 (t, C-14), 44.11 (s, C-8), 38.73 (d, C-3), 32.05 (t, C-6), 30.36 (t, C-2), 28.92 (q, C-17), 27.35 (q, C-16), 21.52 (q, 9-$\underline{C}H_3CO$), 21.29 (q, 13-$\underline{C}H_3CO$), 20.54 (q, 7-$\underline{C}H_3CO$), 14.03 (q, C-19), 10.95 (q, C-18); EIMS m/z (%) 564 (M^+ - i-PrOH, 5), 446 (15), 298 (17), 238 (36), 131 (80), and 149 (23), HREIMS m/z 564.2323 (M - i-PrOH)$^+$, calcd for $C_{32}H_{36}O_9$, 564.2359; ^1H-^1H COSY correlations ($CDCl_3$, H/H): 2a/2b, 2a/3, 5/6a, 5/6b, 6a/6b, 6a/7, 6b/7, 9/10, 13/14a, 13/14b, 14a/14b, 20a/20b, 22/23, and 25/27; NOESY correlations ($CDCl_3$, H/H): 2a/2b, 2a/3, 2a/20a, 2b/9, 2b/16, 2b/19, 3/7, 3/14a, 5/6b, 5/20b, 6a/6b, 7/10, 7/18, 9/19, 10/18, 13/14b, 13/17, 14a/14b, 14b/16, 14b/17, 16/17, 20a/20b, 20b/23, 22/25, 23/25, 25/26, and 26/27; HMBC correlations ($CDCl_3$, C/H), 1/16, 1/17, 2/3, 2/17, 3/9, 3/19, 3/20a, 3/20b, 4/3, 5/20a, 5/20b, 7/3, 7/5, 8/3, 9/3, 11/18, 15/16, 15/17, 20/3, 21/23, 23/29, 24/22, 25/23, 25/26, 27/25, 7-$CH_3\underline{C}O$/7, 9-$CH_3\underline{C}O$/9, and 13-$CH_3\underline{C}O$/13.

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