New Taxane Analogues from the Needles of *Taxus canadensis*

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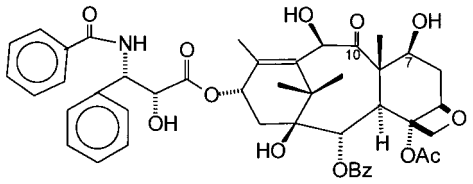
Eight minor taxanes have been identified for the first time in *Taxus canadensis* needles. Four of these metabolites are new taxane analogues: 7-acetyl-10-deacetyltaxol (**1**), 2′-acetyl-7-*epi*-cephalomannine (**2**), 10-deacetyl-10-oxo-7-*epi*-cephalomannine (**3**), and 10-acetylglycollylbaccatin VI (**4**).

Taxus canadensis Marsh. (Taxaceae), a low trailing shrub ubiquitous in the Quebec region, has been investigated by our research group since 1992.[1−3] We have discovered a variety of taxanes specific to this species, in particular an abundant taxane 9-dihydro-13-acetylbaccatin III[4,5] and a family of bicyclic taxanes, the canadensenes.[6−8] The composition of taxanes[9−11] reflects the biosynthetic diversity, and with this publication we suggest that the analysis of the major and minor taxanes in the needles of the Canadian yew is complete. Non-taxane metabolites and the very minor taxanes (less than 1 mg per kilogram of dried needles) are not included. In the present work, the detailed structures of eight minor taxane analogues isolated from the needles of *Taxus canadensis* for the first time were characterized, and four of them are new analogues. They were identified as 7-acetyl-10-deacetyltaxol, **1**, 2′-acetyl-7-*epi*-cephalomannine, **2**, 10-deacetyl-10-oxo-7-*epi*-cephalomannine, **3**, and 10-acetylglycollylbaccatin VI, **4**. Four other metabolites found in other yews are characterized for the first time in the needles of the Canadian yew.



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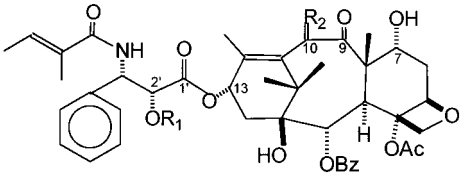
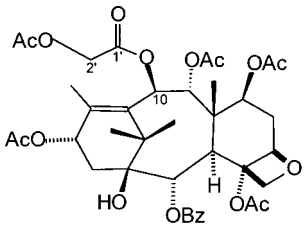


R_1 = Ac, R_2 = OAc, H **2**

R_1 = H, R_2 = O **3**



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Results and Discussion

The methylene chloride extract of *T. canadensis* needles was analyzed, and its taxanes were purified by repetitive chromatography, preparative or semipreparative HPLC, and preparative TLC.

Taxane **1** was isolated as an analogue of Taxol, and its retention time on HPLC was 38.8 min versus 36.5 min for Taxol. The ^{1}H NMR data of **1** (Table 1) was very similar to Taxol.[12,13] The only differences were at H-7 and H-10; H-7 has a chemical shift signal at δ 5.44 (dd, J = 10.5, 7.0 Hz) in **1** (^{1}H−^{1}H COSY experiment), where in Taxol it resonates at δ 4.40 (dd, J = 10.9, 6.7 Hz). The downfield shift of this proton signal suggested the location of an acetate at C-7. On the other hand, H-10 has a chemical shift signal at δ 5.28 (s) in **1**, which is upfield in comparison with H-10 in Taxol, δ 6.27 (s). This was confirmed by the HMBC correlations of H-7 to an acetyl carbonyl (δ 169.3), and OH-10 (δ 3.97 o s) to C-9 (δ 210.5). The relative stereochemistry in **1** as determined by the NOESY correlations was identical to that of Taxol. The structure of **1** was determined as 7-acetyl-10-deacetyltaxol. HRFABMS of **1** confirmed the elemental composition of the $[M + Na]^+$ quasimolecular ions of **1**.

The ^{1}H NMR data of **2** and 7-*epi*-cephalomannine[14] are very similar. The only difference is at C-2′; H-2′ resonates at δ 5.48 (d, J = 3.0 Hz) in **2**, while in 7-*epi*-cephalomannine it occurs at δ 4.72 (dd, J = 5.1, 2.7 Hz). The downfield shift of this proton signal, as well as the additional acetyl singlet (δ 2.10), suggested the location of an acetate at C-2′. The similarity of the NMR data of **2** (Table 2) to that of 7-*epi*-cephalomannine was analogous to the similarity of the data for 2′-acetyl-7-*epi*-taxol (also isolated from *T. canadensis*[3]) to that of 7-*epi*-taxol. HRFABMS of **2** confirmed the elemental composition of the $[M + Na]^+$ quasimolecular ions of **2**.

The NMR data of **3** are shown in Table 3. The ^{1}H NMR spectrum ressembles that of 7-*epi*-cephalomannine except

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Table 1. NMR Spectral Data for Taxane **1** in $CDCl_3$

position	δ ^{1}H mult.[a] (*J* in Hz)	δ ^{13}C[b]	HMBC	NOESY
1		78.4		
2	5.67 d (7.0)	74.9	1, 3, 8, 14, 166.7	3/OH-10, 20b, Me-17, Me-19
3	3.97 o d	46.2	1, 2, 4, 7, 8, 19, 20	7, 10
4		80.8		
5	4.91 d (9.2)	84.0	4, 7	6a
6a	2.52 ddd (14.6; 9.2; 7.0)	33.4	7, 8	5, 6b, 7
	1.92 o m			
6b			7	6a
7	5.44 dd (10.5, 7.0)	72.0	19, 169.3	3, 6a, 10
8		56.4		
9		210.5		
10	5.28 s	74.7	9, 11, 12, 15	3/OH-10, 7, Me-18
OH-10	3.97 o s		9	see H-3
11		135.7		
12		138.3		
13	6.19 t (8.6)	72.6	12	14a, Me-16, Me-18
14a, b	2.30 m	36.1	1, 2, 15	3, 13
15		42.8		
16	1.19 s	26.6	1, 11, 15, 17	13, Me-18
17	1.08 s	20.6	1, 11, 15, 16	2, 3/OH-10, Me-16, Me-19
18	1.81 s	14.4	11, 12, 13	3/OH-10, 10
19	1.85 s	11.1	3, 7, 8, 9	2, 20b
20a	4.32 d (8.5)	76.7	3, 4	20b, Bz-o
20b	4.23 d (8.5)		3, 5	2, 20a, Me-19
OAc	2.39 s	22.8	169.3	
	1.98 s	21.1		
OBz				
C═O		166.7		
Ph-q		126.8		
o	8.12 d (7.4)	130.2	C═O, Ph-o, Ph-p	14, 20a, 2′, Bz-m
m	7.50 t (7.2)	129.1	Ph-q	
p	7.61 t (7.4)	133.9	Ph-o	
C═O 1′		172.2		
CH 2′	4.78 br s	73.5	1′	3′, Ac
OH 2′	3.50 br d (3.3)		1′, 2′, 3′	
CH 3′	5.79 dd (9.2, 2.8)	55.2	3′-Ph-q	2′, Ac, NH, Ph
Ph 3′	7.28−7.40 m			
NH 4′	7.06 d (9.2)		5′	2′, 3′, 7, Ph
C═O 5′		166.6		
Ph 5′-o	7.75 d (8.1)	127.2	5′, Ph	2′, 3′, Ac
m	7.40 o m			
p	7.47 m			

[a] Mult., multiplicity: br, broad; d, doublet; m, multiplet; o, overlapping; s, singlet; t, triplet. The precision of the coupling constants is ±0.5 Hz. [b] The ^{13}C chemical shifts were extracted from the HMQC and HMBC (for quarternary carbons) experiments (±0.2 ppm).

for the absence of the signals for H-10 at δ 6.78 and the acetate at C-10 (δ 2.19). In addition, in the ^{13}C NMR of **3**, the signals at δ 140.7 and 142.5 assigned to C-11 and C-12, respectively, are shifted downfield relative to their respective carbons in 7-*epi*-cephalomannine (δ 133.3 and 139.7). These values are characteristic of a 9,10-diketo moiety, where the conjugation of the C-10-keto with the 11,12 double bond causes the deshielding of these two carbon signals. Indeed, they were very similar to 10-deacetyl-10-oxobaccatin V (δ 140.9 for C-11 and δ 146.6 for C-12), also identified for the first time in this plant but originally isolated from the stems and needles of *Taxus chinensis*.[15] The structure of **3** is thus established as 10-deacetyl-10-oxo-7-*epi*-cephalomannine. In addition to taxane **3** and 10-deacetyl-10-oxobaccatin V, we isolated a third 9,10-diketo-taxane from the needles of the Canadian yew: 10-deacetyl-10-oxo-7-*epi*-taxol, which was first found in the bark of *Taxus brevifolia*.[16] HRFABMS confirmed the elemental composition of the $[M + Na]^+$ quasimolecular ions of these three taxanes.

The structure of taxane **4** was established as 10-acetyl-glycollylbaccatin VI, by comparison of its ^{1}H and ^{13}C NMR data (Table 4) with those of 10-glycollylbaccatin VI.[5] In the ^{1}H NMR spectrum, the downfield shift of the methylene protons at 2′ from δ 4.09 (d, J = 16.6 Hz) and 4.03 (d, J = 16.6 Hz) in 10-glycollylbaccatin VI to δ 4.57 (d, J = 16.0 Hz) and 4.47 (d, J = 16.0 Hz) in compound **4** indicated that an acetoxy substituent was present at C-2′. HMBC correlations of the methylene protons at 2′ to C-1′ and an acetyl carbonyl carbon at δ 170.0 further confirm the structure of **4**. The stereochemistry of compound **4**, as determined by NOESY correlations, is the same as that of 10-glycollylbaccatin VI.

In addition, four known taxanes were isolated for the first time from this plant: *N*-debenzoyl-*N*-hexanoyl-7-*epi*-taxol, first isolated from the roots of *Taxus yunnanensis*,[17] 10-deacetylcephalomannine from the needles of *Taxus baccata*,[18] 10-deacetyl-10-oxo-7-*epi*-taxol from the bark of *T. brevifolia*,[16] and 10-deacetyl-10-oxo-baccatin V from the needles and stems of *T. chinensis*.[15]

According to the known structure−activity relationship of Taxol, substitutions at C-7 or C-10 do not appear to affect the bioactivity.[19] We therefore suspected that Taxol and the new taxane 7-acetyl-10-deacetyltaxol should have similar bioactivity. Indeed, in vitro studies of cytotoxicity to the breast adenocarcinoma cell line MCF7 revealed that 7-acetyl-10-deacetyltaxol (**1**) is cytotoxic (IC_{50}= 10 nM for **1** compared to 2 nM for Taxol). Some C-10- and C-2-modified Taxol analogues discovered by Ojima et al.[20] showed improved activities. On the other hand, we found that a C-10-keto group reduces the bioactivity. Indeed, 10-deacetyl-10-oxo-7-*epi*-cephalomannine **3** and 10-deacetyl-

Table 2. NMR Spectral Data for Taxane **2** in $CDCl_3$

position	δ ^{1}H mult.[a] (*J* in Hz)	δ ^{13}C[b]	HMBC	NOESY
1		79.3		
2	5.75 d (7.5)	75.1		20, Me-17, Me-19
3	3.92 d (7.5)	40.2		10
4				
5	4.92 dd (10.1, 3.5)	82.5		
6a	2.37 m	35.2		
6b	2.29 m			
7	3.70 m	75.7		Me-19
OH-7	4.67 d (11.6)			
8		57.3		
9		207.0		
10	6.82 s	77.9	169.2	Me-18
11		132.9		
12		140.3		
13	6.21 br t (9.5)	71.5		Me-16
14a	2.34 m	35.5		
14b	2.15 o m			
15		42.4		
16	1.21 s	25.8	1, 11, 15, 17	13
17	1.14 s	21.2	1, 11, 15, 16	2, Me-19
18	1.89 d (0.9)	14.5	11, 12, 13	10
19	1.66 s	16.1	3, 7, 8, 9	2, 6, 7, 17, 20
20a,b	4.37 s	77.4		2, 19
OAc	2.50 s	22.5	171.6	
	2.18 s	20.5	169.2	
	2.10 s	20.3	169.5	
OBz				
Ph-o	8.15 d (7.9)	130.2		
m	7.52 t (7.6)	128.7		
p	7.61 t (7.6)			
C=O 1′				
CH 2′	5.48 d (3.0)	74.0		
CH 3′	5.84 dd (9.7, 3.0)			
Ph 3′	7.40−7.28 m	126.3		
		128.9		
NH 4′	6.44 d (9.0)			
C=O 5′				
α =C*Me*	1.78 br s	12.5		
β =C*H*	6.39 qq (6.8, 1.3)			*β* =C*Me*
β =C*Me*	1.71 dq (6.8, 1.0)	13.9		*β* =C*H*

[a] Mult., multiplicity: br, broad; d, doublet; m, multiplet; o, overlapping; s, singlet; t, triplet. The precision of the coupling constants is ±0.5 Hz. [b] The ^{13}C chemical shifts were extracted from the HMQC and HMBC (for quarternary carbons) experiments (±0.2 ppm).

10-oxo-7-*epi*-taxol, previously found in the bark of *T. brevifolia*,[15] had IC_{50} values of 80 and 64 nM, respectively, compared to 2 and 6 nM for Taxol and cephalomannine (Figure 1). These results will be further confirmed with assays such as apoptosis induction.

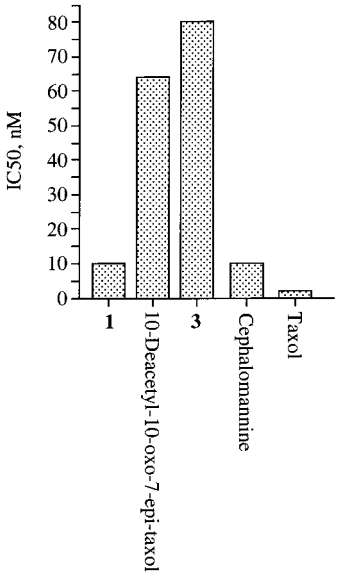

Figure 1. Antiproliferative activity of new taxanes. Exponentially growing cells were continuously exposed to compounds **1**, **3**, 10-deacetyl-10-oxo-7-*epi*-taxol, cephalomannine, and Taxol, as described in the Experimental Section. The graph represents the concentration that inhibits 50% cell growth (mean of quadruplicate samples).

Experimental Section

General Experimental Procedures. Optical rotations were recorded on a Jasco DIP-370 digital polarimeter. The NMR and HRFABMS data were obtained with the instruments and conditions reported previously.[8] Similarly, silica gel column chromatography, preparative TLC, and analytical HPLC were performed as described.[8] The spraying reagent for TLC plates was 10% H_2SO_4 in EtOH followed by heating the plates to visualize the spots. Preparative HPLC was carried out on a Waters Delta Prep 3000 instrument coupled to a UV 486 tunable absorbance detector set at 227 nm (Waters) using one Partisil 10 ODS-2 MAG-20 preparative column (22 × 500 mm) and a 50 min linear gradient method (25% to 100% of CH_3CN in H_2O, flow rate 18 mL/min). Semipreparative HPLC was performed on the same system as the preparative HPLC but using two Partisil 10 ODS-2 MAG-9 semipreparative columns (Whatman) connected in series (9.4 × 500 mm), and a 50 min gradient method (25% to 100% of CH_3CN in H_2O) at a flow rate of 3 mL/min was used

Plant Material. *Taxus canadensis* Marsh was collected in September 1997 at St-Jean, Quebec, Canada, and stored at 4 °C before drying when needed. Several specimens (voucher # lz97-03) have been deposited in the herbarium of the Montreal Botanical Garden.

Table 3. NMR Spectral Data for Taxane **3** in $CDCl_3$

position	δ ^{1}H mult.[a] (*J* in Hz)	δ ^{13}C[b]	HMBC	NOESY
1		78.7		
OH-1	1.91 s			
2	5.87 d (7.6)	74.9	1, 3, 8, 14, 166.6	OH-1, Me-17, Me-19
3	4.01 d (7.6)	39.3	1, 2, 4, 7/20, 8, 19	20a/OH-7, 14a
4		80.9		
5	4.88 dd (8.1, 4.3)	82.6	4	6, OH-7/20a
6a,b	2.26 m	32.2		
7	3.85 br ddd (11.0, 4.5, 2.0)	77.3		6a, OH-7/20a, Me-19
OH-7	4.42 o d (11.0)	7		Me-18, see also 20a
8		56.3		
9		206.7		
10				
11		140.7		
12		142.5		
13	6.20 t (8.1)	71.8		14b, Me-16
14a	2.45 m	36.1		
14b	2.31 m			
15		39.7		
16	1.23 s	25.8	1, 11, 15, 17	13
17	1.13 s	22.5	1, 11, 15, 16	2, OH-1, Me-16, Me-19
18	1.76 s	14.1	11, 12, 13	3, 2′, OH-7/20a
19	1.73 s	14.9	3, 7, 8, 9	2, 7, 20a, 20b
20a	4.41 d (8.6)	77.3		3, 5, 6, 20b
b	4.33 d (8.6)		4	20a, Me-19
OAc	2.48 s	22.2	171.8	
OBz C=O		166.6		
Ph-q		128.3		
o	8.16 d (7.7)	130.5	Ph-o, Ph-p, 166.6	
m	7.53 t (7.9)	129.2	Ph-q	Ph-q
p	7.63 t (7.2)	134.0	Ph-m	Ph-m
C=O 1′				
CH 2′	4.73 br t (3.1)	73.2		3′, Me-18, OAc
OH 2′	3.54 d (4.1)			
CH 3′	5.61 dd (9.0, 2.6)	55.1		2′, NH, OAc
Ph 3′	7.40−7.30 m	137.6		
		129.2		
		126.9		
		128.7		
NH 4′	6.44 d (8.9)		5′	3′
C=O 5′		168.9		
Me 6′	1.78 s	12.4	5′, 6′, 7′	
=C 6′		130.7		
Me 7′	1.71 d (6.9)	13.8	6′, 7′	
=CH 7′	6.42 q (6.9)	132.3		6′

[a] Mult., multiplicity: br, broad; d, doublet; m, multiplet; o, overlapping; s, singlet; t, triplet. The precision of the coupling constants is ±0.5 Hz. [b] The ^{13}C chemical shifts were extracted from the HMQC and HMBC (for quarternary carbons) experiments (±0.2 ppm).

Extraction, Isolation, and Purification of Taxanes. Dried and ground needles of *T. canadensis* (4.7 kg) were extracted and treated as described previously[8] to yield 119 g of a dark brown extract. This extract was fractionated using dry-column chromatography on silica gel (Si gel 60, 70−230 mesh, Selecto Science, 1.5 kg, 8 × 83 cm), eluted with CH_2Cl_2−*i*-PrOH (9:1, 3.5 L). The elution was stopped as the solvents went through the whole column and reached the bottom. The Si gel was then cut into 19 equal bands, and each band was individually eluted with EtOAc−MeOH (1:1, 600 mL). The eluent of the Si gel bands 5 through 8 was combined and evaporated to afford 38 g of residue A, which was then subjected to Si gel column chromatography (840 g, 9.5 × 22 cm) with hexane (1 L), hexane−CH_2Cl_2 (3:1 and 1:1, each 2 L), CH_2Cl_2 (2 L), CH_2Cl_2−EtOAc (4:1, 3:2, 2:3, and 1:4, each 2 L), EtOAc (2 L), and EtOAc−MeOH [4:1 (2 L) and 3:2 (4 L)] to yield fractions B (10.0−11.2 L) and C (14.0−15.4 L).

Fraction B (5.6 g) was applied onto a Si gel column (125 g, 4.5 × 20 cm) and eluted with CH_2Cl_2 (200 mL), CH_2Cl_2−EtOAc (9:1, 8:2, 7:3, 6:4, 1:1, 4:6, 3:7, 2:8, and 1:9, each 200 mL), EtOAc (200 mL), and EtOAc−MeOH (9:1 and 8:2, each 200 mL), yielding B1 (720−1000 mL), B2 (1000−1100 mL), B3 (1100−1300 mL), and B4 (2500−2620 mL). B1 was further purified by preparative HPLC and repetitive preparative TLC (hexane−*n*-BuOH, 8:2, and EtOAc) to afford **2** (0.7 mg) and 10-acetylglycollylbaccatin VI **4** (1.1 mg). Preparative HPLC of the B2 fraction followed by preparative TLC (CH_2Cl_2−Me_2CO, 8:2) and semipreparative HPLC produced *N*-debenzoyl-*N*-hexanoyl-7-*epi*-taxol (0.8 mg). Preparative HPLC followed by repetitive preparative TLC (EtOAc and CH_2Cl_2−Me_2CO, 8:2) as well as semipreparative HPLC of fraction B3 led to pure taxane **1** (1.8 mg). The same steps were used for fraction B4 (preparative HPLC and preparative TLC with EtOAc) to obtain pure 10-deacetylcephalomannine (1.0 mg).

Fraction C (2.4 g) was purified by a silica gel column (62 g, 2.5 × 29 cm), eluting with CH_2Cl_2 (200 mL), CH_2Cl_2−Me_2CO (95:5, 90:10, 85:15, 80:20, 75:25, 70:30, 60:40, and 30:70, each 200 mL), and Me_2CO (200 mL), to afford C1 (820−900 mL). Further preparative HPLC separation of C1 yielded taxane **3** (1.4 mg), 10-deacetyl-10-oxo-7-*epi*-taxol (2.5 mg), and 10-deacetyl-10-oxo-baccatin V (5.7 mg).

7-Acetyl-10-deacetyltaxol (1): amorphous gum; $[\alpha]^{22}_D$ −44.0° (*c* 0.05, $CHCl_3$); ^{1}H and ^{13}C NMR, HMBC, and NOESY spectral data, see Table 1; FABMS *m*/*z* 854 $[M + H]^+$; HRFABMS *m*/*z* 854.3385 (calcd for $C_{47}H_{52}NO_{14}$ 854.3388); HPLC, t_R = 38.8 min; visualized as a green spot on TLC plate with R_f = 0.80 (EtOAc).

2′-Acetyl-7-*epi*-cephalomannine (2): amorphous gum; $[\alpha]^{24}_D$ +15.0° (*c* 0.01, $CHCl_3$); ^{1}H and ^{13}C NMR, HMBC, and NOESY spectral data, see Table 2; FABMS *m*/*z* 896 $[M + Na]^+$; HRFABMS *m*/*z* 896.3468 (calcd for $C_{47}H_{55}NO_{15}Na$ 896.3469); HPLC, t_R = 42.5 min; visualized as a black spot on TLC plate with R_f = 0.80 (EtOAc).

Table 4. NMR Spectral Data for Taxane **4** in $CDCl_3$

position	δ ^{1}H mult.[a] (*J* in Hz)	δ ^{13}C[b]	HMBC	NOESY
1		78.9		
2	5.85 d (6.0)	73.1	1, 3, 8, 14, 166.7	9, Me-17, Me-19
3	3.15 d (6.0)	47.2	7, 8, 20	7, Me-18
4		81.6		
5	4.95 d (8.8)	83.7		6a
6a	2.48 dt (15.0, 8.2)	34.3		5, 6b, 7
6b	1.87 ddd (15.0, 10.0, 1.2)			6a, Me-19
7	5.53 dd (9.1, 8.0)	71.5	170.3	3, 6a, 6b,10, Me-18
8		45.9		
9	6.02 d (11.5)	74.3	7/10, 8, 170.2	2, Me-17, Me-19
10	6.31 d (11.5)	71.5	9, 15, 165.9	3, 7, Me-18
11		133.2		
12		142.2		
13	6.16 t (8.9)	69.5		14, Me-16
14a,b	2.20 o m	35.0		
15		42.8		
16	1.23 s	28.1	1, 11, 15, 17	13, Me-17
17	1.75 s	22.1	1, 11, 15, 16	2, 9, Me-16
18	2.04 d (1.0)	14.8	11, 12, 13	3, 7, 10
19	1.59 s	12.5	3, 7, 8, 9	2, 9, 20b
20a	4.32 d (8.3)	76.3	3, 4	20b
20b	4.11 d (8.3)		5	20a, Me-19
OAc	2.28 s	22.6	169.0	
	2.18 s	20.9	170.3	
	2.15 s	20.3	170.2	
	2.14 s	21.1	170.0	
	2.09 s	20.7	168.9	
OBz				
C═O		166.7		
Ph-o	8.08 d (7.3)	129.9		
m	7.47 t (7.3)	128.5		
p	7.60 t (7.0)	133.5		
C═O 1′		165.9		
CH_2 2′	4.57 d (16.0)	60.2	1′, 170.0	
	4.47 d (16.0)		1′, 170.0	

[a] Mult., multiplicity: br, broad; d, doublet; m, multiplet; o, overlapping; s, singlet; t, triplet. The precision of the coupling constants is ±0.5 Hz. [b] The ^{13}C chemical shifts were extracted from the HMQC and HMBC (for quarternary carbons) experiments (±0.2 ppm).

***N*-Debenzoyl-*N*-hexanoyl-7-*epi*-taxol:** amorphous gum; $[\alpha]^{22}_D$ −38.3° (*c* 0.06, $CHCl_3$); ^{1}H NMR data (with ^{1}H−^{1}H COSY) are identical to the literature data;[13] FABMS *m*/*z* 886 $[M + K]^+$; HRFABMS *m*/*z* 886.3414 (calcd for $C_{46}H_{57}NO_{14}K$ 886.3416); HPLC, t_R = 42.1 min; visualized as a black spot on TLC plate with R_f = 0.75 (CH_2Cl_2−MeOH, 9:1).

10-Deacetylcephalomannine: amorphous gum; $[\alpha]^{22}_D$ −20.0° (*c* 0.02, $CHCl_3$); ^{1}H NMR data (with ^{1}H−^{1}H COSY) are identical to the literature data;[14] FABMS *m*/*z* 812 $[M + Na]^+$; HRFABMS *m*/*z* 812.3259 (calcd for $C_{43}H_{51}NO_{13}Na$ 812.3258); HPLC, t_R = 30.9 min; visualized as a black spot on TLC plate with R_f = 0.45 (EtOAc).

10-Deacetyl-10-oxo-7-*epi*-cephalomannine (3): amorphous gum; $[\alpha]^{24}_D$ −1.2° (*c* 0.05, $CHCl_3$); ^{1}H and ^{13}C NMR, HMBC, and NOESY spectral data, see Table 3; FABMS *m*/*z* 810 $[M + Na]^+$; HRFABMS *m*/*z* 810.3098 (calcd for $C_{43}H_{49}NO_{13}Na$ 810.3102); HPLC, t_R = 37.5 min; visualized as a brown spot on TLC plate with R_f = 0.80 (EtOAc).

10-Deacetyl-10-oxo-7-*epi*-taxol: amorphous gum; $[\alpha]^{22}_D$ −25.0° (*c* 0.06, $CHCl_3$); ^{1}H NMR data (with ^{1}H−^{1}H COSY) are identical to the literature data;[15] FABMS *m*/*z* 832 $[M + Na]^+$; HRFABMS *m*/*z* 832.2946 (calcd for $C_{45}H_{47}NO_{13}Na$ 832.2945); HPLC, t_R = 38.3 min; visualized as a brown spot on TLC plate with R_f = 0.80 (EtOAc).

10-Deacetyl-10-oxobaccatin V: amorphous gum; $[\alpha]^{22}_D$ −89.1° (*c* 0.22, $CHCl_3$); ^{1}H NMR data (with ^{1}H−^{1}H COSY) are identical to the literature data;[16] FABMS *m*/*z* 565 $[M + Na]^+$; HRFABMS *m*/*z* 565.2047 (calcd for $C_{29}H_{34}O_{10}Na$ 565.2049); HPLC, t_R = 29.8 min; visualized as a brown spot on TLC plate with R_f = 0.70 (EtOAc).

10-Acetylglycollylbaccatin VI (4): amorphous gum; $[\alpha]^{24}_D$ −2.9° (*c* 0.12, $CHCl_3$); ^{1}H and ^{13}C NMR, HMBC, and NOESY spectral data see Table 4; FABMS *m*/*z* 811 $[M + K]^+$; HRFABMS *m*/*z* 811.2579 (calcd for $C_{39}H_{48}O_{16}K$ 811.2579); HPLC, t_R = 40.1 min; visualized as a green spot on TLC plate with R_f = 0.75 (EtOAc).

Bioactivity Assays. In vitro cytotoxicity to the breast adenocarcinoma cell line MCF7 was determined using the 3-(4,5-dimethylthiazo-2-yl)-2,5-diphenyltetrazolium bromide (MTT) metabolic assay.[21] Briefly, exponentially growing cells (1×10^3 cells per 100 μL) were seeded in 96-well plates and incubated for 16 h. Cells were then exposed continuously to taxanes. Cell survival was evaluated 96 h later by replacing the culture media with 150 μL of fresh medium containing 50 μL of 2.5 mg/mL of MTT (Sigma, St. Louis, MO) in phosphate buffer solution, pH 7.4. After 3−4 h of incubation at 37 °C, the medium and MTT were removed, and 200 μL of DMSO was added to dissolve the precipitate of reduced MTT, followed by the addition of 25 μL of glycine buffer (0.1 M glycine plus 0.1 M NaCl, pH 10.5). The absorbance was determined at 570 nm with a microplate reader (BIORAD). The MTT assay allows for the measurement of the cell proliferation rate, which is proportional to the capacity of viable cells to metabolize formazan to metabolites that absorb at OD 540. A decrease in OD values reflects inhibition of cell proliferation.

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