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Taxus canadensis Abundant Taxane: Conversion to Paclitaxel and Rearrangements

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Abstract—An efficient conversion of *Taxus canadensis* abundant taxane, 9-dihydro-13-acetylbaccatin III to baccatin III is described. Since the synthesis of paclitaxel from baccatin III has been reported, this work can be used for additional supply of this powerful anticancer drug. In addition, new taxanes derived from skeletal rearrangements originating from oxidation–reduction reactions of the Canadian yew major taxane, are reported.

The Canadian yew (*Taxus canadensis*), a low trailing bush very common in Quebec, is an interesting plant with unusual taxanes specific to this yew.[1–7] Its major taxane, isolated from the needles, was identified as 9-dihydro-13-acetylbaccatin III **1** in 1992 simultaneously by our group[1] and Gunawardana et al.[8] (Fig. 1). Depending on the collection site, it is 5 to 7 times more abundant than its co-metabolite paclitaxel **2**. 9-Dihydro-13-acetylbaccatin III **1** has only been found as traces in the bark of one other yew, *Taxus chinensis*.[9] Since *T. canadensis* is more widespread[10] than *Taxus brevifolia*, from which paclitaxel was originally isolated, a conversion of **1** to **2** would be of immense value. Acid and base rearrangement products of taxane **1** emphasize its unusual chemistry.[11–13] The structure of **1** is very similar to the core skeleton of paclitaxel, with a 9α-hydroxyl group instead of a ketone and a C-13-acetyl group instead of the side chain. Baccatin III **3** has been chemically converted to paclitaxel.[14a,b] A priori, the conversion of taxane **1** to baccatin III **3** or paclitaxel **2** seems trivial. It would require protecting the 7-hydroxyl, oxidizing C-9, deacetylating C-13 and either deprotecting C-7 to form **3** or attaching the C-13-side chain and then deprotecting the C-7 to form **2**. This approach was only partly feasible, and the efficient conversion of **1** to **3** followed a different route, which is described in this publication. In addition, we learned more about the chemistry of this unique natural taxane from some rearrangement reactions.

Results and Discussion

Conversion of 9-dihydro-13-acetylbaccatin III 1 to baccatin III 3 or paclitaxel 2: approach 1

The first approach of the conversion of 9-dihydro-13-acetylbaccatin III **1** to baccatin III **3** (and hence to paclitaxel **2**) depended on the relative reactivities of C-7 and C-9. A mild oxidizing agent such as pyridinium dichromate (PDC) oxidized the 7β-OH preferentially over the 9α-OH of 9-dihydro-13-acetylbaccatin III **1** to give taxane **4** (Scheme 1). Upon purification of taxane **4**, it was unstable which led to opening of the oxetane, C-4 to C-20 acetyl migration and dehydration to give the D-seco derivative **5**, 9-dihydro-13-acetyl-D-seco-5,6-dehydrobaccatin III. The instability of taxane **4** is reminiscent of the results obtained by Kingston[15] and Potier[16] on the oxidation products of paclitaxel. Under Jones' oxidation conditions, both C-7 and C-9 hydroxyls of taxane **1** are oxidized to give taxane **6**. Taxane **6** is unstable during chromatography on silica and converts to the D-seco derivative, 13-acetyl-D-seco-5,6-dehydrobaccatin III **7** (Scheme 1, Table 1). Most alkylating reagents preferentially attack C-7. Acetylation of **1** with acetic anhydride in pyridine and Jones' oxidation gave 7,13-diacetylbaccatin III **8**. Unfortunately, selective deacetylation of **8** to give **3** was unsuccessful. We were

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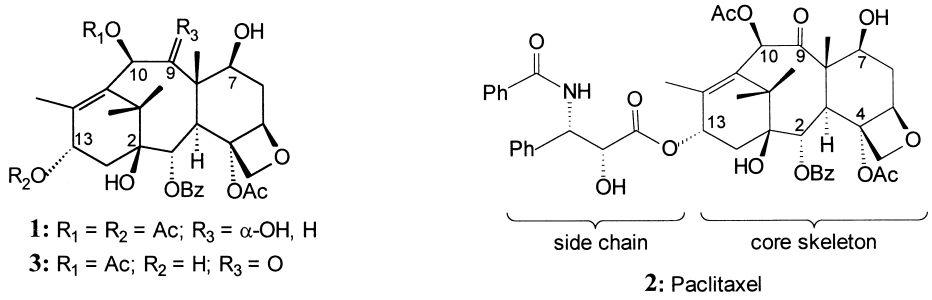
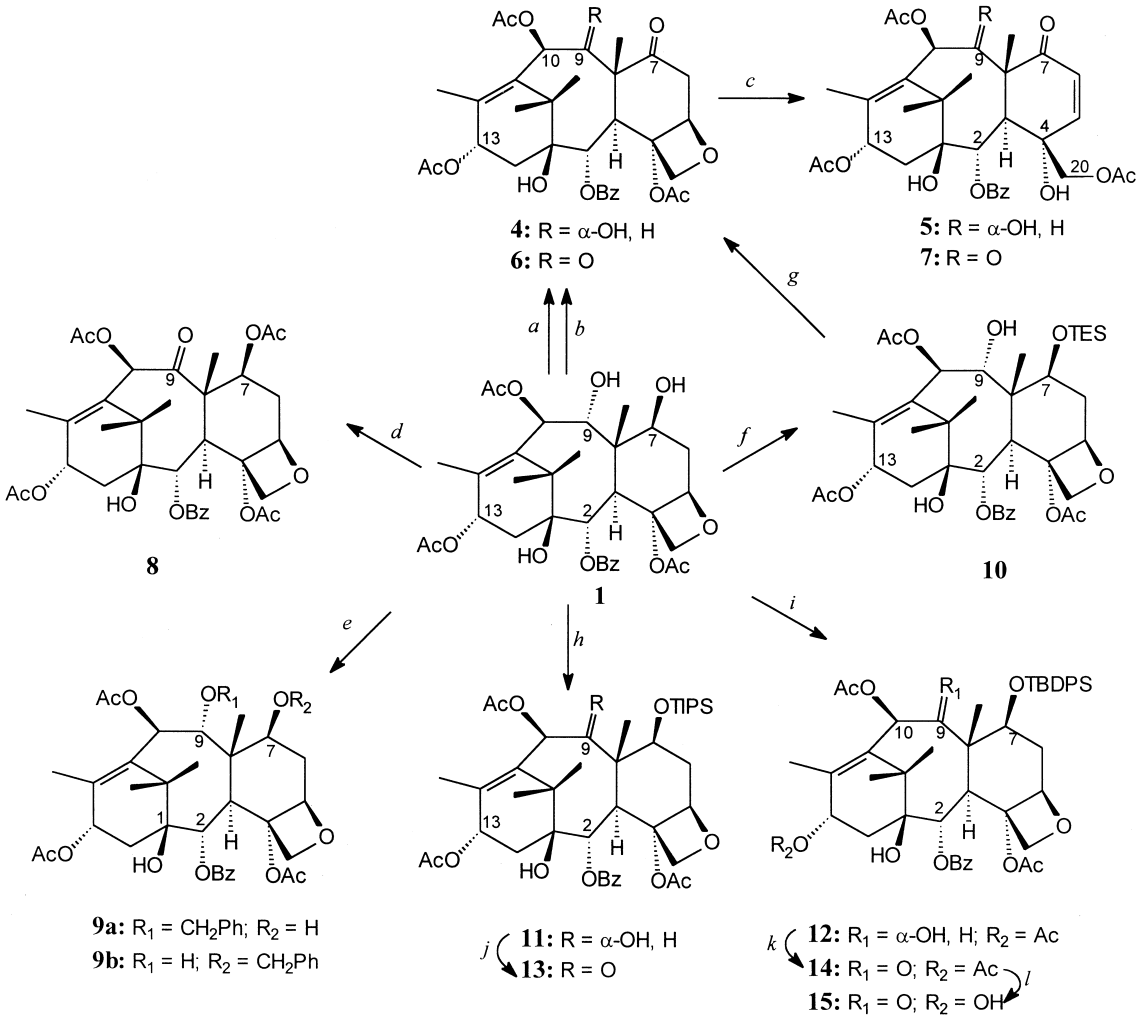


Figure 1. Some metabolites in the Canadian yew: the abundant taxane 9-dihydro-13-acetylbaccatin III **1**, paclitaxel **2** and baccatin III **3**.



Scheme 1. Conversion of 9-dihydro-13-acetylbaccatin III **1** to taxanes **4**–**15**. TES: triethylsilyl; TIPS: triisopropylsilyl; TBDPS: *tert*-butyldiphenylsilyl. Reagents and conditions: (a) pyridinium dichromate, CH_2Cl_2, 23 °C, 4.5 h, 13%; (b) CrO_3 in concentrated H_2SO_4:H_2O (3:7), acetone, 23 °C, 30 min, 69%; (c) silica gel chromatography (EtOAc), 100%; (d) i. Ac_2O, pyridine, 23 °C, 18 h; ii. CrO_3 in concentrated H_2SO_4:H_2O (3:7), acetone, 0 °C, 1 h, 54%; (e) Benzyl bromide, Ag_2O, 23 °C, 18 h, 47% for **9a**, 6% for **9b**; (f) triethylsilyl chloride, pyridine, 23 °C, 72 h, 75%; (g) CrO_3 in concentrated H_2SO_4:H_2O (3:7), acetone, 23 °C, 30 min; (h) triisopropylsilyl chloride, imidazole, DMF, 23 °C, 72 h, 77% based on recovered starting material; (i) *t*-butyldiphenylsilyl chloride, imidazole, DMF, 23 °C, 72 h, 81% based on recovered starting material; (j) CrO_3 in concentrated H_2SO_4:H_2O (3:7), acetone, 23 °C, 30 min, 21%; (k) CrO_3 in concentrated H_2SO_4:H_2O (3:7), acetone, 23 °C, 30 min, 77%; (l) (Method A): *n*-BuLi, THF, −44 °C, 2.5 h, 46% based on recovered starting material, (method B): $NaBH_4$, THF/0.05 M KPO_4 buffer, pH 7, 2:1, 23 °C, 8 h, 66%.

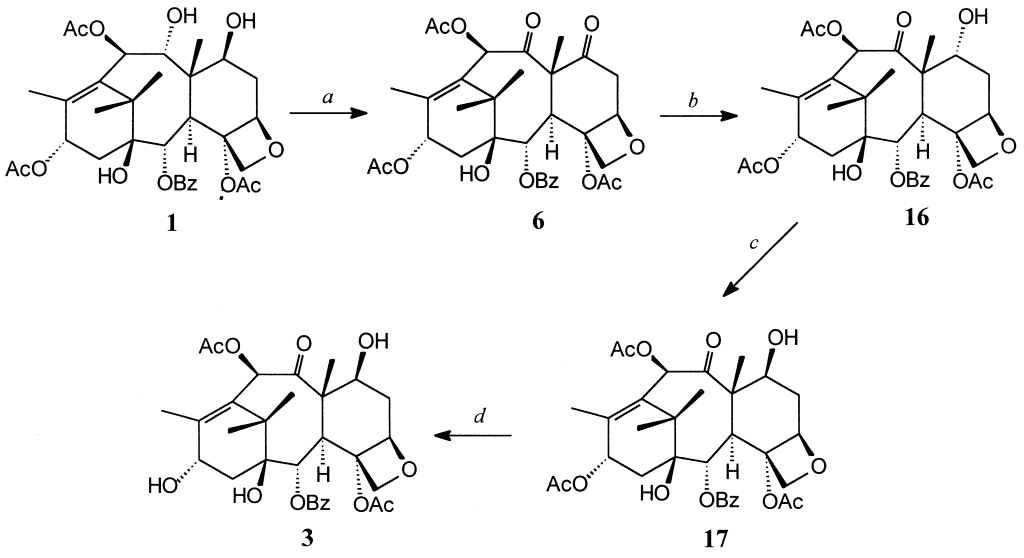
surprised to find that benzylation of taxane **1** proceeds predominantly on C-9 instead of C-7 to give **9a** as a major product and **9b** as a minor (Scheme 1). These compounds could not be used efficiently for the conversion of **1** to baccatin III **3** or to paclitaxel **2**. Silylating reagents can react preferentially only with the C-7 hydroxyl and not with the C-9 (Scheme 1).[17] Indeed, 9-dihydro-13-acetylbaccatin III **1** with triethylsilyl chloride in pyridine[17] gave 7-triethylsilyl-9-dihydro-13-acetylbaccatin III **10**. Similarly, 7-triisopropylsilyl-9-dihydro-13-acetylbaccatin III **11** and 7-*t*-butyldiphenylsilyl-9-dihydro-13-acetylbaccatin III **12** were obtained from

Table 1. ^{1}H and ^{13}C NMR data for taxane **7** in $CDCl_3$

Position	δ ^{1}H mult.[a] (*J* in Hz)	δ ^{13}C[b]	HMBC	NOESY[c]
1		77.6		
2	5.58 d (6.3)	74.2	1, 3, 8, 14, 166.7	3^{w}, Me-17^{s}, Me-19^{s}, $20b^{w}$
3	4.06 d (6.3)	53.9	1, 4, 8, Me-19, 20	2^{m}, 10^{w}, $14a^{s}$, 18^{s}, OH-4^{m}
4		73.7		
OH-4	3.39 s		3, 4, 5, 20	3^{S}, 5^{w}, $14a^{s}$, $20b^{s}$, Bz-O^{w}
5	6.76 d (10.5)	153.4	3	6^{s}, $20b^{w}$, OH-4^{w}
6	5.98 d (10.3)	123.7	8	5^{s}
7		197.3		
8		63.0		
9		199.1		
10	6.36 s	76.7	9, 11, 12, 15, 168.9	3^{w}, Me-18^{s}
11		133.6		
12		140.4		
13	5.88 br m	70.1	11, 12, 170.2	$14b^{s}$, Me-16^{s}, Me-18^{w}
14a	2.80 dd (15.1; 4.1)	35.7	1,2, 13, 15	3^{w}, 13^{w}, $14b^{s}$, OH-4^{w}
14b	2.47 dd (15.2; 10.5)		1, 2, 12, 13	13^{m}, $14a^{s}$
15		42.3		
16	1.12 s	27.6	1, 11, 15, Me-17	13^{s}, $14b^{w}$, 17^{w}
17	1.22 s	18.5	1, 11, 15, Me-16	2^{s}, 16^{m}
18	1.85 br s	15.3	11, 12, 13	3^{w}, 10^{s}
19	1.59 s	17.8	3, 7, 8, 9	2^{s}, $14b^{w}$, Me-17^{m}, $20b^{s}$
20a	4.35 d (12.2)	68.3	4, 5, 171.0	2^{w}, Me-19^{s}, OH-4^{w}
20b	4.31 d (12.2)		171.0	19^{s}
OAc	2.23 s	20.7, 168.9		
	2.17 s	21.0, 170.2		
	1.82 s	20.0, 171.0		
OBz:		166.7		
ortho	8.08 d (7.6)	129.9		
meta	7.51 t (7.5)	128.7		
para	7.63 t (7.2)	133.7		
C-1		130.1		

[a]Mult. multiplicity: s, singlet; d, doublet; t, triplet; dd, doublet of doublet; br, broad; m, multiplet; o, overlapping. The precision of the coupling constants is ±0.5 Hz.
[b]The ^{13}C chemical shifts were extracted from the HMQC and HMBC experiments (for quaternary carbons) (±0.2 ppm).
[c]NOESY intensities are marked as strong (s), medium (m) or weak (w).

the reaction of **1** with triisopropylsilyl chloride or *t*-butyldiphenylsilyl chloride and imidazole in dimethylformamide, respectively. These different silyl protecting groups were used in search of one which would be stable to the conditions required for the oxidation of the 9α-OH. Taxane **10** was unreactive to 0.1 equivalents of tetrapropylammonium perruthenate (TPAP), a mild oxidizing agent,[18] and 3 equivalents of 4-methylmorpholine *N*-oxide (NMO). Even after 6 days at room temperature, primarily starting material **10** was obtained with some recovered **1** isolated by the concomitant cleavage of the C-7 triethylsilyl group. The C-9 hydroxyl group was also unreactive to the following oxidation conditions: pyridinium chlorochromate (PCC) in CH_2C1_2, and to CrO_3 in pyridine:CH_2C1_2. Jones' oxidation of **10** afforded 7-oxo-l3-acetylbaccatin III **6**. This compound can also be obtained directly from Jones' oxidation of taxane **1**. Indeed, under the acidic conditions of Jones' oxidation, the triethylsilyl group of **10** was hydrolyzed. The derived taxane **1** was oxidized on C-7 and C-9 to give the diketone **6**. Upon purification on silica, **6** rearranged to the D-seco derivative, 13-acetyl-D-seco-5,6-dehydrobaccatin III **7** (Scheme 1). Taxane **11** could not be oxidized with pyridinium dichromate in CH_2Cl_2. Jones' oxidation of **11** gave the desired product 7-triisopropylsilyl-13-acetylbaccatin III **13** with 21% yield. Unfortunately, the yield could not be improved and the reaction conditions were not always reproducible. The low yield was attributed to the deprotection of C-7 under the acidic oxidation conditions. The 7-triisopropylsilylprotecting group was successfully removed to give 13-acetylbaccatin III (taxane **17**, Scheme 2), in 24% yield with 7-*epi*-13-acetylbaccatin III (taxane **16**) as well as starting material. A more stable C-7 protecting group was needed and a *t*-butyldiphenylsilyl group was chosen (taxane **12**). Indeed, 7-*t*-butyldiphenylsilyl-13-acetylbaccatin III **14** was readily obtained from Jones' oxidation of **12** in 77% yield. In order to obtain baccatin III only two steps remained: 13-deacetylation and deprotection of C-7. Deacetylation at C-13 could be done with *n*-BuLi at −44 °C to give 7-*t*-butyldiphenylsilylbaccatin III **15** in 29% yield (46% yield based on recovered starting material).[17,19] A preferable method using $NaBH_4$ in THF/phosphate buffer at room temperature[13] increased the yield of **15** to 66% (72% based on recovered starting material). Another advantage of this last method is that by adding more reagent, the reaction can be run to completion. Unfortunately, after intense investigation, we did not succeed in deprotecting C-7. The conditions used on 7-*t*-butyldiphenylsilyl-13-acetylbaccatin III **14** or 7-*t*-butyldiphenylsilylbaccatin III **15** were the following: (1) 2.5% HC1 in 95% ethanol at 0 °C, following Greene's procedure even after 72 h was unsuccessful;[14a] (2) treatment with 50% aqueous CF_3COOH–dioxane at 25 °C;[20] (3) 3% methanolic HCl at ambient temperature;[20] (4) basic hydrolysis with 2 N NaOH in 50% ethanol;[20] (5) acidic hydrolysis with hydrogen fluoride–pyridine did not alter the starting



Scheme 2. Conversion of 9-dihydro-13-acetylbaccatin III **1** to baccatin III **3**. Reagents and conditions: (a) CrO_3 in concentrated H_2SO_4:H_2O (3:7), acetone, 23 °C, 30 min, 69%; (b) $NaBH_4$, MeOH, 4 °C, 2 h, 82%; (c) DBU, toluene, 80 °C, 1.5 h, 67% (based on recovered starting material); (d) $NaBH_4$, THF: 0.05 M KPO_4 buffer, pH 7, 2:1, 23 °C, 10 h, 48%.

taxane **14**; (6) tetra-*n*-butylammonium fluoride (the usual method to cleave silyl ethers) caused C-2 debenzoylation as the main product on taxane **14**; (7) in order to avoid the hydrolysis of the C-2 benzoyl we employed a polymer supported reagent to provide the fluoride ion. Amberlyst® A-26 is a macroreticular anion-exchange resin containing quaternary ammonium groups in the F^- form.[21] It is interesting to note that although the above resin failed to deprotect either **14** or **15**, it easily deprotected 7-*t*-butyldiphenylsilyl-9-dihydro-l3-acetylbaccatin III **12**, where *C-9 is not a keto-group*. The ketone at C-9 hinders the removal of C-7-*t*-butyldiphenylsilyl group.

Conversion of 9-dihydro-13-acetylbaccatin III 1 to baccatin III 3 or paclitaxel 2: approach 2

The approach we decided to use was reduction of the C-7 keto-group of taxane **6**. The first step was to prevent its conversion to the D-secoderivative **7** (Scheme 1). Indeed, if the reaction mixture after oxidation was quenched under non-aqueous conditions with $KHCO_3$, dried over $MgSO_4$, and only filtered through silica gel with ether, very little conversion to the D-seco derivative resulted. The desired 7-oxo-13-acetylbaccatin III **6** obtained in 69% yield (Scheme 2) was identified by its detailed NMR data. High resolution mass spectrometry confirmed the elemental composition of the sodiated quasimolecular ion of **6**. Reduction of the more reactive keto-group on C-7 with $NaBH_4$ produced exclusively 7-*epi*-13-acetylbaccatin III **16** with 82% yield. The NOESY data showed a correlation between the C-7 proton and the methyl group at C-19, and a correlation between the OH-7 and the proton at C-3, thereby confirming a C-7α-OH. The stereochemistry at this center was reversed by treating **16** in toluene with the bulky base 1,8-diazabicyclo[5,4,0]undec-7-ene at 80 °C.[22,23] One single product was obtained, taxane **17**[24] in 67% yield (Scheme 2). Deacetylation at C-13 was done by reductive cleavage[13] to give baccatin III[25] **3** in 48% yield. The synthetic steps from baccatin III to paclitaxel having been well established,[14a,b] this constitutes an efficient conversion from *T. canadensis* abundant taxane to paclitaxel **2**. Indeed, the reactions are easy to perform and the Canadian yew is widespread.[10]

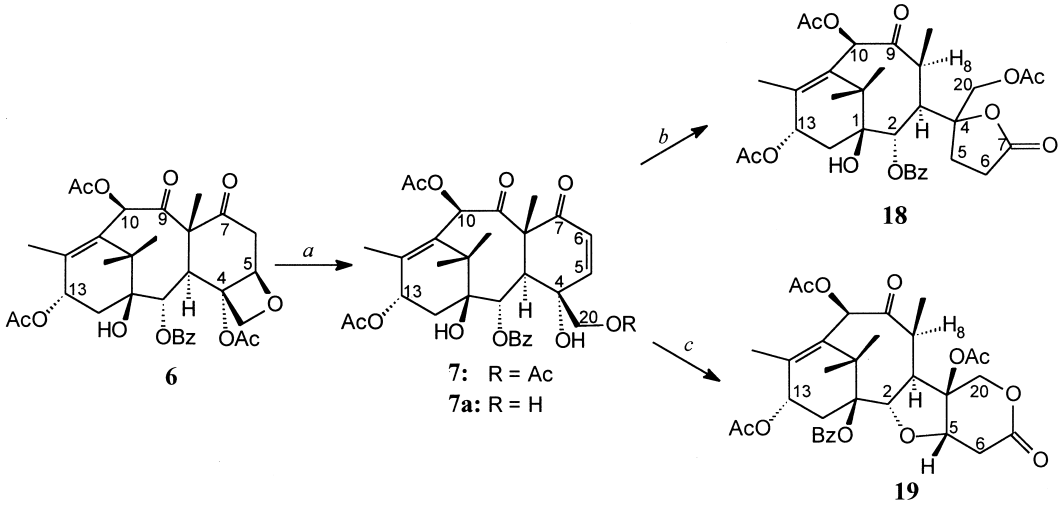
Rearrangement reactions

In an attempt to directly obtain the desired C-7-β-stereoisomer **17**, bulky reducing reagents were used. Lithium tri-*tert*-butoxyaluminohydride reduction of 7-oxo-13-acetylbaccatin III **6** was monitored by analytical HPLC. The products obtained were the D-seco derivative **7**, as well as the C-7-α-stereoisomer **16**, previously obtained from treatment with sodium borohydride (Scheme 2) in equal proportions. We can therefore conclude that not only silica but base reactions can cause the opening of the oxetane and rearrangement to the D-secoderivative.[15,16] The reduction of 7-oxo-l3-acetylbaccatin III **6** with tetrabutylammonium borohydride, was monitored by analytical HPLC. Over time the starting material **6**, was converted to the D-seco derivative **7**, which in turn was converted quantitatively to a new rearranged compound **18**. The NMR data of **18** (Table 2) correspond to the structure shown in Scheme 3. The C-5–C-6 vinyl protons of the αβ-unsaturated ketone in **7** are not found in **18** and there is a proton on C-8 (3.14). There are proton multiplets for H-5 a/b and H-6 a/b. The distinction between C-5 and C-6 derives from HMBC correlations of H-20 (4.08) with C-5 (26.7). There are three acetyls and they are located on C-10, C-20 and C-13. The acetyls on C-10 and C-20 are confirmed by the HMBC correlations of H-10 (6.23) and H-20 (4.08) with carbonyl acetyls 169.8 and 170.3, respectively. The third acetyl has been placed on C-13 because of the deshielding effect of H-13. The benzoyl has remained on C-2 as seen from the HMBC correlations of H-2 (5.73) with the benzoyl carbonyl at 166.7. The NOESY experiment showed a strong correlation between H-8 (3.14), H-3 (3.76), H-10 (6.23) confirming an α-stereochemistry, as is shown in Scheme 3. High

Table 2. ^{1}H and ^{13}C NMR for taxane **18** in $CDCl_3$

Position	δ ^{1}H mult.[a] (*J* in Hz)	δ ^{13}C[b]	HMBC	NOESY[c]
1		78.4		
2	5.73 d (7.4)	72.9	1,3, 8, 14, 166.7	3^{w}, Me-17^{s}, Me-19^{s}
3	3.76 dd (7.3; 2.3)	44.8		2^{s}, 8^{s}, 10^{s}, 18^{s}, $20a^{w}$, $20b^{s}$
4		86.8		
5a	2.19	26.7		$5b^{s}$, Me-19^{s}
5b	1.84			
6a/b	2.51/2.44	28.5		
7		175.1		
8	3.14 br m	46.1		3^{s}, 10^{s}, Me-19^{s}, $5b^{w}$
9		202.0		
10	6.23 s	76.3	9, 11, 12, 15, 169.8	3^{s}, 8^{s}, Me-18^{s}
11		135.1		
12		139.9		
13	5.91 dd (10.1; 3.0)	69.2	11	
14a	2.56 dd (16.5; 9.7)	36.6	1, 2, 12, 13	13^{w}, Me-16^{s}
14b	2.33 br dd (15.8; 3.1)			$14a^{s}$, Me-18^{s}, $20a^{s}$
15		42.2		
16	1.13 s	19.7	1, 11, 15, Me-17	13^{w}, $14a^{w}$
17	1.09 s	27.2	1, 11, 15, Me-16	2^{w}
18	1.93 s	15.8	11, 12, 13	
19	1.41 d (6.8)	10.3	3, 8, 9	2^{s}, 8^{w}, Me-17^{s}
20a	4.75 br m	72.0		$14b^{s}$, $20b^{s}$, $5b^{w}$
20b	4.08 d (11.4)		4, 5, 170.3	3^{s}, Me-19^{w}, $20a^{s}$
OAc	2.26 s	21.0, 170.3		
	2.22 s	20.8, 169.8		
	2.03 s	20.7, 169.5		
OBz:		166.7		
ortho	7.96 d (7.5)	129.8		
meta	7.50 t (7.9)	129.0		
para	7.63 t (7.5)	134.0		
C-1		129.1		

[a]Mult., multiplicity: s, singlet; d, doublet; t, triplet; dd, doublet of doublet; br, broad; m, multiplet; o, overlapping. The precision of the coupling constants is ±0.5 Hz.
[b]The ^{13}C chemical shifts were extracted from the HMQC and HMBC experiments (for quaternary carbons) (±0.2 ppm).
[c]NOESY intensities are marked as strong (s), medium (m) or weak (w).



Scheme 3. Conversion of 7-oxo-13-acetylbaccatin III **6** to taxanes **18** and **19**. Reagents and conditions: (a) silica gel chromatography (EtOAc), 100%; (b) *n*-Bu_4NBH_4, CH_2Cl_2, 23 °C, 30 min, 20%; (c) Lithium tri-*sec*butylborohydride, THF, 4 °C, 2 h, 30%.

resolution mass spectrometry confirmed the elemental composition of the sodiated quasimolecular ion of taxane **18**. This rearranged taxane is somewhat similar to one of the products of the rearrangement of 13-oxo-D-seco-5,6-dehydrobaccatin III (similar structure as **7**, Scheme 3, but with a ketone at C-13) with KCN in DMF.[16] The formation of taxane **18** can be explained first by a 1,4[26] reduction of the αβ-unsaturated ketone in ring C. A retro-Claisen reaction with traces of water on the C-7 ketone will lead to cleavage of ring C followed by lactonization to give taxane **18**. This mechanism[15,26] (Fig. 2) and the product **18** are reminiscent of the six-membered ring lactone obtained from 7-oxo-D-secotaxol upon catalytic reduction with mild aqueous/alcoholic work-up. Another bulky reducing agent used on taxane **6** was lithium tri-*sec*-butylborohydride (L-Selectride®). The

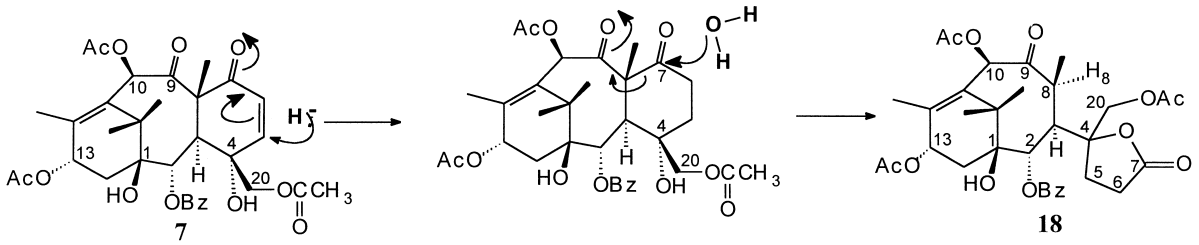


Figure 2. Proposed mechanism for the formation of the rearranged taxane **18**.

reaction was monitored by analytical HPLC and showed two major compounds being produced: 13-acetyl-D-seco-5,6-dehydrobaccatin III **7**, 13-acetyl-D-seco-5,6-dehydro-20-deacetylbaccatin III **7a** (Scheme 3), as well as some starting material, 7-oxo-13-acetylbaccatin III **6**. Therefore 7-oxo-13-acetylbaccatin III **6** upon treatment with L-Selectride® is converted to the D-seco derivative **7**, which is in turn deacetylated to form **7a**. After standard work up and purification on silica gel, only two products **7** and **7a** were obtained since the remaining starting material was converted to **7**. Under more forceful conditions, longer reaction time and more molar equivalents of L-Selectride®, 7-oxo-13-acetylbaccatin III **6** was converted to two major compounds purified by HPLC: the C-20 deacetylated D-seco derivative **7a**, and a new taxane **19** (Scheme 3). Comparing the NMR data of **19** (Table 3) to those of the D-seco derivative **7** (Table 1), we observe the disappearance of the two vinyl protons of the C-5,C-6 double bond. The chemical shifts in **19** of both carbon (74.6 ppm) and proton (4.07 ppm) at C-5 confirm the presence of an oxygen atom. In addition, the protons at C-6 show an HMBC correlation with a carbonyl group at 168.9 ppm. The C-7 carbonyl group in **7** was shifted from 197.3 to 168.9 ppm in **19**, indicating the formation of a lactone and showed an HMBC correlation with the protons at C-20. The benzoyl group in **19** migrated from C-2 to C-1 as observed by the upfield shift of the C-2 proton from 5.58 to 4.84 ppm and the downfield shift of the C-1 carbon from 77.6 to 88.1 ppm. The NOESY data show a strong correlation between the new proton at C-8 (2.85 ppm) and the proton at C-3, and a strong correlation between the proton at C-5 and that at C-2, and the methyl protons at C-19. In addition, the NMR data are

Table 3. ^{1}H and ^{13}C NMR data for taxane **19** in $CDCl_3$

Position	δ ^{1}H mult.[a] (*J* in Hz)	δ ^{13}C[b]	HMBC	NOESY[c]
1		88.1		
2	4.84 od (9.3)	81.6	1, 3, 8	5^{m}, Me-17^{s}, Me-19^{s}
3	3.34 dd (9.4; 2.9)	44.3		2^{m}, 6b/8/14b^{m}, 18^{m}, 20b^{m}
4		83.3		
5	4.07 dm (6.6)	74.6		2^{m}, 6a^{m}, Me-19^{m}, 20a^{m}
6a	3.05 dd (17.6; 6.8)	33.2	4, 5, 168.9	5^{m}, 6b^{s}
6b	2.80 dd (17.6; 2.9)			5^{w}, 6a^{s}, 20b^{w}
7		168.9		
8	2.85 om	44.3		3^{s}, 10^{w}, 14a^{s}, 19^{m}, 20b^{m}
9		202.4		
10	6.27 s	76.3	9, 11, 12, 15, 169.6 (Ac)	3^{w}, Me-18^{s}
11		134.7		
12		140.5		
13	5.92 b r d(10.2)	68.7	11, 12, 170.0 (Ac)	14a^{s}, Me-16^{s}, Me-18^{w}
14a	3.23 dd (16.8;10.5)	33.2	1, 2, 13, 12	13^{m}, 14b^{s}, Me-16^{m}
14b	2.85 om		1, 2, 13, 15	
15		43.3		
16	1.22 s	27.3	1, 11, 15, Me-17	2^{s}, 13^{w}, 14a^{m}
17	1.23 s	20.8	1, 11, 15, Me-16	2^{s}, 13^{w}, Me-19^{w}
18	1.92 s	15.6	11, 12, 13	3^{w}, 10^{s}
19	1.46 d (6.8)	13.2	3, 9, 8	2^{s}, 5^{w}, 8^{s}, Me-17^{m}
20a	4.81 od (12.0)	67.8	4, 5, 168.9	3^{m}, 6b/8/14b^{m}, 20b^{s}
20b	4.33 d (12.0)		4, 5, 168.9	3^{m}, 5^{w}, 6b/8/14b^{m}, 20a^{s}
OAc	2.22 s	20.5, 169.6		
	2.18 s	20.8, 170.0		
	2.11 s	20.8, 170.2		
OBz:		164.8		
ortho	7.95 d (7.6)	129.5		
meta	7.45 t (7.8)	128.3		
para	7.56 t (7.6)	133.0		
C-1		131.5		

[a]Mult., multiplicity: s, singlet; d, doublet; t, triplet; dd, doublet of doublets; br, broad; m, multiplet; o, overlapping. The precision of the coupling constants is ±0.5 Hz.
[b]The ^{13}C chemical shifts were extracted from the HMQC and HMBC experiments (for quaternary carbons) (±0.2 ppm).
[c]NOESY intensities are marked as strong (s), medium (m) or weak (w).

very similar to the NMR data of the base rearrangement of another D-seco derivative derived from 13-oxobaccatin III.[16] Indeed, the compounds differ only by the substituent on C-l3 (an α-acetoxy-C-l3 in taxane **19** and a keto-group in ref 16). Comparison of the respective NMR data confirm our structural determination. The formation of taxane **19** can be explained by the same mechanism shown by Potier's group.[16] High resolution mass spectrometry confirmed the elemental composition of the sodiated quasimolecular ion of taxane **19**.

Conclusion

The chemistry of the conversion of the Canadian yew abundant taxane, 9-dihydro-13-acetylbaccatin III, to baccatin III and hence to paclitaxel in four steps was unexpected. These reactions could be used to increase the supply of paclitaxel. Obviously the transformation of *T. baccata* major taxane, 10-deacetylbaccatin III to baccatin III[14a] is preferable. Unfortunately, the supply of the European yew is limited, while *T. canadensis* seems to be widespread[10,27] and additional supply of paclitaxel and taxanes could be useful. The new skeletons obtained from rearrangement reactions will add to the ongoing investigation of the roles of cycles B and C in tubulin binding. In addition, these structures could be used as a backbone to couple to inhibitors of cellular targets which have been shown to confer resistance to taxanes.

Experimental

Instrumentation

Flash chromatography was performed on Silica Gel 60, 230–400 mesh (EM Science). Thin layer chromatography was conducted on Silica Gel 60 F_{254} pre-coated TLC plates, 0.25 mm (EM Science). $MgSO_4$ was the drying agent used in all work up procedures. Analytical HPLC was performed on a Waters 600^E delivery system coupled to a PDA 996 detector. Preparative and semi-preparative HPLC were carried out on a Waters Delta Prep 3000 instrument coupled to a UV 486 Tunable Absorbance detector set at 227 nm (Waters, Montreal, Quebec, Canada). Analytical HPLC was performed with two Whatman partisil 10 ODS-2 analytical columns in series (4.6×250 mm). Semi-preparative HPLC was performed with two Whatman partisil 10 ODS-2 Mag 9 semi-preparative columns in series (9.4×250 mm). Preparative HPLC was performed with one partisil 10 ODS-2 MAG-20 preparative column (22×500 mm).

NMR and mass spectrometry measurement

All the NMR data were obtained at room temperature on a Varian UNITY-500 spectrometer operating at 499.84 MHz for proton and at 125.70 MHz for carbon-13. The NMR spectra were obtained on 5–10 mg dissolved in 0.3–0.4 mL of $CDCl_3$. The solvent was used as an internal reference (7.25 ppm for proton and 77.0 ppm for carbon-13). The various 2D spectra were acquired and processed using standard procedures. For phase sensitive 2D experiments (NOESY and HMQC), the data were acquired using the hypercomplex phase mode. The NOESY experiment was obtained using a mixing time of 0.3 s and a relaxation delay of 1 s. The intensity of the cross-peaks in the NOESY experiment is designated as strong (s), medium (m) and weak (w). Positive ion Fast Atom Bombardment Mass Spectra (FAB MS) were obtained with a Vacuum Generators ZAB-HS double-focussing instrument using a xenon beam having 8 kV energy at 1 mA equivalent neutral current. Low resolution mass spectra were obtained in glycerol. Samples were dissolved in 0.2 μL DMSO before addition of 0.5 μL glycerol. FABHRMS was similarly obtained in glycerol–DMSO at a resolving power of 12,000.

9-Dihydro-13-acetyl-D-seco-5,6-dehydrobaccatin III 5. 9-Dihydro-13-acetylbaccatin III **1** was isolated from the needles of *T. canadensis* as previously described.[1,2] 9-Dihydro-13-acetylbaccatin III **1** (15 mg; 0.024 mmol) in CH_2Cl_2 (3 mL) was treated with pyridinium dichromate (29 mg; 0.077 mmol) at 23 °C for 4.5 h. The mixture was diluted in CH_2Cl_2 and washed with brine, dried, filtered and evaporated in vacuo. The residue was purified by semi-preparative HPLC (25–100% CH_3CN in H_2O, 50 min gradient at a flow rate of 3 mL/min) affording 9-dihydro-13-acetyl-D-seco-5,6-dehydrobaccatin III **5** (2 mg, 13%, R_t = 32.97 min). FABHRMS: $C_{33}H_{40}O_{12}Na$ [M + Na$^+$] required 651.2418, found 651.2420; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.10 (d, J = 7.6 Hz, 2H, H-2,6 of OBz), 7.61 (t, J = 7.3 Hz, 1H, H-4 of OBz), 7.50 (t, J = 7.5 Hz, 2H, H-3,5 of OBz), 6.69 (d, J = 10.3 Hz, 1H, H-5), 6.20 (d, J = 10.3 Hz, 1H, H-10), 5.88 (d, J = 10.8 Hz, 1H, H-6), 5.75 (br m, 1H, H-13), 5.73 (br d, 1H, H-2), 4.38 (d, J = 12.2 Hz, 1H, H-20a), 4.37 (d, J = 12.7 Hz, 1H, H-20b), 4.32 (d, J = 11.7 Hz, 1H, OH-9), 4.19 (t, J = 11.2 Hz, 1H, H-9), 3.42 (d, J = 5.8 Hz, 1H, H-3), 3.24 (s, 1H, OH-4), 2.73 (dd, J = 15.1, 3.4 Hz, 1H, H-14a), 2.46 (dd, J = 15.6, 10.3 Hz, 1H, H-14b), 2.16 (s, 3H, OAc), 2.10 (s, 3H, OAc), 1.84 (s, 3H, OAc), 1.72 (s, 3H, H-18), 1.63 (s, 3H, H-19), 1.58 (s, 3H, H-17), 1.09 (s, 3H, H-16); ^{13}C NMR ($CDCl_3$, HMQC data) δ 206.1 (C-7), 170.9 (CO–OAc), 170.5 (CO–OAc), 169.9 (CO–OAc), 166.8 (CO–OBz), 152.8 (C-5), 138.1 (C-12), 136.7 (C-11), 133.8 (C-4 of OBz), 130.1 (C-2,6 of OBz), 129.3 (C-1 of OBz), 128.9 (C-3,5 of OBz), 124.6 (C-6), 77.6 (C-1), 75.2 (C-9), 74.8 (C-4), 73.3 (C-10), 72.3 (C-2), 71.2 (C-13), 69.0 (C-20), 53.9 (C-3), 51.3 (C-8), 41.8 (C-15), 36.5 (C-14), 29.3 (C-16), 21.3 (OAc), 21.1 (OAc), 20.3 (OAc), 20.2 (C-17), 19.5 (C-19), 15.7 (C-18).

7-Oxo-13-acetylbaccatin III 6. 9-Dihydro-13-acetylbaccatin III **1** (10 mg; 0.016 mmol) was dissolved in acetone (1.5 mL) and treated with Jones' reagent (50 μL of a 1 mL solution of CrO_3 (0.20 g) in concentrated H_2SO_4:water (3:7)), at 23 °C for 30 min. The reaction was quenched with $KHCO_3$, dried, and filtered through dry silica gel. The column was eluted with ether and the expected 7-oxo-13-acetylbaccatin III **6** was obtained (6.9 mg, 69%). FABHRMS: $C_{33}H_{38}O_{12}Na$ [M + Na$^+$] required 649.2261, found 649.2261; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.09 (d, J = 7.8 Hz, 2H, H-2,6 of OBz), 7.63 (t, J = 7.3 Hz, 1H, H-4 of OBz), 7.49 (t, J = 7.6 Hz, 2H,

H-3,5 of OBz), 6.46 (s, 1H, H-10), 6.12 (t, $J=8.7$ Hz, 1H, H-13), 5.75 (d, $J=6.7$ Hz, 1H, H-2), 5.09 (d, $J=6.3$ Hz, 1H, H-5), 4.45 (d, $J=8.4$ Hz, 1H, H-20a), 4.31 (d, $J=6.7$ Hz, 1H, H-3), 4.27 (d, $J=8.2$ Hz, 1H, H-20b), 3.06 (dd, $J=18.9$, 6.5 Hz, 1H, H-6a), 2.85 (d, $J=18.8$ Hz, 1H, H-6b), 2.33 (s, 3H, OAc), 2.23 (om, 2H, H-l4a/b), 2.21 (s, 3H, OAc), 2.18 (s, 3H, OAc), 2.05 (s, 3H, H-18), 1.85 (s, 3H, H-19). 1.19 (s, 3H, H-17), 1.16 (s, 3H, H-16); ^{13}C NMR ($CDCl_3$, HMQC data) δ 205.6 (C-9), 199.8 (C-7), 170.1 (CO–OAc), 169.6 (CO–OAc), 169.0 (CO–OAc), 166.9 (CO–OBz), 141.5 (C-12), 133.9 (C-4 of OBz), 132.8 (C-11), 130.0 (C-2,6 of OBz), 129.0 (C-1 of OBz), 128.7 (C-3,5 of OBz), 84.6 (C-5), 79.0 (C-1), 78.6 (C-4), 77.2 (C-10), 76.3 (C-20), 74.0 (C-2), 69.4 (C-13), 64.2 (C-8), 44.8 (C-3), 42.9 (C-15), 41.7 (C-6), 35.7 (C-14), 25.9 (C-l7), 22.2 (OAc), 21.2 (OAc), 20.9 (OAc), 20.8 (C-16), 14.5 (C-19), 14.2 (C-18).

13-Acetyl-D-seco-5,6-dehydrobaccatin III 7. 9-Dihydro-13-acetylbaccatin III **1** (10 mg; 0.016 mmol) was dissolved in acetone (1.5 mL) and treated with Jones' reagent (50 μL of a 1 mL solution of CrO_3 (0.20 g) in concentrated H_2SO_4:water (3:7)), at 23 °C for 30 min. The solution was diluted with ethyl acetate, washed with a saturated solution of $NaHCO_3$ and brine to neutrality, dried, filtered and evaporated. Before purification by chromatography on silica gel, the product obtained, as confirmed by NMR, was 7-oxo-13-acetylbaccatin III **6**. Chromatography on silica gel (EtOAc) afforded 13-acetyl-D-seco-5,6-dehydrobaccatin III **7** (10 mg, 100%). FABHRMS: $C_{33}H_{38}O_{12}Na$ [$M+Na^+$] required 649.2261, found 649.2261; ^{1}H and ^{13}C NMR, HMBC and NOESY (see Table 1).

7,13-Diacetylbaccatin III 8. To a solution of acetic anhydride (60 μL) in pyridine (1.0 mL) was added, dropwise over 20 min, a solution of 9-dihydro-13-acetylbaccatin III **1**(38 mg; 0.060 mmol) in pyridine (1.0 mL). The mixture was stirred at 23 °C for 18 h, then diluted with ethyl acetate, washed with brine, dried, and evaporated. The residue was dissolved in acetone (2.0 mL) and treated with Jones' reagent (200 μL of a 1 mL solution of CrO_3 (0.20 g) in concentrated H_2SO_4:water (3:7)), at 0 °C for 1 h. The solution was diluted with ethyl acetate, washed with a saturated solution of $NaHCO_3$ and brine to neutrality, dried, filtered and evaporated. The residue was purified by chromatography on silica gel (EtOAc:hexane, 65:35) affording 7,13-diacetylbaccatin III (taxane **8**, 22 mg, 54% over two steps). FABHRMS: $C_{35}H_{42}O_{13}Na$ [$M+Na^+$] required 693.2523, found 693.2526; ^{1}H NMR ($CDC1_3$, 500 MHz) δ 8.08 (d, $J=7.3$ Hz, 2H, H-2,6 of OBz), 7.62 (t, $J=7.1$ Hz, 1H, H-4 of OBz), 7.49 (t, $J=7.8$ Hz, 2H, H-3,5 of OBz), 6.26 (s, 1H, H-10), 6.17 (br t, $J=8.6$ Hz, 1H, H-13), 5.66 (d, $J=7.1$ Hz, 1H, H-2), 5.59 (dd, $J=10.5$, 7.0 Hz, 1H, H-7), 4.97 (d, $J=8.5$ Hz, 1H, H-5), 4.32 (d, $J=8.3$ Hz, 1H, H-20a), 4.16 (d, $J=8.3$ Hz, 1H, H-20b), 3.96 (d, $J=6.6$ Hz, 1H, H-3), 2.61 (ddd, $J=14.4$, 8.1, 7.1 Hz, 1H, H-6a), 2.34 (s, 3H, OAc), 2.25 (d, $J=9.0$ Hz, 1H, H-14a), 2.21 (s, 3H, OAc), 2.18 (s, 3H, OAc), 2.04 (s, 3H, OAc), 1.96 (br s, 3H, H-18), 1.83 (om, 1H, H-6b), 1.80 (s, 3H, H-19), 1.64 (s, 1H, OH-1), 1.21 (s, 3H, H-16), 1.16 (s, 3H, H-17); ^{13}C NMR ($CDCl_3$, HMQC data) δ 202.0 (C-9), 170.4 (CO–OAc), 170.2 (CO–OAc), 169.6 (CO–OAc), 168.9 (CO–OAc), 166.9 (CO–OBz), 141.2 (C-12), 133.7 (C-4 of OBz), 132.2 (C-11), 130.1 (C-2,6 of OBz), 128.8 (C-3,5 of OBz), 83.8 (C-5), 80.7 (C-4), 78.6 (C-1), 76.2 (C-20), 75.3 (C-10), 74.2 (C-2), 71.2 (C-7), 69.3 (C-13), 56.0 (C-8), 47.1 (C-3), 42.9 (C-15), 35.3 (C-14), 33.2 (C-6), 26.0 (C-16), 22.2 (OAc), 21.1 (OAc), 20.8 (OAc), 20.5 (C-17), 20.5 (OAc), 14.5 (C-18), 10.4 (C-19).

9-Benzyloxy-13-acetylbaccatin III 9a and 7-benzyloxy-13-acetylbaccatin III 9b. A solution of 9-dihydro-13-acetylbaccatin III (0.15 g; 0.24 mmol) in DMF (9 mL) was treated with freshly prepared Ag_2O (83 mg; 0.36 mmol). The solution was cooled to 0 °C and benzyl bromide (0.030 mL; 0.25 mmol) was added. The mixture was stirred at 23 °C for 18 h. The slurry was then filtered through a bed of dry silica gel, and rinsed through with ethyl acetate. The organic solution was then washed with brine, dried, and evaporated. The residue was chromatographed through silica gel (EtOAc:hexane, gradient of 60:40–75:25) to give **9a** (80 mg, 47%) and **9b** (11 mg; 6%). FABHRMS of **9a**: $C_{40}H_{48}O_{12}Na$ [$M+Na^+$] required 743.3044, found 743.3041; ^{1}H NMR of **9a** ($CDCl_3$, 500 MHz) δ 8.10 (d, $J=7.1$ Hz, 2H, H-2,6 of OBz), 7.62 (t, $J=7.3$ Hz, 1H, H-4 of OBz), 7.49 (t, $J=7.8$ Hz, 2H, H-3,5 of OBz), 7.42–7.28 (m, 5H, benzyl), 6.32 (d, $J=11.0$ Hz, 1H, H-10), 6.16 (t, $J=8.8$ Hz, 1H, H-13), 5.82 (d, $J=5.6$ Hz, 1H, H-2), 5.22 (s, 1H, OH-7), 4.98 (d, $J=10.7$ Hz, 1H, CH_2 of benzyl), 4.95 (d, $J=8.8$ Hz, 1H, H-5), 4.85 (d, $J=10.8$ Hz, 1H, CH_2 of benzyl), 4.54 (d, $J=11.0$ Hz, 1H, H9), 4.32 (om, 1H, H-7), 4.32 (od, $J=8.3$ Hz, 1H, H-20a), 4.13 (d, $J=8.3$ Hz, 1H, H-20b), 3.03 (d, $J=5.8$ Hz, 1H, H-3), 2.61 (dt, $J=15.1$, 8.5, 8.5 Hz, 1H, H-6a), 2.27 (s, 3H, OAc), 2.19 (s, 3H, OAc), 2.22 (om, 2H, H-14a/b), 1.96 (s, 3H, OAc), 1.83 (om, 1H, H-6b), 1.98 (s, 3H, H-18), 1.79 (s, 3H, H-17), 1.78 (s, 3H, H-19), 1.74 (s, 1H, OH-1), 1.27 (s, 3H, H-16); ^{13}C NMR of **9a** ($CDCl_3$, HMQC data) δ 170.4 (CO–OAc), 169.3 (CO–OAc), 169.0 (CO–OAc), 167.1 (CO–OBz), 140.6 (C-12), 136.9 (C-1 of CH_2 benzyl), 133.8 (C-4 of OBz), 133.6 (C-11), 130.1 (C-2,6 of OBz), 129.1 (C-1 of OBz), 128.8 (C-3,5 of OBz), 128.7 (C-3,5 of CH_2 benzyl), 128.2 (C-4 of CH_2 benzyl), 126.9 (C-2,6 of CH_2 benzyl), 86.4 (C-9), 84.2 (C-5), 81.8 (C-4), 78.5 (C-1), 78.4 (CH_2 of benzyl), 76.3 (C-20), 73.5 (C-2), 73.5 (C-10), 72.2 (C-7), 69.6 (C-l3), 46.8 (C-8), 46.5 (C-3), 42.9 (C-15), 37.2 (C-6), 35.5 (C-14), 28.2 (C-16), 22.8 (OAc), 22.7 (C-17), 21.2 (OAc), 21.1 (OAc), 14.8 (C-18), 12.9 (C-19). FABHRMS of **9b**: $C_{40}H_{48}O_{12}Na$ [$M+Na^+$] required 743.3044, found 743.3042; ^{1}H NMR of **9b** ($CDCl_3$, 500 MHz) δ 8.08 (d, $J=7.3$ Hz, 2H, H-2,6 of OBz), 7.60 (t, $J=7.6$ Hz, 1H, H-4 of OBz), 7.47 (t, $J=7.6$ Hz, 2H, H-3,5 of OBz), 7.41–7.33 (m, 5H, benzyl), 6.21 (d, $J=11.0$ Hz, 1H, H-10), 6.16 (t, $J=8.5$ Hz, 1H, H-13), 5.74 (d, $J=5.9$ Hz, 1H, H-2), 5.15 (d, $J=10.2$ Hz, 1H, OH-9), 4.98 (d, $J=9.0$ Hz, 1H, H-5), 4.69 (d, $J=10.7$ Hz, 1H, CH_2 of benzyl), 4.63 (d, $J=10.5$ Hz, 1H, CH_2 of benzyl), 4.30 (ot, 1H, H-9), 4.31 (od, $J=8.0$ Hz, 1H, H-20a), 4.22 (dd, $J=10.0$, 7.1 Hz, 1H, H-7), 4.17 (d, $J=8.3$ Hz, 1H, H-20b), 3.07 (d, $J=5.9$ Hz, 1H, H-3), 2.75 (ddd, $J=14.6$, 9.2, 7.0 Hz, 1H, H-6a), 2.28 (s, 3H, OAc), 2.19 (s, 3H, OAc), 2.18 (om,

2H, H-14a/b), 2.15 (s, 3H, OAc), 1.97 (dd, $J=14.2$, 11.2 Hz, 1H, H-6b), 1.85 (s, 3H, H-19), 1.83 (s, 3H, H-18), 1.70 (s, 3H, H-17), 1.25 (s, 3H, H-16); ^{13}C NMR of **9b** ($CDCl_3$, HMQC data) δ 170.5 (CO–OAc), 170.5 (CO–OAc), 169.4 (CO–OAc), 167.0 (CO–OBz), 138.5 (C-12), 136.3 (C-1 of CH_2 benzyl), 135.7 (C-11), 133.7 (C-4 of OBz), 130.1 (C-2,6 of OBz), 128.7 (C-2,6 of CH_2 benzyl), 128.6 (C-3,5 of CH_2 benzyl), 128.5 (C-3,5 of OBz), 128.4 (C-4 of CH_2 benzyl), 83.7 (C-5), 82.0 (C-7), 78.8 (C-1), 76.6 (C-20), 76.3 (C-9), 73.3 (C-2), 72.5 (C-10), 71.5 (CH_2 of benzyl), 68.8 (C-13), 47.8 (C-3), 45.2 (C-8), 43.1 (C-15), 35.2 (C-14), 33.9 (C-6), 28.3 (C-16), 22.9 (OAc), 22.5 (C-17), 21.4 (OAc), 21.3 (OAc), 14.8 (C-18), 13.0 (C-19).

7-Triethylsilyl-9-dihydro-13-acetylbaccatin III 10. 9-Dihydro-13-acetylbaccatin III (35 mg; 0.056 mmol) in pyridine (5 mL) was treated with triethylsilyl chloride (0.19 mL; 1.1 mmol) at 4 °C. The solution was allowed to equilibrate to 23 °C and was stirred for 72 h. The reaction was quenched by addition of ice–water. The pyridine was evaporated in vacuo and the aqueous residue was extracted with EtOAc. The combined extracts were dried, filtered and evaporated in vacuo. The residue was purified by chromatography on silica gel (EtOAc: hexane, 45:55) affording 7-triethylsilyl-9-dihydro-13-acetylbaccatin III (taxane **10**, 31 mg, 75%). FABHRMS: $C_{39}H_{56}O_{12}Si+H^+$ [$M+H^+$] required 745.3619, found 745.3622; ^{1}H NMR ($CDC1_3$, 500 MHz) δ 8.07 (d, $J=7.5$ Hz, 2H, H-2,6 of OBz), 7.59 (t, $J=7.6$ Hz, 1H, H-4 of OBz), 7.46 (t, $J=7.5$ Hz, 2H, H-3,5 of OBz), 6.16 (ot, 1H, H-13), 6.15 (od, $J=10.7$ Hz, 1H, H-10), 5.73 (d, $J=5.9$ Hz, 1H, H-2), 5.32 (d, $J=9.7$ Hz, 1H, OH-9), 4.92 (d, $J=9.2$ Hz, 1H, H-5), 4.55 (dd, $J=10.1$, 7.1 Hz, 1H, H-7), 4.32 (t, $J=10.5$ Hz, 1H, H-9), 4.30 (d, $J=8.2$ Hz, 1H, H-20a), 4.16 (d, $J=8.3$ Hz, 1H, H-20b), 3.05 (d, $J=6.0$ Hz, 1H, H-3), 2.48 (ddd, $J=13.8$, 8.2, 7.7 Hz, 1H, H-6a), 2.27 (s, 3H, OAc), 2.18 (s, 3H, OAc), 2.17 (om, 2H, H-14a/b), 2.11 (s, 3H, OAc), 1.98 (om, 1H, H-6b), 1.93 (s, 3H, H-18), 1.81 (s, 3H, H-19), 1.69 (s, 3H, H-17), 1.24 (s, 3H, H-16), 1.00 (t, $J=8.0$ Hz, 9H, H-triethylsilyl-CH_3), 0.73 (q, $J=7.9$ Hz, 6H, H-triethylsilyl-CH_2); ^{13}C NMR ($CDCl_3$, HMQC data) δ 170.4 (CO–OAc), 170.3 (CO–OAc), 169.5 (CO–OAc), 167.0 (CO–OBz), 138.4 (C-12), 135.8 (C-11), 133.6 (C-4 of OBz), 130.1 (C-2,6 of OBz), 129.3 (C-1 of OBz), 128.6 (C-3,5 of OBz), 83.8 (C-5), 81.9 (C-4), 78.9 (C-1), 76.5 (C-20), 76.3 (C-9), 76.3 (C-7), 73.5 (C-2), 72.6 (C-10), 69.9 (C-13), 47.4 (C-3), 44.9 (C-8), 43.1 (C-15), 38.0 (C-6), 35.3 (C-14), 28.4 (C-16), 22.8 (OAc), 22.6 (C-17), 21.3 (OAc), 21.3 (OAc), 14.9 (C-18), 12.6 (C-19), 6.7 (C-triethylsilyl-CH_3), 5.2 (C-triethylsilyl-CH_2).

7-Triisopropylsilyl-9-dihydro-13-acetylbaccatin III 11. 9-Dihydro-13-acetylbaccatin III **1** (30 mg; 0.048 mmol) in DMF (1.0 mL) was treated with imidazole (79 mg; 1.2 mmol) and triisopropylsilyl chloride (0.13 mL; 0.61 mmol) at 23 °C for 72 h. The reaction mixture was diluted in EtOAc and washed with brine, dried, filtered and evaporated in vacuo. The residue was purified by chromatography on silica gel (gradient of EtOAc:hexane, 50:50, to EtOAc, 100%) affording 7-triisopropylsilyl-9-dihydro-13-acetylbaccatin III (**11**, 22 mg, 59%), and recovered 9-dihydro-13-acetylbaccatin III (**1**, 7 mg, 23%). FABHRMS: $C_{42}H_{62}O_{12}Si+H^+$ [$M+H^+$] required 787.4089, found 787.4091; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.07 (d, $J=7.6$ Hz, 2H, H-2,6 of OBz), 7.59 (t, $J=7.2$ Hz, 1H, H-4 of OBz), 7.46 (t, $J=7.8$ Hz, 2H, H-3,5 of OBz), 6.15 (t, $J=8.5$ Hz, 1H, H-13), 6.10 (d, $J=11.0$ Hz, 1H, H-10), 5.75 (d, $J=5.3$ Hz, 1H, H-2), 5.49 (d, $J=9.5$ Hz, 1H, OH-9), 4.91 (d, $J=9.1$ Hz, 1H, H-5), 4.69 (dd, $J=10.3$, 7.4 Hz, 1H, H-7), 4.37 (t, $J=10.5$ Hz, 1H, H-9), 4.30 (d, $J=8.5$ Hz, 1H, H-20a), 4.17 (d, $J=8.7$ Hz, 1H, H-20b), 3.07 (d, $J=5.7$ Hz, 1H, H-3), 2.58 (ddd, $J=12.9$, 8.3, 7.7 Hz, 1H, H-6a), 2.26 (s, 3H, OAc), 2.18 (s, 3H, OAc), 2.15 (om, 2H, H-14a/b), 2.10 (s, 3H, OAc), 2.07 (om, 1H, H-6b), 1.95 (s, 3H, H-18), 1.84 (s, 3H, H-19), 1.69 (s, 3H, H-17), 1.23 (s, 3H, H-16), 1.12 (m, 21H, isopropyl-H); ^{13}C NMR ($CDCl_3$, HMQC data) δ 170.4 (CO–OAc), 170.1 (CO–OAc), 169.4 (CO–OAc), 167.0 (CO–OBz), 138.6 (C-12), 135.6 (C-11), 133.6 (C-4 of OBz), 130.1 (C-2,6 of OBz), 129.3 (C-1 of OBz), 128.6 (C-3,5 of OBz), 83.7 (C-5), 81.7 (C-4), 78.9 (C-1), 77.3 (C-7), 76.7 (C-20), 76.2 (C-9), 73.6 (C-2), 73.3 (C-10), 69.9 (C-13), 47.3 (C-3), 45.3 (C-8), 43.0 (C-15), 37.8 (C-6), 35.3 (C-14), 28.4 (C-16), 22.8 (OAc), 22.5 (C-17), 21.3 (OAc), 21.2 (OAc), 18.2 (isopropyl-CH_3), 18.1 (isopropyl-CH_3), 14.9 (C-18), 13.5 (C-Si), 12.8 (C-19).

7-*t*-Butyldiphenylsilyl-9-dihydro-13-acetylbaccatin III 12. 9-Dihydro-13-acetylbaccatin III **1** (92 mg; 0.15 mmol) in DMF (1.4 mL) was treated with imidazole (0.16 g; 2.3 mmol) and *t*-butyldiphenylsilyl chloride (0.51 mL; 2.0 mmol) at 23 °C for 72 h. The reaction mixture was diluted in EtOAc and washed with brine, dried, filtered and evaporated in vacuo. The residue was purified by chromatography on silica gel (gradient of EtOAc:hexane, 50:50, to EtOAc, 100%) affording 7-*t*-butyldiphenylsilyl-9-dihydro-13-acetylbaccatin III (**12**, 75 mg, 59%), and recovered 9-dihydro-13-acetylbaccatin III (**1**, 25 mg, 27%). FABHRMS: $C_{49}H_{60}O_{12}Si+H^+$ [$M+H^+$] required 869.3932, found 869.3936; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.04 (d, $J=7.5$ Hz, 2H, H-2,6 of OBz), 7.90 (m, 2H, H-2,6 of Si-Ph_1), 7.64 (d, $J=6.9$ Hz, 2H, H-2,6 of Si-Ph_2), 7.57 (t, $J=7.1$ Hz, 1H, H-4 of OBz), 7.50–7.30 (om, 8H, remaining aromatic protons of OBz, $SiPh_1$, Si-Ph_2), 6.06 (t, $J=8.6$ Hz, 1H, H-13), 6.02 (d, $J=11.2$ Hz, 1H, H-10), 5.73 (d, $J=6.0$ Hz, 1H, H-2), 5.63 (d, $J=9.5$ Hz, 1H, OH-9), 4.61 (d, $J=9.1$ Hz, 1H, H-5), 4.53 (dd, $J=10.2$, 7.0 Hz, 1H, H-7), 4.43 (t, $J=10.4$ Hz, 1H, H-9), 4.20 (d, $J=8.2$ Hz, 1H, H-20a), 4.12 (d, $J=8.3$ Hz, 1H, H-20b), 2.89 (d, $J=5.9$ Hz, 1H, H-3), 2.18 (om, 1H, H-6a), 2.14 (s, 3H, OAc), 2.13 (s, 3H, OAc), 2.11 (s, 3H, OAc), 2.10 (om, 2H, H-14a/b), 2.01 (m, 1H, H-6b), 1.95 (s, 3H, H-19), 1.69 (s, 3H, H-18), 1.53 (s, 3H, H-17), 1.19 (s, 3H, H-16), 1.04 (s, 9H, H-Si-*t*-Bu); ^{13}C NMR ($CDCl_3$, HMQC data) δ 170.4 (CO–OAc), 170.1 (CO–OAc), 168.6 (CO–OAc), 167.0 (CO–OBz), 139.0 (C-12), 136.2 (C-2,6 of Si-Ph_1), 136.0 (C-2,6 of Si-Ph_2), 135.2 (C-11), 133.6 (C-4 of OBz), 130.1 (C-2,6 of OBz), 133.9, 130.9, 130.5, 129.8, 129.3, 128.6, 128.3, 127.5 (remaining aromatic C of OBz, Si-Ph_1, Si-Ph_2), 83.6 (C-5), 81.5 (C-4), 78.8 (C-1), 78.4 (C-7), 76.8 (C-20), 76.1 (C-9), 73.6 (C-2), 73.6 (C-10), 69.7 (C-13), 47.4 (C-3), 45.3 (C-8), 42.9 (C-15), 38.2 (C-6), 35.2 (C-14), 28.4 (C-16), 26.9 (C-Si-*t*-Bu),

22.7 (OAc), 22.4 (C-18), 21.2 (OAc), 21.2 (OAc), 19.0 (C-Si), 14.2 (C-17), 13.2 (C-19).

7-Triisopropylsilyl-13-acetylbaccatin III 13. 7-Triisopropylsilyl-9-dihydro-13-acetylbaccatin III **11** (14 mg; 0.018 mmol) was dissolved in acetone (2.6 mL) and treated with Jones' reagent (120 μL of a 1 mL solution of CrO_3 (0.20 g) in concentrated H_2SO_4:water (3:7)), at 23 °C for 30 min. The solution was diluted with ethyl acetate, washed with a saturated solution of $NaHCO_3$ and brine to neutrality, dried, filtered and evaporated. Chromatography on silica gel (EtOAc:hexane, 50:50) afforded 7-triisopropylsilyl-13-acetylbaccatin III (taxane **13**, 3 mg, 21%). FABHRMS: $C_{42}H_{60}O_{12}Si + H^+$ [M + H$^+$] required 785.3932, found 785.3930; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.07 (d, J = 7.6 Hz, 2H, H-2,6 of OBz), 7.59 (t, J = 7.2 Hz, 1H, H-4 of OBz), 7.46 (t, J = 7.8 Hz, 2H, H-3,5 of OBz), 6.47 (s, 1H, H-10), 6.15 (br t, J = 8.3 Hz, 1H, H-13), 5.67 (d, J = 7.1 Hz, 1H, H-2), 4.95 (br d, J = 8.6 Hz, 1H, H-5), 4.62 (dd, J = 10.7, 6.6 Hz, 1H, H-7), 4.31 (d, J = 8.5 Hz, 1H, H-20a), 4.16 (d, J = 8.3 Hz, 1H, H-20b), 3.84 (d, J = 7.1 Hz, 1H, H-3), 2.60 (ddd, J = 14.4, 9.8, 6.6 Hz, 1H, H-6a), 2.33 (s, 3H, OAc), 2.23 (om, 2H, H-14a/b), 2.21 (s, 3H, OAc), 2.16 (s, 3H, OAc), 2.07 (s, 3H, H-18), 1.97 (ddd, J = 13.4, 11.2,2.0 Hz, 1H, H-6b), 1.72 (s, 3H, H-19), 1.23 (s, 3H, H-17), 1.16 (s, 3H, H-16), 1.04 (m, 21H, isopropyl-H).

13-Acetylbaccatin III 17. 7-Triisopropylsilyl-13-acetylbaccatin III **13** was deprotected using the following conditions: tetra-*n*-butylammonium fluoride in THF at 0 °C for 18 h. The mixture was analyzed by analytical HPLC (25–100% CH_3CN in H_2O, 50 min gradient at a flow rate of 1 mL/min) and showed the formation of taxane **17** (R_t 32.78 min, 24%), taxane **16** (R_t 37.66 min, 16%) and starting material **13** (R_t 60.56 min, 43%). The identity of taxane **17** was confirmed by comparison with standard 13-acetylbaccatin III[24] with an additional gradient (R_t 38.70 min, analytical HPLC, 25–100% CH_3CN in H_2O, 70 min gradient at a flow rate of 1 mL/min).

7-*t*-Butyldiphenylsilyl-13-acetylbaccatin III 14. 7-*t*-Butyldiphenylsilyl-9-dihydro-13-acetylbaccatin III **12** (95 mg; 0.11 mmol) dissolved in acetone (16 mL) was treated with Jones' reagent (0.79 mL of a 1 mL solution of CrO_3 (0.20 g) in concentrated H_2SO_4:water, 3:7) at 23 °C for 30 min. The reaction mixture was diluted in ethyl acetate and washed with a saturated solution of $NaHCO_3$ and with brine to neutrality. The organic phase was dried, filtered and evaporated in vacuo. The residue was purified by chromatography on silica gel (EtOAc:hexane, 40:60) affording 7-*t*-butyldiphenylsilyl-13-acetylbaccatin III (**14**, 73 mg, 77%). FABHRMS: $C_{49}H_{58}O_{12}Si + H^+$ [M + H$^+$] required 867.3776, found 867.3772; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.04 (d, J = 7.8 Hz, 2H, H-2,6 of OBz), 7.72 (m, 2H, H-2,6 of Si-Ph_1), 7.58 (od, 2H, H-2,6 of Si-Ph_2), 7.58 (ot, 1H, H-4 of OBz), 7.50–7.30 (om, 8H, remaining aromatic protons of OBz, SiPh_1, Si-Ph_2), 6.15 (s, 1H, H-10), 6.03 (t, J = 8.7 Hz, 1H, H-13), 5.64 (d, J = 6.8 Hz, 1H, H-2), 4.69 (d, J = 9.3 Hz, 1H, H-5), 4.34 (dd, J = 10.4,6.6 Hz, 1H, H-7), 4.21 (d, J = 8.3 Hz, 1H, H-20a), 4.11 (d, J = 8.3 Hz, 1H, H-20b), 3.65 (d, J = 6.8 Hz, 1H, H-3), 2.23 (om, 1H, H-6a), 2.19 (s, 3H, OAc), 2.17 (om, 2H, H-14a/b), 2.14 (s, 3H, OAc), 2.12 (s, 3H, OAc), 1.94 (m, 1H, H-6b), 1.83 (s, 3H, H-19), 1.58 (s, 3H, H-18), 1.23 (s, 3H, H-17), 1.10 (s, 3H, H-16), 0.94 (s, 9H, H-Si-*t*-Bu); ^{13}C NMR ($CDCl_3$, HMQC data) δ 202.1 (C-9), 170.1 (CO–OAc), 169.1 (CO–OAc), 168.9 (CO–OAc), 167.0 (CO–OBz), 141.4 (C-12), 136.1 (C-2,6 of Si-Ph_1), 136.0 (C-2,6 of Si-Ph_2), 134.4 (C-11), 133.6 (C-4 of OBz), 130.0 (C-2,6 of OBz), 132.8, 131.7, 129.6, 129.3, 128.6, 128.0, 127.3 (remaining aromatic C of OBz, Si-Ph_1, Si-Ph_2), 84.0 (C-5), 80.7 (C-4), 78.9 (C-1), 76.4 (C-20), 75.9 (C-10), 74.8 (C-2), 73.3 (C-7), 69.6 (C-13), 58.6 (C-8), 47.0 (C-3), 43.1 (C-15), 37.4 (C-6), 35.3 (C-14), 26.5 (C-16), 26.4 (C-Si-*t*-Bu), 22.4 (OAc), 21.2 (OAc), 20.9 (OAc), 20.6 (C-17), 19.0 (C-Si), 13.7 (C-18), 10.5 (C-19).

7-*t*-Butyldiphenylsilylbaccatin III 15. (Method A): 7-*t*-Butyldiphenylsilyl-13-acetylbaccatin III **14** (80 mg; 0.092 mmol) was dissolved in tetrahydrofuran (18 mL) and cooled to −44 °C. To this solution a 2.5 M solution of *n*-BuLi in hexanes (0.12 mL; 0.29 mmol) was added and the mixture was stirred at −44 °C for 1 h. *n*-BuLi (0.12 mL) was added again and the reaction was stirred for an additional 1.5 h. The reaction was quenched with brine and diluted in EtOAc. The organic layer was separated, washed with brine to neutrality, dried, filtered and evaporated in vacuo. The residue was purified by chromatography on silica gel (EtOAc:hexane, gradient of 40:60 to 50:50) affording 7-*t*-butyldiphenylsilylbaccatin III (**15**, 22 mg, 29%) and recovered starting material, 7-*t*-butyldiphenylsilyl-13-acetylbaccatin III (**14**, 30 mg, 38%). (Method B): To a solution of 7-*t*-butyldiphenylsilyl-13-acetylbaccatin III **14** (24 mg; 0.028 mmol) in THF (0.9 mL) was added 0.05 M potassium phosphate buffer, pH 7.0 (0.45 mL). The opaque solution was treated with $NaBH_4$ (4×4 mg; 0.11 mmol) at 23 °C over a period of 8 h. The reaction was quenched by dilution with brine. The mixture was diluted in EtOAc, washed with brine to neutrality, dried, filtered and evaporated in vacuo. The residue was purified by chromatography as in method A, affording 7-*t*-butyldiphenylsilylbaccatin III (**15**, 15 mg, 66%) and recovered starting material, 7-*t*-butyldiphenylsilyl-13-acetylbaccatin III (**14**, 2 mg, 8%). FABHRMS of **15**: $C_{47}H_{56}O_{11}Si + H^+$ [M + H$^+$] required 825.3670, found 825.3673; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.08 (d, J = 6.3 Hz, 2H, H-2,6 of OBz), 7.73 (m, 2H, H-2,6 of Si-Ph_1), 7.58 (ot, 1H, H-4 of OBz), 7.57 (od, 2H, H-2,6 of Si-Ph_2), 7.48 (om, 3H, H-3,4,5 of Si-Ph_1), 7.45 (ot, J = 7.5 Hz, 2H, H-3,5 of OBz), 7.38 (t, J = 7.3 Hz, 1H, H-4 of Si-Ph_2), 7.32 (t, J = 7.6 Hz, 2H, H-3,5 of Si-Ph_2), 6.11 (s, 1H, H-10), 5.61 (d, J = 7.1 Hz, 1H, H-2), 4.77 (om, 1H, H-13), 4.77 (om, 1H, H-5), 4.35 (dd, J = 10.5, 6.8 Hz, 1H, H-7), 4.23 (d, J = 8.5 Hz, 1H, H-20a), 4.12 (d, J = 8.3 Hz, 1H, H-20b), 3.69 (d, J = 6.9 Hz, 1H, H-3), 2.23 (ddd, J = 14.6, 9.5, 6.6 Hz, 1H, H-6a), 2.18 (om, 2H, H-14a/b), 2.16 (s, 3H, OAc), 2.14 (s, 3H, OAc), 1.95 (ddd, J = 15.1, 10.7, 2.0 Hz, 1H, H-6b), 1.88 (d, J = 4.9 Hz, 1H, OH-13), 1.84 (s, 3H, H-19), 1.69 (s, 3H, H-18), 1.58 (s, 1H, OH-1), 1.21 (s, 3H, H-17), 0.97 (s, 3H, H-16), 0.95 (s, 9H, H-Si-*t*-Bu); ^{13}C NMR ($CDCl_3$, HMQC data) δ 202.4 (C-9), 170.0 (CO–OAc), 169.4 (CO–OAc), 167.1 (CO–OBz), 144.5 (C-12), 136.2 (C-2,6 of Si-Ph1), 136.2 (C-2,6 of Si-Ph_2), 133.7 (C-4 of OBz), 132.0

(C-11), 130.1 (C-2,6 of OBz), 130.1 (C-3,5 of OBz), 129.6 (C-4 of $SiPh_2$), 128.5 (C-3,5 of Si-Ph_1), 127.9 (C-4 of Si-Ph_1), 127.4 (C-3,5 of Si-Ph_2), 83.8 (C-5), 80.5 (C-4), 78.6 (C-1), 76.4 (C-10), 76.4 (C-20), 74.5 (C-2), 73.2 (C-7), 67.7 (C-13), 58.5 (C-8), 47.1 (C-3), 42.5 (C-15), 37.8 (C-14), 37.3 (C-6), 26.3 (C-16), 26.3 (C-Si-*t*-Bu), 22.5 (OAc), 20.8 (OAc), 19.7 (C-17), 18.9 (C-Si), 13.7 (C-18), 10.1 (C-19).

7-*Epi*-13-acetylbaccatin III 16. 7-Oxo-13-acetylbaccatin III **6** (46 mg; 0.073 mmol) was dissolved in methanol (10 mL) and treated with $NaBH_4$ (6 mg; 0.16 mmol) at 4 °C, for 2 h. The reaction was quenched by dilution with brine. The solution was extracted with dichloromethane, and the combined organic layers were dried, filtered and evaporated in vacuo. The residue was purified by chromatography on silica gel (EtOAc:hexane, 50:50) affording 7-*epi*-13-acetylbaccatin III (**16**, 38 mg, 82%). FABHRMS: $C_{33}H_{40}O_{12}Na$ $[M+Na^+]$ required 651.2418, found 651.2420; ^1H NMR ($CDCl_3$, 500 MHz) δ 8.08 (dd, $J=7.8$, 0.7 Hz, 2H, H-2,6 of OBz), 7.63 (t, $J=7.3$ Hz, 1H, H-4 of OBz), 7.50 (t, $J=7.5$ Hz, 2H, H-3,5 of OBz), 6.83 (s, 1H, H-10), 6.13 (br t, $J=8.0$ Hz, 1H, H-13), 5.75 (d, $J=7.3$ Hz, 1H, H-2), 4.95 (dd, $J=9.3$, 3.2 Hz, 1H, H-5), 4.66 (d, $J=11.7$ Hz, 1H, OH-7), 4.40 (d, $J=8.5$ Hz, 1H, H-20a), 4.35 (d, $J=8.5$ Hz, 1H, H-20b), 3.96 (d, $J=7.3$ Hz, 1H, H-3), 3.70 (ddd, $J=11.7$, 4.6, 1.7 Hz, 1H, H-7), 2.41 (s, 3H, OAc), 2.36 (ddd, $J=15.9$, 9.5, 2.0 Hz, 1H, H-6a), 2.27 (om, 1H, H-6b), 2.27 (om, 2H, H-14a/b), 2.21 (s, 3H, OAc), 2.20 (s, 3H, OAc), 1.87 (d, $J=1.2$ Hz, 3H, H-18), 1.65 (s, 3H, H-19), 1.19 (s, 3H, H-16), 1.15 (s, 3H, H-17); ^{13}C NMR ($CDCl_3$, HMQC data) δ 207.3 (C-9), 171.6 (CO–OAc), 170.2 (CO–OAc), 169.4 (CO–OAc), 167.0 (CO–OBz), 140.6 (C-12), 133.9 (C-4 of OBz), 133.0 (C-11), 130.0 (C-2,6 of OBz), 129.3 (C-1 of OBz), 128.6 (C-3,5 of OBz), 82.5 (C-5), 82.1 (C-4), 79.0 (C-1), 78.1 (C-10), 77.5 (C-20), 75.4 (C-7), 75.2 (C-2), 69.6 (C-13), 57.5 (C-8), 42.3 (C-15), 40.2 (C-3), 35.8 (C-14), 35.2 (C-6), 25.8 (C-16), 22.3 (OAc), 20.8 (OAc), 20.8 (OAc), 20.6 (C-17), 15.9 (C-19), 15.0 (C-18).

13-Acetylbaccatin III 17. To a solution of 7-*epi*-13-acetylbaccatin III **16** (7 mg; 0.011 mmol) in toluene (0.5 mL) was added 1,8-diazabicyclo[5,4,0]undec-7-ene (55 μL; 0.37 mmol) and the mixture was stirred at 80 °C for 1.5 h. The reaction mixture was then diluted in EtOAc and washed with dilute HCl, a saturated solution of $NaHCO_3$ and brine. The organic layer was then dried, filtered and evaporated in vacuo. The residue was purified by semi-preparative HPLC (25–100% CH_3CN in H_2O, 50 min gradient at a flow rate of 3 mL/min) affording 13-acetybbaccatin III (**17**, 2 mg, 29%, $R_t=33.58$ min) and recovered 7-*epi*-13-acetylbaccatin III (**16**, 4 mg, 57%, $R_t=37.98$ min). FABHRMS of **17**: $C_{33}H_{40}O_{12}Na$ $[M+Na^+]$ required 651.2418, found 651.2420; ^1H NMR ($CDCl_3$, 500 MHz) δ 8.07 (d, $J=7.6$ Hz, 2H, H-2,6 of OBz), 7.61 (t, $J=7.5$ Hz, 1H, H-4 of OBz), 7.48 (t, $J=7.4$ Hz, 2H, H-3,5 of OBz), 6.30 (s, 1H, H-10), 6.18 (dd, $J=9.5$, 8.2 Hz, 1H, H-13), 5.66 (d, $J=7.2$ Hz, 1H, H-2), 4.97 (dd, $J=9.8$, 1.6 Hz, 1H, H-5), 4.43 (br m, 1H, H-7), 4.30 (d, $J=8.1$ Hz, 1H, H-20a), 4.16 (d, $J=8.5$ Hz, 1H, H-20b), 3.82 (d, $J=6.9$ Hz, 1H, H-3), 2.55 (ddd, $J=14.7$, 9.4, 6.2 Hz, 1H, H-6a), 2.46 (br d, $J=3.0$ Hz, 1H, OH-7), 2.32 (s, 3H, OAc), 2.24 (om, 2H, H-14a/b), 2.24 (s, 3H, OAc), 2.20 (s, 3H, OAc), 1.90 (d, $J=1.1$ Hz, 3H, H-18), 1.67 (s, 3H, H-19), 1.23 (s, 3H, H-16), 1.13 (s, 3H, H-l7); ^{13}C NMR ($CDCl_3$, HMQC data) δ 203.4 (C-9), 170.9 (CO–OAc), 169.6 (CO–OAc), 169.2 (CO–OAc), 166.6 (CO–OBz), 142.5 (C-12), 134.2 (C-4 of OBz), 132.2 (C-11), 130.3 (C-2,6 of OBz), 128.8 (C-3,5 of OBz), 84.6 (C-5), 80.5 (C-4), 78.7 (C-1), 76.3 (C-20), 75.8 (C-10), 75.1 (C-2), 72.4 (C-7), 69.7 (C-13), 58.1 (C-8), 45.6 (C-3), 42.6 (C-15), 35.6 (C-14), 35.6 (C-6), 26.7 (C-16), 22.4 (OAc), 21.4 (C-17), 21.1 (OAc), 20.9 (OAc), 15.0 (C-18), 9.4 (C-l9).

Baccatin III 3. To a solution of 13-acetylbaccatin III **17** (10 mg; 0.016 mmol) in THF (0.6 mL) was added 0.05 M potassium phosphate buffer, pH 7.0 (0.3 mL). The opaque solution was treated with $NaBH_4$ (2×5 mg; 0.13 mmol) at 23 °C over a period of 10 h. The reaction was quenched by dilution with brine. The solution was extracted with dichloromethane, and the combined organic layers were dried, filtered and evaporated in vacuo. The residue was purified by semi-preparative HPLC (25–100% CH_3CN in H_2O, 50 min gradient at a flow rate of 3 mL/min) affording **3** (4.5 mg, 48%, $R_t=28.45$ min). FABHRMS: $C_{31}H_{38}O_{11}Na$ $[M+Na^+]$ required 609.2312, found 609.2313; The NMR spectroscopic properties of **3** were identical to those of baccatin III.

Reduction of 7-oxo-13-acetylbaccatin III 6 with lithium tri-*tert*-butoxyaluminohydride. Lithium tri-*tert*-butoxyaluminohydride (9 mg; 0.035 mmol) was added to THF (0.875 mL) at 4 °C. To this cooled solution was added dropwise 7-oxo-13-acetylbaccatin III **6** (5 mg; 0.008 mmol) dissolved in THF (0.125 mL). The solution was stirred at 4 °C for 30 min and the reaction was quenched by dilution with brine. The solution was diluted with ether, washed with brine, dried, filtered and evaporated in vacuo. The residue was purified by chromatography on silica gel (EtOAc:CH_2Cl_2, 20:80) affording **7** (1 mg, 20%) (Scheme 1) and **16** (1 mg, 20%) (Scheme 2).

Taxane 18. 7-Oxo-13-acetylbaccatin III **6** (15 mg; 0.024 mmol) was dissolved in CH_2Cl_2 (1.5 mL). To this solution was added *n*-Bu_4NBH_4 (6 mg; 0.023 mmol) and the mixture was stirred at 23 °C for 30 min. The reaction was stopped by addition of a potassium phosphate buffer, pH 7.0. The solution was extracted with CH_2Cl_2 and the combined organic layers were washed with brine, dried, filtered and evaporated in vacuo. The residue was purified by semi-preparative HPLC (25–100% CH_3CN in H_2O, 70 min gradient at a flow rate of 3 mL/min) affording **18** (3 mg, 20%, $R_t=43.93$ min). FABHRMS: $C_{33}H_{40}O_{12}Na$ $[M+Na^+]$ required 651.2417, found 651.2420. For ^1H NMR and ^{13}C NMR data see Table 2.

13-Acetyl-D-seco-5,6-dehydro-20-deacetylbaccatin III 7a. 7-Oxo-13-acetylbaccatin III **6** (5 mg; 0.008 mmol) was dissolved in THF (1 mL), and was reduced with a 1.0 M solution of lithium tri-*sec*-butylborohydride (L-Selectride®) (10 μL; 0.010 mmol) at 4 °C for 1 h. More L-Selectride® (10 μL; 0.010 mmol) was added and after 30 min at 4 °C the reaction was quenched by dilution with brine. The solution was diluted with ether, washed

with brine, dried, filtered and evaporated in vacuo. The residue was purified by chromatography on silica gel (EtOAc:hexane, 50:50) affording **7** (3 mg, 60%) and **7a** (2 mg, 43%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.84 (d, J = 7.6 Hz, 2H, H-2,6 of OBz), 7.61 (t, J = 7.4 Hz, 1H, H-4 of OBz), 7.45 (t, J = 7.3 Hz, 2H, H-3,5 of OBz), 6.62 (d, J = 9.5 Hz, 1H, H-5), 6.66 (s, 1H, H-10), 5.38 (d, J = 9.5 Hz, 1H, H-6), 5.89 (br m, 1H, H-13), 5.79 (d, J = 9.5 Hz, 1H, H-2), 4.76 (d, J = 11.7 Hz, 1H, H-20a), 4.42 (od, 1H, H-20b), 4.40 (od, 1H, H-3), 2.46 (dd, J = 16.1, 10.0 Hz, 1H, H-14a), 2.36 (dd, J = 16.3, 3.9 Hz, 1H, H-14b), 2.25 (s, 3H, OAc), 2.21 (s, 3H, OAc), 1.92 (br s, 3H, H-18), 1.38 (s, 3H, H-19), 1.14 (s, 3H, H-17), 1.12 (s, 3H, H-16); ^{13}C NMR ($CDCl_3$, HMQC data) δ 206.3 (C-9), 201.7 (C-7), 170.2 (CO–OAc), 169.7 (CO–OAc), 166.7 (CO–OBz), 143.7 (C-5), 139.3 (C-12), 135.7 (C-11), 134.3 (C-4 of OBz), 129.7 (C-1 of OBz), 129.5 (C-2,6 of OBz), 129.0 (C-3,5 of OBz), 119.9 (C-6), 79.1 (C-1), 78.5 (C-4), 76.4 (C-10), 75.8 (C-20), 73.6 (C-2), 69.5 (C-13), 63.9 (C-8), 47.3 (C-3), 41.8 (C-15), 36.3 (C-14), 27.6 (C-16), 22.2 (C-19), 20.7 (OAc), 20.7 (OAc), 19.1 (C-17), 15.7 (C-18).

Taxane 19. A 1.0 M solution of lithium tri-*sec*-butylborohydride in THF (32 μL, 0.032 mmol) was added to THF (0.85 mL) at 4 °C. To this cooled solution was added dropwise 7-oxo-13-acetylbaccatin III **6** (5 mg; 0.008 mmol) dissolved in THF (165 μL). The solution was stirred for 2 h at 4 °C. The reaction was quenched with brine and extracted with ether, dried, filtered and evaporated in vacuo. The residue was purified by semi-preparative HPLC (25–100% CH_3CN in H_2O, 50 min gradient at a flow rate of 3 mL/min) affording **19** (1.45 mg, 30%, R_t = 43.25 min) and 13-acetyl-D-seco-5,6-dehydro-20-deacetylbaccatin III **7a** (1.25 mg, 27%, R_t = 35.07 min). FABHRMS of **19**: $C_{33}H_{38}O_{12}Na$ [M + Na$^+$] required 649.2261, found 649.2260; For ^{1}H and ^{13}C NMR data see Table 3.

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