Samarium Diiodide-Mediated Deoxygenation of Taxol: A One-Step Synthesis of 10-Deacetoxytaxol

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Received February 25, 1994

Taxol (**1**), a complex diterpene isolated in small quantities from the stem bark of *Taxus brevifolia* Nutt.,[1] the needles of the Himalayan *Taxus wallichiana* Zucc.,[2] and other yew species,[3] has recently been approved by the FDA for the treatment of cisplatin refractory ovarian cancer. Taxol (**1**) has captured the attention of the scientific community because of its exciting antitumor activity, unique mechanism of action, limited availability, and complex structure.[4-6] Currently, taxol (**1**) is undergoing extensive clinical trials to fully evaluate its potential against several other forms of cancer.[7] Structure–activity relationship studies of taxol analogues are of current interest to identify the taxol pharmacophore.[4-6,8] Recent reports[9-13] on the synthesis and biological evaluation of 10-deacetoxytaxol (**2**), prompted us to disclose our results on a high-yielding one-step synthesis of **2** via a SmI_2-mediated deoxygenation of taxol (**1**).[14] 10-Deacetoxytaxol (**2**) possesses biological activity comparable to taxol (**1**).[9,10]

Since the 10-acetoxy group of taxol (**1**) is located adjacent to the C-9 keto group, we reasoned that it might be possible to effect deoxygenation at C-10 with SmI_2.[15,16] We felt that this reaction might be suitable for the deoxygenation of taxol (**1**) because the reaction occurs under mild conditions and in the presence of a number of other functional groups.[17] It is also of note that the SmI_2-mediated deoxygenation can be applied successfully to sterically encumbered substrates.[17]

Prior approaches by Kingston *et al.*[9] and Chen *et al.*[11] utilized the Barton deoxygenation of 10-deacetylbaccatin III as the key step toward the synthesis of 10-deacetoxytaxol (**2**). The synthesis of **2** was accomplished by both groups in six steps (11 and 14% overall yield, respectively). Chen *et al.*[10] and Holton *et al.*[12] also disclosed a four-step synthesis of 10-deacetoxytaxol (**2**) in 4% overall yield from taxol (**1**) via a Yarovenko reagent–mediated dehydration of the C-10 hydroxyl group. Recently, a direct deoxygenation of 7-*epi*-taxol with tributyltin hydride and AIBN was reported by Chen *et al.*[13] However, this method provided poor yields and a mixture of products when taxol (**1**) or baccatin III (**3**) were subjected to the same reaction conditions.[13]

Our initial investigations involved modifications of baccatin III (**3**), a more readily available diterpene[18,19] which can be converted to taxol (**1**) in a few steps.[20,21] Treatment of a THF solution of baccatin III (**3**) with SmI_2,[22] in the presence of *tert*-butyl alcohol for 15 h, produced 10-deacetoxybaccatin III (**5**) in 45% yield together with about 40% of a 2:1 mixture[23] of 10-deacetoxy-7-*epi*-baccatin III (Figure 1, **7**)[24] and 10-deacetoxy-7-*epi*-13-oxobaccatin III (Figure 1, **8**). Additionally, 10% of the starting material, baccatin III (**3**), was recovered. 10-Deacetoxy-7-*epi*-13-oxobaccatin III (**8**) was characterized by ^1H NMR, ^{13}C NMR, and high resolution FAB MS. The ^1H NMR data for **8** are in good agreement with chemical shifts reported for 7-*epi*-13-oxobaccatin III.[25] The ^{13}C NMR of **8** is characterized by the presence of two ketone carbonyl groups, C-9 at 210.0 ppm and C-13 at 197.4 ppm. Similar ^{13}C NMR data were reported by McLaughlin *et al.* for 13-oxobaccatin III (C-9 at 202.05 ppm and C-13 at 197.96 ppm).[26] The oxidation of 10-deacetoxy-7-*epi*-baccatin III (**7**) to 10-deacetoxy-7-*epi*-13-oxobaccatin III (**8**) is presumably due to the reaction of **7** with *t*-BuOSmI_2, which is the oxidation product formed in the reduction of **3** with SmI_2 in the presence of *tert*-butyl alcohol.[27] The oxidation of **7** occurred slowly and the formation of **8** was observed by TLC only after about 4 h reaction time. It is interesting to note that 10-deacetoxy-7-*epi*-baccatin III (**7**) but not 10-deacetoxybaccatin III (**5**)

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(22) The investigations with *tert*-butyl alcohol as the proton source were carried out using 2 equiv of commercially available 0.1 M SmI_2 solution in THF. In these reactions we recovered considerable amounts of starting material. We then used 5 equiv of the commercially available 0.1 M SmI_2 solution in our studies with acetic acid as the proton source. No starting materials were recovered under these reaction conditions. Presumably, the SmI_2 concentration of the commercially available solution had decreased during storage. However, when we utilized a freshly prepared SmI_2 solution, only 2.5–3 equiv of SmI_2 were needed.
(23) The ratio of **7** and **8** was determined by ^1H NMR.
(24) The structures of the 7-*epi*-derivatives **7**–**9** were assigned by ^1H NMR in analogy to the ^1H NMR data for 7-*epi*-taxol.[38] The ^1H NMR resonance for H-7 of taxol (**1**) is found at 4.36 ppm and at 3.70 ppm for 7-*epi*-taxol. Similar chemical shifts were observed for 10-deacetoxybaccatin III (**5**) at 4.33 ppm, 10-deacetoxy-7-*epi*-baccatin III (**7**) at 3.73 ppm, 10-deacetoxytaxol (**2**) at 4.25 ppm, and 10-deacetoxy-7-*epi*-taxol (**9**) at 3.74 ppm.
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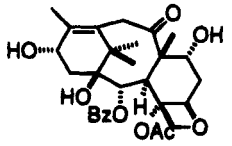
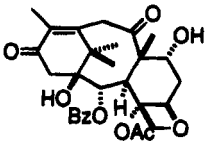
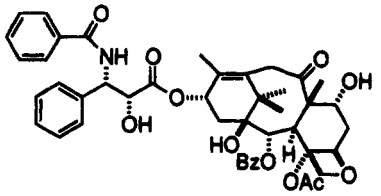


10-deacetoxy-7-*epi*-baccatin III (7)



10-deacetoxy-7-*epi*-13-oxobaccatin III (8)



10-deacetoxy-7-*epi*-taxol (9)

Figure 1. Structures of 10-deacetoxy-7-*epi*-baccatin III (**7**), 10-deacetoxy-7-*epi*-13-oxobaccatin III (**8**), and 10-deacetoxy-7-*epi*-taxol (**9**).

underwent allylic oxidation with *t*-BuOSmI$_2$. It has been suggested that the lack of reactivity of the C-13 hydroxyl group in 10-deacetoxybaccatin III (**5**) is probably due to hydrogen bonding with the C-4 acetyl carbonyl.[28,29] This hydrogen bond may be weakened in 10-deacetoxy-7-*epi*-baccatin III (**7**) due to competing hydrogen bonding between the C-7 *epi*-hydroxyl and the 4-acetoxy group.[30]

Since a considerable amount of 10-deacetoxy-7-*epi*-baccatin III (**7**) was formed during the SmI$_2$ reaction, we hoped that protection of the 7-hydroxyl group as a triethylsilyl ether would prevent the epimerization at C-7 and thus provide a better yield of the desired product. However, treatment of 7-triethylsilylbaccatin III (**4**)[18] with SmI$_2$/*tert*-butyl alcohol at room temperature for 24 h resulted in quantitative recovery of the starting material. This result is in agreement with observations by Chen *et al.*, who found that deoxygenation of 7-(triethylsilyl)taxol could not be effected with tributyltin hydride.[13] Presumably, the 7-triethylsilyl protecting group sterically encumbers the 9-keto group and prevents reaction.

The second, more successful strategy to suppress the formation of 10-deacetoxy-7-*epi*-baccatin III (**7**) involved a change from *tert*-butyl alcohol to acetic acid as the proton source.[22] Thus, treatment of baccatin III (**3**) with SmI$_2$ and acetic acid for 5 min yielded 10-deacetoxybaccatin III (**5**) in 86% yield as the sole reaction product (Scheme 1). This reaction is very reproducible at a scale of 15 mg (0.025 mmol) but when the reaction was carried out at a larger scale (30 mg, 0.05 mmol), we observed the formation of 87% 10-deacetoxybaccatin III (**5**), accompanied by 7% 10-deacetoxy-7-*epi*-baccatin III (**7**). 10-Deacetoxybaccatin III (**5**) and 10-deacetoxy-7-*epi*-baccatin III (**7**) can be easily separated by flash column chromatography.[31] 10-Deacetoxybaccatin III (**5**) was converted to the known compound 7-(triethylsilyl)-10-deacetoxybaccatin III (**6**) by treatment of **5** with triethylsilyl chloride in pyridine. Comparison of the spectral data of **6** (^{1}H NMR) with literature data verified the structural assignment for compound **5**.[12] 7-(Triethylsilyl)-10-deacetoxybaccatin III (**6**) has been converted to 10-dehydroxytaxotére in two steps.[12]

We were able to extend the SmI$_2$ reduction toward the direct deoxygenation of taxol (**1**). Treatment of taxol (**1**) with SmI$_2$ and acetic acid[22] provided 10-deacetoxytaxol (**2**) in 91% yield (Scheme 2).[32] Again some epimerization (6%) at C-7 was observed, when the reaction was carried out at a 50 mg scale. When taxol (**1**) was treated with SmI$_2$ and *tert*-butyl alcohol for 15 h, 10-deacetoxytaxol (**2**) was obtained in 37% yield together with 5% 10-deacetoxy-7-*epi*-taxol (**9**) and 54% of recovered taxol (**1**).[22]

The formation of C-7 epimerized products is presumably due to a retroaldol reaction. Similar retroaldol reactions are known to generate 7-*epi*-taxol from taxol (**1**) in the presence of polar solvents,[26,33] in cell culture medium,[34] under the influence of base,[13,25] and in the presence of Lewis acids.[35] In an effort to learn more about the influence of our reaction conditions on the epimerization at C-7, we investigated the behavior of baccatin III (**3**) and 10-deacetoxybaccatin III (**5**) in the presence of *t*-BuOSmI$_2$ and Sm(OAc)$_3$.[27] When THF solutions of baccatin III (**3**) and 10-deacetoxybaccatin III (**5**) were treated for 20 min with Sm(OAc)$_3$ we did not observe (^{1}H NMR and TLC) formation of C-7 epimerized products. Likewise, no epimerization was seen after subjecting a THF solution of baccatin III (**3**) for 20 min to *t*-BuOSmI$_2$. However, 10-deacetoxybaccatin III (**5**) readily epimerized under the same reaction conditions. 10-Deacetoxy-7-*epi*-baccatin III (**7**) formed within 1 minute and after a reaction time of 20 min, we observed (^{1}H NMR) a 2:1 ratio of 10-deacetoxy-7-*epi*-baccatin III (**7**) and 10-deacetoxybaccatin III (**5**). Thus, our studies suggested that *t*-BuOSmI$_2$ was responsible for the observed C-7 epimerization of 10-deacetoxybaccatin III (**5**). This may be due to the fact that *t*-BuOSmI$_2$ has more coordination sites available at the metal than Sm(OAc)$_3$ to initiate a Lewis acid-catalyzed epimerization. Of interest is also the observation that *t*-BuOSmI$_2$ readily epimerized 10-deacetoxybaccatin III (**5**) but did not cause epimerization of baccatin III (**3**) under the same reaction conditions. Possibly, the sterically less hindered and presumably conformationally more flexible C-9 keto group in 10-deacetoxybaccatin III (**5**) can more easily participate in the retroaldol reaction than can the C-9 keto group of baccatin III (**3**).

In summary, we have developed a high-yield one-step procedure for the synthesis of 10-deacetoxytaxol (**2**) from taxol (**1**) and 10-deacetoxybaccatin III (**5**) from baccatin III (**3**) via reduction with SmI$_2$ in the presence of acetic acid as the proton source.

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(29) It was recently shown that the C-13 hydroxyl group of a baccatin III derivative, devoid of the 4-acetyl group, was significantly more reactive than the C-13 hydroxyl group in baccatin III. Samaranayake, G.; Neidigh, K. A.; Kingston, D. G. I. *J. Nat. Prod.* **1993**, *56*, 884–898.

(30) It has been suggested that the C-7 epimerization may be partly due to hydrogen bonding between the C-4 acetate carbonyl and the 7-*epi* hydroxyl group.[28] Hydrogen bonding between the C-4 acetate carbonyl and the 7-*epi* hydroxyl group was observed in the X-ray structure of 7-*epi*-baccatin III. Castellano, E. E.; Hodder, O. J. R. *Acta Crystallogr. Sect. B* **1973**, *29*, 2566–2570.

(31) Thin layer chromatography on silica gel with ethyl acetate as the mobile phase reveals R_f values for **5** and **7** of 0.5 and 0.73, respectively.

(32) The ^{1}H NMR and FAB mass spectral data of 10-deacetoxytaxol (**2**) are identical with those reported by Kingston.[9]

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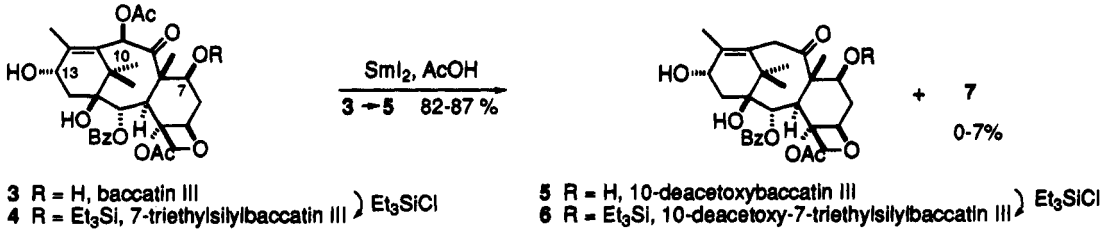
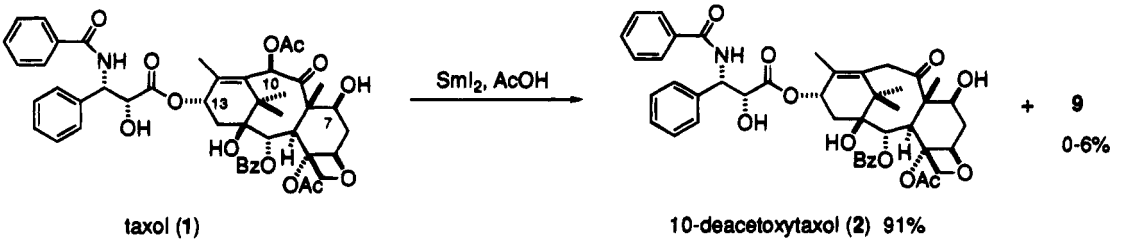
Scheme 1



Scheme 2



Experimental Section

For a description of general experimental procedures please see ref 36. All reactions were performed under a positive atmosphere of nitrogen or argon in oven-dried glassware. The commercially available 0.1 M solution of SmI_2 in THF was obtained from Aldrich. The freshly prepared SmI_2 solution was made according to the procedure of Kagan.[37]

Procedure for the Deoxygenation of Taxol (1) with SmI_2 and Acetic Acid as the Proton Source. Taxol (1) (50 mg, 0.058 mmol) in THF (1.5 mL) and acetic acid (8.7 μL) was treated with a freshly prepared SmI_2 solution (1.46 mL of a 0.1 M THF solution, 0.146 mmol) and stirred for 20 min at room temperature. After adding another 0.5 equiv of SmI_2 (0.29 mL of a 0.1 M THF solution, 0.029 mmol), the reaction was stirred for another 5 min and then poured into a saturated K_2CO_3 solution. The aqueous phase was extracted with ether (2 × 10 mL). The combined extracts were dried over anhydrous Na_2SO_4. The solvent was evaporated and the residue purified by silica gel flash column chromatography using ethyl acetate/hexanes (gradient of 35:65 to 50:50 ratio) as the eluent to afford **2** as a colorless foam (41.8 mg, 91%).

Procedure for the Deoxygenation of Taxol (1) with SmI_2 and *tert*-Butyl Alcohol as the Proton Source.[22] Taxol (1) (10 mg, 0.0117 mmol) in THF (0.5 mL) and *tert*-butyl alcohol (0.5 mL) was treated with SmI_2 (0.23 mL of a 0.1 M commercially available THF solution, 0.023 mmol) and stirred at room temperature for 15 h. The reaction mixture was then poured into saturated K_2CO_3. The aqueous phase was extracted with ether (2 × 10 mL). The combined extracts were dried over anhydrous Na_2SO_4. The solvent was evaporated and the residue purified by silica gel flash column chromatography using ethyl acetate/hexanes (gradient of 35:65 to 50:50 ratio) as the eluent to afford **2** (3.6 mg, 37%) as a colorless foam and 5.4 mg (54%) of starting material.

10-Deacetoxytaxol (2): colorless solid, mp 165–167 °C dec (CH_2Cl_2/pentane); $[\alpha]_D$ −74.3° (c = 0.26, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 8.10 (2H, d, J = 7.2 Hz), 7.74 (2H, d, J = 6.9 Hz), 7.60 (1H, t, J = 7.2), 7.54–7.28 (10H, m), 7.08 (1H, d, J = 9.0 Hz), 6.09 (1H, bt, J = 7.2 Hz,), 5.77 (1H, dd, J = 2.4, 9.0 Hz), 5.67 (1H, d, J = 6.9 Hz), 4.92 (1H, d, J = 7.8 Hz), 4.76 (1H, d, J = 2.1 Hz), 4.28 (1H, d, J = 8.1 Hz), 4.25 (1H, m), 4.17 (1H, d, J = 8.4 Hz), 4.02 (1H, d, J = 6.9 Hz), 3.75 (1H, d, J = 15.9 Hz), 3.64 (1H, bs), 3.40 (1H, b d, J = 15.6 Hz), 2.59 (1H, m), 2.35 (3H, s), 2.28 (2H, m), 1.78 (1H, m), 1.64 (3H, s), 1.62 (3H, s), 1.15 (3H, s), 1.14 (3H, s); HRMS-FAB m/z calcd for $C_{45}H_{49}NO_{12}$Li (M + Li) 802.3415, found 802.3394.

Procedure for the Deoxygenation of Baccatin III (3) with SmI_2 and Acetic Acid as the Proton Source. Baccatin III (3) (30 mg, 0.050 mmol) in THF (1.0 mL) and acetic acid (0.0054 mL) was treated with a freshly prepared SmI_2 solution (1.25 mL of a 0.1 M THF solution, 0.125 mmol), stirred for 10 min at room temperature, and then poured into saturated K_2CO_3. The aqueous phase was extracted with ether (2 × 15 mL). The combined extracts were dried over anhydrous Na_2SO_4. The solvent was evaporated and the residue purified by silica gel flash column chromatography using ethyl acetate/hexanes (gradient of 35:65 to 50:50 ratio) as the eluent to afford **5** as a colorless foam (22.6 mg, 87%).

Procedure for the Deoxygenation of Baccatin III (3) with SmI_2 and *tert*-Butyl Alcohol as the Proton Source.[22] Baccatin III (3) (15 mg, 0.025 mmol) in THF (0.5 mL) and *tert*-butyl alcohol (0.5 mL) was treated with SmI_2 (0.5 mL of a 0.1 M commercially available THF solution, 0.05 mmol), stirred for 15 h at room temperature, and then poured into saturated K_2CO_3. The aqueous phase was extracted with ether (2 × 10 mL). The combined extracts were dried over anhydrous Na_2SO_4. The solvent was evaporated and the residue purified by silica gel flash column chromatography using ethyl acetate/hexanes (gradient of 35:65 to 50:50 ratio) as the eluent to afford 6.1 mg of **5** as a colorless foam (45%), 5.4 mg (40%) of a 2:1 mixture of 10-deacetoxy-7-*epi*-baccatin III (**7**), and 10-deacetoxy-7-*epi*-13-oxo-baccatin III (**8**). About 1.5 mg (10%) of **3** was recovered as well.

10-Deacetoxybaccatin III (5): colorless solid, mp 206–208 °C dec (CH_2Cl_2/pentane); $[\alpha]_D$ −105.5° (c = 0.60, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 8.09 (2H, d, J = 7.2 Hz), 7.59 (1H, t, H = 7.5 Hz), 7.46 (2H, t, J = 7.8 Hz), 5.63 (1H, d, J = 6.9 Hz), 4.95 (1H, d, J = 7.8 Hz), 4.80 (1H, bs), 4.33 (1H, m), 4.30 (1H, d, J = 8.4 Hz), 4.14 (1H, d, J = 8.1 Hz), 4.16 (1H, d, J = 6.3 Hz), 3.81 (1H, d, J = 15.6 Hz), 3.44 (1H, b d, J = 15 Hz), 2.62 (1H, m), 2.27 (3H, s), 2.25 (2H, m), 1.92 (3H, s), 1.78 (1H, m), 1.61 (3H, s), 1.11 (3H, s), 1.04 (3H, s); HRMS-FAB m/z calcd for $C_{29}H_{36}O_9$Li (M + Li) 535.2519, found 535.2538.

10-Deacetoxy-7-(triethylsilyl)baccatin III (6). After adding triethylsilyl chloride (0.038 mL, 0.229 mmol) to **5** (6 mg, 0.0114 mmol) in pyridine (0.57 mL), the reaction mixture was stirred at room temperature for 20 h. The reaction mixture was then poured into water (2 mL). The aqueous phase was extracted with CH_2Cl_2 (2 × 10 mL). The combined CH_2Cl_2 solutions were extracted with 3 N HCl (2 × 2 mL) and then dried over anhydrous Na_2SO_4. The solvent was evaporated and the residue purified by silica gel flash column chromatography using ethyl acetate/hexanes (gradient of 35:65 to 50:50 ratio) as the eluent to afford **6** in 83% yield as a colorless foam. Recrystallization provided a colorless solid: mp 122–125 °C (CH_2Cl_2/pentane); $[\alpha]_D$ −78.9° (c = 0.17, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 8.09 (2H, d, J = 7.2 Hz), 7.58 (1H, bt, J = 7.2 Hz), 7.45 (2H, t, J = 7.8 Hz), 5.59 (1H, d, J = 6.6 Hz), 4.94 (1H, d, J = 7.8 Hz), 4.80 (1H, bt), 4.49 (1H, dd, J = 10.5 Hz, 6.9 Hz), 4.27 (1H, d, J = 8.1 Hz), 4.13 (1H, d, J = 8.1 Hz), 4.08 (1H, d, J = 6.9 Hz), 3.75 (1H,

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Table 1. ^{1}H NMR Data for Aliphatic Protons and NH in ppm for 1–2 and 5–9[a]

protons at	1	2	5	6	7	8	9
C-2	5.67 (d, 7.0)	5.67 (d, 6.9)	5.63 (d, 6.9)	5.59 (d, 6.6)	5.71 (d, 7.5)	5.81 (d, 6.9)	5.74 (d, 7.2)
C-2′	4.78 (d, 2.6)	4.76 (d, 2.1)					4.76 (bs)
C-3	3.77 (d, 7.0)	4.02 (d, 6.9)	4.16 (d, 6.3)	4.08 (d, 6.9)	4.32 (d, 7.2)	4.26 (d, 7.2)	4.17 (d, 7.2)
C-3′	5.76 (dd, 2.0, 9.0)	5.77 (dd, 2.4, 9.0)					5.79 (dd, 2.4, 9)
C-4 OAc	2.36 (s)	2.35 (s)	2.27 (s)	2.26 (s)	2.35 (s)	2.25 (s)	2.48 (s)
C-5	4.92 (d, 8.0)	4.92 (d, 7.8)	4.95 (d, 7.8)	4.94 (d, 7.8)	4.91 (dd, 4.2, 8.6)	4.88 (dd, 3.9, 9.2)	4.88 (dd, 5.1, 7.8)
C-6a	1.85 (m)	1.78 (m)	1.78 (m)	1.85 (m)	1.97 (m)	2.22–2.24 (m)	2.18–2.47 (m)
C-6b	2.49 (m)	2.59 (m)	2.62 (m)	2.47 (m)	2.20–2.28 (m)	2.22–2.24 (m)	2.18–2.47 (m)
C-7	4.36 (m)	4.25 (m)	4.33 (m)	4.49 (dd, 6.9, 10.5)	3.73 (ddd, 2.4, 4.8, 11.7)	3.74 (ddd, 2.1, 4.5, 12)	3.74 (dd, 3.3, 12)
C-10	6.26 (s)	3.75, 3.40 (ABq, 15.9)	3.44, 3.81 (ABq, 15.6)	3.37, 3.75 (ABq, 15)	3.42, 4.11 (ABq, 16.2)	3.70, 4.32 (ABq, 15.9)	3.39, 4.06 (ABq, 16.3)
C-10 OAc	2.22 (s)						
C-13	6.20 (bt, 9)	6.09 (bt, 7.2)	4.80 (bs)	4.80 (bt)	4.78 (bs)		6.14 (bt, 7.2)
C-14	2.28 (m)	2.28 (m)	2.25 (m)	2.24 (m)	2.20–2.28 (m)	2.64, 3.03 (ABq, 10.8)	2.18–2.47 (m)
C-16/17	1.13 (s)	1.14 (s)	1.04 (s)	1.03 (s)	1.01 (s)	1.13 (s)	1.06 (s)
C-17/16	1.21 (s)	1.15 (s)	1.11 (s)	1.12 (s)	1.03 (s)	1.18 (s)	1.13 (s)
C-18	1.77 (s)	1.64 (s)	1.92 (s)	1.94 (s)	1.84 (s)	1.86 (s)	1.63 (s)
C-19	1.67 (s)	1.62 (s)	1.61 (s)	1.60 (s)	1.57 (s)	1.56 (s)	1.59 (s)
C-20	4.17, 4.27 (ABq, 8)	4.17, 4.28 (ABq, 8.1)	4.14, 4.30 (ABq, 8.1)	4.13, 4.27 (ABq, 8.1)	4.38, 4.39 (ABq, 8.7)	4.33, 4.39 (ABq, 8.7)	4.39 (s)
NH	7.22 (d, 9)	7.08 (d, 9)					7.00 (d, 9)

[a] Multiplicities and coupling constants in hertz are given in parentheses. The spectrum of 1 was recorded at 500 MHz; all other data were obtained at 300 MHz.

d, J = 14.7 Hz), 3.37 (1H, b d, J = 15.2 Hz), 2.47 (1H, m), 2.26 (3H, s), 2.24 (2H, m), 1.94 (3H, s), 1.85 (1H, m), 1.60 (3H, s), 1.12 (3H, s), 1.03 (3H, s), 0.93 (9H, t, J = 7.8 Hz), 0.55 (6H, m); HRMS-FAB m/z calcd for $C_{35}H_{51}O_9Si$ (MH^+) 643.3302, found 643.3303.

10-Deacetoxy-7-*epi*-baccatin III (7): colorless solid, mp 135–138 °C (CH_2Cl_2/pentane); $[\alpha]_D$ −91.8° (c = 0.34, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.11 (2H, d, J = 6.9 Hz), 7.60 (1H, t, J = 7.2 Hz), 7.47 (2H, t, J = 7.5 Hz), 5.71 (1H, d, J = 7.5 Hz), 4.91 (1H, dd, J = 4.2, 8.6 Hz), 4.78 (1H, bs), 4.72 (1H, d, J = 11.7 Hz), 4.39 (1H, d, J = 8.7 Hz), 4.38 (1H, d, J = 8.7 Hz), 4.32 (1H, d, J = 7.2 Hz), 4.11 (1H, d, J = 16.2 Hz), 3.73 (1H, ddd, J = 2.4, 4.8, 11.7 Hz), 3.42 (1H, b d, J = 16.2 Hz), 2.35 (3H, s), 2.20–2.28 (3H, m), 1.97 (1H, m), 1.84 (3H, s), 1.57 (3H, s), 1.03 (3H, s), 1.01 (3H, s); HRMS-FAB m/z calcd for $C_{29}H_{36}O_9Li$ 535.2519, found 535.2498.

10-Deacetoxy-7-*epi*-13-oxobaccatin III (8): colorless solid, mp 201–203 °C (CH_2Cl_2/pentane); $[\alpha]_D$ −38.9° (c = 0.54, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.07 (2H, d, J = 7.2 Hz), 7.63 (1H, t, J = 7.2 Hz), 7.49 (2H, t, J = 7.8 Hz), 5.81 (1H, d, J = 6.9 Hz), 4.88 (1H, dd, J = 3.9, 9.2 Hz), 4.46 (1H, d, J = 12 Hz), 4.39 (1H, d, J = 8.7 Hz), 4.33 (1H, d, J = 8.7 Hz), 4.32 (1H, d, J = 15.9 Hz), 4.26 (1H, d, J = 7.2 Hz), 3.74 (1H, ddd, J = 2.1, 4.5, 12 Hz), 3.70 (1H, b d, J = 15.3 Hz), 3.03 (1H, d, J = 19.8 Hz), 2.64 (1H, d, J = 19.8 Hz), 2.25 (3H, s), 2.24–2.22 (2H, m), 1.86 (3H, s), 1.56 (3H, s), 1.18 (3H, s), 1.13 (3H, s). HRMS-FAB m/z calcd for $C_{29}H_{34}O_9Li$: 533.2363, found 533.2358.

10-Deacetoxy-7-*epi*-taxol (9): colorless solid, mp 156–159 °C dec (CH_2Cl_2/pentane); $[\alpha]_D$ −46.2° (c = 0.42, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.15 (2H, d, J = 6.9 Hz), 7.71 (2H, d, J = 6.9 Hz), 7.61 (1H, t, J = 7.5 Hz), 7.55–7.30 (10H, m), 7.00 (1H, d, J = 9 Hz), 6.14 (1H, bt, J = 7.2 Hz), 5.79 (1H, dd, J = 2.4, 9 Hz), 5.74 (1H, d, J = 7.2 Hz), 4.88 (1H, dd, J = 5.1, 7.8 Hz), 4.76 (1H, bs), 4.56 (1H, d, J = 11.7 Hz), 4.39 (2H, s), 4.17 (1H, d, J = 7.2 Hz), 4.06 (1H, d, J = 16.5 Hz), 3.74 (1H, dd, J = 3.3, 12 Hz), 3.46 (1H, d, J = 4.5 Hz), 3.39 (1H, b d, J = 16.3 Hz), 2.48 (3H, s), 2.47–2.18 (4H, m), 1.63 (3H, s), 1.59 (3H, s), 1.13 (3H, s), 1.06 (3H, s); FAB MS m/z calcd for $C_{45}H_{49}NO_{12}$ 795, found 795.

General Procedure Used for the Reaction of *t*-BuOSmI$_2$ with Baccatin III (3) and *t*-BuOSmI$_2$ with 10-Deacetoxybaccatin III (5). SmI_2 (0.42 mL of a commercially available 0.1 M solution in THF, 0.042 mmol) was added to di-*tert*-butyl peroxide (0.0039 mL, 0.025 mmol) at room temperature.[27] Decoloration of the deep blue color to yellow occurred immediately. After stirring for 15 min, baccatin III (3) (5 mg, 0.0085 mmol) or 10-deacetoxybaccatin III (5) (5 mg, 0.0092 mmol) in THF (0.5 mL) was added. The reaction was followed by TLC. After 20 min the reaction was worked up as described above and analyzed by ^{1}H NMR.

General Procedure Used for the Reaction between Sm(OAc)$_3$ and Baccatin III (3) and between Sm(OAc)$_3$·H$_2$O and 10-Deacetoxybaccatin III (5). $Sm(OAc)_3{\cdot}H_2O$ (12.5 mg, 0.038 mmol) was added to a solution of baccatin III (3) (4.5 mg, 0.0077 mmol) or 10-deacetoxybaccatin III (5) (4.5 mg, 0.0083 mmol) in THF (0.5 mL) at room temperature. The reaction was followed by TLC. After 20 min the reaction was worked up as described above and analyzed by ^{1}H NMR.

Acknowledgment. These studies were supported by a grant from the National Institutes of Health (CA 55160) and the J. R. and Inez Jay Research Fund at the University of Kansas. We are also grateful to the Kansas Health Foundation for a postdoctoral fellowship awarded to Z. S. Cheruvallath. A mixture of taxol (1)[39] and cephalomannine was provided to us for these studies by the National Cancer Institute. The authors would also like to thank G. C. B. Harriman and T. C. Boge for a literature search on the SmI_2 reaction, for suggesting the use of acetic acid as the proton source, and for helpful discussions.

Supplementary Material Available: Copies of ^{1}H NMR spectra of **2**, **5–9** (6 pages). The material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(39) Taxol (1) was obtained from a mixture of cephalomannine and taxol as described by Kingston: Kingston, D. G. I.; Gunatilaka, A. A. L.; Ivey, C. A. *J. Nat. Prod.* **1992**, *55*, 259–261.