Pergamon

Tetrahedron Vol. 50, No. 23, pp. 6881-6890, 1994

0040-4020/94 $7.00+0.00

0040-4020(94)E0333-O

Cleavage Reactions of 10-Deacetylbaccatin III. Retrosynthetic Approach to the Total Synthesis of Taxol Derivatives.

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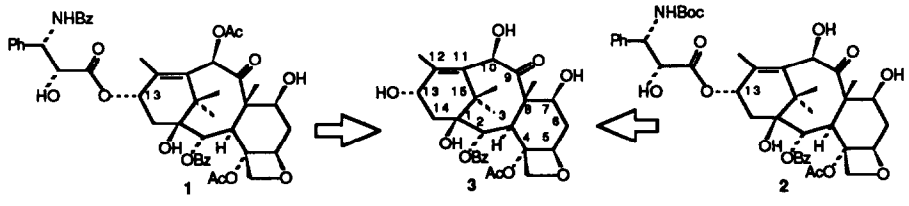
Abstract: With the aim to study disconnection/connection reactions of the taxane skeleton, the synthesis of products resulting from the cleavage of the C(1)-C(2), C(9)-C(10) and C(11)-C(12) bonds of 10-deacetylbaccatin III, a taxol precursor, is described. They represent models to study ring closure reactions starting from highly functionalized taxane derivatives.

Taxol® **1**, a diterpene isolated in only low yield from the bark of several species of the *Taxus* genus,[1] and Taxotère® **2**, a semisynthetic analogue,[2] are currently the most promising new drugs studied in the field of cancer chemotherapy.[3] In spite of scarcity of Taxol **1** from natural sources, each of these substances can now be fortunately secured in good yield from the appropriate hydroxyl-protected side-chain[4] and 10-deacetylbaccatin III **3**, a natural precursor from the leaves of European yew, *Taxus baccata*.[5]



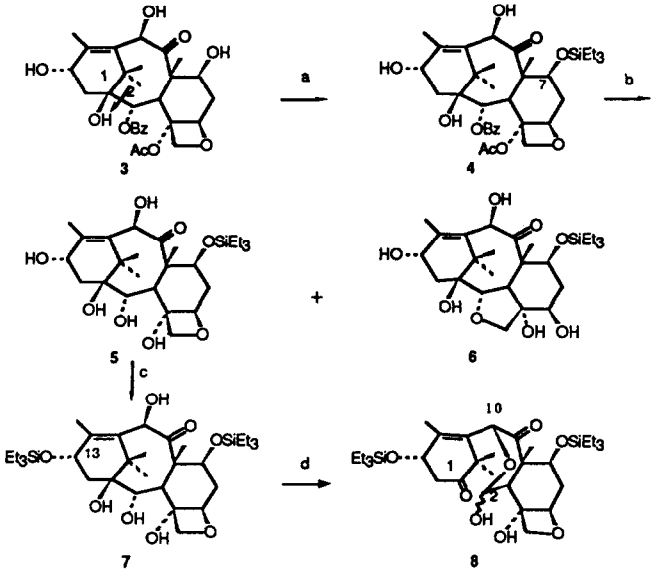
The unusually potent antileukemic and tumor inhibitory properties of Taxol **1**, combined with its highly challenging structure have stimulated considerable synthetic activity[6] in a number of laboratories, most of them with the aim of its total synthesis. We decided to investigate disconnection/connection reactions of 10-deacetylbaccatin III **3**, as means to study chemical properties of the cleavage products and to help in the choice of a synthetic scheme. Moreover, this approach could show some new aspects of the reactivity of this complex molecule and lead to interesting new compounds.

In the present paper we describe reactions we carried out starting from 10-deacetylbaccatin III **3**, which seems to be suited for cleavage reactions of the C(1)-C(2), C(9)-C(10) and C(11)-C(12) bonds.

Cleavage of the C(1)-C(2) bond

Periodate oxidation of a 2-debenzoyl derivative of **3** could be an easy reaction to realize the cleavage of the C(1)-C(2) bond. The C(7)-hydroxyl of 10-deacetylbaccatin III **3** was first protected as its triethylsilyl ether **4**,[4a] in order to avoid its epimerization *via* retroaldolization,[7] during the alkaline treatment necessary to hydrolyse the C(2) and C(4)-ester moieties. The C(13)-hydroxy group was inert under these conditions. The ester functionalities were then cleanly hydrolyzed with 0.25 N sodium methoxide in methanol, giving **5** in 63% yield and **6**, in 23% yield. This latter compound results from the rearrangement of the γ-hydroxy-oxetane into a tetrahydrofuran ring, when the C(2) hydroxyl is deacylated.[8] Deacetylation of the C(4) hydroxyl rendering the C(13)-hydroxyl of **5** less hindered, this position could be selectively protected as triethylsilyl ether **7**. A 2D-COSY experiment clearly shows coupling between C(2)-H/OH and C(10)-H/OH, indicating that these positions were not affected by the silylation reaction. Sodium metaperiodate oxidation of **7**, performed in aqueous EtOH at pH 5,[9] gave the ketolactol **8**, by reaction of the C(10)-hydroxyl with the newly formed C(2)-carbaldehyde functionality (Scheme 1). This compound exists as a mixture of isomers at the C(2) position. During its purification on silica gel a small amount of a 11,13-diene was formed by elimination of the C(13)-triethylsilyloxy group.

Scheme 1

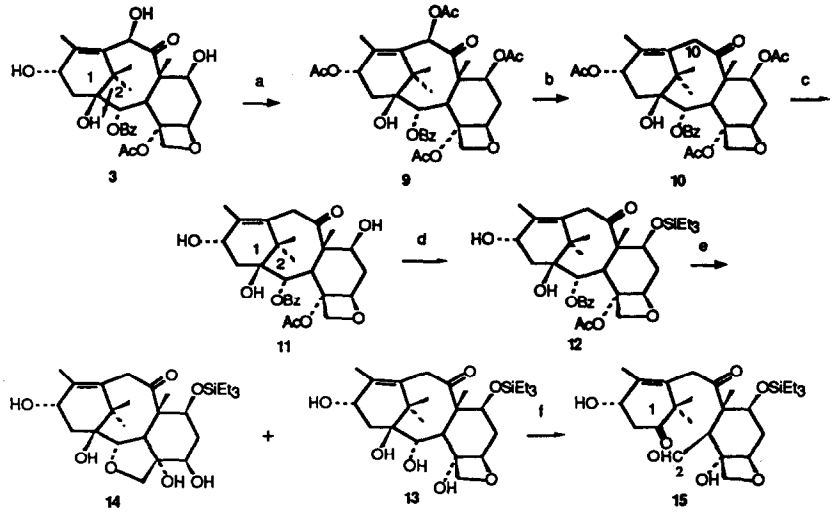


a) Et_3SiCl (10 eq.), py, rt, 24 h (93%); b) 0.25 N MeONa / MeOH, rt, 4 h, **5** (63%), **6** (23%); c) Et_3SiCl (1.1 eq.), py, rt, 3 min (quantitative); d) $NaIO_4$, pH 5 buffer, EtOH, rt, 1.5 h (75%).

To prevent the lactolization reaction, the protection of the C(10)-hydroxyl would be necessary. As we found difficulties to introduce a base-resistant protective group at this position, we prepared a 10-deoxy compound (Scheme 2).

Treatment of **3** with acetic anhydride and a catalytic amount of DMAP in pyridine gave the 7,10,13-triacetyl derivative **9**[10] which was reduced to 7,13-diacetyl-10-deacetoxybaccatin III **10** with samarium diiodide, in the presence of MeOH.[11] Reaction with diisobutylaluminium hydride effected the selective cleavage of the C(7) and C(13)-acetyl groups and the C(7)-hydroxyl of **11** was then protected as triethylsilyl ether **12**. Hydrolysis of the C(2) and C(4) ester functionalities with methanolic sodium methoxide gave a mixture of diol **13** in 60% yield and of its tetrahydrofuran rearranged analogue **14**. Oxidation of **13** with sodium metaperiodate at pH 5 led to keto-aldehyde **15**, which represents a good candidate for the study of intramolecular pinacolic reactions.

Scheme 2



a) Ac_2O, py, DMAP (cat.), rt, 24 h (87%); b) SmI_2 (8 eq.), MeOH (4 eq.), THF, rt, 6 h (97%); c) DIBAH (10 eq.), THF, -78°C, 5 h (80%); d) Et_3SiCl (20 eq.), py, rt, 24 h (98%); e) 0.25 N MeONa / MeOH, rt, 5 h, **13** (60%), **14** (30%); f) $NaIO_4$, EtOH, pH 5, rt, 1.25 h (99%).

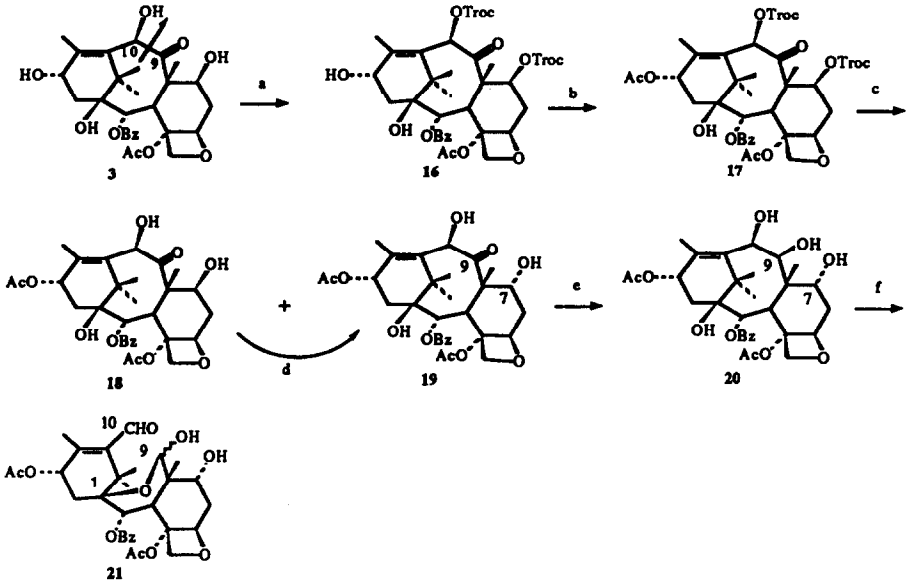
Cleavage of the C(9)-C(10) bond

Direct cleavage of the C(9)-C(10)-ketol system with periodic acid, potassium permanganate or lead tetracetate being unsuccessful, reduction of the C(9)-ketone was carried out before periodate cleavage. To our knowledge, the chemical reduction of this ketone has not been described.[12] However, we found that its reduction by diborane proceeds cleanly in the 7α-hydroxy-series. Furthermore, this electrophilic reagent did not affect the ester functionalities. 7,10-di-trichloroethylcarbonyl-baccatin III (di-Troc) **16**[7b] was reacted with acetic anhydride in pyridine to afford the 13-acetyl derivative **17**. The cleavage of the O-Troc protective groups, realized with Zn in refluxing methanol,[7b] gave a mixture of 13-acetyl-10-deacetylbaccatin III, **18**, and 13-acetyl-10-deacetyl-7-*epi*-baccatin III, **19**. The 7β-hydroxy compound **18** could be epimerized by heating in deoxygenated toluene in the presence of a catalytic amount of DBU. Reduction of the (9)-ketone of **19** was then effected by $BH_3{\cdot}SMe_2$ in toluene giving 1β,7α,9β,10β-tetrol **20**. Assistance of the 7α-hydroxy-group could be involved to explain this stereoselective reduction which led to the 9β-hydroxy derivative as the only product. The 7β-hydroxy isomer is

not reduced under these conditions. The stereochemistry at C(9) was confirmed by the presence of a nOe interaction between the C(9)-H and the C(3)-H in a 2D-NOESY experiment. Oxidative cleavage of the C(9)-C(10) bond led to lactol-aldehyde **21**, as a single isomer, but we were unable to establish the stereochemistry of the hemiacetal hydroxyl.

Until now, our efforts to efficiently protect the C(1)-hydroxyl to prevent this cyclisation reaction have been unsuccessful.

Scheme 3

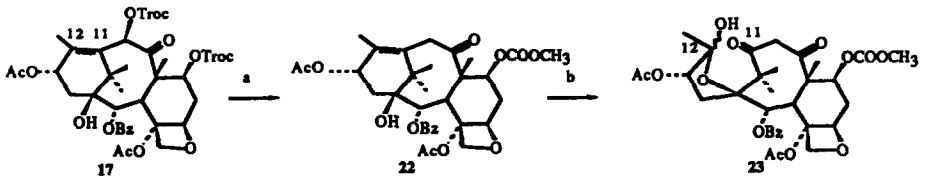


a) Troc-Cl (2 eq.), py, 80°C, 5 min (93 %); b) Ac_2O, py, DMAP (cat.), rt, 24 h (quantitative); c) Zn, MeOH, reflux, 15 h, **18** (48%), **19** (52%); d) DBU (cat.), toluene, 80°C, 0.5 h (80 %); e) $BH_3{\cdot}SMe_2$ (3 eq.), toluene, 0°C, 2 h, then rt, 2 h (84%); f) $NaIO_4$, EtOH, pH 5, rt, 2 h (97%).

Cleavage of the C(11)-C(12) bond.

The cleavage of an olefinic linkage can be carried out by periodate oxidation after OsO_4 or $KMnO_4$ *cis*-hydroxylation,[13] or by direct RuO_4 oxidation.[14] 7-triethylsiloxybaccatin III **4** remained unchanged upon standard treatment with OsO_4 or RuO_4. However, we found that the 10-deoxy analogues underwent C(11)-C(12) double bond cleavage with RuO_4. Therefore, reductive elimination of the C(10)-carbonate of 13-acetyl-7,10-di-Troc-10-deacetyl-baccatin III **17** with SmI_2/MeOH in THF (Scheme 4) was carried out to give **22** in which we observed the concomitant transformation of the C(7)-O-Troc into a methyl carbonate. RuO_4 oxidation cleaved the 11,12-double bond to give ketolactol **23**, as a single product, of which configuration at C(12) has not been established. This structure was assigned by ^{13}C-^{1}H correlation, COSY and NOESY experiments, specially concerning the hemiketal linkage between the C(12)-ketone and the C(1)-hydroxyl.

Scheme 4



a) SmI_2 (8 eq.), THF, MeOH (4 eq.), rt, 20 min (88%); b) RuO_2 (1 eq.), CH_2Cl_2, aqueous $NaIO_4$ (2.5 eq.), rt, 4 h (76%).

The analogue of compound **21** with at C(13) the Taxotère® side-chain, possesses all the functionalities of the South-part of active compounds and shows a 50% inhibition of the rate of diassembly (IC_{50}) of tubuline with concentration 400-fold that of Taxotère®.[3]

Thus, with these four compounds, **8**, **15**, **21** and **23**, in our hands, our efforts are currently concentrated on ring closure studies.

Acknowledgments: We thank Professor P. Potier for his encouragement. S. Py is grateful to the "Ligue nationale contre le Cancer" for a grant. Rhône-Poulenc Rorer is thanked for a gift of 10-deacetylbaccatin III 3. J. Dubois is thanked for having carried out the tubuline test.

Experimental

Melting points (m.p.) were determined in capillary tubes and are uncorrected. Optical rotations, $[\alpha]_D$ were measured in $CHCl_3$ with 0.5% EtOH, or in MeOH, at 20°C, on a PERKIN-ELMER 241 polarimeter. IR spectra were determined with a NICOLET FT-IR 205 spectrometer. ^1H and ^{13}C NMR spectra were recorded on BRUKER AC-200, AC-250, AC-300 or WM-400 instruments, and they were performed in $CDCl_3$, unless otherwise stated. Chemical shifts (δ) are expressed in ppm, coupling constants in Hz, assignments are based on ^1H-^1H et ^1H-^{13}C correlations. 2D-NOESY experiments were performed at 250 MHz, with a 600 ms mixing time. Mass spectra (MS) were run on Kratos MS-80 (FAB or LSIMS) or AEI MS-9 (CI) spectrometers. Diethyl ether and tetrahydrofuran were distilled from sodium-benzophenone ketyl, dichloromethane from phosphorous pentoxide, toluene from sodium. Other solvents and reagents were purified by standard procedures as necessary.[15] The nomenclature which is used for new compounds is derived from baccatin III used as reference. Numbering of the carbon atoms follows the natural product numbering system. Column chromatography was performed on Merck Kieselgel 60, flash column chromatography on Merck Kieselgel 60H. Analytical thin layer chromatography was performed using pre-coated foils F 1500/LS 254, Schleicher & Schuell.

2-debenzoyl-4,10-bisdeacetyl-7,13-bistriethylsilylbaccatin III, 7.
Chlorotriethylsilane (0.045 mL, 0.23 mmol), was added to a solution of **5** (129 mg, 0.21 mmol) in pyridine (3 mL). The reaction proceeded nearly instantaneously, at room temperature, under argon. The medium was made neutral with aqueous sodium bicarbonate and extracted three times with CH_2Cl_2. After evaporation of the solvent, the residue was purified by silicagel column chromatography to give **7** (131 mg, quantitative), as a white foam, amorphous; $[\alpha]_D$ = -73 (c=1.4, $CHCl_3$); Anal. calcd. for $C_{32}H_{58}O_8Si_2$ %: C 61.30, H 9.32; found %: C 61.32, H 9.39; IR ($CHCl_3$) ν, cm^{-1}: 3531, 3463, 3363 (O-H), 1700 (C=O ketone), 1606 (C=C), 1268 (C-O); FABMS m/z: 649 $[M+Na]^+$, 535 $[M+Na-SiEt_3]^+$, 237, 149, 115; ^1H NMR (200 MHz) δ: 0.52 (6H, q, J=8, CH_2Si, C-7), 0.72 (6H, q, J=8, CH_2Si, C-13), 0.92 (9H, t, J=8, $\underline{CH_3}CH_2Si$, C-7), 0.98 (9H, t, J=8, $\underline{CH_3}CH_2Si$, C-13), 1.01 (3H, s, C-16H_3), 1.08 (3H, s, C-17H_3), 1.61 (3H, s, C-19H_3), 1.96 (3H, s, C-18H_3), 2.07 (2H, m, C-6H and C-14H), 2.43 (2H, m, C-6H and C-14H), 3.22 (1H, s, OH), 3.26 (1H, d, J=6, C-3H), 3.46 (1H, d, J=9, OH), 3.74 (1H, dd, J=9, J'=6, C-2H), 3.94 (1H, dd, J=11, J'=6, C-7H), 4,17 (2H, 2s, 2 OH), 4.43 and 4.72 (2H, 2d, J=8, C-20H_2), 4.64 (1H, bd, J=9, C-13H), 4.73 (1H, dd, J=9, J'=2, C-5H), 5.11 (1H, d, J=2, C-10H).

1-Deoxy-2-debenzoyloxy-4,10-deacetyl-7,13-triethylsilyl-1,2-dioxo-1,2-*seco*-baccatin III, 2,10-hemiacetal, 8.

Sodium metaperiodate (97 mg, 0.44 mmol) was added to a solution of **7** (103 mg, 0.16 mmol) in EtOH (10 mL) and aqueous acetic acid/ammonia buffered solution (pH 5-6, 7 mL). The reaction was stirred at room temperature for 1.5 h. Aqueous $Na_2S_2O_7$ was added before extraction with CH_2Cl_2. The organic phases were washed with brine, dried over $MgSO_4$ and evaporated. Column chromatography of the residue gave **8** (77 mg, 75%), amorphous, Anald calc. for $C_{32}H_{56}O_8Si_2$, 0.5 OH_2 %: C 60.64, H 9.06, Si 8.85; found %: C 60.63, H 8.78, Si 8.96; CIMS (NH_3) m/z: 642 $[M+NH_4]^+$, 624 $[M+NH_4-H_2O]^+$; ^1H NMR (200 MHz) 2β OH isomer, δ: 0.58 (12H, m, 2 CH_2Si), 0.88 (9H, t, J=8, CH_3CH_2Si), 0.92 (9H, t, J=8, CH_3CH_2Si), 0.95 (3H, s, C-17H_3), 1.22 (3H, s, C-16H_3), 1.66 (3H, s, C-19H_3), 1.87 (3H, s, C-18H_3), 2.43 (2H, m, C-6H and C-14H), 3.22 (1H, s, OH), 3.26 (1H, d, J=6, C-3H), 4.18 (1H, t, J=7, C-7H), 4.42 and 5,17 (2H, 2d, J=8, C-20H_2), 4.64 (1H, bd, J=9, C-13H), 4.73 (1H, dd, J=9, J'=2, C-5H), 5.44 (1H, bs, C-10H), 5.46 (1H, s, C-2H).

7,13-Diacetyl-10-deacetoxy-baccatin III, 10.

7,13-Diacetylbaccatin III **9**[10] (2.44 g, 3.6 mmol) was introduced in a septum-closed round-bottomed flask with a magnetic stirrer. Through a needle, successively vacuum and introduction of argon were effected many times. THF (20 mL) was added to dissolve **9** and then, SmI_2 (96 mL of 0.3 M solution in THF, 28.8 mmol) and MeOH (0.15 mL) were added. The mixture was stirred for 6 h at room temperature. Aqueous 10% HCl (5 mL) was added and the organic products were extracted three times with ethyl acetate. The combined organic phases were washed with brine, dried on $MgSO_4$ and evaporated to give **10** (2.162 g, 97%), after purification by flash chromatography, as white crystals (MeOH); m.p. 226-228° (MeOH); $[\alpha]_D$ = -96 (c=0.43, $CHCl_3$); Anal. calcd. for $C_{33}H_{40}O_{11}$ %: C, 64.68; H, 6.58; O, 28.74 found %: C, 64.61; H, 6.70; O, 28.47; IR ($CHCl_3$) ν, cm^{-1}: 3438 (O-H), 1731 (C=O esters), 1710 (C=O ketone), 1606 (C=C), 1269-1244 (C-O esters), 1213 (C-O ether); LSIMS m/z: 635 $[M+Na]^+$, 613 $[M+H]^+$, 595 $[M+H-H_2O]^+$, 575 $[M+Na-AcOH]^+$, 237; ^1H NMR (300 MHz,) δ: 1.12 (3H, s, C-16H_3), 1.19 (3H, s, C-17H_3), 1.60 (1H, m, C-6H), 1.76 (3H, s, C-19H_3), 1.89 (3H, s, C-18H_3), 2.03 (3H, s, OAc), 2.21 (3H, s, OAc), 2.26 (2H, m, C-14H_2), 2.37 (3H, s, OAc), 2.53 (1H, ddd, J=15, J'=9, J"=7, C-6H), 3.31 (1H, dq, J=16, J'=2, C-10H), 4.00 (1H, d, J=16, C-10H), 4.18 (1H, d, J=8, C-3H), 4.18 (1H, d, J=8, C-20H_β), 4.33 (1H, d, J=8, C-20H_α), 4.97 (1H, dd, J=9, J'=1, C-5H), 5.65 (1H, d, J=7, C-7H), 5.69 (1H, d, J=7, C-2H), 6.11 (1H, tq, J=8, C-13H), 7.49, 7.63, 8.09 (5H, Ar); ^{13}C NMR (75 Mhz) δ: 11.13 (C-19), 14.31 (C-18), 21.02 ($CO\underline{C}H_3$), 21.31 ($CO\underline{C}H_3$), 22.56 ($CO\underline{C}H_3$), 23.04 (C-16), 25.30 (C-17), 33.42 (C-6), 36.03 (C-14), 43.77 (C-15), 45.42 (C-10), 46.15 (C-3), 58.64 (C-8), 69.87 (C-13), 70,98 (C-7), 75.10 (C-2), 76.61 (C-20), 78.92 (C-1), 80.88 (C-4), 83.84 (C-5), 128.68 (m-Ar), 129.46 (qAr), 129.78 (o-Ar), 133.03 (C-11), 133.68 (p-Ar), 134.20 (C-12), 166.88 (C=O ester),169.66 (C=O ester), 170.16 (C=O ester), 170.41 (C=O ester), 208.04 (C-9); ^{13}C-^1H NMR correlations led to these assignments.

10-Deacetoxy-baccatin III, 11.

DIBAH (14 mL of a 1.5 M solution in toluene, 21 mmol) was added to a solution of **10** (1.264 g, 2 mmol) in THF (40 mL) at -78°C. The mixture was stirred for 5 h at -78°C under argon. After completion of the reaction monitored by TLC, acetic acid (1.5 mL) was added. Stirring was continued for 1 h at -78°C and the reaction was warmed to room temperature. Aqueous 10% HCl (10 mL) and ethyl acetate (50 mL) were added before filtration of the mixture on Celite 545. The aqueous phase was extracted three times with ethyl acetate. The combined organic phases were washed twice with brine, dried on $MgSO_4$ and evaporated. The residue was purified by flash chromatography to give **11** (0.844 g, 80%) as white crystals (MeOH); m.p. 206-207°C (MeOH); Anal. calcd. for $C_{29}H_{36}O_9$ %: C, 65.89, H, 6.86, O, 27.24 found %: C, 65.61; H, 7.12; O, 26.98; $[\alpha]_D$ = -79 (c=1.07, MeOH); IR (nujol) ν, cm^{-1}: 3488, 3356 (O-H), 1725 (C=O esters), 1706 (C=O ketone), 1600 (C=C), 1275, 1250 (C-O esters), 1075 (C-O ethers); CIMS (isobutane) m/z: 529 $[M+H]^+$, 511 $[M+H-H_2O]^+$, 493 $[M+H-2H_2O]^+$; ^1H NMR (250 MHz) δ: 1.07 (3H, s, C-16H_3), 1.15 (3H, s, C-17H_3), 1.64 (3H, s, C-19H_3), 1.80 (1H, ddd, J=14, J'=11, J"=2, C-6H_α), 1,.97 (3H, bs, C-18H_3), 2.27 (2H, m, C-14H_2), 2.30 (3H, s, OAc), 2.65 (1H, ddd, J=14, J'=9, J"=7, C-6H_β), 3.47 (1H, dd, J=16, J'=3, C-10H), 3.83 (1H, d, J=16, C-10H), 4.19 (1H, d, J=7, C-3H), 4.17 and 4.32 (2H, 2d, J=8, C-20H_2), 4.38 (1H, dd, J=11, J'=7, C-7H), 4.84 (1H, m, C-13H), 4.99 (1H, dd, J=9, J'=2, C-5H), 5.66 (1H, d, J=7, C-2H), 7.43, 7.56, 8.03 (5H, Ar); 2D-NOESY experiment led to these assigments; ^{13}C NMR (75 MHz) δ: 10.08 (C-19), 14.77 (C-18), 22.64 ($CO\underline{C}H_3$), 22.64 (C-16), 25.64 (C-17), 36.64 (C-6), 39.03 (C-14), 43.54 (C-15), 45.76 (C-10), 46.79 (C-3H), 60.03 (C-8), 67.36 (C-13), 70.81 (C-7), 75.33 (C-2), 76.73 (C-20), 78.87 (C-1), 81.08 (C-4), 83.57 (C-5), 128.64 (m-Ar), 129.63 (qAr), 130.10 (o-Ar), 132.07 (C-11), 133.61 (p-Ar), 137.52 (C-12), 167.11 (C=O ester), 170.95 (C=O ester), 210.43 (C-9); ^{13}C-^1H NMR correlations led to these assigments.

7-Triethylsilyl-10-deacetoxy-baccatin III, 12.
Chlorotriethylsilane (2.5 mL, 14.8 mmol) was added to a solution of **11** (389 mg, 0.74 mmol) in pyridine (37 mL). The mixture was stirred for 24 h at room temperature. Aqueous $NaHCO_3$ was added before extraction of the organic compounds with CH_2Cl_2. The organic phases were washed with brine, dried on $MgSO_4$ and evaporated to give **12** (465 mg, 98%) after purification by flash chromatography, as crystals ($CHCl_3$); m.p. 203° ($CHCl_3$); $[\alpha]_D$ = -80 (c=0.8, $CHCl_3$); IR ($CHCl_3$) ν, cm^{-1}: 3500 (O-H), 1731 (C=O esters), 1706 (C=O ketone), 1602 (C=C), 1267 and 1248 (C-O esters), 1216 (C-O ether); CIMS (isobutane) m/z: 643 $[M+H]^+$, 625 $[M+H-H_2O]^+$, 607 $[M+H-2H_2O]^+$, 583 $[M+H-AcOH]^+$, 565 $[M+H-H_2O-AcOH]^+$, 547 $[M+H-2H_2O-AcOH]^+$; ^1H NMR (200MHz) δ: 0.56 (6H, q, J=7,5, CH_2-silyl), 0.93 (9H, t, J=7,5, CH_3-silyl), 1.00 (3H, s, C-17H_3), 1.09 (3H, s, C-16H_3), 1.59 (3H, s, C-19H_3), 1.82 (1H, m, C-6H), 1.93 (3H, bs, C-18H_3), 2.23 (2H, 2d, J=8, C-14H_2), 2.25 (3H, s, $COCH_3$), 2.46 (1H, m, C-6H), 3.34 (1H, dq, J=15, J'=2, C-10H), 3.75 ((1H, d, J=15, C-10H), 4.07 (1H, d, J=6, C-3H), 4.11 (1H, d, J=8, C-20H), 4.26 (1H, d, J=8, C-20H), 4.49 (1H, dd, J=10, J'=7, C-7H), 4.78 (1H, m, C-13H), 4.93 (1H, dd, J=9, J'=1, C-5H), 5.57 (1H, d, J=6, C-2H), 7.42, 7.55, 8.15 (5H, Ar); ^{13}C NMR (75 MHz) δ: 5.37 (CH_2Si), 6.81 ($\underline{C}H_3CH_2Si$), 10.26 (C-19), 14.98 (C-18), 22.33 (C-16), 22.70 ($CO\underline{C}H_3$), 25.96 (C-17), 37.36 (C-6), 39.11 (C-14), 43.66 (C-15), 45.68 (C-10), 46.82 (C-3), 60.07 (C-8), 67.76 (C-13), 72.14 (C-7), 75.27 (C-2), 76.68 (C-20), 78.86 (C-1), 80.91 (C-4), 84.46 (C-5), 128.55 (m-Ar), 129.61 (qAr), 130.08 (o-Ar), 132.58 (C-11), 133.49 (p-Ar), 137.01 (C-12), 166.99 (C=O ester), 170.69 (C=O ester), 207.83 (C-9); ^{13}C-^1H NMR correlations led to these assignments.

7-Triethylsilyl-2-debenzoyl-4-deacetyl-10-deacetoxy-baccatin III, 13.
A solution of **12** (111 mg, 0.16 mmol) in 0.25 N methanolic sodium methoxide (6.4 mL, 1.6 mmol) was stirred at room temperature. After completion of the reaction monitored by TLC, the medium was made neutral by addition of Dowex IRC 50 (H^+). After filtration, the solvent was evaporated to give a residue which was purified by silica gel column chromatography. Elution with CH_2Cl_2/MeOH 97:3 gave **13** (48 mg, 60%), elution with CH_2Cl_2/MeOH 95:5 gave tetrahydrofuran isomer (24 mg, 31%).

- Compound **13**: amorphous; $[\alpha]_D$ = -131 (c=1,1, MeOH); IR ($CHCl_3$) ν, cm^{-1}: 3465 (OH), 3388 (O-H), 1699 (C=O ketone), 1602 (C=C), 1216 (C-O); CI HRMS: $[M+H]^+$ 497.2890 (calcd for $C_{26}H_{45}O_7Si$ 497.2934), M^+ 496.2866 (calcd. for $C_{26}H_{44}O_7Si$ 496.2856), $[M-Et]^+$ 467.2464 (calcd for $C_{24}H_{39}O_7Si$ 467.2464); FABMS m/z: 519 $[M+Na]^+$, 501 $[M+Na-H_2O]^+$, 461, 327, 281, 237, 199, 161, 149, 133, 121, 115, 103; ^1H NMR (CD_3OD, 250 MHz) δ: 0.59 (6H, q, J=7.5, CH_2-silyl), 0.94 (9H, t, J=7.5, CH_3-silyl), 0.98 (3H, s, C-16H_3), 1.03 (3H, s, C-17H_3), 1.45 (3H, s, C-19H_3), 1.86 (1H, ddd, J=15, J'=11, J"=4, C-6H), 1.91 (3H, bs, C-18H_3), 2.27 (2H, m, C-14H_2), 2.48 (1H, ddd, J=15, J'=9, J"=6, C-6H), 3.31 (1H, dq, J=15, J'=1, C-10H), 3.42 (1H, d, J=6, C-3H), 3.71 (1H, d, J=15, C-10H), 3.74 (1H, d, J=6, C-2H), 4.18 (1H, dd, J=11, J'=6, C-7H), 4.39 and 4.72 (2H, 2d, J=8, C-20H_2), 4,55 (1H, m, C-13H), 4.98 (1H, dd, J=10 et J'=4, C-5H); ^{13}C NMR (CD_3OD, 75 MHz) δ: 6.15 (CH_2Si), 7.11 ($\underline{C}H_3CH_2Si$), 10.65 (C-19), 16.80 (C-18), 21.54 (C-16), 28.23 (C-17), 38.62 (C-14), 39.02 (C-6), 43.95 (C-15), 46.79 (C-10), 51.88 (C-3), 61.52 (C-8), 69.49 (C-13), 73.87 (C-7), 74.40 (C-2), 75.29 (C-10), 76.68 (C-1), 77.66 (C-4), 82.56 (C-20), 88.65 (C-5), 135.74 (C-11), 137.63 (C-12), >210 (C-9).

- Compound **14**: amorphous, $[\alpha]_D$ = -52 ($CHCl_3$ c=1.06); ^1H NMR ($CDCl_3$, 250 MHz) δ: 0.48 (2H, q, J=8, $SiCH_2$), 0.85 (3H, t, J=8, $CH_2\underline{C}H_3$), 0.94 (3H, s, C-17H_3), 0.97 (3H, s, C-16H_3), 1.17 (3H, s, C-19H_3), 1.74 (3H, s, C-18H_3), 1.67 and 1.92 (2H, 2m, C-6H_2), 2.43 (2H, m, C-14H_2), 3.32 and 3.51 (2H, AB, J=10, C-10H_2), 3.46 (1H, d, j=6, C-3H), 3.63 and 3.77 (2H, AB, J=10, C-20H_2), 3.89 (1H, dd, J=10, J'=3, C-7H), 4.13 (1H, m, C-5H), 4.23 (1H, d, J=6, C-2H), 4.40 (1H, m, C-13H), 5.02 (1H, br s, OH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 4.62 ($SiCH_2$), 6.58 ($SiCH_2\underline{C}H_3$), 15.13 (C-19), 16.32 (C-18), 21.01 (C-16), 26.76 (C-17), 36.59 (C-6), 37.97 (C-14), 42.67 (C-15), 45.95 (C-10), 51.49 (C-3), 58.42 (C-8), 68.40 (C-13), 70.03 (C-7), 73.36 (C-1), 73.89 (C-20), 75.85 (C-5), 84.86 (C-2), 85.01 (C-4), 135.94 (C-11), 136.35 (C-12).

7-Triethylsilyl-13-deacetoxy-1,3-dioxo-1,3-*seco*-baccatin III, 15.
A buffered solution of sodium metaperiodate (117 mg in 3 mL of pH 5 buffer, AcOH/NH_4OH) was added to a solution of **13** (136 mg, 0.27 mmol) in EtOH (5 mL). The mixture was stirred for 1.25 h at room temperature. Aqueous $Na_2S_2O_7$ was added and the organic products were extracted with CH_2Cl_2. The organic phases were washed successively with aqueous $NaHCO_3$ and brine, dried on $MgSO_4$ and evaporated to give **15** (132 mg, 99%), obtained without further purification; amorphous; $[\alpha]_D$ = + 13 (c=1.1, $CHCl_3$); IR ($CHCl_3$) ν, cm^{-1}: 3420 (O-H), 1718, 1680 (C=O); CIMS (isobutane) m/z: 551 $[M+C_4H_9]^+$, 495 $[M+H]^+$, 477 $[M+H-H_2O]^+$, 459 $[M+H-2H_2O]^+$; ^1H NMR (300 MHz) δ: 0.57 (6H, q, J=8, CH_2-silyl), 0.93 (9H, t, J=8, CH_3-silyl), 1.04 (3H, s, C-16H_3), 1.16 (3H, s, C-17H_3), 1.68 (3H, s, C-18H_3), 1.72 (3H, s, C-19H_3), 1.97 (1H, ddd, J=14, J'=11,

J''=4, C-6H$_\beta$), 2.46 (1H, ddd, J=14, J'=9, J''=6, C-6H$_\alpha$), 2.70 (1H, dd, J=14, J'=4, C-14H$_\alpha$), 2.93 (1H, dd, J=14, J'=5, C-14H$_\beta$), 3.42 (1H, d, J=20, C-10H), 3.62 (1H, s, C-3H), 3.91 (1H, d, J=20, C-10H), 4.05 (1H, dd, J=11, J'=6, C-7H), 4.32 (1H, m, C-13H), 4.39 (1H, d, J=8, C-20H$_\beta$), 4.61 (1H, d, J=8, C-20H$_\alpha$), 4.87 (1H, dd, J=9, J'=3, C-5H), 5.45 (1H, bs, OH en 13), 9.34 (1H, s, C-2H); ^{13}C NMR (75 MHz) δ: 5.79 (CH_2Si), 7.03 ($\underline{C}H_3CH_2Si$), 10.21 (C-19), 19.04 (C-18), 22.72 (C-16), 24.94 (C-17), 37.06 (C-6), 41.80 (C-10), 45.20 (C-14), 48.33 (C-8), 54.41 (C-15), 62.33 (C-3), 71.58 (C-13), 71.85 (C-4), 75.25 (C-7), 78.84 (C-20), 87.41 (C-5), 132.88 (C-11), 134.80 (C-12), 200.48 (C-2), 212.37 (C-1), 216.11 (C-9); ^{13}C-^{1}H NMR correlations led to these assignments. The following NOESY interactions were observed in 2D experiments. H-2 / H-20$_\beta$, H-2 / H-3, H-2 / H-19, H-2 / H-16, H-3 / 13-OH, H-3 / H-16, H-3 / H-7, H-5 / H-20$_\alpha$, H-5 / H-6$_\alpha$, H-20$_\beta$ / H-20$_\alpha$, H-20$_\beta$ / H-19, H-13 / H-14$_\alpha$, H-13 / H-14$_\beta$, H-13 / H-18, H-7 / H-6$_\alpha$, H-7 / SiEt$_3$, H-10 / H-10, H-10 / H-16, H-10 / H-17, H-16 / H-14$_\alpha$, H-17 / H-14$_\beta$.

7,10-ditrichloroethylcarbonyl-13-acetyl-10-deacetyl-baccatin III, 17.

Acetic anhydride (0.1 mL, 1.15 mmol) and DMAP (catalytic) were added to a solution of **16**[7b] (205 mg, 0.23 mmol) in pyridine (1 mL). The mixture was stirred under argon for 24 h. Aqueous $NaHCO_3$ was added and the organic compounds were extracted with CH_2Cl_2. The organic phases were washed with brine, dried on $MgSO_4$ and evaporated to give **17** (214 mg, quantitative), after purification by flash chromatography, as white crystals (MeOH); m.p. 230°C (MeOH, dec.); $[\alpha]_D$ = -60 (c=0.56, $CHCl_3$); Anal. calcd. for $C_{37}H_{40}O_{15}Cl_6$ %: C, 47.46; H, 4.32 found %: C, 47.81; H, 4.54; IR ($CHCl_3$) ν, cm^{-1}: 3396 (O-H), 1775 and 1750 (C=O carbonates), 1735 (C=O esters, ketone), 1603 (C=C), 1251 (C-O esters), 1218 (C-O ethers); LSIMS (NBA+Li) m/z: 941 [M+Li]$^+$, ^{15}Cl, 749 [M+Li-Cl$_3$CH$_2$OCOO]$^+$, ^{15}Cl, 105; ^{1}H NMR (250 MHz) δ: 1.18 (3H, s, C-16H$_3$), 1.26 (3H, s, C-17H$_3$), 1.86 (3H, s, C-19H$_3$), 2.03 (3H, bs, C-18H$_3$), 2.09 (1H, m, C-6H), 2.22 (3H, s, OAc), 2.27 (2H, m, C-14H$_2$), 2.37 (3H, s, OAc), 2.63 (1H, ddd, J=14, J'=9, J''=7, C-6H), 3.94 (1H, d, J=7, C-3H), 4.17 and 4.33 (2H, d, J=9, C-20H$_2$), 4.60 and 4,.92 (2H, d, J=12, CH_2 Troc), 4.78 (2H, s, CH_2 Troc), 4.98 (1H, bd, J=9, C-5H), 5.58 (1H, dd, J=11, J'=7, C-7H), 5.68 (1H, d, J=7, C-2H), 6.19 (1H, bt, J=9, C-13H), 6.25 (1H, s, C-10H), 7.50, 7.62, 8.07 (5H, Ar); ^{13}C NMR (75 MHz) δ: 11.37 (C-19), 15.58 (C-18), 21.35 (C-16), 21.91 ($COCH_3$), 23.17 ($CO\underline{C}H_3$), 26.95 (C-17), 33.92 (C-6), 36.21 (C-14), 43.64 (C-15), 47.76 (C-3), 56.86 (C-8), 70.19 (C-13), 74.88 (C-2), 76.93 (C-20), 77.14 (C-7), 77.77 (CH_2-Troc), 78.08 (CH_2-Troc), 79.39 (C-1), 79.94 (C-10), 81.34 (C-4), 84.35 (C-5), 94.90 (CCl_3-Troc), 129.41 (mAr), 129.74 (qAr), 130.71 (oAr), 132.43 (C-11), 134.54 (p-Ar), 143.86 (C-12), 153.92 (C=O Troc), 153.97 (C=O Troc), 167.46 (C=O ester), 170.59 (C=O ester), 170.82 (C=O ester), 201.49 (C-9); ^{13}C-^{1}H NMR correlations led to these assignments.

13-Acetyl-10-deacetyl-7-*epi*-baccatin III, 19

Powdered zinc (excess) was added to a solution of **17** (500 mg, 0.534 mmol) in MeOH (30 mL). The suspension was refluxed and stirred for 15 h, under argon. After cooling, the mixture was filtered through Celite 545. The solvent was evaporated under reduced pressure. The residue was purified by chromatography on silicagel column to give **18** (163 mg, 52%) and **19** (150 mg, 48%).

Catalytic DBU (2 mg) was added to a deoxygenated solution of **18** (150 mg) in toluene (10 mL). The mixture was refluxed under argon for 0.5 h. Ethyl acetate was added and the solution was washed with brine and evaporated to give **19** (120 mg, 80%) and unchanged **18** (22.5 mg, 15%), after purification by flash chromatography (CH_2Cl_2/MeOH 95/5 as eluent).

Compound 19: white crystals (CH_2Cl_2/heptane), m.p. 168°C (CH_2Cl_2 /heptane), 205-207°C (MeOH); Anal. Calcd for $C_{31}H_{38}O_{11}$, H_2O %: C, 61.58, H, 6.67, O, 31.75; found %: C, 61.69, H, 6.47, O, 31.63; $[\alpha]_D$= -66 (c=0.85, $CHCl_3$); IR ($CHCl_3$) ν, cm^{-1}: 3650 (O-H), 1748, 1730 ($\nu_{C=O}$ esters); 1715 (C=O ketone); FABMS m/z: 609 [M+Na]$^+$, 591 [M+Na-H_2O]$^+$, 569, 551; ^{1}H NMR (200 MHz), δ: 1.06 (3H, s, C-16H$_3$), 1.16 (3H, s, C-17H$_3$), 1.67 (3H, s, C-19H$_3$), 1.83 (3H, s, C-18H$_3$), 2.20 (3H, s, OAc), 2.24-2.35 (4H, m, C-6H$_2$, C-14H$_2$)?, 2.38 (3H, s, OAc), 3.63 (1H, m, C-7H), 3.94 (1H, d, J=7, C-3H), 4.37 (2H, d, J=9, C-20H$_2$), 4.67 (1H, d, J=12, C7-O$\underline{H}$), 4.91 (1H, m, C-5H), 5.44 (1H, s, C-10H), 5.70 (1H, d, J=7, C-2H), 6.11 (1H, t, J=9, C-13H), 7.48, 7.60 and 8.07 (5H, Ar).^{13}C NMR (75 MHz), δ: 14.89 (C-18), 16.79 (C-19), 20.18 (C-16), 21.29 ($CO\underline{C}H_3$), 22.52 ($COCH_3$), 26.02 (C-17), 35.45 (C-6)?, 36.48 (C-14) , 40.48 (C-3H), 42.46 (C-15), 57.40 (C-8), 69.95 (C-13H), 75.52 (C-2H), 75.89 (C-7H), 77.83 (C-20), 78.21 (C-10H), 79.25 (C-1), 82.36 (C-4), 82.62 (C-5), 128.79 (mAr), 129.52 (qAr), 130.07 (oAr), 133.80 (pAr), 135.58 (C-11), 138.73 (C-12), 167.01 (C=O, ester), 170.11 (C=O ester), 171.89 (C=O ester), 209.76 (C-9). ^{13}C-^{1}H NMR correlations led to these assignments.

13-Acetyl-9-dihydro-10-deacetyl-7-*epi*-baccatin III, 20.
Boron-methyl sulfide complex (1.0 mL of 1.4 M solution in toluene, 8 mmol) was added to a solution of **19** (100 mg, 0.17 mmol) in anhydrous THF (10 mL), at 0°C under argon. The solution was kept at 0°C for 2 h and was further stirred for 2 h at room temperature. Methanol (2 mL) was added dropwise at 0°C. The mixture was stirred for 30 min. The solvents were evaporated to give **20** (84 mg, 84%) after purification by flash chromatography, as a white solid; FABMS m/z: 611 $[M+Na]^+$; IR ($CHCl_3$) ν, cm^{-1}: 3470 (OH), 1730 (C=O ester); ^1H NMR (200MHz), δ: 1.24 (3H, s, CH_3), 1.56 (3H, s, CH_3), 1.61 (3H, s, CH_3), 1.70 (3H, s, CH_3), 1.82-2.02 (1H, m, H-6), 2.16 (3H, s, CH_3), 2.25-2.30 (3H, m, C-14H_2, C-6H_2), 2.33 (3H, s, CH_3), 3.34 (1H, d, J=5.5, C-3H), 3.88 (1H, m, C-7H), 4.08-4.16 (1H, m, C-10H), 4.25 and 4.38 (2H, 2d, J=8.10, C-20H_2), 4.88 (1H, m, C-5H), 5.37 (1H, m, C-9H), 5.95 (1H, d, J=5.6, C-2H), 6.17 (1H, m, C-13H), 7.41-7.58 and 8.04-8.09 (5H, m, Ar); ^{13}C NMR, δ: 15.68 (CH_3), 16.93 (CH_3), 21.38 (CH_3), 22.99 (CH_3), 23.44 (CH_3), 29.23 (CH_3), 35.78 (C-6), 35.88 (C-14), 41.04 (C-3), 42.31 (C-15), 47.12 (C-8), 70.77 (C-7), 72.00 (C-13), 75.46 (C-10), 78.14 (C-2), 78.48 (C-20), 79.32 (C-9), 79.40 (C-1), 84.02 (C-4), 84.11 (C-5), 128.69 (mAr), 129.90 (qAr), 130.17 (oAr), 133.54 (pAr), 136.51 (C-11), 138.96 (C-12), 167.22 (ester), 170.68 (ester), 171.44 (ester).

13-Acetyl-9,10-dicarbaldehyde-10-deacetyl-7-*epi*-9,10-*seco*-baccatin III, 1,9 hemiketal, 21.
A solution of sodium metaperiodate (60 mg) in a pH 5~6 buffered solution (AcOH, NH_4OH)) was added to a solution of **20** (80mg, 0.136mmol) in ethanol (8 mL) at room temperature. The mixture was stirred for 2 h and then was extracted three times by CH_2Cl_2 (3x15mL). The combined organic phases were washed with aqueous $S_2O_7Na_2$ (10%, 2x10mL), brine (1x10mL) and evaporated to give after silicagel column chromatography **21** (77 mg, 97%) as a white solid; CIMS m/z: 587 $[M+H]^+$, 569 $[M+H-H_2O]^+$; IR ($CHCl_3$) ν, cm^{-1}: 3460 (OH), 1740 (C=O ester); 1690 (CHO), 1602 (C=C); ^1H NMR (200MHz), δ: 1.40 (3H, s, CH_3), 1.42 (3H, s, CH_3), 1.44 (3H, s, CH_3), 1.48 (3H, s, CH_3), 1.80 (3H, s, CH_3), 1.82-1.92 (1H, m, C-6H_2), 1.97 (3H, s, CH_3), 2.20-2.50 (3H, m, C-14H_2, C-6H_2), 3.32 (1H, d, J=11.6, C-3H), 3.96-4.00 (1H, m, C-7H), 4.16 (1H, d, J=10.6, OH), 4.50 and 4.94 (2H, 2d, J=9, C-20H_2), 4.8 (1H, m, C-5H), 5.28 (1H, m, C-13H), 5.56 (1H, d, J=12, C-2H), 5.71 (1H, br s, C-9H), 7.41-7.60 and 7.84-7.88 (5H, m, Ar), 10.14 (CHO); ^{13}C NMR (75 MHz), δ: 8.76 (CH_3), 16.07 (CH_3), 20.71 (CH_3), 21.01 (CH_3), 25.26 (CH_3), 26.04 (CH_3), 35.69 (C-14), 37.08 (C-3), 41.20 (C-6), 43.66 (C-15), 44.54 (C-8), 69.08 (C-13), 69.99 (C-7), 74.11 (C-2), 75.55 (C-1), 76.80 (C-20), 81.11 (C-4), 82.87 (C-5), 92.12 (C-9), 128.68 (mAr), 129.45 (oAr), 139.9 (qAr), 133.22 (pAr), 141.15 (C-11), 143.45 (C-12), 166.0 (C=O ester), 170.92 (C=O ester), 171.56 (C=O ester), 194.76 (CHO).

7-Methoxycarbonyl-13-acetyl-10-deacetoxy-24-baccatin III, 22.
In a round-bottomed flask, **17** (612 mg, 0.66 mmol) and a stirring bar were introduced. The flask was closed with a septum and through a needle, vacuum and argon introduction were carried out, alternatively, three times, to eliminate air. **17** was dissolved by addition of THF (5 mL). SmI_2 (17.5 mL of a 0.3 M solution in THF, 5.25 mmol) and MeOH (0.1 mL, 4 eq.) were added. The mixture was stirred for 0.5 h at room temperature. Aqueous 5% HCl was poured (5 mL) and the organic products were extracted three times with ethyl acetate. The combined organic phases were successively washed with aqueous $Na_2S_2O_7$ and brine, dried over $MgSO_4$ and evaporated. Purification of the residue by flash chromatography (CH_2Cl_2/MeOH 99/1) gave **22**, crystals (MeOH), m.p. > 250°C,$[\alpha]_D$= -107 (c=0.83, $CHCl_3$); $C_{33}H_{40}O_{12}$, Anal. calcd %: C 63.03, H 6.42, O 30.55; found %: C 63.20, H 6.55, O 30.68; IR ($CHCl_3$) ν, cm^{-1}: 3525 (O-H), 1744 (C=O ester, ketone), 1605 (C=C), 1275-1251 (C-O ester), 1219 (C-O ether); ICMS m/z: 629 $[M+H]^+$, 611 $[M+H-H_2O]^+$, 569 $[M+H-AcOH]^+$, 551 $[M+H-H_2O-AcOH]^+$, 507 $[M+H-PhCOOH]^+$, 449, 447 $[M+H-PhCOOH-AcOH]^+$; ^1H NMR (300 MHz) δ: 1.10 (3H, s, C-16H_3), 1.14 (3H, s, C-17H_3), 1.72 (3H, s, C-19H_3), 1.87 (3H, br s, C-18H_3), 1.96 (1H, ddd, J=15, J'=11, J''=1, C-6H), 2.17 (3H, s, OAc), 2.23 (2H, m, C-14H_2), 2.33 (3H, s, OAc), 2.61 (1H, ddd, J=15, J'=9, J''=7, C-6H), 3.35 (1H, dq, J=16, J'=1, C-10H), 3.75 (3H, s, OCH_3), 4.04 (1H, d, J=16, C-10H), 4.16 (1H, d, J=7, C-3H), 4.16 and 4.29 (2H, d, J=8, C-20H_2), 4.94 (1H, dd, J=9, J'=1, C-5H), 5,44 (1H, dd, J=11, J'=7, C-7H), 5,66 (1H, d, J=7, C-2H), 6,08 (1H, bt, J=9, C-13H), 7.40,7.53 and 7.99 (5H, Ar); ^{13}C NMR (75 MHz) δ: 11.13 (C-19), 14.35 (C-18), 21.32 ($COCH_3$), 22.59 ($COCH_3$), 23.11 (C-16), 25.41 (C-17), 33.46 (C-6), 36.12 (C-14), 43.88 (C-15), 45.60 (C-10), 46.30 (C-3), 55.16 (OCH_3), 58.71 (C-8), 69.95 (C-13), 75.14 (C-2), 75.38 (C-7), 76.51 (C-20), 79.05 (C-1), 80.93 (C-4), 83.81 (C-5), 128.75 (mAr), 129.50 (qAr), 130.14 (oAr), 133.17 (C-11), 133.72 (pAr), 134.33 (C-12), 155.07 (OCOOMe), 166.95 (C=O, ester), 169.71 (C=O ester), 170.38 (C=O ester), 207.46 (C-9). ^{13}C-^1H correlations led to these assignments.

7-Methoxycarbonyl-13-acetyl-dioxo-11,12-deacetoxy-10-*seco*-11,12-baccatin III, 1,12 hemiketal, 23
Sodium metaperiodate (172 mg, 0.8 mmol) in water (10 mL) and solid RuO_2 (47 mg, 1.1 eq.) were added to a solution of **22** (204 mg, 0.32 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred for 4 h at room temperature

and then filtered on Celite 545. The organic phase was separated, washed with aqueous $Na_2S_2O_7$ and brine, dried over $MgSO_4$ and evaporated. The residue was purified by flash chromatography (CH_2Cl_2/MeOH 99/1, as eluent) and gave **23** (160 mg, 76%), as an amorphous solid, Anal. calcd. for $C_{33}H_{40}O_{14}$: % C 59.99, H 6.09, O 33.91: found: % C 59.79, H 6.08, O 33.81; $[\alpha]_D$ = +28 (c=0.75, $CHCl_3$); IR ($CHCl_3$) ν, cm^{-1}: 3452 (O-H); 1730 (C=O, carbonate, ester, ketone); 1602 (C=C); 1265 (C-O, ester); 1216 (C-O, ether); ICMS m/z: 661 $[M+H]^+$; 643 $[M+H-H_2O]^+$, 601 $[M+H-AcOH]^+$; ^1H NMR (300 MHz) δ: 1.26 (3H, s, C-16H_3), 1.31 (3H, s, C-17H_3), 1.86 (3H, s, C-19H_3), 2,03 (3H, bs, C-18H3), 2.09 (1H, m, C-6H), 2.22 (3H, s, OAc), 2.27 (2H, m, C-14H_2), 2.37 (3H, s, OAc), 2.63 (1H, ddd, J=14, J'=9, J"=7, C-6H), 3.94 (1H, d, J=7, C-3H), 4.17 and 4.33 (2H, d, J=9, C-20H_2), 4.60 and 4.92 (2H, d, J=12, CH_2Troc), 4.78 (2H, s, CH_2 Troc), 4.98 (1H, br d, J=9, C-5H), 5.58 (1H, dd, J=11, J'=7, C-7H), 5.68 (1H, d, J=7, C-2H), 6.19 (1H, bt, J=9, C-13H), 6.25 (1H, s, C-10H), 7.50, 7. 62 and 8.07 (5H, Ar); ^{13}C NMR (75 MHz) δ: 11.13 (C-19), 14.35 (C-18), 21.32 ($COCH_3$), 22.59 ($COCH_3$), 23.11 (C-16), 25.41 (C-17), 33.46 (C-6), 36.12 (C-14), 43.88 (C-15), 45.60 (C-10), 46.30 (C-3), 55.16 (OCH_3), 58.71 (C-8), 69.95 (C-13), 75.14 (C-2), 75.38 (C-7), 76.51 (C-20), 79.05 (C-1), 80.93 (C-4), 83.81 (C-5H), 128.75 (mAr), 129.50 (qAr), 130.14 (oAr), 133.17 (C-11), 133.72 (pAr), 134.33 (C-12), 155.07 (OCOOMe), 166.95 (C=O, ester), 169.71 (C=O, ester),170.38 (C=O, ester), 207.46 (C-9).^{13}C-^1H NMR correlations led to these assignments.

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(*Received in Belgium* 14 *January* 1994; *accepted* 17 *March* 1994)