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A Formal Total Synthesis of Taxol Aided by an Automated Synthesizer

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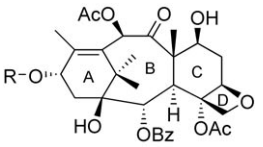
Abstract: A 36-step synthesis was carried out in automated synthesizers to provide a synthetic key intermediate of taxol. A key step involved a microwave-assisted alkylation reaction to construct the ABC ring system from an AC precursor. Subsequent formation of the D ring afforded baccatin III, a well-known precursor of taxol.

Keywords: antitumor agents · automated synthesis · natural products · synthetic methods · total synthesis

Introduction

The total syntheses of structurally complex natural products have been possible for more than a century. These endeavors are crucially dependent on the formulation of an elegant synthetic design and extensive experimental studies. Generally, the latter involves careful analysis of each step in the overall sequence to optimize conditions and maximize yields. In the modern laboratory, automation[1] of the various operations, including reaction setup, workup, purification, and analysis, is an ideal solution for increasing efficiency in organic synthesis. Since the first report of a solid-phase synthesis by Merrifield,[2] simply repeated cycles of coupling reactions and deprotections have been applied to the automated syntheses of biopolymers such as oligopeptides,[2] oligonucleotides,[3] and, more recently, oligosaccharides.[4,5] In recent years, automation has also been utilized for applications such as the optimization of reaction conditions, routine syntheses of structurally similar compounds, such as building blocks for combinatorial synthesis,[6] and the bulk synthesis of important intermediates. In the total syntheses of complex molecules, however, one needs long sequences that include not only simple transformations but also challenging key reactions. It is a worthy goal to develop a versatile synthesizer that can be adapted for such tasks and to demonstrate its application in the automated synthesis of a complex molecule. We report herein our 36-reaction pathway for the supply of the synthetic key intermediate **32** by utilizing the automated synthesizers, modified Sol-capa and ChemKonzert. From intermediate **32**, we completed the total synthesis of (±)-baccatin III (**2**), itself a precursor to the potent antitumor agent taxol (paclitaxel; **1**).



taxol (**1**): (R = )

baccatin III (**2**): (R = H)

Taxol (**1**) consists of a highly functionalized ABCD ring system, including a strained eight-membered B ring.[7] The total synthesis of taxol has been reported by six groups after extensive efforts.[8–13] We envisioned a synthetic route through the sequential formation of the AC→ABC→ABCD ring systems.

Results and Discussion

Synthesis of Rings A and C

Both rings A and C were prepared from geraniol (**3**).[14,15] After acetylation of **3** and epoxidation of **4**, Ti^{III}-catalyzed radical cyclization of **5** provided oxycyclogeranyl acetates **6** as a mixture of alkenyl isomers in 72% yield[16] which were converted into A ring hydrazone **9** in eight steps as previously reported (Scheme 1).[17] Protection of alcohol **6** as an

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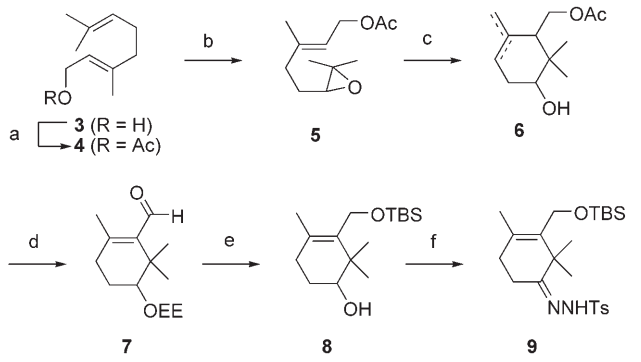
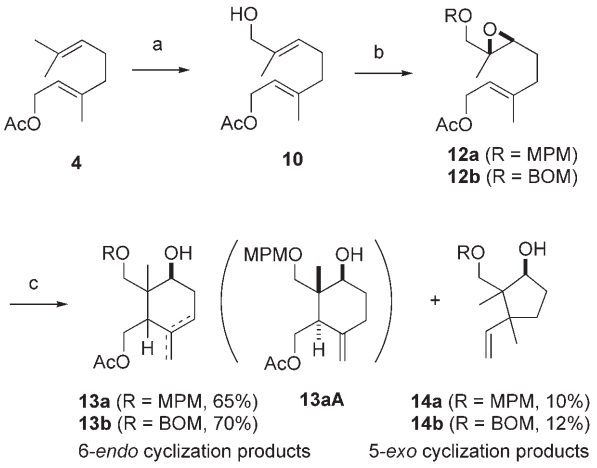


Scheme 1. Automated synthesis of **9**. Reaction conditions: a) Ac_2O, DMAP, Et_3N; b) 1) *N*-bromosuccinimide, *t*BuOH/H_2O; 2) Et_3N, ***toluene***, reflux (90%); c) ***[Cp$_2$TiCl$_2$] (10 mol%)***, ***Mn***, ***Et$_3$B***, ***2,6-lutidine·HCl***, THF, room temperature (72%); d) 1) ethyl vinyl ether, camphorsulfonic acid, CH_2Cl_2; 2) NaOH, ***MeOH/THF/H$_2$O***; 3) SO_3·pyridine, DMSO, Et_3N, CH_2Cl_2; 4) DBU, CH_2Cl_2; e) 1) $NaBH_4$, ***MeOH/THF/H$_2$O***; aq. HCl; 2) TBSCl, Et_3N, CH_2Cl_2; f) 1) SO_3·pyridine, DMSO, Et_3N, CH_2Cl_2; 2) H_2NNHTs, THF (10% in 8 steps). DMAP = 4-dimethylaminopyridine, Cp = cyclopentadienyl, DMSO = dimethyl sulfoxide, DBU = 1,8-diazabicyclo[5.4.0]undecene, TBS = *tert*-butyldimethylsilyl, EE = ethoxyethyl, Ts = *p*-toluenesulfonyl.



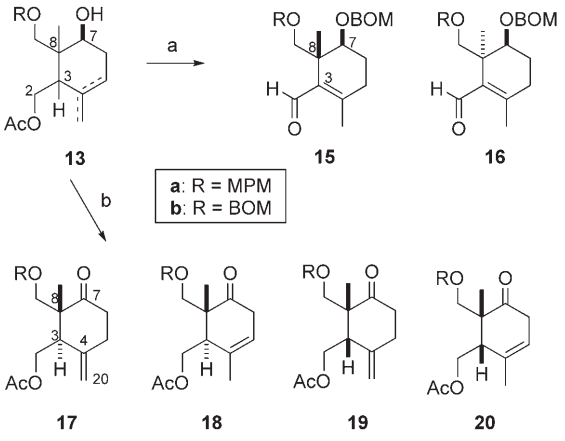
Scheme 2. a) 1) SeO_2, *t*BuO_2H, salicylic acid, ***hexane***; 2) $NaBH_4$, ***MeOH/THF/H$_2$O*** (48%); b) 1) $VO(acac)_2$, *t*BuO_2H, ***toluene***; 2) for **12a**: MPM trichloroacetimidate (**11**), TfOH, Et_2O (89%); for **12b**: BOMCl, DIPEA, CH_2Cl_2 (98%); c) [Cp_2TiCl_2] (4 equiv), Zn, THF, 0°C, 3.5 h. acac = acetylacetonate, MPM = 4-methoxyphenylmethyl, Tf = trifluoromethanesulfonyl, BOM = benzyloxymethyl, DIPEA = *N,N*-diisopropylethylamine.

ethoxyethyl ether, deprotection of the acetyl group, oxidation of the resultant alcohol, and isomerization of alkenyl isomers provided enal **7**. Reduction of **7**, deprotection of the ethoxyethyl group by treatment with acid in situ, and selective protection of the primary alcohol with TBSCl afforded **8**. Oxidation of the secondary alcohol in **8** and hydrazone formation provided **9** in 10% overall yield from **6**.[18,19] These reactions were then performed with a commercially available automated synthesizer, Sol-capa,[20] after some modification. The Ti^{III}-mediated cyclization of **5** reported previously[17,21] was not suited for use in the synthesizer owing to the large amount of stoichiometrically produced (2–3 equiv) Ti salt precipitates. However, the Ti^{III}-catalyzed cyclization described above was compatible for use in the synthesizer. We also modified some conditions (printed in bold italics font in the scheme legends) to adapt the reactions for use in the synthesizer. In particular, when methanol was used as solvent, automated extraction did not work because the sensor would not recognize the difference in electroconductivities between the aqueous and organic layers. We therefore used a mixed solvent, such as THF/MeOH/H_2O, to avoid the problem.

In the preparation of the C ring, stoichiometric Ti^{III}-mediated cyclization of the MPM ether **12a** and BOM ether **12b**,[17] prepared from hydroxygeranyl acetate **10**, was investigated initially (Scheme 2). Treatment of **12a** and **12b** with [Cp_2TiCl][22] (prepared in situ from [Cp_2TiCl_2] (4 equiv)) and Zn in THF at 0°C for 3.5 h provided 6-*endo* cyclization products **13a** and **13b** in 65% and 70% yields, respectively, with 5-*exo* cyclization by-products **14a** (10%) and **14b** (12%). The ratios of isomers **13** shown in Table 1 were determined after conversion into the corresponding Δ^3 enals **15** and **16**,[17] and 7-ketones **17**–**20** (Scheme 3). It can be seen that the MPM protecting group induced higher exo

Table 1. Stereoselectivity in the Ti^{III}-mediated radical cyclization of **12**.

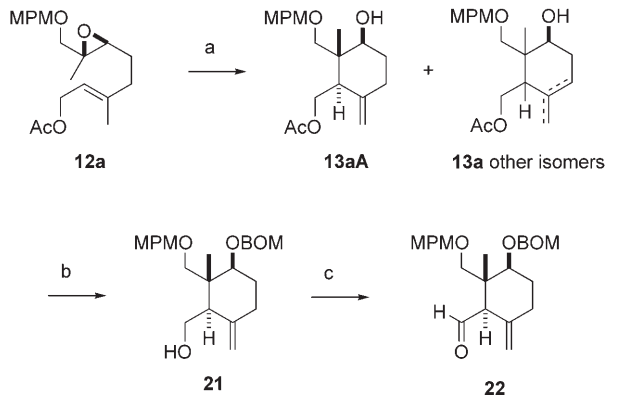
R	*cis*/*trans* (7-OH, 8-Me) **15/16**	*trans*/*cis* (8-Me, 3-H) (**17+18**)/(**19+20**)	*exo*/*endo* ($\Delta^{4,(20)}$, Δ^4) (**17+19**)/(**18+20**)
MPM	5:1	8:1	7:1
BOM	4.5:1	5:1	2.5:1



Scheme 3. a) 1) BOMCl, DIPEA, CH_2Cl_2; 2) NaOH, MeOH; 3) TPAP, NMO, CH_2Cl_2 (61%); 4) DBU, CH_2Cl_2; b) TPAP, NMO, CH_2Cl_2. TPAP = tetrapropylammonium perruthenate, NMO = *N*-methylmorpholine oxide.

alkene selectivity as well as stereoselectivity in the 6-*endo* cyclization to afford the desired **13aA**, which can be directly converted into C ring aldehyde **22**.[23]

To allow the synthesis of the C-ring moiety in an automated synthesizer, we carried out a Ti^{III}-catalyzed cyclization of **12a** (Scheme 4). The catalytic reaction (10 mol% [Cp_2TiCl_2]) led to the desired 6-*endo* cyclization products



Scheme 4. Automated synthesis of **22**. a) ***[Cp$_2$TiCl$_2$] (10 mol%)***, ***Mn***, ***Et$_3$B***, ***TMSCl***, ***K$_2$CO$_3$***, THF, 0°C (61%); b) 1) BOMCl, DIPEA, CH_2Cl_2; 2) NaOH, ***MeOH/THF/H$_2$O***, (72%); 3) automated purification (82%); c) TPAP, NMO, CH_2Cl_2 (85%). TMS = trimethylsilyl.

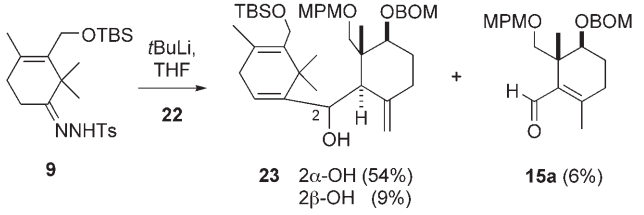
13a in 61% yield, but the addition of lutidine·HCl salt utilized in the preparation of the A ring unit gave only an epoxide-opened product, that is, an undesired chlorohydrin. Owing to the difficulty of the isolation of the desired **13aA**, the 6-*endo* cyclization products **13a** were used in the next reaction as a mixture. Protection of the secondary alcohol as a BOM ether and deprotection of the acetyl group provided the respective alcohols in 72% combined yield. Purification by automated column chromatography with a Combi flash Sg 100c unit was carried out repeatedly to isolate the desired **21** in 82% yield. Oxidation of **21** furnished aldehyde **22** in 85% yield.

All the synthetic protocols from **4** to **22** were performed in the automated synthesizer Sol-capa without affecting the yields of the products.

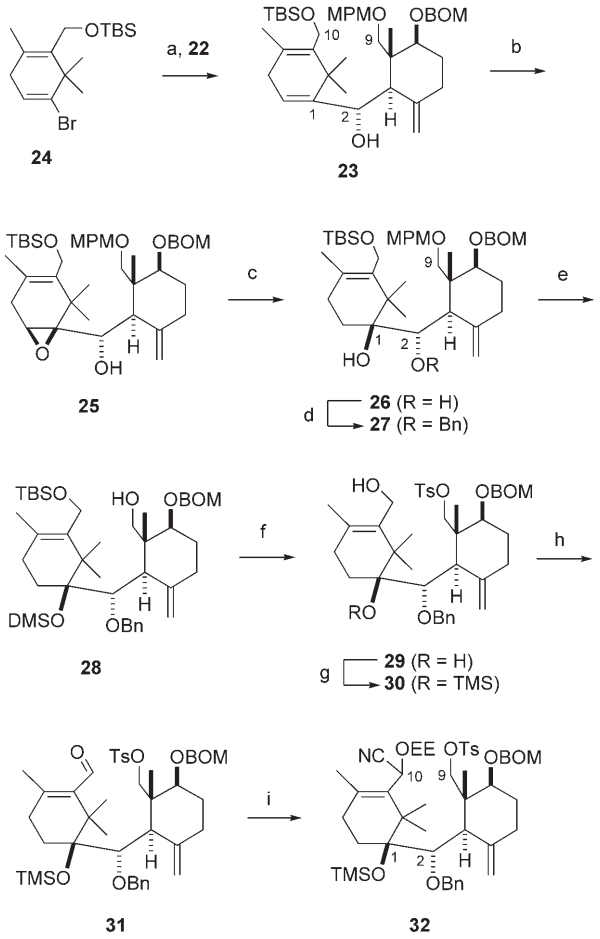
Synthesis of the Cyclization Precursor 32

The Shapiro coupling reaction of **9** with aldehyde **22** provided the desired product **23** (54%) and its C2 epimer (9%) together with α,β-unsaturated aldehyde **15a** (R = MPM) (6%), probably because excess *t*BuLi base was employed, resulting in deprotonation at the α position of the aldehyde **22** (Scheme 5).[9,18,19,24]

Therefore, **9** was converted into vinyl bromide **24** in 70% yield by treatment with *t*BuLi in THF and 1,2-dibromoethane. Lithiation of **24**, followed by coupling with aldehyde **22** in the presence of $CeCl_3$ provided **23** in 78% yield (12:1 ratio of isomers; Scheme 6). Stereoselective epoxidation (75% yield), regioselective ring opening of the epoxide **25** with $LiAlH_4$, and reprotection of the partially deprotected 10-OH group as a TBS ether provided 1,2-diol **26** (64%) accompanied by recovered epoxide **25** (15%). As protection of the 1,2-diol as a dibenzyl ether proceeded in low yield, selective monobenzyl protection of 2-OH was performed (82%). Without protection of the hindered 1-OH group, DDQ oxidation of **27** formed a *p*-methoxybenzylidene acetal between the 1-OH and 9-OH groups. Temporary protection of 1-OH in **27** as a dimethylsilyl (DMS) ether,[25] followed by deprotection of the MPM group afforded **28** (60%). The resultant alcohol was converted into a tosylate leaving group, and deprotection of the TBS and DMS



Scheme 5. Coupling reaction of the vinyl anion produced from **9** with aldehyde **22**.



Scheme 6. Automated synthesis of the cyclization precursor **32**. a) *t*BuLi, $CeCl_3$, THF, −78°C; then **22**, (78%) (2α-OH/2β-OH 12:1); b) $VO(acac)_2$, $tBuO_2H$, benzene (75%); c) 1) $LiAlH_4$, Et_2O; 2) TBSCl, imidazole, CH_2Cl_2 (64%; recovered starting material 15%); d) aqueous KOH, BnBr, Bu_4NHSO_4 (82%); e) 1) Me_2SiHCl, imidazole, DMF; 2) DDQ, CH_2Cl_2/H_2O (60%); f) 1) TsCl, DMAP, $CHCl_3$, 50°C; 2) TBAF, THF (53%); g) 1) TMSOTf, 2,6-lutidine, DIPEA; 2) TBAF (66%; recovered starting material 12%); h) TPAP, NMO, CH_2Cl_2 (quant.); i) 1) TMSCN, [18]crown-6, KCN, 1M HCl, THF (93%); 2) ethyl vinyl ether, camphorsulfonic acid, CH_2Cl_2 (93%). Bn = benzyl, DMF = *N*,*N*-dimethylformamide, DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, TBAF = tetrabutylammonium fluoride, DMS = dimethylsilyl.

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groups provided diol **29** (53%). Both hydroxy groups in **29** were simultaneously protected as TMS ethers, but the primary TMS ether was selectively removed to afford **30** (66%), and some diol **29** was recovered (12%). Oxidation of allylic alcohol **30** followed by cyanohydrin formation at the C10 furnished **32**. We performed all the reactions described in Scheme 6 in an automated synthesizer, ChemKonzert,[26] originally developed by us (Figure 1).

As a result, 36 steps of the synthesis of the key intermediate **32** from geraniol (**3**), including three C–C bond formations, 10 oxidation and reduction reactions, 16 protection and deprotection sequences, and seven other transformation reactions, were performed in the automated synthesizer on a scale between 100 mg and 300 g.

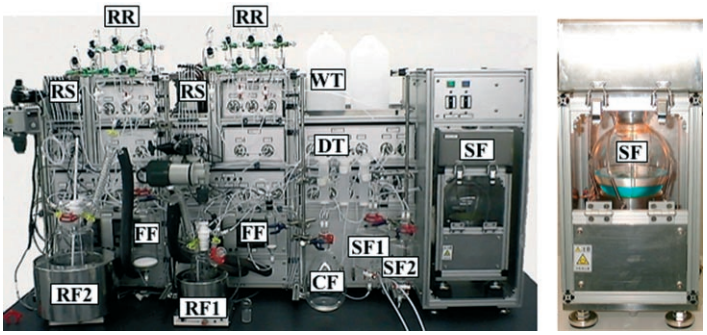
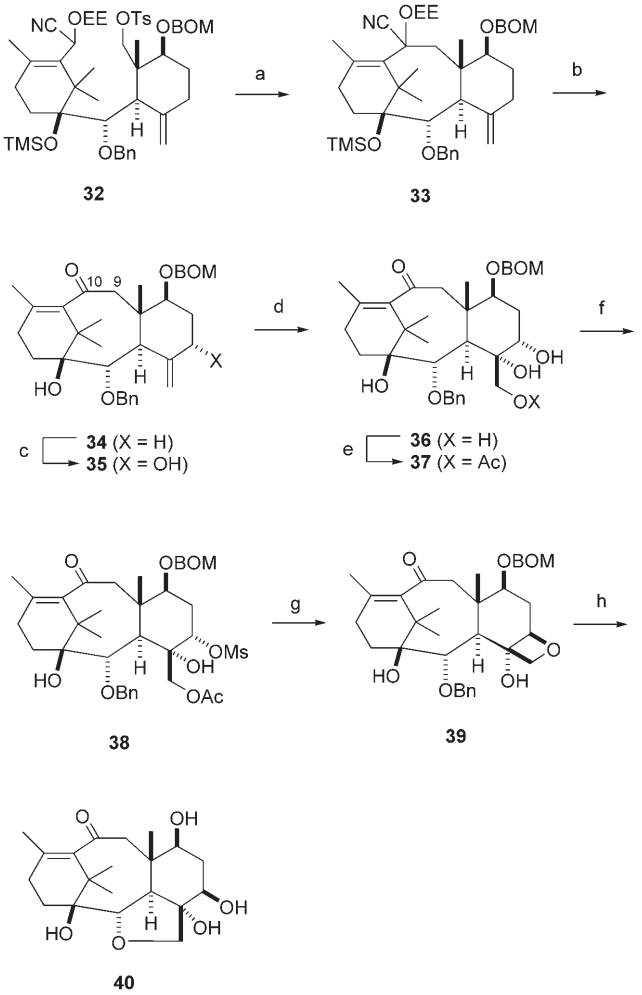


Figure 1. Left: Full picture of ChemKonzert. Right: Two layers separated in a centrifugal separator (rotation speed 1500 rpm). ChemKonzert consists of two reaction vessels (RF) (i.e. 500 and 1000 mL), a centrifugal separator (SF) (700 mL), two receivers (SF1, SF2) (500 mL), two glass filters (FF) (100 and 500 mL), twelve substrate and reagent reservoirs (RR) (100–200 mL), six solvent and washing bottles (RS) (500 mL), three drying pads (DT), a round flask (CF) (1000 mL), two washing solvent tanks (WT), and a computer controller. The glassware is interconnected with teflon tubes, and solutions are transferred under reduced pressure by using a diaphragm pump. Separation of organic and aqueous layers is performed by measuring the electroconductivity of the two different phases with a sensor, and the liquid flow is regulated by solenoid valves controlled with Windows software (KonzertMeister). The users input the procedures in the computer and add substrates and reagents to the reservoirs and fill the solvents. The synthesizer carried out the reaction procedures as follows: the substrate and reagents in RR were added to the reaction vessel RF at a controlled reaction temperature under a nitrogen atmosphere. After the reaction was complete (checking by TLC and/or HPLC by hand), quenching reagent in RR was added to the reaction vessel RF, and the mixture was transferred to a centrifugal separator SF with removal of the precipitate through a glass-filter FF. After the centrifugal separation, the organic phase was transferred to a vessel SF. The aqueous solution was taken back to the reaction vessel RF. After addition of the extraction solvent from RS, the mixture was stirred and then transferred to the centrifugal separator. After three or four extractions, the combined organic solution in SF was washed with aqueous solutions of sodium bicarbonate and sodium chloride in RS in the reaction vessel RF. The organic layer was separated in SF and transferred to another vessel SF. The organic layer SF was then passed through a $MgSO_4$ or Na_2SO_4 plug DT for drying. The filtrate was stored in a round flask CF for purification after evaporation of the solvent (manual). Silica-gel column chromatography was performed with a CombiFlash unit. Unless purification was necessary, the filtrate was directly transferred to another reaction vessel RF, concentrated under reduced pressure, and the next reaction was carried out sequentially. Finally, the whole apparatus was washed with water and acetone from WT and dried under reduced pressure.

Cyclization Reaction of 32

Intramolecular alkylation of the protected cyanohydrin **32** was carried out as previously reported (Scheme 7).[24,27] Treatment of **32** with $LiN(TMS)_2$ for 10 h in refluxing dioxane afforded the cyclization product **33** in 46% yield. The crucial eight-membered ring formation was effectively assisted by microwave irradiation[28] in the presence of excess $LiN(TMS)_2$. The reaction period was dramatically decreased from 10 h to 15 min (49% yield).



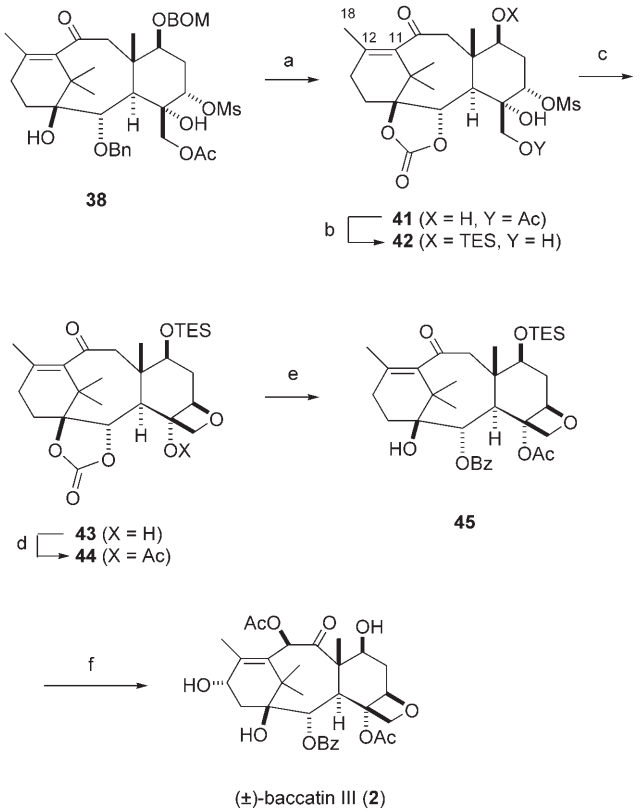
Scheme 7. a) $LiN(TMS)_2$, dioxane, microwave irradiation, 145°C, 15 min (49%); b) 1) camphorsulfonic acid, MeOH; 2) 1 M NaOH, Et_2O (82%); c) SeO_2, $tBuO_2H$, salicyclic acid, hexane, 55°C (92%); d) OsO_4–quinuclidine, NMO, $tBuOH/H_2O$, 0°C, $NaBH_4$ (64%; recovered starting material 19%); e) AcCl, DMAP, CH_2Cl_2 (79%); f) MsCl, DMAP, CH_2Cl_2 (84%); g) 1) K_2CO_3, MeOH, room temperature; 2) DBU, toluene, 110°C (69%); h) H_2, $Pd(OH)_2$ (20%), EtOH, room temperature. Ms = methanesulfonyl.

Total Synthesis of Baccatin III (2)

Further transformations were carried out manually. Hydrolysis of cyanohydrin ether **33** to ketone **34**,[29] regio- and stereo-selective allylic oxidation, and dihydroxylation of exo-alkene **35** with OsO_4–quinuclidine complex provided **36**

(Scheme 7).[23] Selective acetylation of the primary alcohol in **36**, followed by mesylation of the secondary alcohol in **37** afforded **38**. Removal of the acetyl group in **38**, followed by treatment with DBU in refluxing toluene[8,30] provided oxetane **39** in 69% yield. Hydrogenolysis of **39**, however, did not give the desired tetraol but cyclic ether **40**. Surprisingly, the oxetane was opened by the adjacent 2-OH group to form a five-membered ether under relatively neutral reaction conditions.[9b,30]

To circumvent this problem, we converted **38** into 1,2-carbonate **41** prior to the formation of the oxetane ring (Scheme 8). Hydrogenolysis of the benzyl and benzyloxy-



Scheme 8. a) 1) H_2, Pd/C (10%), EtOAc, room temperature; 2) triphosgene, pyridine, CH_2Cl_2, 0°C (75%); b) 1) TESCl, pyridine, 40°C; 2) K_2CO_3, MeOH, 0°C (80%); c) DIPEA, HMPA, 100°C (77%, recovered starting material 20%); d) Ac_2O, DMAP, CH_2Cl_2 (70%); e) PhLi, THF, −78°C (70%); f)[10] 1) *t*BuOK, $(PhSeO)_2O$, THF, −78→0°C; 2) *t*BuOK, THF, −78°C (90%), 3) Ac_2O, DMAP, pyridine (50%), 4) PCC, celite, NaOAc, benzene, 85°C; 5) $NaBH_4$, MeOH (80%); 6) HF·pyridine, THF (80%). TES = triethylsilyl, HMPA = hexamethylphosphoric triamide, PCC = pyridinium chlorochromate. Bz = benzoyl.

methyl ethers in **38**, followed by treatment with triphosgene provided carbonate **41**. TES protection of 7-OH and removal of the acetyl group afforded **42**. Oxetane formation without deconjugation of Δ^{11}-alkene to $\Delta^{12(18)}$-exo methylene was crucial. Treatment of **42** with DIPEA in HMPA at 100°C provided the desired **43** in 77% yield with recovery of the starting material **42** (20%).[31] Acetylation and addition of phenyl lithium to the 1,2-carbonate group of **44** provided benzoate **45**,[18] which is a racemic form of the Danishefsky intermediate (m.p. 214–216°C) for the synthesis of taxol (**1**).[10] Some modification of the reported six-step procedures[8,10] led to the total synthesis of (±)-baccatin III (**2**) (m.p. 221–223°C), whose spectral data were identical to those previously reported.[9b]

Conclusions

We have achieved the total synthesis of (±)-baccatin III (**2**) from epoxide **12a** with a single stereogenic feature. Since optically active epoxide **12a** is prepared by a Sharpless asymmetric epoxidation, this route could be applied to the synthesis of optically active taxol. We have demonstrated that our originally developed synthesizers, modified Sol-capa and ChemKonzert, efficiently allowed a 36-step synthesis to provide the synthetic key intermediate **32** after tuning the reaction conditions to make them suitable for use in the synthesizers. Ultimately, it should be noted that a single PhD student (S.F.) carried out the entire sequence of the total synthesis of baccatin III (**2**) from geraniol (**3**) based on the supply of the synthetic key intermediate **32** utilizing the above automated synthesizers. It can be seen that the automated synthesizer can be utilized in broad areas of organic syntheses. As the synthetic route is still too long to supply enough taxol, we are currently developing a much more efficient synthetic sequence.

Experimental Section

General

Melting points were measured on a Yanako micro melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a JEOL model EX-270 (270 MHz) or a ECA-400 (400 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: $\delta = 7.26$ ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), and assignment. ^{13}C NMR spectra were recorded on a JEOL model EX-270 (67.8 MHz) or a JEOL model ECP-400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: $\delta = 77.0$ ppm). Infrared spectra were recorded on a Perkin–Elmer Spectrum One FT-IR spectrometer. Mass spectra were obtained on AppliedBioSystems Mariner TK3500 Biospectrometry Workstation (ESI-TOF) mass spectrometers. HRMS (ESI-TOF) were calibrated with angiotensin I (SIGMA), bradykinin (SIGMA), and neurotensin (SIGMA) as internal standards. Automated column chromatography was performed on a Combi flash Sg 100c with Isco Redi Sep Flash Column. The automated synthesizer Sol-capa was purchased from MORITEX Corporation.

Synthesis

4: A solution of geraniol (**3**) (300 g, 1.95 mol), Et_3N (298 mL, 2.14 mol) and a catalytic amount of DMAP in the reaction flask was manually treated dropwise with acetic anhydride (320 mL, 3.39 mol) at 10°C under N_2. The resulting mixture was stirred at 40°C for 7 h, the reaction mixture was automatically worked up as described below. The reaction mixture was transferred to the extraction flask. The reaction flask was washed with EtOAc (No. 0) and the solution was transferred to the ex-

traction flask. This washing process was repeated twice (No. 0). The reaction mixture in the extraction flask was quenched by the addition of H_2O (No. 1). The organic phase was transferred to the receiver flask 2, and the aqueous phase was transferred to the receiver flask 1. The aqueous phase in the receiver flask 1 was transferred to the extraction flask and extracted with EtOAc (No. 6). This extraction process was repeated again (No. 5). The organic phase in the receiver flask 2 was transferred to the extraction flask and washed with NaCl (10% aqueous, No. 2). The resulting organic phase was dried by passing through a $MgSO_4$ plug and transferred to a round-bottomed flask. After this automated work-up, the obtained solution was concentrated in vacuo and the residue (398 g) was distilled to afford geranyl acetate (**4**) as a pale yellow oil (374 g, 1.91 mol, 98%). B.p. 111 °C/6 mmHg; $R_f = 0.56$ (hexane/EtOAc 67:33); IR (neat): $\tilde{\nu}$= 2916, 1738, 1442, 1376, 1233, 1022, 954 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): $\delta = 1.60$ (br s, 3H), 1.69 (s, 3H), 1.70 (s, 3H), 2.00–2.98 (m, 4H), 2.06 (s, 3H), 4.59 (d, 2H, $J = 7.3$ Hz), 5.09 (t, 1H, $J = 6.6$ Hz) 5.35 ppm (tq, 1H, $J = 1.0$, 7.3 Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 16.4$, 17.7, 21.0, 25.7, 26.3, 39.5, 61.4, 118.3, 123.7, 131.8, 142.2, 171.1 ppm.

10: A solution of geranyl acetate (**4**) (220 g, 1.12 mol) in hexane (60 mL) in the reaction flask was manually treated with SeO_2 (5.0 g, 40 mmol), salicylic acid (12.4 g, 89.8 mmol), and $tBuO_2H$ (>70% aqueous, 364 mL) at room temperature. The resulting mixture was stirred at 60 °C for 3 days, and the reaction mixture was then worked up automatically as described below. The reaction mixture was transferred to the extraction flask. The reaction flask was washed with EtOAc (No. 0) and the solution was transferred to the extraction flask. This washing process was repeated twice (No. 0). The reaction mixture in the extraction flask was quenched by the addition of $Na_2S_2O_3$ (50% aqueous, No. 1). The organic phase was transferred to the receiver flask 2, and the aqueous phase was transferred to the receiver flask 1. The aqueous phase in the receiver flask 1 was transferred to the extraction flask and extracted with EtOAc (No. 6). This extraction process was repeated again (No. 5). The organic phase in the receiver flask 2 was transferred to the extraction flask and washed with NaCl (10% aqueous, No. 2). The resulting organic phase was dried by passing through a $MgSO_4$ plug and transferred to a round-bottomed flask. After this automated work-up, the obtained solution was concentrated in vacuo to afford a crude mixture of allylic alcohol **10** and enal (265 g). The mixture of allylic alcohol **10** and enal in H_2O (60 mL), THF (60 mL), and MeOH (30 mL) in the reaction flask was manually treated with $NaBH_4$ (15.0 g, 0.40 mol) in several portions at 0 °C. The resulting mixture was stirred at the same temperature for 10 min and quenched by addition of HCl (1 M aqueous). The reaction mixture was automatically worked up as described below. The reaction mixture was transferred to the extraction flask. The reaction flask was washed with EtOAc (No. 0) and the solution was transferred to the extraction flask. This washing process was repeated twice (No. 0). The organic phase was transferred to the receiver flask 2, and the aqueous phase was transferred to the receiver flask 1. The aqueous phase in the receiver flask 1 was transferred to the extraction flask and extracted with EtOAc (No. 6). This extraction process was repeated again (No. 5). The organic phase in the receiver flask 2 was transferred to the extraction flask and washed with $NaHCO_3$ (5% aqueous, No. 2) and NaCl (10% aqueous, No. 3). The resulting organic phase was dried by passing through a $MgSO_4$ plug and transferred to a round-bottomed flask. After this automated workup, the obtained solution was concentrated in vacuo. The residue (232 g) was distilled to give allylic alcohol **10** as a yellow oil (113 g, 533 mmol, 48%) and recovered geranyl acetate **(4)** as a pale yellow oil (27.2 g, 128 mmol, 11%). B.p. 135 °C/2 mmHg; $R_f = 0.48$ (hexane/EtOAc 50:50); IR (neat): $\tilde{\nu}$= 3408, 2924, 1735, 1443, 1380, 1233, 1022 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): $\delta = 1.67$ (s, 3H), 1.71 (s, 3H), 1.62–1.84 (m, 2H), 2.05 (s, 3H), 2.02–2.25 (m, 2H), 3.99 (s, 2H), 4.58 (d, 2H, $J = 7.3$ Hz), 5.28–5.44 ppm (m, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 13.7$, 16.4, 21.0, 25.7, 39.1, 61.4, 68.8, 118.6, 125.2, 135.2, 141.8, 171.3 ppm.

11: A solution of *p*-anisyl alcohol (100 g, 0.724 mol) and DBU (10.8 mL, 72.4 mmol) in dry CH_2Cl_2 (120 mL) in the reaction flask was manually treated with trichloroacetonitrile (69 mL, 0.69 mol) at 0 °C under N_2. The resulting mixture was stirred at the same temperature for 5 min, and the reaction mixture was automatically worked up as described below. The reaction mixture was quenched by addition of NaCl (10% aqueous) and H_2O (No. 0). The resulting mixture was transferred to the extraction flask. The reaction flask was washed with Et_2O (No. 0), and the solution was transferred to the extraction flask. This washing process was repeated again (No. 0). The organic phase was transferred to the receiver flask 2, and the aqueous phase was transferred to the receiver flask 1. The aqueous phase in the receiver flask 1 was transferred to the extraction flask and extracted with Et_2O (No. 6). This extraction process was repeated again (No. 5). The organic phase in the receiver flask 2 was transferred to the extraction flask and washed with HCl (1 M aqueous, No. 2), $NaHCO_3$ (5% aqueous, No. 3), and NaCl (10% aqueous, No. 4). The resulting organic phase was dried by passing through a $MgSO_4$ plug and transferred to a round-bottomed flask. After this automated workup, the obtained solution was concentrated in vacuo to afford MPM imidate **11** as a yellow oil (197 g), which was used in the next reaction without further purification.

12a: A solution of allylic alcohol **10** (100 g, 0.472 mol) in toluene (260 mL) in the reaction flask was treated manually with $VO(acac)_2$ (1.3 g, 4.7 mmol) and $tBuO_2H$ (>70% aqueous, 85 mL) at 0 °C. The resulting mixture was stirred at room temperature for 6 h, and the reaction mixture was automatically worked up as described below. The reaction mixture was transferred to the extraction flask. The reaction flask was washed with EtOAc (No. 0) and the solution was transferred to the extraction flask. This washing process was repeated twice (No. 0). The reaction mixture in the extraction flask was quenched by the addition of $Na_2S_2O_3$ (10% aqueous, No. 1). The organic phase was transferred to the receiver flask 2, and the aqueous phase was transferred to the receiver flask 1. The aqueous phase in the receiver flask 1 was transferred to the extraction flask and extracted with EtOAc (No. 6). This extraction process was repeated again (No. 5). The organic phase in the receiver flask 2 was transferred to the extraction flask and washed with $NaHCO_3$ (5% aqueous, No. 2) and NaCl (10% aqueous, No. 3). The resulting organic phase was dried by passing through a $MgSO_4$ plug and transferred to a round-bottomed flask. After this automated workup, the obtained solution was concentrated in vacuo. The residue (120 g) was used for the next reaction without further purification. A solution of the crude epoxy alcohol (92 g, ca. 0.36 mol) in dry Et_2O (500 m) in the reaction flask was treated manually with TfOH (0.1 M in Et_2O, 4.0 mL, 0.40 mmol) and MPM imidate **11** (123 g, 0.44 mol) at 0 °C under N_2. The resulting mixture was stirred at the same temperature for 5 min, and the reaction mixture was worked up automatically as described below. The reaction mixture was transferred to the extraction flask. The reaction flask was washed with Et_2O (No. 0) and the solution was transferred to the extraction flask. This washing process was repeated twice (No. 0). The resulting mixture was quenched by addition of $NaHCO_3$ (5% aqueous, No. 1). The organic phase was transferred to the receiver flask 2, and the aqueous phase was transferred to the receiver flask 1. The organic phase in the receiver flask 2 was transferred to the extraction flask and washed with NaCl (10% aqueous, No. 2). The resulting solution was dried by passing through a $MgSO_4$ plug and transferred to a round-bottomed flask. After this automated work-up, the obtained solution was concentrated in vacuo. The residue (178 g) was diluted with CH_2Cl_2 and hexane to induce crystallization. The white crystals of trichloroacetamide were removed by filtration. The filtrate was concentrated in vacuo. The residue was purified by column chromatography to afford MPM ether **12a** as a colorless oil (112 g, 0.32 mmol, 89% over two steps). $R_f = 0.51$ (hexane/EtOAc 67:33); IR (neat): $\tilde{\nu}$= 3627, 2936, 2858, 1735, 1615, 1515, 1247, 1092, 1034, 821 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): $\delta = 1.32$ (s, 3H), 1.62–1.77 (m, 2H), 1.72 (s, 3H), 2.05 (s, 3H), 2.08–2.31 (m, 2H) 2.85 (t, 1H, J= 6.3 Hz), 3.40 (d, 1H, $J = 10.9$ Hz), 3.47 (d, 1H, $J = 10.9$ Hz), 3.81 (s, 3H), 4.45 (d, 1H, $J = 11.5$ Hz), 4.51 (d, 1H, $J = 11.5$ Hz), 4.58 (d, 2H, J= 7.3 Hz), 5.38 (t, 1H, $J = 7.3$ Hz) 6.88 (d, 2H, $J = 8.6$ Hz), 7.26 ppm (d, 2H, $J = 8.6$ Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 14.6$, 16.5, 21.1, 26.6, 36.2, 55.3, 60.0, 60.5, 61.3, 72.9, 74.4, 113.9, 119.1, 129.4, 130.3, 141.2, 159.3, 171.2 ppm ; HRMS (ESI-TOF): calcd for $[C_{20}H_{28}O_5+Na]^+$ 371.1829, found: 371.1829.

Ti^{III}-catalyzed cyclization of **12a**: Manganese (3.51 g, 65.0 mmol) and K_2CO_3 (15.5 g, 112 mmol) were placed in the reaction flask. A supernatant of $[Cp_2TiCl]$ in THF (100 mL) (prepared in situ from $[Cp_2TiCl_2]$ (2.90 g, 11.6 mmol) and Mn (0.84 mg, 16 mmol) in dry THF (130 mL)),

TMSCl (11.9 mL, 94 mmol), and Et_3B (97 mL, 97 mmol, 1.0 M in THF) was added to the solution of epoxide **12a** (15.0 g, 43.1 mmol) in dry THF (120 mL) at 0 °C under N_2. The resulting mixture was stirred at the same temperature for 7 h under N_2, quenched by the addition of HCl (3 M aqueous, 210 mL) with stirring at room temperature for 5 min, and diluted with Et_2O (500 mL). The reaction mixture was automatically worked up as described below. The reaction mixture was transferred to the extraction flask. The reaction flask was washed with Et_2O (No. 0), and the solution was transferred to the extraction flask. The organic phase was transferred to the receiver flask 2, and the aqueous phase was transferred to the receiver flask 1. The organic phase in the receiver flask 2 was transferred to the extraction flask and washed with $NaHCO_3$ (5% aqueous, No. 1) and NaCl (10% aqueous, No. 2). The resulting organic phase was dried by passing through a $MgSO_4$ plug and transferred to a round-bottomed flask. After this automated workup, the obtained solution was concentrated in vacuo. The residue (18.6 g) was filtered through silica gel to afford 6-*endo* cyclization products **13a** (9.14 g, 26.3 mmol, 61%). Major isomer **13aA** was isolated by preparative HPLC (column Silica-3301-N (8 mm i.d., 300 mm), eluent hexane/EtOAc 75:25, flow rate 2.1 mL min^{-1}, t_R 24 min), R_f = 0.53 (hexane/EtOAc 50:50); m.p. 81–82 °C; IR (neat): $\tilde{\nu}$= 3480, 2938, 1735, 1614, 1515, 1368, 1302, 1248, 1094, 1034, 821 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 0.80 (s, 3H), 1.38–1.55 (m, 1H), 1.75–1.90 (m, 1H), 2.01 (s, 3H), 2.00–2.14 (m, 1H), 2.25–2.38 (m, 1H), 2.28–2.40 (m, 1H), 3.38 (d, 1H, J = 9.2 Hz), 3.56 (d, 1H, J = 9.2 Hz), 3.81 (s, 3H), 3.78–3.92 (m, 1H), 4.16 (dd, 1H, J = 4.3, 11.5 Hz), 4.28 (dd, 1H, J = 8.6, 11.5 Hz), 4.46 (br s, 2H), 4.60 (s, 1H), 4.93 (s, 1H), 6.88 (d, 2H, J = 8.6 Hz), 7.25 ppm (d, 2H, J = 8.6 Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 11.4, 21.1, 31.2, 33.5, 43.3, 45.2, 55.4, 61.9, 73.3, 73.8, 76.1, 109.6, 114.0, 129.3, 130.1, 144.9, 159.4, 171.2 ppm; HRMS (ESI-TOF) calcd for $[C_{20}H_{29}O_5+H]^+$ 349.2010, found 349.2011; elemental analysis: calcd for $C_{20}H_{29}O_5$ (%): C 68.94, H 8.10; found: C 68.61, H 8.29.

21: A mixture of alcohols **13a** (44.0 g, 0.126 mol) in dry CH_2Cl_2 (126 mL) in the reaction flask was treated manually with iPr$_2$NEt (107 mL, 0.632 mol) and BOMCl (44.0 mL, 0.316 mol) at 0 °C under N_2. The resulting mixture was stirred at the same temperature for 1 h, and the reaction mixture was automatically worked up as described below. The resulting solution was quenched by the addition of H_2O (No. 0) and transferred to the extraction flask. The reaction flask was washed with Et_2O (No. 0), and the solution was transferred to the extraction flask. This washing process was repeated again (No. 0). The organic phase was transferred to the receiver flask 2, and the aqueous phase was transferred to the receiver flask 1. The aqueous phase in the receiver flask 1 was transferred to the extraction flask and extracted with Et_2O (No. 6). This extraction process was repeated again (No. 5). The organic phase was transferred to extraction flask and washed with HCl (1 M aqueous, No. 1), $NaHCO_3$ (5% aqueous, No. 2) and NaCl (10% aqueous, No. 3). The resulting solution was dried by passing through a $MgSO_4$ plug and transferred to a round-bottomed flask. After this automated workup, the obtained solution was concentrated in vacuo to afford crude BOM ether (61 g), which was used for the next reaction without further purification. A solution of the crude BOM ether (30 g, < 62 mmol) in H_2O (96 mL), THF (96 mL) and MeOH (32 mL) in the reaction flask was treated manually with NaOH (9.9 g, 0.25 mol) at 0 °C. The resulting mixture was stirred at 30 °C for 10 h, and the reaction mixture was automatically worked up as described below. The resulting solution was treated with NaCl (10% aqueous) and H_2O (No. 0). The mixture was transferred to the extraction flask. The reaction flask was washed with Et_2O (No. 0), and the solution was transferred to the extraction flask. This washing process was repeated again (No. 0). The organic phase was transferred to the receiver flask 2, and the aqueous phase was transferred to the receiver flask 1. The aqueous phase in the receiver flask 1 was transferred to the extraction flask and extracted with EtOAc (No. 6). This extraction process was repeated again (No. 5). The organic phase was transferred to the extraction flask and washed with HCl (1 M aqueous, No. 1), $NaHCO_3$ (5% aqueous, No. 2) and NaCl (10% aqueous, No. 3). The resulting solution was dried by passing through a $MgSO_4$ plug and transferred to a round-bottomed flask. After this automated workup, the obtained solution was concentrated in vacuo. The residue (27.9 g) was simply filtered through a short silica-gel plug to afford alcohols (19.0 g, 44.6 mmol, 72%). The mixtures were repeatedly purified through a Combi flash Sg 100c (Isco Redi Sep Flash Column 110 g, 25% EtOAc in hexane, flow rate 10 mL min^{-1}) to isolate alcohol **21** (15.6 g, > 80% RI purity). HPLC analysis (column Silica-3301-N (8 mm i.d., X 300 mm), eluent hexane/EtOAc 80:20, flow rate 2.0 mL min^{-1}) t_R = 18 min; IR (neat): $\tilde{\nu}$= 3426, 2938, 2882, 1612, 1513, 1454, 1248, 1098, 1038, 736, 698 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 0.87 (s, 3H), 1.58–1.92 (m, 2H), 1.98–2.13 (m, 1H), 2.25–2.35 (m, 1H), 2.30–2.47 (m, 1H), 3.31 (d, 1H, J = 9.2 Hz), 3.38 (d, 1H, J = 9.2 Hz), 3.72 (dd, 1H, J = 7.9, 10.9 Hz), 3.79 (s, 3H), 3.73–3.89 (m, 2H), 4.39 (br s, 2H), 4.56 (d, 1H, J = 11.2 Hz), 4.64 (d, 1H, J = 11.2 Hz), 4.66 (br s, 1H), 4.71 (d, 1H, J = 6.9 Hz), 4.80 (d, 1H, J = 6.9 Hz), 4.92 (br s, 1H), 6.86 (d, 2H, J = 8.6 Hz), 7.21 (d, 2H, J = 8.6 Hz), 7.23–7.40 ppm (m, 5H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 14.5, 28.2, 31.2, 43.3, 50.0, 55.3, 60.8, 65.5, 69.8, 73.0, 73.8, 94.4, 110.0, 113.8, 127.1, 127.8, 128.7, 129.2, 130.3, 137.9, 146.9, 159.3 ppm; HRMS (ESI-TOF): calcd for $[C_{26}H_{34}O_5Si+Na]^+$: 449.2298; found: 449.2299.

22: The alcohol **21** (1.30 g, 3.05 mmol) in dry CH_2Cl_2 (15 mL) was treated with NMO (1.1 g, 9.1 mmol) and a catalytic amount of TPAP at room temperature under argon. The dark green suspension was stirred at the same temperature for 30 min, diluted with Et_2O and treated with florisil. The mixture was filtered on celite and the filtrate was concentrated in vacuo. The residue was purified by utilizing the automated column machine Combi flash Sg 100c (Isco Redi Sep Flash Column 35 g, 10–12% EtOAc in hexane, flow rate 15 mL min^{-1}) to afford aldehyde **22** (1.1 g, 2.6 mmol) in 85% yield. R_f = 0.49 (hexane/EtOAc 67:33); IR (neat): $\tilde{\nu}$= 2939, 2877, 1716, 1612, 1514, 1247, 1097, 1037, 820, 737, 698 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.18 (s, 3H), 1.73–1.88 (m, 2H), 2.07–2.23 (m, 1H), 2.35–2.55 (m, 1H), 2.89 (d, 1H, J = 3.3 Hz), 3.32 (s, 2H), 3.80 (s, 3H), 3.73–3.85 (m, 1H), 4.37 (s, 2H), 4.56 (d, 1H, J = 8.9 Hz), 4.61 (d, 1H, J = 8.9 Hz), 4.64 (br s, 1H), 4.72 (d, 1H, J = 6.9 Hz), 4.81 (d, 1H, J = 6.9 Hz), 4.97 (br s, 1H), 6.86 (d, 2H, J = 8.6 Hz), 7.21 (d, 2H, J = 8.6 Hz), 7.13–7.42 (m, 5H), 9.81 ppm (d, 1H, J = 3.3 Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 16.0, 27.0, 30.2, 44.0, 55.3, 60.4, 69.9, 73.0, 74.1, 94.0, 112.8, 113.8, 127.8, 127.9, 128.5, 129.2, 130.4, 137.8, 142.7, 159.2, 202.0 ppm; HRMS (ESI-TOF): calcd for $[C_{26}H_{32}O_5+Na]^+$: 447.2142; found: 447.2141.

24: All glassware placed in ChemKonzert (see Figure 1) were dried. RF1 was dried again at 80 °C for 30 min under reduced pressure and cooled to room temperature. Then a solution of tosylhydrazone **9** (1.3 g, 2.9 mmol) in THF (7.0 mL) was added manually to RF1 and cooled to −25 °C under N_2. The solution was treated with tBuLi (1.7 M in pentane, 7.9 mL, 13 mmol) at the same temperature manually, stirred at −25 °C for 30 min, warmed to 10 °C, and stirred at the same temperature for 30 min. The resulting solution was treated with dibromoethane (1.2 mL, 15 mmol, RR1), diluted with hexane (40 mL, RS3), and quenched by the addition of H_2O (60 mL, RS4). The mixture was filtered with FF1 and transferred to SF. After centrifugation, the two phases were separated. The aqueous phase in SF1 was transferred to RF1 and extracted with hexane (40 mL, RS3). This extraction process was repeated twice. The organic phase in SF2 was transferred to RF1 and washed with HCl (1 M aqueous, 40 mL, RS6), $NaHCO_3$ (5% aqueous, 40 mL, RS5), and NaCl (10% aqueous, 40 mL, RR8). The resulting organic phase was dried by passing through DT1 ($MgSO_4$) and transferred to a round-bottomed flask (CF1). The organic solution was concentrated in vacuo. The residue was filtered through a silica-gel plug (eluent hexane) to afford vinyl bromide **24** as a colorless oil (700 mg, 2.03 mmol, 70%). IR (neat): $\tilde{\nu}$= 2930, 2857, 1463, 1253, 1134, 1058, 922, 837, 774 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 0.09 (s, 6H), 0.90 (s, 9H), 1.26 (s, 6H), 1.72 (s, 3H), 2.67 (t, 2H, J = 3.6 Hz), 4.18 (s, 2H), 5.98 ppm (t, 1H, J = 3.6 Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = −5.3, 18.4, 18.8, 26.0, 27.6, 29.3, 35.9, 41.6, 59.5, 125.4, 128.3, 134.5, 134.5 ppm.

23: After all glassware was dried, RF1 was dried again at 80 °C for 30 min under reduced pressure and cooled to room temperature. The 100-mL three-necked flask (RF2) with a solution of vinyl bromide **24** (0.90 g, 2.6 mmol) in THF (9.0 mL) and a dry ice–acetone bath were then attached to ChemKonzert. The solution was treated with tBuLi (1.7 M in pentane, 3.0 mL, 5.1 mmol) at −78 °C manually under N_2 and stirred at the same temperature for 30 min. A cooled (−20 °C) suspension of $CeCl_3$

(1.6 g, 6.5 mmol) in THF (30 mL, RF1) was then transferred to RF2. The resulting mixture was stirred at −78 °C for 1 h and treated dropwise with a solution of aldehyde **22** (0.50 g, 1.2 mmol) in THF (2.5 mL, RR9) at the same temperature. RR9 was then washed with THF (2.0 mL, RR12), and the solution was transferred to RF2. The resulting mixture was stirred at −78 °C for 30 min and transferred to RF1. RF2 was washed twice with hexane (20 mL, RS2), and the solution was transferred to RF1. The reaction was then quenched by the addition of HCl (1 M aqueous, 40 mL, RS6) and transferred to SF. After centrifugation, the two phases were separated. The aqueous phase in SF1 was transferred to RF1 and extracted with Et_2O (40 mL, RS1). This extraction process was repeated twice. The organic phase in SF2 was transferred to RF1 and washed with $NaHCO_3$ (5% aqueous, 40 mL, RS5) and NaCl (10% aqueous, 40 mL, RS4). The resulting organic phase was dried by passing through DT1 ($MgSO_4$) and transferred to a round-bottomed flask (CF1). The obtained solution was concentrated in vacuo. The residue (1.1 g) was purified by utilizing the automated column machine Combi flash Sg 100c (Isco Redi Sep Flash Column, 0–20% EtOAc in hexane, flow rate 7.5 mL min^{-1}) to afford allylic alcohol **23** (647 mg, 0.94 mmol, 78%). R_f = 0.47 (hexane/EtOAc 50:50); IR (neat): $\tilde{\nu}$ = 3435, 2931, 1614, 1514, 1463, 1250, 1093, 1037, 837 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = −0.05 (s, 6H), 0.77 (s, 9H), 0.95 (s, 3H), 1.07 (s, 3H), 1.20 (s, 3H), 1.40–1.52 (m, 1H), 1.58 (s, 3H) 1.77–1.88 (m, 1H), 1.87 (br s, 1H), 1.90–2.00 (m, 1H), 2.43–2.55 (m, 2H), 2.52–2.68 (m, 1H), 2.97 (d, 1H, J = 9.2 Hz), 3.23 (d, 1H, J = 9.2 Hz), 3.64 (s, 3H), 3.73 (br s, 1H), 4.00 (d, 1H, J = 11.1 Hz), 4.08 (d, 1H, J = 11.1 Hz), 4.18 (br s, 1H), 4.22 (s, 2H), 4.51 (s, 2H), 4.57 (br s, 1H), 4.68 (d, 1H, J = 7.3 Hz), 4.80 (d, 1H, J = 7.3 Hz), 4.89 (s, 1H), 5.52 (t, 1H, J = 3.4 Hz), 6.70 (d, 2H, J = 8.7 Hz), 7.05 (d, 2H, J = 8.7 Hz), 7.00–7.25 ppm (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = −5.3 (CH_3), 18.5 (C), 19.2 (CH_3), 19.6 (CH_3) 26.1 (CH_3), 26.3 (CH_3), 27.4 (CH_2), 28.1 (CH_3), 29.3 (CH_2), 33.2 (CH_2), 38.2 (C), 43.7 (C), 53.5 (CH), 55.3 (CH_3), 59.0 (CH_2), 67.8 (CH), 70.3 (CH_2), 73.0 (CH_2), 77.0 (CH_2), 77.6 (CH), 94.1 (CH_2), 113.7 (CH), 115.6 (CH_2), 122.1 (CH), 127.9 (CH), 128.0 (CH), 128.5 (CH), 128.9 (CH), 129.5 (C), 130.7 (C), 135.1 (C), 137.5 (C), 141.4 (C), 143.8 (C), 159.1 ppm (C).

25: A solution of allylic alcohol **23** (0.95 g, 1.4 mmol) in benzene (60 mL) in RF1 was cooled to 10 °C and treated with *t*BuOOH (5.0–6.0 M in decane, 0.55 mL) and $VO(acac)_2$ (22 mg, 0.084 mmol) manually. The resulting mixture was stirred at 10 °C for 2 h, diluted with Et_2O (120 mL, RS2), quenched by the addition of $NaHCO_3$ (5% aqueous, 60 mL, RS5), and transferred to SF. After centrifugation, the two phases were separated. The aqueous phase in SF1 was transferred to RF1 and extracted with EtOAc (60 mL, RS1). This extraction process was repeated twice. The organic phase in SF2 was transferred to RF1 and washed twice with $Na_2S_2O_3$ (10% aqueous, 40 mL, RS6) and NaCl (10% aqueous, 40 mL, RS4). The resulting organic phase was dried by passing through DT1 ($MgSO_4$) and transferred to a round-bottomed flask (CF1). The obtained solution was concentrated in vacuo. The residue (1.24 g) was purified by utilizing the automated column machine Combi flash Sg 100c (Isco Redi Sep Flash Column, 10–30% EtOAc in hexane, flow rate 15 mL min^{-1}) to afford epoxide **25** as a colorless oil (742 mg, 1.05 mmol, 75%). R_f = 0.45 (hexane/Et_2O 33:67); IR (neat): $\tilde{\nu}$ = 3428, 2933, 2885, 1614, 1515, 1250, 1082, 1043, 837, 774, 749 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 0.07 (s, 6H), 0.90 (s, 9H), 1.21 (s, 3H), 1.25 (s, 3H), 1.29 (s, 3H), 1.72 (s, 3H), 1.58–1.78 (m, 1H), 1.82–1.97 (m, 1H), 1.98–2.12 (m, 1H), 2.43 (br s, 2H), 2.48–2.65 (m, 1H), 2.66 (br s, 1H), 3.30 (s, 2H), 3.45 (s, 1H), 3.80 (s, 3H), 3.75–3.83 (m, 1H), 4.07 (d, 1H, J = 11.6 Hz), 4.17 (d, 1H, J = 11.6 Hz), 4.35 (br s, 1H), 4.38 (s, 2H), 4.52 (br s, 1H), 4.60 (d, 1H, J = 11.9 Hz), 4.65 (d, 1H, J = 11.9 Hz), 4.78 (d, 1H, J = 7.3 Hz), 4.89 (d, 1H, J = 7.3 Hz), 4.93 (br s, 1H), 6.85 (d, 2H, J = 8.6 Hz), 7.20 (d, 2H, J = 8.6 Hz), 7.25–7.40 ppm (m, 5H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = −5.3, 18.4, 19.9, 22.0, 26.1, 26.9, 28.1, 30.3, 31.7, 32.4, 39.1, 44.2, 49.6, 55.3, 57.0, 59.1, 64.5, 66.6, 70.1, 73.1, 75.4, 77.5, 94.0, 113.7, 113.7, 125.7, 127.8, 127.9, 128.5, 129.1, 130.5, 134.2, 137.5, 147.0, 159.1 ppm; HRMS (ESI-TOF): calcd for $[C_{42}H_{62}O_7Si+H]^+$: 707.4338; found: 707.4324.

26: RF1 was dried at 70 °C for 10 min under reduced pressure. A solution of epoxy alcohol **25** (0.47 g, 0.66 mmol) in Et_2O (5 mL) was placed in RF1 and concentrated under reduced pressure. The resulting oil was treated with $LiAlH_4$ (0.35 M in Et_2O, 53 mL, 19 mmol) manually and stirred at 40 °C for 2 h. The resulting mixture was cooled to −10 °C, diluted with Et_2O (100 mL, RS2), and quenched dropwise with Na_2SO_4 (4% aqueous, 10 mL, RR1) while controlling the temperature of the reaction mixture. The generated aluminum salt was then dissolved by the addition of H_2SO_4 (5% aqueous, 200 mL, RS6). The mixture was filtered with FF1 and transferred to SF. After centrifugation, the two phases were separated. The aqueous phase in SF1 was transferred to RF1 and extracted with EtOAc (120 mL, RS1). This extraction process was repeated twice. The organic phase in SF2 was transferred to RF1 and washed with $NaHCO_3$ (5% aqueous, 40 mL, RS5) and NaCl (10% aqueous, 40 mL, RS4). The resulting organic phase was dried by passing through DT1 ($MgSO_4$) and transferred to a round-bottomed flask (CF1). The obtained solution was concentrated in vacuo to afford a mixture of diol **26** and the triol obtained by partial deprotection of the TBS ether, which was used for the next reaction without further purification. A solution of the crude mixture in CH_2Cl_2 (8 mL) was placed in RF1 and treated with imidazole (0.25 g, 3.6 mmol) and TBSCl (0.24 g, 1.7 mmol) manually at room temperature. The resulting solution was stirred at the same temperature for 1 h, quenched by the addition of H_2O (40 mL, RR1), diluted with Et_2O (40 mL, RS2), and transferred to SF. After centrifugation, the two phases were separated. The aqueous phase in SF1 was transferred to RF1 and extracted with Et_2O (40 mL, RS2). This extraction process was repeated twice. The organic phase in SF2 was transferred to RF1 and washed with HCl (1 M aqueous, 40 mL, RS6) and $NaHCO_3$ (5% aqueous, 40 mL, RS5) and NaCl (10% aqueous, 40 mL, RS4). The resulting organic phase was dried by passing through DT1 ($MgSO_4$) and transferred to a round-bottomed flask (CF1). The obtained solution was concentrated in vacuo. The residue (0.59 g) was purified by utilizing the automated column machine Combi flash Sg 100c (Isco Redi Sep Flash Column, 10–30% EtOAc in hexane, flow rate 15 mL min^{-1}) to afford diol **26** as a colorless oil (300 mg, 0.42 mmol, 64%) as well as recovered epoxide **25** (70 mg, 0.099 mmol, 15%). R_f = 0.46 (hexane/Et_2O 50:50); IR (neat): $\tilde{\nu}$ = 3408, 2929, 2856, 1733, 1613, 1514, 1362, 1302, 1250, 1095, 1036, 836, 773 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 0.06 (s, 6H), 0.88 (s, 9H), 1.11 (s, 3H), 1.13 (s, 3H), 1.16 (s, 3H), 1.66 (s, 3H), 1.57–1.68 (m, 1H), 1.58–2.25 (m, 6H), 1.98–2.12 (m, 1H), 2.44 (s, 1H), 2.60–2.80 (m, 1H), 3.23 (d, 1H, J = 8.9 Hz), 3.33 (d, 1H, J = 8.9 Hz), 3.75–3.82 (m, 1H), 3.80 (s, 3H), 4.09 (d, 1H, J = 10.9 Hz), 4.13 (br s, 1H), 4.16 (d, 1H, J = 10.9 Hz), 4.35 (d, 1H, J = 11.9 Hz), 4.41 (d, 1H, J = 11.9 Hz), 4.60 (d, 1H, J = 11.6 Hz), 4.65 (d, 1H, J = 11.6 Hz), 4.78 (d, 1H, J = 6.9 Hz), 4.87 (d, 1H, J = 6.9 Hz), 4.87 (s, 1H), 5.00 (s, 1H), 6.86 (d, 2H, J = 8.6 Hz), 7.21 (d, 2H, J = 8.6 Hz), 7.25–7.40 ppm (m, 5H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = −5.3, 18.3, 18.8, 19.3, 23.3, 25.6, 26.0, 27.6, 28.1, 30.1, 31.1, 43.9, 44.3, 48.2, 55.3, 59.3, 70.2, 70.5, 73.0, 75.7, 76.2, 77.7, 94.0, 113.7, 114.5, 128.0, 128.0, 128.6, 129.1, 130.2, 130.6, 136.9, 137.4, 147.6, 159.1 ppm; HRMS (ESI-TOF): calcd for $[C_{42}H_{64}O_7Si+Na]^+$: 731.4314; found: 731.4312.

27: A 100-mL three-necked flask (RF1) with diol **26** (0.50 g, 0.71 mmol) was attached to ChemKonzert. The oil was then treated with KOH (50% aqueous, 5.0 mL), BnBr (1.7 mL, 14 mmol), and Bu_4NHSO_4 (0.48 g, 1.4 mmol) manually at room temperature. The resulting mixture was stirred at the same temperature for 5 h, quenched by the addition of H_2O (40 mL, RR1), diluted with Et_2O (40 mL, RS1), and transferred to SF. After centrifugation, the two phases were separated. The aqueous phase in SF1 was transferred to RF1 and extracted with Et_2O (40 mL, RS2). This extraction process was repeated twice. The organic phase in SF2 was transferred to RF1 and washed with HCl (1 M aqueous, 40 mL, RS6), $NaHCO_3$ (5% aqueous, 40 mL, RS5) and NaCl (10% aqueous, 40 mL, RS4). The resulting organic phase was dried by passing through DT1 ($MgSO_4$) and transferred to a round-bottomed flask (CF1). The obtained solution was concentrated in vacuo. The residue (1.88 g) was purified by utilizing the automated column machine Combi flash Sg 100c (Isco Redi Sep Flash Column, 0–30% EtOAc in hexane, flow rate 15 mL min^{-1}) to afford benzyl ether **27** as a solid (465 mg, 0.58 mmol, 82%). R_f = 0.48 (hexane/Et_2O 67:33); m.p. 87–88 °C; IR (neat): $\tilde{\nu}$ = 3558, 2932, 1613, 1515, 1464, 1361, 1250, 1043, 836, 773, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.05 (s, 6H), 0.89 (s, 9H), 0.92 (s, 3H), 1.08 (s, 3H), 1.17 (s, 3H), 1.67 (s, 3H), 1.55–2.25 (m, 8H), 2.37 (br s, 1H), 3.51 (d, 1H, J = 9.7 Hz), 3.62 (d, 1H, J = 9.7 Hz), 3.79 (s, 3H), 3.73–3.87 (m, 1H), 4.10 (d, 1H, J = 11.1 Hz), 4.15 (d, 1H, J = 11.1 Hz), 4.22 (br s, 1H), 4.36 (d, 1H, J =

11.1 Hz), 4.46 (d, 1H, J=11.1 Hz), 4.47 (d, 1H, J=12.1 Hz), 4.66 (d, 1H, J=12.1 Hz), 4.67 (d, 1H, J=11.6 Hz), 4.71 (d, 1H, J=6.8 Hz), 4.73 (d, 1H, J=6.8 Hz), 4.84 (d, 1H, J=11.6 Hz), 5.03 (s, 1H), 5.50 (s, 1H), 6.84 (d, 2H, J=8.7 Hz), 7.23 (d, 2H, J=8.7 Hz), 7.18–7.42 ppm (m, 10H); ^{1}H NMR (400 MHz, CD_3OD): δ=0.04 (s, 3H), 0.05 (s, 3H), 0.85 (s, 3H), 0.89 (s, 9H), 1.12 (s, 3H), 1.37 (s, 3H), 1.47–1.91 (m, 1H), 1.63 (s, 3H), 1.83–2.20 (m, 7H) 2.32 (br s, 1H), 3.53 (d, 1H, J=9.7 Hz), 3.62 (d, 1H, J=9.7 Hz), 3.75 (br s, 3H), 3.77 (dd, 1H, J=4.3, 11.6 Hz), 4.06 (d, 1H, J=11.1 Hz), 4.19 (br s, 1H), 4.20 (d, 1H, J=11.1 Hz), 4.34 (d, 1H, J=11.1 Hz), 4.45 (d, 1H, J=11.1 Hz), 4.47 (d, 1H, J=12.1 Hz), 4.59 (d, 1H, J=12.1 Hz), 4.66 (d, 1H, J=11.6 Hz) 4.67 (d, 1H, J=6.3 Hz), 4.69 (d, 1H, J=6.3 Hz), 4.99 (d, 1H, J=11.6 Hz), 4.99 (d, 1H, J=1.9 Hz), 5.56 (br s, 1H), 6.83 (d, 2H, J=8.7 Hz), 7.24 (d, 2H, J=8.7 Hz), 7.15–7.40 ppm (m, 10H, a); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ=−5.3, 13.7, 18.4, 19.6, 26.1, 27.4, 29.9, 30.7, 36.5, 42.5, 46.1, 48.3, 55.3, 59.8, 69.5, 72.9, 73.1, 73.9, 79.3, 79.8, 81.4, 95.0, 113.7, 114.4, 126.9, 127.2, 127.7, 127.8, 128.3, 128.5, 129.8, 130.1, 130.9, 136.1, 138.1, 139.1, 146.3, 159.2 ppm; ^{13}C NMR (100 MHz, CD_3OD): δ=−4.3 (CH_3), 14.9 (CH_3), 20.0 (C), 20.6 (CH_3), 27.3 (CH_3), 27.3 (CH_3), 29.0 (CH_2), 31.8 (CH_2), 32.6 (CH_2), 38.5 (CH_2), 44.1 (C), 50.2 (3), 56.5 (CH_3), 61.9 (C10), 71.3 (CH_2), 74.6 (CH_2), 74.8 (CH_2), 76.2 (CH_2), 81.6 (C7), 82.58 (C1), 84.6 (C2), 96.5 (CH_2), 115.3 (C20), 115.5 (CH), 128.6 (CH), 128.8 (CH), 129.4 (CH), 129.7 (CH), 130.0 (CH), 130.2 (CH), 131.7 (CH), 132.3 (C), 133.1 (C), 137.7 (C), 140.2 (C), 141.7 (C), 148.4 (C), 161.5 ppm (C); HRMS (ESI-TOF): calcd for $[C_{49}H_{70}O_7Si+Na]^+$: 821.4783; found: 821.4783; elemental analysis: calcd for $C_{49}H_{70}O_7Si$ (%): C 73.64, H 8.83; found: C 73.62, H 8.97.

28: A 200-mL three-necked flask (RF2) with **27** (0.30 g, 0.38 mmol) was attached to ChemKonzert. The oil was then treated with DMF (5.0 mL), imidazole (0.20 g, 3.0 mmol), and Me_2HSiCl (0.17 mL, 1.5 mmol) manually at room temperature. The resulting mixture was stirred at the same temperature for 5 min, diluted with Et_2O (80 mL, RS2) and quenched by the addition of H_2O (20 mL, RS4) and NaCl (10%, 20 mL, RS6). The resulting mixture was then transferred to SF. After centrifugation, the two phases were separated. The aqueous phase in SF1 was transferred to RF2 and extracted with Et_2O (80 mL, RS2). The organic phase in SF2 was transferred to RF2 and washed with NaCl (10% aqueous, 40 mL, RS6). After separation of the phases, the organic phase was transferred to SF2, and the aqueous phase in SF1 was transferred to DRAIN2. RF2 was washed with Et_2O (40 mL, RS2), and the resulting solution was transferred to SF. RF2 was then washed with H_2O and acetone and dried under reduced pressure. The organic phase in SF2 was dried by passing through DT1 ($MgSO_4$) and transferred to RF1, and the solution in SF was transferred to RF2 through SF2 and DT1. The crude solution was concentrated under reduced pressure, diluted with CH_2Cl_2 (6 mL, RR7), and transferred to RF1 containing DDQ (0.21 g, 0.94 mmol). RF2 was then washed twice with CH_2Cl_2 (6 mL, RR10; 8 mL, RR9), and the resulting solution was transferred to RF1. The mixture was treated with buffer (pH 7 aqueous, 3 mL, RR1), stirred at room temperature for 25 min in RF1, and quenched by the addition of $NaHCO_3$ (5% aqueous, 40 mL, RS5), H_2O (20 mL, RS4), and NaCl (10% aqueous, 20 mL, RS6). The resulting mixture was filtered with FF1 and transferred to SF. FF1 was then washed with Et_2O (60 mL, RS2), and the resulting solution was transferred to SF. After centrifugation, the two phases were separated. The aqueous phase in SF1 was transferred to RF1 and extracted with Et_2O (80 mL, RS2). This extraction process was repeated twice. The organic phase in SF2 was transferred to RF1 and washed twice with NaCl (10% aqueous, 40 mL, RS6). The resulting organic phase was dried by passing through DT2 ($MgSO_4$) and transferred to a round-bottomed flask (CF1). RF1, SF, and SF2 were then washed with Et_2O (40 mL, RS2). The obtained solution was concentrated in vacuo. The residue (0.26 g) was purified by utilizing the automated column machine Combi flash Sg 100c (Isco Redi Sep Flash Column, 0–13% EtOAc in hexane, flow rate 7.5 mL min^{-1}) to afford alcohol **28** as a colorless oil (168 mg, 0.23 mmol, 60%). R_f=0.37 (hexane/Et_2O 80:20); IR (neat): $\tilde{\nu}$=3460, 2952, 2122, 1739, 1471, 1373, 1251, 1046, 903, 837, 732, 696, 668 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.02 (d, 3H), 0.11 (d, 3H), 0.12 (s, 6H), 0.74 (s, 3H), 0.92 (s, 3H), 1.06 (s, 3H), 1.31 (s, 3H), 1.48–1.62 (m, 1H), 1.66 (s, 3H), 2.14 (br s, 1H), 1.90–2.25 (m, 7H), 3.59 (dd, 1H, J=6.8, 12.1 Hz), 3.69 (dd, 1H, J=5.3, 11.6 Hz), 3.73 (dd, 1H, J=4.8, 12.1 Hz), 4.03 (br s, 1H), 4.13 (d, 1H, J=10.6 Hz), 4.22 (d, 1H, J=10.6 Hz), 4.49 (d, 1H, J=12.6 Hz), 4.59 (d, 1H, J=11.6 Hz), 4.66 (d, 1H, J=11.6 Hz), 4.73–4.85 (m, 1H), 4.80 (s, 2H), 5.01 (d, 1H, J=12.6 Hz), 5.09 (br s, 1H), 5.84 (br s, 1H), 7.17–7.40 ppm (m, 10H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ=−5.4, −5.0, 1.1, 1.3, 12.9, 18.6, 19.6, 26.2, 27.7, 29.7, 31.2, 37.0, 43.4, 46.8, 47.6, 60.1, 64.2, 69.9, 73.7, 78.9, 81.4, 84.0, 94.0, 114.8, 126.0, 126.4, 127.8, 128.0, 128.1, 128.1, 128.5, 135.2, 137.9, 140.1, 145.6 ppm; HRMS (ESI-TOF): calcd for $[C_{43}H_{68}O_6Si_2+Na]^+$:759.4447; found: 759.4447.

29: A 200-mL three-necked flask (RF2) with alcohol **28** (0.29 g, 0.39 mmol) was attached to ChemKonzert. The oil was then treated with $CHCl_3$ (4.1 mL), DMAP (0.19 g, 1.6 mmol), and TsCl (0.17 g, 0.9 mmol) manually at room temperature. The resulting mixture was stirred at 50 °C for 1 h, diluted with Et_2O (80 mL, RS2), and quenched by the addition of H_2O (20 mL, RS4) and NaCl (10%, 20 mL, RS6). The resulting mixture was then transferred to SF. After centrifugation, the two phases were separated. The aqueous phase in SF1 was transferred to RF1 and extracted with Et_2O (40 mL, RS2). This extraction process was repeated twice. The organic phase in SF2 was transferred to RF1 and washed with NaCl (10% aqueous, 40 mL, RS6). After the phases were separated, the organic phase was transferred to SF2, and the aqueous phase in SF1 was transferred to DRAIN2. RF2 was washed with Et_2O (40 mL, RS2), and resulting solution was transferred to SF. RF2 was then washed with H_2O and acetone and dried under reduced pressure. The organic phase in SF2 was dried by passing through DT1 ($MgSO_4$) and transferred to RF1, and the solution in SF was transferred to RF2 through SF2 and DT1. The crude solution was concentrated under reduced pressure, diluted with THF (6 mL, RR7), and transferred to RF1 containing TBAF (0.62 g 2.4 mmol). RF2 was then washed twice with THF (6 mL, RR10; 8 mL, RR9) twice, and the resulting solution was transferred to RF1. The mixture in RF1 was stirred at 70 °C for 1 h, quenched by the addition of H_2O (20 mL) and NaCl (10% aqueous, 20 mL, RS6), and diluted with EtOAc (80 mL, RS3). The resulting mixture was transferred to SF. After centrifugation, the two phases were separated. The aqueous phase in SF1 was transferred to RF1 and extracted with EtOAc (80 mL, RS3). This extraction process was repeated twice. The organic phase in SF2 was transferred to RF1 and washed twice with NaCl (10% aqueous, 40 mL, RS6). The resulting organic phase was dried by passing through DT2 ($MgSO_4$) and transferred to a round-bottomed flask (CF1). RF1, SF, and SF2 were then washed with EtOAc (40 mL, RS3). The obtained solution was concentrated in vacuo. The residue (0.35 g) was purified by utilizing the automated column machine Combi flash Sg 100c (Isco Redi Sep Flash Column, 0–60% EtOAc in hexane, flow rate 7.5 mL min^{-1}) to afford diol **29** as a colorless oil (149 mg, 0.21 mmol, 53%). R_f=0.46 (hexane/EtOAc 33:67); IR (neat): $\tilde{\nu}$=3433, 2947, 2895, 1454, 1366, 1190, 1043, 967, 834, 754, 698, 667, 555 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.98 (s, 3H), 1.08 (s, 3H), 1.22 (s, 3H), 1.50–1.80 (m, 2H), 1.77 (s, 3H), 1.88–2.12 (m, 4H), 2.16–2.30 (m, 2H), 2.30 (s, 1H), 2.42 (s, 3H), 3.55 (dd, 1H, J=4.8, 10.4 Hz), 4.08 (d, 1H, J=14.5 Hz), 4.12 (d, 1H, J=9.7 Hz), 4.13 (s, 1H), 4.23 (d, 1H, J=9.7 Hz), 4.23 (d, 1H, J=14.5 Hz), 4.42 (d, 1H, J=12.1 Hz), 4.55 (d, 1H, J=7.2 Hz), 4.57 (d, 1H, J=7.2 Hz), 4.59 (d, 1H, J=12.1 Hz), 4.67 (d, 1H, J=11.6 Hz), 4.77 (d, 1H, J=11.6 Hz), 5.05 (br s, 1H), 5.44 (br s, 1H), 7.34 (d, 2H, J=8.2 Hz), 7.20–7.40 (m, 10H), 7.80 ppm (d, 2H, J=8.2 Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ=13.8, 19.5, 21.7, 25.1, 27.4, 29.6, 30.1, 30.1, 35.5, 42.5, 45.4, 48.3, 59.4, 69.6, 71.9, 73.9, 78.5, 79.4, 80.9, 94.9, 115.2, 126.9, 127.5, 127.8, 127.8, 128.2, 128.5, 128.5, 130.0, 132.5, 132.6, 136.8, 137.8, 138.4, 145.2, 145.4 ppm; HRMS (ESI-TOF): calcd for $[C_{42}H_{54}O_8S+Na]^+$: 741.3432; found: 741.3429.

30: A solution of diol **29** (0.11 g, 0.15 mmol) in dry 2,6-lutidine (0.24 mL) was treated with iPr$_2$NEt (0.26 mL, 1.5 mmol) and TMSOTf (0.11 mL, 0.59 mmol) manually at 0 °C under Ar. The resulting mixture was stirred at the same temperature for 1 h, quenched by addition of $NaHCO_3$ (20 mL saturated aqueous solution), diluted with Et_2O (40 mL), and transferred to RF2 manually. The resulting solution was transferred to SF. After centrifugation, the two phases were separated. The aqueous phase in SF1 was transferred to RF1 and extracted with Et_2O (40 mL, RS2). The aqueous phase was then transferred back to RF1, treated with HCl (1 M aqueous, 20 mL, RR1) and NaCl (10% aqueous, 20 mL, RS6), and reextracted with EtOAc (40 mL, RS3). After separation of the phases, the organic phase in SF2 was transferred to RF1 and washed with

$NaHCO_3$ (5% aqueous, 40 mL, RS5) and NaCl (10% aqueous, 40 mL, RS6). After separation of the phases, the organic phase was transferred to SF2, and the aqueous phase in SF1 was transferred to DRAIN2. RF2 was washed with Et_2O (60 mL, RS2), and the resulting solution was transferred to SF. RF2 was then washed with H_2O and acetone and dried under reduced pressure. The organic phase in SF2 was dried by passing through DT1 (Na_2SO_4) and transferred to RF1, and the solution in SF was transferred to RF2 through SF2 and DT1. The crude solution was concentrated under reduced pressure, diluted with THF (6 mL, RR7), and transferred to RF1 containing TBAF (0.12 g, 0.46 mmol). RF2 was then washed twice with THF (6 mL, RR10; 8 mL, RR9), and the resulting solution was transferred to RF1. The mixture in RF1 was stirred at room temperature for 1 h, quenched by the addition of H_2O (20 mL, RS4) and NaCl (10% aqueous, 20 mL, RS6), and diluted with EtOAc (40 mL, RS3). The resulting mixture was transferred to SF. After centrifugation, the two phases were separated. The aqueous phase in SF1 was transferred to RF1 and extracted with EtOAc (40 mL, RS3). This extraction process was repeated twice. The organic phase in SF2 was transferred to RF1 and washed with NaCl (10% aqueous, 40 mL, RS6). The resulting organic phase was dried by passing through DT2 ($MgSO_4$) and transferred to a round-bottomed flask (CF1). RF1, SF, and SF2 were then washed with EtOAc (40 mL, RS3). The obtained solution was concentrated in vacuo. The residue (90 mg) was purified by utilizing the automated column machine Combi flash Sg 100c (Isco Redi Sep Flash Column, flow rate 7 mL min^{-1}) to afford alcohol **30** (78 mg, 0.099 mmol, 66%) as a colorless oil as well as recovered diol **29** (13 mg, 0.018 mmol, 12%) as a colorless oil. R_f=0.58 (hexane/EtOAc 1:1); IR (neat): $\tilde{\nu}$= 3444, 2952, 1365, 1177, 1105, 1043, 966, 837, 555 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.79 (d, 2H, J=8.2 Hz), 7.30 (d, 2H, J=8.2 Hz), 7.16–7.45 (m, 10H), 5.82 (br s, 1H), 5.06 (br s, 1H), 4.93 (d, 1H, J= 12.6 Hz), 4.57 (d, 1H, J=12.1 Hz), 4.52 (d, 1H, J=12.6 Hz), 4.50 (d, 1H, J=6.8 Hz), 4.42 (d, 1H, J=6.8 Hz), 4.36 (d, 1H, J=12.1 Hz), 4.25 (d, 1H, J=9.7 Hz), 4.13 (d, 1H, J=9.7 Hz), 4.20 (d, 1H, J=11.6 Hz), 4.11 (d, 1H, J=11.6 Hz), 3.95 (s, 1H), 3.45 (dd, 1H, J=4.3, 11.4 Hz), 1.45–2.50 (m, 8H), 2.42 (s, 3H), 2.38 (s, 1H), 1.69 (s, 3H), 1.22 (s, 3H), 1.04 (s, 3H), 0.81 (s, 3H), 0.03 ppm (s, 9H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ= 145.1, 144.7, 139.7, 137.9, 136.5, 132.6, 131.9, 129.9, 128.5, 128.3, 128.2, 127.8, 127.7, 126.6, 125.7, 114.9, 95.0, 85.3, 83.4, 80.0, 74.0, 71.6, 69.4, 59.5, 47.8, 46.0, 42.2, 36.5, 30.7, 30.5, 30.5, 29.8, 28.0, 21.7, 19.6, 12.8, 3.5 ppm; HRMS (ESI-TOF): calcd for $[C_{42}H_{62}O_8SSi+Na]^+$: 813.3827; found: 813.3835.

31: The disposable silica-gel plug (Isco Redi Sep Flash Column 4 g) and the 50-mL three-necked flask (RF2) with **30** (120 mg, 0.15 mmol) was attached to ChemKonzert. The oil was then treated with CH_2Cl_2 (3 mL), NMO (0.055 g, 0.47 mmol), and TPAP (2.8 mg, 7.9 μmol) manually at room temperature. The resulting mixture was stirred at the same temperature for 30 min and transferred to the disposable silica-gel plug. RF2 was then washed twice with mixed solvent (hexane/EtOAc 75:25, 5 mL, RR7; 5 mL, RR10) twice, and the resulting solution was transferred to the disposable silica-gel plug. The crude mixture was filtered through the disposable silica-gel plug, eluting with mixed solvent (hexane/EtOAc 75:25, 70 mL, RR9) and transferred to a round-bottomed flask (CF1). The obtained solution was concentrated in vacuo to afford enal **31** (118 mg, 0.15 mmol, quant.). R_f=0.42 (hexane/Et_2O 50:50); IR (neat): $\tilde{\nu}$=2953, 1674, 1367, 1251, 1178, 1094, 837, 754, 667, 555 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ=0.02 (s, 9H), 0.84 (s, 3H), 1.20 (s, 3H), 1.27 (s, 3H), 2.00 (s, 3H), 1.47–2.35 (m, 9H), 2.43 (s, 3H), 3.45 (dd, 1H, J=4.6, 11.2 Hz), 3.98 (br s, 1H), 4.02 (d, 1H, J=9.9 Hz), 4.29 (d, 1H, J= 9.9 Hz), 4.38 (d, 1H, J=11.9 Hz), 4.49 (d, 1H, J=12.5 Hz), 4.52 (d, 1H, J=6.9 Hz), 4.57 (d, 1H, J=6.9 Hz), 4.60 (d, 1H, J=11.9 Hz), 4.94 (d, 1H, J=12.5 Hz), 5.10 (br s, 1H), 5.79 (br s, 1H), 7.16–7.40 (m, 10H), 7.30 (d, 2H, J=8.6 Hz), 7.79 (d, 2H, J=8.6 Hz), 9.98 ppm (s, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ=3.3, 13.1, 19.6, 21.7, 27.5, 29.8, 30.5, 30.5, 32.8, 36.4, 41.4, 46.0, 48.4, 69.5, 71.4, 73.9, 80.1, 82.3, 84.7, 95.3, 115.6, 126.7, 127.7, 127.8, 128.2, 128.3, 128.5, 129.9, 132.7, 137.9, 139.3, 140.0, 144.4, 145.1, 150.6, 193.2 ppm; HRMS (ESI-TOF): calcd for $[C_{45}H_{60}O_8SSi+Na]^+$: 813.3827; found: 813.3835.

32: A solution of enal **31** (118 mg, 0.15 mmol) in TMSCN (1.0 mL, 7.9 mmol) was treated with a catalytic amount of KCN and [18]crown-6 at room temperature manually and stirred at the same temperature for 1 h under argon in a 200-mL three-necked flask. The reaction flask RF2 was then attached to ChemKonzert. The reaction mixture was diluted with THF (4 mL, RR7) and treated dropwise with HCl (1 M aqueous, 3 mL, RR1) at 10 °C. The resulting mixture was stirred at room temperature for 2 h. The resulting solution was diluted with EtOAc (60 mL, RS3), treated with NaCl (10% aqueous, 40 mL, RS6), and transferred to SF. After centrifugation, the two phases were separated. The organic phase in SF2 was dried by passing through DT1 (Na_2SO_4) and transferred to a round-bottomed flask (CF1). RF2, SF, and SF2 were then washed with EtOAc (60 mL, RS3). The obtained solution was concentrated in vacuo. The residue (120 mg) was filtered through a silica-gel plug (flash column chromatography), eluting with hexane/Et_2O (70:30) to afford a diastereomeric mixture of cyanohydrins as a colorless oil (116 mg, 0.14 mmol, 93%). The solution of the cyanohydrin (116 mg, 0.14 mmol) in CH_2Cl_2 (3 mL) was treated with camphorsulfonic acid (0.027 g, 0.11 mmol) and ethyl vinyl ether (0.032 mL, 0.33 mmol) manually at 0 °C in a 200-mL three-necked flask (RF2). The resulting solution was stirred at the same temperature for 5 min and quenched by the manual addition of Et_3N (0.50 mL, 3.6 mmol). The reaction flask RF2 was then attached to ChemKonzert, and the reaction mixture was diluted with EtOAc (40 mL, RS3) and treated with $NaHCO_3$ (5% aqueous, 40 mL, RS5). The resulting mixture was transferred to SF. After centrifugation, the two phases were separated. The organic phase in SF2 was transferred to RF2 and washed with NaCl (10% aqueous, 40 mL, RS6). The resulting organic phase was dried by passing through DT1 (Na_2SO_4) and transferred to a round-bottomed flask (CF1), dried by passing through DT1 (Na_2SO_4), and transferred to a round-bottomed flask (CF1). The obtained solution was concentrated in vacuo. The residue (0.12 g) was filtered through a silica-gel plug (flash column chromatography) eluting with hexane/Et_2O (60:40) to afford the protected cyanohydrin **32** as a colorless oil (116 mg, 0.13 mmol, 93%).

33: A solution of $HN(TMS)_2$ (0.48 mL, 2.3 mmol) in dry dioxane (2.0 mL) was treated with BuLi (1.59 M in hexane, 1.3 mL, 2.0 mmol) at 6 °C under argon and stirred at room temperature for 30 min. The resulting clear solution was treated dropwise with a solution of protected cyanohydrin **32** (20 mg, 0.023 mmol) in dry dioxane (1.4 mL) at room temperature. The resulting mixture was stirred at 145 °C for 15 min in a microwave synthesizer, quenched by the addition of NH_4Cl (saturated aqueous solution), and extracted with EtOAc. The organic phase was washed with $NaHCO_3$ (saturated aqueous solution) and brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. The residue was filtered through a silica-gel plug (flash column chromatography) eluting with hexane/Et_2O (85:15) to afford cyclization product **33** as a colorless oil (8.0 mg, 0.011 mmol, 49%).

34: A solution of protected cyanohydrin **33** (27 mg, 0.037 mmol) in MeOH (2 mL) was treated with camphorsulfonic acid (22 mg, 0.096 mmol) at room temperature. The resulting solution was stirred at the same temperature for 1 h. The reaction was quenched by the addition of brine, and the organic components were extracted with Et_2O. The solution was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was used for the next reaction without further purification. A solution of the crude cyanohydrin in Et_2O (0.3 mL) was treated with NaOH (1 M aqueous, 0.3 mL, 0.3 mmol) at room temperature. The resulting solution was stirred at the same temperature for 1 h, quenched by the addition of brine, and extracted with Et_2O. The solution was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was filtered through a silica-gel plug (flash column chromatography) eluting with hexane/Et_2O (70:30) to afford ketone **34** as a colorless oil (17 mg, 0.030 mmol, 82%): R_f=0.43 (hexane/Et_2O 50:50); IR (neat): $\tilde{\nu}$=3527, 2936, 1675, 1455, 1376, 1103, 1042, 737, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.08 (s, 3H), 1.21 (s, 3H), 1.29 (s, 3H), 1.55 (ddd, 1H, J=5.8, 11.2, 17.9 Hz), 1.75 (s, 3H), 1.72–1.86 (m, 1H), 1.87–2.13 (m, 3H), 2.13–2.25 (m, 1H), 2.15–2.28 (m, 1H), 2.60 (d, 1H, J=14.8 Hz), 2.75 (ddd, 1H, J=5.8, 13.5, 19.3 Hz), 2.89 (d, 1H, J=14.8 Hz), 2.94 (br d, 1H, J= 4.3 Hz), 3.28 (dd, 1H, J=5.3, 11.2 Hz), 3.84 (br d, 1H, J=4.3 Hz), 4.53 (d, 1H, J=10.9 Hz), 4.62 (d, 1H, J=11.9 Hz), 4.69 (d, 1H, J=11.9 Hz), 4.81 (d, 1H, J=7.3 Hz), 4.85 (d, 1H, J=10.9 Hz), 4.88 (d, 1H, J= 7.3 Hz), 4.97 (br s, 1H), 5.31 (br s, 1H), 7.20–7.46 ppm (m, 10H);

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.6 (C19), 22.4 (C16 or C17), 22.5 (C18), 26.8 (C16 or C17), 28.5 (C14), 29.6 (C6), 31.9 (C13), 36.5 (C5), 39.5 (C15), 45.5 (C8), 48.2 (C3), 51.9 (C9), 69.9 (BOM CH_2Ph), 75.9 (Bn CH_2Ph), 79.5 (C1), 80.9 (C7), 83.2 (C2), 94.9 (BOM OCH_2O), 113.5 (C20), 127.7 (Ph), 127.8 (Ph), 127.9 (Ph), 128.2 (Ph), 128.5 (Ph), 128.8 (Ph), 137.3 (Ph), 138.1 (Ph), 138.4 (C12), 144.3 (C4), 145.8 (C11), 204.6 ppm (C10); HRMS (ESI-TOF): calcd for $[C_{35}H_{44}O_5+Na]^+$: 567.3081; found: 567.3080.

35: A solution of alkene **34** (18 mg, 0.033 mmol) in 1.0 mL of hexane was treated with SeO_2 (23 mg, 0.21 mmol), salicylic acid (9.1 mg, 0.066 mmol) and *t*BuO_2H (>70% aqueous, 0.086 mL). The resulting mixture was stirred at 55 °C for 30 min, quenched by the addition of $Na_2S_2O_3$ (10%, aqueous), and the mixture was stirred for 3 h. The solution was extracted with EtOAc. The organic phase was washed with $Na_2S_2O_3$ (10% aqueous), $NaHCO_3$ (saturated aqueous solution), and brine, dried over anhydrous $MgSO_4$ and concentrated in vacuo to yield an oil. The residue was filtered through a silica-gel plug (flash column chromatography), eluting with hexane/EtOAc (70:30) to afford allylic alcohol **35** as a colorless oil (17 mg, 0.030 mmol, 92%): R_f = 0.50 (hexane/EtOAc 50:50); IR (neat): $\tilde{\nu}$ = 3479, 2938, 1673, 1455, 1105, 1041, 1028, 753, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.01 (s, 3H), 1.22 (s, 3H), 1.31 (s, 3H), 1.64 (ddd, 1H, *J* = 3.9, 11.1, 13.5 Hz), 1.84 (s, 3H), 1.77–1.89 (m, 1H), 2.08–2.22 (m, 2H), 2.18 (ddd, 1H, *J* = 3.4, 5.3, 13.5 Hz), 2.57 (d, 1H, *J* = 15.5 Hz), 2.70 (dt, 1H, *J* = 9.7, 14.7 Hz), 2.90 (d, 1H, *J* = 15.5 Hz), 3.48 (d, 1H, *J* = 4.4 Hz), 3.61 (dd, 1H, *J* = 5.3, 11.1 Hz), 3.88 (d, 1H, *J* = 4.4 Hz), 4.21 (br s, 1H), 4.58 (d, 1H, *J* = 10.6 Hz), 4.61 (d, 1H, *J* = 12.1 Hz), 4.70 (d, 1H, *J* = 12.1 Hz), 4.82 (d, 1H, *J* = 10.6 Hz), 4.83 (d, 1H, *J* = 6.8 Hz), 4.87 (d, 1H, *J* = 6.8 Hz), 5.16 (s, 1H), 5.48 (s, 1H), 7.22–7.50 ppm (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.9 (C8), 21.2 (C18), 22.3 (C16 or C17), 26.8 (C16 or C17), 28.7 (C14), 31.6 (C13), 36.7 (C6), 39.3 (C15), 42.2 (C3), 45.9 (C8), 51.1 (C9), 69.7 (BOM CH_2Ph), 75.7 (C5), 75.7 (Bn CH_2Ph), 77.4 (C7), 79.5 (C1), 83.1 (C2), 95.2 (BOM OCH_2O), 115.0 (C20), 127.6 (Ph), 127.7 (Ph), 127.8 (Ph), 128.2 (Ph), 128.4 (Ph), 128.7 (Ph), 137.0 (Ph), 138.0 (Ph), 139.4 (C12), 145.1 (C11), 147.3 (C4), 203.9 ppm (C10); HRMS (ESI-TOF): calcd for $[C_{35}H_{44}O_6+Na]^+$: 583.3030; found: 583.3023.

36: A solution of quinuclidine (2.0 mg, 18 μmol) in *t*BuOH (2.4 mL) and H_2O (2.4 mL) was treated with OsO_4 (0.05 M in THF, 89 μL, 4.5 μmmol) at room temperature. The resulting solution was stirred at the same temperature for 10 min. The quinuclidine–OsO_4 complex thus prepared was used in the following reaction. A solution of the allylic alcohol **35** (4.3 mg, 7.7 μmol) in *t*BuOH (1.8 mL) and H_2O (1.8 mL) was treated with NMO (3.1 mg, 27 μmol) at room temperature. The resulting mixture was then cooled to 0 °C, treated dropwise with the quinuclidine–OsO_4 complex (1.0 mL) in five separate portions (at 2.5-h intervals), and stirred at the same temperature. The resulting solution was treated with $NaBH_4$ (20 mg, 0.52 mmol) at 0 °C, stirred at the same temperature for 10 min, and acidified by the addition of NH_4Cl (saturated aqueous solution). The *t*BuOH was then removed in vacuo, and the residue was diluted with EtOAc and treated with HCl (1 M aqueous). The solution was extracted with EtOAc. The organic phase was washed with brine, dried over anhydrous $MgSO_4$ and concentrated in vacuo to yield an oil. The residue was purified by thin-layer chromatography (hexane/EtOAc = 33:67) to afford triol **36** as a colorless oil (2.9 mg, 4.9 μmol, 64%) together with recovered allylic alcohol **35** (0.8 mg, 1.4 μmol, 19%) as a colorless oil. R_f = 0.46 (hexane/EtOAc 29:71); IR (neat): $\tilde{\nu}$ = 3468, 2925, 2854, 1735, 1671, 1454, 1261, 1041, 800, 752, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (s, 3H), 1.21 (s, 3H), 1.35 (s, 3H), 1.75 (ddd, 1H, *J* = 2.4, 11.6, 15.5 Hz), 1.63–1.85 (m, 1H), 1.85 (s, 3H), 2.10–2.24 (m, 1H), 2.27 (ddd, 1H, *J* = 3.9, 4.8, 15.5 Hz), 2.32–2.46 (m, 1H), 2.54 (d, 1H, *J* = 15.5 Hz), 2.60–2.74 (m, 1H), 2.78 (d, 1H, *J* = 15.5 Hz), 3.05 (d, 1H, *J* = 4.8 Hz), 3.51 (dd, 1H, *J* = 4.8, 11.6 Hz), 3.69 (d, 1H, *J* = 11.1 Hz), 3.89 (dd, 1H, *J* = 1.5, 11.1 Hz), 3.92 (d, 1H, *J* = 4.8 Hz), 3.94 (dd, 1H, *J* = 2.4, 3.9 Hz), 4.62 (d, 1H, *J* = 12.1 Hz), 4.72 (d, 1H, *J* = 12.1 Hz), 4.75 (d, 1H, *J* = 10.1 Hz), 4.83 (d, 1H, *J* = 6.8 Hz), 4.87 (d, 1H, *J* = 10.1 Hz), 4.88 (d, 1H, *J* = 6.8 Hz), 7.20–7.55 ppm (m, 10H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 19.8, 21.2, 23.9, 28.7, 31.1, 33.0, 33.2, 40.6, 45.9, 46.4, 52.9, 65.8, 71.0, 71.2, 77.7, 78.9, 79.4, 82.3, 84.4, 96.5 (BOM OCH_2O), 128.9 (Ph), 129.3 (Ph), 129.6 (Ph), 129.8 (Ph), 129.8 (Ph), 129.9 (Ph), 139.3 (Ph), 139.8 (Ph), 141.8 (C12), 146.4 (C11), 206.2 ppm (C10); HRMS (ESI-TOF): calcd for $[C_{35}H_{46}O_8+Na]^+$: 617.3085; found: 617.3075.

37: A solution of the triol **36** (34.3 mg, 57.7 μmol) in dry CH_2Cl_2 (18 mL) was treated with DMAP (140 mg, 1.15 mmol) at room temperature. The resulting mixture was then cooled to −40 °C and treated dropwise with AcCl (9.1 μL, 0.12 mmol) at the same temperature. The resulting solution was warmed to 0 °C, stirred at the same temperature for 1 h, diluted with EtOAc, and quenched by the addition of HCl (1 M aqueous). The solution was extracted with EtOAc. The organic phase was washed with a saturated aqueous solution of $NaHCO_3$ and with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo to yield an oil. The residue was purified by thin-layer chromatography (hexane/EtOAc = 33:67) to afford acetate **37** as a colorless oil (33.2 mg, 52.1 μmol, 90%): R_f = 0.50 (hexane/EtOAc 40:60); IR (neat): $\tilde{\nu}$ = 3479, 2926, 1739, 1674, 1455, 1371, 1260, 1233, 1039, 752, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (s, 3H), 1.20 (s, 3H), 1.35 (s, 3H), 1.53–1.78 (m, 2H), 1.84 (s, 3H), 1.95 (s, 3H), 2.16 (ddd, 1H, *J* = 3.4, 10.6, 18.9 Hz), 2.26 (dt, 1H, *J* = 4.8, 14.5 Hz), 2.46–2.60 (m, 1H), 2.54 (d, 1H, *J* = 15.5 Hz), 2.60–2.73 (m, 1H), 2.78 (d, 1H, *J* = 15.5 Hz), 3.02 (d, 1H, *J* = 5.3 Hz), 3.52 (dd, 1H, *J* = 4.8, 11.6 Hz), 3.89 (d, 1H, *J* = 5.3 Hz), 3.91 (dd, 1H, *J* = 4.8, 13.5 Hz), 4.35 (d, 1H, *J* = 11.6 Hz), 4.42 (d, 1H, *J* = 11.6 Hz), 4.62 (d, 1H, *J* = 12.1 Hz), 4.72 (d, 1H, *J* = 12.1 Hz), 4.83 (d, 1H, *J* = 10.6 Hz), 4.83 (d, 1H, *J* = 6.8 Hz), 4.87 (d, 1H, *J* = 6.8 Hz), 4.92 (d, 1H, *J* = 10.6 Hz), 7.20–7.40 ppm (m, 10H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 19.5, 20.6, 20.8, 23.1, 27.8, 28.2, 31.1, 31.8, 38.8, 44.2, 45.3, 51.5, 66.2, 69.9, 70.4, 76.5, 76.8, 76.9, 80.7, 83.9 95.6 (OCH_2O), 127.6 (Ph), 127.8 (Ph), 128.1 (Ph), 128.4 (Ph), 128.6 (Ph), 129.0 (Ph), 136.5 (Ph), 138.2 (Ph), 140.0 (C12), 144.6 (C11), 171.0 (Ac), 202.6 ppm (C10); HRMS (ESI-TOF): calcd for $[C_{37}H_{48}O_9+Na]^+$: 659.3191; found: 659.3196.

38: A solution of the diol **37** (33.2 mg, 52.1 μmol) in dry CH_2Cl_2 (4.1 mL) was treated with DMAP (127 mg, 1.04 mmol) and MsCl (40 μL, 0.52 mmol) at room temperature. The resulting mixture was stirred at the same temperature for 15 min, diluted with EtOAc, and quenched by the addition of HCl (1 M aqueous). The solution was extracted with EtOAc. The organic phase was washed with a saturated aqueous solution of $NaHCO_3$ and with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo to yield an oil. The residue was purified by thin-layer chromatography (hexane/EtOAc = 50:50) to afford mesylate **38** (31.0 mg, 43.4 μmol, 83%) as a colorless oil: R_f = 0.51 (hexane/EtOAc 33:67); IR (neat): $\tilde{\nu}$ = 3502, 2946, 1940, 1673, 1356, 1236, 1177, 1039, 753 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (s, 3H), 1.19 (s, 3H), 1.34 (s, 3H), 1.67–1.79 (m, 1H), 1.87 (s, 3H), 1.92 (ddd, 1H, *J* = 2.9, 4.8, 15.0 Hz), 2.01 (s, 3H), 2.37 (ddd, 1H, *J* = 4.4, 11.6, 15.0 Hz), 2.28–2.38 (m, 1H), 2.57 (d, 1H, *J* = 15.5 Hz), 2.48–2.60 (m, 1H), 2.62–2.75 (m, 1H), 2.77 (d, 1H, *J* = 15.5 Hz), 2.92 (d, 1H, *J* = 4.8 Hz), 2.95 (s, 3H), 3.46 (dd, 1H, *J* = 4.8, 11.6 Hz), 3.94 (d, 1H, *J* = 4.8 Hz), 4.31 (d, 1H, *J* = 12.1 Hz), 4.55 (d, 1H, *J* = 12.1 Hz), 4.61 (d, 1H, *J* = 12.1 Hz), 4.70 (d, 1H, *J* = 12.1 Hz), 4.80 (d, 1H, *J* = 10.6 Hz), 4.83 (dd, 1H, *J* = 2.9, 4.4 Hz), 4.86 (br s, 2H), 4.95 (d, 1H, *J* = 10.6 Hz) 7.30–7.48 ppm (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.8 (CH_3), 20.4 (CH_3), 20.7 (CH_3), 22.9 (CH_3), 27.8 (CH_3), 28.2 (CH_2), 31.6 (CH_2), 32.0 (CH_2), 38.5 (CH_3), 38.7 (C), 44.0 (C), 46.6 (C), 51.4 (CH_2), 65.9 (CH_2), 68.9 (CH_2), 75.2 (CH), 76.2 (CH_2), 76.7 (C), 80.4 (C), 81.0 (CH), 83.5 (CH), 95.6 (CH_2), 127.6 (CH), 127.6 (CH), 128.2 (CH), 128.4 (CH), 128.6 (CH), 128.9 (CH), 136.2 (C), 137.7 (C), 140.8 (C), 144.4 (C), 170.8 (C), 201.6 ppm (C); HRMS (ESI-TOF): calcd for $[C_{38}H_{50}O_{11}S+Na]^+$: 737.2966; found: 737.2969.

39: A solution of acetate **38** (3.6 mg, 5.0 μmol) in MeOH (0.5 mL) was treated with K_2CO_3 (5.0 mg, 36 μmol) at room temperature, stirred at the same temperature for 5 min, and quenched by the addition of NH_4Cl (saturated aqueous solution). The solution was extracted with EtOAc. The organic phase was washed with a saturated aqueous solution of $NaHCO_3$ and with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo to yield an oil. The residue was used for the next reaction without further purification. A solution of crude diol (3.5 mg) in dry toluene (1.2 mL) was treated with DBU (80 μL, 536 μmol) at room temperature, stirred at 110 °C for 10 min, and cooled to room temperature. The resulting solution was diluted with EtOAc and quenched by the addition of H_2O. The solution was extracted with EtOAc. The organic phase was washed with

brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo to yield an oil. The residue was purified by thin-layer chromatography (hexane/EtOAc = 33:67) to afford oxetane **39** (2.0 mg, 3.5 μmol, 69%) as a colorless oil: $R_f = 0.43$ (hexane/EtOAc 50:50); IR (neat): $\tilde{\nu}$ = 3492, 2927, 1673, 1455, 1039, 972, 736, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.19$ (s, 3H), 1.37 (s, 3H), 1.40 (s, 3H), 1.68 (s, 3H), 1.75 (dddd, 1H, $J = 0.9$, 3.4, 10.1, 13.5 Hz), 2.01 (ddd, 1H, $J = 3.4$, 10.2, 15.0 Hz), 2.14 (ddd, 1H, $J = 3.4$, 10.2, 19.6 Hz), 2.23(d, 1H, $J = 4.8$ Hz), 2.29 (ddd, 1H, $J = 3.4$, 10.1, 13.5 Hz), 2.62 (d, 1H, $J = 15.5$ Hz), 2.57–2.69 (m, 2H), 2.94 (d, 1H, $J = 15.5$ Hz), 3.24 (dd, 1H, $J = 7.3$, 10.2 Hz), 3.94 (d, 1H, $J = 4.8$ Hz), 4.34 (d, 1H, $J = 7.8$ Hz), 4.58 (d, 1H, $J = 11.6$ Hz), 4.66 (d, 1H, $J = 10.6$ Hz), 4.68 (dd, 1H, $J = 3.4$, 10.2 Hz), 4.71 (d, 1H, $J = 11.6$ Hz), 4.77 (d, 1H, $J = 7.8$ Hz), 4.80 (d, 1H, $J = 7.3$ Hz), 4.84 (d, 1H, $J = 10.6$ Hz), 4.89 (d, 1H, $J = 7.3$ Hz) 7.26–7.42 ppm (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.2 (C19), 21.1 (C18), 23.1 (C16 or C17), 27.7 (C16 or C17), 28.1 (C14), 31.4 (C13), 35.7 (C6), 38.7 (C15), 43.3 (C8), 50.5 (C3), 51.0 (C9), 69.9 (CH_2Ph), 75.3 (C4), 77.1 (CH_2Ph), 79.3 (C7), 79.3 (C1), 80.4 (C20), 82.5 (C2), 85.5 (C5), 95.4 (OCH_2O), 127.7 (Ph), 127.8 (Ph), 127.8 (Ph), 128.3 (Ph), 128.4 (Ph), 128.9 (Ph), 136.8 (Ph), 137.8 (Ph), 138.5 (C12), 145.5 (C11), 202.7 ppm (C10); HRMS (ESI-TOF): calcd for $[C_{35}H_{49}O_7+H]^+$: 577.3160; found: 577.3160.

40: $Pd(OH)_2$ (20% on carbon, 20 mg, 28.4 μmol) in EtOH (1 mL) was placed under an atmosphere of hydrogen and treated with a solution of benzyl ether **39** (1.8 mg, 3.1 μmol) in EtOH (1 mL). The resulting mixture was stirred at the same temperature for 5 min, filtered through celite, and concentrated in vacuo to afford an oil. The residue was purified by thin-layer chromatography ($CHCl_3$/MeOH 75:25) to afford the five-membered ring ether **40** (1.0 mg, 2.7 μmol, 88%) as a colorless oil: $R_f = 0.41$ ($CHCl_3$/MeOH 75:25); ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.00$ (s, 3H), 1.03 (s, 3H), 1.09 (s, 3H), 1.63 (s, 3H), 1.50–2.60 (m, 6H), 2.48 (d, 1H, $J = 14.0$ Hz), 2.53 (d, 1H, $J = 6.3$ Hz) 2.56 (d, 1H, $J = 14.0$ Hz), 3.42 (dd, 1H, $J = 2.0$, 11.6 Hz), 3.52 (d, 1H, $J = 10.2$ Hz), 3.69 (dd, 1H, $J = 1.0$, 10.2 Hz), 4.04 (dd, 1H, $J = 5.8$, 12.1 Hz), 4.10 ppm (d, 1H, $J = 6.3$ Hz).

41: Pd (10% on carbon, 10 mg, 9.4 μmol) in EtOAc (0.5 mL) was placed under an atmosphere of hydrogen and treated with a solution of benzyl ether **38** (2.5 mg, 3.5 μmol) in EtOAc (0.4 mL). The resulting mixture was stirred at the same temperature for 5 min, filtered through celite, and concentrated in vacuo to afford an oil. The residue was used for the next reaction without further purification. A solution of crude tetrol in dry CH_2Cl_2 (2.5 mL) was treated with pyridine (75 μL, 1.1 mmol) and triphosgene (34 mg, 0.12 μmol) at 0°C, stirred at the same temperature for 45 min, and quenched by the addition of a saturated aqueous solution of $NaHCO_3$. The resulting solution was diluted with EtOAc and acidified by the addition of HCl (1 M aqueous). The solution was extracted with EtOAc. The organic phase was washed with a saturated aqueous solution of $NaHCO_3$ and with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo to yield an oil. The residue was purified by thin-layer chromatography ($CHCl_3$/MeOH 90:10) to afford carbonate **41** (1.4 mg, 2.6 μmol, 75%) as a white solid. $R_f = 0.44$ ($CHCl_3$/MeOH 90:10); IR (neat): $\tilde{\nu}$ = 3486, 2925, 1800, 1739, 1674, 1354, 1233, 1174, 1034, 918, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 0.99$ (s, 3H), 1.28 (s, 3H), 1.40 (s, 3H), 1.87 (s, 3H), 1.93–2.05 (m, 2H), 2.16 (s, 3H), 2.14–2.23 (m, 1H), 2.40 (d, 1H, $J = 16.0$ Hz), 2.36–2.46 (m, 1H), 2.81 (d, 1H, $J = 4.4$ Hz), 2.70–2.85 (m, 1H), 2.95 (d, 1H, $J = 16.0$ Hz), 2.93–3.01 (m, 1H), 3.04 (s, 3H), 3.60–3.70 (m, 1H), 4.47 (d, 1H, $J = 12.1$ Hz), 4.58 (d, 1H, $J = 12.1$ Hz), 4.69 (t, 1H, $J = 2.9$ Hz), 4.76 ppm (d, 1H, $J = 4.4$ Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 18.4 (CH_3), 20.8 (CH_3), 20.9 (CH_3), 21.8 (CH_3), 23.6 (CH_2), 26.7 (CH_3), 30.7 (CH_2), 33.9 (CH_2), 38.1 (C), 38.9 (CH_3), 41.8 (CH), 45.3 (C), 51.7 (CH_2), 64.7 (CH_2), 68.3 (CH), 74.4 (C), 80.1 (CH), 81.4 (CH), 93.0 (C), 142.5 (C), 143.3 (C), 153.0 (C), 171.1 (C), 201.0 ppm (C); HRMS (ESI-TOF): calcd for $[C_{24}H_{34}O_{11}S+Na]^+$: 553.1714; found: 553.1715.

42. A solution of diol **41** (12.0 mg, 22.6 μmol) in pyridine (2 mL) was treated with TESCl (340 μL, 2.02 mmol) at room temperature, stirred at 40°C for 2.5 h, diluted with EtOAc, and quenched by the addition of HCl (1 M aqueous). The solution was extracted with EtOAc. The organic phase was washed with a saturated aqueous solution of $NaHCO_3$ and with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo to yield an oil. The residue was used for the next reaction without further purification. A solution of the crude acetate in MeOH (8 mL) was treated with K_2CO_3 (20 mg, 0.14 mmol) at 0°C, stirred at the same temperature for 5 min, and quenched by the addition of NH_4Cl (saturated aqueous solution). The solution was extracted with EtOAc. The organic phase was washed with a saturated aqueous solution of $NaHCO_3$ and with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo to yield an oil. The residue was purified by thin-layer chromatography (hexane/EtOAc 50:50) to afford diol **42** (10.9 mg, 18.1 μmol, 80%) as a white solid. $R_f = 0.51$ (hexane/EtOAc 40:60); IR (neat): $\tilde{\nu}$ = 3480, 2957, 1799, 1675, 1354, 1236, 1175, 1120, 1036, 970, 917, 744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 0.64$ (q, 6H, $J = 7.8$ Hz), 0.85 (s, 3H), 0.97 (t, 9H, $J = 7.8$ Hz), 1.27 (s, 3H), 1.35 (s, 3H), 1.85 (br s, 3H), 1.86 (ddd, 1H, J = 1.9, 11.6, 15.5 Hz), 1.96 (ddd, 1H, $J = 2.4$, 10.6, 14.0 Hz), 2.15 (ddd, 1H, $J = 3.9$, 4.8, 15.5 Hz), 2.18 (d, 1H, $J = 16.4$ Hz), 2.36 (ddd, 1H, $J = 2.9$, 10.6, 20.3 Hz), 2.71–2.83 (m, 1H), 2.85 (d, 1H, $J = 4.8$ Hz), 2.98 (d, 1H, $J = 16.4$ Hz), 3.06 (br s, 3H), 3.01–3.11 (m, 1H), 3.63 (dd, 1H, $J = 4.8$, 11.1 Hz), 3.69 (dd, 1H, $J = 4.8$, 11.6 Hz), 4.15 (dd, 1H, $J = 3.9$, 11.1 Hz), 4.74 (d, 1H, $J = 4.8$ Hz), 4.74 ppm (dd, 1H, $J = 1.9$, 3.9 Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 5.1$ (CH_2), 6.9 (CH_3), 18.5 (CH_3), 20.6 (CH_3), 21.3 (CH_3), 23.6 (CH_2), 26.4 (CH_3), 30.4 (CH_2), 34.6 (CH_2), 38.1 (C), 38.6 (CH_3), 41.1 (CH), 45.8 (C), 51.8 (CH_2), 62.7 (CH_2), 69.6 (CH), 73.8 (C), 80.6 (CH), 82.9 (CH), 93.4 (C), 141.5 (C), 142.3 (C), 153.9 (C), 201.0 ppm (C); HRMS (ESI-TOF): calcd for $[C_{28}H_{46}O_{10}SSi+Na]^+$: 625.2473; found: 625.2471.

43: A solution of diol **42** (2.5 mg, 4.1 μmol) in dry HMPA (5.6 mL) was treated with iPr$_2$NEt (56 μL, 0.32 mmol) at room temperature, stirred at 100°C for 5.5 h, and cooled to room temperature. The resulting solution was diluted with EtOAc and quenched by the addition of H_2O. The solution was extracted with EtOAc. The organic phase was washed with brine, dried over anhydrous Na_2SO_4, and the remaining HMPA was then removed at 90°C under reduced pressure (≈600 Pa). The residue was purified by thin-layer chromatography (hexane/EtOAc 33:67) to afford oxetane **43** (1.6 mg, 3.1 μmol, 77%) as a white solid together with recovered diol **42** (0.5 mg, 0.8 μmol, 20%) as a white solid. $R_f = 0.51$ (hexane/EtOAc 43:57); IR (neat): $\tilde{\nu}$ = 3455, 2926, 1806, 1680, 1456, 1237, 1118, 1016, 843, 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 0.61$ (q, 6H, J = 7.7 Hz), 0.97 (t, 9H, $J = 7.7$ Hz), 1.27 (s, 3H), 1.33 (s, 3H), 1.36 (s, 3H), 1.73 (s, 3H), 1.87–1.98 (m, 1H), 1.93–2.02, (m, 1H), 2.12 (d, 1H, J = 5.3 Hz), 2.11–2.32 (m, 1H), 2.28 (d, 1H, $J = 16.4$ Hz), 2.31–2.47 (m, 1H), 2.68–2.82 (m, 2H), 3.11 (d, 1H, $J = 16.4$ Hz), 3.45 (dd, 1H, $J = 7.3$, 9.2 Hz), 4.45 (d, 1H, $J = 9.2$ Hz), 4.74 (br d, 1H, $J = 5.3$ Hz), 4.74 (d, 1H, $J = 9.2$ Hz), 4.85 ppm (d, 1H, $J = 5.3$ Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 5.3$ (CH_2), 7.0 (CH_3), 15.9 (CH_3), 21.3 (CH_3), 21.7 (CH_3), 23.6 (CH_2), 25.9 (CH_3), 30.1 (CH_2), 37.8 (CH_2), 38.3 (C), 44.9 (C), 45.3 (CH), 52.8 (CH_2), 72.9 (CH), 74.9 (C), 80.4 (CH), 81.6 (CH_2), 92.9 (C), 140.2 (C), 142.6 (C), 153.5 (C), 201.9 ppm (C); HRMS (ESI-TOF): calcd for $[C_{27}H_{42}O_7Si+Na]^+$: 507.2773; found: 507.2774.

44: A solution of alcohol **43** (6.1 mg, 12.0 μmol) in dry CH_2Cl_2 (0.4 mL) was treated with DMAP (18.1 mg, 0.148 mmol) and Ac_2O (7.6 μL, 74 μmol) at room temperature, stirred at the same temperature for 4.5 h, diluted with EtOAc, and quenched by the addition of H_2O. The solution was extracted with EtOAc. The organic phase was washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo to yield an oil. The residue was purified by thin-layer chromatography (hexane/EtOAc 50:50) to afford acetate **44** (4.6 mg, 8.38 μmol, 70%) as a white solid. $R_f = 0.42$ (hexane/EtOAc 60:40); IR (neat): $\tilde{\nu}$ = 2923, 1807, 1733, 1681, 1239 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 0.63$ (q, 6H, $J = 7.7$ Hz), 0.98 (t, 9H, $J = 7.7$ Hz), 1.26 (s, 3H), 1.37 (s, 3H), 1.40 (s, 3H), 1.72 (br s, 3H), 1.85 (ddd, 1H, $J = 1.9$, 9.2, 15.0 Hz), 1.85–1.95, (m, 1H), 1.96–2.09 (m, 2H), 2.17 (s, 3H), 2.51 (ddd, 1H, $J = 7.7$, 7.7, 15.0 Hz), 2.66–2.78 (m, 1H), 2.84 (d, 1H, $J = 5.3$ Hz), 3.24 (d, 1H, $J = 16.4$ Hz), 3.77 (dd, 1H, $J = 7.7$, 9.2 Hz), 4.55 (d, 1H, $J = 8.7$ Hz), 4.66 (d, 1H, $J = 8.7$ Hz), 4.85 (d, 1H, J = 5.3 Hz), 4.91 ppm (br d, 1H, $J = 7.7$ Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 5.3, 7.0, 16.2, 20.9, 21.4, 22.1, 23.7, 25.5, 29.3, 38.1, 38.2, 41.3, 45.5, 52.0, 72.3, 72.4, 80.0, 81.3, 84.3, 92.4, 139.7, 142.3, 153.2, 170.5, 201.6 ppm; HRMS (ESI-TOF): calcd for $[C_{29}H_{44}O_5Si+Na]^+$: 571.2698; found: 571.2687.

45:[10] A solution of carbonate **44** (1.7 mg, 3.1 μmol) in dry THF (1.7 mL) was treated dropwise with PhLi (1.05 M in cyclohexane/Et_2O, 15 μL, 16 μmol) at −78 °C, stirred at the same temperature, and quenched by the addition of AcOH (1 M in THF, 64 μL, 64 μmol). The resulting mixture was warmed to 0 °C, diluted with EtOAc, and treated with $NaHCO_3$ (saturated aqueous solution). The solution was extracted with EtOAc. The organic phase was washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo to yield an oil. The residue was purified by thin-layer chromatography (hexane/EtOAc 67:33) to afford benzoate **45** (1.4 mg, 2.2 μmol, 70 %) as a white solid. R_f = 0.53 (hexane/EtOAc 50:50); m.p. 214–216 °C (decomposed); IR (neat): $\tilde{\nu}$ = 3494, 2957, 1732, 1679, 1454, 1274, 1245, 1099, 750, 711 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 0.65 (q, 6H, J = 8.2 Hz), 0.99 (t, 9H, J = 8.2 Hz), 1.15 (s, 3H), 1.37 (s, 3H), 1.42 (s, 3H), 1.65–1.75 (m, 1H), 1.77 (br s, 3H), 1.74–1.85 (m, 1H), 1.86–1.98 (m, 1H), 2.29 (s, 3H), 2.21–2.32 (m, 1H), 2.44–2.55 (m, 1H), 2.59 (d, 1H, J = 15.5 Hz), 2.60–2.73 (m, 1H), 3.11 (d, 1H, J = 5.8 Hz), 3.16 (d, 1H, J = 15.5 Hz), 3.74 (t, 1H, J = 8.7 Hz), 4.17 (d, 1H, J = 8.2 Hz), 4.35 (d, 1H, J = 8.2 Hz), 4.91 (d, 1H, J = 9.2 Hz), 5.90 (d, 1H, J = 5.8 Hz), 7.41–7.56 (br t, 2H), 7.55–7.65 (br t, 1H), 8.05–8.19 ppm (br d, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 5.3 (TES CH_2), 7.0 (TES CH_3), 16.1 (CH_3), 20.1 (CH_3), 22.3 (CH_3), 22.8 (CH_3), 26.0 (14), 26.7 (CH_3), 30.2 (C13), 38.0 (C6), 39.6 (C8 or C15), 44.2 (C3), 44.7 (C8 or C15), 50.4 (C9), 72.7 (C7), 73.4 (C2), 76.4 (C20), 80.1 (C1 or C4), 82.4 (C1 or C4), 84.5 (C5), 128.6 (Ph), 129.4 (Ph), 130.1 (Ph), 133.6 (Ph), 138.2 (C12), 144.7 (C11), 167.0 (Bz), 170.0 (Ac), 202.2 ppm (C10); HRMS (ESI-TOF): calcd for $[C_{35}H_{50}O_8Si+Na]^+$: 649.3167; found: 649.3148.

α-Hydroxyketone derived from **45**: A solution of benzoate **45** (0.6 mg, 0.1 μmol) in dry THF (0.3 mL) was treated dropwise with *t*BuOK (0.25 M in THF, 52 μL, 13 μmol) at −78 °C, warmed to −40 °C, and stirred at the same temperature for 45 min. The resulting solution was transferred through a cannula to a solution of $(PhSeO_2)O$ (98 %, ACROS, 10.4 mg, 28.9 μmol) in dry THF (0.3 mL) at 0 °C. The resulting suspension was stirred at 0 °C for 20 min, diluted with EtOAc, and poured into a saturated solution of $NaHCO_3$. The organic phase was washed with aqueous $Na_2S_2O_3$ (10 %) and a saturated aqueous solution of $NaHCO_3$, dried over anhydrous Na_2SO_4, and concentrated in vacuo to yield an oil. The residue was used for the next reaction without further purification. The crude α-hydroxy ketone (1.8 mg) in dry THF (0.3 mL) was treated dropwise with *t*BuOK (0.25 M in THF, 50 μL, 13 μmol) at −78 °C, stirred at the same temperature for 30 min, and quenched by the addition of AcOH (0.8 M in dry THF, 45 μL, 36 μmol). The resulting solution was stirred at the same temperature for 10 min, allowed to warm for 10 min, diluted with EtOAc, and poured into a saturated aqueous solution of $NaHCO_3$. The organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo to yield an oil. The residue was purified by thin-layer chromatography (hexane/EtOAc 67:33) to afford the benzoate α-hydroxyketone (0.6 mg, 0.09 μmol, ≈90 %) as a white solid.

13-Deoxy-7-*O*-TES-baccatin III: A solution of the benzoate α-hydroxy ketone (1.0 mg, 1.6 μmol) in pyridine (0.5 mL) was treated with DMAP (10.4 mg, 85.1 μmol) and Ac_2O (52 μmol, 0.56 mmol) at room temperature and stirred at the same temperature for 2 h. The resulting solution was diluted with EtOAc and poured into ice-cooled HCl (1 M aqueous). The organic phase was washed with $NaHCO_3$ (saturated aqueous solution), dried over anhydrous Na_2SO_4, and concentrated in vacuo to yield an oil. The residue was purified by thin-layer chromatography (toluene/EtOAc 91:9) to afford 13-deoxy-7-*O*-TES-baccatin III (0.5 mg, 7 μmol, ca. 50 %) as a white solid.

7-*O*-TES-baccatin III: A solution of 13-deoxy-7-*O*-TES-baccatin III (0.3 mg, 0.4 μmol) in dry benzene (0.5 mL) was treated with dry celite (10.6 mg), dry NaOAc (4.9 mg, 60 μmol), and PCC (7.1 mg, 33 μmol) at room temperature and stirred at 85 °C for 2 h. The resulting mixture was cooled to room temperature, diluted with Et_2O, and filtered through a silica-gel plug (flash-column chromatography), eluting with Et_2O, to afford crude 13-oxo-7-*O*-TES-baccatin III. The crude oil was used for the next reaction without further purification. A solution of the crude 13-oxo-7-*O*-TES-baccatin III (0.3 mg) in MeOH (0.25 mL) was treated with $NaBH_4$ (3.0 mg, 79 μmol) every 30 min for 2 h at room temperature, quenched by the addition of NH_4Cl (saturated aqueous solution), and stirred vigorously for 15 min. The resulting mixture was diluted with EtOAc, washed with a saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, and concentrated in vacuo to yield an oil. The residue was purified by thin-layer chromatography (hexane/EtOAc 67:33) to afford 7-*O*-TES-baccatin III (0.2 mg, 0.3 μmol, ca. 80 %) as a white solid.

2: A solution of 7-*O*-TES-baccatin III (0.2 mg, 0.3 μmol) in dry THF (0.66 mL) was treated with HF·pyridine (84 μL) at 0 °C and stirred at room temperature for 3 h. The resulting mixture was diluted with Et_2O and washed with saturated solutions of $NaHCO_3$ (twice), $CuSO_4$, NaCl, and $NaHCO_3$. The resulting solution was dried over anhydrous Na_2SO_4 and concentrated in vacuo to yield an oil. The residue was purified by thin-layer chromatography (EtOAc) to afford (±)-baccatin III (**2**) (0.1 mg, 0.2 μmol, ≈80 %) as a white solid. M.p. 221–223 °C (decomp.); R_f = 0.59 (ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.07–817 (2H, br d), 7.57–7.66 (1H, br t), 7.44–7.55 (2H, br t), 6.33 (1H, s), 5.63 (1H, d, J = 7.3 Hz), 4.99 (1H, d, J = 8.7 Hz), 4.90 (1H, t, J = 7.7 Hz), 4.47 (1H, dd, J = 6.8, 11.1 Hz), 4.31 (1H, d, J = 8.2 Hz), 4.16 (1H, d, J = 8.2 Hz), 3.88 (1H, d, J = 7.3 Hz), 2.57 (1H, ddd, J = 7.3, 9.7, 16.4 Hz), 2.25–2.35 (2H, m), 2.29 (3H, s), 2.25 (3H, s), 2.06 (3H, s), 1.87 (1H, ddd, J = 2.4, 11.1, 16.5 Hz), 1.68 (3H, s), 1.11 ppm (6H, s).

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