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Efficient synthesis of the functional central core lactides, a constituent of antibiotic fattiviracins

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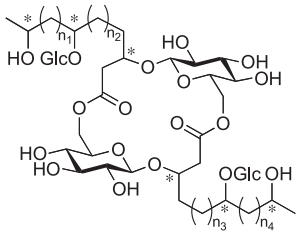
ABSTRACT

An efficient convergent synthetic method has been developed for preparation of various stereoisomers and derivatives of fattiviracins via a common lactide. The synthetic route comprises seco acids prepared by the β-selective glycosylation of chiral 3-hydroxy-4-pentanoate obtained by enzymatic kinetic resolution. The regioselective protection of four individual hydroxy groups was achieved via the 4,6-*O*-benzylidenation of the glucose moiety from its TMS ethers. The dimeric cyclization of the seco acids under control of reaction concentration afforded the desired lactide without using KH. Our convergent synthetic method was successfully applied to direct installation of side chains to the lactide by cross metathesis to synthesize fattiviracin derivatives. We achieved improvements to the reported method with respect to: (1) synthesis of a convergent synthetic intermediate; (2) stereoselectivity in glycosylation; and (3) establishment of a low cost route suitable for large scale synthesis.

1. Introduction

An antiherpetic agent was discovered from a *Streptomyces* species, and found to be identical to *Streptomyces microflavus* No. 2445.[1] The antiherpetic agent was named fattiviracin (FV) and has a lactide as a C_2 symmetric core. *S. microflavus* No. 2445 produces 13 types of FVs (Fig. 1), and determination of each absolute structure has been hampered by the difficult isolation.[1] The fattiviracins, especially FV-8, have been reported to exhibit activity against enveloped DNA viruses such as in the herpes family, HSV-1 and VZV, and enveloped RNA viruses such as influenza A and B, and three strains of HIV-1.[2] FV-8 acts on HIV-1 particles directly without lysis of the particles, inhibiting viral entry into the host cell.[2a] This mode of action is different from other antiviral agents that inhibit reverse transcriptase or protease in the HIV-1 particles. Therefore, FV has potential to be a new type of antiviral agent.

The cycloviracins, structurally related to FV, were isolated from *Kibdelosporangium albatum* so. nov. (R761-7). Cycloviracin B_1 exhibits activity against the herpes simplex and HIV viruses.[3] In addition, a similar glycolipid, glucolipsin A, was reported to be an inhibitor against Cdc25 phosphatase and protein tyrosine phosphatase 1B (PTP1B), which are regulatory enzymes in the cell cycle[3] (Fig. 2).



family	carbon number of fatty acid					
	long chain	n_1	n_2	short chain	n_3	n_4
FV-1,2,3	unidentified					
FV-4,5	22	5	11	22	11	5
FV-6,7,8	24	5	13	22	11	5
FV-9	24	5	13	24	11	7
FV-10,11,12	26	7	13	24	11	7
FV-13	28	9	13	24	11	7

Figure 1. Structure of fattiviracins.

These glycolipids have been attractive targets for synthetic organic chemists, since glycolipids possess unique biological activities and structures. For example, since these lactides are C_2 symmetric compounds, Fürstner et al.[4,5] adopted a strategy to

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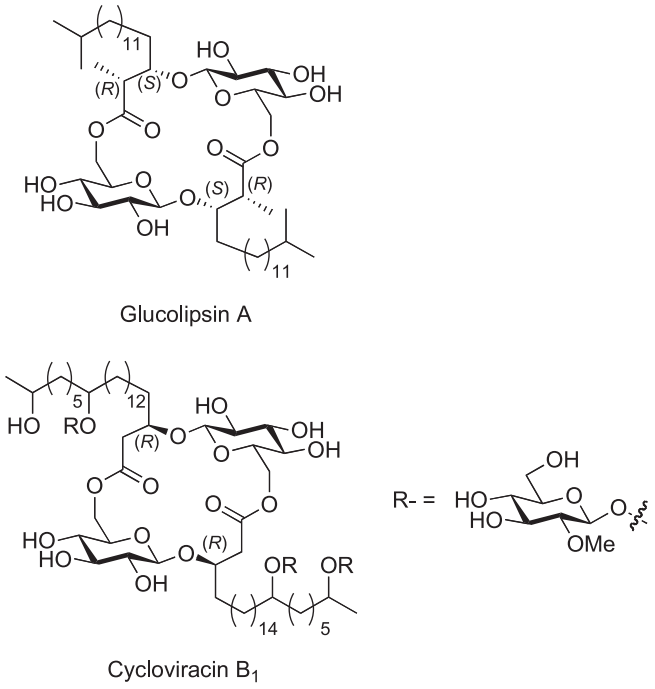


Figure 2.

cyclize two seco acid molecules directly. The cyclization was performed in the presence of KH to construct the lactide in good yield. It was determined that the glycolipids uptake KH to aid in the ring closure. In this manner, the total syntheses of cycloviracin B_1[4] and glucolipsin A were completed.[5]

Cleophax et al. have undertaken a convergent strategy to synthesize derivatives of these glycolipids.[6] They prepared the macrocyclic core of cycloviracin and glucolipsin by exploiting the same type of cyclization as Fürstner's. However, the syntheses of derivatives employing the macrocyclic core lactides have not been reported to date.

While these synthetic strategies are fascinating, they do have some drawbacks: (1) β-stereoselectivity in the glycosylations is not perfect; (2) the starting material, levoglucosan, is expensive; and (3) it is difficult to prepare derivatives, including many kinds of side chains, in order to study structure–activity relationships. Thus, a novel synthetic route to prepare many kinds of diastereomers should be developed in order to determine the absolute stereochemistry of six stereocenters, with the exception of the sugar moiety in FV.

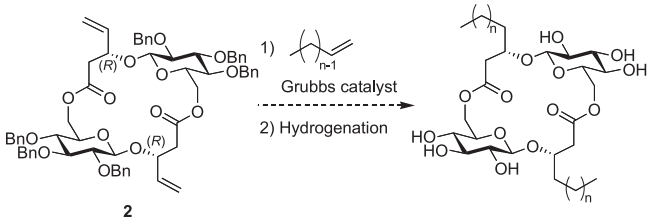
Our goal to design a synthetic route for FV includes the following: (1) achievement of perfect β-selectivity in glycosylation; (2) utilization of low cost starting materials; and (3) development of a convergent synthetic route to generate many kinds of stereoisomers and derivatives via a common lactide.

2. Results and discussion

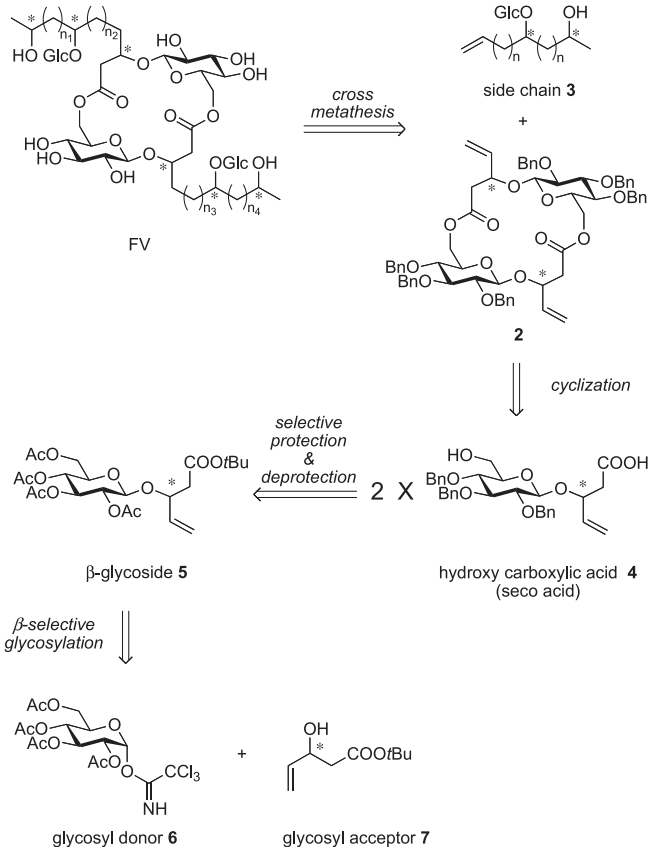
2.1. Retrosynthesis

A convergent synthetic method is required to achieve the synthesis of various FV derivatives. Our strategy includes the design of the common intermediate **2** and the connection of various side chains to this common intermediate (Scheme 1).

The retrosynthesis of FV is shown in Scheme 2. Each derivative of FV could be synthesized through a cross metathesis reaction[7] between the cyclic intermediate **2** and side chains **3**.



Scheme 1. Late stage of synthetic plan.

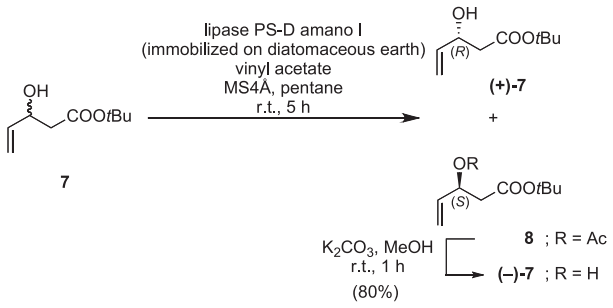


Scheme 2. Retrosynthetic analysis.

The key intermediate **2** could be directly constructed by cyclization of two molecules of seco acid **4**, which could be derived from β-glycoside **5**. For efficient synthesis of **5**, stereoselective construction of the anomeric position would be required to avoid having to separate anomeric isomers. The β-glycoside **5** was segmented into an easily preparable glycosyl donor **6**,[8] which has acyl group to take advantage of neighboring group participation, and a chiral glycosyl acceptor **7**. The chiral induction of glycosyl acceptor **7** would be envisioned to come from kinetic resolution by lipase.

2.2. Syntheses of glycosyl acceptor and glycosyl donor

A racemic mixture of **7** was prepared by aldol reaction between *tert*-butyl acetate and acrolein. According to the previous reports,[9] kinetic resolution of the racemic alcohol **7** was carried out with lipase PS-D Amano I, immobilized on diatomaceous earth, in pentane with excess vinyl acetate at ambient temperature for 60 h to provide enantioenriched alcohol (+)-**7** (45%, 99% ee) and acetate derivative **8** (42%, 70% ee) (Scheme 3). In order to prevent the overesterification, arose from longer reaction times, we decided to revise the reaction conditions being followed with chiral HPLC.



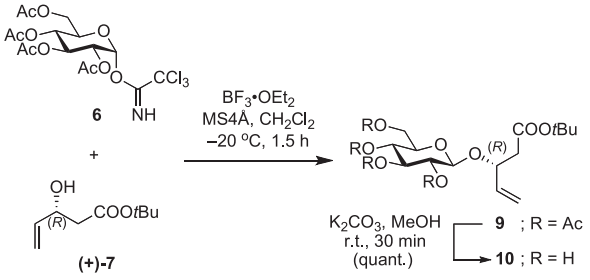
Scheme 3. Enzymatic kinetic resolution and methanolysis.

Monitoring by chiral HPLC (DAICEL Chiral Pack IC, hexane/2-propanol=98:2) during kinetic resolution provides the enantiopurities of all compounds in the reaction, and the enantiopurity of (+)-**7** reached 99% ee in 5 h. The antipode (−)-**7** was obtained by removal of the acetyl group of **8** with K_2CO_3 in MeOH in 99% ee.[10]

Once both highly optically pure glycosyl acceptors were in hand, we turned our attention to the preparation of the glycosyl donor. The 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl imidate (**6**) was selected and synthesized from commercially available penta-*O*-acetyl-β-D-glucose.

2.3. Glycosylation

For the synthesis of the desired seco acid, 3*R*-(+)-**7** as a glycosyl acceptor was chosen for glycosylation with glycosyl donor **6** because (+)-**7** was available directly after kinetic resolution. As shown in Scheme 4, these reactions were carried out in the presence of 4 Å molecular sieves in dichloromethane. The use of 1.2 equiv of $BF_3 \cdot OEt_2$ as a Lewis acid and 2.0 equiv of the acceptor (+)-**7**, gave the best results (69% yield).[11] The stereochemistry of the β-glycosides was determined from the coupling constant, $^3J_{H1',H2'}$, of approximately 8.1 Hz, as would be expected for glycosides with the β-D-glucopyranosyl (1,2-trans) stereochemistry. Removal of the Ac group in glycoside **9** by methanolysis gave **10** in quantitative yield. We thus achieved the preparation of the desired β-glycoside in fewer steps using an inexpensive glucose derivative as the starting material.

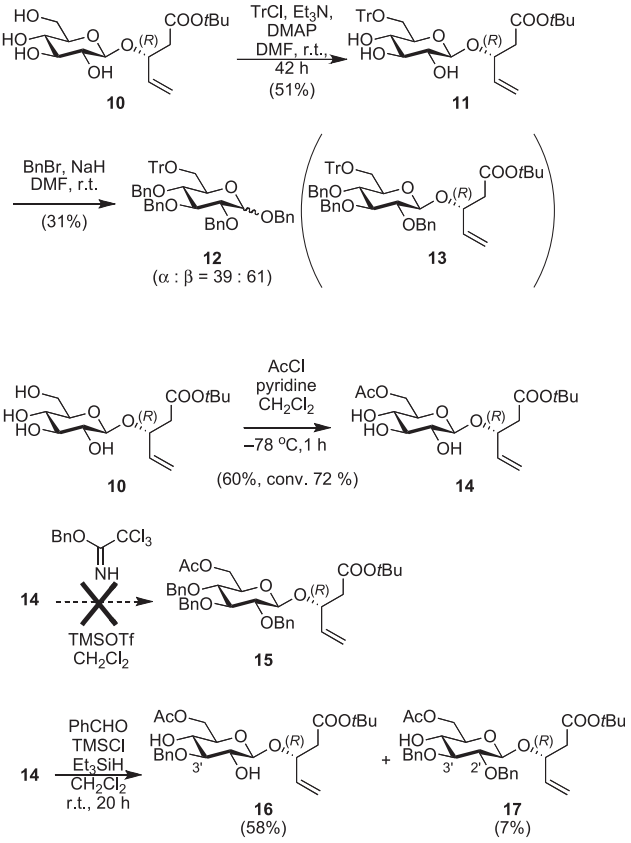


Scheme 4. Glycosylation of (+)-**7** with **6**.

2.4. First generation synthesis

2.4.1. Mono Bn approach. For the synthesis of seco acid **4**, benzyl (Bn) group was chosen to protect the C-2, 3, 4 positions in the sugar moiety. First, the selective protection of the 6-OH with a trityl group gave **11**. Subsequent benzylation (BnBr, NaH) of the hydroxy groups at C-2, 3, 4 afforded 1-benzyloxy compound **12** as an anomeric mixture instead of the desired **13**. This result suggests that unexpected E1cB elimination occurred after deprotonation by a strong base, followed by benzylation at the C-1 position. Thus, we took another approach (Scheme 5).

The next approach using benzyl-2,2,2-trichloroacetimidate in the presence of Lewis acid for the benzylation was attempted. First,



Scheme 5. Benzylation of sugar hydroxy groups.

selective acetylation of the C-6 alcohol at −78 °C under dilute conditions afforded **14** in moderate yield. Unfortunately, benzylation with benzyl-2,2,2-trichloroacetimidate in the presence of TMSOTf did not proceed at low temperature (−40 °C), but resulted in a complex mixture inseparable by flash column chromatography. We believe that mono-*O*-Bn or di-*O*-Bn products were generated, and TMSOTf caused decomposition of the β-oxyester moiety.

Then, focused on benzylation using PhCHO and a corresponding reductive reagent via TMS ether as reported by Fukase and Izumi.[12] Attempts to protect the alcohols using benzaldehyde, excess TMSCl and triethyl silane as a reductive reagent afforded 3′-benzyloxy product **16** in 58% yield and 2′,3′-di-*O*-benzyloxy product **17** in 7% yield, though the desired 2′,3′,4′-tri-*O*-benzyloxy product was not detected. A downfield shift in the ^{1}H NMR spectrum after acetylation of **16** and **17** led to plausible structures for each compound as shown in Scheme 5. These results indicate that the reactivity of the C3-hydroxy group is even higher under mild acidic conditions, but the C-2 hydroxy group has less activity and the C-4 hydroxy group has no reactivity under these benzylation conditions (Fig. 3).

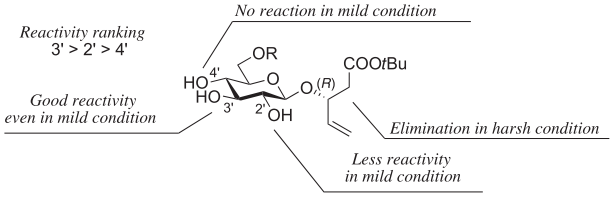
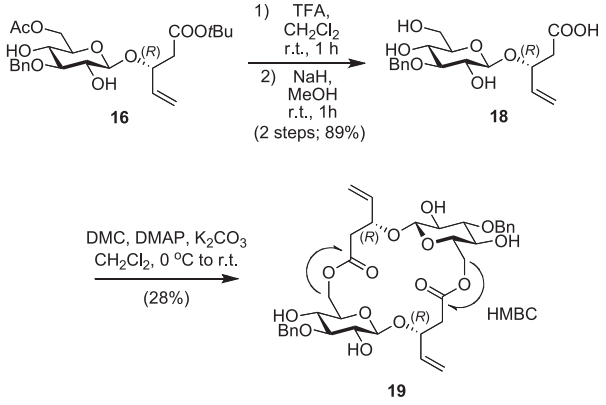


Figure 3. Reactivity of hydroxy groups.

2.4.2. Dimeric cyclization of mono Bn compound. With the mono-*O*-Bn compound **16** in hand, we attempted cyclization according to the reaction shown in Scheme 6. Deprotection of the *tert*-butyl ester under acidic conditions with TFA provided the carboxylic acid, and the Ac group was removed by methanolysis to afford the desired

seco acid **18** in excellent yield. We predicted that the most reactive C-6 hydroxy group would smoothly cyclize to the product **19** even in the presence of free hydroxy groups at C-2 and C-4, whose reactivities were proved to be lower in the previous benzylation.



Scheme 6. Cyclization with monobenzyl compound.

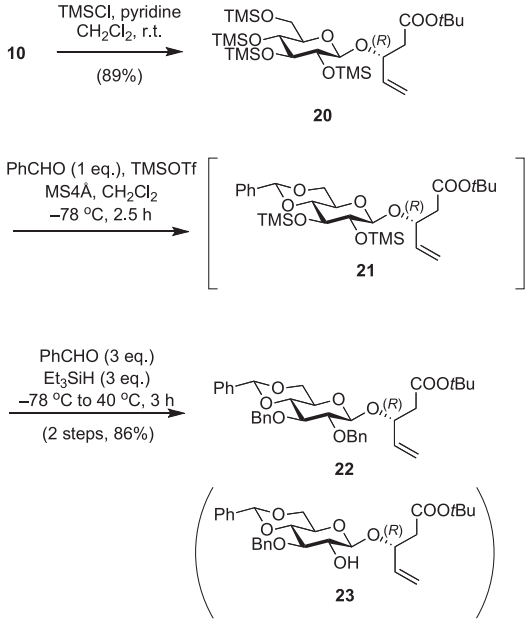
The cyclization of **18** with DMC reported by Fürstner et al.[4,5] provided the desired cyclic product **19**. NMR studies on the product **19** confirmed the proposed structure, evidenced by a cross peak between C6′-H and C-1 observed in HMBC experiments.

Based on these results, even the substrate with only partial protection of the hydroxy groups is applicable to the cyclization. However, this synthetic route has some low yielding reactions such as 6-OH selective protection and benzylation, and is not suitable for obtaining significant quantities of material. Moreover, low solubility of **18** and **19** in organic solvents due to the free hydroxy groups causes low yields in the coupling reaction. These results suggest that complete protection of the C-2, 3, 4 hydroxy groups is required to afford an efficient synthetic route.

2.5. Second generation synthesis

2.5.1. Approach from 4,6-benzylidene intermediate. Faced with these problems, we evaluated another approach to the desired seco acid. In the previous study,[9] protection of the C-2 and C-3 hydroxy groups with benzyl groups was achieved using the combination of benzaldehyde and a reductive reagent under mild acidic conditions. The remaining protection of C-4 might be solved by formation of a 4,6-benzylidene acetal followed by ring opening to give the 4-benzyloxy group. Hung et al. has reported a combinatorial and highly regioselective method[13] that can be used to protect individual hydroxy groups of a monosaccharide such as glucose. This approach can be used to install an orthogonal protecting group pattern in a one-pot manner. In particular, it was reported that 4,6-*O*-benzylidenation and 3-*O*-benzylation from 2,3,4,6-tetra-*O*-TMS glucose derivatives could be carried out as a one-pot reaction.

To apply Hung's methodology, delicate tetra-*O*-TMS compound **20** was prepared from the glycoside **10**, by treating, with TMSCl in pyridine. For large scale synthesis, the reaction temperature was set to −78 °C for the one-pot reaction. The details of the procedure include formation of the 4,6-*O*-benzylidene acetal by treatment of **20** with PhCHO and a catalytic amount of TMSOTf in the first step and then addition of PhCHO and Et_3SiH gave the benzyl ether in the second step. Our first attempt at this one-pot reaction at −78 °C gave **23** having a 3-benzyl ether as well as a small amount of the desired **22** having the 2,3-*O*-benzyl ether. Addition of excess PhCHO and Et_3SiH and warming the reaction mixture up to −40 °C from −78 °C in the second step provided **22** in 86% yield. Since this reaction is reproducible, it is suitable for large scale synthesis (Scheme 7).

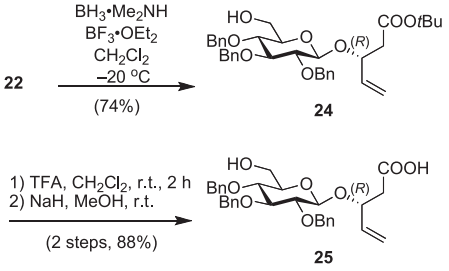


Scheme 7. One-pot 4,6-*O*-benzylidene, 2,3-di-*O*-benzylation.

Applying Hung's method to protect the hydroxy groups at C-2, C-3 and especially C-4 effectively solved the issue of benzylating the hindered hydroxy groups. The reaction using TMS ether as the substrate is different from Fukase's method,[12] which generates water during the reaction. Our method does not generate water, thus avoiding decomposition of the delicate side chain bearing the β-oxoester moiety.

*2.5.2. Synthesis of the seco acid **25**.* With protected compound **22** plausibly in hand, regioselective opening of the 4,6-*O*-benzylidene acetal was attempted to give 4-benzyloxy and 6-free hydroxy compound. Although BH_3 is usually used for reductive-opening of acetals, chemoselective reduction was required for the glycoside **24** possesses the ester and the double bond. Several reducing agents were screened to reveal that the yield of reduction with $BH_3{\cdot}Me_2NH$[14] at −20 °C was much higher.[15]

Attempts to remove the *tert*-butyl group with TFA in CH_2Cl_2 furnished a 6-*O*-trifluoroacetylated product as well as the desired **25**. Based on these results, we altered the procedure to remove the *tert*-butyl group first, followed by methanolysis in the second step to give **25** in high yield (Scheme 8).

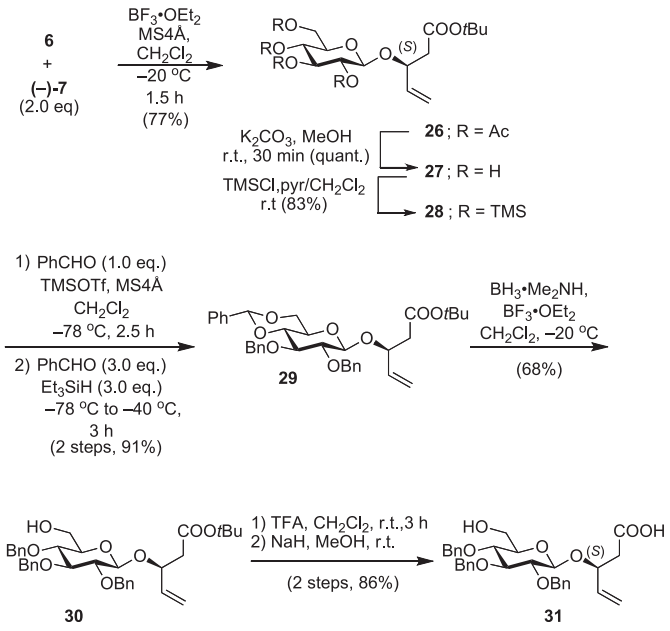


Scheme 8. Deprotection of *tert*-butyl group.

This reaction sequence via the benzylidene acetal enabled us to prepare the desired seco acid **25**.

As described above, we have established a low cost synthetic route to prepare the seco acid. This route also revised the efficiency comparing with the current synthesis with respect to the protecting group manipulation after the glycosylation.

2.5.3. Synthesis of seco acid from (3S)-acceptor. Having optimized the synthesis of seco acid **25** from (3*R*)-acceptor (+)-**7**, we applied this reaction sequence to (3*S*)-acceptor (−)-**7** (Scheme 9) to furnish seco acid **31**. This result suggests that no difference is observed in reactivity between the diastereomers.

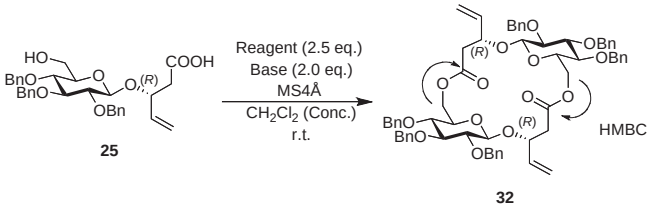


Scheme 9. Synthesis of (3*S*)-seco acid **31**.

2.5.4. Cyclization of the seco acids. With both seco acids **25** and **31** in hand, we optimized the reaction conditions for cyclization to obtain the desired lactides. Fürstner et al.[4,5] and Cleophax et al.[6] reported the same type of cyclization for synthesis of cycloviracin B_1 and glucolipsin A. Both of them used DMC[16] and KH in the presence of DMAP to synthesize the corresponding lactides. Reactivity of the cyclization depended upon the structure of the substrates, which resulted in various yields.

Our preliminary research showed that DMC was more suitable than other reagents[17] (Table 1, entries 1 and 2). Surprisingly, changing the concentrations of DMC and DMAP in CH_2Cl_2 dramatically improved yields of the cyclized product (entries 3–5). Contrary to our expectations, the reaction without DMAP proceeded smoothly in 61% yield (entry 6). Based on the report by Fürstner, we attempted cyclization with KH, which resulted in a lower yield than under non-KH conditions (entry 7).

Table 1
Cyclization of (3*R*)-seco acid **25**



Entry	Reagent	Base	Concn (M)	Yield (%)
1	EDCI	DMAP	0.1	15
2	MNBA	DMAP	0.1	Trace
3	DMC	DMAP	0.01	9
4	DMC	DMAP	0.1	52
5	DMC	DMAP	0.2	41
6	DMC	—	0.1	61
7	DMC	KH[a]	0.1	41

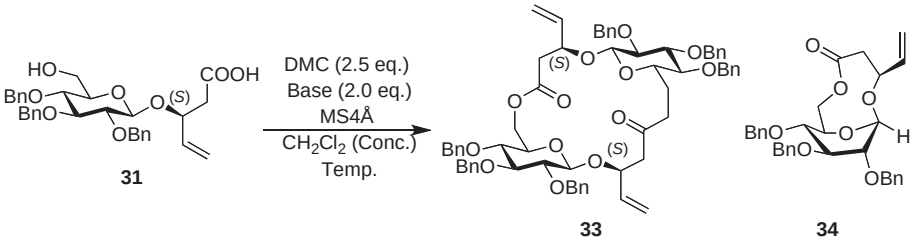
[a] Excess amount of KH was employed.

In addition, we confirmed that cyclized compound **32** had the correct C_2 symmetry by the perfectly overlapping peaks at symmetric positions in the ^{1}H NMR spectrum. The observation of a cross peak between C6′–H and C1 in the HMBC experiments also supported the cyclized structure.

We next turned to the cyclization of seco acid **31** (Table 2). Under conditions similar to those described for **25**, the cyclization of **31** occurred in moderate yield to give not only desired product **33** but also self-cyclized product **34** (Table 2, entry 1), the conformation of which is shown in Figure 4, based on the ^{1}H NMR coupling constants. In the reactions at lower concentrations in CH_2Cl_2, the yields of **33** decreased while those of **34** increased (Table 2, entries 2 and 5). This phenomenon is explained by an intramolecular lactonization, which occurred more easily in dilute conditions, rather than an intermolecular cyclization. The dimeric cyclization product **33** was not obtained in higher yields, despite lowering the temperature (0 °C, entry 3), adding DMAP (entries 4–6), and KH (entry 7).

It seems that seco acids **25**, **31**, and the compounds reported by Fürstner would form appropriate conformations that facilitated the formation of cyclic dimers in CH_2Cl_2. In addition, DMC is the most suitable condensation reagent in all cases. The differences in the seco acids between ours and Fürstner's reflect their reactivities in

Table 2
Cyclization of (3*S*)-seco acid **31**



Entry	Base	Concn (M)	Temp	**33** (%)	**34** (%)
1	—	0.1	rt	42	28
2	—	0.01	rt	23	37
3	—	0.1	0 °C	39	9
4	DMAP	0.1	rt	36	14
5	DMAP	0.01	rt	33	19
6	DMAP	0.1	0 °C	27	5
7	KH[a]	0.1	rt	29	21

[a] Excess amount of KH was employed.

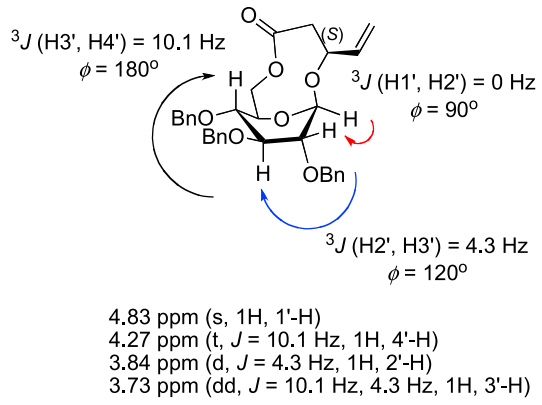
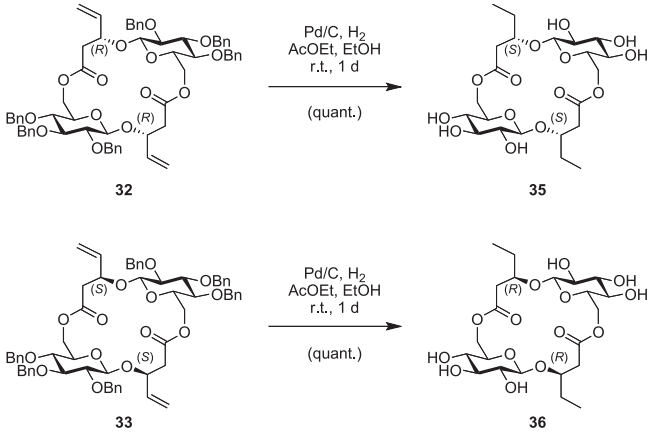


Figure 4. Conformation of intramolecular cyclization product **34**.

terms of molecular size and existence of olefin. In Fürstner's case, although the compounds are too large to be close to one other, they succeeded in forming highly interfacial complexes with the aid of KH, which should be expected to assist orientation of the hydroxy group and carboxy group in the ring closure to achieve the desired cyclization. In our case, the smaller substrate has a better chance to ring close without KH, and increasing the concentration of the substrate improved the cyclization.

Thus, we achieved cyclization to generate the desired lactide in reasonable yield without KH.

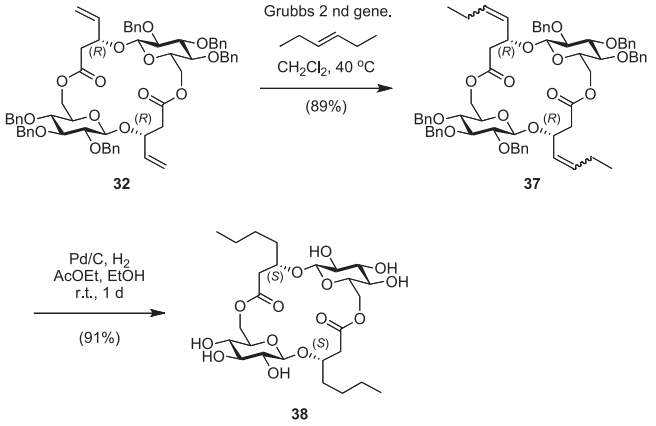
2.5.5. C–C bond formation after the cyclization. With the desired lactide in hand, we attempted C–C bond formation followed by deprotection for the synthesis of FV and its derivatives. To deprotect the benzyl group and reduce the double bond at the same time, we performed hydrogenation before the C–C bond formation. The hydrogenation of **32** and **33** in EtOAc and EtOH caused the simultaneous deprotection of Bn and reduction of the double bond to furnish desired **35** and **36**, respectively, in quantitative yields (Scheme 10).



Scheme 10. Hydrogenation of the lactides **32** and **33**.

We then turned our focus on the C–C bond formation (Scheme 11) to demonstrate the syntheses of new derivatives of FV.

The cross metathesis of **32** with *trans*-3-hexene in the presence of Grubbs second generation catalyst according to Basu's report[18] furnished a mixture of **37** whose structure was difficult to determine.[19] According to the established deprotection procedure described above, hydrogenation and deprotection of **37** proceeded in high yield to give **38**. Thus, we have achieved a convergent synthesis of **38** from the core lactide. This strategy has never been utilized to synthesize derivatives of FV and similar compounds so far.



Scheme 11. C–C bond formation by cross metathesis.

3. Conclusion

In conclusion, we have described the first example of a convergent synthetic route to fattiviracin and its derivatives. Key features of the synthetic scheme to provide seco acids are: (1) the β-selective glycosylation of chiral acceptors (+)-**7** or (−)-**7** prepared by enzymatic kinetic resolution and (2) the regioselective protection of four hydroxy groups via 4,6-benzylidenation from TMS ethers. The dimeric cyclization of the seco acid by controlling the reaction concentrations afforded the desired lactides without using KH. Our convergent synthetic route was successfully applied to direct installation of side chains to lactide by cross metathesis aiming at synthesizing fattiviracin derivatives. We achieved improvements in (1) synthesis of a convergent synthetic intermediate, (2) stereoselectivity in glycosylation, and (3) establishment of a route suitable for large scale synthesis at a significantly lower cost compared to previous reports.[4–6] Further syntheses of other derivatives of FV are in progress in our laboratory.

4. Experimental section

4.1. General remarks

Dry THF, toluene, ethyl ether, and CH_2Cl_2 were purchased from Kanto Chemical Co. Precoated silica gel plates with a fluorescent indicator (Merck 60 F_{254}) were used for analytical and preparative thin layer chromatography. Flash column chromatography was carried out with Kanto Chemical silica gel (Kanto Chemical, silica gel 60N, spherical neutral, 0.040–0.050 mm, Cat. No. 37 563-84). ^{1}H NMR spectra were recorded at 300 or 400 MHz and ^{13}C NMR spectra were recorded at 75 or 100 MHz on Varian VXR-300 (300 MHz), Varian XL-400 (400 MHz), or Varian UNITY-400 (400 MHz) spectrometers. The chemical shifts are expressed in parts per million downfield from the internal solvent peaks for $CDCl_3$ (7.26 ppm, ^{1}H NMR), CD_3OD (3.31, 4.84 ppm, ^{1}H NMR), $CDCl_3$ (77.0 ppm, ^{13}C NMR), CD_3OD (49.0 ppm, ^{13}C NMR), or D_2O (the end of both fields; 0, 200 ppm, ^{13}C NMR) and *J* values are given in hertz. The coupling patterns are denoted s (singlet), d (doublet), dd (double doublet), ddd (double double doublet), t (triplet), dt (double triplet), q (quartet), m (multiplet), or br (broad). High-performance liquid chromatography (HPLC) was carried out using a Senshu UV–vis Detector (SSC-5410) and Senshu HPLC-pump (SSC-3461) with DAICEL Chiral Pack IC (hexane/2-propanol=98:2, UV; 210 nm). All infrared spectra were measured on a JASCO FT/IR-460 spectrometer. High- and low-resolution mass spectra were measured on a JEOL JMS-T100 LP and JEOL JMS-AX505 HA spectrometers. Optical rotations were measured by using JASCO DIP-370 polarimeter. Melting points were measured on a Yanagimoto Micro Apparatus.

4.2. Procedure

*4.2.1. Synthesis of glycosyl acceptor and glycosyl donor. 4.2.1.1. (3R)-3-Hydroxy-4-pentenoic acid tert-butyl ester ((+)-**7**) and (3S)-3-acetoxy-4-pentenoic acid tert-butyl ester (**8**).* To a solution of **7** (16.4 g, 94.9 mmol), vinyl acetate (26.3 mL, 285 mmol), and MS4 Å (15 g) in *n*-pentane (200 mL) at ambient temperature was added Lipase PS-D amano I (immobilized on diatomaceous earth, Wako Pure Chemical Industries, Ltd.) (10.4 g) in one portion. The reaction mixture was stirred for 5 h at ambient temperature. The heterogeneous mixture was filtered through Celite, rinsed with Et_2O (50 mL). The resulting solution was washed with H_2O (2×200 mL) and brine (200 mL). The organic layers were dried with sodium sulfate, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, pentane/Et_2O=6:1→3:1) afforded (+)-**7** (7.28 g, 42.3 mmol, 45%) as colorless liquid and **8** (9.60 g, 44.8 mmol, 47%) as colorless liquid.

Compound (+)-**7**: R_f=0.28 (hexane/AcOEt=3:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.86 (ddd, *J*=17.4, 10.4, 5.3 Hz, 1H, 4-H), 5.29 (dt, *J*=17.4, 1.3 Hz, 1H, 5-H (trans)), 5.12 (ddd, *J*=10.4, 1.5, 1.3 Hz, 1H, 5-H (cis)), 4.47 (ddddd, *J*=8.1, 5.3, 4.4, 1.5, 1.3 Hz, 1H, 3-H), 2.49 (dd, *J*=16.2, 4.4 Hz, 1H, 2-H), 2.41 (dd, *J*=16.2, 8.1 Hz, 1H, 2-H), 1.44 (s, 9H, –*t*-Bu).

Compound **8**: R_f=0.46 (hexane/AcOEt=3:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.81 (ddd, *J*=17.0, 10.6, 6.3 Hz, 1H, 4-H), 5.58 (dddt, *J*=8.1, 6.3, 5.9, 1.3 Hz, 1H, 3-H), 5.28 (dt, *J*=17.0, 1.3 Hz, 1H, 5-H (trans)), 5.18 (dt, *J*=10.6, 1.3 Hz, 1H, 5-H (cis)), 2.58 (dd, *J*=15.4, 8.1 Hz, 1H, 2-H), 2.49 (dd, *J*=15.4, 5.9 Hz, 1H, 2-H), 2.03 (s, 3H, –COC*H*$_3$), 1.44 (s, 9H, –*t*-Bu).

*4.2.1.2. (3S)-3-Hydroxy-4-pentenoic acid tert-butyl ester ((−)-**7**).* To a solution of **8** (9.60 g, 44.8 mmol) in MeOH (200 mL) at ambient temperature was added K_2CO_3 (1.24 g, 8.96 mmol) in one portion. The reaction mixture was stirred for 1 h at ambient temperature before it was quenched by slow addition of AcOH. To the mixture wad added saturated aqueous solution of $NaHCO_3$ (100 mL) and H_2O (30 mL). The resulting mixture was extracted with Et_2O (3×100 mL) The combined organic layer was washed with H_2O (2×200 mL) and brine (200 mL) and dried with sodium sulfate, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, pentane/Et_2O=3:1) afforded (−)-**7** (6.13 g, 35.6 mmol, 80%) as colorless liquid.

*4.2.2. Glycosylation. 4.2.2.1. (3R)-3-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyloxy)-4-pentenoic acid tert-butyl ester (**9**).* To a solution of **6** (39.2 mg, 0.0796 mmol), (+)-**7** (27.4 mg, 0.159 mmol), and MS4 Å (200 mg) in CH_2Cl_2 (0.8 mL) at −20 °C was added $BF_3\cdot OEt_2$ (12 μL, 3.59 μmol) dropwise. The reaction mixture was stirred for 1.5 h at −20 °C before it was quenched by addition of saturated aqueous solution of $NaHCO_3$ (2 mL). This mixture was filtered through Celite, rinsed with AcOEt (10 mL). The resulting solution was washed with H_2O (2×10 mL) and brine (10 mL). The organic layer was dried with sodium sulfate, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, hexane/AcOEt=4:1→3:1) afforded **9** (27.7 mg, 0.0551 mmol, 69%, β only) as colorless oil. R_f=0.32 (benzene/AcOEt=3:1); $[\alpha]_D^{21}$ +0.76 (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.85 (ddd, *J*=17.3, 10.4, 7.2 Hz, 1H, 4-H), 5.24 (dt, *J*=17.3, 1.2 Hz, 1H, 5-H (trans)), 5.17 (dd, *J*=9.5, 9.4 Hz, 1H, 3′-H), 5.13 (dt, *J*=10.4, 1.2 Hz, 1H, 5-H (cis)), 5.03 (dd, *J*=9.8, 9.4 Hz, 1H, 4′-H), 4.95 (dd, *J*=9.5, 8.1 Hz, 1H, 2′-H), 4.60 (d, *J*=8.1 Hz, 1H, 1′-H), 4.46 (br dddt, *J*=8.4, 7.2, 4.8, 1.2 Hz, 1H, 3-H), 4.20 (dd, *J*=12.2, 5.1 Hz, 1H, 6′-H), 4.07 (dd, *J*=12.2, 2.5 Hz, 1H, 6′-H), 3.64 (ddd, *J*=9.8, 5.1, 2.5 Hz, 1H, 5′-H), 2.55 (dd, *J*=16.0, 8.4 Hz, 1H, 2-H), 2.36 (dd, *J*=16.0, 4.8 Hz, 1H, 2-H), 2.05 (s, 3H, –OCOCH_3), 2.04 (s, 3H, –OCOCH_3), 2.00 (s, 3H, –OCOCH_3), 1.97 (s, 3H, –OCOCH_3), 1.42 (s, 9H, –*t*-Bu); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 170.6 (–*O*COCH$_3$), 170.2 (–*O*COCH$_3$), 169.5 (C-1), 169.4 (–*O*COCH$_3$), 169.4 (–*O*COCH$_3$), 137.4 (C-4), 116.8 (C-5), 100.0 (C-1′), 80.9 (–*O*C(CH$_3$)$_3$), 78.7 (C-3), 73.0 (C-3′), 71.7 (C-5′), 71.3 (C-2′), 68.5 (C-4′), 62.0 (C-6′), 41.3 (C-2), 28.1 (–C(*C*H$_3$)$_3$), 20.7 (–OCO*C*H$_3$), 20.6 (–OCO*C*H$_3$), 20.6 (–OCO*C*H$_3$); IR (KBr, cm^{-1}) ν: 2979,1756,1369,1223,1040; HRMS (FAB-pos, NBA matrix) *m*/*z* 525.1950 [M+Na]$^+$, calcd for $C_{23}H_{34}O_{12}Na$: 525.1948 [M+Na].

*4.2.2.2. (3R)-3-(β-D-Glucopyranosyloxy)-4-pentenoic acid tert-butyl ester (**10**).* To a solution of **9** (32.8 mg, 0.0653 mmol) in MeOH (2 mL) at ambient temperature was added NaH (0.1 mg, 0.00327 mmol, 60% disp.) in one portion. The reaction mixture was stirred for 1.5 h at ambient temperature before it was quenched by addition of Duolite to neutralize the mixture. This mixture was filtered, rinsed with MeOH (10 mL). The resulting solution was concentrated under reduced pressure to afford **10** (23.2 mg, 0.0694 mmol, quant.) as yellow oil. The resulting oil of **10** was used in the next step without further purification. R_f=0.53 ($CHCl_3$/MeOH=3:1); $[\alpha]_D^{21}$ −6.13 (*c* 1.13, MeOH); ^{1}H NMR (300 MHz, CD_3OD) δ: 5.90 (ddd, *J*=17.3, 10.6, 6.4 Hz, 1H, 4-H), 5.24 (dt, *J*=17.3, 1.3 Hz, 1H, 5-H (trans)), 5.10 (dt, *J*=10.6, 1.3 Hz, 1H, 5-H (cis)), 4.52 (br dddt, *J*=7.0, 6.4, 6.3, 1.3 Hz, 1H, 3-H), 4.34 (d, *J*=7.8 Hz, 1H, 1′-H), 3.79 (dd, *J*=11.9, 2.2 Hz, 1H, 6′-H), 3.62 (dd, *J*=11.9, 5.3 Hz, 1H, 6′-H), 3.40–3.21 (m, 3H, 3′-H, 4′-H, 5′-H), 3.17 (dd, *J*=9.0, 7.8 Hz, 1H, 2′-H), 2.63 (dd, *J*=15.4, 7.0 Hz, 1H, 2-H), 2.45 (dd, *J*=15.4, 6.3 Hz, 1H, 2-H), 1.42 (s, 9H, –*t*-Bu); ^{13}C NMR (75 MHz, CD_3OD) δ: 172.2 (C-1), 139.2 (C-4), 116.8 (C-5), 103.3 (C-1′), 82.3 (–*O*C(CH$_3$)$_3$), 78.6 (C-3), 78.0 (C-3′), 77.9 (C-5′), 75.3 (C-2′), 71.5 (C-4′), 62.7 (C-6′), 42.1 (C-2), 28.4 (–C(*C*H$_3$)$_3$); IR (KBr, cm^{-1}) ν: 3391, 2979, 2928, 1726, 1368, 1158, 1077; HRMS (FAB-pos, NBA matrix); *m*/*z* 357.1527 [M+Na]$^+$, calcd for $C_{15}H_{26}O_8Na$: 357.1525 [M+Na].

*4.2.3. First generation synthesis. 4.2.3.1. (3R)-3-(6-O-Trityl-β-D-glucopyranosyloxy)-4-pentenoic acid tert-butyl ester (**11**).* To a solution of **10** (79.2 mg, 0.237 mmol) in DMF (0.2 mL) at ambient temperature were added TrCl (72.7 mg, 0.261 mmol), Et_3N (75 μL), DMAP (1.5 mg, 0.0123 mmol). The reaction mixture was stirred at ambient temperature for 42 h before it was concentrated in vacuo. Purification by flash column chromatography (silica gel, hexane/AcOEt=2:1→1:2) afforded **11** (70.2 mg, 0.122 mmol, 51%) as white solid. R_f=0.16 (hexane/AcOEt=1:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.46–7.16 (m, 15H, Ph–*H*), 5.85 (ddd, *J*=17.1, 10.6, 6.6 Hz, 1H, 4-H), 5.35 (dt, *J*=17.1, 1.2 Hz, 1H, 5-H (trans)), 5.15 (dt, *J*=10.6, 1.2 Hz, 1H, 5-H (cis)), 4.49 (br dddt, *J*=9.7, 6.6, 3.6, 1.2 Hz, 1H, 3-H), 4.31 (d, *J*=7.8 Hz, 1H, 1′-H), 3.57–3.28 (m, 6H, 2′-H, 3′-H, 4′-H, 5′-H, 6′-H$_2$), 2.59 (dd, *J*=16.6, 9.7 Hz, 1H, 2-H), 2.45 (dd, *J*=16.6, 3.6 Hz, 1H, 2-H), 1.42 (s, 9H, –*t*-Bu).

*4.2.3.2. Tetra-O-benzyl-6-O-trityl-α (and/or β)-D-glucopyranose (**12**).* A solution of **11** (70.2 mg, 0.122 mmol) in DMF (1 mL) at ambient temperature was treated with NaH (29.2 mg, 0.730 mmol, 60% disp.) followed by cooling the flask to 0 °C and adding BnBr (72 μL, 0.609 mmol) dropwise to this mixture. After warming to ambient temperature, the reaction mixture was stirred at ambient temperature for 1 h. The reaction was quenched with H_2O (1 mL). The resulting mixture was extracted with AcOEt (3 mL×3). The organic layer was washed with H_2O (10 mL×5), brine (10 mL), and dried with sodium sulfate, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, hexane/AcOEt=9:1) to afford **12** (29.6 mg, 0.0378 mmol, 31%, α/β=39:61) as white solid. R_f=0.43 (hexane/AcOEt=3:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.70–6.80 (m, 70H, Ph–*H*), 5.09 (d, *J*=11.7 Hz, 1H, –C*H*$_2$Ph), 5.03 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.99 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.96 (d, *J*=3.8 Hz, 1H, 1α-H), 4.91 (d, *J*=11.0 Hz, 1H,

–C*H*$_2$Ph), 4.82 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.80 (d, *J*=11.0 Hz, 2H, –C*H*$_2$Ph), 4.80 (d, *J*=12.0 Hz, 1H, –C*H*$_2$Ph), 4.78 (d, *J*=11.7 Hz, 1H, –C*H*$_2$Ph), 4.73 (d, *J*=12.0 Hz, 1H, –C*H*$_2$Ph), 4.71 (d, *J*=10.3 Hz, 2H, –C*H*$_2$Ph), 4.64 (d, *J*=12.0 Hz, 1H, –C*H*$_2$Ph), 4.63 (d, *J*=12.0 Hz, 1H, –C*H*$_2$Ph), 4.57 (d, *J*=7.3 Hz, 1H, 1β-H), 4.38 (d, *J*=10.3 Hz, 1H, –C*H*$_2$Ph), 4.31 (d, *J*=10.3 Hz, 1H, –C*H*$_2$Ph), 4.03 (t, *J*=9.2 Hz, 1H, 3α-H), 3.92–3.80 (m, 1H, 5α-H), 3.84 (t, *J*=9.2 Hz, 1H, 3β-H), 3.72–3.57 (m, 5H, 2α-H, 4α-H, 2β-H, 4β-H, 5β-H), 3.47 (dd, *J*=10.0, 1.6 Hz, 1H, 6β-H), 3.46–3.40 (m, 1H, 6α-H), 3.28 (dd, *J*=10.0, 4.0 Hz, 1H, 6β-H), 3.20 (dd, *J*=10.3, 4.5 Hz, 1H, 6α-H); LR-MS (FAB-pos, NBA matrix) *m*/*z* 805 [M+Na]$^+$, calcd for $C_{53}H_{50}O_6Na$: 805.35 [M+Na].

*4.2.3.3. (3R)-3-(6-O-Acetyl-β-D-glucopyranosyloxy)-4-pentenoic acid tert-butyl ester (**14**).* To a solution of **10** (154 mg, 0.460 mmol) in CH_2Cl_2 (60 mL) and pyridine (56 μL, 0.689 mmol) at −78 °C was added a solution of AcCl (36 μL, 0.505 mmol) in CH_2Cl_2 (1.4 mL) dropwise. The reaction mixture was stirred at −78 °C for 1 h before it was quenched with MeOH (5 mL). After warming the resulting mixture to ambient temperature, the reaction mixture was concentrated in vacuo. Purification by flash column chromatography (silica gel, $CHCl_3$/MeOH=50:1→40:1→30:1→10:1) afforded **14** (104 mg, 0.276 mmol, 60%, conversion yield 72%) as colorless oil while **10** (26.9 mg, 0.0805 mmol, 17%) was recovered. R_f=0.33 ($CHCl_3$/MeOH=10:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.85 (ddd, *J*=17.3, 10.4, 6.7 Hz, 1H, 4-H), 5.33 (dt, *J*=17.3, 1.0 Hz, 1H, 5-H (trans)), 5.17 (dt, *J*=10.4, 1.0 Hz, 1H, 5-H (cis)), 4.48 (br dddt, *J*=9.7, 6.7, 3.7, 1.0 Hz, 1H, 3-H), 4.37 (dd, *J*=12.0, 4.5 Hz, 1H, 6′-H), 4.31 (d, *J*=7.8 Hz, 1H, 1′-H), 4.27 (dd, *J*=12.0, 1.8 Hz, 1H, 6′-H), 3.57 (t, *J*=8.8 Hz, 1H, 3′-H), 3.50–3.36 (m, 2H, 4′-H, 5′-H), 3.36 (dd, *J*=9.1, 7.8 Hz, 1H, 2′-H), 2.62 (dd, *J*=16.7, 9.7 Hz, 1H, 2-H), 2.45 (dd, *J*=16.7, 3.7 Hz, 1H, 2-H), 2.07 (s, 3H, –OCOCH_3), 1.42 (s, 9H, –*t*-Bu); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 171.6 (–*C*OOR), 171.4 (–*C*OOR), 136.7 (C-4), 117.1 (C-5), 102.6 (C-1′), 81.9 (–O*C*(CH_3)$_3$), 78.8 (C-3), 75.9 (C-3′), 84.4 (C-2′), 74.1 (C-5′), 69.7 (C-4′), 63.4 (C-6′), 40.7 (C-2), 28.0 (–C(*C*H_3)$_3$), 20.8 (–OCO*C*H_3) HRMS (FAB-pos, NBA matrix) *m*/*z* 399.1631 [M+Na]$^+$, calcd for $C_{17}H_{28}O_9Na$: 399.1631 [M+Na].

*4.2.3.4. (3R)-3-(6-O-Acetyl-3-O-benzyl-β-D-glucopyranosyloxy)-4-pentenoic acid tert-butyl ester (**16**) and (3R)-3-(6-O-acetyl-2, 3-di-O-benzyl-β-D-glucopyranosyloxy)-4-pentenoic acid tert-butyl ester (**17**).* To a solution of **14** (155 mg, 0.412 mmol) in CH_2Cl_2 (4 mL) at ambient temperature were added TMSCl (1.64 mL, 13.0 mmol), PhCHO (132 μL, 1.30 mmol), and Et_3SiH (415 μL, 2.60 mmol). The reaction mixture was stirred at ambient temperature for 20 h before it was concentrated. The residue was purified by flash column chromatography (hexane/AcOEt=6:1→5:1→4:1→3:1→2:1) to afford **16** (112 mg, 0.240 mmol, 58%) as colorless oil and **17** (14.9 mg, 0.0268 mmol, 7%) as colorless oil.

Compound **16**: R_f=0.22 (hexane/AcOEt=3:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.44–7.24 (m, 5H, Ph–*H*), 5.85 (ddd, *J*=17.3, 10.6, 6.9 Hz, 1H, 4-H), 5.35 (dt, *J*=17.3, 1.0 Hz, 1H, 5-H (trans)), 5.19 (dt, *J*=10.6, 1.0 Hz, 1H, 5-H (cis)), 5.09 (d, *J*=11.7 Hz, 1H, –C*H*$_2$Ph), 4.75 (d, *J*=11.7 Hz, 1H, –C*H*$_2$Ph), 4.50 (br dddt, *J*=10.0, 6.9, 3.2, 1.0 Hz, 1H, 3-H), 4.40–4.20 (m, 3H, 1′-H, 6′-H$_2$), 3.54 (t, *J*=8.1 Hz, 1H, 2′-H), 3.51–3.38 (m, 3H, 3′-H, 4′-H, 5′-H), 2.63 (dd, *J*=16.9, 10.0 Hz, 1H, 2-H), 2.47 (dd, *J*=16.9, 3.2 Hz, 1H, 2-H), 2.06 (s, 3H, –OCOCH_3), 1.47 (s, 9H, –*t*-Bu); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 171.4 (–*C*OOR), 171.3 (–*C*OOR), 138.6, 136.7 (C-4), 128.6, 128.1, 127.9, 117.1 (C-5), 103.1 (C-1′), 83.3 (C-3′), 81.8 (–O*C*(CH_3)$_3$), 79.2 (C-3), 75.3 (C-2′), 74.7 (–*C*H$_2$Ph), 73.8 (C-5′), 69.3 (C-4′), 63.4 (C-6′), 40.6 (C-2), 28.0 (–C(*C*H_3)$_3$), 20.8 (–OCO*C*H_3); HRMS (FAB-pos, NBA matrix) *m*/*z* 489.2107 [M+Na]$^+$, calcd for $C_{24}H_{34}O_9Na$: 489.2101 [M+Na].

Compound **17**: R_f=0.35 (hexane/AcOEt=3:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.42–7.24 (m, 10H, Ph–*H*), 5.94 (ddd, *J*=17.3, 10.4, 7.0 Hz, 1H, 4-H), 5.28 (dt, *J*=17.3, 1.2 Hz, 1H, 5-H (trans)), 5.16 (dt, *J*=10.4, 1.2 Hz, 1H, 5-H (cis)), 4.93 (d, *J*=11.3 Hz, 1H, –C*H*$_2$Ph), 4.91 (d, *J*=11.3 Hz, 1H, –C*H*$_2$Ph), 4.68 (d, *J*=11.3 Hz, 2H, –C*H*$_2$Ph), 4.58 (br dddt, *J*=7.0, 6.9, 6.6, 1.2 Hz, 1H, 3-H), 4.53 (d, *J*=7.5 Hz, 1H, 1′-H), 4.34 (dd, *J*=11.9, 4.7 Hz, 1H, 6′-H), 4.26 (dd, *J*=11.9, 1.9 Hz, 1H, 6′-H), 3.50–3.30 (m, 4H, 2′-H, 3′-H, 4′-H, 5′-H), 2.70 (dd, *J*=15.4, 6.9 Hz, 1H, 2-H), 2.49 (dd, *J*=15.4, 6.6 Hz, 1H, 2-H), 2.07 (s, 3H, –OCOCH_3), 1.42 (s, 9H, –*t*-Bu).

^{13}C NMR (75 MHz, $CDCl_3$) δ: 171.4 (–*C*OOR), 169.7 (–*C*OOR), 138.4, 138.3, 137.8 (C-4), 128.6, 128.3, 128.2, 128.0, 127.9, 127.7, 116.7 (C-5), 102.6 (C-1′), 83.8 (C-3′), 81.6 (C-2′), 80.9 (–O*C*(CH_3)$_3$), 78.2 (C-3), 75.3 (–*C*H$_2$Ph), 74.7 (–*C*H$_2$Ph), 73.3 (C-5′), 69.9 (C-4′), 63.4 (C-6′), 41.5 (C-2), 28.1 (–C(*C*H_3)$_3$), 20.1 (–OCO*C*H_3); HRMS (FAB-pos, NBA matrix) *m*/*z* 579.2575 [M+Na]$^+$, calcd for $C_{31}H_{40}O_9Na$: 579.2570 [M+Na].

*4.2.3.5. (3R)-3-(4,6-Di-O-acetyl-2,3-di-O-benzyl-β-D-glucopyranosyloxy)-4-pentenoic acid tert-butyl ester (**17**-Ac).* To a solution of **17** (20 mg, 0.0359 mmol) in CH_2Cl_2 (0.2 mL), and pyridine (0.2 mL) at ambient temperature were added Ac_2O (10 μL, 0.108 mmol) and DMAP (0.5 mg, 3.59 μmol). The reaction mixture was stirred at ambient temperature for 1 h before it was quenched with H_2O (3 mL). The resulting mixture was extracted with AcOEt (3 mL×3). The combined organic layer was washed with saturated aqueous solution of $CuSO_4$ (10 mL), H_2O (10 mL×3), and brine (10 mL), dried with sodium sulfate, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, hexane/AcOEt=2:1) afforded **17**-Ac (19.3 mg, 0.0322 mmol, 90%) as colorless oil. R_f=0.44 (hexane/AcOEt=3:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.40–7.17 (m, 10H, Ph–*H*), 5.94 (ddd, *J*=17.2, 10.4, 7.0 Hz, 1H, 4-H), 5.27 (dt, *J*=17.2, 1.2 Hz, 1H, 5-H (trans)), 5.16 (dt, *J*=10.4, 1.2 Hz, 1H, 5-H (cis)), 4.98 (dd, *J*=10.0, 9.1 Hz, 1H, 4′-H), 4.91 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.79 (d, *J*=11.3 Hz, 1H, –C*H*$_2$Ph), 4.66 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.62–4.50 (m, 1H, 3-H), 4.58 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.53 (d, *J*=7.6 Hz, 1H, 1′-H), 4.17 (dd, *J*=12.2, 5.7 Hz, 1H, 6′-H), 4.04 (dd, *J*=12.2, 2.5 Hz, 1H, 6′-H), 3.57 (t, *J*=9.1 Hz, 1H, 3′-H), 3.54–3.45 (m, 2H, 2′-H, 5′-H), 2.70 (dd, *J*=15.5, 7.0 Hz, 1H, 2-H), 2.49 (dd, *J*=15.5, 6.4 Hz, 1H, 2-H), 2.05 (s, 3H, –OCOCH_3), 1.89 (s, 3H, –OCOCH_3), 1.42 (s, 9H, –*t*-Bu).

*4.2.3.6. (3R)-3-(3-O-Benzyl-β-D-glucopyranosyloxy)-4-pentenoic acid (**18**).* To a solution of **16** (19.0 mg, 0.0407 mmol) in CH_2Cl_2 (1 mL) at ambient temperature was added TFA (0.2 mL) in one portion. The reaction mixture was stirred for 1 h at ambient temperature, before it was concentrated under reduced pressure to remove TFA.

To a solution of the residue in MeOH (1 mL) at ambient temperature was added NaH (0.6 mg, 0.0145 mmol, 60% disp.) in one portion. The reaction mixture was stirred for 1 h at ambient temperature before it was quenched by addition of Duolite to neutralize the mixture. This mixture was filtered, rinsed with MeOH (5 mL). The resulting solution was concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, $CHCl_3$/MeOH/AcOH=5:1:0.1) afforded **18** (13.3 mg, 0.0362 mmol, 89%) as colorless oil. R_f=0.25 ($CHCl_3$/MeOH/AcOH=100:10:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.42–7.22 (m, 5H, Ph–*H*), 5.87 (ddd, *J*=17.2, 10.3, 6.9 Hz, 1H, 4-H), 5.30(d, *J*=17.2 Hz, 1H, 5-H (trans)), 5.18 (d, *J*=10.3 Hz, 1H, 5-H (cis)), 4.98 (d, *J*=11.6 Hz, 1H, –C*H*$_2$Ph), 4.73 (d, *J*=11.6 Hz, 1H, –C*H*$_2$Ph), 4.59–4.47 (m, 1H, 3-H), 4.40 (d, *J*=7.6 Hz, 1H, 1′-H), 3.86–3.63 (m, 2H, 6′-H$_2$), 3.59–3.37 (m, 3H, 2′-H, 3′-H, 4′-H), 3.35–3.26 (m, 1H, 5′-H), 2.70 (dd, *J*=15.9, 9.5 Hz, 1H, 2-H), 2.54 (dd, *J*=15.9, 2.5 Hz, 1H, 2-H).

*4.2.3.7. (3R,3′R)-3-(3-O-Benzyl-2,4-dihydroxy-β-D-glucopyranosyloxy)-4-pentenoic acid bimol. cyclic ester (**19**).* To a solution of **18** (46 mg, 0.125 mmol) in CH_2Cl_2 (7 mL) at ambient temperature were added DMC (52.9 mg, 0.313 mmol), K_2CO_3 (34.6 mg, 0.250 mmol) in one portion. The mixture was stirred at 0 °C for 2 h followed by addition of DMAP (30.5 mg, 0.250 mmol) to this mixture.

After it was warmed to rt, the reaction mixture was stirred at ambient temperature for 17 h. The resulting mixture was filtered through Celite, rinsed with $CHCl_3$ (10 mL), and concentrated in vacuo. Purification of the residue by flash column chromatography (silica gel, $CHCl_3$) afforded **19** (12.0 mg, 0.0171 mmol, 28%) as colorless oil. R_f=0.52 ($CHCl_3$/MeOH/AcOH=100:10:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.46–7.18 (m, 10H, Ph–*H*), 5.83 (ddd, *J*=17.3, 10.7, 6.3 Hz, 2H, 4-H), 5.30 (d, *J*=17.3 Hz, 2H, 5-H (trans)), 5.18 (d, *J*=10.7 Hz, 2H, 5-H (cis)), 5.02 (d, *J*=11.0 Hz, 2H, –C*H*$_2$Ph), 4.77–4.63 (m, 2H, 3-H), 4.73 (d, *J*=11.0 Hz, 2H, –C*H*$_2$Ph), 4.48 (dd, *J*=11.4, 1.3 Hz, 2H, 6′-H), 4.44 (d, *J*=7.8 Hz, 2H, 1′-H), 3.95 (dd, *J*=11.4, 9.8 Hz, 2H, 6′-H), 3.69–3.55 (m, 2H, 5′-H), 3.59 (br dd, *J*=8.5, 7.8 Hz, 2H, 2′-H), 3.42 (t, *J*=8.5 Hz, 2H, 3′-H), 3.36 (t, *J*=8.5 Hz, 2H, 4′-H), 2.96 (dd, *J*=13.9, 4.5 Hz, 2H, 2-H), 2.47 (dd, *J*=13.9, 11.0 Hz, 2H, 2-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 169.2 (C-1), 138.2, 135.6 (C-4), 128.7, 128.1, 128.1, 117.9 (C-5), 99.6 (C-1′), 83.6 (C-3′), 74.8 (–*C*H$_2$Ph), 74.4 (C-3), 74.2 (C-2′), 73.4 (C-5′), 70.1 (C-4′), 65.0 (C-6′), 39.8 (C-2); LR-MS (FAB-pos, NBA matrix) *m*/*z* 723 $[M+Na]^+$, calcd for $C_{36}H_{44}O_{14}Na$: 723.26 [M+Na].

*4.2.4. Second generation synthesis. 4.2.4.1. (3R)-3-(2,3,4,6-Tetra-O-trimethylsilyl-β-D-glucopyranosyloxy)-4-pentenoic acid tert-butyl ester (**20**).* To a solution of **10** (1.31 g, 3.92 mmol) in CH_2Cl_2 (20 mL) and pyridine (20 mL) at ambient temperature was added TMSCl (5.0 mL, 39.2 mmol) dropwise. The reaction mixture was stirred for 3 h at ambient temperature before it was quenched by addition of H_2O (20 mL). The resulting mixture was extracted with hexane (3×20 mL). The organic layer was washed with H_2O (3×60 mL) and brine (60 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, hexane/AcOEt=5:1) to remove a little amount of pyridine, afforded **20** (2.18 g, 3.50 mmol, 89%) as colorless oil. R_f=0.56 (hexane/AcOEt=6:1); $[\alpha]_D^{22}$ −4.11 (*c* 1.78, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.89 (ddd, *J*=17.2, 10.4, 6.6 Hz, 1H, 4-H), 5.24 (dt, *J*=17.2, 1.4 Hz, 1H, 5-H (trans)), 5.10 (dt, *J*=10.4, 1.4 Hz, 1H, 5-H (cis)), 4.54 (dddt, *J*=7.9, 6.6, 6.0, 1.4 Hz, 1H, 3-H), 4.31 (d, *J*=7.5 Hz, 1H, 1′-H), 3.76 (dd, *J*=11.3, 2.1 Hz, 1H, 6′-H), 3.64 (dd, *J*=11.3, 5.1 Hz, 1H, 6′-H), 3.43 (t, *J*=8.4 Hz, 1H, 4′-H), 3.36 (t, *J*=8.4 Hz, 1H, 3′-H), 3.24 (dd, *J*=8.4, 7.5 Hz, 1H, 2′-H), 3.15 (ddd, *J*=8.4, 5.1, 2.1 Hz, 1H, 5′-H), 2.68 (dd, *J*=15.1, 6.0 Hz, 1H, 2-H), 2.43 (dd, *J*=15.1, 7.9 Hz, 1H, 2-H), 1.44 (s, 9H, –*t*-Bu), 0.15 (s, 9H, –Si(C*H*$_3$)$_3$), 0.15 (s, 9H, –Si(C*H*$_3$)$_3$), 0.14 (s, 9H, –Si(C*H*$_3$)$_3$), 0.10 (s, 9H, –Si(C*H*$_3$)$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 170.0 (C-1), 137.9 (C-4), 116.1 (C-5), 101.5 (C-1′), 80.7 (–O*C*(CH$_3$)$_3$), 78.1 (C-3′), 76.7 (C-5′), 76.2 (C-3), 75.2 (C-2′), 71.5 (C-4′), 62.1 (C-6′), 41.3 (C-2), 28.1 (–C(*C*H$_3$)$_3$), 1.3 (–Si(*C*H$_3$)$_3$), 1.2 (–Si(*C*H$_3$)$_3$), 0.9 (–Si(*C*H$_3$)$_3$), −0.3 (–Si(*C*H$_3$)$_3$); IR (KBr, cm^{-1}) ν: 2957, 2902, 1733, 1251, 1091, 843.

*4.2.4.2. (3R)-3-(2,3-Di-O-benzyl-4,6-O-benzylidene-β-D-glucopyranosyloxy)-4-pentenoic acid tert-butyl ester (**22**).* To a suspension of **20** (2.16 g, 3.47 mmol) and MS4 Å (3 g) in CH_2Cl_2 (30 mL) at −78 °C were added PhCHO (386 μL, 3.82 mmol) and TMSOTf (127 μL, 0.700 mmol) dropwise. The reaction mixture was stirred for 2.5 h at −78 °C. To this mixture were added Et_3SiH (1.66 mL, 10.4 mmol), PhCHO (1.05 mL, 10.4 mmol), and TMSOTf (127 μL, 0.700 mmol) dropwise. The reaction mixture was stirred for 1 h at −78 °C and for 2 h at −40 °C before it was quenched with Et_3N. After warmed up to ambient temperature, the resulting mixture was filtered through Celite, rinsed with CH_2Cl_2 (30 mL), and concentrated in vacuo. Purification of the residue by flash column chromatography (silica gel, hexane/AcOEt=20:1→15:1→10:1→8:1→6:1) afforded **22** (1.80 g, 2.99 mmol, 86%) as white solid. R_f=0.24 (hexane/AcOEt=4:1); $[\alpha]_D^{24}$ −16.9 (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.56–7.20 (m, 15H, Ph–*H*), 5.91 (ddd, *J*=17.2, 10.4, 7.0 Hz, 1H, 4-H), 5.55 (s, 1H, –O$_2$C*H*Ph), 5.30 (dt, *J*=17.2, 1.0 Hz, 1H, 5-H (trans)), 5.18 (dt, *J*=10.4, 1.0 Hz, 1H, 5-H (cis)), 4.89 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.88 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.77 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.73 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.63 (d, *J*=7.8 Hz, 1H, 1′-H), 4.59 (br dtt, *J*=7.0, 6.6, 1.0 Hz, 1H, 3-H), 4.31 (dd, *J*=10.4, 5.0 Hz, 1H, 6′-H), 3.77 (dd, *J*=10.4, 9.9 Hz, 1H, 6′-H), 3.73 (dd, *J*=9.1, 8.2 Hz, 1H, 3′-H), 3.67 (t, *J*=9.1 Hz, 1H, 4′-H), 3.46 (dd, *J*=8.2, 7.8 Hz, 1H, 2′-H), 3.38 (br ddd, *J*=9.9, 9.1, 5.0 Hz, 1H, 5′-H), 2.70 (dd, *J*=15.4, 6.6 Hz, 1H, 2-H), 2.47 (dd, *J*=15.4, 7.0 Hz, 1H, 2-H), 1.41 (s, 9H, –*t*-Bu); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 169.6 (C-1), 138.5, 138.4, 137.5, 137.3 (C-4), 128.9, 128.3, 128.3, 128.2, 128.0, 127.6, 127.6, 126.0, 117.0 (C-5), 102.6 (C-1′), 101.1 (–O$_2$CHPh), 82.1 (C-2′), 81.4 (C-4′), 81.1 (C-3′), 81.0 (–O*C*(CH$_3$)$_3$), 77.9 (C-3), 75.3 (–*C*H$_2$Ph), 75.1 (–*C*H$_2$Ph), 68.8 (C-6′), 66.0 (C-5′), 41.5 (C-2), 28.1 (–C(*C*H$_3$)$_3$); IR (KBr, cm^{-1}) ν: 2978, 2872, 1728, 1454, 1367, 1088; HRMS (FAB-pos, NBA matrix); *m*/*z* 625.2778 $[M+Na]^+$, calcd for $C_{36}H_{42}O_8Na$: 625.2777 [M+Na].

*4.2.4.3. (3R)-3-(2,3,4-Tri-O-benzyl-β-D-glucopyranosyloxy)-4-pentenoic acid tert-butyl ester (**24**).* To a solution of **22** (15 mg, 0.0249 mmol) in CH_2Cl_2 (1.5 mL) at −20 °C was added $BH_3\cdot Me_2NH$ (7.4 mg, 0.125 mmol) dropwise. The mixture was stirred at −20 °C for 30 min. To this mixture was added $BF_3\cdot OEt_2$ (15.7 μL, 0.125 mmol) dropwise. The reaction mixture was stirred at −20 °C for 2 h before it was quenched with saturated $NaHCO_3$ (1 mL). The resulting mixture was extracted with AcOEt (3×3 mL). The organic layer was washed with saturated aqueous solution of $NaHCO_3$ (10 mL) and brine (10 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (hexane/AcOEt=8:1→6:1→4:1→3:1) afforded **24** (10.1 mg, 0.0167 mmol, 67%, conversion yield 74%) as colorless oil. R_f=0.24 (hexane/AcOEt=2:1); $[\alpha]_D^{25}$ +16.8 (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.40–7.20 (m, 15H, Ph-*H*), 5.94 (ddd, *J*=17.3, 10.4, 7.0 Hz, 1H, 4-H), 5.28 (dt, *J*=17.3, 1.2 Hz, 1H, 5-H (trans)), 5.17 (dt, *J*=10.4, 1.2 Hz, 1H, 5-H (*cis*)), 4.92 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.91 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.83 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.78 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.68 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.64–4.56 (m, 1H, 3-H), 4.59 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.56 (d, *J*=7.8 Hz, 1H, 1′-H), 3.82 (dd, *J*=11.6, 2.6 Hz, 1H, 6′-H), 3.65 (t, *J*=8.9 Hz, 1H, 3′-H), 3.60 (dd, *J*=11.6, 5.7 Hz, 1H, 6′-H), 3.46 (dd, *J*=9.7, 8.9 Hz, 1H, 4′-H), 3.42 (dd, *J*=8.9, 7.8 Hz, 1H, 2′-H), 3.34 (br ddd, *J*=9.7, 5.7, 2.6 Hz, 1H, 5′-H), 2.68 (dd, *J*=15.4, 7.3 Hz, 1H, 2-H), 2.48 (dd, *J*=15.4, 6.3 Hz, 1H, 2-H), 1.42 (s, 9H, –*t*-Bu); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 169.7 (C-1), 138.5, 138.4, 138.3 (C-4), 137.9, 128.5, 128.3, 128.3, 128.1, 128.0, 127.9, 127.8, 127.6, 127.6, 116.5 (C-5), 102.4 (C-1′), 84.6 (C-3′), 82.2 (C-2′), 81.1 (–O*C*(CH$_3$)$_3$), 78.0 (C-3), 77.9 (C-4′), 75.7 (–*C*H$_2$Ph), 75.0 (C-5′), 75.0 (–*C*H$_2$Ph), 74.8 (–*C*H$_2$Ph), 62.3 (C-6′), 41.7 (C-2), 28.1 (–C(*C*H$_3$)$_3$); IR (KBr, cm^{-1}) ν: 3460, 2977, 2875, 1730, 1366, 1071; HRMS (FAB-pos, NBA matrix) *m*/*z* 627.2947 $[M+Na]^+$, calcd for $C_{36}H_{44}O_8Na$: 627.2934 [M+Na].

*4.2.4.4. (3R)-3-(2,3,4-Tri-O-benzyl-β-D-glucopyranosyloxy)-4-pentenoic acid (**25**).* To a solution of **24** (500 mg, 0.827 mmol) in CH_2Cl_2 (13 mL) at ambient temperature was added TFA (2 mL) in one portion. The reaction mixture was stirred for 2 h at ambient temperature, before it was concentrated under reduced pressure to remove TFA. The resulting residue was used in the next step without further purification.

To a mixture of the previous reaction residue in MeOH (7 mL) at ambient temperature was added NaH (60% disp.) in one portion. The reaction mixture was stirred at ambient temperature before it was quenched by addition of Duolite to neutralize the mixture. This mixture was filtered, rinsed with MeOH. The resulting solution was concentrated under reduced pressure. Purification of the residue by flash column chromatography (hexane/AcOEt:AcOH=50:10:1→30:10:1→10:10:1) afforded **25** (400 mg, 0.729 mmol, 88%) as white solid. R_f=0.24 (hexane/AcOEt/AcOH=10:10:1); $[\alpha]_D^{25}$ +16.8 (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$); δ: 7.36–7.21 (m, 15H, Ph–*H*), 5.95 (ddd, *J*=17.3, 10.4, 6.9 Hz, 1H, 4-H), 5.23 (br dt, *J*=17.3, 1.0 Hz, 1H, 5-H (trans)), 5.19 (br dt, *J*=10.4, 1.0 Hz, 1H, 5-H (cis)), 4.89

(d, J=11.0 Hz, 1H, –CH_2Ph), 4.87 (d, J=11.0 Hz, 1H, –CH_2Ph), 4.82 (d, J=11.0 Hz, 1H, –CH_2Ph), 4.78 (d, J=11.0 Hz, 1H, –CH_2Ph), 4.70–4.50 (m, 1H, 3-H), 4.68 (d, J=11.0 Hz, 1H, –CH_2Ph), 4.58 (d, J=11.0 Hz, 1H, –CH_2Ph), 4.56 (d, J=7.8 Hz, 1H, 1′-H), 3.81 (dd, J=11.9, 2.6 Hz, 1H, 6′-H), 3.65 (t, J=8.9 Hz, 1H, 3′-H), 3.59 (dd, J=11.9, 5.7 Hz, 1H, 6′-H), 3.46 (dd, J=9.7, 8.9 Hz, 1H, 4′-H), 3.42 (dd, J=8.9, 7.8 Hz, 1H, 2′-H), 3.35 (br ddd, J=9.7, 5.7, 2.5 Hz, 1H, 5′-H), 2.72 (dd, J=15.8, 8.4 Hz, 1H, 2-H), 2.55 (dd, J=15.8, 4.8 Hz, 1H, 2-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 174.8 (C-1), 138.3, 137.9, 137.8 (C-4), 128.5, 128.5, 128.4, 128.4, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 127.6, 116.9 (C-5), 102.3 (C-1′), 84.6 (C-3′), 82.1 (C-2′), 77.9 (C-3), 77.8 (C-4′), 75.7 (–CH$_2$Ph), 75.1 (C-5′), 75.0 (–CH$_2$Ph), 74.9 (–CH$_2$Ph), 62.2 (C-6′), 40.2 (C-2); IR (KBr, cm^{-1}) ν: 3439, 3063, 3031, 2915, 1714, 1070; HRMS (FAB-pos, NBA matrix) m/z 571.2326 [M+Na]$^+$, calcd for $C_{32}H_{36}O_8Na$: 571.2308 [M+Na].

*4.2.4.5. (3S)-3-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyloxy)-4-pentenoic acid tert-butyl ester (**26**).* The glycosylation was performed according to the procedure (3.0 mL of CH_2Cl_2, 0 °C, 4 h) employing imidate donor **6** (423 mg, 0.859 mmol), acceptor (−)-**7** (296 mg, 1.72 mmol), and $BF_3\cdot OEt_2$ (130 μL, 1.03 mmol) to give **26** (334 mg, 0.665 mmol, 77%, β only) as colorless oil from the crude product after flash column chromatography (hexane/AcOEt=3:1→2:1). R_f=0.38 (benzene/AcOEt=3:1); $[\alpha]_D^{22}$ −12.8 (c 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.66 (ddd, J=17.2, 10.3, 7.5 Hz, 1H, 4-H), 5.28 (br d, J=17.2 Hz, 1H, 5-H (trans)), 5.27 (br d, J=10.3 Hz, 1H, 5-H (cis)), 5.17 (t, J=9.4 Hz, 1H, 3′-H), 5.07 (dd, J=9.6, 9.4 Hz, 1H, 4′-H), 4.97 (dd, J=9.4, 8.1 Hz, 1H, 2′-H), 4.57 (d, J=8.1 Hz, 1H, 1′-H), 4.53 (br ddd, J=7.5, 7.2, 6.6 Hz, 1H, 3-H), 4.26 (dd, J=12.2, 4.8 Hz, 1H, 6′-H), 4.10 (dd, J=12.2, 2.5 Hz, 1H, 6′-H), 3.64 (ddd, J=9.7, 4.8, 2.5 Hz, 1H, 5′-H), 2.62 (dd, J=15.0, 6.6 Hz, 1H, 2-H), 2.40 (dd, J=15.0, 7.2 Hz, 1H, 2-H), 2.08 (s, 3H, –OCOCH_3), 2.02 (s, 3H, –OCOCH_3), 2.01 (s, 3H, –OCOCH_3), 1.99 (s, 3H, –OCOCH_3), 1.42 (s, 9H, –t-Bu); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 170.6 (–OCOCH$_3$), 170.3 (–OCOCH$_3$), 169.4 (C-1), 169.2 (–OCOCH$_3$), 169.2 (–OCOCH$_3$), 135.9 (C-4), 118.8 (C-5), 97.6 (C-1′), 80.8 (–OC(CH$_3$)$_3$), 76.1 (C-3), 72.9 (C-3′), 71.6 (C-5′), 71.3 (C-2′), 68.4 (C-4′), 61.9 (C-6′), 42.0 (C-2), 28.0 (–C(CH$_3$)$_3$), 20.7 (–OCOCH$_3$), 20.6 (–OCOCH$_3$), 20.6 (–OCOCH$_3$), 20.5 (–OCOCH$_3$); IR (KBr, cm^{-1}) ν: 2979,1757,1368,1225,1041; HRMS (FAB-pos, NBA matrix); m/z 525.1948 [M+Na]$^+$, calcd for $C_{23}H_{34}O_{12}Na$: 525.1948 [M+Na].

*4.2.4.6. (3S)-3-(β-D-Glucopyranosyloxy)-4-pentenoic acid tert-butyl ester (**27**).* According to the synthesis of **10**, deacetylation of **26** (310 mg, 0.623 mmol) gave **27** (212 mg, 0.634 mmol, quant.) as yellow oil. R_f=0.33 ($CHCl_3$/MeOH=4:1); $[\alpha]_D^{23}$ −23.4 (c 1.62, MeOH); ^{1}H NMR (300 MHz, CD_3OD) δ: 5.76 (ddd, J=17.3, 10.0, 7.6 Hz, 1H, 4-H), 5.39 (dt, J=17.3, 1.0 Hz, 1H, 5-H (trans)), 5.28 (dt, J=10.0, 1.0 Hz, 1H, 5-H (cis)), 4.70–4.61 (m, 1H, 3-H), 4.31 (d, J=7.8 Hz, 1H, 1′-H), 3.87 (dd, J=11.7, 1.9 Hz, 1H, 6′-H), 3.65 (dd, J=11.7, 5.7 Hz, 1H, 6′-H), 3.45–3.15 (m, 4H, 2′-H, 3′-H, 4′-H, 5′-H), 2.62 (dd, J=14.7, 7.5 Hz, 1H, 2-H), 2.46 (dd, J=14.7, 7.5 Hz, 1H, 2-H), 1.45 (s, 9H, –t-Bu); ^{13}C NMR (75 MHz, CD_3OD) δ: 172.1 (C-1), 137.8 (C-4), 119.5 (C-5), 100.6 (C-1′), 82.2 (–OC(CH$_3$)$_3$), 78.0 (C-3′), 77.9 (C-5′), 76.1 (C-3), 75.0 (C-2′), 71.8 (C-4′), 62.9 (C-6′), 43.2 (C-2), 28.3 (–C(CH$_3$)$_3$); IR (KBr, cm^{-1}) ν: 3388, 2979, 2930, 1727, 1368, 1160, 1076; HRMS (FAB-pos, NBA matrix) m/z 357.1521 [M+Na]$^+$, calcd for $C_{15}H_{26}O_8Na$: 357.1525 [M+Na].

*4.2.4.7. (3S)-3-(2,3,4,6-Tetra-O-trimethylsilyl-β-D-glucopyranosyloxy)-4-pentenoic acid tert-butyl ester (**28**).* According to the synthesis of **20**, protection of **27** (200 mg, 0.610 mmol) gave **28** (310 mg, 0.498 mmol, 83%) as colorless oil from the crude product after flash column chromatography (hexane/AcOEt=12:1). R_f=0.53 (hexane/AcOEt=4:1); $[\alpha]_D^{21}$ −11.7 (c 2.43, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.66 (ddd, J=17.2, 10.1, 8.5 Hz, 1H, 4-H), 5.30 (br dd, J=17.2, 1.6 Hz, 1H, 5-H (trans)), 5.27 (br dd, J=10.1, 1.6 Hz, 1H, 5-H (cis)), 4.63 (dt, J=8.5, 6.2 Hz, 1H, 3-H), 4.24 (d, J=7.5 Hz, 1H, 1′-H), 3.79 (dd, J=11.3, 2.1 Hz, 1H, 6′-H), 3.64 (dd, J=11.3, 5.4 Hz, 1H, 6′-H), 3.45–3.34 (m, 2H, 3′-H, 4′-H), 3.26 (dd, J=8.6, 7.5 Hz, 1H, 2′-H), 3.34 (br ddd, J=8.9, 5.4, 2.1 Hz, 1H, 5′-H), 2.69 (dd, J=14.5, 6.2 Hz, 1H, 2-H), 2.39 (dd, J=14.5, 8.5 Hz, 1H, 2-H), 1.42 (s, 9H, –t-Bu), 0.15 (s, 9H, –Si(CH_3)$_3$), 0.14 (s, 9H, –Si(CH_3)$_3$), 0.14 (s, 9H, –Si(CH_3)$_3$), 0.12 (s, 9H, –Si(CH_3)$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 169.5 (C-1), 136.0 (C-4), 119.7 (C-5), 98.7 (C-1′), 80.5 (–OC(CH$_3$)$_3$), 78.5 (C-3′), 76.6 (C-5′), 75.6 (C-2′), 74.5 (C-3), 71.8 (C-4′), 62.2 (C-6′), 42.2 (C-2), 28.1 (–C(CH$_3$)$_3$), 1.4 (–Si(CH$_3$)$_3$), 1.3 (–Si(CH$_3$)$_3$), 0.9 (–Si(CH$_3$)$_3$), −0.3 (–Si(CH$_3$)$_3$); IR (KBr, cm^{-1}) ν: 2957, 2901, 1737, 1251, 1092, 843; HRMS (FAB-pos, NBA matrix) m/z 645.3112 [M+Na]$^+$, calcd for $C_{15}H_{26}O_8Na$: 645.3107 [M+Na].

*4.2.4.8. (3S)-3-(2,3-Di-O-benzyl-4,6-O-benzylidene-β-D-glucopyranosyloxy)-4-pentenoic acid tert-butyl ester (**29**).* According to the synthesis of **22**, protection of **28** (295 mg, 0.474 mmol) gave **29** (259 mg, 0.430 mmol, 91%) as white solid from the crude product after flash column chromatography (hexane/AcOEt=12:1→8:1→4:1). R_f=0.29 (hexane/AcOEt=4:1); $[\alpha]_D^{25}$ −23.0 (c 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.52–7.22 (m, 15H, Ph–H), 5.73 (ddd, J=17.1, 10.3, 7.9 Hz, 1H, 4-H), 5.56 (s, 1H, –O$_2$CHPh), 5.34 (ddd, J=17.1, 1.5, 0.7 Hz, 1H, 5-H (trans)), 5.27 (ddd, J=10.3, 1.5, 0.7 Hz, 1H, 5-H (cis)), 4.89 (d, J=11.0 Hz, 1H, –CH_2Ph), 4.88 (d, J=11.0 Hz, 1H, –CH_2Ph), 4.78 (d, J=11.0 Hz, 1H, –CH_2Ph), 4.74 (d, J=11.0 Hz, 1H, –CH_2Ph), 4.61 (br ddd, J=7.9, 7.2, 6.9 Hz, 1H, 3-H), 4.60 (d, J=7.8 Hz, 1H, 1′-H), 4.35 (dd, J=10.4, 4.8 Hz, 1H, 6′-H), 3.77 (dd, J=10.4, 10.0 Hz, 1H, 6′-H), 3.72 (dd, J=9.1, 8.2 Hz, 1H, 3′-H), 3.66 (t, J=9.1 Hz, 1H, 4′-H), 3.45 (dd, J=8.2, 7.8 Hz, 1H, 2′-H), 3.37 (br ddd, J=10.0, 9.1, 4.8 Hz, 1H, 5′-H), 2.66 (dd, J=14.8, 6.9 Hz, 1H, 2-H), 2.47 (dd, J=14.8, 7.2 Hz, 1H, 2-H), 1.44 (s, 9H, –t-Bu); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 169.4 (C-1), 138.5, 138.3, 137.3, 136.1 (C-4), 128.9, 128.3, 128.2, 128.2, 128.0, 127.7, 127.6, 126.0, 119.3 (C-5), 101.1 (–O$_2$$C$HPh), 100.2 (C-1′), 81.9 (C-2′), 81.5 (C-4′), 80.9 (C-3′), 80.7 (–OC(CH$_3$)$_3$), 75.8 (C-3), 75.3 (–CH$_2$Ph), 75.1 (–CH$_2$Ph), 68.8 (C-6′), 65.9 (C-5′), 42.4 (C-2), 28.1 (–C(CH$_3$)$_3$); IR (KBr, cm^{-1}) ν: 2978, 2871, 1730, 1454, 1367, 1089; HRMS (FAB-pos, NBA matrix) m/z 625.2781 [M+Na]$^+$, calcd for $C_{36}H_{42}O_8Na$: 625.2777 [M+Na].

*4.2.4.9. (3S)-3-(2,3,4-Tri-O-benzyl-β-D-glucopyranosyloxy)-4-pentenoic acid tert-butyl ester (**30**).* According to the synthesis of **24**, reaction of **29** (1.60 g, 2.65 mmol) gave **30** (1.09 g, 1.80 mmol, 68%) as colorless oil from the crude product after flash column chromatography (hexane/AcOEt=8:1→6:1→4:1→3:1). R_f=0.32 (hexane/AcOEt=2:1); $[\alpha]_D^{25}$ +3.39 (c 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.20–7.10 (m, 15H, Ph–H), 5.60 (ddd, J=17.4, 10.1, 7.3 Hz, 1H, 4-H), 5.18 (dt, J=17.4, 1.0 Hz, 1H, 5-H (trans)), 5.18 (dt, J=10.1, 1.0 Hz, 1H, 5-H (cis)), 4.78 (d, J=11.0 Hz, 1H, –CH_2Ph), 4.77 (d, J=11.0 Hz, 1H, –CH_2Ph), 4.69 (d, J=11.0 Hz, 1H, –CH_2Ph), 4.63 (d, J=11.0 Hz, 1H, –CH_2Ph), 4.55 (d, J=11.0 Hz, 1H, –CH_2Ph), 4.50–4.41 (m, 1H, 3-H), 4.46 (d, J=11.0 Hz, 1H, –CH_2Ph), 4.35 (d, J=7.8 Hz, 1H, 1′-H), 3.70 (dd, J=11.7, 2.6 Hz, 1H, 6′-H), 3.53–3.45 (m, 1H, 3′-H), 3.50 (dd, J=11.7, 5.2 Hz, 1H, 6′-H), 3.37–3.24 (m, 2H, 2′-H, 4′-H), 3.19 (br ddd, J=7.1, 5.2, 2.6 Hz, 1H, 5′-H), 2.47 (dd, J=14.8, 7.5 Hz, 1H, 2-H), 2.30 (dd, J=14.8, 6.2 Hz, 1H, 2-H), 1.29 (s, 9H, –t-Bu); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 169.8 (C-1), 138.5, 138.3, 137.9, 136.2 (C-4), 128.4, 128.4, 128.3, 128.2, 128.0, 127.8, 118.6 (C-5), 100.1 (C-1′), 84.6 (C-3′), 82.2 (C-2′), 80.9 (–OC(CH$_3$)$_3$), 78.0 (C-4′), 75.9 (C-3), 75.7 (–CH$_2$Ph), 75.0 (C-5′), 74.9 (–CH$_2$Ph), 74.8 (–CH$_2$Ph), 62.3 (C-6′), 42.4 (C-2), 28.1 (–C(CH$_3$)$_3$); IR (KBr, cm^{-1}) ν: 3439, 2873, 1729, 1365, 1070; HRMS (FAB-pos, NBA matrix) m/z 627.2935 [M+Na]$^+$, calcd for $C_{36}H_{44}O_8Na$: 627.2934 [M+Na].

*4.2.4.10. (3S)-3-(2,3,4-Tri-O-benzyl-β-D-glucopyranosyloxy)-4-pentenoic acid (**31**).* According to the synthesis of **25**, reaction of **30** (1.75 g, 2.89 mmol) gave **31** (1.36 g, 2.48 mmol, 86%) as colorless oil from the crude product after flash column chromatography

(hexane/AcOEt/AcOH=40:10:1→30:10:1→20:10:1). R_f=0.13 (hexane/AcOEt/AcOH=15:10: 1); $[\alpha]_D^{25}$ +15.7 (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.40–7.17 (m, 15H, Ph–*H*), 5.80 (ddd, *J*=17.3, 10.4, 7.0 Hz, 1H, 4-H), 5.37 (dt, *J*=17.3, 1.0 Hz, 1H, 5-H (trans)), 5.24 (dt, *J*=10.4, 1.0 Hz, 1H, 5-H (cis)), 4.91 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.91 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.83 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.79 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.74–4.56 (m, 1H, 3-H), 4.70 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.60 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.52 (d, *J*=7.8 Hz, 1H, 1′-H), 3.87 (dd, *J*=11.9, 2.3 Hz, 1H, 6′-H), 3.66 (dd, *J*=11.9, 5.8 Hz, 1H, 6′-H), 3.65 (t, *J*=9.1 Hz, 1H, 3′-H), 3.49 (t, *J*=9.1 Hz, 1H, 4′-H), 3.43 (dd, *J*=9.7, 7.8 Hz, 1H, 2′-H), 3.35 (br ddd, *J*=9.1, 5.8, 2.3 Hz, 1H, 5′-H), 2.71 (dd, *J*=15.5, 8.5 Hz, 1H, 2-H), 2.58 (dd, *J*=15.5, 4.3 Hz, 1H, 2-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 174.9 (C-1), 138.5, 138.2, 137.9, 136.2 (C-4), 128.4, 128.3, 128.1, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 118.2 (C-5), 101.2 (C-1′), 84.6 (C-3′), 82.0 (C-2′), 77.6 (C-4′), 76.6 (C-3), 75.6 (–CH_2Ph), 75.0 (–CH_2Ph), 75.0 (–CH_2Ph), 75.0 (C-5′), 62.0 (C-6′), 41.2 (C-2); IR (KBr, cm^{-1}) ν: 3429, 3063, 3031, 2911, 1719, 1070; HRMS (FAB-pos, NBA matrix); *m*/*z* 571.2307 $[M+Na]^+$, calcd for $C_{32}H_{36}O_8Na$: 571.2308 [M+Na].

*4.2.4.11. (3R,3′R)-3-(2,3,4-Tri-O-benzyl-β-D-glucopyranosyloxy)-4-pentenoic acid bimol. cyclic ester (**32**).* To a suspension of **25** (50 mg, 0.0911 mmol) and MS4 Å (200 mg) in CH_2Cl_2 (1 mL) at ambient temperature was added DMC (39 mg, 0.228 mmol) in one portion. The reaction mixture was stirred for 20 h at ambient temperature. The resulting mixture was filtered through Celite, rinsed with CH_2Cl_2 (5 mL), and concentrated in vacuo. Purification of the residue by flash column chromatography (silica gel, hexane/AcOEt=6:1) afforded **32** (29.3 mg, 0.0276 mmol, 61%) as white solid. R_f=0.24 (hexane/AcOEt/AcOH=10:10:1); $[\alpha]_D^{24}$ +10.6 (*c* 0.30, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.34–7.08 (m, 30H, Ph-*H*), 5.76 (ddd, *J*=17.3, 10.4, 6.9 Hz, 2H, 4-H), 5.23 (d, *J*=17.3 Hz, 2H, 5-H (trans)), 5.10 (d, *J*=10.4 Hz, 2H, 5-H (cis)), 4.87 (d, *J*=11.0 Hz, 2H, –C*H*$_2$Ph), 4.80 (d, *J*=11.0 Hz, 2H, –C*H*$_2$Ph), 4.78 (d, *J*=11.0 Hz, 2H, –C*H*$_2$Ph), 4.71 (d, *J*=11.0 Hz, 2H, –C*H*$_2$Ph), 4.66–4.54 (m, 2H, 3-H), 4.62 (d, *J*=11.0 Hz, 2H, –C*H*$_2$Ph), 4.48 (d, *J*=11.0 Hz, 2H, –C*H*$_2$Ph), 4.48 (d, *J*=8.5 Hz, 2H, 1′-H), 4.29 (d, *J*=10.8 Hz, 2H, 6′-H), 3.76 (t, *J*=10.8 Hz, 2H, 6′-H), 3.66–3.52 (m, 4H, 3′-H, 5′-H), 3.41 (t, *J*=8.5 Hz, 2H, 2′-H), 3.24 (t, *J*=9.2 Hz, 2H, 4′-H), 2.92 (dd, *J*=13.3, 4.1 Hz, 2H, 2-H), 2.34 (dd, *J*=13.3, 11.6 Hz, 2H, 2-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 169.3 (C-1), 138.3, 138.0, 137.4, 135.8 (C-4), 128.5, 128.5, 128.4, 128.2, 128.1, 128.1, 127.9, 127.8, 127.7, 117.6 (C-5), 102.2 (C-1′), 84.7 (C-3′), 81.9 (C-2′), 78.2 (C-4′), 75.8 (–CH_2Ph), 75.1 (–CH_2Ph), 74.7 (C-3), 72.8 (C-5′), 64.9 (C-6′), 40.1 (C-2); IR (KBr, cm^{-1}) ν: 3031, 2901, 1739, 1068; HRMS (FAB-pos, NBA matrix) *m*/*z* 1083.4528 $[M+Na]^+$, calcd for $C_{64}H_{68}O_{14}Na$: 1083.4507 [M+Na].

*4.2.4.12. (3S,3′S)-3-(2,3,4-Tri-O-benzyl-β-D-glucopyranosyloxy)-4-pentenoic acid bimol. cyclic ester (**33**) and (3S)-3-(2,3,4-tri-O-benzyl-β-D-glucopyranosyloxy)-4-pentenolactone (**34**).* According to the synthesis of **25**, reaction of **31** (50 mg, 0.0911 mmol) gave **33** (20.4 mg, 0.0192 mmol, 42%) as white solid and **34** (13.4 mg, 0.0250 mmol, 28%) as colorless oil from the crude product after flash column chromatography (hexane/AcOEt=4:1).

Compound **33**: R_f=0.38 (hexane/AcOEt/AcOH=15:10:1); $[\alpha]_D^{25}$ +13.0 (*c* 0.30, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.37–7.22 (m, 30H, Ph–*H*), 5.70 (ddd, *J*=17.6, 9.8, 7.8 Hz, 2H, 4-H), 5.29 (br d, *J*=9.8, 2H, 5-H (cis)), 5.28 (br d, *J*=17.6 Hz, 2H, 5-H (trans)), 4.94 (d, *J*=11.0 Hz, 2H, –C*H*$_2$Ph), 4.92 (d, *J*=11.0 Hz, 2H, –C*H*$_2$Ph), 4.84 (d, *J*=11.0 Hz, 2H, –C*H*$_2$Ph), 4.78–4.66 (m, 2H, 3-H), 4.77 (d, *J*=11.0 Hz, 2H, –C*H*$_2$Ph), 4.71 (d, *J*=11.0 Hz, 2H, –C*H*$_2$Ph), 4.67 (dd, *J*=11.4, 1.9 Hz, 2H, 6′-H), 4.56 (d, *J*=11.0 Hz, 2H, –C*H*$_2$Ph), 4.48 (d, *J*=9.8 Hz, 2H, 1′-H), 3.76 (dd, *J*=11.4, 8.4 Hz, 2H, 6′-H), 3.65 (t, *J*=8.9 Hz, 2H, 3′-H), 3.46 (dd, *J*=8.9, 7.8 Hz, 2H, 2′-*H*), 3.43 (ddd, *J*=9.8, 8.4, 1.9 Hz, 2H, 5′-H), 3.34 (dd, *J*=9.8, 8.9 Hz, 2H, 4′-H), 2.90 (dd, *J*=15.0, 5.6 Hz, 2H, 2-H), 2.56 (dd, *J*=15.0, 9.1 Hz, 2H, 2-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 169.2 (C-1), 138.4, 138.2, 137.5, 136.2 (C-4), 128.5, 128.4, 128.4, 128.2, 128.2, 128.0, 127.8, 127.8, 127.7, 119.5 (C-5), 99.9 (C-1′), 84.6 (C-3′), 82.0 (C-2′), 78.1 (C-4′), 75.7 (C-3), 75.1 (–CH_2Ph), 75.1 (–CH_2Ph), 75.0 (–CH_2Ph), 72.9 (C-5′), 63.9 (C-6′), 41.6 (C-2); IR (KBr, cm^{-1}) ν: 3031, 2919, 1734, 1068; HRMS (FAB-pos, NBA matrix); *m*/*z* 1083.4513 $[M+Na]^+$, calcd for $C_{64}H_{68}O_{14}Na$: 1083.4507 [M+Na].

Compound **34**: R_f=0.47 (hexane/AcOEt/AcOH=15:10:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.37–7.25 (m, 15H, Ph–*H*), 5.84 (ddd, *J*=17.2, 10.4, 5.1 Hz, 1H, 4-H), 5.28 (dt, *J*=17.2, 1.5 Hz, 1H, 5-H (trans)), 5.17 (dt, *J*=10.4, 1.5 Hz, 1H, 5-H (cis)), 4.94 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.92 (dd, *J*=11.9, 3.2 Hz, 1H, 6′-H), 4.83 (s, 1H, 1′-H), 4.74–4.70 (m, 2H, –C*H*$_2$Ph), 4.67 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.60 (d, *J*=11.7 Hz, 1H, –C*H*$_2$Ph), 4.51 (d, *J*=11.7 Hz, 1H, –C*H*$_2$Ph), 4.33–4.23 (m, 1H, 3-H), 4.27 (t, *J*=10.1 Hz, 1H, 4′-H), 4.00 (d, *J*=11.9 Hz, 1H, 6′-H), 3.84 (d, *J*=4.3 Hz, 1H, 2′-*H*), 3.79 (dd, *J*=10.1, 3.2 Hz, 1H, 5′-H), 3.73 (dd, *J*=10.1, 4.3 Hz, 1H, 3′-H), 2.57 (dd, *J*=11.6, 10.8 Hz, 1H, 2-H), 2.49 (dd, *J*=11.6, 2.9 Hz, 1H, 2-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 173.7 (C-1), 138.2, 138.1, 137.4 (C-4), 137.3, 128.5, 128.4, 128.3, 128.1, 128.0, 127.9, 127.8, 127.8, 127.6, 115.3 (C-5), 101.8 (C-1′), 84.4 (C-2′), 83.6 (C-3′), 80.3 (C-3), 76.3 (C-5′), 75.2 (–CH_2Ph), 73.5 (C-4′), 73.3 (–CH_2Ph), 71.7 (–CH_2Ph), 63.3 (C-6′), 43.3 (C-2); HRMS (FAB-pos, NBA matrix); *m*/*z* 553.2203 $[M+Na]^+$, calcd for $C_{32}H_{34}O_7Na$: 553.2202 [M+Na].

*4.2.5. After the cyclization. 4.2.5.1. (3S,3′S)-3-(β-D-Glucopyranosyloxy)-4-pentanoic acid bimol. cyclic ester (**35**).* A solution of **32** (14.0 mg, 0.0132 mmol) in AcOEt (2 mL) and EtOH (4 mL) was treated with 10 wt% palladium on activated carbon (18.0 mg). The reaction flask was flushed with air and hydrogen atmospheres sequentially. The reaction mixture was then placed under an atmosphere of hydrogen and stirred for 24 h. The heterogeneous mixture was filtered through Celite, rinsed with MeOH (10 mL), and concentrated in vacuo. Purification of the residue by flash column chromatography (silica gel, $CHCl_3$/MeOH=7:1) afforded **35** (9.6 mg, 0.0183 mmol, quant.) as white solid. R_f=0.17 ($CHCl_3$/MeOH=3:1); $[\alpha]_D^{26}$ +3.56 (*c* 0.33, MeOH); ^{1}H NMR (300 MHz, CD_3OD) δ: 4.43 (dd, *J*=11.4, 1.6 Hz, 2H, 6′-H), 4.36 (d, *J*=7.8 Hz, 1H, 1′-H), 4.15 (br ddd, *J*=11.0, 7.6, 3.8 Hz, 2H, 3-H), 3.95 (dd, *J*=11.4, 10.0 Hz, 2H, 6′-H), 3.55 (dt, *J*=10.0, 1.6 Hz, 2H, 5′-H), 3.38 (t, *J*=9.1 Hz, 2H, 3′-H), 3.19 (dd, *J*=9.1, 7.8 Hz, 2H, 2′-H), 3.16 (dd, *J*=10.0, 9.1 Hz, 2H, 4′-H), 2.93 (dd, *J*=13.9, 3.8 Hz, 2H, 2-H), 2.34 (dd, *J*=13.9, 11.0 Hz, 2H, 2-H), 1.67–1.43 (m, 4H, 4-H), 0.93 (t, *J*=7.3 Hz, 6H, 5-H); ^{13}C NMR (75 MHz, CD_3OD) δ: 172.3 (C-1), 101.0 (C-1′), 78.1 (C-3′), 75.5 (C-3), 75.1 (C-5′), 74.9 (C-2′), 72.4 (C-4′), 66.5 (C-6′), 40.6 (C-2), 29.0 (C-4), 9.8 (C-5); IR (KBr, cm^{-1}) ν: 3401,2925,1727;HRMS (FAB-pos, NBA+DTT matrix) *m*/*z* 547.2017 $[M+Na]^+$, calcd for $C_{22}H_{36}O_{14}Na$: 547.2003 [M+Na].

*4.2.5.2. (3R,3′R)-3-(β-D-Glucopyranosyloxy)-4-pentanoic acid bimol. cyclic ester (**36**).* According to the synthesis of **32**, deprotection of **33** (19.0 mg, 0.0179 mmol) gave **36** (10.8 mg, 0.0206 mmol, quant.) as white solid from the crude product after flash column chromatography ($CHCl_3$/MeOH=7:1). R_f=0.50 ($CHCl_3$/MeOH=3:1); $[\alpha]_D^{23}$ +9.39 (*c* 0.50, MeOH); ^{1}H NMR (300 MHz, CD_3OD) δ: 4.44 (dd, *J*=11.7, 2.1 Hz, 2H, 6′-H), 4.35 (d, *J*=7.8 Hz, 1H, 1′-H), 4.01 (dd, *J*=11.7, 7.4 Hz, 2H, 6′-H), 3.99–3.89 (m, 2H, 3-H), 3.47 (ddd, *J*=9.5, 7.4, 2.1 Hz, 2H, 5′-H), 3.36 (t, *J*=8.9 Hz, 2H, 3′-H), 3.24 (dd, *J*=9.5, 8.9 Hz, 2H, 4′-H), 3.18 (dd, *J*=8.9, 7.8 Hz, 2H, 2′-H), 2.96 (dd, *J*=15.5, 5.3 Hz, 2H, 2-H), 2.46 (dd, *J*=15.5, 7.5 Hz, 2H, 2-H), 1.67–1.53 (m, 4H, 4-H), 1.01 (t, *J*=7.5 Hz, 6H, 5-H); ^{13}C NMR (75 MHz, CD_3OD) δ: 173.2 (C-1), 105.7 (C-1′), 80.7 (C-3), 77.8 (C-3′), 75.1 (C-2′), 74.6 (C-5′), 71.9 (C-4′), 65.4 (C-6′), 42.3 (C-2), 29.1 (C-4), 10.1 (C-5); IR (KBr, cm^{-1}) ν: 3422,2925,1736; HRMS (FAB-pos, NBA+DTT matrix) *m*/*z* 547.1995 $[M+Na]^+$, calcd for $C_{22}H_{36}O_{14}Na$: 547.2003 [M+Na].

*4.2.5.3. (3S,3′S)-3-(β-D-Glucopyranosyloxy)-4-heptanoic acid bimol. cyclic ester (**38**).* To a solution of **32** (10.4 mg, 9.80 μmol) in CH_2Cl_2 (1.6 mL) were added *trans*-3-hexene (12.2 μL, 0.0980 mmol) and Grubbs second generation catalyst (1.7 mg, 0.196 μmol). The reaction mixture was stirred at 40 °C for 4 days, while *trans*-3-hexene (12.2 μL, 0.0980 mmol) and Grubbs second generation catalyst (1.7 mg, 0.196 μmol) were added each 24 h. The resulting mixture was concentrated in vacuo. Purification of the residue by flash column chromatography (silica gel, hexane/AcOEt=8:1→6:1) afforded **37** (9.7 mg, 0.00868 mmol, 89%) as white solid.

A solution of **37** (9.5 mg, 8.50 μmol) in AcOEt (1 mL) and EtOH (2 mL) was treated with 10 wt % palladium on activated carbon (10.0 mg). The reaction flask was flushed with air and hydrogen atmospheres sequentially. The reaction mixture was then placed under an atmosphere of hydrogen and stirred for 24 h. The heterogeneous mixture was filtered through Celite, rinsed with MeOH (10 mL), and concentrated in vacuo. Purification of the residue by flash column chromatography (silica gel, $CHCl_3$/MeOH=7:1) afforded **38** (4.5 mg, 7.75 μmol, 91%) as yellow solid. R_f=0.29 ($CHCl_3$/MeOH=3:1); $[\alpha]_D^{26}$ +2.47 (*c* 0.23, MeOH); ^{1}H NMR (300 MHz, CD_3OD) δ: 4.48 (dd, *J*=11.6, 1.6 Hz, 2H, 6′-H), 4.37 (d, *J*=7.8 Hz, 1H, 1′-H), 4.28–4.16 (m, 2H, 3-H), 3.93 (dd, *J*=11.6, 9.8 Hz, 2H, 6′-H), 3.53 (dt, *J*=9.8, 1.6 Hz, 2H, 5′-H), 3.38 (t, *J*=8.9 Hz, 2H, 3′-H), 3.18 (dd, *J*=8.9, 7.8 Hz, 2H, 2′-H), 3.16 (dd, *J*=9.8, 8.9 Hz, 2H, 4′-H), 2.93 (dd, *J*=13.8, 4.0 Hz, 2H, 2-H), 2.34 (dd, *J*=13.8, 10.7 Hz, 2H, 2-H), 1.59–1.43 (m, 4H, 4-H), 1.40–1.18 (m, 8H, 5-H, 6-H), 0.96–0.82 (m, 6H, 7-H); ^{13}C NMR (75 MHz, CD_3OD) δ: 172.3 (C-1), 100.8 (C-1′), 78.2 (C-3′), 75.3 (C-5′), 75.0 (C-2′), 74.1 (C-3), 72.3 (C-4′), 66.5 (C-6′), 40.7 (C-2), 36.2 (C-4), 30.8 (C-5), 30.8 (C-6), 14.4 (C-7); IR (KBr, cm^{-1}) ν: 3423,2958,2925,2855,1737,1082; HRMS (FAB-pos, NBA matrix) *m/z* 603.2636 $[M+Na]^+$, calcd for $C_{26}H_{44}O_{14}Na$: 603.2629 [M+Na].

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2010.04.007. This data include MOL files and InChIKeys of the most important compounds described in this article.

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