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Vinyl Grignard-mediated Stereoselective Carbocyclization of Lactone Acetals

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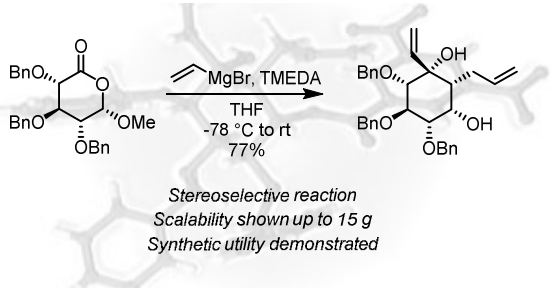


Abstract

A novel Ferrier-type carbocyclization is reported. It involves a carbohydrate-derived lactone acetal synthesized from methyl α-D-glucopyranoside, which upon treatment with excess vinylmagnesium bromide provides a highly substituted carbocyclic product as a single stereoisomer. The yield is greatly increased when *N,N,N',N'*-tetramethylethylenediamine is added to the reaction mixture. Optimized reaction conditions have been applied to lactone acetals derived from other carbohydrates. Based on the obtained results, a possible reaction mechanism has been proposed. Furthermore, scalability of the reaction up to 15 g scale and derivatization of the carbocyclic product has been demonstrated, including the formation of a rare *trans*-bicyclo[4.3.0]nonene scaffold via a ring-closing metathesis. The structure of this and all carbocyclized products were confirmed by X-ray crystallographic analysis.

Introduction

Carbasugars are stable analogues of carbohydrates where the endocyclic oxygen has been replaced with a carbon atom. These highly oxygenated alicyclic molecules form the central scaffold of various natural and synthetic products of biological importance.[1] Many methods have been adopted towards the synthesis of carbasugars from carbohydrates[2-5] or non-carbohydrate precursors.[6-8] Generally, utilization of carbohydrates from the natural chiral pool for synthesis of complex enantiopure compounds have shown many advantages.[9-12] The classical approach for assembling carbacycles from carbohydrate precursors exploits the well-known Ferrier carbocyclization (or

Ferrier II reaction) using an exo-glycal derived from a carbohydrate precursor (Scheme 1a).[13-16] Originally, the reaction proceeds in aqueous acetone with stoichiometric $HgCl_2$ but other conditions have been implemented to provide the β-hydroxy-cyclohexanone **2**.[17-19] This reaction remains a valuable tool for creating a highly functionalized cyclohexane framework.[20-22]

Scheme 1. **Ferrier carbocyclization and newly found carbocyclization**

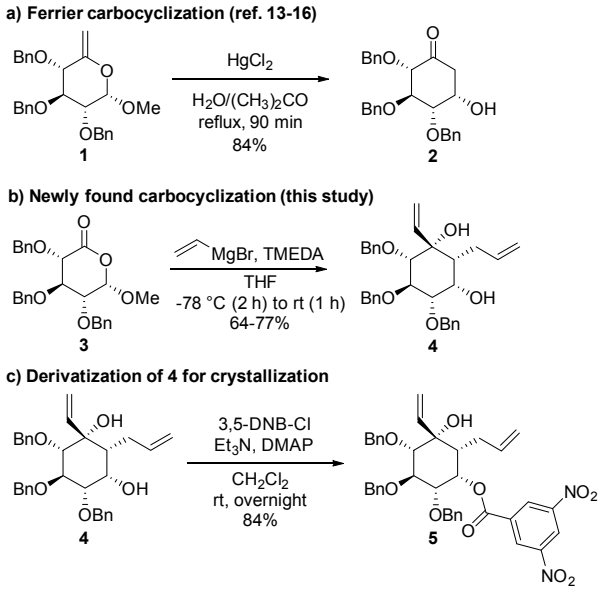
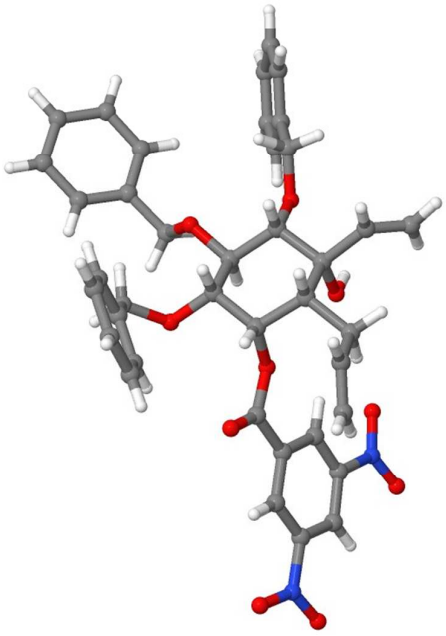


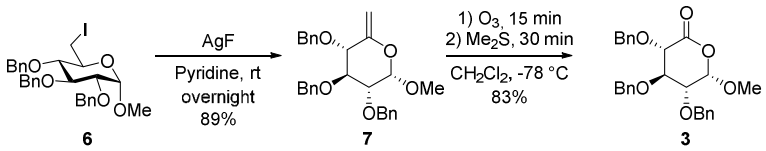
Figure 1. Molecular structure of 5



Results and Discussion

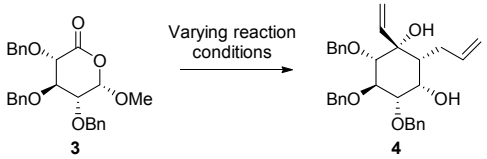
We recently discovered a novel reaction, which can be considered a variety of the Ferrier carbocyclization, where a lactone acetal **3** (or pseudolactone[23]) upon treatment with vinylmagnesium bromide resulted in the carbocyclic product **4** as the only stereoisomer (Scheme 1b). We have studied this reaction in detail and in this paper, we report on our findings. First, the structure and stereochemistry of the carbocyclic product **4** was confirmed by single crystal X-ray crystallographic analysis of the crystalline 3,5-dinitrobenzoyl (3,5-DNB) derivative **5** (Scheme 1c and Figure 1). The lactone acetal starting material for the carbocyclization **3** was prepared from the known iodide **6** by elimination followed by ozonolysis of the resulting exo-cyclic double bond (Scheme 2).[24,25] The elimination step from this iodide has been reported several times with different bases including *t*-BuOK, NaH and DBU,[16,19,26] but in our hands satisfactory and reproducible results were only achieved with AgF in pyridine.

Scheme 2. Synthesis of the substrate 3 from primary iodide 6



To explore this new type of carbocyclization, the influence on product yield by varying reaction conditions was explored (Table 1). Excess Grignard reagent was added as a commercial 1 M solution in THF and THF, Et_2O and toluene were tested as co-solvents (entry 1-3). As the most coordinating solvent, THF provided the best initial result. *N,N,N',N'*-Tetramethylethylenediamine (TMEDA) was added to the reaction mixture and was found to result in a large increase in yield independent of the co-solvent (entries 4-6). Omitting the co-solvent and simply conducting the reaction in the commercial THF solution of vinylmagnesium bromide further increased the yield slightly (entry 7). The reaction was furthermore carried out at different temperatures and with varying amounts of both vinylmagnesium bromide and TMEDA establishing the conditions in entry 7 with 9 equivalents of Grignard reagent (of which 3 is consumed in the reaction) and 1.2 equivalents of TMEDA per Grignard reagent going from -78 °C to rt as the optimal conditions. The results in Table 1 were all obtained on a 300 mg scale and up-scaling of the reaction was found to have a beneficial effect on the reaction yield as 64% of the carbocyclic product **4** was achieved on this scale while 70% was achieved on 1 g scale and 77% on 15 g scale.

Table 1. **Optimization of reaction conditions**

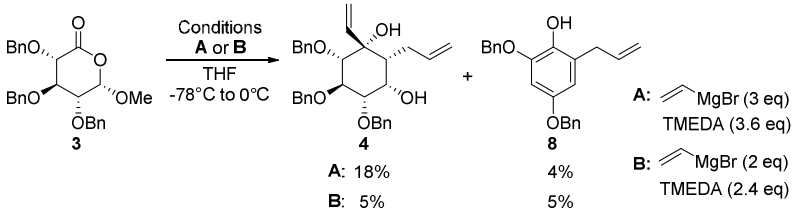


Entry	Grignard/TMEDA[a]	Temp. (°C)[b]	Additive	Yield[c]
1	9/-	-78 to rt	THF	34%
2	9/-	-78 to rt	Et_2O	25%
3	9/-	-78 to rt	Toluene	26%
4	9/1.2	-78 to rt	THF	60%
5	9/1.2	-78 to rt	Et_2O	57%
6	9/1.2	-78 to rt	Toluene	60%
7	**9/1.2**	**-78 to rt**	**-**	**64%**
8	9/0.6	-78 to rt	-	55%
9	9/2.4	-78 to rt	-	62%
10	6/1.2	-78 to rt	-	52%
11	9/1.2	0 to rt	-	28%
12	9/1.2	-78 to -35[d]	-	46%
13	9/1.2	-78 to rt[e]	-	40%
14	9/-	-78 to rt	CuCN· 2LiCl	14%

[a]Equiv. vinylMgBr compared to **3** and equiv. TMEDA compared to vinylMgBr. [b]Unless other is stated, the reaction was stirred at -78 °C for 2 h followed by 1 h at rt. [c]Isolated yield in comparison to the amount of **3**. [d]6 h at -78 °C. [e]6 h at -78 °C, then rt overnight.

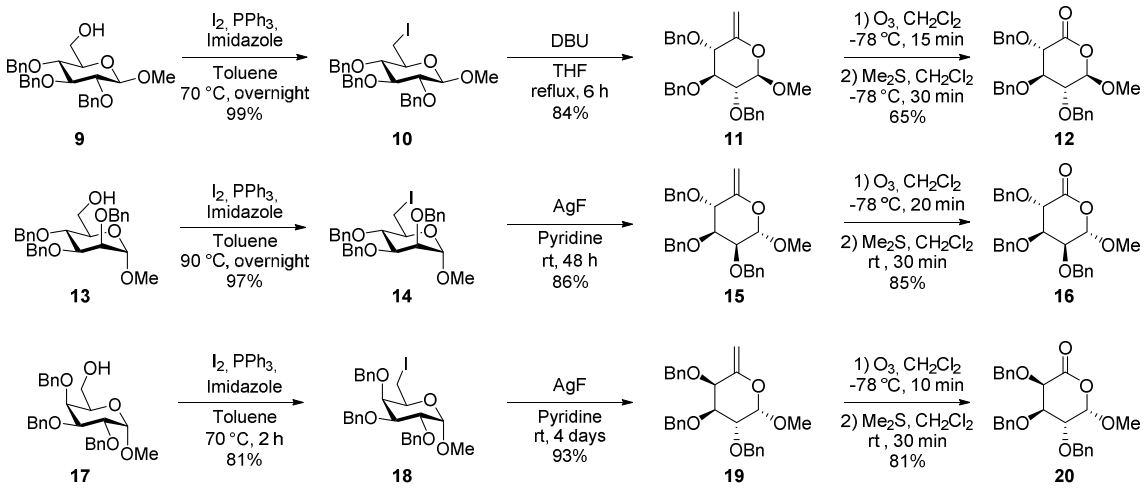
To investigate the reaction efficiency and to potentially isolate reaction intermediates, lactone acetal **3** was treated with a lower amount of Grignard reagent. The amount of TMEDA was maintained at 1.2 equivalents per Grignard reagent. When 2 or 3 equivalents of Grignard reagent were used, the carbocyclic product **4** was obtained in 5% and 18% yield, respectively. The only other product that could be isolated was the aromatized product **8** (Scheme 3), that was obtained in yields of 4% and 5%, respectively.

Scheme 3. Formation of aromatized compound 8 with lower amounts of Grignard reagent



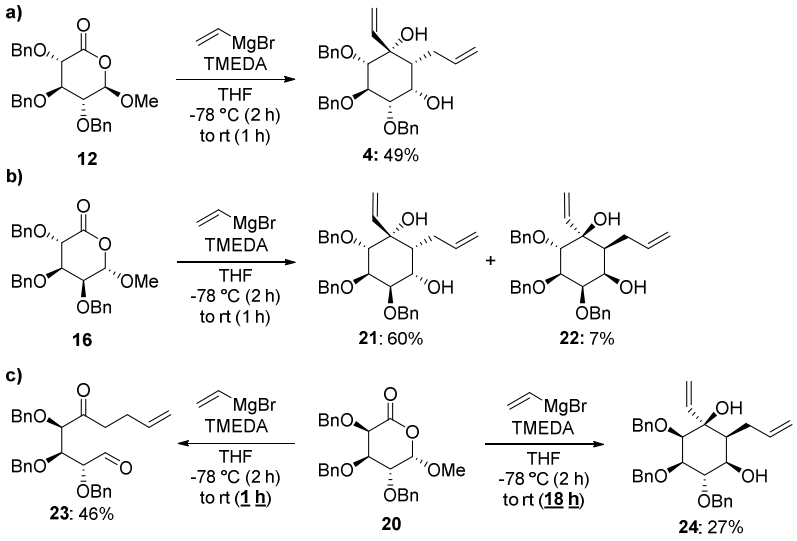
Next, it was chosen to investigate whether other carbohydrate-derived lactone acetals would undergo the newly discovered reaction. Therefore, the anomeric epimer of **3** (**12**) and lactone acetals derived from D-mannose (**16**) and D-galactose (**20**) were synthesized (Scheme 4). The syntheses resembles the synthesis of **3**, starting with conversion of the free alcohol into the iodide followed by elimination and ozonolysis.[4,27,28]

Scheme 4. Synthesis of substrates 12, 16 and 20



It was first shown that **12** underwent the same reaction as **3** to give **4**, albeit in a slightly diminished yield of 49% (Scheme 5a). The D-mannose-derived lactone acetal **16** afforded a combined yield of 67% of carbocyclic products with the same relative orientation of the substituents on the new stereocenters with the major product **21** resembling the original product **4** derived from D-glucose (Scheme 5b).

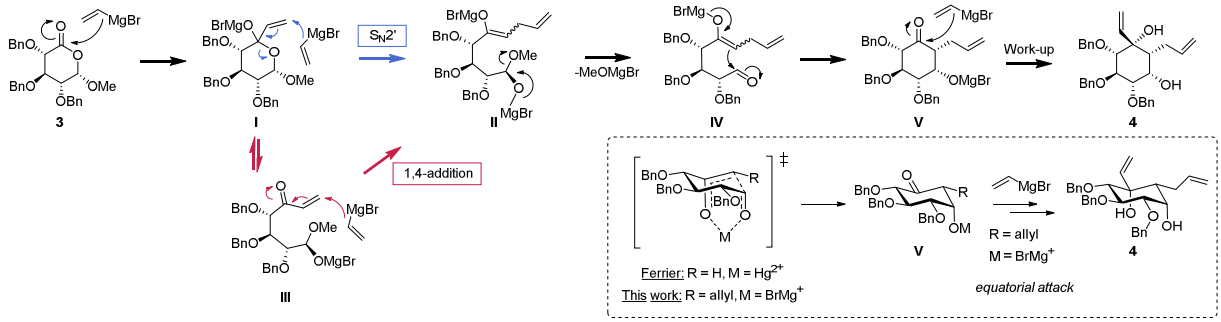
Scheme 5. Carbocyclization from other substrates



When the reaction conditions were applied to the substrate derived from D-galactose **20** a prolonged reaction time at room temperature was found to be required to obtain the carbocyclic product. Reaction for just 1 h at ambient temperature resulted in open-chain compound **23** containing an aldehyde functionality, while prolonging the reaction time increased the yield of carbocyclic product **24** to 27%. The new stereocenters of **24** were all found to have the opposite stereochemistry compared to the original product **4**. The stereochemistry of the carbocyclic products **21**, **22** and **24** was also determined by X-ray crystallographic analysis. Compound **21** was crystallized without any need for derivatization in contrast to the compounds **22** and **24**, which were crystallized as their camphanic acid ester derivatives (Supporting Information).

Based on the above-mentioned results and inspired by the mechanism suggested by Valéry and co-workers for their addition of two equivalents of vinylmagnesium bromide to a glucono-1,5-lactone,[29] we envisage the reaction to occur through either of the following two mechanisms via a S_N2' reaction or a 1,4-addition (Scheme 6).

Scheme 6. Suggested mechanism and reasoning for stereochemical outcome



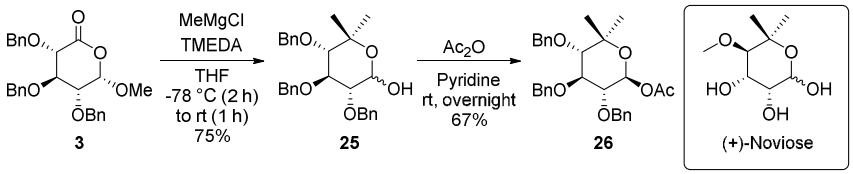
Addition of the first equivalent of vinylmagnesium bromide to the carbonyl carbon gives the tetrahedral intermediate **I**. This intermediate can then either react with another equivalent of vinylmagnesium bromide in an S_N2' reaction to give the open-chain intermediate **II** (blue arrows)**,** or the Grignard reagent can attack the unsaturated carbonyl of the open-chain intermediate **III** in a 1,4-addition (red arrows) giving the same intermediate **II**. After revealing the aldehyde functionality of **IV**, an intramolecular aldol reaction can occur with attack of the enolate onto the aldehyde. Surprisingly, the aldehyde of **IV** is not attacked by the Grignard reagent in solution, but instead participates in the ring-closing aldol step. The isolation of **23** from the D-galactose-derived substrate **20** confirms the existence of intermediate **II** and/or **IV** in the reaction pathway. After ring-closing another molecule of vinylmagnesium bromide can attack the ketone to give the observed product **4** after acidic work-up. Given the proposed involvement of either a Michael addition or S_N2' reaction of vinyl-MgBr, CuCN·2LiCl known to promote conjugate addition of Grignard reagents was explored as an additive without success (Table 1, Entry 14).[30]

For the Ferrier carbocyclization it is believed that the stereochemistry of the β-carbon of the cyclohexanone is determined by a coordination between the mercuric ion and the two oxygen atoms from the resulting hydroxy and carbonyl group, respectively (Scheme 6 (box)). This belief has been substantiated by literature examples where substrates that would adopt one chair conformation gives the opposite stereochemistry at this carbon compared to substrates that would adopt the other possible chair conformation in the transition state.[15,19,31] The stereochemical outcome of the newly discovered reaction on the substrate **4** can also be explained from the coordination of the magnesium ion to two of the oxygens in the transition state of the cyclization step (Scheme 6 (box)) where the chair conformation with the three benzyl ethers and the allyl group in equatorial positions

is adopted. Attack of the last equivalent of vinylmagnesium bromide from the least hindered equatorial trajectory sets the final stereocenter. It is interesting to notice that for all carbocyclic products obtained from different lactone acetals the substituents on the new stereocenters were found to have the same relative orientation providing some evidence for the proposed transition state in Scheme 6 with coordination of the magnesium ion. Changing the stereochemistry of one stereocenter neighboring the acetal functionality, as with the D-mannose-derived substrate **16,** probably causes the two possible chair conformations in the transition state to become closer in energy due to one of the substituents changing from an equatorial to axial orientation. This enables the formation of two diastereomeric carbocyclic products which is also seen by the formation of both compound **21** and **22** (Scheme 5b). Surprisingly, changing the stereochemistry of the carbon center next to the carbonyl, as in the substrate **20** derived from D-galactose, has a major influence on the reaction outcome as both the opposite diastereomer compared to the original reaction is isolated and the reaction yield is greatly diminished.

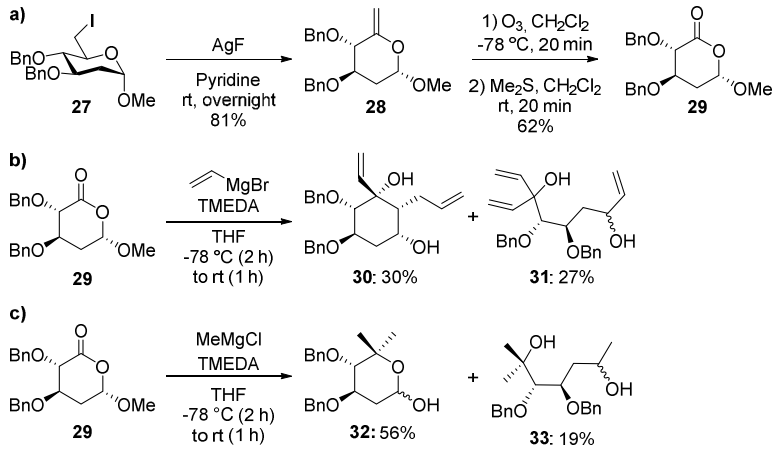
Still enticed by the reaction, it was decided to explore the outcome of treatment of **3** with other Grignard reagents like MeMgCl. The product of the reaction of **3** with MeMgCl was found to be the hemiacetal **25** (Scheme 7), which is a stereoisomeric analogue of the natural compound (+)-noviose, being a carbohydrate fragment of the naturally occurring antitumor agent novobiocin.[32-34] For easier purification and identification, hemiacetal **25** was acetylated to give **26** as a single isomer. Even though a carbocyclic product is not seen with the methyl Grignard reagent, this reaction has some similarity to the carbocyclization as the product hemiacetal is not attacked by excess methylmagnesium chloride. It was surprising to us that the aldehyde functionality of intermediate **IV** (Scheme 6) and hemiacetal of **25** (Scheme 7) was not attacked by Grignard reagent in solution. A reason for this could be a stabilized hemiacetal (intermediate **II**, Scheme 6) through coordination of magnesium to the neighboring ether oxygen. Also, due to the presence of a neighboring electron withdrawing ether functional group, intermediate **II** could have a diminished tendency to expel MeOMgBr and thereby reveal a strongly electron deficient and highly reactive aldehyde.[35]

Scheme 7. Reaction with MeMgCl



For further investigation of this hypothesis, a substrate derived from 2-deoxy-D-glucose **29** was synthesized and subjected to the carbocylization conditions (Scheme 8a-b).[36] From this lactone acetal a cyclized product **30** was obtained in 30% yield with a stereochemical outcome resembling that obtained from the D-glucose-derived starting material **3**. The stereochemistry of this compound was again determined by X-ray crystallographic analysis of the camphanic acid ester derivative (Supporting Information). Additionally, an open-chain compound **31** was isolated in 27% yield. The formation of **31** is proposed to occur through a mechanism that includes the same initial attack of Grignard reagent to the carbonyl as proposed in Scheme 6. After ring-opening, the aldehyde is revealed and attacked by another Grignard reagent and eventually **31** is obtained after a 1,2-addition to the ketone. Products of this type was not found for derivatives **3, 12, 16** and **20** with a benzyl ether flanking the aldehyde carbon atom.

Scheme 8. a) Synthesis of lactone acetal 29 b) Carbocyclization of 29 c) Reaction of 29 with MeMgCl



Lactone acetal **29** was also reacted with the methyl Grignard reagent (Scheme 8c). Again, a hemiacetal **32** resembling **25** was obtained but also the open-chain compound **33** was isolated, analogously to the result obtained from the reaction between **29** and vinylmagnesium bromide. These results with both methyl- and vinyl Grignard reagents support our hypothesis that the ether group next to the acetal is important for the reactivity of the intermediate hemiacetal/aldehyde.

To demonstrate the synthetic utility of these carbocyclic products, a route for further derivatization was pursued for the carbocyclic product **4**. We investigated whether the diene would undergo ring-

closing metathesis (RCM) (Scheme 9). This transformation could be challenging as the product is a five-membered ring *trans*-fused to a six-membered ring, which could imply some ring strain. However, **34** was indeed obtained in 68% yield with the Hoveyda-Grubbs (HG) 2nd generation catalyst. The structure of **34** was confirmed by X-ray crystallographic analysis (Figure 2). The double bond could subsequently be dihydroxylated with catalytic osmium tetroxide and *N*-methylmorpholine *N*-oxide (NMO) in a yield of 74%. The expected *anti*-addition to the cyclic allylic alcohol was rationalized by the $^{3}J_{HH}$ coupling constants and 1D-ROESY experiments (Supporting Information).[37-38] The bicyclic system with a six-membered ring *trans*-fused to a five-membered ring is a motif well-known as the C- and D-ring of steroids including examples such as cholesterol, testosterone and estradiol. Furthermore, **35** resembles a group of polyhydroxylated bicyclic compound compounds which have shown activity as glucosidase inhibitors.[39-40] Further exploration of these highly substituted carbocyclic compound in the synthesis of potential glycosidase inhibitors is currently ongoing in our group.

Scheme 9. Derivatization of carbocyclic product

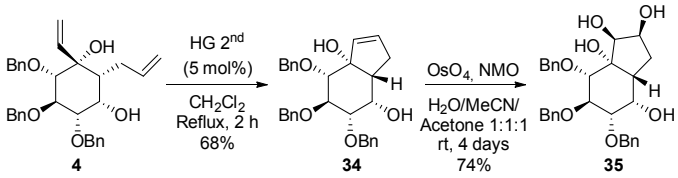
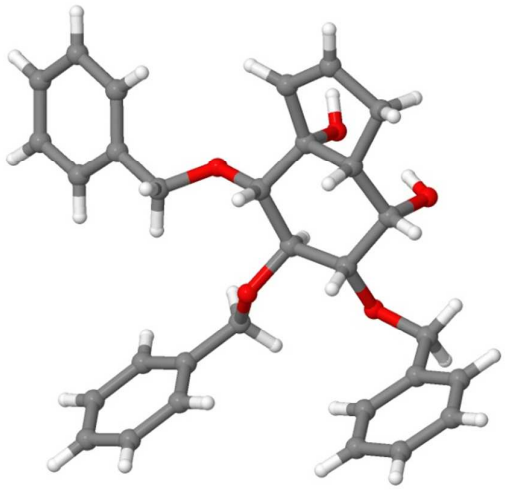


Figure 2. Molecular structure of 34



Conclusion

In conclusion, a novel type of carbocyclization has been presented and a mechanism proposed. The reaction was found to be operationally straightforward even on large scale and was applied to substrates of varying stereochemistry and substituents. The structures of carbocyclic molecules were verified by X-ray crystallographic analysis. The transformation of lactone acetals into highly substituted carbocyclic structures makes it possible to obtain more complex molecules than e.g. with the Ferrier carbocyclization and have the potential to be a key reaction for the synthesis of new biological relevant compounds. Furthermore, it circumvents the use of the toxic mercury salts which is used for the Ferrier carbocyclization.

Experimental Section

General

All reagents were except otherwise stated used as purchased without further purification. All reactions with air- and moisture sensitive compounds were conducted in flame-dried glassware under an atmosphere of nitrogen or argon. CH_2Cl_2, THF, MeCN and toluene were dried over aluminium oxide via a solvent purification system. Pyridine was dried over molecular sieves. DMF was purchased as anhydrous. Flash column chromatography was carried out either with a silica gel 60 Å pore size, 230-400 mesh particle size or a silica gel 60 (0.015-0.040 mm). TLC-analysis was carried out on silica gel on aluminum foil (Kieselgel 60, F254). The TLC-plates were observed under UV-light or visualized by using C-mol stain (cerium(IV) sulfate and ammonium molybdate in 10% sulfuric acid) or $KMnO_4$ stain ($KMnO_4$ and NaOH in H_2O) and heating to dryness. ^{1}H-, gCOSY- and gHMQC-NMR were recorded at 400 MHz and ^{13}C-NMR and DEPT-135 at 100 MHz. Signals from $CDCl_3$ (δ 7.26 ppm for proton and δ 77.16 ppm for carbon) and C_6D_6 (δ 7.16 ppm for proton and δ 128.06 ppm for carbon) were used as internal references. Assignment of NMR-spectra is based on gCOSY-, gHMQC- and DEPT-135 techniques. 1D-ROESY experiments (SI) were conducted with a 500 MHz NMR spectrometer equipped with a 5mm ^{1}H-^{13}C-^{15}N TXI probe. Mass spectra were recorded on a MicroTOF-Q High Performance LC-MS system. Melting points are uncorrected. Optical rotations are given in deg*cm^2*g^{-1} and concentrations are given in g/100 mL.

(3*S*,4*R*,5*R*,6*S*)-3,4,5-Tris(benzyloxy)-6-methoxytetrahydro-2*H*-pyran-2-one (3)

7 (2.555 g, 5.72 mmol) was dissolved in dry CH_2Cl_2 (125 mL). The solution was cooled to -78 °C. O_2 was bubbled through the solution for 5 min followed by O_3 for 15 min until the solution turned light blue. O_2 was then again bubbled through the solution for 5 min followed by nitrogen for

5 min. Me_2S (0.85 mL, 11.4 mmol, 2 eq) was added to the solution at -78 °C. The mixture was stirred for 30 min while being allowed to reach rt. The reaction mixture was concentrated under reduced pressure and subsequently purified by flash column chromatography (CH_2Cl_2) to afford **3** (2.121 g, 4.73 mmol, 83%) as a white solid. R_f (CH_2Cl_2) 0.36. $[\alpha]_D^{299K}$ -46.5 (*c* 0.4, $CHCl_3$). Mp 92.1-94.3 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.47-7.22 (m, 15H, Ar*H*), 5.09 (d, J_{gem} 11.2 Hz, 1H, C*H*HPh), 4.98 (d, $J_{6,5}$ 2.5 Hz, 1H, H6), 4.82 (d, J_{gem} 12.1 Hz, 1H, C*H*HPh), 4.75 (s, 2H, CH_2Ph), 4.73 (d, J_{gem} 11.2 Hz, 1H, CH*H*Ph), 4.72 (d, J_{gem} 12.1 Hz, 1H, CH*H*Ph), 4.15 (t, $J_{4,3/5}$ 7.9 Hz, 1H, H4), 4.03 (d, 1H, H3), 3.74 (dd, 1H, H5), 3.55 (s, 3H, *C*H_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 169.9 (*C*=O, C2), 138.0, 137.6, 137.3 (Ar*C*), 128.7-128.0 (Ar*C*H), 100.7 (C6), 79.3 (C3), 78.8 (C4), 76.8 (C5), 74.9, 74.4, 73.8 (*C*H_2Ph), 57.5 (*C*H_3). HRMS(ESI): Calcd. for $C_{27}H_{28}O_6Na^+$ m/z 471.1778; found m/z 471.1783. NMR-data were in accordance with previously reported data.[41]

General procedure for carbocyclization

For the optimization of the reaction conditions, the following procedure was followed with varying amounts of vinylmagnesium bromide and TMEDA and at varying temperatures. When a co-solvent was used, it was added to the starting material **3** before the addition of any other reagents. When CuCN*2LiCl was used, it was premixed with the Grignard reagent in the place of TMEDA. The vinylmagnesium bromide was purchased as a 1 M solution in THF. However, it was titrated to a concentration of 0.9 M.[42]

(1*R*,2*R*,3*S*,4*S*,5*R*,6*S*)-2-Allyl-4,5,6-tris(benzyloxy)-1-vinylcyclohexane-1,3-diol (4)

Vinylmagnesium bromide (0.9 M in THF, 6.7 mL, 6.0 mmol, 9 eq) and TMEDA (1.1 mL, 7.4 mmol, 11 eq) were mixed at rt and added to **3** (0.299 g, 0.67 mmol) at -78 °C. The mixture was stirred at -78 °C for 2 h and was then allowed to reach rt. It was stirred at this temperature for 1 h before being quenched with water and 1 M aq. HCl. The solution was extracted with CH_2Cl_2 (x3). The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (CH_2Cl_2/EtOAc 100:1 → 25:1) to give **4** (0.215 g, 0.43 mmol, 64%) as a colorless oil. R_f (CH_2Cl_2/EtOAc 20:1) 0.67. $[\alpha]_D^{293K}$ -52.2 (*c* 0.5, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.43-7.27 (m, 15H, Ar*H*), 5.85-5.72 (dddd, J_{trans} 17.1 Hz, J_{cis} 10.2 Hz, J_{vic} 8.3 Hz, J_{vic} 6.2 Hz, 1H, allyl C*H*=CH_2), 5.64 (dd, J_{trans} 17.1 Hz, J_{cis} 10.5 Hz, 1H, vinyl C*H*=CH_2), 5.45 (dd, J_{gem} 1.6 Hz, 1H, vinyl CH=C*H*H), 5.36

(dd, 1H, vinyl CH=CH*H*), 5.14 (d, 1H, allyl CH=C*H*H), 5.09 (d, 1H, allyl CH=CH*H*), 5.00 (d, J_{gem} 10.7 Hz, 1H, C*H*HPh), 4.86 (d, J_{gem} 10.7 Hz, 1H, CH*H*Ph), 4.82 (d, J_{gem} 10.4 Hz, 1H, C*H*HPh), 4.81 (d, J_{gem} 11.7 Hz, 1H, C*H*HPh), 4.75 (d, J_{gem} 11.7 Hz, 1H, CH*H*Ph), 4.56 (d, J_{gem} 10.4 Hz, 1H, CH*H*Ph), 4.18-4.13 (m, 1H, H3), 4.12 (t, $J_{5,4/6}$ 9.5 Hz, 1H, H5), 3.49-3.40 (m, 2H, 2xO*H*), 3.45 (dd, $J_{4.3}$ 3.0 Hz, 1H, H4), 3.37 (d, 1H, H6), 2.51 (ddd, J_{gem} 14.4 Hz, $J_{\underline{CH}H,2}$ 10.9 Hz, 1H, allyl C*H*H), 2.36-2.27 (m, 1H, allyl CH*H*), 1.37 (dt, $J_{2,3/CH\underline{H}}$ 3.0 Hz, 1H, H2). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_c (ppm) 140.9 (vinyl *C*H=CH_2), 139.0, 138.4, 138.1 (Ar*C*), 136.6 (allyl *C*H=CH_2), 128.6-127.7 (Ar*C*H), 117.2 (allyl CH=*C*H_2), 116.5 (vinyl CH=*C*H_2), 85.0 (C6), 82.9 (C4), 80.4 (C5), 79.8 (C1), 76.2, 76.2, 72.4 (*C*H_2Ph), 68.5 (C3), 42.3 (C2), 28.7 (allyl *C*H_2). HRMS(ESI): Calcd. for $C_{32}H_{36}O_5Na^+$ m/z 523.2455; found m/z 523.2463.

(1*S*,2*R*,3*R*,4*S*,5*R*,6*S*)-2-Allyl-4,5,6-tris(benzyloxy)-3-hydroxy-3-vinylcyclohexyl 3,5-dinitrobenzoate (5)

4 (0.205 g, 0.41 mmol) was dissolved in dry CH_2Cl_2 (6 mL). The solution was cooled to 0 °C before the addition of Et_3N (0.11 mL, 0.82 mmol, 2 eq), DMAP (0.011 g, 0.041 mmol, 0.1 eq) and 3,5-dinitrobenzoyl chloride (0.143 g, 0.61 mmol, 1.5 eq). The reaction mixture was stirred overnight at rt. The reaction mixture was diluted with CH_2Cl_2 and subsequently washed with 1 M aq. HCl, sat. aq. $NaHCO_3$ and brine. The organic phase was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (Pentane/CH_2Cl_2 1:2 → 1:4) to afford **5** (0.239 g, 0.34 mmol, 84%) as white crystals. The compound was recrystallized from diethyl ether to produce crystals suitable for X-ray crystallography. R_f (Pentane/CH_2Cl_2 1:2) 0.51. $[\alpha]_D^{299K}$ -4.0 (*c* 1.0, $CHCl_3$). Mp 152.6-154.8 °C (Et_2O). ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 9.31 (d, J_{meta} 2.3 Hz, 2H, Ar*H*), 9.23 (t, 1H, Ar*H*), 7.39-7.24 (m, 15H, Ar*H*), 5.88 (t, $J_{1,2/6}$ 2.5 Hz, 1H, H1), 5.83-5.70 (m, 2H, allyl C*H*=CH_2, vinyl C*H*=CH_2), 5.52 (d, J_{trans} 17.0 Hz, 1H, vinyl CH=C*H*H), 5.44 (d, J_{cis} 10.6 Hz, 1H, vinyl CH=CH*H*), 5.09 (d, J_{cis} 10.0 Hz, 1H, allyl CH=C*H*H), 4.97-4.82 (m, 4H, allyl CH=CH*H*, 3xC*H*HPh), 4.76 (d, J_{gem} 10.5 Hz, 1H, CH*H*Ph), 4.66 (d, J_{gem} 10.1 Hz, 1H, CH*H*Ph), 4.61 (d, J_{gem} 10.9 Hz, 1H, CH*H*Ph), 4.08 (t, $J_{5,4/6}$ 9.6 Hz, 1H, H5), 3.67 (dd, 1H, H6), 3.47 (d, 1H, H4), 2.82 (s, 1H, O*H*), 2.44-2.35 (m, 1H, allyl C*H*H), 2.23-2.11 (m, 1H, allyl CH*H*), 1.71-1.65 (m, 1H, H2). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 162.2 (*C*=O), 148.8 (Ar*C*-NO_2), 142.2 (allyl *C*H=CH_2), 138.7, 137.8, 137.8 (Ar*C*), 135.8 (vinyl *C*H=CH_2), 134.5 (Ar*C*-C=O), 130.1, 128.5-127.7, 122.4 (Ar*C*H), 118.1 (allyl CH=*C*H_2), 116.9 (vinyl CH=*C*H_2), 84.6 (C4), 81.1 (C6), 79.6 (C5), 78.1 (C3), 76.5, 76.1, 72.7

(*C*H_2Ph), 70.7 (C1), 42.8 (C2), 29.0 (allyl C*H*$_2$). HRMS(ESI) Calcd. for $C_{39}H_{38}N_2O_{10}NH_4^+$ m/z 712.2865; found m/z 712.2867.

Methyl 2,3,4-tri-*O*-benzyl-5-methylene-α-D-xylopyranoside (7)

6 (3.682 g, 6.44 mmol) was dissolved in dry pyridine (40 mL) and transferred to a flask containing AgF (3.266 g, 25.7 mmol, 4 eq) under an atmosphere of nitrogen. The reaction mixture was stirred in the dark for 48 h at rt. The reaction mixture was concentrated under reduced pressure and subsequently purified by flash column chromatography (CH_2Cl_2) to afford **7** (2.555 g, 5.72 mmol, 89%) as a white solid. R_f (CH_2Cl_2) 0.47. $[\alpha]_D^{293K}$ -22.2 (*c* 0.4, $CHCl_3$), lit. -18 (*c* 1.3, $CHCl_3$)[43]. Mp 55.3-57.1 °C, lit. 57-58 °C.[16] ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.42-7.31 (m, 15H, Ar*H*), 4.97-4.72 (m, 6H, 3xC*H*HPh, 2xCH*H*Ph, H6a), 4.78-4.75 (bs, 1H, H6b), 4.72 (d, J_{gem} 12.2 Hz, 1H, CH*H*Ph), 4.68 (d, $J_{1,2}$ 3.4 Hz, 1H, H1), 4.03 (t, $J_{3,2/4}$ 9.2 Hz, 1H, H3), 3.96 (dt, $J_{4,6a/6b}$ 1.9 Hz, 1H, H4), 3.65 (dd, 1H, H2), 3.47 (s, 3H, C*H*$_3$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 153.7 (C5), 138.7, 138.1, 138.1 (Ar*C*), 128.5-127.7 (Ar*C*H), 99.1 (C1), 96.9 (C6), 81.3 (C4), 79.6 (C3), 79.3 (C2), 75.8, 74.6, 73.7 (*C*H_2Ph), 55.5 (*C*H_3). HRMS(ESI): Calcd. for $C_{28}H_{30}O_5Na^+$ m/z 469.1985; found m/z 469.1987. NMR-data were in accordance with previously reported data.[44]

2-Allyl-4,6-bis(benzyloxy)phenol (8)

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.46-7.30 (m, 10H, Ar*H* Bn), 6.53 (d, J_{meta} 2.7 Hz, 1H, H3/H5), 6.42 (d, J_{meta} 2.7 Hz, 1H, H3/H5), 6.00 (ddt, J_{trans} 17.1 Hz, J_{cis} 10.2 Hz, J_{vic} 6.5 Hz, 1H, C*H*=CH_2), 5.36 (s, 1H, O*H*), 5.13-5.05 (m, 2H, CH=C*H*$_2$), 5.05 (s, 2H, C*H*$_2$Ph), 4.97 (s, 2H, C*H*$_2$Ph), 3.40 (dt, ^4J 1.2 Hz, 2H, C*H*$_2$CH=CH_2). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 152.1 (C4/C6), 146.1 (C4/C6), 138.1, 137.4 (Ar*C*), 136.6 (*C*H=CH_2), 136.4 (Ar*C*), 128.9-127.8 (Ar*C*H Bn), 126.2 (Ar*C*), 115.8 (CH=*C*H_2), 107.6 (C3/C5), 99.6 (C3/C5), 71.4, 70.9 (*C*H_2Ph), 34.2 (*C*H_2CH=CH_2). HRMS(ESI) Calcd. for $C_{23}H_{22}O_3H^+$ m/z 347.1642; found m/z 347.1646.

Methyl 2,3,4-tri-*O*-benzyl-6-deoxy-6-iodo-β-D-glucopyranoside (10)

9 (2.006 g, 4.3 mmol) was dissolved in dry toluene (80 mL) under an atmosphere of nitrogen. Imidazole (0.598 g, 8.6 mmol, 2 eq), PPh_3 (2.837 g, 10.8 mmol, 2.5 eq) and I_2 (1.319 g, 5.2 mmol, 1.2 eq) were added. The reaction mixture was stirred overnight at 70 °C. The reaction mixture was allowed to reach rt before it was quenched with 10% aq. $Na_2S_2O_3$ (30 mL) and subsequently stirred

for 10 min. The aqueous phase was extracted with EtOAc (x3). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography (Pentane/CH_2Cl_2 5:1 → Pentane/EtOAc 10:1) affording **10** (2.456 g, 4.3 mmol, 99%) as a white solid. R_f (Pentane/EtOAc 30:1) 0.50. $[\alpha]_D^{293K}$ +19.0 (*c* 2.0, $CHCl_3$). Mp 87.5-88.7 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.41-7.30 (m, 15H, Ar*H*), 5.00 (d, J_{gem} 11.0 Hz, 1H, C*H*HPh), 4.98 (d, J_{gem} 11.1 Hz, 1H, C*H*HPh), 4.96 (d, J_{gem} 11.0 Hz, 1H, C*H*HPh), 4.83 (d, J_{gem} 11.0 Hz, 1H, CH*H*Ph), 4.76 (d, J_{gem} 11.1 Hz, 1H, CH*H*Ph), 4.73 (d, J_{gem} 11.0 Hz, 1H, CH*H*Ph), 4.42 (d, $J_{1,2}$ 7.8 Hz, 1H, H1), 3.73 (t, $J_{3,2/4}$ 9.0 Hz, 1H, H3), 3.65 (s, 3H, CH_3), 3.56 (dd, $J_{6a,6b}$ 10.3 Hz, $J_{6a,5}$ 2.3 Hz, 1H, H6a), 3.51 (dd, 1H, H2), 3.44 (t, $J_{4,5}$ 9.0 Hz, 1H, H4), 3.30 (dd, $J_{6b,5}$ 7.2 Hz, 1H, H6b), 3.24 (ddd, 1H, H5). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 138.6, 138.5, 138.0 (Ar*C*), 128.6-127.8 (Ar*C*H), 104.5 (C1), 84.3 (C3), 82.5 (C2), 81.4 (C4), 75.7, 75.4, 74.8 (*C*H_2Ph), 73.9 (C5), 55.3 (*C*H_3), 6.5 (C6). HRMS(ESI): Calcd. for $C_{28}H_{31}IO_5NH_4^+$ m/z 592.1554; found m/z 592.1560

Methyl 2,3,4-tri-*O*-benzyl-5-methylene-β-D-xylopyranoside (11)

10 (2.231 g, 3.88 mmol) was dissolved in dry THF (30 mL) under an atmosphere of nitrogen. DBU (2.32 mL, 15.5 mmol, 4 eq) was added and the reaction mixture was heated to reflux for 6 h. The reaction mixture was allowed to reach rt and left stirring overnight. The reaction mixture was quenched with sat. aq. NH_4Cl. The aqueous phase was extracted with EtOAc (x3). The combined organic layers were washed with H_2O and brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (Pentane/EtOAc 15:1) affording **11** (1.450 g, 3.25 mmol, 84%) as a white solid. R_f (Pentane/EtOAc 30:1) 0.52. $[\alpha]_D^{293K}$ -41.9 (*c* 2.0, $CHCl_3$). Mp 63.1-65.8 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.43-7.31 (m, 15H, Ar*H*), 4.85-4.78 (m, 5H, H6a, 3xC*H*HPh, CH*H*Ph), 4.76-4.71 (m, 3H, H6b, 2xCH*H*Ph), 4.68 (d, $J_{1,2}$ 6.3 Hz, 1H, H1), 4.13 (dt, $J_{4,3}$ 7.8 Hz, $J_{4,6a/6b}$ 1.3 Hz, 1H, H4), 3.71 (dd, $J_{3,2}$ 6.9 Hz, 1H, H3), 3.66-3.61 (m, 1H, H2), 3.62 (s, 3H, *C*H_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 153.9 (C5), 138.4, 138.3, 138.0 (Ar*C*), 128.5-127.7 (Ar*C*H), 104.1 (C1), 94.7 (C6), 82.2 (C3), 81.5 (C2), 78.4 (C4), 74.4, 73.9, 73.1 (*C*H_2Ph), 57.0 (*C*H_3). HRMS(ESI): Calcd. for $C_{28}H_{30}O_5Na^+$ m/z 469.1985; found m/z 469.1988.

(3*S*,4*R*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-6-methoxytetrahydro-2*H*-pyran-2-one (12)

11 (1.229 g, 2.75 mmol) was dissolved in dry CH_2Cl_2 (55 mL). The solution was degassed for 5 min with nitrogen before it was cooled to -78 °C. O_2 was bubbled through the solution for 5 min followed by O_3 for 15 min until the solution turned blue. O_2 was bubbled through the solution for 5 min followed by nitrogen for 5 min. Me_2S (0.40 mL, 5.51 mmol, 2 eq) was added to the solution at -78 °C and the reaction mixture was stirred for 30 min while allowed to reach rt. The reaction mixture was concentrated under reduced pressure and subsequently purified by flash column chromatography (Pentane/EtOAc 10:1) to afford **12** (0.804 g, 1.79 mmol, 65%) as a yellow oil. R_f (Pentane/EtOAc 5:1) 0.41. $[\alpha]_D^{293K}$ -48.9 (*c* 2.0, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.36-7.32 (m, 2H, Ar*H*), 7.29-7.14 (m, 13H, Ar*H*), 5.05 (dd, $J_{6,5}$ 2.5 Hz, $J_{6,4}$ 0.7 Hz, 1H, H6), 4.97 (d, J_{gem} 11.2 Hz, 1H, C*H*HPh), 4.64 (d, J_{gem} 11.8 Hz, 1H, C*H*HPh), 4.56 (d, J_{gem} 11.2 Hz, 1H, CH*H*Ph), 4.54 (d, J_{gem} 11.8 Hz, 1H, CH*H*Ph), 4.41 (d, J_{gem} 11.9 Hz, 1H, C*H*HPh), 4.37 (d, J_{gem} 11.9 Hz, 1H, CH*H*Ph), 4.36 (d, $J_{3,4}$ 8.2 Hz, 1H, H3), 3.77 (ddd, $J_{4,5}$ 2.5 Hz, 1H, H4), 3.70 (t, 1H, H5), 3.43 (s, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 169.8 (*C*=O, C2), 137.6, 137.4, 137.0 (Ar*C*), 128.6-127.9 (Ar*C*H), 103.1 (C6), 80.1 (C4), 79.0 (C5), 77.7 (C3), 73.9, 73.5, 71.9 (*C*H_2Ph), 57.3 (*C*H_3). HRMS(ESI): Calcd. for $C_{27}H_{28}O_6H^+$ m/z 449.1959; found m/z 449.1959.

Methyl 2,3,4-tri-*O*-benzyl-6-deoxy-6-iodo-α-D-mannopyranoside (14)

13 (18.225 g, 39.2 mmol) was dissolved in dry toluene (225 mL). PPh_3 (25.734 g, 98.1 mmol, 2.5 eq), imidazole (5.354 g, 78.6 mmol, 2 eq) and I_2 (11.957 g, 47.1 mmol, 1.2 eq) were added. The reaction mixture was heated to 90 °C and stirred at this temperature for 2 h before being allowed to reach rt. The reaction was quenched by the addition of 10% aq. $Na_2S_2O_3$. The aqueous phase was extracted with EtOAc (x3) and the resulting organic phase was washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude residue was purified was flash column chromatography (Pentane/CH_2Cl_2 3:1 → CH_2Cl_2) to give **14** (21.763 g, 37.9 mmol, 97%) as a slightly yellow oil. R_f (CH_2Cl_2) 0.57. $[\alpha]_D^{299K}$ +30.4 (*c* 2, $CHCl_3$), lit. +26 (*c* 1.39, $CHCl_3$).[27] ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.41-7.27 (m, 15H, Ar*H*), 4.98 (d, J_{gem} 11.0 Hz, 1H, C*H*HPh), 4.75 (d, J_{gem} 12.4 Hz, 1H, C*H*HPh), 4.75 (d, $J_{1,2}$ 1.5 Hz, 1H, H1), 4.71 (d, J_{gem} 12.4 Hz, 1H, CH*H*Ph), 4.67 (d, J_{gem} 11.0 Hz, 1H, CH*H*Ph), 4.60 (s, 2H, CH_2Ph), 3.88 (dd, $J_{3,4}$ 9.3 Hz, $J_{3,2}$ 3.2 Hz, 1H, H3), 3.80-3.73 (m, 2H, H2, H4), 3.56 (dd, $J_{6a,6b}$ 10.2 Hz, $J_{6a,5}$ 2.4 Hz, 1H, H6a), 3.54-3.48 (m, 1H, H5), 3.37 (s, 3H, CH_3), 3.35-3.29 (m, 1H, H6b). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 138.1, 138.1, 138.1 (Ar*C*), 128.3-127.5 (Ar*C*H), 98.8 (C1), 79.7 (C3), 78.4 (C4), 75.2 (*C*H_2Ph), 74.5 (C2),

72.5, 71.9 (*C*H_2Ph), 71.3 (C5), 54.9 (*C*H_3), 7.1 (C6). HRMS(ESI): Calcd. for $C_{28}H_{31}IO_5NH_4^+$ m/z 592.1554; found m/z 592.1563. NMR-data were in accordance with previously reported data.[27]

Methyl 2,3,4-tri-*O*-benzyl-5-methylene-α-D-lyxopyranoside (15)

14 (8.794 g, 15.3 mmol) was dissolved in dry pyridine (90 mL) and added to a flask containing AgF (7.702 g, 60.7 mmol, 4 eq), which was weighed under an atmosphere of nitrogen. The reaction mixture was stirred at rt for 48 h in the dark and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (CH_2Cl_2) to give **15** (5.903 g, 13.2 mmol, 86%) as a colorless oil. R_f (Pentane/EtOAc 8:1) 0.46. $[\alpha]_D^{299K}$ -27.2 (*c* 1, CH_3OH), lit. -18.2 (*c* 1, CH_3OH).[45] ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.40-7.27 (m, 15H, Ar*H*), 4.84-4.72 (m, 8H, H1, H6a+b, 3xC*H*HPh, 2xCH*H*Ph), 4.67 (d, J_{gem} 12.0 Hz, 1H, CH*H*Ph), 4.37 (dt, $J_{4,5}$ 8.6 Hz, $J_{4,6a/6b}$ 1.6 Hz, 1H, H4), 3.90 (dd, $J_{3,2}$ 3.0 Hz, 1H, H3), 3.87 (t, $J_{2,1}$ 3.0 Hz, 1H, H2), 3.42 (s, 3H, C*H*$_3$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 154.9 (C5), 138.6, 138.3 (Ar*C*), 128.4-127.6 (Ar*C*H), 100.8 (C1), 96.7 (C6), 78.7 (C4), 76.6 (C2), 75.7 (C3), 73.7, 73.3, 73.0 (*C*H_2Ph), 55.5 (*C*H_3). HRMS(ESI): Calcd. for $C_{28}H_{30}O_5Na^+$ m/z 469.1985; found m/z 469.1992. NMR-data were in accordance with previously reported data.[46]

(3*S*,4*R*,5*S*,6*S*)-3,4,5-Tris(benzyloxy)-6-methoxytetrahydro-2*H*-pyran-2-one (16)

15 (5.903 g, 13.2 mmol) was dissolved in dry CH_2Cl_2 (250 mL) and the solution was cooled to -78 °C. O_2 was bubbled through the solution for 5 min, followed by O_3 for 20 min, O_2 for 5 min and N_2 for 10 min. Me_2S (2.0 mL, 26.8 mmol, 2 eq) was added and the reaction mixture was allowed to reach rt and was stirred at this temperature for 30 min. The mixture was concentrated *in vacuo* and the crude residue was purified by flash column chromatography (Pentane/EtOAc 7:1) to give **16** (5.058 g, 11.3 mmol, 85%) as a colorless oil. R_f (CH_2Cl_2) 0.37. $[\alpha]_D^{299K}$ -31.0 (*c* 2, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.46-7.27 (m, 15H, Ar*H*), 5.14 (d, J_{gem} 11.0 Hz, 1H, C*H*HPh), 5.08 (d, $J_{6,5}$ 2.6 Hz, 1H, H6), 4.81 (d, J_{gem} 12.0 Hz, 1H, C*H*HPh), 4.76 (d, J_{gem} 11.0 Hz, 1H, CH*H*Ph), 4.76 (d, J_{gem} 11.9 Hz, 1H, C*H*HPh), 4.72 (d, J_{gem} 12.0 Hz, 1H, CH*H*Ph), 4.64 (d, J_{gem} 11.9 Hz, 1H, CH*H*Ph), 4.47 (d, $J_{3,4}$ 9.3 Hz, 1H, H3), 4.12 (dd, $J_{4,5}$ 2.6 Hz, 1H, H4), 3.94 (t, 1H, H5), 3.48 (s, 3H, C*H*$_3$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 170.4 (*C*=O, C2), 138.0, 137.6, 137.5 (Ar*C*), 128.6-127.6 (Ar*C*H), 101.8 (C6), 77.4 (C3), 76.5 (C4), 75.1 (*C*H_2Ph), 74.5 (C5), 73.4, 73.2 (*C*H_2Ph), 56.9 (O*C*H_3). HRMS(ESI): Calcd. for $C_{27}H_{28}O_6NH_4^+$ m/z 466.2224; found m/z 466.2227.

Methyl 2,3,4-tri-*O*-benzyl-6-deoxy-6-iodo-α-D-galactopyranoside (18)

17 (3.399 g, 7.3 mmol) was dissolved in dry toluene (140 mL). Imidazole (0.998 g, 15 mmol, 2 eq), PPh_3 (4.799 g, 18 mmol, 2.5 eq) and I_2 (2.231 g, 8.8 mmol, 1.2 eq) were added to the solution. The reaction mixture was stirred at 70 °C for 2 h, cooled to rt and quenched by the addition of 10% $Na_2S_2O_3$. The aqueous phase was extracted with EtOAc (x3). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (Pentane/CH_2Cl_2 3:1 → 1:2) to afford **18** (3.397 g, 5.9 mmol, 81%) as a colorless oil. R_f (Pentane/EtOAc 20:1) 0.43. $[\alpha]_D^{293K}$ +20.9 (*c* 2.0, $CHCl_3$), lit. +23 (*c* 1.1, $CHCl_3$).[27] ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.48-7.27 (m, 15H, Ar*H*), 5.08 (d, J_{gem} 11.2 Hz, 1H, C*H*HPh), 4.94 (d, J_{gem} 11.7 Hz, 1H, C*H*HPh), 4.87 (d, J_{gem} 12.1 Hz, 1H, C*H*HPh), 4.80 (d, J_{gem} 11.7 Hz, 1H, CH*H*Ph), 4.72 (d, J_{gem} 12.1 Hz, 1H, CH*H*Ph), 4.68 (d, $J_{1,2}$ 3.5 Hz, 1H, H1), 4.67 (d, J_{gem} 11.2 Hz, 1H, CH*H*Ph), 4.09-4.03 (m, 2H, H2, H4), 3.97 (dd, $J_{3,2}$ 10.3 Hz, $J_{3,4}$ 2.3 Hz, 1H, H3), 3.88 (t, $J_{5,6a/6b}$ 6.8 Hz, 1H, H5), 3.45 (s, 3H, C*H*$_3$), 3.28-3.24 (m, 1H, H6a), 3.10 (dd, $J_{6a,6b}$ 10.1 Hz, 1H, H6b). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 138.7, 138.4, 138.3 (Ar*C*), 128.5-127.6 (Ar*C*H), 98.9 (C1), 79.1 (C3), 76.0 (C2), 75.8 (C4), 75.1, 73.7, 73.7 (*C*H_2Ph), 71.3 (C5), 55.8 (*C*H_3), 3.7 (C6). HRMS(ESI): Calcd. for $C_{28}H_{31}IO_5NH_4^+$ m/z 592.1554; found m/z 592.1561. NMR-data were in accordance with previously reported data.[27,28]

Methyl 2,3,4-tri-*O*-benzyl-5-methylene-β-L-arabinopyranoside (19)

18 (2.833 g, 4.9 mmol) was dissolved in dry pyridine (40 mL) and transferred to a flask containing AgF (2.523 g, 20 mmol, 4 eq) under an atmosphere of nitrogen. The reaction mixture was stirred in the dark for 96 h at rt. The reaction mixture was concentrated under reduced pressure and the crude residue was purified by flash column chromatography (CH_2Cl_2) to afford **19** (2.039 g, 4.6 mmol, 93%) as a colorless oil. R_f (CH_2Cl_2) 0.69. $[\alpha]_D^{293K}$ +13.6 (*c* 2.0, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.44-7.27 (m, 15H, Ar*H*), 4.92 (d, J_{gem} 12.0 Hz, 1H, C*H*HPh), 4.79-4.69 (m, 5H, H1, H6a, 2xC*H*HPh, CH*H*Ph), 4.61 (d, J_{gem} 11.9 Hz, 1H, CH*H*Ph), 4.47-4.41 (m, 2H, H6b, CH*H*Ph), 4.18 (dd, $J_{2,3}$ 9.8 Hz, $J_{2,1}$ 2.5 Hz, 1H, H2), 4.07 (d, $J_{4,3}$ 2.5 Hz, 1H, H4), 3.97 (dd, 1H, H3), 3.43 (s, 3H, C*H*$_3$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 151.7 (C5), 138.7, 138.7, 138.0 (Ar*C*), 128.5-127.6 (Ar*C*H), 102.0 (C6), 100.0 (C1), 76.7 (C3), 75.8 (C2), 74.9 (C4), 74.1, 72.6, 69.4 (*C*H_2Ph), 55.8 (*C*H_3). HRMS(ESI): Calcd. for $C_{28}H_{30}O_5Na^+$ m/z 469.1985; found m/z 469.1990.

(3*R*,4*R*,5*R*,6*S*)-3,4,5-Tris(benzyloxy)-6-methoxytetrahydro-2*H*-pyran-2-one (20)

19 (1.853 g, 4.2 mmol) was dissolved in dry CH_2Cl_2 (80 mL). The solution was cooled to -78 °C. O_2 was bubbled through the solution for 5 min followed by O_3 for 10 min until the solution turned light blue. O_2 was again bubbled through the solution for 5 min followed by nitrogen for 5 min. Me_2S (0.61 mL, 8.3 mmol, 2 eq) was added to the solution at -78 °C and the reaction mixture was stirred for 30 min while being allowed to reach rt. The reaction mixture was concentrated under reduced pressure and the crude residue was purified by flash column chromatography (Pentane/EtOAc 10:1 → 4:1) to afford **20** (1.513 g, 3.4 mmol, 81%) as a colorless oil. R_f (Pentane/EtOAc 7:1) 0.38. $[\alpha]_D^{293K}$ +104.5 (*c* 2.0, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.39-7.25 (m, 13H, Ar*H*), 7.20-7.15 (m, 2H, Ar*H*), 5.24 (d, $J_{6,5}$ 3.0 Hz, 1H, H6), 5.06 (d, J_{gem} 12.0 Hz, 1H, C*H*HPh), 4.83 (d, J_{gem} 11.9 Hz, 1H, C*H*HPh), 4.67 (d, J_{gem} 12.0 Hz, 1H, C*H*HPh), 4.64 (d, J_{gem} 12.0 Hz, 1H, CH*H*Ph), 4.59 (d, J_{gem} 11.9 Hz, 1H, CH*H*Ph), 4.53 (d, J_{gem} 12.0 Hz, 1H, CH*H*Ph), 4.53 (d, $J_{3,4}$ 3.8 Hz, 1H, H3), 3.98 (t, $J_{4,5}$ 3.8 Hz, 1H, H4), 3.85 (dd, 1H, H5), 3.58 (s, 3H, C*H*$_3$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 169.1 (*C*=O, C2), 137.8, 137.5, 137.4 (Ar*C*), 128.6-127.9 (Ar*C*H), 102.2 (C6), 76.6 (C4), 75.9 (C5), 74.6 (C3), 73.8, 73.6, 73.5 (*C*H_2Ph), 57.9 (*C*H_3). HRMS(ESI) Calcd. for $C_{27}H_{28}O_6NH_4^+$ m/z 466.2224; found m/z 466.2232.

(1*R*,2*R*,3*S*,4*R*,5*R*,6*S*)/(1*S*,2*S*,3*R*,4*R*,5*R*,6*S*)-2-Allyl-4,5,6-tris(benzyloxy)-1-vinylcyclohexane-1,3-diol (21 and 22)

Vinylmagnesium bromide (0.9 M in THF, 11.7 mL, 10.5 mmol, 9 eq) and TMEDA (1.9 mL, 13 mmol, 11 eq) were mixed at rt and added to **16** at -78 °C. The reaction mixture was stirred at -78 °C for 2 h and allowed to reach rt and stirred at this temperature for 1 h. The reaction was quenched by the addition of water and 1 M aq. HCl. The aqueous phase was extracted with CH_2Cl_2 (x3). The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (CH_2Cl_2/EtOAc 200:1 → 100:1 → 25:1) to give **21** (0.355 g, 0.71 mmol, 60%) and **22** (0.043 g, 0.086 mmol, 7%) as colorless oils. **21** crystallized on standing. **21**: R_f (Pentane/EtOAc 4:1) 0.45. $[\alpha]_D^{299K}$ -49.9 (*c* 2.0, $CHCl_3$). Mp 90.4-91.7 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.32-7.13 (m, 15H, Ar*H*), 5.69 (dd, J_{trans} 17.0 Hz, J_{cis} 10.9 Hz, 1H, vinyl C*H*=CH_2), 5.59-5.56 (m, 1H, allyl C*H*=CH_2), 5.27 (dd, J_{gem} 1.3 Hz, 1H, vinyl CH=C*H*H), 5.25 (dd, 1H, vinyl CH=CH*H*), 5.05-4.98 (m, 1H, allyl CH=C*H*H), 4.95 (d, J_{cis} 10.0 Hz, 1H, allyl CH=CH*H*), 4.76 (d, J_{gem} 10.2 Hz, 1H,

C*H*HPh), 4.70 (d, J_{gem} 12.2 Hz, 1H, C*H*HPh), 4.59 (s, 2H, CH_2Ph), 4.55 (d, J_{gem} 12.2 Hz, 1H, CH*H*Ph), 4.52 (d, J_{gem}, 10.2 Hz, 1H, CH*H*Ph), 3.97-3.91 (m, 2H, H4, H5), 3.83 (t, $J_{3,2/4}$ 3.3 Hz, 1H, H3), 3.75-3.70 (m, 1H, H6), 2.87 (bs, 1H, O*H*), 2.28 (ddd, J_{gem} 14.4 Hz, $J_{C\underline{H}H,2}$ 11.3 Hz, J_{vic} 8.3 Hz, 1H, allyl C*H*H), 2.16 (dtd, $J_{CH\underline{H},2/vic}$ 3.3 Hz, ^4J 1.6 Hz, 1H, allyl CH*H*), 1.84 (dt, 1H, H2). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 141.5 (vinyl *C*H=CH_2), 138.8, 138.8, 138.3 (Ar*C*), 136.8 (allyl *C*H=CH_2), 128.5-127.6 (Ar*C*H), 116.7 (allyl CH=*C*H_2), 115.8 (vinyl CH=*C*H_2), 81.6 (C6), 80.7 (C1), 78.1, 77.5 (C4, C5), 76.1, 73.2, 72.7 (*C*H_2Ph), 69.1 (C3), 39.1 (C2), 28.3 (allyl *C*H_2). HRMS(ESI): Calcd. for $C_{32}H_{36}O_5NH_4^+$ m/z 518.2901; found m/z 518.2908. **22**: R_f (Pentane/EtOAc 6:1) 0.58. $[\alpha]_D^{299K}$ -7.9 (*c* 2.0, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.31-7.15 (m, 13H, Ar*H*), 7.11-7.05 (m, 2H, Ar*H*), 5.88 (ddd, J_{trans} 17.2 Hz, J_{cis} 10.8 Hz, $J_{H,OH}$ 1.6 Hz, 1H, vinyl C*H*=CH_2), 5.72 (dddd, J_{trans} 16.9 Hz, J_{cis} 10.1 Hz, J_{vic} 8.6 Hz, J_{vic} 6.0 Hz, 1H, allyl C*H*=CH_2), 5.42 (dd, J_{gem} 2.2 Hz, 1H, vinyl CH=C*H*H), 5.18 (dd, 1H, vinyl CH=CH*H*), 5.03 (d, 1H, allyl CH=C*H*H), 4.95 (d, 1H, allyl CH=CH*H*), 4.61 (d, J_{gem} 11.8 Hz, 1H, C*H*HPh), 4.51 (d, J_{gem} 11.9 Hz, 1H, C*H*HPh), 4.43-4.38 (m, 3H, C*H*HPh, 2xCH*H*Ph), 4.25 (d, J_{gem} 11.5 Hz, 1H, CH*H*Ph), 4.20-4.16 (m, 2H, H3, O*H*(1)), 3.83-3.80 (m, 1H, H5), 3.64 (t, $J_{4,5/3}$ 3.4 Hz, 1H, H4), 3.55 (d, $J_{6,5}$ 3.2 Hz, 1H, H6), 2.82 (d, $J_{OH,3}$ 1.8 Hz, 1H, O*H*(3)), 2.47 (ddd, J_{gem} 14.3 Hz, $J_{C\underline{H}H,2}$ 11.4 Hz, 1H, allyl C*H*H), 2.17-2.09 (m, 1H, allyl CH*H*), 1.64 (dt, $J_{2,3/CH\underline{H}}$ 2.8 Hz, H2). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 140.9 (vinyl *C*H=CH_2), 138.1, 137.8, 137.8 (Ar*C*), 137.2 (allyl *C*H=CH_2), 128.6-127.8 (Ar*C*H), 116.8 (allyl CH=*C*H_2), 115.4 (vinyl CH=*C*H_2), 81.4 (C6), 76.6 (C5), 75.9 (C1), 75.7 (C4), 74.0, 73.0, 70.3 (*C*H_2Ph), 68.5 (C3), 41.6 (C2), 29.1 (allyl *C*H_2). HRMS(ESI): Calcd. for $C_{32}H_{36}O_5H^+$ m/z 501.2636; found m/z 501.2946.

(2*R*,3*R*,4*R*)-2,3,4-Tris(benzyloxy)-5-oxonon-8-enal (23)

Vinylmagnesium bromide (0.9 M in THF, 4.6 mL, 4.2 mmol, 9 eq) was mixed with TMEDA (0.76 mL, 5.1 mmol, 11 eq) at rt. The mixture was slowly added to **20** (0.207 g, 0.46 mmol) at -78 °C. The reaction was stirred at this temperature for 2 h followed by rt for 1 h before it was quenched with H_2O. The reaction mixture was extracted with CH_2Cl_2 (x3). The combined organic layers were washed with 1 M aq. HCl and brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography ($CHCl_3$/EtOAc 100:1) to afford **23** (0.100 g, 0.21 mmol, 46%) as a colorless oil. R_f ($CHCl_3$/EtOAc 100:1) 0.55. $[\alpha]_D^{298K}$ +2.3 (*c* 2.0, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 9.79 (d, $J_{1,2}$ 0.7 Hz, 1H, CHO), 7.36-7.24 (m, 15H, Ar*H*), 5.69 (ddt, J_{trans} 16.9 Hz, J_{cis} 10.2 Hz, $J_{8,7}$ 6.6 Hz, 1H, H8), 4.95-4.86 (m, 2H, H9a, H9b), 4.62-4.51 (m, 5H, 3xC*H*HPh, 2xCH*H*Ph), 4.46 (d, J_{gem} 11.7 Hz, 1H, CH*H*Ph), 4.32 (dd, $J_{3,2}$

5.2 Hz, $J_{3,4}$ 4.0 Hz, 1H, H3), 4.11 (d, 1H, H4), 3.96 (dd, 1H, H2), 2.74 (ddd, $J_{6a,6b}$ 18.7 Hz, J_{vic} 9.0 Hz, J_{vic} 5.9 Hz, 1H, H6a), 2.55 (ddd, J_{vic} 8.9 Hz, J_{vic} 5.9 Hz, 1H, H6b), 2.22-2.12 (m, 1H, H7a), 2.08-1.99 (m, 1H, H7b). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 210.1 (*C*=O, C5), 200.9 (*C*=O, C1), 137.5 (C8), 137.2, 137.0, 136.8 (Ar*C*), 128.6-128.0 (Ar*C*H), 115.06 (C9), 83.2 (C4), 81.9 (C2), 81.8 (C3), 73.8, 73.3, 73.2 (*C*H_2Ph), 39.1 (C6), 27.0 (C7). HRMS(ESI) Calcd. for $C_{30}H_{32}O_5H^+$ m/z 473.2323; found m/z 473.2327.

(1*S*,2*S*,3*R*,4*S*,5*R*,6*R*)-2-Allyl-4,5,6-tris(benzyloxy)-1-vinylcyclohexane-1,3-diol (24)

Vinylmagnesium bromide (0.9 M solution in THF, 4.5 mL, 4.1 mmol, 9 eq) was mixed with TMEDA (0.74 mL, 5.0 mmol, 11 eq) at rt and added to **20** (0.202 g, 0.45 mmol) at -78 °C. The resultant mixture was stirred for 2 h at -78 °C. The reaction mixture was allowed reach to rt and stirred for an additional 18 h before it was quenched with H_2O. The reaction mixture was extracted with CH_2Cl_2 (x3). The combined organic layers were washed with 1 M aq. HCl and brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography ($CHCl_3$/EtOAc 100:1) to afford **24** (0.061 g, 0.12 mmol, 27%) as a colorless oil. R_f ($CHCl_3$/EtOAc 100:1) 0.48. $[\alpha]_D^{293K}$ +4.5 (*c* 2.0, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.31-7.16 (m, 13H, Ar*H*), 7.14-7.10 (m, 2H, Ar*H*), 5.68 (dddd, J_{trans} 16.7 Hz, J_{cis} 9.9 Hz, J_{vic} 8.5 Hz, J_{vic} 6.0 Hz, 1H, allyl C*H*=CH_2), 5.56 (dd, J_{trans} 17.0 Hz, J_{cis} 10.5 Hz, 1H, vinyl C*H*=CH_2), 5.34 (dd, J_{gem} 1.6 Hz, 1H, vinyl CH=C*H*H), 5.24 (dd, 1H, vinyl CH=CH*H*), 5.03 (d, 1H, allyl CH=C*H*H), 4.94 (d, 1H, allyl CH=CH*H*), 4.56 (d, J_{gem} 11.7 Hz, 1H, C*H*HPh), 4.42 (d, J_{gem} 12.1 Hz, 1H, C*H*HPh), 4.42-4.35 (m, 3H, C*H*HPh, 2xCH*H*Ph), 4.32 (d, J_{gem} 12.1 Hz, 1H, CH*H*Ph), 3.96 (t, $J_{4,3/5}$ 3.1 Hz, 1H, H4), 3.85-3.78 (m, 2H, H3, H5), 3.64 (d, $J_{OH,3}$ 11.4 Hz, 1H, O*H*(3)), 3.51 (d, $J_{6,5}$ 3.7 Hz, 1H, H6), 2.97 (s, 1H, O*H*), 2.45 (ddd, J_{gem} 14.0 Hz, $J_{CHH,2}$ 11.3 Hz, 1H, allyl C*H*H), 2.24-2.14 (m, 1H, allyl CH*H*), 1.66 (dt, $J_{2,3/CHH}$ 3.1 Hz, 1H, H2). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 142.0 (vinyl *C*H=CH_2), 138.1, 138.0, 137.8 (Ar*C*), 137.3 (allyl *C*H=CH_2), 128.6-127.8 (Ar*C*H), 116.5 (allyl CH=*C*H_2), 115.8 (vinyl CH=*C*H_2), 79.0 (C1), 77.6 (C6), 75.9 (C5), 75.8 (C4), 73.1, 72.4, 72.4 (*C*H_2Ph), 68.2 (C3), 41.5 (C2), 28.6 (allyl *C*H_2). HRMS(ESI) Calcd. for $C_{32}H_{36}O_5H^+$ m/z 501.2636; found m/z 501.2636.

2,3,4-Tri-*O*-benzyl-5,5-dimethyl-α/β-D-xylopyranose (25)

Methylmagnesium chloride (3 M solution in THF, 2.0 mL, 6.1 mmol, 9 eq) was mixed with TMEDA (1.1 mL, 7.4 mmol, 11 eq) at rt. The mixture was slowly added to **3** (0.303 g, 0.67 mmol) at -78 °C and stirred at this temperature for 2 h followed by 1 h at rt. The reaction was quenched with H_2O and subsequently extracted with CH_2Cl_2 (x3). The combined organic layers were washed with 1 M aq. HCl and brine before drying over $MgSO_4$. The organic phase was filtered, concentrated under reduced pressure and purified by flash column chromatography (CH_2Cl_2/EtOAc 40:1 → 30:1) to afford **25** (0.228 g, 0.51 mmol, 75%) as a colorless oil consisting of a mixture of isomers. *Major isomer*: R_f (CH_2Cl_2/EtOAc 30:1) 0.31. ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.43-7.30 (m, 15H, Ar*H*), 5.01 (d, J_{gem} 11.2 Hz, 1H, C*H*HPh), 5.00-4.94 (m, 3H, H1, 2xC*H*HPh), 4.84 (d, J_{gem} 10.8 Hz, 1H, CH*H*Ph), 4.83 (d, J_{gem} 11.0 Hz, 1H, CH*H*Ph), 4.70 (d, J_{gem} 11.2 Hz, 1H, CH*H*Ph), 3.93 (d, $J_{OH,1}$ 5.7 Hz, O*H*), 3.79 (t, $J_{3,4/2}$ 9.4 Hz, 1H H3), 3.44 (dd, $J_{2,1}$ 7.8 Hz, 1H, H2), 3.38 (d, 1H, H4), 1.35 (s, 3H, CH_3), 1.32 (s, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 138.7, 138.6, 138.5 (Ar*C*), 128.6-127.7 (Ar*C*H), 93.4 (C1), 84.9 (C4), 84.7 (C2), 82.3 (C3), 75.9, 75.8 (*C*H_2Ph), 75.4 (C5), 75.0 (*C*H_2Ph), 28.4 (*C*H_3), 19.2 (*C*H_3). HRMS(ESI): Calcd. for $C_{28}H_{32}O_5Na^+$ m/z 471.2142; found m/z 471.2144.

Acetyl 2,3,4-tri-*O*-benzyl-5,5-dimethyl-β-D-xylopyranose (26)

25 (0.050 g, 0.11 mmol) was dissolved in dry pyridine (1 mL). Acetic anhydride (1 mL) was added and the reaction mixture was stirred overnight before it was concentrated under reduced pressure. The residue was co-evaporated with toluene (x3). The crude product was purified by flash column chromatography (CH_2Cl_2) to afford **26** (0.037 g, 0.08 mmol, 67%) as a white solid. R_f (CH_2Cl_2) 0.37. $[\alpha]_D^{293K}$ -7.8 (*c* 1.0, $CHCl_3$). Mp 114.8-116.2 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.36-7.29 (m, 15H, Ar*H*), 5.87 (d, $J_{1,2}$ 8.3 Hz, 1H, H1), 4.94 (d, J_{gem} 11.2 Hz, 1H, C*H*HPh), 4.90 (d, J_{gem} 10.8 Hz, 1H, C*H*HPh), 4.82 (d, J_{gem} 10.8 Hz, 1H, CH*H*Ph), 4.81 (d, J_{gem} 11.4 Hz, 1H, C*H*HPh), 4.75 (d, J_{gem} 11.4 Hz, 1H, CH*H*Ph), 4.68 (d, J_{gem} 11.2 Hz, 1H, CH*H*Ph), 3.84 (t, $J_{3,2/4}$ 9.4 Hz, 1H, H3), 3.56 (dd, 1H, H2), 3.36 (d, $J_{4,3}$ 9.4 Hz, 1H, H4), 2.06 (s, 3H, acetyl CH_3), 1.36 (s, 3H, CH_3), 1.29 (s, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 169.5 (*C*=O), 138.5, 138.5, 138.3 (Ar*C*), 128.6-127.7 (Ar*C*H), 90.9 (C1), 84.8 (C4), 82.7 (C3), 82.4 (C2), 76.3 (C5), 75.9, 75.9, 75.2 (*C*H_2Ph), 28.2 (*C*H_3), 21.3 (acetyl *C*H_3), 19.0 (*C*H_3). HRMS(ESI): Calcd. for $C_{30}H_{34}O_6Na^+$ m/z 513.2248; found m/z 513.2253.

Methyl 3,4-di-*O*-benzyl-2-deoxy-5-methylene-α-D-xylopyranoside (28)

AgF (0.320 g, 0.64 mmol, 3.9 eq) was added to a vial under an atmosphere of nitrogen. **27** was dissolved in dry pyridine (3 mL) and transferred to the vial containing AgF. The reaction mixture was stirred at rt overnight in the dark. The crude mixture was concentrated *in vacuo* and purified by flash column chromatography (Pentane/CH_2Cl_2 1:1 → 1:2 → CH_2Cl_2) to give **28** as a colorless oil (0.176 g, 0.52 mmol, 81%). R_f (Pentane/Et_2O 4:1) 0.55. $[\alpha]_D^{298\ K}$ +30.0 (*c* 2, $CHCl_3$), lit. +27.9 (c 1.3, $CHCl_3$)[47]. ^{1}H-NMR (400 MHz, C_6D_6): δ_H (ppm) 7.39 (d, J_{ortho} 7.3 Hz, 2H, Ar*H*), 7.30 (d, J_{ortho} 7.3 Hz, 2H, Ar*H*), 7.25-7.12 (m, 6H, Ar*H*), 5.02 (d, $J_{6a,4}$ 1.3 Hz, 1H, H6a), 4.93 (d, $J_{6b,4}$ 1.3 Hz, 1H, H6b), 4.75 (d, J_{gem} 11.8 Hz, 1H, C*H*HPh), 4.71 (d, J_{gem} 11.8 Hz, 1H, CH*H*Ph) 4.70 (t, $J_{1,2eq/2ax}$ 3.2 Hz, 1H, H1), 4.58 (d, J_{gem} 11.9 Hz, 1H, C*H*HPh), 4.46 (d, J_{gem} 11.9 Hz, 1H, CH*H*Ph), 4.10 (ddd, $J_{3,2ax}$ 9.6 Hz, $J_{3,4}$ 8.0 Hz, $J_{3,2eq}$ 4.5 Hz, 1H, H3), 3.98 (dt, 1H, H4), 3.26 (s, 3H, CH_3), 2.27 (ddd, $J_{2eq,2ax}$ 13.3 Hz, 1H, H2eq), 1.80 (ddd, 1H, H2ax). ^{13}C-NMR (100 MHz, C_6D_6): δ_C (ppm) 155.7 (C5), 139.3, 139.0 (Ar*C*), 128.5-127.6 (Ar*C*H), 100.0 (C1), 96.7 (C6), 79.9 (C4), 76.3 (C3), 73.3, 72.1 (*C*H_2Ph), 55.0 (*C*H_3), 35.6 (C2). HRMS(ESI): Calcd. for $C_{21}H_{24}O_4H^+$ m/z 341.1749; found m/z 341.1747. ^{13}C-NMR-data were in accordance with previously reported data obtained in $CDCl_3$.[47]

(3*S*,4*R*,6*S*)-3,4-Bis(benzyloxy)-6-methoxytetrahydro-2*H*-pyran-2-one (29)

28 (2.842 g, 8.35 mmol) was dissolved in dry CH_2Cl_2 (130 mL). The solution was cooled to -78 °C and bubbled through with O_2 for 5 min, O_3 for 20 min and again O_2 followed by N_2 for 5 min and 10 min, respectively. Me_2S (1.3 mL, 17.4 mmol, 2 eq) was added and the reaction mixture was allowed to reach rt. The mixture was concentrated *in vacuo* and purified by flash column chromatography (Pentane/EtOAc 19:1 → 9:1) to give **29** (1.763 g, 5.15 mmol, 62%) as a colorless oil. R_f (CH_2Cl_2) 0.38. $[\alpha]_D^{300K}$ +12.1 (*c* 2, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.50-7.26 (m, 10H, Ar*H*), 5.25 (t, $J_{1,2eq/2ax}$ 3.3 Hz, 1H, H1), 5.10 (d, J_{gem} 11.3 Hz, 1H, C*H*HPh), 4.75 (d, J_{gem} 11.3 Hz, 1H, CH*H*Ph), 4.71 (d, J_{gem} 11.6 Hz, 1H, C*H*HPh), 4.63 (d, J_{gem} 11.6 Hz, 1H, CH*H*Ph), 4.12 (td, $J_{3,4/2ax}$ 8.1 Hz, $J_{3,2eq}$ 4.6 Hz, 1H, H3), 4.04 (d, 1H, H4), 3.52 (s, 3H, CH_3), 2.33 (dt, $J_{2eq,2ax}$ 14.0 Hz, 1H, H2eq), 2.08 (ddd, 1H, H2ax). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 170.1 (*C*=O), 137.8, 137.3 (Ar*C*), 128.4-127.6 (Ar*C*H), 101.1 (C1), 79.2 (C4), 74.1 (*C*H_2Ph), 73.4 (C3), 72.5 (*C*H_2Ph), 56.8 (*C*H_3), 34.0 (C2). HRMS(ESI): Calcd. for $C_{20}H_{22}O_5NH_4^+$ m/z 360.1805; found m/z 360.1808.

(1*R*,2*R*,3*R*,5*R*,6*S*)-2-Allyl-5,6-bis(benzyloxy)-1-vinylcyclohexane-1,3-diol (30) and (4*S*,5*R*)-4,5-bis(benzyloxy)-3-vinylnona-1,8-diene-3,7-diol (31)

Vinylmagnesium bromide (0.9 M in THF, 18 mL, 16.5 mmol, 9 eq) and TMEDA (3.0 mL, 20 mmol, 11 eq) were mixed at rt. The mixture was added to the lactone acetal **29** (0.626 g, 1.83 mmol) at -78 °C. The reaction mixture was stirred at -78 °C for 2 h before it was allowed to reach rt and stirred at this temperature for 1 h. The reaction was quenched by the addition of 1 M aq. HCl. The mixture was extracted with CH_2Cl_2 (x3) and the combined organic phases were washed with brine and subsequently dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (Pentane/EtOAc 20:1 → 15:1 → 9:1) to give **30** (0.216 g, 0.55 mmol, 30%) and **31** (0.195 g, 0.49 mmol, 27%) as a mixture of isomers. Both compounds were colorless oils. **30**: R_f (CH_2Cl_2) 0.30. $[\alpha]_D^{298K}$ -64.3 (*c* 2, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm) 7.36-7.12 (m, 10H, Ar*H*), 5.68 (m, 2H, allyl C*H*=CH_2, vinyl C*H*=CH_2), 5.28 (d, J_{cis} 10.1 Hz, 1H, vinyl CH=C*H*H), 5.27 (d, J_{trans} 17.4 Hz, 1H, vinyl CH=CH*H*), 5.03 (d, J_{trans} 17.0 Hz, 1H, allyl CH=C*H*H), 4.96 (d, J_{cis} 9.9 Hz, 1H, allyl CH=CH*H*), 4.77 (d, J_{gem} 10.3 Hz, 1H, C*H*HPh), 4.64 (d, J_{gem} 11.4 Hz, 1H, C*H*HPh), 4.58 (d, J_{gem} 11.4 Hz, 1H, CH*H*Ph), 4.55 (d, J_{gem} 10.3 Hz, 1H, CH*H*Ph), 4.05-3.85 (m, 2H, H3, H5), 3.55 (d, $J_{OH,3}$ 9.6 Hz, 1H, O*H*(3)), 3.28 (d, $J_{6,5}$ 9.0 Hz, 1H, H6), 2.89 (s, 1H, O*H*(1)), 2.54-2.40 (dt, $J_{4eq,4ax}$ 13.2 Hz, $J_{4eq,5/3}$ 4.2 Hz, 1H, H4eq), 2.37-2.26 (m, 1H, allyl C*H*H), 2.20-2.10 (m, 1H, allyl CH*H*), 1.45-1.32 (m, 2H, H4ax, H2). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 141.5 (vinyl *C*H=CH_2), 138.8, 138.2 (Ar*C*), 137.0 (allyl *C*H=CH_2), 128.5-127.7 (Ar*C*H), 116.8 (allyl CH=*C*H_2), 115.9 (vinyl CH=*C*H_2), 85.6 (C6), 81.0 (C1), 76.2 (C5), 76.0, 72.5 (*C*H_2Ph), 67.4 (C3), 45.0 (C2), 37.8 (C4), 29.1 (allyl *C*H_2). HRMS(ESI): Calcd. for $C_{25}H_{30}O_4NH_4^+$ m/z 412.2482; found m/z 412.2484. **31a**: R_f (Pentane/EtOAc 5:1) 0.54. ^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm) 7.39-7.27 (m, 10H, Ar*H*), 6.14 (dd, J_{trans} 17.4 Hz, J_{cis} 10.6 Hz, 1H, H2), 6.06 (dd, J_{trans} 17.3 Hz, J_{cis} 10.6 Hz, 1H, vinyl C*H*=CH_2), 5.83 (ddd, J_{trans} 17.2 Hz, J_{cis} 10.4 Hz, $J_{8,7}$ 5.4 Hz, 1H, H8), 5.43 (dd, J_{trans} 17.3 Hz, J_{gem} 1.4 Hz, 1H, H1a), 5.40 (dd, J_{trans} 17.3 Hz, J_{gem} 1.3 Hz, 1H, vinyl CH=C*H*H), 5.26-5.14 (m, 3H, H1b, vinyl CH=CH*H*, H9a), 5.08 (dt, $J_{gem/9b,7}$ 1.4 Hz, 1H, H9b), 4.75 (d, J_{gem} 11.3 Hz, 1H, C*H*HPh), 4.66 (2xd, 2H, CH*H*Ph, C*H*HPh), 4.52 (d, J_{gem} 11.0 Hz, 1H, CH*H*Ph), 4.27-4.20 (m, 1H, H7), 4.00 (ddd, $J_{5,6a}$ 8.6 Hz, $J_{5,4}$ 4.9 Hz, $J_{5,6b}$ 3.9 Hz, 1H, H5), 3.52 (d, 1H, H4), 3.33 (s, 1H, O*H*), 2.07 (bs, 1H, O*H*), 1.95 (ddd, $J_{6a,6b}$ 14.7 Hz, $J_{6a,7}$ 3.4 Hz, 1H, H6a), 1.82 (ddd, $J_{6b,7}$ 8.7 Hz, 1H, H6b). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 141.1, 140.7, 140.7 (*C*H=CH_2), 138.2, 137.9 (Ar*C*), 128.6-128.0 (Ar*C*H), 114.3 (C9), 114.1 (C1, vinyl CH=*C*H_2), 83.9 (C4), 78.5 (C3), 77.2 (C5), 75.2, 73.3

(*C*H_2Ph), 70.3 (C7), 39.4 (C6). HRMS(ESI): Calcd. for $C_{25}H_{30}O_4NH_4^+$ m/z 412.2482; found m/z 412.2484. **31b**: R_f (Pentane/EtOAc 5:1) 0.43. ^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm) 7.39-7.25 (m, 10H, Ar*H*), 6.14 (dd, J_{trans} 17.3 Hz, J_{cis} 10.7 Hz, 1H, H2), 6.07 (dd, J_{trans} 17.3 Hz, J_{cis} 10.7 Hz, 1H, vinyl C*H*=CH_2), 5.78 (ddd, J_{trans} 16.3 Hz, J_{cis} 10.4 Hz, $J_{8,7}$ 5.9 Hz, 1H, H8), 5.44 (dd, J_{trans} 17.1 Hz, J_{gem} 1.3 Hz, 1H, H1a), 5.40 (dd, J_{trans} 16.8 Hz, J_{gem} 1.2 Hz, 1H, vinyl CH=C*H*H), 5.24-5.13 (m, 3H, H1b, vinyl CH=CH*H*, H9a), 5.08 (d, 1H, H9b), 4.76 (d, J_{gem} 11.4 Hz, 1H, C*H*HPh), 4.69 (d, J_{gem} 11.4 Hz, 1H, CH*H*Ph), 4.64 (d, J_{gem} 11.0 Hz, 1H, C*H*HPh), 4.49 (d, J_{gem} 11.0 Hz, 1H, CH*H*Ph), 4.22-4.15 (m, 1H, H7), 3.92 (dt, $J_{5,6a}$ 7.1 Hz, $J_{5,4/6b}$ 5.2 Hz, 1H, H5), 3.55 (d, 1H, H4), 3.44 (bs, 1H, O*H*), 2.64 (bs, 1H, O*H*), 2.00-1.82 (m, 2H, H6a+b). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 140.8, 140.7, 140.5 (*C*H=CH_2), 138.2, 137.7 (Ar*C*), 128.6-128.0 (Ar*C*H), 114.7, 114.1, 114.0 (CH=*C*H_2), 83.6 (C4), 78.6 (C5), 78.4 (C3), 75.3, 72.9 (*C*H_2Ph), 71.4 (C7), 39.4 (C6). HRMS(ESI): Calcd. for $C_{25}H_{30}O_4NH_4^+$ m/z 412.2482; found m/z 412.2488.

2-Deoxy-5,5-dimethyl-α/β-D-xylopyranose (32) and (3*S*,4*R*)-3,4-bis(benzyloxy)-2-methyl-heptane-2,6-diol (33)

Methylmagnesium chloride (3 M in THF, 1.9 mL, 5.7 mmol, 9 eq) and TMEDA (1.0 mL, 6.7 mmol, 11 eq) were mixed at rt and added to **29** (0.214 g, 0.63 mmol) at -78 °C. The reaction mixture was stirred at this temperature for 2 h and was then allowed to reach rt and stirred at this temperature for 1 h. The reaction was quenched with water and 1 M aq. HCl. The aqueous phase was extracted with CH_2Cl_2 (x3). The organic phase was washed with brine, dried over $MgSO_4$, filtered and concentrated. Flash column chromatography (CH_2Cl_2/EtOAc 19:1 → 5:1) afforded **32** (0.119 g, 0.35 mmol, 56%) as a 0.4:1 mixture of α/β-anomers and **33** (0.044 g, 0.12 mmol, 19%) as a 1:0.6 mixture of isomers. **32**: R_f (CH_2Cl_2/EtOAc 5:1) 0.57. **32α**: ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.38-7.26 (m, 10H, Ar*H*), 5.35 (t, $J_{1,2ax/2eq}$ 3.6 Hz, 1H, H1), 4.89 (d, J_{gem} 11.4 Hz, 1H, C*H*HPh), 4.69-4.59 (m, 3H, CH*H*Ph, CH_2Ph), 4.04 (ddd, $J_{3,2ax}$ 8.8 Hz, $J_{3,4}$ 7.7 Hz, $J_{3,2eq}$ 4.4 Hz, 1H, H3), 3.23 (d, 1H, H4), 2.80 (bs, 1H, O*H*), 2.22 (dt, $J_{2eq,2ax}$ 13.2 Hz, 1H, H2eq), 1.83 (ddd, 1H, H2ax), 1.40 (s, 3H, CH_3), 1.31 (s, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 138.8, 138.7 (Ar*C*), 128.6-127.8 (Ar*C*H), 91.9 (C1), 83.8 (C4), 77.4 (C5), 75.2 (*C*H_2Ph), 74.6 (C3), 72.0 (*C*H_2Ph), 36.1 (C2), 28.0, 25.3 (*C*H_3). **32β**: ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.38-7.26 (m, 10H, Ar*H*), 5.02-4.97 (m, 2H, H1, C*H*HPh), 4.69-4.59 (m, 3H, CH*H*Ph, CH_2Ph), 3.75 (ddd, $J_{3,2ax}$ 11.5 Hz, $J_{3,4}$ 9.2 Hz, $J_{3,2eq}$ 4.9 Hz, 1H, H3), 3.27 (d, 1H, H4), 3.11 (bs, 1H, O*H*), 2.43 (ddd, $J_{2eq,2ax}$ 12.4 Hz, $J_{2eq,1}$ 2.3 Hz, 1H, H2eq), 1.53 (td, $J_{2ax,1}$ 10.0 Hz, 1H, H2ax), 1.31 (s, 3H, CH_3), 1.22

(s, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 138.9, 138.5 (Ar*C*), 128.6-127.8 (Ar*C*H), 89.9 (C1), 85.4 (C4), 77.4 (C5), 75.8 (C3), 75.7, 71.9 (*C*H_2Ph), 39.5 (C2), 28.8, 19.6 (*C*H_3). HRMS(ESI): Calcd. for $C_{21}H_{26}O_4Na^+$ m/z 365.1723; found m/z 365.1724. **33**: R_f (Pentane/EtOAc 1:1) 0.59. **33a**: ^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm) 7.39-7.25 (m, 10H, Ar*H*), 4.88 (d, J_{gem} 11.3 Hz, 1H, C*H*HPh), 4.77 (d, J_{gem} 11.0 Hz, 1H, C*H*HPh), 4.63 (d, J_{gem} 11.3 Hz, 1H, CH*H*Ph), 4.52 (d, J_{gem} 11.0 Hz, 1H, CH*H*Ph), 3.94-3.87 (m, 2H, H4, H6), 3.34 (d, $J_{3,4}$ 5.3 Hz, 1H, H3), 1.94-1.70 (m, 2H, H5a, H5b), 1.28 (s, 6H, C(CH_3)$_2$), 1.15 (d, $J_{7,6}$ 6.2 Hz, 3H, CH_3(H7)).^{13}C-NMR (100 MHz, $CDCl_3$): δ (ppm) 138.3, 137.7 (Ar*C*), 128.7-127.9 (Ar*C*H), 85.4 (C3), 79.4 (C4), 75.1, 73.2 (*C*H_2Ph), 73.1 (C2), 67.6 (C6), 42.3 (C5), 27.4 (C(*C*H_3)(CH$_3$)), 26.6 (C(CH$_3$)(*C*H_3)), 23.9 (*C*H_3). **33b**: ^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm) 7.39-7.25 (m, 10H, Ar*H*), 4.85 (d, J_{gem} 11.2 Hz, 1H, C*H*HPh), 4.74 (d, J_{gem} 11.2 Hz, 1H, C*H*HPh), 4.61 (d, J_{gem} 11.2 Hz, 1H, CH*H*Ph), 4.57 (d, J_{gem} 11.2 Hz, 1H, CH*H*Ph), 4.04-3.95 (m, 2H, H4, H6), 3.32 (d, $J_{3,4}$ 5.1 Hz, 1H, H3), 1.94-1.70 (m, 2H, H5a, H5b), 1.28 (s, 6H, C(CH_3)$_2$), 1.19 (d, $J_{7,6}$ 6.1 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ (ppm) 138.4, 138.3 (Ar*C*), 128.7-127.9 (Ar*C*H), 85.8 (C3), 76.6 (C4), 75.1 (*C*H_2Ph), 73.4 (*C*H_2Ph), 73.2 (C2), 65.3 (C6), 42.4 (C5), 27.3 (C(*C*H_3)(CH$_3$)), 26.8 (C(CH$_3$)(*C*H_3)), 24.2 (*C*H_3). HRMS(ESI): Calcd. for $C_{22}H_{30}O_4Na^+$ m/z 381.2036; found m/z 381.2042.

(1*R*,2*S*,3*S*,4*R*,5*S*,6*R*)-3,4,5-Tris(benzyloxy)-bicyclo[4.3.0]non-7-ene-2,6-diol (34)

4 (0.657 g, 1.3 mmol) was dissolved in dry CH_2Cl_2 (13 mL). The solution was heated to reflux and Hoveyda-Grubbs 2nd generation catalyst (0.043 g, 0.069 mmol, 0.05 eq) was added. The reaction mixture was stirred at reflux temperature for 2 h. The crude mixture was concentrated and purified by flash column chromatography (Pentane/EtOAc 4:1 → 2:1) to give **34** as white crystals (0.419 g, 0.89 mmol, 68%). R_f (CH_2Cl_2/EtOAc 10:1) 0.31. $[\alpha]_D^{299K}$ +23.9 (*c* 2, $CHCl_3$). Mp 95.3-97.3 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.35-7.15 (m, 15H, Ar*H*), 6.07 (d, $J_{7,8}$ 5.4 Hz, 1H, H7), 5.78 (d, 1H, H8), 4.96 (d, J_{gem} 10.5 Hz, 1H, C*H*HPh), 4.84 (d, J_{gem} 11.3 Hz, 1H, C*H*HPh), 4.77 (d, J_{gem} 10.5 Hz, 1H, CH*H*Ph), 4.75 (d, J_{gem} 11.8 Hz, 1H, C*H*HPh), 4.65 (d, J_{gem} 11.3 Hz, 1H, CH*H*Ph), 4.63 (d, J_{gem} 11.8 Hz, 1H, CH*H*Ph), 4.23 (d, $J_{OH,2}$ 9.3 Hz, 1H, O*H*(2)), 4.18-4.11 (m, 2H, H2, H4), 3.49 (dd, $J_{3,4}$ 9.4 Hz, $J_{3,2}$ 3.4 Hz, 1H, H3), 3.43 (d, $J_{5,4}$ 8.7 Hz, 1H, H5), 3.05 (s, 1H, O*H*(6)), 2.77 (dd, $J_{9a,9b}$ 15.7 Hz, $J_{9a,1}$ 10.0 Hz, 1H, H9a), 2.23 (dd, $J_{9b,1}$ 6.8 Hz, 1H, H9b), 1.58 (t, 1H, H1). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 138.9 (Ar*C*), 138.3 (C7), 138.3, 138.2 (Ar*C*), 133.2 (C8), 128.6-127.7 (Ar*C*H), 86.0 (C6), 84.6 (C3), 84.1 (C5), 82.8 (C4), 76.5, 75.2, 72.0 (*C*H_2Ph), 67.8 (C2), 45.5 (C1), 30.5 (C9). HRMS (ESI): Calcd. for $C_{30}H_{32}O_5Na^+$ m/z 495.2142; found m/z 495.2146.

(1*R*,2*S*,3*S*,4*R*,5*S*,6*S*,7*S*,8*S*)-3,4,5-Tris(benzyloxy)-bicyclo[4.3.0]nonane-2,6,7,8-tetraol (35)

34 (0.270 g, 0.57 mmol) was dissolved in a 1:1:1 mixture of H_2O/MeCN/Me_2CO (10 mL). *N*-Methylmorpholine *N*-oxide (0.110 g, 0.94 mmol, 1.6 eq) was added. The mixture was cooled to 0 °C before the addition of OsO_4 (2.5 wt.% in *t*BuOH, 0.7 mL, 0.056 mmol, 0.1 eq). The reaction mixture was stirred at rt for 4 days before the addition of sat. aq. Na_2SO_3. After extraction with EtOAc (x3), the combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (CH_2Cl_2/EtOAc 4:1 → 2:1) to give **35** (0.214 g, 0.42 mmol, 74%) as a white solid. R_f (EtOAc) 0.56. $[\alpha]_D^{299K}$ + 45.0 (*c* 2, $CHCl_3$). Mp 141.2-142.6 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.42-7.21 (m, 15H, Ar*H*), 4.96 (d, J_{gem} 10.8 Hz, 1H, C*H*HPh), 4.89 (d, J_{gem} 11.4 Hz, 1H, C*H*HPh), 4.88 (d, J_{gem} 10.8 Hz, 1H, CH*H*Ph), 4.78 (d, J_{gem} 11.4 Hz, 1H, CH*H*Ph), 4.72 (s, 2H, CH_2Ph), 4.54 (ddd, $J_{8,9a}$ 8.3 Hz, $J_{8,7}$ 5.2 Hz, $J_{8,9b}$ 2.5 Hz, 1H, H8), 4.12-4.07 (m, 2H, H2, H4), 3.72 (d, $J_{5,4}$ 9.4 Hz, 1H, H5), 3.64 (d, 1H, H7), 3.47 (dd, $J_{3,4}$ 9.5 Hz, $J_{3,2}$ 3.3 Hz, 1H, H3), 3.39 (bs, 1H, O*H*), 2.74 (bs, 1H, O*H*), 2.52 (ddd, $J_{9a,9b}$ 13.5 Hz, $J_{9a,1}$ 11.7 Hz, 1H, H9a), 2.32 (bs, 1H, O*H*), 1.98 (ddd, $J_{1,9b}$ 9.2 Hz, $J_{1,2}$ 2.2 Hz, 1H, H1), 1.80 (bs, 1H, O*H*), 1.49 (ddd, 1H, H9b). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 138.8, 138.7, 138.0 (Ar*C*), 128.5-127.6 (Ar*C*H), 85.6 (C6), 83.6 (C3), 81.2 (C4), 80.0 (C5), 76.2 (*C*H_2Ph), 74.6 (C7), 74.5, 72.6 (*C*H_2Ph), 71.5 (C8), 68.5 (C2), 39.2 (C1), 31.3 (C9). HRMS (ESI): Calcd. for $C_{30}H_{34}O_7NH_4^+$ m/z 524.2643; found m/z 524.2647.

Derivatization of 22, 24 and 30

***O*-((1*R*,2*S*,3*S*,4*S*,5*R*,6*R*)-2-Allyl-4,5,6-tris(benzyloxy)-3-hydroxy-3-vinylcyclohexyl) (1*S*,4*R*)-camphanoate (36)**

22 (0.050 g, 0.10 mmol) was dissolved in dry CH_2Cl_2 (2 mL). Et_3N (0.08 mL, 0.57 mmol, 5.7 eq), DMAP (0.012 g, 0.11 mmol, 1.1 eq) and (1*S*)-(-)-camphanic chloride (0.056 g, 0.26 mmol, 2.6 eq) were added. The reaction mixture was stirred at 40 °C overnight. 1M aq. HCl was added. The mixture was extracted with CH_2Cl_2 (x3). The combined organic phases were washed with sat. aq. $NaHCO_3$, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (Pentane/Et_2O 2:1) to give **36** (0.055 g, 0.081 mmol, 81%), which was crystallized from CH_2Cl_2 and heptane to give colorless crystals. R_f (Pentane/Et_2O 2:1) 0.50. $[\alpha]_D^{299K}$ -29.6 (*c* 2.0, $CHCl_3$). Mp 125.1-126.9 °C (CH_2Cl_2/Heptane). ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.40-7.25 (m, 13H, Ar*H*), 7.16-7.09 (m, 2H, Ar*H*), 5.96 (ddd, J_{trans} 17.2 Hz, J_{cis} 10.7 Hz,

$J_{H,OH}$ 1.4 Hz, 1H, vinyl C*H*=CH_2), 5.84 (t, $J_{1,2/6}$ 3.4 Hz, 1H, H1), 5.78 (dddd, J_{trans} 17.0 Hz, J_{cis} 10.1 Hz, J_{vic} 8.0 Hz, J_{vic} 6.6 Hz, 1H, allyl C*H*=CH_2), 5.57 (dd, J_{gem} 2.0 Hz, 1H, vinyl CH=C*H*H), 5.30 (dd, 1H, vinyl CH=CH*H*), 5.06 (d, J_{cis} 10.1 Hz, 1H, allyl CH=C*H*H), 5.00 (dd, J_{trans} 17.0 Hz, ^4J 1.4 Hz, 1H, allyl CH=CH*H*), 4.70 (d, J_{gem} 11.8 Hz, 1H, C*H*HPh), 4.61 (d, J_{gem} 11.4 Hz, 1H, C*H*HPh), 4.49 (d, J_{gem} 11.4 Hz, 1H, C*H*HPh), 4.47 (d, J_{gem} 11.4 Hz, 1H, CH*H*Ph), 4.41 (d, J_{gem} 11.8 Hz, 1H, CH*H*Ph), 4.33 (d, J_{gem} 11.4 Hz, 1H, CH*H*Ph), 4.08 (d, 1H, O*H*), 3.84-3.77 (m, 2H, H5, H6), 3.60 (d, 1H, H4), 2.31-2.13 (m, 3H, allyl CH_2, C*H*H-CH_2), 2.03 (dt, $J_{2,CHH}$ 10.5 Hz, $J_{2,CHH}$ 3.4 Hz, 1H, H2), 1.77 (ddd, J_{gem} 13.8 Hz, J_{vic} 9.0 Hz, J_{vic} 4.8 Hz, 1H, CH*H*-CH_2), 1.56-1.40 (m, 2H, CH_2-CH_2), 1.00 (s, 3H, CH_3), 0.88 (s, 6H, C(CH_3)$_2$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 178.2 (*C*=O), 167.1 (*C*=O), 140.7 (vinyl *C*H=CH_2), 138.2, 137.5, 137.2 (Ar*C*), 136.1 (allyl *C*H=CH_2), 128.6-127.8 (Ar*C*H), 117.6 (allyl CH=*C*H_2), 116.0 (vinyl CH=*C*H_2), 91.7 (O_2C-*C*-OCO), 80.9 (C4), 77.0 (C5), 75.1 (C3), 74.4 (C6), 74.0, 73.6, 71.3 (*C*H_2Ph), 69.1 (C1), 55.0, 54.1 (C_Q), 41.7 (C2), 30.9 (*C*H_2-CH_2), 29.5 (allyl *C*H_2), 29.1 (CH_2-*C*H_2), 16.9 (C(*C*H_3)CH_3), 16.9 (C(CH_3)*C*H_3), 9.72 (*C*H_3). HRMS(ESI): Calcd. for $C_{42}H_{48}O_8NH_4^+$ m/z 698.3687; found m/z 698.3699.

_O_-((1_R_,2_S_,3_S_,4_R_,5_R_,6_S_)-2-Allyl-4,5,6-tris(benzyloxy)-3-hydroxy-3-vinylcyclohexyl) (1_S_,4_R_)-camphanoate (37)

24 (0.101 g, 0.20 mmol) was dissolved in dry CH_2Cl_2 (4 mL). Et_3N (0.17 mL, 1.2 mmol, 6 eq), DMAP (0.011 g, 0.10 mmol, 0.5 eq) and (1*S*)-(-)-camphanic chloride (0.109 g, 0.50 mmol, 2.5 eq) were added. The reaction mixture was stirred at 40 °C overnight. The reaction mixture was allowed to reach rt before it was quenched with 1 M aq. HCl. The aqueous phase was extracted with CH_2Cl_2 (x3). The combined organic layers were washed with 1 M aq. HCl, sat. aq. Na_2CO_3 and brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by flash column chromatography (Pentane/Et_2O 4:1) to afford **37** (0.089 g, 0.13 mmol, 64%) as colorless crystals. R_f (Pentane/Et_2O 2:1) 0.36. $[\alpha]_D^{293K}$ +26.5 (*c* 2.0, $CHCl_3$). Mp 130.1-132.5 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.31-7.18 (m, 12H, Ar*H*), 7.16-7.11 (m, 3H, Ar*H*), 5.61-5.44 (m, 3H, allyl C*H*=CH_2, vinyl C*H*=CH_2, vinyl CH=C*H*H), 5.27 (dd, J_{cis} 7.8 Hz, J_{gem} 4.5 Hz, 1H, vinyl CH=C*H*H), 5.13 (t, $J_{1,2/6}$ 2.9 Hz, 1H, H1), 5.96-4.87 (m, 2H, allyl CH=CH_2), 4.67 (d, J_{gem} 11.2 Hz, 1H, C*H*HPh), 4.54 (d, J_{gem} 11.9 Hz, 1H, C*H*HPh), 4.47 (d, J_{gem} 11.8 Hz, 1H, C*H*HPh) 4.44-4.35 (m, 3H, 3xCH*H*Ph), 3.86 (t, $J_{6,5}$ 2.9 Hz, 1H, H6), 3.78 (bs, 1H, O*H*), 3.76 (t, $J_{5,4}$ 2.9 Hz, 1H, H5), 3.49 (d, 1H, H4), 2.35-2.24 (m, 1H, allyl C*H*H), 2.24-2.13 (m, 1H, allyl CH*H*), 1.98-1.84 (m, 2H, H2, C*H*H), 1.55-1.46 (m, 1H, C*H*H), 1.45-1.36 (m, 1H, CH*H*), 1.32 (ddd, J_{gem} 12.4 Hz, J_{vic} 9.0 Hz, J_{vic} 3.6 Hz, 1H, CH*H*), 0.96 (s, 3H, CH_3), 0.90 (s, 3H, CH_3), 0.85 (s, 3H, CH_3). ^{13}C-NMR

(100 MHz, $CDCl_3$): δ_C (ppm) 177.9 (*C*=O), 167.0 (*C*=O), 140.5 (vinyl *C*H=CH_2), 138.0, 137.6, 137.1 (Ar*C*), 136.1 (allyl *C*H=CH_2), 128.9-127.9 (Ar*C*H), 117.3 (allyl CH=*C*H_2), 116.6 (vinyl CH=*C*H_2), 91.4 (O_2C-*C*-OCO), 77.7 (C3), 77.6 (C4), 76.3 (C5), 74.7 (*C*H_2Ph), 74.4 (C6), 73.2, 72.8 (*C*H_2Ph), 70.5 (C1), 54.9 (C_Q), 54.1 (C_Q), 42.3 (C2), 30.1 (*C*H_2), 29.0 (*C*H_2), 28.8 (allyl *C*H_2), 17.0 (*C*H_3), 16.9 (*C*H_3), 9.8 (*C*H_3). HRMS(ESI): Calcd. for $C_{42}H_{48}O_8NH_4^+$ m/z 698.3687; found m/z 698.3681.

***O*-((1*R*,2*R*,3*R*,4*S*,5*R*)-2-Allyl-4,5-bis(benzyloxy)-3-hydroxy-3-vinylcyclohexyl) (1*S*,4*R*)-camphanoate (38)**

30 (0.052 g, 0.13 mmol) was dissolved in dry CH_2Cl_2 (2 mL). Et_3N (0.11 mL, 0.79 mmol, 6 eq), DMAP (0.015 g, 0.13 mmol, 1 eq) and (1*S*)-(-)-camphanic chloride (0.072 g, 0.33 mmol, 2.5 eq) were added. The reaction mixture was stirred at 40 °C overnight before the addition of 1 M aq. HCl. The mixture was extracted with CH_2Cl_2 (x3) and the combined organic phases were washed with sat. aq. $NaHCO_3$ and brine. The organic phase was dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (Pentane/EtOAc 10:1 → 5:1) to give **38** (0.065 g, 0.11 mmol, 86%), which was obtained as colorless crystals after recrystallization from CH_2Cl_2. R_f (Pentane/Et_2O 2:1) 0.56. $[\alpha]_D^{299K}$ -39.2 (*c* 1, $CHCl_3$). Mp 104.0-108.5 °C (CH_2Cl_2). ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.38-7.21 (m, 10H, Ar*H*), 5.75 (dd, J_{trans} 17.0 Hz, J_{cis} 10.5 Hz, 1H, vinyl C*H*=CH_2), 5.65 (m, 1H, allyl C*H*=CH_2), 5.43 (d, 1H, vinyl CH=C*H*H), 5.37 (d, 1H, vinyl CH=CH*H*), 5.31-5.26 (m, 1H, H1), 5.01 (d, J_{cis} 10.0 Hz, 1H, allyl CH=C*H*H), 4.95 (d, J_{trans} 17.0 Hz, 1H, allyl CH=CH*H*), 4.85 (d, J_{gem} 10.2 Hz, 1H, C*H*HPh), 4.68-4.61 (m, 3H, CH*H*Ph, C*H*$_2$Ph), 3.88 (ddd, $J_{5,6ax}$ 11.5 Hz, $J_{5,4}$ 9.2 Hz, $J_{5,6eq}$ 4.4 Hz, 1H, H5), 3.36 (d, 1H, H4), 2.61-2.36 (m, 3H, O*H*, H6a, C*H*H-CH_2), 2.33-2.21 (m, 1H, allyl C*H*H), 2.17-2.04 (m, 1H, allyl CH*H*), 2.04-1.94 (m, 1H, CH*H*-CH_2), 1.93-1.82 (m, 1H, CH_2-C*H*H), 1.73-1.54 (m, 3H, H2, H6b, CH_2-CH*H*), 1.08 (s, 3H, C*H*$_3$), 0.99 (s, 3H, C*H*$_3$), 0.85 (s, 3H, C*H*$_3$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 177.9 (*C*=O), 166.7 (*C*=O), 142.3 (vinyl *C*H=CH_2), 138.5, 138.1 (Ar*C*), 136.0 (allyl *C*H=CH_2), 128.6-127.7 (Ar*C*H), 117.5 (allyl CH=*C*H_2), 116.3 (vinyl CH=*C*H_2), 91.3 (O_2C-*C*-OCO), 85.8 (C4), 78.4 (C3), 76.2 (*C*H_2Ph), 74.9 (C5), 72.5 (*C*H_2Ph), 70.5 (C1), 54.9, 53.8 (C_Q), 45.0 (C2), 34.6 (C6), 30.9 (*C*H_2-CH_2), 29.2 (CH_2-*C*H_2), 29.0 (allyl *C*H_2), 17.1 (*C*H_3), 16.9 (*C*H_3), 9.8 (*C*H_3). HRMS(ESI): Calcd. for $C_{35}H_{42}O_7NH_4^+$ m/z 592.3269; found m/z 592.3272.

Determination of stereochemistry of 35

The compound **35** was derivatized to **39** to induce crystallinity. However, no crystals of **39** were obtained. Therefore, 2D-NOESY and 1D-ROESY NMR experiments were carried out for determination of stereochemistry of **39** (and thereby also of **35**) (Supporting Information).

(1*R*,2*S*,3*S*,4*R*,5*S*,6*R*,7*R*,8*S*)-2-*O*-((1*S*,4*R*)-Camphanoyl)-3,4,5-tris(benzyloxy)-7,8-*O*-isopropylidene-bicyclo[4.3.0]nonane-2,6,7,8-tetraol (39)

35 (0.124 g, 0.25 mmol) was dissolved in dry acetone (12 mL). *p*-TsOH (0.057 g, 0.30 mmol, 1.2 eq) and $MgSO_4$ was added. The reaction mixture was stirred at rt for 15 min before it was neutralized with Et_3N. The mixture was concentrated *in vacuo*, diluted with CH_2Cl_2, washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude residue was dissolved in dry CH_2Cl_2 (12 mL). Et_3N (0.17 mL, 1.2 mmol, 5 eq), DMAP (0.028 g, 0.25 mmol, 1 eq) and (1*S*)-(-)-camphanic chloride (0.143 g, 0.66 mmol, 2.7 eq) were added. The reaction mixture was stirred at rt overnight. The solvent was evaporated *in vacuo* and the crude residue was purified by flash column chromatography (Pentane/EtOAc 4:1 → 3:1) to give **39** (0.141 g, 0.19 mmol, 79%) as a colorless oil. R_f (Pentane/EtOAc 3:1) 0.58. $[\alpha]_D^{299K}$ +34.0 (*c* 2, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H (ppm) 7.39-7.24 (m, 15H, Ar*H*), 5.83 (t, $J_{2,1/3}$ 3.0 Hz, 1H, H2), 4.93 (d, J_{gem} 10.6 Hz, 1H, C*H*HPh), 4.85 (d, J_{gem} 11.0 Hz, 1H, C*H*HPh), 4.83-4.76 (m, 3H, 2xCH*H*Ph, H8), 4.73 (d, J_{gem} 11.0 Hz, 1H, C*H*HPh), 4.61 (d, J_{gem} 11.0 Hz, 1H, CH*H*Ph), 4.18 (d, $J_{7,8}$ 5.5 Hz, 1H, H7), 4.01 (t, $J_{4,5/3}$ 9.5 Hz, 1H, H4), 3.77 (d, 1H, H5), 3.64 (dd, 1H, H3), 2.55-2.44 (m, 2H, C*H*H-CH_2, O*H*), 2.07-1.80 (m, 4H, H1, H9a, CH*H*-CH_2, CH_2-C*H*H), 1.74 (dd, $J_{9b,9a}$ 12.6 Hz, $J_{9b,1}$ 5.7 Hz, 1H, H9b), 1.65 (ddd, J_{gem} 13.3 Hz, J_{vic} 9.3 Hz, J_{vic} 4.2 Hz, 1H, CH_2-CH*H*), 1.42 (s, 3H, CH_3), 1.29 (s, 3H, CH_3), 1.07 (s, 6H, 2xCH_3), 0.80 (s, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C (ppm) 178.0 (*C*=O), 166.9 (*C*=O), 138.8, 138.6, 137.7 (Ar*C*), 128.5-127.7 (Ar*C*H), 110.5 (isoprop. *C*$(CH_3)_2$), 91.5 (O_2C-*C*-OCO), 83.5 (C7), 81.6 (C6), 81.5 (C3), 80.9 (C4), 80.6 (C5), 79.5 (C8), 76.3, 74.9, 72.8 (*C*H_2Ph), 55.0, 54.3 (C_Q), 38.9 (C1), 30.6 (*C*H_2-CH_2), 30.5 (C9), 29.2 (CH_2-*C*H_2), 26.3, 24.0, 16.9, 16.5, 9.8 (*C*H_3). HRMS(ESI): Calcd. for $C_{43}H_{50}O_{10}NH_4^+$ m/z 744.3742; found m/z 744.3749.

Supporting Information

Schemes for derivatization of **22**, **24**, **30** and **35**. Determination of stereochemistry of **35** and **39**, X-ray diffraction analysis data, ^{1}H- and ^{13}C-NMR spectra (PDF).

Crystal structure data (CIF).

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