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ORIGINAL PAPER

Synthesis of 3-deoxy-2-uloses via the indium-mediated allylation reaction

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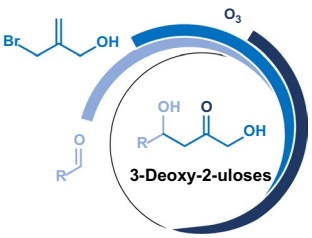
Abstract

We utilized the indium-mediated allylation reaction for the synthesis of carbohydrate structures containing the 3-deoxy-2-ulose motif, a barely investigated compound class. The stereoselective outcome can be controlled by the presence or absence of a chelating group in α-position to the carbonyl function. By introduction of an UV-active allyl building block, we enabled epimer separation by HPLC towards the synthesis of 3-deoxy-D-*glycero*-D-*galacto*-2-nonulose, the carboxyl-reduced analogue of widely distributed 3-deoxy-D-*glycero*-D-*galacto*-nonulosonic acid (Kdn). Ozonolysis of the introduced 2-*C*-methylidenepropan-1-ol motif provided the desired 3-deoxy-2-uloses.

Graphical abstract



Keywords Carbohydrates · 3-Deoxy-2-uloses · Indium-mediated allylation · Organometallic compounds · Ozonolysis

Introduction

The indium-mediated allylation reaction has proven to be an efficient and reliable C–C bond formation method offering many advantages over traditional organometallic compounds [1–3]. Typically, it allows for high regio-, enantio-, as well as diastereoselectivity and tolerates a wide range of functional groups [4–7]. Moreover, indium-mediated allylations can be performed in water, rendering the possibility to fully avoid the use of dry and flammable solvents. This allows for safer and environmentally friendly chemistry, satisfying the demands of green chemistry [1–4]. The reactions generally proceed under mild conditions at room temperature without any promoter, in contrast to the use of other metals such as zinc or tin, which requires acid catalysis, elevated temperatures or sonication, often leading to increasing amounts of undesired side products [8, 9]. Because of

Dedicated to Professor Dr. Heinz Falk on the happy occasion of his 80th birthday anniversary.

Walther Schmid: deceased, Dec 2017.

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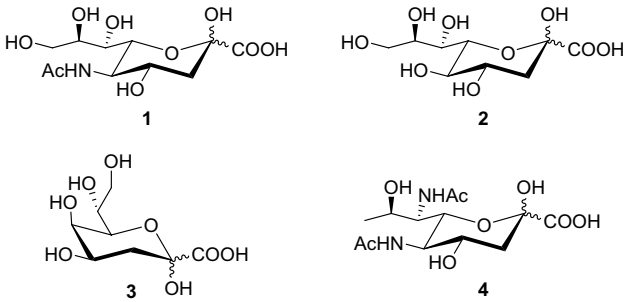
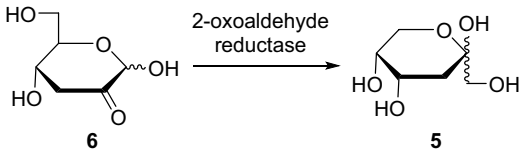


Fig. 1 Natural products (Neu5Ac, **1**), (Kdn, **2**), (Kdo, **3**), (Leg, **4**) synthesized via an indium-mediated allylation reaction

Scheme 1

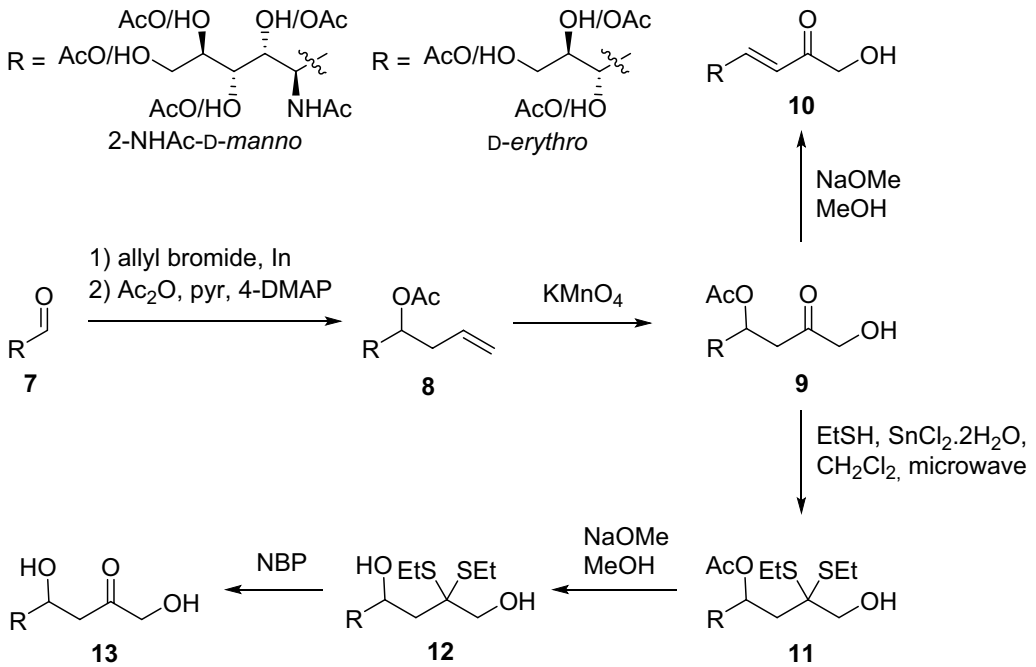


its superior reactivity, the indium-mediated allylation has been applied in numerous natural product syntheses by us and others, e.g. *N*-acetylneuraminic acid (Neu5Ac, **1**) [10, 11], 3-deoxy-D-*glycero*-D-*galacto*-nonulosonic acid (Kdn, **2**) [12], 3-deoxy-D-*manno*-2-octulosonic acid (Kdo, **3**) [13] or legionaminic acid (Leg, **4**) [14, 15] (Fig. 1).

An intriguing compound class that has hardly been addressed by organic synthesis is the 3-deoxy-2-ulose representing an interesting and rare subcategory of the ketose family. Being the C-1 reduced analogue of naturally essential ulosonic acids, these structures have potential biological importance and therefore are attractive target molecules [16]. A naturally occurring representative is 3-deoxy-D-*erythro*-2-hexulose (3-deoxy-D-fructose, **5**), which has been found in mammalian blood and urine [17–19] in concentrations that are elevated in diabetes [20]. As degradation product, it arises from 3-deoxyglucosone (**6**), a key intermediate in the nonenzymatic polymerization and browning of proteins by glucose (Maillard reaction), which is also formed in vivo by D-fructose [21], D-fructose-3-phosphate [22], or Amadori adducts to proteins [19]. In mammals, a significant proportion of 3-deoxyglucosone (**6**) is reduced to 3-deoxy-D-*erythro*-2-hexulose (**5**) presumably to decrease its reactivity, thus being less damaging to tissues (Scheme 1) [23].

An earlier approach of our group regarding the synthesis of 3-deoxy-2-uloses utilized the indium-mediated allylation reaction employing allyl bromide for the elongation of different aldoses, such as *N*-acetyl-D-mannosamine or D-erythrose (Scheme 2). The terminal allyl moiety of **8** was subsequently oxidized using potassium permanganate under acidic conditions yielding the desired 3-deoxy-2-ulose functionality in **9**. However, the acidity of the 3-deoxy position prohibited standard de-*O*-acetylation methods as elimination product **10** was formed exclusively. Hence, a thioketal moiety was introduced at position C-2 to give **11** and enabled de-*O*-acetylation to **12**. Final removal of the thioketal yielded 3-deoxy-2-ulose **13** [24].

Scheme 2



Herein, we report a novel approach towards 3-deoxy-2-uloses by elongating selected aldoses using 2-(bromomethyl)prop-2-en-1-ol (**14**) in an indium-mediated allylation reaction. The presence or absence of a chelating group next to the carbonyl function directs the formation of the corresponding *syn*- or *anti*-product respectively, as we verify during the synthesis of 3-deoxy-D-*erythro*-2-hexulose (**5**) and 3-deoxy-D-*gluco*-2-octulose (**15**). Thus, introduction of an appropriate protecting group in α-position provides diastereoselective control. A benzyl protected allyl building block (2-(benzyloxymethyl)allyl bromide, **16**) can be employed to enable UV detection for epimer separation by HPLC of the epimeric mixture obtained after the elongation reaction.

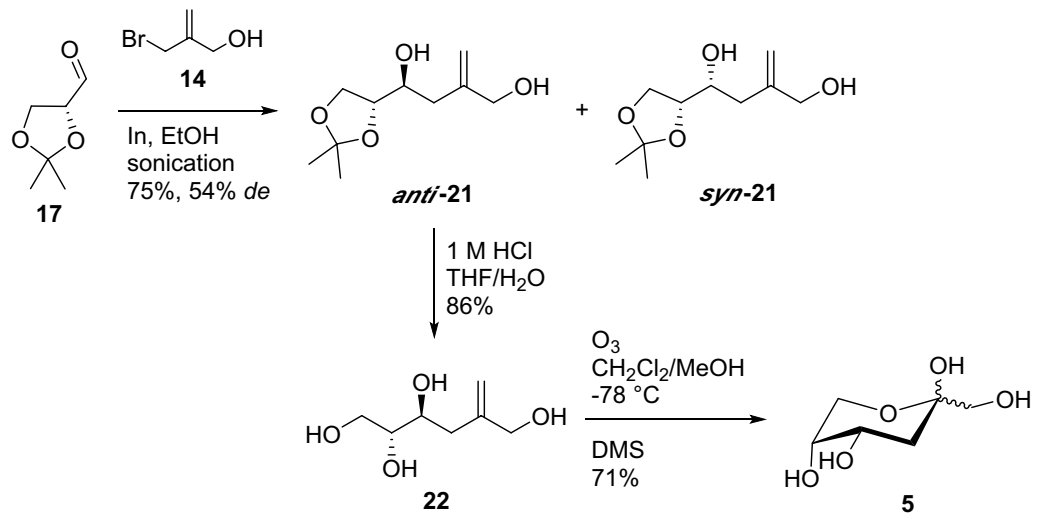
Results and discussions

The indium-mediated allylation using 2-(bromomethyl)prop-2-en-1-ol (**14**) was applied on three different aldoses—2,3-*O*-isopropylidene-D-glyceraldehyde (**17**), D-arabinose (**18**), and D-mannose (**19**)—introducing a 2-*C*-methylidenepropan-1-ol motif. Allyl component **14** was synthesized starting from triethyl phosphonoacetate (**20**) performing a known Horner-Wadsworth-Emmons protocol [25], followed by bromination [25] and DIBAL-H-reduction [26]. Due to the volatility of the allyl building block **14**, the yield for its preparation is modest. After allylation, the generated epimeric mixtures could be separated by conventional silica gel chromatography, when employing 2,3-*O*-isopropylidene-D-glyceraldehyde (**17**) and D-arabinose (**18**) as starting materials. However, for the separation of the epimers obtained from the elongation of D-mannose (**19**), HPLC had to be performed. To enable UV-detection during HPLC, a benzyl protected allyl building block **16** has been used. Final ozonolysis of the elongated aldoses provided the desired 3-deoxy-2-uloses in good to excellent yields.

2,3-*O*-Isopropylidene-D-glyceraldehyde (**17**) has been synthesized from D-mannitol via a known isopropylidene-protection procedure [27] and subsequent oxidative diol cleavage [28]. During the indium-mediated allylation, the absolute configuration of the newly formed stereocenter at position C-4 is influenced by the presence or absence of a chelating group in α-position to the reacting carbonyl function. Hence, an isopropylidene-protected hydroxyl function in neighboring position acts as weak chelating group and allows for the preferred formation of the *anti*-product (2,3-dideoxy-5,6-*O*-isopropylidene-2-*C*-methylidene-D-*erythro*-hexitol, ***anti*-21**) as demonstrated by the elongation of 2,3-*O*-isopropylidene-D-glyceraldehyde (**17**) (Scheme 3). The resulting epimeric mixture was separated by column chromatography. Removal of the isopropylidene group under acidic conditions and subsequent ozonolysis furnished the keto functionality at position C-2. 3-Deoxy-D-*erythro*-2-hexulose (**5**) was obtained in a yield of 35% over 3 steps.

The allylation of D-arabinose (**18**) employing 2-(bromomethyl)prop-2-en-1-ol (**14**) favored the formation of the corresponding *syn*-product (1,4,5,6,7,8-hexa-*O*-acetyl-2,3-dideoxy-2-*C*-methylidene-D-*gluco*-octitol, ***syn*-23**) due to the strong chelating hydroxyl group in α-position to the aldehyde function. Per-*O*-acetylation facilitated epimer separation via column chromatography. Zemplén saponification provided 2,3-dideoxy-2-*C*-methylidene-D-*gluco*-octitol (**24**). The stereochemical relation between the initial α-substituent and the newly formed hydroxyl group of compound **24** has been confirmed by X-ray analysis (Fig. 2). Subsequent ozonolysis generated the keto function at position C-2. 3-Deoxy-D-*gluco*-2-octulose (**15**) was obtained in a yield of 47% over 3 steps (Scheme 4).

Scheme 3



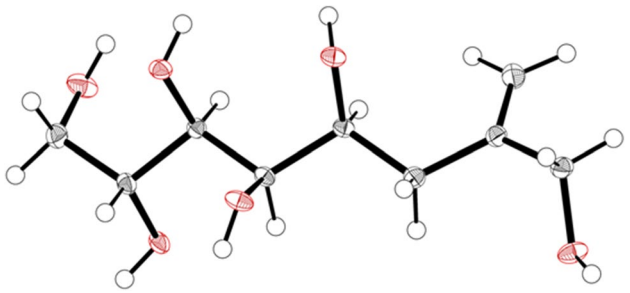
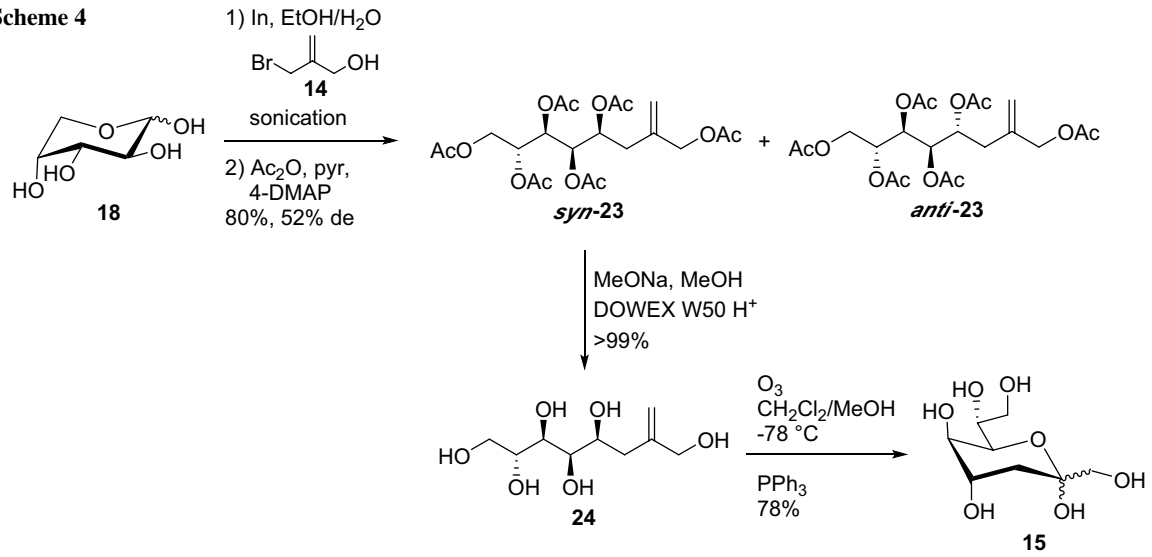


Fig. 2 X-ray analysis of compound **24** confirming its D-*gluco*-configuration

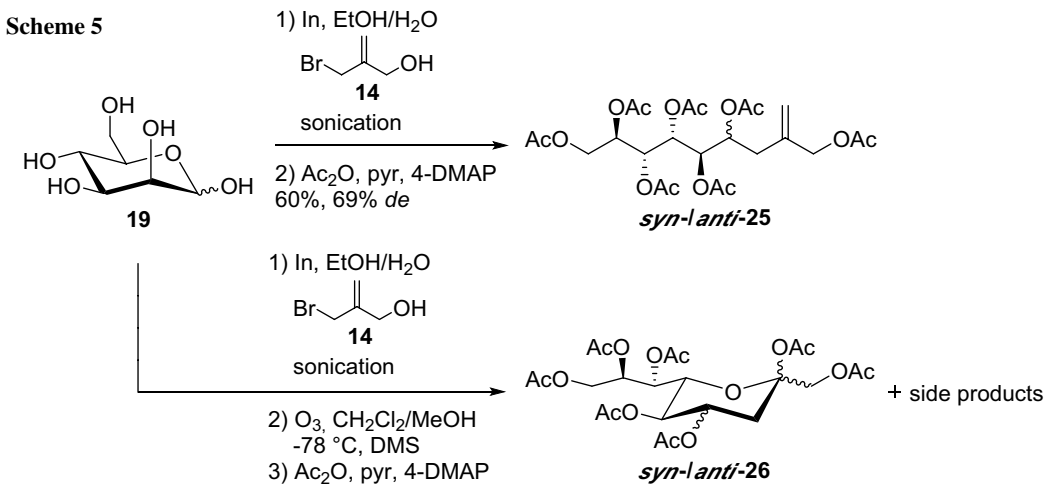
The elongation of D-mannose (**19**) utilizing allyl species **14** preferred the formation of the *syn*-product (1,4,5,6,7,8,9-hepta-*O*-acetyl-2,3-dideoxy-2-*C*-methylidene-D-*glycero*-D-*galacto*-nonitol, ***syn*-25**) according to D-arabinose (**18**). However, separation of the generated epimers in both, their unprotected or per-*O*-acetylated form, could not be accomplished via column chromatography. Also, performing ozonolysis directly after allylation followed by per-*O*-acetylation to compounds ***syn*-/*anti*-26** did not facilitate isolation of the epimers, but led to an even more complex compound mixture containing epimers, their corresponding anomers as well as side products by elimination, which turned out to be inseparable by conventional column chromatography (Scheme 5).

We decided to tackle this challenge using HPLC. To enable detection via UV-absorbance, we employed 2-(benzyloxymethyl)allyl bromide (**16**) as allyl species for the elongation in the indium-mediated allylation reaction. Compound **16** was synthesized starting from triethyl phosphonoacetate (**20**) according to a known Horner-Wadsworth-Emmons protocol [25] to provide ethyl 2-(hydroxymethyl)acrylate (**27**).

Scheme 4



Scheme 5



O-Benzylation was achieved using benzyl trichloroacetimidate (**28**) which was synthesized according to a known procedure [29, 30]. Early benzylation in the allyl building block synthesis decreases the volatility of subsequent intermediates, thus facilitating the workup processes. DIBAL-H-reduction and bromination via Appel reaction [31, 32] gave allyl species **16** in a yield of 37% over 4 steps (Scheme 6).

Allylation of D-mannose (**19**) using compound **16** gave a mixture of epimers in a ratio of 4:1. Due to the presence of a strong chelating hydroxyl group next to the reacting carbonyl function, we termed the major product ***syn*-31**. The epimeric mixture was per-*O*-acetylated and purification via normal-phase HPLC was conducted (Scheme 7). Although separation of the epimers (***syn*-/*anti*-31**) was accomplished using heptane/ethyl acetate as eluent (6:1 v/v), elaborate conditions such as cooling of the column to 15 °C were necessary to give two separated peaks at retention times of 107 and 112 min on an analytical scale (Fig. 3). Having overcome this demanding separation problem in principle, upscaling to a semi-preparative scale has not been conducted yet. Observed yields and diastereoselectivities of performed indium-mediated allylation reactions are presented in Table 1.

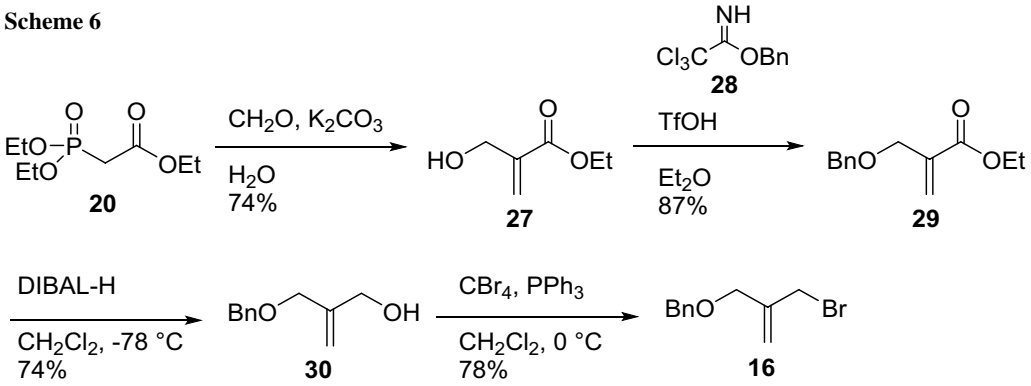
Conclusion

We developed a straightforward method for the synthesis of 3-deoxy-2-uloses. Elongation of simple aldoses via an indium-mediated allylation reaction introduced a 2-*C*-methylidenepropan-1-ol motif. Depending on the initial substrate, epimer separation by column chromatography was facilitated via protecting group manipulations. In case of D-mannose, a benzyl protected allyl species was employed for the elongation to introduce UV-activity to the compounds, thus allowing for separation of the epimeric mixture using HPLC. Subsequent ozonolysis gave the respective 3-deoxy-2-ulose in good to excellent yields. By this method the stereochemical outcome can be controlled by the introduction of an appropriate protecting group in α-position to the carbonyl function prior to the elongation, emphasizing the indium-mediated allylation reaction as a powerful tool for the synthesis of 3-deoxy-2-uloses.

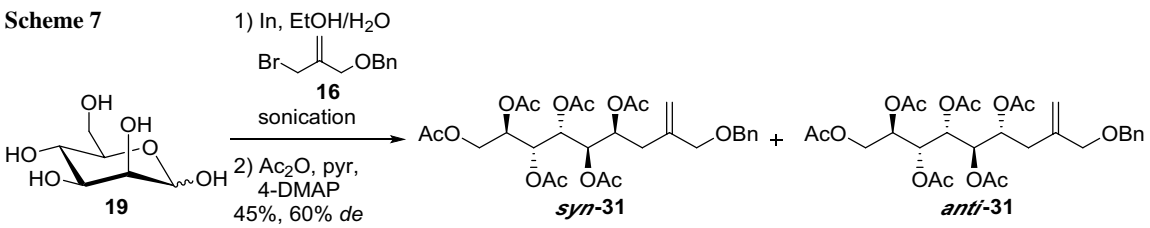
Experimental

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV III 400, Bruker AV III 600, or Bruker AV III HD 700 respectively. Chemical shifts (δ) are reported in parts per million (ppm) and spectra were calibrated using solvent signals of $CDCl_3$ or D_2O. Signal multiplicity is indicated by one or more of the following: s (singlet); d (doublet); t (triplet); q (quartet); m (multiplet); br (broad). NMR analysis was assisted by the spin simulation software DAISY (part of Bruker Top Spin software). Assignment of anomers was achieved by NOESY-NMR experiments. High resolution mass spectra (HRMS) were recorded on a Bruker maXis UHR-TOF spectrometer in ESI mode. Optical rotations were measured on a Schmidt-Haensch Digital Polarimeter Unipol

Scheme 6



Scheme 7



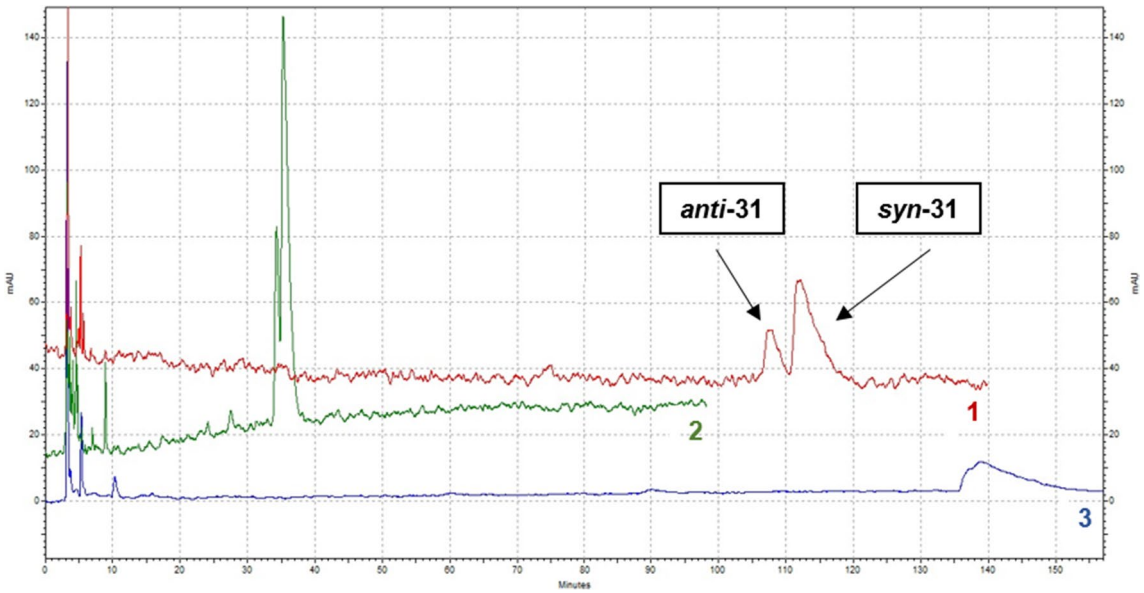


Fig. 3 Separation of epimeric mixture (***syn-/anti*-31**) by HPLC: Macherey–Nagel NUCLEODUR® 100-5 column, 15 °C column temperature, detection at 254 nm, eluents: **1**: heptane/ethyl acetate = 86/14, **2**: heptane/ethyl acetate = 80/20, **3**: heptane/ethyl acetate = 87/13

Table 1 Yields and diastereoselectivities observed in the indium-mediated allylation reactions

Starting material	Allyl species	Product	Combined yield/%	Syn/anti
2,3-*O*-isopropylidene-D-glyceraldehyde (**17**)	**14**	**anti-21**	75	1:3
D-arabinose (**18**)	**14**	**syn-23**	80[a]	3:1
D-mannose (**19**)	**14**	**syn-25**[b]	60[a]	5:1
D-mannose (**19**)	**16**	**syn-31**[b]	45[a]	4:1

[a]Combined yields after allylation and subsequent per-*O*-acetylation

[b]Referring to results obtained by us [5–7, 9, 14, 16] and others [1–4, 10–13, 15], which confirm the influence of the strong chelating effect of a hydroxyl group in α-position to the carbonyl function, we termed the major products ***syn*-25** and ***syn*-31**, respectively

L 2000. Sonication was performed using a Bandelin Sonorex Digiplus DL 512 H ultrasonic unit. Ozonolysis was executed operating an Anseros COM-AD-04 ozone generator. HPLC analyses were carried out on a Knauer system using Macherey-Nagel NUCLEODUR® 100-5 and NUCLEODUR® 100-3 C_{18} ec columns. Column chromatography was performed using Macherey-Nagel silica gel 60 (0.04–0.063 mm, 240–400 mesh). TLC monitoring was carried out on precoated Merck silica gel 60 F_{254} glass plates. Compounds were visualized by treatment with a Mo–Ce$(SO_4)_2$ complex solution (48 g $(NH_4)_6Mo_7O_{24}$ and 2 g $CeSO_4$ in 1 dm^3 10% H_2SO_4) followed by heating. Filtrations over celite were performed with Celite® S by Sigma-Aldrich®. Solvents were distilled, if necessary, prior to use. Reagents were purchased from commercial suppliers and were used without further purification.

Ethyl 2-(bromomethyl)acrylate A known procedure [25] was used for the synthesis of ethyl 2-(bromomethyl)-acrylate. Starting from 33.63 g triethyl phosphonoacetate (**20**, 150.0 mmol), 18.43 g of ethyl 2-(bromomethyl)acrylate (95.46 mmol) with a yield of 64% over 2 steps was obtained. NMR signals correspond to published NMR data [25].

2-(Bromomethyl)prop-2-en-1-ol (14) A known procedure [26] was used for the synthesis of compound **14**. Starting from 5.02 g ethyl 2-(bromomethyl)acrylate (26.0 mmol), 2.40 g of compound **14** (15.9 mmol) with a yield of 61% was obtained. NMR signals correspond to published NMR data [26].

2,3-*O*-Isopropylidene-D-glyceraldehyde (17) Compound **17** was prepared according to a known isopropylidene protection procedure [27] and oxidative 1,2-diol cleavage protocol [28]. Starting from 25.10 g D-mannitol (137.8 mmol), 2.706 g of compound **17** (207.9 mmol) was obtained with a yield of 75% over 2 steps. NMR signals were found to correspond to NMR data in the literature [28].

2,3-Dideoxy-5,6-*O*-isopropylidene-2-*C*-methylidene-D-*erythro*-hexitol (anti-21, $C_{10}H_{18}O_4$) 2,3-*O*-Isopropylidene-D-glyceraldehyde (**17**, 108 mg, 0.830 mmol) and 175 mg 2-(bromomethyl)prop-2-en-1-ol (**14**, 1.16 mmol, 1.4 equiv.) were dissolved in 5 cm^3 ethanol. Indium powder (133 mg, 1.16 mmol, 1.4 equiv.) was added and the

suspension was sonicated at 45 °C for 18 h. The reaction mixture was cooled to room temperature and the pH was adjusted to 7 with 1 M aqueous sodium hydroxide solution. The suspension was filtered over a plug of celite which was subsequently rinsed with 20 cm^3 ethanol. The filtrate was concentrated under reduced pressure and the epimeric mixture was purified by column chromatography with heptane/ethyl acetate (1:3 v/v) as eluent to give 97 mg compound ***anti*-21** (0.48 mmol) as white solid and 29 mg ***syn*-21** (0.143 mmol) as colorless oil (75%, 54% *de*).

***anti*-21**: ^{1}H NMR (600.25 MHz, $CDCl_3$, 25 °C): $\delta = 5.118$ (s, 1H, H-1′a), 4.987 (s, 1H, H-1′b), 4.067 (m, 2H, H-1), 4.014 (m, 1H, H-6a), 4.964 (m, 1H, H-5), 3.907 (m, 1H, H-6b), 3.741 (m, 1H, H-4), 3.492 (s br, 1H, OH), 3.320 (s br, 1H, OH), 2.435 (d, $^2J_{3a,3b} = 14.3$ Hz, 1H, H-3a), 2.137 (dd, $^2J_{3b,3a} = 14.3$ Hz, $^2J_{3b,4} = 9.2$ Hz, 1H, H-3b), 1.401 (s, 3H, CH_3), 1.333 (s, 3H, CH_3) ppm; ^{13}C NMR (150.93 MHz, $CDCl_3$, 25 °C): $\delta = 145.21$ (C-2), 114.89 (C-1′), 109.33 ($\underline{C}(CH_3)_2$), 78.41 (C-5), 71.27 (C-4), 66.41 (C-1), 65.90 (C-6), 37.93 (C-3), 26.69 (CH_3), 25.34 (CH_3) ppm; HRMS (ESI^+): $m/z = 225.1102$ ($[M+Na]^+$), calcd. for $C_{10}H_{18}NaO_4^+$ 225.1097; $[\alpha]_D^{20} = +0.5$ ($c = 6.5$, methanol); $R_f = 0.5$ (heptane/ethyl acetate = 1:3).

***syn*-21**: ^{1}H NMR (600.25 MHz, $CDCl_3$, 25 °C): $\delta = 5.134$ (s, 1H, H-1′a), 4.972 (s, 1H, H-1′b), 4.156–4.097 (m, 2H, H-1), 4.089–4.003 (m, 2H, H-5, H-6a), 3.819–3.746 (m, 1H, H-6b), 3.745–3.655 (m, 1H, H-4), 3.492 (s br, 1H, OH), 3.320 (s br, 1H, OH), 2.434 (d, $^2J_{3a,3b} = 14.2$ Hz, 1H, H-3a), 2.137 (dd, $^2J_{3b,3a} = 14.2$ Hz, $^3J_{3b,4} = 9.2$ Hz, 1H, H-3b), 1.401 (s, 3H, CH_3), 1.333 (s, 3H, CH_3) ppm; ^{13}C NMR (150.93 MHz, $CDCl_3$, 25 °C): $\delta = 145.41$ (C-2), 114.62 (C-1′), 109.77 ($\underline{C}(CH_3)_2$), 78.69 (C-5), 71.90 (C-4), 66.58 (C-1), 66.17 (C-6), 38.17 (C-3), 26.78 (CH_3), 25.42 (CH_3) ppm; HRMS (ESI^+): $m/z = 225.1098$ ($[M+Na]^+$), calcd. for $C_{10}H_{18}NaO_4^+$ 225.1097; $[\alpha]_D^{20} = +0.8$ ($c = 2.6$, methanol); $R_f = 0.4$ (heptane/ethyl acetate = 1:3).

2,3-Dideoxy-2-*C*-methylidene-D-*erythro*-hexitol (22, $C_7H_{14}O_4$) Compound ***anti*-21** (182 mg, 0.900 mmol) was dissolved in 5 cm^3 water and 5 cm^3 tetrahydrofuran and the pH was adjusted to 4 with 1 M aqueous hydrochloride solution. After complete consumption of the starting material as monitored by TLC, the solution was neutralized using saturated aqueous sodium hydrogen carbonate solution. The mixture was concentrated and purified by column chromatography with dichloromethane/methanol (4:1 v/v) as eluent to give 126 mg compound **22** (0.777 mmol, 86%) as colorless oil. ^{1}H NMR (600.25 MHz, D_2O, 25 °C): $\delta = 5.148$ (s, 1H, H-1′a), 5.035 (s, 1H, H-1′b), 4.122–4.033 (m, 2H, H-1), 3.844–3.736 (m, 2H, H-4, H-6a), 3.638–3.583 (m, 2H, H-5, H-6b), 2.462 (dd, $^2J_{3a,3b} = 14.8$ Hz, $^3J_{3a,4} = 2.3$ Hz, 1H, H-3a), 2.154 (dd, $^2J_{3b,3a} = 14.8$ Hz, $^3J_{3b,4} = 10.2$ Hz, 1H, H-3a) ppm; ^{13}C NMR (150.93 MHz, D_2O, 25 °C): $\delta = 144.72$ (C-2), 112.63 (C-1′), 74.60 (C-5), 69.92 (C-4), 64.28 (C-1), 62.42 (C-6), 35.79 (C-3) ppm; HRMS (ESI^+): $m/z = 185.0774$ ($[M+Na]^+$), calcd. for $C_7H_{14}NaO_4^+$ 185.0784; $[\alpha]_D^{20} = -7.8$ ($c = 0.3$, methanol); $R_f = 0.5$ (dichloromethane/methanol = 4:1).

3-Deoxy-D-*erythro*-hexulose (5) Compound **22** (126 mg, 0.777 mmol) was dissolved in 6 cm^3 methanol and 6 cm^3 dichloromethane and the solution was cooled to − 78 °C. Ozone was led through the reaction mixture via a gas inlet tube until the solution's color turned yellow. The mixture was purged with air for 10 min and 171 mm^3 of dimethyl sulfide (2.33 mmol, 3 equiv.) was added. The reaction solution was slowly warmed to 0 °C and the pH was adjusted to 7 with 1 M aqueous sodium hydroxide solution. The cooling bath was removed and the mixture was stirred at ambient temperature for 6 h. The mixture was concentrated and purified by column chromatography with dichloromethane/methanol (4:1 v/v) as eluent to give 91 mg compound **5** (0.554 mmol, 71%) as colorless oil. ^{1}H NMR (700.40 MHz, D_2O, 25 °C): β-pyranose:α-furanose:keto isomer:β-furanose:α-pyranose = 1.00:0.40:0.32:0.30:0.17; δ (β-pyranose) = 4.118 (ddd, $^3J_{4,3a} = 12.5$ Hz, $^3J_{4,3b} = 5.0$ Hz, $^3J_{4,5} = 3.3$ Hz, 1H, H-4), 4.026 (dd, $^2J_{6a,6b} = 12.8$ Hz, $^3J_{6a,5} = 1.4$ Hz, 1H, H-6a), 3.875 (ddd, $^3J_{5,4} = 3.3$ Hz, $^3J_{5,6b} = 2.2$ Hz, $^3J_{5,6a} = 1.4$ Hz, 1H, H-5), 3.765 (dd, $^2J_{6b,6a} = 12.8$ Hz, $^3J_{6b,5} = 2.2$ Hz, 1H, H-6b), 3.516 (d, $^2J_{1a,1b} = 11.6$ Hz, 1H, H-1a), 3.510 (d, $^2J_{1b,1a} = 11.6$ Hz, 1H, H-1b), 1.832 (dd, $^2J_{3a,3b} = 13.6$ Hz, $^3J_{3a,4} = 12.5$ Hz, 1H, H-3a), 1.823 (dd, $^2J_{3b,3a} = 13.6$ Hz, $^3J_{3b,4} = 5.0$ Hz, 1H, H-3b) ppm; δ (α-furanose) = 4.277 (ddd, $^3J_{4,3a} = 7.4$ Hz, $^3J_{4,5} = 4.5$ Hz, $^3J_{4,3b} = 4.1$ Hz, 1H, H-4), 4.172 (ddd, $^3J_{5,6b} = 5.6$ Hz, $^3J_{5,4} = 4.5$ Hz, $^3J_{5,6a} = 3.7$ Hz, 1H, H-5), 3.725 (dd, $^2J_{6a,6b} = 12.3$ Hz, $^3J_{6a,5} = 3.7$ Hz, 1H, H-6a), 3.619 (dd, $^2J_{6b,6a} = 12.3$ Hz, $^3J_{6b,5} = 5.6$ Hz, 1H, H-6b), 3.569 (d, $^2J_{1a,1b} = 11.9$ Hz, 1H, H-1a), 3.562 (d, $^2J_{1b,1a} = 11.9$ Hz, 1H, H-1b), 2.446 (dd, $^2J_{3a,3b} = 14.2$ Hz, $^3J_{3a,4} = 7.4$ Hz, 1H, H-3a), 1.951 (dd, $^2J_{3b,3a} = 14.2$ Hz, $^3J_{3b,4} = 4.1$ Hz, 1H, H-3b) ppm; δ (keto isomer) = 4.433 (d, $^2J_{1a,1b} = 19.0$ Hz, 1H, H-1a), 4.370 (d, $^2J_{1b,1a} = 19.0$ Hz, 1H, H-1b), 4.112 (ddd, $^3J_{4,3b} = 9.2$ Hz, $^3J_{4,5} = 6.6$ Hz, $^3J_{4,3a} = 3.5$ Hz, 1H, H-4), 3.750 (dd, $^2J_{6a,6b} = 11.8$ Hz, $^3J_{6a,5} = 3.3$ Hz, 1H, H-6a), 3.626 (ddd, $^3J_{5,6b} = 7.0$ Hz, $^3J_{5,4} = 6.6$ Hz, $^3J_{5,6a} = 3.3$ Hz, 1H, H-5), 3.593 (dd, $^2J_{6b,6a} = 11.8$ Hz, $^3J_{6b,5} = 7.0$ Hz, 1H, H-6b), 2.763 (dd, $^2J_{3a,3b} = 16.2$ Hz, $^3J_{3a,4} = 3.5$ Hz, 1H, H-3a), 2.683 (dd, $^2J_{3b,3a} = 16.2$ Hz, $^3J_{3b,4} = 9.2$ Hz, 1H, H-3b) ppm; δ (β-furanose) = 4.429 (ddd, $^3J_{4,3b} = 7.2$ Hz, $^3J_{4,3a} = 7.1$ Hz, $^3J_{4,5} = 5.5$ Hz, 1H, H-4), 3.950 (ddd, $^3J_{5,6b} = 6.2$ Hz, $^3J_{5,4} = 5.5$ Hz, $^3J_{5,6a} = 3.9$ Hz, 1H, H-5), 3.770 (dd, $^2J_{6a,6b} = 12.1$ Hz, $^3J_{6a,5} = 3.9$ Hz, 1H, H-6a), 3.673 (dd, $^2J_{6a,6b} = 12.1$ Hz, $^3J_{6b,5} = 6.2$ Hz, 1H, H-6b), 3.602 (s,

2H, H-1), 2.290 (dd, $^{2}J_{3a,3b}$ = 13.6 Hz, $^{3}J_{3a,4}$ = 7.1 Hz, 1H, H-3a), 2.171 (dd, $^{2}J_{3b,3a}$ = 13.6 Hz, $^{3}J_{3b,4}$ = 7.2 Hz, 1H, H-3b) ppm; δ (α-pyranose) = 4.159 (dddd, $^{3}J_{4,3a}$ = 5.1 Hz, $^{3}J_{4,3b}$ = 3.4 Hz, $^{3}J_{4,5}$ = 3.1 Hz, $^{3}J_{4,6b}$ = 0.9 Hz, 1H, H-4), 3.937 (dd, $^{2}J_{6a,6b}$ = 11.5 Hz, $^{3}J_{6a,5}$ = 9.6 Hz, 1H, H-6a), 3.814 (ddd, $^{3}J_{5,6a}$ = 9.6 Hz, $^{3}J_{5,6b}$ = 4.9 Hz, $^{3}J_{5,4}$ = 3.1 Hz, 1H, H-5), 3.662 (ddd, $^{2}J_{6b,6a}$ = 11.5 Hz, $^{3}J_{6b,5}$ = 4.9 Hz, $^{3}J_{6b,4}$ = 0.9 Hz, 1H, H-6b), 3.500 (d, $^{2}J_{1a,1b}$ = 11.8 Hz, 1H, H-1a), 3.470 (d, $^{2}J_{1b,1a}$ = 11.8 Hz, 1H, H-1b), 1.995 (dd,$^{2}J_{3a,3b}$ = 14.5 Hz, $^{3}J_{3a,4}$ = 5.1 Hz, 1H, H-3a), 1.940 (dd, $^{2}J_{3b,3a}$ = 14.5 Hz, $^{3}J_{3b,4}$ = 3.4 Hz, 1H, H-3b) ppm; ^{13}C NMR (176.12 MHz, D_2O, 25 °C): δ (β-pyranose) = 97.40 (C-2), 67.53 (C-1), 67.25 (C-5), 64.95 (C-4), 64.01 (C-6), 32.31 (C-3) ppm; δ (α-furanose) = 105.84 (C-2), 85.74 (C-5), 71.31 (C-4), 65.18 (C-1), 61.52 (C-6), 41.49 (C-3) ppm; δ (keto isomer) = 211.83 (C-2), 74.34 (C-5), 68.00 (C-1), 67.88 (C-4), 62.41 (C-6), 41.45 (C-3) ppm; δ (β-furanose) = 105.49 (C-2), 86.26 (C-5), 70.98 (C-4), 65.43 (C-1), 62.53 (C-6), 41.52 (C-3) ppm; δ (α-pyranose) = 96.49 (C-2), 66.82 (C-4), 66.15 (C-5), 65.79 (C-1), 58.72 (C-6), 34.39 (C-3) ppm; ^{1}H NMR signals correspond to published NMR data [33]. HRMS (ESI^{+}): *m/z* = 187.0579 ([M + Na]$^{+}$), calcd. For $C_6H_{12}NaO_5^{+}$ 187.0577; $[\alpha]_D^{20}$ = − 3.4 (*c* = 1.1, methanol); R_f = 0.4 (dichloromethane/methanol = 4:1).

1,4,5,6,7,8-Hexa-*O*-acetyl-2,3-dideoxy-2-*C*-methylidene-D-*gluco*-octitol (syn-23, $C_{21}H_{30}O_{12}$) 2-(Bromomethyl)prop-2-en-1-ol (**14**, 616 mg, 4.08 mmol, 1.5 equiv.) was dissolved in 16 cm^3 ethanol and 4 cm^3 water. Indium powder (468 mg, 4.08 mmol, 1.5 equiv.) and 408 mg D-arabinose (**18**, 2.72 mmol) were added and the suspension was sonicated at 45 °C for 6 h. The reaction mixture was filtered over celite which was subsequently rinsed with 20 cm^3 ethanol. The filtrate was evaporated yielding a colorless oil. The oil was taken up in 10 cm^3 pyridine, treated with 10 cm^3 acetic anhydride, and cooled to 0 °C. 4-(Dimethylamino)pyridine (17 mg, 0.14 mmol, 0.05 equiv.) was added and the solution was stirred for 3 h while reaching room temperature. After no further conversion was observed via TLC analysis, the reaction mixture was diluted with toluene forming a homogenous pressure-maximum azeotrope with pyridine [34], thus facilitating concentration. The residue was taken up in 30 cm^3 ethyl acetate and was washed with water (3 × 10 cm^3) and 10 cm^3 brine. The organic layer was dried over magnesium sulfate, filtered and concentrated yielding a colorless oil. Separation of the resulting epimers was achieved via column chromatography using heptane/ethyl acetate (1:1 v/v) as eluent to give 779 mg compound ***syn*-23** (1.64 mmol) as colorless oil and 250 mg compound ***anti*-23** (0.527 mmol) as colorless oil (80%, 51% *de*).

***syn*-23**: ^{1}H NMR (600.25 MHz, $CDCl_3$, 25 °C): δ = 5.422 (dd, $^{3}J_{6,7}$ = 7.3 Hz, $^{3}J_{6,5}$ = 3.9 Hz, 1H, 6-H), 5.278 (dd, $^{3}J_{5,4}$ = 6.9 Hz, $^{3}J_{5,6}$ = 3.9 Hz, 1H, 5-H), 5.186 (ddd, $^{3}J_{4,3b}$ = 9.2 Hz, $^{3}J_{4,5}$ = 6.9 Hz, $^{3}J_{4,3a}$ = 3.6 Hz, 1H, 4-H), 5.141 (d, $^{2}J_{1'a,1'b}$ = 0.9 Hz, 1H, 1′-Ha), 5.059 (ddd, $^{3}J_{7,6}$ = 7.3 Hz, $^{3}J_{7,8b}$ = 5.4 Hz, $^{3}J_{7,8a}$ = 3.1 Hz, 1H, 7-H), 5.028 (d, $^{2}J_{1'b,1'a}$ = 0.9 Hz, 1H, 1′-Hb), 4.608 (d, $^{2}J_{1a,1b}$ = 13.2 Hz, 1H, 1-Ha), 4.443 (d, $^{2}J_{1b,1a}$ = 13.2 Hz, 1H, 1-Hb), 4.244 (dd, $^{2}J_{8a,8b}$ = 12.5 Hz, $^{3}J_{8a,7}$ = 3.1 Hz, 1H, 8-Ha), 4.117 (dd, $^{2}J_{8b,8a}$ = 12.5 Hz, $^{3}J_{8b,7}$ = 5.4 Hz, 1H, 8-Hb), 2.459 (dd, $^{2}J_{3a,3b}$ = 14.3 Hz, $^{3}J_{3a,4}$ = 3.6 Hz, 1H, 3-Ha), 2.300 (dd, $^{2}J_{3b,3a}$ = 14.3 Hz, $^{3}J_{3b,4}$ = 9.2 Hz, 1H, 3-Hb), 2.1304 (s, 3H, OAc), 2.0856 (s, 3H, OAc), 2.0620 (s, 3H, OAc), 2.0582 (s, 3H, OAc), 2.0491 (s, 3H, OAc), 2.0153 (s, 3H, OAc) ppm; ^{13}C NMR (150.93 MHz, $CDCl_3$, 25 °C): δ = 170.58 ((C=O)–CH_3), 170.48 ((C=O)–CH_3), 169.96 ((C=O)–CH_3), 169.90 ((C=O)–CH_3), 169.80 ((C=O)–CH_3), 169.79 ((C=O)–CH_3), 138.69 (2-C), 117.53 (1′-C), 70.72 (5-C), 69.24 (4-C), 68.63 (7-C), 68.59 (6-C), 66.22 (1-C), 61.49 (8-C), 34.73 (3-C), 20.86 ((C=O)–CH_3), 20.75 ((C=O)–CH_3), 20.68 ((C=O)–CH_3), 20.66 ((C=O)–CH_3), 20.60 ((C=O)–CH_3), 20.52 ((C=O)–CH_3) ppm; HRMS (ESI^{+}): *m/z* = 497.1634 ([M + Na]$^{+}$), calcd. for $C_{21}H_{30}O_{12}Na^{+}$ 497.1635; $[\alpha]_D^{20}$ = + 0.3 (*c* = 1.0, dichloromethane); R_f = 0.4 (heptane/ethyl acetate = 1:1).

***anti*-23**: ^{1}H NMR (400.27 MHz, $CDCl_3$, 25 °C): δ = 5.431 (dd, $^{3}J_{6,7}$ = 8.7 Hz, $^{3}J_{6,5}$ = 2.7 Hz, 1H, 6-H), 5.272 (dd, $^{3}J_{5,4}$ = 7.5 Hz, $^{3}J_{5,6}$ = 2.7 Hz, 1H, 5-H), 5.134 (ddd, $^{3}J_{4,3a}$ = 8.2 Hz, $^{3}J_{4,5}$ = 7.5 Hz, $^{3}J_{4,3b}$ = 4.5 Hz, 1H, 4-H), 5.093 (d, $^{2}J_{1'a,1'b}$ = 0.9 Hz, 1H, 1′-Ha), 5.068 (ddd, $^{3}J_{7,6}$ = 8.7 Hz, $^{3}J_{7,8b}$ = 5.5 Hz, $^{3}J_{7,8a}$ = 2.8 Hz, 1H, 7-H), 4.983 (d, $^{2}J_{1'b,1'a}$ = 0.9 Hz, 1H, 1′-Hb), 4.560 (d, $^{2}J_{1a,1b}$ = 13.2 Hz, 1H, 1-Ha), 4.515 (d, $^{2}J_{1b,1a}$ = 13.2 Hz, 1H, 1-Hb), 4.208 (dd, $^{2}J_{8a,8b}$ = 12.5 Hz, $^{3}J_{8a,7}$ = 2.8 Hz, 1H, 8-Ha), 4.068 (dd, $^{2}J_{8b,8a}$ = 12.5 Hz, $^{3}J_{8b,7}$ = 5.5 Hz, 1H, 8-Hb), 2.333 (dd, $^{2}J_{3a,3b}$ = 14.3 Hz, $^{3}J_{3a,4}$ = 8.2 Hz, 1H, 3-Ha), 2.306 (dd, $^{2}J_{3b,3a}$ = 14.3 Hz, $^{3}J_{3b,4}$ = 4.5 Hz, 1H, 3-Hb), 2.085 (s, 3H, OAc), 2.077 (s, 3H, OAc), 2.073 (s, 3H, OAc), 2.053 (s, 3H, OAc), 2.039 (s, 3H, OAc), 1.988 (s, 3 H, OAc) ppm; ^{13}C NMR (100.66 MHz, $CDCl_3$, 25 °C): δ = 170.58 ((C=O)–CH_3), 170.56 ((C=O)–CH_3), 170.06 ((C=O)–CH_3), 169.90 ((C=O)–CH_3), 169.87 ((C=O)–CH_3), 169.77 ((C=O)–CH_3), 139.00 (2-C), 116.68 (1‘-C), 70.57 (5-C), 68.12 (7-C), 68.04 (6-C), 67.56(4-C), 66.22 (1-C), 61.89 (8-C), 35.38 (3-C), 20.55–20.89 (6×(C=O)–CH_3) ppm; HRMS (ESI^{+}): *m/z* = 497.1633 ([M + Na]$^{+}$), calcd. for $C_{21}H_{30}O_{12}Na^{+}$ 497.1629; R_f = 0.4 (heptane/ethyl acetate = 1:1).

2,3-Dideoxy-2-*C*-methylidene-D-*gluco*-octitol (24, $C_9H_{18}O_6$) Compound *syn*-23 (133 mg, 0.280 mmol) was dissolved in 10 cm^3 methanol and the solution was treated with 2 mg sodium methoxide (0.037 mmol, 0.13 equiv.).

The mixture was stirred for 3 h until no further conversion could be observed via TLC analysis. The solution was neutralized using DOWEX W50 ion exchange resin (H^+ form) which was subsequently filtered. The filtrate was concentrated to give 62 mg compound **24** (0.28 mmol, > 99%) as a white solid. Single crystals were grown by recrystallization in water/acetone [29]. ^{1}H NMR (600.25 MHz, D_2O, 25 °C): δ = 5.159 (d, $^2J_{1'a,1'b}$ = 1.2 Hz, 1H, 1′-Ha), 5.046 (d, $^2J_{1'b,1'a}$ = 1.2 Hz, 1H, 1′-Hb), 4.098 (d, $^2J_{1a,1b}$ = 14.5 Hz, 1H, 1-Ha), 4.090 (d, $^2J_{1b,1a}$ = 14.5 Hz, 1H, 1-Hb), 3.941 (ddd, $^3J_{4,3b}$ = 9.5 Hz, $^3J_{4,5}$ = 5.7 Hz, $^3J_{4,3a}$ = 3.9 Hz, 1H, 4-H), 3.823 (dd, $^2J_{8a,8b}$ = 11.9 Hz, $^3J_{8a,7}$ = 3.0 Hz, 1H, 8-Ha), 3.772 (ddd, $^3J_{7,6}$ = 8.2 Hz, $^3J_{7,8b}$ = 6.3 Hz, $^3J_{7,8a}$ = 3.0 Hz, 1H, 7-H), 3.711 (dd, $^3J_{5,4}$ = 5.7 Hz, $^3J_{5,6}$ = 2.3 Hz, 1H, 5-H), 3.689 (dd, $^3J_{6,7}$ = 8.2 Hz, $^3J_{6,5}$ = 2.3 Hz, 1H, 6-H), 3.643 (dd, $^2J_{8b,8a}$ = 11.9 Hz, $^3J_{8b,7}$ = 6.3 Hz, 1H, 8-Hb), 2.419 (dd, $^2J_{3a,3b}$ = 14.5 Hz, $^3J_{3a,4}$ = 3.9 Hz, 1H, 3-Ha), 2.216 (dd, $^2J_{3b,3a}$ = 14.5 Hz, $^3J_{3b,4}$ = 9.5 Hz, 1H, 3-Hb) ppm; ^{13}C NMR (150.93 MHz, D_2O, 25 °C): δ = 144.47 (2-C), 112.94 (1′-C), 71.96 (5-C), 71.32 (6-C), 71.05 (7-C), 70.59 (4-C), 64.25 (1-C), 62.78 (8-C), 36.29 (3-C) ppm; HRMS (ESI$^+$): *m/z* = 245.0998 ([M + Na]$^+$), calcd. for $C_9H_{18}O_6Na^+$ 245.0996; m.p.: 124–126 °C; $[\alpha]_D^{20}$ = − 0.1 (*c* = 1.0, water); R_f = 0.7 (1-butanol/acetone/water = 4:4:2).

CCDC 1899885 contains the supplementary crystallographic data for compound **24**. These data can be obtained from The Cambridge Crystallographic Data Centre, www.ccdc.cam.ac.uk/data_request/cif.

3-Deoxy-D-*gluco*-octulose (15, $C_8H_{16}O_7$) Compound **24** (51 mg, 0.23 mmol) was dissolved in 10 cm3 methanol and 10 cm3 dichloromethane and the solution was cooled to − 78 °C. Ozone was led through the reaction mixture via a gas inlet tube until the solution's color turned blue. The mixture was purged with air for 15 min, treated with 121 mg triphenylphosphine (0.46 mmol, 2.0 equiv.) and stirred overnight at room temperature. The solvents were removed under reduced pressure and the residue was taken up in 20 cm^3 dichloromethane and 20 cm^3 water. The aqueous phase was washed with dichloromethane (3 × 10 cm^3). The aqueous layer was concentrated and the resulting oil was purified by column chromatography using dichloromethane/methanol (4:1 v/v) as eluent to give 40 mg compound **15** (0.18 mmol, 78%) as a colorless oil. ^{1}H NMR (600.25 MHz, D_2O, 25 °C): β-pyranose:keto isomer:α-furanose:β-furanose: = 1.00:0.19:0.18:0.09; δ (β-pyranose) = 4.120 (dd, $^3J_{6,7}$ = 9.0 Hz, $^3J_{6,5}$ = 1.4 Hz, 1H, 6-H), 4.111 (ddd, $^3J_{4,3a}$ = 3.7 Hz, $^3J_{4,5}$ = 3.6 Hz, $^3J_{4,3b}$ = 2.8 Hz, 1H, 4-H), 3.862 (ddd, $^3J_{5,4}$ = 3.6 Hz, $^3J_{5,6}$ = 1.4 Hz, $^4J_{5,3b}$ = 1.0 Hz, 1H, 5-H), 3.855 (ddd, $^3J_{7,6}$ = 9.0 Hz, $^3J_{7,8b}$ = 6.0 Hz, $^3J_{7,8a}$ = 2.9 Hz, 1H, 7-H), 3.835 (dd, $^2J_{8a,8b}$ = 12.0 Hz, $^3J_{8a,7}$ = 2.9 Hz, 1H, 8-Ha), 3.664 (dd, $^2J_{8b,8a}$ = 12.0 Hz, $^3J_{8b,7}$ = 6.0 Hz, 1H, 8-Hb), 3.456 (s, 2H, 1-Ha, 1-Hb), 2.024 (dd, $^2J_{3a,3b}$ = 14.9 Hz, $^3J_{3a,4}$ = 3.7 Hz, 1H, 3-Ha), 1.782 (ddd, $^2J_{3b,3a}$ = 14.9 Hz, $^3J_{3b,4}$ = 2.8 Hz, $^4J_{3b,5}$ = 1.0 Hz, 1H, 3-Hb) ppm; δ (keto isomer) = 4.435 (dd, $^2J_{1a,1b}$ = 19.2 Hz, $^4J_{1a,3b}$ = 0.6 Hz, 1H, 1-Ha), 4.380 (dd, $^2J_{1b,1a}$ = 19.2 Hz, $^4J_{1b,3b}$ = 0.6 Hz, 1H, 1-Hb), 4.257 (ddd, $^3J_{4,3a}$ = 9.4 Hz, $^3J_{4,5}$ = 5.7 Hz, $^3J_{4,3b}$ = 3.5 Hz, 1H, 4-H), 3.827 (dd, $^2J_{8a,8b}$ = 12.0 Hz, $^3J_{8a,7}$ = 3.0 Hz, 1H, 8a-H), 3.773 (ddd, $^3J_{7,6}$ = 8.2 Hz, $^3J_{7,8b}$ = 6.3 Hz, $^3J_{7,8a}$ = 3.0 Hz, 1H, 7-H), 3.740 (dd, $^3J_{5,4}$ = 5.7 Hz, $^3J_{5,6}$ = 2.4 Hz, 1H, 5-H), 3.655 (dd, $^2J_{8b,8a}$ = 12.0 Hz, $^3J_{8b,7}$ = 6.3 Hz, 1H, 8-Hb), 3.627 (dd, $^3J_{6,7}$ = 8.2 Hz, $^3J_{6,5}$ = 2.4 Hz, 1H, 6-H), 2.750 (dd, $^2J_{3a,3b}$ = 16.3 Hz, $^3J_{3a,4}$ = 9.4 Hz, 1H, 3-Ha), 2.713 (dddd, $^2J_{3b,3a}$ = 16.3 Hz, $^3J_{3b,4}$ = 3.5 Hz, $^4J_{3b,1a}$ = 0.6 Hz, $^4J_{3b,1b}$ = 0.6 Hz, 1H, 3-Hb) ppm; δ (α-furanose) = 4.614 (ddd, $^3J_{4,3a}$ = 6.3 Hz, $^3J_{4,5}$ = 4.4 Hz, $^3J_{4,3b}$ = 3.3 Hz, 1H, 4-H), 4.294 (dd, $^3J_{5,6}$ = 5.0 Hz, $^3J_{5,4}$ = 4.4 Hz, 1H, 5-H), 3.921 (dd, $^3J_{6,7}$ = 6.8 Hz, $^3J_{6,5}$ = 5.0 Hz, 1H, 6-H), 3.814 (dd, $^2J_{8a,8b}$ = 12.0 Hz, $^3J_{8a,7}$ = 3.3 Hz, 1H, 8-Ha), 3.785 (ddd, $^3J_{7,8b}$ = 6.9 Hz, $^3J_{7,6}$ = 6.8 Hz, $^3J_{7,8a}$ = 3.3 Hz, 1H, 7-H), 3.678 (dd, $^2J_{8b,8a}$ = 12.0 Hz, $^3J_{8b,7}$ = 6.9 Hz, 1H, 8-Hb), 3.653 (s, 2H, 1-Ha, 1-Hb), 2.305 (dd, $^2J_{3a,3b}$ = 14.5 Hz, $^3J_{3a,4}$ = 6.3 Hz, 1H, 3-Ha), 2.241 (dd, $^2J_{3b,3a}$ = 14.5 Hz, $^3J_{3b,4}$ = 3.3 Hz, 1H, 3-Hb) ppm; δ (β-furanose) = 4.538 (ddd, $^3J_{4,3a}$ = 5.6 Hz, $^3J_{4,5}$ = 4.1 Hz, $^3J_{4,3b}$ = 1.9 Hz, 1H, 4-H), 4.122 (dd, $^3J_{5,6}$ = 5.3 Hz, $^3J_{5,4}$ = 4.1 Hz, 1H, 5-H), 3.979 (dd, $^3J_{6,7}$ = 6.9 Hz, $^3J_{6,5}$ = 5.3 Hz, 1H, 6-H), 3.814 (dd, $^2J_{8a,8b}$ = 11.6 Hz, $^3J_{8a,7}$ = 3.3 Hz, 1H, 8-Ha), 3.789 (ddd, $^3J_{7,6}$ = 6.9 Hz, $^3J_{7,8b}$ = 6.9 Hz, $^3J_{7,8a}$ = 3.3 Hz, 1H, 7-H), 3.677 (dd, $^2J_{8b,8a}$ = 11.6 Hz, $^3J_{8b,7}$ = 6.9 Hz, 1H, 8-Hb), 3.597 (d, $^2J_{1a,1b}$ = 11.8 Hz, 1H, 1-Ha), 3.589 (d, $^2J_{1b,1a}$ = 11.8 Hz, 1H, 1-Hb), 2.417 (dd, $^2J_{3a,3b}$ = 14.3 Hz, $^3J_{3a,4}$ = 5.6 Hz, 1H, 3-Ha), 2.055 (dd, $^2J_{3b,3a}$ = 14.3 Hz, $^3J_{3b,4}$ = 1.9 Hz, 1H, 3-Hb) ppm; ^{13}C NMR (150.93 MHz, D_2O, 25 °C): δ (β-pyranose) = 97.25 (2-C), 69.97 (7-C), 68.09 (1-C), 67.98 (4-C), 67.15 (6-C), 66.24 (5-C), 63.57 (8-C), 30.70 (3-C) ppm; δ (keto isomer) = 212.14 (2-C), 72.33 (5-C), 71.65 (6-C), 71.64 (7-C), 69.36 (4-C), 68.55 (1-C), 63.35 (8-C), 42.15 (3-C) ppm; δ (α-furanose) = 105.37 (2-C), 81.19 (5-C), 72.52 (4-C), 72.24 (7-C), 71.18 (6-C), 66.09 (1-C), 62.97 (8-C), 44.01 (3-C) ppm; δ (β-furanose) = 105.96 (2-C), 83.67 (5-C), 72.56 (4-C), 72.28 (7-C), 71.58 (6-C), 65.73 (1-C), 62.97 (8-C), 42.58 (3-C) ppm; HRMS (ESI$^+$): *m/z* = 247.0791 ([M + Na]$^+$), calcd. For $C_9H_{18}O_6Na^+$ 247.0788; = $[\alpha]_D^{20}$0.3 (*c* = 1.0, water); R_f = 0.5 (1-butanol/acetone/water (5:4:1).

1,4,5,6,7,8,9-Hepta-*O*-acetyl-2,3-dideoxy-2-*C*-methylidene-D-*glycero*-D-*galacto*-nonitol (syn-25, $C_{24}H_{34}O_{14}$) D-Mannose (200 mg, **19**, 1.11 mmol) and 251 mg 2-(bromomethyl)prop-2-en-1-ol (**14**, 1.67 mmol, 1.5 equiv.) were dissolved in 8 cm^3 ethanol and 2 cm^3 water. Indium powder (191 mg, 1.67 mmol, 1.5 equiv.) was added and the

suspension was sonicated at 45 °C for 18 h. The reaction mixture was cooled to room temperature and the pH was adjusted to 7 with 1 M aqueous sodium hydroxide solution. The suspension was filtered over a plug of celite which was subsequently rinsed with 30 cm^3 of methanol. The filtrate was concentrated under reduced pressure and the residue was dissolved in 6 cm^3 pyridine and 6 cm^3 acetic anhydride. The mixture was cooled with an ice bath, treated with 7 mg 4-(dimethylamino)pyridine (0.06 mmol, 0.5 equiv.) and stirred overnight. The mixture was concentrated and the addition of toluene facilitated the process by forming a homogenous pressure-maximum azeotrope with pyridine [34]. The residue was taken up in 20 cm^3 ethyl acetate and was washed with water (3 × 10 cm^3) and 10 cm^3 brine. The organic layer was dried over magnesium sulfate, filtered and concentrated. The epimeric mixture ***syn-/anti*-25** could be partially separated from the per-*O*-acetylated starting material by performing column chromatography using heptane/ethyl acetate (10/1 v/v) as eluent. However, the respective epimers could not be isolated. The conversion of 60% (542 mg mixture with 1,2,3,4,6-penta-*O*-acetyl-D-mannose, 0.672 mmol of epimeric products) over two steps and the diastereoselective excess of 69% could be determined by means of NMR.

Ethyl 2-(benzyloxymethyl)acrylate (29, $C_{13}H_{16}O_3$) A suspension of 386 mg sodium hydride (60% dispersion, 9.65 mmol, 0.5 equiv.) in 30 cm^3 anhydrous diethyl ether under argon was cooled to 0 °C. Benzyl alcohol (4.0 cm^3, 39 mmol, 2 equiv.) was slowly added and the reaction mixture was stirred for 30 min at 0 °C. Subsequently, 3.9 cm^3 trichloroacetonitrile (39 mmol, 2 equiv.) was slowly added and the solution was allowed to stir at room temperature for three hours. The reaction was stopped by the addition of 30 cm^3 saturated aqueous bicarbonate solution. The aqueous phase was extracted with diethyl ether (3 × 30 cm^3) and the combined organic layers were dried over magnesium sulfate. After filtration, the eluate was concentrated to give crude benzyl 2,2,2-trichloroacetminidate (**28**) in form of a brown oil. To a mixture of 2.51 g ethyl 2-(hydroxymethyl)acrylate (**27**, 19.3 mmol) in 50 cm^3 anhydrous diethyl ether under argon, 170 mm^3 trifluoromethanesulfonic acid (1.92 mmol, 0.1 equiv.) was added followed by freshly prepared crude benzyl 2,2,2-trichloroacetimidate (**28**, 39 mmol, 2 equiv.). The solution was stirred for 42 h at room temperature. After complete consumption of the starting material, 30 cm^3 aqueous hydrochloric acid solution (2 M) was added and the mixture was stirred for 10 min. The organic phase was separated and washed with saturated bicarbonate solution (2 × 30 cm^3) followed by 30 cm^3 of brine. After concentration, 50 cm^3 heptane was added to the resulted white precipitate and the suspension was filtered and washed with 30 cm^3 of heptane. The organic solution was dried over magnesium sulfate, filtered, and concentrated. The residue was purified by column chromatography using heptane/ethyl acetate (19/1 14/1 v/v) as eluent to give 3.70 g ethyl 2-(benzyloxymethyl)acrylate (**29**, 16.8 mmol, 87%) as a yellowish liquid. ^{1}H NMR (600.25 MHz, $CDCl_3$, 25 °C): δ = 7.407–7.326 (m, 4H, H-7, H-8), 7.326–7.270 (m, 1H, H-9), 6.324 (dd, $^3J_{4a,3}$ = 1.5 Hz, $^2J_{4a,4b}$ = 1.4 Hz, 1H, H-4a), 5.927 (dd, $^3J_{4b,3}$ = 1.9 Hz, $^2J_{4b,4a}$ = 1.4 Hz, 1H, H-4a), 4.594 (s, 2H, H-5), 4.248 (dd, $^3J_{3,4b}$ = 1.9 Hz, $^3J_{3,4a}$ = 1.5 Hz, 2H, H-3), 4.226 (q, $^3J_{1',2'}$ = 7.2 Hz, 2H, H-1′), 1.304 (t, $^3J_{2',1'}$ = 7.2 Hz, 3H, H-2′) ppm; ^{13}C NMR (150.93 MHz, $CDCl_3$, 25 °C): δ = 166.04 (C-1), 138.23 (C-6), 137.57 (C-2), 128.56 (C-8), 127.82 (C-9), 127.77 (C-7), 125.81 (C-4), 72.89 (C-5), 68.52 (C-3), 60.85 (C-1′), 14.34 (C-2′) ppm; HRMS (ESI^+): *m/z* = 243.0992 ($[M+Na]^+$), calcd. for $C_{13}H_{16}NaO_3^+$ 243.0992; R_f = 0.5 (heptane/ethyl acetate = 4:1).

2-(Benzyloxymethyl)-prop-2-en-1-ol (30, $C_{11}H_{14}O_2$) Ethyl 2-(benzyloxymethyl)acrylate (**29**, 3.70 g, 16.8 mmol) was dissolved in anhydrous dichloromethane and cooled to − 78 °C. DIBAL-H solution (39 cm^3, 1 M in dichloromethane, 39 mmol, 2.3 equiv.) was slowly added over 30 min. After stirring for an hour at − 78 °C, the solution was allowed to warm to 0 °C using an ice bath. The reaction was stopped by slowly adding 75 cm^3 of a saturated potassium sodium tartrate solution. The ice bath was removed and the mixture was stirred overnight at room temperature. The organic layer was separated and the aqueous phase was extracted with dichloromethane (3 × 50 cm^3). The combined organic layers were washed with 50 cm^3 brine, dried over magnesium sulfate, filtered, and concentrated. The residue was purified by column chromatography using heptane/ethyl acetate (4/1 v/v) as eluent to give 2.21 g 2-(benzyloxymethyl)-prop-2-en-1-ol (**30** , 12.4 mmol, 74%) as a yellowish oil. ^{1}H NMR (600.25 MHz, $CDCl_3$, 25 °C): δ = 7.400–7.319 (m, 4H, H-7, H-8), 7.319–7.272 (m, 1H, H-9), 5.211 (dd, $^2J_{4a,4b}$ = 1.7 Hz, $^3J_{4a,3}$ = 0.9 Hz, 1H, H-4a), 5.161 (dd, $^2J_{4b,4a}$ = 1.7 Hz, $^3J_{4b,3}$ = 1.0 Hz, 1H, H-4b), 4.528 (s, 2H, H-5), 4.206 (d, $^3J_{1,OH}$ = 5.4 Hz, 2H, H-1), 4.106(dd, $^3J_{3,4b}$ = 1.0 Hz, $^3J_{3,4a}$ = 0.9 Hz, 2H, H-3), 1.895 (m, 1H, OH) ppm; ^{13}C NMR (150.93 MHz, $CDCl_3$, 25 °C): δ = 145.14 (C-2), 138.08 (C-6), 128.60–127.90 (C-7, C-8, C-9), 113.75 (C-4), 72.50 (C-5), 72.00 (C-3), 64.81 (C-1) ppm; HRMS (ESI^+): *m/z* = 201.0887 ($[M+Na]^+$), calcd. for $C_{11}H_{14}NaO_2^+$ 201.0886; R_f = 0.5 (heptane/ethyl acetate = 1:1).

2-(Benzyloxymethyl)allyl bromide (16, $C_{11}H_{13}BrO$) Triphenylphospine (3.47 g, 13.2 mmol, 2 equiv.) and 4.39 g tetrabromomethane (13.24 mmol, 2 equiv.) were dissolved in 150 cm^3 of anhydrous dichloromethane under argon, cooled to 0 °C and stirred for 15 min. Subsequently, a solution of 1.18 g compound **30** (6.62 mmol) in 15 cm^3 anhydrous dichloromethane was added. The reaction was monitored by

TLC and was completed after 3 h. After concentration, the residue was dissolved in 50 cm^3 diethyl ether, and 50 cm^3 of heptane was added under stirring. The resulting precipitate was filtered over celite and washed with 10 cm^3 heptane. The eluate was washed with water (3 × 50 cm^3) and 50 cm^3 brine, dried over magnesium sulfate, filtered, and concentrated. The residue was purified by column chromatography using heptane/ethyl acetate (19/1 v/v) as eluent to give 1.24 g 2-(benzyloxymethyl)allyl bromide (**16**, 5.14 mmol, 78%) as colorless liquid. ^{1}H NMR (600.25 MHz, $CDCl_3$, 25 °C): δ = 7.511–7.326 (m, 4H, H-7, H-8), 7.326–7.272 (m, 1H, H-9), 5.359 (ddd, $^2J_{4a,4b}$ = 1.2 Hz, $^3J_{4a,3}$ = 0.8 Hz, $^3J_{4a,1}$ = 0.8 Hz, 1H, H-4a), 5.271 (ddd, $^3J_{4b,3}$ = 1.3 Hz, $^2J_{4b,4a}$ = 1.2 Hz, $^3J_{4b,1}$ = 0.2 Hz, 1H, H-4b), 4.537 (s, 2H, H-5), 4.156 (dd, $^3J_{3,4b}$ = 1.3 Hz, $^3J_{4a,3}$ = 0.8 Hz, 2H, H-3), 4.053 (dd, $^3J_{1,4a}$ = 0.8 Hz, $^3J_{1,4b}$ = 0.2 Hz, 2H, H-1) ppm; ^{13}C NMR (150.93 MHz, $CDCl_3$, 25 °C): δ = 142.51 (C-2), 138.14 (C-6), 128.58–127.88 (C-7, C-8, C-9), 117.44 (C-4), 72.59 (C-5), 70.49 (C-3), 33.21 (C-1) ppm; HRMS (ESI$^+$): *m/z* = 263.0038 ([M + Na]$^+$), calcd. for $C_{11}H_{13}BrNaO^+$ 263.0042; R_f = 0.5 (heptane/ethyl acetate = 14:1).

4,5,6,7,8,9-Hexa-*O*-acetyl-1-*O*-benzyl-2,3-dideoxy-2-*C*-methylidene-D-*glycero*-D-*galacto*-nonitol (syn-31, $C_{29}H_{38}O_{13}$) D-Mannose (**19**, 200 mg, 1.11 mmol) and 401 mg 2-(benzyloxymethyl) allyl bromide (**16**, 1.67 mmol, 1.5 equiv.) were dissolved in 8 cm^3 ethanol and 2 cm^3 water. Indium powder (191 mg, 1.67 mmol, 1.5 equiv.) was added and the suspension was sonicated at 45 °C for 18 h. The reaction mixture was cooled to room temperature and the pH was adjusted to 7 with 1 M aqueous sodium hydroxide solution. The suspension was filtered over a plug of celite which was subsequently rinsed with 30 cm^3 of methanol. The filtrate was concentrated and the residue was dissolved in 6 cm pyridine and 6 cm^3 acetic anhydride. The mixture was cooled with an ice bath, treated with 7 mg 4-(dimethylamino)pyridine (0.06 mmol, 0.5 equiv.) and stirred overnight. The reaction mixture was concentrated and the addition of toluene facilitated the process by forming a homogenous pressure-maximum azeotrope with pyridine [34]. The residue was taken up in 20 cm^3 ethyl acetate and was washed with water (3 × 10 cm^3) and 10 cm^3 brine. The organic layer was dried over magnesium sulfate, filtered, and concentrated. The epimeric mixture could be separated from the per-*O*-acetylated starting material by performing column chromatography using heptane/ethyl acetate (2/1 v/v) as eluent. The epimers ***syn*-31** and ***anti*-31** could not be separated by conventional column chromatography but by HPLC using a Macherey–Nagel NUCLEODUR® 100–5 column. For successful separation, the column was cooled to 15 °C. The analytes were detected at 254 nm and the eluent applied consisted of heptane/ethyl acetate = 86/14. The conversion of 45% (298 mg, 0.501 mmol) over two steps and the diastereoselective excess of 60% could be determined by means of NMR. HRMS (ESI$^+$): *m/z* = 617.2209 ([M + Na]$^+$), calcd. for $C_{29}H_{38}NaO_{13}^+$ 617.2205; R_f = 0.5 (heptane/ethyl acetate = 1:1).

***syn*-31** : ^{1}H NMR (600.25 MHz, $CDCl_3$, 25 °C): δ = 7.400–7.309 (m, 4H, H-3″, H-4″), 7.309–7.266 (m, 1H, H-5″), 5.433 (dd, $^3J_{6,5}$ = 10.0 Hz, $^3J_{6,7}$ = 2.0 Hz, 1H, H-6), 5.316 (dd, $^3J_{7,8}$ = 8.6 Hz, $^3J_{7,6}$ = 1.97 Hz, 1H, H-7), 5.189 (dd, $^3J_{5,6}$ = 10.0 Hz, $^3J_{5,4}$ = 2.0 Hz, 1H, H-5), 5.127 (ddd, $^3J_{4,3b}$ = 9.3 Hz, $^3J_{4,3a}$ = 4.0 Hz, $^3J_{4,5}$ = 2.0 Hz, 1H, H-4), 5.071 (m, 1H, H-1″a), 4.981 (ddd, $^3J_{8,7}$ = 8.6 Hz, $^3J_{8,9b}$ = 5.4 Hz, $^3J_{8,9a}$ = 2.9 Hz, 1H, H-8), 4.955 (s, 1H, H-1″b), 4.506 (d, $^2J_{1'a,1'b}$ = 11.9 Hz, 1H, H-1′a), 4.406 (d, $^2J_{1'b,1'a}$ = 11.9 Hz, 1H, H-1′b), 4.211 (dd, $^2J_{9a,9b}$ = 12.5 Hz, $^3J_{9a,8}$ = 2.9 Hz, 1H, H-9a), 4.095 (d, $^2J_{1a,1b}$ = 12.75 Hz, 1H, H-1a), 4.021 (dd, $^2J_{9b,9a}$ = 12.5 Hz, $^3J_{9b,8}$ = 5.4 Hz, 1H, H-9b), 3.886 (d, $^2J_{1b,1a}$ = 12.75 Hz, 1H, H-1b), 2.328 (dd, $^2J_{3a,3b}$ = 14.2 Hz, $^3J_{3a,4}$ = 4.0 Hz, 1H, H-3a), 2.126 (dd, $^2J_{3b,3a}$ = 14.2 Hz, $^3J_{3b,4}$ = 9.3 Hz, 1H, H-3b), 2.127 (s, 3H, OAc), 2.085 (s, 3H, OAc), 2.058 (s, 3H, OAc), 2.035 (s, 3H, OAc), 2.007 (s, 3H, OAc), 1.994 (s, 3H, OAc) ppm; ^{13}C NMR (150.93 MHz, $CDCl_3$, 25 °C): δ = 170.69 ((C=O)–CH_3), 170.39 ((C=O)–CH_3), 170.16 ((C=O)–CH_3), 170.10 ((C=O)–CH_3), 170.09 ((C=O)–CH_3), 169.81 ((C=O)–CH_3), 141.16 (C-2), 138.41 (C-2″), 128.52 (C-4″), 127.89 (C-3″), 127.75 (C-5″), 116.23 (C-1″), 72.46 (C-1), 71.97 (C-1′), 69.67 (C-5), 68.35 (C-8), 68.08 (C-4), 67.65 (C-7), 67.18 (C-6), 62.06 (C-9), 35.32 (C-3), 21.08 ((C=O)–CH_3), 20.98 ((C=O)–CH_3), 20.93 ((C=O)–CH_3), 20.85 ((C=O)–CH_3), 20.83 ((C=O)–CH_3), 20.75 ((C=O)–CH_3) ppm.

***anti*-31**: ^{1}H NMR (600.25 MHz, $CDCl_3$, 25 °C): δ = 7.400–7.309 (m, 4H, H-3″, H-4″), 7.309–7.266 (m, 1H, H-5″), 5.411 (dd, $^3J_{6,5}$ = 9.4 Hz, $^3J_{6,7}$ = 2.2 Hz, 1H, H-6), 5.371 (dd, $^3J_{7,8}$ = 9.2 Hz, $^3J_{7,6}$ = 2.2 Hz, 1H, H-7), 5.202 (dd, $^3J_{5,6}$ = 9.4 Hz, $^3J_{5,4}$ = 2.2 Hz, 1H, H-5), 5.118 (s, 1H, H-1″a), 5.067 (ddd, $^3J_{4,3a}$ = 10.8 Hz, $^3J_{4,5}$ = 2.2 Hz, $^3J_{4,3b}$ = 0.5 Hz, 1H, H-4), 5.051 (ddd, $^3J_{8,7}$ = 9.2 Hz, $^3J_{8,9b}$ = 5.4 Hz, $^3J_{8,9a}$ = 2.8 Hz, 1H, H-8), 4.955 (s, 1H, H-1′′b), 4.544 (d, $^2J_{1'a,1'b}$ = 12.0 Hz, 1H, H-1′a), 4.481 (d, $^2J_{1'b,1'a}$ = 12.0 Hz, 1H, H-1′b), 4.203 (dd, $^2J_{9a,9b}$ = 12.5 Hz, $^3J_{9a,8}$ = 2.8 Hz, 1H, H-9a), 4.036 (dd, $^2J_{9b,9a}$ = 12.5 Hz, $^3J_{9b,8}$ = 5.4 Hz, 1H, H-9b), 3.945 (d, $^2J_{1a,1b}$ = 12.7 Hz, 1H, H-1a), 3.907 (d, $^2J_{1b,1a}$ = 12.7 Hz, 1H, H-1b), 2.518 (dd, $^2J_{3a,3b}$ = 15.1 Hz, $^3J_{3a,4}$ = 10.8 Hz, 1H, H-3a), 2.349 (dd, $^2J_{3b,3a}$ = 15.1 Hz, $^3J_{3b,4}$ = 0.5 Hz, 1H, H-3b), 2.079 (s, 3H, OAc), 2.062 (s, 6H, 2xOAc), 2.050 (s, 3H, OAc), 2.046 (s, 3H, OAc), 1.957 (s, 3H, OAc) ppm; ^{13}C NMR (150.93 MHz, $CDCl_3$, 25 °C): δ = 170.41–169.89 (6x((C=O)-CH_3)), 141.38 (C-2), 138.46 (C-2″), 128.48 (C-4″), 127.83 (C-3″), 127.70 (C-5″), 115.10 (C-1″), 73.07 (C-1), 72.02 (C-1′), 70.82 (C-4), 69.82 (C-5),

68.06 (C-8), 67.82 (C-7), 67.59 (C-6), 61.99 (C-9), 31.89 (C-3), 21.08–20.75 (6x(C = O)-$\underline{C}H_3$) ppm.

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