DOI: 10.1002/ejoc.201000623

Permanganate Oxidation Revisited: Synthesis of 3-Deoxy-2-uloses via Indium-Mediated Chain Elongation of Carbohydrates

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Keywords: Carbohydrates / Allylation / Oxidation / Indium / Thioketals

Application of the Barbier-type indium-mediated allylation method to suitable substrates offers access to carbohydrates bearing a terminal olefin moiety. The C–C bond forming reaction generates a defined stereochemistry of the new chiral center and tolerates a wide variety of starting aldehydes thus allowing modifications in the carbohydrate backbone. Further transformations of the alkene moiety via an environmentally benign and subtle controlled protocol using potassium permanganate gives rise to the structural motif of 3-deoxy-2-uloses in good yields. The final part of the reaction sequence focuses on the deprotection of the acetyl groups essential for the success of the oxidation step. The acidic and labile 3-deoxy position of the target molecule is prone to elimination applying standard deacetylation conditions and therefore demands derivatisation of the molecule. The introduction of a thioketal moiety using microwave conditions shows promising results and subsequent standard transformations are applicable leading to the desired products.

Introduction

Carbohydrates are essential for many biological processes,[1] yet the family of the ketoses is less widespread than aldoses.[2] Despite their relatively minor occurrence their biological function is unquestioned. They play key roles in many biochemical pathways, such as glycolysis[3] or cell–cell interactions.[4]

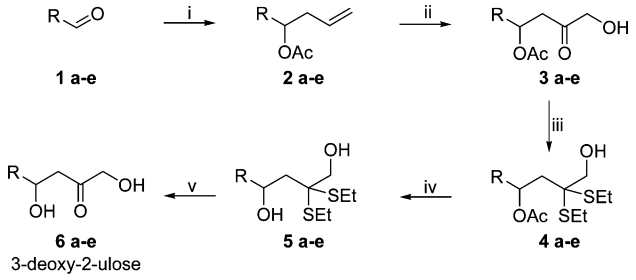
Deoxyketoses represent an essential subcategory among the ketose family. They frequently occur in very low concentrations in nature and their isolation is usually difficult and demanding.[5] But there is an increasing interest to investigate their properties and precise mode of action and higher carbohydrate analogues demand attention regarding to new therapeutic targets.[6]

Modern organic chemistry developed many strategies to produce rare carbohydrates. Total synthesis provides these compounds independently from natural sources[7] and is able to produce non-natural analogues.[8] Aldol reactions[9] as well as Grignard type reagents[10] make use of the carbonyl functionality to construct and modify the carbohydrate backbone. The deoxygenation of sugars has been extensively used to synthesize deoxy analogues.[11] These approaches need sophisticated protecting group strategies and mostly rely on the selective removal of halogens or sulfur-containing groups.

Alternatively, research focuses on the application of enzymes such as aldolases, and their use in organic synthesis.[12] General application is often rendered by limited substrate or solvent tolerance and stability.[13] However, numerous excellent preparative methods have been published.[14] The consecutive utilization of epimerases, isomerases and dehydrogenases shows promising results.[15]

Our synthetic approach focused on the preparation of different members of the 3-deoxy-2-ulose family. These C1-reduced analogues of 3-deoxy-2-ulosonic acids (sialic acids, etc.) have been scarcely examined although their biological importance has been reported.[16]

Here we present a chemical method leading to this structural motif, which offers nearly unlimited variety in the carbohydrate backbone. We applied an indium-mediated allylation to different aldoses for chain elongation. The key step in our synthesis is the oxidation of the terminal double bond to introduce the hydroxy ketone moiety. Thus, we thoroughly reinvestigated the well known and environmentally benign oxidation of olefins with potassium permanganate in acidic media.[17,18] This reaction type led directly to the desired 3-deoxy-2-uloses in good to excellent yields (Scheme 1).



Scheme 1. Reagents and conditions: (i) allyl bromide, In, ultrasound; then Ac_2O, DMAP, pyridine; (ii) $KMnO_4$, buffer/acetone; (iii) EtSH, $SnCl_2 \cdot 2H_2O$, DCM, microwave; (iv) NaOMe, MeOH; (v) *N*-bromophthalimide, THF/H_2O.

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201000623.

Results and Discussion

Our approach leading to 3-deoxy-2-uloses is outlined in Scheme 1. We started with the chain elongation of five different commonly available carbohydrates (Table 1) leading to bioactive target molecules. The indium mediated allylation of aldehydes generated a system containing a terminal double bond and additionally introduced the 3-deoxy functionality. The stereochemistry of the new chiral center formed during the Barbier-type reaction was influenced by the functional group attached to the α-C-atom (Table 1).[19] Free hydroxyl groups achieved a *threo* configuration via chelation control. This *syn* relation is found between C4 and C5 in *N*-acetyl-D-neuraminic acid (Neu5Ac), 3-deoxy-D-*glycero*-D-*galacto*-nonulosonic acid (KDN), 3-deoxy-D-*gluco*-octulosonic acid (4-epi-KDO) and D-*arabino*-3-deoxy-heptulosonic acid (DAH). Starting from *O*-isopropylidene-protected alcohols the reaction offered access to *erythro*-configured products found in 3-deoxy-D-*manno*-octulosonic acid (KDO) and 3-deoxy-D-*erythro*-2-hexulose (3-deoxy-D-fructose). Only in case of D-arabinose-derived products separation of the diastereomers by conventional column chromatography could be achieved. In all other cases the major diastereomeric products were purified at a later stage of the synthesis.

Table 1. Diastereoselectivities observed during chain elongation reaction.

Entry	Starting material	*threo*/*erythro*	Product	Combined yield
1	*N*-acetyl-D-mannosamine (**1a**)	4:1	**2a**	74%
2	D-mannose (**1b**)	5:1	**2b**	95%
3	D-arabinose (**1c**)	7:1	**2c**[20]	99%
4	D-erythrose (**1d**)	8:1	**2d**	78%
5	*O*-isopropylidene-D-glyceraldehyde (**1e**)	1:3	**2e**	76%

The oxidation with potassium permanganate was investigated using a variety of substrates.[21] Since it is an unselective oxidant, free hydroxyl groups led to numerous byproducts and to partly decomposition of the molecules. In order to prevent overoxidatition and cleavage, protecting groups had to be introduced and peracetylation ensured the preservation of the carbohydrate backbone.

In our first efforts towards the oxidation of the terminal double bond we applied conditions reported by Bonini et al.[22] using a solvent system containing 0.03 M acetic acid and acetone in a ratio of 1:4. However, the yields obtained with our substrates were rather low (Table 2, entry 5) and additionally to the desired hydroxy ketone a remarkable amount of byproduct was isolated mostly resulting from dihydroxylation of the double bond.

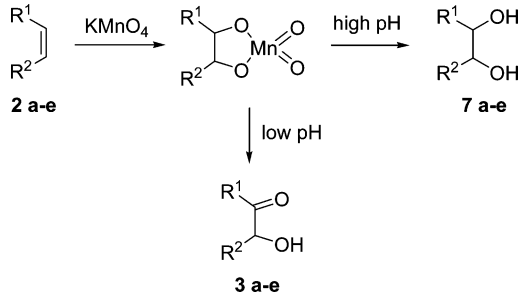
During the reaction the pH value increased dramatically due to the release of hydroxy ions. As reported earlier[23] the reaction mechanism proceeds via a cyclic manganate(VI) ester as the key intermediate in the oxidation (Scheme 2), which is formed initially via a [3+2] cycloaddition.[24] At high pH-values hydrolysis of this cyclic ester

Table 2. Optimization of pH value.

Entry	Alkene	pH value[a]	Hydroxy ketone (% yield)	Dihydroxylation (% yield)
1	**2b**	7,5	**3b** (31)	**7b** (7)
2	**2b**	5	**3b** (21)	**7b** (28)
3	**2b**	4	**3b** (51)	**7b** (14)
4	**2b**	3	**3b** (59)	**7b** (1)
5	**2b**	acetic acid[b]	**3b** (16)	**7b** (13)
6	**2c**	5	**3c** (31)	**7c** (26)
7	**2c**	4	**3c** (50)	**7c** (12)
8	**2c**	3	**3c** (58)	**7c** (9)
9	**2c**	2,5	**3c** (42)	**7c** (10)

[a] Solvent: 1 M acetic acid buffer/acetone, 1:4. [b] c = 0.03 M.[22]

is preferred and leads to dihydroxylated products **7a**–**e**,[25] whereas acidic reaction conditions generate hydroxy ketone moieties via oxidative cleavage of the intermediate manganate ester.[26] Consequently, we examined the pH-dependency of the product ratio of **3a**–**e** and **7a**–**e** in different 1 M acetate buffer/acetone systems (Table 2). The optimum results were obtained using the conditions shown in entries 4 and 8 at pH = 3.



Scheme 2. Possibilities of permanganate oxidation.

Since the amount of water present in the reaction media proved to be crucial regarding to the yield of the oxidation[27] we decided to increase the amount of aqueous buffer to optimize the conditions towards the desired hydroxy ketone formation (Table 3). The best results were obtained using acetate buffer and acetone in a ratio 1:1. Further increase of the aqueous component resulted in decreasing yields mainly because of solubility problems of our substrates (Table 3, entry 4). The optimization of the solvent system was accompanied by a decrease of the reaction time and formation of decomposition products.

Table 3. Optimization of solvent composition.

Entry	Alkene	Solvent (buffer[a]/acetone)	Product (% yield)
1	**2d**	1:4[22]	**3d** (27)
2	**2d**	2:3	**3d** (45)
3	**2d**	1:1	**3d** (53)
4	**2d**	5:1	**3d** (34)
5	**2a**	1:1	**3a** (52)
6	**2b**	1:1	**3b** (64)
7	**2c**	1:1	**3c** (65)
8	**2e**	1:1	**3e** (60)

[a] Acetic acid buffer (1 M).

The removal of the acetyl groups could not be achieved by Zemplén deacetylation or comparable basic protocols. Instead of a deprotection an α,β-unsaturated compound was formed exclusively. Attempts towards deprotection via acidic transesterification approaches failed and change of the protection group to benzyl ethers were unsuccessful due to the attack of the permanganate to the benzyl moieties.

Since the acidity of the deoxy position α to the carbonyl group prohibited standard deprotection methods we decided to establish a thioketal moiety to enable deacetylation (Scheme 1). However, the formation of acetals of labile compounds is often crucial. Strong acidic reaction conditions often limit the application and additionally long reaction times up to days are required leading frequently to moderate to poor yields. Attempts to enhance the reaction rate by heating did not improve the product formation, since elimination products were obtained as major components. Recently, deoxy sugars have been synthesized using microwave conditions[28] without decomposition or side reactions. Adopting this approach to our substrates and providing energy using microwave irradiation resulted in a less complicated product distribution. The use of tin chloride as Lewis acid additionally improved the yields (50–60%) and shortened the reaction time to minutes.

The cleavage of thioketals is usually achieved using *N*-halosuccinimide in aqueous acetone.[29] Application of this method to our substrates provided good yields but separation from the hydrophilic succinimide using standard column chromatography was not successful and caused decomposition of the unprotected carbohydrates. Additionally, the acidic reaction medium induced the formation of an isopropylidene ketal as byproduct. By using the more lipophilic *N*-bromophthalimide as deprotecting reagent and a mixture of THF/H_2O as solvent we obtained the products after neutralisation and extraction of the aqueous phase with dichloromethane and lyophilisation in excellent yields and purity.

Following our route developed we were able to synthesize a variety of bioactive 3-deoxy-2-uloses (Figure 1). The deoxyketoses **6a**–**e** were accessible starting with *N*-acetyl-D-mannosamine (leading to **6a**[30]), D-mannose (leading to **6b**), D-arabinose (leading to **6c**), D-erythrose (leading to **6d**[16]) and *O*-isopropylidene-D-glyceraldehyde (leading to **6e**[33]) as starting material in the initial chain-elongation reaction.

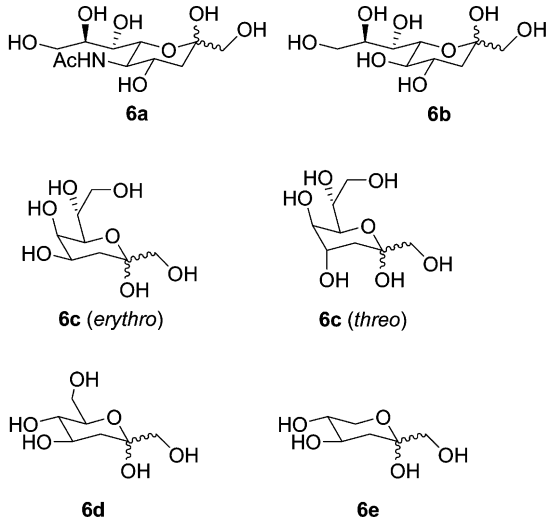


Figure 1. 3-Deoxy-2-uloses synthesized.

Conclusions

We herein report on a straightforward synthetic route towards the 3-deoxy-2-ulose family, which opens access to a great variety of bioactive carbohydrates in excellent yields. Starting from chain-elongated carbohydrate derivatives with terminal double bonds we were able to introduce the hydroxy ketone moiety by potassium permanganate oxidation in acidic media. In addition, we present a new method for the preparation of thioketals for unreactive and labile compounds using microwave conditions within very short reaction times.

Experimental Section

General Methods: ^1H and ^{13}C NMR spectra were recorded at 400 MHz on a Bruker Avance DPX 400 using $CDCl_3$ or CD_3OD for calibration. MS experiments were done in the ESI mode on a Finnigan MAT 900 spectrometer. Flash chromatography was performed using Merck silica gel 60 (0.004–0.063 mm). TLC monitoring was done on Merck plates (silica gel 60 F_{254}), compounds were visualized by treatment with a solution of $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ (48 g) and $Ce(SO_4)_2$ (2 g) in 10% H_2SO_4 (1 L), followed by heating. Solvents were distilled, if necessary, before use. *O*-Isopropylidene-D-glyceraldehyde was prepared following literature procedure.[32] Optical rotations were measured on a Perkin–Elmer Polarimeter 341. Microwave reactions were performed using a Biotage Initiator. Chemicals were purchased in reagent grade.

General Procedure for the Allylation of Aldoses. Synthesis of 2a–e (Method A): The monosaccharide was dissolved in the corresponding solvent and indium powder and allyl bromide were added. The reaction was sonicated until complete consumption of the starting material (3–18 h) as judged by TLC (acetone/ 2-propanol/water: 5:4:1). After evaporation of the solvent pyridine, acetic anhydride and DMAP were added. After completion of the reaction (TLC: EtOAc/PE: 1:1) excess of reagents was removed under reduced pressure and the precipitate was diluted with ethyl acetate and extracted 3 times with 0.1 N HCl. The organic phase was washed with brine and dried with $MgSO_4$. Evaporation of the solvent produced the crude compounds **2a**–**e**, which were purified by column chromatography on silica gel.

General Procedure for the Oxidation with Potassium Permanganate. Synthesis of 3a–e (Method B): The alkene **2a**–**e** was dissolved in a mixture of acetone and 1 M acetate buffer (pH = 3) in a 1:1 ratio. Potassium permanganate was solubilised in the same solvent and added dropwise to the reaction medium. When the purple colour disappeared the precipitate was removed by filtration through celite and washed with dichloromethane. The organic phase was dried with $MgSO_4$ and evaporation of the solvent led to the compounds **3a**–**e**, which were used in the next reaction step without purification.

General Procedure for the Thioketal Formation. Synthesis of 4a–e (Method C): Compound **3a**–**e** (0.02–0.06 mmol) was dissolved in dichloromethane (1 mL) in a microwave tube and EtSH (2 mL) and

1 equiv. $SnCl_2{\cdot}2H_2O$ was added. After irradiation in a microwave generator for 7 min at 75 °C the reaction mixture was washed with water and the organic phase dried with $MgSO_4$. The solvent was removed and the crude product was purified via column chromatography on silica gel and separation of the diastereomers was achieved (PE/EtOAc: 3:1).

General Procedure for the Deacetylation. Synthesis of 5a–e (Method D): The peracetylated thioketal **4a**–**e** was dissolved in dry MeOH (c = 0.015 mmol/mL) and 0.1 equiv. of NaOMe were added. After completion of the reaction dry ice was added to quench the reaction. The solvent was removed under reduced pressure and the product was purified using column chromatography on silica gel (DCM/MeOH: 5:1).

General Procedure for the Deprotection of the Thioketal. Synthesis of 6a–e (Method E): Compound **5a**–**e** was dissolved in H_2O (c = 0.018 mmol/mL) at 10 °C and a solution of 6 equiv. of *N*-bromophthalimide in THF (c = 0.1 mmol/mL) was added dropwise until the yellow colour remained. After 15 min the reaction was diluted with water and extracted 4 times with DCM. The aqueous phase was adjusted to pH = 7 with ion exchange resin (OH^- form) and after filtration the solvent was removed by lyophilisation.

1,2,3,4,6-Penta-*O*-acetyl-5-acetylamino-5,7,8,9-tetradeoxy-D-*glycero*-D-*galacto*-8-nonenitol (2a): *N*-Acetyl-D-mannosamine hydrate (100 mg, 0.42 mmol) was treated according to method A with indium (191 mg, 4 equiv., 1.66 mmol) and allyl bromide (216 μL, 6 equiv., 2.52 mmol) in EtOH/0.1 N HCl: 6:1 (3.5 mL). Purification was achieved using column chromatography and PE/EtOAc: 1:1 as eluent; yield 147 mg (74%) of inseparable diastereomers [*glycero-galacto* (**2a**)/*glycero-talo*: 4:1]. ^{1}H NMR (400 MHz, $CDCl_3$): δ (**2a**) = 5.69 (m, 1 H, H8) 5.61 (d, J = 10.52 Hz, 1 H, NH) 5.30 (dd, J = 8.25, J = 2.16 Hz, 1 H, H3) 5.19 (dd, J = 2.16, J = 10.52 Hz, 1 H, H4) 5.04 (m, 1 H, H9a) 5.00 (m, 1 H, H9b) 4.97 (m, 1 H, H2) 4.79 (m, 1 H, H6) 4.42 (m, 1 H, H5) 4.20 (dd, J = 3.09, J = 12.48 Hz, 1 H, H1a) 3.93 (m, 1 H, H1b) 2.18 (m, 2 H, H7a, H7b) 2.07–1.96 (6s, 18 H, 6 CH_3, OAc/NHAc) ppm. ^{13}C NMR (400 MHz. $CDCl_3$): δ (**2a**) = 174.9 (C=O, NHAc) 170.5–189.8 (5 C=O, OAc) 132.9 (C8) 119.0 (C9) 71.0 (C6) 69.2 (C2) 68.6 (C4) 68.4 (C3) 62.5 (C1) 49.2 (C5) 36.3 (C7) 23.5 –21.0 (6 CH_3, OAcNHAc) ppm. MS (ESI): m/z = 496.2 $[M + Na]^+$.

1,2,3,4,5,6-Hexa-*O*-acetyl-7,8,9-trideoxy-D-*glycero*-D-*galacto*-8-nonenitol (2b): D-Mannose (303 mg, 1.68 mmol) was dissolved (20 mL, EtOH/0.1 N HCl: 10:1) and indium powder (386 mg, 2 equiv., 3.36 mmol) and allyl bromide (580 μL, 4 equiv., 6.8 mmol) were added and treated according to method A (PE/EtOAc: 1:2); yield 759 mg (95%) of inseparable diastereomers [*glycero-galacto* (**2b**)/*glycero-talo*: 5:1]. ^{1}H NMR ($CDCl_3$): δ (**2b**) = 5.57 (m, 1 H, H8) 5.34 (dd, J = 1.90, J = 9.88 Hz, 1 H, H5) 5.20 (dd, J = 1.90, J = 8.65 Hz, 1 H, H3) 5.05 (dd, J = 1.9, J = 9.88 Hz, 1 H, H4) 4.95 (m, 1 H, H9a) 4.91 (m, 1 H, H9b) 4.87 (m, 1 H, H2) 4.83 (m, 1 H, H6) 4.08 (dd, J = 2.80, J = 12.42 Hz, 1 H, H1a) 3.89 (dd, J = 5.28, J = 12.42 Hz, 1 H, H1b) 2.07 (m, 2 H, H7a, H7b) 1.99–1.90 (6s, 18 H, 6 CH_3, OAc) ppm. ^{13}C NMR ($CDCl_3$): δ (**2b**) = 170.2–169.3 (6 C=O, OAc) 132.4 (C8) 118.1 (C9) 69.3 (C6) 68.8 (C2) 67.9 (C4) 67.2 (C3) 66.7 (C5) 61.6 (C1) 35.4 (C7) 20.6–20.3 (6 CH_3, OAc) ppm. MS (ESI): m/z = 497.2 $[M + Na]^+$.

1,2,3,4,5-Penta-*O*-acetyl-6,7,8-trideoxy-D-*manno*-7-octenitol [2c (*erythro*)] and 1,2,3,4,5-Penta-*O*-acetyl-6,7,8-trideoxy-D-*gluco*-7-octenitol [2c (*threo*)]: D-Arabinose (1 mmol, 150 mg) was treated according to method A in EtOH/H2O: 4:1 (10 mL) with indium (172 mg, 1.5 equiv., 1.5 mmol) and allyl bromide (345 μL, 5 equiv., 5 mmol). The crude product was purified with column chromatography (PE/EtOAc: 5:1) and the separation of the diastereomers was achieved {*manno* [**2c** (*erythro*)]/*gluco* [**2c** (*threo*)]: 1:7}; yield 400 mg [99%; R_f[**2c** (*erythro*)] = 0.35, PE/EtOAc = 2:1; R_f[**2d** (*threo*)] = 0.28, PE/EtOAc = 2:1]. [**2c** (*erythro*)] α_D^{20} = +24.2 (c = 16.6 mg/mL DCM). ^{1}H NMR ($CDCl_3$): δ [**2c** (*erythro*)] = 5.71 (m, 1 H, H7) 5.44 (dd, J = 8.84, J = 2.25 Hz, 1 H, H3) 5.30 (dd, J = 8.08, J = 2.25 Hz, 1 H, H5) 5.07 (m, 1 H, H2) 5.05 (m, 2 H, H8a, H8b) 5.00 (m, 1 H, H4) 4.21 (dd, J = 12.63, J = 2.77 Hz, 1 H, H1a) 4.06 (dd, J = 12.63, J = 5.56 Hz, 1 H, H1b) 2.36 (m, 1 H, H6a) 2.24 (m, 1 H, H6b) 2.09–2.01 (5s, 15 H, 5 CH_3, OAc) ppm. ^{13}C NMR ($CDCl_3$): δ [**2c** (*erythro*)] = 170.6–169.7 (5 C=O, OAc) 132.7 (C7) 118.4 (C8) 70.1 (C5) 69.1 (C4) 68.1 (C2) 67.6 (C3) 61.9 (C1) 35.6 (C6) 20.4–20.2 (5 CH_3, OAc) ppm. MS (ESI): m/z = 425.1 $[M + Na]^+$. [**2c** (*threo*)] α_D^{20} = +26.4 (c = 128 mg/mL DCM). ^{1}H NMR ($CDCl_3$): δ [**2c** (*threo*)] = 5.57 (m, 1 H, H7) 5.25 (dd, J = 4.22, J = 6.30 Hz, 1 H, H3) 5.14 (dd, J = 4.22, J = 6.90 Hz, 1 H, H4) 4.98–4.86 (m, 4 H, H2, H5, H8a, H8b) 4.08 (dd, J = 3.31, J = 12.30 Hz, 1 H, H1a) 3.96 (dd, J = 5.63, J = 12.30 Hz, 1 H, H1b) 2.26 (m, 1 H, H6a) 2.16 (m, 1 H, H6b) 1.96–1.87 (5s, 15 H, 5 CH_3, OAc) ppm. ^{13}C NMR ($CDCl_3$): δ = 170.1–169.5 (5 C=O, OAc) 131.9 (C7) 118.6 (C8) 70.4 (C5) 70.1 (C4) 68.7 (C2) 68.5 (C3) 61.2 (C1) 34.9 (C6) 20.5–20.2 (5 CH_3, OAc) ppm. MS (ESI): m/z = 425.1 $[M + Na]^+$.

1,2,3,4-Tetra-*O*-acetyl-5,6,7-trideoxy-D-*arabino*-6-heptenitol (2d): 2,3-Di-*O*-formyl-D-erythrose was prepared starting from D-glucose according to the literature procedure.[31] The erythrose derivative (103 mg, 0.58 mmol) was deformylated with Dowex W50 ion exchange resin (50 mg, H^+ form) in water (1.5 mL) for 3 h at 60 °C. The solution was filtered and the carbohydrate was treated according to method A using EtOH (6 mL), indium (75 mg, 1.1 equiv., 0.65 mmol) and allyl bromide (150 μL, 3 equiv., 1.7 mmol). After conversion and purification (PE/EtOAc = 3:1) 149 mg of **2d** (78%) were obtained as a mixture of inseparable diastereomers [*arabino* (**2d**)/*ribo*: 8:1]. ^{1}H NMR ($CDCl_3$): δ (**2d**) = 5.66 (m, 1 H, H6) 5.26 (dd, J = 2.86, J = 8.43 Hz, 1 H H4) 5.16 (m, 1 H, H2) 5.12–5.02 (m, 3 H, H3, H7a, H7b) 4.19 (dd, J = 2.77, J = 12.42 Hz, 1 H, H1a) 4.09 (dd, J = 5.09, J = 12.42 Hz, 1 H, H1b) 2.42–2.19 (m, 2 H, H5a H5b) 2.10–2.00 (4s, 12 H, 4 CH_3, OAc) ppm. ^{13}C NMR ($CDCl_3$): δ (**2d**) = 170.5–169.7 (4 C=O, OAc) 132.3 (C6) 118.6 (C7) 70.1 (C2) 69.7 (C4) 68.4 (C3) 61.9 (C1) 35.4 (C5) 20,7–20.5 (4 CH_3, OAc) ppm. MS (ESI): m/z = 353.2 $[M + Na]^+$.

1,2,3-Tri-*O*-acetyl-4,5,6-trideoxy-D-*erythro*-5-hexenitol (2e): *O*-Isopropylidene-D-glyceraldehyde[32] (48 mg, 0.369 mmol) was dissolved in EtOH (5 mL) and indium powder (59 mg, 1.4 equiv., 0.52 mmol) and allyl bromide (93 μL, 3 equiv., 1.08 mmol) were added. The reaction was completed within 3 h of sonication and after removal of the solvent dioxane (1 mL), water (5 mL) and Dowex W50 ion exchange resin (40 mg, H^+-form) were added. After 1 h the solvent was removed and the crude product was peracetylated by dissolving in pyridine (5 mL) and acetic anhydride (5 mL) and adding DMAP (5 mg). After complete conversion **2e** was purified via column chromatography using PE/EtOAc: 4:1 as the eluent; yield 72 mg (76%) as a mixture of inseparable diastereomers [*erythro* (**2e**)/*threo*: 3:1]. ^{1}H NMR ($CDCl_3$): δ (**2e**) = 5.72 (m, 1 H, H5) 5.18–5.07 (m, 4 H, H2, H3, H6a, H6b) 4.31 (m, 1 H, H1a) 4.16 (m, 1 H, H1b) 2.44–2.29 (m, 2 H, H4a, H4b) 2.07–2.04 (3s, 9 H, 3 CH_3, OAc) ppm. ^{13}C NMR ($CDCl_3$): δ (**2e**) = 170.7–170.0 (3 C=O, OAc) 132.4 (C5) 118.6 (C6) 71.5 (C2) 70.5 (C3) 61.9 (C1) 34.9 (C4) 20.9–20.7 (3 CH_3, OAc) ppm. MS (ESI): m/z = 281.2 $[M + Na]^+$.

4,6,7,8,9-Penta-*O*-acetyl-5-acetylamino-3,5-dideoxy-D-*glycero*-D-*galacto*-2-nonulose (3a): Alkene **2a** (18 mg, 0.036 mmol) was treated according to method B in 5 mL of solvent and was oxidized with

$KMnO_4$ (8 mg, 1.4 equiv., 0.05 mmol) in 5 mL of solvent; yield 10 mg (52%) of inseparable diastereomers [*glycero-galacto* (**3a**)/*glycero-talo*: 4:1] ^{1}H NMR ($CDCl_3$): δ (**3a**) = 5.61 (d, J = 10.61 Hz, 1 H, NH) 5.38 (dd, J = 2.27, J = 8.40 Hz, 1 H, H7) 5.29 (dd, J = 2.27, J = 10.28 Hz, 1 H, H6) 5.19 (m, 1 H, H4) 5.04 (m, 1 H, H8) 4.40 (m, 1 H, H5) 4.25 (dd, J = 3.06, J = 12.54 Hz, 1 H, H9a) 4.16 (d, J = 15.05 Hz, 2 H, H1a, H1b) 3.99 (dd, J = 5.63, J = 12.54 Hz, 1 H, H9b) 2.67 (dd, J = 8.19, J = 16.64 Hz, 1 H, H3a) 2.55 (dd, J = 5.38, J = 16.64 Hz, 1 H, H3b) 2.11–2.01 (6s, 18 H, 6 CH_3, OAc/NHAc) ppm. ^{13}C NMR ($CDCl_3$): δ (**3a**) = 206.7 (C2) 171.3–170.1 (6 C=O, OAc/NHAc) 69.2 (C8) 68.7 (C1) 68.3 (C6) 68.2 (C7) 68.1 (C4) 62.4 (C9) 49.6 (C5) 39.7 (C3) 23.6–21.0 (6 CH_3, OAc/NHAc) ppm. MS (ESI): m/z = 528.1 $[M + Na]^+$.

4,5,6,7,8,9-Hexa-*O*-acetyl-3-deoxy-D-*glycero*-D-*galacto*-2-nonulose (3b): Compound **2b** (190 mg, 0.4 mmol) was dissolved in 10 mL of the solvent mixture and treated according to method B with $KMnO_4$ (108 mg, 1.7 equiv., 0.68 mmol) in 10 mL solvent; yield 129 mg (64%) of inseparable diastereomers [*glycero-galacto* (**3b**)/*glycero-talo*: 5:1]. ^{1}H NMR ($CDCl_3$): δ (**3b**) = 5.48 (dd, J = 2.00, J = 10.11 Hz, 1 H, H6) 5.36 (dd, J = 2.00, J = 8.98 Hz, 1 H, H7) 5.27 (m, 1 H, H4) 5.08 (dd, J = 1.68, J = 10.11 Hz, 1 H, H5) 5.00 (m, 1 H, H8) 4.19 (dd, J = 2.70, J = 12.59 Hz, 1 H, H9a) 4.14 (d, J = 5.53 Hz, 2 H, H1a, H1b) 4.02 (dd, J = 12.59, J = 5.21 Hz, 1 H, H9b) 2.57 (m, 2 H, H3a, H3b) 2.11–2.02 (6s, 18 H, 6 CH_3, OAc) ppm. ^{13}C NMR ($CDCl_3$): δ (**3b**) = 205.1 (C2) 170.6–169.7 (6 C=O, OAc) 68.8 (C5) 68.1 (C1) 67.9 (C8) 67.3 (C7) 66.7 (C6) 66.5 (C4) 61.8 (C9) 38.9 (C3) 20.8–20.5 (6 CH_3, OAc) ppm. MS (ESI): m/z = 529.3 $[M + Na]^+$.

4,5,6,7,8-Penta-*O*-acetyl-3-deoxy-D-*manno*-2-octulose [3c (*erythro*)]: The substrate **2c** (*erythro*) (35 mg, 0.087 mmol) was solubilised in 5 mL solvent and $KMnO_4$ (16 mg, 1.1 equiv., 0.1 mmol) in 5 mL solvent was used for the oxidation following method B; yield 24.4 mg (65%). ^{1}H NMR ($CDCl_3$): δ = 5.41 (m, 1 H, H7) 5.37 (m, 1 H, H5) 5.36 (m, 1 H, H4) 5.09 (m, 1 H, H6) 4.24 (m, 2 H, H8a, H8b) 4.23 (m, 1 H, H1a) 4.11 (m, 1 H, H1b) 2.73 (m, 2 H, H3a, H3b) 2.10–2.02 (5s, 15 H, 5 CH_3, OAc) ppm. ^{13}C NMR ($CDCl_3$): δ = 205.7 (C2) 170.6–169.7 (5 C=O, OAc) 70.3 (C4) 68.5 (C8) 68.3 (C6) 67.6 (C7) 66.6 (C5) 61.7 (C1) 39.5 (C3) 20.79–20.59 (5 CH_3, OAc) ppm. MS (ESI): m/z = 457.2 $[M + Na]^+$.

4,5,6,7,8-Penta-*O*-acetyl-3-deoxy-D-*gluco*-2-octulose [3c (*threo*)]: Compound **2c** (*threo*) (120 mg, 0.298 mmol) was dissolved in 10 mL solvent and $KMnO_4$ (52 mg, 1.1 equiv., 0.33 mmol) in 10 mL solvent was used for the oxidation following method B; yield 84 mg (65%). ^{1}H NMR ($CDCl_3$): δ = 5.42 (m, 3 H, H4, H5, H6) 5.03 (m, 1 H, H7) 4.22 (dd, J = 3.26, J = 12.61 Hz, 1 H, H8a) 4.16 (d, J = 2.67 Hz, 2 H, H1a, H1b) 4.10 (dd, J = 5.64, J = 12.61 Hz, 1 H, H8b) 2.71 (m, 2 H, H3a, H3b) 2.03–1.98 (5s, 15 H, 5 CH_3, OAc) ppm. ^{13}C NMR ($CDCl_3$): δ = 202.8 (C2) 170.5–169.8 (5 C=O, OAc) 70.1 (C5) 68.8 (C6) 68.6 (C7) 68.4 (C1) 67.6 (C4) 61.3 (C8) 39.1 (C3) 20.6–20.3 (5 CH_3, OAc) ppm. MS (ESI): m/z = 457.1 $[M + Na]^+$.

4,5,6,7-Tetra-*O*-acetyl-3-deoxy-D-*arabino*-2-heptulose (3d): Alkene **2d** (66.8 mg, 0.2 mmol) was dissolved in 5 mL of solvent and oxidised with $KMnO_4$ (48 mg, 1.5 equiv., 0.3 mmol) in 5 mL solvent according to method B; yield 38.5 mg (53%) of inseparable diastereomers [*arabino* (**3d**)/*ribo*: 8:1]. ^{1}H NMR ($CDCl_3$): δ (**3d**) = 5.58 (m, 1 H, H4) 5.26 (dd, J = 2.31, J = 8.94 Hz, 1 H, H5) 5.11 (m, 1 H, H6) 4,24–4.15 (m, 4 H, H1a, H1b, H7a, H7b) 2.63 (m, 2 H, H3a, H3b) 2.21–2.02 (4s, 12 H, 4 CH_3, OAc) ppm. ^{13}C NMR ($CDCl_3$): δ (**3d**) = 205.6 (C2) 170.6–169.8 (4 C=O, OAc) 70.1 (C5) 68.8 (C6) 68.2 (C7) 66.4 (C4) 61.8 (C1) 39.3 (C3) 20.8–20.6 (4 CH_3, OAc) ppm. MS (ESI): m/z = 385.2 $[M + Na]^+$.

4,5,6-Tri-*O*-acetyl-3-deoxy-D-*erythro*-2-hexulose (3e): Substrate **2e** (78.5 mg, 0.24 mmol) was dissolved in 10 mL solvent and treated according to method B with $KMnO_4$ (62 mg, 1.5 equiv., 0.39 mmol) in 5 mL solvent; yield 52 mg (60%) of inseparable diastereomers [*erythro* (**3e**)/*threo*: 3:1]. ^{1}H NMR ($CDCl_3$): δ (**3e**) = 5.54 (m, 1 H, H4) 5.27 (m, 1 H, H5) 4.28 (m, 1 H, H6a) 4.23 (m, 2 H, H1a, H1b) 4.07 (dd, J = 6.84, J = 11.85 Hz, 1 H, H6b) 2.72–2.69 (m, 2 H, H3a, H3b) 2.11–2.05 (3s, 9 H, 3 CH_3, OAc) ppm. ^{13}C NMR ($CDCl_3$): δ (**3e**) = 206.0 (C2) 170.9–170.2 (3 C=O, OAc) 71.2 (C5) 68.9 (C1) 67.8 (C4) 62.4 (C6) 39.6 (C3) 21.1–21.0 (3 CH_3, OAc) ppm. MS (ESI): m/z = 313.1 $[M + Na]^+$.

4,6,7,8,9-Penta-*O*-acetyl-5-acetylamino-3,5-dideoxy-D-*glycero*-D-*galacto*-2-nonulose Diethyl Dithioketal (4a): Treatment of **3a** (13 mg, 0.026 mmol) according to method C yielded in 8 mg (51%; R_f = 0.32 PE/EtOAc: 2:1) of **4a**. a_D^{20} = +18.2 (4.5 mg/mL DCM). ^{1}H NMR ($CDCl_3$): δ = 5.68 (d, J = 10.61 Hz, 1 H, NH) 5.32 (dd, J = 8.97, J = 1.14 Hz, 1 H, H7) 5.19 (m, 1 H, H6) 5.18 (m, 1 H, H4) 5.04 (m, 1 H, H8) 4.52 (m, 1 H, H5) 4.27 (dd, J = 12.45, J = 3.06 Hz, 1 H, H9a) 3.97 (dd, J = 12.45, J = 5.89 Hz, 1 H, H9b) 3.66 (m, 2 H, H1a, H1b) 2.68–2.59 (m, 4 H, 2 CH_2, SEt) 2,17–2.02 (6s, 6 CH_3, OAc/NHAc) 2.10 (m, 1 H, H3a) 1.86 (m, 1 H, H3b) 1.26–1.20 (m, 6 H, 2 CH_3, SEt) ppm. ^{13}C NMR ($CDCl_3$): δ = 170.8–169.9 (6 C=O, OAc/NHAc) 69.0 (C6) 68.9 (C8) 68.5 (C4) 68.0 (C7) 64.8 (C1) 64.2 [C2, $C(SEt)_2$] 62.1 (C9) 50.9 (C5) 37.0 (C3) 23.3 (CH_3, NHAc) 22.3–22.2 (2 CH_2, SEt) 21.2–20.7 (5 CH_3, OAc) 13.9–13.8 (2 CH_3, SEt) ppm. MS (ESI): m/z = 634.2 $[M + Na]^+$.

4,5,6,7,8,9-Hexa-*O*-acetyl-3-deoxy-D-*glycero*-D-*galacto*-2-nonulose Diethyl Dithioketal (4b): Compound **3b** (15 mg, 0.03 mmol) was treated according to method C; yield 9.2 mg (50%; R_f = 0.31 PE/EtOAc: 2:1) a_D^{20} = +9.2 (12.5 mg/mL DCM). ^{1}H NMR ($CDCl_3$): δ = 5.32 (dd, J = 9.60, J = 2.02 Hz, 1 H, H5) 5.28 (m, 1 H, H4) 5.25 (dd, J = 8.59, J = 2.53 Hz, 1 H, H7) 5.10 (dd, J = 9.60, J = 2.53 Hz, 1 H, H6) 4.93 (m, 1 H, H8) 4.15 (dd, J = 12.45, J = 2.91 Hz, 1 H, H9a) 3.95 (dd, J = 12.45, J = 5.30 Hz, 1 H, H9b) 3.61 (m, 1 H, H1a) 3.50 (m, 1 H, H1b) 2.57–2.50 (m, 4 H, 2 CH_2, SEt) 2.05–1.97 (6s, 6 CH_3, OAc) 1.96 (m, 2 H, H3a, H3b) 1.19–1.13 (m, 6 H, 2 CH_3, SEt) ppm. ^{13}C NMR ($CDCl_3$): δ = 170.9–170.3 (6 C=O, OAc) 70.8 (C6) 68.8 (C8) 68.1 (C7) 67.6 (C4) 67.5 (C5) 65.0 (C1) 64.6 [C2, $C(SEt)_2$] 62.3 (C9) 36.9 (C3) 22.8–22.6 (2 CH_2, SEt) 21.7–21.1 (6 CH_3, OAc) 14.5–14.3 (2 CH_3, SEt) ppm. MS (ESI): m/z = 635.2 $[M + Na]^+$.

4,5,6,7,8-Penta-*O*-acetyl-3-deoxy-D-*manno*-2-octulose Diethyl Dithioketal [4c (*erythro*)]: Treatment of **3c** (*erythro*) (14.4 mg, 0.033 mmol) according to method C resulted in 10 mg (56%) of **4c** (*erythro*). a_D^{20} = +21.6 (12.3 mg/mL DCM). ^{1}H NMR ($CDCl_3$): δ = 5.45 (m, 1 H, H4) 5.41 (dd, J = 7.96, J = 3.45 Hz, 1 H, H6) 5.19 (dd, J = 5.05, J = 3.45 Hz, 1 H, H5) 5.13 (m, 1 H, H7) 4.25 (dd, J = 12.38, J = 2.79 Hz, 1 H, H8a) 4.11 (dd, J = 12.38, J = 5.48 Hz, 1 H, H8b) 3.59 (dd, J = 8.40, J = 12.17 Hz, 1 H, H1a) 3.47 (dd, J = 5.07, J = 12.17 Hz, 1 H, H1b) 2.66–2.58 (m, 4 H, 2 CH_2, SEt) 2.21 (m, 1 H, H3a) 2.10–2.01 (5s, 15 H, 5 CH_3, OAc) 2.05 (m, 1 H, H3b) 1.25–1.20 (m, 6 H, 2 CH_3, SEt) ppm. ^{13}C NMR ($CDCl_3$): δ = 170.6–169.9 (5 C=O, OAc) 71.1 (C5) 68.6 (C7) 68.3 (C4) 67.6 (C6) 64.7 (C1) 64.2 [C2, $C(SEt)_2$] 61.7 (C8) 35.9 (C3) 22.5–22.3 (2 CH_2, SEt) 21.3–20.7 (5 CH_3, OAc) 14.1–13.9 (2 CH_2, SEt) ppm. MS (ESI): m/z = 563.3 $[M + Na]^+$.

4,5,6,7,8-Penta-*O*-acetyl-3-deoxy-D-*gluco*-2-octulose Diethyl Dithioketal [4c (*threo*)]: Treatment of **3c** (*threo*) (16.4 mg, 0.038 mmol) according to method C resulted in 11.5 mg (56%) of **4c** (*threo*). a_D^{20} = +32.1 (14 mg/mL DCM). ^{1}H NMR ($CDCl_3$): δ = 5.41 (m, 1 H, H4) 5.38 (m, 1 H, H6) 5.23 (dd, J = 4.12, J = 6.44 Hz, 1 H, H5) 5.10 (m, 1 H, H7) 4.26 (dd, J = 3.04, J = 12.45 Hz, 1 H, H8a)

4.09 (dd, J = 5.64, J = 12.45 Hz, 1 H, H8b) 3.65 (dd, J = 5.05, J = 12.01 Hz, 1 H, H1a) 3.53 (d, J = 8.05, 12.01 Hz, 1 H, H1b) 2.71–2.57 (m, 4 H, 2 CH_2, SEt) 2.11–2.09 (m, 2 H, H3a, H3b) 2.12–2.04 (5s, 15 H, 5 CH_3, OAc) 1.28–1.19 (m, 6 H, 2 CH_3, SEt) ppm. ^{13}C NMR ($CDCl_3$): δ = 170.6–169.8 (5 C=O, OAc) 71.1 (C5) 68.9 (C7) 68.5 (C6) 67.8 (C4) 64.6 (C1) 64.0 [C2, $C(SEt)_2$] 61.7 (C8) 36.0 (C3) 22.4–22.3 (2 CH_2, SEt) 21.2–20.5 (5 CH_3, OAc) 14.0–13.7 (2 CH_3, SEt) ppm. MS (ESI): m/z = 563.3 $[M + Na]^+$.

4,5,6,7-Tetra-*O*-acetyl-3-deoxy-D-*arabino*-2-heptulose Diethyl Dithioketal (4d): Dissolving **3d** (15 mg, 0.041 mmol) and treatment according to method C yielded 10 mg of **4d** (52%; R_f = 0.27 PE/EtOAc: 2:1). α_D^{20} = +23.5 (5.9 mg/mL DCM). ^1H NMR ($CDCl_3$): δ = 5.57 (m, 1 H, H4) 5.25 (dd, J = 8.08, J = 3.16 Hz, 1 H, H5) 5.05 (m, 1 H, H6) 4.26 (dd, J = 12.50, J = 2.75 Hz, 1 H, H7a) 4.13 (dd, J = 12.50, J = 5.09 Hz, 1 H, H7b) 3.64 (dd, J = 11.49, J = 7.45 Hz, 1 H, H1a) 3.54 (dd, J = 11.49, J = 4.92 Hz, 1 H, H1b) 2.66–2.57 (m, 4 H, 2 CH_2, SEt) 2.13–2.04 (4s, 12 H, 4 CH_3, OAc) 2.05 (m, 2 H, H3a, H3b) 1.26–1.21 (m, 6 H, 2 CH_3, SEt) ppm. ^{13}C NMR ($CDCl_3$): δ = 170.7–169.9 (4 C=O, OAc) 72.0 (C5) 68.6 (C6) 67.1 (C4) 64.5 (C1) 64.2 [C2, $C(SEt)_2$] 61.8 (C7) 36.7 (C3) 22.4–22.3 (2 CH_2, SEt) 21.2–20.7 (4 CH_3, OAc) 14.0–13.8 (2 CH_3, SEt) ppm. MS (ESI): m/z = 491.2 $[M + Na]^+$.

4,5,6-Tri-*O*-acetyl-3-deoxy-D-erythro-2-hexulose Diethyl Dithioketal (4e): Compound **3e** (17 mg, 0.058 mmol) was treated according to method C yielding 13.5 mg (59%; R_f = 0.20 PE/EtOAc: 2:1) of inseparable diastereomers [*erythro* (**4e**)/*threo*: 3:1]. ^1H NMR ($CDCl_3$): δ (**4e**) = 5.52 (m, 1 H, H4) 5.16 (m, 1 H, H5) 4.27 (dd, J = 12.12, J = 3.79 Hz, 1 H, H6a) 4.13 (dd, J = 12.12, J = 7.58 Hz, 1 H, H6b) 3.55 (m, 2 H, H1a, H1b) 2.66–2.58 (m, 4 H, 2 CH_2, SEt) 2.16 (m, 1 H, H3a) 2.05 (m, 1 H, H3b) 2.07–2.05 (3s, 9 H, 3 CH_3, OAc) 1.27–1.18 (m, 6 H, 2 CH_3, SEt) ppm. ^{13}C NMR ($CDCl_3$): δ (**4e**) = 170.6–169.9 (3 C=O, OAc) 72.8 (C5) 69.1 (C4) 64.7 (C1) 64.4 [C2, $C(SEt)_2$] 61.8 (C6) 35.8 (C3) 22.5–22.3 (2 CH_2, SEt) 21.1–20.7 (3 CH_3, OAc) 14.0–13.9 (2 CH_3, SEt) ppm. MS (ESI): m/z = 419.2 $[M + Na]^+$.

5-Acetylamino-3,5-dideoxy-D-*glycero*-D-*galacto*-2-nonulose Diethyl Dithioketal (5a): Treatment of **4a** (13 mg, 0.021 mmol) according to method D yielded 7.6 mg (90%) of **5a**. α_D^{20} = –21.9 (3.2 mg/mL MeOH). ^1H NMR (CD_3OD): δ = 4.66 (m, 1 H, H4) 3.89 (m, 1 H, H8) 3.84 (m, 1 H, H5) 3.81 (m, 1 H, H1a) 3.79 (m, 1 H, H9a) 3.71 (m, 1 H, H7) 3.65 (m, 1 H, H1b) 3.61 (m, 1 H, H9b) 3.39 (dd, J = 0.25, J = 8.84 Hz, 1 H, H6) 2.70–2.59 (m, 4 H, 2 CH_2, SEt) 2.04 (m, 1 H, H3a) 2.02 (s, 3 H, CH_3, NHAc) 1.84 (m, 1 H, H3b) 1.24–1.20 (m, 6 H, 2 CH_3, SEt) ppm. ^{13}C NMR (CD_3OD): δ = 174.4 (C=O, NHAc) 72.6 (C7) 71.4 (C6) 69.8 (C8) 67.9 (C1) 67.1 (C4) 65.9 [C2, $C(SEt)_2$] 65.2 (C9) 57.2 (C5) 43.1 (C3) 23.7–23.1 (2 CH_2, SEt) 22.5 (CH_3, NHAc) 14.5–14.1 (2 CH_3, SEt) ppm. MS (ESI): m/z = 424.2 $[M + Na]^+$.

3-Deoxy-D-*glycero*-D-*galacto*-2-nonulose Diethyl Dithioketal (5b): Compound **5b** was prepared according to method D starting from substrate **4b** (20 mg, 0.033 mmol); yield 11 mg (93%). α_D^{20} = +7.2 (4 mg/mL MeOH). ^1H NMR (CD_3OD): δ = 4.43 (m, 1 H, H4) 3.88 (m, 1 H, H6) 3.81 (m, 1 H, H9a) 3.80 (m, 1 H, H1a) 3.79 (m, 1 H, H7) 3.70 (m, 1 H, H8) 3.69 (m, 1 H, H1b) 3.63 (m, 1 H, H9b) 3.51 (dd, J = 9.09, J = 1.52 Hz, 1 H, H5) 2.75–2.57 (m, 4 H, 2 CH_2, SEt) 2.19 (dd, J = 14.53,16, J = 9.60 Hz, 1 H, H3a) 1.99 (dd, J = 14.53, J = 0.63 Hz, 1 H, H3b) 1.24–1.20 (m, 6 H, 2 CH_3, SEt) ppm. ^{13}C NMR (CD_3OD): δ = 74.7 (C5) 73.3 (C8) 71.4 (C7) 70.9 (C6) 69.0 (C4) 68.2 (C1) 66.1 [C2, $C(SEt)_2$] 65.2 (C9) 42.9 (C3) 23.7–23.0 (2 CH_2, SEt) 14.5–14.3 (2 CH_3, SEt) ppm. MS (ESI): m/z = 383.1 $[M + Na]^+$.

3-Deoxy-D-*manno*-2-octulose Diethyl Dithioketal [5c (*erythro*)]: Substrate **4c** (*erythro*) (21 mg, 0.039 mmol) was treated following method D yielding 12.5 mg (97%) of **5c** (*erythro*) after purification. α_D^{20} = –15.7 (6.3 mg/mL MeOH). ^1H NMR (CD_3OD): δ = 4.15 (m, 1 H, H4) 3.79 (m, 2 H, H7, H8a) 3.78 (m, 1 H, H1a) 3.69 (m, 1 H, H1b) 3.67 (m, 1 H, H6) 3.63 (m, 1 H, H8b) 3.57 (dd, J = 7.96, J = 1.14 Hz, 1 H, H5) 2.76–2.62 (m, 4 H, 2 CH_2, SEt) 2.39 (dd, J = 15.00, J = 9.53 Hz, 1 H, H3a) 1.83 (dd, J = 15.00, J = 1.05 Hz, 1 H, H3b) 1.24–1.20 (m, 6 H, 2 CH_3, SEt) ppm. ^{13}C NMR (CD_3OD): δ = 73.6 (C5) 73.1 (C6) 71.1 (C7) 69.9 (C4) 68.4 (C1) 66.1 [C2, $C(SEt)_2$] 65.1 (C8) 42.8 (C3) 23.8–22.7 (2 CH_2, SEt) 14.5–14.2 (2 CH_3, SEt) ppm. MS (ESI): m/z = 329.2 $[M – H]^-$.

3-Deoxy-D-*gluco*-2-octulose Diethyl Dithioketal [5c (*threo*)]: Substrate **4c** (*threo*) (15.9 mg, 0.03 mmol) was treated following method D yielding 9.5 mg (96%) of **5c** (*threo*) after purification. α_D^{20} = +10.3 (5 mg/mL MeOH). ^1H NMR (CD_3OD): δ = 4.25 (m, 1 H, H4) 3.78 (m, 1 H, H1a) 3.77 (m, 1 H, H8a) 3.68 (m, 1 H, H1b) 3.69–3.60 (m, 3 H, H5, H6, H7) 3.63 (m, 1 H, H8b) 2.71–2.59 (m, 4 H, 2 CH_2, SEt) 2.05 (m, 2 H, H3a, H3b) 1.24–1.99 (m, 6 H, 2 CH_3, SEt) ppm. ^{13}C NMR (CD_3OD): δ = 73.8 (C6, C7) 73.2 (C5) 71.4 (C4) 68.3 (C1) 65.9 [C2, $C(SEt)_2$] 64.8 (C8) 42.5 (C3) 23.7–22.9 (2 CH_2, SEt) 14.5–14.3 (2 CH_3, SEt) ppm. MS (ESI): m/z = 329.2 $[M – H]^-$.

3-Deoxy-D-*arabino*-2-heptulose Diethyl Dithioketal (5d): Compound **4d** (9 mg, 0.019 mmol) was treated according to method D; yield 5.2 mg (91%). α_D^{20} = +8.5 (2 mg/mL MeOH). ^1H NMR (CD_3OD): δ = 4.38 (m, 1 H, H4) 3.79 (m, 1 H, H7a) 3.78 (m, 1 H, H1a) 3.68 (m, 1 H H1b) 3.65 (m, 1 H, H6) 3.62 (m, 1 H, H7b) 3.35 (dd, J = 8.08, J = 2.02, Hz, 1 H, H5) 2.71–2.60 (m, 4 H, 2 CH_2, SEt) 2.17 (dd, J = 15.30, J = 9.47 Hz, 1 H, H3a) 1.95 (dd, J = 15.30, J = 0.66 Hz, 1 H, H3b) 1.30–1.20 (m, 6 H, 2 CH_3, SEt) ppm. ^{13}C NMR (CD_3OD): δ = 75.9 (C5) 73.2 (C6) 68.8 (C4) 68.2 (C1) 66.1 [C2, $C(SEt)_2$] 65.1 (C7) 42.9 (C3) 23.7–23.0 (2 CH_2, SEt) 14.5–14.4 (2 CH_3, SEt) ppm. MS (ESI): m/z = 323.2 $[M + Na]^+$.

3-Deoxy-D-*erythro*-2-hexulose Diethyl Dithioketal (5e): Synthesis of **5e** following method D starting from compound **4e** (17 mg, 0.043 mmol) yielded 11 mg (95%) after purification as inseparable diastereomers [*erythro* (**5e**)/*threo*: 3:1]. ^1H NMR (CD_3OD): δ (**5e**) = 4.15 (m, 1 H, H4) 3.75 (m, 3 H, H1a, H1b, H6a) 3.69 (m, 1 H, H6b) 3.56 (m, 1 H, H5) 2.70–2.56 (m, 4 H, 2 CH_2, SEt) 2.10 (dd, J = 15.00, J = 9.30 Hz, 1 H, H3a) 1.93 (dd, J = 15.00, J = 0.5 Hz, 1 H, H3b) 1.26–1.22 (m, 6 H, 2 CH_3, SEt) ppm. ^{13}C NMR (CD_3OD): δ (**5e**) = 74.3 (C5) 70.0 (C4) 66.3 (C6) 64.8 [C2, $C(SEt)_2$] 66.3 (C1) 40.5 (C3) 22.8–22.1 (2 CH_2, SEt) 14.1–14.0 (2 CH_3, SEt) ppm. MS (ESI): m/z = 293.1 $[M + Na]^+$.

5-Acetylamino-3,5-dideoxy-D-*glycero*-D-*galacto*-2-nonulose (6a): Compound **5a** (8.4 mg, 0.021 mmol) was treated according to method E yielding 5.3 mg of **6a** (86%). α_D^{20} = +23.4 (2.15 mg/mL MeOH). ^1H NMR (CD_3OD, pyranose): δ = 4.04 (m, 1 H, H4) 3.93 (dd, J = 9.98, J = 0.63 Hz, 1 H, H6) 3.81 (dd, J = 2.78, J = 11.21 Hz, 1 H, H9a) 3.72 (m, 1 H, H5) 3.70 (m, 1 H, H7) 3.63 (dd, J = 5.81, J = 11.21 Hz, 1 H, H9b) 3.49 (m, 1 H, H8) 3.47 (d, J = 11.36 Hz, 1 H, H1a) 3.36 (d, J = 11.36 Hz, 1 H, H1b) 2.02 (m, 1 H, H3a) 2.02 (s, 3 H, CH_3, NHAc) 1.76 (dd, J = 11.87, J = 12.38 Hz, 1 H, H3b) ppm. ^{13}C NMR (CD_3OD, pyranose): δ = 175.2 (C=O, NHAc) 98.6 (C2) 71.6 (C7) 71.3 (C6) 70.4 (C8) 69.5 (C1) 68.3 (C4) 64.9 (C9) 54.6 (C5) 39.5 (C3) 22.7 (CH_3, NHAc) ppm. MS (ESI): m/z = 318.2 $[M + Na]+$. HRMS calcd. for $C_{11}H_{21}O_8NNa$: 318.1165; found 318.1162.

3-Deoxy-D-*glycero*-D-*galacto*-2-nonulose (6b): Compound **5b** (5 mg, 0.014 mmol) was treated according to method E yielding 3.4 mg of **6b** (96%). α_D^{20} = –26.6 (1.5 mg/mL MeOH). ^1H NMR (CD_3OD,

pyranose): δ = 3.94 (m, 1 H, H4) 3.85 (m, 1 H, H9a) 3.81 (m, 1 H, H7) 3.66 (m, 1 H, H8) 3.64 (m, 1 H, H9b) 3.54 (m, 1 H, H6) 3.44 (m, 1 H, H1a) 3.37 (m, 1 H, H5) 3.36 (m, 1 H, H1b) 1.92 (dd, J = 5.27, J = 12.98 Hz, 1 H, H3a) 1.75 (dd, J = 1.28, J = 12.98 Hz, 1 H, H3b) ppm. ^{13}C NMR (CD_3OD, pyranose): δ = 98.6 (C2) 72.5 (C8) 72.2 (C4, C6) 70.9 (C5) 70.1 (C7) 69.4 (C1) 65.2 (C9) 38.6 (C3) ppm. MS (ESI): m/z = 277.1 [M + Na]+. HRMS calcd. for $C_9H_{18}O_8Na$: 277.0899; found 277.0896.

3-Deoxy-D-*manno*-2-octulose [6c (*erythro*)]: Compound **5c** (*erythro*) (64 mg, 0.194 mmol) was treated according to method E yielding 41 mg of **6c** (*erythro*) (94%). a_D^{20} = +28.0 (2.5 mg/mL MeOH). ^{1}H NMR (CD_3OD, pyranose): δ = 3.98 (m, 1 H, H4) 3.96 (m, 1 H, H5) 3.82 (m, 1 H, H7) 3.79 (m, 1 H, H6) 3.75 (dd, J = 3.17, J = 11.65 Hz, 1 H, H8a) 3.63 (dd, J = 5.09, J = 11.65 Hz, 1 H, H8b) 3.44 (d, J = 11.30 Hz, 1 H, H1a) 3.40 (d, J = 11.30 Hz, 1 H, H1b) 1.87 (m, 1 H, H3a) 1.70 (dd, J = 1.47, J = 4.52 Hz, 1 H, H3b) ppm. ^{13}C NMR (CD_3OD, pyranose): δ = 98.6 (C2) 72.2 (C6) 71.2 (C7) 69.7 (C1) 68.4 (C5) 67.9 (C4) 64.8 (C8) 34.0 (C3) ppm. HRMS calcd. for $C_8H_{16}O_7Na$: 247.0794; found 247.0792.

3-Deoxy-D-*gluco*-2-octulose [6c (*threo*)]: Compound **5c** (*threo*) (11 mg, 0.033 mmol) was treated according to method E yielding 7 mg of **6c** (*threo*) (95%). a_D^{20} = +56.0 (3.7 mg/mL MeOH). ^{1}H NMR (CD_3OD, pyranose): δ = 4.11 (dd, J = 1.34, J = 8.37 Hz, 1 H, H6) 3.99 (m, 1 H, H4) 3.85 (m, 1 H, H7) 3.80 (m, 1 H, H5) 3.77 (dd, J = 3.41, J = 11.43 Hz, 1 H, H8a) 3.64 (dd, J = 5.72, J = 11.43 Hz, 1 H, H8b) 3.37 (m, 2 H, H1a, H1b) 2.11 (dd, J = 3.68, J = 14.29 Hz, 1 H, H3a) 1.69 (dd, J = 2.97, J = 14.29 Hz, 1 H, H3b) ppm. ^{13}C NMR (CD_3OD, pyranose): δ = 98.4 (C2) 71.6 (C7) 69.7 (C4) 69.4 (C1) 68.2 (C6) 67.8 (C5) 64.7 (C8) 31.5 (C3) ppm. HRMS calcd. for $C_8H_{16}O_7Na$: 247.0794; found 247.0799.

3-Deoxy-D-*arabino*-2-heptulose (6d): Compound **5d** (22 mg, 0.073 mmol) was treated according to method E yielding 13.6 mg (96%) of **6d** (spectroscopic data agree with the literature[16,34]) a_D^{20} = +25.7 (1.4 mg/mL MeOH). ^{1}H NMR (CD_3OD, pyranose): δ = 3.91 (m, 1 H, H4) 3.77 (m, 2 H, H7a, H7b) 3.70 (m, 1 H, H6) 3.44 (d, J = 11.12 Hz, 1 H, H1a) 3.38 (d, J = 11.12 Hz, 1 H, H1b) 3.27 (m, 1 H, H5) 1.95 (dd, J = 5.05, J = 11.76 Hz, 1 H, H3a) 1.66 (dd, J = 11.76, J = 12.88 Hz, 1 H, H3b) ppm. ^{13}C NMR (CD_3OD, pyranose): δ = 98.2 (C2) 74.6 (C6) 73.0 (C5) 70.6 (C4) 69.4 (C1) 62.7 (C7) 39.1 (C3) ppm. MS (ESI): m/z = 217.1 [M + Na]$^+$.

3-Deoxy-D-*erythro*-2-hexulose (6e): Compound **5e** (20 mg, 0.074 mmol) was treated according to method E yielding 9 mg (74%) of inseparable diastereomers. Spectroscopical data agree with published data[33] (mixture of pyranose, furanose and open-chain form). MS (ESI): m/z = 187.1 [M + Na]$^+$.

Supporting Information (see also the footnote on the first page of this article): ^{1}H- and ^{13}C-NMR spectra of compound **6a**–**d**.

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[34] NMR shifts for compound **6d** in ref.[16] represent the furanose form, which can be found after equilibration in D_2O.

Received: May 4, 2010
Published Online: July 16, 2010

