New Derivatives of Levoglucosan by Tandem Epoxide Allyl Alcohol Rearrangement-Cuprate Cross-Coupling[‡]

Karsten Krohn,*[a] Dietmar Gehle,[a] and Ulrich Flörke[a]

Dedicated to Prof. R. R. Schmidt on the occasion of his 70th birthday

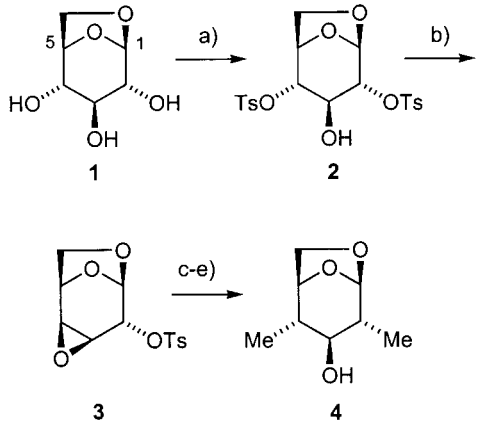
Keywords: 1,6-Anhydro sugars / Chiral building blocks / Branched sugars / Černý epoxide / Gilman cuprates / Epoxide rearrangement / Vinyl tosylate cross coupling

The alkylated allyl alcohols **6a**, **7**, and **8** (R = Me, Et, *n*Bu) were formed in the reaction of the Černý epoxide **3** with the Cyano–Gilman cuprates. The one-pot reaction was initiated by base-catalyzed epoxide allyl alcohol rearrangement to compound **5**, followed by unprecedented vinyl tosylate cross-coupling with the cuprates, to form the alkylation products **6a**, **7**, and **8**. The allyl alcohol **6a** was transformed into a number of new branched 1,6-anhydro sugars in series of highly stereoselective reactions. The products are stereochemically complementary to most known Černý epoxide derivatives and may be useful as chiral building blocks for polypropionate-derived natural products.

Introduction

In connection with our ongoing research in the area of highly deoxygenated sugars,[1] we wanted to investigate the possibility to further improve the use of 1,6-anhydro sugars as starting materials for a diversity of chiral bioactive natural products, in particular polypropionate-derived macrolides. 1,6-Anhydro sugars, such as 1,6-anhydro-β-D-glucopyranose [levoglucosan (**1**)], readily available by pyrolysis of starch or cellulose,[2–4] offer a number of advantages for this purpose. First, the hydroxy groups at the anomeric center at C-1 and the primary hydroxy group at C-6 are protected "internally" and the 1,6-anhydro bridge can be opened at any stage under mild acidic conditions.[5–7] The various functionalities thus generated at C-1 and C-6 can be used to incorporate the chiral fragment into the larger context of target molecules. Furthermore, the rigid $^1C_4$ conformation allows highly regio- and stereoselective reactions (reviews:[8–10]) Accordingly, this approach was investigated for example by Shafizadeh et al.,[11] Kochetkov et al.,[12] Černý et al.,[8] Procter et al.,[5] and others.[13–17] In more recent times, levoglucosan (**1**) was used to prepare a variety of advanced chiral building blocks.[18–23]

However, the rigid $^1C_4$ conformation of **1** and the shielding by the 1,6-anhydro bridge also limits the stereochemical diversity. Only a comparatively small number of well defined isomeric branched methyl derivatives of **1** are readily available. Many interesting isomers are only obtained as minor side products.[10] An example for one of the best investigated routes to the dimethyl compound **4** proceeds through the selective di-tosylation of **1** to produce the monoalcohol **2**, which is cyclized to the "Černý" epoxide **3**.[24] This epoxide was converted in three steps to the 2,4-dideoxy-2,4-dimethyl-1,6-anhydro-β-D-glucopyranose derivative **4** by reaction with methylmagnesium chloride in the presence of catalytic amounts of cuprous bromide or iodide (Normant cuprate, Scheme 1).[20,25] The regioselectivity of the nucleophilic attack is controlled by the Fürst–Plattner



Scheme 1. a) TsCl, acetone/pyridine, 1:1, 2 h, 0 °C, 71%; b) NaOMe, CH_2Cl_2, 2 h, room temp., 92%; c) MeMgCl (4 equiv.), CuI (cat.), THF, 40 °C, 12 h, 79%; d) NaOMe, CH_2Cl_2, 2 h, room temp., 96%, e) CuCN (4 equiv.), RLi (8 equiv.), Et_2O/THF, –78 °C to –20 °C, 2 h, 81%.

[‡] Highly Deoxygenated Sugars, 3. Part 2: Ref.[1]

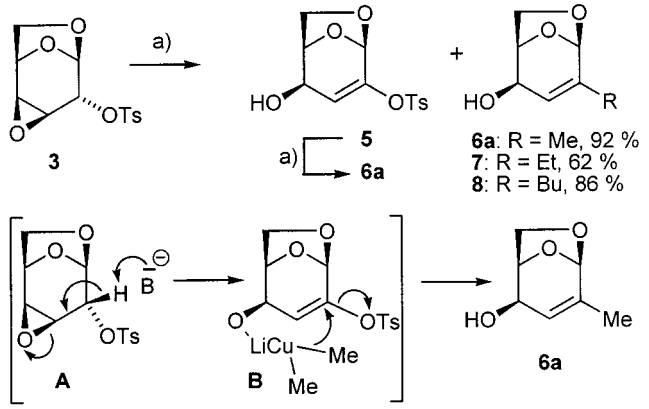
[a] Department Chemie, University of Paderborn, Warburger Straße 100, 33098 Paderborn, Germany
E-mail: Karsten.Krohn@uni-paderborn.de

rule[26] (regioselective addition at C-4 and C-2 in the two successive epoxide openings). The stereochemistry of the nucleophilic addition is directed by the shielding of the top side by the 1,6-anhydro bridge resulting in bottom attack. The reaction time was shortened and the chemical yield improved by using the Gilman cuprate instead of the Normant cuprate in the last epoxide opening [step e) in Scheme 1].

Results and Discussion

In the course of our investigations we were able to reproduce results of the synthesis of the branched sugar **4** and then extend the investigation of the Černý epoxides by reaction of **3** with the Cyano–Gilman cuprates (or higher order cuprates[27]; see also ref.[28–30]). The use of these reagents, easily prepared by mixing alkyllithium and copper cyanide, afforded completely different types of products than are known from Normant cuprates. Also, the yields were much higher and, more importantly, the stereochemistry was mostly complementary to that known from Černý epoxides. The discovery might open the door to an entire new field in the well established investigation of 1,6-anhydro-β-D-glucopyranose and give access to a large number of unknown chiral building blocks. Only part of the area is explored in this first communication.

The very first experiment using the Cyano–Gilman cuprates gave a surprising result. Thus, treatment of epoxide **3** in THF solution with the Gilman methyl cuprate afforded alcohol **6a** as the only detectable product in 92% yield (Scheme 2). The position of the double bond in **6a** was assigned by analysis of the HMBC NMR spectrum showing ^3J couplings of the anomeric 1-H (δ = 5.27 ppm) with the olefinic carbon C-3 and of 4-H (δ = 4.71 ppm) with the olefinic carbon C-2. Furthermore, the assignment and connectivity of each carbon atom was assured by $^1J_{CC}$ couplings from the 1D-SELINQUATE experiments.



Scheme 2. a) CuCN (4 equiv.), RLi (8 equiv.), Et_2O/THF, –78 °C to –20 °C, 2 h.

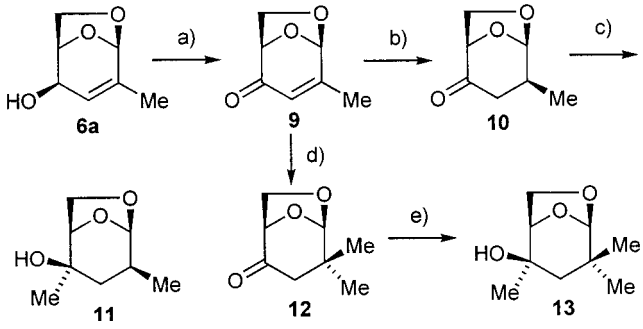
Evidently, the reaction is initiated by base-catalyzed epoxide allyl alcohol rearrangement as shown in the bottom part of Scheme 2. The subsequent cross-coupling of the vinyl tosylate with the cuprate is unprecedented. Such reactions are only known for the much more reactive vinyl triflates.[31–33] Possibly, anchimeric assistance facilitates the substitution of the tosyl group, as indicated in Scheme 2, supported by the usual coordination of the copper to the double bond, as known from alkenylation or arylation with Gilman cuprates.[31] This view of the two-step mechanism was supported by the conversion of the allyl alcohol intermediate **5**, isolated in one case in the corresponding reactions with the ethyl cuprate, to the substitution product **6a** under the same reaction conditions used for conversion of **3** to **6a** (Scheme 2).

The tandem reactions are very reproducible and yields were in the range of 90% even at a 20 g scale. Also, they are general and the corresponding ethyl and *n*-butyl Gilman cuprates gave the same type of allyl alcohol **7** (62%) and **8** (86%). The yield was lower in the reaction of the ethyl Gilman cuprate because the commercial ethyllithium was very dilute and in this case 30% of the tosylate **5** was also isolated. The branched (4*R*)-allyl alcohol fragment of the 1,6-anhydro sugar **6a** is found in many macrolide fragments such as for example phorbazol,[34] streptovaricin,[35] or leinamycin.[36]

The stereochemistry of the hydroxy group at C-4 of **6a** is inverted with respect to the levoglucosan (**1**). A set of stereochemically complementary products can be constructed starting form this allyl alcohol. To demonstrate the potential of the new 1,6-anhydro sugar **6a**, we conducted a number of simple experiments to prepare a series of new derivatives, which may be useful as chiral building blocks in natural product synthesis and synthesis of branched sugars.

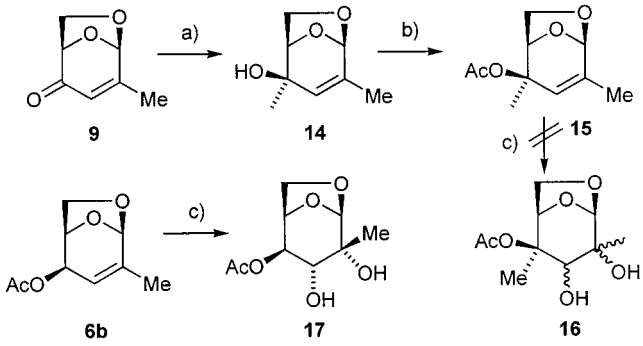
As expected, the allyl alcohol **6a** is easily oxidized to the α,β-unsaturated ketone **9** by treatment with activated manganese dioxide or pyridinium chromate (PDC). Hydrogenation of the double bond in **9** exclusively occurs from the bottom side of the bicyclic molecule to afford the saturated ketone **10** with equatorial orientation of the methyl group in contrast to the axial position in most of the Černý epoxide opening products such as **4**.[8] Grignard reaction of ketone **10** using methylmagnesium chloride affords the tertiary alcohol **11** in 93% isolated yield. In this case, addition occurs from the bottom side of the molecule resulting in a compound with methyl groups in both axial and equatorial position. Conjugate addition of Gilman cuprate yields ketone **12** with geminal methyl groups at C-2, a structural feature quite often occurring in macrolides as for example epothilone A.[37] Subsequent Grignard reaction of ketone **12** with methylmagnesium chloride afforded the trimethyl tertiary alcohol **13**. All reactions proceeded in high yields and no traces of isomeric products could be detected by TLC analysis of the crude reaction mixtures. It is noteworthy that the advantage of this anhydrosugar based "chiral pool" approach may reside in the construction of unusual substitution patterns rather than the 1,3-sequence of methyl and hydroxy groups found in "normal" polypropionate-derived natural products. For example, the substitution pattern and the (2*S*,3*R*) stereochemistry of compound **11** is present in more than 100 polypropionate-derived com-

pounds, including lankanolide,[38] amphidinolide,[39] the large groups of erythronolides,[40] and the cytochalasins (Scheme 3).[41]



Scheme 3. a) PDC, CH_2Cl_2, 24 h, room temp., 93% or MnO_2, Et_2O, reflux, 24 h, 82%; b) Pd/C, H_2, MeOH, 2 h, 94%; c) MeMgCl, Et_2O, –20 °C, 20 min, 93%; d) CuCN (2.5 equiv.), MeLi (2.5 equiv.), THF/Et_2O, –78 °C, 1 h, 89%; e) MeMgCl, Et_2O, 0 °C, 30 min, 92%.

Similarly as performed for the saturated derivative **10**, the stereochemical outcome of the reactions of the unsaturated ketone **9**, and the allyl acetates **6b** and **15** were investigated. (Scheme 4). As with the saturated ketone **10**, the Grignard reaction of the unsaturated ketone **9** with methylmagnesium chloride was highly selective and attack of the nucleophile occurred from the bottom side to yield the



Scheme 4. a) MeMgCl, Et_2O, –78 °C to room temp., 30 min, 98%; b) Ac_2O, Et_3N, DMAP, CH_2Cl_2, 0 °C to room temp. 5 h, 96%; c) OsO_4, NMO, acetone/H_2O, room temp., 4 h, 72%.

branched unsaturated sugar **14** exclusively in 91% isolated yield. The methyl group at C-4 in compound **14** is situated in an axial position and both top and bottom sides of the double bond are now sterically shielded. In fact, this shielding is so effective that the corresponding acetate **15** did not at all undergo *cis*-hydroxylation to **16** with osmium tetroxide, a reaction usually proceeding quite easily. However, in the absence of the axial C-4 methyl group as in **6b** the steric hindrance is absent and *cis*-hydroxylation is performed to yield **17** as the only isomer. It is noteworthy that olefinic building blocks with 100% *Z*-stereochemistry, not easily attained by other methods, are available upon opening of the pyran ring of **6a**, **6b**, **9**, or **14** to open-chain building blocks.

Finally, we investigated the stereoselectivity of the reduction of the carbonyl group at C-4 of ketone **10** and hydrogenation of the 2,3-double bond in the allylic alcohol **6a** and the acetate **6b**. The hydrogenation of **6a** and **6b** gave a ratio 87:13 and 77:23 (by GC) of **18a**:**20a** and **18b**:**20b**, respectively. This decrease in selectivity might be linked to the specific hydrogenation mechanism in which some steps might be partially reversible leading to some equilibration.[31] Treatment of **10** with sodium borohydride in ethanol or ether also afforded a mixture of epimeric alcohols **18a** and **19** but in a better than 92:8 ratio in favor of the major product **18a**. Fortunately, in the reduction with lithium triethyl borohydride (superhydride), the axial alcohol **19** could not be detected any more on TLC and **18a** was the only product isolated in 88% yield. So the desired alcohol was also available in a highly stereoselective reaction. The *cis* stereochemistry of the alcohol and the methyl group was confirmed by X-ray single-crystal analysis of the corresponding acetate **18b** as shown in Figure 1<yigr1>. Compound **18b** now also served as a reliable "relay", further supporting the unambiguous stereochemical assignment of the other derivatives in addition to the NMR coupling constants, chemical shifts, and NOE experiments (Scheme 5).

In summary, the unexpected tandem epoxide allyl alcohol rearrangement-vinyl tosylate substitution of the Černý epoxide **3** to yield the allyl alcohols **6a**, **7**, and **8** have opened the way to a large variety of stereochemically complementary new branched sugar derivatives that may be useful as chiral building blocks.

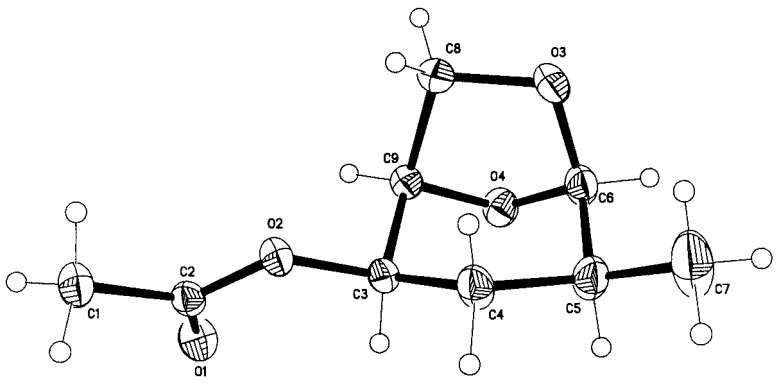
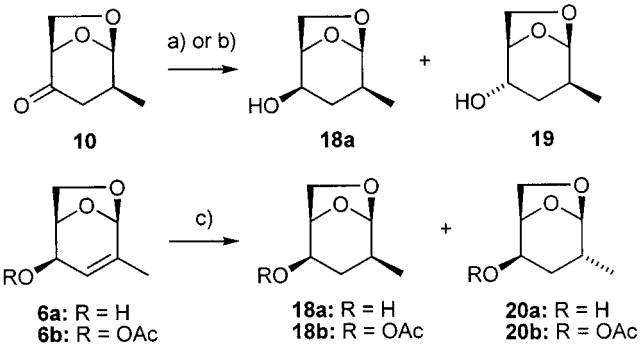


Figure 1. The molecule **18b** in the crystal.



Scheme 5. a) $NaBH_4$/EtOH or Et_2O, 16 h, 92%, 84% de; b) $LiHEt_3$ (superhydride)/Et_2O, 0.5 h, 88%, 100% *de*, c) Pd/C, H_2, MeOH.

Experimental Section

General: For general methods and instrumentation see ref.[1] Ratios of mixtures were generally determined by integration of the ^1H NMR spectra or GC analysis. GC: Hewlett–Packard 5890 Series II. NMR: Bruker Avance 500 (500/125 MHz) spectrometer.

1,6-Anhydro-2,4-di-*O*-tolylsulfonyl-β-D-glucopyranose (2): Prepared according to a procedure of Černý et al.[24] M.p. 118 °C (ref.[24] 119–121 °C). $[a]_D^{20}$ = –44 (*c* = 0.99, $CHCl_3$), [ref.[24] –43 (*c* = 0.96, $CHCl_3$)]. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.46 (s, 3 H, Ar-CH_3), 2.47 (s, 3 H, Ar–CH_3), 2.94 (br. s, 1 H, OH), 3.68 (dd, $J_{6a,6b}$ = 7.8, $J_{6a,5}$ = 5.2 Hz, 1 H, 6a-H), 3.96 (br. s, 1 H, 3-H), 4.02 (d, $J_{6b,6a}$ = 7.8 Hz, 1 H, 6b-H), 4.22 (d, $J_{2,3}$ = 3.0 Hz, 1 H, 2-H), 4.38 (d, $J_{4,3}$ = 3.5 Hz, 1 H, 4-H), 4.65 (d, $J_{5,6a}$ = 5.2 Hz, 1 H, 5-H), 5.34 (s, 1 H, 1-H), 7.37 (m, 4 H, Ar-H), 7.82 (dd, $J_{Ar,Ar}$ = 8.0, $J_{Ar,Ar}$ = 8.0 Hz, 4 H, Ar-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 27.7 (q, CH_3-Ar), 66.2 (t, C-6), 69.6 (d, C-3), 74.8 (d, C-5), 77.8 (d, C-2), 79.0 (d, C-4), 99.9 (d, C-1), 127.9 (d, C-Ar), 127.8 (d, C-Ar), 130.0 (d, C-Ar), 130.1 (d, C-Ar), 132.9 (s, C-Ar), 133.1 (s, C-Ar), 145.4 (s, C-Ar), 145.5 (s, C-Ar) ppm.

1,6:3,4-Dianhydro-2-*O*-tolylsulfonyl-β-D-galactopyranose (3): Prepared according to a procedure of Černý et al.[24] M.p. 149 °C (ref.[24] 148–150 °C). $[a]_D^{20}$ = –43 (*c* = 1.2, CH_2Cl_2), [ref.[24] –42 (*c* = 2.0, $CHCl_3$)]. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.48 (s, 3 H, Ar-CH_3), 3.15 (d, $J_{3,4}$ = 4.0 Hz, 1 H, 3-H), 3.52 (dd, $J_{6a,6b}$ = 6.7, $J_{6a,5}$ = 4.8 Hz, 1 H, 6a-H), 3.63 (dd, $J_{4,3}$ = 4.0, $J_{4,5}$ = 4.8 Hz, 1 H, 4-H), 3.96 (d, $J_{6a,6b}$ = 6.7 Hz, 1 H, 6b-H), 4.41 (s, 1 H, 2-H), 4.86 (dd, $J_{5,4}$ = 4.8, $J_{5,6a}$ = 4.8 Hz, 1 H, 5-H), 5.19 (s, 1 H, 1-H), 7.40 (d, $J_{Ar,Ar}$ = 7.9 Hz, 2 H, Ar-H), 7.87 (d, $J_{Ar,Ar}$ = 7.9 Hz, 2 H, Ar-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.7 (q, Tos-CH_3), 47.6 (d, C-3), 52.9 (d, C-4), 64.8 (t, C-6), 71.6 (d, C-2), 71.8 (d, C-5), 98.1 (d, C-1), 128.0 (d, 2×C-Ar), 130.2 (d, 2×C-Ar), 132.8 (s, C-Ar), 145.7 (s, C-Ar) ppm.

Cuprate Addition to Epoxide 3, General Procedure: A suspension of CuCN (4 equiv.) in freshly distilled dry diethyl ether was treated under argon at –78 °C with a solution of the respective organolithium compound (8 equiv.) over a period of 5 min. The solution was then warmed to 0 °C and during this time the suspension became transparent. After stirring for 10 min at 0 °C, the mixture was cooled to –78 °C and a solution of epoxide **3** in dry THF was added. The resulting yellow solution was stirred at –78 °C for 1 h and was then warmed up to –20 °C. After complete conversion of the starting material (ca. 2 h, at –20 °C, TLC monitoring) the reaction was quenched by dropwise addition of water (15 mL) and then a saturated aqueous NH_4Cl solution (15 mL) was added. The biphasic mixture was stirred until the aqueous phase turned blue. The aqueous phase was washed with diethyl ether (5×20 mL), and the combined ethereal phases were dried (Na_2SO_4), evaporated at reduced pressure, and purified by column chromatography (CH_2Cl_2/acetone, 95:5).

1,6-Anhydro-2,3-dideoxy-2-methyl-β-D-*threo*-hex-2-enopyranose (6a): Quantities of reagents and solvent used: CuCN (2.82 g, 31.5 mmol, 4 equiv.) in dry diethyl ether (75 mL); methyllithium (1.6 M in diethyl ether, 39.4 mL, 63 mmol, 8 equiv.); 1,6:3,4-Dianhydro-2-*O*-tolylsulfonyl-β-D-galactopyranose (**3**) (2.35 g, 7.9 mmol) in dried THF (100 mL). Yield of **6a** (colorless oil): 1.03 g (7.25 mmol, 92%). $[a]_D^{20}$ = –7.2 (*c* = 0.57, MeOH). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.72 (s, 3 H, H-CH_3), 2.69 (br. s, 1 H, OH), 3.84 (dd, $J_{6a,6b}$ = 7.5, $J_{6a,5}$ = 7.5 Hz, 1 H, 6a-H), 4.11 (dd, $J_{6b,6a}$ = 7.5, $J_{6b,5}$ = 1.8 Hz, 1 H. 6b-H), 4.48 (ddd, $J_{5,6a}$ = 7.5, $J_{5,6b}$ = 1.8, $J_{5,4}$ = 4.8 Hz, 1 H, 5-H), 4.70 (br. s, 1 H, 4-H), 5.26 (s, 1 H, 1-H), 5.29 (s, 1 H, 3-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 18.3 (q, C-7), 62.3 (t, C-6), 67.2 (d, C-4), 74.3 (d, C-5), 99.4 (d, C-1), 122.3 (d, C-3), 136.9 (s, C-2) ppm. IR (film): $\tilde{\nu}$ = 3402 cm^{-1} (s, O–H), 2975 (s, C–H), 2903 (m, C–H), 1682 (w, C=C), 1450 (m, C–H), 1372 (s, C–H), 1279 (s, C–O), 1087 (s, C–O). MS (EI, 70 eV): *m*/*z* (%) = 142 (50) [M^+], 111 (25), 99 (95), 82 (89), 71 (75), 57 (65), 43 (100). HREIMS: calcd. for $C_7H_{10}O_3$[M^+]: 142.0629; found 142.0620. $C_7H_{10}O_3$ (142.15): calcd. C 59.14, H 7.09; found C 58.87, H 7.39.

1,6-Anhydro-2,3-dideoxy-2-ethyl-β-D-*threo*-hex-2-enopyranose (7): Quantities of reagents used: CuCN (600 mg, 6.71 mmol, 4 equiv.) diethyl ether (30 mL); ethyllithium (0.5 M in diethyl ether, 26.8 mL, 13.4 mmol, 8 equiv.); 1,6:3,4-Dianhydro-2-*O*-tolylsulfonyl-β-D-galactopyranose (**3**) (500 mg, 1.67 mmol), THF (30 mL). Yield of **7** (colorless oil): 161 mg (1.03 mmol, 62%) and allyl alcohol **5** (colorless oil): 150 mg (0.5 mmol, 30%).

Data of 7: $[a]_D^{20}$ = –9.1 (*c* = 0.78, MeOH). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.28 (t, $J_{8,7}$ = 7.3 Hz, 3 H, 8-H), 1.68 (br. s, 1 H, OH), 2.10 (q, $J_{8,7}$ = 7.3 Hz, 2 H, 7-H), 3.89 (ddd, $J_{6a,6b}$ = 8.0, $J_{6a,5}$ = 6.0, $J_{6a,4}$ = 1.2 Hz, 1 H, 6a-H), 4.15 (dd, $J_{6b,6a}$ = 8.0, $J_{6b,5}$ = 1.9 Hz, 1 H. 6b-H), 4.55 (ddd, $J_{5,6a}$ = 6.0, $J_{5,6b}$ = 1.9, $J_{5,4}$ = 4.7 Hz, 1 H, 5-H), 4.81 (ddd, $J_{4,5}$ = 4.7, $J_{4,3}$ = 2.1, $J_{4,6a}$ = 1.2 Hz, 1 H, 4-H), 5.30 (m, 1 H, 3-H), 5.35 (s, 1 H, 1-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2 (q, C-8), 25.2 (t, C-7), 62.4 (t, C-6), 67.6 (d, C-4), 75.1 (d, C-5), 99.1 (d, C-1), 120.0 (d, C-3), 142.8 (s, C-2). IR (film): $\tilde{\nu}$ = 3400 cm^{-1} (s, O–H), 2971 (s, C–H), 2897 (m, C–H), 1679 (w, C=C), 1453 (m, C–H), 1370 (s, C–H), 1269 (s, C–O), 1088 (s, C–O) ppm. MS (EI, 70 eV): *m*/*z* (%) = 156 (10) [M^+], 110 (5), 96 (15), 86 (45), 84 (74), 57 (15), 51 (30), 49 (100), 43 (15). HREIMS [M^+] calcd. for $C_8H_{12}O_3$: 156.0786; found 156.0774. $C_8H_{12}O_3$ (156.18): calcd. C 61.52, H 7.74; found C 61.18, H 7.69.

Data of 1,6-Anhydro-2,3-dideoxy-2-*O*-tolylsulfonyl-β-D-*threo*-hex-2-enopyranose (5): $[a]_D^{20}$ = –12.2 (*c* = 0.58, MeOH). ^1H NMR (500 MHz, $CDCl_3$): δ = 2.46 (s, 3 H, Ar–CH_3), 3.04 (br. s, 1 H, OH), 3.78 (ddd, $J_{6a,6b}$ = 8.2, $J_{6a,5}$ = 6.0, $J_{6a,4}$ = 1.2 Hz, 1 H, 6a-H), 4.01 (dd, $J_{6b,6a}$ = 8.2, $J_{6b,5}$ = 1.8 Hz, 1 H, 6b-H), 4.47 (ddd, $J_{5,6a}$ = 6.0, $J_{5,6b}$ = 1.8, $J_{5,4}$ = 4.7 Hz, 1 H, 5-H), 4.80 (ddd, $J_{4,5}$ = 4.7, $J_{4,3}$ = 2.4, $J_{4,6a}$ = 1.2 Hz, 1 H, 4-H), 5.25 (s, 1 H, 1-H), 5.40 (s, 1 H, 3-H), 7.36 (d, $J_{Ar,Ar}$ = 8.0 Hz, 2 H, H-Ar), 7.81 (d, $J_{Ar,Ar}$ = 8.0 Hz, 2 H, H-Ar) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.8 (q, Ar–CH_3), 62.6 (t, C-6), 66.4 (d, C-4), 74.7 (d, C-5), 96.6 (d, C-1), 115.3 (d, C-3), 128.5 (d, C-Ar), 129.9 (d, C-Ar), 131.9 (s, C-Ar), 146.0 (s, C-2), 146.7 (s, C-Ar) ppm. IR (film): $\tilde{\nu}$ = 3462 cm^{-1} (s, O–H), 2960 (m, C–H), 2919 (m, C–H), 2851 (m, C–H), 1631 (w, C=C), 1372 (m, C–H), 1263 (s, C–O), 1177 (s, C–O), 1175 (s, S–O). MS (EI, 70 eV): *m*/*z* (%) = 298 (1) [M^+], 227 (51), 155 (100), 139 (55), 98 (75), 91 (100), 69 (40), 57 (51), 41 (35). HREIMS calcd. for

$C_{13}H_{14}O_6S$: 298.0511; found 298.0510. $C_{13}H_{14}O_6S$ (298.31): calcd. C 52.34, H 4.73; found C 52.57, H 4.35.

1,6-Anhydro-2-butyl-2,3-dideoxy-β-D-*threo*-hex-2-enopyranose (8): Quantities of reagents: CuCN (5.6 g, 62.9 mmol, 4 equiv.), diethyl ether (60 mL), butyllithium (2.5 M in hexane, 50.4 mL, 126.1 mmol, 8 equiv.); 1,6:3,4-Dianhydro-2-*O*-tolylsulfonyl-β-D-galactopyranose (**3**) (4.7 g, 15.8 mmol), THF (150 mL). Yield of **8** (colorless oil): 2.50 g, (13.6 mmol, 86%); yield of **5** (colorless oil): 150 mg, (0.5 mmol, 3%). $[\alpha]_D^{20}$ = –15.0 (*c* = 0.92, MeOH). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.89 (t, $J_{10,9}$ = 7.4 Hz, 3 H, 10-H), 1.28–1.35 (m, 2 H, 9-H), 1.37–1.43 (m, 2 H, 8-H), 2.01 (t, $J_{7,8}$ = 7.6 Hz, 2 H. 7-H), 2.62 (br. s, 1 H, OH), 3.83 (ddd, $J_{6a,6b}$ = 7.5, $J_{6a,5}$ = 5.9, $J_{6a,4}$ = 1.2 Hz, 1 H, 6a-H), 4.11 (dd, $J_{6b,6a}$ = 7.5, $J_{6b,5}$ = 1.7 Hz, 1 H, 6b-H), 4.48 (ddd, $J_{5,6a}$ = 5.9, $J_{5,6b}$ = 1.7, $J_{5.4}$ = 3.7 Hz, 1 H, 5-H), 4.72 (m, 1 H, 4-H), 5.26 (m, 1 H, 3-H), 5.32 (s, 1 H, 1-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.8 (q, C-10), 22.2 (t, C-9), 29.0 (t, C-8), 32.1 (t, C-7), 62.3 (t, C-6), 67.4 (d, C-4), 75.1 (d, C-5), 99.0 (d, C-1), 121.3 (d, C-3), 141.0 (s, C-2) ppm. IR (film): $\tilde{\nu}$ = 3400 cm^{-1} (m, O–H), 2960 (m, C–H), 2929 (m, C–H), 2867 (m, C–H), 1693 (m, C=C), 1594 (m, C–H), 1465 (s, C–H), 1367 (s, C–H), 1175 (s, C–O), 989 (s, C–O) ppm. MS (EI, 70 eV): *m*/*z* (%) = 184 (50) [M$^+$], 155 (8),141 (22), 111 (22), 95 (78), 86 (45), 82 (100), 61 (42), 57 (92), 54 (88), 43 (60), 41 (80). HREIMS calcd. for $C_{10}H_{16}O_3$: 184.1099; found 184.1094. $C_{10}H_{16}O_3$ (184.23): calcd. C 65.19, H 8.75; found C 64.41, H 8.63.

4-*O*-Acetyl-1,6-anhydro-2,3-dideoxy-2-methyl-β-D-*threo*-hex-2-enopyranose (6b): A solution of **6a** (2 g, 14.1 mmol) in anhydrous CH_2Cl_2 (80 mL) was treated at 0 °C with a solution of triethylamine (2.4 mL, 16.9 mmol, 1.2 equiv.), acetyl chloride (1.2 mL, 16.9 mmol, 1.2 equiv.) and DMAP (cat.). After 1 h of stirring, the solution was warmed to 20 °C and was kept for an additional 5 h at this temperature. After complete conversion (TLC monitoring), the mixture was poured into ice-water. The phases were separated and the organic phase was extracted with water (2 × 30 mL). The organic phase was dried (Na_2SO_4), concentrated at reduced pressure and purified by flash chromatography (PE/EtOAc, 9:1–3:1) to afford 2.1 g (12.0 mmol, 85%) of the acetate **6b** as a colorless oil. $[\alpha]_D^{20}$ = –48.7 (*c* = 0.7, MeOH). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.72 (s, 3 H, H-7), 2.05 (s, 3 H, H-Ac), 3.85 (ddd, $J_{6a,6b}$ = 7.5, $J_{6a,5}$ = 5.9, $J_{6a,4}$ = 1.2 Hz, 1 H, 6a-H), 4.06 (dd, $J_{6b,6a}$ = 7.5, $J_{6b,5}$ = 1.9 Hz, 1 H, 6b-H), 4.63 (m, 1 H, 5-H), 5.27–5.28 (m, 2 H, 1-H, 3-H), 5.66 (m, 1 H, 4-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.3 (q, C-7), 21.0 (q, Ac-CH_3), 63.2 (t, C-6), 70.2 (d, C-4), 72.3 (d, C-5), 99.6 (d, C-1), 118.3 (d, C-3), 139.1 (s, C-2), 170.3 (s, Ac-CO) ppm. IR (film): $\tilde{\nu}$ = 2970 cm^{-1} (m, C–H), 2908 (m, C–H), 2360 (m, O–C–O), 2334 (m, O–C–O), 1744 (m, C=C), 1698 (m, C=O), 1455 (s, C–H), 1372 (s, C–H), 1227 (s, C–O), 1093 (s, C–O), 1031 (s, C–O). MS (EI, 70 eV): *m*/*z* (%) = 184 (8) [M$^+$], 142 (70), 124 (10), 111 (8), 95 (22), 82 (20), 71 (10), 57 (9), 53 (9), 43 (100). HREIMS calcd. for $C_9H_{12}O_4$: 184.0736; found 184.0736. $C_9H_{12}O_4$ (184.19): calcd. C 58.69, H 6.57; found C 58.56, H 6.84.

1,6-Anhydro-2,3-dideoxy-2-methyl-β-D-*glycero*-hex-2-enopyran-4-ulose (9): A solution of **6a** (5.98 g, 42 mmol) in dry CH_2Cl_2 (300 mL) was treated with PDC (31.6 g, 84 mmol, 2 equiv.). The mixture was stirred at 20 °C and after complete conversion of the starting material (TLC monitoring, ca. 24 h) the solution was diluted by addition of diethyl ether (500 mL), the precipitate filtered off (Celite, washed with diethyl ether, 100 mL), and the filtrate was evaporated at reduced pressure. The residue was purified by flash chromatography (CH_2Cl_2/acetone, 100:0 to 98:2) to obtain ketone **9** (5.5 g, 39 mmol, 93%) as colorless crystals. M.p. 45 °C. $[\alpha]_D^{20}$ = +398 (*c* = 1.05, MeOH). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.08 (d, $J_{7,3}$ = 1.5 Hz, 3 H, 7-H), 3.60 (dd, $J_{6a,6b}$ = 8.0, $J_{6a,5}$ = 1.4 Hz, 1 H, 6a-H), 4.06 (dd, $J_{6b,6a}$ = 8.0, $J_{6b,5}$ = 7.5 Hz, 1 H. 6b-H), 4.48 (dd, $J_{5,6b}$ = 7.5, $J_{5,6a}$ = 1.4 Hz, 1 H, 5-H), 5.58 (s, 1 H, 1-H), 5.85 (d, $J_{3,7}$ = 1.5 Hz, 1 H, 3-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.6 (q, C-7), 63.5 (t, C-6), 78.8 (d, C-5), 100.1 (d, C-1), 122.8 (d, C-3), 160.9 (s, C-2), 194.3 (s, C-4) ppm. IR (film): $\tilde{\nu}$ = 2971 cm^{-1} (s, C–H), 2893 (m, C–H), 1719 (w, C=C), 1693 (s, C=C), 1631 (s, C=O), 1434 (m, C–H), 1377 (s, C–H), 1310 (s, C–H), 1253 (s, C–O), 1087 (s, C–O) ppm. MS (EI, 70 eV): *m*/*z* (%) = 140 (64) [M$^+$], 111 (9), 99 (20), 97 (100), 82 (42), 71 (14), 69 (42), 57 (15), 43 (38), 41 (79), 29 (12), 27 (21). HREIMS calcd. for $C_7H_8O_3$: 140.0473; found 40.0471. $C_7H_8O_3$ (140.15): calcd. C 59.99, H 5.75; found C 60.15, H 5.44.

1,6-Anhydro-2,3-dideoxy-2-methyl-β-D-*threo*-hexopyran-4-ulose (10): A solution of ketone **9** (900 mg, 6.42 mmol) in methanol (50 mL) was treated with Pd/C (12 mg, 10%) and the mixture was stirred under hydrogen at atmospheric pressure for 2 h. The suspension was filtered through Celite and concentrated to afford a single isomer **10** as a colorless oil (820 mg, 5.78 mmol, 94%). $[\alpha]_D^{20}$ = –11.7 (*c* = 0.24, MeOH). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.00 (d, $J_{7,2}$ = 7.0 Hz, 3 H, 7-H), 2.03 (dd, $J_{3a,3b}$ = 17.0, $J_{3a,2}$ = 10.0 Hz, 1 H, 3a-H), 2.30 (m, 1 H. 2-H), 2.48 (dd, $J_{3b,3a}$ = 17.0, $J_{3b,2}$ = 7.1 Hz, 1 H, 3b-H), 3.86–3.92 (m, 2 H, 6-H), 4.41 (d, $J_{5,6a}$ = 5.2 Hz, 1 H, 5-H), 5.34 (s, 1 H, 1-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 16.2 (q, C-7), 38.1 (d, C-2), 40.2 (t, C-3), 67.4 (t, C-6), 78.5 (d, C-5), 104.3 (d, C-1), 203.8 (s, C-4) ppm. IR (film): $\tilde{\nu}$ = 2960 cm^{-1} (s, C–H), 2897 (m, C–H), 1651 (s, C=O), 1558 (s, C–H), 1481 (s, C–H), 1450 (s, C–H), 1377 (s, C–H), 1325 (s, C–H), 1294 (s, C–O), 1134 (s, C–O), 1041 (s, C–O). MS (EI, 70 eV): *m*/*z* (%) = 142 (12) [M$^+$], 114 (26), 99 (100), 85 (14), 71 (56), 55 (46), 46 (30), 41 (38), 29 (9), 27 (12). HREIMS calcd. for $C_7H_{10}O_3$: 142.0629; found 142.0629. $C_7H_{10}O_3$ (142.15): calcd. C 59.14, H 7.09; found C 58.87, H 7.09.

1,6-Anhydro-2,3-dideoxy-2,4-dimethyl-β-D-lyxopyranose (11): A solution of **10** (190 mg, 1.33 mmol) in dried diethyl ether (15 mL) was treated at 0 °C by dropwise addition of MeMgCl (0.53 mL, 1.2 equiv., 3 M in THF. After complete conversion of the starting material (ca. 20 min), the reaction was quenched by addition of water (15 mL) followed by extraction of the aqueous phase with diethyl ether (3 × 10 mL). The combined organic phases were dried (Na_2SO_4), concentrated at reduced pressure and the residue purified by filtration through a small pad of silica to afford **11** (188 mg, 1.23 mmol, 93%) as colorless crystals. M.p. 67 °C. $[\alpha]_D^{20}$ = –105 (*c* = 0.53, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.89 (d, $J_{7,2}$ = 5.6 Hz, 3 H, 7-H), 1.39 (dd, $J_{3a,3b}$ = 13.0, $J_{3a,2}$ = 12.0 Hz, 1 H, 3a-H), 1.46 (s, 3 H, 8-H), 1.64 (dd, $J_{3b,3a}$ = 13.0, $J_{3b,2}$ = 4.8 Hz, 1 H, 3b-H), 1.84 (m, 1 H, 2-H), 3.71 (dd, $J_{6a,6b}$ = 7.8, $J_{6a,5}$ = 5.1 Hz, 1 H, 6a-H), 4.02 (dd, $J_{5,6a}$ = 5.1, $J_{5,6b}$ = 1.8 Hz, 1 H, 5-H), 4.14 (dd, $J_{6b,6a}$ = 7.8, $J_{6b,5}$ = 1.8 Hz, 1 H, 6b-H), 5.17 (s, 1 H, 1-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 16.2 (q, C-7), 26.6 (q, C-8), 35.5 (d, C-2), 39.5 (t, C-3), 65.3 (t, C-6), 68.9 (s, C-4), 79.4 (d, C-5), 104.3 (d, C-1) ppm. IR (film): $\tilde{\nu}$ = 3456 cm^{-1} (m, O–H), 2960 (s, C–H), 2929 (C–H), 2898 (s, C–H), 1475 (m, C–H), 1448 (m, C–H), 1367 (m, C–H), 1337 (m, C–H), 1289 (w, C–O), 1170 (m, C–O), 1150 (s, C–O), 1093 (m, C–O), 1056 (s, C–O), 984 (m, C–O). MS (EI, 70 eV): *m*/*z* (%) = 158 (6) [M$^+$], 143 (8), 127 (7), 116 (42), 115 (62), 100 (42), 97 (54), 85 (38), 73 (39), 71 (62), 70 (69), 55 (94), 43 (100), 41 (54), 27 (29). HREIMS calcd. for $C_8H_{14}O_3$: 158.0942; found 158.0924. $C_8H_{14}O_3$ (158.19): calcd. C 60.74, H 8.92; found C 60.91, H 8.89.

1,6-Anhydro-2,3-dideoxy-2-dimethyl-β-D-*glycero*-hexopyran-4-ulose (12): A suspension of CuCN (800 mg, 8.9 mmol. 2.5 equiv.) in

freshly distilled dry diethyl ether (30 mL) was treated under argon at –78 °C with methyllithium (5.6 mL, 2.5 equiv., 1.6 M solution in diethyl ether), which was added via syringe over a period of 5 min. Upon warming up to 0 °C the solution became clear. The mixture was kept for 10 min at 0 °C, then cooled to –78 °C and treated with a solution of ketone **9** (500 mg, 3.6 mmol) in dry THF (30 mL) by addition over a period of 1 h. The resulting solution was stirred at –78 °C for 1 h and then warmed up to 20 °C. After complete conversion of the starting material (1 h), water was added dropwise until the vigorous hydrolysis was finished. Saturated NH_4Cl solution (20 mL) was added and the biphasic mixture was stirred for 1 h. The precipitate was filtered and washed with diethyl ether. Extraction of the aqueous phase with diethyl ether (3 × 10 mL) and concentration of the dried combined organic phases gave **12** (496 mg, 3.17 mmol, 89%). $[\alpha]_D^{20}$ = –17.0 (*c* = 1.21, MeOH). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.08 (s, 3 H, 7-H), 1.09 (s, 3 H, 8-H), 2.20 (ddd, $J_{3a,3b}$ = 16.6, $J_{3a,1}$ = 1.6, $J_{3a,5}$ = 1.6 Hz, 1 H, 3a-H), 2.32 (d, $J_{3b,3a}$ = 16.6 Hz, 1 H, 3b-H), 3.92 (dd, $J_{6a,6b}$ = 8.3, $J_{6a,5}$ = 5.3 Hz, 1 H, 6a-H), 3.97 (dd, $J_{6b,6a}$ = 8.3, $J_{6b,5}$ = 0.9 Hz, 1 H, 6b-H), 4.45 (ddd, $J_{5,6a}$ = 5.3, $J_{5,6b}$ = 0.9, $J_{5,3a}$ = 1.6 Hz, 1 H, 5-H), 5.12 (d, $J_{1,3}$ = 1.6 Hz, 1 H, 1-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 24.8, 25.1 (2 × q, C-7, C-8), 41.6 (s, C-2), 47.0 (t, C-3), 67.0 (t, C-6), 78.4 (d, C-5), 107.7 (d, C-1), 204.2 (s, C-4). IR (film): $\tilde{\nu}$ = 2970 cm^{-1} (s, C–H), 2893 (s, C–H), 1729 (s, C=O), 1465 (m, C–H), 1418 (m, C–H), 1377 (m, C–H), 1315 (m, C–H), 1289 (s, C–O), 1118 (s, C–O), 1085 (s, C–O) ppm. MS (EI, 70 eV): *m*/*z* (%) = 156 (44) [M$^+$], 113 (100), 111 (26), 95 (24), 85 (16), 71 (34), 67 (19), 55 (20), 43 (48), 41 (12). HREIMS calcd. for $C_8H_{12}O_3$: 156.0786; found 156.0786. $C_8H_{12}O_3$ (156.18): calcd. C 61.52, H 7.74; found C 61.40, H 7.83.

1,6-Anhydro-2,3-dideoxy-2-dimethyl-4-methyl-β-D-*threo*-pyranose (13): A solution of **12** (138 mg, 0.88 mmol) in dried diethyl ether (15 mL) was treated at 0 °C with MeMgCl (0.35 mL, 1.2 equiv. 3 M in THF) by dropwise addition. After 30 min the conversion was complete and water was added to quench the reaction. The aqueous phase was extracted with diethyl ether (3 × 10 mL), the combined organic phases were washed with water, dried (Na_2SO_4) and evaporated at reduced pressure. The residue was purified by flash chromatography (CH_2Cl_2/acetone, 95:5) to afford **13** (139 mg, 0.81 mmol, 92%) as a colorless oil. $[\alpha]_D^{20}$ = –84 (*c* = 0.75, $CDCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.93 (s, 3 H, 7-H), 1.06 (s, 3 H, 8-H), 1.47 (d, $J_{3a,3b}$ = 13.6 Hz, 1 H, 3a-H), 1.54 (s, 3 H, 9-H), 1.59 (d, $J_{3b,3a}$ = 13.6 Hz, 1 H, 3b-H), 3.70 (dd, $J_{6a,6b}$ = 7.8, $J_{6a,5}$ = 5.4 Hz, 1 H, 6a-H), 4.04 (dd, $J_{5,6a}$ = 5.4, $J_{5,6b}$ = 0.6 Hz, 1 H, 5-H), 4.18 (dd, $J_{6b,6a}$ = 7.8, $J_{6b,5}$ = 0.6 Hz, 1 H, 6b-H), 4.90 (s, 1 H, 1-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 24.3, 27.0 (2 × q, C-7, C-8), 28.7 (q, C-9), 37.5 (s, C-2), 44.7 (t, C-3), 64.7 (t, C-6), 68.3 (s, C-4), 79.6 (d, C-5), 107.4 (d, C-1) ppm. IR (film): $\tilde{\nu}$ = 3451 cm^{-1} (m, O–H), 2960 (s, C–H), 2924 (C–H), 2893 (s, C–H), 1486 (m, C–H), 1448 (m, C–H), 1377 (m, C–H), 1367 (m, C–H), 1289 (w, C–O), 1196 (m, C–O), 1103 (s, C–O), 1062 (m, C–O), 1015 (m, C–O). MS (EI, 70 eV): *m*/*z* (%) = 172 (4) [M$^+$], 157 (8), 129 (49), 116 (22), 111 (20), 99 (14), 95 (9), 85 (18), 71 (42), 70 (100), 55 (79), 43 (64), 41 (24). HREIMS calcd. for $C_9H_{16}O_3$: 172.1099; found 172.1100. $C_9H_{16}O_3$ (172.22): calcd. C 62.77, H 9.36; found C 62.51, H 9.21.

1,6-Anhydro-2,3-dideoxy-2,4-dimethyl-β-D-*threo*-hex-2-enopyranose (14): A solution of ketone **9** (1.2 g, 8.56 mmol) in dry THF (80 mL) was treated at –78 °C with MeMgCl (3.4 mL, 10.3 mmol, 1.2 equiv., 3 M in THF) by dropwise addition. The solution was warmed up to 20 °C and was quenched with water (20 mL) after 30 min (TLC monitoring) followed by extraction of the aqueous phase with diethyl ether (3 × 50 mL). The combined organic phases were dried (Na_2SO_4) and concentrated at reduced pressure to obtain **14** as an oil (1.31 g, 8.34 mmol, 98%). $[\alpha]_D^{20}$ = +53.4 (*c* = 0.79, MeOH). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.44 (s, 3 H, 8-H), 1.71 (d, $J_{7,3}$ = 1.5 Hz, 3 H, 7-H), 1.90 (br. s, 1 H, OH), 3.86 (dd, $J_{6a,6b}$ = 8.1, $J_{6a,5}$ = 6.0 Hz, 1 H, 6a-H), 4.12 (dd, $J_{6b,6a}$ = 8.1, $J_{6b,5}$ = 1.8 Hz, 1 H. 6b-H), 4.22 (ddd, $J_{5,6b}$ = 1.8, $J_{5,6a}$ = 6.0, $J_{5,3}$ = 1.8 Hz, 1 H, 5-H), 5.18 (dd, $J_{3,7}$ = 1.5, $J_{3,5}$ = 1.8 Hz, 1 H, 3-H), 5.25 (s, 1 H, 1-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 18.2 (q, C-7), 27.1 (q, C-8), 62.8 (t, C-6), 71.2 (s, C-4), 79.2 (d, C-5), 99.6 (d, C-1), 126.1 (d, C-3), 135.0 (s, C-2) ppm. IR (film): $\tilde{\nu}$ = 3446 cm^{-1} (s, O–H), 2965 (s, C–H), 2924 (s, C–H), 2893 (m, C–H), 1734 (s, C=C), 1450 (m, C–H), 1377 (m, C–H), 1310 (m, C–H), 1248 (m, C–O), 1089 (s, C–O), 1015 (m, C–O). MS (EI, 70 eV): *m*/*z* (%) = 156 (32) [M$^+$], 113 (90), 111 (33), 95 (29), 86 (38), 85 (22), 84 (54), 71 (47), 67 (31), 67 (31), 55 (26), 47 (14), 43 (100), 41 (28), 29 (12), 27 (13). HREIMS calcd. for $C_8H_{12}O_3$: 156.0786; found 156.0786. $C_8H_{12}O_3$ (156.18): calcd. C 61.52, H 7.74; found C 61.38, H 7.92.

4-*O*-Acetyl-1,6-anhydro-2,3-dideoxy-2,4-dimethyl-β-D-*threo*-hex-2-enopyranose (15): A solution of **14** (620 mg, 3.97 mmol in anhydrous CH_2Cl_2 (20 mL) was acetylated at 0 °C by addition of triethylamine (2.1 mL, 15.6 mmol), Ac_2O (1.6 mL, 15.6 mmol), and DMAP (cat.). After 1 h the solution was warmed to 20 °C and was kept at that temperature for an additional 5 h, and was then quenched by pouring into ice-water. The phases were separated and the organic phase was extracted with water (2 × 30 mL), sat. $NaHCO_3$ (2 × 10 mL) and brine. After drying (Na_2SO_4) the combined organic phases were concentrated at reduced pressure and the crude product was purified by flash chromatography (PE/EtOAc, 9:1–3:1) to yield **15** as a colorless oil (747 mg, 3.77 mmol, 95%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.69 (s, 3 H, 8-H), 1.72 (d, $J_{7,3}$ = 1.7 Hz, 3 H, 7-H), 2.02 (s, 3 H, Ac-H), 3.88 (dd, $J_{6a,6b}$ = 8.0, $J_{6a,5}$ = 6.0 Hz, 1 H, 6a-H), 3.97 (dd, $J_{6b,6a}$ = 8.0, $J_{6b,5}$ = 2.0 Hz, 1 H, 6b-H), 4.83 (dd, $J_{5,6b}$ = 2.0, $J_{5,6a}$ = 6.0 Hz, 1 H, 5-H), 5.25 (s, 1 H, 1-H), 5.57 (br. s, 1 H, 3-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 18.2 (q, C-7), 22.0 (q, Ac-CH_3), 22.9 (q, C-8), 63.1 (t, C-6), 77.3 (d, C-5), 81.4 (s, C-4), 99.6 (d, C-1), 122.4 (d, C-3), 136.6 (s, C-2), 170.3 (s, Ac-CO) ppm. MS (EI, 70 eV): *m*/*z* (%) = 156 (32) [M$^+$], 113 (90), 111 (33), 95 (29), 86 (38), 85 (22), 84 (54), 71 (47), 67 (31), 67 (31), 55 (26), 47 (14), 43 (100), 41 (28), 29 (12), 27 (13). HREIMS calcd. for $C_{10}H_{14}O_4$: 198.0892; found 198.0891.

4-*O*-Acetyl-1,6-anhydro-2-methyl-β-D-gulopyranose (17): A solution of **6b** (250 mg, 1.36 mmol) in acetone/water, (1:2, 3 mL) was treated with a mixture of OsO_4 (0.1 mL of a solution of 0.5 g in 5 mL *t*BuOH) and NMO (202 mg, 1.5 mmol, 1.1 equiv.) and the mixture was stirred at 20 °C for 4 h. After complete conversion of the starting material (TLC monitoring), solid $NaHSO_3$ (50 mg) was added and the mixture was stirred for 1 h. The suspension was filtered through a pad of Florisil and eluted with EtOAc (100 mL). The ethyl acetate solution was washed with water (5 mL), dried (Na_2SO_4), filtered and purified by silica gel column chromatography (CH_2Cl_2/MeOH, 95:5) to yield **17** as a single isomer (oil, 213 mg, 0.98 mmol, 72%). $[\alpha]_D^{20}$ = +18.4 (*c* = 0.74, MeOH). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.29 (s, 3 H, 7-H), 2.13 (s, 3 H, Ac-H), 2.89 (br. s, 2 H, 2 × OH), 3.56 (d, $J_{3,4}$ = 9.0 Hz, 1 H, 3-H), 3.69 (ddd, $J_{6a,6b}$ = 8.0, $J_{6a,5}$ = 4.7, $J_{6a,4}$ = 0.8 Hz, 1 H, 6a-H), 3.98 (d, $J_{6b,6a}$ = 8.0 Hz, 1 H. 6b-H), 4.53 (dd, $J_{5,6a}$ = 4.7, $J_{5,4}$ = 4.6 Hz, 1 H, 5-H), 4.94 (ddd, $J_{4,5}$ = 4.6, $J_{4,3}$ = 9.0, $J_{4,6a}$ = 0.8 Hz, 1 H, 4-H), 5.16 (s, 1 H, 1-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.4 (q, C-7), 21.0 (q, Ac-CH_3), 64.6 (t, C-6), 71.6 (d, C-3), 72.3 (d, C-5), 73.1 (d, C-4), 74.4 (s, C-2), 104.6 (d, C-1), 171.3 (s, Ac-CO) ppm. IR (film): $\tilde{\nu}$ = 3472 cm^{-1} (s, OH), 2986 (m, C–H), 2908 (m, C–H), 1739 (w, C=O), 1344 (m, C–H), 1243 (s, C–H), 1118 (s, C–O), 1036 (s, C–O), 968 (s, C–O). MS (CI, *i*Bu, 70 eV): *m*/*z* (%) = 219 (12) [M$^+$+1], 201 (3), 89 (9), 59 (8), 57 (100), 55 (7), 43 (14), 41 (4), 39

(7), 27 (3). $C_9H_{14}O_6$ (218.2): calcd. C 49.54, H 6.47; found C 48.99, H 6.77.

4-*O*-Acetyl-1,6-anhydro-2,3-dideoxy-2-methyl-β-D-*lyxo*-pyranose (18b): A solution of **6b** (890 mg, 4.83 mmol) in methanol (50 mL) was stirred under hydrogen at atmospheric pressure for 4 h in the presence of Pd/C (25 mg, 10%). The suspension was filtered through Celite and concentrated in vacuo to afford a mixture of diastereomers **18b** and **20b** as colorless oil (827 mg, 4.4 mmol, 54%de, 92%). A single crystal of the main isomer was used for X-ray analysis. ^{1}H NMR (500 MHz, $CDCl_3$) major isomer **18b**: δ = 0.81 (d, $J_{7,2}$ = 6.7 Hz, 3 H, H-7), 1.21 (dd, $J_{3a,2}$ = 12.0, $J_{3a,4}$ = 12.0 Hz, 1 H, 3a-H), 1.80 (m, 1 H, 2-H), 1.90 (m, 1 H, 3b-H), 1.96 (s, 3 H, H-Ac), 3.63 (ddd, $J_{6a,6b}$ = 7.8, $J_{6a,5}$ = 4.9, $J_{6a,4}$ = 0.5 Hz, 1 H, 6a-H), 3.95 (d, $J_{6b,6a}$ = 7.8 Hz, 1 H, 6b-H), 4.36 (m, 1 H, 5-H), 4.87 (m, 1 H, 4-H), 5.08 (s, 1 H, 1-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) major isomer **18b**: δ = 16.1 (q, C-7), 20.9 (q, Ac-CH_3), 30.2 (t, C-3), 35.8 (d, C-2), 65.1 (t, C-6), 68.0 (d, C-4), 72.6 (d, C-5), 104.2 (d, C-1), 169.9 (s, Ac-CO) ppm. IR (film): $\tilde{\nu}$ = 2970 cm^{-1} (s, C–H), 2903 (s, C–H), 2882 (m, C–H), 2365 (w, O–C–O), 1750 (s, C=O), 1460 (s, C–H), 1367 (s, C–H), 1237 (s, C–O), 1129 (s, C–O), 1046 (s, C–O), 979 (s, C–O). MS (EI, 70 eV): *m*/*z* (%) = 186 (13) [M$^+$], 143 (28), 141 (28), 115 (10), 101 (22), 97 (40), 85 (23), 83 (23), 71 (24), 57 (24), 55 (25), 43 (100), 28 (65). $C_9H_{14}O_4$ (186.21): calcd. C 58.05, H 7.58; found C 57.97, H 7.79.

1,6-Anhydro-2,3-dideoxy-2-methyl-β-D-lyxopyranose (18a): A solution of **6a** (200 mg, 1.41 mmol) in methanol (30 mL) was stirred under hydrogen at atmospheric pressure for 4 h in the presence of Pd/C (8 mg, 10%). The suspension was filtered through Celite and concentrated to afford a colorless oil as a mixture of diastereomers of **18a** and **20a** (182 mg, 1.3 mmol, 74%de, 90%). ^{1}H NMR (500 MHz, $CDCl_3$) major isomer **18a**: δ = 0.86 (d, $J_{7,2}$ = 6.9 Hz, 3 H, H-7), 1.15 (dd, $J_{3a,2}$ = 12.0, $J_{3a,4}$ = 12.0 Hz, 1 H, 3a-H), 1.80 (m, 1 H, 2-H), 1.89 (m, 1 H, 3b-H), 2.70 (br., 1 H, OH), 3.63 (dd, $J_{6a,6b}$ = 7.6, $J_{6a,5}$ = 4.7 Hz, 1 H, 6a-H), 3.91 (m, 1 H, 4-H), 4.03 (d, $J_{6b,6a}$ = 7.6 Hz, 1 H, 6b-H), 4.30 (dd, $J_{5,6a}$ = 4.7, $J_{5,4}$ = 4.4 Hz, 1 H, 5-H), 5.12 (s, 1 H, 1-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) major isomer **18a**: δ = 16.1 (q, C-7), 33.6 (t, C-3), 35.8 (d, C-2), 63.5 (t, C-6), 65.9 (d, C-4), 75.4 (d, C-5), 104.1 (d, C-1). IR (film): $\tilde{\nu}$ = 3425 cm^{-1} (br., O–H), 2965 (s, C–H), 2960 (s, C–H), 2893 (s, C–H), 2360 (w, O–C–O), 1460 (s, C–H), 1382 (s, C–H), 1129 (s, C–O), 1036 (s, C–O), 968 (s, C–O) ppm4. MS (EI, 70 eV): *m*/*z* (%) = 144 (50) [M$^+$], 101 (65), 98 (62), 97 (20), 83 (60), 73 (52), 71 (69), 57 (90), 55 (100), 47 (60), 43 (59), 41 (57), 39 (40), 27 (38). HREIMS calcd. for $C_7H_{12}O_3$: 144.0786; found 144.0782. $C_7H_{12}O_3$ (144.17): calcd. C 58.32; H 8.39; found C 58.01, H 8.32.

Crystal Structure Analysis of 18b:[42,43] $C_9H_{14}O_4$, M_r = 186.20, orthorhombic, space group $P2_12_12_1$, a = 5.5670(7), b = 6.4641(8), c = 26.291(3) Å, V = 946.1(2) Å^3, Z = 4, $D_{calcd.}$ = 1.307 g/cm^3, F(000) = 400, T = 120(2) K. Bruker AXS SMART APEX, graphite-monochromated, λ(Mo-K_α) = 0.71073 Å, μ = 0.102 mm^{-1}, colorless crystal, size 0.35 × 0.35 × 0.40 mm^3, 7692 intensities collected $3.1 < \theta < 27.8°$, $-7 < h < 7$, $-8 < k < 8$, $-34 < l < 32$, 1360 independent intensities (R_{int} = 0.044). The title compound crystallizes in the noncentrosymmetric space group $P2_12_12_1$; however, in the absence of significant anomalous scattering effects, the Flack parameter is essentially meaningless. Accordingly, Friedel pairs were merged. The present configuration of **18b** follows the known one of starting material **6b**. Structure solved by direct and conventional Fourier methods, full-matrix least-squares refinement based on F^2 and 120 parameters, all but H atoms refined anisotropically, H atoms from Fourier maps placed on idealized positions and refined with riding model with U = 1.5 U_{iso}(methyl-C) and 1.2 U_{iso}(C). CH_3 groups were rotated but not to tip. Refinement converged at $R_1[F > 4\sigma(F)]$ = 0.051, wR_2(all data) = 0.148, S = 1.093, min./max. height in final ΔF map –0.26/0.71 e·Å^{-3}. Figure 1 shows the molecular structure.

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