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Carbohydrate chiral-pool approach to four enantiomerically pure 2-naphthylmethyl 3-hydroxy-2-methylbutanoates

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ABSTRACT

D-Glucose, L-xylose, and D- and L-arabinose were sources of chirality to obtain four enantiomerically pure 3-hydroxy-2-methylbutanoic acids, which were reacted with 2-naphthyldiazomethane to furnish their fluorescent 2-naphthylmethyl esters.

1. Introduction

Batumin **1**, 2*E*,10*Z*,12*E*-20-(3-aminocarboxy)-2-methyl-1-oxo-butylamino-7-methylene-17-oxo-19-oxy-3,5,15-trimethyleicosa-2,10,12-trienoic acid, is an antibiotic produced by the strains of *Pseudomonas batumici* (Fig. 1).[1] It shows very good activity particularly against Gram-negative bacteria, e.g., *Staphylococcus aureus*,[2,3] which pose a serious health problem due to their resistance against antibiotics in current use. Batumin's basic structural elucidation was performed, except for establishing the configurations of the five stereogenic carbon centers. Compound which has the same gross molecular composition dubbed as kalimantacin A, was isolated from a fermentation broth of *Alcaligenes sp. YL-02632S*. Kalimantacin A has the same set of configurations of the C=C bonds but its absolute configurations remain unknown.[4–6] It is not clear at this time if batumin and kalimantacin A are the same compounds or if they differ at the configurations of the stereogenic centers. In principle, compound **1** can be degraded in a basic medium to release 3-hydroxy-2-methylbutanoic acid **2** (Fig. 1). It should be possible to establish absolute configurations of **2** by chiral HPLC by comparison of its mobility with the four reference 3-hydroxy-2-methylbutanoic acids, which have the known configurations. In this way, the configurations of the left fragment containing two stereogenic carbon atoms in **1** can be obtained, which would be an initial step to solve the still lacking full stereochemical constitution of **1**.

Reported here is a carbohydrate-based chiral-pool approach to obtain all four enantiomerically pure (within accuracy of their ^{1}H and ^{13}C NMR spectra recorded at 500 MHz and 125 MHz, respectively) 3-hydroxy-2-methylbutanoic acids **20**, **33**, **48**, and **56** in a form of their fluorescent 2-naphthylmethyl esters. Preliminary results of this work were published.[7]

The syntheses of chiral **2** with variable enantiomeric purities were realized before via aldol condensations[8–16] (in some cases enzymatic resolution step was involved[8,9]), enantioselective reductions of carbonyl group,[17,18] or by acetoxymercuration followed by chiral resolution.[19]

In this work, we opted for the application of monosaccharides to obtain the enantiomerically pure targets **20**, **33**, **48**, and **56** in order to avoid a necessity to perform chiral separations, which can be difficult. Additionally, the starting sugars have well-established absolute configurations, which assure that the targets have predictable stereochemistry.

2. Results and discussion

The basic idea of transformation of the starting sugars 1,2;5,6-di-*O*-isopropylidene-D-*gluco*-furanose **3**, 5-*O*-*tert*-butyldimethylsilyl-1,2-*O*-isopropylidene-L-*xylo*-furanose **25**, 5-*O*-*tert*-butyldiphenylsilyl-1,2-*O*-isopropylidene-D-*arabino*-furanose **35**, and its

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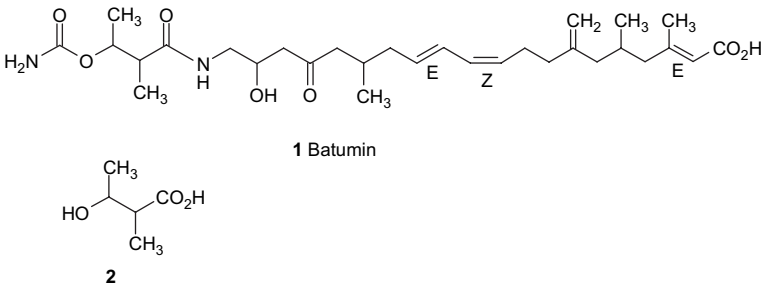


Figure 1. Structure of batumin and of 3-hydroxy-2-methylbutanoic acid, a possible degradation product of batumin.

L-enantiomer **49** into the targets **20**, **33**, **48**, and **56**, respectively, is shown in Figure 2. In all four cases, the stereocenters at the atoms C4 in the substrates were preserved and the bulky 1,2-*O*-isopropylidene moieties were used to install predictably the C3 methyl groups in the intermediates **7**, **28**, **39**, and **54** via oxidation, Wittig methylenation, and hydrogenation. In the case of D- and L-arabinose, this sequence was 100% stereoselective, whereas for D-glucose **3** and L-xylose **25** the selectivity was ca. 90%, however, a simple crystallization furnished pure stereoisomers at the C3 at a later stage (see below). The lateral groups attached to C4 in the substrates were transformed into the methyl groups and the C2 atoms functioned as the latent carboxyl groups.

The synthesis of the (2*R*,3*R*) compound **20** is shown in Scheme 1. Commercial 1,2;5,6-di-*O*-isopropylidene-*D*-*gluco*-furanose **3** was oxidized to **4** using CrO_3–Py–Ac_2O system by analogy to the other oxidations[20,21] and subjected to Wittig methylenation to give **5**. Catalytic hydrogenation over Pd–C rather than RaNi[22] furnished a separable mixture of **6** and **7** in a proportion ca. 1:10 by ^{1}H NMR (roughly the same proportion of **6** to **7** was obtained using much more synthetically demanding thiol-catalyzed free-radical redox process),[23] and an unexpected monoisopropylidenated compound **8**. Cleavage of 5,6-acetonide was most probably a result of the presence of small quantity of $PdCl_2$ in the batch of the catalyst. In a hydrogen atmosphere, $PdCl_2$ was reduced to liberate HCl, which cleaved the more reactive 5,6-acetonide. The same explanation was given to rationalize the alleged hydrogenolysis of the *tert*-butyldimethylsilyl ethers, which eventually turned out to be a simple hydrolysis.[24,25] The D-*allo* stereoisomer **7** was isolated by flash chromatography and subjected to 'dehomologation'[26,27] ((a) H_5IO_6–EtOAc and (b) $NaBH_4$–EtOH) to give 3-deoxy-3-*C*-methyl-D-*ribo* epimer **10** via the aldehyde **9**. Conventional tosylation furnished a highly crystalline **11**, which served as a substrate for 'deoxygenative substitution' ($-CH_2OTs \rightarrow -CH_3$) using $LiBH(Et)_3$ to get another methyl group (**11** → **13**). Since chromatographic separation of **6** and **7** was inconvenient, the 'dehomologation' step was performed on the mixture **6** and **7** obtained after hydrogenation of **5** over Adam's catalyst (PtO_2). The mixture of both epimeric compounds **12** thus obtained was subjected to tosylation and crystallization from EtOAc. This simple crystallization step furnished a pure D-*ribo* compound **11** in 54% yield counting on **6** and **7**. The

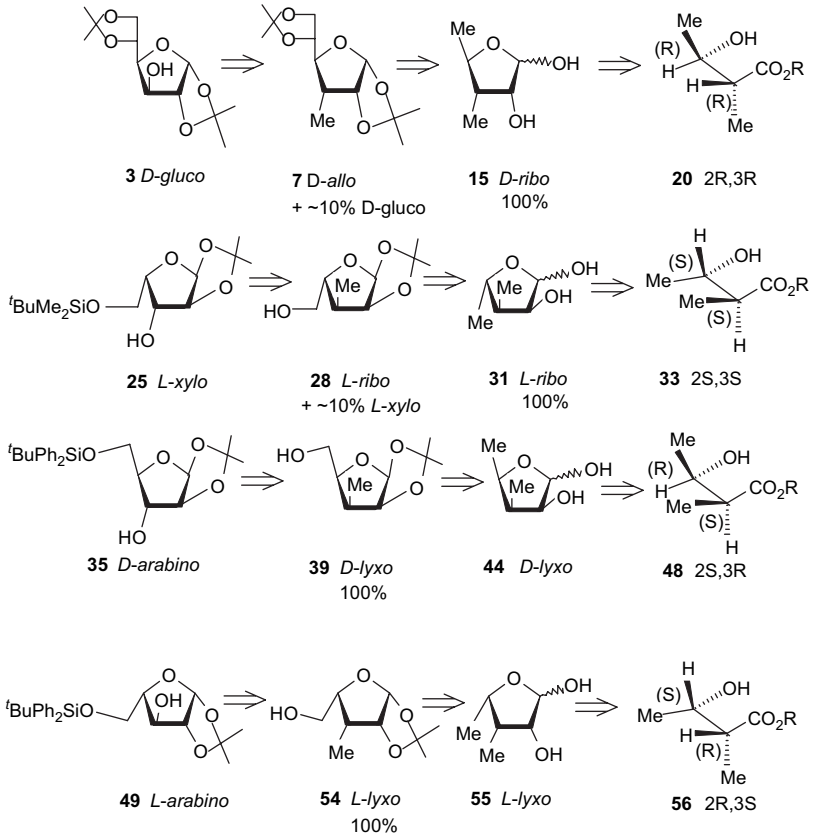
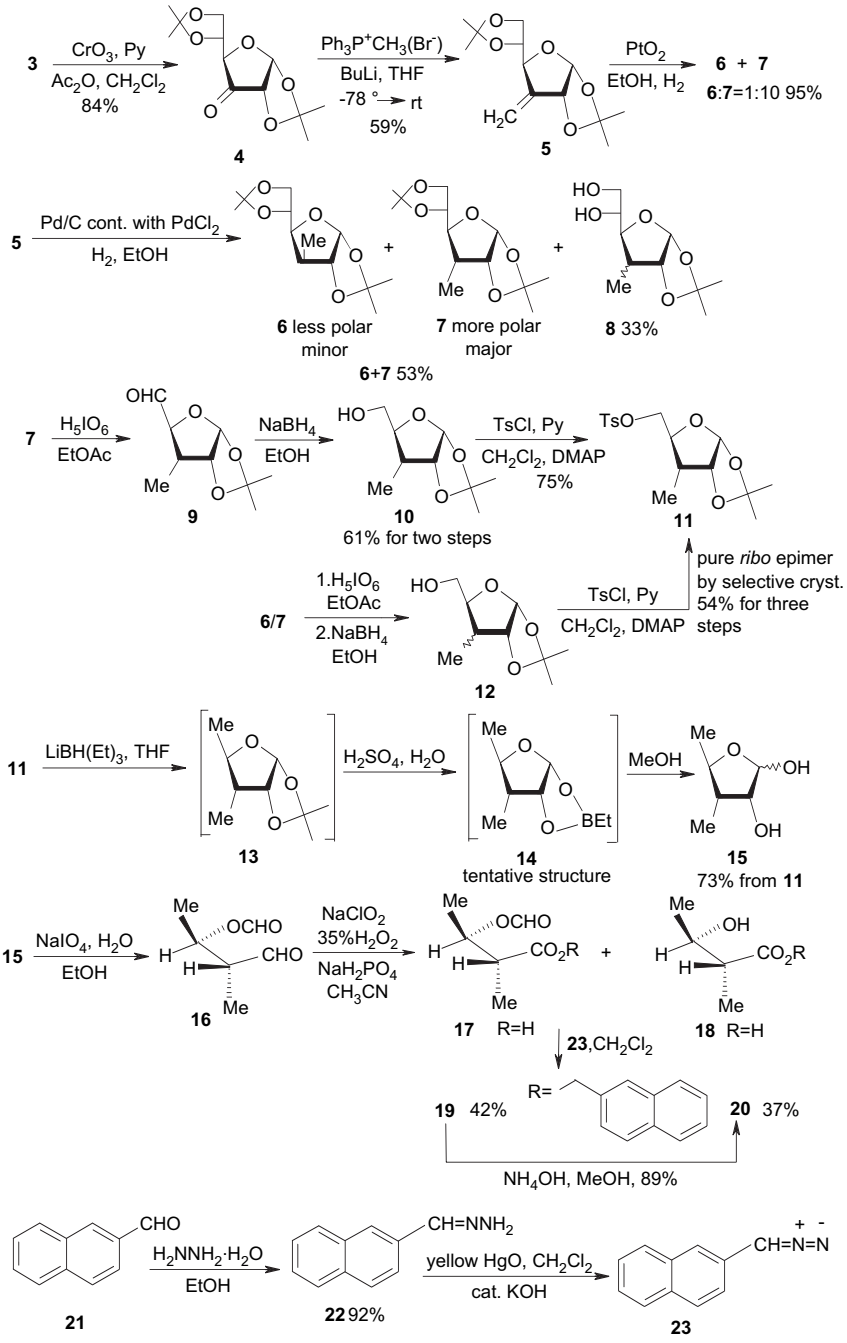


Figure 2. Utilization of chirality present in D-glucose, L-xylose, and D- and L-arabinose to obtain the targets **20**, **33**, **48**, and **56** with predictable configurations.



Scheme 1. Obtention of 2-naphthylmethyl (3*R*)-hydroxy-(2*R*)-methylbutanoate **20** from D-glucose.

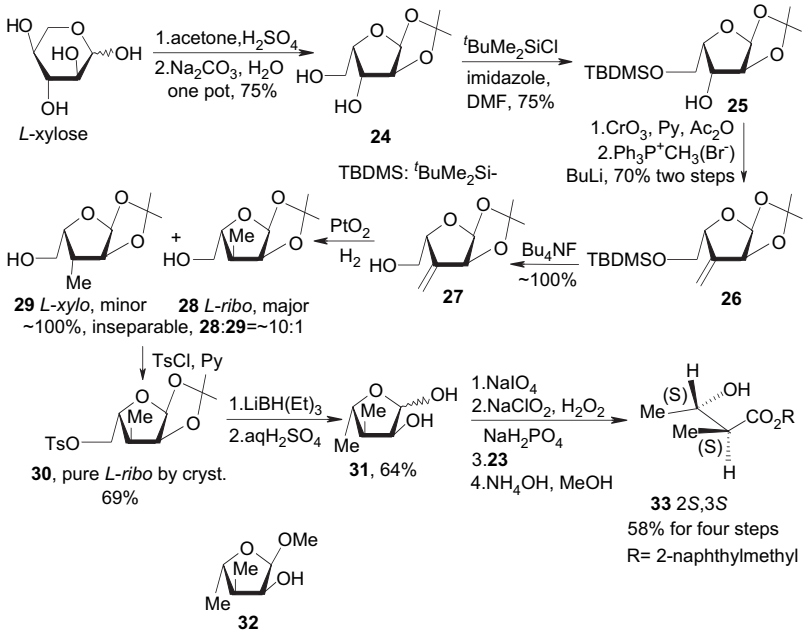
configuration (3*R*) in the tosylate **11** was confirmed by X-ray analysis.[28] Tosylate **11** was then treated with $LiBH(Et)_3$, a donor of a very soft 'supernucleophilic' hydrogen anion, to give 3,5-dideoxy-3-*C*-methyl-1,2-*O*-isopropylidene-D-*ribo*-furanose **13**. Tronchet and Graf described a different route to **13** starting from 3,5-dideoxy-1,2-*O*-isopropylidene-3*C*-(*E*,*Z*)-methylthiomethylene-α-D-*erythro*-pentofuranose by RaNi hydrogenation/desulfurization followed by preparative gas chromatography to separate it from the C3 D-*xylo* epimer.[29] The isolation of **13** was skipped and acid hydrolysis of the 1,2-acetonide function was performed by the addition of aq H_2SO_4 directly to the reaction mixture still containing the boron compounds to give the diol **15** presumably via a cyclic borate **14** (see Section 3). Borates derived from vicinal diols are known to be quite stable, e.g., they survive on HBr–AcOH or PBr_3 treatment but can be easily cleaved by methanolysis.[30] Consequently, repeated co-evaporations of the extracts with MeOH furnished 3,5-dideoxy 3-*C*-methyl-D-*ribo*-furanose **15** isolated in 73% counting on **11**. (Two alternative procedures to remove the isopropylidene function in **13**: I_2–MeOH[31] and $FeCl_3 \cdot 6H_2O$–CH_2Cl_2,[32] were inefficient.) In this way, both methyl groups were properly installed and the carboxyl group was ready to be formed. The vicinal diol system in **15** was cleaved with $NaIO_4$ to give the transient aldehyde **16**, which was immediately subjected to oxidation using $NaClO_2$–H_2O_2–NaH_2PO_4 system.[33] TLC at this stage showed two products: a major formyloxy acid **17** and a minor more polar hydroxy acid **18**, visualized as yellow spots on a blue background upon revelation with an acid–base indicator bromocresol green.[34,35] Both **17** and **18** were not isolated, but instead they were esterified with freshly prepared 2-naphthyldiazomethane **23** obtained from the hydrazone **22**[36] by KOH catalyzed HgO oxidation by analogy to the other

arylhydrazones.[37,38] The esterifications with **23** can be referred to as titrations: loss of the red-orange color of a CH_2Cl_2 solution of **23** was nearly instantaneous and was accompanied by evolution of nitrogen. Addition of **23** was stopped when a reddish color indicating the presence of the excess of **23** persisted. The procedure routinely took ca. 1–2 min. TLC of these mixtures showed a strong fluorescent spot of the formate **19** (major) and a more polar 2-naphthylmethyl (3*R*)-hydroxy-(2*R*)-methylbutanoate **20** (minor), accompanied by UV absorbing compounds having R_fs values similar to those of **19**. The presence of these impurities was not surprising since it is known that in situ generated aryl diazomethanes are in general not more than 85% pure,[39] and also the transient naphthylmethyl carbenes can decompose to form by-products.

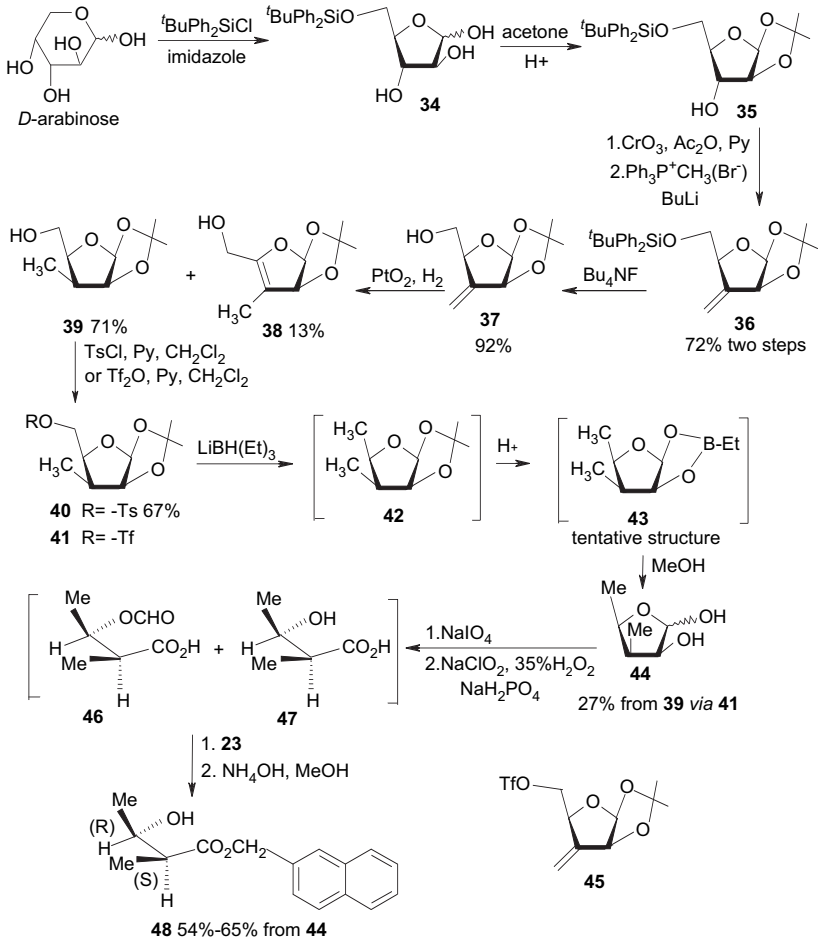
It should be pointed out that tagging of the organic acids with fluorescent 1-napthylmethyl or 1-napthylethyl groups was applied to facilitate their detections during HPLC analysis.[40] Both **19** and the target **20** could be isolated at this stage, and the formate **19** could be easily transformed to **20** by ammonolysis using aq NH_4OH in MeOH. However, it was much more convenient to perform this deprotection on a crude esterification mixture and to isolate **20** in a cumulative yield of ca. 70% for four steps counting on the diol **15**. Comparison of the ^1H and ^{13}C NMR spectra of the (2*R*,3*R*) target **20** with those of the (2*S*,3*R*) epimer **48** (see below) showed that no inversion of configuration at the C2 atom via enolization took place during this sequence and that **20** is a pure enantiomer within the limits of the 500 MHz (^1H) and 125 MHz (^{13}C) measurements.

The enantiomeric (2*S*,3*S*) product **33** was obtained from L-xylose as shown in Scheme 2. 1,2-*O*-Isopropylidene-L-*xylo*-furanose **24** was prepared in a one-pot reaction by analogy to the D-enantiomer.[41] Selective protection of the primary OH group by silylation (→**25**) by analogy to its D-enantiomer,[27,42] followed by CrO_3–Py–Ac_2O oxidation and Wittig methylenation as described before (**3**→**4**→**5**) furnished the olefin **26**. Conventional desilylation and hydrogenation over Adam's catalyst furnished inseparable mixture of the major (~90%) L-*ribo* epimer **28** and the L-*xylo* epimer **29**, formed in the same proportion as compounds *allo* **7** and *gluco* **6**. Tosylation of this mixture and subsequent crystallization furnished pure *C*3 L-*ribo* epimer **30**, which is an enantiomer of D-compound **11** described above. Obviously, the NMR data of **30** match with those of **11** and both compounds have the opposite optical rotations. Transformation of **30** to the diol **31** and further to 2-naphthylmethyl (3*S*)-hydroxy-(2*S*)-methylbutanoate **33** proceeded exactly as described above for the D-series. Again, both (2*S*,3*S*) **33** and (2*R*,3*R*) **20** differ only in the sign of their optical rotations.

The other two targets, which have (2*S*,3*R*) and (2*R*,3*S*) configuration, viz. **48** and **56**, respectively, were obtained in a stereospecific way using D-arabinose (Scheme 3) and L-arabinose (Scheme 4). Selective *tert*-butyldiphenylsilylation of D-arabinose followed by isopropylidenation was performed by analogy to the known process described for L-arabinose[20,21] to furnish *tert*-butyldiphenylsilyl-1,2-*O*-isopropylidene-D-*arabino*-furanose **35**.[43] Oxidation at the position C3 followed by Wittig methylenation furnished the olefin **36**. Tebbe's reagent (μ-chloro-μ-methylene[bis-(cyclopentadienyl)titanium]-dimethylaluminum) could also be used,[21] but its price is rather high. Two-step Peterson olefination ((1) Me_3SiCH_2Li and (2) NaH) was an alternative,[21] but a single step Wittig reaction seemed to be the simplest, and permitted the obtention of **36** in 72% yield for two steps. Desilylation furnished **37**, which was subjected to hydrogenation over Adam's catalyst to furnish two products. The less polar **38** had a double bond migrated to the 3,4-position and was isolated in 13% yield, whereas the necessary 3-deoxy-1,2-*O*-isopropylidene-3-*C*-methyl-D-lyxofuranose **39** was obtained in 71% yield. Formation of **38** undoubtedly reflects a steric difficulty to install four *syn* oriented substituents inside a lyxofuranosyl ring. At the same time, it is known that tetrasubstituted olefins are quite resistant toward hydrogenation,[44] so persistence of **38** under such conditions is not surprising. The alcohol **39** was converted to its 5-*O*-tosylate **40**, which, however, turned out to be unreactive toward substitution using $LiBH(Et)_3$. This inertness again reflects a steric congestion in the *lyxo* ring in **40**. The triflate **41**, however, reacted with $LiBH(Et)_3$ to give **42** even though decomposition was visible on TLC. Further steps to obtain the 3,5-dideoxy-3-*C*-methyl-D-lyxofuranose **44** proceeded as described above for the D-*ribo* (**11**→**15**) and L-*ribo* (**30**→**31**) series. It is evident that a combination of the best known leaving group (–OTf) and a supernucleophilic properties of the $LiBH(Et)_3$ partly offsets the steric hindrance in **41**, even though a yield of the isolated **44** was 27%, much less than in the case of the less congested compounds **11** and **30**. It should be pointed out that application of the triflate **45**, which is less congested than **41** due to lack of the *C*3 methyl group, did not improve the yield of **44** (data not shown). Further transformation of **44** proceeded following the procedure



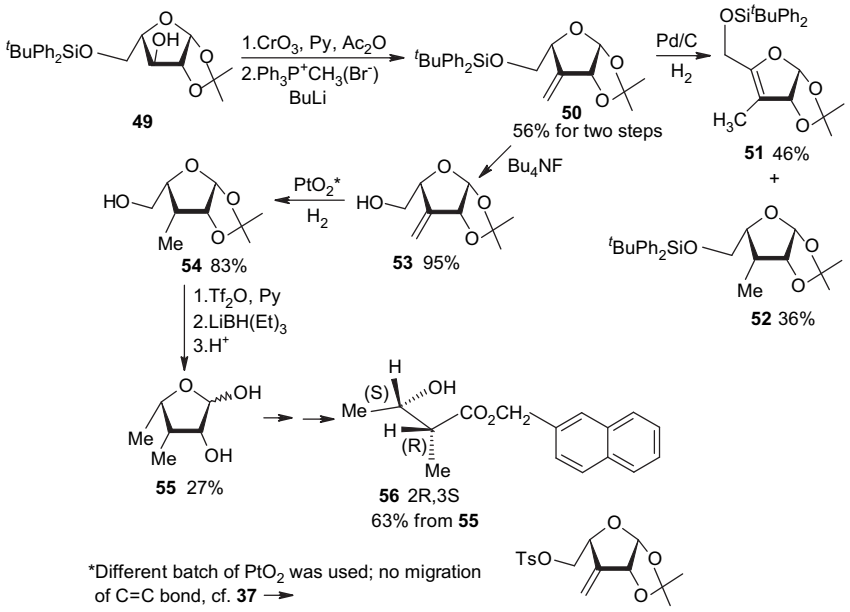
Scheme 2. Obtention of 2-naphthylmethyl (3*S*)-hydroxy-(2*S*)-methylbutanoate **33** from L-xylose.



Scheme 3. Obtention of 2-naphthylmethyl (3*R*)-hydroxy-(2*S*)-methylbutanoate **47** from D-arabinose.

used above (**15**→**20** and **31**→**33**) via the intermediates **46** and **47**, which were deformylated without separation to furnish the third target 2-naphthylmethyl (3*R*)-hydroxy-(2*S*)-methylbutanoate **48**.

The last target **56**, which has (2*R*,3*S*) configuration was obtained from L-arabinose (Scheme 4) following the same directions as those applied to D-arabinose, starting with the known *tert*-butyldiphenylsilyl-1,2-*O*-isopropylidene-L-*arabino*-furanose **49**[20,21] via the olefin **50** with two noticeable differences. Firstly, attempted hydrogenation of **50** over Pd–C catalyst resulted in migration of the carbon–carbon double bond in a much higher extend than in the



Scheme 4. Obtention of 2-naphthylmethyl (3*S*)-hydroxy-(2*R*)-methylbutanoate **56** from L-arabinose.

case of the desilylated D-compound **37**, and the unwanted olefin **51** was obtained in 46% yield, whereas the necessary L-lyxo-3-*C*-methyl product **52** was obtained in 36% yield. This was presumably a result of a bulk of the *tert*-butyldiphenylsilyl group. Also, palladium promotes migrations of the C=C bonds to a greater extent than platinum.[45] Secondly, hydrogenation of the desilylated intermediate **53** over Adam's catalyst (a *different* batch of PtO_2 was used than the one for hydrogenation of **37**) resulted in the *absence* of the transposition of the C=C bond and permitted isolation of the necessary *C*3-Me-L-*lyxo* product **54** in 83% yield. These subtle differences probably reflect variations of the properties of surfaces of platinum catalyst.

It should be pointed out that a tosylate **57** was unreactive toward $LiBH(Et)_3$ just like the more congested **40**.

Further transformation of the alcohol **54** to 3,5-dideoxy-3-*C*-methyl-L-lyxofuranose **55** and its subsequent conversion to 2-naphthylmethyl (3*S*)-hydroxy-(2*R*)-methylbutanoate **56** proceeded exactly as described for their enantiomeric equivalents.

In summary, all four enantiomerically pure 3-hydroxy-2-methylbutanoic acids as fluorescent 2-naphthylmethyl esters were synthesized starting from easily available carbohydrates.

The application of the targets **20**, **33**, **48**, and **56** to establish absolute configurations of the degradation product **2** after its conversion to 2-naphthylmethyl ester will be published in due course.

3. Experimental

3.1. General

All glasswares were dried at 104 °C. Evaporations were performed on a Büchi evaporator coupled to a membrane pump. Vacuums were broken using a balloon filled with nitrogen in the case of moisture-sensitive products. Moisture-sensitive liquids were transferred using dry syringes under atmosphere of nitrogen or argon. THF was freshly distilled from sodium–benzophenone. CH_2Cl_2 was dried by distillation from P_2O_5. Anhydrous acetone was prepared by shaking with P_2O_5 for ca. 20 min, filtration, and distillation. Dry DMF containing molecular sieves was obtained from Aldrich. NMR spectra were recorded on a Bruker 300 MHz and Bruker Avance II 500 MHz spectrometers using $CDCl_3$–TMS unless otherwise stated. Electron impact exact mass measurements were performed on the MS5OTS Kratos instrument at 50 eV, whereas the electrospray measurements on the APEX-Qe Bruker instrument. Optical rotations were taken on a Perkin–Elmer 341 automatic polarimeter in $CHCl_3$ (distilled from P_2O_5, i.e., ethanol-free) using a 1-dm tube for Na line at ca. 24 °C. Flash chromatography was performed using a 230–400 mesh silica gel from ICN or Acros. TLC plates (Fluka) with a fluorescent indicator were used for analysis of the reaction mixtures. The chromatograms were visualized using 10% H_2SO_4 in MeOH unless otherwise stated and charring at 120–130 °C. 'Bromocresol green reagent' used for detection of the carboxylic acids means 0.4% solution of bromocresol green in EtOH and 0.1 N aq NaOH added just to change a color to blue.[34,35] 'CrO_3–H_2SO_4 system' means 2% CrO_3 in 10% H_2SO_4. 'Xylene' means a mixture of isomers. Pyridine was stored over pellets of KOH. Dry ethyl acetate was prepared by distillation. Early distillate containing azeotropic mixture with water was rejected and the late fraction was used. Na_2SO_4 was used to dry the extracts.

3.2. 3-Deoxy-1,2;5,6-di-*O*-isopropylidene-3-*C*-methylene-D-*ribo*-hexofuranose 5

To a magnetically stirred mixture of CrO_3 (10.0 g, 100 mmol) in 100 ml of dry CH_2Cl_2 was added pyridine (16.2 ml, 200 mmol) under nitrogen. The mixture immediately turned dark brown and became warm again. Nearly all CrO_3 solubilized. After 30 min, solid 1,2;5,6-di-*O*-isopropylidene-D-*gluco*-furanose **3** (6.55 g, 25.2 mmol) was added immediately followed by Ac_2O (9.8 ml, 100 mmol). The mixture became warm again. TLC in 2:1 hexane–EtOAc after 45 min showed an elongated spot of the ulose **4**, which is slightly more polar than **3**. Most of CH_2Cl_2 was evaporated. Addition of 100 ml of 1:1 toluene–EtOAc mixture precipitated most of the chromium compounds. The decanted solution and the washings of the precipitated black solid tar were pushed through a 60–200 mesh silica gel column prepared in 1:2 toluene–EtOAc using an overpressure. Elution with 1:2 toluene–EtOAc, evaporation, co-evaporation with xylenes, and final drying furnished **4** (5.44 g, 84%), which was used for a Wittig reaction without characterization.

A magnetically stirred suspension of methyltriphenylphosphonium bromide (98%, 10.7 g, 30 mmol) in THF (100 ml) under nitrogen with EtOH–dry ice external cooling was treated with 2.5 M *n*-BuLi in hexane (11.2 ml, 28 mmol) dropwise. The mixture turned yellow. After the addition of *n*-BuLi, cooling was stopped for 30 min and re-applied again. A solution of **4** in 60 ml of THF was added dropwise for ca. 10 min. Cooling bath was removed. After 1.5 h, TLC showed that all **4** reacted forming a less polar **5** with R_f 0.36 in 9:1 hexane–EtOAc. The solids were filtered on a sintered glass. Evaporation and flash chromatography in 9:1 hexane–EtOAc gave **5** (3.2 g, 59% counted on **4**) as a colorless oil. $[\alpha]_D^{24}$ +109.4 (*c* 2.6, $CHCl_3$).

^1H ($CDCl_3$, 300 MHz): 5.81 (d, J_{12}=4.0 Hz, 1H, H1), 5.50 (dd, J=1.3, 1.8 Hz, 1H, =CH_2), 5.45 (dd, J=0.8, 2.2 Hz, 1H, =CH_2), 4.89 (apparent dd, J=1.0 Hz, J_{21}=4.0 Hz, 1H, H2), 4.67–4.64 (m, 1H), 4.09–4.03 (m, 2H), 3.97–3.90 (m, 1H), 1.52, 1.44, 1.37, and 1.36 (four s, 3H each, isopropylidene Me). ^{13}C (75 MHz): 146.8, 113.4, 112.5, 109.7, 104.5, 82.1, 79.2, 77.3, 66.7, 27.3, 27.0, 26.5, 25.4.

3.3. 3-Deoxy-1,2;5,6-di-*O*-isopropylidene-3-*C*-methyl-D-*gluco*-furanose 6, 3-deoxy-1,2;5,6-di-*O*-isopropylidene-3-*C*-methyl-D-*allo*-furanose 7, and 3-deoxy-1,2-*O*-isopropylidene-3-*C*-*allo*/*gluco*-furanose 8

3.3.1. Hydrogenation of *5* using Pd–C contaminated with $PdCl_2$

To a solution of **5** (3.2 g, 12.5 mmol) in EtOH (20 ml, 96%) was added Pd–C (0.31 g 10%) under a blanket of argon. Hydrogenation was performed in a Parr apparatus at the initial pressure of 35 psi. After 7 h of shaking, TLC showed the presence of the minor **6**, slightly less polar than the major **7** (R_f of a mid-point was 0.40 in 9:1 hexane–EtOAc, run twice), and **8** at a start. R_f of **8** was 0.44 in 20:1 CH_2Cl_2–MeOH. The mixture was passed through a bed of Celite (attention: used Pd catalyst is pyrophoric and should not be left dry) and the solvent was evaporated. Flash chromatography in 20:3 hexane–EtOAc gave 0.07 g of **6**, 0.02 g of a mixture of **6** and **7**, and 0.72 g of **7**. Total yield of **6** and **7** was 53%. Further elution with 20:1 CH_2Cl_2–MeOH gave **8** (0.89 g, 33%).

3.3.2. Hydrogenation of *5* using PtO_2

To a solution of **5** (7.39 g, 28.9 mmol) in 20 ml of 96% EtOH was added $PtO_2 \cdot H_2O$ (0.33 g). Hydrogenation in a Parr apparatus at the initial pressure of 40 psi for 7 h followed by filtration through Celite (attention: used Pt is pyrophoric and should not be left dry) and evaporation furnished 7.11 g, 95% of a mixture **6** and **7**. This mixture was used in a dehomologation step without chromatography.

Compound ***6***. ^1H (300 MHz): 5.78 (d, J_{12}=3.5 Hz, 1H, H1), 4.36 (d, J_{21}=3.5 Hz, 1H, H1), 4.13 (dd, J=5.4, 7.9 Hz, 1H), 4.09–3.99 (m, 2H), 3.94 (dd, J=5.4, 7.9 Hz, 1H), 2.45 (dq, J_{34}=4.0 Hz, J_{H3-Me}=7.4 Hz, 1H, H3), 1.52, 1.41, 1.35, 1.31(four s, 3H each, isopropylidene Me), 0.96 (d, J_{Me-H3}=7.5 Hz, 3H, C3–Me). ^{13}C (75 MHz): 111.2, 109.2, 104.8, 86.5, 80.7, 73.5, 68.4, 40.6, 26.8, 26.7, 26.1, 25.3, 11.1.

Compound **7**. ^{1}H (300 MHz): 5.76 (d, J_{12}=3.6 Hz, 1H, H1), 4.55 (t, J=4.2 Hz, 1H, H2), 4.11–4.02 (m, 2H), 3.97–3.89 (m, 1H), 3.73 (ddd, J=3.6, 6.9, 13.6 Hz, 1H), 1.95 (ddq, J_{32}=4.7 Hz, J_{34}=9.7 Hz, J_{H3-Me}= 6.8 Hz, 1H, H3), 1.51, 1.43, 1.35, 133 (four s, 3H each, isopropylidene Me), 1.19 (d, J_{Me-H3}=6.8 Hz, 3H, C3–Me). ^{13}C (75 MHz): 111.6, 109.5, 104.9, 83.5, 82.7, 77.6, 67.2, 42.4, 26.8, 26.5, 26.3, 25.2, 10.1.

Compound **8**. ^{1}H (300 MHz), major epimer: 5.77 (d, J_{12}=3.6 Hz, 1H, H1), 4.56 (t, J=4.2 Hz, 1H, H2), 3.87 (dd, J=4.2, 10.1 Hz, 1H), 3.81–3.71 (unresolved, 2H), 2.71 and 2.50 (two br s, exchangeable, –OH), 2.04 (ddq, J_{32}=4.6 Hz, J_{H3-Me}=6.6 Hz, J_{34}=10.7 Hz, 1H, H3), 1.52 and 1.33 (two s, 3H each, isopropylidene Me), 1.15 (d, J_{Me-H3}= 6.8 Hz, 3H, C3 Me). ^{13}C (75 MHz): 11.7, 104.6, 83.8, 83.4, 72.6, 63.3, 40.3, 26.7, 26.3, 10.0. HRMS (electrospray) calcd for $C_{10}H_{18}O_5$+Na^+: 241.10521, found: 241.10432.

3.4. 3-Deoxy-1,2-*O*-isopropylidene-3-*C*-methyl-D-*ribo*-furanose 10

To a magnetically stirred solution of the *allo* epimer **7** (0.72 g, 2.8 mmol) in dry EtOAc (15 ml) was added H_5IO_6 (0.76 g, 3.4 mmol). The mixture turned opaque within several seconds. Stirring was continued for 1 h 45 min. TLC in 18:3 hexane–EtOAc showed that all substrate with R_f 0.40 reacted to form the aldehyde **9** with R_f 0.18. The mixture was filtered through a sintered glass and nearly all solvent was evaporated. Small quantity of solid material appeared. Et_2O was added and the mixture was passed through a bed of Celite. The volatiles were evaporated. The residue was solubilized in technical grade EtOH (20 ml) and $NaBH_4$ (0.07 g, 1.9 mmol) was added in one portion while maintaining magnetic stirring. After 2 h, TLC showed a new more polar alcohol **10** with R_f 0.51 in 20:0.5 CH_2Cl_2–MeOH. Evaporation and flash chromatography in 20:0.4 CH_2Cl_2–MeOH gave **10** (0.32 g, 61%).

^{1}H (300 MHz): 5.80 (d, J_{12}=3.6 Hz, 1H, H1), 4.58(t, J=4.1 Hz, 1H, H2), 3.92–3.81 (three groups of multiplets, 2H), 3.55 (ddd, $J_{5''4}$=3.6 Hz, $J_{5''\text{-OH}}$=7.4 Hz, $J_{5''5'}$=12.0 Hz, 1H, H5″), 2.29 (dd, $J_{OH\text{-}5'}$= 4.9 Hz, $J_{OH\text{-}5''}$=7.8 Hz, 1H, exchangeable, –OH), 2.07 (ddq, J_{32}=4.7 Hz, $J_{3\text{-Me}}$=6.8 Hz, J_{34}=10.2 Hz, 1H, H3), 1.51 and 1.34 (two s, 3H each, isopropylidene Me), 1.07 (d, $J_{Me\text{-}3}$=6.8 Hz, 3H, C3-Me). ^{13}C (75 MHz): 111.5, 104.8, 83.1, 83.0, 61.3, 38.0, 26.6, 26.2, 9.1. HRMS (electrospray) calcd for $C_9H_{16}O_4$+Na^+: 211.09410, found: 211.09376.

3.5. 3-Deoxy-1,2-isopropylidene-3*C*-methyl-5-*O*-tosyl-D-*ribo*-furanose 11

3.5.1. *From* D-*ribo alcohol* ***10***

Compound **10** (0.32 g, 1.7 mmol) was conventionally tosylated using TsCl (0.65 g, 3.4 mmol) in CH_2Cl_2 (20 ml), pyridine (1 ml), and cat. DMAP overnight. Few drops of water were added to destroy the excess of TsCl for 1 h. Partition between CH_2Cl_2 and dil HCl, washing the organic phase with water, drying, evaporation, and crystallization from EtOAc gave **11** (0.45 g, 75%) with R_f 0.26 in 4:1 hexane–EtOAc.

3.5.2. *From a mixture of* ***6*** *and* ***7*** *obtained by hydrogenation of* ***5*** *over Adam's catalyst via epimeric alcohols* ***12***

To a cold (ice bath) magnetically stirred solution of **6** and **7** (7.3 g, 28.3 mmol) in dry EtOAc was added H_5IO_6 (8.4 g, 36.8 mmol) in one portion under the atmosphere of nitrogen. The cooling bath was removed. After 2.5 h, the mixture was worked-up as described for **9** to furnish yellowish oil. This oil was solubilized in 80 ml of 96% EtOH, cooled in ice bath, and treated with $NaBH_4$ (1.0 g, 28.3 mmol) added portionwise while maintaining magnetic stirring; 30 min later dil acetic acid was added to neutrality (indicator paper) and the volatiles were evaporated. The residue was solubilized in EtOAc and the resulting opaque solution was washed with water. The organic phase was dried, filtered, evaporated, and finally dried on an oil pump to furnish epimeric alcohols **12**. Dry CH_2Cl_2 was added followed by pyridine (7.5 ml), cat. quantity of DMAP, and TsCl (10.1 g, 53.2 mmol). After an overnight reaction, TLC showed a single spot of the products (R_f 0.26 in 4:1 hexane–EtOAc) and a fast moving spot of TsCl. Extraction was performed as described above. TsCl still present was removed by flash chromatography in hexane–EtOAc, gradient 4:1→3:1, and the epimeric tosylates were crystallized from EtOAc at rt overnight to furnish a pure *ribo* epimer **11** (5.22 g, 54%) together with 2.55 g of the mixture of the *ribo*/*xylo* tosylates.

Mp 120–123 °C (EtOAc), $[\alpha]_D^{24}$ +22.1 (*c* 6, $CHCl_3$). ^{1}H (300 MHz): 7.80 (d, J=8.2 Hz, 2H, H aromatic), 7.34 (d, J=8.2 Hz, 2H, H aromatic), 5.68 (d, J_{12}=3.5 Hz, 1H, H1), 4.52 (t, J=4.1 Hz, 1H, H2), 4.23 (dd, $J_{5'4}$=2.5 Hz, $J_{5'5''}$=11.1 Hz, 1H, H5́), 4.07 (dd, $J_{5''4}$=3.9 Hz, $J_{5''5'}$=11.1 Hz, 1H, H5″), 3.86 (dt, $J_{45'}$=$J_{45''}$=3.2 Hz, J_{43}=10.3 Hz, 1H, H4), 2.44 (s, 3H, Me), 2.02 (ddq, J_{32}=4.5 Hz, $J_{3\text{-Me}}$=7.5 Hz, J_{34}=10.0H, 1H, H3), 1.46 and 1.31 (two s, 3H each, isopropylidene Me), 1.03 (d, J_{Me-H3}=6.8 Hz, 3H, C3–Me). ^{13}C (75 MHz): 144.9, 132.8, 129.8, 128.0, 111.7, 104.8, 82.5, 79.9, 68.5, 39.2, 29.7, 26.3, 21.6, 9.0. HRMS (electrospray) calcd for $C_{16}H_{22}O_6S$+H^+: 343.12099, found: 343.12031.

3.6. 3,5-Dideoxy-3-*C*-methyl-D-*ribo*-furanose 15

To a solution of the tosylate **11** (2.9 g, 8.4 mmol) in THF (20 ml) under nitrogen was injected 1 M $LiBH(Et)_3$ (15 ml) at rt and the mixture was left overnight. TLC showed that all **11** with R_f 0.26 disappeared to form a faint, weakly charring spot of **13** with R_f 0.65 in 4:1 hexane–EtOAc. H_2SO_4 (1 M, 30 ml) was cautiously added (1.5 M H_2SO_4 could also be used). Two layers were formed. Small volume of technical grade THF (~10 ml) was added to achieve homogeneity. Slightly opaque solution was magnetically stirred overnight. TLC showed that the product having a putative structure **14** was *less* polar than the acetonide **13**. The mixture was transferred to a separatory funnel charged with CH_2Cl_2–water and exhaustive extraction (3×) was performed. The organic phase was washed once with water. Combined water phases were extracted with EtOAc (3×) and the combined organic phases were washed with water. To the CH_2Cl_2 phase was added methanol (200 ml) and the volatiles were evaporated. To the residue, MeOH was added again (300 ml) and was subsequently evaporated. This was repeated two more times. The EtOAc layer was treated in the same manner. TLC of the combined residues showed that **14** was no longer present. The newly formed diol **15** showed R_f 0.38 in 20:1.3 CH_2Cl_2–MeOH. Flash chromatography in this system furnished **15**, 0.82 g as an oil in 73% cumulative yield counted on a tosylate **11**. Diol **15** chars more intensely while using 2% CrO_3 in 10% aq H_2SO_4 than using 10% H_2SO_4 in MeOH. In another run yield of **15** was 54%.

$[\alpha]_D^{24}$ +27.9 (*c* 5.7, $CHCl_3$, after 30 min). ^{1}H (500 MHz): 5.383 (d, J_{12}=3.8 Hz, H1), 5.191 (s, H1), 5.11 (br s, exchangeable, –OH), 4.038 (t, J=4.5 Hz, H2), 3.943 (d, J_{23}=4.3 Hz, H2), 3.891 (dq, $J_{4\text{-Me}}$=6.0 Hz, J_{43}=10.2 Hz, H4), 3.859 (dq, $J_{4\text{-Me}}$=6.1 Hz, J_{43}=10.3 Hz), 3.70 and 3.28 (two br s, exchangeable, –OH), 2.006 (m of 14 lines, $J_{3\text{-Me}}$=6.9 Hz, J_{34}=~9.6 Hz, J_{32}=4.3 Hz, H3), 1.705 (m of 14 lines, $J_{3\text{-Me}}$=6.6 Hz, J_{34}=9.6 Hz, J_{32}=~5.5 Hz, H3), 1.277 (d, J_{Me-H4}=6.2 Hz, terminal Me), 1.183 (d, J_{Me-H4}=6.1 Hz), 1.001 (d, J_{Me-H2}=7.0 Hz, C2–Me), 0.995 (d, J_{Me-H2}=6.9 Hz, C2–Me). ^{13}C (75 MHz): 102.29, 97.13, 80.91, 78.81, 78.51, 73.58, 44.84, 42.28, 20.68, 18.82, 9.73, 9.16. HRMS (EI) calcd for $C_6H_{12}O_3$–OH: 115.07589, found: 115.07717.

3.7. 2-Naphthylmethyl (3*R*)-formyloxy-(2*R*)-methylbutanoate 19 and 2-napthylmethyl (3*R*)-hydroxy-(2*R*)-methylbutanoate 20

3.7.1. *Procedure A*

To a magnetically stirred solution of the diol **15** (011 g, 0.83 mmol) in EtOH (8 ml) was added $NaIO_4$ (0.21 g, 1 mmol),

solubilized in minimum volume of distd H_2O (~2 ml). The mixture became opaque immediately. After 1.5 h, TLC showed a high migrating very weakly charring spot (R_f 0.87 in 20:1 CH_2Cl_2–MeOH) and a small amount of unreacted **15**. Few milligrams of solid $NaIO_4$ were added to complete the diol cleavage. The mixture was filtered through sintered glass and evaporated at ca. 20 °C. Addition of CH_3CN (8 ml) precipitated some more white solid. Filtration and evaporation were repeated. To the residue solubilized in CH_3CN (25 ml) was added $NaClO_2$ (80% pure, 0.26 g, 2.21 mmol) in minimum volume of distd water, followed by 0.2 ml of 35% H_2O_2 and $NaH_2PO_4 \cdot 2H_2O$ (0.066 g, 0.42 mmol) in minimum volume of distd water. The additions were done in this order. The mixture was stirred for 2 h. TLC run in 20:1 CH_2Cl_2 and revealed in bromocresol green reagent showed two yellow elongated spots on a blue background: the upper more intense one belonging to the *O*-formylated acid **17** and the more polar spot belonging to the hydroxy acid **18**. The reaction mixture was filtered through Celite and the volatiles were evaporated and dried on an oil pump. The residual oil was solubilized in CH_2Cl_2 (20 ml) and a freshly prepared solution of 2-naphthyldiazomethane **23** was added using a Pasteur pipette. Addition of **23** was continued until reddish color persisted and evolution of nitrogen ceased. TLC at this point showed the presence of strongly UV absorbing spots of **19** with R_f 0.65 and **20** with R_f 0.30 in 4:1 hexane–EtOAc. Several other UV absorbing spots were present presumably arising from the decomposition of **23**. Upon spraying with a CrO_3–H_2SO_4 system and heating at 120–130 °C both **19** and **20** form reddish-brown spots. Evaporation of the solvent and flash chromatography using a gradient of EtOAc in hexane, 1:19→1:3, furnished **19** (0.10 g, 42%) and **20** (0.081 g, 37%).

*3.7.2. Procedure B: 2-naphthylmethyl (3R)-hydroxy-(2R)-methylbutanoate **20** from 2-naphthylmethyl (3R)-formyloxy-(2R)-methylbutanoate **19***

To a solution of the formate **19** in MeOH (6 ml) was added one drop of concd NH_4OH. After 1 h, TLC showed a complete conversion of **19** to a more polar **20** (system as above). Evaporation and flash chromatography furnished **20** (0.080 g, 89%).

*3.7.3. Procedure C: 2-naphthylmethyl (3R)-hydroxy-(2R)-methylbutanoate **20** from a mixture of **19** and **20** without chromatographic separation as in procedure A*

Isolation of the formate **19** can be skipped and a crude mixture after the esterification with **23** can be subjected to ammonolysis. Thus, evaporation of CH_2Cl_2, solubilization in MeOH (10 ml), and addition of few drops of concd NH_4OH transformed **19** to **20** for ~45 min. Evaporation of the solvent and flash chromatography using a gradient of EtOAc in hexane, 1:4→1:3, furnished **20** in ~70% yield counting on the diol **15**.

*Compound **19***. ^{1}H (300 MHz): 7.90 (s, 1H, CHO), 7.84–7.81 (m, 4H, H aromatic), 7.50–7.43 (m, 3H, H aromatic), 5.29 (s, 2H, –OCH_2–), 5.27 (quintette, J=6.6 Hz, 1H, H3), 2.80 (quintette, J=7.2 Hz, 1H, H2), 1.26 (d, J=6.4 Hz, 3H, terminal Me), 1.21 (d, J=7.1 Hz, 3H, C2–Me). ^{13}C (75 MHz): 173.3, 160.2, 133.2, 133.1, 128.4, 128.0, 127.7, 127.5, 126.4, 126.3, 125.9, 71.5, 66.6, 44.6, 17.0, 12.8. HRMS (electrospray) calcd for $C_{17}H_{18}O_4$+Na^+: 309.11029, found: 309.10968; calcd for $C_{17}H_{18}O_4$+K^+: 325.08420, found: 325.08357.

*Compound **20***. $[\alpha]_D^{24}$ −24.1 (*c* 5, $CHCl_3$). ^{1}H (500 MHz): 7.85–7.82 (4H, H aromatic), 7.51–7.44 (3H, H aromatic), 5.32 (s, 2H, –OCH_2–), 3.92 (quintette of broadened lines, J=6.3 Hz, 1H, H3), 2.64 (br s, exchangeable, –OH), 2.54 (quintette, J=7.2 Hz, 1H, H2), 1.222 (d, J=6.4 Hz, 3H, terminal Me), 1.216 (d, J=7.2 Hz, 3H, C2–Me). ^{13}C (75 MHz): 175.7, 133.14, 133.09, 128.4, 128.0, 127.7, 127.3, 126.32, 126.29, 125.7, 69.4, 66.5, 47.1, 20.7, 14.1. HRMS (electrospray) calcd for $C_{16}H_{18}O_3$+Na^+: 281.11483, found: 281.11465.

3.8. 2-Naphthylmethyl hydrazone 22

To a magnetically stirred solution of 2-naphthylcarbaldehyde **21** (15.0 g, 96 mmol) in techn. EtOH (70 ml) was added hydrazine hydrate (100%, 9.6 g, 9.3 ml, 188 mmol) via a syringe for ~5 min with external cooling in ice bath. After the addition was complete, cooling bath was removed and semi-solid slurry was left overnight at rt. The semi-solid mixture was cooled, filtered on a sintered glass, and washed with an ice-cold 1:1 EtOH–Et_2O and finally with ice-cold Et_2O. Final drying on an oil pump gave the crude hydrazone **22** (15.0 g, 92%). Mp 148–151 °C (EtOH), lit.[36] 149–150 °C.

^{1}H (300 MHz, $CDCl_3$+a drop of DMSO-d_6): 7.88–7.76 (m, 6H), 7.51–7.41 (m, 2H), 5.9 (br s, exchangeable, –NH_2). ^{13}C (75 MHz): 141.3, 132.7, 132.6, 125.68, 125.52, 125.46, 122.2. HRMS (electrospray) calcd for $C_{11}H_{10}N_2$+H^+: 171.09167, found: 172.09165.

3.9. 2-Naphthylmethyldiazomethane 23

A mixture of the hydrazone **22** (1.08 g, 6.4 mmol) in CH_2Cl_2 (40 ml), yellow HgO (1.96 g, 9.0 mmol), and a small crushed pellet of KOH was magnetically stirred for 3 h. The initial bright yellow-orange color of the heterogeneous mixture gradually faded and a gray deposit of mercury appeared. Stirring was stopped and after sedimentation of the solids the orange-red solution of **23** was pipetted for the esterification step. This solution was always freshly prepared. Although we have never experienced any problem with this preparation, it should be remembered that any diazo compound is potentially unstable.

3.10. 1,2-*O*-Isopropylidene-L-*xylo*-furanose 24

L-Xylose (20 g, 134 mmol) in 520 ml of dry acetone and 20 ml of concd H_2SO_4 were stirred magnetically for 50 min. The flask was cooled in ice-water bath and a solution of 26 g, 246 mmol of anhyd Na_2CO_3 in 225 ml of water was gradually added to keep the internal temperature below 20 °C and to avoid excessive frothing; 2.5 h after the end of addition, solid anhyd Na_2CO_3 (14 g, 132 mmol) was added for 15 min to neutralize all H_2SO_4. Stirring was continued for 10 min more. TLC showed a spot with R_f 0.45 (CH_2Cl_2–MeOH). The solids were filtered and acetone was evaporated. The residual oil was purified by flash chromatography in CH_2Cl_2–MeOH, 30:1→20:1, to furnish **24** (19.0 g, 75%) as a syrup, which solidified upon storage in a refrigerator. An alternative one-pot preparation described for L-xylose is much longer and was considered less convenient.[46]

$[\alpha]_D^{24}$ +18.2 (*c* 3.4, $CHCl_3$), commercial D-form from the Aldrich has $[\alpha]_D^{24}$ −19.2 (*c* 1, H_2O). ^{1}H (300 MHz): 5.99 (d, J_{12}=3.6 Hz, 1H, H1), 4.53 (d, J_{21}=3.6 Hz, 1H, H2), 4.33 (br s, 1H), 4.19–4.02 (m, 4H, one proton exchangeable), 1.49 and 1.33 (two s, 3H each, isopropylidene Me). ^{13}C (75 MHz): 111.8, 104.8, 85.6, 78.6, 76.9, 61.1, 26.7, 26.1. HRMS (electrospray) calcd for $C_8H_{14}O_5$+Na^+: 213.07736, found: 213.07320.

3.11. 5-*O*-*tert*-Butyldimethylsilyl-1,2-*O*-isopropylidene-L-*xylo*-furanose 25

To a solution of the diol **24** 18.5 g, 97.4 mmol in dry DMF (Aldrich, sold with molecular sieves) 100 ml under a blanket of nitrogen, was added imidazole 16.5 g, 240 mmol and *tert*-butyldimethylsilyl chloride 14.8 g, 110 mmol. After an overnight reaction, TLC showed one spot with R_f 0.45 in 4:1 hexane–EtOAc. Conventional extraction and flash chromatography in hexane–EtOAc, 17:3→4:1, furnished 22 g, 75% of **25**.

$[\alpha]_D^{24}$ +11.0 (*c* 5.4, $CHCl_3$). ^{1}H (300 MHz): 5.96 (d, J_{12}=3.6 Hz, 1H, H1), 4.51 (d, J_{21}=3.6 Hz, 1H, H2), 4.38 (d, J=2.7 Hz, 1H), 3.37 (apparent t, J=2.5 Hz, 2H, one H exchangeable), 4.15–4.08 (unresolved, 2H, H5), 1.48 and 1.32 (two s, 3H each, isopropylidene Me), 0.89 (s,

9H, ^{t}Bu), 0.11 (s, 6H, Me_2Si). ^{13}C (75 MHz): 111.5, 105.0, 85.6, 78.1, 77.1, 62.4, 26.8, 26.1, 25.7, 18.1, −5,5, −5.7. HRMS (electrospray) calcd for $C_{14}H_{28}O_5Si+H^+$: 305.17786, found: 305.17726.

3.12. 5-*O*-*tert*-Butyldimethylsilyl-3-deoxy-1,2-*O*-isopropylidene-3-*C*-methylene-L-*erythro*-pentofuranose 26

A complex of $CrO_3\cdot Py$ was prepared by the addition of pyridine (16.9 ml, 209 mmol) to CrO_3 (10.4 g, 104 mmol) in dry CH_2Cl_2 (200 ml) under nitrogen while maintaining stirring for 30 min. To this dark brown solution was added **25** (10.0 g, 32.9 mmol) in 40 ml of dry CH_2Cl_2 immediately followed by Ac_2O (10.2 ml, 108 mmol). The mixture became warm. TLC (hexane–EtOAc 17:3) showed a conversion of **25** into a slightly less polar product. After 10 min, the excess of chromium compounds was precipitated by the addition of 240 ml of 1:1 EtOAc and toluene mixture. Black solids were washed twice with 1:1 EtOAc–toluene. The original supernatant and the washings were applied on top of a silica gel (70–200 mesh) column prepared in 2:1 EtOAc–toluene. Slight overpressure was used to push the solution through the gel. Elution with 2:1 EtOAc–toluene was performed. The fractions containing the product were pooled together, evaporated, and co-evaporated with xylenes. Final drying was performed on an oil pump.

To a suspension of $Ph_3P^+Me(Br^-)$ (98%, 17.5 g, 48 mmol) in 600 ml of THF cooled with EtOH–dry ice was injected 2.5 M BuLi in hexane (18.2 ml, 45.5 mmol) with constant magnetic stirring. After the addition, cooling bath was removed for 50 min and re-applied again. A solution of the abovementioned oxidation product in 100 ml of THF was added via a syringe and the mixture was left to reach rt overnight. TLC showed a complete conversion of the substrate with R_f 0.44 into a strongly charring spot of the olefin **25** with R_f 0.80 in 17:3 hexane–EtOAc. The solids were filtered on a sintered glass and THF was evaporated. The resulting yellow oil was solubilized in CH_2Cl_2 and washed with water. The extract was dried and evaporated, and the residue was purified by flash chromatography in 19:1 hexane–EtOAc to furnish **26** (6.9 g, 70%) as an oil for two steps.

$[\alpha]_D^{24}$ −127.6 (*c* 3.9, $CHCl_3$). ^1H (300 MHz): 5.85 (d, J_{12}=4.1 Hz, 1H, H1), 5.42 (dd, J=1.2, 2.2 Hz, 1H), 5.27 (t, J=1.7 Hz, 1H), 4.91–4.87 (m, 1H), 4.78–4.74 (m, 1H), 3.76 (dd, $J_{5'4}$=4.1 Hz, $J_{5'5''}$=10.6 Hz, 1H, H5′), 3.68 (dd, $J_{5''4}$=3.8 Hz, $J_{5''5'}$=10.6 Hz, 1H, H5″), 1.50 and 1.39 (two s, 3H each, isopropylidene Me), 0.88 (s, 9H, ^{t}Bu), 0.06 and 0.05 (two s, 6H, Me_2Si). ^{13}C (75 MHz): 147.6, 112.5, 111.5, 104.9, 81.99, 81.96, 80.8, 65.6, 27.5, 27.3, 25.8, 18.2, −5.4, −5.5. HRMS (electrospray) calcd for $C_{15}H_{28}O_4Si+H^+$: 301.18295, found: 301.18239.

3.13. 3-Deoxy-1,2-*O*-isopropylidene-3-*C*-methylene-L-*erythro*-pentofuranose 27

The silane **26** (6.2 g, 20.7 mmol) in technical grade THF (30 ml) was deprotected with 1 M Bu_4NF–THF (22 ml) overnight. R_f of the product is 0.43 in 1:1 hexane–EtOAc. Evaporation of THF and flash chromatography in the same system furnished 3.8 g, quantitative yield, of **27**.

$[\alpha]_D^{24}$ −183.7 (*c* 2.8, $CHCl_3$). ^1H (300 MHz): 5.87 (d, J_{12}=4.0 Hz, 1H, H1), 5.48 (dd, J=0.9, 2.3 Hz, 1H), 5.19 (dd, J=1.2, 2.1 Hz, 1H), 4.93–4.91 (m, 1H), 4.85–4.80 (m, 1H), 3.88 (d, $J_{5'5''}$=11.9 Hz, 1H, H5′), 3.67 (dd, $J_{5''4}$=4.4 Hz, $J_{5''5'}$=12.0 Hz, 1H, H5″), 2.16 (br s, exchangeable, 1H, –OH), 1.52 and 1.39 (two s, 3H each, isopropylidene Me). ^{13}C (75 MHz): 145.5, 112.6, 112.2, 104.4, 82.0, 80.0, 63.4, 21.4, 27.1. HRMS (electrospray) calcd for $C_9H_{14}O_4+Na^+$: 209.07845, found: 209.07818.

3.14. 3-Deoxy-1,2-*O*-isopropylidene-3-*C*-methyl-L-*ribo*-furanose 28 and 3-deoxy-1,2-*O*-isopropylidene-3-*C*-methyl-L-*xylo*-furanose 29

Hydrogenation of the olefin **27** (3.6 g, 19.3 mmol) in 96% EtOH (22 ml) and $PtO_2\cdot H_2O$ (0.102 g) at the initial pressure of 45 psi was performed in a Parr apparatus for 2.5 h. Filtration of Pt (attention: pyrophoric) on the bed of Celite, evaporation, and drying furnished 3.6 g, approximately quantitative yield, of both epimeric 3-*C*-methyl products **28** and **29** in ∼10:1 proportion, which are inseparable under the flash chromatography conditions.

^{13}C (75 MHz): 111.6, 111.5, 104.9, 104.5, 86.8, 83.1, 80.2, 62.1, 40.5, 26.7, 26.3, 26.1, 10.9. HRMS (electrospray): calcd for $C_9H_{16}O_4+Na^+$=211.09410, found: 211.09380.

3.15. 3-Deoxy-1,2-*O*-isopropylidene-3-*C*-methyl-5-*O*-tosyl-L-*ribo*-furanose 30

Tosylation of the **28** and **29** mixture and crystallization of the major *C*-3-methyl L-*ribo* epimer proceeded as described for the enantiomeric compound **11** derived from D-glucose. Compound **30** was obtained in 69% yield together with 26% of the mixture 3-*C*-methyl-5-*O*-tosyl L-*ribo*/*xylo* compounds, inseparable under the conditions of flash chromatography.

Mp 119–122 °C (EtOAc), $[\alpha]_D^{24}$ −21.4 (*c* 7, $CHCl_3$). For ^1H and ^{13}C NMR data see enantiomeric compound **11**. HRMS (electrospray) calcd for $C_{16}H_{22}O_6S+H^+$: 343.12097, found: 343.12054.

3.16. 3,5-Dideoxy-3*C*-methyl-L-*ribo*-furanose 31

Compound **30** was converted to **31** in 64% yield following the procedure described for the transformation of its D-*ribo* enantiomer **11** to obtain **15**.

$[\alpha]_D^{24}$ −26.0 (*c* 1.8, $CHCl_3$). For NMR data see compound **15**. HRMS (EI) calcd for $C_6H_{12}O_3-OH$: 115.07589, found: 115.07611.

3.17. *O*-Methyl 3,5-dideoxy-3-*C*-methyl-α-L-*ribo*-furanoside 32

An unexpected glycosylation took place during conversion of **30** to **31** in one case, evidently due to the presence of acid in the crude CH_2Cl_2 and EtOAc extracts. The residue after evaporation of both solvents was solubilized in MeOH and left overnight at rt, and evaporation was reassumed next day to destroy any borates present. TLC (CH_2Cl_2–MeOH 20:1.3) showed the presence of two compounds: **32** with R_f 0.62 and **31** with R_f 0.41. Flash chromatography in the same system furnished **32** (0.43 g, 28%) and **31** (0.30 g 22%). This unwanted glycosylation can be avoided by performing all evaporations and chromatography in 1 day.

^1H (500 MHz): 4.74 (s, 1H, H1), 3.97 (d, J_{23}=3.9 Hz, 1H, H1), 3.90 (dq, $J_{4\text{-Me}}$=6.1 Hz, J_{43}=9.3 Hz, 1H, H4), 3.35 (s, 3H, –OMe), 2.51 (br s, exchangeable, –OH), 1.98 (ddq, J_{34}=9.3 Hz, J_{23}=3.8 Hz, $J_{3\text{-Me}}$=7.0 Hz, 1H, H3), 1.28 (d, $J_{\text{Me-4}}$=6.1 Hz, 3H, C4-Me), 1.04 (d, $J_{\text{Me-4}}$=7.0 Hz, 3H, C3–Me). ^{13}C (75 MHz): 108.9, 80.9, 80.7, 54.3, 42.7, 20.9, 9.3. HRMS (EI) calcd for $C_7H_{17}O_3-CH_3$: 115.07590, found: 115.07692.

3.18. 2-Naphthylmethyl (3*S*)-hydroxy-(2*S*)-methyl-butanoate 33

Transformation of the diol **31** to the target **33** was performed as described for the enantiomeric compound **15**→**20** in 58% cumulative yield.

$[\alpha]_D^{24}$ +24.0 (*c* 6.8, $CHCl_3$). For NMR data see compound **20**. HRMS (electrospray) calcd for $C_{16}H_{18}O_3+K^+$: 297.08874, found: 297.08869.

3.19. 5-*O*-*tert*-Butyldiphenylsilyl-D-*arabino*-furanose 34

D-Arabinose (30 g, 0.2 mol) was solubilized in dry DMF (300 ml) with warming to ca. 100 °C. When the temperature of this solution dropped to ca. 50 °C, imidazole (27.2 g, 0.4 mol) and *tert*-butyldiphenylsilyl chloride (55 g, 52 ml, 0.2 mol) were added under nitrogen, and the whole was stirred at 55–60 °C for 2.5 h. Extraction

(1 M HCl–CH_2Cl_2), washing of the organic phase with water, drying, and evaporation furnished a yellowish oil. TLC (hexane–EtOAc, 2:3) showed the product with R_f 0.4 and impurities moving with the solvent front. Flash chromatography using a gradient of EtOAc in hexane, 2:3→1:1→3:2, gave **34** (49 g, 63%) as a colorless oil.

^{1}H (300 MHz): 5.43 (br s, H1α, integration of both signals was ca. 3:1), 5.30 (dd, J_{12}=3.6 Hz, $J_{1\text{-OH}}$=7.5 Hz, H1β, integration of both signals was ca. 3:1). ^{13}C (75 MHz): 135.64, 135.60, 131.86, 131.64, 130.24, 130.20, 130.13, 128.01, 127.96, 103.5, 97.0, 87.3, 83.1, 78.8, 78.2, 77.9, 76.7, 64.5, 64.1,26.8, 26.7, 19.2, 19.0. HRMS (electrospray) calcd for $C_{21}H_{28}O_5Si+Na^+$: 411.15984, found: 411.15892.

3.20. 5-*O*-*tert*-Butyldiphenylsilyl-1,2-*O*-isopropylidene-D-*arabino*-furanose 35

Compound **34** (32 g, 82.5 mmol) in dry acetone (360 ml), concd H_2SO_4 (1.6 ml), and $CuSO_4$ (dried at ca. 150 °C for 4 h, 36 g) were stirred under nitrogen for 7 h. The solids were filtered on a sintered glass. The filtrate was neutralized using cold concd NH_4OH and the solids were filtered again. TLC showed a spot of **35** with R_f 0.39 (in hexane–EtOAc 4:1) and a minor less polar compound. Evaporation and flash chromatography in hexane–EtOAc, 5:1→4:1, gave **35** (25 g, 71%) as a syrup. For the next oxidation step, a crude olefination product could be used.

$[\alpha]_D^{24}$ +5.6 (*c* 3.2, $CHCl_3$); L-enantiomer:[20] $[\alpha]_D^{24}$ −5 (*c* 1.2, $CHCl_3$). ^{1}H (300 MHz): 7.68–7.65 (m, 4H, H aromatic), 7.44–7.35 (m, 6H, H aromatic), 5.87 (d, J_{12}=4.0 Hz, 1H, H1), 4.53 (d, J_{21}=4.0 Hz, 1H, H2), 4.42 (t, *J*=3.1 Hz, 1H, H3), 4.06 (dt, *J*=2.4, 6.6, 6.6 Hz, 1H), 3.87–3.77 (m, 2H, H5), 1.32 and 1.28 (two s, 3H each, isopropylidene Me), 1.06 (s, 9H, ^{t}Bu). ^{13}C (75 MHz): 135.61, 135.58, 133.21, 133.17, 129.81, 129.79, 127.8, 112.53, 105.6, 87.5, 87.1, 76.3, 63.7, 26.9, 26.8, 26.1, 19.2. HRMS (electrospray) calcd for $C_{24}H_{32}O_5Si+Na^+$: 451.19168, found: 451.19078.

3.21. 3-Deoxy-5-*O*-*tert*-butyldiphenylsilyl-1,2-*O*-isopropylidene-3-*C*-methylene-*D*-*threo*-furanose 36

To a stirred suspension of CrO_3 (10.1 g, 100 mmol) in dry CH_2Cl_2 (200 ml) under nitrogen was added pyridine (16.2 ml, 200 mmol). After 25 min, a solution of **35** (11.0 g, 25.7 mmol) in dry CH_2Cl_2 (120 ml) was added followed immediately by Ac_2O (9.5 ml, 100 mmol). Stirring was continued for 17 min. The reaction was quenched by the addition of 200 ml of 1:1 EtOAc–toluene. The dark supernatant was applied on top of a 60–200 mesh silica gel column prepared in 2:1 EtOAc–toluene. Black residue after decantation was washed twice with 1:1 EtOAc–toluene and the washings were also applied on the column. Elution with 2:1 EtOAc–toluene, evaporation of the volatiles, co-evaporation with xylene, and drying on an oil pump gave colorless oil (R_f 0.32 in 6:1 hexane–EtOAc), which was solubilized in dry THF and added dropwise to a Wittig reagent prepared from $Ph_3P^+CH_3(Br^-)$ (98%, 14.3 g, 40 mmol) suspended in 350 ml of dry THF and 2.5 M BuLi in hexane (15.2 ml, 38 mmol) as described for the synthesis of **5** and **26**. The cooling bath was removed. After 4 h, TLC showed that the substrate with R_f 0.32 reacted to form strongly charring new product with R_f 0.58 in 6:1 hexane–EtOAc. Filtration through Celite and evaporation furnished yellow-brown oil, which was solubilized in CH_2Cl_2 and washed with water. The organic phase was dried and evaporated. The residue was subjected to flash chromatography in 15:1 hexane–EtOAc to yield **36** as oil (7.9 g, 72%) for two steps.

$[\alpha]_D^{24}$ +3.2 (*c* 7.2, $CHCl_3$). ^{1}H (300 MHz): 7.71–7.66 (m, 4H, H aromatic), 7.41–7.33 (m, 6H, H aromatic), 5.80 (d, J_{12}=3.9 Hz, 1H, H1), 5.45 (dd, *J*=0.8, 2.0 Hz, 1H), 5.32 (t, *J*=1.4 Hz, 1H), 4.85 (dt, *J*=0.9, 0.9, 3.9 Hz, 1H), 4.60 (tt, *J*=1.8, 1.8, 6.7, 6.7 Hz, 1H), 3.89 (dd, $J_{5'4}$=6.4 Hz, $J_{5'5''}$=10.0 Hz, 1H, H5′), 3.76 (dd, $J_{5''4}$=6.9 Hz, $J_{5''5'}$=10.0 Hz, 1H, H5″), 1.34 and 1.31 (two s, 3H each, isopropylidene –Me), 1.06 (s, 9H, ^{t}Bu). ^{13}C (75 MHz): 145.7, 135.7, 134.8, 133.4, 133.3, 129.7, 129.6, 127.70, 127.67, 114.0, 113.1, 105.4, 83.1, 81.4, 67.2, 27.3, 26.8, 26.5, 10.2. HRMS (electrospray) calcd for $C_{25}H_{32}O_4Si+Na^+$: 447.19677, found: 447.19620.

3.22. 3-Deoxy-1,2-*O*-isopropylidene-3-*C*-methylene-*D*-*threo*-furanose 37

Olefin **36** (7.9 g, 18.6 mmol) in technical grade THF (50 ml) was treated with 1 M Bu_4NF (20 ml, 20 mmol) for 2 h. TLC showed a new spot with R_f 0.31 in 3:2 hexane–EtOAc. Evaporation of the solvent and flash chromatography in 55:45 hexane–EtOAc gave **37** (4.5 g, 92%) as oil.

A convenient shortcut to get **37** is to skip a chromatography after the Wittig reaction and to add Bu_4NF directly to the THF solution of the crude extract. Thus, starting from 16.2 g of **35**, 5.1 g of the alcohol **37** was obtained in a cumulative yield of 72% for three steps.

$[\alpha]_D^{24}$ −28.4 (*c* 6.2, $CHCl_3$). ^{1}H (300 MHz): 5.85 (d, J_{12}=3.9 Hz, 1H, H1), 5.49 (dd, *J*=1.0, 2.1 Hz, 1H), 5.27 (t, *J*=1.5 Hz, 1H), 4.90 (dt, *J*=1.0, 1.0, 3.9 Hz, 1H, H2), 4.65 (ddd, *J*=2.0, 4.1, 6.3 Hz, 1H, H4), 3.82 (dd, $J_{5'4}$=7.1 Hz, $J_{5'5''}$=11.7 Hz, 1H, H5′), 3.70 (dd, $J_{5''4}$=4.2 Hz, $J_{5''5'}$=11.7 Hz, 1H, H5″), 2.70 (br s, exchangeable, –OH), 1.56 and 1.36 (two s, 3H each, isopropylidene –Me). ^{13}C (75 MHz): 145.0, 113.7, 113.4, 105.2, 83.7, 81.2, 65.8, 27.2, 26.5. HRMS (electrospray) calcd for $C_9H_{14}O_4+Na^+$: 209.07900, found: 209.07799.

3.23. 4-Hydroxymethyl-3,4-ene-1,2-*O*-isopropylidene-3-*C*-methyl-L-*glycero*-pentofuranose 38 and 3-deoxy-1,2-*O*-isopropylidene-3-*C*-methyl-*D*-*lyxo*-furanose 39

Olefin **37** (2.41 g, 12.9 mmol) in abs EtOH (20 ml) and 0.1777 g of PtO_2 were hydrogenated in a Parr apparatus at the initial pressure of 38 psi for 2.5 h. TLC showed the olefin **38** with R_f 0.58, the main compound **39** with R_f 0.36 (hexane–EtOAc 1:1), and two more polar unidentified compounds present in small concentration. Compound **39** is slightly more polar than the substrate **37**. Filtration through Celite (attention: dry Pt is pyrophoric), evaporation of the solvent, and flash chromatography in 1:1 hexane–EtOAc gave **38** (0.31 g, 13%) and **39** (1.73 g, 71%). Both **38** and **39** are oils.

Compound ***38***. $[\alpha]_D^{24}$ +4.5 (*c* 4.8, $CHCl_3$). ^{1}H (300 MHz): 5.96 (d, J_{12}=5.3 Hz, 1H, H1), 5.11 (d of unresolved quintettes, four *J*=0.9 Hz, J_{21}=5.3 Hz, 1H, H1), 4.17 (s, 2H, H5), 2.259 (br s, exchangeable, 1H, –OH), 1.76, 1.45 and 1.43 (three s, 3H each, isopropylidene –Me, C3–Me). ^{13}C (75 MHz): 151.0, 111.9, 108.0, 103.8, 87.2, 55.7, 28.0, 27.9, 9.1. HRMS (electrospray) calcd for $C_9H_{14}O_4+Na^+$: 209.07900, found: 209.07840.

Compound ***39***. $[\alpha]_D^{24}$ +44.4 (*c* 1.4, $CHCl_3$). ^{1}H (300 MHz): 5.84 (d, J_{12}=3.9 Hz, 1H, H1), 4.58 (dd, J_{21}=3.9 Hz, J_{23}=5.3 Hz, 1H, H1), 4.23 (ddd, $J_{45''}$=4.0 Hz, J_{43}=8.3 Hz, $J_{45'}$=9.8 Hz, 1H, H4), 3.94 (dd, $J_{5'4}$=10.0 Hz, $J_{5'5''}$=11.4 Hz, 1H, H5′), 3.52 (dt, $J_{5''\text{-OH}}$=3.9 Hz, *J*=10.6, 10.6 Hz, 1H, H5) [after decoupling of the doublet at δ 2.24: 3.96 (dd, $J_{5'4}$=9.8 Hz, $J_{5'5''}$=11.5 Hz), 3.53 (dd, $J_{5''4}$=4.0 Hz, $J_{5''5'}$=11.5 Hz)], 2.46 (m of 14 lines, J_{32}=5.4 Hz, $J_{3\text{-Me}}$=7.4 Hz, J_{34}=8.3 Hz, 1H, H3), 2.24 (d, *J*=9.1 Hz, exchangeable, 1H, –OH), 1.56 and 1.31 (two s, 3H each, isopropylidene –Me), 1.10 (d, $J_{\text{Me-3}}$=7.4 Hz, 3H, C3–Me). ^{13}C (75 MHz): 112.1, 105.9, 84.2, 82.3, 62.6, 38.7, 26.5, 25.5, 7.7. HRMS (electrospray) calcd for $C_9H_{16}O_4+Na^+$: 211.09465, found: 211.09403.

3.24. 3-Deoxy-1,2-*O*-ispopropylidene-3-*C*-methyl-5-*O*-tosyl-D-*lyxo*-furanose 40

Alcohol **39** (0.090 g, 0.48 mmol) in dry CH_2Cl_2 (10 ml), pyridine (1 ml), cat. DMAP, and TsCl (0.45 g, 2.4 mmol) were stored under nitrogen for 24 h. TLC (hexane–EtOAc 1:1) showed a complete conversion to the less polar **40**. Extraction (CH_2Cl_2–dil HCl),

washing of the organic phase with water, drying, evaporation, and flash chromatography in 3:2 hexane–EtOAc gave the product (0.11 g, 67%) as a syrup.

^{1}H (300 MHz): 7.81(d, J=8.2 Hz, 2H, H aromatic), 7.34 (d, J=8.2 Hz, 2H, H aromatic), 5.74 (d, J_{12}=3.7 Hz, 1H, H1), 4.49 (t, J=4.3 Hz, 1H, H2), 4.30–4.19 (unresolved, 3H), 2.34 (s, 4H, H3 and –PhMe), 1.30 and 1.24 (two s, 3H each, isopropylidene –Me), 1.08 (d, $J_{Me\text{-}3}$=7.3 Hz, C3-Me). ^{13}C (75 MHz): 144.7, 132.7, 129.7, 128.0, 111.8, 105.9, 81.9, 80.3, 70.0, 39.2, 26.2, 25.2, 21.5, 8.1. HRMS (electrospray) calcd for $C_{16}H_{22}O_6S$+Na^+: 365.10349, found: 365.10276.

3.25. 3,5-Dideoxy-3-*C*-methyl-D-*lyxo*-furanose 44

To a cold (ice bath) solution of the alcohol **39** (1.3 g, 6.9 mmol) in dry CH_2Cl_2 (30 ml) and pyridine (2 ml) with magnetic stirring was added dropwise trifluoromethanesulfonic anhydride (2.4 g, 1.4 ml, 8.5 mmol). After 25 min, extraction was performed (CH_2Cl_2–dil HCl). The organic phase was washed with ice water, dried, filtered through sintered glass, evaporated, and dried on an oil pump to furnish red-orange thick oil. The vacuums were broken using nitrogen in a balloon. All the work-up should be performed rapidly (ca. 30 min) to avoid decomposition of the triflate **41**. Dry THF (30 ml) was added and the flask was cooled in an ice bath. To the stirred solution was injected 1 M LiBH(Et)$_3$ in THF (10 ml). The initial red-orange color turned yellow immediately. The homogenous mixture was left overnight at rt. Small quantity of unreacted **41** was still present and more LiBH(Et)$_3$ (3.0 ml) was added and the reaction was continued for 24 h more. TLC showed that the substrate **41** with R_f 0.22 all reacted forming a faint brown-yellow spot of the substitution product **42** with R_f 0.38 (in hexane–EtOAc 10:1) and a black spot at the application point. The reaction mixture was cooled in ice bath and 4 ml of 3 M H_2SO_4 was cautiously added (frothing) followed by 10 ml of 1 M H_2SO_4. Cooling bath was removed and hydrolysis was continued overnight. TLC (hexane–EtOAc 10:1) showed the presence of a new compound, presumably **43**, which was less polar than **42**. Exhaustive extraction was performed using CH_2Cl_2 (3×) and EtOAc (3×) as described for **14** and **15**. The extracts were evaporated and co-evaporated several times with MeOH to break the putative borate **43** and to release the diol **44**. Flash chromatography of the residual yellowish oil in 20:1.3 CH_2Cl_2–MeOH furnished **44** (0.25 g, 27%) as oil, counting on the alcohol **39**.

$[\alpha]_D^{24}$ +32.3 (c 1.6, $CHCl_3$, after 30 min). ^{1}H (500 MHz, after D_2O exchange): 5.28 (d, J_{12}=4.6 Hz, H1), 5.27 (d, J_{12}=1.6 Hz, H1), 4.42 (quintette, $J_{4\text{-}Me}$=6.6 Hz, J_{43}=6.6 Hz, H4), 4.12 (quintette, $J_{4\text{-}Me}$=6.5 Hz, J_{43}=6.5 Hz, H4), 4.10 (dd, J_{21}=5.1 Hz, J_{23}=6.4 Hz, H2), 4.08 (dd, J_{21}=1.5 Hz, J_{23}=5.4 Hz, H2), 2.46 (m of 10 lines, J_{32}=5.5 Hz, J_{34}=7.3 Hz, $J_{3\text{-}Me}$=7.3 Hz, H3), 2.28 (m of 6 lines, J=7.0 Hz, H3), 1.22 (d, $J_{Me\text{–}H}$=6.6 Hz, terminal –Me), 1.17 (d, $J_{Me\text{–}H}$=6.6 Hz, terminal –Me), 1.02 (d, $J_{Me\text{–}H}$=7.3 Hz, C2-Me), 0.98 (d, $J_{Me\text{–}H}$=7.3 Hz, C2–Me). ^{13}C (75 MHz): 101.6, 96.5, 79.1, 77.1, 76.5, 73.5, 39.0, 38.2, 17.9, 17.6, 8.2, 7.5. HRMS (EI) calcd for $C_6H_{12}O_3-CH_3$: 117.05517, found: 117.05518.

3.26. 2-Naphthylmethyl (3*R*)-hydroxy-(2*S*)-methylbutanoate 48

To a magnetically stirred solution of the diol **44** (0.16 g, 1.6 mmol) in EtOH (20 ml) was added $NaIO_4$ (0.38 g, 1.8 mmol) in 4 ml of distd H_2O. The mixture turned opaque immediately. After 2 h, TLC (CH_2Cl_2–MeOH 20:1.3) showed that all substrate has reacted. The solids were filtered on a sintered glass and EtOH was evaporated. To the residue was added CH_3CN (20 ml). Small quantity of the precipitated solids was again removed by filtration. To the resulting clear solution was added $NaClO_2$ (80%, 0.38 g, 3.2 mmol) solubilized in a minimum volume of distd H_2O followed by $NaH_2PO_4\cdot 2H_2O$ (0.076 g, 0.49 mmol) in minimum volume of H_2O and 35% H_2O_2 (0.3 ml) in this order. The resulting yellow homogenous mixture was stirred for 30 min. TLC at this stage showed the main spot of **46** and much less intense spot of the more polar **47**. Revelation was done using a bromocresol green reagent: both **45** and **46** formed yellow spots on a blue background. The mixture was passed through a bed of Celite, evaporated, and solubilized in distd CH_2Cl_2. Addition of freshly prepared 2-naphthyldiazomethane **23** was continued until evolution of nitrogen subsided and a reddish color persisted. The solvent was evaporated. The residue was solubilized in MeOH (15 ml) and seven drops of concd NH_4OH were added. After 40 min, TLC (hexane–EtOAc 3:1) showed an UV absorbing spot of **48** with R_f 0.34 accompanied by several much less polar spots. Spraying with a CrO_3–H_2SO_4 system and heating reveals **48** as a reddish-brown spot. Evaporation of the solvent and flash chromatography in 3:1 hexane–EtOAc furnished **48** as a glassy material, 0.17 g, 54% counting on **44**.

$[\alpha]_D^{24}$ +0.5 (c 6, $CHCl_3$). ^{1}H (500 MHz, after D_2O exchange): 7.84–7.81 (m, 4H, H aromatic), 7.50–7.43 (m, 3H, H aromatic), 5.30 (s, 2H, –OCH_2–), 4.09 (dq, J_{32}=4.0 Hz, $J_{3\text{-}Me}$=6.3 Hz, 1H, H3), 2.62 (br s, residual OH), 2.57 (dq, J_{23}=3.9 Hz, $J_{2\text{-}Me}$=7.2 Hz, 1H, H2), 1.22 (d, $J_{Me\text{-}2}$= 7.3 Hz, 3H, C2–Me), 1.17 (d, $J_{Me\text{-}3}$=6.4 Hz, 3H, terminal Me). ^{13}C (125 MHz): 175.70, 133.10, 133.07, 128.43, 127.93, 127.67, 127.35, 126.32, 126.30, 125.70, 67.95, 66.50, 45.57, 19.80, 10.98. HRMS (electrospray) calcd for $C_{16}H_{18}O_3$+Na^+: 281.11483, found: 281.11477.

3.27. 5-*O*-*tert*-Butyldiphenylsilyl-3-deoxy-1,2-*O*-isopropylidene-3-*C*-methylene-L-*threo*-pentofuranose 50

Compound **50**[21] was obtained from **49**[20,21] following the directions for the D-enantiomer **35** in 56% yield for two steps, rather than using Tebbe's reagent or Peterson's olefination as described before.[21]

$[\alpha]_D$ −3.3 (c 6, $CHCl_3$). For NMR data see **36**.

3.28. 5-*O*-*tert*-Butyldiphenylsilyl-3,4-ene-1,2-*O*-isopropylidene-3-*C*-methyl-D-*glycero*-pentofuranose 51 and 5-*O*-*tert*-butyldiphenylsilyl-3-deoxy-1,2-*O*-isopropylidene-3-*C*-methyl-L-*lyxo*-furanose 52

Olefin **50** (0.41 g, 1.37 mmol) in EtOH (25 ml) and 10% Pd–C (0.05 g) were hydrogenated at the initial pressure of 40 psi in a Parr apparatus for 5 h. TLC showed traces of unreacted substrate and a less polar compound **51** with R_f 0.46 and the product **52** with R_f 0.19 (hexane–EtOAc 15:1). Filtration through Celite, evaporation, and flash chromatography in a gradient of EtOAc in hexane, 1:15→2:15, gave **51** (oil, 0.19 g, 46%) and **52** (oil, 0.15 g, 36%).

*Compound **51***. $[\alpha]_D^{24}$ +2.7 (c 2.3, $CHCl_3$). ^{1}H (300 MHz): 7.71–7.69 (m, 4H, H aromatic), 7.41–7.36 (m, 6H, H aromatic), 5.92 (d, J_{12}=5.3 Hz, 1H, H1), 5.01 (d, J_{12}=5.3 Hz, 1H, H2), 4.19 (s, 2H, H5), 1.61 (s, 3H) and 1.45 (s, 6H): isopropylidene Me and C3–Me, 1.05 (s, 9H, ^{t}Bu). ^{13}C (75 MHz): 151.1, 135.70, 135.67, 133.21, 133.16, 129.8, 127.8, 111.7, 108.0, 103.9, 87.4, 57.5, 28.0, 26.8, 19.3, 9.2. HRMS (electrospray) calcd for $C_{25}H_{32}O_4Si$+Na^+: 447.19622, found: 447.19566.

*Compound **52***. $[\alpha]_D^{24}$ −32.8 (c 3.8, $CHCl_3$). ^{1}H (300 MHz): 7.69–7.66 (m, 4H, H aromatic), 7.43–7.33 (m, 6H, H aromatic), 5.75 (d, J_{12}=3.9 Hz, 1H, H1), 4.49 (t, J_{12}=J_{23}=4.5 Hz, 1H, H2), 4.24 (dt, $J_{45''}$=5.6 Hz, J_{43}=7.5 Hz, $J_{45'}$=7.6 Hz, 1H, H4), 3.97 (dd, $J_{5'4}$=7.6 Hz, $J_{5'5''}$=10.2 Hz, 1H, H5′), 3.77 (dd, $J_{5''4}$=5.3 Hz, $J_{5''5'}$=10.3 Hz, 1H, H5″), 2.42 (ddq, J_{32}=4.8 Hz, J_{34}=7.4 Hz, $J_{3\text{-}Me}$=7.3 Hz, 1H, H3), 1.27 and 1.24 (two s, 3H each, isopropylidene Me), 1.19 (d, $J_{Me\text{-}3}$=7.3 Hz, 3H, C3-Me), 1.05 (s, 9H, ^{t}Bu). ^{13}C (75 MHz): 135.58, 135.54, 133.6, 133.4, 129.54, 129.52, 127.6, 111.6, 105.8, 84.2, 82.5, 64.3, 39.3, 26.8, 26.4, 25.5, 19.1, 8.6. HRMS (electrospray) calcd for $C_{25}H_{34}O_4Si$+Na^+: 449.21187, found: 449.21146.

3.29. 3-Deoxy-1,2-*O*-isopropylidene-3-*C*-methylene-L-*threo*-pentofuranose 53

Compound **53** was obtained from **50** as described for its D-enantiomer **37** in 95% yield.

$[\alpha]_D^{24}$ +28.8 (*c* 5, $CHCl_3$). For NMR data see **37**. HRMS (electrospray) calcd for $C_9H_{14}O_4+Na^+$: 209.07845, found: 209.07787.

3.30. 3-Deoxy-1,2-*O*-isopropylidene-3-*C*-methyl-L-*lyxo*-furanose 54

Compound **53** was subjected to hydrogenation over Adam's catalyst as described for its D-enantiomer **37** to furnish **54** in 83% yield. A different batch of Adam's catalyst was used than in the case of **37** and no migration of the C=C bond to the C3–C4 position was seen.

$[\alpha]_D^{24}$ −44.4 (*c* 2.5, $CHCl_3$). For NMR data see **39**. HRMS (EI) calcd for $C_9H_{16}O_4-Me$: 173.08137, found: 173.08187.

3.31. 3,5-Dideoxy-3-*C*-methyl-*L*-*lyxo*-furanose 55

Compound **55** was obtained as described for its D-enantiomer **44** in 27% cumulative yield.

$[\alpha]_D^{24}$ −38.1 (*c* 3.2, $CHCl_3$, after 30 min). For NMR data see **44**. HRMS (EI) calcd for $C_6H_{12}O_3-Me$: 117.05517, found: 117.05431.

3.32. 2-Naphthylmethyl (3*S*)-hydroxy-(2*R*)-methylbutanoate 56

Compound **56** was prepared from **55** as described for its enantiomer **48** in 63% cumulative yield.

$[\alpha]_D^{24}$ −0.2 (*c* 3, $CHCl_3$). For NMR data see **48**. HRMS (electrospray) calcd for $C_{16}H_{18}O_3+H^+$: 259.13286, found: 259.13281.

3.33. 3-Deoxy-1,2-*O*-ispropylidene-3-*C*-methylene-5-*O*-tosyl-L-*threo*-pentofuranose 57

Compound **53** (0.22 g, 1.2 mmol) in dry CH_2Cl_2 (10 ml), pyridine (1 ml), cat. DMAP, and TsCl (0.5 g, 2.6 mmol) were left for 48 h. TLC showed a new compound with R_f 0.46 in 3:1 hexane–EtOAc. Extraction (CH_2Cl_2–dil HCl), drying, evaporation, and flash chromatography using a gradient of EtOAc in hexane, 1:4→1:3, furnished 0.29 g, 72% of glassy **57**.

^1H (300 MHz): 7.81–7.78 (m, 2H), 7.35 (br s, 1H, H aromatic), 7.33 (br s, 1H, H aromatic), 5.77 (d, J_{12}=3.7 Hz, 1H, H1), 5.50 (dd, J=0.8, 1.9 Hz, 1H, =CH_2), 5.30 (t, J=1.3 Hz, 1H, =CH_2), 4.81 (dt, J=0.9, 0.9 Hz, J_{21}=3.7 Hz, 1H, H2), 4.68 (q of triplets, J=1.8, 1.8 Hz, $J_{45''}$=5.4 Hz, $J_{45'}$=7.3 Hz, 1H, H4), 4.19 (dd, $J_{5'4}$=7.4 Hz, $J_{5'5''}$=10.1 Hz, 1H, H5′), 4.10 (dd, $J_{5''4}$=5.3 Hz, $J_{5''5'}$=10.1 Hz, 1H, H5″), 2.44 (s, 3H, Ph–Me), 1.34 and 1.30 (two s, 3H each, isopropylidene Me). ^{13}C (75 MHz): 144.8, 143.6, 132.7, 129.8, 128.0, 115.4, 113.4, 105.6, 80.9, 79.5, 71.8, 27.0, 16.2, 21.6. HRMS (electrospray) calcd for $C_{16}H_{20}O_6S+Na^+$: 363.08730, found: 363.08764.

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