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Novel formal synthesis of stereospecifically C-6 deuterated D-glucose employing configurationally stable alkoxymethyllithiums

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ABSTRACT

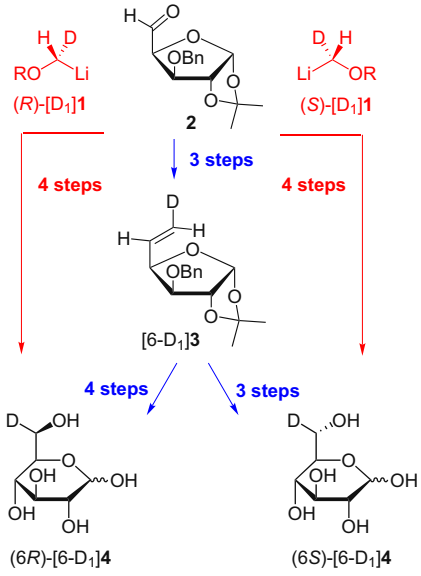
The synthesis and testing of configurational stability of chirally monodeuterated PMB- and THP-substituted oxymethyllithiums are described. Macroscopically they are configurationally stable up to −35 °C, the limit of their chemical stability, and microscopically even up to 0 °C. Furthermore, THP-protected oxy-[D_1]methyllithium has been applied in the formal synthesis of (6*R*)-[6-D_1]-D-glucose (four steps, 40% yield), an example of its use as a homochiral hydroxymethyl synthon.

1. Introduction

Chirally deuterated sugars have been widely used to elucidate mechanisms of biosynthesis and chemical reactions. As such, stereospecifically C-6 deuterated D-galacto- and D-glucopyranosides facilitated studies concerning the preferred conformation of the C-5/C-6 bond of some simple sialosaccharides,[1] and chirally deuterated [6-D_1]-D-glucose fed to *Streptomyces ribosidificus* shed light onto the biosynthesis of the antibiotic ribostamycin.[2] The latter was also applied to investigate the stereochemical course of the Ferrier reaction.[3] Despite the usefulness of such substrates, only very few regio- and stereospecific syntheses have been reported.

The first synthesis of (6*S*)-and (6*R*)-[6-D_1]-D-glucose ([6-D_1]**4**) was achieved by Kakinuma in 1977.[4] He started from aldehyde **2**, converting it to xylohexenofuranose [6-D_1]**3**. (6*R*)-[6-D_1]**4** was then prepared utilising a reaction sequence of epoxidation/chromatographic separation/epoxide opening and (6*S*)-[6-D_1]**4** directly via dihydroxylation (Scheme 1).

Ohrui et al. also synthesised both diastereomers employing stereospecific photo-bromination.[5] The latest synthesis of (6*S*)-[6-D_1]-D-glucose was performed by Xu and Price via stereospecific reduction of both anomers of methyl 2,3,4-tri-*O*-benzyl D-*gluco*-[6-D_1]hexodialdo-1,5-pyranoside with (*R*)-Alpine-Borane® to give protected (6*S*)-[6-D_1]glucoses (almost 100% (*S*)).[6]



Scheme 1. Synthesis of stereospecifically C-6 deuterated D-glucose [6-D_1]4 according to Kakinuma (blue) and our own strategy (red).

We have recently been successful in testing the configurational stability of several chiral methyllithiums.[7] These compounds are chiral by virtue of the hydrogen isotopes protium and deuterium, as well as a heteroatom or heteroatom containing substituent

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necessary for the carbanion to retain its configuration. Among these compounds diisopropylcarbamoyloxy-,[7a] chloro-,[7c] 2,4,6-triisopropylbenzoyloxy-[7e] and amino-substituted methyllithiums[7d] displayed generally high up to complete configurational stability depending on the reaction conditions.

We envisioned these methyllithiums to be versatile chiral methyl synthons. To prove their usefulness we decided to prepare [6-D_1]**4** by employing configurationally stable chiral oxymethyllithiums [D_1]**1**. The key step in our approach was their addition to aldehyde **2**, which could be easily prepared from D-glucose (**4**) according to literature procedures[8] and had already been used by Kakinuma.[4]

Depending on the stereochemistry of the newly formed asymmetric centre, the former carbonyl group of the aldehyde, this would lead to a protected glucofuranose, if the configuration was (5*R*) (non-chelated Felkin–Ahn product). In case of C-5 turning out to be (*S*)-configured (chelation of lithium with the aldehyde), one would get the L-*ido* isomer, respectively. Due to the conformational flexibility of the furanose ring and various chelation possibilities, the stereochemical outcome was difficult to predict. But the work of Bonnaffé et al., who tested the addition of several organometallic reagents to **2**, showed that organolithiums, if not too bulky, favoured the D-*gluco* isomer, substantiating the success of our approach.[9]

2. Results and discussion

2.1. Testing of the configurational stability of THP- and PMB-substituted alkoxymethyllithiums

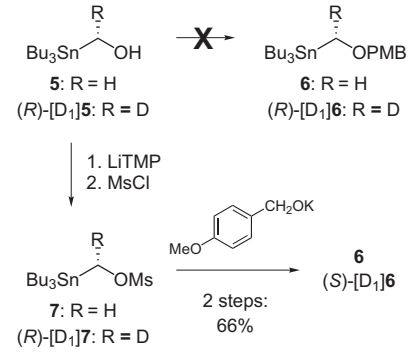
When comparing the carbamoyloxy- and aroyloxy-methyllithiums tested,[7a,e] the choice for their application as deuterium-labelling synthons lay with the latter, as deprotection of the ester moiety by reduction generally proceeded more readily. But still the conditions therefore were harsh (refluxing with excess $LiAlH_4$ in THF), making the use of a differently protected oxymethyllithium desirable.

In their seminal report Still and Sreekumar managed to prove that α-alkoxy-substituted organolithiums could be configurationally stable.[10] In their wake quite a number of alkoxymethyllithiums have been examined towards their configurational stability, and found not to racemise over a period of up to 30 min at −78 °C.[11] We thought them very well suited for our purpose, plus their testing would increase the still limited knowledge about the configurational stability of methyllithiums.

Initially, the *para*-methoxybenzyl group was used as protecting group because it can be introduced and removed easily. It is also one of the most significant protecting groups in organic chemistry, as it can be selectively cleaved under hydrogenolytic, oxidative (with DDQ or CAN), or Lewis acidic conditions.[12] We also reasoned that acetals would probably be more (chemically) stable due to an additional complexation of lithium by the second oxygen atom. In this case the THP protecting group was preferred, due to the existence of several very mild methods for its introduction. Furthermore, Hutchinson and Fuchs had already synthesised unlabelled THP-protected oxymethyllithium **11**, thus proving the feasibility of this approach and outweighing the disadvantage of the additional stereogenic centre.[13] But we had to find a new way for its generation, as tributyl(iodomethyl)stannane was not a viable starting material in our case.

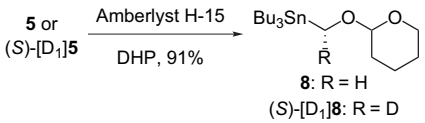
According to previous work in our laboratory, enantiopure tributylstannylmethanol ([D_1]**5**) was used as a common precursor.[7a] Tin–lithium exchange proceeding under retention of configuration would thus deliver the deuterated alkoxymethyllithiums in a stereospecific way, following prior protection of the alcohol.

Transformation of tributylstannylmethanol into the PMB-ether proved tricky. Direct conversion, despite screening different bases in combination with PMBCl and Bundle's reagent (PMB trichloroacetimidate),[14] gave low yields at best. Transformation into the mesylate[7b] and subsequent S_N2 reaction with the potassium salt of *para*-methoxybenzyl alcohol gave the best result with an overall yield of 64% (Scheme 2). When repeated with the labelled compound, inversion of configuration at the deuterated carbon atom was assumed to occur.



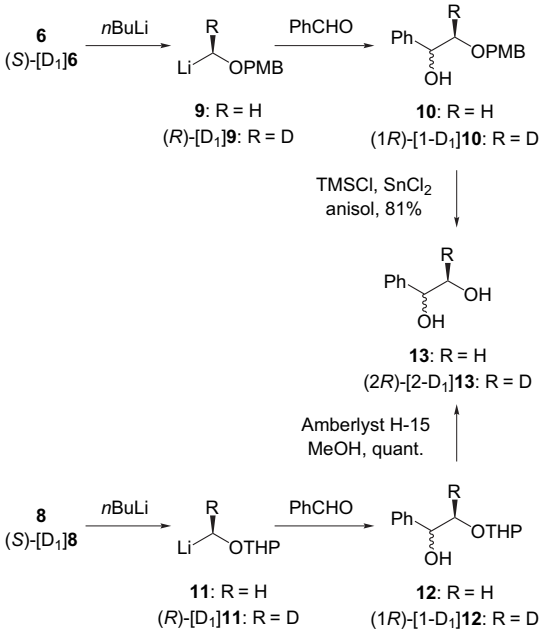
Scheme 2. Towards the preparation of **6** and [D_1]**6**. Ms=methanesulfonyl; TMP=2,2,6,6-tetramethylpiperidinyl.

In comparison, preparation of the PMB-ether proceeded straightforward. Treatment of tributylstannylmethanol with DHP in the presence of the cation exchange resin Amberlyst H-15 delivered **8** and later on labelled [D_1]**8** in 91% yield (Scheme 3).[15]



Scheme 3. Preparation of PMB-ethers **8** and [D_1]**8**.

Before starting with the determination of the configurational stability of the chiral alkoxymethyllithiums, we wanted to test their chemical stability first. Therefore, unlabelled **6** and **8** were transmetalated with *n*BuLi and quenched with benzaldehyde in analogy to the carbamoyloxy and aroyloxy series at various temperatures with THF as solvent (Scheme 4, Table 1).[7a,e]



Scheme 4. Testing of the chemical and configurational stability of alkoxymethyllithiums **9** and **11**.

Table 1
Testing of the chemical stability of alkoxymethyllithiums **9** and **11**

Entry	Substrate	Temp (°C)	Time (min)	Yield (%)
1	**6**	−78	3	84
2	**6**	−50	3	66
3	**6**	−30	3	—
4	**8**	−78	10	70
5[a]	**8**	−78	10	24
6	**8**	−78	60	59
7	**8**	−50	1	51
8	**8**	−30	0.75	21

[a] The reaction was performed in Et_2O/TMEDA.

For both substrates the best yields were obtained at −78 °C and trapping after a few minutes (**6**: entry 1, 84%; **8**: entry 4, 70%). In case of the PMB-ether the time between transmetalation and trapping was extended to 1 h, in which slight decomposition occurred (entry 6). Also, when using Et_2O/TMEDA instead of THF the yield dropped to almost a third (entry 5). At −50 °C decomposition increased significantly for both organolithiums, an indication for their chemical instability (entries 2 and 7). At −30 °C only product derivated from the THP-protected oxymethyllithium could be isolated, but not from the PMB-protected one (entries 3 and 8).

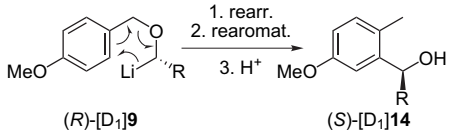
With these results in hand testing of the configurational stability could proceed (Scheme 4, Table 2). For PMB-protected oxymethyllithium [D_1]**9**, this was done macroscopically at −78 and −50 °C and microscopically (with benzaldehyde present upon transmetalation) at 0 °C (entries 1–3). Determination of the configuration at the deuterated centre was done after deprotection and transformation into the known bis-(*R*)-Mosher ester.[7a] In all cases complete retention of configuration was observed. The same qualitative result was found for THP-substituted oxymethyllithium [D_1]**11**, which was completely configurationally stable at −78 and −35 °C (entries 4 and 5).

Table 2
Testing of the configurational stability of alkoxymethyllithiums (*R*)-[D_1]**9** and (*R*)-[D_1]**11**

Entry	Substrate	Temp (°C)	Time (min)	Yield (%)	ee (%)
1	(*S*)-[D_1]**6**	−78	30	87	99
2	(*S*)-[D_1]**6**	−50	10	61[a]	99
3	(*S*)-[D_1]**6**	0	—	46[b]	99
4	(*S*)-[D_1]**8**	−78	60	50	99
5	(*S*)-[D_1]**8**	−35	0.5	62	98

[a] 10% of (*R*)-[D_1]**14**.
[b] 4% of (*R*)-[D_1]**14**.

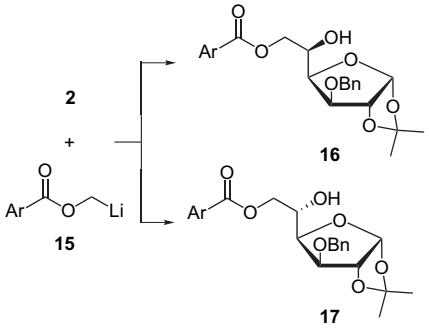
Remarkable was the formation of the side product [D_1]**14** resulting from [D_1]**9**. It was isolated in a few percents when performing the reaction at or above −50 °C (see footnotes of Table 2) and probably resulted from a [2,3]-Wittig rearrangement (Scheme 5). Its (*R*)-Mosher ester showed a broadened singlet in the ^{1}H NMR spectrum at δ=5.29 ppm for the CHD group, indicating that the rearranged product had at least 95% ee. We tentatively assign (*S*)-configuration to the chiral centre, assuming inversion[7d] of configuration, which is the rule for Wittig rearrangements.



Scheme 5. [2,3]-Wittig rearrangement as side reaction of PMB-protected oxymethyllithium **9**.

2.2. Synthesis of *ido*- and *gluco*-type reference compounds

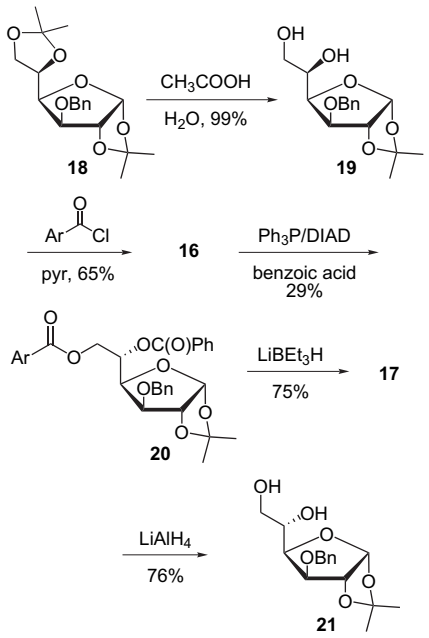
Addition of an alkoxymethyllithium to aldehyde **2** can lead to a substituted *gluco* or *ido*furanose, making a distinction between these two necessary. As we decided to initially perform the reaction with aroyloxymethyllithium **15**, which had been intensively examined in our laboratory,[7e] we expected **16** and/or **17** as products (Scheme 6).



Scheme 6. Possible products of addition of aroyloxymethyllithium **15** to aldehyde **2**. Ar=2,4,6-(*i*-Pr)$_3$C$_6$H$_2$.

To be able to distinguish between these two, the independent synthesis of reference compounds seemed prudent, especially with respect to the determination of the ee at C-6 in the deuterated series later on.

Therefore, one of the isopropylidene groups of **18**, an intermediate in the synthesis of aldehyde **2**, was selectively removed to give diol **19**,[8a] which could then be esterified with 2,4,6-triisopropylbenzoyl chloride at the primary hydroxyl group, yielding 65% of the protected glucofuranose **16** and approximately 10% of the dibenzoylated compound as side product (Scheme 7).



Scheme 7. Synthesis of reference compounds. Ar=2,4,6-(*i*-Pr)$_3$C$_6$H$_2$.

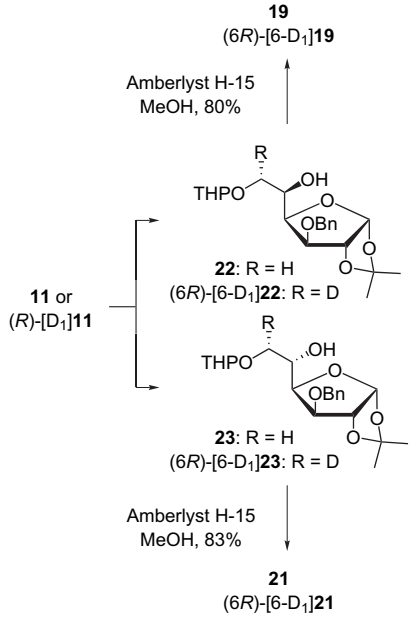
Mitsunobu reaction with benzoic acid gave **20** in low yield (29%). This was probably due to steric hindrance and difficulties at purification, as the starting material had a very similar R_f value to the product. Selective removal of the benzoyl group with Superhydride finally gave protected L-*ido*furanose **17**. A sample of it was

further treated with $LiAlH_4$ to cleave the second, more hindered 2,4,6-triisopropylbenzoyl ester to yield **21**, which would work as a general *ido*-reference for differently substituted oxymethyllithiums after deprotection, the same as **19**, its *gluco*-counterpart.

2.3. Towards the synthesis of stereospecifically C-6 deuterated D-glucose

With these reference compounds in hand, aroyloxmethyllithium **15** was quenched with aldehyde **2** 10 min after its generation from the respective stannane by tin–lithium exchange (Scheme 6).[7e] Under these conditions no racemisation had been detected in previous experiments with benzaldehyde as electrophile. ^1H NMR spectroscopy of the crude product revealed that a mixture of *gluco*- and *ido*-type in a ratio of 4:1 was formed, contaminated with a lot of side products. In the end glucofuranose **16** could be isolated in a yield of only 31%. Additionally, the side product methyl 2,4,6-triisopropylbenzoate was found in a yield of 40%, probably due to protonation of **15** by the enoliseable aldehyde **2**.

Not satisfied with this result, we switched to the THP-protected oxymethyllithium **11**, which seemed superior to its PMB analogue in terms of ease of introduction and lack of side reactions. Transmetalation was effected at −78 °C and aldehyde **2** was added 5 min after the addition of *n*BuLi. Unlabelled **11** again delivered the *gluco*- to *ido*-type (**22**/**23**) in a ratio of 4:1 (Scheme 8). Isolation of the products by flash chromatography was easier than before, when the aroyloxy-substituted methyllithium was used, as there were fewer side products formed. In the end homogenous **22** and **23** could be obtained in yields of 55% and 13%, respectively. The assignment of absolute configurations was secured by removal of the THP groups, which worked in a yield of about 80%, and comparing their spectra to those of the reference compounds.



Scheme 8. Formal synthesis of (6*R*)-[6-D_1]-D-glucose and (6*R*)-[6-D_1]-L-idose.

Finally, repeating the experiment with labelled (*R*)-[D_1]**11**, 43% of (6*R*)-[6-D_1]**22** and 12% of (6*R*)-[6-D_1]**23** could be isolated. Cleavage of the PMB-ether gave (6*R*)-[6-D_1]**19** and (6*R*)-[6-D_1]**21**, completing the formal synthesis of D-glucose and L-idose stereospecifically deuterated at C-6, as removal of the remaining protecting groups (benzyl and isopropylidene) had already been performed by Kakinuma.[4]

Comparison of the ^1H NMR spectra with those of the unlabelled compounds proved complete retention of configuration at C-6 (99% ee) on addition of the chiral oxymethyllithium to the carbonyl group, as only one signal for the CHDO group was visible in the ^1H NMR spectrum, apart from 2% of the unlabelled compound (Fig. 1).

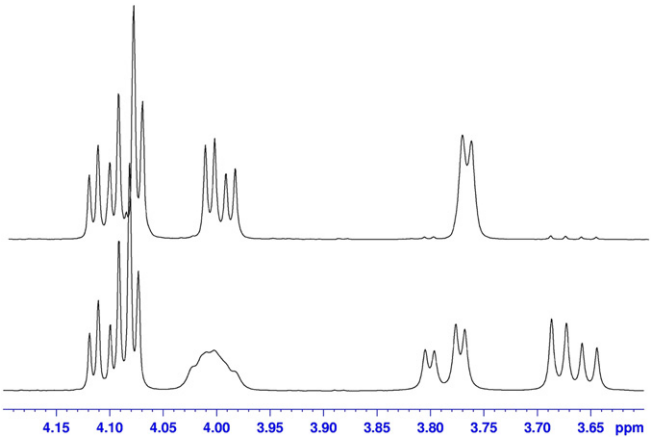


Figure 1. Comparison of the relevant parts in the ^1H NMR spectra (400 MHz, $CDCl_3$) of unlabelled **19** (bottom) and (6*R*)-[6-D_1]**19** (top).

3. Conclusions

In summary, we have proven PMB- and THP-protected oxymethyllithiums to be macroscopically configurationally stable up to −35 °C and microscopically up to 0 °C. They were prepared by tin-lithium exchange, aged and quenched with benzaldehyde. This allowed direct comparison to other methyllithiums tested, which they exceeded both in chemical, as well as configurational stability. Furthermore, the use of THP-protected oxy-[D_1]methyllithium as a versatile chiral hydroxymethyl synthon was shown by its application in the formal synthesis of (6*R*)-[6-D_1]**4** (four steps in a combined yield of 40% starting from the known sugar aldehyde **2**).

4. Experimental

4.1. General information

$^1H/^{13}C$ (*J* modulated) NMR spectra were measured, unless otherwise specified, at 300 K on a Bruker Avance DPX 250, DRX 400 or DRX 600 at 250.13/62.90 MHz, 400.13/100.61 MHz or 600.13/150.92 MHz, respectively. 2D spectra were recorded on the DRX 400. All chemical shifts (δ) are given in ppm. They were referenced either to residual $CHCl_3$ (δ_H=7.24)/toluene (CHD_2: δ_H=2.09)/THF (OCHD: δ_H=3.57) or $CDCl_3$ (δ_C=77.00)/toluene-d_8 (CHD_2: δ_C=21.04)/THF-d_8 (OCD_2: δ_C=67.20). IR spectra were run on a silicon disc on a Perkin–Elmer 1600 FT-IR spectrometer.[16] Optical rotations were measured at 20 °C on a Perkin–Elmer 351 polarimeter in a 1 dm cell. Melting points were determined on a Reichert Thermovar instrument and are uncorrected. Flash chromatography was performed with Merck silica gel 60 (230–400 mesh) and monitored by TLC, carried out on 0.25 mm thick Merck plates, silica gel $60F_{254}$. Spots were visualised by UV and/or dipping the plate into a solution of $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ (23.0 g) and $Ce(SO_4)_2\cdot 4H_2O$ (1.0 g) in 10% aqueous H_2SO_4 (500 mL), followed by heating with a heat gun.

TMEDA and pyridine were refluxed over powdered CaH_2, toluene over sodium/benzophenone, then distilled and stored over molecular sieves (4 Å). CH_2Cl_2 was dried by passing through aluminium oxide 90 active neutral (0.063–0.200 mm, activity I) and stored over molecular sieves (3 Å). Et_2O was refluxed over $LiAlH_4$,

THF over potassium and distilled prior to use. All other chemicals were used as supplied in the highest available purity from Aldrich, Fluka, or Merck.

All glass-ware for moisture sensitive reactions was dried for several hours at 100 °C. Reactions at −78 °C were performed in an acetone/dry ice bath. Small quantities of reagents (μL) were measured with appropriate syringes (Hamilton). The experimental procedures, when identical for the non-deuterated and deuterated compounds, were generally given for the former. The deuterium content of all compounds lay between 97 and 98%.

4.2. Synthesis

*4.2.1. Tributylstannylmethyl para-methoxybenzyl ether (**6**) and (S)-[D$_1$]**6**.* To a solution of KO*t*-Bu (293 mg, 2.60 mmol) in dry THF (15 mL) was added *para*-methoxybenzyl alcohol (468 mg, 3.40 mmol dissolved in 1 mL of THF) at 0 °C under argon; 15 min later tributylstannylmethyl mesylate[7b] (750 mg, 1.70 mmol dissolved in 1 mL of dry THF) was added and stirring was continued for another 1.5 h. Afterwards, the reaction was quenched with 1 M HCl (10 mL) and hexane (10 mL) was added. The organic phase was separated, washed with brine, dried ($MgSO_4$), and then concentrated under reduced pressure. The crude product was purified by flash chromatography (hexane/Et_2O 50:1, R_f 0.36) to yield **6** as a colourless oil (611 mg, 81%). IR (Si): ν_{max} 2955, 2927, 1512, 1457, 1247, 1041 cm^{-1}; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 7.21 (m, 2H$_{arom}$), 6.85 (m, 2H$_{arom}$), 4.33 (s, 2H, OCH_2), 3.79 (s, 3H, OCH_3), 3.70 (s, J($^{117/119}$Sn)=14.7 Hz, 2H, $SnCH_2O$), 1.53–1.44 (m, 6H, $3SnCH_2CH_2$), 1.28 (sext, J=7.3 Hz, 6H, 3 $Sn(CH_2)_2CH_2$), 0.92–0.84 (m, J($^{117/119}$Sn)=51.0, 49.0 Hz, 6H, $3SnCH_2$), 0.87 (t, J=7.3 Hz, 9H, $3Sn(CH_2)_3CH_3$); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 159.0, 131.0, 129.1 (2C), 113.6 (2C), 76.8, 61.1 (J($^{117/119}$Sn)=366.4, 350.3 Hz), 55.2, 29.1 (3C, J($^{117/119}$Sn)=20.6 Hz,), 27.3 (3C, J($^{117/119}$Sn)=52.8 Hz), 13.7 (3C), 9.0 (3C, J($^{117/119}$Sn)=320.5, 306.7 Hz). *Compound (**S**)-[**D$_1$**]**6***: The spectroscopic data were identical to those of **6**, except for ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 3.68 (br s, J($^{117/119}$Sn)=14.1 Hz, 1H, CHD) and ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 60.7 (t, J=21.4 Hz, CHD).

*4.2.2. Tributylstannylmethyl-tetrahydropyranyl ether (**8**) and (S)-[D$_1$]**8**.* A mixture of **5** (333 mg, 1.04 mmol), DHP (174 mg, 2.07 mmol) and Amberlyst H-15 (210 mg) in hexane (6 mL) was stirred for 3.5 h at rt. Then the catalyst was removed via filtration. The reaction mixture was concentrated under reduced pressure and purified by flash chromatography (hexane/CH_2Cl_2 2:1, R_f 0.24) to yield **8** as a colourless oil (382 mg, 91%). IR (Si): ν_{max} 2955, 2925, 2871, 2852, 1465, 1052, 1021 cm^{-1}; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 4.37 (t, J=3.0 Hz, 1H, OCHO), 3.97 (d [AB-sys.], J=10.6 Hz, J($^{117/119}$Sn)=15.2 Hz, 1H, OCH_2Sn), 3.78 (ddd, J=11.5, 8.8, 2.9 Hz, 1H, OCH_2), 3.57 (d [AB-sys.], J=10.6 Hz, J($^{117/119}$Sn)=15.2 Hz, 1H, OCH_2Sn), 3.51–3.44 (m, 1H, OCH_2), 1.81–1.71 (m, 1H, CH_2), 1.69–1.40 (m, 5H, $3CH_2$), 1.54–1.44 (m, 6H, $3SnCH_2CH_2$), 1.29 (sext, J=7.3 Hz, 6H, $3Sn(CH_2)_2CH_2$), 0.92–0.86 (m, 6H, $3SnCH_2$), 0.86 (t, J=7.3 Hz, 9H, $3Sn(CH_2)_3CH_3$); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 101.4 (J($^{117/119}$Sn)=37.5 Hz), 61.6, 57.5 (J($^{117/119}$Sn)=368.7, 351.8 Hz), 30.7, 29.1 (3C, J($^{117/119}$Sn)=20.7 Hz), 27.3 (3C, J($^{117/119}$Sn)=51.3 Hz), 25.6, 19.3, 13.7 (3C), 9.1 (3C, J($^{117/119}$Sn)=322.8, 309.0 Hz). *Compound (**S**)-[**D$_1$**]**8***: The spectroscopic data were identical to those of **8**, except for ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 3.95 (br s, J($^{117/119}$Sn)=14.9 Hz, 1H, OCHD, dia. A), 3.55 (br s, J($^{117/119}$Sn)=14.9 Hz, 1H, OCHD, dia. B) and ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 57.2 (t, J=21.4 Hz, OCHD).

*4.2.3. 2-Hydroxy-2-phenylethyl para-methoxybenzyl ether (**10**) and (1R)-[1-D$_1$]**10**.* Tributylstannylmethyl *para*-methoxybenzyl ether (**6**) (150 mg, 0.34 mmol) dissolved in dry THF (2 mL) was cooled to the respective bath temperature (see Tables 1 and 2) under argon atmosphere. *n*BuLi (0.26 mL, 1.6 M solution in hexane, 0.41 mmol) was added and the reaction quenched with benzaldehyde (0.34 mL, 2 M solution in dry Et_2O, 0.68 mmol) after several minutes. It was stirred for further 30 min at low temperature, before 1 M HCl (4 mL) was added. The organic phase was separated and the aqueous one extracted with Et_2O (3×4 mL). The combined organic layers were dried ($MgSO_4$), concentrated and purified by flash chromatography (hexane/EtOAc 4:1, R_f 0.16) to yield **10**. IR (Si): ν_{max} 3449, 3031, 2858, 1612, 1514, 1249, 1174, 1103, 1034 cm^{-1}; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 7.36–7.21 (m, 7H$_{arom}$), 6.88–6.83 (m, 2H$_{arom}$), 4.87 (br d [X-part of ABX-sys.], J=7.8 Hz, 1H, *CH*OH), 4.50 (AB-sys., J_{AB}=11.4 Hz, 2H, OCH_2Ph), 3.77 (s, 3H, OCH_3), 3.51 (AB-part of ABX-sys., J=9.6, 9.6, 3.0 Hz, 2H, CH_2O), 2.86 (d, J=1.8 Hz, 1H, OH); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 159.3, 140.2, 129.8, 129.4 (2C), 128.3 (2C), 127.8, 126.1 (2C), 113.9 (2C), 75.5, 73.0, 72.8, 55.2. *Compound (1R)-[1-D$_1$]**10***: The spectroscopic data were identical to those of **10**, except for ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 4.91–4.86 (m, 1H, *CH*OH), 3.58 (dt, J=3.0, ~1 Hz, 1H, CHD, dia. A), 3.44 (dt, J=9.6, ~1 Hz, 1H, CHD, dia. B), 2.83 (s, 1H, OH); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 75.1 (t, J=21.1 Hz, CHD, dia. A), 75.1 (t, J=21.1 Hz, CHD, dia. B), 72.74 and 72.71 (CHOH, dias. A and B).

*4.2.4. Deprotection of PMB-protected diol (1R)-[1-D$_1$]**10** to (2R)-[2-D$_1$]**13**[12].* PMB-ether **10** (56 mg, 0.22 mmol), TMSCl (72 mg, 0.66 mmol), anisol (36 mg, 0.33 mmol) and $SnCl_2$ (4 mg, 0.22 mmol) were dissolved in dry CH_2Cl_2 (1 mL) and stirred for 1.5 h at rt. Afterwards, a saturated aqueous solution of $NaHCO_3$ (2 mL) was added, the organic phase separated and the aqueous one extracted with EtOAc (4×2 mL). The combined organic layers were dried ($MgSO_4$), concentrated under reduced pressure and the residue was purified by flash chromatography (hexane/EtOAc 1:2) to yield diol **13** (25 mg, 81%) as colourless crystals.

*4.2.5. Transmetalation **8** and (S)-[D$_1$]**8**, quenching of the respective oxymethyllithiums **11** and (R)-[D$_1$]**11** with benzaldehyde, and deprotection of **12** and (1R)-[1-D$_1$]**12**.* A solution of **8** (122 mg, 0.3 mmol) in dry solvent (2 mL) was cooled to the respective temperature (see Tables 1 and 2) under argon. It was then transmetalated with *n*BuLi (144 μL, 2.5 M solution in hexane, 0.36 mmol) and quenched after various periods of time with benzaldehyde (0.30 mL, 2 M solution in dry THF, 0.6 mmol). After stirring at bath temperature for 30 min, a saturated solution of $NaHCO_3$ (2 mL) was added, the organic phase separated and the aqueous one extracted with Et_2O. The combined organic layers were dried ($MgSO_4$), concentrated under reduced pressure and immediately deprotected. Therefore, Amberlyst H-15 (100 mg) and MeOH (2 mL) were added and the mixture stirred for 3 h at rt. Afterwards, the catalyst was filtered off, the filtrate concentrated and the residue purified by flash chromatography (hexane/EtOAc 1:2) to yield diol **13**.

In one instance the intermediate product **12** was purified by flash chromatography (hexane/EtOAc 3:1, R_f 0.30) for analytical purposes and to determine the yield of deprotection (quantitative). NMR data revealed the existence of two diastereomers in a ratio of 2:1 (A/B). **12**: IR (Si): ν_{max} 3441, 3030, 2942, 2869, 1137, 1123, 1031 cm^{-1}; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 7.40–7.23 (m, 5H$_{arom}$), 4.91–4.85 (m [X-part of ABX-sys.], 1H, OCHPh), 4.605 (t, J=4.8 Hz, 1H, OCHO, dia. A), 4.598 (t, J=4.8 Hz, 1H, OCHO, dia. B), 3.95–3.80 (m, 2H, OCH_2, OH dia. B), 3.89 (dd [AB-part of ABX-sys.], J=10.4, 3.0 Hz, 1H, OCH_2, dia. A), 3.81 (dd [AB-part of ABX-sys.], J=11.4, 3.0 Hz, 1H, OCH_2, dia. B), 3.64 (dd [AB-part of ABX-sys.], J=11.4, 9.1 Hz, 1H, OCH_2, dia. B), 3.55–3.47 (m, 1H, OCH_2), 3.51 (dd [AB-part of ABX-sys.], J=10.4, 8.6 Hz, 1H, OCH_2, dia. A), 3.05 (d, J=2.5 Hz, 1H, OH, dia. A), 1.89–1.72 (m, 2H, CH_2), 1.66–1.49 (m, 4H, $2CH_2$); *Diastereomer A*: ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 140.4, 128.3 (2C), 127.7, 126.2 (2C), 100.0, 73.8, 73.0, 63.0, 30.60, 25.3, 19.8; *Diastereomer B*: ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 140.3, 128.3 (2C), 127.6, 126.2 (2C), 100.3, 75.7, 73.8, 63.5, 30.8, 25.1, 20.1.

*4.2.6. 2-Methyl-5-methoxyphenyl-[D_1]methanol {(S)-[1-D_1]**14**}.* Compound (*S*)-[1-D_1]**14** was isolated in less than 10% yield when performing the transmetalation of (*S*)-[D_1]**8** and quenching of (*R*)-[D_1]**11** at temperatures of −50 °C or above. It could only be partly separated from (1*R*)-[1-D_1]**10**, as the two had virtually the same R_f value. ^{1}H NMR (250.13 MHz, $CDCl_3$): δ 7.06 (d, *J*=8.3 Hz, $1H_{arom}$), 6.94 (d, *J*=2.8 Hz, $1H_{arom}$), 6.73 (dd, *J*=8.3, 2.8 Hz, $1H_{arom}$), 4.64 (br s, 1H, CHD), 3.78 (s, 3H, OCH_3), 2.25 (s, 3H, $PhCH_3$); OH not determined.

*4.2.7. (R)-Mosher ester of (1R)-[1-D_1]**10** and (S)-[D_1]**14**.* A 1:1 mixture of (1*R*)-[1-D_1]**10** and (*S*)-[D_1]**14** (0.05+0.05 mmol), dry pyridine (0.25 mL) and (*S*)-MTPACl (300 μL, 0.5 M solution in dry CH_2Cl_2, 0.15 mmol) in dry CH_2Cl_2 (2 mL) were stirred over night at rt. Afterwards, CH_2Cl_2 (10 mL) and 1 M HCl (10 mL) were added, the organic layer was separated, washed with a saturated solution of $NaHCO_3$ and dried ($MgSO_4$). The solvent was removed under reduced pressure. The residue was purified by flash chromatography (hexane/EtOAc 10:1), giving the (*R*)-Mosher esters of (1*R*)-[1-D_1]**10** (R_f 0.15) in 74% and of (*S*)-[D_1]**14** (R_f 0.23) in 83% yield as oils. *Compound (1R)-[1-D_1]**10** MTPA-(R)*: ^{1}H NMR (250.13 MHz, $CDCl_3$): δ 7.47 (d, *J*=7.8 Hz, $2H_{arom}$), 7.33–7.03 (m, $10H_{arom}$), 6.83–6.78 (m, $2H_{arom}$), 6.25 (d, *J*=3.3 Hz, 1H, OCHPh) and 6.19 (d, *J*=9.3 Hz, 1H, OCHPh), 4.49 and 4.40 (br s, 2H, OCH_2Ph), 3.79 and 3.78 (s, 3H, $PhOCH_3$), 3.76 (br d, *J*=9.3 Hz, 1H CHD) and 3.60 (br d, *J*=3.3 Hz, 1H, CHD), 3.55 (q, *J*=1.0 Hz, 3H, OCH_3) and 3.44 (q, *J*=1.0 Hz, OCH_3). Two diastereomers, determination of ee impossible! *Compound (S)-[1-D_1]**14** MTPA-(R)*: ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 7.43 (br d, *J*=6.8 Hz, $2H_{arom}$), 7.40–7.30 (m, $3H_{arom}$), 7.05 (d, *J*=8.3 Hz, $1H_{arom}$), 6.85 (d, *J*=2.5 Hz, $1H_{arom}$), 6.77 (dd, *J*=2.5, 8.3 Hz, $1H_{arom}$), 5.29 (br s, 1H, CHD), 3.72 (s, 3H, $PhOCH_3$), 3.51 (br s, 3H, OCH_3), 2.18 (s, 3H, $ArCH_3$); ee at least 95%.

*4.2.8. 3-O-Benzyl-1,2-O-isopropylidene-α-D-glucofuranose (**19**).* A solution of 3-*O*-benzyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose[8] (700 mg, 2.0 mmol) in 85% acetic acid was stirred for one day at ambient temperature, before the solvent was removed on a rotary evaporator. The crude product was purified by flash chromatography (hexane/EtOAc 1:2, R_f 0.30) to give diol 19 (629 mg, 99%) as a colourless syrup. IR (Si): ν_{max} 3450, 3032, 2986, 1375, 1216, 1077, 1020 cm^{-1}; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 7.37–7.27 (m, $5H_{arom}$), 5.91 (d, *J*=3.8 Hz, 1H, H-1), 4.71 (d [AB-sys.], 11.6 Hz, 1H, OCH_2Ph), 4.60 (d, *J*=3.8 Hz, 1H, H-2), 4.53 (d [AB-sys.], 11.6 Hz, 1H, OCH_2Ph), 4.10 (dd, *J*=7.8, 3.3 Hz, 1H, H-4), 4.08 (d, *J*=3.3 Hz, 1H, H-3), 4.00 (ddd, *J*=7.8, 5.6, 3.5 Hz, 1H, H-5), 3.79 (dd, *J*=11.6, 3.5 Hz, 1H, H-6a), 3.66 (dd, *J*=11.6, 5.6 Hz, 1H, H-6b), 2.59 (br s, 1H, OH), 2.28 (br s, 1H, OH), 1.46 (s, 3H, CH_3), 1.30 (s, 3H, CH_3); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 137.2, 128.7 (2C), 128.2, 127.8 (2C), 111.8, 105.1, 82.1, 82.0, 79.8, 72.1, 69.3, 64.4, 26.7, 26.2.

*4.2.9. 3-O-Benzyl-1,2-O-isopropylidene-6-O-(2,4,6-triisopropylbenzoyl)-α-D-glucofuranose (**16**).* A solution of diol **19** (250 mg, 0.8 mmol) and 2,4,6-triisopropylbenzoyl chloride (235 mg, 0.88 mmol) in dry pyridine (2.5 mL) was stirred for 8 h at 90 °C. Pyridine was then removed under reduced pressure, the residue dissolved in 1 M HCl (4 mL) and extracted with EtOAc (3×5 mL). The combined organic layers were dried ($MgSO_4$), concentrated under reduced pressure and purified by flash chromatography (hexane/EtOAc 7:1, R_f 0.26) to give 2,4,6-triisopropylbenzoate **16** (280 mg, 65%) as a colourless foam. Furthermore, the bis(2,4,6-triisopropylbenzoylated) compound was isolated in 10% yield (65 mg). This procedure was not optimised. *Compound **16***: $[\alpha]_D^{20}$ −18.3 (*c* 1.38, acetone); IR (Si): ν_{max} 3505, 2962, 2932, 1727, 1252, 1218, 1139, 1077 cm^{-1}; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 7.36–7.25 (m, $5H_{arom}$), 6.99 (s, $2H_{arom}$), 5.93 (d, *J*=3.8 Hz, 1H, H-1), 4.52 (d, [AB-sys.], *J*=11.6 Hz, 2H, OCH_2Ph), 4.60 (d, *J*=3.5 Hz, 1H, H-2), 4.55 (dd, *J*=11.6, 3.2 Hz, 1H, H-6a), 4.52 (d, [AB-sys.], *J*=11.6 Hz, 2H, OCH_2Ph), 4.37 (dd, *J*=11.6, 6.8 Hz, 1H, H-6b), 4.30–4.22 (m, 1H, H-5), 4.13 (dd, *J*=7.8, 3.3 Hz, 1H, H-4), 4.09 (d, *J*=3.3 Hz, 1H, H-3), 2.87 (sept, *J*=6.8 Hz, 1H, $CH(CH_3)_2$), 2.84 (sept, *J*=6.8 Hz, 2H, $2CH(CH_3)_2$), 2.46 (d, *J*=5.3 Hz, 1H, OH), 1.44 (s, 3H, CH_3), 1.30 (s, 3H, CH_3), 1.224 (d, *J*=6.8 Hz, 6H, $CH(CH_3)_2$), 1.219 (d, *J*=6.8 Hz, 6H, $CH(CH_3)_2$), 1.208 (d, *J*=6.8 Hz, 6H, $CH(CH_3)_2$); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 171.0, 150.3, 144.7 (2C), 137.1, 130.2, 128.7 (2C), 128.2, 127.9 (2C), 120.9 (2C), 111.9, 105.3, 82.1, 82.0, 79.7, 72.3, 67.8, 67.1, 34.4, 31.5 (2C), 26.8, 26.2, 24.2 (4C), 23.9 (2C). Assignment was assisted by 2D spectra. Anal. Calcd for $C_{32}H_{44}O_7$: C, 71.08; H, 8.20. Found: C, 71.09; H, 8.07.

*4.2.10. 5-O-Benzoyl-3-O-benzyl-1,2-O-isopropylidene-6-O-(2,4,6-triisopropylbenzoyl)-α-L-idofuranose (**20**).* A solution of **16** (243 mg, 0.45 mmol), Ph_3P (152 mg, 0.58 mmol), benzoic acid (71 mg, 0.58 mmol) and DIAD (117 mg, 0.58 mmol) in dry toluene (4 mL) was stirred over night under argon at 100 °C. A drop of water was added and the solvent removed under reduced pressure. The crude mixture, which still contained some starting material, was then flash chromatographed (hexane/EtOAc 7:1, R_f 0.37) to yield **20** (84 mg, 29%) as homogenous glassy product. This procedure was not optimised. Furthermore some product was lost during chromatography, as it had almost the same R_f value as the starting material. IR (Si): ν_{max} 2963, 2931, 1728, 1269, 1248, 1106, 1073, 1026 cm^{-1}; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 8.02–7.97 (m, $2H_{arom}$), 7.53–7.48 (m, $1H_{arom}$), 7.40–7.30 (m, $7H_{arom}$), 6.95 (s, $2H_{arom}$), 5.96 (d, *J*=3.8 Hz, 1H, H-1), 5.73 (ddd [X-part of ABX-sys.], *J*=8.3, 4.3, 2.8 Hz, 1H, H-5), 4.66 (dd [AB-part of ABX-sys.], *J*=12.5, 2.8 Hz, 1H, H-6a), 4.65 (d, *J*=3.8 Hz, 1H, H-2), 4.73 (d [AB-sys.], *J*=11.6 Hz, 1H, OCH_2Ph), 4.54 (dd, *J*=8.3, 3.5 Hz, 1H, 4-H), 4.50 (d [AB-sys.], *J*=11.6 Hz, 1H, OCH_2Ph), 4.39 (dd [AB-part of ABX-sys.], *J*=12.5, 4.3 Hz, 1H, H-6b), 4.01 (d, *J*=3.5 Hz, 1H, H-3), 2.85 (sept, *J*=6.8 Hz, 1H, $CH(CH_3)_2$), 2.70 (sept, *J*=6.8 Hz, 2H, $2CH(CH_3)_2$), 1.43 (s, 3H, CH_3), 1.29 (s, 3H, CH_3), 1.21 (d, *J*=6.8 Hz, 6H, $CH(CH_3)_2$), 1.14 (d, *J*=6.8 Hz, 6H, $CH(CH_3)_2$), 1.11 (d, *J*=6.8 Hz, 6H, $CH(CH_3)_2$); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 170.5, 165.7, 150.2, 144.8 (2C), 136.5, 133.0, 130.0 (2C), 129.9 (2C), 128.7 (2C), 128.3, 128.2 (2C), 128.2 (2C), 120.8 (2C), 111.8, 105.1, 81.8, 81.3, 78.5, 71.7, 71.1, 63.2, 34.4, 31.5 (2C), 26.8, 26.2, 24.14 (2C), 24.07 (2C), 23.9 (2C).

*4.2.11. 3-O-Benzyl-1,2-O-isopropylidene-6-O-(2,4,6-triisopropylbenzoyl)-α-L-idofuranose (**17**).* To a solution of **20** (80 mg, 0.124 mmol) in dry THF (2 mL) was added Superhydride (0.5 mL, 1 M solution in THF, 0.5 mmol) at −40 °C under argon. After stirring for 1 h and allowing the temperature in the cooling bath to rise continuously to −20 °C, the reaction was quenched with acetone (0.5 mL) and water (3 mL). The organic phase was separated, and the aqueous one extracted with Et_2O (3×4 mL). The combined organic layers were washed with water, dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by flash chromatography (hexane/EtOAc 5:1; TLC: hexane/EtOAc 2:1, R_f 0.44) to yield protected L-*ido*furanose **17** (50 mg, 75%) as colourless crystals, which were recrystallised from hexane. Mp 111 °C (hexane); $[\alpha]_D^{20}$ −37.5 (*c* 0.97, acetone); IR (Si): ν_{max} 3510, 2963, 2932, 2871, 1727, 1457, 1383, 1252, 1076 cm^{-1}; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 7.37–7.27 (m, $5H_{arom}$), 6.98 (s, $2H_{arom}$), 5.99 (d, *J*=3.8 Hz, 1H, H-1), 4.72 (d [AB-sys.], *J*=11.9 Hz, 1H, OCH_2Ph), 4.64 (d, *J*=3.8 Hz, 1H, H-2), 4.49 (d [AB-sys.], *J*=11.9 Hz, 1H, OCH_2Ph), 4.38 (dd, *J*=11.2, 3.9 Hz, 1H, H-6a), 4.31 (dd, *J*=11.2, 5.7 Hz, 1H, H-6b), 4.27–4.21 (m, 1H, 5-H), 4.24 (d, *J*=3.2 Hz, 1H, H-4), 4.00 (d, *J*=3.2 Hz, 1H, H-3), 2.93 (d, *J*=1.8 Hz, 1H, OH), 2.87 (sept, *J*=6.8 Hz, 2H, $2CH(CH_3)_2$), 2.86 (sept, *J*=6.8 Hz, 1H, $CH(CH_3)_2$), 1.43 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.22 (d, *J*=6.8 Hz, 6H, $CH(CH_3)_2$), 1.21 (d, *J*=6.8 Hz, 6H, $CH(CH_3)_2$), 1.20 (d, *J*=6.8 Hz, 6H, $CH(CH_3)_2$); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 170.7, 150.2, 144.9 (2C), 136.5, 130.2, 128.7 (2C), 128.4, 128.0 (2C), 120.8 (2C), 112.0, 105.0, 82.8, 82.3, 79.6,

72.0, 68.7, 65.5, 34.4, 31.5 (2C), 26.8, 26.3, 24.2 (2C), 24.1 (2C), 23.93 (2C). Anal. Calcd for $C_{32}H_{44}O_7$: C, 71.08; H, 8.20. Found: C, 71.05; H, 8.16.

*4.2.12. 3-O-Benzyl-1,2-O-isopropylidene-α-L-idofuranose (**21**).* A solution of **17** (37 mg, 0.068 mmol) and $LiAlH_4$ (10 mg, 0.27 mmol) in dry THF (1.5 mL) was stirred for 2 h at 70 °C. The reaction was quenched with acetone (1 mL) followed by water (2 mL). Tartaric acid was added to dissolve the resulting precipitate, the organic phase was separated and the aqueous one extracted with EtOAc (3×3 mL). The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by flash chromatography (hexane/EtOAc 1:2, R_f 0.27) to give diol **21** (16 mg, 76%) as a colourless syrup. IR (Si): ν_{max} 3460, 2930, 1374, 1218, 1166, 1072, 1028 cm^{-1}; ^1H NMR (400.13 MHz, $CDCl_3$): δ 7.38–7.26 (m, $5H_{arom}$), 5.97 (d, J=3.8 Hz, 1H, H-1), 4.71 (d [AB-sys.], J=11.9 Hz, 1H, OCH_2Ph), 4.64 (d, J=3.8 Hz, 1H, H-2), 4.46 (d [AB-sys.], J=11.9 Hz, 1H, OCH_2Ph), 4.19 (dd, J=5.1, 3.5 Hz, 1H, H-4), 4.05 (dt, J=5.1, 4.6 Hz, 1H, H-5), 4.00 (d, J=3.5 Hz, 1H, H-3), 3.68–3.54 (m, 2H, H-6), 3.02 (br s, 1H, OH), 2.14 (br s, 1H, OH), 1.46 (s, 3H, CH_3), 1.31 (s, 3H, CH_3); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 136.6, 128.7 (2C), 128.4, 127.9 (2C), 112.0, 104.9, 82.9, 82.2, 79.7, 71.9, 70.4, 63.6, 26.8, 26.3.

Similarly, the *gluco*-type **16** (85 mg, 0.16 mmol) gave **19** in 83% (41 mg) after flash chromatography (hexane/EtOAc 1:2, R_f 0.30).

*4.2.13. 3-O-Benzyl-1,2-O-isopropylidene-6-O-(2,4,6-triisopropylbenzoyl)-α-D-glucofuranose (**16**).* To a solution of tributylstannylmethyl 2,4,6-triisopropylbenzoate[7e] (250 mg, 0.45 mmol) in dry THF (2 mL) under argon was added *n*BuLi (0.34 mL, 1.6 M solution in hexane, 0.54 mmol) at −78 °C; 5 min later the reaction was quenched with **2** (150 mg, 0.54 mmol, in 0.5 mL of THF) and kept for further 30 min at bath temperature. Afterwards, a saturated solution of $NaHCO_3$ (2 mL) was added, the organic phase separated and the aqueous one extracted with Et_2O (3×3 mL). The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by flash chromatography (hexane/EtOAc 7:1) to yield the product as a colourless syrup (75 mg, 31%). ^1H NMR analysis of the crude product revealed a ratio of 4:1 for **16**/**17**.

*4.2.14. 3-O-Benzyl-1,2-O-isopropylidene-6-O-tetrahydropyranyl-α-D-glucofuranose (**22**) and (6R)-[6-D_1]**22** and 3-O-benzyl-1,2-O-isopropylidene-6-O-tetrahydropyranyl-α-L-idofuranose (**23**) and (6R)-[6-D_1]**23**.* A solution of tributylstannylmethyl tetrahydropyranyl ether (**8**, 122 mg, 0.30 mmol) in dry THF (1.5 mL) was treated with *n*BuLi (0.23 mL, 1.6 M solution in hexane, 0.36 mmol) at −78 °C under argon; 5 min later the reaction was quenched with aldehyde **2** (100 mg, 0.36 mmol) and stirred for further 30 min at bath temperature. Afterwards, a saturated solution of $NaHCO_3$ (2 mL) was added, the organic phase separated and the aqueous one extracted with Et_2O. The combined organic layers were dried ($MgSO_4$), concentrated under reduced pressure and purified by flash chromatography (hexane/EtOAc 3:1; TLC: hexane/EtOAc 1:1, R_f 0.64) to give the protected D-glucose **22** (65 mg, 55%) and the protected L-idose **23** (15 mg, 13%, R_f 0.38) as colourless oils. Starting from (*S*)-[D_1]**8**, 43% of (6*R*)-[6-D_1]**22** and 12% of (6*R*)-[6-D_1]**23** were isolated.

*4.2.14.1. Compound **22**.* Two inseparable diastereomers (11:9); IR (Si): ν_{max} 3451, 3031, 2938, 2869, 1076, 1024 cm^{-1}; ^1H NMR (400.13 MHz, $CDCl_3$): δ 7.35–7.24 (m, $5H_{arom}$), 5.89 (d, J=3.5 Hz, 1H, H-1), 4.66 (AB-sys., J_{AB}=11.6 Hz, 2H, OCH_2Ph), 4.59–4.51 (m, 2H, H-2, $CH_{acetate}$), 4.18–4.02 (m, 3H, H-3, H-4, H-5), 3.95–3.81 (m, 1H, OCH_2-THP), 3.89 (dd [AB-part of ABX-sys.], J=11.1, 3.0 Hz, 1H, H-6a, major dia.), 3.83 (dd [AB-part of ABX-sys.], J=11.1, 2.3 Hz, 1H, H-6a, minor dia.), 3.75 (dd [AB-part of ABX-sys.], J=11.1, 5.1 Hz, 1H, H-6b), 3.54–3.45 (m, 1H, OCH_2-THP), 3.25 (br d, J=3.0 Hz, 1H, OH, minor dia.), 3.20 (br d, J=3.0 Hz, 1H, OH, major dia.), 1.84–1.69 (m, 2H, CH_2-THP), 1.63–1.43 (m, 4H, $2CH_2$-THP), 1.46 (s, 3H, CH_3, major dia.), 1.45 (s, 3H, CH_3, minor dia.), 1.29 (s, 3H, CH_3, major dia.), 1.28 (s, 3H, CH_3, minor dia.); ^{13}C NMR (100.61 MHz, $CDCl_3$): *Major Dia.*: δ 137.6, 128.4 (2C), 127.8, 127.7 (2C), 111.7, 105.1, 100.5, 82.4, 81.9, 79.8, 72.4, 70.8, 67.7, 63.4, 30.7, 26.8, 26.3, 25.2 (1C, CH_2-THP), 20.14 (1C, CH_2-THP); *Minor Dia.*: ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 137.6, 128.4 (2C), 127.8, 127.7 (2C), 111.6, 105.1, 99.6, 82.4, 81.9, 79.9, 72.4, 70.9, 67.9, 62.7, 30.6, 26.7, 26.3, 25.2, 19.7.

*4.2.14.2. (6R)-[6-D_1]**22**.* Two inseparable diastereomers (1:1); the spectroscopic data were identical to those of **22**, except for ^1H NMR (400.13 MHz, $CDCl_3$): δ 3.87 (d, J=2.8 Hz, 1H, CHD) and 3.81 (br s, 1H, CHD), 3.22 (br s, 1H, OH) and ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 70.6 (t, J=22.2 Hz, 1C, CHD) and 70.5 (t, J=21.8 Hz, 1C, CHD).

*4.2.14.3. Compound **23**.* Two inseparable diastereomers (4:3); IR (Si): ν_{max} 3497, 2936, 2873, 1124, 1075, 1031 cm^{-1}; ^1H NMR (400.13 MHz, $CDCl_3$): δ 7.36–7.26 (m, $5H_{arom}$), 5.976 and 5.971 (d, J=3.8 Hz, 1H, H-1), 4.698 and 4.693 (d [AB-sys.], J=11.6 Hz, 1H, OCH_2Ph), 4.63 (d, J=3.8 Hz, 1H, H-2), 4.57–4.52 (m, 1H, $CH_{acetate}$), 4.48 (d [AB-sys.], J=11.6 Hz, 1H, OCH_2Ph), 4.26 (dd, J=5.3, 3.5 Hz, 1H, H-4, minor dia.) and 4.22 (dd, J=5.3, 3.5 Hz, 1H, H-4, major dia.), 4.18–4.11 (m, 1H, H-5), 4.00 (br s, 1H, H-3), 3.88–3.70 (m, 2H, OCH_2-THP, H-6a), 3.56–3.40 (m, 2H, H-6b, OCH_2-THP), 3.21 (br d, J=3.0 Hz, 1H, OH, major dia.), 3.08 (br d, J=3.0 Hz, 1H, OH, minor dia.), 1.83–1.38 (m, 6H, $3CH_2$-THP), 1.46 (s, 3H, CH_3), 1.31 (s, 3H, CH_3); ^{13}C NMR (100.61 MHz, $CDCl_3$): *Major Dia.*: δ 136.8, 128.6 (2C), 128.2, 127.8 (2C), 111.8, 104.9, 99.3, 83.2, 82.2, 79.8, 71.8, 69.4, 68.9, 62.3, 30.5, 26.8, 26.4, 25.3, 19.5; *Minor Dia.*: 136.9, 128.6 (2C), 128.2, 127.8 (2C), 111.8, 104.9, 99.4, 83.0, 82.3, 79.6, 71.9, 69.3, 68.5, 62.5, 30.5, 26.8, 26.4, 25.3, 19.6.

*4.2.14.4. (6R)-[6-D_1]**23**.* Two inseparable diastereomers (3:2). The spectroscopic data were identical to those of **23**, except for ^1H NMR (400.13 MHz, $CDCl_3$): δ 4.13 (t, J=5.3 Hz 1H, H-5), 3.71 (d, J=5.3 Hz, 1H, CHD) and 3.48 (d, J=5.8 Hz, 1H, CHD) and ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 68.5 (t, J=22.2 Hz, 1C, CHD), 68.2 (t, J=21.4 Hz, 1C, CHD).

*4.2.15. 3-O-Benzyl-1,2-O-isopropylidene-α-D-glucofuranose (**19**) and (6R)-[6-D_1]**19**—cleavage of the PMB ether.* A solution of D-glucose derivative **22** (65 mg, 0.16 mmol) in MeOH (1 mL) and Amberlyst H-15 (50 mg) was stirred for 3 h at rt. The catalyst was filtered off, the mixture concentrated under reduced pressure and purified by flash chromatography (hexane/EtOAc 1:1, R_f 0.15) to give 80% (40 mg) of diol **19**. *Compound (**6R**)-[**6-D_1**]**19***: The spectroscopic data were identical to those of **19**, except for ^1H NMR (400.13 MHz, $CDCl_3$): δ 4.00 (dd, J=7.6, 3.5 Hz, 1H, H-5), 3.77 (d, J=3.5 Hz, 1H, CHD) and ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 64.0 (t, J=21.8 Hz, 1C, CHD).

*4.2.16. 3-O-Benzyl-1,2-O-isopropylidene-α-L-idofuranose (**21**) and (6R)-[6-D_1]**21**—cleavage of the PMB ether.* L-Idose derivative **23** (15 mg, 0.04 mmol) was converted to **21** (10 mg, 83%, hexane/EtOAc 1:2, R_f 0.23) in analogy to **19** above. (**6R**)-[**6-D_1**]**21**: The spectroscopic data were identical to those of **21**, except for ^1H NMR (400.13 MHz, $CDCl_3$): δ 3.57 (d, J=5.8 Hz, 1H, CHD) and ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 63.3 (t, J=22.2 Hz, 1C, CHD).

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