

Intramolecular 1,8-Hydrogen-Atom Transfer Reactions in (1!4)-O-Disaccharide Systems: Conformational and Stereochemical Requirements

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Abstract: The stereochemical and conformational factors controlling the intramolecular hydrogen-atom transfer (HAT) reaction between the two pyranose units in a (1!4)-O-disaccharide when promoted by a primary 6-O-yl radical are studied. Models with α -d-Glcp-(1!4)- β -d-Glcp, α -l-Rhamp-(1!4)- α -d-Galp or α -d-Manp-(1!4)- β -l-

Gulp skeletons led exclusively to the abstraction of the hydrogen from H—C-5⁹ and the formation, through a nine-membered transition state, of a 1,3,5-

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trioxocane ring system in a stable boat-chair conformation. Notwithstanding, derivatives of α -l-Rhamp-(1!4)- α -d-Glcp or α -d-Manp-(1!4)- α -d-Galp exclusively abstract the hydrogen from H—C-1⁹ through a seven-membered transition state and, therefore, lead to an interglycosidic spiro *ortho* ester.

Introduction

Radical reactions in the carbohydrate field have gained considerable importance in the last decades, with a wide range of organic synthetic applications.^[1] Intramolecular hydrogen-atom transfer (HAT) is one of the most interesting processes because it allows the functionalisation with high regioselectivity of remote positions; however, this reaction has been comparatively less investigated in sugars.^[2] Effective 1,*n*-hydrogen-atom transfer has been observed from Csp³-H to alkyl and aryl C radicals with *n* = 4–7,^[3] but 1,5-hydrogen-atom transfer is by far the most common intramolecular HAT reaction when promoted by an alkoxy radical, as a

result of the more favourable entropy of activation of the six-membered transition state.^[4] Although examples of 1,6-hydrogen-atom transfer (through a seven-membered transition state) from reactive carbon atoms to alkoxy radicals have also been described,^[5] only those cases in which the hydrogen atom to be abstracted is bonded to an oxygen-substituted carbon atom could be considered of synthetic interest.^[6]

Only a few cases of intramolecular HAT reactions that proceed via eight- or higher-membered transition states have been reported, limiting their applications to well-suited skeletons such as steroids, in which adverse entropic effects are avoided.^[7] With these considerations in mind, we envisioned that an intramolecular HAT reaction through a higher than seven-membered transition state might be possible if we were able to obtain models with some minimum conditions: a restricted conformational mobility to reduce the entropic barrier, a low-energy transition state and finally, a suitable distance (aprox. 3 Å) between the alkoxy radical and the hydrogen atom to be abstracted.^[8] These requirements can be found in (1!4)-O-disaccharide systems, such as peracetylated *b*-maltose and methyl *b*-maltoside, in accord with previously reported X-ray crystallographic^[9] and molecular mechanics^[10] analysis, respectively. This *b*-maltose unit has a preferred conformation centred around the *exo*-anomeric effect and a *syn* geometry of the glycosidic bond (*F* = –34.2, *Y* = –28.3 ϕ) and a C-6—O \cdots H—C-5⁹ distance of 2.5 Å.^[11] A study of the transition state of the C-6—O \cdots H—C-5⁹ HAT reaction gave a similar situation around the glycosi-

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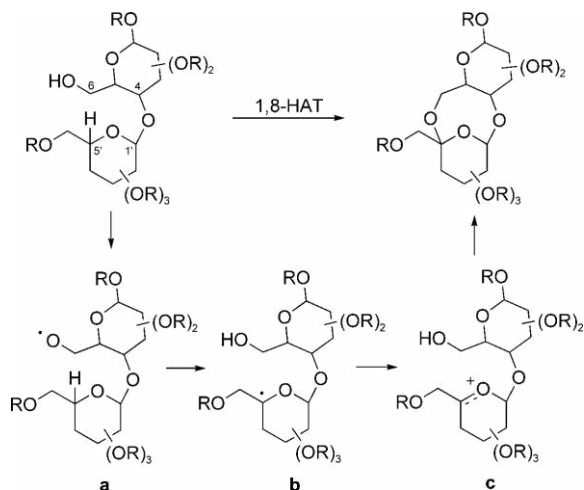
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dic torsion angles ($F = -32.7$, $Y = -37.3^\circ$) and a distance of 3.14 \AA between the alkoxy radical and $\text{H}-\text{C}-5'$.^[12]

Based on these data, we decided to investigate the intramolecular 1,8-hydrogen-atom transfer reaction between the two pyranose units in suitably substituted (1,4)-*O*-disaccharides. As depicted in Scheme 1, under oxidative condi-

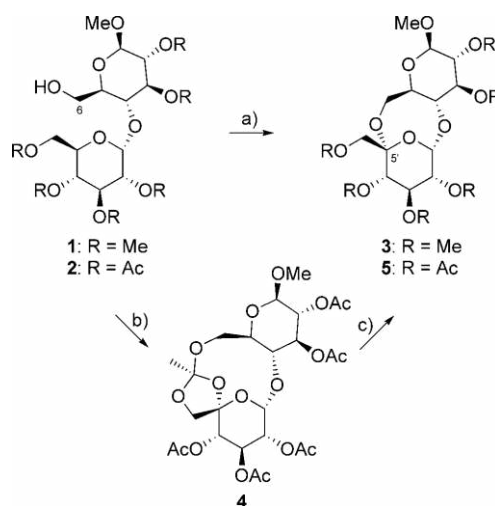


Scheme 1. Mechanism of intramolecular 1,8-hydrogen-atom transfer.

tions, the electrophilic 6-*O*-yl radical (a) generated from the corresponding alcohol would abstract a hydrogen atom at C-5' through a nine-membered transition state to produce a nucleophilic carbon radical (b) that can be subsequently oxidised to an oxonium ion (c). This intermediate could be intramolecularly trapped by the alcohol to give a 1,3,5-trioxocane cyclised derivative. We have described the preliminary results in two short communications^[13] and we now report here the full details of this reaction and its extension to other disaccharide models.

Results and Discussion

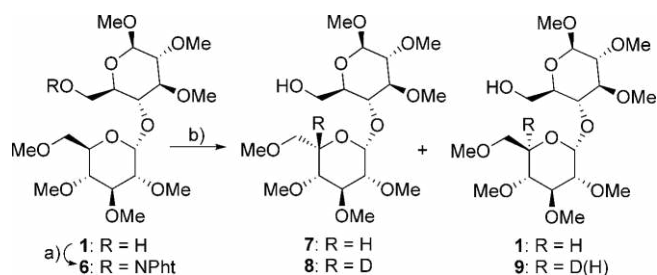
Firstly, to examine the viability of the process, we prepared the known *b*-maltose derivatives **1**^[14] and **2**^[15] (Scheme 2). The C-6 alkoxy radicals were generated by oxidation of the primary alcohol with (diacetoxyiodo)benzene (DIB) in the presence of iodine, under visible light irradiation. The result of the HAT reaction for **1** showed a direct C-5' functionalisation through a nine-membered transition state to give the 1,3,5-trioxocane derivative **3** in 56 % yield, which adopts a restricted, highly stable boat-chair conformation.^[16] When the reaction was performed with the alcohol **2**, a rare 1,3,5,7-tetraoxocane ring system **4** was obtained in good yield. Compound **4** is a reasonably stable crystalline solid the structure of which was deduced by extensive NMR spectroscopic analysis, including bidimensional experiments, and determined unambiguously by X-ray crystallography.^[17] Moreover, this orthoacetate is hydrolysed under very mild



Scheme 2. HAT under oxidative conditions in *b*-maltose. a) DIB (1.7 equiv), iodine (0.7 equiv), CH_2Cl_2 , *h\nu*, RT, 1.5 h, 56 %; b) DIB (1.5 equiv), iodine (0.7 equiv), CH_2Cl_2 , *h\nu*, RT, 1.5 h, 62 %; c) CDCl_3 , RT, 60 h, 100 %. DIB=(diacetoxyiodo)benzene.

acidic conditions with concomitant ring contraction to afford the desired 1,3,5-trioxocane derivative **5** in quantitative yield.

To achieve additional insight into the HAT reaction mechanism, the alkoxy radical was also generated under reductive conditions by reaction of a *N*-hydroxyphthalimide derivative with the $n\text{Bu}_3\text{SnH}/\text{AIBN}$ or $n\text{Bu}_3\text{SnD}/\text{AIBN}$ systems in benzene solutions.^[18] For this purpose, we prepared the 6-*O*-phthalimido derivative **6** by treatment of alcohol **1** with *N*-hydroxyphthalimide under Mitsunobu conditions^[19] (Scheme 3). The reaction of permethylated phthalimide **6**



Scheme 3. HAT under reductive conditions in *b*-maltose. a) DEAD (4 equiv), *N*-hydroxyphthalimide (4 equiv), PPh_3 (4 equiv), THF, 0°C , 30 min, 82 %; b) $n\text{Bu}_3\text{SnH}$ or $n\text{Bu}_3\text{SnD}$ (9 equiv), AIBN (0.16 equiv), PhH, reflux, 1 h, 86–78 %. DEAD= diethyl azodicarboxylate, AIBN= azobisisobutyronitrile, NPh= phthalimide.

with $n\text{Bu}_3\text{SnH}/\text{AIBN}$ afforded a separable mixture of two compounds: a new disaccharide **7** formed by hydrogen abstraction at C-5' and radical quenching with inversion of configuration and the starting maltose derivative **1**, which could arise by abstraction and retention of configuration at C-5', by simple reduction of the 6-*O*-yl radical prior to the abstraction or by a combination of these two mechanisms.

It is important to note that by using this protocol one of the *d*-glucose moieties in the maltose derivative **1** has been transformed into a rare *b*-l-idopyranosyl unit in which the pyranose ring has been changed from a 4C_1 to a 1C_4 conformation leaving the C-2', C-3' and C-4' substituents in axial positions, as can be deduced from the coupling constants of the ring hydrogen atoms in the 1H NMR spectrum.^[20] Since the *α*-l-iduronic-(1!4)-*α*-*d*-Glc_p unit is present as a repetitive fragment in the heparin, this methodology may be of interest for the synthesis of heparinoids.^[21]

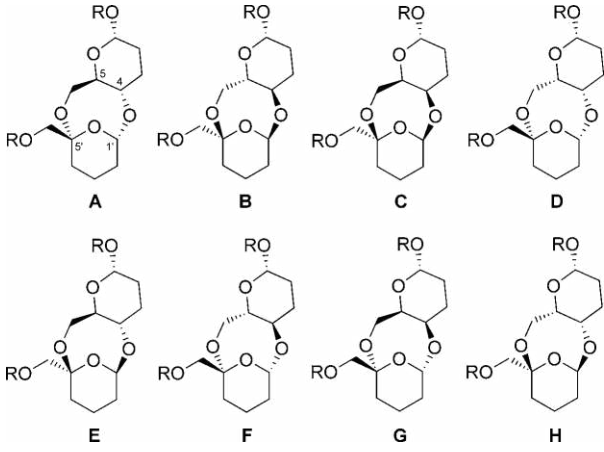
To clarify the HAT mechanism, the reduction of the phthalimide **6** was also accomplished with *n*Bu₃SnD, affording compound **8** with complete deuteration at C-5' and compound **9**, which showed 57 % of deuterium labelling, the reduction of the 6-*O*-yl radical consequently being responsible for the unlabelled molecules. These results have also allowed us to conclude that the abstraction at C-5' takes place with a 60 % yield.

Encouraged by these initial results, which may provide access to a synthetically useful methodology towards remote functionalisation of the C-5' carbon atom or towards the inversion of configuration at this centre, we decided to investigate whether this protocol is exclusive to *b*-maltose or, on the contrary, can be extended to other disaccharides. With this in mind, we studied the configurational and conformational requirements of the intramolecular 1,8-HAT and we, therefore, examined the conformation of the 1,3,5-trioxocane ring for all 16 possible disaccharide diastereoisomers of the four chiral centres involved in the cyclisation step (C-5', C-1', C-4 and C-5). An analysis using molecular mechanics calculations revealed that only four structural arrangements (A–D) could easily accommodate 1,3,5-trioxocane rings in stable boat-chair conformations with similar minimised energies ($DE \leq 1.5$ kcalmol⁻¹) as shown in Table 1. Among them can be identified two pairs of diastereoisomers, A–B and C–D, with very similar energies ($DDE \leq 0.4$ kcalmol⁻¹). In these pairs, the C-5', C-1', C-4 and C-5 atoms are in an enantiomeric relationship.

The next lowest energies correspond to a structural arrangement in which the 1,3,5-trioxocane rings adopt theoretically less-stable boat-boat (E and F) and crown ether (G and H) conformations, which are approximately 3 and 6.5 kcalmol⁻¹, respectively, more energetic than arrangement A. In these cases, the formation of the 1,3,5-trioxocane ring would be energetically disfavoured, such that the HAT reaction could alternatively take place at C-1' through a seven-membered transition state giving a spiro *ortho* ester, an interesting structural motif present in several antibiotics of the orthosomycin^[22] and erythromycin^[23] families, the syntheses of which have attracted the attention of many research groups.^[24] The remainder of the eight isomers not depicted in Table 1 display energy values too high for the 1,8-HAT reaction to take place, and in fact the *syn* relative disposition between substituents at C-5' and C-1' would only allow abstraction at C-1'.

Because the less-energetic structural arrangement A has been investigated previously with the *b*-maltose derivatives,

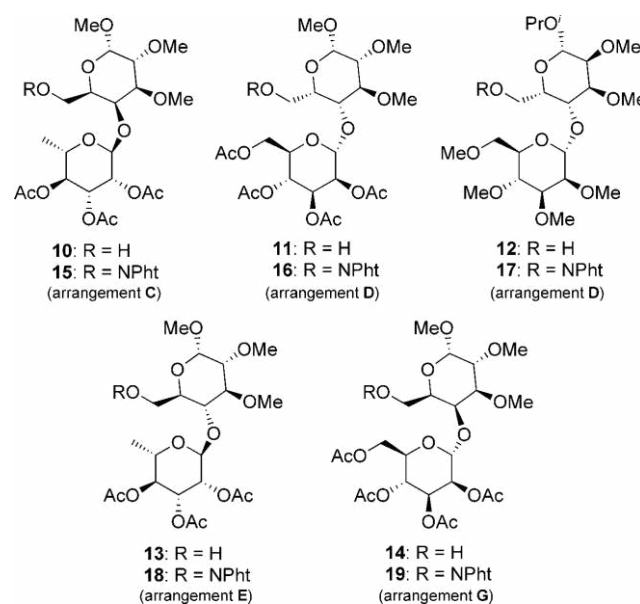
Table 1. Conformations of the 1,3,5-trioxocane ring.^[a]



Arrangement	C-5'	C-1'	C-4	C-5	Conformation	<i>DE</i> [kcalmol ⁻¹]
A ^[b]	<i>S</i>	<i>S</i>	<i>S</i>	<i>R</i>	boat-chair	0
B	<i>R</i>	<i>R</i>	<i>R</i>	<i>S</i>	boat-chair	0.3
C	<i>R</i>	<i>R</i>	<i>R</i>	<i>R</i>	boat-chair	1.1
D	<i>S</i>	<i>S</i>	<i>S</i>	<i>S</i>	boat-chair	1.5
E	<i>R</i>	<i>R</i>	<i>S</i>	<i>R</i>	boat-boat	3.3
F	<i>S</i>	<i>S</i>	<i>R</i>	<i>S</i>	boat-boat	3.9
G	<i>S</i>	<i>S</i>	<i>R</i>	<i>R</i>	crown ether	6.3
H	<i>R</i>	<i>R</i>	<i>S</i>	<i>S</i>	crown ether	10.6

^[a] For simplification, substituents at C-2', C-3', C-2' and C-4' in the carbohydrate skeleton were not considered in the calculation. ^[b] *b*-Maltose arrangement.

we decided to extend the protocol to other disaccharides encompassed in other arrangements to confirm our hypothesis. With this aim, we synthesized a variety of disaccharide models: *α*-l-Rhamp-(1!4)-*α*-*d*-Gal_p **10**, *α*-*d*-Man_p-(1!4)-*b*-l-Idop **11** and *α*-*d*-Man_p-(1!4)-*b*-l-Gulp **12** which, after a HAT reaction, could provide structural arrangements C and D, both slightly more energetic than *b*-maltose. Addi-

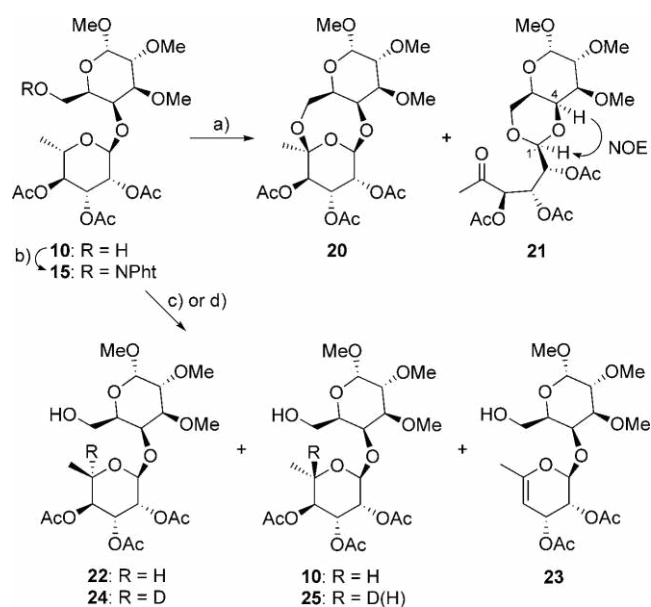


tionally, we have also prepared disaccharides α -l-Rhamp-(1!4)- α -d-Glcp 13 and α -d-Manp-(1!4)- α -d-Galp 14 in which the 1,8-hydrogen-atom transfer would lead to the energetically disfavoured arrangements E and G, respectively.

All the required precursor disaccharides 10–14 were efficiently synthesized by the classical Lewis acid mediated glycosylation of suitably protected d-galactopyranose, l-idopyranose, d-mannopyranose and d-glucopyranose derivatives as glycosyl acceptors with 2,3,4-tri-*O*-acetyl- α -l-rhamnopyranosyl^[25] and 2,3,4,6-tetra-*O*-acetyl- α -d-mannopyranosyl^[26] trichloroacetimidates as glycosyl donors, as described in the Supporting Information.^[27]

Moreover, to study the HAT reaction under reductive conditions and acquire additional insight into its mechanism, the phthalimido derivatives 15–19 were also prepared from the corresponding alcohol and *N*-hydroxyphthalimide under Mitsunobu conditions in accordance with a previously described protocol.^[19]

Firstly, we carried out the HAT reaction with the disaccharide α -l-Rhamp-(1!4)- α -d-Galp 10 under oxidative conditions by treatment with the DIB/iodine system, as shown in Scheme 4. The reaction proceeded in good overall yield, affording the trioxocane 20 as the main product (88 %) together with a small amount of methyl ketone 21 in which the *S* configuration at C-1' was assigned by the NOE interaction observed between H-1' and H-4. Since compound 21 is presumably formed by partial acid-catalysed rearrangement of 20 under the reaction conditions, we can conclude that the reaction occurs with complete regioselectivity by abstraction of the hydrogen atom at C-5' in nearly quantitative yield.



Scheme 4. HAT study of arrangement C. a) DIB (1.7 equiv), iodine (1 equiv), CH₂Cl₂, reflux, 1.5 h, 20 (88%), 21 (10%); b) DEAD (2.5 equiv), *N*-hydroxyphthalimide (2.5 equiv), PPh₃ (2.5 equiv), THF, 0 °C, 1.5 h, 84 %, c) *n*Bu₃SnH (1 equiv), AIBN (0.1 equiv), PhH, reflux, 1.5 h, 22 (52%), 10 (22%), 23 (5%); d) *n*Bu₃SnD (2 equiv), AIBN (0.2 equiv), PhH, reflux, 2 h, 24 (45%), 25 (18%, D/H, 7:3), 23 (15%).

Next, the HAT reaction was carried out under reductive conditions with the phthalimide 15 by treatment with *n*Bu₃SnH/AIBN. In this case, three compounds were obtained: disaccharide 22 formed by hydrogen-atom abstraction at C-5' and radical quenching by the stannane with inversion of configuration, the precursor alcohol 3 that could arise by abstraction at C-5' or by reduction of the 6-*O*-yl radical and finally the olefin 23 formed by reductive elimination of the acetate group at C-4'.

Similar to the reduction of 6, in the inverted alcohol 22, the initial α -l-rhamnopyranosyl moiety has been transformed into a 6-deoxy-*b*-d-gulopyranosyl derivative, the pyranose ring changing from a ¹C₄ to a ⁴C₁ conformation, as deduced from NMR spectroscopic data.

Repetition of the reduction of phthalimide 15 by using *n*Bu₃SnD as reagent on this occasion showed, after careful analysis of the isotopic distribution, total substitution of deuterium at C-5' in compound 24, whereas 70 % of deuterium labelling was found in the alcohol 25, and, therefore, the reduction of the 6-*O*-yl radical is responsible for the unlabelled molecules. Furthermore, the formation of unlabelled olefin 23 sustains the mechanism of free-radical reductive *b*-elimination proposed above. These results have also allowed us to establish that the abstraction at C-5' occurs with an inversion/retention ratio of approximately 3.7:1.^[28]

Next, we investigated the HAT reactions in arrangement D to determine the influence of the l-configuration in the pyranose ring from which the abstraction is made. The initial studies were performed by starting from the disaccharide 11; however, analysis of the coupling constants of the ring hydrogen atoms in this substrate reveals that the l-idopyranose moiety seems to be closer to a ⁴C₁ conformation (Figure 1), so the 1,8 abstraction should be disfavoured versus a 1,6-HAT reaction.

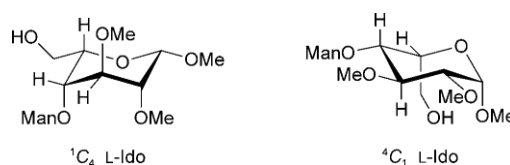
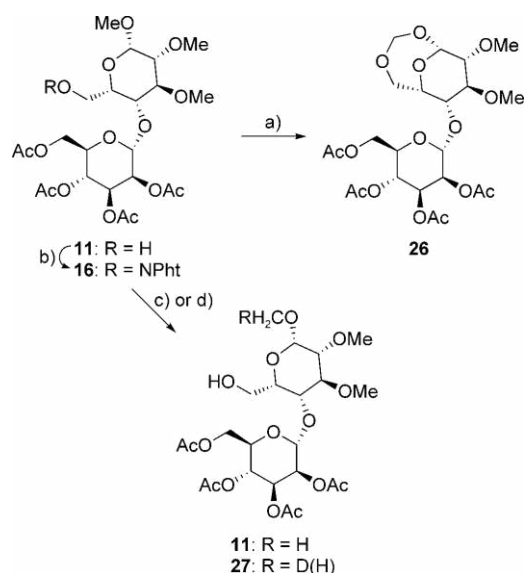


Figure 1. Chair conformations for the l-idose moiety in 11.

Treatment of compound 11 with the DIB/iodine system under visible light irradiation surprisingly afforded as the sole product the methylene derivative 26 in 62 % yield (Scheme 5). This reaction has been described previously for carbohydrates as an efficient and selective methodology to remove methoxy protecting groups,^[29] although as far as we know this is the first case in which an eight-membered transition state is involved.

As expected, when the HAT reaction of the phthalimide 16 was carried out under reductive conditions with *n*Bu₃SnH/AIBN, only the alcohol precursor 11 was obtained in 55% yield. To confirm the possible mechanism, the reduction of this phthalimide 16 was also carried out with



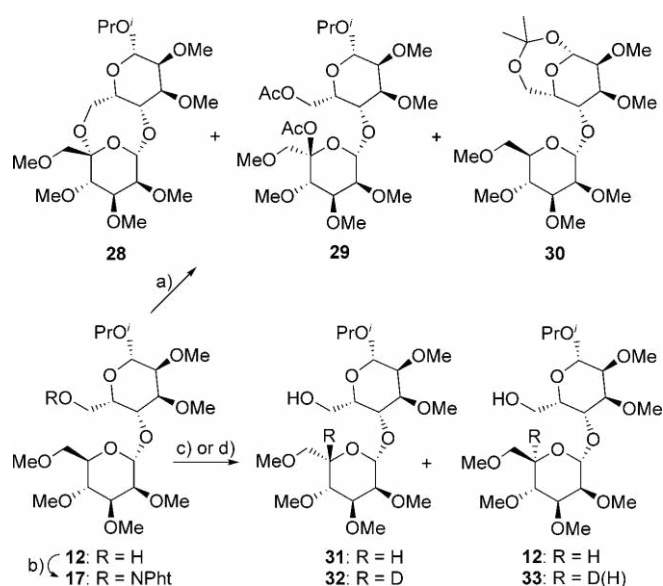
Scheme 5. HAT study of arrangement D. a) DIB (1.5 equiv), iodine (0.6 equiv), CH_2Cl_2 , *h\nu*, RT, 2 h, 62 %; b) DEAD (2.5 equiv), *N*-hydroxyphthalimide (2.5 equiv), PPh_3 (2.5 equiv), THF, 08C, 3 h, 61 %; c) $n\text{Bu}_3\text{SnH}$ (1.5 equiv), AIBN (0.2 equiv), PhH, reflux, 1 h, 55 %; d) $n\text{Bu}_3\text{SnD}$ (3 equiv), AIBN (0.2 equiv), PhH, reflux, 2 h, 54 %, D/H, 7:3.

$n\text{Bu}_3\text{SnD}$ producing the substrate 27 with 70 % of deuterium labelling in the methoxy group at C-1 and, therefore, the reduction of the *O*-radical is responsible for the 30 % of unlabelled molecules.

The formation of compounds 26 and 27 seems to indicate the greater stability of the ${}^4\text{C}_1$ chair conformation; no products originating from the other conformation were detected within the limits of the NMR spectroscopy.

In an effort to avoid this, we prepared the alcohol 12, which possesses an *l*-gulose unit and a more voluminous group at the anomeric carbon atom. In this case, the values of the coupling constants of the *l*-gulose unit ($J_{1,2} = 7.8$, $J_{2,3} = J_{3,4} = 3.4$, $J_{4,5} = 1.5$ Hz) are consistent with the required ${}^1\text{C}_4$ conformation. The results obtained for the HAT reaction of this disaccharide 12 are illustrated in Scheme 6. When the reaction was carried out under oxidative conditions, three compounds were isolated after acetylation: the trioxocane derivative 28 (42 %) as a main product together with the acetate 29 and the isopropylidene derivative 30. The acetate group at C-5' of 29 could be easily distinguished by 2D HSQC and HMBC experiments, whereas the coupling constants deduced from the ${}^1\text{H}$ NMR spectra showed that the d-mannopyranose ring had been inverted to a ${}^1\text{C}_4$ chair conformation. The stereochemistry at C-5' was tentatively assigned as *R* on the basis of the absence of the NOE interactions between H-1' and H₂-6'.

The results suggest that the abstraction at C-5' (compounds 28 and 29), through a nine-membered transition state, competes favourably with the abstraction of the hydrogen atom of the isopropyl group (compound 30) through an eight-membered TS in a ratio of C-5'/C-*i*Pr 75:25, which



Scheme 6. HAT study of arrangement D. a) DIB (1.7 equiv), iodine (1 equiv), CH_2Cl_2 , *h\nu*, RT, 1.5 h; then Ac O, Py, 3 h, 28 (42 %), 29 (25 %), 30 (23 %); b) DEAD (2.5 equiv), *N*-hydroxyphthalimide (2.5 equiv), PPh_3 (2.5 equiv), THF, 08C, RT, 3 h, 49 %; c) $n\text{Bu}_3\text{SnH}$ (1.5 equiv), AIBN (0.2 equiv), PhH, reflux, 1 h, 31 (80 %), 12 (13 %); d) $n\text{Bu}_3\text{SnD}$ (1.5 equiv), AIBN (0.2 equiv), PhH, reflux, 1 h, 32 (83 %), 33 (14 %, D/H 55:45).

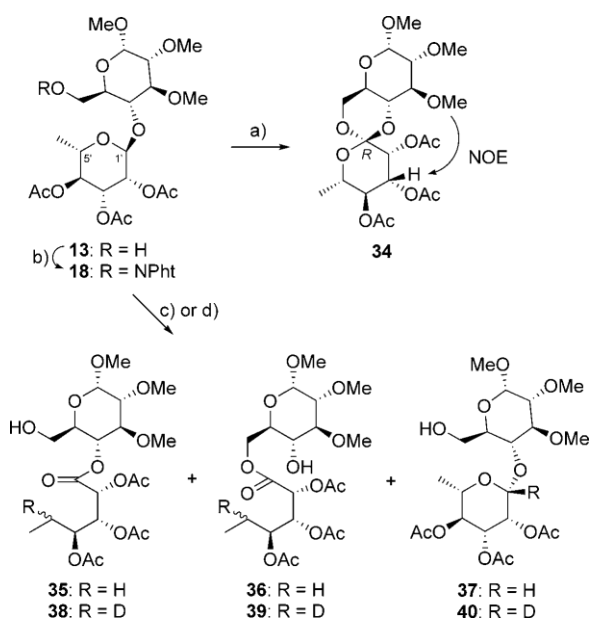
indicates a conformational change from ${}^1\text{C}_4$ to ${}^4\text{C}_1$ of the *l*-gulose ring during the process.

On the other hand, the reduction of phthalimide 17 by treatment with $n\text{Bu}_3\text{SnH}$ /AIBN led preferentially to the inverted alcohol 32 together with a small amount of the precursor 12. Repetition of the experiment with $n\text{Bu}_3\text{SnD}$ /AIBN gave compounds 32 (83 %) and 33 (14 %), in which the deuterium is only incorporated at C-5', with no deuterium detected at other positions within NMR limits; thus under reductive conditions only 1,8-HAT is taking place.

The difference in behaviour observed between the oxidative and reductive conditions could be due to the fact that the alkoxy radical is being generated under two different processes, especially in terms of temperature. This fact together with the different rates of the HAT reactions and the inversion of the pyranose ring may explain the results obtained.

Once the HAT process had been studied in the arrangements with a boat-chair conformation, we next turned our attention to the energetically disfavoured arrangements that could adopt boat-boat or crown ether conformations.

For arrangement E (boat-boat), the disaccharide α -*l*-Rhamp-(14)- α -*d*-GlcP 13 was the substrate of choice (Scheme 7). When alcohol 13 was reacted with DIB and iodine under the standard conditions, the spiro *ortho* ester 34 was obtained in a 79 % yield with complete regio- and stereoselectivity; therefore, the abstraction occurred exclusively at C-1' and no compounds resulting from abstraction at C-5' could be detected in the crude reaction mixture. The configuration at the spiro centre was tentatively assigned as



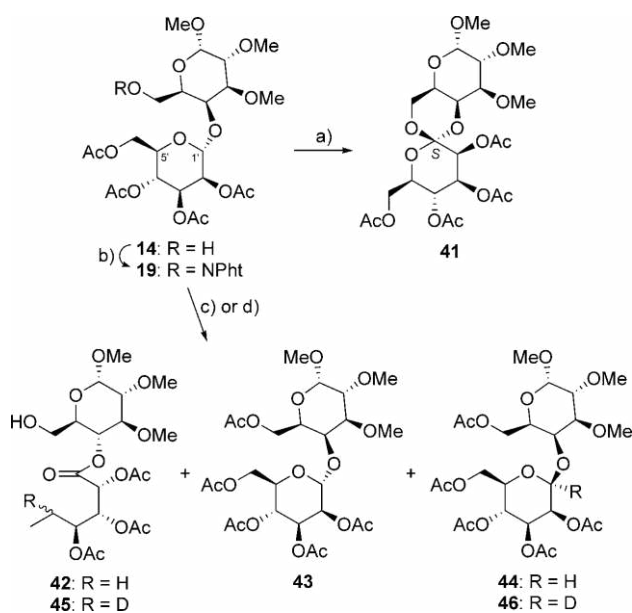
Scheme 7. HAT study of arrangement E. a) DIB (2.5 equiv), iodine (1 equiv), CH_2Cl_2 , *h\nu*, RT, 2.5 h, 79 %; b) DEAD (2.5 equiv), *N*-hydroxyphthalimide (2.5 equiv), PPh_3 (2.5 equiv), THF, 0 $^\circ\text{C}$, 1 h, 94 %, c) $n\text{Bu}_3\text{SnH}$ (2 equiv), AIBN (0.2 equiv), PhH, reflux, 2 h, 35 (48 %), 36 (4 %), 37 (9 %), 13 (8 %); d) $n\text{Bu}_3\text{SnD}$ (2 equiv), AIBN (0.2 equiv), PhH, reflux, 3 h, 38 (28 %), 39 (36 %), 40 (7 %), 13 (7 %).

R on the basis of the NOE interaction observed between the hydrogen at C-3' and the methoxy group at C-3.^[30]

However, when the HAT reaction was conducted under reductive conditions with $n\text{Bu}_3\text{SnH}$, the situation was clearly different. The expected compound 37, formed by abstraction at C-1' and radical reduction by the stannane with inversion of configuration, was obtained in poor yield.^[31] Instead, the ester 35 was the main reaction product, originated also by abstraction at C-1', but in which the radical was stabilised by *b*-fragmentation of the C-5'—O bond prior to the stannane quenching. Besides this, a small amount of transesterified ester 36 was also obtained as a consequence of migration of the ester group from the secondary (C-4') to primary positions (C-6').^[32]

The experiment was also carried out with $n\text{Bu}_3\text{SnD}$. NMR spectroscopic analysis of the isotopic distribution in compounds 38 and 39 showed a complete substitution by deuterium at C-5'. Moreover, the total deuteration of 40 and the isolation of a small amount of the undeuterated alcohol precursor 37 indicated that the abstraction at C-1' proceeded with total inversion of configuration.

Finally, we decided to study the HAT process for the disaccharide α -d-Manp-(1 \rightarrow 4)- α -d-Galp 14, encompassed in rearrangement G (crown ether), the results of which are shown in Scheme 8. Similar to the previous substrate, the HAT reaction under oxidative conditions led to the spiro *ortho* ester 41 in nearly quantitative yield; the process occurred with total regio- and stereoselectivity, abstracting only the hydrogen atom at C-1'. Based on the absence of NOE interactions between the H-2' and the hydrogen atoms



Scheme 8. HAT study of arrangement G. a) DIB (1.7 equiv), iodine (1 equiv), CH_2Cl_2 , *h\nu*, RT, 1 h, 95 %; b) DEAD (2.5 equiv), *N*-hydroxyphthalimide (2.5 equiv), PPh_3 (2.5 equiv), THF, 0 $^\circ\text{C}$, 3 h, 96 %, c) $n\text{Bu}_3\text{SnH}$ (2.4 equiv), AIBN (0.4 equiv), PhH, reflux, 2.5 h, 42 (52 %); then Ac_2O , Py, 43 (19 %), 44 (6 %); d) $n\text{Bu}_3\text{SnD}$ (2 equiv), AIBN (0.4 equiv), PhH, reflux, 2.5 h, 45 (57 %); then Ac_2O , Py, 43 (12 %), 46 (2 %).

at C-4 or C-6, the stereochemistry at the spiro centre has been tentatively assigned as *S*.

Furthermore, in the HAT reaction under reductive conditions by using the phthalimide 19 and $n\text{Bu}_3\text{SnH}$ as the reagent, the predictable compound 44, generated by abstraction at C-1' and radical reduction by the stannane with inversion of configuration, was obtained in only 6 % yield. The ester 42 was the main reaction product, formed by abstraction at C-1' and subsequent *b*-fragmentation of the C-5'—O bond followed by radical-stannane quenching.

In addition, the reduction with $n\text{Bu}_3\text{SnD}$ allowed us to confirm the proposed structures. From the analysis of the isotopic distribution in the isolated products, we concluded that a complete deuteration had taken place in compounds 45 and 46, whereas product 43 remains unlabelled, which indicates that the abstraction at C-1' took place with total inversion, as occurred with the disaccharide 13.

Conclusions

The results described herein confirm that the modelling proposed is consistent in predicting the regioselectivity of the hydrogen-atom transfer reactions in (1 \rightarrow 4)-*O*-disaccharide systems. If a 1,3,5-trioxocane ring is formed in a stable boat-chair conformation, the abstraction would occur preferentially at C-5', whereas if this process is energetically disfavoured, close to boat-boat or crown ether conformations, the abstraction should occur mainly at C-1'. Nevertheless, as we could see for the disaccharides derived from α -d-Manp-(1 \rightarrow

4)-*b*-l-Idop and α -d-Manp-(1 \rightarrow 4)-*b*-l-Gulp (arrangement D), the abstraction step can be influenced not only by the stereochemistry of the trioxocane ring carbon atoms (C-5', C-1', C-4 and C-5), but also by the nature and relative disposition of other substituents of the sugar molecule, especially those which control the pyranose ring conformation.

This methodology, which has been extended to various disaccharide models, is a useful protocol for the remote functionalisation of the C-5' carbon atom or for the inversion of configuration at this centre without modifying the remainder of the sugar, and is, therefore, of special interest in the synthesis of chiral synthons and other carbohydrate derivatives.

Experimental Section

General methods: Melting points were determined with a hot-stage apparatus. Optical rotations were measured at the sodium line at ambient temperature in CHCl₃ solutions. IR spectra were recorded in film unless otherwise stated. NMR spectra were determined at 500 MHz for ¹H and 125.7 MHz for ¹³C in CDCl₃ unless otherwise stated, in the presence of TMS as the internal standard. Mass spectra were determined at 70 eV unless otherwise stated. Merck silica gel 60 PF (0.063–0.2 mm) was used for column chromatography. Circular layers of 1 mm of Merck silica gel 60 PF₂₅₄ were used on a Chromatotron for centrifugally assisted chromatography. Commercially available reagents and solvents were analytical grade or were purified by standard procedures prior to use. All reactions involving air- or moisture-sensitive materials were carried out under a nitrogen atmosphere. The spray reagents for TLC analysis were conducted with 0.5 % vanillin in H₂SO₄/EtOH 4:1 and further heating until development of colour.

General procedure for the oxidative HAT: A solution of the corresponding alcohol (1 mmol) in dry CH₂Cl₂ (40 mL) containing DIB (1.7 mmol) and iodine (1 mmol) under nitrogen was irradiated with two 80 W tungsten-filament lamps at room temperature, monitoring by TLC (1–4 h). The reaction mixture was then poured into 10 % aqueous Na₂S₂O₃ and extracted with CH₂Cl₂, dried over Na₂SO₄ and concentrated. Chromatography of the residue (hexanes/EtOAc) gave the respective cyclised compounds.

General procedure for the reductive HAT: A solution of the corresponding phthalimide (1 mmol) in dry benzene (75 mL) containing *n*Bu₃SnH/*n*Bu₃SnD and AIBN was heated at reflux for 1–3 h. After cooling to room temperature, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in CH₃CN, washed with *n*-hexane and the combined more-polar extracts were concentrated under reduced pressure. The residue was purified by chromatotron chromatography (hexanes/EtOAc) to afford the respective reduced compounds.

Methyl 5,6-anhydro-(2,3,4,6-tetra-*O*-methyl- α -d-xylo-hexos-5-ulopyranosyl)-(1 \rightarrow 4)-2,3-di-*O*-methyl- β -d-galactopyranoside (3): Following the general procedure for oxidative HAT and by using in this case dry CH₂Cl₂ (50 mL), the alcohol 1 afforded after column chromatography (hexanes/EtOAc 4:6) the title compound 3 (56 %) as a syrup. [α]_D = +45.5 (*c* = 0.83 in CHCl₃); ¹H NMR (500 MHz, CDCl₃): δ = 2.93 (dd, *J* = 9.1, 7.8 Hz, 1H), 3.25 (dd, *J* = 9.1, 9.1 Hz, 1H), 3.26 (dd, *J* = 9.3, 3.8 Hz, 1H), 3.32 (ddd, *J* = 9.7, 9.7, 4.0 Hz, 1H), 3.40 (s, 3H), 3.41 (d, *J* = 8.8 Hz, 1H), 3.47 (d, *J* = 9.7 Hz, 1H), 3.488 (s, 3H), 3.490 (d, *J* = 7.9 Hz, 1H), 3.493 (s, 3H), 3.55 (s, 3H), 3.55 (dd, *J* = 9.3, 9.3 Hz, 1H), 3.59 (s, 3H), 3.62 (s, 3H), 3.65 (s, 3H), 3.78 (dd, *J* = 9.6, 9.6 Hz, 1H), 3.83 (dd, *J* = 11.9, 4.3 Hz, 1H), 3.91 (dd, *J* = 11.5, 10.0 Hz, 1H), 4.15 (d, *J* = 7.8 Hz, 1H), 5.20 ppm (d, *J* = 3.4 Hz, 1H); ¹H NMR (500 MHz, C₆D₆): δ = 3.25 (s, 3H), 3.25 (dd, *J* = 8.4, 8.4 Hz, 1H), 3.31 (dd, *J* = 9.5, 3.5 Hz, 1H), 3.33 (s, 3H), 3.34 (s, 3H), 3.36 (ddd, *J* = 9.7, 9.7, 4.1 Hz, 1H), 3.39 (dd, *J* = 9.2, 9.2 Hz, 1H), 3.42 (d, *J* = 10.1 Hz, 1H), 3.62 (d, *J* = 10.2 Hz, 1H), 3.66 (s, 3H), 3.72 (s, 3H), 3.76 (s, 3H), 3.77 (dd, *J* = 9.4, 9.4 Hz, 1H), 3.78 (s, 3H), 3.84 (d, *J* = 9.6 Hz,

1H), 3.98 (dd, *J* = 11.5, 4.0 Hz, 1H), 4.09 (dd, *J* = 10.8, 10.8 Hz, 1H), 4.16 (d, *J* = 7.7 Hz, 1H), 4.32 (dd, *J* = 9.6, 9.6 Hz, 1H), 5.27 ppm (d, *J* = 3.3 Hz, 1H); ¹³C NMR (125.7 MHz, CDCl₃): δ = 57.0 (CH₃), 58.0 (CH₃), 59.3 (CH₃), 60.5 (CH₃), 60.9 (CH₃), 61.1 (CH₃), 61.5 (CH₃), 64.5 (CH₂), 69.7 (CH), 71.4 (CH₂), 79.1 (2 \times CH), 80.5 (CH), 81.3 (CH), 83.7 (CH), 83.8 (CH), 97.1 (CH), 101.2 (C), 104.4 ppm (CH); IR (film): $\tilde{\nu}$ = 2935, 2840, 1082 cm⁻¹; MS (70 eV, EI): *m/z* (%): 438 (1) [M]⁺, 393 (9), 365 (79), 350 (45), 277 (32), 233 (95); HRMS (EI): *m/z*: calcd for C₁₉H₃₄O₁₁: 438.2101 [M]⁺; found: 438.2088; elemental analysis calcd (%) for C₁₉H₃₄O₁₁ (438.47): C 52.05, H 7.82; found: C 52.13, H 8.19.

Orthoacetate 4: Following the general procedure for oxidative HAT and by using in this case DIB (1.5 mmol) and iodine (0.7 mmol) in dry CH₂Cl₂ (43 mL), precursor 2 gave after chromatotron chromatography (hexanes/EtOAc 6:4) compound 4 (62 %) as a crystalline solid. M.p. 195.5–196.5, 210.3–211.5 \times C (*n*-pentane/EtOAc); [α]_D = –3.0 (*c* = 0.220 in CHCl₃); ¹H NMR (500 MHz, CDCl₃): δ = 1.56 (s, 3H), 2.01 (s, 6H), 2.02 (s, 6H), 2.07 (s, 3H), 3.47 (s, 3H), 3.56 (br d, *J* = 9.7 Hz, 1H), 3.74 (d, *J* = 9.0 Hz, 1H), 4.02 (br dd, *J* = 11.7, 2.5 Hz, 1H), 4.10 (br dd, *J* = 9.2, 3.1 Hz, 1H), 4.18 (d, *J* = 9.1 Hz, 1H), 4.18 (m, 1H), 4.38 (d, *J* = 8.1 Hz, 1H), 4.81 (dd, *J* = 8.6, 8.6 Hz, 1H), 4.89 (dd, *J* = 10.4, 5.3 Hz, 1H), 5.07 (d, *J* = 10.2 Hz, 1H), 5.21 (dd, *J* = 9.4, 9.4 Hz, 1H), 5.43 (d, *J* = 5.1 Hz, 1H), 5.74 ppm (dd, *J* = 10.2, 10.2 Hz, 1H); ¹H NMR (500 MHz, C₆D₆): δ = 1.47 (s, 3H), 1.61 (s, 3H), 1.64 (s, 3H), 1.73 (s, 3H), 1.88 (s, 3H), 1.91 (s, 3H), 3.15 (s, 3H), 3.20 (d, *J* = 10.6 Hz, 1H), 3.60 (d, *J* = 9.2 Hz, 1H), 3.79 (dd, *J* = 12.8, 2.8 Hz, 1H), 3.95 (m, 2H), 3.96 (d, *J* = 8.5 Hz, 1H), 4.13 (d, *J* = 7.8 Hz, 1H), 4.93 (dd, *J* = 10.6, 5.0 Hz, 1H), 5.06 (dd, *J* = 9.2, 9.2 Hz, 1H), 5.09 (d, *J* = 9.9 Hz, 1H), 5.33 (d, *J* = 5.0 Hz, 1H), 5.36 (dd, *J* = 9.2, 9.2 Hz, 1H), 6.14 ppm (dd, *J* = 10.2, 10.2 Hz, 1H); ¹³C NMR (125.7 MHz, CDCl₃): δ = 20.3 (CH₃), 20.4 (CH₃), 20.5 (CH₃), 20.6 (CH₃), 21.0 (CH₃), 22.5 (CH₃), 56.7 (CH₃), 64.2 (CH₂), 66.9 (CH), 68.0 (CH), 70.3 (CH), 72.4 (CH₂), 72.6 (CH), 73 (br, CH), 74.7 (CH), 75.2 (CH), 96.0 (CH), 101.3 (CH), 103.1 (C), 124.8 (C), 169.4 (C), 169.6 (C), 169.8 (C), 170.3 (C), 170.5 ppm (C); ¹³C NMR (125.7 MHz, C₆D₆): δ = 19.9 (CH₃), 20.1 (CH₃), 20.2 (CH₃), 20.4 (CH₃), 20.9 (CH₃), 23.0 (CH₃), 56.0 (CH₃), 65.0 (CH₂), 67.5 (CH), 68.5 (CH), 70.8 (CH), 72.5 (CH₂), 72.8 (CH), 74 (br, CH), 75.5 (CH), 75.8 (CH), 96.8 (CH), 101.4 (CH), 103.5 (C), 125.4 (C), 169.0 (C), 169.1 (C), 169.4 (C), 170.3 ppm (2 \times C); IR (film): $\tilde{\nu}$ = 1754 cm⁻¹; MS (FAB): *m/z* (%): 629 (27) [M+Na]⁺, 607 (100), 575 (68); HRMS (FAB): *m/z*: calcd for C₂₅H₃₄O₁₇Na: 629.1694 [M+Na]⁺; found: 629.1667; elemental analysis calcd (%) for C₂₅H₃₄O₁₇ (606.53): C 49.51, H 5.65; found: C 49.52, H 5.81.

Methyl 5,6-anhydro-(2,3,4,6-tetra-*O*-acetyl- α -d-xylo-hexos-5-ulopyranosyl)-(1 \rightarrow 4)-2,3-di-*O*-methyl- β -d-galactopyranoside (5): A solution of orthoacetate 4 (15 mg, 0.025 mmol) in CDCl₃ (0.5 mL) was kept at room temperature for 60 h. Concentration under reduced pressure afforded the title compound 5 (15 mg, 0.025 mmol, quant.) as a syrup. [α]_D = –14.5 (*c* = 0.220 in CHCl₃); ¹H NMR (500 MHz, CDCl₃): δ = 2.00 (s, 6H), 2.01 (s, 3H), 2.02 (s, 3H), 2.06 (s, 3H), 2.10 (s, 3H), 3.43 (d, *J* = 9.1 Hz, 1H), 3.47 (s, 3H), 3.85 (d, *J* = 11.7 Hz, 1H), 3.87 (d, *J* = 11.7 Hz, 1H), 4.08 (d, *J* = 11.2 Hz, 1H), 4.14 (d, *J* = 11.7 Hz, 1H), 4.29 (dd, *J* = 9.6, 9.6 Hz, 1H), 4.43 (d, *J* = 7.6 Hz, 1H), 4.78 (dd, *J* = 8.6, 8.6 Hz, 1H), 4.91 (dd, *J* = 10.7, 5.1 Hz, 1H), 5.13 (d, *J* = 9.7 Hz, 1H), 5.22 (dd, *J* = 9.6, 9.6 Hz, 1H), 5.61 (d, *J* = 4.5 Hz, 1H), 5.76 ppm (dd, *J* = 10.2, 10.2 Hz, 1H); ¹³C NMR (125.7 MHz, CDCl₃): δ = 20.4 (CH₃), 20.5 (CH₃), 20.6 (2 \times CH₃), 20.7 (CH₃), 21.0 (CH₃), 57.2 (CH₃), 60.5 (CH₂), 65.6 (CH), 65.6 (CH₂), 68.7 (CH), 69.6 (CH), 70.2 (CH), 72.4 (CH), 74.4 (CH), 75.5 (CH), 95.1 (CH), 96.5 (C), 101.7 (CH), 169.6 (2 \times C), 169.7 (C), 170.3 (C), 170.4 (C), 170.5 ppm (C); IR (film): $\tilde{\nu}$ = 1748 cm⁻¹; MS (70 eV, EI): *m/z* (%): 591 (< 1) [M–CH₃]⁺, 546 (< 1), 533 (11), 505 (5), 491 (9); HRMS (EI): *m/z*: calcd for C₂₄H₃₁O₁₇: 591.1561 [M–CH₃]⁺; found: 591.1507; elemental analysis calcd (%) for C₂₅H₃₄O₁₇ (606.53): C 49.51, H 5.65; found: C 49.58, H 5.37.

Reductive HAT of methyl 2,3,4,6-tetra-*O*-methyl- α -d-glucopyranosyl-(1 \rightarrow 4)-2,3-di-*O*-methyl-6-*O*-phthalimido- β -d-glucopyranoside (6)

Method A (*n*Bu₃SnH): Following the general procedure and by using *n*Bu₃SnH (9 mmol) and AIBN (0.16 mmol) in dry benzene (16 mL), precursor 6 gave after chromatography (EtOAc) methyl 2,3,4,6-tetra-*O*-

methyl-*b*-l-idopyranosyl-(114)-2,3-di-*O*-methyl-*b*-d-glucopyranoside (7) (43%) as a colourless oil and the precursor alcohol 1 (43%).

Compound 8: [α] = +33.0 ($c = 0.61$ in CHCl_3); $^1\text{H NMR}$ (500 MHz, CDCl_3): $d = 3.02$ (dd, $J = 9.0, 7.9$ Hz, 1H), 3.08 (br s, 1H), 3.20 (br d, $J = 9.9$ Hz, 1H), 3.25 (dd, $J = 9.2, 9.2$ Hz, 1H), 3.35 (s, 3H), 3.41 (s, 3H), 3.42 (br s, 1H), 3.43 (s, 3H), 3.46 (dd, $J = 10.1, 3.4$ Hz, 1H), 3.49 (s, 3H), 3.55 (s, 3H), 3.56 (s, 3H), 3.63 (s, 3H), 3.68 (dd, $J = 12.7, 1.9$ Hz, 1H), 3.72 (dd, $J = 9.6, 9.6$ Hz, 1H), 3.73 (dd, $J = 2.5, 2.5$ Hz, 1H), 3.82 (dd, $J = 9.5, 9.5$ Hz, 1H), 3.96 (ddd, $J = 8.6, 3.0, 2.0$ Hz, 1H), 4.14 (d, $J = 7.7$ Hz, 1H), 4.18 (dd, $J = 12.7, 1.9$ Hz, 1H), 4.90 ppm (s, 1H); $^1\text{H NMR}$ (500 MHz, C_6D_6): $d = 2.94$ (br s, 1H), 3.00 (s, 3H), 3.09 (s, 3H), 3.09 (m, 1H), 3.12 (s, 3H), 3.14 (dd, $J = 9.5, 8.5$ Hz, 1H), 3.28 (s, 3H), 3.29 (dd, $J = 10.2, 8.3$ Hz, 1H), 3.39 (dd, $J = 9.5, 4.8$ Hz, 1H), 3.41 (br s, 1H), 3.43 (s, 3H), 3.51 (s, 3H), 3.56 (br s, 1H), 3.57 (s, 3H), 3.70 (dd, $J = 9.5, 7.6$ Hz, 1H), 4.01 (dd, $J = 9.5, 9.5$ Hz, 1H), 3.92–3.97 (m, 2H), 4.10 (d, $J = 7.6$ Hz, 1H), 4.31 (br d, 1H), 5.18 ppm (s, 1H); $^{13}\text{C NMR}$ (125.7 MHz, CDCl_3): $d = 56.6$ (CH₃), 57.8 (CH₃), 58.5 (CH₃), 58.9 (CH₃), 60.18 (CH₂), 60.23 (CH₃), 60.4 (CH₃), 61.1 (CH₃), 71.9 (CH₂), 73.8 (CH), 74.6 (CH), 74.9 (CH), 75.2 (CH), 76.4 (CH), 77.1 (CH), 83.9 (CH), 86.2 (CH), 102.0 (CH), 104.2 ppm (CH); $^{13}\text{C NMR}$ (50.3 MHz, C_6D_6): $d = 56.0$ (CH₃), 57.09 (CH₃), 57.14 (CH₃), 58.4 (CH₃), 59.7 (CH₃), 59.9 (CH₃), 60.6 (CH₃), 61.6 (CH₂), 71.7 (CH₂), 73.8 (CH), 75.1 (CH), 75.3 (CH), 75.7 (CH), 76.78 (CH), 76.84 (CH), 84.2 (CH), 86.5 (CH), 101.3 (CH), 104.7 ppm (CH); IR (film): $\tilde{\nu} = 3494$ cm⁻¹; MS (70 eV, EI): m/z (%): 408 (< 1) [$M - \text{CH}_3\text{OH}$]⁺, 377 (< 1), 308 (4), 275 (9), 265 (45); HRMS (EI): m/z calcd for $\text{C}_{18}\text{H}_{32}\text{O}_{10}$: 408.1995 [$M - \text{CH}_3\text{OH}$]⁺; found: 408.1977; elemental analysis calcd (%) for $\text{C}_{19}\text{H}_{36}\text{O}_{11}$ (440.68): C 51.81, H 8.24; found: C 52.07, H 7.85.

Method B ($n\text{Bu}_3\text{SnD}$): Following the general procedure and by using $n\text{Bu}_3\text{SnH}$ (9 mmol) and AIBN (0.16 mmol) in dry benzene (16 mL), precursor 6 gave after chromatography (EtOAc) methyl 2,3,4,6-tetra-*O*-methyl-*b*-l-(5-²H₁)idopyranosyl-(114)-2,3-di-*O*-methyl-*b*-d-glucopyranoside (8) (37%) and methyl 2,3,4,6-tetra-*O*-methyl- α -d-[²H₁]glucopyranosyl-(114)-2,3-di-*O*-methyl-*b*-d-glucopyranoside (9) (41%), $^1\text{H}/^2\text{H}$ ratio, 43:57.

Compound 8: $^1\text{H NMR}$ (500 MHz, C_6D_6): $d = 2.95$ (br d, $J = 2.1$ Hz, 1H), 3.00 (s, 3H), 3.10 (s, 3H), 3.11 (s, 3H), 3.11 (m, 1H), 3.14 (dd, $J = 9.0, 7.8$ Hz, 1H), 3.28 (s, 3H), 3.30 (dd, $J = 9.2, 9.2$ Hz, 1H), 3.39 (d, $J = 9.6$ Hz, 1H), 3.41 (br d, $J = 3.2$ Hz, 1H), 3.43 (s, 3H), 3.51 (s, 3H), 3.56 (br d, $J = 2.6$ Hz, 1H), 3.57 (s, 3H), 3.69 (d, $J = 9.6$ Hz, 1H), 3.98 (m, 1H), 4.01 (dd, $J = 9.5, 9.5$ Hz, 1H), 4.10 (d, $J = 7.7$ Hz, 1H), 4.32 (br d, $J = 11.8$ Hz, 1H), 5.19 ppm (d, $J = 1.3$ Hz, 1H); $^{13}\text{C NMR}$ (125.7 MHz, C_6D_6): $d = 56.27$ (CH₃), 57.38 (CH₃), 57.40 (CH₃), 58.7 (CH₃), 60.0 (CH₃), 60.2 (CH₃), 60.8 (CH₃), 61.8 (CH₂), 71.9 (CH₂), 75.3 (CH), 75.6 (CH), 76.0 (CH), 77.0 (CH), 77.1 (CH), 84.5 (CH), 86.8 (CH), 101.6 (CH), 105.0 ppm (CH); MS (FAB): m/z (%): 464 (100) [$M + \text{Na}$]⁺, 442 (10), 307 (25), 289 (13); HRMS (FAB): m/z calcd for $\text{C}_{18}\text{H}_{32}\text{O}_{10}$: 464.2218 [$M + \text{Na}$]⁺; found: 464.2211.

Compound 9: $^{13}\text{C NMR}$ (50.3 MHz, C_6D_6): $d = 56.3$ (CH₃), 59.0 (2 × CH₃), 59.9 (CH₃), 60.2 (CH₃), 60.3 (CH₃), 60.6 (CH₃), 61.8 (CH₂), 72.0 (CH), 72.240 (CH₂), 72.298 (CH₂), 74.3 (CH), 75.5 (CH), 80.47 (CH), 80.53 (CH), 82.7 (CH), 84.1 (CH), 84.9 (CH), 86.9 (CH), 97.8 (CH), 104.6 ppm (CH); MS (FAB): m/z (%): 464/463 (29/21) [$M + \text{Na}$]⁺, 410/409 (7/6); HRMS (FAB): m/z calcd for $\text{C}_{18}\text{H}_{32}\text{O}_{10}$: 464.2218/463.2155 [$M + \text{Na}$]⁺; found: 464.2229/463.2162.

Oxidative HAT of methyl 2,3,4-tri-*O*-acetyl- α -l-rhamnopyranosyl-(114)-2,3-di-*O*-methyl- α -d-galactopyranoside (10): Following the general procedure, in this case without irradiation and heating at reflux, the alcohol 10 gave after chromatography (hexanes/EtOAc 25:75) methyl 5,6-anhydro-(2,3,4-tri-*O*-acetyl-6-deoxy- α -l-lyxo-hexos-5-ulopyranosyl)-(114)-2,3-di-*O*-methyl- α -d-galactopyranoside (20) (88%) as a white crystalline solid and methyl (1³S)-4,6-*O*-(2,3,4-tri-*O*-acetyl-6-deoxy- α -l-lyxo-hexos-5-ulosylidene)-2,3-di-*O*-methyl- α -d-galactopyranoside (21) (10%) as a colourless oil.

Compound 20: M.p. 216.5–217.4 °C (acetone/*n*-hexane); [α]_D = +98.1 ($c = 0.270$ in CHCl_3); $^1\text{H NMR}$ (400 MHz, CDCl_3): $d = 1.37$ (s, 3H), 1.95 (s, 3H), 2.08 (s, 3H), 2.15 (s, 3H), 3.39 (s, 3H), 3.43 (s, 3H), 3.48 (dd, $J = 10.1, 3.2$ Hz, 1H), 3.52 (s, 3H), 3.54 (m, 1H), 3.67 (dd, $J = 10.1, 3.7$ Hz, 1H), 3.91 (dd, $J = 13.2, 2.1$ Hz, 1H), 4.08 (dd, $J = 13.2, 1.6$ Hz, 1H), 4.17

(br d, $J = 3.2$ Hz, 1H), 4.85 (d, $J = 1.6$ Hz, 1H), 4.95 (d, $J = 3.7$ Hz, 1H), 5.36 (d, $J = 10.6$ Hz, 1H), 5.58 (dd, $J = 3.2, 1.6$ Hz, 1H), 5.63 ppm (dd, $J = 10.6, 3.2$ Hz, 1H); $^{13}\text{C NMR}$ (100.6 MHz, CDCl_3): $d = 20.6$ (2 × CH₃), 20.8 (CH₃), 21.9 (CH₃), 55.4 (CH₃), 58.1 (CH₃), 59.1 (CH₃), 63.6 (CH₂), 66.3 (CH), 66.7 (CH), 69.6 (CH), 70.7 (CH), 73.8 (CH), 77.1 (CH), 78.4 (CH), 98.0 (CH), 98.1 (CH), 100.4 (C), 169.6 (C), 169.8 (C), 170.5 ppm (C); IR (film): $\tilde{\nu} = 2933, 2838, 1755, 1372, 1224, 1049$ cm⁻¹; MS (FAB): m/z (%): 515 (8) [$M + \text{Na}$]⁺, 493 (8) [$M + \text{H}$]⁺, 491 (7), 461 (40), 154 (100); HRMS (FAB): m/z calcd for $\text{C}_{21}\text{H}_{32}\text{O}_{13}\text{Na}$: 515.1741 [$M + \text{Na}$]⁺; found: 515.1755; elemental analysis calcd (%) for $\text{C}_{21}\text{H}_{32}\text{O}_{13}$ (492.47): C 51.22, H 6.55; found: C 51.44, H 6.33.

Compound 21: [α]_D = +54.2 ($c = 0.310$ in CHCl_3); $^1\text{H NMR}$ (500 MHz, CDCl_3): $d = 2.04$ (s, 3H), 2.07 (s, 3H), 2.17 (s, 3H), 2.22 (s, 3H), 3.41 (s, 3H), 3.43 (s, 3H), 3.52 (s, 3H), 3.54 (m, 1H), 3.59 (dd, $J = 10.0, 3.1$ Hz, 1H), 3.62 (dd, $J = 10.0, 3.1$ Hz, 1H), 3.81 (dd, $J = 12.5, 1.7$ Hz, 1H), 4.10 (dd, $J = 3.1, 1.1$ Hz, 1H), 4.12 (dd, $J = 12.5, 1.5$ Hz, 1H), 4.73 (d, $J = 4.2$ Hz, 1H), 4.91 (d, $J = 3.1$ Hz, 1H), 5.26 (dd, $J = 7.5, 4.2$ Hz, 1H), 5.43 (d, $J = 1.9$ Hz, 1H), 5.90 ppm (dd, $J = 7.5, 1.9$ Hz, 1H); $^{13}\text{C NMR}$ (125.7 MHz, CDCl_3): $d = 20.5$ (CH₃), 20.6 (CH₃), 20.7 (CH₃), 26.5 (CH₃), 55.6 (CH₃), 57.0 (CH₃), 59.0 (CH₃), 62.3 (CH), 68.0 (CH), 69.0 (CH₂), 69.8 (CH), 73.0 (CH), 76.3 (CH), 76.7 (CH), 77.0 (CH), 98.4 (CH), 99.0 (CH), 169.3 (C), 169.7 (C), 170.1 (C), 201.7 ppm (C); IR (film): $\tilde{\nu} = 2923, 2836, 1748, 1372, 1218, 1049$ cm⁻¹; MS (70 eV, EI): m/z (%): 492 (1) [M]⁺, 449 (> 1), 363 (7), 233 (12), 75 (100); HRMS (EI): m/z calcd for $\text{C}_{21}\text{H}_{32}\text{O}_{13}$: 492.1843 [M]⁺; found: 492.1859; elemental analysis calcd (%) for $\text{C}_{21}\text{H}_{32}\text{O}_{13}$: C 51.22, H 6.55; found: C 51.14, H 6.78.

Reductive HAT of methyl 2,3,4-tri-*O*-acetyl- α -l-rhamnopyranosyl-(114)-2,3-di-*O*-methyl-6-*O*-phthalimido- α -d-galactopyranoside (15)

Method A ($n\text{Bu}_3\text{SnH}$): Following the general procedure and by using $n\text{Bu}_3\text{SnH}$ (1 mmol) and AIBN (0.1 mmol), the phthalimide 15 afforded after chromatography (hexanes/EtOAc, 50:50:130:70) methyl 2,3,4-tri-*O*-acetyl-6-deoxy-*b*-d-gulopyranosyl-(114)-2,3-di-*O*-methyl- α -d-galactopyranoside (22) (52%) as a crystalline solid, the precursor alcohol 10 (22%), described in the Supporting Information, and methyl 2,3-di-*O*-acetyl-4,6-dideoxy-*b*-d-erythro-hex-4-enopyranosyl-(114)-2,3-di-*O*-methyl- α -d-galactopyranoside (23) (5%) as a colourless oil.

Compound 22: M.p. 153.2–154.9 °C (acetone/*n*-hexane); [α]_D = +60.0 ($c = 0.530$ in CHCl_3); $^1\text{H NMR}$ (500 MHz, CDCl_3): $d = 1.19$ (d, $J = 6.4$ Hz, 3H), 2.03 (s, 3H), 2.13 (s, 3H), 2.17 (s, 3H), 3.23 (m, 1H), 3.39 (s, 3H), 3.47 (dd, $J = 10.1, 3.5$ Hz, 1H), 3.48 (s, 3H), 3.49 (s, 3H), 3.57 (dd, $J = 10.1, 3.0$ Hz, 1H), 3.63 (m, 1H), 3.77–3.83 (m, 2H), 4.15 (dddd, $J = 6.5, 6.5, 6.5, 1.3$ Hz, 1H), 4.19 (br d, $J = 3.1$ Hz, 1H), 4.81 (d, $J = 3.5$ Hz, 1H), 4.83 (dd, $J = 3.7, 1.4$ Hz, 1H), 4.94 (d, $J = 8.3$ Hz, 1H), 5.04 (dd, $J = 8.3, 3.5$ Hz, 1H), 5.34 ppm (dd, $J = 3.6, 3.6$ Hz, 1H); $^{13}\text{C NMR}$ (100.6 MHz, CDCl_3): $d = 15.715$ (CH₃), 20.6 (CH₃), 20.7 (CH₃), 20.8 (CH₃), 55.4 (CH₃), 58.4 (CH₃), 59.1 (CH₃), 60.2 (CH₂), 67.9 (CH), 68.4 (CH), 68.8 (CH), 69.0 (CH), 70.100 (CH), 73.3 (CH), 78.0 (CH), 79.2 (CH), 97.9 (CH), 99.8 (CH), 168.9 (C), 169.5 (C), 169.8 ppm (C); IR (film): $\tilde{\nu} = 3506, 2940, 2840, 1748, 1372, 1222, 1045$ cm⁻¹; MS (FAB): m/z (%): 518 (6) [$M + \text{Na} + \text{H}$]⁺, 517 (21) [$M + \text{Na}$]⁺, 391 (32), 273 (63), 73 (100); HRMS (FAB): m/z calcd for $\text{C}_{21}\text{H}_{35}\text{O}_{13}\text{Na}$: 518.1975 [$M + \text{Na} + \text{H}$]⁺; found: 518.1984; elemental analysis calcd (%) for $\text{C}_{21}\text{H}_{35}\text{O}_{13}$: C 51.01, H 6.93; found: C 51.15, H 6.89.

Compound 23: [α]_D = -33.8 ($c = 0.290$ in CHCl_3); $^1\text{H NMR}$ (400 MHz, CDCl_3): $d = 1.83$ (s, 3H), 2.05 (s, 3H), 2.10 (s, 3H), 2.21 (dd, $J = 9.8, 7.5$ Hz, 1H), 3.41 (s, 3H), 3.50 (s, 3H), 3.51 (s, 3H), 3.57–3.58 (m, 2H), 3.60–3.75 (m, 2H), 3.82 (ddd, $J = 6.6, 6.6, 1.3$ Hz, 1H), 4.24 (dd, $J = 1.1, 1.1$ Hz, 1H), 4.66 (br d, $J = 3.7$ Hz, 1H), 4.85 (d, $J = 1.6$ Hz, 1H), 5.25 (dd, $J = 5.0, 5.0$ Hz, 2-H), 5.30 (d, $J = 5.3$ Hz, 1H), 5.51 ppm (ddd, $J = 5.3, 3.7, 1.6$ Hz, 1H); $^{13}\text{C NMR}$ (100.6 MHz, CDCl_3): $d = 19.5$ (CH₃), 20.8 (CH₃), 20.9 (CH₃), 55.4 (CH₃), 58.7 (CH₃), 59.1 (CH₃), 61.4 (CH₂), 64.1 (CH), 66.0 (CH), 69.6 (CH), 73.4 (CH), 78.0 (CH), 79.6 (CH), 95.1 (CH), 97.9 (CH), 98.4 (CH), 151.1 (C), 169.9 (C), 170.2 ppm (C); IR (film): $\tilde{\nu} = 3468, 2935, 2834, 1747, 1682, 1372, 1247, 1049$ cm⁻¹; MS (70 eV, EI): m/z (%): 435 (< 1) [$M + \text{H}$]⁺, 402 (< 1), 374 (1), 212 (11), 88 (100); HRMS (EI): m/z calcd for $\text{C}_{19}\text{H}_{31}\text{O}_{11}$: 435.1866 [$M + \text{H}$]⁺; found: 435.1877; elemental analysis calcd (%) for $\text{C}_{19}\text{H}_{31}\text{O}_{11}$ (434.43): C 52.53, H 6.96; found: C 52.23, H 6.90.

Method B (*n*Bu₃SnD): Following the general procedure and by using *n*Bu₃SnD (2 mmol) and AIBN (0.2 mmol), the phthalimide 15 gave after column chromatography (hexanes/EtOAc 50:50:30:70) methyl 2,3,4-tri-*O*-acetyl-6-deoxy-*b*-d-(5-²H₁)gulopyranosyl-(1⁴)-2,3-di-*O*-methyl- α -d-galactopyranoside (24) (45%), methyl 2,3,4-tri-*O*-acetyl- α -l-[5-²H₁]rhamnopyranosyl-(1⁴)-2,3-di-*O*-methyl- α -d-galactopyranoside (25) (18%, ¹H/²H ratio, 3:7), both as colourless oils, and the olefin 23 (15%).

Compound 24: ¹H NMR (500 MHz, CDCl₃): *d* = 1.18 (s, 3H), 2.02 (s, 3H), 2.12 (s, 3H), 2.16 (s, 3H), 3.24 (m, 1H), 3.38 (s, 3H), 3.46 (dd, *J* = 10.1, 3.5 Hz, 1H), 3.47 (s, 3H), 3.48 (s, 3H), 3.56 (dd, *J* = 10.1, 3.0 Hz, 1H), 3.63 (m, 1H), 3.76–3.82 (m, 2H), 4.19 (dd, *J* = 3.0, 0 Hz, 1H), 4.80 (d, *J* = 3.5 Hz, 1H), 4.81 (d, *J* = 3.7 Hz, 1H), 4.94 (d, *J* = 8.3 Hz, 1H), 5.03 (dd, *J* = 8.3, 3.5 Hz, 1H), 5.33 ppm (dd, *J* = 3.6, 3.6 Hz, 1H); ¹³C NMR (100.6 MHz, CDCl₃): *d* = 15.576 (CH₃), 20.6 (CH₃), 20.7 (CH₃), 20.7 (CH₃), 55.4 (CH), 58.4 (CH), 59.0 (CH), 60.2 (CH), 67.9 (CH), 68.4 (CH), 69.0 (CH), 70.036 (CH), 73.3 (CH), 78.0 (CH), 79.2 (CH), 97.9 (CH), 99.8 (CH), 168.8 (C), 169.5 (C), 169.8 ppm (C); MS (FAB): *m/z* (%): 519 (2) [*M*+Na+H]⁺, 518 (7), 355 (10), 274 (27), 73 (100); HRMS (FAB): *m/z*: calcd for C₂₁H₃₄²HO₁₃Na: 519.2038 [*M*+Na+H]⁺; found: 519.2014.

Compound 25: ¹H NMR (500 MHz, CDCl₃): *d* = 1.22 (s, 3H), 1.23 (d, *J* = 6.6 Hz, 3H), 1.99 (s, 3H), 2.05 (s, 3H), 2.14 (s, 3H), 3.42 (s, 3H), 3.47 (s, 3H), 3.54 (s, 3H), 3.56 (dd, *J* = 10.1, 2.9 Hz, 1H), 3.64 (dd, *J* = 10.1, 3.5 Hz, 1H), 3.66 (m, 1H), 3.80–3.86 (m, 2H), 3.98 (dddd, *J* = 10.0, 6.3, 6.3, 6.3 Hz, 1H), 4.12 (d, *J* = 2.7, 0 Hz, 1H), 4.88 (d, *J* = 3.5 Hz, 1H), 5.05 (d, *J* = 2.1 Hz, 1H), 5.071 (d, *J* = 10.0 Hz, 1H), 5.073 (dd, *J* = 9.8, 9.8 Hz, 1H), 5.31 (dd, *J* = 10.0, 3.3 Hz, 1H), 5.47 ppm (dd, *J* = 3.3, 2.1 Hz, 1H); ¹³C NMR (100.6 MHz, CDCl₃): *d* = 17.350 (CH₃), 17.489 (CH₃), 20.7 (CH₃), 20.8 (CH₃), 20.9 (CH₃), 55.4 (CH₃), 58.8 (CH₃), 59.3 (CH₃), 62.0 (CH₂), 67.5 (CH), 69.0 (CH), 69.8 (CH), 69.9 (CH), 70.869 (CH), 70.932 (CH), 75.1 (CH), 78.0 (CH), 79.8 (CH), 98.1 (CH), 99.7 (CH), 169.8 (C), 170.0 (C), 170.0 ppm (C); MS (FAB): *m/z* (%): 519 (7) [*M*+Na+H]⁺, 518 (26), 517 (5), 274 (46), 273 (27), 73 (100); HRMS (FAB): *m/z*: calcd for C₂₁H₃₄²HO₁₃Na/C₂₁H₃₅O₁₃Na: 519.2038/518.1975 [*M*+Na+H]⁺; found: 519.2042/518.1970.

2,3,4,6-tetra-*O*-acetyl- α -d-mannopyranosyl-(1⁴)-2,3-di-*O*-methyl-1,6-*O*-methylene-*b*-l-idopyranoside (26): Following the general procedure for the oxidative HAT and by using in this case DIB (1.5 mmol) and iodine (0.6 mmol) in dry CH₂Cl₂ (35 mL), precursor 11 gave after chromatotron chromatography (hexanes/EtOAc 1:1) the title compound 26 (62%) as a foam: [*a*]_D²⁰ = + 46.1 (*c* = 0.466 in CHCl₃); ¹H NMR (400 MHz, CDCl₃): *d* = 2.00 (s, 3H), 2.04 (s, 3H), 2.08 (s, 3H), 2.15 (s, 3H), 3.06 (dd, *J* = 9.0, 2.9 Hz, 1H), 3.49 (dd, *J* = 12.5, 3.7 Hz, 1H), 3.54 (s, 3H), 3.63 (s, 3H), 3.83 (dd, *J* = 9.8, 7.4 Hz, 1H), 3.86 (m, 1H), 3.91 (dd, *J* = 9.8, 9.8 Hz, 1H), 4.09 (dd, *J* = 12.2, 2.6 Hz, 1H), 4.17–4.22 (m, 2H), 4.23 (dd, *J* = 12.2, 5.8 Hz, 1H), 4.88 (d, *J* = 7.2 Hz, 1H), 5.09 (d, *J* = 6.9 Hz, 1H), 5.19 (d, *J* = 1.6 Hz, 1H), 5.23 (dd, *J* = 9.8, 9.8 Hz, 1H), 5.26 (m, 1H), 5.33 (dd, *J* = 3.2, 1.9 Hz, 1H), 5.41 ppm (d, *J* = 3.2 Hz, 1H); ¹³C NMR (100.6 MHz, CDCl₃): *d* = 20.6 (CH₃), 20.7 (2 × CH₃), 20.8 (CH₃), 59.2 (CH₃), 61.3 (CH₃), 62.8 (CH₂), 66.4 (CH₂), 67.0 (CH), 68.6 (CH), 69.2 (CH), 69.4 (CH), 76.8 (CH), 77.2 (CH), 80.0 (CH), 82.8 (CH), 91.2 (CH₂), 95.5 (CH), 99.6 (CH), 169.68 (C), 169.71 (C), 169.8 (C), 170.5 ppm (C); IR (film): $\tilde{\nu}$ = 2939, 1748, 1371, 1224, 1043 cm⁻¹; MS (70 eV, EI): *m/z* (%): 550 (< 1) [*M*]⁺, 491 (< 1), 459 (< 1), 331 (100), 169 (97); HRMS (EI): *m/z*: calcd for C₂₃H₃₄O₁₅: 550.1898 [*M*]⁺; found: 550.1886; elemental analysis calcd (%) for C₂₃H₃₄O₁₅: C 50.18, H 6.23; found: C 50.28, H 6.22.

Reductive HAT of methyl 2,3,4,6-tetra-*O*-acetyl- α -d-mannopyranosyl-(1⁴)-2,3-di-*O*-methyl-6-*O*-phthalimido-*b*-l-idopyranoside (16)

Method A (*n*Bu₃SnH): Following the general procedure and by using *n*Bu₃SnH (1.5 mmol) and AIBN (0.2 mmol), the phthalimide 16 gave after column chromatography (hexanes/EtOAc 30:70), the alcohol 11 (55%) described in the Supporting Information.

Method B (*n*Bu₃SnD): Following the general procedure and by using *n*Bu₃SnD (3 mmol) and AIBN (0.2 mmol), the phthalimide 16 afforded after column chromatography (hexanes/EtOAc 30:70) methyl 2,3,4,6-tetra-*O*-acetyl- α -d-mannopyranosyl-(1⁴)-2,3-di-*O*-methyl-*b*-l-[1-

OMe-²H]idopyranoside (27) (54%, ¹H/²H ratio, 3:7) as a colourless oil: ¹H NMR (400 MHz, CDCl₃): *d* = 1.99 (s, 3H), 2.04 (s, 3H), 2.09 (s, 3H), 2.15 (s, 3H), 3.26 (dd, *J* = 7.1, 3.2 Hz, 1H), 3.52 (s, 3H), 3.539 (br s, 2H), 3.544 (s, 3H), 3.56 (s, 3H), 3.74 (dd, *J* = 7.1, 7.1 Hz, 1H), 3.79 (dd, *J* = 6.9, 4.8 Hz, 1H), 3.84 (m, 1H), 3.96 (m, 1H), 4.01 (ddd, *J* = 6.6, 4.8, 4.8 Hz, 1H), 4.04 (ddd, *J* = 9.3, 5.8, 2.4 Hz, 1H), 4.09 (dd, *J* = 12.2, 2.4 Hz, 1H), 4.24 (dd, *J* = 12.2, 5.8 Hz, 1H), 4.74 (d, *J* = 2.9 Hz, 1H), 5.09 (d, *J* = 1.3 Hz, 1H), 5.24 (dd, *J* = 9.5, 9.5 Hz, 1H), 5.27 (dd, *J* = 3.2, 1.8 Hz, 1H), 5.29 ppm (dd, *J* = 9.5, 3.4 Hz, 1H); ¹³C NMR (100.6 MHz, CDCl₃): *d* = 20.6 (CH₃), 20.7 (2 × CH₃), 20.8 (CH₃), 56.867 (CH₂, *t*, *J*_{CD} = 22.6 Hz), 57.145 (CH₃), 59.5 (CH₃), 60.1 (CH₃), 62.3 (CH₂), 62.7 (CH₂), 66.4 (CH), 68.7 (CH), 69.3 (CH), 69.7 (CH), 75.0 (CH), 75.3 (CH), 77.6 (CH), 79.9 (CH), 98.2 (CH), 99.7 (CH), 169.6 (C), 169.8 (C), 169.9 (C), 170.6 ppm (C); MS (70 eV, EI): *m/z* (%): 494 (< 1) [*M*+HCO]⁺, 493 (< 1), 478 (< 1), 477 (< 1), 331 (72), 88 (100); HRMS (EI): *m/z*: calcd for C₂₁H₃₂²HO₁₃/C₂₁H₃₃O₁₃: 494.1984/493.1921 [*M*+HCO]⁺; found: 494.1992/493.1920.

Oxidative HAT of isopropyl 2,3,4,6-tetra-*O*-methyl- α -d-mannopyranosyl-(1⁴)-2,3-di-*O*-methyl-*b*-l-gulopyranoside (12): Following the general procedure and by using in this case dry CH₂Cl₂ (47 mL), the alcohol 12 gave after acetylation of the reaction crude and chromatotron chromatography of the residue (hexanes/EtOAc 4:6) isopropyl (5⁷R)-5⁷,6-anhydro-2³,4³,6³-tetra-*O*-methyl- α -d-lyxo-hexos-5⁷-ulopyranosyl-(1⁴)-2,3-di-*O*-methyl-*b*-l-gulopyranoside (28) (42%) as a colourless oil and an inseparable mixture of isopropyl (5⁷R)-5⁷-*O*-acetyl-2³,4³,6³-tetra-*O*-methyl- α -d-lyxo-hexos-5⁷-ulopyranosyl-(1⁴)-6-*O*-acetyl-2,3-di-*O*-methyl-*b*-l-gulopyranoside (29) (25%) and 2,3,4,6-tetra-*O*-methyl- α -d-mannopyranosyl-(1⁴)-1,6-*O*-isopropylidene-2,3-di-*O*-methyl-*b*-l-gulopyranose (30) (23%).

Compound 28: [*a*]_D²⁰ = + 75.5 (*c* = 0.102 in CHCl₃); ¹H NMR (400 MHz, C₆D₆): *d* = 1.11 (d, *J* = 6.1 Hz, 3H), 1.22 (d, *J* = 6.1 Hz, 3H), 3.14 (s, 3H), 3.22 (s, 3H), 3.31 (s, 3H), 3.33 (s, 3H), 3.38 (d, *J* = 10.3 Hz, 1H), 3.48 (s, 3H), 3.49 (m, 1H), 3.54 (dd, *J* = 3.4, 3.4 Hz, 1H), 3.57 (dd, *J* = 8.2, 3.2 Hz, 1H), 3.62 (s, 3H), 3.64 (d, *J* = 10.3 Hz, 1H), 3.70 (dd, *J* = 2.6, 1.6 Hz, 1H), 3.78 (dd, *J* = 3.7, 1.1 Hz, 1H), 3.86 (dd, *J* = 13.2, 1.9 Hz, 1H), 3.91 (dd, *J* = 13.0, 2.4 Hz, 1H), 3.98 (sep, *J* = 6.1 Hz, 1H), 4.28 (d, *J* = 10.3 Hz, 1H), 4.32 (dd, *J* = 10.3, 2.6 Hz, 1H), 4.98 (d, *J* = 7.9 Hz, 1H), 4.99 ppm (d, *J* = 1.9 Hz, 1H); ¹³C NMR (100.6 MHz, C₆D₆): *d* = 22.1 (CH₃), 23.9 (CH₃), 57.7 (CH₃), 59.1 (CH₃), 59.4 (CH₃), 59.5 (CH₃), 59.7 (CH₃), 60.9 (CH₃), 64.5 (CH₂), 70.6 (CH), 71.4 (CH), 72.8 (CH₂), 74.7 (CH), 77.5 (CH), 77.8 (CH), 78.5 (CH), 79.0 (CH), 80.3 (CH), 98.6 (CH), 100.4 (CH), 102.5 ppm (C); IR (film): $\tilde{\nu}$ = 2926, 1457, 1376, 1114, 1030 cm⁻¹; MS (70 eV, EI): *m/z* (%): 466 (5) [*M*]⁺, 421 (4), 393 (28), 261 (100); HRMS (EI): *m/z*: calcd for C₂₁H₃₈O₁₁: 466.2414 [*M*]⁺; found: 466.2397; elemental analysis calcd (%) for C₂₁H₃₈O₁₁ (466.52): C 54.07, H 8.21; found: C 54.14, H 8.31.

Compound 29: ¹H NMR (500 MHz, C₆D₆): *d* = 1.10 (d, *J* = 6.0 Hz, 3H), 1.23 (d, *J* = 6.3 Hz, 3H), 1.77 (s, 3H), 1.82 (s, 3H), 3.09 (s, 3H), 3.22 (s, 3H), 3.23 (s, 3H), 3.276 (s, 3H), 3.279 (s, 3H), 3.49 (dd, *J* = 8.3, 2.8 Hz, 1H), 3.51 (s, 3H), 3.62–3.64 (m, 1H), 3.64 (dd, *J* = 8.3, 3.1 Hz, 1H), 3.83 (dd, *J* = 3.4, 3.4 Hz, 1H), 3.93 (d, *J* = 3.1 Hz, 1H), 4.10 (d, *J* = 10.3 Hz, 1H), 4.12 (dd, *J* = 3.7, 1.7 Hz, 1H), 4.19 (d, *J* = 10.3 Hz, 1H), 4.34 (ddd, *J* = 7.1, 4.6, 1.1 Hz, 1H), 4.57 (m, 1H), 4.65 (dd, *J* = 11.7, 7.4 Hz, 1H), 4.78 (dd, *J* = 11.7, 4.6 Hz, 1H), 5.05 (d, *J* = 8.0 Hz, 1H), 5.33 ppm (d, *J* = 8.3 Hz, 1H).

Compound 30: ¹H NMR (500 MHz, C₆D₆): *d* = 1.29 (s, 3H), 1.55 (s, 3H), 3.14 (s, 3H), 3.19 (s, 3H), 3.22 (s, 3H), 3.23 (s, 3H), 3.27 (s, 3H), 3.41 (dd, *J* = 10.3, 1.7 Hz, 1H), 3.44 (s, 3H), 3.47 (dd, *J* = 3.7, 2.0 Hz, 1H), 3.53 (dd, *J* = 10.3, 4.3 Hz, 1H), 3.62 (m, 1H), 3.68 (dd, *J* = 3.1, 2.0 Hz, 1H), 3.74 (dd, *J* = 9.7, 9.7 Hz, 1H), 3.78 (ddd, *J* = 9.7, 5.1, 1.7 Hz, 1H), 3.95 (dd, *J* = 6.3, 6.3 Hz, 1H), 3.99 (dd, *J* = 12.8, 7.7 Hz, 1H), 4.04 (dd, *J* = 9.4, 3.4 Hz, 1H), 4.14 (dd, *J* = 12.5, 8.0 Hz, 1H), 4.52–4.60 (m, 1H), 5.26 (d, *J* = 2.0 Hz, 1H), 5.32 ppm (d, *J* = 2.0 Hz, 1H); ¹³C NMR (125.7 MHz, C₆D₆): mixture of 29 and 30: *d* = 20.5 (CH₃), 21.7 (CH₃), 22.3 (CH₃), 23.5 (CH₃), 23.9 (CH₃), 27.6 (CH₃), 57.0 (CH₃), 57.2 (CH₃), 58.5 (CH₃), 58.9 (2 × CH₃), 59.0 (2 × CH₃), 59.1 (2 × CH₃), 59.2 (CH₃), 59.4 (CH₃), 60.3 (CH₃), 60.9 (CH₂), 64.8 (CH₂), 71.2 (CH), 71.4 (CH), 71.5 (CH₂), 71.6 (CH), 72.1 (CH₂), 73.6 (CH), 75.1 (CH), 75.6 (CH), 76.8 (CH), 77.0

(CH), 77.1 (CH), 77.2 (CH), 77.7 (CH), 77.8 (CH), 77.9 (CH), 78.0 (CH), 79.3 (CH), 82.2 (CH), 94.5 (CH), 96.6 (CH), 99.9 (CH), 100.3 (CH), 102.1 (C), 104.6 (C), 168.6 (C), 170.0 ppm (C).

Reductive HAT of isopropyl 2,3,4,6-tetra-*O*-methyl- α -*D*-mannopyranosyl-(1 \rightarrow 4)-2,3-di-*O*-methyl-6-*O*-phthalimido-*b*-*D*-gulopyranoside (17)

Method A (*n*Bu₃SnH): Following the general procedure and by using *n*Bu₃SnH (1.5 mmol) and AIBN (0.2 mmol), the phthalimide 17 gave after column chromatography (hexanes/EtOAc 2:8) isopropyl 2,3,4,6-tetra-*O*-methyl-*b*-*D*-gulopyranosyl-(1 \rightarrow 4)-2,3-di-*O*-methyl-*b*-*D*-gulopyranoside (31) (80 %) as a colourless oil and the precursor alcohol 12 (13 %), described in the Supporting Information.

Compound 31: [α]_D = + 63.7 (*c* = 0.160 in CHCl₃); ¹H NMR (500 MHz, C₆D₆): *d* = 1.09 (d, *J* = 6.0 Hz, 3H), 1.19 (d, *J* = 6.0 Hz, 3H), 3.00 (s, 3H), 3.02 (dd, *J* = 3.9, 1.5 Hz, 1H), 3.10 (s, 3H), 3.20 (s, 3H), 3.278 (s, 3H), 3.281 (dd, *J* = 9.6, 1.8 Hz, 1H), 3.30 (s, 3H), 3.45 (dd, *J* = 8.1, 3.0 Hz, 1H), 3.51 (s, 3H), 3.57 (m, 1H), 3.58 (dd, *J* = 3.3, 3.3 Hz, 1H), 3.61 (dd, *J* = 8.0, 3.3 Hz, 1H), 3.72 (dd, *J* = 9.6, 6.0 Hz, 1H), 3.80 (dd, *J* = 3.3, 3.3 Hz, 1H), 3.89 (sep, *J* = 6.3 Hz, 1H), 4.00 (ddd, *J* = 10.8, 9.9, 5.4 Hz, 1H), 4.11 (m, 1H), 4.12 (dd, *J* = 4.2, 1.2 Hz, 1H), 4.23 (ddd, *J* = 9.3, 5.1, 1.2 Hz, 1H), 4.37 (ddd, *J* = 10.8, 9.9, 6.0 Hz, 1H), 4.97 (d, *J* = 8.1 Hz, 1H), 5.04 ppm (d, *J* = 8.1 Hz, 1H); ¹³C NMR (125.7 MHz, C₆D₆): *d* = 22.2 (CH₃), 24.0 (CH₃), 58.1 (CH₃), 58.7 (CH₃), 59.1 (CH₃), 59.4 (CH₃), 59.6 (CH₃), 59.8 (CH₃), 60.3 (CH₂), 71.1 (CH), 71.7 (CH₂), 72.6 (CH), 72.9 (CH), 75.2 (CH), 77.3 (CH), 77.8 (CH), 78.6 (CH), 78.9 (CH), 80.0 (CH), 99.6 (CH), 101.7 ppm (CH); IR (film): $\tilde{\nu}$ = 3505 (OH), 2928, 1371, 1097, 1052 cm⁻¹; MS (70 eV, EI): *m/z* (%): 408 (1) [M—(CH₃)₂CHOH]⁺, 261 (32), 219 (44), 187 (72), 88 (100); HRMS (EI): *m/z*: calcd for C₁₈H₃₂O₁₀: 408.1995 [M—(CH₃)₂CHOH]⁺; found: 408.2005; elemental analysis calcd (%) for C₂₁H₄₀O₁₁ (468.54): C 53.83, H 8.61; found: C 54.08, H 8.38.

Method B (*n*Bu₃SnD): Following the general procedure and by using *n*Bu₃SnD (1.5 mmol) and AIBN (0.2 mmol), the phthalimide 17 afforded after column chromatography (hexanes/EtOAc 2:8) isopropyl 2,3,4,6-tetra-*O*-methyl-*b*-*D*-(5¹-²H)gulopyranosyl-(1 \rightarrow 4)-2,3-di-*O*-methyl-*b*-*D*-gulopyranoside (32) (83 %) and isopropyl 2,3,4,6-tetra-*O*-methyl- α -*D*-(5¹-²H)mannopyranosyl-(1 \rightarrow 4)-2,3-di-*O*-methyl-*b*-*D*-gulopyranoside (33) (14 %), ¹H/²H ratio, 45:55, both as colourless oils.

Compound 32: ¹H NMR (400 MHz, C₆D₆): *d* = 1.09 (d, *J* = 6.0 Hz, 3H), 1.18 (d, *J* = 6.3 Hz, 3H), 3.00 (s, 3H), 3.01 (d, *J* = 3.7 Hz, 1H), 3.10 (s, 3H), 3.20 (s, 3H), 3.278 (s, 3H), 3.281 (d, *J* = 9.4 Hz, 1H), 3.30 (s, 3H), 3.45 (dd, *J* = 8.3, 3.1 Hz, 1H), 3.51 (s, 3H), 3.57 (d, *J* = 9.1 Hz, 1H), 3.58 (dd, *J* = 3.4, 3.4 Hz, 1H), 3.61 (dd, *J* = 8.0, 2.8 Hz, 1H), 3.74 (dd, *J* = 9.4, 6.0 Hz, 1H), 3.80 (dd, *J* = 3.4, 3.4 Hz, 1H), 3.89 (sep, *J* = 6.1 Hz, 1H), 4.00 (ddd, *J* = 10.8, 9.9, 5.4 Hz, 1H), 4.12 (dd, *J* = 3.7, 1.4 Hz, 1H), 4.23 (dd, *J* = 9.7, 5.3, 1.4 Hz, 1H), 4.36 (ddd, *J* = 10.6, 10.6, 5.7 Hz, 1H), 4.97 (d, *J* = 8.0 Hz, 1H), 5.04 ppm (d, *J* = 8.0 Hz, 1H); ¹³C NMR (125.7 MHz, C₆D₆): *d* = 22.2 (CH₃), 24.0 (CH₃), 58.1 (CH₃), 58.8 (CH₃), 59.1 (CH₃), 59.4 (CH₃), 59.6 (CH₃), 59.8 (CH₃), 60.3 (CH₂), 71.1 (CH), 71.606 (CH₂), 72.9 (CH), 75.2 (CH), 77.3 (CH), 77.734 (CH), 78.6 (CH), 78.9 (CH), 80.0 (CH), 99.6 (CH), 101.7 ppm (CH); MS (70 eV, EI): *m/z* (%): 409 (4) [M—(CH₃)₂CHOH]⁺, 306 (47), 261 (15), 188 (26), 88 (100); HRMS (EI): *m/z*: calcd for C₁₈H₃₁O₁₀: 409.2058 [M—(CH)₂CHOH]⁺; found: 409.2047.

Compound 33: ¹H NMR (500 MHz, C₆D₆): *d* = 1.07 (d, *J* = 6.0 Hz, 3H), 1.16 (d, *J* = 6.3 Hz, 3H), 3.06 (s, 3H), 3.17 (s, 3H), 3.23 (s, 3H), 3.26 (s, 3H), 3.29 (s, 3H), 3.37 (dd, *J* = 7.2, 6.0 Hz, 1H), 3.40–3.44 (m, 4H), 3.50 (s, 3H), 3.50–3.54 (m, 3H), 3.56 (dd, *J* = 7.8, 3.0 Hz, 1H), 3.60 (dd, *J* = 7.2, 2.9 Hz, 1H), 3.74 (dd, *J* = 3.3, 3.3 Hz, 1H), 3.88 (sep, *J* = 6.3 Hz, 1H), 3.97 (ddd, *J* = 11.1, 5.7, 5.7 Hz, 1H), 4.04 (m, 1H), 4.13 (m, 1H), 4.24 (ddd, *J* = 8.7, 5.6, 1.6 Hz, 1H), 4.26 (dd, *J* = 3.6, 1.2 Hz, 1H), 5.03 (d, *J* = 7.8 Hz, 1H), 5.13 ppm (d, *J* = 2.7 Hz, 1H); ¹³C NMR (125.7 MHz, C₆D₆): *d* = 22.1 (CH₃), 24.0 (CH₃), 57.7 (CH₃), 58.8 (CH₃), 59.1 (CH₃), 59.3 (CH₃), 59.4 (CH₃), 59.5 (CH₃), 60.4 (CH₂), 71.2 (CH), 72.2 (CH), 72.956 (CH₂), 73.017 (CH₂), 73.27 (CH), 73.32 (CH), 77.7 (CH), 77.870 (CH), 77.931 (CH), 79.0 (CH), 79.7 (CH), 81.3 (CH), 97.9 (CH), 100.0 ppm (CH); MS (70 eV, EI): *m/z* (%): 409/408 (< 1) [M—(CH₃)₂CHOH]⁺, 339 (8), 306 (3), 188 (28), 88 (100); HRMS (EI): *m/z*: calcd for C₁₈H₃₁²H₁₀/C₁₈H₃₂O₁₀: 409.2058/408.1995 [M—(CH₃)₂CHOH]⁺; found: 409.2058/408.1981.

Methyl (1*R*)-4-*O*-(2,3,4-tri-*O*-acetyl-*D*-rhamnopyranosylidene)-2,3-di-*O*-methyl- α -*D*-glucopyranoside (34): Following the general procedure for the oxidative HAT and by using in this case DIB (2.5 mmol), the alcohol 13 gave after chromatotron chromatography (hexanes/EtOAc 60:40) the title compound 34 (79 %) as a crystalline solid. M.p. 194.2–195.6 °C (*n*-hexane/EtOAc); [α]_D = + 40.6 (*c* = 0.315 in CHCl₃); ¹H NMR (500 MHz, CDCl₃): *d* = 1.28 (d, *J* = 6.3 Hz, 3H), 1.95 (s, 3H), 2.04 (s, 3H), 2.16 (s, 3H), 3.23 (dd, *J* = 8.9, 3.7 Hz, 1H), 3.40 (s, 3H), 3.53 (s, 3H), 3.55 (dd, *J* = 9.3, 9.3 Hz, 1H), 3.58 (dd, *J* = 9.3, 9.3 Hz, 1H), 3.64 (s, 3H), 3.74–3.79 (m, 2H), 3.88 (dd, *J* = 9.9, 5.1 Hz, 1H), 3.98 (dd, *J* = 10.4, 10.4 Hz, 1H), 4.80 (d, *J* = 3.7 Hz, 1H), 5.09 (dd, *J* = 9.9, 9.9 Hz, 1H), 5.27 (dd, *J* = 10.1, 3.5 Hz, 1H), 5.37 ppm (d, *J* = 3.5 Hz, 1H); ¹³C NMR (100.6 MHz, CDCl₃): *d* = 17.5 (CH₃), 20.6 (CH₃), 20.76 (CH₃), 20.79 (CH₃), 55.3 (CH₃), 59.6 (CH₃), 61.2 (CH₃), 61.6 (CH), 62.9 (CH₂), 68.4 (CH), 69.6 (CH), 70.0 (CH), 70.6 (CH), 73.5 (CH), 79.5 (CH), 81.4 (CH), 98.6 (CH), 108.1 (C), 169.7 (C), 169.89 (C), 169.94 ppm (C); IR (film): $\tilde{\nu}$ = 2916, 2839, 1754, 1373, 1222, 1092, 1044 cm⁻¹; MS (70 eV, EI): *m/z* (%): 492 (1) [M]⁺, 461 (3), 304 (44), 262 (27), 88 (100); HRMS (EI): *m/z*: calcd for C₂₁H₃₂O₁₃: 492.1843 [M]⁺; found: 492.1827; elemental analysis calcd (%) for C₂₁H₃₂O₁₃ (492.47): C 51.22, H 6.55; found: C 51.23, H 6.39.

Reductive HAT of methyl 2,3,4-Tri-*O*-acetyl- α -*D*-rhamnopyranosyl-(1 \rightarrow 4)-2,3-di-*O*-methyl-6-phthalimido- α -*D*-glucopyranoside (18)

Method A (*n*Bu₃SnH): Following the general procedure and by using *n*Bu₃SnH (2 mmol) and AIBN (0.2 mmol), the phthalimide 18 gave after column chromatography (hexanes/EtOAc 60:40:150:50) methyl 4-*O*-(2,3,4-tri-*O*-acetyl-5,6-dideoxy-*l*-*lyxo*-hexonoyl)-2,3-di-*O*-methyl- α -*D*-glucopyranoside (35) (48 %), methyl 6-*O*-(2,3,4-tri-*O*-acetyl-5,6-dideoxy-*l*-*lyxo*-hexonoyl)-2,3-di-*O*-methyl- α -*D*-glucopyranoside (36) (4 %), methyl 2,3,4-tri-*O*-acetyl-6-deoxy-*b*-*D*-mannopyranosyl-(1 \rightarrow 4)-2,3-di-*O*-methyl- α -*D*-glucopyranoside (37) (9 %) and the precursor alcohol 13 (8 %), described in the Supporting Information, all as colourless oils.

Compound 35: [α]_D = + 54.8 (*c* = 0.155 in CHCl₃); ¹H NMR (500 MHz, CDCl₃): *d* = 0.91 (t, *J* = 7.4 Hz, 3H), 1.61 (q, *J* = 7.4 Hz, 2H), 2.06 (s, 3H), 2.11 (s, 3H), 2.13 (s, 3H), 3.32 (dd, *J* = 9.6, 3.6 Hz, 1H), 3.43 (s, 3H), 3.49 (s, 3H), 3.51 (s, 3H), 3.59–3.70 (m, 3H), 3.63 (dd, *J* = 9.6, 9.6 Hz, 1H), 4.87 (d, *J* = 3.6 Hz, 1H), 4.91 (dd, *J* = 9.6, 9.6 Hz, 1H), 5.15 (d, *J* = 6.5 Hz, 1H), 5.20 (ddd, *J* = 6.4, 6.4, 4.4 Hz, 1H), 5.42 ppm (dd, *J* = 6.5, 4.2 Hz, 1H); ¹³C NMR (100.6 MHz, CDCl₃): *d* = 9.435 (CH₃), 20.4 (CH₃), 20.6 (CH₃), 20.7 (CH₃), 23.6 (CH₂), 55.4 (CH₃), 58.9 (CH₃), 60.1 (CH₃), 60.8 (CH₂), 69.4 (CH), 70.3 (CH), 71.0 (CH), 71.3 (CH), 72.034 (CH), 72.9 (CH), 81.5 (CH), 97.4 (CH), 167.4 (C), 169.6 (C), 170.1 (C), 170.2 ppm (C); IR (film): $\tilde{\nu}$ = 3500, 2938, 1748, 1373, 1220, 1048 cm⁻¹; MS (70 eV, EI): *m/z* (%): 463 (< 1) [M—C₂H₅]⁺, 434 (1), 403 (1), 231 (23), 101 (11), 88 (100); HRMS (EI): *m/z*: calcd for C₁₉H₂₇O₁₃: 463.1452 [M—C₂H₅]⁺; found: 463.1455; elemental analysis calcd (%) for C₂₁H₃₄O₁₃ (494.49): C 51.01, H 6.93; found: C 51.12, H 6.96.

Compound 36: [α]_D = + 40.7 (*c* = 0.290 in CHCl₃); ¹H NMR (500 MHz, CDCl₃): *d* = 0.91 (t, *J* = 7.2 Hz, 3H), 1.58–1.64 (m, 2H), 2.08 (s, 3H), 2.11 s, (3H), 2.13 (s, 3H), 3.00 (br s, 1H), 3.21 (dd, *J* = 9.2, 3.4 Hz, 1H), 3.43 (s, 3H), 3.44–3.47 (m, 2H), 3.51 (s, 3H), 3.64 (s, 3H), 3.75 (ddd, *J* = 7.6, 3.8, 1.9 Hz, 1H), 4.20 (dd, *J* = 11.8, 1.9 Hz, 1H), 4.54 (dd, *J* = 11.8, 4.2 Hz, 1H), 4.82 (d, *J* = 3.4 Hz, 1H), 5.14 (d, *J* = 6.9 Hz, 1H), 5.23 (ddd, *J* = 7.6, 6.1, 3.8 Hz, 1H), 5.40 ppm (dd, *J* = 7.2, 3.8 Hz, 1H); ¹³C NMR (100.6 MHz, CDCl₃): *d* = 9.5 (CH₃), 20.4 (CH₃), 20.6 (CH₃), 20.8 (CH₃), 23.7 (CH₂), 55.3 (CH₃), 58.7 (CH₃), 61.3 (CH₃), 64.5 (CH₂), 69.0 (CH), 69.7 (CH), 69.8 (CH), 71.1 (CH), 72.0 (CH), 81.7 (CH), 82.5 (CH), 97.6 (CH), 167.6 (C), 169.6 (C), 170.1 (C), 170.5 ppm (C); IR (film): $\tilde{\nu}$ = 3488, 2938, 1748, 1373, 1220, 1063 cm⁻¹; MS (70 eV, EI): *m/z* (%): 463 (1) [M—C₂H₅]⁺, 431 (2), 403 (1), 365 (16), 231 (34), 101 (22), 88 (100); HRMS (EI): *m/z*: calcd for C₁₉H₂₇O₁₃: 463.1452 [M—C₂H₅]⁺; found: 463.1444; elemental analysis calcd (%) for C₂₁H₃₄O₁₃ (494.49): C 51.01, H 6.93; found: C 51.22, H 6.83.

Compound 37 (contaminated with small amounts of alcohols 35 and 36): ¹H NMR (500 MHz, CDCl₃): *d* = 1.28 (d, *J* = 6.5 Hz, 3H), 1.99 (s, 3H), 2.05 (s, 3H), 2.15 (s, 3H), 3.19 (dd, *J* = 9.5, 3.8 Hz, 1H), 3.39 (s, 3H), 3.50 (s, 3H), 3.51–3.58 (m, 2H), 3.59 (s, 3H), 3.64–3.72 (m, 3H), 3.81–3.89 (m, 1H), 4.80 (d, *J* = 3.4 Hz, 1H), 4.98 (d, *J* = 0.8 Hz, 1H), 5.01 (dd, *J* = 10.3, 2.7 Hz, 1H), 5.03 (dd, *J* = 10.3, 10.3 Hz, 1H), 5.46 ppm (dd, *J* = 2.7,

0.8 Hz, 1H); ¹³C NMR (100.6 MHz, CDCl₃): δ = 17.2 (CH₃), 20.6 (CH₃), 20.7 (CH₃), 20.8 (CH₃), 55.2 (CH₃), 59.0 (CH₃), 61.3 (CH₃), 61.9 (CH₂, C-6), 69.0 (CH), 69.9 (CH), 70.4 (CH), 70.602 (CH), 70.9 (CH), 75.9 (CH), 82.3 (CH), 82.7 (CH), 97.6 (CH), 98.8 (CH), 169.8 (C), 170.0 (C), 170.1 ppm (C).

Method B (*n*Bu₃SnD): Following the general procedure and by using *n*Bu₃SnD (2 mmol) and AIBN (0.2 mmol), the phthalimide 18 afforded after column chromatography (hexanes/EtOAc 60:40!50:50) methyl 4-*O*-(2,3,4-tri-*O*-acetyl-5,6-dideoxy-1-(5-²H₁)*lyxo*-hexonoyl)-2,3-di-*O*-methyl- α -*D*-glucopyranoside (38) (28%), methyl 6-*O*-(2,3,4-tri-*O*-acetyl-5,6-dideoxy-1-(5-²H₁)*lyxo*-hexonoyl)-2,3-di-*O*-methyl- α -*D*-glucopyranoside (39) (36%), methyl 2,3,4-tri-*O*-acetyl-6-deoxy-*b*-1-(1-²H₁)mannopyranosyl-(114)-2,3-di-*O*-methyl- α -*D*-glucopyranoside (40) (7%), and the precursor alcohol 13 (7%), all as colourless oils.

Compound 38: ¹H NMR (500 MHz, CDCl₃): δ = 0.90 (d, *J* = 7.6 Hz, 3H), 1.59 (m, 1H), 2.07 (s, 3H), 2.12 (s, 3H), 2.14 (s, 3H), 2.41 (br s, 1H), 3.32 (dd, *J* = 9.5, 3.4 Hz, 1H), 3.44 (s, 3H), 3.50 (s, 3H), 3.51 (s, 3H), 3.59–3.69 (m, 3H), 3.64 (dd, *J* = 9.5, 9.5 Hz, 1H), 4.88 (d, *J* = 3.4 Hz, 1H), 4.91 (dd, *J* = 9.5, 9.5 Hz, 1H), 5.16 (d, *J* = 6.5 Hz, 1H), 5.20 (dd, *J* = 8.4, 4.2 Hz, 1H), 5.42 ppm (dd, *J* = 6.5, 4.2 Hz, 1H); ¹³C NMR (100.6 MHz, CDCl₃): δ = 9.360 (CH₃), 20.4 (CH₃), 20.6 (CH₃), 20.8 (CH₃), 23.4 (CH, *t*, *J*_{CD} = 19.0 Hz), 55.4 (CH₃), 58.9 (CH₃), 60.2 (CH₃), 60.9 (CH₂), 69.4 (CH), 70.3 (CH), 71.0 (CH), 71.4 (CH), 72.044 (CH), 79.7 (CH), 81.6 (CH), 97.5 (CH), 167.5 (C), 169.6 (C), 170.1 (C), 170.3 ppm (C); MS (70 eV, EI): *m/z* (%): 464 (< 1) [*M*–C₂H₅D]⁺, 435 (2), 404 (1), 232 (25), 101 (17), 88 (100); HRMS (EI): *m/z*: calcd for C₁₉H₂₈O₁₃: 464.1530 [*M*–C₂H₅D]⁺; found: 464.1544.

Compound 39: ¹H NMR (500 MHz, CDCl₃): δ = 0.89 (d, *J* = 7.3 Hz, 3H), 1.59 (dddd, *J* = 8.0, 8.0, 8.0, 8.0 Hz, 1H), 2.07 (s, 3H), 2.10 (s, 3H), 2.12 (s, 3H), 3.04 (br s, 1H), 3.20 (dd, *J* = 9.5, 3.4 Hz, 1H), 3.42 (s, 3H), 3.43–3.46 (m, 2H), 3.50 (s, 3H), 3.63 (s, 3H), 3.74 (ddd, *J* = 7.5, 3.9, 2.0 Hz, 1H), 4.19 (dd, *J* = 12.0, 2.0 Hz, 1H), 4.53 (dd, *J* = 12.0, 4.2 Hz, 1H), 4.81 (d, *J* = 3.5 Hz, 1H), 5.13 (d, *J* = 7.1 Hz, 1H), 5.21 (dd, *J* = 8.2, 3.7 Hz, 1H), 5.39 ppm (dd, *J* = 7.2, 3.7 Hz, 1H); ¹³C NMR (100.6 MHz, CDCl₃): δ = 9.3 (CH₃), 20.4 (CH₃), 20.6 (CH₃), 20.8 (CH₃), 23.3 (CH, *t*, *J*_{CD} = 20.0 Hz), 55.3 (CH₃), 58.6 (CH₃), 61.3 (CH₃), 64.5 (CH₂), 69.0 (CH), 69.7 (CH), 69.8 (CH), 71.1 (CH), 71.9 (CH), 81.7 (CH), 82.5 (CH), 97.6 (CH), 167.6 (C), 169.6 (C), 170.1 (C), 170.5 ppm (C); MS (70 eV, EI): *m/z* (%): 464 (< 1) [*M*–C₂H₅D]⁺, 432 (1), 403 (1), 366 (10), 232 (17), 101 (35), 88 (100); HRMS (EI): *m/z*: calcd for C₁₉H₂₈O₁₃: 464.1530 [*M*–C₂H₅D]⁺; found: 464.1510.

Compound 40 (contaminated with small amounts of alcohols 38 and 39): ¹H NMR (500 MHz, CDCl₃): δ = 1.28 (d, *J* = 6.1 Hz, 3H), 1.99 (s, 3H), 2.05 (s, 3H), 2.16 (s, 3H), 3.19 (dd, *J* = 9.5, 3.4 Hz, 1H), 3.40 (s, 3H), 3.50 (s, 3H), 3.51–3.58 (m, 2H), 3.59 (s, 3H), 3.64–3.72 (m, 3H), 3.80–3.89 (m, 1H), 4.80 (d, *J* = 3.4 Hz, 1H), 5.01 (dd, *J* = 10.3, 3.0 Hz, 1H), 5.03 (dd, *J* = 10.3, 10.3 Hz, 1H), 5.46 ppm (dd, *J* = 2.7 Hz, 1H); ¹³C NMR (100.6 MHz, CDCl₃): δ = 17.2 (CH₃), 20.6 (CH₃), 20.7 (CH₃), 20.8 (CH₃), 55.2 (CH₃), 58.9 (CH₃), 61.3 (CH₃), 62.0 (CH₂), 68.9 (CH), 69.9 (CH), 70.4 (CH), 70.570 (CH), 70.9 (CH), 75.9 (CH), 82.3 (CH), 82.7 (CH), 97.7 (CH), 169.8 (C), 170.0 (C), 170.1 ppm (C).

Methyl (1*S*)-4,6-*O*-(2,3,4,6-tetra-*O*-acetyl- α -*D*-mannopyranosylidene)-2,3-di-*O*-methyl- α -*D*-galactopyranoside (41): Following the general procedure for the oxidative HAT, the alcohol 14 gave after chromatotron chromatography (hexanes/EtOAc 45:55) the title compound 41 (95%) as a crystalline solid. M.p. 183–184°C (*n*-hexane/EtOAc); [α]_D²⁰ = + 81.1 (*c* = 0.460 in CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ = 1.95 (s, 3H), 2.04 (s, 3H), 2.07 (s, 3H), 2.15 (s, 3H), 3.40 (s, 3H), 3.48 (s, 3H), 3.54 (s, 3H), 3.59 (dd, *J* = 10.0, 3.4 Hz, 1H), 3.61 (m, 1H), 3.68 (dd, *J* = 10.1, 3.4 Hz, 1H), 3.82 (ddd, *J* = 10.1, 5.6, 2.6 Hz, 1H), 3.86 (dd, *J* = 12.2, 1.6 Hz, 1H), 4.15 (dd, *J* = 12.2, 2.6 Hz, 1H), 4.26–4.30 (m, 3H), 4.90 (d, *J* = 3.4 Hz, 1H), 5.27 (dd, *J* = 10.0, 10.0 Hz, 1H), 5.39 (dd, *J* = 10.1, 3.4 Hz, 1H), 5.46 ppm (d, *J* = 3.4 Hz, 1H); ¹³C NMR (100.6 MHz, CDCl₃): δ = 20.6 (CH₃), 20.7 (2 × CH₃), 20.8 (CH₃), 55.5 (CH₃), 58.1 (CH₃), 59.2 (CH₃), 61.6 (CH), 62.6 (CH₃), 63.2 (CH₃), 65.7 (CH), 66.0 (CH), 69.5 (CH), 70.0 (CH), 70.3 (CH), 76.7 (CH), 76.9 (CH), 98.4 (CH), 108.3 (C), 169.7 (C), 169.7 (2 × C), 170.5 ppm (C); IR (film): $\tilde{\nu}$ = 2935, 2834, 1747, 1372, 1223, 1046 cm⁻¹; MS (70 eV, EI): *m/z* (%): 519 (2) [*M*–CH₃O]⁺, 477 (11), 389 (13), 304

(15), 88 (100); HRMS (EI): *m/z*: calcd for C₂₂H₃₁O₁₄: 519.1714 [*M*–CH₃O]⁺; found: 519.1738; elemental analysis calcd (%) for C₂₂H₃₁O₁₅ (550.51): C 50.18, H 6.23; found: C 50.05, H 6.09.

Reductive HAT of methyl 2,3,4,6-tetra-*O*-acetyl- α -*D*-mannopyranosyl-(114)-2,3-di-*O*-methyl-6-*O*-phthalimido- α -*D*-galactopyranoside (19)

Method A (*n*Bu₃SnH): Following the general procedure and by using *n*Bu₃SnH (2.4 mmol) and AIBN (0.4 mmol), the phthalimide 19 gave after column chromatography (hexanes/EtOAc 30:70) methyl 4-*O*-(2,3,4,6-tetra-*O*-acetyl-5-deoxy-*D*-*lyxo*-hexonoyl)-2,3-di-*O*-methyl- α -*D*-galactopyranoside (42) (52%), and a mixture of two compounds that under standard acetylation and further chromatotron chromatography (hexanes/EtOAc 40:60) yielded methyl 2,3,4,6-tetra-*O*-acetyl- α -*D*-mannopyranosyl-(114)-6-*O*-acetyl-2,3-di-*O*-methyl- α -*D*-galactopyranoside (43) (19%) and methyl 2,3,4,6-tetra-*O*-acetyl-*b*-*D*-mannopyranosyl-(114)-6-*O*-acetyl-2,3-di-*O*-methyl- α -*D*-galactopyranoside (44) (6%), both as colourless oils.

Compound 42: [α]_D²⁰ = + 54.8 (*c* = 0.023 in CHCl₃); ¹H NMR (500 MHz, CDCl₃): δ = 1.85–1.96 (m, 2H), 2.04 (s, 3H), 2.08 (s, 3H), 2.14 (s, 6H), 2.42 (dd, *J* = 6.5, 6.5 Hz, 1H), 3.36 (s, 3H), 3.43 (s, 3H), 3.48 (dd, *J* = 10.0, 3.7 Hz, 1H), 3.51 (s, 3H), 3.64 (dd, *J* = 10.0, 3.4 Hz, 1H), 3.63–3.70 (m, 2H), 3.95 (ddd, *J* = 7.0, 7.0, 0 Hz, 1H), 4.07 (ddd, *J* = 11.4, 6.0, 6.0 Hz, 1H), 4.10 (ddd, *J* = 11.4, 7.4, 5.7 Hz, 1H), 4.90 (d, *J* = 3.7 Hz, 1H), 5.15 (d, *J* = 6.8 Hz, 1H), 5.46 (dd, *J* = 6.8, 3.7 Hz, 1H), 5.49 (ddd, *J* = 10.3, 4.0, 4.0 Hz, 1H), 5.53 ppm (dd, *J* = 3.4, 0 Hz, 1H); ¹³C NMR (125.7 MHz, CDCl₃): δ = 20.4 (CH₃), 20.70 (CH₃), 20.75 (CH₃), 20.8 (CH₃), 20.8 (CH₃), 55.5 (CH₃), 57.6 (CH₃), 59.1 (CH₃), 60.190 (CH₃), 60.4 (CH₃), 68.1 (CH), 68.5 (CH), 69.218 (CH), 70.2 (CH), 71.3 (CH), 77.4 (2 × CH), 98.0 (CH), 167.8 (C), 169.7 (C), 170.0 (2 × C), 170.8 ppm (C); IR (film): $\tilde{\nu}$ = 3499, 2924, 1746, 1372, 1218 cm⁻¹; MS (70 eV, EI): *m/z* (%): 535 (34) [*M*–OH]⁺, 521 (26), 331 (22), 289 (34), 88 (100); HRMS (EI): *m/z*: calcd for C₂₃H₃₅O₁₄: 535.2027 [*M*–OH]⁺; found: 535.2031; elemental analysis calcd (%) for C₂₃H₃₆O₁₅ (552.52): C 50.00, H 6.57; found: C 50.00, H 6.83.

Compound 43: [α]_D²⁰ = + 81.6 (*c* = 0.024 in CHCl₃); ¹H NMR (500 MHz, CDCl₃): δ = 2.01 (s, 3H), 2.04 (s, 3H), 2.06 (s, 3H), 2.11 (s, 3H), 2.16 (s, 3H), 3.42 (s, 3H), 3.48 (s, 3H), 3.52 (s, 3H), 3.54 (dd, *J* = 10.1, 2.8 Hz, 1H), 3.62 (dd, *J* = 10.4, 3.5 Hz, 1H), 3.89 (ddd, *J* = 6.9, 6.9, 0 Hz, 1H), 4.06 (dd, *J* = 12.3, 2.2 Hz, 1H), 4.08 (dd, *J* = 11.0, 7.6 Hz, 1H), 4.11 (dd, *J* = 2.8, 0 Hz, 1H), 4.33 (dd, *J* = 11.3, 6.6 Hz, 1H), 4.36 (dd, *J* = 12.6, 3.5 Hz, 1H), 4.51 (ddd, *J* = 9.8, 3.1, 3.1 Hz, 1H), 4.917 (d, *J* = 1.6 Hz, 1H), 4.919 (d, *J* = 3.5 Hz, 1H), 5.18 (dd, *J* = 3.1, 1.9 Hz, 1H), 5.34–5.40 ppm (m, 2H); ¹³C NMR (125.7 MHz, CDCl₃): δ = 20.72 (2 × CH₃), 20.75 (CH₃), 20.8 (CH₃), 20.9 (CH₃), 55.4 (CH₃), 58.3 (CH₃), 58.4 (CH₃), 61.8 (CH₂), 62.1 (CH₂), 65.8 (CH), 67.4 (CH), 68.7 (CH), 68.8 (CH), 70.1 (CH), 74.9 (CH), 77.0 (CH), 78.5 (CH), 97.6 (CH), 98.8 (CH), 169.7 (C), 169.9 (C), 170.2 (C), 170.3 (C), 170.8 ppm (C); IR (film): $\tilde{\nu}$ = 2930, 2845, 1748, 1229 cm⁻¹; MS (70 eV, EI): *m/z* (%): 594 (< 1) [*M*]⁺, 503 (< 1), 492 (< 1), 331 (46), 169 (36), 88 (100); HRMS (EI): *m/z*: calcd for C₂₅H₃₈O₁₆: 594.2160 [*M*]⁺; found: 594.2156; elemental analysis calcd (%) for C₂₅H₃₈O₁₆ (594.56): C 50.50, H 6.44; found: C 50.49, H 6.41.

Compound 44: [α]_D²⁰ = + 0.071 (*c* = 0.206 in CHCl₃); ¹H NMR (500 MHz, CDCl₃): δ = 2.00 (s, 3H), 2.04 (s, 3H), 2.06 (s, 3H), 2.09 (s, 3H), 2.18 (s, 3H), 3.38 (s, 3H), 3.50 (s, 3H), 3.51 (s, 3H), 3.54–3.58 (m, 2H), 3.61 (ddd, *J* = 10.1, 5.4, 2.8 Hz, 1H), 3.89 (ddd, *J* = 7.8, 3.8, 0.9 Hz, 1H), 4.14 (dd, *J* = 12.0, 7.9 Hz, 1H), 4.18 (dd, *J* = 12.0, 5.4 Hz, 1H), 4.20 (m, 1H), 4.23 (dd, *J* = 11.7, 4.1 Hz, 1H), 4.24 (dd, *J* = 12.0, 3.5 Hz, 1H), 4.83 (d, *J* = 2.8 Hz, 1H), 4.99 (d, *J* = 0.9 Hz, 1H), 5.06 (dd, *J* = 10.1, 3.5 Hz, 1H), 5.22 (dd, *J* = 10.1, 10.1 Hz, 1H), 5.53 ppm (dd, *J* = 3.5, 0.9 Hz, 1H); ¹³C NMR (125.7 MHz, CDCl₃): δ = 20.6 (CH₃), 20.7 (2 × CH₃), 20.77 (CH₃), 20.80 (CH₃), 55.2 (CH₃), 58.9 (CH₃), 59.1 (CH₃), 62.6 (CH₂), 64.2 (CH₂), 66.5 (CH), 68.0 (CH), 68.742 (CH), 71.0 (CH), 72.0 (CH), 72.3 (CH), 77.8 (CH), 79.9 (CH), 97.7 (CH), 97.9 (CH), 169.6 (C), 170.0 (C), 170.4 (C), 170.6 (C), 170.7 ppm (C); IR (film): $\tilde{\nu}$ = 2928, 2842, 1746, 1370, 1227 cm⁻¹; MS (70 eV, EI): *m/z* (%): 594 (< 1) [*M*]⁺, 563 (< 1), 531 (< 1), 492 (2), 417 (2), 328 (88), 88 (100); HRMS (EI): *m/z*: calcd for C₂₅H₃₈O₁₆: 594.2160 [*M*]⁺; found: 594.2176; elemental analysis calcd (%) for C₂₅H₃₈O₁₆ (594.56): C 50.50, H 6.44; found: C 50.46, H 6.31.

Method B (*n*Bu₃SnD): Following the general procedure and by using *n*Bu₃SnD (2.4 mmol) and AIBN (0.4 mmol), the phthalimide 19 gave

after chromatotron chromatography (hexanes/EtOAc 30:70) methyl 4-O-(2,3,4,6-tetra-O-acetyl-5-deoxy-d-(5-²H)lyxo-hexonoyl)-2,3-di-O-methyl- α -d-galactopyranoside (45) (57 %) and a mixture of two compounds that under standard acetylation and further chromatotron chromatography (hexanes/EtOAc 30:70) yielded methyl 2,3,4,6-tetra-O-acetyl- α -d-mannopyranosyl-(1 \rightarrow 4)-6-O-acetyl-2,3-di-O-methyl- α -d-galactopyranoside (43) (12 %) and methyl 2,3,4,6-tetra-O-acetyl- β -d-(1-²H)mannopyranosyl-(1 \rightarrow 4)-6-O-acetyl-2,3-di-O-methyl- α -d-galactopyranoside (46) (2 %), both as colourless oils.

Compound 45: ¹H NMR (500 MHz, CDCl₃): δ = 1.85–1.95 (m, 1H), 2.04 (s, 3H), 2.08 (s, 3H), 2.14 (s, 6H), 2.45 (dd, J = 6.6, 6.6 Hz, 1H), 3.36 (s, 3H), 3.43 (s, 3H), 3.48 (dd, J = 10.0, 3.7 Hz, 1H), 3.50 (s, 3H), 3.63 (dd, J = 10.0, 3.4 Hz, 1H), 3.64–3.70 (m, 2H), 3.95 (ddd, J = 6.9, 6.9 Hz, 1H), 4.07 (dd, J = 11.4, 6.0 Hz, 1H), 4.10 (dd, J = 11.1, 6.0 Hz, 1H), 4.90 (d, J = 3.7 Hz, 1H), 5.15 (d, J = 6.8 Hz, 1H), 5.46 (dd, J = 6.6, 3.7 Hz, 1H), 5.48 (dd, J = 6.0, 4.0 Hz, 1H), 5.53 ppm (dd, J = 2.8, 0 Hz, 1H); ¹³C NMR (100.6 MHz, CDCl₃): δ = 20.4 (CH₃), 20.67 (CH₃), 20.72 (CH₃), 20.8 (CH₃), 29.6 (CHD, t, J_{CD} = 21.2 Hz), 55.4 (CH₃), 57.6 (CH₃), 59.1 (CH₃), 60.092 (CH₂), 60.3 (CH₂), 68.0 (CH), 68.4 (CH), 69.143 (CH), 70.1 (CH), 71.3 (CH), 77.32 (CH), 77.36 (CH), 97.9 (CH), 167.7 (C), 169.7 (C), 169.97 (C), 170.00 (C), 170.8 ppm (C); MS (70 eV, EI): m/z (%): 536 (10) [M—OH]⁺, 522 (11), 322 (19), 290 (41), 88 (100); HRMS (EI): m/z : calcd for C₂₃H₃₄^2HO₁₄: 536.2090 [M—OH]⁺; found: 536.2109.

Compound 46 (contaminated with small amounts of 43): ¹H NMR (400 MHz, CDCl₃): δ = 2.00 (s, 3H), 2.04 (s, 3H), 2.06 (s, 3H), 2.09 (s, 3H), 2.18 (s, 3H), 3.38 (s, 3H), 3.50 (s, 3H), 3.51 (s, 3H), 3.54–3.58 (m, 2H), 3.61 (m, 1H), 3.90 (m, 1H), 4.12–4.25 (m, 5H), 4.83 (d, J = 2.6 Hz, 1H), 5.05 (dd, J = 10.0, 3.4 Hz, 1H), 5.21 (dd, J = 10.1, 10.1 Hz, 1H), 5.53 ppm (d, J = 3.4 Hz, 1H); ¹³C NMR (100.6 MHz, CDCl₃): δ = 20.6 (CH₃), 20.7 (2 \times CH₃), 20.76 (CH₃), 20.79 (CH₃), 55.2 (CH₃), 58.9 (CH₃), 59.1 (CH₃), 62.6 (CH₂), 64.2 (CH₂), 66.5 (CH), 68.0 (CH), 68.666 (CH), 71.0 (CH), 71.9 (CH), 72.2 (CH), 77.8 (CH), 79.8 (CH), 97.8 (CH), 169.7 (C), 170.1 (C), 170.4 (C), 170.68 (C), 170.71 ppm (C).

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