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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-Glc*p*-(1→4)-β-D-Glc*p*, α-L-Rham*p*-(1→4)-α-D-Gal*p* or α-D-Man*p*-(1→4)-β-L-Gul*p* skeletons led exclusively to the abstraction of the hydrogen from H–C-5′ and the formation, through a nine-membered transition state, of a 1,3,5-trioxocane ring system in a stable boat–chair conformation. Notwithstanding, derivatives of α-L-Rham*p*-(1→4)-α-D-Glc*p* or α-D-Man*p*-(1→4)-α-D-Gal*p* exclusively abstract the hydrogen from H–C-1′ through a seven-membered transition state and, therefore, lead to an interglycosidic spiro *ortho* ester.

Keywords: carbohydrates · disaccharides · esters · radical reactions · trioxocane

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 Csp^3-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 alkoxyl 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 alkoxyl radical and the hydrogen atom to be abstracted.[8] These requisites can be found in (1→4)-*O*-disaccharide systems, such as peracetylated β-maltose and methyl β-maltoside, in accord with previously reported X-ray crystallographic[9] and molecular mechanics[10] analysis, respectively. This β-maltose unit has a preferred conformation centred around the *exo*-anomeric effect and a *syn* geometry of the glycosidic bond ($\Phi=-34.2$, $\Psi=-28.3°$) and a C-6–O···H–C-5′ distance of 2.5 Å.[11] A study of the transition state of the C-6–O···H–C-5′ HAT reaction gave a similar situation around the glycosi-

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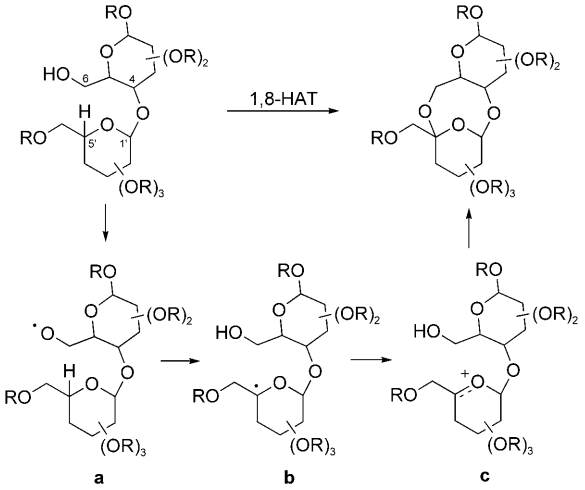
dic torsion angles ($\Phi = -32.7$, $\Psi = -37.3°$) and a distance of 3.14 Å between the alkoxyl radical and H–C-5′.[12]

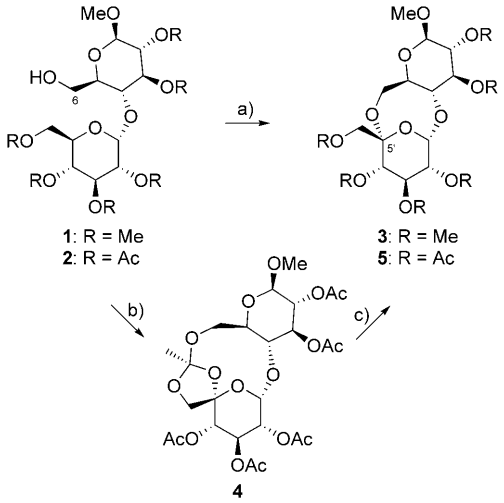
Based on these data, we decided to investigate the intramolecular 1,8-hydrogen-atom transfer reaction between the two pyranose units in suitably substituted (1→4)-*O*-disaccharides. As depicted in Scheme 1, under oxidative conditions, the electrophilic 6-*O*-yl radical (**a**) generated from the corresponding 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.



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

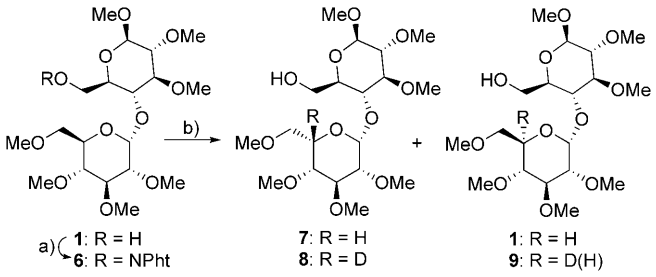
Results and Discussion

Firstly, to examine the viability of the process, we prepared the known β-maltose derivatives **1**[14] and **2**[15] (Scheme 2). The C-6 alkoxyl 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-tetraoxecane 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 acidic conditions with concomitant ring contraction to afford the desired 1,3,5-trioxocane derivative **5** in quantitative yield.



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

To achieve additional insight into the HAT reaction mechanism, the alkoxyl radical was also generated under reductive conditions by reaction of a *N*-hydroxyphthalimide derivative with the nBu$_3$SnH/AIBN or nBu$_3$SnD/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** with nBu$_3$SnH/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.



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

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 β-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 ^{1}H 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]

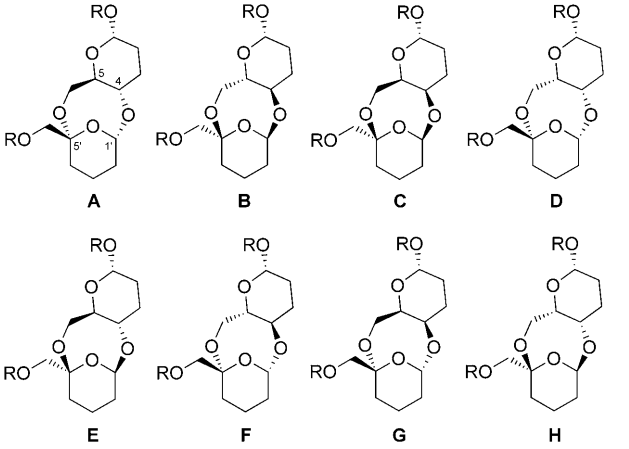
To clarify the HAT mechanism, the reduction of the phthalimide **6** was also accomplished with nBu$_3$SnD, affording compound **8** with complete deuteration at C-5′ and compound **9**, which showed 57% of deuterium labelling, the reduction of the 6-*O*-yl radical consequently being responsible for 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 β-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 ($\Delta E \leq 1.5$ kcal mol^{-1}) as shown in Table 1. Among them can be identified two pairs of diastereoisomers, **A**–**B** and **C**–**D**, with very similar energies ($\Delta\Delta E \leq 0.4$ kcal mol^{-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 kcal mol^{-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 erythromicin[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 β-maltose derivatives,

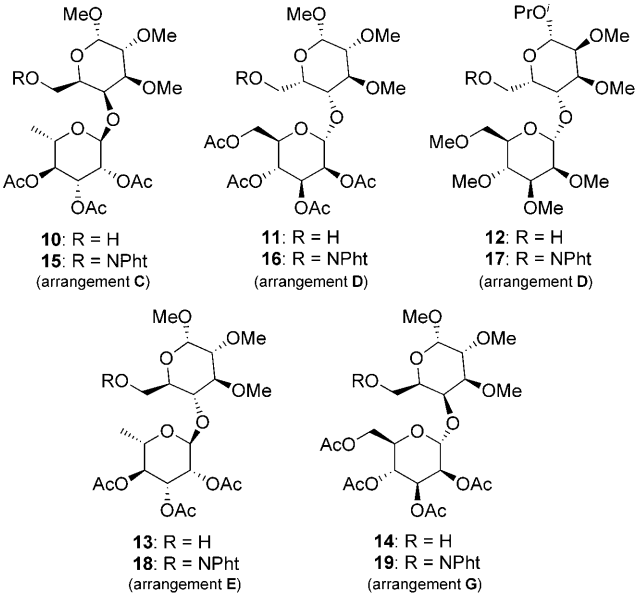
Table 1. Conformations of the 1,3,5-trioxocane ring.[a]



Arrangement	C-5′	C-1′	C-4	C-5	Conformation	ΔE [kcal mol^{-1}]
A[b]	*S*	*S*	*S*	*R*	boat–chair	0
B	*R*	*R*	*R*	*S*	boat–chair	0.3
C	*R*	*R*	*R*	*R*	boat–chair	1.1
D	*S*	*S*	*S*	*S*	boat–chair	1.5
E	*R*	*R*	*S*	*R*	boat–boat	3.3
F	*S*	*S*	*R*	*S*	boat–boat	3.9
G	*S*	*S*	*R*	*R*	crown ether	6.3
H	*R*	*R*	*S*	*S*	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] β-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-Rham*p*-(1→4)-α-D-Gal*p* **10**, α-D-Man*p*-(1→4)-β-L-Ido*p* **11** and α-D-Man*p*-(1→4)-β-L-Gul*p* **12** which, after a HAT reaction, could provide structural arrangements **C** and **D**, both slightly more energetic than β-maltose. Addi-

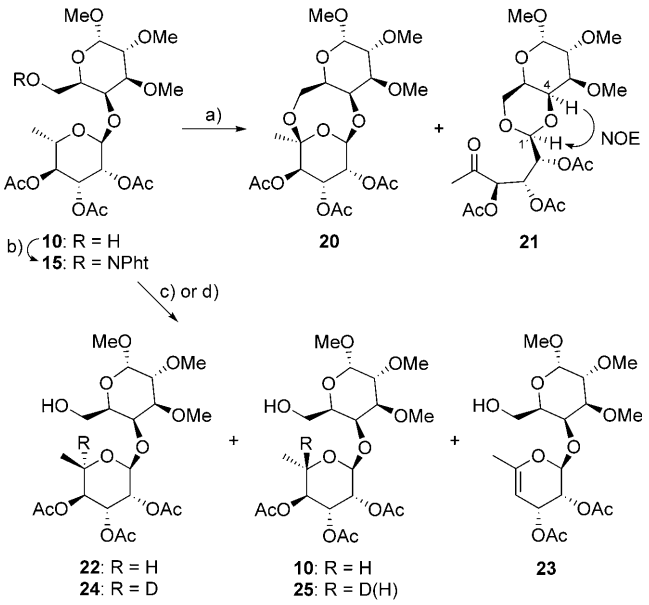


tionally, we have also prepared disaccharides α-L-Rham*p*-(1→4)-α-D-Glc*p* **13** and α-D-Man*p*-(1→4)-α-D-Gal*p* **14** in which the 1,8-hydrogen-atom transfer would lead to the energetically disfavoured arrangements **E** and **G**, respectively.

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-Rham*p*-(1→4)-α-D-Gal*p* **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), CH_2Cl_2, reflux, 1.5 h, **20** (88%), **21** (10%); b) DEAD (2.5 equiv), *N*-hydroxyphthalimide (2.5 equiv), PPh_3 (2.5 equiv), THF, 0 °C, 1.5 h, 84%, c) nBu$_3$SnH (1 equiv), AIBN (0.1 equiv), PhH, reflux, 1.5 h, **22** (52%), **10** (22%), **23** (5%); d) nBu$_3$SnD (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 nBu$_3$SnH/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-β-D-gulopyranosyl derivative, the pyranose ring changing from a $^1C_4$ to a $^4C_1$ conformation, as deduced from NMR spectroscopic data.

Repetition of the reduction of phthalimide **15** by using nBu$_3$SnD 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 β-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 $^4C_1$ conformation (Figure 1), so the 1,8 abstraction should be disfavoured versus a 1,6-HAT reaction.

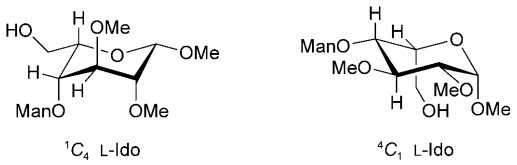
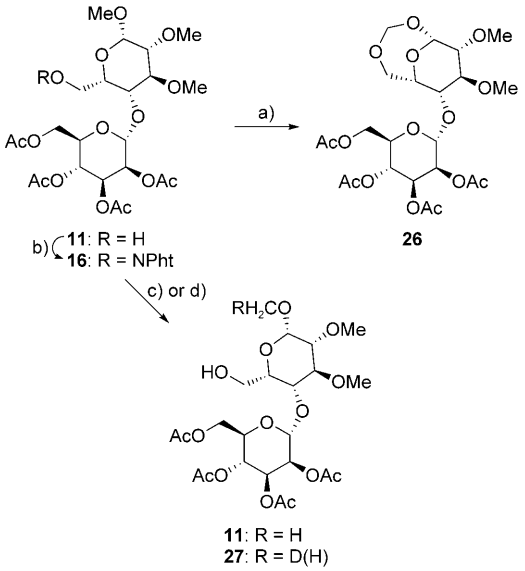


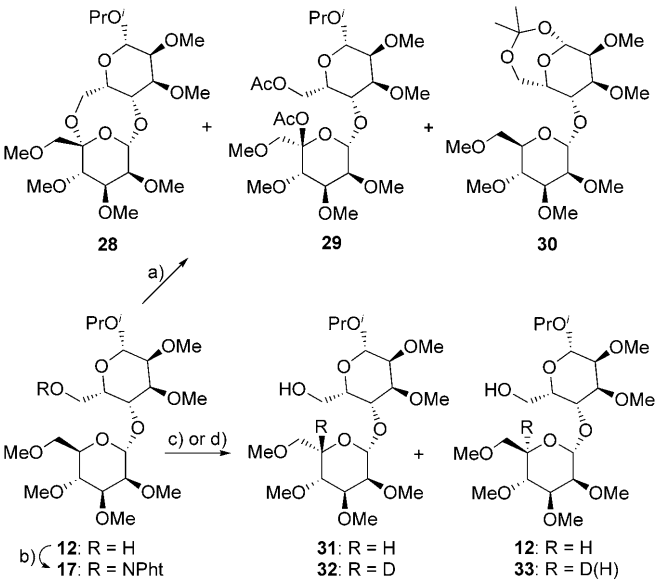
Figure 1. Chair conformations for the L-idose moiety in **11**.

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 nBu$_3$SnH/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, *hν*, RT, 2 h, 62%; b) DEAD (2.5 equiv), *N*-hydroxyphthalimide (2.5 equiv), PPh_3 (2.5 equiv), THF, 0°C, 3 h, 61%, c) nBu$_3$SnH (1.5 equiv), AIBN (0.2 equiv), PhH, reflux, 1 h, 55%; d) nBu$_3$SnD (3 equiv), AIBN (0.2 equiv), PhH, reflux, 2 h, 54%, D/H, 7:3.



Scheme 6. HAT study of arrangement **D**. a) DIB (1.7 equiv), iodine (1 equiv), CH_2Cl_2, *hν*, RT, 1.5 h; then Ac_2O, 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, 0°C→RT, 3 h, 49%; c) nBu$_3$SnH (1.5 equiv), AIBN (0.2 equiv), PhH, reflux, 1 h, **31** (80%), **12** (13%); d) nBu$_3$SnD (1.5 equiv), AIBN (0.2 equiv), PhH, reflux, 1 h, **32** (83%), **33** (14%, D/H 55:45).

nBu$_3$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 $^4C_1$ 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 $^1C_4$ 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}H NMR spectra showed that the D-mannopyranose ring had been inverted to a $^1C_4$ 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 H_2-6′.

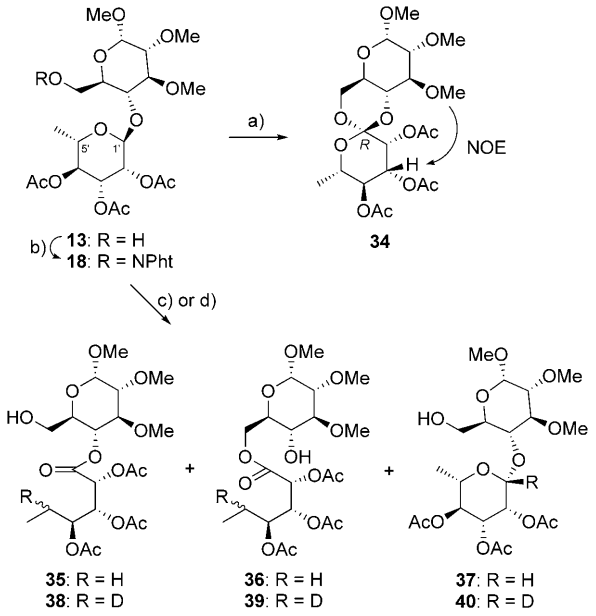
The results suggest that the abstraction at C-5′ (compounds **28** and **29**), through a nine-membered transition state, competes favourably with the abstraction of the hydrogen atom of the isopropyl group (compound **30**) through an eight-membered TS in a ratio of C-5′/C–*i*Pr 75:25, which indicates a conformational change from $^1C_4$ to $^4C_1$ of the L-gulose ring during the process.

On the other hand, the reduction of phthalimide **17** by treatment with nBu$_3$SnH/AIBN led preferentially to the inverted alcohol **32** together with a small amount of the precursor **12**. Repetition of the experiment with nBu$_3$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.

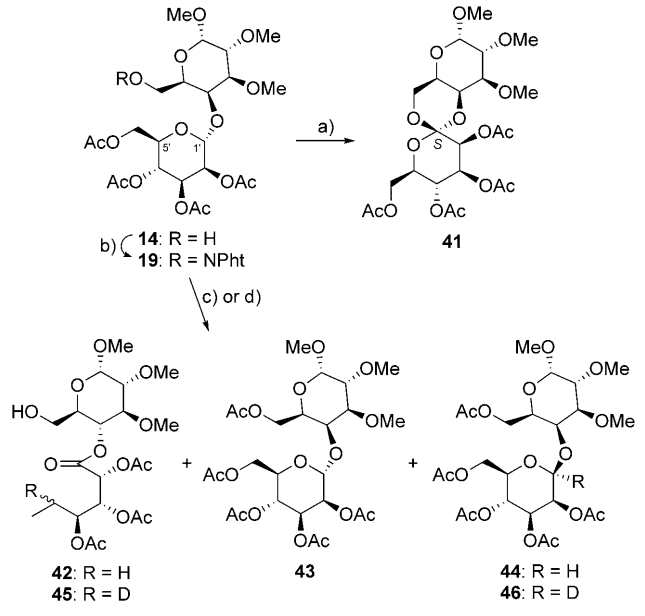
The difference in behaviour observed between the oxidative and reductive conditions could be due to the fact that the alkoxyl radical is being generated under two different processes, especially in terms of temperature. This fact together with the different rates of the HAT reactions and the inversion 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-Rham*p*-(1→4)-α-D-Glc*p* **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, *hv*, RT, 2.5 h, 79%; b) DEAD (2.5 equiv), *N*-hydroxyphthalimide (2.5 equiv), PPh_3 (2.5 equiv), THF, 0°C, 1 h, 94%, c) nBu_3SnH (2 equiv), AIBN (0.2 equiv), PhH, reflux, 2 h, **35** (48%), **36** (4%), **37** (9%), **13** (8%); d) nBu_3SnD (2 equiv), AIBN (0.2 equiv), PhH, reflux, 3 h, **38** (28%), **39** (36%), **40** (7%), **13** (7%).



Scheme 8. HAT study of arrangement **G**. a) DIB (1.7 equiv), iodine (1 equiv), CH_2Cl_2, *hv*, RT, 1 h, 95%; b) DEAD (2.5 equiv), *N*-hydroxyphthalimide (2.5 equiv), PPh_3 (2.5 equiv), THF, 0°C, 3 h, 96%, c) nBu_3SnH (2.4 equiv), AIBN (0.4 equiv), PhH, reflux, 2.5 h, **42** (52%); then Ac_2O, Py, **43** (19%), **44** (6%); d) nBu_3SnD (2 equiv), AIBN (0.4 equiv), PhH, reflux, 2.5 h, **45** (57%); then Ac_2O, Py, **43** (12%), **46** (2%).

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 nBu_3SnH, 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 β-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 nBu_3SnD. 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-Man*p*-(1→4)-α-D-Gal*p* **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 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 nBu_3SnH 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 β-fragmentation of the C-5′–O bond followed by radical-stannane quenching.

In addition, the reduction with nBu_3SnD 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→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-Man*p*-(1→

4)-β-L-Ido*p* and α-D-Man*p*-(1→4)-β-L-Gul*p* (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 $CHCl_3$ solutions. IR spectra were recorded in film unless otherwise stated. NMR spectra were determined at 500 MHz for ^1H and 125.7 MHz for ^{13}C in $CDCl_3$ 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 PF_{254} 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 H_2SO_4/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 CH_2Cl_2 (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 $Na_2S_2O_3$ and extracted with CH_2Cl_2, dried over Na_2SO_4 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*Bu_3SnH/*n*Bu_3SnD 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 CH_3CN, 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→4)-2,3-di-*O*-methyl-β-D-galactopyranoside (3): Following the general procedure for oxidative HAT and by using in this case dry CH_2Cl_2 (50 mL), the alcohol **1** afforded after column chromatography (hexanes/EtOAc 4:6) the title compound **3** (56%) as a syrup. $[\alpha]_D=+45.5$ ($c=0.83$ in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): $\delta=2.93$ (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, C_6D_6): $\delta=3.25$ (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); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta=57.0$ (CH_3), 58.0 (CH_3), 59.3 (CH_3), 60.5 (CH_3), 60.9 (CH_3), 61.1 (CH_3), 61.5 (CH_3), 64.5 (CH_2), 69.7 (CH), 71.4 (CH_2), 79.1 (2×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 $C_{19}H_{34}O_{11}$: 438.2101 $[M]^+$; found: 438.2088; elemental analysis calcd (%) for $C_{19}H_{34}O_{11}$ (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 CH_2Cl_2 (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 °C (*n*-pentane/EtOAc); $[\alpha]_D=-3.0$ ($c=0.220$ in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): $\delta=1.56$ (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, C_6D_6): $\delta=1.47$ (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); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta=20.3$ (CH_3), 20.4 (CH_3), 20.5 (CH_3), 20.6 (CH_3), 21.0 (CH_3), 22.5 (CH_3), 56.7 (CH_3), 64.2 (CH_2), 66.9 (CH), 68.0 (CH), 70.3 (CH), 72.4 (CH_2), 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); ^{13}C NMR (125.7 MHz, C_6D_6): $\delta=19.9$ (CH_3), 20.1 (CH_3), 20.2 (CH_3), 20.4 (CH_3), 20.9 (CH_3), 23.0 (CH_3), 56.0 (CH_3), 65.0 (CH_2), 67.5 (CH), 68.5 (CH), 70.8 (CH), 72.5 (CH_2), 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×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 $C_{25}H_{34}O_{17}Na$: 629.1694 $[M+Na]^+$; found: 629.1667; elemental analysis calcd (%) for $C_{25}H_{34}O_{17}$ (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→4)-2,3-di-*O*-methyl-β-D-galactopyranoside (5): A solution of orthoacetate **4** (15 mg, 0.025 mmol) in $CDCl_3$ (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. $[\alpha]_D=-14.5$ ($c=0.220$ in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): $\delta=2.00$ (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); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta=20.4$ (CH_3), 20.5 (CH_3), 20.6 (2 × CH_3), 20.7 (CH_3), 21.0 (CH_3), 57.2 (CH_3), 60.5 (CH_2), 65.6 (CH), 65.6 (CH_2), 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×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) $[M-CH_3]^+$, 546 (<1), 533 (11), 505 (5), 491 (9); HRMS (EI): *m*/*z*: calcd for $C_{24}H_{31}O_{17}$: 591.1561 $[M-CH_3]^+$; found: 591.1507; elemental analysis calcd (%) for $C_{25}H_{34}O_{17}$ (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→4)-2,3-di-*O*-methyl-6-*O*-phthalimido-β-D-glucopyranoside (6)

Method A (*n*Bu_3SnH): Following the general procedure and by using *n*Bu_3SnH (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-β-L-idopyranosyl-(1→4)-2,3-di-*O*-methyl-β-D-glucopyranoside (**7**) (43%) as a colourless oil and the precursor alcohol **1** (43%).

Compound ***8***: $[\alpha]_D = +33.0$ ($c = 0.61$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 3.02$ (dd, $J = 9.0$, 7.9 Hz, 1H), 3.08 (brs, 1H), 3.20 (brd, $J = 9.9$ Hz, 1H), 3.25 (dd, $J = 9.2$, 9.2 Hz, 1H), 3.35 (s, 3H), 3.41 (s, 3H), 3.42 (brs, 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}H NMR (500 MHz, C_6D_6): $\delta = 2.94$ (brs, 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 (brs, 1H), 3.43 (s, 3H), 3.51 (s, 3H), 3.56 (brs, 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}C NMR (125.7 MHz, $CDCl_3$): $\delta = 56.6$ (CH_3), 57.8 (CH_3), 58.5 (CH_3), 58.9 (CH_3), 60.18 (CH_2), 60.23 (CH_3), 60.4 (CH_3), 61.1 (CH_3), 71.9 (CH_2), 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}C NMR (50.3 MHz, C_6D_6): $\delta = 56.0$ (CH_3), 57.09 (CH_3), 57.14 (CH_3), 58.4 (CH_3), 59.7 (CH_3), 59.9 (CH_3), 60.6 (CH_3), 61.6 (CH_2), 71.7 (CH_2), 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) $[M-CH_3OH]^+$, 377 (<1), 308 (4), 275 (9), 265 (45); HRMS (EI): *m/z*: calcd for $C_{18}H_{32}O_{10}$: 408.1995 $[M-CH_3OH]^+$; found: 408.1977; elemental analysis calcd (%) for $C_{19}H_{36}O_{11}$ (440.68): C 51.81, H 8.24; found: C 52.07, H 7.85.

Method B (*n*Bu$_3$SnD): Following the general procedure and by using *n*Bu$_3$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-β-L-(5-^{2}H$_1$)idopyranosyl-(1→4)-2,3-di-*O*-methyl-β-D-glucopyranoside (**8**) (37%) and methyl 2,3,4,6-tetra-*O*-methyl-α-D-[5-^{2}H$_1$]glucopyranosyl-(1→4)-2,3-di-*O*-methyl-β-D-glucopyranoside (**9**) (41%, ^{1}H/^{2}H ratio, 43:57).

Compound ***8***: ^{1}H NMR (500 MHz, C_6D_6): $\delta = 2.95$ (brd, $J = 2.1$ 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 (brd, $J = 3.2$ Hz, 1H), 3.43 (s, 3H), 3.51 (s, 3H), 3.56 (brd, $J = 2.6$ 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 (brd, $J = 11.8$ Hz, 1H), 5.19 ppm (d, $J = 1.3$ Hz, 1H); ^{13}C NMR (125.7 MHz, C_6D_6): $\delta = 56.27$ (CH_3), 57.38 (CH_3), 57.40 (CH_3), 58.7 (CH_3), 60.0 (CH_3), 60.2 (CH_3), 60.8 (CH_3), 61.8 (CH_2), 71.9 (CH_2), 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) $[M+Na]^+$, 442 (10), 307 (25), 289 (13); HRMS (FAB): *m/z*: calcd for $C_{19}H_{35}{}^2H_1NaO_{11}$: 464.2218 $[M+Na]^+$; found: 464.2211.

Compound ***9***: ^{13}C NMR (50.3 MHz, C_6D_6): $\delta = 56.3$ (CH_3), 59.0 ($2\times CH_3$), 59.9 (CH_3), 60.2 (CH_3), 60.3 (CH_3), 60.6 (CH_3), 61.8 (CH_2), 72.0 (CH), 72.240 (CH_2), 72.298 (CH_2), 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) $[M+Na]^+$, 410/409 (7/6); HRMS (FAB): *m/z*: calcd for $C_{19}H_{35}{}^2H_1NaO_{11}$/$C_{19}H_{36}NaO_{11}$: 464.2218/463.2155 $[M+Na]^+$; found: 464.2229/463.2162.

Oxidative HAT of methyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)-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 chromatotron chromatography (hexanes/EtOAc 25:75) methyl 5,6-anhydro-(2,3,4-tri-*O*-acetyl-6-deoxy-α-L-*lyxo*-hexos-5-ulopyranosyl)-(1→4)-2,3-di-*O*-methyl-α-D-galactopyranoside (**20**) (88%) as a white crystalline solid and methyl (1′*S*)-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); $[\alpha]_D = +98.1$ ($c = 0.270$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.37$ (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 (brd, $J = 3.2$ 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}C NMR (100.6 MHz, $CDCl_3$): $\delta = 20.6$ ($2\times CH_3$), 20.8 (CH_3), 21.9 (CH_3), 55.4 (CH_3), 58.1 (CH_3), 59.1 (CH_3), 63.6 (CH_2), 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) $[M+Na]^+$, 493 (8) $[M+H]^+$, 491 (7), 461 (40), 154 (100); HRMS (FAB): *m/z*: calcd for $C_{21}H_{32}O_{13}Na$: 515.1741 $[M+Na]^+$; found: 515.1755; elemental analysis calcd (%) for $C_{21}H_{32}O_{13}$ (492.47): C 51.22, H 6.55; found: C 51.44, H 6.33.

Compound ***21***: $[\alpha]_D = +54.2$ ($c = 0.310$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 2.04$ (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}C NMR (125.7 MHz, $CDCl_3$): $\delta = 20.5$ (CH_3), 20.6 (CH_3), 20.7 (CH_3), 26.5 (CH_3), 55.6 (CH_3), 57.0 (CH_3), 59.0 (CH_3), 62.3 (CH), 68.0 (CH), 69.0 (CH_2), 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 $C_{21}H_{32}O_{13}$: 492.1843 $[M]^+$; found: 492.1859; elemental analysis calcd (%) for $C_{21}H_{32}O_{13}$: 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-(1→4)-2,3-di-*O*-methyl-6-*O*-phthalimido-α-D-galactopyranoside (15)

Method A (*n*Bu$_3$SnH): Following the general procedure and by using *n*Bu$_3$SnH (1 mmol) and AIBN (0.1 mmol), the phthalimide **15** afforded after chromatography (hexanes/EtOAc, 50:50→30:70) methyl 2,3,4-tri-*O*-acetyl-6-deoxy-β-D-gulopyranosyl-(1→4)-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-β-D-*erythro*-hex-4-enopyranosyl-(1→4)-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); $[\alpha]_D = +60.0$ ($c = 0.530$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.19$ (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 (brd, $J = 3.1$ 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}C NMR (100.6 MHz, $CDCl_3$): $\delta = 15.715$ (CH_3), 20.6 (CH_3), 20.7 (CH_3), 20.8 (CH_3), 55.4 (CH_3), 58.4 (CH_3), 59.1 (CH_3), 60.2 (CH_2), 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) $[M+Na+H]^+$, 517 (21) $[M+Na]^+$, 391 (32), 273 (63), 73 (100); HRMS (FAB): *m/z*: calcd for $C_{21}H_{35}O_{13}Na$: 518.1975 $[M+Na+H]^+$; found: 518.1984; elemental analysis calcd (%) for $C_{21}H_{34}O_{13}$ (494.49): C 51.01, H 6.93; found: C 51.15, H 6.89.

Compound ***23***: $[\alpha]_D = -33.8$ ($c = 0.290$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.83$ (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 (brd, $J = 3.7$ 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}C NMR (100.6 MHz, $CDCl_3$): $\delta = 19.5$ (CH_3), 20.8 (CH_3), 20.9 (CH_3), 55.4 (CH_3), 58.7 (CH_3), 59.1 (CH_3), 61.4 (CH_2), 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) $[M+H]^+$, 402 (<1), 374 (1), 212 (11), 88 (100); HRMS (EI): *m/z*: calcd for $C_{19}H_{31}O_{11}$: 435.1866 $[M+H]^+$; found: 435.1877; elemental analysis calcd (%) for $C_{19}H_{30}O_{11}$ (434.43): C 52.53, H 6.96; found: C 52.23, H 6.90.

Method B (*n*Bu$_3$SnD): Following the general procedure and by using *n*Bu$_3$SnD (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-β-D-(5-^{2}H$_1$)gulopyranosyl-(1→4)-2,3-di-*O*-methyl-α-D-galactopyranoside (**24**) (45%), methyl 2,3,4-tri-*O*-acetyl-α-L-[5-^{2}H$_1$]rhamnopyranosyl-(1→4)-2,3-di-*O*-methyl-α-D-galactopyranoside (**25**) (18%, ^{1}H/^{2}H ratio, 3:7), both as colourless oils, and the olefin **23** (15%).

Compound ***24***: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=1.18$ (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); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta=15.576$ (CH_3), 20.6 (CH_3), 20.7 (CH_3), 20.7 (CH_3), 55.4 (CH_3), 58.4 (CH_3), 59.0 (CH_3), 60.2 (CH_2), 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 $C_{21}H_{34}{}^2HO_{13}Na$: 519.2038 $[M+Na+H]^+$; found: 519.2014.

Compound ***25***: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=1.22$ (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); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta=17.350$ (CH_3), 17.489 (CH_3), 20.7 (CH_3), 20.8 (CH_3), 20.9 (CH_3), 55.4 (CH_3), 58.8 (CH_3), 59.3 (CH_3), 62.0 (CH_2), 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 $C_{21}H_{34}{}^2HO_{13}Na/C_{21}H_{35}O_{13}Na$: 519.2038/518.1975 $[M+Na+H]^+$; found: 519.2042/518.1970.

Methyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl-(1→4)-2,3-di-*O*-methyl-1,6-*O*-methylene-β-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 CH_2Cl_2 (35 mL), precursor **11** gave after chromatotron chromatography (hexanes/EtOAc 1:1) the title compound **26** (62%) as a foam: $[\alpha]_D=+46.1$ ($c=0.466$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=2.00$ (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); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta=20.6$ (CH_3), 20.7 (2 × CH_3), 20.8 (CH_3), 59.2 (CH_3), 61.3 (CH_3), 62.8 (CH_2), 66.4 (CH_2), 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 (CH_2), 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 $C_{23}H_{34}O_{15}$: 550.1898 $[M]^+$; found: 550.1886; elemental analysis calcd (%) for $C_{23}H_{34}O_{15}$ (550.51): 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-(1→4)-2,3-di-*O*-methyl-6-*O*-phthalimido-β-L-idopyranoside (16)

Method A (*n*Bu$_3$SnH): Following the general procedure and by using *n*Bu$_3$SnH (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*Bu$_3$SnD): Following the general procedure and by using *n*Bu$_3$SnD (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-(1→4)-2,3-di-*O*-methyl-β-L-[1-OMe-^{2}H]idopyranoside (**27**) (54%, ^{1}H/^{2}H ratio, 3:7) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=1.99$ (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); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta=20.6$ (CH_3), 20.7 (2×CH_3), 20.8 (CH_3), 56.867 (CH_2, t, $J_{CD}=22.6$ Hz), 57.145 (CH_3), 59.5 (CH_3), 60.1 (CH_3), 62.3 (CH_2), 62.7 (CH_2), 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 $C_{21}H_{32}{}^2HO_{13}/C_{21}H_{33}O_{13}$: 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-(1→4)-2,3-di-*O*-methyl-β-L-gulopyranoside (12): Following the general procedure and by using in this case dry CH_2Cl_2 (47 mL), the alcohol **12** gave after acetylation of the reaction crude and chromatotron chromatography of the residue (hexanes/EtOAc 4:6) isopropyl (5′*R*)-5′,6-anhydro-2′,3′,4′,6′-tetra-*O*-methyl-α-D-*lyxo*-hexos-5′-ulopyranosyl-(1→4)-2,3-di-*O*-methyl-β-L-gulopyranoside (**28**) (42%) as a colourless oil and an inseparable mixture of isopropyl (5′*R*)-5′-*O*-acetyl-2′,3′,4′,6′-tetra-*O*-methyl-α-D-*lyxo*-hexos-5′-ulopyranosyl-(1→4)-6-*O*-acethyl-2,3-di-*O*-methyl-β-L-gulopyranoside (**29**) (25%) and 2,3,4,6-tetra-*O*-methyl-α-D-mannopyranosyl-(1→4)-1,6-*O*-isopropylidene-2,3-di-*O*-methyl-β-L-gulopyranose (**30**) (23%).

Compound ***28***: $[\alpha]_D=+75.5$ ($c=0.102$ in $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): $\delta=1.11$ (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); ^{13}C NMR (100.6 MHz, C_6D_6): $\delta=22.1$ (CH_3), 23.9 (CH_3), 57.7 (CH_3), 59.1 (CH_3), 59.4 (CH_3), 59.5 (CH_3), 59.7 (CH_3), 60.9 (CH_3), 64.5 (CH_2), 70.6 (CH), 71.4 (CH), 72.8 (CH_2), 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 $C_{21}H_{38}O_{11}$: 466.2414 $[M]^+$; found: 466.2397; elemental analysis calcd (%) for $C_{21}H_{38}O_{11}$ (466.52): C 54.07, H 8.21; found: C 54.14, H 8.31.

Compound ***29***: ^{1}H NMR (500 MHz, C_6D_6): $\delta=1.10$ (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***: ^{1}H NMR (500 MHz, C_6D_6): $\delta=1.29$ (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); ^{13}C NMR (125.7 MHz, C_6D_6; mixture of **29** and **30**): $\delta=20.5$ (CH_3), 21.7 (CH_3), 22.3 (CH_3), 23.5 (CH_3), 23.9 (CH_3), 27.6 (CH_3), 57.0 (CH_3), 57.2 (CH_3), 58.5 (CH_3), 58.9 (2×CH_3), 59.0 (2×CH_3), 59.1 (2×CH_3), 59.2 (CH_3), 59.4 (CH_3), 60.3 (CH_3), 60.9 (CH_2), 64.8 (CH_2), 71.2 (CH), 71.4 (CH), 71.5 (CH_2), 71.6 (CH), 72.1 (CH_2), 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→4)-2,3-di-*O*-methyl-6-*O*-phthalimido-β-L-gulopyranoside (17)

Method A (*n*Bu$_3$SnH): Following the general procedure and by using *n*Bu$_3$SnH (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-β-L-gulopyranosyl-(1→4)-2,3-di-*O*-methyl-β-L-gulopyranoside (**31**) (80%) as a colourless oil and the precursor alcohol **12** (13%), described in the Supporting Information.

*Compound **31***: $[\alpha]_D = +63.7$ ($c = 0.160$ in $CHCl_3$); ^{1}H NMR (500 MHz, C_6D_6): $\delta = 1.09$ (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); ^{13}C NMR (125.7 MHz, C_6D_6): $\delta = 22.2$ (CH_3), 24.0 (CH_3), 58.1 (CH_3), 58.7 (CH_3), 59.1 (CH_3), 59.4 (CH_3), 59.6 (CH_3), 59.8 (CH_3), 60.3 (CH_2), 71.1 (CH), 71.7 (CH_2), 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) $[M-(CH_3)_2CHOH]^+$, 261 (32), 219 (44), 187 (72), 88 (100); HRMS (EI): *m*/*z*: calcd for $C_{18}H_{32}O_{10}$: 408.1995 $[M-(CH_3)_2CHOH]^+$; found: 408.2005; elemental analysis calcd (%) for $C_{21}H_{40}O_{11}$ (468.54): C 53.83, H 8.61; found: C 54.08, H 8.38.

Method B (*n*Bu$_3$SnD): Following the general procedure and by using *n*Bu$_3$SnD (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-β-L-(5′-^{2}H)gulopyranosyl-(1→4)-2,3-di-*O*-methyl-β-L-gulopyranoside (**32**) (83%) and isopropyl 2,3,4,6-tetra-*O*-methyl-α-D-[5′-^{2}H]mannopyranosyl-(1→4)-2,3-di-*O*-methyl-β-L-gulopyranoside (**33**) (14%, ^{1}H/^{2}H ratio, 45:55), both as colourless oils.

*Compound **32***: ^{1}H NMR (400 MHz, C_6D_6): $\delta = 1.09$ (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); ^{13}C NMR (125.7 MHz, C_6D_6): $\delta = 22.2$ (CH_3), 24.0 (CH_3), 58.1 (CH_3), 58.8 (CH_3), 59.1 (CH_3), 59.4 (CH_3), 59.6 (CH_3), 59.8 (CH_3), 60.3 (CH_2), 71.1 (CH), 71.606 (CH_2), 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) $[M-(CH_3)_2CHOH]^+$, 306 (47), 261 (15), 188 (26), 88 (100); HRMS (EI): *m*/*z*: calcd for $C_{18}H_{31}{}^2HO_{10}$: 409.2058 $[M-(CH_3)_2CHOH]^+$; found: 409.2047.

*Compound **33***: ^{1}H NMR (500 MHz, C_6D_6): $\delta = 1.07$ (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); ^{13}C NMR (125.7 MHz, C_6D_6): $\delta = 22.1$ (CH_3), 24.0 (CH_3), 57.7 (CH_3), 58.8 (CH_3), 59.1 (CH_3), 59.3 (CH_3), 59.4 (CH_3), 59.5 (CH_3), 60.4 (CH_2), 71.2 (CH), 72.2 (CH), 72.956 (CH_2), 73.017 (CH_2), 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) $[M-(CH_3)_2CHOH]^+$, 339 (8), 306 (3), 188 (28), 88 (100); HRMS (EI): *m*/*z*: calcd for $C_{18}H_{31}{}^2HO_{10}$/$C_{18}H_{32}O_{10}$: 409.2058/408.1995 $[M-(CH_3)_2CHOH]^+$; found: 409.2058/408.1981.

Methyl (1*R*)-4,6-*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); $[\alpha]_D = +40.6$ ($c = 0.315$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.28$ (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); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 17.5$ (CH_3), 20.6 (CH_3), 20.76 (CH_3), 20.79 (CH_3), 55.3 (CH_3), 59.6 (CH_3), 61.2 (CH_3), 61.6 (CH), 62.9 (CH_2), 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 $C_{21}H_{32}O_{13}$: 492.1843 $[M]^+$; found: 492.1827; elemental analysis calcd (%) for $C_{21}H_{32}O_{13}$ (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-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-methyl-6-phthalimido-α-D-glucopyranoside (18)

Method A (*n*Bu$_3$SnH): Following the general procedure and by using *n*Bu$_3$SnH (2 mmol) and AIBN (0.2 mmol), the phthalimide **18** gave after column chromatography (hexanes/EtOAc 60:40→50:50) 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-β-L-mannopyranosyl-(1→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***: $[\alpha]_D = +54.8$ ($c = 0.155$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.91$ (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); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 9.435$ (CH_3), 20.4 (CH_3), 20.6 (CH_3), 20.7 (CH_3), 23.6 (CH_2), 55.4 (CH_3), 58.9 (CH_3), 60.1 (CH_3), 60.8 (CH_2), 69.4 (CH), 70.3 (CH), 71.0 (CH), 71.3 (CH), 72.034 (CH), 79.6 (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) $[M-C_2H_7]^+$, 434 (1), 403 (1), 231 (23), 101 (11), 88 (100); HRMS (EI): *m*/*z* calcd for $C_{19}H_{27}O_{13}$: 463.1452 $[M-C_2H_7]^+$; found: 463.1455; elemental analysis calcd (%) for $C_{21}H_{34}O_{13}$ (494.49): C 51.01, H 6.93; found: C 51.12, H 6.96.

*Compound **36***: $[\alpha]_D = +40.7$ ($c = 0.290$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.91$ (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); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 9.5$ (CH_3), 20.4 (CH_3), 20.6 (CH_3), 20.8 (CH_3), 23.7 (CH_2), 55.3 (CH_3), 58.7 (CH_3), 61.3 (CH_3), 64.5 (CH_2), 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) $[M-C_2H_7]^+$, 431 (2), 403 (1), 365 (16), 231 (34), 101 (22), 88 (100); HRMS (EI): *m*/*z*: calcd for $C_{19}H_{27}O_{13}$: 463.1452 $[M-C_2H_7]^+$; found: 463.1444; elemental analysis calcd (%) for $C_{21}H_{34}O_{13}$ (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**)*: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.28$ (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); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ=17.2 (CH_3), 20.6 (CH_3), 20.7 (CH_3), 20.8 (CH_3), 55.2 (CH_3), 59.0 (CH_3), 61.3 (CH_3), 61.9 (CH_2, 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*Bu$_3$SnD): Following the general procedure and by using *n*Bu$_3$SnD (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-L-(5-^{2}H$_1$)*lyxo*-hexonoyl)-2,3-di-*O*-methyl-α-D-glucopyranoside (**38**) (28%), methyl 6-*O*-(2,3,4-tri-*O*-acetyl-5,6-dideoxy-L-(5-^{2}H$_1$)*lyxo*-hexonoyl)-2,3-di-*O*-methyl-α-D-glucopyranoside (**39**) (36%), methyl 2,3,4-tri-*O*-acetyl-6-deoxy-β-L-(1-^{2}H$_1$)mannopyranosyl-(1→4)-2,3-di-*O*-methyl-α-D-glucopyranoside (**40**) (7%), and the precursor alcohol **13** (7%), all as colourless oils.

*Compound **38***: ^{1}H NMR (500 MHz, $CDCl_3$): 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); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ=9.360 (CH_3), 20.4 (CH_3), 20.6 (CH_3), 20.8 (CH_3), 23.4 (CH, t, J_{CD}=19.0 Hz), 55.4 (CH_3), 58.9 (CH_3), 60.2 (CH_3), 60.9 (CH_2), 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) $[M-C_2H_5D]^+$, 435 (2), 404 (1), 232 (25), 101 (17), 88 (100); HRMS (EI): m/z: calcd for $C_{19}H_{28}O_{13}$: 464.1530 $[M-C_2H_5D]^+$; found: 464.1544.

*Compound **39***: ^{1}H NMR (500 MHz, $CDCl_3$): 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); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ=9.3 (CH_3), 20.4 (CH_3), 20.6 (CH_3), 20.8 (CH_3), 23.3 (CH, t, J_{CD}=20.0 Hz), 55.3 (CH_3), 58.6 (CH_3), 61.3 (CH_3), 64.5 (CH_2), 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) $[M-C_2H_5D]^+$, 432 (1), 403 (1), 366 (10), 232 (17), 101 (35), 88 (100); HRMS (EI): m/z: calcd for $C_{19}H_{28}O_{13}$: 464.1530 $[M-C_2H_5D]^+$; found: 464.1510.

*Compound **40** (contaminated with small amounts of alcohols **38** and **39**)*: ^{1}H NMR (500 MHz, $CDCl_3$): 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); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ=17.2 (CH_3), 20.6 (CH_3), 20.7 (CH_3), 20.8 (CH_3), 55.2 (CH_3), 58.9 (CH_3), 61.3 (CH_3), 62.0 (CH_2), 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-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); $[\alpha]_D$=+81.1 (c=0.460 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): 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); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ=20.6 (CH_3), 20.7 (2 × CH_3), 20.8 (CH_3), 55.5 (CH_3), 58.1 (CH_3), 59.2 (CH_3), 61.6 (CH), 62.6 (CH_2), 63.2 (CH_2), 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) $[M-CH_3O]^+$, 477 (11), 389 (13), 304 (15), 88 (100); HRMS (EI): m/z: calcd for $C_{22}H_{31}O_{14}$: 519.1714 $[M-CH_3O]^+$; found: 519.1738; elemental analysis calcd (%) for $C_{23}H_{34}O_{15}$ (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-(1→4)-2,3-di-*O*-methyl-6-*O*-phthalimido-α-D-galactopyranoside (19)

Method A (*n*Bu$_3$SnH): Following the general procedure and by using *n*Bu$_3$SnH (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-(1→4)-6-*O*-acetyl-2,3-di-*O*-methyl-α-D-galactopyranoside (**43**) (19%) and methyl 2,3,4,6-tetra-*O*-acetyl-β-D-mannopyranosyl-(1→4)-6-*O*-acetyl-2,3-di-*O*-methyl-α-D-galactopyranoside (**44**) (6%), both as colourless oils.

*Compound **42***: $[\alpha]_D$=+54.8 (c=0.023 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): 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); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ=20.4 (CH_3), 20.70 (CH_3), 20.75 (CH_3), 20.8 (CH_3), 30.0 (CH_2), 55.5 (CH_3), 57.6 (CH_3), 59.1 (CH_3), 60.190 (CH_2), 60.4 (CH_2), 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 $C_{23}H_{35}O_{14}$: 535.2027 $[M-OH]^+$; found: 535.2031; elemental analysis calcd (%) for $C_{23}H_{36}O_{15}$ (552.52): C 50.00, H 6.57; found: C 50.00, H 6.83.

*Compound **43***: $[\alpha]_D$=+81.6 (c=0.024 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): 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); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ=20.72 (2×CH_3), 20.75 (CH_3), 20.8 (CH_3), 20.9 (CH_3), 55.4 (CH_3), 58.3 (CH_3), 58.4 (CH_3), 61.8 (CH_2), 62.1 (CH_2), 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 $C_{25}H_{38}O_{16}$: 594.2160 $[M]^+$; found: 594.2156; elemental analysis calcd (%) for $C_{25}H_{38}O_{16}$ (594.56): C 50.50, H 6.44; found: C 50.49, H 6.41.

*Compound **44***: $[\alpha]_D$=+0.071 (c=0.206 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): 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); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ=20.6 (CH_3), 20.7 (2×CH_3), 20.77 (CH_3), 20.80 (CH_3), 55.2 (CH_3), 58.9 (CH_3), 59.1 (CH_3), 62.6 (CH_2), 64.2 (CH_2), 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 $C_{25}H_{38}O_{16}$: 594.2160 $[M]^+$; found: 594.2176; elemental analysis calcd (%) for $C_{25}H_{38}O_{16}$ (594.56): C 50.50, H 6.44; found: C 50.46, H 6.31.

Method B (*n*Bu$_3$SnD): Following the general procedure and by using *n*Bu$_3$SnD (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-^{2}*H*)*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-manno-pyranosyl-(1→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-^{2}H)mannopyranosyl-(1→4)-6-*O*-acetyl-2,3-di-*O*-methyl-α-D-galactopyranoside (**46**) (2%), both as colourless oils.

Compound ***45***: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.85$–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); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 20.4$ (CH_3), 20.67 (CH_3), 20.72 (CH_3), 20.8 (CH_3), 29.6 (CHD, t, $J_{CD} = 21.2$ Hz), 55.4 (CH_3), 57.6 (CH_3), 59.1 (CH_3), 60.092 (CH_2), 60.3 (CH_2), 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 $C_{23}H_{34}{}^2HO_{14}$: 536.2090 $[M-OH]^+$; found: 536.2109.

Compound ***46*** *(contaminated with small amounts of* ***43****)*: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.00$ (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); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 20.6$ (CH_3), 20.7 ($2\times CH_3$), 20.76 (CH_3), 20.79 (CH_3), 55.2 (CH_3), 58.9 (CH_3), 59.1 (CH_3), 62.6 (CH_2), 64.2 (CH_2), 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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