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A Substituent-Directed Strategy for the Selective Synthesis of L-Hexoses: An Expeditious Route to L-Idose

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L-Hexoses are rare but biologically significant components of various important biomolecules. However, most are prohibitively expensive (if commercially available) which limits their study and biotechnological exploitation. New, efficient methods to access L-hexoses and their derivatives are thus of great interest. In a previous study, we showcased a stereoselective Bu_3SnH-mediated transformation of a 5-*C*-bromo-D-glucuronide to an L-iduronide. We have now drawn inspiration from this result to derive a new methodology – one that can be harnessed to access other L-hexoses. DFT calculations demonstrate that a combination of a β-F at the anomeric position and a methoxycarbonyl substituent at C-6 is key to optimising the selectivity for the L-hexose product. Our investigations have also culminated in the development of the shortest known synthetic route to a derivative of L-idose from a commercially available starting material (45% yield over 3 steps). Collectively, these results address the profound lack of understanding of how to synthesise L-hexoses in a stereoselective fashion.

Introduction

Carbohydrates are often challenging synthetic targets due to their stereochemical complexity. In this context, L-sugars pose additional synthetic challenges beyond those found with their more abundant D-configured counterparts, due to the much lower availability of L-configured building blocks within the chiral pool.[1] Despite their low natural abundance, L-sugars are immensely important in biology. For example, L-guluronic acid is a key component of medicinally and industrially significant alginates;[2] L-iduronic acid (L-IdoA) is a component of mammalian glycosaminoglycans (GAGs) which regulate numerous biological processes such as anticoagulation and angiogenesis;[3] L-altruronic acid (L-AltA) manifests in the capsular polysaccharides of numerous pathogenic bacteria;[4] and 2-acetamido-2-deoxy-L-altruronic acid (L-AltNAcA) is a component of the surface antigen of *Shigella sonnei*.[5] Based on their prominent biological roles, L-sugars are attractive targets for pharmaceutical synthesis.[6]

Many L-sugars are prohibitively expensive or commercially unavailable. Striking examples are L-idose and L-IdoA, which are currently priced at US $1580/g (aq. solution) and $38000/g ($Na^+$ salt), respectively.[7] This problem severely hinders progress on any research project requiring access to them. Existing synthetic methodologies towards L-sugars have been reviewed by several authors including ourselves,[1c] Zulueta *et al.*,[1b] and Frihed *et al.*[1a] Since the publication of these reviews, innovative contributions to the field have been made by Wan *et al.*,[8] Wang *et al.*,[9] and Hsu and Chang.[10] However, there still exists a broad set of substantial limitations within the field of L-sugar synthesis. Current synthetic routes are often lengthy, require tedious protecting group strategies, and are typically centred upon onerous functional group manipulations. A narrow scope is often the downfall of the select few methods which avoid these limitations. Therefore, the demand for new methodologies is strong.

One of the shortest routes to L-hexoses involves C-5 epimerisation of D-hexoses via free radical reduction. So far, this strategy has largely been limited to members of the L-IdoA family, which can be accessed via the reduction of D-GlcA configured substrates.[11] Mixtures of D- and L-configured products are often obtained, yields are variable, and chromatographic separation of mixtures is required. We recently demonstrated that the stereoselectivity of the Bu_3SnH-mediated radical reduction of 5-*C*-bromo-D-glucuronides was strongly dependent on the anomeric substituent.[11] Notably, when the anomeric substituent was a β-fluoride (**1**, Scheme 1), the reduction proceeded with complete selectivity for the L-ido product (**2**) under very mild conditions. This confirmed the results of Blanchard *et al.*[12] Hyperconjugative effects[13] and Sn–F interactions were proposed to explain the stereochemical role of the β-fluoride.

Herein we report key substrate design features that determine the success of the β-F effect. A series of 5-*C*-bromides varying in their anomeric substituents, protecting groups, and C-6 substituents are surveyed as substrates for the Bu_3SnH-mediated reduction. The results reveal the important discovery that the selectivity requires not only an anomeric β-F group but the combination of a β-F with a methoxycarbonyl group at C-6. Density functional theory (DFT) calculations reveal why this combination of substituents is linked to optimal selectivity. This study provides new insights into how to prepare derivatives of L-IdoA and L-idose in a stereoselective manner and represents a key step forward in the development of a unified synthetic route to L-hexoses.

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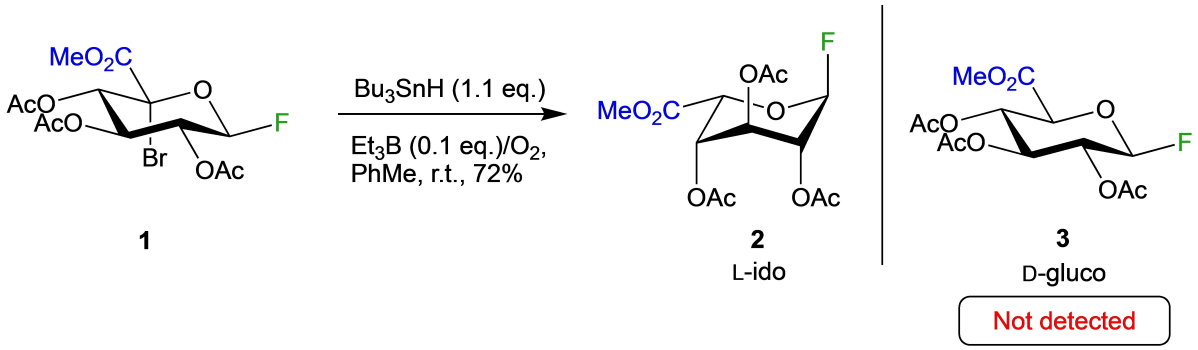


Scheme 1. Free radical reduction of the 5-*C*-bromo-D-glucuronide **1** proceeds with complete selectivity for the L-ido product **2**.[11]

Results and Discussion

Our studies commenced by investigating the influence of the protecting groups and C-6 substituents on reduction selectivity. Four 5-*C*-bromides (**4**–**7**, Figure 1), all accessible through a common synthetic pathway, were prepared in order to determine the stereochemically-important structural features for the reduction. Compared to **1**, which bears acetate protecting groups and a methoxycarbonyl group at C-6, the target substrates **4** and **5** differ in terms of protecting group (**4**, benzoate) or C-6 substituent (**5**, CH_2OAc), while **6** differs in both of these ways. The 5-*C*-bromide **7** is analogous to **6** but contains a β-OBz group as the anomeric substituent rather than a β-F.

The syntheses of **4**–**6** involved transformations of the known α-glycosyl bromides[14] **8**, **11**, and **14** (Scheme 2) into the respective β-fluorides **9**, **12**, and **15** via treatment with AgF in dry acetonitrile in yields of 80–98%. The synthesis of **7** was undertaken from **13**, which was prepared according to the procedure of Sail and Kováč.[15] The 5-*C*-bromide moieties were then installed by photobromination.[16] Thus, the 5-*C*-bromides **6** and **7** were prepared by irradiation of **15** and **13**, respectively, with Br_2 and K_2CO_3 in carbon tetrachloride[17] at reflux (**6**: 61%, 5 h; **7**: 51%, 6 h). Photobromination of **15** was also performed in the greener solvent benzotrifluoride ($PhCF_3$) at reflux.[18] A comparable yield of **6** was acquired (54%).

Bromination of the glycosyl fluoride **9** under the same conditions proceeded swiftly (2 h) to generate an inseparable mixture of the novel epimeric 5-*C*-bromides **4** and **10** (2.7:1) in good combined yield (78%). Based on its small $^3J_{H\text{-}H}$ values, the 5-*C*-bromo-α-L-idosyl fluoride **10** was determined to favour a $^1C_4$ chair conformation. The lack of stereoselectivity observed for the photobromination of **9** is unprecedented, as photobromination at C-5 of D-hexose derivatives typically results in products with the bromine selectively introduced onto the α face of the ring.[19] In contrast to the benzoate-protected fluoride **13**, photobromination of the acetate-protected glycosyl fluoride **12** proved challenging. Somsák and Ferrier reported that α-bromination of the C-4 acetate group is possible under photobromination conditions.[19a] Therefore, in the interest of improving chemo- and regioselectivity, our initial experiments aimed to utilise *N*-bromosuccinimide (NBS) as a mild source of the bromine radical. Thus, **12** was irradiated in the presence of NBS in CCl_4 at reflux. However, no trace of the desired bromide **5** was detected by ^1H NMR spectroscopy after 6 h. This result contrasted with a previous study by Praly *et al.* who reported the formation of **5** in 56% yield after 2 h.[20] Photobromination of **12** with molecular bromine provided the desired 5-*C*-

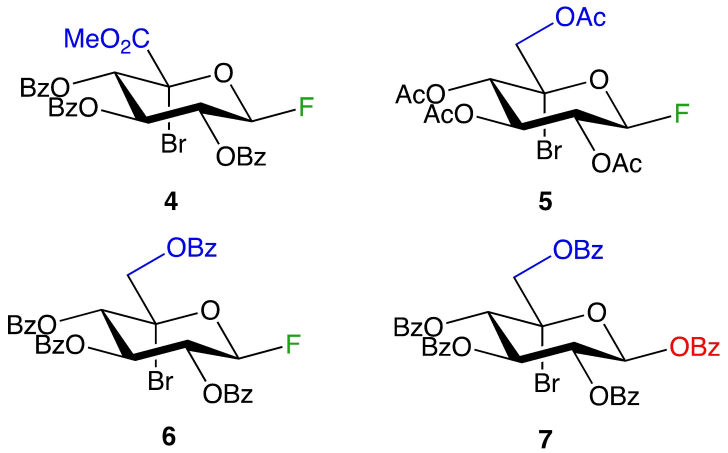
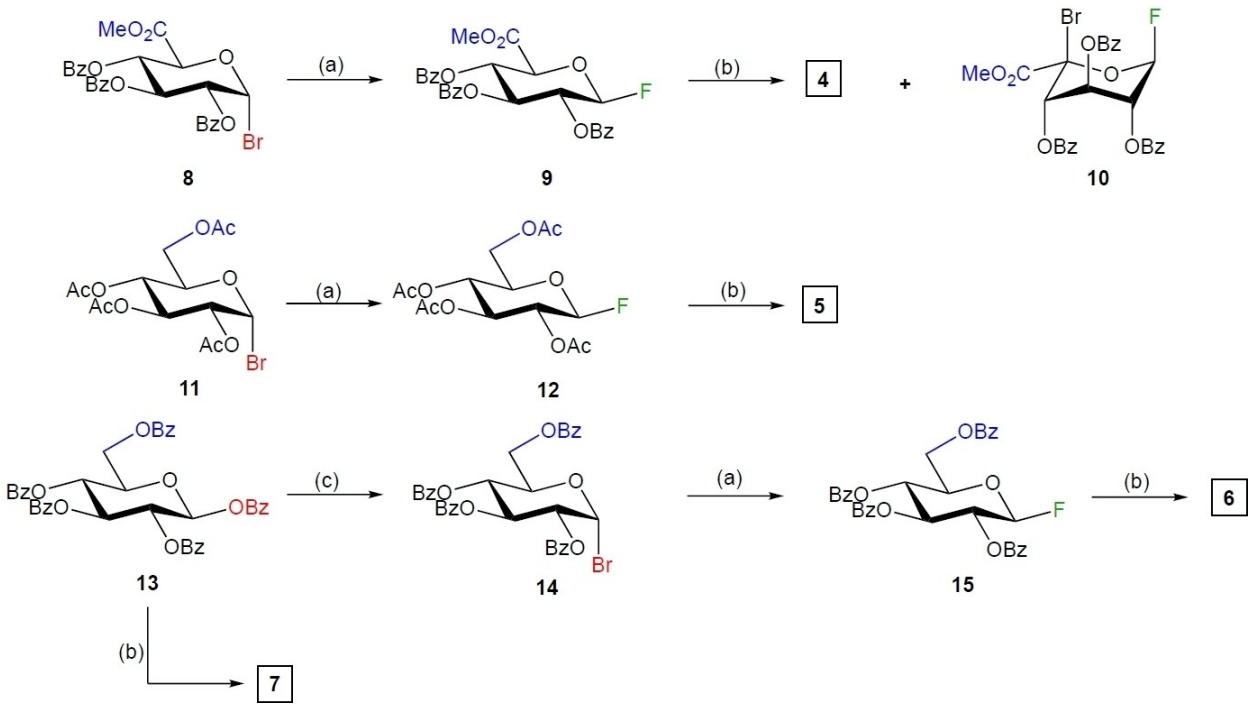


Figure 1. Structures of target 5-*C*-bromides **4**–**7**.

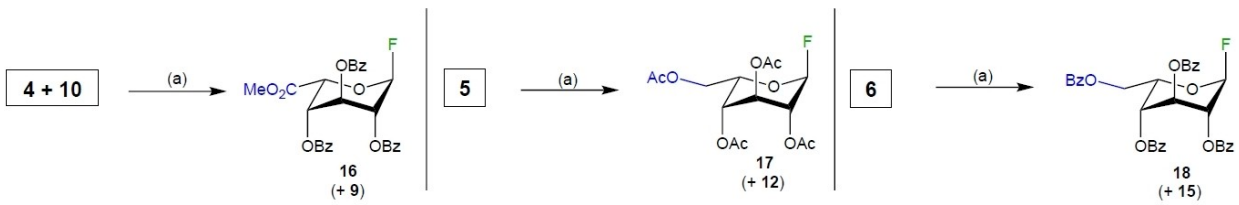


Scheme 2. Synthetic routes employed to access 5-*C*-bromides **4**–**7** (a) AgF, MeCN, r.t., on. (**9**: 80%; **12**: 98%; **15**: 89%); (b) Br_2, K_2CO_3, CCl_4, hν, ↑↓ (**4**:**10** 2.7:1, 78% (combined), 2 h; **5**: 8%, 2 h; **6**: 61%, 5 h; $PhCF_3$, ↑↓, 54%, 6 h; **7**: 51%, 6 h); (c) 33% HBr/AcOH, AW300 MS, CH_2Cl_2, 0 °C – r.t., o/n., 97%.

bromide **5** in a low yield (8%, starting material recovery: 49%) and notably, α-bromination of the C-4 acetate was avoided. The specific rotation of **5** ($[\alpha]_D^{23}$ −58.1 (*c.* 0.26 acetone)) was not in close agreement with that reported by Praly *et al.* ($[\alpha]_D^{23}$ −109 (*c.* 0.75 acetone)). However, the ^1H, ^{13}C, and ^{19}F NMR data were in accord, and HRMS data were consistent with the structure.

Free radical reductions were performed by treating bromides **4**–**7** with tributyltin hydride at room temperature in toluene (Scheme 3). Triethylborane was used as the initiator since we had previously found it to give the best yield and least product degradation.[11] The reductions of **5**–**7** were performed on the pure materials, while the reduction of **4** was studied using the 2.7:1 mixture of C-5 epimers **4** and **10** obtained from the photobromination. The stereoselectivity was measured by ^1H NMR analysis of the crude reduction mixtures. The yields and stereoselectivities of the reductions are shown in Table 1, along with those previously obtained in the highly stereoselective reduction of **1**.

The reduction of the epimeric 5-*C*-bromides **4**/**10** generated a mixture of the novel L-iduronosyl fluoride **16** and the D-



Scheme 3. Free radical reduction of 5-*C*-bromides **4** (as a mixture with **10**), **5** and **6** yields L-ido products **16**–**18**. (a) Bu_3SnH (1.5 eq.), Et_3B (0.1 eq.)/O_2, PhMe, r.t.

Table 1. Stereoselectivities and yields of the Bu_3SnH mediated reductions of 5-*C*-bromides **1**, **4**–**7**, and **10**.

Substrate/s	Anomeric substituent	Protecting group	C-6 substituent	Product/s	Selectivity (L:D)/ Combined yield [%]
1	β-F	Ac	$-CO_2Me$	**2** (L) & **3** (D)	1:0/72[11]
4, **10** (2.7:1)	β-F	Bz	$-CO_2Me$	**16** (L) & **9** (D)	2.9:1/89
5	β-F	Ac	$-CH_2OAc$	**17** (L) & **12** (D)	1:1.4/75
6	β-F	Bz	$-CH_2OBz$	**18** (L) & **15** (D)	2.0:1/94
7	β-OBz	Bz	$-CH_2OBz$	**19** (L) & **13** (D)	0:1/77

glucuronosyl fluoride **9** in a ratio of 2.9:1. The yield was excellent (89% combined), but the selectivity was lower than observed with **1**. Thus, acetate is a superior protecting group choice to benzoate in this synthetic route to L-IdoA derivatives. The reduction of 5-*C*-bromide **5**, bearing acetate protecting groups and a CH_2OAc group at C-6, yielded an inseparable mixture of the novel L-idosyl fluoride **17** and the D-glucosyl fluoride **12** in a ratio of 1:1.4 (75% combined yield). This result reveals that the C-6 substituent plays a key role in controlling the selectivity: $-CO_2Me$ being superior to $-CH_2OAc$ for favouring the L-ido product.

The 5-*C*-bromide **6**, containing benzoate protecting groups and a CH_2OBz group at C-6, was studied next. Its reduction yielded a readily separable mixture of the new L-idosyl fluoride **18** and the D-glucosyl fluoride **15** in a ratio of 2.0:1 and in excellent combined yield (94%). Compared with the peracetylated analogue **5**, the result obtained with the perbenzoate derivative **6** represents a notable increase in L-ido selectivity as well as a substantial improvement in product separability and overall yield.

The final substrate for the reduction was 5-*C*-bromide **7**, which is analogous to **6** but bears a β-benzoate instead of a β-fluoride at the anomeric position. The reduction of **7** gave only the D-gluco derivative **13** (77% yield); no measurable quantity of the L-ido pentabenzoate was produced. Comparing this result with that for 5-*C*-bromide **6** reaffirms the importance of the β-fluoride substituent to the L-ido selectivity.

Taken together, these results define a set of substrate design strategies for the selective formation of L-ido sugars. Optimal L-ido selectivity is obtained with the combination of an anomeric β-fluoride, acetate protecting groups, and a methoxycarbonyl group at C-6 (**1**). However, the benzoate-protected substrate **6** is also noteworthy. By reduction of **6**, compound **18**, a protected, crystalline derivative of L-idose equipped with glycosyl donor functionality, can be achieved from commercially available **14** in only three synthetic steps and in an overall yield of 45%. To the best of our knowledge, this represents the shortest synthetic route to a derivative of L-idose from a commercially available starting material developed to date. Attractively, intermediates **15** and **6** are both bench-stable and are amenable to chromatographic purification. It is noteworthy that **15** is an isolable by-product of the reduction of **6**, and can therefore be recycled to obtain more of the desired L-ido product **18**. Thus, reduction of **6** represents a new synthetic route to L-idose which contends very strongly with current methodologies.[1a,b]

We performed DFT calculations to understand the origins of stereocontrol in the radical reduction. Previously, we have used calculations to examine the role of the β-fluoride.[11] In the present work, we have focused on the role of the C-6 substituent which has emerged from our experiments reported above. We therefore calculated transition states (TSs) for the reduction of **5**, containing a C-6 CH_2OAc group. These TSs can be compared to those previously calculated[11] for the reduction of **1** to determine the effects of different C-6 substituents. The TSs for hydrogen atom transfer from a model stannane, Me_3SnH, to the respective C-5 radicals were optimised at the B3LYP/6-31G(d)-LANL2DZ level of theory. Single point energies were then calculated with B3LYP-D3(BJ)/Def2-TZVPP and were used to compute Gibbs free energies for each TS in solution. All calculations used the SMD implicit solvent model to represent the solvent used experimentally in the respective reaction (benzene for **1**, toluene for **5**).

Figures 2 and 3 show the reductions of 1 and 5, respectively. Part a of each figure shows the energies of the TSs and part b of each figure shows the geometries of key TSs. Six ring conformations were considered for each reduction: three for the TS leading to the L-ido product (featuring hydrogen atom transfer to the β-face of the ring) and three for the TS leading to the D-gluco product (featuring transfer to the α-face). The structures of the TSs for reduction of **1**, previously reported by us,[11] are labelled **TS1-A** to **TS6-A**. In this reaction, transition states **TS1-A**, **TS2-A**, and **TS3-A** lead to the L-ido product **2** and feature $^4C_1$ chair, $^1C_4$ chair, and ^2S_O skew-boat pyranose ring conformations, respectively. **TS2-A** could not be located on the potential energy surface, but the other two TSs were located. Transition states **TS4-A**, **TS5-A**, and **TS6-A** all lead to the D-gluco product **3** and feature $^4C_1$ chair, $^1C_4$ chair, and $^1S_5$ skew-boat (close to $^{1,4}B$) conformations, respectively.

For the reduction of **1**, we previously reported that transition states **TS3-A** and **TS4-A** were the major contributors to the reaction, lying at least 1.4 kcal/mol lower in energy than the other TSs. For the reduction of **5**, we calculated a corresponding set of six TSs, which are shown as **TS1-B**–**TS6-B** in Figure 3. Conformational sampling was performed to identify the lowest-energy conformation of the C-6 substituent. The general conformational features of the rest of the structures mimicked those of **TS1-A**–**TS6-A**. In this way, the stereoelectronic effects within the pyranose ring are conserved ongoing from series **A** to series **B**.

Whereas the reduction of **1** favoured **TS3-A**, the reduction of **5** is predicted to favour **TS4-B**. There are two high-energy transition states, **TS1-B** and **TS5-B**, which do not contribute significantly to the reaction ($\geq$3.5 kcal/mol). Two other transition states, **TS3-B** and **TS6-B**, lie at 0.4 kcal/mol and 1.8 kcal/mol relative to **TS4-B**, respectively, and make minor contributions to the reaction. Based on the free energies of the two major TSs, the calculations predict an L-ido:D-gluco selectivity of 34:66 at the experimental temperature of 25 °C. When other TS conformers are incorporated into the Boltzmann analysis, the calculated selectivity increases to 38:62, in excellent agreement with the experimental result (42:58).

The calculations, therefore, indicate that the difference between the experimental selectivities for **1** and **5** can be attributed to a reversal in the relative energies of the two important transition states **TS3** and **TS4**. For substrate **1**, **TS3** is favoured relative to **TS4**; for substrate **5**, **TS4** is favoured relative to **TS3**. To understand these differences in stability, we analysed the steric and stereoelectronic effects of various individual groups. A set of computational experiments was performed in which specific groups were removed from the TSs, or replaced by H, and the energy difference ($\Delta\Delta E^{\ddagger}$) between the truncated versions of the two TSs was calculated.[21] These computations utilised single point potential energies at the B3LYP-D3(BJ)/

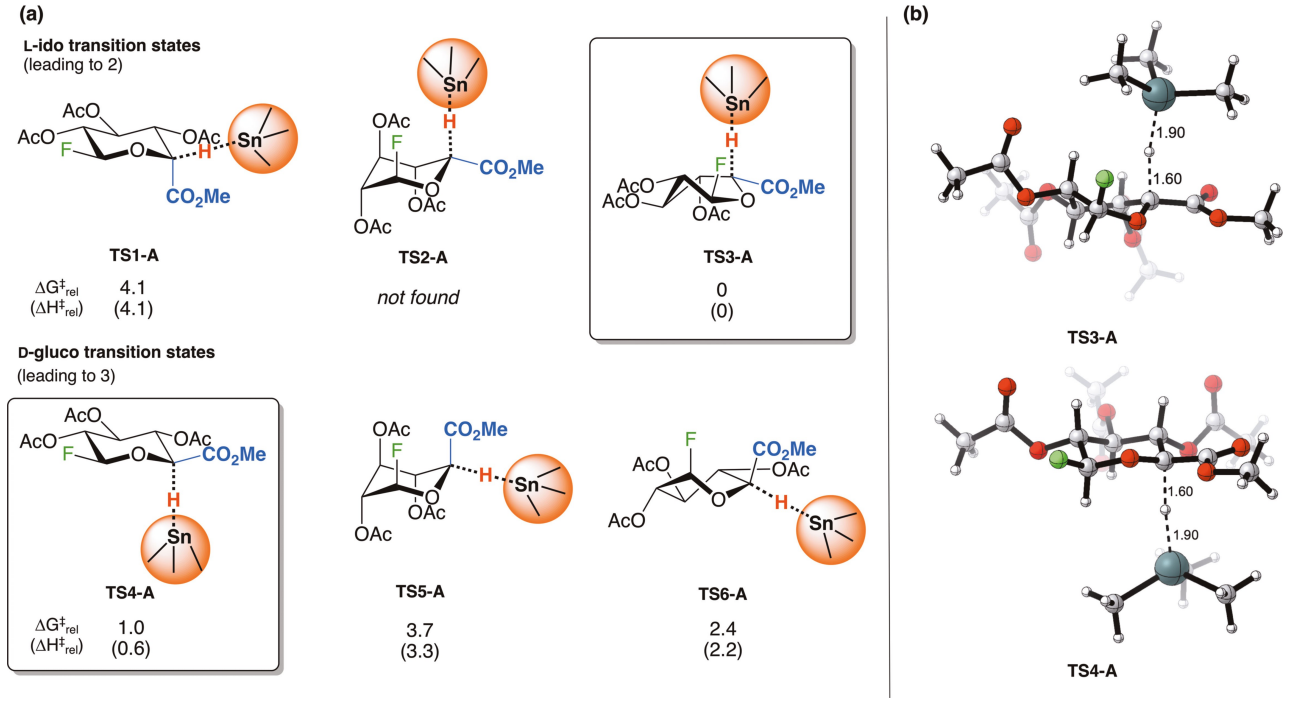


Figure 2. (a) Transition states for the reaction of **1** with Me_3SnH, computed with B3LYP-D3(BJ)/Def2-TZVPP-SMD(benzene)//B3LYP/6-31G(d)-LANL2DZ-SMD (benzene). $\triangle G^{\ddagger}_{rel}$ and $\triangle H^{\ddagger}_{rel}$ in kcal/mol. Data for **1** are taken from reference 11. (b) Optimised geometries of TS3-A and TS4-A. Bond lengths in Å.

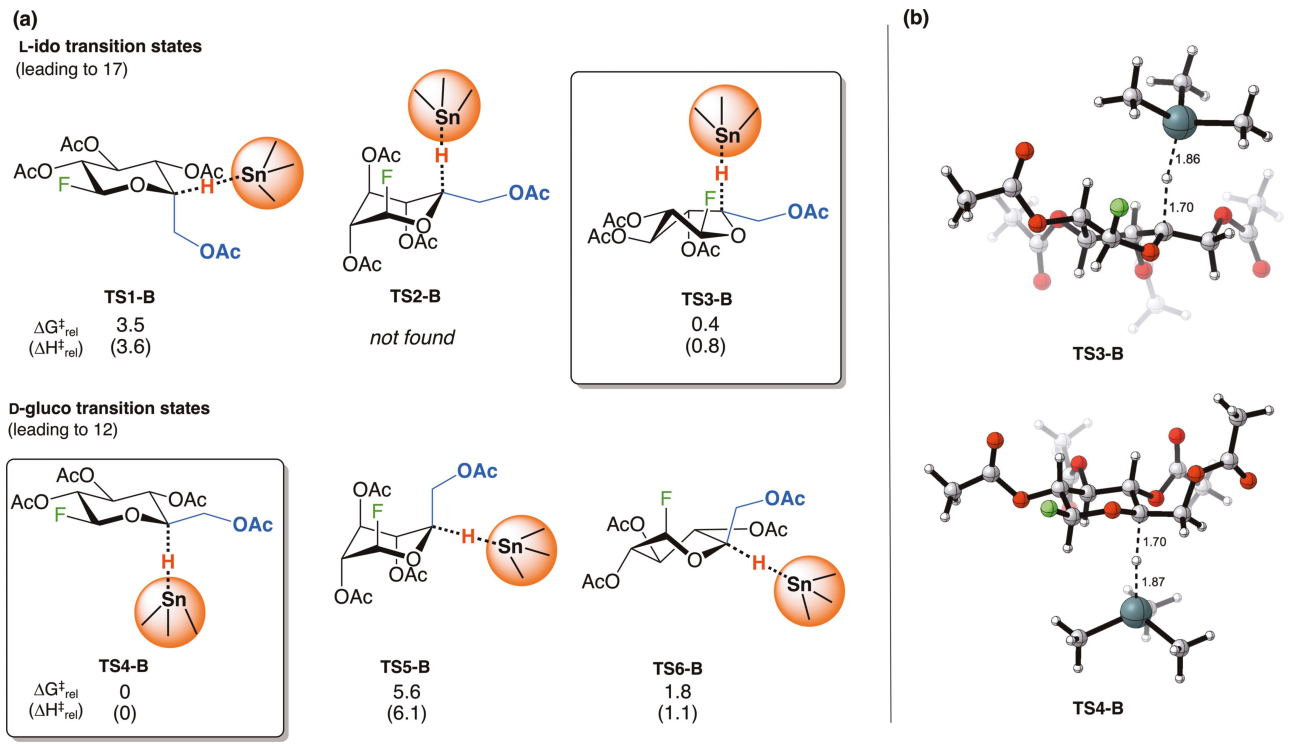


Figure 3. (a) Transition states for the reaction of **5** with Me_3SnH, computed with B3LYP-D3(BJ)/Def2-TZVPP-SMD(toluene)//B3LYP/6-31G(d)-LANL2DZ-SMD (toluene). $\triangle G^{\ddagger}_{rel}$ and $\triangle H^{\ddagger}_{rel}$ in kcal/mol. (b) Optimised geometries of TS3-B and TS4-B. Bond lengths in Å.

Def2-TZVPP-SMD(toluene) level of theory. The results are shown in Table 2.

For reference, the computed values of $\Delta\Delta E^{\ddagger}$ (**TS4** relative to **TS3**) for the unmodified TSs are 1.3 kcal/mol for **1** and

Table 2. Calculated differences in energy ($\Delta\Delta E^{\ddagger}$) between structurally modified versions of **TS3** and **TS4** in the reductions of **1** and **5**.[a]

Modification	$\Delta\Delta E^{\ddagger}$ *(TS4-A–TS3-A)*	$\Delta\Delta E^{\ddagger}$ *(TS4-B–TS3-B)*
None	1.3	−0.8
Me_3SnH removed	0.6	−1.3
C-4-OAc replaced by H	−0.7	−2.0
C-6 substituent (CO_2Me or CH_2OAc) replaced by H	2.5	2.5
1-F replaced by H	−3.2	−5.3

[a] $\Delta\Delta E^{\ddagger}$ (kcal/mol) at the B3LYP-D3(BJ)/Def2-TZVPP-SMD(toluene) level of theory.

−0.8 kcal/mol for **5**. These values mirror the $\Delta\Delta G^{\ddagger}$ values, which were 1.0 and −0.4 kcal/mol, respectively. In our first structural modification experiment, we removed the stannane, leaving only the C-5 radical remaining (Figure 4). This alteration had a relatively small impact, lowering $\Delta\Delta E^{\ddagger}$ by 0.5–0.7 kcal/mol, which suggests that the selectivity is primarily underpinned by stereoelectronic effects within the radical itself rather than by the interactions of the radical with the stannane.[22] The role of the C-4 OAc group was examined by replacing OAc with a hydrogen atom. After making this alteration, the $\Delta\Delta E^{\ddagger}$ values for both substrates decreased by 1.2–2.0 kcal/mol, making the D-gluco structure **TS4** more stable than the L-ido structure **TS3**. This result can be attributed to hyperconjugative interactions between the 4-OAc group and the forming C–H bond. Newman projections are drawn in Figure 5a to highlight that in **TS3**, the 4-OAc group is antiperiplanar with the forming C–H bond, but in **TS4** the same two groups are *gauche*. Thus, the 4-OAc group provides stronger hyperconjugative stabilization to **TS3** than to **TS4**.

We next investigated the C-6 CO_2Me and CH_2OAc groups. Upon replacement of these groups by H, **TS3** is preferred by 2.5 kcal/mol relative to **TS4**. The same value of $\Delta\Delta E^{\ddagger}$ is obtained for both **1** and **5** due to the fact that the truncated structures are chemically identical and have negligible differences in their conformations. In this experiment, the truncated TSs for **1** favour the same product as the TSs for **1** itself, whereas the truncated TSs for **5** display the opposite selectivity than for **5** itself. This result can be explained by the electronic nature of the substituent: the electron density of the forming C–H bond is delocalized onto the π system of the CO_2Me group in **1**, but the CH_2OAc group of **5** provides no avenue for conjugation. Instead, the TS energies for **5** depend on hyperconjugative interactions between the forming bond and the C-6–O bond. As illustrated in the Newman projections in Figure 5b, the two TSs differ with respect to the amount of hyperconjugative stabilisation provided by C6–O. In **TS4-B**, this bond is arranged in an antiperiplanar relationship with respect to the forming bond but in **TS3-B** it adopts a *gauche* relationship; the *gauche* relationship avoids clashing between the lone pairs of the pyranose and C-6 oxygen atoms. The C-6–O bond, therefore, provides less hyperconjugative stabilisation to **TS3-B** than to **TS4-B**. This explains why changing the C-6 substituent from CO_2Me to CH_2OAc causes the stereoselectivity to change from favouring the L-ido product to favouring the D-gluco product.

In a further experiment, we replaced the C-1 fluorine atom by H. This modification had a large effect, altering $\Delta\Delta E^{\ddagger}$ by 4.5 kcal/mol in both cases and making the D-gluco transition state **TS4** strongly favoured. If the Sn–F interaction had been the major contributor to selectivity, then a similar large change in $\Delta\Delta E^{\ddagger}$ would have been expected to result from removing the stannane. That a large effect is only seen for removal of F allows the effect of the β-F substituent to be traced to stereoelectronic factors. In **TS4**, the ring is a $^4C_1$ chair, which places both ring oxygen lone pairs *gauche* to the C–F bond (Figure 5c). In **TS3**, by contrast, the ring is a ^2S_O skew-boat, which places one of the ring oxygen lone pairs antiperiplanar to the C–F bond. The hyperconjugative interaction between the O

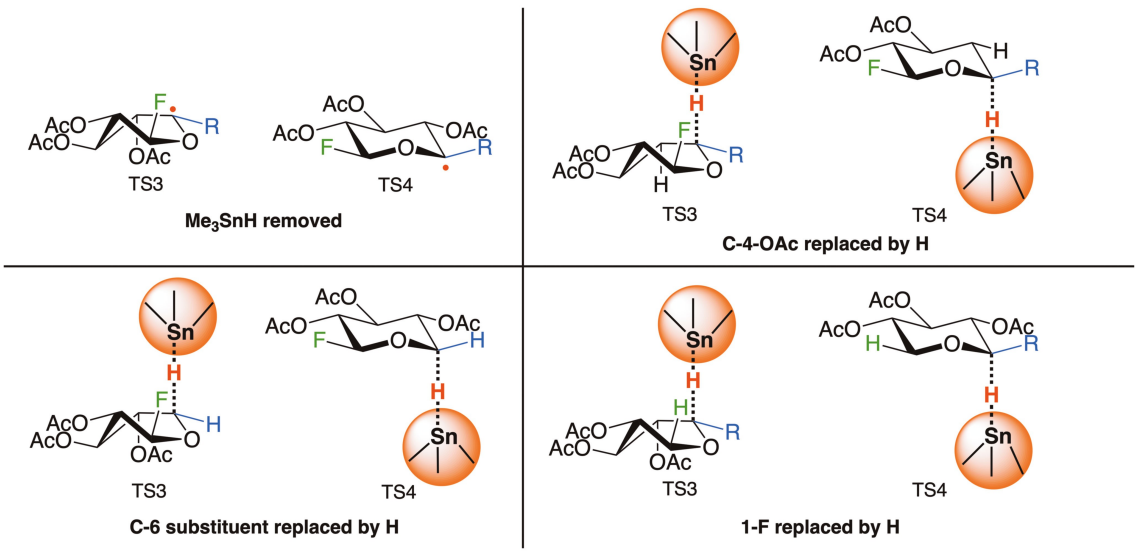


Figure 4. Structural modifications performed on transition states **TS3**-(**A**, R=CO_2Me; **B**, R=CH_2OAc) and **TS4**-(**A**, R=CO_2Me; **B**, R=CH_2OAc).

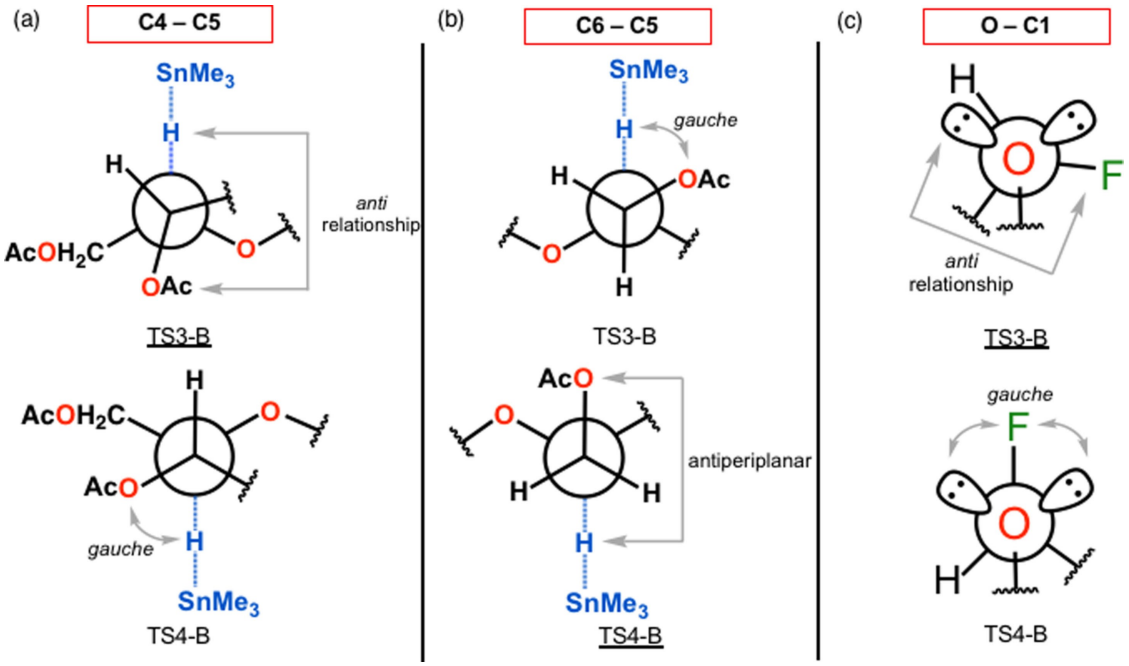


Figure 5. Newman projections of selected bonds in **TS3-B** and **TS4-B**. In each case, the TS bearing the stronger stabilising interaction is underlined.

lone pair and C–F σ* orbital stabilises **TS3** and exerts a major influence on the L-ido : D-gluco selectivity.

Conclusions

Radical reduction of 5-*C*-bromo-β-D-glucosyl fluorides with tributyltin hydride has yielded a series of new and bench-stable derivatives of L-IdoA and L-idose which possess glycosyl donor functionality. For optimal stereoselectivity in the synthesis of L-IdoA from D-glucurono-6,3-lactone, the best substrate design features a β-fluoride at the anomeric position, a methoxycarbonyl group as the C-6 substituent, and acetates as the protecting groups. However, when the method is utilised to access L-idose from D-glucose, a perbenzoylated substrate provides an attractive combination of selectivity, separability, and overall yield. Thus, we highlight that this methodology provides a new, expeditious route from D-glucose to an L-idose derivative requiring only three steps from commercially available **14** and with minimal chromatography. Of further practical note is that the major by-products recovered from the reductions, the D-glucosyl fluorides, are the precursors to the starting 5-*C*-bromides. This introduces an element of recyclability, which, when paired with the high yielding nature of the reduction, makes possible a short and efficient route to L-IdoA and L-idose. Benzotrifluoride has successfully been implemented as a green alternative to carbon tetrachloride for photobrominations. We are also currently investigating the catalytic generation of Bu_3SnH as an environmentally benign protocol for the reduction.[23] Our DFT calculations explain the importance of the β-fluoride and C-6 methoxycarbonyl group in optimising the selectivity for the L-ido products. Conveniently, these functional groups can readily be installed across the family of D-hexoses. We are now applying the results of this investigation to develop optimised syntheses of other L-hexoses from various commercially available and inexpensive D-hexoses. We will report our findings in due course.

Experimental Section

General

Reaction solvents were acquired in anhydrous form where possible and stored over 3 Å molecular sieves (MS). Photobrominations were performed with a 500 W Arlec lamp, fitted with a linear tungsten halogen tube. The lamp was positioned at a distance of 20 cm from the reaction vessels. All experiments were performed in oven-dried glassware under an inert atmosphere (N_2 or Ar). All reactions were monitored by thin-layer chromatography (TLC) using Merck Silica gel 60 F_{254} aluminium-backed sheets. Developed compounds were visualised under ultraviolet light and/or with anisaldehyde dip. Flash chromatography was performed on silica gel (230–400 mesh, Grace). NMR spectra were measured on Bruker AV or AS 300 and 500 MHz spectrometers at 20 °C, using $CDCl_3$ as solvent (99.8 atom % D). The residual solvent peaks served as internal references ($CDCl_3$: δ_H H = 7.26 and δ_C = 77.0 ppm). ^{19}F NMR spectra were referenced externally to monofluorobenzene (δ_F = −113.5 ppm). Coupling constants are reported in hertz (Hz) and chemical shifts are reported in parts per million (ppm). Structure elucidations were aided by 2D experiments, including ^1H–^1H COSY, ^1H–^{19}F COSY, HSQC, HMBC, and NOESY experiments. Melting points were obtained using a Digimelt MPA161 melting point apparatus and are uncorrected. Optical rotations were measured on a Jasco P-2000 polarimeter and are reported in units of 10^{-1} deg cm^2 g^{-1}. Low and high-resolution electrospray ionisation mass spectrometry (LR/HRMS) data were obtained with Bruker HCT and Bruker micrOTOFQ spectrometers respectively, in positive ionisation mode.

Theoretical calculations

Density functional theory calculations on the reduction of **5** were performed using Gaussian 16.[24] Our computational procedure utilised a similar methodology to that used in our previous study of the reduction of **1**.[11] The geometries of transition states for reduction of **5** were optimised with B3LYP[25] using a mixed basis set consisting of LANL2DZ on Sn and 6-31G(d) on all other atoms. The solvent (toluene) was modelled with the SMD implicit solvent model.[26] Harmonic vibrational frequencies were calculated to confirm that transition states had one imaginary frequency, and also to compute thermochemical data. Errors in computed entropies introduced by the harmonic treatment of low-frequency modes were addressed using Truhlar's quasiharmonic approximation[27] in which all harmonic frequencies below 100 cm^{-1} were raised to exactly 100 cm^{-1} before evaluation of the vibrational component of the thermal contribution to entropy. Single-point energy calculations were performed at the B3LYP-D3(BJ)[28]/Def2-TZVPP level of theory in SMD toluene. The default "ultrafine" pruned (99,590) integration grid of Gaussian 16 was used. Gibbs free energies in solution were computed by adding the B3LYP zero-point energy and thermochemical corrections to the B3LYP-D3(BJ) solution-phase electronic energies. A standard state of 298.15 K and 1 mol/L was used.

Synthesis

General procedure for anomeric fluorination with AgF

The glycosyl bromide (1 eq.) was dissolved in dry MeCN (35 mM). AgF (3.5 eq.) was added and the heterogeneous mixture was stirred in the dark o/n. at r.t. under $Ar_{(g)}$. The product was filtered through silica and concentrated under reduced pressure.

Methyl (2,3,4-Tri-O-benzoyl-1-fluoro-1-deoxy-β-D-glucopyran)uronate – 9

The glycosyl bromide **8** (590 mg, 1.0 mmol) was subjected to the conditions outlined in the general procedure to afford 470 mg (80%) of the glycosyl fluoride **9** as a colourless oil after purification by flash chromatography (80:1 PhMe:EtOAc). $[\alpha]_D^{23} = +23.9$ (*c.* 0.95, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.69 (s, 3H, $-OCH_3$), 4.68 (d, 1H, $J_{4,5}$ = 6.4 Hz), 5.53 (ddd, 1H, $J_{1,2}$ = 4.1 Hz, $J_{2,3}$ = 6.5 Hz, $J_{2,F}$ = 9.4 Hz, H-2), 5.81 (dd, 1H, $J_{1,F}$ = 50.3 Hz, H-1), 5.82 (dd, 1H, $J_{3,4}$ = 6.7 Hz, H-3), 5.95 (dd, 1H), 7.33–4.42 (m, 6H), 7.51–7.59 (m, 3H), 7.94–8.02 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 52.9 ($-OCH_3$), 67.7 (C-4), 68.7 (d, $J_{3,F}$ = 4.0 Hz, C-3), 69.3 (d, $J_{2,F}$ = 34.1 Hz, C-2), 72.5 (d, $J_{5,F}$ = 2.2 Hz, C-5), 105.6 (d, $J_{1,F}$ = 226.5 Hz, C-1), 128.4(2), 128.4(7), 128.5(0), 128.5(4), 128.6, 128.7, 129.9(1), 130.0, 130.6(1), 129.9(1), 133.6(3), 133.7, 164.8, 165.0, 165.1, 167.2. ^{19}F NMR (470 MHz, $CDCl_3$): δ −131.6 (dd, $J_{1,F}$ = 51.0 Hz, $J_{2,F}$ = 8.6 Hz). LRMS: *m/z* 1067.4 [2 M + Na]$^+$. HRMS: calcd for $C_{56}H_{46}F_2O_{18}Na$ 1067.2549 found *m/z* 1067.2610 [2 M + Na]$^+$.

2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl fluoride – 12

The glycosyl bromide **11** (620 mg, 1.5 mmol) was subjected to the conditions outlined in the general procedure to afford 520 mg (98%) of the glycosyl fluoride **12** as a colourless oil. $[\alpha]_D^{23} = +20.4$ (*c.* 1.0, $CHCl_3$) lit.[29] +20.8. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.03 (s, 3H, $-CH_3$), 2.04 (s, 3H, $-CH_3$), 2.09 (s, 3H, $-CH_3$), 2.10 (s, 3H, $-CH_3$), 3.88–3.92 (m, 1H, H-5), 4.21 (dd, 1H, B part of ABX system, $J_{5,6b}$ = 2.5 Hz, $J_{6a,6b}$ = 12.2 Hz, H-6b), 4.26 (dd, 1H, A part of ABX system, $J_{5,6a}$ = 5.0 Hz, H-6a), 5.07–5.12 (m, 1H, H-2), 5.17–5.23 (m, 2H, H-3, H-4), 5.35 (dd, 1H, $J_{1,2}$ = 6.0 Hz, $J_{1,F}$ = 52.2 Hz, H-1). ^{13}C NMR (125 MHz, $CDCl_3$): δ 20.5 (3×$-CH_3$), 20.7 ($-CH_3$), 61.7 (C-6), 67.4 (C-4), 71.1 (d, $J_{2,F}$ = 30.2 Hz, C-2), 71.7 (d, $J_{3,F}$ = 7.6 Hz, C-3), 71.9 (d, $J_{5,F}$ = 3.9 Hz, C-5), 106.1 (d, $J_{1,F}$ = 222.5 Hz, C-1), 169.1, 169.3, 170.0, 170.6. ^{19}F NMR (470 MHz, $CDCl_3$): δ −137.1 (dd, $J_{1,F}$ = 52.2 Hz, $J_{2,F}$ = 10.4 Hz). The ^{1}H and ^{13}C NMR spectra were in accord with the literature.[29] LRMS: *m/z* 373.1 [M + Na]$^+$.

2,3,4,6-Tetra-O-benzoyl-β-D-glucopyranosyl fluoride – 15

The glucosyl bromide **14** (1.0 g, 1.6 mmol) was subjected to the conditions outlined in the general procedure to afford 830 mg (89%) of the glucosyl fluoride **15** as a white foam. R_f 0.16 (10:1 hexane:EtOAc); $[\alpha]_D^{24} = +47.3$ (*c.* 0.7, $CHCl_3$) lit.[30] +43.4; ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.41 (ddd, 1H, $J_{5,6a}$ = 3.7 Hz, $J_{5,6b}$ = 5.3 Hz, $J_{4,5}$ = 9.1 Hz, H-5), 4.56 (dd, 1H, B part of ABX system, $J_{6a,6b}$ = 12.4 Hz, H-6b), 4.71 (dd, 1H, A part of ABX system, H-6a), 5.60 (ddd, 1H, $J_{1,2}$ = 5.6 Hz, $J_{2,3}$ = 9.2 Hz, $J_{2,F}$ = 9.5 Hz, H-2), 5.71 (dd, 1H, $J_{1,F}$ = 51.5 Hz, H-1), 5.82 (dd, 1H, $J_{3,4}$ = 9.1 Hz, H-4), 5.87 (dd, 1H, H-3), 7.31–7.37 (m, 4H), 7.38–7.44 (m, 4H), 7.45–7.58 (m, 4H), 7.87–7.91 (m, 2H), 7.91–7.94 (m, 2H), 7.99–8.02 (m, 2H), 8.03–8.06 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 62.9 (C-6), 68.1 (C-4), 71.3 (d, $J_{2,F}$ = 16.4 Hz, C-2), 71.5 (d, $J_{3,F}$ = 7.2 Hz, C-3), 72.6 (d, $J_{5,F}$ = 3.0 Hz, C-5), 106.5 (d, $J_{1,F}$ = 224.0 Hz, C-1), 128.4(2), 128.4(4), 128.4(8), 128.5(1), 128.5(9), 128.6, 128.7, 129.4, 129.8(3), 129.8(7), 129.9(0), 129.9(7), 133.2, 133.5, 133.6(1), 133.6(2), 164.9, 165.0, 165.5, 166.1. ^{19}F NMR (470 MHz, $CDCl_3$): δ −134.3 (dd, $J_{1,F}$ = 51.4 Hz, $J_{2,F}$ = 9.1 Hz). The ^{1}H and ^{13}C NMR spectra were in accord with the literature.[30] LRMS: *m/z* 621.5 [M + Na]$^+$.

General procedure for photobromination

The substrate (1 eq.), Br_2 (5 eq.), and K_2CO_3 (10 mg/mL) were combined in dry CCl_4 (15 mM). The mixture was irradiated at reflux under $Ar_{(g)}$. The mixture was then cooled to r.t. before it was diluted with $CHCl_3$ and washed with 1.0 M $Na_2S_2O_3$ (3x). The product was then washed with sat. $NaHCO_3$ (1x) and brine (1x) before it was dried ($MgSO_4$), filtered, and concentrated under reduced pressure.

Methyl (2,3,4-Tri-O-benzoyl-5-C-bromo-1-deoxy-1-fluoro-β-D-glucopyran)uronate – 4 & Methyl (2,3,4-Tri-O-benzoyl-5-C-bromo-1-deoxy-1-fluoro α-L-idopyran)uronate – 10

The glucosyl fluoride **9** (220 mg, 0.42 mmol) was brominated according to the general procedure (2 h) to afford 196 mg (78%) of **4** and **10** in ratio of 2.7:1 as an inseparable mixture after purification by flash chromatography (80:1 PhMe:EtOAc). Key data for **4**: ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.82 (s, 3H, $-CH_3$), 5.76 (ddd, 1H, $J_{1,2}$ = 7.5 Hz, $J_{2,F}$ = 12.9 Hz, H-2), 5.92 (d, 1H, $J_{3,4}$ = 10.0 Hz, H-4), 6.01 (dd, 1H, $J_{1,F}$ = 50.0 Hz, H-1), 6.11 (dd, 1H, $J_{2,3}$ = 10.0 Hz, H-3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 54.4 ($-CH_3$), 70.0 (C-4), 70.3 (d, $J_{3,F}$ = 10.5 Hz, C-3), 70.6 (d, $J_{2,F}$ = 24.9 Hz, C-2), 88.3 (d, $J_{5,F}$ = 6.7 Hz, C-5), 106.5 (d, $J_{1,F}$ = 228.5 Hz, C-1), 163.9, 164.5, 164.7, 165.2. ^{19}F NMR (470 MHz, $CDCl_3$): δ −149.0 (dd, $J_{1,F}$ = 50.0 Hz, $J_{2,F}$ = 12.9 Hz).

Key data for **10**: ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.75 (s, 3H, $-CH_3$), 5.60–5.63 (m, 1H, H-2), 5.72–5.74 (m, 1H, H-3), 6.15 (ap. d, 1H, $J_{1,F}$ = 49.0 Hz, H-1), 6.17 (d, 1H, $J_{3,4}$ = 2.9 Hz, H-4). ^{13}C NMR (125 MHz, $CDCl_3$): δ 53.8 ($-CH_3$), 64.9 (d, $J_{2,F}$ = 35.0 Hz, C-2), 65.8 (C-3), 69.8 (C-4), 77.9 (C-5), 105.0 (d, $J_{1,F}$ = 236.3 Hz, C-1), 163.5, 164.6(1), 164.6(3), 165.2. ^{19}F NMR (470 MHz, $CDCl_3$): δ −133.5 (dd, $J_{1,F}$ = 48.5 Hz, $J_{2,F}$ = 6.3 Hz). Data for **4** and **10**: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.10–7.19 (m, 2H), 7.30–7.35 (m, 3H), 7.38–7.52 (m, 10H), 7.53–7.58 (m, 3H), 7.60–7.66 (m, 1H), 7.79–7.87 (m, 4H), 7.97–8.03 (m, 6H), 8.21–8.25 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 128.2(1), 128.2(5), 128.3(1),

128.3(6), 128.4, 128.5, 128.6, 128.7, 129.0, 129.8, 129.9, 130.0(0), 130.0(5), 130.0(8), 130.5, 133.6, 133.7, 133.8, 133.9, 134.0. LRMS: *m/z* 601.8 $[M+H]^+$; HRMS: calcd for $C_{28}H_{22}BrFO_9Na$ 623.0329 found 623.0314 $[M+Na]^+$.

2,3,4,6-Tetra-O-acetyl-5-C-bromo-β-D-glucopyranosyl fluoride – 5

The glucosyl fluoride **12** (215 mg, 0.61 mmol) was brominated according to the general procedure (2 h) to afford 21 mg (8%) of the 5-*C*-bromide **5** as a colourless oil, after purification by flash chromatography (8:1 PhMe:EtOAc). $[\alpha]_D^{23} = -58.1$ (*c.* 0.26, acetone) lit.[20] −109. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.02 (CH_3), 2.09 (CH_3), 2.11 (CH_3), 2.13 (CH_3), 4.40 (d, 1H, $J_{6a,6b}$ = 12.2 Hz, H-6b), 4.55 (d, 1H, H-6a), 5.27 (ddd, 1H, $J_{1,2}$ = 7.6 Hz, $J_{2,3}$ = 9.7 Hz, $J_{2,F}$ = 14.3 Hz, H-2), 5.29 (d, 1H, $J_{3,4}$ = 9.8 Hz, H-4), 5.53 (dd, 1H, H-3), 5.67 (dd, 1H, $J_{1,F}$ = 51.8 Hz, H-1). ^{13}C NMR (125 MHz, $CDCl_3$): δ 20.4(4) (CH_3), 20.4(7) (CH_3), 20.4(8) (CH_3), 20.5 (CH_3), 65.6 (C-6), 68.0 (C-4), 70.4 (d, $J_{2,F}$ = 24.3 Hz, C-2), 70.5 (d, $J_{3,F}$ = 10.4 Hz, C-3), 94.7 (d, $J_{5,F}$ = 7.5 Hz, C-5), 106.7 (d, $J_{1,F}$ = 220.0 Hz, C-1), 168.9, 169.1, 169.6, 169.7. ^{19}F NMR (470 MHz, $CDCl_3$): δ −149.8 (dd, $J_{1,F}$ = 52.0 Hz, $J_{2,F}$ = 14.0 Hz). The ^{1}H and ^{13}C NMR spectra were in accord with the literature.[20] LRMS: 451.0 $[M+Na]^+$. HRMS: calcd for $C_{14}H_{18}BrFO_9Na$ $[M+Na]^+$ 451.0016 found 451.0011 $[M+Na]^+$.

2,3,4,6-Tetra-O-benzoyl-5-C-bromo-β-D-glucopyranosyl fluoride – 6

The glucosyl fluoride **15** (210 mg, 0.35 mmol) was brominated according to the general procedure (5 h) to afford 140 mg (61% isolated, 81% based on recovered starting material) of the bromide **6** as a white foam after purification by flash chromatography (*stepwise gradient* 1:1:0.05 hexane:PhMe:EtOAc→1:1:0.1 hexane:PhMe:EtOAc→EtOAc). R_f 0.38 (1:1:0.05 hexane:PhMe:EtOAc); $[\alpha]_D^{23} = +19.6$ (*c.* 0.19, $CHCl_3$) lit.[31] +23.5; ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.67 (d, 1H, B part of AB system, $J_{6a,6b}$ = 12.3 Hz, H-6b), 5.01 (d, 1H, A part of AB system, H-6a), 5.77 (ddd, 1H, $J_{1,2}$ = 7.3 Hz, $J_{2,3}$ = 9.3 Hz, $J_{2,F}$ = 13.1 Hz, H-2), 5.95 (d, 1H, $J_{3,4}$ = 9.9 Hz, H-4), 5.99 (dd, 1H, $J_{1,F}$ = 51.9 Hz, H-1), 6.20 (dd, 1H, H-3), 7.27–7.32 (m, 2H), 7.35–7.47 (m, 5H), 7.48–7.64 (m, 5H), 7.80–7.85 (m, 2H), 7.94–7.98 (m, 2H), 8.00–8.05 (m, 2H), 8.10–8.15 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 66.3 (C-6), 69.1 (C-4), 70.8 (d, $J_{3,F}$ = 9.8 Hz, C-3), 71.0 (d, $J_{2,F}$ = 25.0 Hz, C-2), 95.5 (d, $J_{5,F}$ = 6.7 Hz, C-5), 106.9 (d, $J_{1,F}$ = 224.8 Hz, C-1), 128.0, 128.3(2), 128.3(7), 128.4, 128.5(2), 128.5(7), 128.5(8), 128.9, 129.8, 130.0(1), 130.0(5), 130.1, 133.4, 133.5, 133.7, 133.9, 164.4, 164.8, 165.1, 165.3. ^{19}F NMR (470 MHz, $CDCl_3$): δ −147.5 (dd, $J_{1,F}$ = 51.9 Hz, $J_{2,F}$ = 13.1 Hz). The ^{1}H and ^{13}C NMR spectra were in accord with the literature.[31] LRMS: *m/z* 699.0 $[M+Na]^+$.

1,2,3,4,6-Penta-O-benzoyl-5-C-bromo-β-D-glucopyranose – 7

The perbenzoate **13** (200 mg, 0.29 mmol) was brominated according to the general procedure (6 h) to afford 123 mg (51%) of the bromide **7** as a white foam after purification by flash chromatography (*stepwise gradient* 1:1:0.05 hexane:PhMe:EtOAc→1:1:0.1 hexane:PhMe:EtOAc→EtOAc). The product was observed to decompose at r.t. and was therefore stored under $Ar_{(g)}$ at −20 °C. R_f 0.30 (1:1:0.05 hexane:MePh:EtOAc); $[\alpha]_D^{23} = -13.8$ (*c.* 0.50, $CHCl_3$) lit. [32] −12.0; ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.70 (d, 1H, B part of AB system, $J_{6a,6b}$ = 12.2 Hz, H-6b), 4.95 (d, 1H, A part of AB system, H-6a), 5.96 (d, 1H, $J_{3,4}$ = 9.7 Hz, H-4), 5.99 (dd, 1H, $J_{1,2}$ = 8.5 Hz, $J_{2,3}$ = 9.7 Hz, H-2), 6.35 (dd, 1H, H-3), 6.79 (d, 1H, H-1), 7.27–7.62 (m, 15H, Ar–H), 7.81–7.85 (m, 2H, Ar–H), 7.93–7.99 (m, 4H, Ar–H), 8.02–8.06 (m, 2H, Ar–H), 8.08–8.11 (m, 2H, Ar–H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 66.6 (C-6), 69.5 (C-4), 69.9 (C-2), 71.3 (C-3), 92.4 (C-1), 96.6 (C-5), 128.2, 128.3, 128.4, 128.5(0), 128.5(3), 128.5(8), 129.7, 129.9(6), 129.9(9), 130.1, 130.2, 164.1, 164.5, 165.1(2), 165.1(9), 165.3. The ^{1}H and ^{13}C NMR spectra were in accord with the literature.[32] LRMS: *m/z* 802.6 $[M+Na]^+$.

General procedure for tributyltin hydride reduction

The substrate (1 eq.) was dissolved in anhydrous toluene (40 mM) and stirred under $Ar_{(g)}$. Bu_3SnH (1.0 M in hexanes, 1.5 eq.) and Et_3B (1.0 M in hexanes, 0.1 eq.) were added and the solution was stirred at r.t. until complete consumption of starting material was confirmed by TLC. The product mixture was concentrated under reduced pressure before the resulting crude residue was dissolved in acetonitrile and washed with hexane (3x). The acetonitrile phase was then concentrated, and an aliquot was subjected to analysis by ^{1}H NMR spectroscopy.

Methyl (2,3,4-Tri-O-benzoyl-1-deoxy-1-fluoro–α-L-idopyran)uronate – 16

The mixture of 5-*C*-bromides **4** and **10** (120 mg, 0.21 mmol) was reduced according to the general procedure (1 h) to afford an inseparable mixture of the L-idosyl fluoride **16** and the D-glucosyl fluoride **9** in a ratio of 2.9:1 (96 mg, 89%, combined), as determined by ^{1}H NMR spectroscopy, as a white foam. The product was purified by flash chromatography (80:1 PhMe:EtOAc). Key data for **16**: ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.78 (s, 3H, $-CH_3$), 5.26 (d, 1H, $J_{4,5}$ = 1.9 Hz, H-5), 5.31 (m, 1H, H-2), 5.61 (m, 1H, H-4), 5.73 (m, 1H, H-3), 5.99 (ap. d, $J_{1,F}$ = 46.9 Hz, H-1). ^{13}C NMR (125 MHz, $CDCl_3$): δ 52.8 (CH_3), 64.6 (d, $J_{2,F}$ = 38.2 Hz, C-2), 65.3 (C-3), 66.4 (C-4), 67.7 (d, $J_{5,F}$ = 2.6 Hz, C-5), 104.7 (d, $J_{1,F}$ = 227.8 Hz, C-1). ^{19}F NMR (470 MHz, $CDCl_3$): δ −136.5 (dd, $J_{1,F}$ = 46.1 Hz, $J_{2,F}$ = 3.9 Hz). LRMS: *m/z* 1066.6 $[2M+Na]^+$.

2,3,4,6-Tetra-O-acetyl-α-L-idopyranosyl fluoride – 17

The 5-*C*-bromide **5** (18 mg, 0.042 mmol) was reduced according to the general procedure (1 h) to afford an inseparable mixture of the L-idosyl fluoride **17** and the D-glucosyl fluoride **12** in a ratio of 1:1.4 (11 mg, 75%, combined), as determined by ^{1}H NMR spectroscopy, as a white foam. The product was purified by flash chromatography (5:1 PhMe:EtOAc). Key data for **17**: ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.55–4.58 (m, 1H, H-5), 4.89–4.92 (m, 2H, H-2, H-4), 5.02–5.05 (m, 1H, H-3), 5.57 (ap. d, 1H, $J_{1,F}$ = 49.1 Hz, H-1). ^{13}C NMR (125 MHz, $CDCl_3$): δ 64.8 (d, $J_{2,F}$ = 38.0 Hz, C-2), 65.3 (C-4), 65.5 (C-3), 65.9 (d, $J_{5,F}$ = 2.7 Hz, C-5), 104.5 (d, $J_{1,F}$ = 225.4 Hz, C-1). ^{19}F NMR (470 MHz, $CDCl_3$): δ −133.7 (dd, $J_{1,F}$ = 48.7 Hz, $J_{2,F}$ = 6.1 Hz). LRMS: *m/z* 373.3 $[M+Na]^+$.

2,3,4,6-Tetra-O-benzoyl-α-L-idopyranosyl fluoride – 18

The 5-*C*-bromide **6** (30 mg, 0.04 mmol) was reduced according to the general procedure (4 h) to give a mixture of the L-idosyl fluoride **18** and the D-glucosyl fluoride **15** (25 mg, 94%, combined) in a ratio of 2.0:1, as determined by ^{1}H NMR spectroscopy. The product was purified by flash chromatography (*stepwise gradient* 8:1:0.1 hexane:EtOAc:PhMe→2:1 PhMe:EtOAc→EtOAc) and was subsequently crystallised from Et_2O/hexane. Data for **18**: R_f 0.20 (10:1:0.1 hexane:EtOAc:PhMe; m.p. (°C): 140.0–140.5; $[\alpha]_D^{24} = -2.7$ (*c.* 0.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.57 (dd, B part of ABX, 1H, $J_{6a,6b}$ = 11.7 Hz, $J_{5,6b}$ = 5.2 Hz, H-6b), 4.74 (dd, A part of ABX spin system, 1H, $J_{5,6a}$ = 5.1 Hz, H-6a), 5.02 (ddd, 1H, $J_{4,5}$ = 1.4 Hz, H-5), 5.31–5.34 (m, 1H, H-2), 5.44–5.48 (m, 1H, H-4), 5.68–5.72 (m, 1H, H-3), 5.90 (ap. d, 1H, $J_{1,F}$ = 47.6 Hz), 7.17 (m, 2H), 7.38–7.45 (m, 4H),

7.46–7.53 (m, 3H), 7.56 (m, 1H), 7.59–7.65 (m, 2H), 7.87 (m, 2H), 8.03 (m, 2H), 8.11–8.17 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 62.8 (C-6), 65.3 (d, $J_{2,F}$ = 39.1 Hz, C-2), 65.5 (C-4), 65.6 (C-3), 66.3 (d, $J_{5,F}$ = 3.8 Hz, C-5), 104.6 (d, $J_{1,F\ 0}$ = 225.6 Hz, C-1), 128.3, 128.4, 128.5, 128.6, 128.8, 128.9, 129.4, 129.7, 129.9, 130.1, 130.2, 133.2, 133.6, 133.7, 133.8, 164.3, 164.8, 165.1, 166.1.^{19}F NMR (470 MHz, $CDCl_3$): δ −134.5 (dd, $J_{1,F}$ = 47.8 Hz, $J_{2,F}$ = 4.0 Hz). LRMS: *m/z* 621.1 $[M+Na]^+$; HRMS: calcd for $C_{34}H_{27}FO_9Na$ $[M+Na]^+$ 621.1537 found 621.1518 $[M+Na]^+$.

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Conflict of Interest

The authors declare no conflict of interest.

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