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Synthesis of Branched Iminosugars through a Hypervalent Iodine(III)-Mediated Radical-Polar Crossover Reaction

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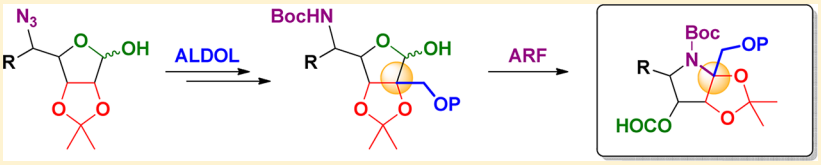
Supporting Information



ABSTRACT: The synthesis of a novel type of branched iminosugars is described. This synthetic strategy is based on two key reactions: first, an aldol reaction with formaldehyde in order to introduce selectively the hydroxymethyl branch, and second, a tandem β-fragmentation-intramolecular cyclization reaction. The combination of both reactions afforded a battery of compounds exhibiting a great structural complexity, with the concomitant formation of a quaternary center, starting from readily available aldoses. With this approach we have demonstrated the usefulness of the fragmentation of anomeric alkoxyl radicals (ARF) promoted by the PhIO/I_2 system for the preparation of new compounds with potential interest for both medicinal and synthetic chemists.

1. INTRODUCTION

Radical-polar crossover reactions,[1] also called radical-ionic cascades, are radical-initiated processes that, however, do not terminate homolytically, but heterolytically. For these transformations to take place, radical initiators are not needed. Instead, the reagents employed have the ability to give or accept an electron. The radical intermediates thus generated become ionic, either by oxidation or reduction, resulting in the respective cations or anions that evolve from this point on in a heterolytic manner. Samarium iodide is the most common reagent for these reactions to end in an anionic form, by converting the radical intermediate into a nucleophile.[2,3] On the other side, the radical species can be generated by oxidation of the substrate by transferring one electron to a metal center, such as Mn^{III}/Cu^{II},[4] Ce^{IV},[5] and Fe^{III}.[6] Most recently, nonmetallic systems such as hypervalent iodine reagents, and especially iodoso-derivatives, have also been used, traditionally, for the radical coupling between phenolic aromatics.[7]

In this regard, our research group has been devoted to the development of new synthetic strategies based on alkoxyl radicals, mainly in the carbohydrate field. One of our main findings is the β-fragmentation of anomeric alkoxyl radicals[8] that relies upon the formation, in a first step, of an anomeric alkoxyl radical by the action of acetylhypoiodite, generated in situ by the hypervalent iodine(III) reagent and iodine. This radical then undergoes, under mild conditions, a β-fragmentation of the C1−C2 bond. The evolution of this reaction has been shown to depend on the nature of the protecting group at C−2,[9] and in the case of electron donating groups, such as ethers, the C−2 radical intermediate is oxidized (by an excess of reagent) to give an oxonium ion that can be trapped intra- or intermolecularly by different nucleophiles, thus making the whole process a radical-polar crossover reaction (Scheme 1).[10,11]

In this context, we have reported a methodology for the synthesis of several polyhydroxylated nitrogen heterocycles.[12,13] The versatility of this procedure became clear after the synthesis of several iminosugar skeletons, prepared both in the furanose and the pyranose form. The relevance of these polyhydroxylated alkaloids, structurally related to cyclic carbohydrates, stems from the fact that they can bind specifically to the active sites of the glycosidases, by mimicking either the corresponding substrate or its transition state, thus inhibiting the enzymatic catalysis.[14]

Another tandem β-fragmentation−cyclization process that has also been studied in our laboratory involves the conversion of aldoses into ketoses.[15] This methodology, which represents an effective alternative to the alkaline isomerization of Lobry de Bruyn-Alberda van Ekestein,[16] uses as starting material readily available aldoses to which a hydroxymethyl branch has been introduced at position C−2 by means of an aldol reaction with formaldehyde.[17]

With this consideration in mind, we envisaged a combination of both strategies in order to prepare novel iminosugars exhibiting a hydroxymethyl group at the anomeric position.[18] The resulting iminoketoses[19] would represent an intermediate state between iminoaldoses and imino-C-glycosides, and also, they could be considered as interesting synthons, giving rise quickly to homoiminosugars by regioselective reduction, among other modifications.[20]

A careful search in the literature showed that there are many references related to the synthesis of iminosugars[21] and imino-C-glycosides,[22] but as far as we know, there are no synthetic references to this type of ketose.

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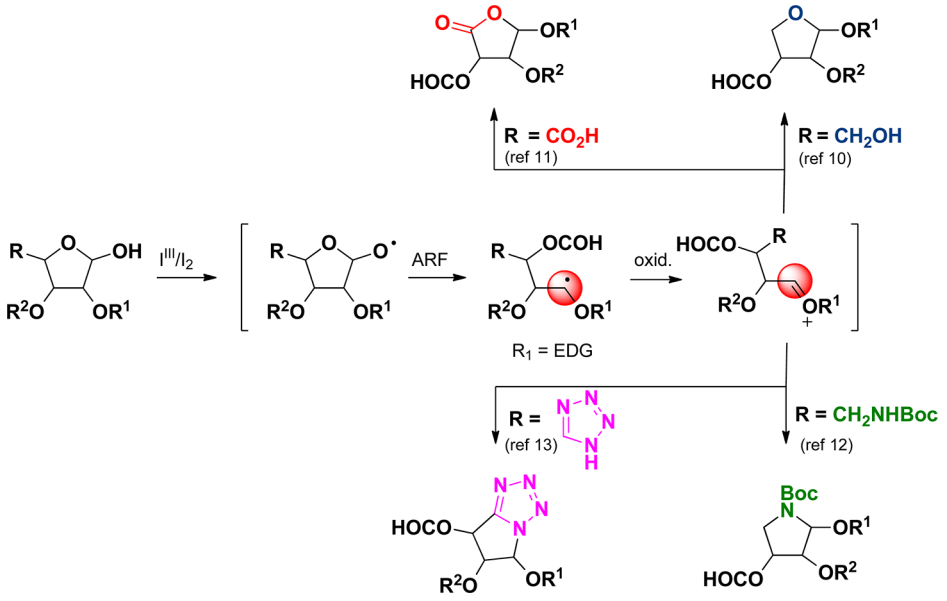
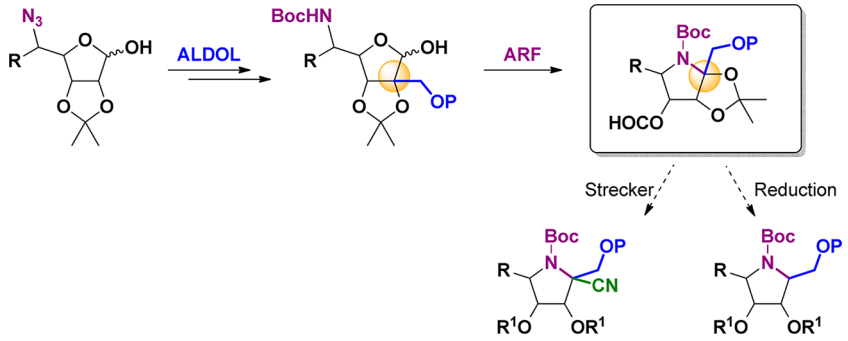
Scheme 1. Anomeric Alkoxyl Radical Fragmentation (ARF): Mechanism and Applications



Scheme 2. Synthesis of Iminoketoses



Herein, we report the efficient synthesis of several iminoketopentoses and iminoketohexoses from carbohydrates, by the concatenation of the two methodologies presented above (Scheme 2).

2. RESULTS AND DISCUSSION

In order to test the viability of our synthetic approach, a battery of substrates showing different stereochemistry, protecting groups and substitution pattern was prepared, starting with 5-amino-5-deoxy-D-ribo derivatives **4a** and **4b**, which were synthesized from the readily available azide **1** (Scheme 3).[23] Aldol reaction with aqueous formaldehyde and methanol in the presence of excess potassium carbonate afforded the corresponding aldol **2**[24] in good yield, as an anomeric mixture. It should be noted here that a careful control of the pH is necessary to obtain the desired products rapidly and in good yields, since cross-Cannizzaro side reactions may compete under longer reaction times.[25] The selective protection of the new primary alcohol, either with TBSCl or PivCl, provided the silyl derivative **3a** and the pivalate **3b**, respectively. Hydrogenation of the azides and in situ protection of the resulting free amines with di-*tert*-butyldicarbonate afforded D-ribo compounds **4a** and **4b** in good yields. Lyxose derivatives **8a** and **8b**, presenting the opposite stereochemistry at positions C−2 and C−3, were synthesized from 5-azido-5-deoxy-D-lyxose (**5**)[12] following a similar protocol (Scheme 3).

For the synthesis of precursors **16a** and **16b**, where the internal nucleophile is located on a secondary position, 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose was used as starting material (Scheme 4). Initially, an analogous synthetic route as that described in Scheme 3 was assayed for the preparation of compounds **16a** and **16b**; however, the aldol reaction carried out in the final steps of the synthesis with more elaborated intermediates proved to be very sluggish, and the desired product was obtained in very low yield. In order to avoid this, we decided to perform the aldol reaction in a first step, as described in the literature.[26] Thus, when compound **9** was treated with formaldehyde in methanol, under our optimized conditions, the corresponding aldol product was obtained in 88% yield, which was treated with benzoyl chloride to afford the dibenzoate **10**. Deprotection of the 5,6-*O*-isopropylidene and further protection of the primary alcohol as TBS ether afforded the silyl derivative **11** in 95% yield. The substitution of the secondary alcohol by the azide moiety was accomplished in a two-step procedure: first was the activation of the alcohol as a triflate ester, and then the nucleophilic substitution with sodium azide afforded the desired L-gulo azide **13** in good yield. The deprotection of both benzoate esters and the selective protection of the primary alcohol as TBS ether or pivalate ester afforded compounds **15a** and **15b** in good yields after the two steps. Finally, hydrogenation of the azide and in situ protection as BOC carbamate led to compounds **16a** and **16b**.

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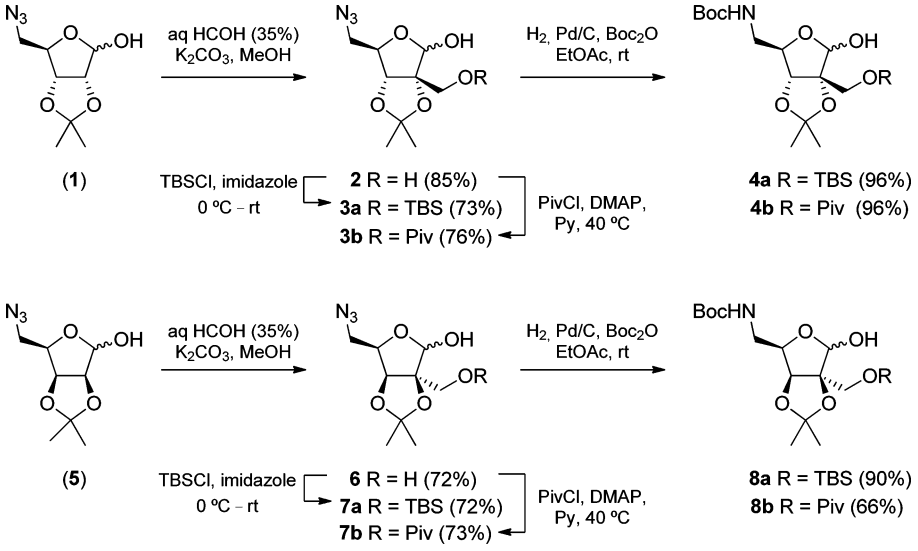
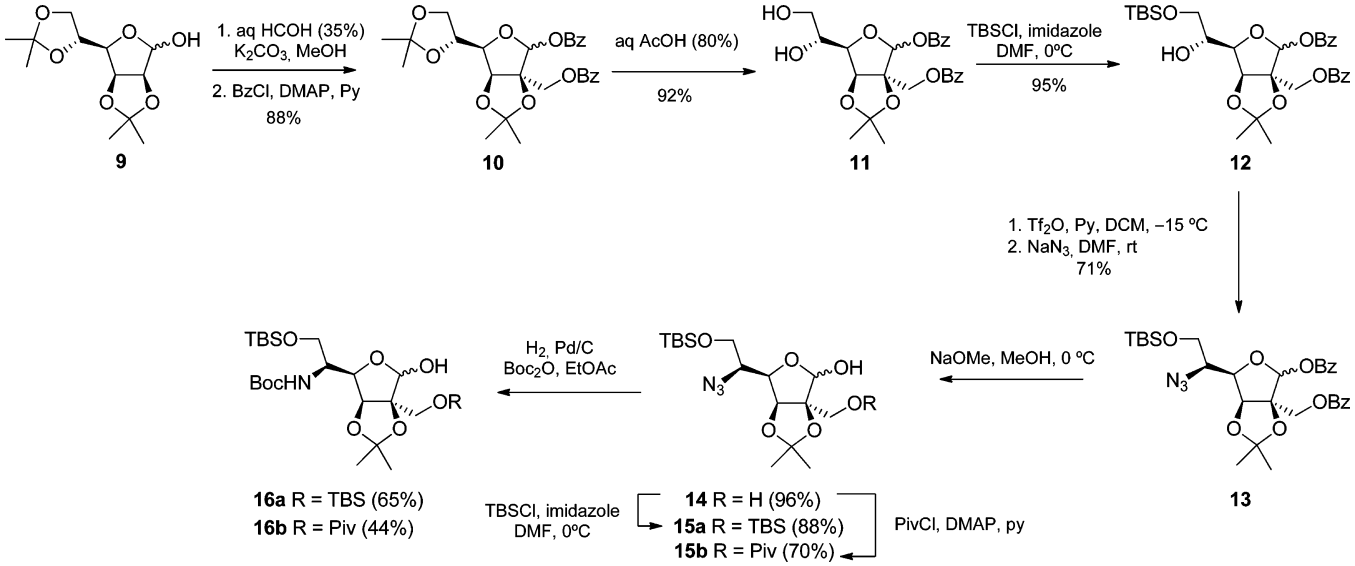
Scheme 3. Synthesis of Substrates for the Pentofuranose Series



Scheme 4. Synthesis of Substrates for the Hexofuranose Series (I)



In order to prepare the precursors **23a**, **23b** and **29**, epoxide **17**,[13] also derived from D-mannose, was used as a common starting material (Scheme 5). On the one hand, treatment of **17** with neat TBAF·2HF[27] provided fluorohydrin **18** as a colorless oil in 91% yield; on the other, the deoxygenated compound **24** was obtained, also in very good yield, by the reductive opening of the epoxide with $LiAlH_4$. Activation of the resulting secondary alcohols as triflate esters and subsequent displacement with sodium azide yielded the azides **19** and **25**, which were afterward treated with CAN to remove the anomeric PMB protecting group. From this point on, the synthetic scheme used was similar to the first one. Aldol reaction, selective protection of the resulting diols and hydrogenation of the azide with in situ formation of the carbamate, furnished compounds **23a**, **23b** and **29** in good yields.

Finally, compounds **35a** and **35b**, both presenting the internal nucleophile at the primary, yet more distant C−6 position, were synthesized in order to widen the scope of this methodology. The synthesis started from epoxide **30**, easily prepared from dibenzoate **11** by treatment, with Ph_3P and DEAD under Mitsunobu conditions. Nucleophilic opening with sodium azide and protection of the resulting secondary alcohol as TBS-ether using TBSOTf afforded compound **32** in good yield. Methanolysis of both benzoates and selective protection of the primary alcohol led to the silylated compound **34a** and the pivalate **34b**, which were hydrogenated and selectively protected to obtain compounds **35a** and **35b**, respectively, in good yields (Scheme 6).

With the aim of demonstrating the synthetic usefulness of our methodology toward the preparation of potential glycosidase inhibitors and structurally related derivatives, the hemiacetalic precursors **4**, **8**, **16**, **23**, **29** and **35** were submitted to photolysis upon treatment with iodosylbenzene[28] and I_2, as oxidizing system, under the conditions specified in Table 1.

When the reaction was performed with the silylated D-ribo-derivative **4a**, we were pleased to find that the expected cyclic iminoketose **36** was obtained in 61% yield as a single compound (entry 1). The ^1H and ^{13}C NMR spectra of this compound showed at room temperature a mixture of conformers due to the restricted rotation of the nitrogen−carbon bond of the

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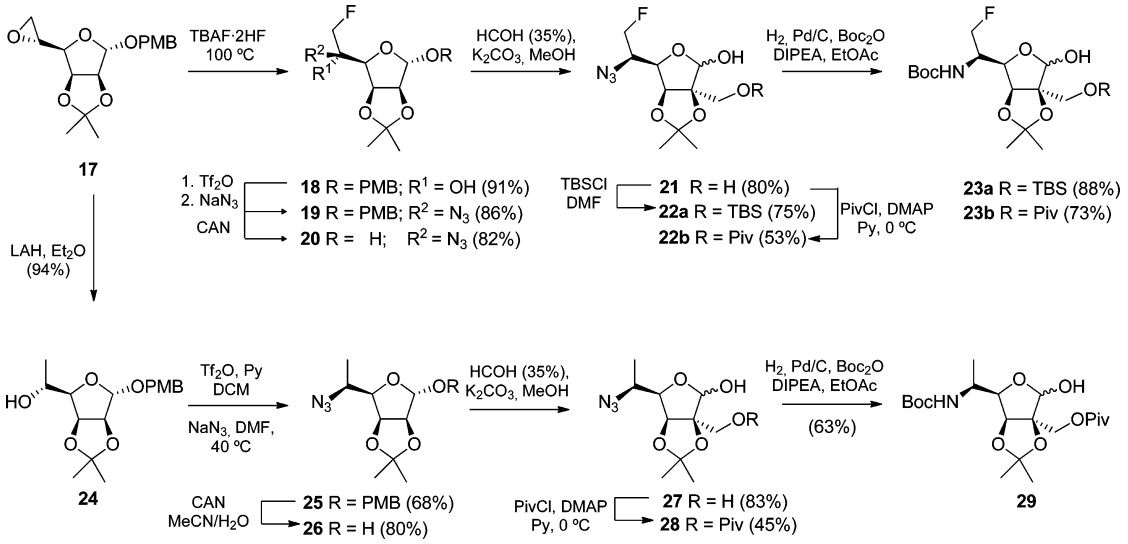
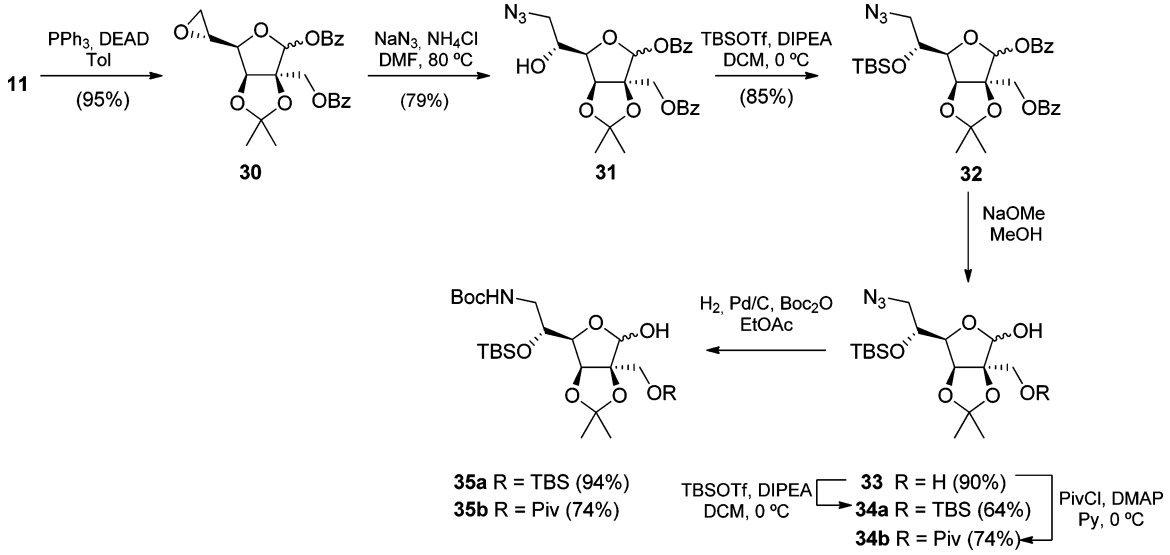
Scheme 5. Synthesis of Substrates for the Hexofuranose Series (II)



Scheme 6. Synthesis of the Substrates for the Hexopyranose Series



carbamate group. However, when these were recorded at 70 °C, sharp well-resolved spectra were obtained in accordance with the proposed structure.

Next, the reaction with pivalate **4b** was carried out. The introduction of an ester group, as in this case, would allow us to evaluate the influence of the protecting group of the hydroxymethyl branch during the cyclization step. In this specific case, the corresponding iminoketose **37** was obtained with an improved yield of 71% and also as a single isomer (entry 2). It is worth mentioning that these compounds have been formed after four consecutive reaction steps: formation of the anomeric alkoxyl radical (A), scission of the C1−C2 bond with concomitant formation of the formate group (B), oxidation of the C2−radical to the corresponding tertiary oxycarbenium (C), and finally, nucleophilic capture of this cationic intermediate by the carbamate group (Scheme 7). This result would translate into an approximate 90% average yield for each individual step.

In order to evaluate the stereoelectronic requirements affecting this reaction, compound **8a**, derived from D-lyxose, was reacted under the same reaction conditions. The corresponding cyclized compound **38** was obtained in a low yield, despite the reaction mixture was allowed to react for a longer time (entry 3). The slowdown in the nucleophilic capture results in an increased lifetime on the intermediates, which leads to partial decomposition of the substrate. Similarly to what happened with the D-ribose analogue **4b**, a better result was obtained when pivalate **8b** was used as starting material in the photolysis (entry 4).

Compound **16a**, which is characterized for having two bulky *tert*-butyldimethylsilyl groups, afforded, after 4 h of reaction, the doubly branched iminoketose **40** in a moderate 46% yield along with a minor compound identified as the alcohol **40a** (entry 5). 2D experiments showed that the free alcohol in **40a** was located in C−1, thus alleviating the steric congestion of the protected cyclized product. Once again, when the reaction was carried out with pivalate **16b**, the corresponding iminoketose **41** was obtained in a slightly higher yield (58%) and in a shorter reaction time (entry 6). It should be noted here that, in this case, no other cyclized compound was isolated, highlighting the higher robustness of pivalate in comparison to TBS-ether under these reaction conditions.

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The fragmentation reaction on the fluorinated compound **23a** led to the formation of the iminoketohexose **42**, albeit in low yield. In this case a different iminosugar **42a**, proceeding from a double fragmentation pathway, was identified as the major product, producing a combined yield for the cyclization reaction of 72%. Once iminoketose **42** is formed, the deprotection of the silyl group can take place in the reaction medium, generating a primary alcohol which, under these oxidizing conditions,

Table 1. Conversion of C−2 Branched Aminoaldoses into Iminoketoses[a]

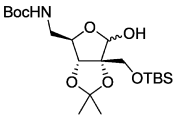
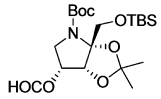
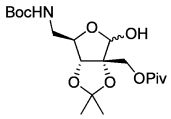
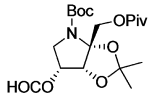
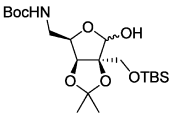
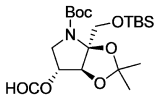
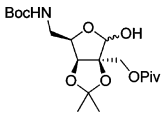
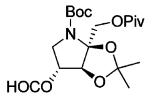
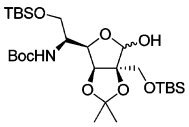
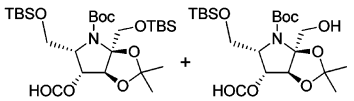
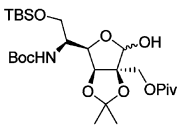
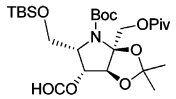
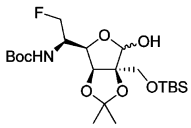
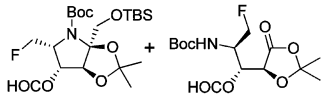
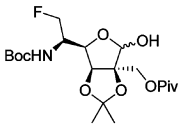
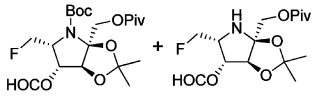
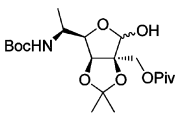
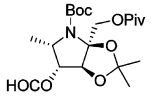
Entry	Substrate	Solvent	Conditions PhIO	Conditions I_2	Conditions t(h)	Product/s (yield %)[b]
1	 **4a**	DCM	2.2	1.2	1.0	 **36** (61)
2	 **4b**	DCM	2.2	1.2	2.0	 **37** (71)
3	 **8a**	DCM	2.5	1.1	5.0	 **38** (35)
4	 **8b**	DCE	2.5	1.1	2.0	 **39** (58)
5	 **16a**	DCM	2.0	1.2	4.0	 **40** (46) **40a** (10)
6	 **16b**	DCM	2.0	1.2	2.0	 **41** (58)
7[c]	 **23a**	DCE	2.5	0.5	1.5	 **42** (25) **42a** (47)
8[c]	 **23b**	DCE	2.5	0.5	1.0	 **43** (39) **43a** (8)
9[d]	 **29**	DCE	2.5	1.1	2.5	 **44** (50)

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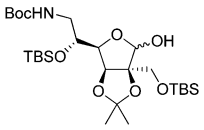
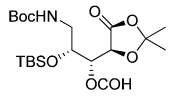
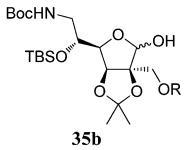
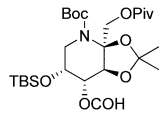
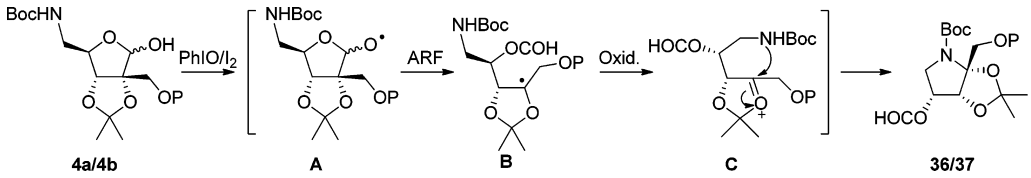
Table 1. continued

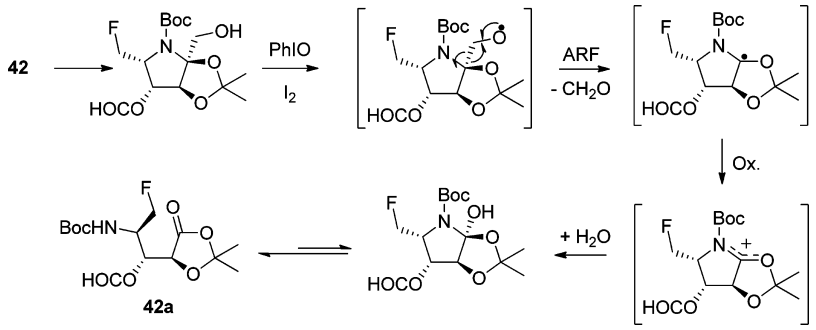
Entry	Substrate	Solvent	Conditions PhIO	I_2	t(h)	Product/s (yield %)[b]
10	 **35a**	DCM	2.0	1.2	20	 **45** (33)
11	 **35b**	DCM	2.0	1.2	4.0	 **46** (46)

[a]Reaction conditions: All reactions were performed in dry DCM or DCE (40 mL/mmol) under irradiation with two 80 W tungsten-filament lamps at room temperature, containing PhIO (2−2.5 equiv) and I_2 (0.5−1.2 equiv). [b]Isolated yield after chromatography. [c]$NaHCO_3$ 100% w/w was added. [d]The reaction was carried out at 80 °C.

Scheme 7. Mechanism of the Tandem ARF-Cyclization Reaction



Scheme 8. Plausible Mechanism for the Synthesis of Compound 42a



undergoes a second fragmentation to generate an acyliminium cation that is finally trapped by water (Scheme 8).[29] A thorough study of the NMR spectra of this compound indicated that its open form is prevalent in solution instead of the aminal form.

According to the previous examples where the pivalate derivatives afforded the corresponding cyclized products in better yields, a similar trend for compound **23b** was expected. However, we were disappointed to find a very complex reaction mixture, where the cyclized compound **43** was isolated as a major compound but in a lower yield (39%), along with another trace compound identified as the free amine (**43a**, 8%). These unexpected results give an idea of the influence that a single fluorine atom can exert on the reactivity and stability of neighboring functional groups.

The photolysis of the 6-deoxyfuranose **29** furnished the iminoketose **44** in a moderate yield after 2 h of reaction. This time, no other side products derived from partial deprotection were detected. Surprisingly, compound **44** was obtained in a lower yield than compound **41**, despite the fact that the carbamate group in the 6-deoxy substrate is less hindered than on the other, where the bulky TBS-ether group flanks the carbamate. These results show that the reaction outcome is not influenced by the steric encumbrance of the nucleophile as much as by the electronic effects induced by vicinal groups.

Next, compounds **35a** and **35b** were synthesized in order to exploit this procedure toward preparing iminoketohexoses in the pyranose form. However, the desired iminoketohexose was not obtained as a product of the photolysis of the hemiacetal **35a**; instead, the major product identified in the reaction mixture was compound **45**, which comes from the deprotection of the silyl group and further fragmentation, following a mechanism similar to that explained in Scheme 8. It should be noted that this reaction, despite presenting the nucleophilic carbamate in a primary position, needs about 20 h to be completed. Such long reaction times cause the decomposition of the intermediate in the reaction media. Similarly to what happened to compound **42a**, NMR spectra of **45** also showed that this structure preferred to adopt the open carbonyl form rather than the hemiaminal form. Interestingly, the photolysis of compound **35b** afforded the expected iminoketose **46** in 46% yield. The successful formation of this homologated iminosugar broadens the scope of this methodology toward the synthesis of novel iminoketoses, also in the pyranose form, and gives an idea of the versatility of this combined process.

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3. CONCLUSION

In summary, we have presented here the first approach to the synthesis of polyhydroxylated iminoketoses by using tandem β-fragmentation−intramolecular cyclization, promoted by the readily available and nontoxic iodosylbenzene, as a key step. These compounds present a well-defined quaternary center, and in general, they are obtained under mild conditions, with short reaction times and moderate to good overall yields. Moreover, simple modifications on these polyfunctionalized scaffolds may lead to more elaborated synthetic derivatives, also possessing interesting pharmacological features. Biological evaluation assays against a set of commercial glycosidases are currently under study and will be reported in due course.

4. EXPERIMENTAL SECTION

General Methods. Optical rotations were measured with a polarimeter at the sodium line at ambient temperature in $CHCl_3$ solutions. IR spectra were recorded CCl_4 unless otherwise stated, with an FTIR instrument. NMR spectra were recorded with a 400 MHz spectrometer for ^1H, 100.6 MHz for ^{13}C, and 376.5 MHz for ^{19}F in $CDCl_3$ unless otherwise stated, in the presence of TMS as internal standard. Structures were elucidated by COSY, DEPT, HSQC and NOESY experiments. Mass spectra were recorded with a spectrometer by using EI-TOF (70 eV) or by using electrospray ionization (ESI^+-TOF), as specified in each case. Elemental analyses were performed with an analyzer using a CHN method. 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 (1:4) and further heating until development of color.

*5-Azido-5-deoxy-2,3-O-isopropylidene-D-ribofuranose (**1**).* Sodium methoxide (254 mg, 4.70 mmol) was added to a solution of the 5-azido-1-*O*-benzoyl-5-deoxy-2,3-*O*-isopropylidene-β-D-ribofuranose[23] (1.50 g, 4.70 mmol) in dry methanol (50 mL, 10 mL/mmol) under nitrogen and in an ice/water bath. The reaction was stirred until reaching room temperature (1h), and then the solvent was removed under reduced pressure. The resulting extract was dissolved in EtOAc and washed with brine; the organic phase was dried over anhydrous sodium sulfate and evaporated under a vacuum. The residue was purified by column chromatography (hexanes−EtOAc, 80:20) to yield **1** (986 mg, 4.59 mmol, 97%) as a colorless oil: IR 3611, 3462, 2991, 2103, 1271 cm^{-1}. NMR showed a mixture of anomers in a 2:1 ratio. Major isomer: ^1H NMR δ_H 1.30 (3H, s), 1.46 (3H, s), 3.37 (1H, dd, J = 5.8, 12.7 Hz), 3.55 (1H, dd, J = 7.3, 12.7 Hz), 4.30 (1H, ddd, J = 1.1, 5.8, 7.3 Hz), 4.61 (1H, d, J = 5.9 Hz), 4.63 (1H, dd, J = 1.1, 5.9 Hz), 5.45 (1H, s); ^{13}C NMR δ_C 24.8 (CH_3), 26.4 (CH_3), 53.9 (CH_2), 82.1 (CH), 85.4 (CH), 86.0 (CH), 103.3 (CH), 112.7 (C). Minor isomer: ^1H NMR δ_H 1.37 (3H, s), 1.55 (3H, s), 3.39 (1H, dd, J = 3.7, 12.7 Hz), 3.51 (1H, dd, J = 4.0, 12.7 Hz), 4.23 (1H, ddd, J = 2.6, 3.7, 4.0 Hz), 4.63 (1H, dd, J = 2.6, 6.7 Hz), 4.66 (1H, dd, J = 4.0, 6.7 Hz), 5.40 (1H, d, J = 4.0 Hz); ^{13}C NMR δ_C 24.7 (CH_3), 26.1 (CH_3), 53.0 (CH_2), 79.5 (CH), 79.6 (CH), 81.6 (CH), 96.9 (CH), 114.6 (C); MS (EI-TOF) m/z (rel intensity) 200 [$(M - CH_3)^+$, 21], 159 (27), 101 (9), 59 (100); HRMS (EI-TOF) m/z [$M - CH_3]^+$ Calcd for $C_7H_{10}N_3O_4$ 200.0671, found 200.0664. Anal. Calcd for $C_8H_{13}N_3O_4$: C, 44.65; H, 6.09; N, 19.53. Found: C, 44.91; H, 6.35; N, 19.22.

*5-Azido-5-deoxy-2-C-hydroxymethyl-2,3-O-isopropylidene-D-ribofuranose (**2**).* Potassium carbonate (860 mg, 100% w/w) was added to a 35% aqueous solution of formaldehyde (8.0 mL, 2 mL/mmol), and the mixture was stirred until a clear solution was observed. A solution of compound **1** (860 mg, 4.0 mmol) in dry methanol (18 mL, 4.5 mL/mmol) was then added dropwise while heating at 80 °C. After 2 h, the solvent was removed under a vacuum, and the residue was extracted twice with EtOAc and washed with brine. The organic phase was dried over anhydrous sodium sulfate and concentrated under a vacuum. The residue was purified by column chromatography (hexanes−EtOAc, 70:30 → 1:1) to yield compound **2** (830 mg, 3.39 mmol, 85%) as a colorless oil: IR 3610, 2996, 2103, 1373, 1244 cm^{-1}. NMR showed a mixture of anomers in a 2:1 ratio. Major isomer: ^1H NMR δ_H 1.37 (3H, s), 1.44 (3H, s), 3.29 (1H, dd, J = 6.0, 12.6 Hz), 3.53 (1H, dd, J = 8.1, 12.6 Hz), 3.79 (1H, d, J = 12.0 Hz), 3.86 (1H, d, J = 12.0 Hz), 4.24 (1H, ddd, J = 1.2, 6.0, 8.1 Hz), 4.45 (1H, d, J = 1.2 Hz), 5.42 (1H, s); ^{13}C NMR δ_C 27.4 (CH_3), 27.8 (CH_3), 52.1 (CH_2), 63.1 (CH_2), 80.5 (CH), 84.9 (CH), 93.3 (C), 104.6 (CH), 113.8 (C). Minor isomer: ^1H NMR δ_H 1.42 (3H, s), 1.54 (3H, s), 3.40 (1H, dd, J = 5.0, 13.0 Hz), 3.46 (1H, dd, J = 4.8, 13.0 Hz), 3.77 (2H, s), 4.26 (1H, ddd, J = 2.1, 4.8, 5.0 Hz), 4.45 (1H, d, J = 2.1 Hz), 5.18 (1H, s); ^{13}C NMR δ_C 26.9 (CH_3), 27.0 (CH_3), 53.3 (CH_2), 62.9 (CH_2), 83.3 (CH), 84.5 (CH), 91.2 (C), 97.8 (CH), 115.3 (C); MS (EI-TOF) m/z (rel intensity) 230 [$(M - CH_3)^+$, 20], 131 (19), 96 (46), 91 (25), 59 (100); HRMS (EI-TOF) m/z [$M - CH_3]^+$ Calcd for $C_8H_{12}N_3O_5$ 230.0777, found 230.0777. Anal. Calcd for $C_9H_{15}N_3O_5$: C, 44.08; H, 6.17; N, 17.13. Found: C, 44.32; H, 6.19; N, 17.06.

*5-Azido-2-C-(tert-butyldimethyl)silyloxymethyl-5-deoxy-2,3-O-isopropylidene-D-ribofuranose (**3a**).* To a solution of diol **2** (565 mg, 2.30 mmol) in dry DMF (5.8 mL, 2.5 mL/mmol) at 0 °C and under nitrogen were added imidazole (313 mg, 4.60 mmol) and then TBSCl (380 mg, 2.50 mmol), and the mixture was stirred for 4 h. It was poured into an ice/water mixture and extracted several times with diethyl ether. The organic phase was dried over sodium sulfate and concentrated under a vacuum. The resulting crude was purified by column chromatography (hexanes−EtOAc, 95:5 → 85:15) to obtain compound **3a** (600 mg, 1.67 mmol, 73%) as a colorless oil: IR 3600, 3500, 2931, 2103, 1256 cm^{-1}. NMR showed a mixture of anomers in a 5:1 ratio. Major isomer: ^1H NMR (500 MHz) δ_H 0.077 (3H, s), 0.080 (3H, s), 0.89 (9H, s), 1.42 (3H, s), 1.54 (3H, s), 3.34 (1H, dd, J = 6.0, 12.9 Hz), 3.38 (1H, dd, J = 6.0, 12.9 Hz), 3.71 (1H, d, J = 10.6 Hz), 3.74 (1H, d, J = 10.6 Hz), 4.20 (1H, ddd, J = 1.9, 6.0, 6.0 Hz), 4.52 (1H, d, J = 1.9 Hz), 5.12 (1H, s); ^{13}C NMR (125.7 MHz) δ_C −5.7 (CH_3), −5.6 (CH_3), 18.3 (C), 25.8 (3 × CH_3), 27.1 (CH_3), 27.3 (CH_3.), 51.6 (CH_2), 63.1 (CH_2), 80.4 (CH), 83.6 (CH), 90.7 (C), 97.7 (CH), 114.7 (C). Minor isomer: ^1H NMR (500 MHz) δ_H 0.09 (3H, s), 0.10 (3H, s), 0.90 (9H, s), 1.38 (3H, s), 1.45 (3H, s), 3.30 (1H, dd, J = 6.8, 12.8 Hz), 3.53 (1H, dd, J = 6.8, 12.8 Hz), 3.80 (1H, d, J = 10.8 Hz), 3.93 (1H, d, J = 10.8 Hz), 4.21 (1H, ddd, J = 1.5, 6.8, 6.8 Hz), 4.48 (1H, d, J = 1.5 Hz), 5.35 (1H, s); ^{13}C NMR (125.7 MHz) δ_C −5.7 (CH_3), −5.6 (CH_3), 18.2 (C), 25.7 (3 × CH_3), 27.7 (CH_3), 27.8 (CH_3), 53.2 (CH_2), 63.5 (CH_2), 84.2 (CH), 84.5 (CH), 93.0 (C), 105.4 (CH), 113.9 (C); MS (EI-TOF) m/z (rel intensity) 344 [$(M - CH_3)^+$, 5], 302 (1), 171 (7), 159 (15), 75 (100); HRMS (EI-TOF) m/z [$M - CH_3]^+$ Calcd for $C_{14}H_{26}N_3O_5Si$ 344.1642, found 344.1634. Anal. Calcd for $C_{15}H_{29}N_3O_5Si$: C, 50.12; H, 8.13; N, 11.69. Found: C, 50.34; H, 8.17; N, 11.62.

*5-(tert-Butoxycarbonyl)amino-2-C-(tert-butyldimethyl)-silyloxymethyl-5-deoxy-2,3-O-isopropylidene-D-ribofuranose (**4a**).* To a solution of azide **3a** (170 mg, 0.47 mmol) in EtOAc (7.0 mL, 15 mL/mmol) were added di-*tert*-butyl dicarbonate (155 mg, 0.71 mmol) and 10% Pd/C (17 mg, 10% w/w). Three vacuum/hydrogen cycles were performed, and the mixture was stirred under hydrogen atmosphere for 1 h. The reaction mixture was then filtered over a Celite pad and washed twice with ethyl acetate, and the combinated filtrates were evaporated. The crude was purified by column chromatography (hexanes−EtOAc, 85:15 → 70:30) to yield compound **4a** (195 mg, 0.45 mmol, 96%) as a colorless oil: IR 3458, 3373, 2932, 1719, 1504, 1252, 1170, 1103 cm^{-1}. NMR showed a mixture of anomers in a 5:3 ratio. Major isomer: ^1H NMR (500 MHz, DMSO-d_6) δ_H 0.037 (3H, s), 0.041 (3H, s), 0.87 (9H, s), 1.32 (3H, s), 1.37 (9H, s), 1.43 (3H, s), 2.93−3.05 (1H, m), 3.12−3.21 (1H, m), 3.56 (1H, d, J = 11.0 Hz), 3.67 (1H, d, J = 11.0 Hz), 3.89 (1H, ddd, J = 0.9, 5.4, 9.1 Hz), 4.39 (1H, d, J = 0.9 Hz), 5.11 (1H, d, J = 4.1 Hz), 6.64 (1H, d, J = 4.1 Hz), 6.83 (1H, dd, J = 6.0, 6.0 Hz); ^{13}C NMR (125.7 MHz, DMSO-d_6) δ_C −5.7 (CH_3), −5.6 (CH_3), 18.0 (C), 25.8 (3x CH_3), 26.9 (CH_3), 27.5 (CH_3), 28.1 (3x CH_3), 43.2 (CH_2), 62.5 (CH_2), 81.9 (C), 83.8 (CH), 84.0 (CH), 94.3 (C), 103.2 (CH), 112.3 (C), 155.5 (C). Minor isomer: ^1H NMR (500 MHz, DMSO-d_6) δ_H 0.06 (6H, s), 0.86 (9H, s), 1.28 (3H, s), 1.31 (9H, s), 1.39 (3H, s), 2.93−3.05 (1H, m), 3.12−3.21 (1H, m), 3.71 (1H, d, J = 11.7 Hz),

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3.74 (1H, d, J = 11.7 Hz), 3.93 (1H, ddd, J = 2.4, 6.8, 6.8 Hz), 4.28 (1H, d, J = 2.4 Hz), 4.92 (1H, d, J = 7.3 Hz), 5.83 (1H, d, J = 7.0 Hz), 6.88 (1H, dd, J = 5.8, 5.8 Hz); ^{13}C NMR (125.7 MHz, DMSO-d_6) δ_C −5.6 (CH_3), −5.4 (CH_3), 17.9 (C), 25.7 (3 × CH_3), 27.3 (CH_3), 27.7 (CH_3), 28.0 (3 × CH_3), 41.5 (CH_2), 63.7 (CH_2), 77.8 (C), 79.5 (CH), 82.7 (CH), 90.9 (C), 96.6 (CH), 113.7 (C), 155.6 (C); MS (EI-TOF) m/z (rel intensity) 418 [$(M - CH_3)^+$, 1], 376 (1), 304 (78), 57 (100); HRMS (EI-TOF) m/z [$M - CH_3$]$^+$ Calcd for $C_{19}H_{36}NO_7Si$ 418.2261, found 418.2246. Anal. Calcd for $C_{20}H_{39}NO_7Si$: C, 55.40; H, 9.07; N, 3.23. Found: C, 55.40; H, 9.06; N, 3.22.

*5-Azido-5-deoxy-2,3-O-isopropylidene-2-C-pivaloyloxymethyl-D-ribofuranose (**3b**).* To a solution of compound **2** (146 mg, 0.60 mmol) in dry pyridine (3 mL, 5 mL/mmol) were added, under nitrogen and at 0 °C, DMAP (14 mg, 0.11 mmol, 10% w/w) and pivaloyl chloride (88 μL, 0.72 mmol), and then the mixture was allowed to warm up to room temperature and stirred for 24 h. The reaction was poured into 10% aqueous HCl and extracted twice with EtOAc. The organic phase was washed with sodium bicarbonate and brine, dried over sodium sulfate and concentrated under a vacuum. The crude was purified by column chromatography (hexanes−EtOAc, 90:10 → 80:20) to yield compound **3b** (150 mg, 0.46 mmol, 76%) as a white solid: IR 3609, 3449, 2974, 2937, 2103, 1734, 1381, 1280 cm^{-1}. NMR showed a mixture of anomers in a 2:1 ratio. Major isomer: ^{1}H NMR δ_H 1.21 (9H, s), 1.46 (3H, s), 1.56 (3H, s), 3.43 (1H, dd, J = 4.5, 13.0 Hz), 3.48 (1H, dd, J = 4.5, 13.0 Hz), 3.85 (1H, d, J = 8.0 Hz), 4.20 (1H, d, J = 12.0 Hz), 4.26 (1H, ddd, J = 2.4, 4.5, 4.5 Hz), 4.32 (1H, d, J = 12.0 Hz), 4.48 (1H, d, J = 2.4 Hz), 5.19 (1H, d, J = 8.0 Hz); ^{13}C NMR δ_C 27.0 (3 × CH_3), 27.2 (CH_3), 27.3 (CH_3), 38.8 (C), 52.4 (CH_2), 64.0 (CH_2), 80.5 (CH), 83.6 (CH), 89.7 (C), 98.2 (CH), 115.7 (C), 177.9 (C). Minor isomer: ^{1}H NMR δ_H 1.20 (9H, s), 1.42 (3H, s), 1.46 (3H, s), 3.33 (1H, dd, J = 5.8, 12.7 Hz), 3.57 (1H, dd, J = 7.6, 12.7 Hz), 4.00 (1H, bs), 4.25 (1H, d, J = 12.2 Hz), 4.26 (1H, ddd, J = 1.3, 5.8, 7.6 Hz), 4.41 (1H, d, J = 1.3 Hz), 4.44 (1H, d, J = 12.2 Hz), 5.41 (1H, bs); ^{13}C NMR δ_C 27.1 (3 × CH_3), 27.6 (CH_3), 28.0 (CH_3), 38.8 (C), 53.7 (CH_2), 63.7 (CH_2), 84.5 (CH), 85.1 (CH), 92.8 (C), 104.0 (CH), 114.1 (C), 178.3 (C); MS (EI-TOF) m/z (rel intensity) 314 [$(M - CH_3)^+$, 8], 215 (6), 96 (47), 57 (100); HRMS (EI-TOF) m/z [$M - CH_3$]$^+$ Calcd for $C_{13}H_{20}N_3O_6$ 314.1352, found 314.1352. Anal. Calcd for $C_{14}H_{23}N_3O_6$: C, 51.06; H, 7.04; N, 12.76. Found: C, 51.35; H, 7.13; N, 12.63.

*5-(tert-Butoxycarbonyl)amino-5-deoxy-2,3-O-isopropylidene-2-C-pivaloyloxymethyl-D-ribofuranose (**4b**).* To a solution of azide **3b** (240 mg, 0.73 mmol) in EtOAc (11.0 mL, 15 mL/mmol) were added di-*tert*-butyl dicarbonate (238 mg, 1.1 mmol) and 10% Pd/C (24 mg, 10% w/w). Three vacuum/hydrogen cycles were performed, and the mixture was stirred under hydrogen atmosphere for 2 h. The reaction mixture was then filtered over a Celite pad and washed twice with ethyl acetate, and the combined filtrates were evaporated. The crude was purified by column chromatography (hexanes−EtOAc, 90:10 → 70:30) to yield compound **4b** (282 mg, 0.70 mmol, 96%) as a colorless oil: IR 3459, 3373, 2980, 2937, 1731, 1718, 1510, 1247, 1158 cm^{-1}. NMR showed a mixture of anomers in a 2:1 ratio (only major one is described): ^{1}H NMR (500 MHz, DMSO-d_6) δ_H 1.15 (9H, s), 1.35 (3H, s), 1.36 (9H, s), 1.37 (3H, s), 3.02 (1H, ddd, J = 5.4, 5.4, 13.8 Hz), 3.14 (1H, ddd, J = 6.9, 9.6, 13.8 Hz), 3.76 (1H, bs), 3.92 (1H, dd, J = 5.3, 9.6 Hz), 4.14 (1H, d, J = 12.2 Hz), 4.22 (1H, d, J = 12.2 Hz), 4.47 (1H, s), 5.19 (1H, d, J = 3.8 Hz), 6.84−6.89 (1H, m); ^{13}C NMR (125.7 MHz, DMSO-d_6) δ_C 26.8 (3 × CH_3), 27.6 (CH_3), 27.7 (CH_3), 28.1 (3 × CH_3), 38.2 (C), 43.1 (CH_2), 63.9 (CH_2), 77.9 (C), 84.1 (CH), 84.2 (CH), 92.4 (C), 102.8 (CH), 112.6 (C), 155.6 (C), 177.3 (C); MS (EI-TOF) m/z (rel intensity) 388 [$(M - CH_3)^+$, 1], 312 (7), 245 (10), 199 (24), 57 (100); HRMS (EI-TOF) m/z [$M - CH_3$]$^+$ Calcd for $C_{18}H_{30}NO_8$ 388.1971, found 388.1965. Anal. Calcd for $C_{19}H_{33}NO_8$: C, 56.56; H, 8.24; N, 3.47. Found: C, 56.41; H, 8.41; N, 3.36.

*5-Azido-5-deoxy-2,3-O-isopropylidene-D-lyxofuranose (**5**).* Sodium methoxide (157 mg, 2.91 mmol) was added to a solution of 5-azido-1-*O*-benzoyl-5-deoxy-2,3-*O*-isopropylidene-α-D-lyxofuranose[12] (740 mg, 2.32 mmol) in dry methanol (25 mL, 10 mL/mmol) under nitrogen and in an ice/water bath. The reaction was stirred at room temperature for 1.5 h. Then, the solvent was removed under reduced pressure. The resulting extract was dissolved in EtOAc and washed with brine; the organic phase was dried over anhydrous sodium sulfate and removed under a vacuum. The residue was purified by column chromatography (hexanes−EtOAc, 90:10 → 70:30) to yield **5** (467 mg, 2.17 mmol, 93%) as a colorless oil: IR 3611, 2992, 2949, 2101, 1373, 1270 cm^{-1}. NMR showed a mixture of anomers in a 5:1 ratio. Major isomer: ^{1}H NMR δ_H 1.32 (3H, s), 1.46 (3H, s), 2.71 (1H, bs), 3.52 (1H, dd, J = 4.8, 12.2 Hz), 3.57 (1H, dd, J = 6.6, 12.2 Hz), 4.30 (1H, ddd, J = 3.7, 4.8, 6.6 Hz), 4.63 (1H, d, J = 5.8 Hz), 4.75 (1H, dd, J = 3.7, 5.8 Hz), 5.41 (1H, s); ^{13}C NMR δ_C 24.7 (CH_3), 25.9 (CH_3), 49.9 (CH_2), 78.8 (CH), 79.7 (CH), 85.5 (CH), 101.2 (CH), 112.9 (C). Minor isomer: ^{1}H NMR δ_H 1.38 (3H, s), 1.54 (3H, s), 2.71 (1H, bs), 3.55−3.62 (2H, m), 3.68 (1H, ddd, J = 3.7, 6.5, 6.5 Hz), 4.55 (1H, dd, J = 3.7, 6.1 Hz), 4.69 (1H, dd, J = 3.4, 6.1 Hz), 5.04 (1H, d, J = 3.7 Hz); ^{13}C NMR δ_C 24.9 (CH_3), 25.7 (CH_3), 49.4 (CH_2), 74.4 (CH), 78.7 (CH), 79.3 (CH), 97.0 (CH), 113.6 (C); MS (EI-TOF) m/z (rel intensity) 200 [$(M - CH_3)^+$, 71], 159 (17), 135 (17), 59 (100); HRMS (EI-TOF) m/z [$M - CH_3$]$^+$ Calcd for $C_7H_{10}N_3O_4$ 200.0671, found 200.0671. Anal. Calcd for $C_8H_{13}N_3O_4$: C, 44.65; H, 6.09; N, 19.53. Found: C, 44.35; H, 5.94; N, 19.28.

*5-Azido-5-deoxy-2-C-hydroxymethyl-2,3-O-isopropylidene-D-lyxofuranose (**6**).* Potassium carbonate (573 mg, 100% w/w) was added to a 35% aqueous solution of formaldehyde (5.0 mL, 2 mL/mmol), and the mixture was stirred until a clear solution was observed. A solution of compound **5** (573 mg, 2.66 mmol) in dry methanol (13 mL, 5 mL/mmol) was then added dropwise while heating at 80 °C. After 2 h, the solvent was removed under a vacuum, and the residue was extracted twice with EtOAc and washed with brine. The organic phase was dried over anhydrous sodium sulfate and concentrated under a vacuum. The residue was purified by column chromatography (hexanes−EtOAc, 70:30 → 1:1) to yield compound **6** (470 mg, 1.92 mmol, 72%) as a colorless oil: IR 3565, 3421, 2990, 2103, 1271 cm^{-1}. NMR showed a mixture of anomers in a 2:1 ratio. Major isomer: ^{1}H NMR (500 MHz) δ_H 1.41 (3H, s), 1.47 (3H, s), 3.24 (1H, bs), 3.54 (1H, dd, J = 5.2, 12.7 Hz), 3.59 (1H, dd, J = 7.6, 12.7 Hz), 3.84 (1H, d, J = 11.9 Hz), 3.99 (1H, d, J = 11.9 Hz), 4.32 (1H, ddd, J = 3.1, 5.2, 7.6 Hz), 4.61 (1H, d, J = 3.1 Hz), 5.41 (1H, s); ^{13}C NMR (125.7 MHz) δ_C 27.4 (CH_3), 27.5 (CH_3), 49.8 (CH_2), 63.4 (CH_2), 79.5 (CH), 82.9 (CH), 94.0 (C), 103.7 (CH), 114.2 (C). Minor isomer: ^{1}H NMR (500 MHz) δ_H 1.47 (3H, s), 1.57 (3H, s), 3.52−3.61 (2H, m), 3.73 (1H, ddd, J = 3.3, 6.3, 6.7 Hz), 3.77 (1H, d, J = 11.5 Hz), 3.81 (1H, d, J = 11.5 Hz), 4.59 (1H, d, J = 3.3 Hz), 4.92 (1H, d, J = 6.7 Hz); ^{13}C NMR (125.7 MHz) δ_C 26.9 (CH_3), 27.1 (CH_3), 49.4 (CH_2), 62.7 (CH_2), 74.5 (CH), 81.9 (CH), 89.7 (C), 97.5 (CH), 114.4 (C); MS (EI-TOF) m/z (rel intensity) 230 [$(M - CH_3)^+$, 61], 110 (32), 96 (100), 71 (45), 59 (100); HRMS (EI-TOF) m/z [$M - CH_3$]$^+$ Calcd for $C_8H_{12}N_3O_5$ 230.0777, found 230.0777. Anal. Calcd for $C_9H_{15}N_3O_5$: C, 44.08; H, 6.17; N, 17.13. Found: C, 44.30; H, 6.34; N, 16.87.

*5-Azido-2-C-(tert-butyldimethyl)silyloxymethyl-5-deoxy-2,3-O-isopropylidene-D-lyxofuranose (**7a**).* To a solution of diol **6** (500 mg, 2.04 mmol) in dry DMF (5.0 mL, 2.5 mL/mmol) at 0 °C and under nitrogen, were added imidazole (280 mg, 4.08 mmol), DMAP (25 mg, 0.2 mmol), and TBSCl (355 mg, 2.35 mmol), and the mixture was stirred for 2 h at room temperature and then poured into an ice/water mixture and extracted several times with diethyl ether. The organic phase was dried over sodium sulfate and concentrated under a vacuum. The resulting crude was purified by column chromatography (hexanes−EtOAc, 95:5 → 85:15) to obtain compound **7a** (530 mg, 1.48 mmol, 72%) as a colorless oil: IR 3608, 3524, 2989, 2104, 1256 cm^{-1}. NMR showed a mixture of anomers in a 4:1 ratio. Major isomer: ^{1}H NMR δ_H 0.08 (3H, s), 0.09 (3H, s), 0.90 (9H, s), 1.43 (3H, s), 1.54 (3H, s), 3.53 (1H, dd, J = 6.6, 12.5 Hz), 3.58 (1H, dd, J = 6.6, 12.5 Hz), 3.67 (1H, ddd, J = 2.9, 6.6, 6.6 Hz), 3.74 (2H, s), 4.58 (1H, d, J = 2.9 Hz), 4.80 (1H, bs), 5.01 (1H, bs); ^{13}C NMR δ_C −5.3 (CH_3), −5.2 (CH_3), 18.5 (C), 26.1 (3 × CH_3), 27.2 (CH_3), 27.3 (CH_3), 49.8 (CH_2), 63.5 (CH_2), 75.0 (CH), 83.0 (CH), 89.2 (C), 97.6 (CH), 114.3 (C). Minor isomer: ^{1}H NMR δ_H 0.13 (6H, s), 0.91 (9H, s), 1.38 (3H, s), 1.47 (3H, s), 3.52−3.57 (1H, m), 3.60 (1H, dd, J = 6.4, 12.7 Hz), 3.83 (1H, d, J = 10.6 Hz), 4.08 (1H, d, J = 10.6 Hz), 4.21 (1H, ddd, J = 2.9, 6.4, 6.4 Hz), 4.56 (1H, d, J = 2.9 Hz), 4.80 (1H, bs), 5.29 (1H, bs); ^{13}C NMR δ_C −5.3 (CH_3), −5.2 (CH_3), 18.5 (C), 26.1 (3 × CH_3), 27.8 (2 × CH_3), 50.0 (CH_2), 64.4 (CH_2), 79.2 (CH), 83.6 (CH), 93.5 (C), 104.9 (CH), 114.6 (C); MS (EI-TOF) m/z (rel intensity) 344 [$(M - CH_3)^+$, 4], 226 (2), 183 (15), 75 (100); HRMS (EI-TOF) m/z [$M - CH_3$]$^+$ Calcd for

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$C_{14}H_{26}N_3O_5Si$, 344.1642, found 344.1641. Anal. Calcd for $C_{15}H_{29}N_3O_5Si$: C, 50.12; H, 8.13; N, 11.69. Found: C, 50.13; H, 7.95; N, 11.65.

*5-(tert-Butoxycarbonyl)amino-2-C-(tert-butyldimethyl)-silyloxymethyl-5-deoxy-2,3-O-isopropylidene-D-lyxofuranose (**8a**).* To a solution of azide **7a** (210 mg, 0.59 mmol) in EtOAc (9.0 mL, 15 mL/mmol) were added di-*tert*-butyl dicarbonate (167 mg, 0.77 mmol) and 10% Pd/C (21 mg, 10% w/w). Three vacuum/hydrogen cycles were performed, and the mixture was stirred under hydrogen atmosphere for 3 h. The reaction mixture was then filtered over a Celite pad, washed twice with ethyl acetate, and the combinated filtrates were evaporated. The crude was purified by column chromatography (hexanes−EtOAc, 80:20 → 70:30) to yield compound **8a** (230 mg, 0.53 mmol, 90%) as an oil: IR 3459, 2954, 2931, 2858, 1718, 1370 cm^{-1}. NMR showed a mixture of anomers in a 2:1 ratio. Major isomer: ^1H NMR (500 MHz, DMSO-d_6) δ_H 0.057 (3H, s), 0.061 (3H, s), 0.88 (9H, s), 1.34 (3H, s), 1.370 (9H, s), 1.42 (3H, s), 3.13−3.24 (2H, m), 3.69 (1H, d, J = 11.5 Hz), 3.76 (1H, d, J = 11.5 Hz), 4.04−4.07 (1H, m), 4.45 (1H, d, J = 3.1 Hz), 5.03 (1H, d, J = 4.4 Hz), 5.73 (1H, d, J = 4.4 Hz), 6.83 (1H, bs); ^{13}C NMR δ_C −5.7 (CH_3), −5.6 (CH_3), 18.1 (C), 25.8 (3 × CH_3), 26.8 (CH_3), 27.0 (CH_3), 28.3 (3 × CH_3), 39.7 (CH_2), 63.1 (CH_2), 74.8 (CH), 79.3 (C), 82.9 (CH), 89.1 (C), 97.0 (CH), 113.7 (C), 155.9 (C). Minor isomer: ^1H NMR (500 MHz, DMSO-d_6) δ_H 0.04 (6H, s), 0.86 (9H, s), 1.33 (3H, s), 1.36 (9H, s), 1.40 (3H, s), 3.13−3.20 (2H, m), 3.51−3.54 (1H, m), 3.66 (2H, s), 4.39 (1H, d, J = 3.1 Hz), 4.75 (1H, d, J = 9.6 Hz), 5.25 (1H, bs), 5.73 (1H, d, J = 9.6 Hz); ^{13}C NMR δ_C −5.7 (CH_3), −5.6 (CH_3), 18.1 (C), 25.7 (3 × CH_3), 27.0 (CH_3), 27.4 (CH_3), 28.3 (3 × CH_3), 39.8 (CH_2), 63.9 (CH_2), 79.0 (CH), 79.3 (C), 83.6 (CH), 93.2 (C), 104.4 (CH), 114.0 (C), 155.9 (C); MS (EI-TOF) m/z (rel intensity) 418 [$(M - CH_3)^+$, 1], 360 (1), 302 (25), 276 (23), 199 (31), 75 (60), 57 (100); HRMS (EI-TOF) m/z [$M - CH_3$]$^+$ Calcd for $C_{19}H_{36}NO_7Si$ 418.2261, found 418.2252. Anal. Calcd for $C_{20}H_{39}NO_7Si$: C, 55.40; H, 9.07; N, 3.23. Found: C, 55.25; H, 9.00; N, 3.27.

*5-Azido-5-deoxy-2,3-O-isopropylidene-2-C-pivaloyloxymethyl-D-lyxofuranose (**7b**).* To a solution of compound **6** (294 mg, 1.20 mmol) in dry pyridine (6 mL, 5 mL/mmol) were added, under nitrogen and at 0 °C, DMAP (30 mg, 10% w/w) and pivaloyl chloride (0.2 mL, 1.68 mmol), and then the mixture was warmed at 40 °C and stirred for 24 h. The reaction was poured into 10% aqueous HCl and extracted twice with EtOAc. The organic phase was washed with sodium bicarbonate and brine, dried over sodium sulfate and concentrated under a vacuum. The crude was purified by column chromatography (hexanes−EtOAc, 90:10 → 80:20) to yield compound **7b** (290 mg, 0.88 mmol, 73%) as a white solid: IR 3446, 2981, 2104, 1736, 1647 cm^{-1}. NMR showed a mixture of anomers in a 3:2 ratio. Major isomer: ^1H NMR δ_H 1.22 (9H, s), 1.43 (3H, s), 1.46 (3H, s), 3.22 (1H, bs), 3.52 (1H, dd, J = 5.4, 12.7 Hz), 3.60 (1H, dd, J = 4.2, 12.7 Hz), 4.28 (1H, ddd, J = 3.1, 4.2, 5.4 Hz), 4.29 (1H, d, J = 12.2 Hz), 4.46 (1H, d, J = 12.2 Hz), 4.50 (1H, d, J = 3.1 Hz), 5.35 (1H, s); ^{13}C NMR δ_C 27.1 (3 × CH_3), 27.5 (CH_3), 27.8 (CH_3), 38.8 (C), 49.6 (CH_2), 63.3 (CH_2), 78.8 (CH), 82.7 (CH), 93.4 (C), 102.6 (CH), 114.5 (C), 178.3 (C). Minor isomer: ^1H NMR δ_H 1.21 (9H, s), 1.46 (3H, s), 1.55 (3H, s), 3.54 (1H, dd, J = 6.4, 12.3 Hz), 3.58 (1H, dd, J = 5.9, 12.3 Hz), 3.68 (1H, ddd, J = 3.0, 5.9, 6.4 Hz), 3.88 (1H, d, J = 12.0 Hz), 4.20 (1H, d, J = 11.7 Hz), 4.26 (1H, d, J = 11.7 Hz), 4.52 (1H, d, J = 3.0 Hz), 4.93 (1H, d, J = 12.0 Hz); ^{13}C NMR δ_C 26.78 (CH_3), 26.84 (CH_3), 27.1 (3 × CH_3), 38.9 (C), 49.2 (CH_2), 63.6 (CH_2), 74.4 (CH), 82.3 (CH), 87.5 (C), 97.7 (CH), 114.7 (C), 177.7 (C); MS (EI-TOF) m/z (rel intensity) 314 [$(M - CH_3)^+$, 9], 215 (2), 139 (2), 96 (75), 57 (100); HRMS (EI-TOF) m/z [$M - CH_3$]$^+$ Calcd for $C_{13}H_{20}N_3O_6$ 314.1352, found 314.1354. Anal. Calcd for $C_{14}H_{23}N_3O_6$: C, 51.06; H, 7.04; N, 12.76. Found: C, 51.19; H, 7.37; N, 13.07.

*5-(tert-Butoxycarbonyl)amino-5-deoxy-2,3-O-isopropylidene-2-C-pivaloyloxymethyl-D-lyxofuranose (**8b**).* To a solution of azide **7b** (284 mg, 0.86 mmol) in EtOAc (12.0 mL, 15 mL/mmol) were added di-*tert*-butyl dicarbonate (375 mg, 1.72 mmol) and 10% Pd/C (50 mg, 20% w/w). Three vacuum/hydrogen cycles were performed, and the mixture was stirred under hydrogen atmosphere for 3 h. The reaction mixture was then filtered over a Celite pad and washed twice with ethyl acetate, and the combinated filtrates were evaporated. The crude was purified by column chromatography (hexanes−EtOAc, 90:10 → 70:30) to yield compound **8b** (230 mg, 0.57 mmol, 66%) as a colorless oil: IR 3596, 2986, 1737, 1705, 1408, 1240 cm^{-1}. NMR showed a mixture of anomers in a 6:1 ratio (only major anomer described): ^1H NMR (500 MHz, DMSO-d_6) δ_H 1.15 (9H, s), 1.36 (12H, s), 1.40 (3H, s), 3.11−3.23 (2H, m), 4.08 (1H, ddd, J = 3.3, 5.9, 8.0 Hz), 4.12 (1H, d, J = 12.2 Hz), 4.29 (1H, d, J = 12.2 Hz), 4.46 (1H, d, J = 3.3 Hz), 5.09 (1H, d, J = 4.0 Hz), 6.50 (1H, d, J = 4.0 Hz), 6.85 (1H, dd, J = 5.2, 5.2 Hz); ^{13}C NMR (125.7 MHz, DMSO-d_6) δ_C 26.8 (3 × CH_3), 27.5 (CH_3), 27.6 (CH_3), 28.2 (3 × CH_3), 38.2 (CH_2), 38.7 (C), 63.1 (CH_2), 77.7 (CH), 80.6 (C), 82.1 (CH), 93.1 (C), 101.4 (CH), 112.8 (C), 155.5 (C), 177.2 (C); MS (EI-TOF) m/z (rel intensity) 403 (M^+, 1), 372 (1), 286 (4), 231 (3), 85 (15), 57 (100); HRMS (EI-TOF) m/z [M]$^+$ Calcd for $C_{19}H_{33}NO_8$ 403.2206, found 403.2190. Anal. Calcd for $C_{19}H_{33}NO_8$: C, 56.56; H, 8.24; N, 3.47. Found: C, 56.66; H, 8.35; N, 3.50.

*2-C-Hydroxymethyl-2,3:5,6-di-O-isopropylidene-D-mannofuranose (**9a**).*[26] Potassium carbonate (750 mg) was added to a 35% aqueous solution of formaldehyde (7.5 mL, 1.5 mL/mmol), and the mixture was stirred until a clear solution was observed. A solution of compound **9** (1.30 g, 5.00 mmol) in dry methanol (10 mL, 2 mL/mmol) was then added dropwise while heating at 80 °C. After 20 h, the solvent was removed under a vacuum, and the residue was extracted twice with EtOAc and washed with brine. The organic phase was dried over anhydrous sodium sulfate and concentrated under a vacuum. The residue was purified by column chromatography (hexanes−EtOAc, 70:30 → 1:1) to yield compound **9a** (1.27 g, 4.39 mmol, 88%) as an oil: IR 3615, 3419, 2989, 2937, 1456, 1371 cm^{-1}. NMR showed a mixture of anomers in a 2:1 ratio. Major isomer: ^1H NMR δ_H 1.38 (3H, s), 1.42 (3H, s), 1.45 (3H, s), 1.47 (3H, s), 2.60 (1H, bs), 3.16 (1H, bs), 3.86 (1H, d, J = 11.9 Hz), 3.99 (1H, d, J = 11.9 Hz), 4.04 (1H, dd, J = 4.7, 8.7 Hz), 4.10 (1H, dd, J = 6.1, 8.7 Hz), 4.16 (1H, dd, J = 3.0, 7.7 Hz), 4.40 (1H, ddd, J = 4.7, 6.1, 7.7 Hz), 4.67 (1H, d, J = 3.0 Hz), 5.38 (1H, s); ^{13}C NMR δ_C 25.1 (CH_3), 26.9 (CH_3), 27.3 (2 × CH_3), 63.6 (CH_2), 66.6 (CH_2), 73.1 (CH), 81.1 (CH), 82.8 (CH), 93.7 (C), 103.8 (CH), 109.2 (C), 113.8 (C). Minor isomer: ^1H NMR δ_H 1.37 (3H, s), 1.44 (3H, s), 1.49 (3H, s), 1.56 (3H, s), 1.87 (1H, bs), 3.51 (1H, dd, J = 2.9, 8.2 Hz), 3.77 (1H, d, J = 11.7 Hz), 3.81 (1H, d, J = 11.7 Hz), 3.87 (1H, d, J = 11.0 Hz), 4.05 (1H, dd, J = 4.3, 8.8 Hz), 4.11 (1H, dd, J = 6.1, 8.9 Hz), 4.38 (1H, ddd, J = 4.3, 6.1, 8.3 Hz), 4.65 (1H, d, J = 2.8 Hz), 4.89 (1H, d, J = 11.0 Hz); ^{13}C NMR δ_C 25.2 (CH_3), 26.8 (CH_3), 26.97 (CH_3), 27.02 (CH_3), 62.8 (CH_2), 67.1 (CH_2), 72.9 (CH), 76.4 (CH), 81.9 (CH), 89.5 (C), 97.6 (CH), 109.4 (C), 114.1 (C); MS (EI-TOF) m/z (rel intensity) 275 [$(M - CH_3)^+$, 35], 217 (14), 199 (22), 101 (100); HRMS (EI-TOF) m/z [$M - CH_3$]$^+$ Calcd for $C_{12}H_{19}O_7$ 275.1131, found 275.1134. Anal. Calcd for $C_{13}H_{22}O_7$: C, 53.78; H, 7.64. Found: C, 53.78; H, 7.68.

*1-O-Benzoyl-2-C-benzoyloxymethyl-2,3:5,6-di-O-isopropylidene-D-mannofuranose (**10**).* To a solution of compound **9a** (900 mg, 3.10 mmol) in dry pyridine (10 mL, 3 mL/mmol) was added, under nitrogen and at 0 °C, DMAP (40 mg, 0.31 mmol) and benzoyl chloride (1.08 mL, 9.3 mmol), and the mixture was stirred for 13 h and allowed to reach room temperature. The reaction was poured into aqueous HCl and extracted with EtOAc. The organic phase was washed with sodium bicarbonate and brine, dried over sodium sulfate and concentrated under a vacuum. The residue was purified by column chromatography (hexanes−EtOAc, 90:10) to afford **10** (1.29 g, 2.59 mmol, 84%) as an oil: IR 2990, 2938, 2884, 1731, 1266 cm^{-1}. NMR showed a mixture of anomers in a 5:2 ratio. Major isomer: ^1H NMR δ_H 1.38 (3H, s), 1.45 (3H, s), 1.48 (3H, s), 1.56 (3H, s), 4.04 (1H, dd, J = 4.0, 9.0 Hz), 4.13 (1H, dd, J = 6.1, 9.0 Hz), 4.15 (1H, dd, J = 3.3, 8.3 Hz), 4.48 (1H, ddd, J = 4.0, 6.1, 8.3 Hz), 4.72 (1H, d, J = 11.9 Hz), 4.78 (1H, d, J = 11.9 Hz), 4.88 (1H, d, J = 3.3 Hz), 6.54 (1H, s), 7.34−7.48 (6H, m), 7.91−8.00 (4H, m); ^{13}C NMR δ_C 25.1 (CH_3), 27.0 (CH_3), 27.4 (CH_3), 27.5 (CH_3), 63.7 (CH_2), 67.0 (CH_2), 72.6 (CH), 82.6 (CH), 82.9 (CH), 93.4 (C), 101.7 (CH), 109.6 (C), 115.2 (C), 128.4 (2 × CH), 128.5 (2 × CH), 129.2 (C), 129.4 (C), 129.6 (2 × CH), 129.7 (2 × CH), 133.3 (CH), 133.6 (CH), 164.7 (C), 166.1 (C). Minor isomer: ^1H NMR δ_H 1.40 (3H, s), 1.43 (3H, s), 1.44 (3H, s), 1.45 (3H, s), 4.11−4.18 (3H, m), 4.55 (1H, ddd, J = 4.9, 6.0, 7.7 Hz), 4.70 (1H, d, J = 11.7 Hz), 4.74 (1H, d, J = 11.7 Hz), 4.80 (1H, d, J = 4.0 Hz), 6.22 (1H, s), 7.51−7.61 (6H, m), 8.04−8.12 (4H, m); ^{13}C NMR δ_C 25.3 (CH_3), 26.2 (CH_3),

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26.3 (CH_3), 26.9 (CH_3), 64.4 (CH_2), 66.7 (CH_2), 73.4 (CH), 79.8 (CH), 81.4 (CH), 89.8 (C), 99.0 (CH), 109.4 (C), 115.1 (C), 128.5 (2 × CH), 128.6 (2 × CH), 129.2 (C), 129.4 (C), 129.7 (2 × CH), 129.9 (2 × CH), 133.4 (CH), 133.5 (CH), 164.9 (C), 166.0 (C); MS (EI-TOF) m/z (rel intensity) 483 [$(M - CH_3)^+$, 22], 425 (10), 272 (11), 114 (50), 105 (100); HRMS (EI-TOF) m/z [$M - CH_3]^+$ Calcd for $C_{26}H_{27}O_9$ 483.1655, found 483.1652. Anal. Calcd for $C_{27}H_{30}O_9$: C, 65.05; H, 6.07. Found: C, 65.12; H, 6.27.

*1-O-Benzoyl-2-C-benzoyloxymethyl-2,3-O-isopropylidene-D-mannofuranose (**11**).* Compound **10** (1.20 g, 2.41 mmol) was dissolved in 80% aqueous acetic acid (25 mL, 10 mL/mmol) and stirred for 20 h at room temperature. The solvent was evaporated under a vacuum, and the residue thus obtained was extracted with EtOAc and sodium bicarbonate; the organic phase was washed with brine, dried over sodium sulfate and concentrated under a vacuum. The crude was purified by column chromatography (hexanes−EtOAc, 85:15 → 1:1 → 0:100) to afford diol **11** (1.01 g, 2.21 mmol, 92%) as a white solid: IR 3443, 2990, 1731, 1271 cm^{-1}. NMR showed a mixture of anomers in a 5:1 ratio. Major isomer: ^1H NMR δ_H 1.47 (3H, s), 1.56 (3H, s), 2.34 (2H, bs), 3.72 (1H, dd, J = 5.6, 11.7 Hz), 3.88 (1H, dd, J = 3.2, 11.7 Hz), 4.12 (1H, ddd, J = 3.2, 5.6, 8.2 Hz), 4.26 (1H, dd, J = 3.2, 8.3 Hz), 4.70 (1H, d, J = 12.0 Hz), 4.78 (1H, d, J = 12.0 Hz), 4.93 (1H, d, J = 3.2 Hz), 6.58 (1H, s), 7.34−7.49 (6H, m), 7.91−7.99 (4H, m); ^{13}C NMR δ_C 27.52 (CH_3), 27.54 (CH_3), 63.7 (CH_2), 64.0 (CH_2), 69.6 (CH), 81.6 (CH), 83.1 (CH), 93.2 (C), 101.4 (CH), 115.2 (C), 128.4 (2 × CH), 128.5 (2 × CH), 129.1 (C), 129.3 (C), 129.6 (2 × CH), 129.7 (2 × CH), 133.3 (CH), 133.6 (CH), 164.7 (C), 166.1 (C). Minor isomer: ^1H NMR δ_H 1.42 (3H, s), 1.43 (3H, s), 2.35 (2H, bs), 3.81 (1H, dd, J = 5.3, 11.6 Hz), 3.94 (1H, dd, J = 2.8, 11.6 Hz), 4.09−4.15 (1H, m), 4.23−4.29 (1H, m), 4.67 (1H, d, J = 11.9 Hz), 4.73 (1H, d, J = 11.9 Hz), 4.90 (1H, d, J = 4.5 Hz), 6.26 (1H, s), 7.51−7.62 (6H, m), 8.05−8.10 (4H, m); ^{13}C NMR δ_C 26.2 (CH_3), 26.3 (CH_3), 63.8 (CH_2), 64.4 (CH_2), 70.5 (CH), 77.2 (CH), 79.4 (CH), 90.2 (C), 98.8 (CH), 115.6 (C), 128.5 (2 × CH), 128.6 (2 × CH), 129.1 (C), 129.3 (C), 129.7 (2 × CH), 129.8 (2 × CH), 133.5 (2 × CH), 164.9 (C), 166.0 (C); MS (EI-TOF) m/z (rel intensity) 443 [$(M - CH_3)^+$, 10], 321 (3), 295 (4), 114 (36), 105 (100); HRMS (EI-TOF) m/z [$M - CH_3]^+$ Calcd for $C_{23}H_{23}O_9$ 443.1342, found 443.1340. Anal. Calcd for $C_{24}H_{26}O_9$: C, 62.88; H, 5.72. Found: C, 62.84; H, 5.83.

*1-O-Benzoyl-2-C-benzoyloxymethyl-6-O-(tert-butyldimethyl)silyl-2,3-O-isopropylidene-D-mannofuranose (**12**).* To a solution of diol **11** (700 mg, 1.53 mmol) in dry DMF (4.0 mL, 2.5 mL/mmol) at 0 °C and under nitrogen were added imidazole (260 mg, 3.83 mmol) and TBSCl (277 mg, 1.84 mmol), and the mixture was stirred for 1.5 h at room temperature. Then, it was poured into an ice/water mixture and extracted several times with diethyl ether. The organic phase was dried over sodium sulfate and concentrated under a vacuum. The resulting crude was purified by column chromatography (hexanes−EtOAc, 90:10 → 80:20) to obtain compound **12** (834 mg, 1.46 mmol, 95%) as a colorless oil: IR 3565, 3065, 2954, 2930, 2883, 1731, 1270 cm^{-1}. NMR showed a mixture of anomers in a 5:1 ratio. Major isomer: ^1H NMR δ_H −0.06 (3H, s), 0.00 (3H, s), 0.77 (9H, s), 1.47 (3H, s), 1.55 (3H, s), 2.73 (1H, bs), 3.77 (1H, dd, J = 3.7, 10.3 Hz), 3.84 (1H, dd, J = 3.2, 10.3 Hz), 4.01−4.09 (1H, m), 4.23 (1H, dd, J = 2.9, 8.7 Hz), 4.72 (1H, d, J = 11.9 Hz), 4.78 (1H, d, J = 11.9 Hz,), 4.95 (1H, d, J = 2.9 Hz), 6.56 (1H, s), 7.31−7.47 (6H, m), 7.89−8.00 (4H, m); ^{13}C NMR δ_C −5.8 (CH_3), −5.5 (CH_3), 18.1 (C), 25.6 (4 × CH_3), 25.8 (CH_3), 63.6 (CH_2), 63.7 (CH_2), 68.7 (CH), 81.0 (CH), 83.1 (CH), 93.1 (C), 101.4 (CH), 114.9 (C), 128.3 (4 × CH), 129.2 (C), 129.4 (C), 129.59 (2 × CH), 129.63 (2 × CH), 133.2 (CH), 133.4 (CH), 164.6 (C), 166.1 (C). Minor isomer: ^1H NMR δ_H 0.077 (3H, s), 0.082 (3H, s), 0.89 (9H, s), 1.44 (3H, s), 1.45 (3H, s), 3.83 (1H, dd, J = 4.5, 10.3 Hz), 3.91 (1H, dd, J = 2.9, 10.3 Hz), 4.15 (1H, d, J = 4.0 Hz), 4.14−4.19 (1H, m), 4.68 (1H, d, J = 11.9 Hz), 4.74 (1H, d, J = 11.9 Hz), 4.90 (1H, d, J = 4.0 Hz), 6.25 (1H, s), 7.49−7.60 (6H, m), 8.04−8.11 (4H, m); ^{13}C NMR δ_C −5.5 (2 × CH_3), 18.2 (C), 26.2 (CH_3), 26.3 (CH_3), 27.5 (3 × CH_3), 63.9 (CH_2), 64.5 (CH_2), 69.8 (CH), 78.8 (CH), 81.8 (CH), 89.7 (C), 98.6 (CH), 115.1 (C), 128.3 (2 × CH), 128.5 (2 × CH), 129.2 (C), 129.4 (C), 129.7 (2 × CH), 129.8 (2 × CH), 133.31 (CH), 133.32 (CH), 164.8 (C), 165.9 (C); MS (EI-TOF) m/z (rel intensity) 557 [$(M - CH_3)^+$, 6], 393 (20), 335 (5), 185 (16), 105 (100); HRMS (EI-TOF) m/z [$M - CH_3]^+$ Calcd for $C_{29}H_{37}O_9Si$ 557.2207, found 557.2208. Anal. Calcd for $C_{30}H_{40}O_9Si$: C, 62.91; H, 7.04. Found: C, 62.92; H, 7.00.

*5-Azido-1-O-benzoyl-2-C-benzoyloxymethyl-6-O-(tert-butyldimethyl)silyl-5-deoxy-2,3-O-isopropylidene-L-gulofuranose (**13**).* To a solution of alcohol **12** (1.00 g, 1.75 mmol) in dry DCM (7 mL, 4 mL/mmol) were added, under nitrogen and at −15 °C, pyridine (0.54 mL, 7.00 mmol) and then triflic anhydride dropwise (0.53 mL, 3.15 mmol), and the mixture was stirred for 30 min at this temperature. The reaction was purified by flash chromatography (DCM) affording the corresponding triflate (1.17 g, 1.66 mmol, 95%), which was dissolved in dry DMF (8 mL, 4.5 mL/mmol). Sodium azide (340 mg, 5.25 mmol) was added in one portion under nitrogen, and the mixture was stirred at room temperature for 12 h. The reaction was poured into ice and extracted with ether. The organic phase was dried over sodium sulfate and concentrated under a vacuum. The crude was purified by column chromatography (hexanes−EtOAc, 90:10 → 85:15) to yield compound **13** (750 mg, 1.25 mmol, 71% after two steps) as a colorless oil: IR 3068, 2929, 2857, 2102, 1730, 1270 cm^{-1}. NMR showed a mixture of anomers in a 5:1 ratio. Major isomer: ^1H NMR δ_H 0.10 (6H, s), 0.91 (9H, s), 1.45 (3H, s), 1.57 (3H, s), 3.78 (1H, ddd, J = 3.7, 4.8, 8.6 Hz), 3.88 (1H, dd, J = 4.8, 10.9 Hz), 3.92 (1H, dd, J = 3.7, 10.9 Hz), 4.37 (1H, dd, J = 2.9, 8.6 Hz), 4.67 (1H, d, J = 12.2 Hz), 4.74 (1H, d, J = 2.9 Hz), 4.77 (1H, d, J = 12.2 Hz), 6.65 (1H, s), 7.32−7.49 (6H, m), 7.90−8.00 (4H, m); ^{13}C NMR δ_C −5.6 (CH_3), −5.5 (CH_3), 18.2 (C), 25.8 (3 × CH_3), 27.5 (2 × CH_3), 62.2 (CH), 63.2 (CH_2), 63.6 (CH_2), 81.6 (CH), 82.5 (CH), 93.6 (C), 101.0 (CH), 115.2 (C), 128.4 (4 × CH), 129.2 (C), 129.3 (C), 129.65 (2 × CH), 129.72 (2 × CH), 133.3 (CH), 133.5 (CH), 164.5 (C), 166.1 (C). Minor isomer: ^1H NMR δ_H 0.06 (3H, s), 0.08 (3H, s), 0.86 (9H, s), 1.40 (3H, s), 1.42 (3H, s), 3.84−3.94 (3H, m), 4.33 (1H, dd, J = 4.4, 8.5 Hz), 4.67−4.77 (2H, m), 4.70 (1H, d, J = 4.4 Hz), 6.31 (1H, s), 7.50−7.62 (6H, m), 8.04−8.14 (4H, m); ^{13}C NMR δ_C −5.7 (CH_3), −5.6 (CH_3), 18.1 (C), 25.7 (3x CH_3), 26.1 (CH_3), 26.2 (CH_3), 63.3 (CH), 64.4 (CH_2), 63.7 (CH_2), 78.9 (CH), 81.4 (CH), 90.1 (C), 98.9 (CH), 115.2 (C), 128.4 (2 × CH), 128.6 (2 × CH), 129.1 (C), 129.4 (C), 129.7 (2 × CH), 129.9 (2 × CH), 133.2 (CH), 133.4 (CH), 164.9 (C), 165.9 (C); MS (EI-TOF) m/z (rel intensity) 582 [$(M - CH_3)^+$, 2], 540 (1), 390 (7), 240 (19), 179 (57), 105 (100); HRMS (EI-TOF) m/z [$M - CH_3]^+$ Calcd for $C_{29}H_{36}N_3O_8Si$ 582.2272, found 582.2256. Anal. Calcd for $C_{30}H_{39}N_3O_8Si$: C, 60.28; H, 6.58; N, 7.03. Found: C, 60.30; H, 6.55; N, 6.89.

*5-Azido-6-O-(tert-butyldimethyl)silyl-2-C-(tert-butyldimethyl)-silyloxymethyl-5-deoxy-2,3-O-isopropylidene-L-gulofuranose (**15a**).* Sodium methoxide (54 mg, 1.01 mmol) was added to a solution of azide **13** (300 mg, 0.50 mmol) in dry methanol (5 mL, 10 mL/mmol) under nitrogen and in an ice/water bath. The reaction was stirred at room temperature for 2 h, and then the solvent was removed under reduced pressure. The resulting residue was dissolved in EtOAc and washed with brine; the organic phase was dried over anhydrous sodium sulfate and evaporated under a vacuum. The residue was purified by column chromatography (hexanes−EtOAc, 90:10 → 70:30) to yield diol **14** (187 mg, 0.48 mmol, 96%) as a colorless oil. To a solution of diol **14** (85 mg, 0.22 mmol) in dry DMF (1.5 mL, 7 mL/mmol) at 0 °C and under nitrogen were added imidazole (37 mg, 0.55 mmol) and TBSCl (40 mg, 0.24 mmol), and the mixture was stirred for 2 h at room temperature. It was then poured into an ice/water mixture and extracted several times with diethyl ether. The organic phase was dried over sodium sulfate and concentrated under a vacuum. The resulting crude was purified by column chromatography (hexanes−EtOAc, 90:10) to obtain compound **15a** (97 mg, 0.19 mmol, 88%) as a colorless oil: IR 3528, 2952, 2859, 2103, 1469, 1381, 1255, 1109 cm^{-1}. NMR showed a mixture of anomers in a 4:1 ratio (only the major anomer is described): ^1H NMR δ_H 0.07 (6H, s), 0.086 (3H, s), 0.090 (3H, s), 0.87 (9H, s), 0.90 (9H, s), 1.41 (3H, s), 1.53 (3H, s), 3.62 (1H, ddd, J = 3.4, 4.5, 9.0 Hz), 3.69 (1H, dd, J = 2.7, 9.0 Hz), 3.72 (2H, s), 3.79 (1H, d, J = 12.2 Hz), 3.85 (1H, d, J = 4.5 H), 3.86 (1H, d, J = 3.4 Hz), 4.56 (1H, d, J = 2.7 Hz), 4.99 (1H, d, J = 12.2 Hz); ^{13}C NMR δ_C −5.7 (2 × CH_3), −5.6 (CH_3), −5.5 (CH_3), 18.17 (C), 18.23 (C), 25.8 (6 × CH_3), 26.9 (CH_3),

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27.0 (CH_3), 62.4 (CH), 63.0 (CH_2), 63.3 (CH_2), 75.3 (CH), 82.5 (CH), 89.1 (C), 96.8 (CH), 113.7 (C); MS (ESI-TOF) m/z (rel intensity) 526 [$(M + Na)^+$, 100]; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{22}H_{45}N_3O_6Si_2Na$ 526.2745, found 526.2740.

*5-(tert-Butoxycarbonyl)amino-6-O-(tert-butyldimethyl)silyl-2-C-(tert-butyldimethyl)silyloxymethyl-5-deoxy-2,3-O-isopropylidene-L-gulofuranose (**16a**).* To a solution of azide **15a** (90 mg, 0.18 mmol) in EtOAc (3.0 mL, 15 mL/mmol) were added di-*tert*-butyl dicarbonate (58 mg, 0.27 mmol) and 10% Pd/C (18 mg, 20% w/w). Three vacuum/hydrogen cycles were performed, and the mixture was stirred under hydrogen atmosphere for 13 h. The reaction mixture was then filtered over a Celite pad, washed twice with ethyl acetate, and the combinated filtrates were evaporated. The crude was purified by column chromatography (hexanes−EtOAc, 90:10) to yield compound **16a** (67 mg, 0.116 mmol, 65%) as a foam: IR 3611, 3523, 3456, 2955, 2858, 1718, 1498, 1254, 1108 cm^{-1}. NMR showed a mixture of anomers in a 2:1 ratio (only the major anomer is described): ^{1}H NMR (500 MHz, DMSO-d_6) δ_H 0.01 (3H, s), 0.03 (3H, s), 0.04 (3H, s), 0.05 (3H, s), 0.85 (9H, s), 0.87 (9H, s), 1.33 (3H, s), 1.36 (9H, s), 1.38 (3H, s), 3.57−3.65 (2H, m), 3.66 (1H, d, J = 11.7 Hz), 3.73 (1H, d, J = 11.7 Hz), 3.82 (1H, dddd, J = 5.3, 9.1, 9.1, 13.5 Hz), 3.97 (1H, dd, J = 2.6, 9.1 Hz), 4.41 (1H, d, J = 2.6 Hz), 5.03 (1H, d, J = 3.8 Hz), 6.37 (1H, d, J = 3.8 Hz), 6.46 (1H, d, J = 9.1 Hz); ^{13}C NMR (125.7 MHz, 70 °C) δ_C −5.6 (CH_3), −5.5 (CH_3), −5.4 (2 × CH_3), 18.28 (C), 18.30 (C), 25.9 (3 × CH_3), 26.0 (3 × CH_3), 27.0 (CH_3), 27.1 (CH_3), 28.5 (3 × CH_3), 51.9 (CH), 63.1 (CH_2), 63.5 (CH_2), 74.7 (CH), 79.1 (C), 83.3 (CH), 89.5 (C), 96.8 (CH), 113.7 (C), 155.6 (C); MS (ESI-TOF) m/z (rel intensity) 600 [$(M + Na)^+$, 100]; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{27}H_{55}NO_8Si_2Na$ 600.3364, found 600.3358.

*5-Azido-6-O-(tert-butyldimethyl)silyl-5-deoxy-2,3-O-isopropylidene-2-C-pivaloyloxymethyl-L-gulofuranose (**15b**).* To a solution of diol **14** (128 mg, 0.33 mmol) in dry pyridine (2 mL, 6 mL/mmol) were added, under nitrogen and at 0 °C, DMAP (13 mg, 10% w/w) and pivaloyl chloride (61 μL, 0.495 mmol), and then the mixture was warmed to room temperature and stirred for 5 h. The reaction was poured into 10% aqueous HCl and extracted twice with EtOAc. The organic phase was washed with sodium bicarbonate and brine, dried over sodium sulfate and concentrated under a vacuum. The crude was purified by column chromatography (hexanes−EtOAc, 90:10) to yield compound **15b** (108 mg, 0.23 mmol, 70%) as a colorless oil: IR 3526, 3457, 2956, 2932, 2859, 2104, 1737, 1462, 1255, 1125 cm^{-1}. NMR showed a mixture of anomers in a 5:3 ratio. Major isomer: ^{1}H NMR δ_H 0.08 (3H, s), 0.09 (3H, s), 0.90 (9H, s), 1.21 (9H, s), 1.42 (3H, s), 1.46 (3H, s), 3.15 (1H, bs), 3.64 (1H, ddd, J = 3.3, 5.1, 9.3 Hz), 3.82 (1H, dd, J = 5.1, 10.9 Hz), 3.88 (1H, dd, J = 3.3, 10.9 Hz), 4.26 (1H, dd, J = 3.0, 9.3 Hz), 4.29 (1H, d, J = 12.4 Hz), 4.45 (1H, d, J = 12.4 Hz), 4.47 (1H, d, J = 3.0 Hz), 5.38 (1H, s); ^{13}C NMR δ_C −5.5 (2 × CH_3), 18.2 (C), 25.8 (3 × CH_3), 27.2 (3 × CH_3), 27.6 (CH_3), 27.8 (CH_3), 38.8 (C), 62.4 (CH), 63.2 (CH_2), 63.3 (CH_2), 79.3 (CH), 82.4 (CH), 93.6 (C), 102.3 (CH), 114.4 (C), 178.2 (C). Minor isomer: ^{1}H NMR δ_H 0.077 (3H, s), 0.081 (3H, s), 0.89 (9H, s), 1.20 (9H, s), 1.45 (3H, s), 1.55 (3H, s), 3.61−3.66 (1H, m), 3.72 (1H, dd, J = 3.0, 8.8 Hz), 3.82−3.88 (2H, m), 4.20 (1H, d, J = 11.6 Hz), 4.24 (1H, d, J = 11.6 Hz), 4.51 (1H, d, J = 3.0 Hz), 4.92 (1H, d, J = 9.6 Hz); ^{13}C NMR δ_C −5.68 (CH_3), −5.66 (CH_3), 18.2 (C), 25.8 (3 × CH_3), 26.87 (CH_3), 26.89 (CH_3), 27.2 (3 × CH_3), 38.8 (C), 62.1 (CH), 63.2 (CH_2), 63.5 (CH_2), 75.1 (CH), 82.4 (CH), 87.7 (C), 97.2 (CH), 114.4 (C), 177.7 (C); MS (ESI-TOF) m/z (rel intensity) 496 [$(M + Na)^+$, 100]; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{21}H_{39}N_3O_7SiNa$ 496.2455, found 496.2449.

*5-(tert-Butoxycarbonyl)amino-6-O-(tert-butyldimethyl)silyl-5-deoxy-2,3-O-isopropylidene-2-C-pivaloyloxymethyl-L-gulofuranose (**16b**).* To a solution of azide **15b** (95 mg, 0.20 mmol) in EtOAc (3.0 mL, 15 mL/mmol) were added di-*tert*-butyl dicarbonate (66 mg, 0.3 mmol) and 10% Pd/C (20 mg, 20% w/w). Three vacuum/hydrogen cycles were performed, and the mixture was stirred under hydrogen atmosphere for 12 h. The reaction mixture was then filtered over a Celite pad, washed twice with ethyl acetate, and the combinated filtrates were evaporated. The crude was purified by column chromatography (hexanes−EtOAc, 90:10 → 80:20) to yield compound **16b** (48 mg, 0.09 mmol, 44%) as an oil: IR 3613, 3454, 2957, 2859, 1733, 1500, 1254, 1154 cm^{-1}. NMR showed a mixture of anomers in a 3:2 ratio (only the major anomer is described): ^{1}H NMR (500 MHz, 70 °C) δ_H 0.06 (3H, s), 0.07 (3H, s), 0.91 (9H, s), 1.23 (9H, s), 1.42 (3H, s), 1.45 (9H, s), 1.50 (3H, s), 2.64 (1H, bs), 3.72 (1H, dd, J = 6.0, 10.7 Hz), 3.77 (1H, dd, J = 4.1, 10.7 Hz), 3.82 (1H, dd, J = 3.5, 10.4 Hz), 3.97−4.07 (1H, m), 4.30 (1H, d, J = 12.0 Hz), 4.49 (1H, d, J = 12.0 Hz), 4.50 (1H, d, J = 3.5 Hz), 4.79−4.86 (1H, m), 4.87 (1H, d, J = 11.7 Hz); ^{13}C NMR (125.7 MHz, 70 °C) δ_C −5.4 (2 × CH_3), 18.3 (C), 26.0 (3 × CH_3), 27.00 (CH_3), 27.02 (CH_3), 27.3 (3 × CH_3), 28.5 (3 × CH_3), 39.0 (C), 51.9 (CH), 63.2 (CH_2), 64.0 (CH_2), 74.7 (CH), 79.5 (C), 83.2 (CH), 88.2 (C), 97.4 (CH), 114.5 (C), 155.7 (C), 177.7 (C); MS (ESI-TOF) m/z (rel intensity) 570 [$(M + Na)^+$, 100]; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{26}H_{49}NO_9SiNa$ 570.3074, found 570.3076.

*p-Methoxybenzyl 6-Deoxy-6-fluoro-2,3-O-isopropylidene-α-D-mannofuranoside (**18**).* Freshly prepared TBAF·2HF[27] (1530 mg, 5.09 mmol) was added dropwise to a flask containing epoxide **17**[13] (820 mg, 2.55 mmol), and then the mixture was heated under nitrogen at 95 °C, for 60 h. Once cooled, the reaction mixture was poured into water and extracted with EtOAc. The organic phase was washed with brine, dried over sodium sulfate and concentrated under a vacuum. The crude was purified by column chromatography (hexanes−EtOAc, 80:20) to yield fluorohydrin **18** (790 mg, 2.31 mmol, 91%) as a colorless oil: $[\alpha]_D$ +78.4 (c 0.51); IR ($CHCl_3$) 3507, 3020, 1613, 1514, 1250, 1082 cm^{-1}; ^{19}F NMR δ_F −234.1 (1F, s); ^{1}H NMR δ_H 1.32 (3H, s), 1.47 (3H, s), 3.80 (3H, s), 4.01 (1H, dd, J = 3.8, 8.3 Hz), 4.16 (1H, dddd, J = 2.8, 5.0, 8.3 Hz, $^3J_{FH}$ = 23.3 Hz), 4.41 (1H, d, J = 11.4 Hz), 4.56 (1H, ddd, J = 5.0, 9.7 Hz, $^2J_{FH}$ = 47.4 Hz), 4.57 (1H, d, J = 11.4 Hz), 4.64 (1H, d, J = 5.8 Hz), 4.65 (1H, ddd, J = 2.8, 9.7 Hz, $^2J_{FH}$ = 47.5 Hz), 4.86 (1H, dd, J = 3.8, 5.8 Hz), 5.09 (1H, s), 6.85−6.90 (2H, m), 7.21−7.26 (2H, m); ^{13}C NMR δ_C 24.6 (CH_3), 25.9 (CH_3), 55.3 (CH_3), 68.8 (CH_2), 69.3 (CH, d, $^2J_{FC}$ = 18.4 Hz), 77.9 (CH, d, $^3J_{FC}$ = 6.4 Hz), 80.0 (CH), 84.8 (CH_2, d, $^1J_{FC}$ = 169.5 Hz), 84.9 (CH), 105.1 (CH), 112.8 (C), 113.9 (2 × CH), 129.3 (C), 129.8 (2 × CH), 159.5 (C); MS (EI-TOF) m/z (rel intensity) 342 (M^+, 5), 327 [$(M - CH_3)^+$, 6], 221 (19), 163 (38), 121 (100); HRMS (EI-TOF) m/z [M − CH_3]$^+$ Calcd for $C_{17}H_{23}FO_6$ 342.1479, found 342.1477. Anal. Calcd for $C_{17}H_{23}FO_6$: C, 59.64; H, 6.77. Found: C, 59.80; H, 6.74.

*p-Methoxybenzyl 5-Azido-5,6-dideoxy-6-fluoro-2,3-O-isopropylidene-β-L-gulofuranoside (**19**).* To a solution of alcohol **18** (660 mg, 1.93 mmol) in dry DCM (15.0 mL, 8 mL/mmol) were added at −20 °C and under N_2, pyridine (0.6 mL, 7.74 mmol) and triflic anhydride (0.58 mL, 3.47 mmol), and the reaction was stirred at this temperature for 1 h before being poured into a cold 10% aqueous HCl solution and extracted with DCM. The organic phase was dried over anhydrous sodium sulfate and concentrated under a vacuum. The residue was used in the next step without further purification. Thus, to a solution of the resulting triflate in DMF (9.5 mL, 5.0 mL/mmol) was added sodium azide (627 mg, 9.65 mmol), and the reaction was heated at 40 °C for 15 h. The reaction was poured into ice/water and extracted with EtOAc. The organic layer was dried and concentrated under a vacuum. The residue was purified by column chromatography (hexanes−EtOAc, 90:10) to afford the title compound **19** (611 mg, 1.66 mmol, 86%) as a colorless oil: $[\alpha]_D$ +75.7 (c 0.59); IR 2939, 2099, 1613, 1514, 1251, 1085 cm^{-1}; ^{19}F NMR δ_F −230.6 (1F, s); ^{1}H NMR δ_H 1.27 (3H, s), 1.45 (3H, s), 3.79 (3H, s), 3.90 (1H, dddd, J = 2.5, 4.1, 9.0 Hz, $^3J_{FH}$ = 26.6 Hz), 4.21 (1H, dd, J = 3.5, 9.0 Hz), 4.44 (1H, d, J = 11.3 Hz), 4.627 (1H, dd, J = 2.5 Hz, $^2J_{FH}$ = 47.0 Hz), 4.629 (1H, dd, J = 4.1 Hz, $^2J_{FH}$ = 47.2 Hz), 4.64 (1H, d, J = 11.3 Hz), 4.65 (1H, d, J = 5.9 Hz), 4.71 (1H, dd, J = 3.5, 5.9 Hz), 5.11 (1H, s), 6.86−6.91 (2H, m), 7.24−7.29 (2H, m); ^{13}C NMR δ_C 24.6 (CH_3), 25.9 (CH_3), 55.2 (CH_3), 61.0 (CH, d, $^2J_{FC}$ = 17.6 Hz), 68.7 (CH_2), 78.5 (CH, d, $^3J_{FC}$ = 6.4 Hz), 79.4 (CH), 82.7 (CH_2, d, $^1J_{FC}$ = 172.3 Hz), 85.3 (CH), 104.6 (CH), 112.9 (C), 113.9 (2 × CH), 128.9 (C), 129.9 (2 × CH), 159.4 (C); MS (ESI-TOF) m/z (rel intensity) 390 [$(M + Na)^+$, 100]; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{17}H_{22}FN_3O_5Na$ 390.1441, found 390.1444. Anal. Calcd for $C_{17}H_{22}FN_3O_5$: C, 55.58; H, 6.04; N, 11.44. Found: C, 55.88; H, 6.06; N, 11.07.

*5-Azido-5,6-dideoxy-6-fluoro-2,3-O-isopropylidene-L-gulofuranose (**20**).* To a solution of **19** (570 mg, 1.55 mmol) in a 9:1 mixture of CH_3CN/H_2O (15.5 mL, 10 mL/mmol) was added, at 0 °C,

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CAN (1.70 g, 3.10 mmol), and the resulting suspension was stirred at that temperature for 2 h and then was poured into an aqueous sodium bicarbonate solution and extracted with EtOAc. The organic phase was dried over sodium sulfate and concentrated under a vacuum. The residue was purified by column chromatography (hexanes−EtOAc, 85:15) to afford compound **20** (314 mg, 1.27 mmol, 82%) as a colorless oil: IR 3599, 2992, 2102, 1378, 1269, 1088 cm^{-1}. NMR showed a mixture of anomers in a 6:1 ratio (only the major anomer is described): ^{19}F NMR δ_F −230.2 (1F, s); ^1H NMR δ_H 1.31 (3H, s), 1.46 (3H, s), 2.79 (1H, bs), 3.89 (1H, dddd, J = 2.9, 4.4, 9.1 Hz, $^3J_{FH}$ = 25.4 Hz), 4.30 (1H, dd, J = 3.5, 9.1 Hz), 4.64 (1H, dd, J = 4.5 Hz, $^2J_{FH}$ = 47.2 Hz), 4.65 (1H, dd, J = 2.9 Hz, $^2J_{FH}$ = 46.7 Hz), 4.66 (1H, d, J = 5.9 Hz), 4.74 (1H, dd, J = 3.5, 5.9 Hz), 5.44 (1H, s); ^{13}C NMR δ_C 24.6 (CH_3), 25.9 (CH_3), 61.2 (CH, d, $^2J_{FC}$ = 18.4 Hz), 78.8 (CH, d, $^3J_{FC}$ = 7.1 Hz), 79.3 (CH), 82.7 (CH_2, d, $^1J_{FC}$ = 172.3 Hz), 85.7 (CH), 101.0 (CH), 113.0 (C); MS (EI-TOF) m/z (rel intensity) 232 [(M − CH_3)$^+$, 44], 159 (24), 73 (31), 59 (100); HRMS (EI-TOF) m/z [M − CH_3]$^+$ Calcd for $C_8H_{11}FN_3O_4$ 232.0734, found 232.0726. Anal. Calcd for $C_9H_{14}FN_3O_4$: C, 43.72; H, 5.71; N, 17.00. Found: C, 43.64; H, 5.68; N, 17.29.

*5-Azido-2-C-(tert-butyldimethyl)silyloxymethyl-5,6-dideoxy-6-fluoro-2,3-O-isopropylidene-L-gulofuranose (**22a**).* Potassium carbonate (500 mg, 200% w/w) was added to a 35% aqueous solution of formaldehyde (1.3 mL, 2 mL/mmol), and the mixture was stirred until a clear solution was observed. A solution of compound **20** (250 mg, 1.01 mmol) in dry methanol (2 mL, 2 mL/mmol) was then added dropwise while heating at 80 °C. After 2 h, the solvent was removed under a vacuum, and the residue was extracted twice with EtOAc and washed with brine. The organic phase was dried over anhydrous sodium sulfate and concentrated under a vacuum. The residue was purified by rotatory chromatography (hexanes−EtOAc, 80:20 → 60:40) to yield compound **21** (224 mg, 0.81 mmol, 80%) as a colorless oil. To a solution of diol **21** (110 mg, 0.4 mmol) in dry DMF (2 mL, 5 mL/mmol) at 0 °C and under nitrogen were added imidazole (60 mg, 0.88 mmol) and then TBSCl (72 mg, 0.48 mmol), and the mixture was stirred for 4 h. It was poured into an ice/water mixture and extracted several times with diethyl ether. The organic phase was dried over sodium sulfate and concentrated under a vacuum. The resulting crude was purified by column chromatography (hexanes−EtOAc, 90:10) to obtain compound **22a** (118 mg, 0.30 mmol, 75%) as a colorless oil: IR ($CHCl_3$) 3500, 2932, 2104, 1258, 1106 cm^{-1}. NMR showed a mixture of anomers in a 3:2 ratio. Major isomer: ^{19}F NMR δ_F −230.0 (1F, s); ^1H NMR δ_H 0.08 (6H, s), 0.88 (9H, s), 1.41 (3H, s), 1.53 (3H, s), 3.71 (1H, dd, J = 2.8, 8.6 Hz), 3.73 (1H, d, J = 10.3 Hz), 3.75 (1H, d, J = 10.3 Hz), 3.84 (1H, d, J = 12.1 Hz), 3.86−3.97 (1H, m), 4.58 (1H, d, J = 2.8 Hz), 4.57−4.71 (2H, m), 5.02 (1H, d, J = 12.1 Hz); ^{13}C NMR δ_C −5.65 (2 × CH_3), 18.1 (C), 25.7 (3 × CH_3), 26.7 (CH_3), 26.9 (CH_3), 61.0 (CH, d, $^2J_{FC}$ = 17.7 Hz), 63.1 (CH_2), 75.0 (CH, d, $^3J_{FC}$ = 7.1 Hz), 82.3 (CH), 82.8 (CH_2, d, $^1J_{FC}$ = 172.3 Hz), 88.9 (C), 97.1 (CH), 114.0 (C). Minor isomer: ^{19}F NMR δ_F −230.1 (1F, s); ^1H NMR δ_H 0.12 (3H, s), 0.13 (3H, s), 0.91 (9H, s), 1.38 (3H, s), 1.47 (3H, s), 3.83 (1H, d, J = 10.7 Hz), 3.86−3.97 (1H, m), 4.06 (1H, d, J = 10.7 Hz), 4.24 (1H, dd, J = 2.8, 8.8 Hz), 4.56 (1H, d, J = 2.8 Hz), 4.57−4.71 (2H, m), 5.34 (1H, d, J = 6.0 Hz); ^{13}C NMR δ_C −5.7 (CH_3), −5.6 (CH_3), 18.1 (C), 25.7 (3 × CH_3), 27.3 (CH_3), 27.4 (CH_3), 61.2 (CH, d, $^2J_{FC}$ = 18.4 Hz), 63.8 (CH_2), 79.2 (CH, d, $^3J_{FC}$ = 7.1 Hz), 82.8 (CH_2, d, $^1J_{FC}$ = 172.3 Hz), 82.9 (CH), 93.4 (C), 104.3 (CH), 114.3 (C); MS (ESI-TOF) m/z (rel intensity) 414 [(M + Na)$^+$, 100)]; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{16}H_{30}FN_3O_5SiNa$ 414.1836, found 414.1832.

*5-(tert-Butoxycarbonyl)amino-2-C-(tert-butyldimethyl)-silyloxymethyl-5,6-dideoxy-6-fluoro-2,3-O-isopropylidene-L-gulofuranose (**23a**).* To a solution of azide **22a** (110 mg, 0.28 mmol) in EtOAc (4.2 mL, 15 mL/mmol) were added di-*tert*-butyl dicarbonate (74 mg, 0.34 mmol), DIPEA (49 μL, 0.28 mmol) and 10% Pd/C (22 mg, 20% w/w). Three vacuum/hydrogen cycles were performed, and the mixture was stirred under hydrogen atmosphere for 15 h. The reaction mixture was then filtered over a Celite pad, washed twice with ethyl acetate, and the combined filtrates were evaporated. The crude was purified by column chromatography (hexanes−EtOAc, 90:10 → 80:20) to yield compound **23a** (115 mg, 0.25 mmol, 88%) as a colorless oil: IR ($CHCl_3$) 3442, 1708, 1502, 1369 cm^{-1}. NMR showed a mixture of anomers in a 7:2 ratio. Major isomer: ^{19}F NMR δ_F −232.7 (0.2F, s), −231.2 (0.8F, s); ^1H NMR (500 MHz, 70 °C) δ_H 0.118 (3H, s), 0.120 (3H, s), 0.91 (9H, s), 1.42 (3H, s), 1.45 (9H, s), 1.54 (3H, s), 3.72 (1H, dd, J = 3.0, 6.8 Hz), 3.75 (2H, s), 4.11−4.20 (1H, m), 4.52 (1H, dd, J = 1.0 Hz, $^2J_{FH}$ = 47.3 Hz), 4.53 (1H, dd, J = 4.7 Hz, $^2J_{FH}$ = 47.0 Hz), 4.60 (1H, d, J = 3.0 Hz), 4.88 (1H, bs), 4.97 (1H, d, J = 6.3 Hz); ^{13}C NMR δ_C −5.60 (CH_3), −5.58 (CH_3), 18.2 (C), 25.8 (3 × CH_3), 26.8 (CH_3), 27.0 (CH_3), 28.5 (3 × CH_3), 50.8 (CH, d, $^2J_{FC}$ = 20.1 Hz), 63.6 (CH_2), 74.2 (CH, d, $^3J_{FC}$ = 5.3 Hz), 80.1 (C), 82.8 (CH_2, d, $^1J_{FC}$ = 170.6 Hz), 83.1 (CH), 89.5 (C), 97.2 (CH), 114.1 (C), 155.6 (C). Minor isomer: ^{19}F NMR δ_F −229.8 (0.4F, s), −228.9 (0.6F, s); ^1H NMR (500 MHz, 70 °C) δ_H 0.125 (3H, s), 0.131 (3H, s), 0.93 (9H, s), 1.37 (3H, s), 1.38 (3H, s), 1.47 (9H, s), 3.61 (1H, d, J = 9.8 Hz), 3.67 (1H, d, J = 9.8 Hz), 4.11−4.20 (1H, m), 4.18−4.24 (1H, m), 4.56−4.63 (2H, m), 4.61 (1H, d, J = 8.5 Hz), 5.30 (1H, bs); ^{13}C NMR δ_C −5.7 (CH_3), −5.5 (CH_3), 18.4 (C), 25.9 (3 × CH_3), 26.6 (CH_3), 27.2 (CH_3), 28.4 (3 × CH_3), 51.8 (CH, d, $^2J_{FC}$ = 22.3 Hz), 67.5 (CH_2), 78.4 (CH, d, $^3J_{FC}$ = 4.2 Hz), 79.6 (C), 80.8 (CH_2, d, $^1J_{FC}$ = 170.6 Hz), 83.6 (CH), 93.5 (C), 104.4 (CH), 114.3 (C), 155.3 (C); MS (ESI-TOF) m/z (rel intensity) 488 [(M + Na)$^+$, 100]; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{21}H_{40}FNO_7SiNa$ 488.2456, found 488.2445. Anal. Calcd for $C_{21}H_{40}FNO_7Si$: C, 54.17; H, 8.66; N, 3.01. Found: C, 54.21; H, 8.43; N, 3.11.

*5-Azido-5,6-dideoxy-6-fluoro-2,3-O-isopropylidene-2-C-pivaloyloxymethyl-L-gulofuranose (**22b**).* To a solution of compound **21** (110 mg, 0.4 mmol) in dry pyridine (2 mL, 5 mL/mmol) were added, under nitrogen and at 0 °C, DMAP (11 mg, 10% w/w) and pivaloyl chloride (100 μL, 0.81 mmol), and then the mixture was warmed to room temperature and stirred for 10 h. The reaction was poured into 10% aqueous HCl and extracted twice with DCM. The organic phase was washed with sodium bicarbonate and brine, dried over sodium sulfate and concentrated under a vacuum. The crude was purified by column chromatography (hexanes−EtOAc, 90:10 → 1:1) to yield compound **22b** (75 mg, 0.21 mmol, 53%) as a colorless oil: IR ($CHCl_3$) 3597, 3516, 3354, 2983, 2104, 1731, 1279, 1151, 1123 cm^{-1}. NMR showed a mixture of anomers in a 3:2 ratio. Major isomer: ^{19}F NMR δ_F −230.5 (1F, s); ^1H NMR δ_H 1.21 (9H, s), 1.46 (3H, s), 1.56 (3H, s), 3.73 (1H, dd, J = 2.9, 8.5 Hz), 3.84−3.96 (2H, m), 4.19 (1H, d, J = 11.7 Hz), 4.30 (1H, d, J = 11.7 Hz), 4.53 (1H, dd, J = 0.8, 2.9 Hz), 4.63 (2H, dd, J = 3.6 Hz, $^2J_{FH}$ = 47.0 Hz), 4.95 (1H, d, J = 11.1 Hz); ^{13}C NMR δ_C 26.6 (CH_3), 26.8 (CH_3), 27.1 (3 × CH_3), 38.9 (C), 60.8 (CH, d, $^2J_{FC}$ = 18.4 Hz), 63.5 (CH_2), 74.9 (CH, d, $^3J_{FC}$ = 7.1 Hz), 82.1 (CH), 82.7 (CH_2, d, $^1J_{FC}$ = 172.3 Hz), 87.5 (C), 97.6 (CH), 114.7 (C), 177.7 (C). Minor isomer: ^{19}F NMR δ_F −230.0 (1F, s); ^1H NMR δ_H 1.22 (9H, s), 1.42 (3H, s), 1.48 (3H, s), 3.07 (1H, bs), 3.84−3.96 (1H, m), 4.310 (1H, dd, J = 0.5, 6.1 Hz), 4.311 (1H, d, J = 12.2 Hz), 4.45 (1H, d, J = 12.2 Hz), 4.50 (1H, d, J = 2.9 Hz), 4.62 (2H, dd, J = 7.2 Hz, $^2J_{FH}$ = 47.2 Hz), 5.40 (1H, s); ^{13}C NMR δ_C 27.1 (3 × CH_3), 27.5 (CH_3), 27.6 (CH_3), 38.8 (C), 61.0 (CH, d, $^2J_{FC}$ = 19.1 Hz), 63.2 (CH_2), 79.1 (CH, d, $^3J_{FC}$ = 7.1 Hz), 82.3 (CH), 82.6 (CH_2, d, $^1J_{FC}$ = 172.3 Hz), 93.6 (C), 102.4 (CH), 114.7 (C), 178.1 (C); MS (ESI-TOF) m/z (rel intensity) 384 [(M + Na)$^+$, 100)]; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{15}H_{24}FN_3O_6Na$ 384.1547, found 384.1550.

*5-(tert-Butoxycarbonyl)amino-5,6-dideoxy-6-fluoro-2,3-O-isopropylidene-2-C-pivaloyloxymethyl-L-gulofuranose (**23b**).* To a solution of azide **22b** (108 mg, 0.30 mmol) in EtOAc (4.5 mL, 15 mL/mmol) were added di-*tert*-butyl dicarbonate (98 mg, 0.45 mmol), DIPEA (51 μL, 0.30 mmol) and 10% Pd/C (21 mg, 20% w/w). Three vacuum/hydrogen cycles were performed, and the mixture was stirred under hydrogen atmosphere for 15 h. The reaction mixture was then filtered over a Celite pad, washed twice with ethyl acetate, and the combined filtrates were evaporated. The crude was purified by rotatory chromatography (hexanes−EtOAc 80:20) to yield compound **23b** (95 mg, 0.22 mmol, 73%) as a colorless oil: IR ($CHCl_3$) 2983, 1725, 1504, 1369, 1281 cm^{-1}. ^1H and ^{13}C NMR spectra were too complex to be described due to the mixture of anomers and rotamers. However when both of them were attempted to be registered at a higher temperature, the product decomposed before reaching the coalescence temperature. MS (ESI-TOF) m/z (rel intensity) 458 [(M + Na)$^+$, 100]; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{20}H_{34}FNO_8Na$

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458.2166, found 458.2170. Anal. Calcd for $C_{20}H_{34}FNO_8$: C, 55.16; H, 7.87; N, 3.22. Found: C, 55.26; H, 7.63; N, 3.34.

*p-Methoxybenzyl 6-Deoxy-2,3-O-isopropylidene-α-D-mannofuranoside (**24**).* To a solution of epoxide **17** (740 mg, 2.3 mmol) in dry ether (23 mL, 10 mL/mmol) was added lithium aluminum hydride (220 mg, 5.75 mmol), and the reaction mixture was heated at reflux for 3 h. Once cooled, the excess of hydride was destroyed by a dropwise addition of an aqueous sodium sulfate solution till the effervescence ceased, and then stirring was continued for 30 min. The mixture was filtrated, and the filtrate was extracted with EtOAc and saturated ammonium chloride. The organic phase was dried over sodium sulfate and concentrated under a vacuum. The residue was purified by column chromatography (hexanes−EtOAc, 70:30) to yield alcohol **24** (700 mg, 2.16 mmol, 94%) as a colorless oil: $[\alpha]_D$ +78.7 (*c* 0.55); IR 3607, 2982, 2937, 1613, 1514, 1250 cm^{-1}; ^1H NMR δ_H 1.31 (3H, s), 1.34 (3H, d, *J* = 6.4 Hz), 1.47 (3H, s), 3.77 (1H, ddd, *J* = 0.5, 3.8, 7.3 Hz), 3.80 (3H, s), 4.09 (1H, dddd, *J* = 6.4, 6.4, 6.4, 7.3 Hz), 4.42 (1H, d, *J* = 11.7 Hz), 4.59 (1H, d, *J* = 11.7 Hz), 4.62 (1H, d, *J* = 6.0 Hz), 4.85 (1H, dd, *J* = 3.8, 6.0 Hz), 5.10 (1H, s), 6.85−6.89 (2H, m), 7.23−7.27 (1H, m); ^{13}C NMR δ_C 20.4 (CH_3), 24.5 (CH_3), 25.9 (CH_3), 55.2 (CH_3), 66.5 (CH), 68.6 (CH_2), 80.0 (CH), 83.2 (CH), 85.0 (CH), 104.9 (CH), 112.6 (C), 113.8 (2 × CH), 129.4 (C), 129.7 (2 × CH), 159.3 (C); MS (EI-TOF) *m*/*z* (rel intensity) 324 (M^+, 2), 309 (3), 203 (7), 157 (4), 145 (28), 121 (100); HRMS (EI-TOF) *m*/*z* $[M]^+$ Calcd for $C_{17}H_{24}O_6$ 324.1573, found 324.1572. Anal. Calcd for $C_{17}H_{24}O_6$: C, 62.95; H, 7.46. Found: C, 62.82; H, 7.62.

*p-Methoxybenzyl 5-Azido-5,6-dideoxy-2,3-O-isopropylidene-β-L-gulofuranoside (**25**).* To a solution of alcohol **24** (600 mg, 1.85 mmol) in dry DCM (15.0 mL, 8 mL/mmol) were added at −20 °C and under N_2, pyridine (0.57 mL, 7.4 mmol) and triflic anhydride (0.62 mL, 3.47 mmol), and the reaction was stirred at this temperature for 45 min before pouring into a cold aqueous HCl solution and extracted with DCM. The organic phase was dried over anhydrous sodium sulfate and concentrated under a vacuum. Next, to a solution of the resulting residue in DMF (10 mL, 5.0 mL/mmol) was added sodium azide (601 mg, 9.25 mmol), and the reaction was stirred at room temperature for 16 h. The solvent was removed under a vacuum, and the residue was solved in water and extracted with EtOAc. The organic layer was washed with brine, dried over sodium sulfate and concentrated under a vacuum. The residue was purified by rotatory chromatography (hexanes−EtOAc, 98:2) to afford the title compound **25** (440 mg, 1.26 mmol, 68%) as a colorless oil: $[\alpha]_D$ +51.3 (*c* 0.32); IR ($CHCl_3$) 2997, 2940, 2093, 1612, 1514, 1250 cm^{-1}; ^1H NMR δ_H 1.26 (3H, d, *J* = 6.4 Hz), 1.28 (3H, s), 1.44 (3H, s), 3.79 (3H, s), 3.82 (1H, dddd, *J* = 6.4, 6.4, 6.4, 9.3 Hz), 3.89 (1H, dd, *J* = 3.1, 9.3 Hz), 4.44 (1H, d, *J* = 11.4 Hz), 4.61 (1H, d, *J* = 5.9 Hz), 4.63 (1H, dd, *J* = 3.1, 5.9 Hz), 4.64 (1H, d, *J* = 11.4 Hz), 5.08 (1H, s), 6.85−6.90 (2H, m), 7.25−7.30 (2H, m); ^{13}C NMR δ_C 16.0 (CH_3), 24.8 (CH_3), 26.0 (CH_3), 55.2 (CH_3), 57.1 (CH), 68.6 (CH_2), 79.7 (CH), 83.5 (CH), 85.2 (CH), 104.9 (CH), 112.6 (C), 113.9 (2 × CH), 129.1 (C), 129.9 (2 × CH), 159.4 (C); MS (EI-TOF) *m*/*z* (rel intensity) 349 (M^+, 16), 334 (6), 246 (7), 142 (11), 121 (100); HRMS (EI-TOF) *m*/*z* $[M]^+$ Calcd for $C_{17}H_{23}N_3O_5$ 349.1638, found 349.1640. Anal. Calcd for $C_{17}H_{23}N_3O_5$: C, 58.44; H, 6.64; N, 12.03. Found: C, 58.62; H, 6.63; N, 12.12.

*5-Azido-5,6-dideoxy-2,3-O-isopropylidene-L-gulofuranose (**26**).* To a solution of **25** (370 mg, 1.06 mmol) in DCM (10 mL, 10 mL/mmol) was added, at 0 °C, trifluoroacetic acid (1.0 mL, 10% v/v), and the resulting mixture was stirred at that temperature for 2 h. The reaction was poured into an aqueous sodium bicarbonate solution and extracted with DCM. The organic phase was dried over sodium sulfate and concentrated under a vacuum. The residue was purified by rotatory chromatography (C_6H_6−EtOAc, 90:10) to afford the compound **26** (195 mg, 0.85 mmol, 80%) as a colorless oil: IR ($CHCl_3$) 3596, 3361, 3020, 2991, 2943, 2093, 1381, 1215, 1090 cm^{-1}. NMR showed a mixture of anomers in a 10:1 ratio (only the major anomer is described): ^1H NMR δ_H 1.285 (3H, d, *J* = 6.5 Hz), 1.287 (3H, s), 1.44 (3H, s), 3.53 (1H, bs), 3.79 (1H, dddd, *J* = 6.5, 6.5, 6.5, 9.4 Hz), 3.98 (1H, dd, *J* = 3.5, 9.4 Hz), 4.60 (1H, d, *J* = 5.9 Hz), 4.67 (1H, dd, *J* = 3.5, 5.9 Hz), 5.40 (1H, s); ^{13}C NMR δ_C 15.8 (CH_3), 24.7 (CH_3), 26.0 (CH_3), 57.3 (CH), 79.6 (CH), 83.4 (CH), 85.6 (CH), 101.1 (CH), 112.7 (C); MS (EI-TOF) *m*/*z* (rel intensity) 214 [$(M - CH_3)^+$, 37], 159 (61), 212 (15), 73 (89), 59 (100); HRMS (EI-TOF) *m*/*z* $[M - CH_3]^+$ Calcd for $C_8H_{12}N_3O_4$ 214.0828, found 214.0823. Anal. Calcd for $C_9H_{15}N_3O_4$: C, 47.16; H, 6.60; N, 18.33. Found: C, 47.11; H, 6.67; N, 18.28.

*5-Azido-5,6-dideoxy-2,3-O-isopropylidene-2-C-pivaloyloxymethyl-L-gulofuranose (**28**).* Potassium carbonate (370 mg, 200% w/w) was added to a 35% aqueous solution of formaldehyde (1.6 mL, 2 mL/mmol), and the mixture was stirred until a clear solution was observed. A solution of compound **26** (185 mg, 0.81 mmol) in dry methanol (3.5 mL, 4.5 mL/mmol) was then added dropwise while heating at 80 °C. After 2 h, the solvent was removed under a vacuum, and the residue was extracted twice with EtOAc and washed with brine. The organic phase was dried over anhydrous sodium sulfate and concentrated under a vacuum. The residue was purified by rotatory chromatography (hexanes−EtOAc, 80:20 → 60:40) to yield compound **27** (173 mg, 0.67 mmol, 83%) as a colorless oil. NMR showed a mixture of anomers in a 3:1 ratio. To a solution of compound **27** (160 mg, 0.618 mmol) in dry pyridine (3 mL, 5 mL/mmol) were added, under nitrogen and at 0 °C, DMAP (16 mg, 10% w/w) and pivaloyl chloride (1.84 mL, 1.50 mmol), and then the mixture was warmed to room temperature and stirred for 38 h. The reaction was poured into 10% aqueous HCl and extracted twice with EtOAc. The organic phase was washed with sodium bicarbonate and brine, dried over sodium sulfate and concentrated under a vacuum. The crude was purified by column chromatography (hexanes−EtOAc, 95:5 → 85:15) to yield compound **28** (95 mg, 0.277 mmol, 45%) as a colorless oil: IR ($CHCl_3$) 3692, 3596, 2096, 1728, 1382, 1155, 1091 cm^{-1}. NMR showed a mixture of anomers in a 9:2 ratio (major anomer is only described): ^1H NMR δ_H 1.23 (9H, s), 1.28 (3H, d, *J* = 6.7 Hz), 1.42 (3H, s), 1.48 (3H, s), 2.90 (1H, bs), 3.78−3.87 (1H, m), 4.01 (1H, dd, *J* = 3.0, 9.3 Hz), 4.30 (1H, d, *J* = 12.2 Hz), 4.44 (1H, d, *J* = 3.0 Hz), 4.45 (1H, d, *J* = 12.2 Hz), 5.38 (1H, d, *J* = 1.8 Hz); ^{13}C NMR δ_C 15.9 (CH_3), 27.2 (3 × CH_3), 27.6 (CH_3), 27.8 (CH_3), 38.9 (C), 57.1 (CH), 63.3 (CH_2), 82.6 (CH), 83.8 (CH), 93.4 (C), 102.5 (CH), 114.4 (C), 178.2 (C); MS (EI-TOF) *m*/*z* (rel intensity) 328 [$(M - CH_3)^+$, 3], 215 (5), 110 (63), 57 (100); HRMS (EI-TOF) *m*/*z* $[M - CH_3]^+$ Calcd for $C_{14}H_{22}N_3O_6$ 328.1509, found 328.1516. Anal. Calcd for $C_{15}H_{25}N_3O_6$: C, 52.47; H, 7.34; N, 12.24. Found: C, 52.19; H, 7.20; N, 12.35.

*5-(tert-Butoxycarbonyl)amino-5,6-dideoxy-2,3-O-isopropylidene-2-C-pivaloyloxymethyl-L-gulofuranose (**29**).* To a solution of azide **28** (157 mg, 0.457 mmol) in EtOAc (7.0 mL, 15 mL/mmol) were added di-*tert*-butyl dicarbonate (120 mg, 0.548 mmol) and 10% Pd/C (30 mg, 20% w/w). Three vacuum/hydrogen cycles were performed, and the mixture was stirred under hydrogen atmosphere for 2.5 h. The reaction mixture was then filtered over a Celite pad, washed twice with ethyl acetate, and the combined filtrates were evaporated. The crude was purified by column chromatography (hexanes−EtOAc, 90:10 → 70:30) to yield compound **29** (120 mg, 0.288 mmol, 63%) as a colorless oil: IR ($CHCl_3$) 3443, 1725, 1680, 1415, 1369, 1160 cm^{-1}. ^1H and ^{13}C NMR spectra were too complex to be described due to the mixture of anomers and rotamers. However when both of them were attempted to be registered at a higher temperature, the product decomposed before reaching the coalescence temperature. MS (ESI-TOF) *m*/*z* (rel intensity) 440 [$(M + Na)^+$, 100]; HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ Calcd for $C_{20}H_{35}NO_8Na$ 440.2260, found 440.2274. Anal. Calcd for $C_{20}H_{35}NO_8$: C, 57.54; H, 8.45; N, 3.35. Found: C, 57.73; H, 8.31; N, 3.38.

*5,6-Anhydro-1-O-benzoyl-2-C-benzoyloxymethyl-2,3-O-isopropylidene-D-mannofuranose (**30**).* To a solution of diol **11** (2.0 g, 4.37 mmol) in dry toluene (17 mL, 4 mL/mmol) were added, under nitrogen, triphenylphosphine (1.26 g, 4.80 mmol) and diethylazodicarboxilate (DEAD) dropwise (790 μL, 5.02 mmol). Then, the reaction was heated at reflux for 2 h, and the solvent was removed under a vacuum. The residue was purified by column chromatography (hexanes−EtOAc, 95:5 → 75:25) to yield epoxide **30** (1.83 g, 4.16 mmol, 95%) as a colorless oil: IR 3065, 2994, 2939, 1737, 1376, 1277 cm^{-1}. NMR showed a mixture of anomers in a 5:1 ratio. Major isomer: ^1H NMR δ_H 1.49 (3H, s), 1.59 (3H, s), 2.80 (1H, dd, *J* = 2.4, 5.0 Hz), 2.93 (1H, dd, *J* = 4.0, 5.0 Hz), 3.39 (1H, ddd, *J* = 2.4, 4.0, 6.5 Hz), 3.88 (1H, dd, *J* = 3.1, 6.5 Hz), 4.71 (1H, d, *J* = 12.2 Hz), 4.79 (1H, d, *J* = 12.2 Hz), 4.92 (1H, d, *J* = 3.1 Hz), 6.59 (1H, s), 7.34−7.44 (4H, mz),

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7.51−7.58 (2H, m), 7.90−7.99 (4H, m); ^{13}C NMR δ_C 27.48 (CH_3), 27.52 (CH_3), 46.6 (CH_2), 48.3 (CH), 63.6 (CH_2), 83.0 (CH), 83.1 (CH), 93.4 (C), 101.4 (CH), 115.3 (C), 128.4 (2 × CH), 128.5 (2 × CH), 129.1 (C), 129.3 (C), 129.6 (2 × CH), 129.7 (2 × CH), 133.3 (CH), 133.6 (CH), 164.7 (C), 166.1 (C). Minor isomer: ^{1}H NMR δ_H 1.44 (3H, s), 1.46 (3H, s), 2.86 (1H, dd, J = 2.6, 5.0 Hz), 2.98 (1H, dd, J = 3.7, 5.0 Hz), 3.49 (1H, ddd, J = 2.6, 3.7, 6.6 Hz), 3.88 (1H, dd, J = 4.8, 6.6 Hz), 4.69 (1H, d, J = 11.9 Hz), 4.74 (1H, d, J = 11.9 Hz), 4.88 (1H, d, J = 4.8 Hz), 6.29 (1H, s), 7.39−7.49 (4H, mz), 7.56−7.63 (2H, m), 8.04−8.12 (4H, m); ^{13}C NMR δ_C 26.1 (2 × CH_3), 46.4 (CH_2), 49.1 (CH), 64.4 (CH_2), 80.9 (CH), 81.8 (CH), 90.1 (C), 98.9 (CH), 115.5 (C), 128.5 (2 × CH), 128.6 (2 × CH), 129.2 (C), 129.4 (C), 129.7 (2 × CH), 129.9 (2 × CH), 133.4 (CH), 133.5 (CH), 164.9 (C), 166.0 (C); MS (EI-TOF) m/z (rel intensity) 425 [$(M - CH_3)^+$, 6], 214 (12), 113 (31), 105 (100); HRMS (EI-TOF) m/z [$M - CH_3$]$^+$ Cacld for $C_{23}H_{21}O_8$ 425.1236, found 425.1229. Anal. Calcd for $C_{24}H_{24}O_8$: C, 65.45; H, 5.49. Found: C, 65.22; H, 5.84.

*6-Azido-1-O-benzoyl-2-C-benzoyloxymethyl-6-deoxy-2,3-O-isopropylidene-D-mannofuranose (**31**).* To a solution of epoxide **30** (1.82 g, 4.14 mmol) in dry DMF (20 mL, 5 mL/mmol), under nitrogen, were added sodium azide (1.88 g, 28.95 mmol) and ammonium chloride (222 mg, 4.14 mmol), and the mixture was stirred at 80 °C for 4 h. The solvent was removed under a vacuum, and the residue was extracted with EtOAc and water. The organic phase was dried over anhydrous sodium sulfate and concentrated under a vacuum. The crude was purified by column chromatography (hexanes−EtOAc, 80:20) to afford compound **31** (1.59 g, 3.29 mmol, 79%) as a colorless oil: IR 3612, 3506, 3068, 2992, 2939, 2104, 1733, 1271, 1108 cm^{-1}. NMR showed a mixture of anomers in a 5:1 ratio. Major isomer: ^{1}H NMR δ_H 1.48 (3H, s), 1.56 (3H, s), 2.60 (1H, d, J = 5.0 Hz), 3.48 (1H, dd, J = 6.0, 12.9 Hz), 3.60 (1H, dd, J = 3.4, 12.8 Hz), 4.16−4.24 (1H, m), 4.21 (1H, dd, J = 2.7, 6.9 Hz), 4.70 (1H, d, J = 12.2 Hz), 4.80 (1H, d, J = 12.2 Hz), 4.93 (1H, d, J = 2.7 Hz), 6.57 (1H, s), 7.35−7.44 (4H, m), 7.52−7.58 (2H, m), 7.91−7.99 (4H, m); ^{13}C NMR δ_C 27.6 (2 × CH_3), 54.1 (CH_2), 63.6 (CH_2), 68.9 (CH), 81.8 (CH), 82.8 (CH), 93.3 (C), 101.4 (CH), 115.4 (C), 128.46 (2 × CH), 128.51 (2 × CH), 129.1 (C), 129.3 (C), 129.65 (2 × CH), 129.72 (2 × CH), 133.3 (CH), 133.6 (CH), 164.6 (C), 166.1 (C). Minor isomer: ^{1}H NMR δ_H 1.42 (3H, s), 1.43 (3H, s), 2.68 (1H, d, J = 4.8 Hz), 3.52 (1H, dd, J = 6.4, 13.0 Hz), 3.67 (1H, dd, J = 2.9, 13.0 Hz), 4.16−4.24 (1H, m), 4.37 (1H, dddd, J = 2.9, 4.8, 6.4, 9.0 Hz), 4.68 (1H, d, J = 11.9 Hz), 4.73 (1H, d, J = 11.9 Hz), 4.91 (1H, d, J = 5.0 Hz), 6.28 (1H, s), 7.44−7.50 (4H, m), 7.57−7.63 (2H, m), 8.06−8.09 (4H, m); ^{13}C NMR δ_C 26.1 (CH_3), 26.3 (CH_3), 53.8 (CH_2), 64.5 (CH_2), 70.0 (CH), 79.8 (CH), 81.5 (CH), 90.4 (C), 98.9 (CH), 116.0 (C), 128.5 (2 × CH), 128.6 (2 × CH), 129.1 (C), 129.4 (C), 129.77 (2 × CH), 129.83 (2 × CH), 133.50 (CH), 133.52 (CH), 164.8 (C), 166.0 (C); MS (ESI-TOF) m/z (rel intensity) 506 [$(M + Na)^+$, 100]; HRMS (ESI-TOF) m/z [$M + Na$]$^+$ Calcd for $C_{24}H_{25}N_3O_8Na$ 506.1539, found 506.1531. Anal. Calcd for $C_{24}H_{25}N_3O_8$: C, 59.62; H, 5.21; N, 8.69. Found: C, 59.35; H, 5.47; N, 8.98.

*6-Azido-1-O-benzoyl-2-C-benzoyloxymethyl-5-O-(tert-butyldimethyl)silyl-6-deoxy-2,3-O-isopropylidene-D-mannofuranose (**32**).* To a solution of alcohol **31** (215 mg, 0.445 mmol) in dry DCM (3 mL, 7 mL/mmol) at 0 °C and under nitrogen, was added diisopropylethylamine (155 μL, 0.89 mmol) and *tert*-butyldimethylsilyl triflate (153 μL, 0.668 mmol), and the mixture was stirred for 12 h. Then, it was poured into a saturated aqueous ammonium chloride solution and extracted with DCM. The organic phase was dried over sodium sulfate, concentrated under a vacuum and purified by column chromatography (hexanes−EtOAc, 90:10 → 80:20) to yield compound **32** (226 mg, 0.379 mmol, 85%) as a colorless oil: IR 2932, 2858, 2104, 1734, 1270, 1106 cm^{-1}. NMR showed a mixture of anomers in a 5:1 ratio (only the major anomer is described): ^{1}H NMR δ_H 0.15 (3H, s), 0.16 (3H, s), 0.92 (9H, s), 1.43 (3H, s), 1.53 (3H, s), 3.34 (1H, dd, J = 4.0, 13.0 Hz), 3.57 (1H, dd, J = 2.6, 13.0 Hz), 4.19 (1H, ddd, J = 2.6, 4.0, 8.8 Hz), 4.31 (1H, dd, J = 2.9, 8.8 Hz), 4.71 (1H, d, J = 11.9 Hz), 4.78 (1H, d, J = 11.9 Hz), 4.79 (1H, d, J = 2.9 Hz), 6.54 (1H, s), 7.34−7.43 (4H, m), 7.50−7.56 (2H, m), 7.91−7.98 (4H, m); ^{13}C NMR δ_C −5.2 (CH_3), −4.3 (CH_3), 18.0 (C), 25.7 (3 × CH_3), 27.2 (CH_3), 27.4 (CH_3), 54.6 (CH_2), 63.9 (CH_2), 69.1 (CH), 81.8 (CH), 82.3 (CH), 93.1 (C), 101.4 (CH), 114.6 (C), 128.40 (2 × CH), 128.42 (2 × CH), 129.3 (C), 129.4 (C), 129.6 (2 × CH), 129.7 (2 × CH), 133.2 (CH), 133.5 (CH), 164.7 (C), 166.1 (C); MS (ESI-TOF) m/z (rel intensity) 620 [$(M + Na)^+$, 100]; HRMS (ESI-TOF) m/z [$M + Na$]$^+$ Calcd for $C_{30}H_{39}N_3O_8SiNa$ 620.2404, found 620.2413. Anal. Calcd for $C_{30}H_{39}N_3O_8Si$: C, 60.28; H, 6.58; N, 7.03. Found: C, 60.25; H, 6.53; N, 6.99.

*6-Azido-5-O-(tert-butyldimethyl)silyl-2-C-(tert-butyldimethyl)-silyloxymethyl-6-deoxy-2,3-O-isopropylidene-D-mannofuranose (**34a**).* Sodium methoxide (54 mg, 1.0 mmol) was added to a solution of azide **32** (300 mg, 0.50 mmol) in dry methanol (7.5 mL, 15 mL/mmol) under nitrogen and in an ice/water bath. The reaction was stirred at room temperature for 5 h, and then the solvent was removed under reduced pressure. The residue was purified by column chromatography (hexanes−EtOAc, 80:20 → 70:30) to yield diol **33** (175 mg, 0.45 mmol, 90%) as a colorless oil. To a solution of diol **33** (84 mg, 0.216 mmol) in dry DCM (1.5 mL, 6 mL/mmol) at 0 °C and under nitrogen were added diisopropylethylamine (75 μL, 0.434 mmol) and then TBSOTf (75 μL, 0.326 mmol), and the mixture was stirred for 24 h at room temperature. It was poured into a brine solution and extracted several times with DCM. The organic phase was dried over sodium sulfate and concentrated under a vacuum. The resulting crude was purified by column chromatography (hexanes−EtOAc, 90:10 → 80:20) to obtain compound **34a** (70 mg, 0.139 mmol, 64%) as a colorless oil: IR 3520, 2931, 2859, 2103, 1469, 1254 cm^{-1}. NMR showed a mixture of anomers in a 4:1 ratio (only the major anomer is described): ^{1}H NMR δ_H 0.08 (3H, s), 0.09 (3H, s), 0.10 (3H, s), 0.13 (3H, s), 0.895 (9H, s), 0.904 (9H, s), 1.41 (3H, s), 1.51 (3H, s), 3.29 (1H, dd, J = 4.2, 12.7 Hz), 3.56 (1H, dd, J = 2.5, 12.7 Hz), 3.59 (1H, dd, J = 2.9, 8.9 Hz), 3.72 (1H, d, J = 10.6 Hz), 3.74 (1H, d, J = 10.6 Hz), 3.86 (1H, d, J = 11.6 Hz), 4.08 (1H, ddd, J = 2.5, 4.2, 8.9 Hz), 4.58 (1H, d, J = 2.9 Hz), 4.95 (1H, d, J = 11.6 Hz); ^{13}C NMR δ_C −5.63 (CH_3), −5.61 (CH_3), −5.3 (CH_3), −4.2 (CH_3), 18.0 (C), 18.2 (C), 25.71 (3 × CH_3), 25.73 (3 × CH_3), 26.3 (CH_3), 26.9 (CH_3), 54.7 (CH_2), 63.3 (CH_2), 69.4 (CH), 75.9 (CH), 82.0 (CH), 88.6 (C), 97.2 (CH), 113.1 (C); MS (EI-TOF) m/z (rel intensity) 488 [$(M - CH_3)^+$, 1], 446 [$(M - C_4H_9)^+$, 1], 331 (1), 285 (1), 169 (4), 117 (10), 73 (100); HRMS (EI-TOF) m/z [$M - CH_3$]$^+$ Calcd for $C_{21}H_{42}N_3O_6Si_2$ 488.2612, found 488.2610. Anal. Calcd for $C_{22}H_{45}N_3O_6Si_2$: C, 52.45; H, 9.00; N, 8.34. Found: C, 52.60; H, 9.11; N, 8.00.

*5-O-(tert-Butyldimethyl)silyl-2-C-(tert-butyldimethyl)-silyloxymethyl-6-(tert-butoxycarbonyl)amino-6-deoxy-2,3-O-isopropylidene-D-mannofuranose (**35a**).* To a solution of compound **34a** (65 mg, 0.129 mmol) in EtOAc (2.0 mL, 15 mL/mmol) were added di-*tert*-butyl dicarbonate (37 mg, 0.168 mmol) and 10% Pd/C (13 mg, 20% w/w). Three vacuum/hydrogen cycles were performed, and the mixture was stirred under hydrogen atmosphere for 20 h. The reaction mixture was then filtered over a Celite pad, washed twice with ethyl acetate, and the combined filtrates were evaporated. The crude was purified by column chromatography (hexanes−EtOAc, 90:10 → 80:20) to yield compound **35a** (70 mg, 0.121 mmol, 94%) as a colorless oil: IR 3520, 3460, 2955, 2931, 2858, 1720, 1505, 1252, 1174 cm^{-1}. NMR showed a mixture of anomers in a 3:1 ratio (only the major anomer is described): ^{1}H NMR (500 MHz, 70 °C) δ_H 0.09 (6H, s), 0.10 (3H, s), 0.12 (3H, s), 0.89 (9H, s), 0.91 (9H, s), 1.41 (3H, s), 1.44 (9H, s), 1.51 (3H, s), 3.29 (1H, dd, J = 4.6, 9.8 Hz), 3.40 (1H, dd, J = 4.1, 9.8 Hz), 3.41 (1H, dd, J = 3.1, 8.5 Hz), 3.70 (1H, d, J = 12.0 Hz), 3.73 (1H, d, J = 10.4 Hz), 3.75 (1H, d, J = 10.4 Hz), 4.02 (1H, ddd, J = 4.1, 4.6, 8.5 Hz), 4.57 (1H, d, J = 3.1 Hz), 4.77, (1H, bs), 4.90 (1H, d, J = 12.0 Hz); ^{13}C NMR (125.7 MHz, 70 °C) δ_C −5.61 (CH_3), −5.59 (CH_3), −5.1 (CH_3), −4.4 (CH_3), 18.1 (C), 18.2 (C), 25.8 (6 × CH_3), 26.6 (CH_3), 27.0 (CH_3), 28.5 (3 × CH_3), 45.1 (CH_2), 63.6 (CH_2), 68.7 (CH), 78.0 (CH), 78.9 (C), 82.5 (CH), 88.8 (C), 97.6 (CH), 113.2 (C), 156.0 (C); MS (ESI-TOF) m/z (rel intensity) 600 [$(M + Na)^+$, 100]; HRMS (ESI-TOF) m/z [$M + Na$]$^+$ Calcd for $C_{27}H_{55}NO_8Si_2Na$ 600.3364, found 600.3372.

*6-Azido-5-O-(tert-butyldimethyl)silyl-6-deoxy-2,3-O-isopropylidene-2-C-pivaloyloxymethyl-D-mannofuranose (**34b**).* To a solution of diol **33** (80 mg, 0.20 mmol) in dry pyridine (1.0 mL, 5 mL/mmol) were added, under nitrogen and at 0 °C, DMAP (catalytic amount) and pivaloyl chloride (32 μL, 0.260 mmol), and then the mixture was warmed to room temperature and stirred for 24 h. The reaction was

poured into 10% aqueous HCl and extracted twice with EtOAc. The organic phase was washed with sodium bicarbonate and brine, dried over sodium sulfate and concentrated under a vacuum. The crude was purified by column chromatography (hexanes−EtOAc, 95:5 → 90:10) to yield compound **34b** (70 mg, 0.148 mmol, 74%) as a colorless oil: IR 3611, 3524, 2957, 2932, 2103, 1737, 1253, 1101 cm^{-1}. NMR showed a mixture of anomers in a 4:1 ratio (only the major anomer is described): ^1H NMR δ_H 0.10 (3H, s), 0.13 (3H, s), 0.89 (9H, s), 1.23 (9H, s), 1.46 (3H, s), 1.53 (3H, s), 3.31 (1H, dd, J = 3.9, 13.0 Hz), 3.56 (1H, dd, J = 2.5, 13.0 Hz), 3.61 (1H, dd, J = 2.8, 8.8 Hz), 3.87 (1H, d, J = 11.7 Hz), 4.10 (1H, ddd, J = 2.5, 3.8, 8.7 Hz), 4.21 (1H, d, J = 11.9 Hz), 4.28 (1H, d, J = 11.9 Hz), 4.53 (1H, d, J = 2.8 Hz), 4.90 (1H, d, J = 11.6 Hz); ^{13}C NMR δ_C −5.3 (CH_3), −4.2 (CH_3), 18.0 (C), 25.7 (3 × CH_3), 26.3 (CH_3), 26.8 (CH_3), 27.1 (3 × CH_3), 38.9 (C), 54.6 (CH_2), 63.9 (CH_2), 69.2 (CH), 75.4 (CH), 81.8 (CH), 87.2 (C), 97.7 (CH), 113.9 (C), 177.8 (C); MS (EI-TOF) m/z (rel intensity) 458 [$(M - CH_3)^+$, 2], 358 (13), 238 (12), 57 (100); HRMS (EI-TOF) m/z $[M - CH_3]^+$ Calcd for $C_{20}H_{36}N_3O_7Si$ 458.2323, found 458.2338. Anal. Calcd for $C_{21}H_{39}N_3O_7Si$: C, 53.25; H, 8.30; N, 8.87. Found: C, 53.42; H, 8.19; N, 8.72.

*5-O-(tert-Butyldimethyl)silyl-6-(tert-butoxycarbonyl)amino-6-deoxy-2,3-O-isopropylidene-2-C-pivaloyloxymethyl-D-mannofuranose (**35b**).* To a solution of azide **34b** (70 mg, 0.148 mmol) in EtOAc (2.0 mL, 15 mL/mmol) were added di-*tert*-butyl dicarbonate (48 mg, 0.22 mmol) and 10% Pd/C (14 mg, 20% w/w). Three vacuum/hydrogen cycles were performed, and the mixture was stirred under hydrogen atmosphere for 3 h. The reaction mixture was then filtered over a Celite pad, washed twice with ethyl acetate, and the combined filtrates were evaporated. The crude was purified by column chromatography (hexanes−EtOAc, 90:10 → 80:20) to yield compound **35b** (73 mg, 0.133 mmol, 90%) as a colorless oil: IR 3460, 2932, 1726, 1504, 1250 cm^{-1}. NMR showed a mixture of anomers in a 2:1 ratio (only the major anomer is described): ^1H NMR (500 MHz, 70 °C) δ_H 0.09 (3H, s), 0.12 (3H, s), 0.88 (9H, s), 1.22 (9H, s), 1.43 (9H, s), 1.45 (3H, s), 1.53 (3H, s), 3.28 (1H, ddd, J = 4.4, 4.8, 13.7 Hz), 3.407 (1H, ddd, J = 4.0, 7.1, 13.7 Hz), 3.411 (1H, dd, J = 3.1, 8.5 Hz), 4.02 (1H, ddd, J = 4.0, 4.8, 8.5 Hz), 4.21 (1H, d, J = 12.0 Hz), 4.26 (1H, d, J = 12.0 Hz), 4.49 (1H, d, J = 3.1 Hz), 4.76 (1H, bs), 4.84 (1H, s); ^{13}C NMR (125.7 MHz, 70 °C) δ_C −5.1 (CH_3), −4.4 (CH_3), 18.1 (C), 25.8 (3 × CH_3), 26.6 (CH_3), 26.9 (CH_3), 27.2 (3 × CH_3), 28.5 (3 × CH_3), 38.9 (C), 45.0 (CH_2), 64.0 (CH_2), 68.6 (CH), 77.6 (CH), 79.0 (C), 82.3 (CH), 87.5 (C), 98.0 (CH), 113.9 (C), 155.9 (C), 177.7 (C); MS (ESI-TOF) m/z (rel intensity) 570 [$(M + Na)^+$, 100]; HRMS (ESI-TOF) m/z $[M + Na]^+$ Calcd for $C_{26}H_{49}NO_9SiNa$ 570.3074, found 570.3073.

General Procedure for the Synthesis of Iminosugars 36−46. A solution of the corresponding hemiacetal (1 mmol) in dry DCM or DCE (40 mL) containing PhIO (2.0−2.5 equiv) and iodine (0.5−1.2 equiv) was irradiated with 80 W tungsten-filament lamps at room temperature for 1−20 h. The reaction mixture was then poured into aqueous sodium thiosulfate and extracted with DCM. The organic phase was dried and concentrated in vacuo. Column chromatography of the residue (hexanes−EtOAc mixtures) afforded the desired cyclic imino-compounds.

*5-(tert-Butoxycarbonyl)amino-1-O-(tert-butyldimethyl)silyl-5-deoxy-4-O-formyl-2,3-O-isopropylidene-α-D-ribulofuranose (**36**).* Following the general procedure [DCM, PhIO (2.2 equiv), I_2 (1.2 equiv)], compound **4a** (53 mg, 0.12 mmol) afforded, after 1 h, the iminosugar **36** (32 mg, 0.07 mmol, 61%) as a colorless oil: $[\alpha]_D$ −21.7 (c 0.18); IR 2980, 2931, 2858, 1737, 1715, 1367, 1254 cm^{-1}; ^1H NMR (500 MHz, 70 °C) δ_H 0.07 (3H, s), 0.08 (3H, s), 0.91 (9H, s), 1.39 (3H, s), 1.46 (9H, s), 1.49 (3H, s), 3.53 (1H, dd, J = 8.2, 9.8 Hz), 3.75 (1H, d, J = 10.7 Hz), 3.88 (1H, dd, J = 8.2, 9.8 Hz), 4.12−4.56 (1H, bs), 4.61 (1H, d, J = 3.9 Hz), 5.17 (1H, ddd, J = 3.9, 8.2, 8.2 Hz), 8.06 (1H, s); ^{13}C NMR (125.7 MHz, 70 °C) δ_C −5.5 (2 × CH_3), 18.2 (C), 25.8 (3 × CH_3), 26.7 (CH_3), 27.4 (CH_3), 28.4 (3x CH_3), 48.6 (CH_2), 63.9 (CH_2), 68.5 (CH), 80.4 (C), 82.6 (CH), 99.9 (C), 113.7 (C), 137.7 (C), 159.8 (CH); MS (EI-TOF) m/z (rel intensity) 431 (M^+, 1), 318 (100), 216 (58), 186 (23); HRMS (EI-TOF) m/z $[M]^+$ Calcd for $C_{20}H_{37}NO_7Si$ 431.2339, found 431.2355. Anal. Calcd for $C_{20}H_{37}NO_7Si$: C, 55.66; H, 8.64; N, 3.25. Found: C, 55.59; H, 8.45; N, 3.20.

*5-(tert-Butoxycarbonyl)amino-5-deoxy-4-O-formyl-2,3-O-isopropylidene-1-O-pivaloyl-α-D-ribulofuranose (**37**).* Following the general procedure [DCM, PhIO (2.2 equiv), I_2 (1.2 equiv)], compound **4b** (57 mg, 0.14 mmol) afforded, after 2 h, the iminosugar **37** (40 mg, 0.10 mmol, 71%) as a colorless oil: $[\alpha]_D$ −43.1 (c 0.10); IR 2980, 1738, 1705, 1394, 1173 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6, 75 °C) δ_H 1.17 (9H, s), 1.38 (3H, s), 1.406 (9H, s), 1.414 (3H, s), 3.41 (1H, dd, J = 9.8, 9.8 Hz), 3.83 (1H, dd, J = 7.9, 9.8 Hz), 4.32 (1H, d, J = 11.3 Hz), 4.68 (1H, d, J = 11.3 Hz), 4.72 (1H, d, J = 3.9 Hz), 5.10 (1H, ddd, J = 3.9, 7.9, 9.8 Hz), 8.24 (1H, s); ^{13}C NMR (125.7 MHz, DMSO-d_6, 75 °C) δ_C 26.3 (CH_3), 26.7 (3 × CH_3), 27.0 (CH_3), 27.8 (3 × CH_3), 38.1 (C), 47.6 (CH_2), 62.5 (CH_2), 67.0 (CH), 79.9 (C), 81.3 (CH), 96.9 (C), 112.9 (C), 152.2 (C), 161.3 (CH), 176.4 (C); MS (EI-TOF) m/z (rel intensity) 386 [$(M - CH_3)^+$, 1], 286 (25), 255 (36), 186 (99), 57 (100); HRMS (EI-TOF) m/z $[M - CH_3]^+$ Calcd for $C_{18}H_{28}NO_8$ 386.1815, found 386.1810. Anal. Calcd for $C_{19}H_{31}NO_8$: C, 56.85; H, 7.78; N, 3.49. Found: C, 57.06; H, 8.17; N, 3.31.

*5-(tert-Butoxycarbonyl)amino-1-O-(tert-butyldimethyl)silyl-5-deoxy-4-O-formyl-2,3-O-isopropylidene-β-D-xylulofuranose (**38**).* Following the general procedure [DCM, PhIO (2.2 equiv), I_2 (1.2 equiv)], compound **8a** (44 mg, 0.10 mmol) afforded, after 5 h, the compound **38** (15 mg, 0.04 mmol, 35%) as a colorless oil: $[\alpha]_D$ +13.8 (c 0.174); IR 2931, 2857, 1737, 1702, 1370, 1216 cm^{-1}; ^1H NMR (500 MHz, 70 °C) δ_H 0.10 (6H, s), 0.93 (9H, s), 1.41 (3H, s), 1.43 (3H, s), 1.49 (9H, s), 3.55 (1H, d, J = 12.7 Hz), 3.86−3.94 (1H, m), 3.96 (1H, dd, J = 4.5, 12.7 Hz), 4.32 (1H, d, J = 10.7 Hz), 4.63 (1H, s), 5.23 (1H, d, J = 4.5 Hz), 8.01 (1H, s); ^{13}C NMR (125.7 MHz, 70 °C) δ_C −5.5 (CH_3), −5.3 (CH_3), 18.4 (C), 25.9 (3 × CH_3), 27.0 (CH_3), 27.7 (CH_3), 28.5 (3 × CH_3), 52.4 (CH_2), 63.7 (CH_2), 72.0 (CH), 80.5 (C), 84.4 (CH), 101.1 (C), 112.9 (C), 153.6 (C), 159.5 (CH); MS (EI-TOF) m/z (rel intensity) 431 (M^+, 1), 416 (1), 318 (41), 216 (31), 170 (31), 57 (100); HRMS (EI-TOF) m/z $[M]^+$ Calcd for $C_{20}H_{37}NO_7Si$ 431.2339, found 431.233. Anal. Calcd for $C_{20}H_{37}NO_7Si$: C, 55.66; H, 8.64; N, 3.25. Found: C, 55.73; H, 8.70; N, 3.27.

*5-(tert-Butoxycarbonyl)amino-5-deoxy-4-O-formyl-2,3-O-isopropylidene-1-O-pivaloyl-β-D-xylulofuranose (**39**).* Following the general procedure [DCE, PhIO (2.5 equiv), I_2 (1.1 equiv)], compound **8b** (200 mg, 0.50 mmol) afforded, after 2 h, the iminosugar **39** (115 mg, 0.29 mmol, 58%) as a colorless oil: $[\alpha]_D$ +35.6 (c 0.89); IR 2981, 2936, 1736, 1704, 1394, 1159 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6, 70 °C) δ_H 1.17 (9H, s), 1.37 (3H, s), 1.38 (3H, s), 1.42 (9H, s), 3.51 (1H, d, J = 12.8 Hz), 3.87 (1H, dd, J = 4.7, 12.8 Hz), 4.35 (1H, d, J = 11.6 Hz), 4.52 (1H, s), 4.67 (1H, d, J = 11.6 Hz), 5.13 (1H, d, J = 4.7 Hz), 8.21 (1H, s); ^{13}C NMR (125.7 MHz, 70 °C) δ_C 27.17 (CH_3), 27.23 (3 × CH_3), 27.3 (CH_3), 28.4 (3 × CH_3), 38.9 (C), 52.1 (CH_2), 63.5 (CH_2), 71.6 (CH), 81.1 (C), 84.8 (CH), 98.7 (C), 113.0 (C), 153.4 (C), 159.3 (CH), 177.5 (C); MS (EI-TOF) m/z (rel intensity) 401 (M^+, 1), 355 (3), 230 (37), 128 (100), 57 (100); HRMS (EI-TOF) m/z $[M]^+$ Calcd for $C_{19}H_{31}NO_8$ 401.2050, found 401.2053. Anal. Calcd for $C_{19}H_{31}NO_8$: C, 56.85; H, 7.78; N, 3.49. Found: C, 56.92; H, 7.75; N, 3.70.

*5-(tert-Butoxycarbonyl)amino-1,6-di-O-(tert-butyldimethyl)silyl-5-deoxy-4-O-formyl-2,3-O-isopropylidene-α-L-sorbofuranose (**40**) and 5-(tert-Butoxycarbonyl)amino-6-O-(tert-butyldimethyl)silyl-5-deoxy-4-O-formyl-2,3-O-isopropylidene-α-L-sorbofuranose (**40a**).* Following the general procedure [DCM, PhIO (2.0 equiv), I_2 (1.2 equiv)], compound **16a** (50 mg, 0.09 mmol) afforded after 4 h, the iminosugar **40** (23 mg, 0.04 mmol, 46%) along with other minor cyclized compounds, of which **40a** (4 mg, 0.009 mmol, 10%) could be characterized. **Compound 40.** Colorless oil: $[\alpha]_D$ +56.2 (c 0.4); IR 2955, 2930, 2858, 1739, 1703, 1471, 1255, 1161, 1090 cm^{-1}; ^1H NMR (500 MHz, 70 °C) δ_H 0.04 (3H, s), 0.06 (3H, s), 0.081 (3H, s), 0.084 (3H, s), 0.88 (9H, s), 0.92 (9H, s), 1.39 (3H, s), 1.43 (3H, s), 1.48 (9H, s), 3.64 (1H, dd, J = 9.1, 9.3 Hz), 3.78 (1H, d, J = 10.7 Hz), 4.16 (1H, dd, J = 4.6, 9.3 Hz), 4.28 (1H, ddd, J = 4.6, 5.0, 9.1 Hz), 4.30 (1H, d, J = 10.7 Hz), 4.52 (1H, d, J = 1.0 Hz), 5.49 (1H, ddd, J = 0.7, 1.0, 5.0 Hz), 8.04 (1H, s); ^{13}C NMR (125.7 MHz, 70 °C) δ_C −5.52 (CH_3), −5.47 (CH_3), −5.3 (CH_3), −5.2 (CH_3), 18.2 (C), 18.4 (C), 25.9 (3 × CH_3), 26.0 (3 × CH_3), 26.9 (CH_3), 27.7 (CH_3), 28.5 (3 × CH_3), 60.0 (CH_2), 61.6 (CH), 63.9 (CH_2), 72.4 (CH), 80.6 (C), 82.4 (CH), 102.4 (C), 112.6 (C), 154.4 (C), 159.4 (CH); MS (ESI-TOF) m/z (rel intensity) 576 [$(M + H)^+$, 100], 598 [$(M + Na)^+$, 44].

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HRMS (ESI-TOF) m/z $[M + H]^+$ Calcd for $C_{27}H_{54}NO_8Si_2$ 576.3388, found 576.3381. **Compound 40a.** Colorless oil: $[\alpha]_D$ +14.5 (c 0.1); ^1H NMR (500 MHz) δ_H 0.15 (6H, s), 0.95 (9H, s), 1.38 (3H, s), 1.42 (3H, s), 1.49 (9H, s), 3.73 (1H, d, J = 10.2 Hz), 3.75−3.81 (1H, m), 4.11 (1H, dd, J = 4.0, 11.2 Hz), 4.19 (1H, ddd, J = 4.0, 4.2, 8.7 Hz), 4.34 (1H, d, J = 10.2 Hz), 4.36 (1H, d, J = 7.0 Hz), 4.49 (1H, d, J = 10.2 Hz), 4.84 (1H, dd, J = 4.2, 10.2 Hz), 8.05 (1H, s); ^{13}C NMR (125.7 MHz) δ_C −5.5 (CH_3), −5.4 (CH_3), 18.4 (C), 25.9 (3 × CH_3), 26.5 (CH_3), 27.4 (CH_3), 28.4 (3 × CH_3), 60.9 (CH_2), 61.4 (CH), 65.3 (CH_2), 70.3 (CH), 81.2 (C), 87.6 (CH), 101.4 (C), 112.5 (C), 159.5 (C), 160.4 (CH); MS (EI-TOF) m/z (rel intensity) 462 [$(M + H)^+$, 1], 446 (1), 334 (16), 304 (44), 246 (26), 57 (100). HRMS (EI-TOF) m/z $[M + H]^+$ Calcd for $C_{21}H_{40}NO_8Si$ 462.2523, found 462.2509.

*5-(tert-Butoxycarbonyl)amino-6-O-(tert-butyldimethyl)silyl-5-deoxy-4-O-formyl-2,3-O-isopropylidene-1-O-pivaloyl-α-L-sorbofuranose (**41**).* Following the general procedure [DCM, PhIO (2.2 equiv), I_2 (1.2 equiv)], compound **16b** (27 mg, 0.05 mmol) afforded, after 2 h, compound **41** (16 mg, 0.029 mmol, 58%) as a colorless oil: $[\alpha]_D$ +58.2 (c 0.29); IR 2957, 2931, 2858, 1736, 1706, 1479, 1367, 1255 cm^{-1}; ^1H NMR (500 MHz, 70 °C) δ_H 0.04 (3H, s), 0.07 (3H, s), 0.89 (9H, s), 1.23 (9H, s), 1.43 (3H, s), 1.44 (3H, s), 1.49 (9H, s), 3.66 (1H, dd, J = 9.3, 9.3 Hz), 4.18 (1H, dd, J = 4.3, 9.3 Hz), 4.29 (1H, d, J = 12.0 Hz), 4.27−4.31 (1H, m), 4.40 (1H, s), 4.85 (1H, d, J = 12.0 Hz), 5.51 (1H, d, J = 4.7 Hz), 8.04 (1H, s); ^{13}C NMR (125.7 MHz, 70 °C) δ_C −5.5 (CH_3), −5.4 (CH_3), 18.2 (C), 25.9 (3 × CH_3), 27.1 (CH_3), 27.3 (3 × CH_3), 27.7 (CH_3), 28.4 (3 × CH_3), 38.9 (C), 59.9 (CH_2), 61.5 (CH), 64.0 (CH_2), 72.2 (CH), 81.2 (C), 82.8 (CH), 100.3 (C), 112.9 (C.), 154.0 (C), 159.3 (CH), 177.6 (C); MS (ESI-TOF) m/z (rel intensity) 568 [$(M + Na)^+$, 100]; HRMS (ESI-TOF) m/z $[M + Na]^+$ Calcd for $C_{26}H_{47}NO_9SiNa$ 568.2918, found 568.2911. Anal. Calcd for $C_{26}H_{47}NO_9Si$: C, 57.22; H, 8.68; N, 2.57. Found: C, 57.08; H, 8.66; N, 2.70.

*5-(tert-Butoxycarbonyl)amino-1-(tert-butyldimethyl)silyl-5,6-dideoxy-6-fluoro-4-O-formyl-2,3-O-isopropylidene-α-L-sorbofuranose (**42**) and 4-(tert-Butoxycarbonyl)amino-4,5-dideoxy-5-fluoro-3-O-formyl-1,2-O-isopropylidene-L-xylonic acid (**42a**).* To a solution of **23a** (38 mg, 0.081 mmol) in dry DCE (4 mL, 50 mL/mmol) were added PhIO (45 mg, 0.204 mmol), I_2 (10 mg, 0.04 mmol) and $NaHCO_3$ (40 mg, 100% w/w), and the resulting suspension was irradiated with two 80 W tungsten-filament lamps at room temperature for 1.5 h. Then, the reaction mixture was poured into aqueous sodium thiosulfate and extracted with DCM. The organic phase was dried over sodium sulfate, concentrated under a vacuum and purified by rotatory chromatography (hexanes−EtOAc, 90:10 → 70:30) to afford the fluorinated iminosugars **42** (9.5 mg, 0.021 mmol, 25%) and **42a** (13 mg, 0.038 mmol, 47%). **Compound 42.** Colorless oil: $[\alpha]_D$ +96.2 (c 0.55); IR ($CHCl_3$) 2955, 2935, 1731, 1711, 1696, 1385, 1370, 1164, 1149 cm^{-1}; ^1H NMR (500 MHz, 70 °C) δ_H 0.09 (6H, s), 0.93 (9H, s), 1.41 (3H, s), 1.44 (3H, s), 1.49 (9H, s), 3.82 (1H, d, J = 10.7 Hz), 4.24 (1H, d, J = 10.7 Hz), 4.46−4.51 (1H, m), 4.51 (1H, ddd, J = 8.5, 8.5 Hz, $^2J_{FH}$ = 45.1 Hz), 4.58 (1H, d, J = 1.3 Hz), 4.81 (1H, ddd, J = 3.8, 8.5 Hz, $^2J_{FH}$ = 41.0 Hz), 5.53 (1H, dd, J = 1.3, 5.0 Hz), 8.07 (1H, s); ^{13}C NMR (125.7 MHz, 70 °C) δ_C −5.5 (CH_3), −5.2 (CH_3), 18.4 (C), 26.0 (3 × CH_3), 27.0 (CH_3), 27.8 (CH_3), 28.4 (3 × CH_3), 59.4 (CH, d, $^2J_{FC}$ = 25.4 Hz), 63.9 (CH_2), 72.2 (CH), 79.8 (CH_2, d, $^1J_{FC}$ = 169.5 Hz), 81.3 (C), 83.0 (CH), 101.8 (C), 113.1 (C), 156.2 (C), 159.2 (CH); MS (ESI-TOF) m/z (rel intensity) 486 [$(M + Na)^+$, 100]; HRMS (ESI-TOF) m/z $[M + Na]^+$ Calcd for $C_{21}H_{38}FNO_7SiNa$ 486.2299, found 486.2299. Anal. Calcd for $C_{21}H_{38}FNO_7Si$: C, 54.40; H, 8.26; N, 3.02. Found: C, 54.37; H, 8.46; N, 3.12. **Compound 42a.** Colorless oil: $[\alpha]_D$ +6.3 (c 0.65); IR ($CHCl_3$) 3438, 2985, 1797, 1736, 1713, 1503, 1272, 1157 cm^{-1}; ^{19}F NMR δ_F −231.0 (1F, s); ^1H NMR (500 MHz) δ_H 1.43 (9H, s), 1.56 (3H, s), 1.66 (3H, s), 4.34 (1H, ddddd, J = 3.5, 4.3, 6.0, 9.2 Hz, $^3J_{FH}$ = 25.5 Hz), 4.42 (1H, ddd, J = 4.3, 9.9 Hz, $^2J_{FH}$ = 47.0 Hz), 4.56 (1H, ddd, J = 3.5, 9.9 Hz, $^2J_{FH}$ = 46.2 Hz), 4.67 (1H, d, J = 3.5 Hz), 4.98 (1H, d, J = 9.2 Hz), 5.57 (1H, dd, J = 3.5, 6.0 Hz), 8.09 (1H, s); ^{13}C NMR (125.7 MHz) δ_C 26.5 (CH_3), 26.7 (CH_3), 28.2 (3 × CH_3), 50.9 (CH, d, $^2J_{FC}$ = 21.2 Hz), 69.4 (CH, d, $^3J_{FC}$ = 3.2 Hz), 73.3 (CH), 80.4 (C), 82.6 (CH_2, d, $^1J_{FC}$ = 172.7 Hz), 112.0 (C), 155.1 (C), 159.4 (CH), 169.3 (C); EM (ESI-TOF) m/z (rel intensity) 358 [$(M + Na)^+$, 100]; HRMS (ESI-TOF) m/z $[M + Na]^+$ Calcd for $C_{14}H_{22}FNO_7Na$ 358.1278, found 358.1277.

*5-(tert-Butoxycarbonyl)amino-5,6-dideoxy-6-fluoro-4-O-formyl-2,3-O-isopropylidene-1-O-pivaloyl-α-L-sorbofuranose (**43**) and 5-Amino-5,6-dideoxy-6-fluoro-4-O-formyl-2,3-O-isopropylidene-1-O-pivaloyl-α-L-sorbofuranose (**43a**).* Following the general procedure [DCE, PhIO (2.5 equiv), I_2 (0.5 equiv)], compound **23b** (47 mg, 0.108 mmol) afforded, after 1 h, the fluorinated iminosugars **43** (18 mg, 0.042 mmol, 39%) and **43a** (3 mg, 0.009 mmol, 8%). **Compound 43.** Colorless oil: $[\alpha]_D$ +76.2 (c 1.09); IR 2985, 1730, 1699, 1480, 1377, 1151, 1016 cm^{-1}; ^1H NMR (500 MHz, 70 °C) δ_H 1.24 (9H, s), 1.44 (3H, s), 1.45 (3H, s), 1.50 (9H, s), 4.34 (1H, d, J = 12.0 Hz), 4.46 (1H, d, J = 1.6 Hz), 4.46−4.52 (1H, m), 4.54 (1H, ddd, J = 7.7, 8.8 Hz, $^2J_{FH}$ = 45.4 Hz), 4.81 (1H, d, J = 12.0 Hz), 4.85 (1H, ddd, J = 3.8, 8.8 Hz, $^2J_{FH}$ = 54.2 Hz), 5.41 (1H, ddd, J = 1.3, 1.6, 5.5 Hz), 8.08 (1H, s); ^{13}C NMR δ_C 27.0 (CH_3), 27.2 (3 × CH_3), 27.7 (CH_3), 28.2 (3 × CH_3), 38.8 (C), 59.0 (CH, d, $^2J_{FC}$ = 24.7 Hz), 63.5 (CH_2), 71.5 (CH), 79.5 (CH_2, d, $^1J_{FC}$ = 173.7 Hz), 81.9 (C), 82.4 (CH), 99.7 (C), 113.2 (C), 155.4 (C), 159.3 (CH), 177.7 (C); EM (ESI-TOF) m/z (rel intensity) 456 [$(M + Na)^+$, 100]; HRMS (ESI-TOF) m/z $[M + Na]^+$ Calcd for $C_{20}H_{32}FNO_8Na$ 456.2010, found 456.2011. Anal. Calcd for $C_{20}H_{32}FNO_8$: C, 55.42; H, 7.44; N, 3.23. Found: C, 55.50; H, 7.66; N, 3.36. **Compound 43a.** Colorless oil: $[\alpha]_D$ +50.8 (c 0.25); IR 3353, 2989, 1731, 1677, 1480, 1375, 1149, 1112 cm^{-1}; ^{19}F NMR δ_F −227.8 (1F, s); ^1H NMR (500 MHz) δ_H 1.25 (9H, s), 1.421 (3H, s), 1.425 (3H, s), 4.29 (1H, d, J = 12.0 Hz), 4.42−4.47 (1H, m), 4.490 (1H, d, J = 12.0 Hz), 4.491 (1H, s), 4.52 (1H, d, J = 4.7 Hz), 4.66 (1H, ddd, J = 8.7, 8.7 Hz, $^2J_{FH}$ = 45.7 Hz), 5.20 (1H, ddd, J = 4.7, 8.7 Hz, $^2J_{FH}$ = 46.3 Hz), 8.13 (1H, s); ^{13}C NMR δ_C 26.6 (CH_3), 27.2 (3 × CH_3), 27.5 (CH_3), 38.9 (C), 59.7 (CH, d, $^2J_{FC}$ = 24.4 Hz), 64.3 (CH_2), 70.9 (CH, d, $^3J_{FC}$ = 2.1 Hz), 79.8 (CH_2, d, $^1J_{FC}$ = 166.3 Hz), 85.1 (CH), 98.6 (C), 114.1 (C), 163.4 (CH), 177.8 (C); MS (ESI-TOF) m/z (rel intensity) 356 [$(M + Na)^+$, 100]; HRMS (ESI-TOF) m/z $[M + Na]^+$ Calcd for $C_{15}H_{24}FNO_6Na$ 356.1485, found 356.1488.

*5-(tert-Butoxycarbonyl)amino-5,6-dideoxy-4-O-formyl-2,3-O-isopropylidene-1-O-pivaloyl-α-L-sorbofuranose (**44**).* Following the general procedure [DCE, PhIO (2.5 equiv), I_2 (1.1 equiv)], compound **29** (30 mg, 0.072 mmol) was stirred at 80 °C for 2.5 h to afford iminosugar **44** (15 mg, 0.036 mmol, 50%) as a colorless oil: $[\alpha]_D$ +57.5 (c 0.57); IR ($CHCl_3$) 2985, 1729, 1701, 1458, 1373, 1156 cm^{-1}; ^1H NMR (500 MHz, 70 °C) δ_H 1.24 (9H, s), 1.28 (3H, d, J = 6.3 Hz), 1.42 (3H, s), 1.43 (3H, s), 1.50 (9H, s), 4.31 (1H, dddd, J = 6.0, 6.3, 6.3, 6.3 Hz), 4.32 (1H, d, J = 12.0 Hz), 4.38 (1H, d, J = 1.3 Hz), 4.83 (1H, d, J = 12.0 Hz), 5.34 (1H, ddd, J = 1.3, 1.3, 6.0 Hz), 8.08 (1H, dd, J = 0.8, 1.3 Hz); ^{13}C NMR δ_C 14.3 (CH_3), 27.0 (CH_3), 27.2 (3 × CH_3), 27.6 (CH_3), 28.3 (3 × CH_3), 38.8 (C), 56.1 (CH), 63.7 (CH_2), 73.5 (CH), 81.0 (C), 82.2 (CH), 99.6 (C), 112.8 (C), 154.1 (C), 159.6 (CH), 177.8 (C); EM (ESI-TOF) m/z (rel intensity) 438 [$(M + Na)^+$, 100]; HRMS (ESI-TOF) m/z $[M + Na]^+$ Calcd for $C_{20}H_{33}NO_8Na$ 438.2104, found 438.2112. Anal. Calcd for $C_{20}H_{33}NO_8$: C, 57.82; H, 8.01; N, 3.37. Found: C, 57.87; H, 8.34; N, 3.39.

*5-(tert-Butoxycarbonyl)amino-4-(tert-butyldimethyl)silyl-5-deoxy-3-O-formyl-1,2-O-isopropylidene-D-arabinonic acid (**45**).* Following the general procedure [DCM, PhIO (2.0 equiv), I_2 (1.2 equiv)], compound **35a** (35 mg, 0.06 mmol) afforded, after 20 h, compound **45** (9.5 mg, 0.02 mmol, 33%) as a colorless oil: IR 3440, 2985, 1796, 1736, 1712, 1498 cm^{-1}; ^1H NMR (500 MHz, 70 °C) δ_H 0.14 (3H, s), 0.17 (3H, s), 0.93 (9H, s), 1.46 (9H, s), 1.56 (3H, s), 1.65 (3H, s), 3.16 (1H, ddd, J = 4.1, 6.3, 14.5 Hz), 3.41 (1H, ddd, J = 4.1, 5.7, 14.5 Hz), 4.02 (1H, ddd, J = 4.1, 4.1, 7.9 Hz), 4.78 (1H, d, J = 2.2 Hz), 4.76 (1H, dd, J = 5.7, 6.3 Hz), 5.36 (1H, dd, J = 2.2, 7.9 Hz), 8.03 (1H, s); ^{13}C NMR (125.7 MHz, 70 °C) δ_C −5.0 (CH_3), −4.4 (CH_3), 18.1 (C), 25.8 (3 × CH_3), 26.6 (CH_3), 26.9 (CH_3), 28.5 (3 × CH_3), 42.7 (CH_2), 69.6 (CH), 71.4 (CH), 73.7 (CH), 79.0 (C), 111.5 (C), 155.8 (C), 159.1 (CH), 170.1 (C); EM (ESI-TOF) m/z (rel intensity) 470 [$(M + Na)^+$, 100]; HRMS (ESI-TOF) m/z $[M + Na]^+$ Calcd for $C_{20}H_{37}NO_8SiNa$ 470.2186, found 470.2185.

*6-(tert-Butoxycarbonyl)amino-5-O-(tert-butyldimethyl)silyl-6-deoxy-4-O-formyl-2,3-O-isopropylidene-1-O-pivaloyl-β-D-fructopyranose (**46**).* Following the general procedure [DCM, PhIO (2.0 equiv),

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I_2 (1.2 equiv)], compound **35b** (27 mg, 0.05 mmol) afforded, after 4 h, the compound **46** (12 mg, 0.02 mmol, 46%) as a colorless oil: $[\alpha]_D$ +5.1 (*c* 0.57); IR 2958, 2932, 2859, 1736, 1697, 1368, 1255, 1163, 1099 cm^{-1}; ^1H NMR (500 MHz, 70 °C) δ_H 0.10 (3H, s), 0.12 (3H, s), 0.89 (9H, s), 1.18 (9H, s), 1.26 (3H, s), 1.45 (3H, s), 1.48 (9H, s), 3.22 (1H, dd, *J* = 9.6, 13.2 Hz), 3.91 (1H, dd, *J* = 4.5, 13.2 Hz), 4.27 (1H, d, *J* = 3.1 Hz), 4.25−4.30 (1H, m), 4.35 (1H, d, *J* = 11.7 Hz), 4.76 (1H, d, *J* = 11.7 Hz), 5.41 (1H, dd, *J* = 3.1, 3.1 Hz), 8.07 (1H, s); ^{13}C NMR (125.7 MHz, 70 °C) δ_C −4.92 (CH_3),−4.87 (CH_3), 18.1 (C), 25.8 (3 × CH_3), 26.6 (CH_3), 27.3 (3 × CH_3), 27.6 (CH_3), 28.4 (3 × CH_3), 38.9 (C), 44.9 (CH), 62.0 (CH_2), 64.3 (CH), 70.3 (CH), 77.3 (CH), 80.9 (C), 90.2 (C), 110.0 (C), 154.8 (C), 159.4 (CH), 177.4 (C); MS (EI-TOF) *m*/*z* (rel intensity) 474 [$(M - CH_3 - C_4H_8)^+$, 1], 458 (2), 444 (1), 373 (1), 314 (4), 129 (10), 57 (100); HRMS (EI-TOF) *m*/*z* [$M - CH_3 - C_4H_8]^+$ Calcd for $C_{21}H_{36}NO_9Si$ 474.2159, found 474.2164. Anal. Calcd for $C_{26}H_{47}NO_9Si$: C, 57.22; H, 8.68; N, 2.57. Found: C, 57.06; H, 8.99; N, 2.46.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^1H and ^{13}C NMR spectra for all new compounds. This material is available free of charge via Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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