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Citation: Liu, Zilei, Yoshihara, Akihide, Kelly, Ciarán, Heap, John T., Marqvorsen, Mikkel H. S., Jenkinson, Sarah F., Wormald, Mark R., Otero, José M., Estévez, Amalia, Kato, Atsushi, Fleet, George W. J., Estévez, Ramón J. and Izumori, Ken (2016) 6-Deoxyhexoses froml-Rhamnose in the Search for Inducers of the Rhamnose Operon: Synergy of Chemistry and Biotechnology. Chemistry: A European Journal, 22 (35). pp. 12557-12565. ISSN 0947-6539

Published by: Wiley-Blackwell

URL: https://doi.org/10.1002/chem.201602482 <https://doi.org/10.1002/chem.201602482>

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NEWCASTLE

6-Deoxyhexoses from L-Rhamnose in the Search for Inducers of the Rhamnose Operon: Synergy of Chemistry and Biotechnology

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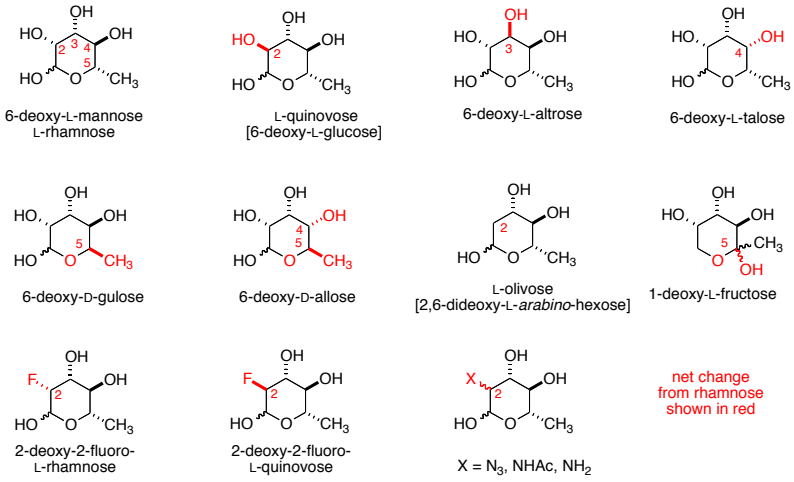
TOC



ABSTRACT

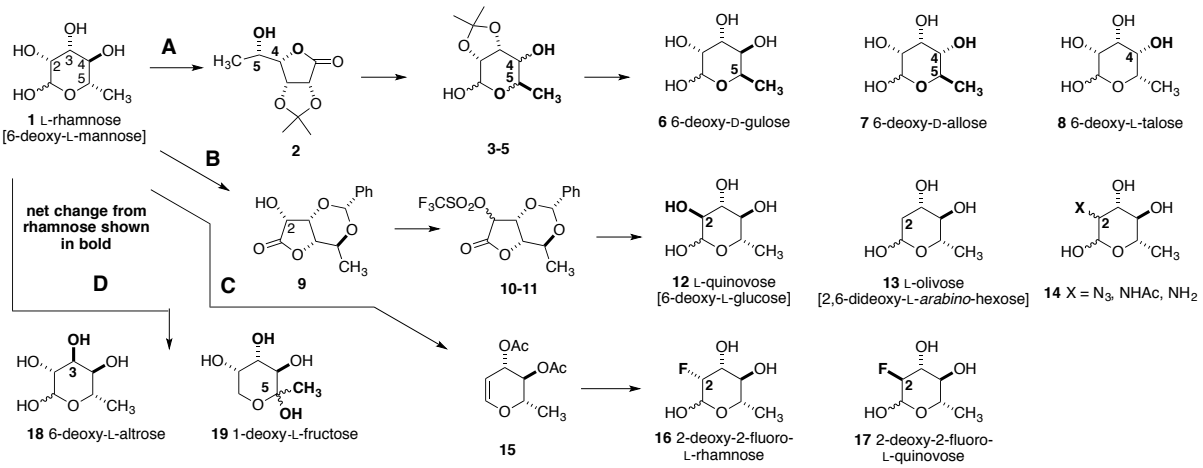
In the search for alternative non-metabolizable inducers in the L-rhamnose promoter system, the synthesis of fifteen 6-deoxyhexoses from L-rhamnose demonstrates the value of synergy between biotechnology and chemistry. The readily available 2,3-acetonide of rhamnonolactone allows inversion of configuration at C4 and/or C5 of rhamnose to give 6-deoxy-D-allose, 6-deoxy-D-gulose and 6-deoxy-L-talose. Highly crystalline 3,5-benzylidene rhamnonolactone gives easy access to L-quinovose [6-deoxy-L-glucose], L-olivose and rhamnose analogue with C2 azido, amino and acetamido substituents. Electrophilic fluorination of rhamnal gives a mixture of 2-deoxy-2-fluoro-L-rhamnose and 2-deoxy-2-fluoro-L-quinovose. Biotechnology provides access to 6-deoxy-L-altrose and 1-deoxy-L-fructose.

KEY WORDS: rhamnose operon, rhamnonolactone, 6-deoxyhexose, rare sugar

INTRODUCTION

In biotechnology, control over gene expression is often useful, such as in the production of proteins of interest. This is typically achieved by assembling a DNA construct in which the gene of interest is placed under the control of a promoter (a regulatory DNA sequence) which responds to a known external stimulus. Numerous inducible gene expression systems have been reported, exploiting inducible promoters which respond to natural or synthetic stimuli such as sugars, antibiotics and metals.[1] L-Rhamnose [6-deoxy-L-mannose] is readily metabolized by *E. coli*[2] and the metabolism of L-rhamnose is precisely controlled. L-Rhamnose works as inducer of the operon encoding the enzymes required for its metabolism, *rhaBAD*.[3] The L-rhamnose promoter system, P_{rhaBAD}, is used extensively for the heterologous expression of many genes of interest in *E. coli* and other bacteria.[4] Its many advantages over alternative promoter systems include: non-leaky basal expression, titratable concentration-dependent expression and the ability to achieve higher levels of expression.[5] However, due to L-rhamnose metabolism and its auto-repression of the P_{rhaBAD} promoter,[6] induction is transient, which limits its application. This system could be improved by the development of a non-metabolizable analogue of L-rhamnose, an approach which has been developed for only a few other inducible expression systems.[7] No 6-deoxyhexose analogues have been tested for this purpose previously.

The chemotherapeutic potential of interfering with L-rhamnose metabolic pathways in bacteria and in plants has long been recognized, and is safe because L-rhamnose has no role in mammalian metabolism.[8] Synthetic inducers/antagonists of the rhamnose operon might also be useful as antimicrobials, targeting pathogens requiring rhamnose-incorporation into their cell walls for survival. Control or suppression of expression of the genes encoding rhamnose metabolic enzymes may allow control of biosynthesis of TDP-rhamnose and thus of cell wall construction of a number of pathogens.[9] For example, a rhamnose inducible promoter was reported to be essential to *Burkholderia cenocepacia*.[10] Other L-rhamnose metabolic enzymes, such as L-rhamnosidases and L-rhamnose isomerase, are also potential targets. Iminosugars affecting rhamnose processing enzymes may have potential as antibiotics.[11] The identification of synthetic inducers or antagonists of the L-rhamnose metabolic pathway will be valuable tools for biotechnology.



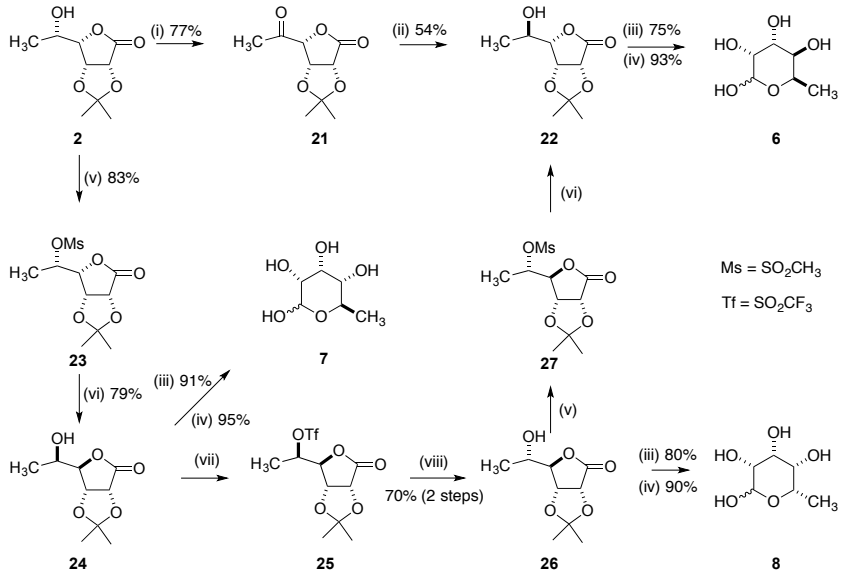
Scheme 1: Strategy for synthesis of rhamnose mimics

A recent study, which evaluated the effect of some 35 analogues of rhamnose on the operon, required access to 6-deoxyhexoses.[12] This paper describes the conversion of L-rhamnose **1**, the cheapest 6-deoxyhexose,[13] into 15 isomers and other analogues of rhamnose as free sugars by four different

strategies [Scheme 1]. Nucleophilic substitution of either pyranose or furanose derivatives of rhamnose[14] is easy neither to set up the precursor nor to perform S_N2 displacements of sulfonates. However efficient S_N2 reactions in rhamnonolactones can allow isomerization at C5, C4 and C2. The 2,3-acetonide of rhamnonolactone **2** is readily available from L-rhamnose in multigram scale by a well-established procedure. [15] Lactone **2** allows access to the 3 diastereomeric lactols **3**-**5** as intermediates in the synthesis of 6-deoxy-D-gulose **6**, 6-deoxy-D-allose **7** and 6-deoxy-L-talose **8** (strategy A). Unlike many lactone acetonides, **2** is not crystalline and is usually contaminated with the corresponding 3,5-acetonide. The highly crystalline benzylidene lactone **9,** with only C2 OH free, was prepared from L-rhamnose on a 50 g scale by a reported procedure (strategy B). [16] High yield nucleophilic substitution of the epimeric *manno*- **10** and *gluco*- **11** C2 triflates allowed the syntheses of the epimer at C2 L-quinovose **12**, the dideoxy hexose L-olivose **13** and both epimers of analogues with nitrogen introduced at C2 **14**; 2-nitrogen substituted analogues are also useful building blocks for the synthesis of bioactive glycoconjugates. [17] It was not possible to introduce fluorine at C2 by an S_N2 reaction; strategy C uses diacetyl rhamnal **15** for the non-stereoselective introduction of electrophilic fluorine to allow access to the 2-fluoro analogues of rhamnose **16** and quinovose **17**. It is not easy to access C3 of rhamnonolactone (or rhamnose) chemically; [18] however, a highly efficient biotechnological synthesis of the C3 epimer **18** allows the preparation of multigram quantities (strategy D). Rhamnose may also be converted to **19** where the anomeric hydroxyl group has been transposed from C1 to C5. Thus a combination of biotechnology and chemistry has allowed the preparation of some 15 analogues of rhamnose *as free sugars* for evaluation as inducers of the rhamnose operon.

SYNTHESIS

A Stereoisomers at C4 and C5 of rhamnose from 2,3-*O*-isopropylidene rhamnonolactone 2



Scheme 2: (i) Dess-Martin periodinane, CH_2Cl_2 (ii) $NaBH_4$, MeOH, rt (iii) DIBALH, CH_2Cl_2, -78 ^oC, (iv) DOWEX® 50WX8-100 (H^+ form), H_2O, rt (v) $MeSO_2Cl$, DMAP, pyridine, 0 ^oC (vi) KOH, H_2O:1,4-dioxane, rt (vii) $(CF_3SO_2)_2O$, pyridine, CH_2Cl_2 (viii) CF_3COONa, pentanone

The acetonide of rhamnonolactone **2** allowed easy access to three diastereomeric lactones at C4 and C5 **22**, **24** and **26** [Scheme 2]. There are very few examples of S_N2 reactions[19] at C5 of **2**. The difficulty probably arises from the extra steric hindrance because of the *cis*-relationship of the isopropylidene protecting group and the C4-side chain; S_N2 displacements at C5 of the C4-epimeric

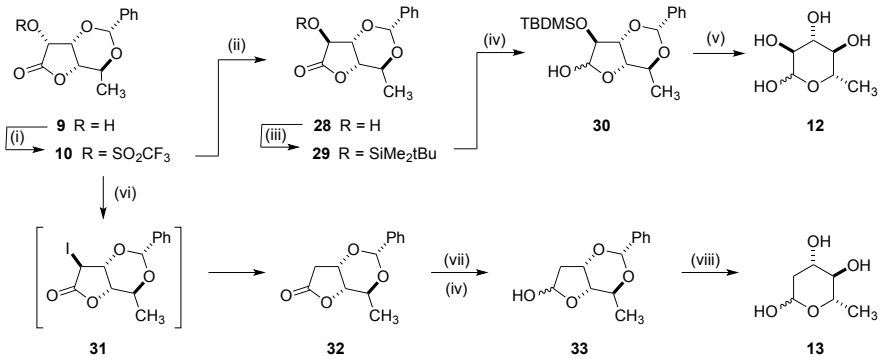
talono-lactone **24**, where there is a corresponding *trans* arrangement, are efficient.[20] All attempts to use oxygen nucleophiles [acetate or trifluoroacetate in DMF, butanone or pentanone] on either the mesylate **23** or the corresponding triflate gave no indication of the formation of the *gulo*-epimer **22**. Accordingly, inversion of configuration at C5 was achieved by Dess-Martin oxidation of **2** in dichloromethane to give the crystalline ketone **21** (77%). Reduction of **21** with sodium borohydride ar room temperature showed little diastereoselectivity to give crystalline **22**[21] (54%) and the D-*gulo*-lactone **2** in a 1.5:1 ratio. No improvement in the ratio was found at lower temperatures or use of cyanoborohydride and other conditions led to competitive reduction of the lactone; a similar lack diastereoselectivity has been found in analogous systems.[22] The two lactones **2** and **22** were readily separable by chromatography. Reduction of **22** with diisobutylaluminum hydride (DIBALH) in dichloromethane afforded the lactols **3** (75%). In the reduction of 2,3-protected lactones, no attempts were made to analyze the ratio of 2,3-*O*-isopropylidene pyranoses and furanoses formed. Acid ion exchange catalyzed hydrolysis of the lactols at room temperature gave 6-deoxy-D-gulose **6**[23], a syrup, (93%) predominantly as the β-pyranose form.

Esterification of the free alcohol in **2** with mesyl chloride in pyridine gave the mesylate **23** (83%); treatment of **23** with aqueous potassium hydroxide in 1,4-dioxane caused inversion of configuration at both C4 and C5 by Payne rearrangements[24] to form the D-*allono*-lactone **24** (79%). Nucleophilic displacement at C5 of the *allono*-lactone **24** where the side chain is *trans* to the isopropylidene protecting group was efficient. Thus reaction of **24** with triflic anhydride in dichloromethane in the presence of pyridine gave the corresponding triflate **25** which, with sodium trifluoroacetate in pentanone at room temperature followed by work-up with methanol,[25] gave the *talono*-lactone **26** in 70% yield. DMF is not an appropriate solvent since the solvent competes with trifluoroacetate as a nucleophile; the mesylate of **24** did not give S_N displacement by trifluoroacetate.

An identical two-step procedure for the reduction and hydrolysis of the protected *allono*- **24** and *talono*- **26** lactones gave 6-deoxy-D-allose **7**[26] and 6-deoxy-L-talose **8**[27], in overall yields of 83% and 72%, *via* the lactols **4** and **5** respectively.

For the rhamnose operon assays, it was very important to establish that there was no contamination of 6-deoxy-D-gulose **6** with rhamnose arising from incomplete separation of **2** and **22** in the reduction of ketone **21**. Accordingly, an alternative approach to 6-deoxy-gulonolactone **22** by a double inversion of C4 and C5 of the *talono*-lactone **26** was investigated. Sequential formation of the mesylate **27** from **26**, followed by treatment with aqueous potassium, hydroxide gave **22** in 76% which was identical to that prepared from the reduction of the ketone **21**. A sample of 6-deoxy-D-gulose **6** by this route gave an identical response in the rhamnose operon experiments to that derived from the ketone;[12] this established that there was no contamination with rhamnose in the synthesis *via* **21**.

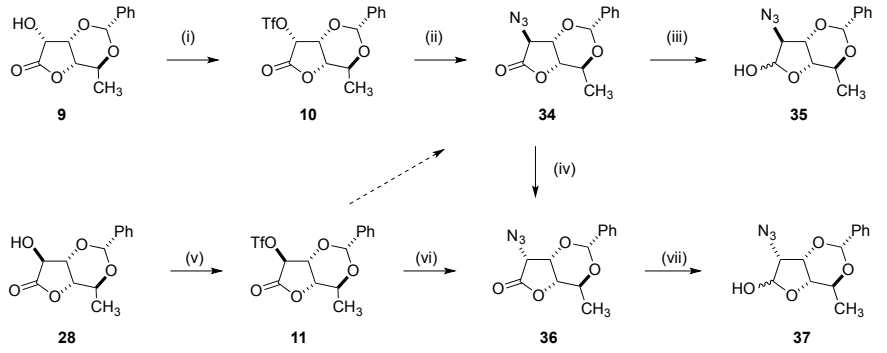
B 2-Substituted rhamnose analogues from 3,5-*O*-benzylidene rhamnonolactone 9



Scheme 3: (i) $(CF_3SO_2)_2O$, pyridine, THF, -20 ^oC, 95% (ii) CF_3COOCs, butanone, 60 ^oC, 4 h, 90% (iii) TBDMSCl, imidazole, DMF, 71% (iv) DIBALH, CH_2Cl_2, -78 ^oC, 1 h, 88% (v) DOWEX® 50WX8-200 (H^+ form), H_2O, rt, 15 h, 100% (vi) LiI:$3H_2O$, butanone, 60 ^oC, 16 h, 74% (vii) DIBALH, CH_2Cl_2, -78 ^oC, 3 h, 96% (viii) DOWEX® 50WX8-200 (H^+ form), H_2O, rt, 18 h, 100%

The highly crystalline benzylidene lactone **9** was directly obtained from rhamnose on a 50 g scale as previously described. [28] Esterification of the C2-OH group in **9** with triflic anhydride in THF afforded the triflate **10**[16] which is an ideal intermediate for S_N2 reactions at C2 of rhamnose. Although the crude triflate **10** may be used directly in subsequent reactions, **10** is a stable triflate which can be purified by column chromatography. For the preparation of L-quinovose [6-deoxy-L-glucose] **12**, reaction of **10** with cesium trifluoroacetate in butanone[29] gave the inverted alcohol **28**[16] (90%) [Scheme 3]. Attempts to reduce **28** directly gave complex mixtures but prior protection of **28** with TBDMS chloride in DMF in the presence of imidazole afforded the TBDMS ether **29** (71%); DIBALH reduction of the fully protected lactone **29** formed the protected lactols **30** (88%). Removal of the silyl and benzylidene protecting groups in **30** by ion exchange gave L-quinovose **12**[30] (100%) with an identical ^1H NMR spectrum to that of an authentic sample of D-quinovose [see SI].

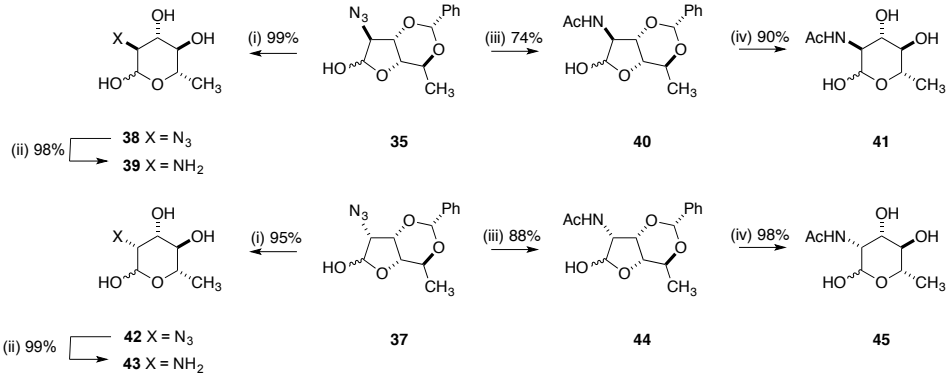
Treatment of the triflate **10** with lithium iodide hydrate in butanone gave the iodide **31** by rapid S_N2 displacement of the triflate which underwent further attack by iodide to give iodine[31] and the deoxygenated lactone **32** (74%). Reduction of **32** by DIBALH in dichloromethane afforded the lactols **33** (96%) which on hydrolysis by acid ion exchange resin gave L-olivose **13**[32] (100%).



Scheme 4: (i) $(CF_3SO_2)_2O$, pyridine, THF, -20 ^oC, 95% (ii) NaN_3, DMF, -40 ^oC, 75% (iii) DIBALH, CH_2Cl_2, -78 ^oC, 3 h, 84% (iv) see text 85% **36** from **10** (v) $(CF_3SO_2)_2O$, pyridine, THF, -20 ^oC (vi) NaN_3, DMF, -40 ^oC, 70% **36** and 24% **34** [over two steps] (vii) DIBALH, CH_2Cl_2, -78 ^oC, 3 h, 87%

In a number of cases it has been established that azide displacement of a triflate at C2 of a lactone may result in isolation of the azide with either retention or inversion of configuration. [25,33] For the preparation of C2 nitrogen derivatives of rhamnose and quinovose, high yield S_N2 substitution of the

triflate **10** with sodium azide in DMF gave the kinetic *gluco*-azide **34** with inversion or the thermodynamic *manno*-azide **36** with retention, respectively [Scheme 4]. Reaction of the stable triflate **10** with sodium azide in DMF at -40 °C formed the inverted *gluco*-azide **34** (75%). After column purification, the *gluco*-azide **34** was reduced by DIBALH in dichloromethane to the lactols **35** (84%). When the S_N2 reaction was conducted at room temperature, **10** formed the thermodynamic *manno*-azide **36** (85%). The initially formed **34** was converted to the more stable all *cis*-azide **36** under the reaction conditions. The two azides were readily distinguishable by TLC and easily separable by column chromatography. The triflate **11** derived from the *gluco*-alcohol **28** was less stable than the *manno*-triflate **10**. When crude triflate **11** in DMF was treated with sodium azide at -20 °C, the *manno*-azide **36** (70%) was isolated together with the less stable *gluco*-azide **34** (24%); there is competition between azide displacement to give **36** (70%) and epimerization of triflate **11** to the more stable triflate **10** which then forms the less stable azide **34** (24%). Reduction of **36** with DIBALH in dichloromethane gave the *manno*-lactols **37** (87%). After the reduction, there was no indication of any epimerization of the *gluco*- **35** to the *manno*- **37** lactols.

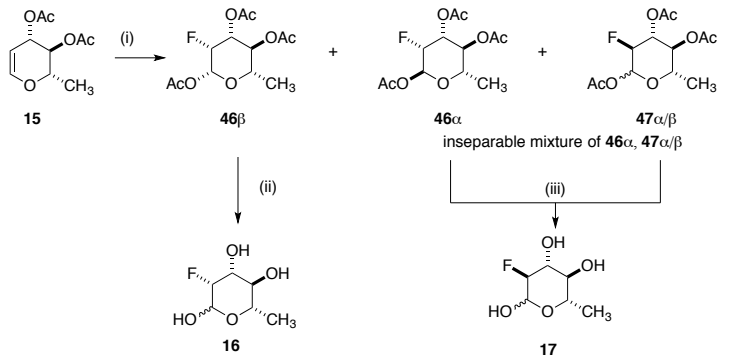


Scheme 5: (i) DOWEX® 50WX8-200 (H^+ form), H_2O, rt (ii) H_2, 10% Pd/C, HCl (iii) H_2, 10% Pd/C, Ac_2O, (iv) DOWEX® 50WX8-200 (H^+ form), H_2O

Hydrolysis of the protected *gluco*-lactols **35** by acid ion exchange resin gave the quinovose azide **38** (99%) [Scheme 5]. Hydrogenation of **38** in the presence of palladium on carbon and hydrochloride acid afforded the hydrochloride salt of 2-amino-2,6-dideoxy-L-glucose **39**[34] (98%). Hydrogenation of the azide **35** in the presence of acetic anhydride and palladium in ethyl acetate/1,4-dioxane gave the protected *gluco*-acetamide **40** (74%). Removal of the benzylidene acetal in **40** by DOWEX-catalysed hydrolysis in aqueous ethanol afforded acetamido-quinovose **41**[34] (90%). Identical procedures on the rhamno-azide **37** gave the azido- **42** (95%), amino- **43**[34] (100%) and acetamido- **45** (80% from **37**) rhamnose analogues in equally high yields.

C 2-Deoxy-2-fluoro-L-rhamnose 16 and 2-Deoxy-2-fluoro-L-quinovose 17 from 3,4-di-*O*-acetyl rhamnal

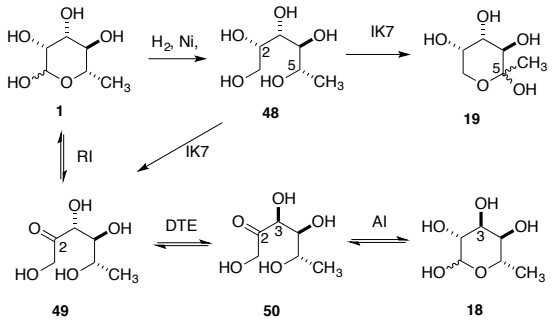
It was not possible either to displace the triflates in **10** by any of a number of nucleophilic sources of fluoride (including TASF, TBAF and CsF) or to introduce fluorine directly by reaction of the alcohol **9** with DAST[35] or Xtalfluor[36].



Scheme 6: (i) SelectFluor, water, MeCN; then Ac_2O in pyridine, 27% of pure **46β** (ii) CF_3COOH, H_2O, 100% (iii) CF_3COOH, H_2O, 100% (mixture of free sugars), then pure **17** was isolated by preparative HPLC

Accordingly, treatment of diacetylrhamnal **15** with SelectFluor in aqueous acetonitrile[37] followed by acetylation with acetic anhydride in pyridine during the workup caused electrophilic fluorination to give a mixture of the four sugar triacetates **46α/β** and **47** [Scheme 6] with little stereoselectivity. One of the 4 triacetates, the β-fluoro-rhamnose **46β**, was isolated as a pure crystalline solid. Hydrolysis of **46β** gave a pure sample of previously unknown 2-deoxy-2-fluoro-rhamnose **16** (27% overall yield) for biological evaluation. Hydrolysis of the mixture of **46α** and **47α/β** gave a mixture of fluoro-rhamnose **16** and fluoro-quinovose **17** (38% yield); a pure sample of fluoro-quinovose **17** was obtained by preparative HPLC.

D 1-Deoxy-L-fructose and 6-deoxy-L-altrose from rhamnose by biotechnology



Scheme 7: (i) H_2, Raney Ni, H_2O (ii) IK7 (iii) RI (iv) DTE (v) AI

The biotechnology of Izumoring[38] allows access to substantial amounts of rare deoxy sugars from rhamnose in water without the need for any protection. Hydrogenation of rhamnose **1** in the presence of Raney nickel gave L-rhamnitol **48** (96%) [Scheme 7]. Oxidation of the (*4S,5S*) diol in **48** by *Enterobacter aerogenes* IK7 (IK7) afforded 1-deoxy-L-fructose **19**; 37 g of **19** were obtained by direct crystallization of the crude oxidation product from 50 g of rhamnose **1**.[39] Longer times of the reaction of **48** with IK7 gave oxidation of the (*2S,3S*) diol to form rhamnulose [6-deoxy-L-fructose] **49** (10%);[41] **49** was also be obtained by L-rhamnose isomerase (RI) equilibration with **1**. [30] D-Tagatose-3-epimerase (DTE) equilibrates all C3 epimeric pairs of deoxyketoses[40] and equilibrated **49** at C3 to give 6-deoxy-L-psicose **50**.[41] Reaction of **50** with L-arabinose isomerase (AI) afforded 6-deoxy-L-altrose **18** allowing the ready preparation of 10 g of **18**.

NMR analysis of synthetic free 6-deoxy-hexoses

1. 6-Deoxy-D-gulose 6

Table 1: ^{1}H and ^{13}C NMR data of 6-deoxy-D-gulose **6** (D_2O), α-py:β-py = 1:10

		C1	C2	C3	C4	C5	C6
α pyranose	^{1}H /*J*	5.11[a]/3.0[b]	3.88/3.0/3.3	4.01/3.3/4.0	3.75/4.0/1.0	4.37/1.0/6.6	1.21/6.6
	^{13}C	91.9	63.8	70.0	70.6	61.5	13.8
β pyranose	^{1}H/*J*	4.85/8.3	3.57/8.3/3.2	4.07/3.2/3.2	3.62/3.2/0.6	4.10/0.6/6.5	1.22/6.5
	^{13}C	92.8	68.0	70.4	71.0	68.4	14.3

[a]: ppm; [b]: Hz.

The synthesis and characterization, but not the NMR analysis, of 6-deoxy-D-gulose **6** has been reported. [23] ^{1}H and ^{13}C NMR spectra of **6** in D_2O, pH=8.0, showed two spin-systems [Table 1], confirmed as pyranose forms by the HMBC correlations between C1 and H5 (D-gulose also exists mainly in the pyranose form[42]). The α and β pyranose anomers could be identified by the magnitude of coupling constant of anomeric proton ($J_{1,2}$ of β anomer was 8.3 Hz because of the *trans*-diaxial configuration; $J_{1,2}$ of α anomer was 3.0 Hz) and were present in an α-pyranose:β-pyranose ratio of 1:10.

2. 6-Deoxy-L-talose 8

Table 2: ^{1}H and ^{13}C NMR data of 6-deoxy-L-talose **8** (D_2O), α-py:β-py:α-fu:β-fu = 1.00:0.72:0.36:0.14

		C1	C2	C3	C4	C5	C6
α pyranose	^{1}H /*J*	5.21[a]/1.3[b]	3.80/1.3/3.2	3.91/3.2/3.2	3.74/3.2/1.0	4.17/1.0/6.7	1.24/6.7
	^{13}C	95.3	71.0	66.0	72.8	67.6	16.4
β pyranose	^{1}H/*J*	4.77/1.1	3.85/1.1/3.3	3.75/3.3/3.3	3.66/3.3/1.0	3.69/1.0/6.5	1.27/6.5
	^{13}C	94.6	71.8	69.3	71.7	71.9	16.2
α furanose	^{1}H /*J*	5.23/1.6	3.97/1.6/4.9	4.20/4.9/6.4	3.71/6.4/6.4	3.83/6.4/6.3	1.23/6.3
	^{13}C	101.3	76.0	71.7	86.4	69.5	18.7
β furanose	^{1}H /*J*	5.35/2.6/1.3	4.08/*na*[c]	4.08/*na*	3.90/*na*	3.84/*na*	1.22/6.4
	^{13}C	96.8	71.6	71.3	87.1	67.9	19.0

[a]: ppm; [b]: Hz; [c]: can not be assigned due to overlaps or weak signals.

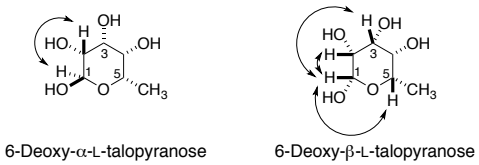


Figure 1: Key ROESY correlations of 6-deoxy-α-L-talopyranose and 6-deoxy-β-L-talopyranose

^{1}H and ^{13}C NMR spectra of 6-deoxy-L-talose **8** in D_2O, pH=7.8, showed four spin-systems [Table 2], confirmed as the pyranose and furanose forms by the HMBC correlations between C1 and H5 (pyranose) and H4 (furanose). The α- and β-anomers of the pyranose forms of **8** were identified from the ROESY spectra, the H1 of the β-anomer showing strong correlations with H3 and H5 whereas the H1 of the α-anomer only showed a strong correlation with H2 [Figure 1]. The furanose forms were more difficult to analyze. The β-anomer was tentatively assigned on the basis of a stronger H1 to H2 ROESY correlation (SI). In addition, the ^{13}C data in this study agree with a previous report. [43]

3. 6-Deoxy-D-allose 7

Table 3: ^{1}H and ^{13}C NMR data of 6-deoxy-D-allose **7** (D_2O), α-py:β-py:α-fu:β-fu = 0.11:1.00:0.03:0.04

		C1	C2	C3	C4	C5	C6

α pyranose	^{1}H /*J*	5.08[a]/3.4[b]	3.70/3.4/3.4	4.12/*na*[c]	3.36/*na*	4.04/9.4/6.4	1.26/6.4
	^{13}C	93.4	68.0	72.1	72.3	63.5	17.2
β pyranose	^{1}H/*J*	4.85/8.3	3.40/8.3/3.0	4.12/3.0/2.8	3.36/2.8/9.8	3.82/9.8/6.3	1.24/6.3
	^{13}C	93.9	72.1	71.7	72.9	70.1	17.6
α furanose	^{1}H /*J*	5.35/4.2	4.04/*na*	4.16/5.9/3.9	4.00/3.9/3.8	3.93/*na*	1.20/6.7
	^{13}C	96.6	71.8	69.4	87.8	67.6	17.9
β furanose	^{1}H /*J*	5.22/2.3	3.94/*na*	4.30/5.2/5.2	3.82/*na*	3.93/*na*	1.22/6.7
	^{13}C	101.1	76.1	70.7	86.3	68.1	17.9

[a]: ppm; [b]: Hz; [c]: can not be assigned due to overlaps or weak signals.

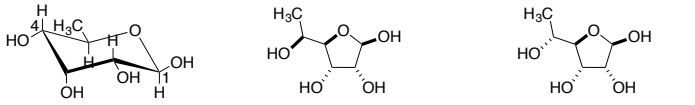


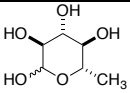
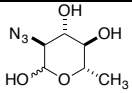
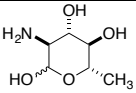
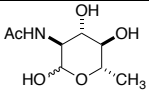
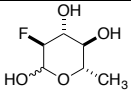
Figure 2: 6-Deoxy-β-D-allopyranose in a $^{4}C_{1}$ conformation and 6-deoxy-α-L-talofuranose and 6-deoxy-β-D-allofuranose

The NMR data of 6-deoxy-β-D-allopyranose has been previously reported although in a different solvent. [44] ^{1}H and ^{13}C NMR spectra of 6-deoxy-D-allose **7** in D_2O, pH=6.1, showed four spin-systems [Table 3], confirmed as the pyranose and furanose forms by the HMBC correlations between H1 and C5 (pyranose) and C4 (furanose) (SI). The β-anomer of the pyranose forms was identified by the large *trans*-diaxial coupling between H1 and H2 and a strong ROESY correlation between H1 and H5 [Figure 2] The analysis of furanose forms was more difficult. The β-anomer was tentatively assigned on the basis of a weak H1 to H4 ROESY correlation, not observed for the α-anomer.

Since 6-deoxy-β-D-allofuranose has an identical ring conformation to 6-deoxy-α-L-talofuranose (they only differ by the configuration at C5) [Figure 2], the NMR parameters of the α- and β-furanose forms of **7** should be very similar to the β- and α-furanose forms **8** respectively. This provides additional support for the assignment of the furanose α- and β-anomers in **7** and **8**.

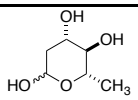
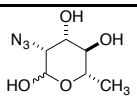
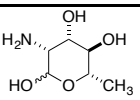
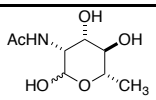
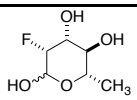
4 L-*gluco*-analogues and L-*manno*-analogues

Table 4: NMR comparison of anomeric protons of L-*gluco*-analogues

	L-*gluco*-series				
					
	12	**38**	**39**	**41**	**17**
H1α/$J_{1,2}$	5.10[a]/3.8[b]	5.29/3.7	5.38/3.5	5.06/3.5	5.38/4.0
C1α	93.2	91.6	89.5	91.0	89.7
H1β/$J_{1,2}$	4.55/7.9	4.67/8.1	4.91/8.4	4.59/8.5	4.87/7.9
C1β	96.9	95.5	93.1	95.4	92.5

[a]: ppm; [b]: Hz.

Table 5: NMR comparison of anomeric protons of L-*manno*-analogues

	L-*manno*-series				
					
	13	**42**	**43**	**45**	**16**
H1α/$J_{1,2}$	5.31[a]/3.7[b]	5.20/1.1	5.32/1.2	4.85/1.1	5.30/1.8
$J_{1,2}$,	1.0	*na*[c]	*na*	*na*	*na*
C1α	91.7	92.7	90.8	94.8	91.8
H1β/$J_{1,2}$	4.91/9.8	5.01/1.1	5.17/1.5	4.72/1.5	4.98/0
$J_{1,2}$,	2.0	*na*	*na*	*na*	*na*
C1β	93.8	93.4	91.3	95.0	92.7

[a]: ppm; [b]: Hz; [c]: not available.

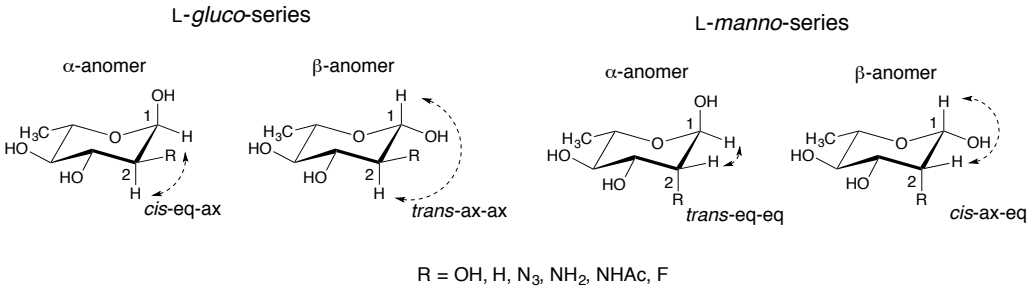


Figure 3: Conformations of 2-substituted L-quinovose and L-rhamnose

The ten L-*gluco*-series and L-*manno*-series targets synthesized from benzylidene protected L-rhamnonolactone **9**, have similar NMR spectra to those of glucose and mannose. [45]

Table 5: NMR comparison of anomeric protons of L-manno-analogues and **错误! 未找到引用源。** show the anomeric ^{1}H, ^{13}C shifts and their coupling constants, in D_2O. The pyranose forms were the predominant (>95% NMR ratio) in all analogues as judged by the intensities of the ^{13}C NMR peaks in the region associated with pyranose forms (δ = 93 – 97 ppm) compared to the intensities in the region associated with furanose forms (whose anomeric carbons are generally at lower field). In the L-*gluco*-series (**12**, **38**, **39**, **41, 17)** and L-olivose **13**, the ^{1}H NMR peaks of β-anomeric protons were showed larger coupling constants ($J_{1,2}$ = 8 - 9 Hz) than their α counterparts ($J_{1,2}$ = 3 - 4 Hz) because of the *trans*-diaxial configuration [Figure 3]. In contrast, in the L-*manno*-series, the magnitude of the coupling constants of anomeric protons were similar due to the *trans*-diequatorial or *cis*-equatorial-axial configurations ($J_{1,2}$ = 0 - 2 Hz) [Figure 3], while the ^{1}H peaks of α-anomers were in lower field than their β counterparts, which was consistent with NMR data of L-rhamnose. [45c]

CONCLUSION

This paper describes the efficient production of 15 6-deoxy-sugars from L-rhamnose by a synergy of chemical synthesis and biotechnology as part of a project to find alternative non-metabolizable inducers to rhamnose for the L-rhamnose operon. Several inducers with different activities were identified: 1-deoxy-L-fructose **19** and 6-deoxy-L-altrose **18** were weak inducers; L-olivose **13** and 6-deoxy-2-fluoro-L-rhamnose **16** were moderate inducers. Further studies explored their induction kinetics and confirmed L-olivose **13**, 6-deoxy-2-fluoro-L-rhamnose **16** and 6-deoxy-L-altrose **18** were

poorly metabolized in *E. coli.* and gave sustained induction.[12] Such inducers with different strength could be used for different purposes e.g. production of toxic protein, production of certain protein in constant rate. Rhamnonolactones have rarely been used as chirons[46] but are ideal intermediates for the chemical modification of rhamnose. Full NMR characterization of several 6-deoxyhexoses has been provided for the first time.

EXPERIMENTAL SECTION

General Experimental

All commercial reagents were used as supplied. Solvents were used as supplied (Analytical or HPLC grade), without prior purification. Thin layer chromatography (TLC) was performed on aluminium sheets coated with 60 F_{254} silica. Plates were visualised using a 0.2% w/v cerium (IV) sulfate and 5% ammonium molybdate solution in 2 M sulfuric acid. Melting points were recorded on a Kofler hot block and are uncorrected. Optical rotations of the protected sugars were recorded on a Perkin-Elmer 241 polarimeter with a path length of 1 dm; concentrations are quoted in g 100 mL^{-1}. Optical rotations were recorded on a Jasco R1030 polarimeter, Na^+ lamp, (Jasco, Tokyo, Japan) at 20 °C, polarimeter with a path length of 1 dm. Infrared spectra were recorded on a Perkin-Elmer 1750 IR Fourier Transform spectrophotometer using thin films on a diamond ATR surface (thin film). Only the characteristic peaks are quoted. Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker AMX 500 (^{1}H: 500 MHz and ^{13}C: 125.7 MHz) or Bruker AVIII 400 HD nanobay and Bruker DQX 400 (^{1}H: 400 MHz, ^{13}C: 100.6 MHz and ^{19}F: 375 MHz) or Bruker DPX 250 (^{1}H: 250 MHz and ^{13}C: 62.5 MHz) or Varian Mercury 300 (^{1}H: 300 MHz, ^{13}C: 75 MHz) spectrometers in the deuterated solvent stated. ^{1}H and ^{13}C NMR spectra were assigned by utilizing 2D COSY, HSQC and HMBC spectra. All chemical shifts (δ) are quoted in ppm and coupling constants (*J*) in Hz. Residual signals from the solvents were used as an internal reference. For solutions in D_2O acetonitrile was used as an internal reference. HRMS measurements were made using a microTOF mass analyzer using electrospray ionization (ESI) or an HP 5988A mass spectrometer using chemical ionization (CI). Commercial sample of 6-deoxy-D-glucose was kindly provided by Carbosynth Limit.

A. Stereoisomers at C4 and C5 of rhamnose from 2,3-*O*-isopropylidene rhamnonolactone 2

2,3-*O*-Isopropylidene-L-rhamnono-1,4-lactone 2

Concentrated sulphuric acid (0.3 mL) was added to a suspension of anhydrous copper sulphate (25 g) in a solution of L-rhamnono-1,4-lactone (5.29 g, 32.65 mmol) in acetone (400 mL) and the mixture was stirred at rt overnight. TLC analysis (methanol/ethyl acetate, 1:9) showed the consumption of the starting material (R_f 0.4) and the formation of one product (R_f 0.7). The reaction mixture was neutralized with potassium carbonate (8 g) and filtered through Celite®, which was washed with acetone (2 x 25 mL). The liquids were removed *in vacuo* and the resulting crude solid was purified by flash column chromatography (ethyl acetate/ hexane, 1:1) to give the acetonide **2** (4.56 g, 69%) as a colourless oil.

$[\alpha]_D^{20}$ = -47.8 (*c* = 2.7 in $CHCl_3$) {lit.[15a] $[\alpha]_D^{23}$ = -28 (*c* = 1.2 in Me_2CO)}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 4.94 (dd, $J_{3,2}$ 5.5 Hz, $J_{3,4}$ 3.6 Hz, 1H; H3), 4.82 (br-d, $J_{2,3}$ 5.5 Hz, 1H; H2), 4.16 (dd, $J_{4,5}$ = 8.3 Hz, $J_{4,3}$ = 3.6 Hz, 1H; H4), 4.09 (dq, $J_{5,4}$ = 8.3 Hz, $J_{5,6}$ = 6.3 Hz, 1H; H5), 2.33 (br-s, 1H; OH), 1.46 (s, 3H; CH_3), 1.39 (s, 3H; CH_3), 1.37 (d, $J_{6,5}$ = 6.3 Hz, 3H; H6); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 173.9 (C=O), 114.5 ($\underline{C}(CH_3)_2$), 82.0 (C4), 76.3 (C2), 76.2 (C3), 65.8 (C5), 26.8 (CH_3), 26.0 (CH_3), 20.3 (C6); IR (thin film): ν_{max} = 3465 (OH), 1784 (C=O); *m/z* (CI+ve): 203.2 ($[M+H]^+$, 85%), 187.1 ($[M-CH_3]^+$, 100%); HRMS *m/z* (CI+ve): found 203.0929 $[M+H]^+$; $C_9H_{15}O_5^+$ requires 203.0919;.

6–Deoxy-2,3-*O*-isopropylidene-L-*lyxo*-hex-5-ulosono-1,4-lactone 21

Dess-Martin periodinane (3.00 g, 6.80 mmol) was added in three portions to a solution of the alcohol **2** (1.10 g, 5.44 mmol) in dichloromethane (26 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 2 h, after which TLC analysis (diethyl ether) revealed the absence of starting material (R_f 0.6) and the formation of one major product (R_f 0.8). The reaction mixture was filtered through Celite®, which was washed with dichloromethane (2 x 10 mL), and the liquids were concentrated *in vacuo*. The residue was then dissolved in dichloromethane (30 mL) and washed with sodium thiosulfate (sat. aq., 15 mL) and brine (15 mL). The organic layer was dried (anhydr. Na_2SO_4) and concentrated *in vacuo;* the residue was purified by flash column chromatography (ethyl acetate/hexane, 1:1) affording the ketone **21** (0.85 g, 77%) as a white solid.

m.p.: 142-144 ºC; {lit.[11b] m.p.: 124-125 ºC} $[\alpha]_D^{20}$ = +3.5 (*c* = 2.2 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.08 (dd, $J_{3,4}$ = 4.9 Hz, $J_{3,2}$ = 4.4 Hz, 1H; H3), 4.87 (d, $J_{3,4}$ = 4.9 Hz, 1H; H4), 4.83 (d, $J_{2,3}$ = 4.4 Hz, 1H; H2), 2.28 (s, 3H; H6), 1.43 (s, 3H; CH_3), 1.35 (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.4 (C=O), 173.1 (C=O), 114.9 ($\underline{C}(CH_3)_2$), 81.6 (C4), 77.5 (C2), 75.7 (C3), 27.8 (C6), 26.7 (CH_3), 25.8 (CH_3); IR (thin film): ν_{max} = 1789 (C=O), 1724 (C=O); *m/z* (CI+ve): 223.0 ([M+Na]$^+$, 100%); HRMS (ESI+ve) found 223.0571 [M+Na]$^+$; $C_9H_{12}NaO_5^+$ requires 223.0577.

6-Deoxy-2,3-*O*-isopropylidene-D-gulono-1,4-lactone 22 (from ketone 21)

Sodium borohydride (0.015 g, 0.40 mmol) was added in two portions to a solution of the ketone **21** (0.230 g, 1.15 mmol) in methanol (1.2 mL). The reaction mixture was stirred at rt for 15 min, when TLC analysis (diethyl ether) revealed the transformation of the starting material (R_f 0.8) into one major product (R_f 0.6). Ammonium chloride (sat. aq., 3 mL) was added and the mixture was extracted with ethyl acetate (5 x 5 mL). ^{1}H-NMR analysis of the crude mixture showed an approximate 1.5:1 ratio of the major products, the D-gulono- **22** and L-rhamnono-1,4-lactone **2** derivatives. Flash column chromatography of the mixture (ethyl acetate/hexane, 1:1) yielded lactone **22** (R_f 0.6) as a white solid (0.126 g, 54%).

m.p.: 183-185 ºC; $[\alpha]_D^{20}$ = -82.0 (*c* = 0.4 in $CHCl_3$) {lit.[21] m.p.: 142-144 ºC; $[\alpha]_D^{20}$ -64.1 (*c* = 1.2 in EtOH)}; ^{1}H NMR (250 MHz, CD_3OD): δ = 4.98 (d, $J_{2,3}$ 5.5 Hz, 1H; H2), 4.86 - 4.80 (m, 1H; H3), 4.32 (dd, $J_{4,5}$ 8.8 Hz, $J_{4,3}$ 3.8 Hz, 1H; H4), 4.01-4.10 (m, 1H; H5), 1.44 (s, 3H; CH_3), 1.41 (s, 3H; CH_3), 1.31 (d, $J_{6,5}$ 6.4 Hz, 3H; H6); ^{13}C NMR (62.5 MHz, CD_3OD): δ = 176.5 (C=O), 114.8 ($\underline{C}(CH_3)_2$), 85.4 (C4), 78.3 (C2), 78.1 (C3), 67.5 (C5), 27.1 (CH_3), 26.0 (CH_3), 18.4 (C6); IR (thin film): ν_{max} = 3421 (OH), 1774 (C=O); *m/z* (CI+ve): 203.2 ([M+H]$^+$, 80%), 187.2 ([M-CH_3], 100%); HRMS *m/z* (CI+ve): found 203.0918 [M+H]$^+$; $C_9H_{15}O_5^+$ requires 203.0919.

6-Deoxy-2,3-*O*-isopropylidene-D-gulose 3

Diisobutylaluminium hydride (25 % wt. in toluene, 1.17 mL, 2.04 mmol) was added dropwise to a solution of 6-deoxy-2,3-*O*-isopropylidene-D-gulono-1,4-lactone **22** (0.165 g, 0.82 mmol) in anhydrous DCM (2.4 mL) at -78 °C. The reaction mixture was stirred at -78 °C for 30 min, until TLC (hexane/ethyl acetate, 1:1) indicated the formation of one major product (R_f 0.2). The reaction mixture was quenched with methanol and allowed to warm to rt. Ethyl acetate (2 mL), potassium dihydrogen orthophosphate (2 g) and sodium hydrogen carbonate (sat. aq., 2 mL) were added and the mixture was stirred for 10 min. The mixture was dried (anhydr. Na_2SO_4), filtered through Celite®, the solids were washed with ethyl acetate (3 x 10 mL) and the liquids were concentrated *in vacuo*. Flash column chromatography (hexane/ethyl acetate, 1:1) of the residue provided 6-deoxy-2,3-*O*-isopropylidene-D-gulose, **3** as a white solid (0.12 g, 75%).

$[\alpha]_D^{20}$ = -37.8 (*c* = 4.8 in $CHCl_3$); Major component: ^{1}H NMR (250 MHz, CD_3OD): δ = 5.30 (s, 1H; H1), 4.78 (d, $J_{2,3}$ = 5.9 Hz, 1H; H2), 4.59 (a-d, $J_{3,2}$ = 5.9 Hz, 1H; H3), 3.98 (m, 1H; H5), 3.92 (dd, $J_{4,5}$

= 8.3 Hz, $J_{4,3}$ = 3.5 Hz, 1H; H4), 1.46 (s, 3H; CH_3), 1.35 (s, 3H; CH_3), 1.30 (d, $J_{6,5}$ = 6.3 Hz, 3H; H6); ^{13}C NMR (62.5 MHz, CD_3OD): δ = 113.4 ($\underline{C}(CH_3)_2$), 102.0 (C1), 87.5 (C2), 85.7 (C4), 81.3 (C3), 67.7 (C5), 26.4 (CH_3), 24.9 (CH_3), 19.3 (C6); IR (thin film): ν_{max} = 3420 (OH); *m/z* (CI+ve): 205.2 ($[M+H]^+$, 30%), 187.2 ($[M-OH]^+$, 100%); HRMS *m/z* (CI+ve): found 205.1071 $[M+H]^+$; $C_9H_{17}O_5^+$ requires 205.1076.

6-Deoxy-D-gulose 6

DOWEX® 50WX8-100 (H^+ form) (0.07 g) was added into a solution of the lactols **3** (0.074 g, 0.36 mmol) in water (2 mL); after stirring at rt for 24 h, TLC analysis (hexane/ethyl acetate, 1:1.5) indicated the absence of the starting material (R_f 0.5) and the formation of one polar major product (R_f 0.0). The resin was filtered and washed with water (2 x 2 mL), the liquids were concentrated *in vacuo* and the residue was purified by column chromatography (methanol/dichloromethane, 1:6), to obtain a 10:1 mixture of β- and α- anomers of 6-deoxy-D-gulopyranose, **6** respectively (0.055 g, 93%), as a syrup.

$[\alpha]_D^{20}$ = -20.3 (*c* = 0.6 in H_2O) {lit. [23] $[\alpha]_D^{20}$ = -39 (*c* = 2.0 in H_2O)}; ^{1}H NMR (400 MHz, CD_3OD): δ = 5.11 (d, $J_{1,2}$ = 3.0 Hz, 1H; H1α), 4.85 (d, $J_{1,2}$ = 8.3 Hz, 1H; H1β), 4.37 (dq, $J_{5,4}$ = 1.0 Hz, $J_{5,6}$ = 6.6 Hz, 1H; H5α), 4.10 (dq, $J_{5,4}$ = 0.6 Hz, $J_{5,6}$ = 6.5 Hz, 1H; H5β), 4.07 (t, $J_{3,4}$ = $J_{3,2}$ = 3.2 Hz, 1H; H3β), 4.01 (dd, $J_{3,2}$ = 3.3 Hz, $J_{3,4}$ = 4.0 Hz, 1H; H3α), 3.88 (dd, $J_{2,3}$ = 3.0 Hz, $J_{2,1}$ = 3.3 Hz, 1H; H2α), 3.75 (dd, $J_{4,5}$ = 1.0 Hz, $J_{4,3}$ = 4.0 Hz, 1H; H4α), 3.62 (dd, $J_{4,5}$ = 0.6 Hz, $J_{4,3}$ = 3.2 Hz, 1H; H4β), 3.57 (dd, $J_{2,3}$ = 3.2 Hz, $J_{2,1}$ = 8.3 Hz, 1H; H2β), 1.22 (d, $J_{6,5}$ = 6.5 Hz, 3H; H6β), 1.21 (d, $J_{6,5}$ = 6.6 Hz, 3H; H6α); 13C NMR (100 MHz, D_2O): δ = 92.8 (C1β), 91.9 (C1α), 71.0 (C4β), 70.6 (C4α), 70.4 (C3β), 70.0 (C3α), 68.4 (C5β), 68.0 (C2β), 63.8 (C2α), 61.5 (C5α), 14.3 (C6β), 13.8 (C6α); IR (thin film): ν_{max} = 3367 (OH); *m/z* (CI+ve): 165.1 ($[M+H]^+$, 3%), 147.1 ($[M-OH]^+$, 100%); HRMS *m/z* (CI+ve): found 165.0768 $[M+H]^+$; $C_6H_{13}O_5^+$ requires 165.0763.

6-Deoxy-2,3-*O*-isopropylidene-D-allono-1,4-lactone 24

Methanesulfonyl chloride (2.97 mL, 38.33 mmol) and *N*,*N*-dimethylaminopyridine (0.37 g, 3.07 mmol) were added under argon to a solution of the protected lactone **2** (6.20 g, 30.66 mmol) in anhydrous pyridine (30 mL) at 0 °C. The reaction mixture was stirred at 0 ºC for 3 h, after which TLC analysis (hexane/ethyl acetate, 1:1.5, 2 runs) indicated the consumption of the starting material (R_f 0.3) and the formation of one major product (R_f 0.4). The mixture was concentrated *in vacuo* and co-evaporated with toluene (3 x 20 mL) and the residue was dissolved in dichloromethane (60 mL) and washed with water (40 mL) and with brine (40 mL). The organic layer was dried (anhydr. Na_2SO_4) and concentrated *in vacuo*, and the residue was purified by flash column chromatography (ethyl acetate/hexane, 1:1.3) affording the mesylate **23** (7.13 g, 83 %) as a white solid.

$[\alpha]_D^{20}$ = -39.5 (*c* = 1.9 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.98 (dq, $J_{5,6}$ = 6.6 Hz, $J_{5,4}$ = 7.7 Hz, 1H; H5), 4.85-4.90 (m, 2H; H2, H3), 4.42 (dd, $J_{4,3}$ = 2.7 Hz, $J_{4,5}$ = 7.7 Hz, 1H; H4), 3.06 (s, 3H; CH_3-SO_3), 1.60 (d, $J_{6,5}$ = 6.6 Hz, 1H; H6), 1.48 (s, 3H; CH_3), 1.39 (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.9 (C=O), 114.7 ($\underline{C}(CH_3)_2$), 79.1 (C4), 76.2 (C2), 75.4 (C3, C5), 38.7 (CH_3-SO_3), 26.9 (CH_3), 26.0 (CH_3), 18.9 (C6); IR (thin film): ν_{max} = 1774 (C=O); *m/z* (CI+ve): 281.4 ($[M+H]^+$, 53%), 157.3 ($[M-C_3H_7O_3S]^+$, 100%); HRMS *m/z* (CI+ve): found 303.0509 $[M+Na]^+$; $C_{10}H_{16}O_7S^+$ requires 303.0508.

A solution of mesylate **23** in 1,4-dioxane (113 mL) and aqueous potassium hydroxide (0.85 M, 90 mL, 76.3 mmol) was stirred at rt overnight. The reaction mixture was acidified to pH 1 with hydrochloric acid (2 M, aq.) and extracted with ethyl acetate (6 x 100 mL). TLC analysis (hexane/ethyl acetate, 1:1) indicated the transformation of the starting material (R_f 0.3) into a mixture of lactone **24** (minor component, R_f 0.3) and base line material (major component, R_f 0.0). The pooled organic extracts

were stirred in presence of anhydrous Na_2SO_4 at rt overnight in order to complete the lactonization to **24**. The solids were filtered off and the reaction mixture concentrated *in vacuo*. Flash column chromatography (diethyl ether/hexane, 2.5:1) of the residue afforded the *allono*-lactone **24** (4.07 g, 79 %; 66% over two steps) as white solid.
m.p.: 165-167 ºC; $[\alpha]_D^{20}$ = -62.1 (*c* = 3.2 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.78 (d, $J_{2,3}$ = 2.2 Hz, 1H; H2), 4.76 (d, $J_{3,2}$ = 2.2 Hz, 1H; H3), 4.38 (d, $J_{4,5}$ = 2.2 Hz, 1H; H4), 4.10 (dq, $J_{5,6}$ = 6.7 Hz, $J_{5,4}$ = 2.2 Hz, 1H; H5), 3.36 (br-s, 1H; OH), 1.42 (s, 3H; CH_3), 1.34 (s, 3H; CH_3), 1.27 (d, $J_{6,5}$ = 6.3 Hz, 3H; H6); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.2 (C=O), 113.1 ($\underline{C}(CH_3)_2$), 86.6 (C4), 75.8 (C2), 75.7 (C3), 66.6 (C5), 26.7 (CH_3), 25.4 (CH_3), 18.4 (C6); IR (thin film): ν_{max} = 3432 (OH), 1788 (C=O); *m/z* (CI+ve): 203.2 ($[M+H]^+$, 68%), 187.2 ($[M-CH_3]^+$, 100%); HRMS *m/z* (CI+ve): found 203.0918 $[M+H]^+$; $C_9H_{15}O_5^+$ requires 203.0913.

6-Deoxy-2,3-*O*-isopropylidene-L-talono-1,4-lactone 26
Triflic anhydride (0.6 mL, 3.56 mmol) was added dropwise to a solution of the *gulono*-lactone (0.6 g, 2.97 mmol) and anhydrous pyridine (0.72 mL, 8.91 mmol) in anhydrous dichloromethane (20 mL) at -30 °C. The reaction mixture was stirred between -30 and -10 °C for 1 h, after which TLC (hexane/ethyl acetate, 1:1) showed the consumption of the starting material (R_f 0.3) and the formation of one major product (R_f 0.6). The reaction mixture was diluted with DCM (30 mL) and washed with hydrochloric acid (1 M, aq. 10 mL). The organic layer was dried (anhydrous Na_2SO_4), filtered and the solvent removed *in vacuo* affording triflate **25** (1.10 g) as white solid.
A solution of the crude triflate **25** and sodium trifluoroacetate (1.21 g, 8.91 mmol) in pentanone (10 mL) was stirred at rt for 2 h, when TLC analysis (hexane/ethyl acetate, 1:1) showed the transformation of the starting material (R_f 0.6) into a mixture of its trifluoroacetate derivative (R_f 0.5) and **26** (R_f 0.3). Methanol (10 mL) was added and the reaction mixture was stirred at rt for 6 h, until TLC analysis (hexane/ethyl acetate, 1:1) showed the total transformation of the major component into the reaction product **26** (R_f 0.3). The reaction mixture was concentrated *in vacuo*, and the residue was dissolved in ethyl acetate (10 mL) and washed with water (3 x 5 mL). The organic layer was dried (anhydr. Na_2SO_4), filtered and concentrated in *vacuo*. Flash column chromatography (ethyl acetate/hexane, 1:1) of the residue afforded the *talono*-lactone **26** (0.42 g, 70%) as a white solid.
m.p.: 58-61ºC; $[\alpha]_D^{20}$ = -26.6 (*c* = 3.1 in $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 4.80 (d, $J_{2,3}$ = 5.6 Hz, 1H; H2), 4.73 (d, $J_{3,2}$ = 5.6 Hz, 1H; H3), 4.41 (d, $J_{4,5}$ = 1.5 Hz, 1H; H4), 4.01 (dq, $J_{5,6}$ = 6.5 Hz, $J_{5,4}$ = 1.5 Hz, 1H; H5), 2.45 (br-s, 1H; OH), 1.44 (s, 3H; CH_3), 1.36 (s, 3H; CH_3), 1.35 (d, $J_{6,5}$ = 6.5 Hz, 3H; H6); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 175.5 (C=O), 113.1 ($\underline{C}(CH_3)_2$), 85.8 (C4), 78.9 (C2), 75.2 (C3), 67.5 (C5), 26.8 (CH_3), 25.5 (CH_3), 19.4 (C6); IR (thin film): ν_{max} = 3436 (OH), 1773 (C=O); *m/z* (CI+ve): 203.2 ($[M+H]^+$, 70%), 187.2 ($[M-CH_3]^+$, 100%); HRMS *m/z* (CI+ve): found 203.0934 $[M+H]^+$; $C_9H_{15}O_5^+$ requires 203.0929.

6-Deoxy-2,3-O-isopropylidene-α-D-allose 4
Diisobutylaluminum hydride (25 % wt in toluene, 0.64 mL, 1.12 mmol) was added dropwise to a solution of the *allono*-lactone **24** (0.09 g, 0.45 mmol) in anhydrous dichloromethane (0.70 mL) at -78 °C. The reaction mixture was stirred at -78 °C for 30 min until TLC (hexane/ethyl acetate 1:1) indicated the comsumption of the starting material (R_f 0.4) and formation of one major product (R_f 0.3). The reaction was quenched with methanol and allowed to warm to rt. Ethyl acetate (2 mL), potassium dihydrogen orthophosphate (2 g) and sodium hydrogen carbonate (sat. aq., 2 mL) were added and the mixture was stirred for 10 min. The mixture was dried (anhydrous Na_2SO_4), filtered through Celite®. The solids were washed with ethyl acetate (3 x 10 mL) and the liquids were concentrated *in vacuo*. Flash column chromatography (ethyl acetate/hexane, 1:1) of the crude afforded the lactols **4** (0.55 g, 91%) as a pale yellow oil.

$[\alpha]_D^{20}$ = -41.0 (*c* = 0.7 in $CHCl_3$); Major component: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.40 (s, 1H; H1), 4.87 (d, $J_{2,3}$ = 5.9 Hz, 1H; H2), 4.56 (d, $J_{3,2}$ = 5.9 Hz, 1H; H3), 4.15 (br-s, 1H; OH), 3.91-4.02 (m, 2H; H4, H5), 1.48 (s, 3H; CH_3), 1.32 (s, 3H; CH_3), 1.25 (d, $J_{6,5}$ = 6.6 Hz, 3H; H6); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 111.9 ($\underline{C}(CH_3)_2$), 102.1 (C1), 91.5 (C2), 86.5 (C4), 79.3 (C3), 67.9 (C5), 26.1 (CH_3), 24.5 (CH_3), 18.3 (C6); IR (thin film): ν_{max} = 3371 (OH); *m/z* (CI+ve): 205.2 ($[M+H]^+$, 68%), 187.2 ([M-OH]$^+$, 100%); HRMS *m/z* (CI+ve): found 205.1078 $[M+H]^+$; $C_9H_{17}O_5^+$ requires 205.1076.

6-Deoxy-D-allose 7

DOWEX® 50WX8-100 (H^+ form) (0.3 g) was added to a solution of crude 6-deoxy-2,3-O-isopropylidene-D-allofuranose **4** (0.3 g, 1.47 mmol) in water (8.5 mL). After stirring at rt for 24 h, TLC analysis (ethyl acetate) indicated the absence of the starting material (R_f 0.8) and the formation of one polar major product (R_f 0.0). The resin was filtered and washed with water (2 x 8 mL), the liquids were concentrated *in vacuo* and the residue was purified by column chromatography (methanol/dichloromethane, 1:6) to obtain 6-deoxy-D-allose **7** (0.23 g, 95%), as a white solid.

m.p.: 144-146 ºC (methanol/dichloromethane), {lit.[26] 151-152 ºC}, $[\alpha]_D^{20}$ (initial) = -7.0 (*c* = 0.33 in H_2O), $[\alpha]_D^{20}$ (eqm. after 30 min) = +2.0 (*c* = 0.33 in H_2O); ^{1}H NMR (500 MHz, D_2O): **Pyranose**: δ = 5.08 (d, $J_{1,2}$ = 3.4 Hz, 1H; H1α), 4.85 (d, $J_{1,2}$ = 8.3 Hz, 1H; H1β), 4.12 (dd, $J_{3,4}$ = 2.8 Hz, $J_{3,2}$ = 3.0 Hz, 1H; H3β), 4.12 (m (weak), 1H; H3α), 4.04 (dq, $J_{5,6}$ = 6.4 Hz, $J_{5,4}$ = 9.4 Hz, 1H; H5α), 3.82 (dq, $J_{5,6}$ = 6.3 Hz, $J_{5,4}$ = 9.8 Hz, 1H; H5β), 3.70 (t, $J_{2,1}$ = $J_{2,3}$ = 3.4 Hz, 1H; H2α), 3.40 (dd, $J_{2,3}$ = 3.0 Hz, $J_{2,1}$ = 8.3 Hz, 1H; H2β), 3.36 (dd, $J_{4,3}$ = 2.8 Hz, $J_{4,5}$ = 9.8 Hz, 1H; H4β), 3.36 (m (weak), 1H; H4α), 1.26 (d, $J_{6,5}$ = 6.4 Hz, 3H; H6α), 1.24 (d, $J_{6,5}$ = 6.3 Hz, 3H; H6β); **Furanose**: δ = 5.35 (d, $J_{1,2}$ = 4.2 Hz, 1H; H1α), 5.22 (d, $J_{1,2}$ = 2.3 Hz, 1H; H1β), 4.30 (t, $J_{3,2}$ = $J_{3,4}$ = 5.2 Hz, 1H; H3β), 4.16 (dd, $J_{3,4}$ = 3.9 Hz, $J_{3,2}$ = 5.9 Hz, 1H; H3α), 4.04 (m (weak), 1H; H2α), 4.00 (dd, $J_{4,5}$ = 3.8 Hz, $J_{4,3}$ = 3.9 Hz, 1H; H4α), 3.94 (m (weak), 1H; H2β), 3.93 (m (weak), 2H; H5α and H5β), 3.82 (m (weak), 1H; H4β), 1.22 (d, $J_{6,5}$ = 6.7 Hz, 3H; H6β), 1.20 (d, $J_{6,5}$ = 6.7 Hz, 3H; H6α); ^{13}C NMR (125 MHz, D_2O): **Pyranose**: δ = 94.0 (C1β), 93.4 (C1α), 72.9 (C4β), 17.2 (C6α), 72.3 (C4α), 72.1 (C2β, C3α), 71.7 (C3β), 68.0 (C2α), 70.1 (C5β), 63.5 (C5α), 17.6 (C6β), **Furanose**: δ = 101.1 (C1β), 96.6 (C1α), 87.8 (C4α), 86.3 (C4β), 76.1 (C2β), 71.8 (C2α), 70.7 (C3β), 69.4 (C3α), 68.1 (C5β), 67.6 (C5α), 17.9 (C6α, C6β),; IR (thin film): ν_{max} = 3377 (OH); *m/z* (CI+ve): 165.1 ($[M+H]^+$, 5%), 147.2 ([M-OH], 100%); HRMS *m/z* (CI+ve): found 165.0764 $[M+H]^+$; $C_6H_{13}O_5^+$ requires 165.0763.

6-Deoxy-2,3-*O*-isopropylidene-L-talose 5

Diisobutylaluminum hydride (25 % wt. in toluene, 3 mL, 5.23 mmol) was added dropwise to a solution of the *talono*-lactone **26** (0.5 g, 2.47 mmol) in anhydrous dichloromethane (7 mL) at -78 °C. The reaction mixture was stirred at -78 °C for 30 min, until TLC (hexane/ethyl acetate, 1:1) indicated the consumption of the starting material (R_f 0.3) and formation of one major product (R_f 0.4). The reaction was quenched with methanol and allowed to warm to rt. Ethyl acetate (2 mL), potassium dihydrogen orthophosphate (2 g) and sodium hydrogen carbonate (sat. aq., 2 mL) were added and the mixture was stirred for 10 min. The mixture was dried (anhydr. Na_2SO_4) and filtered through Celite®. The solids were washed with ethyl acetate (3 x 10 mL) and the liquids concentrated *in vacuo*. Flash column chromatography (hexane/ethyl acetate, 1:1) of the residue provided the *talo*-lactols **5** (0.40 g, 1.97 mmol, 80% yield) as a colourless oil.

$[\alpha]_D^{20}$ = -3.7 (*c* = 0.8 in $CHCl_3$); Major component: ^{1}H NMR (250 MHz, CDCl): δ = 5.24 (s, 1H; H1), 4.89 (br-s, 1H; OH), 4.61 (d, $J_{2,3}$ = 5.9 Hz, 1H; H2), 4.40 (d, $J_{3,2}$ = 5.9 Hz, 1H; H3), 4.00 (d, $J_{4,5}$ = 2.0 Hz, 1H; H4), 3.63-3.77 (m, 1H; H5), 1.33 (s, 3H; CH_3), 1.18 (s, 3H; CH_3), 1.09 (d, $J_{6,5}$ = 6.4 Hz, 3H; H6); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 111.9 ($\underline{C}(CH_3)_2$), 102.5 (C1), 90.6 (C2), 86.2 (C4), 82.3 (C3), 67.7 (C5), 26.2 (CH_3), 24.5 (CH_3), 19.4 (C6); IR (thin film): ν_{max} = 3370 (OH); *m/z* (CI+ve): 205.2

([M+H]$^+$, 2%), 187.2 ([M-OH]$^+$, 100%); HRMS *m/z* (CI+ve): found 205.1070 [M+H]$^+$; $C_9H_{17}O_5^+$ requires 205.1075.

6-Deoxy-L-talose 8

DOWEX® 50WX8-100 (H^+ form) (0.3 g) was added into a solution of the lactols **5** (0.3 g, 1.47 mmol) in water (8.5 mL). After stirring at rt for 24 h, TLC analysis (ethyl acetate) indicated the absence of the starting material (R_f 0.8) and the formation of one polar major product (R_f 0.0). The resin was filtered off and washed with water (2 x 8 mL), the filtrate was concentrated *in vacuo* and the residue was purified by column chromatography (methanol/dichloromethane 1:6) to obtain 6-deoxy-D-talose **8** as a white solid (0.216 g, 90%).

m.p.: 126-128 ºC (methanol/dichloromethane); $[\alpha]_D^{20}$ (initial) = -49 (*c* = 0.14 in H_2O), $[\alpha]_D^{20}$ (eqm. after 30 min) = -21; {lit.[27] m.p. 119-121 ºC, $[\alpha]_D^{20}$ = -20.5 (*c* = 2.28 in H_2O)}; ^{1}H NMR (500 MHz, D_2O): **Pyranose**: δ = 5.21 (d, $J_{1,2}$ = 1.3 Hz, 1H; H1α), 4.77 (d, $J_{1,2}$ = 1.1 Hz, 1H; H1β), 4.17 (dq, $J_{5,4}$ = 1.0 Hz, $J_{5,6}$ = 6.7 Hz, 1H; H5α), 3.91 (t, $J_{3,2}$ = $J_{3,4}$ = 3.2 Hz, 1H; H3α), 3.85 (dd, $J_{2,1}$ = 1.1 Hz, $J_{2,3}$ = 3.3 Hz, 1H; H2β), 3.80 (dd, $J_{2,1}$ = 1.3 Hz, $J_{2,3}$ = 3.2 Hz, 1H; H2α), 3.75 (t, $J_{3,2}$ = $J_{3,4}$ = 3.3 Hz, 1H; H3β), 3.74 (dd, $J_{4,5}$ = 1.0 Hz, $J_{4,3}$ = 3.2 Hz, 1H; H4α), 3.69 (dq, $J_{5,4}$ = 1.0 Hz, $J_{5,6}$ = 6.5 Hz, 1H; H5β), 3.66 (dd, $J_{4,5}$ = 1.0 Hz, $J_{4,3}$ = 3.3 Hz, 1H; H4β), 1.27 (d, $J_{6,5}$ = 6.5 Hz, 3H; H6β), 1.24 (d, $J_{6,5}$ = 6.7 Hz, 3H; H6α), **Furanose**: δ = 5.35 (d, *J* = 1.3 Hz, *J* = 2.6 Hz, 1H; H1β), 5.23 (d, $J_{1,2}$ = 1.6 Hz, 1H; H1α), 4.20 (dd, $J_{3,2}$ = 4.9 Hz, $J_{3,4}$ = 6.4 Hz, 1H; H3α), 4.08 (m (weak), 2H; H2β and H3β), 3.97 (dd, $J_{2,1}$ = 1.6 Hz, $J_{2,3}$ = 4.9 Hz, 1H; H2α), 3.90 (m (weak), 1H; H4β), 3.84 (m (weak), 1H; H5β), 3.83 (dq, $J_{5,6}$ = 6.3 Hz, $J_{5,4}$ = 6.4 Hz, 1H; H5α), 3.71 (t, $J_{4,5}$ = $J_{4,3}$ = 6.4 Hz, 1H; H4α), 1.23 (d, $J_{6,5}$ = 6.3 Hz, 3H; H6α), 1.22 (d, $J_{6,5}$ = 6.4 Hz, 3H; H6β); ^{13}C NMR (125 MHz, D_2O): **Pyranose**: δ = 95.3 (C1α), 94.6 (C1β), 72.8 (C4α), 71.9 (C5β), 71.8 (C2β), 71.7 (C4β), 71.0 (C2α), 69.3 (C3β), 67.6 (C5α), 66.0 (C3α), 16.4 (C6α), 16.2 (C6β), **Furanose**: δ = 101.3 (C1α), 96.8 (C1β), 87.1 (C4β), 86.4 (C4α), 76.0 (C2α), 71.7 (C3α), 71.6 (C2β), 71.3 (C3β), 69.5 (C5α), 67.9 (C5β), 19.0 (C6β), 18.7 (C6α); IR (thin film): ν_{max} = 3386 (OH); *m/z* (CI+ve): 165.1 ([M+H]$^+$, 1%), 147.1 ([M-OH]$^+$, 100%); HRMS *m/z* (CI+ve): found 165.0765 [M+H]$^+$; $C_6H_{13}O_5^+$ requires 165.0760.

6-Deoxy-2,3-O-isopropylidene-D-gulono-1,4-lactone 22 (from *talono*-lactone 26)

Methanesulfonyl chloride (0.1 mL, 1.28 mmol) and *N*,*N*-dimethylaminopyridine (0.013 g, 0.10 mmol) were added under argon to a solution of the *talono*-lactone **26** (0.21 g, 1.03 mmol) in anhydrous pyridine (1.4 mL) at 0 °C. The reaction mixture was stirred at 0 ºC for 3 h, when TLC (hexane/ethyl acetate, 1:1) showed the consumption of starting material (R_f 0.3) and the formation of one reaction product (R_f 0.4). The solvent was evaporated *in vacuo* and the residue co-evaporated with toluene (3 x 2 mL). The residue was dissolved in DCM (10 mL) and washed with water (5 mL) and brine (5 mL). The organic layer was dried (anhydr. Na_2SO_4), filtered and concentrated in *vacuo*, affording mesylate **27** (0.25 g, 86 %) as a white solid.

m.p.: 75 ºC (ethyl acetate/hexane); $[\alpha]_D^{20}$ = -36.7 (*c* = 0.4 in MeOH); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.04 (dq, $J_{5,6}$ = 6.6 Hz, $J_{5,4}$ = 1.7 Hz, 1H; H5), 4.76-4.81 (m, 2H; H3, H4), 4.55 (d, *J* = 7.7 Hz, 1H; H2), 3.06 (s, 3H; CH_3-SO_3), 1.54 (d, $J_{6,5}$ = 6.6 Hz, 1H; H6), 1.45 (s, 3H; CH_3), 1.37 (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.6 (C=O), 113.9 ($\underline{C}(CH_3)_2$), 83.6 (C4), 78.2 (C2), 76.8 (C5), 74.7 (C3), 39.6 (CH_3-SO_3), 26.8 (CH_3), 25.6 (CH_3), 17.4 (C6); IR (thin film): ν_{max} = 1781 (C=O); *m/z* (CI+ve): 281.4 ([M+H]$^+$, 35%), 157.3 ([M-$C_3H_7O_3S$]$^+$, 100%); HRMS *m/z* (CI+ve): found 281.0706 [M+H]$^+$; $C_{10}H_{17}O_7S^+$ requires 281.0703.

Aqueous potassium hydroxide (0.60 M, 3.9 mL, 2.34 mmol) was added to a solution of crude mesylate **27** (0.22 g, 0.78 mmol) in 1,4-dioxane (5 mL) and the mixture was stirred at rt overnight. The reaction mixture was acidified to pH 1 with hydrochloric acid (2 M, aq.) and extracted with ethyl

acetate (6 x 10 mL). TLC analysis (hexane/ethyl acetate, 1:1) indicated the transformation of the starting material (R_f 0.4) into a mixture of lactone **22** (R_f 0.2) and its carboxylic acid precursor (R_f 0.0). The pooled organic extracts were stirred in presence of Na_2SO_4 (anhydr.) at rt overnight, filtered and concentrated *in vacuo*. Flash column chromatography (ethyl acetate/hexane, 1:1) of the solid residue afforded the *gulono*-lactone **22** (0.12 g, 76%) as a white solid. This sample was identical to that prepared above from ketone **21** and was converted to 6-deoxy-D-gulose **6** as described above for biological evaluation.

B. 2-Substituted rhamnose analogues from 3,5-*O*-benzylidene rhamnonolactone 9

3,5-*O*-Benzylidene-2-*O*-trifluoromethanesulfonyl-L-rhamnono-1,4-lactone 10

Trifluoromethanesulfonyl anhydride (2.70 mL, 16.0 mmol) was added dropwise to a solution of the benzylidene lactone **9** (2.0 g, 8.0 mmol) and anhydrous pyridine (1.93 mL, 24.0 mmol) in anhydrous THF (30 mL) at -20 °C. After 2 h, TLC (cyclohexane/ethyl acetate, 1:1) indicated the consumption of the starting material (R_f 0.54) and the formation of one major product (R_f 0.61). The reaction mixture was diluted with dichloromethane (10 mL) and washed with HCl (2 M, aq., 3 x 40 mL). The organic layer was dried ($MgSO_4$) and the solvent was removed in *vacuo* to give the residue which was purified by flash chromatography (cyclohexane/ethyl acetate, 5:1→3:1) to obtain pure triflate **10** (2.9 g, 95%) as a white solid.

m.p.: 115-117 °C; $[\alpha]_D^{20}$ = -78 (*c* = 0.69 in $CHCl_3$) {lit.[16] m.p.: 139-140 °C; $[\alpha]_D^{20}$ = -63.9 (*c* = 0.69 in CH_3CN)}; ^{1}H NMR (400 MHz, CD_3CN): δ = 7.46–7.42 (m, 5H; -Ar), 5.97 (s, 1H; H7), 5.85 (d, $J_{2,3}$ = 3.9 Hz, 1H; H2), 5.23 (dd, $J_{3,4}$ = 1.7 Hz, $J_{3,2}$ = 3.9 Hz, 1H; H3), 4.60 (dq, $J_{5,4}$ = 0.8 Hz, $J_{5,6}$ = 7.3 Hz, 1H; H5), 4.38 (br-s, 1H; H4), 1.55 (d, $J_{6,5}$ = 7.3 Hz, 3H; H6); ^{13}C NMR (100 MHz, CD_3CN): δ = 168.6 (C=O), 126.7, 128.9, 129.8, 137.9 (-Ar), 92.1 (C7), 81.1 (C2), 73.8 (C4), 71.0 (C3), 69.9 (C5), 14.4 (C6); IR (thin film): ν_{max} = 1780 (C=O); *m/z* (ESI+ve): 405 ([M+Na]$^+$, 100%); HRMS (ESI+ve): found 405.0226 [M+Na]$^+$; $C_{14}H_{13}F_3NaO_7S^+$ requires 405.0226.

3,5-*O*-Benzylidene-6-deoxy-L-glucono-1,4-lactone 28

Cesium trifluoroacetate (4.45 g, 18.2 mmol) was added to a solution of triflate **10** (2.9 g, 7.6 mmol) in butanone (30 mL). The reaction mixture was then stirred at 60 °C for 4 h until TLC (cyclohexane/ethyl acetate, 1:1) indicated the disappearance of starting material (R_f 0.61) and the formation of one major product (R_f 0.57). Solvent was removed *in vacuo* to give a residue that was purified by flash chromatography (cyclohexane/ethyl acetate, 5:1→3:1) to obtain the *glucono*-lactone **28** (1.8 g, 90%) as a white solid.

m.p.: 146-148 °C; $[\alpha]_D^{20}$ = -80 (*c* = 0.90 in MeCN) {lit.[16] m.p.: 145-148 °C; $[\alpha]_D^{20}$ = -84.1 (*c* = 1.15 in CH_3CN)}; ^{1}H NMR (400 MHz, CD_3CN): δ = 7.39–7.46 (m, 5H; -Ar), 5.92(s, 1H; H7), 4.66 (d, $J_{3,4}$ = 2.0 Hz, 1H; H3), 4.57 (q, $J_{5,6}$ = 7.2 Hz, 1H; H5), 4.47 (br-s, 1H; H4), 4.14 (br-s, 1H; H2), 1.54 (d, $J_{6,5}$ = 7.2 Hz, 3H; H6); ^{13}C NMR (100 MHz, CD_3CN): δ = 175.6 (C=O), 127.1, 129.2, 129.6, 139.1 (-Ar), 92.8 (C7), 77.5 (C4), 75.5 (C3), 73.8 (C2), 73.8 (C2), 15.3 (C6); IR (thin film): ν_{max} = 1785 (C=O); *m/z* (ESI+ve): 405 ([M+Na]$^+$, 100%); HRMS (ESI+ve): found 273.0726 [M+Na]$^+$; $C_{13}H_{14}NaO_5^+$ requires 273.0733.

3,5-*O*-Benzylidene-2-*O*-*tert*-butyldimethylsilyl-6-deoxy-L-glucono-1,4-lactone 29

tert-Butyldimethylsilyl chloride (111 mg, 0.74 mmol) and imidazole (78 mg, 1.14 mmol) were added to a solution of **28** (143 mg, 0.57 mmol) in anhydrous DMF (3 mL). The reaction mixture was stirred at rt for 15 h until TLC (cyclohexane/ethyl acetate, 1:1) showed the formation of one major product (R_f 0.8). Then the mixture was diluted with ethyl acetate (10 mL) and washed with half saturated

brine (10 mL). The organic phase was dried ($MgSO_4$), filtered and solvent removed *in vacuo* to give a residue that was purified by flash chromatography (cyclohexane/ethyl acetate, 7:1→5:1) to yield the silyl ether **29** (148 mg, 71%) as a white solid.
m.p.: 58-60 °C; $[\alpha]_D^{20}$ = -70.9 (*c* = 1.17 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.47 (m, 5H; -Ar), 5.8 (s, 1H; H7), 4.59 (dq, $J_{5,4}$ = 0.8 Hz, $J_{5,6}$ = 7.1 Hz, 1H; H5), 4.10 (d, $J_{3,4}$ = 2.3 Hz, 1H; H3), 4.39 (dd, $J_{4,5}$ = 1.8 Hz, $J_{4,3}$ = 2.3 Hz, 1H; H4), 4.23 (s, 1H; H2), 1.56 (d, $J_{6,5}$ = 7.1 Hz, 3H; H6), 0.92 (s, 9H; 3 x CH_3), 0.20 (s, 3H; CH_3), 0.18 (s, 3H; CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.8 (C=O), 126.3, 128.4, 129.4, 137.3 (-Ar), 92.7 (C7), 77.2 (C4), 75.4 (C3), 73.9 (C2), 68.8 (C5), 25.5 (CH_3), 15.5 (C6), -4.9 (CH_3), -5.2 (CH_3); IR (thin film): ν_{max} = 1793 (C=O); *m/z* (ESI+ve): 387 ($[M+Na]^+$, 100%); HRMS (ESI+ve): found 387.1597 $[M+Na]^+$; $C_{19}H_{28}NaO_5Si^+$ requires 387.1598.

3,5-*O*-Benzylidene-2-*O*-*tert*-butyldimethylsilyl-6-deoxy-L-glucose 30
Diisobutylaluminium hydride (25% w/v in toluene, 0.30 mL, 0.53 mmol) was added dropwise to a solution of **29** (148 mg, 0.41 mmol) in anhydrous dichloromethane (3 mL) at -78 °C. The reaction mixture was stirred at -78°C for 1 h until mass spectrometry showed the formation of desired product peak and disappearance of starting material peak (*m/z* 364). Then the mixture was diluted with ethyl acetate (10 mL) and potassium sodium tartrate (sat. aq., ~0.5 mL) was added. After stirring for 8 h, the mixture was diluted with water (10 mL) and extracted with ethyl acetate (3 x 10 mL). Organic phase was dried ($MgSO_4$), filtered and solvent was removed *in vacuo* to obtain a residue that was further purified *via* flash chromatography (cyclohexane/ethyl acetate, 7:1→5:1) to yield the lactols **30** as a syrup (α:β ratio 5:4) (130 mg, 88%).
$[\alpha]_D^{20}$ = -10 (*c* = 0.27 in $CHCl_3$); ^{1}H NMR (400 MHz, CD_3CN): δ = 7.24-7.14 (m, 10H; -Arα, -Arβ), 5.54 (s, 1H; H7α), 5.54 (s, 1H; H7β), 5.24 (dd, $J_{1,2}$ = 3.6 Hz, $J_{1,OH}$ = 11.3 Hz, 1H; H1β), 4.78 (d, $J_{1,OH}$ = 10.7 Hz, 1H; H1α), 4.15-4.18 (m, 3H; H3α, H3β, H5α), 4.07 (a-q, $J_{5,6}$ = 7.2 Hz, 1H; H5β), 3.90 (d, $J_{2,1}$ = 3.5 Hz, 1H; H2β), 3.88 (br-s, 1H; H2α), 3.80 (d, $J_{OH,1}$ = 11.1 Hz, 1H; OHβ), 3.64 (br-s, 2H; H4α, H4β), 3.59 (d, $J_{OH,1}$ = 10.7 Hz, 1H; OHα), 1.23 (d, $J_{6,5}$ = 7.2 Hz, 3H; H6α), 1.19 (d, $J_{6,5}$ = 7.2 Hz, 3H; H6β), 0.72 (s, 9H; 3 x CH_3 (β)), 0.69 (s, 9H; 3 x CH_3 (α)), -0.04 (s, 3H; CH_3), -0.06 (s, 3H; CH_3), -0.08 (s, 6H; 2 x CH_3); ^{13}C NMR (100 MHz, CD_3CN): δ = 127.2, 127.3, 129.2, 129.4, 129.8, 130.0, 139.8, 140.0 (-Arα, -Arβ), 105.3 (C1α), 98.9 (C1β), 93.4 (C7α), 93.1 (C7β), 81.7 (C2α), 79.6, 78.9 (C3α, C3β), 77.2 (C2β), 78.4, 75.5 (C4α, C4β), 71.5 (C5α), 71.2 (C5β), 26.2, 26.1 (3 x CH_3 (α), 3 x CH_3 (β)), 16.6 (C6α), 16.3 (C6β), -4.9 (CH_3), -4.8 (2 x CH_3), -4.7 (CH_3); *m/z* (ESI+ve): 389 ($[M+Na]^+$, 100%); HRMS (ESI+ve): found 389.1755 $[M+Na]^+$; $C_{19}H_{30}NaO_5Si^+$ requires 389.1755.

L-Quinovose [6-Deoxy-L-glucose] 12
DOWEX® 50WX8-200 (H^+ form) (100 mg) was added to a solution of lactol **30** (130 mg, 0.36 mmol) in water (5 mL). After stirring at rt for 15 h mass spectrometry indicated the completion of reaction, the resin was filtered off and water was removed *in vacuo* to yield 6-deoxy-L-glucose **12** as a syrup (α:β ratio 3:5) (58 mg, 100%).
$[\alpha]_D^{20}$ = -40 (*c* = 1.39 in H_2O) {lit.[30] $[\alpha]_D^{20}$ = -27 (*c* = 2 in H_2O), commercial sample of 6-deoxy-D-glucose: $[\alpha]_D^{20}$ = +27 (*c* = 2 in H_2O)}; ^{1}H NMR (400 MHz, D_2O): δ = 5.10 (d, $J_{1,2}$ = 3.8 Hz, 1H; H1α), 4.55 (d, $J_{1,2}$ = 7.9, 1H; H1β,), 3.85 (dq, $J_{5,6}$ = 6.3 Hz, $J_{5,4}$ = 9.6 Hz, 1H; H5α), 3.58 (t, $J_{3,2}$ = $J_{3,4}$ = 9.5 Hz, 1H; H3α), 3.47 (dd, $J_{2,1}$ = 3.8 Hz, $J_{2,3}$ = 9.9 Hz, 1H; H2α), 3.42 (dq, $J_{5,6}$ = 6.2 Hz, $J_{5,4}$ = 9.5 Hz, 1H; H5β), 3.36 (t, $J_{3,2}$ = $J_{3,4}$ = 9.3 Hz, 1H; H3β), 3.17 (dd, $J_{2,1}$ = 7.9 Hz, $J_{2,3}$ = 9.3 Hz, 1H; H2β), 3.08 (t, $J_{4,3}$ = $J_{4,5}$ = 9.3 Hz, 1H; H4β), 3.07 (t, $J_{4,3}$ = $J_{4,5}$ = 9.5 Hz, 1H; H4α), 1.21 (d, $J_{6,5}$ = 6.1 Hz, 3H; H6β), 1.19 (d, $J_{6α,5α}$ = 6.3 Hz, 3H; H6α); ^{13}C NMR (100 MHz, D_2O): δ = 96.9 (C1β), 93.2 (C1α), 76.7 (C3β), 76.4 (C4α), 76.1 (C4β), 75.6 (C2β), 73.6 (C3α), 73.1 (C5β), 72.9 (C2α), 68.6 (C5α), 17.9 (C6α, C6β);

m/z (ESI+ve): 165 ($[M+H]^+$, 100%); HRMS (ESI+ve): found 165.0757 $[M+H]^+$; $C_6H_{13}O_5^+$ requires 165.0757.

3,5-*O*-Benzylidene-2,6-dideoxy-L-*arabino*-hexono-1,4-lactone 32

Lithium iodide hydrate (917 mg, 4.91 mmol) was added to a solution of triflate **10** (300 mg, 0.79 mmol) in butanone (10 mL). The reaction mixture was stirred at 60 °C for 16 h until TLC (cyclohexane/ethyl acetate, 1:1) showed the disappearance of starting material (R_f 0.57) and formation of one major product (R_f 0.39). Then sodium thiosulfate (sat. aq., sat, 10 mL) was added. After stirring at rt for 10 min, the reaction mixture was extracted with ethyl acetate (3 x 10 mL), the organic phase was dried ($MgSO_4$) and the solvent was removed in *vacuo* to give a residue which was purified by flash chromatography (cyclohexane/ethyl acetate, 4:1→1:1) to obtain the deoxylactone **32** (137 mg, 74%) as a white solid.

m.p.: 100-102 °C; $[\alpha]_D^{20}$ = -61.6 (*c* = 0.25 in MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.38 (m, 5H; -Ar), 5.8 (s, 1H; H7), 4.78 (br-dd, $J_{3,4}$ = 3.7 Hz, $J_{3,2'}$ = 4.6 Hz, 1H; H3), 4.48 (dq, $J_{5,4}$ = 2.4 Hz, $J_{5,6}$ = 7.0 Hz, 1H; H5), 4.16 (br-dd, $J_{4,3}$ = 3.7 Hz, $J_{4,5}$ = 2.4 Hz, 1H; H4), 2.82 (dd, $J_{2',3}$ = 4.6 Hz, J_{gem} = 17.7 Hz, 1H; H2'), 2.74 (d, J_{gem} = 17.6 Hz, 1H; H2), 1.53 (d, $J_{6,5}$ = 7.0 Hz, 3H; H6); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.2 (C=O), 126.5, 128.7, 129.6, 137.8 (-Ar), 93.8 (C7), 79.1 (C4), 70.7 (C3), 68.5 (C5), 37.5 (C2), 16.7 (C6); IR (thin film): ν_{max} = 1780 (C=O); *m/z* (ESI+ve): 235 ($[M+H]^+$, 100%); HRMS (ESI+ve): found 298.0798 $[M+Na]^+$; $C_{13}H_{13}N_3NaO_4^+$ requires 298.0798.

3,5-*O*-Benzylidene-2,6-dideoxy-L-*arabino*-hexose 33

Diisobutylaluminium hydride (25% wt. in toluene, 0.32 mL, 0.56 mmol) was added dropwise to a solution of **32** (100 mg, 0.43 mmol) in anhydrous dichloromethane (4 mL) at -78 °C. The reaction mixture was stirred at -78 °C for 3 h until TLC (cyclohexane/ethyl acetate, 1:1) indicated the disappearance of starting material (R_f 0.42) and the formation of one product (R_f 0.49). Also mass spectrometry showed the formation of desired product peak (*m/z* 259). Then the mixture was diluted with ethyl acetate (5 mL) and potassium sodium tartrate (sat. aq., ~0.5 mL) was added. After stirring for 5 h, the mixture was diluted with water (5 mL) and extracted with ethyl acetate (3 x 5 mL). The organic phase was dried ($MgSO_4$), filtered and solvent was removed *in vacuo* to obtain a residue that was further purified *via* flash chromatography (cyclohexane/ethyl acetate 5:1 to 1:1) to yield the benzylidene lactols **33** as a white solid (α:β ratio 10:1) (96 mg, 96%).

m.p.: 90-92 °C; $[\alpha]_D^{20}$ = -34 (*c* = 0.27 in MeOH); ^{1}H NMR (400 MHz, CD_3Cl): δ = 7.34-7.54 (m, 10H; -Arα, -Arβ), 5.83 (t, $J_{1,2}$ = $J_{1,2'}$ = 4.7 Hz, 1H; H1α), 5.78 (s, 1H; H7β), 5.73 (s, 1H; H7α), 5.46 (d, $J_{2,1}$ = 5.1 Hz, 1H; H1β), 4.61 (br-s, 2H; H3α, H3β), 4.54 (a-q, $J_{5,6}$ = 7.0 Hz, 1H; H5β), 4.41 (a-q, $J_{5,6}$ = 7.0 Hz, 1H; H5α), 3.9 (br-s, 1H; H4α), 3.7 (br-s, 1H; H4β), 2.47 (dd, $J_{2',3}$ = 5.7 Hz, J_{gem} = 14.5 Hz, 1H; H2α'), 2.28 (d, J_{gem} = 14.0 Hz, 1H; H2β'), 2.19 (dt, $J_{2,1}$ = $J_{2,3}$ = 4.7 Hz, J_{gem} = 14.0 Hz, 1H; H2β), 2.12 (dt, $J_{2,1}$ = $J_{2,3}$ = 4.5 Hz, J_{gem} = 14.3 Hz, 1H; H2α), 1.50 (d, $J_{6,5}$ = 7.0 Hz, 3H; H6β), 1.49 (d, $J_{6,5}$ = 7.0 Hz, 3H; H6α); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 126.4, 126.5, 128.6, 128.7, 128.8, 129.2, 129.5, 129.6 (-Arα, -Arβ), 99.6 (C1β), 98.7 (C1α), 93.3 (C7α, C7β), 79.5 (C4β), 77.5 (C4α), 74.8 (C3α), 73.8 (C3β), 70.8 (C5β), 69.7 (C5α), 41.9 (C2α), 41.5 (C2β), 17.2 (C6α), 17.0 (C6β); *m/z* (ESI+ve): 237 ($[M+H]^+$, 100%); HRMS (ESI+ve): found 237.1118 $[M+H]^+$; $C_{13}H_{17}O_4^+$ requires 237.1120.

L-Olivose [2,6-Dideoxy-L-*arabino*-hexose] 13

DOWEX® 50WX8-200 (H^+ form) (100 mg) was added into a solution of lactol **33** (90 mg, 0.38 mmol) in water (5 mL). After stirring at rt for 18 h and mass spectrum indicated the completion of reaction, the resin was filtered off and water was removed *in vacuo* to yield L-olivose **13** as a syrup (α:β ratio 1:1) (56 mg, 100%).

$[\alpha]_D^{20}$ = -13 (*c* = 0.49 in H_2O) {lit.[32] $[\alpha]_D^{20}$ = -20 (*c* = 0.80 in H_2O)}; ^{1}H NMR (400 MHz, D_2O): δ = 5.31 (a-dd, $J_{1,2'}$ = 1.0 Hz, $J_{1,2}$ = 3.7 Hz, 1H; H1α), 4.91 (dd, $J_{1,2'}$ = 2.0 Hz, $J_{1,2}$ = 9.8 Hz, 1H; H1β), 3.91-3.83 (m, 2H; H3α, H5α), 3.66 (ddd, $J_{3,2'}$ = 5.0 Hz, $J_{3,4}$ = 9.0 Hz, $J_{3,2}$ = 12.0 Hz, 1H; H3β), 3.41 (dq, $J_{5,6}$ = 6.3 Hz, $J_{5,4}$ = 9.5 Hz, 1H; H5β), 3.10 (t, $J_{4,3}$ = $J_{4,5}$ = 9.3 Hz, 1H; H4α), 3.05 (t, $J_{4,3}$ = $J_{4,5}$ = 9.3 Hz, 1H; H4β), 2.25 (ddd, $J_{2',1}$ = 2.0 Hz, $J_{2',3}$ = 5.0 Hz, J_{gem} = 12.3, 1H; H2β'), 2.13 (ddd, $J_{2',1}$ = 1.0 Hz, $J_{2',3}$ = 5.1 Hz, J_{gem} = 13.4 Hz, 1H; H2α'), 1.51 (dt, $J_{2,1}$ = 9.9 Hz, $J_{2,3}$ = J_{gem} = 12.0 Hz, 1H; H2β), 1.28 (d, $J_{6,5}$ = 6.3 Hz, 3H; H6β), 1.25 (d, $J_{6,5}$ = 6.4 Hz, 3H; H6α); ^{13}C NMR (100 MHz, D_2O): δ = 93.8 (C1β), 91.7 (C1α), 77.4 (C4α), 76.8 (C4β), 72.5 (C5β), 70.7 (C3β), 68.5, 68.3 (C3α, C5α), 40.3 (C2β), 38.2 (C2α), 17.5 (C6β, C6α); *m/z* (ESI+ve): 171 ([M+Na]$^+$, 100%); HRMS (ESI+ve): found 149.0808 [M+H]$^+$; $C_6H_{13}O_4^+$ requires 149.0808.

3,5-*O*-Benzylidene-2-azido-2,6-dideoxy-L-glucono-1,4-lactone 34

Sodium azide (16.6 mg, 0.26 mmol) was added to a solution of triflate **10** (100 mg, 0.26 mmol) in anhydrous DMF. The mixture was stirred at -30 °C for 6 h until TLC (cyclohexane/ethyl acetate, 1:1) indicated the formation of the only product (R_f 0.68). After being diluted with ethyl acetate (5 mL), the mixture was washed with half saturated brine (10 mL). The organic phase was dried ($MgSO_4$), filtered and solvent was removed *in vacuo* to obtain a crude solid that was purified *via* flash chromatography (cyclohexane/ethyl acetate 5:1) to yield the azido lactone **34** as a white solid (53.3 mg, 75%).

m.p.: 70-74 °C; $[\alpha]_D^{20}$ = -150 (*c* = 0.89 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.46 (m, 5H; -Ar), 5.8 (s, 1H; H7), 4.57 (dq, $J_{5,4}$ = 1.8 Hz, $J_{5,6}$ = 7.2 Hz, 1H; H5), 4.51 (d, $J_{3,4}$ = 2.9 Hz, 1H; H3), 4.31 (t, $J_{4,3}$ = $J_{4,5}$ = 2.4 Hz, 1H; H4), 4.24 (s, 1H; H2), 1.54 (d, $J_{6,5}$ = 7.2 Hz, 3H; H6); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.3 (C=O), 137.2, 129.6, 128.8, 126.5 (-Ar), 93.4 (C7), 77.5 (C4), 73.7 (C3), 68.7 (C5), 63.0 (C2), 16.0 (C6); IR (thin film): ν_{max} = 2112 (s, N_3); *m/z* (ESI+ve): 298 ([M + Na]$^+$, 100%); HRMS (ESI+ve): found 298.0796 [M+Na]$^+$; $C_{12}H_{19}FNaO_5^+$ requires 298.0798.

3,5-*O*-Benzylidene-2-azido-2,6-dideoxy-L-glucose 35

Diisobutylaluminium hydride (25% w/v in toluene, 0.34 mL, 0.60 mmol) was added dropwise to a solution of **34** (150 mg, 0.55 mmol) in anhydrous dichloromethane (5 mL) at -78 °C. The reaction mixture was stirred at -78 °C for 2 h until mass spectrometry showed the formation of desired product peak (*m/z* 300) and disappearance of starting material peak (*m/z* 298). Then the mixture was diluted with ethyl acetate (5 mL) and potassium sodium tartrate (sat. aq., ~0.5 mL) was added. After stirring for 5 h, the mixture was diluted with water (5 mL) and extracted with ethyl acetate (3 x 5 mL). The organic phase was dried ($MgSO_4$), filtered and solvent was removed *in vacuo* to obtain a crude product that was further purified *via* flash chromatography (cyclohexane/ethyl acetate 7:1) to yield the benzylidene lactol **35** as a colourless oil (α:β ratio 5:4) (126 mg, 84%).

$[\alpha]_D^{20}$ = -142 (*c* = 1.70 in MeOH); ^{1}H NMR (400 MHz, CD_3CN): δ = 7.25-7.14 (m, 10H; -Arα, -Arβ); 5.59 (s, 1H; H7β), 5.52 (s, 1H; H7α), 5.46 (dd, $J_{1,2}$ = 4.1 Hz, $J_{1,OH}$ = 6.7 Hz, 1H; H1β), 4.94 (d, $J_{1,OH}$ = 9.5 Hz, 1H; H1α), 4.50 (d, $J_{OH,1}$ = 6.9 Hz, 1H; OHβ), 4.32 (br-d, $J_{3,2}$ = $J_{3,4}$ = 2.7 Hz, 1H; H3β), 4.24 (t, $J_{3,4}$ = $J_{3,2}$ = 2.5 Hz, 1H; H3α), 4.14 (dq, $J_{5,4}$ = 2.3 Hz, $J_{5,6}$ = 7.0 Hz, 1H; H5β), 4.00 (dq, $J_{5,4}$ = 2.6 Hz, $J_{5,6}$ = 7.0 Hz, 1H; H5α), 4.00 (dq, $J_{5,4}$ = 2.6 Hz, $J_{5,6}$ = 7.0 Hz, 1H; H5α), 3.81-3.84 (m, 2H; H2α, H2β), 3.67 (t, $J_{4,3}$ = $J_{4,5}$ = 2.7 Hz, 1H; H4α), 3.59 (t, $J_{4,3}$ = $J_{4,5}$ = 2.6 Hz, 1H; H4β), 1.21 (d, $J_{6,5}$ = 7.0 Hz, 3H; H6β), 1.17 (d, $J_{6,5}$ = 7.2 Hz, 3H; H6α); ^{13}C NMR (100 MHz, CD_3CN): δ = 126.2, 126.3, 128.3, 128.4, 128.9, 129.1, 138.5, 138.8 (-Arα, -Arβ), 101.5 (C1α), 98.1 (C1β), 93.0 (C7β), 92.8 (C7α), 77.7 (C4β), 77.1 (C3α), 76.2 (C3β), 75.6 (C4α), 70.1 (C5β), 69.7 (C5α), 70.2, 66.8 (C2α, C2β), 15.8, 15.6 (C6α, C6β); IR (thin film): ν_{max} = 2110 (s, N_3); *m/z* (ESI+ve): 300 ([M + Na]$^+$, 100%); HRMS (ESI+ve): found 300.0905 [M+Na]$^+$; $C_{19}H_{30}NaO_5Si^+$ requires 300.0905.

3,5-*O*-Benzylidene-2-azido-2, 6-dideoxy-L-mannono-1,4-lactone 36

A) From the *manno*-triflate 10

Sodium azide (260 mg, 4.0 mmol) was added to a solution of triflate **10** (1.5 g, 4.0 mmol) in anhydrous DMF at 0 °C. The mixture was stirred at 0 °C for 1.5 h after which it was stirred at room temperature overnight. After 12 hours TLC analysis (cyclohexane/ethyl acetate, 1:1) indicated the formation of the only product (R_f 0.38). The mixture was diluted with ethyl acetate (50 mL), washed with brine (50 mL), half saturated brine (50 mL) and then brine (50 mL) again. The organic phase was dried ($MgSO_4$), filtered and reduced *in vacuo* to obtain a crude solid which was purified by flash column chromatography (cyclohexane/ethyl acetate 2:1→1:2) to afford the *manno*-azido **36** as a colourless solid (932 mg, 85%); none of the epimeric *gluco*-azide **34** was isolated under these conditions.

B) From the *gluco*-triflate 11

Triflic anhydride (1.11 mL, 6.5 mmol) was added dropwise to a solution of benzylidene lactone **28** (800 mg, 3.2 mmol) and anhydrous pyridine (1.25 mL, 15.5 mmol) in anhydrous THF (10 mL) at -20 °C. After stirring at -20 °C for 8 h, TLC (cyclohexane/ethyl acetate, 1:1) indicated the formation of one major product (R_f 0.70). The reaction mixture was diluted with DCM (10 mL) and washed with HCl (2 M, aq. 3 x 10 mL). The organic layer was dried ($MgSO_4$) and the solvent was removed *in vacuo* to give the crude triflate **11** (1.3 g) which was not stable to chromatography and was used without further purification.

Sodium azide (204.8 mg, 3.2 mmol) was added into a solution of the crude triflate **11** (1.3 g) in anhydrous DMF (20 mL). The mixture was stirred at -40 °C for 18 h until TLC (cyclohexane/ethyl acetate, 1:1) indicated the formation of one major product (R_f 0.42) and one minor product (R_f 0.68). After being diluted with ethyl acetate (20 mL), the mixture was washed with half saturated brine (20 mL). The organic phase was dried ($MgSO_4$), filtered and solvent was removed *in vacuo* to obtain a crude that was further purified *via* flash chromatography (cyclohexane/ethyl acetate 5:1 to 1:1) to yield the azido lactone **36** as a white solid (616 mg, 70%) and **34** (211 mg, 24%).

m.p.: 148 - 152 °C; $[\alpha]_D^{20}$ = -70 (c = 0.52 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.38 (m, 5H; -Ar), 5.9 (s, 1H; H7), 4.87 (dd, $J_{3,4}$ = 2.1 Hz, $J_{3,2}$ = 4.0 Hz, 1H; H3), 4.57 (br-dq, $J_{5,4}$ = 1.7 Hz, $J_{5,6}$ = 7.3 Hz, 1H; H5), 4.12 (t, $J_{4,3}$ = $J_{4,5}$ = 1.7 Hz, 1H; H4), 4.04 (d, $J_{2,3}$ = 4.1 Hz, 1H; H2), 1.56 (d, $J_{6,5}$ = 7.3 Hz, 3H; H6); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.8 (C=O), 137.0, 129.7, 128.7, 126.5 (-Ar), 93.0 (C7), 75.0 (C4), 72.5 (C3), 69.3 (C5), 62.0 (C2), 15.7 (C6); IR (thin film): ν_{max} = 2109 (s, N_3), 1789 (C=O); *m/z* (ESI+ve): 298 ($[M + H]^+$, 100%); HRMS (ESI+ve): found 298.0798 $[M+Na]^+$; $C_{12}H_{19}FNaO_5^+$ requires 298.0798.

3,5-*O*-Benzylidene-2-azido-2, 6-dideoxy-L-mannose 37

Diisobutylaluminium hydride (25% w/v in toluene, 0.83 mL, 1.46 mmol) was added dropwise to a solution of **36** (310 mg, 1.13 mmol) in anhydrous dichloromethane (10 mL) at -78 °C. The reaction mixture was stirred at -78 °C for 3 h until TLC (cyclohexane/ethyl acetate, 1:1) indicated the consumption of starting material (R_f 0.42) and the formation of one product (R_f 0.50). Then the mixture was diluted with ethyl acetate (10 mL) and potassium sodium tartrate (sat. aq., ~1.0 mL) was added. After stirring for 5 h, the mixture was diluted with water (10 mL) and extracted with ethyl acetate (3 x 10 mL). Organic phase was dried ($MgSO_4$), filtered and solvent was removed *in vacuo* to obtain a crude that was further purified *via* flash chromatography (cyclohexane/ethyl acetate 3:1 to 1:1) to yield the lactol **37** as a white solid (α:β ratio 2:1) (270 mg, 87%).

$[\alpha]_D^{20}$ = -84 (c = 0.75 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.51-7.34 (m, 10H; -Arα, -Arβ), 5.80 (s, 1H; H7α), 5.78 (s, 1H; H7β), 5.71 (d, $J_{1,2}$ = 5.0 Hz, 1H; H1β), 5.38 (d, $J_{1,2}$ = 4.7 Hz, 1H; H1α), 4.69 (t, $J_{3,2}$ = $J_{3,4}$ = 3.2 Hz, 1H; H3α), 1.46 (d, $J_{6,5}$ = 7.3 Hz, 3H; H6β), 4.62 (dd, $J_{3,4}$ = 2.5 Hz, $J_{3,2}$ = 4.1 Hz, 1H; H3β), 4.46 (dq, $J_{5,4}$ = 1.3 Hz, $J_{5,6}$ = 7.3 Hz, 1H; H5α), 4.35 (dq, $J_{5,4}$ = 1.6 Hz, $J_{5,6}$ = 7.3 Hz,

1H; H5β), 4.03 (br-t, $J_{4,3} = J_{4,5} = 1.8$ Hz, 1H; H4β), 3.74 (dd, $J_{2,1} = 4.1$ Hz, $J_{2,1} = 5.0$ Hz, 1H; H2β), 3.72 (br-t, $J_{4,3} = J_{4,5} = 1.8$ Hz, 1H; H4α), 3.64 (dd, $J_{2,3} = 3.2$ Hz, $J_{2,1} = 4.7$ Hz, 1H; H2α), 1.49 (d, $J_{6,5} = 7.3$ Hz, 3H; H6α); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 126.2, 126.5, 128.6, 128.8, 129.3, 129.5, 137.5, 138.0 (-Arα, -Arβ), 100.6 (C1β), 98.3 (C1α), 93.2 (C7α, C7β), 77.0 (C4α, C4β), 74.8 (C3β), 74.1 (C3α), 71.1 (C5α), 70.2 (C5β), 68.7 (C2β), 63.5 (C2α), 16.7 (C6α), 16.6 (C6β); IR (thin film): ν_{max} = 2110 (s, N_3); *m/z* (ESI+ve): 300 ([M + Na]$^+$, 100%); HRMS (ESI+ve): found 300.0901 [M+Na]$^+$; $C_{19}H_{30}NaO_5Si^+$ requires 300.0905.

2-Azido-2,6-dideoxy-L-glucose 38

DOWEX® 50WX8-200 (H^+ form) (100 mg) was added to a solution of the protected lactol **35** (100 mg, 0.36 mmol) in water / 1,4-dioxane (1:1, 5 mL). After stirring at RT for 21 h, the mass spectrum indicated the completion of reaction; the resin was filtered off and water was removed *in vacuo* to yield the azide **38** as a light yellow syrup (α:β ratio 2:5) (67 mg, 99%).

$[\alpha]_D^{20}$ = +1.6 (*c* = 0.80 in H_2O); ^{1}H NMR (400 MHz, D_2O): δ = 5.29 (d, $J_{1,2} = 3.7$ Hz, 1H; H1α), 4.67 (d, $J_{1,2} = 8.1$ Hz, 1H; H1β), 3.90 (dq, $J_{5,6} = 6.3$ Hz, $J_{5,4} = 9.6$ Hz, 1H; H5α), 3.79 (dd, $J_{3,4} = 9.3$ Hz, $J_{3,2} = 10.2$ Hz, 1H; H3α), 3.47 (dq, $J_{5,6} = 6.2$ Hz, $J_{5,4} = 9.5$ Hz, 1H; H5β), 3.46 (dd, $J_{2,1} = 3.4$ Hz, $J_{2,3} = 10.3$ Hz, 1H; H2α), 3.43 (t, $J_{3,2} = J_{3,4} = 9.3$ Hz, 1H; H3β), 3.27 (dd, $J_{2,1} = 8.1$ Hz, $J_{2,3} = 9.9$ Hz, 1H; H2β), 3.21 (t, $J_{4,3} = J_{4,5} = 9.5$ Hz, 1H; H4α), 3.20 (t, $J_{4,3} = J_{4,5} = 9.3$ Hz, 1H; H4β), 1.28 (d, $J_{6,5} = 6.1$ Hz, 3H; H6β), 1.26 (d, $J_{6,5} = 6.3$ Hz, 3H; H6α); ^{13}C NMR (100 MHz, D_2O): δ = 95.5 (C1β), 91.6 (C1α), 75.9 (C4α), 75.4 (C4β), 74.6 (C3β), 72.6 (C5β), 71.6 (C3α), 68.2 (C5α), 67.7 (C2β), 64.4 (C2α), 17.3 (C6α, C6β),; IR (thin film): ν_{max} = 2110 (s, N_3); *m/z* (ESI+ve): 212 ([M + Na]$^+$, 100%); HRMS (ESI+ve): found 190.0820 [M+H]$^+$; $C_6H_{13}O_5^+$ requires 190.0822.

2-Amino-2,6-dideoxy-L-glucose hydrochloride 39

10% Palladium on charcoal (10 % wt., 15 mg) and aqueous HCl (2M, 0.1 mL) was added to a solution of **38** (67 mg, 0.36 mmol) in water (3 mL). The reaction mixture was flushed with nitrogen, argon and hydrogen gas sequentially. The reaction mixture was stirred vigorously for 2 h at RT under hydrogen atmosphere until the completion of reaction was confirmed by mass spectrometry (*m/z* (ESI+ve): 164 [M+H]$^+$). After filtration, the solvent was removed *in vacuo* to afford the HCl salt of **39** as a brown gum (α:β ratio 1:1) (70 mg, 98%).

$[\alpha]_D^{20}$ = -49.6 (*c* = 0.29 in H_2O) {lit. [34] $[\alpha]_D^{20}$ = -50 (*c* = 1.1 in H_2O)}; ^{1}H NMR (400 MHz, D_2O): δ = 5.38 (d, $J_{1,2} = 3.5$ Hz, 1H; H1α), 4.91 (d, $J_{1,2} = 8.4$ Hz, 1H; H1β), 3.95 (dq, $J_{5,6} = 6.3$ Hz, $J_{5,4} = 9.6$ Hz, 1H; H5α), 3.82 (t, $J_{3,2} = J_{3,4} = 9.7$ Hz, 1H; H3α), 3.62 (t, $J_{3,2} = J_{3,4} = 9.3$ Hz, 1H; H3β), 3.54 (dq, $J_{5,6} = 6.2$ Hz, $J_{5,4} = 9.3$, 1H; H5β), 3.30 (dd, $J_{2,1} = 3.5$ Hz, $J_{2,3} = 10.7$ Hz, 1H; H2α), 3.22 (t, $J_{4,3} = J_{4,5} = 9.2$ Hz, 1H; H4β), 3.21 (t, $J_{4,3} = J_{4,5} = 9.3$ Hz, 1H; H4α), 3.00 (dd, $J_{2,1} = 8.7$ Hz, $J_{2,3} = 10.4$ Hz, 1H; H2β), 1.30 (d, $J_{6,5} = 6.1$ Hz, 3H; H6β), 1.27 (d, $J_{6,5} = 6.3$ Hz, 3H; H6α); ^{13}C NMR (100 MHz, D_2O): δ = 93.0 (C1β), 89.5 (C1α), 75.6, 75.5 (C4α, C4β), 72.8 (C5β), 72.3 (C3β), 70.0 (C3α), 68.2 (C5α), 57.5 (C2β), 55.1 (C2α), 17.2, 17.1 (C6α, C6β); *m/z* (ESI+ve): 164 ([M + H]$^+$, 100%); HRMS (ESI+ve): found 164.0916 [M+H]$^+$; $C_6H_{14}NO_4^+$ requires 164.0917.

3,5-*O*-Benzylidene-2-acetamido-2, 6-dideoxy-L-glucose 40

10% Palladium on charcoal (10 % wt., 20 mg) and acetic anhydride (0.050 mL, 0.51 mmol) were added in a solution of lactol **35** (140 mg, 0.51 mmol) in ethyl acetate / 1,4-dioxane (2:1, 6 mL). The reaction mixture was flushed with nitrogen, argon and hydrogen gas sequentially. The reaction mixture was stirred vigorously for 4 h at rt under hydrogen atmosphere until TLC (ethyl acetate/methanol, 9:1) showed the disappearance of starting material (R_f 0.98) and the formation of the product (R_f 0.71). After filtration, the solvent was removed *in vacuo* to afford a residue that was

purified *via* flash chromatography (ethyl acetate / ethanol 15:1) to yield the protected azide **40** as a white solid (α:β ratio 3:1) (110.7 mg, 74%).
m.p.: 131-133 °C; $[\alpha]_D^{20}$ = +2.3 (*c* = 0.86 in MeOH); ^{1}H NMR (400 MHz, CD_3CN): δ = 7.50-7.38 (10H, m, 1H; -Arα, -Arβ), 6.67 (2H, br-s, NHα and NHβ), 5.82 (1H, s, H7β), 5.75 (1H, s, H7α), 5.58 (br-d, 1H, $J_{1,2}$ = 3.8 Hz; H1α,), 5.11 (d, $J_{1,2}$ = 9.8 Hz,, 1H; H1β), 4.84 (br-s, 2H; OHα and OHβ), 4.44 (br-d, $J_{3,2}$ = 2.9 Hz, 1H; H3β), 4.41 (m, 1H; H3α), 4.39 (dq, $J_{5,4}$ = 1.7 Hz, $J_{5,6}$ = 7.1 Hz, 1H; H5β), 4.26-4.29 (m, 1H; H2α), 4.26 (dq, $J_{5,4}$ = 2.9 Hz, $J_{5,6}$ = 7.0 Hz, 1H; H5α), 4.11 (br-dd, $J_{2,3}$ = 3.0 Hz, $J_{2,1}$ = 9.9 Hz, 1H; H2β), 3.88 (t, $J_{4,3}$ = $J_{4,5}$ = 3.1 Hz, 1H; H4α), 3.85 (t, $J_{4,3}$ = $J_{4,5}$ = 2.4 Hz, 1H; H4β), 1.91 (s, 3H; CH_3(β)), 1.91 (s, 3H; CH_3(α)), 1.45 (d, $J_{6,5}$ = 7.2 Hz, 3H; H6β), 1.41 (d, $J_{6,5}$ = 7.0 Hz, 3H; H6α); ^{13}C NMR (100 MHz, CD_3CN): δ = 171.1 (C=O(α), C=O(β)), 127.1, 127.2, 129.2, 129.3, 129.8, 130.0, 140.1 (-Arα, -Arβ), 103.2 (C1β), 96.2 (C1α), 94.1 (C7α), 93.8 (C7β), 79.5 (C3α), 78.5 (C3β), 77.6 (C4β), 76.3 (C4α), 71.2 (C5β), 70.2 (C5α), 63.0 (C2β), 59.3 (C2α), 23.2 (CH_3(α)), 23.0 (CH_3(β)), 17.1 (C6α), 16.9 (C6β); IR (thin film): ν_{max} = 1673 (C=O); *m/z* (ESI+ve): 294 ($[M + H]^+$, 100%); HRMS (ESI+ve): found 294.1335 $[M+H]^+$; $C_{15}H_{20}NO_5^+$ requires 294.1336.

2-Acetamido-2,6-dideoxy-L-glucose 41
DOWEX® 50WX8-200 (H^+ form) (100 mg) was added into a solution of **40** (110 mg, 0.38 mmol) in water / ethanol (1:1, 5 mL). After stirring at rt for 15 h, TLC (ethyl acetate/methanol, 9:1) indicated the disappearance of **40** (R_f 0.71) and the formation of a new spot (R_f 0.17). Then resin was filtered off and solvent was removed *in vacuo* to yield **41** as a white solid (α:β ratio 10:3) (69 mg, 90%).
m.p.: 180-184 °C; $[\alpha]_D^{20}$ = -53 (*c* = 0.22 in MeOH), $[\alpha]_D^{20}$ = -48 (*c* = 1.0 in H_2O) {lit.[34] m.p.: 201-204, $[\alpha]_D^{20}$ = -54 to -15 (initial to eqm, *c* = 1.0 in H_2O)}; ^{1}H NMR (500 MHz, CD_3OD): δ = 5.06 (d, $J_{1,2}$ = 3.5 Hz, 1H; H1α), 4.59 (d, $J_{1,2}$ = 8.5 Hz, 1H; H1β), 3.91 (dq, $J_{5,6}$ = 6.3 Hz, $J_{5,4}$ = 9.1 Hz, 1H; H5α), 3.87 (dd, $J_{2,1}$ = 3.5 Hz, $J_{2,3}$ = 10.7 Hz, 1H; H2α), 3.68 (dd, $J_{3,4}$ = 8.9 Hz, $J_{3,2}$ = 10.7 Hz, 1H; H3α), 3.62 (dd, $J_{2,1}$ = 8.5 Hz, $J_{2,3}$ = 10.4 Hz, 1H; H2β), 3.42 (dd, $J_{3,4}$ = 8.8 Hz, $J_{3,2}$ = 10.4 Hz, 1H; H3β), 3.34-3.38 (m, 1H; H5β), 3.07 (t, $J_{4,3}$ = $J_{4,5}$ = 8.8 Hz, 1H; H4β), 3.06 (t, $J_{4,3}$ = $J_{4,5}$ = 9.0 Hz, 1H; H4α), 2.02 (s, 3H; CH_3α), 2.02 (s, 3H; CH_3β), 1.32 (d, $J_{6,5}$ 6.3 Hz, 3H; H6β), 1.26 (d, $J_{6,5}$ 6.3 Hz, 3H; H6α); ^{13}C NMR (100 MHz, CD_3OD): δ = 172.8 (C=O(α)), 172.3 (C=O(β)), 95.4 (C1β), 91.0 (C1α), 76.8 (C4α), 76.1 (C4β), 74.4 (C3β), 71.9 (C5β), 71.4 (C3α), 66.8 (C5α), 57.6 (C2β), 54.8 (C2α), 21.5 (CH_3α), 21.3 (CH_3β), 16.9 (C6β), 16.8 (C6α); IR (thin film): ν_{max} = 1633 (s, C=O); *m/z* (ESI+ve): 228 ($[M + Na]^+$, 100%); HRMS (ESI+ve): found 228.0838 $[M+Na]^+$; $C_8H_{15}NNaO_5^+$ requires 228.0842.

2-Azido-2,6-dideoxy-L-mannose 42
DOWEX@ 50WX8-200 (90 mg) was added into a solution of the protected rhamnono-azide **37** (47 mg, 0.17 mmol) in water / 1,4-dioxane (1:1, 3 mL). After stirring at rt for 18 h, TLC (ethyl acetate/methanol 9:1) indicated the disappearance of **37** (R_f 0.50). Then resin was filtered off and solvent was removed *in vacuo* to yield the azide **42** as a light yellow gum (α:β ratio 7:10) (30 mg, 95%).
$[\alpha]_D^{20}$ = +9.4 (*c* = 0.30 in H_2O); ^{1}H NMR (400 MHz, D_2O): δ = 5.20 (d, $J_{1,2}$ = 1.1 Hz, 1H; H1α), 5.01 (d, $J_{1,2}$ = 1.1 Hz, 1H; H1β), 4.04 (a-dq, $J_{2,1}$ = 1.1 Hz, $J_{2,3}$ = 3.7 Hz, 1H; H2β), 3.99-4.02 (m, 2H; H2α, H3α), 3.87 (dq, $J_{5,6}$ = 6.4 Hz, $J_{5,4}$ = 9.6 Hz, 1H; H5α), 3.81 (dd, $J_{3,2}$ = 3.8 Hz, $J_{3,4}$ = 9.5 Hz, 1H; H3β), 3.41 (dq, $J_{5,6}$ = 6.3 Hz, $J_{5,4}$ = 9.5 Hz, 1H; H5β), 3.40 (t, $J_{4,3}$ = $J_{4,5}$ = 9.6 Hz, 1H; H4α), 3.30 (t, $J_{4,3}$ = $J_{4,5}$ = 9.5 Hz, 1H; H4β), 1.27 (d, $J_{6,5}$ = 6.4 Hz, 3H; H6β), 1.25 (d, $J_{6,5}$ = 6.8 Hz, 3H; H6α); ^{13}C NMR (100 MHz, D_2O): δ = 93.4 (C1β), 92.7 (C1α), 72.9 (C4α, C3β, C5β), 72.4 (C4β), 70.5 (C3α), 68.9 (C5α), 66.7 (C2β), 65.2 (C2α), 17.3, 17.2 (C6α, C6β); IR (thin film): ν_{max} = 2106 (s, N_3); *m/z* (ESI+ve): 212 ($[M + Na]^+$, 100%); HRMS (ESI+ve): found 212.0641 $[M+Na]^+$; $C_6H_{11}NaO_4^+$ requires 212.0642.

2-Amino-2,6-dideoxy-L-mannose hydrochloride salt 43

10% Palladium on charcoal (10 % wt., 10 mg) and aqueous HCl (2 M, 0.1 mL) was added to a solution of the azide **42** (71 mg, 0.38 mmol) in H_2O (5 mL). The reaction mixture was flushed with nitrogen, argon and hydrogen gas sequentially. The reaction mixture was stirred vigorously for 2 h at rt under hydrogen atmosphere until the completion of reaction was confirmed by mass spectrometry (*m/z* (ESI+ve): 164 $[M+H]^+$). After filtration, the solvent was removed *in vacuo* to afford the HCl salt of **43** as an off white solid (α:β pyranose ratio 1:2) (75 mg, 99%).
m.p.: 186-190 °C; $[\alpha]_D^{20}$ = +21 (*c* = 0.26 in H_2O) [lit.[34] m.p.: 170–175 °C (decomp), $[\alpha]_D^{20}$ = +25.5 (*c* = 0.4 in H_2O)]; ^{1}H NMR (400 MHz, D_2O): δ = 5.32 (d, $J_{1,2}$ = 1.2 Hz, 1H; H1α), 5.17 (d, $J_{1,2}$ = 1.5 Hz, 1H; H1β), 4.10 (dd, $J_{3,2}$ = 4.7 Hz, $J_{3,4}$ = 9.6 Hz, 1H; H3α), 3.97 (dq, $J_{5,6}$ = 6.3 Hz, $J_{5,4}$ = 9.6 Hz, 1H; H5α), 3.92 (dd, $J_{3,2}$ = 4.6 Hz, $J_{3,4}$ = 9.6 Hz, 1H; H3β), 3.69 (dd, $J_{2,1}$ = 1.2 Hz, $J_{2,3}$ = 4.6 Hz, 1H; H2β), 3.63 (dd, $J_{2,1}$ = 1.3 Hz, $J_{4,5}$ = 4.6 Hz, 1H; H2α), 3.48 (dq, $J_{5,6}$ = 6.1 Hz, $J_{5,4}$ = 9.6 Hz, 1H; H5β), 3.36 (t, $J_{4,3}$ = $J_{4,5}$ = 9.6 Hz, 1H; H4α), 3.31 (t, $J_{4,3}$ = $J_{4,5}$ = 9.6 Hz, 1H; H4β), 1.30 (d, $J_{6,5}$ = 6.1 Hz, 3H; H6β), 1.28 (d, $J_{6,5}$ = 6.3 Hz, 3H; H6α); ^{13}C NMR (100 MHz, D_2O): δ = 91.3 (C1β), 90.8 (C1α), 72.8 (C5β), 72.1 (C4α), 71.9 (C4β), 69.7 (C3β), 68.5 (C5α), 67.1 (C3α), 56.3 (C2β), 55.1 (C2α), 17.2, 17.1 (C6α, C6β); *m/z* (ESI+ve): 164 ($[M + H]^+$, 100%); HRMS (ESI+ve): found 164.0917 $[M+H]^+$; $C_6H_{14}NO_4^+$ requires 164.0917.

3,5-*O*-Benzylidene-2-acetamido-2, 6-dideoxy-L-mannose 44
10% Palladium on charcoal (10 % wt., 20 mg) and acetic anhydride (0.043 mL, 0.43 mmol) were added in a solution of lactol **37** (120 mg, 0.43 mmol) in ethyl acetate / 1,4-dioxane (2:1, 6 mL). The reaction mixture was flushed with nitrogen, argon and hydrogen gas sequentially. The reaction mixture was stirred vigorously for 5 h at rt under hydrogen atmosphere until TLC (ethyl acetate/methanol 9:1) showed the disappearance of starting material (R_f 0.6) and the formation of the product (R_f 0.86). After filtration, the solvent was removed *in vacuo* to afford a residue that was purified *via* flash chromatography (ethyl acetate / ethanol 20:1) to yield the **44** as a white solid (α:β ratio 1:10) (110 mg, 88%).
m.p.: 178-180 °C; $[\alpha]_D^{20}$ = -26 (*c* = 0.82 in MeOH); ^{1}H NMR (400 MHz, CD_3OD): δ = 7.58 - 7.36 (m, 10H; -Arα, -Arβ), 5.85 (s, 1H; H7α), 5.82 (s, 1H; H7β), 5.46 (d, $J_{1,2}$ = 6.0 Hz, 1H; H1β), 5.33 (d, $J_{1,2}$ = 5.2 Hz, 1H; H1α), 4.58 (dd, $J_{3,4}$ = 1.8 Hz, $J_{3,2}$ = 4.1 Hz, 1H; H3β), 4.53-4.56 (m, 2H; H2α, H3α), 4.43 (dd, $J_{2,3}$ = 4.3 Hz, $J_{2,1}$ = 6.0 Hz, 1H; H2β), 4.39-4.35 (m, 1H; H5α), 4.32 (q, $J_{5,6}$ = 7.0 Hz, 1H; H5β), 4.07 (br-s, 1H; H4β), 3.82 (t, $J_{4,3}$ = $J_{4,5}$ = 3.0 Hz, 1H; H4α), 2.03 (s, 3H; CH_3(α)), 2.00 (s, 3H; CH_3(β)), 1.49 (d, $J_{6,5}$ = 7.2 Hz, 3H; H6β), 1.46 (d, $J_{6,5}$ = 7.0 Hz, 3H; H6α); ^{13}C NMR (100 MHz, CD_3OD): δ = 174.6 (C=O(β)), 174.3 (C=O(α)), 128.4, 128.5, 129.9, 130.1, 130.7, 130.8, 140.7 (-Arα, -Arβ), 102.8 (C1β), 97.6 (C1α), 95.9 (C7α), 94.3 (C7β), 79.6 (C4α), 78.2 (C4β), 75.4 (C3β), 74.5 (C3α), 72.7 (C5β), 72.2 (C5α), 62.4 (C2β), 57.2 (C2α), 23.2 (CH_3(α), CH_3(β)), 17.8 (C6α), 17.0 (C6β); IR (thin film): ν_{max} = 1653 (C=O); *m/z* (ESI+ve): 294 ($[M + H]^+$, 100%); HRMS (ESI+ve): found 294.1330 $[M+H]^+$; $C_{15}H_{20}NO_5^+$ requires 294.1336.

2-Acetamido-2, 6-dideoxy-L-mannose 45
DOWEX® 50WX8-200 (H^+ form) (90 mg) was added into a solution of **44** (90 mg, 0.31 mmol) in water / ethanol (1:1, 5 mL). After stirring at RT for 15 h, TLC (ethyl acetate/methanol 9:1) indicated the disappearance of **44** (Rf 0.86) and the formation of a new spot (R_f 0.17). Then resin was filtered off and solvent was removed *in vacuo* to yield **45** as a white solid (α:β pyranose ratio 5:2) (60 mg, 98%).
m.p.: 144-146 °C; $[\alpha]_D^{20}$ = +8.9 (*c* = 0.36 in MeOH); ^{1}H NMR (400 MHz, CD_3OD): δ = 4.85 (d, $J_{1,2}$ = 1.1 Hz, 1H; H1α), 4.72 (d, $J_{1,2}$ = 1.5 Hz, 1H; H1β), 4.31 (dd, $J_{2,1}$ = 1.3 Hz, $J_{2,3}$ 4.4, 1H; H2β), 4.15 (dd, $J_{2,1}$ = 1.4 Hz, $J_{4,5}$ = 4.7 Hz, 1H; H2α), 3.86 (dd, $J_{3,2}$ = 4.7 Hz, $J_{3,4}$ = 9.6 Hz, 1H; H3α), 3.75 (dq, $J_{5,6}$ = 6.3 Hz, $J_{5,4}$ = 9.3 Hz, 1H; H5β), 3.50 (dd, $J_{3,2}$ = 4.6 Hz, $J_{3,4}$ = 9.2 Hz, 1H; H3β), 3.22 (t, $J_{4,3}$ = $J_{4,5}$ = 9.6

Hz, 1H; H4α), 3.14-3.18 (m, 1H; H5α), 3.11 (t, $J_{4,3} = J_{4,5} = 9.3$ Hz, 1H; H4β), 1.96 (s, 3H; CH_3α), 1.91 (s, 3H; CH_3β), 1.22 (d, $J_{6,5} = 6.0$ Hz, 3H; H6β), 1.17 (d, $J_{6,5} = 6.3$ Hz, 3H; H6α); ^{13}C NMR (100 MHz, CD_3OD): δ = 175.5 (C=O(β)), 174.3 (C=O(α)), 95.0 (C1β), 94.8 (C1α), 74.4 (C4α), 74.2 (C4β), 74.0 (C3β), 70.2 (C3α), 69.1 (C5β), 56.1 (C2β), 55.6 (C2α), 50.0 (C5α), 22.9 (CH_3β), 22.7 (CH_3α), 18.2 (C6α), 18.1 (C6β); IR (thin film): ν_{max} = 1636 (C=O); *m/z* (ESI+ve): 228 ([M + Na]$^+$, 100%); HRMS (ESI+ve): found 228.0840 [M+H]$^+$; $C_8H_{15}NNaO_5^+$ requires 228.0842.

C 2-Deoxy-2-fluoro-L-rhamnose 16 and 2-Deoxy-2-fluoro-L-quinovose 17 from 3,4-di-*O*-acetyl rhamnal

1, 3, 4-Tri-*O*-acetyl-2-fluoro-2, 6-dideoxy-β-L-mannose 46β

Selectfluor (2.16 g, 6.1 mmol) was added to a solution of diacetyl rhamnal **15** (1.0 g, 4.6 mmol) in acetonitrile/water (40 mL, 3:1) at 0 °C. The reaction mixture was stirred at rt for 16 h until TLC (cyclohexane/ethyl acetate, 1:1) showed the disappearance of starting material (R_f 0.81). After removing solvent *in vacuo*, the mixture was dissolved into ethyl acetate (20 mL) and was washed with water (20 mL). Organic phase was dried ($MgSO_4$), filtered and solvent was removed *in vacuo* to obtain a residue (900 mg) which was dissolved into acetic anhydride/pyridine (20 mL, 1:1). The mixture was stirred for 6 h until TLC (hexane/ethyl acetate, 1:1) showed the formation of two major products (R_f 0.80, R_f 0.78). After removing solvent *in vacuo*, the residue was purified *via* flash chromatography (cyclohexane/ethyl acetate, 7:1) to yield **46β** (400 mg, 30%) with minor impurities. A mixture of **46α** and **47** (500 mg, 38%) was also isolated from chromatography. **46β** was further purified by crystallization in ether to obtain pure **46β** as a white solid (360 mg, 27%)

m.p.: 124-126 °C; $[\alpha]_D^{20}$ = -84 (*c* = 0.40 in MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.21 (dd, $J_{1,2}$ = 2.2 Hz, $J_{1,F}$ = 7.0, 1H; H1), 5.22 (ddd, $J_{3,2}$ = 2.6 Hz, $J_{3,4}$ = 10.3 Hz, $J_{3,F}$ = 24.2 Hz, 1H; H3), 5.18 (ddd, $J_{4,F}$ = 2.0 Hz, $J_{4,5}$ = 8.3 Hz, $J_{4,3}$ = 10.3 Hz, 1H; H4), 4.75 (dt, $J_{2,1} = J_{2,3}$ = 2.2 Hz, $J_{2,F}$ = 48.9 Hz, 1H; H2), 3.96 (dq, $J_{5,6}$ = 6.4 Hz, $J_{5,4}$ = 8.8 Hz, 1H; H5), 2.16 (s, 3H; CH_3), 2.12 (s, 3H; CH_3), 2.07 (s, 3H; CH_3), 1.24 (d, $J_{6,5}$ 6.4 Hz, 3H; H6); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.3 (C=O), 169.6 (C=O), 168.3 (C=O), 90.1 (d, $J_{1,F}$ = 31 Hz; C1), 86.2 (d, $J_{2,F}$ = 180 Hz; C2), 70.2 (C4), 69.4 (d, $J_{3,F}$ 17 Hz; C3), 68.8 (C5), 20.9 (CH_3), 20.7 (CH_3), 20.6 (CH_3), 17.3 (C6); ^{19}F NMR (376 MHz, $CDCl_3$): δ = -203.6 (dddd, $J_{F,4}$ = 2.3 Hz, $J_{F,1}$ = 7.0 Hz, $J_{3,F}$ = 26.0 Hz, $J_{3,F}$ = 48.0 Hz); IR (thin film): ν_{max} = 1760, 1742 (C=O); *m/z* (ESI+ve): 315 ([M+H]$^+$, 100%); HRMS (ESI+ve): found 315.0851 [M+Na]$^+$; $C_{12}H_{19}FNaO_5^+$ requires 315.0851.

2,6-Dideoxy-2-fluoro-L-mannose (2-Deoxy-2-fluoro-L-rhamnose) 16

Trifluoroacetic acid (1 mL) was added to a solution of **46β** (170 mg) in water (2 mL). The mixture was stirred at 60 °C for 12 h until TLC (ethyl acetate/methanol 9:1) showed the disappearance of starting material (R_f 0.96) and the formation of one product (R_f 0.68). Solvent was removed *in vacuo* to obtain 2,6-dideoxy-2-fluoro-mannose **16** as a colorless syrup (α:β ratio 5:3) (96 mg, 100%).

$[\alpha]_D^{20}$ = -3.5 (*c* = 0.91 in H_2O); ^{1}H NMR (400 MHz, D_2O): δ = 5.30 (dd, $J_{1,2}$ = 1.8 Hz, $J_{1,F}$ = 7.5 Hz, 1H; H1α), 4.98 (d, $J_{1,F}$ = 20.5 Hz, 1H; H1β), 4.79 (dd, $J_{2,3}$ = 2.5 Hz, $J_{2,F}$ = 51.2 Hz, 1H; H2β), 4.75 (dt, $J_{2,3} = J_{2,1}$ = 2.2 Hz, $J_{2,F}$ = 49.3 Hz, 1H; H2α), 3.90-3.95 (m, 1H; H5α), 3.86 (ddd, $J_{3,2}$ = 2.5 Hz, $J_{3,4}$ = 9.7 Hz, $J_{3,F}$ = 31.4 Hz, 1H; H3α), 4.72 (ddd, $J_{3,2}$ = 2.6 Hz, $J_{3,4}$ = 9.5 Hz, $J_{3,F}$ = 30.8 Hz, 1H; H3β), 3.43-3.50 (m, 1H; H5β), 3.45 (t, $J_{4,3} = J_{4,5}$ = 9.7 Hz, 1H; H4α), 3.40 (dt, $J_{4,F}$ = 1.0 Hz, $J_{4,3} = J_{4,5}$ = 9.5 Hz, 1H; H4β), 1.31 (d, $J_{6,5}$ = 6.1 Hz, 3H; H6β), 1.29 (d, $J_{6,5}$ = 6.3 Hz, 3H; H6α); ^{13}C NMR (100 MHz, D_2O): δ = 92.7 (C1β, d, $J_{1,F}$ = 16 Hz), 92.1 (C2β, d, $J_{2,F}$ = 179 Hz), 91.8 (C1α, d, $J_{1,F}$ = 45 Hz), 91.1 (C2α, d, $J_{2,F}$ = 171 Hz), 72.8 (C4α), 72.6 (C5β), 72.4 (C4β), 72.1 (C3β, d, $J_{3,F}$ = 18 Hz), 69.7 (C3α, d, $J_{3,F}$ = 18 Hz), 68.9 (C5α), 17.2 (C6α, C6β); ^{19}F NMR (376 MHz, D_2O): δ = -204.5 (ddd, $J_{F,1}$ = 7.0 Hz, $J_{F,3}$ = 32.0 Hz, $J_{F,2}$ = 49.2 Hz), -223.0 (ddd, $J_{F,1}$ = 20.6 Hz, $J_{F,3}$ = 30.9 Hz, $J_{F,2}$ = 51.5 Hz); *m/z*

(ESI+ve): 189 ([M + Na]$^+$, 100%); HRMS (ESI+ve): found 189.0532 [M+Na]$^+$; $C_6H_{11}FNaO_4^+$ requires 189.0534.

2,6-Dideoxy-2-fluoro-L-glucose (2-Deoxy-2-fluoro-L-quinovose) 17

Trifluoroacetic acid (2.5 mL) was added to a solution of the mixture of **46α** and **47α/β** (200 mg, obtained from the preparation of **46β**) in water (2.5 mL). The mixture was stirred at 60 °C for 12 h until mass spectrum showed the completion of the reaction. After removing solvent *in vacuo*, **17** (5.2 mg) was purified from the mixture (94 mg, containing **16** and **17**) *via* HPLC.

$[\alpha]_D^{20}$ -38 (c 0.26, H_2O) {lit.[32] $[\alpha]_D^{20}$ -35 (*c* 0.27, H_2O)}; ^{1}H NMR (400 MHz, D_2O): δ = 5.38 (d, $J_{1,2}$ = 4.0 Hz, 1H; H1α), 4.87 (dd, $J_{1,F}$ = 2.5 Hz, $J_{1,2}$ = 7.9 Hz, 1H; H1β), 4.42 (ddd, $J_{2,1}$ = 4.0 Hz, $J_{2,3}$ = 9.5 Hz, $J_{2,F}$ = 49.3 Hz, 1H; H2α), 4.09 (ddd, $J_{2,1}$ = 7.9 Hz, $J_{2,3}$ = 9.2 Hz, $J_{2,F}$ = 51.5 Hz, 1H; H2β), 3.91 (dq, $J_{5,6}$ = 6.3 Hz, $J_{5,4}$ = 9.5 Hz, 1H; H5α), 3.90 (ddd, $J_{3,4}$ = 9.3 Hz, $J_{3,2}$ = 9.5 Hz, $J_{3,F}$ = 13.3 Hz, 1H; H3α), 3.73 (td, $J_{3,4}$ = $J_{3,2}$ = 9.2 Hz, $J_{3,F}$ = 15.1 Hz, 1H; H3β), 3.52 (dq, $J_{5,6}$ = 6.3 Hz, $J_{5,4}$ = 9.6 Hz, 1H; H5β), 3.21 (dd, $J_{4,3}$ = 9.2 Hz, $J_{4,5}$ = 9.6 Hz, 1H; H4β), 3.19 (dd, $J_{4,3}$ = 9.3 Hz, $J_{4,5}$ = 9.5 Hz, 1H; H4α), 1.28 (d, $J_{6,5}$ = 6.3 Hz, 3H; H6β), 1.25 (d, $J_{6,5}$ = 6.3 Hz, 3H; H6α); ^{13}C NMR (100 MHz, D_2O): 92.5 (d, $J_{1,F}$ 23.5 Hz; C1β), 92.4 (d, $J_{2,F}$ 182.8 Hz; C2β), 89.7 (d, $J_{2,F}$ 185.6 Hz; C2α), 88.7 (d, $J_{1,F}$ 21.3 Hz; C1α), 73.9 (d, $J_{4,F}$ 7.9 Hz; H4α), 73.8 (d, $J_{4,F}$ 7.9 Hz; H4β), 73.0 (d, $J_{3,F}$ 17 Hz; H3β), 71.3 (d, $J_{5,F}$ 1.3 Hz; C5β), 70.1 (d, $J_{3,F}$ 17 Hz; C3α), 66.5 (d, $J_{5,F}$ 1.2 Hz; C5α), 15.7 (C6α, C6β); ^{19}F NMR (376 MHz, D_2O): δ = -199.4 -199.0 (m, Fα and Fβ); *m/z* (ESI+ve): 189 ([M + Na]$^+$, 100%).

Acknowledgements

This work was supported by the Biotechnology and Biological Sciences Research Council [BB/M011321/1 to JTH], the Leverhulme Trust (GWJF), Xunta de Galicia (proyect GRC2014/040) and Galchimia S.A..

Supporting Information

Supporting Information: Copies of NMR spectra (^{1}H, ^{13}C and ^{19}F). This material is available free of charge via the Internet at http://pubs.acs.org/.

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