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Bicyclic Iminosugars

Conformationally Restricted Oxazolidin-2-one Fused Bicyclic Iminosugars as Potential Glycosidase Inhibitors

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Abstract: The synthesis of fused bicyclic oxazolidin-2-one (OZO) iminosugars was achieved through a tandem Staudinger reduction/retro-Michael/intramolecular Michael addition from the corresponding OZO azidosugars. Those precursors, based on both aldopentofuranoses and ketofuranohexoses backbones, were obtained following alkylation and oxidation of the related oxazolidine-2-thione (OZT) azidosugars. Eight OZO based iminosugars were isolated in good yields and evaluated for their potency as glycosidases inhibitors, thus extending the family of known 1-Deoxynojirimycin (DNJ) bicyclic analogues.

Introduction

Glycoside hydrolases or glycosidases (GHs)[1a] are carbohydrate processing enzymes responsible for the hydrolysis of the glycosidic bond, which is a widespread biological process. Thus, glycosidases can be used as therapeutic targets for the treatment of several diseases such as diabetes, viral infection, lysosomal storage disorder or cancers. This is why great efforts have been made over recent years to design and synthesize selective and potent inhibitors for potential therapeutical applications, as well as tools for chemical biology and extremely useful probes for a better understanding of the mode of action of these enzymes.[1b–1g] Most GHs inhibitors are carbohydrate mimetics[2] and among them, iminosugars (sugars with an endocyclic nitrogen atom) have attracted considerable attention since the discovery of nojirimycin **A**.[3] At physiological pH, the nitrogen atom of the iminosugar is protonated and these charged species mimic the cationic transition state of the natural substrate, which allows the carbohydrate analogue to compete and inhibit the hydrolysis process. Thus, iminosugars display a high therapeutical potential, which is illustrated by *N*-butyl-1-deoxynojirimycin **B** (Miglustat, Zavesca™) and Miglitol **C** (Glyset™), both clinically used for the control of Gaucher's disease related to disturbed lysosomal storage and type II diabetes, respectively (Figure 1).[4] As a result, much effort has been made around the structural variation of 1-deoxynojirimycin **D** (DNJ)-like compounds. However, despite their therapeutic potential, most iminosugars suffer from a low specificity probably due to their flexible conformation. Conse-

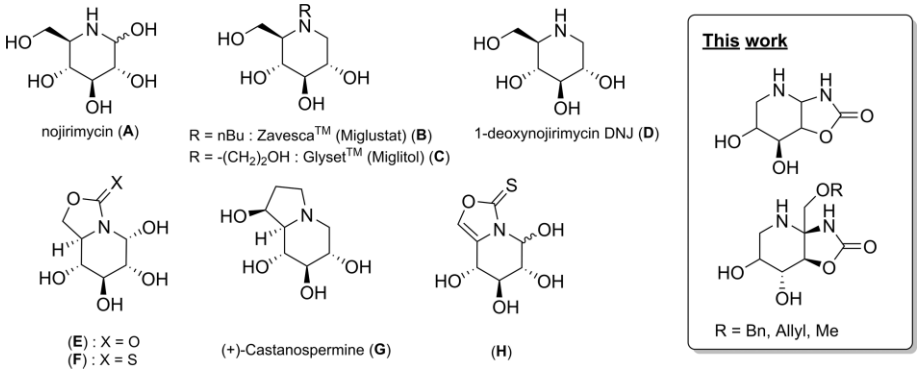

Figure 1. Examples of iminosugars used as therapeutics, synthetic analogues and proposed work.

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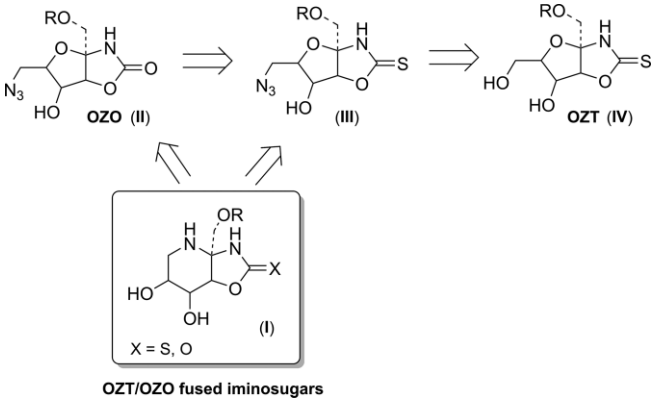
quently, bicyclic iminosugars such as pyrrolidizines, indolizidines and nortropanes have attracted attention due to their rigid structures, which induce higher and more specific GH inhibitory activity.[5] The synthesis of conformationally locked iminosugars such as imidazopiperidine derivatives, triazole and tetrazole fused iminosugars, has also been explored. Indeed the modification of the sp^3 nitrogen atom into a sp^2 function such as pseudoamide type (urea, thiourea, carbamate) led to innovative glycomimetics with increased selectivities and retaining good inhibitory activities.[6] For example, compounds **E** & **F** are potent and selective inhibitors of yeast α-glucosidase (K_i = 2.2 μM and 40 μM respectively with complete α specificity).[7] Our group has also reported the synthesis of castanospermine **G** analogues bearing oxazole-2-(3)-thione moieties **H**.[8]

In this work, we explored the synthesis of modified oxazolidinethiones (OZT) and oxazolidinones (OZO) iminosugars (**I**) (Scheme 1)**.** We were concerned with the development of efficient synthetic pathways towards common precursors amenable to both OZT and OZO fused iminosugars. Both aldopentoses and ketohexoses templates were targeted, in order to thoroughly investigate the structure-activity relationship of these novel glycomimetics as potential glycosidase inhibitors. Our synthetic approach relies on an innovative tandem Staudinger reduction-aminocyclisation of OZT azidosugars (**III**) or OZO azidosugars (**II**) accessible from native sugars via the corresponding OZT sugars (**IV**).[9]



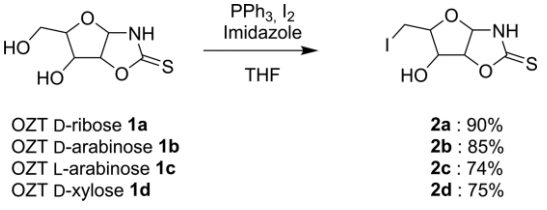
Scheme 1. Retrosynthetic pathway to bicyclic OZT(O) fused iminosugars (ketohexoses and pentoses).

Results and Discussion

Two main approaches are used to introduce the OZT function in the sugar precursors, either from a β-amino alcohol with a thionocarbonyl source such as thiophosgene or carbon disulfide, or directly on reducing sugars by reacting with thiocyanic acid.[9,10] This last approach was the one favored in this work since it gives a rapid access to the OZT using safe, non-toxic reagents in mild conditions, usually in good yields. It also has the advantage of rapidly giving the parent OZO derivatives through oxidation. Four different pentoses series have been explored, while for the ketohexoses, we chose to work from 1-*O*-benzyl-D-fructopyranose and 1-*O*-protected-L-sorbopyranose (methyl, benzyl and allyl).

Synthesis of OZO(T) Azidosugars

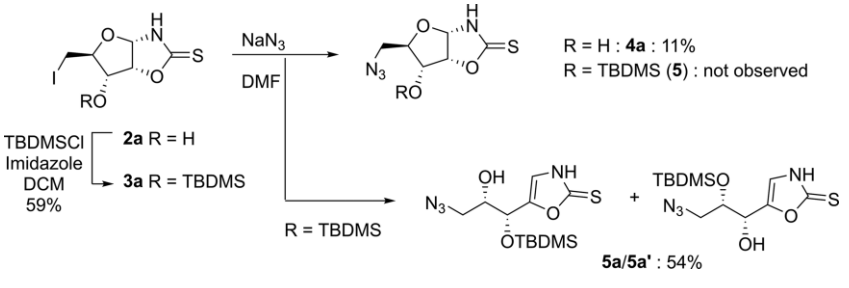
The OZT fused sugars were obtained from native D-ribose, D-xylose, D- and L-arabinose, following previously reported procedure.[9a] The primary alcohol position was then activated through Garegg's iodination[11] and the OZT 5-iodosugars **2a**–**2d** were obtained in good yields ranging from 74 % to 90 % (Scheme 2).



Scheme 2. Synthesis of fused OZT 5-iodopentoses- **2a**–**2d**.

The following step was the introduction of the azido moiety through nucleophilic displacement of the iodo group. When first working on the D-ribose based OZT **2a**, classical conditions using sodium azide in DMF led to the desired compound **4a** but in a poor 11 % yield, mainly due to the degradation of the starting material (Scheme 3). Prior protection of the free hydroxyl at the C-3 position with a *tert*-butyldimethylsilyl group (TBDMS) did not allow the formation of the desired azide. Based on the isolated products, we assume that the unstable 5-azido product undergoes ring opening at the hemiaminal *C*-1 position followed by tautomeric equilibrium to lead to the oxazole-2-thione **5a** in 54 % yield. This product was observed by NMR spectroscopy as a mixture of two isomers **5a** and **5a′** resulting from the migration of the TBDMS group on both hydroxyl groups. Similar results were obtained when performing the reactions in D-*arabino* series (data not shown).

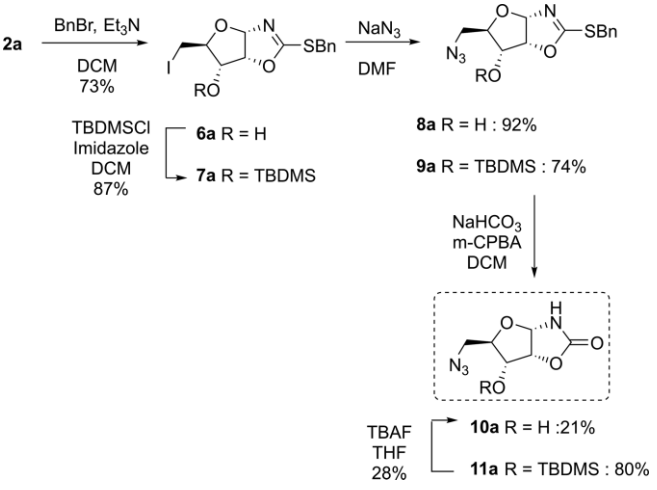
To avoid these parasite reactions, we decided to focus on the preparation of the corresponding OZO (Scheme 4). Thus,



Scheme 3. Synthesis of OZT 5-azido-D-ribose derivative **4a**.

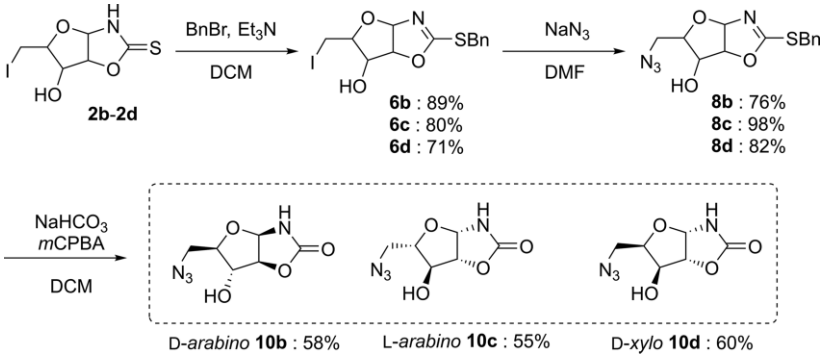
OZT 5-iodo-D-ribofuranose **2a** was alkylated using benzyl bromide in the presence of triethylamine in dichloromethane and the *S*-benzylated product was obtained in a good 73 % yield. *S*-Alkylation could be assessed by ^{13}C NMR spectroscopy, from the chemical shift of *C*=*S* which moved from 189 ppm down to 173 ppm after alkylation. Subsequent nucleophilic substitution of the iodogroup with sodium azide was successful and gave the desired 5-azido compound **8a** in an excellent 92 % yield. From there, the OZO function could be obtained through an oxidative desulfurisation with *m*-chloroperbenzoic acid (*m*-CPBA) and sodium bicarbonate.[9b,9f] However, the OZO 5-azido-D-ribose **10a** was only isolated in a low 21 % yield. The protection of 3-OH with a TBDMS increased the yield of the oxidation up to 80 % (**11a**). The desilylation step was unfortunately quite low yielding (28 %), making the overall synthetic pathway less interesting than the direct one.

With this synthetic sequence in hands, similar conditions were applied to the OZT 5-iodo-D-*arabino*, L-*arabino* and D-*xylo* derivatives **2b**–**2d** (Scheme 5). The three OZTs **8b**–**8d** could be obtained in good yields (58–78 %) over 2 steps and the corresponding final OZO 5-iodosugars derivatives **10b**–**10d** were obtained with yields close to 60 %.



Scheme 4. Synthesis of OZO 5-azido-D-ribose **10a**.

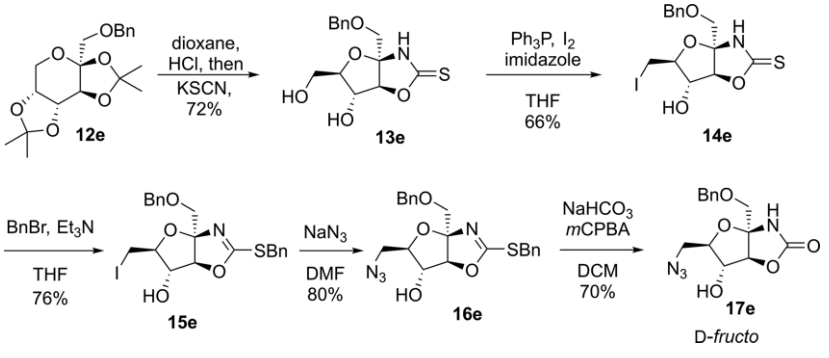
The azido group could be installed using the usual three steps sequence involving Garegg's iodination, *S*-benzylation and nucleophilic displacement of the iodine with sodium azide to give



Scheme 5. Exemplification with pentoses.

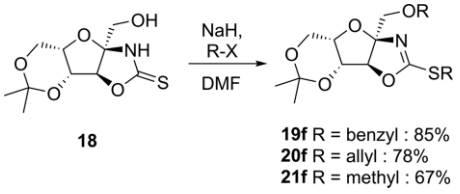
In the D-fructose series, we decided to apply similar conditions as for aldopentoses (Scheme 6). 1-*O*-benzyl-2:3,4:5-di-*O*-isopropylidene-D-fructose **12e** was first prepared from D-fructose in two steps.[9b,9d] Acid hydrolysis of both acetals afforded the 1-*O*-benzyl-D-fructopyranose which could be directly condensed with potassium thiocyanate to give the desired OZT 1-*O*-benzyl-D-fructofuranose **13e** in 72 % yield over two steps. **16e** with a 40 % overall yield. Finally, oxidation with *m*CPBA afforded the desired OZO **17e** in a good 70 % yield.

In the L-sorbose series, we slightly modified our strategy in order to simultaneously introduce both alkyl groups at a later stage in the sequence and then perform the transformation of the OZT into OZO before introducing the azido group. The synthetic pathway is shorter than the one described for the



Scheme 6. Synthesis of OZO 6-azido-1-*O*-benzyl-D-fructose **17e**.

D-*fructo* series and allows the introduction of diverse protecting groups on the C-1 position later in the sequence. To this end, the OZT group was introduced on native L-sorbose to give the OZT furanose, which conformation was locked by the introduction of the 4,6-*O*-*iso*propylidene group (Scheme 7). From this OZT furano intermediate **18**, bisalkylation could be achieved using either benzyl bromide, allyl bromide or methyl iodide as the electrophile in *N*,*N*-dimethylformamide, in the presence of sodium hydride. The bisalkylated products **19–21f** were thus isolated in good yields ranging from 67 to 85 %.



Scheme 7. L-Sorbose approach: synthesis of bisalkylated intermediates.

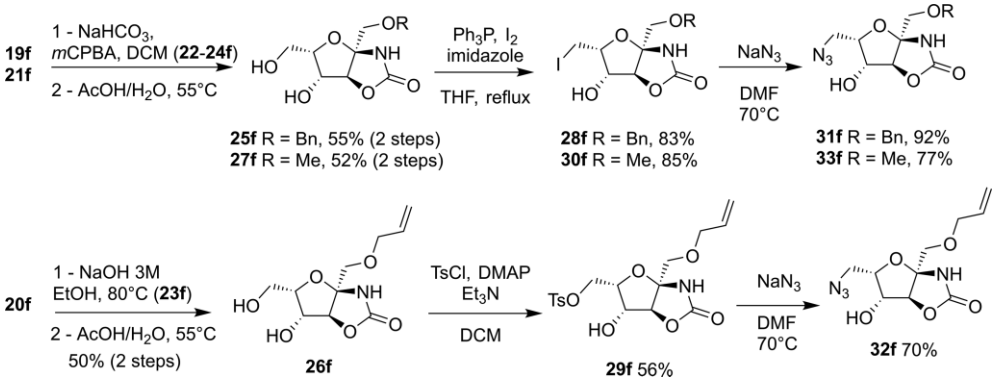
Bisalkylated products **19f** and **21f** were then submitted to *m*-CPBA oxidation to form the corresponding OZO, followed by acid hydrolysis of the isopropylidene acetal (Scheme 8). Benzyl- and methyl OZO **19f** and **21f** were obtained in reasonable yields of 55 and 52 % respectively. Introduction of the azide was achieved in the usual conditions, by nucleophilic substitution of the 6-iodo derivatives **28f** and **30f** with sodium azide. Finally, the L-sorbo OZO precursors **31f** and **33f** were obtained over 6 steps in 15 and 11 % yields from L-sorbose. For the allyl derivative, due to the presence of the reactive double bond and the possible side reactions, the formation of the OZO could be achieved using a basic hydrolysis with sodium hydroxide in ethanol. Once the acetal hydrolyzed, the desired OZO 1-*O*-allyl-sugar **26f** was obtained in 50 % yield over 2 steps. The synthesis of the 6-iodo derivative under Garegg's conditions also turned out to be problematic with a very low 17 % yield, so the azido group was installed via the tosylate **29f** with an overall yield of 39 % over two steps for compound **32f**.

Finally, we managed to access OZT 5-azidoD-ribose **4a**, OZO 5-azidoaldopentoses **10a**–**10d** and OZT 6-azidoketohexoses **17e** and **31–33f**, which were then engaged in the cyclisation towards the corresponding iminosugars.

Synthesis of Iminosugars. One-Pot Staudinger Reduction/ retro-Michael/Michael Addition

Cyclisation of the aldopentoses derivatives was first studied. The OZT 5-azido-D-ribose was first submitted to Staudinger reduction[12] using 5 equivalents of triphenylphosphine in a 5:1 THF/water mixture at room temperature overnight (Table 1, entry 1). Unfortunately, only the aminosugar **34a** could be isolated, in a very low 7 % yield, rather than the desired iminosugar. As a control experiment, the reduction conditions were also applied to the *S* and 3-*O*-protected compounds **9a** and the corresponding aminosugar **35a** was isolated in a much better 86 % yield (entry 2). When moving to OZO derivatives, the 3-*O*-TBDMS protected D-ribose derivative gave the iminosugar **37a/a′** in 51 % yield (entry 3). These iminosugars were formed as a mixture of 2 isomers (separable by column chromatography) resulting from the migration of the silylated protecting group from the 3- to the 4-OH position. When changing the conditions to Pd/C in ethanol and ammonium formate, the iminosugar **37a/a′** was isolated in a lower 44 % yield and the migration of the silyl group was also observed (entry 4). In both cases, the aminosugar **36a** was also observed up to 30 % but could not be isolated as a pure product. For the unprotected azide **10a**, the OZO D-*ribo*-iminosugar **38a** was observed by NMR analysis of the crude mixture but could not be isolated due to purification difficulties and separation of the polar iminosugar from the triphenylphosphine oxide by-product (entry 5). Reverse phase silica gel column chromatography was also attempted with no success. To overcome this problem, supported PS-PPh_3 was used but, once again, the iminosugar **38a** was detected but not isolated pure. However, the structure of **38a** could be confirmed by comparison with a pure sample obtained from desilylation of iminosugars **37a** and **37a′**. More interestingly, the D-*xylo* precursor **10d** allowed the formation of the corresponding iminosugar **38d** in a moderate 41 % yield (entry 8) while D- and L-*arabino* azides led to iminosugars **38b** and **38c** in good 67 % and 66 % yields respectively (entries 6 and 7).

The optimized conditions for the aldopentose azides were then applied to the ketohexoses derivatives (Table 2). We first studied the cyclisation of one OZT derivative we already had in hands. However, the OZT azido L-*sorbo* derivative **44f** gave



Scheme 8. L-Sorbose approach: synthesis of OZO 1-*O*-protected-6-azido sugars.

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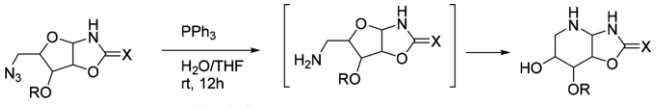
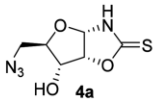
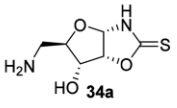
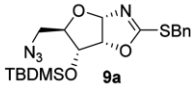
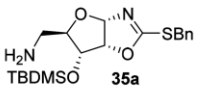
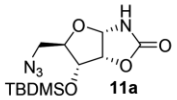
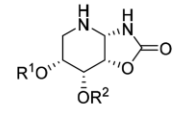
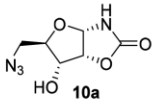
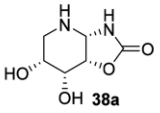
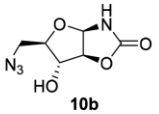
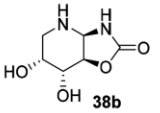
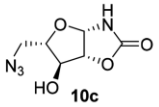
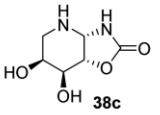
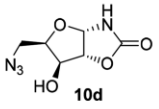
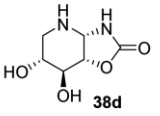
Table 1. Staudinger reduction of pentoses-derived OZO(T) sugars.

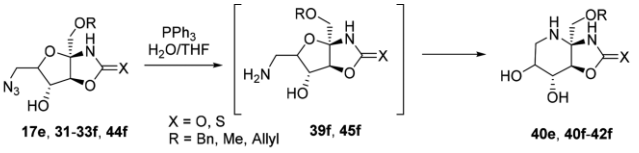


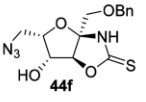
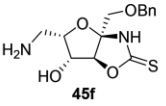
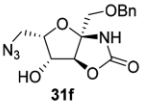
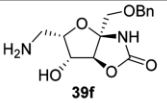
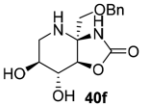
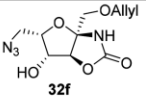
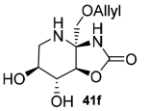
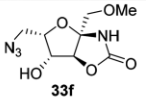
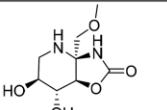
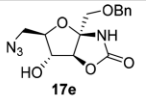
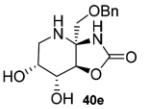
entry	series	product	yield
1	 **4a** D-*ribo*	 **34a**	7%[a]
2	 **9a** D-*ribo*	 **35a**	86%[a]
3	 **11a** D-*ribo*	 **37a**: R^1 = H, R^2 = TBDMS **37a'**: R^1 = TBDMS, R^2 = H	51%[b]
4[b]			44%[c]
5	 **10a** D-*ribo*	 **38a**	ni[d]
6	 **10b** D-*arabino*	 **38b**	67%
7	 **10c** L-*arabino*	 **38c**	66%
8[e]	 **10d** D-*xylo*	 **38d**	41%[d]

[a] Iminosugar not detected. [b] Global yield: the 3-OTBDMS **37a** (15 %) and 4-OTBDMS **37a'** (36 %) iminosugars were isolated; aminosugar **36a** was also detected. [c] Using HCO_2NH_4, Pd/C, EtOH, 12 h, 45 °C; global yield: 3-OTBDMS (14 %) and 4-OTBDMS (30 %); aminosugar **36a** was also detected but couldn't be purified. [d] Both PPh_3 and PPh_3-PS. [e] 4 % of SM **10d** also recovered. [f] 5 % of aminosugar **36d** also isolated.

solely the aminosugar **45f** in 50 % yield. When we heated the reaction at 50 °C, the aminosugar **45f** was isolated with a lower 22 % yield whereas the corresponding iminosugar was not detected (entries 1 and 2). At room temperature the OZO derivative **31f** gave the aminosugar **39f**, which was identified by NMR but could not be isolated as a pure product (entry 3). Heating the reaction at 50 °C overnight gave the desired iminosugar **40f** in a good 67 % yield (entry 4). All the other OZO azidoketohexoses **17e**, **32f**–**33f** gave also the desired iminosugars **40e** and **40f**–**42f** in moderate to good yields from 55 to 70 %. Neither the nature of the protecting group (benzyl, allyl or methyl) nor the sugar series influenced the good outcome of the reaction (entries 5 to 7).

Table 2. Staudinger reduction applied to ketohexoses OZT **44f** and OZO **17e**, **31–33f**.



entry	starting azide	conditions	product	yield
1[a]	 **44f** L-*sorbo*	r.t., o/n	 **45f**	50%[b]
2		50°C, o/n		22%[b]
3	 **31f** L-*sorbo*	r.t., 6h	 **39f**	ni[c]
4		50°C, 4h	 **40f**	67%[d]
5	 **32f** L-*sorbo*	50°C, 4h	 **41f**	70%[d]
6	 **33f** L-*sorbo*	50°C, 5h	 **42f**	62%[d]
7	 **17e** D-*fructo*	50°C, 15h	 **40e**	55%[d]

[a] **44f** was prepared from iodation/azidation of OZT 1-*O*-Bn-L-sorbose[9b] (see SI for experimental details). [b] Iminosugar not detected. [c] ni = could not be isolated. [d] Amino sugar not detected.

While optimizing the cyclisation of the benzylated L-*sorbo* derivative **31f**, the reaction was completed after 4 h at 50 °C (entry 4). However, after silica gel column chromatography, the iminosugar **40f** was obtained as a mixture of two compounds, shown to be isomers by mass spectrometry analysis. Careful comparison with previous results (entry 3) revealed these two compounds as the aminosugar **39f** and the iminosugar **40f**. The equilibrium between both forms is favored in polar, protic media. NMR monitoring of a solution of a 45:55 mixture amino/iminosugar (obtained from column chromatography), in deuterated methanol showed that the ratio evolves over time: after 8 days, an equilibrium is reached at a 25:75 ratio of amino/imino forms (see supporting information, Figure S2). Finally, the whole procedure was optimised to isolate the pure iminosugar and avoid the formation of the amino form. To this end we discovered that all the work-up, purification and analyses should be carried out in non-protic solvents as much as possible (entries 4–7).

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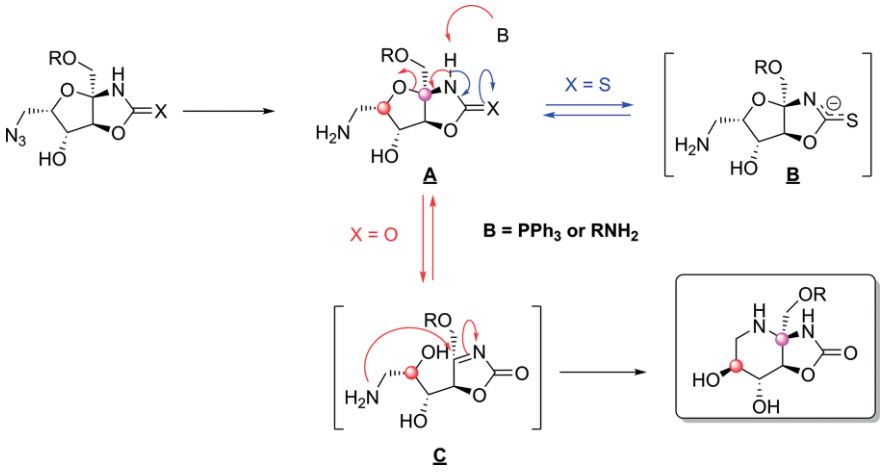

Scheme 9. Postulated mechanism: one-pot retro-Michael/Michael addition (example of L-*sorbo* series).

Finally, we proposed the following mechanism for this cyclisation (Scheme 9 - example of L-*sorbo* derivative): following Staudinger reduction of the azido group into the amine **A**, the cyclisation can occur through a retro-Michael reaction leading to the imine intermediate **C** followed by a Michael addition of the amine onto the C-2 position (C-1 for the pentoses). This retro-Michael reaction can be catalysed by traces of base or nucleophile, such as triphenylphosphine or another amine residue. However, for the OZT, the softer sulfur atom is a better stabilizing group for the negative charge than the oxygen atom **B**, which probably disfavors the formation of the imine intermediate and terminates the reaction at the amino-OZT product.

To summarise, the preparation and the cyclisation of the OZT azidosugars turned out more problematic than the OZO analogues. Indeed, no OZT iminosugar could be isolated, only the corresponding aminosugars that were quite unstable (degradation when heating). However, eight OZO-fused bicyclic iminosugars were synthetized: compounds **40–42f** and **40e** based on ketohexoses scaffolds and **38a-d** based on aldopentoses (Figure 2).

All the structures were confirmed by NMR spectroscopy (^{1}H, ^{13}C and 2D correlations). The high field shift of the pseudoanomeric carbon resonance (signals observed around 66 ppm for the pentoses (C-1) and 75 ppm for the ketohexoses (C-2), with Δ ppm of around 20 ppm) confirmed the aminoketalic bicyclic structure. For the pentoses iminosugars, the vicinal proton-proton coupling constants around the six-membered ring are indicative of a $^4C_1$ chair conformation for the D-*xylo* iminosugar **38d** and the L-*arabino* **38c** (Figure 3), with the α-pseudoanomeric substituent being axial, thus fitting the anomeric effect (see supporting information for detailed *J* values, Table S2. On the contrary, the D-*arabino* derivative adopts a $^1C_4$ conformation, the β-pseudoanomeric substituent thus being also axial. For the D-*ribo* derivative, coupling constants were not clearly discriminant but we assumed a $^1C_4$ chair, due to similar $J_{1,2}$ value and $J_{4,5}$ values in favor of H4 being equatorial. Overall, some coupling constants values were slightly lower to what was expected, especially close to the junction with the OZO (notably $J_{2\text{-}3}$ ca. 6.5–6.8Hz for **38b**–**d**), so it is likely that the chair conformation is somehow twisted. In the ketohexoses family, the L-*sorbo* derivatives display large $J_{4,5}$ and medium $J_{3,4}$ coupling constant values, in agreement with a $^2C_5$ conformation (only OBn derivative **40f** shown). In addition, a large $J_{5,6}$ coupling constant, could be measured for **40f** which reinforces the hypothesis that H5 is axial. Similarly, the D-*fructo* derivative is likely to adopt a $^2C_5$ conformation due to $J_{3,4}$ and $J_{5,6}$ values similar to the L-*sorbo* derivatives (Figure 3 and SI).

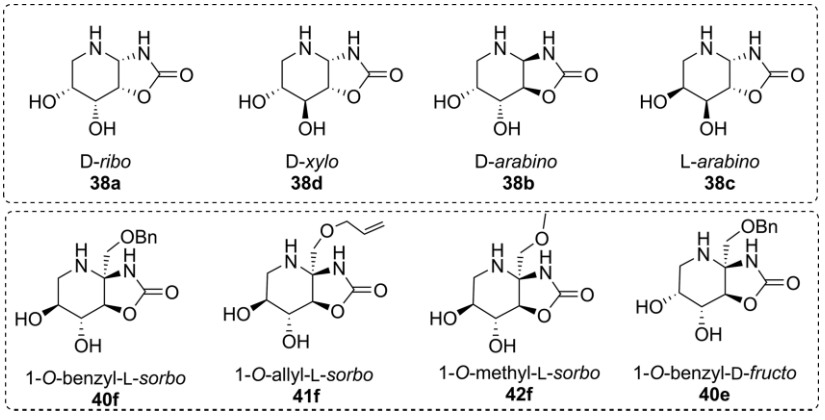

Figure 2. Summary of prepared OZO fused iminosugars.

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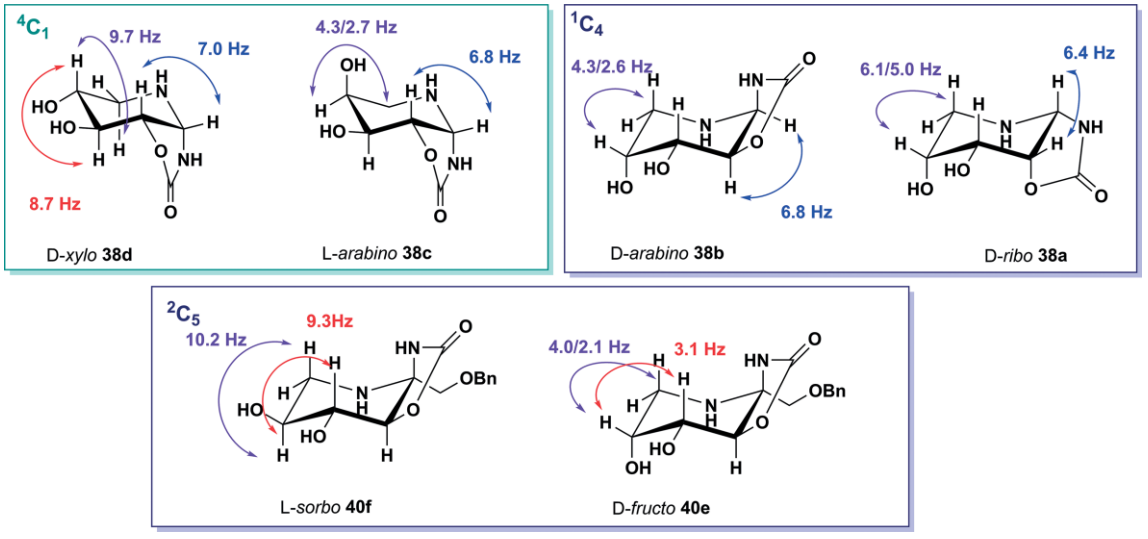

Figure 3. Conformational analysis of bicyclic iminosugars (400 MHz NMR; aldopentoses spectra were recorded in CD_3OD, for ketohexoses different solvents had to be used, see SI for experimental details).

Conformational Analysis – Molecular Modelling

Conformational analysis of each series of iminosugars was performed on a DFT-6-31G++ level using Spartan software in polar solvent (see experimental part and SI for more details). Conformational search followed by minimization of each conformer was achieved. The results for the pentose series are in agreement with the conclusions of the NMR analysis in favour of a

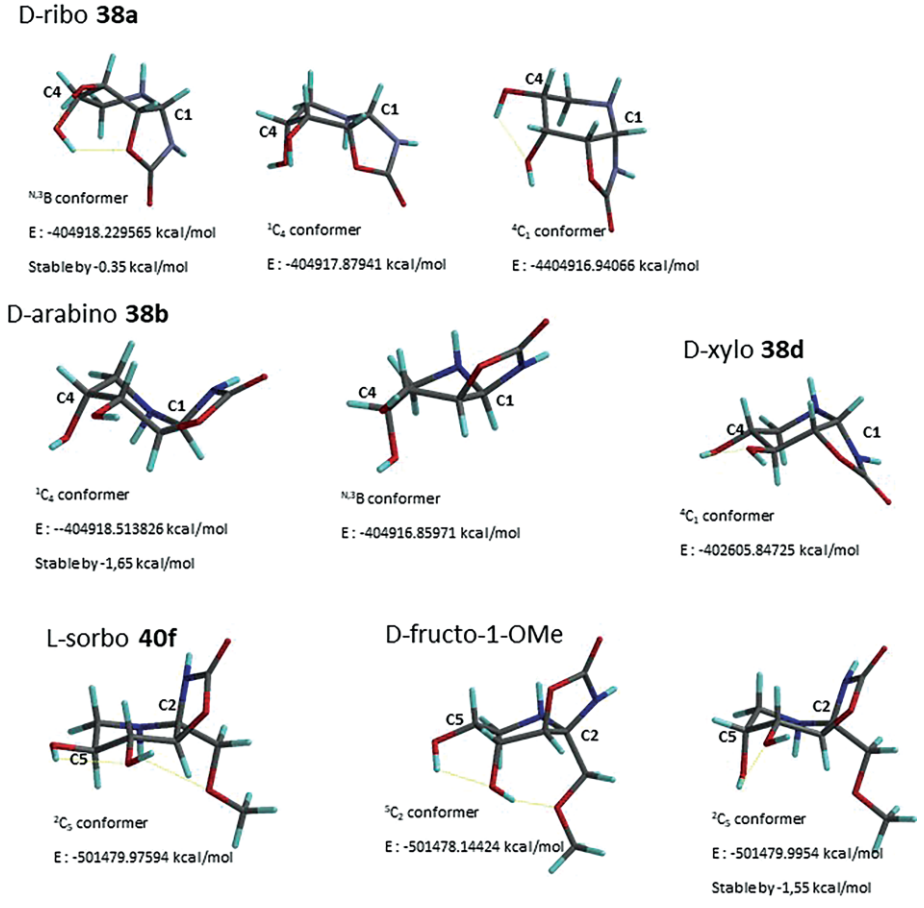

Figure 4. Geometrically DFT-optimised conformations of iminosugars **38a**, **38b** and **38d** of the pentose series together with the L-*sorbo* **40f** and the 1-*O*–Me D-*fructo* compounds.[a]

$^4C_1$ conformation for the D-*xylo* derivative **38d** and a $^1C_4$ conformation for the D-*arabino* **38b** and D-*ribo* derivatives **38a** (Figure 4). Similarly, to the NMR data analysis, the determination of the D-*ribo* conformer **38a** proved to be more difficult as two closely related conformers were in balance: a $^1C_4$ conformer showing 5 possible energy minimum conformers representing a Boltzmann weight of 0.263 while the boat structures (4 conformers) represent a heavier Boltzmann weight of 0.486. The possible $^4C_1$ conformer proved far less important (0.046 BW). Relying on the NMR data, the most probable conformer in solution might be the $^1C_4$ with a much higher flexibility. On the contrary, only the $^4C_1$ conformer of the D-xylopyranose **38d** was observed. For the ketohexose series, the conformational search was performed on 1-*O*-methyl derivatives such as L-*sorbo* **42f**. In both series, the optimised conformers turned out to be a $^2C_5$ structure.

Glycosidase Inhibitory Activity

The inhibitory potency of the synthesized compounds was assessed against a range of GHs: α/β-D-glucosidase, α/β-D-galactosidase, α/β-D-mannosidase, and β-D-glucuronidase (see SI, Figures S1, S2 and Table S1). Unfortunately, most of the compounds showed little or no inhibition when assayed at 1 mM. Still, only OZO D-*arabino* and L-*arabino* iminosugars **38b** and **38c** were able to inhibit around 40 % of β-D-glucosidase and α-D-galactosidase activities respectively. Both compounds turned out to be competitive inhibitors of each enzyme with respective K_i values of 68.3 ± 2.2 μM (β-Glu) and 445 ± 90 μM (α-Gal), hence exhibiting similar inhibition constants as previously reported sp^2-iminosugars, in the sub-millilolar range.[7b] Iminosugar **38b** derived from β-D-arabinopyranose, could eventually be structurally related to β-D-glucopyranose, as C-1 and C-4 stereochemistry are conserved. More interestingly, the OZO iminosugar **38c** based on β-L-arabinopyranose, is more closely related to the structure of α-D-galactopyranose. Thus, there is still a reasonable scope for variations in the structure of these mixed OZO iminosugar structures to further improve their inhibitory potency and understand their selectivity and mechanisms of interaction with glycosidases.

Conclusion

We have developed a novel and efficient synthetic pathway towards 1,2-fused oxazolidinone iminosugars a new class of glycosidase inhibitors. Our strategy relies on an innovative Staudinger reduction/retro-Michael/aza-Michael sequence and allowed for the preparation of both aldopentoses and ketohexoses based bicyclic OZO iminosugars. Eight novel compounds were synthesized and evaluated as potential GHs inhibitors, thus extending the family of conformationally restricted bicyclic DNJ analogues. Both D- and L-*arabino* based iminosugars showed moderate inhibition properties with remarkable selectivity on β-D-glucosidase and α-D-galactosidase respectively, thus encouraging the synthesis of novel GHs inhibitors built with this unusual scaffold.

Experimental Section

General methods. Flash silica column chromatography was performed on silica gel 60N (spherical, neutral, 40–63 μm) or using a Reveleris® flash chromatography system. The reactions were monitored by thin layer chromatography (TLC) on silica gel 60F254 precoated aluminium plates. Compounds were visualized under UV light and by charring with a 10 % H_2SO_4 ethanolic solution spray or a solution of potassium permanganate. Solvents were dried by standard methods: THF was purified with a dry station GT S100 immediately prior use, dichloromethane was distilled from P_2O_5; methanol and *N*,*N*-dimethylformamide were dried with molecular sieves; pyridine and triethylamine were dried with potassium hydroxide. Molecular sieves were activated prior use by heating for 4 h at 500 °C. All other commercial solvents and reagents were used without further purification. All reactions were carried out under dry argon atmosphere. Melting points were determined in open capillary tubes using a Büchi 510 apparatus and are uncorrected. The infrared spectra of compounds were recorded on a Perkin–Elmer PARAGON 1000 PC instrument, and values are reported in cm^{-1}. Optical rotation were recorded on a Jasco P2000 polarimeter at 20 °C, values are given in deg dm^{-1} g^{-1} mL with concentrations reported in g/100mL. ^1H NMR and ^{13}C NMR were recorded with Bruker Avance II 250 MHz or an Avance III HD Nanobay 400 MHz spectrometer. Assignments of both ^1H and ^{13}C signals were based on DEPT 135 sequence, homo- and heteronuclear 2D correlations. Chemical shifts are reported in parts per million (ppm) using tetramethylsilane as the internal standard. Coupling constants (*J*) are reported and expressed in Hertz (Hz), splitting patterns are designated as b (broad), s (singlet), d (doublet), dd (doublet of doublet), q (quartet), dt (doublet of triplet), ddd (doublet of doublet of doublet), m (multiplet). High-resolution mass spectra (HRMS) were performed on a Maxis Bruker 4G by the "Federation de Recherche" ICOA/CBM (FR2708) platform in the electrospray ionisation (ESI) mode. The following solvents have been abbreviated: ethyl acetate (EA), petroleum ether (PE), tetrahydrofuran (THF), and DMF (*N*,*N*-dimethylformamide), DMSO (dimethyl sulfoxide).

Glucosidase inhibition assay.

α-D-glucosidase (from *S. cerevisiae*), β-D-glucosidase (from almonds), α-D-galactosidase (from green coffee beans), β-D-galactosidase (from *E. coli*), α-D-mannosidase (from jack beans), β-D-glucuronidase (from bovine liver) were purchased from Sigma (St Louis, USA). β-D-mannosidase (from *D. thermophilum*) was cloned, and expressed as described previously.[13] 4-nitrophenylglycosides substrates were purchased from Carbosynth (UK).

GHs activities were assayed for 30 minutes at 37 °C in 200 μL reaction mixture containing 4-nitrophenylglycoside substrate, inhibitor (1 mM) in Tris buffer (50 mM, pH 7.0) or 2-(*N*-morpholino)ethanesulfonic (MES) buffer (50 mM, pH 5.0) (individual conditions, e.g. origin and concentration of enzymes, substrate concentration, ••• are reported in supporting information, table S1). After incubation, 100 μL of 1 M sodium carbonate was added, and the amount of released para-nitrophenol was quantified by absorbance measurement at 405 nm (ε_{405} = 19500 M^{-1} cm^{-1}). Product formation rates were extracted and uncatalytic activities were determined using DMSO instead of inhibitor as control. Means and standard deviations were calculated from 3 independent data.

Enzyme inhibition mechanism and Ki calculation were done by determining enzymatic activities in presence of a range of substrate and inhibitor concentrations for the corresponding enzyme. Model fitting and constants determination from 3 independent experiments were done using Prism 4 (GraphPad).

DFT calculations.

Quantum chemical calculations using the density functional theory (DFT) method were performed. The initial geometries for these compounds have been generated using molecular modeling Spartan Student (wavefunction.in). Automated complete geometry optimizations were performed using the DFT method by employing B3LYP/6-31 G** basic set function on Spartan Student software. SCF model: A restricted hybrid HF-DFT SCF calculation was performed using Pulay DIIS + Geometric Direct Minimization Polarizable Continuum solvation model was applied. Solvation: C-PCM dielectric = 37.22. Cartesian coordinates are detailed in the supporting information.

Synthesis of OZO(T) azidosugars.

D-*ribo*, *arabino* and *xylo* furanosylamines **1a,1b** and **1d** were prepared following literature procedures **9**[a,b] OZT 6-Azido-1-*O*-benzyl-L-sorbose **44f** was prepared from 1-*O*-benzyl-2-*N*,3-*O*-thiocarbonyl-α-L-sorbofuranosylamine **9**[b] .

1-*N*,2-*O*-Thiocarbonyl-β-L-arabinofuranosylamine (1c). L-Arabinose (3 g, 19.6 mmol, 1 equiv.) was suspended in water (0.5 M) then KSCN (4.5 g, 46.3 mmol, 2.4 equiv.) and HCl 37 % (10 mL, 6.1 equiv.) were added. The pink solution obtained was stirred at 55 °C for 24–48h. Water was removed by co-evaporation with toluene under reduced pressure and the crude product was purified by silica gel column chromatography using pure EA, to yield the desired product **1c** as a brown solid (3.1 g, 83 %). R_f = 0.66 (EA/MeOH, 90:10); m.p. 130–134 °C; $[\alpha]_D^{20}$ = +54 (*c* 1, MeOH); ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ (ppm) = 3.17–3.37 (m, 2H, H-5), 3.85–3.92 (m, 1H, H-4), 3.23–3.26 (m, 1H, H-3), 4.95 (t, 1H, ^3J = 5.4 Hz, OH-5), 5.05 (d, 1H, $^3J_{1\text{-}2}$ = 5.7 Hz, H-2), 5.70 (d, 1H, $^3J_{OH\text{-}3}$ = 4.3 Hz, OH-3), 5.80 (d, 1H, $^3J_{1\text{-}2}$ = 5.7Hz, H-1), 10.82 (s, 1H, NH); ^{13}C NMR (62.5 MHz, [D$_6$]DMSO): δ (ppm) = 60.9 (CH$_2$-5), 74.3 (CH-3), 87.1 (CH-4), 89.3 (CH-1), 91.5 (CH-2), 188.2 (C=S); IR (neat) (ν, cm^{-1}) = 3304 (OH + NH), 1482 (C-N), 1034 (C=S); HRMS (ESI$^+$): *m/z* = calculated for $C_6H_{10}NO_4S$ ([M + H]$^+$): 192.0325, found 192.0329.

General procedure 1: iodation of OZT sugar. OZT sugar (1 equiv.) was dissolved in THF (0.3 M) and cooled to 0 °C, then Ph_3P (2 equiv.), imidazole (2 equiv.) and iodine (2.5 equiv.) were added and the suspension was stirred for 2h at r.t. The resulting mixture was concentrated under reduced pressure then purified by silica gel column chromatography using PE/EA, yielding **2a**–**2d**, **14e**.

5-Deoxy-5-iodo-1-*N*,2-*O*-thiocarbonyl-α-D-ribofuranosylamine (2a). General procedure 1 was followed using OZT **1a** (710 mg, 3.72 mmol) and gave after purification (PE/AE: 30:70) the desired OZT iodo compound **2a** as a yellow solid (1.01 g, 90 %). R_f = 0.71 (EA/PE: 90:10); m.p. 171–174 °C; $[\alpha]_D^{20}$ = +24 (*c* 0.33, MeOH); ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ (ppm) = 3.26–3.33 (m, 2H, H-5b and H-4), 3.53–3.57 (m, 1H, H-5a), 3.72–3.77 (m, 1H, H-3), 5.16 (t, 1H, $^3J_{2\text{-}3}$ = $^3J_{2\text{-}1}$ = 5.3 Hz, H-2), 5.73 (d, 1H, $^3J_{1\text{-}2}$ = 5.5Hz, H-1), 5.88 (d, 1H, $^3J_{OH\text{-}3}$ = 6.2 Hz, OH), 10.79 (s, 1H, NH); ^{13}C NMR (62.5 MHz, [D$_6$]DMSO): δ (ppm) = 6.5 (CH$_2$-5), 74.9 (CH-3), 77.0 (CH-4), 84.8 (CH-2), 87.5 (CH-1), 189.5 (C=S); IR (neat) (ν̃, cm^{-1}) = 3279 (OH + NH), 1518 (C-N), 1073 (C=S), 601 (C-I); HRMS (ESI$^+$): *m/z* = calculated for $C_6H_9INO_3S$ ([M + H]$^+$): 301.9342, found 301.9341.

5-Deoxy-5-iodo-1-*N*,2-*O*-thiocarbonyl-β-D-arabinofuranosylamine (2b). General procedure 1 was followed using OZT **1b** (697 mg, 3.65 mmol) and gave after purification (PE/EA, 70:30) the desired OZT iodo compound **2b** as a white solid (934 mg, 85 %). R_f = 0.45 (PE/EA: 50:50); m.p. 169–173 °C; $[\alpha]_D^{20}$ = –24 (*c* 0.407, MeOH); ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ (ppm) = 3.14 (dd, 1H, $^3J_{5b\text{-}4}$ = 7.3 Hz, $^3J_{5b\text{-}5a}$ = 10.5 Hz, H-5b), 3.19 (dd, 1H, $^3J_{5a\text{-}4}$ = 7.1 Hz, $^3J_{5a\text{-}5b}$ = 10.5 Hz, H-5a), 4.04 (td, 1H, $^3J_{4\text{-}3}$ = 2.2 Hz, $^3J_{4\text{-}5a}$ = $^3J_{4\text{-}5b}$ = 7.2 Hz, H-4), 4.24–4.27 (m, 1H, H-3), 5.11 (dd, 1H, $^3J_{2\text{-}3}$ = 1.1 Hz, $^3J_{2\text{-}1}$ = 5.6 Hz, H-2), 5.88 (d, 1H, $^3J_{1\text{-}2}$ = 5.6 Hz, H-1), 5.95 (d, 1H, $^3J_{OH\text{-}3}$ = 4.4 Hz, OH-3), 10.99 (s, 1H, NH); ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ (ppm) = 6.2 (CH$_2$-5), 76.4 (CH-3), 85.4 (CH-4), 89.5 (CH-1), 91.2 (CH-2), 188.1 (C=S); IR (neat) (ν̃, cm^{-1}) = 3296 (NH + OH), 1151 (C=S), 1035 (CN), 607 (C-I); HRMS (ESI$^+$): *m/z* = calculated for $C_6H_9INO_3S$ ([M + H]$^+$): 301.9342, found 301.9341.

5-Deoxy-5-iodo-1-*N*,2-*O*-thiocarbonyl-β-L-arabinofuranosylamine (2c). General procedure 1 was followed using OZT **1c** (1.70 g, 8.89 mmol) and gave after purification (PE/EA: 60:40) the desired OZT iodo compound **2c** as a white solid (1.97 g, 74 %). R_f = 0.52 (PE/EA: 40:60); m.p. 172–176 °C; $[\alpha]_D^{20}$ = +52 (*c* 1, MeOH); ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ (ppm) = 3.14 (dd, 1H, $^3J_{5b\text{-}4}$ = 7.3 Hz, $^3J_{5b\text{-}5a}$ = 10.5 Hz, H-5b), 3.19 (dd, 1H, $^3J_{5a\text{-}4}$ = 7.1 Hz, $^3J_{5a\text{-}5b}$ = 10.5 Hz, H-5a), 4.04 (td, 1H, $^3J_{4\text{-}3}$ = 2.3 Hz, $^3J_{4\text{-}5a}$ = $^3J_{4\text{-}5b}$ = 7.2 Hz, H-4), 4.24–4.26 (m, 1H, H-3), 5.12 (dd, 1H, $^3J_{2\text{-}3}$ = 0.6Hz, $^3J_{2\text{-}1}$ = 5.7 Hz, H-2), 5.89 (d, 1H, $^3J_{1\text{-}2}$ = 5.7 Hz, H-1), 5.96 (d, 1H, $^3J_{OH\text{-}3}$ = 4.4 Hz, OH), 10.99 (s, 1H, NH); ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ (ppm) = 6.2 (CH$_2$-5), 76.4 (CH-3), 85.5 (CH-4), 89.6 (CH-1), 91.3 (CH-2), 188.1 (C=S); IR (neat) (ν̃, cm^{-1}) = 3311 (OH + NH), 1488 (C-N), 1036 (C=S), 607 (C-I); HRMS (ESI$^+$): *m/z* = calculated for $C_6H_9INO_3S$ ([M + H]$^+$): 301.9342, found 301.9341.

5-Deoxy-5-iodo-1-*N*,2-*O*-thiocarbonyl-α-D-xylofuranosylamine (2d). General procedure 1 was followed using OZT **1d** (1.7 g, 8.90 mmol) and gave after purification (PE/EA, 50:50) the desired OZT iodo compound **2d** as a white solid (2.01 g, 75 %). R_f = 0.3 (PE/EA: 50:50); m.p. 168–170 °C; $[\alpha]_D^{20}$ = +24 (*c* 0.33, MeOH); ^{1}H NMR (250 MHz, CDCl$_3$): δ (ppm) = 3.22 (dd, 1H, $^3J_{5b\text{-}4}$ = 7.2 Hz, $^3J_{5b\text{-}5a}$ = 9.8 Hz, H-5b), 3.28–3.36 (m, 1H, H-5a), 3.90 (td, 1H, $^3J_{4\text{-}3}$ = 2.6 Hz, $^3J_{4\text{-}5a}$ = $^3J_{4\text{-}5b}$ = 6.9 Hz, H-4), 4.23 (dd, 1H, $^3J_{3\text{-}4}$ = 2.7 Hz, $^3J_{3\text{-}OH}$ = 5.3 Hz, H-3), 5.12 (d, 1H, $^3J_{2\text{-}1}$ = 5.4 Hz, H-2), 5.81 (d, 1H, $^3J_{OH\text{-}2}$ = 5.3 Hz, OH), 5.88 (d, 1H, $^3J_{1\text{-}2}$ = 5.4 Hz, H-1), 10.8 (s, 1H, NH); ^{13}C NMR (62.5 MHz, CDCl$_3$): δ (ppm) = 0.0 (CH$_2$-5), 72.6 (CH-3), 80.4 (CH-4), 88.7 (CH-1), 90.0 (CH-2), 188.4 (C=S); IR (cm^{-1}) (neat) (ν̃, cm^{-1}) = 3314 (NH +OH), 1155 (C=S), 628 (C-I); HRMS (ESI$^+$): *m/z* = calculated for $C_6H_9INO_3S$ ([M + H]$^+$): 301.9342, found 301.9339.

1-*O*-Benzyl-6-deoxy-6-iodo-2-*N*,3-*O*-thiocarbonyl-β-D-fructofuranosylamine (14e). General procedure 1 was followed using OZT **13e**[9b] (3.70 g, 8.7 mmol), triphenylphosphine (2.0 equiv.), imidazole (2.5 equiv.) and iodine (2.0 equiv.) for 5 hours. The desired OZT iodo compound **14e** was obtained after purification (PE/EA = 70:30) as a white sticky foam (2.40 g, 66 %). R_f = 0.49 (PE/EA: 70:30); $[\alpha]_D^{20}$ = –21 (*c* 1.02, MeOH); ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) = 3.11–3.18 (m, 2H, H-6b, OH), 3.22 (dd, 1H, $^2J_{6a\text{-}6b}$ = 10.5 Hz, $^3J_{6a\text{-}5}$ = 6.7 Hz, H-6a), 3.68 (d, 1H, $^2J_{1b\text{-}1a}$ = 9.9 Hz, H-1b), 3.76 (d, 1H, $^2J_{1a\text{-}1b}$ = 9.9 Hz, H-1a), 4.42–4.49 (m, 1H, H-5), 4.54 (d, 1H, $^3J_{4\text{-}OH}$ = 9.3 Hz, H-4), 4.61 (d, 1H, ^2J = 11.8 Hz, CH$_2$ Bn), 4.67 (d, 1H, ^2J = 11.8 Hz, CH$_2$ Bn), 5.01 (s, 1H, H-3), 7.29–7.49 (m, 5H, CH Ar); ^{13}C NMR (100 MHz, CDCl$_3$): δ (ppm) = 3.8 (CH$_2$-6), 69.8 (CH$_2$-1), 74.4 (CH$_2$ Bn), 76.5 (CH-4), 89.3 (CH-5), 93.1 (CH-3), 100.1 (C-2), 128.3 (CH Ar), 128.8 (CH Ar), 129.0 (CH Ar), 136.1 (Cq Ar), 188.4 (C=S); IR (neat) (ν̃, cm^{-1}) = 3233 (NH+OH), 3028 (C$_{sp2}$-H), 1310 (C-O), 1091 (C=S), 1027 (C-N), 510 (C-I); HRMS (ESI$^+$): *m/z* = calculated for $C_{14}H_{17}INO_4S$ ([M + H]$^+$): 421.9917, found 421.9917.

1-*O*-Benzyl-6-deoxy-6-iodo-2-*N*,3-*O*-thiocarbonyl-α-L-sorbofuranosylamine (43f). General procedure 1 was followed using 1-*O*-benzyl-2-*N*,3-*O*-thiocarbonyl-α-L-sorbofuranosylamine **9**[b] (860 mg, 2.8 mmol) and gave after silica gel column chromatography (PE/EA: 70:30) the desired product as a brown oil (680 mg, 59 %). R_f = 0.71 (PE/EA: 50:50); ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) = 2.98 (d, 1H, $^3J_{OH\text{-}4}$= 10.5 Hz, OH), 3.23–3.31 (m, 2H, CH$_2$-6), 3.67 (d,

1H, $^2J_{1b\text{-}1a}$ = 9.9 Hz, H-1b), 3.76 (d, 1H, $^2J_{1a\text{-}1b}$ = 9.9 Hz, H-1a), 4.28–4.32 (m, 1H, H-5), 4.47 (dd, 1H, $^3J_{4\text{-}OH}$ = 10.5 Hz, $^3J_{5\text{-}4}$ = 2.4 Hz, H-4), 4.60 (d, 1H, ^2J = 11.8 Hz, CH_2Bn), 4.67 (d, 1H, ^2J = 11.8 Hz, CH_2Bn), 5.01 (s, 1H, H-3), 7.26–7.41 (m, 5H, CH Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = –3.0 (CH_2-6), 69.3 (CH_2-1), 73.7 (CH-4), 74.3 (CH_2 Bn), 82.3 (CH-5), 91.8 (CH-3), 99.0 (C-2), 128.2 (CH Ar), 128.9 (CH Ar), 129.0 (CH Ar), 136.0 (Cq Ar), 189.0 (C=S); MS (ESI$^+$): *m/z* = 422.0 ([M + H]$^+$), 439.0 ([M + Na]$^+$).

General procedure 2: benzylation of OZT sugars.

OZT iodosugar (1 equiv.) was dissolved in THF (0.1 M) and cooled to –5 °C, then the Et_3N (4 equiv.) and BnBr (2 equiv.) were added and the solution was stirred for 2 h at r.t. The resulting mixture was concentrated under reduced pressure and then purified by silica gel column chromatography using PE/EA, yielding **6a**-**d**.

2-Benzylsulfanyl-4,5-dihydro-(5-deoxy-5-iodo-α-D-ribofuranoso) [2,1-d]-1,3-oxazole (**6a**). General procedure 2 was followed using OZT **2a** (1.13 g, 3.74 mmol) and gave after purification (PE/EA: 90:10) the desired OZT iodo compound **6a** as an orange solid (1.07 g, 73 %). R_f = 0.85 (PE/EA: 50:50); m.p. 86–88 °C; $[\alpha]_D^{20}$ = +35 (*c* 0.39, $CHCl_3$); ^{1}H NMR (250 MHz, CD_3OD): δ (ppm) = 3.17 (ddd, 1H, $^3J_{4\text{-}5a}$ = 2.8 Hz, $^3J_{4\text{-}5b}$ = 6.0 Hz, $^3J_{4\text{-}3}$ = 8.9 Hz, H-4), 3.31–3.38 (m, 1H, H-5b), 3.59 (dd, 1H, $^3J_{5a\text{-}4}$ = 2.8 Hz, $^3J_{5a\text{-}5b}$ = 11.1 Hz, H-5a), 3.91 (dd, 1H, $^3J_{3\text{-}2}$ = 5.5 Hz, $^3J_{3\text{-}4}$ = 8.9 Hz, H-3), 4.32 (d, 1H, ^2J = 13.3 Hz, CH_2 Bn), 4.39 (d, 1H, ^2J = 13.3 Hz, CH_2 Bn), 4.99 (t, 1H, $^3J_{2\text{-}3}$ = $^3J_{2\text{-}1}$ = 5.4 Hz, H-2), 5.96 (d, 1H, $^3J_{1\text{-}2}$ = 5.3 Hz, H-1), 7.29–7.39 (m, 3H, CH Ar), 7.42–7.46 (m, 2H, CH Ar); ^{13}C NMR (62.5 MHz, CD_3OD): δ (ppm) = 4.9 (CH_2-5), 36.8 (CH_2 Bn), 77.0 (CH-3), 78.0 (CH-4), 84.9 (CH-2), 99.7 (CH-1), 128.7 (CH Ar), 129.7 (CH Ar), 130.0 (CH Ar), 137.9 (Cq Ar), 173.2 (N=CS); IR (neat) ($\tilde{\nu}$, cm^{-1}) = 3184 (OH), 1566 (C=N), 606 (C-I); HRMS (ESI$^+$): *m/z* = calculated for $C_{13}H_{15}INO_3S$ ([M + H]$^+$): 391.9812, found 391.9810.

2-Benzylsulfanyl-4,5-dihydro-(5-deoxy-5-iodo-α-D-arabinofuranoso) [2,1-d]-1,3-oxazole (6b). General procedure 2 was followed using OZT **2b** (500 mg, 1.66 mmol) and gave after purification (PE/EA: 70:30) the desired OZT iodo compound **6b** as a brown oil (578 mg, 89 %). R_f = 0.53 (PE/EA: 50:50); $[\alpha]_D^{20}$ = –44 (*c* 0.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 2.88 (dd, 1H, $^3J_{5b\text{-}4}$ = 9.5 Hz, $^3J_{5b\text{-}5a}$ = 10.3 Hz, H-5b), 3.04–3.09 (m, 1H, OH), 3.09 (dd, 1H, $^3J_{5a\text{-}4}$ = 5.3 Hz, $^3J_{5a\text{-}5b}$ = 10.3 Hz, H-5a), 4.18 (ddd, 1H, $^3J_{4\text{-}3}$ = 2.5 Hz, $^3J_{4\text{-}5a}$ = 5.3 Hz, $^3J_{4\text{-}5b}$ = 9.5 Hz, H-4), 4.25 (d, 1H, ^2J = 13.4 Hz,CH_2 Bn), 4.29 (d, 1H, ^2J = 13.4 Hz,CH_2 Bn), 4.42–4.43 (m, 1H, H-3), 4.91 (dd, 1H, $^3J_{2\text{-}3}$ = 1.2 Hz, $^3J_{2\text{-}1}$ = 5.9 Hz, H-2), 6.14 (d, 1H, $^3J_{1\text{-}2}$ = 5.9 Hz, H-1), 7.25–7.39 (m, 5H, CH Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 5.1 (CH_2-5), 36.5 (CH_2 Bn), 78.6 (CH-3), 85.9 (CH-4), 90.2 (CH-2), 101.1 (CH-1), 128.0 (CH Ar), 128.8 (CH Ar), 129.2 (CH Ar), 136.2 (Cq Ar), 170.3 (C=N); IR (neat) ($\tilde{\nu}$, cm^{-1}) = 3241 (OH), 1579 (C=N), 606 (C-I); HRMS (ESI$^+$): *m/z* = calculated for $C_{13}H_{15}INO_3S$ ([M + H]$^+$): 391.9812, found 391.9811.

2-Benzylsulfanyl-4,5-dihydro-(5-deoxy-5-iodo-β-L-arabinofuranoso) [2,1-d]-1,3-oxazole (6c). General procedure 2 was followed using OZT **2c** (1.43 g, 4.75 mmol) and gave after purification (PE/EA: 70:30) the desired OZT iodo compound **6c** as a colorless oil (1.49 g, 80 %). R_f = 0.53 (PE/EA: 50:50); $[\alpha]_D^{20}$ = +39 (*c* 1, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 2.90 (t, 1H, $^3J_{5b\text{-}5a}$ = $^3J_{5b\text{-}4}$ = 9.7 Hz, H-5b), 3.09 (dd, 1H, $^3J_{5a\text{-}4}$ = 5.4 Hz, $^3J_{5a\text{-}4}$ = 10.4 Hz, H-5a), 3.76 (bs, 1H, OH), 4.16–4.20 (m, 1H, H-4), 4.26 (s, 2H,CH_2 Bn), 4.41–4.42 (m, 1H, H-3), 4.93 (d, 1H, $^3J_{2\text{-}3}$ = 5.8 Hz, H-2), 6.13 (d, 1H, $^3J_{1\text{-}2}$ = 5.8 Hz, H-1), 7.24–7.41 (m, 5H, CH Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 5.2 (CH_2-5), 36.4 (CH_2 Bn), 78.4 (CH-3), 85.7 (CH-4), 90.3 (CH-2), 100.8 (CH-1), 128.0 (CH Ar), 128.8 (CH Ar), 129.1 (CH Ar), 136.0 (Cq Ar), 170.5 (N=CS); IR (neat) ($\tilde{\nu}$, cm^{-1}) = 3233 (OH), 1580 (C=N), 607 (C-I); HRMS (ESI$^+$): *m/z* = calculated for $C_{13}H_{15}INO_3S$ ([M + H]$^+$): 391.9812, found 391.9810.

2-Benzylsulfanyl-4,5-dihydro-(5-deoxy-5-iodo-α-D-xylofuranoso) [2,1-d]-1,3-oxazole (**6d**). General procedure 2 was followed using OZT **2d** (926 mg, 3.08 mmol) and gave after purification (PE/EA: 80:20) the desired OZT iodo compound **6d** as a white solid (856 mg, 71 %). R_f = 0.67 (PE/EA: 50:50); m.p. 144–146 °C $[\alpha]_D^{20}$ = +46 (*c* 0.48, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ (ppm) = 2.66 (d, 1H, $^3J_{OH\text{-}3}$ = 5.6 Hz, OH), 3.23–3.35 (m, 2H, CH_2-5), 3.86 (ddd, 1H, $^3J_{4\text{-}3}$ = 2.6 Hz, $^3J_{4\text{-}5a}$ = 5.9 Hz, $^3J_{4\text{-}5b}$ = 8.8 Hz, H-4), 4.26 (d, 1H, ^2J = 13.2 Hz, CH_2 Bn), 4.32 (d, 1H, ^2J = 13.2 Hz, CH_2 Bn), 4.40–4.43 (m, 1H, H-3), 4.88 (d, 1H, $^3J_{2\text{-}1}$ = 5.4 Hz, H-2), 6.19 (d, 1H, $^2J_{1\text{-}2}$= 5.4 Hz, H-1), 7.28–7.40 (m, 5H, CH Ar); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ (ppm) = –2.1 (CH_2-5), 36.6 (CH_2 Bn), 74.5 (CH-3), 79.4 (CH-4), 88.2 (CH-2), 100.4 (CH-1), 128.0 (CH Ar), 128.9 (CH Ar), 129.1 (CH Ar), 136.1 (Cq Ar), 170.4 (N=CS); IR (neat) ($\tilde{\nu}$, cm^{-1}) = 3473 (OH), 1589 (C=N), 616 (C-I); HRMS (ESI$^+$): *m/z* = calculated for $C_{13}H_{15}INO_3S$ ([M + H]$^+$): 391.9812, found 391.9810.

2-Benzylsulfanyl-4,5-dihydro-(1-O-benzyl-6-deoxy-6-iodo-β-D-fructofuranoso) [2,1-d]-1,3-oxazole (15e). General procedure 2 was followed using OZT **14e** (500 mg, 1.19 mmol) during 24h and gave after purification (PE/EA: 70:30) the desired product **15e** as a yellow oil (465 mg, 76 %). R_f = 0.64 (PE/EA: 70:30); $[\alpha]_D^{20}$ = –28 (*c* 1.04, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 2.87 (t, 1H, $^2J_{6b\text{-}6a}$ = $^3J_{6b\text{-}5}$ = 10.0 Hz, H-6b), 3.04 (dd, 1H, $^2J_{6a\text{-}6b}$ = 10.2 Hz, $^3J_{6a\text{-}5}$ = 6.0 Hz, H-6a), 3.54 (d, 1H, $^2J_{1b\text{-}1a}$ = 10.0 Hz, H-1b), 3.40–3.65 (bs, 1H, O-H), 3.96 (d, 1H, $^2J_{1a\text{-}1b}$ = 10.0 Hz, H-1a), 4.22 (d, 1H, ^2J = 13.3 Hz, CH_2 SBn), 4.26 (d, 1H, ^2J = 13.3 Hz, CH_2 SBn), 4.38 (dd, $^3J_{5\text{-}6a}$ = 6.0 Hz, $^3J_{5\text{-}6b}$ = 9.9 Hz, H-5), 4.41 (bs, 1H, H-4), 4.57 (d, 1H, ^2J = 11.7 Hz, CH_2 OBn), 4.68 (d, 1H, ^2J = 11.7 Hz, CH_2 OBn), 4.76 (s, 1H, H-3), 7.24–7.41 (m, 10H, CH Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 4.4 (CH_2-6), 36.6 (CH_2 SBn), 72.0 (CH_2-1), 74.2 (CH_2 OBn), 76.7 (CH-4), 88.5 (CH-5), 90.9 (CH-3), 110.7 (C-2), 128.0 (CH Ar), 128.1 (CH Ar), 128.4 (CH Ar), 128.8 (CH Ar), 129.1 (CH Ar), 136.2 (Cq Ar), 136.8 (Cq Ar), 170.4 (C-S); IR (neat) ($\tilde{\nu}$, cm^{-1}) = 3399 (NH + OH), 3062 (C_{sp2}-H), 2863, 1581 (N=C), 1109 (C-O), 1027 (C-N), 695 (C-S), 513 (C-I); HRMS (ESI$^+$): *m/z* = calculated for $C_{21}H_{23}INO_4S$ ([M + H]$^+$): 512.0387, found 512.0388.

General procedure 3: silylation of OZT sugars.

OZT iodosugar (1 equiv.) was dissolved in anhydrous DMF (0.1 M) then imidazole (2.5 equiv.) and TBDMSCl (1.2 equiv.) were added and the solution was stirred overnight at r.t. Ethyl acetate was added, and the resulting solution was washed with water 4 times and dried with $MgSO_4$. The resulting mixture was filtered, concentrated under reduced pressure and then purified by silica gel column chromatography using PE/EA, yielding **3a** and **7a**.

3-*tert*-Butyldimethysilyl-5-deoxy-5-iodo-1-*N*,2-*O*-thiocarbonyl-α-D-ribofuranosylamine (3a). General procedure 3 was followed using OZT **2a** (2.78 g, 9.23 mmol) and gave after purification (PE/EA, 95:5) the desired silylated compound **3a** as a white solid (2.26 g, 59 %). R_f = 0.79 (EA/PE: 50:50); m.p. 138–140 °C; $[\alpha]_D^{20}$ = +63 (*c* 0.49, $CHCl_3$); ^{1}H NMR (250 MHz, CD_3OD): δ (ppm) = 0.24, 0.25 (s × 2, 6H, $Si(CH_3)_2$)), 1.00 (s, 9H, $SiC(CH_3)_3$), 3.34–3.40 (m, 2H, H-5b, H-4), 3.56–3.63 (m, H-5a), 4.07 (dd, 1H, $^3J_{3\text{-}2}$ = 5.2 Hz, $^3J_{3\text{-}4}$ = 8.4 Hz, H-3), 5.20 (t, 1H, $^3J_{2\text{-}1}$ = $^3J_{2\text{-}3}$ = 5.3 Hz, H-2), 5.79 (d, 1H,$^3J_{1\text{-}2}$ = 5.3 Hz, H-1); ^{13}C NMR (62.5 MHz, CD_3OD): δ (ppm) = –4.4 ($Si(CH_3)_2$), –4.6 ($Si(CH_3)_2$), 5.2 (CH_2-5), 18.9 ($SiC(CH_3)_3$), 26.2 ($SiC(CH_3)_3$), 77.9 (CH-3), 78.1 (CH-4), 85.9 (CH-2), 89.4 (CH-1), 192.1 (C=S); IR (neat) ($\tilde{\nu}$, cm^{-1}) = 3180 (NH), 1484 (C-N), 1247 (C-O), 1146 (C=S), 632 (CI); HRMS (ESI$^+$): *m/z* = calculated for $C_{12}H_{23}INO_3SSi$ ([M + H]$^+$): 416.0207, found 416.0205.

2-Benzylsulfanyl-4,5-dihydro-(3-*tert*-butyldimethylsilyl-5-deoxy-5-iodo-α-D-ribofuranoso) [2,1-d]-1,3-oxazole (7a). General procedure 3 was followed using OZT **6a** (613 mg, 1.48 mmol) and gave after purification (PE/EA: 80:20) the desired product **7a** as an orange oil (650 mg, 87 %). R_f = 0.95 (PE/EA: 50:50); $[\alpha]_D^{20}$ = +67 (*c* 0.49, $CHCl_3$); ^{1}H NMR (250 MHz, CD_3OD): δ (ppm) = 0.22 (s, 6H, $Si(CH_3)_2$), 0.97 (s, 9H, $SiC(CH_3)_3$), 3.07 (ddd, 1H, $^3J_{4\text{-}5a}$ = 3.1 Hz, $^3J_{4\text{-}5b}$ = 4.8 Hz, $^3J_{4\text{-}3}$ = 8.2 Hz, H-4), 3.33 (dd, 1H, $^3J_{5b\text{-}4}$ = 4.8 Hz, $^3J_{5b\text{-}5a}$ = 11.3 Hz, H-5b), 3.56 (dd, 1H, $^3J_{5a\text{-}4}$ = 3.1 Hz, $^3J_{5a\text{-}5b}$ = 11.3 Hz, H-5a), 4.02 (dd, 1H, $^3J_{3\text{-}2}$ = 5.4 Hz, $^3J_{3\text{-}4}$ = 8.4 Hz, H-3), 4.32 (s, 2H, CH_2 Bn), 4.94 (t, 1H, $^3J_{2\text{-}3}$ = $^3J_{2\text{-}1}$ = 5.4 Hz, H-2), 5.98 (d, 1H, $^3J_{1\text{-}2}$ = 5.4 Hz, CH-1), 5.3 Hz, H-1), 7.31–7.38 (m, 3H, CH Ar), 7.42–7.46 (m, 2H, CH Ar); ^{13}C NMR (62.5 MHz, CD_3OD): δ (ppm) = –4.5 ($Si(CH_3)_2$), –4.2 ($Si(CH_3)_2$), 5.6 (CH_2-5), 18.8 ($SiC(CH_3)_3$), 26.2 ($SiC(CH_3)_3$), 36.7 (CH_2 Ar), 77.6 (CH-4), 78.0 (CH-3), 84.1 (CH-2), 100.0 (CH-1), 128.7 (CH Ar), 129.7 (CH Ar), 129.9 (CH Ar), 137.9 (Cq Ar), 172.9 (N=CS); IR (cm^{-1}) (neat) (ṽ, cm^{-1}) = 1591 (N=C), 1251 (C-O), 672 (C-I); HRMS (ESI^+): *m/z* = calculated for $C_{19}H_{29}INO_3SSi$ ($[M + H]^+$): 506.0677, found 506.0675.

General procedure 4: synthesis of OZT azidosugars.

Iodosugar derivative (1 equiv.) was dissolved in anhydrous DMF (0.05 M) then NaN_3 (5 equiv.) was added and the solution was heated at 80 °C for 3h. Ethyl acetate was added and the resulting solution was washed with water 4 times and dried with $MgSO_4$. The resulting mixture was filtered, concentrated under reduced pressure and then purified by silica gel column chromatography using PE/EA.

5-Azido-5-deoxy-1-*N*,2-*O*-thiocarbonyl-α-D-ribofuranosylamine (4a). General procedure 4 was followed using OZT **3a** (1.12 g, 3.71 mmol) and gave after purification (PE/AE: 80:20) the desired OZT azido compound **4a** as a brown solid (88 mg, 11 %). R_f = 0.68 (EA/PE: 50:50); m.p. 138–140 °C; $[\alpha]_D^{20}$ = +54 (*c* 1, MeOH); ^{1}H NMR (250 MHz, CD_3OD): δ (ppm) = 3.42 (dd, 1H, $^3J_{5b\text{-}4}$ = 5.3 Hz, $^3J_{5b\text{-}5a}$ = 13.6 Hz, H-5b), 3.70 (dd, 1H, $^3J_{5a\text{-}4}$ = 2.5 Hz, $^3J_{5a\text{-}5b}$ = 13.6 Hz, H-5a), 3.79 (ddd, 1H, $^3J_{4\text{-}5a}$ = 2.5 Hz, $^3J_{4\text{-}5b}$ = 5.3 Hz, $^3J_{4\text{-}3}$ = 9.3 Hz, H-4), 4.12 (dd, 1H, $^3J_{3\text{-}2}$ = 5.3 Hz, $^3J_{3\text{-}4}$ = 9.3 Hz, H-3), 5.19 (t, 1H, $^3J_{2\text{-}3}$ = $^3J_{2\text{-}1}$ = 5.3 Hz, H-2), 5.82 (d, 1H, $^3J_{1\text{-}2}$ = 5.3 Hz, H-1); ^{13}C NMR (62.5 MHz, CD_3OD): δ (ppm) = 51.6 (CH_2-5), 73.5 (CH-3), 79.0 (CH-4), 86.2 (CH-2), 89.5 (CH-1), 192.1 (C=S); IR (neat) (ṽ, cm^{-1}) = 3274 (OH + NH), 2101 (N_3), 1517 (C-N), 1111 (C=S); HRMS (ESI^+): *m/z* = calculated for $C_6H_9N_4O_3S$ ($[M + H]^+$): 217.0390, found 217.0391.

5-((1R,2R)-3-Azido-1-*O*-*tert*-butyldimethylsilyloxy-2-hydroxypropyl)-2-(3H)-oxazolethione & 5-((1R,2R)-3-Azido-2-*O*-*tert*-butyldimethylsilyloxy-1-hydroxypropyl)-2-(3H)-oxazolethione (5a/5a'). Obtained following general procedure 4 from OZT 3a (1.00 g, 2.47 mmol) after purification (PE/EA: 94:6) as a 2:1 mixture of isomers 5a/5a′ as an orange oil (441 mg, 54 %). R_f = 0.5 (PE/EA: 50:50); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 0.00 (s, 3H, $Si(CH_3)_2$), 0.02 (s, 1.5H, $Si(CH_3)_2$′), 0.10 (s, 3H, $Si(CH_3)_2$), 0.12 (s, 1.5H, $Si(CH_3)_2$′), 0.85, 0.87 (s × 2, 15H, $SiC(CH_3)_3$), 3.45 (d, 1H, ^3J = 4.2 Hz, CH_2N′), 3.46–3.55 (m, 2H, CH_2N), 4.02–4.14 (m, 1.5H, H-2, H-2′), 4.58 (d, 1H, ^3J = 6.6 Hz, H-1), 4.65 (d, 0.5H, ^3J = 6.3 Hz, H-1′), 6.84 (bs, 1.5H, H-4 oxazole), 11.49 (bs, 1.2H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = –5.0 ($Si(CH_3)_2$), –4.6 ($Si(CH_3)_2$), –4.4 ($Si(CH_3)_2$), 18.0 ($SiC(CH_3)_3$′), 18.1 ($SiC(CH_3)_3$), 25.7 ($SiC(CH_3)_3$), 25.8 ($SiC(CH_3)_3$), 52.9 (CH_2N), 53.3 (CH_2N′), 67.4 (CH-1′), 67.9 (CH-1), 72.3 (CH-2), 72.5 (CH-2′), 113.8 (CH-4 oxazole′), 114.1 (CH-4 oxazole), 149.0 (C-2 oxazole′), 149.3 (C-2 oxazole), 178.89 (C=S′); 178.94 (=CS); IR (neat) (ṽ, cm^{-1}) = 3126 (OH + NH), 2101 (N_3), 1651 (C=C), 1471 (C=N), 1252 (C-O), 1077 (C=S); HRMS (ESI^+): *m/z* = calculated for $C_{12}H_{23}N_4O_3SSi$ ($[M + H]^+$): 331.1255, found 331.1254.

2-Benzylsulfanyl-4,5-dihydro-(5-azido-5-deoxy-α-D-ribofuranoso) [2,1-d]-1,3-oxazole (8a). General procedure 4 was followed using OZT **6a** (1.89 g, 4.85 mmol) and gave after purification (PE/EA: 90:10) the desired product **8a** as a brown oil (1.37 g, 92 %). R_f = 0.81 (PE/EA: 80:20); $[\alpha]_D^{20}$ = +23 (*c* 0.22, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 3.06 (bs, 1H, OH), 3.37 (dd, 1H, $^3J_{5b\text{-}4}$ = 4.6 Hz, $^3J_{5b\text{-}5a}$ = 13.3 Hz, CH_2-5), 3.37 (dd, 1H, $^3J_{4\text{-}5a}$ = 2.8 Hz, $^3J_{4\text{-}5b}$ = 4.6 Hz, $^3J_{4\text{-}3}$ = 9.1 Hz, H-4), 3.66 (dd, 1H, $^3J_{5a\text{-}4}$ = 2.8 Hz, $^3J_{5a\text{-}5b}$ = 13.3 Hz, H-5a), 4.05 (dd, 1H, $^3J_{3\text{-}2}$ = 5.7 Hz, $^3J_{3\text{-}4}$ = 9.1 Hz, H-3), 4.27 (d, 1H, ^2J = 13.3 Hz, CH_2 Bn), 4.32 (d, 1H, ^2J = 13.3 Hz, CH_2 Bn), 4.85 (t, 1H, $^3J_{2\text{-}3}$ = $^3J_{2\text{-}1}$ = 5.5 Hz, H-2), 5.99 (d, 1H, $^3J_{1\text{-}2}$ = 5.2 Hz, CH-1), 7.24–7.39 (m, 5H, CH Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 36.5 (CH_2 Ar), 50.2 (CH_2-5), 72.5 (CH-3), 76.8 (CH-4), 82.4 (CH-2), 98.9 (CH-1), 127.8 (CH Ar), 128.7 (CH Ar), 128.9 (CH Ar), 136.1 (Cq Ar), 170.8 (C=N); IR (neat) (ṽ, cm^{-1}) = 3241 (OH), 2096 (N_3), 1581 (C=N); HRMS (ESI^+): *m/z* = calculated for $C_{13}H_{15}N_4O_3S$ ($[M + H]^+$): 307.0859, found 307.0861.

2-Benzylsulfanyl-4,5-dihydro-(5-azido-3-*tert*-butyldimethylsilyl-5-deoxy-α-D-ribofuranoso) [2,1-d]-1,3-oxazole (9a). General procedure 4 was followed using OZT **7a** (373 mg, 0.739 mmol) and gave after purification (PE/EA, 80:20) the desired product **9a** as a yellow oil (230 mg, 74 %). R_f = 0.84 (PE/EA: 20:80); $[\alpha]_D^{20}$ = +77 (*c* 0.22, $CHCl_3$); ^{1}H NMR (250 MHz, CD_3OD): δ (ppm) = 0.19, 0.21 (s × 2, 6H, $Si(CH_3)_2$), 0.97 (s, 9H, $SiC(CH_3)_3$), 3.34 (dd, 1H, $^3J_{5b\text{-}4}$ = 4.6 Hz, $^3J_{5b\text{-}5a}$ = 13.4 Hz, H-5b), 3.49 (ddd, 1H, $^3J_{4\text{-}5a}$ = 2.6 Hz, $^3J_{4\text{-}5b}$ = 4.6 Hz, $^3J_{4\text{-}3}$ = 8.8 Hz, H-4), 3.64 (dd, 1H, $^3J_{5a\text{-}4}$ = 2.6 Hz, $^3J_{5a\text{-}5b}$ = 13.4 Hz, H-5a), 4.21 (dd, 1H, $^3J_{3\text{-}2}$ = 5.4 Hz, $^3J_{3\text{-}4}$ = 8.8 Hz, H-3), 4.33 (s, 2H, CH_2 Bn), 4.93 (t, 1H, $^3J_{2\text{-}3}$ = $^3J_{2\text{-}1}$ = 5.4Hz, H-2), 6.00 (d, 1H, $^3J_{1\text{-}2}$ = 5.4 Hz, H-1), 7.29–7.38 (m, 3H, CH Ar), 7.42–7.46 (m, 2H, CH Ar); ^{13}C NMR (62.5 MHz, CD_3OD): δ (ppm) = –4.9 ($Si(CH_3)_2$), –4.5 ($Si(CH_3)_2$), 18.9 ($SiC(CH_3)_3$), 26.2 ($SiC(CH_3)_3$), 36.7 (CH_2 Ar), 51.2 (CH_2-5), 74.3 (CH-3), 78.7 (CH-4), 83.9 (CH-2), 100.4 (CH-1), 128.7 (CH Ar), 129.7(CH Ar), 130.0 (CH Ar), 137.9 (Cq Ar), 173.1 (N=CS); IR (cm^{-1}) (neat) (ṽ, cm^{-1}) = 2097 (N_3), 1592 (N=C), 1251 (C-O); HRMS (ESI^+): *m/z* = calculated for $C_{19}H_{29}N_4O_3SSi$ ($[M + H]^+$): 421.1724, found 421.1729.

2-Benzylsulfanyl-4,5-dihydro-(5-azido-5-deoxy-β-D-arabinofuranoso) [2,1-d]-1,3-oxazole (8b). General procedure 4 was followed using OZT **6b** (371 mg, 0.95 mmol) and gave after purification (PE/EA, 95:5) the desired OZT **8b** as a white solid (221 mg, 76 %). R_f = 0.67 (PE/EA: 60:40); m.p. 95–98 °C; $[\alpha]_D^{20}$ = +2 (*c* 0.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 2.85 (bs, 1H, OH), 3.14 (dd, 1H, $^3J_{5b\text{-}4}$ = 6.1 Hz, $^3J_{5b\text{-}5a}$ = 12.9 Hz, H-5b), 3.25 (dd, 1H, $^3J_{5a\text{-}4}$ = 6.5 Hz, $^3J_{5a\text{-}5b}$ = 12.9 Hz, H-5a), 4.04 (ddd, 1H, $^3J_{4\text{-}3}$ = 3.5 Hz, $^3J_{4\text{-}5a}$ = $^3J_{4\text{-}5b}$ = 6.3 Hz, H-4), 4.26 (dd, 1H, $^3J_{3\text{-}2}$ = 1.6 Hz, $^3J_{3\text{-}4}$ = 3.6 Hz, H-3), 4.28 (s, 2H, CH_2 Bn), 4.88 (dd, 1H, $^3J_{2\text{-}3}$ = 1.6 Hz, $^3J_{2\text{-}1}$ = 5.9 Hz, H-2), 6.07 (d, 1H, $^3J_{1\text{-}2}$ = 5.9 Hz, H-1), 7.27–7.39 (m, 5H, CH Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 36.5 (CH_2 Bn), 51.9 (CH_2-5), 77.6 (CH-3), 83.6 (CH-4), 90.2 (CH-2), 100.7 (CH-1), 128.0 (CH Ar), 128.8 (CH Ar), 129.2 (CH Ar), 136.2 (Cq Ar), 170.3 (C=N); IR (neat) (ṽ, cm^{-1}) = 3172 (OH), 2101 (N_3), 1584 (C=N); HRMS (ESI^+): *m/z* = calculated for $C_{13}H_{15}N_4O_3S$ ($[M + H]^+$): 307.0859, found 307.0858.

2-Benzylsulfanyl-4,5-dihydro-(5-azido-5-deoxy-β-L-arabinofuranoso) [2,1-d]-1,3-oxazole (8c). General procedure 4 was followed using OZT **6c** (650 mg, 1.66 mmol) and gave the desired OZT **8c** as a white solid (500 mg, 98 %); it was used in the next step without any further purification. R_f = 0.53 (PE/EA: 40:60); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 3.14 (dd, 1H, $^3J_{5b\text{-}4}$ = 5.9 Hz, $^2J_{5b\text{-}5a}$ = 12.9 Hz, H-5b), 3.22 (dd, 1H, $^3J_{5a\text{-}4}$ = 6.6 Hz, $^2J_{5a\text{-}5b}$ = 12.9 Hz, H-5a), 3.53 (bs, 1H, OH), 4.04 (td, 1H, $^3J_{4\text{-}3}$ = 3.4 Hz, $^3J_{4\text{-}5a}$ = $^3J_{4\text{-}5b}$ = 6.3 Hz, H-4),4.24–4.25 (m, 1H, H-3), 4.27 (s, 2H, CH_2 Bn), 4.89 (dd, 1H, $^3J_{2\text{-}3}$ = 1.6 Hz, $^3J_{2\text{-}1}$ = 6.0 Hz, H-2), 6.05 (d, 1H, $^3J_{1\text{-}2}$ = 5.9 Hz, H-1),

7.26–7.38 (m, 5H, CH Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 36.4 (CH_2 Bn), 51.9 (CH_2-5), 77.3 (CH-3), 83.6 (CH-4), 90.3 (CH-2), 100.6 (CH-1), 128.0 (CH Ar), 128.8 (CH Ar), 129.2 (CH Ar), 136.0 (Cq Ar), 170.5 (C=N); IR (neat) (ṽ, cm^{-1}) = 3176 (OH), 2102 (N_3), 1584 (C=N); HRMS (ESI$^+$): *m/z* = calculated for $C_{13}H_{15}N_4O_3S$ ([M + H]$^+$): 307.0859, found 307.0861.

2-Benzylsulfanyl-4,5-dihydro-(5-azido-5-deoxy-α-D-xylofuranoso) [2,1-d]-1,3-oxazole (8d). General procedure 4 was followed using OZT **6d** (250 mg, 0.64 mmol) and gave after purification (PE/EA: 90:10) the desired OZT azido compound **8d** as a white solid (161 mg, 82 %). R_f = 0.74 (PE/EA: 70:30); m.p. 117–120 °C; $[\alpha]_D^{20}$ = +18 (*c* 0.48, $CHCl_3$); M.S (IS$^+$): *m/z* = 307.0 [M + H]$^+$, 329.0 [M + Na]$^+$; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 3.11 (bs, 1H, OH), 3.58–3.66 (m, 2H, CH_2-5), 3.70 (td, 1H, $^3J_{4\text{-}3}$ = 2.8 Hz, $^3J_{4\text{-}5a}$ = $^3J_{4\text{-}5b}$ = 5.9 Hz, H-4), 4.24–4.32 (m, 2H, CH_2 Bn and H-3), 4.30 (d, 1H, ^2J = 13.2 Hz, CH_2 Bn), 4.83 (d, 1H, $^3J_{2\text{-}1}$ = 5.4 Hz, H-2), 6.15 (d, 1H, $^3J_{1\text{-}2}$ = 5.4 Hz, H-1), 7.28–7.38 (m, 5H, CH Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 36.5 (CH_2 Bn), 48.9 (CH_2-5), 74.7 (CH-3), 77.0 (CH-4), 88.4 (CH-2), 99.7 (CH-1), 128.0 (CH Ar), 128.8 (CH Ar), 129.1 (CH Ar), 136.1 (Cq Ar), 170.5 (C=N); IR (cm^{-1}) (neat) (ṽ, cm^{-1}) = 3139 (OH), 2088 (N_3), 1584 (C=N).

2-Benzylsulfanyl-4,5-dihydro-(6-azido-1-*O*-benzyl-6-deoxy-β-D-fructofuranoso)[2,1-d]-1,3-oxazole (16e). General procedure 4 was followed using OZT **15e** (393 mg, 0.77 mmol) in anhydrous DMF (0.08 M) with sodium azide (250 mg, 3.84 mmol, 5.0 equiv.). The reaction mixture was heated at 80 °C for 3h. After usual workup, silica gel column chromatography (PE/EA: 80:20) gave the desired product **16e** as a colourless oil (264 mg, 80 %). R_f = 0.28 (PE/EA: 80:20); $[\alpha]_D^{20}$ = +13 (*c* 1.04, MeOH); ^{1}H NMR (250 MHz, $CDCl_3$): δ (ppm) = 3.02 (dd, 1H, $^2J_{6b\text{-}6a}$ = 12.8 Hz, $^3J_{6b\text{-}5}$ = 6.1 Hz, H-6b), 3.17 (dd, 1H, $^2J_{6a\text{-}6b}$ = 12.8 Hz, $^3J_{6a\text{-}5}$ = 7.8 Hz, H-6a), 3.47 (d, 1H, $^3J_{OH\text{-}4}$ = 11.0 Hz, OH), 3.59 (d, 1H, $^2J_{1b\text{-}1a}$ = 10.0 Hz, H-1b), 4.00 (d, 1H, $^2J_{1a\text{-}1b}$ = 10.0 Hz, H-1a), 4.15–4.34 (m, 4H, H-4, H-5, CH_2 SBn), 4.58 (d, 1H, ^2J = 11.7 Hz, CH_2 OBn), 4.71 (d, 1H, ^2J = 11.7 Hz, CH_2 OBn), 4.76 (s, 1H, H-3), 7.22–7.44 (m, 10H, CH Ar); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ (ppm) = 36.4 (CH_2 SBn), 52.0 (CH_2-6), 72.2 (CH_2-1), 74.2 (CH_2 OBn), 76.1 (CH-4), 86.9 (CH-5), 90.8 (CH-3), 110.4 (C-2), 128.0 (CH Ar), 128.2 (CH Ar), 128.5 (CH Ar), 128.8 (CH Ar), 128.9 (CH Ar), 129.2 (CH Ar), 136.1 (Cq Ar), 136.9 (Cq Ar), 170.2 (C-S); IR (neat) (ṽ, cm^{-1}) = 3408 (NH + OH), 3062 (C_{sp2}-H), 2919 (C-H), 2098 (N_3), 1581 (N=C), 1099 (C-O), 1027 (C-N), 636 (C-S); HRMS (ESI$^+$): *m/z* = calculated for $C_{21}H_{23}N_4O_4S$ ([M + H]$^+$): 427.1434, found 427.1429.

General procedure 5: oxidation of OZT into OZO.

Azidosugar derivative (1 equiv.) **8a-d, 9a** was dissolved in anhydrous DCM (0.1 M) then $NaHCO_3$ (3 equiv.) was added and the reaction mixture was cooled to 0 °C. The *m*-CPBA (3 equiv.) was added and the solution was stirred for 20 min at 0 °C. The reaction mixture was warmed up to r.t and allowed to react for 12h at r.t. The solution was neutralized by addition of $Na_2S_2O_5$ and then concentrated under reduced pressure. The resulting residue was dissolved in methanol and filtered. The resulting filtrate was concentrated under reduced pressure and then purified by silica gel column chromatography using PE/EA, yielding **10a-d**, **11a** and **17e**.

5-Azido-3-*O*-*tert*-butyldimethysilyl-1-*N*,2-*O*-carbonyl-5-deoxy-α-D-ribofuranosylamine (11a). General procedure 5 was followed using OZT **9a** (215 mg, 0.512 mmol) and gave after purification (PE/EA, 85:15) the desired product **11a** as a white solid (129 mg, 80 %). R_f = 0.26 (PE/EA: 80:20); m.p. 86–89 °C; $[\alpha]_D^{20}$ = +80 (*c* 0.43, $CHCl_3$); ^{1}H NMR (250 MHz, CD_3OD): δ = 0.19, 0.21 (s × 2, 6H, $Si(CH_3)_2$)), 0.97 (s, 9H, $SiC(CH_3)_3$), 3.32–3.39 (m, 1H, H-5b), 3.69 (dd, 1H, $^3J_{5a\text{-}4}$ = 2.6 Hz, $^3J_{5a\text{-}5b}$ = 13.7 Hz, H-5a), 3.85 (ddd, 1H, $^3J_{4\text{-}5a}$ = 2.6 Hz, $^3J_{4\text{-}5b}$ = 4.5 Hz, $^3J_{4\text{-}3}$ = 8.9 Hz, H-4), 4.20 (dd, 1H, $^3J_{3\text{-}2}$ = 5.3 Hz, $^3J_{3\text{-}4}$ = 8.9 Hz, H-3), 4.96 (t, 1H, $^3J_{2\text{-}1}$ = $^3J_{2\text{-}3}$ = 5.3 Hz, H-2), 5.71 (d, 1H, $^3J_{1\text{-}2}$ = 5.3 Hz, H-1); ^{13}C NMR (62.5 MHz, CD_3OD): δ (ppm) = –5.0 ($Si(CH_3)_2$), –4.6 ($Si(CH_3)_2$), 18.9 ($SiC(CH_3)_3$), 26.1 ($SiC(CH_3)_3$), 51.2 (CH_2-5), 73.7 (CH-3), 78.8 (CH-4), 80.3 (CH-2), 86.9 (CH-1), 160.9 (C=O); IR (neat) (ṽ, cm^{-1}) = 3325 (NH), 2104 (N_3), 1753 (C=O), 1251 (C-O); HRMS (ESI$^+$): *m/z* = calculated for $C_{12}H_{23}N_4O_4Si$ ([M + H]$^+$): 315.1483, found 315.1483.

5-Azido-1-*N*,2-*O*-carbonyl-5-deoxy-α-D-ribofuranosylamine (10a). *Method A:* general procedure 5 was followed using OZT **8a** (1.300 g, 4.25 mmol) and gave after purification (PE/EA, 50:50) the desired product **10a** as a white solid (180 mg, 21 %). *Method B*: 5-azido-5-deoxy-3-*O*-*tert*-butyldimethysilyl-1-*N*,2-*O*-carbonyl-α-D-ribofuranosylamine **11a** (0.5 g, 1.6 mmol, 1 equiv.) was suspended in dry THF (12 mL, 0.12 M) at 0 °C, then TBAF (1M in THF) (3.8 mL, 3.8 mmol, 2.4 equiv.) was added. The solution was stirred at room temperature overnight then diluted with ethyl acetate. The organic phase was washed twice with brine, dried with $MgSO_4$, filtered and the solvent evaporated under reduced pressure. The crude product was purified by silica gel column chromatography using PE/AE (50:50) to give the desired product **10a** as a white solid (90 mg, 28 %). R_f = 0.40 (PE/EA: 20:80); m.p. 116–121 °C; $[\alpha]_D^{20}$ = +36 (*c* 1.3, MeOH); M.S (IS$^+$): *m/z* = 201.0 [M + H]$^+$; ^{1}H NMR (400 MHz, CD_3OD): δ (ppm) = 3.38 (dd, 1H, $^3J_{5b\text{-}4}$ = 5.4 Hz, $^2J_{5b\text{-}5a}$ = 13.6 Hz, H-5b), 3.65 (dd, 1H, $^3J_{5a\text{-}4}$ = 2.6 Hz, $^2J_{5a\text{-}5b}$ = 13.6 Hz, H-5a), 3.82–3.86 (m, 1H, H-4), 4.02 (dd, 1H, $^3J_{3\text{-}2}$ = 5.4 Hz, $^3J_{3\text{-}4}$ = 9.3 Hz, H-3), 4.95 (t, 1H, $^3J_{2\text{-}3}$ = $^3J_{2\text{-}1}$ = 5.3 Hz, H-2), 5.68 (d, 1H, $^3J_{1\text{-}2}$ = 5.3 Hz, H-1); ^{13}C NMR (100 MHz, CD_3OD): δ (ppm) = 51.7 (CH_2-5), 73.0 (CH-3), 78.3 (CH-4), 80.6 (CH-2), 86.5 (CH-1), 160.6 (C=O); IR (neat) (ṽ, cm^{-1}) = 3300 (NH), 2099 (N_3), 1716 (C=O).

5-Azido-1-*N*,2-*O*-carbonyl-5-deoxy-β-D-arabinofuranosylamine (10b). General procedure 5 was followed using OZT **8b** (1.35 g, 4.39 mmol) and gave after purification (PE/EA: 50:50) the desired OZO **10b** as a white solid (509 mg, 58 %). R_f = 0.24 (PE/EA: 50:50); m.p. 133–137 °C; $[\alpha]_D^{20}$ = +32 (*c* 0.34, MeOH); ^{1}H NMR (400 MHz, CD_3OD): δ (ppm) = 3.33–3.41 (m, 2H, CH_2-5), 4.03 (ddd, 1H, $^3J_{4\text{-}3}$ = 3.5 Hz, $^3J_{4\text{-}5a}$ = 4.5 Hz, $^3J_{4\text{-}5b}$ = 6.7Hz, H-4), 4.21 (dd, 1H, $^3J_{3\text{-}2}$ = 1.4 Hz, $^3J_{3\text{-}4}$ = 3.6 Hz, H-3), 4.86 (dd, 1H, $^3J_{2\text{-}3}$ = 1.4 Hz, $^3J_{2\text{-}1}$ = 5.6 Hz, H-2), 5.72 (d, 1H, $^3J_{1\text{-}2}$ = 5.6 Hz, H-1); ^{13}C NMR (100 MHz, CD_3OD): δ (ppm) = 53.4 (CH_2-5), 77.4 (CH-3), 85.6 (CH-4), 88.1 (CH-2 or CH-1), 88.2 (CH-1 or CH-2), 159.8 (C=O); IR (neat) (ṽ, cm^{-1}) = 3296 (NH + OH), 2100 (N_3), 1731 (C=O), 1093 (CN); HRMS (ESI$^+$): *m/z* = calculated for $C_6H_9N_4O_4$ ([M + H]$^+$): 201.0618, found 201.0618, 223.0 [M + Na]$^+$.

5-Azido-1-*N*,2-*O*-carbonyl-5-deoxy-β-L-arabinofuranosylamine (10c). General procedure 5 was followed using OZT **8c** (500 mg, 1.63 mmol) and gave after purification (PE/EA: 60:40 to 40:60) the desired OZO **10c** as a white solid (180 mg, 55 %). R_f = 0.45 (PE/EA: 20:80); m.p. 128–132 °C; $[\alpha]_D^{20}$ = –51 (*c* 1, MeOH); ^{1}H NMR (400 MHz, CD_3OD): δ (ppm) = 3.33–3.41 (m, 2H, CH_2-5), 4.03 (ddd, 1H, $^3J_{4\text{-}3}$ = 3.6 Hz, $^3J_{4\text{-}5a}$ = 4.9 Hz, $^3J_{4\text{-}5b}$ = 6.8 Hz, H-4), 4.22 (dd, 1H, $^3J_{3\text{-}2}$ = 1.4 Hz, $^3J_{3\text{-}4}$ = 3.7 Hz, H-3), 4.86 (dd, 1H, $^3J_{2\text{-}3}$ = 1.4 Hz, $^3J_{2\text{-}1}$ = 5.7 Hz, H-2), 5.72 (d, 1H, $^3J_{1\text{-}2}$ = 5.7 Hz, H-1); ^{13}C NMR (100 MHz, CD_3OD): δ (ppm) = 53.4 (CH_2-5), 77.4 (CH-3), 85.6 (CH-4), 88.1 (CH-2 or CH-1), 88.2 (CH-1 or CH-2), 159.9 (C=O); IR (neat) (ṽ, cm^{-1}) = 3302 (OH + NH), 2102 (N_3), 1728 (C=O), 1034 (C-N); HRMS (ESI$^+$): *m/z* = calculated for $C_6H_9N_4O_4$ ([M + H]$^+$): 201.0618, found 201.0622.

5-Azido-1-*N*,2-*O*-carbonyl-5-deoxy-α-D-xylofuranosylamine (10d). General procedure 5 was followed using OZT **8d** (1.26 g, 4.12 mmol) and gave after purification (PE/EA: 50:50) the desired OZO **10d** as a brown oil (495 mg, 60 %). R_f = 0.43 (PE/EA: 20:80); $[\alpha]_D^{20}$ = –18 (*c* 0.96, MeOH); ^{1}H NMR (400 MHz, CD_3OD): δ (ppm) = 3.48–3.58 (m, 2H, CH_2-5), 4.05 (ddd, 1H, $^3J_{4\text{-}3}$ = 2.9 Hz, $^3J_{4\text{-}5a}$ = 5.3 Hz,

$^3J_{4\text{-}5b}$ = 7.1 Hz, H-4), 4.24 (d, 1H, $^3J_{3\text{-}2}$ = 2.8 Hz, H-3), 4.87 (d, 1H, $^3J_{2\text{-}1}$ = 5.4 Hz, H-2), 5.79 (d, 1H, $^3J_{1\text{-}2}$ = 5.4 Hz, H-1); ^{13}C NMR (100 MHz, CD_3OD): δ (ppm) = 50.4 (CH_2-5), 74.8 (CH-3), 79.4 (CH-4), 86.7 (CH-2), 87.4 (CH-1), 160.1 (C=O); IR (cm^{-1}) (neat) ($\tilde{\nu}$, cm^{-1}) = 3241 (NH + OH), 2088 (N_3), 1694 (C=O), 1082 (CN); HRMS (ESI^+): *m/z* = calculated for $C_6H_9N_4O_4S$ ([M + H]$^+$): 201.0618, found 201.0619.

6-Azido-1-*O*-benzyl-2-*N*,3-*O*-carbonyl-6-deoxy-β-D-fructofuranosylamine (17e). General procedure 5 was followed using OZT **16e** (1.14 g, 2.7 mmol) and gave after silica gel column chromatography (PE/EA: 60:40) the desired product **17e** as a yellow oil (600 mg, 70 %). R_f = 0.32 (PE/EA: 60:40); $[\alpha]_D^{20}$ = +22 (*c* 1.04, MeOH); ^{1}H NMR (400 MHz, CD_3OD): δ (ppm) = 3.35–3.43 (dd, 1H, $^2J_{6b\text{-}6a}$ = 13.3 Hz, $^3J_{6b\text{-}5}$ = 6.6 Hz, H-6b), 3.48 (dd, 1H, $^2J_{6a\text{-}6b}$ = 13.3 Hz, $^3J_{6a\text{-}5}$ = 4.4 Hz, H-6a), 3.72 (d, 1H, $^2J_{1b\text{-}1a}$ = 10.3 Hz, H-1b), 3.77 (d, 1H, $^2J_{1a\text{-}1b}$ = 10.3 Hz, H-1a), 4.16 (dt, 1H, $^3J_{5\text{-}6b}$ = 6.6 Hz, $^3J_{5\text{-}4}$ = $^3J_{5\text{-}6a}$ = 4.4 Hz, H-5), 4.30 (dd, 1H, $^3J_{4\text{-}5}$ = 4.4 Hz, $^3J_{4\text{-}3}$ = 2.1 Hz, H-4), 4.66 (d, 1H, ^2J = 11.9 Hz, CH_2 Bn), 4.69 (d, 1H, ^2J = 11.9 Hz), 4.84 (d, 1H, $^3J_{3\text{-}4}$ = 2.1 Hz, H-3), 7.32–7.45 (m, 5H, CH Ar); ^{13}C NMR (100 MHz, CD_3OD): δ (ppm) = 53.1 (CH_2-6), 71.3 (CH_2-1), 74.5 (CH_2-Bn), 78.1 (CH-4), 85.5 (CH-5), 88.8 (CH-3), 97.6 (C-2), 128.7 (CH Ar), 128.8 (CH Ar), 129.4 (CH Ar), 139.0 (Cq Ar), 159.2 (C=O); IR (neat) ($\tilde{\nu}$, cm^{-1}) = 3217 (NH + OH), 2081 (N_3), 2372, 2405, 1728 (C=O); HRMS (ESI^+): *m/z* = calculated for $C_{14}H_{17}N_4O_5$ ([M + H]$^+$): 321.1193, found 321.1192.

General procedure 6: O- and S-protection of OZT ketoses.

OZT iodosugar (1 equiv.) **18** was dissolved in anhydrous DMF (0.3 M) and cooled to –5 °C, then sodium hydride 60 % (2.5 equiv.) was added portionwise, and after ten minutes, BnBr or allyl bromide or methyl iodide (2.5 equiv.) was added dropwise. The reaction mixture was stirred at –5 °C, 30 min and then overnight at r.t. The reaction mixture was quenched by addition of cold water and diluted with EA. The organic phase was washed 3 times with cold water, twice with a saturated aqueous NaCl solution, dried with $MgSO_4$ and filtered. The solvent was evaporated under reduced pressure. The residue was purified by silica gel flash column chromatography using PE/EA to give the desired bisalkylated compounds **19–21f**.

2-Benzylsulfanyl-4,5-dihydro-(1-O-benzyl-4,6-*O*-isopropylidene-α-L-sorbofuranoso) [2,1-d]-1,3-oxazole (19f). General procedure 6 was followed using 4,6-*O*-isopropylidene-2-*N*,3-*O*-thiocarbonyl-α-L-sorbofuranosylamine **18** (2.5 g, 9.6 mmol) and gave after purification (PE/EA: 80:20) the desired bisprotected OZT **19f** as a colourless oil (3.59 g, 85 %). R_f = 0.24 (PE/EA: 80:20); $[\alpha]_D^{20}$ = –65 (*c* 0.91, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ (ppm) = 1.33 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 3.58 (q, 1H, $^3J_{5\text{-}6}$ = $^3J_{5\text{-}4}$ = 2.0 Hz, H-5), 3.82 (d, 1H, $J_{1b\text{-}1a}$ = 10.5 Hz, H-1b), 3.91 (d, 1H, $^2J_{1a\text{-}1b}$ = 10.5 Hz, H-1a), 4.06 (d, 2H, $^3J_{6\text{-}5}$ = 2.0Hz, CH_2-6), 4.25 (d, 1H, ^2J = 13.2 Hz, CH_2 *S*Bn), 4.32 (d, 1H, $^3J_{4\text{-}5}$ = 2.4 Hz, H-4), 4.37 (d, 1H, ^2J = 13.2 Hz, CH_2*S*Bn), 4.64 (s, 2H, CH_2 *O*Bn), 4.78 (s, 1H, H-3), 7.25–7.40 (m, 10H, CH Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 18.8 (CH_3), 29.0 (CH_3), 35.7 (CH_2 S-Bn), 59.7 (CH_2-6), 71.0 (CH-5), 71.5 (CH_2-1), 73.2 (CH-4), 73.7 (CH_2 O-Bn), 88.3 (CH-3), 97.9 (C-2 or Cq *i*Pr), 109.4 (Cq *i*Pr or C-2), 127.6 (CH Ar), 127.7 (CH Ar), 127.8 (CH Ar), 128.4 (CH Ar), 128.8 (CH Ar), 129.2 (CH Ar), 136.4 (Cq Ar), 138.4 (Cq Ar), 169.0 (C-S); IR (neat) ($\tilde{\nu}$, cm^{-1}) = 3059 (C_{sp2}-H), 1596 (C=N), 1114 (C-O), 1072, 696 (C-S); HRMS (ESI^+): *m/z* = calculated for $C_{24}H_{28}NO_5S$ ([M + H]$^+$): 442.1682, found 442.1687.

2-Allylsulfanyl-4,5-dihydro-(1-*O*-allyl-4,6-*O*-isopropylidene-α-L-sorbo furanoso) [2,1-d]-1,3-oxazole (20f). General procedure 6 was followed using 4,6-*O*-isopropylidene-2-*N*,3-*O*-thiocarbonyl-α-L-sorbofuranosylamine **18** (3.0 g, 11.5 mmol) and gave after purification (PE/EA, 80:20 to 70:30) the desired bisprotected OZT **20f** as a colourless oil (3.04 g, 78 %). R_f = 0.56 (PE/EA: 70:30); $[\alpha]_D^{20}$ = –73 (*c* 1.01, MeOH); ^{1}H NMR (250 MHz, $CDCl_3$): δ (ppm) = 1.38 (s, 3H, CH_3), 1.44 (s, 3H, CH_3), 3.64 (bs, 1H, H-5), 3.68 (dm, 2H, ^2J = 10.0 Hz, CH_2O allyl), 3.78 (d, 1H, $^2J_{1b\text{-}1a}$ = 10.5 Hz, H-1b), 3.86 (d, 1H, $^2J_{1a\text{-}1b}$ = 10.5 Hz, H-1a), 4.02–4.17 (m, 4H, CH_2S allyl, CH_2-6), 4.35 (bs, 1H, H-4), 4.75 (s, 1H, H-3), 5.11–5.33 (m, 4H, =CH_2 *O*- and *S*-allyl), 5.82–6.00 (m, 2H, HC= *O*- and *S*-allyl); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 18.9 (CH_3), 29.0 (CH_3), 35.0 (CH_2 *O*-allyl), 59.7 (CH_2-6 or CH_2 *S*-allyl), 71.0 (CH-5), 71.5 (CH_2-1), 72.8 (CH_2 *S*-allyl or CH_2-6), 73.3 (CH-4), 88.2 (CH-3), 97.9 (C-2 or *i*Pr), 109.4 (*i*Pr or C-2), 117.0 (=CH_2 *O*- or *S*-allyl), 118.9 (=CH_2 *O*- or *S*-allyl), 132.4 (=CH *O*-allyl), 134.8 (=CH *S*-allyl), 168.8 (C-S); IR (neat) ($\tilde{\nu}$, cm^{-1}) = 2995 (C-H), 1598 (C=N), 1113 (C-O), 1075, 919 (C_{sp2}-H), 849 (C-S); HRMS (ESI^+): *m/z* = calculated for $C_{16}H_{24}NO_5S$ ([M + H]$^+$): 342.1367, found 342.1372.

2-Methylsulfanyl-4,5-dihydro-(4,6-*O*-isopropylidene-1-*O*-methyl-α-L-sorbofuranoso) [2,1-d]-1,3-oxazole (21f). General procedure 6 was followed using 4,6-*O*-isopropylidene-2-*N*,3-*O*-thiocarbonyl-α-L-sorbofuranosylamine **18** (5.04 g, 19.3 mmol) and gave after purification (PE/EA, 50:50) the desired bisprotected OZT **21f** as a colourless oil (3.74 g, 67 %). R_f = 0.49 (PE/EA: 50:50); $[\alpha]_D^{20}$ = –84 (*c* 1.02, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.40 (s, 3H, CH_3 *i*Pr), 1.45 (s, 3H, CH_3 *i*Pr), 2.51 (s, 3H, SCH_3), 3.46 (s, 3H, OCH_3), 3.64–3.67 (m, 1H, H-5), 3.69 (d, 1H, $^2J_{1b\text{-}1a}$ = 10.3 Hz, H-1b), 3.83 (d, 1H, $^2J_{1a\text{-}1b}$ = 10.3 Hz, H-1a), 4.03–4.13 (m, 2H, CH_2-6), 4.37 (d, 1H, $^3J_{4\text{-}5}$ = 2.3 Hz, H-4), 4.73 (s, 1H, H-3); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 14.8 (CH_3 *i*Pr), 18.8 (S-CH_3), 29.1 (CH_3 *i*Pr), 59.7 (CH_2-6), 60.0 (O-CH_3), 70.9 (CH-5), 73.2 (CH-4), 74.1 (CH_2-1), 88.4 (CH-3), 97.9 (C-2 or Cq *i*Pr), 109.2 (Cq *i*Pr or C-2), 170.3 (C-S); IR (neat) ($\tilde{\nu}$, cm^{-1}) = 2933 (C-H), 1598 (C=N), 1194 (C-O), 1114 (C-N), 1072, 849 (C-S); HRMS (ESI^+): *m/z* = calculated for $C_{12}H_{20}NO_5S$ ([M + H]$^+$): 290.105670, found 290.105873.

General procedure 7: oxidation of OZT ketoses into OZO

The bisprotected OZT (1.0 equiv.) **19–21f** was dissolved in DCM (0.1 M). Sodium bicarbonate (5.0 equiv.) was added at 0 °C. After 10 minutes *m*-CPBA (3.5 equiv.) was added. The reaction was stirred at r.t. for the next 15 hours, then was stopped by adding cooled water and sodium metabisulfite (1.85 equiv.) and diluted with DCM. The organic phase was washed three times with 1 M NaOH solution and twice with a saturated aqueous NaCl solution, dried with $MgSO_4$ and filtered. The solvent was evaporated under reduced pressure. The residue was purified by silica gel flash column chromatography using PE/EA to give the desired 1-*O*-protected OZO **22–24f**.

1-*O*-Benzyl-2-*N*,3-*O*-carbonyl-4,6-*O*-isopropylidene-α-L-sorbofuranosylamine (22f). General procedure 7 was followed using 1-*O*,*S*-dibenzyl-4,6-*O*-isopropylidene-2-*N*,3-*O*-thiocarbonyl-α-L-sorbofuranosylamine **19f** (1.3 g, 2.9 mmol) and gave after purification (PE/EA, 50:50) the desired OZO **22f** as a white foam (567 mg, 58 %). R_f = 0.41 (PE/EA: 50:50); $[\alpha]_D^{20}$ = –45 (*c* 1.11, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ (ppm) = 1.33 (s, 3H, CH_3), 1.44 (s, 3H, CH_3), 3.67 (d, 1H, $^2J_{1b\text{-}1a}$ = 10.2 Hz, H-1b), 3.77 (d, 1H, $^2J_{1a\text{-}1b}$ = 10.2 Hz, H-1a), 3.94 (q, 1H, $^3J_{5\text{-}6a}$ = $^3J_{5\text{-}6a}$ = $^3J_{5\text{-}4}$ = 2.2 Hz, H-5), 4.01 (bd, 1H, $^2J_{6a\text{-}6b}$ = 13.7 Hz, H-6b), 4.09 (dd, $^3J_{6a\text{-}5}$ = 2.2 Hz, $^2J_{6a\text{-}6b}$ = 13.6 Hz, 1H, H-6a), 4.40 (d, 1H, $^3J_{4\text{-}5}$ = 2.2 Hz, H-4), 4.60 (d, 1H, ^2J = 12.1 Hz, CH_2 Bn), 4.66 (d, 1H, ^2J = 12.1 Hz, CH_2 Bn), 4.67 (s, 1H, H-3), 6.19 (bs, 1H, NH), 7.27–7.39 (m, 5H, CH Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 18.7 (CH_3), 29.0 (CH_3), 59.7 (CH_2-6), 70.3 (CH_2-1), 71.5 (CH-5), 72.7 (CH-4), 73.7 (CH_2 Bn), 85.7 (CH-3), 96.0 (C-2 or Cq *i*Pr), 98.0 (Cq *i*Pr or C-2), 128.0 (CH Ar), 128.1 (CH Ar), 128.6 (CH Ar), 137.3 (Cq Ar), 156.9 (C=O); IR (neat) ($\tilde{\nu}$, cm^{-1}) = 3312 (NH), 3043 (C_{sp2}-H), 1762

(C=O), 1377 (C-O), 1058 (C-N); HRMS (ESI^+): *m/z* = calculated for $C_{17}H_{22}NO_6$ ($[M + H]^+$): 336.1440, found 336.1441.

1-*O*-Allyl-2-*N*,3-*O*-carbonyl-4,6-*O*-isopropylidene-α-L-sorbofuranosylamine (23f). The OZT 4,6-*O*-bisallylated **20f** (690 mg, 2.0 mmol, 1.0 equiv.) was dissolved in 16.0 mL of EtOH and 4.0 mL of 3 M NaOH solution. The mixture was heated at 80 °C for 5 h. The mixture was then cooled down at r.t. and diluted with EA. The organic layer was washed four times with a saturated aqueous NaCl solution, dried with $MgSO_4$ and then filtered. The solvent was evaporated under reduced pressure. The desired product **23f** was obtained as a colourless oil and was used without any further purification (0.42 g, 72 %). R_f = 0.50 (PE/EA: 50:50); $[\alpha]_D^{20}$ = –49 (*c* 0.69, MeOH); ^1H NMR (250 MHz, $CDCl_3$): δ (ppm) = 1.38 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 3.67 (d, 1H, $^2J_{1b\text{-}1a}$ = 10.3 Hz, H-1b), 3.78 (d, 1H, $^2J_{1a\text{-}1b}$ = 10.3 Hz, H-1a), 3.95–3.99 (m, 1H, H-5), 4.04–4.17 (m, 4H, CH_2-6, CH_2 allyl), 4.42 (d, 1H, $^3J_{4\text{-}5}$ = 2.2 Hz, H-4), 4.68 (s, 1H, H-3), 5.19–5.33 (m, 2H, =CH_2), 5.89 (ddt, $^3J_{trans}$ = 17.3 Hz, $^3J_{cis}$ = 10.3 Hz, $^2J_{gem}$ = 5.7 Hz, 1H, HC=allyl), 6.15 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 18.8 (CH_3), 29.1 (CH_3), 59.8 (CH_2-6 or CH_2 allyl), 70.6 (CH_2-1), 71.5 (CH-5), 72.7 (CH-4), 72.8 (CH_2 allyl or CH_2-6), 85.7 (CH-3), 95.9 (C-2 or Cq *i*Pr), 98.0 (Cq *i*Pr or C-2), 118.1 (=CH_2), 134.0 (HC=), 156.9 (C=O); IR (neat) (ṽ, cm^{-1}) = 3291 (N-H), 1766 (C=O), 1378 (C-O), 1061 (C-N), 848 (C_{sp2}-H); HRMS (ESI^+): *m/z* = calculated for $C_{13}H_{20}NO_6$ ($[M + H]^+$): 286.1285, found 286.1286.

2-*N*,3-*O*-Carbonyl-1-*O*-methyl-4,6-*O*-isopropylidene-α-L-sorbofuranosylamine (24f). General procedure 7 was followed using 1-*O*,*S*-dimethyl-4,6-*O*-isopropylidene-2-*N*,3-*O*-thiocarbonyl-α-L-sorbofuranosylamine **21f** (2.5 g, 8.7 mmol) and gave after purification (PE/EA, 50:50) the desired OZO **24f** as a colourless oil (1.23 g, 55 %). R_f = 0.27 (PE/EA: 50:50); $[\alpha]_D^{20}$ = –54 (*c* 1.08, MeOH); ^1H NMR (250 MHz, $CDCl_3$): δ (ppm) = 1.39 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 3.46 (s, 3H, OCH_3), 3.62 (d, 1H, $^2J_{1b\text{-}1a}$ = 10.1 Hz, H-1b), 3.73 (d, 1H, $^2J_{1a\text{-}1b}$ = 10.1 Hz, H-1a), 3.95–4.00 (m, 1H, H-5), 4.04 (dm, 1H, $^3J_{6b\text{-}6a}$ = 13.6 Hz, H-6b), 4.14 (dd, 1H, $^3J_{6a\text{-}5}$ = 2.3 Hz, $^3J_{6a\text{-}6b}$ = 13.6 Hz, H-6a), 4. 43 (d, 1H, $^3J_{4\text{-}5}$ = 2.3 Hz, H-4), 4.68 (s, 1H, H-3), 5.92 (bs, 1H, NH); ^{13}C NMR (100 MHz, CD_3OD): δ (ppm) = 19.0 (CH_3), 29.4 (CH_3), 59.8 (O-CH_3), 60.7 (CH_2-6), 72.6 (CH-5), 73.5 (CH_2-1), 74.1 (CH-4), 86.7 (CH-3), 97.4 (C-2 or Cq *i*Pr), 99.1 (Cq *i*Pr or C-2), 159.7 (C=O); IR (neat) (ṽ, cm^{-1}) = 3288 (NH + OH), 2939 (C-H), 1765 (C=O), 1198 (C-N), 1114 (C-O), 1056; HRMS (ESI^+): *m/z* = calculated for $C_{11}H_{18}NO_6$ ($[M + H]^+$): 260.1128, found 260.1126.

General procedure 8: deprotection of 4,6-O-isopropylidene.

The OZO 4,6-*O*-isopropylidene monoprotected (1.0 equiv.) was dissolved in a mixture acetic acid/water, 4:1 (0.05–0.1 M) and the reaction mixture was stirred at 55 °C for 4 h. The solvent was evaporated under reduced pressure and the residue co-evaporated several times with toluene. The desired product was used in most cases without any further purification in the next step.

1-*O*-Benzyl-2-*N*,3-*O*-carbonyl-α-L-sorbofuranosylamine (25f). General procedure 8 was followed using OZO 4,6-*O*-isopropylidene **22f** (500 mg, 1.5 mmol) and gave the desired product **25f** as a colourless oil (450 mg, 97 %). R_f = 0.36 (PE/EA: 60:40); ^1H NMR (250 MHz, $CDCl_3$): δ (ppm) = 3.70 (d, 1H, $^2J_{1b\text{-}1a}$ = 10.0 Hz, H-1b), 3.73–3.84 (m, 2H, H-1a, OH-4), 3.93–4.09 (m, 2H, CH_2-6), 4.11–4.18 (m, 1H, H-5), 4.30–4.38 (m, 1H, H-4), 4.60 (d, 1H, ^2J = 11.9 Hz, CH_2 Bn), 4.66 (d, 1H, ^2J = 11.9 Hz, CH_2 Bn), 4.70 (s, 1H, H-3), 6.01 (bs, 1H, NH), 7.28–7.44 (m, 5H, CH Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 61.1 (CH_2-6), 70.7 (CH_2-1), 74.2 (CH_2 Bn), 75.2 (CH-4), 80.3 (CH-5), 86.8 (CH-3), 95.3 (C-2), 128.2 (CH Ar), 128.7 (CH Ar), 128.9 (CH Ar), 136.5 (Cq Ar), 156.7 (C=O); IR (neat) (ṽ, cm^{-1}) = 3298 (NH + OH), 1746 (C=O), 1366 (C-O), 1097 (C-O), 1038 (C-N); HRMS (ESI^+): *m/z* = calculated for $C_{14}H_{18}NO_6$ ($[M + H]^+$): 296.1128, found 296.1129.

1-*O*-Allyl-2-*N*,3-*O*-carbonyl-α-L-sorbofuranosylamine (26f). General procedure 8 was followed using 4,6-*O*-isopropylidene OZO **23f** (800 mg, 2.8 mmol) and gave after silica gel column chromatography (PE/EA: 50:50 to pure EA) the desired product **26f** as a brown oil (352 mg, 51 %). R_f = 0.46 (EA); $[\alpha]_D^{20}$ = –9 (c 1.02, MeOH); ^1H NMR (250 MHz, CD_3OD): δ (ppm) = 3.62 (d, 1H, $^2J_{1b\text{-}1a}$ = 10.3 Hz, H-1b), 3.71 (d, 1H, $^2J_{1a\text{-}1b}$ = 10.3 Hz, H-1a), 3.77 (dd, 1H, $^3J_{6b\text{-}6a}$ = 11.6 Hz, $^3J_{6b\text{-}5}$ = 6.4 Hz, H-6b), 3.86 (dd, 1H, $^3J_{6a\text{-}6b}$ = 11.6 Hz, $^3J_{6a\text{-}5}$ = 4.9 Hz, H-6a), 4.03 (ddd, 1H, $^3J_{5\text{-}4}$ = 2.8 Hz, $^3J_{5\text{-}6a}$ = 4.9 Hz, $^3J_{5\text{-}6b}$ = 6.4 Hz, H-5), 4.08 (dt, 2H, ^3J = 5.6 Hz, ^4J = 1.45 Hz, CH_2 allyl), 4.24 (d, 1H, $^3J_{4\text{-}5}$ = 2.8 Hz, H-4), 4.67 (s, 1H, H-3), 5.20 (dm, 1H, $^3J_{cis}$= 10.4 Hz, = CH_2), 5.31 (dq, 1H, $^3J_{trans}$ = 17.3 Hz, $^3J_{cis}$= ^4J = $^2J_{gem}$ = 1.7 Hz, =CH_2), 5.93 (ddt, 1H, $^3J_{trans}$ = 17.3 Hz, $^3J_{cis}$ = 10.4 Hz, ^3J = 5.6 Hz, HC=); ^{13}C NMR (100 MHz, CD_3OD): δ (ppm) = 60.6 (CH_2-6), 71.2 (CH_2-1), 73.5 (CH_2 allyl), 75.1 (CH-4), 82.1 (CH-5), 87.8 (CH-3), 97.3 (C-2), 117.7 (=CH_2 allyl), 135.6 (HC= allyl), 159.9 (C=O); IR (neat) (ṽ, cm^{-1}) = 3339 (NH + OH), 1743 (C=O), 1374 (C-O), 1042 (C-N), 972 (C_{sp2}-H); HRMS (ESI^+): *m/z* = calculated for $C_{10}H_{16}NO_6$ ($[M + H]^+$): 246.0972, found 264.0971.

2-*N*,3-*O*-Carbonyl-1-*O*-methyl-α-L-sorbofuranosylamine (27f). General procedure 8 was followed using OZO 4,6-*O*-isopropylidene **24f** (1.16 g, 4.5 mmol) and gave the desired product **27f** as a white solid (930 mg, 95 %). R_f = 0.30 (EA); ^1H NMR (250 MHz, CD_3OD): δ (ppm) = 3.43 (s, 3H, OCH_3), 3.56 (d, 1H, $^2J_{1b\text{-}1a}$ = 10.2 Hz, H-1b), 3.64 (d, 1H, $^2J_{1a\text{-}1b}$ = 10.2 Hz, H-1a), 3.77 (dd, 1H, $^3J_{6b\text{-}6a}$ = 11.6 Hz, $^3J_{6b\text{-}5}$ = 6.4 Hz, H-6b), 3.86 (dd, 1H, $^3J_{6a\text{-}6b}$ = 11.6 Hz, $^3J_{6a\text{-}5}$ = 4.9 Hz, H-6a), 3.77(ddd, 1H, $^3J_{5\text{-}4}$ = 2.8 Hz, $^3J_{5\text{-}6a}$ = 4.9 Hz, $^3J_{5\text{-}6b}$ = 6.4 Hz, H-5), 4.23 (d, 1H, $^3J_{4\text{-}5}$ = 2.8 Hz, H-4), 4.64 (s, 1H, H-3); ^{13}C NMR (100 MHz, CD_3OD): δ (ppm) = 59.7 (CH_3), 60.6 (CH_2-6), 73.7 (CH_2-1), 82.0 (CH-4), 87.8 (CH-5), 97.1 (CH-3), 159.9 (C=O); IR (neat) (ṽ, cm^{-1}) = 3380 (NH + OH), 2995 (C-H), 1743 (C=O), 1370 (C-O), 1022 (C-N); HRMS (ESI^+): *m/z* = calculated for $C_8H_{14}NO_6$ ($[M + H]^+$): 220.0815, found 220.0814.

General Procedure 9: iodation of OZO 1-O-protected ketoses.

OZO 4,6-unprotected **25–27f** (1.0 equiv.) were dissolved in THF (0.2M) under argon atmosphere. Then triphenylphosphine (2.0 equiv.) and imidazole (2.0 equiv.) were added. After 10 minutes iodine (1.5 equiv.) was added. The mixture was heated at 60 °C for the next 3 h. The solvent was evaporated under reduced pressure. The residue was dissolved in EA and water. Once the layers were separated, the aqueous phase was extracted 2 times with EA. The combined organic phases were washed three times with water and twice with a saturated aqueous NaCl solution, dried with $MgSO_4$ and then filtered. The solvent was evaporated under reduced pressure. The residue was purified by silica gel flash column chromatography using PE/EA (70:30) to give the desired compounds **28–30f**.

1-*O*-Benzyl-2-*N*,3-*O*-carbonyl-6-deoxy-6-iodo-α-L-sorbofuranosylamine (28f). General procedure 9 was followed using OZO **25f** (1.19 g, 4 mmol) and gave after silica gel column chromatography (PE/EA: 70:30) the desired product **28f** as a pale yellow solid (1.37 g, 83 %). R_f = 0.39 (PE/EA: 60:40); m.p. 124–125 °C; $[\alpha]_D^{20}$ = –14 (*c* 1.05, MeOH); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 3.14 (bs, 1H, OH), 3.20–3.35 (m, 2H, CH_2-6), 3.64 (d, 1H, $^2J_{1b\text{-}1a}$ = 9.8 Hz, H-1b), 3.76 (d, 1H, $^2J_{1a\text{-}1b}$ = 9.8 Hz, H-1a), 4.29–4.40 (m, 2H, H-4, H-5), 4.60 (d, 1H, ^2J = 11.8 Hz, CH_2 Bn), 4.67 (d, 1H, ^2J = 11.8 Hz, CH_2 Bn), 4.78 (s, 1H, H-3), 5.90 (bs, 1H, NH), 7.27–7.46 (m, 5H, CH Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = –2.2 (CH_2-6), 70.2 (CH_2-1), 73.8 (CH-4 or CH-5), 74.2 (CH_2 Bn), 82.0 (CH-5 or CH-4), 86.5 (CH-3), 95.7 (C-2), 128.2 (CH Ar), 128.8 (CH Ar), 129.0 (CH Ar), 136.2 (Cq Ar), 156.6 (C=O); IR (neat)

($\tilde{\nu}$, cm^{-1}) = 3257 (NH + OH), 1740 (C=O), 1416 (C=C), 1366 (C-O), 1028 (C-O), 1045(C-N); HRMS (ESI^+): *m/z* = calculated for $C_{14}H_{17}INO_5$ ($[M + H]^+$): 406.0145, found 406.0146.

1-*O*-Allyl-2-*N*,3-*O*-carbonyl-6-*O*-*p*-toluenesulfonyl-α-L-sorbofuranosylamine (29f). The 4,6-unprotected OZO **26f** (100 mg, 0.41 mmol, 1.0 equiv.) was dissolved in 5.0 mL of anhydrous DCM under argon atmosphere. Then triethylamine (0.18 mL, 1.22 mmol, 3.0 equiv.) and DMAP (0.005 g, 0.04 mmol, 0.1 equiv.) were added. After 10 min, 4-toluenesulfonyl chloride (0.094 g, 0.49 mmol, 1.2 equiv.) was added at 0 °C. The reaction was stirred for the next 15 h at r.t. The reaction mixture was diluted with DCM and water. The organic layer was washed once with ammonium chloride, once with a saturated aqueous sodium bicarbonate solution and twice with a saturated aqueous NaCl solution, dried with $MgSO_4$ and filtered. The solvent was evaporated under reduced pressure. The residue was purified by silica gel flash column chromatography using PE/EA (50:50 to 30:70). The desired product was obtained as a yellow oil (91 mg, 56 %). R_f = 0.67 (PE/EA: 30:70); $[\alpha]_D^{20}$ = –2 (*c* 1.05, MeOH); ^1H NMR (250 MHz, $CDCl_3$): δ (ppm) = 2.46 (s, 3H, CH_3), 3.41 (d, 1H, $^3J_{OH\text{-}4}$ = 10.3 Hz, OH), 3.65 (d, 1H, $^2J_{1b\text{-}1a}$ = 10.1 Hz, H-1b), 3.73 (d, 1H, $^2J_{1a\text{-}1b}$ = 10.1 Hz, H-1a), 4.06 (dm, 2H, ^3J = 5.8 Hz, CH_2 allyl), 4.13–4.41 (m, 4H, H-4, H-5, CH_2-6), 4.72 (s, 1H, H-3), 5.20–5.25 (m, 1H, =CH_2 allyl), 5.28 (dq, 1H, $^3J_{cis}$ = 10.3 Hz, $^2J_{gem}$ = ^4J = 1.5 Hz, = CH_2 allyl), 5.83 (ddt, 1H, $^3J_{trans}$ = 17.2 Hz, $^3J_{cis}$ = 10.3 Hz, ^3J = 5.8 Hz, HC= allyl), 6.43 (bs, 1H, NH), 7.37 (dm, 2H, ^3J = 8.6 Hz, CH Ar), 7.81 (dm, 2H, ^3J = 8.6 Hz, CH Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 21.5 (CH_3), 67.1 (CH_2-6), 69.8 (CH_2-1), 72.6 (CH_2 allyl), 73.2 (CH-4 or CH-5), 78.5 (CH-5 or CH-4), 85.8 (CH-3), 95.5 (C-2), 118.9 (=CH_2 allyl), 127.9 (CH Ar), 129.9 (CH Ar), 132.2 (Cq Ar), 132.7 (CH= allyl), 145.1 (Cq Ar), 156.5 (C=O); IR (neat) ($\tilde{\nu}$, cm^{-1}) = 3360 (NH + OH), 1755 (C=O), 1598 (C=C), 1369 (S=O), 1173 (S=O), 1074 (C-O); HRMS (ESI^+): *m/z* = calculated for $C_{17}H_{22}NO_8S$ ($[M + H]^+$): 400.1060, found 400.1058.

2-*N*,3-*O*-Carbonyl-6-deoxy-6-iodo-1-*O*-methyl-α-L-sorbofuranosylamine (30f). General procedure 9 was followed using OZO **27f** (2.16 g, 9.9 mmol) and gave after silica gel column chromatography (PE/EA: 70:30) the desired product **30f** as a white foam (2.77 g, 85 %). R_f = 0.30 (PE/EA: 50:50); m.p. 162–163 °C; $[\alpha]_D^{20}$ = –11 (*c* 1.02, MeOH); ^1H NMR (400 MHz, CD_3OD): δ (ppm) = 3.27 (dd, 1H, $^2J_{6b\text{-}6a}$ = 9.7 Hz, $^3J_{6b\text{-}5}$ = 6.4 Hz, H-6b), 3.37 (dd, 1H, $^2J_{6a\text{-}6b}$ = 9.7 Hz, $^3J_{6a\text{-}5}$ = 7.7 Hz, H-6a), 3.42 (s, 3H, OCH_3), 3.55 (d, 1H, $^2J_{1b\text{-}1a}$ = 10.2 Hz, H-1b), 3.61 (d, 1H, $^2J_{1a\text{-}1b}$ = 10.2 Hz, H-1a), 4.21 (ddd, 1H, $^3J_{5\text{-}4}$ = 2.7 Hz, $^3J_{5\text{-}6b}$ = 6.4 Hz, $^3J_{5\text{-}6a}$ = 7.7 Hz, H-5), 4.29 (d, 1H, $^3J_{4\text{-}5}$ = 2.7 Hz, H-4), 4.70 (s, 1H, H-3); ^{13}C NMR (100 MHz, CD_3OD): δ (ppm) = –1.8 (CH_2-6), 59.7 (OCH_3), 73.6 (CH_2-1), 74.7 (CH-4) 82.5 (CH-), 87.7 (CH-3), 97.6 (C-2), 159.73 (C=O); IR (neat) ($\tilde{\nu}$, cm^{-1}) = 3170 (NH + OH), 1739 (C=O), 1376 (C-O), 1060 (C-O), 1030 (C-N), 509 (C-I); HRMS (ESI^+): *m/z* = calculated for $C_8H_{13}INO_5$ ($[M + H]^+$): 329.9832, found 329.9831.

General Procedure 10: azidation of 1-*O*-protected ketoses OZOs.

The 6-iodo/6-*O*Ts derivative **28–30f** (1.0 equiv.) was dissolved in anhydrous DMF (0.15M) under argon atmosphere. After 10 minutes, sodium azide (4.0 equiv.) was added. The mixture was heated at 70 °C for the next 15 hours. The reaction mixture was quenched by addition of cold water and diluted with EA. The aqueous phase was extracted 2 more times with EA. The combined organic phases were washed 3 times with cold water, twice with a saturated aqueous NaCl solution, dried with $MgSO_4$ and filtered. The solvent was evaporated under reduced pressure. The residue was purified by silica gel flash column chromatography (PE/EA: 55:45) to give the desired 6-iodoOZOs **31–33f**.

6-Azido-1-*O*-benzyl-6-deoxy-2-*N*,3-*O*-carbonyl-α-L-sorbofuranosylamine (31f). General procedure 10 was followed using OZO **28f** (1.20 g, 3.0 mmol) and gave after silica gel column chromatography (PE/EA: 55:45) the desired product **31f** as a yellow solid (0.95 g, 92 %). R_f = 0.27 (PE/EA: 60:40); m.p. 107–110 °C; $[\alpha]_D^{20}$ = +3 (*c* 0.97, MeOH); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 3.20 (bs, 1H, OH), 3.50–3.62 (m, 2H, CH_2-6), 3.68 (d, 1H, $^2J_{1b\text{-}1a}$ = 9.8 Hz, H-1b), 3.80 (d, 1H, $^2J_{1a\text{-}1b}$ = 9.8 Hz, H-1a), 4.16–4.28 (m, 2H, H-4, H-5), 4.62 (d, 1H, ^2J = 11.8 Hz, CH_2 Bn), 4.68 (d, 1H, ^2J = 11.8 Hz, CH_2 Bn), 4.75 (s, 1H, H-3), 5.67 (bs, 1H, NH), 7.28–7.44 (m, 5H, CH Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 49.5 (CH_2-6), 70.2 (CH_2-1), 74.0 (CH-4 or CH-5), 74.3 (CH_2 Bn), 80.0 (CH-5 or CH-4), 86.4 (CH-3), 95.3 (C-2), 128.2 (CH Ar), 128.8 (CH Ar), 129.0 (CH Ar), 136.2 (Cq Ar), 156.3 (C=O); IR (neat) ($\tilde{\nu}$, cm^{-1}) = 3238 (NH + OH), 3030 (C_{sp2}-H), 2104 (N_3), 1741 (C=O), 1661 (C=C) 1073 (C-O); HRMS (ESI^+): *m/z* = calculated for $C_{14}H_{17}N_4O_5$ ($[M + H]^+$): 321.1193, found 321.1191.

1-*O*-Allyl-6-azido-2-*N*,3-*O*-carbonyl-6-deoxy-α-L-sorbofuranosylamine (32f). General procedure 10 was followed using OZO **29f** (99 mg, 0.25 mmol) and gave after silica gel column chromatography (PE/EA: 55:45) the desired product **32f** as a yellow solid (0.47 g, 70 %). R_f = 0.35 (PE/EA: 60:40); m.p. 73–74 °C; $[\alpha]_D^{20}$ = +10 (*c* 1.01, MeOH); ^1H NMR (250 MHz, $CDCl_3$): δ (ppm) = 3.34 (d, 1H, $^3J_{OH\text{-}4}$ = 10.6 Hz, OH), 3.54–3.63 (m, 2H, CH_2-6), 3.68 (d, 1H, $^2J_{1b\text{-}1a}$ = 9.9 Hz, H-1b), 3.78 (d, 1H, $^3J_{1a\text{-}1b}$ = 9.9 Hz, H-1a), 4.12 (dm, 2H, ^3J = 5.8 Hz, CH_2 allyl), 4.18–4.31 (m, 2H, H-4, H-5), 4.78 (s, 1H, H-3), 5.26–5.37 (m, 2H, =CH_2), 5.93 (ddt, 1H, $^3J_{trans}$ = 17.2 Hz, $^3J_{cis}$ = 10.3 Hz, ^3J = 5.8 Hz, HC= allyl), 6.26 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 49.5 (CH_2-6), 70.3 (CH_2-1), 73.1 (CH_2 allyl), 73.9 (CH-4 or CH-5), 80.1 (CH-5 or CH-4), 86.4 (CH-3), 95.4 (C-2), 119.5 (=CH_2 allyl), 132.9 (=CH allyl), 156.5 (C=O); IR (neat) ($\tilde{\nu}$, cm^{-1}) = 3254 (NH + OH), 2104 (N_3), 1737 (C=O), 1288 (C-O), 1042 (C-N), 666 (C_{sp2}-H); HRMS (ESI^+): *m/z* = calculated for $C_{10}H_{15}N_4O_5$ ($[M + H]^+$): 271.1036, found 271.1035.

6-Azido-2-*N*,3-*O*-carbonyl-6-deoxy-1-*O*-methyl-α-L-sorbofuranosylamin>e (33f). General procedure 10 was followed using OZO **30f** (714 mg, 2.17 mmol) and gave after silica gel column chromatography (PE/EA: 40:60) the desired product **33f** as a colourless oil (406 mg, 77 %). R_f = 0.36 (PE/EA: 40:60); $[\alpha]_D^{20}$ = +9 (*c* 1.04, MeOH); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 3.32 (d, 1H, $^3J_{OH\text{-}4}$ = 10.3 Hz, OH), 3.49 (s, 3H, CH_3), 3.61–3.57 (m, 2H, CH_2-6), 3.65 (d, 1H, ^2J = 9.9 Hz, H-1a), 3.74 (d, 1H, ^2J = 9.9 Hz, H-1b), 4.21 (ddd, 1H, $^3J_{5\text{-}4}$ = 2.5 Hz, ^3J = 5.6 Hz, ^3J = 6.4 Hz, H-5), 4.24 (dd, 1H, $^3J_{4\text{-}5}$ = 2.5 Hz, $^3J_{4\text{-}OH}$ = 10.1 Hz, H-4), 4.76 (s, 1H, H-3), 6.29 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 49.4 (CH_2-6), 59.9 (CH_3), 73.0 (CH_2-1), 73.8 (CH-4), 79.9 (CH-5), 86.3 (CH-3), 95.4 (C-2), 156.9 (C=O); IR (neat) ($\tilde{\nu}$, cm^{-1}) = 3318 (NH + OH), 2936 (C-H), 2100 (N_3), 1746 (C=O), 1259 (C-O), 1110 (C-O), 1038 (C-N); HRMS (ESI^+): *m/z* = calculated for $C_8H_{13}N_4O_5$ ($[M + H]^+$): 245.088, found 245.0877.

6-Azido-1-*O*-benzyl-6-deoxy-2-*N*,3-*O*-thiocarbonyl-α-L-sorbofuranosylamine (44f). General procedure 10 was followed using OZT **43f** (1.20 g, 3.0 mmol) and gave after silica gel column chromatography (PE/EA: 70:30) the desired product **44f** (0.14 g, 40 %). R_f = 0.63 (PE/EA: 50:50); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 3.15 (d, 1H, $J_{OH,4}$ = 10.2 Hz, OH), 3.59 (d, 2H, $^3J_{6\text{-}5}$ = 6.1Hz, CH_2-6), 3.71 (d, 1H, $^2J_{1b\text{-}1a}$ = 10.0 Hz, H-1b), 3.80 (d, 1H, $^2J_{1a\text{-}1b}$ = 9.9 Hz, H-1a), 4.17 (td, 1H, $^3J_{5\text{-}6}$ = 6.1 Hz, $^3J_{5\text{-}4}$ = 2.6 Hz, H-5), 4.34 (dd, 1H, $^3J_{4\text{-}5}$ = 2.5 Hz, $^3J_{4\text{-}OH}$ = 10.2 Hz, H-4), 4.61 (d, 1H, ^2J = 11.8 Hz, CH_2 Bn), 4.68 (d, 1H, ^2J = 11.8 Hz, CH_2 Bn), 4.97 (s, 1H, H-3); 7.26–7.41 (m, 5H, CH Ar), 7.52 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 49.2 (CH_2-6), 69.3 (CH_2-1), 73.8 (CH-4), 74.3 (CH_2 Bn), 80.3 (CH-5), 91.7 (CH-3), 98.7 (C-2), 128.2 (CH Ar), 128.8 (CH Ar), 129.0 (CH Ar), 136.1 (Cq Ar), 189.0 (C=S); MS (ESI^+): *m/z* = 337.5 ([M + H] +); 359.5 ([M + Na] $^+$).

Synthesis of iminosugars.

General procedure 11: Staudinger reduction/cyclisation.

a) *For pentoses derivatives*: OZT/OZO sugar derivative (1 equiv.) was dissolved in H_2O/THF (1:5, 0.1 M) then Ph_3P (5 equiv.) was added and the solution was stirred for overnight at r.t. The resulting mixture was concentrated under reduced pressure and then purified by silica gel column chromatography using EA/MeOH.

b) *For ketoses derivatives*: OZO/OZT sugar derivative (1 equiv.) was dissolved in H_2O/THF (1:4, 0.05 M) then Ph_3P (1 equiv.) was added and the solution was heated at 50 °C for 3–15h. The resulting mixture was concentrated under reduced pressure, co-evaporated three times with toluene and then purified by silica gel column chromatography using EA/acetone.

5-Amino-5-deoxy-1-*N*,2-*O*-thiocarbonyl-α-D-ribofuranosylamine (34a). Aminosugar **34a** was isolated as a colorless oil (9 mg, 7 %) from OZT **4a** (150 mg, 0.69 mmol) in conditions of general procedure 11a, after purification (PE/EA: 50:50). R_f = (PE/EA: 80:20); $[\alpha]_D^{20}$ = +30 (*c* 0.13, MeOH); M.S (IS^+): *m/z* = 191.0 [M + H]$^+$, 213.0 [M + Na]$^+$; ^{1}H NMR (250 MHz, CD_3OD): δ (ppm) = 2.83 (dd, 1H, $^3J_{5b\text{-}4}$ = 6.7 Hz, $^3J_{5b\text{-}5a}$ = 13.6 Hz, H-5b), 3.07 (dd, 1H, $^3J_{5a\text{-}4}$ = 3.2 Hz, $^3J_{5a\text{-}5b}$ = 13.6 Hz, H-5a), 3.66 (ddd, 1H, $^3J_{4\text{-}5a}$ = 3.2 Hz, $^3J_{4\text{-}5b}$ = 6.7 Hz, $^3J_{4\text{-}3}$ = 9.6 Hz H-4), 3.96 (dd, 1H, $^3J_{3\text{-}2}$ = 5.3 Hz, $^3J_{3\text{-}4}$ = 9.5 Hz, H-3), 5.15 (t, 1H, $^3J_{2\text{-}1}$ = $^3J_{2\text{-}3}$ = 5.3 Hz, H-2), 5.76 (d, 1H, $^3J_{1\text{-}2}$ = 5.3 Hz, H-1); ^{13}C NMR (62.5 MHz, CD_3OD): δ (ppm) = 42.9 (CH_2-5), 74.3 (CH-3), 79.6 (CH-4), 86.5 (CH-2), 89.5 (CH-1), 192.1(C=S); IR (neat) (ṽ, cm^{-1}) = 3371 (NH + OH), 1118 (C=S).

2-Benzylsulfanyl-4,5-dihydro-(3-*O*-tertbutyldimethylsilyl-5-amino-5-deoxy-α-D-ribofuranoso) [2,1-d]-1,3-oxazole (35a). Amino sugar **35a** was isolated as an orange oil (488 mg, 86 %), following reaction of OZT **9a** (604 mg, 1.44 mmol) in conditions of general procedure 11a, after purification (PE/EA: 50:50). R_f = 0.27 (PE/EA: 90:10); $[\alpha]_D^{20}$ = +61 (*c* 0.75, $CHCl_3$); ^{1}H NMR (250 MHz, CD_3OD): δ (ppm) = 0.15, 0.17 (s × 2, 6H, $Si(CH_3)_2$), 0.93 (s, 9H, $SiC(CH_3)_3$), 2.72 (dd, 1H, $^3J_{5b\text{-}4}$ = 7.1 Hz, $^3J_{5b\text{-}5a}$ = 13.4 Hz, H-5b), 2.96 (dd, 1H, $^3J_{5a\text{-}4}$ = 3.0 Hz, $^3J_{5a\text{-}5b}$ = 13.4 Hz, H-5a), 3.38 (ddd, 1H, $^3J_{4\text{-}5a}$ = 3.0 Hz, $^3J_{4\text{-}5b}$ = 7.1 Hz, $^3J_{4\text{-}3}$ = 8.9Hz, H-4), 3.99 (dd, 1H, $^3J_{3\text{-}2}$ = 5.4 Hz, $^3J_{3\text{-}4}$ = 8.9 Hz, H-3), 4.29 (s, 2H, CH_2 Bn), 4.88 (t, 1H, $^3J_{2\text{-}1}$ = $^3J_{2\text{-}3}$ = 5.4 Hz, H-2), 5.94 (d, 1H, $^3J_{1\text{-}2}$ = 5.4 Hz, H-1), 7.26–7.35 (m, 3H, CH Bn), 7.38–7.42 (m, 2H, CH Bn); ^{13}C NMR (62.5 MHz, CD_3OD): δ (ppm) = –4.9 ($Si(CH_3)_2$), –4.4 ($Si(CH_3)_2$), 18.9 ($SiC(CH_3)_3$), 26.2 ($SiC(CH_3)_3$), 36.7 (CH_2 Ar), 43.3 (CH_2-5), 75.4 (CH-3), 80.2 (CH-4), 84.3 (CH-2), 100.3 (CH-1), 128.8 (CH Ar), 129.7(CH Ar), 130.0 (CH Ar), 137.9 (Cq Ar), 172.7 (N=CS); IR (neat) (ṽ, cm^{-1}) = 3386 (NH_2), 1591 (N=C),, 1250 (C-O); HRMS (ESI^+): *m/z* = calculated for $C_{19}H_{31}N_2O_3SSi$ ([M + H]$^+$): 395.1819, found 395.1817.

5-Amino-1-*N*,2-*O*-carbonyl-5-deoxy-α-D-xylofuranosylamine (36d). Amino sugar **36d** was isolated as a colorless oil (17 mg, 5 %) following reaction of OZT **10d** (406 mg, 2.03 mmol) in conditions of general procedure 11a, after purification (EA/MeOH: 95:5). R_f = 0.28 (EA/MeOH: 80:20); M.S (IS^+): *m/z* = 175.0 [M + H]$^+$; ^{1}H NMR (400 MHz, CD_3OD): δ (ppm) = 3.27–3.33 (m, 1H, H-5b), 3.52 (dd, 1H, $^3J_{5a\text{-}4}$ = 6.9 Hz, $^3J_{5a\text{-}5b}$ = 14.2 Hz, H-5a), 3.93 (td, 1H, $^3J_{4\text{-}3}$ = 2.6 Hz, $^3J_{4\text{-}5a}$ = $^3J_{4\text{-}5b}$ = 6.6 Hz, H-4), 4.18 (d, 1H, $^3J_{3\text{-}4}$ = 2.6 Hz, H-3), 4.87 (d, 1H, $^3J_{2\text{-}1}$ = 5.4 Hz, H-2), 5.74 (d, 1H, $^3J_{1\text{-}2}$ = 5.4 Hz, H-1); ^{13}C NMR (100 MHz, CD_3OD): δ (ppm) = 39.0 (CH_2-5), 74.6 (CH-3), 79.9 (CH-4), 86.5 (CH-2), 87.3 (CH-1), 160.3 (C=O); IR (neat) (ṽ, cm^{-1}) = 3241 (NH + OH), 1703 (C=O), 1082 (CN).

4/3-*O*-*tert*-Butyldimethylsilyl-5-amino-1-*N*,2-*O*-carbonyl-5-deoxy-α-D-ribopyranosylamine (37a/37a′).

Method A: general procedure 11a was followed using azidoOZO **11a** (300 mg, 0.96 mmol) and purification was achieved through silica gel column chromatography (PE/EA, 50:50).

Method B: azidoOZO **11a** (270 mg, 0.860 mmol, 1 equiv.) was dissolved in 10 mL of EtOH at room temperature. Pd/C (183 g, 1.720 mmol, 2 equiv.) and HCO_2NH_4 (163 mg, 2.580 mmol, 3 equiv.) were added and the reaction mixture was allowed to react for 12 hours at 44 °C. It was then filtered through celite and the solvent evaporated under reduced pressure. The crude residue was purified by silica gel column chromatography using EA as eluent.

4-*O*-*tert*-Butyldimethylsilyl-2-*N*,3-*O*-carbonyl-1,5-dideoxy-1,5-imino-α-D-ribopyranosylamine (37a).

Method A: 15 % yield, white solid; *Method B:* 14 % yield. R_f = 0.31 (EA/MeOH: 85:15); m.p. 134–137; $[\alpha]_D^{20}$ = +33 (*c* 0.36, MeOH); ^{1}H NMR (250 MHz, $CDCl_3$): δ (ppm) = 0.066, 0.096 (s × 2, 6H, $Si(CH_3)_2$), 0.89 (s, 9H, $SiC(CH_3)_3$), 2.83 (dd, 1H, $^3J_{4\text{-}5b}$ = 5.0 Hz, $^3J_{5b\text{-}5a}$ = 13.7 Hz, H-5b), 3.07 (dd, 1H, $^3J_{5a\text{-}4}$ = 5.5 Hz, $^3J_{5a\text{-}5b}$ = 13.7 Hz, H-5a), 3.77–3.86 (m, 1H, H-3), 3.91 (q, 1H, $^3J_{4\text{-}3}$ = $^3J_{4\text{-}5a}$ = $^3J_{4\text{-}5b}$ = 4.9 Hz, H-4), 4.59 (dd, 1H, $^3J_{2\text{-}3}$ = 4.3 Hz, $^3J_{2\text{-}1}$ = 6.3 Hz, H-2), 4.79 (d, 1H, $^3J_{1\text{-}2}$ = 6.5 Hz, H-1), 6.53 (bs, 1H, NH or OH); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ (ppm) = –4.7 ($Si(CH_3)_2$), –4.5 ($Si(CH_3)_2$), 18.3 ($SiC(CH_3)_3$), 25.8 ($SiC(CH_3)_3$), 25.9 ($SiC(CH_3)_3$), 44.2 (CH_2-5), 66.0 (CH-1), 66.6 (CH-4), 68.9 (CH-3), 76.4 (CH-2), 159.3 (C=O); IR (neat) (ṽ, cm^{-1}) = 3290 (NH + OH), 1723 (C=O), 1248 ($SiCH_3$); HRMS (ESI^+): *m/z* = calculated for $C_{12}H_{25}N_2O_4Si$ ([M + H]$^+$): 289.1578, found 289.1580.

3-*O*-*tert*-Butyldimethylsilyl-2-*N*,3-*O*-carbonyl-1,5-dideoxy-1,5-imino-α-D-ribopyranosylamine (37a′). Method A: 36 % yield, white solid; Method B: 30 % yield. R_f = 0.17 (EA/MeOH: 85:15); m.p. 98–102 °C; $[\alpha]_D^{20}$ = +30 (*c* 0.36, MeOH); ^{1}H NMR (250 MHz, $CDCl_3$): δ (ppm) = 0.13, 0.15 (s × 2, 6H, $Si(CH_3)_2$), 0.93 (s, 9H, $SiC(CH_3)_3$), 2.83 (dd, 1H, $^3J_{5b\text{-}4}$ = 4.3 Hz, $^3J_{5b\text{-}5a}$ = 14.0 Hz, H-5b), 3.07 (dd, 1H, $^3J_{5a\text{-}4}$ = 4.8 Hz, $^3J_{5a\text{-}5b}$ = 14.0 Hz, H-5a), 3.83 (q, 1H, $^3J_{4\text{-}3}$ = $^3J_{4\text{-}5a}$ = $^3J_{4\text{-}5b}$ = 3.9 Hz, H-4), 3.91 (t, 1H, $^3J_{3\text{-}2}$ = $^3J_{3\text{-}4}$ = 4.2 Hz, H-3), 4.44–4.48 (m, 1H, H-2), 4.71 (d, 1H, $^3J_{1\text{-}2}$ = 5.9 Hz, H-1), 6.53 (bs, 1H, NH or OH); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ (ppm) = –4.7 ($Si(CH_3)_2$), –4.5 ($Si(CH_3)_2$), 18.3 ($SiC(CH_3)_3$), 25.8 ($SiC(CH_3)_3$), 25.9 ($SiC(CH_3)_3$), 44.2 (CH_2-5), 66.0 (CH-1), 66.6 (CH-4), 68.9 (CH-3), 76.4 (CH-2), 159.3 (C=O); IR (neat) (ṽ, cm^{-1}) = 3272 (NH + OH), 1749 (C=O), 1244 (C-O); HRMS (ESI^+): *m/z* = calculated for $C_{12}H_{25}N_2O_4Si$ ([M + H]$^+$): 289.1578, found 289.1580.

2-*N*,3-*O*-Carbonyl-1,5-dideoxy-1,5-imino-α-D-ribopyranosylamine (38a). To a solution of 3- and 4-*O*-silylated iminosugars **37a** and 3**7a′** (0.135 g, 0.469 mmol) in THF/H_2O (6:1 (28 mL) at 0 °C, was added TFA (12 mL). The reaction mixture was then allowed to react 4 hours at room temperature. After evaporation under reduced pressure, the crude residue was purified using silica gel column chromatography (EA/MeOH: 80:20) to give the deprotected iminosugar **38a** as a white solid (13 mg, 16 %). R_f = 0.23 (EA/MeOH: 80:20); m.p 90–93 °C; $[\alpha]_D^{20}$ = +23 (*c* 1.29, MeOH); ^{1}H NMR (400 MHz, CD_3OD): δ (ppm) = 2.85 (dd, 1H, $^3J_{5b\text{-}4}$ = 5.0 Hz, $^3J_{5b\text{-}5a}$ = 13.6 Hz, H-5b), 2.95 (dd, 1H, $^3J_{5a\text{-}4}$ = 6.1 Hz, $^3J_{5a\text{-}5b}$ = 13.6 Hz, H-5a), 3.81–3.84 (bq, $^3J_{4\text{-}3}$ = $^3J_{4\text{-}5a}$ = $^3J_{4\text{-}5b}$ = 4.8 Hz, 1H, H-4), 3.91 (t, 1H, $^3J_{3\text{-}4}$ = $^3J_{3\text{-}2}$ = 4.2 Hz, H-3), 4.57 (dd, 1H, $^3J_{2\text{-}3}$ = 4.2 Hz, $^3J_{2\text{-}1}$ = 6.4 Hz, H-2), 4.78 (d, 1H, $^3J_{1\text{-}2}$ = 6.4 Hz, H-1); ^{13}C NMR (100 MHz, CD_3OD): δ (ppm) = 44.4 (CH_2-5), 66.8 (CH-1), 67.2 (CH-4), 68.6 (CH-3), 77.8 (CH-2), 161.6 (C=O); IR (neat) (ṽ, cm^{-1}) = 3242 (NH + OH), 1716 (C=O), 1082 (CN); HRMS (ESI^+): *m/z* = calculated for $C_6H_{11}N_2O_4$ ([M + H]$^+$): 175.0713, found 175.0714.

2-*N*,3-*O*-Carbonyl-1,5-dideoxy-1,5-imino-β-D-arabinopyranosylamine (38b). General procedure 11a was followed using OZO **10b** (247 mg, 1.24 mmol). Purification using silica gel column chroma-

tography (pure EA) gave the desired product **38b** as an orange oil (76 mg, 67 %). R_f = 0.31 (EA/MeOH: 90:10); $[\alpha]_D^{20}$ = –155 (*c* 1, MeOH); ^{1}H NMR (400 MHz, CD_3OD): δ (ppm) = 2.82 (dd, 1H, $^3J_{5b\text{-}4}$ = 4.3 Hz, $^3J_{5b\text{-}5a}$ = 13.9 Hz, H-5b), 2.96 (dd, 1H, $^3J_{5a\text{-}4}$ = 2.6 Hz, $^3J_{5a\text{-}5b}$ = 13.9 Hz, H-5a), 3.78 (dd, 1H, $^3J_{3\text{-}4}$ = 3.0 Hz, $^3J_{3\text{-}2}$ = 6.6 Hz, H-3), 3.83 (dt, 1H, $^3J_{4\text{-}5a}$ = $^3J_{4\text{-}3}$ = 2.9 Hz, $^3J_{4\text{-}5b}$ = 4.3 Hz, H-4), 4.42 (t, 1H, $^3J_{2\text{-}3}$ = $^3J_{2\text{-}1}$ = 6.7 Hz, H-2), 5.00 (d, 1H, $^3J_{1\text{-}2}$ = 6.8 Hz, H-1); ^{13}C NMR (100 MHz, CD_3OD): δ (ppm) = 44.5 (CH_2-5), 67.6 (CH-1), 68.6 (CH-4), 72.3 (CH-3), 80.2 (CH-2), 161.1 (C=O); IR (neat) ($\tilde{\nu}$, cm^{-1}) = 3276 (NH + OH), 1718 (C=O), 1076 (C-N); HRMS (ESI$^+$): *m/z* = calculated for $C_6H_{11}N_2O_4$ ([M + H]$^+$): 175.0713, found 175.0716.

2-*N*,3-*O*-Carbonyl-1,5-dideoxy-1,5-imino-β-L-arabinopyranosylamine (38c). General procedure 11a was followed using OZO **10c** (250 mg, 1.25 mmol). Purification using silica gel column chromatography (EA/MeOH: 90:10) gave the desired product **38c** as a white solid (145 mg, 66 %). R_f = 0.36 (EA/MeOH: 70:30); m.p. 117–120 °C; $[\alpha]_D^{20}$ = +153 (*c* 0.44, MeOH); ^{1}H NMR (400 MHz, CD_3OD): δ (ppm) = 2.82 (dd, 1H, $^3J_{5b\text{-}4}$ = 4.3 Hz, $^3J_{5b\text{-}5a}$ = 13.8 Hz, H-5b), 2.95 (dd, 1H, $^3J_{5a\text{-}4}$ = 2.7 Hz, $^3J_{5a\text{-}5b}$ = 13.9 Hz, H-5a), 3.77 (dd, 1H, $^3J_{3\text{-}4}$ = 3.0 Hz, $^3J_{3\text{-}2}$ = 6.5 Hz, H-3), 3.82 (dt, 1H, $^3J_{4\text{-}3}$ = $^3J_{4\text{-}5a}$ = 2.9 Hz, $^3J_{4\text{-}5b}$ = 4.3 Hz, H-4), 4.41 (t, 1H, $^3J_{2\text{-}3}$ = $^3J_{2\text{-}1}$ = 6.7 Hz, H-2), 4.98 (d, 1H, $^3J_{1\text{-}2}$ = 6.8 Hz, H-1); ^{13}C NMR (100 MHz, CD_3OD): δ (ppm) = 44.6 (CH_2-5), 67.6 (CH-1), 68.6 (CH-4), 72.3 (CH-3), 80.2 (CH-2), 161.2 (C=O); IR (neat) ($\tilde{\nu}$, cm^{-1}) = 3328 (OH + NH), 1723(C=O), 1024 (C-N); HRMS (ESI$^+$): *m/z* = calculated for $C_6H_{11}N_2O_4$ ([M + H]$^+$): 175.0713, found 175.0715.

2-*N*,3-*O*-Carbonyl-1,5-dideoxy-1,5-imino-α-D-xylopyranosylamine (38d). General procedure 11a was followed using OZO **10d** (406 mg, 2.03 mmol). Purification using silica gel column chromatography (EA/MeOH: 80:20) gave the desired product **38d** as a white solid (146 mg, 41 %). R_f = 0.21 (EA/MeOH: 80:20); m.p. 153–156 °C; $[\alpha]_D^{20}$ = +44 (*c* 0.27, MeOH); ^{1}H NMR (400 MHz, CD_3OD): δ (ppm) = 2.68 (dd, 1H, $^3J_{4\text{-}5b}$ = 9.7 Hz, $^3J_{5b\text{-}5a}$ = 12.7 Hz, H-5b), 2.88 (dd, 1H, $^3J_{5a\text{-}4}$ = 4.6 Hz, $^3J_{5a\text{-}5b}$ = 12.7 Hz, H-5a), 3.40 (ddd, 1H, $^3J_{4\text{-}5a}$ = 4.6 Hz, $^3J_{4\text{-}3}$ = 8.7 Hz, $^3J_{4\text{-}5b}$ = 9.7Hz, H-4), 3.55 (dd, 1H, $^3J_{3\text{-}2}$ = 6.5 Hz, $^3J_{3\text{-}4}$ = 8.8 Hz, H-3), 4.24 (t, 1H, $^3J_{2\text{-}1}$ = $^3J_{2\text{-}3}$ = 6.8 Hz, H-2), 5.02 (d, 1H, $^3J_{1\text{-}2}$ = 7.0 Hz, H-1); ^{13}C NMR (100 MHz, CD_3OD): δ (ppm) = 44.3 (CH_2-5), 68.5 (CH-1), 70.8 (CH-4), 77.3 (CH-3), 81.3 (CH-2), 161.2 (C=O); IR (neat) ($\tilde{\nu}$, cm^{-1}) = 3241 (NH + OH), 1696 (C=O), 1082 (CN); HRMS (ESI$^+$): *m/z* = calculated for $C_6H_{11}N_2O_4$ ([M + H]$^+$): 175.0713, found 175.0718.

1-*O*-Benzyl-2-*N*,3-*O*-carbonyl-2,6-dideoxy-2,6-imino-β-D-fructopyranosylamine (40e). General procedure 11b was followed using OZO **17e** (100 mg, 0.31 mmol). Purification using silica gel column chromatography (pure EA then EA/Acetone, 50:50) gave the desired product **40e** as a pale yellow sticky solid (54 mg, 55 %). R_f = 0.34 (EA/MeOH: 90:10); $[\alpha]_D^{20}$ = –69 (*c* 0.88, EA); ^{1}H NMR (400 MHz, (CD_3CN): δ (ppm) = 2.14 (bs, 1H, NH), 2.80 (dd, 1H, $^2J_{6b\text{-}6a}$ = 14.0 Hz, $^3J_{6b\text{-}5}$ = 4.0 Hz, H-6b), 2.89 (dd, 1H, $^2J_{6a\text{-}6b}$ = 14.0 Hz, $^3J_{6a\text{-}5}$ = 2.1 Hz, H-6a), 3.03 (bs, 1H, OH), 3.36–3.47 (bs, 1H, OH), 3.42 (d, 1H, $^2J_{1b\text{-}1a}$ = 9.3 Hz, H-1b), 3.49 (d, 1H, $^2J_{1a\text{-}1b}$ = 9.3 Hz, H-1a), 3.65 (dd, 1H, $^3J_{4\text{-}3}$ = 6.5 Hz, $^3J_{4\text{-}5}$ = 3.1 Hz, H-4), 3.68–3.73 (m, 1H, H-5), 4.18 (d, 1H, $^3J_{3\text{-}4}$ = 6.5 Hz, H-3), 4.52–4.61 (m, 2H, CH_2 Bn), 5.74 (bs, 1H, NH), 7.28–7.41 (m, 5H, CH Ar); ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) = 44.2 (CH_2-6), 68.0 (CH-5), 73.5 (CH-4), 74.0 (CH_2 Bn), 74.6 (CH_2-1), 75.2 (C-2), 80.5 (CH-3), 128.7 (CH Ar), 129.4 (CH Ar), 139.1 (Cq Ar), 158.2 (C=O); IR (neat) ($\tilde{\nu}$, cm^{-1}) = 3307 (NH + OH), 1732 (C=O); HRMS (ESI$^+$): *m/z* = calculated for $C_{14}H_{19}N_2O_5$ ([M + H]$^+$): 295.1288, found 295.1287.

1-*O*-Benzyl-2-*N*,3-*O*-carbonyl-2,6-dideoxy-2,6-imino-α-L-sorbopyranosylamine (40f). General procedure 11b was followed using OZO **31f** (100 mg, 0.31 mmol). Purification using silica gel column chromatography (pure EA then EA/Acetone, 50:50) gave the desired product **40f** as a white sticky solid (62 mg, 67 %). R_f = 0.42 (EA/MeOH: 90:10); $[\alpha]_D^{20}$ = –71 (*c* 0.81, EA); ^{1}H NMR (400 MHz, D_2O): δ (ppm) = 2.73 (dd, 1H, $^2J_{6b\text{-}6a}$ = 12.8 Hz, $^3J_{6b\text{-}5}$ = 10.2 Hz, H-6b), 3.01 (dd, 1H, $^2J_{6a\text{-}6b}$ = 12.8 Hz, $^3J_{6a\text{-}5}$ = 4.6 Hz, H-6a), 3.50–3.56 (m, 1H, H-5), 3.58 (d, 1H, $^2J_{1b\text{-}1a}$ = 10.2 Hz, H-1b), 3.63 (d, 1H, $^2J_{1a\text{-}1b}$ = 10.2 Hz, H-1a), 3.69 (dd, 1H, $^3J_{4\text{-}5}$ = 9.3 Hz, $^3J_{4\text{-}3}$ = 6.7 Hz, H-4), 4.32 (d, 1H, $^3J_{3\text{-}4}$ = 6.7 Hz, H-3), 4.64–6.70 (m, 2H, CH_2 Bn), 7.37–7.65 (m, 5H, CH Ar); ^{13}C NMR (62.5 MHz, [D_6]DMSO): δ (ppm) = 44.1 (CH_2-6), 69.7 (CH-5), 72.5 (CH_2 Bn), 74.1 (CH_2-1), 74.5 (C-2), 77.2 (CH-4), 81.1 (CH-3), 127.4 (CH Ar), 127.5 (CH Ar), 128.3 (CH Ar), 138.0 (Cq Ar), 157.5 (C=O); IR (neat) ($\tilde{\nu}$, cm^{-1}) = 3307 (NH + OH), 1743 (C=O); HRMS (ESI$^+$): *m/z* = calculated for $C_{14}H_{19}N_2O_5$ ([M + H]$^+$): 295.1288, found 295.1288.

1-*O*-Allyl-2-*N*,3-*O*-carbonyl-2,6-dideoxy-2,6-imino-α-L-sorbopyranosylamine (41f). General procedure 11b was followed using OZO **32f** (100 mg, 0.37 mmol). Purification using silica gel column chromatography (pure EA then EA/Acetone, 50:50) gave the desired product **41f** as a yellow foam (63 mg, 70 %). R_f = 0.32 (EA/MeOH: 90:10); $[\alpha]_D^{20}$ = –72 (*c* 0.81, EA); ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ (ppm) = 2.62–2.71 (m, 1H, H-6b), 2.93 (dd, 1H, $^2J_{6a\text{-}6b}$ = 12.6 Hz, $^3J_{6a\text{-}5}$ = 4.5 Hz, H-6a), 3.33–3.41 (m, 1H, H-5), 3.42 (d, 1H, $^2J_{1b\text{-}1a}$ = 9.2 Hz, H-1b), 3.46 (d, 1H, $^2J_{1a\text{-}1b}$ = 9.2 Hz, H-1a), 3.51 (ddd, 1H, $^3J_{4\text{-}5}$ = 9.0 Hz, $^3J_{4\text{-}3}$ = 6.7 Hz, $^3J_{4\text{-}OH}$ = 4.6 Hz, H-4), 4.01 (d, 1H, $^3J_{OH\text{-}5}$ = 4.3 Hz, OH-5), 4.03–4.11 (m, 3H, H-3, CH_2-allyl), 4.54 (d, 1H, $^3J_{OH\text{-}4}$ = 4.6 Hz, OH-4), 5.15 (dq, 1H, $^3J_{cis}$ = 10.6 Hz, $^2J_{gem}$ = ^4J = 1.5 Hz, =CH_2 allyl), 5.29 (dq, 1H, $^3J_{trans}$ = 17.3 Hz, $^2J_{gem}$ = ^4J = 1.8 Hz, =CH_2 allyl), 5.90 (ddt, 1H, $^3J_{trans}$= 17.3 Hz, $^3J_{cis}$= 10.6 Hz, ^3J = 5.4 Hz, HC= allyl), 6.46 (bs, 1H, NH); ^{13}C NMR (100 MHz, $(CD_3)_2CO$): δ (ppm) = 45.0 (CH_2-6), 71.2 (CH-5), 72.8 (CH_2-allyl), 75.0 (CH_2-1), 75.6 (C-2), 78.6 (CH-4), 81.9 (CH-3), 117.2 (=CH_2), 135.5 (HC= allyl), 157.9 (C=O); IR (neat) ($\tilde{\nu}$, cm^{-1}) = 3296 (NH + OH), 1749 (C=O); HRMS (ESI$^+$): *m/z* = calculated for $C_{10}H_{17}N_2O_5$ ([M + H]$^+$): 245.1131, found 245.1130.

6-Amino-2-*N*,3-*O*-carbonyl-6-deoxy-1-*O*-methyl-α-L-sorbopyranosylamine (42f). General procedure 11b was followed using OZO **33f** (145 mg, 0.59 mmol). Purification using silica gel column chromatography (pure EA then EA/Acetone, 50:50) gave the desired product **42f** as a pale yellow sticky solid (80 mg, 62 %). R_f = 0.27 (EA/MeOH: 90:10); $[\alpha]_D^{20}$ = –89 (*c* 0.60, EA); ^{1}H NMR (400 MHz, [D_6]DMSO): δ (ppm) = 2.37–2.44 (m, 1H, CH_2-6a), 2.63 (bs, 1H, NH), 2.72 (td, 1H, $J_{6b\text{-}5}$ = 3.4 Hz, $J_{6b\text{-}6a}$ = 12.5 Hz, CH_2-6b), 3.09–3.16 (m, 1H, H-5), 3.19–3.26 (m, 3H, 2H of CH_2-1 and 1H, H-4), 3.29 (s, 1H, CH_3), 3.88 (d, 1H, $J_{3\text{-}4}$ = 6.4 Hz, H-3), 4.85 (d, 1H, $J_{OH\text{-}5}$ = 4.6 Hz, OH-5), 5.35 (d, 1H, $J_{OH\text{-}4}$ = 5.1 Hz, OH-4), 7.51 (s, 1H, NH); ^{13}C NMR (100 MHz, $(CD_3)_2SO$): δ (ppm) = 44.0 (CH_2-6), 58.9 (CH_3), 69.6 (CH-5), 74.3 (CH_2-1), 76.5 (CH-4), 77.1 (CH-3), 80.9 (C-2), 157.4 (C=O); IR (neat) ($\tilde{\nu}$, cm^{-1}) = 3359 (NH + OH), 1739 (C=O); HRMS (ESI$^+$): *m/z* = calculated for $C_8H_{15}N_2O_5$ ([M + H]$^+$): 219.0975, found 219.0976.

6-Amino-1-*O*-benzyl-6-deoxy-2-*N*,3-*O*-thiocarbonyl-α-L-sorbopyranosylamine (45f). General procedure 11a was followed using OZT **44f** (170 mg, 0.51 mmol). Purification using silica gel column chromatography (EA/MeOH: 90:10) gave the aminosugar **45f** as a white solid (78 mg, 50 %). R_f = 0.15 (EA/MeOH: 80:20); m.p 87–91 °C; $[\alpha]_D^{20}$ = –10.4 (*c* 0.193, MeOH); M.S (IS$^+$): *m/z* = 311.4 ([M + H]$^+$); ^{1}H NMR (400 MHz, CD_3OD): δ (ppm) = 2.98 (dd, 2H, ^3J = 1.5 Hz, $^3J_{6\text{-}5}$ = 5.8 Hz, CH_2-6), 3.69 (d, 1H, ^2J = 10.4 Hz, CH_2-1a), 3.77 (d, 1H, ^2J = 10.4 Hz, CH_2-1b), 3.93 (td, 1H, $^3J_{5\text{-}6}$ = 5.7 Hz, $^3J_{5\text{-}4}$ = 2.9 Hz, CH-5), 4.30 (d, 1H, $^3J_{4\text{-}5}$ = 2.9 Hz, CH-4), 4.62 (d, 2H, ABq, CH_2 Bn), 4.89 (s, 1H, CH-3), 7.26–7.36 (m, 5H, CH Ar). ^{13}C NMR (100 MHz, CD_3OD): δ (ppm) = 40.6 (CH_2-6), 70.6 (CH_2-1), 74.7 (CH_2 Bn), 75.4 (CH-4), 82.3 (CH-5), 92.6 (CH-3), 100.8 (C-2), 128.9 (CH Ar), 129.0 (CH Ar), 129.5

(CH Ar), 139.0 (Cq Ar), 190.8 (C=S); IR (neat) ($\tilde{\nu}$, cm^{-1})= 3160 (NH + OH), 1093 (C=S), 997 (CN).

Supporting Information: ^{1}H and ^{13}C NMR spectra of all new compounds, details for glycosidases inhibition evaluation and DFT calculation (cartesian coordinates for each conformer).

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Keywords: Iminosugar · Oxazolidinone · Oxazolidinethione · Glycosidase inhibitor

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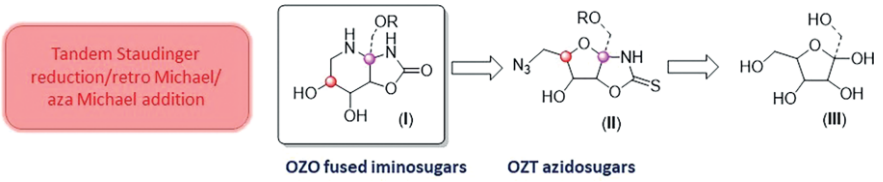
Bicyclic Iminosugars



The synthesis of unprecedented bicyclic oxazolidin-2-one (OZO) fused iminosugars is described. The key step involves a tandem Staudinger/retro Michael/aza Michael sequence from OZO azidosugars, themselves obtained through oxidation of oxazolidin-2-thione (OZT) precursors. The iminosugars were subsequently evaluated as glycosidase inhibitors.

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