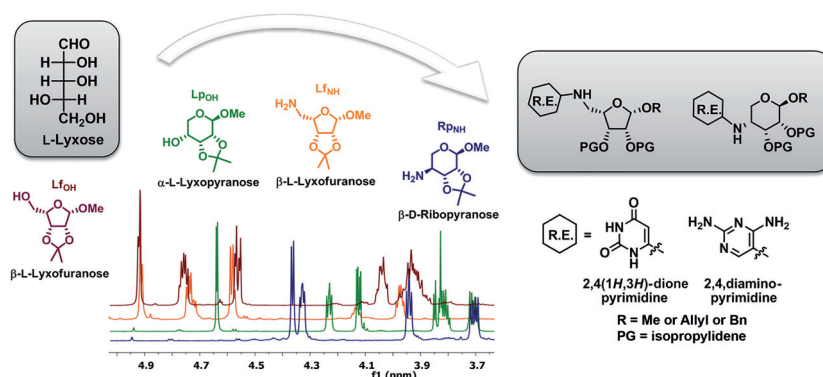


Investigations towards the Synthesis of 5-Amino-L-lyxofuranosides and 4-Amino-lyxopyranosides and NMR Analysis

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Received: 02.04.2017

Accepted after revision: 12.05.2017

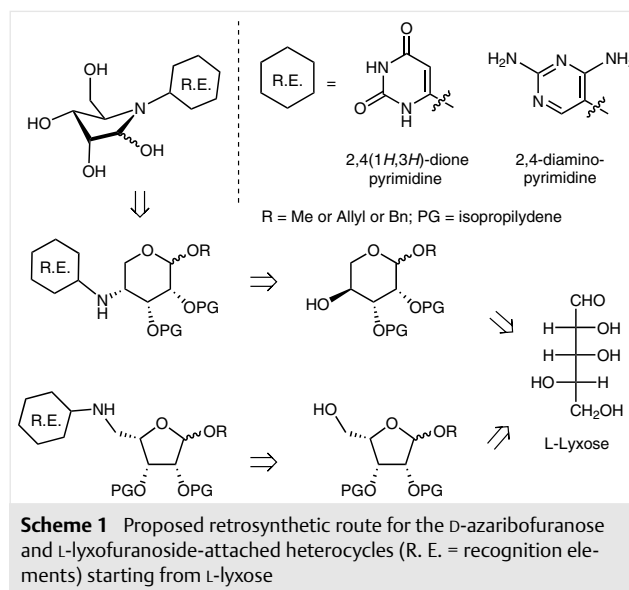
Published online: 01.06.2017

DOI: 10.1055/s-0036-1588859; Art ID: so-2017-d0014-op

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Abstract The reactivity of trifluoromethanesulfonyl esters derived from L-lyxofuranosides and L-lyxopyranosides was investigated with various 5-aminopyrimidines as nucleophiles with the expectation to synthesize *N*-substituted 5-amino-ribosugars. The lyxopyranoside forms were found to be unreactive, while the lyxofuranoside forms were found to be reactive with 5-aminopyrimidines, yielding novel *N*-substituted 5-amino-lyxofuranosides. We report on the synthesis of these novel *N*-substituted lyxofuranosides and the systematic analyses of NMR data that demonstrate trends within each series: furano-, pyrano-, β- and α- anomers of L-lyxose and β-D-ribofuranoside forms. The data call for caution when identifying these monosaccharides in isomeric mixtures.

Key words L-lyxofuranoses, L-lyxopyranoses, D-ribofuranoses, conformation analysis, heterocycles, NMR spectroscopy



In our research exploring the self-assembly properties of alternative recognition elements such as 5-aminouracil and 2,4,5-triaminopyrimidine substituted-pyrrolidines, it was necessary to develop new *N*-substituted 4-amino-D-ribofuranose sugars.¹⁻³ We proposed the corresponding L-lyxopyranose derivatives as outlined in Scheme 1 as intermediates en route to the final pyrrolidine compounds. This synthetic approach is based on the fact that nucleophiles can attack the C(4) position of a substituted lyxopyranose sugar (with a good leaving group at the C(4)-position) through a bimolecular nucleophilic substitution (S_N2) displacement, resulting in the corresponding ribopyranose framework.⁴⁻⁷ However, the synthesis of *N*-substituted 4-amino-D-ribofuranose derivatives proved problematic with amino pyrimidine heterocycles, presumably due to the poor nucleophilicity of these alternative amino nucleobases.

For comparison, we also studied the S_N2 reaction with the L-lyxofuranosyl series with the awareness that 5-amino-heterocycles may react more readily at a primary carbon. When comparing the results of the L-lyxopyranose and L-lyxofuranose series, we found that there could be some uncertainty in the assignments as α/β anomeric mixtures of alcohols derived from L-lyxose when they are actually furanoside/pyranoside mixtures.⁸ To clarify this issue, we have synthesized, measured NMR spectra and contrasted the chemical shift trends of the furanosyl and pyranosyl L-lyxose series – both from this work and those in the literature – and came to the conclusion that identifying the minor compound in isomeric mixtures of monosaccharides can be crucial and should always rely on accurate identification based on corroborating NMR techniques.

The starting lyxofuranosides **1–3** were obtained in a one-pot reaction, in which protection of the anomeric position and formation of the acetal were accomplished by heating the starting L-lyxose in the presence of acetone and the appropriate alcohol in acidic medium for short periods of time. Characterization of small amounts of impurities that co-eluted with the desired products showed discrepancies with the results described earlier.⁸ Instead of mixtures of anomers, we identified trace amounts of pyranose products **5–7**. In our hands, we could not find mixtures of anomers in any of the cases. The synthesis of starting materials in the L-lyxopyranose series was accomplished by following existing procedures (Scheme 2).^{5–7,9–12} L-Lyxopyranosides **5–7** were prepared in a stepwise fashion. First, protection of the anomeric position by a regular Fischer glycosidation was conducted with corresponding anhydrous alcohol in the presence of an acid. The reaction produced, what we originally thought to be, anomeric mixtures of **4a–c**. The ketal protection of these mixtures led to the pyranosyl compounds **5–7** (Scheme 2) and small amounts of the corresponding isomers. We had assumed **5** could be mixed with its anomer to a small amount and this was not considered problematic because both anomers would lead to the desired pyrrolidine scaffolds as formulated in Scheme 1. In fact, it turned out to be a mixture of furanose and pyranose forms, which was difficult to purify. Detailed analysis by NMR (see Figure S.54 in the Supporting Information) showed that alcohols **5** and **6** indeed contained small amounts of furanose forms (**1** and **2**, respectively), instead of mixtures of (misassigned) anomers.⁸ It is noticeable that the chemical shifts of both isomer protons (**5** and **1**) are quite different; for example, 0.5 ppm in CDCl₃ between both isomers for the anomeric protons (see Table 2), which may have suggested they actually were more different than simply anomers. NOESY NMR spectroscopic analysis of the

pure starting materials (**1–3** and **5–7**) showed that the major anomer is β for L-lyxofuranosyl and α for L-lyxopyranosyl alcohols (see also Supporting Information).

To access the sugars tagged with different alternative recognition elements, the corresponding 5-position of the furanosides and 4-position of the pyranosides were modified with good leaving groups that facilitated the attack of different nucleophiles through S_N2 mechanism. In the case of the α -L-lyxopyranose series, inversion of configuration at C(4) generates the β -D-ribofuranose sugar. Four different nucleophiles were selected for this study (Figure 1). Sodium azide **8** was chosen based on the fact that it would lead to a precursor of the corresponding amino compound.^{4,13} This approach could allow for a later introduction of heterocycles via nucleophilic aromatic substitution. Along with the heterocycles 5-aminouracil **10** and 2,4,5-triaminopyridine **11**, benzyl amine **9** was also utilized for comparison.

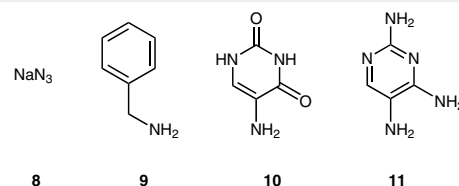
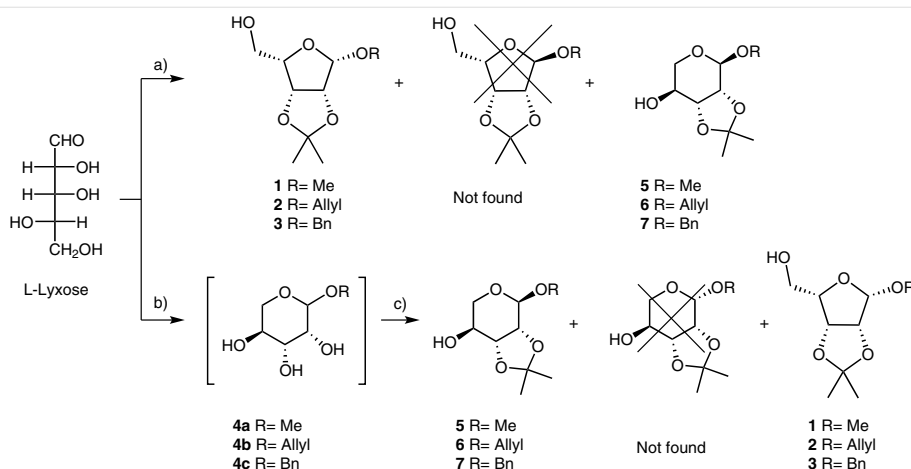
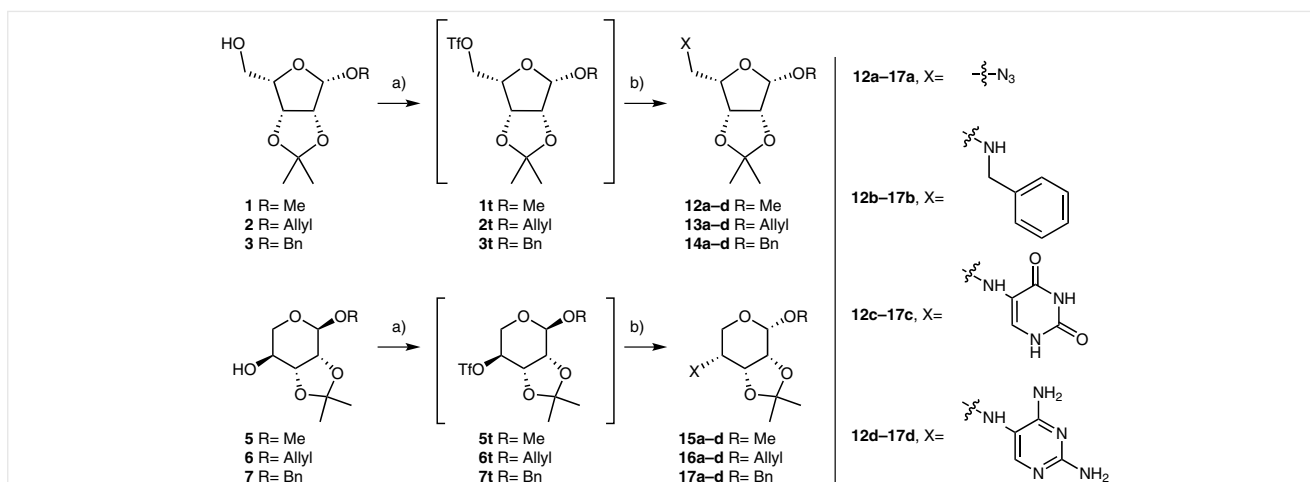


Figure 1 Nucleophiles utilized for the S_N2 reactions with L-lyxose derivatives

The trifluoromethane sulfonate esters of alcohols (at (C)4 position for the pyranose and (C)5 position for the furanose series) were generated with trifluoromethanesulfonic anhydride in the presence of DMAP and pyridine at -20 °C.^{6,7} Reactions were quenched by aqueous work-up upon consumption of starting material. The subsequent S_N2 reaction was conducted on the crude triflate intermediates



Scheme 2 Synthesis of the ketal-protected β -furanosides and α -pyranosides of L-lyxose. *Reagents and conditions:* (a) Acetone, ROH, H₂SO₄, 60 °C, 4 h (1: 72% and 5: <5%; 2: 48% and 6: <5%; 3: 37% and 7: <5%); (b) ROH, reflux, H⁺, 3 h; (c) HCl, acetone, DMP, r.t., 16 h (yields after two steps: 5: 36% and 1: <20%; 6: 41% and 2: <10%; 7: 30% and 3: <5%).



Scheme 3 Generation of the trifluoromethanesulfonyl esters of L-xylose and subsequent S_N2 reaction with nucleophiles **8-11**. Reagents and conditions: (a) TiF_2O , DMAP, CH_2Cl_2 , Py, -20°C to r.t., 4 h; (b) **8-11**, DMF, different conditions: see Table 1.

1t-3t and **5t-7t** (no purification was attempted due to their instability). The corresponding mesylate leaving groups were not used because they did not react even with sodium azide; whereas the triflate intermediates promptly reacted with the latter nucleophile (Scheme 3 and Table 1, entries 1 and 2). Reaction of the triflate of **1** with **10** over three days at room temperature led to poor yields (entry 3). The use of 3.0 equivalents of heterocycles **10** and **11** and higher temperature (probably increasing the solubility of the heterocycles and the speed of the reaction) led to higher product yields. The use of *N,O*-bis(trimethylsilyl)acetamide (BSA) increased the solubility of 5-aminouracil **10** and resulted in further improvement of product yields (entry 5), but did not help in the case of **11** (entry 7).

Reactions of triflates with different nucleophiles at 70°C for up to two days generated by-products resulting from the hydrolysis or decomposition of the starting materials. In the β -L-lyxofuranose series, 2,4,5-triaminopyrimidine **11** produced higher yields than 5-aminouracil **10** when reacting with the **1t-3t** triflates, perhaps reflecting the higher nucleophilicity of the 5- NH_2 group in **11**. For comparison, 5-aminolixofuranose **18** was synthesized by hydrogenation of azide **12a** (see Scheme 5).

Analyses of the NMR spectra of amines **12c-d**, **13c-d** and **14d**, obtained through S_N2 reaction with the corresponding trifluoromethanesulfonates, showed similar features when compared with the corresponding alcohols **1-3**, respectively (Table 2) and with amine **18**. As expected, the electronic nature of the substituents affected the ^1H and ^{13}C NMR shift values; that is, substitution of the hydroxy at C(5) with an amino group produced an upfield shift of 20 ppm in the ^{13}C NMR spectra and up to 0.6 ppm in the ^1H NMR spectra (Table 2 and Table 3, entries 1 and 5). NOESY NMR spectra of the products of the S_N2 reaction confirmed the β -L-lyxofuranosyl form of the compounds. Figure 2 illustrates the NMR spectrum of compound **12c**. Nuclear Overhauser

Table 1 Reaction Conditions and Products Obtained from the S_N2 Reaction Outlined in Scheme 3

Entry	Alcohol	Nucleophile	Conditions	Product	Overall yield (%) ^a
1	1	8	r.t., 4 h	12a	75
2	5 ^b	8	r.t., 4 h	15a ^c	68
3	1	10	r.t., 3d	12c	<5
4	1	10	70°C , 48 h	12c	9
5	1	10	BSA, 70°C , 48 h	12c	47
6	1	11	70°C , 48 h	12d	56
7	1	11	BSA, 70°C , 48 h	12d	33
8	2	10	BSA, 70°C , 48 h	13c	45
9	2	11	70°C , 48 h	13d	48
10	3	11	70°C , 48 h	14d	26
11	5 ^b	10	BSA, 70°C , 48 h	12c	5
12	5	10	BSA, 70°C , 48 h	15c	–
13	5 ^b	11	70°C , 48 h	12d	5
14	5	11	70°C , 48 h	15d	–
15	5	9	70°C , 24 h	15b	63
16	6	10	BSA, 70°C , 48 h	16c	–
17	6	11	70°C , 48 h	16d	–

^aYields determined after isolation and purification by column chromatography; ‘–’ indicates no reaction.

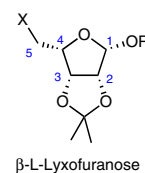
^bStarting material **5** was utilized as a mixture of isomers (mixed with **1**).

^cBy-product **12a** was isolated (ca. 5%) by column chromatography.

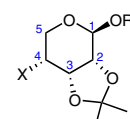
effect (nOe) correlations between the proton at the anomeric position with protons at the C(2) and C(4) positions confirmed the expected β -form, in agreement with the starting materials and the anomeric effect. This was consistent with the NOESY spectra of the alcohol starting materials.

Table 2 ¹H and ¹³C NMR Chemical Shift Values [δ, ppm] of Monosaccharides in DMSO-*d*₆

Entry	Product	Ring ^a	R	X	H-1	H-2	H-3	H-4	H-5	C-1	C-2	C-3	C-4	C-5
1	1	Lf	Me	OH	4.81	4.49	4.70	3.85	3.51, 3.64	106.3	84.3	79.1	80.6	58.9
2	2	Lf	Allyl	OH	4.95	4.53	4.72	3.90	3.55, 3.64	104.8	84.4	79.1	80.7	58.9
3	3	Lf	Bn	OH	5.01	4.58	4.76	3.98	3.59, 3.68	104.7	84.4	79.1	80.8	58.9
4	19^b	Lf	H	OH	5.10	4.42	4.68	4.00	3.50, 3.62	100.0	85.6	79.5	80.0	59.2
5	18	Lf	Me	NH ₂	4.92	4.57	4.79	4.10	2.92, 3.15	106.2	85.4	79.1	75.8	38.0
6	12c	Lf	Me	NH-U ^c	4.83	4.51	4.73	4.01	3.03, 3.17	106.3	84.4	79.5	77.8	42.8
7	12d	Lf	Me	NH-Py ^d	4.86	4.55	4.79	4.03	3.08, 3.22	106.4	84.4	79.3	77.4	42.7
8	13c	Lf	Allyl	NH-U ^c	4.98	4.57	4.76	4.05	3.01, 3.21	104.8	84.6	79.5	77.8	42.8
9	13d	Lf	Allyl	NH-Py ^d	4.98	4.58	4.81	4.04	3.03, 3.16	104.6	84.3	79.3	77.9	43.4
10	14d	Lp	Benzyl	NH-Py ^d	5.05	4.63	4.83	4.12	3.08, 3.22	105.2	84.9	79.8	77.8	43.0
11	5	Lp	Me	OH	4.59	3.95	3.95	3.58	3.38, 3.45	99.5	77.0 ^e	74.5 ^e	66.5	62.0

^a Lf = β-L-lyxofuranoside; Lp = α-L-lyxopyranoside.^b For comparison, compound **19** was made by hydrogenolysis of **3** (see Scheme 5).^c U = 5-uracil.^d Py = 5-(2,4-diamino)pyrimidine.^e Assignments may be interchanged.

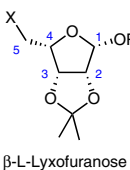
β-L-Lyxofuranose



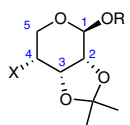
α-L-Lyxopyranose

Table 3 ¹H and ¹³C NMR Chemical Shift Values [δ, ppm] of Monosaccharides in CDCl₃

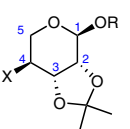
Entry	Product	Ring ^a	R	X	H-1	H-2	H-3	H-4	H-5	C-1	C-2	C-3	C-4	C-5
1	1	Lf	Me	OH	4.92	4.56	4.76	4.03	3.90, 3.95	107.2	85.3	80.4	79.4	61.2
2	2	Lf	Allyl	OH	5.02	4.57	4.72	4.03	3.81, 3.87	105.1	85.0	80.0	79.4	60.7
3	3	Lf	Bn	OH	5.15	4.71	4.81	4.13	3.94, 4.00	105.2	85.3	80.5	79.3	61.5
4	12a	Lf	Me	N ₃	4.91	4.57	4.70	4.08	3.50, 3.57	106.2	84.0	78.6	77.3	48.7
5	18	Lf	Me	NH ₂	4.89	4.56	4.72	3.94	3.04, 3.04	107.1	85.2	80.7	80.1	40.9
6	5	Lp	Me	OH	4.64	4.12	4.23	3.81	3.71, 3.82	99.9	74.4	76.2	67.3	63.3
7	6	Lp	Allyl	OH	4.76	4.14	4.20	3.81	3.67, 3.75	97.8	74.5	76.6	67.4	62.9
8	7	Lp	Bn	OH	4.84	4.18	4.24	3.81	3.73, 3.81	97.3	74.5	76.5	67.3	62.8
9	15a	Rp	Me	N ₃	4.47	4.00	4.50	3.81	3.71, 3.81	100.9	75.3	72.9	54.9	60.2
10	20	Rp	Me	NH ₂	4.37	3.94	4.34	3.21	3.71, 3.43	101.9	75.7	75.4	49.9	65.1
11	15b	Rp	Me	NHBn	4.33	3.90	4.46	3.15	3.40, 3.85	102.4	75.8	72.9	52.1	63.5
12	21	Rp	Me	NHCHO	4.42	4.03	4.35	4.61	3.44, 3.82	100.1	75.1	72.5	43.0	61.0
13	22	Rp	Me	NHBz	4.47	4.09	4.47	4.76	3.51, 3.97	101.2	75.4	73.0	44.8	61.4

^a Lf = β-L-lyxofuranoside; Lp = α-L-lyxopyranoside; Rp = β-D-ribofuranoside.

β-L-Lyxofuranose



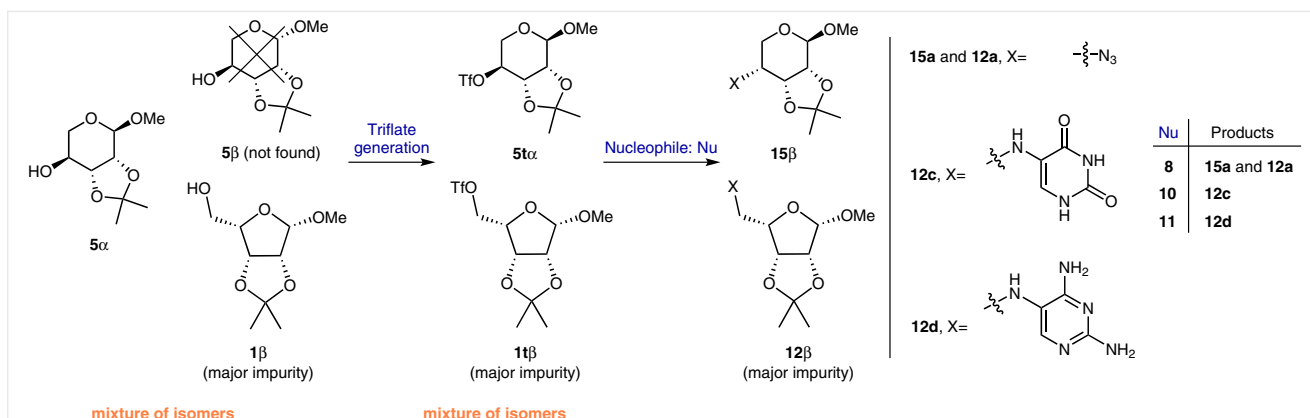
α-L-Lyxopyranose



β-D-Ribopyranose

In the α-L-lyxopyranosyl series, only NaN₃ and BnNH₂ (Table 1, entries 2 and 15) were successful in reacting with triflate **5t**, resulting in inversion of configuration at the C(4) position by nucleophilic substitution giving D-ribofuranose derivatives **15a** and **15b**, respectively. When reactions were run with heterocycles **10** and **11**, degradation of triflate **5t** was mostly observed, with only very small amounts of the substituted products being isolated; this reflects the poor nucleophilicity of heterocycles **10** and **11**. Analysis of the resulting compounds revealed that the reaction products

(expected **15c** and **15d**) had the β-L-lyxofuranose form instead of the anticipated β-D-ribofuranose form. NMR comparisons with prepared furanoses showed that these reaction products were the same as **12c** and **12d**. Both pyranose and furanose triflates reacted with good nucleophiles such as azide **8** and benzylamine **9** (Scheme 4) in S_N2 reactions. Therefore, in these cases, while the isolated major product was the pyranosyl derivative, a minor (furanosyl) product was isolated in small yields or, in some cases, 'lost' during the purification procedures. However, regarding the reac-



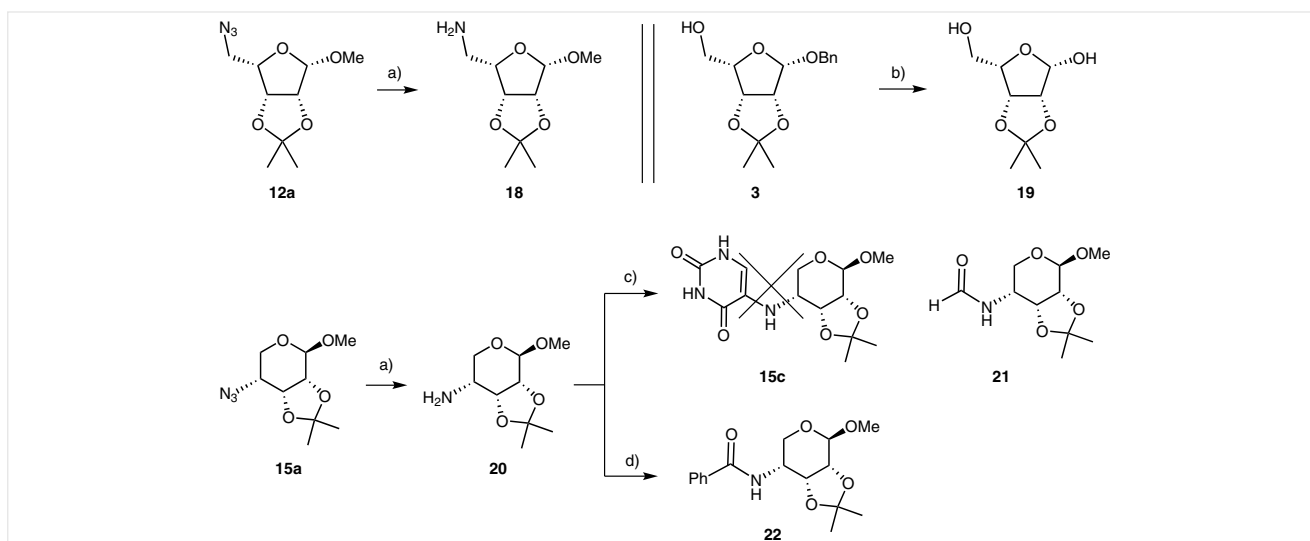
Scheme 4 Reaction scheme for the mixture of isomers of **5** and subsequent S_N2 reactions with nucleophiles

tion of pyrimidines **10** and **11** with **5t** (mixed with its isomer), it seemed that the minor compound (the furanose form, **1t**) is the only isomer able to react with poor nucleophiles (Table 1, entries 11 and 13), whereas the pyranose form **5t** is not reactive with **10** and **11**. When S_N2 reactions were repeated starting with pure pyranoses **5–7** and nucleophiles **10** and **11**, the expected ribopyranoses **15c/d**, **16c/d**, and **17c/d** were not formed (Table 1, entries 12, 14, 16–19), confirming our previous results that only the furanose forms undergo reaction.

We attempted an alternative synthesis of **15c** as depicted in Scheme 5. It is known that 5-bromouracil can act as an electrophile and be attacked by amines under different reaction conditions (heat without solvent,^{14–16} reflux,^{16–18} or microwave¹⁹). Therefore, we prepared aminosugar **20** and reacted it with 5-bromouracil. Unfortunately, this ‘in-

verse approach’ in DMF did not generate the expected compound (**15c**), but rather led to the *N*-formylated sugar derivative **21**. We did not explore this pathway further, but suspect that the 5-bromouracil assisted in the formylation process. Heterocycle-assisted *N*-formylation reactions under mild conditions have been described utilizing imidazole with primary amines.²⁰ Full characterization of **21** revealed the NMR trends to be consistent with the rest of the β -D-ribose compounds and was comparable to compound **22** prepared via a different route.

To address the question of dealing with mixtures of anomers versus mixtures of furanoses and pyranoses,⁸ we scrutinized the ¹H and ¹³C NMR data of our compounds to find trends in chemical shifts, supported by other NMR spectroscopic techniques that would prove useful in assigning the structures. Table 2 and Table 3 summarize the full charac-



Scheme 5 Generation of the amines **18** and **20** for the ‘inverse approach’ in which the sugar acts as the nucleophile with a leaving group on the heterocycle. Attempted synthesis of **15c**. Synthesis of **19** and **22** are shown for comparison. *Reagents and conditions:* (a) H_2 , Pd/C (5%), MeOH, r.t., 6 h (**18**: 95%; **20**: 95%); (b) H_2 , Pd(OH)₂, MeOH, r.t., 20 h (98%); (c) 5-bromouracil, DMF, 70 °C, 16 h (**21**: 56% and **15c**: not found); (d) BzCl, DIPEA, CH₂Cl₂, r.t., 16 h (82%).

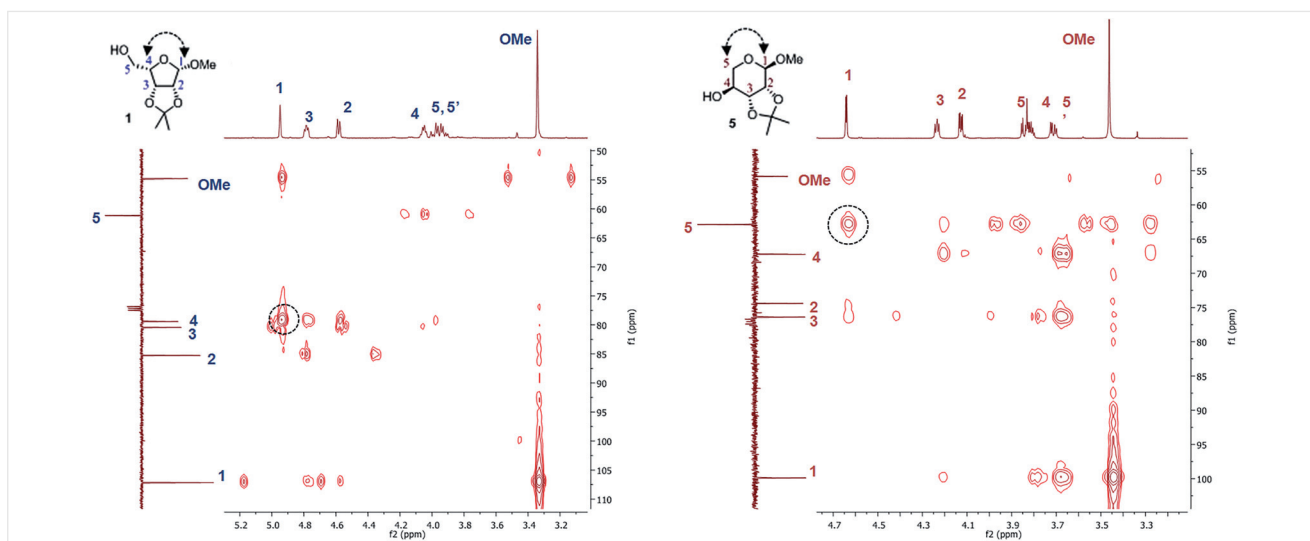


Figure 2 HMBC (^1H - ^{13}C , CDCl_3) spectra of the alcohols **1** and **5**. Correlations highlighted with a dashed circle corroborate unambiguously the configuration of the furanose and pyranose forms, respectively

terization of the sugar derivatives that we have obtained, documenting trends within and between the furanose and pyranose series. Extensive NMR measurements were conducted using the same deuterated solvent ($\text{DMSO-}d_6$) system both for the already published products and related compounds originally reported in CDCl_3 (Table 2), and for the heterocycle-attached furanose compounds, which are insoluble in CDCl_3 (Table 3). Analyses were carried out by HSQC and COSY NMR spectroscopy of all the structures, in addition to NOESY spectroscopy to confirm the configuration of the pyranose or furanose rings and the configuration in the anomeric position (see Figure 3 and the Supporting Information); HMBC spectroscopy was used to corroborate the configuration of the rings (see Figure 2 and the Supporting Information) of some of the starting materials and several products.

In general, the trends in chemical shift for pyranosides versus furanosides (within a sugar series) are consistent, and independent of solvent and substituents in the anomeric position. For example, in ^1H NMR spectra for the lyxo series, all shifts except for the $\text{C}(5)\text{H}_2$, are more downfield (ca. 0.5–0.3 ppm) in the furanose form when compared with the pyranose form. The same trend is observed in the ^{13}C NMR (12–4 ppm) for both the lyxo and the ribo series, as documented in Table 2 (entries 1–3 and entries 11 and 12) and Table 3 (entries 1–3 and entries 6 and 7).

There is also a consistent trend for the different anomers within a given series. The signals for the anomeric position for β -L-lyxofuranosyl compounds appear around 4.8–5.0 ppm in ^1H NMR spectra and 104–107 ppm in ^{13}C NMR spectra; whereas the corresponding values for the α -L-lyxopyranosyl forms are consistently more upfield: around 4.6–4.8 ppm in the ^1H NMR spectra and below 100 ppm in the

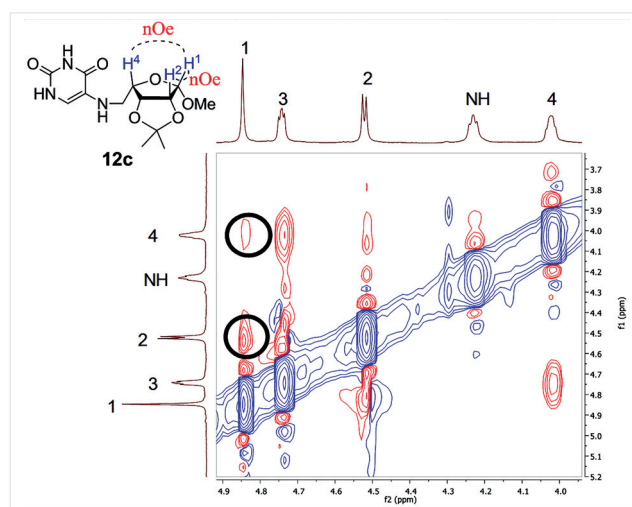


Figure 3 NOESY (^1H - ^1H , $\text{DMSO-}d_6$) spectrum that corroborates the β -configuration of **12c**

^{13}C NMR spectra (Table 2, entries 1–8; Table 3). The substitution of the hydroxyl in the $\text{C}(5)$ position by an amine in the furanose series up-shifted the CH_2 -signal by 20 ppm in the ^{13}C NMR spectra and by around 0.6 ppm in the ^1H NMR spectra (Table 2, entries 1–4 versus 5–10). In the ribopyranose series, substitution in position $\text{C}(4)$ affected the chemical shift values of position $\text{C}(4)$ and $\text{C}(5)$ depending on the nature of the substituent, as evidenced in Table 3, entries 10 vs. 12 and 13 and entries 10 vs. 11, respectively.

Thus, caution must be exercised to determine whether the compounds are mixtures of furanose/pyranose (in the ribo- or lyxo-series) versus mixtures of anomers (in the ribo- and lyxo-series).⁸ Further NMR spectroscopic (e.g.,

HMBC and NOESY) studies need to be performed to confirm the α - or β - versus furanose- or pyranose-configuration of the sugars at hand.

In conclusion, in our attempts to synthesize *N*-substituted 5-amino-lyxopyranose derivatives, we have demonstrated that only the 5-*O*-trifluoromethanesulfonate *L*-lyxofuranoside derivative reacts with 5-aminouracil and 2,4,5-triaminopyrimidine as nucleophiles; S_N2 reactions with 4-*O*-triflate *L*-lyxopyranoside derivatives with these heterocyclic nucleophiles were unsuccessful. A detailed NMR spectroscopic characterization of both the starting materials and products enabled us to identify trends in chemical shifts for the corresponding lyxosides and ribosides (in the pyrano and furano series versus the α - and β -anomers). Identifying trends on chemical shifts within each series and also exceptions between them, will be of utility in future investigations. These exceptions point out the potential pitfalls in attempting to recognize mixtures of anomers versus mixtures of furanosides/pyranosides based on trends in chemical shifts alone.

All reagents were obtained from commercial sources and used without purification. Anhydrous solvents were purchased from EMD Chemicals. All experiments were performed under a nitrogen or argon atmosphere. Thin-layer chromatography (TLC) was performed on silica gel 60 Å F_{254} from Angela Technologies, and visualized under a UV lamp and/or by staining with a solution of phosphomolybdic acid (PMA) in ethanol. Flash column chromatography was performed on silica gel 60 Å with particle size 35–70 μm purchased from Acros Organics. NMR spectra were recorded at 20 °C with a Bruker DRX-600, AV-600 (600 MHz for ^1H and 150 MHz for ^{13}C) or an AV-400 (400 MHz for ^1H and 100 MHz for ^{13}C). Chemical shifts (δ) are given in parts per million (ppm). ^1H and ^{13}C chemical shifts in CDCl_3 were referenced to chloroform at $\delta = 7.26$ and 77.16 ppm, respectively. ^1H and ^{13}C chemical shifts in $\text{DMSO-}d_6$ were referenced to dimethyl sulfoxide at $\delta = 2.50$ and 39.52 ppm, respectively. NMR peak assignments were made based on COSY, HSQC and/or NOESY 2D experiments. Mass spectra were measured with an Agilent ESI-TOF or a ThermoElectron Finnigan LTQ ion trap mass spectrometer.

Synthesis of the Protected Furanoside Sugars

The protection of the furanose sugars was developed by following the same procedure described by Coleman et al.²¹ *L*-Lyxose (1.20 g, 8.00 mmol, 1 equiv) was dissolved in the corresponding freshly distilled alcohol (10 equiv) and anhydrous acetone (4.70 mL, 48.0 mmol, 8 equiv). The flask was immersed in an ice bath and concentrated sulfuric acid (3–4 Pasteur pipette drops) was added dropwise. The mixture was stirred at reflux until disappearance of the starting material, as monitored by TLC (3–5 h, depending on the alcohol). The reaction was quenched with saturated aq. NaHCO_3 solution and the aqueous solution was extracted three times with EtOAc. The combined organic layers were dried with anhydrous Na_2SO_4 , filtered and evaporated to dryness. Analysis of the crude material by ^1H NMR spectroscopy showed mixtures of furanose and pyranose products up to 1:0.10 ratio (depending on the reaction). The crude reaction mixture was subjected to column chromatography to afford the corresponding pro-

tected lyxofuranoside. Traces (>5%) of the corresponding 2,3-*O*-isopropylidene- α -*L*-lyxopyranoside were found in the crude material in all cases.

Methyl 2,3-*O*-Isopropylidene- β -*L*-lyxofuranoside (1)²²

Yield: 1.17 g (72%); oil; R_f (hexanes/EtOAc, 8:2) = 0.18.

^1H NMR (400 MHz, CDCl_3): $\delta = 4.92$ (s, 1 H, H-1), 4.74–4.78 (m, 1 H, H-3), 1.29 (s, 3 H, CCH_3), 4.56 (d, $J = 5.9$ Hz, 1 H, H-2), 4.01–4.06 (m, 1 H, H-4), 3.87–3.97 (m, 2 H, H-5a, H-5b), 3.32 (s, 3 H, OCH_3), 2.42 (br s, 1 H, OH), 1.45 (s, 3 H, CCH_3).

^{13}C NMR (100 MHz, CDCl_3): $\delta = 112.8$ ($\text{C}(\text{CH}_3)_2$), 107.2 (C-1), 80.4 (C-3), 85.3 (C-2), 79.4 (C-4), 61.2 (C-5), 54.8 (OCH_3), 26.0 (CCH_3), 24.7 (CCH_3).

^1H NMR (600 MHz, $\text{DMSO-}d_6$): $\delta = 4.81$ (s, 1 H, H-1), 4.68–4.75 (m, 2 H, H-3, OH), 4.49 (d, $J = 5.9$ Hz, 1 H, H-2), 3.85 (dd, $J = 9.6, 5.9$ Hz, 1 H, H-4), 3.61–3.67 (m, 1 H, H-5b), 3.51–3.57 (m, 1 H, H-5a), 3.22 (s, 3 H, OCH_3), 1.34 (s, 3 H, CCH_3), 1.24 (s, 3 H, CCH_3).

^{13}C NMR (150 MHz, $\text{DMSO-}d_6$): $\delta = 111.4$ ($\text{C}(\text{CH}_3)_2$), 106.3 (C-1), 84.3 (C-2), 80.6 (C-4), 79.1 (C-3), 58.9 (C-5), 53.9 (OCH_3), 26.0 (CCH_3), 24.7 (CCH_3).

ESI(+)-MS: m/z calcd. for $\text{C}_9\text{H}_{17}\text{O}_5$ [$\text{M} + \text{H}$]⁺: 205.11; found: 205.11.

Data in agreement with the literature²² (*ent*-1).

Allyl 2,3-*O*-Isopropylidene- β -*L*-lyxofuranoside (2)⁸

Yield: 884 mg (48%); oil; R_f (hexanes/EtOAc, 8:2) = 0.25.

^1H NMR (600 MHz, CDCl_3): $\delta = 5.81$ (dddd, $J = 17.5, 10.4, 6.4, 5.5$ Hz, 1 H, $\text{CH}=\text{CH}_2$), 5.21 (d, $J = 17.2$ Hz, 1 H, $\text{CH}=\text{CH}_2$ -*trans*), 5.12 (d, $J = 10.4$ Hz, 1 H, $\text{CH}=\text{CH}_2$ -*cis*), 5.02 (s, 1 H, H-1), 4.72 (dd, $J = 5.7, 4.3$ Hz, 1 H, H-3), 4.57 (d, $J = 5.7$ Hz, 1 H, H-2), 4.09 (dd, $J = 12.3, 5.5$ Hz, 1 H, $\text{OCHHCH}=\text{CH}_2$), 4.03 (dd, $J = 9.4, 5.1$ Hz, 1 H, H-4), 3.90 (dd, $J = 12.3, 6.4$ Hz, 1 H, $\text{OCHHCH}=\text{CH}_2$), 3.81–3.87 (m, 2 H, H-5a, H-5b), 2.75 (br s, 1 H, OH), 1.39 (s, 3 H, CCH_3), 1.24 (s, 3 H, CCH_3).

^{13}C NMR (150 MHz, CDCl_3): $\delta = 133.7$ ($\text{CH}=\text{CH}_2$), 117.4 ($\text{CH}=\text{CH}_2$), 112.5 ($\text{C}(\text{CH}_3)_2$), 105.1 (C-1), 85.0 (C-2), 80.0 (C-3), 79.5 (C-4), 67.7 ($\text{OCH}_2\text{CH}=\text{CH}_2$), 60.7 (C-5), 25.7 (CCH_3), 24.4 (CCH_3).

^1H NMR (600 MHz, $\text{DMSO-}d_6$): $\delta = 5.89$ (dddd, $J = 16.2, 10.8, 5.9, 5.0$ Hz, 1 H, $\text{CH}=\text{CH}_2$), 5.25 (dd, $J = 17.3, 1.7$ Hz, 1 H, $\text{CH}=\text{CH}_2$ -*trans*), 5.12 (dd, $J = 10.4, 1.6$ Hz, 1 H, $\text{CH}=\text{CH}_2$ -*cis*), 4.95 (s, 1 H, H-1), 4.70–4.75 (m, 2 H, H-3, OH), 4.53 (d, $J = 5.5$ Hz, 1 H, H-2), 4.09 (dd, $J = 13.3, 5.0$ Hz, 1 H, $\text{OCHHCH}=\text{CH}_2$), 3.94 (dd, $J = 13.3, 5.9$ Hz, 1 H, $\text{OCHHCH}=\text{CH}_2$), 3.88–3.92 (m, 1 H, H-4), 3.64 (dt, $J = 11.2, 5.6$ Hz, 1 H, H-5b), 3.51–3.57 (m, 1 H, H-5a), 1.34 (s, 3 H, CCH_3), 1.24 (s, 3 H, CCH_3).

^{13}C NMR (150 MHz, $\text{DMSO-}d_6$): $\delta = 134.6$ ($\text{CH}=\text{CH}_2$), 116.7 ($\text{CH}=\text{CH}_2$), 111.4 ($\text{C}(\text{CH}_3)_2$), 104.8 (C-1), 84.4 (C-2), 80.7 (C-4), 79.1 (C-3), 67.1 ($\text{OCH}_2\text{CH}=\text{CH}_2$), 58.9 (C-5), 26.0 (CCH_3), 24.7 (CCH_3).

ESI(+)-MS: m/z calcd. for $\text{C}_{11}\text{H}_{19}\text{O}_5$ [$\text{M} + \text{H}$]⁺: 231.12; found: 231.12.

ESI(+)-MS: m/z calcd. for $\text{C}_{11}\text{H}_{18}\text{NaO}_5$ [$\text{M} + \text{Na}$]⁺: 253.10; found: 253.10.

Data in agreement with the literature.⁸

Benzyl 2,3-*O*-Isopropylidene- β -*L*-lyxofuranoside (3)²³

Yield: 828 mg (37%); yellow oil; R_f (hexanes/EtOAc, 9:1) = 0.10.

^1H NMR (600 MHz, CDCl_3): $\delta = 7.28$ –7.37 (m, 5 H, *H*-Bn), 5.15 (s, 1 H, H-1), 4.81 (dd, $J = 5.6, 3.8$ Hz, 1 H, H-3), 4.66–4.71 (m, 2 H, *CHHPH*, H-2), 4.50 (d, $J = 11.7$ Hz, 1 H, *CHHPH*), 4.11–4.15 (m, 1 H, H-4), 4.00 (dd, $J = 11.5, 4.9$ Hz, 1 H, H-5b), 3.94 (dd, $J = 11.7, 4.5$ Hz, 1 H, H-5a), 1.82 (br s, 1 H, OH), 1.47 (s, 3 H, CCH_3), 1.31 (s, 3 H, CCH_3).

^{13}C NMR (150 MHz, CDCl_3): δ = 137.2 (C-Bn), 128.5 (C-Bn), 128.1 (C-Bn), 127.9 (C-Bn), 112.7 ($\text{C}(\text{CH}_3)_2$), 105.2 (C-1), 85.3 (C-2), 80.5 (C-3), 79.3 (C-4), 69.0 (OCH_2Ph), 61.5 (C-5), 25.8 (CCH_3), 24.4 (CCH_3).

^1H NMR (600 MHz, $\text{DMSO}-d_6$): δ = 7.28–7.39 (m, 5 H, H-Bn), 5.01 (s, 1 H, H-1), 4.76 (dd, J = 5.9, 5.0 Hz, 1 H, H-3), 4.76 (br. s, 1 H, OH), 4.62 (d, J = 11.9 Hz, 1 H, CHHPh), 4.58 (d, J = 5.9 Hz, 1 H, H-2), 4.46 (d, J = 11.9 Hz, 1 H, CHHPh), 3.98 (dd, J = 9.3, 5.8 Hz, 1 H, H-4), 3.68 (dt, J = 11.2, 5.6 Hz, 1 H, H-5b), 3.56–3.62 (m, 1 H, H-5a), 1.35 (s, 3 H, CCH_3), 1.25 (s, 3 H, CCH_3).

^{13}C NMR (150 MHz, $\text{DMSO}-d_6$): δ = 137.6 (C-Bn), 128.3 (C-Bn), 127.8 (C-Bn), 127.6 (C-Bn), 111.4 ($\text{C}(\text{CH}_3)_2$), 104.7 (C-1), 84.4 (C-2), 80.8 (C-4), 79.1 (C-3), 67.9 (OCH_2Ph), 58.9 (C-5), 26.0 (CCH_3), 24.6 (CCH_3).

ESI(+)-MS: m/z calcd. for $\text{C}_{15}\text{H}_{21}\text{O}_5$ [M + H] $^+$: 281.33; found: 281.33.

Data in agreement with the literature²³ (ent-3).

Methyl α -L-Lyxopyranoside (4a)^{4,6,7}

To a methanolic HCl solution (0.5% w/v), prepared in situ by the reaction of acetyl chloride (0.1 mL, 0.7 mmol) in anhydrous MeOH (7.5 mL), was added L-lyxose (1.5 g, 10 mmol, 1.0 equiv) under an argon atmosphere. The resulting suspension was heated under reflux for 4 h until disappearance of L-lyxose. The cooled solution was neutralized with Amberlist[®] basic resin IRA 400 (2 g) with stirring. The resin was filtered and washed several times with MeOH. The filtrate and washings were combined and evaporated to give a colorless syrup, which was recrystallized in EtOAc to afford a mixture of isomers where the major compound was 4a.

Yield: 1.64 g (70%); white amorphous solid; R_f ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) = 0.15.

^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ = 4.76–4.81 (m, 2 H, 2 \times OH), 4.65 (d, J = 5.5 Hz, 1 H, OH), 4.39–4.44 (m, 1 H, H-1), 3.55–3.61 (m, 3 H, C-2, C-4, OH), 3.36–3.50 (m, 2 H, H-3, H-5b), 3.25 (s, 3 H, OCH_3), 3.22–3.27 (m, 1 H, H-5a).

^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ = 101.7 (C-1), 71.3 (C-3), 69.8 (C-2), 66.9 (C-4), 63.1 (C-5), 54.7 (OCH_3).

Data in agreement with the literature.^{4,6,7}

Synthesis of the Protected Pyranose Sugars 4b and 4c

L-Lyxose (1.5 g, 10 mmol, 1 equiv) was dissolved in the corresponding freshly distilled alcohol (allyl or benzyl alcohol, 100 mmol, 10 equiv). The solution was immersed in an ice bath and H_2SO_4 (6.1 mol%) was added dropwise. The solution was warmed to r.t., heated to reflux for 3 h and stirred overnight at r.t. Reaction progress was monitored by TLC (90:10, $\text{CH}_2\text{Cl}_2/\text{MeOH}$) and the reaction was quenched with Amberlyst A-26(OH) resin (2 g). The mixture was shaken for 30 min, filtered, and the resin was washed with MeOH. The combined filtrate and washings was evaporated and the residue was washed several times with diethyl ether (30 mL each) to remove the excess alcohol. The residue was subjected to column chromatography ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1 and hexanes/EtOAc, 2:8, respectively) to afford products 4b and 4c, respectively.

Allyl α -L-Lyxopyranoside (4b)¹⁰

Yield: 1.34 g (71%); white amorphous solid; R_f ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) = 0.40.

^1H NMR (600 MHz, $\text{DMSO}-d_6$): δ = 5.88 (dddd, J = 17.1, 10.4, 5.6, 4.8 Hz, 1 H, $\text{CH}=\text{CH}_2$), 5.25 (d, J = 17.1 Hz, 1 H, $\text{CH}=\text{CH}_2$ -trans), 5.14 (d, J = 10.4 Hz, 1 H, $\text{CH}=\text{CH}_2$ -cis), 4.76–4.81 (m, 2 H, 2 \times OH), 4.65 (d, J =

5.5 Hz, 1 H, OH), 4.56 (d, J = 2.8 Hz, 1 H, H-1), 4.09 (dd, J = 13.3, 4.8 Hz, 1 H, $\text{OCHHCH}=\text{CH}_2$), 3.91 (dd, J = 13.3, 5.6 Hz, 1 H, $\text{OCHHCH}=\text{CH}_2$), 3.55–3.61 (m, 2 H, H-2, H-4), 3.49 (dd, J = 10.8, 4.9 Hz, 1 H, H-5b), 3.44–3.47 (m, 1 H, H-3), 3.26 (dd, J = 10.8, 9.4 Hz, 1 H, H-5a).

^{13}C NMR (150 MHz, $\text{DMSO}-d_6$): δ = 134.9 ($\text{CH}=\text{CH}_2$), 116.6 ($\text{CH}=\text{CH}_2$), 99.8 (C-1), 71.3 (C-3), 69.9 (C-2), 67.4 ($\text{OCH}_2\text{CH}=\text{CH}_2$), 66.9 (C-4), 63.4 (C-5).

ESI(+)-MS: m/z calcd for $\text{C}_8\text{H}_{15}\text{O}_5$ [M + H] $^+$: 191.09; found: 191.09.

ESI(-)-MS: m/z calcd for $\text{C}_8\text{H}_{13}\text{O}_5$ [M - H] $^-$: 189.08; found: 189.08.

ESI(+)-MS: m/z calcd for $\text{C}_8\text{H}_{14}\text{O}_5\text{Na}$ [M + Na] $^+$: 213.07; found: 213.07.

ESI(-)-MS: m/z calcd for $\text{C}_8\text{H}_{14}\text{O}_5\text{Cl}$ [M + Cl] $^-$: 225.05; found: 225.05.

Data in agreement with the literature¹⁰ (ent-4b).

Benzyl α -L-Lyxopyranoside (4c)^{9,12,24}

Yield: 1.44 g (60%); white amorphous solid; R_f (hexanes/EtOAc, 2:8) = 0.15.

^1H NMR (600 MHz, $\text{DMSO}-d_6$): δ = 7.26–7.39 (m, 5 H, H-Bn), 4.80 (d, J = 5.0 Hz, 2 H, 2 \times OH), 4.66 (d, J = 5.6 Hz, 1 H, OH), 4.60 (s, 1 H, H-1), 4.60 (d, J = 12.0 Hz, 1 H, CHHPh), 4.41 (d, J = 12.0 Hz, 1 H, CHHPh), 3.56–3.63 (m, 2 H, H-2, H-4), 3.55 (dd, J = 10.0, 5.2 Hz, 1 H, H-5b), 3.48 (dd, J = 8.3, 5.5, 3.0 Hz, 1 H, H-3), 3.31 (dd, J = 10.0, 10.0 Hz, 1 H, H-5a).

^{13}C NMR (150 MHz, $\text{DMSO}-d_6$): δ = 138.0 (C-Bn), 128.3 (C-Bn), 127.7 (C-Bn), 127.5 (C-Bn), 99.8 (C-1), 71.2 (C-3), 69.9 (C-2 or C-4), 68.2 (OCH_2Ph), 66.8 (C-4 or C-2), 63.4 (C-5).

ESI(+)-MS: m/z calcd for $\text{C}_{12}\text{H}_{17}\text{O}_5$ [M + H] $^+$: 241.11; found: 241.11.

ESI(+)-MS: m/z calcd for $\text{C}_{12}\text{H}_{16}\text{NaO}_5$ [M + Na] $^+$: 263.09; found: 263.09.

ESI(-)-MS: m/z calcd for $\text{C}_{12}\text{H}_{15}\text{O}_5$ [M - H] $^-$: 239.09; found: 239.09.

ESI(-)-MS: m/z calcd for $\text{C}_{12}\text{H}_{16}\text{O}_5\text{Cl}$ [M + Cl] $^-$: 275.07; found: 275.07.

Data in agreement with the literature^{9,12,24} (ent-4c).

General Procedure for the 2,3-Di-O-isopropylidene Protection of Pyranoses

To the corresponding 1-O-protected pyranoside (5 mmol, 1 equiv), was added anhydrous acetone (1.83 mL, 215 mmol, 5 equiv), 2,2-dimethoxypropane (1.85 mL, 15 mmol, 3 equiv) and concentrated HCl (3–5 Pasteur pipette drops). The solution was stirred for 18 h at r.t. The reaction was quenched with a saturated solution NaHCO_3 and extracted with CH_2Cl_2 (3 times). The combined organic layers were dried with anhydrous Na_2SO_4 , filtered, and solvent was removed in vacuo. Analysis of the ^1H NMR spectrum of the crude product showed mixtures of pyranose and furanose products up to 1:0.25 ratios (depending on the reaction). The products were purified and isolated by flash silica column chromatography with hexanes/EtOAc as the eluent.

Methyl 2,3-O-Isopropylidene- α -L-lyxopyranoside (5)^{4,6,7,10}

Yield: 520 mg (51%); yellow oil; R_f (hexanes/EtOAc, 1:1) = 0.55.

^1H NMR (600 MHz, CDCl_3): δ = 4.64 (d, J = 2.6 Hz, 1 H, H-1), 4.23 (dd, J = 6.0, 4.8 Hz, 1 H, H-3), 4.12 (dd, J = 6.0, 2.7 Hz, 1 H, H-2), 3.79–3.86 (m, 2 H, H-5b, H-4), 3.71 (dd, J = 11.2, 4.6 Hz, 1 H, H-5a), 3.46 (s, 3 H, OCH_3), 2.97 (d, J = 8.0 Hz, 1 H, OH), 1.51 (s, 3 H, CCH_3), 1.35 (s, 3 H, CCH_3).

^{13}C NMR (150 MHz, CDCl_3): δ = 109.7 ($\text{C}(\text{CH}_3)_2$), 99.9 (C-1), 76.2 (C-3), 74.4 (C-2), 67.3 (C-4), 63.3 (C-5), 56.0 (OCH_3), 27.6 (CCH_3), 25.7 (CCH_3).

^1H NMR (400 MHz, DMSO- d_6): δ = 5.18 (d, J = 5.4 Hz, 1 H, OH), 4.59 (d, J = 1.9 Hz, 1 H, H-1), 3.90–3.97 (m, 2 H, H-3, H-2), 3.54–3.62 (m, 1 H, H-4), 3.45 (dd, J = 11.5, 4.4 Hz, 1 H, H-5b), 3.35–3.40 (m, 1 H, H-5a), 3.31 (s, 3 H, OCH₃), 1.41 (s, 3 H, CCH₃), 1.27 (s, 3 H, CCH₃).

^{13}C NMR (100 MHz, DMSO- d_6): δ = 108.2 (C(CH₃)₂), 99.5 (C-1), 77.6 (C-3 or C-2), 74.5 (C-2 or C-3), 66.5 (C-4), 62.0 (C-5), 54.9 (OCH₃), 28.0 (CCH₃), 26.2 (CCH₃).

Data in agreement with the literature^{4,6,7,10} (ent-5).

Allyl 2,3-O-Isopropylidene- α -L-lyxopyranoside (6)^{4,6,7,10}

Yield: 655 mg (57%); yellow oil; R_f (hexanes/EtOAc, 1:1) = 0.70.

^1H NMR (600 MHz, CDCl₃): δ = 5.87 (ddt, J = 16.3, 10.4, 1.2 Hz, 1 H, CH=CH₂), 5.29 (dd, J = 16.3, 1.4 Hz, 1 H, CH=CH₂-trans), 5.20 (d, J = 10.4 Hz, 1 H, CH=CH₂-cis), 4.76–4.79 (m, 1 H, H-1), 4.25 (ddd, J = 12.8, 5.3, 1.2 Hz, 1 H, OCHHCH=CH₂), 4.20 (t, J = 5.3 Hz, 1 H, H-3), 4.12–4.15 (m, 1 H, H-2), 4.05 (ddd, J = 12.8, 6.2, 1.2 Hz, 1 H, OCHHCH=CH₂), 3.78–3.83 (m, 1 H, H-4), 3.75 (dd, J = 11.6, 3.8 Hz, 1 H, H-5b), 3.67 (dd, J = 11.6, 5.9 Hz, 1 H, H-5a), 3.38–3.44 (m, 1 H, OH), 1.47 (s, 3 H, CCH₃), 1.32 (s, 3 H, CCH₃).

^{13}C NMR (150 MHz, CDCl₃): δ = 133.5 (CH=CH₂), 118.0 (CH=CH₂), 109.5 (C(CH₃)₂), 97.8 (C-1), 76.7 (C-3), 74.6 (C-2), 68.8 (OCH₂CH=CH₂), 67.4 (C-4), 62.9 (C-5), 27.7 (CCH₃), 25.7 (CCH₃).

ESI(+)-MS: m/z calcd for C₁₁H₁₉O₅ [M + H]⁺: 231.12; found: 231.12.

ESI(+)-MS: m/z calcd for C₁₁H₁₈O₅Na [M + Na]⁺: 253.10; found: 253.10.

^1H NMR (600 MHz, DMSO- d_6): δ = 5.85–5.95 (m, 1 H, CH=CH₂), 5.27–5.32 (m, 1 H, CH=CH₂), 5.13–5.21 (m, 2 H, CH=CH₂, OH), 4.67–4.71 (m, 1 H, H-1), 4.15 (dt, J = 16.2, 8.1 Hz, 1 H, OCHHCH=CH₂), 3.93–4.04 (m, 3 H, OCHHCH=CH₂, H-2, H-3), 3.54–3.62 (m, 1 H, H-4), 3.39–3.49 (m, 2 H, H-5a, H-5b), 1.41 (s, 3 H, CCH₃), 1.28 (s, 3 H, CCH₃).

^{13}C NMR (150 MHz, DMSO- d_6): δ = 134.4 (CH=CH₂), 116.8 (CH=CH₂), 108.2 (C(CH₃)₂), 97.8 (C-1), 75.6 (C-3 or C-2), 74.5 (C-2 or C-3), 67.7 (OCH₂CH=CH₂), 66.5 (C-4), 62.4 (C-5), 28.0 (CCH₃), 26.2 (CCH₃).

Data in agreement with the literature^{4,6,7,10} (ent-6).

Benzyl 2,3-O-Isopropylidene- α -L-lyxopyranoside (7)^{9,12,24}

Yield: 700 mg (50%); white amorphous solid; R_f (hexanes/EtOAc, 8:2) = 0.20.

^1H NMR (600 MHz, CDCl₃): δ = 7.29–7.39 (m, 5 H, H-Bn), 4.84 (d, J = 2.5 Hz, 1 H, H-1), 4.81 (d, J = 11.8 Hz, 1 H, CHHPh), 4.57 (d, J = 11.8 Hz, 1 H, CHHPh), 4.23 (d, J = 5.4 Hz, 1 H, H-3), 4.18 (dd, J = 6.0, 2.5 Hz, 1 H, H-2), 3.78–3.84 (m, 2 H, H-4, H-5b), 3.73 (dd, J = 11.4, 5.8 Hz, 1 H, H-5a), 3.00 (br s, 1 H, OH), 1.46 (s, 3 H, CCH₃), 1.34 (s, 3 H, CCH₃).

^{13}C NMR (150 MHz, CDCl₃): δ = 136.6 (C-Bn), 128.5 (C-Bn), 128.1 (C-Bn), 127.9 (C-Bn), 109.5 (C(CH₃)₂), 97.3 (C-1), 74.5 (C-2), 76.5 (C-3), 69.6 (CH₂Ph), 67.3 (C-4), 62.8 (C-5), 27.4 (CCH₃), 25.6 (CCH₃).

Data in agreement with the literature^{9,12,24} (ent-7).

General Procedure for the Triflate Formation Reaction

Pyridine (0.10 mL, 1.20 mmol) and 4-(dimethylamino)pyridine (6.00 mg, 5 mol%) in anhydrous CH₂Cl₂ (5 mL) was treated slowly with 1 M solution of trifluoromethanesulfonic anhydride in CH₂Cl₂ (1.30 mL, 1.30 mmol) at –20 °C under argon atmosphere. The reaction mixture was stirred at –20 °C for 5 min. The corresponding alcohol (1.00 mmol) in CH₂Cl₂ (2 mL) was added via a cannula, the mixture was stirred at –20 °C for 15 min and then warmed to r.t. The reaction was monitored by TLC until disappearance of the starting material (30 min to 2 h) indicated completion of the reaction. The mixture was poured into a mixture of 25 mL ice-water and 10 mL CH₂Cl₂ and the

organic layer was separated. The aqueous phase was extracted with CH₂Cl₂ three times. The combined organic layers were washed with water and brine, dried with anhydrous Na₂SO₄, filtered and evaporated to give the intermediate triflate product as pale-yellow gummy solid. The product was used without further purification.

General Procedure for the S_N2 Reaction; Method A

The crude trifluoromethanesulfonate intermediate (1.00 mmol) was dissolved in freshly distilled DMF (10 mL), then the corresponding nucleophile (**8** or **9**, 3.00 mmol) was added. The suspension was stirred at r.t. overnight, then the reaction mixture was evaporated to dryness. The residue was dissolved in a mixture of CH₂Cl₂ and water. The organic layer was separated and washed with water and brine, dried with anhydrous MgSO₄, filtered and evaporated to obtain an oily residue, which, on purification by silica gel flash chromatography, afforded the expected product.

Methyl 5-Azido-5-deoxy-2,3-O-isopropylidene- β -L-lyxofuranoside (12a)

Yield: 172 mg (overall yield 75 %); oil; R_f (Hexanes/EtOAc, 9:1) = 0.58.

^1H NMR (600 MHz, CDCl₃): δ = 4.91 (s, 1 H, H-1), 4.70 (dd, J = 5.9, 3.7 Hz, 1 H, H-3), 4.57 (d, J = 5.9 Hz, 1 H, H-2), 4.08 (ddd, J = 7.6, 5.2, 3.9 Hz, 1 H, H-4), 3.57 (dt, J = 12.8, 6.4 Hz, 1 H, H-5b), 3.47–3.52 (m, 1 H, H-5a), 3.34 (s, 1 H, OCH₃), 1.46 (s, 1 H, CCH₃), 1.31 (s, 1 H, CCH₃).

^{13}C NMR (150 MHz, CDCl₃): δ = 111.9 (C(CH₃)₂), 106.2 (C-1), 84.0 (C-2), 78.6 (C-3), 77.3 (C-4), 53.7 (OCH₃), 48.7 (C-5), 25.0 (CCH₃), 23.8 (CCH₃).

ESI(+)-MS: m/z calcd. for C₉H₁₅N₃O₄Na [M + Na]⁺: 252.10; found: 252.10.

Methyl 4-Azido-4-deoxy-2,3-O-isopropylidene- β -D-ribofuranoside (15a)^{4,6,7}

Yield: 156 mg (overall yield 68 %); oil; R_f (hexanes/EtOAc, 9:1) = 0.56.

^1H NMR (600 MHz, CDCl₃): δ = 4.48–4.52 (m, 1 H, H-3), 4.47 (d, J = 3.8 Hz, 1 H, H-1), 4.00 (dd, J = 6.3, 3.8 Hz, 1 H, H-2), 3.78–3.84 (m, 2 H, H-4, H-5b), 3.69–3.74 (m, 1 H, H-5a), 3.41 (s, 3 H, OCH₃), 1.53 (s, 3 H, CCH₃), 1.35 (s, 3 H, CCH₃).

^{13}C NMR (150 MHz, CDCl₃): δ = 110.8 (C(CH₃)₂), 100.9 (C-1), 75.3 (C-2), 72.9 (C-3), 60.2 (C-5), 56.4 (OCH₃), 54.9 (C-4), 26.9 (CCH₃), 25.6 (CCH₃).

ESI(+)-MS: m/z calcd for C₉H₁₆N₃O₄ [M + H]⁺: 230.11; found: 230.11.

ESI(+)-MS: m/z calcd. for C₉H₁₅N₃O₄Na [M + Na]⁺: 252.10; found: 252.10.

Data in agreement with the literature^{4,6,7}

Methyl 4-Benzylamino-4-deoxy-2,3-O-isopropylidene- β -D-ribofuranoside (15b)

Yield: 184 mg (overall yield 63 %); oil; R_f (hexane/EtOAc, 13:7) = 0.66.

^1H NMR (600 MHz, CDCl₃): δ = 7.28–7.36 (m, 4 H, H-Bn), 7.22–7.27 (m, 1 H, H-Bn), 4.46 (dd, J = 5.4, 3.8 Hz, 1 H, H-3), 4.33 (d, J = 5.3 Hz, 1 H, H-1), 3.88–3.92 (m, 2 H, NCHHPh, H-2), 3.81–3.87 (m, 2 H, H-5b, NCHHPh), 3.45 (s, 3 H, OCH₃), 3.37–3.43 (m, 1 H, H-5a), 3.15 (ddd, J = 11.0, 5.6, 3.6 Hz, 1 H, H-4), 1.35 (s, 3 H, CCH₃), 1.23 (s, 3 H, CCH₃).

^{13}C NMR (150 MHz, CDCl₃): δ = 140.2 (C-Bn), 128.5 (C-Bn), 128.1 (C-Bn), 127.2 (C-Bn), 109.7 (C(CH₃)₂), 102.4 (C-1), 75.8 (C-2), 72.9 (C-3), 63.5 (C-5), 56.6 (OCH₃), 52.1 (C-4), 51.1 (PhCH₂NH), 27.6 (CCH₃), 25.8 (CCH₃).

ESI(+)-HRMS: m/z calcd for $C_{16}H_{24}NO_4$ [M + H]⁺: 294.1700; found: 294.1701.

General Procedure for the S_N2 Reaction; Method B

The crude trifluoromethanesulfonate intermediate (1.00 mmol) was dissolved in distilled DMF (10 mL), then the corresponding nucleophile (**10** or **11**, 3.00 mmol) was added. The suspension was stirred at 70 °C until consumption of the starting material was observed (reaction monitored by TLC), then the reaction mixture was evaporated to dryness. The residue was filtered through a pad of Celite® and silica. The pad was washed several times with EtOAc/MeOH (9:1) to avoid dissolving the excess of nucleobase that did not react during the reaction. The filtrate and washings were combined and evaporated. The residue was purified by silica gel flash chromatography to afford the expected product.

Methyl 5-Deoxy-2,3-O-isopropylidene-5-(uracil-5-ylamino)-β-L-lyxofuranoside (**12c**)

Yield: 147 mg (overall yield 47%); yellow amorphous solid; R_f (EtOAc/MeOH, 9:1) = 0.66.

¹H NMR (600 MHz, DMSO-*d*₆): δ = 11.16 (s, 1 H, NH-uracil), 10.18 (s, 1 H, NH-uracil), 6.47 (d, J = 3.4 Hz, 1 H, CH-uracil), 4.83 (s, 1 H, H-1), 4.71–4.74 (m, 1 H, H-3), 4.51 (d, J = 5.9 Hz, 1 H, H-2), 4.21–4.23 (m, 1 H, NHCH₃), 4.00–4.03 (m, 1 H, H-4), 3.21 (s, 3 H, OCH₃), 3.16–3.19 (m, 1 H, H-5b), 2.95–3.06 (m, 1 H, H-5a), 1.36 (s, 3 H, CCH₃), 1.25 (s, 3 H, CCH₃).

¹³C NMR (150 MHz, DMSO-*d*₆): δ = 161.4 (CO-uracil), 149.5 (CO-uracil), 123.7 (C-uracil), 113.7 (CH-uracil), 111.7 (C(CH₃)₂), 106.3 (C-1), 84.4 (C-2), 79.5 (C-3), 77.8 (C-4), 54.0 (OCH₃), 42.8 (C-5), 26.0 (CCH₃), 24.7 (C(CH₃)₂).

ESI(+)-HRMS: m/z calcd for $C_{13}H_{20}N_3O_6$ [M + H]⁺: 314.1347; found: 314.1352.

ESI(-)-HRMS: m/z calcd for $C_{13}H_{18}N_3O_6$ [M - H]⁻: 312.1201; found: 312.1199.

ESI(+)-HRMS: m/z calcd for $C_{13}HN_3O_6Na$ [M + Na]⁺: 336.1166; found: 336.1168.

Methyl 5-Deoxy-5-(2,4-diaminopyrimidin-5-ylamino)-2,3-O-isopropylidene-β-L-lyxofuranoside (**12d**)

Yield: 174 mg (overall yield, 56%); brown-orange amorphous solid; R_f (EtOAc/MeOH, 95:5) = 0.65.

¹H NMR (150 MHz, DMSO-*d*₆): δ = 7.39 (br. s, 2 H, NH₂-pyrimidine), 7.05 (br. s, 2 H, NH₂-pyrimidine), 7.01 (s, 1 H, CH-pyrimidine), 4.86 (s, 1 H, H-1), 4.79 (dd, J = 5.6, 3.7 Hz, 1 H, H-3), 4.68–4.72 (m, 1 H, NH), 4.55 (d, J = 5.9 Hz, 1 H, H-2), 4.03 (dd, J = 9.6, 5.9 Hz, H-4), 3.21 (s, 3 H, OCH₃), 3.20–3.23 (m, H-5b), 3.05–3.12 (m, 1 H, H-5a), 1.37 (s, 3 H, CCH₃), 1.27 (s, 3 H, CCH₃).

¹³C NMR (150 MHz, DMSO-*d*₆): δ = 159.0 (C-pyrimidine), 151.2 (C-pyrimidine), 121.0 (C-pyrimidine), 118.3 (CH-pyrimidine), 111.8 (C(CH₃)₂), 106.4 (C-1), 84.4 (C-2), 79.3 (C-3), 77.4 (C-4), 54.1 (OCH₃), 42.7 (C-5), 26.0 (CCH₃), 24.8 (CCH₃).

ESI(+)-HRMS: m/z calcd for $C_{13}H_{22}N_5O_4$ [M + H]⁺: 312.1666; found: 312.1670.

ESI(+)-HRMS: m/z calcd for $C_{13}H_{21}N_5O_4Na$ [M + Na]⁺: 334.1486; found: 334.1485.

Allyl 5-Deoxy-2,3-O-isopropylidene-5-(uracil-5-ylamino)-β-L-lyxofuranoside (**13c**)

Yield: 152 mg (overall yield 45%); pale-yellow amorphous solid; R_f (CH₂Cl₂/MeOH, 95:5) = 0.20.

¹H NMR (600 MHz, DMSO-*d*₆): δ = 11.16 (s, 1 H, NH-uracil), 10.55 (s, 1 H, NH-uracil), 6.49 (d, J = 5.4 Hz, 1 H, CH-uracil), 5.83–5.92 (m, 1 H, CH=CH₂), 5.24 (d, J = 17.3 Hz, 1 H, CH=CH₂-*trans*), 5.15 (d, J = 10.2 Hz, 1 H, CH=CH₂-*cis*), 4.98 (s, 1 H, H-1), 4.76 (dd, J = 10.9, 7.1 Hz, 1 H, H-3), 4.57 (d, J = 5.8 Hz, 1 H, H-2), 4.21–4.25 (m, 1 H, NH), 4.00–4.09 (m, 2 H, H-4, OCH₂CH=CH₂), 3.92–3.98 (m, 1 H, H-5b), 3.18–3.25 (m, 1 H, H-5a), 2.98–3.04 (m, 1 H, CHNH), 1.38 (s, 3 H, CCH₃), 1.26 (s, 3 H, CCH₃).

¹³C NMR (150 MHz, DMSO-*d*₆): δ = 161.4 (CO-uracil), 149.4 (CO-uracil), 134.6 (CH=CH₂), 123.7 (C-uracil), 116.9 (CH=CH₂), 113.7 (CH-uracil), 111.7 (C(CH₃)₂), 104.8 (C-1), 84.6 (C-2), 79.5 (C-3), 77.8 (C-4), 67.3 (OCH₂CH=CH₂), 42.8 (C-5), 26.0 (CCH₃), 24.7 (CCH₃).

ESI(+)-HRMS: m/z calcd. for $C_{15}H_{22}N_3O_6$ [M + H]⁺: 340.1509; found: 340.1507.

ESI(+)-HRMS: m/z calcd. for $C_{15}H_{21}N_3NaO_6$ [M + Na]⁺: 362.1328; found: 362.1325.

Allyl 5-Deoxy-5-(2,4-diaminopyrimidin-5-ylamino)-2,3-O-isopropylidene-β-L-lyxofuranoside (**13d**)

Yield: 162 mg (overall yield 48%); brown-orange solid; mp 146–148 °C; R_f (CH₂Cl₂/MeOH, 9:1) = 0.23; R_f (CH₂Cl₂/MeOH, 9:1) = 0.20.

¹H NMR (600 MHz, DMSO-*d*₆): δ = 7.40 (s, 1 H, CH-pyrimidine), 6.34 (br. s, 2 H, NH₂), 5.82–5.93 (m, 1 H, CH=CH₂), 5.49 (br. s, 2 H, NH₂), 5.24 (dd, J = 17.2, 1.7 Hz, CH=CH₂-*trans*), 5.14 (dd, J = 10.4, 1.5 Hz, 1 H, CH=CH₂-*cis*), 4.98 (s, 1 H, H-1), 4.84 (br. s, 1 H, NH), 4.81 (dd, J = 5.8, 3.7 Hz, 1 H, H-3), 4.58 (d, J = 5.9 Hz, 1 H, H-2), 4.08 (dd, J = 13.2, 5.1 Hz, 1 H, OCHHCH=CH₂), 4.04 (ddd, J = 6.2, 6.2, 3.8 Hz, 1 H, H-4), 3.95 (dd, J = 13.2, 5.8 Hz, 1 H, OCHHCH=CH₂), 3.12–3.20 (m, 1 H, H-5b), 2.99–3.05 (m, 1 H, H-5a), 1.37 (s, 3 H, CCH₃), 1.27 (s, 3 H, CCH₃).

¹³C NMR (150 MHz, DMSO-*d*₆): δ = 158.0 (C-pyrimidine), 136.7 (C-pyrimidine), 134.6 (OCH₂CH=CH₂), 126.7 (CH-pyrimidine), 119.4 (C-pyrimidine), 116.9 (OCH₂CH=CH₂), 111.6 (C(CH₃)₂), 104.6 (C-1), 84.3 (C-2), 79.3 (C-3), 77.9 (C-4), 67.1 (OCH₂CH=CH₂), 43.4 (C-5), 26.0 (CCH₃), 24.8 (CCH₃).

ESI(+)-HRMS: m/z calcd. for $C_{15}H_{24}N_5O_4$ [M + H]⁺: 338.1828; found: 338.1822.

ESI(+)-HRMS: m/z calcd. for $C_{15}H_{23}N_5NaO_4$ [M + Na]⁺: 362.1328; found: 362.1325.

Benzyl 5-Deoxy-5-(2,4-diaminopyrimidin-5-ylamino)-2,3-O-isopropylidene-β-L-lyxofuranoside (**14d**)

Yield: 100 mg (overall yield 26%); brown-orange amorphous solid.

¹H NMR (600 MHz, DMSO-*d*₆): δ = 7.23–7.39 (m, 5 H, H-Bn), 7.03 (s, 1 H, CH-pyrimidine), 7.00–7.05 (br. s, 2 H, NH₂), 5.05 (s, 1 H, H-1), 4.83 (dd, J = 5.8, 3.6 Hz, 1 H, H-3), 4.73 (dd, J = 7.2, 5.0 Hz, 1 H, NH), 4.63 (d, J = 6.0 Hz, 1 H, H-2), 4.61 (d, J = 11.8 Hz, 1 H, CHHPh), 4.47 (d, J = 11.8 Hz, 1 H, CHHPh), 4.09–4.14 (m, 1 H, H-4), 3.22 (dd, J = 12.9, 5.0 Hz, 1 H, H-5b), 3.08 (dd, J = 12.9, 7.2 Hz, 1 H, H-5a), 1.34 (s, 3 H, CCH₃), 1.23 (s, 3 H, CCH₃).

¹³C NMR (150 MHz, DMSO-*d*₆): δ = 159.6 (C-pyrimidine), 151.6 (C-pyrimidine), 138.0 (C-Bn), 129.0 (C-Bn), 128.6 (C-Bn), 128.4 (C-Bn), 122.1 (CH-pyrimidine), 119.7 (C-pyrimidine), 112.5 (C(CH₃)₂), 105.2 (C-1), 84.9 (C-2), 79.8 (C-3), 77.8 (C-4), 68.8 (OCH₂Ph), 43.0 (C-5), 26.4 (CCH₃), 25.1 (CCH₃).

ESI(+)-HRMS: m/z calcd. for $C_{19}H_{25}N_5O_4$ [M + H]⁺: 387.1907; found: 387.1911.

ESI(+)-HRMS: m/z calcd. for $C_{19}H_{24}N_5NaO_4$ [M + Na]⁺: 409.1726; found: 409.1736.

General Procedure for the Reduction of the Azides

Pd/C (5% w/w) (100 mg) was added to the corresponding azide (230 mg, 1.00 mmol) in anhydrous MeOH (5 mL) and the reaction mixture was stirred under an atmosphere of hydrogen (1 atm) until completion of the reaction as monitored by TLC (hexanes/EtOAc, 9:1). The reaction mixture was filtered over a pad of Celite® and evaporated to dryness. The product was sufficiently pure to be used without any further purification.

Methyl 5-Amino-5-deoxy-2,3-O-isopropylidene-β-L-lyxofurano- side (18)

Yield: 193 mg (95%); white amorphous solid; R_f (CH₂Cl₂/MeOH, 95:5) = 0.25.

¹H NMR (600 MHz, CDCl₃): δ = 4.89 (s, 1 H, H-1), 4.72 (dd, J = 5.8, 3.9 Hz, 1 H, H-3), 4.56 (d, J = 5.8 Hz, 1 H, H-2), 3.92–3.96 (m, 1 H, H-4), 3.32 (s, 3 H, OCH₃), 2.99–3.09 (m, 2 H, H-5a, H-5b), 1.45 (s, 1 H, CCH₃), 1.30 (s, 1 H, CCH₃).

¹³C NMR (150 MHz, CDCl₃): δ = 112.7 (C(CH₃)₂), 107.1 (C-1), 85.2 (C-2), 80.7 (C-3), 80.1 (C-4), 54.6 (OCH₃), 40.9 (C-5), 26.1 (CCH₃), 24.8 (CCH₃).

¹H NMR (600 MHz, DMSO-*d*₆): δ = 4.92 (s, 1 H, H-1), 4.79 (dd, J = 5.9, 3.8 Hz, 1 H, H-3), 4.57 (d, J = 5.9 Hz, 1 H, H-2), 4.07–4.13 (m, 1 H, H-4), 3.27 (s, 3 H, OCH₃), 3.15 (dd, J = 13.3, 3.3 Hz, 1 H, H-5'), 2.92 (dd, J = 13.3, 9.0 Hz, 1 H, H-5), 1.37 (s, 1 H, CCH₃), 1.26 (s, 1 H, CCH₃).

¹³C NMR (151 MHz, DMSO-*d*₆): δ = 112.0 (C(CH₃)₂), 106.2 (C-1), 85.4 (C-2), 79.1 (C-3), 75.8 (C-4), 54.1 (OCH₃), 38.0 (C-5), 25.8 (CCH₃), 24.5 (CCH₃).

ESI(+)-HRMS: m/z calcd. for $C_9H_{18}NO_4$ [M + H]⁺: 204.1230; found: 204.1221.

Methyl 4-Amino-4-deoxy-2,3-O-isopropylidene-β-D-ribo- pyranoside (20)^{4,6,7}

Yield: 193 mg (95%); white amorphous solid; R_f (CH₂Cl₂/MeOH, 95:5) = 0.25.

¹H NMR (600 MHz, CDCl₃): δ = 4.37 (dd, J = 5.3, 3.9 Hz, 1 H, H-1), 4.34 (d, J = 4.9 Hz, 1 H, H-3), 3.94 (dd, J = 13.2, 8.0 Hz, 1 H, H-2), 3.71 (dd, J = 10.8, 5.6 Hz, 1 H, H-5b), 3.46 (s, 3 H, OCH₃), 3.41–3.45 (m, 1 H, H-5a), 3.18–3.24 (m, 1 H, H-4), 1.53 (s, 3 H, CCH₃), 1.37 (s, 3 H, CCH₃).

¹³C NMR (150 MHz, CDCl₃): δ = 109.9 (C(CH₃)₂), 101.9 (C-1), 75.7 (C-2), 74.5 (C-3), 65.1 (C-5), 56.4 (OCH₃), 49.9 (C-4), 27.5 (CCH₃), 25.6 (CCH₃).

ESI(+)-HRMS: m/z calcd. for $C_9H_{18}NO_4$ [M + H]⁺: 204.1230; found: 204.1224.

Data in agreement with the literature.^{4,6,7}

2,3-O-Isopropylidene-L-lyxofuranose (19)

A suspension of the benzyl protected compound **3** (140 mg, 0.5 mmol, 1.0 equiv) with Pd(OH)₂ in anhydrous MeOH was stirred at r.t. under an atmosphere of hydrogen for 1 day. The suspension was filtered through a pad of Celite® and washed several times with MeOH. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (hexanes/EtOAc, 3:7) to afford the expected product **19**.

Yield: 650 mg (98%); R_f (hexanes/EtOAc, 7:3) = 0.50.

¹H NMR (600 MHz, DMSO-*d*₆): δ = 6.31 (d, J = 3.8 Hz, 1 H, C'OH), 5.10 (d, J = 3.8 Hz, 1 H, H-1), 4.65–4.72 (m, 2 H, OH, H-3), 4.42 (d, J = 5.8 Hz, 1 H, H-2), 3.97–4.03 (m, 1 H, H-4), 3.62 (dt, J = 11.2, 5.5 Hz, 1 H, H-5b), 3.46–3.53 (m, 1 H, H-5a), 1.32 (s, 3 H, CCH₃), 1.22 (s, 3 H, CCH₃).

¹³C NMR (150 MHz, DMSO-*d*₆): δ = 111.2 (C(CH₃)₂), 100.0 (C-1), 85.6 (C-2), 80.0 (C-4), 79.5 (C-3), 59.2 (C-5), 26.0 (CCH₃), 24.7 (CCH₃).

ESI(+)-HRMS: m/z calcd for $C_8H_{15}O_5$ [M + H]⁺: 191.0914; found: 191.0909.

Methyl 4-Deoxy-4-formamido-2,3-O-isopropylidene-β-D-ribo- pyranoside (21)

A solution of 5-bromouracil (573 mg, 3.00 mmol) and 4-deoxy-4-amino-2,3-O-isopropylidene-β-D-ribofuranoside **20** (203 mg, 1.00 mmol) in anhydrous dimethylformamide (5 mL) was stirred at 70 °C overnight. The mixture was allowed to cool, then saturated aqueous NaHCO₃ was added. The aqueous phase was extracted three times with EtOAc and the organic layers were combined, dried with Na₂SO₄, filtered and evaporated. The oily residue was purified by column chromatography (hexanes/EtOAc, 7:3) to afford the expected pure product **21**.

Yield: 231 mg (56%); white amorphous solid; R_f (hexane/EtOAc, 7:3) = 0.5.

¹H NMR (600 MHz, CDCl₃): δ = 8.16 (s, 1 H, COH), 6.01 (d, J = 7.7 Hz, 1 H, NH), 4.58–4.64 (m, 1 H, H-4), 4.42 (d, J = 4.2 Hz, 1 H, H-1), 4.35 (dd, J = 6.0, 4.2 Hz, 1 H, H-3), 4.03 (dd, J = 6.0, 4.4 Hz, 1 H, H-2), 3.82 (dd, J = 10.6, 5.7 Hz, 1 H, H-5b), 3.43 (s, 3 H, OCH₃), 3.42–3.45 (m, 1 H, H-5a), 1.49 (s, 3 H, CCH₃), 1.32 (s, 3 H, CCH₃).

¹³C NMR (150 MHz, CDCl₃): δ = 160.8 (CHO), 110.1 (C(CH₃)₂), 100.1 (C-1), 75.1 (C-2), 72.5 (C-3), 61.0 (C-5), 56.3 (OCH₃), 43.0 (C-4), 27.1 (CCH₃), 25.4 (CCH₃).

ESI(+)-HRMS: m/z calcd. for $C_{10}H_{18}NO_5$ [M + H]⁺: 232.1179; found: 232.1181.

ESI(+)-HRMS: m/z calcd. for $C_{10}H_{17}NNaO_5$ [M + Na]⁺: 254.0999; found: 254.1003.

Methyl 4-Benzoylamino-4-deoxy-2,3-O-isopropylidene-α-D-ri- bopyranoside (22)

To a solution of methyl 4-deoxy-4-amino-2,3-O-isopropylidene-β-D-ribofuranoside **20** (190 mg, 0.80 mmol, 1.0 equiv) and DIPEA (0.31 mL, 1.76 mmol, 2.2 equiv) in anhydrous dimethylformamide (5 mL), benzoyl chloride (0.21 mL, 1.82 mmol, 2.0 equiv) was slowly added at 0 °C under an argon atmosphere. The solution was stirred at 70 °C overnight. The mixture was allowed to cool, then saturated aqueous NaHCO₃ was added. The aqueous phase was extracted three times with EtOAc and the organic layers were combined, dried with Na₂SO₄, filtered and evaporated. The oily residue was purified by chromatography (hexanes/EtOAc, 7:3) to afford the expected pure product **22**.

Yield: 201 mg (82%); white amorphous solid; R_f (hexanes/EtOAc, 9:1) = 0.50.

¹H NMR (600 MHz, CDCl₃): δ = 7.79 (d, J = 7.2 Hz, 2 H, H-Bz), 7.51 (dd, J = 7.4, 7.2 Hz, 1 H, H-Bz), 7.44 (dd, J = 7.4, 7.4 Hz, 2 H, H-Bz), 6.48 (d, J = 8.8 Hz, 1 H, NHCO), 4.74–4.80 (m, 1 H, H-4), 4.45–4.49 (m, 2 H, H-3, H-1), 4.09 (dd, J = 6.1, 4.5 Hz, 1 H, H-2), 3.97 (dd, J = 10.6, 6.5 Hz, 1 H, H-5b), 3.49–3.54 (m, 1 H, H-5a), 3.49 (s, 3 H, OCH₃), 1.54 (s, 3 H, CCH₃), 1.38 (s, 3 H, CCH₃).

¹³C NMR (150 MHz, CDCl₃): δ = 167.7 (CO), 131.8 (C-Bz), 128.6 (C-Bz), 127.1 (C-Bz), 110.2 (C(CH₃)₂), 101.2 (C-1), 75.4 (C-2), 73.0 (C-3), 61.4 (C-5), 59.4 (OCH₃), 44.8 (C-4), 27.3 (CCH₃), 25.6 (CCH₃).

ESI(+)-HRMS: m/z calcd. for $C_{16}H_{22}NO_5$ [$M + H$]⁺: 308.1492; found: 308.1492.

Funding Information

This work was supported jointly by the NSF Center for Chemical Evolution, Grant CHE-1504217.

Acknowledgment

We are grateful to Mr. Richard Mosesso for the purification of some starting materials and Dr. Clémentine Gibard for the assistance in running selected NMR spectra.

Supporting Information

Supporting information for this article is available online at <https://doi.org/10.1055/s-0036-1588859>. It contains ¹H, APT (or ¹³C) and 2D (HSQC and/or COSY) NMR spectral data of all compounds in CDCl₃ and/or DMSO-*d*₆. It also contains HMBC of the compounds **1**, **5** and **12c**, NOESY NMR spectra of compounds **2**, **3**, **5**, **6**, **12c**, **15a** and **18**, a figure comparing APT NMR of lyxofuranoside **1–3** and lyxopyranosides **5–7**, a figure comparing ¹H NMR among the compounds **1** and **5**, and crude material of **5**, and experimental procedures for the synthesis of starting materials **1–7** and compound **19**.

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