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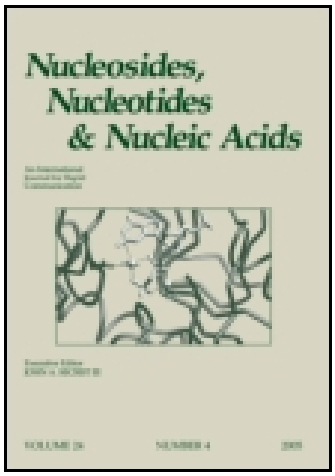

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THIOSUGARS. VIII.* PREPARATION OF NEW 4′-THIO-L-LYXO PYRIMIDINE NUCLEOSIDE ANALOGUES

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THIOSUGARS. VIII.* PREPARATION OF NEW 4′-THIO-L-LYXO PYRIMIDINE NUCLEOSIDE ANALOGUES

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ABSTRACT

Reaction of 1-*O*-acetyl-2,3,5-tri-*O*-benzyl-4-thio-L-lyxofuranose with silylated pyrimidine bases and subsequent deprotection with boron tribromide led to 4′-thio-L-lyxo pyrimidine nucleosides. The 5-bromo-6-methyl derivative was prepared from methyl 2,3,5-tri-*O*-acetyl-4-thio-L-lyxofuranoside. Deacetylation was performed with sodium methoxide. The anomers were separated by HPLC and their configurations assigned by NMR spectroscopy and X-ray structural analyses. The biological activity of the nucleosides was tested.

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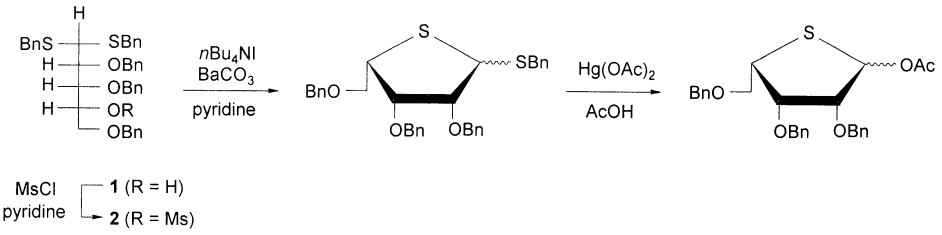
INTRODUCTION

Nucleoside analogues containing either modified nucleobases or unnatural carbohydrate moieties have found wide-spread interest in synthetic chemistry[1]. In particular, their biological activity as compared with the natural nucleosides has initiated intense research activities in the last decade. Prominent examples, which have already found medicinal application as *anti*-HIV[2] (AZT, L-3TC) or *anti*-HSV (Penciclovir®) drugs, are 2′,3′-dideoxy- or acyclocarba-nucleoside derivatives and can, therefore, act as chain terminators. It seems, however, worthwhile to synthesise and test also 4′-thio-nucleoside analogues[3] since the lipophilicity of a nucleoside and hence its ability to penetrate into a cell should be increased by the replacement of oxygen by sulfur in the furanose ring. We have, therefore, recently prepared uracil analogues with the unnatural 4-thio-L-arabino-[4a] and 2-deoxy-4-thio-L-*threo*-configuration[4b] of the carbohydrate.

RESULTS AND DISCUSSION

D-Ribose dibenzyldithioacetal **1** was prepared in three steps from D-ribose according to literature procedures[5–7] and transformed into benzyl 1,4-dithio-L-lyxofuranoside **3** *via* the mesylate **2**. The best result (82% yield) was obtained by heating the crude mesylate **2** at 110 °C in the presence of tetrabutylammonium iodide and barium carbonate in dry pyridine[6–9]. Heating of **2** with sodium iodide and barium carbonate in dry acetone[5,10] gave only 28% of **3**. In both cases only one anomer was formed. It was not possible to decide on the basis of NMR (NOE) spectra whether it was the α- or β-anomer of **3**. We have, however, proved the inversion of the configuration at C-4, which leads from the D-*ribo* to the L-*lyxo* series for analogous compounds[7,11]. Transformation of the dithiosugar **3** into the more suitable 1-*O*-acetyl-2,3,5-tri-*O*-benzyl-4-thio-L-lyxofuranose (**4**) was achieved under the Seebach conditions[12–14] by using mercuric acetate in glacial acetic acid. We obtained a 76% yield of **4** with an α:β ratio of 1:10 (Scheme 1). The anomeric



Scheme 1.

configurations of **4** could be assigned by NOE spectroscopy. The α-anomer showed an NOE between H-1/H-5 and the β-anomer a significant NOE between H-1/H-2.

Compound **4** was then transformed into protected 4′-thionucleosides by using various silylated nucleobases[15,16] in the presence of trimethylsilyl trifluoromethanesulfonate (TMSOTf) as coupling reagent[6,17,18]. The protected 4′-thio-L-lyxouridine **5** was obtained with 88% yield as anomeric mixture with an α:β ratio of 1:2. The protected 4′-thio-L-lyxothymidine **6** (68% yield) exhibited an α:β ratio of 2:1. In the case of the protected uridine nucleoside **5** the anomers could be separated by silica gel chromatography, whereas for **6** a separation failed. The anomeric structures of **5** and **6** were assigned by measurement of NOE spectra. The observed NOE interactions between H-6 and H-2′, H-3′ and H-4′ doubtlessly indicated the α-anomer, whereas the observed NOE between H-6 and the two H-5′ protons proved the β-structure (Fig. 1).

The protected 6-methyl-4′-thio-L-lyxouridine derivative **7** was isolated with a yield of 80% (α-**7**:β-**7** = 10:1). The anomers were separated by column chromatography. The configuration of β-**7** could be assigned by the NOEs of H-1′ with H-2′ and H-3′ and of the methyl protons of the nucleobase with one of the two protons at C-5′ (Fig. 2). The α-anomer showed an intense NOE between the methyl group of the nucleobase and the H-1′ proton of the sugar moiety.

The synthesis of the protected 5,6-dimethyl-4′-thio-L-lyxouridine derivative **8** yielded 70% of one pure anomer. It was not possible to assign its structure by NOE measurements. Comparison of the one-dimensional NMR spectra of **8** with those of **7** led us to the conclusion that the obtained anomer exhibits α-configuration.

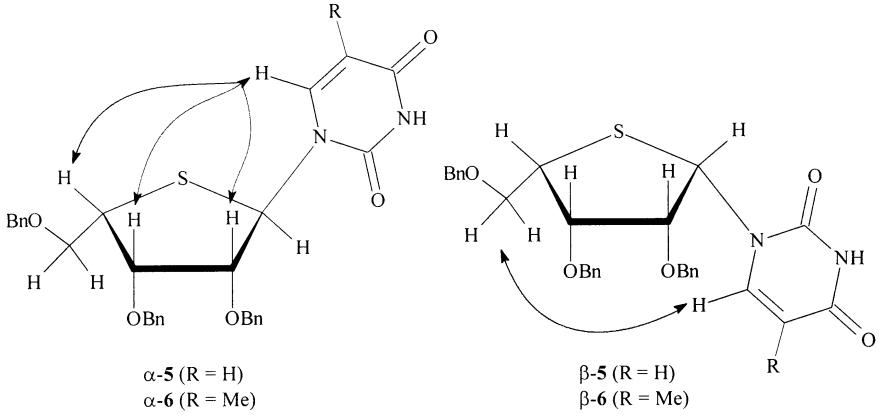


Figure 1. Observed NOE contacts for the α- and β-anomers of **5** and **6**.

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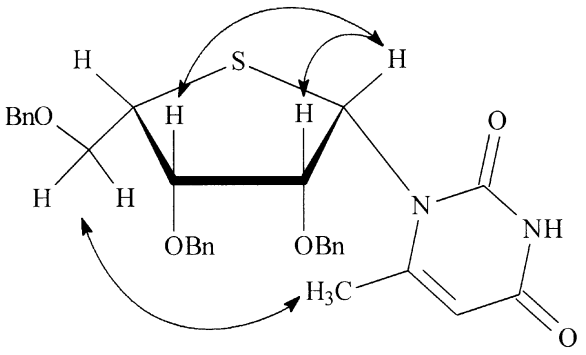
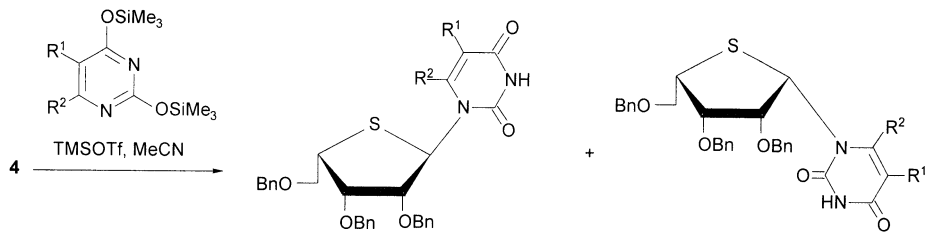


Figure 2. Observed NOE contacts for the β-anomer of **7**.

Coupling of **4** with silylated 5-halo-6-methyluracil[16] yielded protected 5-iodo-6-methyl-4′-thio-L-lyxouridine **9** with 53% and 5-bromo-6-methyl-4′-thio-L-lyxouridine **10** with 55%, respectively. Both 4′-thio-L-lyxo nucleosides were obtained as one pure anomer. Again the NOE measurements did not allow configurational assignments, but the one-dimensional NMR spectra of **9** and **10** are very similar to that of α-7 (Scheme 2).

The final and crucial step was then the cleavage of the benzyl protecting groups of the nucleosides **5**–**10**. We achieved this by reaction of these nucleosides with boron tribromide at −90 °C[6,13,19]. In order to get satisfactory results it was necessary that after quenching the excess boron tribromide the resulting hydrobromic acid had to be neutralised. Without neutralisation of the reaction mixture we were only able to isolate ill-defined hydrobromides of the unprotected nucleosides. The best reagent for the neutralisation was



α-**5**: $R^1 = R^2 = H$
α-**6**: $R^1 = Me$, $R^2 = H$
α-**7**: $R^1 = H$, $R^2 = Me$
8: $R^1 = R^2 = Me$
9: $R^1 = I$, $R^2 = Me$
10: $R^1 = Br$, $R^2 = Me$

β-**5**: $R^1 = R^2 = H$
β-**6**: $R^1 = Me$, $R^2 = H$
β-**7**: $R^1 = H$, $R^2 = Me$

Scheme 2.

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silver carbonate[7]. It should be mentioned that obviously a tight silver complex was formed when the silver carbonate got to long in contact with the nucleoside, *e.g.* over night. As a consequence, it was no longer possible to isolate the nucleoside from the solution without acidifying the silver residue which inevitably led again to hydrohalides. The best compromise was a neutralisation time of half an hour. We also tested sodium hydrogencarbonate[13] or pyridine[6] instead of silver carbonate. This led, however, to the formation of large amounts of soluble salts, the separation of which from the nucleoside, *e.g.* by Sephadex LH 20 column chromatography was lengthy and expensive, whereas the silver salts could be easily filtered off.

Cleavage of the uridine derivative **5** with boron tribromide gave both anomers of the unprotected nucleoside **11**. The anomers could be separated by crystallisation from water, which yielded 11% of pure β-**11**. Removal of traces of β-**11** from α-**11** was achieved by reversed phase HPLC to give α-**11** in 69% yield. The unprotected anomers of the analogous thymidine nucleoside **12** were only separable by HPLC. The yields were 23% α-**12** and 15% β-**12**, respectively. Cleavage of the benzyl groups of the 6-methyluridine derivative **7** gave the pure major anomer α-**13** with a yield of 21% after HPLC separation. The minor anomer β-**13** was isolated with a yield of 13%. It was possible to grow single crystals of α-**12** and α-**13** from water and determine the structures by X-ray diffraction analyses which proved undoubtedly their α-configuration (Fig. 3 and 4).

Removal of the benzyl groups of the 5,6-dimethyl-4′-thio-L-lyxouridine derivative **8** led to 7% of **14**. Repetition of the NOE experiment with the unprotected nucleoside **14** to assign its anomeric structure failed as mentioned before for **8**. However, **14** crystallised from water-methanol and the α-configuration was proved by X-ray diffraction analysis (Fig. 5). The thiofuranose moieties of the three methyl-substituted nucleoside analogues α-**12**, α-**13** and **14** exhibit envelope conformations at C-3′, whereas C-1′, C-2′, C-4′ and S nearly form a plane with torsion angles of only 2.1° (α-**12**), 3.3° (α-**13**) and −2.6° (**14**) at the bonds between sulfur and the anomeric centre (C1′). The torsion angles C2-N1-C1′-S between the pyrimidine ring and the sugar part are −135.3° (α-**12**), 63.2° (α-**13**) and 59.3° (**14**) (Fig. 3−5), *i.e.* a methyl substituent at C-6 causes steric hindrance with the sulfur atom.

Unprotected 5-iodo-6methyl-4′-thio-L-lyxouridine **15** was obtained after chromatography and recrystallisation from water with a yield of 9%. The 5-bromo-6-methyl-4′-thio-L-lyxouridine derivative **16** could not be isolated after treatment of **10** with boron tribromide (Scheme 3).

However, we found an alternative pathway which made the desired nucleoside **16** accessible. The acetate **4** was first treated with boron tribromide followed by immediate acetylation to give the thiosugar **17** as a 2:1 mixture of anomers with a yield of 55%. The exchange of the anomeric acetyl group by the methoxy group occurs during the work-up with methanol in the presence of hydrobromic acid. Coupling of **17** with 5-bromo-6-methy

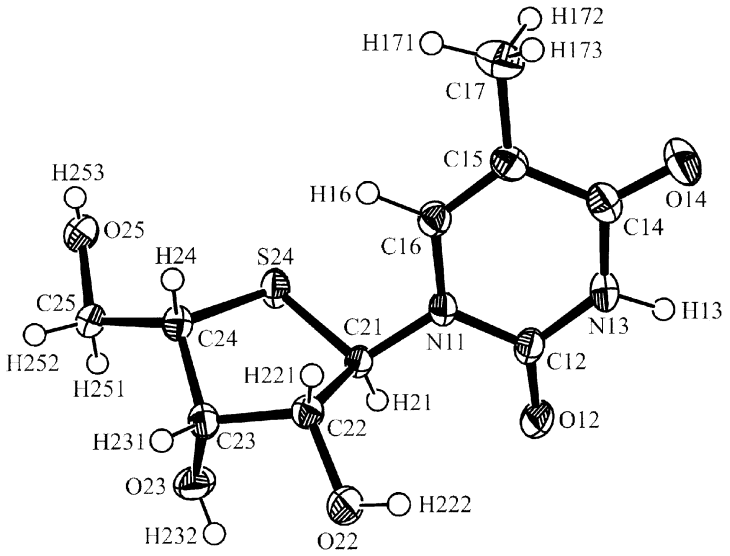

Figure 3. ORTEP view of the X-ray diffraction structure of α-**12** with atom numbering. Thermal ellipsoids are drawn at the 50% probability level.

l-2,4-bis-*O*-(trimethylsilyl)uracil[16] in the presence of trimethylsilyl triflate gave 30% nucleoside **18** (α-anomer). Cleavage of the acetyl groups with sodium methoxide yielded the unprotected 5-bromo-6-methyl-4′-thio-L-lyxouridine **16** (7% after recrystallisation) (Scheme 4).

Biological tests were performed with the 4′-thiouridine and 4′-thiothymidine analogues α-**11**, β-**11**, β-**12**, α-**12** as well as with the 6-methyl-4′-thionucleoside analogues α-**13**, β-**13**, α-**14**, α-**15** and α-**16**. No significant inhibitor activities against the following viruses were found for these L-lyxonucleoside analogues at subtoxic concentrations: HIV-1 (III_B), HIV-2 (ROD), HSV-1, HSV-2, VZV (OKA), HCMV (Davis), Vaccinia V., Vesicular stomatitis V., Parainfluenza-3 V., Reovirus-3, Sindbis V., Coxsackie V. B4, Punta Toro V., Respiratory syncytial V.

EXPERIMENTAL

Melting points were taken on an Electrothermal apparatus (values are corrected). NMR measurements were carried out with Bruker AMX 400 (400 MHz) and DRX 500 (500 MHz) spectrometers. Chemical shifts (ppm) are related to Me_4Si. Standard correlation techniques were used for assignments. IR spectra were recorded on an ATI Mattson Genesis spectrometer. Mass spectra were measured on Varian CH 7 (70 eV, EI) and VG Analytical

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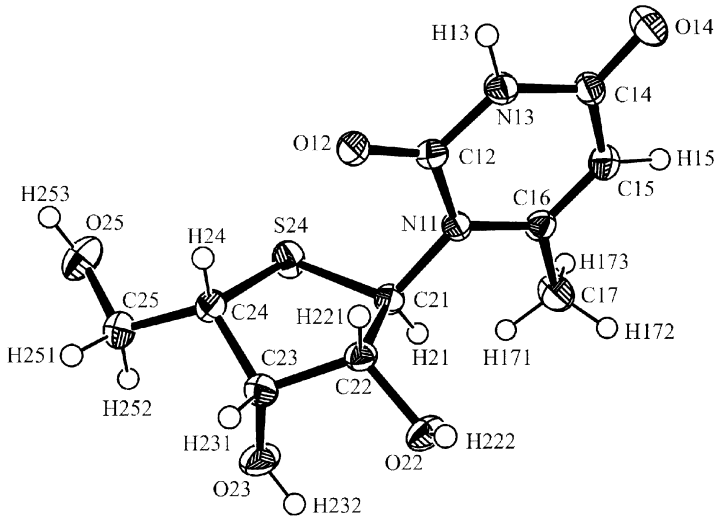

Figure 4. ORTEP view of the X-ray diffraction structure of α-**13** with atom numbering. Thermal ellipsoids are drawn at the 50% probability level.

70–250 S (FAB MS, FAB HRMS, HRMS). For FAB and FAB HRMS *meta*-nitrobenzyl alcohol (mNBA) was used as matrix. HPLC (Merck-Hitachi equipment): semipreparative HPLC was carried out with a LiChro-CART 250-10 column containing LiChrosher 100 RP-18 (10 μm) and analytical HPLC was performed with a EcoCART 125-3 column containing

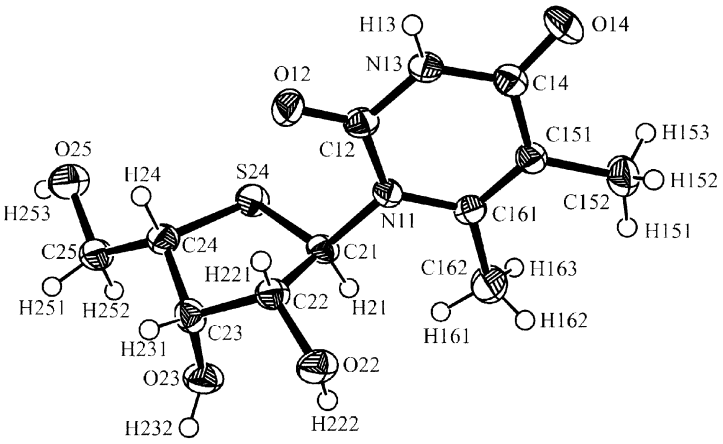

Figure 5. ORTEP view of the X-ray diffraction structure of α-**14** with atom numbering. Thermal ellipsoids are drawn at the 50% probability level.

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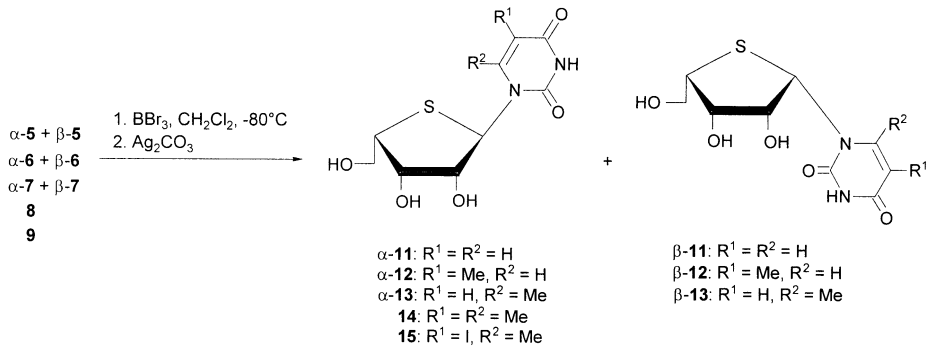
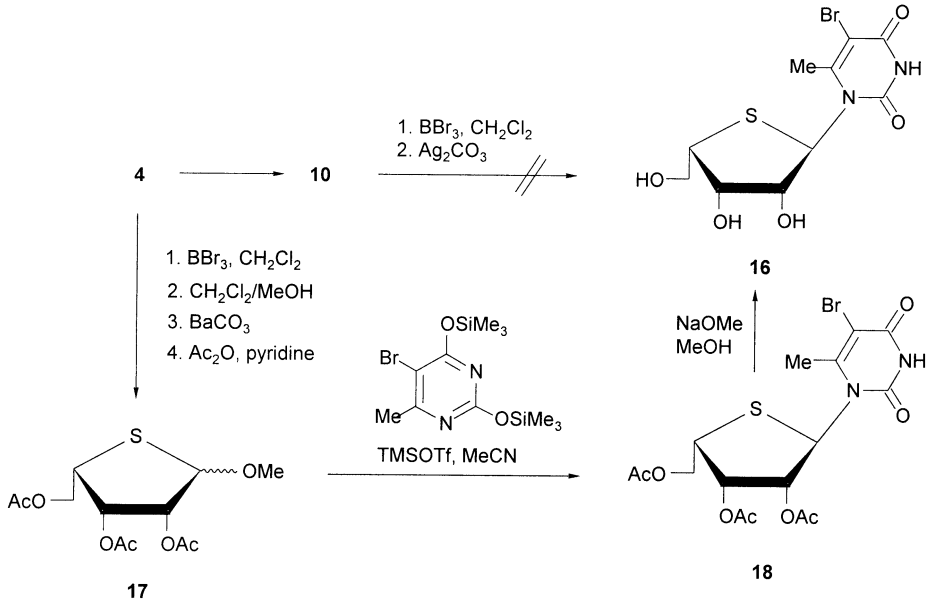


Scheme 3.



Scheme 4.

LiChrosher 100 RP-18 end capped (5 μm). Solvents for HPLC were obtained from Merck (MeCN, HPLC grade) and Riedel-de Haën (water, HPLC grade). Optical rotations were measured with Perkin Elmer Polarimeter 341. TLC was carried out on Merck PF_{254} foils (detection: UV light, iodine vapour, or EtOH-H_2SO_4 spray/200 °C), and column chromatography on Merck Kieselgel 60 (70–230 mesh). Solvents were purified and dried according to standard laboratory procedures[20].

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X-ray structure analyses.—The crystal data and a summary of experimental details for α-**12**, α-**13** and **14** are given in Table 1. The data collection was performed on a KappaCCD Nonius diffractometer, with graphite monochromated Mo K_α radiation (0.71073 Å) in the rotation Φ scan mode. The structures were solved by direct methods using the SIR-97[21] program, and refined by full-matrix-block least-squares on F^2 using all data and the SHELXL-97[22] program. Full crystallographic details, excluding structure features, have been deposited with the Cambridge Crystallographic Data Centre. These data may be obtained, on request, from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. Tel. +44-1223-336408, Fax +44-1223-336033, E-mail deposit@ccdc.cam.ac.uk. Deposition number CCDC 142899 (α-**13**), CCDC 142900 (**14**) and 142901 (α-**12**).

Benzyl 2,3,5-tri-*O*-benzyl-1,4-dithio-L-lyxofuranoside (3). *Method A*: 2,3,5-Tri-*O*-benzyl-D-ribose dibenzyldithioacetal (**1**)[5–7] (29.72 g, 45.66 mmol) was dissolved in dry pyridine (200 mL) and cooled to 0 °C. A solution of mesyl chloride (7.0 mL, 10.29 g, 89.83 g) in dry pyridine (50 mL) was added and the reaction mixture was stirred at room temperature for 24 h. After the reaction was finished the excess of mesyl chloride was quenched with water (300 mL) and the solution was evaporated. The residue was dissolved in $CHCl_3$, washed with dilute hydrochloric acid, water and sat. $NaHCO_3$ solution. The organic phase was separated, dried with $MgSO_4$ and evaporated to give the crude mesylate **2** in quantitative yield (32.97 g). This was dissolved in dry acetone (900 ml), sodium iodide (71.93 g, 0.48 mol) and barium carbonate (141.3 g, 0.72 mol) were added and the mixture stirred for 24 h at 60 °C. After the reaction mixture was cooled to room temperature the solids were filtered off and the acetone was removed. The residue was dissolved in $CHCl_3$, extracted with water, the organic phase separated, dried with $MgSO_4$ and evaporated. The resulting crude product was purified by column chromatography (petroleum ether-EtOAc 4:1, $R_f = 0.42$) to give one pure anomer of **3** (6.93 g, 28%) as a pale yellow syrup. – *Method B*: Mesylation of **1** was carried out as described for method A. The crude mesylate **2** (33.27 g, 45.64 mmol) and tetrabutylammonium iodide (16.98 g, 45.97 mmol) were dissolved in dry pyridine (380 mL), barium carbonate (9.19 g, 46.57 mmol) was added and the mixture was heated at 110 °C for 2 h. After the reaction was completed the mixture was cooled to room temperature and worked up as described for method A to yield **3** (20.31 g, 82%) as one pure anomer. $[\alpha]_D^{20} = +75.2$ ($c = 1.0$ in $CHCl_3$); IR (film): $\nu = 3086, 3063, 3030, 2920, 2826, 1492, 1455, 1361, 1311, 1241, 1208, 1124, 1090, 1028, 912, 736, 698\ cm^{-1}$; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.20–7.36$ (m, 20H, CH_{arom}), 4.71 (d, 1H, $J_{A,B}$ 11.7 Hz, OCH_2Ph), 4.60 (d, 1H, $J_{A,B}$ 11.7 Hz, OCH_2Ph), 4.47–4.54 (m, 4H, OCH_2Ph), 4.45 (d, 1H, H-1), 4.27 (dd, 1H, H-3), 3.88 (dd, 1H, H-5_b), 3.84 (dd, 1H, H-2),

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3.80 (s, 2H, SCH_2Ph), 3.69 (ddd, 1H, H-4), 3.58 (dd, 1H, H-5$_a$) ppm. $J_{1,2}=6.6$, $J_{2,3}=3.1$, $J_{3,4}=5.0$, $J_{4,5a}=7.1$, $J_{4,5b}=6.8$, $J_{5a,5b}=9.3$ Hz; ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=138.2$ (C_{arom}), 138.1, 137.80, 137.78, 129.1 (CH_{arom}), 128.6, 128.5, 128.43, 128.37, 127.9, 127.82, 127.81, 127.80, 127.74, 127.71, 127.2, 86.9 (C-2), 79.0 (C-3), 73.5 (O*C*H$_2$Ph), 73.3, 73.0, 70.4 (C-5), 51.3 (C-1), 46.3 (C-4), 36.4 (2C, each S*C*H$_2$Ph) ppm; ^{1}H and ^{13}C NMR data in agreement with the lower resolved spectra of ref[6b]. MS (70 eV, EI): m/z (%): 542 (0.01) [M^+], 181 (5), 108 (5), 92 (10), 91 (100) [$C_7H_7^+$], 65 (8); $C_{33}H_{34}O_3S_2$ (542.77): calcd C 73.03, H 6.31, S 11.81; found C 72.11[23], H 6.33, S 11.53.

1-*O*-Acetyl-2,3,5-tri-*O*-benzyl-4-thio-L-lyxofuranose (4). A solution of benzyl 1,4-dithio-L-lyxofuranoside **3** (8.94 g, 16.47 mmol) and mercuric acetate (10.41 g, 32.67 mmol) in glacial acetic acid (220 mL) was stirred at room temperature for 1.5 h. After removal of the acetic acid under reduced pressure the residue was dissolved in EtOAc, diluted with petroleum ether and kept overnight at −5 °C. The precipitated mercuric salts were filtered off, the solvents were removed and the crude product was purified by silica gel column chromatography (petroleum ether-EtOAc 4:1; $R_{f,\alpha,\beta}=0.26$) to give **4** (5.96 g, 76%) as a pale yellow syrup with an anomeric ratio of 1:10 (α:β). The anomers were not separable. IR (film): $\nu=3087$, 3063, 3030, 2924, 2865, 1745 (C=O), 1498, 1452, 1369, 1311, 1246, 1228, 1101, 1016, 912, 847, 794, 739, 700, 606 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): α-**4**: $\delta=7.27-7.41$ (m, 15H, CH_{arom}), 6.25 (d, 1H, H-1), 4.46–4.70 (m, 6H, C*H*$_2$Ph), 4.25 (dd, 1H, H-3), 3.94–3.96 (m, 1H, H-5$_b$), 3.91 (dd, 1H, H-2), 3.55 (dd, 1H, H-5$_a$), 3.48–3.52 (m, 1H, H-4), 2.03 (s, 3H, CH_3), ppm. $J_{1,2}=4.9$, $J_{2,3}=3.2$, $J_{3,4}=4.0$, $J_{4,5a}=6.5$, $J_{5a,5b}=9.0$ Hz; β-**4**: $\delta=7.27-7.41$ (m, 15H, CH_{arom}), 6.02 (d, 1H, H-1), 4.46–4.70 (m, 6H, C*H*$_2$Ph), 4.25 (dd, 1H, H-3), 4.10 (dd, 1H, H-2), 3.98 (dd, 1H, H-5$_b$), 3.78 (ddd, 1H, H-4), 3.69 (dd, 1H, H-5$_a$), 2.04 (s, 3H, CH_3), ppm. $J_{1,2}=3.7$, $J_{2,3}=3.5$, $J_{3,4}=5.7$, $J_{4,5a}=8.0$, $J_{4,5b}=5.6$, $J_{5a,5b}=9.3$Hz; ^{13}C NMR (126 MHz, $CDCl_3$): α-**4**: $\delta=171.3$ (CO), 139.5 (C_{arom}), 138.5, 138.1, 129.0 (CH_{arom}), 128.9, 128.6, 128.44, 128.41, 128.37, 128.2, 128.1, 128.0, 84.7 (C-2), 79.1 (C-3), 76.9 (C-1), 73.93 (*C*H$_2$Ph), 73.87, 72.9, 70.2 (C-5), 46.7 (C-4), 21.8 (CH_3), ppm; β-**4**: $\delta=$ 171.3 (CO), 138.1 (C_{arom}), 137.9, 137.7, 128.40 (CH_{arom}), 128.38, 128.36, 127.78, 127.77, 127.75, 127.7, 127.61, 127.57, 84.4 (C-2), 80.5 (C-1), 79.4 (C-3), 73.30 (*C*H$_2$Ph), 73.26, 72.6, 71.0 (C-5), 46.4 (C-4), 21.0 (CH_3), ppm; FAB MS: m/z: 479 [M+H]; $C_{28}H_{30}O_5S$ (478.61): calcd C 70.27, H 6.32, S 6.70; found C 68.65[23], H 6.26, S 6.68.

1-(2,3,5-Tri-*O*-benzyl-4-thio-L-lyxofuranosyl)uracil (5). A solution of **4** (414 mg, 0.87 mmol), 2,4-bis-*O*-(trimethylsilyl)uracil[15] (850 mg, 3.31 mmol) and molecular sieves A4 (50 mg) in dry MeCN (15 mL) was cooled to −18 °C and TMSOTf (0.50 mL, 615 mg, 2.77 mmol) was added. The reaction mixture

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was stirred for 2 h and the temperature was allowed to rise to room temperature. Then the mixture was quenched with an excess of sat. $NaHCO_3$ solution and stirred for another 0.5 h. The solids were filtered off and the filtrate was extracted with $CHCl_3$. The organic phase was separated, dried with $MgSO_4$ and evaporated. The resulting crude product was purified by silica gel chromatography (petroleum ether-EtOAc 1:1, $R_{f,\beta} = 0.21$, $R_{f,\alpha} = 0.15$) to give separated anomers α-**5** (132 mg, 29%) and β-**5** (270 mg, 59%). Both anomers are white solids. α-**5**: M.p. 45–47 °C; $[a]_D^{20} = -62.1$ ($c = 1.0$ in $CHCl_3$); β-**5**: M.p. 41–43 °C; $[a]_D^{20} = +89.0$ ($c = 1.0$ in $CHCl_3$); IR (KBr): α-**5**: $\nu = 3192$ (NH), 3086, 3062, 3031, 2925, 2859, 1690 (C=O), 1495, 1454, 1380, 1246, 1207, 1129, 1077, 1027, 808, 738, 699, 550, 515 cm^{-1}; β-**5**: $\nu = 3060$, 3029, 2924, 2857, 1680 (C=O), 1495, 1456, 1384, 1266, 1208, 1121, 1086, 1048, 1025, 806, 736, 697, 605, 551 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): α-**5**: $\delta = 8.50$ (ws, 1H, NH), 7.28–7.37 (m, 16H, H-6, CH_{arom}), 6.26 (d, 1H, H-1′), 5.55 (dd, 1H, H-5), 4.85 (d, 1H, $J_{A,B}$ 11.7 Hz, C*H*$_2$Ph), 4.67 (d, 1H, $J_{A,B}$ 11.7 Hz, C*H*$_2$Ph), 4.65 (d, 1H, $J_{A,B}$ 12.5 Hz, C*H*$_2$Ph) 4.50 (s, 2H, C*H*$_2$Ph), 4.31 (d, 1H, $J_{A,B}$ 12.5 Hz, C*H*$_2$Ph), 4.22 (dd, 1H, H-3′), 3.91 (dd, 1H, H-2′), 3.84–3.89 (m, 2H, H-4′, H-5′$_b$), 3.56 (dd, 1H, H-5′$_a$) ppm. $J_{1',2'} = 7.8$, $J_{2',3'} = 3.1$, $J_{3',4'} = 3.2$, $J_{4',5'a} = 9.3$, $J_{5'a,5'b} = 12.2$, $J_{5,6} = 8.2$, $J_{5,NH} = 2.3$ Hz; β-**5**: $\delta = 8.82$ (ws, 1H, NH), 8.06 (d, 1H, H-6), 7.29–7.37 (m, 15H, CH_{arom}), 6.41 (d, 1H, H-1′), 5.41 (dd, 1H, H-5), 4.75 (d, 1H, $J_{A,B}$ 10.9 Hz, C*H*$_2$Ph), 4.66 (d, 1H, $J_{A,B}$ 12.0 Hz, C*H*$_2$Ph), 4.58 (d, 1H, $J_{A,B}$ 12.0 Hz, C*H*$_2$Ph), 4.57 (d, 1H, $J_{A,B}$ 10.9 Hz, C*H*$_2$Ph), 4.56 (d, 1H, $J_{A,B}$ 11.9 Hz, C*H*$_2$Ph), 4.51 (d, 1H, $J_{A,B}$ 11.9 Hz, C*H*$_2$Ph), 4.19 (dd, 1H, H-3′), 4.09 (dd, 1H, H-2′), 3.94 (dd, 1H, H-5′$_b$), 3.65 (dd, 1H, H-5′$_a$), 3.60 (ddd, 1H, H-4′), ppm. $J_{1',2'} = 6.8$, $J_{2',3'} = 3.4$, $J_{3',4'} = 4.4$, $J_{4',5'a} = 6.9$, $J_{4',5'b} = 6.7$, $J_{5'a,5'b} = 8.8$, $J_{5,6} = 8.3$, $J_{5,NH} = 2.4$ Hz; ^{13}C NMR (101 MHz, $CDCl_3$): α-**5**: $\delta = 162.1$ (C-4), 149.9 (C-2), 139.9 (C-6), 137.4 (C_{arom}), 137.3, 136.4, 128.3 (CH_{arom}), 128.04, 127.98, 127.9, 127.59, 127.55, 127.49, 127.45, 127.42, 102.4 (C-5), 84.4 (C-2′), 75.7 (C-3′), 73.4 (*C*H$_2$Ph), 73.1, 72.0, 69.0 (C-5′), 62.3 (C-1′), 46.4 (C-4′) ppm. β-**5**: $\delta = 162.8$ (C-4), 151.1 (C-2), 144.2 (C-6), 137.2 (C_{arom}), 136.9, 136.7, 128.14 (CH_{arom}), 128.06, 128.02, 127.8, 127.71, 127.65, 127.5, 127.2, 100.2 (C-5), 82.2 (C-2′), 79.3 (C-3′), 73.8 (*C*H$_2$Ph), 73.1, 73.0, 68.6 (C-5′), 58.4 (C-1′), 46.3 (C-4′) ppm; FAB MS: α-**5**: *m/z*: 531 [M+H]; β-**5**: *m/z*: 531 [M+H]; $C_{30}H_{30}N_2O_5S$ (530.65): calcd C 67.90, H 5.70, N 5.28, S 6.04; α-**5**: found C 67.32, H 5.77, N 5.02, S 5.93; β-5: found C 67.48, H 5.45, N 5.12, S 6.28.

1-(2,3,5-Tri-*O*-benzyl-4-thio-L-lyxofuranosyl)thymine (6) was prepared as described for **5** from **4** (580 mg, 1.21 mmol), 2,4-bis-*O*-(trimethylsilyl) thymine[15] (780 mg, 2.88 mmol), molecular sieves A4 (60 mg), TMSOTf (0.70 mL, 861 mg, 3.87 mmol) and MeCN (20 mL). After chromatographic work-up (petroleum ether-EtOAc 1:1, $R_f = 0.28$) **6** was obtained as an inseparable anomeric mixture (450 mg, 68%) with an α:β ratio of 2:1 (white solid). IR (KBr): $\nu =$ 3184, 3061, 3031, 2924, 2859, 1686, 1495, 1455,

1367, 1308, 1265, 1208, 1133, 1085, 1026, 909, 818, 739, 699, 544, 475 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): α-**6**: $\delta = 8.66$ (ws, 1H, NH), 7.27−7.38 (m, 15H, CH_{arom}), 7.00 (q, 1H, H-6), 6.30 (d, 1H, H-1′), 4.88, (d, 1H, $J_{A,B}$ 11.7 Hz, CH_2Ph) 4.68 (d, 1H, J_{AB} 11.7 Hz, CH_2Ph), 4.50 (s, 2H, CH_2Ph), 4.66 (d, 1H, $J_{A,B}$ 12.6 Hz, CH_2Ph), 4.26 (d, 1H, $J_{AB} = 12.6$ Hz, CH_2Ph), 4.24−4.25 (m, 1H, H-3′), 3.83−3.89 (m, 3H, H-2′, H-4′, H-5′$_b$), 3.51−3.57 (m, 1H, H-5′$_a$), 1.75 (d, 3H, CH_3) ppm. $J_{1',2'} = 8.2$, $J_{6,Me} = 1.2$ Hz; β-**6**: $\delta = 8.72$ (ws, 1H, NH), 7.90 (q, 1H, H-6), 7.27−7.38 (m, 15H, CH_{arom}), 6.45 (d, 1H, H-1′), 4.77 (d, 1H, $J_{A,B}$ 10.7 Hz, CH_2Ph), 4.57 (d, 1H, $J_{AB} =$ 10.7 Hz, CH_2Ph), 4.55−4.67 (m, 4H, CH_2Ph), 4.21 (dd, 1H, H-3′), 4.10 (dd, 1H, H-2′), 4.01 (dd, 1H, H-5′$_b$), 3.69 (dd, 1H, H-5′$_a$), 3.62 (ddd, 1H, H-4′), 1.50 (d, 3H, CH_3), ppm. $J_{1',2'} = 7.0$, $J_{2',3'} = 3.5$, $J_{3',4'} = 4.5$, $J_{4',5'a} = 6.8$, $J_{4',5'b} = 7.1$, $J_{5'a,5'b} = 9.1$, $J_{6,Me} = 1.2$ Hz; ^{13}C NMR (101 MHz, $CDCl_3$): α-**6**: $\delta = 163.3$ (C-4), 150.6 (C-2), 137.9 (C_{arom}), 137.7, 136.9, 135.9 (C-6), 128.6 (CH_{arom}), 128.51, 128.46, 128.4, 128.1, 128.0, 127.9, 127.8, 127.6, 111.3 (C-5), 84.7 (C-2′), 75.8 (C-3′), 73.9 (*C*H_2Ph), 73.5, 72.2, 69.4 (C-5′), 62.1 (C-1′), 46.7 (C4′), 12.5 (CH3) ppm; β-**6**: $\delta =$ 163.8 (C-4), 151.6 (C-2), 140.3 (C-6), 137.7 (C_{arom}), 137.5, 137.3, 128.5 (CH_{arom}), 128.46, 128.34, 128.26, 128.13, 128.05, 128.0, 127.9, 127.8, 109.0 (C-5), 82.9 (C-2′), 79.7 (C-3′), 74.5 (*C*H_2Ph), 73.5, 73.4, 69.0 (C-5′), 58.5 (C-1′), 46.5 (C-4′), 12.1 (CH_3) ppm; FAB MS: m/z: 545 [M+H]; $C_{31}H_{32}N_2O_5S$ (544.68): calcd C 68.36, H 5.92, N 5. 14, S 5.89; found C 67.44[23], H 5.91, N 4.87, S 5.79.

6-Methyl-1-(2,3,5-tri-*O*-benzyl-4-thio-L-lyxofuranosyl)uracil (7) was prepared as described for **5** from **4** (600 mg, 1.25 mmol), 6-methyl-2,4-bis-*O*-(trimethylsilyl)uracil[16] (1.36 g, 5.03 mmol), molecular sieves A4 (75 mg), TMSOTf (0.71 mL, 873 mg, 3.93 mmol) and MeCN (15 mL). After chromatographic work-up (petroleum ether-EtOAc 1:1, $R_{f,\ \beta} = 0.37$, $R_{f,\alpha} = 0.29$) the separated anomers α-7 (497 mg, 73%) and β-7 (51 mg, 7%) were obtained as white solids. α-7: M.p. 90−92 °C; $[\alpha]_D^{20} = -106.9$ ($c = 1.0$ in $CHCl_3$); β-7: M.p. 82−84 °C; $[\alpha]_D^{20} = -89.7$ ($c = 1.0$ in $CHCl_3$); IR (KBr): α-7: $\nu = 3192$ (N-H), 3087, 3061, 3030, 2922, 2860, 1693 (C=O), 1496, 1454, 1370, 1237, 1205, 1126, 1072, 1027, 821, 738, 699, 600, 536, 495, 416 cm^{-1}; β-**7**: $\nu = 3190$ (N-H), 3087, 3061, 3031, 2925, 2859, 1679 (C=O), 1496, 1455, 1394, 1353, 1207, 1153, 1101, 1047, 1026, 911, 822, 737, 699, 650, 616, 541, 513, 428 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): α-**7**: $\delta = 8.64$ (ws, 1H, NH), 7.26−7.38 (m, 15H, CH_{arom}), 5.72 (s, 1H, H-1′), 5.48 (ws, 1H, H-5), 5.05 (d, 1H, H-2′), 4.87 (d, 1H, $J_{A,B}$ 11.8 Hz, CH_2Ph), 4.70 (d, 1H, $J_{A,B}$ 11.8 Hz, CH_2Ph), 4.58 (d, 1H, $J_{A,B}$ 12.2 Hz, CH_2Ph), 4.48 (s, 2H, CH_2Ph), 4.30 (dd, 1H, H-3′), 4.23 (d, 1H, $J_{A,B}$ 12.2 Hz, CH_2Ph), 4.12−4.15 (m, 1H, H-4′), 3.79 (dd, 1H, H-5′$_b$), 3.50 (dd, 1H, H-5′$_a$), 2.22 (ws, 3H, CH_3) ppm. $J_{1',2'} = 0$, $J_{2',3'} = 2.9$, $J_{3',4'} = 2.9$, $J_{4',5'a} = 6.2$, $J_{4',5'b} = 8.8$, $J_{5'a,5'b} = 9.1$ Hz; β-**7**: $\delta = 9.01$ (ws, 1H, NH), 7.26−7.39 (m, 15H, CH_{arom}), 6.73 (d, 1H, H-1′), 5.43 (ws, 1H,

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H-5), 4.75 (d, 1H, $J_{A,B}$ 11.5 Hz CH_2Ph), 4.67 (d, 1H, $J_{A,B}$ 11.8 Hz, CH_2Ph), 4.60 (d, 1H, $J_{A,B}$ 11.8 Hz, CH_2Ph), 4.57 (d, 1H, $J_{A,B}$ 12.0 Hz, CH_2Ph) 4.48 (d, 1H, $J_{A,B}$ 12.0 Hz, CH_2Ph), 4.43 (d, 1H, $J_{A,B}$ 11.5 Hz, CH_2Ph), 4.27 (dd, 1H, H-2′), 4.20 (dd, 1H, H-3′), 4.01–4.05 (m, 2H, H-5′$_a$, H-5′$_b$), 3.81 (ddd, 1H, H-4′), 2.58 (d, 3H, CH_3) ppm. $J_{1',2'} = 5.5$, $J_{2',3'} = 3.6$, $J_{3',4'} = 7.0$, $J_{4',5'a} = 6.0$, $J_{4',5'b} = 7.2$, $J_{5,Me} = 0.6$ = Hz; ^{13}C NMR (126 = MHz, $CDCl_3$): α-**7**: $\delta = 162.3$ (C-4), 154.0 (C-6), 149.7 (C-2), 138.3 (C_{arom}), 137.8, 137.4, 128.6 (CH_{arom}), 128.43, 128.35, 128.24, 128.20, 128.1, 127.84, 127.81, 127.80, 103.1 (C-5), 83.1 (C-2′), 77.2 (C-3′), 74.2 (*C*H_2Ph), 73.3, 73.1, 68.3 (C-5′), 64.5 (C-1′), 48.3 (C4′), 21.0 (CH_3) ppm; β-**7**: $\delta = 161.9$ (C-4), 157.7 (C-6), 152.4 (C-2), 138.0 (C_{arom}), 137.3, 137.0, 128.6 (CH_{arom}), 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.7, 127.5, 104.0 (C-5), 81.4 (C-2′), 79.4 (C-3′), 74.9 (*C*H_2Ph), 73.3, 72.7, 69.6 (C-5′), 58.0 (C-1′), 49.4 (C-4′), 23.8 (CH_3) ppm; FAB MS: α-**7**: *m/z*: 545 [M+H]; β-**7**: *m/z*: 545 [M+H]; FAB HRMS: $C_{31}H_{33}N_2O_5S$: calcd 545.2110; α-**7**: found 545.2103; β-**7**: found 545.2114.

5,6-Dimethyl-(2,3,5-tri-*O*-benzyl-4-thio-α,L-lyxofuranosyl)uracil (8) was prepared as described for **5** from **4** (600 mg, 1.25 mmol), 5,6-dimethyl-2,4-bis-*O*-(trimethylsilyl)uracil[16] (1.42 g, 4.99 mmol), molecular sieves A4 (70 mg), TMSOTf (0.71 mL, 873 mg, 3.93 mmol) and MeCN (15 mL). After chromatographic work-up (petroleum ether-EtOAc 1:1, $R_f = 0.36$) only the α-anomer of **8** could be isolated (488 mg, 70%) as a white solid. M.p. 64 °C; $[\alpha]_D^{20} = -70.8$ ($c = 1.0$ in $CHCl_3$); IR (KBr): $\nu = 3188$ (N-H), 3086, 3060, 3030, 2926, 2865, 1676 (C=O), 1496, 1455, 1343, 1307, 1125, 1073, 1027, 911, 819, 739, 699, 608, 504, 469 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 8.57$ (ws, 1H, NH), 7.24–7.37 (m, 15H, CH_{arom}), 5.80 (s, 1H, H-1′), 5.12 (d, 1H, H-2′), 4.88 (d, 1H, $J_{A,B}$ 11.8 Hz, CH_2Ph), 4.70 (d, 1H, $J_{A,B}$ 11.8 Hz, CH_2Ph), 4.59 (d, 1H, $J_{A,B}$ 12.3 Hz, CH_2Ph), 4.48 (s, 2H, CH_2Ph), 4.31 (dd, 1H, H-3′), 4.25 (d, 1H, $J_{A,B}$ 12.3 Hz, CH_2Ph), 4.15 (ddd, 1H, H-4′), 3.79 (dd, 1H, H-5′$_b$), 3.49 (dd, 1H, H-5′$_a$), 2.20 (d, 3H, CH_3), 1.92 (d, 3H, CH_3) ppm. $J_{1',2'} = 0$, $J_{2',3'} = 3.3$, $J_{3',4'} = 2.9$, $J_{4',5'a} = 6.1$, $J_{4',5'b} = 8.4$, $J_{5'a,5'}b = 9.3$ Hz; ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 163.0$ (C-4), 149.4 (C-6), 148.8 (C-2), 138.4 (C_{arom}), 137.9, 137.6, 128.5 (CH_{arom}), 128.4, 128.3, 128.09, 128.08, 127.83, 127.77, 127.74, 108.9 (C-5), 83.6 (C-2′), 77.5 (C-3′), 74.2 (*C*H_2Ph), 73.2, 68.3 (C-5′), 64.9 (C-1′), 48.2 (C-4′), 17.1 (CH_3), 11.5 ppm; FAB MS: *m/z*: 559 [M+H]; FAB HRMS: $C_{32}H_{35}N_2O_5S$: calcd 559.2267; found 559.2375.

5-Iodo-6-methyl-1-(2,3,5-tri-*O*-benzyl-4-thio-α,L-lyxofuranosyl)uracil (9) was prepared as described for **5** from **4** (591 mg, 1.23 mmol), 5-iodo-6-methyl-2,4-bis-*O*-(trimethylsilyl)uracil[16] (1.92 g, 4.83 mmol), TMSOTf (0.71 mL, 873 mg, 3.93 mmol) and molecular sieves A4 (80 mg) in dry MeCN (15 mL). The resulting crude product was recrystallised from EtOAc to yield the pure α-anomer of **9** (437 mg, 53%) as colourless needles. M.p. 162 °C; $[\alpha]_D^{20} = -79.8$ ($c = 1.0$ in $CHCl_3$); IR (KBr): $\nu = 3207$

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(N-H), 3064, 3031, 2926, 2879, 2847, 2795, 1681 (C=O), 1587, 1496, 1453, 1433, 1402, 1357, 1342, 1288, 1210, 1128, 1073, 1027, 1005, 909, 797, 747, 701, 652, 600, 568, 497, 411 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 8.39$ (ws, 1H, NH), 7.13–7.38 (m, 15H, CH_{arom}), 5.85 (s, 1H, H-1′), 5.00 (bs, 1H, H-2′), 4.88 (d, 1H, $J_{A,B}$ 11.8 Hz, CH_2Ph), 4.71 (d, 1H, $J_{AB} = 11.8$ Hz, CH_2Ph), 4.61 (d, 1H, $J_{A,B}$ 11.8 Hz, CH_2Ph), 4.48 (s, 2H, CH_2Ph), 4.30 (dd, 1H, H-3′), 4.17 (d, 1H, $J_{AB} = 12.3$ Hz, CH_2Ph), 4.11–4.15 (m, 1H, H-4′), 3.78 (dd, 1H, H-5′$_b$), 3.49 (dd, 1H, H-5′$_a$), 2.62 (s, 3H, CH_3) ppm. $J_{1',2'} = 0$, $J_{2',3'} = 3.2$, $J_{3',4'} = 3.2$, $J_{4',5'a} = 6.2$, $J_{4',5'a} = 8.4$, $J_{5'a,5'b} = 9.2$ Hz; ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 159.3$ (C-4), 154.4, (C-2), 148.8 (C-6), 138.2 (C_{arom}), 137.8, 137.4, 128.6 (CH_{arom}), 128.44, 128.39, 128.37, 128.2, 128.1, 127.9, 127.8, 83.5 (C-2′), 76.8–77.3 (C-3′, C-5; the peaks of both carbon atoms were covered by the solvent. Their position could be determined by an HMBC measurement.), 74.3 (*C*H_2Ph), 73.28, 73.27, 68.2 (C-5′), 67.8 (C-1′), 48.5 (C-4′), 26.5 (CH_3) ppm; FAB MS: *m/z*: 671 [M+H]; FAB HRMS: calcd 671.1077; found 671.1343; $C_{31}H_{31}IN_2O_5S$ (670.57): calcd C 55.53, H 4.66, I 18.92, N 4.18, S 4.78; found C 55.52, H 4.61, I 19.26, N 4.10, S 4.96.

5-Bromo-6-methyl-1-(2,3,5-tri-*O*-benzyl-4-thio-α,L-lyxofuranosyl)uracil (10) was prepared as described for **5** from **4** (600 mg, 1.25 mmol), 5-bromo-6-methyl-2,4-bis-*O*-(trimethylsilyl)uracil[16] (1.74 g, 4.98 mmol), molecular sieves A4 (60 mg) and TMSOTf (0.71 mL, 873 mg, 3.93 mmol) in dry MeCN (15 ml). After recrystallisation of the crude product from EtOAc the α-anomer of nucleoside **10** was obtained as colourless needles (430 mg, 55%). M.p. 175 °C; $[\alpha]_D^{20} = -97.6$ ($c = 1.0$ in $CHCl_3$); IR (KBr): $\nu = 3203$ (N-H), 3064, 3030, 2947, 2929, 2866, 2797, 1692 (C=O), 1598, 1496, 1454, 1439, 1402, 1356, 1341, 1290, 1256, 1209, 1162, 1129, 1074, 1026, 1006, 910, 795, 748, 700, 656, 600, 576, 497, 463, 412 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): $\delta = 8.61$ (ws, 1H, NH), 7.13–7.37 (m, 15H, CH_{arom}), 5.80 (s, 1H, H-1′), 5.01 (ws, 1H, H-2′), 4.88 (d, 1H, $J_{A,B}$ 11.8 Hz, CH_2Ph), 4.70 (d, 1H, $J_{AB} = 11.8$ Hz, CH_2Ph), 4.61 (d, 1H, $J_{A,B}$ 12.3 Hz, CH_2Ph), 4.48 (s, 2H, CH_2Ph), 4.30 (dd, 1H, H-3′), 4.18 (d, 1H, $J_{AB} = 12.3$ Hz, CH_2Ph), 4.11–4.16 (m, 1H, H-4′), 3.79 (dd, 1H, H-5′$_b$), 3.50 (dd, 1H, H-5′$_a$), 2.49 (s, 3H, CH_3) ppm. $J_{1',2'} = 0$, $J_{2',3'} = 3.1$, $J_{3',4'} = 3.1$, $J_{4',5'a} = 6.3$, $J_{4',5'b} = 8.3$, $J_{5'a,5'b} = 9.3$ Hz. ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 158.2$ (C-4), 151.7 (C-2), 148.5 (C-6), 138.2 (C_{arom}), 137.8, 137.4, 128.6 (CH_{arom}), 128.43, 128.37, 128.14, 128.08, 127.84, 127.80, 100.3 (C-5), 83.4 (C-2′), 77.3 (C-3′), 74.3 (*C*H_2Ph), 73.28, 73.26, 68.2 (C-5′), 66.5 (C-1′), 48.5 (C-4′), 21.2 (CH_3) ppm. FAB MS: *m/z*: 625 [M+H, for ^{81}Br], 623 [M+H, for ^{79}Br]. $C_{31}H_{31}BrN_2O_5S$ (623.58): calcd C 59.71, H 5.01, Br 12.81, N 4.49, S 5.14; found C 59.34, H 4.98, Br 12.61, N 4.39, S 5.19.

1-(4-Thio-L-lyxofuranosyl)uracil (11). Boron tribromide (0.21 mL, 554 mg, 2.21 mmol) was added into dry CH_2Cl_2 (2.10 mL) and cooled to −90 °C. A solution of **5** (250 mg, 0.47 mmol, α:β = 1:2) in CH_2Cl_2 (3.20 mL)

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was added dropwise under vigorous stirring. The temperature was kept below $-80\,^{\circ}C$. After complete addition stirring was continued at $-90\,^{\circ}C$ for 1 h. Then the excess of boron tribromide was quenched at $-90\,^{\circ}C$ by dropwise adding a 1:1 mixture of CH_2Cl_2-MeOH (8 mL). After the solution had warmed to room temperature silver carbonate (2.18 g, 7.91 mmol) was added to neutralise the hydrobromic acid. After 0.5 h the inorganic salts were filtered off, the solution was evaporated to dryness and the remaining crude product was purified by silica gel chromatography ($CHCl_3$-MeOH 4:1, $R_{f,\alpha} = 0.12$, $R_{f,\beta} = 0.23$), to yield α-**11** (34 mg, 84%) and β-**11** (14 mg, 17%) as white solids. For further work up of the α-anomer it was purified by reversed phase HPLC (MeCN-H_2O 8:92) to yield α-**11** as white solid (28 mg, 69%). β-**11** was recrystallised from water to yield colourless needles (11 mg, 13%). α-**11**: M.p. 234 °C; $[\alpha]_D^{20} = -107.5$ ($c = 1.0$ in MeOH); β-**11**: M.p. 235–238 °C; $[\alpha]_D^{20} = -19.6$ ($c = 1.0$ in MeOH); IR (KBr): α-**11**: $\nu = 3449$ (O-H), 3178 (N-H), 3064, 2977, 2940, 2866, 2824, 1710 (C=O), 1689 (C=O), 1458, 1420, 1390, 1271, 1201, 1147, 1099, 1016, 980, 815, 757, 679, 630, 556, 538, 510, 407 cm^{-1}; β-**11**: $\nu = 3416$ (O-H), 3055, 2930, 2883, 2824, 1688 (C=O), 1466, 1389, 1249, 1179, 1123, 1043, 808, 628, 556, 518, 420 cm^{-1}; 1H NMR (500 MHz, [D_6]Me_2SO): α-**11**: $\delta = 11.18$ (ws, 1H, NH), 8.26 (d, 1H, H-6), 6.11 (d, 1H, H-1′), 5.58–5.60 (m, 2H, 2′-OH, H-5), 5.47 (d, 1H, 3′-OH), 4.92 (dd, 1H, 5′-OH), 4.21 (ddd, 1H, H-2′), 4.16 (ddd, 1H, H-3′), 3.87 (ddd, 1H, H-$5'_b$), 3.60 (ddd, 1H, H-$5'_a$), 3.47 (ddd, 1H, H-4′) ppm. $J_{1',2'} = 7.0$, $J_{2',3'} = 3.7$, $J_{2',OH} = 6.8$, $J_{3',4'} = 4.6$, $J_{3',OH} = 4.5$, $J_{4',5'a} = 7.7$, $J_{4',5'b} = 5.4$, $J_{5'a,5'b} = 10.8$, $J_{5'a,OH} = 5.4$, $J_{5'b,OH} = 5.3$, $J_{5,6} = 8.2$ Hz; β-**11**: $\delta = 11.29$ (ws, 1H, NH), 8.00 (d, 1H, H-6), 5.98 (d, 1H, H-1′), 5.72 (d, 1H, H-5), 5.50 (d, 1H, 2′-OH), 5.20 (d, 1H, 3′-OH), 4.79 (dd, 1H, 5′-OH), 4.23 (ddd, 1H, H-2′), 4.10 (ddd, 1H, H-3′), 3.84 (ddd, 1H, H-4′), 3.76 (ddd, 1H, H-$5'_b$), 3.42 (ddd, 1H, H-$5'_a$) ppm. $J_{1',2'} = 9.1$, $J_{2',3'} = 3.4$, $J_{2',OH} = 6.3$, $J_{3',4'} = 3.4$, $J_{3',OH} = 3.9$, $J_{4',5'a} = 7.6$, $J_{4',5'b} = 6.3$, $J_{5'a,5'b} = 10.7$, $J_{5'a,OH} = 5.8$, $J_{5'b,OH} = 4.8$, $J_{5,6} = 8.1$ Hz; ^{13}C NMR (126 MHz, [D_6]Me_2SO): α-**11**: $\delta = 163.6$ (C-4), 151.8 (C-2), 145.3 (C-6), 100.2 (C-5), 75.2 (C-2′), 73.0 (C-3′), 61.3 (C-5′), 60.2 (C-1′), 51.4 (C-4′) ppm; β-**11**: $\delta = 163.3$ (C-4), 151.6 (C-2), 142.2 (C-6), 102.7 (C-5), 78.5 (C-2′), 72.2 (C-3′), 62.3 (C-1′), 61.5 (C-5′), 50.2 (C-4′) ppm; MS (70 eV, EI): α-**11**: m/z (%): 242 (56) [$M^+ - H_2O$], 224 (19) [$M^+ - 2H_2O$], 194 (67), 181 (9), 151 (28), 131 (34) [$C_5H_7O_2S^+$], 113 (78), 112 (100) [$C_4H_4N_2O_2^+$], 85 (18), 57 (43), 42 (25); β-**11**: m/z (%): 242 (93) [$M^+ - H_2O$], 211 (8), 194 (100), 183 (16), 151 (39), 131 (45) [$C_5H_7O_2S^+$], 113 (67), 112 (77) [$C_4H_4N_2O_2^+$], 87 (21), 57 (48), 55 (22); HRMS: calcd 261.0545 (M^++H), 242.0361 ($M^+ - H_2O$), 244.0256 ($M^+ - 2H_2O$); α-11: found 261.0551, 242.0279, 224.0225; β-**11**: found 261.0592, 224.0258.

1-(4-Thio-L-lyxofuranosyl)thymine (12) was prepared as described for **11** from **6** (500 mg, 0.92 mmol, α:β = 2:1) in CH_2Cl_2 (6.33 mL), boron tribromide (0.42 mL, 1.11g, 4.43 mmol) in CH_2Cl_2 (4.20 mL) and silver

carbonate (4.27 g, 15.49 mmol) to yield the separated anomers α-**12** (45 mg, 26%) and β-**12** (16 mg, 19%) after chromatographic work-up ($CHCl_3$-MeOH 4:1, $R_{f,\alpha} = 0.23$, $R_{f,\beta} = 0.32$). Further purification of the anomers was carried out by reversed phase HPLC (MeCN-H_2O 8:92) to give α-**12** (38 mg, 23%) and β-**12** (13 mg, 15%) as white solids. The anomer α-**12** could be crystallised from water. α-**12**: M.p. 228 °C, under decomposition; $[\alpha]_D^{20} = -20.0$ ($c = 1.0$ in MeOH); β-**12**: M.p. 213 °C; $[\alpha]_D^{20} = -28.2$ ($c = 0.5$ in MeOH); IR (KBr): α-**12**: $\nu = 3435$ (O-H), 2926, 2856, 1750 (C=O), 1688 (C=O), 1473, 1384, 1233, 1121, 1040, 977, 901, 838, 779, 671, 601, 464 cm^{-1}; β-**12**: $\nu = 3476$ (O-H), 3227 (N-H), 2993, 2934, 2905, 2881, 2821, 1695 (C=O), 1465, 1423, 1377, 1334, 1252, 1226, 1200, 1116, 1044, 1020, 896, 772, 654, 541, 425 cm^{-1}; ^1H NMR (500 MHz, [D_6]Me_2SO): α-**12**: $\delta = 11.17$ (ws, 1H, NH), 8.14 (q, 1H, H-6), 6.12 (d, 1H, H-1′), 5.57 (d, 1H, 2′-OH), 5.45 (d, 1H, 3′-OH), 4.95 (dd, 1H, 5′-OH), 4.19 (ddd, 1H, H-2′), 4.16 (ddd, 1H, H-3′), 3.88 (ddd, 1H, H-$5'_b$), 3.63 (ddd, 1H, H-$5'_a$), 3.47 (ddd, 1H, H-4′), 1.77 (d, 3H, CH_3) ppm. $J_{1',2'} = 7.0$, $J_{2',3'} = 3.6$, $J_{2',OH} = 6.4$, $J_{3',4'} = 4.8$, $J_{3',OH} = 4.3$, $J_{4',5'a} = 7.6$, $J_{4',5'b} = 5.4$, $J_{5'a,5'b} = 10.9$, $J_{5'a,OH} = 5.8$, $J_{5'b,OH} = 5.2$, $J_{6,Me} = 1.2$ Hz; β-**12**: $\delta = 11.20$ (ws, 1H, NH), 7.80 (q, 1H, H-6), 5.92 (d, 1H, H-1′), 5.38 (d, 1H, 2′-OH), 5.11 (d, 1H, 3′-OH), 4.71 (dd, 1H, 5′-OH), 4.19 (ddd, 1H, H-2′), 4.03 (ddd, 1H, H-3′), 3.78 (ddd, 1H, H-4′), 3.70 (ddd, 1H, H-$5'_b$), 3.35 (ddd, 1H, H-$5'_a$), 1.76 (d, 3H, CH_3) ppm. $J_{1',2'} = 9.1$, $J_{2',3'} = 3.4$, $J_{2',OH} = 6.4$, $J_{3',4'} = 3.2$, $J_{3',OH} = 3.9$, $J_{4',5'a} = 7.6$, $J_{4',5'b} = 6.2$, $J_{5'a,5'b} = 10.7$, $J_{5'a,OH} = 5.8$, $J_{5'b,OH} = 4.8$, $J_{6,Me} = 1.2$ Hz; ^{13}C NMR (126 MHz, [D_6]Me_2SO): α-**12**: $\delta = 163.2$ (C-4), 150.9 (C-2), 140.2 (C-6), 106.3 (C-5), 74.2 (C-2′), 72.1 (C-3′), 60.3 (C-5′), 59.0 (C-1′), 50.5 (C-4′), 11.9 (CH_3) ppm; β-**12**: $\delta = 163.3$ (C-4), 151.0 (C-2), 136.9 (C-6), 109.8 (C-5), 77.7 (C-2′), 71.6 (C-3′), 61.5 (C-5′), 60.9 (C-1′), 49.6 (C-4′), 11.9 (CH_3), ppm; MS (70 eV, EI): α-**12**: m/z (%): 274 (7) [M^+], 256 (100) [$M^+ - H_2O$], 208 (42), 205 (7), 171 (12), 165 (11), 131 (88) [$C_5H_7O_2S^+$], 126 (94) [$C_5H_6N_2O_2{}^+$], 101 (31), 83 (26), 57 (70), 40 (100); β-**12**: m/z (%): 274 (1) [M^+], 256 (85) [$M^+ - H_2O$], 238 (20) [$M^+ - 2H_2O$], 208 (47), 205 (7), 171 (14), 165 (10), 131 (100) [$C_5H_7O_2S^+$], 126 (53) [$C_5H_6N_2O_2{}^+$], 101 (38), 85 (26), 57 (68), 55 (26); HRMS: calcd 274.0623 (M^+), 256.0518 ($M^+ - H_2O$), 238.0412 ($M^+ - 2H_2O$); α-**12**: found 274.0605, 256.0515; β-**12**: found 256.0527, 238.0413.

6-Methyl-1-(4-thio-L-lyxofuranosyl)uracil (13) was prepared as described for **11** from **7** (518 mg, 0.95 mmol, α:β = 10:1) in CH_2Cl_2 (6.20 mL), boron tribromide (0.46 mL, 1.21 g, 4.85 mmol) in CH_2Cl_2 (4.60 mL) and silver carbonate (4.95 g, 17.95 mmol) to yield after chromatographic work-up ($CHCl_3$-MeOH 4:1, $R_{f,\alpha,\beta} = 0.21$) the unseparated anomers of **13** (74 mg, 28%). Separation of these was carried out by reversed phase HPLC (MeCN-H_2O 7:93) to yield α-**13** (49 mg, 21%) and β-**13** (3 mg, 13%) as white solids, whereas α-**13** could be crystallised from water to give colourless needles. α-**13**: M.p. 244 °C, under decomposition;

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$[\alpha]_D^{20} = -56.0$ ($c = 1.0$ in MeOH); β-**13**: M.p. 206 °C, under decomposition; $[\alpha]_D^{20} = -1.4$ ($c = 0.3$ in MeOH); IR (KBr): α-**13**: $\nu = 3456$ (O-H), 3225 (N-H), 3029, 2935, 2872, 2797, 1697 (C=O), 1664 (C=O), 1474, 1407, 1388, 1237, 1193, 1131, 1096, 1049, 1018, 888, 857, 816, 765, 681, 540, 503 cm^{-1}; β-**13**: $\nu = 3454$ (O-H), 3223 (N-H), 3083, 2934, 2872, 2796, 1697 (C=O), 1665 (C=O), 1474, 1406, 1387, 1336, 1191, 1132, 1096, 1049, 1018, 937, 888, 816, 764, 681, 540, 503 cm^{-1}; ^{1}H NMR (500 MHz, [D$_6$]Me$_2$SO): α-**13**: $\delta = 11.20$ (ws, 1H, NH), 5.54 (s, 1H, H-5), 5.51 (ws, 1H, H-1′), 5.34 (d, 1H, 2′-OH), 5.09 (d, 1H, 3′-OH), 4.99 (ws, 1H, H-2′), 4.74 (dd, 1H, 5′-OH), 4.09 (ddd, 1H, H-3′), 3.80 (ddd, 1H, H-4′), 3.76 (ddd, 1H, H-5′$_b$), 3.43 (ddd, 1H, H-5′$_a$), 2.22 (ws, 3H, CH_3) ppm. $J_{1',2'} = 0$, $J_{2',3'} = 3.9$, $J_{2',OH} = 7.6$, $J_{3',4'} = 2.8$, $J_{3',OH} = 4.2$, $J_{4',5'a} = 6.9$, $J_{4',5'b} = 6.5$, $J_{5'a,5'b} = 10.3$, $J_{5'a,OH} = 5.8$, $J_{5'b,OH} = 4.9$ Hz; β-**13**: $\delta = 11.35$ (ws, 1H, NH), 5.95 (d, 1H, H-1′), 5.61–5.64 (m, 2H, H-5, 3′-OH), 5.45 (d, 1H, 2′-OH), 4.81 (dd, 1H, 5′-OH), 4.34 (ddd, 1H, H-2′), 4.04 (ddd, 1H, H-3′), 3.91 (ddd, 1H, H-5′$_b$), 3.58 (ddd, 1H, H-5′$_a$), 3.45 (ddd, 1H, H-4′), 2.34 (s, 3H, CH_3) ppm. $J_{1',2'} = 8.5$, $J_{2',3'} = 4.7$, $J_{2',OH} = 5.4$, $J_{3',4'} = 2.8$, $J_{3',OH} = 4.7$, $J_{4',5'a} = 7.7$, $J_{4',5'b} = 5.8$, $J_{5'a,5'b} = 10.6$, $J_{5'a,OH} = 5.4$, $J_{5'b,OH} = 4.9$ Hz; ^{13}C NMR (126 MHz, [D$_6$]Me$_2$SO): α-**13**: $\delta = 162.7$ (C-4), 154.7 (C-6), 149.2 (C-2), 105.7 (C-5), 76.2 (C-2′), 72.8 (C-3′), 66.2 (C-1′), 61.0 (C-5′), 52.4 (C-4′), 20.6 (CH_3) ppm; β-**13**: $\delta = 164.3$ (C-4), 157.5 (C-6), 154.3 (C-2), 105.3 (C-5), 77.7 (C-2′), 74.8 (C-3′), 63.3 (C-1′), 62.9 (C-5′), 54.0 (C-4′), 23.4 (CH_3) ppm; MS (70 eV, EI): α-13: m/z (%): 274 (0.3) [M^+], 256 (1) [$M^+ - H_2O$], 238 (10) [$M^+ - 2H_2O$], 208 (8), 165 (5), 131 (19) [$C_5H_7O_2S^+$], 126 (70) [$C_5H_6N_2O_2^+$], 101 (16), 83 (36), 68 (44), 57 (50), 42 (100); β-**13**: m/z (%): 274 (3) [M^+], 256 (6) [$M^+ - H_2O$], 238 (38) [$M^+ - 2H_2O$], 208 (18), 182 (5), 165 (8), 131 (35) [$C_5H_7O_2S^+$], 126 (100) [$C_5H_6N_2O_2^+$], 100 (24), 83 (42), 57 (37), 42 (57); HRMS: calcd 275.0702 (M^++H), 274.0623 (M^+), 256.0518 ($M^+ - H_2O$), 238.0412 ($M^+ - 2H_2O$); α-**13**: found 256.0503, 238.0408; β-13: found 275.0671, 274.0665, 256.0480, 238.0407.

5,6-Dimethyl-1-(4-thio-α,L-lyxofuranosyl)uracil (14) was prepared as described for 11 from **8** (478 mg, 0.86 mmol) in CH_2Cl_2 (6.0 mL), boron tribromide (0.41 mL, 1.08 g, 4.32 mmol) in CH_2Cl_2 (4.10 mL) and silver carbonate (4.48 g, 16.25 mmol) to yield after chromatographic work-up ($CHCl_3$-MeOH 4:1, $R_f = 0.23$) and crystallisation from H_2O-MeOH nucleoside **14** (17 mg, 7%) as colourless needles, which decomposed at 241 °C without melting. $[\alpha]_D^{20} = -62.2$ ($c = 1.0$, MeOH); IR (KBr): $\nu = 3422$ (O-H), 3172 (N-H), 2928, 2822, 1713 (C=O), 1661 (C=O), 1479, 1419, 1350, 1309, 1276, 1178, 1120, 1075, 1046, 1019, 936, 860, 789, 717, 608, 506, 473 cm^{-1}; ^{1}H NMR (500 MHz, [D$_6$]Me$_2$SO): $\delta = 11.22$ (ws, 1H, NH), 5.50 (ws, 1H, H-1′), 5.29 (d, 1H, 2′-OH), 5.06 (d, 1H, 3′-OH), 5.04 (ws, 1H, H-2′), 4.72 (dd, 1H, 5′-OH), 4.08–4.10 (m, 1H, H-3′), 3.74–3.82 (m, 2H, H-4′, H-5′$_b$), 3.43 (ddd, 1H, H-5′$_a$), 2.23 (s, 3H, CH_3), 1.83 (s, 3H, CH_3) ppm. $J_{1',2'} = 0$, $J_{2',OH} = 7.5$, $J_{3',OH} = 3.2$, $J_{4',5'a} = 7.0$, $J_{5'a,5'b} = 10.8$, $J_{5'a,OH} = 5.7$,

$J_{5'b,OH} = 5.3$ Hz; ^{13}C NMR (126 MHz, [D$_6$]Me$_2$SO): $\delta = 162.9$ (C-4), 150.2 (C-2), 149.8 (C-6), 107.9 (C-5), 76.6 (C-2′), 73.1 (C-3′), 61.3 (C-5′), 59.3 (C-1′), 52.6 (C-4′), 17.6 (CH_3), 11.7 (CH_3) ppm; MS (70 eV, EI): m/z (%): 288 (1) [M^+], 270 (12) [$M^+ - H_2O$], 252 (6) [$M^+ - 2H_2O$], 222 (15), 196 (7), 140 (100), 113 (10), 101 (23), 85 (20), 57 (88), 42 (35); HRMS: calcd 270.0674 ($M^+ - H_2O$), 252.0569 ($M^+ - 2H_2O$); found 270.0675, 252.0562.

5-Iodo-6-methyl-1-(4-thio-α,L-lyxofuranosyl)uracil (15) was prepared as described for **11** from **9** (369 mg, 0.55 mmol) in dry CH_2Cl_2 (3.51 mL) and boron tribromide (0.27 mL, 713 mg, 2.85 mmol) in dry CH_2Cl_2 (2.70 mL). After neutralisation with Ag_2CO_3 (2.93 g, 10.63 mmol) and chromatographic work-up ($CHCl_3$-MeOH 4:1, $R_f = 0.26$) **15** was obtained as pale brown solid (19 mg, 9%). Recrystallisation from MeOH yielded pure **15** (12 mg, 5%) as white solid, which decomposes at 211 °C without melting; $[\alpha]_D^{20} = -16.8$ ($c = 0.5$ in MeOH); IR (KBr): $\nu = 3458$, 3172, 2924, 2853, 1712, 1667, 1584, 1448, 1411, 1305, 1165, 1117, 1072, 1049, 1018, 935, 864, 751, 656, 573, 501 cm^{-1}; ^{1}H NMR (400 MHz, [D$_6$]Me$_2$SO): $\delta = 11.88$ (bs, 1H, NH), 5.85 (bs, 1H, H-1′), 5.60 (d, 1H, 2′-OH), 5.33 (d, 1H, 3′-OH), 5.14 (bs, 1H, H-2′), 4.98 (dd, 1H, 5′-OH), 4.28 (ddd, 1H, H-3′), 3.92–4.01 (m, 2H, H-4′, H-5′$_b$), 3.61–3.64 (m, 1H, H-5′$_a$; covered by H_2O), 2.84 (s, 3H, CH_3) ppm. $J_{1',2'} = 0$, $J_{2',3'} = 3.3$ or 4.3, $J_{2',OH} = 7.2$, $J_{3',4'} = 3.3$ or 4.3, $J_{3',OH} = 3.8$, $J_{5'a,OH} = 5.0$, $J_{5'b,OH} = 5.0$ Hz; ^{13}C NMR (101 MHz, [D$_6$]Me$_2$SO): $\delta = 160.5$ (C-4), 155.2 (C-2), 149.6 (C-6), 77.8 (C-5), 76.5 (C-2′), 72.7 (C-3′), 61.0 (2C, C-1′, C-5′), 52.5 (C-4′), 26.6 (CH_3) ppm; MS (70 eV, EI): m/z (%): 252 (7) [$C_5H_5IN_2O_2^+$], 131 (16) [$C_5H_7O_2S^+$], 97 (33), 69 (60), 44 (100).

5-Bromo-6-methyl-1-(4-thio-α,L-lyxofuranosyl)uracil (16). A solution of sodium (1 mg, 0.04 mmol) in dry MeOH (3.0 mL) and a solution of **18** (77 mg, 0.16 mmol) in dry MeOH (3.0 mL) were mixed and stirred for 24 h at room temperature. After addition of water (1.0 mL), the solution was evaporated to dryness and the residue was purified by column chromatography (Sephadex LH 20, MeOH). The resulting pale red solid was recrystallised from MeOH to give the unprotected nucleoside **16** (4 mg, 7%) as white solid, which decomposes at 186 °C without melting; $[\alpha]_D^{20} = -9.6$ ($c = 0.2$ in MeOH); IR (KBr): $\nu = 3448$ (O-H), 3258, 3173 (N-H), 2925, 2855, 2822, 1716 (C=O), 1674 (C=O), 1594, 1454, 1417, 1344, 1304, 1243, 1167, 1117, 1074, 1052, 938, 867, 733, 659, 582, 501 cm^{-1}; ^{1}H NMR (500 MHz, [D$_6$]Me$_2$SO): $\delta = 8.61$ (ws, 1H, NH), 5.63 (s, 1H, H-1′), 5.38 (ws, 1H, 2′-OH), 5.11 (ws, 1H, 3′-OH), 4.95 (ws, 1H, H-2′), 4.75 (dd, 1H, 5′-OH), 4.10 (ddd, 1H, H-3′), 3.75–3.82 (m, 2H, H-4′, H-5′$_b$), 3.44 (ddd, 1H, H-5′$_a$), 2.42 (s, 3H, CH_3) ppm. $J_{1',2'} = 0$, $J_{2',3'} = 3.0$, $J_{3',4'} = 3.0$, $J_{3',OH} = 3.0$, $J_{4',5'a} = 6.7$, $J_{5'a,5'b} = 10.4$, $J_{5'a,OH} = 5.3$, $J_{5'b,OH} = 5.1$ Hz; ^{13}C NMR (126 MHz, [D$_6$]Me$_2$SO): $\delta = 160.3$ (C-4), 154.1, (C-2), 144.9 (C-6), 100.8 (C-5), 77.7 (C-2′), 74.0 (C-3′), 53.8 (C-4′), 22.7 (CH_3) ppm. Because of

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dynamic effects it was not possible to detect the signal of C-1′; MS (70 eV, EI): m/z (%): 354 (0.2) [M^+, for ^{81}Br], 352 (0.2) [M^+, for ^{79}Br], 336 (4) [$M^+ - H_2O$, for ^{81}Br], 334 (4) [$M^+ - H_2O$, for ^{79}Br], 288 (6), 286 (6), 206 (97) [$C_5H_5{}^{81}BrN_2O_2{}^+$], 204 (100) [$C_5H_5{}^{79}BrN_2O_2{}^+$], 163 (56), 161 (55), 131 (45) [$C_5H_7O_2S^+$], 120 (34), 83 (13), 57 (38), 42 (78); HRMS: calcd 205.9514 ($C_5H_5{}^{81}BrN_2O_2{}^+$), 203.9534 ($C_5H_5{}^{79}BrN_2O_2{}^+$); found 205.9508, 203.9529.

Methyl 2,3,5-tri-*O*-acetyl-4-thio-L-lyxofuranoside(17) was prepared in the same way as **11** from **4** (869 mg, 1.82 mmol) in dry CH_2Cl_2 (9.0 mL) and boron tribromide (0.89 mL, 2.35 g, 9.38 mmol) in dry CH_2Cl_2 (8.90 mL). After quenching the reaction with CH_2Cl_2/MeOH 1:1, neutralisation with barium carbonate (6.52 g, 33.04 mmol) and filtration the residue was dissolved in dry pyridine (15.0 mL). Then acetic anhydride (2.85 mL, 3.08 g, 30.17 mmol) was added and the solution was stirred at room temperature for 24 h. After the reaction was completed sat. $NaHCO_3$ solution was added and stirring was continued for another 0.5 h. Then the solution was diluted with water and extracted with $CHCl_3$. The organic phase was separated, dried with Na_2SO_4, concentrated and the resulting crude product was purified by silica gel chromatography (petroleum ether-EtOAc 1:1, $R_{f,a} = 0.38$, $R_{f,b} = 0.27$) to give the minor anomer (99 mg, 18%) and the major anomer (207 mg, 37%) of **17**. Both anomers are colourless syrups. Minor anomer: $[\alpha]_D^{20} = -166.9$ ($c = 1.0$ in $CHCl_3$); Major anomer: $[\alpha]_D^{20} = +143.3$ (c = 1.0 in $CHCl_3$); IR (film): Minor anomer: $\nu = 2992$, 2934, 2830, 1730 (C=O), 1496, 1454, 1371, 1315, 1260, 1112, 1030, 893, 843, 812, 778, 702, 610 cm^{-1}; Major anomer: $\nu = 2993$, 2938, 2830, 1747 (C=O), 1445, 1371, 1229, 1097, 878, 840, 787, 720, 661, 636, 603 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): Minor anomer: $\delta = 5.60$ (dd, 1H, H-3), 5.39 (dd, 2H, H-2), 5.05 (d, 1H, H-1), 4.36 (dd, 1H, H-5_b), 4.17 (dd, 1H, H-5_a), 3.96 (ddd, 1H, H-4), 3.36 (s, 3H, OCH_3), 2.12, 2.11, 2.05 (s, each 3H, $COCH_3$), ppm. $J_{1,2} = 3.7$, $J_{2,3} = 3.7$, $J_{3,4} = 6.3$, $J_{4,5a} = 7.3$, $J_{4,5b} = 7.2$, $J_{5a,5b} = 11.2$ Hz; Major anomer: $\delta = 5.79$ (dd, 1H, H-3), 5.14–5.17 (m, 2H, H-1, H-2), 4.36 (dd, 1H, H-5_b), 4.17 (dd, 1H, H-5_a), 3.82 (ddd, 1H, H-4), 3.35 (s, 3H, OCH_3), 2.12, 2.11, 2.03 (s, each 3H, $COCH_3$) ppm. $J_{2,3} = 4.3$, $J_{3,4} = 5.7$, $J_{4,5a} = 6.6$, $J_{4,5b} = 8.6$, $J_{5a,5b} = 11.0$ Hz; ^{13}C NMR (126 MHz, $CDCl_3$): Minor anomer: $\delta = 170.93$ ($COCH_3$), 170.17, 170.07, 88.83 (C-1), 78.33 (C-2), 72.80 (C-3), 64.58 (C-5), 57.38 (OCH_3), 43.11 (C-4), 20.82 ($CO\mathit{C}H_3$), 20.74, 20.62 ppm; Major anomer: $\delta = 170.41$ ($\mathit{C}OCH_3$), 170.10, 170.01, 87.35 (C-1), 75.27 (C-2), 71.28 (C-3), 63.54 (C-5), 57.28 (OCH_3), 43.12 (C-4), 20.75 ($CO\mathit{C}H_3$), 20.69 ppm; MS (70 eV, EI): Minor anomer: m/z (%): 246 (7), 217 (6), 186 (48), 172 (49), 144 (56), 127 (76), 115 (33), 85 (27), 74 (33), 69 (26), 43 (100) [$C_2H_3O^+$]; Major anomer: m/z (%): 246 (18), 186 (34), 172 (68), 144 (63), 127 (49), 113 (32), 103 (19), 85 (21), 69 (28), 43 (100) [$C_2H_3O^+$]; $C_{12}H_{18}O_7S$ (306.34): calcd C 47.05, H 5.92, S 10.47; Major anomer: found C 46.87, H 6.03, S 9.46.

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5-Bromo-6-methyl-1-(2,3,5-tri-*O*-acetyl-4-thio-α,L-lyxofuranosyl)uracil (18) was prepared as described for **5** from **17** (176 mg, 0.57 mmol), 5-bromo-6-methyl-2,4-bis-*O*-(trimethylsilyl)uracil[16] (780 mg, 2.23 mmol), TMSOTf (0.38 mL, 467 mg, 2.10 mmol) and molecular sieves A4 (35 mg) in dry MeCN (10 mL). After chromatographic work-up (petroleum ether-EtOAc 1:2, $R_f = 0.22$) the α-anomer of **18** could be isolated as a white solid (82 mg, 30%). M.p. 75 °C; $[\alpha]_D^{20} = -51.3$ ($c = 1.0$ in $CHCl_3$); IR (KBr): $\nu = 3205$ (N-H), 3044, 2936, 2816, 1748 (C=O), 1703 (C=O), 1596, 1443, 1402, 1373, 1231, 1046, 901, 769, 667, 593, 497 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 9.14$ (bs, 1H, NH), 6.28 (bs, 1H, H-2′), 5.86 (s, 1H, H-1′), 5.84 (dd, 1H, H-3′), 4.45–4.50 (m, 1H, H-4′), 4.37 (dd, 1H, H-5′$_b$), 4.10 (dd, 1H, H-5′$_a$), 2.57 (s, 3H, CH_3), 2.18, 2.05, 2.04 (s, each 3H, $COCH_3$) ppm. $J_{1',2'} = 0$, $J_{2',3'} = 3.7$, $J_{3',4'} = 3.7$, $J_{4',5'a} = 7.1$, $J_{4',5'b} = 7.6$, $J_{5'a,5'b} = 11.1$ Hz; ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 170.4$ ($COCH_3$), 169.8, 169.5, 158.2 (C-4), 150.4 (C-2), 148.9 (C-6), 101.6 (C-5), 79.5 (C-2′), 76.2 (C-3′), 66.1 (C-1′), 61.7 (C-5′), 47.3 (C-4′), 21.1 ($CO\mathit{C}H_3$), 20.8 (CH_3), 20.7 ($CO\mathit{C}H_3$), 20.5 ppm; FAB MS: m/z: 481 [M+H, for ^{81}Br], 479 [M+H, for ^{79}Br].

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