Synthesis and Structural Elucidation of 2′-Deoxy-4′-thio-L-*threo*-pentofuranosylpyrimidine and -purine Nucleosides[‡]

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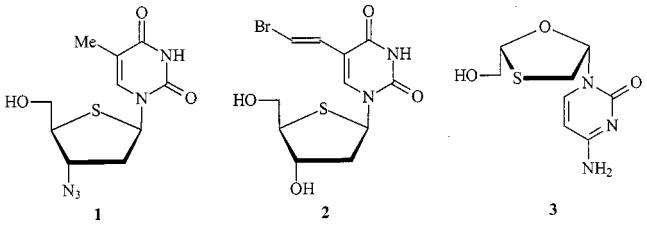
Benzyl 3,5-di-*O*-benzyl-2-deoxy-1,4-dithio-L-*threo*-pentofuranoside (**13**) was used as glycosyl donor for the synthesis of 4′-thio-L-*threo*-pentofuranosyluracil derivatives **23**–**29**. The corresponding cytidine analogue **33** was prepared from **13** via the triazolo derivative **31**. Adenine and hypoxanthine did not react with **13**. Therefore, **13** was transformed into the 1-*O*-acetate **15**, which was a sufficiently reactive donor for the purine bases, yielding 4′-thio-L-*threo*-pentofuranosylpurines **36** and **37**. In most cases it was possible to obtain pure anomers of the deprotected nucleoside analogues, three of which were suitable for X-ray structural analyses.

Introduction

4′-Thionucleosides have been prepared and investigated since the 1960s[1,2] and 1970s.[3,4] Over the last 40 years, numerous articles on this scientific topic have been published.[5] In particular, bioorganic chemists' attention has been drawn to 4′-thionucleosides containing 2-deoxy-4-thio-D-ribose[5] or 4-thio-D-ribose[6] as the sugar moiety, since these compounds are the analogues of the natural DNA and RNA building blocks. As important representatives of this class of substances, 4′-S-AZT (**1**)[7] and 4′-S-BVDU (**2**)[7] should be mentioned (Scheme 1). In 1995, Leydier et al.[8] published the first results on the synthesis of 4′-thio-D-*ribo*-oligonucleotides, the starting material for 4′-thio-RNA. Since the synthesis of 2′,3′-dideoxy-3′-thiacytidine (3-TC, **3**), with its remarkable activity against the AIDS virus,[9] 4′-thionucleosides of the unnatural L configuration have become compounds of increased scientific interest.[10–12]

In 1998, Satoh et al.[13] reported on the synthesis of the 4′-thio-L-*arabino*-nucleosides **4** and **6** and investigated their antiviral activities (Scheme 2). Independently, we have synthesised **4** and the corresponding uridine **5**,[14] as well as the analogous 5-halo derivatives **7**–**9**.[15] In continuation of our synthetic work we report here on the synthesis and structural elucidation of various 2′-deoxy-4-thio-L-*threo*-pentofuranosylnucleosides ["2′-deoxy-4′-thio-L-*lyxo*-furanosylnucleosides"], most of which are new compounds not yet mentioned in the literature.



Scheme 1

Results and Discussion

In 1997 we prepared benzyl 2-deoxy-3,5-di-*O*-methyl-1,4-dithio-L-*threo*-pentofuranoside (**10**) from 2-deoxy-D-ribose, in five steps.[16] Using NOE measurements on **10**, we established the inversion of the D configuration into the L form. Analogously, we converted 2-deoxy-D-ribose into the dithioacetal **11** in two steps, following the synthetic procedures reported by Dyson et al.[17] After mesylation of **11**, the mesylate **12** was cyclised in the presence of tetrabutylammonium iodide and barium carbonate, in pyridine at reflux temperature, to afford the 2-deoxy-1,4-dithio-L-*threo*-pentofuranoside **13** [18] (85% yield), as an anomeric mixture with a ratio of α/β = 2:1 (Scheme 3). The spectroscopic data of **13** are in agreement with those reported by Dyson et al.[17] In 1993, Huang and Hui[19] described the formation of the 2-deoxy-1,4-dithio-D-ribofuranoside **14** from **12**, with the aid of triphenylphosphane/iodine/imidazole. However, our spectroscopic data for **13** agree with those of Huang and Hui's compound **14**, but not with those of the well-known authentic **14**.[17] Tiwari et al.[20] have already repeated Huang and Hui's synthesis and obtained **13** instead of **14**. This means that double inversion – i.e., retention of configura-

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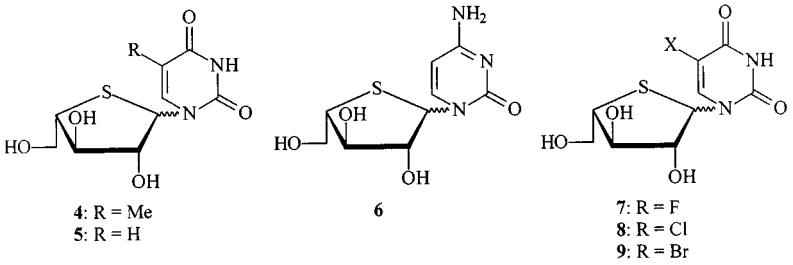
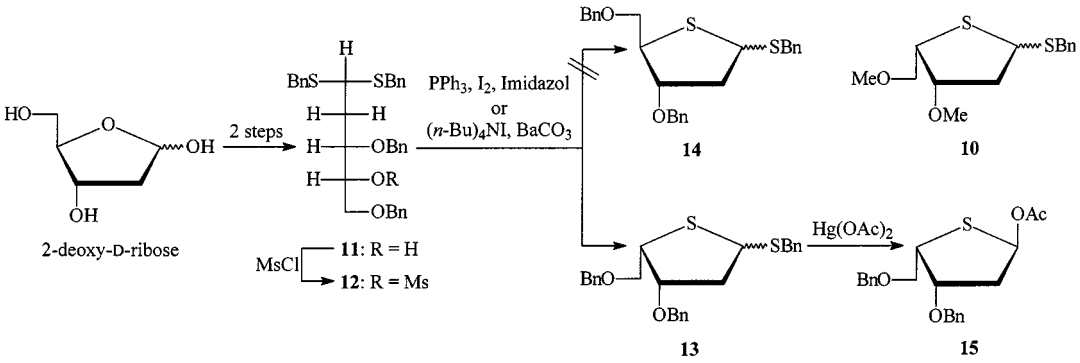


Scheme 2



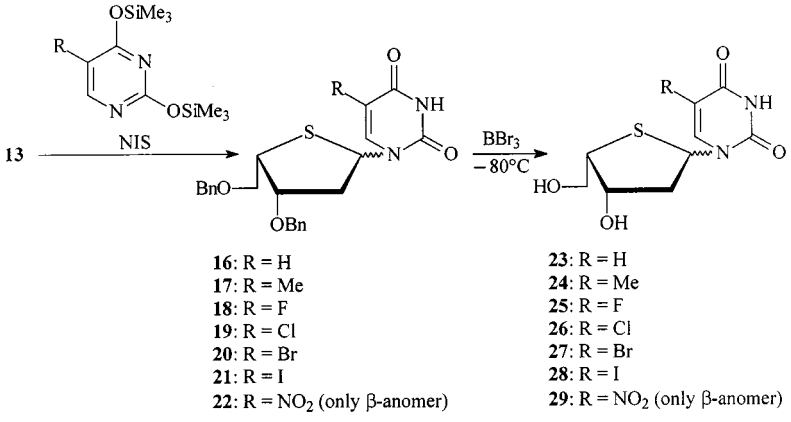
Scheme 3

tion at C-4 in the dithioacetal **12** − had not taken place. Rather, the cyclisation mechanism consists of a single intramolecular S_N2 displacement reaction.[14,16,20] As a consequence, Huang and Hui's thymidine, 5-fluoro- and 5-iodouridine derivatives also do not exhibit the claimed D configuration, but the L form.

Treatment of 1,4-dithiofuranoside **13** with mercuric acetate[21−23] gave the 1-*O*-acetyl-4-thiofuranose **15** as a pure α anomer, with a yield of 64% (Scheme 3).

Treatment of 1,4-dithiofuranoside **13** with 2,4-bis-*O*-trimethylsilyluracil[24] and *N*-iodosuccinimide (NIS)[5,25,26] yielded the benzyl-protected 1-(4-thio-L-*threo*-pentofuranosyl)uridine derivative **16** in 75% yield. The anomers were separated by column chromatography and obtained in an α/β ratio of 2:3. Analogously, the thymidine derivative **17** was obtained from **13** and 2,4-bis-*O*-trimethylsilylthymine[24] as a 1:1 inseparable mixture of anomers, in a yield of 55% (Scheme 4). The anomeric configurations of **16** and **17**, as well as that at C-4, were assigned by NOE measurements. For the α anomers, significant NOE interactions were observed between H-6 of the nucleobase and one of the protons H-2′, as well as H-3′ and H-4′. Moreover, we observed an NOE between H-2′ and H-4′, which is only possible in the L configuration, as well as an NOE between the other H-2′ proton and one of the H-5′ protons. For the β anomers, we observed an NOE between the H-6 proton of the nucleobase and one of the H-2′ protons, as well as an NOE between H-6 and one of the H-5′ protons. The other H-2′ proton and H-3′ showed interactions with H-4′, which again is only possible in the L configuration of the nucleosides **16** and **17**.

Coupling of **13** with silylated 5-fluorouracil[27] yielded the 5-fluorouridine derivative **18**, with an α/β ratio of 1:2 and in 68% yield. The 5-chlorouridine **19** was obtained in a yield of 67% as an anomeric mixture (α/β = 1:3). Treatment of **13** with silylated 5-bromouracil[27] gave the benzyl-protected



Scheme 4

5-bromouridine derivative **20**, with an anomeric ration of 1:2 (α/β) and in a yield of 60%. The 5-iodouridine **21** was obtained from **13** and silylated 5-iodouracil[27] in 72% yield. Again, the α/β ratio was 1:2. Only for **21** was it possible to separate the anomers by column chromatography. The 5-nitrouridine derivative **22** was surprisingly obtained as a pure β anomer, although in a low yield of 26% (Scheme 4). For all 5-substituted uridine derivatives **18**−**22**, the anomeric configurations were assigned by comparison of their NMR spectra with those of **16** and **17**.

Cleavage of the benzyl groups of **16** and **17** was achieved by treatment with boron tribromide at −80 °C.[18,28] After quenching the excess boron tribromide, neutralisation of the formed hydrobromic acid with silver carbonate[14] and reversed-phase HPLC, the separated anomers α-**23** and β-**23** were obtained in yields of 47% and 25%, respectively. It was possible to crystallise α-**23** from water and to determine its structure by X-ray diffraction analysis (cf. Figure 1), clearly confirming the expected L-*threo* configuration, in contrast to Huang and Hui's assumption[19] of a 2-deoxy-D-*ribo* configuration. The separated thymidine derivatives α-**24** and β-**24** were obtained in yields of 27% and 12%, respectively.

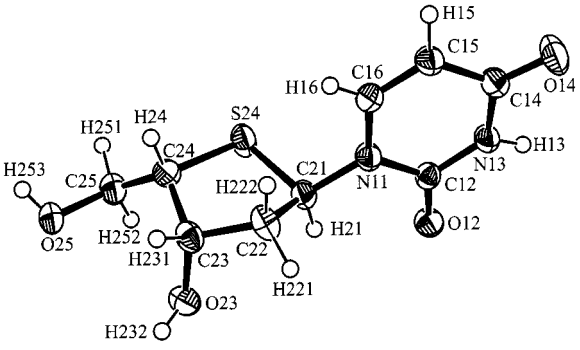


Figure 1. ORTEP view of the X-ray diffraction structure of uridine derivative α-**23**; thermal ellipsoids are drawn at the 50% probability level

Treatment of **18** with boron tribromide gave α-**25** (37%) and β-**25** (11%). Cleavage of the benzyl groups in 5-chlorouridine **19** produced α-**26** (49%) and β-**26** (9%). The unprotected 5-bromouridine derivatives α-**27** and β-**27** were isolated in only 16% and 8% yields. Deprotection of **21** yielded α-**28** (23%) and β-**28** (8%). An X-ray structure analysis was performed on a single crystal of α-**28**, unequivocally confirming the α-L-*threo* configuration (cf. Figure 2), in contrast with Huang and Hui's findings.[19] In all cases, the cleavage reactions were carried out using the anomeric mixtures of the benzylated 5-halouridines **18**−**21**. The anomers of the deprotected products were then separated by reversed-phase HPLC. This was not, however, necessary for the 5-nitrouridine **29**, which was obtained as the pure β anomer (9%) (Scheme 4).

Attempts to synthesise the benzyl-protected cytidine derivative **32** by coupling thiosugar **13** with 2,4-bis-*N*,*O*-trimethylsilylcytosine[24] in the presence of NIS or trimethylsilyl trifluoromethanesulfonate (TMSOTf)[6,23] failed. Only the starting material, together with unidentifiable decomposition products, was recovered in either case. As well as this, a route to **32** via the 4-thionouracil derivative **30**, described for similar cases by Leydier et al.,[6] was unsuccessful. While the first step, thionation of **16** with Lawesson's reagent, worked well with a yield of 82%, no reaction of **30** took place with methanolic ammonia. Eventually, Uenishi's alternative approach[29] to cytidine derivatives via 4-(1,2,4-triazolo) derivatives proved applicable. To be successful, we had to use a large excess of 1,2,4-triazole, phosphoryl chloride and triethylamine, obtaining a 72% yield of **31** (anomeric ratio α/β = 3:2) (Scheme 5). The displacement of the 1,2,4-triazolyl substituent with ammonia resulted in the desired benzyl-protected cytidine derivative **32** in 72% yield. Again, the anomeric ratio was 3:2. Deprotection of **32** with boron tribromide provided the cytidine derivative **33** as mixture of anomers (Scheme 5). A proportion of the α anomer of **33** could be separated from the mixture by column chromatography. The pure β anomer could not be obtained because of intense tailing, even during reversed-phase HPLC. The total yield of the cleavage reaction was 26%.

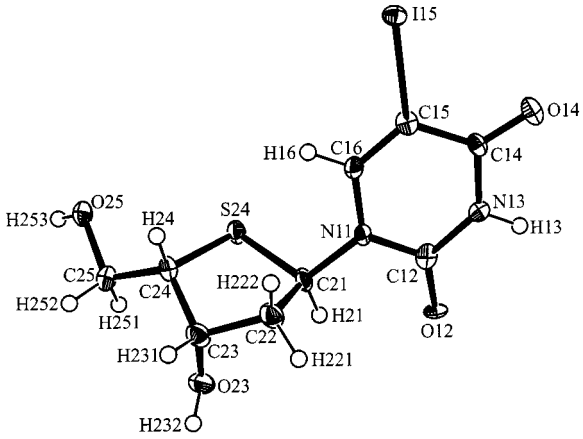
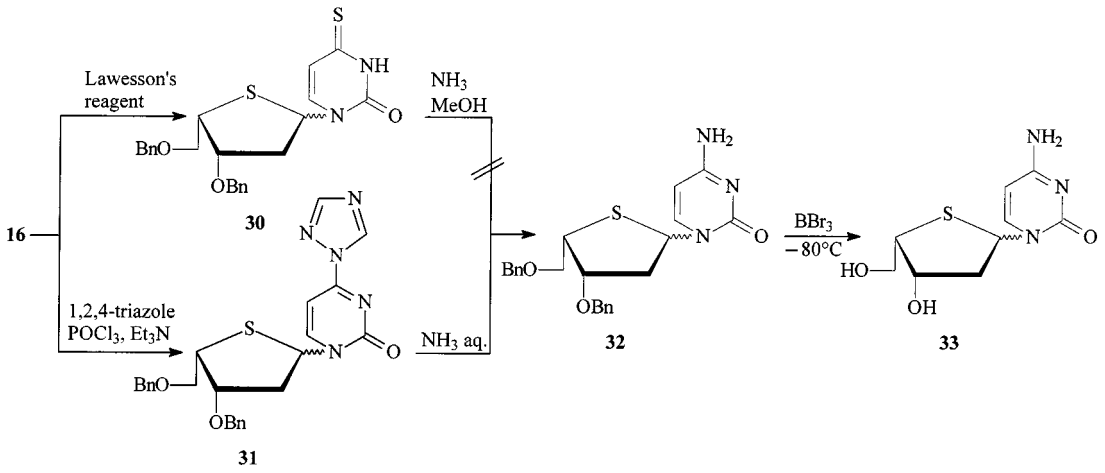
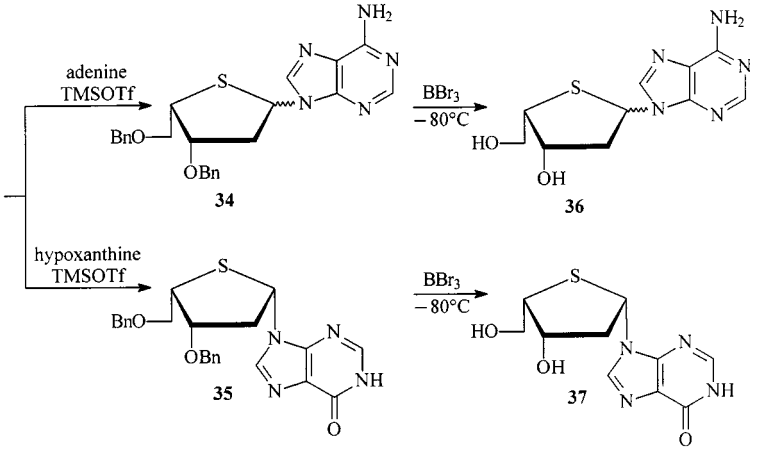


Figure 2. ORTEP view of the X-ray diffraction structure of 5-iodouridine derivative α-**28**; thermal ellipsoids are drawn at the 50% probability level

As shown in Scheme 6, purine nucleoside analogues derived from 2-deoxy-4-thio-L-*threo*-pentofuranose are also accessible. Coupling of the glycosyl donor **15** with adenine in the presence of TMSOTf[6] yielded adenosine derivative **34** with an anomeric ratio of α/β = 1:5 and in 60% yield. Treatment of **15** with hypoxanthine under the same conditions produced the inosine derivative **35**, obtained as the pure β anomer in 68% yield. The pronounced preponderance of the β anomers is surprising, as one would expect steric hindrance to favour the formation of α anomers. Cleavage of the benzyl groups of **34** and **35** with boron tribromide and separation of the anomers by reversed phase HPLC yielded the adenosine analogues α-**36** and β-**36**, together with the inosine derivative **37**. The deprotection steps gave low yields of only 12% of α-**36**, 13% of β-**36** and 6% of **37**, due to the strongly basic properties of the purine moieties; these formed persistent hydrobromides and made workup difficult. However, β-**36** could be crystallised from water as a monohydrate. A single crystal was suitable for X-ray structural analysis. As in the cases of the uridine de-



Scheme 5



Scheme 6

rivatives α-**23** and α-**28**, the anomeric configuration was confirmed, together with the L configuration at the C-4 atom of β-**36** (cf. Figure 3). Like that of α-**28** (cf. Figure 2), the thiofuranose moiety of β-**36** exhibits an envelope conformation, with centres C24, S24, C21 and C22 arranged in nearly coplanar manner and a torsion angle of only −2.5° at the S24−C21 bond (α-**28**: −8.7°), whereas in α-**23**, C21, S24, C24 and C23 nearly form a plane, while the torsion angle at the S24−C24 bond is −8.45°. The plane of the pyrimidine ring and the S24−C21−C22 triangle in α-**23** and α-**28** are situated perpendicularly to each other. Because of its steric requirements, the purine ring, i.e., the C14−N13 edge of β-**36**, exists in a staggered conformation with respect to the S24−C21−H21 triangle (cf. Figure 3).

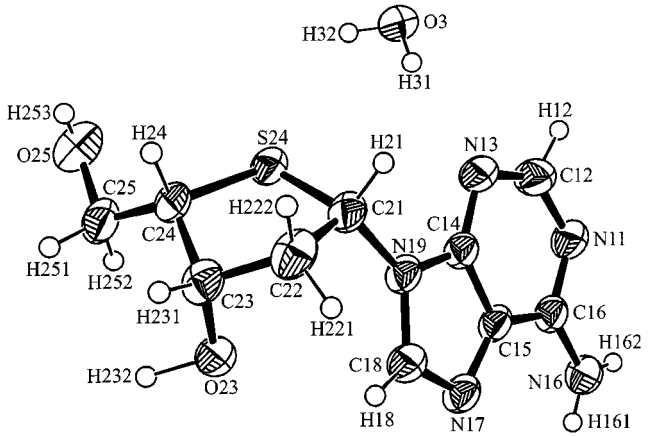


Figure 3. ORTEP view of the X-ray diffraction structure of adenosine derivative β-**36** with one molecule of crystal water; thermal ellipsoids are drawn at the 50% probability level

Experimental Section

General: IR: ATI Mattson Genesis spectrometer. − NMR: Bruker AMX 400 and DRX 500. Chemical shifts (ppm) are relative to Me_4Si (^1H) and $CDCl_3$ (^{13}C, δ = 77.05). Standard correlation techniques were used for assignments. − Mass spectra: Varian CH 7 (EI) and VG Analytical 70−250 S (FAB, HRMS). − Melting points: Electrothermal apparatus (values are corrected). − HPLC (Merck−Hitachi equipment): Semipreparative HPLC was carried out with a LiChroCART 250−10 column containing LiChrosher 100 RP-18 (10 μm), and analytical HPLC was performed with an EcoCART 125-3 column containing LiChrosher 100 RP-18 endcapped (5 μm). Solvents for HPLC were obtained from Merck (MeCN, HPLC grade) and Riedel-de Haën (water, HPLC grade). − 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); R_f(A1) and R_f(A2) correspondent to fast and slowly eluted fractions without

assignment of the anomers. Solvents were purified and dried according to standard laboratory procedures.[30] The pyrimidine bases, adenine and hypoxanthine are commercially available.

X-ray Structure Analysis: The crystal data and a summary of experimental details for the nucleosides α-**23**, α-**28** and β-**36** are given in Table 1. For α-**23** and β-**36**, data collection was performed with a Kappa-CCD Nonius diffractometer with graphite-monochromated Mo-K_α radiation (0.71073 Å) in the rotation Φ scan mode at a temperature of 293 K. The data for α-**28** were collected with an Enraf−Nonius CAD4 diffractometer in the 2θ/ω scan mode with graphite-monochromated Cu-K_α radiation (1.54178 Å) at a temperature of 173 K. The structures were solved by direct methods using the SIR-97[31] program, and refined by full-matrix-block least squares on F^2 using all data and the SHELXL-97[32] program. Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications no. CCDC-142899 (α-**23**), -144783 (α-**28**) and -142901 (β-**36**). Copies of the data can be obtained free of charge on applicaton to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

3,5-Di-*O*-benzyl-2-deoxy-D-ribose Dibenzyl Dithioacetal (11): Compound **11** was prepared from 2-deoxy-D-ribose according to standard procedures. Compound **11** is described in the literature[17,19,20] but with poor spectroscopic data, which are therefore addressed in the Supporting Information (see footnote on first page). − $[\alpha]_D^{20}$ = −45.1 (c = 1.0, $CHCl_3$), ref.[17] $[\alpha]_D^{20}$ = −102 (c = 2.0, EtOH). − $C_{33}H_{36}O_3S_2$ (544.8) calcd. C 72.76, H 6.66, S 11.77; found C 72.05, H 6.80, S 11.65.

Benzyl 3,5-Di-*O*-benzyl-2-deoxy-1,4-dithio-L-*threo*-pentofuranoside (13):[19] A solution of mesyl chloride (5.20 mL, 7.64 g, 66.73 mmol) in dry pyridine (150 mL) was added dropwise into an ice-cold solution of **11** (19.41 g, 35.63 mmol) in dry pyridine (150 mL). The mixture was allowed to warm to room temp. and stirred for 24 h. When the reaction was complete, the pyridine was evaporated and the residue dissolved in CH_2Cl_2 and extracted with 0.1 N HCl, water and saturated $NaHCO_3$ solution to give the crude mesylate **12** (22.0 g). This was dissolved in pyridine (300 mL), tetrabutylammonium iodide (13.22 g, 35.79 mmol) and barium carbonate (7.12 g, 36.07 mmol) were added and the mixture was refluxed for 2.5 h. Solid compounds were filtered off and the pyridine was removed under reduced pressure. The residue was dissolved in CH_2Cl_2 and extracted as described above. The crude product was purified by column chromatography [silica gel, petroleum ether/EtOAc, 4:1, $R_f(\alpha,\beta)$ = 0.25] to give **13** (13.26 g, 85%) as an α/β = 2:1 mixture of anomers; pale yellow syrup. − $C_{26}H_{28}O_2S_2$ (436.6): calcd. C 71.52, H 6.46, S 14.69; found C 71.89, H 7.57,[33] S 14.91.

1-*O*-Acetyl-3,5-di-*O*-benzyl-2-deoxy-4-thio-α,L-*threo*-pentofuranose (15): Thiosugar **13** (1.28 g, 2.93 mmol) and mercuric acetate (1.83 g, 5.74 mmol) were dissolved in glacial acetic acid (60 mL) and stirred at room temperature for 2.5 h. After the reaction was complete (TLC, petroleum ether/EtOAc, 4:1), the solvent was removed, and the residue was diluted with CH_2Cl_2 and filtered through a Celite pad. The crude product was purified by column chromatography [petroleum ether/EtOAc, 4:1, $R_f(\alpha,\beta)$ = 0.22] to yield **15** (673 mg, 64%) as pure α anomer; colourless oil. − $[\alpha]_D^{20}$ = −118.7 (c = 0.9, $CHCl_3$). − $C_{21}H_{24}O_3S$ (356.5): calcd. C 70.76, H 6.79, S 9.00; found C 70.21, H 6.55, S 9.13.

1-(3,5-Di-*O*-benzyl-2-deoxy-4-thio-L-*threo*-pentofuranosyl)uracil (16): NIS (431 mg, 1.92 mmol) was added to a solution of **13** (618 mg, 1.42 mmol), 2,4-bis-*O*-trimethylsilyluracil[24] (474 mg, 1.85 mmol) and 4-Å molecular sieves (20 mg) in dry MeCN (15 mL), and the reaction mixture was stirred for 2 h at room temperature. Then aq. sodium thiosulfate solution was added and stirring was continued 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 concentrated. The resulting crude product was purified by silica gel chromatography [petroleum ether/

Table 1. Crystal data and structure refinement for α-**23**, α-**28** and β-**36**

	α-**23**	α-**28**	β-**36**
Crystal system	tetragonal	triclinic	monoclinic
Space group	$P4_32_12$	P_1	$P2_1$
a [Å]	7.2450(10)	5.1453(17)	4.9140(10)
b [Å]	7.2450(10)	6.2338(10)	8.7000(10)
c [Å]	40.1820(10)	10.379(3)	15.1830(2)
α/β/γ [°]		α = 71.345(18) β = 84.18(3) γ = 76.193(18)	β = 95.300(10)
Crystal size [mm]	0.38 × 0.31 × 0.18	0.70 × 0.25 × 0.20	0.31 × 0.12 × 0.09
$\rho_{calcd.}$ [g cm^{-3}]	1.538	2.007	1.466
F_{000}	1024	180	300
μ [mm^{-1}]	0.308	22.224	0.264
$h/k/l$ limits	0,9/0,6/−50,51	0,6/−7,7/−13,13	0,6/−11,10/−19,19
θ limits [°]	3.98/27.49	4.50/76.31	2.69/27.40
Number of reflections	11060	1447	5353
Independent reflections	1987	1436	2745
Number of reflections with $I \leq 2\sigma(I)$	1660	1436	2494
Weighting scheme [$\Sigma w(F_o^2 - F_c^2)^2$]	$w = 1/[\sigma^2(F_o^2) + (0.0522P)^2 + 0.0343P]$ with $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0832P)^2 + 1.1778P]$ with $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0410P)^2 + 0.1499P]$ with $P = (F_o^2 + 2F_c^2)/3$
Number of parameters	194	164	233
R	0.0366	0.0412	0.0345
R_w	0.0786	0.1090	0.0808
GoF	0.993	1.104	1.060
Largest difference peak and hole [e Å^{-3}]	0.165 and −0.223	2.538 and −2.313	0.147 and −0.153
Refinement of H atoms	difmap/geom	geom	difmap/geom

EtOAc 1:3, $R_f(\beta) = 0.60$, $R_f(\alpha) = 0.43$] to give α-**16** (228 mg, 29%) and β-**16** (159 mg, 59%) as white amorphous solids. − **α-16:** $[\alpha]_D^{20} = -8.9$ ($c = 1.0$, $CHCl_3$). − FAB MS (mNBA); *m/z*: 425 $[M + H]^+$. − FAB HRMS (mNBA): calcd. 425.1535 $[M + H]^+$; found 425.1533. − $C_{23}H_{24}N_2O_4S$ (424.5): calcd. C 65.08, H 5.70, N 6.60, S 7.55; found C 65.18, H 5.97, N 6.36, S 7.64. − **β-16:** $[\alpha]_D^{25} = 10.3$ ($c = 1.0$, $CHCl_3$). − FAB MS (mNBA); *m/z*: 425 $[M + H]^+$. − FAB HRMS (mNBA): calcd. 425.1535 $[M + H]^+$; found 425.1572.

1-(3,5-Di-*O*-benzyl-2-deoxy-4-thio-L-*threo*-pentofuranosyl)thymine (17): Compound **17** was prepared as described for **16**; from **13** (1.5 g, 3.44 mmol), NIS (982 mg, 4.36 mmol), 2,4-bis-*O*-trimethylsilylthymine[24] (1.13 g, 4.18 mmol), 4-Å molecular sieves (80 mg) and MeCN (30 mL). After chromatographic workup [silica gel, petroleum ether/EtOAc, 1:3, $R_f(\alpha,\beta) = 0.39$], **17** (823 mg, 55%) was obtained as an amorphous white solid. The anomers were inseparable (α/β = 1:1). − FAB MS (*m*NBA); *m/z*: 439 $[M + H]^+$. − FAB HRMS (*m*NBA): calcd. 439.1692 $[M + H]^+$; found 439.1679.

1-(3,5-Di-*O*-benzyl-2-deoxy-4-thio-L-*threo*-pentofuranosyl)-5-fluorouracil (18): Compound **18** was prepared as described for **16**; from **13** (240 mg, 0.55 mmol), NIS (182 mg, 0.81 mmol), 5-fluoro-2,4-bis-*O*-trimethylsilyluracil[27] (320 mg, 1.17 mmol), 4-Å molecular sieves (40 mg) and MeCN (12 mL). After chromatographic workup [silica gel, petroleum ether/EtOAc 1:3, $R_f(\alpha,\beta) = 0.58$], **18** (166 mg, 68%) was obtained as an amorphous white solid. The anomers were inseparable (α/β = 1:2). − FAB MS (*m*NBA); *m/z*: 443 $[M + H]^+$. − FAB HRMS (*m*NBA): calcd. 443.1441 $[M + H]^+$; found 443.1455. − $C_{23}H_{23}FN_2O_4S$ (442.5): calcd. C 62.43, H 5.24, F 4.29, N 6.33; found C 61.90, H 5.18, F 4.44, N 6.63.

5-Chloro-1-(3,5-di-*O*-benzyl-2-deoxy-4-thio-L-*threo*-pentofuranosyl)-uracil (19): Compound **19** was prepared as described for **16**; from **13** (400 mg, 0.92 mmol), NIS (307 mg, 1.36 mmol), 5-chloro-2,4-bis-*O*-trimethylsilyluracil[27] (830 mg, 2.85 mmol), 4-Å molecular sieves (50 mg) and MeCN (14 mL). After chromatographic workup [silica gel, petroleum ether/EtOAc 1:3, $R_f(\alpha,\beta) = 0.51$], **19** (283 mg, 67%) was obtained as an amorphous white solid. The anomers were inseparable (α/β = 1:3). − FAB MS (*m*NBA); *m/z*: 459 $[M + H]^+$. − FAB HRMS (*m*NBA): calcd. 459.1145 $[M + H]^+$; found 459.1189. − $C_{23}H_{23}ClN_2O_4S$ (459.0): calcd. C 60.19, H 5.05, N 6.10; found C 60.67, H 5.21, N 6.26.

5-Bromo-1-(3,5-di-*O*-benzyl-2-deoxy-4-thio-L-*threo*-pentofuranosyl)-uracil (20): Compound **20** was prepared as described for **16**; from **13** (507 mg, 1.16 mmol), NIS (384 mg, 1.71 mmol), 5-bromo-2,4-bis-*O*-trimethylsilyluracil[27] (780 mg, 2.32 mmol), 4-Å molecular sieves (50 mg) and MeCN (12 mL). After chromatographic workup [silica gel, petroleum ether/EtOAc 1:3, $R_f(\alpha,\beta) = 0.61$], **20** (352 mg, 60%) was obtained as an amorphous white solid. The anomers were inseparable (α/β = 1:2). − FAB MS (*m*NBA); *m/z*: 505 [M + H, for $^{81}Br]^+$, 503 [M + H, for $^{79}Br]^+$. − $C_{23}H_{23}BrN_2O_4S$ (503.4): calcd. C 54.88, H 4.61, N 5.56, S 6.37; found C 53.83[33], H 4.47, N 5.63, S 6.26.

1-(3,5-Di-*O*-benzyl-2-deoxy-4-thio-L-*threo*-pentofuranosyl)-5-iodouracil (21): Compound **21** was prepared as described for **16**; from **13** (500 mg, 1.15 mmol), NIS (667 mg, 2.96 mmol), 5-iodo-2,4-bis-*O*-trimethylsilyluracil[27] (880 mg, 2.30 mmol), 4-Å molecular sieves (70 mg) and MeCN (15 mL). After chromatographic workup (silica gel, petroleum ether/EtOAc 1:2, $R_{f,\alpha} = 0.35$, $R_{f,\beta} = 0.22$), α-**21** (156 mg, 25%) and β-**21** (296 mg, 47%) were obtained as white solids. − **α-21:** M.p. 82 °C. $-[\alpha]_D^{20} = -6.1$ ($c = 1.0$, $CHCl_3$). − FAB MS (*m*NBA); *m/z*: 551 $[M + H]^+$. − FAB HRMS (*m*NBA): calcd. 551.0502 $[M + H]^+$; found 551.0309. − **β-21:** M.p. 68 °C. − $[\alpha]_D^{25} = +27.4$ ($c = 1.0$, $CHCl_3$). − FAB MS (*m*NBA); *m/z*: 551 $[M + H]^+$. − FAB HRMS (*m*NBA): calcd. 551.0502 $[M + H]^+$; found 551.0423.

1-(3,5-Di-*O*-benzyl-2-deoxy-4-thio-β-L-*threo*-pentofuranosyl)-5-nitrouracil (22): Compound **22** was prepared as described for **16**; from **13** (600 mg, 1.37 mmol), NIS (795 mg, 3.53 mmol), 5-nitro-2,4-bis-*O*-trimethylsilyluracil (1.62 g, 5.37 mmol), 4-Å molecular sieves (60 mg) and MeCN (15 mL). The crude product was recrystallised from EtOAc to give β-**22** (170 mg, 26%) as a white solid. − M.p. 169−172 °C (decomp.). − $[\alpha]_D^{25} = +39.0$ ($c = 1.0$, $CHCl_3$). − FAB MS (*m*NBA); *m/z*: 470 $[M + H]^+$. − FAB MS (*m*NBA); *m/z*: 470 $[M + H]^+$. − FAB HRMS (*m*NBA): calcd. 470.1386 $[M + H]^+$; found 470.1361. − $C_{23}H_{23}N_3O_6S$ (469.5): calcd. C 58.84, H 4.94, N 8.95, S 6.83; found C 58.68, H 5.09, N 8.69, S 6.66.

1-(2-Deoxy-4-thio-L-*threo*-pentofuranosyl)uracil (23):[34] Boron tribromide (1.0 mL, 2.64 g, 10.54 mmol) was added to dry CH_2Cl_2 (10.0 mL); the mixture was cooled to −90 °C. A solution of **16** (948 mg, 2.23 mmol, α/β = 3:2) in CH_2Cl_2 (8.0 mL) was added dropwise with vigorous stirring. The temperature was kept below −80 °C. After complete addition, stirring was continued at −90 °C for 1 h. Then the excess of boron tribromide was quenched at −90 °C by dropwise addition of a 1:1 mixture of CH_2Cl_2/MeOH (16 mL). After the solution had warmed to room temperature, silver carbonate (10.21 g, 37.03 mmol) was added to neutralise the hydrobromic acid. After 0.5 h, the inorganic salts were filtered off, the solution was concentrated to dryness and the remaining crude product was purified by silica gel chromatography [$CHCl_3$/MeOH 4:1, R_f(A1) = 0.35, R_f(A2) = 0.32], followed by reversed-phase HPLC (MeCN/H_2O, 5:95) to yield **α-23** (51 mg, 16%) and **β-23** (41 mg, 19%) as white solids. A portion of **α-23** was used to grow single crystals (colourless sheets), suitable for X-ray structural analysis, from H_2O. − **α-23:** M.p. 180 °C. − $[\alpha]_D^{20} = -91.0$ ($c = 1.0$, MeOH). − IR (KBr): $\tilde{\nu}$ = 3422, 3087, 3047, 2934, 2889, 2833, 1690, 1469, 1426, 1382, 1304, 1241, 1169, 1113, 1068, 1027, 981, 912, 823, 760, 707, 622, 557, 512, 417 cm^{-1}. − ^1H NMR (500 MHz, [D$_6$]DMSO): δ = 11.28 (ws, 1 H, NH), 7.49 (d, 1 H, H-6), 6.32 (dd, 1 H, H-1′), 5.68 (d, 1 H, H-5), 5.08 (d, 1 H, 3′-OH), 4.77 (dd, 1 H, 5′-OH), 4.39−4.42 (m, 1 H, H-3′), 3.93 (ddd, 1 H, H-4′), 3.74 (ddd, 1 H, H-5′$_b$), 3.46 (ddd, 1 H, H-5′$_a$), 2.27 (ddd, 1 H, H-2′$_b$), 2.12 (ddd, 1 H, H-2′$_a$). $J_{1',2'a} = 9.7$, $J_{1',2'b} = 6.6$, $J_{2'a,3'} = 4.4$, $J_{2'b,3'} = 2.2$, $J_{2'a,2'b} = 13.1$, $J_{3',4'} = 3.4$, $J_{3',OH} = 4.4$, $J_{4',5'a} = 7.7$, $J_{4',5'b} = 6.2$, $J_{5'a,5'b} = 10.8$, $J_{5'a,OH} = 5.9$, $J_{5'b,OH} = 4.8$, $J_{5,6} = 8.1$ Hz. − ^{13}C NMR (126 MHz, [D$_6$]DMSO): δ = 163.0 (4-CO), 150.9 (2-CO), 142.0 (C-6), 102.6 (C-5), 72.2 (C-3′), 61.2 (C-5′), 60.5 (C-1′), 57.5 (C-4′), 43.8 (C-2′). − FAB MS (*m*NBA); *m/z*: 245 $[M + H]^+$. − FAB HRMS (*m*NBA): calcd. 245.0596 $[M + H]^+$; found 245.0623. − **β-23:** M.p. 220 °C. − $[\alpha]_D^{20} = -2.2$ ($c = 1.0$, MeOH). − IR (KBr): $\tilde{\nu}$ = 3412, 3045, 2935, 2882, 2816, 1691, 1467, 1392, 1259, 1141, 1097, 1035, 910, 816, 752, 624, 556, 511, 420 cm^{-1}. − ^1H NMR (500 MHz, [D$_6$]DMSO): δ = 11.21 (ws, 1 H, NH), 8.32 (d, 1 H, H-6), 6.10 (dd, 1 H, H-1′), 5.62 (d, 1 H, H-5), 5.35 (d, 1 H, 3′-OH), 4.86 (dd, 1 H, 5′-OH), 4.32−4.37 (m, 1 H, H-3′), 3.85 (ddd, 1 H, H-5′$_b$), 3.62 (ddd, 1 H, H-5′$_a$), 3.54 (ddd, 1 H, H-4′), 2.38 (ddd, 1 H, H-2′$_b$), 2.13 (ddd, 1 H, H-2′$_a$). $J_{1',2'a} = 2.6$, $J_{1',2'b} = 8.2$, $J_{2'a,3'} = 2.7$, $J_{2'b,3'} = 4.1$, $J_{2'a,2'b} = 14.3$, $J_{3',4'} = 4.2$, $J_{3',OH} = 3.7$, $J_{4',5'a} = 7.4$, $J_{4',5'b} = 5.4$, $J_{5'a,5'b} = 10.8$, $J_{5'a,OH} = 5.8$, $J_{5'b,OH} = 5.0$, $J_{5,6} = 8.2$ Hz. − ^{13}C NMR (126 MHz, [D$_6$]DMSO): δ = 163.3 (4-CO), 151.1 (2-CO), 143.4 (C-6), 101.0 (C-5), 72.1 (C-3′), 62.2 (C-1′), 60.9 (C-5′), 58.1 (C-4′), 44.3 (C-2′). − FAB MS (*m*NBA); *m/z*: 245 $[M + H]^+$. − FAB HRMS (*m*NBA): calcd. 245.0585 $[M + H]^+$; found 245.0623.

1-(2-Deoxy-4-thio-L-*threo*-pentofuranosyl)thymine (24): Compound **24**, which has also been obtained as a mixture of anomers by Ti-

wari et al.,[21] was prepared as described for **23**; from **17** (522 mg, 1.19 mmol, α/β = 1:1) in CH_2Cl_2 (4.0 mL), boron tribromide (0.53 mL, 1.40 g, 5.59 mmol) in CH_2Cl_2 (5.3 mL) and silver carbonate (5.39 g, 19.55 mmol). After chromatographic workup [silica gel, $CHCl_3$/MeOH, 4:1, R_f(A1) = 0.40, R_f(A2) = 0.33] and reversed-phase HPLC (MeCN/H_2O, 13:87), the separated anomers **α-24** (41 mg, 27%) and **β-24** (19 mg, 12%) were obtained as white solids. − **α-24:** M.p. 180 °C. − $[\alpha]_D^{20}$ = −79.2 (*c* = 1.0, MeOH). − IR (KBr): $\tilde{\nu}$ = 3416, 3198, 3052, 2930, 2824, 1683, 1470, 1388, 1306, 1245, 1222, 1170, 1125, 1071, 1045, 1020, 985, 958, 904, 797, 765, 692, 635, 585, 534, 481, 416 cm^{-1}. − ^1H NMR (500 MHz, [D$_6$]DMSO): δ = 11.26 (ws, 1 H, NH), 7.79 (q, 1 H, H-6), 6.35 (dd, 1 H, H-1′), 5.06 (d, 1 H, 3′-OH), 4.77 (dd, 1 H, 5′-OH), 4.39−4.42 (m, 1 H, H-3′), 3.95 (ddd, 1 H, H-4′), 3.74 (ddd, 1 H, H-5′$_b$), 3.64 (ddd, 1 H, H-5′$_a$), 2.24 (ddd, 1 H, H-2′$_b$), 2.15 (ddd, 1 H, H-2′$_a$), 1.80 (d, 3 H, CH_3). $J_{1',2'a}$ = 9.8, $J_{1',2'b}$ = 6.7, $J_{2'a,3'}$ = 3.4, $J_{2'b,3'}$ = 2.0, $J_{2'a,2'b}$ = 13.0, $J_{3',4'}$ = 3.3, $J_{3',OH}$ = 4.4, $J_{4',5'a}$ = 7.6, $J_{4',5'b}$ = 6.2, $J_{5'a,5'b}$ = 10.8, $J_{5'a,OH}$ = 5.8, $J_{5'b,OH}$ = 4.9, $J_{6,Me}$ = 1.1 Hz. − ^{13}C NMR (126 MHz, [D$_6$]DMSO): δ = 163.7 (4-CO), 150.9 (2-CO), 137.3 (C-6), 110.4 (C-5), 72.2 (C-3′), 61.2 (C-5′), 60.2 (C-1′), 57.5 (C-4′), 43.7 (C-2′), 12.3 (CH_3). FAB MS (*m*NBA); *m*/*z*: 259 [M + H]$^+$. − FAB HRMS (*m*NBA); calcd. 259.0723 [M + H]$^+$; found 259.0840. − **β-24:** M.p. 220 °C. − $[\alpha]_D^{25}$ = +28.3 (*c* = 1.0, MeOH). − IR (KBr): $\tilde{\nu}$ = 3422, 3065, 2931, 2823, 1687, 1474, 1397, 1278, 1224, 1109, 1081, 1039, 970, 900, 766, 632, 563, 486, 417 cm^{-1}. − ^1H NMR (500 MHz, [D$_6$]DMSO): δ = 11.22 (ws, 1 H, NH), 8.19 (q, 1 H, H-6), 6.12 (dd, 1 H, H-1′), 5.37 (d, 1 H, 3′-OH), 4.87 (dd, 1 H, 5′-OH), 4.34−4.37 (m, 1 H, H-3′), 3.85 (ddd, 1 H, H-5′$_b$), 3.65 (ddd, 1 H, H-5′$_a$), 3.52 (ddd, 1 H, H-4′), 2.38 (ddd, 1 H, H-2′$_b$), 2.13 (ddd, 1 H, H-2′$_a$), 1.76 (d, 3 H, CH_3). $J_{1',2'a}$ = 3.4, $J_{1',2'b}$ = 8.4, $J_{2'a,3'}$ = 3.5, $J_{2'b,3'}$ = 4.2, $J_{2'a,2'b}$ = 14.1, $J_{3',4'}$ = 4.6, $J_{3',OH}$ = 3.7, $J_{4',5'a}$ = 7.2, $J_{4',5'b}$ = 5.7, $J_{5'a,5'b}$ = 10.9, $J_{5'a,OH}$ = 5.8, $J_{5'b,OH}$ = 4.8, $J_{6,Me}$ = 1.2 Hz. − ^{13}C NMR (126 MHz, [D$_6$]DMSO): δ = 163.8 (4-CO), 151.0 (2-CO), 138.9 (C-6), 108.5 (C-5), 72.1 (C-3′), 61.0 (C-5′), 60.2 (C-1′), 57.6 (C-4′), 43.8 (C-2′), 12.7 (CH_3). − FAB HRMS (*m*NBA): calcd. 259.0723 [M + H]$^+$; found 245.0757.

1-(2-Deoxy-4-thio-L-*threo*-pentofuranosyl)-5-fluorouracil (25): Compound **25** was prepared as described for **23**; from **18** (165 mg, 0.39 mmol, α/β = 1:2) in CH_2Cl_2 (1.3 mL), boron tribromide (0.17 mL, 449 mg, 1.79 mmol) in CH_2Cl_2 (1.7 mL) and silver carbonate (1.86 g, 6.75 mmol). After chromatographic workup [silica gel, $CHCl_3$/MeOH, 4:1, R_f(A1) = 0.33, R_f(A2) = 0.25] and reversed-phase HPLC (MeCN/H_2O, 9:91), the separated anomers **α-25** (12 mg, 37%) and **β-25** (7 mg, 11%) were obtained as white solids. − **α-25:** M.p. 213 °C. − $[\alpha]_D^{20}$ = −63.8 (*c* = 1.0, MeOH). − IR (KBr): $\tilde{\nu}$ = 3439, 3213, 3066, 2928, 2807, 1707, 1661, 1479, 1385, 1243, 1122, 1070, 1029, 925, 865, 771, 709, 583, 529 cm^{-1}. − ^1H NMR (500 MHz, [D$_6$]DMSO): δ = 11.32 (ws, 1 H, NH), 8.32 (d, 1 H, H-6), 6.34 (ddd, 1 H, H-1′), 5.09 (d, 1 H, 3′-OH), 4.80 (ws, 1 H, 5′-OH), 4.39−4.42 (m, 1 H, H-3′), 3.99 (ddd, 1 H, H-4′), 3.75 (dd, 1 H, H-5′$_b$), 3.47 (dd, 1 H, H-5′$_a$), 2.28 (ddd, 1 H, H-2′$_b$), 2.16 (ddd, 1 H, H-2′$_a$). $J_{1',2'a}$ = 9.7, $J_{1',2'b}$ = 6.7, $J_{1',F}$ = 1.9, $J_{2'a,3'}$ = 3.3, $J_{2'b,3'}$ = 2.0, $J_{2'a,2'b}$ = 13.0, $J_{3',4'}$ = 3.1, $J_{3',OH}$ = 4.1, $J_{4',5'a}$ = 7.6, $J_{4',5'b}$ = 6.2, $J_{5'a,5'b}$ = 10.8, $J_{6,F}$ = 7.3 Hz. − ^{13}C NMR (126 MHz, [D$_6$]DMSO): δ = 157.5 (d, 4-CO), 149.5 (2-CO), 141.2 (d, C-5), 126.3 (d, C-6), 72.1 (C-3′), 61.2 (C-1′, C-5′), 57.5 (C-4′), 43.7 (C-2′). $J_{4,F}$ = 26.2, $J_{5,F}$ = 231.2, $J_{6,F}$ = 34.4 Hz. − ^{19}F NMR (471 MHz, [D$_6$]DMSO): δ = −166.03 (dd, 1 F, F-5). $J_{F,6}$ = 7.3, $J_{F,NH}$ = 1.5 Hz. − FAB MS (*m*NBA); *m*/*z*: 263 [M + H]$^+$. − MS (70 eV); *m*/*z*: 262 (8) [M$^{+\bullet}$], 133 (54) [$C_5H_9O_2S^{+\bullet}$], 130 (39) [$C_4H_3FN_2O_2^{+\bullet}$], 115 (27) [$C_5H_7OS^{+\bullet}$], 85 (100), 57 (30). − HRMS: calcd. 262.0424 [M$^{+\bullet}$], 133.0323 [$C_5H_9O_2S^{+\bullet}$], 130.0179 [$C_4H_3FN_2O_2^{+\bullet}$], 115.0218 [$C_5H_7OS^{+\bullet}$]; found 262.0434, 133.0315, 130.0170, 115.0185. − **β-25:** M.p. 156−159 °C. − $[\alpha]_D^{25}$ = +2.2 (*c* = 0.7, MeOH). − IR (KBr): $\tilde{\nu}$ = 3427, 3052, 2933, 2822, 1693, 1476, 1397, 1245, 1104, 1036, 971, 906, 829, 749, 682, 534 cm^{-1}. − ^1H NMR (500 MHz, [D$_6$]DMSO): δ = 11.75 (ws, 1 H, NH), 8.60 (d, 1 H, H-6), 6.10 (ddd, 1 H, H-1′), 5.47 (d, 1 H, 3′-OH), 4.91 (ws, 1 H, 5′-OH), 4.34−4.37 (m, 1 H, H-3′), 3.84 (dd, 1 H, H-5′$_b$), 3.64 (dd, 1 H, H-5′$_a$), 3.54 (ddd, 1 H, H-4′), 2.39 (ddd, 1 H, H-2′$_b$), 2.15 (ddd, 1 H, H-2′$_a$). $J_{1',2'a}$ = 2.3, $J_{1',2'b}$ = 8.3, $J_{1',F}$ = 2.0, $J_{2'a,3'}$ = 2.5, $J_{2'b,3'}$ = 4.0, $J_{2'a,2'b}$ = 14.4, $J_{3',4'}$ = 4.0, $J_{3',OH}$ = 3.0, $J_{4',5'a}$ = 7.3, $J_{4',5'b}$ = 5.8, $J_{5'a,5'b}$ = 10.8, $J_{6,F}$ = 8.0 Hz. − ^{13}C NMR (126 MHz, [D$_6$]DMSO): δ = 157.1 (d, 4-CO), 149.6 (2-CO), 139.2 (d, C-5), 127.7 (d, C-6), 72.0 (C-3′), 61.8 (C-1′), 60.8 (C-5′), 58.3 (C-4′), 44.3 (C-2′). $J_{4,F}$ = 26.2, $J_{5,F}$ = 228.3, $J_{6,F}$ = 35.7 Hz. − ^{19}F NMR (471 MHz, [D$_6$]DMSO): δ = −168.10 (d, 1 F, F-5). $J_{F,6}$ = 8.0 Hz. − FAB MS (*m*NBA); *m*/*z*: 263 [M + H]$^+$. − MS (70 eV); *m*/*z*: 262 (6) [M$^{+\bullet}$], 133 (56) [$C_5H_9O_2S^{+\bullet}$], 130 (36) [$C_4H_3FN_2O_2^{+\bullet}$], 115 (29) [$C_5H_7OS^{+\bullet}$], 85 (100), 57 (21). − HRMS: calcd. 262.0424 [M$^{+\bullet}$], 133.0323 [$C_5H_9O_2S^{+\bullet}$], 130.0179 [$C_4H_3FN_2O_2^{+\bullet}$], 115.0218 [$C_5H_7OS^{+\bullet}$]; found 262.0418, 133.0366, 130.0201, 115.0188.

5-Chloro-1-(2-deoxy-4-thio-L-*threo*-pentofuranosyl)uracil (26): Compound **26** was prepared as described for **23**; from **19** (283 mg, 0.62 mmol, α/β = 1:3) in CH_2Cl_2 (3.0 mL), boron tribromide (0.28 mL, 739 mg, 2.95 mmol) in CH_2Cl_2 (2.8 mL) and silver carbonate (2.93 g, 10.63 mmol). After chromatographic workup [silica gel, $CHCl_3$/MeOH, 4:1, R_f(A1) = 0.38, R_f(A2) = 0.30] and reversed-phase HPLC (MeCN/H_2O, 10:90), the separated anomers **α-26** (21 mg, 49%) and **β-26** (11 mg, 9%) were obtained as white solids. − **α-26:** M.p. 200 °C. − $[\alpha]_D^{20}$ = −61.9 (*c* = 1.0, MeOH). − IR (KBr): $\tilde{\nu}$ = 3444, 3168, 3019, 2926, 2839, 1708, 1665, 1468, 1439, 1376, 1345, 1302, 1246, 1197, 1151, 1054, 1024, 980, 899, 844, 746, 649, 628, 579, 521, 457, 417 cm^{-1}. − ^1H NMR (500 MHz, [D$_6$]DMSO): δ = 11.80 (ws, 1 H, NH), 8.33 (s, 1 H, H-6), 6.31 (dd, 1 H, H-1′), 5.07 (d, 1 H, 3′-OH), 4.78 (dd, 1 H, 5′-OH), 4.36−4.40 (m, 1 H, H-3′), 4.01 (ddd, 1 H, H-4′), 3.74 (ddd, 1 H, H-5′$_b$), 3.46 (ddd, 1 H, H-5′$_a$), 2.27 (ddd, 1 H, H-2′$_b$), 2.20 (ddd, 1 H, H-2′$_a$). $J_{1',2'a}$ = 9.7, $J_{1',2'b}$ = 6.7, $J_{2'a,3'}$ = 3.3, $J_{2'b,3'}$ = 2.0, $J_{2'a,2'b}$ = 13.0, $J_{3',4'}$ = 3.3, $J_{3',OH}$ = 4.3, $J_{4',5'a}$ = 7.8, $J_{4',5'b}$ = 6.1, $J_{5'a,5'b}$ = 10.8, $J_{5'a,OH}$ = 5.8, $J_{5'b,OH}$ = 4.8 Hz. − ^{13}C NMR (126 MHz, [D$_6$]DMSO): δ = 159.0 (4-CO), 150.0 (2-CO), 139.3 (C-6), 107.8 (C-5), 72.2 (C-3′), 61.3 (C-1′), 61.2 (C-5′), 57.6 (C-4′), 43.9 (C-2′). − FAB MS (*m*NBA); *m*/*z*: 279 [M + H]$^+$ − FAB HRMS (*m*NBA): calcd. 279.0206 [M + H]$^+$; found 279.0209. − **β-26:** M.p. 190 °C. − $[\alpha]_D^{20}$ = +12.8 (*c* = 1.0, MeOH). − IR (KBr): $\tilde{\nu}$ = 3434, 3057, 2932, 2826, 1693, 1459, 1386, 1257, 1131, 1078, 1037, 971, 904, 797, 754, 626, 525, 443 cm^{-1}. − ^1H NMR (500 MHz, [D$_6$]DMSO): δ = 11.76 (ws, 1 H, NH), 8.67 (s, 1 H, H-6), 6.08 (dd, 1 H, H-1′), 5.43 (d, 1 H, 3′-OH), 4.93 (dd, 1 H, 5′-OH), 4.36 (dddd, 1 H, H-3′), 3.85 (ddd, 1 H, H-5′$_b$), 3.64 (ddd, 1 H, H-5′$_a$), 3.57 (ddd, 1 H, H-4′), 2.38 (ddd, 1 H, H-2′$_b$), 2.18 (ddd, 1 H, H-2′$_a$). $J_{1',2'a}$ = 2.0, $J_{1',2'b}$ = 8.2, $J_{2'a,3'}$ = 2.3, $J_{2'b,3'}$ = 3.8, $J_{2'a,2'b}$ = 14.4, $J_{3',4'}$ = 3.8, $J_{3',OH}$ = 3.4, $J_{4',5'a}$ = 7.4, $J_{4',5'b}$ = 5.6, $J_{5'a,5'b}$ = 10.7, $J_{5'a,OH}$ = 5.7, $J_{5'b,OH}$ = 4.9 Hz. − ^{13}C NMR (126 MHz, [D$_6$]DMSO): δ = 159.2 (4-CO), 150.2 (2-CO), 140.9 (C-6), 105.9 (C-5), 72.1 (C-3′), 62.3 (C-1′), 60.8 (C-5′), 58.6 (C-4′), 44.5 (C-2′). − FAB MS (*m*NBA); *m*/*z*: 279 [M + H]$^+$ − FAB HRMS (*m*NBA): calcd. 279.0206 [M + H]$^+$; found 279.02.09.

5-Bromo-1-(2-deoxy-4-thio-L-*threo*-pentofuranosyl)uracil (27): Compound **27** was prepared as described for **23**; from **20** (570 mg, 1.13 mmol, α/β = 1:2) in CH_2Cl_2 (6.0 mL), boron tribromide (0.51 mL, 1.35 g, 5.35 mmol) in CH_2Cl_2 (5.1 mL) and silver carbonate (5.19 g, 18.82 mmol). After chromatographic workup [silica gel,

$CHCl_3$/MeOH, 4:1, R_f(A1) = 0.37, R_f(A2) = 0.30] and reversed-phase HPLC (MeCN/H_2O, 11:89), the separated anomers **α-27** (20 mg, 16%) and **β-27** (19 mg, 8%) were obtained as white solids. − **α-27:** M.p. 215 °C. − $[\alpha]_D^{20} = -54.7$ (c = 1.0, MeOH). − IR (KBr): $\tilde{\nu}$ = 3437, 3179, 3050, 2931, 2825, 1694, 1448, 1240, 1038, 903, 751, 619, 502, 426 cm^{-1}. − ^1H NMR (500 MHz, [D$_6$]DMSO): δ = 11.76 (ws, 1 H, NH), 8.38 (s, 1 H, H-6), 6.31 (dd, 1 H, H-1′), 5.06 (d, 1 H, 3′-OH), 4.78 (dd, 1 H, 5′-OH), 4.36−4.39 (m, 1 H, H-3′), 4.02 (ddd, 1 H, H-4′), 3.74 (ddd, 1 H, H-5′$_b$), 3.46 (ddd, 1 H, H-5′$_a$), 2.27 (ddd, 1 H, H-2′$_b$), 2.21 (ddd, 1 H, H-2′$_a$). $J_{1',2'a}$ = 9.7, $J_{1',2'b}$ = 6.8, $J_{2'a,3'}$ = 2.2, $J_{2'b,3'}$ = 2.0, $J_{2'a,2'b}$ = 13.0, $J_{3',4'}$ = 3.3, $J_{3',OH}$ = 4.3, $J_{4',5'a}$ = 7.8, $J_{4',5'b}$ = 6.1, $J_{5'a,5'b}$ = 10.8, $J_{5'a,OH}$ = 5.9, $J_{5'b,OH}$ = 4.8 Hz. − ^{13}C NMR (126 MHz, [D$_6$]DMSO): δ = 159.1 (4-CO), 150.2 (2-CO), 141.7 (C-6), 96.4 (C-5), 72.3 (C-3′), 61.3 (C-1′), 61.2 (C-5′), 57.6 (C-4′), 43.9 (C-2′). − MS (70 eV); m/z: 324 (2) [$M^{+\bullet}$, for ^{81}Br], 322 (2) [$M^{+\bullet}$, for ^{79}Br], 306 (8) [$M^{+\bullet} - H_2O$, for ^{81}Br], 304 (8) [$M^{+\bullet} - H_2O$, for ^{79}Br], 192 (7) [$C_4H_3{}^{81}BrN_2O_2^{+\bullet}$], 190 (7) [$C_4H_3{}^{79}BrN_2O_2^{+\bullet}$], 133 (35) [$C_5H_9O_2S^{+\bullet}$], 115 (30) [$C_5H_7OS^{+\bullet}$], 85 (100), 59 (9), 45 (10). − HRMS: calcd. 323.9601 [$M^{+\bullet}$, for ^{81}Br], 321.9603 [$M^{+\bullet}$, for ^{79}Br], 305.9496 [$M^{+\bullet} - H_2O$, for ^{81}Br], 303.9468 [$M^{+\bullet} - H_2O$, for ^{79}Br]; found 323.9628, 321.9602, 305.9524, 303.9491. − **β-27:** M.p. 201−203 °C. − $[\alpha]_D^{25} = +9.2$ (c = 1.0, MeOH). − IR (KBr): $\tilde{\nu}$ = 3428, 3053, 2934, 2826, 1692, 1453, 1267, 1122, 1078, 1035, 970, 833, 755, 618, 522, 435 cm^{-1}. − ^1H NMR (500 MHz, [D$_6$]DMSO): δ = 11.70 (ws, 1 H, NH), 8.75 (s, 1 H, H-6), 6.07 (dd, 1 H, H-1′), 5.42 (d, 1 H, 3′-OH), 5.42 (d, 1 H, 3′-OH), 4.93 (dd, 1 H, 5′-OH), 4.36 (dddd, 1 H, H-3′), 3.85 (ddd, 1 H, H-5′$_b$), 3.64 (ddd, 1 H, H-5′$_a$), 3.57 (ddd, 1 H, H-4′), 2.37 (ddd, 1 H, H-2′$_b$), 2.18 (ddd, 1 H, H-2′$_a$). $J_{1',2'a}$ = 2.0, $J_{1',2'b}$ = 8.0, $J_{2'a,3'}$ = 2.2, $J_{2'b,3'}$ = 3.8, $J_{2'a,2'b}$ = 14.5, $J_{3',4'}$ = 3.8, $J_{3',OH}$ = 3.4, $J_{4',5'a}$ = 7.5, $J_{4',5'b}$ = 5.7, $J_{5'a,5'b}$ = 10.6, $J_{5'a,OH}$ = 5.7, $J_{5'b,OH}$ = 4.8 Hz. − ^{13}C NMR (126 MHz, [D$_6$]DMSO): δ = 159.3 (4-CO), 150.4 (2-CO), 143.5 (C-6), 94.3 (C-5), 72.1 (C-3′), 62.4 (C-1′), 60.9 (C-5′), 58.7 (C-4′), 44.6 (C-2′). − FAB MS (mNBA); m/z: 325 [M + H, for ^{81}Br], 323 [M + H, for ^{79}Br]. − FAB HRMS (mNBA): calcd. 322.9701 [M + H, for ^{79}Br]; found 322.9766.

1-(2-Deoxy-4-thio-L-*threo*-pentofuranosyl)-5-iodouracil (28): Compound **28** was prepared as described for **23**; from **21** (400 mg, 0.73 mmol, α/β = 1:2) in CH_2Cl_2 (3.5 mL), boron tribromide (0.32 mL, 845 mg, 3.37 mmol) in CH_2Cl_2 (3.2 mL) and silver carbonate (3.40 g, 12.33 mmol). After chromatographic workup [silica gel, $CHCl_3$/MeOH 4:1, R_f(A1) = 0.39, R_f(A2) = 0.34] and reversed-phase HPLC (MeCN/H_2O, 12:88), the separated anomers **α-28** (21 mg, 23%) and **β-28** (14 mg, 8%) were obtained as white solids. A portion of **α-28** was used to grow single crystals (colourless needles), suitable for X-ray structural analysis, from H_2O. − **α-17:** M.p. 210 °C (decomp.). − $[\alpha]_D^{20} = -37.2$ (c = 1.0, MeOH). − IR (KBr): $\tilde{\nu}$ = 3427, 3047, 2928, 2816, 1690, 1443, 1240, 1086, 908, 612, 519 cm^{-1}. − ^1H NMR (500 MHz, [D$_6$]DMSO): δ = 11.67 (ws, 1 H, NH), 8.36 (s, 1 H, H-6), 6.32 (dd, 1 H, H-1′), 5.08 (d, 1 H, 3′-OH), 4.80 (dd, 1 H, 5′-OH), 4.38−4.41 (m, 1 H, H-3′), 4.04 (ddd, 1 H, H-4′), 3.76 (ddd, 1 H, H-5′$_b$), 3.48 (ddd, 1 H, H-5′$_a$), 2.27 (ddd, 1 H, H-2′$_b$), 2.23 (ddd, 1 H, H-2′$_a$). $J_{1',2'a}$ = 9.7, $J_{1',2'b}$ = 6.9, $J_{2'a,3'}$ = 3.3, $J_{2'b,3'}$ = 2.1, $J_{2'a,2'b}$ = 13.0, $J_{3',4'}$ = 3.2, $J_{3',OH}$ = 4.3, $J_{4',5'a}$ = 7.8, $J_{4',5'b}$ = 6.0, $J_{5'a,5'b}$ = 10.8, $J_{5'a,OH}$ = 5.9, $J_{5'b,OH}$ = 4.7 Hz. − ^{13}C NMR (126 MHz, [D$_6$]DMSO): δ = 160.5 (4-CO), 150.6 (2-CO), 146.2 (C-6), 72.3 (C-3′), 70.2 (C-5), 61.3 (C-5′), 61.0 (C-1′), 57.6 (C-4′), 43.9 (C-2′). − FAB MS (mNBA); m/z: 371 [M + H]$^+$. − FAB HRMS (mNBA): calcd. 370.9563 [M + H]$^+$; found 370.9476. − **β-28:** M.p. 195 °C (decomp.). − $[\alpha]_D^{25} = +30.4$ (c = 1.0, MeOH) − IR (KBr): $\tilde{\nu}$ = 3431, 3066, 2927, 2853, 1688, 1450, 1385, 1274, 1118, 1077, 1036, 938, 756, 611 cm^{-1}. − ^1H NMR (500 MHz, [D$_6$]DMSO): δ = 11.59 (ws, 1 H, NH), 8.78 (s, 1 H, H-6), 6.05 (dd, 1 H, H-1′), 5.40 (d, 1 H, 3′-OH), 4.93 (dd, 1 H, 5′-OH), 4.36 (dddd, 1 H, H-3′), 3.85 (ddd, 1 H, H-5′$_b$), 3.64 (ddd, 1 H, H-5′$_a$), 3.57 (ddd, 1 H, H-4′), 2.36 (ddd, 1 H, H-2′$_b$), 2.16 (ddd, 1 H, H-2′$_a$). $J_{1',2'a}$ = 2.0, $J_{1',2'b}$ = 8.1, $J_{2'a,3'}$ = 2.1, $J_{2'b,3'}$ = 3.9, $J_{2'a,2'b}$ = 14.4, $J_{3',4'}$ = 3.9, $J_{3',OH}$ = 3.5, $J_{4',5'a}$ = 7.5, $J_{4',5'b}$ = 5.5, $J_{5'a,5'b}$ = 10.6, $J_{5'a,OH}$ = 5.7, $J_{5'b,OH}$ = 4.9 Hz. − ^{13}C NMR (126 MHz, [D$_6$]DMSO): δ = 160.6 (4-CO), 150.8 (2-CO), 148.4 (C-6), 72.1 (C-3′), 67.8 (C-5), 62.2 (C-1′), 60.90 (C-5′), 58.6 (C-4′), 44.7 (C-2′). − FAB MS (mNBA); m/z: 371 [M + H]$^+$. − FAB HRMS (mNBA): calcd. 370.9563 [M + H]$^+$; found 370.9540.

1-(2-Deoxy-4-thio-β-L-*threo*-pentofuranosyl)-5-nitrouracil (29): Compound **29** was prepared as described for **23**; from **22** (170 mg, 0.36 mmol) in CH_2Cl_2 (8.0 mL), boron tribromide (0.17 mL, 449 mg, 1. 97 mmol) in CH_2Cl_2 (1.7 mL) and silver carbonate (1.73 g, 6.27 mmol). After chromatographic workup (silica gel, $CHCl_3$/MeOH, 4:1, R_f = 0.34) and recrystallisation from H_2O, **29** (9 mg, 9%) was obtained as a white solid. − M.p. 186−188 °C. − $[\alpha]_D^{25} = +11.4$ (c = 0.9, MeOH). − IR (KBr): $\tilde{\nu}$ = 3453, 3171, 3076, 2959, 2826, 1708, 1612, 1509, 1456, 1378, 1343, 1303, 1255, 1101, 1018, 989, 906, 818, 757, 698, 624, 604, 512, 486 cm^{-1}. − ^1H NMR (500 MHz, [D$_6$]DMSO): δ = 12.00 (ws, 1 H, NH), 9.84 (s, 1 H, H-6), 6.04 (dd, 1 H, H-1′), 5.29 (d, 1 H, 3′-OH), 4.98 (dd, 1 H, 5′-OH), 4.40 (dddd, 1 H, H-3′), 3.87−3.91 (m, 1 H, H-5′$_b$), 3.63−3.69 (m, 2 H, H-4′, H-5′$_a$), 2.35 (ddd, 1 H, H-2′$_b$), 2.31 (ddd, 1 H, H-2′$_a$). $J_{1',2'a}$ = 1.8, $J_{1',2'b}$ = 6.7, $J_{2'a,3'}$ = 1.8, $J_{2'b,3'}$ = 3.3, $J_{2'a,2'b}$ = 14.5, $J_{3',4'}$ = 3.0, $J_{3',OH}$ = 3.0, $J_{5'a,OH}$ = 5.1, $J_{5'b,OH}$ = 5.1 Hz. − ^{13}C NMR (126 MHz, [D$_6$]DMSO): δ = 154.9 (4-CO), 149.5 (2-CO), 149.3 (C-6), 124.1 (C-5), 72.3 (C-3′), 65.2 (C-1′), 61.1 (C-5′), 59.4 (C-4′), 44.7 (C-2′). − FAB MS (mNBA); m/z: 290 [M + H]$^+$. − FAB HRMS (mNBA): calcd. 290.0447 [M + H]$^+$; found 290.0430.

1-(3,5-Di-*O*-benzyl-2-deoxy-4-thio-L-*threo*-pentofuranosyl)-4-thiouracil (30): A solution of **16** (710 mg, 1.67 mmol, α/β = 2:1) and Lawesson's reagent (388 mg, 0.96 mmol) in dry 1,2-dichloroethane (30 mL) was heated for 2.5 h at 83 °C. After the solution had been allowed to cool to room temperature, the solvent was evaporated, the residue was dissolved in $CHCl_3$ and extracted with water, and the organic phase was separated, dried with $MgSO_4$ and concentrated. The crude product was purified by silica gel column chromatography [petroleum ether/EtOAc, 2:1, R_f(α) = 0.29, R_f(β) = 0.21] to yield **α-30** (405 mg, 83%) and **β-30** (199 mg, 81%) as yellow solids. − **α-30:** M.p. 139−141 °C (decomp.). − $[\alpha]_D^{20} = -6.8$ (c = 1.0, $CHCl_3$). − IR (KBr): $\tilde{\nu}$ = 3077, 3030, 2924, 2854, 1705, 1614, 1454, 1365, 1252, 1136, 1075, 1029, 759, 699 cm^{-1}. − ^1H NMR (500 MHz, $CDCl_3$): δ = 9.56 (ws, 1 H, NH), 7.57 (d, 1 H, H-6), 7.28−7.38 (m, 10 H, ArH), 6.45 (dd, 1 H, H-5), 6.40 (dd, 1 H, H-1′), 4.52, 4.56 (AB system, 2 H, CH_2Ph, J_{AB} = 11.9 Hz), 4.49, 4.62 (AB system, 2 H, CH_2Ph, J_{AB} = 11.9 Hz), 4.31 (ddd, 1 H, H-3′), 4.03 (ddd, 1 H, H-4′), 3.86 (dd, 1 H, H-5′$_b$), 3.66 (dd, 1 H, H-5′$_a$), 2.77 (ddd, 1 H, H-2′$_b$), 1.86 (ddd, 1 H, H-2′$_a$). $J_{1',2'a}$ = 8.3, $J_{1',2'b}$ = 6.8, $J_{2'a,3'}$ = 3.7, $J_{2'b,3'}$ = 3.5, $J_{2'a,2'b}$ = 13.6, $J_{3',4'}$ = 3.8, $J_{4',5'a}$ = 6.9, $J_{4',5'b}$ = 6.4, $J_{5'a,5'b}$ = 9.2, $J_{5,6}$ = 7.7, $J_{5,NH}$ = 1.6 Hz. − ^{13}C NMR (125 MHz, $CDCl_3$): δ = 189.0 (4-CS), 148.1 (2-CO), 137.6 (C_q), 137.4, 135.3 (C-6), 128.53 ($C_{Ar}H$), 128.47, 128.0, 127.9, 127.8, 127.7, 114.1 (C-5), 79.9 (C-3′), 73.6 (CH_2Ph), 71.8(CH_2Ph), 69.2 (C-5′), 61.8 (C-1′), 53.1 (C-4′), 41.5 (C-2′). − FAB MS (mNBA); m/z: 441 [M + H]$^+$. − **β-30:** M.p. 155−157 °C (decomp.). − $[\alpha]_D^{25} = +9.3$ (c =1.0, $CHCl_3$). − IR (KBr): $\tilde{\nu}$ = 3079, 3030, 2925, 2855, 1998, 1615, 1495, 1454, 1368, 1255, 1211, 1178, 1135, 1030, 760, 700, 668 cm^{-1}. − ^1H NMR (500 MHz, $CDCl_3$): δ = 9.43 (ws, 1 H, NH), 8.01 (d, 1 H, H-6), 7.28−7.39 (m, 10 H, ArH), 6.18 (dd, 1 H, H-1′), 6.08 (wd, 1 H, H-5), 4.60, 4.57 (AB system, 2 H, CH_2Ph, J_{AB} = 11.6 Hz), 4.44 (s, 2 H, CH_2Ph), 4.27 (ddd, 1 H, H-

3′), 3.93 (dd, 1 H, H-5′$_b$), 3.77−3.84 (m, 2 H, H-4′, H-5′$_a$), 2.45 (ddd, 1 H, H-2′$_b$), 2.34 (ddd, 1 H, H-2′$_a$). $J_{1',2'a}$ = 7.4, $J_{1',2'b}$ = 3.2, $J_{2'a,3'}$ = 4.0, $J_{2'b,3'}$ = 3.7, $J_{2'a,2'b}$ = 14.4, $J_{3',4'}$ = 4.0, $J_{4',5'b}$ = 6.0, $J_{5'a,5'b}$ = 8.9, $J_{5,6}$ = 7.7, $J_{5,NH}$ < 0.5 Hz. − ^{13}C NMR (125 MHz, $CDCl_3$): δ = 189.2 (4-CS), 148.7 (2-CO), 137.8 (C-6), 137.6, 136.9 (C_q), 128.54, 128.48, 128.1, 127.93, 127.87, 127.8 ($C_{Ar}H$), 112.5 (C-5), 79.8 (C-3′), 73.5 (*C*H$_2$Ph), 71.3, (*C*H$_2$Ph), 68.8 (C-5′), 62.2 (C-1′), 53.6 (C-4′), 41.3 (C-2′). − FAB MS (*m*NBA); *m*/*z*: 441 [M + H]$^+$.

1-(3,5-Di-*O*-benzyl-2-deoxy-4-thio-L-*threo*-pentofuranosyl)-4-(1,2,4-triazol-1-yl)pyrimidine-2(1*H*)-one (31): Phosphoryl chloride (3.0 mL, 5.04 g, 32.87 mmol) was added to a suspension of 1,2,4-triazole (10.42 g, 151 mmol) in anhydrous MeCN (30.0 mL) at room temperature, and the suspension was cooled in an ice bath to 0 °C. Triethylamine (20.0 mL, 14.6 g, 144 mmol) was added to the suspension, the ice bath was removed, a solution of **16** (1.07 g, 2.52 mmol, α/β = 3:2) in MeCN (10.0 mL) was added and the mixture was stirred at room temperature for 2 h. After the reaction was complete, triethylamine (13.8 mL) and water (3.6 mL) were added and stirring was continued for 0.5 h. Solid components were filtered off, the solvents were removed under reduced pressure, and the residue was dissolved in $CHCl_3$ and extracted with satd aq $NaHCO_3$ solution (100 mL) and water (100 mL). The organic phase was dried with $MgSO_4$ and concentrated, and the resulting crude product was purified by silica gel column chromatography [petroleum ether/EtOAc, 1:3, R_f(α,β) = 0.14] to yield pure **31** (825 mg, 72%, α/β = 3:2) as a colourless, resinous solid. The anomers were inseparable. − IR (KBr): $\tilde{\nu}$ = 3116, 3062, 3030, 2924, 2860, 1674, 1626, 1547, 1507, 1465, 1416, 1379, 1364, 1283, 1241, 1178, 1088, 1027, 987, 928, 874, 783, 737, 698, 670, 629 cm^{-1}. − **α-31:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.26 (s, 1 H, $H_{triazole}$), 8.58 (d, 1 H, H-6), 8.12 (s, 1 H, $H_{triazole}$), 7.05−7.38 (m, 10 H, ArH), 7.08 (d, 1 H, H-5), 6.54 (d, 1 H, H-1′), 4.58, 4.54 (AB system, 2 H, C*H*$_2$Ph, J_{AB} = 11.9 Hz), 4.50, 4.65 (AB system, 2 H, C*H*$_2$Ph, J_{AB} = 11.9 Hz), 4.31−4.33 (m, 1 H, H-3′), 4.07 (ddd, 1 H, H-4′), 3.87−3.93 (m, 1 H, H-5′$_b$), 3.70 (dd, 1 H, H-5′$_a$), 3.00 (ddd, 1 H, H-2′$_b$), 1.92 (ddd, 1 H, H-2′$_a$). $J_{1',2'a}$ = 7.2, $J_{1',2'b}$ = 6.9, $J_{2'a,3'}$ = 3.8, $J_{2'b,3'}$ = 4.2, $J_{2'a,2'b}$ = 13.8, $J_{3',4'}$ = 4.3, $J_{4',5'a}$ = 7.5, $J_{4',5'b}$ = 6.0, $J_{5'a,5'b}$ = 9.4, $J_{5,6}$ = 7.3 Hz. − ^{13}C NMR (101 MHz, $CDCl_3$): δ = 158.9, 154.9 (2-CO, C-4), 154.0 ($C_{triazole}$), 147.8 (C-6), 143.3 ($C_{triazole}$), 137.7, 137.4 (C_q), 128.53, 128.47, 127.99, 127.90, 127.8, 127.7 ($C_{Ar}H$), 95.2 (C-5), 78.0 (C-3′), 73.6 (*C*H$_2$Ph), 71.8 (*C*H$_2$Ph), 69.4 (C-5′), 63.8 (C-1′), 52.9 (C-4′), 42.2 (C-2′). − **β-31:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.25 (s, 1 H, $H_{triazole}$), 8.11 (s, 1 H, $H_{triazole}$), 8.08 (d, 1 H, H-6), 7.05−7.38 (m, 10 H, ArH), 6.61 (d, 1 H, H-5), 6.29 (d, 1 H, H-1′), 4.63, 4.59 (AB-system, 2 H, C*H*$_2$Ph, J_{AB} = 11.7 Hz), 4.31−4.33 (m, 1 H, H-3′), 4.28, 4.35 (AB system, 2 H, C*H*$_2$Ph, J_{AB} = 11.3 Hz), 4.00 (dd, 1 H, H-5′$_b$), 3.87−3.93 (m, 1 H, H-4′), 3.85 (dd, 1 H, H-5′$_a$), 2.72 (ddd, 1 H, H-2′$_b$), 2.41 (ddd, 1 H, H-2′$_a$). $J_{1',2'a}$ = 7.1, $J_{1',2'b}$ = 2.1, $J_{2'a,3'}$ = 3.6, $J_{2'b,3'}$ = 2.6, $J_{2'a,2'b}$ = 14.7, $J_{4',5'a}$ = 6.1, $J_{4',5'b}$ = 6.0, $J_{5'a,5'b}$ = 8.4, $J_{5,6}$ = 7.3 Hz. − ^{13}C NMR (101 MHz, $CDCl_3$): δ = 158.8, 154.9 (2-CO, C-4), 153.8 ($C_{triazole}$), 150.5 (C-6), 143.2 ($C_{triazole}$), 137.7, 136.8 (C_q), 128.6, 128.4, 128.1, 128.0, 127.9, 127.8 ($C_{Ar}H$), 93.5 (C-5), 80.1 (C-3′), 73.6 (*C*H$_2$Ph), 71.5 (*C*H$_2$Ph), 68.8 (C-5′), 65.6 (C-1′), 54.4 (C-4′), 41.5 (C-2′). − FAB MS (*m*NBA); *m*/*z*: 476 [M + H]$^+$.

1-(3,5-Di-*O*-benzyl-2-deoxy-4-thio-L-*threo*-pentofuranosyl)cytosine (32): A solution of **31** (774 mg, 1.69 mmol, α/β = 3:2) in 1,4-dioxane (20 mL) and ammonia (25% NH_3 in H_2O, 9.6 mL) was stirred at room temperature for 24 h. The solvents were evaporated, the residue was dissolved in $CHCl_3$ and extracted with water, and the organic phase was separated, dried with $MgSO_4$ and concentrated. The crude product was purified by column chromatography [silica gel; $CHCl_3$/MeOH, 9:1, R_f(β) = 0.23, R_f(α) = 0.14] to yield the cytidines **α-32** (292 mg, 71%) and **β-32** (203 mg, 74%) as white solids. − **α-32:** M.p. 144 °C (decomp.). − $[\alpha]_D^{25}$ = +2.7 (*c* = 1.0, $CHCl_3$). − FAB MS (*m*NBA); *m*/*z*: 424 [M + H]$^+$. − FAB HRMS (*m*NBA): calcd. 424.1695 [M + H]$^+$; found 424.1742. − **β-32**: M.p. 156−158 °C (decomp.). − $[\alpha]_D^{20}$ = −58.1 (*c* = 1.0, $CHCl_3$). − FAB MS (*m*NBA); *m*/*z*: 424 [M + H]$^+$. − FAB HRMS (*m*NBA): calcd. 424.1695 [M + H]$^+$; found 424.1715.

1-(2-Deoxy-4-thio-L-*threo*-pentofuranosyl)cytosine (33):[34] Compound **33** was prepared as described for **23**; from **32** (487 mg, 1.15 mmol, α/β = 3:2) in CH_2Cl_2 (4.0 mL), boron tribromide (0.51 mL, 1.35 g, 5.39 mmol) in CH_2Cl_2 (5.1 mL) and silver carbonate (5.20 g, 18.86 mmol). After chromatographic workup [silica gel, $CHCl_3$/MeOH, 2:1, R_f(β) = 0.31, R_f(α) = 0.27], it was possible to isolate a proportion of **α-33** (27 mg, 16%) as the pure anomer (white solid). **β-33** was obtained as a 1:1 mixture with **α-33** [total: 46 mg, **β-33** (calcd. yield): 23 mg, 21%]. − **α-33:** M.p. 185 °C. − $[\alpha]_D^{20}$ = −61.5 (*c* = 1.0, MeOH). − IR (KBr): $\tilde{\nu}$ = 3404, 3204, 3007, 2929, 1721, 1650, 1529, 1490, 1406, 1277, 1197, 1049, 956, 788, 703, 617, 564 cm^{-1}. − ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 8.09 (ws, 1 H, NH*H*), 8.02 (d, 1 H, H-6), 7.59 (ws, 1 H, N*H*H), 6.31 (dd, 1 H, H-1′), 5.87 (d, 1 H, H-5), 5.05 (ws, 1 H, 3′-OH), 4.74 (ws, 1 H, 5′-OH), 4.37−4.38 (m, 1 H, H-3′), 3.84 (ddd, 1 H, H-4′), 3.70 (dd, 1 H, H-5′$_b$), 3.41 (dd, 1 H, H-5′$_a$), 2.24 (ddd, 1 H, H-2′$_b$), 2.00 (ddd, 1 H, H-2′$_a$). $J_{1',2'a}$ = 9.4, $J_{1',2'b}$ = 6.6, $J_{2'a,3'}$ = 3.6, $J_{2'b,3'}$ = 2.4, $J_{3',4'}$ = 3.5, $J_{4',5'a}$ = 7.6, $J_{4',5'b}$ = 6.3, $J_{5'a,5'b}$ = 10.6, $J_{5,6}$ = 7.6 Hz. − ^{13}C NMR (126 MHz, [D$_6$]DMSO): δ = 44.3 (C-2′), 57.3 (C-4′), 61.2 (C-5′), 61.2 (C-1′), 72.25 (C-3′), 95.0 (C-5), 144.1 (C-6), 157.3, 163.4 (2-CO, C-4). − FAB MS (*m*NBA); *m*/*z*: 244 [M + H]$^+$. − FAB HRMS (*m*NBA): calcd. 244.0756 [M + H]$^+$; found 244.0746. − **β-33:** IR (KBr, 1:1 mixture with α-**33**): $\tilde{\nu}$ = 3389, 2926, 2855, 1714, 1666, 1537, 1405, 1278, 1097, 1075, 1017, 919, 810, 758, 616 cm^{-1}. − ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 8.88 (ws, 1 H, NH*H*), 8.55 (d, 1 H, H-6), 7.92 (ws, 1 H, N*H*H), 6.08 (dd, 1 H, H-1′), 6.03 (d, 1 H, H-5), 5.21 (ws, 1 H, 3′-OH), 4.91 (ws, 1 H, 5′-OH), 4.38−4.41 (m, 1 H, H-3′), 3.89 (dd, 1 H, H-5′$_b$), 3.65 (dd, 1 H, H-5′$_a$), 3.60 (ddd, 1 H, H-4′), 2.38 (ddd, 1 H, H-2′$_b$), 2.21 (ddd, 1 H, H-2′$_a$). $J_{1',2'a}$ = 2.2, $J_{1',2'b}$ = 7.7, $J_{2'a,3'}$ = 2.3, $J_{2'b,3'}$ = 3.8, $J_{3',4'}$ = 3.5, $J_{4',5'a}$ = 7.7, $J_{4',5'b}$ = 5.5, $J_{5'a,5'b}$ = 10.6, $J_{5,6}$ = 7.8 Hz. − ^{13}C NMR (126 MHz, [D$_6$]DMSO): δ = 160.31, 158.9 (2-CO, 4-C), 147.6 (C-6), 93.2 (C-5), 72.4 (C-3′), 63.9 (C-1′), 61.0 (C-5′), 57.7 (C-4′), 44.6 (C-2′).

9-(3,5-Di-*O*-benzyl-2-deoxy-4-thio-L-*threo*-pentofuranosyl)adenine (34): A solution of **15** (1.05 g, 2.95 mmol), adenine (746 mg, 5.52 mmol) and 4-Å molecular sieves (100 mg) in dry MeCN (26 mL) was cooled to −18 °C and TMSOTf (1.94 mL, 2.39 g, 10.74 mmol) was added. The reaction mixture was stirred for 2 h and the temperature was allowed to rise to room temperature. The mixture was then quenched with an excess of saturated aq $NaHCO_3$ 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 concentrated. The resulting crude product was purified by silica gel chromatography [$CHCl_3$/MeOH, 9:1, R_f(α,β) = 0.34] to yield **34** (871 mg, 66%) as an amorphous solid. The anomers were inseparable. FAB MS (*m*NBA); *m*/*z*: 448 [M + H]$^+$. − FAB HRMS (*m*NBA): calcd. 448.1807 [M + H]$^+$; found 448.1849.

9-(3,5-Di-*O*-benzyl-2-deoxy-4-thio-β-L-*threo*-pentofuranosyl)inosine (35): Compound **35** was prepared as described for **34**; from **15** (375 mg, 1.05 mmol), hypoxanthine (287 mg, 2.11 mmol), 4-Å molecular sieves (40 mg), TMSOTf (0.99 mL, 1.22 g, 5.48 mmol) and MeCN (15 mL). After chromatographic workup ($CHCl_3$/MeOH, 9:1, R_f =

0.31), pure **β-35** (322 mg, 68%) was obtained as a white solid. − M.p. 116−118 °C. − $[\alpha]_D^{20}$ = −2.0 (*c* = 1.0, $CHCl_3$). − FAB MS (*m*NBA); *m*/*z* = 449 $[M + H]^+$. − FAB HRMS (*m*NBA): calcd. 449.1647 $[M + H]^+$; found 449.1694.

9-(2-Deoxy-4-thio-L-*threo*-pentofuranosyl)adenine (36): Compound **36** was prepared as described for **23**; from **34** (500 mg, 1.12 mmol, α/β = 1:5) in CH_2Cl_2 (4.0 mL), boron tribromide (0.50 mL, 1.32 g, 5.27 mmol) in CH_2Cl_2 (5.0 mL) and silver carbonate (5.20 g, 18.86 mmol). After chromatographic workup [silica gel, $CHCl_3$/MeOH, 2:1, R_f(α,β) = 0.26] and reversed-phase HPLC (MeCN/H_2O, 8:92), the separated anomers **α-36** (6 mg, 12%) and **β-36** (32 mg, 13%) were obtained as white solids. A portion of **β-36** was used to grow a single crystal (small, colourless needles), which was suitable for X-ray structural analysis. − **α-36:** M.p. 183 °C. − $[\alpha]_D^{20}$ = −13.9 (*c* = 0.3, MeOH). − IR (KBr): $\tilde{\nu}$ = 3440, 3188, 3030, 2956, 2860, 1665, 1603, 1474, 1421, 1372, 1310, 1265, 1180, 1112, 1050, 997, 915, 797, 699, 640, 595, 537, 476 cm^{-1}. − ^1H NMR (500 MHz, [D$_6$]DMSO): δ = 2.47−2.51 (m, 1 H, H-2′$_a$; covered by DMSO), 2.73 (ddd, 1 H, H-2′$_b$), 3.49 (ddd, 1 H, H-5′$_a$), 3.80 (ddd, 1 H, H-5′$_b$), 4.02 (ddd, 1 H, H-4′), 4.54−4.57 (m, 1 H, H-3′), 4.78 (dd, 1 H, 5′-OH), 5.16 (d, 1 H, 3′-OH), 6.32 (dd, 1 H, H-1′), 7.22 (br. s, 2 H, NH_2), 8.13 (s, 1 H, H_{ade}), 8.40 (s, 1 H, H_{ade}). $J_{1',2'a}$ = 6.5, $J_{1',2'b}$ = 9.3, $J_{2'b,3'}$ = 3.6, $J_{2'a,2'b}$ = 12.9, $J_{3',4'}$ = 3.6, $J_{3',OH}$ = 4.0, $J_{4',5'a}$ = 7.6, $J_{4',5'b}$ = 6.1, $J_{5'a,5'b}$ = 10.8, $J_{5'a,OH}$ = 5.8, $J_{5'b,OH}$ = 4.7 Hz. − ^{13}C NMR (126 MHz, [D$_6$]DMSO): δ = 156.2 (C_{ade}), 152.6 (CH_{ade}), 149.4 (C_{ade}), 139.8 (CH_{ade}), 119.4 (C_{ade}), 72.4 (C-3′), 61.2 (C-5′), 58.8 (C-1′), 57.6 (C-4′), 44.3 (C-2′). − FAB MS (*m*NBA); *m*/*z*: 268 $[M + H]^+$. − FAB HRMS (*m*NBA): calcd. 268.0868; found 268.0890. − **β-36:** M.p. 206−208 °C (decomp.). − $[\alpha]_D^{25}$ = +15.0 (*c* = 0.5, MeOH). − IR (KBr): $\tilde{\nu}$ = 3318, 3146, 2969, 2899, 1662, 1604, 1474, 1420, 1372, 1293, 1239, 1208, 1177, 1075, 998, 909, 815, 797, 699, 641, 596, 574, 539 cm^{-1}. − ^1H NMR (500 MHz, [D$_6$]DMSO): δ = 8.47 (s, 1 H, H_{ade}), 8.12 (s, 1 H, H_{ade}), 7.21 (ws, 2 H, NH_2), 6.19 (dd, 1 H, H-1′), 5.56 (ws, 1 H, 3′-OH), 4.88 (ws, 1 H, 5′-OH), 4.45−4.50 (m, 1 H, H-3′), 3.89−3.96 (m, 1 H, H-5′$_b$), 3.63−3.70 (m, 2 H, H-4′, H-5′$_a$), 2.56 (ddd, 1 H, H-2′$_b$), 2.46 (ddd, 1 H, H-2′$_a$). $J_{1',2'a}$ = 2.6, $J_{1',2'b}$ = 8.0, $J_{2'a,3'}$ = 2.9, $J_{2'b,3'}$ = 4.1, $J_{2'a,2'b}$ = 14.2 Hz. − ^{13}C NMR (126 MHz, [D$_6$]DMSO): δ = 156.1 (C_{ade}), 152.4 (CH_{ade}), 149.2 (C_{ade}), 140.7 (CH_{ade}), 118.9 (C_{ade}), 72.6 (C-3′), 61.1 (C-5′), 58.3 (C-4′), 58.2 (C-1′), 44.4 (C-2′). − FAB MS (*m*NBA); *m*/*z*: 268 $[M + H]^+$. − FAB HRMS (*m*NBA): calcd. 268.0868; found 268.0873.

9-(2-Deoxy-4-thio-β-L-*threo*-pentofuranosyl)inosine (37): Preparation of **37** was carried out as described for **23**; using **35** (503 mg, 1.12 mmol) in CH_2Cl_2 (4.0 mL), boron tribromide (0.50 mL, 1.32 g, 5.27 mmol) in CH_2Cl_2 (5.0 mL) and silver carbonate (5.20 g, 18.86 mmol). After chromatographic workup (silica gel, $CHCl_3$/MeOH, 2:1, R_f = 0.27) and reversed-phase HPLC (MeCN/H_2O, 9:91), **37** (19 mg, 6%) was obtained as a white solid. − M.p. 205 °C. − $[\alpha]_D^{25}$ = +41.3 (*c* = 1.0, MeOH). − IR (KBr): $\tilde{\nu}$ = 3422, 3052, 2923, 1697, 1588, 1545, 1415, 1373, 1201, 1093, 971, 906, 789, 648, 599 cm^{-1}. − ^1H NMR (500 MHz, [D$_6$]DMSO): δ = 12.27 (ws, 1 H, NH), 8.43 (s, 1 H, H_{ino}), 8.03 (s, 1 H, H_{ino}), 6.14 (dd, 1 H, H-1′), 5.38 (d, 1 H, 3′-OH), 4.86 (dd, 1 H, 5′-OH), 4.47−4.50 (m, 1 H, H-3′), 3.91 (ddd, 1 H, H-5′$_b$), 3.63−3.69 (m, 2 H, H-4′, H-5′$_a$), 2.55 (ddd, 1 H, H-2′$_b$), 2.45 (ddd, 1 H, H-2′$_a$). $J_{1',2'a}$ = 2.5, $J_{1',2'b}$ = 7.9, $J_{2'a,3'}$ = 2.8, $J_{2'b,3'}$ = 4.0, $J_{2'a,2'b}$ = 14.2, $J_{3',OH}$ = 3.9, $J_{4',5'b}$ = 9.6, $J_{5'a5'b}$ = 9.6, $J_{5'a,OH}$ = 5.7, $J_{5'b,OH}$ = 4.8 Hz. − ^{13}C NMR (126 MHz, [D$_6$]DMSO): δ = 156.7 (C_{ino}), 148.1 (C_{ino}), 145.7 (CH_{ino}), 140.1 (CH_{ino}), 124.0 (C_{ino}), 72.5 (C-3′), 61.1 (C-5′), 58.7 (C-1′), 58.2 (C-4′), 44.5 (C-2′). − FAB MS (*m*NBA); 269 $[M + H]^+$. − FAB HRMS (*m*NBA): calcd. 269.0708 $[M + H]^+$; found 269.0656.

Supporting Information Available: ^1H NMR, ^{13}C NMR, IR and MS data of **11**, **13**, **15**−**22**, **32**, **34**, **35** (see also footnote on the first page of this article).

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[33] The elemental analyses of **13** and **20** deviate by approx. 1% from the calcd. values due to impurities.

[34] The structures of **23** and **33** have been erroneously reported by J.-C. G. Graciet, R. F. Schinazi, "From D- to L-Nucleoside Analogs as Antiviral Agents", in *Advances in Antiviral Drug Design* (Ed.: E. De Clercq), JAI Press Inc., Stamford Connecticut, **1999**, vol. 3, pp. 1−68, esp. p. 55. The cited compounds belong, however, to the 2-deoxy-L-*ribo* rather than the 2-deoxy-L-*threo* series according to ref.[29]

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