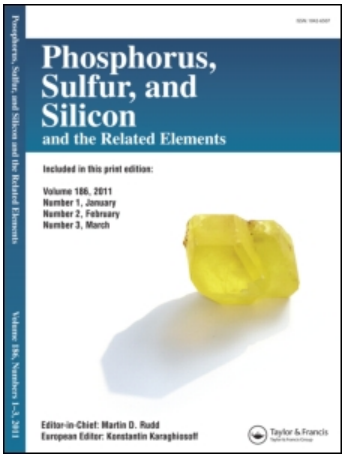

Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Synthesis and Reactions of Anhydro-Azido-thio-D-lyxofuranosides[1]

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To cite this Article Otzen, Dirk , Voss, Jürgen and Adiwidjaja, Gunadi(2006) 'Synthesis and Reactions of Anhydro-Azido-thio-D-lyxofuranosides[1]', Phosphorus, Sulfur, and Silicon and the Related Elements, 181: 6, 1249 — 1270
To link to this Article: DOI: 10.1080/10426500500326545
URL: http://dx.doi.org/10.1080/10426500500326545

Phosphorus, Sulfur, and Silicon, 181:1249–1270, 2006

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500500326545

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Synthesis and Reactions of Anhydro-Azido-thio-D-lyxofuranosides[1]

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*2,5-anhydro-3-azido-2-thio-D-lyxofuranosides and 3,5-anhydro-2-azido-3-thio-D-lyxofuranosides were prepared from methyl D-xylofuranoside or methyl D-ribofuranoside via corresponding 2,3-epoxysugars or the 5-*O*-trityl derivative. The sulfur was introduced into molecules by use of the thio-Mitsunobu reaction. Bicyclic azido-thiosugars were transformed into nucleoside analogues, oxidized to sulfoxides and sulfones, and reduced to bicyclic amino-thiosugars. Structures and configurations of products were determined by NMR spectroscopy or X-ray structure analyses.*

Keywords Azides; cyclization; oxidation; Thiosugars; X-ray diffraction

INTRODUCTION

The carbohydrates described in the following exhibit three particular molecular features. They are thiosugars, they are bicyclic compounds (anhydrosugar-type), and they are substituted with an azido group. Each of these three peculiarities is known as a reason for special chemical and biochemical properties. Especially the thiosugars have recently found widespread chemical and biochemical interest.[2–4] Anhydrosugars as well are interesting synthetic building blocks in carbohydrate chemistry, and the corresponding nucleoside analogues represent precursors for the synthesis of locked nucleic acids.[5] Finally, azidosugars

Received June 2, 2005; accepted June 16, 2005.
The University of Hamburg and the Fonds der Chemischen Industrie are gratefully acknowledged for their financial support.
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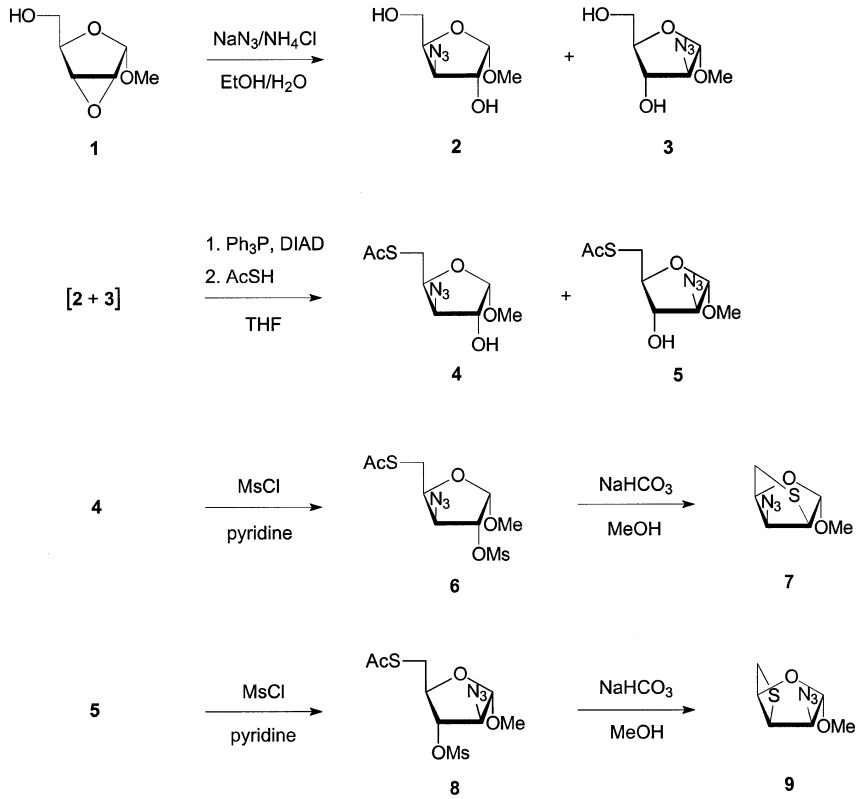
are the most suitable starting compounds for the preparation of the important aminosugars.[6a] Furthermore, the nucleoside analogue azidothymine is known as the first chemotherapeutic drug with a significant activity against HIV.[7,8] In continuation of our studies on mono-[9] and bicyclic[10,11] thiosugars, we present here our results on the synthesis of monosaccharides with a corresponding combination of these three structural moieties.

RESULTS AND DISCUSSION

Syntheses

Methyl 2,3-anhydro-α-D-ribofuranoside (**1**), which is available in large amounts from inexpensive D-xylose,[12] reacted with sodium azide and ammonium chloride in refluxing aqueous ethanol to yield a mixture of the 3-azido-3-deoxy-xylofuranoside **2** and the 2-azido-2-deoxy-arabinofuranoside **3** by a nucleophilic ring opening of the epoxide. Two isomers were formed with good overall yield in a ratio of 3:2 in favor of **3**. This slight regioselectivity is obviously due to steric hindrance of the attack at C-3 by the hydroxymethyl substituent on C-4. Isomers could be separated, by column chromatography, but also the mixture was suitable as starting material for the thio-Mitsunobu reaction with thioacetic acid in the next step. It resulted in an expected 2:3 mixture of the 2-azido- and the 3-azido-5-*S*-thioacetates **4** and **5**. The azido groups of **2** and **3** were not reduced by thioacetic acid or triphenyl phosphine under the conditions of the thio-Mitsunobu reaction as one could expect. Column chromatography led to pure isomers as yellowish syrups. Structures and configurations of **2**, **3**, **4**, and **5** follow from their ^{1}H and ^{13}C NMR spectra. In particular, chemical shifts $\delta(^{13}C)$ of 66.5 ppm for C-3 in **2** and 71.8 ppm for C-2 in **3** as compared with 76.9 ppm for C-2 in **2** and 75.4 ppm for C-3 in **3** are indicative of the respective positions of the azido and the hydroxy substituents. The proton coupling constants $^3J_{1,2} = 4.5$ Hz and $^3J_{1,2} = 2.0$ Hz, respectively, are characteristic of the α-*xylo* configuration of **2** and the α-*arabino* configuration of **3**. Furthermore, X-ray structures of the follow-up products **27** and **29** (see Reactions) corroborate the structural assignments.

The mesylation of **4** gave a 83% yield of the mesylate **6**. Nucleophilic thioester cleavage with sodium hydrogen carbonate and concomitant intramolecular displacement of the mesylate leaving group by the 5-thiolate substituent under a ring closure finally resulted in the bicyclic methyl 2,5-anhydro-3-azido-3-deoxy-2-thio-α-D-lyxofuranoside (**7**) (Scheme 1). In spite of the presence of an azido substituent in the *syn*-2,3-position, which might cause some steric hindrance, the yield

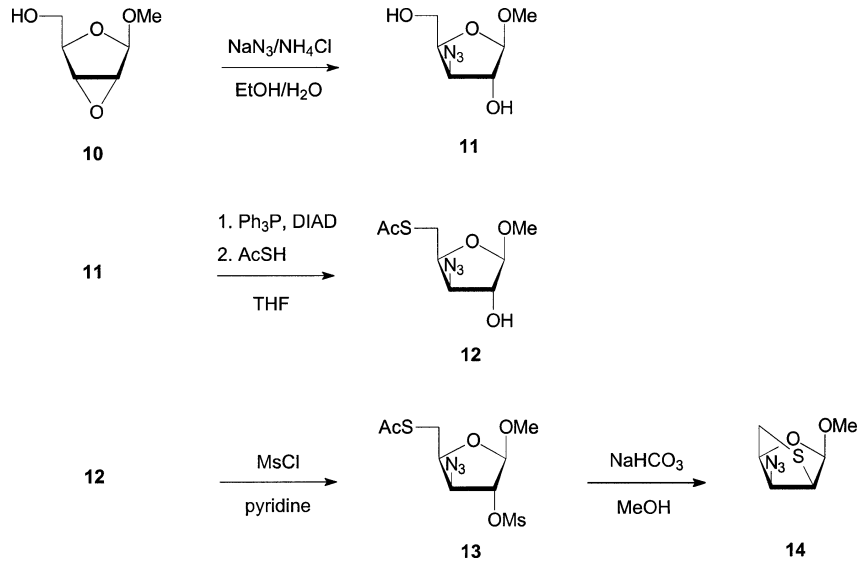


SCHEME 1

of **7** was 75%. The azido group remained unaffected. The mesylate **8** obtained from the 3-azido-5-*S*-thioacetate **5**, on the other hand, reacted with sodium hydrogen carbonate to form the expected thietano-sugar **9** (Scheme 1).

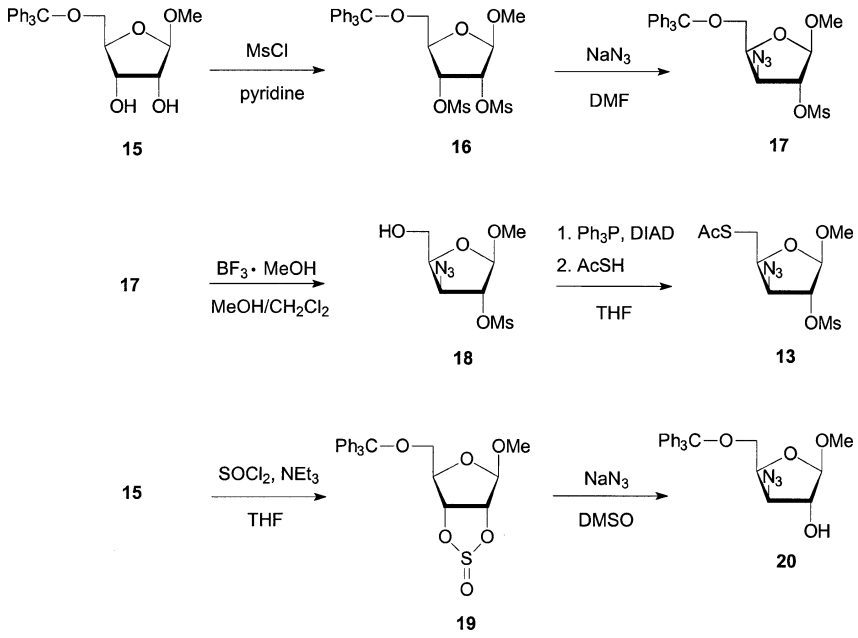
In a related reaction sequence, methyl 2,3-anhydro-β-D-ribofuranoside (**10**), which can be prepared in only two steps from D-xylose,[13] was transformed into methyl 2,5-anhydro-3-azido-3-deoxy-2-thio-β-D-lyxofuranoside (**14**). In the first step, the reaction of **10** with sodium azide, methyl 3-azido-3-deoxy-β-D-xylofuranoside (**11**) was formed with a 74.5% yield as the only isomer. Steric hindrance as well as the electronic repulsion by the β-glycosidic methoxy group in **10** and the known reduced reactivity for nucleophilic substitutions next to anomeric centers[6b,14–16] should be reasons for the regioselectivity in this case as compared with the epoxide ring opening of the α-anomer **1**. We have observed the same pronounced regioselectivities for the

reactions of methyl 2,3-anhydro-α-D- and -α-L-lyxofuranoside with sodium azide, which led to methyl 3-azido-3-deoxy-α-D- and -α-L-arabinofuranoside as the only products with yields of over 90%.[17,18] The thio-Mitsunobu reaction of **11** with thioacetic acid again selectively led to the expected 3-azido-5-*S*-thioacetate **12** with a 79% yield. The mesylation of **12** led to **13**. The subsequent nucleophilic cleavage of the thioester group with sodium hydrogen carbonate under concomitant intramolecular displacement of the mesylate group and ring closure gave 65% of the bicyclic azido-thietano-sugar **14** (Scheme 2). The total yield for the six steps from D-xylose to **14** amounted to 11.4%.



SCHEME 2

We have also explored an alternative route to **14**. First, methyl β-D-ribofuranoside was tritylated.[19] The 5-*O*-trityl-riboside **15** was mesylated to form the dimesylate **16**. Nucleophilic displacement with azide expectedly (see preceeding paragraph) took place with complete regioselectivity to yield the 3-azido-sugar **17** with β-D-*xylo* configuration. The deprotection of **17** gave **18**; the thio-Mitsunobu reaction also provided the precursor **13** for the preparation of the anhydrothio sugar **14** (Scheme 3). This sequence is however unfavorable as compared with the aforementioned D-xylose-based route since it starts from D-ribose, which is more expensive by a factor of five, and it includes seven steps with an overall yield of only 7.6%. Also, methyl 2,3-di-*O*-sulfinyl-5-*O*-trityl-β-D-ribofuranoside (**19**), which we have prepared from **15** by a



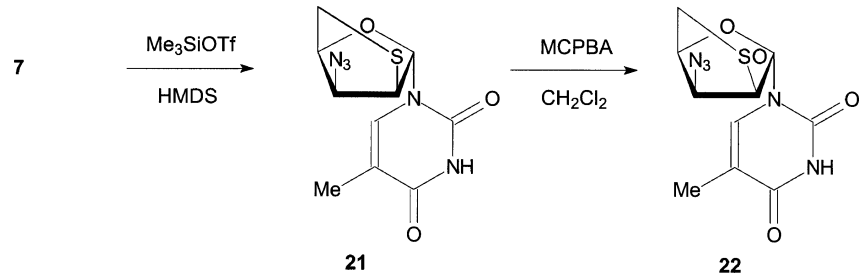
SCHEME 3

reaction with thionyl chloride and triethyl amine, does not offer advantages as an intermediate. The nucleophilic displacement with sodium azide once more occurred in the 3-position under the formation of the β-D-*xylo* derivative **20** with a moderate yield of 50% (Scheme 3). Substitution at the 2-position to form a compound with the desired β-D-*arabino* configuration was not achieved. Furthermore, **20** could not be successfully transformed into **14**.[20,21]

Reactions

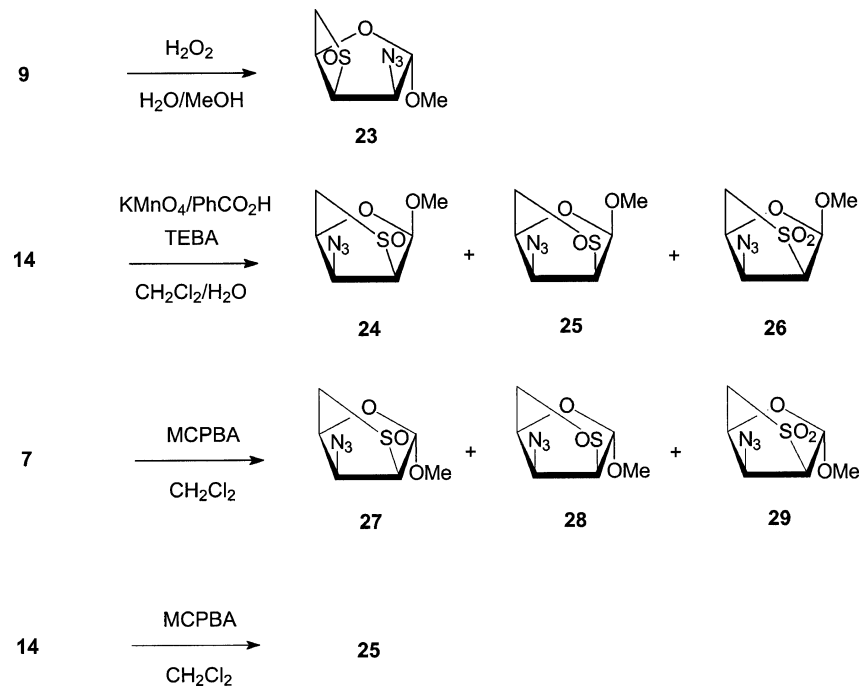
In continuation of our investigations on sulfur-containing nucleoside analogues,[22] we have used **7** as a glycosyl donor. Its reaction with bistrimethylsilylthymine under the *Vorbrüggen* conditions[23] led to **21** with a 54% yield (Scheme 4).

The α-configuration of **21** was proved by NOESY measurements. The proton H-6 of the base moiety exhibits through-space interactions with the three carbohydrate protons H-2′, H-3′, and H-4′, which is only possible if all of these four protons are located below the furanose ring, i.e., if the molecule exhibits the α-D-*lyxo* configuration. The correct connection of the anomeric center with the 1-position of the nucleobase was demonstrated by the characteristic UV spectrum of **21**.



SCHEME 4

Since we were also interested in sulfoxides and sulfones derived from azido-thiosugars,[24] we have studied the oxidation of **7**, **14**, **9**, and **21** with various oxidizing reagents. First, the relatively mild oxidant hydrogen peroxide was used. The oxidation of the thietane **9** gave a 53% yield of the *exo*-sulfoxide **23** as the only product (Scheme 5). Presumably, steric hindrance by the azido substituent in the 2-position had prevented the formation of the diastereoisomeric *endo*-sulfoxide and of



SCHEME 5

the corresponding sulfone. The assignment of the *exo*-configuration to **23** was possible on account of its ^{1}H NMR spectrum. The aniosotropic effect of the sulfoxide group upon the *syn*-proton H-4 caused a downfield shift to 5.23 ppm as compared with 4.42 ppm for the *anti*-proton H-2. This observation agrees with results which we have obtained with several related compounds (see the following paragraph).

Next, we applied potassium permanganate in the presence of benzoic acid under phase transfer catalysis with benzyltriethylammonium chloride, which mixture reacts similarly but not identically as compared with perbenzoic acid.[25] A mixture of the two possible sulfoxides (**24/25**) with yields of 75% and 4%, respectively, together with 7% of the sulfone **26** was formed on reaction with **14** (Scheme 5).

The structural assignment of the two diastereoisomeric sulfoxides was not unequivocal since no discriminating anisotropic effect of the sulfoxide oxygen on neighboring protons was observed. In fact, chemical shifts of H-1 are not significantly different in **24** and **25**, and also the chemical shifts of the two geminal protons H-5 and H-5′ are nearly the same in each of the two compounds. Our presumptive assignment (Scheme 5) rests on the much higher yield of the *exo*-sulfoxide **25**, the formation of which should be favored on stereochemical reasons. The structure and configuration of the sulfone **26**, and as a consequence, also of its precursors **14**, **13**, **12**, and **11**, were proved by an X-ray structure analysis (Figure 1).

Finally, furanosides **7** and **14** and the nucleoside analogue **21** were oxidized with *meta*-chloroperbenzoic acid. Again, a mixture of the two possible diastereoisomeric sulfoxides **28** (40%) and **27** (8%) and the sulfone **29** (34%) was produced from **7**, whereas the β-anomer **14**, not unexpectedly, gave only the *exo*-sulfoxide **25** with a 51% yield (Scheme 5). Since a large amount of the sulfone **29** was produced from **7**, one cannot

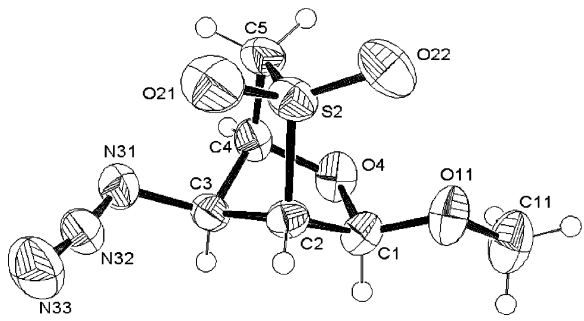


FIGURE 1 ORTEP view of the X-ray diffraction structure of the sulfone **26**; thermal ellipsoids are drawn at the 50% probability level.

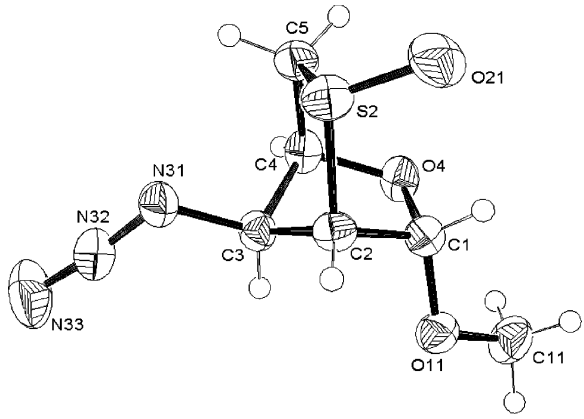


FIGURE 2 ORTEP view of the X-ray diffraction structure of the sulfoxide **27**; thermal ellipsoids are drawn at the 50% probability level.

take the observed relative yields of **28** and **27** as indicative of a corresponding diastereoselectivity of the oxidation reaction. The sulfoxide **27** could be well formed at a higher rate but also could be further oxidized to the sulfone **29** in a fast follow-up reaction.

In this case, X-ray diffraction analyses of **27** (Figure 2) and **29** (Figure 3) left no doubt on the structures of the stereoisomers, although the NMR spectra were no more conclusive than for **24** und **25**. The unequivocal structures of **27** and **29** also corroborate the structural

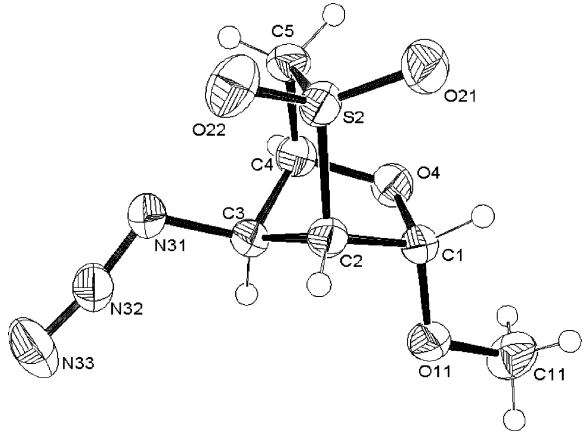
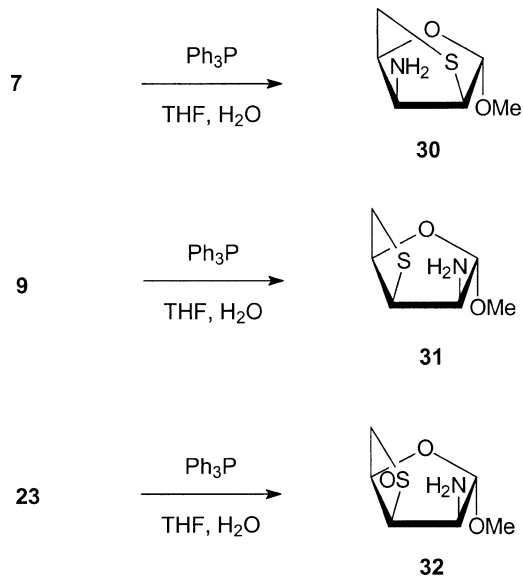


FIGURE 3 ORTEP view of the X-ray diffraction structure of the sulfone **29**; thermal ellipsoids are drawn at the 50% probability level.

assignments of their precursors **7**, **6**, **4**, and **2**, and in addition, of **5** and **3**.

The thymidine derivative **21** gave a 74% yield of the *endo*-sulfoxide **22** (Scheme 4) as the only product. This diastereoselectivity seems to be due to steric repulsion of the azido substituent. It may, in addition, result from the formation of a hydrogen bridge between N-1 of the base in the substrate **21** and the oxidant *meta*-chloroperbenzoic acid, which would direct the transfer of the oxygen to the *endo*-position in **22**. The configuration of **22** was evident from a significant downfield shift to 6.40 ppm for H-1 as compared with 5.80 ppm for H-1 in **21**.

Reduction of the azido group should lead to aminosugars, which are very interesting compounds from a biochemical point of view.[6a] We have, therefore, studied the exemplary reduction of **7**, **9**, and **23**. In particular, we were interested to find out whether the functional groups present in these compounds, i.e., the sulfide and the sulfoxide functions, remain uneffected during the reduction of the azide substituent. We chose triphenylphosphine as a reducing agent, which is known for its good chemoselectivity and yields in azide reductions.[26,27] In fact, all three starting compounds were cleanly transformed into the corresponding aminogars **30**, **31**, and **32**, with yields of 64–69% (Scheme 6).



SCHEME 6

The products exhibited the expected spectroscopic data. The missing azido band and the appearance of an amino band in the IR spectra

revealed the success of the reduction. The NMR spectra are indicative of intact structures of bicyclo-thiosugars. In particular, the unchanged sulfoxide function of **32**, which is, of course, anyhow clearly distinct from compound **31**, is evident from ^{13}C chemical shifts of 75.8 ppm for C-3 and 53.2 ppm for C-5 (**31**: 57.7 ppm and 33.9 ppm, respectively).

Conclusion

We have shown that methyl azido-deoxypentofuranosides can be selectively transformed into the corresponding 5-*S*-acetyl-azido-5-thio derivatives by a thio-Mitsunobu reaction with thioacetic acid. Base-promoted tandem thioacetate splitting/intramolecular cyclization of the 2-*O*-mesyl- and 3-*O*-mesyl-thioacetates yields 3-azido-2,5-thioanhydro- ("thiolano"-) or 2-azido-3,5-thioanhydro- ("thietano"-) pentofuranosides. These can be transformed easily into nucleoside analogues and aminosugars. Oxidation of sulfur leads to sulfoxides and/or sulfones with pronounced chemo- and diastereoselectivity depending on the structure and configuration of the substrate and the nature of the applied oxidant.

EXPERIMENTAL

General Procedure

IR spectra were measured on an ATI Mattson Genesis spectrometer (films or KBr pellets). UV spectra were recorded on a Varian Cary 1 E spectrometer. NMR spectra were measured on a Bruker AMX 400 spectrometer (^1H: 400 MHz, ^{13}C: 100.6 MHz) in $CDCl_3$ if not stated otherwise. Chemical shifts (ppm) are relative to Me_4Si (^1H) and $CDCl_3$ (^{13}C, $\delta = 77.05$). In order to enhance the resolution of the ^1H signals, the spectra were recalculated from the FID by use of the WinNMR software (Bruker). ^1H-^1H-COSY-, ^1H-^{13}C-Cosy-, NOESY-, and DEPT-experiments were performed to assign the signals. Mass spectra were measured on a Finnegan MAT 311 A (EI, 70 eV) spectrometer. Corrected melting points were taken with an Electrothermal apparatus. Optical rotations were measured on a Perkin-Elmer polarimeter 341. TLC was performed on Merck PF_{254} foils. The spots were detected by (a) spraying with 20% H_2SO_4 in EtOH and heating, (b) spraying with 4-methoxybenzaldehyde in 2.5% H_2SO_4 and 0.4% AcOH in EtOH, (c) by UV absorption. Column chromatography (CC) was performed with Merck Kieselgel 60 (70–230 mesh), PE = redistilled petroleum ether.

X-Ray Structure Analyses

The crystal data and a summary of experimental details are given in Table I. Data collection was performed with a Kappa-CCD

TABLE I Crystal Data and Structure Refinement for 27, 29, and 26

Compound	**27**	**29**	**26**
Empirical formula	$C_6H_9N_3O_3S$	$C_6H_9N_3O_4S$	$C_6H_9N_3O_4S$
Formula weight	203.22	219.22	219.22
Crystal system	Orthorhombic	Monoclinic	Orthorhombic
Space group	$P2_12_12_1$	$P2_1$	$P2_12_12_1$
a [Å]	5.494(1)	8.760(1)	8.522(1)
b [Å]	6.706(1)	10.944(1)	10.209(1)
c [Å]	14.265(1)	8.385(1)	10.345(1)
β [°]		110.69(1)	
Z	4	2	4
Crystal size [mm]	0.33 × 0.25 × 0.16	0.37 × 0.27 × 0.23	0.33 × 0.28 × 0.15
$\rho_{calcd.}$ [g cm^{-1}]	1.574	1.624	1.574
μ [mm^{-1}]	0.356	0.355	0.344
$F(000)$	424	228	456
θ limits [°]	2.35/27.48	2.60/30.02	2.80/30.02
$h/k/l$ limits	0, 7/0, 14/0, 18	0, 9/0, 11/-11, 11	0, 12/0, 14/0, 14
Reflections collected	9348	3565	9913
Unique reflections	1169 [R (int) = 0.047]	1376 [R (int) = 0.026]	1565 [R (int) = 0.033]
Number of parameters	143	152	152
R indices (all data)	$R_1 = 0.0318$	$R_1 = 0.0497$	$R_1 = 0.0457$
	$wR_2 = 0.0770$	$wR_2 = 0.1100$	$wR_2 = 0.0837$
Final R indices	$R_1 = 0.0268$	$R_1 = 0.0432$	$R_1 = 0.0324$
[$I > 2\sigma(I)$]	$wR_2 = 0.0739$	$wR_2 = 0.1051$	$wR_2 = 0.0769$
Goodness of fit on F^2	1.036	1.016	1.003
Abs. struct. parameter	0.39(10)	−0.06(13)	0.20(10)
Extinction coefficient	0.015(5)	0.43(3)	0.037(4)
Largest difference peak and hole [e A^{-3}]	0.156 and −0.198	0.582 and −0.631	0.166 and −0.211

Nonius diffractometer with graphite-monochromated Mo-K_α radiation (0.71073 Å) in the rotation Φ scan mode at 293 K. Structures were solved by direct methods using the SIR-97 program[28] and refined by full-matrix block least squares on F^2 using all data and the SHELX-97 program.[29] Crystallographic data reported in this article have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications no. CCDC-272968 (**27**), CCDC-272967 (**29**), and CCDC-272969 (**26**). Copies of data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 IEZ, UK [Fax: (international) + 44-1223/336-033; E-mail: deposit@ccdc.cam.uk].

Methyl 3-Azido-3-deoxy-α-D-xylofuranoside (2) and Methyl 2-azido-2-deoxy-α-D-arabinofuranoside (3)

A solution of methyl 2,3-anhydro-α-D-ribofuranoside[12] (**1**, 5.60 g, 38.2 mmol), NaN_3 (8.47 g, 130.3 mmol), and NH_4Cl (6.56 g, 122.6 mmol) in H_2O (196 mL)/EtOH (46 mL) was heated to 80°C for 72 h. The

solvents were distilled off, and the residue was worked up with H_2O as usual. Purification and separation by CC (EtOAc/PE 3:2) yielded 2.32 g **2** (12.3 mmol, 32.0%) and 3.49 g **3** (18.5 mmol, 48.1%) as colorless syrups. **2** : $R_f = 0.23$. IR: $\nu = 3399$ (OH), 2111 (N_3) cm^{-1}. ^1H NMR: $\delta = 2.83$ (bs, 1H, OH), 3.36 (bs, 1H, OH), 3.48 (s, 3H, OMe), 3.72 (d, 2H, H-5, H-5′), 4.13 (m, 1H, H-3), 4.25 (m, 1H, H-2), 4.27 (m, 1H, H-4), 4.91 (d, 1H, H-1). $J_{1,2} = 4.5$, $J_{3,4} = 7.0$, $J_{4,5} = 4.0$, $J_{4,5'} = 4.0$ Hz. ^{13}C NMR: $\delta = 55.5$ (OMe), 61.7 (C-5), 66.5 (C-3), 76.9 (C-2), 77.0 (C-4), 101.3 (C-1). **3** : $R_f = 0.29$. IR: $\nu = 3391$ (OH), 2113 (N_3) cm^{-1}. ^1H NMR: $\delta = 3.13$ (bs, 1H, OH), 3.43 (s, 3H, OMe), 3.75 (dd, 1H, H-5), 3.84 (dd, 1H, H-5′), 3.92 (dd, 1H, H-2), 3.95 (bs, 1H, OH), 4.02 (m, 1H, H-4), 4.08 (m, 1H, H-3), 4.87 (d, 1H, H-1). $J_{1,2} = 2.0$, $J_{2,3} = 4.0$, $J_{4,5} = 4.2$, $J_{4,5'} = 3.5$, $J_{5,5'} = 12.2$ Hz. ^{13}C NMR: $\delta = 55.4$ (OMe), 61.5 (C-5), 71.8 (C-2), 75.4 (C-3), 83.9 (C-4), 106.6 (C-1).

Methyl 5-S-Acetyl-3-azido-3-deoxy-5-thio-α-D-xylofuranoside (4) and Methyl 5-S-Acetyl-2-azido-2-deoxy-5-thio-α-D-arabinofuranoside (5)

A solution of PPh_3 (9.62 g, 36.7 mmol) in dry THF (100 mL) was stirred at 0°C under an Ar atmosphere. Diisopropyl azodicarboxylate (DIAD, 7.26 g, 6.93 mL, 35.9 mmol) was added. The resulting white suspension was stirred at 0°C for 30 min. Then a solution of a 2:3 mixture of **2** and **3** (5.81 g, 30.7 mmol) and thioacetic acid (vacuum-distilled three times at low temp., 2.93 g, 2.74 mL, 38.5 mmol) in dry THF (100 mL) was slowly added. The resulting yellow solution, which slowly turned green and finally formed a greenish yellow suspension, was stirred at r.t. for 16 h. The THF was distilled off, and the residue was worked up with H_2O as usual. Purification and separation by CC (EtOAc/PE, gradient of 1:4 to 1:2) yielded 2.01 g **4** (8.13 mmol, 26.5%) and 3.32 g **5** (13.4 mmol, 43.7%) as light yellow syrups. **4**: $R_f = 0.26$. IR: $\nu = 3459$ (OH), 2110 (N_3), 1692 (C=O) cm^{-1}. ^1H NMR: $\delta = 2.36$ (s, 3H, MeCO), 2.88 (bs, 1H, OH), 3.07 (dd, 1H, H-5), 3.13 (dd, 1H, H-5′), 3.49 (s, 3H, OMe), 3.99 (dd, 1H, H-3), 4.24 (m, 1H, H-2), 4.28 (m, 1H, H-4), 4.94 (d, 1H, H-1). $J_{1,2} = 4.5$, $J_{2,3} = 4.5$, $J_{3,4} = 5.8$, $J_{4,5} = 6.3$, $J_{4,5'} = 7.0$, $J_{5,5'} = 13.8$ Hz. ^{13}C NMR: $\delta = 29.3$ (C-5), 30.5 (CH_3CO), 55.9 (OMe), 68.0 (C-3), 76.4 (C-4), 77.0 (C-2), 101.3 (C-1), 194.9 (C=O). **5**: $R_f = 0.33$. IR: $\nu = 3448$ (OH), 2107 (N_3), 1694 (C=O) cm^{-1}. ^1H NMR: $\delta = 2.40$ (s, 3H, CH_3CO), 3.06 (bs, 1H, OH), 3.16 (dd, 1H, H-5), 3.25 (dd, 1H, H-5′), 3.40 (s, 3H, OMe), 3.79 (dd, 1H, H-3), 3.91 (dd, 1H, H-2), 4.10 (m, 1H, H-4), 4.83 (d, 1H, H-1). $J_{1,2} = 2.1$, $J_{2,3} = 4.4$, $J_{3,4} = 5.5$, $J_{4,5} = 5.3$, $J_{4,5'} = 5.2$, $J_{5,5'} = 14.3$ Hz. ^{13}C NMR: $\delta = 30.6$ (CH_3CO), 30.8 (C-5), 55.5 (OMe), 71.1 (C-2), 77.7 (C-3), 82.0 (C-4), 106.5 (C-1), 196.7 (C=O).

Methyl 5-S-Acetyl-3-azido-3-deoxy-2-O-mesyl-5-thio-α-D-xylofuranoside (6)

Mesyl chloride (1.37 g, 0.93 mL, 12.0 mmol) was added to a stirred solution of **4** (2.32 g, 9.38 mmol) in dry pyridine (60 mL) at −10°C. After 1 h, the solution was warmed up to r.t. and stirred for 16 h. $CHCl_3$ was added, and the solution was washed subsequently with a 3M Na_2SO_4 solution (3×), satd. $NaHCO_3$ solution (2×), and H_2O (1×). The organic layer was dried with $MgSO_4$ and evaporated. CC of the residue (EtOAc/PE 1:3, $R_f = 0.20$) yielded 2.54 g **6** (7.82 mmol, 83.4%) as a light yellow syrup. IR: $\nu = 2106$ (N_3), 1696 (C=O), 1346 ($MeSO_3$), 1170 ($MeSO_3$) cm^{-1}. ^1H NMR: $\delta = 2.37$ (s, 3H, MeCO), 3.06 (dd, 1H, H-5), 3.13 (s, 3H, $MeSO_3$), 3.21 (dd, 1H, H-5′), 3.45 (s, 3H, OMe), 4.37 (m, 1H, H-4), 4.39 (m, 1H, H-3), 4.82 (dd, 1H, H-2), 5.03 (d, 1H, H-1). $J_{1,2} = 4.2$, $J_{2,3} = 6.0$, $J_{4,5} = 6.1$, $J_{4,5'} = 5.5$, $J_{5,5'} = 13.9$ Hz. ^{13}C NMR: $\delta = 29.5$ (C-5), 30.5 (CH_3CO), 38.7 ($MeSO_3$), 55.7 (OMe), 64.3 (C-3), 75.0 (C-4), 81.3 (C-2), 99.9 (C-1), 194.7 (C=O).

Methyl 2,5-Anhydro-3-azido-3-deoxy-2-thio-α-D-lyxofuranoside (7)

Compound **6** (7.63 g, 23.5 mmol) was dissolved in dry MeOH (analytical grade, 600 mL) under an Ar atmosphere in a carefully dried apparatus. Ar was bubbled through the solution for 2 h, and then dry $NaHCO_3$ (4.20 g, 50.0 mmol) was added. After another 30 min, the Ar current was stopped, and the solution was refluxed until **6** was consumed (tlc control, ca. 3 h). The solvent was evaporated. The residue was dissolved in CH_2Cl_2. The excess of $NaHCO_3$ was filtered, and the CH_2Cl_2 was evaporated. CC (EtOAc/PE 1:3, $R_f = 0.58$) gave **7** (3.30 g, 17.6 mmol, 75.1%) as a colorless syrup. $[\alpha]_D^{20} = +47$ (*c* 0.90, $CHCl_3$). IR: $\nu = 2109$ (N_3) cm^{-1}. ^1H NMR: $\delta = 2.75$ (dd, 1H, H-5), 2.91 (dd, 1H, H-5′), 3.30 (s, 3H, OMe), 3.30 (m, 1H, H-2), 4.43 (m, 1H, H-4), 4.44 (s, 1H, H-3), 4.86 (s, 1H, H-1). $J_{4,5} = 1.0$, $J_{4,5'} = 1.2$, $J_{5,5'} = 10.4$ Hz. ^{13}C NMR: $\delta = 33.6$ (C-5), 48.4 (C-2), 54.0 (OMe), 63.1 (C-3), 75.9 (C-4), 108.5 (C-1). MS; *m/z* : 187 [$M^{+\cdot}$].

Methyl 5-S-Acetyl-2-azido-2-deoxy-2-O-mesyl-5-thio-α-D-arabinofuranoside (8)

Compound **8** was prepared as described for **6** from **5** (2.97 g, 12.0 mmol) and mesyl chloride (1.76 g, 1.20 mL, 15.4 mmol) in pyridine (65 mL). Reaction time: 17 h. CC (EtOAc/PE 1:3, $R_f = 0.25$) gave 3.30 g **8** (10.1 mmol, 84.5%) as a light yellow syrup. IR: $\nu = 2113$ (N_3), 1694 (C=O), 1361 ($MeSO_3$), 1178 ($MeSO_3$) cm^{-1}. ^1H NMR: $\delta = 2.40$ (s, 3H, MeCO), 3.17 (s, 3H, $MeSO_3$), 3.27 (dd, 1H, H-5), 3.32 (dd, 1H, H-5′),

3.39 (s, 3H, OMe), 4.16 (dd, 1H, H-2), 4.30 (m, 1H, H-4), 4.61 (dd, 1H, H-3), 4.89 (d, 1H, H-1). $J_{1,2} = 1.2$, $J_{2,3} = 2.7$, $J_{3,4} = 5.7$, $J_{4,5} = 5.4$, $J_{4,5'} = 5.1$, $J_{5,5'} = 14.4$ Hz. ^{13}C NMR: $\delta = 30.2$ (C-5), 30.5 (CH_3CO), 38.5 ($MeSO_3$), 55.2 (OMe), 70.4 (C-2), 79.6 (C-4), 83.4 (C-3), 106.7 (C-1), 195.0 (C=O).

Methyl 3,5-Anhydro-2-azido-2-deoxy-3-thio-α-D-lyxofuranoside (9)

Compound **9** was prepared as described for **7** from **8** (3.06 g, 9.40 mmol) and $NaHCO_3$ (1.14 g, 16.8 mmol) in MeOH (analytical grade, 340 mL). Reaction time: 3 h. CC (EtOAc/PE 1:2, $R_f = 0.71$) gave 1.00 g **9** (5.34 mmol, 56.8%) as a colorless syrup. $[\alpha]_D^{20} = +26$ (c1.40, $CHCl_3$). IR: $\nu = 2107$ (N_3) cm^{-1}. ^{1}H NMR: $\delta = 3.08$ (dd, 1H, H-5), 3.46 (s, 3H, OMe), 3.47 (dd, 1H, H-5′), 3.93 (dd, 1H, H-2), 4.20 (dd, 1H, H-3), 5.13 (ddd, 1H, H-4), 5.32 (d, 1H, H-1). $J_{1,2} = 3.1$, $J_{2,3} = 6.9$, $J_{3,4} = 6.3$, $J_{4,5} = 3.0$, $J_{4,5'} = 6.3$, $J_{5,5'} = 10.6$ Hz. ^{13}C NMR: $\delta = 31.9$ (C-5), 45.8 (C-3), 56.3 (OMe), 67.2 (C-2), 79.5 (C-4), 108.0 (C-1). MS; m/z: 156 [M − OMe].$^+$ $C_6H_9O_2N_3S$ (187.2): calcd.: C, 38.49; H, 4.85; N, 22.44; S, 17.13; found: C, 38.46; H 4.89: N, 21.30; S, 17.45.

Methyl 3-Azido-3-deoxy-β-D-xylofuranoside (11)

Compound **11** was prepared as described for **2** from methyl 2,3-anhydro-β-D-ribofuranoside[13] (**10**, 2.56 g, 15.5 mmol), NaN_3 (4.02 g, 61.8 mmol), and NH_4Cl (3.04 g, 56.8 mmol) in EtOH (90 mL)/H_2O (20 mL). Reaction time: 12 d. CC (EtOAc/PE, $R_f = 0.27$) gave 2.47 g **11** (13.1 mmol, 74.5%) as a colorless syrup. ^{1}H NMR: $\delta = 2.80$ (bs, 2H, OH), 3.45 (s, 3H, OMe), 3.73 (dd, 1H, H-5), 3.78 (dd, 1H, H-5'), 4.11 (dd, 1H, H-3), 4.36 (dd, 1H, H-2), 4.39 (m, 1H, H-4), 4.86 (d, 1H, H-1). $J_{1,2} = 2.3$, $J_{2,3} = 4.9$, $J_{3,4} = 7.1$, $J_{4,5} = 4.5$, $J_{4,5'} = 4.2$, $J_{5,5'} = 12.3$ Hz. ^{13}C NMR: $\delta = 56.2$ (OMe), 62.1 (C-5), 66.7 (C-3), 80.1 (C-2), 80.5 (C-4), 109.3 (C-1).

Methyl 5-S-Acetyl-3-azido-3-deoxy-5-thio-β-D-xylofuranoside (12)

Compound **12** was prepared as described for **4** from **11** (1.46 g, 7.72 mmol), DIAD (1.74 mL, 9.02 mmol), PPh_3 (2.42 g, 9.22 mmol) and thioacetic acid (0.69 mL, 9.69 mmol) in THF (50 mL). Reaction time: 20 h. CC (EtOAc/PE 1:1, $R_f = 0.36$) gave 1.50 g **12** (6.07 mmol, 78.6%) as a colorless syrup. ^{1}H NMR: $\delta = 2.36$ (s, 3H, CH_3CO), 2.88 (bs, 1H, OH), 3.07 (dd, 1H, H-5), 3.13 (dd, 1H, H-5′), 3.49 (s, 3H, OMe), 3.99 (dd, 1H, H-3), 4.24 (d, 1H, H-2), 4.28 (m, 1H, H-4), 4.94 (s, 1H, H-1). $J_{1,2} = 4.5$, $J_{2,3} = 4.5$, $J_{3,4} = 5.8$, $J_{4,5} = 6.3$, $J_{4,5'} = 7.0$, $J_{5,5'} = 13.8$ Hz.

^{13}C NMR: $\delta = 30.3$ (C-5), 30.5 (CH_3CO), 55.8 (OMe), 67.5 (C-3), 79.6 (C-4), 80.2 (C-2), 109.4 (C-1).

Methyl 5-S-Acetyl-3-azido-3-deoxy-2-O-mesyl-5-thio-β-D-xylofuranoside (13)

Compound **13** was prepared as described for **6** from **12** (1.76 g, 7.10 mmol) and mesyl chloride (0.68 mL, 8.80 mmol) in pyridine (50 mL). Reaction time: 16 h. CC (EtOAc/petroleum ether 1:2, R_f = 0.65) gave 1.87 g **13** (5.75 mmol, 81.0%) as a light yellow syrup. ^{1}H NMR: $\delta = 2.38$ (s, 3H, MeCO), 3.12 (s, 3H, $MeSO_3$), 3.17 (d, 1H, H-5), 3.19 (d, 1H, H-5′), 3.43 (s, 3H, OMe), 4.31 (dd, 1H, H-3), 4.39 (m, 1H, H-4), 4.98 (dd, 1H, H-2), 5.01 (d, 1H, H-1). $J_{1,2} = 1.0$, $J_{2,3} = 2.4$, $J_{3,4} = 5.9$, $J_{4,5} = 6.3$, $J_{4,5'} = 1.3$ Hz. ^{13}C NMR: $\delta = 30.0$ (C-5), 30.5 (CH_3CO), 38.5 ($MeSO_3$), 56.0 (OMe), 65.6 (C-3), 79.7 (C-4), 85.5 (C-2), 106.7 (C-1), 194.9 (C=O).

Methyl 2,5-Anhydro-3-azido-3-deoxy-2-thio-β-D-lyxofuranoside (14)

Compound **14** was prepared as described for **7** from **13** (1.50 g, 4.61 mmol) and $NaHCO_3$ (0.77 g, 9.22 mmol) in MeOH (analytical grade, 120 mL). Reaction time: 2 h. CC (EtOAc/PE 1:3, R_f = 0.40) gave 0.69 g **14** (3.68 mmol, 79.8%) as a colorless syrup. ^{1}H NMR: $\delta = 2.90$ (m, 2H, H-5, H-5′), 3.40 (s, 3H, OMe), 3.50 (m, 1H, H-2), 4.30 (m, 1H, H-3), 4.50 (m, 1H, H-4), 5.20 (m, 1H, H-1). ^{13}C NMR: $\delta = 34.8$ (C-5), 51.2 (C-2), 56.7 (OMe), 64.9 (C-3), 78.8 (C-4), 106.7 (C-1).

Methyl 2,3-di-O-mesyl-5-O-trityl-β-D-ribofuranoside (16)

Compound **16** was prepared as described for **6** from methyl 5-*O*-trityl-β-D-ribofuranoside[19] (**15**, 0.25 g, 0.62 mmol) and mesyl chloride (0.05 mL, 0.65 mmol) in pyridine (5 mL). Reaction time: 66 h. Recrystallisation from EtOAc/PE gave 0.29 g, **16** (0.52 mmol, 84.6%) as a light yellow solid. $R_f = 0.56$ (EtOAc/PE 1:1). ^{1}H NMR: $\delta = 2.86$ (s, 3H, $MeSO_3$), 3.13 (s, 3H, $MeSO_3$), 3.14 (dd, 1H, H-5), 3.49 (s, 3H, OMe), 3.54 (dd, 1H, H-5′), 4.31 (m, 1H, H-4), 5.09 (dd, 1H, H-2), 5.15 (d, 1H, H-1), 5.28 (dd, 1H, H-3), 7.23–7.34 (m, 9H, H_{ar}), 7.44–7.48 (m, 6H, H_{ar}). $J_{1,2} = 1.7$, $J_{2,3} = 4.6$, $J_{3,4} = 6.5$, $J_{4,5} = 3.2$, $J_{4,5'} = 3.5$, $J_{5,5'} = 10.7$ Hz. ^{13}C NMR: $\delta = 37.8$ ($MeSO_3$), 38.4 ($MeSO_3$), 56.1 (OMe), 62.0 (C-5), 76.7 (C-3), 79.6 (C-4), 80.0 (C-2), 87.0 (C_q), 105.8 (C-1), 127.26, 127.30, 128.0, 143.3 (each 1 C_{ar}).

*Methyl 3-Azido-3-deoxy-2-*O*-mesyl-5-*O*-triphenylmethyl-β-*D*-xylofuranoside (17)*

Compound **17** was prepared as described for **2** from **16** (22.73 g, 40.40 mmol) and NaN_3 (12.93 g, 198.9 mmol) in dry DMF (120 mL). The reaction time was 43 h at 110°C. CC (EtOAc/PE 1:2, $R_f = 0.27$) gave **17** (6.93 g, 13.6 mmol, 34.0%) as a light yellow syrup. ^{1}H NMR: $\delta = 3.06$ (s, 3H, $MeSO_3$), 3.33 (dd, 1H, H-5), 3.37 (s, 3H, OMe), 3.40 (dd, 1H, H-5′), 4.28 (dd, 1H, H-3), 4.45 (ddd, 1H, H-4), 4.99 (dd, 1H, H-2), 5.01 (d, 1H, H-1), 7.20–7.49 (m, 15H, ArH). $J_{1,2} = 1.6$, $J_{2,3} = 2.8$, $J_{3,4} = 5.9$, $J_{4,5} = 5.6$, $J_{4,5'} = 5.9$, $J_{5,5'} = 10.0$ Hz. ^{13}C NMR: $\delta = 38.4$ ($MeSO_3$), 56.0 (OMe), 62.8 (C-5), 64.7 (C-3), 79.9 (C-4), 85.1 (C-2), 87.3 (C_q), 106.6 (C-1), 127.0, 127.9, 128.7, 143.6 (C_{ar}).

*Methyl 3-Azido-3-deoxy-2-*O*-mesyl-β-*D*-xylofuranoside (18)*

A solution of BF_3-MeOH complex (20%, 17.8 mmol) in MeOH (10 mL) was added to a solution of **17** (6.93 g, 13.6 mmol) in CH_2Cl_2 (50 mL). The mixture was stirred r.t. for 40 h. Solvents were distilled off, and the residue was purified by CC (EtOAc/PE 1:1, $R_f = 0.37$) to yield 9.93 g **18** (1.96 g, 7.33 mmol, 54.0%) as a light yellow syrup. $R_f = 0.56$ (EtOAc/Pe 2:1). ^{1}H NMR: $\delta = 2.45$ (bs, 1H, OH), 3.14 (s, 3H, $MeSO_3$), 3.48 (s, 3H, OMe), 3.76 (dd, 1H, H-5), 3.81 (dd, 1H, H-5'), 4.36 (dd, 1H, H-3), 4.43 (m, 1H, H-4), 5.07 (d, 1H, H-1), 5.08 (dd, 1H, H-2). $J_{1,2} = 2.1$, $J_{2,3} = 4.6$, $J_{3,4} = 7.2$, $J_{4,5} = 4.1$, $J_{4,5'} = 4.0$, $J_{5,5'} = 12.5$ Hz. ^{13}C NMR: $\delta = 38.4$ ($MeSO_3$), 56.4 (OMe), 61.8 (C-5), 64.8 (C-3), 80.9 (C-4), 86.1 (C-2), 106.7 (C-1).

*Methyl 5-*S*-Acetyl-3-azido-3-deoxy-2-*O*-mesyl-5-thio-β-*D*-xylofuranoside (13)*

Compound **13** was prepared as described for **4** from **18** (0.18 g, 0.67 mmol), DIAD (0.15 mL, 0.79 mmol), PPh_3 (0.21 g, 0.80 mmol), and thioacetic acid (0.06 mL, 0.80 mmol) in dry THF (14 mL). Reaction time: 16 h. CC (EtOAc/PE 1:1) gave 0.18 g **13** (0.55 mmol, 81.6%) with spectroscopic data, which agreed with the ones previously described.

*Methyl 2,3-*O*-Sulfinyl-5-*O*-triphenylmethyl-β-*D*-ribofuranoside (19)*

A solution of **15** (3.30 g, 8.13 mmol) and triethyl amine (4.60 mL, 33.2 mmol) in dry THF (40 mL) was cooled to −17°C. Thionyl chloride (1.20 mL, 16.6 mmol) was dropped in under stirring to maintain the temperature between −15°C and −10°C. Stirring was continued for 1 h. Then EtOAc was added and the solution was washed twice with satd. NaCl solution. The organic solvents were evaporated in a vacuum. CC

of the residue (EtOAc/PE 1:1, $R_f = 0.57$) gave **19** (3.47 g, 7.67 mmol, 94.3%) as a light yellow syrup. ^{1}H NMR: $\delta = 3.51$ (s, 3H, OMe), 3.73 (dd, 1H, H-5), 3.76 (dd, 1H, H-5′), 4.79 (dd, 1H, H-4), 5.10 (d, 1H, H-3), 5.31 (s, 1H, H-2), 5.35 (s, 1H, H-1), 7.25–7.33 (m, 15H, ArH). $J_{4,5} = 2.6$, $J_{4,5'} = 2.4$, $J_{5,5'} = 12.8$ Hz. ^{13}C NMR: $\delta = 56.1$ (OMe), 63.6 (C-5), 85.5 (C-2), 87.2 (C-4), 88.0 (C-3), 108.6 (C-1), 127.3, 127.7, 127.9, 146.9 (C_{ar}).

Methyl 3-Azido-3-deoxy-5-O-triphenylmethyl-β-D-xylofuranoside (20)

A solution of **19** (1.12 g, 2.47 mmol) and NaN_3 (0.66 g, 10.2 mmol) in dry DMSO (15 mL) was heated to 130°C for 40 h. The solvent was distilled off in a vacuum. CC of the residue (EtOAc/PE 1:2) gave **20** (0.53 g, 1.23 mmol, 49.8%) as a light yellow syrup. $R_f = 0.45$ (EtOAc/PE 1:1). IR: $\nu = 3421$ (OH), 2105 (N_3). ^{1}H NMR: $\delta = 2.46$ (d, 1H, OH), 3.29 (dd, 1H, H-5), 3.43 (s, 3H, OMe), 3.39 (dd, 1H, H-5'), 3.95 (d, 1H, H-3), 4.23 (m, 1H, H-2), 4.49 (ddd, 1H, H-4), 4.81 (d, 1H, H-1), 7.20–7.50 (m, 15H, ArH). $J_{1,2} = 1.1$, $J_{2,OH} = 3.6$, $J_{2,3} = 2.5$, $J_{3,4} = 5.6$, $J_{4,5} = 5.7$, $J_{4,5'} = 6.3$, $J_{5,5'} = 9.8$ Hz. ^{13}C NMR: $\delta = 56.2$ (OMe), 62.1 (C-5), 66.8 (C-3), 80.4 (C-2), 80.6 (C-4), 87.1 (C_q), 109.3 (C-1), 127.3, 127.7, 127.9, 146.9 (C_{ar}).

1-(2,5-Anhydro-3-azido-3-deoxy-2-thio-α-D-lyxofuranosyl)thymine (21)

A solution of thymine (0.100 g, 0.793 mmol) and a catalytic amount of $(NH_4)_2SO_4$ in hexamethyldisilazane (HMDS, 2 mL) was refluxed under the exclusion of moisture for 2 h. Excess HMDS was distilled off under Ar and then codistilled with xylene (3×). Compound **7** (0.100 g, 0.534 mmol) in dry acetonitrile (4 mL) was added to the residue under a dry Ar atmosphere. The resulting solution was cooled to −40°C. Trimethylsilyl triflate (0.13 mL, 0.694 mmol) was added under vigorous stirring. Stirring was continued for 2 h at −40°C and finally over night at r.t. The reaction mixture was diluted with CH_2Cl_2 and washed with $NaHCO_3$ solution. The organic layer was dried over Na_2SO_4 and evaporated. CC (EtOAc, $R_f = 0.45$) gave 0.082 g **21** (0.29 mmol, 54.3%) as colorless crystals, m.p. 108°C. $[\alpha]_D^{20} = -38$ (c1.0, $CHCl_3$). UV: $\lambda_{max}(\lg \varepsilon) = 209$ nm (1.23), 267 nm (1.37); $\lambda_{min}(\log \varepsilon) = 234$ nm (0.24). ^{1}H NMR: $\delta = 1.95$ (d, 3H, CH_3), 3.03 (dd, 1H, H-5′$_a$), 3.11 (dd, 1H, 5′$_b$), 3.92 (d, 1H, H-2′), 4.15 (dd, 1H, H-3′), 4.76 (ddd, 1H, H-4′), 5.80 (s, 1H, H-1′), 7.28 (q, 1H, H-6), 9.30 (bs, 1H, NH). $J_{2',3'} = 2.2$, $J_{3',4'} = 2.8$, $J_{4',5'a} = 1.3$, $J_{4',5'b} = 1.8$, $J_{5'a,5b'} = 11.0$, $J_{6,Me} = 1.2$ Hz. ^{13}C NMR: $\delta = 12.8$ (CH_3), 34.6 (C-5′), 50.0 (C-2′), 62.3 (C-3′), 79.0 (C-4′), 92.5 (C-1′), 110.3 (C-5), 133.9 (C-6), 150.0 (C2=O), 163.8 (C4=O).

1-(2,5-Anhydro-3-azido-3-deoxy-2-thio-α-D-lyxofuranosyl)thymine (S)-S-oxide (22)

A solution of *meta*-chloroperbenzoic acid (MCPBA, 70%, 0.049 g, 0.20 mmol) in CH_2Cl_2 (5 mL) was dropped into a solution of **21** (0.032 g, 0.12 mmol) in CH_2Cl_2 (5 mL). After 30 min, (TLC control) satd. $NaHCO_3$-solution and $Na_2S_2O_3$-solution were added. The mixture was extracted with CH_2Cl_2 (3×). The extract was dried with Na_2SO_4 and evaporated. CC (EtOAc/PE 3:1, $R_f = 0.51$) gave 0.025 g **22** (0.080 mmol, 73.8%) as colorless crystals. UV: λ_{max} (lg ε) = 211 nm (0.67), 266 nm (0.76); λ_{min} (log ε) = 235 nm (0.20). IR: ν = 3269 (NH), 2121 (N_3), 1697 (C=O), 1676 (C=O), 1058 (S=O) cm^{-1}. ^1H NMR (CD_3OD): $\delta = 1.93$ (d, 3H, Me), 2.54 (dd, 1H, H-5′$_a$), 3.63 (dd, 1H, 5′$_b$), 4.45 (d, 1H, H-2′), 4.89 (dd, 1H, H-3′), 5.07 (dd, 1H, H-4′), 6.40 (s, 1H, H-1′), 7.63 (q, 1H, H-6), $J_{2',3'} = 2.2$, $J_{3',4'} = 5.6$, $J_{4',5'a} = 2.1$, $J_{4',5'b} = 2.3$, $J_{5'a,5b'} = 14.0$, $J_{6,Me} = 1.2$ Hz. ^{13}C NMR (CD_3OD): $\delta = 11.2$ (CH_3), 55.3 (C-5′), 61.9 (C-2′), 64.1 (C-3′), 79.4 (C-4′), 80.3 (C-1′), 111.7 (C-5), 136.1 (C-6), 151.2 (C2=O), 164.4 (C4=O).

Methyl 3,5-Anhydro-2-azido-2-deoxy-3-thio-α-D-lyxofuranoside (R)-S-oxide (23)

H_2O_2 (30%, 5.0 mL, 90 mmol) was slowly added to a solution of **9** (0.660 g, 3.53 mmol) in MeOH (50 mL). After 72 h of stirring at r.t., the reaction mixture was poured into satd. NaCl-solution and extracted with CH_2Cl_2. The extract was dried with $MgSO_4$ and evaporated. CC (EtOAc/PE 2:1, $R_f = 0.22$) of the residue gave 0.38 g of **23** (1.87 mmol, 53.0%) as colorless crystals, m.p. 163°C. ^1H NMR: $\delta = 3.17$ (ddd, 1H, H-5), 3.36 (s, 3H, OMe), 3.66 (ddd, 1H, H-5′), 3.95 (dddd, 1H, H-3), 4.42 (dd, 1H, H-2), 5.05 (d, 1H, H-1), 5.23 (ddd, 1H, H-4). $J_{1,2} = 1.0$, $J_{2,3} = 7.5$, $J_{3,4} = 5.9$, $J_{3,5} = 0.9$, $J_{3,5'} = 1.1$, $J_{4,5} = 5.7$, $J_{4,5'} = 1.1$, $J_{5,5'} = 13.0$ Hz. ^{13}C NMR: $\delta = 53.1$ (C-5), 55.7 (OMe), 68.9 (C-2), 71.9 (C-3), 74.5 (C-4), 110.9 (C-1).

Methyl 2,5-Anhydro-3-azido-3-deoxy-2-thio-β-D-lyxofuranoside (R)-S-oxide (24), Methyl 2,5-Anhydro-3-azido-3-deoxy-2-thio-β-D-lyxofuranoside (S)-S-oxide (25), and Methyl 2,5-Anhydro-3-azido-3-deoxy-2-thio-β-D-lyxofuranoside S,S-dioxide (26)

Compound **14** (200 mg, 1.07 mmol) was dissolved in CH_2Cl_2 (10 mL). Benzoic acid (131 mg, 1.07 mmol) and benzyltriethylammonium chloride (24 mg, 0.11 mmol) were added, and the mixture was stirred for 10 min. Then, a solution of $KMnO_4$ (338 mg, 2.14 mmol) in H_2O (20 mL) was added, and the two-phase mixture was stirred vigorously

for 12 h. After quenching with $Na_2S_2O_5$, the solution turned colorless and was filtered through celite and extracted with CH_2Cl_2 (2×). The combined organic layers were dried with Na_2SO_4 and evaporated. Purification and separation of the residue by CC (EtOAc/PE 1:1) gave 8 mg **24** (0.04 mmol, 3.7%), 163 mg **25** (0.80 mmol, 75.0%), and 16 mg **26** (0.07 mmol, 6.9%). **24**: colorless syrup. $R_f = 0.22$ (EtOAc/PE 2:1). IR: $\nu = 3446$ (OH), 2129 (N_3), 1057 (S=O) cm^{-1}. ^1H NMR: $\delta = 3.43$ (m, 1H, H-5), 3.44 (m, 1H, H-5′), 3.54 (s, 3H, OMe), 3.70 (m, 1H, H-2), 4.70 (m, 1H, H-4), 4.71 (m, 1H, H-3), 5.30 (d, 1H, H-1). $J_{1,2} = 2.4$ Hz. ^{13}C NMR: $\delta = 58.4$ (OMe), 59.6 (C-5), 62.1 (C-2), 63.3 (C-3), 77.2 (C-4), 103.6 (C-1). MS; $m/z = 218$ [$M^{+\cdot}$]. **25**: slightly yellow syrup: $R_f = 0.23$ (EtOAc/PE 2:1). IR: $\nu = 2131$ (N_3), 1053 (S=O) cm^{-1}. ^1H NMR: $\delta = 3.18$ (ddd, 1H, H-5), 3.28 (m, 1H, H-5′), 3.44 (s, 3H, OMe), 3.67 (m, 1H, H-2), 4.76 (m, 1H, H-4), 4.99 (m, 1H, H-3), 5.36 (s, 1H, H-1). $J_{2,5} = 1.4$, $J_{2,5'} = 0.7$, $J_{4,5} = 1.5$, $J_{4,5'} = 2.1$, $J_{5,5'} = 12.7$ Hz. ^{13}C NMR: $\delta = 56.3$ (OMe), 56.7 (C-5), 63.4 (C-3), 64.8 (C-2), 77.2 (C-4), 102.3 (C-1). **26**: colorless crystals, m.p. 157°C $R_f = 0.32$ (EtOAc/PE 2:1). $[\alpha]_D^{20} = +40$ (c1.0, $CHCl_3$). IR: $\nu = 2121$ (N_3), 1319 (SO_2), 1153 (SO_2) cm^{-1}. ^1H NMR: $\delta = 3.25$ (dd, 1H, H-5), 3.42 (dd, 1H, H-5′), 3.46 (s, 3H, OMe), 4.38 (dd, 1H, H-3), 4.88 (ddd, 1H, H-4), 5.01 (d, 1H, H-2), 5.07 (d, 1H, H-1). $J_{1,2} = 1.1$, $J_{2,3} = 2.2$, $J_{3,4} = 5.7$, $J_{4,5} = 3.3$, $J_{4,5'} = 8.9$, $J_{5,5'} = 14.9$ Hz. ^{13}C NMR: $\delta = 53.6$ (C-5), 57.0 (OMe), 65.8 (C-3), 75.7 (C-4), 84.5 (C-2), 107.4 (C-1). $C_6H_9O_4N_3S$ (219.2): calcd: C, 32.87; H, 4.14; N, 19.17; S, 14.63; found: C, 32.78; H, 4.09; N, 19.22; S, 14.59.

Methyl 2,5-Anhydro-3-azido-3-deoxy-2-thio-α-D-lyxofuranoside (S)-S-oxide (27), Methyl 2,5-Anhydro-3-azido-3-deoxy-2-thio-α-D-lyxofuranoside (R)-S-oxide (28), and methyl 2,5-Anhydro-3-azido-3-deoxy-2-thio-α-D-lyxofuranoside S,S-dioxide (29)

Compound **7** (1.00 g, 5.34 mmol) was oxidized with MCPBA (70%, 2.70 g, 11.0 mmol) in CH_2Cl_2 (150 mL) as described for the preparation of **22**. Reaction time: 30 min. Purification and separation by CC (EtOAc/PE, gradient 1:1 to 2:1) gave 0.090 g **27** (0.44 mmol, 8.2%), 0.430 g **28** (2.12 mmol, 39.7%), and 0.40 g **29** (1.82 mmol, 34.1%). **27**: colorless crystals, m.p. 119°C. $R_f = 0.63$ (EtOAc). IR: $\nu = 3371$ (OH), 2121 (N_3), 976 (S=O) cm^{-1}. ^1H NMR: $\delta = 2.54$ (d, 1H, H-5), 3.46 (s, 3H, OMe), 3.61 (dd, 1H, H-5′), 4.04 (d, 1H, H-3), 4.79 (m, 1H, H-2), 4.84 (m, 1H, H-4), 5.41 (s, 1H, H-1). $J_{3,4} = 2.1$, $J_{4,5} = 2.2$, $J_{5,5'} = 13.4$ Hz. ^{13}C NMR: $\delta = 55.1$ (C-5), 56.4 (OMe), 58.8 (C-2), 64.8 (C-3), 80.2 (C-4), 99.8 (C-1). **28**: colorless syrup. $R_f = 0.37$ (EtOAc). ^1H NMR: $\delta = 2.49$ (d, 1H, H-5), 3.35 (dd, 1H, H-5′), 3.46 (s, 3H, OMe), 3.99 (s, 1H, H-3),

4.74 (s, 2H, H-2, H-4), 5.41 (s, 1H, H-1). $J_{4,5} = 1.5$, $J_{5,5'} = 13.3$ Hz. ^{13}C NMR: $\delta = 55.2$ (C-5), 56.4 (OMe), 63.2 (C-3), 65.9 (C-2), 77.9 (C-4), 98.7 (C-1). **29**: colorless crystals, m.p. 142°C. $R_f = 0.56$ (EtOAc). ^{1}H NMR: $\delta = 3.47$ (s, 3H, OMe), 4.18 (dd, 1H, H-5), 4.30 (dd, 1H, H-2), 4.31 (ddd, 1H, H-5′), 4.89 (ddd, 1H, H-3), 5.04 (dd, 1H, H-4), 5.35 (d, 1H, H-1). $J_{1,2} = 3.2$, $J_{2,3} = 7.9$, $J_{3,4} = 6.1$, $J_{4,5} = 2.0$, $J_{4,5'} = 6.1$, $J_{5,5'} = 14.1$ Hz. ^{13}C NMR: $\delta = 57.0$ (OMe), 64.8 (C-3), 67.4 (C-2), 72.1 (C-5), 83.4 (C-4), 110.7 (C-1). $C_6H_9O_4N_3S$ (219.2): calcd.: C, 32.87; H, 4.14; N, 19.17; S, 14.63; found: C, 32.62; H, 4.09; N, 18.77; S, 14.60.

Methyl 2,5-Anhydro-3-azido-3-deoxy-2-thio-β-D-lyxofuranoside (R)-S-Oxide (25)

Compound **25** was also obtained by the oxidation of **14** (22 mg, 0.12 mmol) with MCPBA (69 mg, 0.40 mmol) in CH_2Cl_2 (15 mL) as described for **28**. Reaction time: 2 h. Yield: 13 mg (0.060 mmol, 50.5%). The spectroscopic data agreed with the ones previously described.

Methyl 3-Amino-2,5-anhydro-3-deoxy-2-thio-α-D-lyxofuranoside (30)

PPh_3 (0.168 g, 0.64 mmol) was added to a solution of **7** (0.100 g, 0.53 mmol) in THF (5 mL). The solution was stirred at r.t. until **7** was consumed (TLC control, ca. 16 h). H_2O (40 μL, 2.0 mmol) was added, and the solution was heated at 60°C for 5 h and then stirred at r.t. for 60 h. The solvent was distilled off in a vacuum. Purification of the residue by CC (EtOAc/PE 3:1 with a trace of NH_3, $R_f = 0.39$) gave 0.055 g **30** (0.34 mmol, 64.2%) as a colorless syrup. IR: $\nu = 3371$ (NH_2), 3324 (NH_2), 3289 (NH_2), 3225 (NH_2) cm^{-1}. ^{1}H NMR: $\delta = 1.68$ (bs, 2H, NH_2), 2.95 (dd, 1H, H-5), 3.33 (dd, 1H, H-2), 3.46 (s, 3H, OMe), 3.50 (dd, 1H, H-5′), 4.18 (ddd, 1H, H-3), 5.05 (dd, 1H, H-1), 5.10 (ddd, 1H, H-4). $J_{1,2} = 3.8$, $J_{1,3} = 0.4$, $J_{2,3} = 7.2$, $J_{3,4} = 6.3$, $J_{4,5} = 2.7$, $J_{4,5'} = 6.4$, $J_{5,5'} = 10.7$ Hz. ^{13}C NMR: $\delta = 31.4$ (C-5), 48.9 (C-3), 56.5 (OMe), 58.4 (C-2), 79.3 (C-4), 111.0 (C-1).

Methyl 2-Amino-3,5-anhydro-2-deoxy-3-thio-α-D-lyxofuranoside (31)

Compound **31** was prepared as described for **30** from **9** (20 mg, 0.107 mmol), PPh_3 (34 mg, 0.128 mmol) in THF (2 mL), and H_2O (4 μL, 0.21 mmol). Reaction times: 16 h/6 h. CC (EtOAc/PE 3:1 with a trace of NH_3, $R_f = 0.46$) gave 11 mg **31** (0.07 mmol, 63.8%) as a colorless syrup. ^{1}H NMR: $\delta = 1.48$ (bs, 2H, NH_2), 2.76 (dd, 1H, H-5), 2.88 (dd, 1H, H-5′), 3.10 (d, 1H, H-2), 3.36 (s, 3H, OMe), 3.92 (m, 1H, H-3), 4.27 (ddd, 1H, H-4), 4.89 (a, 1H, H-1). $J_{2,3} = 2.0$, $J_{3,4} = 2.9$, $J_{4,5} = 1.4$, $J_{4,5'} = 1.8$,

$J_{5,5'} = 10.7$ Hz. ^{13}C NMR: $\delta = 33.9$ (C-5), 52.7 (C-2), 54.9 (OMe), 56.7 (C-3), 78.3 (C-4), 109.6 (C-1).

Methyl 2-Amino-3,5-anhydro-2-deoxy-3-thio-α-D-lyxofuranoside (R)-S-Oxide (32)

Compound **32** was prepared as described for **30** from **23** (22 mg, 0.108 mmol), and PPh_3 (33 mg, 0.124 mmol) in THF (2 mL), and H_2O (4 μL, 0.21 mmol). Reaction times: 16 h/5 h. CC (EtOAc/PE 3:1 with a trace of NH_3, $R_f = 0.24$) gave 13.3 mg **32** (0.075 mmol, 69.4%) as a colorless syrup. ^{1}H NMR: $\delta = 2.02$ (bs, 2H, NH_2), 3.18 (dd, 1H, H-5), 3.30 (s, 3H, OMe), 3.67 (dd, 1H, H-5′), 3.85 (dd, 1H, H-2), 3.91 (dd, 1H, H-3), 4.79 (d, 1H, H-1), 5.22 (ddd, 1H, H-4). $J_{1,2} = 1.4$, $J_{2,3} = 7.3$, $J_{3,4} = 5.7$, $J_{4,5} = 5.8$, $J_{4,5'} = 0.8$, $J_{5,5'} = 12.9$ Hz. ^{13}C NMR: $\delta = 53.2$ (C-5), 55.8 (OMe), 61.0 (C-2), 74.4 (C-4), 75.8 (C-3), 114.3 (C-1).

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[21] The tosylation of **20** to yield ***methyl 3-azido-3-deoxy-2-O-tosyl-5-O-triphenylmethyl-β-D-xylofuranoside***; a subsequent detritylation to form ***methyl 3-azido-3-deoxy-2-O-tosyl-β-D-xylofuranoside*** and a thio-Mitsunobu reaction of the latter with thioacetic acid led to ***methyl 5-S-acetyl-3-azido-3-deoxy-5-thio-2-O-tosyl-β-D-xylofuranoside***. However, a base-promoted cyclization of this thioacetate to form **14** was not possible [20].
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