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Synthesis of 4-cyanophenyl 4-azido-4-deoxy-1,5-dithio-β-D-xylopyranoside [1,2]

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Abstract

L-Arabinose diethyl dithioacetal was converted, via its 4-azido-5-*S*-benzoyl-4-deoxy-2,3-*O*-isopropylidene-5-thio-D-xylose diethyl dithioacetal, into 4-azido-4-deoxy-5-thio-α-D-xylopyranose triacetate **29**. Glycosidation of **29** with 4-cyanothiophenol in the presence of trimethylsilyl triflate gave the 4-cyanophenyl 2,3-di-*O*-acetyl-4-azido-4-deoxy-1,2-dithio-α- and -β-D-xylopyranosides **31** and **33** as well as 3-*O*-acetyl-2,5-anhydro-4-azido-4-deoxy-5-thio-D-lyxose bis(4-cyanophenyl) dithioacetal **34** in a 8:2:1 respective ratio. Treatment of **29** with hydrogen bromide in acetic acid yielded a 1:4 mixture of 2,3-di-*O*-acetyl-4-azido-4-deoxy-5-thio-D-xylopyranosyl bromide **38** and 2,3-di-*O*-acetyl-5-bromo-5-deoxy-4-thio-L-arabinofuranosyl bromide **40**. Reaction of the mixture of bromides **38** and **40** with 4-cyanothiophenol in the presence of potassium carbonate afforded the expected **31** and **33** only in traces, while 2-(1*R*,2*S*,-1,2-di-*O*-acetyl-1,2-dihydroxy-but-3-en-1-yl)-5-cyano-1,3-benzodithiole and 4-cyanophenyl 2,3-di-*O*-acetyl-5-*S*-(4-cyanophenyl)-1,4,5-trithio-α-L-arabinofuranoside (**42**) were isolated in 18% and 20% yield, respectively. The formation of these two derivatives is tentatively explained by involvement of a radical reaction mechanism. When *O*-(2,3-di-*O*-acetyl-4-azido-4-deoxy-5-thio-α-D-xylopyranosyl) trichloroacetimidate was used as donor and boron trifluoride ethyl etherate as promoter, **31** and **33** were formed in excellent yield (96%) in a 2:1 ratio. The glycosides, obtained on deacetylation of **33**, **34**, and **42** showed a significant antithrombotic activity on rats. © 1997 Elsevier Science Ltd.

Keywords: 4,5-Epithio-D-xylose and 5-azido-5-deoxy-4-thio-D-xylose derivatives; 4-Azido-4-deoxy-5-thio-D-xylose derivatives; Glycosidation reactions; Participation of the sulfur atom; Thioglycosides; Oral antithrombotic activity

1. Introduction

In a previous paper [1], we reported on the synthesis of 4-cyanophenyl 2-azido-2-deoxy- and 3-azido-3-deoxy-1,5-dithio-β-D-xylopyranosides. Both compounds showed on rats stronger oral antithrombotic activity as compared to 4-cyanophenyl 1,5-dithio-β-D-xylopyranoside (beciparcil, **1**) [2]. In order to investigate the role of the position of the azido group on the biological activity, synthesis of the corresponding 4-azido-4-deoxy derivative **2** was decided on. L-

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[1] Orally active antithrombotic thioglycosides, Part III. For Part II, see [1].

[2] Presented partly at the XVIIIth International Carbohydrate Symposium, Milan, July 21–26, 1996. Abstr. BP086.

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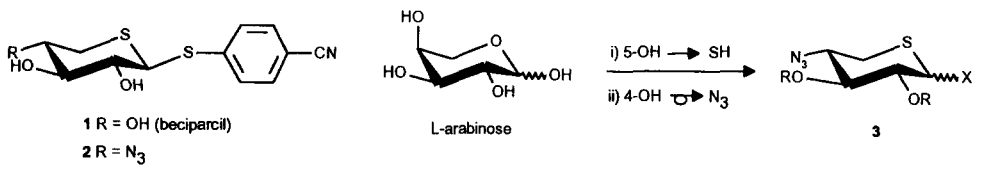
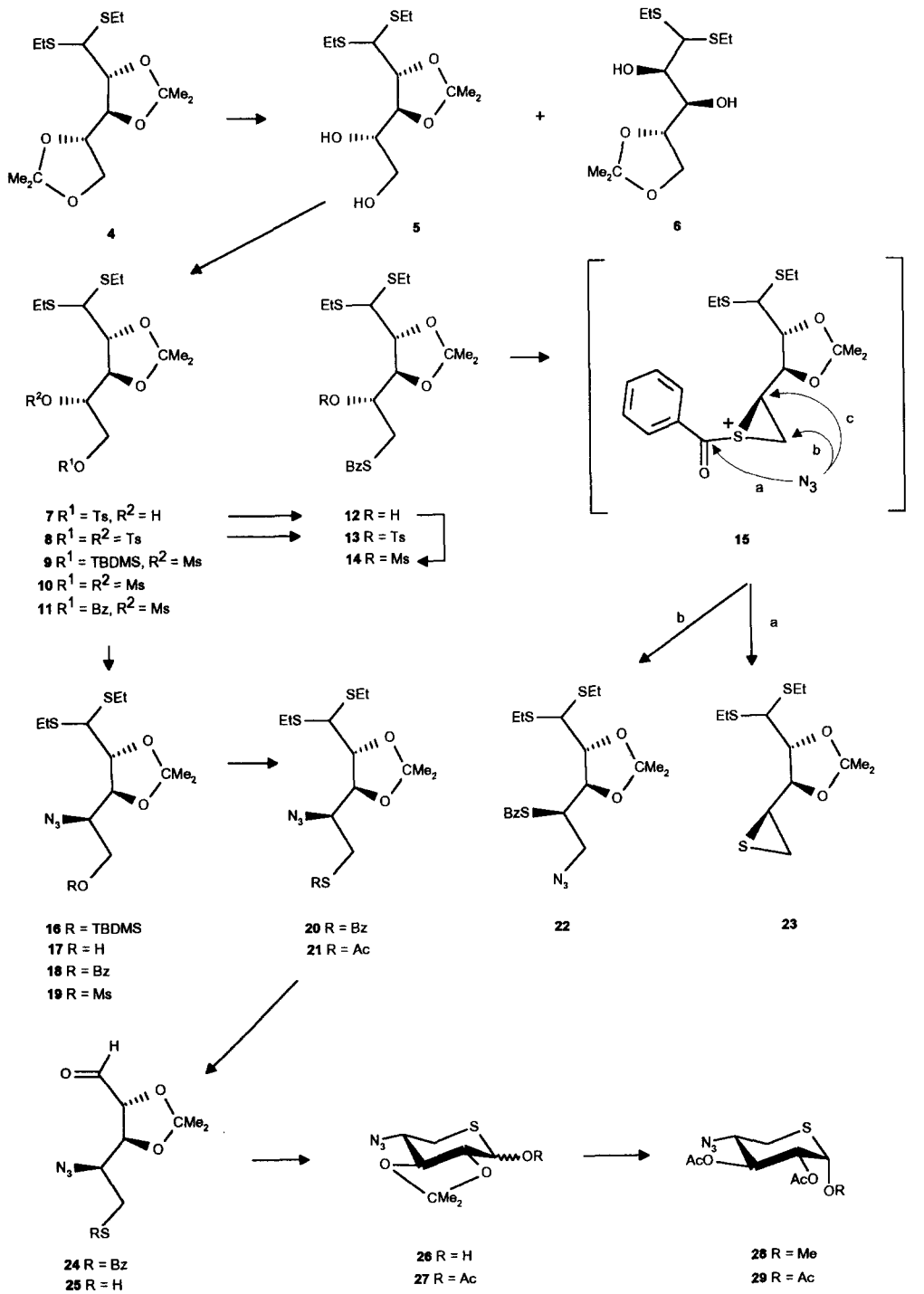


Scheme 1.



Scheme 2.

Arabinose was chosen as starting material, which can be converted into the proper glycosyl donor **3** needed for the glycosidation reaction via two transformations: *i*) introduction of the thiol group at C-5; and *ii*) introduction of the azido group with inversion of the configuration at C-4 (see Scheme 1).

2. Results and discussion

In our first attempt, sequence *i*) → *ii*) was investigated (see Scheme 1). L-Arabinose diethyl dithioacetal was converted with 2,2-dimethoxypropane, in quantitative yield, into its 2,3:4,5-di-*O*-isopropylidene derivative **4** [3]. Partial hydrolysis of **4** in methanol with M hydrochloric acid at 50 °C resulted in the 2,3-*O*-isopropylidene derivative **5** as the main product (91%), together with some L-arabinose diethyl dithioacetal (5%) and traces of the 4,5-*O*-isopropylidene isomer **6**. As an acetal migration (from 2,3-*O* to 4,5-*O*) in **5** under acidic conditions is unlikely to occur [4], **6** is formed either directly from diacetal **4** by selective hydrolysis of the 2,3-*O*-isopropylidene group, or from the reaction of arabinose diethyl dithioacetal with the acetone formed during the hydrolysis.

Partial tosylation of the diol **5** gave the 5-tosylate **7**, which could be smoothly converted with potassium thiobenzoate in acetone into the *S*-benzoate **12**. For the introduction of the azido group at C-4 with inversion of configuration, **12** was treated with tosyl chloride in pyridine, but the reaction was very sluggish (2 d at 60 °C), and the overall yield of **13** (from **5**) remained below 50%. For this reason, the diol **5** was first converted with an excess of tosyl chloride into its ditosylate **8**, which on treatment with potassium thiobenzoate afforded **13** in an overall yield of 67%. The exchange of the tosyloxy group of **13** by azide was carried out in *N*,*N*-dimethylformamide with sodium azide at 60 °C. The reaction was complete in 30 min, and the structure of the formed three compounds was elucidated by NMR spectroscopy after separation by column chromatography. The 5-azido-4-*S*-benzoyl-D-xylose derivative **22** could be isolated as the main product (65%). Its structure became evident by comparing its ^{13}C NMR spectrum with that of **13**. Due to the TsO → BzS exchange at C-4 and the BzS → N_3 exchange at C-5, a strong upfield shift of C-4 (from 80.1 to 45.7 ppm) and a simultaneous downfield shift for C-5 (from 29.4 to 53.7 ppm) was detected. As the value of $J_{3,4}$ 1.5 Hz in **22** differed significantly from that of **13** ($J_{3,4}$ 4.0 Hz), the change of configuration (L-*arabino* → D-*xylo*) can be taken as granted. Benzoyl azide as well as the 4,5-epithio derivative **23** (12%) were isolated as by-products. Their formation is in agreement with the reaction mechanism depicted in Scheme 2. Accordingly, C-4 is attacked first intramolecularly by the sulfur atom of the neighboring benzoylthio group, leading via inversion of configuration at C-4 to the 4,5-episulfonium intermediate **15**, which can be attacked by the azide ion either at the less hindered bridge atom (C-5), yielding **22**, or at the carbonyl group, yielding **23** and benzoyl azide, simultaneously. The intramolecular attack of the benzoylthio group could not be prevented by using mesylate **14** instead of tosylate **13**, as even in this case the 5-azido derivative **22** was formed as the main component. The structure of **23** could be proved chemically too, as it was formed in quantitative yield from the mixed esters **13** and **14**, respectively, on treatment with methanolic sodium methoxide.

In order to avoid this rearrangement reaction, sequence *ii*) → *i*) was investigated. Accordingly, the azide had to be introduced at C-4 first, making the selective activation of HO-4 necessary. For this reason, the terminal hydroxyl group of diol **5** was first protected by *tert*-butyldimethylsilylation to give, after subsequent treatment with mesyl chloride, in a one-pot reaction, the mixed ester **9** (87%). Exchange of the mesyloxy group by azide in *N*,*N*-dimethylformamide was a slow reaction even at 110 °C (15 h), during which partial desilylation took place. The resulting azides **16** and **17** could be separated by column chromatography in 42% and 35% yield, respectively. For the further reaction, the 5-hydroxy derivative **17** was needed. Therefore the crude mixture of **16** and **17** was directly submitted to desilylation in a large scale preparation by treating it with tetrabutylammonium fluoride in tetrahydrofuran, resulting in **17** in 72% yield, i.e. the overall yield from **5** to **17** was 62%. The reaction pathway from **5** to **17** could be further simplified by converting **5** into its dimesylate **10** (100%) and exchanging the terminal mesyloxy group by sodium benzoate affording the mixed ester **11** in high yield (92%). The azide-exchange reaction of **11** gave the expected D-*xylo* derivative **18** (89%), which was debenzoylated to **17** using Zemplén's method. The free hydroxyl group of **17** was mesylated and the resulting ester **19** gave, on treatment with potassium thiobenzoate, the 5-*S*-benzoate **20**. The mercapto groups of **20** were removed in acetone–water with mercury chloride–cadmium

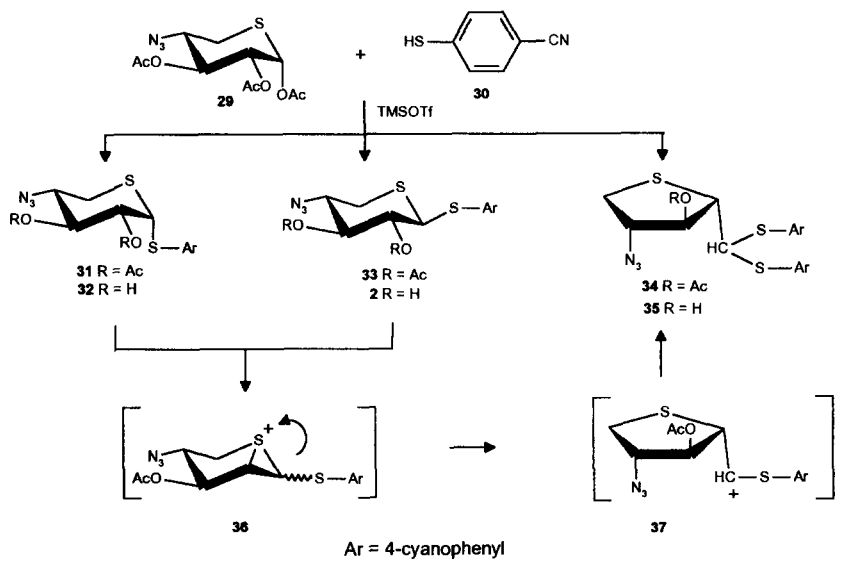
carbonate, and the resulting aldehyde **24** was debenzoylated with sodium methoxide in methanol. In similar reactions, a catalytic amount of sodium methoxide is usually not enough [5,6], because of the acidity of the free thiol group formed. In the present case, however, the thiol group of **25** immediately formed the thiopyranose ring **26**. Therefore, the normal Zemplén conditions were used for the debenzoylation. The structure of **26** was proved by acetylation, whereupon a 2:1 mixture of the corresponding α and β acetates of **27** was formed, which could be resolved by column chromatography. Hydrolysis of crude **26** was carried out with hydrogen chloride in methanol, affording, after acetylation and subsequent column chromatography, the crystalline methyl α-glycoside **28** in 67% yield. The methoxy–acetoxy conversion of **28** was carried out in acetic anhydride–sulfuric acid, and the formed triacetate **29** was used in the glycosidation reactions as donor.

The only drawback of the aforementioned reaction sequence was that the methyl benzoate, formed during the deacylation of **24**, had to be removed by column chromatography, as it prevented the crystallization of **28**. To avoid this step, **19** was treated with potassium thioacetate to give **21** (81%) but, during the removal of the mercapto groups in acetone–water with mercury chloride–cadmium carbonate, decomposition took place and no aldehyde could be isolated.

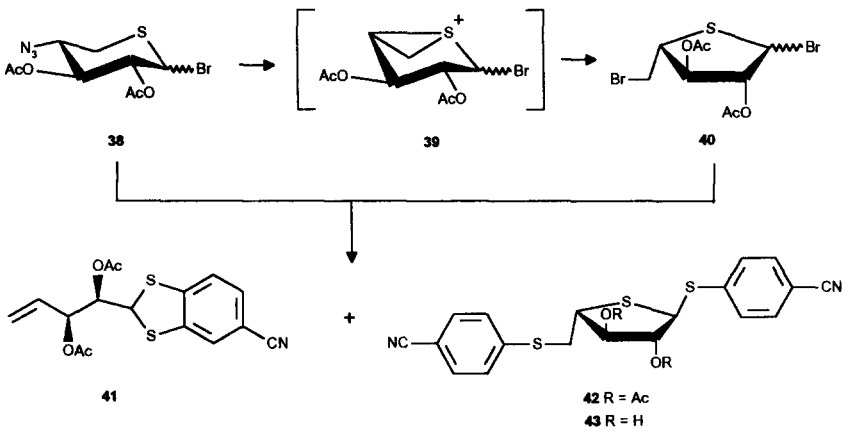
Synthesis of the thioglycosides.—For the glycosidation reaction, the triacetate **29** was used as donor, 4-cyanothiophenol **30** as acceptor and trimethylsilyl triflate as activator of the anomeric acetoxyl group (see Scheme 3). The reaction was carried out in dichloromethane and was completed within 1 h. Under these conditions, an inseparable mixture was obtained (65%) which, according to NMR data, contained three components: the α anomer **31**, the β-glycoside **33**, as well as the 2,5-thioanhydro-D-lyxose mercaptal **34** in a 8:2:1 respective ratio. Deacetylation of the aforementioned mixture afforded **2**, **32**, and **35**, from which the latter could be separated by column chromatography. For structure elucidation, **35** was re-acetylated to **34**, the NOE difference spectra of which was recorded (Table 5) and selective INEPT experiments optimized to 7 Hz heteronuclear coupling were carried out. These proved a three-bond $^{1}H-^{13}C$ connectivity between H-1 (5.18 ppm) and both aromatic C-1′ and C-1″ atoms (140.3 and 140.4 ppm) as well as the α-orientation of C-1. The mercaptal **34** can be formed from both glycoside anomers **31** or **33**, as activation of the 2-acetoxy group by trimethylsilyl triflate can lead via the episulfonium intermediates **36** to the carbonium ion **37** [7,8] which reacts with **30** to yield **34** after deprotonation.

In order to obtain pure **2**, the inseparable mixture of the two anomers **2** and **32** was re-acetylated and, in the absence of **34**, the formed acetates **31** and **33** could be separated by repeated column chromatography. On deacetylation, they gave **32** and **2**, respectively, needed for biological testing.

Because of the preparative difficulties mentioned above and the low ratio of the β anomer **33**, other glycosidation methods were taken into consideration,

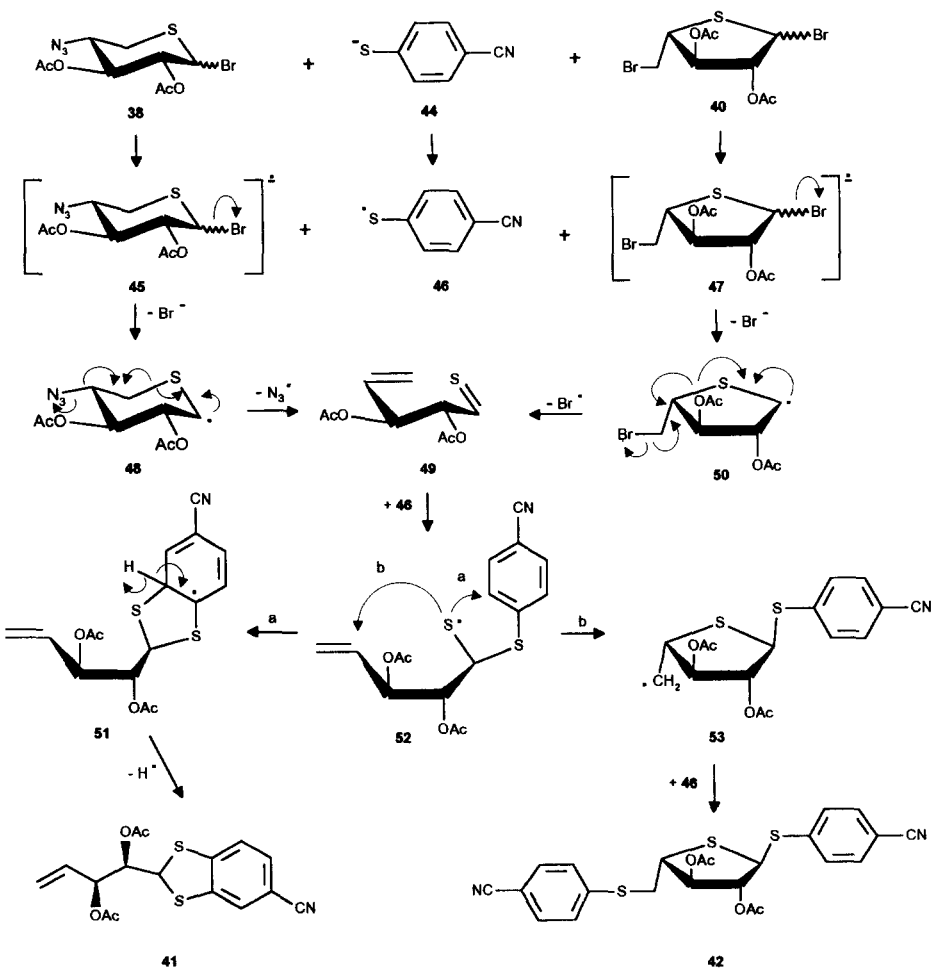


Scheme 3.



Scheme 4.

in particular the reaction of the corresponding acetobromo derivative **38** with the thiolate anion. Accordingly, the α-acetate **29** was treated with hydrogen bromide in acetic acid, but the resulting acetobromo derivative **38** was very unstable and could not be obtained in pure state. NMR investigation of the



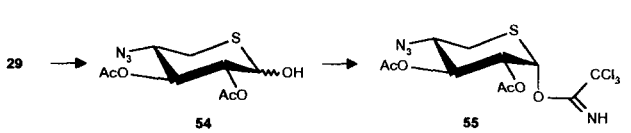
Scheme 5.

crude product revealed, besides **38**, the presence of dibromide **40** as the main component (ratio ~ 1:4). The structure of **40** was evident from the shift of C-4 (from 62.6 to 48.2 ppm) and C-5 (from 28.1 to 34.3 ppm), due to the substitution of the (C-4)–N bond for a (C-4)–S and the (C-5)–S bond for a (C-5)–Br one. Dibromide **40** could be formed via the cyclic episulfonium ion **39** (see Scheme 4), as such intermediates are usually opened by an attack of the corresponding nucleophile at the less hindered bridge atom [7,8]. When the crude mixture of bromides **38** + **40** was reacted (Scheme 4) in acetone with 4-cyanothiophenol in the presence of potassium carbonate at 20 °C the reaction was completed according to TLC within 1 h. The two thioglycoside anomers **31** and **33** were formed in traces only and, from the multicomponent mixture, two compounds, i.e. the open chain unsaturated mercaptal **41** as well as the β-L-arabinofuranoside **42**, containing two 4-cyanothiophenyl groups at C-1 and C-5, could be isolated in 18% and 20% yield, respectively. The ratio of **41** and **42** was not effected when the reaction was carried out at 60 °C, but **31** and **33** were not formed. The structure of **41** was evident from its NMR spectra, proving the presence of the terminal double bond, the two vicinal acetoxy groups, and the dithioacetal moiety. Despite the fact that C-1 is a chiral center, only one diastereomer was observed and isolated, but its relative configuration could not be established. The furanoid structure and the 1,5-position of the arylthio groups in **42** was proved by its NOE difference spectra (Table 5) and selective INEPT experiments optimized to 7 Hz heteronuclear couplings. These proved a three-bond $^{1}H-^{13}C$ connectivity between H-1 (4.89 ppm) and one aromatic C-1′ signal (141.3 ppm), the connectivity between H-5a (3.54 ppm) and the other aromatic C-1″ signal (142.6 ppm), as well as the β-L anomeric configuration. Zemplén deacetylation of **34** and **42** gave **35** and **43**, respectively, which were submitted to biological testing.

While **42** could be formed via substitution of both bromide atoms of **40** by the thiophenolate anion **44**, the formation of **41** can be explained only by a different mechanism (see Scheme 5). Since aromatic thiolate ions react readily via an S_{RN} mechanism [9], it could be presumed that a single-electron transfer (SET) reaction can take place either between bromide **38** or dibromide **40** and the thiolate ion **44**. This reaction would lead to the carbohydrate radical-anions **45** or **47**, respectively, under simultaneous formation of the neutral arylthio radical **46**. The former two radical-anions should yield the neutral carbohydrate radicals **48** and **50**, respectively, via elimination of the bromide ion. Fragmentation of both **48** or **50** could yield the very reactive unsaturated thioaldehyde **49**. Addition of the arylthio radical **46** to the thioaldehyde group of **49** would give a dithioacetal radical **52**. This radical can attack the aromatic ring (route a in Scheme 5), via formation of the cyclic mercapto radical **51**. The latter can undergo stabilization to **41** via elimination of a hydrogen radical. On the other hand, **52** can undergo a cyclization reaction (route b in Scheme 5) [10,11] affording the carbon radical of the thiofuranoside **50** which, on recombination with **46**, would yield the isolated disubstituted derivative **42**. In order to get a deeper insight into the mechanism, the reaction was repeated using 2,2,6,6-tetramethylpiperidine-*N*-oxyl (TEMPO) as scavenger. Under these conditions, the reaction became very sluggish, and even after 5 h at 60 °C only traces of **41** and **42** could be detected. This means that both compounds are probably formed via a radical mechanism.

In our further glycosidation experiments, the trichloroacetimidate procedure [12] was used. Accordingly, triacetate **29** was treated with hydrazine acetate in *N*,*N*-dimethylformamide to yield the 1-hydroxy derivative **54** (75%) as a 9:1 mixture of its α and β anomers (see Scheme 6). Treatment of **54** with trichloroacetonitrile in dichloromethane in the presence of potassium carbonate afforded the crystalline α-imidate **55** (85%). For the coupling of the latter with 4-cyanothiophenol, boron trifluoride ethyl etherate activation was used at −15 °C in acetonitrile, affording the thioglycoside anomers **31** and **33** in good yield (70%) in a 3:1 ratio. When dichloromethane was used as solvent, both the yield (96%) and the anomeric ratio (2:1) were improved.

Biological evaluation.—The oral antithrombotic activity of the β-thiopyranoside **2** (ED_{50} = 6.5 mg/kg), the mercaptal **35** (ED_{50} = 7 mg/kg), and the 1,5-disubstituted thiofuranoside **43** (ED_{50} = 14 mg/kg) was established on rats, using Pescador's model [13] and beciparcil (**1**) as the reference compound (ED_{50} = 25 mg/kg). All compounds were administered orally 3 h before ligation. From the obtained data, it can be seen that exchange of the



Scheme 6.

4-hydroxyl group of **1** by an azido group (**2**) increases the activity 4-fold. More surprising was the high activity of **35** and **43** as they represent structures totally different from **1**. Consequently, the original proposal [2] according to which the thioxylopyranosides exhibit their antithrombotic effect by acting as primers for the biological synthesis of glycosaminoglycans has to be reconsidered.

3. Experimental

General methods.—Organic solns were dried over $MgSO_4$ and concd under diminished pressure at or below 40 °C. TLC: E. Merck precoated Silica Gel 60 F_{254} plates, with hexane–EtOAc mixtures (*A*, 1:1; *B*, 2:1; *C*, 3:1; *D*, 4:1; *E*, 5:1; *F*, 9:1; *G*, 20:1), toluene (*H*), and toluene–MeOH mixtures (*I*, 100:1; *K*, 9:1); detection by spraying the plates with a 0.02 M soln of I_2 and a 0.30 M soln of KI in 10% aq H_2SO_4 soln, followed by heating at ca. 200 °C. For column chromatography, Kieselgel 60 was used. The mp are uncorrected. Optical rotations were determined on 1.0% solns in $CHCl_3$ at 20 °C unless otherwise stated. NMR spectra were recorded with a Bruker AC 250 spectrometer at 250 MHz (^1H) and 62.9 MHz (^{13}C) for solns in $CDCl_3$ (internal Me_4Si) unless

Table 1
Selected ^1H NMR data for 2,3-*O*-isopropylidene-L-arabinose- (**7–14**) and -D-xylose (**16–23**) diethyl dithioacetal derivatives [a] for solutions in $CDCl_3$

Compound	Chemical shifts (δ, ppm)						
	H-1	H-2	H-3	H-4	H-5a	H-5b	CMe_2
7	4.0	4.32	4.0	3.89	4.10	4.25	1.30, 1.42
8	3.85	4.30	4.25	4.77	4.07	4.25	1.29, 1.38
9	3.98	4.50	4.30	4.64	3.85	4.00	1.40, 1.46
10	3.95	4.44	4.34	4.98	4.44	4.63	1.42, 1.48
11	3.95	4.46	4.46	5.15	4.48	4.82	1.46, 1.48
12	4.07	4.40	4.15	3.92	3.21	3.59	1.41, 1.49
13	3.95	4.47	4.50	4.90	3.22	3.46	1.43, 1.47
14	3.96	4.50	4.48	5.02	3.36	3.71	1.44, 1.48
16	3.90	4.35	4.18	3.64	3.90	3.90	1.42, 1.48
17	3.90	4.37	4.23	3.67	3.90	3.90	1.46, 1.48
18	3.94	4.40	4.25	4.00	4.62	4.65	1.44, 1.47
19	3.94	4.36	4.15	3.98	4.48	4.48	1.43, 1.47
20	3.90	4.36	4.21	3.72	3.46	3.46	1.44, 1.46
21	3.90	4.32	4.22	3.56	3.27	3.27	1.44, 1.46
22	3.92	4.15	4.60	4.38		3.58–3.66	1.46, 1.48
23	3.93	4.38	4.01	3.15		2.45–2.55	1.44, 1.47

Compound	Coupling constants (Hz)					
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5a}$	$J_{4,5b}$	$J_{5a,5b}$
8	3.4	6.8	7.2	5.2	2.7	11.4
9	3.1	7.2	7.2	6.8	3.2	11.8
10	3.8	6.9	6.9	6.9	2.3	11.8
11	3.7	nd [b]	nd	7.0	2.5	12.7
12	3.4	6.7	6.7	7.8	2.7	14.3
13	4.5	5.0	4.0	8.1	3.0	14.7
14	4.0	5.0	4.6	7.1	3.6	14.7
16	5.8	7.5	2.1	7.5	5.6	nd
17	5.8	7.4	2.6	4.9	7.5	nd
18	6.2	7.4	2.2	8.1	4.9	11.7
19	6.4	7.4	2.1	6.6	6.6	nd
20	5.9	6.5	2.2	8.2	6.5	nd
21	6.3	6.3	2.4	7.5	7.5	nd
22	6.2	7.5	1.5	8.3	6.7	nd
23	5.6	6.7	6.7	6.7	6.7	1.2

[a] δ 2.60–2.80 (SCH_2CH_3) and 1.30–1.48 ppm (SCH_2CH_3) for all compounds.
[b] nd: Not determined.

Table 2
Selected ^{13}C NMR data for 2,3-*O*-isopropylidene-L-arabinose- **(7–14)** and -D-xylose **(16–23)** diethyl dithioacetal derivatives [a] for solutions in $CDCl_3$

Compound	Chemical shifts (δ, ppm)							
	C-1	C-2	C-3	C-4	C-5	CMe_2	CMe_2	Others
7	53.0	83.7	77.6	71.6	72.0	110.4	26.9, 27.0	21.5 (TsMe)
8	52.7	82.3	78.6 [b]	76.0 [b]	67.4	111.6	26.7, 26.8	21.5 (TsMe)
9	52.9	83.8	82.3 [b]	76.5 [b]	63.1	110.5	26.9, 27.0	38.8 (OMs)
10	52.8	82.6	78.8	76.4	67.9	111.2	26.9, 27.1	39.1, 37.7 (OMs)
11	53.0	82.2	79.5 [b]	77.4 [b]	63.4	111.0	27.0, 27.1	39.0 (OMs), 166.0 (CO)
12	53.0	86.4	80.4	73.0	33.5	110.1	26.9, 27.1	193.2 (CO)
13	53.3	81.3 [b]	80.8 [b]	80.1 [b]	29.4	110.8	26.9, 27.1	21.4 (TsMe), 190.4 (CO)
14	53.1	81.7 [b]	80.5 [b]	79.6 [b]	29.8	110.8	27.0, 27.2	39.0 (OMs), 190.3 (CO)
16	52.7	79.7	78.4	62.9	63.6	111.0	26.9, 27.0	
17	52.5	79.6 [b]	79.5 [b]	62.4	63.0	110.2	26.7, 26.9	
18	52.6	79.6 [b]	78.8 [b]	60.3	64.8	110.4	26.8, 27.0	166.2 (CO)
19	52.4	79.3 [b]	78.2 [b]	60.0	68.6	110.5	26.6, 26.9	37.5 (OMs)
20	53.0	80.7 [b]	79.9 [b]	61.0	30.4	110.4	27.0, 27.2	190.7 (CO)
21	52.7	80.4 [b]	79.6 [b]	60.7	30.4	110.2	26.7, 26.9	30.4 (OAc), 194.5 (CO)
22	53.2	80.9	78.2	45.7	53.7	110.1	27.0, 27.2	190.3 (CO)
23	52.6	83.7 [b]	81.7 [b]	35.6	22.6	109.9	27.2, 27.3	

[a] δ 24.8–25.5 (SCH_2CH_3) and 14.1–14.3 ppm (SCH_2CH_3) for all compounds.
[b] Arbitrary assignment.

Table 3
Selected ^1H NMR data for 4-azido-4-deoxy-5-thio-D-xylopyranose derivatives for solutions in $CDCl_3$ [a]

Compound	Chemical shift (δ)						
	H-1	H-2	H-3	H-4	H-5ax	H-5eq	Others
2 [b]	4.54	3.44	3.34	3.64	2.80	2.66	5.80, 6.00 (OH); 7.60, 7.80 (Ar)
27*α*	6.15	3.98	3.80	3.87	2.82	2.75	1.44, 1.46 (CMe_2); 2.15 (OAc)
27*β*	5.90	3.95	3.48	3.88	2.70	3.03	1.44, 1.47 (CMe_2); 2.12 (OAc)
28	4.60	5.12	5.36	3.78	2.82	2.56	2.05, 2.09 (OAc); 3.40 (OMe)
29	6.06	5.18	5.34	3.86	2.98	2.72	2.02, 2.10, 2.16 (OAc);
31	4.86	5.25	5.36	3.84	3.12	2.74	1.95, 2.12 (OAc); 7.46, 7.60 (Ar)
32 [b]	4.98	3.95	3.44	3.64		2.60–2.80	5.70, 5.95 (OH); 7.55, 7.75 (Ar)
33	4.20	5.16	4.96	3.86		2.66–2.86	2.02, 2.10 (OAc); 7.45–7.60 (Ar)
54*α*	5.13	5.15	5.45	3.82	3.14	2.70	2.10, 2.13 (OAc)
55	6.18	5.18	5.39	3.85	3.00	2.69	1.95, 2.05 (OAc); 8.60 (NH)

Compound	Coupling constants (Hz)						
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5ax}$	$J_{4,5eq}$	$J_{5ax,5eq}$	$J_{1,5eq}$
2 [b]	9.9	8.5	9.0	11.0	4.4	13.4	–
27*α*	2.7	8.8	9.2	10.0	4.8	13.5	< 0.5
27*β*	9.0	9.1	9.3	7.8	4.9	14.3	–
28	2.8	10.0	10.0	11.8	4.4	13.5	< 0.5
29	3.0	10.0	10.0	11.9	4.04	13.7	< 0.5
31	4.1	10.1	9.9	10.7	4.4	13.5	1.2
32 [b]	4.3	9.1	9.2	10.6	4.4	nd [c]	1.0
33	10.6	9.5	9.5	9.5	5.6	nd	–
54*α*	2.8	9.7	9.7	11.8	4.3	13.5	< 0.5
55	3.0	10.1	10.0	13.6	4.3	13.6	< 0.5

[a] Unless otherwise indicated.
[b] Me_2SO-d_6.
[c] nd: Not determined.

Table 4
Selected ^{13}C NMR data for 4-azido-4-deoxy-5-thio-D-xylopyranose derivatives for solutions in $CDCl_3$ [a]

Compound	Chemical shift (δ)					
	C-1	C-2	C-3	C-4	C-5	Others
27α	78.0 [c]	75.4 [c]	71.4 [c]	62.1	28.5	20.7 (OAc); 26.1, 26.7 (CMe_2); 109.4 (CMe_2); 169.1 (CO)
27β	79.8 [c]	79.0 [c]	74.1 [c]	61.0	30.6	20.8 (OAc); 26.6, 26.8 (CMe_2); 110.9 (CMe_2); 169.3 (CO)
28	81.2	74.7	71.0	63.4	25.1	20.5, 20.6 (OAc); 56.3 (OMe); 169.4, 170.1 (CO)
29	73.0	71.0 [c]	70.8 [c]	63.0	26.7	20.4, 20.5, 20.8 (OAc); 169.0, 169.5, 169.6 (CO)
31	51.5	70.9 [c]	74.3 [c]	63.2	26.9	20.3, 20.4 (OAc); 118.1 (CN); 169.2, 169.7 (CO)
32 [b]	54.1	74.0 [c]	75.1 [c]	65.2	27.2	119.0 (CN)
33	50.6	73.3 [c]	75.1 [c]	62.8	31.9	20.5 (OAc); 118.2 (CN); 169.5 (CO)
55	76.0 [c]	73.5 [c]	70.9 [c]	63.0	26.9	20.5, 20.6 (OAc); 90.6 (CCl_3); 160.7 (C=NH); 169.4, 169.8 (CO)

[a] Unless otherwise indicated.
[b] Me_2SO-d_6.
[c] Arbitrary assignment.

otherwise stated (Tables 1–5). Multiplicities of the ^{13}C NMR spectra were obtained from DEPT experiments. The assignment of the protons were based on homonuclear decoupling and DNOE experiments. Connectivities between identified protons and protonated carbons were observed by means of HETCOR and selective INEPT experiments. The ratio of α:β anomeric mixtures was determined by ^1H NMR.

2,3:4,5-Di-O-isopropylidene-L-arabinose diethyl dithioacetal (**4**).—A slurry of L-arabinose diethyl dithioacetal (25.6 g, 0.1 mol) in acetone (125 mL), 2,2-dimethoxypropane (31.2 g; 37 mL, 0.3 mol), and TsOH (100 mg) was stirred at 20 °C for 5 h. Then $NaHCO_3$ was added and the salts were filtered off after 30 min. The residue, obtained on concn of the filtrate, was dissolved in CH_2Cl_2, washed with water, dried, and concd to yield **4** (34 g, 100%) as a colorless syrup: $[\alpha]_D$ −71°, lit. for the D-isomer +86° (*c* 3.6, MeOH) [3]; R_f 0.8 (solvent *F*); ^1H NMR: δ 3.95–4.32 (m, 6 H, H-1, H-2, H-3, H-4, H-5a, H-5b), 2.60–2.80 (m, 4 H, SCH_2CH_3), 1.47, 1.42, 1.37, 1.34 (4 s, 12 H, CMe_2), 1.25 (m, 6 H, SCH_2CH_3); ^{13}C NMR: δ 110.0, 109.5 (CMe_2), 84.3, 78.9, 76.0 (C-2, C-3, C-4), 67.6 (C-5), 52.2 (C-1), 27.2, 26.9, 26.5, 25.1 (CMe_2). Anal. Calcd for $C_{15}H_{28}O_4S_2$: C, 53.54; H, 8.39; S, 19.05. Found: C, 53.70; H, 8.42; S, 18.88.

2,3-O-Isopropylidene-L-arabinose diethyl dithioacetal (**5**) *and 4,5-O-isopropylidene-L-arabinose diethyl dithioacetal* (**6**).—A soln of **4** (34 g, 0.1 mol) in MeOH (340 mL) and M HCl (34 mL) was kept at 50 °C for 40 min. The cooled soln was neutralized with $NaHCO_3$ to give, after filtration and concn, a syrup which was dissolved in CH_2Cl_2–H_2O. The undissolved L-arabinose diethyl dithioacetal (1.3 g, 5%) was filtered off, the organic soln was dried and concd to give crude **5** (27 g, 91%), contaminated with traces of **4** and **6**. Purification by column chromatography

Table 5
NOE data (%) for **34** and **42**

NOE at	Irradiated at							
	34				**42**			
	H-1	H-2	H-3	H-4	H-1	H-4	H-5a	H-5b
H-1		9	4.5				1	
H-2	10		4.2		5	3.8		
H-3	7.7	4.3		4.1	3	4	5	7
H-4		4.5	4.6				3	3
H-5a			2.6	2.4		1.4		31
H-5b				2.7		1	29	

(solvent *C*, then *A*) gave, on concn of the fractions having R_f 0.6 (solvent *A*), **6** (0.3 g, 1%): mp 75–77 °C (hexane–EtOAc); $[\alpha]_D$ +77°; the NMR data were identical with those [14] given for the D-isomer; mp 75–75.5 °C, lit. 70–72 °C [3]; $[\alpha]_D$ −58.5°, lit. −69° (*c* 2.19, $CHCl_3$) [3]. Anal. Calcd for $C_{12}H_{24}O_4S_2$: C, 48.62; H, 8.16; S, 21.63. Found: C, 48.55; H, 8.32; S, 21.49.

Concn of the fractions having R_f 0.5 (solvent *A*) gave **5** (21.3 g, 72%): $[\alpha]_D$ −85°; the NMR data were identical with those [4] given for the D-isomer; $[\alpha]_D$ +87°, lit. +94° (*c* 4.1, MeOH) [3]. Anal. Calcd for $C_{12}H_{24}O_4S_2$: C, 48.62; H, 8.16; S, 21.63. Found: C, 48.50; H, 8.38; S, 21.38.

5-O-p-Toluenesulfonyl-2,3-O-isopropylidene-L-arabinose diethyl dithioacetal (**7**).—To a stirred soln of **5** (6 g, 20 mmol) in pyridine (20 mL), a soln of TsCl (4 g, 21 mmol) in CH_2Cl_2 (20 mL) was added at −5 °C. The mixture was kept at 0 °C for 4 h, then water (1 mL) was added to give, after usual processing and purification of the product by column chromatography (solvent *B*), **7** (6.7 g, 74%) as an unstable syrup, which decomposed slowly on standing at room temperature: $[\alpha]_D$ −54.5°; R_f 0.7 (solvent *B*); R_f 0.3 (solvent *I*). Anal. Calcd for $C_{19}H_{30}O_6S_3$: C, 50.64; H, 6.71; S, 21.43. Found: C, 50.72; H, 6.80; S, 21.27.

4,5-Di-O-p-toluenesulfonyl-2,3-O-isopropylidene-L-arabinose diethyl dithioacetal (**8**).—To a soln of **5** (6 g, 20 mmol) in pyridine (20 mL), TsCl (12 g, 63 mmol) was added at 0 °C. The mixture was kept at room temperature for 24 h to give, after usual processing, **8** (12.5 g, 100%) as a syrup: $[\alpha]_D$ −43°; R_f 0.6 (solvent *I*). Anal. Calcd for $C_{26}H_{36}O_8S_4$: C, 51.63; H, 6.00; S, 21.20. Found: C, 51.52; H, 6.11; S, 21.03.

5-O-tert-Butyldimethylsilyl-4-O-methanesulfonyl-2,3-O-isopropylidene-L-arabinose diethyl dithioacetal (**9**).—To a soln of **5** (7 g, 23.6 mmol) in pyridine (25 mL), *tert*-butyldimethylsilyl chloride (3.75 g, 24.9 mmol) was added at 20 °C, and after 1.5 h MsCl (2 mL, 25.5 mmol). The mixture was kept at room temperature for 24 h to give, after usual processing and column chromatography (solvent *F*), **9** (10 g, 87%) as a syrup: $[\alpha]_D$ −57°; R_f 0.5 (solvent *F*); ^1H NMR: δ 0,92 (s, 9 H, CMe_3) 0.12 (s, 6 H, $SiMe_2$), for further data see Table 1; ^{13}C NMR: δ 25.8, 18.3, −5.5 ($SiMe_2CMe_3$), for further data see Table 2. Anal. Calcd for $C_{19}H_{40}O_6S_3Si$: C, 46.69; H, 8.25; S, 19.68. Found: C, 46.72; H, 8.30; S, 19.45.

4,5-Di-O-methanesulfonyl-2,3-O-isopropylidene-L-arabinose diethyl dithioacetal (**10**).—To a soln of **5** (5.2 g, 17.5 mmol) in pyridine (25 mL), MsCl (4 mL, 51 mmol) was added at 0 °C. After 2 h at room temperature, the mixture was processed in the usual way to give **10** (8 g, 100%), as a syrup: $[\alpha]_D$ −52°; R_f 0.45 (solvent *I*). Anal. Calcd for $C_{14}H_{28}O_4S_4$: C, 37.15; H, 6.24; S, 28.33. Found: C, 36.88; H, 6.30; S, 28.03.

5-O-Benzoyl-4-O-methanesulfonyl-2,3-O-isopropylidene-L-arabinose diethyl dithioacetal (**11**).—To a soln of **10** (9 g, 20 mmol) in DMF (150 mL), NaOBz (3.05 g, 21 mmol) was added and the mixture was stirred at 150 °C for 2 h. After cooling, the slurry was dild with water and was extracted with CH_2Cl_2. The organic soln was washed with water to give, after concn and column chromatography (solvent *B*), **11** (8.8 g, 92%) as a syrup: $[\alpha]_D$ −59°; R_f 0.5 (solvent *B*). Anal. Calcd for $C_{20}H_{30}O_6S_4$: C, 48.56; H, 6.11; S, 25.92. Found: C, 48.39; H, 6.20; S, 25.77.

5-S-Benzoyl-2,3-O-isopropylidene-L-arabinose diethyl dithioacetal (**12**).—To a soln of **7** (6 g, 14.4 mmol) in acetone (30 mL), KSBz (3.5 g, 19.8 mmol) was added and the mixture was stirred at room temperature for 24 h and then concd. The residue was dissolved in CH_2Cl_2, washed with water, to give, after concn, **12** (5.2 g, 94%) as a syrup: $[\alpha]_D$ −65°; R_f 0.7 (solvent *I*). Anal. Calcd for $C_{19}H_{28}O_4S_3$: C, 54.78; H, 6.77; S, 23.09. Found: C, 54.93; H, 6.87; S, 23.25.

5-S-Benzoyl-2,3-O-isopropylidene-4-O-p-toluenesulfonyl-L-arabinose diethyl dithioacetal (**13**).—(a) A soln of **12** (0.8 g, 1.9 mmol) and TsCl (0.5 g, 2.6 mmol) in pyridine (10 mL) was kept at 60 °C for 2 h. Then TsCl (0.3 g, 1.6 mmol) was added and heating was continued for 15 h. Thereafter, further TsCl (0.3 g, 1.6 mmol) was added, and after 15 h at 60 °C, the mixture was poured into water. The formed crystals were filtered and washed with ether to give **13** (0.75 g, 68%): mp 86–88 °C (acetone–hexane); $[\alpha]_D$ −98°; R_f 0.4 (solvent *D*). Anal. Calcd for $C_{26}H_{34}O_6S_4$: C, 54.71; H, 6.00; S, 22.47. Found: C, 54.66; H, 6.08; S, 22.40.

(b) A soln of **8** (3 g, 4.97 mmol) and KSBz (0.9 g, 5.1 mmol) in acetone (15 mL) was stirred at room temperature for 4 d. The residue obtained on concn was dissolved in CH_2Cl_2, washed with water to give, on concn and treatment of the residue with ether–hexane, **13** (1.9 g, 67%), identical with the compound described above.

5-S-Benzoyl-2,3-O-isopropylidene-4-O-methanesulfonyl-L-arabinose diethyl dithioacetal (**14**).—To a soln of **12** (0.84 g, 2 mmol) in pyridine (10 mL), MsCl (0.4 mL, 5.1 mmol) was added. After

3 h at room temperature, the mixture was processed in the usual way to give **14** (0.87 g, 92%): $[\alpha]_D$ −79°; R_f 0.5 (solvent *D*). Anal. Calcd for $C_{20}H_{30}O_6S_4$: C, 48.56; H, 6.11; S, 25.92. Found: C, 48.71; H, 6.18; S, 25.73.

*4-Azido-5-*O*-*tert*-butyldimethylsilyl-4-deoxy-2,3-*O*-isopropylidene-*D*-xylose diethyl dithioacetal* (**16**) *and 4-azido-4-deoxy-2,3-*O*-isopropylidene-*D*-xylose diethyl dithioacetal* (**17**).—A soln of **9** (10 g, 20.5 mmol) and NaN_3 (2 g, 30.8 mmol) in DMF (100 mL) was stirred at 110 °C for 15 h. The residue obtained on concn was dissolved in CH_2Cl_2, washed with water, and concd. The resulting mixture was separated by column chromatography (solvent *G*, then *B*). Concn of the first fraction gave **16** (3.7 g, 42%): $[\alpha]_D$ −62°; R_f 0.9 (solvent *F*); ^{1}H NMR: δ 0.92 (s, 9 H, CMe_3) 0.10 (s, 6 H, SiMe_2), for further data see Table 1; ^{13}C NMR: δ 25.7, 18.1, −5.6 ($SiMe_2CMe_3$), for further data see Table 2. Anal. Calcd for $C_{18}H_{37}N_3O_3S_2Si$: C, 49.62; H, 8.56; N, 9.64; S, 14.72. Found: C, 49.50; H, 8.62; N, 9.55; S, 14.58.

Concn of the second fraction gave **17** (2.3 g, 35%): $[\alpha]_D$ −97°; R_f 0.1 (solvent *F*); R_f 0.3 (solvent *E*). Anal. Calcd for $C_{12}H_{23}N_3O_3S_2$: C, 44.84; H, 7.21; N, 13.07; S, 19.95. Found: C, 44.97; H, 7.28; N, 13.23; S, 19.73.

*4-Azido-4-deoxy-2,3-*O*-isopropylidene-*D*-xylose diethyl dithioacetal* (**17**).—(a) A soln of **16** (3 g, 6.9 mmol) and $Bu_4NF \cdot 3H_2O$ (2.6 g, 8.24 mmol) in THF (30 mL) was kept at room temperature for 20 h and was then concd. The residue was purified by column chromatography (solvent *E*) to yield **17** (2 g, 90%), identical with the compound described above. When the crude mixture of **16** and **17**, obtained from the reaction of mesylate **9** with azide, was submitted to the same procedure without previous separation of the components, the yield was 72% based on **9**.

(b) A soln of **18** (42.5 g, 0.1 mol) in $CHCl_3$ (200 mL) and MeOH (100 mL) was refluxed in the presence of methanolic M NaOMe (0.1 mL) for 1 h. The cooled soln was neutralized with CO_2 to give, on concn and column chromatography of the residue (solvent *E*), **17** (27.5 g, 85.7%), identical with the compound described above.

*4-Azido-5-*O*-benzoyl-4-deoxy-2,3-*O*-isopropylidene-*D*-xylose diethyl dithioacetal* (**18**).—To a stirred soln of **11** (19.2 g, 40 mmol) in DMF (300 mL), NaN_3 (4 g, 61 mmol) was added, and stirring was continued at 100 °C for 20 h. The residue obtained on concn of the mixture was partitioned between CH_2Cl_2 and water. The organic soln was washed with water, and the residue obtained on concn was purified by column chromatography (solvent *H*) to give **18** (13.6 g, 80%): $[\alpha]_D$ −36°; R_f 0.6 (solvent *H*). Anal. Calcd for $C_{12}H_{23}N_3O_3S_2$: C, 44.84; H, 7.21; N, 13.07; S, 19.95. Found: C, 44.97; H, 7.28; N, 13.23; S, 19.73.

*4-Azido-4-deoxy-2,3-*O*-isopropylidene-5-*O*-methanesulfonyl-*D*-xylose diethyl dithioacetal* (**19**).—To a stirred soln of **17** (5.6 g, 17.4 mmol) in pyridine (50 mL), MsCl (2.7 mL, 35 mmol) was added dropwise below 10 °C. The mixture was kept at room temperature for 1 h to give, after usual processing, **19** (6.3 g, 90%) as a syrup: $[\alpha]_D$ −52°; R_f 0.5 (solvent *I*). Anal. Calcd for $C_{13}H_{25}N_3O_5S_3$: C, 39.08; H, 6.31; N, 10.52; S, 24.07. Found: C, 38.97; H, 6.55; N, 10.33; S, 23.88.

*4-Azido-5-*S*-benzoyl-4-deoxy-2,3-*O*-isopropylidene-*D*-xylose diethyl dithioacetal* (**20**).—A soln of **19** (3.5 g, 8.76 mmol) and KSBz (2.2 g, 12.5 mmol) in acetone (40 mL) was boiled for 1 h. The resulting thick slurry was cooled, filtered, and the salts were washed with acetone (20 mL). The filtrate was boiled for 4 h, cooled, and concd. The residue was partitioned between CH_2Cl_2 and water to give, after concn of the organic soln, **20** (3.6 g, 93%): $[\alpha]_D$ −3°; R_f 0.5 (solvent *F*). Anal. Calcd for $C_{19}H_{27}N_3O_3S_3$: C, 51.68; H, 6.16; N, 9.51; S, 21.78. Found: C, 51.54; H, 6.28; N, 9.33; S, 21.73.

*5-*S*-Acetyl-4-azido-4-deoxy-2,3-*O*-isopropylidene-*D*-xylose diethyl dithioacetal* (**21**).—A soln of **19** (0.9 g, 2.25 mmol) and KSAc (0.3 g, 2.63 mmol) in acetone (10 mL) was stirred at room temperature for 2 d to give, after concn and column chromatography (solvent *E*) of the residue, **21** (0.7 g, 81%) as a syrup: $[\alpha]_D$ −33°; R_f 0.7 (solvent *E*). Anal. Calcd for $C_{14}H_{25}N_3O_3S_3$: C, 44.30; H, 6.64; N, 11.07; S, 25.34. Found: C, 44.52; H, 6.39; N, 10.83; S, 25.05.

*5-Azido-4-*S*-benzoyl-5-deoxy-2,3-*O*-isopropylidene-4-thio-D-xylose diethyl dithioacetal* (**22**) *and 4,5-anhydro-2,3-*O*-isopropylidene-4-thio-D-xylose diethyl dithioacetal* (**23**).—To a stirred soln of **13** (7.4 g, 13 mmol) in DMF (140 mL), NaN_3 (3.7 g, 57 mmol) was added, and the mixture was stirred at 60 °C for 30 min. After cooling and filtration, the soln was concd. The residue was partitioned between $CHCl_3$ and water, the organic soln was concd, and the residue submitted to column chromatography (solvent *G*). The fraction having R_f 0.80 gave, on concn, benzoyl azide (0.1 g), identified by IR and NMR spectroscopy. The fraction having R_f 0.45 gave, on concn, **22** (3.7 g, 65%): $[\alpha]_D$ −36°. Anal. Calcd for $C_{19}H_{27}N_3O_3S_3$: C, 51.68; H, 6.16; N, 9.51; S, 21.78. Found: C, 51.55; H, 6.45; N, 9.72; S, 21.52.

The fraction having R_f 0.35 gave, on concn, **23**

(0.46 g,12%): $[\alpha]_D$ −94°; R_f 0.6 (solvent *H*). Anal. Calcd for $C_{12}H_{22}O_2S_3$: C, 48.94; H, 7.53; S, 32.66. Found: C, 48.77; H, 7.60; S, 32.40.

Compound **23** was obtained in ~quantitative yield, when tosylate **13** or mesylate **14** were treated with 1.1 equiv of NaOMe in MeOH.

*4-Azido-5-S-benzoyl-4-deoxy-2,3-O-isopropylidene-5-thio-*D*-xylose* (**24**).—To a stirred soln of **20** (5.7 g, 12.9 mmol) in acetone (140 mL), water (35 mL), $CdCO_3$ (23 g), and subsequently a soln of $HgCl_2$ (26 g) in acetone (70 mL) were added. The slurry was stirred for 20 h, filtered and concd in the presence of Na_2CO_3 (2 g). The residue was partitioned between $CHCl_3$ and water, the precipitated salts were filtered off and washed with $CHCl_3$. The organic soln was washed with 10% aq KI soln and water to give, on concn, **24** (4.5 g, ~100%), containing according to NMR spectroscopy some **24**-hydrate. Therefore, no correct analytical data could be obtained: $[\alpha]_D$ +59°; R_f 0.3 (solvent *B*); ^{1}H NMR: δ 9.85 (d, 1 H, H-1), 4.52 (dd, 1 H, H-2), 4.30 (dd, 1 H, H-3), 1.40, 1.46 (2s, 6 H, CMe_2); $J_{1,2}$ 1.2, $J_{2,3}$ 6.5, $J_{3,4}$ 4.2 Hz; ^{13}C NMR: δ 201.4 (aldehyde), 96.0 (aldehyde-hydrate).

*1-O-Acetyl-4-azido-4-deoxy-2,3-O-isopropylidene-5-thio-*D*-xylose* (**27**).—To a soln of **24** (0.67 g, 2 mmol) in MeOH (10 mL), methanolic M NaOMe (0.1 mL) was added. After 10 min at room temperature, the mixture was neutralized with CO_2 to give, on concn, crude **26** contaminated with BzOMe. This mixture was dissolved in pyridine (5 mL) and treated with Ac_2O (3 mL) to give, after usual processing and column chromatography of the residue (solvent *C*), **27α** (0.25 g, 46%): $[\alpha]_D$ +303°; R_f 0.55 (solvent *C*). Anal. Calcd for $C_{10}H_{15}N_3O_4S$: C, 43.95; H, 5.53; N, 15.37; S, 11.73. Found: C, 43.77; H, 5.60; N, 15.20; S, 11.55.

Concn of the second fraction gave **27β** (0.13 g, 23%): $[\alpha]_D$ +42°; R_f 0.45 (solvent *C*). Anal. Calcd for $C_{10}H_{15}N_3O_4S$: C, 43.95; H, 5.53; N, 15.37; S, 11.73. Found: C 43.81; H, 5.65; N, 15.26; S, 11.52.

*Methyl 2,3-di-O-acetyl-4-azido-4-deoxy-5-thio-α-*D*-xylopyranoside* (**28**).—To a soln of **24** (4.5 g, 13.4 mmol) in MeOH (45 mL), methanolic M NaOMe (0.5 mL) was added. When according to TLC the deacylation was complete (R_f 0.3 → 0.4, solvent *C*), the pH of the soln was adjusted to 1 by adding 20% HCl in MeOH, and the mixture was boiled for 1 h. The cooled soln was concd, and toluene was evaporated from the residue. Then pyridine (15 mL) and Ac_2O (10 mL) were added, and after 20 h at room temperature, the mixture was concd. The residue gave, after column chromatography (solvent *C*), **28** (2.5 g, 67%): mp 85–86 °C (hexane–EtOAc); $[\alpha]_D$ +226°; R_f 0.4 (solvent *C*). Anal. Calcd for $C_{10}H_{15}N_3O_5S$: C, 41.52; H, 5.23; N, 14.52; S, 11.08. Found: C, 41.77; H, 5.33; N, 14.30; S, 10.95.

*1,2,3-Tri-O-acetyl-4-azido-4-deoxy-5-thio-α-*D*-xylopyranose* (**29**).—To a soln of **28** (5.8 g, 8 mmol) in Ac_2O (15 mL), concd H_2SO_4 (1 mL) was added at 0 °C. The mixture was kept at 0 °C for 30 min and at room temperature for 2 h and was thereafter poured into a mixture of $CHCl_3$ (200 mL), ice (35 g), and $NaHCO_3$ (20 g). The organic soln was separated, the aq soln was extracted with $CHCl_3$ (2 × 100 mL), and the combined $CHCl_3$ solns were washed with 5% aq $NaHCO_3$ and water. The residue obtained on concn was purified by column chromatography (solvent *C*) to give **29** (4.9 g, 77%) as a syrup: $[\alpha]_D$ +214°; R_f 0.45 (solvent *C*). Anal. Calcd for $C_{11}H_{15}N_3O_6S$: C, 41.64; H, 4.76; N, 13.24; S, 10.10. Found: C, 41.75; H, 4.80; N, 13.11; S, 9.95.

Reaction of **29** *with 4-cyanothiophenol.*—4-Cyanothiophenol (0.8 g, 5.9 mmol) was added under Ar to a stirred soln of **29** (1.0 g, 3.15 mmol) in CH_2Cl_2 (40 mL), and the mixture was cooled to −10 °C. After addition of Me_3SiOTf (0.6 mL, 3.3 mmol), the temperature was allowed to raise and the mixture was stirred at room temperature for 1 h, then quenched with Et_3N (0.5 mL). The residue, obtained on concn, was submitted to column chromatography (solvent *D*) to yield a 8:2:1 mixture of **31**, **33**, and **34** (1.05 g) which was dissolved in MeOH (20 mL) and deacetylated under Zemplén conditions (M NaOMe, 0.1 mL). After 1 h at room temperature, the mixture was neutralized with CO_2, concd, and submitted to column chromatography (solvent *K*). Concn of the first fraction gave *2,5-anhydro-4-azido-4-deoxy-5-thio-*D*-lyxose bis(4-cyanophenyl) dithioacetal* (**35**, 50 mg, 4%): mp 198–201 °C (ether); $[\alpha]_D$ −102° (*c* 0.5, pyridine); R_f 0.6 (solvent *K*); ^{1}H NMR (Me_2SO-d_6): δ 7.50–7.85 (m, 8 H, aromatic), 6.25 (br s, 1 H, OH), 5.60 (d, 1 H, H-1), 4.00–4.16 (m, 2 H, H-3, H-4), 3.64 (dd, 1 H, H-2), 2.98 (dd, 1 H, H-5a), 2.64 (dd, 1 H, H-5b); $J_{1,2}$ 2.9, $J_{2,3}$ 7.7, $J_{4,5a}$ 6.0, $J_{4,5b}$ 10.3, $J_{5a,5b}$ 10.6 Hz; ^{13}C NMR (Me_2SO-d_6): δ 141.2, 140.8, 133.0, 132.9, 130.2, 129.6, 109.8, 109.3 (aromatic), 118.8, 118.6 (CN), 78.2 (C-3), 66.3 (C-4), 56.7 (C-1), 52.8 (C-2), 29.0 (C-5). Anal. Calcd for $C_{19}H_{15}N_5OS_3$: C, 53.63; H, 3.55; N, 16.46; S, 22.60. Found: C, 53.75; H, 3.62; N, 16.51; S, 22.83.

Concn of the second fraction (R_f 0.3, solvent *K*) gave a 1:4 mixture of **2** and **32** (0.52 g, 54%) which was dissolved in pyridine (10 mL), and Ac_2O (5 mL) was added. After 20 h at room temperature, the

mixture was processed in the usual way. The residue obtained upon concn of the organic soln was purified by column chromatography (solvent *D*). Concn of the first fraction yielded *4-cyanophenyl 2,3-di-O-acetyl-4-azido-4-deoxy-1,5-dithio-β-D-xylopyranoside* (**33**, 125 mg, 19%): mp 115–120 °C (hexane–EtOAc); $[\alpha]_D$ +78° (*c* 0.5, $CHCl_3$); R_f 0.4 (solvent *D*). Anal. Calcd for $C_{16}H_{16}N_4O_4S_2$: C, 48.97; H, 4.11; N, 14.28; S, 16.34. Found: C, 48.82; H, 4.20; N, 14.11; S, 16.51.

Concn of the second fraction gave *4-cyanophenyl 2,3-di-O-acetyl-4-azido-4-deoxy-1,5-dithio-α-D-xylopyranoside* (**31**, 0.5 g, 76%): mp 123–126 °C (hexane–EtOAc); $[\alpha]_D$ +479° (*c* 0.5, $CHCl_3$); R_f 0.35 (solvent *D*). Anal. Calcd for $C_{16}H_{16}N_4O_4S_2$: C, 48.97; H, 4.11; N, 14.28; S, 16.34. Found: C, 49.07; H, 4.08; N, 14.21; S, 16.49.

4-Cyanophenyl 4-azido-4-deoxy-1,5-dithio-β-D-xylopyranoside (**2**).—Deacetylation of **33** (70 mg, 0.18 mmol) with methanolic M NaOMe (0.1 mL) in MeOH (10 mL) yielded, after deionization with Dowex 50W-X resin and concn, **2** (50 mg, 91%): mp 105–110 °C (ether); $[\alpha]_D$ +139° (*c* 0.5, MeOH); R_f 0.3 (solvent *K*). Anal. Calcd for $C_{12}H_{12}N_4O_2S_2$: C, 46.74; H, 3.92; N, 18.1; S, 20.79. Found: C, 46.85; H, 3.89; N, 18.11; S, 20.84.

4-Cyanophenyl 4-azido-4-deoxy-1,5-dithio-α-D-xylopyranoside (**32**).—Deacetylation of **31** (0.4 g, 1.0 mmol) with methanolic M NaOMe (0.1 mL) in MeOH (40 mL) yielded, after deionization with Dowex 50W-X resin and concn, **32** (0.3 g, 95%): $[\alpha]_D$ +698° (*c* 0.5, MeOH); R_f 0.3 (solvent *K*). Anal. Calcd for $C_{12}H_{12}N_4O_2S_2$: C, 46.74; H, 3.92; N, 18.17; S, 20.79. Found: C, 46.65; H, 3.99; N, 18.21; S, 20.88.

3-O-Acetyl-2,5-anhydro-4-azido-4-deoxy-5-thio-D-lyxose bis(4-cyanophenyl) dithioacetal (**34**).—To a stirred soln of **35** (50 mg, 0.1 mmol) in pyridine (1 mL), Ac_2O (0.5 mL) was added, and the soln was kept at room temperature overnight before processing in the usual way. The residue obtained upon concn yielded **34** (50 mg, 91%): $[\alpha]_D$ −202° (*c* 0.166, $CHCl_3$); R_f 0.4 (solvent *D*); ^1H NMR (CD_2Cl_2): δ 7.50–7.65 (m, 6 H, aromatic), 7.40 (m, 2 H, aromatic), 5.49 (dd, 1 H, H-3), 5.18 (d, 1 H, H-1), 4.25 (ddd, 1 H, H-4), 3.67 (dd, 1 H, H-2), 3.05 (dd, 1 H, H-5a), 3.00 (dd, 1 H, H-5b), 2.10 (s, 3 H, OAc); $J_{1,2}$ 4.5, $J_{2,3}$ 5.7, $J_{3,4}$ 7.4, $J_{4,5a}$ 6.4, $J_{4,5b}$ 8.9, $J_{5a,5b}$ 11.2 Hz; ^{13}C NMR (CD_2Cl_2): δ 170.8 (C=O), 140.4, 140.3, 132.9, 132.8, 132.1, 131.8, 111.7, 111.7 (aromatic), 118.5, 118.4 (CN), 80.1 (C-3), 66.9 (C-4), 61.9 (C-1), 53.9 (C-2), 32.0 (C-5), 20.9 (OAc). Anal. Calcd for $C_{21}H_{17}N_5O_2S_3$: C, 53.94; H, 3.66; N, 14.98; S, 20.57. Found: C, 53.82; H, 3.81; N, 14.81; S, 20.51.

Reaction of bromides **38** *and* **40** *with 4-cyanothiophenol.*—To a stirred soln of **29** (0.5 g, 1.57 mmol) in CH_2Cl_2 (10 mL), HBr in AcOH (33%, 2 mL) was added. After stirring for 1 h, the mixture was poured into ice–water and extracted with CH_2Cl_2. The organic layer was washed with 6% aq $NaHCO_3$, water, and concd to yield according to NMR spectroscopy a ~ 1:4 mixture of **38** and **40** (0.5 g): R_f 0.7 (solvent *B*).

38: ^1H NMR: no assignment could be made due to signal overlap; ^{13}C NMR: δ 73.9, 71.4 (C-2, C-3), 62.8 (C-4), 53.05 (C-1), 28.1 (C-5).

40: ^1H NMR: δ 5.74 (d, 1 H, H-1), 5.68 (dd, 1 H, H-3), 5.05 (dd, 1 H, H-2), 3.88 (m, 1 H, H-5a), 3.66 (m, 2 H, H-4, H-5b), 2.10 (s, 6 H, OAc); $J_{1,2}$ 4.5, $J_{2,3}$ 8.9, $J_{3,4}$ 6.1 Hz; ^{13}C NMR: δ 169.8, 169.6 (C=O), 78.0, 77.2 (C-2, C-3), 54.0 (C-1), 48.2 (C-4), 34.3 (C-5), 20.8, 20.5 (OAc).

To a stirred soln of **38** and **40** (0.5 g) in acetone (20 mL), 4-cyanothiophenol (0.28 g, 2.07 mmol) and K_2CO_3 (0.28 g, 2.02 mmol) were added, and stirring was continued for 1 h at room temperature. The salts were filtered off, and the filtrate was concd and submitted to column chromatography (solvent *B*). Concn of the first fraction gave *2-(1R,2S,-1,2-di-O-acetyl-1,2-dihydroxy-but-3-en-1-yl)-5-cyano-1,3-benzodithiole* (**41**, 100 mg, 18%): $[\alpha]_D$ +171° (*c* 0.4, $CHCl_3$); R_f 0.75 (solvent *B*); ^1H NMR: δ 7.35–7.65 (m, 3 H, aromatic), 6.01 (dd, 1 H, H-3), 5.75 (ddd, 1 H, H-4), 5.52 (dd, 1 H, H-2), 5.34 (dd, 1 H, H-5a), 5.27 (dd, 1 H, H-5b), 4.50 (d, 1 H, H-1), 2.20, 1.95 (2s, 6 H, OAc); $J_{1,2}$ 10.1, $J_{2,3}$ 2.1, $J_{3,4}$ 5.3, $J_{4,5a}$ 17.2, $J_{4,5b}$ 10.5, $J_{5a,5b}$ ~ 1 Hz; ^{13}C NMR: δ 169.9, 169.0 (C=O), 148.9, 139.8, 132.4, 131.9, 129.3, 123.6 108.3 (aromatic, C-4), 118.4 (C-5), 118.0 (CN), 72.7, 70.8 (C-2, C-3), 55.8 (C-1), 20.9, 20.4 (OAc). Anal. Calcd for $C_{16}H_{15}NO_4S_2$: C, 55.00; H, 4.33; N, 4.01; S, 18.35. Found: C, 55.11; H, 4.45; N, 4.11; S, 18.47.

Concn of the second fraction yielded a 1:1 mixture of **31** and **33** (37 mg, 6%).

Concn of the third fraction gave *4-cyanophenyl 2,3-di-O-acetyl-5-S-(4-cyanophenyl)-1,4,5-trithio-α-L-arabinofuranoside* (**42**, 150 mg, 20%): $[\alpha]_D$ −133° (*c* 0.4, $CHCl_3$); R_f 0.5 (solvent *B*); ^1H NMR (CD_2Cl_2): δ 7.50–7.65 (m, 4 H, aromatic), 7.45 (m, 2 H, aromatic), 7.35 (m, 2 H, aromatic), 5.46 (dd, 1 H, H-2), 5.33 (dd, 1 H, H-1), 4.89 (d, 1 H, H-1), 3.79 (ddd, 1 H, H-4), 3.54 (dd, 1 H, H-5a), 3.19 (dd, 1 H,

H-5b), 2.08, 2.05 (2s, 6 H, OAc); $J_{1,2}$ 4.8, $J_{2,3}$ 4.9, $J_{3,4}$ 5.6, $J_{4,5a}$ 5.8, $J_{4,5b}$ 8.7, $J_{5a,5b}$ 13.6 Hz; ^{13}C NMR (CD_2Cl_2): δ 170.1, 169.5 (C=O), 142.6, 141.4, 132.8, 132.8, 130.6, 128.3, 110.9, 109.7 (aromatic), 118.6, 118.3 (CN), 81.2 (C-2), 80.1 (C-3), 54.9 (C-1), 50.0 (C-4), 37.0 (C-5), 20.8, 20.8 (OAc). Anal. Calcd for $C_{23}H_{20}N_2O_4S_3$: C, 57.01; H, 4.16; N, 5.78; S, 19.85. Found: C, 57.23; H, 4.07; N, 5.91; S, 19.95.

When the reaction was carried out at reflux temperature, only **41** and **42**, but no traces of **31** and **33**, could be isolated.

If the reaction was carried out in the presence of TEMPO (0.2 equiv), only unchanged bromides **38** and **40** could be detected by TLC and isolated from the reaction mixture even after 5 h at reflux temperature.

*4-Cyanophenyl 5-S-(4-cyanophenyl)-1,4,5-trithio-α-*L*-arabinofuranoside* (**43**).—Deacetylation of **42** (100 mg, 0.2 mmol) with methanolic M NaOMe (0.1 mL) in MeOH (10 mL) yielded, after deionization with Dowex 50W-X resin and concn, **43** (80 mg, 97%): mp 115–119 °C (ether); $[\alpha]_D$ −332° (*c* 0.5, MeOH); R_f 0.3 (solvent *K*); ^1H NMR (Me_2SO-d_6): δ 7.70–7.85 (m, 4 H, aromatic), 7.48 (m, 2 H, aromatic), 7.45 (m, 2 H, aromatic), 5.70 (br s, 1 H, OH), 5.05 (br s, 1 H, OH), 4.78 (d, 1 H, H-1), 3.85 (dd, 1 H, H-2), 3.81 (dd, 1 H, H-3), 3.69 (dd, 1 H, H-5a), 3.44 (ddd, 1 H, H-4), 3.15 (dd, 1 H, H-5b); $J_{1,2}$ 6.8, $J_{2,3}$ 7.2, $J_{3,4}$ 7.2, $J_{4,5a}$ 4.2, $J_{4,5b}$ 9.1, $J_{5a,5b}$ 13.3 Hz. Anal. Calcd for $C_{19}H_{16}N_2O_2S_3$: C, 56.98; H, 4.03; N, 6.99, S, 24.01. Found: C, 56.85; H, 3.89; N, 7.11; S, 24.14.

*2,3-Di-O-acetyl-4-azido-4-deoxy-5-thio-*D*-xylopyranose* (**54**).—Under Ar, hydrazine acetate (0.43 g, 4.67 mmol) was added to a stirred soln of **29** (1.0 g, 3.15 mmol) in DMF (30 mL) at room temperature. After 1 h, EtOAc (50 mL) and CH_2Cl_2 (50 mL) were added, the organic layer was washed with brine, concd, and the residue submitted to column chromatography (solvent *B*) to yield **54** (0.65 g, 75%, α:β ratio 9:1): R_f 0.4 (solvent *B*); ^1H NMR: α anomer, for data see Table 3; β anomer, δ 4.83 (d, 1 H, H-1), $J_{1,2}$ 9.8 Hz, the other signals overlapped with those of the α anomer. Anal. Calcd for $C_9H_{13}N_3O_5S$: C, 39.27; H, 4.76; N, 15.26; S, 11.65. Found: C, 39.33; H, 4.80; N, 15.11; S, 11.73.

*O-(2,3-Di-O-acetyl-4-azido-4-deoxy-5-thio-α-*D*-xylopyranosyl) trichloroacetimidate* (**55**).—To a stirred soln of **54** (0.5 g, 1.8 mmol) in CH_2Cl_2 (10 mL), CCl_3CN (1.8 mL, 18 mmol) and K_2CO_3 (2.5 g, 18 mmol) were added under Ar. After 24 h, the mixture was dild with ether, filtered through Celite, concd, and the residue submitted to column chromatography (solvent *D*) to yield **55** (0.65 g, 85%): mp 68–72 °C (hexane–EtOAc); $[\alpha]_D$ +195° (*c* 0.5, $CHCl_3$); R_f 0.6 (solvent *D*). Anal. Calcd for $C_{11}H_{13}Cl_3N_4O_5S$: C, 31.48; H, 3.12; N,13.35; S, 7.64. Found: C, 31.36; H, 3.25; N, 13.19; S, 7.78.

Reaction of **55** *with 4-cyanothiophenol.*—Under Ar, a stirred soln of **55** (210 mg, 0.5 mmol) and 4-cyanothiophenol (160 mg, 1.18 mmol) in MeCN (10 mL) was cooled to −15 °C, 0.1 M $BF_3 \cdot OEt_2$ in MeCN (0.5 mL) was added, and stirring was continued at −15 °C for 15 min. After addition of Et_3N (0.5 mL), the mixture was concd and submitted to column chromatography (solvent *D*) to give a 3:1 mixture of **31** and **33** (137 mg, 70%).

When the reaction was carried out in CH_2Cl_2, **31** and **33** were formed in a 2:1 ratio (188 mg, 96%).

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