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An economic synthesis of 1,2,3,4-tetra-*O*-acetyl-5-thio-D-xylopyranose and its transformation into 4-substituted-phenyl 1,5-dithio-D-xylopyranosides possessing antithrombotic activity[1,2]

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Abstract

D-Xylose was converted via 1,2-*O*-isopropylidene-α-D-xylofuranose (**4**) into 3-*O*-benzoyl-5-*S*-benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranose which, after methanolysis, acetylation and subsequent acetolysis afforded 1,2,3,4-tetra-*O*-acetyl-5-thio-α-D-xylopyranose (**14**) in an overall yield of 36%. Reaction of **4** with thionyl chloride gave a mixture of the diastereomeric cyclic sulfites, the structures of which were established by X-ray crystallography. Their oxidation with sodium periodate afforded the corresponding cyclic sulfate **23**. Treatment of **23** with potassium thioacetate gave the potassium salt of 5-*S*-acetyl-1,2-*O*-isopropylidene-α-D-xylofuranose 3-*O*-sulfonic acid (**26**) which, after methanolysis, acetylation and subsequent acetolysis afforded **14** in an overall yield of 56%. Treatment of **4** with sulfuryl chloride gave a mixture containing 5-chloro-3-*O*-chlorosulfonyl-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose, 3,7,9,11-tetraoxa-4-thia-10-dimethyl-tricyclo[6,3,0,$0^{2,6}$]undecane S-dioxide and **23** in a 2:3:7 ratio. Tetraacetate **14** was converted into the α-1-bromide **18** as well as into the α-1-*O*-trichloroacetimidate **17**. These three compounds were used as donors for the glycosylation with 4-cyanothiophenol, affording the 4-cyanophenyl 2,3,4-tri-*O*-acetyl-1,5-dithio-α- (**29**) and β-D-xylopyranoside (**30**) in different ratios, depending on the reaction conditions. When donor **18** was used in the presence of potassium carbonate, besides **29** and **30** two aryl C-glycosylated-thioglycosides, i.e. 4-cyano-2-(2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)phenyl 2,3,4-tri-*O*-acetyl-1,5-dithio-α- and β-D-xylopyranoside (**32** and **33**) as well as 4-cyano-2-(2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)phenyl disulfide **34** could be isolated as byproducts. Deacetylation of **30** with sodium methoxide in methanol afforded, besides 4-cyanophenyl 1,5-dithio-β-D-xylopyranoside (**1**), the corresponding 4-[(methoxy)(imino)methyl]phenyl

[1] Orally active antithrombotic thioglycosides, Part V. For Part IV see [1].

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glycoside **2**. The 4-cyano group of **1** was converted into the 4-aminothiocarbonyl, the 4-(methylthio)(imino)methyl, the 4-amidino and the 4-(imino)(hydrazino)methyl group. All of these glycosides showed a significant antithrombotic activity on rats.

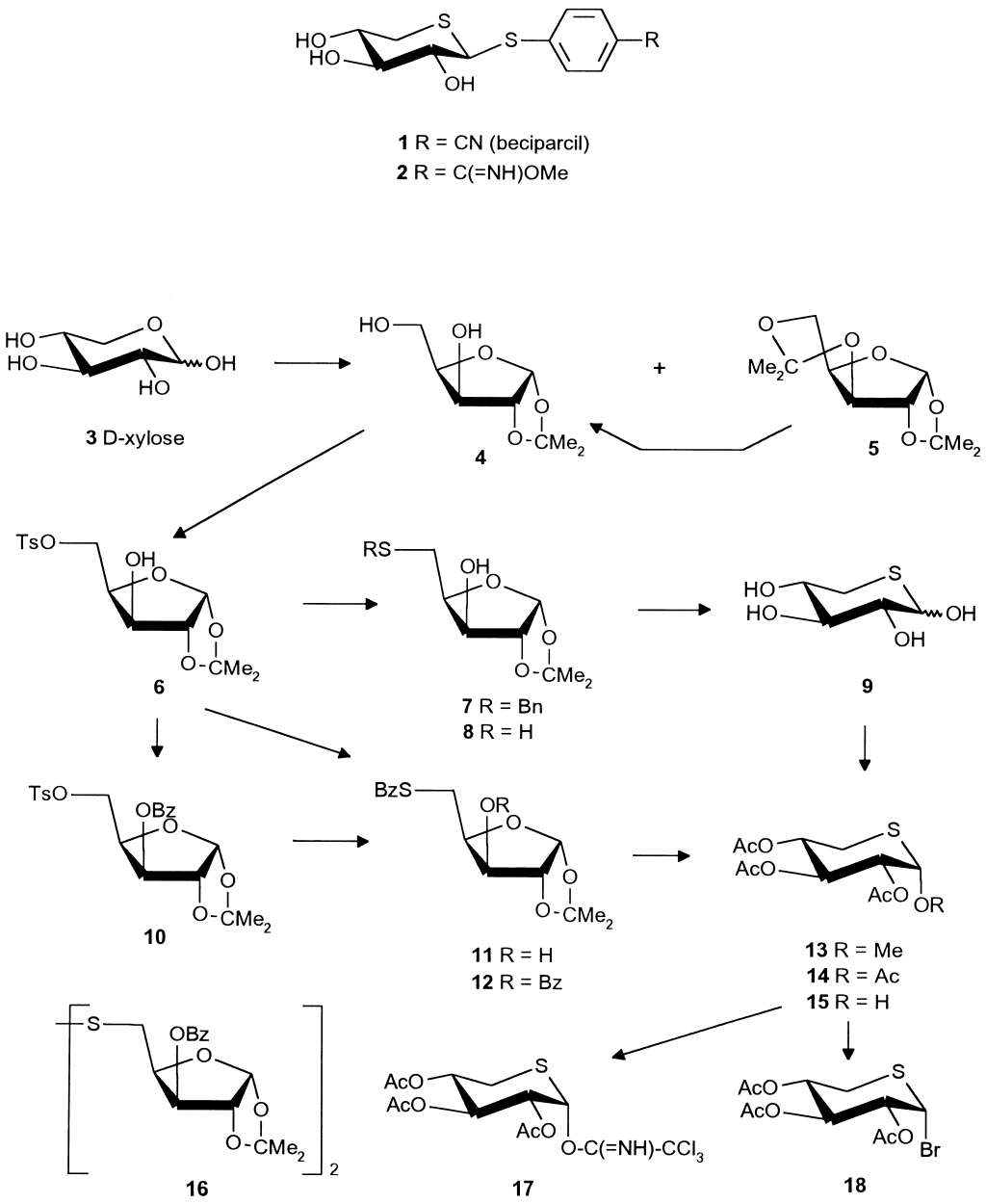
Keywords: 1,2-*O*-Isopropylidene-α-D-xylofuranose cyclic sulfite and sulfate derivatives; 5-Thio-D-xylose derivatives; Glycosidation reactions; Thioglycosides; *C*-Glycosides; Oral antithrombotic activity

1. Introduction

In the previous parts of this series of papers [1–4], we have shown that the oral antithrombotic activity of 4-cyanophenyl 1,5-dithio-β-D-xylopyranoside (beciparcil, **1**) [5] could be significantly increased by replacing the individual hydroxyl groups of the pentose unit with azido groups or by using the hexose congener (5-thio-D-glucopyranose). During the synthesis of **1**, which was needed as a reference compound for the biological experiments, we isolated the corresponding 4-iminoether **2** as a byproduct. As the antithrombotic activity of **2** superseded that of **1**, a research program was initiated, focusing on the structure-activity relationships by transforming the cyano group into different carboxylic acid derivatives.

2. Results and discussion

An economic synthesis of 1,2,3,4-tetra-O-*acetyl-5-thio*-D-*xylopyranose*.—In the previous literature, bromide **18** obtained from D-xylose (**3**) in an eight step process [5] was used as glycosyl donor for the synthesis of **1**. For the conversion of **3** into the 1,2-*O*-isopropylidene derivative **4**, anhydrous copper sulfate with sulfuric acid was used [6] affording a mixture of **4** and the 1,2:3,5-di-*O*-isopropylidene compound **5**, which was converted in 70% yield into **4** by partial hydrolysis with acetic acid. As, according to the simple one pot synthesis of Moravcová et al. [7], **4** can be obtained from **3** in a yield of ~90%, this method was applied by us. However it turned out that the crude **4**, obtained following this procedure, had to be purified by column chromatography before further use since the contaminants (~5% **3**, ~5% **5** and ~10% inorganic salts) decreased dramatically the yield of the next step. This purification could be avoided when the mixture of **4** and **5** was partially hydrolysed in methanol with 0.1 M hydrochloric acid at 40 °C, affording **4** in nearly quantitative yield and 98% purity and containing only 2% of **5**. According to literature [5], the 5-thio group was introduced into **4** by the Whistler procedure [8] using the 5-*O*-tosyl derivative **6** as the key intermediate which was converted via the 5-*S*-benzyl derivative **7** into thiol **8**, applying the reductive debenzylation with sodium in liquid ammonia. For eluding this unpleasant step, we introduced the thio group by a modification of Owen's procedure [9], using potassium thiobenzoate instead of thioacetate as reagent. However, depending on the reaction conditions, a mixture of the *S*-benzoyl (**11**) and the *O*,*S*-dibenzoyl **12** derivative, or a mixture of **12** and the disulfide **16** was obtained. Formation of these mixtures could be avoided by converting first the tosylate **6** into its 3-*O*-benzoate **10** [10], which gave **12** in a very clean reaction. Deacylation of **12** with sodium methoxide in methanol afforded, after acidification, methyl 5-thio-α-D-xylopyranoside which was isolated as its triacetate **13**. Acetolysis of **13** with acetic anhydride-sulfuric acid gave the tetraacetate **14** [9,11] which was converted into the bromide **18** on treatment with hydrogen bromide in acetic acid. A serious drawback of this reaction sequence was the tosylation of **4**, as the high yield (90%) of **6** claimed in literature [5] (without giving experimental details) could not be repeated by us. Only the modest yield (60%) reported by Tipson [12] was attained. On the other hand, the fact that substitution of the 5-*O*-tosyl group by the thiobenzoate could be carried out in satisfactory yield only with the 3-*O*-protected derivative gave us the idea to synthesize a cyclic 3,5-*O*-sulfate. It could be presumed that a proper sulfur nucleophile could attack this ester selectively at the less hindered C-5 atom [13], and the resulting *O*-3-sulfate salt could act as a protecting group which could be selectively removed by hydrolysis [14]. As cyclic sulfates are usually synthesized via the oxidation of cyclic sulfites [13–17], the reaction of diol **4** with thionyl chloride was investigated first, using dichloromethane as solvent and triethylamine as base. The reaction was very fast even at −30 °C



Scheme 1.

and two *exo* and *endo*[3] isomers (**19** and **20**) were formed respectively in a ratio of ~2:1. They differed dramatically in almost all their properties and reactivity, but their MS spectra both gave an $[M+H]^+$ ion at *m*/*z* 237, excluding a dimeric structure.

The structures of **19** and **20** could not be deduced from their NMR spectra, but were established by X-ray crystallography (see Figs. 1 and 2). According to these data, the six membered ring of the cyclic sulfite occupies an almost identical chair conformation in both isomers, and the S→O bond is in "*syn* axial" relation with the axially oriented H-5a in **19**.

As cyclic sulfites can undergo a selective ring opening with strong nucleophiles via simultaneous elimination of sulfur dioxide [18], the reaction of potassium thiobenzoate with **19** and **20** in *N*,*N*-dimethyl formamide was investigated at 100 °C. While **20** was converted into the 5-*S*-benzoate **11** within 30 min, 5 h were needed for a complete

[3] *Exo* and *endo* refers to the orientation of the S→O bond in relation to the sugar furanose ring. The proper chemical name of **19** would be: 1*R*,2*S*,4*R*,7*R*,9*R*-3,5,8,10,12-pentaoxa-4-thia-11-dimethyl-tricyclo[7,3,0,$0^{2,7}$]-dodecane *S*-oxide while in **20** the sulfur has the opposite configuration (4*S*).

conversion of **19** and due to a partial 5-S→3-*O* benzoyl migration a mixture of **11** and **12** was formed. On the other hand, both **19** and **20** were almost instantly oxidized by sodium periodate in the presence of a catalytic amount of ruthenium(III) chloride at room temperature affording the cyclic sulfate **23** in excellent yield. The latter reacted rapidly with potassium thioacetate in acetonitrile to give the corresponding 5-*S*-acetate-3-*O*-sulfonic acid potassium salt **26** in practically quantitative yield. The sulfate ester could be hydrolyzed selectively with aq sulfuric acid according [13,19] and the resulting 3-OH derivative was isolated as its acetate **27**. However, this step was not necessary for the conversion of **26** into **13**, since all protecting groups could be removed simultaneously by boiling a methanolic solution of **26** in the presence of hydrochloric acid, affording after acetylation **13** in excellent yield (95%). The latter could be converted by acetolysis in acetic anhydride-sulfuric acid into **14** in 74% yield, consequently the overall yield of the **3**→**4**→**19**+**20**→**23**→**26**→**13**→**14** reaction sequence (Scheme 2) was 56%, making this approach more economic than that published (36.5%) [5].

For shortening further the synthesis of **14**, the direct transformation of the diol **4** into the cyclic sulfate **23** was considered. *N*,*N*-Sulfuryl diimidazole, which was used successfully [20] for a similar reaction, is too expensive for an economic, large scale synthesis. Therefore, the reaction of **4** with sulfuryl chloride was investigated. When this reaction was carried out in dichloromethane at 20 °C in the presence of triethylamine as base, a complex mixture was formed containing besides $SO_3 \cdot Et_3N$ the 5-chloro-derivative **21**, the sultone **22** and the cyclosulfate **23** in a 2:3:7 ratio. The formation of **21** can be explained via **24** or **25**, in which the terminal ester group undergoes either a fragmentation (route *a*) yielding **21** and sulfur trioxide, or by a substitution reaction with the chloride ion (route *b*). The sultone **22** could be formed from **21** via elimination of chlorine, which is a known reaction under photochemical conditions [21]. Because of the complex reaction and the low yield of **23**, this approach proved to be unsuitable for a large scale synthesis of **14**.

*Synthesis of the 4-cyanophenyl 1,5-dithio-*D*-xylopyranosides*.—Imidate **17** and bromide **18** have been used [22] as 5-thio-D-xylopyranosyl donors and reacted with 4-cyanothiophenol **28**. The highest yield (64%) of the β-anomer **30** was obtained using **18** in the presence of zinc oxide, but the formation of the α-anomer **29** was not mentioned. In order to check the influence of the different reaction conditions on the yield and the anomeric ratio, we applied acetate **14**, imidate **17**, as well as bromide **18** as donors and used in the case of **18**, besides zinc oxide, potassium carbonate as promoter too. From the data listed in Table 1, it can be seen that although the yield was the highest (90%) when acetate **14** was coupled with the aglycon in the presence of trimethylsilyl triflate, the α:β ratio was 3:1. This might be the consequence of a fast anomerisation of the primarily formed β-anomer, catalysed by the presence of the strong Lewis acid. The anomerisation was slower (α:β = 1:1) when imidate **17** was used as donor in the presence of boron trifluoride diethyl etherate, but the highest β-content (α:β ratio 1:4) was obtained in the presence of zinc oxide, using bromide **18** as donor. When the same reaction was carried out in the presence of potassium carbonate, besides **29** and **30** (3:7), their *C*-glycosylated derivatives **32** and **33**, as well as a *C*-glycosylated disulfide **34** could be isolated in 5:2:1 ratio. As proved earlier [1], the diglycosylated type derivatives such as **32** and **33** are not formed via the

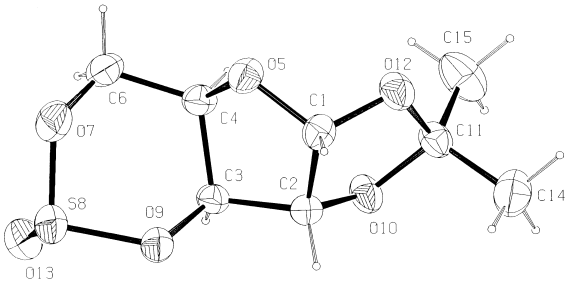


Fig. 1. ORTEP diagram of **19**. Thermal ellipsoids represent 40% probabilities.

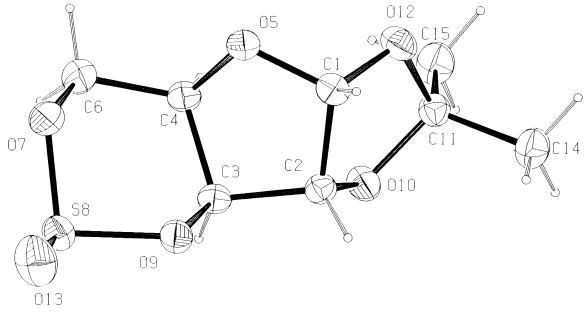
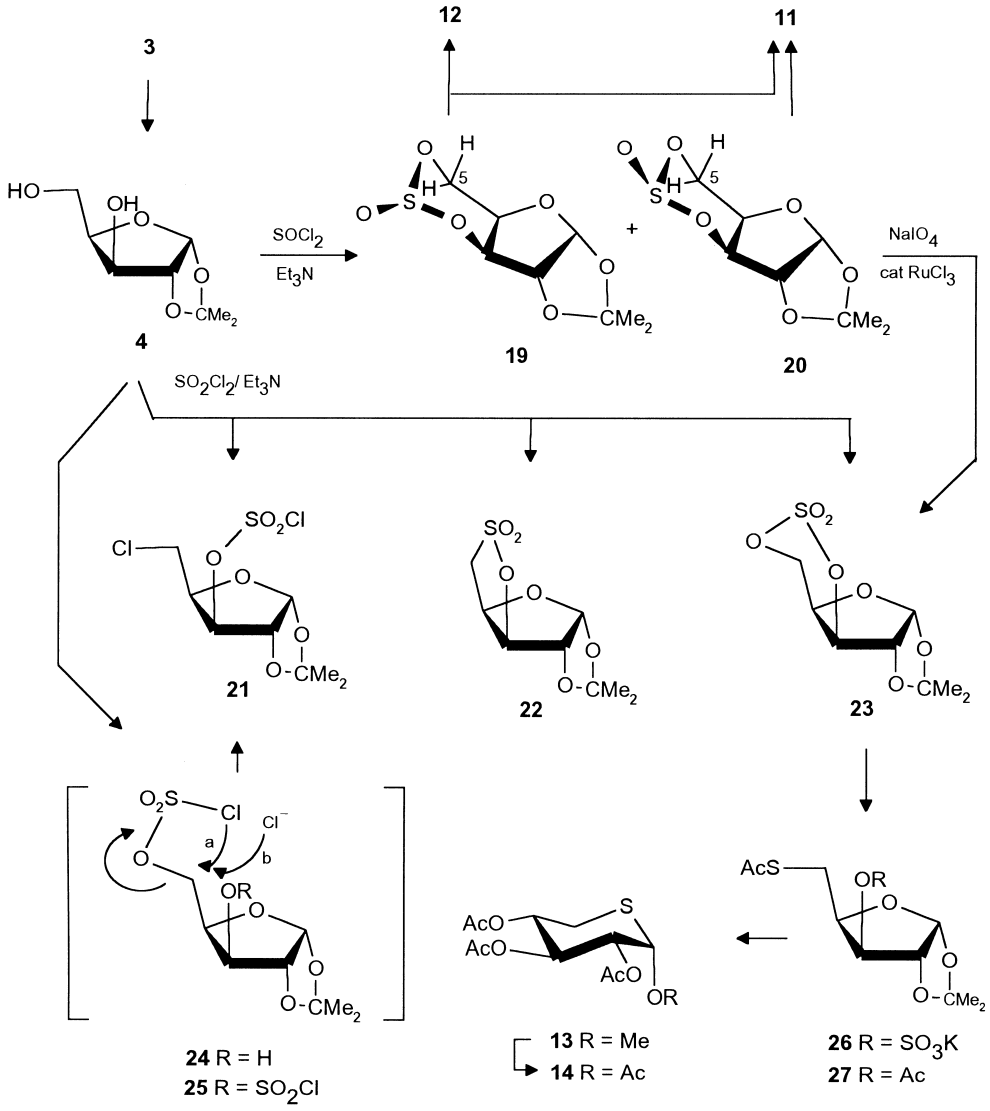


Fig. 2. ORTEP diagram of **20**. Thermal ellipsoids represent 40% probabilities.



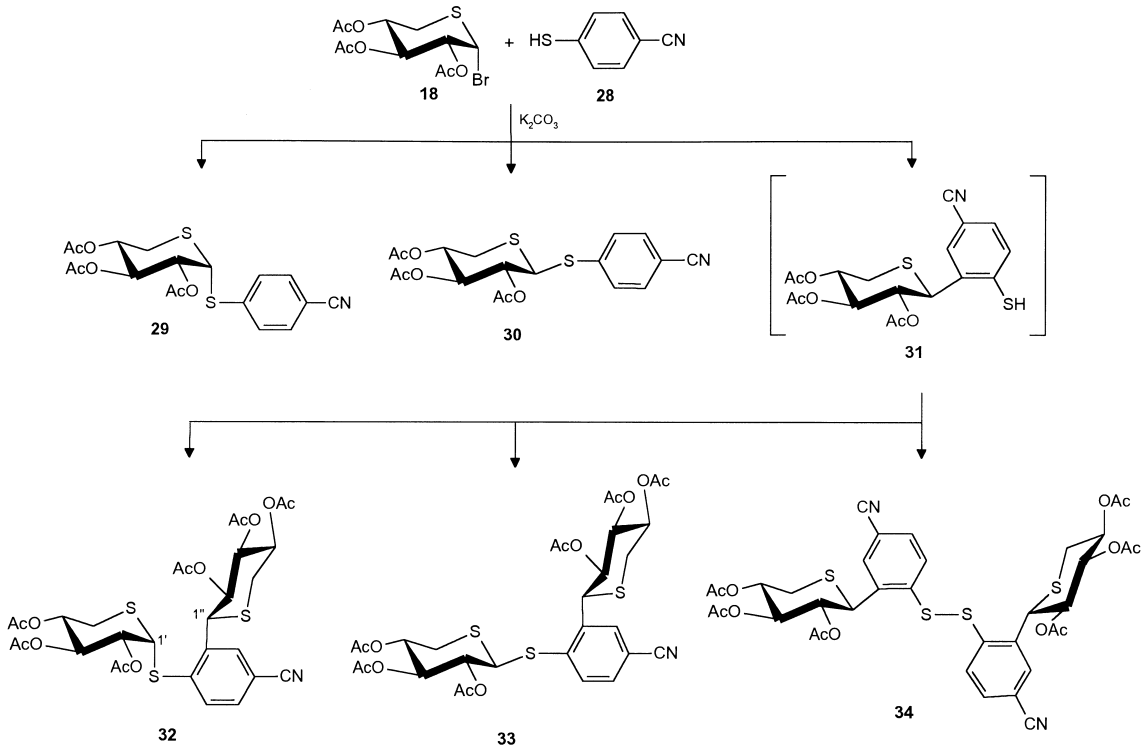
Scheme 2.

Table 1
Glycosydation of 4-cyanothiophenol with some 5-thio-D-xylopyranose donors under different conditions

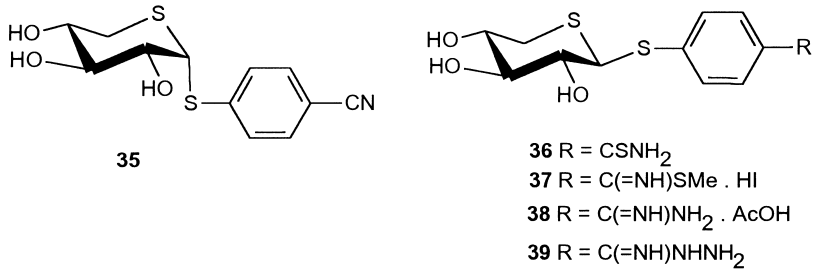
Donor	Promoter	Solvent	Time	Temperature	Yield (**29** + **30**)	α,β ratio (**29**:**30**)
14	TMSOTf	dichloroethane	1 h	r.t.	90%	3:1
17	$BF_3{\cdot}Et_2O$	dichloromethane	0.5 h	0 °C	60%	1:1
18	ZnO	acetonitrile/toluene	0.5 h	50 °C	76%	1:4
18	K_2CO_3	acetone	1 h	refl.	45%	3:7

corresponding *S*-glycosides **29** and **30**. The formation of **34** strongly supported our earlier proposed mechanism [1] according to which the *C*-glycosyl type compound **31** is formed first and is subsequently converted via *S*-glycosylation into the diglycosylated derivatives (**32** and **33**). The intermediate **31** is however air sensitive and is oxidized during work up to **34** (Scheme 3).

Deacetylation of both *S*-glycosides **29** and **30** was carried out under Zemplén's conditions and afforded the crystalline α- **35** and β-anomer **1** in excellent yield. However, when the reaction mixture was not neutralized after completion, the slow addition of methanol to the cyano group took place and, in the case of **1**, after 24 h at room temperature the corresponding iminoether **2** could be



Scheme 3.



Scheme 4.

isolated in a 20% yield. This yield could not be increased essentially by a prolonged reaction time, or by a higher sodium methoxide concentration. Attempts to convert the cyano group directly into a carboxyl group failed, but it reacted readily in pyridine–triethylamine solution with hydrogen sulfide and gave the corresponding thioamide **36** in high yield. Methylation of **36** with methyl iodide in acetone afforded the highly crystalline methylthioimine **37** the methylthio group of which could be easily exchanged by an amino or a hydrazino group, affording amidine **38** and amidrazone **39**, respectively.

Table 2
Oral antithrombotic activity of **1**, **2**, **36**, **37**, **38** and **39** in rats using Pescador's model [23]

Compound	**1**	**2**	**36**	**37**	**38**	**39**
ED_{50} (mg/kg)	25	10	5	1.5	5	2

Biological results.—The oral antithrombotic activity of **1**, **2**, **36**, **37**, **38**, and **39** was determined in rats, using Pescador's model [23]. All compounds were administered orally 3 h before ligation. From the data listed in Table 2, it can be seen that all beciparcil analogs in which the cyano group of the aglycon was transformed into different carboxylic acid derivatives were more active than beciparcil (**1**) itself. The most active compound was the methylthio-derivative **37** which, in contrary to the methoxy analogue **2**, is stable only as its hydroiodide salt and was selected for further biological testing.

3. Experimental

General methods.—Organic solns were dried over $MgSO_4$ and concentrated under diminished pressure at or below 40 °C. TLC used 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), toluene–MeOH mixture (*F*, 4:1), EtOAc–EtOH mixture (*G*, 9:1) and EtOAc–pyridine–water–AcOH mixture (*H*, 60:20:11:6); with detection by spraying the plates with a 0.02 M soln of I_2 and a 0.3 M soln of KI in a 10% aq H_2SO_4 soln followed by heating at ~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 otherwise stated (Tables 3 and 4). Multiplicities of the ^{13}C NMR spectra were obtained from DEPT experiments. The assignment of the protons were based on homonuclear decoupling and NOE difference 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. Mass spectra were recorded with a Finnigan MAT 8430 mass spectrometer/SS300 data system. For the FAB mode, an Ion Tech FAB gun (8 kV), and 4:1 glycerol–*m*-nitrobenzyl alcohol matrix were used.

Table 3
Selected ^1H NMR data for solutions in $CDCl_3$

Compound	Chemical shift δ					
	H-1	H-2	H-3	H-4	H-5a	H-5b
1[a]	4.44	3.33	3.12	3.47	2.70	2.50
2[a]	4.52	3.34	3.12	3.48	2.62	2.50
11	5.95	4.59	4.10	4.24	3.20	3.58
12	6.01	4.67	5.50	4.60	3.43	3.48
13	4.62	5.15	5.48	5.08	2.83	2.64
14	6.08	5.21	5.44	5.12	3.00	2.80
16	5.95	4.62	5.45	4.67	3.00	
17	6.28	5.28	5.57	5.16	3.06	2.82
18	5.50	4.88	5.53	5.08	3.13	2.93
19	6.03	4.62	4.91	4.19	4.16	4.96
20	6.07	4.72	4.79	4.36	4.57	4.57
20[a]	6.02	4.72	5.12	4.20	4.56	4.80
21	6.00	4.95	5.10	4.57	3.66	3.75
22	6.08	4.88	4.96	5.24	3.46–3.64	
23	6.08	4.76	5.21	4.28	4.86	5.00
26	5.81	4.76	4.40	4.06	3.01	3.06
27	5.90	4.52	5.18	4.34	3.14	3.17
29	4.90	5.28	5.48	5.08	3.14	2.80
30	4.20	5.20	5.02–5.16		2.75	2.87
35[a]	4.92	3.86	3.34	3.48	2.73	2.60
36[a]	4.30	3.28	3.06	3.44	2.64	2.48
37[a]	4.54	3.36	3.12	3.48	2.72	2.52
38[a]	4.42	3.35	3.12	3.45	2.65	2.50
39[a]	4.15	3.24	3.05	3.40	2.58	2.46

Compound	Coupling constants (Hz)					
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5a}$	$J_{4,5b}$	$J_{5a,5b}$
1[a]	10.0	9.8	8.8	10.0	4.3	13.2
2[a]	10.1	8.6	8.6	10.94	4.3	13.3
11	3.7	<1	2.2	4.3	10.0	14.2
12	3.8	<1	2.9	6.7	7.3	13.6
13	2.9	10.2	9.9	11.2	4.7	13.0
14	3.1	10.2	9.9	11.3	4.6	13.1
16	3.8	<1	2.5	nd[b]	nd	nd
17	3.1	10.2	10.0	11.3	4.5	13.2
18	3.4	9.8	9.8	11.2	4.6	13.4
19	3.7	<1	2.1	~1	2.3	13.2
20	3.7	<1	2.7	3.5	3.5	—
20[a]	3.8	<1	2.1	1.4	2.3	13.9
21	3.7	<1	2.7	8.5	5.7	11.2
22	3.3	<1	3.1	4.8	~1	~14
23	3.7	<1	2.1	~1	2.0	12.9
26	3.7	<1	3.2	7.6	5.9	13.7
27	3.7	<1	2.9	7.2	6.9	13.6
29	4.4	10.2	9.9	11.2	4.6	13.4
30	10.3	9.9	nd	10.2	4.0	14.0
35[a]	3.9	8.8	8.8	9.9	3.4	13.4
36[a]	10.1	8.6	8.6	10.6	4.6	13.3
37[a]	11.1	9.5	9.5	11.0	4.1	13.0
38[a]	9.9	8.6	8.6	9.8	4.2	13.2
39[a]	10.1	8.6	8.6	10.7	4.6	13.2

[a] Me_2SO-d_6.
[b] nd, Not determined.

Table 4
Selected ^{13}C NMR data for solutions in $CDCl_3$

Compound	Chemical shift δ					
	C-1	C-2	C-3	C-4	C-5	Others
1[a]	50.6	78.9[b]	75.8[b]	73.0[b]	33.5	
2[a]	51.6	78.9[b]	75.8[b]	73.0[b]	33.6	164.9 (C=NH); 53.2 (OMe)
11	104.7	84.7[b]	80.8[b]	73.9[b]	25.4	
12	104.8	83.5[b]	78.2[b]	77.0[b]	26.8	
14	73.2[b]	72.4[b]	70.8[b]	69.9[b]	26.0	
16	104.6	83.4[b]	77.9[b]	76.8[b]	36.2	
17	76.0[b]	73.7[b]	72.4[b]	69.9[b]	26.2	160.7 (C=NH); 90.7 (CCl_3)
18	53.3	74.3[b]	72.2[b]	70.4[b]	27.6	
19	104.5	83.2	69.0	70.8	55.3	
20	105.5	83.6	79.8	72.0	63.4	
21	104.8	86.8[b]	82.0[b]	78.7[b]	38.1	
22	106.3	85.2[b]	82.3[b]	78.7[b]	52.0	
23	104.4	82.4	87.3	69.2	73.6	
26	104.4	83.4[b]	78.5[b]	78.4[b]	27.1	
27	104.5	83.2[b]	77.7[b]	75.9[b]	26.3	30.2 (SAc); 20.5 (OAc)
30	50.6	73.7[b]	73.4[b]	72.0[b]	31.2	118.1 (CN)
38[a]	51.0	73.0[b]	75.8[b]	79.0[b]	33.6	165.6 ($C(NH_2)_2^+$)
39[a]	52.4	73.0[b]	75.8[b]	79.0[b]	33.7	133.8 (C=NH)

[a] Me_2SO-d_6.
[b] Arbitrary assignment.

Table 5
Crystal data and structure refinement

Compound	**19**	**20**
Empirical formula	$C_8H_{12}O_6S$	
Formula weight	236.24	
Crystal system	tetragonal	orthorhombic
Space group	$P4_12_12$	$P2_12_12_1$
Unit cell dimensions, Å		
a (Å)	7.307(1)	6.704(1)
b (Å)		10.705(1)
c (Å)	39.572(8)	14.279(2)
Volume Å^3	2112.8(6)	1024.8(2)
Z	8	4
Density (calc) (Mg/m^3)	1.485	1.531
μ (mm^{-1})	0.313	0.323 mm^{-1}
F(000)	992	496
Crystal description	colourless blocks	
Crystal size (mm)	0.50×0.20×0.15	0.30×0.10×0.10
Reflections collected	6852	4086
Independent reflections	2929	3480
Data/restraints/parameters	2455/0/138	2738/0/138
Goodness-of-fit on F^2	0.931	0.933
Final *R* indices [$I > 2\sigma(I)$]		
*R*1	0.0353	0.0421
*wR*2	0.0834	0.0841
R indices (all data)		
*R*1	0.0925	0.1371
*wR*2	0.1144	0.1137
Weighting scheme used	$w = 1/[\sigma^2(F_o^2) + (kP)^2]$ where $P = (F_o^2 + 2F_o^2)/3$	
k	0.462	0.463
Absolute structure parameter	−0.06(11)	−0.07(10)
Largest diff. peak and hole (eÅ^{-3})	0.146, −0.164	0.244–0.246

X-ray data[4]: unit cell parameters were determined by least-squares of the setting angles of 25 (**19**: 15.08 $\leq\theta\leq$18.85°, **20**: 13.14 $\leq\theta\leq$15.37°) reflections. Intensity data were collected on an Enraf–Nonius CAD4 diffractometer (graphite monochromator; Mo-K_α radiation, $\lambda = 0.71073$ Å) at 293(2) K in the range 2.06 $\leq\theta\leq$29.45° (**19**, index ranges: $-10 \leq h \leq 10$; $-10 \leq k$ 10; $-54 \leq l$ 54) and 2.38$\leq\theta\leq$32.40° (**20**, index ranges: $-10 \leq h \leq 10$; $-16 \leq k \leq 16$; $-21 \leq l \leq 21$) using ω–θ scans. The intensities of three standard reflections were monitored regularly every 60 min. The intensities of the standard reflections indicated 2% (**19**) and 3% (**20**) decay. The structures were solved by direct methods [24] and refined by anisotropic full matrix least-squares on F^2 [25]. Crystal data and refinement details are shown in Table 5. Hydrogen atomic positions were calculated from assumed geometries. Hydrogen atoms were included in structure factor calculations but they were not refined. The methyl hydrogen atoms were allowed to rotate about the C–CH_3 bonds. Neutral atomic scattering factors and anomalous scattering factors were taken from [26]. Final atomic parameters are listed in Tables 6 and 7, bond lengths and angles are given in Tables 8 and 9.

1,2-O-*Isopropylidene*-α-D-*xylofuranose* (**4**).—A slurry of **3** (150 g) and anhyd $CuSO_4$ (200 g) in acetone (3 L) and H_2SO_4 (15 mL) was stirred at 20 °C for 24 h and was then filtered. Concd NH_4OH (48 mL) was added and the filtered soln was concentrated to yield a syrup containing according to GLC [7] **4** and **5** in a ratio of ~1:9. This mixture was dissolved in MeOH (1.200 L), warmed to 40 °C, and then 0.1 M HCl (330 mL) was added. After 100 min, when **5** (R_f 0.7, solvent *F*) was completely converted into **4** (R_f 0.4, solvent *F*) the mixture was neutralized with solid $NaHCO_3$, filtered, concentrated and then coevaporated with EtOH and toluene. The residue was dissolved in CH_2Cl_2 (500 mL) dried, filtered and concentrated to yield a syrup (190 g, ~100%) containing, according to GLC, 98% of **4** and 2% of **5**.

Reaction of **6** *with potassium thiobenzoate*.—(a) To a soln of **6** [11] (0.7 g) in DMF (10 mL), KSBz

[4] Tables of atomic coordinates, bond lengths, and bond angles have been deposited with the Cambridge Crystallographic Data Centre. These tables may be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, UK, CB2 1EZ.

Table 6
Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$). U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor

Atom	x	y	z	U(eq)
	19			
C-1	10319(3)	−2146(3)	800(1)	47(1)
C-2	9776(3)	−1275(3)	462(1)	46(1)
C-3	9491(3)	726(3)	549(1)	43(1)
C-4	10742(3)	987(2)	853(1)	44(1)
O-5	10597(2)	−707(2)	1031(1)	52(1)
C-6	10258(3)	2553(3)	1080(1)	58(1)
O-7	8324(2)	2595(2)	1158(1)	66(1)
S-8	6985(1)	2724(1)	843(2)	63(1)
O-9	7587(2)	879(2)	646(1)	56(1)
O-10	11363(2)	−1434(2)	262(1)	54(1)
C-11	12424(3)	−2923(3)	385(1)	49(1)
O-12	11946(2)	−3080(2)	733(1)	57(1)
O-13	7570(3)	4234(2)	634(1)	75(1)
C-14	11916(4)	−4667(3)	209(1)	77(1)
C-15	14410(3)	−2447(4)	352(1)	84(1)
	20			
C-1	−1394(4)	851(2)	7145(2)	35(1)
C-2	−1206(4)	1904(2)	6425(1)	33(1)
C-3	−1116(3)	1232(2)	5498(2)	33(1)
C-4	−2260(3)	35(2)	5709(2)	38(1)
O-5	−1643(3)	−263(1)	6645(1)	43(1)
C-6	−1837(4)	−1037(2)	5055(2)	49(1)
O-7	285(3)	−1210(1)	4907(1)	46(1)
S-8	1304(1)	14(1)	4441(1)	40(2)
O-9	979(2)	966(1)	5321(1)	38(1)
O-10	−3055(3)	2530(2)	6476(1)	41(1)
C-11	−3871(4)	2332(2)	7392(2)	36(1)
O-12	−3101(3)	1146(2)	7672(1)	44(1)
O-13	3406(3)	−254(2)	4465(2)	65(1)
C-14	−3186(5)	3343(3)	8056(2)	53(1)
C-15	−6097(4)	2253(3)	7295(2)	52(1)

Table 7
Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($Å^2 \times 10^3$)

Atom	x	y	z	U(iso)
	19			
H-1	9387	−2970	878	60
H-2	8726	−1834	359	60
H-3	9790	1535	366	56
H-4	11981	1129	776	58
H-6a	10948	2464	1286	75
H-6b	10584	3682	971	75
H-14a	10649	−4935	250	104
H-14b	12658	−5649	294	104
H-14c	12115	−4535	−30	104
H-15a	14663	−1357	479	114
H-15b	14700	−2243	118	114
H-15c	15141	−3436	437	114
	20			
H-1	−235	807	7539	45
H-2	−85	2442	6537	43
H-3	−1708	1705	4999	43
H-4	−3663	215	5706	49
H-6a	−2383	−1787	5320	64
H-6b	−2480	−893	4464	64
H-14c	−1755	3376	8060	72
H-14b	−3661	3163	8676	72
H-14c	−3707	4134	7855	72
H-15a	−6433	1596	6865	70
H-15b	−6601	3033	7063	70
H-15c	−6680	2079	7895	70

(0.5 g) was added and the mixture was refluxed for 2 h. After concentration, the residue was dissolved in CH_2Cl_2, washed with water, concentrated and submitted to column chromatography (solvent *D*). Concentration of the first fraction gave 3-*O*-benzoyl-5-*S*-benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranose (**12**, 200 mg, 24%): mp 92–94 °C (hexane); $[\alpha]_D$ −100° (*c* 0.5, $CHCl_3$); R_f 0.6 (solvent *D*); Anal. Calcd for $C_{22}H_{22}O_6S$: C, 63.75; H, 5.35; S, 7.74. Found: C, 63.62; H, 5.18; S, 7.87.

Concentration of the second fraction gave 3-*O*-benzoyl-1,2-*O*-isopropylidene-5-thio-α-D-xylofuranose disulfide (**16**, 350 mg, 56%): $[\alpha]_D$ +68° (*c* 0.5, $CHCl_3$); R_f 0.4 (solvent *D*); Anal. Calcd for $C_{30}H_{34}O_{10}S_2$: C, 58.24; H, 5.54; S, 10.36. Found: C, 58.19; H, 5.47; S, 10.35.

(b) To a soln of **6** (0.7 g) in DMF (10 mL), KSBz (0.5 g) was added and the mixture was stirred at 110 °C for 1.5 h. After concentration, the residue was dissolved in CH_2Cl_2, washed with water, concentrated and submitted to column chromatography (solvent *D*). Concentration of the first fraction gave **12** (200 mg, 24%), identical with the compound described above.

Concentration of the second fraction gave 5-*S*-benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranose (**11**, 240 mg, 38%): mp 146–148 °C (hexane); $[\alpha]_D$ +54°; R_f 0.3 (solvent *D*); Anal. Calcd for $C_{15}H_{18}O_6S$: C, 63.75; H, 5.35; S, 7.74. Found: C, 63.62; H, 5.18; S, 7.87.

3-O-*Benzoyl-5*-S-*benzoyl-1,2*-O-*isopropylidene*-α-D-*xylofuranose* (**12**).—To a soln of **10** [10] (20.3 g) in DMF (110 mL), KSBz (11.9 g) was added and the mixture was stirred at 110 °C for 1 h. After concentration, the residue was dissolved in CH_2Cl_2, washed with water and concentrated to yield **12** (17.8 g, 95%) identical with the compound described above.

1,2-O-*Isopropylidene*-α-D-*xylofuranose 3,5-cyclic sulfites* (**19** *and* **20**).—To a stirred soln of crude **4** (190 g) in CH_2Cl_2 (2 L) and Et_3N (340 mL), thionyl

Table 8
Bond distances and angles

Atom 1	Atom 2	Distance (Å)	
		19	**20**
C-1	O-5	1.410(2)	1.400(3)
C-1	O-12	1.395(2)	1.406(3)
C-1	C-2	1.531(3)	1.531(3)
C-2	O-10	1.410(2)	1.411(3)
C-2	C-3	1.516(3)	1.508(3)
C-3	O-9	1.447(2)	1.455(3)
C-3	C-4	1.522(3)	1.523(3)
C-4	O-5	1.429(2)	1.435(3)
C-4	C-6	1.499(3)	1.506(3)
C-6	O-7	1.447(3)	1.450(3)
O-7	S-8	1.590(2)	1.620(2)
S-8	O-13	1.442(2)	1.438(2)
S-8	O-9	1.617(1)	1.632(2)
O-10	C-11	1.421(2)	1.435(3)
C-11	O-12	1.428(2)	1.428(3)
C-11	C-15	1.498(3)	1.501(3)
C-11	C-14	1.498(3)	1.510(3)

Atom 1	Atom 2	Atom 3	Angle (°)	
			19	**20**
O-12	C-1	O-5	111.4(2)	111.6(2)
O-12	C-1	C-2	105.1(2)	105.1(2)
O-5	C-1	C-2	107.1(2)	107.1(2)
O-10	C-2	C-3	108.6(2)	107.9(2)
O-10	C-2	C-1	104.1(2)	104.1(2)
C-3	C-2	C-1	103.9(2)	104.0(2)
O-9	C-3	C-2	105.5(2)	106.6(2)
O-9	C-3	C-4	111.0(2)	110.8(2)
C-2	C-3	C-4	102.5(1)	102.0(2)
O-5	C-4	C-6	110.3(2)	110.7(2)
O-5	C-4	C-3	103.7(1)	103.1(2)
C-6	C-4	C-3	115.3(2)	115.1(2)
C-1	O-5	C-4	109.6(1)	108.7(2)
O-7	C-6	C-4	112.0(2)	111.9(2)
C-6	O-7	S-8	115.7(1)	111.8(2)
O-13	S-8	O-7	108.2(1)	104.0(1)
O-13	S-8	O-9	106.4(1)	103.8(1)
O-7	S-8	O-9	99.3(1)	97.61(9)
C-3	O-9	S-8	117.0(1)	112.7(1)
C-2	O-10	C-11	108.6(1)	108.1(2)
O-10	C-11	O-12	105.0(2)	104.4(2)
O-10	C-11	C-15	108.7(2)	107.7(2)
O-12	C-11	C-15	109.9(2)	109.6(2)
O-10	C-11	C-14	111.0(2)	110.5(2)
O-12	C-11	C-14	108.6(2)	110.6(2)
C-15	C-11	C-14	113.4(2)	113.6(2)
C-1	O-12	C-11	110.5(1)	110.1(2)

Table 9
Ring torsion angles

Atom 1	Atom 2	Atom 3	Atom 4	Torsion angle (°)	
				19	**20**
Pentafuranose ring O-5 C-1 C-2 C-3 C-4					
O-5	C-1	C-2	O-10	104.8(2)	105.9(2)
O-12	C-1	C-2	O-10	−13.7(2)	−12.9(2)
O-12	C-1	C-2	C-3	−127.4(2)	−125.7(2)
O-5	C-1	C-2	C-3	−8.8(2)	−6.9(2)
O-10	C-2	C-3	O-9	160.5(1)	160.9(2)
C-1	C-2	C-3	O-9	−89.1(2)	−89.0(2)
O-10	C-2	C-3	C-4	−83.2(2)	−82.8(2)
C-1	C-2	C-3	C-4	27.1(2)	27.3(2)
O-9	C-3	C-4	O-5	75.9(2)	74.7(2)
C-2	C-3	C-4	O-5	−36.3(2)	−38.4(2)
O-9	C-3	C-4	C-6	−44.8(2)	−45.8(3)
C-2	C-3	C-4	C-6	−157.0(2)	−159.0(2)
O-12	C-1	O-5	C-4	99.5(2)	96.3(2)
C-2	C-1	O-5	C-4	−14.8(2)	−18.3(2)
C-6	C-4	O-5	C-1	156.5(2)	159.4(2)
C-3	C-4	O-5	C-1	32.4(2)	35.9(2)
Ring S-8 O-7 C-6 C-4 C-3 O-9					
O-5	C-4	C-6	O-7	−70.5(2)	−69.4(3)
C-3	C-4	C-6	O-7	46.6(2)	47.0(3)
C-4	C-6	O-7	S-8	−57.9(2)	−60.8(2)
C-6	O-7	S-8	O-13	−51.6(2)	172.4(2)
C-6	O-7	S-8	O-9	59.1(2)	66.1(2)
C-2	C-3	O-9	S-8	164.8(1)	169.3(1)
C-4	C-3	O-9	S-8	54.5(2)	59.1(2)
O-13	S-8	O-9	C-3	53.7(2)	−172.6(2)
O-7	S-8	O-9	C-3	−58.4(2)	−66.0(2)
Ring O-10 C-2 C-1 O-12 C-11					
C-3	C-2	O-10	C-11	135.0(2)	136.0(2)
C-1	C-2	O-10	C-11	24.7(2)	26.0(2)
C-2	O-10	C-11	O-12	−26.3(2)	−29.2(2)
O-5	C-1	O-12	C-11	−117.7(2)	−120.6(2)
C-2	C-1	O-12	C-11	−2.1(2)	−4.9(2)
O-10	C-11	O-12	C-1	17.0(2)	20.5(2)

chloride (78 mL) was added at −30 °C. Stirring was continued for 15 min, then water (40 mL) was added gradually. The mixture was washed with water, 6% aq $NaHCO_3$, and water to give after concentration a solid crude mixture (231 g, 98%) containing **19** and **20** in a ratio of ~2:1. An aliquot part (10 g) of this mixture was boiled with ether (50 ml) for 15 min to give, after cooling and filtration the *endo* isomer **20** (2.9 g, 29%); mp 132–134 °C (acetone–hexane); $[\alpha]_D$ −10°; R_f 0.4 (solvent *C*); MS: *m/z* 237 $[M+H]^+$. The residue, obtained on concentration of the filtrate, was submitted to column chromatography (solvent *C*). The residue, obtained on concentration of the fractions having R_f 0.7, was crystallized with ether to give the *exo* isomer **19** (6.1 g, 61%); mp 100–102 °C (acetone–hexane); $[\alpha]_D$ +47°; MS: *m/z* 237 $[M+H]^+$. Anal. Calcd for $C_8H_{12}O_6S$: C, 40.67; H, 5.12; S, 13.57. Found for **19**: C, 40.60; H, 5.08; S, 13.35. Found for **20**: C, 40.65; H, 5.15; S, 13.38.

Reaction of **19** *and* **20** *with potassium thiobenzoate*.—(a) A soln of **20** (0.5 g) and KSBz (0.4 g) in DMF (10 mL) was stirred at 100 °C. After 30 min, when according to TLC the starting material was consumed, the mixture was concentrated, the

residue dissolved in CH_2Cl_2 and washed with water to give, after concn and filtration of the residue with water, **11** (0.35 g, 53%) identical with the compound described above.

(b) A similar mixture of **19** had to be heated to 100 °C for 5 h, until the starting material was consumed. The mixture was concentrated, the residue dissolved in CH_2Cl_2 and washed with water. Column chromatography (solvent *D*) of the residue obtained after concentration of the CH_2Cl_2 soln afforded **11** (0.25 g, 38%) and **12** (0.17 g, 19%) identical with the compounds described above.

1,2-O-*Isopropylidene*-α-D-*xylofuranose 3,5*-O-*cyclic sulfate* (**23**).—To a stirred and ice cooled soln of the crude mixture of **19** and **20** (120 g) in EtOAc (600 mL) and CH_3CN (600 mL), $RuCl_3$ hydrate (50 mg) and subsequently a soln of $NaIO_4$ (240 g) in water (2.4 L) was added at such a rate to keep the temperature below 20 °C. The formed slurry was filtered after 30 min and the solid material was washed with water (200 mL) and then separately with EtOAc (3×200 mL). The aq soln was extracted with EtOAc (3×200 mL), then the combined organic solns were washed with 6% aq $NaHCO_3$, and water to give after concn **23** (105 g, 82%); mp 151–155 °C (acetone–hexane); $[\alpha]_D + 21°$ (*c* 1, acetone); R_f 0.5 (solvent *C*); MS *m/z* 253 $[M+H]^+$. The yields from **19** and **20** were 86 and 88%, respectively. Anal. Calcd for $C_8H_{12}O_7S$: C, 38.09; H, 4.80; S, 12.71. Found: C, 38.12; H, 4.75; S, 12.66.

5-S-*Acetyl-1,2*-O-*isopropylidene*-α-D-*xylofuranose 3*-O-*sulfonic acid potassium salt* (**26**).—To a stirred soln of **23** (25.2 g) in CH_3CN (250 mL), KSAc (12 g) was added at room temperature. After 1 h, the mixture was concentrated and the residue was taken up in acetone–ether and the solids were removed by filtration to give **26** (35.5 g, 97%); mp 223 °C dec.; $[\alpha]_D - 20°$ (*c* 1, water); R_f 0.4 (solvent *G*); Anal. Calcd for $C_{10}H_{15}O_8S_2K$: C, 32.78; H, 4.13; S, 17.50; K, 10.67. Found: C, 32.55; H, 4.03; S, 17.64; K, 10.89.

3-O-*Acetyl-5*-S-*acetyl-1,2*-O-*isopropylidene*-α-D-*xylofuranose* (**27**).—To a stirred soln of **26** (3.7 g) in THF (100 mL), concd H_2SO_4 (5 μL) and water (1.8 μL) were added. After 30 min at room temperature, when hydrolysis of the sulfonic ester was complete (R_f 0.4→0.7; solvent *G*), pyridine (20 mL) and Ac_2O (10 mL) were added. The mixture was concentrated after 2 h and the residue purified by column chromatography (solvent *E*) to give **27** (1.8 g, 63%) as syrup; $[\alpha]_D - 17°$; R_f 0.5 (solvent *C*); Anal. Calcd for $C_{12}H_{18}O_6S$: C, 49.64; H, 6.25; S, 11.04. Found: C, 49.60; H, 6.32; S, 10.95.

Methyl 2,3,4-tri-O-*acetyl-5-thio*-α-D-*xylopyranoside* (**13**).—(a) A soln of **12** (2.0 g) in MeOH (50 mL) and 3 M methanolic NaOMe (2.5 mL) was stirred at room temperature for 1 h, then acidified with 10% aq HCl and refluxed for 1 h. After neutralization with Et_3N, the mixture was concentrated, the residue was dissolved in pyridine (10 mL) and Ac_2O (10 mL) was added. The mixture was kept at room temperature for 24 h, then processed the usual way to give after column chromatography (solvent *B*) **13** (0.95 g, 64%): $[\alpha]_D + 196°$; R_f 0.6 (solvent *B*); Anal. Calcd for $C_{12}H_{18}O_7S$: C, 47.05; H, 5.93; S, 10.45. Found: C, 46.88; H, 5.90; S, 10.34.

(b) A soln of **26** (36.6 g) in MeOH (370 mL) and concd HCl (37 mL) was boiled for 1.5 h. The cooled mixture was neutralized with solid $NaHCO_3$, filtered and concentrated. Then, EtOH and toluene were added and destilled off from the residue which was thereafter dissolved in pyridine (80 mL) and Ac_2O (60 mL) was added. The mixture was processed through the usual way after 24 h at room temperature to give a syrup (29.5 g, 96.5%) which, according to NMR contained >90% **13**. Column chromatography (solvent *B*) gave **13** identical with the compound described above.

1,2,3,4-Tetra-O-*acetyl-5-thio*-α-D-*xylopyranose* (**14**).—To a stirred soln of **13** (100 g) in Ac_2O (110 mL), concd H_2SO_4 (7 mL) was added at 0 °C and stirring was continued for 1 h at 0 °C. After adding NaOAc (15 g), the pH was adjusted to ~6 with ice-cold 6% aq $NaHCO_3$ and stirring was continued at room temperature for 2 h. Then, the mixture was extracted with CH_2Cl_2, washed with water, concentrated and submitted to column chromatography (solvent *B*) to give **14** (80.8 g, 74%); mp 98–100 °C (ether–hexane); $[\alpha]_D + 204°$ (*c* 0.5); R_f 0.4 (solvent *B*); lit mp 98–100 °C, $[\alpha]_D + 210°$ (*c* 2.8) [9]; lit mp 99–100 °C, $[\alpha]_D + 219°$ (*c* 2.2) [11].

O-*(2,3,4-Tri*-O-*acetyl-5-thio*-α-D-*xylopyranosyl) trichloroacetimidate* (**17**).—Under argon, hydrazine acetate (0.4 g) was added to a stirred soln of **14** (1.0 g) in DMF (30 mL) at room temperature. After 2 h, EtOAc (50 mL) and CH_2Cl_2 (50 mL) were added, the organic layer was washed with brine, concentrated and the residue submitted to column chromatography (solvent *A*) to yield **15** (0.6 g, 69%): R_f 0.3 (solvent *B*). The resulting compound was dissolved in CH_2Cl_2 (10 mL), CCl_3CN (2.05 mL) and K_2CO_3 (2.8 g) were added under

argon and the mixture was stirred for 24 h at room temperature. After diluting with ether, the mixture was filtered through a bed of Celite, concentrated and the residue submitted to column chromatography (solvent *B*) to yield **17** (0.6 g, 67%): mp 105–108 °C (hexane–EtOAc); lit. [22] 110 °C; $[\alpha]_D$ +221° (*c* 0.5, $CHCl_3$); lit. [22] +227° (*c* 0.42, $CHCl_3$); R_f 0.7 (solvent *B*).

2,3,4-Tri-O-*acetyl*-α-D-*xylopyranosyl bromide* (**18**).—To a stirred soln of **15** (10 g) in CH_2Cl_2 (40 mL), 33% HBr in AcOH (20 mL) was added and stirring was continued for 1 h at room temperature. Then, the mixture was poured into ice-water, extracted with CH_2Cl_2, washed with 6% aq $NaHCO_3$, water and concentrated to yield **18** (10.5 g, 99%): mp 115 °C (hexane), lit. 115 °C [8]; $[\alpha]_D$ +221° (*c* 0.5, $CHCl_3$), lit. [8] +245° (*c* 1.75, MeOH); R_f 0.7 (solvent *B*).

Reaction of **4** *with sulfuryl chloride*.—To a stirred soln of **4** (1.9 g, 10 mmol) in CH_2Cl_2 (30 mL), Et_3N (3.4 mL, 25 mmol) and after cooling to 0 °C a soln of SO_2Cl_2 (0.9 mL, 11 mmol) in CH_2Cl_2 (10 mL) was added. The mixture was kept at 20 °C for 24 h. The solid residue obtained on concentration of the CH_2Cl_2 soln (2.5 g) contained $SO_3{\cdot}Et_3N$, **21**, **22** and **23** in a 3:2:3:7 ratio. Column chromatography (solvent *E*) afforded 5-chloro-3-*O*-chlorosulfonyl-5-deoxy-1,2-*O*-isopropylidene-D-xylofuranose (**21**, 0.15 g, 5%); mp 82–84 °C; $[\alpha]_D$ −74°; R_f 0.55 (solvent *C*); MS: *m*/*z* 308 $[M+H]^+$; Anal. Calcd for $C_8H_{12}Cl_2O_6S$: C, 31.28; H, 3.94; Cl, 23.09; S, 10.44. Found: C, 31.41; H, 4.03; Cl 22.88; S, 10.32.

Concentration of the fraction with R_f 0.5 gave a 1:2 mixture of **22** and **23** (1.6 g). This was dissolved in CH_3CN (20 mL) and KSAc (0.8 g) was added. After 20 h at 20 °C the mixture was concentrated and the residue was taken up in CH_2Cl_2. The solids were removed by filtration to give crude **23** contaminated with KSAc. The organic soln was washed with water to give on concentration 3,7,9,11-tetraoxa-4-thia-10-dimethyl-tricyclo[6,3,0,$0^{2,6}$]undecane *S*-dioxide (**22**, 0.5 g, 21%); mp 150–152 °C; $[\alpha]_D$ +37°; R_f 0.5 (solvent *C*); MS *m*/*z* 237 $[M+H]^+$; Anal. Calcd for $C_8H_{12}O_6S$: C, 40.67; H, 5.12; S, 13.57. Found: C, 40.70; H, 5.18; S, 13.55.

Reaction of **14** *with 4-cyanothiophenol*.—4-Cyanothiophenol (1.3 g) was added under argon to a stirred soln of **14** (1.75 g) in dry 1,2-dichloroethane (25 mL) and the mixture was cooled to −10 °C. After addition of Me_3SiOTf (0.9 mL), the temperature was allowed to raise and the mixture was stirred at room temperature for 1 h, then quenched with Et_3N. The residue, obtained on concentration, was submitted to column chromatography (solvent *A*) to yield a 3:1 mixture of **29** and **30** (1.92 g, 90%).

Reaction of **17** *with 4-cyanothiophenol*.—4-Cyanothiophenol (95 mg) was added under argon to a stirred soln of **17** (250 mg) in dry CH_2Cl_2 (10 mL) and the mixture was cooled to 0 °C. After addition of 0.1 M $BF_3{\cdot}OEt_2$ (1 mL) in CH_2Cl_2, the mixture was stirred at 0 °C for 30 min, then quenched with Et_3N. The residue, obtained on concentration, was submitted to column chromatography (solvent *A*) to yield a 1:1 mixture of **29** and **30** (140 mg, 60%).

Reaction of **18** *with 4-cyanothiophenol*.—(a) 4-Cyanothiophenol (4.4 g) was added to a stirred soln of **18** (10.5 g) in dry toluene (100 mL) and dry MeCN (100 mL). After addition of ZnO (2.8 g), the mixture was stirred at 50 °C for 30 min, then cooled to room temperature, filtered through Celite and concentrated. The residue was submitted to column chromatography (solvent *A*) to yield a 1:4 mixture of **29** and **30** (9.12 g, 76%).

(b) 4-Cyanothiophenol (2.6 g) and K_2CO_3 (2.6 g) were added to a stirred soln of **18** (5 g) in dry acetone (250 mL) and the mixture was refluxed for 1 h. Then the reaction was cooled to room temperature, filtered, the filtrate was concentrated, and the residue was submitted to column chromatography (solvent *A*) to yield on concentration of the first fraction a 3:7 mixture of **29** and **30** (2.67 g, 45%).

Concentration of the second fraction gave 4-cyano-2-(2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)phenyl 2,3,4-tri-*O*-acetyl-1,5-dithio-α-D-xylopyranoside (**32**, 0.95 g, 20%): mp 97–102 °C (hexane); $[\alpha]_D$ +164° (*c* 0.5, $CHCl_3$); R_f 0.4 (solvent *A*); ^{1}H NMR: δ 5.63 (dd, 1 H, H-3), 5.44 (dd, 1 H, H-2″), 5.26 (dd, 1 H, H-3″), 5.22 (dd, 1 H, H-2), 5.21 (ddd, 1 H, H-4″), 5.07 (ddd, 1 H, H-4), 4.87 (d, 1 H, H-1), 4.86 (d, 1 H, H-1″), 3.16 (dd, 1 H, H-5ax), 3.11 (dd, 1 H, H-5″ax), 2.96 (dd, 1 H, H-5″eq), 2.84 (dd, 1 H, H-5eq), 2.10–1.72 (m, 18 H, OAc); $J_{1,2}$ 4.5, $J_{2,3}$ 10.0, $J_{3,4}$ 9.6, $J_{4,5ax}$ 11.0, $J_{4,5eq}$ 4.9, $J_{5ax,5eq}$ 13.5, $J_{1,5eq}$ 1.4, $J_{1'',2''}$ 10.6, $J_{2'',3''}$ 9.6, $J_{3'',4''}$ 9.9, $J_{4'',5''ax}$ 10.5, $J_{4'',5''eq}$ 4.2, $J_{5''ax,5''eq}$ 13.4 Hz; ^{13}C NMR: δ 169.9, 169.8, 169.8, 169.7, 169.5, 168.7 (C=O), 140.3 (C-1′), 139.3 (C-2′), 134.5 (C-6′), 132.0 (C-3′), 131.7 (C-5′), 117.4 (CN), 112.7 (C-4′), 75.2 (C-2), 75.1 (C-2″), 74.3 (C-3″), 72.7 (C-4″), 72.6 (C-4), 69.8 (C-3), 53.1 (C-1), 45.1 (C-1″), 31.0

(C-5″), 26.9 (C-5), 20.8, 20.8, 20.6, 20.5, 20.3, 20.1 (OAc). Anal. Calcd for $C_{29}H_{33}NO_{12}S_3$: C, 50.94; H, 4.86; N, 2.05; S, 14.07. Found: C, 50.99; H, 4.73; N, 2.11; S, 14.13.

Concentration of the third fraction gave 4-cyano-2-(2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)phenyl disulfide (**34**, 0.23 g, 4%): mp 158–163 °C (EtOAc-hexane); $[\alpha]_D + 26°$ (*c* 0.3, $CHCl_3$); R_f 0.35 (solvent *A*); ^{1}H NMR: δ 7.74 (d, 1 H, H-3′), 7.72 (d, 1 H, H-6′), 7.54 (dd, 1 H, H-5′), 5.51 (dd, 1 H, H-2), 5.20 (ddd, 1 H, H-4), 5.17 (dd, 1 H, H-3), 4.59 (d, 1 H, H-1), 2.96 (dd, 1 H, H-5eq), 2.81 (dd, 1 H, H-5ax), 2.05–1.76 (m, 18 H, OAc); $J_{1,2}$ 10.6, $J_{2,3}$ 9.6, $J_{3,4}$ 9.5, $J_{4,5ax}$ 10.1, $J_{4,5eq}$ 4.3, $J_{5ax,5eq}$ 13.5 Hz; ^{13}C NMR: δ 169.8, 169.7, 168.7 (C=O), 141.9 (C-1′), 136.2 (C-2′), 132.4 (C-5′), 131.7 (C-3′), 129.6 (C-6′), 117.4 (CN), 112.6 (C-4′), 74.5 (C-2), 74.1 (C-3), 72.3 (C-4), 44.8 (C-1), 31.3 (C-5), 20.8, 20.5, 20.2 (OAc); MS *m*/*z* 757 $[M+H\text{-}AcOH]^+$. Anal. Calcd for $C_{36}H_{36}N_2O_{12}S_4$: C, 52.93; H, 4.44; N, 3.43; S, 15.70. Found: C, 52.88; H, 4.33; N, 3.51; S, 15.62

Concentration of the fourth fraction gave 4-cyano-2-(2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)phenyl 2,3,4-tri-*O*-acetyl-1,5-dithio-β-D-xylo-pyranoside (**33**, 0.43 g, 9%): mp 117–121 °C (hexane); $[\alpha]_D + 94°$ (*c* 0.5, $CHCl_3$); R_f 0.3 (solvent *A*); ^{1}H NMR: δ 7.76 (d, 1 H, H-3′), 7.73 (d, 1 H, H-6′), 7.54 (dd, 1 H, H-5′), 5.46 (dd, 1 H, H-2″), 5.28 (dd, 1 H, H-2), 5.19 (ddd, 1 H, H-4″), 5.17 (dd, 1 H, H-3″), 5.10 (ddd, 1 H, H-4), 5.08 (dd, 1 H, H-3), 4.76 (d, 1 H, H-1″), 4.18 (d, 1 H, H-1), 2.97 (dd, 1 H, H-5″eq), 2.94 (dd, 1 H, H-5″ax), 2.87 (dd, 1 H, H-5eq), 2.69 (dd, 1 H, H-5ax), 2.01–1.71 (m, 18 H, OAc); $J_{1,2}$ 10.5, $J_{2,3}$ 9.0, $J_{3,4}$ 9.5, $J_{4,5ax}$ 10.5, $J_{4,5eq}$ 4.1, $J_{5ax,5eq}$ 13.3, $J_{1'',2''}$ 10.7, $J_{2'',3''}$ 9.1, $J_{3'',4''}$ 9.2, $J_{4'',5''ax}$ 10.6, $J_{4'',5''eq}$ 4.3, $J_{5''ax,5''eq}$ 13.5 Hz; ^{13}C NMR: δ 169.7, 169.6, 169.6, 169.6, 169.3, 168.7 (C=O), 139.9 (C-1′), 139.0 (C-2′), 133.2 (C-6′), 132.0 (C-5′), 131.8 (C-3′), 117.5 (CN), 112.9 (C-4′), 74.8 (C-2″), 74.2 (C-3″), 73.9 (C-2), 73.8 (C-3), 72.6 (C-4″), 72.0 (C-4), 52.9 (C-1), 45.0 (C-1″), 31.4 (C-5), 31.2 (C-5″), 20.8, 20.7, 20.6, 20.5, 20.5, 20.1 (OAc). Anal. Calcd for $C_{29}H_{33}NO_{12}S_3$: C, 50.94; H, 4.86; N, 2.05; S, 14.07. Found: C, 51.02; H, 4.77; N, 2.09; S, 14.11.

4-Cyanophenyl 2,3,4-tri-O-*acetyl-1,5-dithio*-α-D-*xylopyranoside* (**29**) *and 4-cyanophenyl 2,3,4-tri*-O-*acetyl-1,5-dithio*-β-D-*xylopyranoside* (**30**).—A 1:4 mixture of **29** and **30** (9.12 g) could be separated by crystallization with diethyl ether to yield **30** (6.0 g, 66%): mp 159–162 °C (Et_2O), lit. 155 °C [23]; $[\alpha]_D + 45°$ (*c* 0.5, $CHCl_3$), lit. + 37° (*c* 0.5, $CHCl_3$) [23]; R_f 0.4 (solvent *B*); Anal. Calcd for $C_{18}H_{19}NO_6S_2$: C, 52.80; H, 4.68; N, 3.42; S, 15.66. Found: C, 52.92; H, 4.75; N, 3.36; S, 15.59.

Column chromatography (solvent *B*) of the mother liquor gave **29** (1.1 g, 12%): mp 104–106 °C (hexane); $[\alpha]_D + 368°$ (*c* 0.5, $CHCl_3$); R_f 0.45 (solvent *B*); Anal. Calcd for $C_{18}H_{19}NO_6S_2$: C, 52.80; H, 4.68; N, 3.42; S, 15.66. Found: C, 52.72; H, 4.65; N, 3.47; S, 15.70.

4-Cyanophenyl 1,5-dithio-β-D-*xylopyranoside* (**1**).—A soln of **30** (6.0 g) in MeOH (240 mL) and methanolic M NaOMe (0.1 mL) was stirred for 30 min at room temperature to yield, after deionization with Dowex 50 WX resin and concentration, **1** (4.0 g, 96%): mp 173–175 °C, lit. 175 °C [22]; $[\alpha]_D + 35°$ (*c* 0.5, MeOH), lit. [22] + 36° (*c* 0.5, MeOH); R_f 0.4 (solvent *F*).

4-[(Imino)(methoxy)methyl]phenyl 1,5-dithio-β-D-*xylopyranoside* (**2**).—To a soln of **1** (0.45 g), in dry MeOH (10 mL), methanolic M NaOMe (0.1 mL) was added. After 24 h at room temperature, the mixture was neutralized with solid CO_2 and concentrated. The residue was submitted to column chromatography (solvent *F*) to give, on concentration of the first fraction (R_f = 0.4), the unchanged starting material (350 mg).

Concentration of the second fraction yielded **2** (100 mg, 20%): mp 174–177 °C; $[\alpha]_D + 28°$ (*c* 0.5, MeOH); R_f 0.3 (solvent *F*); Anal. Calcd for $C_{13}H_{17}NO_4S_2$: C, 49.51; H, 5.43; N, 4.44; S, 20.33. Found: C, 49.59; H, 5.33; N, 4.37; S, 20.36.

4-Cyanophenyl 1,5-dithio-α-D-*xylopyranoside* (**35**).—Deacetylation of **29** (0.6 g) with methanolic M NaOMe (0.1 mL) in MeOH (20 mL) yielded, after deionization with Dowex 50 WX resin and concentration, **35** (0.36 g, 87%): mp 136–138 °C; $[\alpha]_D + 626°$ (*c* 0.5, MeOH); R_f 0.4 (solvent *F*); Anal. Calcd for $C_{12}H_{13}NO_3S_2$: C, 50.87; H, 4.62; N, 4.94; S, 22.63. Found: C, 50.99; H, 4.73; N, 5.01; S, 22.57.

4-(Aminothiocarbonyl)phenyl 1,5-dithio-β-D-*xylopyranoside* (**36**).—A stirred soln of **1** (4.0 g) in dry pyridine (60 mL) and Et_3N (60 mL) was saturated with a slow stream of dry H_2S for 2 h. The mixture was kept at room temperature overnight and was then concentrated. The residue was recrystallized from MeOH to yield **36** (3.85 g, 86%): mp 174–179 °C; $[\alpha]_D + 38°$ (*c* 0.5, MeOH); R_f 0.3 (solvent *F*); Anal. Calcd for $C_{12}H_{15}NO_3S_3$: C, 45.41; H, 4.76; N, 4.41; S, 30.30. Found: C, 45.43; H, 4.76; N, 4.29; S, 30.37.

4-[(Imino)(methylthio)methyl]phenyl 1,5-dithio-β-D-xylopyranoside (**37**).—To a stirred soln of **36** (3.85 g) in dry acetone (385 mL), MeI (2.4 mL) was added and the mixture was refluxed for 2 h. After cooling to room temperature, the precipitated crystals were filtered off and washed with ether to give **37** (4.57 g, 82%) as its hydroiodide: mp 197–200 °C; $[\alpha]_D + 45°$ (*c* 0.5, Me_2SO); R_f 0.4 (solvent *F*); Anal. Calcd for $C_{13}H_{18}INO_3S_3$: C, 33.99; H, 3.95; I, 27.63; N, 3.05; S, 20.94. Found: C, 34.13; H, 3.92; I, 27.74; N, 2.92; S, 20.87.

4-Amidinophenyl 1,5-dithio-β-D-xylopyranoside (**38**).—To a soln of **37** (200 mg) in EtOH (10 mL), NH_4OAc (0.1 g) was added and the mixture was stirred at 60 °C for 4 h. After cooling to room temperature, the precipitated crystals were filtered off and washed with ether to give **38** (120 mg, 55%) as its acetate salt: mp 195–199 °C; $[\alpha]_D + 30°$ (*c* 0.5, 50% aq AcOH); R_f 0.6 (solvent *H*); Anal. Calcd for $C_{14}H_{20}N_2O_5S_2$: C, 46.65; H, 5.59; N, 7.77; S, 17.79. Found: C, 46.82; H, 5.66; N, 7.68; S, 17.65.

4-[(Hydrazino)(imino)methyl]phenyl 1,5-dithio-β-D-xylopyranoside (**39**).—To a stirred soln of **37** (200 mg) in EtOH (10 mL), 98% hydrazine hydrate (0.7 mL) was added and stirring was continued at room temperature for 5 h. The precipitated crystals were filtered off and washed with EtOH to give **39** (80 mg, 58%): mp 185–189 °C; $[\alpha]_D + 12°$ (*c* 0.5, pyridine); R_f 0.5 (solvent *H*); Anal. Calcd for $C_{12}H_{17}N_3O_3S_2$: C, 45.70; H, 5.43; N, 13.32; S, 20.33. Found: C, 45.56; H, 5.38; N, 13.17; S, 20.21.

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