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Synthesis of 4-cyanophenyl and 4-nitrophenyl 1,5-dithio-L- and -D-arabinopyranosides possessing antithrombotic activity[1,2]

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Abstract

5-*S*-Benzoyl-2,3-*O*-isopropylidene-5-thio-L-arabinose, prepared from L-arabinose diethyl dithioacetal gave, on treatment with sodium methoxide in methanol, 4-*O*-benzoyl-2,3-*O*-isopropylidene-5-thio-L-arabinopyranose **12** which was converted into its 1-*O*-acetate **14**. Hydrolysis of **12** in acetic acid–water afforded, after acetylation, 1,2,3-tri-*O*-acetyl-4-*O*-benzoyl-5-thio-L-arabinopyranose **17** which was transformed into 2,3-di-*O*-acetyl-4-*O*-benzoyl-5-thio-L-arabinopyranosyl bromide **20**. Zemplén deacylation of **17** gave 5-thio-L-arabinopyranose which was converted via 1,2,3,4-tetra-*O*-acetyl-5-thio-β-L-arabinopyranose **5** into 2,3,4-tri-*O*-acetyl-5-thio-β-L-arabinopyranosyl bromide **6** and into *O*-(2,3,4-tri-*O*-acetyl-5-thio-L-arabinopyranosyl) trichloro-acetimidate **7**. Glycosidation of 4-nitrophenol with **12** under the Mitsunobu conditions afforded 4-nitrophenyl 4-*O*-benzoyl-2,3-*O*-isopropylidene-5-thio-α- and β-L-arabinopyranoside in a ~1:2 ratio. Condensation of the glycosyl donors **6**, **7**, **17**, and **20** with 4-cyano- and 4-nitrobenzenethiol yielded, after deacylation, 4-cyano- and 4-nitrophenyl 1,5-dithio-α- and β-L-arabinopyranosides **28α**, **28β**, **29α** and **29β** in different ratios and yields, depending on the reaction conditions applied. In a similar manner the corresponding D-isomers **30α**, **30β**, **31α** and **31β** were also prepared. All of these glycosides, except **28α**, showed a stronger oral antithrombotic effect in rats as compared to beciparcil, used as reference.

Keywords: 5-Thio-L and D-arabinose derivatives; S→O-benzoyl migration; Glycosidation reactions; Thioglycosides; Oral antithrombotic activity

1. Introduction

In the previous parts of this series of papers [2–5], we have shown that the oral antithrombotic activity of 4-cyanophenyl 1,5-dithio-β-D-xylopyranoside (beciparcil, **1**) [6] 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). It was presumed [6] that these thioglycosides express their antithrombotic activity by acting in vivo as initiators in the biosynthesis of the natural antithrombotic glycosaminoglycans (GAGs), increasing their concentration. Nevertheless the

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

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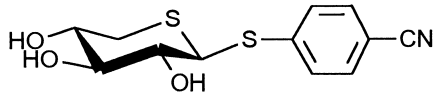
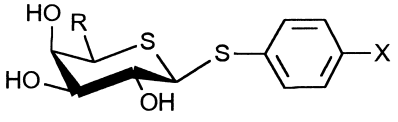
same effect could arise from blocking the galactosyltransferase I enzyme, that binds the primarily formed free GAGs to proteins, yielding the endogenous proteoglycans (PGs), being void of any antithrombotic activity. Accordingly, it was presumed that 1,5-dithio-D-galactopyranosides (**2**) might possess some antithrombotic activity by acting as enzyme inhibitors. As the synthesis of 5-thio-D-galactose would be too demanding, that of its pentose congener (5-thio-L-arabinose), as well as that of its thiopyranosides (**3**) was decided (Scheme 1).

2. Results and discussion

Synthesis of the donor molecules.—For the synthesis of the planned **3** type thioglycosides, proper 5-thio-L-arabinopyranose donors **6** or **7** were needed. Bromide **6** was synthesized recently [7] from the corresponding 5-*O*-tosyl dibenzyl dithioacetal **4**, which is however a rather unstable intermediate, and decomposes easily yielding benzyl 5-*S*-benzyl-1,5-dithio-arabinofuranoside [8,9]. Imidate **7** has not been described so far, but its D-isomer was synthesized [10] using 1,2,3-tri-*O*-acetyl-5-*O*-trityl-D-arabinofuranose **8** as an intermediate which can be obtained from D-arabinose in a multi-step process only. In order to avoid these drawbacks, the readily available [3] and stable 5-*O*-tosylate of 2,3-*O*-isopropylidene-L-arabinose diethyl dithioacetal **9** was used as starting material and converted in excellent yield into the 5-*S*-benzoate **10**. The ethylthio groups of **10** were split off with mercuric oxide in the presence of boron trifluoride etherate [11] and the obtained aldehyde **11** was submitted to the Zemplén deacylation procedure at room temperature using 0.1 equiv of sodium methoxide [12,13]. Under these conditions, instead of deacylation only migration of the benzoyl group from *S*-5 to *O*-4 took place and the formed free thiol group closed immediately to a pyranose ring affording **12** as an anomeric mixture (α:β = 15:85). The cyclic $^4C_1$ (β-L) conformation of the separated **12β** was evident from its NMR spectrum as for H-1, besides a $^3J_{1,2}$ coupling of 2.7 Hz a $^4J_{1,5eq}$ coupling of ~1 Hz could be detected too. Because of the presence of the ring sulfur atom, the trans fused dioxolane ring at C-2,3, which has already been detected in xylopyranosides [14] is well tolerated. The 4-*O*-benzoyl group of **12** could be removed by carrying out the deacylation at reflux temperature yielding crystalline **13**, which proved to be a 1:9 mixture of the α,β-anomers. In pyridine solution, a mutarotation (+252° (5 min)→+230° (24 h)) could be detected. Acetylation of **12** in pyridine with acetic anhydride gave **14** as an anomeric mixture (α:β ~ 2:3) from which a 1:1 mixture could be separated on crystallization from methanol. When the isopropylidene group of **12** was split off in boiling methanol with concd hydrochloric acid, the 4-*O*-benzoyl group remained intact and an anomeric mixture of the corresponding methyl pyranosides was obtained which was isolated after acetylation as its diacetate **15** (α:β ~ 1:6). The ester groups of this mixture could be removed under normal Zemplén conditions affording the crystalline methyl β-pyranoside **16β**. When aqueous acetic acid was used for the hydrolysis of the isopropylidene group of **12**, the 4-*O*-benzoate **18** was obtained in solid state containing the α:β-anomers in a ratio of 1:9. Acetylation of this mixture gave the anomeric mixture of the mixed ester **17**. Debenzoylation of **18** according to Zemplén's method gave crystalline **19β** which yielded the tetra-acetate **5** on acetylation. For comparing the different glycosidation methods, both tetra-esters **5** and **17** were converted by treatment with hydrogen bromide in acetic acid into the corresponding pyranosyl bromides **6** and **20**, respectively, which were used as glycosyl donors. For the same purpose, the anomeric acetyl group of **5** was selectively removed with hydrazine acetate, and the formed anomeric mixture of the 1-OH derivative **21** was converted into its trichloroacetimidate **7**. The benefit of using the 4-*O*-benzoates **17** and **20** in



1 (Beciparcil)

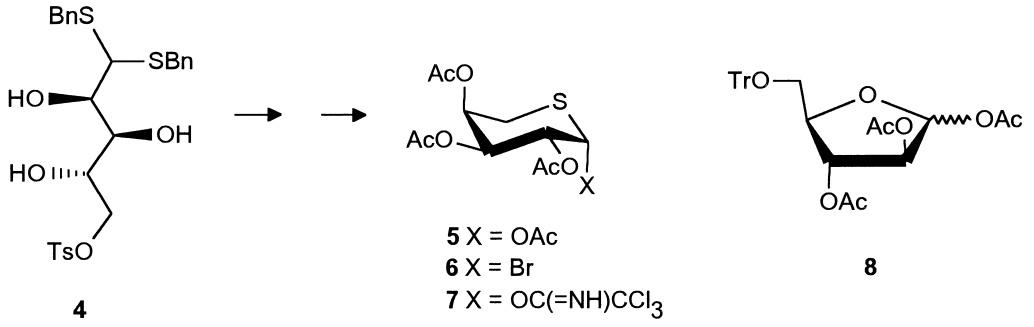


2 R = CH_2OH (β-D-galactopyranoside)
3 R = H (α-L-arabinopyranoside)

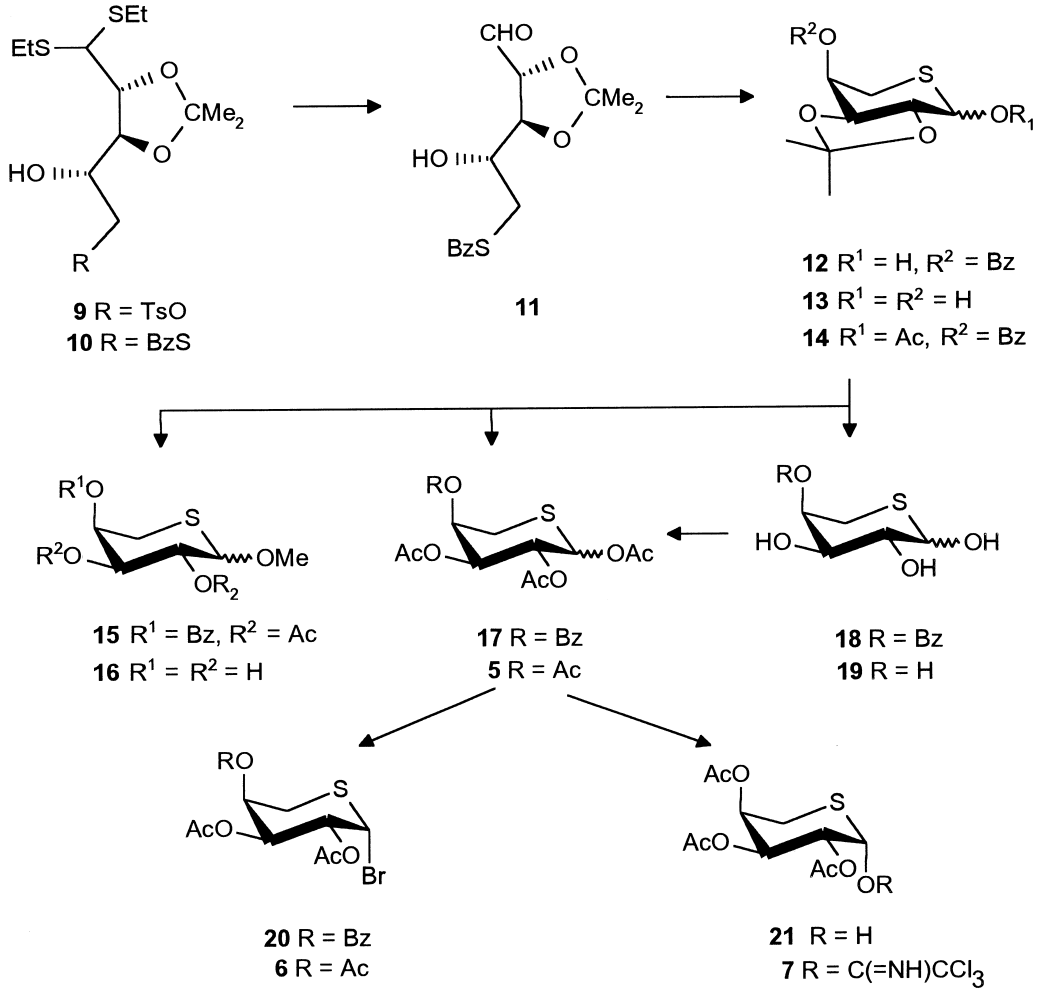
Scheme 1.

the glycosidation reactions was that the formed anomeric mixtures could be separated, while unseparable mixtures were formed when the corresponding 4-*O*-acetate **6** was used as donor (Schemes 2 and 3).

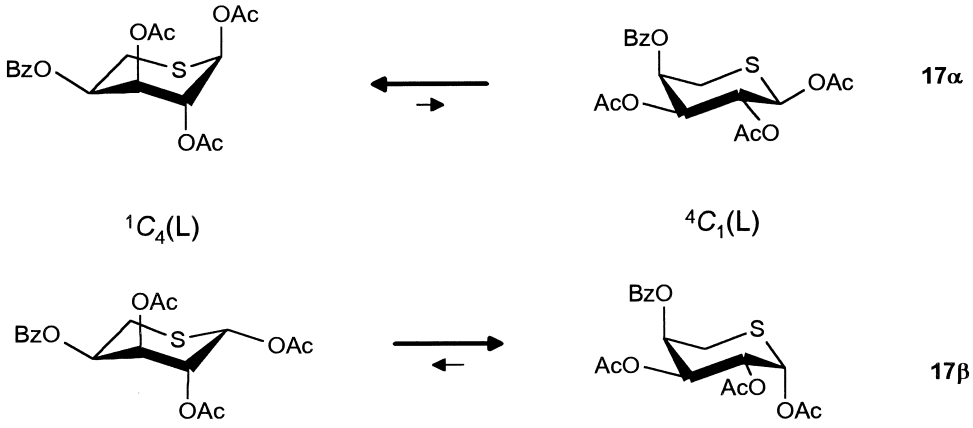
It is worthwhile mentioning that the two anomers of the 4-*O*-benzoyl triacetates (**17α** and **17β**) are formed in a ratio of 1:4, and according to NMR data **17α** adopts preferably the $^1C_4$(L) conformation, while **17β** prefers the $^4C_1$(L) conformation (Scheme 4). That means that, although in **17α** the energy gained by the anomeric effect of the exocyclic sulfur atom [17] compensates the steric strain caused by the 1,3-diaxial arrangement of the two



Scheme 2.



Scheme 3.



Scheme 4.

acetoxy groups, this conformation is energetically less favored than that in **17β** for which no such 1,3-diaxial arrangement exist.

Glycosidation reactions.—As the free anomeric hydroxy group of *O*-isopropylidene protected carbohydrate derivatives can be glycosylated under Mitsunobu conditions [18,19], in a model experiment, the 2,3-*O*-isopropylidene derivative **12** was treated with 4-nitrophenol in the presence of triphenylphosphine and diethyl azodicarboxylate. The resulting anomeric mixture of the nitrophenyl glycosides could be separated by column chromatography affording **22α** and **22β** in 35 and 18.6% yield, respectively. However, when 4-nitro- or 4-cyanobenzenethiol was used as aglycon, no thioglycosides could be isolated.

In our further experiments the *O*-isopropylidene protected 1-acetate **14** was used as donor, trimethylsilyl triflate as activator and 4-cyanobenzenethiol as acceptor. Under these conditions, an α,β-anomeric mixture (7:3) of the corresponding thioglycosides (**23**) was formed in 24% yield, from which the anomers **23α** and **23β** could be separated by column chromatography. Because of this modest yield, deprotection of these glycosides was not attempted.

In all further experiments the 2,3-*O*-acetate derivatives were used as donors, differing in the substitution at C-1 and O-4, and the results are listed in Table 1. The reaction of the acetobromo derivative **6** with the corresponding 4-cyano and 4-nitrobenzenethiol was carried out in acetone in the presence of potassium carbonate at 60 °C. The corresponding thioglycosides **24** and **25** were formed in both cases as 1:1 anomeric mixtures (64 and 61%) which could not be separated by crystallization or column chromatography. When the imidate **7** was used as donor and 4-cyanobenzenethiol as acceptor in 1,2-dichloroethane in the presence of boron trifluoride etherate as promoter, the reaction became much faster and was completed within 15 min even at low temperature (−15 °C). Under these conditions, the anomerisation is a slower process and **24** was obtained in a much higher α:β ratio (1:4) and from this mixture **24β** could be separated by crystallization.

When the 1,2,3-tri-*O*-acetate-4-*O*-benzoate **17** was used as donor, 4-cyanobenzenethiol as acceptor

Table 1
Influence of the reaction conditions on the glycosidation reactions with L-arabinopyranosyl donors

Run	Donor	Acceptor[a]	Promoter	Solvent	Time	Temp. (°C)	Product	Yield (%)	α,β ratio
1	**6**	CN	K_2CO_3	Acetone	2 h	60	**24**	64	1:1[b]
2	**6**	NO_2	K_2CO_3	Acetone	1 h	60	**25**	61	1:1[b]
3	**7**	CN	$BF_3{\cdot}Et_2O$	1,2-Dichloroethane	15 min	−15	**24**	92	1:4
4	**17**	CN	TMSOTf	1,2-Dichloroethane	2 h	20	**26**	87	1:2
5	**17**	NO_2	$BF_3{\cdot}Et_2O$	1,2-Dichloroethane	24 h	20	**27**	81	1:2
6	**20**	CN	K_2CO_3	Acetone	1 h	60	**26**	55	1.3:1
7	**20**	CN	ZnO	Acetonitrile/toluene	30 min	20	**26**	64	1.3:1
8	**20**	NO_2	K_2CO_3	Acetone	2 h	60	**27**	42	1.3:1

[a] Substituent of the 4-substituted thiophenol.
[b] Unseparable mixture.

and trimethylsilyl triflate as promoter the α:β ratio of the corresponding thioglycoside **26** was 1:2 and the reaction reached completion within 2 h at 20 °C. Essentially the same anomeric ratio of **27** was obtained when 4-nitrobenzenethiol was used as aglycon and boron trifluoride etherate as promoter, but the reaction was much slower and was completed after 24 h at 20 °C. For comparison, both **26** and **27** were synthesized also by using the corresponding bromide **20** as donor. The ratio of the anomers (α,β = 1.3:1) did not depend on the aglycon or the applied promoter, but the highest yield and fastest reaction was obtained in the presence of zinc oxide.

The ester groups of all separated isomers could be removed under Zemplén's condition and the resulting thioglycosides **28α**, **28β**, **29α** and **29β** were obtained in crystalline state. In solution ($CDCl_3$), all acylated glycosides (**24**–**27**) adopted the $^4C_1$(L) conformation, independently of the configuration of the anomeric center. However, in the case of the deacylated derivatives **28** and **29**, a $^4C_1(L) \leftrightarrow {}^1C_4(L)$ equilibrium could be detected for both anomers by NMR spectroscopy which in the case of the β-anomers was strongly shifted towards the $^1C_4$(L) conformation. In methanol-d_4 at low temperature (203 K), the two conformers of **28β** gave separated signals and their ratio was 2:8.

All reactions mentioned above were repeated with the corresponding D-isomers too, affording the thioglycosides **30α**, **30β**, **31α** and **31β** which were submitted together with their enantiomers to biological testing (Scheme 5).

Biological results.—The oral antithrombotic activity of **1**, **28α**, **28β**, **29α**, **29β**, **30α**, **30β**, **31α** and **31β** was determined in rats, using Pescador's model [20]. All compounds were administered orally 3 h before ligation. From the data listed in Table 2, it can be seen that while the **28α** isomer was only slightly more active than the reference compound (beciparcil **1**) all other isomers showed a much stronger anticoagulant activity.

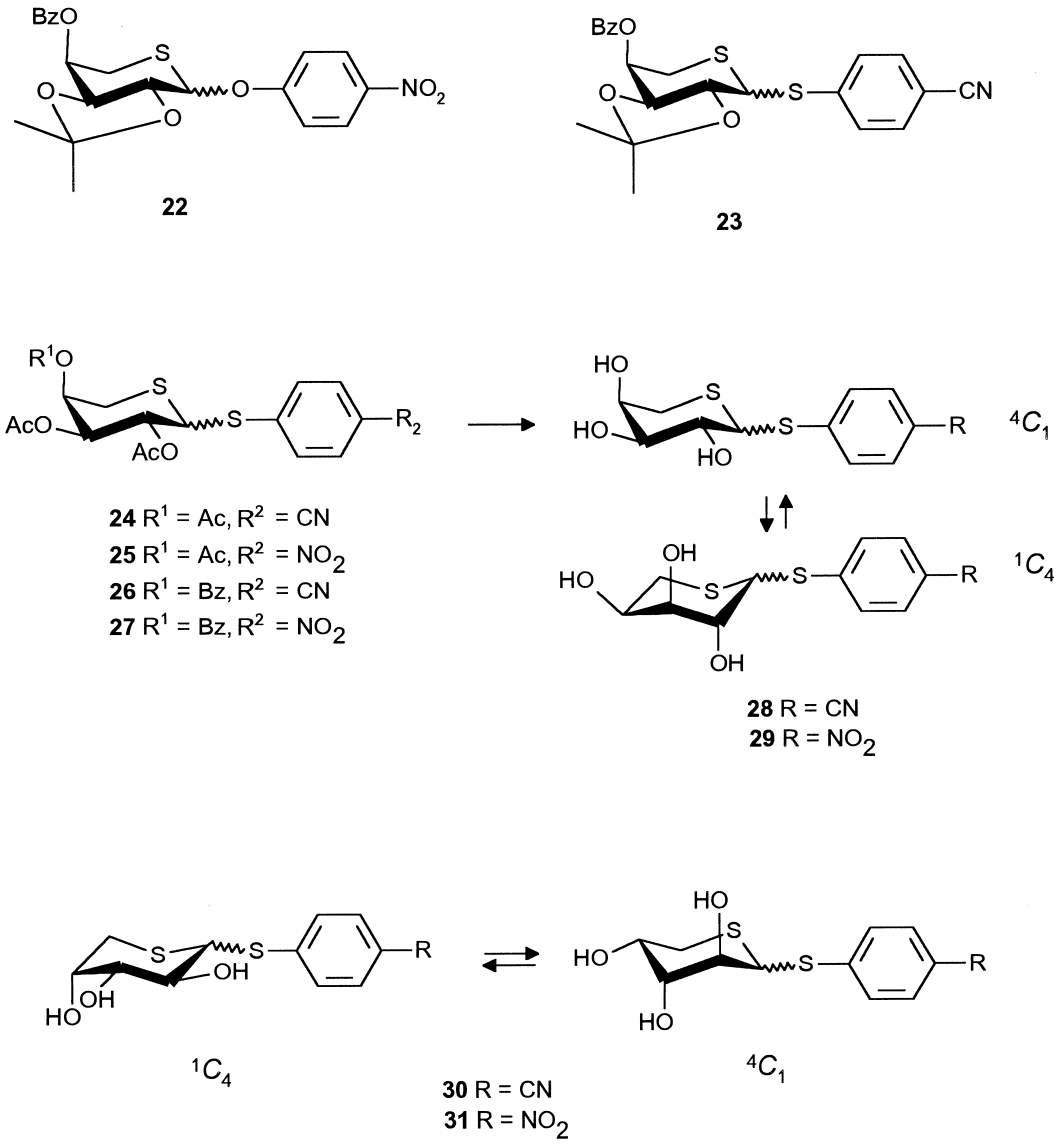
3. Experimental

General methods.—Organic solutions 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*, 1:2; *B*, 2:1; *C*, 3:1; *D*, 5:1), EtOAc–EtOH mixture (*E* 9:1) and toluene–MeOH mixtures (*F*, 4:1; *G*, 9:1); detection by spraying the plates with a 0.02 M solution of I_2 and a 0.3 M solution of KI in 10% aq H_2SO_4 solution 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% solutions in $CHCl_3$ at 20 °C unless stated otherwise. NMR spectra were recorded with a Bruker AC 250 spectrometer at 250 MHz (^{1}H) and 62.9 MHz (^{13}C) for solutions in $CDCl_3$ (internal Me_4Si) unless stated otherwise (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 experiments. The ratio of α:β anomeric mixtures was determined by ^{1}H NMR spectroscopy. Structural formulas of the corresponding intermediates refer to the L-isomers, the data of the corresponding D-enantiomers are indicated by the addition of **-D** to the number of the formulas.

5-S-*Benzoyl-2,3*-O-*isopropylidene-5-thio*-L-*arabinose* (**11**).—To a stirred slurry of HgO (18 g) in THF (400 mL) and water (45 mL), $BF_3{\cdot}Et_2O$ (48%, 12 mL) was added at 0 °C. Thereafter, a solution of **10** [3] (16.6 g, 40 mmol) in THF (40 mL) was added over a period of 30 min. Stirring was continued at 20 °C for 1 h, then the reaction mixture was poured into a stirred slurry of ether (500 mL) and Na_2CO_3 (20 g). The organic solution was washed with 10% aq K_2CO_3 until a pH of ~ 9 was reached and then with water to give on concentration **11** (12.4 g, ~100%) containing, according to NMR spectroscopy, some **11**-hydrate. Therefore, no correct analytical data could be obtained; $[\alpha]_D$ +145°; R_f 0.5 (solvent *A*); ^{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).

5-S-*Benzoyl-2,3*-O-*isopropylidene-5-thio*-D-*arabinose* (**11-D**). $[\alpha]_D$ −147°.

4-O-*Benzoyl-2,3*-O-*isopropylidene-5-thio*-L-*arabinopyranose* (**12**).—A solution of crude **11** (10.9 g, 35 mmol) in MeOH (50 mL) was treated with methanolic 4 M NaOMe (1 mL) at room temperature. The mixture was neutralized with solid CO_2 after 15 min, filtered and concentrated to give crude **12** (10.5 g, 97%) as an anomeric mixture (α:β~15:85). Column chromatography (solvent *B*) afforded **12β** (5.19 g, 48%) as syrup; $[\alpha]_D$ +215°; R_f 0.5 (solvent *B*). Anal. Calcd for $C_{15}H_{18}O_5S$: C, 58.05; H, 5.85; S, 10.33. Found: C, 58.00; H, 5.89;



Scheme 5.

S, 10.25. The same compound could be obtained in 95% yield when acetate **14** was used as starting material.

4-O-*Benzoyl-2,3*-O-*isopropylidene-5-thio*-D-*arabinopyranose* (**12-D**). $[\alpha]_D$ −217°. Anal. Calcd for $C_{15}H_{18}O_5S$: C, 58.05; H, 5.85; S, 10.33. Found: C, 57.95; H, 5.90; S, 10.27.

2,3-O-*Isopropylidene-5-thio*-L-*arabinopyranose* (**13**).—A solution of crude **12** (1.35 g, 5 mmol) or **14** (1.75 g, 5 mmol) in CH_2Cl_2 (10 mL) and MeOH (10 mL) was boiled in the presence of methanolic M NaOMe (0.3 mL) for 1 h to give after neutralization with solid CO_2, filtration and concentration **13** (0.95 g, 93%): mp 123–125 °C (ether–hexane) as an anomeric mixture (α:β ~ 1:9); $[\alpha]_D$ +190°; mutarotation: $[\alpha]_D$ +252° (5 min) → +230° (24 h, *c* 1, pyridine); R_f 0.5 (solvent *D*). Anal. Calcd for $C_8H_{14}O_4S$: C, 46.59; H, 6.85; S, 15.52. Found: C, 46.48; H, 6.90; S, 15.42.

2,3-O-*Isopropylidene-5-thio*-L-*arabinopyranose* (**13-D**). mp 122–125 °C (ether–hexane) anomeric mixture (α:β ~ 1:9); $[\alpha]_D$ −192°; mutarotation: $[\alpha]_D$ +254° (5 min)→ +235° (24 h, *c* 1, pyridine). Anal. Calcd for $C_8H_{14}O_4S$: C, 46.59; H, 6.85; S, 15.52. Found: C, 46.52; H, 6.92; S, 15.48.

Table 2
Oral antithrombotic activity of **1**, **28α**, **28β**, **29α**, **29β**, **30α**, **30β**, **31α**, and **31β** in rats using Pescador's model [20]

Compound	**1**	**28α**	**28β**	**29α**	**29β**	**30α**	**30β**	**31α**	**31β**
ED_{50} (mg/kg)	25	15	5	2	1.5	1	3.5	3.5	3.5

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

Compound	Chemical shifts (δ)						Coupling constants (Hz)						
	H-1	H-2	H-3	H-4	H-5ax	H-5eq	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5ax}$	$J_{4,5eq}$	$J_{5ax,5eq}$	$J_{1,5eq}$
12β	5.42	4.55	4.18	5.85	3.32	2.95	2.7	9.5	2.2	1.8	3.5	14.9	~1
13β	5.35	4.35	4.02	4.64	3.25	2.73	2.6	9.5	2.2	1.9	3.6	14.3	~1
14α	6.02	4.52	3.68	5.78	3.20	3.08	9.2	9.3	2.9	3.4	4.0	14.9	—
14β	6.28	4.62	4.12	5.88	3.26	2.98	2.8	9.7	2.3	1.9	3.4	14.8	~1
15α	4.42	5.15–5.80			3.18	2.68	5.0	nd[b]	nd	~8	3.0	13.4	—
15β	4.73	5.15–5.80			3.22	2.74	2.5	nd	nd	1.4	4.2	14.7	1.6
17α	5.80	5.45	5.28	5.63	3.31	2.81	4.7	nd	nd	9.4	3.3	13.5	—
17β	6.24	5.65	5.43	5.85	3.43	2.88	3.0	10.8	2.9	1.4	4.3	14.9	1.6
18α[a]	4.60	3.90	3.65	5.35	2.75–3.10		6.7	nd	nd	nd	nd	nd	—
18β[a]	4.96	3.95	3.88	5.42	3.03	2.81	2.3	8.7	2.4	1.4	5.8	13.9	~1
20	5.68	5.28	5.49	5.79	3.50	3.00	3.4	10.2	2.9	1.5	4.3	15.0	2.2
22α	5.62	4.72	3.75	5.85	3.24	3.16	8.8	9.1	2.6	2.9	3.7	15.0	—
22β	5.80	4.76	4.38	5.92	3.24	3.02	2.6	9.6	2.3	1.8	3.4	14.8	~1
23α	4.50	4.22	3.63	5.80	3.20	2.96	10.4	8.9	2.2	1.9	3.4	14.9	—
23β	4.92	4.84	4.11	5.85	3.34	3.00	4.0	9.4	2.4	1.7	3.7	14.9	1.0
24α	4.24	5.45	5.05	5.45	2.88	3.03	7.8	7.7	2.8	2.6	6.6	14.2	—
24β	4.85	5.55	5.35	5.46	3.18	2.85	3.9	9.3	2.7	1.7	6.0	14.4	1.2
25α	4.38	5.45	5.06	5.45	2.90	3.06	7.8	7.8	2.9	2.7	6.8	14.4	—
25β	4.91	5.58	5.36	5.45	3.18	2.85	3.7	9.3	2.9	1.7	5.8	14.4	1.4
26α	4.38	5.56	5.15	5.68	2.98–3.20		8.3	8.3	2.8	2.9	5.6	~14	—
26β	4.96	5.67	5.48	5.76	3.36	2.95	3.9	9.5	2.9	~2	5.5	14.6	~1
27α	4.42	5.58	5.18	5.70	3.00–3.20		8.1	8.1	2.6	~3	~6	~14.5	—
27β	5.02	5.70	5.48	5.75	3.36	2.96	3.9	9.5	3.0	1.5	5.6	14.5	1.4
28α[a]	4.42	3.88	3.44	4.02	2.70		7.3	7.2	2.6	nd	nd	nd	—
28β[a]	4.75	4.06	3.66	4.00	2.94	2.26	2.0	5.3	1.8	9.6	3.5	12.5	nd
28β[c]	4.80	4.25	3.82	4.16	3.00	2.54	2.5	6.1	2.4	9.8	3.4	13.0	
28β,($^1C_4$)[c,d]	4.82	4.19	3.85	4.12	2.20	2.30	nd	4.4	nd	12.2	nd	12.2	
28β,($^4C_1$)[c,d]	4.94	4.38	3.60	4.20	nd	2.52	3.9	10.3	nd	nd	nd	12.5	
29α[a]	4.50	3.95	3.48	4.04	2.65–2.85		7.0	6.8	2.5	nd	nd	nd	—
29β[a]	4.82	4.12	3.70	4.05	2.96	2.32	1.9	5.0	2.3	10.3	3.3	12.6	nd

[a] Me_2SO-d_6.
[b] nd, Not determined.
[c] MeOH-d_4.
[d] 203 K.

1-O-*Acetyl-4*-O-*benzoyl-2,3*-O-*isopropylidene-5-thio*-L-*arabinopyranose* (**14**).—Acetylation of crude **12** (11 g, 35.5 mmol) in pyridine (20 mL) with Ac_2O (15 mL) gave, after usual processing and column chromatography (solvent *D*), **14** (9 g, 72%) as a semisolid anomeric mixture (α:β ~4:6). Recrystallization from methanol afforded an α:β ~ 1:1 mixture (3.2 g, 26%): mp 118–120°; $[\alpha]_D$ +230°; R_f 0.6 (solvent *C*). Anal. Calcd for $C_8H_{14}O_4S$: C, 46.59; H, 6.85; S, 15.52. Found: C, 46.48; H, 6.90; S, 15.42.

1-O-*Acetyl-4*-O-*benzoyl-2,3*-O-*isopropylidene-5-thio*-D-*arabinopyranose* (**14-D**). α:β ~1:1 mixture, mp 117–119°. Anal. Calcd for $C_8H_{14}O_4S$: C, 46.59; H, 6.85; S, 15.52. Found: C, 46.51; H, 6.79; S, 15.39.

Methyl 2,3-di-O-*acetyl-4*-O-*benzoyl-5-thio*-L-*arabinopyranoside* (**15**).—A solution of crude **12** (3.5 g, 10 mmol) in MeOH (20 mL) and concd HCl (0.5 mL) was boiled for 15 min, cooled, neutralized with $NaHCO_3$, filtered and concentrated. The residue was dissolved in pyridine (10 mL) and Ac_2O (7 mL) to give after usual processing and column chromatography (solvent *D*) **15** (2.3 g, 58%) as an anomeric mixture (α:β ~1:6); R_f 0.6 (solvent *C*). Anal. Calcd for $C_{17}H_{20}O_7S$: C, 55.43; H, 5.47; S, 8.70. Found: C, 55.25; H, 5.66; S, 8.52.

Methyl 2,3-di-O-*acetyl-4*-O-*benzoyl-5-thio*-D-*arabinopyranoside* (**15-D**). α:β ~1:5 mixture. Anal. Calcd for $C_{17}H_{20}O_7S$: C, 55.43; H, 5.47; S, 8.70. Found: C, 55.29; H, 5.60; S, 8.58.

Methyl 5-thio-β-L-*arabinopyranoside* (**16**).—Deacylation of **15** (1.5 g, 4 mmol) with methanolic M NaOMe (0.1 mL) in MeOH (10 mL) at room temperature afforded after 24 h crystalline **16** (0.24 g, 38%). The residue of the concentrated mother liquor gave, after column chromatography (solvent *E*), a second crop of **16** (0.21 g, 33%): mp 178–180 °C;

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

Compound	Chemical shifts (δ)					
	C-1	C-2	C-3	C-4	C-5	Others
12β	74.6[a]	73.3[a]	71.8[a]	69.1[a]	28.5	108.1 (CMe_2)
14α	77.8[a]	74.6[a]	74.5[a]	67.0[a]	31.5	110.8 (CMe_2)
14β	72.9[a]	72.9[a]	72.6[a]	68.5[a]	29.5	108.6 (CMe_2)
15α	81.7	70.8[a]	69.7[a]	68.8[a]	23.8	57.1 (OMe)
15β	81.9	71.6[a]	69.7[a]	68.3[a]	26.5	56.4 (OMe)
18β[b]	73.9[a]	72.9[a]	72.8[a]	68.6[a]	26.0	
20	55.4	70.9[a]	69.3[a]	69.0[a]	29.5	
22α	80.9[a]	77.9[a]	75.3[a]	67.1[a]	31.7	110.1 (CMe_2)
22β	79.0[a]	73.9[a]	72.6[a]	68.5[a]	29.4	108.8 (CMe_2)
23α	50.7	67.8[a]	73.8[a]	79.6[a]	33.8	108.8 (CMe_2)
23β	52.8	68.4[a]	73.9[a]	74.3[a]	29.5	109.0 (CMe_2)
26α	50.4	69.0[a]	70.6[a]	71.7[a]	29.6	
26β	51.4	68.5[a]	69.1[a]	71.4[a]	28.1	
27α	50.3	69.0[a]	70.6[a]	71.6[a]	29.5	
27β	51.3	68.5[a]	69.0[a]	71.4[a]	28.2	
28α[b]	51.0	75.9[a]	72.3[a]	73.8[a]	30.9	
28β[b]	48.9	65.9[a]	72.6[a]	73.6[a]	29.4	

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

$[\alpha]_D$ +457° (*c* 0.5, water); R_f 0.4 (solvent *E*). Anal. Calcd for $C_6H_{12}O_4S$: C, 39.99; H, 6.71; S, 17.79. Found: C, 40.0; H, 6.75; S, 17.66.

Methyl 5-thio-β-D-*arabinopyranoside* (**16-D**). mp 180–182 °C, lit. 185–186 °C [15], lit. 176–178 °C [16]; $[\alpha]_D$ −457° (*c* 0.5, water); lit. −452° (*c* 0.6, MeOH) [15].

1,2,3-Tri-O-*acetyl-4*-O-*benzoyl-5-thio*-L-*arabinopyranose* (**17**).—Acetylation of **18** (2.7 g, 10 mmol) with Ac_2O (10 mL) in pyridine (15 mL) gave, after usual processing, **17** (3.44 g, 87%) as an anomeric mixture (α:β ~1:4); R_f 0.6 (solvent *C*). Anal. Calcd for $C_{18}H_{20}O_8S$: C, 54.54; H, 5.09; S, 8.09. Found: C, 54.50; H, 5.12; S, 7.98.

1,2,3-Tri-O-*acetyl-4*-O-*benzoyl-5-thio*-D-*arabinopyranose* (**17-D**). α:β ~1:5 mixture. Anal. Calcd for $C_{18}H_{20}O_8S$: C, 54.54; H, 5.09; S, 8.09. Found: C, 54.48; H, 5.02; S, 7.95.

4-O-*Benzoyl-5-thio*-L-*arabinopyranose* (**18**).—A solution of **12** (3.1 g, 10 mmol) in AcOH (30 mL) and H_2O (10 mL) was heated on a steam bath for 30 min to give after concentration, and subsequent coevaporation of the residue with toluene **18β** (1.7 g, 63%); mp 136–138 °C (acetone–ether); $[\alpha]_D$ +295° (*c* 1, acetone); mutarotation: $[\alpha]_D$ +326° (5 min)→ +250° (4 h, *c* 1, pyridine). Concentration of the filtrate gave **18** (0.9 g, 34%) as an anomeric mixture (α:β ~1:3); R_f 0.4 (solvent *C*). Anal. Calcd for $C_{12}H_{14}O_5S$: C, 53.32; H, 5.22; S, 11.86. Found: C, 53.25; H, 5.25; S, 11.81.

4-O-*Benzoyl-5-thio*-D-*arabinopyranose* (**18-D**). mp 138–140 °C (acetone–ether) $[\alpha]_D$ −299° (*c* 1, acetone), mutarotation: $[\alpha]_D$ −330° (5 min)→ −250° (4 h, *c* 1, pyridine). Anal. Calcd for $C_{12}H_{14}O_5S$: C, 53.32; H, 5.22; S, 11.86. Found: C, 53.29; H, 5.27; S, 11.80.

5-Thio-β-L-*arabinose* (**19**).—To a solution of **18** (0.8 g, 2 mmol) in $CHCl_3$ (5 mL) and MeOH (5 mL), a solution of methanolic M NaOMe (0.1 mL) was added at room temperature. The mixture was neutralized with solid CO_2 after 1 h to yield, on concentration and crystallization with EtOH, **19** (0.24 g, 72%): mp 172–174 °C (EtOH); $[\alpha]_D$ +303° (5 min)→ +281° (24 h, *c* 0.5, H_2O). Anal. Calcd for $C_5H_{10}O_4S$: C, 36.14; H, 6.06; S, 19.29. Found: C, 36.03; H, 6.12; S, 18.88.

5-Thio-β-D-*arabinose* (**19-D**). mp 173–175 °C (EtOH); lit. 172–175 °C [15]; $[\alpha]_D$ −300° (5 min)→ −285° (24 h, *c* 0.5, H_2O); lit. −250° (*c* 0.6, H_2O) [15].

1,2,3,4-Tetra-O-*acetyl-5-thio*-β-L-*arabinopyranose* (**5**).—Acetylation of **19** (8.3 g, 50 mmol) with Ac_2O (45 mL) in pyridine (60 mL) gave, after usual processing, **5** (16.0 g, 93%): mp 120–122 °C (EtOH); $[\alpha]_D$ +299°; R_f 0.45 (solvent *B*). Anal. Calcd for $C_{13}H_{18}O_8S$: C, 46.70; H, 5.43; S, 9.59. Found: C, 46.67; H, 5.40; S, 9.52.

1,2,3,4-Tetra-O-*acetyl-5-thio*-β-D-*arabinopyranose* (**5-D**).—mp 120–124 °C (EtOH); lit. 118–120 °C [15], $[\alpha]_D$ −300°; lit. −308° [15].

2,3-Di-O-*acetyl-4*-O-*benzoyl-5-thio*-β-L-*arabinopyranosyl bromide* (**20**).—To a stirred solution of **17** (1.0 g, 2.5 mmol) in dry CH_2Cl_2 (10 mL), 33% hydrogen bromide in acetic acid (5 mL) was added. After 1 h at room temperature, the mixture was poured into ice-water, extracted with CH_2Cl_2, washed with 6% aq $NaHCO_3$, brine and concentrated to yield **20** (1.0 g, 95%): $[\alpha]_D$ +367° (*c* 0.4, $CHCl_3$); R_f 0.7 (solvent *B*). Anal. Calcd for $C_{16}H_{17}BrO_6S$: C, 46.70; H, 5.43; S, 9.59. Found: C, 46.67; H, 5.40; S, 9.52.

O-(2,3,4-Tri-O-*acetyl-5-thio*-β-L-*arabinopyranosyl) trichloroacetimidate* (**7**).—Under argon, hydrazine acetate (0.4 g, 4.3 mmol) was added to a stirred solution of **5** (1.0 g, 3.0 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, concentrated, and the residue submitted to column chromatography (solvent *B*) to yield 2,3,4-tri-*O*-acetyl-5-thio-L-arabinopyranose (**21**, 0.58 g, 66%): R_f 0.3 (solvent *B*). This was dissolved in CH_2Cl_2 (10 mL), CCl_3CN (2.05 mL, 20 mmol) and K_2CO_3 (2.8 g, 20 mmol) were added under argon, and the mixture was stirred at room temperature for 24 h. Then the reaction was diluted with ether, filtered through Celite, concentrated, and the residue was submitted to column chromatography (solvent *B*) to yield **7** (0.74 g, 86%): mp 148–153 °C (ether); $[\alpha]_D$ +313° (*c* 0.47, $CHCl_3$); R_f 0.7 (solvent *B*). Anal. Calcd for $C_{13}H_{16}Cl_3NO_7S$: C, 35.76; H, 3.69; N, 3.21; S, 7.34. Found: C, 35.63; H, 3.82; N, 3.15; S, 7.42. lit. data for **7-D** mp 143–148 °C (ether-petroleum ether); $[\alpha]_D$ −326° [10].

4-Nitrophenyl 4-O-*benzoyl-2,3*-O-*isopropylidene-5-thio*-L-*arabinopyranoside* (**22**).—A solution of **12** (0.31 g, 1 mmol), PPh_3 (0.34 g, 1.3 mmol), 4-nitrophenol (0.22 g, 1.6 mmol) and DEAD (0.25 mL, 1.6 mmol) in toluene (10 mL) was stirred under N_2 for 72 h, concentrated and submitted to column chromatography (solvent *D*). Concentration of the first fraction gave **22β** (80 mg, 18.6%): mp 108–111 °C (ether–hexane); $[\alpha]_D$ +327° (*c* 0.5, $CHCl_3$); R_f 0.6 (solvent *C*). Anal. Calcd for $C_{21}H_{21}NO_7S$: C, 58.46; H, 4.91; N, 3.25; S, 7.43. Found: C, 58.33; H, 5.00; N, 3.33; S, 7.35.

Concentration of the second fraction gave **22α** (150 mg, 35%). mp 93–95 °C (ether–hexane); $[\alpha]_D$ −38° (*c* 0.5, $CHCl_3$); R_f 0.4 (solvent *C*). Anal. Calcd for $C_{21}H_{21}NO_7S$: C, 58.46; H, 4.91; N, 3.25; S, 7.43. Found: C, 58.30; H, 5.07; N, 3.36; S, 7.39.

4-Cyanophenyl 4-O-*benzoyl-2,3*-O-*isopropylidene-1,5-dithio*-L-*arabinopyranoside* (**23**).—Under argon, to a solution of **14** (0.35 g, 1 mmol) and 4-cyanobenzenethiol (0.26 g, 1.85 mmol) in dry CH_2Cl_2 (15 mL) TMSOTf (0.2 mL, 1.1 mmol) was added at −10 °C and the mixture was stirred at −10 °C for 30 min. The reaction was quenched with Et_3N, concentrated and the residue was submitted to column chromatography (solvent C*)*. Concentration of the first fraction gave **23β** (30 mg, 7%): mp 145–150 °C (EtOAc–hexane); $[\alpha]_D$ +392° (*c* 0.5, $CHCl_3$); R_f 0.7 (solvent *C*). Anal. Calcd for $C_{22}H_{21}NO_4S_2$: C, 61.81; H, 4.95; N, 3.28; S, 15.00. Found: C, 61.72; H, 5.07; S, 15.11.

Concentration of the second fraction gave **23α** (70 mg, 17%): mp 90–95 °C (EtOAc–hexane); $[\alpha]_D$ +55° (*c* 0.5, $CHCl_3$); R_f 0.5 (solvent *C*). Anal. Calcd for $C_{22}H_{21}NO_4S_2$: C, 61.81; H, 4.95; N, 3.28; S, 15.00. Found: C, 61.93; H, 4.79; S, 15.05.

Glycosidation of 4-cyanobenzenethiol with **6**.—To a stirred suspension of **6** [7] (1.5 g, 4.2 mmol) and potassium carbonate (0.85 g, 6.15 mmol) in acetone (85 mL), 4-cyanobenzenethiol (0.8 g, 5.9 mmol) was added and the mixture was refluxed for 2 h. After cooling to room temperature, the precipitated salts were filtered off, washed with acetone, the filtrate was concentrated and submitted to column chromatography (solvent *B*) to yield 4-cyanophenyl 2,3,4-tri-*O*-acetyl-1,5-dithio-L-arabinopyranoside (**24**, 1.1 g, 64%) as a 1:1 anomeric mixture. R_f 0.5 (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, 52.91; H, 4.75; N, 3.50; S, 15.72.

Glycosidation of 4-nitrobenzenethiol with **6**.—To a stirred suspension of **6** (1.0 g, 2.8 mmol) and potassium carbonate (0.56 g, 4.05 mmol) in acetone (45 mL), 4-nitrobenzenethiol (0.6 g, 3.9 mmol) was added and the mixture was refluxed for 1 h. After cooling to room temperature, the precipitated salts were filtered off, washed with acetone, the filtrate was concentrated and submitted to column chromatography (solvent *B*) to yield 4-nitrophenyl 2,3,4-tri-*O*-acetyl-1,5-dithio-L-arabinopyranoside (**25**, 0.74 g, 61%) as a 1:1 anomeric mixture. R_f 0.4 (solvent *B*). Anal. Calcd for $C_{17}H_{19}NO_8S_2$: C, 47.55; H, 4.46; N, 3.26; S, 14.93. Found: C, 47.48; H, 4.40; N, 3.17; S, 14.88.

Glycosidation of 4-cyanobenzenethiol with **7**.—Under argon, a suspension of **7** (1.8 g, 4.12 mmol), 4-cyanobenzenethiol (1.3 g, 9.7 mmol) and 4 Å molecular sieve (2.4 g) in 1,2-dichloroethane (80 mL) was stirred at room temperature for

30 min. After cooling to −15 °C, 0.1 M $BF_3{\cdot}Et_2O$ in 1,2-dichloroethane (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 filtered through Celite, washed with 1,2-dichloroethane, the filtrate was concentrated and submitted to column chromatography (solvent *B*) to yield **24** (1.56 g, 92%) as a 1:4 mixture of α and β anomers. R_f 0.5 (solvent *B*). Recrystallization from ether yielded 4-cyanophenyl 2,3,4-tri-*O*-acetyl-1,5-dithio-β-L-arabinopyranoside (**24β**, 1.1 g, 65%): mp 167–169 °C (ether); $[\alpha]_D$ +375° (*c* 0.5, $CHCl_3$); R_f 0.5 (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, 52.73; H, 4.61; N, 3.33; S, 15.58.

Glycosidation of 4-cyanobenzenethiol with **17**.—Under argon, to a stirred solution of **17** (0.8 g, 2 mmol) and 4-cyanobenzenethiol (0.54 g, 4 mmol) in 1,2-dichloroethane (20 mL) TMSOTf (0.4 mL, 2.2 mmol) was added at −10 °C. After stirring at room temperature for 2 h, the reaction was quenched with Et_3N, concentrated and submitted to column chromatography (solvent *B*). Concentration of the first fraction gave 4-cyanophenyl 2,3-di-*O*-acetyl-4-*O*-benzoyl-1,5-dithio-β-L-arabinopyranoside (**26β**, 0.55 g, 58%): mp 161–163 °C (ether); $[\alpha]_D$ +386° (*c* 0.5, $CHCl_3$); R_f 0.6 (solvent *B*). Anal. Calcd for $C_{23}H_{21}NO_6S_2$: C, 58.58; H, 4.49; N, 2.97; S, 13.60. Found: C, 58.67; H, 4.40; N, 2.83; S, 13.55.

Concentration of the second fraction gave 4-cyanophenyl 2,3-di-*O*-acetyl-4-*O*-benzoyl-1,5-dithio-α-L-arabinopyranoside (**26α**, 0.27 g, 29%): $[\alpha]_D$ +15° (*c* 0.5, $CHCl_3$); R_f 0.5 (solvent *B*). Anal. Calcd for $C_{23}H_{21}NO_6S_2$: C, 58.58; H, 4.49; N, 2.97; S, 13.60. Found: C, 58.65; H, 4.53; N, 3.07; S, 13.52.

The corresponding D-isomers, obtained under identical conditions, had the following data: **26β-D**: mp 161–163 °C (ether); $[\alpha]_D$ −383° (*c* 0.5, $CHCl_3$); R_f 0.6 (solvent *B*). **26α-D**: $[\alpha]_D$ −15° (*c* 0.5, $CHCl_3$); R_f 0.5 (solvent *B*).

Glycosidation of 4-nitrobenzenethiol with **17**.—To a stirred solution of **17** (1.14 g, 2.9 mmol) and 4-nitrobenzenethiol (0.5 g, 3.2 mmol) in 1,2-dichloroethane (15 mL), $BF_3{\cdot}Et_2O$ (0.36 mL, 2.9 mmol) was added. The mixture was kept at room temperature for 24 h, then poured into ice-cold 6% aq $NaHCO_3$ solution (25 mL), separated, and the organic layer was washed with water, 6% aq $NaHCO_3$, concentrated and submitted to column chromatography (solvent *B*). Concentration of the first fraction gave 4-nitrophenyl 2,3-di-*O*-acetyl-4-*O*-benzoyl-1,5-dithio-β-L-arabinopyranoside (**27β**, 0.75 g, 53%): mp 173–176 °C (ether); $[\alpha]_D$ +363° (*c* 0.4, $CHCl_3$); R_f 0.6 (solvent *B*). Anal. Calcd for $C_{22}H_{21}NO_8S_2$: C, 53.76; H, 4.31; N, 2.85; S, 13.04. Found: C, 53.88; H, 4.40; N, 2.91; S, 13.14.

Concentration of the second fraction gave 4-nitrophenyl 2,3-di-*O*-acetyl-4-*O*-benzoyl-1,5-dithio-α-L-arabinopyranoside (**27α**, 0.4 g, 28%): $[\alpha]_D$ +1° (*c* 0.5, $CHCl_3$); R_f 0.5 (solvent *B*). Anal. Calcd for $C_{22}H_{21}NO_8S_2$: C, 53.76; H, 4.31; N, 2.85; S, 13.04. Found: C, 53.90; H, 4.35; N, 3.01; S, 13.16.

The corresponding D-isomers were obtained under identical conditions and had the following data: **27β-D**: mp 173–176 °C (ether); $[\alpha]_D$ −374° (*c* 0.5, $CHCl_3$); R_f 0.6 (solvent *B*). **27α-D**: $[\alpha]_D$ −5° (*c* 0.5, $CHCl_3$); R_f 0.5 (solvent *B*).

Glycosidation of 4-cyanobenzenethiol with **20**.—(a) To a stirred suspension of **20** (1.0 g, 2.4 mmol) and potassium carbonate (0.5 g, 3.6 mmol) in acetone (45 mL) 4-cyanobenzenethiol (0.45 g, 3.3 mmol) was added and the mixture was refluxed for 1 h. After cooling to room temperature, the precipitated salts were filtered off, washed with acetone, the filtrate was concentrated and submitted to column chromatography (solvent *B*). Concentration of the first fraction gave **26β** (250 mg, 22%), identical with the compound described above.

Concentration of the second fraction gave **26α** (375 mg, 33%), identical with the compound described above.

(b) To a suspension of **20** (1.0 g, 2.4 mmol) and ZnO (0.3 g) in acetonitrile (10 mL) and toluene (10 mL), 4-cyanobenzenethiol (0.45 g, 3.3 mmol) was added and the mixture was stirred at room temperature for 30 min. The reaction was filtered through Celite, washed with CH_2Cl_2, concentrated and submitted to column chromatography (solvent *B*). Concentration of the first fraction gave **26β** (320 mg, 28%), identical with the compound described above.

Concentration of the second fraction gave **26α** (410 mg, 36%), identical with the compound described above.

Glycosidation of 4-nitrobenzenethiol with **20**.—To a stirred suspension of **20** (1.0 g, 2.4 mmol) and potassium carbonate (0.5 g, 3.6 mmol) in acetone (45 mL) 4-nitrobenzenethiol (0.51 g, 3.3 mmol) was added and the mixture was refluxed for 2 h. After cooling to room temperature, the precipitated salts

were filtered off, washed with acetone, the filtrate was concentrated and submitted to column chromatography (solvent *B*). Concentration of the first fraction gave **27β** (220 mg, 19%), identical with the compound described above.

Concentration of the second fraction gave **27α** (280 mg, 24%), identical with the compound described above.

4-Cyanophenyl 1,5-dithio-α-L-*arabinopyranoside* (**28α**).—(a) Deacetylation of **24** (α:β ~1:1; 1.1 g, 2.7 mmol) with M NaOMe (0.1 mL) in MeOH (25 mL) yielded, after neutralization with solid CO_2, **28α** (200 mg, 26%) which crystallized from the solution; mp 220–222 °C (MeOH); $[\alpha]_D$ −108° (*c* 0.5, pyridine); R_f 0.3 (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, 50.76; H, 4.53; N, 4.91; S, 22.70.

(b) Deacylation of **26α** (410 mg, 0.87 mmol) with M NaOMe (0.1 mL) in MeOH (15 mL) yielded, after neutralization with solid CO_2 and column chromatography (solvent *F*), **28α** (230 mg, 95%), identical with the compound described above.

4-Cyanophenyl 1,5-dithio-β-L-*arabinopyranoside* (**28β**).—(a) Deacetylation of **24β** (1.1 g, 2.7 mmol) with M NaOMe (0.1 mL) in MeOH (25 mL) yielded after processing as described for **28α** in method (b), **28β** (0.66 g, 87%): mp 182–184 °C (ether); $[\alpha]_D$ +162° (*c* 0.5, pyridine); R_f 0.3 (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, 50.76; H, 4.53; N, 4.91; S, 22.70.

(b) Deacylation of **26β** (250 mg, 0.53 mmol) with M NaOMe (0.1 mL) in MeOH (10 mL) yielded, after processing as described for **28α** in method (b), **28β** (140 mg, 95%), identical with the compound described above.

4-Nitrophenyl 1,5-dithio-α-L-*arabinopyranoside* (**29α**).—Deacylation of **27α** (280 mg, 0.57 mmol) with M NaOMe (0.1 mL) in MeOH (15 mL) yielded, after processing as described for **28α** in method (b), **29α** (140 mg, 81%): mp 175–177 °C (ether); $[\alpha]_D$ −106° (*c* 0.5, pyridine); R_f 0.2 (solvent *G*). Anal. Calcd for $C_{11}H_{13}NO_5S_2$: C, 43.55; H, 4.32; N, 4.62; S, 21.14. Found: C, 43.62; H, 4.43; N, 4.71; S, 21.20.

4-Nitrophenyl 1,5-dithio-β-L-*arabinopyranoside* (**29β**).—Deacylation of **27β** (220 mg, 0.45 mmol) with M NaOMe (0.1 mL) in MeOH (15 mL) yielded, after processing as described for **28α** in method (b), **29β** (120 mg, 88%): mp 183–185 °C (ether); $[\alpha]_D$ +165° (*c* 0.5, pyridine); R_f 0.2 (solvent *G*). Anal. Calcd for $C_{11}H_{13}NO_5S_2$: C, 43.55; H, 4.32; N, 4.62; S, 21.14. Found: C, 43.51; H, 4.25; N, 4.57; S, 21.19.

4-Cyanophenyl 1,5-dithio-α-D-*arabinopyranoside* (**30α**).—Deacylation of **26α-D** (1.3 g, 2.8 mmol) with M NaOMe (0.1 mL) in MeOH (70 mL) yielded, after processing as described for **28α** in method (b), **30α** (0.69 g, 89%): mp 219–221 °C (ether); $[\alpha]_D$ +106° (*c* 0.5, pyridine); R_f 0.3 (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, 50.92; H, 4.63; N, 4.79; S, 22.72.

4-Cyanophenyl 1,5-dithio-β-D-*arabinopyranoside* (**30β**).—Deacylation of **26β-D** (1.0 g, 2.15 mmol) with M NaOMe (0.1 mL) in MeOH (50 mL) yielded, after processing as described for **28α** in method (b), **29β** (0.53 g, 88%): mp 181–183 °C (ether); $[\alpha]_D$ −161° (*c* 0.5, pyridine); R_f 0.3 (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, 50.81; H, 4.58; N, 4.90; S, 22.68.

4-Nitrophenyl 1,5-dithio-α-D-*arabinopyranoside* (**31α**).—Deacylation of **27α-D** (0.53 g, 1.1 mmol) with M NaOMe (0.1 mL) in MeOH (25 mL) yielded, after processing as described for **28α** in method (b), **31α** (0.26 g, 79%): mp 175–177 °C (ether); $[\alpha]_D$ +106° (*c* 0.5, pyridine); R_f 0.2 (solvent *G*). Anal. Calcd for $C_{11}H_{13}NO_5S_2$: C, 43.55; H, 4.32; N, 4.62; S, 21.14. Found: C, 43.63; H, 4.40; N, 4.68; S, 21.19.

4-Nitrophenyl 1,5-dithio-β-D-*arabinopyranoside* (**31β**).—Deacylation of **27β-D** (390 mg, 0.79 mmol) with M NaOMe (0.1 mL) in MeOH (20 mL) yielded, after processing as described for **28α** in method (b), **29β** (200 mg, 83%): mp 183–185 °C (ether); $[\alpha]_D$ −165° (*c* 0.5, pyridine); R_f 0.2 (solvent *G*). Anal. Calcd for $C_{11}H_{13}NO_5S_2$: C, 43.55; H, 4.32; N, 4.62; S, 21.14. Found: C, 43.52; H, 4.28; N, 4.59; S, 21.17.

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References

[1] É. Bozó, S. Boros, J. Kuszmann, E. Gács-Baitz, and L. Párkányi, *Carbohydr. Res.*, 308 (1998) 297–310.
[2] É. Bozó, S. Boros, and J. Kuszmann, *Carbohydr. Res.*, 304 (1997) 271–280.
[3] É. Bozó, S. Boros, and J. Kuszmann, *Carbohydr. Res.*, 302 (1997) 149–162.

[4] É. Bozó, S. Boros, and J. Kuszmann, *Carbohydr. Res.*, 301 (1997) 23–32.
[5] É. Bozó, S. Boros, and J. Kuszmann, *Carbohydr. Res.*, 299 (1997) 59–67.
[6] F. Bellamy, V. Barberousse, N. Martin, P. Masson, J. Millet, S. Samreth, Ch. Sepulchre, J. Théveniaux, and D. Horton, *Eur. J. Med. Chem.*, 30 (1995) 101–115.
[7] C. Lépine, C. Roy, and D. Delorme, *Tetrahedron. Lett.*, 35 (1994) 1843–1846.
[8] N.A. Hughes and R. Robson, *J. Chem. Soc. (C)*, 1966, 2366–2368.
[9] J.Harness and N.A. Hughes, *J. Chem. Soc., Chem. Commun.*, (1971) 811.
[10] H. Hashimoto and M. Izumi, *Tetrahedron. Lett.*, 34 (1993) 4949–4952.
[11] P. Norris, D. Horton, and B.R. Levine, *Tetrahedron Lett.*, 36 (1995) 7811–7814.
[12] J. Kuszmann and B. Podányi, *Carbohydr. Res.*, 225 (1992) 247–267.
[13] Gy. Hodosi, G. Galambos, B. Podányi, and J. Kuszmann, *Carbohydr. Res.*, 225 (1992) 269–278.
[14] N. Morishima, S. Koto, Ch. Kusuhara, and S. Zen, *J. Chem. Soc. Jpn.*, 55 (1982) 631–632.
[15] N.A. Hughes and N.M. Munkombwe, *Carbohydr. Res.*, 136 (1985) 397–409.
[16] N.A. Hughes, K.M. Kuhajda, and D.A. Miljkovic, *Carbohydr. Res.*, 257 (1994) 299–304.
[17] E. Juaristi and G. Cuevas, *Tetrahedron*, 48 (1992) 5019–5087 and refs. cited therein.
[18] E. Grochowski and J. Jurczak, *Carbohydr. Res.*, 50 (1975) C15.
[19] G. Grienkiewicz, *Polish J. Chem.*, 53 (1979) 15710–1579.
[20] D. Bagdy, G. Szabó, É. Barabás, and S. Bajusz, *Thromb. Haemost.*, 68 (1992) 125–129.