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Synthesis of 4-cyano- and 4-nitrophenyl 2,5-anhydro-1,6-dithio-α-D-gluco- and -α-L-guloseptanosides carrying different substituents at C-3 and C-4☆

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Dedicated to Professor András Lipták on the occasion of his 65th birthday

Abstract

Treatment of 1,6:2,5-dianhydro-3,4-di-*O*-methanesulfonyl-1-thio-D-glucitol in methanol with sodium hydroxide afforded 1,6:2,5:3,4-trianhydro-1-thio-allitol, 1,4:2,5-dianhydro-6-methoxy-1-thio-D-galactitol, 1,6:2,5-dianhydro-4-*O*-methyl-1-thio-D-glucitol, 1,6:2,5-dianhydro-3-*O*-methanesulfonyl-1-thio-D-glucitol and 1,6:2,5-dianhydro-4-deoxy-1-thio-D-*erythro*-hex-3-ulose (**14**) in 5, 4, 28, 5.5 and 41% yield, respectively. Formation of these derivatives can be explained via a common sulfonium intermediate. Reduction of **14** with sodium borohydride and subsequent acetylation afforded 3-*O*-acetyl-1,6:2,5-dianhydro-4-deoxy-1-thio-D-*xylo*-hexitol, the absolute configuration of which was proved by X-ray crystallography. The 1,6:2,5-dianhydro-1-thio-D-hexitol derivatives in which the free OH groups were protected by acetylation, methylation or mesylation were converted by a Pummerer reaction of their sulfoxides into the corresponding 1-*O*-acetyl hexoseptanose derivatives which were used as donors for the glycosidation of 4-cyano- and 4-nitrobenzenethiol, respectively. The Pummerer reaction of 1,6:2,5-dianhydro-4-deoxy-3-*O*-methyl-1-thio-D-*xylo*-hexitol *S*-oxide gave, besides 1-*O*-acetyl-2,5-anhydro-3-deoxy-4-*O*-methyl-6-thio-α-L- (**23**) and 1-*O*-acetyl-2,5-anhydro-4-deoxy-3-*O*-methyl-6-thio-α-D-*xylo*-hexoseptanose (**25**), 1-*O*-acetyl-4-deoxy-2,6-thioanhydro-D-*lyxo*-hexopyranose, formed in a rearrangement reaction. The same rearrangement took place, when a mixture of **23** and **25** was used as donor in the glycosidation reaction with 4-cyanobenzenethiol, applying trimethylsilyl triflate as promoter. The oral antithrombotic activity of the obtained α-thioglycosides was determined in rats, using Pescador's model.

Keywords: Antithrombotic thioglycosides; Sulfonium intermediates; Pummerer reaction

1. Introduction

In a previous paper [1] we have shown that, in contrast to the statement of the literature [2], the oral antithrombotic effect of 4-cyanophenyl 1,5-dithio-pentopyranosides is

☆ Orally active antithrombotic thioglycosides, Part XI. For Part X, see Ref. [1].

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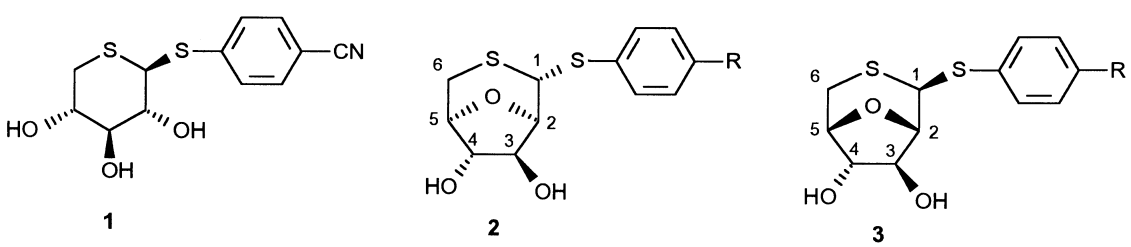
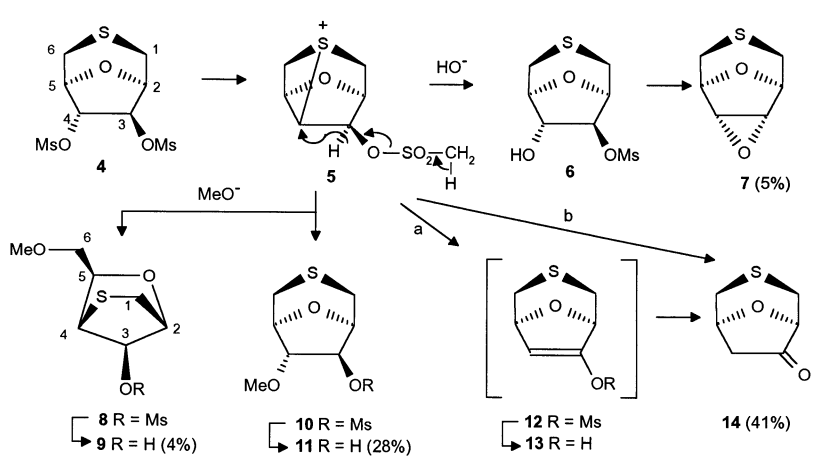
not restricted to the β-D-*xylo* configuration (**1**) as e.g., the overbridged, 2,5-anhydro-1,6-dithio-D-gluco- (**2**) and L-guloseptanosides (**3**) possess a much stronger biological activity (Scheme 1). For checking the structure–activity relationship in this type of thioglycosides, the role of the free OH groups at C-3 and/or C-4 was studied by synthesising analogues of **2** and **3**, in which OH-4 was either eliminated, methylated or exchanged with retention of configuration with an azido group, while OH-3 was kept intact or was converted into its methyl ether or mesyl ester.

2. Results and discussion

For the synthesis of the aforementioned thioglycosides, the 3,4-dimesylate of the corresponding 1,6-thioanhydro-D-glucitol derivative **4** was chosen as starting material, which can be prepared from 1,6-dibromo-1,6-dideoxy-D-mannitol in seven steps [3,4]. When **4** was treated in methanol with 40% aqueous sodium hydroxide, a complex mixture was formed, from which the monomesylate **6** (5.5%), epoxide **7** (5%), two monohydroxy–monomethoxy derivatives **9** (4%) and **11** (28%), as well as the ketone **14** (41%) could be isolated after column chromatography (Scheme 2). The formation of all these derivatives can be explained via the sulfonium intermediate **5** [3]. Attack of the OH^- ion at C-4 will lead with retention of configuration to the hydroxy–mesylate **6** which undergoes a trans elimination of methanesulfonic acid affording the known [3] allo epoxide **7**. A similar attack of the MeO^- ion at C-4 will result in the methoxy–mesylate **10**, the mesyl group of which will be split off in an E1cB type process [5] via regeneration of the 3-OH group affording **11**. Furthermore, the MeO^- ion can attack the less polar, but less crowded C-6 bridge atom of **5** too, when rearrangement to the 1,4:2,5-dianhydro-3-*O*-methanesulfonyl-6-methoxy-1-thio-D-galactitol isomer **8** takes place. The mesyl group of the latter will be split off as mentioned above yielding the isolated methoxy–hydroxy derivative **9**. The main attack of the base occurs however either at H-3 (route a), splitting it off as a proton resulting in the enol–ester **12** from which the



Scheme 1.



Scheme 2.

mesyl group is removed by the base yielding **13** which rearranges immediately to the 3-keto compound **14**. Another possibility would be an attack of the base on the methyl group of the mesyloxy substituent (route b) the deprotonation of which could trigger a chain reaction in which the mesyl group would be first eliminated as a sulfene [5] and the formed 3-oxy anion would form directly **14** via migration of H-3 to C-4 in a pinacoline-type rearrangement. The absolute configuration of **14** had to be established, as deprotonation of **4** at C-4 could not be ruled out and this process would lead via a similar reaction sequence to the isomeric 4-keto derivative, indistinguishable by NMR spectroscopy from **14**. For this reason **14** was reduced with sodium borohydride, but from the theoretically possible two isomers **15** and **18** only the former was formed which was converted into its crystalline acetate **16**. The stereoselectivity of the reduction is a consequence of the steric arrangement of **14**, in which the thioether bridge is 'endo' related to the keto group, therefore the borohydride ion can approach the latter only from the less hindered 'exo' side, excluding the formation of **18**. The hydroxy derivative **15**, obtained as a by-product from **4** on reduction with LAH [5] had probably the same structure, but as the configuration of this compound was only deduced from the mechanism suggested for this reaction [5], this structure had still to be established. The absolute D-*xylo* configuration of **16** was finally established by X-ray crystallography (Fig. 1).

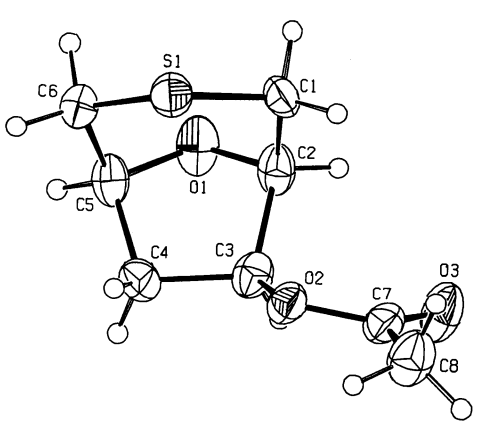
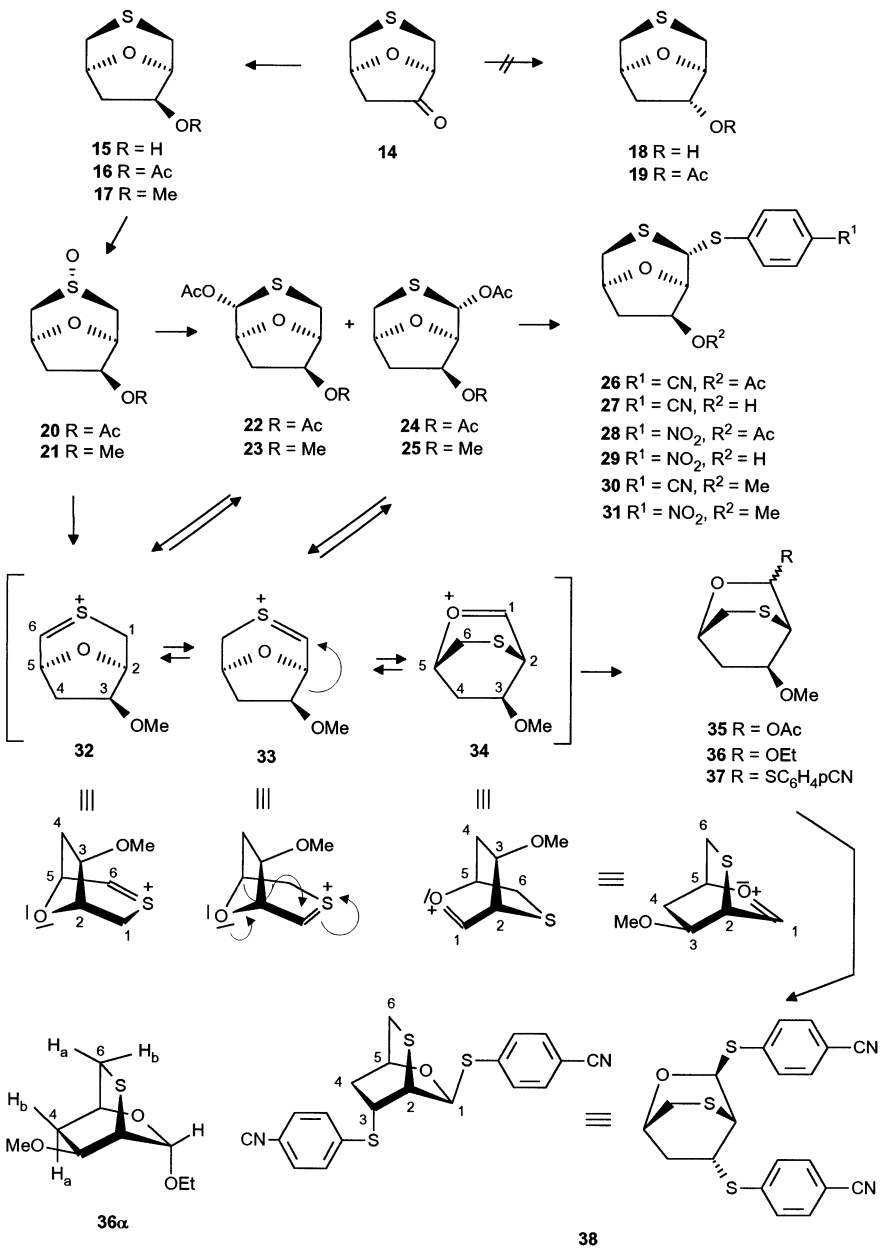


Fig. 1. ORTEP plot [15] (using the program PLATON) of **16**. Thermal ellipsoids represent 40% probabilities.

Both the acetate **16** as well as the 3-*O*-methyl ether **17**, which was obtained from **15** by methylation with methyl iodide in the presence of sodium hydride, were converted with hydrogen peroxide in acetic acid into the corresponding sulfoxides **20** and **21**, respectively. Pummerer rearrangement of **20** gave a mixture from which the 3-deoxy-α-L- **22** and the 4-deoxy-α-D-*xylo*-diacetate **24** could be isolated by column chromatography in a yield of 2 and 71%, respectively. When **24** was applied as donor in the glycosylation reaction with 4-cyanobenzenethiol and trimethylsilyl triflate as promoter, the corresponding α-D-septanoside **26** was obtained in excellent yield (97%) and gave, after deacetylation according to Zemplén, **27** which was submitted to biological testing. When 4-nitrobenzenethiol was used as acceptor, and borontrifluoride etherate as promoter, the resulting acetylated thioglycoside **28** afforded **29** after deacetylation (Scheme 3).

When the methoxy derivative **21** was submitted to the Pummerer reaction, besides a 1:4 mixture of the isomeric monoacetates **23** and **25** the 4-deoxy-2,6-thioanhydro-D-*lyxo*-hexopyranose acetate **35** as well as its ethyl pyranoside **36α** could be isolated in a yield of 40, 9.5 and 5%, respectively. The rearranged structure of the last two derivatives was established by NMR spectroscopy comparing their data with those of the thioseptanose acetates **23** and **25**. Formation of **35** and **36** can be explained via the isomeric sulfenium ions **32** and **33**, which are the hypothetical intermediates of the Pummerer reaction [6] and are in equilibrium with each other [1]. However **33** is probably in an equilibrium with the oxocarbenium ion **34** formed in a pinacoline-type rearrangement reaction via a shift of the C-3–C-2 bond to C-1 (Scheme 3). As **34** should be much more reactive than **33** the acetoxy anion will attack the former yielding the D-lyxopyranose acetate **35**. This was obtained as a single isomer, the anomeric configuration of which could not be established by NMR spectroscopy. Nevertheless, it is most probably an α anomer as its optical rotation ($[\alpha]_D$ + 23°) is very similar to that of the corresponding ethyl α-glycoside **36α**[1] ($[\alpha]_D$ + 17°).

[1] **36α** is probably formed from **35** during work up (evaporation with EtOH).



Scheme 3.

The structure of **36α** and **38** was established by NMR spectroscopy by the following data. According to selective INEPT experiments, there was a three-bond $^{1}H-^{13}C$ connectivity in **36α** between H-1 (5.26 ppm) and C-3 (70.4 ppm) proving the quasi-equatorial (β) arrangement of H-1. On the other hand, a long range coupling $^{4}J_{4a,6b}$ of 2.3 Hz indicated the W-arrangement of H-4a and H-6b, enabling their identification. The corresponding $^{3}J_{3,4a}$ and $^{3}J_{3,4b}$ coupling constants of 9.5 and 2.7 Hz could be determined accordingly. Location of the two 4-cyanophenylthio groups in **38** at C-1 and C-3 was evident from the shift of the corresponding signals in the ^{13}C NMR spectra (85.0 and 44.1 ppm) compared to those of **36α** (100.8 and 70.4 ppm). Furthermore, selective INEPT measurements showed a three-bond connectivity between H-1 as well as H-3 and the aromatic C-1′ carbon atoms. Besides a long range coupling $^{4}J_{4a,6b}$ of 2.2 Hz, an intensive cross-peak between H-4b and H-6a could be detected too in full agreement with the steric arrangement of these protons in **38**. The inversion of configuration at C-3 was evident from the change in the value of the $J_{3,4a}$ and

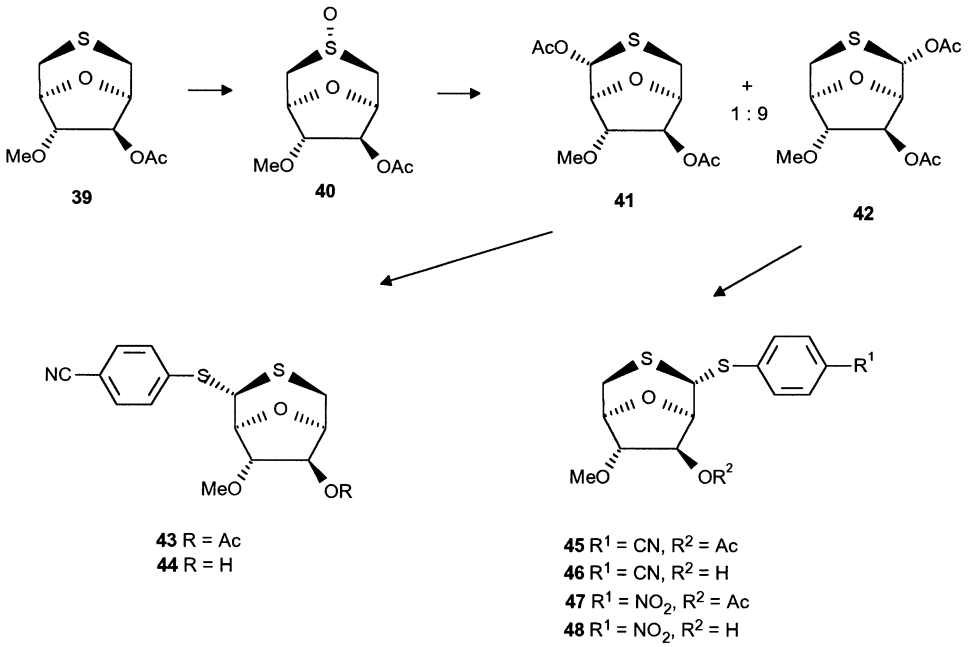
$J_{3,4b}$ coupling constants (9.5 → 4.8 and 2.7 → 11.0 Hz, respectively). In accordance with this arrangement, no NOE effect was observed between H-1 and H-3. The anomeric configuration of **38** was deduced further from the results of the selective INEPT experiments, as no three-band $^{1}H-^{13}C$ connectivity could be detected between H-1 (6.28 ppm) and C-3 (44.1 ppm) and a strong NOE effect was observed on the aromatic protons on irradiating H-6b.

The mechanism of the rearrangement, depicted in Scheme 3 was further backed by the fact that, when the isomeric mixture of the 1-*O*-acetates **23** and **25** was used as donor in the glycosidation reaction with 4-cyanobenzenethiol in the presence of trimethylsilyl tri -flate as promoter, instead of the corresponding 4-deoxy-α-D-*xylo*-hexoseptanoside **30**, only the thioglycoside of 2,6-thioanhydro-β-D-*arabino*-hexopyranoside **38**, carrying a second 4-cyanothiophenol substituent at C-3 could be isolated in 26% yield. The formation of **38** might be explained by the same sulfenium ion intermediate **33** mentioned above, which can be formed from both, **23** and **25** in the presence of trimethylsilyl triflate according to the mechanism depicted in Scheme 3 [1] and reacts via the oxocarbenium intermediate **34** to give first the rearranged thioglycoside **37**, the 3-*O*-methyl group of which is then activated by trimethylsilyl triflate and undergoes a substitution reaction via inversion of configuration affording **38**. The same glycoside **38** was obtained in a yield of 97%, when acetate **35** was used as donor. The desired 3-*O*-methyl thioseptanosides **30** and **31** were finally synthesised by methylating the 3-OH group of the corresponding glycosides **27** and **29**, respectively, using methyl iodide in the presence of sodium hydride in *N*,*N*-dimethylformamide.

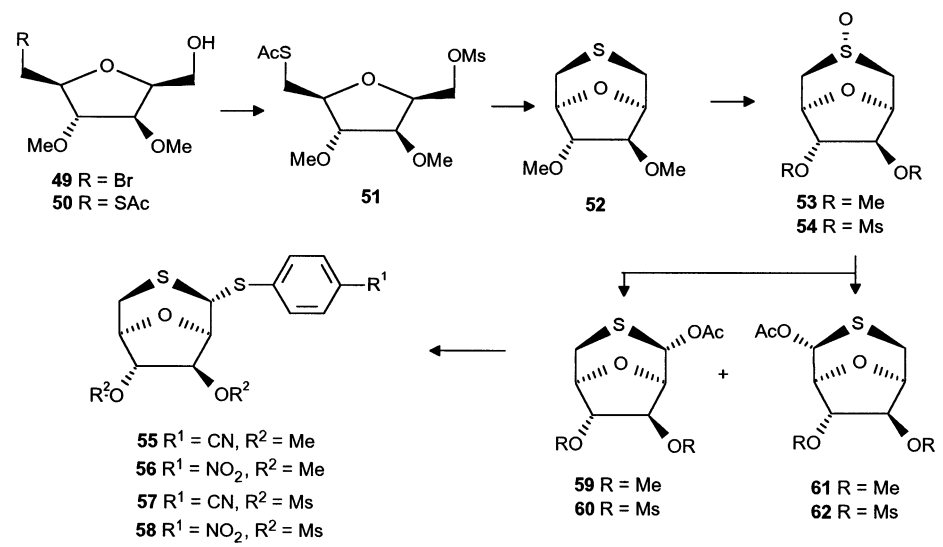
For the synthesis of the 4-*O*-methyl thioseptanosides **46** and **48**, the 3-*O*-acetyl-4-*O*-methyl-glucitol derivative **39**, which was obtained from **11** by acetylation, was converted via oxidation and Pummerer reaction of the obtained sulfoxide **40** into a 1:9 mixture of the isomeric acetates **41** and **42**. This mixture could be separated by column chromatography, and the major component **42** was used as donor for the glycosidation of both, 4-cyano- and 4-nitrobenzenethiol affording **45** and **47** which on deacetylation gave **46** and **48**, respectively. Similar glycosidation of the minor component **41** with 4-cyanobenzenethiol gave **44** via **43** (Scheme 4).

For checking the influence of the free 3-OH group of the aforementioned 3-hydroxy-4-methoxy-thioglycosides on the antithrombotic activity, the corresponding 3,4-di-*O*-methyl derivatives were synthesised too. Theoretically these derivatives could be obtained by methylating the free 3-OH group of **46** and **48** but, as shown above, these thioglycosides could be obtained in a multistep synthesis only, the overall yield of which was too low for using them as starting material in any further reaction. For this reason, 2,5-anhydro-6-bromo-6-deoxy-3,4-di-*O*-methyl-D-glucitol **49** was applied as starting material, which can be easily obtained from D-mannitol in few steps [7]. Reaction of **49** with potassium thioacetate afforded **50**, which after mesylation and treatment of the obtained mixed ester **51** with methanolic sodium methoxide, gave the thioether **52** in excellent yield (Scheme 5). This was converted into the sulfoxide **53** the Pummerer rearrangement of which afforded the two isomeric acetates **59** and **61** in a ratio of 9:1. They were used without separation for the glycosylation of both, 4-cyano- and 4-nitrobenzenethiol and the formed thioglycosides **55** and **56** were isolated by column chromatography. By analogy, the corresponding 3,4-di-*O*-mesylates **57** and **58** were also synthesised, using the known [9] sulfoxide **54** as starting material.

Finally, we decided to synthesise such analogs, in which the 4-OH group of **2** or **3** is exchanged by azide, as similar substitution in **1** type compounds led to a substantial increase in the antithrombotic activity [8]. As starting material 1,6-anhydro-3-*O*-tetrahydropyranyl-4-*O*-mesyl-6-thio-D-glucitol **63** [1] was chosen, the mesyloxy group of which could be exchanged by azide with retention of configuration affording **64** via an **5** type (OMs = OTHP) sulfonium intermediate (Scheme 6). After removing the tetrahydropyranyl group in methanol with an ion exchange resin (H^+), the resulting hydroxy derivative **65** was acetylated and the acetate **66**

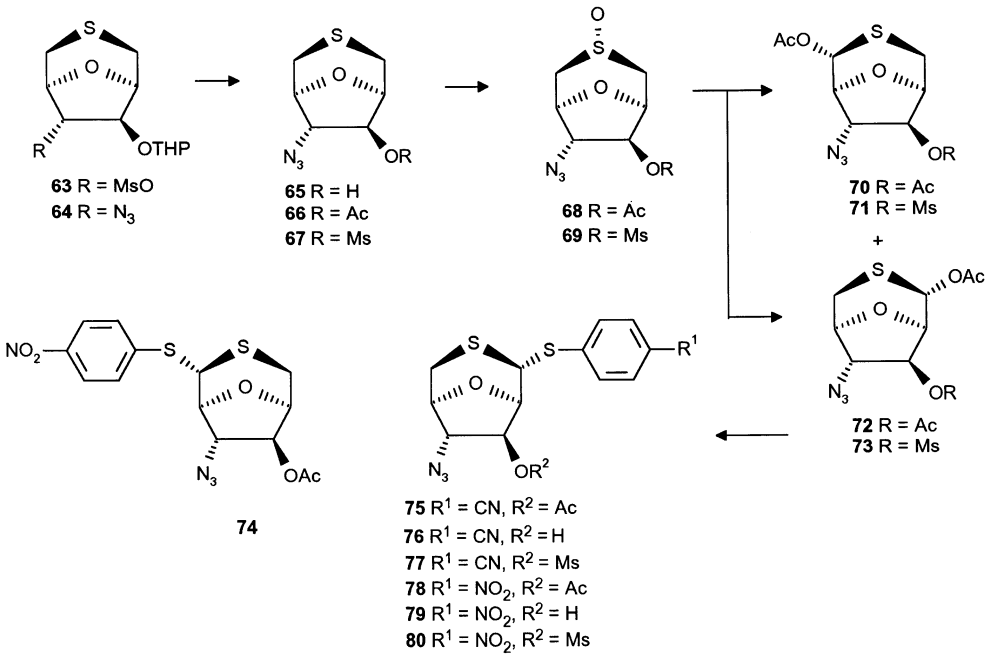


Scheme 4.



Scheme 5.

converted via the Pummerer reaction of its sulfoxide **68** into a 1:4 mixture of the corresponding 1-*O*-acetates **70** and **72**. This mixture was used as donor in the glycosidation of 4-cyanobenzenethiol and gave, after column chromatography, the corresponding thioglucoside **75**. When 4-nitrobenzenethiol was used as aglycon, besides **78** the corresponding L-gulo isomer **74** could also be isolated in traces. Deacetylation of **75** and **78** afforded **76** and **79**, respectively. For checking the influence of the 3-OH group of these derivatives on the biological activity, the corresponding 3-*O*-mesyl compounds **77** and **80** were also prepared



Scheme 6.

applying analogous reactions, i.e., converting the known [3] 3-*O*-mesylate **67** via its sulfoxide **69** into the 1-*O*-acetyl isomers **71** and **73** and using this mixture for the glycosylation of 4-cyano- and 4-nitrobenzenethiol.

Biological results.—The oral antithrombotic activity of **27**, **29**, **30**, **31**, **38**, **44**, **46**, **48**, **55**, **56**, **57**, **58**, **76**, **77**, **79** and **80** was determined in rats, using Pescador's model [10] and **2** as reference compound. All compounds were administered orally 3 h before ligation at a dose of 2 mg/kg. From the data listed in Table 1, it can be seen that although there exists no straightforward structure–activity relationship in this type of thioglycosides, blocking of the 4-OH group by methylation (**44**, **46**, **48**) or its substitution by an azido group (**76**, **79**) seems to have little influence on the activity when the 3-OH group is still present. Blocking of the latter by methylation (**31**, **55**, **56**) or mesylation (**57**, **58**, **77**) decreases the activity in most cases. It is worthwhile mentioning, that the 2,6-thioanhydro-D-*arabino*-hexopyranoside **38**, carrying a second 4-cyanothiophenol substituent at C-3 was as active (38%) as **1**.

3. Experimental

General methods.—Organic solns were dried over $MgSO_4$ and concd under diminished pressure at or below 40 °C. TLC: E. Merck precoated Silica Gel 60 F_{254} plates, with EtOAc (A), EtOAc–hexane mixtures (B, 1:1; C, 1:2; D, 1:4), toluene–MeOH mixture (E, 9:1), and toluene–acetone mixture (F, 4:1); detection by spraying the plates with a 0.02 M soln of I_2 and a 0.3 M soln of KI in 10% aq H_2SO_4 soln followed by heating at ca. 200 °C. For column chromatography, Kieselgel 60 was used. The mp are uncorrected. Optical rotations were determined on 1.0% solns in $CHCl_3$ at 20 °C unless stated otherwise. 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 stated otherwise. Multiplicities of the ^{13}C NMR spectra were obtained from DEPT experiments. The assignment of the protons was based on homonuclear decoupling experiments. The selective INEPT pulse sequence was optimised to a heteronuclear coupling constant of 7 Hz. The ratio of α:β anomeric mixtures was determined by ^1H NMR.

Table 1
Oral antithrombotic activity of 4-cyanophenyl and 4-nitrophenyl 2,5-anhydro-1,6-dithio-α-D-glucoseptanosides differently substituted at C-3 and C-4 in rats using Pescador's model [10]

Compound	**2**	**27**	**29**	**30**	**31**	**44** [a]	**46**	**48**	**55**	**56**	**57**	**58**	**76**	**77**	**79**	**80**
C-3–R	OH	OH	OH	OMe	OMe	OH	OH	OH	OMe	OMe	OMs	OMs	OH	OMs	OH	OMs
C-4–R	OH	H	H	H	H	OMe	OMe	OMe	OMe	NO_2	OMs	OMs	N_3	N_3	N_3	N_3
C-4′–R	CN	CN	NO_2	CN	NO_2	CN	CN	NO_2	CN	NO_2	CN	NO_2	CN	CN	NO_2	NO_2
Inhibition (%) [b]	37	17	39	33	9	38	46	44	16	28	15	27	47	12	20	37

[a] α-L-Guloseptanoside.
[b] Percentage inhibition at an oral dose of 2 mg/kg.

X-ray data (see Section 4). Unit cell parameters were determined by least-squares of the setting angles of 25 ($40.87 \leq \theta \leq 44.71°$) reflections. Intensity data were collected on an Enraf–Nonius CAD4 diffractometer (graphite monochromator; Cu K_α radiation, $\lambda =$ 1.54180 Å) at 293(2) K in the range $3.80 \leq \theta \leq 74.52°$ using ω–2θ scans. The intensities of three standard reflections were monitored regularly (every 60 min). The intensities of the standard reflections indicated a crystal decay

Table 2
Crystal data and structure refinement of **16**

Empirical formula	$C_8H_{12}O_3S$
Formula weight	188.24
Temperature (K)	293(2)
Radiation	Cu K_α
Wavelength, λ (Å)	1.54180
Crystal system	monoclinic
Space group	$P2_1$
Unit cell dimensions	
a (Å)	5.529(1)
b (Å)	6.989(1)
c (Å)	11.633(2)
β (°)	90.20(1)
Volume (Å^3)	449.52(13)
Z	2
D_{calc} (g/cm^3)	1.391
Absorption coefficient, μ (mm^{-1})	2.940
F(000)	200
Crystal colour	transparent
Crystal description	prism
Crystal size (mm)	$0.40 \times 0.30 \times 0.30$
Absorption correction	psi-scan
Max. and min. transmission	0.998 and 0.890
θ Range for data collection (°)	$3.80 \leq \theta \leq 74.52$
Index ranges (°)	$-6 \leq h \leq 6$, $-8 \leq k \leq 8$, $-14 \leq l \leq 14$
Reflections collected	2219
Number of standard reflections	3
Decay (%)	22.00
Independent reflections	1811 [$R_{int} = 0.0244$]
Reflections [$I > 2\sigma(I)$]	1774
Refinement method	full-matrix least-squares on F^2
Data/restraints/parameters	1811/1/110
Goodness-of-fit on F^2	1.1
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0466$, $wR_2 = 0.1190$
R indices (all data)	$R_1 = 0.0471$, $wR_2 = 0.1199$
Absolute structure parameter	−0.01(2)
Max. and mean shift/esd	0.004, 0.000
Largest difference peak and hole (e Å^{-3})	0.361 and −0.627

Table 3
Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) of **16** [a]

	x	*y*	*z*	U_{eq}
S-1	8804(1)	10080.1(7)	3343.1(5)	48(1)
O-1	4466(3)	7293(4)	3789(2)	59(1)
O-2	7972(3)	7054(3)	1206(1)	45(1)
O-3	4792(4)	7203(4)	11(2)	67(1)
C-1	5870(4)	9962(4)	2647(2)	47(1)
C-2	4806(4)	7967(4)	2637(2)	47(1)
C-3	6401(4)	6412(4)	2114(2)	46(1)
C-4	7944(5)	5690(4)	3128(2)	50(1)
C-5	6859(4)	6714(4)	4161(2)	48(1)
C-6	8278(5)	8476(4)	4535(2)	47(1)
C-7	6935(4)	7333(4)	173(2)	46(1)
C-8	8754(5)	7868(6)	−716(2)	64(1)

[a] U(eq) is defined as one third of the trace of the orthogonalised U_{ij} tensor.

Table 4
Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters of **16** ($Å^2 \times 10^3$)

	x	*y*	*z*	U_{iso}
H-1a	4766	10816	3040	61
H-1b	6025	10408	1861	61
H-2	3243	7989	2237	61
H-3	5380	5367	1830	60
H-4a	7814	4313	3210	66
H-4b	9631	6031	3029	66
H-5	6727	5820	4807	62
H-6a	9818	8080	4858	61
H-6b	7387	9144	5129	61
H-8a	8317	7295	−1438	89
H-8b	10322	7418	−484	89
H-8c	8792	9234	−799	89

of 22% (the data were corrected for decay). An empirical absorption correction (psi-scans) [11] was applied to the data.

The structure was solved by direct methods [12] and refined by full-matrix least-squares anisotropic least-squares on F^2 [13]. Crystal data and refinement details are shown in Table 2. Hydrogen atomic positions were calculated from assumed geometries. Scattering factors and their anomalous contributions were taken from [14]. Final atomic parameters are given in Tables 3 and 4, bond lengths, bond angles and torsion angle in Table 5. Selected ^{1}H NMR chemical shifts (δ) and coupling constants (Hz) for solns of the compounds under investigation in $CDCl_3$ are given in Tables 6 and 7, respectively. Table 8 lists selected ^{13}C NMR data for solns in $CDCl_3$.

*Reaction of 1,6:2,5-dianhydro-3,4-di-*O*-methanesulfonyl-1-thio-*D*-glucitol* (**4**) *with NaOH.*—A stirred soln of **4** (19.2 g, 60 mmol) [3,4] in MeOH (400 mL) and 40% aq NaOH (50 mL) was refluxed for 4 h. After cooling to rt the mixture was neutralised with solid CO_2, filtered through Celite, concd and the residue was submitted to column chromatography (solvent C, then B). Concentration of the first fraction gave 1,6:2,5-dianhydro-4-deoxy-D-*erythro*-hex-3-ulose (**14**, 3.56 g, 41%): mp 55–60 °C (hexane); $[\alpha]_D$ +72° (*c* 0.5, $CHCl_3$); R_f 0.7 (solvent C). Anal. Calcd for $C_6H_8O_2S$: C, 49.98; H, 5.59; S, 22.24. Found: C, 50.03; H, 5.62; S, 22.21.

Concentration of the second fraction gave 1,6:2,5:3,4-trianhydro-1-thio-allitol (**7**, 0.43 g, 5%): mp 104–105 °C (hexane); lit. 105–106 °C [3]; R_f 0.6 (solvent C).

Concentration of the third fraction gave 1,6:2,5-dianhydro-4-*O*-methyl-1-thio-D-glucitol (**11**, 2.97 g, 28%): mp 68–70 °C (ether); lit. 75–76 °C [16]; $[\alpha]_D$ +28° (*c* 0.5, $CHCl_3$); lit. $[\alpha]_D$ +31° [16]; R_f 0.4 (solvent B).

Concentration of the fourth fraction gave 1,4:2,5-dianhydro-6-methoxy-1-thio-D-galactitol (**9**, 425 mg, 4%) as an oil: $[\alpha]_D$ −36° (*c* 0.5, $CHCl_3$); R_f 0.3 (solvent B). Anal. Calcd for $C_7H_{12}O_3S$: C, 47.71; H, 6.86; S, 18.19. Found: C, 47.75; H, 6.90; S, 18.23.

Table 5
Bond lengths (Å) and angles (°) of **16**

S-1–C-6	1.807(3)	S-1–C-1	1.813(2)
O-1–C-2	1.433(3)	O-1–C-5	1.448(3)
O-2–C-7	1.343(3)	O-2–C-3	1.442(3)
O-3–C-7	1.203(3)	C-1–C-2	1.513(5)
C-2–C-3	1.528(4)	C-3–C-4	1.538(3)
C-4–C-5	1.523(4)	C-5–C-6	1.523(4)
C-7–C-8	1.493(4)		
C-6–S-1–C-1	99.7(1)	C-2–O-1–C-5	104.4(2)
C-7–O-2–C-3	116.4(2)	C-2–C-1–S-1	113.1(2)
O-1–C-2–C-1	110.4(2)	O-1–C-2–C-3	102.5(2)
C-1–C-2–C-3	115.7(2)	O-2–C-3–C-2	114.8(2)
O-2–C-3–C-4	109.3(2)	C-2–C-3–C-4	104.3(2)
C-5–C-4–C-3	103.4(2)	O-1–C-5–C-6	109.2(2)
O-1–C-5–C-4	104.9(2)	C-6–C-5–C-4	113.7(2)
C-5–C-6–S-1	111.5(2)	O-3–C-7–O-2	123.1(2)
O-3–C-7–C-8	125.2(2)	O-2–C-7–C-8	111.7(2)

Table 6
Selected ^{1}H NMR data for solutions in $CDCl_3$

Compound	Chemical shifts (δ)								
	H-1a	H-1b	H-2	H-3	H-4a	H-4b	H-5	H-6a	H-6b
9	2.74	2.84	4.17	4.55	3.33		4.30	3.60	3.68
14	3.13	2.42	4.13		2.72	2.53	4.95	3.49	2.27
16	3.15	2.20	4.45	5.17	2.68	2.21	4.45	3.30	2.12
17	3.12	2.36	4.30	4.10	2.50	2.20	4.50	3.30	2.10
20	2.84	3.48	4.74	5.12	2.64	1.70	4.57	2.84	3.50
21	2.85	3.64	4.65	4.12	2.45	1.68	4.60	2.88	3.56
22	6.07		4.38	[c]	5.18		4.52	3.30	2.48
24	5.37		4.36	5.15	2.66	2.15	4.54	3.45	2.10
25	5.54		4.33	4.13	2.54	2.20	4.59	3.49	2.15
26	4.15		4.55	5.19	2.73	2.22	4.62	3.57	2.17
27 [a]	4.59		4.13	4.40	2.45	1.98	4.48	3.28	2.26
28	4.22		4.57	5.21	2.75	2.24	4.63	3.58	2.18
29 [a]	4.67		4.18	4.42	2.46	2.00	4.50	3.30	2.30
30	4.36		4.38	4.17	2.52	2.20	4.61	3.53	2.15
31	4.43		4.41	4.18	2.53	2.22	4.62	3.55	2.17
35	6.32		3.15	4.05	2.00–2.20	2.00–2.20	4.40	2.55	3.21
36α	5.26		3.01	4.11	2.50	1.49	4.27	2.69	2.93
38	6.28		3.01	4.33	2.10	2.50	4.40	2.82	3.57
40	2.75	3.24	4.84	5.07	3.72		4.40	2.82	3.50
41	6.00		4.20	4.53	5.18		4.81	3.25	2.25
42	5.25		4.70	5.23	4.41		4.40	3.45	2.30
43	4.20		4.35	4.38	5.20		4.88	3.40	2.05
44 [a]	4.90		4.06–4.16	4.06–4.16	4.20		4.45	3.12	2.35
45	3.97		4.83	5.18	4.42		4.42	3.50	2.32
46 [a]	4.57		4.38	4.25	4.10		4.30	3.18	2.42
47	4.03		4.86	5.19	4.44		4.44	3.52	2.32
48 [a]	4.63		4.43	4.28	4.12		4.30	3.21	2.46
50	3.78–3.88	3.78–3.88	4.06	3.79	3.58		3.90	3.25	3.12
51	4.30–4.50	4.30–4.50	4.25	3.73	3.58		3.94	3.22	3.08
52	3.12	2.28	4.56	3.98	4.25–4.32	4.25–4.32	4.25–4.32	3.22	2.20
53 [a]	2.57	3.43	4.74	3.87	3.62		4.40	2.53	3.68
55	4.28		4.61	4.02	4.28		4.42	3.45	2.24
56	4.35		4.63	4.03	4.30		4.43	3.50	2.26
57	4.32		4.80	5.28	5.72		4.64	3.49	2.48
58 [a]	4.70		4.88	5.38	5.65		4.70	3.35	2.70
59	5.51		4.55	3.97	4.27		4.38	3.45	2.24
64 [b]	3.09	2.34	4.50	4.32	4.60		4.24	3.19	2.23
64 [b]	3.09	2.47	4.49	4.44	4.50		4.26	3.20	2.23
66	3.14	2.14	4.70	5.17	4.53		4.32	3.22	2.28
68 [a]	2.62	3.50	4.84	5.03	4.14		4.45	2.62	3.78
69 [a]	2.72	3.58	4.90	5.13	4.41		4.53	2.65	3.85
70	5.43		4.27	4.34	5.19		4.80	3.33	2.19
71	6.02		4.28	4.85	5.03		4.70	3.32	2.65
72	5.37		4.64	5.19	4.50		4.40	3.45	2.30
73	5.50		4.64	5.08	4.72		4.46	3.47	2.35
74	4.40		4.23	4.49	5.20		4.83	3.44	2.23
75	4.08		4.77	5.18	4.52		4.42	3.50	2.35
76 [a]	4.58		4.25–4.45	4.25–4.45	4.25–4.45	4.25–4.45	4.25–4.45	3.20	2.55
77	4.33		4.73	5.07	4.72		4.48	3.55	2.38
78	4.15		4.80	5.18	4.53		4.43	3.53	2.37
79 [a]	4.65		4.25–4.50	4.25–4.50	4.25–4.50	4.25–4.50	4.25–4.50	3.20	2.58
80	4.40		4.75	5.08	4.72		4.50	3.56	2.40

[a] Me_2SO-d_6.
[b] Signals of the two THP-diastereomers.
[c] H-3a 2.60, H-3b 2.38 ppm.

Table 7
Selected ^{1}H NMR data for solutions in $CDCl_3$

Compound	Coupling constants (Hz)												
	$J_{1a,1b}$	$J_{1a,2}$	$J_{1b,2}$	$J_{2,3}$	$J_{3,4a}$	$J_{3,4b}$	$J_{4a,4b}$	$J_{4a,5}$	$J_{4b,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$	$J_{1b,6b}$
9	10.9	0.8	1.9	2.5	2.3			2.3		6.3	7.7	9.8	
14	12.9	2.9	1.2				17.8	7.6	~0	2.7	~1	13.4	~1
16	13.4	3.4	~1	6.4	11.2	5.0	13.2	7.7	<1	2.4	~1	12.9	~1
17	13.4	3.4	~1	6.3	11.2	5.0	12.7	7.8	1.7	2.7	~1	12.9	~1
20	13.2	~3	~1	6.9	11.5	3.4	14.4	8.5	0.7	~2.5	~1.5	~13	~1
21	13.3	3.4	~1.5	~7	9.5	3.3	13.9	9.5	<1	~2.5	~1.5	~12	~1
22		3.4		[b]	9.7	4.9	[c]	4.8		3.4	~1	13.7	<1
24		1.7		6.8	10.7	5.0	13.4	7.8	1.6	2.7	~1.5	12.9	~1
25		1.7		6.6	10.3	5.1	12.9	7.9	1.9	2.7	~1.5	12.7	~1
26		~1		6.4	11.0	4.9	13.4	7.8	1.5	2.4	~1.5	13.2	~1
27 [a]		~1		6.6	11.0	5.1	12.7	7.8	1.4	2.4	~1.5	13.2	~1
28		~1		6.8	11.0	5.1	13.2	7.6	1.5	2.4	~1.5	13.2	~1
29 [a]		~1		6.6	11.0	5.0	12.5	7.9	1.5	2.4	~1.5	12.9	~1
30		~1		7.1	10.3	4.9	13.0	7.8	1.5	2.5	~1.5	13.0	~1
31		~1		6.3	10.3	4.9	12.7	7.8	1.5	2.4	~1.5	12.8	~1
35		2.9		3.5	8.8	~3	nd [d]	~4	~2	2.2	~3	10.8	
36α		2.7		4.1	9.5	2.7	14.5	4.8	~1.5	~1	4.4	11.0	
38		2.7		2.8	4.8	11.0	14.9	5.1	1.2	2.3	~2	11.5	
40	13.0	2.9	~1	~7	~2			~0		2.9	~1.5	12.5	~1
41		3.4		~0	2.9			6.8		3.4	~1.5	13.7	~1
42		~2		6.8	3.2			nd		2.9	1.7	12.9	~1
43		1.3		~0	2.7			6.6		3.2	~1	13.9	~1
44 [a]		~1.5		~0	2.6			5.9		3.2	~1	13.2	~1
45		~1		6.6	2.7			nd		2.4	~1.5	13.2	~1
46 [a]		~1		7.1	2.9			~0		2.4	~1.5	13.2	~1
47		~1		6.8	2.9			nd		2.7	~2	13.4	~1
48 [a]		~1		7.1	2.7			~0		2.4	~1.5	13.2	~1
50	nd	~5	~5	4.9	2.0			3.7		5.9	6.9	13.7	
51	11.0	4.6	6.8	4.1	~1			2.7		6.4	7.1	13.9	
52	13.2	3.2	~1	6.8	3.4			nd		2.7	~1.5	13.2	~1
53 [a]	12.5	3.4	~2	6.9	2.2			~0		2.9	~2	12.5	~1.5
55		~1		6.8	2.8			nd		~2	~1.5	13.2	~1
56		~1		6.6	2.7			~0		2.7	~1.5	13.2	~1
57		~1.5		6.8	2.7			~0		2.2	~1.5	13.7	~1
58 [a]		~1		6.8	2.7			~0		~2.5	~1.5	13.9	~1
59		1.7		6.8	2.8			~0		3.2	~2	13.0	~1
64	13.2	3.2	~1	6.8	3.2			~0		2.4	~1.5	13.2	~1
66	13.7	3.2	~1	6.8	3.4			~0		2.6	~1	13.4	~1
68 [a]	~13	~3	~2	~7	~2.5			~0		~3	~2	12.5	~2
69 [a]	12.9	3.2	2.4	7.1	2.7			~0		2.9	2.4	12.2	2.4
70		2.7		~0	3.2			~7		3.4	nd	13.7	<1
71		3.3		~0	3.7			6.8		3.4	~1.5	14.2	<1
72		2.2		7.1	3.7			~0		2.9	1.7	13.4	<1
73		1.9		6.8	3.7			~0		2.7	~1.5	13.2	~1
74		~1.5		~0	3.4			6.6		2.7	~1	13.9	~1
75		~1		6.8	3.2			~0		2.7	~2	13.8	~1
76 [a]		~1		nd	nd			nd		2.4	~1.5	13.2	~1
77		~1		6.6	3.7			~0		2.4	~1.5	13.2	~1
78		~1		6.8	3.4			~0		2.6	~2	13.7	~1
79 [a]		~1		nd	nd			nd		2.2	~1	13.1	~1
80		~1		6.8	3.4			~0		2.4	~1.5	13.7	~1

[a] Me_2SO-d_6.
[b] $J_{2,3a}$ 7.3, $J_{2,3b}$ 1.5 Hz.
[c] $J_{3a,3b}$ 14.1 Hz.
[d] nd, not determined.

Table 8
Selected ^{13}C NMR data for solutions in $CDCl_3$

Compound	Chemical shifts (δ)						
	C-1	C-2	C-3	C-4	C-5	C-6	Others
9	34.5	77.7	75.5	52.0	80.2	73.4	59.0 (OMe)
14	26.4	75.6	213.7	40.7	73.4	30.5	
16	25.2	73.1 [a]	73.3 [a]	34.0	73.4 [a]	31.4	170.8 (CO); 20.7 (OAc)
17	24.8	73.8	81.3	33.9	73.5	31.7	58.6 (OMe)
20	52.5	72.7 [a]	73.2 [a]	34.8	74.3 [a]	56.2	170.3(CO); 20.6 (OAc)
21	52.1	75.1	80.6	34.6	72.9	56.1	58.3 (OMe)
22	70.3	73.1 [a]	31.3	73.3 [a]	74.6 [a]	27.8	168.9, 170.7 (CO); 20.6, 20.7 (OAc)
24	68.2	76.2	72.6	33.2	72.9	29.8	169.8, 170.6 (CO); 20.7, 21.2 (OAc)
25	68.4	76.6	80.6	32.7	72.7	29.8	169.8 (CO); 21.1 (OAc); 58.5 (OMe)
26	46.1	76.8	74.0	33.8	73.8	30.0	170.8 (CO); 20.9 (OAc); 118.6 (CN)
28	45.8	76.6	73.9	33.6	73.7	29.9	170.8 (CO); 20.8 (OAc)
30	45.5	74.0 [a]	81.5	33.1	77.3 [a]	30.2	58.7 (OMe);118.6 (CN)
31	45.4	74.0	81.5	33.1	77.3	30.2	58.7 (OMe)
35	91.2	33.8	76.5	33.2	66.0	29.3	169.8 (CO); 21.0 (OAc); 55.9 (OMe)
36α	100.8	36.5	70.4	33.9	65.4	29.2	62.8, 15.0 (OEt); 55.7 (OMe)
38	85.0	37.7	44.1	32.4	65.8	29.7	118.2, 118.6 (CN)
40	51.3	74.4 [a]	78.2 [a]	86.6	79.7 [a]	54.2	169.8 (CO); 20.5 (OAc); 57.0 (OMe)
41	68.2	75.2 [a]	79.4 [a]	80.1 [a]	84.9 [a]	27.2	168.8, 170.3 (CO); 20.7 (OAc); 57.1 (OMe)
42	67.6	78.2	79.2	87.1	78.0	27.1	169.8, 170.1 (CO); 20.7, 21.1 (OAc); 57.1 (OMe)
43	49.5	81.2	88.1	79.6	76.0	22.9	170.2 CO); 20.7 (OAc); 57.1 (OMe); 118.4 (CN)
45	45.4	78.5 [a]	78.7 [a]	87.0	80.6 [a]	27.2	170.3 CO); 20.7 (OAc); 57.0 (OMe); 118.4 (CN)
47	45.3	78.5 [a]	78.8 [a]	87.0	80.6 [a]	27.2	170.4 (CO); 20.7 (OAc); 57.0 (OMe)
50	61.0	80.8 [a]	85.6 [a]	86.7 [a]	81.5 [a]	31.9	195.1 (CO); 57.2, 57.4 (OMe); 30.3 (SAc)
51	68.5	78.7 [a]	84.3 [a]	86.0 [a]	82.6 [a]	31.8	194.9 (CO); 57.3, 57.2 (OMe); 37.3 (Ms); 30.4 (SAc)
52	24.3	75.7 [a]	88.3 [a]	88.4 [a]	78.2 [a]	29.1	57.0, 58.7 (OMe)
55	45.4	79.2	88.7	87.6	78.4	27.4	57.1, 58.8 (OMe); 118.5 (CN)
56	45.4	79.3	88.8	87.6	78.5	27.5	57.2, 58.9 (OMe)
59	68.2	77.9 [a]	87.9 [a]	87.8 [a]	78.5 [a]	27.3	169.9 (CO); 21.1 (OAc); 57.1, 58.7 (OMe)
64 [b]	24.5	76.2	85.6	68.8	79.8	29.3	
64 [b]	24.6	76.8	83.4	68.7	78.8	29.2	
66	24.7	75.6 [a]	79.2 [a]	68.4	80.0 [a]	29.2	170.4 CO); 20.6 (OAc);
70	69.4 [a]	81.5 [a]	67.8 [a]	79.3 [a]	75.2 [a]	22.8	169.8, 170.2 (CO); 20.7, 21.2 (OAc);
71	68.2	75.6 [a]	65.6	80.4 [a]	82.7 [a]	27.0	168.6 (CO); 20.6 (OAc); 38.1 (OMs)
72	67.4 [a]	78.2 [a]	79.1 [a]	68.2 [a]	79.3 [a]	27.4	169.8, 170.2 (CO); 20.7, 21.2 (OAc)
73	67.0 [a]	78.2 [a]	78.9 [a]	67.4 [a]	81.9 [a]	27.4	169.6 (CO); 21.1 (OAc); 38.2 (OMs)
75	45.8	78.7 [a]	79.6 [a]	68.1	80.3 [a]	27.4	170.2 (CO); 20.6 (OAc); 118.3 (CN)
78	45.7	78.7 [a]	79.7 [a]	68.1	80.4 [a]	27.5	170.4 (CO); 20.7 (OAc)
80	44.8	78.8 [a]	79.2 [a]	67.4	83.4 [a]	27.7	38.1 (OMs)

[a] Arbitrary assignment.
[b] Signals of the two THP-diastereomers.

Concentration of the fifth fraction gave 1,6:2,5-dianhydro-3-*O*-methanesulfonyl-1-thio-D-glucitol (**6**, 0.8 g, 5.5%): mp 99–101 °C (hexane); lit. 98–100 °C [3]; $[\alpha]_D$ +19° (*c* 0.5, $CHCl_3$); lit. $[\alpha]_D$ +17.5° (*c* 1, $CHCl_3$) [3]; R_f 0.2 (solvent B).

3-O-Acetyl-1,6:2,5-dianhydro-4-deoxy-1-thio-D-xylo-*hexitol* (**16**).—To a stirred soln of **14** (2.5 g, 17.3 mmol) in EtOH (85 mL), $NaBH_4$ (2.4 g, 63.5 mmol) was added at rt and stirring was continued for 30 min. The mixture was neutralised with 4% aq HCl, concd and toluene (50 mL) was evaporated from the residue. The resulting residue was acetylated in a mixture of pyridine (20 mL) and Ac_2O (10 mL) to give, after the usual processing and column chromatography (solvent D), **16** (2.88 g, 88%): mp 87–88 °C (acetone); $[\alpha]_D$ +5° (*c* 0.5, $CHCl_3$); R_f 0.4 (solvent D). Anal. Calcd for $C_8H_{12}O_3S$: C, 51.04; H, 6.43; S, 17.03. Found: C, 51.07; H, 6.46; S, 17.08

*1,6:2,5-Dianhydro-4-deoxy-3-*O*-methyl-1-thio-*D*-xylo-hexitol* (**17**).—To a stirred soln of **16** (3.3 g, 17.5 mmol) in MeOH (50 mL), 1 M NaOMe (0.1 mL) in MeOH was added at rt and stirring was continued for 1 h. The mixture was neutralised with solid CO_2, concd and toluene (25 mL) was evaporated from the residue. The residue was dissolved in dry DMF (25 mL) and 80% NaH (0.65 g, 21.7 mmol) in oil was added. After stirring at rt for 30 min, MeI (1.5 mL, 24 mmol) was added and stirring was continued for 1 h. The mixture was poured into ice-water, extracted with CH_2Cl_2, concd and the residue was submitted to column chromatography (solvent B) to give **17** (1.91 g, 68%) as an oil: $[\alpha]_D$ +46° (*c* 0.5, $CHCl_3$); R_f 0.7 (solvent B). Anal. Calcd for $C_7H_{12}O_2S$: C, 52.47; H, 7.55; S, 20.01. Found: C, 52.44; H, 7.53; S, 19.98.

*3-*O*-Acetyl-1,6:2,5-dianhydro-4-deoxy-1-thio-*D*-xylo-hexitol* S-*oxide* (**20**).—To a stirred soln of **16** (2.88 g, 15.3 mmol) in AcOH (45 mL) 33% aq H_2O_2 (2.2 mL) was added and the mixture was kept overnight at rt. The reaction was concd and EtOH (50 mL) was evaporated from the residue to give, after crystallisation with ether, **20** (2.62 g, 84%): mp 139–143 °C (ether); $[\alpha]_D$ −7° (*c* 0.5, $CHCl_3$); R_f 0.3 (solvent A). Anal. Calcd for $C_8H_{12}O_4S$: C, 47.05; H, 5.92; S, 15.70. Found: C, 47.09; H, 5.98; S, 15.67.

*1,6:2,5-Dianhydro-4-deoxy-3-*O*-methyl-1-thio-*D*-xylo-hexitol* S-*oxide* (**21**).—Oxidation of **17** (1.55 g, 9.67 mmol) was carried out as described for **20** to give **21** (1.70 g, 100%) as an oil: $[\alpha]_D$ +12°; R_f 0.2 (solvent A). Anal. Calcd for $C_8H_{12}O_4S$: C, 47.71; H, 6.86; S, 18.19. Found: C, 47.69; H, 6.88; S, 18.22.

*1,4-Di-*O*-acetyl-2,5-anhydro-3-deoxy-6-thio-α-L-xylo-hexoseptanose* (**22**) *and 1,3-di-*O*-acetyl-2,5-anhydro-4-deoxy-6-thio-α-*D*-xylo-hexoseptanose* (**24**).—A soln of **20** (2.2 g, 10.77 mmol) in Ac_2O (22 mL) was stirred at 80 °C for 15 h. The mixture was concd and toluene (30 mL) was evaporated from the residue. The resulting residue was submitted to column chromatography (solvent C). Concentration of the first fraction gave **22** (60 mg, 2%) as an oil: $[\alpha]_D$ +22° (*c* 0.5, $CHCl_3$); R_f 0.5 (solvent C). Anal. Calcd for $C_{10}H_{14}O_5S$: C, 48.77; H, 5.73; S, 13.02. Found: C, 48.81; H, 5.68; S, 13.07.

Concentration of the second fraction gave **24** (1.88 g, 71%) as an oil: $[\alpha]_D$ +261°; R_f 0.4 (solvent C). Anal. Calcd for $C_{10}H_{14}O_5S$: C, 48.77; H, 5.73; S, 13.02. Found: C, 48.75; H, 5.69; S, 13.06.

*1-*O*-Acetyl-2,5-anhydro-3-deoxy-4-*O*-methyl-6-thio-α-L-xylo-hexoseptanose* (**23**), *1-*O*-acetyl-2,5-anhydro-4-deoxy-3-*O*-methyl-6-thio-α-*D*-xylo-hexoseptanose* (**25**), *1*-O*-acetyl-2,6-anhydro-4-deoxy-3-*O*-methyl-6-thio-*D*-lyxo-hexopyranose* (**35**) *and ethyl 2,6-anhydro-4-deoxy-3-*O*-methyl-6-thio-α-*D*-lyxo-hexopyranoside* (**36α**).—A soln of **21** (1.7 g, 9.6 mmol) in Ac_2O (20 mL) was stirred at 100 °C for 5 h. The mixture was concd and EtOH (30 mL) was evaporated from the residue. The resulting residue was submitted to column chromatography (solvent C). Concentration of the first fraction gave **36α** (100 mg, 5%) as an oil: $[\alpha]_D$ +17° (*c* 0.5, $CHCl_3$); R_f 0.8 (solvent C). Anal. Calcd for $C_9H_{16}O_3S$: C, 52.92; H, 7.89; S, 15.70. Found: C, 52.97; H, 7.85; S, 15.73.

Concentration of the second fraction gave **35** (200 mg, 9.5%) as an oil: $[\alpha]_D$ +23° (*c* 0.5, $CHCl_3$); R_f 0.6 (solvent C). Anal. Calcd for $C_9H_{14}O_4S$: C, 49.53; H, 6.47; S, 14.69. Found: C, 49.56; H, 6.50; S, 14.71.

Concentration of the third fraction gave a 1:4 mixture of **23** and **25** (0.85 g, 40%): $[\alpha]_D$ +227° (*c* 0.5, $CHCl_3$); R_f 0.4 (solvent C). Anal. Calcd for $C_9H_{14}O_4S$: C, 49.53; H, 6.47; S, 14.69. Found: C, 49.51; H, 6.44; S, 14.65.

*4-Cyanophenyl 3-*O*-acetyl-2,5-anhydro-4-deoxy-1,6-dithio-α-*D*-xylo-hexoseptanoside* (**26**).—To a soln of **24** (1.3 g, 5.3 mmol) and 4-cyanobenzenethiol (1.43 g, 10.6 mmol) in dry 1,2-dichloroethane (25 mL) TMSOTf (0.98 mL, 5.3 mmol) under argon, was added at −10 °C. After stirring at rt for 1 h, the reaction was quenched with Et_3N, concd and submitted to column chromatography (solvent C) to give **26** (1.65 g, 97%): mp 139–144 °C (EtOAc–hexane); $[\alpha]_D$ +389°; R_f 0.5 (solvent C). Anal. Calcd for $C_{15}H_{15}NO_3S_2$: C, 56.05; H, 4.70; N, 4.36; S, 19.95. Found: C, 56.09; H, 4.76; N, 4.40; S, 19.91.

*4-Cyanophenyl 2,5-anhydro-4-deoxy-1,6-dithio-α-*D*-xylo-hexoseptanoside* (**27**).—To a soln of **26** (1.65 g, 5.1 mmol) in MeOH (30 mL), 1 M NaOMe (0.1 mL) in MeOH was added and the mixture was stirred at rt for 1

h. After neutralising with solid CO_2 the mixture was concd to give, after column chromatography (solvent B), **27** (1.0 g, 70%): mp 42–44 °C (EtOH–water); $[\alpha]_D$ +519°(*c* 0.5 MeOH); R_f 0.4 (solvent B). Anal. Calcd for $C_{13}H_{13}NO_2S_2$: C, 55.89; H, 4.69; N, 5.01; S, 22.95. Found: C, 55.85; H, 4.73; N, 5.05; S, 22.91.

4-Nitrophenyl 3-O-acetyl-2,5-anhydro-4-deoxy-1,6-dithio-α-D-xylo-hexoseptanoside (**28**).—To a stirred soln of **24** (1.3 g, 5.3 mmol) and 4-nitrobenzenethiol (80% pure, 1.08 g, 5.5 mmol) in dry 1,2-dichloroethane (25 mL), $BF_3{\cdot}Et_2O$ (0.65 mL, 5.4 mmol) was added. After stirring at rt for 3 h, the mixture was poured into ice-cold 6% aq $NaHCO_3$ soln (50 mL), separated and the organic layer was washed with 6% aq $NaHCO_3$, water, concd and submitted to column chromatography (solvent C) to give **28** (1.8 g, 100%) as an oil: $[\alpha]_D$ +398°; R_f 0.5 (solvent C). Anal. Calcd for $C_{14}H_{15}NO_5S_2$: C, 49.25; H, 4.43; N, 4.10; S, 18.78. Found: C, 49.28; H, 4.46; N, 4.07; S, 18.81.

4-Nitrophenyl 2,5-anhydro-4-deoxy-1,6-dithio-α-D-xylo-hexoseptanoside (**29**).—To a soln of **28** (1.8 g, 5.3 mmol) in MeOH (50 mL), 1 M NaOMe (0.1 mL) in MeOH was added and the mixture was stirred at rt overnight. After neutralising with solid CO_2 the mixture was concd to give, after column chromatography (solvent B), **29** (1.3 g, 82%) as an oil: $[\alpha]_D$ +421°(*c* 0.5 MeOH); R_f 0.4 (solvent B). Anal. Calcd for $C_{12}H_{13}NO_4S_2$: C, 48.15; H, 4.38; N, 4.68; S, 21.42. Found: C, 48.18; H, 4.33; N, 4.65; S, 21.39.

4-Cyanophenyl 2,5-anhydro-4-deoxy-3-O-methyl-1,6-dithio-α-D-xylo-hexoseptanoside (**30**).—To a soln of **27** (0.9 g, 3.2 mmol) in DMF (10 mL), 50% NaH (0.2 g, 4.2 mmol) in oil was added and the mixture was stirred at rt for 30 min, then MeI (1.5 mL, 24 mmol) was added and the reaction was stirred at rt overnight. The mixture was poured into ice-water, extracted with EtOAc, concd and the residue was submitted to column chromatography (solvent B) to give **30** (0.66 g, 70%): mp 175–183 °C (ether); $[\alpha]_D$ +560°(*c* 0.5 $CHCl_3$); R_f 0.8 (solvent B). Anal. Calcd for $C_{14}H_{15}NO_2S_2$: C, 57.31; H, 5.15; N, 4.77; S, 21.86. Found: C, 57.34; H, 5.19; N, 4.81; S, 21.90.

4-Nitrophenyl 2,5-anhydro-4-deoxy-3-O-methyl-1,6-dithio-α-D-xylo-hexoseptanoside (**31**).—To a soln of **27** (1.3 g, 4.34 mmol) in DMF (15 mL) 50% NaH (0.25 g, 5.2 mmol) in oil was added and the mixture was stirred at rt for 30 min, then MeI (1.5 mL, 24 mmol) was added and the reaction was stirred at rt overnight. The mixture was poured into ice-water, extracted with EtOAc, concd and the residue was submitted to column chromatography (solvent B) to give **31** (0.96 g, 70%): mp 91–93 °C (ether); $[\alpha]_D$ +611°(*c* 0.5 $CHCl_3$); R_f 0.8 (solvent B). Anal. Calcd for $C_{13}H_{15}NO_4S_2$: C, 49.82; H, 4.82; N, 4.47; S, 20.46. Found: C, 49.80; H, 4.86; N, 4.51; S, 20.42.

4-Cyanophenyl 3-S-(4-cyanophenyl)-2,6-thioanhydro-4-deoxy-2,3-dithio-β-D-arabino-hexopyranoside (**38**).—(i) Glycosidation of 4-cyanobenzenethiol with a 1:4 mixture of **23** and **25** (0.42 g, 1.92 mmol) was carried out as described for **26** to give, after column chromatography (solvent C), **38** (0.2 g, 26%): mp 130–133 °C (ether); $[\alpha]_D$ +318° (*c* 0.5, $CHCl_3$); R_f 0.5 (solvent C). Anal. Calcd for $C_{20}H_{16}N_2OS_3$: C, 60.58; H, 4.07; N, 7.06; S, 24.26. Found: C, 60.55; H, 4.06; N, 7.03; S, 24.22.

(ii) To a soln of **35** (0.17 g, 0.78 mmol) and 4-cyanobenzenethiol (0.25 g, 1.85 mmol) in dry 1,2-dichloroethane (10 mL) under argon, TMSOTf (0.15 mL, 0.75 mmol) was added at 0 °C. After stirring at 0 °C for 30 min, the reaction was quenched with Et_3N, concd and submitted to column chromatography (solvent C) to give **38** (0.3 g, 97%), identical to the compound described above.

3-O-Acetyl-1,6:2,5-dianhydro-4-O-methyl-1-thio-D-glucitol (**39**).—Acetylation of **11** (2.2 g, 12.5 mmol) with Ac_2O (5 mL) in pyridine (10 mL) gave, after the usual processing, **39** (2.67 g, 98%): mp 79–80 °C (ether–hexane); lit. 80–82 °C [16]; R_f 0.7 (solvent C).

3-O-Acetyl-1,6:2,5-dianhydro-4-O-methyl-1-thio-D-glucitol S-oxide (**40**).—Oxidation of **39** (2.67 g, 12.2 mmol) was carried out as described for **20** to give **40** (2.46 g, 86%): mp 153–157 °C (ether); $[\alpha]_D$ −46° (*c* 0.5 $CHCl_3$); R_f 0.3 (solvent A). Anal. Calcd for $C_9H_{14}O_5S$: C, 46.14; H, 6.02; S, 13.69. Found: C, 46.18; H, 6.07; S, 13.71.

1,4-Di-O-acetyl-2,5-anhydro-3-O-methyl-6-thio-α-L-guloseptanose (**41**) *and 1,3-di-O-*

acetyl-2,5-anhydro-4-O-*methyl-6-thio-α*-D-*glucoseptanose* (**42**).—A soln of **40** (2.46 g, 10.5 mmol) in Ac_2O (25 mL) was stirred at 100 °C for 10 h. The mixture was concd and toluene (30 mL) was evaporated from the residue. The resulting residue was submitted to column chromatography (solvent C). Concentration of the first fraction gave **41** (220 mg, 7.5%) as an oil: $[\alpha]_D$ −30° (*c* 0.3, $CHCl_3$); R_f 0.55 (solvent C). Anal. Calcd for $C_{11}H_{16}O_6S$: C, 47.82; H, 5.84; S, 11.60. Found: C, 47.81; H, 5.88; S, 11.57.

Concentration of the second fraction gave **42** (2.45 g, 84%) as an oil: $[\alpha]_D$ +186° (*c* 0.5, $CHCl_3$); R_f 0.5 (solvent C). Anal. Calcd for $C_{11}H_{16}O_6S$: C, 47.82; H, 5.84; S, 11.60. Found: C, 47.84; H, 5.81; S, 11.63.

4-Cyanophenyl 4-O-*acetyl-2,5-anhydro-3*-O-*methyl-1,6-dithio-α-*L-*guloseptanoside* (**43**).—Glycosidation of 4-cyanobenzenethiol with **41** (170 mg, 0.6 mmol) was carried out as described for **26** to give, after column chromatography (solvent C), **43** (190 mg, 88%) as an oil: $[\alpha]_D$ −483° (*c* 0.36, $CHCl_3$); R_f 0.5 (solvent C). Anal. Calcd for $C_{16}H_{17}NO_4S_2$: C, 54.68; H, 4.88; N, 3.99; S, 18.25. Found: C, 54.71; H, 4.86; N, 4.03; S, 18.21.

4-Cyanophenyl 2,5-anhydro-3-O-*methyl-1,6-dithio-α-*L-*guloseptanoside* (**44**).—Deacetylation of **43** (190 mg, 0.54 mmol) was performed as described for **27** to give, after column chromatography (solvent E), **44** (130 mg, 78%): mp 166–168 °C (ether); $[\alpha]_D$ −536°(*c* 0.3 acetone); R_f 0.4 (solvent E). Anal. Calcd for $C_{14}H_{15}NO_3S_2$: C, 54.35; H, 4.89; N, 4.53; S, 20.73. Found: C, 54.33; H, 4.83; N, 4.55; S, 20.71.

4-Cyanophenyl 3-O-*acetyl-2,5-anhydro-4*-O-*methyl-1,6-dithio-α*-D-*glucoseptanoside* (**45**).—Glycosidation of 4-cyanobenzenethiol with **42** (1.2 g, 4.3 mmol) was carried out as described for **26** to give, after column chromatography (solvent C), **45** (1.21 g, 79%) as an oil: $[\alpha]_D$ +364° (*c* 0.5, $CHCl_3$); R_f 0.55 (solvent C). Anal. Calcd for $C_{16}H_{17}NO_4S_2$: C, 54.68; H, 4.88; N, 3.99; S, 18.25. Found: C, 54.65; H, 4.82; N, 4.01; S, 18.22.

4-Cyanophenyl 2,5-anhydro-4-O-*methyl-1,6-dithio-α*-D-*glucoseptanoside* (**46**).—Deacetylation of **45** (1.21 g, 3.4 mmol) was performed as described for **27** to give, after column chromatography (solvent F), **44** (0.9 g, 84%): mp 140–141 °C (ether); $[\alpha]_D$ +522°(*c* 0.5 MeOH); R_f 0.4 (solvent F). Anal. Calcd for $C_{14}H_{15}NO_3S_2$: C, 54.35; H, 4.89; N, 4.53; S, 20.73. Found: C, 54.31; H, 4.84; N, 4.50; S, 20.76.

4-Nitrophenyl 3-O-*acetyl-2,5-anhydro-4*-O-*methyl-1,6-dithio-α*-D-*glucoseptanoside* (**47**).—Glycosidation of 4-nitrobenzenethiol with **42** (1.2 g, 4.3 mmol) was carried out as described for **28** to give, after column chromatography (solvent C), **47** (1.6 g, 99%) as an oil: $[\alpha]_D$ +398° (*c* 0.5, $CHCl_3$); R_f 0.55 (solvent C). Anal. Calcd for $C_{15}H_{17}NO_6S_2$: C, 48.51; H, 4.61; N, 3.77; S, 17.26. Found: C, 48.54; H, 4.62; N, 3.80; S, 17.22.

4-Nitrophenyl 2,5-anhydro-4-O-*methyl-1,6-dithio-α*-D-*glucoseptanoside* (**48**).—Deacetylation of **47** (1.6 g, 4.3 mmol) was performed as described for **27** to give, after column chromatography (solvent F), **44** (1.0 g, 70%): mp 145–147 °C (ether); $[\alpha]_D$ +570° (*c* 0.5 MeOH); R_f 0.4 (solvent F). Anal. Calcd for $C_{13}H_{15}NO_5S_2$: C, 47.40; H, 4.59; N, 4.25; S, 19.47. Found: C, 47.44; H, 4.54; N, 4.20; S, 19.46.

6-S-*Acetyl-2,5-anhydro-3,4-di*-O-*methyl-6-thio*-D-*glucitol* (**50**).—A soln of **49** (5.1 g, 20 mmol) [7] and potassium thioacetate (2.74 g, 24 mmol) in DMF (25 mL) was stirred at 100 °C for 1 h. The residue obtained on concentration was dissolved in CH_2Cl_2 (50 mL), washed with water, dried and concd to give, after column chromatography (solvent B), **50** (4.35 g, 87%): $[\alpha]_D$ +68°; R_f 0.4 (solvent B). Anal. Calcd for $C_{10}H_{18}O_5S$: C, 47.98; H, 7.25; S, 12.81. Found: C, 47.82; H, 7.30; S, 12.66.

6-S-*Acetyl-2,5-anhydro-1*-O-*methanesulfonyl-3,4-di*-O-*methyl-6-thio*-D-*glucitol* (**51**).—To a stirred soln of **50** (3.25 g, 13 mmol) in pyridine (15 mL) mesyl chloride (1.23 mL, 15.6 mmol) was added at 0 °C. After 30 min the mixture was processed the usual way to give on concentration **51** (4.18 g, 98%) as syrup, $[\alpha]_D$ +49°; R_f 0.6 (solvent B). Anal. Calcd for $C_{11}H_{20}O_7S_2$: C, 40.23; H, 6.14; S, 19.53. Found: C, 40.11; H, 6.22; S, 19.44.

1,6:2,5-Dianhydro-3,4-di-O-*methyl-1-thio*-D-*glucitol* (**52**).—To a stirred soln of **51** (16.4 g, 50 mmol) in dioxane (160 mL), 4.5 M

methanolic NaOMe (12.2 mL, 55 mmol) was added and the slurry was heated on a steam bath for 2 h. The cooled mixture was diluted with water (300 mL) and extracted with CH_2Cl_2. The organic soln was washed with water, dried, concd, and the residue distilled at 26.6 Pa to give **52** as colourless liquid (7 g, 78%), $bp_{0.2}$ 75–80 °C; $[\alpha]_D$ +5°; R_f 0.8 (solvent B). Anal. Calcd for $C_8H_{14}O_3S$: C, 50.50; H, 7.42; S, 16.85. Found: C, 50.48; H, 7.38; S, 12.82.

1,6:2,5-Dianhydro-3,4-di-O-*methyl-1-thio*-D-*glucitol* S-*oxide* (**53**).—Oxidation of **52** (1.0 g, 5.25 mmol) was carried out as described for **20** to give **53** (0.92 g, 85%): mp 81–83 °C (ether); $[\alpha]_D$ −21° (*c* 0.5, acetone); R_f 0.2 (solvent A). Anal. Calcd for $C_8H_{14}O_4S$: C, 46.59; H, 6.84; S, 15.55. Found: C, 46.63; H, 6.88; S, 15.57.

4-Cyanophenyl 2,5-anhydro-3,4-di-O-*methyl-1,6-dithio*-α-D-*glucoseptanoside* (**55**).—Glycosidation of 4-cyanobenzenethiol with a 9:1 mixture of **59** and **61** (0.6 g, 2.4 mmol) was carried out as described for **26** to give, after column chromatography (solvent C), **55** (0.7 g, 90%) as an oil: $[\alpha]_D$ +440° (*c* 0.5, $CHCl_3$); R_f 0.5 (solvent C). Anal. Calcd for $C_{15}H_{17}NO_3S_2$: C, 55.70; H, 5.30; N, 4.33; S, 19.83. Found: C, 55.74; H, 5.27; N, 4.30; S, 19.82.

4-Nitrophenyl 2,5-anhydro-3,4-di-O-*methyl-1,6-dithio*-α-D-*glucoseptanoside* (**56**).—Glycosidation of 4-nitrobenzenethiol with a 9:1 mixture of **59** and **61** (0.6 g, 2.4 mmol) was carried out as described for **28** to give, after column chromatography (solvent C), **56** (0.73 g, 88%) as an oil: $[\alpha]_D$ +378° (*c* 0.5, $CHCl_3$); R_f 0.5 (solvent C). Anal. Calcd for $C_{14}H_{17}NO_5S_2$: C, 48.96; H, 4.99; N, 4.08; S, 18.67. Found: C, 48.98; H, 4.96; N, 4.07; S, 18.71.

4-Cyanophenyl 2,5-anhydro-3,4-di-O-*methanesulfonyl-1,6-dithio*-α-D-*glucoseptanoside* (**57**).—Glycosidation of 4-cyanobenzenethiol with **60** [9] (0.5 g, 1.33 mmol) was carried out as described for **26** to give, after column chromatography (solvent B, then A), **57** (0.53 g, 88%): mp 157–163 °C (ether); $[\alpha]_D$ +216° (*c* 0.5, $CHCl_3$); R_f 0.6 (solvent B). Anal. Calcd for $C_{15}H_{17}NO_7S_4$: C, 39.90; H, 3.79; N, 3.10; S, 28.40. Found: C, 39.88; H, 3.83; N, 3.12; S, 28.44.

4-Nitrophenyl 2,5-anhydro-3,4-di-O-*methanesulfonyl-1,6-dithio*-α-D-*glucoseptanoside* (**58**).—Glycosidation of 4-nitrobenzenethiol with **60** (0.5 g, 1.33 mmol) was carried out as described for **28** to give **58** (0.58 g, 93%): mp 117–123 °C (ether); $[\alpha]_D$ +250° (*c* 0.5, $CHCl_3$); R_f 0.6 (solvent B). Anal. Calcd for $C_{14}H_{17}NO_9S_4$: C, 35.66; H, 3.63; N, 2.97; S, 27.20. Found: C, 35.62; H, 3.66; N, 2.95; S, 27.17.

1-O-*Acetyl-2,5-anhydro-3,4-di*-O-*methyl-6-thio*-α-D-*glucoseptanose* (**59**) *and 1*-O-*acetyl-2,5-anhydro-3,4-di*-O-*methyl-6-thio*-α-L-*gulose ptanose* (**61**).—A soln of **53** (3.3 g, 16 mmol) in Ac_2O (35 mL) was stirred at 100 °C for 5 h. The mixture was concd and toluene (30 mL) was evaporated from the residue to give, after column chromatography (solvent C), a 9:1 mixture of **59** and **61** (2.66 g, 67%) as an oil: $[\alpha]_D$ +180° (*c* 0.5, $CHCl_3$); R_f 0.4 (solvent C). Anal. Calcd for $C_{10}H_{16}O_5S$: C, 48.37; H, 6.50; S, 12.91. Found: C, 48.41; H, 6.53; S, 12.96.

1,6:2,5-Dianhydro-4-azido-4-deoxy-3-O-*tetrahydropyranyl-1-thio*-D-*glucitol* (**64**).—To a soln of **63** [1] (5.4 g, 16.6 mmol) in DMF (55 mL) NaN_3 (2.5 g, 38.5 mmol) was added and the mixture was stirred at 110 °C for 1 h. After cooling to rt the reaction was poured into ice-water, extracted with ether and concd to give **64** (4.5 g, 100%) as an oil: R_f 0.8 (solvent C). Anal. Calcd for $C_{11}H_{17}N_3O_3S$: C, 48.69; H, 6.32; N, 15.49; S, 11.82. Found: C, 48.71; H, 6.33; N, 15.52; S, 11.86.

3-O-*Acetyl-1,6:2,5-dianhydro-4-azido-4-deoxy-1-thio*-D-*glucitol* (**66**).—To a soln of **64** (4.27 g, 15.7 mmol) in MeOH (65 mL) Dowex 50WX ion exchange resin (1.5 g) was added and the mixture was stirred at rt for 24 h. Then the resin was filtered off, washed with MeOH and the filtrate was concd. The residue was acetylated with Ac_2O (5 mL) in pyridine (10 mL) to give, after the usual processing, **66** (2.96 g, 82%): mp 40–46 °C (hexane); $[\alpha]_D$ +39.5° (*c* 0.5, $CHCl_3$); R_f 0.8 (solvent C). Anal. Calcd for $C_8H_{11}N_3O_3S$: C, 41.91; H, 4.84; N, 18.33; S, 13.99. Found: C, 41.94; H, 4.80; N, 18.37; S, 13.95.

3-O-*Acetyl-1,6:2,5-dianhydro-4-azido-4-deoxy-1-thio*-D-*glucitol* S-*oxide* (**68**).—Oxidation of **66** (2.2 g, 9.6 mmol) was carried out as described for **20** to give **68** (2.1 g, 89%): mp

98–105 °C (ether); $[\alpha]_D$ +9° (*c* 0.5, acetone); R_f 0.4 (solvent A). Anal. Calcd for $C_8H_{11}N_3O_4S$: C, 39.18; H, 4.52; N, 17.13; S, 13.07. Found: C, 39.20; H, 4.57; N, 17.15; S, 13.09.

*1,6:2,5-Dianhydro-4-azido-4-deoxy-3-*O*-methanesulfonyl-1-thio-*D*-glucitol* S-*oxide* (**69**).—Oxidation of **67** [3] (2.5 g, 9.4 mmol) was carried out as described for **20** to give **69** (2.5 g, 94%): mp 133–138 °C (ether); $[\alpha]_D$ +3° (*c* 0.5, acetone); R_f 0.3 (solvent A). Anal. Calcd for $C_7H_{11}N_3O_5S_2$: C, 29.89; H, 3.94; N, 14.94; S, 22.80. Found: C, 29.91; H, 3.92; N, 14.97; S, 22.77.

*1,4-Di-*O*-acetyl-2,5-anhydro-3-azido-3-deoxy-6-thio-α-*L*-guloseptanose* (**70**) *and 1,3-di-*O*-acetyl-2,5-anhydro-4-azido-4-deoxy-6-thio-α-*D*-glucoseptanose* (**72**).—A soln of **68** (2.1 g, 7.3 mmol) in Ac_2O (20 mL) was stirred at 100 °C for 5 h. The mixture was concd and toluene (30 mL) was evaporated from the residue to give, after column chromatography (solvent C), a 1:4 mixture of **70** and **72** (1.7 g, 81%) as an oil: R_f 0.5 (solvent C). Anal. Calcd for $C_{10}H_{13}N_3O_5S$: C, 41.81; H, 4.56; N, 14.63; S, 11.16. Found: C, 41.85; H, 4.53; N, 14.66; S, 11.20.

*1-*O*-Acetyl-2,5-anhydro-3-azido-3-deoxy-4-*O*-methanesulfonyl-6-thio-α-*L*-guloseptanose* (**71**) *and 1-*O*-acetyl-2,5-anhydro-4-azido-4-deoxy-3-*O*-methanesulfonyl-6-thio-α-*D*-glucoseptanose* (**73**).—A soln of **69** (2.5 g, 8.9 mmol) in Ac_2O (25 mL) was stirred at 100 °C for 5 h. The mixture was concd and toluene (30 mL) was evaporated from the residue. The resulting residue was submitted to column chromatography (solvent C). Concentration of the first fraction gave **71** (150 mg, 5%) as an oil: $[\alpha]_D$ +14° (*c* 0.5, $CHCl_3$); R_f 0.45 (solvent C). Anal. Calcd for $C_9H_{13}N_3O_6S_2$: C, 33.43; H, 4.05; N, 13.00; S, 19.83. Found: C, 33.46; H, 4.03; N, 13.03; S, 19.87.

Concentration of the second fraction gave **73** (1.5 g, 52%) as an oil: $[\alpha]_D$ +84° (*c* 0.5, $CHCl_3$); R_f 0.4 (solvent C). Anal. Calcd for $C_9H_{13}N_3O_6S_2$: C, 33.43; H, 4.05; N, 13.00; S, 19.83. Found: C, 33.40; H, 4.08; N, 12.98; S, 19.80.

*4-Cyanophenyl 3-*O*-acetyl-4-azido-4-deoxy-2,5-anhydro-1,6-dithio-α-*D*-glucoseptanoside* (**75**).—Glycosidation of 4-cyanobenzenethiol with a 1:4 mixture of **70** and **72** (0.5 g, 1.74 mmol) was carried out as described for **26** to give, after column chromatography (solvent D), **75** (0.45 g, 71%) as an oil: $[\alpha]_D$ +403° (*c* 0.5, $CHCl_3$); R_f 0.7 (solvent C). Anal. Calcd for $C_{15}H_{14}N_4O_3S_2$: C, 49.71; H, 3.89; N, 15.46; S, 17.69. Found: C, 49.75; H, 3.84; N, 15.42; S, 17.72.

*4-Cyanophenyl 4-azido-4-deoxy-2,5-anhydro-1,6-dithio-α-*D*-glucoseptanoside* (**76**).—Deacetylation of **75** (0.45 g, 1.2 mmol) was performed as described for **27** to give, after column chromatography (solvent C), **76** (0.36 g, 90%) as an oil: $[\alpha]_D$ +456° (*c* 0.5 MeOH); R_f 0.3 (solvent C). Anal. Calcd for $C_{13}H_{12}N_4O_2S_2$: C, 48.74; H, 3.78; N, 17.49; S, 20.02. Found: C, 48.77; H, 3.75; N, 17.52; S, 19.99.

*4-Cyanophenyl 4-azido-4-deoxy-2,5-anhydro-3-*O*-methanesulfonyl-1,6-dithio-α-*D*-glucoseptanoside* (**77**).—Glycosidation of 4-cyanobenzenethiol with **73** (0.7 g, 2.16 mmol) was carried out as described for **26** to give, after column chromatography (solvent EH 1:2), **77** (0.58 g, 67%): mp 94–96 °C (ether); $[\alpha]_D$ +344° (*c* 0.5, $CHCl_3$); R_f 0.6 (solvent C). Anal. Calcd for $C_{14}H_{14}N_4O_4S_3$: C, 42.20; H, 3.54; N, 14.06; S, 24.14. Found: C, 42.22; H, 3.51; N, 14.02; S, 24.17.

*4-Nitrophenyl 4-*O*-acetyl-3-azido-3-deoxy-2,5-anhydro-1,6-dithio-α-*L*-guloseptanoside* (**74**) *and 4-nitrophenyl 3-*O*-acetyl-4-azido-4-deoxy-2,5-anhydro-1,6-dithio-α-*D*-glucoseptanoside* (**78**).—Glycosidation of 4-nitrobenzenethiol with a 1:4 mixture of **70** and **72** (0.62 g, 2.16 mmol) was carried out as described for **28** to give, after column chromatography (solvent D), **78** (0.4 g, 48%) as an oil: $[\alpha]_D$ +394° (*c* 0.5, $CHCl_3$); R_f 0.7 (solvent C). Anal. Calcd for $C_{14}H_{14}N_4O_5S_2$: C, 43.97; H, 3.69; N, 14.65; S, 16.77. Found: C, 43.93; H, 3.71; N, 14.69; S, 16.73.

Concentration of the second fraction gave, after crystallisation with hexane, **74** (20 mg, 2%): mp 174–177 °C (hexane); $[\alpha]_D$ −447.5° (*c* 0.4 $CHCl_3$); R_f 0.65 (solvent C). Anal. Calcd for $C_{14}H_{14}N_4O_5S_2$: C, 43.97; H, 3.69; N, 14.65; S, 16.77. Found: C, 43.95; H, 3.66; N, 14.63; S, 16.79.

*4-Nitrophenyl 4-azido-4-deoxy-2,5-anhydro-1,6-dithio-α-*D*-glucoseptanoside* (**79**).—Deacetylation of **78** (0.4 g, 1.04 mmol) was performed as described for **27** to give, after column chromatography (solvent C), **79** (0.34 g, 96%): mp 96–101 °C (hexane); $[\alpha]_D$ +476° (*c* 0.5 MeOH); R_f 0.4 (solvent C). Anal. Calcd for $C_{12}H_{12}N_4O_4S_2$: C, 42.34; H, 3.55; N, 16.46; S, 18.84. Found: C, 42.38; H, 3.54; N, 16.49; S, 18.80.

Glycosidation of 4-nitrobenzenethiol with **73** (0.7 g, 2.16 mmol) was carried out as described for **28** to give, after column chromatography (solvent C), **80** (0.49 g, 54%): mp 77–79 °C (ether); $[\alpha]_D$ +324° (*c* 0.5, $CHCl_3$); R_f 0.6 (solvent C). Anal. Calcd for $C_{13}H_{14}N_4O_6S_3$: C, 37.31; H, 3.37; N, 13.39; S, 22.99. Found: C, 37.28; H, 3.41; N, 13.42; S, 23.02.

4. Supplementary material

Full crystallographic details, excluding structural features, have been deposited with the Cambridge Crystallographic Data Centre (CCDC number for **16**: 146871). These data may be obtained, on request, from: The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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References

[1] É. Bozó, J. Kuszmann, *Carbohydr. Res.*, 325 (2000) 143–149.
[2] F. Bellamy, V. Barberousse, N. Martin, P. Masson, J. Millet, S. Samreth, Ch. Sepulchre, J. Théveniaux, D. Horton, *Eur. J. Med. Chem.*, 30 (1995) 101–115.
[3] J. Kuszmann, P. Sohár, *Carbohydr. Res.*, 27 (1973) 157–168.
[4] J. Kuszmann, P. Sohár, *Carbohydr. Res.*, 35 (1974) 97–102.
[5] É. Bozó, S. Boros, J. Kuszmann, E Gács-Baitz, *Tetrahedron*, 55 (1999) 8095–8102.
[6] J. Kuszmann, P. Sohár, Gy. Horváth, *Tetrahedron*, 27 (1971) 5055–5061.
[7] J. Kuszmann, *Carbohydr. Res.*, 73 (1979) 93–101.
[8] G. Szabó, É. Bozó, É. Barabás, R. Kedves, K. Csomor, J. Kuszmann, *Drugs Future*, 24 (1999) 1241–1248 and references cited therein.
[9] J. Kuszmann, P. Sohár, *Acta Chim. Hung.*, 88 (1976) 167–171.
[10] D. Bagdy, G. Szabó, É. Barabás, S. Bajusz, *Thromb. Haemost.*, 68 (1992) 125–129.
[11] A.C. North, D.C. Philips, F. Mathews, *Acta Crystallogr., Sect. A*, 24 (1968) 350–359.
[12] G.M. Sheldrick, SHELXS-97, Program for Crystal Structure Solution, University of Göttingen, Germany, 1997.
[13] G.M. Sheldrick, SHELXL-97, Program for Crystal Structure Refinement, University of Göttingen, Germany, 1997.
[14] A.J.C. Wilson (Ed.), *International Tables for X-ray Crystallography*, Vol. C, Kluwer Academic, Dordrecht, 1992.
[15] A.L. Spek, *Acta Crystallogr., Sect. A*, 46 (1990) C34.
[16] J. Kuszmann, P. Sohár, *Acta Chim. Hung.*, 83 (1974) 373–379.