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Synthesis of 4-cyano and 4-nitrophenyl 1,6-dithio-D-manno-, L-ido- and D-glucoseptanosides possessing antithrombotic activity☆,☆☆

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Abstract

1,6-Anhydro-3,4-*O*-isopropylidene-1-thio-D-mannitol was converted into its sulfoxide which after hydrolysis, acetylation and subsequent Pummerer rearrangement gave the penta-*O*-acetyl-1-thio-D-mannoseptanose anomers in excellent yield. This anomeric mixture was used as donor for the glycosylation of 4-nitro- and 4-cyanobenzenethiol in the presence of boron trifluoride etherate and trimethylsilyl triflate, respectively, to yield the corresponding thioseptanosides in high yield. The same strategy was applied for the synthesis of the corresponding L-idothioseptanosides using 1,6-anhydro-3,4-*O*-isopropylidene-1-thio-L-iditol as starting material. The penta-*O*-acetyl-D-glucothioseptanose donors could not be synthesised the same way, as the Pummerer reaction of the corresponding tetra-*O*-acetyl-1,6-thioanhydro-1-thio-D-glucitol sulfoxides led to an inseparable mixture of the corresponding L-gulo- and D-glucothioseptanose anomers. Therefore, D-glucose diethyl dithioacetal was converted via its 2,3,4,5-tetra-*O*-acetyl-6-*S*-acetyl derivative into an anomeric mixture of its 6-thio-septanose and -furanose peracetates which could be separated by column chromatography. Condensation of the 6-thio-glucoseptanose peracetates with 4-cyano- and 4-nitrobenezenethiol in the presence of boron trifluoride etherate afforded anomeric mixtures of the corresponding thioseptanosides. The D-manno-, L-ido- and D-glucothioseptanosides obtained after Zemplén deacetylation of these mixtures were tested for their oral antithrombotic activity.

Keywords: 6-Thiosugars; D-manno-, L-ido- and D-glucothioseptanose peracetates; Thioseptanosides; Oral antithrombotic activity

1. Introduction

In our previous papers,[2,3] we showed that 4-substituted phenyl 2,5-anhydro-1,6-dithio-D-glucoseptanosides (**1**) possess oral antithrombotic activity. For our further structure–activity studies, we decided to check the influence of the 2,5-anhydro bridge on the biological activity, i.e., to synthesise the corresponding D-manno- (**2**), L-ido- (**3**), and D-gluco-6-thioseptanosides (**4**) (Scheme 1).

2. Results and discussion

Synthesis of the D-*mannoseptanosides*.—For the synthesis of the required donor molecule, 1,6-anhydro-3,4-*O*-isopropylidene-1-thio-D-mannitol (**5**)[4] was chosen as starting material the isopropylidene group of which was hydrolysed with aqueous trifluoroacetic acid (Scheme 2). Acetylation of the crude product resulted, however, in a relatively low yield (30%) of an inseparable mixture containing the needed tetra-*O*-acetate **8** and its ring-contracted 2,6-anhydro-D-glucitol isomer **6** in a 1:1 ratio. The latter is formed during hydrolysis via a transannular attack of the sulfur atom on the C-2(5) carbon atom§ and subsequent hydrolysis of the formed episulfonium intermediate.[4,5] The mixture of the tetra-

☆ Orally active antithrombotic thioglycosides, Part XV. For Part XIV, see Ref. 1.

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§ Because of the C_2 symmetry of the molecule, C-2 and C-5 are equivalent, consequently attack of the sulfur atom on either of them will lead to the same isomer.

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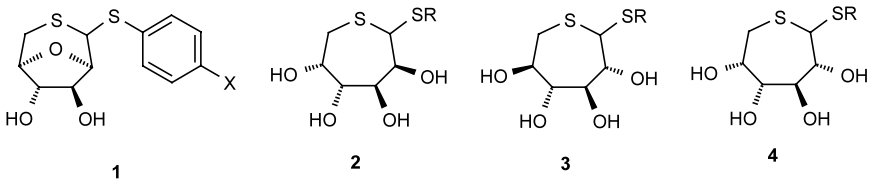
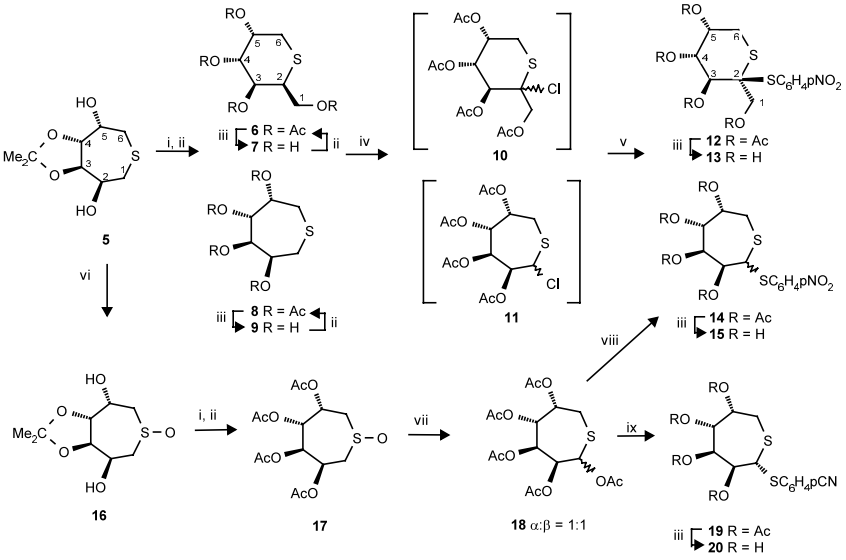


Scheme 1.

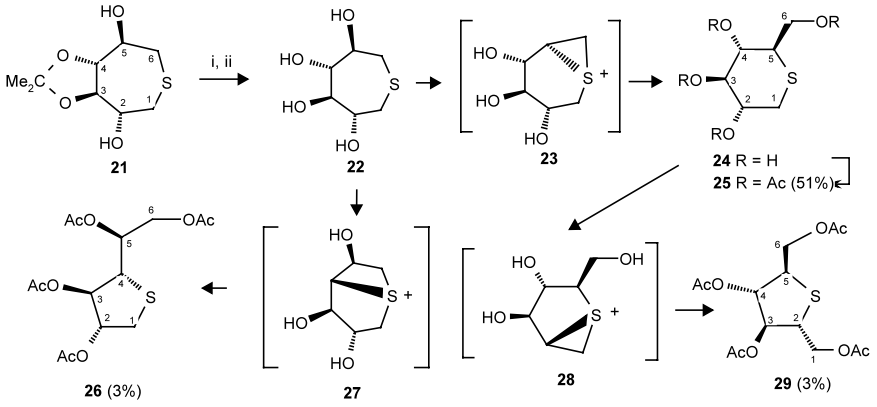


Scheme 2. (i) TFA/H_2O. (ii) Ac_2O/Py. (iii) NaOMe/MeOH. (iv) NCS. (v) $HSC_6H_4pNO_2$/ZnO. (vi) $NaIO_4$. (vii) Ac_2O. (viii) $HSC_6H_4pNO_2/BF_3{\cdot}Et_2O$. (ix) HSC_6H_4pCN/TMSOTf.

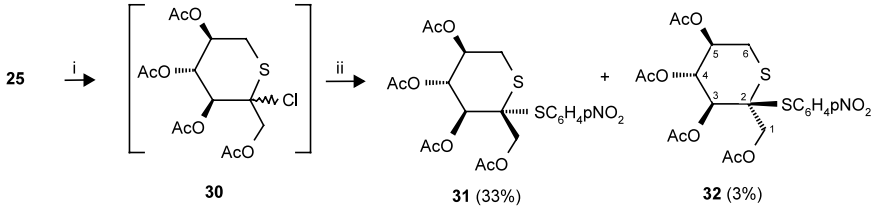
acetates **6** and **8** was deacetylated, but from the resulting mixture of the tetrahydroxy compounds **7** and **9** only the latter could be partially separated. Reacetylation of **9** afforded **8**. Treatment of a mixture of the tetraacetates **6** and **8** with *N*-chlorosuccinimide in toluene[2] afforded the corresponding chlorides **10** and **11**, which gave **13** and **15** on treatment with 4-nitrobenzenethiol in the presence of zinc oxide and subsequent Zemplén deacetylation of the intermediate derivatives **12** and **14** in a yield of 12.5 and 6%, respectively. Although the low yield of **15α** could be increased to 26% using pure **9** as donor, because of this relatively low yield as well as the difficulties in separating the mixtures of **6** and **8**, another approach was tried. For avoiding the ring contraction reaction mentioned above, the thioether **5** was converted into its sulfoxide **16** prior to hydrolysis. Hydrolysis of the *O*-isopropylidene group of **16** and subsequent acetylation afforded the tetraacetate **17** in excellent yield. Pummerer rearrangement of **17** gave a 1:1 mixture of the corresponding α- and β-pentaacetates (**18αβ**) and this was used without separation for the glycosidation of 4-nitrobenzenethiol in the presence of boron trifluoride etherate to give a 95:5 α,β-anomeric mixture of the thioseptanosides **14** in excellent yield (98%). After deacetylation according to Zemplén, the crystalline α anomer **15α** was obtained. When 4-cyanobenzenethiol was used as aglycon and trimethylsilyl triflate as promoter, the corresponding acetylated α-thioglycoside **19** was formed which afforded the thioseptanoside **20** after deacetylation. Both **15α** and **20** were submitted to biological testing.

Synthesis of the L-*idoseptanosides.*—By analogy to the aforementioned synthesis, 1,6-thioanhydro-3,4-*O*-isopropylidene-L-iditol (**21**)[4] was chosen as starting material for the donor molecule (Scheme 3). Hydrolysis of the isopropylidene group with aqueous trifluoroacetic acid and subsequent acetylation led, however, not to **22**, but to a mixture from which the 1,5-thioanhydro-D-glucitol[¶] pentaacetate **25** was isolated as the main component (51%) and the 1,4-thioanhydro-D-altritol[¶] **26** (3%) as well as the 2,5-thioanhydro-D-mannitol pentaacetate **29** as by-products (3%). That means that during hydrolysis, the ring sulfur atom can attack not only C-2(5) by forming an episulfonium intermediate (**23**) but C-3(4) as well, and the more strained four membered ring of the bicyclic sulfonium ion **27** so

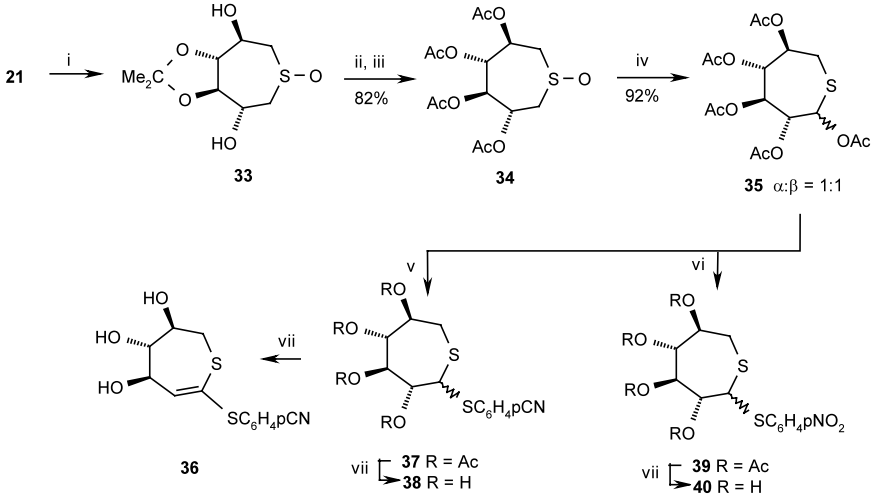
[¶] Due to the C_2 symmetry of the starting material attack of the sulfur atom at C-2 leads to 2,6-thioanhydro-L-gulitol and that at C-3 to 3,6-thioanhydro-L-talitol, but both are equivalent with the mentioned structures **25** and **26**.



Scheme 3. (i) TFA/H_2O. (ii) Ac_2O/Py.



Scheme 4. (i) NCS. (ii) $HSC_6H_4pNO_2$/ZnO.

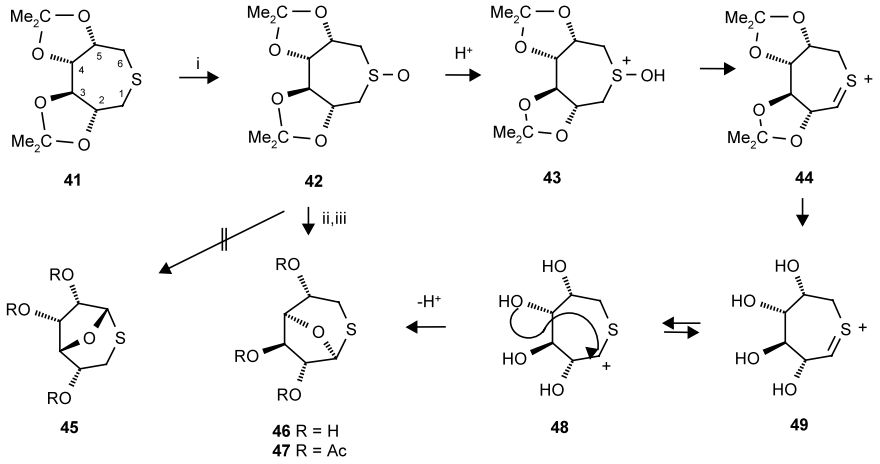


Scheme 5. (i) $NaIO_4$. (ii) TFA/H_2O. (iii) Ac_2O/Py. (iv) Ac_2O. (v) $HSC_6H_4pCN/BF_3{\cdot}Et_2O$. (vi) $HSC_6H_4pNO_2/BF_3{\cdot}Et_2O$. (vii) NaOMe/MeOH.

formed will be opened at the less hindered carbon atom, yielding after acetylation **26**. On the other hand, the tetrahydrothiopyrane ring of **24** can undergo a further ring contraction via the episulfonium ion **28** leading, after acetylation, to **29**. Similar ring-transformation reactions were described for hydroxy containing thiepane derivatives using Mitsunobu conditions.[5]

When the tetraacetate **25** was treated with *N*-chlorosuccinimide in toluene, the resulting anomeric chlorides (**30**) were too unstable to be separated and were therefore converted directly into their thioglycosides using 4-nitrobenzenethiol in the presence of zinc oxide (Scheme 4). Similarly to the aforementioned mannitol derivatives chlorination took place at the tertiary carbon atom, as only the two anomeric 2,6-dithio-L-*xylo*-hex-2-ulopyranosides **31** and **32** were formed and could be separated in yields of 33 and 3%, respectively.

For avoiding the unwanted rearrangement reactions which occurred during the acidic treatment of **21**, the strategy used successfully for the synthesis of the donor **18** was applied, i.e., **21** was converted via its sulfoxide **33** into the tetraacetate **34** the Pummerer rearrangement



Scheme 6. (i) $NaIO_4$. (ii) TFA/H_2O. (iii) Ac_2O/Py.

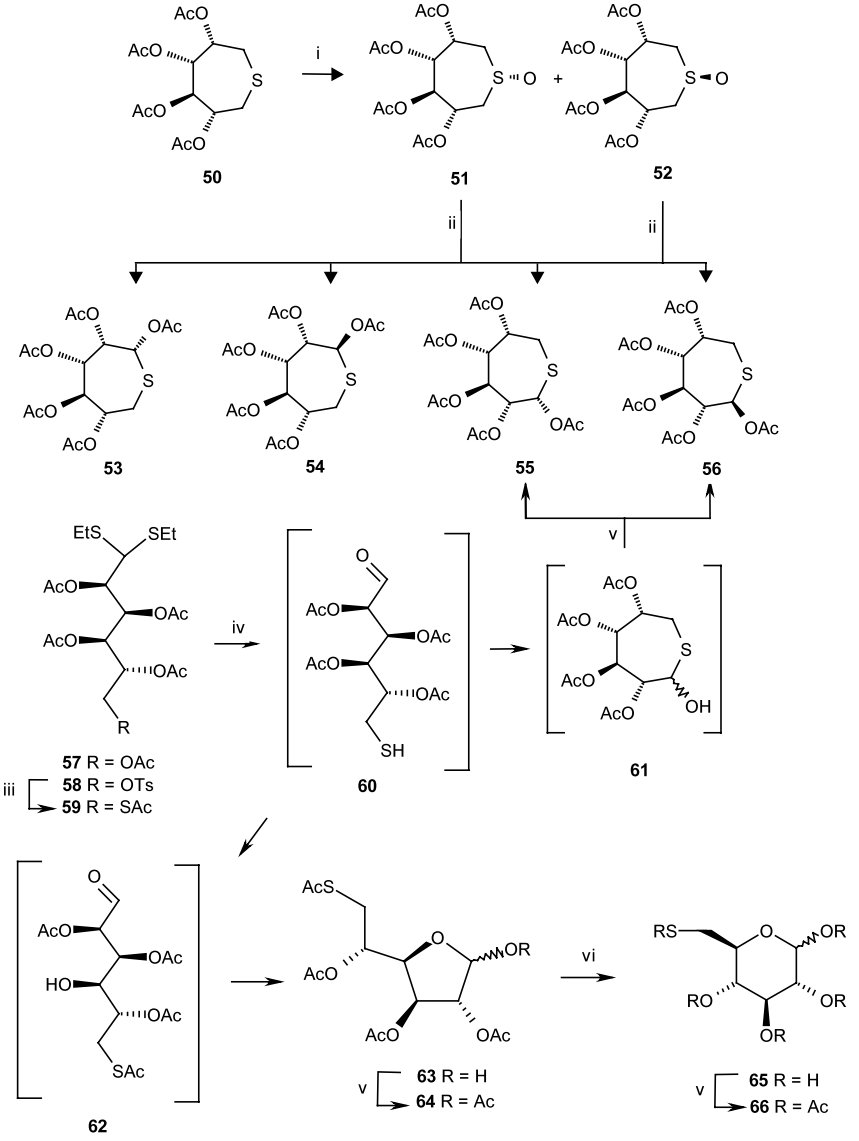
of which afforded a 1:1 anomeric mixture of the corresponding pentaacetates **35** (Scheme 5). This mixture was used without separation for the glycosidation of 4-cyanobenzenethiol in the presence of trimethylsilyl triflate, but the anomeric mixture of the corresponding thioglycosides (**37**) was accompanied by several inseparable by-products. However, when boron trifluoride etherate was applied as promoter, **37** was obtained in satisfactory yield as a 1:1.5 mixture of the α and β anomers which could not be separated even by repeated column chromatography. In an analogous way the condensation of **35** with 4-nitrobenzenethiol afforded **39α** and **39β** in a similar ratio which could be separated by column chromatography. Zemplén deacetylation of the anomeric mixture of **37** afforded an inseparable mixture of **38α** + **38β** and the unsaturated 2-deoxy-1-ene derivative **36** which could be separated as a by-product. They were submitted to biological testing together with the 4-nitrobenzene anomers **40α** and **40β**, obtained on Zemplén deacetylation of **39α** and **39β**, respectively.

Synthesis of the D-*glucoseptanosides.*—For the synthesis of these thioglycosides di-*O*-isopropylidene-1,6-thioanhydro-D-glucitol **41**[6] was chosen as starting material, but for avoiding any rearrangement during hydrolysis of the isopropylidene groups, the compound was converted with sodium periodate into its sulfoxide **42** (Scheme 6). The two diastereomers, differing in the chirality of the sulfoxide group, i.e., the (*S*)-*S*-oxide **42α** and the (*R*)-*S*-oxide **42β** could be separated, and their stereochemistry was established by NMR, as according to the literature[7–10] an axial sulfoxide is associated with a larger geminal coupling constant of the α-methylene protons as compared to an equatorial one. Moreover, the significant deshielding of the protons that are in a syn–axial arrangement to an axial sulfoxide can be used to assign the configuration of the S=O centre. The measured larger geminal $^2J_{1a,1b}$ and $^2J_{6a,6b}$ couplings (Table 3), as well as the observed downfield shift of the H-2 and H-5 protons (Table 2) of the β-sulfoxides (the sulfoxide oxygen assumes an axial orientation in the dominant conformation) relative to the α-sulfoxides (oxygen is equatorial) are diagnostic of the sulfoxide configuration. When a mixture of in **42α** and **42β** was treated with aqueous trifluoroacetic acid, an unexpected ring closure reaction took place, as after acetylation only the triacetate of the corresponding 1,4-anhydro-derivative **47** could be isolated.‖ This is most probably formed via protonation of the sulfoxide group (**43**) and subsequent elimination of water. Hydrolysis of the resulting S-C(1) ylide **44** would give **49**, the polarised C-1 atom of which can be attacked by the OH-4 group (**48**) resulting in the overbridged structure **46**. The latter gives on acetylation the isolated triacetate **47**. As the sulfoxide group in **42** is flanked by two methylene groups, theoretically the L-gulofuranose isomer **45** could be formed in an analogous reaction via an S-C(6) ylide, but in **45** all three acetoxy groups would be cis related which is a sterically unfavoured arrangement.

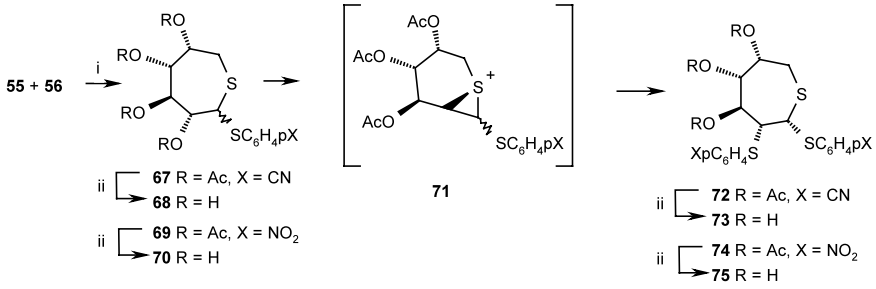
For overcoming the above mentioned difficulties, 1,6-thioanhydro-D-glucitol tetraacetate **50**[11] was used as starting material for the synthesis of the glycosyl donor (Scheme 7). As this molecule does not belong to the C_2 symmetry group, on oxidation with sodium periodate two sulfoxide isomers **51** and **52** were formed, which could be separated by column chromatography. Their structure was assigned by NMR spectroscopy as described for the isomers of **42**. Pummerer rearrangement of both isomers resulted, according to NMR spectroscopy, in a mixture of four compounds: the two L-gulothioseptanose **53** and **54** as well as the two D-glu-

‖ The synthesis of **47** was recently published by Hughes and Todhunter[12] using a different route. This compound can be regarded as a 1,6-anhydro-6-thio-β-D-glucofuranose derivative.

cothioseptanose anomers **55** and **56**, and differed only in their ratio. Attempts to separate these four pentaacetate isomers by column chromatography failed, as only a mixture of the two 1,2-trans-glycosides **54** + **56** could be partly separated from the mixture of the 1,2-cis-glycosides **53** + **55**. For this reason the approach applied by Whistler and Campbell[13] for the synthesis of the analogous 6-thio-D-galactoseptanose acetates was adopted next for the synthesis of the donor D-glucoseptanose pentaacetates **55** + **56**. Accordingly D-glucose diethyl dithioacetal was treated with 1.1 equiv of *p*-toluenesulfonyl chloride in pyridine and subsequently with acetic anhydride, affording a 9:1 mixture of the 6-*O*-tosylate **58** and the pentaacetate **57**, which were separated by column chromatography. Conversion of **58** with potassium thioacetate in acetone afforded the 6-*S*-acetate **59** in ~quantitative yield. Reaction of the latter with mercury oxide/mercury chloride in aqueous acetone and subsequent treatment with hydrogen sulfide in the presence of pyridine led, after acetylation, to a mixture containing according to GLC and NMR spectroscopy, the two anomers of the glucofuranoside **64α** and **64β** as well as the required anomeric mixture of the thioseptanoside acetates **55** + **56** in a ratio of 1:1:2:4. While the former two anomers could not be separated from each other by column chromatography, we succeeded in separating **55** and **56**. Formation of the furanose isomers **64** means that, during the hydrolysis of the mercapto groups of **59**, not only the expected *S*-deacetylation takes place, but the thiol intermediate **60** undergoes a partial acetyl migration, resulting in the 2,3,5,6-tetraacetate **62** which undergoes a cyclisation to the furanose derivative **63** yielding on acetylation **64**. It is worthwhile mentioning that, when all acetyl groups



Scheme 7. (i) $NaIO_4$. (ii) Ac_2O. (iii) KSAc. (iv) $HgCl_2/HgO/H_2O$. (v) Ac_2O/Py. (vi) NaOMe/MeOH.



Scheme 8. (i) HSC_6H_4pX, $BF_3{\cdot}Et_2O$. (ii) NaOMe/MeOH.

Table 1
Oral antithrombotic activity of 4-substituted phenyl 1,6-dithio-hexoseptanosides in rats using Pescador's model[14]

Configuration	D-*gluco*[a]		D-*manno*			L-*ido*			D-*gluco*		
Compound	**1**	**1**	**15α**	**20**	**36**[b]	**38**[c]	**40α**	**40β**	**68β**	**70α**	**70β**
R[d]	CN	NO_2	NO_2	CN	CN	CN	NO_2	NO_2	CN	NO_2	NO_2
Inhibition[e] (%)	37	50	37	43	30	26	48	29	27	24	19

[a] Reference compounds: 2,5-anhydro-derivatives.[2]
[b] 1-en-D-*arabino*.
[c] α,β Anomer ratio 1:1.6.
[d] Substituent of the phenyl aglycon.
[e] Inhibition % at an oral dose of 2 mg/kg.

of **64** are removed by Zemplén deacetylation, a furanose → pyranose isomerisation takes place, and after acetylation only a 1:1 mixture of the corresponding pentaacetate pyranose anomers **66α** and **66β** can be isolated. That means that, during the demercaptalisation process, only the 4-*O*-acetyl group migrates to the 6-thiol group while the 5-*O*-acetyl group remains intact. Otherwise the pyranose pentaacetates **66** should be formed as by-products instead of the furanose anomers **64**.

As, during the glycosidation reactions with the appropriate thiols, α,β-anomeric mixtures were formed even when the pure β-pentaacetate **56** was used as donor, in further experiments the α,β-anomeric pentaacetate mixture was used for this purpose. Condensation of a 1:2 α,β-anomeric mixture of the glucoseptanose pentaacetates **55** + **56** with 4-cyanobenzenethiol in the presence of boron trifluoride etherate afforded, besides a 1:2 mixture of the α and β anomers of **67**, some further by-products (Scheme 8). From this mixture, pure **67β** could be isolated after column chromatography and subsequent crystallisation which gave **68β** after Zemplén deacetylation. Deacetylation of the residue, obtained after separation of **67β**, afforded a mixture from which **68α** as well as the 1,2,6-trithio derivative **73** could be separated by column chromatography in low yield. That means that, during the glycosidation reaction, the boron trifluoride can activate the 2-*O*-acetyl group of **67**, which is eliminated via a transannular participation reaction of the ring sulfur atom, forming the sulfonium intermediate **71** with inversion of configuration at C-2. Attack of this episulfonium ion by a 4-cyanobenezenethiol molecule will lead, via a second inversion at C-2, to the trithio derivatives **72** which on deacetylation affords **73**. When 4-nitrobenzenethiol was used as aglycon in the aforementioned glycosidation reaction, a mixture was obtained, containing besides a 1:2 mixture of the α and β anomers of **69** the corresponding trithio derivative **74** as by-product. From this mixture **69β** as well as **74** could be separated by column chromatography and crystallisation. Zemplén deacetylation of the anomeric mixture of **69** afforded **70α** and **70β**, respectively, which could be separated. The thioseptanosides **68β**, **70α** and **70β** were submitted to biological testing.

Deacetylation of the trithio-derivative **74** afforded **75**. Although the anomeric configuration of **73** and **75** was suggested to be α by comparing its NMR data with those of the two pentaacetate anomers **55** and **56**, the large negative value of their optical rotation ($[\alpha]_D$ − 560 and − 562°, respectively) indicated rather the presence of a β anomer.

Biological results.—The oral antithrombotic activity of **15α**, **20**, **36**, **38**, **40α**, **40β**, **73α**, **73β**, **75α** and **75β** was determined on rats, using Pescador's model.[14] All compounds were administered orally 3 h before ligation. From the data listed in Table 1, it can be seen that the biological activity of the D-mannoseptanosides **15α** and

20 and the α-L-idoseptanoside **40α** was in the range of the corresponding 2,5-anhydro-glucoseptanosides **1** which were used as reference compounds, but no generally valid structure activity relationship could be established.

3. Experimental

General methods.—Organic solutions were dried over $MgSO_4$ and concentrated under diminished pressure at or below 40 °C. TLC: E. Merck precoated Silica Gel 60 F_{254} plates, with hexane–EtOAc mixtures (A, 1:1; B, 2:1; C, 3:1), EtOAc (D), toluene–MeOH mixtures (E, 4:1), CH_2Cl_2–MeOH mixtures (F, 95:5; G, 9:1), toluene–acetone mixtures (H, 2:1) and EtOAc–EtOH mixtures (I, 9:1); detection by spraying the plates with a 0.02 M solution of I_2 and a 0.30 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. Mp are uncorrected. Optical rotations were determined at 20 °C. The NMR spectra were recorded on a Varian INOVA™ spectrometer operating at 500 MHz (^1H) by using a Varian 5 mm $^1H\{^{13}C/^{15}N\}$ PFG Indirect·nmr™ probe. ^1H chemical shifts are given relative to TMS (δ_{TMS} 0.00 ppm) as measured in Me_2SO-d_6 and $CDCl_3$ at 30 °C. ^1H assignments were straightforward by a concerted use of standard high-field one- and two-dimensional (2D) NMR methods: 1D DPFGSE-NOE (selective excitation by I-Burp2 shaped pulses) and 2D ^1H–^1H shift correlations (PFG-DQFCOSY, PFG-HSQC, PFG-HMBC). The obtained scalar and NOE connectivities provided abundant information to ensure unambiguous spectral assignments. Chemical shifts are given in Table 2 and coupling constants in Table 3. A detailed conformational analysis of the prepared glucoseptanosides will be published in a forthcoming paper.

GLC was conducted with a Chrompack CP-9000 Gaschromatograph, using a glass capillary column RH-5ms$^+$ (30 m × 0.25 mm) coated with polyimide; temperature 12 °C × min^{-1} from 185 to 325 °C; carrier gas nitrogen, v_{lin} 16.8 cm × s^{-1}, v_{split} 24.9 cm × s^{-1}, inlet pressure 60 kPa, make up gas nitrogen; detection by FID.

1,3,4,5-Tetra-O-*acetyl-2,6-anhydro-2-thio*-D-*glucitol* (**6**) *and 2,3,4,5-tetra*-O-*acetyl-1,6-anhydro-1-thio*-D-*mannitol* (**8**).—A solution of **5**[4] (9.1 g, 41.3 mmol) in 0.1 M aq trifluoroacetic acid (90 mL) was refluxed for 2 h, then concentrated and the residue was acetylated in 2:1 pyridine–Ac_2O (120 mL) overnight. After usual work-up, the residue was submitted to column chromatography (solvent B) to yield, according to NMR spectroscopy, a 1:1 mixture of **6** and **8** (4.3 g, 30%).

1,6-Anhydro-1-thio-D-*mannitol* (**9**).—Deacetylation of a 1:1 mixture of **6** and **8** (2.5 g, 7.2 mmol) with 3 M NaOMe (0.1 mL) in MeOH (50 mL) yielded, after neutralisation with solid CO_2 and column chromatography (solvent E) **9** (0.5 g, 39%): mp 122–124 °C (ether), Lit.[4] mp 120–122 °C; 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, 39.91; H, 6.78; S, 17.83.

Concentration of the second fraction gave a 4:1 mixture of 2,6-anhydro-2-thio-D-glucitol **7** and **9** (0.77 g, 60%).

Acetylation of **9** (0.6 g) with Ac_2O (5 mL) in pyridine (10 mL) afforded **8** (0.92 g, 79%) as a syrup: $[\alpha]_D$ −74.5° (*c* 0.6, $CHCl_3$); R_f 0.4 (solvent B). Anal. Calcd for $C_{14}H_{20}O_8S$: C, 48.27; H, 5.79; S, 9.20. Found: C, 48.32; H, 5.78; S, 9.24.

Conversion of the mixture of **6** + **8** *into the thioglycosides* **12** *and* **14**.—To a slurry of a 1:1 mixture of **6** + **8** (1.0 g, 2.87 mmol) in toluene (10 mL), NCS (0.38 g, 2.85 mmol) was added and the mixture was stirred for 1 h at 20 °C. During this period, **6** + **8** was gradually dissolved and succinimide precipitated. This was filtered off and was washed with toluene (5 mL). The filtrate, containing **10** and **11** (R_f 0.6 (solvent B) was added dropwise over a period of 30 min to a stirred slurry of freshly fused ZnO (0.3 g, 3.7 mmol) and 4-nitrobenzenethiol (purity 80%) (0.67 g, 3.45 mmol) in MeCN (15 mL). Stirring was continued for 30 min at 20 °C, then the mixture was filtered through Celite. The residue obtained on concentration of the filtrate was dissolved in MeOH (20 mL) and deacetylated with 3 M NaOMe (0.1 mL). After neutralisation with solid CO_2, the mixture was concentrated and submitted to column chromatography (solvent F, then G). Concentration of the first fraction yielded 4-nitrophenyl 1,6-dithio-D-mannoseptanoside (**15α**, 60 mg, 6%): mp 162–164 °C (ether); $[\alpha]_D$ +75° (*c* 0.5, pyridine); R_f 0.7 (solvent G). Anal. Calcd for $C_{12}H_{15}NO_6S_2$: C, 43.23; H, 4.54; N, 4.20; S, 19.24. Found: C, 43.29; H, 4.57; N, 4.16; S, 19.22.

Concentration of the second fraction gave 4-nitrophenyl 1,6-dithio-β-D-fructopyranoside (**13**, 120 mg, 12.5%): mp 98–102 °C; $[\alpha]_D$ −234° (*c* 0.5, pyridine); R_f 0.6 (solvent G). The β configuration was proved by NMR, as there was a NOE effect between the aromatic H-2′, H-6(β) and H-4, as well as between H-1 and H-3. Anal. Calcd for $C_{12}H_{15}NO_6S_2$: C, 43.23; H, 4.54; N, 4.20; S, 19.24. Found: C, 43.21; H, 4.57; N, 4.23; S, 19.24.

4-Nitrophenyl 2,3,4,5-tetra-O-*acetyl-1,6-dithio*-D-*mannoseptanoside* (**14**).—(i) To a slurry of **8** (0.7 g, 2.0 mmol) in toluene (10 mL), NCS (0.27 g, 2.0 mmol) was added and the mixture was stirred for 2 h at 20 °C. During this period, **8** gradually dissolved and succinimide precipitated. This was filtered off and was washed with toluene (5 mL). The filtrate, containing **11** (R_f 0.6

Table 2
^{1}H NMR data for **6**–**75** as measured in [a]$CDCl_3$ and [b]Me_2SO-d_6 at 30 °C at 500 MHz

Compound	Chemical shifts (δ)								
	H-1a	H-1b	H-2	H-3	H-4	H-5	H-6a	H-6b	Others
6[a, #]	4.06	4.13	3.44	5.27	5.19	5.25	2.91	2.64	1.98, 2.01, 2.05, 2.07 (OAc)
8[a, #]	2.80–2.90			5.37–5.39			2.80–2.90		2.00, 2.04 (OAc)
9[b,§]	2.43	2.79	3.92	3.74	3.74	3.92	2.43	2.79	4.67 br (2-OH, 3-OH)
13[b]	3.60	3.91		4.18	3.75	4.06	2.43	2.90	5.14 (1-OH), 5.17 (3-OH), 4.66 (4-OH, 5-OH)
14α[a]	4.52		5.52	5.74	5.57	5.43	3.10	2.94	2.12 (2-OAc), 2.06 (3-OAc), 2.14 (4-OAc), 2.07 (5-OAc)
15α[b]	4.60		4.00	4.09	3.81	4.00	2.84	2.72	5.54 (2-OH), 4.83 (3-OH), 4.59 (4-OH), 4.84 (5-OH)
16[a]	3.54	3.04	4.56	4.04	4.28	4.47	3.54	3.13	2.87 br s (2-OH, 5-OH), 1.42 $C(CH_3)_2$
17[a]	3.14	3.66	5.77	5.39	5.19	5.24	3.46	3.38	2.05 (2-OAc), 2.12 (3-OAc), 2.17 (4-OAc), 2.10 (5-OAc)
18α[a]	5.91		5.67	5.44	5.53	5.33	3.26	2.74	2.09 (1-OAc), 2.07 (2-OAc), 2.13 (3-OAc), 2.13 (4-OAc), 2.08 (5-OAc)
18β[a]	6.08		5.77	5.50	5.38–5.42		2.98	3.37	2.10 (1-OAc), 2.14 (2-OAc), 2.04 (3-OAc), 2.05 (4-OAc), 2.17 (5-OAc)
19[a]	4.45		5.49	5.73	5.56	5.42	3.07	2.94	2.05, 2.06, 2.11, 2.13 (OAc)
20[b]	4.55		3.98	4.10	3.82	4.00	2.82	2.75	5.55 (2-OH), 4.85 (3-OH), 4.62 (4-OH), 4.88 (5-OH)
25[a]	2.83	2.60	4.94–5.02		5.14	3.11	4.07	4.18	1.95 (2-OAc), 1.94 (3-OAc), 1.96 (4-OAc), 2.00 (6-OAc)
26[a, #]	3.23	2.94	5.26	5.29	3.44	5.20	4.09	4.36	2.00, 2.02, 2.04, 2.04 (OAc)
29[a, #]	4.08	4.22	3.57	5.29	5.29	3.57	4.08	4.22	2.01, 2.02 (OAc)
31[a]	4.32	4.95		5.33	5.39	4.94	2.71	3.04	2.19 (1-OAc), 2.11 (3-OAc), 1.98 (4-OAc), 2.00 (5-OAc)
32[a]	4.02	4.52		5.64	5.75	5.14	2.90	3.27	1.80 (1-OAc), 2.06 (3-OAc), 2.01 (4-OAc), 2.07 (5-OAc)
33[b]	2.80	3.55	3.96	3.49	3.84–3.92		3.27	2.89	5.68 (2-OH), 5.46 (5-OH), 1.32 $C(CH_3)_2$
34[a]	3.52	3.21	5.68	5.26–5.30		5.41	3.51	3.21	2.04, 2.09, 2.11, 2.14 (OAc)
35α[a, #]	5.87			5.33–5.45		5.06	2.72	3.06	2.01, 2.02, 2.03, 2.05, 2.08, (OAc)
35β[a, #]	6.08		5.34	5.40	5.44	5.22	3.40	2.83	1.99, 2.02, 2.04, 2.08, 2.18 (OAc)
36[b]			6.43	4.18	3.30	3.58	3.01	2.66	5.10 br (3-OH, 4-OH, 5-OH)
38α[b, #]	4.55		3.44	3.47–3.51		3.56	2.87	2.68	5.43 (2-OH), 5.09 (3-OH), 4.97 (4-OH), 4.99 (5-OH)
38β[b, #]	4.85		3.89	3.57	3.42	3.49	2.87	2.71	5.69 (2-OH), 5.06 (3-OH), 4.90 (4-OH), 4.95 (5-OH)
39α[a]	4.41		5.31	5.39	5.50	5.15	2.86	3.01	2.02, 2.03, 2.03, 2.03 (OAc)
39β[a]	4.78		5.55	5.38	5.39	5.28	3.37	2.81	2.06 (2-OAc), 2.06 (3-OAc), 2.04 (4-OAc), 2.04 (5-OAc)
40α[b]	4.62			3.44–3.54		3.57	2.89	2.70	5.11 (2-OH), 5.47 (3-OH), 5.00 (4-OH), 5.00 (5-OH)
40β[b]	4.90		3.92	3.59	3.44	3.51	2.89	2.76	5.10 br (2-OH, 3-OH, 4-OH, 5-OH)
42α[b]	3.13	3.75	3.81	4.23	4.15	4.52	3.56	3.00	1.33, 1.36 $C(CH_3)_2$, 1.27, 1.39 $C(CH_3)_2$
42β[b]	2.90	3.41	4.23	4.09	4.29	4.78	3.06	3.20	1.35, 1.37 $C(CH_3)_2$, 1.30, 1.39 $C(CH_3)_2$
47[a]	5.00		5.61	5.36	4.65	4.81	2.79	3.59	2.13 (2-OAc), 2.17 (3-OAc), 2.18 (5-OAc)
51[a]	3.62	3.32	5.12	5.27	5.22	5.32	3.48	3.41	2.08 (2-OAc), 2.10 (3-OAc), 2.18 (4-OAc), 2.09 (5-OAc)
52[a]	3.26–3.30		5.73	5.26	5.34	5.69	3.21	3.15	2.04 (2-OAc), 2.12 (3-OAc), 2.14 (4-OAc), 2.06 (5-OAc)
53[a, #]	6.07		5.71	5.27	5.54	5.07	3.48	2.66	2.05 (1-OAc), 2.21 (2-OAc), 2.06 (3-OAc), 2.05 (4-OAc), 2.04 (5-OAc)
54[a, #]	5.75		5.37	5.25	5.73	5.20	2.79	3.30	2.13 (1-OAc), 2.16 (2-OAc), 2.03 (3-OAc), 2.04 (4-OAc), 2.05 (5-OAc)
55[a]	6.05		5.35	5.61	5.42	5.44	3.18	2.87	2.18 (1-OAc), 2.02 (2-OAc), 2.04 (3-OAc), 2.05 (4-OAc), 2.12 (5-OAc)
56[a]	6.01		5.26	5.44	5.32	5.36	2.92–3.02		2.10 (1-OAc), 2.04 (2-OAc), 2.10 (3-OAc), 2.11 (4-OAc), 2.10 (5-OAc)
67α[a, #]	4.52		5.60	5.73	5.24	5.44	3.16	2.90	2.09 (2-OAc), 2.04 (3-OAc), 2.06 (4-OAc), 2.17 (5-OAc)
67β[a]	4.46		5.18	5.54	5.42	5.37	2.96	3.02	2.06 (2-OAc), 2.12 (3-OAc), 2.13 (4-OAc), 2.08 (5-OAc)
68α[b]	4.74		3.87	4.00	3.63	4.10	2.69	3.01	5.61 (2-OH), 5.17 (3-OH), 4.47 (4-OH), 4.94 (5-OH)
68β[b]	4.74		3.60	3.77–3.88		4.01	2.88	2.62	5.46 (2-OH), 5.12 (3-OH), 4.89 (4-OH), 4.94 (5-OH)
69α[b, #]	4.58		5.61	5.74	5.26	5.45	3.17	2.92	2.05, 2.06, 2.10, 2.17 (OAc)
69β[b]	4.51		5.20	5.55	5.43	5.38	2.95–3.06		2.06 (2-OAc), 2.13 (3-OAc), 2.14 (4-OAc), 2.09 (5-OAc)
70α[b, #]	4.79		3.87	4.01	3.63	4.10	2.69	3.04	5.64 (2-OH), 5.17 (3-OH), 4.46 (4-OH), 4.94 (5-OH)
70β[b]	4.80		3.63	3.80–3.88		4.28	2.94	2.63	5.10 (2-OH), 5.14 (3-OH), 4.92 (4-OH), 4.96 (5-OH)
73[b]	5.78		3.30	3.96	3.20	4.00	2.58	2.90	3.40 br s (3,4,5-OH)
74[a]	4.89		3.51	5.88	4.86	5.41	2.92–2.95		2.02 (3-OAc), 2.01 (4-OAc), 2.21 (5-OAc)
75[b]	5.89		3.35	3.96	3.22	3.99	2.80	2.91	5.44 (3-OH), 4.73 (4-OH), 4.71 (5-OH)

§ Measured at 300 MHz.

Chemical shifts are determined from the mixture of the respective isomers (**6**+**8**, **26**+**29**, **35α**+**35β**, **38α**+**38β**, **53**+**55**, **54**+**56**, **67α**+**67β**, **69α**+**69β**, **70α**+**70β**).

Table 3
^{1}H–^{1}H coupling data for **6**–**75** as measured in [a]$CDCl_3$ and [b]Me_2SO-d_6 at 30 °C at 500 MHz

Compound	Coupling constants (Hz)									
	$^3J_{1a,2}$	$^3J_{1b,2}$	$^3J_{2,3}$	$^3J_{3,4}$	$^3J_{4,5}$	$^3J_{5,6a}$	$^3J_{5,6b}$	$^2J_{6a,6b}$	$^2J_{1a,1b}$	Others
6[a, #]	7.1	6.8	3.0	6.3	2.9	9.7	3.7	13.8	11.1	
9[b,§]	3.3	8.9	n.r.						13.4	
13[b]				9.2	2.9	4.3	1.8	13.9	11.6	$^3J_{1a,1\text{-OH}} = 3.9$, $^3J_{1b,1\text{-OH}} = 4.3$
14α[a]	7.2		2.1	8.2	3.1	7.5	4.5	15.7		
15α[b]	7.8		2.1	7.3	2.7	7.5	3.4	14.7		$^3J_{2,2\text{-OH}} = 5.5$, $^3J_{3,3\text{-OH}} = 5.4$, $^3J_{4,4\text{-OH}} = 4.6$, $^3J_{5,5\text{-OH}} = 4.7$
16[a]	~8.0	7.8	3.3	9.2	2.4	n.d.	3.3	13.9	13.6	
17[a]	1.0	9.7	1.5	6.4	1.7	9.6	1.7	14.6	14.9	
18α[a]	8.1		1.4	7.1	3.2	8.8	4.5	15.7		
18β[a]	2.9		2.8	8.9	n.d.	7.2	2.0	15.2		
19[a]	7.3		1.9	8.1	2.9	4.6	7.2	15.6		
20[b]	7.8		1.7	7.3	2.4	3.7	6.5	14.6		$^3J_{2,2\text{-OH}} = 5.4$, $^3J_{3,3\text{-OH}} = 5.4$, $^3J_{4,4\text{-OH}} = 4.6$, $^3J_{5,5\text{-OH}} = 4.4$
25[a]	10.8	3.9	n.d.	10.6	9.2	3.4	5.8	12.0	13.4	
26[a, #]	2.9	4.9	2.9	2.0	10.3	5.0	2.6	12.3	12.1	
29[a, #]	6.7	7.9	3.0						11.4	
31[a]				9.8	9.6	4.9	11.2	13.5	12.1	
32[a]				9.9	9.7	4.7	11.2	13.3	12.1	
33[b]	3.0	4.6	8.6	8.6	n.d.	9.5	4.8	12.6	13.9	$^3J_{2,2\text{-OH}} = 4.2$, $^3J_{5,5\text{-OH}} = 4.2$
34[a]	7.5	1.9	7.4	3.3	8.9	1.9	9.3	14.1	14.2	
35α[a, #]	7.4		n.d.	n.d.	n.d.	4.0	11.3	15.4		
35β[a, #]	3.1		~9	~9	~9	3.4	3.7	16.3		
36[b]			3.7	9.6	7.6	3.2	8.4	14.4		
38α[b, #]	7.9		~8	n.d.	n.d.	4.4	6.0	15.3		$^3J_{2,2\text{-OH}} = 4.4$, $^3J_{3,3\text{-OH}} = 2.9$, $^3J_{4,4\text{-OH}} = 3.8$, $^3J_{5,5\text{-OH}} = 4.4$
38β[b, #]	3.4		6.8	8.5	8.5	4.4	9.3	14.4		$^3J_{2,2\text{-OH}} = 5.7$, $^3J_{3,3\text{-OH}} = 4.1$, $^3J_{4,4\text{-OH}} = 3.5$, $^3J_{5,5\text{-OH}} = 3.5$
39α[a]	8.2		8.4	9.2	8.5	4.3	7.7	15.7		
39β[a]	4.1		8.8	8.2	8.3	4.0	5.7	15.8		
40α[b]	7.8		n.d.	n.d.	n.d.	3.9	6.1	15.4		$^3J_{2,2\text{-OH}} = 1.9$, $^3J_{3,3\text{-OH}} = 4.3$
40β[b]	3.6		6.9	8.5	8.1	4.5	9.3	14.5		
42α[b]	11.8	2.3	8.9	8.4	6.8	12.0	2.3	12.8	11.1	
42β[b]	11.3	2.4	8.9	7.8	6.4	11.4	2.1	14.5	13.8	
47[a]	0.6		2.7	7.5	2.7	3.3	3.6	14.9		
51[a]	10.1	2.3	7.1	5.2	1.3	10.0	2.8	13.2	13.6	
52[a]	9.4	1.8	7.9	4.3	1.0	10.1	2.5	14.5	14.6	
53[a, #]	4.9		0.9	9.4	7.3	10.8	3.8	15.2		
54[a, #]	5.2		1.4	8.7	7.4	3.4	3.8	16.6		
55[a]	2.9		9.2	7.8	2.8	8.2	5.0	15.4		
56[a]	7.0		4.6	8.6	1.8			n.d.		$^3J_{5,6a} + {}^3J_{5,6b} = 12.0$
67α[a, #]	4.1		7.6	8.6	2.0	6.1	4.0	15.5		
67β[a]	8.4		4.0	8.4	1.8	8.9	4.5	14.7		
68α[b]	3.1		6.5	8.3	1.7	5.0	2.5	14.5		$^3J_{2,2\text{-OH}} = 6.6$, $^3J_{3,3\text{-OH}} = 5.0$, $^3J_{4,4\text{-OH}} = 3.8$, $^3J_{5,5\text{-OH}} = 4.1$
68β[b]	8.3		5.2	7.0	1.5	8.9	4.3	14.1		$^3J_{2,2\text{-OH}} = 6.6$, $^3J_{3,3\text{-OH}} = 4.6$, $^3J_{4,4\text{-OH}} = 4.1$, $^3J_{5,5\text{-OH}} = 4.7$
69α[b, #]	4.1		7.6	8.6	2.1	6.1	4.0	15.5		
69β[b]	8.6		3.8	8.4	1.8	8.7	4.6	14.7		
70α[b, #]	3.1		6.5	8.3	1.5	5.0	2.6	14.4		$^3J_{2,2\text{-OH}} = 6.6$, $^3J_{3,3\text{-OH}} = 5.0$, $^3J_{4,4\text{-OH}} = 3.8$, $^3J_{5,5\text{-OH}} = 4.1$
70β[b]	8.4		5.2	~7	1.5	8.9	4.2	14.0		$^3J_{2,2\text{-OH}} = 6.6$, $^3J_{3,3\text{-OH}} = 4.5$, $^3J_{4,4\text{-OH}} = 4.1$, $^3J_{5,5\text{-OH}} = 4.7$
73[b]	2.5		9.6	9.0	2.8	4.3	1.7	13.9		
74[a]	3.2		9.7	9.5	2.9			n.d.		$^3J_{5,6a} + {}^3J_{5,6b} = 5.8$
75[b]	2.7		9.6	8.8	2.8	4.4	1.8	13.9		$^3J_{3,3\text{-OH}} = 5.5$, $^3J_{4,4\text{-OH}} = 5.8$, $^3J_{5,5\text{-OH}} = 3.7$

§ Measured at 300 MHz.
# Chemical shifts are determined from the mixture of the respective isomers (**6**+**8**, **26**+**29**, **35α**+**35β**, **38α**+**38β**, **53**+**55**, **54**+**56**, **67α**+**67β**, **69α**+**69β**, **70α**+**70β**).
n.d., not determined; n.r., not resolved.

(solvent B) was added dropwise over a period of 30 min to a stirred slurry of freshly fused ZnO (0.21 g, 2.6 mmol) and 4-nitrobenzenethiol (purity 80%) (0.47 g, 2.4 mmol) in MeCN (15 mL). Stirring was continued for 30 min at 20 °C, then the mixture was filtered through Celite. The residue obtained on concentration of the filtrate was submitted to column chromatography (solvent B, then A) to yield **14α** (320 mg, 26%) as an oil: $[\alpha]_D$ +72° (*c* 0.55, $CHCl_3$); R_f 0.4 (solvent B). Anal. Calcd for $C_{20}H_{23}NO_{10}S_2$: C, 47.90; H, 4.62; N, 2.79; S, 12.79. Found: C, 47.93; H, 4.59; N, 2.82; S, 12.75.

(ii) Under argon, to a stirred solution of **18** (1.32 g, 3.25 mmol) and 4-nitrobenzenethiol (purity 80%) (0.66 g, 3.4 mmol) in dry 1,2-dichloroethane (20 mL) $BF_3{\cdot}Et_2O$ (0.4 mL, 3.0 mmol) was added at 20 °C. The mixture was kept at 20 °C for 2 h and then poured into an ice-cold 6% aq $NaHCO_3$ solution (50 mL). The separated organic layer was washed with water, 6% aq $NaHCO_3$ and concentrated. The residue was submitted to column chromatography (solvent B, then A) to yield **14** (1.6 g, 98%) as an oil which, according to NMR spectroscopy, contained **14α** and **14β** in a ratio of 19:1.

*4-Nitrophenyl 1,6-dithio-α-*D*-mannoseptanoside* (**15α**).—To a solution of a 19:1 α:β mixture of **14** (1.6 g, 3.2 mmol) in MeOH (50 mL), 3 M NaOMe in MeOH (0.1 mL) was added at rt. The solution was made neutral after 1 h with solid CO_2 and the precipitated material was filtered and washed with ether to give **15α** (0.68 g, 64%) identical with that obtained above.

*1,6-Anhydro-3,4-*O*-isopropylidene-1-thio-*D*-mannitol S-oxide* (**16**).—To a solution of $NaIO_4$ (6.5 g, 30.4 mmol) in water (20 mL), a solution of **5** (6.66 g, 30.2 mmol) in acetone (120 mL) was added dropwise and the resulting mixture was stirred at 20 °C for 2 h. The precipitated crystals were filtered off and washed with acetone. The residue obtained on concentration of the filtrate was submitted to column chromatography (solvent E) to yield **16** (7.1 g, 99%): mp 77–80 °C (ether–hexane); $[\alpha]_D$ −76° (*c* 0.5, MeOH); R_f 0.3 (solvent E). Anal. Calcd for $C_9H_{16}O_5S$: C, 45.75; H, 6.83; S, 13.57. Found: C, 45.72; H, 6.80; S, 13.55.

*2,3,4,5-Tetra-*O*-acetyl-1,6-anhydro-1-thio-*D*-mannitol S-oxide* (**17**).—A solution of **16** (7.1 g, 41.3 mmol) in 0.1 M aq trifluoroacetic acid (70 mL) was refluxed for 2 h, then concentrated and the residue was acetylated in 2:1 pyridine–Ac_2O (100 mL) overnight. After usual work-up, the residue was recrystallised from ether–hexane to yield **17** (8.37 g, 82%): mp 130–133 °C; $[\alpha]_D$ −3° (*c* 0.5, MeOH); R_f 0.3 (solvent D). Anal. Calcd for $C_{14}H_{20}O_9S$: C, 46.15; H, 5.53; S, 8.80. Found: C, 46.18; H, 5.55; S, 8.83.

*1,2,3,4,5-Penta-*O*-acetyl-1-thio-*D*-mannoseptanose* (**18**).—A solution of **17** (8.0 g, 22 mmol) in Ac_2O (80 mL) was stirred at 140 °C for 17 h. The mixture was concentrated and toluene (100 mL) was evaporated from the residue. The obtained residue was submitted to column chromatography (solvent B). Concentration of the first fraction gave **18α** (200 mg, 2%) as an oil: $[\alpha]_D$ +139° (*c* 0.5, $CHCl_3$); R_f 0.4 (solvent B). Anal. Calcd for $C_{16}H_{22}O_{10}S$: C, 47.29; H, 5.46; S, 7.89. Found: C, 47.33; H, 5.45; S, 7.83.

Concentration of the second fraction gave a 1:1 mixture of **18α** and **18β** (8.44 g, 95%).

Concentration of third fraction gave **18β** (130 mg, 1.5%) as an oil: $[\alpha]_D$ −196° (*c* 0.5, $CHCl_3$); R_f 0.35 (solvent B). Anal. Calcd for $C_{16}H_{22}O_{10}S$: C, 47.29; H, 5.46; S, 7.89. Found: C, 47.27; H, 5.41; S, 7.85.

*4-Cyanophenyl 2,3,4,5-tetra-*O*-acetyl-1,6-dithio-*D*-mannoseptanoside* (**19**).—Under argon, to a stirred solution of **18** (203 mg, 0.5 mmol) and 4-cyanobenzenethiol (140 mg, 1 mmol) in dry 1,2-dichloroethane (10 mL), TMSOTf (0.12 mL, 0.6 mmol) was added at −10 °C. After stirring at −10 °C for 30 min, the reaction was quenched with Et_3N, concentrated and the residue submitted to column chromatography (solvent B) to give **19** (200 mg, 83%) as a syrup which, according to NMR spectroscopy, was a 19:1 mixture of the α and β anomers: $[\alpha]_D$ +55° (*c* 1, $CHCl_3$); R_f 0.35 (solvent B). Anal. Calcd for $C_{21}H_{23}NO_8S_2$: C, 52.38; H, 4.81; N, 2.91; S, 13.32. Found: C, 52.65; H, 5.03; N, 2.61; S, 13.21.

*4-Cyanophenyl 1,6-dithio-α-*D*-mannoseptanoside* (**20**).—To a solution of **19** (400 mg) in $CHCl_3$ (10 mL) and MeOH (10 mL), 1 M NaOMe in MeOH (0.05 mL) was added at rt. The solution was made neutral after 1 h with solid CO_2, and the residue of the concentrated solution was submitted to column chromatography (solvent I) to yield **20** (120 mg, 46%): mp 158–160 °C (ether); $[\alpha]_D$ +69° (*c* 0.5, pyridine); R_f 0.6 (solvent I). 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, 4.77; N, 4.42; S, 20.31.

*2,3,4,6-Tetra-*O*-acetyl-1,5-anhydro-1-thio-*D*-glucitol* (**25**), *2,3,5,6-tetra-*O*-acetyl-1,4-anhydro-1-thio-*D*-altritol* (**26**) *and 1,3,4,6-tetra-*O*-acetyl-2,5-anhydro-2-thio-*D*-mannitol* (**29**).—A solution of **21**[4] (2.5 g, 11.3 mmol) in 0.1 M aq trifluoroacetic acid (25 mL) was refluxed for 2 h, then concentrated and the residue was acetylated in 2:1 pyridine–Ac_2O (45 mL) overnight. After usual work-up, the residue was submitted to column chromatography (solvent B). Concentration of the first fraction gave a 1:1 mixture of **26** and **29** (235 mg, 6%): R_f 0.4 (solvent B).

Concentration of the second fraction gave **25** (2.02 g, 51%): mp 108–110 °C (ether); $[\alpha]_D$ +44° (*c* 0.5, $CHCl_3$); R_f 0.3 (solvent B). Anal. Calcd for $C_{14}H_{20}O_8S$: C, 48.27; H, 5.79; S, 9.20. Found: C, 48.30; H, 5.77; S, 9.16.

*4-Nitrophenyl 1,3,4,5-tetra-*O*-acetyl-2,6-dithio-β-*L*-xylo-hex-2-ulopyranoside* (**31**) *and 4-nitrophenyl 1,3,4,5-tetra-*O*-acetyl-2,6-dithio-α-*L*-xylo-hex-2-ulopyranoside* (**32**).—To a slurry of **25** (1.25 g, 3.6 mmol) in toluene

(15 mL), NCS (0.48 g, 3.6 mmol) was added and the mixture was stirred for 1 h at 20 °C. During this period **25** was gradually dissolved and succinimide precipitated. This was filtered off and was washed with toluene (5 mL). The filtrate, containing **30** (R_f 0.7, solvent B) was added dropwise over a period of 30 min to a stirred slurry of freshly fused ZnO (0.38 g, 4.7 mmol) and 4-nitrobenzenethiol (purity 80%) (0.85 g, 4.4 mmol) in MeCN (20 mL). Stirring was continued for 1 h at 20 °C, then the mixture was filtered through Celite. The residue obtained on concentration of the filtrate was submitted to column chromatography (solvent B). Concentration of the first fraction gave **32** (50 mg, 3%): mp 128–132 °C (ether); $[\alpha]_D$ −101° (*c* 0.3, $CHCl_3$); R_f 0.6 (solvent B); The β configuration was proved by NMR, as there was a NOE effect between the aromatic H-2′, H-6(β) and H-4, as well as between H-1 and H-3. Anal. Calcd for $C_{20}H_{23}NO_{10}S_2$: C, 47.90; H, 4.62; N, 2.79; S, 12.79. Found: C, 47.88; H, 4.64; N, 2.77; S, 12.76.

Concentration of the second fraction gave **31** (0.6 g, 33%) as an oil: $[\alpha]_D$ +89° (*c* 0.3, $CHCl_3$); R_f 0.5 (solvent B); The α configuration was proved by NMR, as there was a NOE effect between the aromatic H-2′, and H-3, as well as between H-1, H-4 and H-6(β). Anal. Calcd for $C_{20}H_{23}NO_{10}S_2$: C, 47.90; H, 4.62; N, 2.79; S, 12.79. Found: C, 47.87; H, 4.63; N, 2.76; S, 12.80.

*1,6-Anhydro-3,4-*O*-isopropylidene-1-thio-*L*-iditol* S-*oxide* (**33**).—To a solution of $NaIO_4$ (12.5 g, 58.44 mmol) in water (260 mL), a solution of **21** (12.2 g, 55.38 mmol) in acetone (220 mL) and water (100 mL) was added dropwise and the resulted mixture was stirred at 20 °C for 2 h. The precipitated crystals were filtered off and washed with acetone. The residue obtained on concentration of the filtrate was submitted to column chromatography (solvent E) to yield **33** (12.95 g, 99%): mp 235–240 °C; $[\alpha]_D$ +35° (*c* 0.5, pyridine); R_f 0.3 (solvent E). Anal. Calcd for $C_9H_{16}O_5S$: C, 45.75; H, 6.83; S, 13.57. Found: C, 45.78; H, 6.85; S, 13.60.

*2,5-Anhydro-2,3,4,5-tetra-*O*-acetyl-1-thio-*L*-iditol* S-*oxide* (**34**).—A solution of **33** (7.5 g, 31.7 mmol) in 0.1 M aq trifluoroacetic acid (90 mL) was refluxed for 2 h, then concentrated and the residue was acetylated in 2:1 pyridine–Ac_2O (100 mL) overnight. After usual work-up, the residue was submitted to column chromatography (solvent E) to yield **34** (8.54 g, 74%): mp 133–135 °C (ether); $[\alpha]_D$ −13° (*c* 1.0, MeOH); R_f 0.5 (solvent E). Anal. Calcd for $C_{14}H_{20}O_9S$: C, 46.15; H, 5.53; S, 8.80. Found: C, 46.12; H, 5.51; S, 8.78.

*1,2,3,4,5-Penta-*O*-acetyl-1-thio-*L*-idoseptanose* (**35**).—A solution of **34** (6.7 g, 18.4 mmol) in Ac_2O (70 mL) was stirred at 100 °C for 20 h. The mixture was concentrated and toluene (100 mL) was evaporated from the residue. The residue was submitted to column chromatography (solvent A) to yield, according to NMR spectroscopy, a 1:1 mixture of **35α** and **35β** (6.85 g, 92%): mp 105–107 °C (EtOAc–hexane); R_f 0.6 (solvent A). Anal. Calcd for $C_{16}H_{22}O_{10}S$: C, 47.29; H, 5.46; S, 7.89. Found: C, 47.27; H, 5.43; S, 7.87.

*4-Cyanophenyl 2-deoxy-1,6-dithio-*L*-xylo-hex-1-eno-septanoside* (**36**) *and 4-cyanophenyl 1,6-dithio-*L*-idoseptanoside* (**38**).—To a solution of **37** (500 mg, 1.04 mmol) in MeOH (50 mL), 3 M NaOMe in MeOH (0.05 mL) was added at rt. The solution was made neutral after 1 h with solid CO_2, and the residue of the concentrated solution was submitted to column chromatography (solvent E). Concentration of the first fraction gave **36** (35 mg, 11%): mp 118–120 °C (ether); $[\alpha]_D$ −268° (*c* 0.4, pyridine); R_f 0.4 (solvent E). Anal. Calcd for $C_{13}H_{13}NO_3S_2$: C, 52.86; H, 4.44; N, 4.74; S, 21.71. Found: C, 52.81; H, 4.46; N, 4.72; S, 21.77.

Concentration of the second fraction gave **38** (190 mg, 58%) as a 1:1.5 mixture of α:β anomers: R_f 0.3 (solvent E). Anal. Calcd for $C_{13}H_{15}NO_4S_2$: C, 49.82; H, 4.82; N, 4.47; S, 20.46. Found: C, 52.81; H, 4.46; N, 4.72; S, 21.77.

*4-Cyanophenyl 2,3,4,5-tetra-*O*-acetyl-1,6-dithio-*L*-idoseptanoside* (**37**).—Under argon, to a stirred solution of **34** (2.03 g, 5 mmol) and 4-cyanobenzenethiol (0.81 g, 6 mmol) in dry 1,2-dichloroethane (30 mL), $BF_3{\cdot}Et_2O$ (0.65 mL, 5.3 mmol) was added at rt. After 2 h, the reaction was poured into ice-cold 6% aq $NaHCO_3$ solution (60 mL). The separated organic solution was washed with water, dried, concentrated and the residue submitted to column chromatography (solvent B) to give **37** (1.7 g, 69%) which, according to ^1H NMR spectroscopy, was a 1:1.5 mixture of the α and β anomers: δ 4.36 (1 H, d, $J_{1,2}$ 8.1 Hz, H-1β) and 4.73 (1 H, d, $J_{1,2}$ 4.1 Hz, H-1α) R_f 0.3 (solvent B). Anal. Calcd for $C_{21}H_{23}NO_8S_2$: C, 52.38; H, 4.81; N, 2.91; S, 13.32. Found: C, 52.65; H, 5.03; N, 2.61; S, 13.21.

*4-Nitrophenyl 2,3,4,5-tetra-*O*-acetyl-1,6-dithio-*L*-idoseptanoside* (**39**).—The reaction of 4-nitrobenzenethiol (0.66 g, 80% purity, 3.4 mmol) with **35** (1.32 g, 3.25 mmol) was carried out as described for **37** to give after column chromatography (solvent B) **39** (1.53 g, 94%) which, according to NMR spectroscopy, was a 2:3 mixture of the α and β anomers: R_f 0.3 (solvent B). They could be separated by repeated column chromatography (solvent B). Concentration of the first fraction gave **39β** (0.82 g): mp 165–168 °C (ether); $[\alpha]_D$ +225° (*c* 1.0, $CHCl_3$); R_f 0.6 (solvent A). Anal. Calcd for $C_{20}H_{23}NO_{10}S_2$: C, 47.90; H, 4.62; N, 2.79; S, 12.79. Found: C, 47.93; H, 4.65; N, 2.82; S, 12.83.

Concentration of the second fraction gave **39α** (0.55 g): mp 155–158 °C (ether); $[\alpha]_D$ −80° (*c* 1.0, $CHCl_3$); R_f 0.55 (solvent A). Anal. Calcd for $C_{20}H_{23}NO_{10}S_2$: C, 47.90; H, 4.62; N, 2.79; S, 12.79. Found: C, 47.88; H, 4.60; N, 2.77; S, 12.75.

*4-Nitrophenyl 1,6-dithio-α-*L*-idoseptanoside* (**40α**).—To a solution of a **39α** (0.55 g, 1.0 mmol) in MeOH (50 mL), 3 M NaOMe in MeOH (0.1 mL) was added at rt. The solution was made neutral after 1 h with solid CO_2,

concentrated and the residue was washed with water to yield **40α** (234 mg, 64%): mp 75–77 °C (ether); $[\alpha]_D$ −240° (*c* 0.5, pyridine); R_f 0.3 (solvent E). Anal. Calcd for $C_{12}H_{15}NO_6S_2$: C, 43.23; H, 4.54; N, 4.20; S, 19.24. Found: C, 43.20; H, 4.62; N, 4.19; S 19.19.

*4-Nitrophenyl 1,6-dithio-β-*L*-idoseptanoside* (**40β**).—Deacetylation of **39β** (0.59 g, 1.2 mmol) was performed as described for **39α** to yield **40β** (325 mg, 83%): mp 181–184 °C (ether); $[\alpha]_D$ −27° (*c* 1.0, pyridine); R_f 0.3 (solvent E). Anal. Calcd for $C_{12}H_{15}NO_6S_2$: C, 43.23; H, 4.54; N, 4.20; S, 19.24. Found: C, 43.27; H, 4.57; N, 4.16; S 19.29.

*2,3:4,5-Di-*O*-isopropylidene-1,6-anhydro-1-thio-*D*-glucitol* S-*oxide* (**42**).—To a solution of $NaIO_4$ (1.95 g, 9.12 mmol) in water (60 mL), a solution of **41**[6] (2.33 g, 8.95 mmol) in acetone (50 mL) was added dropwise and the resulted mixture was stirred at 20 °C for 1 h. The precipitated crystals were filtered off and washed with acetone. The residue obtained on concentration of the filtrate was submitted to column chromatography (solvent H). Concentration of the first fraction yielded **42β** (*R*)-*S*-oxide (0.51 g, 21%): mp 229–232 °C (ether); $[\alpha]_D$ +72° (*c* 0.5, acetone); R_f 0.4 (solvent H). Anal. Calcd for $C_{12}H_{20}O_5S$: C, 52.16; H, 7.29; S, 11.60. Found: C, 52.19; H, 7.31; S, 11.57.

Concentration of the second fraction gave a 1.7:1 mixture of **42β** (*R*)-*S*-oxide and **42α** (*S*)-*S*-oxide (1.75 g, 71%).

Concentration of the third fraction yielded **42α** (*S*)-*S*-oxide (90 mg, 3.6%): mp 222–226 °C (ether); $[\alpha]_D$ +2° (*c* 0.5, acetone); R_f 0.3 (solvent H). Anal. Calcd for $C_{12}H_{20}O_5S$: C, 52.16; H, 7.29; S, 11.60. Found: C, 52.13; H, 7.25; S, 11.62.

*2,3,5-Tri-*O*-acetyl-1,6-anhydro-1-thio-β-*D*-glucofuranose* (**47**).—A solution of a 1.7:1 mixture of **42**(*R*)- and (*S*)-*S*-oxide (1.75 g, 6.3 mmol) in 0.1 M aq trifluoroacetic acid (20 mL) was refluxed for 1.5 h, then concentrated and the residue was acetylated in 2:1 pyridine–Ac_2O (30 mL) overnight. After usual work-up, the residue was submitted to column chromatography (solvent B) to yield **47** (0.78 g, 40%) as an oil: $[\alpha]_D$ −114° (*c* 1.0, $CHCl_3$); R_f 0.4 (solvent B); Lit.[12] $[\alpha]_D$ −90° (*c* 1.0, $CHCl_3$). Both, the ^1H as well as the ^{13}C NMR data were identical with those given in Lit. [12]. Anal. Calcd for $C_{12}H_{16}O_7S$: C, 39.56; H, 4.43; S, 8.80. Found: C, 39.60; H, 4.47; S, 8.77.

*2,3,4,5-Tetra-*O*-acetyl-1,6-anhydro-1-thio-*D*-glucitol (*S*)-*S*-oxide* (**51**) *and (*R*)-*S*-oxide* (**52**).—To a stirred solution of **50**[8] (5.2 g, 15 mmol) in acetone (100 mL), a solution of $NaIO_4$ (5.5 g, 25.7 mmol) in water (35 mL) was added at rt. After 2 h further $NaIO_4$ (0.5 g, 2.3 mmol) was added to the formed slurry and stirring was continued for 20 h. The precipitate was filtered off and washed with acetone (50 mL). The combined filtrate was concentrated, the residue was dissolved in CH_2Cl_2, washed with water, dried and concentrated. According to NMR spectroscopy, the solid residue contained **51** and **52** in a ratio of 1:3. It was dissolved in hot EtOAc (50 mL) and hexane (30 mL) was added. After cooling, the precipitated crystals were filtered and washed with hexane to give **52** (3.1 g, 58%), mp 174–177 °C, $[\alpha]_D$ −58° (*c* 1, $CHCl_3$), R_f 0.4 (solvent C). The residue (2 g) obtained on concentration of the filtrate was submitted to column chromatography (solvent D). Eluted first was unchanged **50** (0.6 g, 11.5%). Concentration of the second fraction gave **51** (0.8 g, 15%) mp 137–141 (EtOAc–hexane); $[\alpha]_D$ −18° (*c* 1, $CHCl_3$); R_f 0.45 (solvent D). Anal. Calcd for $C_{14}H_{20}O_9S$: C, 46.15; H, 5.53; S, 8.80. Found for **51**: C, 46.11; H, 5.62; S 8.72. Found for **52**: C, 46.09; H, 5.59; S, 8.82.

Pummerer reaction of **51** *and* **52**.—A solution of **51** + **52** (2.6 g, 18.4 mmol) in Ac_2O (26 mL) was stirred at 100 °C for 7 h. The mixture was concentrated and toluene (50 mL) was evaporated from the residue. The obtained residue was submitted to column chromatography (solvent A). Concentration of the first fraction gave, according to NMR spectroscopy, a 1:1 mixture of **54** and **56** (0.78 g, 27%): R_f 0.5 (solvent A). Anal. Calcd for $C_{16}H_{22}O_{10}S$: C, 47.29; H, 5.46; S, 7.89. Found: C, 47.23; H, 5.49; S, 7.82.

Concentration of the second fraction gave, according to NMR spectroscopy, a 1.2:2.8:1:1.7 mixture of **53**, **54**, **55** and **56** (1.9 g, 65.5%): R_f 0.50 + 0.45 (solvent A). Anal. Calcd for $C_{16}H_{22}O_{10}S$: C, 47.29; H, 5.46; S, 7.89. Found: C, 47.19; H, 5.43; S, 7.92.

Concentration of the third fraction gave, according to NMR spectroscopy, a 3:7 mixture of **53** and **55** (180 mg, 6%): R_f 0.45 (solvent A). Anal. Calcd for $C_{16}H_{22}O_{10}S$: C, 47.29; H, 5.46; S, 7.89. Found: C, 47.25; H, 5.45; S, 7.84.

*1,2,3,4,5-Penta-*O*-acetyl-6-thio-α-*D*- (**55**) *and -β-*D*-glucoseptanose* (**56**) *as well as 1,2,3,5-*O*-acetyl-6-*S*-acetyl-*D*-glucofuranose* (**64**).—To a stirred solution of **59** (10.5 g, 20 mmol) in acetone (200 mL) and water (25 mL), $HgCl_2$ (25 g) and yellow HgO (25 g) were added. The slurry was stirred for 36 h at rt, filtered and the residue was washed with hot acetone (100 mL). Pyridine (37 mL) was added to the filtrate and thereafter a stream of H_2S was passed through it until all mercury salts precipitated. The formed dark brown precipitate was removed by filtration and the filtrate was concentrated at 25 °C. The residue was dissolved in chloroform (200 mL), washed three times with water (3 × 30 mL), dried and concentrated. The remaining syrup was dissolved in pyridine (100 mL) and concentrated to half of its volume at 30 °C. The remaining solution was kept under argon for 24 h at rt, then cooled to 0 °C and treated with Ac_2O (20 mL). The mixture was kept at rt for 24 h to give after usual processing a syrup (7.8 g, 94%), which on TLC (solvent C) showed two distinguished set of spots at R_f ~0.4 and ~0.3. According to GLC and NMR, this mixture contained **55**, **56**, **64α**

and **64β** in a ratio of 2:4:1:1 and was submitted to column chromatography (solvent C).

Concentration of the first fraction (R_f 0.4) gave a syrup (1.6 g, 19%) which according to GLC and NMR contained **64α** and **64β** in a ratio of ~1:1. ^{1}H NMR ($CDCl_3$): **64α** δ 6.44 (d, $J_{1,2}$ 4.4, 1 H, H-1), 5.52 (dd, $J_{2,3}$ 3.3, $J_{3,4}$ 4.9 Hz, 1 H, H-3), 5.20 (ddd, $J_{4,5}$ 5.1, $J_{5.6a}$ 6.8, $J_{5.6b}$ 3.4 Hz, 1 H, H-5), 5.18 (dd, 1 H, H-2), 4.44 (dd, 1 H, H-4), 3.54 (dd, $J_{6a,6b}$ 14.0 Hz, 1 H, H-6b), 3.02 (dd, 1 H, H-6a), 2.33 (s, 3 H, SAc), 2.12–1.96 (OAc); ^{13}C NMR: δ 93.4 (C-1), 30.2 (S-Ac), 29.9 (C-6), **64β** δ 6.10 (s, $J_{1,2}$ ~0, 1 H, H-1), 5.39 (d, $J_{2,3}$ ~0, $J_{3,4}$ 4.6 Hz, 1 H, H-3), 5.28 (ddd, $J_{4,5}$ 5.1, $J_{5.6a}$ 6.4, $J_{5.6b}$ 3.4 Hz, 1 H, H-5), 5.10 (s, 1 H, H-2), 4.47 (dd, 1 H, H-4), 3.60 (dd, $J_{6a,6b}$ 14.0 Hz, 1 H, H-6b), 3.00 (dd, 1 H, H-6a), 2.33 (s, 3 H, SAc), 2.12–1.96 (OAc); ^{13}C NMR: δ 98.6 (C-1), 30.4 (C-6), 30.2 (S-Ac). Anal. Calcd for $C_{16}H_{22}O_{10}S$: C, 47.29; H, 5.46; S, 7.89. Found: C, 47.42; H, 5.62; S, 7.53.

The second fraction (R_f 0.35) afforded on concentration **56** (1,7 g, 20.5%): mp 95–97 °C (ether–hexane), $[\alpha]_D$ −59°; ^{1}H NMR ($CDCl_3$): δ 6.01 (d, $J_{1,2}$ 6.8, 1 H, H-1), 5.53 (dd, $J_{2,3}$ 4.6, $J_{3,4}$ 8.5 Hz, 1 H, H-3), 5.40–5.27 (m, 2 H, H-4,5), 5.24 (dd, 1 H, H-2), 2.98 (d, $J_{5,6a} \sim J_{5,6b}$ 5.8 Hz, 2 H, H-6a,6b), 2.12, 2.11, 2.11, 2.10, 2.04 (5 s, 5 × 3 H, OAc); ^{13}C NMR: δ 75.9, 74.9, 70.7, 69.6, 68.9 (C-1,2,3,4,5), 28.0 (C-6). Anal. Calcd for $C_{16}H_{22}O_{10}S$: C, 47.29; H, 5.46; S, 7.89. Found: C, 47.21; H, 5.45; S, 7.78.

The third fraction (R_f 0.30) gave on concentration **55** (0.58 g, 7%) as a syrup, $[\alpha]_D$ +109° ^{1}H NMR ($CDCl_3$): δ 6.05 (d, $J_{1,2}$ 2.9, 1 H, H-1), 5.62 (dd, $J_{2,3}$ 9.3, $J_{3,4}$ 7.6 Hz, 1 H, H-3), 5.48–5.38 (m, 2 H, H-4,5), 5.35 (dd, 1 H, H-2), 3.18 (dd, $J_{5,6b}$ 8.1, $J_{6a,6b}$ 15.1 Hz, 1 H, H-6b), 2.86 (dd, $J_{5,6a}$ 4.6 Hz, 1 H, H-6a), 2.18, 2.13, 2.05, 2.04, 2.02 (5 s, 5 × 3 H, OAc); ^{13}C NMR: δ 74.7, 71.1, 71.0, 70.4, 67.8 (C-1,2,3,4,5), 26.8 (C-6). Anal. Calcd for $C_{16}H_{22}O_{10}S$: C, 47.29; H, 5.46; S, 7.89. Found: C, 47.39; H, 5.65; S, 7.62.

2,3,4,5,6-Penta-O-*acetyl*- (**57**) *and 2,3,4,5-tetra*-O-*acetyl-6*-O-p-*toluenesulfonyl*-D-*glucose diethyl dithioacetal* (**58**).—To a stirred solution of D-glucose diethyl dithioacetal (14.3 g, 50 mmol), TsCl (10.5 g, 55 mmol) was added at 0 °C. After 30 min the temperature was raised to 20 °C, after 20 min the mixture was cooled with ice and Ac_2O (50 mL) was added. The mixture was kept at rt overnight to give after usual processing a syrup (30 g) which was submitted to column chromatography using solvent C for elution.

Concentration of the first fraction gave **57** (2.3 g, 9.2%), mp 43–45 °C (EtOH–water), R_f 0.3 (solvent C). Lit.[15] mp 45–47 °C. ^{1}H NMR ($CDCl_3$): δ 5.76 (dd, $J_{2,3}$ 7.3, $J_{3,4}$ 2.9 Hz, 1 H, H-3), 5.43 (dd, $J_{4,5}$ 8.1 Hz, 1 H, H-4), 5.28 (dd, $J_{1,2}$ 4.2, 1 H, H-2), 5.06 (ddd, $J_{5.6a}$ 4.8, $J_{5.6b}$ 3.2 Hz, 1 H, H-5), 4.23 (dd, $J_{6a,6b}$ 12.7 Hz, 1 H, H-6b), 4.11 (dd, 1 H, H-6a), 4.07 (d, 1 H, H-1), 2.90–2.45 (m, 4 H, S-CH_2CH$_3$), 2.15, 2.09, 2.08, 2.06 and 2.05 (5 s, 5 × 3 H, OAc) 1.33 and 1.23 (2 t, 2 × 3 H, S-CH$_2$CH_3); ^{13}C NMR: δ 72.1, 70.0, 68.4, 68.3 (C-2,3,4,5), 61.4 (C-6), 50.7 (C-1)

Concentration of the second fraction gave **58** (23.1 g, 76%) as a syrup, $[\alpha]_D$ +9°. Lit.[16] $[\alpha]_D$ +8° (*c* 4, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.78 and 7.38 (2 d, 4 H, aromatic) 5.71 (dd, $J_{2,3}$ 7.6, $J_{3,4}$ 2.6 Hz, 1 H, H-3), 5.38 (dd, $J_{4,5}$ 8.1 Hz, 1 H, H-4), 5.23 (dd, $J_{1,2}$ 4.2, 1 H, H-2), 5.01 (ddd, $J_{5.6a}$ 4.2, $J_{5.6b}$ 2.9 Hz, 1 H, H-5), 4.18 (dd, $J_{6a,6b}$ 11.2 Hz, 1 H, H-6b), 4.11 (d, 1 H, H-1), 4.10 (dd, 1 H, H-6a), 2.85–2.45 (m, 4 H, S-CH_2CH$_3$), 2.45 (s, 3 H, TsCH$_3$), 2.09, 2.07, 2.02 and 2.01 (4 s, 4 × 3 H, OAc) 1.29 and 1.23 (2 t, 2 × 3 H, S-CH$_2$CH_3); ^{13}C NMR: δ 72.0, 69.8, 67.9, 67.8 (C-2,3,4,5), 66.4 (C-6), 50.6 (C-1).

2,3,4,5-Tetra-O-*acetyl-6*-S-*acetyl*-D-*glucose diethyl dithioacetal* (**59**).—To a stirred solution of **58** (12.2 g, 20 mmol) in acetone (250 mL), KSAc (2.96 g, 26 mmol) was added and the slurry was boiled for 5 h when according to TLC the reaction was completed. The residue of the concentrated mixture was dissolved in $CHCl_3$, washed with water, dried and concentrated to give **59** (10 g, 98%) as a syrup. $[\alpha]_D$ +25°. Anal. Calcd for $C_{20}H_{32}O_9S_3$: C, 46.86; H, 6.29; S, 18.76. Found: C, 46.72; H, 6.11; S, 18.52. ^{1}H NMR ($CDCl_3$): δ 5.78 (dd, $J_{2,3}$ 7.1, $J_{3,4}$ 3.2 Hz, 1 H, H-3), 5.35 (dd, $J_{4,5}$ 7.1 Hz, 1 H, H-4), 5.29 (dd, $J_{1,2}$ 4.6, 1 H, H-2), 5.01 (ddd, $J_{5.6a}$ 6.6, $J_{5.6b}$ 3.2 Hz, 1 H, H-5), 4.07 (d, 1 H, H-1), 3.33 (dd, $J_{6a,6b}$ 14.6 Hz, 1 H, H-6b), 2.99 (dd, 1 H, H-6a), 2.90–2.40 (m, 4 H, S-CH_2CH$_3$), 2.33 (s, 3 H, SAc), 2.16, 2.09, 2.05 and 2.03 (4 s, 4 × 3 H, OAc) 1.32 and 1.23 (2 t, 2 × 3 H, S-CH$_2$CH_3); ^{13}C NMR: δ 71.9, 70.1, 69.9, 69.2 (C-2,3,4,5), 50.8 (C-1), 29.0 (C-6).

1,2,3,4-Tetra-O-*acetyl-6*-S-*acetyl*-D-*glucopyranose* (**66**).—To a solution of a 1:1 α,β-anomeric mixture of the furanose compound **64** (3.2 g) in MeOH (30 mL), 3 M methanolic NaOMe (3.5 mL) was added at rt. The mixture was neutralised after 30 min with solid CO_2 and kept for 20 h at rt. The residue obtained on concentration was dissolved in pyridine (15 mL) and Ac_2O (10 mL) was added. After 20 h at rt, the mixture was processed by the usual way to give on concentration of the CH_2Cl_2 solution a syrup (2.75 g, 86%) which, according to NMR spectroscopy and GLC measurements, contained **66α** and **66β** in a ratio of ~1:1. After column chromatography (solvent B), the same mixture solidified and was filtered with ether–hexane (2.4 g, 75%), mp 88–92 °C (ether–hexane); R_f 0.45 (solvent B). ^{1}H NMR ($CDCl_3$): **66α** δ 6.26 (d, $J_{1,2}$ 3.6, 1 H, H-1), 5.43 (dd, $J_{2,3}$ 10.2, $J_{3,4}$ 9.5 Hz, 1 H, H-3), 5.05 (dd, 1 H, H-2), 5.01 (dd, $J_{4,5}$ 10.0 Hz, 1 H, H-4), 4.02 (dd, $J_{5,6b} \sim J_{5,6a}$ 4.4 Hz, 1 H, H-5), 3.18 (d, 2 H, H-6a,6b), 2.33 (s, 3 H, SAc), 2.17, 2.08, 2.01, 2.00 (4 s, 4 × 3 H, OAc); ^{13}C NMR: δ 88.8 (C-1), 70.6, 69.8, 69.7, 69.1 (C-2,3,4,5), 29.6 (C-6), **66β** δ 5.68 (d, $J_{1,2}$ 8.0, 1 H,

H-1), 5.20 (m, $J_{2,3} \sim J_{3,4}$ 9.5 Hz, 1 H, H-3), 5.15–4.95 (m, 2 H, H-2,4), 3.81 (dd, $J_{5,6b}$ 3.5, $J_{5,6a}$ 5.9 Hz, 1 H, H-5), 3.20 (dd, $J_{6a,6b}$ 14.4 Hz, 1 H, H-6b), 3.16 (dd, 1 H, H-6a), 2.33 (s, 3 H, SAc), 2.10, 2.09, 2.02, 2.01 (4 s, 4 × 3 H, OAc); ^{13}C NMR: δ 91.5 (C-1), 73.6, 72.6, 70.2, 69.7 (C-2,3,4,5), 29.6 (C-6). Anal. Calcd for $C_{16}H_{22}O_{10}S$: C, 47.29; H, 5.46; S, 7.89. Found: C, 47.35; H, 5.65; S, 7.68.

From this mixture, **66α** could be separated after repeated column chromatography, mp 114–118 °C (ether–hexane); Lit.[17] mp 102–104 °C, R_f 0.40 (solvent B); $[\alpha]_D$ +80°; Lit.[16] $[\alpha]_D$ +38° (*c* 1.1, $CHCl_3$). Anal. Calcd for $C_{16}H_{22}O_{10}S$: C, 47.29; H, 5.46; S, 7.89. Found: C, 47.30; H, 5.55; S, 7.81.

4-Cyanophenyl 2,3,4,5-tetra-O-*acetyl-1,6-dithio*-D-*glucoseptanoside* (**67**).—The reaction of 4-cyanobenzenethiol (950 mg, 7 mmol) with 1:2 mixture of **55** + **56** (2.45 g, 6 mmol) was carried out in the presence of $BF_3{\cdot}Et_2O$ (0.8 mL, 6.5 mmol) as described for **37** to give after column chromatography (solvent B, R_f 0.35) a semisolid material (2.7 g) which, according to NMR spectroscopy, was a mixture containing besides different by-products **67α** and **67β** as the main components in a ratio of 1:2.5. On treatment with ether–hexane, **67β** (1.6 g, 55.4%) was obtained; mp 160–163 °C (MeOH), $[\alpha]_D$ −20° (*c* 1, $CHCl_3$); R_f 0.35 (solvent B). Anal. Calcd for $C_{21}H_{23}NO_8S_2$: C, 52.38; H, 4.81; N, 2.91; S, 13.32. Found: C, 52.40; H, 4.85; N, 2.88; S, 13.27.

The residue (1 g) obtained on concentration of the mother liquor contained, according to NMR spectroscopy, besides different by-products **67α** and **67β** in a ratio of 3:1 which could not be separated.

4-Cyanophenyl 1,6-dithio-D-*glucoseptanoside* (**68**) *and 4-cyanophenyl 2*-S-*(4-cyanophenyl)-1,2,6-trithio*-D-*glucoseptanoside* (**73**).—(i) Deacetylation of **67β** (270 mg) was performed as described for **20** to give after column chromatography (solvent E) **68β** (150 mg, 85.3%), mp 130–133 °C; $[\alpha]_D$ −113° (*c* 0.8, pyridine); R_f 0.30 (solvent E). Anal. Calcd for $C_{13}H_{15}NO_4S_2$: C, 49.82; H, 4.82; N, 4.47; S, 20.46. Found: C, 49.88; H, 4.87; N, 4.40; S, 20.32

(ii) When the residue (900 mg), obtained on concentration of the mother liquor of **67β** was deacetylated in a similar way a mixture (380 mg) containing **68α**, **68β** and **73** was obtained which could be separated by column chromatography (solvent E).

Concentration of the first fraction gave **73** (60 mg, 2.3%), mp 100–105 °C (ether); $[\alpha]_D$ −560° (*c* 0.4, pyridine); R_f 0.40 (solvent E). Anal. Calcd for $C_{20}H_{18}N_2O_3S_3$: C, 55.79; H, 4.21; N, 6.51; S, 22.34. Found: C, 55.63; H, 4.27; N, 6.57; S, 22.31.

Concentration of the second fraction gave **68α** (205 mg, 10.7%), mp 165–170 °C (ether); $[\alpha]_D$ −18° (*c* 0.25, pyridine); R_f 0.35 (solvent E). Anal. Calcd for $C_{13}H_{15}NO_4S_2$: C, 49.82; H, 4.82; N, 4.47; S, 20.46. Found: C, 49.76; H, 4.80; N, 4.42; S, 20.23.

Concentration of the third fraction gave **68β** (50 mg, 2%), identical with that, described above.

4-Nitrophenyl 2,3,4,5-tetra-O-*acetyl-1,6-dithio*-D-*glucoseptanoside* (**69**) *and 4-nitrophenyl 3,4,5-tri*-O-*acetyl-2*-S-*(4-nitrophenyl)-1,2,6-trithio*-D-*glucoseptanoside* (**74**).—The reaction of 4-nitrobenzenethiol (1.2 g, 80% purity, 3 mmol) with 1:2 mixture of **55** + **56** (2 g, 5 mmol) was carried out as described for **37** to give after column chromatography (R_f 0.35, solvent B) a solid material (2.1 g, 84%) which contained, according to NMR spectroscopy, besides different by-products **69α** and **69β** as the main components in a ratio of 1:9. Recrystallisation of this mixture from MeOH (20 mL) gave **69β** (1.5 g, 58%), mp 149–151 °C; $[\alpha]_D$ −9°; R_f 0.30 (solvent E). Anal. Calcd for $C_{20}H_{23}NO_{10}S_2$: C, 47.90; H, 4.62; N, 2.79; S, 12.79. Found: C, 47.87; H, 4.71; N, 2.62; S, 12.83.

The residue obtained on concentration of the mother liquor gave, after repeated column chromatography (solvent B), **74** (140 mg, 4.6%) as a syrup; $[\alpha]_D$ −168° (*c* 0.8, $CHCl_3$); R_f 0.35 (solvent B). Anal. Calcd for $C_{24}H_{24}N_2O_{10}S_3$: C, 48.31; H, 4.05; N, 4.70; S, 16.12. Found: C, 48.55; H, 4.26; N, 4.62; S, 15.95.

Concentration of the further fractions gave a mixture (1.1 g) which, according to NMR spectroscopy, contained **69α** and **69β** in a ratio of 1:2, but these two anomers could not be separated.

4-Nitrophenyl 1,6-dithio-D-*glucoseptanoside* (**70**).—(i) Deacetylation of **69β** (500 mg) was carried out as described for **15α** to give after column chromatography (solvent E) **70β** (252 mg, 75%), mp 145–149 °C (ether); $[\alpha]_D$ −98° (*c* 1, pyridine); R_f 0.30 (solvent E). Anal. Calcd for $C_{12}H_{15}NO_6S_2$: C, 43.23; H, 4.54; N, 4.20; S, 19.24. Found: C, 43.27; H, 4.62; N, 4.12; S, 19.17.

(ii) When the residue (1 g) obtained after separation of **74** was submitted to deacetylation, as described for **15α**, a mixture (620 mg, 73%) was obtained which, according to NMR spectroscopy, contained **69α** and **69β** in a ratio of 1:2 which could not be separated; mp 129–134 °C (ether); $[\alpha]_D$ −56° (*c* 1, pyridine); R_f 0.30 (solvent E). Anal. Calcd for $C_{12}H_{15}NO_6S_2$: C, 43.23; H, 4.54; N, 4.20; S, 19.24. Found: C, 43.19; H, 4.60; N, 4.10; S, 19.09.

4-Nitrophenyl 2-S-*(4-nitrophenyl)-1,2,6-trithio*-D-*glucoseptanoside* (**75**).—Deacetylation of **74** (100 mg) was performed as described for **15α** to give after column chromatography (solvent E) **75** (70 mg, 91%), mp 196–205 °C (ether); $[\alpha]_D$ −562° (*c* 0.5, pyridine); R_f 0.40 (solvent E). Anal. Calcd for $C_{18}H_{18}N_2O_7S_3$: C, 45.95; H, 3.86; N, 5.95; S, 20.44. Found: C, 45.87; H, 3.60; N, 5.77; S, 20.09.

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