Synthesis and configurational assignments of 3-substituted 2-deoxy-4-thio-D-*erythro*-pentofuranose derivatives

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A new route is described to 1-*O*-acetyl-2-deoxy-4-thio-α,β-D-*erythro*-pentofuranose derivatives starting from L-arabinose. This route is amenable to variation in the 3-substituent and the 3-*O*-benzoyl and 3-azido derivatives were obtained in 17 and 15% yields, respectively, making this procedure easily the most economical entry to 4′-thionucleosides. The anomeric configuration of these and other thiosugars is established unequivocally.

Introduction

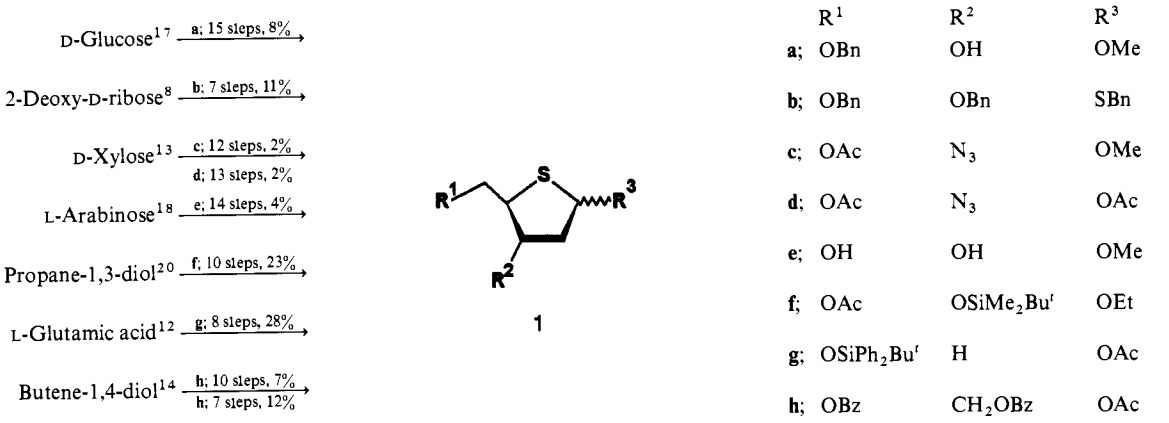
The synthesis of nucleosides in which the sugar moiety is modified (to be different from ribose or 2-deoxyribose) has been the subject of extensive investigation since it was recognised that such compounds could interfere with DNA replication. Several 2′-deoxy and 2′,3′-dideoxynucleosides are reported to have antiviral activity and anti-tumour activity.[1–5] A modification of particular interest is the replacement of the furanose ring oxygen atom with a sulfur atom, a structural change which is known to lead to an increase in the metabolic stability of a nucleoside towards phosphorylase enzymes.[6] Consequently 2′-deoxy-4′-thionucleosides could be especially advantageous to an antiviral strategy when incorporated into a DNA matrix.[7] Recent work in this area includes the synthesis of the pyrimidine nucleosides, 4′-thiothymidine and related 5-substituted 2′-deoxy-4′-thiouridines,[7–11] 3′-deoxy-4′-thiothymidine,[12] 3′-azido-3′-deoxy-4′-thiothymidine and related 3′-azido-2′,3′-dideoxy-4′-thiouridines,[9,12,13] and several purine 4′-thionucleosides.[7] Similar 4′-thionucleosides have been obtained from a branched sugar.[14] The synthesis of oligonucleotides incorporating 4′-thionucleosides has also been reported.[15,16]

Extensive biological study of 4′-thionucleosides requires efficient synthesis of the 4-thiosugar precursors. Published routes (Scheme 1) to 2-deoxy-4-thioribose starting from a carbohydrate are multistep procedures with a low overall yield which are not suitable for the large-scale synthesis of nucleoside precursors. For example, the synthesis of methyl 5-*O*-benzyl-2-deoxy-4-thio-α,β-D-*erythro*-pentofuranoside **1a** from 1,2:5,6-di-*O*-isopropylidene-α-D-glucose required 14 steps[17] with an overall yield of 11%, and an alternative strategy starting from L-arabinose[18] required the same number of steps with a yield of ~ 4%. A shorter route designed by Walker and co-workers[8] starting from 2-deoxy-D-ribose gave benzyl 3,5-di-*O*-benzyl-2-deoxy-1,4-dithio-α,β-D-*erythro*-pentofuranoside **1b** in 11% overall yield in seven steps.[8] A similar route was proposed by Huang and Hui[10] but this does not give the correct stereochemical control at the ring-closure step[19] and the product is an L-sugar as is evident from comparison of their NMR data for 4′-thiothymidine with those of other workers.[7,9] Several groups[11,12,14] have employed non-saccharide starting materials but these routes are generally of restricted application particularly when the target is a 3-substituted 2-deoxy-4-thioribose. For example, Samuelsson and co-workers[14] have described two variants of a route from (*Z*)-but-2-ene-1,4-diol in which the 3-substituent can only be the hydroxymethyl group. Notably Uenishi[11,20] has developed a stereospecific route from propane-1,3-diol which gives access to either the D or the L form of ethyl 5-*O*-acetyl-3-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-4-thio-α,β-D-*erythro*-pentofuranoside **1f**. Both of these routes, starting from an aliphatic diol, require an asymmetric induction step.

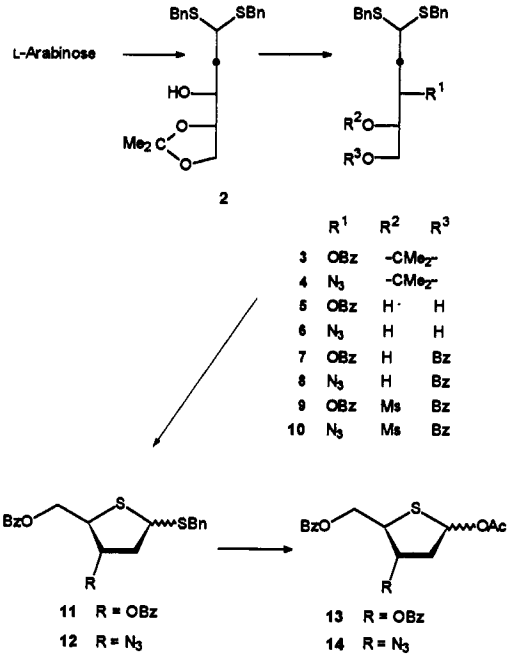
We have reported recently[13] a more versatile strategy for the synthesis of 2-deoxy-4-thioribose derivatives (*e.g.* **1c** and **1d**) starting from D-xylose. This route, which allows the 3-substituent to be varied at an early point in the sequence, is particularly attractive for the formation of 4′-thionucleosides with desirable 3′-substituents. Thus we were able to obtain 3′-azido-3′-deoxy-4′-thiothymidine, the 4′-thio analogue of AZT, in ~ 1% yield from D-xylose. Since the discovery of the antiviral activity of AZT (3′-azido-3′-deoxythymidine) there has been strong interest in the formation of other 3′-azidonucleosides and our methodology is superior to the conventional procedure[9,12] which involves the introduction of the azido group at the 3′-position of a β-pyrimidine nucleoside *via* a 2,3′-anhydro intermediate. Our method gives essentially unlimited choice of nucleoside base and an improved overall yield. We have extended our search for efficient syntheses of thionucleoside precursors and we now report a method for the preparation of 1-*O*-acetyl-3,5-di-*O*-benzoyl-2-deoxy-4-thio-α,β-D-*erythro*-pentofuranoside **13** and its 3-azido analogue **14** from L-arabinose. Particular features of this new route are its adaptability in terms of the nature of the group introduced at C-3, the control of the stereochemistry at this carbon atom and the mild conditions required for subsequent steps which means that the 3-substituent can include groups sensitive to strong acids and bases.

Results and discussion

The full route is shown in Scheme 2. The key derivative of L-arabinose is 2-deoxy-4,5-*O*-isopropylidene-L-*erythro*-pentose dibenzyl dithioacetal **2**. This starting material was obtained from L-arabinose in four steps (61% overall) according to a procedure developed by Wong and Gray.[21] Compound **2** has only one free hydroxy group and hence substitution of this group provides a regiospecific and stereospecific route to derivatisation, Thus with the Mitsunobu reagents[22] and benzoic acid the 3-*O*-benzoyl derivative **3** was obtained with complete inversion. A similar Mitsunobu reaction with the complex[23] $Zn(N_3)_2(C_6H_5N)_2$ gave the corresponding 3-azido derivative **4** again with complete inversion. Selective removal of the 4,5-*O*-isopropylidene group and reprotection of these sites



Scheme 1



Scheme 2

by benzoylation of the primary 5-OH group and mesylation of the 4-OH group gave the derivatives **9** and **10** which each have a good leaving group in the correct configuration at C-4 as required for the final thioacetal cyclisation step. Treatment with tetrabutylammonium iodide (TBAI) and barium carbonate in dimethylformamide (DMF) or hexamethylphosphoric triamide (HMPT) (both of these solvents are better than pyridine[15] at solvating cations) gave the corresponding cyclised products benzyl 3,5-di-*O*-benzoyl-2-deoxy-1,4-dithio-α,β-D-*erythro*-pentofuranoside **11** and benzyl 3-azido-5-*O*-benzoyl-2,3-dideoxy-1,4-dithio-α,β-D-*erythro*-pentofuranoside **12**, in good yield. It is notable that as a consequence of starting from L-arabinose, only a single inversion is required to produce a D-thiosugar compared with the double inversion which is necessary for the routes which start from 2-deoxy-D-ribose[8] or D-xylose.[13]

Compounds **11** and **12** were both obtained as an anomeric pair with an α,β ratio of 1:6. The configuration of these species was difficult to assign (see below) but the major isomer was probably the β-form. Evidently the cyclisation shows some stereoselectivity which could be useful if the anomers could be separated easily. However, this was not achieved. Even after careful chromatography only a partial separation could be effected in both cases, sufficient only to allow the determination of some reference spectroscopic data.

An alternative method[14] for the conversion of dithioacetal **7** to compound **11** which avoids the formation of a mesyl derivative was also investigated. Thus treatment of compound **7** with chlorodiphenylphosphine (4 mol equiv.), iodine (4 mol equiv.) and imidazole (6 mol equiv.) at room temperature gave compound **11** as an anomeric mixture (α,β ratio 1:6) in 72% yield after chromatography.

Compounds **11** and **12** were converted to the corresponding 1-*O*-acetyl derivatives, **13** and **14** respectively. Glycosyl acetates are more versatile for the formation of nucleosides from a range of heterocyclic substrates. The anomers of the 3-*O*-benzoyl compound **13** and the 3-azido compound **14** were readily separated by chromatography and each anomer was obtained optically pure, in both cases.

The overall yield of 1-*O*-acetyl-3,5-di-*O*-benzoyl-2-deoxy-4-thio-α,β-D-*erythro*-pentofuranose **13** was 17% based on L-arabinose (10 steps). This compares very favourably (Scheme 1) with the yield (~2%) for the analogous derivative obtained by the routes starting from D-xylose[13] and with the route from 2-deoxy-D-ribose[8] bearing in mind the cost of this starting material. Thus the L-arabinose route described in this work is undoubtedly the most attractive method of generating 2-deoxy-4-thio-D-ribose derivatives for further nucleoside work. The corresponding yield of the azido derivative **14** was 15%, and thus direct entry to 3′-azido nucleosides can be achieved much more efficiently than has been possible hitherto.

Configurational assignments

Although several workers have made glycosides of 2-deoxy-4-thio-D-*erythro*-pentofuranose **1** with various different groups in the 3 and 5 positions (see Scheme 1), little attempt has been made to separate anomers and to assign the respective configurations. Generally, chromatographic separation of the anomers of these compounds is difficult and in most previous work[7,9,11,12,14] with this thiosugar system, this problem has been avoided and nucleosides were formed directly, using the anomeric mixture. The nucleosides are relatively easily separated and characterised. The assignment of the configuration of 4′-thionucleosides has been reviewed and discussed in detail.[24]

The methyl 2-deoxy-4-thio-D-*erythro*-pentofuranoside anomers (**1**, $R^1 = R^2 = OH$, $R^3 = OMe$) were separated by Nayak and Whistler[17] who reported the optical rotation values $[\alpha]_D^{25}$ +314° and $[\alpha]_D^{25}$ −278° for the α-anomer and the β-anomer, respectively. These values were confirmed by Fu and Bobek.[18] However the assignment of configuration was based on Hudson's rules and was not confirmed by modern spectroscopic data. In our earlier work[13] we separated the methyl glycoside anomers **1c** and assigned the configurations on the basis of optical rotation by comparison with the results of Nayak and Whistler. The anomers of compound **1c** had

rotations of $[\alpha]_D^{23}$ +251† and $[\alpha]_D^{23}$ −188 and were assigned the α and β configuration, respectively. A similar assignment was made for the 1-*O*-acetyl derivatives **1d** on the basis of optical rotations, α-anomer $[\alpha]_D^{23}$ +261 and β-anomer $[\alpha]_D^{23}$ −195.

Uenishi has recently reported[20] the assignment of the configurations of the anomeric ethyl glycosides **1f** on the basis of 'typical' NMR patterns for the anomeric protons. Based on this assignment the α-anomer has $[\alpha]_D^{25}$ −87.2 and the β-anomer has $[\alpha]_D^{25}$ +196.8. We feel that this assignment is not absolutely secure and that there is some uncertainty in this area, particularly concerning the relationship of configuration to optical rotation. We have attempted to find unequivocal spectroscopic criteria which are applicable across a range of structures of type **1** and which resolve these apparent contradictions. From the present work and our previous work we had available three anomeric pairs of 1-*O*-acetyl-2-deoxy-4-thio-D-*erythro*-pentofuranoside derivatives **1d**, **13** and **14**, and the methyl glycosides **1c**, and have examined these compounds in detail.

Selected NMR data and other physical parameters are collected in Table 1 for compounds **1c**, **1d**, **13** and **14** and together with some data for the ethyl glycosides **1f**.[20] Considering the optical rotations there is a very clear parallel with the results of Nayak and Whistler, each pair of anomers having one compound with a high positive rotation and one with a somewhat smaller negative rotation. It is very unlikely that the structural variations across the set could induce large mutually opposite changes in the anomeric rotations and hence a *common configuration can be assumed* with confidence for those anomers with the same sign of rotation. This assumption is reinforced by the R_f-values which indicate that the higher running member of an anomeric pair is always the anomer with a negative rotation.

Some trends are also apparent in the chemical shifts. In each case protons H-1 and H-4 have a higher frequency chemical shift for the same anomer and the H-2 protons are consistently nearly coincident for one anomer and separated by 0.2–0.3 ppm for the other anomer. These trends are similar to those which have been noted for regular 2′-deoxynucleosides[25] and 2′-deoxy-4′-thionucleosides[24] which are characterised by a high frequency shift for H-1′ and a small separation of the H-2′ protons in the β-configuration, in most but not all cases. These 'rules' break down for nucleosides which have sugar substituents similar to those in the simple sugars examined here and hence none of the above trends in chemical shift can be regarded as a compelling rationale for reversing the assignments of Nayak and Whistler. Notably the sugar derivatives **1d**, **13** and **14** show a separation between the H-2 protons (ΔH-2) in the range 0.2–0.4 ppm for *both anomers* when measured in acetone, further undermining the confidence of an anomeric assignment on the basis of ΔH-2.

Coupling constants involving H-1 of a 2-deoxy-4-thiopentofuranose are obviously related to configuration and other couplings may also be indicative if the change in the position of the anomeric group induces a regular consequential change of the average conformation. However, the direct attribution of configuration on the basis of the measurable ^3J-values is complicated by the existence of two conformations for the pentofuranose ring (the well known South and North conformations both of which will contribute to the average conformation), by the sensitivity of ^3J to different substituents at C-1 and C-3 either directly or through induced changes in the conformation and by the lack of any absolute assignment of the H-2*exo* and H-2*endo* protons. On the basis of the couplings to H-1 (Table 1), the common criterion for distinguishing nucleoside anomers, *i.e.* the pattern of the H-1 multiplet (which is usually a 'triplet' for the β-anomers and a double doublet for the α-anomer[24]) is not applicable to the simple thiosugars. These so-called 'typical' patterns arise due to the difference in the magnitude of $J_{1,2exo}$. For the 2-deoxy-4-thiosugars, there is only a small difference between the $J_{1,2exo}$-values and there is no consistent trend. Most other couplings are likewise poorly characteristic of configuration. The exception is $J_{3,4}$ which has a value of 1.7–3.9 Hz in one anomer and 5.9–7.6 Hz in the other anomer. The coupling $J_{2endo,3}$ also shows a regular difference between anomers but neither of these trends can be regarded as a definitive indicator of configuration without further support.

Four-bond couplings are much less sensitive to substituents effects and we have examined the spectra of some of the 2-deoxy-4-thiopentofuranose compounds under high-resolution conditions (in deuteriated acetone) to measure ^4J-values. Of particular importance is the unequivocal assignment of the pair of H-2 protons as *exo* and *endo*. We find that both anomers of the 4-thiopentofuranose derivatives (Table 1) show a ^4J coupling in the range 0.4–0.8 Hz between H-4 and one of the H-2 protons. Coupling to the other H-2 proton is $\leqslant$0.2 Hz, *i.e.* usually below the resolution in the spectrum. Inspection of a molecular model shows that when the 4-thiopentofuranose ring is in a South conformation with C-2 *endo* (a $^2T_3$ or similar form) the H-2*exo* and H-4 protons have a synperiplanar relationship and, crucially, the H-2*exo*–H-4 pathway approaches the classical planar shape required for maximum four-bond coupling. Any coupling of H-4 to the anticlinal H-2*endo* will be much smaller since H-4 is virtually orthogonal to the C-4–C-3–C-2 pathway. In a North conformation ($^3T_2$ or similar form) the coupling of H-4 should be small to both H-2 protons. On the basis of the limited X-ray structural data[24] both the α- and β-2′-deoxy-4′-thionucleosides exist in a South conformation in the solid state and this is also probably the predominant form in solution[26] also although further study is required to confirm this. In any case an assignment of H-2*exo* is possible for all the 4-thiopentofuranose derivatives on the basis of $^4J_{2exo,4}$ >0.4 Hz in both the α- and β-anomers.

Significantly, the observation of a large value for $^4J_{2exo,4}$ implies an average conformation for the 4-thiopentofuranose ring which should also produce significant long-range coupling to H-1 ($^4J_{1,3}$ and $^4J_{1,4}$) in the α-anomer (pseudoequatorial proton) and negligible coupling in the β-anomer (pseudoaxial proton). This is exactly what is observed for the anomer pairs **1d**, **13** and **14**. Due to a multiplicity of couplings the H-1 multiplet does not show fully resolved long-range splittings in the α-anomer of azide **14**, but the line width of about 1.1 Hz is consistent with $^4J_{1,3}$ ~0.5 Hz and couplings to H-4 and H-5 in the range 0.1–0.25 Hz. In sharp contrast, the H-1 multiplet in the β-anomer of azide **14** shows *negigible long-range coupling*, having a residual line width of ~0.3 Hz. Similar features are found for the other compounds (Table 1) and in triester **13** the α-anomer shows a resolved $^4J_{1,3}$ coupling of 0.52 Hz in H-3. Thus the anomeric configurations which were only tentative on the basis of the normal NMR criteria are confirmed.

Although nuclear Overhauser enhancement (NOE) effects can often give an unequivocal assignment of configuration for 4′-thionucleosides on the basis of inter-ring and intra-ring contacts[24] the results are not always unambiguous, due to spectral degeneracy and conformational variability. This is particularly the case for the sugars dealt with here since the preferred ring conformations for 2-deoxy-4-thiosugars are not known with any certainty and there is likely to be greater variation with 3-substituent due to the intrinsically greater flexibility inherent in the larger ring size. Thus 2-D NOE and NOE difference spectra were used to support rather than define configurational assignments.

The crucial protons are H-1 and H-4. The α-anomer (large ΔH-2) of compounds **1d**, **13** and **14** has an H-1↔H-2*endo* contact which is much stronger than the H-1↔H-2*exo*

† $[\alpha]_D$-Values are now given in units of 10^{-1} deg cm^2 g^{-1}.

Table 1 NMR and other data[a] applied to configurational assignment in the 2-deoxy-4-thio-D-*erythro*-pentofuranose system **1**

R^1	R^2	R^3	Config.	R_f	$[\alpha]_D$	H-1	H-2*en*	H-2*ex*	H-3	H-4	$J_{1,2en}$	$J_{1,2ex}$	$J_{2en,3}$	$J_{2ex,3}$	$J_{3,4}$	$J_{1,3}$	$J_{2ex,4}$
OBz	OBz	OAc	β	0.39	+203	6.21	2.53	2.62	5.72	4.03	5.6	1.6	4.3	2.2	1.7	~0	0.76
OBz	OBz	OAc	α	0.47	−105	6.10	2.46	2.70	5.75	3.88	5.7	2.8	7.8	5.4	5.9	0.50	0.49
OBz	N_3	OAc	β	0.30	+247	6.21	2.59	2.53	4.29	3.82	5.3	2.5	5.1	3.5	2.9	~0	0.72
OBz	N_3	OAc	α	0.35	−167	6.06	2.36	2.61	4.24	3.65	5.2	1.8	10.4	5.3	7.6	~0.5	0.5
OAc	N_3	OAc	β	0.15	+261[b]	6.15	2.49	2.48	4.18	3.65	5.1	3.0	4.0	4.8	3.0	~0	0.73
OAc	N_3	OAc	α	0.20	−195[b]	6.00	2.28	2.53	4.11	3.49	5.2	1.9	10.5	5.6	7.0	~0.5	0.50
OAc	N_3	OMe	β	0.40	+251	5.17	2.49	2.39	4.09	3.65	5.6	2.4	5.8	4.4	3.9	~0	0.4
OAc	N_3	OMe	α	0.55	−188	4.91	2.15	2.48	4.08	3.45	4.7	1.6	10.4	5.9	7.0	0.45	0.5
OAc[c]	OTBDMS[d]	OEt	β	0.40	+197	5.17											
OAc[c]	OTBDMS[d]	OEt	α	0.46	−87	5.00											

[a] Chemical shifts in ppm relative to $SiMe_4$, coupling constants in Hz, rotations in units of 10^{-1} deg cm^2 g^{-1} determined in $CHCl_3$. [b] The values given in the original report[13] were in error. [c] Taken from Uenishi *et al.*[20] [d] TBDMS = $SiMe_2Bu^t$.

Table 2 Configuration criteria for 2-deoxy-4-thio-D-*erythro*-pentofuranoses

Diagnostic	Characteristic value or range	
	α-Anomer	β-Anomer
δ(H-1) and δ(H-4)	Low frequency[a]	High frequency[a]
Δ(H-2)	≥0.24	≤0.1
$w_{\frac{1}{2}}$(H-1)[b]	> 1.0 Hz	~0.3 Hz
$J_{1,3}$ (Hz)	~0.5	~0
$J_{2endo,3}$ (Hz)	7.8–10.5	4.0–5.8
$J_{3,4}$ (Hz)	5.9–7.6	1.7–3.9
$[\alpha]_D$	Negative value	Positive value

[a] Relative shift between anomers. [b] The width of each line in the double doublet.

contact, and the H-1↔H-4 contact is weak or absent. In the other anomer, enhancements at H-2 are not diagnostic and the H-1↔H-4 contact is present. Both anomers show NOE effects between H-1 and the H-3, H-5 group of protons and these interactions thus have little diagnostic value. The general pattern of NOE contacts is very similar in the anomeric methyl glycosides **1c** and there is also a strong cross peak between the methoxy protons and the H-3,H-5 multiplet in the spectrum of the β-anomer and a correspondingly weak peak for the α-anomer. These results provide support for the assignments made above.

From a consideration of the analysis made above we are confident that the assignment of the anomeric configurations of the 2-deoxy-4-thio-*erythro*-pentofuranose system can be made on the basis of the criteria detailed in Table 2.

Conclusions

The results discussed above show that consistent assignments of the anomeric configuration in the 4-thiosugars are possible on the basis of spectroscopic data. It follows that the assignment we made originally[13] for the anomers of compounds **1c** and **1d** must be reversed and that the compounds with positive optical rotations have a β-configuration. It also follows that the assignment of configuration for the methyl 2-deoxy-4-thio-D-*erythro*-pentofuranoside anomers obtained by Nayak and Whistler[17] must also be reversed. This may imply that Hudson's isorotation rules do not apply directly to 4-thio-D-pentofuranose systems. It remains to be established whether the reversal of the 'Hudson' assignment in this class of sugar is a general phenomenon.

Experimental

General procedures

Melting temperatures (uncorrected) were determined using an Electrothermal capillary apparatus with a digital thermometer. Optical rotations were obtained at ambient temperature on a JASCO model DIP-370 digital polarimeter, and are given in units of 10^{-1} deg cm^2 g^{-1}. IR spectra were measured as thin films with a Perkin-Elmer 983G spectrometer. NMR spectra were recorded with a JEOL GX270 or Bruker 300WB spectrometer using standard conditions with a data point resolution of ~0.1 Hz. ^{1}H chemical shifts were measured relative to Me_4Si, and ^{13}C chemical shifts relative to $CDCl_3$ (δ_C 77.05) or $(CD_3)_2SO$ (δ_C 39.5). *J*-Values are in Hz. Data for phenyl groups are not reported. Standard heteronuclear correlation techniques were used where required for assignment. High-resolution spectra were obtained with $(CD_3)_2CO$ as solvent, using 128k data points and appropriate line narrowing to give a residual half-height line width of ~0.2 Hz. TLC was carried out using Kieselgel $60F_{254}$ plates (Merck), with detection by UV light or phosphomolybdic acid spray. Silica Gel 60 was used for column chromatography. Elemental analyses were carried out with a Fisons EA 1108 CHN Analyser. We have found with the series of compounds reported here and with other compounds[13] that it is exceptionally difficult to obtain correct analytical results for compounds containing the azido group, especially in the presence of a benzylthio group. Multiple analysis with different, spectroscopically pure, samples of such compounds invariably gives low values for nitrogen.

2-Deoxy-4,5-*O*-isopropylidene-L-*erythro*-pentose dibenzyl dithioacetal 2

L-Arabinose was converted to L-arabinose dibenzyl dithioacetal (90%) by the method of MaloneyHuss;[27] R_f 0.45 (EtOAc); mp 150–151 °C; $[\alpha]_D^{23}$ −16.6 (*c* 2.6, pyridine) {lit.,[27] $[\alpha]_D^{23}$ −18.7° (pyridine)}. The reaction of this compound with acetone according to the procedure of Wong and Gray[21] gave 2,3:4,5-*di*-O-*isopropylidene*-L-*arabinose dibenzyl dithioacetal* as a pale yellow syrup (90%); R_f 0.80 (hexanes–Et_2O, 1:1); $[\alpha]_D^{23}$ −99.6 (*c* 1.7, $CHCl_3$); $\delta_H(CDCl_3)$ 1.06, 1.27, 1.35 and 1.42 (4 s, 12 H, 4 × Me), 3.88 (d, 1 H, $J_{1,2}$ 6.9, H-1), 4.33 (dd, 1 H, $J_{2,3}$ 2.4, H-2) and 3.75–4.04 (m, 8 H, H-3, -4, -5a, -5b, 2 × CH_2Ph); $\delta_C(CDCl_3)$ 25.3, 26.3, 26.9, 27.2, 109.6 and 110.3 (2 × Me_2C), 35.0 and 35.5 (2 × CH_2Ph), 51.5 (C-1), 83.6 (C-2), 78.9 (C-3), 77.0 (C-4) and 67.5 (C-5) (Found: 65.25; H, 6.9. $C_{25}H_{32}O_4S_2$ requires C, 65.2; H, 6.95%).

Following the method of Wong and Gray[21] this protected arabinose derivative was converted to 2-deoxy-4,5-*O*-isopropylidene-L-*erythro*-pent-1-enose dibenzyl dithioacetal, which was reduced directly to give compound **2**. After chromatographic purification on silica gel, compound **2** was obtained as a syrup (75% over two steps); R_f 0.45 (hexanes–Et_2O, 1:1); $[\alpha]_D^{23}$ +12.5 (*c* 0.9, $CHCl_3$); $\delta_H(CDCl_3)$ 1.30 and 1.37 (2 s, 6 H, 2 × Me), 1.805 (m, 1 H, $J_{1,2a}$ 5.5, $J_{2a,3}$ 9.2, $J_{2a,2b}$ 14.6, H-2a), 1.91 (m, 1 H, $J_{1,2b}$ 9.2, $J_{2b,3}$ 2.9, H-2b), 3.7–3.9 (m, 9 H, H-1, -3, -4, -5a, -5b and 2 × CH_2Ph) and 2.28 (d, 1 H, 3-OH); $\delta_C(CDCl_3)$ 25.2, 26.5 and 109.1 (Me_2C), 34.5 and 35.1 (2 × CH_2Ph), 47.2 (C-1), 38.5 (C-2), 69.5 (C-3), 78.0 (C-4) and 65.4 (C-5) (Found: C, 65.4; H, 7.2. $C_{22}H_{28}O_3S_2$ requires C, 65.3; H, 6.9%).

3-*O*-Benzoyl-2-deoxy-4,5-*O*-isopropylidene-L-*threo*-pentose dibenzyl dithioacetal 3 and 3-azido-2,3-dideoxy-4,5-*O*-isopropylidene-L-*threo*-pentose dibenzyl dithioacetal 4

Diisopropyl azodicarboxylate (11.6 ml, 59.4 mmol) was added to a vigorously stirred solution of triphenylphosphine (15.6 g, 59.4 mmol) in anhydrous toluene (200 ml) at 0 °C. After 30 min at this temperature a precipitate was formed. A solution of compound **2** (12.0 g, 29.7 mmol) and benzoic acid (7.2 g, 59.4 mmol) in anhydrous toluene (50 ml) was added dropwise over a period of 10 min. Stirring was continued for 2 h at 0 °C and for 1 h at room temperature. The clear yellow solution was concentrated under reduced pressure to a syrup. This residue was chromatographed on a silica gel column (hexanes–Et_2O, 19:1) to give *compound* **3** as a syrup (10.5 g, 75%): R_f 0.75 (hexanes–Et_2O, 1:1); $[\alpha]_D^{23}$ +16.5 (*c* 1.6, $CHCl_3$); $\delta_H(CDCl_3)$ 3.54 (dd, 1 H, $J_{1,2a}$ 9.0, $J_{1,2b}$ 6.1, H-1), 2.11 (m, 1 H, $J_{2a,3}$ 4.4, H-2a), 2.31 (m, 1 H, $J_{2b,3}$ 8.7, $J_{2a,2b}$ 14.6, H-2b), 5.37 (m, 1 H, H-3), 3.91 (m, 1 H, $J_{3,4}$ 3.3, H-4), 3.65 (m, 1 H, $J_{4,5a}$ 5.8, $J_{5a,5b}$ 8.4, H-5a), 3.85 (m, 1 H, $J_{4,5b}$ 6.7, H-5b) and 3.73–3.80 (m, 4 H, 2 × CH_2Ph); $\delta_C(CDCl_3)$ 25.2, 26.2 and 109.5 (Me_2C), 34.6 and 34.9 (2 × CH_2Ph), 46.0 (C-1), 36.5 (C-2), 70.9 (C-3), 75.7 (C-4), 65.3 (C-5) and 165.7 (CO) (Found: C, 68.3; H, 6.5. $C_{29}H_{32}O_4S_2$ requires C, 68.5; H, 6.3%).

The analogous azido derivative 4 was obtained using the procedure described previously[13] using the complex[23] $Zn(N_3)_2{\cdot}(C_5H_5N)_2$. The crude material was chromatographed on silica gel (hexanes–Et_2O, 9:1) to give *azide* 4 as a pale yellow syrup (75%); R_f 0.67 (hexanes–ether, 1:1); $[\alpha]_D^{23}$ −12.3 (*c* 1.6, $CHCl_3$); $\delta_H(CDCl_3)$ 3.65 (dd, 1 H, $J_{1,2a}$ 10.0, $J_{1,2b}$ 5.0, H-1), 1.68 (m, 1 H, $J_{2a,3}$ 4.0, $J_{2a,2b}$ 14.4, H-2a), 1.87 (m, 1 H, $J_{2b,3}$ 9.8, H-2b), 3.37 (m, 1 H, $J_{3,4}$ 5.5, H-3), 3.51 (m, 1 H, H-5a) and 3.78 (m, 6 H, H-4, -5b and 2 × CH_2Ph); $\delta_C(CDCl_3)$ 24.2, 25.4 and 108.9 (Me_2C), 33.6 and 34.4 (2 × CH_2Ph), 46.2 (C-1), 35.9 (C-2), 60.0 (C-3), 76.5 (C-4) and 65.1 (C-5) (Found: C, 61.3; H, 6.3; N, 9.4. $C_{22}H_{27}N_3O_2S_2$ requires C, 61.5; H, 6.3; N, 9.8%).

3-*O*-Benzoyl-2-deoxy-L-*threo*-pentose dibenzyl dithioacetal 5 and 3-azido-2,3-dideoxy-L-*threo*-pentose dibenzyl dithioacetal 6

A suspension of Amberlyst resin (15 Wet) (25 g) in a solution of compound **3** (10.0 g, 19.7 mmol) in ethanol (150 ml) was stirred for 12 h at 50 °C. After removal of the resin the residue was concentrated under reduced pressure and then chromatographed on silica gel (hexanes–acetone, 4:1) to give *compound* **5** as a viscous syrup (8.3 g, 90%); R_f 0.75 (hexanes–acetone, 2:3); $[\alpha]_D^{23}$ −18.3 (*c* 0.3, $CHCl_3$) $\delta_H(CDCl_3)$ 3.7–3.9 (m, 6 H, H-1, -4 and 2 × CH_2Ph), 1.84 (m, 1 H, $J_{1,2a}$ 9.3, $J_{2a,3}$ 3.2, $J_{2a,2b}$ 14.5, H-2a), 2.08 (m, 1 H, $J_{1,2b}$ 5.5, $J_{2b,3}$ 9.3, H-2b), 5.38 (m, 1 H, $J_{3,4}$ 3.6, H-3), 4.26 (m, 1 H, $J_{4,5a}$ 6.5, $J_{5a,5b}$ 11.5, H-5a) and 4.32 (m, 1 H, $J_{4,5b}$ 5.0, H-5b); $\delta_C(CDCl_3)$ 34.6 and 35.1 (2 × CH_2Ph), 47.3 (C-1), 39.1 (C-2), 69.1 (C-3), 70.0 (C-4), 66.1 (C-5) and 166.7 (CO) (Found: C, 66.6; H, 6.0. $C_{26}H_{28}O_4S_2$ requires C, 66.7; H, 6.0%).

In the same way azide 4 (10.0 g, 23.3 mmol) was converted to compound **6**. The crude material was chromatographed on silica gel (hexanes–acetone, 4:1) to give *title compound* **6** as a syrup (8.15 g, 90%); R_f 0.51 (Et_2O); $[\alpha]_D^{23}$ +35.2 (*c* 1.2, $CHCl_3$); $\delta_H(CDCl_3)$ 3.65 (m, 1 H, H-1), 1.89 (m, 1 H, $J_{1,2a}$ 9.3, $J_{2a,3}$ 5.8, $J_{2a,2b}$ 14.5, H-2a), 2.07 (m, 1 H, $J_{1,2b}$ 5.7, $J_{2b,3}$ 8.9, H-2b), 3.55 (m, 1 H, H-3), 3.32 (m, 1 H, H-4), 3.5 (m, 2 H, H-5a and -5b) and 3.8 (m, 4 H, 2 × CH_2Ph); $\delta_C(CDCl_3)$ 33.6 and 34.3 (2 × CH_2Ph), 46.6 (C-1), 35.9 (C-2), 60.6 (C-3), 72.7 (C-4) and 62.9 (C-5) (Found: C, 58.4; H, 6.3; N, 10.1. $C_{19}H_{23}N_3O_2S_2$ requires C, 58.6; H, 5.95; N, 10.8%).

3,5-Di-*O*-benzoyl-2-deoxy-L-*threo*-pentose dibenzyl dithioacetal 7 and 3-azido-5-*O*-benzoyl-2,3-dideoxy-L-*threo*-pentose dibenzyl dithioacetal 8

A solution of benzoyl chloride (2.1 g, 16.5 mmol) in $CHCl_3$ (5 ml) was added to a solution of compound **5** (7.0 g, 14.9 mmol) in pyridine (30 ml) at −10 °C. The mixture was stirred for 4 h at 0 °C, then was poured into ice–water and extracted with CH_2Cl_2. The organic phase was washed sequentially with HCl (0.1 M) and water, then dried (Na_2SO_4), concentrated under reduced pressure, and chromatographed on silica gel (hexanes–Et_2O, 4:1) to give *title compound* **7** as a solid (6.0 g, 70%); R_f 0.45 (hexanes–Et_2O, 1:1); mp 107–108 °C; $[\alpha]_D^{23}$ +6.1 (*c* 0.3, $CHCl_3$); $\delta_H(CDCl_3)$ 3.58 (dd, 1 H, $J_{1,2a}$ 9.2, $J_{1,2b}$ 5.8, H-1), 2.23 (m, 1 H, $J_{2a,3}$ 4.6, $J_{2a,2b}$ 14.5, H-2a), 2.38 (m, 1 H, $J_{2b,3}$ 8.4, H-2b), 5.48 (m, 1 H, $J_{3,4}$ 3.5, H-3), 3.83 (m, 1 H, H-4) and 4.30 (d, 2 H, $J_{4,5}$ 5.1, H-5a and -5b); $\delta_C(CDCl_3)$ 34.5 and 34.9 (2 × CH_2Ph), 46.2 (C-1), 36.1 (C-2), 72.3 (C-3), 70.4 (C-4), 66.0 (C-5) and 165.9 and 166.6 (2 × CO) (Found: C, 69.5; H, 5.7. $C_{33}H_{32}O_5S_2$ requires C, 69.35; H, 5.6%).

Compound **6** (10.0 g, 25.7 mmol) was benzoylated similarly at −10 °C and the crude product was chromatographed on silica gel (hexanes–ether, 9:1) to give *azide* **8** as a syrup (10.2 g, 80%); R_f 0.43 (hexanes–Et_2O, 1:1); $[\alpha]_D^{23}$ +41.6 (*c* 2.1, $CHCl_3$); $\delta_H(CDCl_3)$ 3.63 (m, 3 H, H-1, -3 and -4), 1.97 (m, 1 H, $J_{1,2a}$ 9.2, $J_{2a,3}$ 5.0, $J_{2a,2b}$ 14.2, H-2a), 2.05 (m, 1 H, $J_{1,2b}$ 6.8, $J_{2b,3}$ 8.6, H-2b), 4.26 (m, 2 H, H-5a and -5b) and 3.79 (m, 4 H, 2 × CH_2Ph); $\delta_C(CDCl_3)$ 34.5 and 35.2 (2 × CH_2Ph), 47.1 (C-1), 36.6 (C-2), 61.3 (C-3), 71.7 (C-4), 66.4 (C-5) and 166.6 (CO) (Found: C, 63.5; H, 5.5; N, 8.2. $C_{26}H_{27}N_3O_3S_2$ requires C, 63.3; H, 5.5; N, 8.5%).

3,5-Di-*O*-benzoyl-2-deoxy-4-*O*-mesyl-L-*threo*-pentose dibenzyl dithioacetal 9 and 3-azido-5-*O*-benzoyl-2,3-dideoxy-4-*O*-mesyl-L-*threo*-pentose dibenzyl dithioacetal 10

Methanesulfonyl chloride (0.3 g, 2.6 mmol) was added, dropwise, to a stirred solution of compound **7** (1.0 g, 1.74 mmol) in dichloromethane (10 ml) and triethylamine (1 ml) at 0 °C. The reaction mixture was maintained at 0 °C for 30 min, and at room temperature for 2 h, then was poured into cold water. The organic phase was washed with water, dried ($NaSO_4$), and concentrated under reduced pressure. The residue was chromatographed on silica gel to give dibenzoate **9** as a syrup (1.08 g, 95%); R_f 0.45 (hexanes–Et_2O, 1:1); $[\alpha]_D^{23}$ −22.1 (*c* 2.5, $CHCl_3$); $\delta_H(CDCl_3)$ 3.48 (dd, 1 H, $J_{1,2a}$ 9.6, $J_{1,2b}$ 5.3, H-1), 2.07 (m, 1 H, $J_{2a,3}$ 3.5, $J_{2a,2b}$ 14.5, H-2a), 2.27 (m, 1 H, $J_{2b,3}$ 9.2, H-2b), 5.58 (m, 1 H, H-3), 4.88 (m, 1 H, H-4), 4.25 (d, 1 H, $J_{4,5a}$ 7.4, $J_{5a,5b}$ 12.5, H-5a), 4.39 (m, 1 H, $J_{4,5b}$ 3.4, H-5b), 2.82 (s, 3 H, Me) and 3.75–3.9 (m, 4 H, 2 × CH_2Ph); $\delta_C(CDCl_3)$ 34.5 and 34.9 (2 × CH_2Ph), 38.7 (Me), 46.2 (C-1), 36.3 (C-2), 69.9 (C-3), 78.5 (C-4), 63.1 (C-5) and 165.2 and 165.6 (2 × CO). This mesyl ester was not very stable and was used directly for the next step.

Compound **8** (10.0 g, 20.3 mmol) was mesylated by exactly the same method to give azide **10** as a syrup (9.2 g, 80%); R_f 0.33 (hexanes–Et_2O, 1:1); $[\alpha]_D^{23}$ −41.6 (*c* 2.3; $CHCl_3$); $\delta_H(CDCl_3)$ 3.74 (dd, 1 H, $J_{1,2a}$ 9.0, $J_{1,2b}$ 5.8, H-1), 1.91 (m, 1 H, $J_{2a,3}$ 3.5, $J_{2a,2b}$ 14.5, H-2a), 1.96 (m, 1 H, $J_{2b,3}$ 9.2, H-2b), 3.86 (m, 1 H, H-3), 4.67 (m, 1 H, H-4), 4.34 (d, 1 H, $J_{4,5a}$ 6.8, $J_{5a,5b}$ 12.1, H-5a), 4.45 (m, 1 H, $J_{4,5b}$ 3.6, H-5b), 3.02 (s, 3 H, Me) and 3.82 (m, 4 H, 2 × CH_2Ph); $\delta_C(CDCl_3)$ 34.2 and 35.2 (2 × CH_2Ph), 38.8 (Me), 47.2 (C-1), 36.5 (C-2), 59.7 (C-3), 79.8 (C-4), 63.3 (C-5) and 165.8 (CO). This compound was also unstable and hence was not analysed but used directly for the next step.

Benzyl 3,5-di-*O*-benzoyl-2-deoxy-1,4-dithio-α,β-D-*erythro*-pentofuranoside 11 and benzyl 3-azido-5-*O*-benzoyl-2,3-dideoxy-1,4-dithio-α,β-D-*erythro*-pentofuranoside 12

$BaCO_3$ (0.24 g, 1.2 mmol) and TBAI (0.45 g, 1.2 mmol) were added to a solution of compound **9** (0.4 g, 0.6 mmol) in dry HMPA or DMF (5 ml) and the mixture was stirred for 4 h at 100 °C, then was cooled, filtered, and then the filtrate was poured into ice-cold water and extracted with diethyl ether. The organic phase was washed with water, dried (Na_2SO_4), and concentrated under reduced pressure. The

residue was chromatographed on silica gel (hexanes–ether, 9:1) to give dibenzoate **11** as a syrup (9.5 g, 70%), α:β ratio 1:6 (NMR).

Alternatively chlorodiphenylphosphine (2.5 ml, 13.98 mmol), imidazole (1.42 g, 20.97 mmol), iodine (3.54 g, 13.98 mmol) and compound **7** (2.0 g, 3.49 mmol) were stirred in dry acetonitrile (165 ml) at room temperature for 15 min and the reaction mixture was then concentrated to a syrup. This residue was taken up in CH_2Cl_2 and this organic phase was washed (10% aq. sodium hydrogensulfite, then water) and dried ($MgSO_4$) and concentrated to a syrup. Chromatography of the residue (toluene) gave two components. The first compound was an impure sample of the intermediate, 3,5-di-*O*-benzoyl-2-deoxy-4-iodo-D-*erythro*-pentose dibenzyl dithioacetal, obtained as a yellow gum (0.26 g, 11%); R_f 0.33 (toluene); $\delta_H(CDCl_3)$ 3.58 (dd, 1 H, $J_{1,2a}$ 10.7, $J_{1,2b}$ 4.1, H-1), 2.14 (m, 1 H, $J_{2b,3}$ 2.7, $J_{2a,2b}$ 14.8, H-2a), 2.47 (m, 1 H, $J_{2b,3}$ 9.8, H-2b), 5.16 (m, 1 H, $J_{3,4}$ 3.4, H-3), 4.62 (m, 1 H, H-4), 4.39 (m, 1 H, H-5a), 4.58 (m, 1 H, H-5b), 3.69 and 3.78 (ABq, 2 H, *J* 13.4, CH_2Ph) and 3.80 (s, 2 H, CH_2Ph); $\delta_C(CDCl_3)$ 34.4 and 35.2 (2 × CH_2Ph), 45.9 (C-1), 39.0 (C-2), 71.3 (C-3), 30.9 (C-4), 66.2 (C-5) and 165.2 and 165.6 (2 × CO).

The second component was compound **11**, obtained as a solid (1.2 g, 74%), mp 96–97 °C, α:β ratio 1:6 (NMR); R_f 0.26 (toluene) (Found: C, 66.9; H, 5.1. $C_{26}H_{24}O_4S_2$ requires C, 67.2; H, 5.2%). This anomeric mixture could not be effectively separated by further chromatography and the NMR data were obtained from the mixture; β-anomer (**11β**) $\delta_H(CDCl_3)$ 4.50 (dd, 1 H, $J_{1,2a}$ 8.2, $J_{1,2b}$ 5.9, H-1), 2.34 (m, 1 H, $J_{2a,3}$ 4.4, $J_{2a,2b}$ 13.7, H-2a), 2.44 (m, 1 H, $J_{2b,3}$ 4.0, H-2b), 5.70 (m, 1 H, $J_{3,4}$ 2.8, H-3), 3.84 (m, 1 H, $J_{4,5a}$ 8.5, $J_{4,5b}$ 6.0, H-4), 4.35 (m, 1 H, $J_{5a,5b}$ 11.5, H-5a) and 4.42 (m, 1 H, H-5b); $\delta_C(CDCl_3)$ 36.9 (CH_2Ph), 52.2 (C-1), 41.4 (C-2), 78.6 (C-3), 49.8 (C-4), 66.0 (C-5) and 165.5 and 166.1 (2 × CO); α-anomer (**11α**) $\delta_H(CDCl_3)$ 3.8 (s, 2 H, CH_2Ph), 4.43 (dd, 1 H, $J_{1,2a}$ 4.2, $J_{1,2b}$ 7.4, H-1), 2.30 (m, 1 H, $J_{2a,3}$ 4.3, $J_{2a,2b}$ 14.3, H-2a), 2.70 (m, 1 H, $J_{2b,3}$ 5.3, H-2b), 5.57 (m, 1 H, H-3), 4.05 (m, 1 H, $J_{3,4}$ 4.0, $J_{4,5a} = J_{4,5b}$ = 7.0, H-4) and 4.35 (d, 2 H, H-5a and -5b); $\delta_C(CDCl_3)$ 37.6 (CH_2Ph), 52.1 (C-1), 41.6 (C-2), 78.2 (C-3), 49.9 (C-4) and 65.4 (C-5).

In a similar way compound **10** (7.6 g, 13.4 mmol) was converted to compound **12**. After chromatography on silica gel (hexanes–ether, 9:1), azide **12** was obtained as a syrupy mixture of anomers (3.32 g, 65%) (α:β ratio 1:6) [although this anomeric mixture contained no impurities by NMR it would not give acceptable results for elemental analysis]. This anomeric mixture could not be effectively separated by chromatography but the mixture gave the following data: β-anomer (**12β**): $\delta_H(CDCl_3)$ 4.3–4.50 (m, 4 H, H-1, -3, -5a and -5b), 2.33 (m, 1 H, $J_{1,2a} = J_{2a,3}$ = 5.4, $J_{2a,2b}$ 13.8, H-2a), 2.39 (m, 1 H, $J_{1,2b}$ 6.2, $J_{2b,3}$ 6.2, H-2b), 3.66 (m, 1 H, H-4) and 3.83 (s, 2 H, CH_2Ph); $\delta_C(CDCl_3)$ 36.4 (CH_2Ph), 48.3 (C-1), 40.7 (C-2), 64.8 (C-3), 50.4 (C-4), 65.2 (C-5) and 166.0 (CO). α-anomer (**12α**): $\delta_H(CDCl_3)$ 4.3–4.50 (m, 4 H, H-1, -3, -5a and -5b), 2.16 (m, 1 H, $J_{1,2a}$, $J_{2a,3}$ 6.9, 7.2 and $J_{2a,2b}$ 13.6, H-2a), 2.63 (m, 1 H, $J_{1,2b}$, $J_{2b,3}$ 5.6, 6.7, H-2b), 4.00 (m, 1 H, H-4) and 3.86 (s, 2 H, CH_2Ph); $\delta_C(CDCl_3)$ 37.1 (CH_2Ph), 48.3 (C-1), 41.4 (C-2), 65.3 (C-3), 51.4 (C-4), 64.8 (C-5) and 166.0 (CO).

1-*O*-Acetyl-3,5-di-*O*-benzoyl-2-deoxy-4-thio-α,β-D-*erythro*-pentofuranose 13 and 1-*O*-acetyl-3-azido-5-*O*-benzoyl-2,3-dideoxy-4-thio-α,β-D-*erythro*-pentofuranose 14

A solution of compound **11** (2.5 g, 4.95 mmol) and mercury(II) acetate (3.95 g, 12.4 mmol) in glacial acetic acid (50 ml) was stirred for 2 h at room temperature. The mixture was poured into ice-cold water, and extracted with CH_2Cl_2 (2 × 100 ml). The extract was washed successively with saturated aq. Na_2CO_3 and water, then dried (Na_2SO_4), and concentrated under reduced pressure. The crude material was chromatographed on silica gel (hexanes–Et_2O, 2:3) to give an anomeric mixture, α:β ratio 1:1 (NMR) (Found: C, 63.3; H, 4.9. $C_{21}H_{20}O_6S$ requires C, 63.0; H, 5.0%).

This mixture of anomers was carefully rechromatographed (hexanes–Et_2O, 4:1 then 2:3) to give the separate anomers. The first fraction, with R_f 0.47 (hexanes–Et_2O, 1:1), identified as the α-*anomer* **13α**, was a solid (0.94 g, 44%), mp 125–126 °C, $[\alpha]_D^{23}$ −105 (*c* 1.2, $CHCl_3$); $\delta_H(CDCl_3)$ 2.00 (s, 3 H, COMe), 6.10 (dd, 1 H, $J_{1,2a}$ 5.7, $J_{1,2b}$ 2.8, H-1), 2.46 (m, 1 H, $J_{2a,3}$ 7.8, $J_{2a,2b}$ 13.8, H-2a), 2.70 (m, 1 H, $J_{2b,3}$ 5.4, H-2b), 5.75 (m, 1 H, H-3), 3.88 (m, 1 H, $J_{3,4}$ 5.9, $J_{4,5a}$ 6.0, $J_{4,5b}$ 7.5, H-4), 4.42 (m, 1 H, $J_{5a,5b}$ 11.5, H-5a) and 4.50 (m, 1 H, H-5b); $\delta_C(CDCl_3)$ 21.1 (CO*Me*), 77.3 (C-1), 40.6 (C-2), 79.0 (C-3), 50.1 (C-4), 65.9 (C-5), 165.7 and 166.1 (2 × *C*OPh) and 170.3 (*C*OMe). The fraction with R_f 0.39 (hexanes–Et_2O, 1:1), identified as the β-*anomer* **13β** was a solid (0.88 g, 41%), mp 79–80 °C; $[\alpha]_D^{23}$ +203 (*c* 2.0, $CHCl_3$); $\delta_H(CDCl_3)$ 1.96 (s, 3 H, COMe), 6.22 (dd, 1 H, $J_{1,2a}$ 5.6, $J_{1,2b}$ 1.6, H-1), 2.53 (m, 1 H, $J_{2a,3}$ 4.3, $J_{2a,2b}$ 15.1, H-2a), 2.62 (m, 1 H, $J_{2b,3}$ 2.2, $J_{2b,4}$ 0.78, H-2b), 5.71 (m, 1 H, H-3), 4.03 (m, 1 H, $J_{3,4}$ 1.7, H-4), 4.25 (m, 1 H, $J_{4,5a}$ 8.4, $J_{5a,5b}$ 11.6, H-5a) and 4.34 (m, 1 H, $J_{4,5b}$ 6.0, H-5b); $\delta_C(CDCl_3)$ 21.1 and 170.3 (COMe), 81.1 (C-1), 40.1 (C-2), 78.3 (C-3), 52.3 (C-4), 65.1 (C-5) and 165.7 and 166.1 (2 × *C*OPh).

A similar reaction was carried out with compound **12** (0.82 g, 2.13 mmol). The crude product was chromatographed (hexanes–Et_2O, 1:1) to give an *anomeric mixture*, α:β ratio 1:1 (NMR) as a pale yellow oil (0.6 g, 80%) (Found: C, 52.0; H, 4.5; N, 12.8. $C_{14}H_{15}N_3O_4S$ requires C, 52.3; H, 4.7; N, 13.1%). This mixture of anomers was carefully rechromatographed (hexanes–Et_2O, 8:2) to give the separate anomers. The first fraction, with R_f 0.35 (hexanes–Et_2O, 1:1), identified as the α-*anomer* **14α**, was obtained as a pale yellow oil (0.25 g, 36%), $[\alpha]_D^{23}$ −167 (*c* 1.5, $CHCl_3$); $\delta_H(CDCl_3)$ 2.03 (s, 3 H, COMe), 6.06 (dd, 1 H, $J_{1,2a}$ 5.2, $J_{1,2b}$ 1.8, H-1), 2.36 (m, 1 H, $J_{2a,3}$ 10.4, $J_{2a,2b}$ 13.5, H-2a), 2.61 (m, 1 H, $J_{2b,3}$ 5.3, H-2b), 4.24 (m, 1 H, H-3), 3.65 (m, 1 H, $J_{3,4}$ 7.6, H-4), 4.46 (m, 1 H, $J_{4,5a}$ 6.0, $J_{5a,5b}$ 11.6, H-5a) and 4.61 (m, 1 H, $J_{4,5b}$ 6.4, H-5b); $\delta_C(CDCl_3)$ 21.1 and 170.0 (COMe), 78.5 (C-1), 41.4 (C-2), 64.6 (C-3), 50.4 (C-4), 65.5 (C-5) and 166.1 (*C*OPh). The second fraction, with R_f 0.30 (hexanes–Et_2O, 1:1), identified as the β-*anomer* **14β**, was obtained as a pale yellow oil (0.29 g, 43%), $[\alpha]_D^{23}$ +247 (*c* 1.6, $CHCl_3$); $\delta_H(CDCl_3)$ 2.01 (s, 3 H, COMe), 6.21 (dd, 1 H, $J_{1,2a}$ 2.5, $J_{1,2b}$ 5.3, H-1), 2.53 (m, 1 H, $J_{2a,3}$ 3.5, $J_{2a,2b}$ 14.5, H-2a), 2.59 (m, 1 H, $J_{2b,3}$ 5.1, H-2b), 4.29 (m, 1 H, H-3), 3.82 (m, 1 H, $J_{3,4}$ 2.9, H-4) and 4.30 (d, 1 H, $J_{4,5}$ 7.1, H-5); $\delta_C(CDCl_3)$ 21.1 and 170.4 (COMe), 80.2 (C-1), 39.2 (C-2), 64.8 (C-3), 52.0 (C-4), 64.9 (C-5) and 166.1 (*C*OPh).

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