Diastereoselective Free-radical Reactions. Part 1. Preparation of 2-Deoxy-β-glycosides by Synthesis and Reductive Decarboxylation of 3-Deoxyulosonic Acid Glycosides

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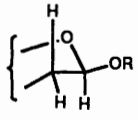
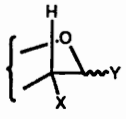
A general procedure for the synthesis of 2-deoxy-β-D-glycosides involving the preparation of 3-deoxyulosonic acid glycosides from glycals and their reductive decarboxylation is described.

The rational design and implementation of diastereoselective free-radical reactions represents a major challenge to organic chemists. We report here the details of a method for the preparation of 2-deoxy-β-D-glycosides in which the anomeric configuration is determined by diastereoselective hydrogen atom transfer to alkoxyglycos-1-yl radicals.[1,2]

2-Deoxy-β-glycosidic linkages (**1**) occur widely in Nature for example in the aureolic acid group of antitumor antibiotics;[3] the orthosomycin,[4] sporaviridin,[5] and angucycline[6] groups of antibiotics; in certain cardiac glycosides[7] and in the recently isolated antitumoral agents calicheamicin and esperamicin.[8] Synthesis of such glycosidic linkages,[9] an area of considerable current interest, is usually achieved with the aid of a glycosyl donor (**2**) bearing an equatorial substituent in the 2-position capable of providing anchimeric assistance in the glycosylation step. This auxiliary is then removed reductively in a subsequent reaction.



(1)



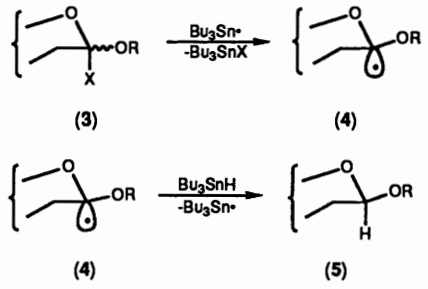
(2)

X = OAc, SPh, I, SePh, *etc.*
Y = Br, Cl, OC(=NH)CCl_3, F

Two general approaches can be identified: those corresponding essentially to a classical Koenigs–Knorr glycosylation and employing a glycosyl donor with an appropriately placed 2-substituent,[10,11] and those in which this stereodirecting entity is introduced in the course of the glycosylation reaction by addition across a glycal double bond.[12] The approach which we describe here is based on a fundamentally different concept in so far as it requires no stereodirecting auxiliary and consequently no further manipulation of the product after glycosylation.

Since the initial independent reports[13] of the Baldwin and Giese groups on the selective α-facial trapping of tetra-*O*-acetylglucos-1-yl radicals by both electron deficient alkenes and tributyltin deuteride considerable use has been made[14] in organic synthesis of simple furanosyl and pyranosyl radicals. Tetra-*O*-acetylmannos-1-yl radicals on the other hand are quenched from the β-face. This variation of stereoselectivity with configuration has been attributed[15] to the adoption, by the intermediate sp^2 hydridised glycosyl radicals, of conformations in which the singly occupied orbital is periplanar with and stabilised by interaction with the β-C–O bond. A similar effect of a β-C–O bond has been invoked to explain the migration, under certain conditions, of acetoxy groups in per-*O*-acetylglycosyl radicals.[16]

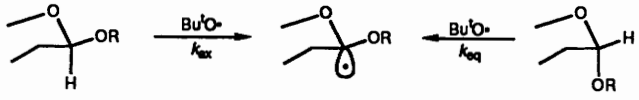
We were attracted to the idea, outlined in Scheme 1, of preparing β-glycosides by the reaction of an anomeric mixed orthoester (**3**) with tributyltin hydride, *via* a free-radical chain mechanism in which the intermediate 1-alkoxyglycos-1-yl radical (**4**) would be trapped from the axial direction giving the β-glycoside (**5**).



(3) (4) (4) (5)

Scheme 1. X = halogen, SPh, SePh, NO_2 *etc.*

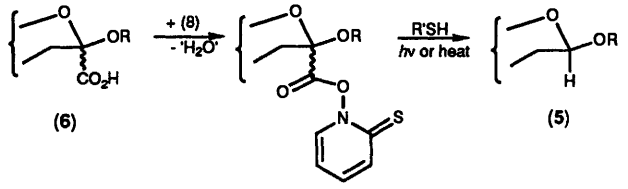
Reports[17] on the differing rates of hydrogen abstraction from *cis*-and *trans*-2-alkoxy-4-methyltetrahydropyan (Scheme 2) and related diastereoisomeric pairs, and more importantly on the σ-nature of the unique radical formed[18] with $g = 2.0029$ and $a_H = 28.92(1H)$ and 3.99(1H) with the single electron in the axial position were strongly supportive of this hypothesis. The stereochemical consequences of 1-alkoxyglycosyl radical chemistry should therefore be dominated by stereoelectronic effects at the anomeric centre and not by any substituents, or lack of substituents, at the 2-position.



Scheme 2. $k_{ax} = 8$, $k_{eq} = 1$ (relative rates of hydrogen abstraction by triplet benzophenone at ambient temperature).

Initially we turned our attention to the preparation of anomeric mixed orthoesters (**3**). A variety of approaches were investigated[19] but we were unable to isolate molecules of the general type (**3**), despite their observation[19] by ^{13}C NMR in various reaction mixtures [(**3**; X = SPh, R = $C_{10}H_{21}$), δ(C-1):111.6] owing to their presumed instability under the conditions employed. Subsequently Kahne *et al.* have been able to prepare and isolate compounds of the type (**3**; X = SMe, R = alkyl) [δ(C-1):108.7] by methylation of thionolactones followed by trapping of the intermediate oxathienium ions with alcohols;[2] an approach that we had investigated and abandoned[19,20] owing to poor reproducibility in the reaction of lactones[21] with Lawesson's reagent.

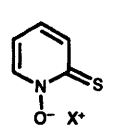
We were therefore constrained to look for an alternative source of 1-alkoxyglycosyl radicals (**4**) and were attracted to the possibility of their generation by radical decarboxylation of ulosonic acid glycosides by means of the Barton *O*-acyl thiohydroxamate chemistry.[22] The revised plan, outlined in Scheme 3, required the formation of *O*-acyl thiohydroxamates (**7**) of ulosonic acid glycosides (**6**) by their effective condensation with the thiohydroxamic acid (**8**) and their photochemical or thermal decarboxylation in the presence of a tertiary thiol.



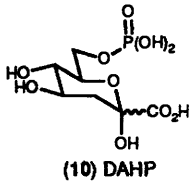
Scheme 3.

This scheme was particularly attractive in so far as various 3-deoxyulosonic acids (**10**)–(**13**) and their glycosides occur naturally and are both stable and isolable.[23]

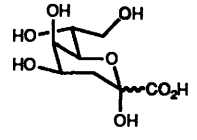
Initially, in order to test the compatibility of the ulosonic acid function with the thiohydroxamate chemistry, the sodium salt of an azeotropically dried sample of commercial 2,3:4,6-di-*O*-isopropylidene-2-keto-L-gulonic acid (**14**)[24] was treated with oxalyl chloride in benzene to give the corresponding chloride (**15**). This acyl chloride was treated with the sodium salt (**9**) of



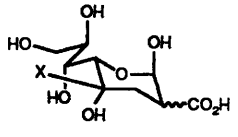
(**8**) X = H
(**9**) X = Na



(**10**) DAHP



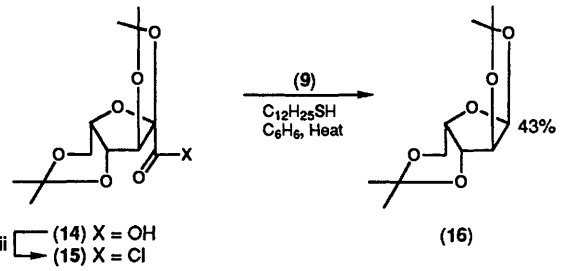
(**11**) KDO



(**12**) X = AcNH, NANA
(**13**) X = OH, KDN

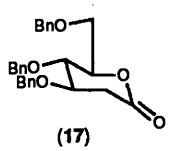
the thiohydroxamic acid (**8**) and t-dodecanethiol in benzene at reflux, leading after chromatographic work-up to the L-xylose derivative (**16**)[25] in 43% isolated yield (Scheme 4). We find that commercial t-dodecanethiol, a mixture of isomers and a convenient, cheap and relatively odourless thiol, is equally efficient in this reductive decarboxylation procedure as the previously recommended t-butanethiol[22] or triethylmethanethiol.[26]

Bearing in mind the eventual aim of a general 2-deoxy-β-glycoside synthesis it was essential that we develop a broadly applicable short and high-yielding method for the introduction of the carboxy group required as the radical precursor. None of the various literature syntheses[27] of ulosonic acids were thought to meet the criterion of generality; it was decided therefore to investigate methods of one-carbon homologation of pyranose derivatives. Initially, we studied the reaction of tris(methylthio)methyl-lithium[28] with the aldonolactone (**17**) prepared by oxidation of tri-*O*-benzyl-D-glucal (**20**) with pyridinium chlorochromate.[29] This approach was, however, abandoned owing to the complexity of the trithio-orthoester hydrolysis step, a problem also encountered by other workers.[30]

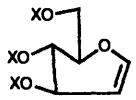


Scheme 4. *Reagents:* i, NaH; ii, $(COCl)_2$.

Attempts at the reaction of the glycosyl chloride (**21**) with sodium or mercuric cyanide in a variety of solvents also proved unsatisfactory; variable yields have been recorded by other workers for related systems.[31]

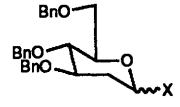


(**17**)



(**18**) X = H
(**19**) X = Ac
(**20**) X = Bn
Bn = CH_2Ph

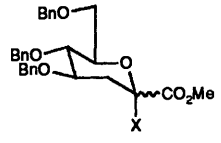
Eventually, encouraged both by the work of Ley[32] and Beau[33] and by our own subsequent work with 2-arylsulphonyltetrahydroyrans[19] we turned to glycopyranosyl phenylsulphones as precursors to ulosonic acid derivatives. Thus benzylation of D-glucal (**18**), itself prepared by saponification of triacetyl-D-glucal (**19**) with a catalytic quantity of sodium methoxide in methanol,[34] with sodium hydride and benzyl chloride in dimethyl sulphoxide according[35] to Guthrie gave tri-*O*-benzyl-D-glucal (**20**) in high yield. Sequential treatment of (**20**) with hydrogen chloride in toluene, thiophenol and ethyldi-isopropylamine (Hunig's base) in dichloromethane, and eventually *m*-chloroperoxybenzoic acid (MCPBA) and solid sodium hydrogen carbonate in dichloromethane gave a 72% overall yield of the white crystalline glucopyranosyl phenyl sulphone (**22**)[33] as a 1:6 α:β mixture. Attempts at the direct addition of toluene-*p*-sulphinic acid to the glucal led to complex reaction mixtures. Deprotonation of (**22**) with lithium diisopropylamide (LDA) in tetrahydrofuran (THF) at −78 °C followed by quenching with dimethyl carbonate gave 73% of the sulphone ester (**29**) which we assign as the β-sulphone in accordance with the work of Ley[32] in a related series. Somewhat surprisingly, methyl cyanoformate (Mander's reagent)[36] failed to yield any (**29**) on attempted reaction with the lithium salt of (**22**). Reductive desulphonylation of (**29**) with lithium naphthalenide in THF followed by quenching with methanol gave a 1:2 mixture of the esters (**23**) and (**24**) in 76% combined yield. In order to prepare a glycosyl donor the lithium salt of (**24**) was quenched with hexachloroethane leading to the unstable chloride (**30**) of unassigned anomeric configuration. Attempted purification of (**30**) by chromatography on silica gel resulted in decomposition. However it proved possible to prepare an *O*-methyl glycoside by treatment of crude (**30**) with silver(I) sulphate in methanol. In this manner an unassigned 5:1



(**21**) X = αβ-Cl
(**22**) X = αβ-SO_2Ph
(**23**) X = β-CO_2Me
(**24**) X = α-CO_2Me
(**25**) X = αβ-OMe
(**26**) X = αβ-OC_6H_4-4-Me
(**27**) X = αβ-*O*-3β-cholestanyl
(**28**) X = αβ-SPh

mixture of the methyl glycosides (**31**) and (**32**) was obtained in 30% overall yield from the ester (**23**). Attempted direct use of (**29**) as a glycosyl donor with activation by magnesium bromide, as advocated recently by Ley[37] for other glycopyranosyl sulphones, failed, probably due to the equatorial orientation of the sulphone entity.

Given the evident instability of the chloride (**30**) and the obvious preference for a stable isolable glycosyl donor we turned to thioglycosides. Although extensively employed as simple glycosyl donors it is only recently that their use has been extended to the ulosonic acids.[38] Treatment of (**24**) with LDA in THF at −78 °C followed by quenching with diphenyl disulphide gave a 30% yield of the methyl ulosonate thioglycosides (**33**) and (**34**). In a more expeditious procedure (**29**) was treated with two equivalents of lithium naphthalenide and



(**29**) X = β-SO_2Ph
(**30**) X = αβ-Cl
(**31**)† X = α-OMe
(**32**)† X = β-OMe
(**33**) X = α-SPh
(**34**) X = β-SPh
(**35**) X = αβ-OC_6H_4-4-Me
(**36**) X = αβ-OAc
(**37**) X = αβ-O-3β-cholestanyl

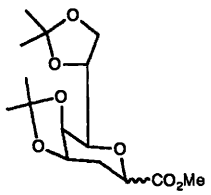
† Assignments may be reversed.

subsequently diphenyl disulphide to give a 1:1.6 ratio of (**33**) and (**34**) in 62% isolated yield. Both isomers were stable to silica gel chomatography and the major one was obtained in crystalline form from methanol. The observation of a nuclear Overhauser effect (NOE) between the *ortho*-hydrogens of the phenylthio group and the 3β-hydrogen led us to assign the major isomer as the β-phenylthioglycoside (**34**). Supportive evidence is provided by the related work of Beau[33] involving reductive desulphonylation of the tris(t-butyldimethylsilyl) analogue of (**29**) and more especially by the work[39] of Claesson in which it was demonstrated, by a combination of chemical correlations and X-ray crystallography, that quenching of the lithium salt of the closely related ester (**38**) with a range of carbon electrophiles takes place from the β-face.

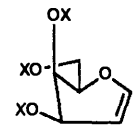
An even more efficient procedure for the preparation of compounds (**33**) and (**34**) involved sequential treatment of the sulphone (**22**) with LDA; dimethyl carbonate; lithium naphthalenide, and finally diphenyl disulphide resulting in a 75% isolated mixture of the two phenylthioglycosides. In this manner a mixture of (**33**) and (**34**) can be prepared *via* a simple two pot procedure from tri-*O*-benzyl-D-glucal (**20**) in good overall yield, in a minimum of time and with only a single chromatographic purification step. Although it is possible to separate (**33**) and (**34**) chromatographically this is unnecessary as the mixture serves equally well in the glycosylation reaction.

Having successfully developed a route to a stable 3-deoxyulosonate glycosyl donor in the *arabino*-series we then investigated its extension to the *lyxo*-series. D-Galactal (**39**)[40] was treated with an excess of t-butyldimethylsilyl chloride and imidazole in dimethylformamide according to the general procedure of Corey[41] giving an 86% yield of the persilyl-D-galactal (**40**). In common with Kinzy and Schmidt[42] we noted the relative difficulty of introducing the third silyl group.

Treatment of (**40**) with hydrogen chloride in toluene and subsequently with Hunig's base and thiophenol in dichloromethane gave a 76% yield of the phenylthioglycosides (**41**) rich in the β-anomer (α:β = 1:13.7). Alternatively, stirring of (**40**) and thiophenol over powdered molecular sieves in dichlormethane with 10 mol % of camphor-10-sulphonic acid gave a 15:1 α:β mixture of (**41**) in 60% yield. Oxidation of the



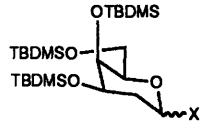
(**38**)

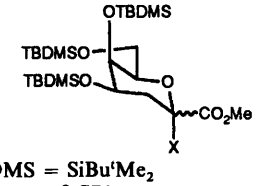


(**39**) X = H
(**40**) X = $SiBu^tMe_2$

former β-rich mixture with MCPBA in dichloromethane gave 67% of a 1:12 (α:β) mixture of the sulphones (**42**). The sulphones (**42**) were also obtained in 96% yield by oxidation of (**41**) with magnesium monoperoxyphthalate[43] in absolute ethanol.

An anomeric mixture of the sulphones (**42**) was then subjected sequentially to treatment with butyl-lithium; dimethyl carbonate; lithium naphthalenide and finally diphenyl disulphide giving a 1:8 α:β mixture of the thioglycosides (**46**) in 63% isolated yield. The major isomer was tentatively assigned the β-phenylthio configuration in accordance with the *arabino*-series (*vide supra*).

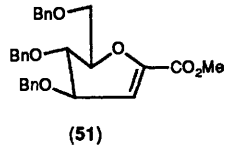




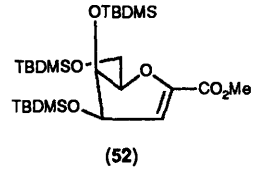
TBDMS = $SiBu^tMe_2$

(**41**) X = αβ-SPh
(**42**) X = αβ-SO_2Ph
(**43**) X = αβ-OMe
(**44**) X = αβ-O-C_6H_4-4-Me
(**45**) X = αβ-O-3β-cholestanyl
(**46**) X = αβ-SPh
(**47**) X = αβ-OMe
(**48**) X = αβ-OC_6H_4-4-Me
(**49**) X = αβ-O-3β-cholestanyl
(**50**) X = αβ-O-C_6H_{11}-c

Thioglycosides have been activated with a variety of mercuric salts,[44] copper salts,[45] *N*-bromosuccinimide (NBS),[46] nitrosyl tetrafluoroborate,[47] methyl trifluoromethanesulphonate,[48] and a variety of sulphenium[49] and selenenium[38] cation donors. For our part we have simply used mercuric salts and NBS to activate the thioglycosides (**33**), (**34**), and (**46**) towards coupling with some simple model alcohols. The results of the various coupling reactions undertaken are summarised in Table 1.



(**51**)



(**52**)

For the most part reaction mixtures were complex and coupling yields are only modest; no attempt was made to optimise conditions for coupling. A possible, although as yet unexplored, solution lies with the recently described methyl ulosonate fluorides.[50]

Finally we turned to the key reductive decarboxylation step. Saponification of the ester (**31**) gave 90% of the corresponding acid (**53**). Similarly the acid (**54**) was prepared by saponification of (**32**) in 86% yield. Repeated attempts at the formation of an acyl chloride from (**53**) and its sodium salt with oxalyl chloride and a catalytic amount of dimethylformamide were unsuccessful and thus it was decided to prepare the key *O*-acyl thiohydroxamate by coupling of (**53**) with (**8**) by means of dicyclohexylcarbodi-imide (DCC). In the event, stirring of (**53**) with a molar equivalent each of (**8**) and DCC in ether for 1 h at room temperature followed by filtration to remove the

Table 1.

Entry	Donor	Alcohol	Activating agent	Solvent	Products (% yield)
1	(**34**)	MeOH	NBS	MeOH	(**31**)(85)
2	(**33**) + (**34**)(1:1.62)	MeOH	$Hg(OAc)_2$	MeOH	(**31**)(43) + (**32**)(18)
3	(**34**)	4-MeC_6H_4OH	$HgCl_2$	CH_2Cl_2	(**35**)(47) + (**51**)(18)
4	(**34**)	4-MeC_6H_4OH	$Hg(OAc)_2$	CH_2Cl_2	(**35**)(18) + (**36**)(62)
5	(**33**)	3β-Cholestanol	NBS	CH_2Cl_2	(**37**)(25)
6	(**46**)	MeOH	$Hg(OAc)_2$	MeOH	(**47**)(67)
7	(**46**)	4-MeC_6H_4OH	$HgCl_2$	CH_2Cl_2	(**48**)(54)
8	(**46**)	3β-Cholestanol	NBS	CH_2Cl_2	(**49**)(39)
9	(**46**)	c-$C_6H_{11}OH$	NBS	CH_2Cl_2	(**50**)(29) + (**52**)(35)

Table 2.

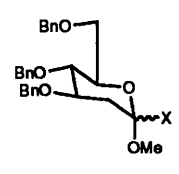
Entry	Methyl ulosonate	Method	Products (% yield)	α:β Ratio
1	(**53**)	DCC	(**25**)(36)*	1:10
2	(**53**)	(**55**)	(**25**)(40)*	1:10
3	(**35**)	DCC	(**26**)(12)	>5:95
4	(**37**)	(**55**)	(**27**)(50) + (**17**)(23)	1:11
5	(**47**)	(**55**)	(**43**)(55)	1:10
6	(**48**)	(**55**)	(**44**)(34)	1:16
7	(**49**)	(**55**)	(**45**)(44)	1:8
8	(**33**) + (**34**)	(**55**)	(**28**)(50)	1:8
9	(**46**)	(**55**)	(**41**)(48)	1:18

* Yields calculated from the isolated acid.

precipitated dicyclohexylurea gave, as anticipated,[22] a bright yellow solution. On addition of t-dodecanethiol and photolysis with a 500 W tungsten lamp at room temperature the 2-deoxyglucoside (**25**) was formed in 36% yield from (**53**) (Table 2, entry 1). The α:β ratio, as determined by ^1H NMR spectroscopy was 1:10 so vindicating the initial hypothesis that 2-deoxy-β-D-glycosides could be prepared by diastereofacial hydrogen atom transfer to the appropriate alkoxyglycosyl radicals.

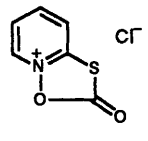
Although the DCC procedure for the generation of *O*-acylthiohydroxamates proved successful it has a major disadvantage in so far as filtration is required prior to photolysis. A solution to this experimental inconvenience was found in the thiohydroxamic acid derivative (**55**)[22] which couples directly with carboxylic acids without any external reagents being required. Thus, stirring of the triethylammonium salts of a mixture of (**53**) and (**54**) with (**55**) in a 1:1 mixture of dichloromethane and THF followed by addition of the thiol and photolysis gave 40% of (**25**) again as a 1:10 α:β mixture. Table 2 summarises the various reductive decarboxylations carried out and the anomeric ratios of the products obtained.

For all cases examined the α:β ratio is at least 1:8 and in several cases significantly higher, in good agreement with the results observed[2] by Kahne by the mixed orthoester method. It is also interesting to note (Table 2, entries 8 and 9) that 2-deoxy-β-thioglycosides can also be prepared by this method with good selectivity.



(**53**)† X = β-CO_2H
(**54**)† X = α-CO_2H

† Assignments could be reversed.



(**55**)

Evidently once the requirement for an improved coupling procedure is met the method outlined here presents we believe an attractive, conceptually different, approach to 2-deoxy-β-D-glycoside synthesis.

Experimental

M.p.s are uncorrected and were determined with a Kofler hot-stage microscope. Optical rotations were measured with an Optical Activity AA-10 polarimeter. IR spectra were recorded as chloroform solutions with a Perkin-Elmer 983 spectrophotometer. ^1H NMR spectra were obtained at 60, 200, or 400 MHz as deuteriochloroform solutions with JEOL PMX 60, Varian XL 200 and VXR 400 instruments respectively. Chemical shifts (δ) are in ppm downfield from tetramethylsilane as internal standard. All solvents were dried and distilled by standard techniques. Tetrahydrofuran (THF) was distilled under nitrogen from sodium benzophenone ketyl immediately prior to use. Ether refers to diethyl ether and petroleum to the fraction boiling in the range 40–60 °C.

1,2; 5,6-*Di*-O-*isopropylidene*-α-L-xylo-*furanose* (**16**).—Sodium hydride (80% in oil; 84 mg, 2.78 mmol) was added to a stirred solution of a sample of acid (**14**) previously dried by azeotropic distillation with benzene (381 mg, 1.39 mmol) in benzene (3 ml) at room temperature under a nitrogen atmosphere. When gas evolution had ceased (20 min) pyridine (2 drops) and subsequently oxalyl chloride (0.24 ml, 2.78 mmol) were added and the solution stirred at room temperature for 30 min. The solution of crude acid chloride so formed was then added dropwise under nitrogen to a stirred suspension of (**9**) (414 mg, 2.78 mmol) and t-dodecanethiol (0.654 ml, 2.78 mmol) in benzene (4 ml) at reflux. After 1 h at reflux the reaction mixture was allowed to cool to room temperature, filtered on Celite, and concentrated to give an oil which was purified by chromatography on silica gel [eluant ether–petroleum (35:65)] to give the title compound (**16**) (137 mg, 43%) as a white crystalline solid with m.p. 39–40 °C [lit.,[25] 43–45 °C (corrected); for D-enantiomer[51] 39–41 °C (uncorrected)] (Found: $M - Me^+$, 215.0903. Calc. for $C_{10}H_{15}O_5$: 215.0919); δ(200 MHz) 1.33 (3 H, s), 1.39 (3 H, s), 1.45 (3 H, s), 1.50 (3 H, s), 4.03 (1 H, m), 4.09 (2 H, m), 4.30 (1 H, d, *J* 2.47 Hz, 3-H), 4.52 (1 H, d, *J* 3.63 Hz, 2-H), and 6.01 (1 H, d, *J* 3.63 Hz, 1-H).

Phenyl 3,4,6-*Tri*-O-*benzyl*-2-*deoxy*-1-*sulphonyl*-αβ-D-arabino-*pyranoside* (**22**).—A stream of hydrogen chloride was passed into a stirred solution of compound (**20**)[35] (10.0 g, 24 mmol) in dry toluene (30 ml) at 0 °C for 10 min. After a further 10 min, the solvent was evaporated under reduced pressure and the oily residue of (**21**) taken up in dichloromethane (25 ml) and treated at room temperature with thiophenol (3.70 ml, 36 mmol) and then Hunig's base (6.27 ml, 36 mmol). After being stirred for 1 h at room temperature the solution was washed successively with 2M aqueous potassium hydroxide (50 ml), 2M hydrochloric

acid (50 ml), water (50 ml), and brine (50 ml), dried ($MgSO_4$), and concentrated to give the crude sulphide (**28**). The reaction mixture was dissolved in dichloromethane (30 ml) and treated with sodium hydrogen carbonate (4.84 g, 57 mmol) and subsequently with a solution of *m*-chloroperoxybenzoic acid (11.7 g, 57.6 mmol) in dichloromethane (100 ml) with stirring at 0 °C over 30 min. After being stirred for a further 90 min, the solution was filtered and concentrated under reduced pressure to give the crude sulphone. Crystallisation of this from methanol afforded the sulphone (**22**)[33] as a white microcrystalline solid as a 1:6 α:β mixture of anomers with m.p. 94–97 °C; $\bar{\nu}_{max}$ 3 025, 2 858, 1 601, 1 585, 1 495, 1 448, 1 361, 1 321, 1 311, 1 147, 1 111, and 1 077 cm^{-1}; δ(200 MHz) β-anomer: 1.71 (1 H, dt, *J* 12 and 11 Hz, 2ax.-H), 2.72 (1 H, ddd, *J* 11, 5 and 2.1 Hz, 2eq.-H), 3.35–3.75 (5 H, m), 4.39 (1 H, dd, *J* 12 and 2.1 Hz, 1-H), 4.44–4.76 (5 H, m), 4.86 (1 H, d, *J* 11 Hz), 7.19–7.37 (15 H, m), 7.47 (2 H, m), 7.59 (1 H, m), and 7.92 (2 H, m); α-anomer had 4.82 (1 H, dd, *J* 6.9 and 3.2 Hz, 1-H).

Methyl [*Phenyl* 4,5,7-*Tri*-O-*benzyl*-3-*deoxy*-2-*sulphonyl*-β-D-arabino-2-*heptulopyranoside*]*onate* (**29**).—A stirred solution of (**22**) (5.00 g, 8.95 mmol) in THF (10 ml) at −70 °C under nitrogen was treated with 1M LDA in THF (10.74 ml, 10.74 mmol). After 15 min dimethyl carbonate (0.98 ml, 11.63 mmol) was added dropwise and the reaction mixture allowed to warm to room temperature over 1 h. The reaction was quenched with saturated aqueous ammonium chloride (10 ml) and brine (50 ml) and extracted with ether (2 × 30 ml). The combined extracts were washed with dilute hydrochloric acid and brine and dried ($MgSO_4$). After removal of the volatiles chromatography of the residue on silica gel [eluant petroleum–ether (1:1)] provided the *sulphone ester* (**29**) as a colourless gum (4.04 g, 73%) which crystallised from ether as needles, m.p. 88 °C;[52] $[\alpha]_D^{30}$ +56° (*c* 2, $CHCl_3$); $\bar{\nu}_{max}$ 3 025, 2 938, 2 860, 1 738, 1 585, 1 492, 1 448, 1 361, 1 308, 1 141, 1 101, 1 074, 907, and 603 cm^{-1}; δ(200 MHz) 2.90–2.93 (2 H, m, 2 2-H), 3.39 (3 H, s, CO_2Me), 3.54 (1 H, dd, *J* 9.69 and 2.54 Hz), 3.68–3.73 (2 H, m, 2 6-H), 4.05 (1 H, m), 4.34–4.70 (7 H, m), 7.16–7.42 (17 H, m), 7.61 (1 H, m), and 7.90 (2 H, m) (Found: C, 68.5; H, 5.85. $C_{35}H_{36}O_8S$ requires C, 68.12; H, 5.88%).

Methyl [4,5,7-*Tri*-O-*benzyl*-2,3-*dideoxy*-β-D-arabino-2-*heptulopyranosid*]*onate* (**23**) *and Methyl* [4,5,7-*Tri*-O-*benzyl*-2,3-*dideoxy*-α-D-arabino-2 *heptulopyranosid*]*onate* (**24**).—A solution of sulphone ester (**29**) (0.719 g, 1.16 mmol) in THF (15 ml) at −75 °C under N_2 was treated with 1M lithium naphthalenide (2.4 ml, 2.4 mmol) dropwise over 1 min. After 5 min methanol (0.5 ml) was added to the brown solution. The reaction mixture was then allowed to warm to 0 °C after which it was poured onto water (50 ml) and extracted with ether (3 × 20 ml). The combined extracts were washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the crude residue on silica gel [eluant: ether–petroleum (1:1)] gave first the α-*ester* (**24**) as a colourless syrup (282 mg, 51%) with $[\alpha]_D^{30}$ +44° (*c* 2, $CHCl_3$); $\bar{\nu}_{max}$ 3 059, 3 025, 2 919, 2 865, 1 735, 1 601, 1 491, 1 444, 1 358, 1 231, 1 197, 1 111, 1 074, 1 027, 994, 843, and 817 cm^{-1}; δ(200 MHz) 1.88 (1 H, m, 2ax.-H), 2.56 (1 H, m, 2eq.-H), 3.58–3.79 (5 H, m), 3.71 (3 H, s, CO_2Me), 4.48–4.72 (6 H, m, 5 × PhCH_2O, 1-H), 4.85 (1 H, d, *J* 11 Hz, 1 PhCH_2O), and 7.13–7.37 (15 H, m). Further elution gave the β-*ester* (**23**) (140 mg, 25%) as a colourless oil with $\bar{\nu}_{max}$ 3 059, 3 025, 2 911, 2 865, 1 741, 1 491, 1 445, 1 358, 1 264, 1 211, 1 178, 1 154, 1 111, 1 077, and 1 024; δ(200 MHz) 1.71 (1 H, ddd, *J* 3 × 12 Hz, 2ax.-H), 2.50 (1 H, ddd, *J* 12, 5 and 2 Hz, 2eq.-H), 3.46–3.76 (5 H, m), 3.77 (3 H, s, CO_2Me), 4.02 (1 H, dd, *J* 12 and 2 Hz, 1-H), 4.51–4.75 (5 H, m), 4.89 (1 H, d, *J* 11 Hz, PhCH_2O), and 7.14–7.36 (15 H, m) [Found for a mixture of (**23**) and (**24**): C, 73.05; H, 6.7. $C_{29}H_{32}O_6$ requires C, 73.09; H, 6.77%].

Methyl [*Methyl* 4,5,7-*Tri*-O-*benzyl*-3-*deoxy*-α-D-arabino-*heptulopyranosid*]*onate* (**31**) *and Methyl* [*Methyl* 4,5,7-*Tri*-O-*benzyl*-3-*deoxy*-β-D-arabino-2-*heptulopyranosid*]*onate* (**32**) via *the Chloride* (**30**).—A solution of ester (**24**) (393 mg, 0.82 mmol) in THF (5 ml) under nitrogen at −70 °C was treated with 1M LDA in THF (0.99 ml, 0.99 mmol). After 20 min at −70 °C, a solution of hexachloroethane (390 mg, 1.65 mmol) in THF (2 ml) was added and the mixture allowed to warm to room temperature. The reaction mixture was then poured into water (50 ml) and extracted with ether (2 × 25 ml). The combined extracts were washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure to give crude (**30**) which was dissolved in dry ether (10 ml) and added to a stirred suspension of silver sulphate (1.00 g), calcium sulphate (0.2 g), and a crystal of iodine in anhydrous methanol (5 ml) at room temperature. After being stirred at room temperature overnight, the reaction mixture was filtered and after concentration the filtrate purified by chromatography on silica gel [eluant: ether–petroleum (35:65)] to give first the *major anomer* (**31**) as a colourless oil (105 mg, 25%), $[\alpha]_D^{30}$ +36.5° (*c* 2, $CHCl_3$); $\bar{\nu}_{max}$ 2 925, 2 865, 1 745, 1 431, 1 361, 1 198, 1 091, and 997 cm^{-1}; δ(200 MHz) 1.79 (1 H, dd, *J* 13 and 12 Hz, 2ax.-H), 2.73 (1 H, dd, *J* 13 and 4.4 Hz, 2eq.-H), 3.38 (3 H, s, OMe), 3.78 (3 H, s, CO_2Me), 3.44–3.84 (5 H, m), 4.51–4.73 (5 H, m), 4.89 (1 H, d, *J* 10 Hz), and 7.18–7.39 (15 H, m). Further elution gave the *minor isomer* (**32**) as a colourless oil (21 mg, 5%), $[\alpha]_D^{30}$ +38° (*c* 1, $CHCl_3$); $\bar{\nu}_{max}$ 3 019, 2 919, 2 865, 1 748, 1 431, 1 361, 1 164, 1 104, 1 047, 995, and 897 cm^{-1}; δ(200 MHz) 1.75 (1 H, dd, *J* 12 and 11 Hz, 2ax.-H), 2.56 (1 H, dd, *J* 12 and 4 Hz, 2eq.-H), 3.23 (3 H, s, OMe), 3.81 (3 H, s, CO_2Me), 3.50–3.82 (4 H, m), 4.00 (1 H, m, 3-H), 4.52–4.70 (5 H, m), 4.90 (1 H, d, *J* 10.8 Hz), and 7.17–7.36 (15 H, m) (Found for a mixture of anomers: C, 71.0; H, 6.7. $C_{30}H_{34}O_7$ requires C, 71.13: H, 6.77%).

Methyl [*Phenyl* 4,5,7-*Tri*-O-*benzyl*-3-*deoxy*-2-*thio*-α-D-arabino-2-*heptulopyranosid*]*onate* (**33**) *and Methyl* [*Phenyl* 4,5,7-*Tri*-O-*benzyl*-3-*deoxy*-2-*thio*-β-D-2-arabino-*heptulopyranosid*]*onate* (**34**).—A stirred solution of the sulphone (**22**) (1.00 g, 1.79 mmol) in THF (3 ml) at −75 °C under nitrogen was treated with 1M LDA in THF (2.15 ml, 2.15 mmol) and after 15 min with dimethyl carbonate (0.2 ml, 2.33 mmol). After a further 1 h at −75 °C 1M lithium naphthalenide in THF (4.5 ml, 4.5 mmol) was added. The dark brown solution was then treated with diphenyl disulphide (782 mg, 3.57 mmol) in THF (2 ml) and the mixture allowed to warm slowly to 0 °C over 1 h. The reaction mixture was then poured onto brine (50 ml) and extracted with ether (2 × 30 ml). The combined extracts were washed with dilute hydrochloric acid and brine and dried ($MgSO_4$). After removal of the volatiles under reduced pressure the residue was purified by chromatography on silica gel eluting with a gradient of ether in petroleum (from 1:3 to 3:7) to give first the crystalline β-*phenylthio glycoside* (**34**) (449 mg, 43%), m.p. 78–80 °C (MeOH); $[\alpha]_D^{30}$ +19.5° (*c* 2 in $CHCl_3$); $\bar{\nu}_{max}$ 3 019, 2 905, 2 865, 1 735, 1 584, 1 441, 1 361, 1 197, 1 091, 1 017, 900, and 817 cm^{-1}; δ(200 MHz) 1.84 (1 H, dd, *J* 13 and 12 Hz, 2ax.-H), 2.96 (1 H, dd, *J* 12 and 5 Hz, 2eq.-H), 3.48 (3 H, s, CO_2Me), 3.42–3.65 (3 H, m), 3.79 (2 H, d), 4.56–4.66 (5 H, m), 4.88 (1 H, d, *J* 10.8 Hz), 7.18–7.38 (18 H, m), and 7.58 (2 H, m) (Found: C, 71.65; H, 6.3. $C_{35}H_{36}O_6S$ requires: C, 71.89; H, 6.21%). Further elution gave the α-*phenylthioglycoside* (**33**) as a colourless oil (332 mg, 32%), $[\alpha]_D^{30}$ +108° (*c* 3.5 in $CHCl_3$); $\bar{\nu}_{max}$ 3 019, 2 905, 2 865, 1 738, 1 581, 1 448, 1 361, 1 201, 1 094, 898, and 633 cm^{-1}; δ(200 MHz) 2.12 (1 H, dd, *J* 14 and 10 Hz, 2ax.-H), 2.81 (1 H, dd, *J* 14 and 5 Hz, 2eq.-H), 3.51 (3 H, s, CO_2Me), 3.30–3.84 (4 H, m), 3.98 (1 H, m), 4.35–4.68 (5 H, m), 4.90 (1 H, d, *J* 10.9 Hz), and 7.18–7.47 (20 H, m) (Found: C, 71.9; H, 6.05. $C_{35}H_{36}O_6S$ requires C, 71.89; H, 6.21%).

Tri-O-t-butyldimethylsilyl-D-galactal (**40**).—Imidazole (9.78 g, 144 mmol) and D-galactal (3.00 g, 20.5 mmol) (**39**)[40] were added successively to a stirred solution of t-butyldimethylsilyl chloride (10.86 g, 72 mmol) in dry dimethylformamide (21 ml). The mixture was heated to 60 °C and stirred under a nitrogen atmosphere for 48 h before cooling to room temperature. After being poured onto water (100 ml) the reaction mixture was extracted with ether (3 × 35 ml) and the combined extracts were washed with 2M hydrochloric acid, water, and brine and dried ($MgSO_4$). Concentration and distillation yielded the *persilylated galactal* (**40**) as a colourless syrup (8.65 g, 86%), b.p. 170 °C (oven)/0.01 mmHg; $[\alpha]_D^{20}$ −37° (*c* 1, $CHCl_3$); $\bar{\nu}_{max}$ 2 951, 2 932, 2 852, 1 638, 1 463, 1 254, 1 087, 834, and 776 cm^{-1}; δ(200 MHz) 0.04–0.08 (18 H, m), 0.85–0.89 (27 H, m), 3.84–4.11 (5 H, m), 4.65 (1 H, m, 2-H), and 6.22 (1 H, d, *J* 7 Hz, 1-H) (Found: C, 58.75; H, 10.75. $C_{24}H_{52}O_4Si_3$ requires C, 58.96; H, 10.72%).

Phenyl 3,4,6-*Tri*-O-(*t-butyldimethylsilyl*)-2-*deoxy*-1-*thio*-αβ-D-lyxo-*pyranoside* (**41**).—A solution of compound (**40**) (1.00 g, 2.05 mmol) in dry toluene (3 ml) was treated at 0 °C with a solution of hydrogen chloride (82 mg, 2.25 mmol) in toluene (6.2 ml). After 10 min the solvent was removed under reduced pressure and the residue taken up in dry dichloromethane (3 ml) and treated successively with thiophenol (0.27 ml, 2.7 mmol) and Hunig's base (0.46 ml, 2.7 mmol) at room temperature. After 1.5 h at room temperature the reaction mixture was diluted with dichloromethane and washed with 2M hydrochloric acid, 2M potassium hydroxide, water, and brine, and dried ($MgSO_4$). Concentration of the solution and purification of the crude product by chromatography on silica gel [eluant dichloromethane–petroleum (1.20)] afforded the *phenyl thio-deoxygalactoside* (**41**) as a colourless syrup (0.92 g, 76%) with an α:β ratio of 1:13.7 with $\bar{\nu}_{max}$ 2 951, 2 925, 2 852, 1 581, 1 468, 1 371, 1 254, 1 104, 1 027, 834, and 775 cm^{-1} (Found: C, 60.15; H, 9.65. $C_{30}H_{58}O_4SSi_3$ requires C, 60.15; H, 9.76%). The β-anomer had δ(200 MHz) 0.06–0.08 (18 H, m), 0.90 (27 H, s), 1.76 (1 H, m, 2eq.-H), 2.19 (1 H, ddd, *J* 3 × 12 Hz, 2ax.-H), 3.38 (1 H, t, *J* 6.4 Hz, 4-H), 3.67–3.82 (4 H, m), 4.74 (1 H, dd, *J* 12 and 2.2 Hz, 1-H), and 7.20–7.54 (5 H, m). The α-anomer had δ(200 MHz) 0.01–0.16 (18 H, m) 0.82, 0.85, 0.91 (27 H, 3 s), 1.80 (1 H, m, 2-H), 2.49 (1 H, m, 2-H), 3.60–3.75 (2 H, m), 3.89 (1 H, s), 4.03 (1 H, m, 3-H), 4.14 (1 H, t), 5.62 (1 H, d, *J* 4.8 Hz, 1-H), 7.26 (3 H, m), and 7.50 (2 H, m).

Thiogalactoside (**41**) *by Direct Camphor-10-sulphonic Acid Catalysed Addition of Thiophenol to* (**40**).—Thiophenol (1.77 ml, 17.3 mmol) and powdered 4 Å molecular sieves (0.25 g) followed by camphor-10-sulphonic acid (100 mg, 0.43 mmol) were added to a solution of the silylated galactal (**40**) (2.11 g, 4.32 mmol) in dry dichloromethane (6 ml) at room temperature. After being stirred for 48 h at room temperature the reaction mixture was filtered on Celite and washed successively with 2M aqueous sodium hydroxide, water, and brine, dried ($CaCl_2$) and concentrated. Chromatography of the residue on silica gel [eluant dichloromethane–petroleum (1:6)] gave (**41**) as a colourless syrup (1.55 g, 60%) as a 15:1 α:β anomeric mixture. The thiogalactoside (**41**) prepared in this manner differed only in the ratio of the two anomers from the sample prepared above.

Phenyl 3,4,6-*Tri*-O-(*t-butyldimethylsilyl*)-2-*deoxy*-1-*sulphonyl*-αβ-D-lyxo-*pyranoside* (**42**).—Crude phenylthiogalactoside (**41**) (2.50 g, 5.11 mmol), prepared by addition of hydrogen chloride and then thiophenol to compound (**40**), was dissolved in dichloromethane (25 ml) and treated with sodium hydrogen carbonate (1.03 g, 12.3 mmol). A solution of *m*-chloroperoxybenzoic acid (2.49 g, 12.3 mmol) in dichloromethane (40 ml) was then added at 0 °C with stirring over 1 h. After a total of 3 h at 0 °C the reaction mixture was washed with 2M aqueous sodium hydroxide, water, and brine, and then dried ($CaCl_2$). Concentration and chromatography of the solution on silica gel [eluant ether–petroleum (1:9)] gave the *sulphone* (**42**) as a colourless oil (2.15 g, 67%) with a 1:12 α:β ratio and $\bar{\nu}_{max}$ 2 939, 2 885, 2 852, 1 462, 1 445, 1 371, 1 318, 1 251, 1 147, 1 107, 1 051, 1 031, 894, 837, 780, and 684 cm^{-1} (Found: C, 57.35; H, 9.25. $C_{30}H_{58}O_6SSi_3$ requires: C, 57.10; H, 9.26%). The β-anomer had δ(200 MHz) 0.10–0.14 (18 H, m), 0.62 (9 H, s), 0.85 (9 H, s), 0.88 (9 H, s), 1.81 (1 H, ddd, 2ax.-H), 1.99 (1 H, m, 2eq.-H), 3.34 (1 H, t, *J* 6 Hz, 4-H), 3.58–3.73 (4 H, m), 4.45 (1 H, dd, *J* 12 and 2 Hz, 1-H), 7.46–7.70 (3 H, m), and 7.86–7.94 (2 H, m). The α-anomer had δ(200 MHz) 0.01–0.15 (18 H, m), 0.85, 0.86, 0.93 (27 H, 3 s), 2.33–2.42 (2 H, m, 2-H), 3.56 (2 H, m), 3.87 (1 H, s), 4.40 (2 H, m), 4.78 (1 H, dd, *J* 6.3 and 2.2 Hz, 1-H), 7.49–7.64 (3 H, m), and 7.89 (2 H, m).

Phenylsulphonylgalactoside (**42**) *by Oxidation of* (**41**) *with Magnesium Monoperoxyphthalate* (*MMPP*).—To a stirred solution of phenylthiogalactoside (**41**) (0.25 g, 0.42 mmol) in absolute ethanol (5 ml) at 5 °C was added MMPP (0.241 g, 0.44 mmol) portionwise over 5 min. The reaction mixture was stirred overnight at room temperature and then poured into chloroform and washed with dilute aqueous sodium hydrogen carbonate water, and brine. The extract was dried ($CaCl_2$) and evaporated under reduced pressure to give the sulphone (**42**) (0.25 g, 96%) as a colourless syrup differing from the sample prepared above only in anomeric ratio.

Methyl [*Phenyl* 4,5,7-*Tri*-O-(*t-butyldimethylsilyl*)-2-*deoxy*-2-*thio*-αβ-D-lyxo-2-*heptulopyranosid*]*onate* (**46**).—A stirred solution of sulphone (**42**) (0.43 g, 0.68 mmol) in THF (3 ml) at −70 °C under nitrogen was treated with 2.4M butyl-lithium in hexanes (0.34 ml, 0.82 mmol). After 15 min the yellow solution was treated with dimethyl carbonate (0.075 ml, 0.89 mmol). After a further 45 min 1M lithium naphthalenide in THF (1.7 ml, 1.7 mmol) was added. A solution of diphenyl disulphide (0.298 g, 1.36 mmol) in THF (1.5 ml) was then added and the reaction mixture allowed to warm to room temperature over 1 h. The mixture was poured into dilute aqueous sodium hydrogen carbonate and extracted with ether (3 × 25 ml). The combined extracts were washed with dilute hydrochloric acid, water, and brine, dried ($MgSO_4$), and evaporated under reduced pressure. The resultant oil was chromatographed on silica gel eluting with a gradient of petroleum–ether (100:0→19:1) to afford the *title compound* (**46**) as a white crystalline mass (0.429 g, 63%) with a 1:8 αβ anomeric ratio and m.p. 99–100 °C; $\bar{\nu}_{max}$ 2 950, 2 925, 2 885, 2 852, 1 738, 1 464, 1 254, 1 104, 1 047, 834, and 777 cm^{-1} (Found: C, 58.3; H, 9.35. $C_{32}H_{60}O_6SSi_3$ requires C, 58.49; H, 9.20%). The major isomer had δ(200 MHz) 0.08–0.16 (18 H, m), 0.87 (9 H, s), 0.92 (9 H, s), 0.95 (9 H, s), 2.14 (1 H, dd, *J* 14 and 4 Hz, 2eq.-H), 2.39 (1 H, dd, *J* 14 and 12 Hz, 2ax.-H), 3.54 (3 H, s, CO_2Me), 3.71–3.95 (3 H, m), 4.17 (2 H, m), and 7.28–7.45 (5 H, m). The minor isomer had δ(200 MHz) 0.01–0.08 (18 H, m), 0.87–0.90 (27 H, m), 2.10–2.34 (2 H, m, 2-H), 3.34–3.55 (2 H, m), 3.60 (3 H, s), 3.72–3.79 (3 H, m), and 7.29–7.59 (5 H, m).

Methyl Glycoside (**31**) *by Reaction of the Thioglycoside* (**34**) *with NBS and Methanol*.—A solution of the β-sulphide ester (**34**) (0.936 g, 1.60 mmol) in dry dichloromethane (2 ml) and methanol (5 ml) was stirred at room temperature with powdered 4 Å molecular sieves for 5 min and then treated with NBS (0.314 g, 1.76 mmol). After 2 h the reaction mixture was concentrated under reduced pressure, diluted with further dichloromethane, and filtered. Purification of the filtrate by chromatography on silica gel [eluant ether–petroleum (3:7)] gave the glycoside (**31**) (0.690 g, 85%) identical with the sample described above.

Methyl Glycosides (**31**) *and* (**32**) *by Reaction of Compounds* (**33**) *and* (**34**) *with Mercuric Acetate and Methanol.*—To a solution of a mixture of the anomers (**33**) and (**34**) (0.247 g, 0.42 mmol) in methanol (3 ml) and dichloromethane (1 ml) was added mercuric acetate (0.134 g, 0.42 mmol). The reaction mixture was stirred at room temperature for 24 h, after which sodium sulphide nonahydrate (151 mg, 0.63 mmol) was added and the mixture stirred for a further 30 min. The reaction mixture was then filtered on Celite to remove the black precipitate and after concentration the residue purified by chromatography on silica gel [eluant ether–petrol (3:7)] to give the methyl glycosides (**32**) (38.3 mg, 18%) and (**31**) (92.6 mg, 43%) identical with the samples isolated above.

Methyl [p-*Tolyl* 4,5,7-*tri*-O-*Benzyl*-2-*deoxy*-αβ-D-arabino-2-*heptulopyranosid*]*onate* (**35**) *and* 1-*Methoxycarbonyl*-3,4,6-*tri*-O-*benzyl*-D-*glucal* (**51**).—A solution of sulphide (**34**) (0.449 g, 0.77 mmol) and *p*-cresol (0.166 g, 1.54 mmol) in dichloromethane was treated with powdered 4 Å molecular sieves and mercuric chloride (0.229 g, 0.85 mmol). The reaction mixture was heated to reflux with stirring for 6 h and then allowed to cool to room temperature, when it was diluted with ether and filtered on Celite. The filtrate was washed with 1M aqueous potassium hydroxide, water, and brine, dried ($MgSO_4$), and evaporated to give a yellow syrup (0.46 g). Chromatography on silica gel [eluant ether–petroleum (3:7)] afforded the p-*tolyl glycoside* (**35**) as a colourless oil (0.212 g, 47%) of undetermined anomeric configuration with $\tilde{\nu}_{max}$ 2 918, 2 865, 1 745, 1 431, 1 361, 1 150, 1 104, 1 048, and 997 cm^{-1}; δ(200 MHz) 1.85 (1 H, dd, *J* 2 × 12 Hz, 2ax.-H), 2.30 (3 H, s), 2.75 (1 H, dd, *J* 12 and 6 Hz, 2eq.-H), 3.69–3.94 (7 H, m), 4.20 (1 H, m, 3-H), 4.49–4.94 (6 H, m), 6.98 (4 H, s), and 7.18–7.37 (15 H, m) (Found: C, 74.45; H, 6.55. $C_{36}H_{38}O_7$ requires C, 74.21; H, 6.57%). Further elution gave the *methoxycarbonylglucal* (**51**) as a white crystalline solid (64 mg, 18%), m.p. 70–72 °C (ether–petroleum); $\tilde{\nu}_{max}$ 2 898, 2 865, 1 732, 1 652, 1 431, 1 351, 1 267, 1 107, 1 025, and 897 cm^{-1}; δ(200 MHz) 3.80 (3 H, s, CO_2Me), 3.84 (2 H, d, *J* 4 Hz, 2 × 6-H), 3.95 (1 H, m, 4-H), 4.12–4.31 (2 H, m), 4.50–4.84 (6 H, m), 6.12 (1 H, d, *J* 3 Hz, 2-H), and 7.23–7.35 (15 H, m) (Found: C, 73.55; H, 6.4. $C_{29}H_{30}O_6$ requires C, 73.40; H, 6.37%).

p-*Tolylglycoside* (**35**) *and Acetate* (**36**).—A solution of glycosyl donor (**34**) (0.534 g, 0.91 mmol) and *p*-cresol (0.198 g, 1.83 mmol) in dichloromethane (3 ml) was stirred with powdered molecular sieves (0.1 g) and mercuric acetate (0.437 g, 1.37 mmol) at room temperature for 4 h. The reaction mixture was then diluted with ether, filtered through Celite, and washed with 1M potassium hydroxide, water, and brine, and then dried ($MgSO_4$). The filtrate was evaporated and taken up again in ether, the insoluble mercury salts removed by filtration, and the filtrate concentrated under reduced pressure to give a yellow oil (0.54 g) which was chromatographed on silica gel [eluant ether–petroleum (1:2→1:1)] to give the *p*-tolyl glycoside (**35**) identical with the sample isolated above and subsequently the *acetate* (**36**) as a colourless syrup (0.303 g, 62%) with $\tilde{\nu}_{max}$ 3 025, 2 912, 2 865, 1 755, 1 448, 1 364, 1 205, 1 104, 1 048, and 920 cm^{-1}; δ(200 MHz) 1.90 (1 H, dd, *J* 12 and 11 Hz, 2ax.-H), 2.06 (3 H, s), 2.67 (1 H, dd, *J* 12 and 5 Hz, 2eq.-H), 3.65–4.00 (8 H, m), 4.51–4.72 (5 H, m), 4.90 (1 H, d, *J* 10.6 Hz), and 7.18–7.38 (15 H, m) (Found: C, 69.7; H, 6.4. $C_{31}H_{34}O_8$ requires C, 69.65; H, 6.41%).

Methyl [3β-*Cholestanyl* 4,5,7-*Tri*-O-*benzyl*-2-*deoxy*-αβ-D-arabino-2-*heptulopyranosid*]*onate* (**37**).—A stirred solution of the sulphide (**33**) (0.332 g, 0.57 mmol) and 3β-cholestanol (0.265 g, 0.68 mmol) in dry dichloromethane (4 ml) was treated with NBS (0.121 g, 0.68 mmol), and powdered molecular sieves (0.1 g). After being stirred at room temperature for 4 h the reaction mixture was diluted with ether, washed with dilute aqueous sodium thiosulphate, 1M hydrochloric acid, and brine, and then dried ($MgSO_4$). Concentration of the solution and chromatography of the residue on silica gel [eluant ether–petroleum (1:4)] gave the *cholestanyl glycoside* (**37**) a single unassigned anomer, as a colourless syrup (0.120 g, 25%) with $\tilde{\nu}_{max}$ 2 919, 2 858, 1 739, 1 600, 1 461, 1 361, 1 092, 1 022, and 900 cm^{-1}; δ(200 MHz) 0.63 (3 H, s), 0.77 (3 H, s), 0.88 (6 H, d, *J* 7.2 Hz), 0.91 (3 H, d, *J* 6.6 Hz), 0.80–2.00 (36 H, m, *steroid* + 2ax.-H), 2.76 (1 H, dd, *J* 12 and 4 Hz, 2eq.-H), 3.70 (3 H, s, CO_2Me), 3.45–3.90 (6 H, m), 4.58–4.66 (5 H, m), 4.89 (1 H, d, *J* 10.8 Hz), and 7.24–7.38 (15 H, m).

Methyl [*Methyl* 4,5,7-*Tri*-O-(t-*butyldimethylsilyl*)-2-*deoxy*-αβ-lyxo-2-*heptulopyranosid*]*onate* (**47**).—A solution of the glycosyl donor (**46**) (0.250 g, 0.38 mmol) in methanol (2 ml) was stirred with powdered molecular sieves (0.1 g) and mercuric acetate (0.133 g, 0.42 mmol) for 24 h at room temperature. The reaction mixture was then diluted with dichloromethane (2 ml), filtered on Celite, and concentrated under reduced pressure. The residue was chromatographed on silica gel [eluant ether–petroleum (1:25)] to afford the *methyl glycoside* (**47**) as a colourless oil (0.148 g, 67%) with an unassigned 1:2.7 anomeric ratio; $\tilde{\nu}_{max}$ 2 952, 2 932, 2 885, 2 852, 1 742, 1 464, 1 254, 1 174, 1 084, 1 042, 837, and 777 cm^{-1} (Found: C, 56.2; H, 10.45. $C_{27}H_{58}O_7Si_3$ requires C, 56.01; H, 10.10%). The major isomer had δ(200 MHz) 0.06–0.12 (18 H, m), 0.89, 0.90, and 0.91 (27 H, 3 s), 2.03 (1 H, dd, *J* 12 and 4 Hz, 2eq.-H), 2.29 (1 H, dd, *J* 2 × 12 Hz, 2ax.-H), 3.37 (3 H, s, OMe), 3.79 (3 H, s, CO_2Me), and 3.50–3.82 (5 H, m). The minor isomer had δ(200 MHz) 0.06–0.10 (18 H, m), 0.80–0.90 (27 H, m), 1.82 (1 H, dd, *J* 12 and 4 Hz, 2eq.-H), 2.10 (1 H, dd, *J* 2 × 12 Hz, 2ax.-H), 3.20 (3 H, s, OMe), 3.78 (3 H, s, CO_2Me), 3.45–3.63 (4 H, m), and 4.01 (1 H, m, 3-H).

p-*Tolyl* [*Methyl* 4,5,7-*Tri*-O-(*t-butyldimethylsilyl*)-2-*deoxy*-αβ-D-lyxo-2-*heptulopyranosid*]*onate* (**48**).—To a stirred suspension of the thioglycoside (**46**) (0.250 g, 0.38 mmol) and powder 4 Å molecular sieves (0.1 g) and *p*-cresol (41 mg, 0.38 mmol) in dry dichloromethane at room temperature was added mercuric chloride (0.114 g, 0.42 mmol). After being stirred for 48 h at room temperature the reaction mixture was diluted with dichloromethane, filtered on Celite, and evaporated to dryness. The residue was chromatographed on silica gel [eluant petroleum–ether–triethylamine (100:2:0.1) to give the p-*tolyl glycoside* (**48**) as colourless syrup (0.135 g, 54%) as an unassigned 2:1 mixture of anomers with $\tilde{\nu}_{max}$ 2 952, 2 925, 2 852, 1 758, 1 504, 1 465, 1 254, 1 107, 1 054, 834, and 777 cm^{-1}; δ(200 MHz) 0.01–0.14 (18 H, m), 0.86–0.95 (27 H, m), 2.05–2.26 (5 H, m), 3.58 (minor) + 3.64 (major) (3 H, 2 s, CO_2Me), 3.30–4.30 (5 H, m), 6.99 (4 H, s), and 7.20–7.60 (5 H, m) (Found: C, 60.6; H, 9.7. $C_{33}H_{62}O_7Si_3$ requires C, 60.50; H, 9.54%).

Methyl [3β-*Cholestanyl* 4,5,7-*Tri*-O-(*t-butyldimethylsilyl*)-2-*deoxy*-αβ-D-lyxo-2-*heptulopyranosid*]*onate* (**49**).—NBS (30 mg, 0.17 mmol) was added to a stirred suspension of the glycosyl donor (**46**) (100 mg, 0.15 mmol) and 3β-cholestanol (118 mg, 0.30 mmol) and powdered molecular sieves in dichloromethane (1.3 ml) at room temperature. After being stirred for 30 min at room temperature the reaction mixture was diluted with ether, filtered on Celite, and evaporated to dryness. The residue was chromatographed on silica gel [eluant petroleum–ether (40:1)] to provide the *cholestanyl glycoside* (**49**) as a colourless syrup (56 mg, 39%), an unassigned 1:2.6 mixture of anomers, with $\tilde{\nu}_{max}$ 2 925, 2 852, 1 758, 1 464, 1 171, 1 107, 1 054, and 837 cm^{-1}; δ(200 MHz) 0.50–0.11 (18 H, m), 0.60–2.05 (75 H, m), 3.74 (major) + 3.89 (minor) (3 H, 2 s, CO_2Me), and 3.40–4.25 (6 H, m) (Found: C, 68.35; H, 11.35. $C_{53}H_{102}O_7Si_3$ requires C, 68.04; H, 11.00%).

Methyl [*Cyclohexyl* 4,5,7-*Tri*-O-(*t-butyldimethylsilyl*-2-*deoxy*-αβ-D-lyxo-2-*heptulopyranosid*']*onate* (**50**) *and* 1-*Methoxycarbonyl*-3,4,6-*tri*-O-(*t-butyldimethylsilyl*)-D-*galactal* (**52**).—A stirred solution of the thioglycoside (**46**) (0.200 g, 0.30 mmol) and cyclohexanol (0.061 g, 0.61 mmol) in dichloromethane (2 ml) over 4 Å molecular sieves was treated at room temperature with NBS (60 mg, 0.36 mmol). After being stirred for 3 h at room temperature the reaction mixture was diluted with ether, filtered on Celite, and evaporated to dryness. The residue was chromatographed on silica gel [eluant petroleum–ether (40:1)] to give the *cyclohexyl glycoside* (**50**), an undefined single anomer, as a colourless oil (57 mg, 29%); $\bar{\nu}_{max}$ 2 925, 2 852, 1 750, 1 462, 1 254, 1 054, 834, 777, and 734 cm^{-1}; δ(200 MHz) 0.05–0.10 (18 H, m), 0.89 (18 H, s), 0.92 (9 H, s), 1.15–2.10 (12 H, m), 3.75 (3 H, s, CO_2Me), 3.50–3.84 (5 H, m), and 4.06 (1 H, m, 3-H) (Found: C, 59.35; H, 10.2. $C_{32}H_{68}O_7Si_3$ requires C, 59.39; H, 10.28%). Further elution gave the *glycal* (**52**) also as a colourless oil (59 mg, 35%); $\bar{\nu}_{max}$ 2 951, 2 926, 2 885, 2 852, 1 735, 1 645, 1 464, 1 254, 1 101, 837, 777, and 734 cm^{-1}; δ(200 MHz) 0.05–0.12 (18 H, m), 0.89 (18 H, s), 0.92 (9 H, s), 3.80 (3 H, s, CO_2Me), 3.87–4.36 (5 H, m), and 5.83 (1 H, d, *J* 3.2 Hz, 2-H) (Found: C, 57.1; H, 9.95. $C_{26}H_{54}O_6Si_3$ requires C, 57.09; H, 9.95%).

Methyl 4,5,7-*Tri*-O-*benzyl*-2-*deoxy*-α-D-arabino-2-*heptulopyranosidonic Acid* (**54**).—A solution of the ester (**32**) (0.587 g, 1.16 mmol) in methanol (3 ml) was treated at room temperature with a solution of potassium hydroxide (0.130 g, 2.32 mmol) in water (0.5 ml). After being stirred for 7 h at room temperature the reaction mixture was poured into dilute hydrochloric acid and the precipitated solid extracted into ether (2 × 25 ml). The extracts were washed with brine, dried ($MgSO_4$), and evaporated to give the *acid* (**54**) as a colourless oil (0.515 g, 90%); $\bar{\nu}_{max}$ 3 419, 2 918, 2 865, 1 782, 1 761, 1 735, 1 361, 1 094, and 900 cm^{-1}; δ(200 MHz) 1.74 (1 H, dd, *J* 13.3 and 11 Hz, 2ax.-H), 2.59 (1 H, dd, *J* 13.3 and 4.8 Hz, 2eq.-H), 3.24 (3 H, s, OMe), 3.46–3.80 (4 H, m), 4.01 (1 H, m, 3-H), 4.47–4.69 (5 H, m), 4.90 (1 H, d, *J* 11 Hz), 6.81 (1 H, bs, CO_2H), and 7.17–7.36 (15 H, m).

Methyl 4,5,7-*Tri*-O-*benzyl*-2-*deoxy*-β-D-arabino-2-*heptulopyranosidonic Acid* (**53**).—Saponification of (**31**) (0.332 g, 0.66 mmol) as described for (**54**) above gave the *acid* (**53**) (0.279 g, 0.57 mmol) as a colourless oil; $\bar{\nu}_{max}$ 3 429, 2 892, 1 778, 1 755, 1 725, 1 361, 1 094, and 900 cm^{-1}; δ(200 MHz) 1.81 (1 H, dd, *J* 13 and 11 Hz, 2ax.-H), 2.71 (1 H, dd, *J* 13 and 5 Hz, 2eq.-H), 3.38 (3 H, s, OMe), 3.56–3.80 (5 H, m), 4.51–4.70 (5 H, m), 4.88 (1 H, d, *J* 10.9 Hz), 7.16–7.36 (15 H, m), and 9.13 (1 H, br s).

General Procedure for Decarboxylation by means of Dicyclohexylcarbodi-imide (*DCC*) *and* (**8**): *Methyl* 3,4,6-*Tri*-O-*benzyl*-2-*deoxy*-αβ-D-gluco-*pyranoside* (**25**).—To a stirred solution of the acid (**53**) (0.150 g, 0.305 mmol) and thiohydroxamic acid (**8**) (39 mg, 0.35 mmol) in dry ether (2 ml) was added DCC (63 mg, 0.305 mmol). The reaction mixture was shielded from the light and stirred at room temperature for 1 h. The resulting yellow solution was filtered on Celite into a flask containing t-dodecanethiol (0.144 ml, 0.61 mmol). The resultant solution was photolysed at room temperature under nitrogen with a 500 W tungsten lamp for 1 h. After concentration under reduced pressure, chromatography on silica gel [eluant ether–petroleum (3:7)] of the residue gave the methyl glycoside (**25**), a 1:10 α:β mixture of anomers, as a colourless oil (50 mg, 36%); $\bar{\nu}_{max}$ 3 019, 2 919, 2 865, 1 431, 1 361, 1 162, 1 101, 1 049, and 996 cm^{-1}; δ(200 MHz, β-anomer) 1.63 (1 H, ddd, *J* 12,11 and 9.7 Hz, 2ax.-H), 2.32 (1 H, ddd, *J* 12,5 and 2 Hz, 2eq.-H), 3.50 (3 H, s, OMe), 3.35–3.76 (5 H, m), 4.35 (1 H, dd, *J* 9.7 and 2 Hz, 1-H), 4.52–4.72 (5 H, m), 4.90 (1 H, d, *J* 10.9 Hz), and 7.18–7.38 (15 H, m). The minor α-anomer had δ 3.30 (OMe) (Found: C, 74.7; H, 7.25. $C_{28}H_{32}O_5$ requires C, 74.98; H, 7.19%).

p-*Tolyl* 3,4,6-*Tri*-O-*benzyl*-2-*deoxy*-β-D-gluco-*pyranoside* (**26**).—The heptulosonate glycoside (**35**) (152 mg, 0.26 mmol) was saponified as described for compound (**54**) above and the crude acid decarboxylated according to the general procedure using DCC outlined above. Chromatography on silica gel [eluant ether–petroleum (10:1)] of the crude product gave the 2-*deoxy*-β-*glucoside* (**26**) as a colourless oil (17 mg, 12%); δ(400 MHz) 1.93 (1 H, ddd, *J* 12.4, 12, and 9.8 Hz, 2ax.-H), 2.29 (3 H, s, Ar*Me*), 2.51 (1 H, ddd, *J*, 12.4, 4.8, and 2 Hz 2eq.-H), 3.56–3.83 (5 H, m), 4.52–4.74 (5 H, m), 4.92 (1 H, d, *J* 10.8 Hz), 5.02 (1 H, dd, *J* 9.8 and 2 Hz, 1-H), 6.949 (2 H, m), 7.04 (2 H, m), and 7.22–7.38 (15 H, m).

General Procedure for Decarboxylation by Reaction of Acids with the Salt (**55**) *and Thiol*: *Methyl Glycoside* (**25**).—A solution of the acid (**53**) (245 mg, 0.50 mmol) in THF–chloroform (1:1; 2 ml) was stirred with the salt (**55**) (104 mg, 0.55 mmol) and triethylamine (55 mg, 0.55 mmol) under nitrogen, in the dark, at room temperature for 1.5 h. (If necessary, the solution should be clarified by filtration on Celite at this stage). t-Dodecanethiol (0.23 ml, 1 mmol) was then added and the mixture photolysed with a 500 W tungsten lamp under nitrogen at room temperature until colourless. Evaporation and chromatography gave the glycoside (**25**) (90 mg, 40%) identical with the sample isolated above and in the same anomeric ratio.

3β-*Cholestanyl* 3,4,6-*Tri*-O-*benzyl*-2-*deoxy*-β-D-gluco-*pyranoside* (**27**).—A solution of cholestanyl heptulosonide (**37**) (82 mg, 0.095 mmol) in THF (3 ml), and methanol (2 ml) was stirred for 36 h at room temperature with potassium hydroxide (27 mg, 0.4 mmol) in water (0.5 ml). The reaction mixture was poured into dilute hydrochloric acid and extracted with ether (2 × 10 ml). The combined extracts were washed with brine, dried ($MgSO_4$), and evaporated to give the crude corresponding acid (74 mg, 92%) as a white foam. This crude acid was subjected to the general procedure for decarboxylation with (**55**) to give after chromatography on silica gel [eluant ether–petroleum (1:9)] the cholestanyl 2-deoxyglucoside (**27**) as a white amorphous solid (35 mg, 50%) with a 1:11 α:β ratio. Crystallisation from propan-2-ol gave the pure β-anomer, m.p. 105–106 °C lit.,[11] 105.5–106 °C); $\bar{\nu}_{max}$ 2 919, 2 858, 1 601, 1 491, 1 461, 1 361, 1 094, 1 024, and 900 cm^{-1}; δ(400 MHz) 0.66–1.99 (47 H, m), 2.32 (1 H, ddd, *J* 12.4, 5 and 1.8 Hz, 2eq.-H), 3.43–3.80 (6 H, m), 4.56–4.71 (6 H, m, 5 × $PhCH_2O$, 1-H), 4.91 (1 H, d, *J* 10.8 Hz, $PhCH_2O$), and 7.22–7.38 (15 H, m). The α-anomer had δ(400 MHz) 2.26 (1 H, dd, *J* 12.9 and 5.7 Hz, 2eq.-H), and 5.14 (1 H, d, *J* 2.9 Hz, 1-H). Further elution gave the lactone (**17**) (8.5 mg, 23%) identified by TLC comparison with an authentic sample.

Methyl *Tri*-O-(*t-butyldimethylsilyl*)-2-*deoxy*-β-D-galacto-*pyranoside* (**43**).—Saponification of (**47**) (0.148 g, 0.26 mmol) as described for (**54**) and decarboxylation of the crude acid according to the general procedure with (**55**) gave after chromatography on silica gel [eluant ether–petroleum (100:3)] the 2-*deoxygalactoside* (**43**), a 1:9.6 α:β mixture, as a colourless oil (64.5 mg, 55%); $\bar{\nu}_{max}$ 2 951, 2 924, 2 852, 1 465, 1 384, 1 254, 1 104, 1 068, 1 031, 834, and 777 cm^{-1}; δ(200 MHz, β-anomer) 0.07–0.10 (18 H, m), 0.90 (27 H, m), 1.71 (1 H, m, 2eq.-H), 1.99 (1 H, ddd, *J* 2 × 10, 9.7 Hz, 2ax.-H), 3.27 (1 H, t, *J* 6.6 Hz, 4-H), 3.49 (3 H, s, OMe), 3.50–3.81 (4 H, m), 4.34 (1 H, dd, *J* 9.7 and 2.2 Hz, 1-H). The α-anomer had δ 1.64 (1 H, m, 2eq.-H), 2.12 (1 H, dt, 2eq.-H), 3.30 (3 H, s, OMe), and 4.76 (1 H, d, *J* 4 Hz, 1-H) (Found: C, 58.0; H, 10.8. $C_{25}H_{56}O_5Si_3$ requires C, 57.64; H, 10.83%).

p-*Tolyl* 3,4,6-*Tri*-O-(*t-butyldimethylsilyl*)-2-*deoxy*-β-D-galacto-*pyranoside* (**44**).—Saponification of the heptulosonide (**48**)

(0.147 g, 0.22 mmol) as described for (**54**) and decarboxylation by the standard procedure with (**55**) gave, after chromatography on silica gel [eluant petroleum–ether–triethylamine (100:1:0.1)], the *2-deoxygalactoside* (**44**) as a colourless syrup (45 mg, 34%) with a 1:16 α:β ratio; $\tilde{\nu}_{max}$ 2 932, 2 885, 2 852, 1 608, 1 585, 1 507, 1 464, 1 384, 1 222, 1 171, 1 101, 1 057, 1 029, 954, 937, and 837 cm^{-1}; δ(200 MHz, β-anomer) 0.05–0.13 (18 H, m), 0.90 (9 H, s), 0.92 (18 H, s), 1.84 (1 H, m, 2eq.-H), 2.26 (3 H, s, Ar*Me*), 2.20–2.31 (1 H, m, 2ax.-H), 3.43 (1 H, t, 4-H), 3.66–3.82 (4 H, m), 4.99 (1 H, dd, *J* 9.8 and 2.3 Hz, 1-H), and 6.93–7.07 (4 H, m). The α-anomer had δ 5.52 (1 H, m, 1-H) (Found: C, 62.35; H, 10.4. $C_{31}H_{60}O_5Si_3$ requires C, 62.36; H, 10.13%).

3β-*Cholestanyl* 3,4,6-*Tri*-O-(*t-butyldimethylsilyl*)-2-*deoxy*-β-D-galacto-*pyranoside* (**45**).—Saponification of the heptulosonide (**49**) (0.126 g, 0.14 mmol) as described for (**27**) above and decarboxylation of the resultant crude acid according to the general procedure with (**55**) gave, after chromatography on silica gel [eluant ether–petroleum (1:100)] the *title compound* (**45**), 1:8 α:β mixture, as a colourless oil (42.3 mg, 44%); $\tilde{\nu}_{max}$ 2 925, 2 852, 1 465, 1 375, 1 171, 1 101, 1 057, 1 028, and 835 cm^{-1}; δ(200 MHz, β-anomer) 0.05–0.09 (18 H, m), 0.64 (3 H, s, 18-Me), 0.79 (3 H, s, 19-Me), 0.8–2.04 (69 H, m), 3.24 (1 H, t, *J* 6.0 Hz, 4-H), 3.61–3.73 (5 H, m), and 4.55 (1 H, dd, *J* 9.5 and 1.7 Hz, 1-H). The α-anomer had δ 5.02 (1 H, bd, 1-H) (Found: C, 69.65; H, 11.75. $C_{51}H_{100}O_5Si_3$ requires C, 69.80; H, 11.48%).

Phenyl 3,4,6-*Tri*-O-*benzyl*-2-*deoxy*-1-*thio*-β-D-gluco-*pyranoside* (**28**).—Saponification of a mixture of (**33**) and (**34**) (150 mg, 0.26 mmol) as described for (**54**) and decarboxylation of the crude acid by the general procedure with (**55**) gave, after chromatography on silica gel [eluant ether–petroleum (15:85)], first the β-glycoside (59.6 mg, 44.5%) with δ(200 MHz) 1.83 (1 H, ddd, *J* 3 × 12 Hz, 2ax.-H), 2.48 (1 H, dd, *J* 12 and 4 Hz, 2eq.-H), 4.76 (1 H, d, *J* 12 Hz, 1-H) [lit.,[33] δ 4.70 (1 H, dd, *J* 11.7 and 2.0 Hz]. Further elution gave the α-anomer (7.6 mg, 5.5%); δ(200 MHz) 2.15 (1 H, ddd, *J* 2 × 14 and 6 Hz, 2ax.-H), 2.48 (1 H, dd, *J* 14 and 4 Hz, 2eq.-H), and 5.71 (1 H, d, *J* 6 H, 1-H) [lit.,[33] δ 5.65 (1 H, dd, *J* 5.6 and 1.3 Hz, 1-H].

Phenyl Tri-O-(*t-butyldimethylsilyl*)-2-*deoxy*-1-*thio*-β-D-galacto-*pyranoside* (**41**).—Saponification of the heptulosonide (**46**) (200 mg, 0.30 mmol) as described for (**54**) and decarboxylation of the crude acid according to the general procedure with (**55**) gave after chromatography on silica gel [eluant ether–petroleum (1:100)] the thiogalactoside (**41**), a 1:18 α:β mixture of anomers, as a colourless oil with spectral characteristics identical with the samples described above.

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