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PREPARATION OF PYRANOID GLYCAL DERIVATIVES FROM PHENYL THIOGLYCOSIDES AND GLYCOSYL PHENYL SULPHONES*

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ABSTRACT

Phenyl thioglycopyranosides with various protecting groups (acetal, ether, ester) underwent reductive lithiation at C-1, followed by rapid elimination of the 2-substituent, when treated with lithium naphthalenide in tetrahydrofuran at low temperature. Thus, pyranoid glycal derivatives with acid-labile protecting groups were obtained in excellent yields. Glycopyranosyl phenyl sulphones were prepared quantitatively by oxidation of the corresponding phenyl thioglycosides with catalytic amounts of ruthenium trichloride in the presence of sodium periodate in a biphasic solvent system. These compounds also gave rise to pyranoid glycal derivatives in excellent yields when treated with lithium naphthalenide in tetrahydrofuran at low temperature. A β-linked 2′-deoxydisaccharide glycal derivative was also prepared from the corresponding disaccharide phenyl thioglycoside. Phenyl thioglycopyranosides carrying a 2-xanthate group underwent a radical reductive elimination when treated with tributyltin hydride, to afford glycal derivatives in good yields under neutral conditions.

INTRODUCTION

Glycals are useful precursors in synthetic carbohydrate chemistry[1]. Of particular importance are the conversions of glycals into efficient glycosyl donors for the stereoselective synthesis of either 2-amino-2-deoxy-D-glycopyranosides[2–4] or 2-deoxy-α- and -β-glycopyranosides[5–11]. Pyranoid glycals are usually prepared[12] by modifications of the classical Fischer–Zach method involving reduction of acetylated pyranosyl halides in acetic acid. 3,4,6-Tri-*O*-acetyl-D-glucal, now on the market, is obtained in this way. Unfortunately, the acidic conditions of this procedure preclude the preparation of glycal derivatives with acid-sensitive protecting groups, especially acetals. 4,6-*O*-Benzylidene-D-glucal[13] and 4,6-*O*-isopropylidene-

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D-glucal[14] were obtained by acetalation of acid-sensitive D-glucal, and the yields were poor. An alternative and efficient method for the preparation of pyranoid glycal derivatives with base-stable protecting groups involves the formation of an unstable C-1 anion from a glycosyl halide either with lithium in liquid ammonia[15] or with sodium naphthalenide in tetrahydrofuran at room temperature[16], followed by elimination of the 2-alkoxy group. On the other hand, reductive elimination of 2-*O*-mesylaldosyl chlorides with active zinc dust in the presence of iodide gave pyranoid glycals in high yields[17].

Treatment[18] of phenyl 2,3,4,6-tetra-*O*-benzyl-1-thio-β-D-glucopyranoside with 2 equiv. of lithium naphthalenide in tetrahydrofuran at −78° for 15 min resulted in the quantitative formation of 3,4,6-tri-*O*-benzyl-D-glucal. Thus, the selective reductive lithiation of a sulphide in the presence of benzyl ethers[19] occurred without difficulty at the anomeric centre and was followed, as expected, by rapid elimination of the 2-benzyloxy group.

Phenyl thioglycosides are stable under a variety of reaction conditions (acylation, alkylation, acetalation) and they have attracted considerable attention[20]. The conversion of a phenyl thioglycoside into a glycal derivative, under mild conditions, avoids the need for a glycosyl halide, and parallels their use as glycosylating agents in the synthesis of oligosaccharides. We now report on the scope of this novel reaction.

RESULTS AND DISCUSSION

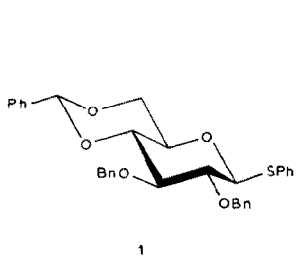
Phenyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside* (**1**), selected first as a typical candidate for glycal synthesis, was prepared easily from phenyl 1-thio-β-D-glucopyranoside and contains both acid-sensitive (benzylidene acetal) and radical anion-sensitive (benzyl ether) protecting groups. Treatment of **1** with 2 equiv. of lithium naphthalenide in tetrahydrofuran at −78° gave a nearly quantitative yield of the crystalline glucal derivative **21**.

Attention was then turned to variously protected galactopyranosides. Phenyl 1-thio-β-D-galactopyranoside, obtained by *O*-deacetylation (sodium methoxide in methanol)[23] of phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranoside[24], was isopropylidenated in nearly quantitative yield using 2-methoxypropene in *N,N*-dimethylformamide[25] in the presence of a catalytic amount of camphorsulphonic acid. The crystalline phenyl 2,3:4,6-di-*O*-isopropylidene-1-thio-β-D-galactopyranoside (**2**) underwent a clean lithium naphthalenide-mediated reductive elimination to give the crystalline glycal derivative **26** (85%). The formation of **26** can be explained easily if it is assumed that the elimination of acetone[15,16] occurred in an intermediate unstable α-glycosyl-lithium derivative[18].

Treatment of phenyl 1-thio-β-D-galactopyranoside with 2,2-dimethoxypropane in the presence of a catalytic amount of camphorsulphonic acid gave phenyl 3,4-*O*-isopropylidene-6-*O*-(1-methoxy-1-methylethyl)-1-thio-β-D-galacto-

*This compound[21] was recently used by Nicolaou *et al.*[22] as a synthesis intermediate.

pyranoside as the key non-isolated intermediate **3**. Acidic work-up gave phenyl 3,4-*O*-isopropylidene-1-thio-β-D-galactopyranoside[26] (**4**), whereas benzylation or benzoylation followed by removal of the acid-labile 6-*O*-(1-methoxy-1-methylethyl) group[27] gave either phenyl 2-*O*-benzyl- (**6**, ~60%) or 2-*O*-benzoyl-3,4-*O*-isopropylidene-1-thio-β-D-galactopyranoside (**10**, ~60%). Compound **4** was converted into the 2,6-di-*O*-benzyl (**5**), -methyl (**7**), -acetyl (**8**), and benzoyl (**9**) derivatives using conventional methods.



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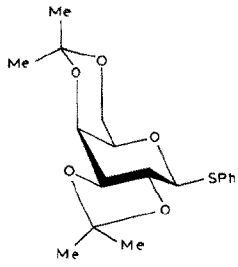

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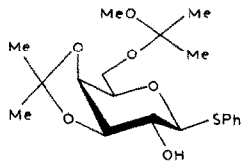

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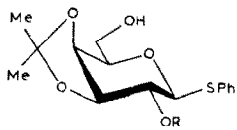
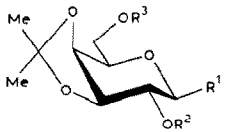
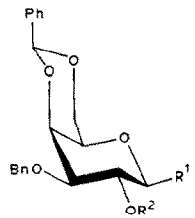


4 R = H
6 R = Bn
10 R = Bz
11 R = CSSMe



5 R^1 = SPh, R^2 = R^3 = Bn
7 R^1 = SPh, R^2 = R^3 = Me
8 R^1 = SPh, R^2 = R^3 = Ac
9 R^1 = SPh, R^2 = R^3 = Bz
12 R^1 = SO_2Ph, R^2 = R^3 = Bn
13 R^1 = SO_2Ph, R^2 = R^3 = Me
14 R^1 = SO_2Ph, R^2 = R^3 = Ac
15 R^1 = SO_2Ph, R^2 = R^3 = Bz

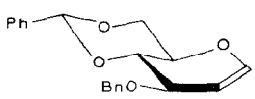


16 R^1 = H, R^2 = Bn
17 R^1 = SPh, R^2 = Bn
18 R^1 = SPh, R^2 = H
19 R^1 = SPh, R^2 = CSSMe
20 R^1 = SO_2Ph, R^2 = Bn

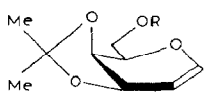
As expected, reductive lithiation of phenyl 2,6-di-*O*-benzyl- (**5**) and 2,6-di-*O*-methyl-3,4-*O*-isopropylidene-1-thio-β-D-galactopyranoside (**7**) gave the galactal derivatives **22** and **24**, respectively, in almost quantitative yields. Likewise, reductive elimination of **6** gave **23** (92%), demonstrating that the methodology is compatible with the presence of an unprotected hydroxyl group.

Phenyl 2,6-di-*O*-acetyl- (**8**) and 2,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-1-thio-β-D-galactopyranoside (**9**), which are esterified at position 2, were studied next. Reductive lithiation of **8** gave a mixture of the glycal derivative **23** (68%) and the diol **4** (17%). Thus, the 2-*O*-acetyl group was eliminated with electron transfer occurring selectively on the anomeric sulphur. This outcome is in sharp contrast to

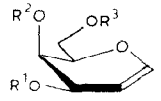
the behaviour of the dibenzoate **9** in that no galactal derivative was formed and the electron transfer occurred preferentially on the ester functions[28], leading to a mixture of monobenzoate **10** (16%) and diol **4** (58%).



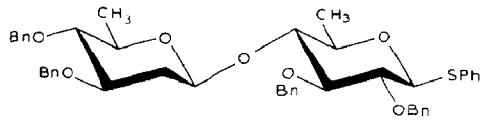
21



22 R = Bn
23 R = H
24 R = Me
25 R = Ac



26 R^1 = H, R^2, R^3 = Me_2C
27 R^1 = H, R^2, R^3 = PhCH
28 R^1 = Bn, R^2, R^3 = PhCH



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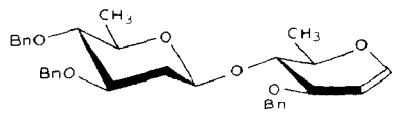

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Reductive lithiation of phenyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside[21] (**17**) was slow, so that concomitant *O*-debenzylation at C-3 occurred to yield the crystalline galactal derivative **27** (75%). When compared with the quantitative conversion of **1** into the glucal derivative **21** as reported above, this result emphasizes the influence of the configuration on the kinetic course of the reductive elimination.

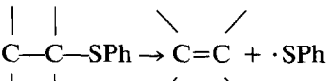
Anomeric phenyl sulphones undergo rapid reductive lithiation[29]. An extension of the reaction for the preparation of glycal derivatives was investigated. Phenyl thioglycosides are oxidized quantitatively into the corresponding sulphones[30] (in a few min at room temperature) in the presence of sodium periodate and catalytic amounts of ruthenium trichloride, in the biphasic system carbon tetrachloride–water–acetonitrile[31]. Benzyl ethers and alcohols[32] were oxidized at a much lower rate under these conditions. In a typical example, **7** was oxidized into the crystalline sulphone **13** (90%). Reductive lithiation of **13** gave the galactal derivative **24** (85%), identical to the compound prepared above from the thiogalactoside **7**. Similarly, **5** was oxidized to the sulphone **12**, which gave the glycal derivative **22** (95%) by reductive lithiation. Oxidation of **8** afforded the crystalline sulphone **14** in almost quantitative yield. Treatment of **14** with lithium naphthalenide gave a mixture of the galactal derivatives **25** (41%) and **23** (47%). Interestingly, 82% of **23** was isolated when the crystalline sulphone **15** was submitted to reductive lithiation. This result contrasts with the behaviour of the corresponding thioglycoside **9** where selective reduction of the benzoate group occurred, so that no trace of the galactal derivative could be detected in the reaction mixture. This example demonstrates that it is possible to modulate the course of the elimination when a

2-ester group is present. Therefore, the reductive elimination of an anomeric sulphone protected at C-2 by reducible and base-sensitive protecting groups (acetyl or benzoyl) is possible, which enlarges the scope of the methodology.

Selective reductive lithiation of the crystalline phenyl sulphone **20** gave the expected galactal derivative **28** (30%). A major side reaction was the fast deprotonation of either naphthalene or tetrahydrofuran by the strongly basic C-1 anion, leading to crystalline **16** (46%).

The scope of this procedure was demonstrated by the smooth conversion of the disaccharide derivative **29** into the crystalline glycal derivative **30** (92%), a key intermediate in the synthesis of orthosomycin fragments[33]. The sensitivity of the 2′-deoxyglycosidic linkage in **29** precludes the use of acidic conditions, and the presence of reducible benzyl ethers calls for a selective reducing system.

Lythgoe and Waterhouse reported[34] a 1,2-elimination reaction with a radical mechanism



which has been applied to the synthesis of vinyl ethers[35]. Extension to the preparation of glycal derivatives was investigated. Compound **11** was easily obtained as described above for the preparation of **6** and **10**, with the intermediate **3** being converted into a 2-xanthate prior to acidic work-up. Treatment of **11** with tributyltin hydride in boiling toluene for a few min in the presence of catalytic amounts of α,α'-azobisisobutyronitrile gave (93%) a glycal derivative identical to **23** obtained by lithium naphthalenide-mediated reductive elimination. Phenyl 4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside was selectively converted into the crystalline phenyl 3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside (**18**) using the tin methodology[36]. Xanthation of **18** gave **19**, which underwent radical reductive elimination to give **28** (90%). To our knowledge, this represents the first example of the synthesis of substituted pyranoid glycals from phenyl thioglycosides by a neutral radical process and is complementary to existing methods.

The methodologies presented here allow the efficient preparation of variously protected pyranoid glycals, which are useful intermediates in organic synthesis.

EXPERIMENTAL

General methods. — Melting points were determined with a Büchi Model 510 capillary apparatus and are uncorrected. Optical rotations were measured at 20 ±2° with a Perkin–Elmer Model 241 polarimeter. C.i. (ammonia)-mass spectra were obtained with a Nermag R10-10 spectrometer. Elemental analyses were performed at the University Pierre et Marie Curie (Paris VI). ^{1}H-N.m.r. spectra were recorded with a Cameca 250 and a Bruker AM-400 spectrometer for solutions in

$CDCl_3$ or C_6D_6 (internal Me_4Si). ^{13}C-N.m.r. spectra were recorded at 100.57 MHz with a Bruker AM-400 spectrometer for solutions in $CDCl_3$, adopting 77.0 p.p.m. for the central line of $CDCl_3$. Assignments were aided by the J-MOD technique[37,38]. Reactions were monitored by t.l.c. on Silica Gel 60 F_{254} (Merck) and detection by charring with sulfuric acid. Flash column chromatography[39] was performed on Silica Gel 60 (230–400 mesh, Merck).

Phenyl 2,3:4,6-di-O-isopropylidene-1-thio-β-D-galactopyranoside (**2**). — 2-Methoxypropene (1.3 mL, 13.5 mmol) was added dropwise at room temperature under argon to a stirred solution of phenyl 1-thio-β-D-galactopyranoside[23,24] (0.81 g, 3 mmol) in anhydrous *N,N*-dimethylformamide (20 mL) containing (±)-10-camphorsulphonic acid (60 mg). The mixture was stirred for 1 h at room temperature, then treated with triethylamine (0.5 mL), and concentrated. Column chromatography (750:250:1 ether–hexane–triethylamine) of the residue gave **2** (1.01 g, 95%), m.p. 101–103° (from hexane), $[\alpha]_D$ −66° (*c* 1, chloroform). N.m.r. data: ^1H (C_6D_6), δ 7.92–7.88 and 7.16–7.04 (2 m, 5 H, Ph), 4.67 (d, 1 H, $J_{1,2}$ 9.5 Hz, H-1), 4.20 (dd, 1 H, $J_{2,3}$ 9.2 Hz, H-2), 3.88 (dd, 1 H, $J_{3,4}$ 2.6, $J_{4,5}$ 0.8 Hz, H-4), 3.85 (dd, 1 H, $J_{5,6a}$ 1.6, $J_{6a,6b}$ 12.8 Hz, H-6a), 3.48 (dd, 1 H, $J_{5,6b}$ 2.2 Hz, H-6b), 3.24 (dd, 1 H, H-3), 2.47 (ddd, 1 H, H-5), 1.48, 1.38, 1.30, and 1.08 (4 s, each 3 H, 2 CMe_2); ^{13}C ($CDCl_3$), δ 132.82, 131.43, 128.27, and 127.59 (aromatic), 110.07 (dioxolane CMe_2), 98.01 (dioxane CMe_2), 84.62 (C-1), 79.09, 70.23, 69.35, and 66.14 (C-2,3,4,5), 62.67 (C-6), 28.61 and 18.25 (dioxane CMe_2), 26.30 and 25.90 (dioxolane CMe_2).

Anal. Calc. for $C_{18}H_{24}O_5S$: C, 61.34; H, 6.86. Found: C, 61.38; H, 6.90.

Phenyl 2,6-di-O-benzyl-3,4-O-isopropylidene-1-thio-β-D-galactopyranoside (**5**). — Sodium hydride (1.6 g of a 60% dispersion in oil, 40 mmol) was added in small portions to a solution of phenyl 3,4-*O*-isopropylidene-1-thio-β-D-galactopyranoside[26] (**4**; 3.12 g, 10 mmol) in dry *N,N*-dimethylformamide (50 mL) with stirring and cooling in ice–water. The mixture was then stirred for 30 min at room temperature, benzyl bromide (3.6 mL, 30 mmol) was added dropwise, and the mixture was stirred overnight at room temperature. The excess of sodium hydride was decomposed by the dropwise addition of methanol (15 mL). Volatile material was evaporated and a solution of the residue in dichloromethane was washed with water, dried, and concentrated. Column chromatography (30:1 toluene–ethyl acetate) of the residue gave **5** (4.68 g, 95%), m.p. 61–62° (from hexane), $[\alpha]_D$ −22° (*c* 1, chloroform). ^1H-N.m.r. data ($CDCl_3$): δ 7.63–7.26 (m, 15 H, 3 Ph), 4.86 and 4.72 (2 d, 2 H, J_{gem} 11.5 Hz, OCH_2Ph), 4.69 (d, 1 H, $J_{1,2}$ 9.6 Hz, H-1), 4.63 and 4.55 (2 d, 2 H, J_{gem} 12.0 Hz, OCH_2Ph), 4.29 (dd, 1 H, $J_{2,3}$ 6.0, $J_{3,4}$ 5.8 Hz, H-3), 4.24 (dd, 1 H, $J_{4,5}$ 1.8 Hz, H-4), 3.97 (ddd, 1 H, $J_{5,6a} = J_{5,6b} = 6.0$ Hz, H-5), 3.82 (m, 2 H, H-6), 3.55 (dd, 1 H, H-2), 1.42 and 1.35 (2 s, each 3 H, CMe_2).

Anal. Calc. for $C_{29}H_{32}O_5S$: C, 70.70; H, 6.55. Found: C, 70.63; H, 6.49.

Phenyl 2-O-benzyl-3,4-O-isopropylidene-1-thio-β-D-galactopyranoside (**6**). — A mixture of phenyl 1-thio-β-D-galactopyranoside (817 mg, 3 mmol), 2,2-dimethoxypropane (30 mL, 244 mmol), and (±)-10-camphorsulphonic acid (30 mg)

was stirred for 48 h at room temperature under argon. Triethylamine (0.2 mL) was then added, and the volatile material was evaporated. A solution of the residue in dry tetrahydrofuran (12 mL) was stirred with sodium hydride (240 mg of a 60% dispersion in oil, 6 mmol) for 30 min at room temperature, benzyl bromide (1.45 mL, 12 mmol) was added, and the mixture was stirred for 2 h at 45° under argon and then cooled at 0°. Methanol and then water were added to destroy the excess of sodium hydride. The mixture was extracted twice with ether, and the combined extracts were dried and concentrated. A solution of the residue in methanol (6 mL) was treated with (±)-10-camphorsulphonic acid (8 mg) for 10 min at room temperature, the reaction being monitored by t.l.c. (2:1 hexane–ethyl acetate). Triethylamine (0.2 mL) was added and the mixture was concentrated. Column chromatography (600:400:1 hexane–ethyl acetate–triethylamine) of the residue gave **6** as a syrup (710 mg, 59%), $[\alpha]_D$ −1.5° (*c* 0.9, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.60–7.32 (m, 10 H, 2 Ph), 4.90 and 4.74 (2 d, 2 H, J_{gem} 11.5 Hz, OCH_2Ph), 4.72 (d, 1 H, $J_{1,2}$ 9.5 Hz, H-1), 4.34 (dd, 1 H, $J_{2,3} = J_{3,4} = 6.0$ Hz, H-3), 4.23 (dd, 1 H, $J_{4,5}$ 1.9 Hz, H-4), 4.00 (dd, 1 H, $J_{5,6a}$ 6.5, $J_{6a,6b}$ 10.5 Hz, H-6a), 3.90–3.80 (m, 2 H, H-5,6b), 3.58 (dd, 1 H, H-2), 1.44 and 1.39 (2 s, each 3 H, CMe_2).

Anal. Calc. for $C_{22}H_{26}O_5S$: C, 65.65; H, 6.51. Found: C, 65.46; H, 6.62.

*Phenyl 3,4-*O*-isopropylidene-2,6-di-*O*-methyl-1-thio-β-*D*-galactopyranoside* (**7**). — Sodium hydride (1.34 g of a 60% dispersion in oil, 33.5 mmol) was added to a solution of **4** (3.12 g, 10 mmol) in dry tetrahydrofuran (40 mL) with stirring and cooling in ice–water. The mixture was stirred for 30 min at room temperature, methyl iodide (4.5 mL, 72 mmol) was added, and the mixture was stirred for 2 h at 50°, further additions of sodium hydride (0.45 g of a 60% dispersion in oil, 11 mmol) and methyl iodide (2.3 mL, 37 mmol) being made after 90 min. The mixture was cooled to 0° and methanol and then water were added to destroy the excess of sodium hydride. The mixture was extracted twice with ether, and the combined extracts were dried and concentrated. Column chromatography (2:1 hexane–ethyl acetate) of the residue gave **7** as a syrup (3.23 g, 95%), $[\alpha]_D$ −23° (*c* 1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.64–7.26 (m, 5 H, Ph), 4.60 (d, 1 H, $J_{1,2}$ 9.5 Hz, H-1), 4.20 (m, 2 H, H-3,4), 3.91 (ddd, 1 H, $J_{4,5}$ 1.7, $J_{5,6a} = J_{5,6b} = 6.5$ Hz, H-5), 3.70 (m, 2 H, H-6a,6b), 3.56 and 3.41 (2 s, each 3 H, 2 OMe), 3.29 (dd, 1 H, $J_{2,3}$ 6.0 Hz, H-2), 1.49 and 1.36 (2 s, each 3 H, CMe_2).

Anal. Calc. for $C_{17}H_{24}O_5S$: C, 59.98; H, 7.10. Found: C, 60.12; H, 7.09.

*Phenyl 2,6-di-*O*-acetyl-3,4-*O*-isopropylidene-1-thio-β-*D*-galactopyranoside* (**8**). — Acetic anhydride (10 mL) was added to a solution of **4** (1 g) in pyridine (10 mL). After 3 h at room temperature, the reaction mixture was concentrated. Column chromatography (3:2 hexane–ethyl acetate) of the residue gave **8** as a syrup (1.2 g, 95%), $[\alpha]_D$ +32° (*c* 1.25, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.61–7.34 (m, 5 H, Ph), 5.10 (m, 1 H, H-2), 4.65 (d, 1 H, $J_{1,2}$ 11.0 Hz, H-1), 4.42 (m, 2 H, H-6a,6b), 4.26 (m, 2 H, H-3,4), 4.05 (ddd, 1 H, $J_{4,5}$ 1.5, $J_{5,6a} = J_{5,6b} =$ 6.0 Hz, H-5), 2.16 and 2.12 (2 s, each 3 H, 2 Ac), 1.55 and 1.35 (2 s, each 3 H, CMe_2).

Anal. Calc. for $C_{19}H_{24}O_7S$: C, 57.56; H, 6.10. Found: C, 57.82; H, 6.10.

Phenyl 2,6-di-O-benzoyl-3,4-O-isopropylidene-1-thio-β-D-galactopyranoside (**9**). — Benzoyl chloride (0.9 mL, 7.8 mmol) was added to a solution of **4** (800 mg, 2.6 mmol) in anhydrous pyridine (4.8 mL) containing 4-dimethylaminopyridine (~5 mg) with stirring and cooling in ice–water. The mixture was stirred for 5 min at 0°, when t.l.c. (1:1 hexane–ethyl acetate) showed the reaction to be complete. After the addition of methanol (0.4 mL), the solution was concentrated, and the residue was crystallized from ethanol to give **9** (1.15 g, 86%), m.p. 129–131°, $[\alpha]_D$ +29° (*c* 1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.15 and 7.73–7.10 (2 m, 15 H, 3 Ph), 5.41 (dd, 1 H, $J_{1,2}$ 10.0, $J_{2,3}$ 6.8 Hz, H-2), 4.85 (d, 1 H, H-1), 4.80 (dd, 1 H, $J_{5,6a}$ 4.0, $J_{6a,6b}$ 12.0 Hz, H-6a), 4.67 (dd, 1 H, $J_{5,6b}$ 8.0 Hz, H-6b), 4.45 (dd, 1 H, $J_{3,4}$ 6.0 Hz, H-3), 4.39 (dd, 1 H, $J_{4,5}$ 2.5 Hz, H-4), 4.29 (m, 1 H, H-5), 1.63 and 1.38 (2 s, each 3 H, CMe_2).

Anal. Calc. for $C_{29}H_{28}O_7S$: C, 66.91; H, 5.42. Found: C, 66.96; H, 5.44.

Phenyl 2-O-benzoyl-3,4-O-isopropylidene-1-thio-β-D-galactopyranoside (**10**). — A mixture of phenyl 1-thio-β-D-galactopyranoside (250 mg, 0.9 mmol), 2,2-dimethoxypropane (9 mL, 73 mmol), and (±)-10-camphorsulphonic acid (8 mg) was stirred for 48 h at room temperature under argon. Triethylamine (60 μL) was then added and the solution was concentrated. To a solution of the residue in anhydrous pyridine (1.5 mL) containing 4-dimethylaminopyridine (~3 mg) at 0° was added benzoyl chloride (0.16 mL, 1.4 mmol). After 5 min, methanol (0.2 mL) was added and the solution was concentrated. The residue was taken up in methanol (2 mL), then treated with (±)-10-camphorsulphonic acid (3 mg) for 5 min at room temperature. Triethylamine (0.1 mL) was added, and the solution was concentrated. Column chromatography (600:400:1 hexane–ethyl acetate–triethylamine) of the residue gave **10** as a solid (230 mg, 60%) melting below 30°, $[\alpha]_D$ +51° (*c* 1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.15 and 7.68–7.30 (2 m, 10 H, 2 Ph), 5.35 (dd, 1 H, $J_{1,2}$ 10.0, $J_{2,3}$ 7.2 Hz, H-2), 4.85 (d, 1 H, H-1), 4.43 (dd, 1 H, $J_{3,4}$ 5.8 Hz, H-3), 4.31 (dd, 1 H, $J_{4,5}$ 1.9 Hz, H-4), 4.10–3.80 (m, 3 H, H-5,6a,6b), 1.59 and 1.35 (2 s, each 3 H, CMe_2).

Anal. Calc. for $C_{22}H_{24}O_6S$: C, 63.44; H, 5.81. Found: C, 63.10; H, 5.95.

Phenyl 3-O-benzyl-4,6-O-benzylidene-1-thio-β-D-galactopyranoside (**18**). — A mixture of phenyl 4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside (360 mg, 1 mmol) and dibutyltin oxide (300 mg, 1.2 mmol) in acetonitrile (20 mL) was heated to reflux overnight in the presence of activated, powdered molecular sieve (4 Å, 300 mg). Tetrabutylammonium bromide (320 mg, 1 mmol) and benzyl bromide (0.5 mL, 4.2 mmol) were added and boiling under reflux was continued for 1 h. The cooled mixture was filtered, the solids were washed with dichloromethane, and the combined filtrate and washings were concentrated. Column chromatography (2:1, then 3:2 hexane–ethyl acetate) of the residue gave **18** (312 mg, 70%), which crystallized from hexane–ethyl acetate; m.p. 165–167°, $[\alpha]_D$ +11° (*c* 1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.67–7.15 (m, 15 H, 3 Ph), 5.41 (s, 1 H, C*H*Ph), 4.70 (m, 2 H, OCH_2Ph), 4.50 (d, 1 H, $J_{1,2}$ 9.5 Hz, H-1), 4.32 (dd, 1 H, $J_{5,6a}$ 1.8, $J_{6a,6b}$ 12.0

Hz, H-6a), 4.12 (dd, 1 H, $J_{3,4}$ 3.8, $J_{4,5}$ 1.0 Hz, H-4), 3.95 (dd, 1 H, $J_{5,6b}$ 1.8 Hz, H-6b), 3.93 (dd, 1 H, $J_{2,3}$ 9.5 Hz, H-2), 3.50 (dd, 1 H, H-3), 3.40 (m, 1 H, H-5), 2.50 (bd, 1 H, OH); ($CDCl_3$ + CCl_3CONCO): δ 8.48 (s, 1 H, NH), 7.70–7.26 (m, 15 H, 3 Ph), 5.50 (s, 1 H, C*H*Ph), 5.32 (dd, 1 H, $J_{1,2} = J_{2,3}$ = 10.0 Hz, H-2), 4.75 (d, 1 H, H-1), 4.72 and 4.60 (2 d, 2 H, J_{gem} 13.0 Hz, OCH_2Ph), 4.38 (dd, 1 H, $J_{5,6a}$ 1.5, $J_{6a,6b}$ 12.5 Hz, H-6a), 4.26 (dd, 1 H, $J_{3,4}$ 3.5, $J_{4,5}$ 1.0 Hz, H-4), 4.02 (dd, 1 H, $J_{5,6b}$ 1.5 Hz, H-6b), 3.76 (ddd, 1 H, H-3), 3.50 (ddd, 1 H, H-5).

Anal. Calc. for $C_{26}H_{26}O_5S$: C, 69.31; H, 5.82. Found: C, 69.25; H, 5.91.

*General procedure for catalytic oxidation of phenyl 1-thio-β-*D*-hexopyranosides.* — Ruthenium(III) chloride hydrate (5 mg) and sodium periodate (900 mg, 4.2 mmol) were added to a mixture of phenyl 1-thio-β-D-hexopyranoside (1 mmol), acetonitrile (10 mL), carbon tetrachloride (10 mL), and water (15 mL). The biphasic mixture was stirred vigorously for 3–10 min at room temperature and the reaction was monitored by t.l.c. (the phenyl sulphones usually migrated more slowly than the phenyl thioglycosides). Dichloromethane (10 mL) was then added, the phases were separated, the aqueous phase was extracted three times with dichloromethane, and the combined organic extracts were dried and concentrated. The crude product containing the remaining ruthenium species was purified by column chromatography on silica gel.

*2,6-Di-*O*-benzyl-3,4-*O*-isopropylidene-β-*D*-galactopyranosyl phenyl sulphone* (**12**). — Oxidation of **5** (492 mg, 1 mmol), followed by column chromatography (2:1 hexane–ethyl acetate), gave **12** (467 mg, 89%), $[\alpha]_D$ +5° (*c* 1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.04–7.96 (m, 5 H, Ph), 7.66–7.24 (m, 10 H, 2 Ph), 4.84 (m, 2 H, OCH_2Ph), 4.47 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.42–4.36 (m, 3 H, H-3 and OCH_2Ph), 4.20 (dd, 1 H, $J_{3,4}$ 6.5, $J_{4,5}$ 2.5 Hz, H-4), 4.13 (dd, 1 H, $J_{2,3}$ 5.0 Hz, H-3), 3.81 (m, 1 H, H-5), 3.74–3.57 (m, 2 H, H-6a,6b), 1.38 and 1.30 (2 s, each 3 H, CMe_2).

Anal. Calc. for $C_{29}H_{32}O_7S$: C, 66.39; H, 6.15. Found: C, 66.10; H, 6.20.

*3,4-*O*-Isopropylidene-2,6-di-*O*-methyl-β-*D*-galactopyranosyl phenyl sulphone* (**13**). — Oxidation of **7** (350 mg, 1 mmol), followed by column chromatography (1:1 hexane–ethyl acetate), gave **13** (345 mg, 90%), m.p. 125–126° (from ethanol), $[\alpha]_D$ −3° (*c* 1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.95 and 7.70–7.50 (2 m, 5 H, Ph), 4.28 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.27 (dd, 1 H, $J_{2,3}$ 5.2, $J_{3,4}$ 6.0 Hz, H-3), 4.12 (dd, 1 H, $J_{4,5}$ 2.5 Hz, H-4), 3.79 (dd, 1 H, H-2), 3.68 (ddd, 1 H, $J_{5,6a}$ 5.0, $J_{5,6b}$ 7.0 Hz, H-5), 3.60 (dd, 1 H, $J_{6a,6b}$ 11.0 Hz, H-6a), 3.50 (s, 3 H, OMe), 3.40 (dd, 1 H, H-6b), 3.15 (s, 3 H, OMe), 1.33 and 1.24 (2 s, each 3 H, CMe_2). Mass spectrum: *m/z* 390 (M^+ +18).

Anal. Calc. for $C_{17}H_{24}O_7S$: C, 54.82; H, 6.49. Found: C, 54.83; H, 6.60.

*2,6-Di-*O*-acetyl-3,4-*O*-isopropylidene-β-*D*-galactopyranosyl phenyl sulphone* (**14**). — Oxidation of **8** (1.35 g, 3.4 mmol), followed by column chromatography (1:1 hexane–ethyl acetate), gave **14** (1.42 g, 97%), m.p. 169–170° (from ethanol), $[\alpha]_D$ +58° (*c* 1.45, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.20 and 7.77–7.60 (2 m, 5 H, Ph), 5.32 (dd, 1 H, $J_{1,2}$ 9.3, $J_{2,3}$ 6.2 Hz, H-2), 4.40 (d, 1 H, H-1), 4.35–4.25 (m, 3 H, H-3,6a,6b), 4.18 (dd, 1 H, $J_{3,4}$ 5.5, $J_{4,5}$ 2.2 Hz, H-4), 3.97 (ddd, 1 H, $J_{5,6a}$

7.0, $J_{5,6b}$ 4.5 Hz, H-5), 2.19 and 2.00 (2 s, each 3 H, 2 Ac), 1.34 and 1.29 (2 s, each 3 H, CMe_2). Mass spectrum: *m/z* 446 (M^+ + 18).

Anal. Calc. for $C_{19}H_{24}O_9S$: C, 53.26; H, 5.65. Found: C, 53.34; H, 5.63.

2,6-Di-O-benzoyl-3,4-O-isopropylidene-β-D-galactopyranosyl phenyl sulphone (**15**). — Oxidation of **9** (210 mg, 0.4 mmol), followed by column chromatography (dichloromethane), gave **15** (190 mg, 91%), m.p. 220–221° (from hexane–ethyl acetate), $[\alpha]_D$ +35° (*c* 1.3, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.15, 7.98, and 7.70–7.46 (3 m, 15 H, 3 Ph), 5.67 (dd, 1 H, $J_{1,2}$ 9.0, $J_{2,3}$ 6.0 Hz, H-2), 4.66 (d, 1 H, H-1), 4.60 (m, 2 H, H-6), 4.52 (dd, 1 H, $J_{3,4}$ 6.0 Hz, H-3), 4.35 (dd, 1 H, $J_{4,5}$ 2.0 Hz, H-4), 4.20 (m, 1 H, H-5), 1.48 and 1.34 (2 s, each 3 H, CMe_2). Mass spectrum: *m/z* 570 (M^+ + 18).

Anal. Calc. for $C_{29}H_{28}O_9S$: C, 63.03; H, 5.11. Found: C, 62.93; H, 5.10.

2,3-Di-O-benzyl-4,6-O-benzylidene-β-D-galactopyranosyl phenyl sulphone (**20**). — Oxidation of **17**[21] (540 mg, 1 mmol), followed by column chromatography (2:1 hexane–ethyl acetate), gave **20** (550 mg, 95%), m.p. 164–166° (from ethanol), $[\alpha]_D$ −3° (*c* 1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.11 and 7.68–7.32 (2 m, 20 H, 4 Ph), 5.42 (s, 1 H, C*H*Ph), 5.01 and 4.92 (2 d, 2 H, J_{gem} 10.0 Hz, OCH_2Ph), 4.75 (m, 2 H, OCH_2Ph), 4.55 (d, 1 H, $J_{1,2}$ 9.5 Hz, H-1), 4.22 (dd, 1 H, $J_{2,3}$ 9.5 Hz, H-2), 4.19 (dd, 1 H, $J_{5,6a}$ 1.5, $J_{6a,6b}$ 12.0 Hz, H-6a), 4.08 (dd, 1 H, $J_{3,4}$ 3.1, $J_{4,5}$ 1.0 Hz, H-4), 3.91 (dd, 1 H, $J_{5,6b}$ 1.5 Hz, H-6b), 3.71 (dd, 1 H, H-3), 3.40 (ddd, 1 H, H-5).

Anal. Calc. for $C_{33}H_{32}O_7S$: C, 69.21; H, 5.63. Found: C, 69.06; H, 5.61.

General procedure for reductive lithiation of phenyl 1-thio-β-D-hexopyranosides and β-D-hexopyranosyl phenyl sulphones. —Small chips of lithium (69 mg, 10 mmol), previously washed with dry hexane, were added under argon at room temperature to a solution of naphthalene (1.28 g, 10 mmol) in anhydrous tetrahydrofuran (10 mL, distilled from Na–benzophenone). The mixture was stirred (glass-coated magnetic bar) overnight at room temperature under argon. The resulting dark-green solution of lithium naphthalenide could be stored for a few days under argon in the refrigerator.

The M lithium naphthalenide solution (2–5 mL)* was transferred dropwise under argon by standard syringe techniques to a solution of phenyl 1-thio-β-D-hexopyranoside or β-D-hexopyranosyl phenyl sulphone (1 mmol) in anhydrous tetrahydrofuran (5 mL) at −78°. The reaction was indicated by a change of colour (from dark-green to light-brown) of the solution, and was monitored by t.l.c. After the starting material had disappeared, the mixture was allowed to reach room temperature and stirring was continued for 15 min. The mixture was neutralized by the dropwise addition of tetrahydrofuran–acetic acid (4:1, ~0.6 mL). When the substrate contained substituents able to react with an excess of lithium naphthalenide (*O*-benzyl groups in other positions than C-2), the reaction mixture was stirred for 30 min at −78° after disappearance of the starting material (t.l.c.), then neutralized at −78° by addition of tetrahydrofuran–acetic acid (4:1), and allowed to reach room temperature.

*Where there was unavoidable concomitant cleavage of protecting groups (reductive lithiations of **8**, **14**, **15**, and **17**), >2 mol of lithium naphthalenide was required.

The neutralized reaction mixture was concentrated and toluene was evaporated several times from the residue, a solution of which in dichloromethane was washed with water, dried, and concentrated.

*1,5-Anhydro-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-*D-arabino-*hex-1-enitol* (**21**). — Reductive lithiation of **1**[21] (541 mg, 1 mmol) followed by column chromatography(1000:1 toluene–triethylamine, then 1000:1 dichloromethane–triethylamine), gave **21** (318 mg, 98%), m.p. 101–102° (from hexane), $[\alpha]_D$ −41° (*c* 1.1, chloroform). ^{1}H-N.m.r. data (C_6D_6): δ 7.66–7.10 (m, 10 H, 2 Ph), 6.12 (dd, 1 H, $J_{1,2}$ 6.2, $J_{1,3}$ 1.6 Hz, H-1), 5.30 (s, 1 H, C*H*Ph), 4.78 and 4.62 (2 d, 2 H, J_{gem} 12.5 Hz, OCH_2Ph), 4.72 (dd, 1 H, $J_{2,3}$ 2.0 Hz, H-2), 4.28 (ddd, 1 H, $J_{3,4}$ 7.5 Hz, H-3), 4.15 (dd, 1 H, $J_{5,6a}$ 5.2, $J_{6a,6b}$ 10.4 Hz, H-6a), 3.95 (dd, 1 H, $J_{4,5}$ 10.0 Hz, H-4), 3.72 (ddd, 1 H, $J_{5,6b}$ 10.2 Hz, H-5), 3.50 (dd, 1 H, H-6b).

Anal. Calc. for $C_{20}H_{20}O_4$: C, 74.05; H, 6.21. Found: C, 73.98; H, 6.26.

*1,5-Anhydro-2-deoxy-4,6-*O*-isopropylidene-*D-lyxo-*hex-1-enitol* (**26**). — Reductive lithiation of **2** (352 mg, 1 mmol), followed by column chromatography (2000:1000:3 ethyl acetate–hexane–triethylamine), gave **26** (158 mg, 85%), m.p. 48–50°, $[\alpha]_D$ +18° (*c* 1.1, chloroform). N.m.r. data: ^{1}H (C_6D_6), δ 6.31 (dd, 1 H, $J_{1,2}$ 6.2, $J_{1,3}$ 1.8 Hz, H-1), 4.74 (ddd, 1 H, $J_{2,3} = J_{2,4}$ = 1.6 Hz, H-2), 4.24 (m, 1 H, $J_{3,4}$ 5.2, $J_{3,OH}$ 11.8, $J_{3,5}$ ~0.5 Hz, H-3), 3.74 (dd, 1 H, $J_{5,6a}$ 2.0, $J_{6a,6b}$ 12.6 Hz, H-6a), 3.57 (ddd, 1 H, $J_{4,5}$ ~0.8 Hz, H-4), 3.33 (dd, 1 H, $J_{5,6b}$ 1.6 Hz, H-6b), 2.96 (m, 1 H, H-5), 2.44 (d, 1 H, OH), 1.42 and 1.13 (2 s, each 3 H, CMe_2); ^{13}C ($CDCl_3$), δ 143.73 (C-1), 102.04 (C-2), 99.20 (*C*Me_2), 67.80, 64.78, and 62.46 (C-3, C-4, and C-5), 62.96 (C-6), 29.26 and 18.54 (C*Me*$_2$).

Anal. Calc. for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 58.08; H, 7.68.

*1,5-Anhydro-6-*O*-benzyl-2-deoxy-3,4-*O*-isopropylidene-*D-lyxo-*hex-1-enitol* (**22**). — Reductive lithiation of **5** (493 mg, 1 mmol), followed by column chromatography (800:200:1 hexane–ethyl acetate–triethylamine), gave **22** (268 mg, 97%), isolated as an oil, 150°/0.5 Pa (Kugelrohr apparatus), $[\alpha]_D$ +18° (*c* 1.2, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.42–7.30 (m, 5 H, Ph), 6.45 (d, 1 H, $J_{1,2}$ 6.4 Hz, H-1), 4.82 (ddd, 1 H, $J_{2,3}$ 3.0, $J_{2,4}$ 1.5 Hz, H-2), 4.70 and 4.59 (2 d, 2 H, J_{gem} 12.0 Hz, OCH_2Ph), 4.67 (dd, 1 H, $J_{3,4}$ 6.0 Hz, H-3), 4.31 (ddd, 1 H, $J_{4,5}$ 1.0 Hz, H-4), 4.13 (ddd, 1 H, $J_{5,6a}$ 7.5, $J_{5,6b}$ 5.2 Hz, H-5), 3.86 (dd, 1 H, $J_{6a,6b}$ 10.0 Hz, H-6a), 3.75 (dd, 1 H, H-6b), 1.47 and 1.35 (2 s, each 3 H, CMe_2).

Anal. Calc. for $C_{16}H_{20}O_4$: C, 69.55; H, 7.30. Found: C, 69.43; H, 7.25.

Reductive lithiation of **12** (524 mg, 1 mmol), followed by column chromatography (800:200:1 hexane–ethyl acetate–triethylamine), gave **22** (263 mg, 95%).

*1,5-Anhydro-2-deoxy-3,4-*O*-isopropylidene-*D-lyxo-*hex-1-enitol* (**23**). — Reductive lithiation of **6** (403 mg, 1 mmol), followed by column chromatography (3:2 hexane–ethyl acetate), gave **23** (171 mg, 92%), isolated as a syrup, $[\alpha]_D$ +28° (*c* 1.9, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 6.49 (d, 1 H, $J_{1,2}$ 6.1 Hz, H-1), 4.87 (ddd, 1 H, $J_{2,3}$ 2.9, $J_{2,4}$ 1.5 Hz, H-2), 4.74 (dd, 1 H, $J_{3,4}$ 6.5 Hz, H-3), 4.35 (ddd, 1 H, $J_{4,5}$ 1.5 Hz, H-4), 4.10–3.80 (m, 3 H, H-5,6a,6b), 2.5 (m, 1 H, OH), 1.48 and 1.37 (2 s, each 3 H, CMe_2).

Anal. Calc. for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 57.80; H, 7.71.

Reductive lithiation of **8** (396 mg, 1 mmol), followed by column chromatography (3:2, then 1:1 hexane–ethyl acetate), gave **23** (127 mg, 68%) and **4** (53 mg, 17%).

Reductive lithiation of **9** (521 mg, 1 mmol), followed by column chromatography (2:1, then 3:2 hexane–ethyl acetate), gave **10** (67 mg, 16%), then **4** (181 mg, 58%). No trace of **23** could be detected.

Reductive lithiation of **14** (428 mg, 1 mmol), followed by column chromatography (4:1, then 3:2 hexane–ethyl acetate), gave 6-*O*-acetyl-1,5-anhydro-2-deoxy-3,4-*O*-isopropylidene-D-*lyxo*-hex-1-enitol (**25**; 94 mg, 41%), isolated as a syrup, $[\alpha]_D$ +16° (*c* 1.2, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 6.47 (d, 1 H, $J_{1,2}$ 6.5 Hz, H-1), 4.88 (ddd, 1 H, $J_{2,3}$ 2.9, $J_{2,4}$ 1.2 Hz, H-2), 4.72 (dd, 1 H, $J_{3,4}$ 6.2 Hz, H-3), 4.43 (m, 2 H, H-6), 4.32 (ddd, 1 H, $J_{4,5}$ 1.0 Hz, H-4), 4.16 (ddd, 1 H, $J_{5,6a}$ 7.0, $J_{5,6b}$ 5.0 Hz, H-5), 2.14 (s, 3 H, OAc), 1.47 and 1.36 (2 s, each 3 H, CMe_2).

Anal. Calc. for $C_{11}H_{16}O_5$: C, 57.88; H, 7.07. Found: C, 58.17; H, 7.24.

Eluted next was **23** (144 mg, 47%).

Reductive lithiation of **15** (553 mg, 1 mmol), followed by column chromatography (2:1, then 3:2 hexane–ethyl acetate), gave **23** (251 mg, 82%).

*1,5-Anhydro-2-deoxy-3,4-*O*-isopropylidene-6-*O*-methyl-*D-lyxo-*hex-1-enitol* (**24**). — Reductive lithiation of **7** (340 mg, 1 mmol), followed by column chromatography (3:1 hexane–ethyl acetate), gave **24** (192 mg, 96%), isolated as a syrup, $[\alpha]_D$ +19° (*c* 1.7, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 6.49 (d, 1 H, $J_{1,2}$ 6.2 Hz, H-1), 4.85 (ddd, 1 H, $J_{2,3}$ 3.0, $J_{2,4}$ 1.5 Hz, H-2), 4.72 (dd, 1 H, $J_{3,4}$ 6.5 Hz, H-3), 4.30 (ddd, 1 H, $J_{4,5}$ 1.5 Hz, H-4), 4.12 (ddd, 1 H, $J_{5,6a}$ 8.0, $J_{5,6b}$ 4.8 Hz, H-5), 3.80 (dd, 1 H, $J_{6a,6b}$ 10.5 Hz, H-6a), 3.68 (dd, 1 H, H-6b), 3.49 (s, 3 H, OMe), 1.49 and 1.37 (2 s, each 3 H, CMe_2).

Anal. Calc. for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 59.87; H, 7.98.

Reductive lithiation of **13** (372 mg, 1 mmol), followed by column chromatography (3:1 hexane–ethyl acetate), gave **24** (170 mg, 85%).

*1,5-Anhydro-4,6-*O*-benzylidene-2-deoxy-*D-lyxo-*hex-1-enitol* (**27**). — Reductive lithiation of **17**[21] (541 mg, 1 mmol), followed by column chromatography (2:1, then 3:2, and 1:1 hexane–ethyl acetate), gave **27** (176 mg, 75%), m.p. 151–152° (from ethyl acetate–hexane), $[\alpha]_D$ +47° (*c* 1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.60–7.30 (m, 5 H, Ph), 6.48 (dd, 1 H, $J_{1,2}$ 6.8, $J_{1,3}$ 2.0 Hz, H-1), 5.73 (s, 1 H, C*H*Ph), 4.78 (ddd, 1 H, $J_{2,3} = J_{2,4} = 1.8$ Hz, H-2), 4.52 (m, 1 H, H-3), 4.40 (dd, 1 H, $J_{5,6a}$ 2.0, $J_{6a,6b}$ 12.5 Hz, H-6a), 4.25 (bd, 1 H, $J_{3,4}$ 5.0 Hz, H-4), 4.08 (dd, 1 H, $J_{5,6b}$ 1.5 Hz, H-6b), 3.95 (bs, 1 H, H-5), 2.45 (d, 1 H, $J_{3,OH}$ 11.8 Hz, OH).

Anal. Calc. for $C_{13}H_{14}O_4$: C, 66.66; H, 6.02. Found: C, 66.77; H, 5.95.

Reductive lithiation of **20** (573 mg, 1 mmol), followed by column chromatography (3:1 hexane–ethyl acetate), gave 1,5-anhydro-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-D-*lyxo*-hex-1-enitol (**28**; 97 mg, 30%) as an amorphous solid, $[\alpha]_D$ +122° (*c* 1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.70–7.30 (m, 10 H, 2 Ph), 6.55 (dd, 1 H, $J_{1,2}$ 6.5, $J_{1,3}$ 2.0 Hz, H-1), 5.69 (s, 1 H, C*H*Ph), 4.87 (ddd, 1 H, $J_{2,3} = J_{2,4} = 1.5$ Hz, H-2), 4.73 (m, 2 H, OCH_2Ph), 4.40 (m, 2 H, H-3,6a), 4.31 (bd, 1

H, $J_{3,4}$ 3.5 Hz, H-4), 4.08 (dd, 1 H, $J_{5,6b}$ 1.0, $J_{6a,6b}$ 12.0 Hz, H-6b), 3.90 (bs, 1 H, H-5).

Anal. Calc. for $C_{20}H_{20}O_4$: C, 74.06; H, 6.22. Found: C, 73.87; H, 6.26.

Eluted next was 1,5-anhydro-2,3-di-*O*-benzyl-4,6-*O*-benzylidene-D-galactitol (**16**; 199 mg, 46%), m.p. 95–97° (ethyl acetate–hexane), $[\alpha]_D$ +76° (*c* 0.8, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.70–7.30 (m, 10 H, 2 Ph), 5.55 (s, 1 H, C*H*Ph), 4.90 and 4.70 (2 d, 2 H, J_{gem} 12.0 Hz, OCH_2Ph), 4.84 (m, 2 H, OCH_2Ph), 4.29 (dd, 1 H, $J_{5,6a}$ 1.5, $J_{6a,6b}$ 12.5 Hz, H-6a), 4.24 (dd, 1 H, $J_{3,4}$ 3.5, $J_{4,5}$ 1.0 Hz, H-4), 4.22–4.05 (m, 2 H, H-1*e*,2), 4.00 (dd, 1 H, $J_{5,6b}$ 1.8 Hz, H-6b), 3.61 (dd, 1 H, $J_{2,3}$ 9.1 Hz, H-3), 3.32–3.20 (m, 2 H, H-1*a*,5).

Anal. Calc. for $C_{27}H_{28}O_5$: C, 74.98; H, 6.53. Found: C, 74.67; H, 6.45.

*1,5-Anhydro-3-*O*-benzyl-2,6-deoxy-4-*O*-(3,4-di-*O*-benzyl-2,6-dideoxy-β-*D*-arabino-hexopyranosyl)-*D*-arabino-hex-1-enitol* (**30**). — Reductive lithiation of phenyl 2,3-di-*O*-benzyl-6-deoxy-4-*O*-(3,4-di-*O*-benzyl-2,6-dideoxy-β-D-*arabino*-hexopyranosyl)-1-thio-β-D-glucopyranoside (**29**; 747 mg, 1 mmol), followed by column chromatography (6:1 hexane–ethyl acetate), gave **30** (488 mg, 92%), m.p. 80–83°, $[\alpha]_D$ −45° (*c* 0.75, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.43–7.30 (m, 15 H, 3 Ph), 6.40 (dd, 1 H, $J_{1,2}$ 6.0, $J_{1,3}$ 1.0 Hz, H-1), 5.00 and 4.70 (2 d, 2 H, J_{gem} 11.0 Hz, CH_2Ph), 4.91 (dd, 1 H, $J_{2,3}$ 3.0 Hz, H-2), 4.74 (dd, 1 H, $J_{1',2'a}$ 10.0, $J_{1',2'e}$ 2.0 Hz, H-1′), 4.73 and 4.65 (2 d, 2 H, J_{gem} 12.0 Hz, CH_2Ph), 4.70 (m, 2 H, CH_2Ph), 4.21 (ddd, 1 H, $J_{3,4}$ 5.0 Hz, H-3), 4.12 (dq, 1 H, $J_{4,5}$ 7.0, $J_{5,6}$ 7.0 Hz, H-5), 3.82 (dd, 1 H, H-4), 3.66 (ddd, 1 H, $J_{2'e,3'}$ 5.0, $J_{2'a,3'}$ 10.0, $J_{3',4'}$ 9.0 Hz, H-3′), 3.37 (dq, 1 H, $J_{4',5'}$ 9.0, $J_{5',6'}$ 6.0 Hz, H-5′), 3.19 (dd, 1 H, H-4′), 2.43 (ddd, 1 H, $J_{2'a,2'e}$ 12.0 Hz, H-2′*e*), 1.70 (ddd, 1 H, H-2′*a*), 1.43 (d, 3 H, CH_3-6), 1.35 (d, 3 H, CH_3-6′).

Anal. Calc. for $C_{33}H_{38}O_6$: C, 74.69; H, 7.22. Found: C, 74.66; H, 7.35.

Preparation of glycals by radical reductive elimination. — (a) Synthesis of **23**. A mixture of phenyl 1-thio-β-D-galactopyranoside (500 mg, 1.8 mmol), 2,2-dimethoxypropane (19 mL, 155 mmol), and (±)-10-camphorsulphonic acid (19 mg) was stirred for 48 h at room temperature under argon. Triethylamine (0.1 mL) was then added and the solution was concentrated. To a solution of the residue in dry tetrahydrofuran (8 mL) were added sodium hydride (150 mg of a 60% dispersion in oil, 3.8 mmol) and imidazole (25 mg, 0.37 mmol), and the mixture was stirred for 1 h at room temperature. Carbon disulfide (1.1 mL, 18 mmol) was added, the mixture was stirred for 15 min, methyl iodide (1.15 mL, 18 mmol) was added, and stirring was continued for 1 h at room temperature. Methanol and then water were added to destroy the excess of sodium hydride, the mixture was extracted three times with ether, and the combined extracts were dried and concentrated. A solution of the residue in methanol (5 mL) was treated with (±)-10-camphorsulphonic acid (9 mg), the reaction being monitored by t.l.c. (3:2 hexane–ethyl acetate). Triethylamine (0.4 mL) was added and the mixture was concentrated. Column chromatography (100:50:3, then 25:25:1 hexane–ethyl acetate–triethylamine) of the residue gave **11** (400 mg, 55%), which was immediately submitted to radical elimination. ^{1}H-N.m.r. data ($CDCl_3$): δ 7.60–7.30 (m, 5 H, Ph), 6.18 (dd, 1 H, $J_{1,2}$

9.5, $J_{2,3}$ 6.9 Hz, H-2), 4.82 (d, 1 H, H-1), 4.43 (dd, 1 H, $J_{3,4}$ 5.5 Hz, H-3), 4.30 (dd, 1 H, $J_{4,5}$ 2.0 Hz, H-4), 4.10–3.80 (m, 3 H, H-5,6a,6b), 2.65 (s, 3 H, SMe), 2.20 (m, 1 H, OH), 1.35 and 1.60 (2 s, each 3 H, CMe_2).

A solution of **11** (180 mg, 0.45 mmol) in toluene (3.5 mL) was added dropwise to a refluxing solution of tributyltin hydride (0.58 mL, 2.16 mmol) and α,α'-azobisisobutyronitrile (8 mg) in toluene (6 mL). The mixture was boiled for 5 min, then cooled, and concentrated. Column chromatography (hexane, then 3:2 hexane–ethyl acetate) of the residue gave **23** (77 mg, 93%).

(b) Synthesis of **28**. To a solution of **18** (120 mg, 0.27 mmol) in dry tetrahydrofuran (2 mL) was added sodium hydride (21 mg of a 60% dispersion in oil, 0.53 mmol). The mixture was stirred for 45 min at room temperature, carbon disulfide (0.16 mL, 2.7 mmol) was added, stirring was continued for 15 min, then methyl iodide (0.16 mL, 2.6 mmol) was added. Stirring was continued for 20 min at room temperature, methanol and then water were added, the mixture was extracted three times with ether, and the combined extracts were dried and concentrated. Column chromatography (2:1 hexane–ethyl acetate) of the residue gave **19** (110 mg, 79%).

A solution of **19** (95 mg, 0.18 mmol) in toluene (2 mL) was added dropwise to a refluxing solution of tributyltin hydride (0.24 mL, 0.89 mmol) and α,α'-azobisisobutyronitrile (4 mg) in toluene (4 mL). The mixture was boiled for 10 min, then cooled, and concentrated. A solution of the residue in hexane (6 mL) was kept at 5° for 4 h, the supernatant solution was removed, the residue was extracted with dichloromethane, and the extract was concentrated. Column chromatography (3:1 hexane–ethyl acetate) of the residue gave **28** (52 mg, 90%).

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