Preparation, structure, derivatisation and NMR data of cyclohexane-1,2-diacetal protected carbohydrates

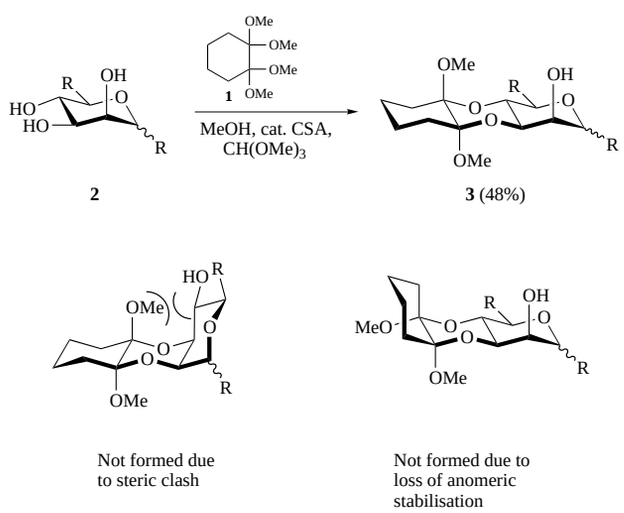
Peter Grice, Steven V. Ley,* Jörg Pietruszka, Henning W. M. Priepke and Stuart L. Warriner

Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge CB2 1EW, UK

Acid catalysed reaction of monosaccharides with 1,1,2,2-tetramethoxycyclohexane results in selective protection of vicinal, diequatorial, diol functionality as a cyclohexane-1,2-diacetal (CDA). This new methodology complements classical cyclic acetal protecting group strategies which in general are not able to mask diols with such diequatorial stereochemistry. The resulting CDA protected derivatives can be readily functionalised to give rapid access to numerous key building blocks for oligosaccharide and natural product synthesis.

As an extension of our dispiroketal (dispoke) methodology we recently introduced the concept of 1,2-diacetals as new, regioselective protecting groups for diequatorial 1,2-diol units in carbohydrates.[1–4] In particular, cyclohexane-1,2-diacetal (CDA) protection of monosaccharide units offers rapid access to important building blocks for oligosaccharide synthesis.[3,5]

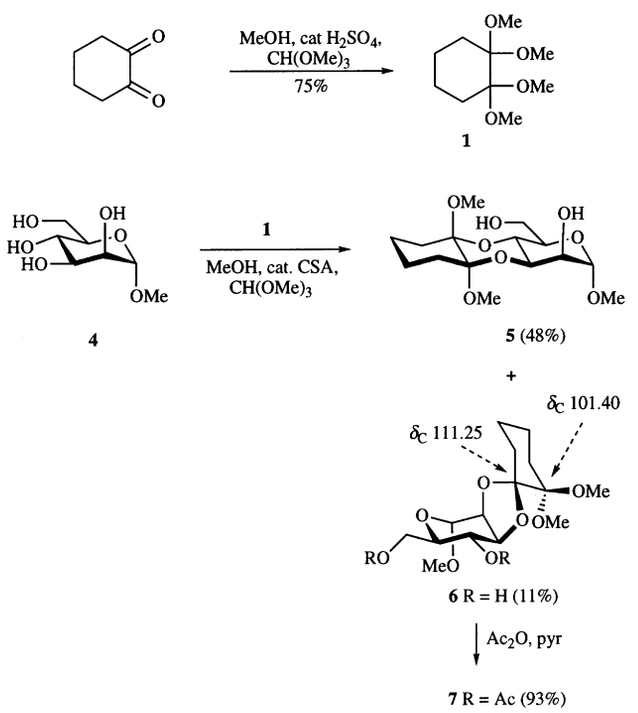
In the reaction of 1,1,2,2-tetramethoxycyclohexane **1** with pyranosides such as **2** regioselective protection of the vicinal diequatorial diol unit is observed (Scheme 1). The selectivity



Scheme 1

arises from the combination of two effects. Protection of the 3,4-diequatorial diol to give product **3** is favoured over the 2,3-*cis* diol as this leads to the sterically less demanding *trans* ring fusion between the dioxane ring (formed by acetalisation) and the pyranoside. Only one diastereoisomer of this compound is produced as the configuration of the acetal centres is controlled by the anomeric effect. The same regulatory elements also control the selectivity of reactions using dispiroketal methodology, however, the use of the more stable 1,1,2,2-tetramethoxycyclohexane **1** instead of 6,6′-bis-dihydropyran (bis-DHP) offers some advantages, particularly for carbohydrate chemistry. Dispiroketal protection reactions are performed in boiling chloroform which can lead to solubility problems when the polyol substrate is very polar. The use of boiling methanol in CDA protections ensures dissolution of the substrate and thermodynamic control in the resulting reaction. As a further advantage, the methoxy groups in the reaction product, *e.g.* **3** can be used as reporter groups in the ^{1}H NMR spectra. In this work we report full experimental details for the protection reactions which have been performed, as well as some useful derivatisations and deprotecting conditions for the resulting CDA protected saccharides. The key NMR characteristics of CDA protected substrates will also be described.

Diacetal **1** is easily synthesised from commercially available cyclohexane-1,2-dione by treatment with methanol, trimethyl orthoformate and catalytic concentrated sulfuric acid (Scheme 2) or may now be obtained from commercial sources.[6]



Scheme 2

With **1** in hand the protection of methyl α-D-mannopyranoside **4**, which did not react with bis-DHP under the standard conditions due to its poor solubility in chloroform, was attempted. Treatment of this monosaccharide with 1.4 equiv. of **1** in boiling methanol with added trimethyl orthoformate and catalytic (±)-camphorsulfonic acid (CSA) for 16 h yielded the 3,4-protected mannopyranoside **5** as the major reaction

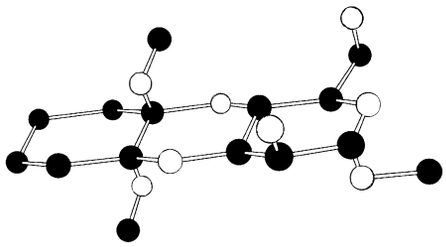


Fig. 1 Representation of the structure of **5** as determined by X-ray crystal structure analysis

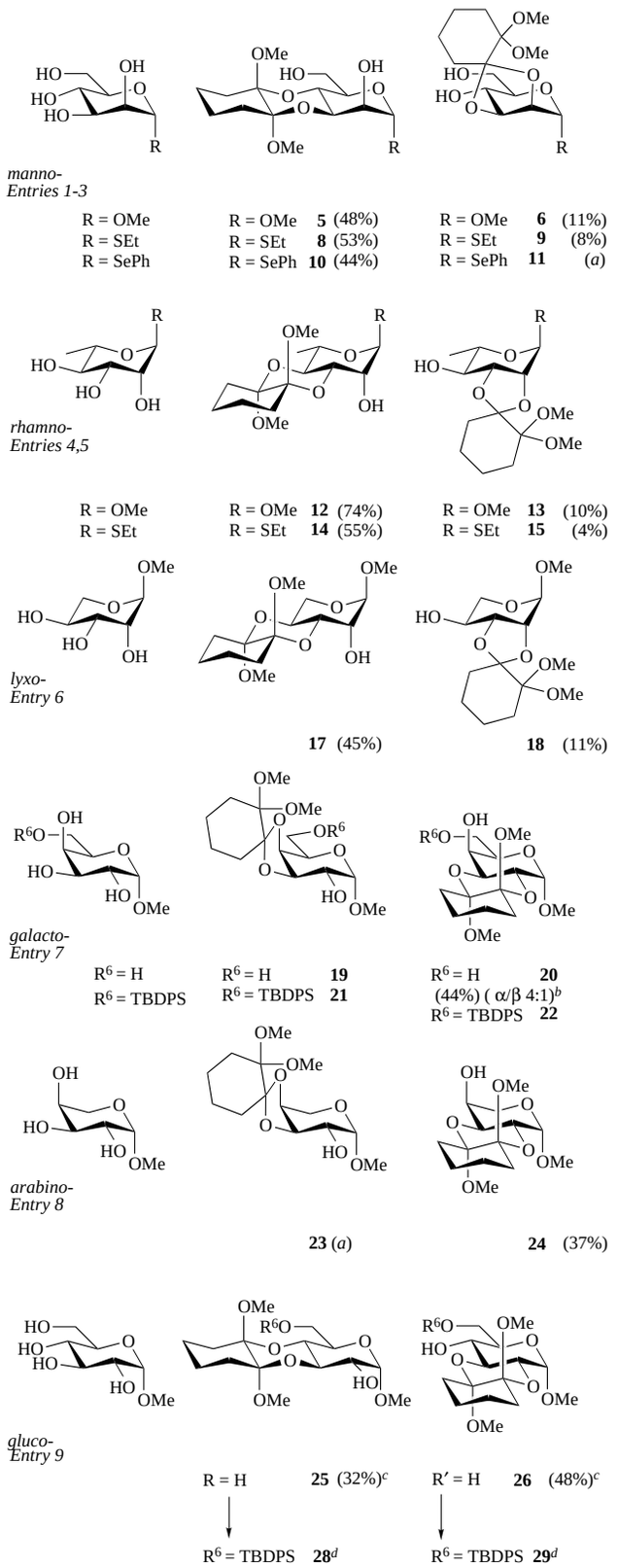
product in 48% yield (Scheme 2). Purification was easily achieved by flash column chromatography and recrystallisation from diethyl ether. The use of trimethyl orthoformate in the reaction prevents any decomposition of the starting acetal by adventitious water (*e.g.* water of crystallisation in the sugar substrate). Competitive protection of the carbohydrate as an orthoformate is not observed as protection with the CDA group and formation of the orthoester are mutually exclusive.[7] The higher thermodynamic stability of the CDA adducts ensures that these are the only products observed. Clearly the reaction conditions for preparation of reagent **1** and the protection are very similar, indeed it is possible to use the cyclohexane-1,2-dione directly in the reaction.[4] However, the hygroscopic nature of cyclohexane-1,2-dione means that we use the easy to handle, stable diacetal **1** as our preferred reagent in these reactions.

The structure of the CDA protected saccharide **5** was unambiguously assigned by X-ray crystallography (Fig. 1).[8] The crystal structure clearly confirmed that, as expected, both *O*-methyl groups in the cyclohexyl moiety of **5** were arranged axially, and the three annulated rings all existed as chair conformers. Comparison with the published structure of methyl α-D-mannopyranoside reveals little change in the conformation of the pyranoside ring.[9] The *gauche-trans* (*gt*) arrangement of the anomeric methoxy group allows for stabilisation from the *exo*-anomeric effect and the 5-C–6-C conformation is *gg*, in agreement with other published mannopyranoside X-ray structures. This conformation allows maximum hyperconjugative stabilisation between 5-CH, 6-CO and 6-CH, 5-CO bonds (the *gauche* effect).[10,11]

The 2,3-*cis* diol fragment reacted only to a minor extent (11%). In this case the product is the *dioxolane* **6** where the CDA group has reacted in a manner analogous to a cyclohexylidene system (Scheme 2). The regiochemistry of protection was confirmed by derivatisation to the diacetate which exhibited the expected downfield shift for 4-H (δ 3.72 in **6**; δ 5.02 in **7**) in the ^{1}H NMR spectrum. The ^{1}H NMR spectrum of **6** is also very similar to the related acetonide,[12] both spectra showing abnormal H–H coupling constants indicating distortion of the pyranose ring away from the idealised chair form by the annulated five membered ring. The five membered ring structure was also confirmed by the significant downfield shift of one of the acetal carbons in the ^{13}C NMR spectrum (δ 111.25 and 101.40 for **6** compared to 99.22 and 98.77 for **5**) which is in the chemical shift range of the 1,3-dioxolanes derived from 1,2-diols and acetone (108–112 ppm).[13] The configuration of the stereogenic centre in the cyclohexane moiety of **6** was inferred from NOE experiments with significant NOEs observed between the acetal methoxy groups and 2-H and 3-H. This shows that these sterically demanding substituents are located on the *exo*-face of the curved system constructed by formation of the dioxolane. Treatment of the by-product **6** in boiling methanol with catalytic CSA for 4 days enabled **5** to be obtained in 35% yield together with 16% of recovered starting material. This result clearly demonstrates that **5** is the thermodynamically most stable product and that the acetalisation process is reversible under the protection conditions.

The new methodology was also applicable to the ethylthio- and phenylseleno-α-mannopyranosides, which are both potential glycosyl donors. Reaction with **1** under our standard conditions produced the 3,4-protected crystalline sugars **8** and **10** as the main reaction products in comparable yields and selectivities to the *O*-glycoside substrate (Table 1, Entries 2, 3). These

Table 1



[a] Other isomers were visible by TLC but were not isolated. [b] Under standard conditions. With 6-TBDPS galactose as starting material only the α isomer is formed. [c] Inseparable. [d] Separable.

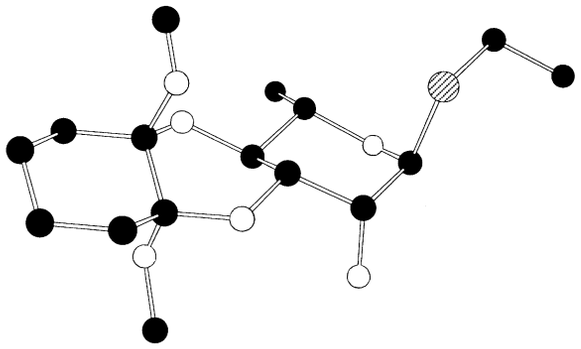


Fig. 2 Representation of the structure of **16** as determined by X-ray crystal structure analysis

yields compare very favourably with classical approaches to this protection pattern. For example, the preparation of methyl 3,4-di-*O*-benzylmannopyranoside is a multistep procedure (7 steps from mannose) which produces the target compound in less than 40% yield.[14] 3,4-Protection can also be achieved using Thiem's two step procedure for the synthesis of methyl 3,4-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)mannopyranoside in 61% yield.[15] This protecting group is, however, rather labile and often incompatible with conventional transformations in carbohydrate chemistry. Our new CDA protected mannosides are, therefore, valuable alternatives to established monosaccharide building blocks. For example, both **8** and **10** can be readily manipulated to give either glycosyl donors or glycosyl acceptors.[16]

Rhamnose (entries 4, 5) and lyxose (entry 6) derived pyranosides, which also bear an axially oriented 2-hydroxy group, could similarly be selectively protected at the 3- and 4-positions in good yields (compounds **12**, **14** and **17**). Dioxolanes **13**, **15** and **18** were also produced as the major by-products. These and other CDA reactions also produce synthetically irrelevant amounts of other minor products. Interestingly, in the case of the *S*-ethyl 1-thiorhamnoside another less polar and crystalline side product could be isolated in 4% yield and was unambiguously identified by X-ray crystal structure analysis to be the 3,4-protected isomer **16**, where the stereochemistry of both CDA acetal centres was inverted relative to the major compound **14** (Fig. 2).[8] This necessitates the adoption of a twist boat conformation by the central dioxane ring. In this conformation nearly all anomeric stabilisation is retained.[17] Hence destabilisation of this isomer arises solely as a result of the boat conformation. While the pyranoside fragment showed normal bond lengths, it should be noted that the cyclohexane ring in the protecting group exhibits a rather short C–C bond length of 1.48 Å (2′-C–3′-C) and a rather long distance between 3′-C and 4′-C of 1.55 Å. The C–O bond lengths at the anomeric centres in the CDA group varied from 1.41 Å (1′-C–1′-O) to 1.44 Å (2′-C–2′-O). In a related area, Waagen *et al.* recently published X-ray data for dihydroxyacetone dimers.[18] Interestingly in this case a 1:1 ratio of chair and boat isomers was obtained under nearly identical reaction conditions [EtOH, $HC(OMe)_3$, cat. H_2SO_4, 96 h, 4 °C].

The next examples of the protection reactions studied were performed with galacto- and arabino-pyranosides which all bear an axial hydroxy group at 4-C. Reaction of these substrates with **1** under standard conditions unfortunately gave less satisfactory results. Although the desired 2,3-adducts **20** and **24** were obtained in about 40% yield, TLC revealed a multitude of side products. Extensive chromatography was required to furnish clean products. The galactoside **20** was obtained only as a 4:1 mixture of α- and β-anomers, indicating a higher tendency for these substrates to anomerise under the reaction conditions. Anomerisation could be suppressed if 6-*O*-*tert*-butydiphenylsilyl (6-*O*-TBDPS) protected galactose was used as the starting material. Under standard reaction conditions the desilylated dioxane **19** was obtained as the clean α-anomer. This could be accounted for by noting that CDA protection inhibits the anomerisation process by resisting formation of the cyclic oxonium ion.[5] Hence, the protected galactoside anomerises more slowly than the starting material. The improved selectivity in the reaction may arise because equilibration to the desired CDA structure is more rapid with the silylated derivative. This could be due to the absence of the 6-hydroxy group in competing equilibration processes and also to the improved solubility of the substrate. After protection desilylation then follows as the slowest process in the system. This may be reinforced by the bulky protecting group on the 6-position making the α configuration of the substrate more favourable. Methanol was required to achieve equilibration to the desired CDA structure. When the solvent was switched to chloroform in this reaction we obtained the silylated dioxolane **21** in 41% yield as the major reaction product while silylated dioxane **22** was produced in only 11% yield.

Methyl α-D-glucopyranoside has also been converted into an inseparable 6:4 mixture of 2,3- and 3,4-protected monosaccharides **26** and **25** using similar methods (entry 9). The two regioisomers could be separated by transformation into the 6-*O*-TBDPS derivatives **28** and **29**. This is the only reaction where CDA and dispoke methodology furnished a comparable ratio of regioisomers.[2] Unsurprisingly, no dioxolane products were observed in the reaction of methyl glucoside, although a further product, which is probably the twisted boat isomer **27**, could be isolated in 2% yield.

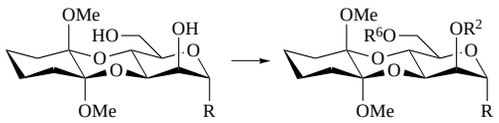
In conclusion we have demonstrated that CDA protection is useful for blocking diequatorial diol units in pyranosides, especially in the case of rhamnose and mannose derivatives where selective protection of the 3 and 4 positions was previously only attainable *via* multistep protection and deprotection procedures.[14,15,19]

Derivatisations and deprotections of CDA protected monosaccharides

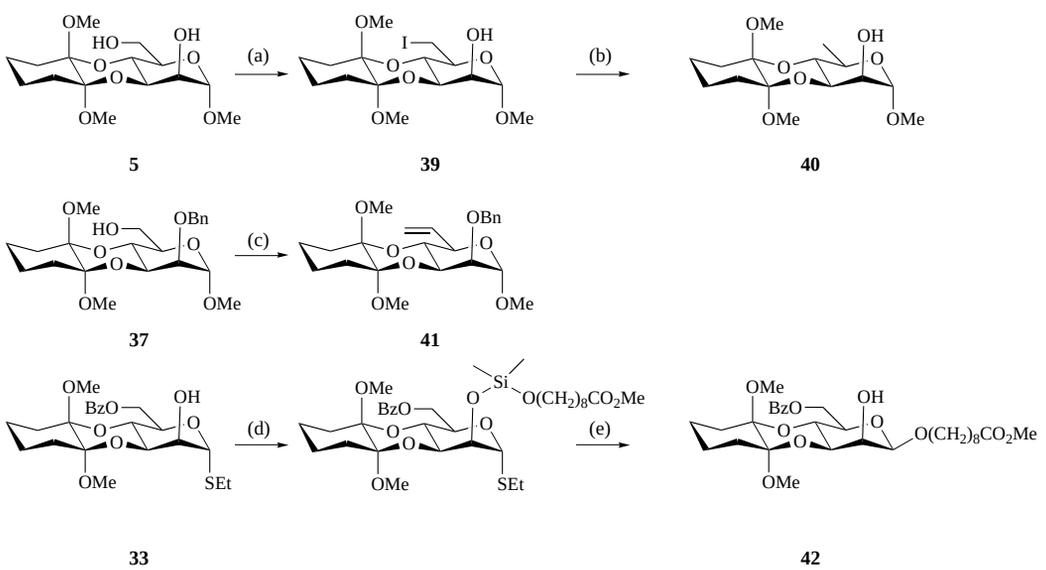
In order to demonstrate the stability of the CDA protected monosaccharides to standard reaction conditions used in carbohydrate chemistry and to obtain useful precursors for oligosaccharide synthesis, procedures for selectively blocking one of the two remaining hydroxy groups in the mannosides **5**, **8** and **10** were investigated. Protection of the primary 6-hydroxy function was easily accomplished by silylation with *tert*-butyldiphenylsilyl chloride (TBDPS-Cl) under standard conditions to give compounds **30**, **31** and **32** in almost quantitative yield (Table 2, entries 1–3). Selective benzoylation of the 6-hydroxy group was also attempted. However, when thioglycoside **8** was mixed with one equivalent of benzoyl chloride in pyridine at room temperature a mixture of the 6-monobenzoate **33**, the 2-monobenzoate **34**, and the 2,6-dibenzoate **35** was obtained (entry 4). To increase the selectivity for the primary position it was necessary to convert **8** into its tributylstannyl ether which was benzoylated *in situ* to produce the desired 6-benzoate **33** in 81% yield together with minor amounts of dibenzoate **35** (entry 5). Alternatively, the 2-benzoate **34** was available in a two step sequence starting from silyl ether **31** in 71% overall yield (entry 6). Application of the stannyl ether methodology to selenoglycoside **10** furnished the 6-benzoate **36** in 76% yield (entry 7).

Rapid selective protection of the 2-position of CDA mannosides **5** and **8** could, surprisingly, be achieved by benzylation with benzyl bromide and sodium hydride in DMF, yielding the 2-benzyl ethers **37** and **38** in 75% and 84% respectively (entries 8, 9). The regioselectivity was unambiguously assigned from the multiplicity of the hydroxy proton in the ^{1}H NMR and by the observation of a long range C–H correlation between the benzylic protons and 2-C of the sugar ring in the HMBC spectrum. The high selectivity for the 2-hydroxy group function is quite surprising although a similar high preference for the secondary over the primary hydroxy group has been reported for the benzylation of methyl 3,4-*O*-isopropylidene-α-D-galactopyrano-

Table 2



Entry	Starting material	Conditions	Product	R	R^2	R^6	Yield (%)
1	**5**	TBDPS-Cl THF, Imidazole	**30**	OMe	H	TBDPS	100
2	**8**	TBDPS-Cl THF, Imidazole	**31**	SEt	H	TBDPS	97
3	**10**	TBDPS-Cl THF, Imidazole	**32**	SePh	H	TBDPS	95
4	**8**	BzCl, pyr 1 equiv.	**33**	SEt	H	Bz	54
			34	SEt	Bz	H	13
			35	SEt	Bz	Bz	28
5	**8**	i, $(Bu_3Sn)_2O$; ii, BzCl	**33**	SEt	H	Bz	81
			34	SEt	Bz	H	0
			35	SEt	Bz	Bz	8
6	**31**	i, BzCl, pyr; ii, TBAF	**34**	SEt	Bz	H	71
7	**10**	i, $(Bu_3Sn)_2O$; ii, BzCl	**36**	SePh	H	Bz	76
8	**5**	NaH, BnBr 1 equiv. DMF	**37**	OMe	Bn	H	75
9	**8**	NaH, BnBr 1 equiv. DMF	**38**	SEt	Bn	H	84



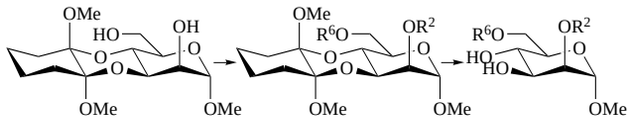
Scheme 3 *Reagents and yields:* (*a*) I_2, PPh_3, imidazole, toluene, 60%; (*b*) Pd/C, NEt_2H, cyclohexane, H_2, 83%; (*c*) i, $(COCl)_2$, DMSO, NEt_3; ii, $Ph_3P^+CH_3Br^-$, BuLi, 63%; (*d*) i, $SiMe_2Cl_2$, pyr; ii, $HO(CH_2)_8CO_2Me$; (*e*) NIS, $MeNO_2$, 61% (3 steps)

side.[20] This reversal of selectivity is not easily explained, however, it should be noted that benzylation is the least sterically demanding of these selective derivatisations and hence will favour the 6-position less than benzoylation or silylation. Furthermore the procedure involves formation of the oxyanion prior to reaction. The pK_a of the two hydroxy groups will affect the population of each oxyanion in solution and their reactivity. The oxyanion at the 2-position is probably more basic and hence more reactive although it will be present in a lower equilibrium concentration. This would account for the observed reactivity profile. This interesting result, however, means that one step procedures are available for selective protection of either the primary 6- or the secondary 2-hydroxy groups of these key mannoside building blocks.

Other transformations which demonstrate the compatability of CDA protection with common organic transformations are shown in Scheme 3. For instance, the CDA protected mannoside **5** was converted, according to the procedure of Garegg and Samuelsson, *via* the iodide **39** into the 2,3-protected D-rhamnoside **40**.[21] Although D-rhamnose is a rather uncommon sugar in nature, α-1,2- and α-1,3-oligo-D-rhamnosides were recently reported as the main components of the polysaccharide portion of A-band lipopolysaccharide from a mutant of *Pseudomonas aeruginosa* strain PAO1.[22] The mannoside **37** could also be transformed *via* Swern oxidation followed by Wittig reaction into vinyl pyranoside **41**. This compound provides versatile functionality for elaboration for carbohydrate based natural product synthesis. Application of a silicon tether based strategy developed by Stork and Bols to *S*-ethyl glycoside **33** produced the β-mannoside **42**.[23,24] These procedures clearly demonstrate the stability of the CDA protecting group to a variety of standard organic transformations.

Deprotection of the CDA moiety is readily achieved under acidic conditions (Table 3). Dimethylation, dibenzylation or dibenzoylation of CDA protected methyl mannoside **5** yields the fully protected glycosides **43**, **44** and **45** respectively. These substrates were used to develop conditions for the deprotection reaction. Firstly aqueous acids were used under different reaction conditions to remove the CDA unit. Deprotection with TFA–water (20:1) produced the unprotected methyl mannosides **46** and **48** instantaneously in good and excellent yields (entries 1 and 4). CDA removal with more dilute acids (entries 2 and 3) required longer reaction times and higher temperatures but also furnished unprotected **47** in good yield. Deprotection of dimethylated CDA mannoside **43**

Table 3



5 R^2,R^6 = Me **43** R^2,R^6 = Me **46**
R^2,R^6 = Bn **44** R^2,R^6 = Bn **47**
R^2,R^6 = Bz **45** R^2,R^6 = Bz **48**

Derivatisations					Deprotections		
Entry	Conditions	Compound	R^2, R^6	Yield (%)	Conditions	Product	Yield (%)
1	KH, MeI, DMF	**43**	Me	99	TFA–H_2O, 20:1, 5 min	**46**	76
2	NaH, BnBr, DMF	**44**	Bn	78	AcOH–THF–H_2O, 4:1:1, 100 h	**47**	90
3	NaH, BnBr, DMF	**44**	Bn	78	TFA–H_2O, 4:6, 16 h	**47**	86
4	BzCl, pyr	**45**	Bz	94	TFA–H_2O, 20:1, 5 min	**48**	96

gives rapid access to methyl α-D-curamicoside, a naturally occurring component of orthosomycin antibiotics.[15,25] We have also demonstrated that these deprotection conditions do not cleave glycosidic linkages and hence cyclohexane-1,2-diacetals are valuable tools for rapid oligosaccharide assembly.[1,5,16]

NMR characteristics of products from CDA protection reactions

In the course of these investigations more than 40 different compounds have been prepared from the CDA reactions. The NMR spectra of these species contain useful diagnostic information for the determination of the product structures. The major reaction products, the CDA dioxane systems have a high degree of symmetry in their structure which is reflected in the NMR spectra. In the ^{1}H NMR spectrum the two methoxy singlets are the characteristic markers. These occur between 3.10 and 3.25 ppm and are usually separated by only 0.01–0.02 ppm, although this separation may rise on subsequent protection, particularly when TBDPS is placed on the 6-hydroxy group (the difference in these cases is nearer 0.1 ppm). Coupling constants around the pyranose ring are identical to the free pyranose systems indicating that there is no distortion of the usual chair conformation of the sugar. The ^{13}C NMR spectrum is the most helpful in the identification of a CDA protected product. The two acetal centres of the protecting group resonate at very similar chemical shifts in the range 98.5–99.5 ppm. The methoxy signals occur between 46 and 47 ppm, usually separated by less than 0.2 ppm and the remainder of the cyclohexane ring gives two sets of two peaks, at 21.3 and 27.0 ppm.

The principal by-products, the dioxolane structures are far less symmetrical which again is reflected in their NMR spectra. The methoxy signals occur at around 3.26 and 3.32 ppm in the ^{1}H NMR spectrum. The protons on the sugar ring also show abnormal coupling constants indicating distortion of the pyranose system. ^{13}C NMR spectroscopy is again very diagnostic. The acetal carbons resonate very differently at around 101 and 111 ppm and the methoxy signals at 49 and 50 ppm. The cyclohexane signals are also spread out giving peaks around 21.5, 22.9, 30.7 and 35.5 ppm. In general the carbon and proton NMR spectra are highly homologous to those of the related isopropylidene protected systems.

The EI mass spectra of all products from these protection reactions show characteristic fragments which arise from the diacetal group. Molecular ions readily lose methyl groups, whilst cleavage of the protecting group at the sugar ring gives a series of peaks at *m/z* 175 [$CO_2Me(CH_2)_4CO_2MeH^+$], 161, 143, 127 and 111. The dioxolane by-products also tend to show a peak at 101 which is usually absent in the desired CDA compounds, however this in itself provides no proof of structure.

Conclusion

Cyclohexane diacetals provide new opportunities for rapid selective protection of monosaccharides. Selective protection of the vicinal diequatorial diol relationship complements the classical chemistry of isopropylidene and benzylidene acetals and as such greatly improves the efficiency of monosaccharide manipulations. In this paper we have demonstrated the efficacy of this methodology on a wide variety of monosaccharide precursors and have shown the stability of the protecting group to a number of standard manipulations. Procedures for high yielding cleavage of the protecting group under acidic conditions have also been developed. This chemistry forms the basis of the assembly of versatile building blocks for oligosaccharide synthesis.

In further studies we have also shown that the CDA protecting group can *tune* the reactivity of glycosyl donors, allowing highly convergent oligosaccharide assembly.[1,5,16] CDA and related BDA (butane-2,3-diacetal) protected units now rest at the heart of our strategy for the efficient synthesis of complex carbohydrates.

Experimental

General procedures

^{1}H NMR spectra were recorded on a Bruker DRX-500, a Bruker AM-400 or a Bruker AC-200 spectrometer as solutions in deuteriochloroform ($CDCl_3$) using the residual $CHCl_3$ as reference (7.26 ppm) unless otherwise stated. All multiplets were analysed as first order couplings. ^{13}C spectra were recorded on a Bruker AC-200 (50.8 MHz) or Bruker AM-400 (100.12 MHz) spectrometer and chemical shifts are quoted relative to the middle peak of $CDCl_3$ (77 ppm). Coupling constants are quoted in Hz. Low and high resolution mass spectra were recorded under EI or positive FAB conditions using a Kratos MS 890 spectrometer. Microanalyses were performed in the University of Cambridge microanalyses laboratory. Optical rotations were measured using an Optical activity AA-1000 polarimeter and are quoted in units of 10^{-1} deg cm^2 g^{-1}. Ether refers to diethyl ether and petrol refers to light petroleum (bp 40–60 °C). All solvents were purified before use: light petroleum was redistilled, benzene, toluene, acetonitrile and dichloromethane were distilled from calcium hydride, ether and tetrahydrofuran (THF) were distilled from sodium–benzophenone ketyl, methanol was distilled from magnesium. Where appropriate, reactions were carried out under an argon atmosphere in oven dried glassware (150 °C overnight). Reagents were either dried by standard procedures or used as purchased. Flash chromatography was carried out using Merck-Kieselgel 60 (0.040–0.063 mm) under pressure. Thin layer chromatography

was visualised with UV light (254 nm) and either acidified ammonium molybdate(IV) or 10% conc. sulfuric acid in methanol as appropriate. X-Ray crystal structures were solved by members of Dr Paul Raithby's group in Cambridge.

Preparation of 1,1,2,2-tetramethoxycyclohexane 1

Conc. sulfuric acid (1 ml) was added to a stirred solution of cyclohexane-1,2-dione (44.8 g, 0.4 mmol) in methanol (100 ml) and trimethyl orthoformate (160 ml). The resulting black solution was heated under reflux for 5 h and then neutralised with sodium hydrogen carbonate (*ca.* 4 g). The solvent was removed under reduced pressure and the residue distilled to furnish **1** (59.5 g, 65%) as a colourless liquid, bp 76 °C, 0.8 mmHg (Found: C, 58.9; H, 9.9. $C_{10}H_{20}O_4$ requires C, 58.8; H, 9.9%); ν_{max}(film)/cm^{-1} 2942, 1462, 1346, 1162, 1089, 1060, 967, 872; δ_H(200 MHz; $CDCl_3$) 1.31–1.48 and 1.60–1.75 (2 × 4 H, 2 × m, 3-H, 4-H, 5-H, 6-H), 3.32 (12 H, s, OMe); δ_C(50 MHz; $CDCl_3$) 21.67 (4-C, 5-C), 30.61 (3-C, 6-C), 49.25 (OMe), 102.07 (1-C, 2-C); *m/z* (EI) 204 (M^+, 2%), 189 (100, $M^+ - Me$), 173 (20, $M^+ - OMe$), 97 (30), 75 (15) (Found: M^+, 204.1362. $C_{10}H_{20}O_4$ requires *M*, 204.1361).

General procedure for CDA protection

CSA (0.15 equiv.) was added to a solution of monosaccharide precursor (1 equiv.), 1,1,2,2-tetramethoxycyclohexane **1** (1.6 equiv.) and dry trimethyl orthoformate (*ca.* 0.1 ml mmol^{-1} of monosaccharide) in dry methanol (*ca.* 1.4 ml mmol^{-1} of monosaccharide). The reaction was heated under reflux for 16 h after which the mixture was neutralised with sodium hydrogen carbonate. The solvent was removed under reduced pressure and the residue purified by column chromatography. Minor products <5% were, in general, not characterised.

(1′*R*)-Methyl 2,3-*O*-(2′,2′-dimethoxycyclohexylidene)-α-D-mannopyranoside 6 and (1′*S*,2′*S*)-methyl 3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-α-D-mannopyranoside 5. Methyl α-D-mannopyranoside **4** (3.46 g, 17.8 mmol) was subjected to the general procedure for CDA protection. Chromatography (gradient elution Et_2O to Et_2O + 4% EtOH) furnished **6** (666 mg, 11%) as an off-white foam and slightly impure **5** which was further purified by slow crystallisation from ether to give **5** (2.83 g, 48%) as colourless cubes.

Compound **6**: $[\alpha]_D^{25}$ +19.8 (*c* 0.89 in $CHCl_3$) (Found: C, 53.8; H, 7.9. $C_{15}H_{26}O_8$ requires C, 53.9; H, 7.8%); δ_H(400 MHz; $CDCl_3$) 1.37–1.87 (8 H, m, 3′-H, 4′-H, 5′-H, 6′-H), 2.17 (1 H, br t, *J* 6.2, 6-OH), 2.74 (1 H, d, *J* 5.0, 4-OH), 3.27 and 3.32 (2 × 3 H, 2 × s, 2 × 2′-OMe), 3.40 (3 H, s, 1-OMe), 3.64 (1 H, ddd, *J* 8.4, 2 × 4.2, 5-H), 3.72 (1 H, ddd, *J* 8.3, 6.5, 5.3, 4-H), 3.80–3.86 (2 H, m, 6-H_A, 6-H_B), 4.30 (1 H, dd, *J* 2 × 6.4, 3-H), 4.41 (1 H, d, *J* 6.3, 2-H), 4.88 (1 H, s, 1-H); δ_C(100 MHz; $CDCl_3$) 21.59 and 22.89 (4′-C, 5′-C), 30.71 and 35.68 (3′-C, 6′-C), 49.13 and 49.98 (2 × 2′-OMe), 55.23 (1-OMe), 62.89 (6-C), 69.56 (4-C), 70.17 (5-C), 76.71 (2-C), 78.37 (3-C), 98.92 (1-C), 101.40 (2′-C), 111.25 (1′-C); *m/z* (EI) 334 (M^+, <10%), 319 (90, $M^+ - Me$), 303 (40, $M^+ - OMe$), 175 (60), 161 (50), 143 (100), 111 (80) (Found: M^+, 334.1632. $C_{15}H_{26}O_8$ requires *M*, 334.1628).

Compound **5**: mp 168 °C (from Et_2O); $[\alpha]_D^{25}$ +191 (*c* 0.94 in $CHCl_3$) (Found: C, 54.0; H, 8.0. $C_{15}H_{26}O_8$ requires C, 53.8; H, 7.8%); δ_H(400 MHz; $CDCl_3$) [1.29–1.43, 1.45–1.55 and 1.62–1.82 (2 H, 2 H and 4 H, 3 × m, 3′-H, 4′-H, 5′-H, 6′-H)], 2.25 (1 H, br t, *J* 5.8, 6-OH), 2.89 (1 H, s, 2-OH), 3.20 and 3.21 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 3.35 (3 H, s, 1-OMe), 3.72–3.86 (3 H, m, 5-H, 6-H_A, 6-H_B), 3.92 (1 H, br s, 2-H), 4.14 (1 H, dd, *J* 10.6, 2.9, 3-H), 4.25 (1 H, dd, *J* 2 × 10.0, 4-H), 4.72 (1 H, d, *J* 0.9, 1-H); δ_C(100 MHz; $CDCl_3$) 21.35 (4′-C, 5′-C), 27.00 (3′-C, 6′-C), 46.79 and 46.93 (1′-OMe, 2′-OMe), 54.88 (1-OMe), 61.41 (6-C), 63.88 (4-C), 68.83 (3-C), 70.05 (2-C), 70.72 (5-C), 98.77 and 99.22 (1′-C, 2′-C), 101.21 (1-C); *m/z* (EI) 334 (M^+, 20%), 319 (80, $M^+ - Me$), 303 (40, $M^+ - OMe$), 287 (40), 271 (50), 244 (60), 175 (30), 159 (20), 143 (90), 127 (60), 111 (80), 101 (100) (Found: M^+, 334.1620. $C_{15}H_{26}O_8$ requires *M*, 334.1628).

X-Ray structure determination of compound **5**.—$C_{15}H_{26}O_8$, *M* 334.4, orthorhombic, space group $P2_12_12_1$, a = 10.312(3), b = 16.910(5), c = 9.533(3) Å, U = 1662.4(8) Å^3, $F(000)$ = 720, D_c = 1.336 Mg m^{-3}, Z = 4, μ(Mo-Kα) = 0.108 mm^{-1}, final $wR(F^2)$ = 0.0792 on 2144 independent reflections, $R(F)$ = 0.0309 for 1952 independent reflections [$I > 2\sigma(I)$].

(1′*R*)-Methyl 4,6-di-*O*-acetyl-2,3-*O*-(2′,2′-dimethoxycyclohexylidene)-α-D-mannopyranoside 7. The dioxolane **6** (151 mg, 0.451 mmol) was stirred for 16 h in pyridine (1.5 ml) and acetic anhydride (0.5 ml). Removal of the solvent under reduced pressure and column chromatography furnished the title compound **7** (175 mg, 93%) as an off-white foam, $[\alpha]_D^{18}$ +4.5 (*c* 0.74 in $CHCl_3$); δ_H(500 MHz; $CDCl_3$) [1.37–1.53 (2 H, m), 1.58 (2 H, t, *J* 7.0), 1.75 (2 H, t, *J* 6.0) and 1.81–1.93 (2 H, m), (3′-H, 4′-H, 5′-H, 6′-H)], 2.08 (6 H, s, 2 × $MeCO_2$), 3.26 and 3.33 (2 × 3 H, 2 × s, 2 × 2′-OMe), 3.39 (3 H, s, 1-OMe), 3.80 (1 H, ddd, *J* 10.2, 5.9, 2.6, 5-H), 4.08 (1 H, dd, *J* 12.1, 2.6, 6-H_A), 4.24 (1 H, dd, *J* 12.1, 5.8, 6-H_B), 4.30 (1 H, dd, *J* 7.4, 6.3, 3-H), 4.45 (1 H, d, *J* 5.9, 2-H), 4.96 (1 H, s, 1-H), 5.02 (1 H, dd, *J* 10.3, 7.5, 4-H); δ_C(100 MHz; $CDCl_3$) 20.71 and 20.92 (4′-C, 5′-C), 21.54 and 22.66 [2 × $MeCO_2$], 30.72 and 35.36 (3′-C, 6′-C), 48.93 and 50.04 (2 × 2′-OMe), 54.95 (1-OMe), 62.62 (6-C), [65.97, 69.61, 75.75 and 77.09 (2-C, 3-C, 4-C, 5-C)], 98.49 (1-C), 101.25 (2′-C), 111.32 (1′-C), 169.64 and 170.63 (2 × CO); *m/z* (EI) 418 (M^+, 5%), 403 (80, $M^+ - Me$), 387 (40, $M^+ - OMe$), 130 (40), 101 (100) (Found: M^+, 418.1839. $C_{19}H_{30}O_{10}$ requires *M*, 418.1839).

(1′*R*)-Ethyl 2,3-*O*-(2′,2′-dimethoxycyclohexylidene)-1-thio-α-D-mannopyranoside 9 and (1′*S*,2′*S*)-ethyl 3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-1-thio-α-D-mannopyranoside 8. Ethyl 1-thio-α-D-mannopyranoside (1.22 g, 5.44 mmol) was subjected to the general procedure for CDA protection. Column chromatography (gradient elution Et_2O–petrol 3:1 to Et_2O + 3% EtOH) furnished **9** (162 mg, 8%) as an off-white foam and slightly impure **8** which was further purified by slow crystallisation (from Et_2O) and further column chromatography to give clean **8** (1.04 g, 53%) as a white solid.

Compound **9**: $[\alpha]_D^{18}$ +119 (*c* 0.63 in $CHCl_3$) (Found: C, 52.6; H, 7.8. $C_{16}H_{28}O_7S$ requires C, 52.7; H, 7.7%); δ_H(400 MHz; $CDCl_3$) 1.28 (3 H, t, *J* 7.4, SCH_2CH_3), [1.40–1.50, 1.57–1.60 and 1.68–1.82 (2 H, 2 H and 4 H, 3 × m, 3′-H, 4′-H, 5′-H, 6′-H)], 2.51 (1 H, dq, *J* 13.1, 7.4, SCH_AH_B), 2.62 (1 H, dq, *J* 13.1, SCH_AH_B), 2.40–2.70 (1 H, br, OH), 3.24 (3 H, s, 2′-OMe), 3.29 (3 H, s, 2′-OMe), 3.75 (1 H, dd, *J* 7.4, 9.7, 4-H), 3.82 (2 H, d, *J* 3.8, 6-H_A, 6-H_B), 3.92 (1 H, dt, *J* 9.8, 3.8, 5-H), 4.19 (1 H, t, *J* 7.0, 3-H), 4.48 (1 H, d, *J* 6.0, 2-H), 5.56 (1 H, s, 1-H); δ_C(100 MHz; $CDCl_3$) 14.12 (SCH_2CH_3), 21.55 and 22.87 (4′-C, 5′-C), 24.23 (SCH_2), 30.70 and 35.95 (3′-C, 6′-C), 49.09 and 49.98 (2 × 2′-OMe), 62.44 (6-C), [69.49, 70.64, 77.84 and 78.55 (2-C, 3-C, 4-C, 5-C)], 83.10 (1-C), 101.34 (2′-C), 111.16 (1′-C); *m/z* (EI) 364 (M^+, 30%), 349 (20, $M^+ - Me$), 332 (60), 287 (40), 189 (50), 175 (50), 127 (30), 111 (20), 101 (100) (Found: M^+, 364.1549. $C_{16}H_{28}O_7S$ requires *M*, 364.1555).

Compound **8**: mp 185 °C (from Et_2O); $[\alpha]_D^{18}$ +281 (*c* 0.72 in $CHCl_3$) (Found: C, 52.7; H, 7.8. $C_{16}H_{28}O_7S$ requires C, 52.7; H, 7.7%); δ_H(400 MHz; $CDCl_3$) 1.19 (3 H, t, *J* 7.4, SCH_2CH_3), 1.32–1.56 and 1.64–1.89 (2 × 4 H, 2 × m, 3′-H, 4′-H, 5′-H, 6′-H), 2.10 (1 H, br t, *J* 6.5, 6-OH), 2.57 (1 H, dq, *J* 12.9, 7.4, SCH_AH_B), 2.65 (1 H, dq, *J* 12.9, 7.4, SCH_AH_B), 2.94 (1 H, s, 2-OH), 3.20 and 3.22 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 3.80 (2 H, m, 6-H_A, 6-H_B), 4.03 (1 H, br s, 2-H), 4.11–4.18 (2 H, m, 3-H, 5-H), 4.31 (1 H, dd, *J* 2 × 10.2, 4-H), 5.30 (1 H, s, 1-H); δ_C(100 MHz; $CDCl_3$) 14.85 (SCH_2CH_3), 21.34 (4′-C, 5′-C), 25.16 (SCH_2), 26.97 and 27.00 (3′-C, 6′-C), 46.83 and 46.91 (1′-OMe, 2′-OMe), 61.40 (6-C), [64.21, 69.48, 70.95 and 71.61 (2-C, 3-C, 4-C, 5-C)], 84.54 (1-C), 98.79 and 99.29 (1′-C, 2′-C); *m/z* (EI) 364 (M^+, 10%), 349 (90), 333 (30), 175 (50), 161 (60), 143 (60), 111 (50), 81 (70), 67 (80), 55 (100) (Found: M^+, 364.1555. $C_{16}H_{28}O_7S$ requires *M*, 364.1555).

(1′*S*,2′*S*)-Phenyl 3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-1-seleno-α-D-mannopyranoside 10. Phenyl 1-seleno-α-D-mannopyranoside (563 mg, 1.83 mmol) was subjected to the standard conditions for CDA protection. Column chromatography (gradient elution Et_2O–petrol 2:1 to Et_2O) furnished impure product which was recrystallised (Et_2O) to give clean **10** (371 mg, 44%). Other isomers were not characterised.

Compound **10**: $[\alpha]_D^{25}$ +325 (*c* 1.16 in $CHCl_3$) (Found: C, 52.2; H, 6.1. $C_{20}H_{28}O_7Se$ requires C, 52.3; H, 6.1%); δ_H(500 MHz; $CDCl_3$) 1.32–1.49 and 1.69–1.85 (2 × 4 H, 2 × m, 3′-H, 4′-H, 5′-H, 6′-H_2), 1.98 (1 H, br t, *J* 6.5, 6-OH), 2.93 (1 H, d, *J* 2.0, 2-OH), 3.20 and 3.27 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 3.74–3.80 (2 H, m, 6-H_A, 6-H_B), 4.16–4.21 (2 H, m, 3-H, 5-H), 4.28 (1 H, br s, 2-H), 4.36 (1 H, dd, *J* 2 × 10.2, 4-H), 5.80 (1 H, s, 1-H), 7.27–7.33 and 7.54–7.59 (3 H and 2 H, 2 × m, Ar-H); δ_C(100 MHz; $CDCl_3$) 21.30 (4′-C, 5′-C), 26.92 and 26.96 (3′-C, 6′-C), 46.83 and 46.96 (1′-OMe, 2′-OMe), 61.06 (6-C), 63.80 (4-C), 69.69 (3-C), 71.98 (2-C), 73.30 (5-C), 85.60 (1-C), 98.78 and 99.33 (1′-C, 2′-C), 127.98 (*para*-C), 128.90 (*ipso*-C), 129.22 and 134.26 (*ortho*- and *meta*-C); *m/z* (EI) 460 (M^+, 25%), 429 (40, $M^+ - OMe$), 271 (60), 127 (100), 99 (40) (Found: M^+, 460.1000. $C_{20}H_{28}O_7Se$ requires *M*, 460.1000).

(1′*S*)-Methyl 2,3-*O*-(2′,2′-dimethoxycyclohexylidene)-α-L-rhamnopyranoside 13 and (1′*R*,2′*R*)-methyl 3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-α-L-rhamnopyranoside 12. Methyl α-L-rhamnopyranoside (331 mg, 1.86 mmol) was subjected to the standard conditions for CDA protection. Column chromatography (gradient elution Et_2O–petrol 1:1 to 3:1) furnished **12** (437 mg, 74%) as an off-white foam, which was recrystallised from ether, and slightly impure **13** (62 mg, 10%).

Compound **13**: (an analytical sample of **13** was purified by extensive chromatography) $[\alpha]_D^{18}$ 14.8 (*c* 0.65 in $CHCl_3$) (Found: C, 56.7; H, 8.4. $C_{15}H_{26}O_7$ requires C, 56.6; H, 8.2%); δ_H(400 MHz; $CDCl_3$) 1.28 (3 H, d, *J* 6.3, 6-H), 1.33–1.60 and 1.64–1.87 (2 × 4 H, 2 × m, 3′-H, 4′-H, 5′-H, 6′-H), 2.59 (1 H, d, *J* 4.8, 4-OH), 3.25 (3 H, s, 2′-OMe), 3.30 (3 H, s, 2′-OMe), 3.36 (3 H, s, 1-OMe), 3.35–3.40 (1 H, m, 4-H), 3.63 (1 H, dq, *J* 8.5, 6.4, 5-H), 4.19 (1 H, dd, *J* 2 × 6.6, 3-H), 4.38 (1 H, d, *J* 6.3, 2-H), 4.80 (1 H, s, 1-H); δ_C(100 MHz; $CDCl_3$) 17.89 (6-C), 21.62 and 22.87 (4′-C, 5′-C), 30.70 and 35.76 (3′-C, 6′-C), 49.05 (2′-OMe), 49.99 (2′-OMe), 54.96 (1-OMe), [66.12, 74.31, 76.72 and 78.56 (2-C, 3-C, 4-C, 5-C)], 98.70 (1-C), 101.38 (2′-C), 111.09 (1′-C); *m/z* (EI) 318 (M^+, <10%), 303 (30, $M^+ - Me$), 101 (70), 84 (100) (Found: M^+, 318.1674. $C_{15}H_{26}O_7$ requires *M*, 318.1678).

Compound **12**: mp 135 °C (from Et_2O); $[\alpha]_D^{18}$ −190 (*c* 0.93 in $CHCl_3$) (Found: C, 56.7; H, 8.1. $C_{15}H_{26}O_7$ requires C, 56.6; H, 8.2%); δ_H(400 MHz; $CDCl_3$) 1.27 (3 H, d, *J* 5.9, 6-H), 1.32–1.57 and 1.62–1.83 (2 × 4 H, 2 × m, 3′-H, 4′-H, 5′-H, 6′-H), 2.43 (1 H, s, 2-OH), 3.19 and 3.21 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 3.35 (3 H, s, 1-OMe), 3.81 (1 H, dq, *J* 9.8, 5.9, 5-H), 3.92 (1 H, dd, *J* 2 × 9.9, 4-H), 3.92 (1 H, br s, 2-H), 4.09 (1 H, dd, *J* 10.0, 3.1, 3-H), 4.66 (1 H, d, *J* 1.0, 1-H); δ_C(100 MHz; $CDCl_3$) 16.53 (6-C), 21.38 (4′-C, 5′-C), 26.98 and 27.08 (3′-C, 6′-C), 46.55 and 46.91 (1′-OMe, 2′-OMe), 54.73 (1-OMe), 66.65 (5-C), 68.94 and 69.07 (3-C, 4-C), 70.30 (2-C), 98.74 and 99.09 (1′-C, 2′-C), 100.94 (1-C); *m/z* (EI) 318 (M^+, <10%), 303 (80, $M^+ - Me$), 287 (40, $M^+ - OMe$), 175 (60), 143 (90), 111 (60), 84 (100), 55 (70) (Found: M^+, 318.1689. $C_{15}H_{26}O_7$ requires *M*, 318.1678).

(1′*S*)-Ethyl 2,3-*O*-(2′,2′-dimethoxycyclohexylidene)-1-thio-α-L-rhamnopyranoside 15, (1′*R*,2′*R*)-ethyl 3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-1-thio-α-L-rhamnopyranoside 14 and (1′*S*,2′*S*)-ethyl 3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-1-thio-α-L-rhamnopyranoside 16. Ethyl 1-thio-α-L-rhamnopyranoside (2.66 g, 12.8 mmol) was subjected to standard CDA protection conditions. Column chromatography (gradient elution Et_2O–petrol 1:1 to 3:1) furnished crystalline **14** (2.46 g, 55%) and **15** (200 mg, 4%). Minor boat dioxolane isomer **16** could also be obtained (0.20 g, 4%) and was submitted for X-ray analysis.

Compound **15**: mp 100 °C (from Et_2O); $[\alpha]_D^{25}$ −123 (*c* 1.30 in $CHCl_3$) (Found: C, 55.0; H, 8.2. $C_{16}H_{28}O_6S$ requires C, 55.15; H, 8.1%); δ_H(400 MHz; $CDCl_3$) 1.27 (3 H, d, *J* 6.2, 6-H), 1.29 (3 H, t, *J* 7.4, SCH_2CH_3), 1.36–1.62 and 1.68–1.90 (2 × 4 H, 2 × m, 3′-H, 4′-H, 5′-H, 6′-H), 2.19 (1 H, br s, 4-OH), 2.51 (1 H, dq, *J* 13.0, 7.4, SCH_AH_B), 2.64 (1 H, dq, *J* 13.0, 7.3, SCH_AH_B), 3.26 (3 H, s, 2′-OMe), 3.31 (3 H, s, 2′-OMe), 3.43 (1 H, ddd, *J* 9.7, 7.6, 3.7, 4-H), 3.93 (1 H, dq, *J* 9.6, 6.2, 5-H), 4.12 (1 H, dd, *J* 2 × 6.6, 3-H), 4.48 (1 H, d, *J* 6.9, 2-H), 5.52 (1 H, s, 1-H); δ_C(100 MHz; $CDCl_3$) 14.60 (SCH_2CH_3), 17.42 (6-C), 21.60 and 22.88 (4′-C, 5′-C), 24.33 (SCH_2), 30.72 and 36.04 (3′-C, 6′-C), 49.05 (2′-OMe), 50.10 (2′-OMe), [65.72, 75.78, 78.15 and 78.53 (2-C, 3-C, 4-C, 5-C)], 79.86 (1-C), 101.32 (2′-C), 111.14 (1′-C); *m/z* (EI) 348 (M^+, 30%), 316 (30), 287 (80), 168 (100), 113 (30) (Found: M^+, 348.1599. $C_{16}H_{28}O_6S$ requires *M*, 348.1606).

Compound **14**: mp 137 °C (from Et_2O); $[\alpha]_D^{18}$ −320 (*c* 0.55 in $CHCl_3$) (Found: C, 55.4; H, 8.1. $C_{16}H_{28}O_6S$ requires C, 55.15; H, 8.1%); δ_H(400 MHz; $CDCl_3$) 1.26 (3 H, d, *J* 6.0, 6-H), 1.27 (3 H, t, *J* 7.5, SCH_2CH_3), 1.32–1.55 and 1.64–1.80 (2 × 4 H, 2 × m, 3′-H, 4′-H, 5′-H, 6′-H), 2.54 (1 H, d, *J* 2.1, 2-OH), 2.58 (1 H, dq, *J* 13.0, 7.4, SCH_AH_B), 2.66 (1 H, dq, *J* 13.0, 7.3, SCH_AH_B), 3.19 and 3.21 (2 × s, 1′-OMe, 2′-OMe), 3.91 (1 H, dd, *J* 2 × 10.0, 4-H), 4.02 (1 H, br s, 2-H), 4.09 (1 H, dd, *J* 10.3, 3.0, 3-H), 4.18 (1 H, dq, *J* 9.9, 6.1, 5-H), 5.24 (1 H, s, 1-H); δ_C(100 MHz; $CDCl_3$) 14.99 (SCH_2CH_3), 16.45 (6-C), 21.37 (4′-C, 5′-C), 25.37 (SCH_2), 26.94 and 27.07 (3′-C, 6′-C), 46.57 and 46.87 (1′-OMe, 2′-OMe), [67.09, 69.45, 69.52 and 71.89 (2-C, 3-C, 4-C, 5-C)], 84.24 (1-C), 98.74 and 99.15 (1′-C, 2′-C); *m/z* (EI) 348 (M^+, 20%), 333 (70, $M^+ - Me$), 317 (50, $M^+ - OMe$), 255 (80), 175 (40), 143 (100), 127 (80), 111 (60), 84 (100) (Found: M^+, 348.1615. $C_{16}H_{28}O_6S$ requires *M*, 348.1606).

Compound **16**: mp 162 °C (from Et_2O); $[\alpha]_D^{18}$ −157 (*c* 0.65 in $CHCl_3$) (Found: C, 55.3; H, 8.2. $C_{16}H_{28}O_6S$ requires C, 55.2; H, 8.1%); δ_H(400 MHz; $CDCl_3$) 1.28 (3 H, t, *J* 7.4, SCH_2CH_3), 1.29 (3 H, d, *J* 6.2, 6-H), [1.46–1.54 (4 H, m), 1.60 (1 H, ddd, *J* 2 × 13.5, 4.0), 1.65 (1 H, ddd, *J* 2 × 13.5, 3.9), 1.88 (1 H, br d, *J* 13.0) and 1.95 (1 H, br d, *J* 13.0) (3′-H, 4′-H, 5′-H, 6′-H)], 2.21 (1 H, d, *J* 3.6, 2-OH), 2.56 (1 H, dq, *J* 13.0, 7.4, SCH_AH_B), 2.65 (1 H, dq, *J* 13.0, 7.3, SCH_AH_B), 3.26 and 3.34 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 3.98 (1 H, dq, *J* 9.5, 6.2, 5-H), 4.07 (1 H, dd, *J* 3.0, 2.5, 2-H), 4.22 (1 H, dd, *J* 11.9, 9.6, 4-H), 4.50 (1 H, dd, *J* 11.0, 3.1, 3-H), 5.23 (1 H, s, 1-H); δ_C(100 MHz; $CDCl_3$) 14.88 (SCH_2CH_3), 16.75 (6-C), 21.64 and 21.72 (4′-C, 5′-C), 25.31 (SCH_2), 28.51 and 28.57 (3′-C, 6′-C), 46.87 and 47.23 (1′-OMe, 2′-OMe), [68.02, 71.66, 72.22 and 72.30 (2-C, 3-C, 4-C, 5-C)], 84.09 (1-C), 100.21 and 100.67 (1′-C, 2′-C); *m/z* (EI) 348 (M^+, <10%), 333 (80, $M^+ - Me$) 316 (50), 269 (60), 254 (60), 143 (60), 127 (100), 111 (50), 84 (60) (Found: M^+, 348.1595. $C_{16}H_{28}O_6S$ requires *M*, 348.1606).

X-Ray structure determination of compound **16**.—$C_{16}H_{28}O_6S$, *M* 348.4, monoclinic, space group $P2_1$, $a = 9.406(2)$, $b = 9.816(2)$, $c = 9.690(2)$ Å, $U = 894.3(3)$ Å^3, $F(000) = 376$, $D_c = 1.294$ Mg m^{-3}, $Z = 2$, μ(Mo-Kα) = 0.208 mm^{-1}, final $wR(F^2) = 0.1668$ on 2932 independent reflections, $R(F) = 0.0593$ for 1917 independent reflections [$I > 2\sigma(I)$].

(1′*S*)-Methyl 2,3-*O*-(2′,2′-dimethoxycyclohexylidene)-β-L-lyxopyranoside 18 and (1′*R*,2′*R*)-methyl 3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-β-L-lyxopyranoside 17. Methyl α-D-lyxopyranoside (300 mg, 1.83 mmol) was subjected to the standard CDA protection conditions. Column chromatography (gradient elution Et_2O–petrol 1:1 to 3:1) furnished **17** (248 mg, 45%) as an off-white foam and **18** (62 mg, 11%).

Compound **18**: $[\alpha]_D^{18}$ +29.5 (*c* 0.78 in $CHCl_3$) (Found: C, 55.4; H, 7.9. $C_{14}H_{24}O_7$ requires C, 55.3; H, 8.0%); δ_H(400 MHz; $CDCl_3$) 1.38–1.60 and 1.66–1.81 (2 × 4 H, 2 × m, 3′-H, 4′-H, 5′-H, 6′-H), 3.26 (3 H, s, 2′-OMe), 3.27 (3 H, s, 2′-OMe), 3.39 (1 H, d, *J* 8.9, OH), 3.43 (3 H, s, 1-OMe), 3.69 (1 H, dd, *J* 11.4, 4.3, 5-H_A), 3.77 (1 H, dddd, *J* 8.4, 3 × 4.2, 4-H), 3.87 (1 H, dd, *J* 11.4, 3.8, 5-H_B), 4.35 (1 H, dd, *J* 6.3, 1.8, 2-H), 4.43 (1 H, dd, *J*

6.8, 4.1, 3-H), 4.65 (1 H, d, *J* 1.8, 1-H); δ_C(100 MHz; $CDCl_3$) 21.60 and 22.89 (4′-C, 5′-C), 30.78 and 35.20 (3′-C, 6′-C), 49.27 (2′-OMe), 55.70 (1-OMe), 63.15 (5-C), [67.10, 75.41 and 76.56 (2-C, 3-C, 4-C)], 99.44 (1-C), 101.65 (2′-C), 111.14 (1′-C); *m/z* (EI) 304 (M^+, <10%), 289 (70, $M^+ - Me$), 214 (50), 143 (60), 129 (80), 111 (60), 101 (100) (Found: M^+, 304.1528. $C_{14}H_{24}O_7$ requires *M*, 304.1522).

Compound **17**: $[\alpha]_D^{18}$ +142 (*c* 0.74 in $CHCl_3$) (Found: C, 53.9; H, 7.8. $C_{14}H_{24}O_7 \cdot 0.5H_2O$ requires C, 53.7; H, 8.0%); δ_H(400 MHz; $CDCl_3$) 1.30–1.58 and 1.62–1.84 (2 × 4 H, 2 × m, 3′-H, 4′-H, 5′-H, 6′-H), 2.94 (1 H, s, 2-OH), 3.19 and 3.20 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 3.33 (3 H, s, 1-OMe), 3.62 (2 H, d, *J* 8.1, 5-H), 3.91 (1 H, br s, 2-H), 4.05 (1 H, dd, *J* 10.5, 2.9, 3-H), 4.32 (1 H, dt, *J* 10.4, 8.1, 4-H), 4.64 (1 H, d, *J* 1.0, 1-H); δ_C(100 MHz; $CDCl_3$) 21.35 (4′-C, 5′-C), 26.99 (3′-C, 6′-C), 46.80 and 46.89 (1′-OMe, 2′-OMe), 54.88 (1-OMe), 60.85 (5-C), 63.67 (4-C), 69.44 (3-C), 70.01 (2-C), 98.71 and 99.37 (1′-C, 2′-C), 101.35 (1-C); *m/z* (EI) 304 (M^+, 10%), 289 (80, $M^+ - Me$), 273 (40, $M^+ - OMe$), 257 (40), 175 (30), 143 (100), 111 (60), 70 (70) (Found: M^+, 304.1522. $C_{14}H_{24}O_7$ requires *M*, 304.1522).

(1′*R*,2′*R*)-Methyl 2,3-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-D-galactopyranoside 20 (alpha and beta isomers). Methyl α-D-galactopyranoside (H_2O-adduct, 1.20 g, 6.16 mmol) was subjected to the standard CDA protection conditions. Column chromatography (gradient elution Et_2O to Et_2O + 4% EtOH) furnished a 4:1 α:β-mixture of **20** (850 mg, 46%). Other isomers were visible by TLC but were not isolated.

In another experiment under standard conditions starting from 6-OTBDPS protected methyl α-galactopyranoside (531 mg, 1.2 mmol), the desilylated derivative **20** could be isolated in a comparable yield (182 mg, 44%) but without contamination with the β-anomer.

Compound **20**: (α-anomer) $[\alpha]_D^{25}$ +10.9 (*c* 0.66 in $CHCl_3$); δ_H(400 MHz; $CDCl_3$) 1.29–1.57 and 1.71–1.89 (2 × 4 H, 2 × m, 3′-H, 4′-H, 5′-H, 6′-H), 2.57 and 2.93 (2 × 1 H, 2 × br s, 2 × OH), 3.19 and 3.20 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 3.41 (s, 1-OMe), 3.78–3.86 (2 H, m, 5-H, 6-H_A), 3.93 (1 H, dd, *J* 10.7, 5.0, 6-H_B), 4.05 (1 H, br d, *J* 1.9, 4-H), 4.23 (1 H, dd, *J* 10.8, 3.0, 3-H), 4.36 (1 H, dd, *J* 10.8, 3.4, 2-H), 4.83 (1 H, d, *J* 3.3, 1-H); δ_C(100 MHz; $CDCl_3$) 21.34 (4′-C, 5′-C), 27.00 and 27.03 (3′-C, 6′-C), 46.81 and 46.84 (1′-OMe, 2′-OMe), 55.28 (1-OMe), 62.91 (6-C), 65.81 (2-C), 66.89 (3-C), 69.60 (4-C), 70.37 (5-C), 98.62 (1-C), 99.03 and 99.07 (1′-C, 2′-C); *m/z* (EI) 334 (M^+, <10%), 319 (40, $M^+ - OMe$), 143 (70), 111 (60), 100 (100) (Found: M^+, 334.1625. $C_{15}H_{26}O_8$ requires *M*, 334.1628).

(1′*R*,2′*R*)-Methyl 6-*O*-*tert*-butyldiphenylsilyl-2,3-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-α-D-galactopyranoside 22 and (1′*S*)-6-*O*-*tert*-butyldiphenylsilyl-3,4-*O*-(2′,2′-dimethoxycyclohexylidene)-α-D-galactopyranoside 21. CSA (36 mg, 0.16 mmol) was added to a stirred solution of methyl 6-*O*-*tert*-butyldiphenylsilyl-α-D-galactopyranoside (489 mg, 1.13 mmol) and **1** (395 mg, 1.93 mmol) in chloroform (5 ml), and the mixture was stirred for 4 h at room temperature. The mixture was neutralised with $NaHCO_3$ (*ca.* 0.1 g), the solvent was removed under reduced pressure, and the crude material was purified by column chromatography (gradient elution Et_2O–petrol 1:2 to 4:1) to furnish slightly impure dioxane **22** (54 mg, 8%) and dioxolane **21** (265 mg, 41%).

Compound **22** (Found: C, 65.0; H, 7.9. $C_{31}H_{44}O_8Si$ requires C, 65.0; H, 7.7%); δ_H(400 MHz; $CDCl_3$) 1.06 [9 H, s, $C(CH_3)_3$], [1.34–1.90 (5 H, m), 1.84 (1 H, br d, *J* 14.0), 2.02 (1 H, br d, *J* 13.5) and 2.28 (1 H, ddd, *J* 2 × 13.5, 3.3) (3′-H, 4′-H, 5′-H, 6′-H)], 2.44 (1 H, br s, OH), [3.24, 3.38 and 3.40 (3 × 3 H, 3 × s, 1′-OMe, 2′-OMe, 1-OMe)], 3.77–3.83 (2 H, m, 6-H_A, 6-H_B), 3.94 (1 H, d, *J* 3.5, 5-H), 4.08 (1 H, br d, *J* 1.7, 4-H), 4.14 (1 H, dd, *J* 10.7, 2.9, 3-H), 4.26 (1 H, dd, *J* 10.7, 3.4, 2-H), 4.81 (1 H, d, *J* 3.3, 1-H), 7.32–7.45 and 7.65–7.72 (6 H, and 4 H, Ar-H); δ_C(100 MHz; $CDCl_3$) 19.25 [*C*$(CH_3)_3$], 21.97 and 22.08 (4′-C, 5′-C), 26.49 and 30.65 (3′-C, 6′-C), 26.86 [C(*C*$H_3)_3$], 47.52 and 48.99 (1′-OMe, 2′-OMe), 55.13 (1-OMe), 62.57 (6-C), [65.35, 68.03, 69.72 and 71.30 (2-C, 3-C, 4-C, 5-C)], 98.49 (1-C), 98.61 and 99.42 (1′-C, 2′-C); *m/z* (+FAB) 1168 (2 M + Na^+, 70%), 596 (70, M + Na^+), 542 (70, $M^+ - MeOH$), 197 (100) (Found: M + Na^+, 595.2697. $C_{31}H_{44}NaO_8Si$ requires *M*, 595.2703).

Compound **21**: $[\alpha]_D^{25}$ +53 (*c* 1.37 in $CHCl_3$) (Found: C, 65.0; H, 7.8. $C_{31}H_{44}O_8Si$ requires C, 65.0; H, 7.7%); δ_H(400 MHz; $CDCl_3$) 1.04 [s, $C(CH_3)_3$], [1.38–1.54, 1.61–1.69 and 1.74–1.82 (4 H, 2 H and 2 H, 3 × m, 3′-H, 4′-H, 5′-H, 6′-H)], 2.21 (1 H, d, *J* 7.0, OH), 3.23 and 3.28 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 3.40 (3 H, s, 1-OMe), 3.86 (1 H, dd, *J* 10.0, 6.7, 6-H_A), 3.96 (1 H, dd, *J* 10.0, 6.6, 6-H_B), 4.05 (1 H, ddd, *J* 2 × 6.6, 2.3, 5-H), 4.15 (1 H, dd, *J* 2 × 6.0, 3-H), 4.15–4.21 (1 H, m, 2-H), 4.24 (1 H, dd, *J* 5.9, 2.3, 4-H), 4.74 (1 H, d, *J* 3.7, 1-H), 7.33–7.45 and 7.65–7.72 (6 H and 4 H, 2 × m, Ar-H); δ_C(100 MHz; $CDCl_3$) 19.16 [*C*$(CH_3)_3$], 21.65 and 22.25 (4′-C, 5′-C), 26.73 [C(*C*$H_3)_3$], 30.97 and 32.62 (3′-C, 6′-C), 49.35 and 49.95 (1′-OMe, 2′-OMe), 55.38 (1-OMe), 63.09 (6-C), [67.95, 69.31, 72.46 and 76.36 (2-C, 3-C, 4-C, 5-C)], 98.98 (1-C), 99.10 (2′-C), 111.57 (1′-C); *m/z* (+FAB) 637 (70%), 596 (M + Na^+, 70), 542 (70, $M^+ - MeOH$), 197 (100) (Found: M + Na^+, 595.2702. $C_{31}H_{44}NaO_8Si$ requires *M*, 595.2703).

(1′*R*,2′*R*)-Methyl 2,3-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-α-L-arabinopyranoside 24. Methyl β-D-arabinopyranoside (319 mg, 1.94 mmol) was subjected to the standard CDA protection conditions. Chromatography (gradient elution Et_2O–petrol 2:1 + 1% EtOH to Et_2O–petrol 5:1 + 4% EtOH) furnished **24** (216 mg, 37%). Other isomers were visible by TLC but were not isolated.

Compound **24**: $[\alpha]_D^{18}$ −25.6 (*c* 0.60 in $CHCl_3$); δ_H(400 MHz; $CDCl_3$) 1.29–1.56 and 1.67–1.92 (2 × 4 H, 2 × m, 3′-H, 4′-H, 5′-H, 6′-H), 2.64 (1 H, br s, OH), 3.18 and 3.20 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 3.40 (3 H, s, 1-OMe), 3.72 (1 H, dd, *J* 12.6, 1.7, 5-H_A), 3.81 (1 H, br d, *J* 12.6, 5-H_B), 3.95 (1 H, br s, 4-H), 4.24 (1 H, dd, *J* 10.7, 3.1, 3-H), 4.36 (1 H, dd, *J* 10.7, 3.3, 2-H), 4.76 (1 H, d, *J* 3.2, 1-H); δ_C(100 MHz; $CDCl_3$) 21.36 and 21.39 (4′-C, 5′-C), 27.01 and 27.04 (3′-C, 6′-C), 46.78 (1′-OMe, 2′-OMe), 55.30 (1-OMe), 62.89 (5-C), [65.94, 66.50, 68.48 (2-C, 3-C, 4-C)], 98.86 (1-C), 99.04 and 99.07 (1′-C, 2′-C); *m/z* (EI) 304 (M^+, <10%) 289 (80, $M^+ - Me$), 273 (20, $M^+ - OMe$), 143 (60), 129 (50), 111 (50), 100 (100), 75 (60) (Found: M^+, 304.1523. $C_{14}H_{24}O_7$ requires *M*, 304.1522).

(1′*R*,2′*R*)-Methyl 2,3-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-α-D-glycopyranoside 26, (1′*S*,2′*S*)-methyl 3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-α-D-glucopyranoside 25 and (1′*R*,2′*R*)-methyl 3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-α-D-glycopyranoside 27. Methyl α-D-glycopyranoside (752 mg, 3.87 mmol) was subjected to standard CDA protection conditions. Column chromatography (gradient elution Et_2O to Et_2O + 5% EtOAc) yielded a 3:2 mixture of 2,3- and 3,4-protected glucosides of **26** and **25** (1.04 g, 80%) and the less polar boat isomer **27** (26.9 mg, 2%).

Compound **26** (Found: C, 52.4; H, 7.8. $C_{15}H_{26}O_8 \cdot 0.5H_2O$ requires C, 52.5; H, 7.9%); δ_H(400 MHz; $CDCl_3$) 1.31–1.57 and 1.65–1.91 (2 × 4 H, 2 × m, 3′-H, 4′-H, 5′-H, 6′-H), 2.03 (1 H, t, *J* 6.4, 6-OH), 2.54 (1 H, d, *J* 2.8, 4-OH), 3.20 and 3.23 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 3.42 (3 H, s, 1-OMe), 3.67 (1 H, dt, *J* 9.5, 3.9, 5-H), 3.78 (1 H, ddd, *J* 2 × 9.4, 2.6, 4-H), 3.81–3.88 (3 H, m, 2-H, 6-H_A, 6-H_B), 4.19 (1 H, dd, *J* 10.5, 9.3, 3-H), 4.75 (1 H, d, *J* 3.4, 1-H); δ_C(100 MHz; $CDCl_3$) 21.37 and 21.40 (4′-C, 5′-C), 26.93 and 27.10 (3′-C, 6′-C), 46.75 and 46.89 (1′-OMe, 2′-OMe), 55.17 (1-OMe), 62.29 (6-C), [68.61, 68.81, 69.76 and 71.96 (2-C, 3-C, 4-C, 5-C)], 98.29 (1-C), 98.47 and 98.82 (1′-C, 2′-C).

Compound **25**: δ_H(400 MHz; $CDCl_3$) 2.16 (1 H, d, *J* 8.5, 2-OH), 3.21 and 3.24 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 4.19 (1 H, dd, *J* 2 × 9.7, 3-H or 4-H), 4.80 (1 H, d, *J* 3.9, 1-H) all other signals overlapped by the major isomer; δ_C(100 MHz; $CDCl_3$) 21.37 (4′-C, 5′-C, overlapped by signals of the major isomer), 26.93 and 27.09 (3′-C, 6′-C, overlapped by the signals of the major isomer), 46.75 and 46.89 (1′-OMe, 2′-OMe, overlapped

by signal of the major isomer), 55.32 (1-OMe), 61.25 (6-C), [66.71, 69.83, 70.00 and 70.61 (2-C, 3-C, 4-C, 5-C)], 98.56 and 98.67 (1′-C, 2′-C), 99.66 (1-C); *m/z* (EI) 334 (M^+, 10%), 319 (10, $M^+ - Me$), 303 (60, $M^+ - OMe$), 271 (40), 198 (100), 159 (40), 142 (90), 127 (60), 111 (65), 100 (100) [Found (+FAB): $M - OMe^+$, 303.1433. $C_{14}H_{23}O_7$ requires $M - OMe^+$, 303.1444).

Compound **27**: $[\alpha]_D^{29}$ +109 (*c* 0.89 in $CHCl_3$); δ_H(400 MHz; $CDCl_3$) 1.20–1.69 and 1.85–2.00 (6 H and 2 H, 2 × m, 3′-H, 4′-H, 5′-H, 6′-H), 2.14 and 2.68 (2 × 1 H, 2 × s, 2 × OH), 3.26 and 3.30 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 3.39 (3 H, s, 1-OMe), 3.55 (1 H, br dd, *J* 2 × 9.0, 4-H), 3.60 (1 H, dt, *J* 9.6, 3.6, 5-H), 3.78–3.87 (2 H, m, 6-H_A, 6-H_B), 4.14 (1 H, dd, *J* 11.2, 3.4, 2-H), 4.55 (1 H, dd, *J* 11.2, 8.6, 3-H), 4.76 (1 H, d, *J* 3.4, 1-H); δ_C(100 MHz; $CDCl_3$) 21.55 and 21.65 (4′-C, 5′-C), 28.25 and 28.36 (3′-C, 6′-C), 47.13 (1′-OMe and 2′-OMe), 55.32 (1-OMe), 62.15 (6-C), [70.66, 71.16, 71.57 and 72.12 (2-C, 3-C, 4-C, 5-C)], 98.69 (1-C), 100.02 and 100.27 (1′-C, 2′-C); *m/z* (EI) 334 (M^+, 10%), 319 (20, M − Me), 303 (60, M − OMe), 287 (25), 159 (20), 143 (50), 127 (50), 111 (40), 100 (100) (Found: M^+, 334.1623. $C_{15}H_{26}O_8$ requires *M*, 334.1628).

General procedure for preparation of 6-*O*-*tert*-butyldiphenylsilyl derivatives of CDA protected monosaccharides

tert-Butyldiphenylsilyl chloride (1.2 equiv.) was added to a solution of CDA protected monosaccharide (1 equiv.) and imidazole (2.2 equiv.) in THF (15 ml $mmol^{-1}$ of monosaccharide) and the mixture stirred at room temperature for 16 h. The precipitate was removed by filtration and washed with Et_2O. The combined filtrates were evaporated under reduced pressure and the residue purified by column chromatography to give the desired silylated derivatives.

(1′*R*,2′*R*)-Methyl 6-*O*-*tert*-butyldiphenylsilyl-2,3-*O*-(1′-2′-dimethoxycyclohexane-1′,2′-diyl)-α-D-glycopyranoside 29 and (1′*S*,2′*S*)-methyl 6-*O*-*tert*-butyldiphenylsilyl-3,4-*O*-(1′-2′-dimethoxycyclohexane-1′,2′-diyl)-α-D-glucopyranoside 28. A 3:2 mixture of 2,3- and 3,4-CDA-protected α-methyl glucopyranoside **26**/**25** (438 mg, 1.31 mmol) was subjected to the standard procedure for silylation. Column chromatography (gradient elution Et_2O–petrol 1:8 to Et_2O) yielded 2,3-protected isomer **29** (367 mg, 49%) and 3,4-protected **28** (270 mg, 36%).

Compound **29**: $[\alpha]_D^{20}$ −11.8 (*c* 0.92 in $CHCl_3$) (Found: C, 63.0; H, 7.6. $C_{31}H_{44}O_8Si{\cdot}H_2O$ requires C, 63.0; H, 7.85%); δ_H(400 MHz; $CDCl_3$) 1.05 [9 H, s, $C(CH_3)_3$], 1.32–1.55 and 1.66–1.92 (2 × 4 H, 2 × m, 3′-H, 4′-H, 5′-H, 6′-H), 2.76 (1 H, br s, OH), 3.21 and 3.25 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 3.37 (3 H, s, 1-OMe), 3.72 (1 H, ddd, *J* 9.3, 2 × 4.7, 5-H), 3.82 (1 H, ddd, *J* 2 × 9.3, 1.0, 4-H), 3.84–3.91 (3 H, m, 2-H, 6-H_A, 6-H_B), 4.21 (1 H, dd, *J* 10.4, 9.4, 3-H), 4.72 (1 H, d, *J* 3.4, 1-H), 7.34–7.46 and 7.66–7.72 (6 H, 4 H, m, Ar-H); δ_C(100 MHz; $CDCl_3$) 19.24 [$C(CH_3)_3$], 21.41 and 21.46 (4′-C, 5′-C), 26.97 and 27.15 (3′-C, 6′-C), 26.84 [$C(CH_3)_3$], 46.77 and 46.86 (1′-OMe, 2′-OMe), 54.96 (1-OMe), 64.70 (6-C), [68.82, 69.78, 69.95 and 71.70 (2-C, 3-C, 4-C, 5-C)], 98.05 (1-C), 98.42 and 98.79 (1′-C, 2′-C); *m/z* (+FAB) 596 (M + Na^+, 20%), 483 (50), 199 (50), 135 (100) (Found: M + Na^+, 595.2740. $C_{31}H_{44}NaO_8Si$ requires *M*, 595.2703).

Compound **28**: $[\alpha]_D^{20}$ +117 (*c* 0.48 in $CHCl_3$) (Found: C, 64.8; H, 7.5. $C_{31}H_{44}O_8Si$ requires C, 65.0; H, 7.7%); δ_H(400 MHz; $CDCl_3$) 1.03 [9 H, s, $C(CH_3)_3$], [1.32–1.57 (4 H, m), 1.64–1.80 (3 H, m) and 1.85 (1 H, br d, *J* 13.5) (3′-H, 4′-H, 5′-H, 6′-H)], 2.10 (1 H, d, *J* 7.7, OH), 3.14 and 3.25 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 3.39 (3 H, s, 1-OMe), 3.75–3.94 (5 H, m, 2-H, 4-H, 5-H, 6-H_A, 6-H_B), 4.08 (1 H, dd, *J* 2 × 10.0, 3-H), 4.80 (1 H, d, *J* 3.9, 1-H), [7.32–7.44 and 7.67–7.74 (6 H and 4 H, 2 × m, Ar-H)]; δ_C(100 MHz; $CDCl_3$) 19.36 [$C(CH_3)_3$], 21.39 (4′-C, 5′-C), 26.97 and 27.09 (3′-C, 6′-C), 26.82 [$C(CH_3)_3$], 46.87 and 46.99 (1′-OMe, 2′-OMe), 54.92 (1-OMe), 62.03 (6-C), [66.42, 70.02, 70.74 and 71.02 (2-C, 3-C, 4-C, 5-C)], 98.44 and 98.61 (1′-C, 2′-C), 99.28 (1-C); *m/z* (+FAB) 1083 (40%), 1050 (60), 1025 (70), 636 (60), 596 (M + Na^+, 50%), 542 (70, M − MeOH), 483 (70), 269 (70), 199 (100), 195 (90), 163 (60) (Found: M + Na^+, 595.2683. $C_{31}H_{44}NaO_8Si$ requires *M*, 595.2703).

(1′*S*,2′*S*)-Methyl 6-*O*-*tert*-butyldiphenylsilyl-3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-dilyl)-α-D-mannopyranoside 30. CDA-derivative **5** (466 mg, 1.39 mmol) was subjected to the general procedure for silylation. Column chromatography (Et_2O–petrol 3:1) yielded **30** (802 mg, 100%), $[\alpha]_D^{25}$ +95.6 (*c* 0.64 in $CHCl_3$); δ_H(400 MHz; $CDCl_3$) 1.05 [9 H, s, $C(CH_3)_3$], 1.30–1.54 and 1.67–1.80 (2 × 4 H, 2 × m, 3′-H, 4′-H, 5′-H, 6′-H), 2.48 (1 H, d, *J* 2.9, OH), [3.09, 3.22 and 3.35 (3 × 3 H, 3 × s, 1′-OMe, 2′-OMe, 1-OMe)], 3.81–3.95 (4 H, m, 2 H, 5-H, 6-H_A, 6-H_B), 4.16 (1 H, dd, *J* 10.3, 2.9, 3-H), 4.21 (1 H, dd, *J* 2 × 9.9, 4-H), 4.73 (1 H, d, *J* 1.0, 1-H), 7.32–7.43 and 7.80–7.85 (6 H, and 4 H, 2 × m, Ar-H); δ_C(100 MHz; $CDCl_3$) 19.37 [$C(CH_3)_3$], 21.34 (4′-C, 5′-C), 26.80 [$C(CH_3)_3$], 27.00 and 27.03 (3′-C, 6′-C), 46.82 and 46.92 (1′-OMe, 2′-OMe), 54.52 (1-OMe), 64.47 (6-C), [63.87, 69.22, 70.20 and 71.78 (2-C, 3-C, 4-C, 5-C)], 98.62 and 99.16 (1′-C, 2′-C), 100.88 (1-C), [127.48, 127.56, 135.66 and 135.91 (*ortho*- and *meta*-C)], [129.46 and 129.50 (*para*-C)], [133.58 and 134.00 (*ipso*-C)]; *m/z* (EI) 557 (M − Me^+, 20%), 541 (80, M − OMe^+), 483 (100), 451 (50), 339 (70), 241 (90), 199 (70), 141 (50), 127 (80) (Found: M − Me^+, 557.2568. $C_{30}H_{41}O_8Si$ requires *M*, 557.2571).

(1′*S*,2′*S*)-Ethyl 6-*tert*-butyldiphenylsilyl-3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-1-thio-α-D-mannopyranoside 31. CDA protected SEt mannose **8** (511 mg, 1.41 mmol) was subjected to the general procedure for silylation. Chromatography (Et_2O–petrol 1:2 to 1:1) yielded **31** (823 mg, 97%), $[\alpha]_D^{18}$ +156 (*c* 1.51 in $CHCl_3$) (Found: C, 63.6; H, 7.7. $C_{32}H_{46}O_7SSi$ requires C, 63.75; H, 7.7%); δ_H(400 MHz; $CDCl_3$) 1.03 [9 H, s, $C(CH_3)_3$], 1.24 (3 H, t, *J* 7.4, SCH_2CH_3), 1.30–1.56 and 1.61–1.80 (2 × 4 H, 2 × m, 3′-H, 4′-H, 5′-H, 6′-H), 2.53 (1 H, dq, *J* 13.0, 7.4, SCH_AH_B), 2.65 (1 H, dq, *J* 13.0, 7.3, SCH_AH_B), *ca.* 2.6 (1 H, OH, obscured by SCH_AH_B), 3.11 and 3.22 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 3.87 (1 H, dd, *J* 11.2, 2.0, 6-H_A), 3.92 (1 H, dd, *J* 11.3, 4.8, 6-H_B), 4.01 (1 H, br s, 2-H), 4.17 (1 H, dd, *J* 10.3, 3.0, 3-H), 4.21 (1 H, ddd, *J* 9.8, 4.6, 1.9, 5-H), 4.29 (1 H, dd, *J* 2 × 10.1, 4-H), 5.33 (1 H, s, 1-H), 7.30–7.43 and 7.67–7.73 (6 H, and 4 H, 2 × m, Ar-H); δ_C(100 MHz; $CDCl_3$) 14.73 (SCH_2CH_3), 19.31 [$C(CH_3)_3$], 21.36 (4′-C, 5′-C), 24.60 (SCH_2CH_3), 26.80 [$C(CH_3)_3$], 26.96 and 27.02 (3′-C, 6′-C), 46.84 and 46.88 (1′-OMe, 2′-OMe), 62.29 (6-C), [64.12, 69.81, 71.57 and 71.89 (2-C, 3-C, 4-C, 5-C)], 83.65 (1-C), 98.69 and 99.22 (1′-C, 2′-C), [127.47, 127.57, 135.61 and 135.94 (*ortho*- and *meta*-C)], 129.47 and 129.51 (*para*-C), 133.45 and 133.99 (*ipso*-C); *m/z* (EI) 513 (M − Me − Bu^{t+}, 20%), 392 (100), 159 (70), 143 (60), 91 (90) (Found: M − Me − Bu^{t+}, 513.1737. $C_{27}H_{33}O_6SSi$ requires *M*, 513.1767).

(1′*S*,2′*S*)-Phenyl 6-*O*-*tert*-butyldiphenylsilyl-3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-1-seleno-α-D-mannopyranoside 32. CDA-derivative **10** (2.29 g, 4.85 mmol) was subjected to the general procedure for silylation. Column chromatography (Et_2O–petrol 1:2 to 1:1) yielded **32** (3.22 g, 95%), $[\alpha]_D^{25}$ +150 (*c* 0.17 in $CHCl_3$) (Found: C, 62.0; H, 6.7. $C_{36}H_{46}O_7SeSi$ requires C, 62.0; H, 6.6%); δ_H(400 MHz; $CDCl_3$) 1.03 [9 H, s, $C(CH_3)_3$], 1.33–1.57 and 1.67–1.83 (2 × 4 H, 2 × m, 3′-H, 4′-H, 5′-H, 6′-H), 2.52 (1 H, d, *J* 2.9, OH), 3.17 and 3.27 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 3.86 (1 H, dd, *J* 10.5, 1.8, 6-H_A), 3.99 (1 H, dd, *J* 10.4, 4.1, 6-H_B), 4.15 (1 H, dd, *J* 10.4, 2.9, 3-H), 4.23 (1 H, ddd, *J* 10.0, 3.8, 1.7, 5-H), 4.31 (1 H, br s, 2-H), 4.45 (1 H, dd, *J* 2 × 10.2, 4-H), 5.83 (1 H, s, 1-H), [7.14–7.44, 7.49–7.55 and 7.64–7.70 (9 H, 2 H and 4 H, 3 × m, Ar-H)]; δ_C(100 MHz; $CDCl_3$) 19.37 [$C(CH_3)_3$], 21.37 (4′-C, 5′-C), 26.88 [$C(CH_3)_3$], 26.98 and 27.06 (3′-C, 6′-C), 46.97 (1′-OMe, 2′-OMe), 62.04 (6-C), [63.58, 70.12, 72.35 and 74.25 (2-C, 3-C, 4-C, 5-C)], 86.36 (1-C), 98.78 and 99.34 (1′-C, 2′-C), [127.48, 127.51, 127.58, 127.79, 129.10, 129.46, 129.48, 129.92, 133.29, 133.63, 134.05, 135.57 and 135.94 (Ar-H)]; *m/z* (+FAB) 1208 (50%), 722 (M + Na, 60), 697 (10, M − H^+), 682 (20, M − Me^+), 510 (60),

365 (50), 197 (50), 135 (100) (Found: 697.2103. $C_{36}H_{45}O_7SeSi$ requires *M*, 697.2099).

(1′*S*,2′*S*)-Ethyl 6-*O*-benzoyl-3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-1-thio-α-D-mannopyranoside 33, (1′*S*,2′*S*)-ethyl 2-*O*-benzoyl-3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-1-thio-α-D-mannopyranoside 34 and (1′*S*,2′*S*)-ethyl 2,6-di-*O*-benzoyl-3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-1-thio-α-D-mannopyranoside 35. *Method A*.—Benzoyl chloride (0.18 ml, 0.22 g, 1.6 mmol) was added at 0 °C to CDA-protected *S*-ethyl mannoside **8** (571 mg, 1.58 mmol) in pyridine (4.0 ml). The reaction was gradually warmed to room temperature and stirred for 2 days. After removal of the solvent under reduced pressure the crude material was purified by column chromatography (gradient elution Et_2O–petrol 1:2 to Et_2O) to furnish, in order of elution, dibenzoylated **35** (124 mg, 28% relative to benzoyl chloride), 2-*O*-benzoylated **34** (96 mg, 13%) and the 6-*O*-protected mannoside **33** (398 mg, 54%).

Method B.—CDA-protected *S*-ethyl mannoside **8** (5.91 g, 16.3 mmol) and bis(tributyltin) oxide (6.65 ml, 13.1 mmol) were refluxed in toluene (55 ml) under Dean–Stark conditions (trap filled with 4 Å mol. sieves) for 2 days. The mixture was cooled to room temperature, benzoyl chloride (2.08 ml, 18.0 mmol) was added and the mixture stirred for 7 h. After quenching with saturated aqueous sodium hydrogen carbonate (20 ml), the mixture was extracted with DCM (3 × 40 ml) and the combined organic layers were dried with Na_2SO_4. The solvent was removed under reduced pressure and the crude reaction mixture was purified by column chromatography to furnish 6-monobenzoylated **33** (6.17 g, 81%) together with traces of 2,6-dibenzoylated compound **35** (608 mg, 8%).

Method C.—In a two step procedure 6-*O*-silylated CDA-derivative **31** was benzoylated using method A. Desilylation in TBAF–THF was followed by column chromatography to yield the 2-benzoylated compound **34** (71% from CDA-protected *S*-ethyl mannoside).

Compound **33**: $[\alpha]_D^{19}$ +220 (*c* 0.63 in $CHCl_3$) (Found: C, 58.1; H, 7.0. $C_{23}H_{32}O_8S{\cdot}0.5H_2O$ requires C, 57.85; H, 7.0%); δ_H(400 MHz; $CDCl_3$), 1.25 (3 H, t, *J* 7.4, SCH_2CH_3), 1.29–1.54 and 1.66–1.83 (2 × 4 H, 2 × m, 3′-H, 4′-H, 5′-H, 6′-H), 2.58 (1 H, dq, *J* 13.0, 7.4, SCH_AH_B), 2.67 (1 H, dq, *J* 13.0, 7.4, SCH_AH_B) [from 200 MHz spectra: *ca.* 2.7 (1 H, br s, OH)], 3.09 and 3.22 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 4.06 (1 H, dd, *J* 2.8, 0.9, 2-H), 4.18 (1 H, dd, *J* 10.2, 3.0, 3-H), 4.38 (1 H, dd, *J* 2 × 9.9, 4-H), 4.43–4.59 (3 H, m, 5-H, 6-H_A, 6-H_B), 5.33 (1 H, s, 1-H), 7.40 (2 H, t, *J* 7.6, *meta*-H), 7.52 (1 H, br t, *J* 7.0, *para*-H), 8.03 (2 H, br d, *J* 7.0, *ortho*-H); δ_C(100 MHz; $CDCl_3$) 14.90 (SCH_2CH_3), 21.32 (4′-C, 5′-C), 25.06 (SCH_2CH_3), 26.94 and 27.01 (3′-C, 6′-C), 46.83 and 46.91 (1′-OMe, 2′-OMe), 63.17 (6-C), [64.43, 69.09, 69.65 and 71.43 (2-C, 3-C, 4-C, 5-C)], 84.54 (1-C), 98.93 and 99.32 (1′-C, 2′-C), 128.33 and 129.66 (*ortho*- and *meta*-C), 130.01 (*ipso*-C), 133.01 (*para*-C), 166.37 (CO); *m/z* (EI) 468 (M^+, 10%), 453 (80, $M^+ - Me$), 437 (20, $M^+ - OMe$), 143 (50), 105 (100) (Found: M^+, 468.1820. $C_{23}H_{32}O_8S$ requires *M*, 468.1818).

Compound **34**: $[\alpha]_D^{25}$ +169 (*c* 1.39 in $CHCl_3$) (Found: C, 59.1; H, 7.0. $C_{23}H_{32}O_8S$ requires C, 58.95; H, 6.9%); δ_H(400 MHz; $CDCl_3$) 1.29 (3 H, t, *J* 7.4, SCH_2CH_3), 1.32–1.81 (8 H, m, 3′-H, 4′-H, 5′-H, 6′-H), 1.86 (1 H, br t, *J ca.* 3–4, OH), 2.65 (2 H, m, SCH_2CH_3), 3.24 and 3.28 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 3.85 (2 H, br s, 6-H_A, 6-H_B), 4.21 (1 H, ddd, *J* 10.0, 2 × 3.4, 5-H), 4.34 (1 H, dd, *J* 10.5, 2.9, 3-H), 4.52 (1 H, dd, *J* 2 × 10.3, 4-H), 5.34 (1 H, dd, *J* 2.9, 1.4, 2-H), 5.40 (1 H, d, *J* 0.7, 1-H), 7.45 (2 H, t, *J* 7.7, *meta*-H), 7.57 (1 H, tt, *J* 7.5, 1.5, *para*-H), 8.07 (2 H, br d, *J* 8, *ortho*-H); δ_C(100 MHz; $CDCl_3$) 15.01 (SCH_2CH_3), 21.30 and 21.40 (4′-C, 5′-C), 25.91 (SCH_2CH_3), 26.91 and 26.99 (3′-C, 6′-C), 46.84 and 46.96 (1′-OMe, 2′-OMe), 61.38 (6-C), [64.64, 67.62, 71.31 and 73.54 (2-C, 3-C, 4-C, 5-C)], 83.26 (1-C), 98.74 and 99.11 (1′-C, 2′-C), 128.44 and 129.91 (*ortho*- and *meta*-C), 130.22 (*ipso*-C), 133.18 (*para*-C), 165.97 (CO); *m/z* (EI) 468 (M^+, <10%), 453 (50, $M^+ - Me$), 437 (30, $M^+ - OMe$), 314 (50), 293 (50), 105 (100), 77 (60) (Found: M^+, 468.1821. $C_{23}H_{32}O_8S$ requires *M*, 468.1818).

Compound **35**: (slightly impure) δ_H(400 MHz; $CDCl_3$) 1.29 (3 H, t, *J* 7.4, SCH_2CH_3), 1.3–1.8 (8 H, m, 3′-H, 4′-H, 5′-H, 6′-H), 2.68 (2 H, m, SCH_2CH_3), 3.14 and 3.25 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 4.39 (1 H, dd, *J* 10.4, 2.9, 3-H), 4.53 (1 H, ddd, *J* 10.2, 4.0, 2.0, 5-H), 4.56 (1 H, dd, *J* 12.7, 2.0, 6-H_A), 4.62 (1 H, dd, *J* 12.1, 4.4, 6-H_B), 4.66 (1 H, dd, *J* 2 × 10.2, 4-H), 5.39 (1 H, dd, *J* 2.8, 1.3, 2-H), 5.45 (1 H, d, *J* 0.9, 1-H), 7.33–7.62 and 8.01–8.13 (6 H and 4-H, 2 × m, Ar-H); δ_C(100 MHz; $CDCl_3$) 15.09 (SCH_2CH_3), 21.29 and 21.38 (4′-C, 5′-C), 25.90 (SCH_2CH_3), 27.87 (3′-C, 6′-C), 46.86 and 46.99 (1′-OMe, 2′-OMe), 62.81 (6-C), [64.60, 67.31, 69.38 and 73.37 (2-C, 3-C, 4-C, 5-C)], 83.24 (1-C), 98.92 and 99.19 (1′-C, 2′-C), [128.36, 128.42, 129.61, 129.90, 133.04, 133.14 and 130.04, 130.32 (2 × *ipso*-C), Ar-C], 165.85 and 166.29 (2 × CO); *m/z* (EI) 572 (M^+, <10%), 557 (80, $M^+ - Me$), 511 (60), 450 (50), 418 (80), 275 (60), 154 (60), 143 (70), 105 (100), 91 (70), 77 (40) (Found: M^+, 572.2118. $C_{30}H_{36}O_9S$ requires *M*, 572.2080).

(1′*S*,2′*S*)-Phenyl 6-*O*-benzoyl-3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-1-seleno-α-D-mannopyranoside 36. CDA protected selenomannoside **10** (936 mg, 2.04 mmol) and bis(tributyltin) oxide (0.78 ml, 1.5 mmol) were refluxed in toluene (25 ml) under Dean–Stark conditions (trap filled with 4 Å molecular sieves) for 24 h. The mixture was cooled to room temperature, benzoyl chloride (2.08 ml, 2.52 g, 18.0 mmol) was added and the mixture stirred for 24 h. After quenching with saturated aqueous sodium hydrogen carbonate solution (20 ml), the mixture was extracted with DCM (3 × 40 ml) and the combined organic layers were dried with Na_2SO_4. The solvent was removed under reduced pressure and the crude reaction mixture was purified by column chromatography to furnish 6-monobenzoylated **36** (878 mg, 76%), δ_H(400 MHz; $CDCl_3$) 1.29–1.60 and 1.67–1.86 (2 × 4 H, 2 × m, 3′-H, 4′-H, 5′-H, 6′-H), 2.74 (1 H, br s, OH), 3.11 and 3.28 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 4.20 (1 H, dd, *J* 10.3, 2.9, 3-H), 4.33 (1 H, br d, *J* 2.0, 2-H), 4.43 (1 H, dd, *J* 2 × 10.0, 4-H), 4.47–4.60 (3 H, m, 5-H, 6-H_A, 6-H_B), 5.86 (1 H, s, 1-H), [7.12–7.28 (3 H, m), 7.40 (2 H, t, *J* 7.7), 7.50–7.61 (3 H, m) and 8.00 (2 H, br d, *J* 7.5), (Ar-H)]; δ_C(100 MHz; $CDCl_3$) 21.34 (4′-C, 5′-C), 26.98 and 27.05 (3′-C, 6′-C), 46.91 and 47.01 (1′-OMe, 2′-OMe), 63.06 (6-C), [64.33, 69.93, 71.29 and 71.99 (2-C, 3-C, 4-C, 5-C)], 85.83 (1-C), 99.01 and 99.43 (1′-C, 2′-C), [127.82, 128.35, 129.19, 129.75, 129.94, 130.15, 133.03 and 133.84 (Ar-C)], 166.36 (CO); *m/z* (EI) 564 (M^+, 30%), 533 (80, $M - Me^+$), 407 (50), 143 (50), 375 (40), 105 (100) (Found: M^+, 564.1261. $C_{27}H_{32}O_8Se$ requires *M*, 564.1262).

(1′*S*,2′*S*)-Methyl 2-*O*-benzyl-3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-α-D-mannopyranoside 37. CDA protected mannoside **5** (20 g, 0.06 mol) was added to a suspension of sodium hydride (2.7 g, of a 60% suspension in mineral oil, 0.07 mol) in DMF (70 ml). The reaction was stirred for 2 h at room temperature. Benzyl bromide (7.84 ml, 0.066 mol) was added slowly and the reaction mixture stirred for 15 h. Saturated aq. ammonium chloride (50 ml) was added and the mixture extracted with Et_2O (2 × 300 ml). The combined organic extracts were washed with brine (200 ml) and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue purified by column chromatography (eluent Et_2O–hexane 1:1) to give the 2-*O*-benzylated derivative **37** (19.1 g, 75%) as a white foam, $[\alpha]_D^{19}$ 33 (*c* 0.96 in $CHCl_3$) (Found: C, 61.9; H, 7.6. $C_{22}H_{32}O_8$ requires C, 62.25; H, 7.6%); δ_H(400 MHz; $CDCl_3$) [1.30–1.45, 1.48–1.57 and 1.65–1.90 (2 H, 2 H and 4 H, 3 × m, 3′-H, 4′-H, 5′-H, 6′-H)], 2.01 (1 H, dd, *J* 5.5, 7.3, 6-OH), 3.23 and 3.24 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 3.31 (3 H, s, 1-OMe), 3.71 (1 H, dd, *J* 1.5, 2.7, 2-H), 3.73–3.85 (3 H, m, 5-H, 6-H_A, 6-H_B), 4.22 (1 H, dd, *J* 2.7, 10.6, 3-H), 4.37 (1 H, dd, *J* 10.6, 9.6, 4-H), 4.63 (1 H, d, *J* 11.7, CH_AH_BPh), 4.66 (1 H, d, *J* 1.5, 1-H), 4.98 (1 H, d, *J* 11.7, CH_AH_BPh), 7.24–7.45 (5 H, m, Ar-H); δ_C(100 MHz; $CDCl_3$) 21.38 and 21.45 (4′-C, 5′-C), 27.04 and 27.16 (3′-C, 6′-C), 46.77 and 46.88 (1′-OMe, 2′-OMe), 54.70 (1-

OMe), 61.80 (6-C), [64.77, 69.67, 71.12 and 76.12 (2-C, 3-C, 4-C, 5-C)], 73.35 (OCH_2Ph), 98.49 and 98.78 (1′-C, 2′-C), 100.80 (1-C), [127.54, 128.16, 128.24 and 138.67 (Ar-C)]; *m/z* (EI) 424 (M^+, 10%), 409 (20, $M^+ - Me$), 392 (100, $M^+ - MeOH$), 143, 91 (Found: M^+, 424.2098. $C_{22}H_{32}O_8$ requires *M*, 424.2097).

(1′*S*,2′*S*)-Ethyl 2-*O*-benzyl-3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-1-thio-α-D-mannopyranoside 38. Sodium hydride (0.08 g of a 60% dispersion in mineral oil, 2.0 mmol) was added to a solution of CDA protected thiomannoside **8** (0.36 g, 1.0 mmol) and benzyl bromide (0.13 ml, 1.05 mmol) in DMF (5 ml) at −10 °C. The mixture was stirred for 1 h at −10 °C then allowed to warm to room temperature overnight. Saturated aqueous ammonium chloride solution (25 ml) was added and the mixture extracted with Et_2O (3 × 20 ml). The combined extracts were washed with water (3 × 10 ml) and brine (10 ml) and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue purified by column chromatography (eluent: petrol–EtOAc 4:1) gave the mono benzylated product **38** (0.38 mg, 84%) as a colourless foam, $[\alpha]_D^{19}$ 226 (*c* 0.93 in $CHCl_3$) (Found: C, 60.9; H, 7.6. $C_{23}H_{34}O_7S$ requires C, 60.8; H, 7.5%); δ_H(500 MHz; $CDCl_3$) 1.23 (3 H, t, *J* 7.4, SCH_2CH_3), [1.33–1.45, 1.50–1.53 and 1.68–1.85 (2 H, 2 H and 4 H, 3 × m, 3′-H, 4′-H, 5′-H, 6′-H)], 1.99 (1 H, br s, OH), 2.54 (1 H, dq, *J* 13.0, 7.4, SCH_AH_B), 2.60 (1 H, dq, *J* 13.0, 7.4, SCH_AH_B), 3.23 and 3.24 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 3.78–3.80 (2 H, m, 6-H_A, 6-H_B), 3.83 (1 H, d, *J* 1.3, 2-H), 4.13 (1 H, dt, *J* 9.9, 3.9, 5-H), 4.20 (1 H, dd, *J* 2.6, 10.5, 3-H), 4.42 (1 H, t, *J* 10.3, 4-H), 4.63 (1 H, d, *J* 11.7, CH_AH_BPh), 4.96 (1 H, d, *J* 11.7, CH_AH_B-Ph), 5.24 (1 H, s, 1-H), [7.27 (1 H, t, *J* 7.3), 7.33 (2 H, t, *J* 7.2) and 7.44 (2 H, d, *J* 7.3) (Ar-H)]; δ_C(50 MHz; $CDCl_3$) 14.87 (SCH_2CH_3), 21.31 and 21.37 (4′-C and 5′-C), 25.35 and 27.02 (3′-C and 6′-C), 26.95 (SCH_2CH_3), 46.73 and 46.78 (1′-OMe, 2′-OMe), 61.61 (6-C), 64.84 (4-C), 70.17 (3-C), 72.29 (5-C), 73.12 (OCH_2Ph), 77.98 (2-C), 84.10 (1-C), 98.41 and 98.76 (1′-C and 2′-C), [127.53, 128.01, 128.22 and 138.52 (Ar-C)]; *m/z* (EI) 439 ($M^+ - Me$), 422 ($M^+ - MeOH$), 361, 91 (Found: $M^+ - Me$, 439.1782. $C_{23}H_{34}O_7S$ requires *M*, 439.1790).

(1′*S*,2′*S*)-Methyl 6-deoxy-3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-6-iodo-α-D-mannopyranoside 39. Iodine (610 mg, 2.40 mmol) was added to a mixture of CDA-derivative **5** (618 mg, 1.85 mmol), imidazole (377 mg, 5.54 mmol) and triphenylphosphine (727 mg, 2.77 mmol) in toluene (40 ml). The mixture was stirred at 75 °C for 3 h, then it was poured into saturated aqueous sodium hydrogen carbonate (45 ml), stirred for 5 min, treated with iodine until the red–brown colour persisted and finally titrated with 10% aqueous sodium thiosulfate until the solution was colourless again. The organic layer was separated and dried ($MgSO_4$). The solvent was removed under reduced pressure and the crude material was purified by column chromatography (gradient elution Et_2O–petrol 1:1 to Et_2O) to yield **39** (496 mg, 60%), $[\alpha]_D^{18}$ +133 (*c* 0.16 in $CHCl_3$) (Found: C, 40.7; H, 5.8. $C_{15}H_{25}IO_7$ requires C, 40.55; H, 5.7%); δ_H(400 MHz; $CDCl_3$) 1.29–1.58 and 1.63–1.82 (2 × 4 H, 2 × m, 3′-H, 4′-H, 5′-H, 6′-H), 2.56 (1 H, s, OH), 3.20, 3.21 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 3.25 (1 H, dd, *J* 10.6, 8.2, 6-H_A), 3.42 (3 H, s, 1-OMe), 3.53 (1 H, dd, *J* 10.6, 2.3, 6-H_B), 3.68 (1 H, ddd, *J* 10.0, 7.7, 2.2, 5-H), 3.92 (1 H, br s, 2-H), 4.02 (1 H, dd, *J* 2 × 10.0, 4-H), 4.12 (1 H, dd, *J* 10.3, 3.0, 3-H), 4.73 (1 H, s, 1-H); δ_C(100 MHz; $CDCl_3$) 5.07 (6-C), 21.32 and 21.36 (4′-C, 5′-C), 26.96 and 27.07 (3′-C, 6′-C), 46.99 and 47.18 (1′-OMe, 2′-OMe), 55.16 (1-OMe), [67.88, 68.58, 70.12 and 70.23 (2-C, 3-C, 4-C, 5-C)], 98.92 and 99.21 (1′-C, 2′-C), 101.19 (1-C); *m/z* (EI) 444 (M^+, 20%), 430 (700), 209 (60), 143 (100), 111 (50) (Found: M^+, 444.0666. $C_{15}H_{25}IO_7$ requires *M*, 444.0647).

(1′*S*,2′*S*)-Methyl 3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-α-D-rhamnopyranoside 40. Iodo compound **39** (466 mg, 1.05 mmol) was stirred with 10% palladium on charcoal (40 mg) and diethylamine in cyclohexane (15 ml) under a hydrogen atmosphere for 16 h. The suspension was filtered and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (gradient elution Et_2O–petrol 3:1 to Et_2O) to yield **40** (276 mg, 83%). Its NMR spectra are identical to the reported data for the L-compound **12**.

Compound **40**: $[\alpha]_D^{18}$ +190 (*c* 0.76 in $CHCl_3$); *m/z* (EI) 318 (M^+, 10%), 303 (70, $M^+ - Me$), 287 (30, $M^+ - OMe$), 175 (40), 143 (100), 111 (50), 84 (100) (Found: M^+, 318.1677. $C_{15}H_{26}O_7$ requires *M*, 318.1678).

(1′*S*,2′*S*)-Methyl 2-*O*-benzyl-6,7-dideoxy-3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-α-D-*manno*-hept-6-enopyranoside 41. Dimethyl sulfoxide (6.7 ml, 0.094 mol) was added to a solution of oxalyl dichloride (40 ml, 0.08 mol) in dichloromethane (300 ml) at −78 °C and stirred for 20 min. A solution of CDA mannose derivative **37** (30.79 g, 0.072 mol) in dichloromethane (80 ml) was added slowly. The mixture was stirred for 40 min and triethylamine (30.1 ml, 0.22 mol) was added. The mixture was stirred at −78 °C for a further 3 h and then concentrated under reduced pressure to give the crude aldehyde which was used directly without further purification.

Butyllithium (1.6 M in hexane, 43 ml, 0.11 mol) was added slowly to a solution of methyl(triphenyl)phosphonium bromide (38.84 g, 0.11 mol) in tetrahydrofuran (150 ml) at −78 °C. The mixture was warmed to 0 °C and stirred for 20 min. This solution was then added to a solution of the crude aldehyde in tetrahydrofuran (300 ml) at 0 °C. The mixture was warmed to room temperature and stirred for 1 h. Saturated aq. ammonium chloride (200 ml) was added and the mixture extracted with Et_2O (2 × 300 ml) and the combined organic extracts dried (Na_2SO_4) and evaporated under reduced pressure. The residue was purified by column chromatography (eluent Et_2O–hexane 3:7) to give alkene **41** (19.2 g, 63%) as a white solid, $[\alpha]_D^{18}$ +130 (*c* 0.93 in $CHCl_3$) (Found: C, 65.8; H, 7.7. $C_{23}H_{32}O_7$ requires C, 65.7; H, 7.7%); δ_H(500 MHz; $CDCl_3$) [1.39–1.42, 1.50–1.54 and 1.70–1.82 (2 H, 2 H and 4 H, 3 × m, 3′-H, 4′-H, 5′-H, 6′-H), 3.19 and 3.24 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 3.32 (3 H, s, 1-OMe), 3.71 (1 H, dd, *J* 1.5, 2.6, 2-H), 4.12–4.15 (2 H, m, 4-H, 5-H), 4.22 (1 H, dd, *J* 10.3, 2.6, 3-H), 4.67 (1 H, d, *J* 12.0, CH_AH_B-Ph), 4.68 (1 H, br s, 1-H), 4.96 (1 H, *J* 12.0, CH_AH_BPh), 5.23 (1 H, dd, *J* 10.4, 0.9, 7-H_A), 5.45 (1 H, dd, *J* 17.3, 0.9, 7-H_B), 5.95 (1 H, dd, *J* 10.4, 6-H), 7.26–7.45 (5 H, m, Ar-H); δ_C(100 MHz; $CDCl_3$) 21.41 and 21.47 (4′-C, 5′-C), 27.08 and 27.14 (3′-C, 6′-C), 46.65 and 46.84 (1′-OMe, 2′-OMe), 54.62 (1-OMe), 68.20 (4-C), 69.84 (3-C), 71.37 (5-C), 73.21 (OCH_2Ph), 76.05 (2-C), 98.57 and 98.74 (1′-C, 2′-C), 100.59 (1-C), 117.73 (C-7), 134.29 (6-C), 127.44, 128.13, 128.18 and 138.8 (Ar-C); *m/z* (EI) 420 (M^+, 0.1%), 405 (5, $M^+ - Me$), 388 (15, $M^+ - MeOH$) (Found: M^+, 420.2163. $C_{23}H_{32}O_7$ requires *M*, 420.2148).

8-(Methoxycarbonyl)octyl 6-*O*-benzoyl-3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-β-D-mannopyranoside 42. A solution of CDA protected mannoside **33** (469 mg, 1.0 mmol), dimethyl(dichloro)silane (0.6 ml, 5.0 mmol) and pyridine (1.5 ml) in toluene (15 ml) was stirred for 1 h at room temperature. The toluene was then removed by distillation, and the reaction cooled to room temperature. 8-(Methoxycarbonyl)octanol (196 mg, 0.78 mmol) was added and the mixture was stirred for 12 h. The mixture was diluted with ether (20 ml) and washed with water (10 ml) and brine (10 ml) and dried ($MgSO_4$). The solvents were removed under reduced pressure and the residue purified by column chromatography (eluent petrol–ether 1:1) to furnish the intermediate silyl-acetal which was used without further purification.

The intermediate (556 mg, 0.78 mmol) was dissolved in nitromethane (24 ml) and *N*-iodosuccinimide (430 mg, 1.9 mmol) was added. The mixture was heated under reflux for 1 h and cooled to room temperature. The mixture was partitioned between DCM and 40% aq. sodium thiosulfate. The organic extract was concentrated under reduced pressure and the residue purified by column chromatography (gradient elution ether–hexane 1:1 to 3:1) to yield the β-glycoside **42** (283 mg, 61%), $[\alpha]_D^{30}$ +8.6 (*c* 0.7 in $CHCl_3$) (Found: C, 61.2; H, 7.7. $C_{31}H_{46}O_{11}\cdot 0.5H_2O$ requires C, 61.7; H, 7.85%); δ_H(500 MHz;

$CDCl_3$) 1.20–1.88 [20 H, m, 3′-H, 4′-H, 5′-H, 6′-H, OCH_2-(CH_2)$_6$$CH_2CO_2Me$], 2.24 (2 H, t, *J* 7.5, CH_2CO_2Me), 2.41 (1 H, d, *J* 1.6, OH), 3.09 and 3.20 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 3.50 [1 H, dt, *J* 9.5, 6.9, $OCH_AH_B(CH_2)_7CO_2Me$], 3.62 (3 H, s, CO_2Me), 3.73 (1 H, ddd, *J* 1.6, 5.6, 9.8, 5-H), 3.84–3.89 [2 H, m, 3-H, $OCH_AH_B(CH_2)_7CO_2Me$], 4.01 (1 H, br, 2-H), 4.34 (1 H, t, *J* 10.1, 4-H), 4.43 (1 H, dd, *J* 5.6, 11.9, 6-H_A), 4.54 (1 H, d, *J* 0.8, 1-H), 4.62 (1 H, dd, *J* 2.3, 11.8, 6-H_B), 7.39 (2 H, t, *J* 7.9, *meta*-H), 7.52 (1 H, tt, *J* 1.2, 7.7, *para*-H), 8.03 (2 H, dd, *J* 1.3, 7.7, *ortho*-H); δ_C(100 MHz; $CDCl_3$) 21.21, 24.73, 25.72, 26.83, 26.92, 28.38, 28.87 and 29.28 [3′-C, 4′-C, 5′-C, 6′-C, OCH_2-(CH_2)$_6$$CH_2CO_2Me$], 33.90 ($CH_2CO_2Me$), 46.67 and 46.80 (1′-OMe and 2′-OMe), 51.31 (CO_2Me), 62.96 (6-C), 63.76 (4-C), 69.67 (2-C), 69.75 [$OCH_2(CH_2)_7CO_2Me$], 70.72 (3-C), 72.21 (5-C), 99.08 and 99.60 (1′-C, 2′-C), 100.08 (1-C, $^1J_{CH}$ 158), [128.19, 129.58, 129.87 and 132.89 (Ar-C)], 166.21 (CH_2CO), 174.12 (Ar*C*O); *m/z* (EI) 1126 ($2M^+$, 5%), 563 (50, $M^+ - OMe^+$), 375, 142 (Found: $M^+ - OMe$, 563.2843. $C_{30}H_{43}O_{10}$ requires *M*, 563.2856).

(1′*S*,2′*S*)-Methyl 3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-2,6-di-*O*-methyl-α-D-mannopyranoside 43. Methyl iodide (0.24 ml, 3.9 mmol) was added to a stirred suspension of CDA-protected methyl mannoside **5** (518 mg, 1.55 mmol) and potassium hydride (173 mg, 4.36 mmol) in DMF (5.0 ml). After 24 h more potassium hydride (*ca.* 50 mg) and methyl iodide (*ca.* 0.10 ml) were added and the mixture stirred for a further 24 h. The reaction was quenched by addition of saturated aqueous ammonium chloride (5 ml) and water (5 ml). Following extraction with ether (3 × 25 ml), the combined organic extracts were dried ($MgSO_4$) and the solvent removed under reduced pressure. The residue was purified by column chromatography (gradient elution Et_2O–petrol 1:1 to Et_2O) to furnish **43** (555 mg, 99%) as a colourless oil, $[\alpha]_D^{18}$ +157 (*c* 0.63 in $CHCl_3$); δ_H(400 MHz; $CDCl_3$) 1.23–1.53 and 1.59–1.82 (2 × 4 H, 2 × m, 3′-H, 4′-H, 5′-H, 6′-H), 3.15 and 3.18 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 3.33 and 3.34 (2 × 3 H, 2 × s, 2-OMe, 6-OMe), 3.41 (1 H, br s, 2-H), 3.44 (3 H, s, 1-OMe), 3.54 (1 H, dd, *J* 10.6, 5.6, 6-H_A), 3.59 (1 H, dd, *J* 10.6, 2.2, 6-H_B), 3.80 (1 H, ddd, *J* 10.0, 5.3, 2.1, 5-H), 4.09–4.18 (2 H, m, 3-H, 4-H), 4.75 (1 H, d, *J* 1.2, 1-H); δ_C(100 MHz; $CDCl_3$) 21.38 and 21.41 (4′-C, 5′-C), 27.05 (3′-C, 6′-C), 46.60 and 46.80 (1′-OMe, 2′-OMe), 54.73 (1-OMe), 58.90 and 59.22 (2-OMe, 6-OMe), [64.22, 68.99 and 70.26 (3-C, 4-C, 5-C)], 70.86 (6-C), 78.70 (2-C), 98.45 and 98.83 (1′-C, 2′-C), 98.93 (1-C); *m/z* (EI) 362 (M^+, 60%), 347 (60, $M^+ - Me$), 331 (40, $M^+ - MeO$), 143 (100), 128 (90), 111 (80), 97 (80) (Found: M^+, 362.1941. $C_{17}H_{30}O_8$ requires *M*, 362.1940).

(1′*S*,2′*S*)-Methyl 2,6-di-*O*-benzyl-3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-α-D-mannopyranoside 44. Protected mannoside **5** (0.50 g, 1.5 mmol) was added to a suspension of sodium hydride (60% in mineral oil, 0.24 g, 3.3 mmol) in DMF (3.5 ml) and the mixture stirred for 16 h under Ar. Benzyl bromide (0.53 ml, 4.5 mmol) and catalytic tetrabutylammonium iodide were added and the mixture was stirred for 16 h. Saturated aqueous ammonium chloride (5 ml) was added and the mixture extracted with Et_2O (2 × 15 ml). The combined organic layers were washed with brine (20 ml), dried ($MgSO_4$) and the solvent removed under reduced pressure. Column chromatography of the residue (gradient elution, Et_2O–petrol 20:80–35:65) gave the title compound **44** (0.60 g, 78%) as a pale yellow oil, $[\alpha]_D^{30}$ 96.5 (*c* 1.14 in $CHCl_3$); δ_H(400 MHz; $CDCl_3$) 1.30–1.80 (8 H, m, 3-H′, 4-H′, 5-H′, 6-H′), 3.09 and 3.19 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 3.28 (3 H, s, 1-OMe), 3.70–3.78 (3 H, m, 2-H, 6-H_A, 6-H_B), 3.91 (1 H, m, 5-H), 4.22 (1 H, dd, *J* 2.7, 9.5, 3-H), 4.37 (1 H, t, *J* 10.4, 4-H), 4.71 (1 H, d, *J* 0.7, 1-H), [4.57 (1 H, d, *J* 12.1), 4.66 (1 H, d, *J* 12.0), 4.64 (1 H, d, *J* 12.1) and 4.97 (1 H, d, *J* 12.0) (2 × CH_2Ph)], [7.43 (2 H, d, *J* 7.1) and 7.20–7.35 (8 H, m) (Ar-H)]; δ_C(100 MHz; $CDCl_3$) 21.40 and 21.46 (4′-C, 5′-C), 27.07 and 27.14 (3′-C, 6′-C), 46.77 and 46.85 (1′-OMe, 2′-OMe), 54.61 (1-OMe), 68.91 (6-C), [64.62, 69.83, 71.12 and 76.20 (2-C, 3-C, 4-C, 5-C)], 73.04 and 73.44 (2 × CH_2Ph), 98.48 and 98.73 (1′-C, 2′-C), 100.41 (1-C), [127.26, 127.33, 127.47, 127.97, 128.15, 128.17, 138.68 and 138.91 (Ar-C)]; *m/z* (EI) 514 (M^+, 5%), 499 (20, M − Me), 482 (95, $M^+ - MeOH$), 189 (20), 181 (40), 159 (20), 143 (75), 127 (50), 111 (35), 91 (100, C_7H_7) (Found: M^+, 514.2587. $C_{29}H_{38}O_8$ requires *M*, 514.2566).

(1′*S*,2′*S*)-Methyl 2,6-di-*O*-benzoyl-3,4-*O*-(1′,2′-dimethoxycyclohexane-1′,2′-diyl)-α-D-mannopyranoside 45. Benzoyl chloride (0.68 ml, 0.82 g, 5.9 mmol) was added to a solution of CDA-protected methyl mannoside **5** (654 mg, 1.96 mmol) in pyridine (8.0 ml) and the mixture stirred for 16 h. The reaction mixture was diluted with DCM (30 ml), washed with 1 M HCl (15 ml), saturated aqueous sodium hydrogen carbonate (15 ml) and brine (15 ml), dried ($MgSO_4$) and the solvent removed under reduced pressure. The residue was chromatographed (Et_2O–petrol 3:1) to furnish dibenzoylated **45** (1.00 g, 94%), $[\alpha]_D^{18}$ +112 (*c* 0.74 in $CHCl_3$) (Found: C, 64.4; H, 6.3. $C_{29}H_{34}O_{10}$ requires C, 64.2; H, 6.3%); δ_H(200 MHz; $CDCl_3$) 1.32–1.79 (8 H, m, 3′-H, 4′-H, 5′-H, 6′-H), 3.16 and 3.27 (2 × 3 H, 2 × s, 1′-OMe, 2′-OMe), 3.44 (3 H, s, OMe), 4.18 (1 H, ddd, *J* 10.0, 2 × 3.0, 5-H), 4.46 (1 H, dd, *J* 10.5, 2.9, 3-H), 4.60 (2 H, d, *J* 3.3, 6-H_A, 6-H_B), 4.63 (1 H, dd, *J* 2 × 10.3, 4-H), 4.89 (1 H, d, *J* 1.5, 1-H), 5.30 (1 H, dd, *J* 2.9, 1.6, 2-H), 7.33–7.65 and 8.04–8.13 (6 H and 4 H, 2 × m, Ar-H); δ_C(100 MHz; $CDCl_3$) 21.29 and 21.39 (4′-C, 5′-C), 26.96 and 27.05 (3′-C, 6′-C), 46.83 and 47.02 (1′-OMe, 2′-OMe), 55.14 (1-OMe), 62.76 (6-C), [64.32, 66.88, 67.00 and 71.53 (2-C, 3-C, 4-C, 5-C)], 98.91 and 99.16 (1′-C, 2′-C), 99.08 (1-C), [128.39, 129.61, 129.90, 133.04, 133.10 and 130.07, 130.30 (2 × *ipso*-C) (Ar-C)], 165.88 and 166.31 (2 × CO); *m/z* (EI) 542 (M^+, 20%), 527 (80, $M^+ - Me$), 511 (10, $M^+ - OMe$), 143 (40), 105 (100), 77 (40) (Found: M^+, 542.2177. $C_{29}H_{34}O_{10}$ requires *M*, 542.2152).

Methyl 2,6-di-*O*-methyl-α-D-mannopyranoside 46 (methyl curamicoside). The CDA-protected mannoside **43** (207 mg, 0.571 mmol) was stirred for 5 min in 19:1 TFA–water mixture (1.0 ml), the solvent was evaporated under reduced pressure, three drops of triethylamine were added and the crude material purified by column chromatography (gradient elution Et_2O to Et_2O + 10% EtOH) to furnish **46** (97 mg, 76%) as a colourless oil, $[\alpha]_D^{18}$ +56.6 (*c* 1.17 in $CHCl_3$) (lit.,[15] +58.6 in MeOH, 20 °C); δ_H(400 MHz; $CDCl_3$) 3.36, 3.39 and 3.43 (3 × 3 H, 3 × s, 1-OMe, 2-OMe, 6-OMe), 3.46 (1 H, dd, *J* 3.6, 1.4, 2-H), 3.59–3.67 (3 H, m, 5-H, 6-H_A, 6-H_B), 3.71 (1 H, dd, *J* 2 × 9.2, 4-H), 3.81 (1 H, dd, *J* 9.5, 3.6, 3-H), 4.02 (2 H, br s, 3-OH, 4-OH), 4.79 (1 H, d, *J* 1.2, 1-H); δ_C(100 MHz; $CDCl_3$), 54.99 (1-OMe), 58.72 and 58.42 (2-OMe, 6-OMe), [69.32, 70.10 and 71.32 (3-C, 4-C, 5-C)], 72.42 (6-C), 79.64 (2-C), 97.41 (1-C); *m/z* (EI) 222 (M^+, <10%), 191 (60, $M^+ - MeO$), 173 (80), 159 (60), 87 (80), 74 (100) (Found: M^+, 222.1100. $C_9H_{18}O_6$ requires *M*, 222.1183).

Methyl 2,6-di-*O*-benzyl-α-D-mannopyranoside 47. *Method A.*—Acetic acid (4 ml) was added to a stirred solution of fully protected mannoside **44** (130 mg, 4.0 mmol) in a mixture of THF (1 ml) and water (1 ml). The mixture was heated to 60 °C for 100 h. Sodium hydrogen carbonate was added until CO_2 evolution ceased and the mixture extracted with Et_2O (2 × 10 ml). The combined organic layers were washed with saturated aqueous sodium hydrogen carbonate (10 ml), dried ($MgSO_4$) and the solvent evaporated under reduced pressure to give the title compound **47** (85 mg, 90%) as a pale yellow oil.

Method B.—Aqueous trifluoroacetic acid (40%, 1 ml) was added to fully protected mannoside **44** (53 mg) and the mixture stirred overnight. Work-up as in procedure A gave the title compound **47** (33 mg, 86%), $[\alpha]_D^{30}$ −5.4 (*c* 0.72 in $CHCl_3$); δ_H(400 MHz; $CDCl_3$) 2.60 (1 H, br, OH), 3.02 (1 H, br s, OH), 3.35 (3 H, s, 1-OMe), 3.66–3.80 (6 H, m, 2-H, 3-H, 4-H, 5-H, 6-H_A, 6-H_B), [4.56 (1 H, d, *J* 11.7), 4.58 (1 H, d, *J* 10.8), 4.64 (1 H, d, *J* 12.6) and 4.71 (1 H, d, *J* 11.7) (2 × CH_2Ph)], 4.80 (1 H, s, 1-H), 7.25–7.40 (10 H, m, Ar-H); δ_C(100 MHz; $CDCl_3$) 54.93 (1-OMe), 70.30 (6-C), 72.98 and 73.59 (2 × CH_2Ph) [69.71, 70.73, 71.57 and 77.83 (2-C, 3-C, 4-C, 5-C)], 98.20 (1-C), [127.64, 127.87, 128.00, 128.39, 128.56, 137.75, 138.21 (Ar-C)]; *m/z* (EI)

374 (M^+, 20%), 373 (20, $M^+ - H$), 343 (30, $M^+ - MeO$), 283 (45, $M^+ - PhCH_2$), 163 (50), 107 (60, $PhCH_2O^+$), 91 (100, $PhCH_2^+$) (Found: M^+, 374.1733. $C_{21}H_{26}O_6$ requires *M*, 374.1729).

Methyl 2,6-di-*O*-benzoyl-α-D-mannopyranoside 48. CDA-protected methyl mannoside **45** (200 mg, 0.368 mmol) was stirred in a 20:1 mixture of TFA–water (2.1 ml) for 5 min. The solvent was removed under reduced pressure and the residue was chromatographed (gradient elution Et_2O–petrol 3:1 to Et_2O) to furnish dibenzoylated **48** (142 mg, 96%), $[\alpha]_D^{25}$ +11.6 (*c* 1.12 in $CHCl_3$) (Found: C, 62.45; H, 5.55. $C_{21}H_{22}O_7$ requires C, 62.7; H, 5.5%); δ_H(200 MHz; $CDCl_3$) [2.38 (1 H, d, *J* 5.0) and 3.13 (1 H, d, *J* 2.7) (3-OH, 4-OH)], 3.44 (3 H, s, 1-OMe), 3.84–3.94 (2 H, m, 3-H, 4-H), 4.16 (1 H, m, 5-H), 4.52 (1 H, dd, *J* 12.2, 1.3, 6-H_A), 4.86 (1 H, d, *J* 1.7, 1-H), 4.91 (1 H, dd, *J* 12.1, 2.9, 6-H_B), 5.37 (1 H, dd, *J* 3.2, 1.7, 2-H), [7.20–7.27 (2 H, m), 7.41–7.53 (3 H, m), 7.58–7.65 (1 H, m), 7.90 (2 H, dd, *J* 8.3, 1.3) and 8.11 (2 H, dd, *J* 8.3, 1.3), (Ar-H)]; δ_C(100 MHz; $CDCl_3$) 55.32 (1-OMe), 63.53 (6-C), [67.94, 70.02, 70.80 and 72.15 (2-C, 3-C, 4-C, 5-C)], 98.89 (1-C), [128.39, 129.54, 129.75, 129.88 (*ortho*- and *meta*-C), 129.45 (*ipso*-C) and 133.32 (*para*-C) (Ar-C)], 166.03 and 167.32 (2 × CO); *m/z* (EI) 371 ($M - Me^+$, 30%), 267 (50), 248 (60), 237 (40), 227 (50), 207 (60), 123 (70), 105 (100), 77 (90), 60 (70) (Found: $M - Me^+$, 371.1122. $C_{20}H_{19}O_7$ requires *M*, 371.1131).

Acknowledgements

We gratefully acknowledge financial support from Agrevo (Fellowship to H. W. M. P.), the Deutsche Forschungsgemeinschaft (Fellowship to J. P.) SmithKline Beecham (Studentship to S. L. W.) the Zeneca Strategic Research Fund and the Ciba Research Fellowship (to S. V. L.).

References

1 P. Grice, S. V. Ley, J. Pietruszka and H. W. M. Priepke, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 197.
2 S. V. Ley, R. Downham, P. J. Edwards, J. E. Innes and M. Woods, *Contemp. Org. Synth.*, 1995, **2**, 365.
3 S. V. Ley, H. W. M. Priepke and S. L. Warriner, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 2290.
4 N. L. Douglas, S. V. Ley, H. M. I. Osborn, D. R. Owen, H. W. M. Priepke and S. L. Warriner, *Synlett*, 1996, 793.
5 S. V. Ley and H. W. M. Priepke, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 2292.
6 Cyclohexane-1,2-dione and 1,1,2,2-tetramethoxycyclohexane are both available from Avocado Research Chemicals, Shore Road, Port of Heysham Industrial Park, Heysham, Lancashire LA3 2XY, England.
7 M. Bouchra, P. Calinaud and J. Gelas, *Carbohydr. Res.*, 1995, **267**, 227.
8 Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, 1997, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 207/68.
9 Methyl α-D-mannopyranoside: (*a*) B. M. Gatehouse and B. J. Poppleton, *Acta Crystallogr., Sect. B*, 1970, **26**, 1761; (*b*) G. A. Jeffrey, R. K. McMulle and S. T. Akagi, *Acta Crystallogr., Sect. B*, 1977, **33**, 728.
10 Man-α(1,2)-Man-α(1)-OMe disaccharide: T. Srikrishnan, M. S. Chowdhary and K. L. Matta, *Carbohydr. Res.*, 1989, **186**, 167.
11 K. Bock and J. Duus, *J. Carbohydr. Chem.*, 1994, **13**, 513.
12 M. E. Evans and F. W. Parrish, *Carbohydr. Res.*, 1977, **54**, 105.
13 (*a*) J. G. Buchanan, M. E. Chacon-Fuertes, A. R. Edgar, S. J. Moorehouse, D. I. Rawson and R. H. Wightman, *Tetrahedron Lett.*, 1980, **21**, 1793; (*b*) J. G. Buchanan, A. R. Edgar, D. I. Rawson, P. Shahidi and R. H. Wightman, *Carbohydr. Res.*, 1982, **100**, 75.
14 T. Ogawa and K. Sasajima, *Carbohydr. Res.*, 1981, **93**, 67. For the 1-*O*-allyl compound see also: H. Paulson and B. Helpap, *Carbohydr. Res.*, 1991, **216**, 289.
15 J. Thiem, V. Duckstein, A. Prahst and M. Matzke, *Liebigs Ann. Chem.*, 1987, 289. TIPDS protection was developed by Markiewicz: W. T. Markiewicz, *J. Chem. Res.* (*S*), 1979, 24.
16 P. Grice, S. V. Ley, J. Pietruszka, H. W. M. Priepke and E. P. E. Walther, *Synlett*, 1995, 781.
17 J. F. Stoddart, *Stereochemistry of Carbohydrates*, Wiley Interscience, New York, 1971, p. 68.
18 V. Waagen, T. K. Barua, H. W. Anthonsen, L. K. Hansen, D. J. Fossli, E. Hough and T. Anthonsen, *Tetrahedron*, 1994, **50**, 10 056.
19 For 3,4-dibenzyl-protected rhamnosides see: (*a*) *O*-methyl: V. Pozsgay, J. R. Brisson and H. J. Jennings, *Can. J. Chem.*, 1987, **65**, 2764; (*b*) For *S*-methyl rhamnoside see: V. Pozsgay and H. J. Jennings, *J. Org. Chem.*, 1988, **53**, 4042.
20 H. M. Flowers, *Carbohydr. Res.*, 1982, **100**, 418.
21 P. J. Garegg and B. Samuelsson, *J. Chem. Soc., Perkin Trans. 1*, 1980, 2866.
22 T. L. Arsenault, D. B. MacLean, W. Zou and W. A. Szarek, *Can. J. Chem.*, 1994, **72**, 1376.
23 G. Stork and G. Kim, *J. Am. Chem. Soc.*, 1992, **114**, 1087.
24 M. Bols, *J. Chem. Soc., Chem. Commun.*, 1993, 791.
25 D. E. Wright, *Tetrahedron*, 1979, **35**, 1207.

Paper 6/05851E
Received 22*nd August* 1996
Accepted 14*th October* 1996