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Dispiroketals in Synthesis (Part 17)[1]: Regioselective Protection of D-Glucopyranoside, D-Galactopyranoside and D-Mannopyranoside Substrates.

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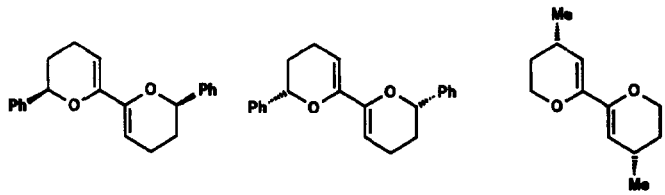
Abstract: Chiral recognition of enantiomeric *trans*-1,2-diol relationships leading to regioselective formation of 1,8,13,16-tetraoxadispiro[5.0.5.4] hexadecanes (dispiroketals) of various D-glucopyranoside, D-galactopyranoside and D-mannopyranoside substrates is described. Regioselectivity is achieved using the enantiomerically pure disubstituted tetrahydro-6,6'-bi-2*H*-pyrans **1**, **2**, **3**, **4** and **5**. Facile removal of the dispiroketal protecting group from a number of the sugar adducts has been achieved.

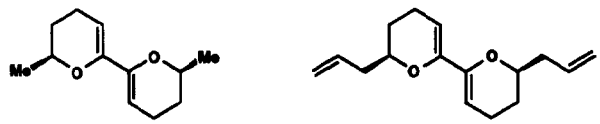
INTRODUCTION

The use of protective agents in the manipulation of carbohydrate substrates is a long established practice. A key element in this is the need for regioselective protection of the carbohydrate substrates to facilitate further processing. The basic sugar unit contains a number of vicinal 1,2-diol units, for which there exist a number of methods for protection (or blocking) of *cis*-1,2-diols which include the use of boronates, carbonates, orthoesters, siloxanes and variously substituted benzylidines and acetonides.[2] Methods for the selective protection of *trans*-1,2-diequatorial diols in the presence of other hydroxyl functions, however, are extremely rare. Two examples of this type of protection are the isomerisation of a disiloxanylidene in a glucose derivative,[3] and the reaction of methyl-α-D-glucopyranoside with 2,2-dimethoxypropane to give only a low yield of a highly unstable *trans*-acetonide.[4] Recently, we have shown that the dispiroketal group (dispoke)[5] is a convienent, effective way to protect 1,2-*trans* diol moieties in monosaccharide substrates,[6] arising from the inherent preference of the dispiroketal moiety for formation at 1,2-*trans* diequatorial diols. This new methodology has been applied to the regioselective protection of D-glucopyranosyl substrates[7] using the enantiomerically pure dienes (**1**), (**2**) and (**5**) (Scheme 1). Regioselectivity arises out of the preference of the anomerically stabilised substituents for equatorial orientations giving a "matched" dispoke adduct with only one pair of vicinal diols.

Herein we wish to report the results of our studies into regioselective protection of a number of D-glucopyranoside, D-galactopyranoside and D-mannopyranoside substrates, using the enantiopure dienes **1**, **2**, **3**, **4**, and **5** shown in Scheme 1.



[2*R*,2'*R*] PDHP 1 [2*S*,2'*S*] PDHP 2 [4*S*,4'*S*] MDHP



[2*S*,2'*S*] MDHP 4 [2*R*,2'*R*] ADHP 5

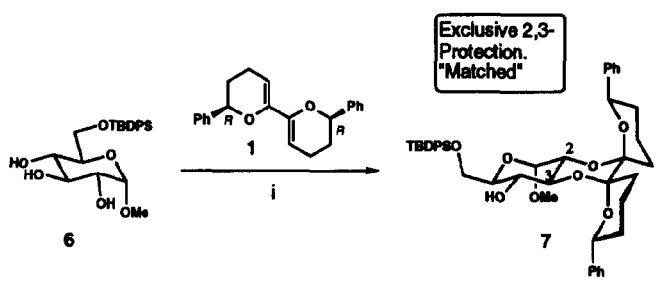
Scheme 1

RESULTS AND DISCUSSION

The reaction of methyl 6-*O*-(*tert*-butyldiphenylsilyl)-α-D-glucopyranose **6**, prepared using the procedure of Hannesian,[8] with enantiomerically pure dienes **1-5** under standard spiroketalisation conditions (catalytic camphorsulfonic acid in boiling chloroform), affords a number of regioselectively protected sugar adducts as their single diastereoisomers and is described below.

Regioselective Protection of D-Glucopyranoside Derivatives:

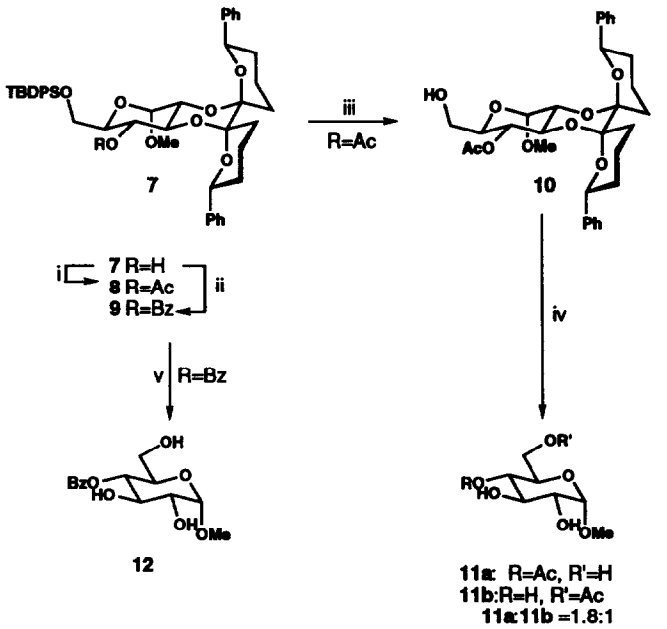
Reaction of [2*R*,2'*R*] 2,2'-diphenyl-3,3',4,4'-tetrahydro-6,6'-bi-2*H*-pyran [2*R*,2'*R*] PDHP 1[9] with D-glucopyranoside derivative **6**, under standard reaction conditions, gave the dispoke adduct **7** as a single diastereoisomer in 88% yield, an outcome which can be accounted for by the operation of multiple anomeric effects (Scheme 2). Complete regioselectivity in this spiroketalisation is observed, a process which is an expression of the chiral "matching" of the C-2 and C-3 vicinal diol moieties with the enantiopure diene **1**.



i) Camphorsulfonic acid (CSA) (catalytic), **1** (1.5 eq.), $CHCl_3$, reflux, overnight, **7**, 88%

Scheme 2

This regioselective 2,3-protection pattern, which forms a characteristic motif with D-glucopyranoside substrates and diene **1**, was proved upon conversion of dispoke adduct **7** into its acetate **8** and into its benzoate **9** (Scheme 3). Proton NMR spectroscopy confirmed the expected protection pattern in both cases. Removal of the spiroketal moiety from the acetate **8** was achieved on treatment with ferric chloride in dichloromethane which gave, in the first instance, desilylated material **10** in 84% yield. This compound, however, was not fully characterised. Longer exposure to Lewis acid generated an inseparable, by flash column chromatography, (1.8:1 **11a**:**11b**), mixture of acetate protected methyl-α-D-glucopyranoside in 63% yield, the ratio being determined by proton NMR spectroscopy. Complications arising from acetate migration to the free C-6 hydroxyl in compound **10**, under the reaction conditions, could be circumvented by blocking of the C-4 hydroxyl as its benzoate, giving **9**. Hence treatment of dispoke adduct **9** with an excess of ferric chloride gave methyl 4-*O*-benzoyl-α-D-glucopyranoside **12** in 41% yield, a product of both dispoke removal and desilylation under the Lewis acidic conditions.

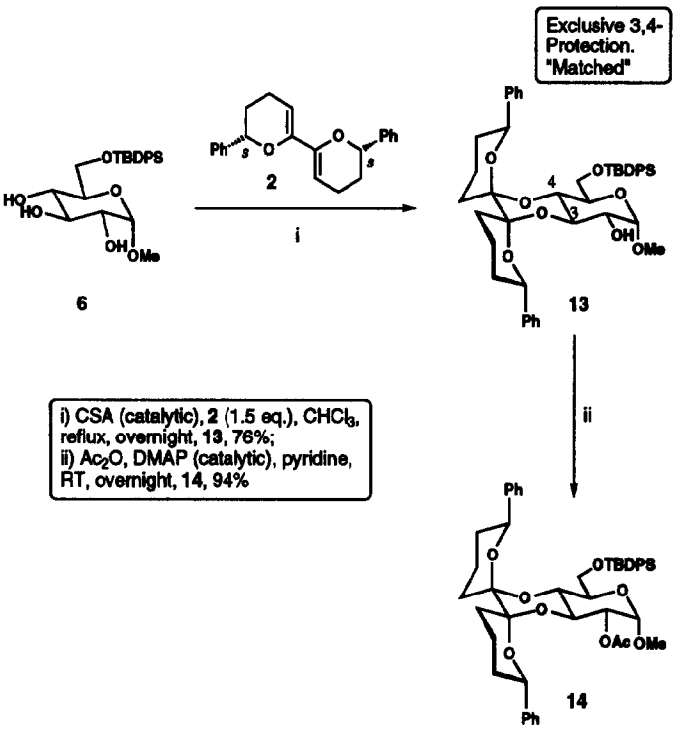


i) Ac_2O, DMAP (catalytic), pyridine, RT, overnight, **8**, 92%; ii) BzCl, DMAP (catalytic), triethylamine, DCM, RT, overnight, **9**, 96%; iii) $FeCl_3$ (excess), CH_2Cl_2, RT, overnight, **10**, 84%; iv $FeCl_3$ (excess), CH_2Cl_2, RT, overnight **11a**:**11b**; 63%; v) $FeCl_3$, (excess), CH_2Cl_2, RT, overnight, **12**, 41%.

Scheme 3

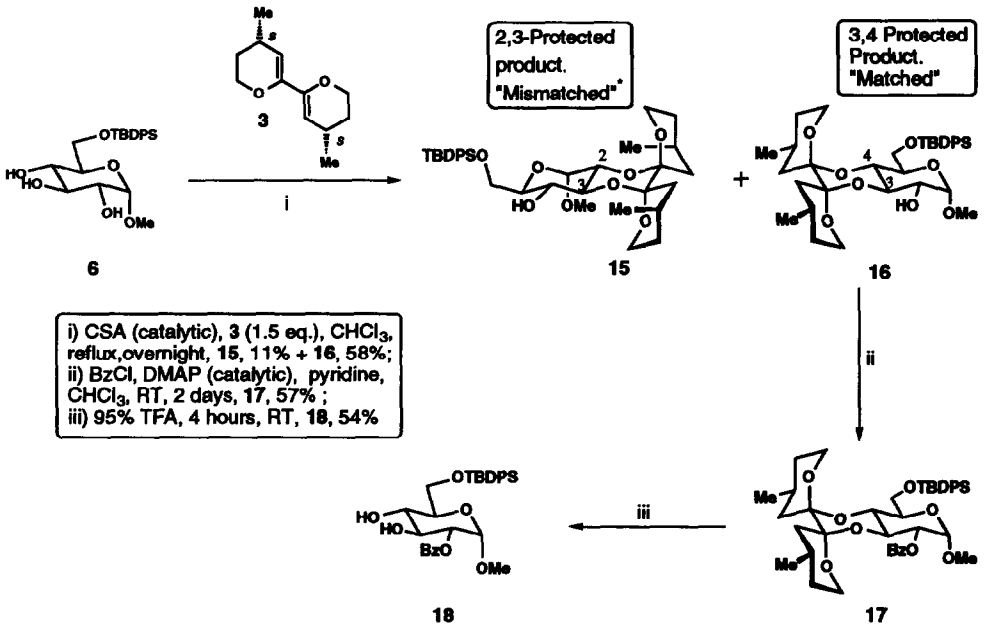
The reaction of methyl 6-*O*-(*tert*-butyldiphenylsilyl)-α-D-glucopyranoside **6** with the enantiomeric diene **2** was also considered, with the expectation that the 3,4-dispiroketal adduct should form exclusively. Indeed this proved to be the case, with the 3,4-protected compound **13** isolated in 76% yield (Scheme 4). This was then further reacted with acetic anhydride to give the fully protected derivative **14** in a pleasing 94% yield.

Hence it can be seen that both the enantiomeric dienes [2*R*,2'*R*] PDHP **1** and [2*S*,2'*S*] PDHP **2** offer an efficient, *complementary*, regioselective protection strategy for D-gluco substrates.



Scheme 4

Reaction of enantiopure [4*S*,4'*S*] 4,4'-dimethyl-3,3'-dihydro-6,6'-bi-2*H*-pyran [4*S*,4'*S*] MDHP **3**[10] with D-glucopyranose derivative **6** under standard conditions gave, in addition to the expected major product of 3,4-protection **16**, obtained as a single diastereoisomer in 58% yield, some "mismatched" product of 2,3-protection **15**, also as a single diastereoisomer in an isolated yield of 11%, (Scheme 5). Again the operation of multiple anomeric effects ensures that a single diastereoisomer predominates for each of the dispoke adducts, both being readily separated by flash column chromatography. A somewhat surprising outcome of the reaction was the appearance of minor amounts of the "mismatched" 2,3-dispoke adduct. It is possible that positioning of the methyl groups in the diene at the 4-position creates less steric differentiation in the transition states of the reaction with the vicinal diols, representing the two sites in the substrate capable of adduct formation with the diene. Reassuringly, however, the "matched" 3,4-adduct is seen to predominate, in keeping with expectation.

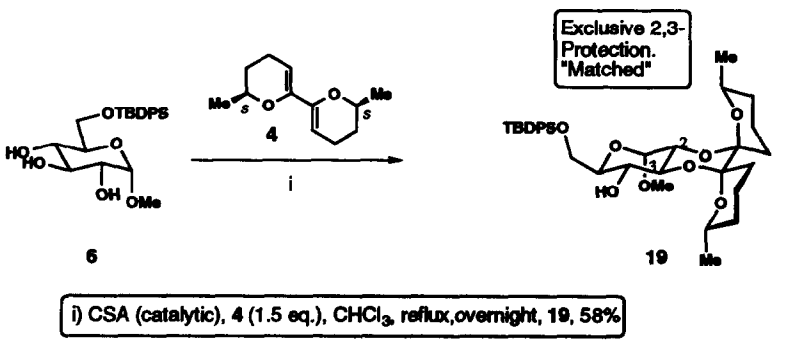


* The conformation of the pyran rings in the "mismatched" adduct has not been established. There is a possibility that one or both of the rings is in a boat conformation. However there is no direct experimental evidence to support this at the present time.

Scheme 5

Further reaction of the major 3,4-adduct **16** with benzoyl chloride furnished the fully protected derivative **17** in 57% yield. The dispiroketal moiety was then removed under acidic conditions with 95% trifluroacetic acid giving methyl-2-*O*-benzoyl-α-D-glucopyranoside **18** in 54% yield.

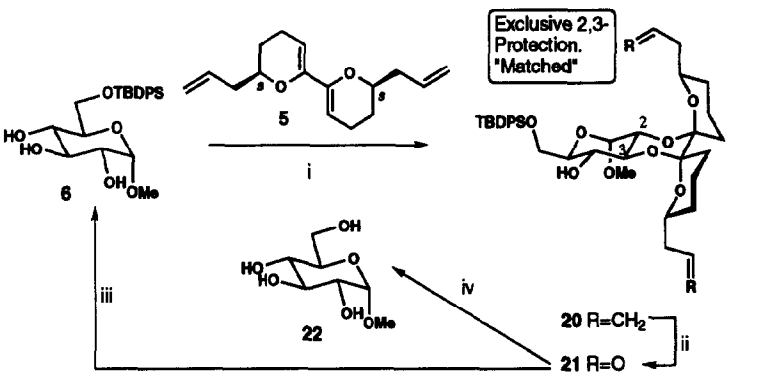
The reaction of enantiopure [2*S*,2'*S*] 2,2'-dimethyl-3,3',4,4'-tetrahydro-6,6'-bi-2*H*-pyran, [2S,2'S] MDHP, **4**[11] with D-glucopyranose substrate **6** under standard conditions gave the 2,3-protected adduct **19**, again as a single diastereoisomer, in 58% yield and as the only spiroketalised product of the reaction (Scheme 6).



Scheme 6

Hopefully it can be appreciated that the enantiopure diene, [2*S*,2'*S*] MDHP **4**, gives exclusive protection at the 2,3-position of the D-glucopyranoside **6** to give only the adduct **19**, in a manner which complements the use of diene [4*S*,4'*S*] MDHP **3**, the latter giving the 3,4-protected dispoke adduct **16** as the major product.

The removal of the dispiroketal moiety thus far has been achieved using either Lewis or protic acid conditions. Another possible route involves preparation of the enantiomerically pure diallyl diene **5** which could be removed using a two step ozonolysis and β-elimination process. The diallyl diene **5** was prepared from 2-allylcyclopentanone,[12] and reacted with D-glucopyranose substrate **6** under refluxing conditions in chloroform with catalytic pyridinium *para*-toluenesulfonate (PPTS). This afforded the dispoke derivative **20** as a single diastereoisomer in 78% yield, where protection of the sugar derivative had taken place exclusively at the 2,3-position (Scheme 7). Removal of the dispiroketal was effected in a two stage procedure involving first the ozonolysis of adduct **20** to the dialdehyde **21** in quantitative yield. Heating **21** in toluene in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) gave methyl 6-*O*-(*tert*-butyldiphenylsilyl)-α-D-glucopyranoside **6** in 56% yield. Alternatively, it was observed that the dialdehyde **21** could also be treated with Schwesinger's base (P_4-*t*-octyl)[13] at 0 °C in tetrahydrofuran (THF) to give methyl-α-D-glucopyranoside (**22**) in 73% yield, resulting from the expected β-elimination and concomitant desilylation.[14]

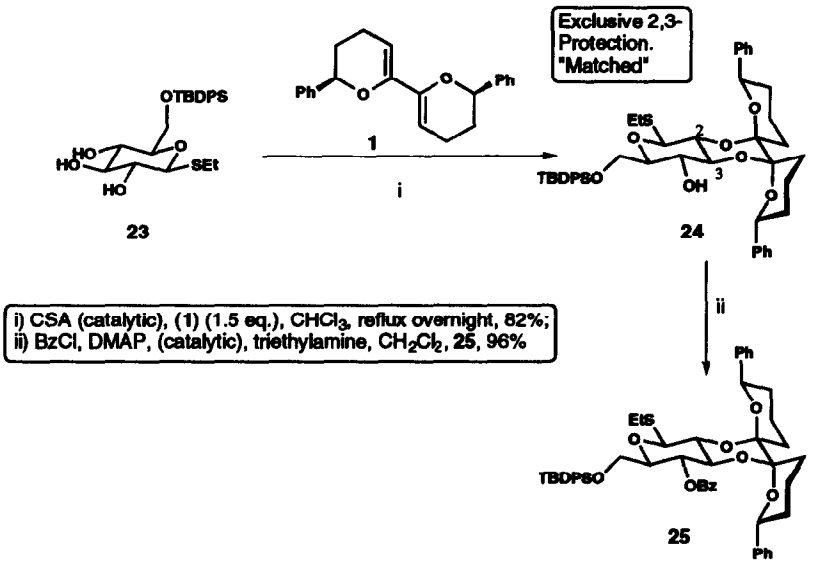


i) PPTS (catalytic), **5** (1.16 eq.), $CHCl_3$, reflux, 2 days, **20**, 78%; ii) O_3, CH_2Cl_2, -78°C then PPh_3 (1.4 eq.), 7 hours, RT, **21**, 100%; iii) DBU (1eq.), $PhCH_3$, 80°C, 21 hours **6**, 56%; iv) P_4-*t*-octyl (1 eq.), 0°C, THF, 2 hours, **22**, 73%

Scheme 7

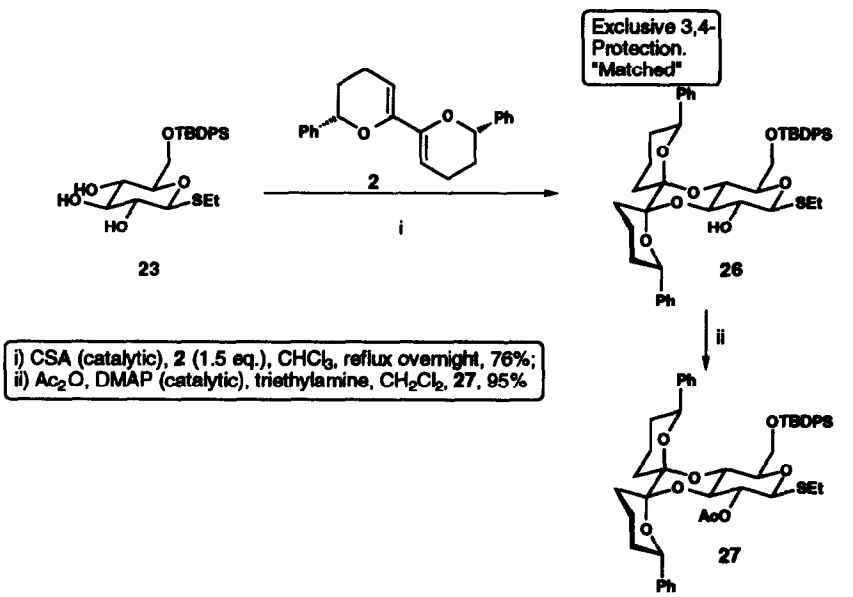
In addition to methyl-α-D-glucopyranosides, a range of β-thioglucopyranosides was also examined for their regioselective protection with enantiomerically pure dienes. The β-thioglucopyranosides represent a more synthetically versatile substrate, allowing the possibility of generating glycosidic linkages with other suitably derivatised substrates.[15]

Hence, reaction of thioethyl 6-*O*-(*tert*-butyldiphenylsilyl)-β-D-glucopyranoside[16] **23** with [2*R*,2'*R*] PDHP **1**, under standard spiroketalisation conditions gave the expected 2,3-dispoke adduct **24** in a good 82% yield (Scheme 8). This product was then further reacted with benzoyl chloride in dichloromethane to give the 4-*O*-benzoyl derivative **25** in 96% yield.



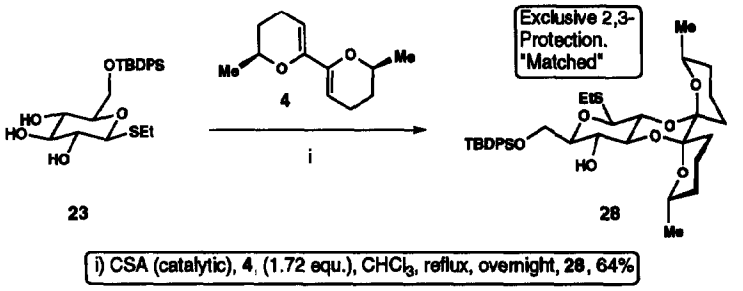
Scheme 8

Regioselective protection at the 3,4- position of the β-thioglucoside **23** was readily achieved by reacting with [2*S*,2'*S*] PDHP, **2** under the standard conditions to give dispoke adduct **26** in 76% yield (Scheme 9). The free hydroxyl at the 2-position could then be protected as its acetate upon reaction with acetic anhydride, giving the dispoke protected derivative **27** in 95% yield.



Scheme 9

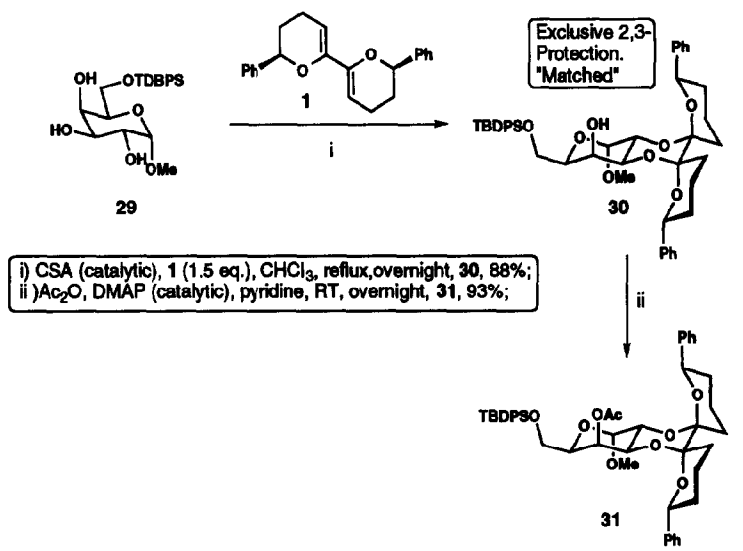
Reaction of the thioethyl 6-*O*-(*tert*-butyldiphenylsilyl)-β-D-glucopyranoside **23** with [2*S*,2'*S*] MDHP **4**, under standard spiroketalisation conditions gave the expected 2,3-dispoke adduct **28** in 64% yield (Scheme 10). The enantiopure diene **4** thus affords the same regioselective protection as [2R,2'R] PDHP **1** but complementary protection to [2*S*,2'*S*] PDHP **2**, where 3,4-protection is the exclusive outcome.



Scheme 10

Regioselective Protection of D-Galactopyranoside Derivatives:

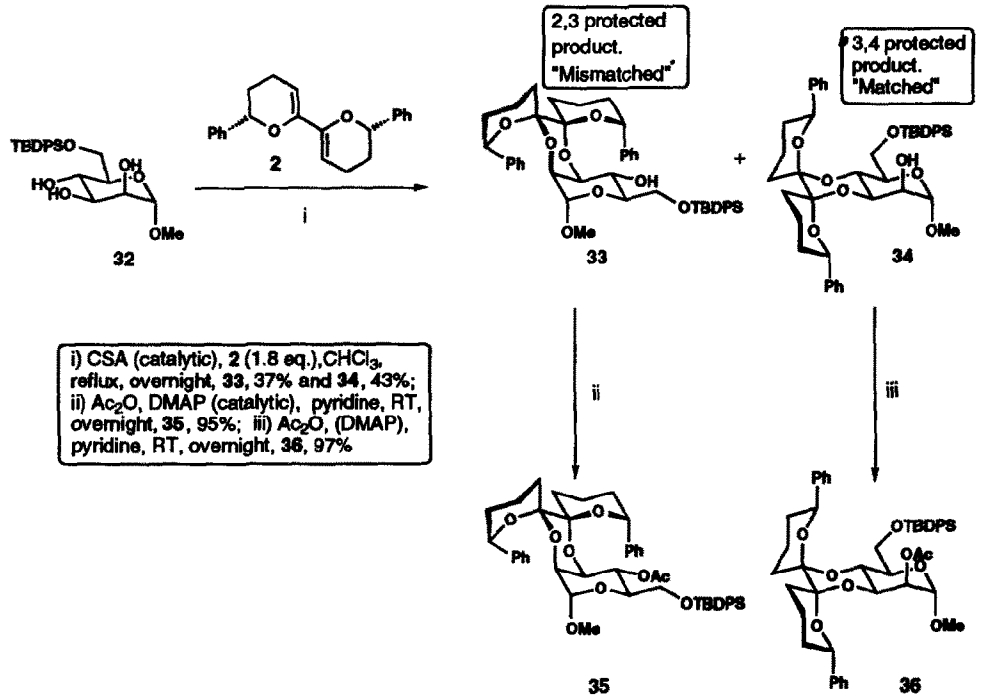
The reaction of enantiomerically pure dienes **1-5** with sugar derivatives is not confined to the use of D-gluco-substrates. The regioselectivity is also observed for galacto- and manno- sugars. Reaction of [2*R*,2'*R*] PDHP **1** with methyl 6-*O*-(*tert*-butyldiphenylsilyl)-α-D-galactopyranoside[17] **29** under standard conditions gave the 2,3-protected galactopyranoside derivative **30** in 88% yield (Scheme 11). This was further protected by reaction with acetic anhydride to give the 4-*O*-acetyl dispoke adduct **31** in 93% yield.



Scheme 11

Regioselective Protection of D-Mannopyranose Derivatives:

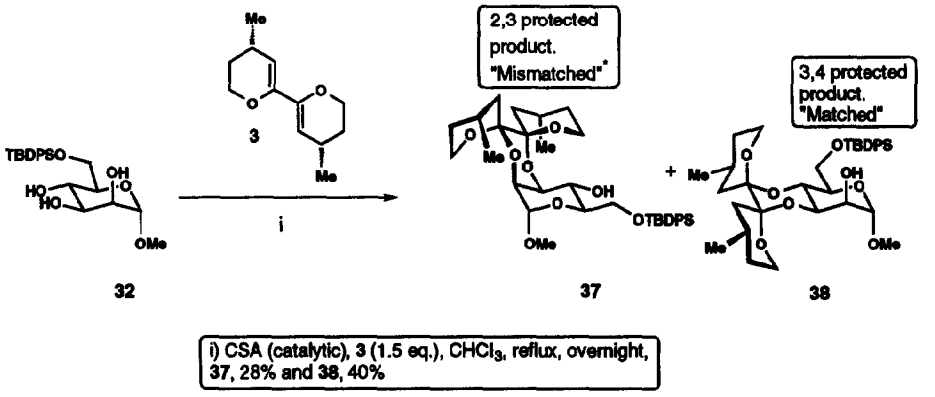
D-Mannopyranoside sugar units represent a third class of compound that may be protected with dispoke. Reaction of the methyl 6-*O*-(*tert*-butyldiphenylsilyl)-α-D-mannopyranoside[18] **32** with enantiomerically pure diene **2** under standard conditions affordes the dispiroketal adducts **33** and **34** as a mixture separable by flash column chromatography (Scheme 12). These adducts arise from protection of both the 2,3- and 3,4-vicinal diol moieties respectively with the chiral diene. The poor regioselectivity is disappointing and can be rationalised by a poor steric differentiation in the transition states leading to the formation of the two adducts **33** and **34**. However, a slight predominance of the expected "matched" 3,4-dispoke adduct is seen. Adduct **33** can then be further protected by reaction with acetic anhydride to give the 4-*O*-acetyl derivative **35** in 95% yield. Adduct **34** can similarly be protected to give the 2-*O*-acetyl derivative **36** in 97% yield by reaction with acetic anhydride.



* The conformation of the pyran rings in the "mismatched" adduct has not been established. There is a possibility that one or both of the rings is in a boat conformation. However there is no direct experimental evidence to support this at the present time.

Scheme 12

Reaction of the enantiomerically pure [4*S*,4'*S*] MDHP **3** with methyl 6-*O*-(*tert*-butyldiphenylsilyl)-α-D-mannopyranose **32** under standard conditions also gave a mixture of 2,3- and 3,4- dispoke protected mannopyranosides **37** and **38** which were again readily separable by flash column chromatography (Scheme 13).



* The conformation of the pyran rings in the "mismatched" adduct has not been established. There is a possibility that one or both of the rings is in a boat conformation. However there is no direct experimental evidence to support this at the present time.

Scheme 13

The mixture of adducts is formed for the same reason, namely a poor steric differentiation in the transition states leading to these adducts **37** and **38**. Again the "matched" 3,4-dispoke **38** is formed as the major product.

SUMMARY AND CONCLUSIONS

In this paper we have demonstrated the use of enantiopure dienes **1-5** in their regioselective protection of a number of D-glucopyranoside, D-galactopyranoside and D-mannopyranoside derivatives. The protection of the sugar unit as a dispiroketal derivative is compatible with a range of protection strategies. This methodology therefore creates new opportunities for the protection of vicinal *trans*-1,2-diol moieties in sugar units, leading to new methods for the construction of oligosaccharides.

EXPERIMENTAL SECTION

Proton and carbon NMR spectra were recorded on Bruker AC200, AC250, WM250, AC400 and DRX500 machines. Chemical shifts are quoted in ppm relative to residual protic solvent ($CHCl_3$, δ_H=7.26) or deuteriochloroform ($CDCl_3$, t, δ_C=77.0). Coupling constants are measured in Hertz. ^{13}C NMR assignments were confirmed by DEPT or APT spectra. Infra-red spectra were recorded on a Perkin-Elmer 983G or 1620 FTIR machine. Mass spectra were recorded on VG-7070B, VG 12-253 or VG ZAB-E instruments at the Department of Chemistry, Imperial College, or at the University of Cambridge Chemistry Department using a Kratos MS890MS spectrometer, or by the SERC mass spectrometry service at Swansea. Microanalyses were performed by the University Chemistry Department microanalytical service, Cambridge. Melting points were determined on a Reichert hot stage apparatus and are uncorrected. Optical rotations were measured with an Optical Activity AA-1000 polarimeter. Flash column chromatography was carried out on Merck Kieselgel 60 (230-400 mesh) and reverse phase chromatography was carried out on Merck Kieselgel 60 (C18) silica. Solvents and reagents were purified by standard procedures where necessary or used as purchased. Analytical

thin layer chromatography was performed using precoated glass-backed plates (Merck Kieselgel 60 F_{254}) and visualised by uv light, or acidic ammonium molybdate. Ozonolyses were run at 140V, O_2=35 l/h.

Methyl 6-*O*-(*tert*-butyldiphenylsilyl)-α-D-glucopyranoside (6)[8]

tert-Butyldiphenylsilylchloride (221 μL, 0.885 mmol) was added to a suspension of methyl α-D-glucopyranoside (150 mg, 0.772 mmol) and imidazole (59 mg, 0.85 mmol) in DMF (5 mL) at 0 °C. The suspension was then stirred at room temperature for 24 hours after which the reaction was diluted with H_2O (10 mL) and extracted with ether (3 x 20 mL). The combined organic extracts were sequentially washed with H_2O (10 mL) and brine (10 mL), dried ($MgSO_4$) and evaporated *in vacuo* to give a colourless gum which was purified by column chromatography on silica gel, eluting with methanol/ether (2:98), to give methyl 6-(*O*-*tert*-butyldiphenylsilyl)-α-D-glucopyranoside **6** as a white solid (307 mg, 0.710 mmol, 92%); m.p. 126-128 °C (lit.[8] 119-121 °C); $[\alpha]_D^{25}$ = + 57.3 (c = 1.00, $CHCl_3$) (lit.[8] $[\alpha]_D^{21}$ = + 61.6 (c = 1.15, $CHCl_3$)); δ_H (200 MHz , $CDCl_3$) 7.65 (4H, m, 4x *o*-TBD*PS*), 7.40 (6H, m, 4x *m*- and 2x *p*- TBD*PS*), 4.74 (1H, d, *J* 3.8, *H*-1), 3.90 (2H, m, 2x *H*-6), 3.80-3.45 (4H, m, *H*-2, *H*-3, *H*-4, *H*-5), 3.38 (3H, s, OCH_3), 1.06 (9H, s, $C(CH_3)_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3287, 3154, 2950, 1472, 1428, 1383, 1362, 1264, 1151, 1112, 1056, 1012, 900, 825, 739, 703; *m/z* (EI) 375 $(M\text{-}C(CH_3)_3)^+$, 357, 343 $(M\text{-}C(CH_3)_3\text{-}CH_3OH)^+$, 241, 199 and 57 $(C(CH_3)_3)^+$; Found $(M\text{-}C(CH_3)_3)^+$ 375.1262. $C_{19}H_{23}O_6Si$ requires 375.1264.

[2'*R*,2''*R*,6'*R*,6''*R*] Methyl 6-*O*-(*tert*-butyldiphenylsilyl)-2-*O*,3-*O*-(6',6''-diphenyloctahydro-2',2''-bipyran-2',2''-diyl)-α-D-glucopyranoside (7)

A solution of methyl 6-*O*-(*tert*-butyldiphenylsilyl)-α-D-glucopyranoside **6** (98 mg, 0.224 mmol), [2*R*,2'*R*] 2,2'-diphenyl-3,3',4,4'-tetrahydro-6,6'-bi-2*H*-pyran (**1**) (107 mg, 0.336 mmol) and camphorsulfonic acid (30 mg, catalytic) in $CHCl_3$ (4 mL) was heated at 70 °C for 18 hours. The orange solution was cooled to room temperature, evaporated *in vacuo* and purified by column chromatography on silica gel, eluting with ether/petrol (2:8), to give *dispoke derivative* **7** as a white foam (147 mg, 0.197 mmol, 88%); $[\alpha]_D^{26}$ = + 36.2 (c = 1.00, $CHCl_3$); δ_H (200 MHz , $CDCl_3$) 7.65 (4H, m, 4x *o*-OTBD*PS*), 7.37 (16H, m, 10x Ph-*H*, 4x *m*- and 2x *p*- OTBD*PS*), 4.85 (1H, dd, *J* 11.6, 2.2, *H*-6'(or *H*-6")), 4.72 (1H, d, *J* 3.5, *H*-1), 4.68 (1H, dd, *J* 11.5, 2.3, *H*-6"(or *H*-6')), 4.12 (1H, d, *J* 9.8, *H*-3), 3.80 (3H, m, *H*-2, $H\text{-}6_A$, $H\text{-}6_B$), 3.67 (2H, m, *H*-4, *H*-5), 3.42 (3H, s, OCH_3), 2.60 (1H, br.s, O*H*), 2.30-1.50 (12H, m, 2x *H*-3', 2x *H*-3", 2x *H*-4', 2x *H*-4", 2x *H*-5', 2x *H*-5"), 1.05 (9H, s, $C(CH_3)_3$); ν_{max} (film)/cm^{-1} 3451, 2930, 2856, 1453, 1428, 1362, 1202, 1168, 1113, 1047, 982, 873, 823, 741, 699; *m/z* (FAB) 773 $(MNa)^+$, 751 $(MH)^+$, 719 $(M\text{-}OCH_3)^+$, 694 $(MH\text{-}C(CH_3)_3)^+$, 661 $(M\text{-}CH_3OH\text{-}C(CH_3)_3)^+$, 319, 135; Found (MH^+) 751.3663. $C_{45}H_{55}O_8Si$ requires 751.3666.

[2'*R*,2''*R*,6'*R*,6''*R*] Methyl 4-*O*-acetyl-6-*O*-(*tert*-butyldiphenylsilyl)-2-*O*,3-*O*-(6',6''-diphenyloctahydro-2',2''-bipyran-2',2''-diyl)-α-D-glucopyranoside (8)

Dispoke derivative **7** (85 mg, 0.113 mmol) and DMAP (1 crystal, catalytic) were dissolved in pyridine (500 μL); acetic anhydride (37 μL, 0.50 mmol) was added under argon at room temperature and the

yellow solution was stirred for 16 hours. The reaction mixture was poured into $NaHCO_3$ (aqueous, saturated, 10 mL) and extracted with ether (3 x 10 mL). The combined organic extracts were sequentially washed with H_2O (5 mL) and HCl (1 M, 10 mL), dried ($MgSO_4$) and evaporated *in vacuo* to give a yellow foam. Purification by column chromatography on silica gel, eluting with ether/petrol (3:7), gave *acetate* **8** as a white solid (82 mg, 0.103 mmol, 92%); m.p. 86-89 °C; $[\alpha]_D^{25}$ = + 66.2 (c = 1.00 in $CHCl_3$); δ_H (200 MHz, $CDCl_3$) 7.65 (4H, m, 4x *o*-TBD*PS*), 7.45 (16H, m, 10x Ph-*H*, 4x *m*- and 2x *p*- TBD*PS*), 4.89 (1H, t, *J* 9.6, *H*-4), 4.80 (1H, d, *J* 3.6, *H*-1), 4.70 (2H, m, *H*-6', *H*-6"), 4.20 (1H, t, *J* 9.6, *H*-3), 3.90 (1H, dd, *J* 10.0, 3.6, *H*-2), 3.80 (1H, m, *H*-5), 3.65 (2H, m, $H\text{-}6_A$, $H\text{-}6_B$), 3.42 (3H, s, OCH_3), 2.13 (3H, s, CH_3CO), 2.10-1.40 (12H, m, 2x *H*-3', 2x *H*-3", 2x *H*-4', 2x *H*-4", 2x *H*-5', 2x *H*-5"), 1.02 (9H, s, $C(CH_3)_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2932, 1746, 1472, 1453, 1428, 1366, 1234, 1217, 1168, 1113, 1046, 982; *m/z* (FAB) 815 $(MNa)^+$, 793 $(MH)^+$, 792 $(M)^+$ 761 $(M\text{-}CH_3O)^+$, 319; Found $(MH)^+$ 793.3730. $C_{47}H_{57}O_9Si$ requires 793.3772; Found: C, 70.94; H, 7.53. $C_{47}H_{56}O_9Si$ requires C, 71.18; H, 7.22%.

[2'*R*,2''*R*,6'*R*,6''*R*] Methyl 4-*O*-acetyl-2-*O*,3-*O*-(6',6''-diphenyloctahydro-2',2''-bipyran-2',2''-diyl)-α-D-glucopyranoside (10)

Ferric chloride (11 mg, 0.067 mmol) was added in one portion to a solution of acetate **8** (14.7 mg, 0.017 mmol) in DCM (1 mL) and the solution was stirred under argon for 16 hours. Water (200 μL) was added and the reaction was stirred for a further 30 minutes, after which the solvents were removed by evaporation *in vacuo* to give a brown oily solid. The product was purified by column chromatography on silica gel eluting, with methanol/ethyl acetate (1:9), to give *dispoke derivative* **10** as a colourless oil (8 mg, 0.16 mmol, 84%); δ_H (200 MHz , $CDCl_3$) 7.35 (10H, m, 2x Ph-*H*), 4.93 (1H, t, *J* 9.7, *H*-4), 4.81 (1H, d, *J* 3.6, *H*-1), 4.72 (2H, m, *H*-6,' *H*-6"), 4.28 (1H, t, *J* 9.7, *H*-3), 3.92 (1H, dd, *J* 10.0, 3.6, *H*-2), 3.60 (3H, m, *H*-5, 2x *H*-6), 3.37 (3H, s, OCH_3), 2.50 (1H, br.t, *J* 3.7, O*H*), 2.14 (3H, s, CH_3CO), 2.20-1.41 (12H, m, 2x *H*-3', 2x *H*-3", 2x *H*-4', 2x *H*-4", 2x *H*-5', 2x *H*-5"); ν_{max} (film)/cm^{-1} 3506, 2935, 1745, 1495, 1453, 1368, 1235, 1168, 1044, 982, 966, 754, 734, 698.

Methyl 4-*O*-acetyl-α-D-glucopyranoside (11a) and Methyl 6-*O*-acetyl-α-D-glucopyranoside (11b)

Ferric chloride (9 mg, 0.053 mmol) was added in one portion to a solution of acetate **8** (14.7 mg, 0.017 mmol) in DCM (1 mL) and the solution was stirred under argon for 16 hours. Water (200 μL) was added and the reaction was stirred for a further 30 minutes, after which the solvents were removed by evaporation *in vacuo* to give a brown oily solid. The product was purified by column chromatography on silica gel, eluting with methanol/ethyl acetate (1:9), to give a 1.8:1 mixture of acetates **11a:11b** as a pale yellow glass (4.0 mg, 0.017mmol, 63%), inseparable by flash column chromatography; δ_H (200 MHz , CD_3OD) 4.73 (0.64H, dd, *J* 10.1, 9.2, $H\text{-}4_{major}$), 4.70 (0.64H, d, *J* 3.7, $H\text{-}1_{major}$), 4.64 (0.36H, d, *J* 3.7, $H\text{-}1_{minor}$), 4.35 (0.36H, dd, *J* 11.8, 2.2, $H\text{-}6_{minor}$), 4.18 (0.36H, dd, *J* 11.8, 5.8, $H\text{-}6_{minor}$), 3.70-3.45 (4.64H, m, $H\text{-}2_{major}$, $H\text{-}2_{minor}$, $H\text{-}3_{major}$, $H\text{-}3_{minor}$, $H\text{-}4_{minor}$, $H\text{-}5_{major}$, $H\text{-}5_{minor}$, $H\text{-}6_{major}$, $H\text{-}6_{major}$), 3.41 (1.93H, s, OCH_{3major}), 3.39 (1.07H, s, OCH_{3minor}), 2.08 (1.93H, s, CH_3CO_{major}), 2.05 (1.07H, s,

CH_3CO_{minor}); ν_{max} ($CHCl_3$)/cm^{-1} 3386, 2924, 1737, 1461, 1376, 1237, 1190, 1154, 1030, 922, 754; *m/z* (EI) 237 (MH^+), 205 (M-OCH_3), 145 (M-OCH_3-CH_3COOH), 116, 74, 60; Found (MH^+) 237.0993. $C_9H_{17}O_7$ requires 237.0974.

[2'*R*,2''*R*,6'*R*,6''*R*] Methyl 4-*O*-benzoyl-6-*O*-(*tert*-butyldiphenylsilyl)-2-*O*,3-*O*-(6',6''-diphenyloctahydro-2',2''-bipyran-2',2''-diyl)-α-D-glucopyranoside (9)

Dispoke derivative **7** (52 mg, 0.069 mmol) and DMAP (1 crystal , catalytic) were dissolved in triethylamine (48 μL, 0.346 mmol) and DCM (1 mL). Benzoyl chloride (16 μL, 0.138 mmol) was added under argon at room temperature and the yellow solution was stirred for 16 hours. The reaction mixture was poured into $NaHCO_3$ (aqueous, saturated, 10 mL) and extracted with ether (3 x 10 mL). The combined organic extracts were sequentially washed with H_2O (5 mL) and HCl (1 M, 10 mL), dried ($MgSO_4$) and evaporated *in vacuo* to give a yellow foam. Purification by column chromatography on silica gel, eluting with ether/petrol (3:7), gave *benzoate* **9** as a white solid (57 mg, 0.066 mmol, 96%); m.p. 215-217 °C; $[\alpha]_D^{25}$ = + 54.8 (c = 1.00 in $CHCl_3$); δ_H (200 MHz, $CDCl_3$) 8.17 (2H, m, 2x *o*- OCOPh-*H*) 7.70-7.20 (23H, m, 10x Ph-*H*, 10x OTBD*PS*, 2x *m*- and *p*- OCOPh-*H*), 5.25 (1H, t, *J* 9.7, *H*-4), 4.90 (1H, d, *J* 3.6, *H*-1), 4.80 (1H, dd, *J* 11.5, 2.2, *H*-6' (or *H*-6'')), 4.62 (1H, br.d, *J* 9.7, *H*-6'' (or *H*-6')), 4.38 (1H, t, *J* 9.7, *H*-3), 4.07 (1H, dd, *J* 10.0, 3.7, *H*-2), 4.07 (1H, overlapped m, *H*-5), 3.81 (2H, m, H-6_A, H-6_B), 3.49 (3H, s, OCH_3), 2.20-1.50 (12H, m, 2x *H*-3', 2x *H*-3'', 2x *H*-4', 2x *H*-4'', 2x *H*-5', 2x *H*-5''), 1.05 (9H, s, C(CH_3)$_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2932, 1787, 1424, 1647, 1601, 1557, 1450, 1387, 1315, 1272, 1213, 1047, 907, 726; *m/z* (FAB) 988 (MCs)$^+$, 855 (MH)$^+$, 824 (MH-OCH_3)$^+$, 319; Found (MH)$^+$ 855.3878. $C_{52}H_{59}O_9Si$ requires 855.3928.

Methyl 4-*O*-benzoyl-α-D-glucopyranoside (12)

Ferric chloride (39 mg, 0.243 mmol) was added in one portion to a solution of benzoate **9** (63 mg, 0.074 mmol) in DCM (5 mL) and the solution was stirred under argon for 4 hours. Water (300 μL) was added and the reaction was stirred for a further 30 minutes after which the solvents were removed by evaporation *in vacuo* to give a brown oily solid. The product was purified by column chromatography on silica gel, eluting with methanol/ethylacetate (1:9), to give methyl 4-*O*-benzoyl-α-D-glucopyranoside **12** as a colourless oil (9 mg, 0.030 mmol, 41%), $[\alpha]_D^{26}$ = + 79.3 (c = 1.00 in $CHCl_3$); δ_H (200 MHz, CD_3OD) 8.05 (2H, m, 2x *o*-OCOPh-*H*), 7.50 (3H, m, 2x *m*- and *p*- OCOPh-*H*), 5.02 (1H, dd, *J* 10.2, 9.3, *H*-4), 4.76 (1H, d, *J* 3.7, *H*-1), 3.89 (1H, t, *J* 9.4, *H*-3), 3.82 (1H, m, *H*-5), 3.55 (3H, m, *H*-2, *H*-6, *H*6'), 3.46 (3H, s, OCH_3); ν_{max} ($CHCl_3$)/cm^{-1} 3415, 2924, 2852, 1723, 1602, 1452, 1273, 1026, 901, 755, 712; *m/z* (EI) 299 (MH^+), 267 (M-OCH_3)$^+$, 178 (MH-OCOPh)$^+$, 177 (M-OCOPh)$^+$, 123 ($PhCOOH_2$)$^+$, 105 (PhCO)$^+$, 77 (Ph); Found (MH)$^+$ 299.1121. $C_{14}H_{18}O_7$ requires 299.1131.

[2'*S*,2''*S*,6'*S*,6''*S*] Methyl 6-*O*-(*tert*-butyldiphenylsilyl)-3-*O*,4-*O*-(6',6''-diphenyloctahydro-2',2''-bipyran-2',2''-diyl)-α-D-glucopyranoside (13)

A solution of methyl 6-*O*-(*tert*-butyldiphenylsilyl)-α-D-glucopyranoside (**6**) (50 mg, 0.116mmol), [2*S*,2'*S*] 2,2'-diphenyl-3,3',4,4'-tetrahydro-6,6'-bi-2*H*-pyran (**2**) (55 mg, 0.173 mmol) and camphorsulfonic acid (20 mg, catalytic) in $CHCl_3$ (2 mL) was heated at 70 °C for 22 hours. The orange solution was cooled to room temperature, evaporated *in vacuo* and the residue was purified by column chromatography on silica gel, eluting with ether/petrol (45:55), to give *dispoke derivative* **13** as a colourless viscous oil (36.7 mg, 0. 088 mmol, 76%); $[\alpha]_D^{25}$ = + 63.0 (c = 1.00, $CHCl_3$); δ_H (200 MHz, $CDCl_3$) 7.72 (4H, m, 4x *o*-OTBD*PS*), 7.40 (16H, m, 10x Ph-*H*, 4x *m*- and 2x *p*- OTBD*PS*), 4.82 (1H, dd, *J* 11.5, 2.1, *H*-6' (or *H*-6")), 4.76 (1H, d, *J* 4.0, *H*-1), 4.45 (1H, br.d, *J* 9.8, *H*-6" (or *H*-6')), 3.06 (2H, t, *J* 9.9, *H*-3, *H*-4), 3.80 (2H, m, *H*-6_A, *H*-6_B), 3.69 (1H, dd, *J* 9.2, 4.0, *H*-2), 3.57 (1H, m, *H*-5), 3.40 (3H, s, O*CH*$_3$), 2.10-1.30 (12H, m, 2x *H*-3', 2x *H*-3", 2x *H*-4', 2x *H*-4", 2x *H*-5', 2x *H*-5"), 1.01 (9H, s, C(*CH*$_3$)$_3$); ν_{max} (film)/cm^{-1} 3474, 2931, 1157, 1112, 1046, 966, 740, 699; *m/z* (FAB) 773 (MNa)$^+$, 751 (MH)$^+$, 694 (MH-C(CH$_3$)$_3$)$^+$, 319, 241, 197; Found (MH)$^+$ 751.3680. $C_{45}H_{55}O_8Si$ requires 751.3666.

[2'*S*,2''*S*,6'*S*,6''*S*] Methyl 2-*O*-acetyl-6-*O*-(*tert*-butyldiphenylsilyl)-3-*O*,4-*O*-(6',6''-diphenyloctahydro-2',2''-bipyran-2',2''-diyl)-α-D-glucopyranoside (14)

Dispoke derivative **13** (25 mg, 0.034 mmol) and DMAP (1 crystal, catalytic) were dissolved in pyridine (500 μL). Acetic anhydride (25 μL, 0.34 mmol) was added at room temperature and the yellow solution was stirred for 16 hours. The reaction mixture was poured into $NaHCO_3$ (aqueous, saturated, 10 mL) and extracted with ether (3 x 10 mL). The combined organic extracts were sequentially washed with H_2O (5 mL) and HCl (1 M, 10 mL), dried ($MgSO_4$) and evaporated *in vacuo* to give a yellow foam. Purification by column chromatography on silica gel, eluting with ether/petrol (4:6), gave *acetate* **14** as a glass (25.5 mg, 0.032 mmol, 94%); $[\alpha]_D^{25}$ = + 40.4 (c = 0.50 in $CHCl_3$); δ_H (200 MHz, $CDCl_3$) 7.65 (4H, m, 4x *o*-TBD*PS*), 7.40 (16H, m, 10x Ph-*H* , 4x *m*- and 2x *p*- TBD*PS*), 4.94 (1H, d, *J* 3.7, *H*-1), 4.80 (2H, m, *H*-2, *H*-6' (or *H*-6")), 4.45 (1H, br.d, *J* 10.7, *H*-6"(or *H*-6')), 4.24 (1H, br.t, *J* 10.4, *H*-3), 4.00-3.40 (4H, m, *H*-4, *H*-5, *H*-6_A, *H*-6_B), 3.35 (3H, s, O*CH*$_3$), 2.17 (3H, s, *CH*$_3$CO), 2.10-1.30 (12H, m, 2x *H*-3', 2x *H*-3", 2x *H*-4', 2x *H*-4", 2x *H*-5', 2x *H*-5"), 1.02 (9H, s, C(*CH*$_3$)$_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2930, 1745, 1453, 1428, 1367, 1238, 1161, 1113, 1044, 981, 965, 742, 699; *m/z* (FAB) 815 (MNa)$^+$, 793 (MH)$^+$, 792 (M)$^+$ 761 (M-CH$_3$O)$^+$, 319; Found (MH)$^+$ 793.3732. $C_{47}H_{57}O_9Si$ requires 793.3772.

[2'*S*,2''*S*,4'*S*,4''*S*] Methyl 6-*O*-(*tert*-butyldiphenylsilyl)-2-*O*-3-*O*-(4',4''-dimethyloctahydro-2',2''-bipyran-2',2''-diyl)-α-D-glucopyranoside (15) and [2'*S*,2''*S*,4'*S*,4''*S*] Methyl 6-*O*-(*tert*-butyldiphenylsilyl)-3-*O*-4-*O*-(4',4''-dimethyloctahydro-2',2''-bipyran-2',2''-diyl)-α-D-glucopyranoside (16)

A solution of methyl 6-*O*-(*tert*-butyldiphenylsilyl)-α-D-glucopyranose (**6**) (100 mg, 0.231 mmol), [4*S*,4'*S*] 4,4'-dimethyl-3,3'-dihydro-6,6'-bi-2*H*-pyran (**3**) (90 mg, 0.346 mmol) and camphorsulfonic acid (5.4 mg, 0.023 mmol, catalytic) in $CHCl_3$ (5 mL) was heated at 70 °C for 15 hours. The solution was cooled

to room temperature, evaporated *in vacuo* and the residue purified by column chromatography on silica gel, eluting with hexane/ethyl acetate (8/2), to give, in order of elution:
dispoke derivative **15** as a colourless glass (R_f 0.44, 16 mg, 0.026 mmol, 11%); $[\alpha]_D^{25}$ = + 60.5 (c = 0.55 in $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 7.71 (4H, m, 4x *o*-Ph-*H*), 7.40 (6H, 4x *m*- and 2x *p*-Ph-*H*), 4.74 (1H, d, *J* 3.3, *H*-1), 4.42 (1H, m, *H*-3), 4.19 (1H, m, *H*-6'), 4.01 (2H, m, *H*-6, *H*-6"), 3.91 (2H, ABX, *H*-6), 3.73 (1H, m, *H*-6'), 3.66 (1H, m, *H*-6"), 3.63 (2H, m, *H*-4, *H*-5), 3.47 (3H, s, OCH_3), 2.02 (2H, m, *H*-4', *H*-4"), 1.89 (1H, m, H-5'$_{eq}$), 1.81 (1H, m, H-5"$_{eq}$), 1.53 (2H, m, H-3'$_{eq}$, H-3"$_{eq}$), 1.21 (4H, m, H-3'$_{ax}$, H-3"$_{ax}$, H-5'$_{ax}$, H-5"$_{ax}$), 1.06 (9H, s, $C(CH_3)_3$), 0.91 (6H, m, 2x CH_3); δ_C(100 MHz, $CDCl_3$): 135.69, 134.81, 133.36, 133.27, 129.73, 127.66, 127.68 (Aromatic *C*), 99.2, 99.08 (*C*-2', *C*-2"), 98.49 (*C*-1) 71.73, 71.59, 71.36, 70.85 (*C*-2, *C*-3, *C*-4, *C*-5), 64.32 (*C*-6), 61.01, 60.78 (*C*-6', *C*-6"), 55.15 (OCH_3), 37.81, 37.71 (*C*-5', *C*-5"), 33.87 (*C*-3', *C*-3"), 26.83 ($C(CH_3)_3$), 24.41 (*C*-4', *C*-4"), 22.33, 22.29 (2x CH_3), 19.28 ($C(CH_3)_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3582, 2932, 1589, 1455, 1428, 1380, 1266, 1112, 1071, 1050, 995, 915, 783, 613; *m/z* (EI) 626 $(M)^+$, 595, 569, 551, 537, 519, 355, 340, 325, 309, 297, 253, 241, 223, 214, 195, 179, 135, 115, 100, 78, 69, 55. Found $(M)^+$ 626.3273. $C_{35}H_{50}O_8Si$ requires 626.3274.
and *dispoke derivative* **16** as a colourless glass (R_f 0.14, 80 mg, 0.128 mmol 58%); $[\alpha]_D^{25}$ = + 110.7 (c = 3.5 in $CHCl_3$) δ_H (500 MHz, $CDCl_3$) 7.71 (4H, m, 4x *o*-Ph-*H*), 7.40 (6H, m, 4x *m*- and 2x *p*-Ph-*H*), 4.83 (1H, d, *J* 3.8, *H*-1,), 3.96 (1H, t, *J* 10.1, *H*-3), 3.87 (2H, m, 2x *H*-6), 3.75 (5H, m, *H*-2, *H*-4, *H*-5, *H*-6', *H*-6"), 3.62 (2H, m, *H*-6', *H*-6"), 3.41 (3H, s, OCH_3), 2.23 (2H, m, *H*-4', *H*-4"), 1.82 (1H, m, H-5'$_{eq}$), 1.74 (2H, m, O*H*, H-3'$_{eq}$), 1.53 (1H, m, H-5"$_{eq}$), 1.38 (1H, m, H-3"$_{eq}$), 1.18 (4H, m, H-3'$_{ax}$, H-3"$_{ax}$, H-5'$_{ax}$, H-5"$_{ax}$), 1.03 (9H, s, $C(CH_3)_3$), 0.89-0.88 (6H, m, 2x CH_3); δ_C (100MHz, $CDCl_3$): 135.89, 135.35, 133.89, 133.17, 129.55, 127.60, 127.51 (Aromatic *C*), 99.41 (*C*-1), 97.37, 97.22 (*C*-2', *C*-2"), 70.81, 70.01, 69.95 (*C*-2, *C*-3, *C*-4), 64.84 (*C*-5), 62.17 (*C*-6), 60.69, 60.77 (*C*-6', *C*-6"), 54.89 (OCH_3), 37.13, 37.03 (*C*-5', *C*-5"), 33.49, 33.39 (*C*-3', *C*-3"), 26.74 ($C(CH_3)_3$), 24.52, 24.48 (*C*-4', *C*-4"), 22.29, 22.19 (2x CH_3), 19.31 ($C(CH_3)_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3418, 3009, 2932, 1456, 1428, 1380, 1264, 1194, 1144, 1112, 1070, 1053, 1018, 984, 916, 867, 824, 704, 615; *m/z* (EI) 626 $(M)^+$, 569, 551, 537, 452, 402, 395, 383, 353. Found $(M)^+$ 626.3256. $C_{35}H_{50}O_8Si$ requires 626.3274.

[2'*S*,2"*S*,4'*S*,4*S*"] Methyl 2-*O*-benzoyl-6-*O*-(*tert*-butyldiphenylsilyl)-3-*O*-4-*O*-(4',4"-dimethyl-2',2"-bipyran-2',2"-diyl)-α-D-glucopyranoside (17)

Dispoke derivative **16** (50 mg, 0.098 mmol) and DMAP (1 crystal, catalytic) were dissolved in $CHCl_3$ (5 mL). Pyridine (7.09 μL, 0.088 mmol) and benzoyl chloride (9.73 μL, 0.084 mmol) were added successively and the solution was stirred at room temperature for 2 days. Although TLC showed some starting material **16** remained, the reaction was quenched with HCl (1M, 10 mL) and the aqueous layer was extracted with DCM (2x 5 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated *in vacuo*. Purification of the residue by column chromatography on silica, gel eluting with hexane/ethyl acetate (95:5), gave *benzoate* **17** (33 mg, 0.046 mmol, 57%) as a colourless glass; $[\alpha]_D^{25}$ = + 132.6 (c=0.85 in $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 7.91 (2H, m, 2x Ph-*H*), 7.72 (4H, m, 4x Ph-*H*), 7.39 (9H, m, 9x Ph-*H*), 5.18 (1H, d, *J* 3.8, *H*-1), 5.06 (1H, dd, *J* 10.5, 3.8, *H*-2), 4.41 (1H, dd, *J* 10.52, 8.47, *H*-3), 3.93-3.81 (6H, m, *H*-4, *H*-5, 2x *H*-6', 2x *H*-6"), 3.66 (2H, m, 2x *H*-6), 3.34 (3H, s, OCH_3), 1.81-1.75 (4H, m, *H*-4', *H*-4", H-5'$_{eq}$.

H-5"eq), 1.51-1.42 (6H, m, *H*-3'ax, *H*-3"ax, *H*-5'ax, *H*-5"ax, *H*-3'eq, *H*-3"eq), 1.09 (9H, s, C(C*H*$_3$)$_3$), 0.91-0.83 (6H, m, 2x C*H*$_3$); δ_C
(100 MHz, $CDCl_3$): 165.97 (*C*OOPh), 135.87, 135.49, 134.50, 133.88, 133.01, 130.54, 129.73, 129.53, 128.85, 128.58, 127.49 (Aromatic *C*), 97.39 (*C*-1), 97.26, 97.14 (*C*-2', *C*-2"), 71.78, 70.35, 66.57, 65,21 (*C*-2, *C*-3, *C*-4, *C*-5), 62.04 (*C*-6), 60.94, 60.82 (*C*-6', *C*-6"), 54.80 (O*C*H$_3$), 37.01, 36.94, 33.53, 33.33 (*C*-3', *C*-3", *C*-5', *C*-5"), 26.69 (C(*C*H$_3$)$_3$), 24.48, 24.40, 22.26. 22.15 (*C*-4', *C*-4", 2x *C*H$_3$), 19.27 (C(CH$_3$)$_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2930, 1742, 1548, 1345, 1285, 1212, 1170, 1112, 1070, 997; *m/z* (EI) 731 $(MH)^+$, 730 $(M)^+$, 705, 641, 589, 551, 533, 503, 393, 353, 333, 323, 287, 269, 253, 195, 163, 135. Also isolated was starting **16** (10 mg, 0.016 mmol, 20 %)

Methyl-2-*O*-benzoyl-α-D-glucopyranoside (18)

Dispoke derivative **17** (70 mg, 0.096 mmol) was dissolved in a solution of trifluoroacetic acid and water (95/5, 3 mL) and the reaction mixture was stirred at room temperature for 4 hours (with monitoring by TLC for the disappearance of starting material). The crude material was purified by flash chromatography on silica gel eluting with ethyl acetate/methanol (95:5) to give pyranoside **18** as a colourless oil (14 mg, 0.047 mmol, 54%). δ_H (400 MHz, $CDCl_3$) 8.06 (2H, d, 2x *o*-Ph-*H*), 7.48 (3H, m, 2x *m*- and *p*-Ph-*H*), 4.97 (1H, d, *J* 3.6, *H*-1), 4.83 (3H, br.s, O*H*), 4.81 (1H, dd, J 10.0, 3.6, *H*-2), 3.99 (1H, dd, *J* 9.2, *H*-3), 3.79 (2H, 2x dd, *J* 11.9, 5.6, 2.1, *H*-6), 3.61 (1H, m, *H*-5), 3.44 (1H, t, *J* 9.3, *H*-4); δ_C (100 MHz, $CDCl_3$): 167.78 (*C*OOPh), 134.44, 131.18, 130.82, 129.54 (Aromatic *C*), 98.51 (*C*-1), 75.56, 73.56, 72.53, 71.91 (*C*-2, *C*-3, *C*-4, *C*-5), 62.57 (*C*-6), 55.58 (O*C*H$_3$).

[2'*S*, 2"*S*, 6'*S*, 6"*S*] Methyl 6-*O*-(*tert*-butyldiphenylsilyl)-2-*O*,3-*O*-(6'6"-dimethyloctahydro-2,2'-bipyran-2',2"-diyl)-α-D-glucopyranoside (19)

A solution of methyl 6-*O*-(tert-butyldiphenylsilyl)-α-D-glucopyranose (**6**) (160 mg, 0.37 mmol), [2*S*,2'*S*] 2,2'-dimethyl-3,3',4,4'-tetrahydro-6,6'-bi-2*H* pyran (**4**) (114 mg, 0.59 mmol) and camphorsulfonic acid (50 mg) in $CHCl_3$ (5mL) was heated at 70 °C for 20 hours. The orange solution was cooled to room temperature, evaporated *in vacuo* and purification of the residue by column chromatography on silica gel, eluting with ether/petrol (2:8), to give *dispoke derivative* **19** as a colourless oil (213 mg, 0.341 mmol, 58%); $[\alpha]_D^{24}$ = -4.6 (c = 1.5 in $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.71 (4H, m, 2x *o*-Ph-*H*), 7.40 (6H, m, 2x *m*- and *p*-Ph-*H*), 7.72 (1H, d, *J* 3.5, *H*-1), 4.10-4.03 (1H, m, *H*-5), 3.94-3.71 (7H, m, *H*-2, *H*-3, *H*-4, 2x *H*-6, *H*-6', *H*-6"), 3.39, (3H, s, O*C*H$_3$), 2.58 (1H, br. s, O*H*), 1.95-1.20 (12H, m, 2x *H*-3', 2x *H*-3", 2x *H*-4', 2x *H*-4", 2x *H*-5', 2x *H*-5"), 1.15-1.06 (6H, m, 2x C*H*$_3$), 1.04 (9H, s, C(C*H*$_3$)$_3$); δ_C (100 MHz, $CDCl_3$): 135.70 (Aromatic *C*-H), 134.82 (Aromatic *C*), 133.30 (Aromatic *C*-H), 133.23 (Aromatic *C*-H), 129.73 (Aromatic *C*-H), 127.70 (Aromatic *C*-H), 98.12 (*C*-1), 97.80 (*C*-6'), 97.38 (*C*-6"), 71.67, 69.74, 68.60, 67.52, 66.04, 66.00, (*C*-2, *C*-3, *C*-4, *C*-5, *C*-2', *C*-2"), 64.46 (*C*-6), 54.85 (O*C*H$_3$) 32.52, 28.05, 27.72 (3x *C*H$_2$), 26.87 (C(*C*H$_3$)$_3$), 21.92, 21.85, (2x *C*H$_3$), 19.29, 18.54, 18.35 (3x *C*H$_2$), 15.28 (*C*(CH$_3$)$_3$); ν($CHCl_3$)/cm^{-1} 3496, 3008, 2953, 2932, 1456, 1428, 1366, 1184, 1113, 1073, 1050, 980, 916, 864, 823, 703, 614; *m/z* (FAB) 649 $(M+Na)^+$, 626 $(M)^+$, 625 $(M-H)^+$, 595, 537, 481, 365, 339, 309, 241, 211, 195, 163. Found $(M-OCH_3)^+$ 595.3121. $C_{34}H_{47}O_7Si$ requires 595.3091.

[2'*R*,2''*R*,6'*R*,6''*R*] Methyl 6-*O*-(*tert*-butyldiphenylsilyl)-2-*O*,3-*O*-(6',6''-diallyl-octahydro-2',2''-bipyran-2',2''-diyl)-α-D-glucopyranoside (20)

A solution of methyl 6-*O*-(*tert*-butyldiphenylsilyl)-α-D-glucopyranoside (**6**) (220 mg, 0.587 mmol), [2*R*,2'*R*] 2,2'-diallyl-3,3'-dihydro-6,6'-bi-2*H*-pyran (**5**) (174 mg, 0.70 mmol) and pyridinium *p*-toluenesulfonate (PPTS) (36 mg, 0.14 mmol, catalytic) in $CHCl_3$ (10 mL) was heated at 70 °C for 48 hours. The reaction was cooled to room temperature, diluted with dichloromethane (20 mL), dried ($MgSO_4$) and evaporated *in vacuo* to give a brown oil. Purification by flash chromatography on silica gel, eluting with ether/petrol (1:9-3:7), gave *dispoke derivative* **20** (309 mg, 0.455 mmol, 78%) as an off-white foam; $[\alpha]_D^{23}$ = -8.8 (c=1.2 in $CHCl_3$); δ_H (200 MHz, $CDCl_3$) 7.72-7.69 (4H, m, 4x *o*-Ph-H), 7.44-7.35 (6H, m, 4x *m*- and 2x *p*-Ph-H), 5.84 (2H, m, C*H*=CH_2), 5.08-4.90 (4H, m, CH=C*H*$_2$), 4.71 (1H, d, *J* 3.5, *H*-1), 4.04 (1H, dd, *J* 10.0, 8.6, *H*-3), 3.90 (2H, m, 2x *H*-6), 3.77-3.69, 3.62 (5H, 2x m, *H*-2, *H*-4, *H*-5, *H*-2', *H*-2''), 3.38 (3H, s, OC*H*$_3$), 2.44 (1H, d, *J* 1.9, O*H*), 2.30-2.16 (4H, m, 2x C*H*$_2$CH=CH_2), 1.94-1.11 (12H, m, 2x *H*-3', 2x *H*-3'', 2x *H*-4', 2x *H*-4'', 2x *H*-5', 2x *H*-5''), 1.06 (9H, s, C(C*H*$_3$)$_3$); δ_C (50 MHz, $CDCl_3$): 135.70, 135.64, 134.92, 134.79, 133.33, 133.20, 129.68, 127.65 (Aromatic*C*), 116.81, 116.64, 98.03, 97.68, 97.28, 71.61, 69.59, 69.45, 69.18, 68.49, 67.51, 64.20, 54.82, 40.42, 40.36, 29.98, 29.74, 28.19, 27.91, 26.82, 19.25, 18.37, 18.24; ν(Film)/cm^{-1} 3518, 3076, 2931, 1641, 1428; *m/z* (FAB) 679 $(MH)^+$. Found 679.3725. $C_{39}H_{55}O_8Si$ requires 679.3666.

[2'*R*,2''*R*,6'*R*,6''*R*] Methyl 6-*O*-(*tert*-butyldiphenylsilyl)-2-*O*,3-*O*-(6',6''-di-(2-oxoethyl)-octahydro-2',2''-bipyran-2',2''-diyl)-α-D-glucopyranoside (21)

Ozone was bubbled into a solution of the diallyl dispoke adduct **20** (48 mg, 0.07 mmol) in dichloromethane (5 mL) at -78 °C for 20 minutes. Argon was bubbled through the solution to remove any residual ozone, then triphenylphosphine (53 mg, 0.20 mmol) was added. The solution was allowed to warm to room temperature and stirred for 7 hours. The solvent was evaporated *in vacuo* and the residue purified by chromatography on silica gel, eluting with ether/petrol (7:3-8:2), to give *dispoke derivative* **21** as a colourless foam (50 mg, 0.07 mmol, 100%); $[\alpha]_D^{23}$ = -3.8 (c = 1.0 in $CHCl_3$); δ_H (200 MHz, $CDCl_3$) 9.84 (1H, t, *J* 2.0, C*H*O), 9.80 (1H, t, *J* 2.0, C*H*O), 7.70 (4H, m, 4x *o*-Ph-*H*), 7.39 (6H, m, 4x *m*- and 2x *p*-Ph-*H*), 4.74 (1H, d, *J* 3.5, *H*-1), 4.40-4.03, 4.00-3.63 and 2.55 (12H, 3x m, *H*-2, *H*-3, *H*-4, *H*-5, 2x *H*-6, 2x C*H*CH$_2$CHO, 2x C*H*$_2$CHO), 3.38 (3H, s, OC*H*$_3$), 2.05-1.10 (12H, m, 2x *H*-3', 2x *H*-3'', 2x *H*-4', 2x *H*-4'', 2x *H*-5', 2x *H*-5''), 1.06 (9H, s, C(C*H*$_3$)$_3$); δ_C (50 MHz, $CDCl_3$): 201.45, 200.71, (2x *C*HO), 135.64, 133.14, 133.03, 129.76, 127.72, (Aromatic *C*), 97.83, 97.58, 97.25, 71.44, 70.04, 68.71, 67.69, 65.45, 65.27, 64.65, 54.98, 49.41, 49.25, 30.33, 30.21, 27.94, 27.72, 26.81, 19.23, 18.18, 17.98; ν(film)/cm^{-1} 3491, 2931, 1724, 1428, 1112, 1032; *m/z* (FAB) 683 $(MH)^+$. Found 683.3211. $C_{37}H_{51}O_{10}Si$ requires 683.3251.

Methyl 6-*O*-(*tert*-butyldiphenylsilyl)-α-D-glucopyranoside (6)

1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) (12 mL, 0.08 mmol) was added to a solution of *dispoke derivative* **21** (29 mg, 0.012 mmol) in toluene (2 mL) at room temperature and the solution was stirred at 80 °C overnight. After cooling to room temperature, ether (3 mL) and water (2 mL) were added, the aqueous layer was extracted with ether (3x 2 mL) and the combined organic layers were dried ($MgSO_4$). After

concentration *in vacuo*, chromatography on silica gel, eluting with ether/petrol (6:4) then ether/methanol (9:1), gave 6-*O*-(tert-butyldiphenylsilyl)-α-D-glucopyranoside (**6**) as a white powder (10 mg, 0.023 mmol, 56%) identical in all respects to that prepared above.

Methyl-α-D-glucopyranoside (22)

Phosphazene base P4-*t*-octyl[13] (1M in hexane, 70 μL, 0.07 mmol) was added to a solution of *dispoke derivative* **21** (25 mg, 0.036 mmol) in THF (0.6 mL) under an argon atmosphere at 0 °C. The deep purple solution was stirred for 2 hours at 0 °C and then poured into water (2 mL). The water was extracted with ether (2 mL) and concentrated under reduced pressure to one quarter of its original volume. Purification by reverse phase column chromatography (C18), eluting with water, gave methyl-α-D-glucopyranoside **22** (5 mg, 0.025 mmol, 73%) as a white solid identical in all respects to an authentic sample.[14]

[2'*R*,2''*R*,6'*R*,6''*R*] Thioethyl 6-*O*-(*tert*-butyldiphenylsilyl)-2-*O*,3-*O*-(6',6''-diphenyloctahydro-2',2''-bipyran-2',2''-diyl)-β-D-glucopyranoside (24)

A solution of thioethyl 6-*O*-(*tert*-butyldiphenylsilyl)-β-D-glucopyranoside[16] (**23**) (340 mg, 0.735 mmol), [2*R*,2'*R*] 2,2'-diphenyl-3,3',4,4'-tetrahydro-6,6'-bi-2*H*-pyran (**1**) (350 mg, 1.102 mmol) and camphorsulfonic acid (50 mg, catalytic) in $CHCl_3$ (2 mL) was heated at 70 °C for 18 hours. The orange solution was cooled to room temperature, evaporated *in vacuo* and the residue purified by column chromatography on silica gel, eluting with ether/petrol (2:8), to give *dispoke derivative* **24** as a white foam (471 mg, 0.603 mmol, 82%); $[\alpha]_D^{26}$ = - 23.8 (c = 1.00, $CHCl_3$); δ_H (200 MHz , $CDCl_3$) 7.67 (4H, m, 4x *o*-OTBD*PS*), 7.37 (16H, m, 10x Ph-*H*, 4x *m*- and 2x *p*- OTBD*PS*), 4.83 (2H, m, *H*-6', *H*-6''), 4.57 (1H, d, *J* 9.8, *H*-1), 3.87 (2H, br.d, *J* 5, *H*-6_A, *H*-6_B), 3.84-3.71 (2H, m, *H*-3, *H*-4), 3.63 (1H, t, *J* 9.4, *H*-2), 3.48 (1H, m, *H*-5), 2.81 (1H, br.s, O*H*), 2.70 (2H, dq, *J* 2.4, 7.4, SCH_2CH_3), 2.20-1.40 (12H, m, 2x *H*-3', 2x *H*-3'', 2x *H*-4', 2x *H*-4'', 2x *H*-5', 2x *H*-5''), 1.28 (3H, t, *J* 7.5, SCH_2CH_3), 1.04 (9H, s, $C(CH_3)_3$); ν_{max} (film)/cm^{-1} 3451, 2929, 2857, 1453, 1428, 1202, 1113, 1044, 980, 966, 742, 700; *m/z* (CI) 780 $(M)^+$, 763 $(M\text{-}OH)^+$, 720, 661, 519, 319, 197, 135; Found $(M)^+$ 780.3447; $C_{46}H_{56}O_7SSi$ requires 780.3516.

[2'*R*,2''*R*,6'*R*,6''*R*] Thioethyl 4-*O*-benzoyl-6-*O*-(*tert*-butyldiphenylsilyl)-2-*O*,3-*O*-(6',6''-diphenyloctahydro-2',2''-bipyran-2',2''-diyl)-β-D-glucopyranoside (25)

Dispoke derivative **24** (471 mg, 0.603 mmol) and DMAP (1 crystal, catalytic) were dissolved in triethylamine (1 mL) and DCM (10 mL) and benzoyl chloride (105 μL, 0.904 mmol) was added under argon at room temperature. The yellow solution was stirred for 16 hours, poured into $NaHCO_3$ (aqueous, saturated 10 mL) and extracted with DCM (3 x 30 mL). The combined organic extracts were sequentially washed with H_2O (30 mL) and HCl (1 M, 30 mL), dried ($MgSO_4$) and evaporated *in vacuo* to give a yellow foam. Purification by column chromatography on silica gel, eluting with ether/petrol (1:9), gave *benzoate* **25** as a white solid (513 mg, 0.58 mmol, 96%); m.p. 180-181 °C; $[\alpha]_D^{24}$ = + 2.3 (c = 1.00 in $CHCl_3$); δ_H (200 MHz, $CDCl_3$)

7.97 (2H, m, 2x *o*- OCOPh-*H*) 7.70-7.20 (23H, m, 10x Ph-*H*, 10x OTBD*PS*, 2x *m*- and *p*- OCOPh-*H*), 5.23 (1H, t, *J* 9.7, *H*-4), 4.82 (1H, br.dd, *J* 11.5, 2.3, *H*-6'(or *H*-6")), 4.62 (1H, d, *J* 9.9, *H*-1), 4.52 (1H, br.dd, *J* 11.3, 2.2, *H*-6"(or *H*-6')), 4.02 (1H, t, *J* 9.5, *H*-3), 3.78 (3H, m, *H*-2, *H*-6_A, *H*-6_B), 3.64 (1H, m, *H*-5), 2.76 (2H, m, SCH_2CH_3), 2.10-1.40 (12H, m, 2x *H*-3', 2x *H*-3", 2x *H*-4', 2x *H*-4", 2x *H*-5', 2x *H*-5"), 1.34 (3H, t, *J* 7.4, SCH_2CH_3), 0.97 (9H, s, $C(CH_3)_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2932, 1731, 1601, 1452, 1428, 1264, 1112, 1043, 1026, 970, 739, 700; *m/z* (FAB) 885 $(MH)^+$, 824 $(MH\text{-}CH_3CH_2S)^+$, 549, 423, 319; Found $(MH)^+$ 885.3866; $C_{53}H_{61}O_8SSi$ requires 885.3856; Found: C, 70.55; H, 6.99. $C_{53}H_{62}O_9SSi$ (**25**·H_2O) requires C, 70.48; H, 6.92%.

[2'*S*,2"*S*,6'*S*,6"*S*] Thioethyl 6-*O*-(*tert*-butyldiphenylsilyl)-3-*O*,4-*O*-(6',6"-diphenyloctahydro-2',2"-bipyran-2',2"-diyl)-β-D-glucopyranoside (26)

A solution of thioethyl 6-*O*-(*tert*-butyldiphenylsilyl)-β-D-glucopyranoside (**23**) (50 mg, 0.105 mmol), [2*S*,2'*S*] 2,2'-diphenyl-3,3',4,4'-tetrahydro-6,6'-bi-2*H*-pyran (**2**) (50 mg, 0.157 mmol) and camphorsulfonic acid (20 mg, catalytic) in $CHCl_3$ (2 mL) was heated at 70 °C for 18 hours. The orange solution was cooled to room temperature, evaporated *in vacuo* and the residue purified by column chromatography on silica gel, eluting with ether/petrol (2:8), to give *dispoke derivative* **26** as a white foam (62 mg, 0. 080 mmol, 76%); $[\alpha]_D^{26}$ = - 9.4 (c = 0.54 in $CHCl_3$); δ_H (200 MHz, $CDCl_3$) 7.70 (4H, m, 4x *o*-OTBD*PS*), 7.37 (16H, m, 10x Ph, 4x *m*- and 2x *p*- OTBD*PS*), 4.84 (1H, dd, *J* 11.4, 2.2, *H*-6' (or *H*-6")), 4.49 (1H, br.d, *J* 10.4, *H*-6" (or *H*-6')), 4.36 (1H, d, *J* 9.4, *H*-1), 3.98 (1H, dd, *J* 11.0, 1.7, *H*-6_A), 3.87-3.76 (2H, m, *H*-6_B, *H*-3), 3.68 (1H, t, *J* 9.5, *H*-4), 3.58-3.49 (2H, m, *H*-2, *H*-5), 2.70 (2H, dq, *J* 1.7, 7.4, SCH_2CH_3), 2.34 (1H, br.d, *J* 1.7, O*H*), 2.20-1.40 (12H, m, 2x *H*-3', 2x *H*-3", 2x *H*-4', 2x *H*-4", 2x *H*-5', 2x *H*-5"), 1.30 (3H, t, *J* 7.5, SCH_2CH_3), 0.97 (9H, s, $C(CH_3)_3$); ν_{max} (film)/cm^{-1} 3444, 2926, 1454, 1428, 1202, 1159, 1113, 1040, 966, 699; *m/z* (CI) 798 $(MNH_4)^+$, 780 $(M)^+$, 736, 632, 518, 319; Found $(M)^+$ 780.3447; $C_{46}H_{56}O_7SSi$ requires 780.3516.

[2'*S*,2"*S*,6'*S*,6"*S*] Thioethyl 2-*O*-acetyl-6-*O*-(*tert*-butyldiphenylsilyl)-3-*O*,4-*O*-(6',6"-diphenyloctahydro-2',2"-bipyran-2',2"-diyl)-β-D-glucopyranoside (27)

Dispoke derivative **26** (51 mg, 0.068 mmol) and DMAP (1 crystal, catalytic) were dissolved in triethylamine (1 mL); DCM (10 mL) and acetic anhydride (20 μL, 0.272 mmol) were added under argon at room temperature. The yellow solution was stirred for 16 hours, poured into $NaHCO_3$ (aqueous, saturated, 10 mL) and extracted with DCM (3 x 10 mL). The combined organic extracts were sequentially washed with H_2O (10 mL) and HCl (1 M, 10 mL), dried ($MgSO_4$) and evaporated *in vacuo* to give a yellow foam. Purification by column chromatography on silica gel, eluting with ether/petrol (2:8), gave *acetate* **27** as a white foam (53 mg, 0.064 mmol, 95%); $[\alpha]_D^{25}$ = - 15.9 (c = 0.57 in $CHCl_3$); δ_H (200 MHz, $CDCl_3$) 7.72 (4H, m, 4x *o*- TBD*PS*) 7.45-7.10 (16H, m, 10x Ph-*H*, 4x *m*- and 2x *p*- OTBD*PS*), 4.99 (1H, t, *J* 9.6, *H*-2), 4.69 (1H, br.dd, *J* 11.6, 2.0, *H*-6'(or *H*-6")), 4.50 (1H, br.d, *J* 10.2, *H*-6"(or *H*-6')), 4.43 (1H, d, *J* 9.8, *H*-1, 3.98 (1H, dd, *J* 11.6, 2.0, *H*-6_A), 3.85 (2H, m, H-3, *H*-6_B), 3.73 (1H, t, *J* 9.6, *H*-4), 3.55 (1H, m,

H-5), 2.69 (2H, dq, *J* 3.2, 7.5, SCH_2CH_3), 2.16 (3H, s, CH_3CO), 2.10-1.40 (12H, m, 2x *H*-3', 2x *H*-3", 2x *H*-4', 2x *H*-4", 2x *H*-5', 2x *H*-5"), 1.34 (3H, t, *J* 7.4, SCH_2CH_3), 1.00 (9H, s, $C(CH_3)_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2930, 2857, 1753, 1453, 1427, 1368, 1228, 1158, 1112, 1042, 965, 909, 872, 823, 737, 700; *m/z* (FAB) 840 $(MNH_4)^+$, 761 $(M-CH_3CH_2S)^+$, 543, 423, 365, 319, 301, 279, 241, 221, 147, 117, 91, 55; Found $(M)^+$ 822.3595; $C_{48}H_{58}O_8SSi$ requires 822.3621.

[2'*S*,2"*S*,6'S,6"S] Thioethyl 6-*O*-(*tert*-butyldiphenylsilyl)-2-*O*,3-*O*-(6',6"-dimethyloctahydro-2',2"-bipyran-2',2"-diyl)-β-D-glucopyranoside (28)

A solution of thioethyl 6-*O*-(*tert*-butyldiphenylsilyl)-β-D-glucopyranoside (**23**) (185 mg, 0.400 mmol), [2*S*,2'*S*] 2,2'-dimethyl-3,3',4,4'-tetrahydro-6,6'-bi-2*H*-pyran (**4**) (134 mg, 0.69 mmol) and camphorsulfonic acid (20 mg, catalytic) in $CHCl_3$ (5 mL) was heated at 70 °C for 24 h. The solution was cooled to room temperature, evaporated *in vacuo* and the residue purified by column chromatography on silica gel, eluting with ether/petrol (5:95-2:8), to give *dispoke derivative* **28** as a white foam (169 mg, 0.258 mmol, 64%); $[\alpha]_D^{26}$ = - 55.6 (c = 2.1 in $CHCl_3$); δ_H (400 MHz , $CDCl_3$) 7.70 (4H, m, 4x *o*-Ph-*H*), 7.44-7.36 (6H, m, 4x *m*- and 2x *p*-Ph-*H*), 4.63 (1H, d, *J* 9.8, *H*-1), 3.94-3.74 and 3.53-3.44 (7H, 2x m, *H*-3, *H*-4, *H*-5, 2x *H*-6, *H*-2', *H*-2"), 3.57 (1H, apparent t, *J* 9.5, *H*-2), 2.72 (2H, m, SCH_3CH_2), 1.87-1.39 and 1.26-1.14 (12H, 2x m, 2x *H*-3', 2x *H*-3", 2x *H*-4', 2x *H*-4", 2x *H*-5', 2x *H*-5"), 1.28 (3H, t, *J* 7.4 SCH_3CH_2), 1.13-1.09 (6H, m, 2x CH_3), 1.05 (9H, s, $C(CH_3)_3$); δ_C (100 MHz , $CDCl_3$): 135.64 (Aromatic *C*-H), 133.03, 129.77 (2x Aromatic *C*), 127.74 (Aromatic *C*-H), 97.93, 97.51 (*C*-6', *C*-6"), 82.65 (*C*-1), 79.64, 73.64, 69.30, 68.05, 66.32, 66.02 (*C*-2, *C*-3, *C*-4, *C*-5, *C*-2', *C*-2"), 64.67 (*C*-6), 32.57, 32.47, 27.97, 27.91 (4x CH_2), 26.82 ($C(CH_3)_3$), 24.25 (CH_2), 21.97, 21.79 (2x CH_2), 19.23 ($C(CH_3)_3$), 18.52, 18.46 (2x CH_2), 15.11 (CH_3CH_2S); ν_{max} (film)/cm^{-1} 3506, 3003, 2972, 2933, 2872, 1472, 1456, 1428, 1383, 1272, 1194, 1137, 1112, 1048, 1032, 986, 942, 908, 824, 703, 610; *m/z* (FAB) 656 $(M)^+$, 655 $(M-H)^+$, 595, 577, 537, 497, 445, 427, 387, 367, 349, 339, 289, 281, 241, 221, 195, 135. Found $(M-H)^+$ 655.3115. $C_{36}H_{51}O_7SSi$ requires 655.3124.

[2'*R*,2"*R*,6'*R*,6"*R*] Methyl 6-*O*-(*tert*-butyldiphenylsilyl)-2-*O*,3-*O*-(6',6"-diphenyloctahydro-2',2"-bipyran-2',2"-diyl)-β-D-galactopyranoside (30)

A solution of methyl 6-*O*-(*tert*-butyldiphenylsilyl)-β-D-galactopyranoside[17] (**29**) (45 mg, 0.104 mmol), [2*R*,2'*R*] 2,2'-diphenyl-3,3',4,4'-tetrahydro-6,6'-bi-2*H*-pyran (**1**) (50 mg, 0.157 mmol) and camphorsulfonic acid (20 mg, catalytic) in $CHCl_3$ (2 mL) was heated at 70 °C for 10 hours. The yellow solution was cooled to room temperature, evaporated *in vacuo* and the residue purified by column chromatography on silica gel, eluting with ether/petrol (2.5:7.5), to give *dispoke derivative* **30** as a colourless foam (69 mg, 0.092 mmol, 88%); $[\alpha]_D^{26}$ = - 5.7 (c = 1.00 in $CHCl_3$); δ_H (200 MHz, $CDCl_3$) 7.69 (4H, m, 4x *o*-OTBD*PS*), 7.39 (16H, m, 10x Ph-*H*, 4x *m*- and 2x *p*- OTBD*PS*), 4.79 (2H, m, *H*-6', *H*-6"), 4.34 (1H, d, *J* 7.9, *H*-1), 4.05-3.78 (5H, m, H-6_A, H-6_B, *H*-2, *H*-3, *H*-4), 3.57 (1H, br.t, *J* 6.3, *H*-5), 3.50 (3H, s, OCH_3), 2.35 (1H, br.s, O*H*), 2.20-1.40 (12H, m, 2x *H*-3', 2x *H*-3", 2x *H*-4', 2x *H*-4", 2x *H*-5', 2x *H*-5"), 1.05 (9H, s, $C(CH_3)_3$); ν_{max} (film)/cm^{-1} 3577, 2934, 1453, 1428, 1266, 1202, 1168, 1112, 1071,

1047, 980, 824, 738, 701; *m/z* (FAB) 773 $(MNa)^+$, 751 $(MH)^+$, 719 $(M\text{-}CH_3O)^+$, 701 $(M\text{-}CH_3O\text{-}H_2O)^+$, 661 $(M\text{-}C(CH_3)_3\text{-}CH_3OH)^+$ 319. Found $(MH)^+$ 751.3670; $C_{45}H_{54}O_8Si$ requires 751.3666.

[2'*R*,2''*R*,6'*R*,6''*R*] Methyl 4-*O*-acetyl-6-*O*-(*tert*-butyldiphenylsilyl)-2-*O*,3-*O*-(6',6''-diphenyloctahydro-2',2''-bipyran-2',2''-diyl)-β-D-galactopyranoside (31)

Dispoke derivative **30** (61 mg, 0.081 mmol) and DMAP (1 crystal, catalytic) were dissolved in pyridine (1 mL), acetic anhydride (59 μL, 0.81 mmol) was added under argon at room temperature and the yellow solution was stirred for 16 hours. The reaction mixture was poured into $NaHCO_3$ (aqueous, saturated, 10 mL) and extracted with ether (3 x 10 mL). The combined organic extracts were sequentially washed with H_2O (5 mL) and HCl (1 M, 10 mL), dried ($MgSO_4$) and evaporated *in vacuo* to give a yellow foam. Purification by column chromatography on silica gel, eluting with ether/petrol (2:8), gave *acetate* **31** as a pale yellow oil (60 mg, 0.076 mmol, 93%); $[\alpha]_D^{26}$ = - 12.6 (c = 1.00 in $CHCl_3$); δ_H (200 MHz, $CDCl_3$) 7.58 (4H, m, 4x *o*-OTBD*PS*), 7.44-7.21 (16H, m, 10x Ph-*H* , 4x *m*- and 2x *p*- OTBD*PS*), 5.44 (1H, br.d, *J* 2.0, *H*-4), 4.81 (2H, m, *H*-6', *H*-6''), 4.36 (1H, d, *J* 7.3, *H*-1), 3.91 (2H, m, *H*-2, *H*-5), 3.67 (3H, m, *H*-3, *H*-6_A, *H*-6_B), 3.49 (3H, s, OCH_3), 2.2-1.4 (12H, m, 2x *H*-3', 2x *H*-3'', 2x *H*-4', 2x *H*-4'', 2x *H*-5', 2x *H*-5''), 1.89 (3H, s, CH_3CO), 1.03 (9H, s, $C(CH_3)_3$); ν_{max} (film)/cm^{-1} 2926, 2853, 1750, 1451, 1428, 1366, 1227, 1168, 1112, 1075, 969, 825, 741, 700.

[2'*S*,2''*S*,6'*S*,6''*S*] Methyl 6-*O*-(*tert*-butyldiphenylsilyl)-2-*O*,3-*O*-(6',6''-diphenyloctahydro-2',2''-bipyran-2',2''-diyl)-α-D-mannopyranoside (33) and [2'*S*,2''*S*,6'*S*,6''*S*] Methyl 6-*O*-(*tert*-butyldiphenylsilyl)-3-*O*,4-*O*-(6',6''-diphenyloctahydro-2',2''-bipyran-2',2''-diyl)-α-D-mannopyranoside (34)

A solution of methyl 6-*O*-(*tert*-butyldiphenylsilyl)-α-D-mannopyranoside[18] (**32**) (71 mg, 0.164 mmol), [2*S*,2'*S*] 2,2'-diphenyl-3,3',4,4'-tetrahydro-6,6'-bi-2*H*-pyran (**2**) (93 mg, 0.292 mmol) and camphorsulfonic acid (30 mg, catalytic) in $CHCl_3$ (2 mL) was heated at 70 °C for 10 hours. The yellow solution was cooled to room temperature, evaporated *in vacuo* and the residue purified by column chromatography on silica gel, eluting with ether/petrol (4:6), to give in order of elution:

Cis *dispoke derivative* **33** as a pale yellow foam (45 mg, 0.061 mmol, 37%); δ_H (200 MHz , $CDCl_3$) 7.63 (4H, m, 4x *o*-OTBD*PS*), 7.52-7.30 (16H, m, 10x Ph-*H*, 4x *m*- and 2x *p*-OTBD*PS*), 4.62 (3H, m, *H*-1, *H*-6', *H*-6''), 4.18 (1H, d, *J* 3.8, *H*-2), 3.83 (1H, dd, *J* 9.4, 3.8, *H*-3), 3.78-3.54 (4H, m, *H*-4, *H*-5, *H*-6_A, *H*-6_B), 3.24 (3H, s, OCH_3), 2.20-1.40 (12H, m, 2x *H*-3', 2x *H*-3'', 2x *H*-4', 2x *H*-4'', 2x *H*-5', 2x *H*-5''), 1.00 (9H, s, $C(CH_3)_3$); ν_{max} (film)/cm^{-1} 3582, 2931, 1492, 1453, 1428, 1202, 1162, 1112, 1047, 980, 875, 823, 740, 699; *m/z* (FAB) 773 $(MNa)^+$, 751 $(MH)^+$, 750 $(M)^+$, 718 $(M\text{-}CH_3OH)^+$, 693 $(M\text{-}C(CH_3)_3)^+$, 675 $(M\text{-}C(CH_3)_3\text{-}OH_2)^+$, 661 $(MH\text{-}CH_3OH\text{-}C(CH_3)_3)^+$, 319; Found $(MH)^+$ 751.3640. $C_{45}H_{55}O_8Si$ requires 751.3666.

and more polar *trans adduct* **34** as a colourless foam (53 mg, 0.071 mmol, 43%); $[\alpha]_D^{26}$ = +28.1 (c = 0.88, $CHCl_3$); δ_H (200 MHz , $CDCl_3$) 7.71 (4H, m, 4x *o*-OTBD*PS*), 7.37 (16H, m, 10x Ph-*H*, 4x *m*- and 2x *p*-OTBD*PS*), 4.73 (2H, m, *H*-1, *H*-6' (or *H*-6'')), 4.37 (1H, br.d, *J* 9.7, *H*-6'' (or *H*-6')), 4.05 (6H, m, *H*-2,

H-3, *H*-4, *H*-5, *H*-6_A, *H*-6_B), 3.36 (3H, s, OC*H*$_3$), 2.25 (1H, d, *J* 2.4, O*H*), 2.10-1.20 (12H, m, 2x *H*-3', 2x *H*-3", 2x *H*-4', 2x *H*-4", 2x *H*-5', 2x *H*-5"), 1.01 (9H, s, C(C*H*$_3$)$_3$) ; *m/z* (FAB) 773 $(MNa)^+$, 751 $(MH)^+$, 750 $(M)^+$, 718 $(M\text{-}CH_3OH)^+$, 693 $(M\text{-}C(CH_3)_3)^+$, 675 $(M\text{-}C(CH_3)_3\text{-}OH_2)^+$, 661 $(MH\text{-}CH_3OH\text{-}C(CH_3)_3)^+$, 319; Found $(MH)^+$ 751.3640. $C_{45}H_{55}O_8Si$ requires 751.3666.

[2'*S*,2"*S*,6'*S*,6"*S*] Methyl 4-*O*-acetyl-6-*O*-(*tert*-butyldiphenylsilyl)-2-*O*,3-*O*-(6',6"-diphenyloctahydro-2',2"-bipyran-2,'2"-diyl)-α-D-mannopyranoside (35)

Dispoke derivative **33** (45 mg, 0.061 mmol) and DMAP (1 crystal, catalytic) were dissolved in pyridine (500 μL), acetic anhydride (50 μL, 0.68 mmol) was added under argon at room temperature and the yellow solution was stirred for 16 hours. The reaction mixture was poured into $NaHCO_3$ (aqueous, saturated, 10 mL) and extracted with ether (3 x 10 mL). The combined organic extracts were sequentially washed with H_2O (5 mL) and HCl (1 M, 10 mL), dried ($MgSO_4$) and evaporated *in vacuo* to give a yellow foam. Purification by column chromatography on silica gel, eluting with ether/petrol (2:8), gave *acetate* **35** as a pale yellow foam (45 mg, 0.057 mmol, 95%); $[\alpha]_D^{26}$ = + 2.3 (c = 0.97 in $CHCl_3$); δ_H (200 MHz, $CDCl_3$) 7.62 (4H, m, 4x OTBD*PS*), 7.44 (16H, m, 10x Ph-*H*, 4x *m*- and 2x *p*- OTBD*PS*), 5.16 (1H, t, *J* 9.8, *H*-4), 4.77 (1H, s, *H*-1), 4.66 (2H, m, *H*-6', *H*-6"), 4.26 (1H, d, *J* 4.0, *H*-2), 4.13 (1H, dd, *J* 9.6, 4.0, *H*-3), 3.84 (1H, m, *H*-5), 3.69 (1H, dd, *J* 11.0, 7.8, *H*-6_A), 3.49 (1H, dd, *J* 11.0, 2.2, *H*-6_B), 3.41 (3H, s, OC*H*$_3$), 1.90 (3H, s, C*H*$_3$CO), 2.20-1.30 (12H, m, 2x *H*-3', 2x *H*-3", 2x *H*-4', 2x *H*-4", 2x *H*-5', 2x *H*-5"), 0.99 (9H, s, C(C*H*$_3$)$_3$); ν_{max} (film)/cm^{-1} 2930, 1750, 1428, 1366, 1232, 1156, 1105, 1040, 698; *m/z* (FAB) 793 $(MH)^+$, 792 $(M)^+$, 761 $(M\text{-}CH_3O)^+$, 735 $(M\text{-}C(CH_3)_3)^+$, 703 $(M\text{-}CH_3OH\text{-}C(CH_3)_3)^+$, 319; Found $(MH)^+$ 793.3733. $C_{47}H_{57}O_9Si$ requires 793.3772.

[2'*S*,2"*S*,6'*S*,6"*S*] Methyl 2-*O*-acetyl-6-*O*-(*tert*-butyldiphenylsilyl)-3-*O*,4-*O*-(6',6"-diphenyloctahydro-2',2"-bipyran-2',2"-diyl)-α-D-mannopyranoside (36)

Dispoke derivative **34** (24 mg, 0.0325 mmol) and DMAP (1 crystal, catalytic) were dissolved in pyridine (500 μL), acetic anhydride (24 μL, 0.325 mmol) was added under argon at room temperature and the yellow solution was stirred for 16 hours. The reaction mixture was poured into $NaHCO_3$ (aqueous, saturated, 10 mL) and extracted with ether (3 x 10 mL). The combined organic extracts were sequentially washed with H_2O (5 mL) and HCl (1 M, 10 mL), dried ($MgSO_4$) and evaporated *in vacuo* to give a yellow foam. Purification by column chromatography on silica gel, eluting with ether/petrol (2:8), gave *acetate* **36** as a pale yellow oil (25 mg, 0.0315 mmol, 97%); $[\alpha]_D^{26}$ = + 22.5 (c = 1.00 in $CHCl_3$); δ_H (200 MHz, $CDCl_3$) 7.73 (4H, m, 4x *o*-OTBD*PS*), 7.44-7.20 (16H, m,10x Ph-*H*, 4x *m*- and 2x *p*- OTBD*PS*), 5.16 (1H, dd, *J* 2.9, 1.5, *H*-2), 4.74 (1H, dd, *J* 11.7, 2.4, *H*-6' (or *H*-6")), 4.65 (1H, d, *J* 1.3, *H*-1), 4.58 (1H, dd, *J* 11.8, 2.3, *H*-6"(or *H*-6')), 4.18 (1H, dd, *J* 9.7, 3.0, *H*-3), 4.08 (1H, t, *J* 9.7, *H*-4), 3.92 (2H, m, *H*-6_A, *H*-6_B), 3.77 (1H, m, *H*-5), 3.32 (3H, s, OC*H*$_3$), 2.02 (3H, s, C*H*$_3$CO), 2.00-1.30 (12H, m, 2x *H*-3', 2x *H*-3", 2x *H*-4', 2x *H*-4", 2x *H*-5', 2x *H*-5"), 0.95 (9H, s, C(C*H*$_3$)$_3$); ν_{max} (film)/cm^{-1} 2930, 1747, 1453, 1428, 1366, 1236, 1165, 1045, 980, 741, 700; *m/z* (FAB) 793 $(MH)^+$, 792 $(M)^+$, 761 $(M\text{-}CH_3O)^+$, 735 $(M\text{-}C(CH_3)_3)^+$, 703 $(M\text{-}CH_3OH\text{-}C(CH_3)_3)^+$, 319; Found $(MH)^+$ 793.3802. $C_{47}H_{57}O_9Si$ requires 793.3772.

[2'*S*,2''*S*,4'*S*,4''*S*] Methyl 6-*O*-(*tert*-butyldiphenylsilyl)-2-*O*-3-*O*-(4',4''-dimethyloctahydro-2',2''-bipyran-2',2''-diyl)-α-D-mannopyranoside (37) and [2'*S*,2''*S*,4'*S*,4''*S*] Methyl 6-*O*-(*tert*-butyldiphenylsilyl)-3-*O*-4-*O*-(4',4''-dimethyloctahydro-2',2''-bipyran-2',2''-diyl)-α-D-mannopyranoside (38)

A solution of methyl 6-*O*-(*tert*-butyldiphenylsilyl)-α-D-mannopyranoside (**32**) (171 mg, 0.396 mmol), [4*S*,4'*S*] 4,4'-dimethyl-3,3'-dihydro-6,6'-bi-2*H*-pyran (**3**) (115 mg, 0.593 mmol) and camphorsulfonic acid (8 mg, catalytic) in $CHCl_3$ (3.5 mL) was heated at 70 °C for 15 hours. The yellow solution was cooled to room temperature, evaporated *in vacuo* and the residue purified by column chromatography on silica gel eluting, with hexane/ethyl acetate (8:2), to give in order of elution:

dispoke derivative **37**, Rf 0.27, (70 mg, 0.112 mmol, 28%); $[\alpha]_D^{26}$ = + 88.4 (c = 0.98 in $CHCl_3$); δ_H (500MHz, $CDCl_3$) 7.70 (4H, m, 4x *o*-Ph-*H*), 7.39 (6H, m, 4x *m*- and 2x *p*-Ph-*H*), 4.61 (1H, s, *H*-1), 4.56 (1H, t, *J* 9.5, *H*-4), 4.20 (1H, m, *H*-6"), 4.12 (1H, d, *J* 3.9, *H*-2), 3.93 (2H, ABX, *H*-6), 3.71 (3H, m, 2x *H*-6', *H*-3), 3.55 (2H, m, *H*-6", *H*-5), 3.28 (3H, s, OCH_3), 2.87 (1H, s, O*H*), 2.02 (1H, m, *H*-4' or *H*-4"), 1.91 (2H, m, H-5'$_{eq}$, *H*-4" or *H*-4'), 1.76 (1H, m, H-5"$_{eq}$), 1.52 (2H, m, H-3'$_{eq}$, H-3"$_{eq}$), 1.15 (4H, m, H-3'$_{ax}$, H-3"$_{ax}$, H-5'$_{ax}$, H-5"$_{ax}$), 1.07 (9H, s, $C(CH_3)_3$), 0.89-0.88 (6H, m, 2x CH_3); δ_C (100 MHz , $CDCl_3$): 135.65, 132.94, 132.91, 129.87, 129.79 (Aromatic *C*), 100.41 (*C*-1), 97.92, 96.95 (*C*-2', *C*-2"), 72.78, 70.75, 69.84 (*C*-2, *C*-3, *C*-4), 65.90 (*C*-5), 65.49 (*C*-6), 61.43, 60.78 (*C*-6', *C*-6"), 54.47 (OCH_3), 38.67, 36.93 (*C*-5', *C*-5"), 33.73, 33.33 (*C*-3', *C*-3"), 26.83 ($C(CH_3)_3$), 24.72, 24.53 (*C*-4', *C*-4"), 22.39, 22.20 (2x CH_3), 19.19 ($C(CH_3)_3$); ν_{max} (film)/cm^{-1} 3582, 2932, 1589, 1455, 1380, 1266, 1112, 1071, 1050, 995, 915, 704, 613; *m/z* (FAB) 649 $(M+Na)^+$, 626 $(M)^+$, 625 $(M-H)^+$, 595, 569, 530, 353, 339, 309, 295, 281, 269, 253, 195, 135. Found $(M-OCH_3)^+$ 595.3117. $C_{34}H_{47}O_7Si$ requires 595.3091.

and *dispoke derivative* **38**, Rf: 0.21, (100 mg, 0.160 mmol, 40%); $[\alpha]_D^{26}$ = + 44.88 (c = 2.33 in $CHCl_3$); δ_H (500 MHz $CDCl_3$) 7.72 (4H, m, 4x *o*-Ph-*H*), 7.39 (6H, m, 4x *m*- and 2x *p*-Ph-*H*), 4.77 (1H, s, *H*-1), 4.04 (1H, d, *J* 6.0, *H*-2), 3.89 (4H, m, *H*-3, *H*-4, 2x *H*-6), 3.83 (1H, m, *H*-5), 3.72 (2H, m, *H*-6', *H*-6"), 3.54 (2H, m, *H*-6', *H*-6"), 3.38 (3H, s, OCH_3), 1.95 (1H, m, *H*-4' or *H*-4"), 1.82 (1H, m, H-5'$_{eq}$), 1.71 (2H, m, H-5"$_{eq}$, *H*-4' or *H*-4"), 1.50 (1H, m, H-3'$_{eq}$), 1.34 (1H, m, H-3"$_{eq}$), 1.16 (4H, m, H-3'$_{ax}$, H-3"$_{ax}$, H-5'$_{ax}$, H-5"$_{ax}$), 1.04 (9H, s, $C(CH_3)_3$), 0.89-0.87 (6H, m, 2x CH_3); δ_C (100 MHz , $CDCl_3$): 135.91, 135.59, 133.95, 133.30, 129.49, 127.59, 127.49 (Aromatic*C*), 100.89 (*C*-1), 98.01, 97.53 (*C*-2', *C*-2"), 71.78, 69.77, 67.77 (*C*-2, *C*-3, *C*-4), 62,62 (*C*-6), 62.07 (*C*-5), 60.86, 60.81 (*C*-6', *C*-6"), 54.52 (OCH_3), 37.14, 36.98 (*C*-5', *C*-5"), 33.48, 33.38 (*C*-3', *C*-3"), 26.73 ($C(CH_3)_3$), 24.51, 24.39 (*C*-4', *C*-4"), 22.28, 22.22 (2x CH_3), 19.27 ($C(CH_3)_3$); ν_{max} (film)/cm^{-1} 3506, 3003, 2972, 2933, 2872, 1472, 1456, 1428, 1383, 1272, 1194, 1137, 1112, 1048, 1032, 986, 942, 908, 824, 703, 610; *m/z* (FAB) 649 $(M+Na)^+$, 626 $(M)^+$, 625 $(M-H)^+$, 595, 568, 537, 517, 339, 309, 289, 267. Found $(M-OCH_3)^+$ 595.3132. $C_{34}H_{47}O_7Si$ requires 595.3091.

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References

1. Dispiroketals in Synthesis (Part 16): Beziudenhoudt, B. C. B., Castle, G. H., Ley, S. V., *Recl. Trav. Chim. Pays-Bas.*, in press.
2. Green, T. W., Wuts, P. G. M., *Protective groups in Organic Synthesis*; Second Edition; Wiley Interscience: New York, 1991.
3. (a): van Boeckel, C. A. A., van Boom, J. H., *Tetrahedron*, **1985**, *41*, 4545, 4557; (b): Verdegaal, C. H. M. Jannse, de Rooij, J. F. M., van Boom, J. H., *Tetrahedron Lett.*, **1980**, *21*, 1571; (c): Oltvoort, G. G., van Boeckel, C. A. A., De Koning, G. A., van Boom, J. H., *Synthesis*, **1981**, 305.
4. (a): De Belder, A. N., *Carbohydr. Chem. Biochem.*, **1977**, *34*, 179; (b): Clode, D. M., *Chem. Rev.*, **1979**, *79*, 491; (c): Ferrier, R. J., Collins, P. M., *Monosaccharide Chemistry*, 1972, Penguin Books; London.
5. Boons, G-J., Entwistle, D. A., Ley, S. V., Woods, M., *Tetrahedron Lett.*, **1993**, *34*, 5649.
6. Hughes, A. B., Ley, S. V., Priepke, H. M. W., Woods, M., *Tetrahedron Lett.*, **1994**, *35*, 773.
7 Entwistle, D. A., Hughes, A. B., Ley, S. V., Visentin, G., *Tetrahedron Lett*, **1994**, *35*, 777
8 Hannesian, S., Lavallée, P., *Can. J. Chem.*, **1975**, *53*, 2975.
9 The preparation of enantiomerically pure dienes **1** and **2** will be reported in due course.
10 For the preparation of enantiomerically pure **3** see : Genicot, C., Ley, S. V., *Synthesis*, in press
11 Boons, G-J., Downham, R., Kim, K-S., Ley, S. V., Woods, M., *Tetrahedron*, **1994**, *50*, 7157.
12 Lorette, N. B., Howard, W. L., *J. Org. Chem.*, **1961**, *26*, 3112.
13 Schwesinger, R., *Nachr. Chem. Tech. Lab.*, **1990**, *38*, 1214
14 Methyl-α-D-glucopyranoside identical to a sample purchased from Aldrich.
15 (a): Veeneman, G. H., van Boom, J. H., *Tetrahedron Lett.*, **1990**, *31*, 275; (b): Toshima, K., Nozaki, H., Innokuchi, H., Nakata, M., Kinoshita, G. H., *Tetrahedron Lett.*, **1993**, *34*, 1911.
16 Entwistle, D. A., Ph.D Thesis, University of London, 1994
17 Eugenia, N. M., Glaudenmans, C. P. J., *J. Org. Chem.*, **1987**, *52*, 5255.
18 Shan, S. H., Jain, R. J., Matta, K. L., *Carbohydr. Res.*, **1990**, *207*, 57.

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