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STUDIES OF THE SELECTIVE SILYLATION OF METHYL α- AND β-D-ALDOHEXOPYRANOSIDES: STABILITY OF THE PARTIALLY PROTECTED DERIVATIVES IN POLAR SOLVENTS

THÉRÈSE HALMOS, ROLAND MONTSERRET, JEAN FILIPPI, AND KOSTAS ANTONAKIS
Institut de Recherches Scientifiques sur le Cancer du C.N.R.S., 94802 Villejuif (France)
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ABSTRACT

Treatment of methyl α- (**1**) and β-D-glucopyranosides, methyl α- (**3**) and β-D-galactopyranosides, and methyl α-D-mannopyranoside (**5**) with 2, 3, or 4 mol. equiv. of *tert*-butyldimethylsilyl (TBDMS) chloride under two conditions afforded mixtures of TBDMS ethers which were identified. The following compounds were isolated in synthetically useful yields, the 2,6-di-TBDMS ether of **1** (70%), the 2,6-di- and 2,3,6-tri-TBDMS ethers of **3** (84% and 57%, respectively), and the 2,6-di-and 3,6-di-TBDMS ethers of **5** (50% and 80%, respectively). In dipolar solvents, no migration of the TBDMS groups was detected between partially silylated hydroxyl groups, but the addition of a base (triethylamine or imidazole) caused migration to vicinal *cis* positions.

INTRODUCTION

The *tert*-butyldimethylsilyl (TBDMS) group[1] is useful for temporary protection of hydroxyl groups since it is stable under a wide range of conditions and is removed readily by reaction with fluoride ion or by treatment with acid. Furthermore, it can be easily replaced by acyl groups using tetrabutylammonium fluoride in the presence of acid anhydrides[2]. The use of this group has been suggested for the selective protection of the primary hydroxyl groups in diols[3], nucleosides[3,4], and other carbohydrate derivatives[5].

Selective protection of secondary hydroxyl groups of ribo- and arabino-nucleosides with *tert*-butyldimethylsilyl chloride (TBDMSCl) has been extensively studied[6–9] and the use of 2′-TBDMS-protected ribonucleosides as building blocks in oligonucleoside syntheses has been recommended[6,10,11]. However, there is little information on the selectivity of the reaction of TBDMSCl with the secondary hydroxyl groups of alkyl hexopyranosides. Di-TBDMS derivatives of the title compounds were prepared by reaction with 2 mol. equiv. of the reagent[12,13]. We now report on the selective reaction of methyl α- (**1**) and β-D-glucopyranoside (**2**), methyl α- (**3**) and β-D-galactopyranoside (**4**), and methyl α-D-mannopyranoside (**5**), using TBDMSCl in *N,N*-dimethylformamide–imidazole[1] (*A*) and in *N,N*-dimethylformamide–triethylamine–4-dimethylaminopyridine[3] (*B*).

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TABLE I

YIELDS (%) OF PARTIALLY PROTECTED METHYL GLYCOSIDES UNDER CONDITIONS *A*

Compound	*TBDMSCl (mol. equiv.)*	*6*[a]	*2,6*	*3,6*	*2,3,6*	*2,4,6*	*2,3,4,6*	*Total*
1	2.2	2	70	11	9			92
	3.2		42	15	7	11		75
	4.3			3	29	42	5	79
2	2.2	31	20	20				71
	3.2		28	29	1		16	74
	4.3		7	17	8		38	70
3	2.2		66	21	10			97
	3.2		84		14			98
	4.3		33		57	6		96
4	2.2		35	43	8			86
	3.2		31		24	25		80
	4.3		20		39	38		97
5	2.2		50	33	9			97 (97)[b]
	3.2		40	16	9	10		75
	4.3		28		21	30	5	84

[a]Positions of TBDMS substituents. [b]The 4,6-isomer was isolated also in 5% yield.

TABLE II

YIELDS (%) OF PARTIALLY PROTECTED METHYL GLYCOSIDES UNDER CONDITIONS *B*

Compound	*TBDMSCl (mol. equiv.)*	*6*[a]	*2,6*	*3,6*	*Tri*	*Total*
1	2.2	2	38	38	12	90
2	2.2	4	38	31	3	76 (80)[b]
3	2.2		38	46	15	99
4	2.2		48	43	8	99
5	2.2		10	80	8	98

[a]Position of TBDMS substituents. [b]The 4,6-isomer was also isolated in 4% yield.

RESULTS AND DISCUSSION

The silylations were performed under two sets of conditions (*A* and *B*, see Experimental) and the products were isolated by column chromatography on silica gel. Product distributions and yields are summarised in Tables I and II. The structures of the products were based upon elemental analyses and 300-MHz ^{1}H-n.m.r. spectroscopy of the acetylated derivatives.

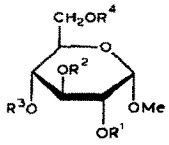
The reaction of methyl α-D-glucopyranoside (**1**) under conditions *A* with 2.2 mol. equiv. of reagent gave 2% of the TBDMS ether **6**, 70% and 11%, respectively, of the di-TBDMS ethers **7** and **8**, and 9% of the tri-TBDMS ether. As expected, **6** was the 6-TBDMS derivative. In the ^{1}H-n.m.r. spectrum of the 3,4-diacetate **10** of **7**, the most shifted signals were those of H-3 (δ 5.30) and H-4 (δ 4.88); thus, the two TBDMS groups in **7** were located at positions 2 and 6. The second TBDMS ether was shown to be the methyl 3,6-di-TBDMS derivative **8**, since, in the ^{1}H-n.m.r. spectrum of its diacetate **11**, the resonances due to H-2 and H-4 were more shifted than that of H-3. The reaction of **1** with 2.2 mol. equiv. of reagent under conditions *B* was much less selective than under conditions *A*: the di-TBDMS ethers **7** and **8** were isolated in equal yields (38%), together with 12% of tri-TBDMS ethers.

The reaction of **1** with 3.3 mol. equiv. of reagent under conditions *A* gave, after chromatography, 42% of the 2,6-di-TBDMS ether **7**, 15% of the 3,6-di-TBDMS ether **8**, 7% of the 2,3,6-tri-TBDMS ether **12** [the most deshielded proton in its acetate **13** was H-4 (δ 4.68)], and 11% of the 2,4,6-tri-TBDMS ether **14** [the most deshielded proton in its acetate **15** was H-3 (δ 5.26)]. Treatment of **1** with 4.3 mol. equiv. of TBDMSCl under conditions *A* gave a mixture of four products, from which the fastest-moving syrupy component (5%) was the tetra-TBDMS ether **16**. The other products were **14** (42%), **12** (29%), and **8** (3%).

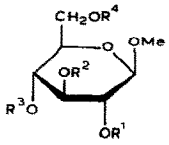
The reaction of methyl β-D-glucopyranoside (**2**) with 2.2 mol. equiv. of TBDMSCl under conditions *A* was incomplete. Chromatography of the product mixture afforded 31% of the 6-TBDMS ether **17**, and 20% each of the 2,6- (**19**) and 3,6-di-TBDMS (**20**) ethers; no trisubstituted derivative was detected. In the ^{1}H-n.m.r. spectrum of the diacetate **21** of **19**, resonances due to H-3 and H-4 appeared as two low-field triplets at δ 5.06 and 4.85, respectively; in the spectrum of the diacetate **22** of **20**, the signal for H-3 was a triplet (δ 3.78) to high-field of the resonances of H-2 (δ 4.84) and H-4 (δ 4.80).

The reaction of **2** with 2.2 mol. equiv. of reagent under conditions *B* was more efficient than under conditions *A*. Thus, only 4% of the TBDMS ether **17** was present in the mixture and the yields of the di-TBDMS ethers **19** and **20** were 38% and 31%, respectively. Also, 4% of the 4,6 di-TBDMS ether was isolated; in the ^{1}H-n.m.r. spectrum of its di-acetate, H-3 (δ 5.01) and H-2 (δ 4.61) were the most deshielded protons. This derivative was not further characterised.

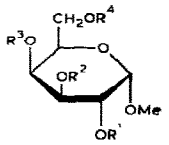
The reaction of **2** with 3.2 mol. equiv. of TBDMSCl under conditions *A* proceeded non-selectively, affording **19** (28%), **20** (29%), the tri-TBDMS ether **23** (1%), and the tetra-TBDMS ether **24** (16%). Compound **23** was shown to be 2,3,6-trisubstituted since, in the ^{1}H-n.m.r. spectrum of its acetate **25**, the low-field signal at δ 4.70 was assigned to H-4. Treatment of **2** with 4.3 mol. equiv. of TBDMSCl under conditions *A* afforded a mixture from which the fastest-moving major component was isolated in 38% yield and identified as the tetra-TBDMS ether **24** (under comparable conditions, the α anomer **1** gave only 8% of tetra-TBDMS ether). From the remainder of the mixture, the 2,3,6-tri-TBDMS ether **23** and the



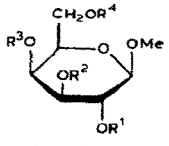
1 $R^1 = R^2 = R^3 = R^4 = H$
6 $R^1 = R^2 = R^3 = H, R^4 = Si$
7 $R^1 = R^4 = Si, R^2 = R^3 = H$
8 $R^1 = R^3 = H, R^2 = R^4 = Si$
9 $R^1 = R^2 = R^3 = Ac, R^4 = Si$
10 $R^1 = R^4 = Si, R^2 = R^3 = Ac$
11 $R^1 = R^3 = Ac, R^2 = R^4 = Si$
12 $R^1 = R^2 = R^4 = Si, R^3 = H$
13 $R^1 = R^2 = R^4 = Si, R^3 = Ac$
14 $R^1 = R^3 = R^4 = Si, R^2 = H$
15 $R^1 = R^3 = R^4 = Si, R^2 = Ac$
16 $R^1 = R^2 = R^3 = R^4 = Si$



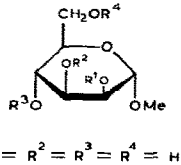
2 $R^1 = R^2 = R^3 = R^4 = H$
17 $R^1 = R^2 = R^3 = H, R^4 = Si$
18 $R^1 = R^2 = R^3 = Ac, R^4 = Si$
19 $R^1 = R^4 = Si, R^2 = R^3 = H$
20 $R^1 = R^3 = H, R^2 = R^3 = Si$
21 $R^1 = R^4 = Si, R^2 = R^3 = Ac$
22 $R^1 = R^3 = Ac, R^2 = R^4 = Si$
23 $R^1 = R^2 = R^4 = Si, R^3 = H$
24 $R^1 = R^2 = R^3 = R^4 = Si$
25 $R^1 = R^2 = R^4 = Si, R^3 = Ac$



3 $R^1 = R^2 = R^3 = R^4 = H$
26 $R^1 = R^4 = Si, R^2 = R^3 = H$
27 $R^1 = R^4 = Si, R^2 = R^3 = Ac$
28 $R^1 = R^3 = H, R^2 = R^4 = Si$
29 $R^1 = R^3 = Ac, R^2 = R^4 = Si$
30 $R^1 = R^2 = R^4 = Si, R^3 = H$
31 $R^1 = R^2 = R^4 = Si, R^3 = Ac$
32 $R^1 = R^3 = R^4 = Si, R^2 = H$
33 $R^1 = R^3 = R^4 = Si, R^2 = Ac$



4 $R^1 = R^2 = R^3 = R^4 = H$
34 $R^1 = R^4 = Si, R^2 = R^3 = H$
35 $R^1 = R^3 = H, R^2 = R^4 = Si$
36 $R^1 = R^4 = Si, R^2 = R^3 = Ac$
37 $R^1 = R^3 = Ac, R^2 = R^4 = Si$
38 $R^1 = R^2 = R^4 = Si, R^3 = H$
39 $R^1 = R^3 = R^4 = Si, R^2 = H$
40 $R^1 = R^2 = R^4 = Si, R^3 = Ac$
41 $R^1 = R^3 = R^4 = Si, R^2 = Ac$



5 $R = R^2 = R^3 = R^4 = H$
42 $R^1 = R^4 = Si, R^2 = R^3 = H$
43 $R^1 = R^4 = Si, R^2 = R^3 = Ac$
44 $R^1 = R^3 = H, R^2 = R^4 = Si$
45 $R^1 = R^3 = Ac, R^2 = R^4 = Si$
46 $R^1 = R^2 = R^4 = Si, R^3 = H$
47 $R^1 = R^3 = R^4 = Si, R^2 = H$
48 $R^1 = R^2 = R^4 = Si, R^3 = Ac$
49 $R^1 = R^3 = R^4 = Si, R^2 = Ac$
50 $R^1 = R^2 = R^3 = R^4 = Si$

Si = *tert*-butyldimethylsilyl

2,6- (**19**) and 3,6-di-TBDMS (**20**) ethers were isolated in yields of 8%, 7%, and 17%, respectively.

The reaction of methyl α-D-galactopyranoside (**3**) under conditions *A* with 2.2 mol. equiv. of TBDMSCl gave a product mixture from which 66% of the 2,6-di-TBDMS derivative (**26**) was isolated crystalline after column chromatography. The ^{1}H-n.m.r. spectrum of the diacetate **27** of **26** showed that the most deshielded protons were H-3 (δ 5.17) and H-4 (δ 5.44). The crystalline 3,6-di-TBDMS ether **28** was also isolated (21%). In the ^{1}H-n.m.r. spectrum of the diacetate **29** of **28**, signals due to H-2 (δ 4.95) and H-4 (δ 5.32) appeared at lower field than that of H-3 (δ 4.12). In addition, a mixture of tri-TBDMS ethers (10%) was isolated which was not further purified.

Treatment of **3** with 2.2 mol. equiv. of TBDMSCl was less selective under conditions *B* and afforded **28** (46%), **26** (38%), and tri-TBDMS ethers (15%). The reaction of **3** under conditions *A* with 3.2 mol. equiv. of TBDMSCl gave 84% of **26**

and 14% of the 2,3,6-tri-TBDMS ether **30**. The ^{1}H-n.m.r. spectrum of the acetate **31** of **30** contained a narrow doublet of doublets at δ 5.25 (J 3.2 and 1.1 Hz), diagnostic of H-4 of a galactopyranoside in the $^4C_1$ conformation.

When **3** was treated with 4.3 mol. equiv. of TBDMSCl under conditions *A*, the formation of the tetra-TBDMS ether was not detected by t.l.c. The major product (57%) was the 2,3,6-tri-TBDMS ether **30**. The 2,4,6-tri-TBDMS ether **32** was also isolated (6%); in the ^{1}H-n.m.r. spectrum of its acetate **33**, the lowest-field doublet of doublets (δ 5.08) was assigned to H-3. The third component of the mixture was the 2,6-di-TBDMS ether **26** (33%).

The reaction of methyl β-D-galactopyranoside (**4**) with 2.2 mol. equiv. of TBDMSCl under conditions *A* afforded a mixture of products which contained no mono-TBDMS ether (t.l.c.). Chromatography of the mixture gave the 2,6- (**34**, 35%, crystalline) and 3,6-di-TBDMS ether (**35**, 43%, amorphous) together with 8% of tri-TBDMS ethers, which were not identified. In the ^{1}H-n.m.r. spectrum of the diacetate **36** of **34**, the signals for H-3 (δ 4.87) and H-4 (δ 5.40) were shifted much more than that of H-2 (δ 3.69). Likewise, for the diacetate **37** of **35**, the signal for H-3 (δ 3.77) appeared at higher field than those of H-2 (δ 5.06) and H-4 (δ 5.31).

Treatment of **4** with 2.2 mol. equiv. of TBDMSCl under conditions *B* caused little change, and the yields for the tri-TBDMS ethers, **34**, and **35** were 8%, 48%, and 43%, respectively. The reaction of **4** under conditions *A* with 3.2 mol. equiv. of TBDMSCl gave, after chromatography, 24% of the 2,3,6- (**38**) and 25% of the 2,4,6-tri-TBDMS ether (**39**), together with a mixture (31%) of two di-TBDMS ethers, which was not further purified. In the ^{1}H-n.m.r. spectrum of the acetate **40** of **38**, the most deshielded signal was a narrow doublet of doublets for H-4 at δ 5.26. Likewise, for the acetate **41** of **39**, the signal for H-3 appeared at lower field (δ 4.76) than those of H-2 (δ 3.80) and H-4 (δ 4.04).

With 4.3 mol. equiv. of TBDMSCl under conditions *A*, **4** afforded a mixture, from which the 2,3,6- (**38**, 39%) and the 2,4,6-tri-TBDMS ether (**39**, 38%) were isolated. The relatively high reactivity of the axial HO-4 compared to that of the equatorial HO-3 is noteworthy. The fraction (20%) of di-TBDMS ethers was not characterised.

Treatment of methyl α-D-mannopyranoside (**5**) under conditions *A* with 2.2 mol. equiv. of TBDMSCl followed by column chromatography gave the 2,6- (**42**, 50%), 3,6- (**44**, 33%), and 4,6-di-TBDMS (5%) derivatives. In the ^{1}H-n.m.r. spectrum of the diacetate **43** of **42**, H-2 (δ 3.98) was more shielded than H-3 (δ 5.15) and H-4 (δ 5.26). Likewise, for the diacetate **45** of **44**, the signal due to H-3 (δ 4.05) appeared at higher field than those of H-2 (δ 5.04) and H-4 (δ 5.03); for the diacetate of the 4,6-isomer, the signals for H-2 (δ 5.17) and H-3 (δ 5.06) were the most shifted. This isomer was not further characterised. The reaction mixture also contained 9% of tri-TBDMS ethers which were not characterised. In contrast, when **5** was treated with 2.2 mol. equiv. of TBDMSCl under conditions *B*, the major product was **44** (80%) and only 10% of **42** was obtained. Thus, depending on the reaction conditions, **42** or **44** could be prepared in synthetically useful yields.

When **5** was treated with 3.2 mol. equiv. of TBDMSCl under conditions *A*, **42** (40%) and **44** (16%) were isolated together with the 2,3,6- (**46**, 9%) and the 2,4,6-tri-TBDMS (**47**, 10%) derivatives. In the ^{1}H-n.m.r. spectrum of the acetate **48** of **46**, the signal for H-4 was a low-field triplet at δ 5.07; for the acetate **49** of **47**, the signal for H-3 was a low-field doublet of doublets at δ 4.91.

The reaction of **5** with 4.3 mol. equiv. of TBDMSCl under conditions *A* gave only 5% of the tetra-TBDMS derivative **50** together with **46** (21%) and **47** (30%). The fraction (28%) of di-TBDMS ethers was not characterised.

Thus, the methyl glycosides examined show good selectivity in their reaction towards TBDMSCl, which depends on the reaction conditions. Several useful derivatives can be obtained, for example, methyl 2,6-di-*O*- and 3,4,6-tri-*O*-*tert*-butyldimethylsilyl-α-D-glucopyranosides, methyl 2,6-di-*O*- and 2,3,6-tri-*O*-*tert*-butyldimethylsilyl-α-D-galactopyranosides, and methyl 2,6- and 3,6-di-*O*-*tert*-butyldimethylsilyl-α-D-mannopyranosides. The differential selectivity observed under conditions *A* and *B* could arise either from different reaction mechanisms or from the migration of the *tert*-butyldimethylsilyl group during the reaction. The migration of the *tert*-butyldimethylsilyl group under basic conditions between *cis*-hydroxyl groups of ribonucleosides[6,7,11,14,15] and between *trans*-diaxial hydroxyl groups of a 1,6-anhydroglucose derivative[16] has been reported. Accordingly, the stability of the partially protected glycosides described above was investigated in various solvents in the presence and absence of added bases.

When solutions of several silylated glycosides in methanol or pyridine were stored at room temperature, no isomerisation was detected during 24 h. In the ribonucleoside field, migration proceeded rapidly in these solvents[7,12,13]. In 0.01M triethylamine in methanol, pyridine, or *N,N*-dimethylformamide, no appreciable rearrangement occurred between *trans*-hydroxyl groups of the derivatives examined, as well as the *cis*-hydroxyl groups of the α-D-galactopyranoside derivative. In contrast, considerable 3→2 migration occurred when methyl 3,6-di-*O*-*tert*-butyldimethylsilyl-α-D-mannopyranoside was treated with methanolic triethylamine. The effect of triethylamine in *N,N*-dimethylformamide was less and it was not detectable in pyridine. In imidazole–*N,N*-dimethylformamide, migration was more pronounced between *cis*-hydroxyl groups. Thus, ~80% of the 3,6-di-TBDMS-mannopyranoside derivative was converted into the 2,6-isomer, and appreciable 3→4 migration occurred in 2,3,6-tri-TBDMS derivatives of both galactopyranosides. Furthermore, in the presence of imidazole, the 3,6-di-TBDMS derivative of the α-D-galactopyranoside gave traces of a new product which was not characterised. Presumably, it was the 4,6-isomer, since, in t.l.c., it migrated as a di-TBDMS derivative and it differed from the 2,6- and the 3,6-isomers.

The above observations suggest that different selectivities under conditions *A* and *B* arise from both migration and different reaction mechanisms. Thus, the 3,6-isomer was formed preferentially on dimolar *tert*-butyldimethylsilylation of methyl α-D-mannopyranoside, as would be expected by analogy with the results of selective acylation[17]. It was isolated in high yield under conditions *B* where migra-

tion was slow, whereas, under conditions *A*, imidazole-catalysed 3→2 migration was efficient, and the main product, the 2,6-isomer, was the result of thermodynamic control. In contrast, the opposite selectivity on dimolar *tert*-butyldimethylsilylation of methyl α-D-glucopyranoside under conditions *A* and *B* could not be explained by migration. Thee greater selectivity under conditions *A* may be associated with lower reaction rates that permit preferential reaction with HO-2, which is the most reactive of the secondary hydroxyl groups[18]. However, under conditions *B*, the reactive species is probably the *tert*-butyldimethylsilyl-4-dimethylaminopyridinium ion[3], the enhanced reactivity of which results in no differentiation between secondary OH groups.

The relatively high yields of the 2,4,6-isomers in the tri- and tetra-molar *tert*-butyldimethylsilylations of **1**, **4**, and **5** contrast with the results of selective acylation[18], where, if formed, they are minor products. However, in the presence of sodium hydride, selective benzylation of methyl 2,6-di-*O*-benzyl-α- and -β-D-galactopyranosides[19] and methyl α-D-glucopyranoside[20] gives the 2,4,6-isomers as major products, showing the enhanced reactivity of HO-4 relative to that of HO-3 in a strongly alkaline medium. Apparently, this is also true for moderately alkaline media, and *tert*-butyldimethylsilylation at position 4 appears to involve direct attack, since no isomerisation occurred with the 2,3,6- and 2,4,6-tri-TBDMS derivatives of **1** and **5**. In contrast, 3→4 migration was appreciable in the 2,3,6-tri-TBDMS derivative of **4**, and production of the 2,4,6-isomer appears to be a result of both direct *tert*-butyldimethylsilylation at position 4 and migration to this position.

In conclusion, the *tert*-butyldimethylsilyl group appears to be a valuable protecting-group for the synthesis of partially protected carbohydrate derivatives. In alkaline media, migration involves only *cis*-hydroxyl groups and these compounds may have value in synthesis if strongly basic conditions are avoided.

EXPERIMENTAL

Experimental methods. — T.l.c. was carried out on Silica Gel 60 F_{254} (Merck), and Silica Gel 60 (230–400 mesh, Merck) was used for flash chromatography[21], with hexane (*A*), and 9:1 (*B*), 39:1 (*C*), and 99:1 (*D*) hexane–ethyl acetate. ^{1}H-N.m.r. spectra were recorded with a Bruker MSL 300 spectrometer. Chemical shifts are relative to the residual proton signal of $CDCl_3$. Optical rotations were measured with a Roussel–Jouan Quick polarimeter. The TBDMS derivatives were acetylated conventionally with acetic anhydride–pyridine. The products, which were usually non-crystalline, were used solely for n.m.r. spectroscopy and were not characterised.

General procedure for the partial tert-*butyldimethylsilylation of* **1–5**. — *Method* A. To a stirred solution of the anhydrous glycoside and imidazole (2 mmol/mmol of TBDMSCl) in anhydrous *N,N*-dimethylformamide (1 mL/mmol of the sugar) was added dropwise a solution of the indicated amount of TBDMSCl in the

same solvent (1–2 mL). Stirring was continued for 24 h at room temperature, the mixture was concentrated *in vacuo* at 30°, and a solution of the residue in dichloromethane was washed with aqueous 10% NH_4Cl and water, dried (Na_2SO_4), and concentrated. The residue was subjected to column chromatography.

Method B. To a stirred solution of the anhydrous glycoside (0.5 mmol), triethylamine (0.167 mL, 1.2 mmol), and 4-dimethylaminopyridine (5 mg, 0.04 mmol) in *N,N*-dimethylformamide (0.5 mL) was added dropwise a solution of TBDMSCl (166 mg, 1.1 mmol) in the same solvent (0.5 mL). The mixture was stored at room temperature for 24 h and processed as in method *A*.

*Reaction of methyl α-*D*-glucopyranoside* (**1**) *with TBDMSCl.* — (*a*) *2.2 Mol.* The product obtained by treatment of **1** (194 mg, 1 mmol) with TBDMS (332 mg, 2.2 mmol) under conditions *A* was purified by flash chromatography (solvent *A* followed by solvent *B*). The first fraction was a mixture (48 mg, 9%) of tri-TBDMS derivatives which was not purified. Eluted second was methyl 3,6-di-*O-tert*-butyldimethylsilyl-α-D-glucopyranoside (**8**; 46 mg, 11%), $[\alpha]_D^{22}$ +80° (*c* 0.15 chloroform); lit.[12] m.p. 46–48°, $[\alpha]_D^{20}$ +74.74° (chloroform).

Anal. Calc. for $C_{19}H_{42}O_6Si_2$: C, 53.99; H, 10.02. Found: C, 54.13; H, 9.90.

Acetylation of **8** gave **11**. ^{1}H-N.m.r. data ($CDCl_3$): δ 4.89 (d, 1 H, *J* 3.7 Hz, H-1), 4.79 (dd, 1 H, *J* 9.9 Hz, H-4), 4.65 (dd, 1 H, *J* 9.7 Hz, H-2), 4.08 (dd, 1 H, *J* 8.8 Hz. H-3), 3.7–3.56 (m, 3 H, H-5,6,6').

Eluted next was methyl 2,6-di-*O-tert*-butyldimethylsilyl-α-D-glucopyranoside (**7**; 296 mg, 70%), isolated as an amorphous solid, $[\alpha]_D^{22}$ +63° (*c* 0.2, chloroform); lit.[12] $[\alpha]_D^{20}$ +12.8° (chloroform).

Anal. Calc. for $C_{19}H_{42}O_6Si_2$: C, 53.99; H, 10.02. Found: C, 54.10; H, 9.99.

Acetylation of **7** gave **10**. ^{1}H-N.m.r. data ($CDCl_3$): δ 5.30 (t, 1 H, *J* 9.3 Hz, H-3), 4.88 (t, 1 H, *J* 10 Hz, H-4), 4.63 (d, 1 H, *J* 3.7 Hz, H-1), 3.78 (m, 1 H, 3.3 Hz, H-5), 3.73 (dd, 1 H, *J* 9.3 Hz, H-2), 3.64 (d, 2 H, H-6,6').

Eluted last was methyl 6-*O-tert*-butyldimethylsilyl-α-D-glucopyranoside (**6**; 6 mg, 2%), $[\alpha]_D^{22}$ +110° (*c* 0.2, chloroform); lit.[22] $[\alpha]_D^{18}$ +114° (methanol).

Anal. Calc. for $C_{13}H_{28}O_6Si$: C, 50.65; H, 9.09. Found: C, 51.0; H, 8.93.

Acetylation of **6** afforded **7**. ^{1}H-N.m.r. data ($CDCl_3$): δ 5.44 (t, 1 H, *J* 9.2 Hz, H-3), 4.98 (t, 1 H, *J* 10 Hz, H-4), 4.90 (d, 1 H, *J* 3.7 Hz, H-1), 4.83 (dd, 1 H, *J* 9.8 Hz, H-2), 3.79 (m, 1 H, *J* 3.3 Hz, H-5), 3.65 (d, 2 H, H-6,6').

Similar fractionation of the mixture of products obtained from **1** after reaction under conditions *B* gave a mixture (32 mg, 12%) of tri-TBDMS derivative **8** (80 mg, 38%), **7** (80 mg, 38%), and **6** (3 mg, 2%).

(*b*) *3.2 Mol.* Column chromatography (solvent *C* followed by solvent *B*) of the mixture of products obtained under conditions *A* gave, first, amorphous methyl 2,4,6-tri-*O-tert*-butyldimethylsilyl-α-D-glucopyranoside (**14**; 59 mg, 11%), $[\alpha]_D^{22}$ +74° (*c* 0.2, chloroform).

Anal. Calc. for $C_{25}H_{56}O_6Si_3$: C, 55.92; H, 10.51. Found: C, 56.13; H, 10.58.

Acetylation of **14** gave **15**. ^{1}H-N.m.r. data ($CDCl_3$): δ 5.26 (dd, 1 H, *J* 8.3 Hz, H-3), 4.58 (d, 1 H, *J* 3.7 Hz, H-1), 3.82–3.51 (m, 4 H, H-4,5,6,6'), 3.53 (dd, 1 H, *J* 9.8 Hz, H-2).

Eluted second was methyl 2,3,6-tri-*O*-*tert*-butyldimethylsilyl-α-D-glucopyranoside (**12**; 37 mg, 7%), m.p. 38°, $[\alpha]_D^{22}$ +50° (*c* 0.2, chloroform).

Anal. Calc. for $C_{25}H_{56}O_6Si_3$: C, 55.92; H, 10.51; Found: C, 56.13; H, 10.41.

Acetylation of **12** afforded **13**. ^{1}H-N.m.r. data ($CDCl_3$): δ 4.68 (dd, 1 H, *J* 9.7 Hz, H-4), 4.63 (d, 1 H, *J* 3.5 Hz, H-1), 3.91 (t, 1 H, *J* 8.7 Hz, H-3), 3.61 (dd, 1 H, *J* 9.1 Hz, H-2), 3.68–3.52 (m, 3 H, H-5,6,6′).

The two last fractions contained **7** (177 mg, 42%) and **8** (63 mg, 15%).

(*c*) *4.3 Mol.* Fractionation (solvent *C* followed by solvent *B*) of the mixture of products obtained after reaction under conditions *A* gave methyl 2,3,4,6-tetra-*O*-*tert*-butyldimethylsilyl-α-D-glucopyranoside (**16**; 32 mg, 5%), **14** (225 mg, 42%), **12** (155 mg, 29%), and **8** (13 mg, 3%).

The structure of **16** was established on the basis of ^{1}H-n.m.r. data and lack of reaction with acetic anhydride–pyridine. The compound was not investigated further.

Reaction of methyl β-D-glucopyranoside (**2**) *with TBDMSCl.* — (*a*) *2.2 Mol.* Three fractions (solvent *B* followed by ethyl acetate) were obtained after reaction under conditions *A*: methyl di-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranoside (**20**; 85 mg, 20%), methyl 2,6-di-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranoside (**19**; 85 mg, 20%), and methyl 6-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranoside (**17**; 96 mg, 31%).

Compound **20** was amorphous, $[\alpha]_D^{22}$ −22° (*c* 0.2, chloroform); lit.[12] m.p. 65°, $[\alpha]_D^{20}$ −20.2° (chloroform).

Anal. Calc. for $C_{19}H_{42}O_6Si_2$: C, 53.99; H, 10.02. Found: C, 54.01; H, 9.99.

Acetylation of **20** afforded **22**. ^{1}H-N.m.r. data ($CDCl_3$): δ 4.84 (dd, 1 H, *J* 9.3 Hz, H-2), 4.80 (dd, 1 H, *J* 9.8 Hz, H-4), 4.22 (d, 1 H, *J* 8 Hz, H-1), 3.78 (dd, 1 H, *J* 8.1 Hz, H-3), 3.61 (m, 2 H, H-6,6′), 3.37 (m, 1 H, H-5).

Compound **19** was a syrup, $[\alpha]_D^{22}$ −32° (*c* 0.2, chloroform); lit.[12] $[\alpha]_D^{20}$ −31.05° (chloroform).

Anal. Calc. for $C_{19}H_{42}O_6Si_2$: C, 53.99; H, 10.02. Found: C, 53.96; H, 9.90.

Acetylation of **19** gave **21**. ^{1}H-N.m.r. data ($CDCl_3$): δ 5.06 (t, 1 H, *J* 9 Hz, H-3), 4.85 (t, 1 H, *J* 9.5 Hz, H-4), 4.15 (d, 1 H, *J* 7.6 Hz, H-1), 3.6 (m, 2 H, H-6,6′), 3.5 (m, 2 H, $J_{2,3}$ 9.1 Hz, H-2,5).

Compound **17** had m.p. 106–107°, $[\alpha]_D^{22}$ −35° (*c* 0.2, chloroform); lit.[12] m.p. 97–99°, $[\alpha]_D^{20}$ −35.92° (chloroform).

Anal. Calc. for $C_{13}H_{28}O_6Si_2$: C, 50.62; H, 9.15. Found: C, 50.17; H, 9.17.

Acetylation of **17** gave **18**. ^{1}H-N.m.r. data ($CDCl_3$): δ 4.99 (t, 1 H, *J* 9.6 Hz, H-4), 4.93 (t, 1 H, *J* 9.7 Hz, H-2), 4.38 (d, 1 H, *J* 8 Hz, H-1), 4.17 (t, 1 H, *J* 9.5 Hz, H-3), 3.69 (m, 2 H, H-6,6′), 3.51 (m, 1 H, H-5).

Fractionation (solvent *A* followed by solvent *B* and ethyl acetate) of the product mixture obtained from **2** under conditions *B* gave a mixture (16 mg, 3%) of the tri-TBDMS derivatives, **20** (131 mg, 31%), **19** (80 mg, 38%), and **17** (6 mg, 4%).

(*b*) *3.2 Mol.* The following fractions (solvent *C* followed by solvent *B*) were obtained after reaction under conditions *A*: methyl 2,3,4,6-tetra-*O*-*tert*-butyl-

dimethylsilyl-β-D-glucopyranoside (**24**; 104 mg, 16%), methyl 2,3,6-tri-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranoside (**23**; 5 mg, 1%), **20** (123 mg, 29%), and **19** (118 mg, 28%).

Compound **24** was a syrup, the structure of which was established on the basis of ^{1}H-n.m.r. data and lack of reaction with acetic anhydride–pyridine, and it was not investigated further.

Compound **23** had $[\alpha]_D^{22}$ −16° (*c* 0.2, chloroform).

Anal. Calc. for $C_{25}H_{56}O_6Si_3$: C, 55.92; H, 10.51. Found: C, 55.85; H, 10.45.

Acetylation of **23** afforded **25**. ^{1}H-N.m.r. data ($CDCl_3$): δ 4.70 (t, 1 H, *J* 8.6 Hz, H-4), 4.07 (d, 1 H, *J* 7.1 Hz, H-1), 3.62 (t, 1 H, *J* 8.5 Hz, H-3), 3.6–3.4 (m, 4 H, H-2,5,6,6′).

(*c*) *4.2 Mol.* Column chromatography (solvent *C* followed by solvent *B*) of the mixture of products obtained after reaction under conditions *A* gave **24** (247 mg, 38%), **23** (43 mg, 8%), **20** (72 mg, 17%), and **19** (30 mg, 7%).

Reaction of methyl α-D-galactopyranoside (**3**) *with TBDMSCl.* — (*a*) *2.2 Mol.* The following fractions (solvent *C* followed by solvent *B*) were obtained after reaction under conditions *A*: a mixture (54 mg, 10%) of tri-TBDMS derivatives, methyl 2,6-di-*O*-*tert*-butyldimethylsilyl-α-D-galactopyranoside (**26**; 279 mg, 66%); methyl 3,6-di-*O*-*tert*-butyldimethylsilyl-α-D-galactopyranoside (**28**; 89 mg, 21%).

Compound **26** had m.p. 132–133°, $[\alpha]_D^{22}$ +76° (*c* 0.2, chloroform).

Anal. Calc. for $C_{19}H_{42}O_6Si_2$: C, 53.99; H, 10.02. Found: C, 53.92; H, 9.97.

Acetylation of **26** gave **27**. ^{1}H-N.m.r. data ($CDCl_3$): δ 5.44 (dd, 1 H, *J* 0.9 Hz, H-4), 5.17 (dd, 1 H, *J* 3 Hz, H-3), 4.68 (d, 1 H, *J* 3.8 Hz, H-1), 4.03 (dd, 1 H, *J* 10.2 Hz, H-2), 3.99 (m, 1 H, *J* 7.2 Hz, H-5), 3.74–3.52 (m, 2 H, H-6,6′).

Compound **28** had m.p. 60–61°, $[\alpha]_D^{22}$ +87° (*c* 0.2, chloroform).

Anal. Calc. for $C_{19}H_{42}O_6Si_2$: C, 53.99; H, 10.02. Found: C, 54.10; H, 9.90.

Acetylation of **28** gave **29**. ^{1}H-N.m.r. data ($CDCl_3$): δ 5.32 (dd, 1 H, *J* 1 Hz, H-4), 5.0–4.90 (m, 2 H, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 9.5 Hz, H-1,2), 4.12 (dd, 1 H, *J* 3.5 Hz, H-3), 3.90 (m, 1 H, *J* 6.3 Hz, H-5), 3.58 (d, 2 H, H-6,6′).

The following fractions were obtained after reaction under conditions *B*; a mixture (40 mg, 15%) of tri-TBDMS derivatives, **26** (80 mg, 38%), and **28** (97 mg, 46%).

(*b*) *3.2 Mol.* Column chromatography (solvent *C* followed by solvent *B*) of the mixture of products obtained after reaction under conditions *A* gave methyl 2,3,6-tri-*O*-*tert*-butyldimethylsilyl-α-D-galactopyranoside (**30**; 75 mg, 14%) and **26** (355 mg, 84%).

Compound **30** was amorphous, $[\alpha]_D^{22}$ +76° (*c* 0.2, chloroform).

Anal. Calc. for $C_{25}H_{56}O_6Si_3$: C, 55.92; H, 10.51. Found: C, 56.13; H, 10.41.

Acetylation of **30** gave **31**. ^{1}H-N.m.r. data ($CDCl_3$): δ 5.25 (dd, 1 H, *J* 1.1 Hz, H-4), 4.68 (d, 1 H, *J* 3.4 Hz, H-1), 3.95–3.88 (m, 3 H, $J_{2,3}$ 9.4 Hz, $J_{3,4}$ 3.2 Hz, H-2,3,5), 3.56 (m, 1 H, H-6), 3.34 (m, 1 H, H-6′).

(*c*) *4.2 Mol.* The following fractions were obtained after reaction under condi-

tions *A*: methyl 2,4,6-tri-*O*-*tert*-butyldimethylsilyl-α-D-galactopyranoside (**32**; 32 mg, 6%), **30** (306 mg, 57%), and **26** (139 mg, 33%).

Compound **32** had $[\alpha]_D^{22}$ +55° (*c* 0.2, chloroform).

Anal. Calc. for $C_{25}H_{56}O_6Si_3$: C, 55.92; H, 10.51. Found: C, 56.31; H, 10.58.

Acetylation of **32** gave **33**. ^{1}H-N.m.r. data ($CDCl_3$): δ 5.08 (dd, 1 H, *J* 2.5 Hz, H-3), 4.65 (d, 1 H, *J* 3.6 Hz, H-1), 4.15 (dd, 1 H, *J* 10.3 Hz, H-2), 4.09 (d, 1 H, *J* 0 Hz, H-4), 3.73 (t, 1 H, *J* 6.4 Hz, H-5), 3.61 (d, 2 H, H-6,6′).

Reaction of methyl β-D-galactopyranoside (**4**) *with TBDMSCl.* — (*a*) *2.2 Mol.* The following fractions (solvent *D* followed by solvent *B*) were obtained after reaction under conditions *A*: a mixture (43 mg, 8%) of tri-TBDMS derivatives, 2,6-di-*O*-*tert*-butyldimethylsilyl-β-D-galactopyranoside (**34**; 148 mg, 35%), methyl 3,6-di-*O*-*tert*-butyldimethylsilyl-β-D-galactopyranoside (**35**; 181 mg, 43%).

Compound **34** had m.p. 84–85°, $[\alpha]_D^{22}$ −13° (*c* 0.18, chloroform); lit.[13] m.p. 86–88°, $[\alpha]_D^{20}$ −20.3° (chloroform).

Anal. Calc. for $C_{19}H_{42}O_6Si_2$: C, 53.99; H, 10.02. Found: C, 53.97; H, 10.01.

Acetylation of **34** gave **36** ^{1}H-N.m.r. data ($CDCl_3$): δ 5.40 (dd, 1 H, *J* 0.9 Hz, H-4), 4.87 (dd, 1 H, *J* 3.4 Hz, H-3), 4.17 (d, 1 H, *J* 7.5 Hz, H-1), 3.69 (dd, 1 H, *J* 9.7 Hz, H-2), 3.70–3.55 (m, 3 H, H-5,6,6′).

Compound **35** was semi-crystalline, $[\alpha]_D^{22}$ −3° (*c* 0.2, chloroform); lit.[13] $[\alpha]_D^{20}$ −4.4° (chloroform).

Anal. Calc. for $C_{19}H_{42}O_6Si_2$: C, 53.99; H, 10.02. Found: C, 53.92; H, 10.03.

Acetylation of **35** gave **37**. ^{1}H-N.m.r. data ($CDCl_3$): δ 5.31 (dd, 1 H, *J* 1 Hz, H-4), 5.06 (dd, 1 H, *J* 9.7 Hz, H-2), 4.26 (d, 1 H, *J* 8.1 Hz, H-1), 3.77 (dd, 1 H, *J* 3.5 Hz, H-3), 3.65–3.45 (m, 3 H, H-5,6,6′).

The following fractions were obtained after reaction under conditions *B*: a mixture (21 mg, 8%) of tri-TBDMS derivatives, **34** (101 mg, 48%), and **35** (91 mg, 43%).

(*b*) *3.2 Mol.* Column chromatography (solvent *D* followed by solvent *B*) of the mixture of products obtained after reaction under conditions *A* gave methyl 2,3,6-tri-*O*-*tert*-butyldimethylsilyl-β-D-galactopyranoside (**38**; 129 mg, 24%), methyl 2,4,6-tri-*O*-*tert*-butyldimethylsilyl-β-D-galactopyranoside (**39**; 134 mg, 25%), and a mixture (131 mg, 31%) of di-TBDMS derivatives.

Compound **38** was a syrup, $[\alpha]_D^{22}$ −2.5° (*c* 0.2, chloroform).

Anal. Calc. for $C_{25}H_{56}O_6Si_3$: C, 55.92; H, 10.51. Found: C, 55.57; H, 10.69.

Acetylation of **38** afforded **40**. ^{1}H-N.m.r. data ($CDCl_3$): δ 5.26 (d, 1 H, *J* 0 Hz, H-4), 4.06 (d, 1 H, *J* 7.4 Hz, H-1), 3.6 (m, 2 H, $J_{3,4}$ 2.2 Hz, H-2,3), 3.65–3.51 (m, 3 H, H-5,6,6′).

Compound **39** was a syrup, $[\alpha]_D^{22}$ −10° (*c* 0.2, chloroform).

Anal. Calc. for $C_{25}H_{56}O_6Si_3$: C, 55.92; H, 10.51. Found: C, 55.96; H, 10.49.

Acetylation of **39** gave **41**. ^{1}H-N.m.r. data ($CDCl_3$): δ 4.76 (dd, 1 H, *J* 2.7 Hz, H-3), 4.11 (d, 1 H, *J* 7.5 Hz, H-1), 4.04 (d, 1 H, *J* 0 Hz, H-4), 3.66 (d, 2 H, H-6,6′), 3.41 (t, 1 H, *J* 6.7 Hz, H-5).

(*c*) *4.3 Mol.* The following fractions (solvent *D* followed by solvent *B*) were

obtained after reaction under conditions *A*: **38** (209 mg, 39%), **39** (204 mg, 38%), and a mixture (84 mg, 20%) of di-TBDMS derivatives.

Reaction of methyl α-D-mannopyranoside (**5**) *with TBDMSCl.* — (*a*) *2.2 Mol.* The following fractions (solvent *D* followed by solvent *B*) were obtained after reaction under conditions *A*: a mixture (48 mg, 9%) of tri-TBDMS derivatives, methyl 3,6-di-*O-tert*-butyldimethylsilyl-α-D-mannopyranoside (**44**; 139 mg, 33%), and methyl 2,6-di-*O-tert*-butyldimethylsilyl-α-D-mannopyranoside (**42**; 211 mg, 50%).

Compound **44** had m.p. 49–50°, $[\alpha]_D^{22}$ +42° (*c* 0.2, chloroform); lit.[13] m.p. 46–48°, $[\alpha]_D^{20}$ +36.9° (chloroform).

Anal. Calc. for $C_{19}H_{42}O_6Si_2$: C, 53.99; H, 10.02. Found: C, 53.92; H, 10.01.

Acetylation of **44** afforded **45**. ^{1}H-N.m.r. data ($CDCl_3$): δ 5.04 (m, 2 H, $J_{2,3}$ 3.6 Hz, H-2,4), 4.61 (d, 1 H, *J* 1.5 Hz, H-1), 4.05 (dd, 1 H, *J* 9.3 Hz, H-3), 3.7–3.57 (m, 3 H, H-5,6,6').

Compound **42** was amorphous, $[\alpha]_D^{22}$ +19° (*c* 0.2, chloroform).

Anal. Calc. for $C_{19}H_{42}O_6Si_2$: C, 53.99; H, 10.02. Found: C, 53.95; H, 9.99.

Acetylation of **42** gave **43**. ^{1}H-N.m.r. data ($CDCl_3$): δ 5.26 (t, 1 H, *J* 9.3 Hz, H-4), 5.15 (dd, 1 H, *J* 9.1 Hz, H-3), 4.53 (d, 1 H, *J* 1.8 Hz, H-1), 3.98 (dd, 1 H, *J* 2.8 Hz, H-2), 3.75–3.6 (m, 3 H, H-5,6,6').

The following compounds were obtained after reaction under conditions *B*: a mixture (43 mg, 8%) of tri-TBDMS derivatives, **44** (338 mg, 80%), and **42** (42 mg, 10%).

(*b*) *3.2 Mol.* Column chromatography (solvent *D* followed by solvent *B*) of the mixture of products obtained after reaction under conditions *A* gave methyl 2,4,6-tri-*O-tert*-butyldimethylsilyl-α-D-mannopyranoside (**47**; 54 mg, 10%), methyl 2,3,6-tri-*O-tert*-butyldimethylsilyl-α-D-mannopyranoside (**46**; 48 mg, 9%), **44** (68 mg, 16%), and **42** (169 mg, 40%).

Compound **47** had $[\alpha]_D^{22}$ +26° (*c* 0.2, chloroform).

Anal. Calc. for $C_{25}H_{56}O_6Si_3$: C, 55.92; H, 10.51. Found: C, 56.07; H, 10.48.

Acetylation of **47** gave **49**. ^{1}H-N.m.r. data ($CDCl_3$): δ 4.91 (dd, 1 H, *J* 9.5 Hz, H-3), 4.47 (d, 1 H, *J* 1.6 Hz, H-1), 4.03 (t, 1 H, *J* 9.4 Hz, H-4), 4.01 (t, 1 H, *J* 2.9 Hz, H-2), 3.49 (m, 1 H, H-5), 3.84–3.73 (m, 2 H, H-6,6').

Compound **46** was a syrup, $[\alpha]_D^{22}$ +16° (*c* 0.2, chloroform).

Anal. Calc. for $C_{25}H_{56}O_6Si_3$: C, 55.92; H, 10.51. Found: C, 56.07; H, 10.56.

Acetylation of **46** gave **48**. ^{1}H-N.m.r. data ($CDCl_3$): δ 5.07 (t, 1 H, *J* 9.3 Hz, H-4), 4.51 (d, 1 H, *J* 2.0 Hz, H-1), 3.92 (dd, 1 H, *J* 9.2 Hz, H-3), 3.77 (t, 1 H, *J* 2.7 Hz, H-2), 3.68–3.52 (m, 3 H, H-5,6,6').

(*c*) *4.3 Mol.* The following fractions (solvent *D* followed by solvent *B*) were obtained after reaction under conditions *A*: methyl tetra-*O-tert*-butyldimethylsilyl-α-D-mannopyranoside (**50**; 32 mg, 5%), **47** (161 mg, 30%), **46** (113 mg, 21%), and a mixture (118 mg, 28%) of di-TBDMS derivatives.

Compound **50** was a syrup, $[\alpha]_D^{22}$ +59° (*c* 0.2, chloroform).

Isomerisation studies. — Equilibration reactions were monitored by t.l.c. (solvent *B*; 8:2 hexane–ethyl acetate; 1:1 light petroleum–dichloromethane). When

migration was detected, the reaction was stopped by acetylation of the mixture, and the relative proportions of the isomers were estimated by ^{1}H.n.m.r. spectroscopy. Compounds **7, 8, 12, 13, 19, 20, 26, 28, 30, 38, 42, 44,** and **46** were studied in the following systems: methanol, pyridine and *N,N*-dimethylformamide, 0.01M triethylamine in methanol, pyridine, and *N,N*-dimethylformamide, and 2M imidazole in *N,N*-dimethylformamide. The concentration of the solution with respect to the glycoside was 0.1M in the experiments with pure solvents and with added triethylamine, and 0.5M in the experiments with imidazole. Systems in which no migration was detected after 24 h at room temperature: methanol, *N,N*-dimethylformamide, pyridine, triethylamine–pyridine. Systems in which isomerisation occurred (24 h, room temperature): triethylamine–methanol: ~10% of **44** from **42**, and ~50% of **42** from **44**; triethylamine–*N,N*-dimethylformamide: traces of **42** from **44**, and traces of **44** from **42**; imidazole–*N,N*-dimethylformamide: ~80% of **42** from **44**, ~10% of **44** from **42**, ~10% of a new di-TBDMS derivative (probably the 4,6-isomer) from **28, 30:32** ~1:1, and **38:39** ~1:5.

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