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SYNTHESIS OF ACETAL-α-GLUCOSIDES. A STEREOSELECTIVE ENTRY INTO A NEW CLASS OF COMPOUNDS*,†

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ABSTRACT

Acetal-glycosides are a new class of compounds, which became of special interest as enzyme inhibitors and cytostatics for the treatment of cancer. In a highly stereoselective glucosidation, acetyl-protected acetal-α-glucosides such as methoxymethyl 2,3,4,6-tetra-*O*-acetal-α-D-glucopyranoside (**5a**) were obtained in 60–80% yield by treatment of 2,3,4,6-tetra-*O*-acetyl-1-*O*-trimethylsilyl-α-D-glucopyranose (**1**) with acetals, *e.g.* dimethoxymethane (**3a**) in the presence of a catalytic amount of trimethylsilyl trifluoromethanesulfonate (**4**) at −70°. The glucosidation involves a new principle, where the reaction does not take place at the anomeric carbon, but with retention at the oxygen of the trimethylsilyloxy group on C-1. The trimethylsilyl derivative **1** may be used as a pure anomer or prepared by *in situ* anomerisation from a mixture of **1** and its β anomer **26**. The yields in the glucosidation can be increased by the addition of acetone or the aldehydes that correspond to the acetals (except formaldehyde). In a one pot synthesis, the reaction of phenylacetaldehyde (**23e**), trimethylsilyl methyl ether (**14a**), and **1** at −70° in the presence of **4** led directly to 1-methoxy-2-phenylethyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside (**5e**). *O*-Deacetylation of the obtained acetyl-protected acetal-α-glucosides gave the free acetal-α-glucosides in excellent yield. Thus **5e** afforded 1-methoxy-2-phenylethyl α-D-glucopyranoside (**6e**). Since the acetal-α-glucosides can be cleaved by enzymic hydrolysis to the corresponding aldehydes under mild conditions, glucose may be used as a protective group for the CHO function. Similarly, 2,3,4,6-tetra-*O*-benzyl-1-*O*-trimethylsilyl-α-D-glucopyranose (**2**) was used to afford benzyl-protected acetal-α-glucosides.

*Dedicated to Professor Dr. Burckhardt Helferich on the hundredth anniversary of his birth.
†Glucosidation, part 6. For part 5 see ref. 1. A preliminary communication of this work has already appeared (ref. 2).
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INTRODUCTION

A multitude of compounds in Nature exist as glycosides[3]. In addition the importance of oligosaccharides, especially glycoconjugates[4], is still growing because of their special biological functions. The basic requirement for the synthesis of these compounds was the development of methods for the stereoselective formation of the glycosidic bond[5]. In this respect the procedures introduced by Helferich[6] have proved to be very effective and are still of great use. However, nearly all methods developed so far are based on an attack at the anomeric carbon of the sugar moiety*. The stereochemistry in these reactions is either controlled by a neighbouring group-active substituent or by the configuration at C-1 of the activated sugar derivative used.

In this paper we describe a new, highly selective glycosidation, in which the anomeric carbon is not involved in the reaction. This procedure is most suitable for the glycosidation of compounds which can form a stabilized carbocation, such as acetals or hemiacetals. The method gives access to glycosides of simple cyclic and acyclic hemiacetals, and thus to a class of compounds which was nearly unknown thus far[8] and not accessible in a general and stereoselective way†. However, the structural element of these compounds is wide-spread in Nature, in substances such as the trehaloses and sucrose as well as the iridoid and secoiridoid glycosides[10].

The acetal-glycosides are of special interest, since they can act as inhibitors for glycosidases[11]. In addition, by using the new method highly cytotoxic aldehydes may be transformed into nontoxic acetal-glycosides, which may release their cytocidal principle by an enzymatic or proton-catalyzed hydrolysis. Thus, these compounds may be useful in the treatment of cancer[12].

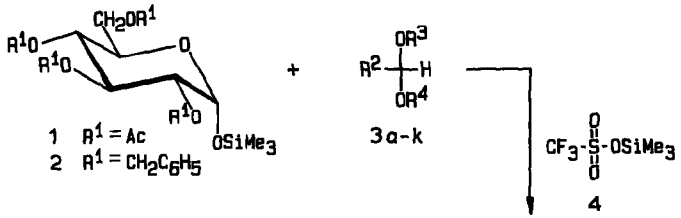
RESULTS AND DISCUSSION

The synthesis of the acetyl-protected acetal-α-glucosides **5a–k** was accomplished by the reaction of 2,3,4,6-tetra-*O*-acetyl-1-*O*-trimethylsilyl-α-D-glucopyranose (**1**) with the acetals **3a–k** in the presence of a catalytic amount of trimethylsilyl trifluoromethanesulfonate (**4**) in dry dichloromethane at $-70°$. In this reaction, which proceeds with retention of configuration at C-1, the acetyl group at C-2 does not behave as a neighboring group-active substituent. The formation of a carbocation at C-1 can be excluded, since in that case β-glucosides should be formed. The reaction time varies from 20 to 60 h, therefore the transformation should be followed by t.l.c. Solvolysis of the tetraacetates **5a–k** with sodium methoxide or potassium carbonate in methanol at 20° afforded the unprotected acetal-glucosides **6a–k** in excellent yields (>90%).

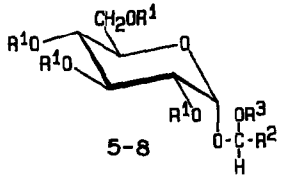
The educt **1** can easily be obtained as a crystalline compound with high

*An exception is the method of von Wartburg[7].

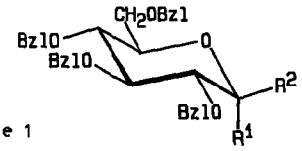
†The new method which was developed by us is already used extensively by other scientists[9].



Series	R^2	R^3	R^4
a	H	CH_3	CH_3
b	H	CH_3	C_6H_5
c	CH_3	C_2H_5	C_2H_5
d	C_3H_7	CH_3	CH_3
e	$CH_2C_6H_5$	CH_3	CH_3
f	$CH_2CH(OCH_3)_2$	CH_3	CH_3
g	$C_2H_4OCH_2C_6H_5$	C_2H_5	C_2H_5
h	CH_2OCH_3	CH_3	CH_3
i	CH_2Cl	CH_3	CH_3
j	CH_2Br	CH_3	CH_3
k	CH_2Br	C_2H_5	C_2H_5



5a-k R^1 = Ac
6a-k R^1 = H
7a-k R^1 = Bzl
8a-k R^1 = Bzl, β-configuration at C-i



Scheme 1

9 R^1=OH R^2=H
10 R^1=H R^2=OH
11 R^1=H R^2=OSiMe3

anomeric purity from the mixture of acetyl-protected trimethylsilyl-α- and -β-glucosides by anomerisation with **4** in dichloromethane[13]. This seems to be a general method which can also be used with great success for other sugars[1].

The reaction of **1** with **3a** gave only one α-glucoside (**5a**), in a 70% yield. However, in using the prochiral acetals **3c–k** a new chiral center is formed in the product, leading to two diastereomers. The asymmetric induction varied from 1:1.2 for **3h** to 3.2:1 for **3e**. Interestingly, the selectivity in the formation of the β-glycosides is lower[14]. The diastereomeric forms of the protected and unprotected acetal-glycosides, **5c–k** and **6c–k** respectively, could be separated by chromatography on silica gel or aluminium oxide, although the separation was sometimes difficult. However, in some cases the diastereomers could be purified by fractional crystallisation.

In the glucosidation symmetric acetals were used mostly but mixed acetals such as **3b** can also be employed. However, the reaction leads to a single product only if either the alkoxy or the phenoxy moiety is removed selectively from **3b** in the transformation. It was found that in the case of **3b** the phenoxy group was lost exclusively to afford **5b**. From this it follows that for the synthesis of phenoxy-substituted acetals of type **5**, diphenyl acetals[15] would have to be employed as reagents.

In a similar manner, as described for **1**, the benzyl-protected 1-*O*-trimethylsilylglucose **2** can be used in the glucosidation of **3**. Thus the reaction of **2** with **3b** in the presence of **4** at −70° yielded 84% of the α-glycoside **7b** within 32 h. Thus, the benzyl protecting group also did not influence the stereochemistry at C-1 in the products. However, glucosidation with **2** was slower than with **1**, and also the amount of catalyst had to be increased to ensure a reasonable rate.

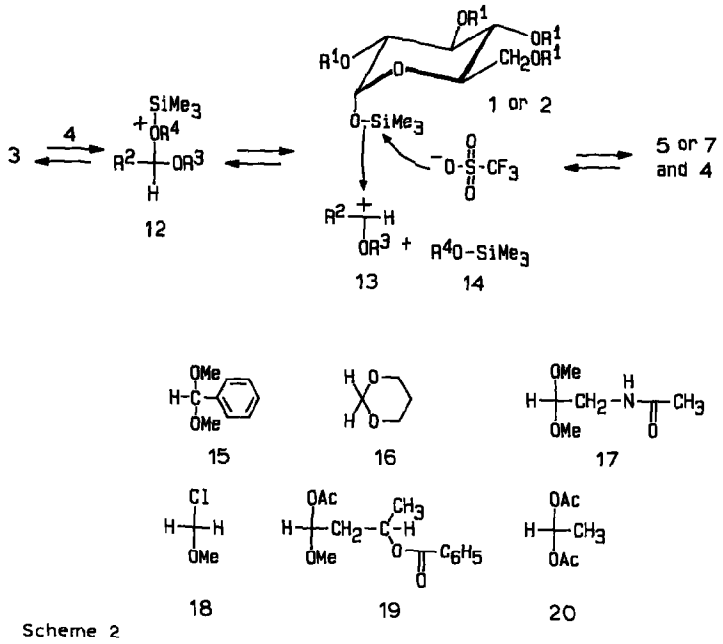
There is another disadvantage in using **2**, namely that the compound cannot be obtained in a high anomeric purity. Thus **9**, the precursor of **2**, could only be synthesized as a 80:20 mixture with the β anomer **10**, which was not removable by chromatography or crystallisation*. The silylation of **9/10** (80:20) with *N*-trimethylsilylacetamide in pyridine[17] gave a 4:5 mixture of **2** and **11**, whereas with hexamethyldisilazane/chlorotrimethylsilane and pyridine an 80:20 mixture of **2** and **11** was obtained, in nearly 100% yield. On using this mixture for the glucosidation of **3b**, **3d–f**, and **3h–k**, 80:20 mixtures of the α-glycosides **7b**, **7d–f**, and **7h–k** and the corresponding β-glycosides **8b**, **8d–f**, and **8h–k** were formed, and these anomers could not be separated. However, purification of the α-glycosides **7** was possible by hydrogenolytic debenzylation and enzymatic hydrolysis of the β-glycosides with emulsin. It is noteworthy that the selectivity in the glucosidation of **2** with prochiral acetals **3c–f** and **3h–k** was higher than with **1**, ranging from 1.5:1 for **3h** to 10:1 for **3e**.

Mechanism and improvement of the method. — Detailed studies on the mechanism of this reaction have not been made so far. But we assume that the first step in the glucosidation is the formation of an oxonium ion **12**, which can collapse to the carbenium ion **13** and the trimethylsilyl alkyl ether **14**. Reaction of **13** with **1** or **2** at the oxygen of the trimethylsilyloxy group gives **5** or **7** with retention of the configuration at C-1, and in addition trimethylsilyl triflate **4**: this explains why **4** is necessary only in a catalytic amount. To exclude the possibility that **12** is directly attacked by **1** or **2** we are currently investigating the reaction with chiral acetals.

The new method of glycosidation is very mild and imposes modest requirements on the educts. Nearly all sugars can be used in this reaction, provided that the trimethylsilyl glycosides are available in sufficient anomeric purity, and that functional groups which could react with **4** are absent. However, there are some acetals which cannot be glycosidated, such as **15**, **16**, and **17**. Chloromethyl methyl ether (**18**) reacting with **1** at 0° gives 60% of the acetal-α-glucoside **5a** with substitution of the halogen atom, and acetylated hemiacetals of type **19** even at −70° afford the corresponding acetal-glycosides, with loss of acetate. In contrast, the diacetate **20** does not react even at 20°. This clearly shows that the rate of the reaction depends on the ease of formation of the oxonium ion **12** and the stability of the proposed intermediate carbocation **13**.

The glucosidation is reversible, although the equilibrium lies on the side of

*For the synthesis of **9/10** a new procedure has been developed which is a combination of the methods published by Koto, Schmidt and Glaudemans[16].

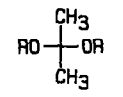


Scheme 2

the products. However, removal of the trimethylsilyl alkyl ether **14** from the reaction mixture can improve the yields and in addition can shorten the reaction time. This is extremely useful in the transformation of highly valuable sugars or acetals. With the addition of acetone to the reaction mixture **14** is transformed into a ketal **21**, which does not react with **1** at −70°. Thus, the reaction of **1** with **3a** and 2 mol of acetone in the presence of a catalytic amount of **4** at −70° yields 91% of **5a** within 24 h. However, the addition of acetone was not useful with methyl phenyl acetals (**3b**) or diphenyl acetals, since **14** ($R^4 = C_6H_5$) does not react with acetone to give the corresponding ketal **22**. Instead of acetone the aldehydes **23** from which the acetals **3** are derived can be used. This procedure was better than the use of acetone for highly sensitive carbohydrates like deoxy sugars or unsaturated sugars. In the glucosidation only 50 mol% of acetone or aldehyde is necessary, but a 5-fold excess did not affect the transformation adversely.

In some cases an increase in the amount of the catalyst **4** provided a better yield in a shorter reaction time, especially when **4** was added in successive increments.

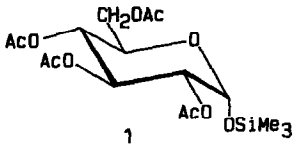
One-pot synthesis of acetal-α-glucosides from aldehydes. — The acetal-α-glucosides **5c–k** and **7c–k** can also be obtained in excellent yield directly from the corresponding aldehydes **23** by the reaction of 1 mole of **1** or **2**, 2 moles of **23**, and 2.5 moles of the trimethylsilyl alkyl ether **14a** or **14c** in the presence of a catalytic amount of trimethylsilyl trifluoromethanesulfonate (**4**; 5–30 mol%) at −70° in dichloromethane. We assume that in the reaction not the acetal[17] **3** but the



21 R= CH_3 or C_2H_5
22 R= C_6H_5

23

3 R= R^3
24 R= H
25 R= $SiMe_3$



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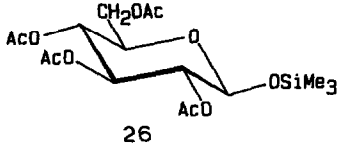

26

hemiacetal **24** or its trimethylsilyl ether **25** acts as starting material for the glucosidation[18].

This procedure not only gives access to the acetal-α-glucosides **5** or **7** in a most simple and convenient way but also opens the possibility of using glucose as a protective group for aldehydes. Thus, after solvolysis of the acetyl groups in **5** to afford **6**, glucose can be removed at pH 6–7 with an α-glucosidase to give back the aldehyde **23** under very mild conditions. However, the one-pot glucosidation is not appropriate in the case of unstable aldehydes.

Glucosidation of **1** *prepared by* in situ *anomerisation.* — In the glucosidations described so far anomerically pure **1** was used. However, the procedure can be simplified even more by using a mixture of the α and β anomer (**1/26**) as starting material. Thus, the mixture of **1** and **26** in any ratio was first treated with 4 mol% of **4** for 10 h at 0°, and afterwards either the acetals **3** were added at 0° or the aldehyde **23** and the trimethylsilyl alkyl ether **14** were added at −70°. The reaction time varied from 2 to 48 h depending on the reactivity of the acetals **3** or the aldehyde **23**. With highly reactive acetals such as **3b, 3d**, and **3e** the glucosidation must be carried out at −10 to −20°. Using this procedure the corresponding β-glucosides were not detected in the raw product (<3%), however, 10–15% of trehaloses were also formed in the reaction. The disaccharides were easily removed by chromatography on silica gel with 1:1 petroleum ether–ethyl acetate as solvent or the formation of trehaloses could be avoided by a modification of the procedure. Thus treatment of a mixture of the trimethylsilyl α,β-glucosides **1/26** and the acetals **3** with 8 mol% of **4** at 0° afforded **5** in an excellent yield without formation of oligosaccharides. However, β-glucosides were obtained as byproducts in 6% yield; they could be removed by enzymatic hydrolysis after deacetylation. With highly reactive acetals this procedure is less useful, since the amount of β-glucosides increases and the overall yield decreases.

TABLE I

^{1}H- AND ^{13}C-N.M.R. PARAMETERS (δ, J) OF **5**, **6**, AND **7** AT 200 MHz[a]

Compounds	*Chemical shifts*							
	H-1 ($J_{1,2}$)	*H-1'* ($J_{1',2'a}/J_{1',2'b}$)	*OCH$_3$*	*OCH$_2$–CH$_3$* ($J_{2',1''}$)	*C-1*	*C-1'*	*C-2'*	*O–CH$_2$–R*
5a	5.32 d (3.75)	4.75[b] (6.5)	3.40		92.61	93.53		55.94
(*R*)-**5d**	5.34 d (3.75)	4.69 t (6.0)	3.30		92.56	102.35	35.54	52.09
(*S*)-**5d**	5.32 d (3.75)	4.53 t (6.0)	3.41		92.56	106.22	36.56	55.36
(*R*)-**5e**	5.29 d (3.75)	[c]	3.36		91.99	101.23	39.64	51.70
(*S*)-**5e**	5.35 d (3.75)	4.74 t (6.0)	3.38		92.66	106.14	41.15	55.58
(*R*)-**5f**	5.35 d (3.75)	4.80 t (6.0)	3.35		92.34	99.53	36.82	52.69
(*S*)-**5f**	5.32 d (3.75)	4.64 dd (5.5/6.5)	3.42		92.73	103.39	37.82	55.58
(*R*)-**5g**	5.38 d (3.75)	[c]		1.15 t (7.0)	92.13	99.43	34.75	61.92
(*S*)-**5g**	5.34 d (3.75)	[c]		1.15 t (7.0)	92.26	102.07	35.33	63.70
(*R*)-**5h**	5.38 d (3.75)	4.81 t (5.25)	3.41		93.35	100.58	72.68	53.87
(*S*)-**5h**	5.40 d (3.75)	4.72 t (5.5)	3.47		91.86	103.09	73.25	56.12
(*R*)-**5i**	5.36 d (3.75)	4.81 t (5.5)	3.42		92.91	101.06	43.51	53.68
(*S*)-**5i**	5.41 d (3.75)	4.71 t (5.5)	3.49		92.13	104.06	44.04	56.36
(*R*)-**5j**	5.36 d (3.75)	4.85 t (5.5)	3.40					

TABLE I *(continued)*

Compounds	*Chemical shifts*							
	H-1 ($J_{1,2}$)	*H-1'* ($J_{1',2'a}/J_{1',2'b}$)	OCH_3	OCH_2–CH_3 ($J_{2',1'}$)	*C-1*	*C-1'*	*C-2'*	*O–CH_2–R*
(*S*)-**5j**	5.41 d (3.75)	4.78 t (5.5)	3.48					
(*R*)-**5k**	5.38 d (3.75)	[c]		1.21 t (7.0)	92.58	100.27	31.66	62.69
(*S*)-**5k**	5.45 d (3.75)	[c]		1.21 t (7.0)	91.92	102.38	32.01	64.57
6a	5.10 d (3.75)	4.82[d] (6.5)	3.45		96.47	94.00		56.33
(*R*)-**6c**	5.13 d (3.75)	4.99 q (5.25)		1.16 t (7.0)				
(*S*)-**6c**	5.09 d (3.75)	4.93 q (5.25)		1.16 t (7.0)				
(*R*)-**6d**	5.10 d (3.75)	4.77 t (5.5)	3.36		96.81	102.22	36.66	52.78
(*S*)-**6d**	5.03 d (3.75)	4.60 dd (5.5/6.5)	3.42		97.84	104.54	37.47	56.01
(*R*)-**6e**	5.10 d (3.75)	4.93 t (6.0)	3.39		97.02	102.98	41.24	53.34
(*S*)-**6e**	5.13 d (3.75)	4.81 dd (4.0/7.0)	3.48		97.02	107.11	42.14	56.22
(*R*)-**6f**	5.12 d (3.75)	4.82 t (6.0)	3.38		96.96	99.90	38.30	53.40
(*S*)-**6f**	5.02 d (3.75)	4.66 dd (5.5/6.5)	3.42		97.84	104.54	39.36	56.01
(*R*)-**6h**	5.14 d (3.75)	4.88 t (5.5)	3.44		97.59	100.75	73.74	54.50
(*S*)-**6h**	5.10 d (3.75)	4.76 t (5.5)	3.48		97.59	104.34	74.47	56.34

(*R*)-**6i**	5.17 d (3.75)	4.91 dd (4.5/6.0)	3.48		97.70	101.80	44.85	54.58
(*S*)-**6i**	5.17 d (3.75)	4.81 dd (4.0/7.5)	3.52		96.73	104.96	45.34	56.69
(*R*)-**6k**	5.16 d (3.75)	4.97 dd (4.5/6.0)		1.19 t (7.0)	97.21	100.61	32.97	63.67
(*S*)-**6k**	5.19 d (3.75)	4.93 dd (4.0/7.5)		1.20 t (7.0)	96.27	103.10	33.27	65.22
7a	5.18 d (3.5)	[c]	3.45		93.41	93.08		56.15
(*R,S*)-**7c**	5.15 d (3.5)	[c]		1.12 t/1.16 t (7.0) (7.0)	93.96	98.27/99.82	20.94/21.01	60.83/62.81
(*R,S*)-**7d**	5.15 d/5.22 d (3.5) (3.5)	[c]	3.36/3.40		93.64	101.09	35.41	51.89
(*R,S*)-**7e**	5.18 d (3.5)	[c]	3.41		93.70/93.64	105.48/101.57	40.09	52.51
(*R,S*)-**7f**	5.16 d/5.21 d (3.5) (3.5)	[c]	3.39/3.42		93.79/93.92	98.70/101.19	36.79	[c]
(*R,S*)-**7h**	5.18 d/5.21 d (3.5) (3.5)	[c]	[c]		94.61/92.94	99.75/102.53	[c]	[c]
(*R,S*)-**7i**	5.17 d/5.22 d (3.5) (3.5)	[c]	3.46/3.48		94.48	100.51	43.66	53.86
(*R,S*)-**7k**	5.17 d/5.23 d (3.5) (3.5)	[c]		1.19 t/1.21 t (7.0) (7.0)	94.16/92.86	99.74/101.81	32.03	62.72

[a]Series **5** and **7** in $CDCl_3$, **6** in acetone-d_6–D_2O. [b]AB-system: δ_A 4.88, δ_B 4.62. [c]Overlapped by other signals. [d]AB-system: δ_A 4.95, δ_B 4.69.

TABLE II

CHEMICAL SHIFT DIFFERENCES FOR (1'*R*) AND (1'*S*) ACETAL-α-GLUCOSIDES **5** AND **6**

Compound	$\delta(1'R) - \delta(1'S)$		
	H-1'	*C-1'*	*O-CH₂R*
5d	+0.16	−3.87	−3.27
5e	—	−4.91	−3.88
5f	+0.16	−3.86	−2.89
5g	—	−2.64	−1.78
5h	+0.09	−2.51	−2.25
5i	+0.11	−3.00	−2.68
5k	—	−2.11	−1.88
6c	+0.06	—	—
6d	+0.17	−4.37	−2.87
6e	+0.12	−4.13	−2.88
6f	+0.16	−4.64	−2.61
6h	+0.12	−3.59	−1.84
6i	+0.10	−3.16	−2.11
6k	+0.04	−2.49	−1.60

Determination of the structures of **5a–k, 6a–k, 7a–f**, and **7h–k**. — The structures of the compounds were determined from ^{1}H- and ^{13}C-n.m.r. data (Table I). Thus the α configuration of the newly formed glycosidic bond was evidenced by a coupling constant, *J*, of 3.75 Hz for the resonance of H-1. In the corresponding β-glucosides[14] signals at δ 4.75–4.85 having *J* 7.5–8 Hz are found for H-1. In the acetyl-protected α-glucosides **5a–k** H-1 absorbs at δ 5.29–5.45, in the benzyl-protected compounds **7a–f** and **7h–k** at δ 5.15–5.23, and in the free glucosides **6a–k** at δ 5.02–5.19.

The configuration* at C-1' can be determined from the chemical shifts of C-1' and H-1'. Our n.m.r. studies[19] of bis-acetals have shown that in compounds having a (1*S*,1'*S*) or (1*R*,1'*R*) configuration the oxygen of the pyran ring system causes a compression of the C-1'–H bond, whereas in compounds having a (1*S*,1'*R*) or (1*R*,1'*S*) configuration this effect is absent. Because of the anomeric effect[20] the C-1–O_{exo} and the C-1'–O_{alkyl} bonds in bis-acetals should be synclinal. This causes a parallel orientation of the C-1–O_{endo} and the C-1'–H bond in the α-glucosides **5, 6**, and **7** having the (*R*) configuration† at C-1', since a parallel orientation of C-1–O_{endo} and C-1'–O_{alkyl} is destabilised by electrostatic repulsive forces. In the acetal-α-glucosides having the (*S*) configuration at C-1' a conformation with a parallel orientation of the C-1–O_{endo} and the C-1'–H bonds would be unfavourable. Thus,

*Primed numbers are used to identify carbon and hydrogen atoms in the aglycon moieties for purposes of discussion and description of n.m.r. spectra only.

†The assignment has been confirmed by an X-ray analysis of (1'*R*)-**5e**.

the compression of the C-1′–H bond[21] in the (1′*R*) acetal-α-glucosides causes an upfield shift of the C-1′ absorption by 2.11–4.91 p.p.m. and a downfield shift of the H-1 resonance by 0.04–0.17 p.p.m. in comparison to the (1′*S*) acetal-α-glucosides. In addition a downfield shift of the carbon in the O–CH_2–R group is found in the (1′*R*) acetal-α-glucosides **5** and **6**.

EXPERIMENTAL

General. — Melting points were determined with a Mettler FP 61 or a Kofler melting-point apparatus, and are uncorrected. Elemental analyses were performed by Mr. Beller, Microanalytical Laboratory, University of Göttingen. Optical rotations were determined with a Perkin–Elmer 241 polarimeter. ^{1}H- and ^{13}C-n.m.r. spectra were recorded with a Varian XL-200 instrument (200 MHz, internal tetramethylsilane). The progress of all reactions was monitored by t.l.c. on DC-Fertigfolien SIL G/UV_{254} (Macherey, Nagel & Co., 0.25 mm). The removal of samples from the reaction mixtures had to be done under completely anhydrous conditions and without changing the temperature in the vessel. Column chromatography was performed on Kieselgel 60 (Merck), Kieselgel 0.040–0.063 and 0.063–0.200 mm (ICN, Biomedicals), and Alumina Woelm N-Super I, type W 200. Solvents used for t.l.c. and column chromatography were: *A*, 1:1 hexane–ethyl acetate; *B*, 6:2:1 chloroform–methanol–hexane; *C*, 1:1 petroleum ether–ethyl acetate; *D*, 3:1 petroleum ether–ethyl acetate; and *E*, 3:1:0.004 hexane–ethyl acetate–triethylamine.

All reactions were carried out under argon and in anhydrous media. It was essential to use pure educts and maintain the stated reaction temperatures, otherwise colouration of the reaction mixtures and loss of selectivity occurred.

General procedures for synthesis:

I. Synthesis of acetal-α-glucosides **5** *from acetals* **3** *and 2,3,4,6-tetra-*O*-acetyl-1-*O*-trimethylsilyl-α-*D*-glucopyranose* (**1**). — To a solution of **1** (420 mg, 1.0 mmol) and **3** (2.0 mmol) in dry dichloromethane (3 mL) at −70° was added trimethylsilyl trifluoromethanesulfonate (**4**; 8 mol%, 0.16 mL of 0.5M solution in dichloromethane or *n*-hexane). The mixture was stirred at −70° until the reaction was complete (20–60 h, t.l.c., silica gel, solvent *A*) and the reaction was quenched by addition of triethylamine (0.5 mL). For workup the solution was either diluted with dichloromethane (20 mL), washed (saturated $NaHCO_3$ solution and brine), and dried (Na_2SO_4), or filtered in a cold state over aluminium oxide (10 g, neutral) with dichloromethane as solvent. Concentration *in vacuo* and column chromatography on silica gel (solvent *A*) afforded **5**.

II. Synthesis of acetal-α-glucosides **5** *from* **1** *and acetals* **3** *with the addition of acetone, or aldehydes* (**23**). — To a solution of **1** (420 mg, 1.0 mmol), **3** (2.0 mmol), and acetone or aldehyde (**23**) corresponding to **3** (0.5–2.5 mmol) in dry

dichloromethane (3 mL) at −70° was added **4** (8 mol%, 0.16 mL of 0.5M solution in dichloromethane or *n*-hexane). The mixture was stirred at −70° for about 20 h and worked up as in general procedure *I*.

III. Synthesis of acetal-α-glucosides **7** *from* **2** *and acetals* **3**. — The reaction was carried out as for glucosidation with **1**; however 30 mol% of **4** (0.60 mL of 0.5M solution in dichloromethane or *n*-hexane) and 1 mL of dichloromethane as solvent were used. The products contained up to 20% of the corresponding β-glucoside, since the **2** used was in fact an 80:20 mixture with **11**.

IV. Synthesis of acetal-α-glucosides **5** *from* **1** *and aldehydes* **23**. — To a solution of **1** (420 mg, 1.0 mmol), aldehyde **23** (2.0 mmol), and trimethylsilyl alkyl ether **14** (2.5 mmol) in dry dichloromethane (5 mL) at −70° was added **4** (8 mol%, 0.16 mL of 0.5M solution in dichloromethane or *n*-hexane). The mixture was stirred for about 24 h (t.l.c.) and worked up as in general procedure *I*.

V. Synthesis of acetal-α-glucosides **5** *from* **1** *and acetals* **3** via in situ *anomerisation*. — *a*. To a solution of a mixture of the trimethylsilyl α and β glucosides **1** and **26** (420 mg, 1.0 mmol) and acetal **3** (2.0 mmol) in dry dichloromethane (5 mL) at 0° was added **4** (8 mol%, 0.16 mL of 0.5M solution in dichloromethane or *n*-hexane). The mixture was stirred for 9–40 h at 0° and worked up as in general procedure *I*. Chromatography afforded **5** and 6–8% of the corresponding β-glucosides.

b. To a solution of a mixture of **1** and **26** (420 mg, 1.0 mmol) in dry dichloromethane (5 mL) at 0° was added **4** (4 mol%, 0.08 mL of 0.5M solution in dichloromethane or *n*-hexane). After stirring for 10 h at 0°, first acetal **3** (2.0 mmol) at 0° or as stated, and after 15 min **4** (0.08 mL of 0.5M solution) were added. After 4 to 40 h the reaction was complete (t.l.c.) and the mixture was worked up as in general procedure *I*. Chromatography on silica gel (solvent *A*) afforded **5** and 10–15% of trehaloses.

VI. Deacetylation of the tetraacetates **5** *to* **6**. — *a*. To a solution of **5** (0.50 mmol) in dry methanol (5 mL) was added sodium methoxide in methanol (1.50 mL of 0.1% solution), and the mixture was stirred for 0.5–3 h at room temperature (t.l.c., solvent *B*). Filtration through silica gel (3 g, solvent methanol), evaporation of the solvent *in vacuo*, and purification by column chromatography (solvent *B*) or crystallisation from ethanol yielded **6**.

b. For sensitive compounds such as the glucosides **5i–k**, potassium carbonate (100 mg) instead of sodium methoxide was used. The reaction and the work up were carried out as in *VIa*.

Synthetic products:

*Methoxymethyl 2,3,4,6-tetra-*O*-acetyl-α-*D*-glucopyranoside* (**5a**). — *a*. The reaction of **1** (420 mg, 1.0 mmol) and **3a** (152 mg, 2.0 mmol) for 50 h according to general procedure *I* gave 275 mg (70%) of **5a** as colourless rhombs.

b. The treatment of **1** (420 mg, 1.0 mmol) with **3b** (276 mg, 2.0 mmol) for 29 h as described in general procedure *I* gave 341 mg (87%) of **5a**.

c. When **1** (420 mg, 1.0 mmol) and **3a** (152 mg, 2.0 mmol) were used as reactants (24 h, general procedure *II*) the yield of **5a** was 356 mg (91%).

d. The reaction of a mixture of **1** and **26** (420 mg, 1.0 mmol) and **3a** (152 mg, 2.0 mmol) for 30 h according to general procedure *Va* afforded 310 mg (79%) of **5a** as a colourless oil, which contained 4% of the β anomer.

e. The treatment of a mixture of **1** and **26** (420 mg, 1.0 mmol) and **3b** (276 mg, 2.0 mmol) for 18 h at −20° according to general procedure *Vb* yielded 321 mg (82%) of **5a**.

Compound **5a** prepared by any of the foregoing procedures had m.p. 108° (from ether–petroleum ether), $[\alpha]_D^{20}$ +158° (*c* 1, chloroform); R_F 0.29 (solvent *A*); ^{1}H-n.m.r. ($CDCl_3$): δ 2.02, 2.04, 2.08, 2.10 (4 s, 12 H, 4 CH_3CO), 3.40 (s, 3 H, OCH_3), 4.05–4.31 (m, 3 H, H-5, 2 × H-6), 4.75 (2 H, AB-system, δ_A 4.88, δ_B 4.62, *J* 6.5 Hz, 2 × H-1′), 4.97 (dd, 1 H, $J_{2,1}$ 3.75, $J_{2,3}$ 10.25 Hz, H-2); 5.10 (t, 1 H, *J* 9.75 Hz, H-4), 5.32 (d, 1 H, $J_{1,2}$ 3.75 Hz, H-1), and 5.53 (dd, 1 H, $J_{3,2}$ 10.3, $J_{3,4}$ 9.75 Hz, H-3); double resonance: δ 5.32→4.97 (d, 1 H, $J_{2,3}$ 10.25 Hz, H-2), 4.10→5.10 (d, 1 H, $J_{4,3}$ 9.75 Hz, H-4); ^{13}C-n.m.r. ($CDCl_3$): δ 20.52, 20.62 (4 CH_3CO), 55.94 (OCH_3), 61.95 (C-6), 67.96 (C-4), 68.57 (C-5), 70.12, 70.46 (C-2,3), 92.61 (C-1), 93.53 (C-1′), 169.48, 169.78, 170.01, and 170.47 (4 CO).

Anal. Calc. for $C_{16}H_{24}O_{11}$ (392.4): C, 48.98; H, 6.17. Found: C, 49.02; H, 6.12.

*Methoxymethyl α-*D*-glucopyranoside* (**6a**). — Compound **5a** (196 mg, 0.50 mmol) treated for 0.5 h according to general procedure *VIa* yielded 102 mg (91%) of **6a** as a colourless oil, $[\alpha]_D^{20}$ +116° (*c* 1, methanol); R_F 0.25 (solvent *B*); ^{1}H-n.m.r. (acetone-d_6–D_2O): δ 3.34–3.87 (m, 6 H, H-2, 3, 4, 5, 2 × H-6), 3.45 (s, 3 H, OCH_3), 4.24 (HDO), 4.82 (2 H, AB-system, δ_A 4.95, δ_B 4.69, *J* 6.5 Hz, 2 × H-1′), and 5.10 (d, 1 H, *J* 3.75 Hz, H-1); ^{13}C-n.m.r. (CD_3OD): δ 56.33 (OCH_3), 62.61 (C-6), 71.68 (C-4), 73.18 (C-5), 74.17 (C-2), 74.91 (C-3), 94.00 (C-1′), and 96.47 (C-1).

Anal. Calc. for $C_8H_{16}O_7$ (224.2): C, 42.86; H, 7.19. Found: C, 42.99; H, 7.26.

*Methoxymethyl 2,3,4,6-tetra-*O*-benzyl-α-*D*-glucopyranoside* (**7a**). — The transformation of **2** (306 mg, 0.50 mmol) and **3b** (138 mg, 1.0 mmol) for 12 h according to general procedure *III* afforded 260 mg (89%) of a colourless oil, $[\alpha]_D^{22}$ +65° (*c* 1, chloroform); R_F 0.36 (solvent *C*); ^{1}H-n.m.r. ($CDCl_3$): δ 3.45 (s, 3 H, OCH_3), 3.51–4.11 (m, 6 H, H-2, 3, 4, 5, 2 × H-6), 4.34–5.02 (m, 10 H, 4 CH_2, 2 × H-1′), 5.18 (d, 1 H, *J* 3.5 Hz, H-1), and 7.02–7.32 (m, 20 H, phenyl).

Anal. Calc. for $C_{36}H_{40}O_7$ (584.7): C, 74.04; H, 6.90. Found: C, 73.92; H, 6.92.

*(1*R,S*)-1-Methoxy-2-phenylethyl 2,3,4,6-tetra-*O*-acetyl-α-*D*-glucopyranoside* (**5e**). — *a.* The reaction of **1** (420 mg, 1.0 mmol) and **3e** (332 mg, 2.0 mmol) for 28 h according to general procedure *I* yielded 380 mg (79%) of **5e** as colourless crystals having a ratio (1′*R*):(1′*S*) of 3.2:1.

b. The transformation of **1** (420 mg, 1.0 mmol), **14e** (R^4 = CH_3; 260 mg, 2.5 mmol), and **23e** (240 mg, 2.0 mmol) for 30 h according to general procedure *IV*

afforded 407 mg (85%) of **5e** as colourless crystals having a ratio (1′*R*):(1′*S*) of 3:1.

c. The reaction of **1/26** (420 mg, 1.0 mmol) and **3e** (332 mg, 2.0 mmol) for 9 h at −10° according to general procedure *Vb* yielded 347 mg (72%) of **5e** as colourless crystals having a ratio (1′*R*):(1′*S*) of 2:1; m.p. 129° (from ether), $[\alpha]_D^{20}$ +150° (*c* 1, chloroform) for (1′*R*):(1′*S*) = 4:1; R_F 0.38 (1′*S*) and 0.35 (1′*R*) (solvent *A*). Isomer (1′*R*)-**5e** was separated by fractional crystallisation from ether and (1′*S*)-**5e** by column chromatography on silica gel (solvent *C*).

(1′*S*)-**5e**: colourless oil, $[\alpha]_D^{20}$ +97° (*c* 1, in chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 1.92, 2.01, 2.03, 2.06 (4 s, 12 H, 4 CH_3CO), 2.91–3.10 (m, 2 H, 2 × H-2′), 3.38 (s, 3 H, OCH_3), 3.96–4.27 (m, 3 H, H-5, 2 × H-6), 4.74 (t, 1 H, *J* 6.0 Hz, H-1′), 4.84–4.94 (m, 1 H, H-2), 5.08 (t, 1 H, *J* 9.8 Hz, 4-H), 5.35 (d, 1 H, *J* 3.75 Hz, H-1), 5.55 (dd, 1 H, $J_{3,2}$ 10.3, $J_{3,4}$ 9.8 Hz, H-3), and 7.19–7.38 (m, 5 H, phenyl).

(1′*R*)-**5e**: colourless crystals, m.p. 133° (from ether), $[\alpha]_D^{20}$ +167° (*c* 1, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 1.99, 2.00, 2.02, 2.07 (4 s, 12 H, 4 CH_3CO), 2.91–3.10 (m, 3 H, 2 × H-2′, H-5), 3.36 (s, 3 H, OCH_3), 3.57 (dd, 1 H, $J_{6a,5}$ 2.3, $J_{6a,6b}$ 12.5 Hz, H-6a), 3.85 (dd, 1 H, $J_{6b,5}$ 4.0, $J_{6b,6a}$ 12.5 Hz, H-6b), 4.84–4.98 (m, 3 H, H-1′, 2, 4), 5.29 (d, 1 H, *J* 3.75 Hz, H-1), 5.40 (dd, 1 H, $J_{3,2}$ 10.3, $J_{3,4}$ 9.8 Hz, H-3), and 7.19–7.38 (m, 5 H, phenyl).

(1′*R*)-**5e**/(1′*S*)-**5e**: ^{13}C-n.m.r. ($CDCl_3$): δ 20.52, 20.55, 20.62, 20.66, 20.70 (4 CH_3CO), 39.64/41.15 (C-2′), 51.70/55.58 (OCH_3), 61.23/61.93 (C-6), 67.16/67.97 (C-4), 67.93/68.51 (C-5), 69.98, 70.38/70.10, 70.65 (C-2, 3), 91.99/92.66 (C-1), 101.23/106.14 (C-1′), 126.63/126.57 (C-6′), 128.57, 129.62/128.36, 129.48 (C-4′, 5′, 7′, 8′), 136.57/136.32 (C-3′), 169.42, 169.94, 170.07, 170.53, 170.58 (*C*=O).

Anal. Calc. for $C_{23}H_{30}O_{11}$ (482.5): C, 57.26; H, 6.27. Found: C, 57.40; H, 6.42.

*(1*R,S*)-1-Methoxy-2-phenylethyl* α-D-*glucopyranoside* (**6e**). — The reaction of **5e** (241 mg, 0.50 mmol) for 0.5 h under the conditions of general procedure *VIa* yielded 150 mg (95%) of **6e** as colourless crystals having a ratio (1′*R*):(1′*S*) of 3.5:1; m.p. 121° (from ethanol), $[\alpha]_D^{20}$ +147° (*c* 1, methanol) for (1′*R*):(1′*S*) = 8:1; R_F 0.37 (solvent *B*); ^{1}H-n.m.r. (acetone-d_6–D_2O): δ 2.90–3.07 (m, 2 H, 2 × H-2′), 3.10–3.84 (m, 6 H, H-2, 3, 4, 5, 2 × H-6), 3.39/3.48 (2 s, 3 H, OCH_3), 3.50 (HDO), 4.81 (dd, 0.3 H, *J* 7.0, *J* 4.0 Hz, H-1′, *S*-epimer), 4.93 (t, 0.7 H, *J* 6.0 Hz, H-1′, *R*-epimer), 5.10/5.13 (2 d, 1 H, *J* 3.75 Hz, H-1), and 7.16–7.38 (m, 5 H, phenyl).

Anal. Calc. for $C_{15}H_{22}O_7$ (314.3): C, 57.32; H, 7.06. Found: C, 57.23; H, 7.15.

*(1*R,S*)-1-Ethoxyethyl* α-D-*glucopyranoside* (**6c**). — The reaction of **1** (210 mg, 0.50 mmol) and **3c** (118 mg, 1.0 mmol) for 33 h according to general procedure *I*, followed by hydrolysis according to general procedure *VIa*, yielded 90 mg (72%) of **6c** as a colourless oil having a ratio (1′*R*):(1′*S*) of 2.5:1; $[\alpha]_D^{20}$ +134° (*c* 1, methanol); lit.[8b] $[\alpha]_D^{20}$ +123° (water).

*(1*R,S*)-1-Methoxybutyl 2,3,4,6-tetra-*O*-acetyl-*α*-D-glucopyranoside* (**5d**). — The reaction of **1** (420 mg, 1.0 mmol) and **3d** (236 mg, 2.0 mmol) for 30 h according to general procedure *I* yielded 355 mg (82%) of **5d** as colourless crystals having a

ratio (1′*R*):(1′*S*) of 2.8:1; m.p. 75.5° (from ether–petroleum ether), $[\alpha]_D^{20}$ +124° (*c* 1, chloroform) for (1′*R*):(1′*S*) = 3:1; R_F 0.41 (solvent *A*).

Anal. Calc. for $C_{19}H_{30}O_{11}$ (434.4): C, 52.53; H, 6.96. Found: C, 52.71; H, 6.87.

*(1*R,S*)-1-Methoxybutyl* α-D-*glucopyranoside* (**6d**). — The treatment of **5d** (217 mg, 0.50 mmol) for 0.5 h according to general procedure *VIa* yielded 128 mg (96%) of colourless crystals having a ratio (1′*R*):(1′*S*) of 3:1; m.p. 93.5° (from ethanol), $[\alpha]_D^{20}$ +147° (*c* 1, methanol); R_F 0.41 (solvent *B*).

Anal. Calc. for $C_{11}H_{22}O_7$ (266.3): C, 49.62; H, 8.33. Found: C, 49.49; H, 8.30.

*(1*R,S*)-1,3,3-Trimethoxypropyl 2,3,4,6-tetra*-O-*acetyl*-α-D-*glucopyranoside* (**5f**). — The reaction of **1** (420 mg, 1.0 mmol) and **3f** (328 mg, 2.0 mmol) for 60 h according to general procedures *I* and *Va* yielded 342 mg (71%) of **5f** as a colourless oil having a ratio (1′*R*):(1′*S*) of 1.7:1; $[\alpha]_D^{20}$ +119° (*c* 1, chloroform); R_F 0.25 (solvent *A*).

Anal. Calc. for $C_{20}H_{32}O_{13}$ (480.5): C, 50.00; H, 6.71. Found: C, 50.18; H, 6.58.

*(1*R,S*)-1,3,3-Trimethoxypropyl* α-D-*glucopyranoside* (**6f**). — The reaction of **5f** (240 mg, 0.50 mmol) for 1 h under the conditions of general procedure *VIa* yielded 146 mg (94%) of **6f** as a colourless oil having a ratio (1′*R*):(1′*S*) of 2:1; $[\alpha]_D^{20}$ +127° (*c* 1, methanol); R_F 0.37 (solvent *B*).

Anal. Calc. for $C_{12}H_{24}O_9$ (312.3): C, 46.15; H, 7.75. Found: C, 46.14; H, 7.90.

*(1*R,S*)-3-Benzyloxy-1-ethoxypropyl 2,3,4,6-tetra*-O-*acetyl*-α-D-*glucopyranoside* (**5g**). — The reaction of **1** (420 mg, 1.0 mmol) and **3g** (357 mg, 1.5 mmol) for 50 h according to general procedure *II* yielded 438 mg (81%) of **5g** as a colourless oil having a ratio (1′*R*):(1′*S*) of 2:1; $[\alpha]_D^{20}$ +119° (*c* 1, chloroform); R_F 0.41 (solvent *A*).

Anal. Calc. for $C_{26}H_{36}O_{12}$ (540.6): C, 57.77; H, 6.71. Found: C, 57.87; H, 6.70.

*(1*R,S*)-1,2-Dimethoxyethyl 2,3,4,6-tetra*-O-*acetyl*-α-D-*glucopyranoside* (**5h**). — The reaction of **1** (420 mg, 1.0 mmol) and **3h** (240 mg, 2.0 mmol) for 55 h according to general procedures *I* and *Va* yielded 310 mg (71%) of **5h** as white crystals having a ratio (1′*R*):(1′*S*) of 1:1.2; m.p. 106° (from ether–petroleum ether, $[\alpha]_D^{20}$ +140° (*c* 1, chloroform); R_F 0.24 (solvent *A*).

Anal. Calc. for $C_{18}H_{28}O_{12}$ (436.4): C, 49.54; H, 6.47. Found: C, 49.47; H, 6.41.

*(1*R,S*)-1,2-Dimethoxyethyl* α-D-*glucopyranoside* (**6h**). — The treatment of **5h** (218 mg, 0.50 mmol) for 0.5 h according to general procedure *VIa* yielded 121 mg (91%) of **6h** as a colourless oil having a ratio (1′*R*):(1′*S*) of 1:1.1; $[\alpha]_D^{20}$ +146° (*c* 1, methanol); R_F 0.24 (solvent *B*).

Anal. Calc. for $C_{10}H_{20}O_8$ (268.2): C, 44.77; H, 7.53. Found: C, 44.70; H, 7.35.

*(1*R,S*)-2-Chloro-1-methoxyethyl 2,3,4,6-tetra*-O-*acetyl*-α-D-*glucopyranoside*

(**5i**). — The reaction of **1** (210 mg, 0.50 mmol) and **3i** (125 mg, 1.0 mmol) for 60 h according to general procedures *I* and *Va* yielded 145 mg (66%) of **5i** as colourless crystals having a ratio (1′*R*):(1′*S*) of 1.5:1; m.p. 120° (from ether–petroleum ether), $[\alpha]_D^{20}$ +128° (*c* 1, chloroform) for (1′*R*):(1′*S*) = 2:1; R_F 0.35 (solvent *A*).

Anal. Calc. for $C_{17}H_{25}ClO_{11}$ (440.8): C, 46.32; H, 5.72; Cl, 8.04. Found: C, 46.20; H, 5.75; Cl, 7.92.

*(1*R,S*)-2-Chloro-1-methoxyethyl* α-D-*glucopyranoside* (**6i**). — The reaction of **5i** (220 mg, 0.50 mmol) for 1.5 h under the conditions of general procedure *VIb* yielded 123 mg (90%) of colourless crystals having a ratio (1′*R*):(1′*S*) of 1.4:1; m.p. 118° (from ethanol), $[\alpha]_D^{20}$ +141° (*c* 1, methanol); R_F 0.28 (solvent *B*).

Anal. Calc. for $C_9H_{17}ClO_7$ (272.7): C, 39.64; H, 6.28. Found: C, 39.50; H, 6.36.

*(1*R,S*)-2-Bromo-1-methoxyethyl 2,3,4,6-tetra*-O-*acetyl*-α-D-*glucopyranoside* (**5j**). — The reaction of **1** (210 mg, 0.50 mmol) and **3j** (169 mg, 1.0 mmol) for 55 h according to general procedures *I* and *Va* yielded 152 mg (63%) of **5j** as a colourless oil having a ratio (1′*R*):(1′*S*) of 2.5:1; $[\alpha]_D^{20}$ +115° (*c* 1, chloroform); R_F 0.34 (solvent *A*).

Anal. Calc. for $C_{17}H_{25}BrO_{11}$ (458.3): C, 42.08; H, 5.19. Found: C, 41.95; H, 5.16.

*(1*R,S*)-2-Bromo-1-ethoxyethyl 2,3,4,6-tetra*-O-*acetyl*-α-D-*glucopyranoside* (**5k**). — The reaction of **1** (420 mg, 1.0 mmol) and **3k** (394 mg, 2.0 mmol) for 60 h according to general procedures *I* and *Va* yielded 359 mg (72%) of **5k** as colourless crystals having a ratio (1′*R*):(1′*S*) of 2.1:1; m.p. 103° (from ether–petroleum ether), $[\alpha]_D^{20}$ +117° (*c* 1, chloroform) for (1′*R*):(1′*S*) = 2.5:1; R_F 0.38 (solvent *A*).

Anal. Calc. for $C_{18}H_{27}BrO_{11}$ (499.3): C, 43.30; H, 5.45. Found: C, 43.17; H, 5.33.

*(1*R,S*)-2-Bromo-1-ethoxyethyl* α-D-*glucopyranoside* (**6k**). — The reaction of **5k** (250 mg, 0.50 mmol) for 1 h according to general procedure *VIb* yielded 156 mg (94%) of **6k** as colourless crystals having a ratio (1′*R*):(1′*S*) of 1.8:1; m.p. 113° (from ethanol), $[\alpha]_D^{20}$ +115° (*c* 1, methanol); R_F 0.44 (solvent *B*).

Anal. Calc. for $C_{10}H_{19}BrO_7$ (331.2): C, 36.27; H, 5.78; Br, 24.13. Found: C, 36.11; H, 5.76; Br, 24.37.

*(1*R,S*)-1-Ethoxyethyl 2,3,4,6-tetra*-O-*benzyl*-α-D-*glucopyranoside* (**7c**). — The reaction of **2** (306 mg, 0.50 mmol), acetaldehyde (**23c**; 33.0 mg, 0.75 mmol), **14c** (173 mg, 1.5 mmol), and 30 mol% of **4** in 1 mL dichloromethane for 3 d according to general procedure *IV* yielded 230 mg (75%) of **7c** having a ratio (1′*R*):(1′*S*) of 2.5:1; R_F 0.48 (solvent *E*).

Anal. Calc. for $C_{38}H_{44}O_7$ (612.8): C, 74.49; H, 7.24. Found: C, 74.50; H, 7.28.

*(1*R,S*)-1-Methoxybutyl 2,3,4,6-tetra*-O-*benzyl*-α-D-*glucopyranoside* (**7d**). — The reaction of **2** (306 mg, 0.50 mmol) and **3d** (177 mg, 1.5 mmol) for 5 d according to general procedure *III* yielded 163 mg (52%) of **7d** having a ratio (1′*R*):(1′*S*) of 7:1; R_F 0.52 (solvent *E*).

Anal. Calc. for $C_{39}H_{46}O_7$ (626.8): C, 74.73; H, 7.39. Found: C, 74.64; H, 7.39.

*(1*R,S*)-1-Methoxy-2-phenylethyl 2,3,4,6-tetra-*O*-benzyl-α-*D*-glucopyranoside* (**7e**). — The reaction of **2** (306 mg, 0.50 mmol) and **3e** (249 mg, 1.5 mmol) for 4 d according to general procedure *III* yielded 162 mg (48%) of **7e** having a ratio (1′*R*):(1′*S*) of 10:1; R_F 0.44 (solvent *E*).

Anal. Calc. for $C_{43}H_{46}O_7$ (674.8): C, 76.53; H, 6.87. Found: C, 76.45; H, 6.94.

*(1*R,S*)-1,3,3-Trimethoxypropyl 2,3,4,6-tetra-*O*-benzyl-α-*D*-glucopyranoside* (**7f**). — The reaction of **2** (306 mg, 0.50 mmol) and **3f** (246 mg, 1.5 mmol) for 3 d according to general procedure *III* yielded 249 mg (74%) of **7f**; R_F 0.31 (solvent *E*).

Anal. Calc. for $C_{40}H_{48}O_9$ (672.8): C, 71.41; H, 7.19. Found: C, 71.57; H, 7.19.

*(1*R,S*)-1,2-Dimethoxyethyl 2,3,4,6-tetra-*O*-benzyl-α-*D*-glucopyranoside* (**7h**). — The reaction of **2** (306 mg, 0.50 mmol) and **3h** (180 mg, 1.5 mmol) for 5 d according to general procedure *III* yielded 151 mg (48%) of **7h** having a ratio (1′*R*):(1′*S*) of 1.5:1; R_F 0.47 (solvent *E*).

Anal. Calc. for $C_{38}H_{44}O_8$ (628.8): C, 72.59; H, 7.05. Found: C, 72.73; H, 7.10.

*(1*R,S*)-2-Chloro-1-methoxyethyl 2,3,4,6-tetra-*O*-benzyl-α-*D*-glucopyranoside* (**7i**). — The reaction of **2** (306 mg, 0.50 mmol) and **3i** (138 mg, 1.5 mmol) for 5 d according to general procedure *III* yielded 199 mg (63%) of **7i** having a ratio (1′*R*):(1′*S*) of 5:1; R_F 0.52 (solvent *E*).

Anal. Calc. for $C_{37}H_{41}ClO_7$ (633.2): C, 70.19; H, 6.53. Found: C, 70.35; H, 6.67.

*(1*R,S*)-2-Bromo-1-ethoxyethyl 2,3,4,6-tetra-*O*-benzyl-α-*D*-glucopyranoside* (**7k**). — The reaction of **2** (306 mg, 0.50 mmol) and **3k** (248 mg, 1.5 mmol) for 4 d according to general procedure *III* yielded 190 mg (55%) of **7k**; R_F 0.44 (solvent *E*).

Anal. Calc. for $C_{38}H_{43}BrO_7$ (691.8): C, 65.89; H, 6.40. Found: C, 65.92; H, 6.41.

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