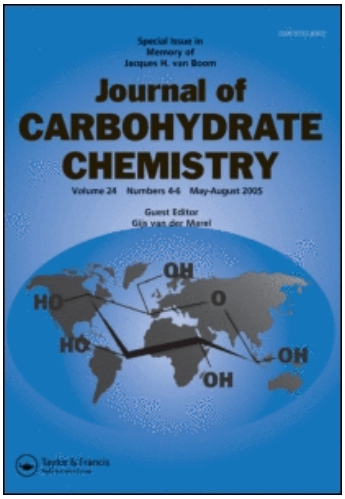

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SYNTHESIS OF 2-(TRIMETHYLSILYL)ETHYL α-d-MANNOPYRANOSIDES REVISITED

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SYNTHESIS OF 2-(TRIMETHYLSILYL)ETHYL α-D-MANNOPYRANOSIDES REVISITED

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ABSTRACT

Glycosylation of 2-(trimethylsilyl)ethanol with various ethyl 1-thioglycosides, which were activated with *N*-iodosuccinimide and silver triflate, was studied. The starting thioglycosides, some prepared for the first time, were obtained conventionally from the corresponding α-1-acetates. When β-1-acetates were more readily available, these were converted to the α-anomers by anomerization, prior to the glycosylation. Using ethyl 1-thioglycosides as glycosyl donors, especially those bearing a pivaloyl or a nonparticipating group at O-2, the corresponding 2-(trimethylsilyl)ethyl α-D-mannopyranosides were obtained in excellent yields.

Key Words: 2-(Trimethylsilyl)ethyl glycosides; Glycosylation; NIS/AgOTf; Anomerization

INTRODUCTION

The importance of 2-(trimethylsilyl)ethyl (SE) glycosides in the chemical synthesis of oligosaccharides lies in the fact that they are stable during many protecting group manipulations, yet the glycosidic 2-(trimethylsilyl)ethyl linkage can be cleaved under conditions which leave interglycosidic linkages in oligosaccharides (essentially) intact. A further desirable property of 2-(trimethylsilyl)ethyl glycosides is that they can be converted to an array of other useful glycosyl derivatives.[1–4] While

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good yields of 2-(trimethylsilyl)ethyl glycosides of most common sugars can be obtained conventionally, synthesis of 2-(trimethylsilyl)ethyl α-D-mannopyranosides is notoriously problematic.[1,5]

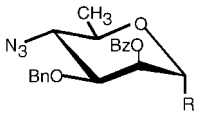
The formation of 2-(trimethylsilyl)ethyl α-D-mannopyranosides from per-*O*-acylated glycosyl chlorides has been studied.[5] Fully acylated mannopyranosyl chlorides having different acyl groups at *O*-2 were treated with 2-(trimethylsilyl)ethanol (SEOH) under the conditions of silver trifluoromethanesulfonate (triflate, AgOTf) mediated Koenigs–Knorr reaction. The highest yield (72%) of the desired product was obtained from 3,4,6-tri-*O*-acetyl-2-*O*-benzoyl-α-D-mannopyranosyl chloride, prepared from 1,3,4,6-tetra-*O*-acetyl-2-*O*-benzoyl-β-D-mannopyranose (**26**).[a] Since the yield of the fully benzoylated SE glycoside **11** from the corresponding glycosyl chloride was only 48%, the author[5] concluded that it was not the presence of the benzoyl group at *O*-2 alone, but ''a proper ensemble of the protecting groups in a mannosyl donor'' that minimizes side reactions and, as a result, affects the yield of 2-(trimethylsilyl)ethyl α-D-mannopyranosides. The same communication reported that, unlike with D-mannose, a high yield of the corresponding 2-(trimethylsilyl)ethyl α-glycoside could be obtained from the fully benzoylated L-rhamnose. Accordingly, we have been able to prepare 2-(trimethylsilyl)ethyl 4-azido-3-*O*-benzyl-2-*O*-benzoyl-4,6-dideoxy-α-D-mannopyranoside (**2**),[6] from the corresponding glycosyl chloride, in 82% yield. However, the need for a large quantity of **2**, in connection with our synthesis of perosamine-containing oligosaccharides suitable for conjugation,[7] rendered even this yield not quite satisfactory. In an attempt to improve the yield, we have glycosylated SEOH using ethyl 4-azido-3-*O*-benzyl-2-*O*-benzoyl-4,6-dideoxy-1-thio-α-D-mannopyranoside (**1**) as a glycosyl donor and obtained the SE glycoside **2** in virtually theoretical yield. That result prompted us to undertake the present study, and here we describe the thioglycoside approach to making a number of useful 2-(trimethylsilyl)ethyl α-D-mannopyranosides. Because of the convenience[8] of its use, silver AgOTf/*N*-iodosuccinimide (NIS) reagent[9] was used as the promoter.

RESULTS AND DISCUSSION

Because of their versatility, thioglycosides have become very popular glycosyl donors in glycoside synthesis. Nevertheless, to our knowledge, thioglycosides have not been employed in syntheses of SE α-D-mannopyranosides. The ethyl 1-thio-D-mannopyranosides used during this work were conveniently prepared from the corresponding α-1-*O*-acetyl derivatives. In the case of **30** and **31**, the preparation was first carried out from the more readily available β-1-acetates **26** and **27**. When the yields of **30** and **31** were not quite satisfactory we turned to conversions of the α-acetates **28** and **29**, as it has been reported[10] that the use of α-anomers resulted in shorter reaction times and cleaner conversions to thioglycosides. In our situation, however, the benefit from the use of the α-compounds was unimpressive. The α-1-acetates **28** and **29**, were conveniently prepared from the β-anomers **26** and **27** by treatment with a mixture of AcOH, Ac_2O and H_2SO_4,

[a]No physical constants or spectral data were reported for this substance, and the compound, as well as its HO-2-free precursor, are erroneously shown (Ref. [5]) as α-anomers.

which is generally used to effect acetolysis. An equilibrium mixture was formed, containing the α- and β-anomers in a ratio of ~93:7 (NMR). The pure α-anomers were then obtained by chromatography, which also gave an unresolved mixture of anomers containing a considerable amount of the β-anomer. The economy of preparation of the α-anomers could be improved by repeated treatment of this unresolved mixture of anomers with the acetolysis reagent (see above), to give product showing the same $\alpha:\beta \simeq 93:7$ ratio (NMR).



	R
1	SEt
2	OSE

In the quest for improving the yield of **2** we treated ethyl 4-azido-2-*O*-benzoyl-4,6-dideoxy-1-thio-α-D-mannopyranoside (**1**) with the NIS/AgOTf reagent and compared the yield of the desired compound **2** with that obtained from 4-azido-2-*O*-benzoyl-4,6-dideoxy-α-D-mannopyranosyl chloride.[6] Monitoring the reaction by thin-layer chromatography (TLC) showed that 1.4 and 1.2 equivalents of NIS and AgOTf, respectively, was necessary to drive the reaction to completion, and that the conversion was a one-product reaction. After processing (see Experimental) and chromatography, the desired SE glycoside **2** was obtained in virtually theoretical yield.

The above results suggested that high yields of other SE mannopyranosides might be generally possible to obtain by way of 1-thioglycosides. Therefore, to ascertain if the thioglycoside functionality alone caused the dramatic change of the situation, glycosylation of SEOH with ethyl 2,3,4,6-tetra-*O*-acetyl-1-thio-α-D-mannopyranoside (**4**) was carried out (since we do not deem this reaction to be preparatively useful, this experiment is not described in the Experimental). Examination of the reaction mixture by TLC showed that several products were formed, and that the desired SE glycoside (**7**) was present in only a relatively small amount. The chromatographic mobility observed for two of the byproducts isolated from this conversion indicated that they were the hemiacetal (**8**), and 2-(trimethylsilyl)ethyl 3,4,6-tri-*O*-acetyl-1-thio-α-D-mannopyranoside (**9**). This corresponded to the previous observation[5] that products of partial deacetylation are formed during reactions of acetylated glycosyl donors with SEOH (cf., also formation of **20** during conversion **15** → **19**). Conventional acetylation of **9** gave the peracetate **7** (TLC, NMR).

To imitate the substitution pattern at positions 1 and 2 in **1**, which gave the optimum yield of the desired product, reaction of ethyl 2,3,4,6-tetra-*O*-benzoyl-1-thio-α-D-mannopyranoside (**10**) with SEOH was examined next. Compound **10** was prepared from ethyl 1-thio-α-D-mannopyranoside[11,12] (**6**), here obtained crystalline for the first time. The NIS/triflic acid-promoted[9] reaction of **10** with SEOH (not described in the Experimental) was rather sluggish and yielded a multicomponent mixture. The same conversion mediated with NIS/AgOTf[9] was virtually instantaneous, but 3.5 equivalents of the promoter were required to leave only trace of the starting thioglycoside unchanged. Analysis of the crude product by TLC showed the presence of two pro-

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Table 1. Amounts of Reagents Used (mmol) in Reactions of 1 mmol of the Starting Thioglycoside with 2 mmols of 2-(Trimethylsilyl)ethanol, and Yields (%) of Products

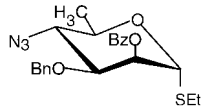
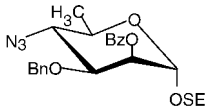
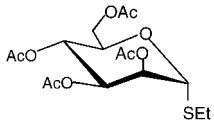
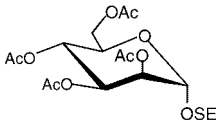
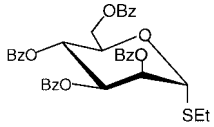
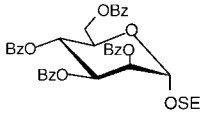
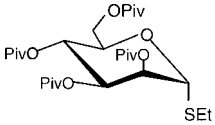
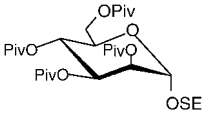
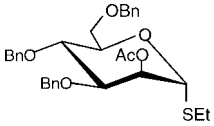
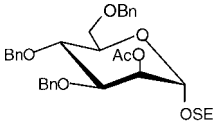
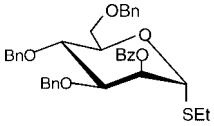
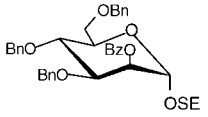
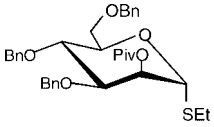
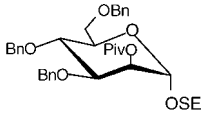
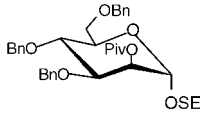
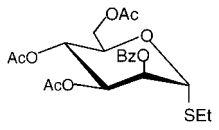
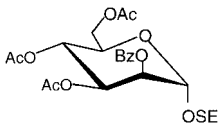
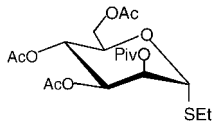
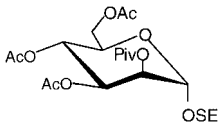
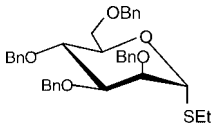
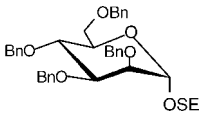
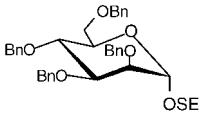
Thioglycoside	Product	NIS	AgOTf	Yield
		1.2	1.4	~100
1	**2**	1.5	1.6	~20%
				
4	**7**	3.5	3.5	52.4
				
10	**11**	3.5	3.5	89
				
13	**14**	1.5	1.5	88.4
				
15	**19**	1.5	1.5	85.2
				
17	**22**	1.5	1.9	87
				
18	**23**			3
				
	24			

Table 1. Continued

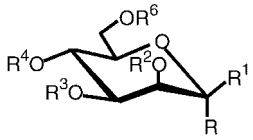
Thyoglycoside	Product	NIS	AgOTf	Yield
 **30**	 **32**	2	2.2	73
 **31**	 **33**	1.3	1.2	71
 **34**	 **35**	1.2	1.2	66
	 **36**			32

ducts. After chromatography, the less polar product was shown to be the desired compound **11**, obtained in 52.4% yield. NMR and MS analysis of the more polar material showed that it was the hemiacetal **12**. The low yield of **11** from **10**, which compared well with that obtained[5] from the corresponding glycosyl chloride, indicated that, as with **4** (*vide supra*), there was no advantage in the use of thioglycoside. Neither did the use of a thioglycoside as a glycosyl donor change the situation in the conversion **30** → **32**. Improved yield of the corresponding SE glycoside was not obtained, compared to that from the glycosyl chloride.[5]

It has been suggested[5] that it is the hydrolysis of orthoesters, which are intermediates in glycoside formation from 2-*O*-acylated glycosyl donors, that causes the low yield of SE mannosides. Kunz[13] found that orthoester formation during glycosylation is suppressed when 2-*O*-pivaloyl glycosyl donors are used, unlike with other 2-*O*-acylated glycosyl donors. When we treated the fully pivaloylated 1-thioglycoside **13** with 2-(trimethylsilyl)ethanol (see Experimental), the desired, hitherto unknown, SE glycoside **14** was virtually the only product formed and, after chromatography, it was isolated crystalline in excellent yield of 87%. In view of the above it was somewhat disappointing to find that the yield of SE glycoside **33** from the 2-*O*-pivaloylated thioglycoside **31**, was not improved compared to that from **30**.

The potential utility of 2-(trimethylsilylethyl) 3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (**20**) for making some (1 → 2)-linked manno-oligosaccharides prompted us to examine glycosylation of SEOH with ethyl 2-*O*-acyl-3,4,6-tri-*O*-benzyl-α-1-thio-D-

mannopyranosides **15**, **17**, and **18**. The yields of the corresponding SE glycosides from these glycosyl donors was high (>80%). The best yield was obtained from the conversion **18** → **23**, which was virtually a one product reaction, yielding 87% of **23**, after chromatography, along with a little of the corresponding β-anomer, 2-(trimethylsilyl)ethyl 2-*O*-pivaloyl-3,4,6-tri-*O*-benzyl-β-D-mannopyranoside **24**.



	R	R1	R2	R3	R4	R6
3	OAc	H	Ac	Ac	Ac	Ac
4	SEt	H	Ac	Ac	Ac	Ac
5	H	SEt	Ac	Ac	Ac	Ac
6	SEt	H	H	H	H	H
7	OSE	H	Ac	Ac	Ac	Ac
8	HOH		Ac	Ac	Ac	Ac
9	OSE	H	OH	Ac	Ac	Ac
10	SEt	H	Bz	Bz	Bz	Bz
11	OSE	H	Bz	Bz	Bz	Bz
12	HOH		Bz	Bz	Bz	Bz
13	SEt	H	Piv	Piv	Piv	Piv
14	OSE	H	Piv	Piv	Piv	Piv
15	SEt	H	Ac	Bn	Bn	Bn
16	SEt	H	H	Bn	Bn	Bn
17	SEt	H	Bz	Bn	Bn	Bn
18	SEt	H	Piv	Bn	Bn	Bn
19	OSE	H	Ac	Bn	Bn	Bn
20	OSE	H	OH	Bn	Bn	Bn
21	HOH		Ac	Bn	Bn	Bn
22	OSE	H	Bz	Bn	Bn	Bn
23	OSE	H	Piv	Bn	Bn	Bn
24	H	OSE	Piv	Bn	Bn	Bn
25	H	Ac	H	Ac	Ac	Ac
26	H	Ac	Bz	Ac	Ac	Ac
27	H	Ac	Piv	Ac	Ac	Ac
28	Ac	H	Bz	Ac	Ac	Ac
29	Ac	H	Piv	Ac	Ac	Ac
30	SEt	H	Bz	Ac	Ac	Ac
31	SEt	H	Piv	Ac	Ac	Ac
32	OSE	H	Bz	Ac	Ac	Ac
33	OSE	H	Piv	Ac	Ac	Ac
34	SEt	H	Bn	Bn	Bn	Bn
35	OSE	H	Bn	Bn	Bn	Bn
36	H	OSE	Bn	Bn	Bn	Bn
37	H	SEt	Bz	Ac	Ac	Ac
38	H	SEt	Piv	Ac	Ac	Ac

Finally, we deemed it interesting to examine the formation of SE glycosides from the fully benzylated mannosyl donor, ethyl 2,3,4,6-tetra-*O*-benzyl-1-thio-α-D-mannopyranoside (**34**). Since it contains only alkyl protecting groups, orthoester formation during SE-glycoside formation can not occur. The conversion **34** → **35** + **36** was high yielding, but produced the SE glycosides with impaired stereoselectivity.

Outcome of the reactions described above, together with the results of others[1,5] confirm that formation of SE α-D-mannopyranosides is not a simple process. Although it is not possible to make a simple generalization, the following observations have been made. Firstly, the use of thioglycosides as glycosylating reagents for SEOH alone can be beneficial, compared to the use of glycosyl chlorides.[5,6] For example, in the conversion **1** → **2**, the use of ethyl 1-thioglycoside as the glycosyl donor, even with the 2-*O*-benzoyl protection, resulted in a one-product reaction and a high yield of the desired product. On the other hand, the use of thioglycosides had no significant effect on the yield of **7** and **11** (see Experimental), compared to the use of glycosyl chlorides.[5,6] Secondly, variously protected ethyl 1-thio α-D-mannopyranosides show different reactivity when treated with the NIS/AgOTf reagent. Therefore, the amount of the NIS/AgOTf reagent needed to drive the reaction to completion varied with the substitution pattern, and it had to be determined for each ethyl 1-thioglycoside (Table 1). Presumably, the same holds also for other 1-thioglycosides. Thirdly, a comparison of yields of the corresponding SE glycosides obtained from thioglycosides **4** and **13**, respectively, 52.4 and 89%, seems to suggest that formation and subsequent hydrolysis of orthoesters during the formation of SE glycosides[5] is a factor that influences the yield of SE mannopyranosides. It is, however, important to note in this context that glycosylation of SEOH with 2-*O*-acetylated glycosyl donors does not necessarily result in a poor yield of SE mannopyranosides (cf. the conversion **15** → **19**). Neither does the presence of the *O*-pivaloyl group at position 2 in a glycosyl donor guarantee excellent yield of the corresponding SE mannopyranoside (cf. the conversion **31** → **33**). Thus, besides simple orthoester formation and its hydrolysis, other phenomena must be involved, which affect the yields of SE α-mannopyranosides. The results here described suggest that these yields are affected not only by the nature of the acyl group at *O*-2, but also by its presence/absence at position 6. This can be confidently concluded from the yields of conversions of the tri-*O*-benzylated donors **15**, **17**, and **18**, which all gave very good yields of the corresponding SE glycosides, as well as from the comparison in the yields of SE α-glycosides obtained from the mannoside **10** (52.4 or 48%[5]), rhamnose[5] (86%), **1** (∼100%), or the corresponding glycosyl chloride[6] (82%).

EXPERIMENTAL

General methods. Unless stated otherwise, optical rotations were measured at ambient temperature for solutions in chloroform ($c \sim 1$), with a Perkin–Elmer automatic polarimeter, Model 341. All reactions were monitored by TLC on Silica gel 60 coated glass slides (Whatman or Analtech). The judgment expressed in Results and Discussion concerning the quality of individual reactions is based mainly on TLC and not on the actual yields. Thus, a reaction is occasionally described as a ''one-product reaction,'' even though the yield reported for that reaction is $< 100\%$, which reflects manipulative losses and not incomplete reactions or formation of by-products. Column chromatography was performed by gradient elution from columns of silica gel. Solvent

Table 2. 1H NMR Chemical Shifts[a] and Peak Multiplicities for Compounds **1,5–7,10–14,16,18,19,22–24,** and **26–38**

Compound	H-1	H-2	H-3	H-4	H-5	H-6	SCH_2CH_3	SCH_2CH_3
1[b]	5.34d	5.63dd	3.85dd	3.55t	4.20–3.90m	1.38d	2.72–2.52m	1.28t
5[c]	4.80d	5.52dd	5.08dd	5.26t	3.72ddd	4.28dd, 4.14dd	2.74q	1.31t
6[d]	5.29bd	4.02dd	3.75, dd, po	3.63t	3.97ddd, po	3.86dd, 3.73dd, po	2.72–2.55m	1.24t
7[e]	4.80d	5.17dd	5.33	5.23t	3.97ddd	4.23dd, 4.08dd		
10	5.58bd	~5.82dd,po	5.84dd, po	6.16	4.84ddd	4.69dd, 4.53dd	2.84–2.66m	1.35t
11[f]	5.13d	5.68dd	5.94dd	6.09t	~4.44m, po	4.70m, 4.48dd, po		
12[g]	5.53d	5.75dd	6.02dd	6.19t	4.68dt	4.78dd, 4.43dd		
13[h]	5.24bd	5.34dd	5.30dd	5.51t	4.44ddd	4.23dd, 4.12dd	2.75–2.57m	1.31t
14[i]	4.79d	5.20dd	5.39dd	5.47t	4.05ddd	4.20dd, 4.13dd		
16[j]	5.38d	4.08dd	3.83dd, po	3.90t	4.16ddd	3.79dd, po, 3.67dd	2.72–2.50m	1.27t
16[k]	5.53bd	4.13dd	3.94dd	4.08t	4.41mpo	3.82dd, 3.69dd	2.52–2.27m	1.07t
18[l]	5.30d	5.44bt	3.95–3.87m	3.95–3.87m	4.20–4.13m	3.82dd, 3.71dd	2.73–2.53m	1.28t
18[m]	5.41d	5.74	4.10dd	4.16t	4.41m, po	3.84dd, 3.66dd	2.45–2.25m	1.04t
19[n]	4.94d	5.69dd	4.22dd	4.14t	4.07m	3.83dd, 3.74dd		
22[o]	5.01d	5.94dd	4.35–4.30m	4.35–4.30m	4.11ddd	3.92dd, 3.78dd		
23[p]	4.82d, po	5.31dd	3.97dd	3.85–3.69m	3.85–3.69m	3.85–3.69m		
24[q]	4.50d, po	5.56dd	3.65dd	3.82–3.72m	3.47ddd	3.82–3.72m		
26[r]	6.00d	5.75dd	5.28dd	5.46t	3.92ddd	4.36dd, 4.22dd		
27[s]	5.89d	5.45dd	5.13dd	5.33t	3.83ddd	4.29dd, 4.16dd		
28[t]	6.41d	5.81dd	5.73dd	5.89t	4.10ddd	4.40dd, 4.16dd		
29[u]	6.08d	5.26dd	5.34dd	5.43t	4.06ddd	4.27dd, 4.12dd		
30[v]	5.44bd	5.59dd	5.38dd	5.49t	4.46ddd	4.35dd, 4.16dd	2.78–2.59m	1.33t
31[w]	5.28d, po	5.34dd	5.25dd, po	5.37t, po	4.39ddd	4.30dd, 4.12dd	2.76–2.57m	1.32t
32[x]	4.87bd	5.90–5.86m	5.90–5.86m	5.90–5.86m	4.17m	4.43dd, 4.32dd		
33[y]	4.83d	5.20dd	5.38–5.29m	5.38–5.29m	4.01ddd	4.24dd, 4.14dd		
34[z]	5.50d	3.94dd	4.07dd	4.30t	~4.42m	3.86dd, 3.73dd	2.58–2.35m	1.12t
35[aa]	5.07d	~3.94, po	4.22dd	4.33t	4.15ddd	4.01–3.91m, 3.85dd		
36[bb]	4.39d	3.87dd, po	3.50dd, po	3.87t, po	~3.45m, po	3.82dd, 3.74dd		
37[cc]	4.89d	5.76dd	5.18dd	5.37t	3.78ddd	4.33dd, 4.20dd	2.75q	1.30t
38[dd]	4.81d	5.50dd	5.06dd	5.29t	3.72ddd	4.28dd, 4.15dd	2.74q	1.30t

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mixtures slightly less polar than those used for TLC were used at the onset of elution. Chemical ionization mass spectra (CIMS, positive or negative ion) were obtained on a Finnigan 4000 quadrupole mass spectrometer with ammonia reagent gas. Fast atom bombardment (FAB) mass data were obtained using a JEOL SX-102 mass spectrometer

Notes to Table 2:

[a]Measured in $CDCl_3$, unless stated otherwise; d, doublet; t, triplet; q, quartet; m, multiplet: b, broad; po, partially overlapped; *not determined due to overlapping signals.

[b]δ_{PhCH_2} 4.73, 4.55 (2 d ^2J 11.2 Hz).

[c]δ_{COCH_3} 2.19s, 2.08s, 2.05s, 1.99s.

[d]Measured in D_2O.

[e]$\delta_{OCH_aCH_2Si}$ 3.76ddd J 6.2 and 9.7; $\delta_{OCH_bCH_2Si}$ 3.51ddd; $\delta_{CH_2CH_2Si}$ 0.94m; $\delta_{(CH_3)_3Si} \sim 0.0$s; δ_{COCH_3} 2.12s, 2.06s, 2.01s, 1.96s.

[f]$\delta_{CH_aCH_2Si}$ 3.95dt, po, J 10.6 Hz; $\delta_{CH_bCH_2Si}$ 3.68dt, po, J 10.0 Hz; $\delta_{CH_2CH_2Si}$ 1.09m; $\delta_{(CH_3)_3}$Si 0.06s.

[g]Data for the α-anomer. Measured after addition of D_2O.

[h]$\delta_{C(CH_3)_3}$ 1.28s, 1.24s, 1.17s, 1.12s.

[i]$\delta_{OCH_aCH_2Si}$ 3.82, 3.80 (2 t, J 10.0); $\delta_{OCH_bCH_2Si}$ 3.56, 3.54 (2 t, J 10.0); $\delta_{CH_2CH_2Si}$ 0.99m; $\delta_{(CH_3)_3Si} \sim 0.03$s; $\delta_{C(CH_3)_3}$ 1.27, 1.24, 1.16, 1.12, 4 s.

[j]δ_{PhCH_2} 4.84–4.48m.

[k]Measured in C_6D_6. δ_{PhCH_2} 4.89, 4.59, 2d, ^2J 11.3 Hz; 4.53, 4.40, 2d, ^2J 12.0 Hz; 4.28s.

[l]δ_{PhCH_2} 4.85–4.46m; δ_{COCH_3} 1.23s.

[m]Measured in C_6D_6; δ_{PhCH_2} 5.03–4.34m; δ_{COCH_3} 1.25s.

[n]Measured in C_6D_6; δ_{PhCH_2} 5.05–4.38m; the signal of OCH_aCH_2Si appears as 2 t (δ 3.83, 3.76), po with the H-6a signal; the signal of OCH_bCH_2Si appears as 2 t at δ 3.39 and 3.37, J 9.7 Hz; $\delta_{CH_2CH_2Si}$ 0.94–0.81m; $\delta_{(CH_3)_3Si} \sim -0.04$s.

[o]Measured in C_6D_6; δ_{PhCH_2} 4.81–4.41m; the signal of OCH_aCH_2Si appears as 2 t (δ 3.84, 3.82), po with the H-6b signal; the signal of OCH_bCH_2Si appears as 2 t at δ 3.41 and 3.38, J 9.3 Hz; $\delta_{CH_2CH_2Si}$ 0.95–0.80m; $\delta_{(CH_3)_3}Si \sim -0.03$s.

[p]δ_{PhCH_2} 4.83–4.44m; the signal of OCH_aCH_2Si is part of m at 3.85–3.69; $\delta_{CH_bCH_2Si}$ 3.49, 3.47 (2 t, J 9.8 Hz); $\delta_{C(CH_3)_3}$ 1.19s; $\delta_{CH_2CH_2Si}$ 0.89m; $\delta_{(CH_3)_3}Si$ −0.02s.

[q]δ_{PhCH_2} 4.87–4.44m; $\delta_{OCH_aCH_2Si}$ 3.99, 3.97 (2 t, J 9.3 Hz); $\delta_{OCH_bCH_2Si}$ 3.58, 3.56 J 9.3 Hz); $\delta_{CH_2CH_2Si}$ 0.93ddd, po, J 7.1 and 8.3; $\delta_{C(CH_3)_3}$ 1.24s; $\delta_{(CH_3)_3Si}$ 0.01s.

[r]δ_{COCH_3} 2.15s, 2.07s, 2.05s, 1.99s.

[s]δ_{COCH_3} 2.09s, 2.08s, 2.05s, 1.99s.

[t]Measured in C_6D_6. δ_{COCH_3} 1.79s, 1.68s, 1.63s, 1.50s.

[u]δ_{COCH_3} 2.18s, 2.09s, 2.05s, 1.99s; $\delta_{C(CH_3)_3}$ 1.28s.

[v]δ_{COCH_3} 2.13s, 2.07s, 1.97s.

[w]δ_{COCH_3} 2.09s, 2.05s, 1.97s, 1.99s; $\delta_{C(CH_3)_3}$ 1.28s.

[x]Measured in C_6D_6; δ_{COCH_3} 1.82s, 1.68s, 1.61s; $\delta_{OCH_aCH_2Si}$, 3.69m; $\delta_{OCH_b}CH_2Si$, 3.30m; $\delta_{CH_2}CH_2Si$ 0.89m; $\delta_{(CH_3)_3}Si \sim 0.01$s.

[y]δ_{COCH_3} 2.09s, 2.04s, 1.97s; $\delta_{OCH_aCH_2Si}$ 3.81ddd; $\delta_{OCH_bCH_2Si}$ 3.57ddd; $\delta_{CH_2CH_2Si}$ 0.99m; $\delta_{(CH_3)_3Si}$ 0.04s; $\delta_{C(CH_3)_3}$ 1.27.

[z]Measured in C_6D_6; δ_{CH_2Ph} 4.99–4.34m, partially overlapped.

[aa]Measured in C_6D_6; δ_{PhCH_2} 5.03–4.48m; the signal of OCH_aCH_2Si is part of m at 4.01–3.83; the signal of OCH_bCH_2Si appears as m at 3.53–3.44; δ $\delta_{CH_2CH_2Si}$ 0.96–0.90m; $\delta_{(CH_3)_3Si} \sim 0.16$s.

[bb]δ_{PhCH_2} 5.02–4.39m; $\delta_{OCH_a}CH_2Si$ 4.12–4.03m; the signal of OCH_bCH_2Si is part of m at 3.55–3.43; $\delta_{CH_2CH_2Si}$ 1.0t; $\delta_{(CH_3)_3Si} \sim 0.03$s.

[cc]δ_{COCH_3} 2.12s, 2.05s, 1.97s.

[dd]δ_{COCH_3} 2.08s, 2.04s, 1.96s.

utilizing a glycerol matrix. Assignments of NMR signals (Tables 2–4), obtained at 300 MHz for ^{1}H and 75 MHz for ^{13}C at 25°C, were made by first-order analysis of spectra and, when feasible, the assignments were supported by APT and/or DEPT experiments, homonuclear decoupling and/or homo- and heteronuclear 2-dimensional correlation spectroscopy. The commercial software supplied with the spectrometers (Varian Gemini or Varian XL 300) was used. The β-anomeric configuration of substances was ascertained by $^{1}H-^{13}C$ coupling constants[14] $J_{C\text{-}1,H\text{-}1}$. Solutions in organic solvents were dried with anhydrous Na_2SO_4 and concentrated at 40°C/2kPa.

Table 3. ^{1}H NMR Coupling Constants[a] for Compounds **1**, **5–7**, **10–14**, **16**, **18**, **19**, **22–24**, and **26–38**

Compound	Coupling Constants (Hz)						
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$
1	1.6	3.2	9.9	9.9	6.2		
5	1.1	3.5	10.1	10.1	6.1	2.6	12.4
6	~1.2	3.3	~9.8	~9.8	2.7	6.4	12.5
7	1.4	3.1	10.2	10.2	6.0	2.3	12.5
10	~1.0	3.1	~10.0	~10.0	2.6	4.5	12.4
11	1.8	3.3	~10.3	~10.3	*	5.0	~13
12	1.8	3.1	10.2	~10	2.6	3.5	12.2
13	1.6	3.3	9.9	10.1	4.4	1.9	12.5
14	1.7	3.1	9.9	9.6	4.4	2.0	12.5
16	1.4	3.1	9.3	9.3	4.5	1.9	11.1
16[b]	1.5	3.6	9.2	9.2	4.8	1.7	10.9
18	1.5	*	*	*	4.3	1.9	10.9
18[b]	1.8	2.9	9.2	9.2	4.6	1.5	11.0
19[b]	1.8	3.3	9.2	~9.2	4.6	1.7	10.8
22[b]	1.8	2.6	*	9.7	4.6	1.7	10.8
23	1.9	3.3	9.1	*	*	*	*
24	~1.0	3.0	9.3	9.3	2.3	4.3	*
26	0.9	3.5	10.3	~10	5.5	2.3	13.0
27	1.2	3.2	10.1	9.8	5.0	2.2	12.7
28	2.0	3.3	10.2	10.2	4.7	2.5	12.3
29	2.1	3.0	10.0	10.0	4.0	2,4	12.2
30	1.8	3.5	10.0	10.0	5.0	2.4	12.3
31	~1.6	3.1	10.0	9.9	4.7	2.3	12.2
32	~1.5	*	*	*	4.9	2.5	12.1
33	1.9	2.9	*	9.9	5.3	2.6	12.4
34[b]	1.4	3.2	10.0	10.0	5.2	1.6	10.9
35[b]	~1.4	3.1	9.3	9.6	*	3.8	~10.7
36	0.8	3.1	9.3	9.3	2.0	5.9	10.6
37	1.1	3.5	10.0	10.1	5.5	2.5	12.2
38	0.9	3.3	10.0	10.0	5.6	2.2	12.7

[a]Measured in $CDCl_3$, unless stated otherwise.
[b]Measured in C_6D_6.
*Not determined due to overlap, or broadening of signal, or second order effect.

NIS and AgOTf were purchased from Aldrich Chemical Company. Before use, NIS was purified by crystallization from dioxane-CCl_4, and dried at 80°C/2 kPa for 2 h, mp 201–202°C. Ethyl 2,3,4,6-tetra-*O*-acetyl-1-thio-α,β-D-mannopyranoside was obtained as described,[15] except that the reaction was performed at room temperature. Essentially the same anomeric mixture was formed within 3–4 h as that described[15] with the reaction time 6–7 days. Chromatography and crystallization yielded the α-anomer **4**, mp 106–107°C (from EtOH), ref. 16, mp 107–108°C. The β-anomer **5** had mp 160–161°C (from EtOH) and $[\alpha]_D$ −64° (*c* 0.9, $CHCl_3$), in accord with literature values reported by Fried and Waltz.[12] The NMR data, hitherto not reported, are in Tables 2–4. Ethyl 2,3,4,6-tetra-*O*-benzoyl-1-thio-α-D-mannopyranoside (**10**) was obtained from **5** as described by Sarbajna and Roy.[11] Ethyl 2,3,4,6-tetra-*O*-benzyl-1-thio-α-D-mannopyranoside (**34**) was obtained from **6** as described by Helander et al.[16] 1,3,4,6-Tetra-*O*-acetyl-β-D-mannopyranose (**25**) was prepared as reported by Bovin et al.[17] Ethyl 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (**17**) was prepared according to Zhang et al.[18] Ethyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (**15**) was obtained as described.[19] The compound crystallized readily from isopropyl ether containing a few drops of hexane, mp 51–53°C, ref. 19 mp 50–51°C. Deacetylation gave ethyl 3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (**16**).[18]

General procedure for preparation of SE glycosides (for amounts of reagents and yields of products, see Table 1). To a solution of the thioglycoside (1 mmol) in dry CH_2Cl_2 (10 mL) was added 2-(trimethylsilyl) ethanol and molecular sieves (powder, 4 Å, 0.5 g), and the mixture was stirred for 15 min. *N*-Iodosuccinimide was added, which resulted in slight pink color development. The stirring was continued for another 15 min, when AgOTf (0.1 M in toluene, freshly prepared and stored in the dark) was added dropwise. Red color developed immediately upon the addition, and kept developing intermittently as the AgOTf solution was added, and it finally changed to yellow, indicating that all starting material that had been activated with NIS was consumed. TLC showed complete conversion of the starting material into the faster moving SE glycoside and, occasionally, to more polar product(s). When conversion of the starting material was incomplete, more NIS was added, followed by ''titration'' with the solution of AgOTf. The reaction mixture was terminated by addition of triethylamine (equimolar to AgOTf). The bright yellow precipitate formed was filtered through a pad of Celite directly into a separating funnel containing excess of 2:1 (v/v) sodium thiosulfate (10%)-sodium bicarbonate (satd) solution. The mixture was extracted with CH_2Cl_2, the organic phase was dried, concentrated, and the crude product was chromatographed. 2-(Trimethylsilyl)ethyl glycosides that were prepared following the above protocol are listed below. In all glycosylations of SEOH, except for the conversions **1** → **2**, and **34** → **35** + **36** a product more polar than the corresponding 1-thioethyl glycoside, presumably[5] the product of hydrolysis of the starting glycosyl donor, was formed.

Ethyl 4-azido-2-*O*-benzoyl-3-*O*-benzyl-4,6-dideoxy-1-thio-α-D-mannopyranoside (1). Benzoyl chloride (0.12 mL, 1.02 mmol) was added to a solution of ethyl 4-azido-3-*O*-benzyl-4,6-dideoxy-1-thio-α-D-mannopyranoside[20] (220 mg, 0.68 mmol) in CH_2Cl_2 (3 mL) containing pyridine (0.17 mL, 2.03 mmol), and the mixture was stirred for 3 h at room temperature. TLC (5:1 hexane-EtOAc) then showed that the reaction was

Table 4. ^{13}C NMR Chemical Shifts for Compounds **1**, **5–7**, **10–14**, **16**, **18**, **19**, **22–24**, and **26–38**[a]

Compound	C-1	C-2	C-3	C-4	C-5	C-6
1[b]	82.31	69.76	76.45	64.55	67.51	18.57
5[c]	82.54	70.39	71.81	65.79	76.58	62.75
6[d]	84.40	72.00	71.26	67.28	73.22	61.01
7[e]	96.99	69.81	69.13	66.27	68.4	62.63
10[f]	82.35	72.14	70.50	67.07	69.23	62.88
11[g]	97.10	70.77	70.11	67.08	68.82	63.10
12[h]	92.28	70.96	69.89	66.83	68.73	62.70
13[i]	82.47	71.06	69.82	65.32	69.31	62.08
14[j]	97.22	69.75	69.40	65.32	68.86	62.19
16[k]	83.35	69.85	80.42	74.49	71.39	68.83
16[l]	84.24	70.57	81.50	75.60	72.72	70.07
18[m]	82.45	69.91	78.77	74.38	71.68	68.91
18[n]	83.31	70.84	79.89	75.42	73.06	70.02
19[o]	98.26	69.73	79.30	75.58	72.78	70.25
22[p]	98.18	70.17	79.37	75.44	72.93	70.26
23[q]	97.18	68.31	78.42	74.32	71.24[r]	69.11
24[s]	98.56	67.71	80.57	74.30	75.46	69.15
26[t]	90.48	68.70	70.75	65.31	73.02	61.97
27[u]	90.38	70.75	65.16	67.83	72.88	61.83
28[v]	91.30	69.79	69.91	66.25	71.65	62.52
29[w]	90.57	67.90	69.09	65.24	70.50	61.86
30[x]	82.24	71.64	69.60	66.31	68.90	62.36
31[y]	82.17	70.68	69.77	65.97	68.73	62.16
32[z]	97.43	70.93	69.93	66.82	69.43	62.86
33[aa]	96.86	69.30	69.42	65.94	68.31	62.36
34[bb]	82.77	77.89	81.64	76.10	73.39	70.34
35[cc]	98.49	76.49	81.51	76.19	73.40	70.67
36[dd]	101.16	73.91	82.33	74.96	75.88	69.74
37[ee]	82.78	71.12	72.09	65.84	76.37	62.80
38[ff]	82.64	70.15	72.09	65.51	76.07	62.56

[a]For conditions of measurements, see Table 1.
[b]δ_{PhCH_2} 71.44; δ_{SCH_2} 25.67; $\delta_{SCH_2CH_3}$ 14.92.
[c]$J_{C\text{-}1,H\text{-}1}$ 151.4 Hz; $\delta_{CH_2CH_3}$ 14.92; $\delta_{CH_2CH_3}$ 25.78; δ_{COCH_3} 20.65, 20.59, 20.51, 20.47.
[d]δ_{SCH_2} 24.94; $\delta_{SCH_2CH_3}$ 14.21.
[e]$\delta_{CH_2CH_2Si}$ 65.81; $\delta_{CH_3CH_3Si}$ 17.80; $\delta_{Si(CH_3)_3}$ − 1.46; δ_{COCH_3} 20.89, 20.70 (3 C).
[f]δ_{SCH_2} 25.61; $\delta_{SCH_2CH_3}$ 14.83.
[g]$J_{C\text{-}1,H\text{-}1}$ 171.2 Hz; $\delta_{CH_2CH_2Si}$ 66.16; $\delta_{CH_2CH_2Si}$ 17.99; $\delta_{(CH_3)_3Si}$ − 1.40.
[h]$J_{C\text{-}1,H\text{-}1}$ 172.1 Hz.
[i]δ_{SCH_2} 25.32; $\delta_{SCH_2CH_3}$ 14.75; $\delta_{C(CH_3)_3}$ 39.05; $\delta_{C(CH_3)_3}$ 38.88, 38.82, 38.75, 38.68; $\delta_{C(CH_3)_3}$ 27.15, 27.09, 27.05, 27.02.
[j]$J_{C\text{-}1,H\text{-}1}$ 170.3 Hz; $\delta_{CH_2CH_2Si}$ 65.89; $\delta_{CH_2CH_2Si}$ 17.89; $\delta_{C(CH_3)_3}$ 38.89, 38.86, 38.77, 38.72; $\delta_{C(CH_3)_3}$ 27.14, 27.12, 27.09, 27.06; $\delta_{Si(CH_3)_3}$ − 1.38.
[k]$\delta_{CH_2CH_3}$ 14.80; $\delta_{CH_2CH_3}$ 24.83; δ_{CH_2Ph} 75.07. 73.38, 72.00.
[l]Measured in C_6D_6; $\delta_{CH_2CH_3}$ 15.25; $\delta_{CH_2CH_3}$ 25.27; δ_{CH_2Ph} 75.50. 73.88, 72.21.
[m]δ_{PhCH_2} 75.10, 73.14; 71.37; $\delta_{CH_2CH_3}$ 14.96; $\delta_{CH_2CH_3}$ 25.45; $\delta_{C(CH_3)_3}$ 39.05; $\delta_{C(CH_3)_3}$ 27.11.

complete and that one product was formed. A little ice, followed by saturated, aqueous $NaHCO_3$ was added, and the mixture was stirred for 2 h. After extraction with CH_2Cl_2, the organic phase was concentrated, and the residue was chromatographed, to give amorphous **1** (285 mg, 98%), $[\alpha]_D + 65°$ (*c* 1.45); CIMS: *m/z* 445 ($[M+18]^+$).

Anal. Calcd for $C_{22}H_{25}N_3O_4S$: C, 61.81; H, 5.89; N 9.83; S, 7.50. Found: C, 61.98; H, 6.00; N 9.9.76; S, 7.60.

2-(Trimethylsilyl)ethyl 4-azido-2-*O*-benzoyl-3-*O*-benzyl-4,6-dideoxy-α-D-mannopyranoside (2). The conversion **1** → **2** was a one product reaction. Chromatography gave, in virtually theoretical yield, compound **2**, which was identical with the independently synthesized substance (NMR, mp), obtained previously[6] in 82% yield.

Ethyl 1-thio-α-D-mannopyranoside (6). Conventional deacetylation (Zemplén) of **4** gave the title compound **6**, mp 126–127°C (from EtOH), $[\alpha]_D + 20.2°$ (*c* 0.85, H_2O).

Anal. Calcd for $C_8H_{16}O_5$: C, 42.84; H,7.19. Found: C, 42.75; H, 6.94.

2-(Trimethylsilyl)ethyl 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranoside (11). One major and a minor product were formed. Chromatography gave first the amorphous **11**, $[\alpha]_D - 42.4°$ (*c* 1.5). CIMS: *m/z* 714 ($[M+18]^+$).

Notes to Table 4 Continued:

[n]Measured in C_6D_6. δ_{PhCH_2} 75.64, 73.68; 72.00; $\delta_{CH_2CH_3}$ 15.30; $\delta_{CH_2CH_3}$ 25.97; $\delta_{C(CH_3)_3}$ 39.39; $\delta_{C(CH_3)_3}$ 27.69.

[o]Measured in C_6D_6; δ_{PhCH_2} 75.65, 73.91, 72.27; $\delta_{CH_2CH_2Si}$ 65.64; $\delta_{CH_2CH_2Si}$ 18.37; δ_{COCH_3} 20.99; $\delta_{Si(CH_3)_3} - 0.99$.

[p]Measured in C_6D_6; δ_{PhCH_2} 75.68, 73.93, 72.08; $\delta_{CH_2CH_2Si}$ 65.72; $\delta_{CH_2CH_2Si}$, 18.35; $\delta_{Si(CH_3)_3} - 0.96$.

[q]δ_{PhCH_2} 75.11, 73.16; 71.24; $\delta_{CH_2CH_2Si}$ 65.11; $\delta_{CH_2CH_2Si}$ 17.84; $\delta_{C(CH_3)_3}$ 38.94; $\delta_{C(CH_3)_3}$ 27.12; $\delta_{Si(CH_3)_3} - 1.41$.

[r]2-Carbon signal.

[s]$J_{C\text{-}1,H\text{-}1}$ 154.7 Hz; δ_{PhCH_2} 75.08, 73.23; 71.00; $\delta_{CH_2CH_2Si}$ 67.05; $\delta_{CH_2CH_2Si}$ 17.86; $\delta_{C(CH_3)_3}$ 39.01; $\delta_{C(CH_3)_3}$ 27.22; $\delta_{Si(CH_3)_3} - 1.35$.

[t]δ_{COCH_3} 20.59 (2 C), 20.54, 20.45.

[u]$J_{C\text{-}1,H\text{-}1}$ 162.4 Hz;δ_{COCH_3} 20.56 (2 C), 20.40, $\delta_{C(CH_3)_3}$ 39.15, $\delta_{C(CH_3)_3}$ 26.98.

[v]Measured in C_6D_6 $J_{C\text{-}1,H\text{-}1}$ 177.8 Hz; δ_{COCH_3} 20.63, 20.52 (2 C), 20.30.

[w]δ_{COCH_3} 20.85, 20.58 (2 C), 20.54; $\delta_{C(CH_3)_3}$ 39.06; $\delta_{C(CH_3)_3}$ 26.99.

[x]$J_{C\text{-}1,H\text{-}1}$ 168.5 Hz;δ_{COCH_3} 20.59, $\delta_{CH_2CH_3}$ 14.74, $\delta_{CH_2CH_3}$ 25.52.

[y]$J_{C\text{-}1,H\text{-}1}$ 168.5 Hz; δ_{COCH_3} 20.60, 20.55, 20.49, $\delta_{CH_2CH_3S}$ 14.76, $\delta_{CH_2CH_3S}$ 25.40; $\delta_{C(CH_3)_3}$ 39.02.

[z]Measured in C_6D_6; δ_{COCH_3} 20.36, 20.23 (2C) $\delta_{CH_2CH_2Si}$ 65.85; $\delta_{CH_2CH_2Si}$ 17.84; $\delta_{Si(CH_3)3} - 1.38$.

[aa]δ_{COCH_3} 20.60, 20.55, 20.51; $\delta_{CH_2CH_2Si}$ 65.72; $\delta_{CH_2CH_2Si}$ 17.73; $\delta_{C(CH_3)3}$ 38.95; $\delta_{Si(CH_3)3} - 1.52$.

[bb]Measured in C_6D_6; $\delta_{CH_2CH_3}$ 15.52, $\delta_{CH_2CH_3}$ 25.78, δ_{PhCH_2} 75.55, 73.82, 72.87; 72.49.

[cc]Measured in C_6D_6; $J_{C\text{-}1,H\text{-}1}$ 166.0 Hz; δ_{PhCH_2} 75.57, 73.90, 73.52, 72.62; $\delta_{CH_2CH_2Si}$ 65.34; $\delta_{CH_2CH_2Si}$ 18.45; $\delta_{Si(CH_3)_3} - 0.93$.

[dd]$J_{C\text{-}1,H\text{-}1}$ 153.5 Hz; δ_{PhCH_2} 75.12, 73.78, 73.43, 71.31; $\delta_{CH_2CH_2Si}$ 67.19; $\delta_{CH_2CH_2Si}$ 18.28, $\delta_{Si(CH_3)_3} - 1.39$.

[ee]$J_{C\text{-}1,H\text{-}1}$ 153.9 Hz; δ_{COCH_3} 20.72, 20.66, 20.60; $\delta_{CH_2CH_3}$ 14.89, $\delta_{CH_2CH_3}$ 25.91.

[ff]$J_{C\text{-}1,H\text{-}1}$ 154.1 Hz; $\delta_{C(CH_3)_3}$ 39.10; $\delta_{C(CH_3)_3}$ 27.06; $\delta_{CH_2CH_3}$ 14.90; $\delta_{CH_2CH_3}$ 25.95; δ_{COCH_3} 20.67, 20.64, 20.50.

Anal. Calcd for $C_{39}H_{40}O_{10}Si$: C, 67.72; H, 5.79. Found: C, 66.86; H, 5.86.

Eluted next was 2,3,4,6-tetra-*O*-benzoyl-α,β-D-mannopyranose (**12**), which was identified by comparison with an authentic sample,[21] (TLC, NMR); CIMS: *m/z* 614 ($[M+18]^+$).

Ethyl 2,3,4,6-tetra-*O*-pivaloyl-1-thio-α-D-mannopyranoside (13). Pivaloylation of **6**, as described below for preparation of **18**, gave the title ethyl 1-thioglycoside **13** in 92% yield, mp 104–105°C (from EtOH), $[\alpha]_D + 58°$ (*c* 0.9); CIMS: *m/z* 578 ($[M+18]^+$).

Anal. Calcd for $C_{28}H_{48}O_9S$: C, 59.97; H, 8.63. Found: C, 60.12; H, 8.65.

2-(Trimethylsilyl)ethyl 2,3,4,6-tetra-*O*-pivaloyl-α-D-mannopyranoside (14). One major product, faster moving than the starting material, and one minor, slower moving product was formed, as shown by TLC (30:1 toluene–acetone). Chromatography gave **14**, mp 82–84°C (from EtOH containing a few drops of water, $[\alpha]_D + 33.5°$ (*c* 0.9); FAB MS: *m/z* 455 ($[M+Na]^+$).

Anal. Calcd for $C_{31}H_{56}O_{10}Si$: C, 60.36; H, 9.15. Found: C, 60.32; H, 9.14.

Ethyl 3,4,6-tri-*O*-benzyl-2-*O*-pivaloyl-1-thio-α-D-mannopyranoside (18). Pivaloyl chloride (1.2 mL, 10 mmol) was added with stirring to a solution of ethyl 3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside[18] (**16**, 2.36 g, 5 mmol) in pyridine (1.2 mL, 15 mmol), and the mixture was stirred at room temperature with exclusion of atmospheric moisture overnight. TLC (15:1 hexane–acetone) showed that the reaction was complete and that one product was formed. Aqueous $NaHCO_3$ solution was added, to destroy excess of the reagent, and the mixture was partitioned between CH_2Cl_2 and aqueous $NaHCO_3$ solution. The organic phase was dried, concentrated, and chromatography gave amorphous compound **18** (3.10 g, 87%), $[\alpha]_D + 71°$ (*c* 0.9); CIMS: *m/z* 596 ($[M+18]^+$).

Anal. Calcd for $C_{34}H_{42}O_6S$: C, 70.56; H, 7.31. Found: C, 70.77; H,7.41.

2-(Trimethylsilyl)ethyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (19). One major and three minor products were formed. Eluted first was the title compound **19**, $[\alpha]_D + 29°$ (*c* 2.8), CIMS: *m/z* 591 ([M-1]).

Anal. Calcd for $C_{33}H_{44}O_7Si$: C, 68.89; H, 7.48. Found: C, 68.98; H, 7.51.

Two of the three minor products formed were isolated in amounts sufficient to be identified by MS and NMR spectroscopy. Eluted next was the product of deacetylation of the major product **19**, 2-(trimethylsilyl)ethyl 3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (**20**, ~20 mg). ^{1}H NMR ($CDCl_3$): δ 4.91 (d, 1 H, $J_{1,2}$ 1.7 Hz, H-1); ^{13}C NMR ($CDCl_3$): δ 98.68 ($J_{C\text{-}1,H\text{-}1}$ 168.6 Hz, C-1), 80.27 (C-3), 75.10, 73.40, 71.91 (3 CH_2Ph), 73.37 (C-4), 70.93 (C-5), 68.96 (C-6), 68.51 (C-2), 64.88 (OCH_2CH_2Si), 17.85 (CH_2Si), −1.37[$(CH_3)_3$]; FAB MS: *m/z* 573 ($[M+Na]^+$), which was not further characterized. When this material was acetylated, the product was indistinguishable from compound **19** described above (TLC, NMR, MS).

Eluted last was the hemiacetal **21**, as indicated by its chromatographic mobility and *m/z* value 515 ($[M+Na]^+$) in the FAB MS spectrum.

2-(Trimethylsilyl)ethyl 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (22). One major product, faster moving that the starting material, and one minor,

slower moving product was formed, as shown by TLC (40:1 toluene–acetone). Chromatography gave the amorphous **22**, $[\alpha]_D - 2.3°$ (*c* 3.4); CIMS: *m/z* 672 ($[M+18]^+$).

Anal. Calcd for $C_{39}H_{46}O_7Si$: C, 71.53; H, 7.08. Found: C, 71.55; H, 7.17.

2-(Trimethylsilyl)ethyl 3,4,6-tri-*O*-benzyl-2-*O*-pivaloyl-α-D-mannopyranoside (23). Three products were formed, the one showing the fastest chromatographic mobility largely predominating. Chromatography (25:1 toluene–EtOAc) gave first the title glycoside **23**, $[\alpha]_D + 29°$ (*c* 0.9); CIMS: *m/z* 652 ($[M+18]^+$).

Anal. Calcd for $C_{37}H_{50}O_7Si$: C, 70.00; H, 7.94. Found: C, 70.06; H, 7.82.

Eluted next was a small amount of material whose NMR spectra showed it to be 2-(trimethylsilyl)ethyl 3,4,6-tri-*O*-benzyl-2-*O*-pivaloyl-β-D-mannopyranoside (**24**).

1,3,4,6-Tetra-*O*-acetyl-2-*O*-benzoyl-β-D-mannopyranose (26). Benzoylation of **25**,[17] as described above for the preparation of **1** gave **26** in virtually theoretical yield, mp 103–104°C (from EtOH), $[\alpha]_D - 65°$ (*c* 0.8); CIMS: *m/z* 470 ($[M+18]^+$).

Anal. Calcd for $C_{21}H_{24}O_{11}$: C, 55.75; H, 5.35 Found: C, 55.68; H, 5.35.

1,3,4,6-Tetra-*O*-acetyl-2-*O*-pivaloyl-β-D-mannopyranose (27). A reaction of the 2-hydroxy compound **25** with pivaloyl chloride, as described above for similar benzoylation gave, after chromatography, the title derivative **27** in virtually theoretical yield, mp 106–107°C (from EtOH), $[\alpha]_D - 20.4°$ (*c* 0.8); CIMS: *m/z* 455 ($[M+18]^+$).

Anal. Calcd for $C_{19}H_{28}O_{11}$: C, 52.77; H, 6.53. Found: C, 52.91; H, 6.47.

1,3,4,6-Tetra-*O*-acetyl-2-*O*-benzoyl-α-D-mannopyranose (28). A solution of **26** (1 g) in 10:4:0.1 Ac_2O:AcOH:H_2SO_4 (6 mL) was kept at room temperature overnight. TLC (3:1 hexane–acetone) showed that a faster moving product was formed. ^1H NMR showed that a ~93:7 equilibrium mixture of α- and β-anomers was present.[b] Solid NaOAc trihydrate was added with stirring, to neutralize the mineral acid, followed by aqueous $NaHCO_3$, to destroy Ac_2O and neutralize AcOH. The resulting mixture was partitioned between CH_2Cl_2 and aqueous $NaHCO_3$ solution, the organic phase was dried, concentrated, and chromatography gave first the pure α-anomer **28** (0.83 g, 83%), mp 102–103°C (from EtOH), $[\alpha]_D - 15°$ (*c* 0.8); FAB MS: *m/z* 475 ($[M+Na]^+$).

Anal. Calcd for $C_{21}H_{24}O_{11}$: C, 55.75; H, 5.35 Found: C, 55.72; H, 5.35.

Eluted next was a mixture of α- and β-anomers. Such mixtures, obtained from several experiments, could be processed as described above, to obtain more of the desired **28**.

1,3,4,6-Tetra-*O*-acetyl-2-*O*-pivaloyl-α-D-mannopyranose (29). Anomerization of **27**, as described above for the preparation of **26** gave, after chromatography, the amorphous **29** (90%), $[\alpha]_D + 42°$ (*c* 0.8); CIMS: *m/z* 455 ($[M+18]^+$).

Anal. Calcd for $C_{19}H_{28}O_{11}$: C, 52.77; H, 6.53. Found: C, 52.79; H, 6.65.

[b]That ratio had not changed when, in a separate experiment, the reaction time was extended to 48 h, as showed by ^1H NMR spectroscopy. The two anomers show almost identical mobility on TLC.

Ethyl 3,4,6-tri-*O*-acetyl-2-*O*-benzoyl-1-thio-α-D-mannopyranoside (30). *A*. From 1,3,4,6-Tetra-*O*-acetyl-2-*O*-benzoyl-β-D-mannopyranose (**26**). Ethanethiol (0.45 mL, 3 mmol) followed by BF_3-etherate (1.5 mL) was added at 0°C, with stirring and exclusion of moisture, to a solution of **26** (1.35 g, 3 mmol) in CH_2Cl_2 (60 mL), and the mixture was kept in a refrigerator (5–7°C) until TLC (3:1 hexane–acetone) showed that almost all starting material was consumed (~3 days). One major and several minor products were formed. The mixture was slowly poured into aqueous $NaHCO_3$, contained in a separatory funnel, the product was extracted with CH_2Cl_2, and chromatography gave first the α-anomer **30** (0.785 g, 58%), mp 66–67°C (from EtOH), $[\alpha]_D + 127°$ (*c* 1.7); CIMS: *m/z* 472 ($[M+18]^+$).

Anal. Calcd for $C_{21}H_{26}O_9S$: C, 55.50; H, 5.77. Found: C, 55.62; H, 5.90.

Eluted next was a small amount of material whose NMR spectra showed it to be ethyl 3,4,6-tri-*O*-acetyl-2-*O*-benzoyl-1-thio-β-D-mannopyranoside (**37**, 45 mg, 3%); CIMS: *m/z* 472 ($[M+18]^+$).

B. From 1,3,4,6-tetra-*O*-acetyl-2-*O*-benzoyl-α-D-mannopyranose (**28**). The reaction of **28**, performed on the same scale as described above but with only 1.2 mL of BF_3-etherate, was terminated after ~24 h. Chromatography gave **30** and **37** in 65 and 2% yield, respectively.

Ethyl 3,4,6-tri-*O*-acetyl-2-*O*-pivaloyl-1-thio-α-D-mannopyranoside (31). *A*. From 1,3,4,6-Tetra-*O*-acetyl-2-*O*-pivaloyl-β-D-mannopyranose (**27**). The reaction, carried out as described above for the preparation of **30** (*B*) gave, after a reaction time of 48 h and chromatography, the α-anomer **31** (680 mg, 52%), 93.5–94°C, $[\alpha]_D + 90°$ (*c* 0.8). CIMS: *m/z* 452 ($[M+18]^+$).

Anal. Calcd for $C_{19}H_{30}O_9S$: C, 52.52; H, 6.96. Found: C, 52.53; H, 7.03.

Eluted next was the amorphous ethyl 3,4,6-tri-*O*-acetyl-2-*O*-pivaloyl-1-thio-β-D-mannopyranoside (**38**, 300 mg, 23%), $[\alpha]_D - 76°$ (c 1.6); CIMS: *m/z* 452 ($[M+18]^+$). Found: C, 53.02; H, 6.77.

B. From 1,3,4,6-tetra-*O*-acetyl-2-*O*-pivaloyl-α-D-mannopyranose (**29**). Reaction as above (*A*) gave compounds **31** and **38** in 60 and 12%, respectively.

2-(Trimethylsilyl)ethyl 3,4,6-tri-*O*-acetyl-2-*O*-benzoyl-α-D-mannopyranoside (32). One major and one minor product were formed. Chromatography (5:1 hexane–acetone) gave **32**, $[\alpha]_D + 15.5°$ (*c* 0.5); CIMS: *m/z* 528 ($[M+18]^+$).

Anal. Calcd for $C_{24}H_{34}O_{10}Si$: C, 56.45; H, 6.71. Found: C, 56.51; H, 6.61.

2-(Trimethylsilyl)ethyl 3,4,6-tri-*O*-acetyl-2-*O*-pivaloyl-α-D-mannopyranoside (33). One major and one minor product were formed. Chromatography (10:1 toluene–acetone) gave **33** $[\alpha]_D + 53°$ (*c* 1.1); CIMS: *m/z* 508 ($[M+18]^+$).

Anal. Calcd for $C_{22}H_{38}O_{10}Si$: C, 53.86; H, 7.81. Found: C, 53.77; H, 7.80.

2-(Trimethylsilyl)ethyl 2,3,4,6-tetra-*O*-benzyl-α- (35) and β-D-mannopyranoside (36). Two products, which showed similar chromatographic mobility were formed, as shown by TLC (10:1 hexane–EtOAc). The α-anomer **35**, eluted first, showed $[\alpha]_D + 48°$ (*c* 0.7). FABMS: *m/z* 663 ($[M+Na]^+$).

Anal. Calcd for $C_{39}H_{48}O_6Si$: C, 73.09; H,7.55. Found: C, 73.03; H,7.70.

The β-anomer **36**,which was eluted next, crystallized on standing. Recrystallization from EtOH gave material melting at 56–59°C, $[\alpha]_D - 13.5°$ (*c* 0.3), FABMS: *m/z* 663 ($[M+Na]^+$). Found: C, 73.16; H, 7.70.

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