J. prakt. Chem. 340 (1998) 204 – 213

Journal für praktische Chemie
Chemiker-Zeitung

Fortschrittsbericht · Progress Report

The Glycosylation of Silylated Alcohols

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Received February 2nd, 1998

Abstract. Reactions of 1-*O*-trimethylsilyl-glycoses, 1-*O*-acyl-glycoses and glycosyl fluorides, respectively, with silylated alcohols (glycodesilylations) are summarized. Synthetic strategies toward oligosaccharides using glycodesilylations are discussed as well and some typical experimental procedures are given.

Contents

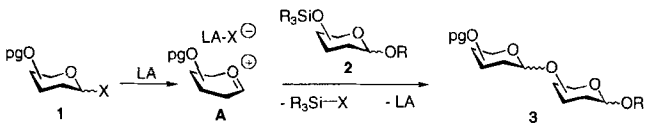
1 Introduction

The efficient chemical construction of complex oligosaccharide structures demands synthetic procedures that allow the highly stereo- and regioselective formation of *O*-glycosidic bonds. Usually, for that purpose, a fully protected saccharide building block which is prone to activation of the anomeric center (glycosyl donor) is condensed with a partially blocked saccharide building block that has those hydroxyls unprotected which are planned to be glycosylated (glycosyl acceptor). Although the "classical" approach toward the chemical synthesis of oligosaccharides has been brought to an overwhelming perfection in recent years [1–5], it still appears to be a rather tedious venture to prepare the needed partially blocked glycosyl acceptors. Often, from a practical point of view, the most time consuming operations during syntheses of complex oligosaccharides are the selective protecting group manipulations which are required to get access to the desired acceptor blocks [6]. Therefore, direct glycosylation of a suitably protected hydroxy group of a glycosyl acceptor block without the need of deblocking this position prior to the glycosylation step is an attractive strategy for oligosaccharide preparation. Thus, in this review, recent examples will be presented that involve the direct glycosylation of silylated alcohols (glycodesilylation) and the application of that strategy to the synthesis of complex oligosaccharides.

2 General Aspects of Glycodesilylations

In general, for the reaction of a glycosyl donor with a silylated alcohol, a glycosyl cation **A** is first generated from a suitable precursor **1** like 1-*O*-silylated or 1-*O*-acylated glycoses and glycosyl fluorides, respectively. The thus generated cation **A** then attacks the silylated oxygen atom of the acceptor **2** to form the *O*-glycoside **3** by cleaving the Si–O bond of **2** (Scheme 1). In this respect, the glycodesilylation resembles the classical Koenigs-Knorr reaction. However, since no acid is generated during glycodesilylation there is no need to add a base to the reaction mixture which often results in the formation of orthoesters in Koenigs-Knorr reactions. Table 1–3 sumarizes glycodesilylations using

1-*O*-silylated glycoses, 1-*O*-acylated glycoses and glycosyl fluorides.



Scheme 1 Principle of the formation of *O*-glycosidic bonds by glycodesilylation LA = Lewis acid, pg = protecting group, R = alkyl or aryl, X = leaving group

2.1 1-*O*-Trimethylsilyl Glycoses as Donors

Using 1-*O*-trimethylsilyl-2,3,4,6-tetra-*O*-acetyl-D-glucopyranose as the donor (Table 1, entries 1–5), Tietze [7] demonstrated that TMSOTf catalyzed glycodesilylation of aryl trimethylsilanes gave almost exclusively the corresponding aryl β-D-glucopyranosides *via* neighboring participation of the acetyl group at position 2 (*i.e.* the configuration of the anomeric center of the donor does not have any influence on the anomeric outcome of the glycosylation). This glycodesilylation procedure has later been extended by Glaudemans [8] to the synthesis of β-(1→6)-linked di- and trisaccharides (Table 1, entries 6–9) from glycosyl acceptors having a regioselectively introducable 6-*O*-*t*-butyl-dimethylsilyl group. The procedure was also compatible to labile diazirin groups in the acceptor (entry 9). When 1-*O*-trimethylsilyl-2,3,4,6-tetra-*O*-benzyl-D-glucopyranose is used as the donor (Table 1, entries 10–17) the corresponding α-glycosides were formed preferentially. For 1-*O*-trimethylsilyl-2,3,5-tri-*O*-benzyl-D-ribofuranoses, Mukaiyama [9] showed that the anomeric selectivity of the glycodesilylation can be governed by the Lewis acid. For example, with a mixture of Ph_2SnO and TMSOTf β-D-furanosides were formed highly selectively (Table 1, entries 18–22) whereas with additionally added $LiClO_4$ (entries 23–27), α-D-furanosides were the main products.

2.2 1-*O*-Acyl Glycoses as Donors

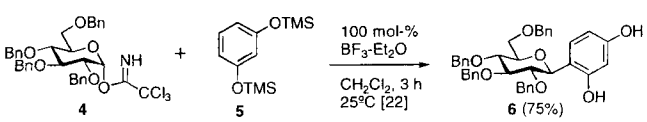
Similar glycodesilylations were studied for 1-*O*-acylated glycosyl donors by Mukaiyama [10] and Charette [11] (Table 2). Once again, high α-selectivities were obtained from trimethylsilylated acceptors and benzyl protected donors with various Lewis acids (entries 1–3 and 9–11). However, when a neighboring active benzoyl group was present at position 2 of the donor, solely the corresponding β-D-glycosides were obtained (entries 4–8). Even different silyl groups may be differentiated as outlined by Charette [11] for 1-trimethylsiloxy-4-*t*-butyldiphenylsiloxy-2-butene (entry 7). Here, glycodesilylation was exclusively found at the more labile TMS group. Thus, the glycodesilylation protocol can be extended to a chemoselective glycosylation procedure (see also below).

2.3 Glycosyl Fluorides as Donors

When glycosyl fluorides are used as donors in glycodesilylations, fluorosilanes are formed. Since the formation of a Si–F bond is thermodynamically favoured the reaction of a glycosyl fluoride with a silylated alcohol is expected to proceed faster than that with an alcohol. Indeed, Kunz [18] found for BF_3-diethylether catalyzed condensations of glycosyl fluorides (Table 3, entries 9–12) that trimethylsilylated alcohols reacted faster than the corresponding unblocked alcohols. Furthermore, triethylamin had to be added for the latter condensations in order to trap the formed HF. No such dependence was, however, found by Thiem [13] who used TiF_4, SnF_4 and TMSOTf in different solvents instead of BF_3-diethylether as the Lewis acid (entries 1 and 3). Even an inverted reactivity was encounterd by Noyori [16] who found for condensations catalyzed by SiF_4 that unblocked alcohols reacted significantly faster than the corresponding trimethylsilylated counterparts (entries 5–7). Obviously, the catalyst plays an important role for the reactivity in glycodesilylations. Nevertheless, the diastereoselectivity of the condensation of glycosyl fluorides with silylated acceptors is apparantly the same as for other glycosyl donors (see above). Acylated glycosyl fluorides result in the formation of β-glycosides (entries 1, 2, 8 and 9) whereas for benzyl protected glycosyl fluorides the selectivity depends on the catalyst and the solvent (entries 3–7 and 12–14). In addition to glycosyl fluorides as donors in glycodesilylations also 1-*O*-unprotected glycoses may be used in combination with special catalysts [20, 21].

2.4 Restrictions for Glycodesilylations

If electron rich aryloxysilanes are used as acceptors for glycodesilylations (*cf.* Table 1, entries 2, 3 and 11, 12) *C*-glycoside formation may interfere with the formation of *O*-glycosides. For example Schmidt reported reactions of glycosyl trichloroacetimidates **4** with 1,3-



Scheme 2

Table 1 Glycodesilylations with 1-*O*-trimethylsilyl glycoses and glycofuranoses

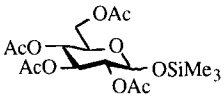
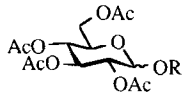
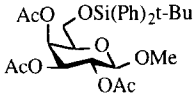
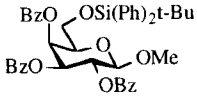
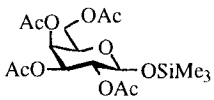
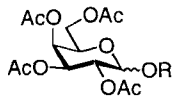
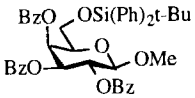
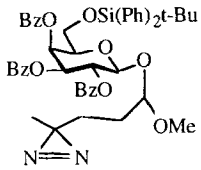
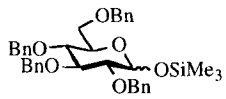
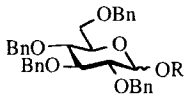
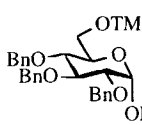
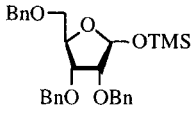
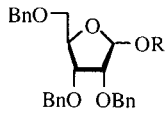
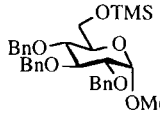
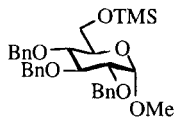
entry	Donor **1**	Acceptor **2**	Lewis acid	conditions	Product **3** yield, anomeric ratio	Ref.
		R-OSiMe$_3$				
1		R=Ph	3 mol-% TMSOTf	CH_2Cl_2 24 h, 20 °C	90% $\alpha:\beta$ = 9:91	[7]
2		R=*p*-Me-Ph			79% $\alpha:\beta$ = 6:94	[7]
3		R=*p*-MeO-Ph			86% $\alpha:\beta$ < 3:97	[7]
4		R=2-Naphthyl			77% $\alpha:\beta$ = 8:92	[7]
5		R=Östron-3-yl			64% $\alpha:\beta$ < 3:97	[7]
6			70 mol-% TMSOTf	CH_2Cl_2 3 d, −70 to −30 °C	70% $\alpha:\beta$ = 0:100	[8]
7			60 mol-% TMSOTf	CH_2Cl_2 2 d, −70 to −30 °C	74% $\alpha:\beta$ = 0:100	[8]
		R-OSiMe$_3$				
8			50 mol-% TMSOTf	$C_2H_4Cl_2$ 2 d, −50 to −30 °C	76% $\alpha:\beta$ = 0:100	[8]
9			75 mol-% TMSOTf	CH_2Cl_2 8 d, −78 °C	54% $\alpha:\beta$ = 0:100	[8]
		R-OSiMe$_3$				
10		R= Ph	3 mol-% TMSOTf	CH_2Cl_2 24 h, 20 °C	75% $\alpha:\beta$ = 88:12	[7]
11		R= *p*-Me-Ph			90% $\alpha:\beta$ = 88:12	[7]
12		R= *p*-MeO-Ph			80% $\alpha:\beta$ = 88:12	[7]
13		R= 2-Naphthyl			53% $\alpha:\beta$ = 40:60	[7]
14		R= Östron-3-yl			69% $\alpha:\beta$ = 25:75	[7]
15		R= Cyclohexyl	$SiCl_3ClO_4$ $Ph_2Sn{=}S$ $LiClO_4$	10 mol-% 150 mol-% 300 mol-% Et_2O, 20 °C	96% $\alpha:\beta$ = 91:9	[9]
16		R = Cholestan-3β-yl			100% $\alpha:\beta$ = 83:17	[9]
17					75% $\alpha:\beta$ = 96:4	[9]

Table 1 (continued)

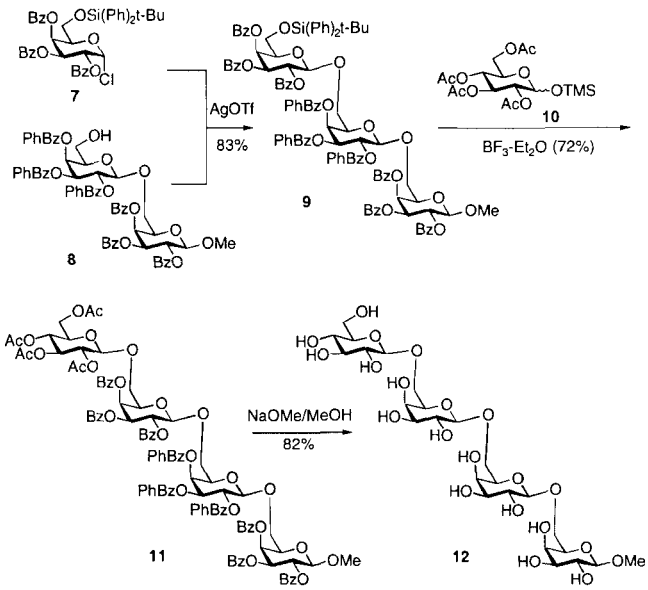
entry	Donor **1**	Acceptor **2**	Lewis acid	conditions	Product **3**	Ref.
						
18		R = Cyclohexyl	$Ph_2Sn{=}O$ TMSOTf CH_2Cl_2	150 mol-% 3 mol-% −23 to 20 °C	100% $\alpha{:}\beta$ = 2:98	[9]
19		R = Cholestan-3β-yl			98% $\alpha{:}\beta$ = 1:99	[9]
20					98% $\alpha{:}\beta$ = 5:95	[9]
21		R = Me			100% $\alpha{:}\beta$ = 1:99	[9]
22		R = *t*-Bu			74% $\alpha{:}\beta$ = 2:98	[9]
23		R= Cyclohexyl	$Ph_2Sn{=}O$ TMSOTf $LiClO_4$ CH_2Cl_2	150 mol-% 3 mol-% 300 mol-% −23 to 20 °C	100% $\alpha{:}\beta$ = 97:3	[9]
24		R = Cholestan-3β-yl			96% $\alpha{:}\beta$ = 99:1	[9]
25					100% $\alpha{:}\beta$ = 95:5	[9]
26		R = Me			100% $\alpha{:}\beta$ = 95:5	[9]
27		R = *t*-Bu			75% $\alpha{:}\beta$ = 98:2	[9]

bis-trimethylsiloxybenzene **5** to give exclusively the corresponding *C*-glycoside **6** [22].

Similar formations of *C*-glycosides were also found for Lewis acid catalyzed condensations of 1-*O*-acylated glycosyl donors with siloxybenzenes [23, 24] and trimethylsilyl enolethers [23], respectively and of glycosyl fluorides with phenols [25, 26].

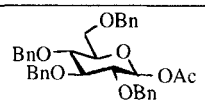
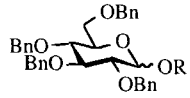
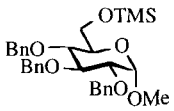
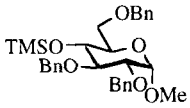
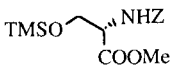
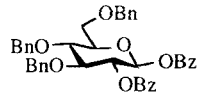
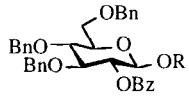
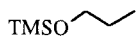
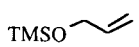
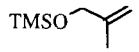
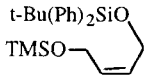
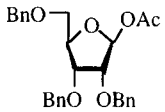
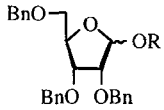
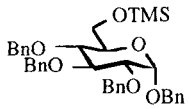
3 Glycodesilylations for Oligosaccharide Syntheses

As outlined in chapter 2, the glycodesilylation protocol appears to be especially useful for the efficient preparation of oligosaccharides. Since silyl groups may be introduced regioselectively into saccharides [6], following glycodesilylation affords oligosaccharides without further manipulation of protecting groups. An example comprises the synthesis of tetrasaccharide methyl glycoside **12** which has been used for epitope mapping of monoclonal antigalactan antibodies [27]. First, silylated galactosyl chloride **7** was condensed with disaccharide methyl galactoside **8** affording silylated trisaccharide **9** [28]. Next, the latter was coupled with 1-*O*-silylated glucosyl donor **10** to give tetrasaccharide **11** [8].



Scheme 3

Table 2 Glycodesilylations with 1-*O*-acetyl and 1-*O*-benzoyl glycopyranoses and glycofuranoses

entry	Donor **1**	Acceptor **2**	Lewis acid	conditions	Product **3** yield, anomeric	Ref.
		R-OTMS				
1			20 mol-% $GaCl_3$/ $AgClO_4$	Et_2O 1 h, 20 °C	95% $\alpha:\beta = 96:4$	[10]
2					84% $\alpha:\beta = 91:9$	[10]
3					86% $\alpha:\beta = 94:6$	[10]
		R-OTMS				
						
4			5 mol-% TMSOTf	$C_2H_4Cl_2$ 1 h, 25 °C	92%	[11]
5					82%	[11]
6				0.5 h, 25 °C	39%	[11]
7				1.5 h, 25 °C	50%	[11]
8		R = cholestan-3β-yl			74%	[11]
		R-OSiMe$_3$				
9		R = cholestan-3β-yl	20 mol-% $SnCl_4/Sn(OTf)_2$ 100 mol-% $LiClO_4$	CH_2Cl_2 5 h, −23 °C	86% $\alpha:\beta = 90:10$	[12]
10		R = n-$C_{18}H_{38}$			71% $\alpha:\beta = 92:8$	[12]
11			10 mol-% $SnCl_4/Sn(OTf)_2$/ $NaIO_4$ 100 mol-% $LiClO_4$	CH_2Cl_2 21 h, −23 °C	66% $\alpha:\beta = 100:0$	[12]

Final deblocking of **11** then afforded tetrasaccharide **12** [8].

Another useful feature of glycodesilylations which may be applied for efficient strategies for oligosaccharide synthesis lies in the discrimination of different silyl groups of the donor moiety. For example, it has been demonstrated for 6-*O*-silylated hexa-*O*-benzoyl-amygdalin (*cf.* Table 3, entry 2) that the dimethylthexylsilyl group was much more faster glycodesilylated by tetra-*O*-acetyl-glucopyranosyl fluoride than the *t*-butyldiphenylsilyl group [14]. The selectivity solely depends on the reaction conditions (amount of Lewis acid). Thus, different silyl protecting groups in one glycosyl donor may be sequentially glycosylated as outlined below. Reac-

Table 3 Glycodesilylations with glycosyl fluorides

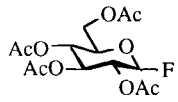
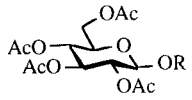
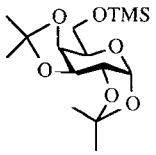
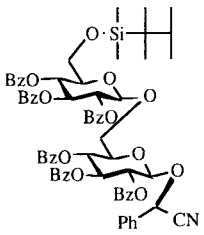
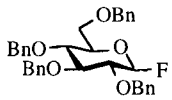
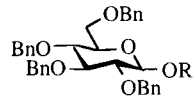
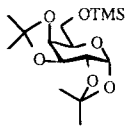
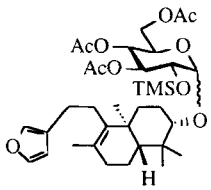
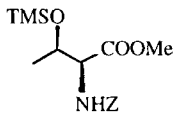
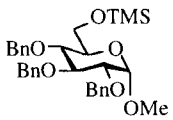
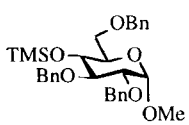
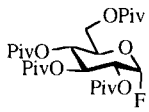
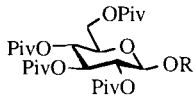
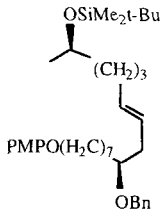
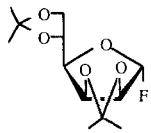
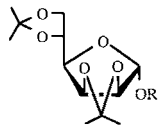
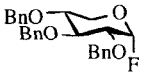
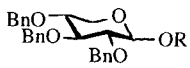
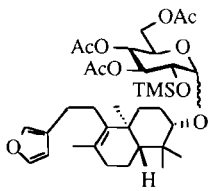
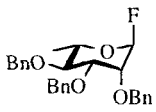
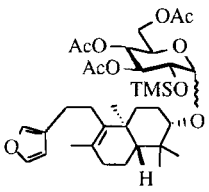
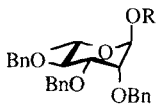
entry	Donor **1**	Acceptor **2**	Lewis acid	conditions	Product **3** yield, anomeric	Ref.
		R-OSiR'$_3$				
1	β-fluoride		50 mol-% TiF_4	MeCN 2 h, 22 °C	60% α:β = 0:100	[13]
2	α-fluoride		10 mol-% BF_3-Et_2O	CH_2Cl_2 24 h, 25 °C	72% α:β = 0:100	[14]
		R-OTMS				
3	β-fluoride		50 mol-% TiF_4, MeCN TiF_4, Et_2O SnF_4,MeCN TMSOTf in Et_2O	 2 h, 0 °C 24 h, 0 °C 2 h, 22 °C 22 h, 22 °C	 88% α:β = 13:87 91% α:β = 58:42 89% α:β = 15:85 85% α:β = 87:13	[13]
4	α-fluoride		8 mol-% TMSOTf	toluene 2 h, 25 °C β-acceptor α-acceptor	 62% α:β = 23:77 43% α:β = 53:47	[15]
5	α/β-fluoride		20 mol-% SiF_4	Et_2O 5 h, 24 °C	65% α:β = 67:33	[16]
6			20 mol-% SiF_4	Et_2O 5 h, 24 °C	68% α:β = 78:22	[16]
7			20 mol-% SiF_4	Et_2O 5 h, 24 °C	66% α:β = 75:25	[16]

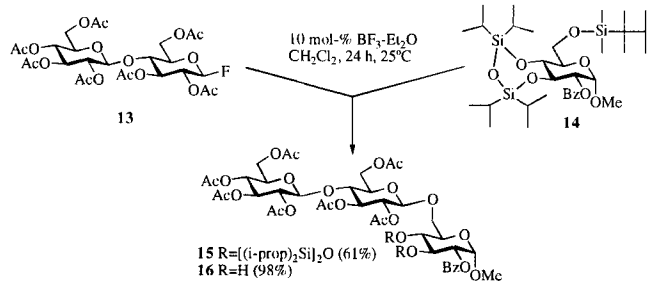
Table 3 (continued)

entry	Donor **1**	Acceptor **2**	Lewis acid	conditions	Product **3**	Ref.
		R-$OSiMe_3$				
8			BF_3–Et_2O	CH_2Cl_2 24 °C	71%	[17]
9		R=CH_2-Ph	420 mol-% BF_3-Et_2O	CH_2Cl_2 10 min, 24 °C	75%	[18]
		R-OTMS				
10		R = cholestan-3β-yl	420 mol-% BF_3-Et_2O	CH_2Cl_2 10 min, 24 °C	67%	[18]
11		R = CH_2-Ph			54%	[18]
		R-OTMS				
12		R = cholestan-3β-yl	420 mol-% BF_3-Et_2O	CH_2Cl_2 10 min, 24 °C	81% α:β = 86:14	[18]
13			8 mol-% TMSOTf	toluene 2 h, 25 °C β-acceptor α-acceptor	51% α:β = 38:62 45% α:β = 0:100	[15, 19]
14		R-OTMS: 	8 mol-% TMSOTf	toluene 2 h, 25 °C β-acceptor α-acceptor	 55% 91%	[15]

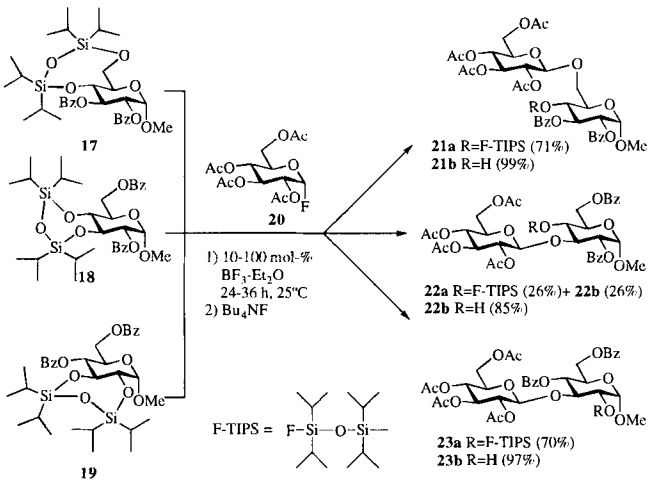
tion of hepta-*O*-acetyl-cellobiosyl fluoride **13** with methyl α-D-glucopyranoside **14** afforded trisaccharide **15** in 61% yield [29]. No glycodesilylation was observed at the siloxane protecting group of the silylated glycosyl acceptor **14**. Trisaccharide **15** was subsequently converted into glycosyl acceptor **16** having positions 3 and 4 at the non-reducing end free for further elongation of the saccharide chain.

3.1 Regioselective Glycodesilylations

In addition to the chemoselective glycodesilylation (*i.e.* discrimination of different silyl protecting groups) regioselective glycodesilylations (*i.e.* discrimination of different positions of the same silyl protecting group) may be realized as well. Condensation of the regioisomers **17**–**19** of 1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl



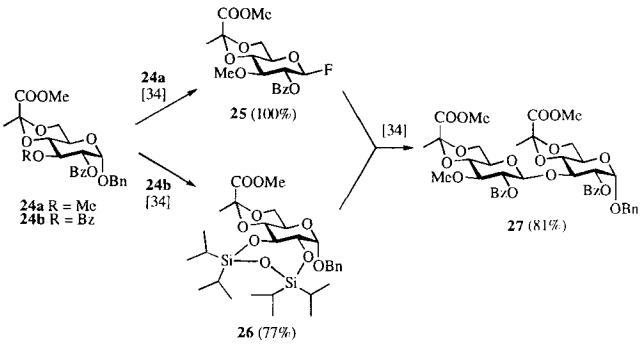
Scheme 4



Scheme 5

protected methyl α-D-glucopyranosides with tetra-*O*-acetyl-glucopyranosyl fluoride **20** afforded the methyl gentiobioside **21** and laminaribiosides **22** and **23**, respectively [30]. The β-(1→3)-selective reaction in case of **23** was especially useful because it resulted in an inverted selectivity compared to the classical glycosylation of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside with halogenoses giving predominantly the corresponding sophorobioside [31, 32]. Subsequent cleavage of the fluorosiloxane residue in compounds **21a**–**23a** gave the corresponding disaccharide acceptors **21b**–**23b** which can be used for the preparation of higher oligosaccharides. This regioselective glycodesilylation procedure also was further extended to various siloxane protected acceptors in the manno and galacto series [29].

The regioselective glycodesilylation can be applied as well to a convergent glycosylation strategy for the efficient preparation of otherwise difficultly to obtain pyruvated saccharides [33, 34] as outlined in scheme 6. First, 4,6-pyruvated benzyl glucoside **24a** was converted in two steps into glycosyl fluoride **25** and glucoside **24b** into the 2,3-siloxane protected counterpart **26**, respectively. Next, donor **25** was regioselectively condensed with silylated acceptor **26** to afford the corresponding doubly pyruvated β-(1→3)-linked laminaribioside **27** in 81% overall yield after subsequent cleavage of the fluorosiloxane residue followed by rebenzoylation of the intermediate. Disaccharide **27** which resembles a fragment of the glycolipid of *Mycobacterium smegmatis* has also been used for the construction of higher oligosaccharides [34].



Scheme 6

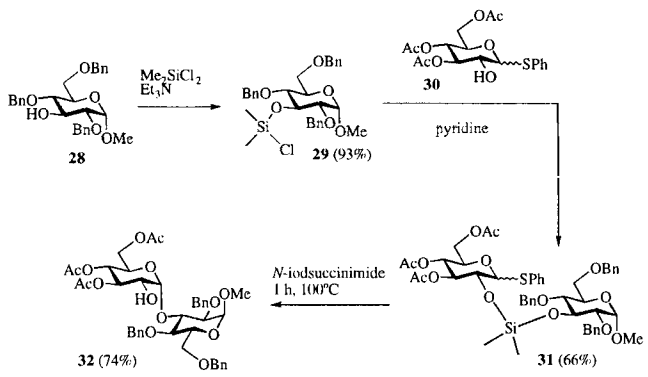
3.2 Intramolecular Glycodesilylations

Intramolecular glycodesilylations can be accomplished when glycosyl donor and glycosyl acceptor are linked by a silylene tether. Stork [35] and Bols [36] used this concept originally based on the intramolecular glycosylation protocol of Hindsgaul [37] for controlling the anomeric outcome of mannosylations and glucosylations, respectively. For example, the partially benzylated methyl glucoside **28** was first condensed with dichlorodimethylsilane followed by coupling of intermediate **29** with thioglucoside **30**. The silylene-tethered saccharide **31** was then converted by intramolecular glycodesilylation into the α-(1→3)-linked disaccharide **32** [38].

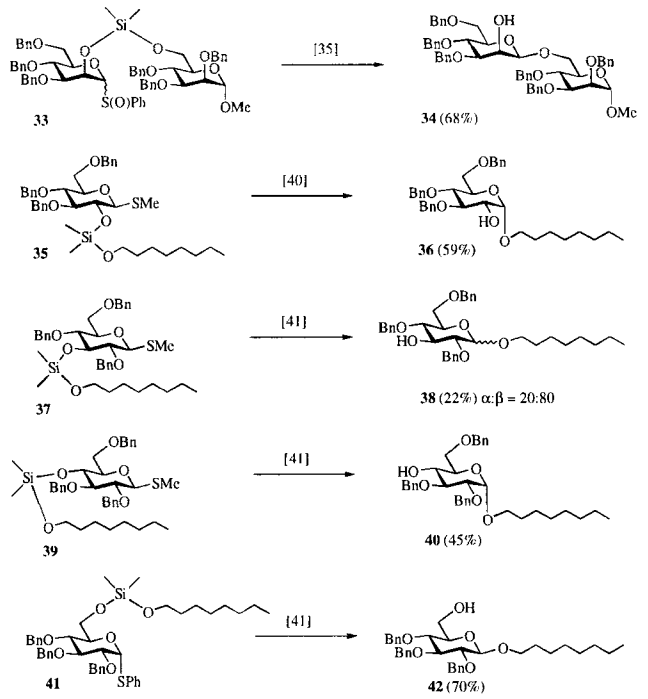
In general, α-glycosides and β-mannosides were predominantly obtained by intramolecular glycodesilylations from various alcohols when the silylene bridge was attached to position 2 of the glycosyl donor (*cf.* Scheme 8 **33**→**34** and **35**→**36**) [39, 40]. However, when the alcohol was tethered to position 3 of glucosyl donors, anomeric mixtures were obtained (*cf.* **37**→**38**). Tethers to position 4 resulted in α-glucosides (*cf.* **39**→**40**) and tethers to position 6 of the donors (pyranoses and furanoses) afforded β-glycosides (*cf.* **41**→**42**) [41]. Therefore, intramolecular glycodesilylations are extremely useful procedures for the selective formation of α- or β-linked saccharides [42] also there are some hints that the reaction does not completely occur intramolecularly [40].

4 Summary

Glycodesilylation of silylated alcohols (glycodesilylation) provides a useful procedure for the efficient prepara-



Scheme 7



Scheme 8

tion of glycosides and oligosaccharides. Various easily available glycosyl donors and Lewis acids can be applied and the diastereoselectivity of the reaction can be governed in many cases. Different silyl protecting groups which are prone to regioselective introduction into a saccharide may be selectively glycodesilylated by proper choice of the reaction conditions. Regioselective glycodesilylations can be realized using the tetraisopropyldisiloxane group. Intramolecular variants of the glycodesilylation protocol provide access to otherwise difficultly to establish anomers.

5 Typical Experimental Procedures

Methyl O-β-D-Glucopyranosyl-(1→6)-β-D-galactopyranosyl-(1→6)-β-D-galactopyranosyl-(1→6)-β-D-galactopyranoside (**12**) [8].

TMSOTf (10% of total 53.3 mg, 0.24 mmol) is added at −78 °C to a stirred solution of **9** (one third of total 0.192 g, 0.1 mmol) and **10** (67 mg, 0.16 mmol) in CH_2Cl_2. The reaction is followed by TLC and subsequent portions of **9** and TMSOTf are added periodically. When the reaction is complete, the mixture is neutralized with triethylamine, diluted with CH_2Cl_2, washed with water, aqueous sodium bicarbonate, and water again, and dried. Concentration, followed by column chromatography yields **11** (146 mg, 72%). A catalytic amount of NaOMe is added at room temperature to a solution of **11** (50 mg, 0.025 mmol) in a 5:1 mixture of MeOH–toluene. The mixture is stirred at 60 °C for 24 h, cooled, neutralized with ion exchange resign and concentrated. Purification of the residue by HPLC affords **12** (17 mg, 82%).

Methyl O-[2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl-(1→4)-2,3,6-tri-O-acetyl-β-D-glucopyranosyl-(1→6)]-2-O-benzoyl-α-D-glucopyranoside (**16**) [30].

BF_3-diethylether (0.012 ml, 0.1 mmol) is added at room temperature to a solution of **13** (0.51 g, 0.8 mmol) and **14** (0.49 g, 0.72 mmol) in CH_2Cl_2 (10 ml). The mixture is stirred for 2.5 h, washed with sodium bicarbonate, dried and concentrated. Chromatography of the residue affords **15** (0.51 g, 61%). Next, pyridine–polyhydrogene fluoride (0.05 ml, 1.8 mmol) is added at room temperature to a solution of **15** (0.23 g, 0.2 mmol) in CH_2Cl_2. The mixture is stirred for 24 h, washed with sodium bicarbonate and dried. Concentration afforded **16** (0.18 g, 98%).

Methyl O-[3,4,6-Tri-O-acetyl-α-D-glucopyranosyl-(1→4)]-2,3,6-tri-O-benzyl-α-D-glucopyranoside (**32**) [38].

N-iodosuccinimide (0.075 mg, 0.33 mmol) is added to a solution of **31** (93 mg, 0.1 mmol) in nitromethane (5 ml), and the mixture is refluxed for 1 h. HCl (25 ml, 1M) is added, the waterlayer is separated and extracted with ethyl acetate. The combined organic layers are washed with sodium bicarbonate and sodium thiosulfate, dried and concentrated. Chromatography of the residue affords **32** (56 mg, 74%).

6 References

[1] H. Paulsen, Chem. Soc. Rev. **1984**, *13*, 15
[2] R. R. Schmidt, Angew. Chem. Int. Ed. Engl. **1986**, *25*, 212
[3] K. Toshima, K. Tatsuta, Chem. Rev. **1992**, *93*, 1503
[4] S. Hanessian (Ed.), Preparative Carbohydrate Chemistry, Marcel Dekker, New York 1997
[5] G. H. Veeneman in Carbohydrate Chemistry (G. J. Boons Ed.), Blackie Akademic & Professional, London 1998, p. 98
[6] T. Ziegler in Carbohydrate Chemistry (G. J. Boons Ed.), Blackie Akademic & Professional, London 1998 p. 21
[7] L.-F. Tietze, R. Fischer, H.-J. Guder, Tetrahedron Lett.

1982, *23*, 4661
[8] E. M. Nashed, C. P. J. Glaudemans, J. Org. Chem. **1989**, *54*, 6116
[9] T. Mukaiyama, K. Matsubara, Chem. Lett. **1992**, 1041
[10] T. Mukaiyama, T. Shimpuku, T. Takashima, S. Kobayashi, Chem. Lett. **1989**, 145
[11] A. B. Charette, J.-F. Maroux, B. Côté, Tetrahedron Lett. **1991**, *32*, 7215
[12] T. Mukaiyama, M. Katsurada, T. Takashima, Chem. Lett. **1991**, 985
[13] M. Kreuzer, J. Thiem, Carbohydr. Res. **1986**, *149*, 347
[14] T. Ziegler, U. Seidl, J. Carbohydr. Chem. **1991**, *10*, 813
[15] H. Yamada, M. Nishizawa, Tetrahedron **1992**, *48*, 3021
[16] S. Hashimoto, M. Hayashi, R. Noyori, Tetrahedron Lett. **1984**, *25*, 1379
[17] B. Ernst, B. Wagner, Helv. Chim. Acta **1989**, *72*, 165
[18] H. Kunz, W. Sager, Helv. Chim. Acta **1985**, *68*, 283
[19] H. Yamada, M. Nishizawa, Tetrahedron Lett. **1987**, *28*, 4315
[20] T. Mukaiyama, S. Suda, Chem. Lett. **1990**, 1143
[21] S. Suda, T. Mukaiyama, Chem. Lett. **1991**, 431
[22] R. R. Schmidt, M. Hoffmann, Tetrahedr. Lett. **1982**, *23*, 409
[23] P. Allevi, M. Anastasi, P. Ciuffreda, A. Fiecchi, J. Chem. Soc., Chem. Commun. **1987**, 1245
[24] D.-I. Kwok, R. A. Outten, R. Huhn, G. D. Daves, J. Org. Chem. **1988**, *53*, 5359.
[25] M. Yamaguchi, A. Horiguchi, A. Fukuda, T. Minami, J. Chem. Soc., Perkin Trans. 1 **1990**, 1079
[26] T. Matsumoto, M. Katsuki, K. Suzuki, Tetrahedron Lett. **1989**, *30*, 833
[27] C. P. J. Glaudemans, Chem. Rev. **1991**, *91*, 25
[28] E. M. Nashed, C. P. J. Glaudemans, J. Org. Chem. **1987**, *52*, 5255.
[29] T. Ziegler, E. Eckhardt, G. Pantkowski, J. Carbohydr. Chem. **1994**, *13*, 81
[30] T. Ziegler, K. Neumann, E. Eckhardt, G. Herold, G. Pantkowski, Synlett **1991**, 699
[31] S. Hanessian, J. Banoub, Carbohydr. Res. **1977**, *53*, C13
[32] K. Takeo, Carbohydr. Res. **1980**, *87*, 147
[33] T. Ziegler, R. Dettmann, F. Bien, C. Jurisch, Trends Org. Chem. **1977**, *6*, 91
[34] T. Ziegler, E. Eckhardt, Tetrahedron Lett. **1992**, *44*, 6615
[35] G. Stork, G. Kim, J. Am. Chem. Soc. **1992**, *114*, 1087
[36] M. Bols, J. Chem. Soc. Chem. Commun. **1992**, 913
[37] F. Barresi, O. Hindsgaul, Synlett **1992**, 759
[38] M. Bols, J. Chem. Soc. Chem. Commun. **1993**, 791
[39] M. Bols, Tetrahedron **1993**, *44*, 10049
[40] M. Bols, Acta Chim. Scand. **1993**, *47*, 829
[41] M. Bols, C. Hansen, Chem. Lett. **1994**, 1049
[42] M. Bols, T. Skrydstrup, Chem. Rev. **1995**, *95*, 1253

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