the previous heterogeneous system, and tolerates some substituents. Study of the catalyst intermediates suggests that the hydride [Cp_2TiH] is a key reactant in the catalytic cycle, as previously proposed for a number of other titanocene-catalyzed reactions.

Experimental Section

1b: [Cp_2TiMe_2] (50 mg, 0.24 mmol) was dissolved in a mixture *n*-hexane/toluene (4/1, 5 mL), pyridine (0.10 mL, 1.2 mmol), and phenylsilane (0.11 mL, 0.72 mmol). Over about one hour, the solution slowly changed color from orange to dark violet. This was accompanied by a slow gas evolution and the formation of violet, needle-shaped crystals of **1b**·$0.25\,C_5H_5N$. The crystals were separated, washed several times with cold hexane, and dried under vacuum (yield: 95 mg, 87%). Elemental analysis for $C_{27}H_{26}NSiTi$ (440.47): found (calcd): C 72.83 (73.62); H 5.99 (5.95); N 3.22 (3.18); Si 5.98 (6.37); Ti 10.26 (10.87). The deuterated form of **1b** was prepared with Ph_2SiD_2 instead of Ph_2SiH_2.

2: [Cp_2TiMe_2] (120 mg, 0.58 mmol) was added to a solution of phenylmethylsilane (0.24 mL, 1.73 mmol) and pyridine (1.0 mL, 12.4 mmol) in *n*-hexane/toluene (6/1; 7.0 mL). The solution turned deep violet after 2 hr without stirring, and dark brown after about a further 1 h. The solution was held at ambient temperatures for another 4 h and at $-20\,^\circ C$ for 24 h to yield dark brown plates suitable for X-ray chrystallographic analysis (yield: 83 mg, 56%). Elemental analysis for $C_{26}H_{26}Ti_2N$ (448.25): found (calcd): C 66.27 (68.98); H 5.12 (5.79); N 3.04 (3.22); Ti 22.33 (22.01).

General procedure for the catalytic hydrosilylation/hydrogenation: PhMeSiH_2 (1.20 mL, 8.75 mmol) and pyridine (0.35 mL, 4.34 mmol) were added to [Cp_2TiMe_2] (0.45 g, 0.43 mmol) in a Schlenk tube. After a short time at room temperature the solution turned blue-violet, and gas was evolved. The mixture was stirred at $80\,^\circ C$ for 8 h and then distilled under vacuum to give pure *N*-(phenylmethylsilyl)-1,2,3,4-tetrahydropyridine (entry 1) (b.p. $57\,^\circ C/0.12$ Torr; yield: 0.88 g, 50%). NMR analysis of the undistilled reaction mixture showed 94% conversion of pyridine. ^1H NMR (499.9 MHz, C_6D_6): $\delta = 0.28$ (d, 3H, $J = 3.3$ Hz, $SiCH_3$), 1.57 (m, 2H, C5-H), 2.00 (m, 2H, C4-H), 2.99 (m, 2H, C6-H), 4.62 (m, 1H, C3-H), 5.01 (q, 1H, $J = 3.3$ Hz, SiH), 6.28 (dt, 1H, $^3J = 7.8$ Hz, $^4J = 3.0$ Hz, C2-H), 7.20 (m, 3H, *m*,*p*-C_6H_5), 7.50 (m, 2H, *o*-C_6H_5); ^{13}C NMR (125.7 MHz, C_6D_6): $\delta = -0.50$ ($SiCH_3$), 22.16, 23.44, 43.79 (C2, C3, C4), 98.69, 123.49 (C5, C6), 128.18, 129.48, 130.13, 134.40 (Ph); ^{29}Si NMR (59.9 MHz, C_6D_6): $\delta = -9.10$; MS (70 eV): *m*/*z* (%): 203 (100) [M^+], 188 (18.5) [$M^+ - Me$], 121 (77) [$M^+ - C_5H_8N$].

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Synthesis of β-Mannosides via Prearranged Glycosides**

Thomas Ziegler* and Gregor Lemanski

Although the chemical synthesis of oligosaccharides has reached a remarkable level several problematic cases of the diastereoselective formation of O-glycosidic bonds demand improvements. In particular, 1,2-*cis*-configurated O-glycosides are often realized solely with difficulties or with significant synthetic efforts. This is especially the case for saccharides that contain β-D-mannosidic and β-L-rhamnosidic linkages. Similarly, α-linked D-galactosyl and D-glucosyl residues are difficult to establish in some cases.

The Koenigs – Knorr reaction in combination with the silver silicate promotor developed by Paulsen et al. is still applied often to the synthesis of β-D-mannosidic and β-L-rhamnosidic linkages.[1] Since this glycosylation procedure and related

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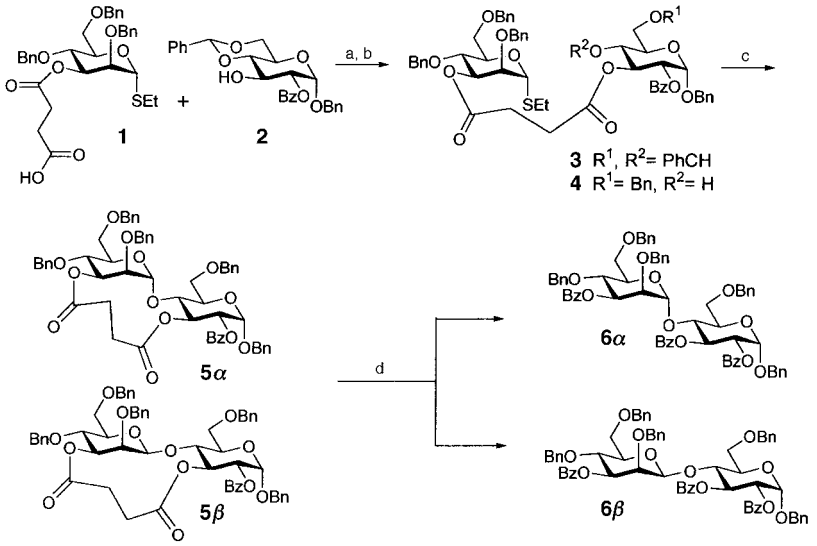
variants[2] are most often only applicable to reactive glycosyl donors and acceptors or to special cases[3] efficient alternatives have been developed in recent years that allow for the selective preparation of 1,2-*cis*-configurated glycosides. The latter are accessible from 2-ulosyl bromides as glycosyl donors by diastereoselective reduction of the carbonyl group.[4] Similarly, β-mannosides can be prepared from β-glucosides by Walden inversion of position 2 by S_N2 reactions.[5] Another method that has been investigated recently for the stereoselective synthesis of 1,2-*cis*-configurated O-glycosides is intramolecular glycosylation.[6] Here, the aglycon is linked first by a labile tether to the glycosyl donor. Next, the aglycon is "delivered" intramolecularly to the anomeric center during glycosylation. However, recent investigations of similar potential intramolecular glycosylations showed that an intermolecular mechanism may also be operative.[7] Furthermore, intramolecular glycosylations involving labile tethers are not suited in all instances to the formation of β-L-rhamnosidic linkages.[8]



Scheme 1. Reagents and conditions: a) **1** (1.0 equiv), **2** (1.0 equiv), DCC (1.2 equiv), CH_2Cl_2, RT, 23 h, 71 % **3**; b) **3** (1.0 equiv), $NaCNBH_3$ (12.5 equiv), HCl in Et_2O, THF, 0 °C, 5 min, 77 % **4**; c) **4** (1.0 equiv), *N*-iodosuccinimide (5.0 equiv), cat. trifluoromethanesulfonate, MeCN, −30 °C, 10 min, 66 % ***5α***; **4** (1.0 equiv), MeOTf (5.0 equiv), MeCN, RT, 3 h, 64 % ***5β***; d) ***5α*** (1.0 equiv), cat. NaOMe, MeOH, RT, 24 h, then BzCl (5.0 equiv), pyridine, RT, 24 h 77 % ***6α***; ***5β*** (1.0 equiv), cat. NaOMe, MeOH, RT, 24 h, then BzCl (5.0 equiv), pyridine, RT, 24 h 76 % ***6β***.

Recently we disclosed a "true" intramolecular glycosylation protocol in which a suitable glycosyl donor and a glycosyl acceptor were linked together by a stable bridge.[8, 9] The following intramolecular glycosylation step leaves the bridge intact and governs the anomeric outcome of the condensation.[10] The glycosylation variant via "prearranged glycosides" can be extended to regioselective glycosylations as well.[11] Although this variant is well suited for the construction of β-L-rhamnosidic, α-D-glucosidic, and α-D-galactosidic linkages it could not be extended yet to the synthesis of biologically important β-D-mannosides.[9] Herein we present methods for linking donor and acceptor that allow for the highly selective formation of β-mannosidic linkages via prearranged glycosides.

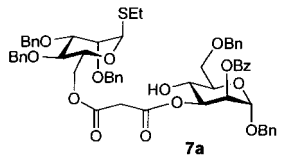
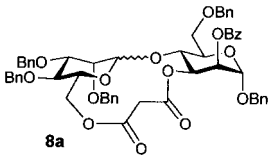
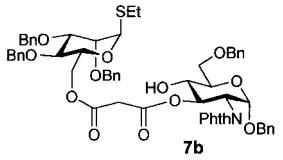
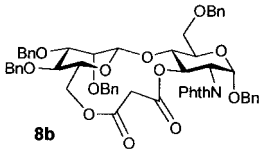
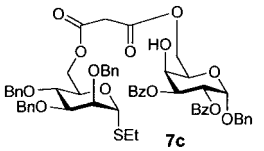
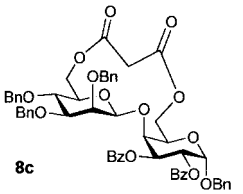
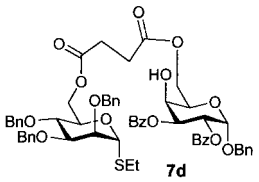
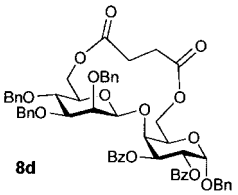
Previously, we used succinyl tethers for the construction of β-D-mannosidic linkages via prearranged glycosides. Similarly to the respective L-rhamnosyl donors, these tethers were used to link the mannosyl donor via its position 2 or 6 with a glycosyl acceptor. However, these mannosylations of appropriate glycosyl acceptors afforded an anomeric ratio α:β of 30:70 (for D-Man*p*-(1→4)-L-Glc*p*[10]), whereas the corresponding β-L-rhamnosides were formed in high yield.[9] Since during intramolecular glycosylation via prearranged glycosides a double diastereoselection influences the anomeric selectivity,[10] and furthermore, solely β-L-Rha*p*-(1→4)-D-Glc*p* disaccharides were obtained from L-rhamnosyl donors with a succinyl bridge at position 3,[9b] 3-O-succinyl-tethered mannosyl donors should afford the corresponding β-D-Man*p*-(1→4)-D-Glc*p* disaccharides.

Indeed, with activation by *N*-iodosuccinimide (NIS) in acetonitrile the intramolecular mannosylation of the prearranged glycoside **4** afforded solely the β-(1→4)-linked disaccharide ***5β***. The latter was characterized as ***6β*** after cleavage of all acyl groups and subsequent rebenzoylation (Scheme 1). In the ^{13}C NMR spectrum the CH coupling constant of $^1J = 158.5$ Hz at the anomeric center of the mannosyl residue in ***6β*** proves the β-configuration unambiguously.[12] Compound **4** is readily accessible from ethyl 1-thio-2,4,6-tri-*O*-benzyl-α-D-mannopyranoside via intermediates **1**–**3**, as described for the corresponding rhamnosylations.[9b] In contrast, activation of **4** with methyl trifluoromethanesulfonate (MeOTf) instead of NIS affords the corresponding α-(1→4)-linked disaccharide ***5α*** (once again characterized as ***6α*** showing a coupling constant of $^1J = 170.9$ Hz). The strong dependence of the anomeric selectivity of the intramolecular mannosylation on the activation procedure is surprising. However, a similar dependence was previously observed for comparable rhamnosylations in less pronounced form.[9b] Thus, α- or β-D-mannosidic linkages can now be established selectively from compound **4** by simple choice of the activator (NIS or MeOTf) for the glycosylation step.

Previous attempts toward intramolecular (1→4)-mannosylations of glycosyl acceptors via prearranged glycosides with a succinyl tether at postion 6 (mannosyl donor) and position 3 (glucosyl acceptor) resulted in low β-selectivities.[9c, 10] However, if the tether is shortened as realized in compound **7** (a malonyl instead of a succinyl tether), excellent selectivities are obtained for β-mannosyl saccharides **8** (Table 1). It is noteworthy that the anomeric selectivity of the intramolecular mannosylation of the glycoside **7** does not strongly depend on the activation procedure but on the glycosyl acceptor. For β-mannosylations (c.f. **7c** and **7d** in Table 1) even the length of the tether has no influence on the selectivity of the glycosylation. Solely the selectivity in case of the disaccharide β-D-Man-(1→4)-D-Man **8a** remains unsatisfactory and needs further optimization. Excellent β-selectivities are observed for the disaccharides β-D-Man-(1→4)-D-Glc ***5β***, β-D-Man-(1→4)-D-GlcN **8b**, and β-D-Man-(1→4)-D-Gal **8c** and **8d**,

  1433-7851/98/3722-3130 $ 17.50+.50/0 *Angew. Chem. Int. Ed.* **1998**, *37*, No. 22

Table 1. Reaction of various prearranged glycosides **7** with *N*-iodosuccinimide (NIS) or methyl trifluoromethanesulfonate (MeOTf) to give the disaccharides **8**.[a]

Prearranged glycoside	Disaccharide	Activator	Yield	α:β
 **7a**	 **8a**	NIS	71 %	67:33
		MeOTf	72 %	50:50
 **7b**	 **8b**	NIS	51 %	0:100
		MeOTf	50 %	0:100
 **7c**	 **8c**	NIS	50 %	0:100
		MeOTf	55 %	0:100
 **7d**	 **8d**	MeOTf	53 %	0:100

[a] Reaction conditions are as described in Scheme 1 under c). Bn = benzyl, Bz = benzoyl, Phth = phthaloyl.

which all can now be applied to the synthesis of complex oligosaccharides.

Experimental Section

6α: 4 Å Molecular sieves (1.32 g) and **4c** (0.55 g, 0.53 mmol) were stirred under Ar for 10 min at 20 °C in MeCN (20 mL), and MeOTf (0.33 g, 2.65 mmol) was added. After stirring for 3 h the mixture was neutralized with Et_3N, diluted with CH_2Cl_2, and filtered through a layer of Celite. The filtrate was washed with water, dried, and concentrated. Chromatography of the residue toluene/ethyl acetate 20:1 on silica gel afforded **5α** (0.33 g, 64 %). Compound **5α** (0.21 g, 0.21 mmol) and a catalytic amount of NaOMe were stirred in MeOH/CH_2Cl_2 (1:2, 10 mL) for 24 h at 20 °C, neutralized by addition of Dowex H^+ ion exchange resin, filtered, and concentrated. The residue was dissolved in pyridine (5 mL), and benzoyl chloride (122 µL, 1.05 mmol) was added. After stirring for 24 h at 20 °C, the mixture was poured into ice-water, and extracted with CH_2Cl_2. The combined organic layers were subsequently washed with aqueous HCl and $NaHCO_3$ solution, dried, and concentrated. Chromatography of the residue in *n*-hexane/ethyl acetate 4:1 on silica gel afforded **6α** (0.15 g, 76 %). $[\alpha]_D^{20} = +43.6$ ($c = 1.8$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 25 °C, 300 MHz, signals of benzoyl and benzyl groups are not given): $\delta = 6.10$ (dd, 1H, $J_{2,3} = 10.3$, $J_{3,4} = 9.2$ Hz; H-3), 5.60 (dd, 1H, $J_{2,3} = 3.0$, $J_{3,4} = 9.4$ Hz; H-3′), 5.33 (d, 1H, $J_{1,2} = 3.8$ Hz; H-1), 5.19 (dd, 1H; H-2), 5.14 (d, 1H, $J_{1,2} = 1.8$ Hz; H-1′), 4.40 (t, 1H, $J_{4,5} = 9.5$ Hz; H-4′), 4.13 (t, 1H, $J_{4,5} = 9.3$ Hz; H-4), 4.03 – 3.98 (m, 1H, $J_{5,6a} = 4.1$, $J_{5,6b} = 2.0$ Hz; H-5), 3.95 (dd, 1H, $J_{6a,6b} = -11.2$ Hz; H-6a), 3.86 – 3.80 (m, 2H, $J_{5,6b} = 3.1$, $J_{6a,6b} = -11.6$ Hz; H-5′,6a′), 3.84 (dd, 1H; H-2′), 3.73 (dd, 1H; H-6b), 3.74 (dd, 1H; H-6b′); ^{13}C NMR ($CDCl_3$, 25 °C, 75.46 MHz, signals of benzoyl and benzyl groups are not given): $\delta = 98.8$ ($J_{C\text{-}1,H\text{-}1} = 170.9$ Hz; C-1′), 95.1 (C-1), 77.7 (C-2′), 76.3 (C-4), 75.6 (C-4′), 73.9, 73.7, 73.5 (C-3,3′,5′), 72.4 (C-2), 70.2 (C-5), 68.8, 68.5 (C-6,6′); elemental analysis: calcd. for $C_{68}H_{64}O_{14}$: C 73.90, H 5.84; found.: C 74.05, H 5.93.

6β: 4 Å Molecular sieves (2 g), **4c** (0.94 g, 0.9 mmol), and NIS (1.01g, 4.5 mmol) were stirred under Ar for 20 min at 20 °C in MeCN (30 mL). The mixture was cooled to −30 °C and TMSOTf (41 µL, 0.25 mmol) was added. After stirring for 10 min, the mixture was neutralized with pyridine, diluted with CH_2Cl_2, and filtered through a layer of Celite. The filtrate was washed subsequently with aqueous $Na_2S_2O_3$ and $NaHCO_3$ solution, dried, and concentrated. Chromatography of the residue with toluene/ethyl acetate 20:1 on silica gel afforded **5β** (0.59 g, 66 %). The deacylation and rebenzoylation of **5β** (0.16 g, 0.16 mmol) as described for **6α** afforded **6β** (0.14 g, 76 %). $[\alpha]_D^{20} = -32.2$ ($c = 1.1$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 25 °C, 300 MHz, signals of benzoyl and benzyl groups are not shown): $\delta = 6.10$ (t, 1H, $J_{2,3} = 10.2$, $J_{3,4} = 9.8$ Hz; H-3), 5.34 (d, 1H, $J_{1,2} = 3.8$ Hz; H-1), 5.21 (dd, 1H; H-2), 5.00 (dd, 1H, $J_{2,3} = 3.1$, $J_{3,4} = 9.8$ Hz; H-3′), 4.44 (s, 1H, $J_{1,2} < 1.0$ Hz; H-1′), 4.33 (t, 1H, $J_{4,5} = 9.8$ Hz; H-4), 4.00 (t, 1H, $J_{4,5} = 9.7$ Hz; H-4′), 4.05 – 3.99 (m, 1H, $J_{5,6a} = 2.8$, $J_{5,6b} = 1.8$ Hz; H-5), 3.89 (bd, 1H; H-2′), 3.74 (dd, 1H, $J_{6a,6b} = -11.2$ Hz; H-6a), 3.66 (dd, 1H, H-6b), 3.44 (dd, 1H, $J_{5,6a} = 4.5$, $J_{6a,6b} = -11.4$ Hz; H-6a′), 3.34 (dd, 1H, $J_{5,6b} = 1.8$ Hz; H-6b′), 3.26 – 3.21 (m, 1H, H-5′); ^{13}C NMR ($CDCl_3$, 25 °C, 75.46 MHz, signals of benzoyl and benzyl groups are not shown): $\delta = 100.6$ ($J_{C\text{-}1,H\text{-}1} = 158.5$ Hz; C-1′), 95.3 (C-1), 76.2, 76.0, 76.0 (C-2′,3′,5′), 74.9 (C-4), 73.0 (C-4′), 72.2 (C-2), 70.9, 70.2 (C-3,5), 68.8, (C-6′), 68.1 (C-6); elemental analysis: calcd. for $C_{68}H_{64}O_{14}$: C 73.90, H 5.84; found: C 74.10, H 5.90.

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Layered Dendritic Block Copolymers**

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Macromolecular engineering of complex molecular architectures through block copolymerization or the introduction of controlled branching has become a common theme of research in polymer science. The interest in these synthetic mesoscopic systems and nanostructures is driven by the possible unique mechanical, rheological, and solution properties. Block copolymers are simply two distinct homopolymers covalently bound at one point, and the molecular architecture, block lengths, and composition can be designed to produce materials with a wide range of properties and morphologies.[1] Furthermore, since the two dissimilar materials are covalently bound, miscibility is enhanced and phase separation is restricted to dimensions of 100 to 400 Å. Dendrimers provide the ultimate standard of a well-defined branched macromolecule, while hyperbranched polymers are less perfect elaborations of such three-dimensional structures.[2, 3] The combination of controlled branching with block copolymerization provides additional opportunities to devise new molecular architectures. For instance, dendrimers have often been used as cores for the preparation of star polymers with a well-defined number of arms.[4] Conversely, Fréchet et al.[5] terminated star polymers with dendrons at their focal point, and layered and segmented dendrimers have been reported by other groups.[6] In addition, Tomalia et al.,[7a] Möller and co-workers,[7b–d] and others have reported successive grafting of polymeric building blocks.[7] These "comb-burst" polymers, or arborescent graft polymers, utilize linear building blocks with narrow polydispersity in the construction of highly and randomly branched polymers. A new type of molecular architecture, denoted dendrimer-like star polymers, based on poly(ε-caprolactone) has been recently reported.[8] These highly branched dendrimer-like star polymers are different from comb-burst polymers because the branching is controlled and resembles that of traditional dendrimers. The use of living polymerization methods in combination with selective and quantitative organic transformations allows the design and preparation of classical polymers with molecular architectures similar to the most advanced dendrimers with layered and segmented block structures.

Here layered dendrimer-like star copolymers are reported. These novel polymers, characterized by a radial architecture, are constructed by alternating layers of high molecular weight polymer and dendrons emanating from a central core (Scheme 1). There are many possible routes to these novel geometries but this paper focuses on the possibility of using living polymerization techniques. These polymers contain multiple hydroxyl groups and are of interest in areas of surgery and medicinal chemistry as well as in nanotechnology. In addition, it is of interest to investigate whether these molecular structures display microphase-separated morphologies. The general synthetic strategy is shown in Scheme 1. A multifunctional core molecule is used as an initiator for the controlled ring opening polymerization of ε-caprolactone. The polymer obtained, G1(6OH), is the first generation of the final triblock copolymer. The chain ends of the six-arm star polymer are capped with functional dendrons of different sizes to produce diblock polymers with 12, 24, or 48 functional end groups. These macromolecules will serve as "macroinitiators" for the growth of an additional layer of poly(ε-caprolactone) or the third layer of the dendrimer-like triblock copolymers (Scheme 1).

The six-arm star polymer G1(6OH) was synthesized by the reaction of one equivalent of a hexafunctional "initiator" and 120 equivalents of caprolactone in the presence of 1/400 equivalents of $Sn(Oct)_2$ under bulk conditions at 110 °C. The initiator is a first-generation hydroxyl-substituted dendrimer based on 2,2-bis(hydroxymethyl)proprionic acid (DMPA).[9] The target degree of polymerization (DP) was 20, and the DP obtained was calculated to be 20.6 by ^{1}H NMR spectroscopy. Protected DMPA or second- and third-generation dendrons derived from it were used to construct the second layer in the triblock dendrimer-like copolymer. The benzylidene-protected DMPA was synthesized in one step according to a procedure reported elsewhere,[10] while the

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