

This article was downloaded by:

On: 23 January 2011

Access details: *Access Details: Free Access*

Publisher *Taylor & Francis*

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



## Journal of Carbohydrate Chemistry

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713617200>

### Prearranged Glycosides. Part 8. Intramolecular $\alpha$ -Galactosylation Via Succinoyl Tethered Glycosides

Thomas Ziegler; Ralf Dettmann; Ariffadhillah; Uwe Zettl

**To cite this Article** Ziegler, Thomas , Dettmann, Ralf , Ariffadhillah and Zettl, Uwe(1999) 'Prearranged Glycosides. Part 8. Intramolecular  $\alpha$ -Galactosylation Via Succinoyl Tethered Glycosides', *Journal of Carbohydrate Chemistry*, 18: 9, 1079 – 1095

**To link to this Article:** DOI: 10.1080/07328309908544056

**URL:** <http://dx.doi.org/10.1080/07328309908544056>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

**PREARRANGED GLYCOSIDES. PART 8. INTRAMOLECULAR  
 $\alpha$ -GALACTOSYLATION VIA SUCCINOYL TETHERED GLYCOSIDES**

Thomas Ziegler,\* Ralf Dettmann, Ariffadhillah and Uwe Zettl

Institute of Organic Chemistry, University of Cologne, Greinstraße 4,  
D-50939 Cologne, Germany

*Received May 25, 1999 - Final Form September 3, 1999*

**ABSTRACT**

Benzyl protected phenyl 1-thio-galactopyranoside donors which were tethered by a succinoyl linker at their positions 2 and 6, respectively, to position 3 of a blocked benzyl glucopyranoside acceptor with a 4-OH group solely afforded the corresponding  $\alpha$ -(1 $\rightarrow$ 4)-linked disaccharides upon intramolecular glycosylation. 4,6-Siloxane protected mannosides react with rearrangement of the siloxane group under similar conditions.

**INTRODUCTION**

Intramolecularisation of glycosylation reactions appears to be an attractive alternative to the classical intermolecular condensation of a glycosyl donor and a glycosyl acceptor. In many cases where the anomeric outcome of such a classical glycosylation is unpleasant due to the formation of anomeric mixtures or even the exclusive formation of an undesired anomer, the intramolecular approach allows the highly stereoselective

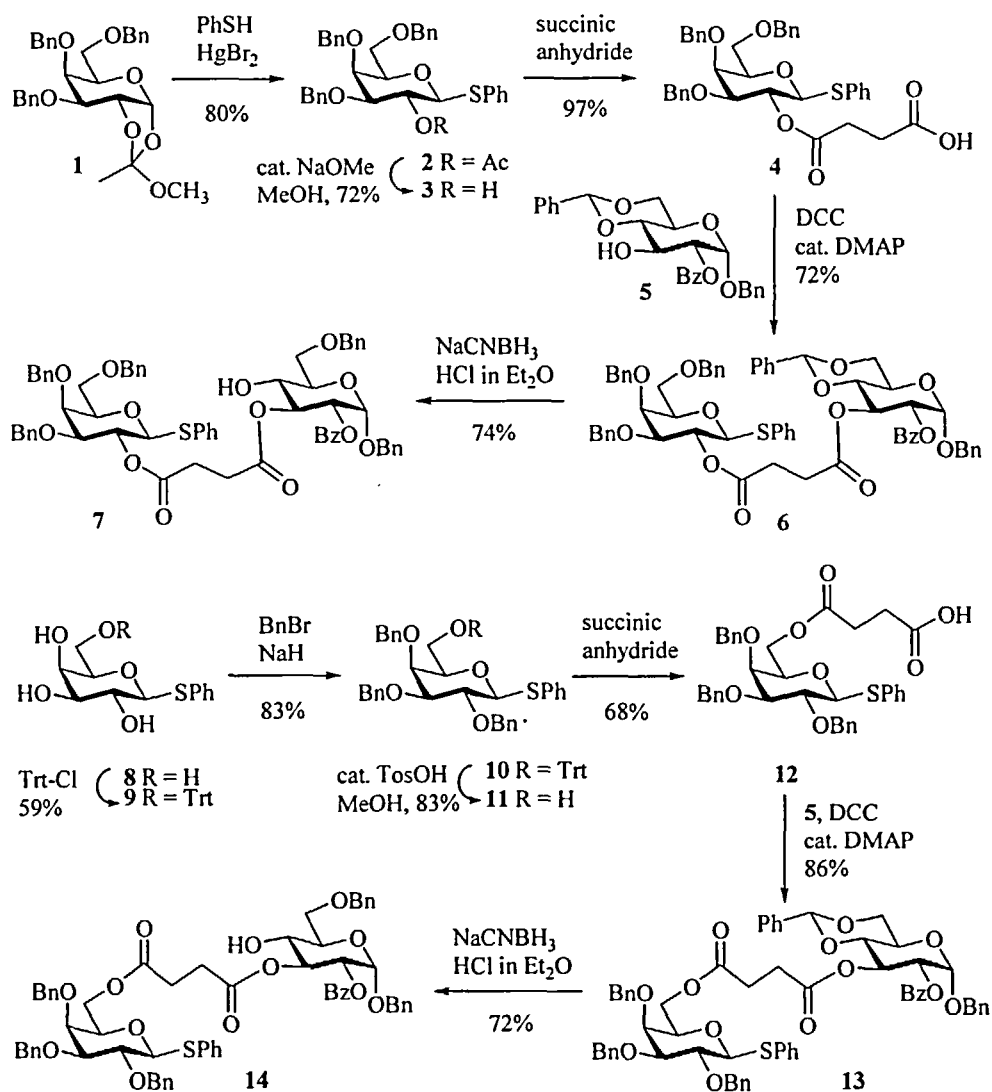
formation of *O*-glycosidic bonds. Furthermore, intramolecular glycosylation resembles enzyme catalyzed glycosylations to some extent and might be regarded as a biomimetic variant, since here glycosyl donor and acceptor are first bound to the enzyme followed by an intramolecular glycosylation step. Two different strategies for intramolecular glycosylations have been followed by several groups so far. On the one hand, glycosyl donor and glycosyl acceptor are first linked together by a labile tether which is cleaved during the glycosylation step. Most commonly, acetals,<sup>1</sup> silylene acetals,<sup>2</sup> carbonates<sup>3</sup> and intermediate orthoesters<sup>4</sup> or dicobaltcarbonyl complexes of alkynes<sup>5</sup> have been used as tethers for that approach. However, it has been shown for some examples that an intermolecular mechanism can be operative as well.<sup>3c,4</sup> On the other hand, glycosyl donor and glycosyl acceptor are first connected by a stable bridge which is not cleaved during glycosylation (prearranged glycosides) and thus, results in the formation of large rings.<sup>6</sup>

Recently, the strategy via prearranged glycosides was successfully applied to the efficient preparation of  $\beta$ -mannosidic linkages.<sup>6k</sup> Furthermore, it was shown that intramolecular glycosylations of prearranged glycosides exclusively gave  $\alpha$ -D-glucopyranosides even when a  $\beta$ -directing neighboring active acyl group was present at position 2 of the glucosyl donor.<sup>6g</sup> Since the latter  $\alpha$ -selective glycosylation proceeded efficiently, we now extended this strategy to the synthesis of  $\alpha$ -D-galactopyranosides, namely the disaccharide structures  $\alpha$ -D-Galp-(1 $\rightarrow$ 4)-D-Glcp and  $\alpha$ -D-Galp-(1 $\rightarrow$ 6)-D-Manp.

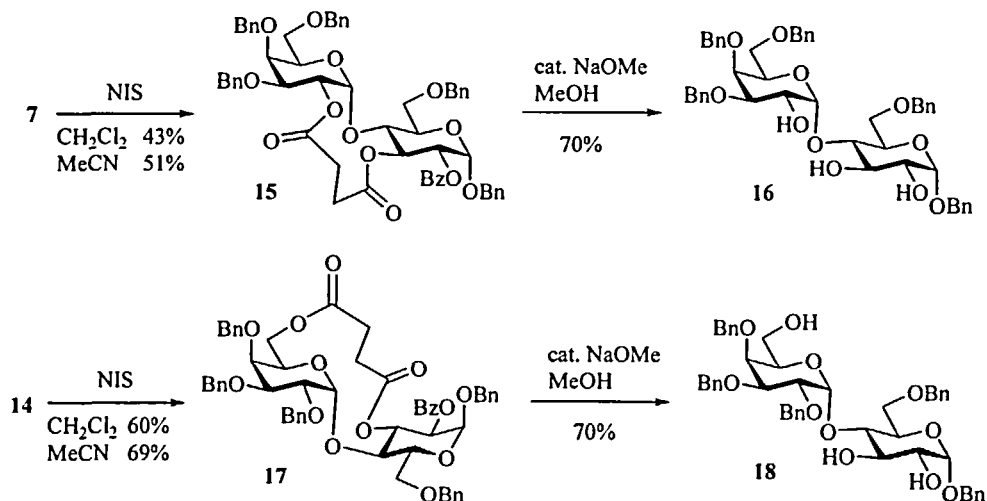
## RESULTS AND DISCUSSION

For the corresponding  $\alpha$ -glucosylations, succinate was chosen as the tether for the galactosylation. Thus, 2,3,6-tri-*O*-benzyl-1,2-*O*-methoxyethylidene- $\alpha$ -D-galactopyranose<sup>7</sup> (**1**) was first converted into phenyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl- $\beta$ -D-galactopyranoside (**2**). Next, deacetylation afforded compound **3** which was treated with succinic anhydride to give succinoylated galactoside **4**. Condensation of the latter with benzyl 2-*O*-benzoyl-4,6-*O*-benzylidene- $\alpha$ -D-glucopyranoside<sup>6j</sup> (**5**) then afforded succinate **6**, the benzylidene acetal of which was finally opened by Garegg's method<sup>8</sup> to give the 2,3-prearranged glycoside **7**. Similarly, the corresponding 3,6-prearranged counterpart

was prepared from phenyl 1-thio- $\beta$ -D-galactopyranoside<sup>9</sup> (**8**) by sequential tritylation of position 6, followed by benzylation of the remaining hydroxyls and cleaving of the trityl group. Thus, compound **11** was prepared in 41% overall yield *via* intermediates **9-10**. Next, succinylation of **11** afforded **12** which was coupled with DCC to acceptor **5** to give the benzylidene derivative **13**. Final reductive cleavage of the benzylidene ring of the latter afforded the 3,6-prearranged glycoside **14**.

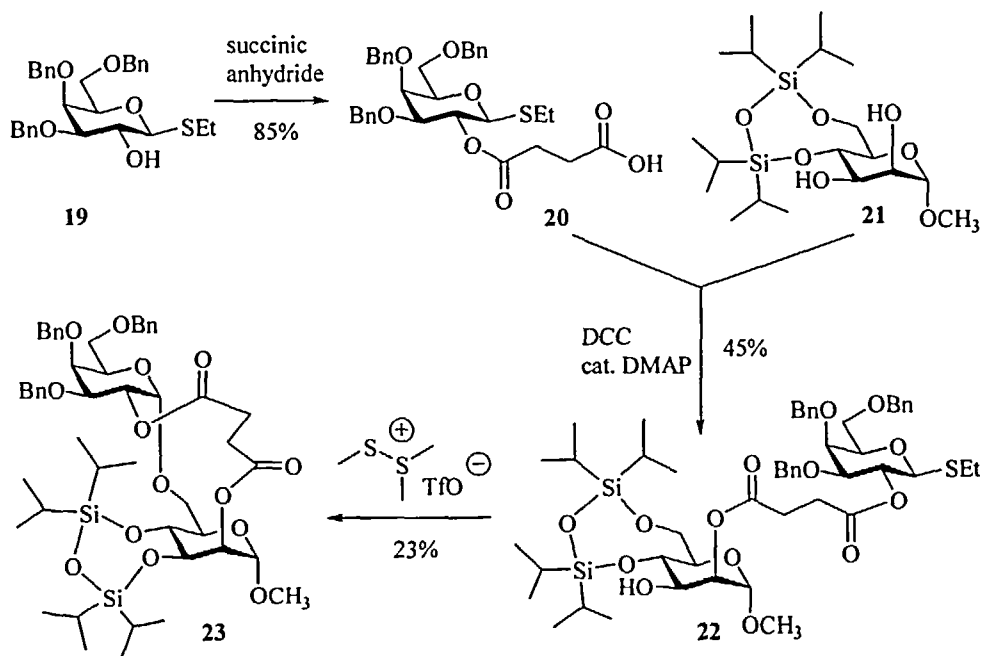


*N*-Iodosuccinimide (NIS) promoted intramolecular glycosylation of the prearranged glycosides **7** and **14** resulted in exclusive formation of the corresponding  $\alpha$ -(1 $\rightarrow$ 4)-linked disaccharides **15** and **17**, respectively. Yields of cyclisation products were slightly higher when acetonitrile was used as the solvent instead of dichloromethane (experimental details for dichloromethane are not shown). However, there was no solvent dependence of the diastereoselectivity of the galactosylation as was found for other intramolecular condensations of prearranged glycosides.<sup>6</sup> The anomeric configuration of the products was clearly evident from their NMR spectra. The coupling constant between C-1 and H-1 of the respective galactose moiety was 170.8 Hz for **15** and 164.5 Hz for **17** which was in good agreement for  $\alpha$ -anomers.<sup>10</sup> Furthermore, the H-H coupling constant  $J_{1,2}$  of the galactosyl residue of compound **17** was 3.6 Hz whereas that of compound **15** could not be determined due to extensive overlapping of the proton signals in the NMR spectra. Therefore, deacylation of **15** and **17** was performed as well. The thus formed disaccharides **16** and **18** showed again typical coupling constants of  $J_{C-1,H1} = 167.0$  Hz and  $J_{1,2} = 3.7$  Hz for **16** and  $J_{C-1,H1} = 170.6$  Hz and  $J_{1,2} = 3.6$  Hz for **18**, respectively.



The formation of the  $\alpha$ -linked products was also in good agreement with the previously observed  $\alpha$ -selectivity of intramolecular glucosylations.<sup>6g</sup> However, it should

be noted that this  $\alpha$ -selectivity of intramolecular glucosylations<sup>6b</sup> and of galactosylations in the case of compound 7 is in sharp contrast to similar mannosylations.<sup>6c</sup> Here  $\alpha$ -mannosides were formed as well, despite the 'inverted' configuration at position 2 of the glycosyl donor. Furthermore, provided that a double diastereoselection (*i.e.*, formation of matched and mismatched pairs during cyclisation) which has been previously shown to govern the diastereoselectivity of intramolecular glycosylations<sup>6j</sup> was also operative here, the  $\alpha$ -selectivity of the cyclisation of 14 (compared to that of 7) was surprising and rather unexpected. Changing the tether from position 2 to position 6 of the galactoside moiety should result in a mismatched case for  $\alpha$ -galactosylation and thus, give also some  $\beta$ -linked product. However, preliminary molecular modelling studies for compounds 15, 17, and their  $\beta$ -(1 $\rightarrow$ 4)-linked counterparts, respectively, using a Monte-Carlo conformation search with the AMBER force field implemented in MacroModel<sup>11</sup> revealed that in both cases performed here the  $\alpha$ -linked products should be favored whereas without any tether (*i.e.*, acetyl groups instead of a succinyl group), the  $\beta$ -(1 $\rightarrow$ 4)-linked product should be favoured in the case related to disaccharide 17.<sup>12</sup>



Another intramolecular galactosylation was tested with a mannosyl acceptor as follows. Ethyl 3,4,6-tri-*O*-benzyl-1-thio- $\beta$ -D-galactopyranoside<sup>13</sup> (**19**) was succinoylated as described above affording galactoside **20**. Next, the latter was condensed with siloxane protected  $\alpha$ -D-mannoside **21**<sup>14</sup> to give succinate **22** in 45% yield. Originally, **21** was chosen as the acceptor since regioselective acylation<sup>14</sup> directly leads to a suitable prearranged glycoside for intramolecular galactosylation and the siloxane group should allow for further glycosylations using the glycodesilylation protocol.<sup>15</sup> However, as a byproduct of the latter condensation, the corresponding prearranged glycoside, which was esterified at position 3 of the mannosyl residue, was formed as well in 35% yield. Since this isomer, however, could not be isolated in pure form, no further experimental details will be given here. Intramolecular galactosylation of **22** was somehow sluggish. Complete decomposition of the starting material occurred with MeOTf as the activator. Solely, when dimethylthiomethylsulfoniumtriflate (DMTST) was used, 23% of disaccharide **23** could be isolated. Obviously, under the acidic conditions, a rearrangement of the siloxane group occurred with subsequent glycosylation of position 6. It is, however, well known that glycosylations of position 3 in 4,6-siloxane protected glycopyranosides are difficult to achieve due to steric reasons and that similar rearrangements of siloxane groups do occur under acidic conditions.<sup>16</sup> Nevertheless, further examples for the intramolecular glycosylation of siloxane protected glycosides related to the conversion **22**→**23** are now under investigation since this strategy would open up an easy access to complex oligosaccharides when combined with the glycodesilylation protocol.<sup>15</sup>

## EXPERIMENTAL

The NMR data were obtained from spectra measured in CDCl<sub>3</sub> solutions (with Me<sub>4</sub>Si as internal standard) at 25 °C with a Bruker AMX 300 spectrometer. <sup>1</sup>H NMR signal assignments were made by first-order analysis of the spectra and by HH-COSY spectra. Of the two magnetically non-equivalent geminal protons at C-6, the one resonating at lower field was allocated H-6a and the one resonating at higher field H-6b. <sup>13</sup>C NMR assignments were made by mutual comparison of the spectra, by DEPT spectra,

and by CH-COSY spectra. Optical rotations were measured at 25 °C with a Perkin-Elmer automatic polarimeter, Model 241. TLC was performed on precoated plastic sheets, Polygram SIL UV<sub>254</sub>, 40 x 80mm (Macherey-Nagel) using appropriately adjusted mixtures of toluene-acetone. Detection was affected by UV light, where applicable, and by charring with 5% H<sub>2</sub>SO<sub>4</sub> in ethanol. CC was performed by eluting from columns of Silica Gel 60 (Merck) with appropriately adjusted mixtures of toluene/acetone. Solutions in organic solvents were dried with anhydr Na<sub>2</sub>SO<sub>4</sub> and concentrated at 2 kPa, <40 °C.

**Phenyl 2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-1-thio-β-D-galactopyranoside (2).** Thiophenol (2.2 mL, 21.6 mmol) was added dropwise at 20 °C to a stirred solution of 1,2-*O*-(1-methoxyethylidene)-3,4,6-tri-*O*-benzyl-α-D-galactopyranose<sup>7</sup> (1) (7.5 g, 14.8 mmol) and HgBr<sub>2</sub> (200 mg, 0.6 mmol) in MeCN (58 mL). The mixture was stirred for 24 h, concentrated and dissolved in dichloromethane (200 mL). The resulting solution was washed with saturated aq NaHCO<sub>3</sub> solution and water, dried and concentrated. Recrystallization of the residue from ethanol afforded 2 (6.90 g, 80%): mp 107-108 °C; [α]<sub>D</sub> +11.3° (*c* 1.0, chloroform); <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 5.40 (t, 1H, J<sub>1,2</sub> = 9.7 Hz, J<sub>2,3</sub> = 9.7 Hz, H-2), 4.66-4.35 (m, 6H, H-1, CH<sub>2</sub>Ph), 3.96 (d, 1H, J<sub>3,4</sub> = 2.7 Hz, J<sub>4,5</sub> < 1.0 Hz, H-4), 3.65-3.59 (m, 3H, H-5,6a,6b), 3.53 (dd, 1H, H-3), 2.00 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 87.1 (C-1), 81.9 (C-3), 78.0 (C-5), 74.8, 74.0, 72.4 (CH<sub>2</sub>Ph), 73.3 (C-4), 70.2 (C-2), 69.2 (C-6), 21.5 (CH<sub>3</sub>).

Anal. Calcd for C<sub>35</sub>H<sub>36</sub>O<sub>6</sub>S (584.7): C, 70.89; H, 6.21. Found: C, 71.10; H, 6.21.

**Phenyl 3,4,6-Tri-*O*-benzyl-1-thio-β-D-galactopyranoside (3).** A solution of 2 (3.94 g, 6.7 mmol) and a catalytic amount of NaOMe in MeOH/toluene (1:1 v/v, 70 mL) was stirred at 75 °C for 2.5 h, cooled to 20 °C, neutralized with ion exchange resin (Dowex 1X8, H<sup>+</sup> form) and concentrated. Recrystallization of the residue from *n*-hexane/ethyl acetate afforded 3 (2.66 g, 72%): mp 88 °C; [α]<sub>D</sub> +3.1° (*c* 1.0, chloroform); <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 4.89 (d, 1H, J = -11.5 Hz, CH<sub>2</sub>Ph), 4.75-4.68 (m, 2H, CH<sub>2</sub>Ph), 4.57 (d, 1H, J = -12.1 Hz, CH<sub>2</sub>Ph), 4.53 (d, 1H, J<sub>1,2</sub> = 9.7 Hz, H-1), 4.46 (d, 2H, CH<sub>2</sub>Ph), 4.04-3.96 (m, 1H, H-2), 3.97 (d, 1H, J<sub>3,4</sub> = 2.5 Hz, J<sub>4,5</sub> < 1.0 Hz, H-4), 3.66 (br.s, 3H, H-5,6a,6b), 3.46 (dd, 1H, J<sub>2,3</sub> = 9.3 Hz, H-3), 2.48 (br.s, 1H, OH); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 88.1 (C-1), 83.6 (C-3), 78.0 (C-5), 74.8, 74.0, 72.8 (CH<sub>2</sub>Ph), 73.6 (C-4), 69.5 (C-2), 69.1 (C-6).

Anal. Calcd for C<sub>33</sub>H<sub>34</sub>O<sub>5</sub>S (542.7): C, 73.04; H, 6.31. Found: C, 72.83; H, 6.39.



**Phenyl 3,4,6-Tri-*O*-benzyl-2-*O*-succinoyl-1-thio- $\beta$ -D-galactopyranoside (4).** A solution of **3** (680 mg, 1.3 mmol), succinic anhydride (1.25 g, 12.5 mmol) and a catalytic amount of DMAP (ca. 10 mg) in pyridine (16 mL) was stirred at 100 °C for 22.5 h. The mixture was concentrated and coevaporated with toluene. Chromatography (toluene/acetone 8:1 v/v) of the residue afforded **4** (780 mg, 97%) as a colorless foam:  $[\alpha]_D +12.4^\circ$  (*c* 1.0, chloroform);  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  5.39 (t, 1H,  $J_{1,2} = 9.7$  Hz,  $J_{2,3} = 9.7$  Hz, H-2), 4.86 (d, 1H,  $J = -11.6$  Hz,  $\text{CH}_2\text{Ph}$ ), 4.61-4.32 (m, 6H, H-1,  $\text{CH}_2\text{Ph}$ ), 3.92-3.50 (m, 5H, H-3,4,5,6a,6b), 2.56-2.53 (m, 4H,  $\text{CH}_2$ );  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  177.8 (COOH), 170.9 (COO), 86.6 (C-1), 81.4 (C-3), 77.6 (C-5), 74.4, 73.6, 72.1 ( $\text{CH}_2\text{Ph}$ ), 73.0 (C-4), 70.0 (C-2), 68.9 (C-6), 29.1, 28.9 ( $\text{CH}_2$ ).

Anal. Calcd for  $\text{C}_{37}\text{H}_{38}\text{O}_8\text{S}$  (642.8): C, 69.14; H, 5.96. Found: C, 68.99; H, 5.94.

**Phenyl 3,4,6-Tri-*O*-benzyl-2-*O*-(2-*O*-benzoyl-1-*O*-benzyl-4,6-*O*-benzylidene- $\alpha$ -D-glucopyranos-3-yloxycarbonylpropanoyl)-1-thio- $\beta$ -D-galactopyranoside (6).** Dicyclohexyl carbodiimide (0.55 g, 2.64 mmol) was added at 20 °C to a solution of **4** (1.5 g, 2.4 mmol), benzyl 2-*O*-benzoyl-4,6-*O*-benzylidene- $\alpha$ -D-glucopyranoside<sup>6j</sup> (**5**) (1.22 g, 2.64 mmol) and a catalytic amount of DMAP (ca. 10 mg) in dichloromethane (40 mL). The mixture was stirred for 20 h and filtered. The filtrate was washed with water, dried and concentrated. Chromatography (toluene/acetone 18:1 v/v) of the residue afforded **6** (1.83 g, 72%) as a colorless foam:  $[\alpha]_D +58.6^\circ$  (*c* 1.0, chloroform);  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  5.87 (t, 1H,  $J_{2,3} = 9.9$  Hz,  $J_{3,4} = 9.9$  Hz, H-3<sub>Glc</sub>), 5.49 (s, 1H, PhCH), 5.36-5.28 (m, 2H, H-1<sub>Glc</sub>, H-2<sub>Gal</sub>), 5.03 (dd, 1H,  $J_{1,2} = 3.8$  Hz, H-2<sub>Glc</sub>), 4.90 (d, 1H,  $J = -11.6$  Hz,  $\text{PhCH}_2$ ), 4.73 (d, 1H,  $J = -12.4$  Hz,  $\text{PhCH}_2$ ), 4.59-4.46 (m, 5H, H-1<sub>Gal</sub>,  $\text{PhCH}_2$ ), 4.24 (dd, 1H,  $J_{5,6a} = 4.8$  Hz,  $J_{6a,6b} = -10.1$  Hz, H-6a<sub>Glc</sub>), 4.09-4.01 (m, 1H, H-5<sub>Glc</sub>), 3.90 (d, 1H,  $J_{3,4} = 2.6$  Hz,  $J_{4,5} < 1.0$  Hz, H-4<sub>Gal</sub>), 3.78-3.48 (m, 5H, H-4<sub>Glc</sub>, 6b<sub>Glc</sub>, 5<sub>Gal</sub>, 6a<sub>Gal</sub>, 6b<sub>Gal</sub>), 3.46 (dd, 1H,  $J_{2,3} = 9.6$  Hz, H-3<sub>Gal</sub>), 2.59-2.46 (m, 4H,  $\text{CH}_2\text{CO}$ );  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  171.2, 170.4 (CO), 165.9 (PhCO), 101.6 (PhCH), 95.9 (C-1<sub>Glc</sub>), 86.5 (C-1<sub>Gal</sub>), 81.2 (C-3<sub>Gal</sub>), 79.1 (C-4<sub>Glc</sub>), 77.5 (C-5<sub>Gal</sub>), 72.9 (C-4<sub>Gal</sub>), 72.4 (C-2<sub>Glc</sub>), 74.3, 73.5, 72.2, 70.0 ( $\text{PhCH}_2$ ), 70.0 (C-2<sub>Gal</sub>), 69.2 (C-3<sub>Glc</sub>), 68.8 (C-6<sub>Glc</sub>), 68.7 (C-6<sub>Gal</sub>), 62.5 (C-5<sub>Glc</sub>), 29.1, 28.8 ( $\text{CH}_2$ ).

Anal. Calcd for  $\text{C}_{64}\text{H}_{62}\text{O}_{14}\text{S}$  (1087.3): C, 70.70; H, 5.75. Found: C, 70.89; H, 5.79.

**Phenyl 3,4,6-Tri-*O*-benzyl-2-*O*-(2-*O*-benzoyl-1,4-di-*O*-benzyl- $\alpha$ -D-glucopyranos-3-yloxycarbonylpropanoyl)-1-thio- $\beta$ -D-galactopyranoside (7).** A saturated solution of HCl in diethyl ether was added dropwise at 0 °C under Ar to a stirred

suspension of **6** (1.4 g, 1.28 mmol), NaCNBH<sub>3</sub> (1.0 g, 16.1 mmol) and molecular sieves 3 Å (1.0 g) in THF (26 mL) until the evolution of gas ceased. The mixture was diluted with dichloromethane and filtered through a layer of Celite. The filtrate was washed with saturated aq NaHCO<sub>3</sub> solution, dried and concentrated. Chromatography (toluene/acetone 14:1 v/v) of the residue afforded **7** (1.04 g, 74%) as a colorless foam:  $[\alpha]_D +59.3^\circ$  (*c* 1.0, chloroform); <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 5.67 (t, 1H, J<sub>2,3</sub> = 9.7 Hz, J<sub>3,4</sub> = 9.7 Hz, H-3<sub>Glc</sub>), 5.38 (d, 1H, J<sub>1,2</sub> = 3.7 Hz, H-1<sub>Glc</sub>), 5.26 (dd 1H, J<sub>1,2</sub> = 9.5 Hz, J<sub>2,3</sub> = 10.3 Hz, H-2<sub>Gal</sub>), 5.00 (t, 1H, H-2<sub>Glc</sub>), 4.92 (d, 1H, J = -11.6 Hz, PhCH<sub>2</sub>), 4.74 (d, 1H, J = -12.3 Hz, PhCH<sub>2</sub>), 4.65-4.37 (m, 9H, H-1<sub>Gal</sub>, PhCH<sub>2</sub>), 4.00-3.95 (m, 2H, H-4<sub>Gal</sub>, 5<sub>Glc</sub>), 3.94-3.51 (m, 7H, H-4<sub>Glc</sub>, 6a<sub>Glc</sub>, 6b<sub>Glc</sub>, 3<sub>Gal</sub>, 5<sub>Gal</sub>, 6a<sub>Gal</sub>, 6b<sub>Gal</sub>), 2.65-2.45 (m, 4H, CH<sub>2</sub>CO); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 172.3, 171.2 (CO), 165.8 (PhCO), 95.1 (C-1<sub>Glc</sub>), 86.5 (C-1<sub>Gal</sub>), 81.2 (C-3<sub>Gal</sub>), 77.5 (C-5<sub>Gal</sub>), 74.4, 73.6, 73.5, 72.4, 69.6 (PhCH<sub>2</sub>), 73.5 (C-3<sub>Glc</sub>), 72.8 (C-4<sub>Gal</sub>), 71.4 (C-4<sub>Glc</sub>), 70.4 (C-2<sub>Glc</sub>), 70.2 (C-5<sub>Glc</sub>), 70.1 (C-2<sub>Gal</sub>), 69.3 (C-6<sub>Glc</sub>), 68.7 (C-6<sub>Gal</sub>), 62.5 (C-5<sub>Glc</sub>), 29.3, 29.1 (CH<sub>2</sub>).

Anal. Calcd for C<sub>64</sub>H<sub>64</sub>O<sub>14</sub>S (1089.3): C, 70.57; H, 5.92. Found: C, 70.37; H, 5.99.

**Phenyl 1-Thio-6-O-trityl-β-D-galactopyranoside (9)**. A solution of phenyl 1-thio-β-D-galactopyranoside<sup>9</sup> (**8**) (1.75 g, 6.4 mmol) and trityl chloride (2.15 g, 7.7 mmol) in pyridine (18 mL) was stirred at 90 °C for 21 h followed at 100 °C for 4 h, and concentrated. The residue was dissolved in dichloromethane (250 mL), washed with aq HCl and NaHCO<sub>3</sub> solution, dried and concentrated. Chromatography (toluene/acetone 4:1 to 2:1 v/v) of the residue afforded **9** (1.96 g, 59%): mp 89 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.60-7.13 (m, 20H, Ph), 4.52 (d, 1H, J<sub>1,2</sub> = 9.6 Hz, H-1), 4.01-2.91 (m, 9H, H-2,3,4,6, OH); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 88.6 (C-1), 87.0 (Ph<sub>3</sub>C), 77.6 (C-5), 74.9, 69.9, 69.7 (C-2,3,4), 63.6 (C-6).

Anal. Calcd for C<sub>31</sub>H<sub>30</sub>O<sub>5</sub>S (514.6): C, 72.35; H, 5.88. Found: C, 72.80; H, 5.87.

**Phenyl 2,3,4-Tri-O-benzyl-1-thio-6-O-trityl-β-D-galactopyranoside (10)**. NaH (0.75 g, 31.4 mmol) was added portionwise with cooling to a solution of **9** (2.8 g, 5.44 mmol) and benzyl bromide (1.94 mL, 16.3 mmol) in DMF (14 mL). The mixture was stirred at 20 °C for 2 h and carefully hydrolyzed by addition of water. The mixture was poured into water and extracted with dichloromethane. The combined extracts were washed with water and saturated aq NaHCO<sub>3</sub> solution, dried and concentrated. Chromatography (*n*-hexane/ethyl acetate 5:1 v/v) of the residue afforded **10** (3.56 g, 83%)

as a colorless oil:  $[\alpha]_D +5.5^\circ$  ( $c$  1.0, chloroform);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  4.85 (d, 1H,  $J = -11.5$  Hz,  $\text{PhCH}_2$ ), 4.77-4.67 (m, 4H,  $\text{PhCH}_2$ ), 4.59 (d, 1H,  $J_{1,2} = 9.6$  Hz, H-1), 4.51 (d, 1H,  $J = -11.5$  Hz,  $\text{PhCH}_2$ ), 3.92-3.87 (m, 2H, H-2,3), 3.55 (m, 1H, H-6a), 3.51 (d, 1H,  $J_{3,4} = 2.6$  Hz,  $J_{4,5} < 1.0$  Hz, H-4), 3.32 (t, 1H,  $J_{5,6} = 6.2$  Hz, H-5), 3.21 (m, 1H, H-6b);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  87.6 (C-1), 86.9 ( $\text{Ph}_3\text{C}$ ), 84.1 (C-4), 77.6 (C-5), 77.3 (C-2), 75.6, 74.1, 72.9 ( $\text{PhCH}_2$ ), 74.0 (C-3), 62.9 (C-6).

Anal. Calcd for  $\text{C}_{52}\text{H}_{48}\text{O}_5\text{S}$  (785.0): C, 79.56; H, 6.16. Found: C, 79.48; H, 6.15.

**Phenyl 2,3,4-Tri-*O*-benzyl-1-thio- $\beta$ -D-galactopyranoside (11).** A solution of 10 (3.0 g, 3.8 mmol) and *p*-TosOH (0.56 g, 3.3 mmol) in chloroform/methanol (2:1 v/v, 140 mL) was stirred at 20 °C for 1 h, washed with saturated aq  $\text{NaHCO}_3$  solution, dried and concentrated. Chromatography (toluene/acetone 8:1 v/v) of the residue afforded 11 (1.73 g, 83%) as a colorless foam:  $[\alpha]_D -16.7^\circ$  ( $c$  1.0, chloroform);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  4.96 (d, 1H,  $J = -11.8$  Hz,  $\text{PhCH}_2$ ), 4.83-4.73 (m, 4H,  $\text{PhCH}_2$ ), 4.64 (d, 1H,  $J_{1,2} = 9.7$  Hz, H-1), 4.63 (d, 1H,  $J = -11.8$  Hz,  $\text{PhCH}_2$ ), 3.95 (t, 1H,  $J_{2,3} = 9.5$  Hz, H-2), 3.86-3.80 (m, 2H, H-3,6a), 3.60 (br.d, 1H,  $J_{3,4} = 2.8$  Hz, H-4), 3.52 (dd, 1H,  $J_{5,6b} = 5.1$  Hz,  $J_{6a,6b} = -11.2$  Hz, H-6b), 3.43 (m, 1H, H-5), 1.76 (br.s, 1H, OH);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  88.1 (C-1), 84.7 (C-4), 79.3 (C-5), 77.2 (C-2), 76.1, 74.6, 73.5 ( $\text{PhCH}_2$ ), 73.7 (C-3), 62.7 (C-6).

Anal. Calcd for  $\text{C}_{33}\text{H}_{34}\text{O}_5\text{S}$  (542.7): C, 73.04; H, 6.31. Found: C, 73.04; H, 6.32.

**Phenyl 2,3,4-Tri-*O*-benzyl-6-*O*-succinoyl-1-thio- $\beta$ -D-galactopyranoside (12).** A solution of 11 (1.55 g, 2.4 mmol), succinic anhydride (1.93 g, 19.3 mmol) and a catalytic amount of DMAP (ca. 10 mg) in pyridine (35 mL) was stirred at 20 °C for 19 h. The mixture was concentrated and coevaporated with toluene. The residue was dissolved in dichloromethane and washed with aq HCl and  $\text{NaHCO}_3$  solution, dried and concentrated. Chromatography (toluene/acetone 5:1 to 4:1 v/v) of the residue afforded 12 (1.25 g, 68%) as a colorless foam:  $[\alpha]_D -16.0^\circ$  ( $c$  1.0, chloroform);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  4.91 (d, 1H,  $J = -11.4$  Hz,  $\text{PhCH}_2$ ), 4.75-4.64 (m, 4H,  $\text{PhCH}_2$ ), 4.57 (d, 1H,  $J = -11.6$  Hz,  $\text{PhCH}_2$ ), 4.55 (d, 1H,  $J_{1,2} = 9.7$  Hz, H-1), 4.23 (dd, 1H,  $J_{5,6a} = 6.8$  Hz,  $J_{6a,6b} = -11.0$  Hz, H-6a), 4.09 (dd, 1H,  $J_{5,6b} = 5.5$  Hz, H-6b), 3.90 (t, 1H,  $J_{2,3} = 9.2$  Hz, H-2), 3.78 (br.s, 1H, H-4), 3.55-3.52 (m, 2H, H-3,5), 2.55-2.43 (m, 4H,  $\text{CH}_2\text{CO}$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  177.2 (COOH), 171.8 (COO), 87.7 (C-1), 84.1 (C-4), 77.3 (C-5), 75.9 (C-2), 75.7, 74.3, 73.0 ( $\text{PhCH}_2$ ), 73.3 (C-3), 63.6 (C-6), 28.8, 28.7 ( $\text{CH}_2$ ).

Anal. Calcd for  $\text{C}_{37}\text{H}_{38}\text{O}_8\text{S}$  (642.8): C, 69.14; H, 5.96. Found: C, 68.84; H, 5.90.

**Phenyl 6-*O*-(2-*O*-Benzoyl-1-*O*-benzyl-4,6-*O*-benzylidene- $\alpha$ -D-glucopyranos-3-yloxy-carbonylpropanoyl)-2,3,4-tri-*O*-benzyl-1-thio- $\beta$ -D-galactopyranoside (13).**

Dicyclohexyl carbodiimide (0.3 g, 1.43 mmol) was added at 20 °C to a solution of **12** (0.92 g, 1.43 mmol), **5** (0.66 g, 1.43 mmol) and a catalytic amount of DMAP (ca. 10 mg) in dichloromethane (25 mL). The mixture was stirred for 20 h and filtered. The filtrate was washed with water, dried and concentrated. Chromatography (toluene/acetone 12:1 v/v) of the residue afforded **13** (1.45 g, 86%) as a colorless foam:  $[\alpha]_D +52.1^\circ$  (*c* 1.0, chloroform);  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  5.77 (t, 1H,  $J_{2,3} = 9.9$  Hz,  $J_{3,4} = 9.9$  Hz, H-3<sub>Glc</sub>), 5.45 (s, 1H, PhCH), 5.18 (d, 1H,  $J_{1,2} = 3.8$  Hz, H-1<sub>Glc</sub>), 4.98 (dd, 1H, H-2<sub>Glc</sub>), 4.85 (d, 1H,  $J = -11.6$  Hz, PhCH<sub>2</sub>), 4.74-4.62 (m, 5H, PhCH<sub>2</sub>), 4.52-4.42 (m, 2H, PhCH<sub>2</sub>), 4.47 (d, 1H,  $J_{1,2} = 9.6$  Hz, H-1<sub>Gal</sub>), 4.19 (dd, 1H,  $J_{5,6a} = 4.8$  Hz,  $J_{6a,6b} = -10.2$  Hz, H-6a<sub>Glc</sub>), 4.04 (dd, 1H,  $J_{5,6a} = 6.9$  Hz,  $J_{6a,6b} = -11.2$  Hz, H-6a<sub>Gal</sub>), 4.00-3.94 (m, 1H, H-5<sub>Glc</sub>), 3.87-3.80 (m, 2H, H-2<sub>Gal</sub>, 6b<sub>Gal</sub>), 3.74-3.63 (m, 3H, H-4<sub>Glc</sub>, 6b<sub>Glc</sub>, 3<sub>Gal</sub>), 3.50-3.37 (m, 2H, H-4<sub>Gal</sub>, 5<sub>Gal</sub>), 2.48-2.26 (m, 4H, CH<sub>2</sub>CO);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  171.8, 171.6 (COO), 166.1 (PhCO), 102.0 (PhCH), 96.2 (C-1<sub>Glc</sub>), 88.1 (C-1<sub>Gal</sub>), 84.5 (C-4<sub>Gal</sub>), 79.5 (C-4<sub>Glc</sub>), 77.7 (C-2<sub>Gal</sub>), 76.2 (C-5<sub>Gal</sub>), 76.1, 74.6, 73.4, 70.3 (PhCH<sub>2</sub>), 73.6 (C-3<sub>Gal</sub>), 72.6 (C-2<sub>Glc</sub>), 69.8 (C-3<sub>Glc</sub>), 69.2 (C-6<sub>Glc</sub>), 63.8 (C-6<sub>Gal</sub>), 63.2 (C-6<sub>Glc</sub>), 29.4, 29.3 (CH<sub>2</sub>).

Anal. Calcd for C<sub>64</sub>H<sub>62</sub>O<sub>14</sub>S (1087.3): C, 70.70; H, 5.75. Found: C, 70.61; H, 5.78.

**Phenyl 6-*O*-(2-*O*-Benzoyl-1,6-di-*O*-benzyl- $\alpha$ -D-glucopyranos-3-yloxy-carbonylpropanoyl)-2,3,4-tri-*O*-benzyl-1-thio- $\beta$ -D-galactopyranoside (14).** A saturated solution of HCl in diethyl ether was added dropwise at 0 °C under Ar to a stirred suspension of **13** (0.8 g, 0.74 mmol), NaCNBH<sub>3</sub> (0.58 g, 9.2 mmol) and molecular sieves 3 Å (0.5 g) in THF (15 mL) until the evolution of gas ceased. Work up as described for **7** and chromatography (toluene/acetone 7:1 v/v) afforded **14** (0.58 g, 72%) as a colorless foam:  $[\alpha]_D +43.0^\circ$  (*c* 1.0, chloroform);  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  5.57 (d, 1H,  $J_{2,3} = 10.2$  Hz,  $J_{3,4} = 9.0$  Hz, H-3<sub>Glc</sub>), 5.16 (d, 1H,  $J_{1,2} = 3.7$  Hz, H-1<sub>Glc</sub>), 4.96 (dd, 1H, H-2<sub>Glc</sub>), 4.89 (d, 1H,  $J = -11.6$  Hz, PhCH<sub>2</sub>), 4.75-4.63 (m, 5H, PhCH<sub>2</sub>), 4.57-4.42 (m, 5H, H-1<sub>Gal</sub>, PhCH<sub>2</sub>), 4.12 (dd, 1H,  $J_{5,6a} = 7.1$  Hz,  $J_{6a,6b} = -11.3$  Hz, H-6a<sub>Glc</sub>), 3.99-3.43 (m, 8H, H-4<sub>Glc</sub>, 5<sub>Glc</sub>, 6b<sub>Glc</sub>, 2<sub>Gal</sub>, 3<sub>Gal</sub>, 4<sub>Gal</sub>, 6a<sub>Gal</sub>, 6b<sub>Gal</sub>), 3.45 (m, 1H, H-5<sub>Gal</sub>), 2.51-2.35 (m, 4H, CH<sub>2</sub>);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  172.8, 172.5 (COO), 166.2 (PhCO), 95.6 (C-1<sub>Glc</sub>), 88.1 (C-1<sub>Gal</sub>), 84.5 (C-4<sub>Gal</sub>), 77.7 (C-2<sub>Gal</sub>), 76.3 (C-5<sub>Gal</sub>), 76.1, 74.7, 74.1, 73.5, 70.0 (PhCH<sub>2</sub>), 73.9 (C-3<sub>Glc</sub>),

73.7 (C-3<sub>Gal</sub>), 71.8 (C-4<sub>Glc</sub>), 70.8 (C-2<sub>Glc</sub>), 70.5 (C-5<sub>Glc</sub>), 69.8 (C-6<sub>Glc</sub>), 64.3 (C-6<sub>Gal</sub>), 29.6, 29.5 (CH<sub>2</sub>).

Anal. Calcd for C<sub>64</sub>H<sub>64</sub>O<sub>14</sub>S (1089.3): C, 70.57; H, 5.92. Found: C, 70.35; H, 5.89.

**Benzyl O-(3',4',6'-Tri-O-benzyl- $\alpha$ -D-galactopyranosyl)-(1 $\rightarrow$ 4)-2-O-benzoyl-6-O-benzyl- $\alpha$ -D-glucopyranoside-2',3-succinate (15).** TMSOTf (15  $\mu$ L, 83  $\mu$ mol) was added at -30 °C under Ar to a stirred suspension of **7** (220 mg, 0.23 mmol), NIS (220 mg, 1.15 mmol) and molecular sieves 3Å (0.2 g) in MeCN (30 mL). The mixture was stirred for 10 min, neutralized by addition of pyridine (1 mL) and warmed to 20 °C. The mixture was diluted with dichloromethane and filtered through a layer of Celite. The filtrate was washed with saturated aq NaHCO<sub>3</sub> solution, dried and concentrated. Chromatography (toluene/acetone 18:1 v/v) of the residue afforded **15** (101 mg, 51%) as a colorless foam:  $[\alpha]_D^{+94.6^\circ}$  (*c* 1.0, chloroform); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  5.79 (dd, 1H, J<sub>2,3</sub> = 10.3 Hz, J<sub>3,4</sub> = 8.4 Hz, H-3<sub>Glc</sub>), 5.24-5.18 (m, 3H, H-1<sub>Glc</sub>, 1<sub>Gal</sub>, 2<sub>Gal</sub>), 4.92 (dd, 1H, J<sub>1,2</sub> = 3.8 Hz, J<sub>2,3</sub> = 10.3 Hz, H-2<sub>Glc</sub>), 4.89 (d, 1H, J = -11.5 Hz, PhCH<sub>2</sub>), 4.96-4.32 (m, 9H, PhCH<sub>2</sub>), 3.98 (t, 1H, J<sub>4,5</sub> = 6.2 Hz, H-5<sub>Gal</sub>), 3.92-3.84 (m, 5H, H-4<sub>Glc</sub>, 5<sub>Glc</sub>, 6<sub>aGlc</sub>, 3<sub>Gal</sub>, 4<sub>Gal</sub>), 3.59 (br.d, 1H, J = 9.7 Hz, H-6<sub>bGlc</sub>), 3.52-3.40 (m, 2H, H-6<sub>aGal</sub>, 6<sub>bGal</sub>), 2.75-2.42 (m, 4H, CH<sub>2</sub>CO); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  171.1, 170.7 (CO), 166.0 (PhCO), 100.9 (J<sub>C-1,H-1</sub> = 170.8 Hz, C-1<sub>Gal</sub>), 95.5 (C-1<sub>Glc</sub>), 80.5 (C-3<sub>Gal</sub>), 73.7, 70.1, 75.2 (PhCH<sub>2</sub>), 73.9 (2C, PhCH<sub>2</sub>), 72.9 (C-2<sub>Gal</sub>), 72.0 (C-2<sub>Glc</sub>), 71.9 (C-3<sub>Glc</sub>), 71.1 (C-5<sub>Gal</sub>), 76.6, 75.6, 70.8 (C-4<sub>Glc</sub>, 5<sub>Glc</sub>, 4<sub>Gal</sub>), 69.8 (C-6<sub>Gal</sub>), 68.3 (C-6<sub>Glc</sub>), 31.0, 30.9 (CH<sub>2</sub>). FABMS (pos.): *m/z* 1001 (M+Na)<sup>+</sup>.

Anal. Calcd for C<sub>58</sub>H<sub>58</sub>O<sub>14</sub> (979.1): C, 71.15; H, 5.97. Found: C, 70.92; H, 5.97.

**Benzyl O-(3,4,6-Tri-O-benzyl- $\alpha$ -D-galactopyranosyl)-(1 $\rightarrow$ 4)-2-O-benzoyl-6-O-benzyl- $\alpha$ -D-glucopyranoside (16).** A solution of **15** (63.3 mg, 65  $\mu$ mol) and a catalytic amount of NaOMe in MeOH/dichloromethane (2:1 v/v, 35 mL) was stirred at 20 °C for 2.5 h, neutralized with ion exchange resin (Dowex 1X8, H<sup>+</sup> form) and concentrated. Chromatography (toluene/acetone 3:1 v/v) of the residue afforded **16** (24 mg, 68%) as a colorless foam:  $[\alpha]_D^{+91.4^\circ}$  (*c* 2.4, chloroform); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  5.14 (d, 1H, J<sub>1,2</sub> = 3.7 Hz, H-1<sub>Gal</sub>), 4.94 (d, 1H, J<sub>1,2</sub> = 3.8 Hz, H-1<sub>Glc</sub>), 4.81 (d, 1H, J = -11.4 Hz, PhCH<sub>2</sub>), 4.72-4.65 (m, 2H, PhCH<sub>2</sub>), 4.59-4.33 (m, 7H, PhCH<sub>2</sub>), 4.18 (dd, 1H, J<sub>2,3</sub> = 10.1 Hz, H-2<sub>Gal</sub>), 4.00 (t, 1H, J<sub>5,6</sub> = 6.3 Hz, H-5<sub>Gal</sub>), 3.91 (br.s, 1H, H-4<sub>Gal</sub>), 3.85 (t, 1H, J<sub>2,3</sub> = 9.2 Hz, J<sub>3,4</sub> = 9.2 Hz, H-3<sub>Glc</sub>), 3.75-3.59 (m, 5H, H-4<sub>Glc</sub>, 5<sub>Glc</sub>, 6<sub>aGlc</sub>, 6<sub>bGlc</sub>, 3<sub>Gal</sub>), 3.55 (dd, 1H, H-2<sub>Glc</sub>), 3.47 (br.d, 2H, H-6<sub>aGal</sub>, 6<sub>bGal</sub>), 2.7 (br.s, 3H, OH); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  101.6 (J<sub>C-1,H-1</sub> =

167.0 Hz, C-1<sub>Gal</sub>), 97.5 (C-1<sub>Glc</sub>), 81.3 (C-5<sub>Glc</sub>), 79.2 (C-3<sub>Gal</sub>), 74.6, 73.5, 73.3, 72.3, 69.7 (PhCH<sub>2</sub>), 74.1 (C-3<sub>Glc</sub>), 73.8 (C-4<sub>Gal</sub>), 71.9 (C-2<sub>Glc</sub>), 70.6 (C-5<sub>Gal</sub>), 70.2 (C-4<sub>Glc</sub>), 69.7 (C-2<sub>Gal</sub>), 69.2 (C-6<sub>Gal</sub>), 68.8 (C-6<sub>Glc</sub>). FABMS (pos.): *m/z* 815 (M+Na)<sup>+</sup>.

**Benzyl *O*-(2',3',4'-Tri-*O*-benzyl- $\alpha$ -D-galactopyranosyl)-(1 $\rightarrow$ 4)-2-*O*-benzoyl-6-*O*-benzyl- $\alpha$ -D-glucopyranoside-3,6'-succinate (17).** Treatment of 14 (220 mg, 0.2 mmol) exactly as described for the preparation of 15 afforded 17 (126 mg, 69%) as a colorless foam:  $[\alpha]_D +80.0^\circ$  (*c* 1.0, chloroform); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  6.09 (t, 1H, J<sub>2,3</sub> = 10.0 Hz, J<sub>3,4</sub> = 10.0 Hz, H-3<sub>Glc</sub>), 5.21 (d, 1H, J<sub>1,2</sub> = 3.6 Hz, H-1<sub>Gal</sub>), 5.14 (d, 1H, J<sub>1,2</sub> = 3.3 Hz, H-1<sub>Glc</sub>), 4.98-4.36 (m, 11H, H-2<sub>Glc</sub>, PhCH<sub>2</sub>), 4.50-4.36 (m, 1H, H-6a<sub>Gal</sub>), 4.28 (t, 1H, J<sub>4,5</sub> = 10.4 Hz, H-4<sub>Glc</sub>), 4.11 (br.d, 1H, J<sub>5,6</sub> = 9.5 Hz, H-5<sub>Gal</sub>), 4.02 (dd, 1H, J<sub>2,3</sub> = 3.5 Hz, H-2<sub>Gal</sub>), 4.01-3.96 (m, 1H, H-6a<sub>Glc</sub>), 3.85-3.68 (m, 3H, H-5<sub>Glc</sub>, 3<sub>Gal</sub>, 4<sub>Gal</sub>), 3.67 (dd, 1H, J<sub>6a,6b</sub> = -11.3 Hz, H-6b<sub>Gal</sub>), 3.35 (dd, 1H, J<sub>6a,6b</sub> = -10.0 Hz, H-6b<sub>Glc</sub>), 2.82-2.12 (m, 4H, CH<sub>2</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  171.1, 170.3 (CO), 165.7 (PhCO), 94.9 (C-1<sub>Glc</sub>), 93.1 (J<sub>C-1,H-1</sub> = 164.5 Hz, C-1<sub>Gal</sub>), 78.9 (C-5<sub>Glc</sub>), 75.7 (C-2<sub>Gal</sub>), 74.7 (C-4<sub>Gal</sub>), 74.4, 74.1, 73.6, 72.8, 69.2 (PhCH<sub>2</sub>), 73.7 (C-2<sub>Glc</sub>), 73.0 (C-4<sub>Glc</sub>), 69.1 (C-3<sub>Gal</sub>), 68.1 (C-6<sub>Glc</sub>), 67.4 (C-3<sub>Glc</sub>), 64.9 (C-6<sub>Gal</sub>), 29.7 (2C, CH<sub>2</sub>). FABMS (pos.): *m/z* 1001 (M+Na)<sup>+</sup>.

Anal. Calcd for C<sub>58</sub>H<sub>58</sub>O<sub>14</sub> (979.1): C, 71.15; H, 5.97. Found: C, 71.00; H, 5.98.

**Benzyl *O*-(2,3,4-Tri-*O*-benzyl- $\alpha$ -D-galactopyranosyl)-(1 $\rightarrow$ 4)-6-*O*-benzyl- $\alpha$ -D-glucopyranoside (18).** Treatment of 17 (61.2 mg, 63  $\mu$ mol) exactly as described for the preparation of 16 afforded 18 (38.3 mg, 68%) as a colorless foam:  $[\alpha]_D +64.0^\circ$  (*c* 3.0, chloroform); <sup>1</sup>H NMR (significant signals, CDCl<sub>3</sub>)  $\delta$  5.01 (br.d, 2H, J<sub>1,2</sub> = 3.7 Hz, H-1<sub>Glc</sub>, H-1<sub>Gal</sub>), 4.08 (dd, 1H, J<sub>2,3</sub> = 10.1 Hz, H-2<sub>Gal</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  101.4 (J<sub>C-1,H-1</sub> = 170.6 Hz, C-1<sub>Gal</sub>), 97.6 (C-1<sub>Glc</sub>), 81.5 (C-5<sub>Gal</sub>), 79.4 (C-3<sub>Gal</sub>), 75.9 (C-2<sub>Gal</sub>), 74.4 (C-4<sub>Gal</sub>), 74.4 (2C, PhCH<sub>2</sub>), 74.2 (C-3<sub>Glc</sub>), 73.3, 72.9, 69.8 (PhCH<sub>2</sub>), 71.9 (C-2<sub>Glc</sub>), 71.6 (C-5<sub>Glc</sub>), 70.1 (C-4<sub>Glc</sub>), 68.6 (C-6<sub>Glc</sub>), 62.3 (C-6<sub>Gal</sub>). FABMS (pos.): *m/z* 815 (M+Na)<sup>+</sup>.

**Ethyl 3,4,6-Tri-*O*-benzyl-2-*O*-succinoyl-1-thio- $\beta$ -D-galactopyranoside (20).** A solution of ethyl 3,4,6-tri-*O*-benzyl-1-thio- $\beta$ -D-galactopyranoside<sup>13</sup> (19) (1.0 g, 2.0 mmol), succinic anhydride (2.0 g, 20 mmol) and DMAP (72 mg, 0.6 mmol) in pyridine (20 mL) was stirred for 48 h at 80 °C. Work up as described for 4 and chromatography (*n*-hexane/ethyl acetate/acetic acid 3:2:0.1 v/v) afforded 20 (1.0 g, 85%) as a colorless foam:  $[\alpha]_D +0.6^\circ$  (*c* 1.5, chloroform); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  5.42 (t, 1H, J<sub>1,2</sub> = 9.7 Hz, J<sub>2,3</sub> =

9.7 Hz, H-2), 4.93 (d, 1H,  $J = -11.3$  Hz, CH<sub>2</sub>Ph), 4.65 (d, 1H,  $J = -12.2$  Hz, CH<sub>2</sub>Ph), 4.56 (d, 1H,  $J = -11.5$  Hz, CH<sub>2</sub>Ph), 4.52 (d, 1H,  $J = -12.0$  Hz, CH<sub>2</sub>Ph), 4.45 (d, 1H,  $J = -11.9$  Hz, CH<sub>2</sub>Ph), 4.40 (d, 1H,  $J = -11.8$  Hz, CH<sub>2</sub>Ph), 4.33 (d, 1H, H-1), 3.97 (d, 1H,  $J_{3,4} = 2.4$  Hz, H-4), 3.59 (br.s, 3H, H-5,6a,6b), 3.54, (dd, 1H, H-3), 2.74-2.56 (m, 6H, CH<sub>2</sub>COO, SCH<sub>2</sub>), 1.23-1.18 (m, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  83.5 (C-1), 81.3 (C-3), 77.4 (C-5), 77.4, 73.5 (PhCH<sub>2</sub>), 72.9 (C-4), 72.0 (PhCH<sub>2</sub>), 70.1 (C-2), 68.5 (C-6), 29.0, 28.8 (CH<sub>2</sub>), 23.5 (SCH<sub>2</sub>), 14.8 (CH<sub>3</sub>).

Anal. Calcd for C<sub>33</sub>H<sub>38</sub>O<sub>8</sub>S (594.7): C, 66.65; H, 6.44. Found: C, 66.59; H, 6.64.

**Ethyl 2-O-[1-O-Methyl-4,6-O-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)- $\alpha$ -D-mannopyranos-3-yloxycarbonylpropanoyl]-3,4,6-tri-O-benzyl-1-thio- $\beta$ -D-galactopyranoside (22).** Dicyclohexyl carbodiimide (0.17 g, 0.8 mmol) was added at 20 °C to a solution of methyl 4,6-O-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)- $\alpha$ -D-mannopyranoside<sup>14</sup> (21) (330 mg, 0.75 mmol), 20 (400 mg, 0.7 mmol) and a catalytic amount of DMAP (ca. 10 mg) in dichloromethane (20 mL) and the solution was stirred for 24 h. Work up as described for 6 and chromatography (toluene/ethyl acetate 15:1 to 5:1 v/v) afforded 22 (338 mg, 45%) as a colorless foam:  $[\alpha]_D +1.2^\circ$  ( $c$  1.1, chloroform); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  5.41 (t, 1H,  $J_{2,3} = 9.7$  Hz, H-2<sub>Man</sub>), 5.18 (dd, 1H,  $J_{2,3} = 3.2$  Hz, H-2<sub>Gal</sub>), 4.73 (d, 1H,  $J_{1,2} = 1.2$  Hz, H-1<sub>Man</sub>), 4.32 (d, 1H,  $J_{1,2} = 9.8$  Hz, H-1<sub>Gal</sub>), 4.19-4.13 (m, 2H, H-4<sub>Gal</sub>, 6a<sub>Gal</sub>), 4.02 (ddd, 1H,  $J_{3,4} = 9.4$  Hz,  $J_{3,OH} = 5.4$  Hz, H-3<sub>Man</sub>), 3.97 (d, 1H,  $J_{3,4} = 2.8$  Hz, H-4<sub>Man</sub>), 3.89 (dd, 1H,  $J_{6a,6b} = -12.5$  Hz,  $J_{5,6b} = 1.0$  Hz, H-6b<sub>Gal</sub>), 3.59 (s, 3H, H-5<sub>Man</sub>, 6a<sub>Man</sub>, 6b<sub>Man</sub>), 3.54 (dd, 1H,  $J_{3,4} = 2.7$  Hz, H-3<sub>Gal</sub>), 3.50 (d, 1H,  $J = 9.4$  Hz, H-5<sub>Gal</sub>), 3.33 (s, 3H, OCH<sub>3</sub>), 2.74-2.53 (m, 6H, CH<sub>2</sub>, SCH<sub>2</sub>), 1.26-1.02 (m, 31H, CH, CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  98.9 (C-1<sub>Man</sub>), 83.4 (C-1<sub>Gal</sub>), 81.4 (C-3<sub>Gal</sub>), 77.5 (C-5<sub>Gal</sub>), 73.0 (C-4<sub>Gal</sub>), 72.7 (C-5<sub>Man</sub>), 72.1 (C-2<sub>Man</sub>), 70.1 (C-3<sub>Man</sub>), 70.0 (C-2<sub>Gal</sub>), 68.5 (C-6<sub>Gal</sub>), 67.2 (C-4<sub>Man</sub>), 60.8 (C-6<sub>Man</sub>), 23.3 (SCH<sub>2</sub>), 17.4, 17.3, 17.2, 17.1, 17.0, 14.8, 13.7, 13.3, 12.5, 12.3 (CH, CH<sub>3</sub>).

Anal. Calcd for C<sub>52</sub>H<sub>76</sub>O<sub>14</sub>SSi<sub>2</sub> (1013.4): C, 61.63; H, 7.56. Found: C, 61.57; H, 7.43.

**Methyl O-(3',4',6'-Tri-O-benzyl- $\alpha$ -D-galactopyranosyl)-(1 $\rightarrow$ 6)-3,4-O-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)- $\alpha$ -D-mannopyranoside-2,2'-succinate (23).** DMTST (129 mg, 0.5 mmol) was added at 20 °C to a mixture of 22 (100 mg, 0.1 mmol) and molecular sieves (4Å, 0.5 g) in CH<sub>2</sub>Cl<sub>2</sub> (5 mL). The mixture was stirred for 4 h,

diluted with dichloromethane and filtered. The filtrate was washed with aq HCl and NaHCO<sub>3</sub> solution, dried and concentrated. Chromatography (toluene/ethyl acetate 15:1 v/v) of the residue afforded **23** (22 mg, 23%) as a colorless foam:  $[\alpha]_D^{+81.7^\circ}$  (*c* 0.3, chloroform); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  5.61 (d, 1H,  $J_{1,2} = 3.8$  Hz, H-1<sub>Gal</sub>), 5.19 (dd, 1H,  $J_{2,3} = 10.3$  Hz, H-2<sub>Gal</sub>), 5.05 (dd, 1H,  $J_{2,3} = 3.3$  Hz, H-2<sub>Man</sub>), 4.91 (d, 1H,  $J = -11.5$  Hz, CH<sub>2</sub>Ph), 4.66 (d, 1H,  $J = -12.6$  Hz, CH<sub>2</sub>Ph), 4.64 (d, 1H,  $J = -12.2$  Hz, CH<sub>2</sub>Ph), 4.55 (d, 1H,  $J = -11.9$  Hz, CH<sub>2</sub>Ph), 4.52 (d, 1H,  $J_{1,2} = 2.2$  Hz, H-1<sub>Man</sub>), 4.48 (d, 1H,  $J = -11.4$  Hz, CH<sub>2</sub>Ph), 4.41 (d, 1H,  $J = -11.6$  Hz, CH<sub>2</sub>Ph), 4.32 (t, 1H,  $J_{3,4} = J_{4,5} = 9.1$  Hz, H-4<sub>Man</sub>), 4.02 (dd, 1H, H-3<sub>Man</sub>) 3.99-3.95 (m, 3H, H-4<sub>Gal</sub>, 5<sub>Gal</sub>, 3<sub>Gal</sub>), 3.85 (br.s, 2H, H-6<sub>aMan</sub>, 6<sub>bMan</sub>), 3.62 (dd, 1H,  $J_{5,6a} = 7.3$  Hz,  $J_{6a,6b} = -9.1$  Hz, H-6<sub>aGal</sub>), 3.56 (dd, 1H,  $J_{5,6b} = 5.8$  Hz, H-6<sub>bGal</sub>), 3.29 (s, 3H, OMe), 3.00 (ddd, 1H,  $J = 17.8$  Hz, 13.2 Hz, 2.6 Hz, CH<sub>2</sub>), 2.72 (ddd, 1H,  $J = 16.8$  Hz, 13.4 Hz, 2.2 Hz, CH<sub>2</sub>), 2.48 (ddd, 1H,  $J = 17.7$  Hz, 4.4 Hz, 2.2 Hz, CH<sub>2</sub>), 2.33 (ddd, 1H,  $J = 17.0$  Hz, 9.3 Hz, 2.7 Hz, CH<sub>2</sub>), 1.15-0.92 (m, 28H, CH, CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  97.9 (C-1<sub>Man</sub>) 96.6 ( $J_{C-1,H-1} = 175.5$  Hz, C-1<sub>Gal</sub>) 76.7 (C-3<sub>Gal</sub>), 74.8 (C-4<sub>Gal</sub>), 74.8, 73.7 (PhCH<sub>2</sub>), 73.5 (C-5<sub>Man</sub>), 72.9 (PhCH<sub>2</sub>), 72.2 (C-2<sub>Gal</sub>), 72.2 (C-2<sub>Man</sub>), 71.9 (C-3<sub>Man</sub>), 69.5 (C-4<sub>Man</sub>), 69.1 (C-5<sub>Gal</sub>), 68.9 (C-6<sub>Gal</sub>), 62.4 (C-6<sub>Man</sub>), 55.1 (OMe), 29.5, 28.9 (CH<sub>2</sub>); 17.5, 17.4, 17.3, 17.2 (CH<sub>3</sub>), 13.0, 12.9, 12.3, 11.9 (CH). FABMS (pos.): *m/z* 973 (M+Na)<sup>+</sup>, 951 (M+H)<sup>+</sup>.

## ACKNOWLEDGMENT

This work was financially supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. The support by the Deutscher Akademischer Austauschdienst (DAAD) for a Ph.D. stipend (A.) is acknowledged as well. We thank Dr. H. Schmickler and C. Schmitz, University of Cologne for measuring the NMR spectra and performing the elemental analyses.

## REFERENCES AND NOTES

1. a) F. Barresi and O. Hindsgaul, *J. Am. Chem. Soc.*, **113**, 9376 (1991); b) F. Barresi and O. Hindsgaul, *Synlett*, 759 (1992); c) F. Barresi and O. Hindsgaul,



- Can. J. Chem.*, **72**, 1447 (1994); d) Y. Ito and T. Ogawa, *Angew. Chem.*, **106**, 1843 (1994); *Angew. Chem. Int. Ed. Engl.*, **33**, 1765 (1994); e) A. Dan, Y. Ito and T. Ogawa, *J. Org. Chem.*, **60**, 4680 (1995); f) A. Dan, Y. Ito and T. Ogawa, *Tetrahedron Lett.*, **36**, 7487 (1995); g) A. Dan, Y. Ito and T. Ogawa, *Carbohydr. Lett.*, **1**, 469 (1996); h) Z.-W. Guo, Y. Nakahara and T. Ogawa, *Tetrahedron Lett.*, **38**, 4799 (1997); i) Y. Ito and T. Ogawa, *J. Am. Chem. Soc.*, **119**, 5562 (1997); j) A. Dan, M. Lergenmüller, M. Amano, Y. Nakahara, T. Ogawa and Y. Ito, *Chem. Eur. J.*, **4**, 2182 (1998).
2. a) G. Stork and G. Kim, *J. Am. Chem. Soc.*, **114**, 1087 (1992); b) M. Bols, *J. Chem. Soc., Chem. Commun.*, 913 (1992); c) M. Bols and T. Skrydstrup, *Chem. Rev.*, **95**, 1253 (1995); M. Bols, *Acta Chem. Scand.*, **50**, 931 (1996); d) G. Stork and J. J. LaClair, *J. Am. Chem. Soc.*, **118**, 247 (1996).
  3. a) S. Inaba, M. Yamada, T. Yoshino and Y. Ishido, *J. Am. Chem. Soc.*, **95**, 2062 (1973); b) T. Iimori, T. Shibazaki and S. Ikegawa, *Tetrahedron Lett.*, **37**, 2267 (1996); c) G. Scheffler and R. R. Schmidt, *Tetrahedron Lett.*, **38**, 2943 (1997).
  4. M. E. Behrendt and R. R. Schmidt, *Tetrahedron Lett.*, **34**, 6733 (1993).
  5. C. Mukai, T. Itoh and M. Hanaoka, *Tetrahedron Lett.*, **38**, 4595 (1997).
  6. a) T. Ziegler and R. Lau, *Tetrahedron Lett.*, **36**, 1417 (1995); b) R. Lau, G. Schüle, U. Schwaneberg and T. Ziegler, *Liebigs Ann.*, 1745 (1995); c) T. Ziegler, G. Lemanski and A. Rakoczy, *Tetrahedron Lett.*, **36**, 8973 (1995); d) S. Valverde, A. M. Gómez, A. Hernández, B. Herrandón and J. C. López, *J. Chem. Soc., Chem. Commun.*, 2005 (1995); e) S. Valverde, A. M. Gómez, J. C. López and B. Herrandón, *Tetrahedron Lett.*, **37**, 1105 (1996); f) G. Schüle and T. Ziegler, *Liebigs Ann.*, 1599 (1996); g) T. Ziegler, A. Ritter and J. Hürtlen, *Tetrahedron Lett.*, **38**, 3715 (1997); h) H. Yamada, K. Imamura and T. Takahashi, *Tetrahedron Lett.*, **38**, 391 (1997); i) U. Huchel and R. R. Schmidt, *Tetrahedron Lett.*, **39**, 7693 (1998); j) T. Ziegler and G. Lemanski, *Eur. J. Org. Chem.*, 163 (1998); k) T. Ziegler and G. Lemanski, *Angew. Chem.*, **110**, 3367 (1998); *Angew. Chem. Int. Ed. Engl.*, **37**, 3129 (1998).
  7. H. F. Vernay, E. S. Rachaman, R. Eby and C. Schuerch, *Carbohydr. Res.*, **86**, 267 (1980).
  8. P. Garegg and H. Hultberg, *Carbohydr. Res.*, **93**, C10 (1981).
  9. N. Janaki, J. R. Patil and J. L. Bose, *Ind. J. Chem.*, **7**, 227 (1968).
  10. a) K. Bock and C. Pedersen, *J. Chem. Soc., Perkin Trans. 2*, 293 (1974); b) K. Bock and C. Pedersen, *Acta Chem. Scand.*, **B29**, 258 (1975).
  11. a) F. Mohamadi, N. G. J. Richards, W. C. Guida, R. Liskamp, M. Lipton, C. Caufield, G. Chang, T. Hendrickson and W. C. Still, *J. Comput. Chem.*, **11**, 440 (1990); b) H. Senderowitz and W. C. Still, *J. Org. Chem.*, **62**, 1427 (1997).
  12. All possible conformations of compounds **15** and **17** and their corresponding  $\beta$ -(1 $\rightarrow$ 4)-linked counterparts were generated by a Monte-Carlo conformation search (1000 steps) and energy-minimized with the AMBER force field. 9, 3, 9, and 9 conformers were found for compounds **15**, its  $\beta$ -anomer, **17** and its  $\beta$ -anomer, respectively, within 3 kcal/mol of the global minima. Compound **15** was calculated to be 12.8 kcal/mol more stable than its  $\beta$ -anomer and compound **17** was calculated to be 7.0 kcal/mol more stable than its  $\beta$ -anomer. Similarly, the  $\alpha$ -(1 $\rightarrow$ 4)-linked 2,3-di-*O*-acetylated disaccharide related to **15** was calculated to be 4.5 kcal/mol more stable than the corresponding  $\beta$ -(1 $\rightarrow$ 4)-linked saccharide,

whereas in the case of the 2,6-di-*O*-acetylated disaccharide related to 17, the  $\beta$ -(1 $\rightarrow$ 4)-linked isomer was found to be 7 kcal/mol more stable. Thus, in the case of conversion 14 $\rightarrow$ 17 a significant influence of the tether on the diastereoselectivity was found.

13. M.-J. L. Thijssen, K. M. Halkens, J. P. Kamerling and J. F. G. Vliegthart, *Bioorg. Med. Chem.*, **2**, 1309 (1994)
14. T. Ziegler, R. Dettmann and J. Grabowski, *Synthesis*, (1999) in press.
15. a) T. Ziegler, K. Neumann, E. Eckhardt, G. Herold and G. Pantkowski, *Synlett*, 699 (1991); b) T. Ziegler, E. Eckhardt and G. Pantkowski, *J. Carbohydr. Chem.*, **13**, 81 (1994); c) T. Ziegler and E. Eckhardt, *Tetrahedron Lett.*, **33**, 6615 (1992).
16. For a recent review on siloxane protected carbohydrates see: T. Ziegler, R. Dettmann, F. Bien and C. Jurisch, *Trends Org. Chem.*, **6**, 91 (1997).