Prearranged Glycosides, 6[◇]

Double Asymmetric Induction During Intramolecular Glycosylation

Thomas Ziegler* and Gregor Lemanski

Institute of Organic Chemistry, University of Cologne,
Greinstraße 4, D-50939 Cologne, Germany
Fax: (internat.) + 49(0)221/470-3078
E-mail: thomas.ziegler@uni-koeln.de

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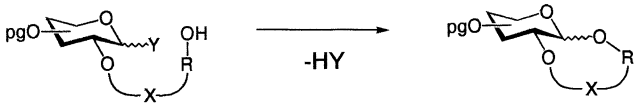
N-Iodosuccinimide activation of prearranged glycosides constructed out of phenyl 2,3,4-tri-*O*-benzyl-1-thio-α-L- and -D-mannopyranosides which are linked by a succinyl spacer via position 6 to position 3 of the benzyl 2-*O*-benzoyl-6-*O*-benzyl-α-L- and -D-glucopyranosides (6,3-prearranged L-Man/L-Glc, D-Man/D-Glc, L-Man/D-Glc, and D-Man/L-Glc) affords α/β-mixtures of the corresponding 3,6′-succinyl bridged disaccharides Man-(1→4)-Glc in 70−78% yield. The diastereoselectivity of the intramolecular glycosylation is independent of the topographic properties of the prearranged glycosides (the α-anomers predominate for L-Man/L-Glc and D-Man/D-Glc) but depends on the geometric properties (the β-anomers predominate for L-Man/D-Glc and D-Man/L-Glc). Thus, a double asymmetric induction is operative during intramolecular glycosylation of prearranged glycosides. Furthermore, the diastereoselectivity strongly depends on the topological properties and on the donor moiety of the prearranged glycosides, since 2,3-prearranged L-Man/D-Glc affords solely the disaccharide α-L-Man-(1→4)-D-Glc whereas the corresponding L-Rha/D-Glc was previously shown to give predominantly the disaccharide β-L-Rha-(1→4)-D-Glc.

In recent years, intramolecular glycosylations have gained significant importance for the stereoselective construction of *O*-glycosidic bonds. In general, two different approaches have been followed by several groups in order to achieve intramolecular glycosylation. In the first approach, a glycosyl donor and a glycosyl acceptor are connected by a temporary, labile tether, which is cleaved in the course of the formation of the *O*-glycosidic bond. In this approach, dialkylsilyl[1][2][3][4][5][6][7] and acetal tethers[8][9][10][11][12][13] have been succesfully used. Furthermore, the glycosyl acceptor can also be attached to the leaving group of the glycosyl donor, either by an orthoester moiety,[14] a carbonate tether,[15][16][17] or by the formation of a complex with the leaving group[18]. However, competition experiments have revealed recently[17] that this approach can also proceed intermolecularly rather than intramolecularly.

Figure 1. Schematic representation of intramolecular glycosylations via prearranged glycosides (pg = protecting group, X = stable tether, Y = leaving group, R−OH = glycosyl acceptor)



In the second approach,[19][20][21][22] which is also followed up by our group[23][24][25][26][27], glycosyl donor and glycosyl acceptor are connected by a stable, persisting bridge (prearranged glycosides) and the subsequent glycosylation step proceeds truly intramolecularly by ring formation (Figure 1). This not only allows control of the anomeric selectivity of the glycosylation but also allows control of the regioselectivity when partially protected acceptor moieties are used. However, the prediction of the stereoselectivity of these intramolecular glycosylations via prearranged glycosides still remains somewhat confusing since various factors (i.e. type and position of the bridging group, of the glycosyl donor, and of the acceptor) can influence the anomeric outcome of the cyclisation. For example, it was recently thought that for intramolecular mannosylations via prearranged glycosides, a double asymmetric induction may govern the diastereoselectivity of the *O*-glycoside formation[25]. Here, we now present evidence that a double diastereoselection is in fact operative during intramolecular mannosylations and that other factors may also influence the anomeric outcome of that approach.

Recently, it was shown for a prearranged glycoside constructed out of phenyl 2,3,4-tri-*O*-benzyl-1-thio-α-D-mannopyranoside which was linked by a succinyl spacer via its position 6 to position 3 of benzyl 2-*O*-benzoyl-6-*O*-benzyl-α-D-glucopyranoside (6,3-prearranged D-Man/D-Glc) that *N*-iodosuccinimide-activated ring closure led to a 2:1 α/β mixture of the corresponding disaccharides D-Man-(1→4)-D-Glc[25]. Although the anomeric selectivity of this intramolecular glycosylation of prearranged glycosides was not satisfactory for the construction of β-mannosidic linkages for preparative purposes, prearranged glycosides of this

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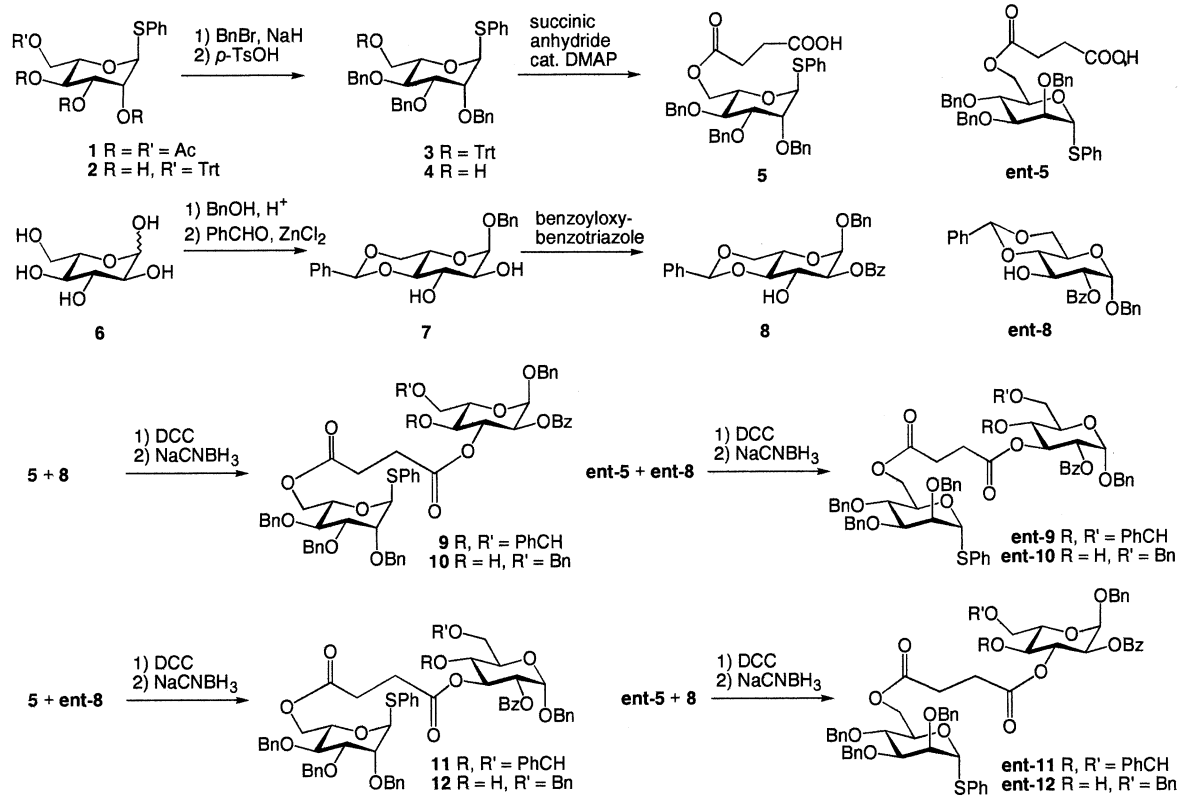
type appeared to be suitable for the evaluation if a double asymmetric induction might be responsible (at least in part) for the anomeric outcome of glycosylations following this approach. Therefore, all still remaining combinations of prearranged mannosyl donors and glucosyl acceptors in the D- and L-series, respectively (i.e. 6,3-prearranged L-Man/L-Glc, L-Man/D-Glc, and D-Man/L-Glc) were prepared as follows and tested for intramolecular 1,4-selective glycosylations.

First, phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-α-L-mannopyranoside (**1**), prepared from 1,2,3,4,6-penta-*O*-acetyl-α-L-mannopyranose[28] as described for the corresponding D-enantiomer[29] was deacetylated and tritylated at position 6, to give **2** (80%). Next, benzylation of the latter afforded **3** (85%), treatment of which with *p*-toluenesulfonic acid then removed the trityl group to give 1-thio-L-mannoside **4** (78%). Finally, **4** was succinylated at position 6 as previously described for the corresponding 1-thio-D-mannoside **ent-5**[25] to give compound **5** (92%). Similarly, L-glucose **6** was first converted into crude benzyl α-L-glucopyranoside treatment of which with benzaldehyde as described in the D series[30] then furnished crystalline **7** (20%). Regioselective benzoylation of the latter with in situ generated 1-benzoyloxybenzotriazole[31] as described in the D series for compound **ent-8**[24] then afforded **8** (78%). To this end, **5** and **ent-5** were condensed with both glucose derivatives **8** and **ent-8**, respectively, and the benzylidene rings of the glucose moieties of the resulting succinyl-linked glycosides **9** (L-Man/L-Glc), **11** (L-Man/D-Glc) and **ent-11** (D-Man/L-Glc) were regioselectively opened[32] as previously described for the conversion of **ent-9** into **ent-10**[25] (D-Man/D-Glc). Thus, all remaining combinations of prearranged glycosides **10** (L-Man/L-Glc), **12** (L-Man/D-Glc) and **ent-12** (D-Man/L-Glc) were obtained.

For the intramolecular glycosylation, the aforementioned prearranged glycosides **10** and **12** were treated under identical conditions with 5 equivalents of *N*-iodosuccinimide and a catalytic amount of trimethylsilyltriflate in MeCN as the solvent, to give mixtures of the corresponding α-linked disaccharides **13a** and **14a** and of the β-linked disaccharides **13b** and **14b**, respectively and of the enantiomers **ent-13**[25] and **ent-14** thereof in 70−78% yield (Scheme 2). The results of the glycosylations are summarized in Table 1. All α/β ratios were determined by HPLC analysis of the crude reaction mixture and by preparative separation and characterisation of the individual products. In general, anomers were assigned unambiguously by determining the respective $^1J_{1\text{-H,C-1}}$ values of their NMR spectra which were found in the range of 162−165 Hz, significant for α-linked disaccharides[33][34] and 153−155 Hz, significant for β-linked disaccharides.

Not unexpectedly, no change in the anomeric selectivity of the intramolecular glycosylation was encountered for the enantiomeric prearranged glycosides **10** and **ent-10** (entries 1 and 2). In both cases, the corresponding α anomers **13a** and **ent-13a** were the main products. Furthermore, the α/β ratios were almost identical. Similarly, for cyclisations of prearranged glycosides **12** and **ent-12**, the β anomers **14b**

Scheme 1. Trt = triphenylmethyl, DCC = dicyclohexyl carbodiimide



Scheme 2. NIS = *N*-iodosuccinimide

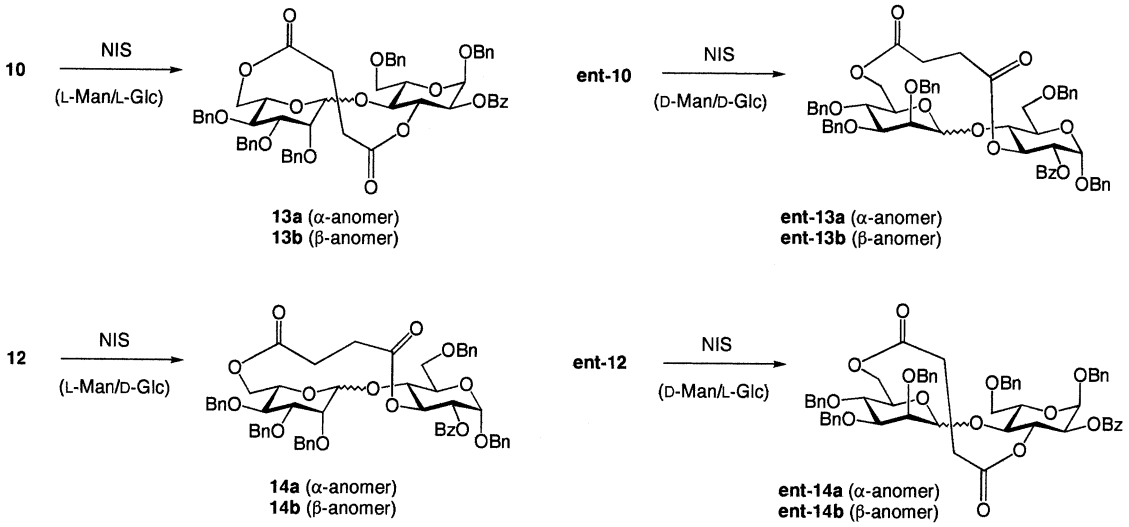


Table 1. Intramolecular glycosylation of prearranged glycosides **10**, **12**, **21**, **23**, and **25**

Entry	Glycoside	Configuration	Products	α/β ratio[a]	Yield[b]
1	**10**	L-Man/L-Glc	**13a**	65:35	51% **13a**
			13b		25% **13b**
2[c]	**ent-10**	D-Man/D-Glc	**ent-13a**	68:32	45% **ent-13a**
			ent-13b		25% **ent-13b**
3	**12**	L-Man/D-Glc	**14a**	44:56	30% **14a**
			14b		45% **14b**
4	**ent-12**	D-Man/L-Glc	**ent-14a**	30:70	22% **ent-14a**
			ent-14b		56% **ent-14b**
5	**21**	L-Man/D-Glc	**22**	100:0	70% **22**
6[c]	**23**	L-Rha/D-Glc	**24a**	18:82	14% **24a**
			24b		60% **24b**
7[c]	**25**	D-Man/D-Glc	**26**	100:0	54% **26**

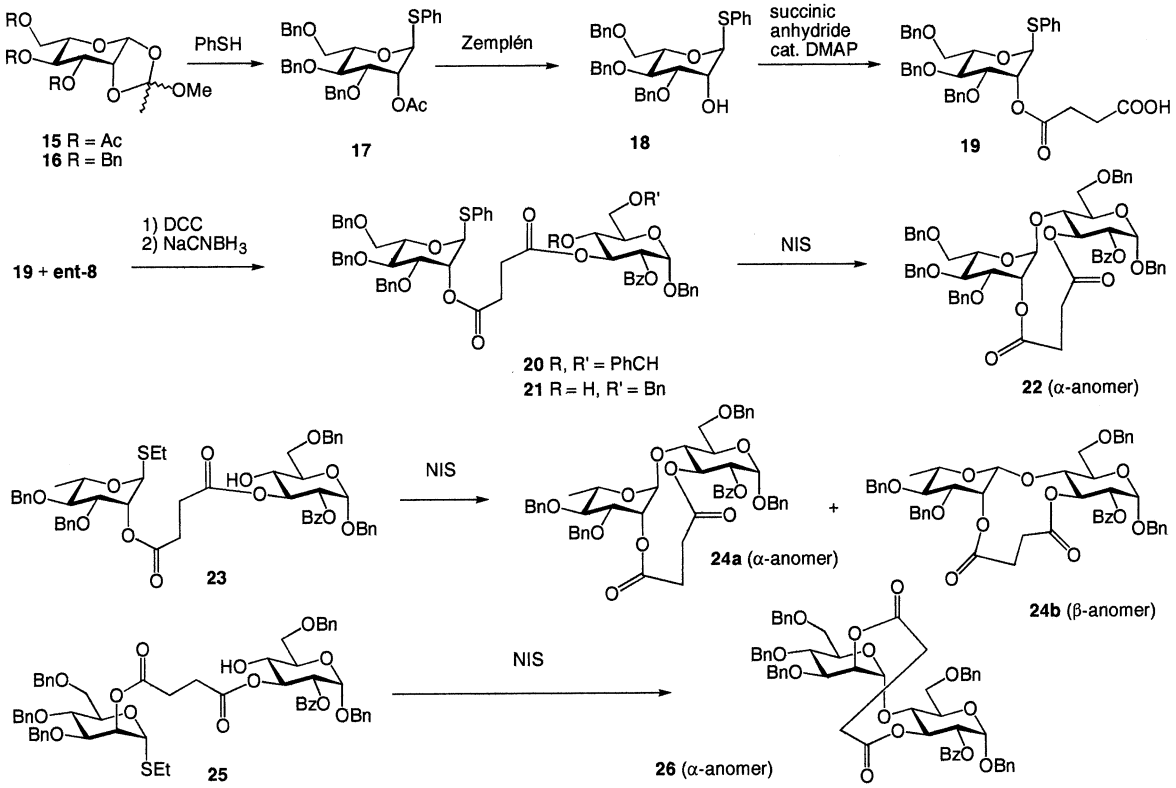
[a] HPLC of the crude reaction mixture. – [b] Isolated yield. – [c] Taken from ref.[25].

and **ent-14b** were the main products (entries 3 and 4) although the ratios differed significantly. The identical diastereoselectivity which was observed upon changing the topographic properties of the prearranged glycosides (entries 1 and 2) as well as the observed inverted selectivity with almost the same magnitude upon changing the geometric properties of the prearranged glycosides (entries 1, 3 and 2, 4, respectively) showed that a double asymmetric induction[35][36] was operative during intramolecular glycosylation. However, other factors like solvent, temperature, and activation procedure of the donor moiety[24] are responsible as well for the anomeric outcome of this glycosylation protocol.

Another important factor which controls the diastereoselectivity of glycosylations via prearranged glycosides beside the geometric properties is the change in the topological properties. This was demonstrated with prearranged glycoside **21** (Scheme 3). Here, the L-mannose moiety was linked by a succinyl bridge at position 2 to position 3 of a D-glucosyl acceptor moiety. Compound **21** was prepared as described in the D series[37] starting from 1,2,3,4,6-penta-*O*-acetyl-α-L-mannopyranose which was converted into the corresponding bromide and treated with 2,6-dimethylpyridine to give the orthoester **15**, obtained as a mixture of diastereomers in 66% yield. Next, the acetate groups were removed and benzylation afforded **16** (62%). Treatment of the latter with thiophenol and $HgBr_2$ gave **17** (68%) which was deacetylated via **18** (92%) and succinylated to give the acid derivative **19** (91%). Condensation of the latter with **ent-8** then afforded intermediate **20** (60%) ring-opening of the benzylidene group of which furnished the prearranged glycoside **21** in 82% yield. *N*-Iodosuccinimide-promoted intramolecular glycosylation of **21** (Table 1, entry 5) resulted in exclusive formation of the α-linked disaccharide **22** (70%). No trace of the corresponding β-linked counterpart could be detected on TLC of the crude reaction mixture. This selectivity clearly showed in comparison with the cyclisation of **12** (enty 3) that the position of the linking bridge and thus, the topological properies of the prearranged glycoside dramatically influence the anomeric selectivity.

It should be noted for the latter conversion of **21** into **22** that the presence of a benzyloxy group at position 6 of the donor moiety (i.e. distant to the reacting center of the donor moiety) has also a strong influence on the diastereoselectivity of the glycosylation. Previously, it was shown for the corresponding prearranged glycoside **23**[25] having a L-rhamnosyl donor moiety instead of an L-mannosyl moiety that intramolecular glycosylation afforded 14% of the α-linked disaccharide **24a** and 60% of the β-linked disaccharide **24b** (entry 6). Although, it is well known for "classical" glycosylations that a distant protecting group in the glycosyl donor may influence the diastereoselectivity of the formation of the glycosidic bond[38][39], no such effect can be considered for the dramatic change in conversions **21** → **22** and **23** → **24**, respectively. In addition, it was previously found[25] that prearranged glycoside **25** afforded solely the α-linked product **26** as well (entry 7). Therefore, it must be assumed that the succinyl bride at position 2 of the donor moiety in prearranged glycosides of type **23** (rhamnosyl do-

Scheme 3. DMAP = 4-dimethylaminopyridine



nor) causes a strong double asymmetric induction upon intramolecular glycosylation. In contrast, for succinyl bridged glycosides of type **21** and **25** (mannosyl donor) it appears to be likely that the induction is rather weak and the glycosylation proceeds by neighboring-group participation of the acyl residue at position 2 of the donor moiety affording α-linked saccharides. Thus, in order to achieve a highly β-selective mannosylation the linking bridge has to be modified in order to allow a double asymmetric induction. Experiments in this direction are now under investigation.

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Experimental Section

General: Thin-layer chromatography (TLC) was performed on precoated plastic sheets, Polygram SIL G/UV$_{254}$, 40 × 80 mm (Macherey−Nagel) using appropriately adjusted mixtures of tetrachloromethane/acetone for the developing. Spots were detected by UV light and by charring with 5% sulfuric acid in ethanol. − CC was performed by elution from columns of silica gel S (Riedel-de Haën, 0.032−0.063 mm) using the given eluents. − Solutions in organic solvents were dried with anhydrous sodium sulfate, and concentrated at < 40°C/< 200 Pa. − NMR spectra were recorded for solutions in $CDCl_3$ (with TMS as an internal standard) at 25°C with a Bruker AC 250 F spectrometer. Proton-signal assignments were made by first-order analysis of the spectra. Of two magnetically nonequivalent geminal protons, the one resonating at lower field was designated as H_a and the one resonating at higher field was designated as H_b. Carbon-signal assignments were made by C,H correlation and by comparison of the peaks with those of related compounds. − Optical rotations were measured at 20°C with a Perkin-Elmer automatic polarimeter, Model 241. − Melting points were determined with a Büchi apparatus, Model SMP-20. − HPLC was performed on Macherey-Nagel Nucleosil 100-5 columns with a Sykam gradient pump system and a Linear 206 PHD diode-array detector.

Phenyl 2,3,4,6-Tetra-O-acetyl-1-thio-α-L-mannopyranoside (**1**): A solution of 1,2,3,4,6-penta-*O*-acetyl-α-L-mannopyranose[28] (2.27 g, 5.8 mmol), thiophenol (1.1 ml, 10.0 mmol), and boron trifluoride−diethyl ether (1.2 ml, 10.1 mmol) in CH_2Cl_2 (20 ml) was stirred at room temp. for 18 h. The mixture was washed with aq. $NaHCO_3$ solution and H_2O and concentrated. Chromatography (CCl_4/acetone, 10:1) of the residue afforded **1** (1.75 g, 69%), $[\alpha]_D$ = −108.8 (c = 1.1, $CHCl_3$). − ^{1}H NMR ($CDCl_3$): δ = 5.51 (s, 1 H, 1-H), 5.49 (br. s, 1 H, 2-H), 5.35−5.29 (m, 2 H, 3-H, 4-H), 4.56 (ddd, $J_{4,5}$ = 9.6 Hz, $J_{5,6a}$ = 6.0 Hz, 1 H, 5-H), 4.33 (dd, $J_{6a,6b}$ = −12.2 Hz, 1 H, 6a-H), 4.11 (dd, $J_{5,6b}$ = 2.4 Hz, 1 H, 6b-H). − ^{13}C NMR ($CDCl_3$): δ = 87.5 (C-1), 70.9 (C-2), 69.5, 69.4 (C-3, 4), 66.5 (C-5), 62.4 (C-6). − $C_{20}H_{24}O_9S$ (440.5): calcd. C 54.54, H 5.49, S 7.28; found C 54.68, H 5.53, S 7.34.

Phenyl 6-O-Trityl-1-thio-α-L-mannopyranoside (**2**): A solution of **1** (1.5 g, 3.4 mmol) and a catalytic amount of NaOMe (1 M in MeOH) in MeOH was stirred for 3 h at room temp., neutralized by addition of ion exchange resign (H^+ form), filtered and concentrated. A solution of thus obtained crude phenyl 1-thio-α-L-mannopyranoside (0.92 g, 3.38 mmol) and chlorotriphenylmethane (1.04 g, 3.72 mmol) in pyridine (10 ml) was stirred at room temp. for 24 h. The mixture was concentrated and the residue was dissolved in CH_2Cl_2. The solution was subsequently washed with aq. HCl and aq. $NaHCO_3$ solution and water and then concentrated. Chromatography (CCl_4/acetone, 2:1 with 0.5% pyridine) of the residue af-

forded **2** (1.43 g, 80%), $[\alpha]_D = -116.7$ (c = 1.2, $CHCl_3$). – ^1H NMR ($CDCl_3$): δ = 5.48 (s, 1 H, 1-H), 4.30–4.22 (m, 1 H, 5-H), 4.15–4.11 (m, 1 H, 4-H), 3.78–3.66 (m, 2 H, 2-H, 3-H), 3.41–3.35 (m, 2 H, 6a-H, 6b-H), 3.15 (br. s, 3 H, OH). – ^{13}C NMR ($CDCl_3$): δ = 87.6 (C-1), 87.4 (Ph_3C), 72.2 (C-3), 71.9 (C-2), 71.4 (C-4), 70.4 (C-5), 64.5 (C-6). – $C_{31}H_{30}O_5S$ (514.6): calcd. C 72.35, H 5.88, S 6.23; found C 72.28, H 5.92, S 6.35.

Phenyl 2,3,4-Tri-O-benzyl-6-O-trityl-α-L-mannopyranoside (**3**): NaH (0.25 g, 10.44 mmol) and benzyl bromide (0.67 ml, 5.61 mmol) were added with stirring at 0°C to a solution of **2** (0.93 g, 1.81 mmol) in DMF (10 ml), and mixture was stirred for 3 h at room temp. MeOH was added in order to destroy excess of NaH and the mixture was poured into H_2O. After extraction with CH_2Cl_2, the extract was washed with H_2O and concentrated. Chromatography (light petroleum ether/ethyl acetate, 2:1) of the residue afforded **3** (1.2 g, 85%), $[\alpha]_D = -70.4$ (c = 1.0, $CHCl_3$). – ^1H NMR ($CDCl_3$): δ = 5.72 (d, $J_{1,2}$ = 1.4 Hz, 1 H, 1-H), 4.30–4.25 (m, $J_{5,6a}$ = 4.6 Hz, $J_{5,6b}$ = 9.7 Hz, 1 H, 5-H), 4.10 (t, $J_{4,5}$ = 9.5 Hz, 1 H, 4-H), 4.00 (dd, $J_{2,3}$ = 3.0 Hz, 1 H, 2-H), 3.85 (dd, $J_{3,4}$ = 9.2 Hz, 1 H, 3-H), 3.53 (dd, $J_{6a,6b}$ = –10.1 Hz, 1 H, 6a-H), 3.30 (dd, 1 H, 6b-H). – ^{13}C NMR ($CDCl_3$): δ = 85.5 (C-1), 86.5 (Ph_3C), 80.0 (C-3), 77.1 (C-2), 75.3 (C-4), 75.0, 72.2, 71.9 ($PhCH_2$), 72.9 (C-5), 62.5 (C-6). – $C_{52}H_{48}O_5S$ (785.0): calcd. C 79.56, H 6.16, S 4.08; found C 79.32, H 6.12, S 4.07.

Phenyl 2,3,4-Tri-O-benzyl-1-thio-α-L-mannopyranoside (**4**): A solution of **3** (1.17 g, 1.49 mmol) and *p*-toluenesulfonic acid (0.06 g, 0.30 mmol) in a mixture of $CHCl_3$ (10 ml) and MeOH (5 ml) was stirred at room temp. for 40 min. The mixture was washed with aq. $NaHCO_3$ solution and water and concentrated. Chromatography (toluene/ethyl acetate, 10:1) of the residue afforded **4** (0.64 g, 78%), $[\alpha]_D = -94.2$ (c = 1.0, $CHCl_3$). – ^1H NMR ($CDCl_3$): δ = 5.51 (d, $J_{1,2}$ = 1.6 Hz, 1 H, 1-H), 4.16-4.09 (m, 1 H, 5-H), 4.04 (t, $J_{4,5}$ = 8.8 Hz, 1 H, 4-H), 3.99 (dd, $J_{2,3}$ = 3.2 Hz, 1 H, 2-H), 3.88 (dd, $J_{3,4}$ = 8.8 Hz, 1 H, 3-H), 3.80-3.78 (m, 2 H, 6a-H, 6b-H), 2.01 (br. s, 1 H, OH). – ^{13}C NMR ($CDCl_3$): δ = 86.1 (C-1), 80.2 (C-3), 76.5 (C-2), 74.9 (C-4), 73.3 (C-5), 62.3 (C-6). – $C_{33}H_{34}O_5S$ (542.7): calcd. C 73.04, H 6.31, S 5.91; found C 72.83, H 6.28, S 6.00.

Phenyl 2,3,4-Tri-O-benzyl-6-O-(3-carboxypropanoyl)-1-thio-α-L-mannopyranoside (**5**): A solution of **4** (0.49 g, 0.90 mmol), succinic anhydride (0.72 g, 7.22 mmol) and a catalytic amount of DMAP in pyridine (20 ml) was stirred at room temp. for 24 h and concentrated. The residue was dissolved in CH_2Cl_2, washed with aq. HCl and aq. $NaHCO_3$ solution and water and concentrated. Chromatography (CCl_4/acetone, 4:1) of the residue afforded **5** (0.54 g, 92%), $[\alpha]_D = -61.9$ (c = 1.0, $CHCl_3$). – ^1H NMR ($CDCl_3$): δ = 5.54 (d, $J_{1,2}$ = 1.6 Hz, 1 H, 1-H), 4.42–4.36 (m, $J_{5,6b}$ = 2.4 Hz, 2 H, 6a-H, 6b-H), 4.31 (ddd, $J_{5,6a}$ = 5.0 Hz, 1 H, 5-H), 4.02 (dd, $J_{2,3}$ = 3.0 Hz, 1 H, 2-H), 4.00 (t, $J_{4,5}$ = 9.3 Hz, 1 H, 4-H), 3.88 (dd, $J_{3,4}$ = 9.4 Hz, 1 H, 3-H), 2.53 (s, 4 H, CH_2CH_2). – ^{13}C NMR ($CDCl_3$): δ = 176.7 (COOH), 172.0 (CO_2CH_2), 85.9 (C-1), 80.2 (C-3), 76.1 (C-2), 74.8 (C-4), 71.1 (C-5), 63.4 (C-6), 28.8, 28.7 (CH_2CH_2). – $C_{37}H_{38}O_8S$ (642.8): calcd. C 69.14, H 5.96, S 4.99; found C 68.93, H 6.02, S 4.96.

Benzyl 4,6-O-Benzylidene-α-L-glucopyranoside (**7**): BnOH (30 ml) and acetyl chloride (1.1 ml, 15.4 mmol) were heated to 110°C and L-glucose (4.0 g, 22.20 mmol) was added within 1 h. The mixture was heated for 4 h and cooled to room temp. $BaCO_3$ (1 g) was added with stirring, the mixture was filtered through a layer of Celite and concentrated. The residue was mixed with benzaldehyde (6 ml) and freshly molten $ZnCl_2$ (2.40 g) and was vigorously stirred at 70°C for 4 h. The resulting solution was poured with stirring into a mixture of H_2O (50 ml) and *n*-hexane (50 ml), the precipitate was collected by filtration and resuspended 2 times in *n*-hexane (50 ml). Recrystallization of the material from EtOH afforded **7** (1.57 g, 20%), m.p. 161°C, $[\alpha]_D = -65.0$ (c = 1.1, $CHCl_3$). – ^1H NMR ($CDCl_3$): δ = 5.23 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 1-H), 4.20 (dd, $J_{5,6a}$ = 4.5 Hz, 1 H, 6a-H), 3.93 (t, $J_{3,4}$ = 9.3 Hz, 1 H, 3-H), 3.83 (dt, $J_{5,6b}$ = 9.8 Hz, 1 H, 5-H), 3.67 (t, $J_{6a,6b}$ = –10.1 Hz, 1 H, 6b-H), 3.57–3.54 (m, $J_{2,3}$ = 9.3 Hz, 1 H, 2-H), 3.47 (t, $J_{4,5}$ = 9.3 Hz, 1 H, 4-H), 3.23 (br. s, 1 H, OH), 2.65 (br. s, 1 H, OH). – ^{13}C NMR ($CDCl_3$): δ = 101.9 (PhCH), 98.1 (C-1), 80.4 (C-4), 72.8 (C-2), 71.7 (C-3), 68.8 (C-6), 62.7 (C-5). – $C_{20}H_{22}O_6$ (358.4): calcd. C 67.03, H 6.19; found C 67.15, H 6.15.

Benzyl 2-O-Benzoyl-4,6-O-benzylidene-α-L-glucopyranoside (**8**): 1-Hydroxybenzotriazole (0.45 g, 3.34 mmol) and Et_3N (0.47 ml, 3.34 mmol) in CH_2Cl_2 (15 ml) were treated with benzoyl chloride (0.39 ml, 3.34 mmol) in CH_2Cl_2 (15 ml) for 30 min. Then, a solution of **7** (1.09 g, 3.04 mmol) and Et_3N (0.42 ml, 3.04 mmol) in CH_2Cl_2 (10 ml) was added. After stirring for 24 h at room temp., the mixture was diluted with CH_2Cl_2, washed with aq. $NaHCO_3$ solution and water and concentrated. Chromatography (CH_2Cl_2/ethyl acetate, 30:1) of the residue afforded **8** (1.10 g, 78%), $[\alpha]_D = -113.8$ (c = 1.0, $CHCl_3$). – ^1H NMR ($CDCl_3$): δ = 5.57 (s, 1 H, PhCH), 5.24 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 1-H), 5.06 (dd, $J_{2,3}$ = 9.7 Hz, 1 H, 2-H), 4.41 (t, $J_{3,4}$ = 9.3 Hz, 1 H, 3-H), 4.28 (dd, $J_{5,6a}$ = 4.8 Hz, 1 H, 6a-H), 4.00 (dt, $J_{5,6b}$ = 9.9 Hz, 1 H, 5-H), 3.78 (t, $J_{6a,6b}$ = –10.2 Hz, 1 H, 6b-H), 3.64 (t, $J_{4,5}$ = 9.4 Hz, 1 H, 4-H), 2.58 (s, 1 H, OH). – ^{13}C NMR ($CDCl_3$): δ = 166.1 (PhCO), 102.1 (PhCH), 96.0 (C-1), 81.5 (C-4), 73.9 (C-2), 68.9 (C-6), 68.8 (C-3), 62.4 (C-5). – $C_{27}H_{26}O_7$ (462.5): calcd. C 70.12, H 5.67; found C 69.93, H 5.72.

Phenyl 6-O-[(2-O-Benzoyl-1-O-benzyl-4,6-O-benzylidene-α-L-glucopyranos-3-yloxy)carbonylpropanoyl]-2,3,4-tri-O-benzyl-1-thio-α-L-mannopyranoside (**9**): DCC (0.20 g, 0.99 mmol) was added at room temp. to a solution of **5** (0.58 g, 0.90 mmol), **8** (0.46 g, 0.99 mmol) and a catalytic amount of DMAP in CH_2Cl_2 (20 ml). The mixture was stirred for 18 h, filtered through a layer of Celite, washed with aq. HCl and H_2O and concentrated. Chromatography (CCl_4/acetone, 15:1) of the residue afforded **9** (0.61 g, 62%), $[\alpha]_D = -100.3$ (c = 1.0, $CHCl_3$). – ^1H NMR ($CDCl_3$): δ = 5.51 (s, 1 H, PhCH), 5.87 (t, $J_{3,4}$ = 9.8 Hz, 1 H, 3-H), 5.53 (d, $J_{1',2'}$ = 1.5 Hz, 1 H, 1′-H), 5.27 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 1-H), 5.06 (dd, $J_{2,3}$ = 9.9 Hz, 1 H, 2-H), 4.31 (dd, $J_{6a,6b}$ = –10.1 Hz, 1 H, 6a-H), 4.29–4.20 (m, $J_{5',6a'}$ = 4.9 Hz, 1 H, 5′-H), 4.18–4.14 (m, 2 H, 6a′-H, 6b′-H), 4.07 (dt, $J_{5,6a}$ = 5.0 Hz, 1 H, 5-H), 3.98–3.93 (m, 1 H, 2′-H), 3.89–3.82 (m, 1 H, 3′-H), 3.81–3.68 (m, $J_{4,5}$ = 9.6 Hz, $J_{5,6b}$ = 9.5 Hz, 2 H, 4-H, 6b-H), 2.56–2.46 (m, 4 H, CH_2CH_2). – ^{13}C NMR ($CDCl_3$): δ = 171.6, 171.2 (CH_2CO_2), 101.6 (PhCH), 95.8 (C-1), 85.4 (C-1′), 80.1 (C-3′), 79.1 (C-4), 75.9 (C-2′), 74.5 (C-4′), 72.3 (C-2), 70.8 (C-5′), 69.2 (C-3), 68.8 (C-6), 63.5 (C-6′), 62.8 (C-5), 29.0, 28.9 (CH_2CH_2). – $C_{64}H_{62}O_{14}S$ (1087.3): calcd. C 70.70, H 5.75, S 2.95; found C 70.50, H 5.81, S 3.12.

Phenyl 6-O-[(2-O-Benzoyl-1,6-di-O-benzyl-α-L-glucopyranos-3-yloxy)carbonylpropanoyl]-2,3,4-tri-O-benzyl-1-thio-α-L-mannopyranoside (**10**): A solution of HCl (satd. in Et_2O) was added at room temp. to a suspension of **9** (0.55 g, 0.51 mmol), $NaCNBH_3$ (0.39 g, 6.28 mmol) and molecular sieves (3 Å) in THF (15 ml) until the evolution of H_2 has ceased. The mixture was diluted with CH_2Cl_2, filtered through a layer of Celite, washed with H_2O and aq. $NaHCO_3$ solution and concentrated. Chromatography (CCl_4/acetone, 10:1) of the residue afforded **10** (0.45 g, 80%), $[\alpha]_D = -103.0$ (c = 1.5, $CHCl_3$). – ^1H NMR ($CDCl_3$): δ = 5.65 (dd, $J_{3,4}$ = 9.4 Hz, 3-H), 5.56 (d, $J_{1',2'}$ = 1.5 Hz, 1 H, 1′-H), 5.24 (d, $J_{1,2}$ = 3.7

Hz, 1 H, 1-H), 5.00 (dd, $J_{2,3}$ = 10.0 Hz, 1 H, 2-H), 4.31−4.23 (m, 3 H, 5′-H, 6a′-H, 6b′-H), 3.98−3.89 (m, $J_{2',3'}$ = 2.9 Hz, 3 H, 5-H, 2′-H, 4′-H), 3.85 (dd, $J_{3',4'}$ = 9.1 Hz, 1 H, 3′-H), 3.80−3.73 (m, 2 H, 4-H, 6a-H), 3.71 (t, $J_{6a,6b}$ = −10.4 Hz, 1 H, 6b-H), 3.29 (d, $J_{4,OH}$ = 3.8 Hz, 1 H, OH), 2.65−2.40 (m, 4 H, CH_2CH_2). − ^{13}C NMR ($CDCl_3$): δ = 172.2 (2 C, CH_2CO_2), 95.1 (C-1), 85.4 (C-1′), 79.9 (C-3′), 76.0, 74.4 (C-2′, 4′), 73.4 (C-3), 71.4 (C-2), 70.8 (C-5′), 70.5 (C-5), 69.7 (C-4), 69.2 (C-6), 63.7 (C-6′), 29.2 (2 C, CH_2CH_2). − $C_{64}H_{64}O_{14}S$ (1089.3): calcd. C 70.57, H 5.92, S 2.94; found C 70.36, H 6.00, S 3.08.

Phenyl 6-O-[(2-O-Benzoyl-1-O-benzyl-4,6-O-benzylidene-α-D-glucopyranos-3-yloxy)carbonylpropanoyl]-2,3,4-tri-O-benzyl-1-thio-α-L-mannopyranoside (**11**): Treatment of compound **5** (0.38 g, 0.59 mmol), **ent-8** (0.30 g, 0.65 mmol), DCC (0.13 g, 0.65 mmol) and a catalytic amount of DMAP in CH_2Cl_2 (20 ml) as described for compound **9** afforded **11** (0.40 g, 63%), $[\alpha]_D$ = +3.9 (*c* = 1.1, $CHCl_3$). − ^{1}H NMR ($CDCl_3$): δ = 5.86 (t, $J_{3,4}$ = 9.8 Hz, 1 H, 3-H), 5.53 (d, $J_{1',2'}$ = 1.5 Hz, 1 H, 1′-H), 5.50 (s, 1 H, PhCH), 5.27 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 1-H), 5.06 (dd, $J_{2,3}$ = 9.9 Hz, 1 H, 2-H), 4.31−4.27 (m, 1 H, 5′-H), 4.26 (dd, $J_{5,6a}$ = 9.9 Hz, 1 H, 6a-H), 4.19−4.10 (m, 2 H, 6a′-H, 6b′-H), 4.07 (dt, $J_{5,6b}$ = 9.9 Hz, 1 H, 5-H), 4.01-3.85 (m, $J_{3',4'}$ = 9.5 Hz, 2 H, 2′-H, 3′-H), 3.73 (t, $J_{4',5'}$ = 9.5 Hz, 1 H, 4′-H), 3.69−3.66 (m, $J_{4,5}$ = 9.8 Hz, $J_{6a,6b}$ = −10.2 Hz, 2 H, 4-H, 6b-H), 2.60-2.44 (m, 4 H, CH_2CH_2). − ^{13}C NMR ($CDCl_3$): δ = 171.5, 171.2 (CH_2CO_2), 101.7 (PhCH), 96.0 (C-1), 85.5 (C-1′), 80.2 (C-3′), 79.2 (C-4), 75.9 (C-2′), 74.6 (C-4′), 72.4 (C-2), 70.9 (C-5′), 69.3 (C-3), 68.9 (C-6), 63.6 (C-6′), 62.9 (C-5), 29.1, 29.0 (CH_2CH_2). − $C_{64}H_{62}O_{14}S$ (1087.3): calcd. C 70.70, H 5.75, S 2.95; found C 70.47, H 5.79, S 2.80.

Phenyl 6-O-[(2-O-Benzoyl-1,6-di-O-benzyl-α-D-glucopyranos-3-yloxy)carbonylpropanoyl]-2,3,4-tri-O-benzyl-1-thio-α-L-mannopyranoside (**12**): Treatment of compound **11** (0.31 g, 0.29 mmol), $NaCNBH_3$ (0.23 g, 3.56 mmol) and molecular sieves (3 Å) in THF (15 ml) with HCl (satd. in Et_2O) as described for compound **10** afforded **12** (0.24 g, 76%), $[\alpha]_D$ = +8.0 (*c* = 1.3, $CHCl_3$). − ^{1}H NMR ($CDCl_3$): δ = 5.65 (dd, $J_{3,4}$ = 9.1 Hz, 1 H, 3-H), 5.57 (d, $J_{1',2'}$ = 1.5 Hz, 1 H, 1′-H), 5.24 (d, $J_{1,2}$ = 3.7 Hz, 1 H, 1-H), 4.96 (dd, $J_{2,3}$ = 10.2 Hz, 1 H, 2-H), 4.35−4.23 (m, 3 H, 5′-H, 6a′-H, 6b′-H), 3.96−3.90 (m, $J_{2',3'}$ = 3.0 Hz, 3 H, 2′-H, 4′-H, 5-H), 3.85 (dd, $J_{3',4'}$ = 9.2 Hz, 1 H, 3′-H), 3.81−3.66 (m, $J_{6a,6b}$ = −10.1 Hz, 3 H, 4-H, 6a-H, 6b-H), 3.25 (br. s, 1 H, OH), 2.60-2.41 (m, 4 H, CH_2CH_2). − ^{13}C NMR ($CDCl_3$): δ = 172.3 (2 C, CH_2CO_2), 95.1 (C-1), 85.4 (C-1′), 80.1 (C-3′), 75.9, 74.2 (C-2′, 4′), 73.5 (C-3), 71.4 (C-2), 70.8 (C-5′), 70.6 (C-5), 69.7 (C-4), 69.1 (C-6), 63.7 (C-6′), 29.2 (2 C, CH_2CH_2). − $C_{64}H_{64}O_{14}S$ (1089.3): calcd. C 70.57, H 5.92, S 2.94; found C 70.79, H 6.07, S 3.05.

Phenyl 6-O-[(2-O-Benzoyl-1-O-benzyl-4,6-O-benzylidene-α-L-glucopyranos-3-yloxy)carbonylpropanoyl]-2,3,4-tri-O-benzyl-1-thio-α-D-mannopyranoside (**ent-11**): Treatment of compound **ent-5** (0.40 g, 0.62 mmol), **8** (0.31 g, 0.68 mmol), DCC (0.14 g, 0.68 mmol) and a catalytic amount of DMAP in CH_2Cl_2 (15 ml) as described for compound **9** afforded **ent-11** (0.43 g, 64%), $[\alpha]_D$ = −4.2 (*c* = 1.1, $CHCl_3$). − NMR data ($CDCl_3$) were identical to those of compound **11**. − $C_{64}H_{62}O_{14}S$ (1087.3): calcd. C 70.70, H 5.75, S 2.95; found C 70.58, H 5.78, S 3.08.

Phenyl 6-O-[(2-O-Benzoyl-1,6-di-O-benzyl-α-L-glucopyranos-3-yloxy)carbonylpropanoyl]-2,3,4-tri-O-benzyl-1-thio-α-D-mannopyranoside (**ent-12**): Treatment of compound **ent-11** (0.38 g, 0.35 mmol), $NaCNBH_3$ (0.27 g, 4.38 mmol) and molecular sieves (3 Å) in THF (15 ml) with HCl (satd. in Et_2O) as described for compound **10** yielded **ent-12** (0.33 g, 85%), $[\alpha]_D$ = −7.8 (*c* = 1.0, $CHCl_3$). − NMR data ($CDCl_3$) were identical to those of compound **12**. − $C_{64}H_{64}O_{14}S$ (1089.3): calcd. C 70.57, H 7.92, S 2.94; found C 70.62, H 5.98, S 2.88.

General Procedure: A suspension of compounds **10**, **12**, **ent-12**, and **21** (1.0 mol equiv.), respectively and molecular sieves (3 Å) in MeCN was stirred at room temp. under Ar for 1 h and then cooled to ≮phen30°C. NIS (5.0 mol equiv.) was added followed by TMSOTf (0.25 mol equiv.). The mixture was stirred for 10 min, neutralized with pyridine, diluted with CH_2Cl_2, and filtered. The filtrate was washed with aq. $NaHCO_3$ and aq. $Na_2S_2O_3$ solution and concentrated. Chromatography (CCl_4/acetone mixtures) of the residue afforded compounds **13**, **14**, **ent-14**, and **22**.

Benzyl O-(2,3,4-Tri-O-benzyl-L-mannopyranosyl)-(1→4)-2-O-benzoyl-6-O-benzyl-α-L-glucopyranoside 3,6′-Succinate (**13**): Treatment of compound **10** (0.40 g, 0.41 mmol) according to the *General Procedure* afforded first **13a** (0.21 g, 21%), $[\alpha]_D$ = −119.5 (*c* = 1.0, $CHCl_3$). − ^{1}H NMR ($CDCl_3$): δ = 6.09 (t, $J_{3,4}$ = 10.0 Hz, 1 H, 3-H), 5.18 (d, $J_{1,2}$ = 3.4 Hz, 1 H, 1-H), 5.03 (d, $J_{1',2'}$ = 1.5 Hz, 1 H, 1′-H), 4.95 (dd, $J_{2,3}$ = 9.7 Hz, 1 H, 2-H), 4.27−4.11 (m, 3 H, 4-H, 6a′-H, 6b′-H), 4.05−4.00 (m, 1 H, 5′-H), 3.71 (dd, $J_{3',4'}$ = 9.0 Hz, 1 H, 3′-H), 3.70−3.59 (m, 1 H, 5-H), 3.64 (t, $J_{4',5'}$ = 9.3 Hz, 1 H, 4′-H), 3.44−3.41 (m, $J_{2',3'}$ = 3.0 Hz, 2 H, 2′-H, 6a-H), 3.39 (dd, $J_{5,6b}$ = 4.0 Hz, $J_{6a,6b}$ = −10.6 Hz, 1 H, 6b-H), 2.90−2.14 (m, 4 H, CH_2CH_2). − ^{13}C NMR ($CDCl_3$): δ = 171.0, 170.5 (CH_2CO_2), 95.1 (C-1), 93.0 (C-1′, $J_{C\text{-}1',1'\text{-}H}$ = 163.8 Hz), 79.0 (C-3′), 75.4 (C-4′), 75.3 (C-2′), 73.7 (C-4), 73.4 (C-2), 70.9 (C-5′), 68.8 (C-6), 68.7 (C-5), 67.5 (C-3), 64.2 (C-6′), 29.9, 29.8 (CH_2CH_2). − $C_{58}H_{58}O_{14}$ (979.10): calcd. C 71.15, H 5.97; found C 71.22, H 5.97.

Eluted next was **13b** (0.10 g, 25%), $[\alpha]_D$ = −39.0 (*c* = 1.0, $CHCl_3$). − ^{1}H NMR ($CDCl_3$): δ = 5.88 (t, $J_{3,4}$ = 8.8 Hz, 1 H, 3-H), 5.27 (d, $J_{1,2}$ = 3.6 Hz, 1 H, 1-H), 5.03 (dd, $J_{2,3}$ = 10.0 Hz, 1 H, 2-H), 4.40−4.37 (m, 1 H, 6a′-H), 4.30 (s, 1 H 1′-H), 4.26 (dd, $J_{5',6b'}$ = 8.9 Hz, 6a′-H, 6b′-H = −11.0 Hz, 1 H, 6b′-H), 4.05 (t, $J_{4,5}$ = 9.4 Hz, 1 H, 5-H), 3.87−3.83 (m, 1 H, 5-H), 3.76 (t, $J_{4',5'}$ = 9.6 Hz, 1 H, 4′-H), 3.58−3.56 (m, $J_{2',3'}$ = 2.6 Hz, 1 H, 2′-H), 3.54−3.47 (m, 1 H, 5′-H), 3.46−3.38 (m, $J_{3',4'}$ = 9.5 Hz, 2 H, 3′-H, 6a-H), 3.36 (dd, 1 H, 6b-H), 2.66−2.31 (m, 4 H, CH_2CH_2). − ^{13}C NMR ($CDCl_3$): δ = 170.6, 170.4 (CH_2CO_2), 103.1 (C-1′, $J_{C\text{-}1',1'\text{-}H}$ = 153.7 Hz), 95.2 (C-1), 82.4 (C-3′), 78.4 (C-4), 75.5 (C-4′), 74.6 (C-2′), 72.5 (C-5′), 72.3 (C-2), 72.1 (C-3), 69.8 (C-5), 68.2 (C-6), 63.3 (C-6′), 29.9, 29.7 (CH_2CH_2). − $C_{58}H_{58}O_{14}$ (979.1): calcd. C 71.15, H 5.97; found C 70.93, H 6.09.

Benzyl O-(2,3,4-Tri-O-benzyl-L-mannopyranosyl)-(1→4)-2-O-benzoyl-6-O-benzyl-α-D-glucopyranoside 3,6′-Succinate (**14**): Treatment of compound **12** (296 mg, 0.30 mmol) according to the *General Procedure* afforded first **14b** (130 mg, 45%), $[\alpha]_D$ = +89.3 (*c* = 0.8, $CHCl_3$). − ^{1}H NMR ($CDCl_3$): δ = 5.75 (t, $J_{3,4}$ = 9.5 Hz, 1 H, 3-H), 5.20 (d, $J_{1,2}$ = 3.7 Hz, 1 H, 1-H), 5.00 (dd, $J_{2,3}$ = 9.9 Hz, 1 H, 2-H), 4.61−4.59 (m, 3 H, 1′-H, $PhCH_2$), 4.01 (t, $J_{4,5}$ = 9.5 Hz, 1 H, 4-H), 3.95−3.72 (m, $J_{6a',6b'}$ = −10.3 Hz, 5 H, 2′-H, 4′-H, 5-H, 6a′-H, 6b′-H), 3.67−3.45 (m, 4 H, 3′-H, 5′-H, 6a-H, 6b-H), 2.83−2.17 (m, 4 H, CH_2CH_2). − ^{13}C NMR ($CDCl_3$): δ = 172.0, 170.0 (CH_2CO_2), 101.6 (C-1′, $J_{C\text{-}1',1'\text{-}H}$ = 153.9 Hz), 95.1 (C-1), 76.9, 75.4 (C-4, 2′), 75.8 (C-4′), 74.9 (C-3′), 72.9 (C-5′), 72.4 (C-2), 71.7 (C-3), 70.7 (C-5), 68.3 (C-6), 63.6 (C-6′), 29.9 (2 C, CH_2CH_2). − $C_{58}H_{58}O_{14}$ (979.1): calcd. C 71.15, H 5.97; found C 70.85, H 5.99.

Eluted next was **14b** (87.1 mg, 30%), $[\alpha]_D$ = +20.4 (*c* = 1.3, $CHCl_3$). − ^{1}H NMR ($CDCl_3$): δ = 6.06 (t, $J_{3,4}$ = 9.7 Hz, 1 H, 3-H), 5.21 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 5.04 (dd, $J_{2,3}$ = 9.5 Hz, 1 H, 2-H), 4.77−4.53 (m, 7 H, 1′-H, $PhCH_2$), 4.36 (t, $J_{4,5}$ = 10.1 Hz, 1 H, 4-H), 3.93−3.88 (m, 1 H, 5′-H), 3.85−3.78 (m, 2 H, 6a′-H, 6b′-H), 3.68 (t, $J_{3'4'}$ = $J_{4',5'}$ = 9.2 Hz, 1 H, 4′-H), 3.61−3.53 (m, 3 H,

2′-H, 3′-H, 5-H), 3.50−3.40 (m, 2 H, 6a-H, 6b-H), 2.86−2.38 (m, 4 H, CH_2CH_2). − ^{13}C NMR ($CDCl_3$): δ = 172.1, 170.4 (CH_2CO_2), 94.8 (C-1), 94.3 (C-1′, $J_{C\text{-}1',1'\text{-}H}$ = 163.7 Hz), 82.2 (C-3′), 76.9, 74.8 (C-4′, 2′), 73.9 (C-4), 73.0 (C-2), 72.7 (C-5′), 70.4 (C-5), 69.5 (C-6), 67.2(C-3), 63.1 (C-6′), 29.9 (2 C, CH_2CH_2). − $C_{58}H_{58}O_{14}$ (979.1): calcd. C 71.15, H 5.97; found C 70.87, H 5.97.

Benzyl O-(2,3,4-Tri-O-benzyl-D-mannopyranosyl)-(1→4)-2-O-benzoyl-6-O-benzyl-α-L-glucopyranoside 3,6′-Succinate (**ent-14**): Treatment of compound **ent-12** (208.6 mg, 0.21 mmol) according to the *General Procedure* afforded first **ent-14b** (117.5 mg, 56%), $[\alpha]_D$ = −90.0 (*c* = 0.8, $CHCl_3$). − NMR data ($CDCl_3$) were identical to those of compound **14a**. − $C_{58}H_{58}O_{14}$ (979.1): calcd. C 71.15, H 5.97; found C 70.94, H 6.04.

Eluted next was **ent-14a** (46.0 mg, 22%), $[\alpha]_D$ = −21.0 (*c* = 1.0, $CHCl_3$). − NMR data ($CDCl_3$) were identical to those of compound **14a**. − $C_{58}H_{58}O_{14}$ (979.1): calcd. C 71.15, H 5.97; found C 70.87, H 5.96.

3,4,6-Tri-O-acetyl-β-L-mannopyranose 1,2-(Methyl orthoacetate) (**15**): A solution of 1,2,3,4,6-tetra-*O*-acetyl-α-L-mannopyranose bromide (9.34 g, 22.27 mmol), prepared from 1,2,3,4,6-tetra-*O*-acetyl-α-L-mannopyranose[28], in CH_2Cl_2 (50 ml) was treated with a mixture of MeOH (50 ml) and lutidin (7 ml) for 14 h at room temp. The mixture was diluted with CH_2Cl_2 (100 ml), washed with aq. $NaHCO_3$ solution and water and concentrated. After coevaporation of toluene, the residue was crystallized from MeOH/H_2O to afforded **15** (4.52 g, 56%) as a 9:1 *exo*/*endo* diastereomeric mixture, m.p. 110−112°C, $[\alpha]_D$ = −18.5 (*c* = 1.1, $CHCl_3$). − ^1H NMR ($CDCl_3$), (*exo* isomer): δ = 5.50 (d, $J_{1,2}$ = 2.6 Hz, 1 H, 1-H), 5.30 (t, $J_{4,5}$ = 9.6 Hz, 1 H, 4-H), 5.15 (dd, $J_{3,4}$ = 9.8 Hz, 1 H, 3-H), 4.62 (dd, $J_{2,3}$ = 3.9 Hz, 1 H, 2-H), 4.25 (dd, $J_{6a,6b}$ = −12.1 Hz, 1 H, 6a-H), 4.14 (dd, 1 H, 6b-H), 3.69 (ddd, $J_{5,6a}$ = 2.8 Hz, $J_{5,6b}$ = 4.8 Hz, 1 H, 5-H), 3.28 (s, 3 H, OCH_3), 2.12, 2.08, 2.06 (s, 9 H, $COCH_3$), 1.74 (s, 3 H, $OCCH_3$). − ^{13}C NMR ($CDCl_3$), (*exo*-isomer): δ = 170.7, 170.4, 169.4 (CO), 124.5 ($C_{quat.}$), 97.4 (C-1), 76.6 (C-3), 71.3 (C-2), 70.6 (C-5), 65.5 (C-4), 62.3 (C-6), 49.4 (OCH_3), 24.4 (CCH_3), 20.7 ($COCH_3$). − $C_{15}H_{22}O_{10}$ (362.3): calcd. C 49.72, H 6.12; found C 49.44, H 6.10.

3,4,6-Tri-O-benzyl-β-L-mannopyranose 1,2-(Methyl orthoacetate) (**16**): A solution of **15** (4.32 g, 11.93 mmol) in MeOH (50 ml) was treated with NH_3 (satd. in MeOH) (10 ml) for 2 h at room temp. and then concentrated. The residue was dissolved in DMF (50 ml) and cooled to 0°C. NaH (1.68 g, 69.85 mmol) and benzyl bromide (4.66 ml, 39.37 mmol) were added and the mixture was stirred for 2 h at room temp. Workup as described for compound **3** and chromatography (light petroleum ether/ethyl acetate, 4:1 with 0.1% NEt_3) of the residue afforded **16** (3.97 g, 62%) as a 9:1 *exo*/*endo* diastereomeric mixture, $[\alpha]_D$ = −30.5 (*c* = 0.8, $CHCl_3$). − ^1H NMR ($CDCl_3$), (*exo* isomer): δ = 5.34 (d, $J_{1,2}$ = 2.5 Hz, 1 H, 1-H), 4.39 (dd, $J_{2,3}$ = 3.9 Hz, 1 H, 2-H), 3.92 (t, $J_{4,5}$ = 9.4 Hz, 1 H, 4-H), 3.78−3.67 (m, $J_{3,4}$ = 9.3 Hz, 3 H, 3-H, 6a-H, 6b-H), 3.44−3.38 (m, 1 H, 5-H), 4.90 (d, *J* = −10.8 Hz, 1 H, $PhCH_2$), 4.78 (s, 2 H, $PhCH_2$), 4.60 (d, *J* = −10.5 Hz, $PhCH_2$), 4.56 (s, 2 H, $PhCH_2$), 3.28 (s, 3 H, OCH_3), 1.74 (s, 3 H, $OCCH_3$). − ^{13}C NMR ($CDCl_3$): δ = 124.0 ($C_{quat.}$), 97.5 (C-1), 79.0 (C-3), 77.1 (C-2), 74.2, 74.1 (C-4, 5), 75.2, 73.3, 72.4 ($PhCH_2$), 69.0 (C-6), 49.8 (OCH_3), 24.4 (CCH_3). − $C_{30}H_{34}O_7$ (506.6): calcd. C 71.13, H 6.76; found C 71.01, H 6.76.

Phenyl 2-O-Acetyl-3,4,6-tri-O-benzyl-1-thio-α-L-mannopyranoside (**17**): $HgBr_2$ (0.11 g, 0.31 mmol) and thiophenol (5.92 ml, 58.02 mmol) were added at room temp. under Ar to a solution of **16** (3.0 g, 5.92 mmol) in MeCN (30 ml). The mixture was heated to 60°C for 5 h, cooled, diluted with CH_2Cl_2, washed with aq. $NaHCO_3$ solution and water and concentrated. Chromatography (light petroleum ether/ethyl acetate, 6:1) of the residue afforded **17** (2.35 g, 68%), $[\alpha]_D$ = −85.2 (*c* = 0.7, $CHCl_3$). − ^1H NMR ($CDCl_3$): δ = 5.61 (dd, $J_{2,3}$ = 2.7 Hz, 1 H, 2-H), 5.54 (d, $J_{1,2}$ = 1.5 Hz, 1 H, 1-H), 4.36−4.31 (m, $J_{5,6a}$ = 4.5 Hz, 1 H, 5-H), 4.02−3.91 (m, $J_{3,4}$ = 9.3 Hz, 2 H, 3-H, 4-H), 3.86 (dd, $J_{6a,6b}$ = −10.9 Hz, 1 H, 6a-H), 3.71 (dd, $J_{5,6b}$ = 1.9 Hz, 1 H, 6b-H), 2.14 (s, 3 H, CH_3CO). − ^{13}C NMR ($CDCl_3$): δ = 170.3 (CO), 86.2 (C-1), 78.5 (C-3), 74.5 (C-4), 72.4 (C-5), 70.3 (C-2), 68.8 (C-6), 21.1 (CH_3). − $C_{35}H_{36}O_6S$ (584.7): calcd. C 71.89, H 6.21, S 5.48; found C 72.00, H 6.25, S 5.55.

Phenyl 3,4,6-Tri-O-benzyl-1-thio-α-L-mannopyranoside (**18**): A solution of **17** (2.30 g, 3.93 mmol) and a catalytic amount of NaOMe (1 M in MeOH) in MeOH was stirred for 3 h at room temp., neutralized by addition of ion exchange resign (H^+ form), filtered and concentrated. Chromatography (*n*-hexane/ethyl acetate, 2:1) of the residue afforded **18** (1.96 g, 92%), $[\alpha]_D$ = −190.2 (*c* = 1.8, $CHCl_3$). − ^1H NMR ($CDCl_3$): δ = 5.62 (d, $J_{1,2}$ = 1.5 Hz, 1 H, 1-H), 4.32 (ddd, $J_{5,6a}$ = 4.5 Hz, $J_{5,6b}$ = 1.9 Hz, 1 H, 5-H), 4.26 (dd, $J_{2,3}$ = 3.0 Hz, 1 H, 2-H), 3.96 (t, $J_{4,5}$ = 9.3 Hz, 4-H), 3.89 (dd, $J_{3,4}$ = 9.0 Hz, 1 H, 3-H), 3.82 (dd, $J_{6a,6b}$ = −10.8 Hz, 1 H, 6a-H), 3.69 (dd, 1 H, 6b-H), 2.25 (br. s, 1 H, OH). − ^{13}C NMR ($CDCl_3$): δ = 87.3 (C-1), 80.2 (C-3), 74.4 (C-4), 72.2 (C-5), 69.8 (C-2), 68.8 (C-6). − $C_{33}H_{34}O_5S$ (542.7): calcd. C 73.04, H 6.32, S 5.91; found C 72.68, H 6.26, S 5.70.

Phenyl 3,4,6-Tri-O-benzyl-2-O-(3-carboxypropanoyl)-1-thio-α-L-mannopyranoside (**19**): Treatment of compound **18** (1.90 g, 3.50 mmol), succinic anhydride (2.80 g, 28.0 mmol) and a catalytic amount of DMAP in pyridine (40 ml) as described for compound **5** afforded crude **19** (2.04 g, 91%), which was used without further purification.

Phenyl 2-O-[(2-O-Benzoyl-1-O-benzyl-4,6-O-benzylidene-α-D-glucopyranos-3-yloxy)carbonylpropanoyl]-3,4,6-tri-O-benzyl-1-thio-α-L-mannopyranoside (**20**): Treatment of compound **19** (1.82 g, 2.83 mmol), **ent-8** (1.31 g, 2.83 mmol), DCC (0.59 g, 2.83 mmol) and a catalytic amount of DMAP in CH_2Cl_2 (50 ml) as described for compound **9** afforded **20** (1.85 g, 60%), $[\alpha]_D$ = −15.3 (*c* = 1.6, $CHCl_3$). − ^1H NMR ($CDCl_3$): δ = 5.89 (t, $J_{3,4}$ = 9.9 Hz, 1 H, 3-H), 5.51 (s, 1 H, PhCH), 5.48 (d, $J_{1',2'}$ = 1.6 Hz, 1 H, 1′-H), 5.46 (dd, $J_{2',3'}$ = 2.6 Hz, 1 H, 2′-H), 5.26 (d, $J_{1,2}$ = 3.8 Hz, 1-H), 5.08 (dd, $J_{2,3}$ = 9.9 Hz, 1 H, 2-H), 4.33−4.30 (m, $J_{5',6a'}$ = 4.6 Hz, 5′-H), 4.26 (dd, $J_{5,6a}$ = 4.9 Hz, $J_{6a,6b}$ = −10.1 Hz, 1 H, 6a-H), 4.07 (dt, $J_{5,6b}$ = 9.9 Hz, 1 H, 5-H), 3.88−3.84 (m, 2 H, 3′-H, 4′-H), 3.79 (dd, $J_{5',6b'}$ = 2.0 Hz, $J_{6a',6b'}$ = −10.9 Hz, 1 H, 6a′-H), 3.73 (t, $J_{4,5}$ = 9.8 Hz, 1 H, 4-H), 3.73−3.71 (m, 1 H, 6b-H), 3.67 (dd, 1 H, 6b′-H), 2.66−2.63 (m, 4 H, CH_2CH_2). − ^{13}C NMR ($CDCl_3$): δ = 171.2, 171.0 (CH_2CO_2), 101.5 (PhCH), 95.9 (C-1), 86.0 (C-1′), 79.2 (C-4), 78.4, 74.5 (C-3′, 4′), 72.3 (C-5′), 72.1 (C-2), 70.5 (C-2′), 69.3 (C-3), 68.8 (2 C, C-6, 6′), 62.8 (C-5), 29.0, 28.9 (CH_2CH_2). − $C_{64}H_{62}O_{14}S$ (1087.3): calcd. C 70.70, H 5.75, S 2.95; found C 70.54, H 5.79, S 3.16.

Phenyl 2-O-[(2-O-Benzoyl-1,6-di-O-benzyl-α-D-glucopyranos-3-yloxy)carbonylpropanoyl]-3,4,6-tri-O-benzyl-1-thio-α-L-mannopyranoside (**21**): Treatment of compound **20** (1.60 g, 1.47 mmol), $NaCNBH_3$ (1.16 g, 18.38 mmol) and molecular sieves (3 Å) in THF (15 ml) with HCl (satd. in Et_2O) as described for compound **10** afforded **21** (1.32 g, 82%), $[\alpha]_D$ = −20.1 (*c* = 1.2, $CHCl_3$). − ^1H NMR ($CDCl_3$): δ = 5.66 (dd, $J_{3,4}$ = 9.2 Hz, 1 H, 3-H), 5.54 (dd, $J_{2',3'}$ = 2.5 Hz, 1 H, 2′-H), 5.48 (d, $J_{1',2'}$ = 1.6 Hz, 1 H, 1′-H), 5.25 (d, $J_{1,2}$ = 3.7 Hz, 1 H, 1-H), 5.04 (dd, $J_{2,3}$ = 10.2 Hz, 1 H, 2-H), 4.34−4.27 (m, 1 H, 5-H), 3.97−3.92 (m, 1 H, 5-H), 3.91−3.88 (m, 2 H, 3′-H,4′-H), 3.85−3.78 (m, $J_{5'6a'}$ = 1.9 Hz, 2 H, 4-H, 6a′-

H), 3.73−3.69 (m, 2 H, 6a-H, 6b-H), 3.68 (dd, $J_{6a',6b'} = -10.9$ Hz, 1 H, 6b′-H), 3.13 (br. s, 1 H, OH), 2.73−2.51 (m, 4 H, CH_2CH_2). − ^{13}C NMR ($CDCl_3$): δ = 172.2, 171.8 (CH_2CO_2), 95.2 (C-1), 78.3, 74.4 (C-3′, 4′), 73.5 (C-3), 72.4 (C-5′), 71.3 (C-2), 70.8 (C-2′), 70.5 (C-5), 69.9 (C-4), 69.2 (C-6), 68.7 (C-6′), 29.4, 29.3 (CH_2CH_2). − $C_{64}H_{64}O_{14}S$ (1089.3): calcd. C 70.57, H 5.92, S 2.94; found C 70.61, H 6.03, S 3.15.

Benzyl O-(3,4,6-Tri-O-benzyl-L-mannopyranosyl)-(1→4)-2-O-benzoyl-6-O-benzyl-α-D-glucopyranoside 2′,3-Succinate (**22**): Treatment of compound **21** (0.69 g, 0.64 mmol) according to the *General Procedure* afforded **22** (0.44 g, 70%), $[\alpha]_D = -85.4$ (*c* = 1.2, $CHCl_3$). − ^1H NMR ($CDCl_3$): δ = 5.76 (dd, $J_{3,4} = 9.3$ Hz, 1 H, 3-H), 5.38−5.36 (m, 1 H, $J_{2',3'} = 3.0$ Hz, 2′-H), 5.26 (d, $J_{1,2} = 3.8$ Hz, 1 H, 1-H), 5.16 (s, 1 H, 1′-H), 4.95 (dd, $J_{2,3} = 10.2$ Hz, 1 H, 2-H), 4.19-4.11 (m, 1 H, 4-H), 3.97−3.77 (m, 3 H, 3′-H, 4′-H, 5′-H), 3.72−3.65 (m, 3 H, 5-H, 6a′-H, 6b′-H), 3.60−3.47 (m, 2 H, 6a-H, 6b-H), 2.60−2.50 (m, 4 H, CH_2CH_2). − ^{13}C NMR ($CDCl_3$): δ = 171.3, 171.2 (CH_2CO_2), 95.1 (C-1), 92.8 (C-1′, $J_{C\text{-}1',1'\text{-}H}$ = 162.5 Hz), 77.4 (C-3′), 76.0 (C-4′), 75.2 (C-4), 73.9 (C-2), 71.8 (C-5′), 71.2 (C-2′), 70.2 (C-5), 69.4 (C-6), 69.1 (C-6′), 67.0 (C-3), 31.2, 30.8 (CH_2CH_2). − $C_{58}H_{58}O_{14}$ (979.1): calcd. C 71.15, H 5.97; found C 70.89, H 6.01.

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