ELSEVIER

Carbohydrate Research 337 (2002) 195–206

CARBOHYDRATE RESEARCH

www.elsevier.com/locate/carres

Efficient intramolecular β-mannoside formation using *m*-xylylene and isophthaloyl derivatives as rigid spacers

Adel A.-H. Abdel-Rahman,[a] El Sayed H. El Ashry,[b] Richard R. Schmidt[a,*]

[a]*Department of Chemistry, University of Konstanz, Fach M 725, D-78457 Konstanz, Germany*
[b]*Department of Chemistry, Faculty of Science, University of Alexandria, Alexandria, Egypt*

Received 28 July 2001; accepted 15 November 2001

Abstract

A series of mannosyl donors linked via position 2 to an *m*-xylylene or an isophthaloyl spacer which was connected to the position 6 of a glucoside acceptor afforded, via intramolecular glycosylation, the corresponding disaccharides with high β anomeric ratio.

Keywords: Glycosides; β-Mannopyranosides; Synthesis; Intramolecular glycosidation; Hetaryl thioglycosides

1. Introduction

As the interest in carbohydrate derivatives with biologically important properties is increasing,[1–4] the development of selective and efficient methods for the construction of glycoside bonds is now becoming more and more important, not only in carbohydrate chemistry but also in organic synthesis in general.[5–13] The practical and stereocontrolled synthesis of oligosaccharides is therefore an area of current interest, and particular attention has recently been paid to the development of regioselective non-enzymatic glycosylation methods that would obviate the need for complex protecting group strategies. Recently, various studies for anomeric stereocontrol have been reported using the intramolecular reaction of a glycosyl donor and a glycosyl acceptor which are connected via a suitable linker.[14] The developed methods can be divided into three classes of spacer-mediated linkages of the acceptor to the donor:[15–17] (i) Leaving group based acceptor–donor linkage; (ii) linkage of the accepting atom via a bifunctional group to the donor; (iii) spacer mediated linkage of acceptor and donor via nonreacting centers. The intramolecular glycosylation approach by 'linkage of the accepting atom to the donor via a bifunctional group' ('intramolecular aglycon delivery', IAD) was originally developed for the synthesis of β-mannopyranosides and later extended to the synthesis of other glycosides. The synthesis of the β-mannosidic linkage is a difficult task[11] because the anomeric effect favors, thermodynamically, the formation of α-mannosides, and participating neighboring groups at 2-*O* also lead to α-mannosides (1,2-*trans* configuration).[18,19]

The 2-*O*-isopropenyl ether derivative of thiomannosides as a donor was used for the acid-catalyzed addition of the 6-*O* or 4-*O*-unprotected acceptors to yield the corresponding isopropylidene ketal derivatives. Then, glycosylation by activation of the thiogroup with *N*-iodosuccinimide (NIS) yielded exclusively β-mannosides in good yields.[20–23] To avoid ketal formation, the methoxybenzylidene acetal was designed as a bifunctional group for the attachment of the acceptor to the glycosyl fluoride donor.[24] Further improvement was achieved with the help of thioglycoside donors.[25,26] The high performance of the methoxybenzylidene acetal method enabled its use for the key step in the total synthesis of the core pentasaccharide unit of *N*-glycoproteins.[27,28] It was demonstrated that the methoxybenzylidene acetal method is also suitable in polymer-supported synthesis.[29] In another approach to the synthesis of β-mannosides applying the 'linkage of

* Corresponding author. Tel.: +49-7531-882538; fax: +49-7531-883135.
E-mail addresses: eelashry@link.net (E.S.H. El Ashry), richard.schmidt@uni-konstanz.de (R.R. Schmidt).

0008-6215/02/$ - see front matter
PII: S0008-6215(01)00306-8

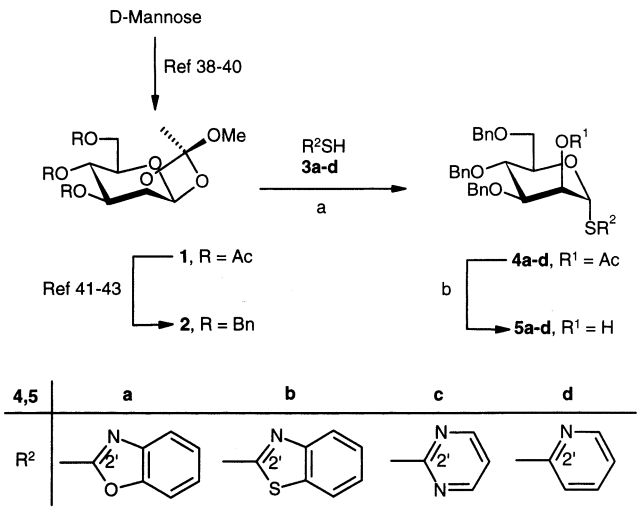
the accepting atom via a bifunctional group', a silicon-tethered 'disaccharide' was used for intramolecular glycosylations applying sulfoxide activation.[30] Further improvement of the method concerning the preparation of the silicon-tethered 'disaccharide' also enabled the use of secondary hydroxy groups in the acceptors.[31]

Variation of the tethering position at the donor and the acceptor moiety, of the length of the tethering group, and of the activation method gave a large number of interesting results [see (iii)].[14,32–34] For the synthesis of Manβ(1→4)Gal disaccharides, (6,6′)-tethered glycoside precursors were also used.[33] The 'spacer-mediated linkage via nonreacting centers' concept was also employed for the investigation of the regio- and stereoselectivity of intramolecular glycosylation reactions using phthaloyl or isophthaloyl spacers.[35–37] In order to obtain the desired close proximity between the glycosyl donor and acceptor moiety, the rigid spacer concept was designed.[14–17] As this leads to a structurally rigid array, a highly diastereoselective glycosylation under construction of a large ring should be enforced. As a powerful example for a rigid spacer, the *m*-xylylene moiety and derivatives were chosen. Excellent results in the formation of various glycosidic linkages were obtained.[14–17]

These results prompted us to apply this concept to β-mannoside formation using *m*-xylylene and also isophthaloyl derivatives as rigid spacers.

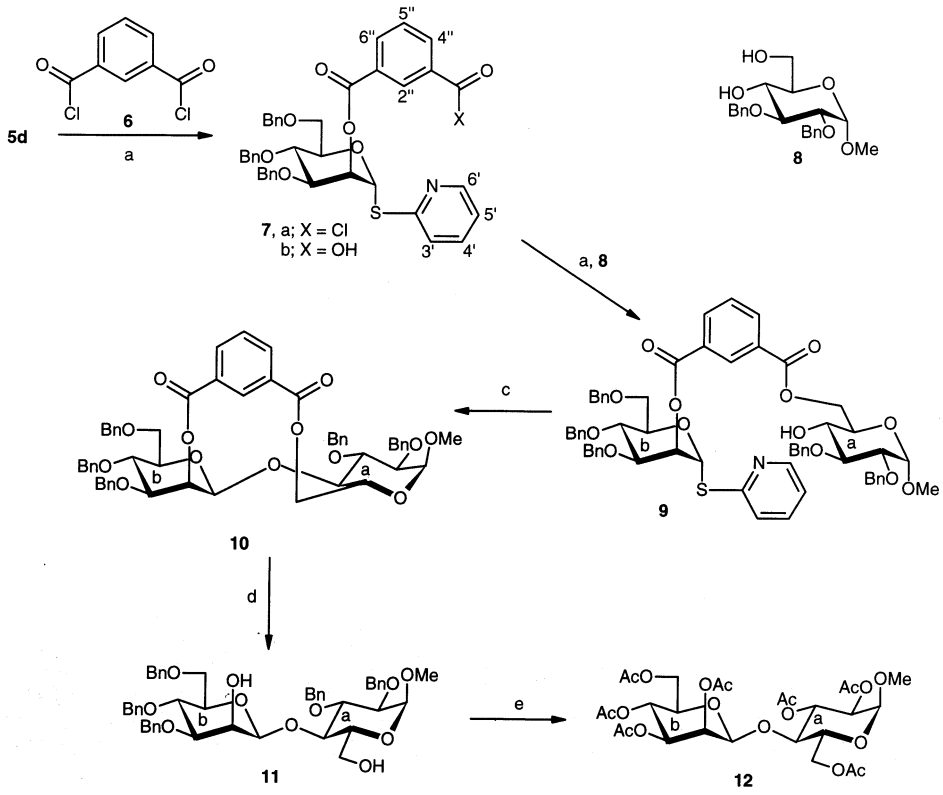
2. Results and discussion

Synthesis of glycosyl donors.—The known 3,4,6-tri-*O*-acetyl-β-D-mannopyranose orthoacetate (**1**)[38–40] was transformed into 3,4,6-tri-*O*-benzyl-β-D-mannopyranose orthoacetate (**2**)[41–43] (Scheme 1). Treatment of a solution of **2** in acetonitrile with 2-mercaptobenzoxazole (**3a**), 2-mercaptobenzothiazole (**3b**), 2-mercaptopyrimidine (**3c**) and 2-mercaptopyridine (**3d**) in the presence of catalytic amounts of mercury(II) bromide gave thioglycoside donors **4a**–**d** in 87–93% yields. The protons in the ^{1}H NMR spectra of **4a**–**d** were assigned by ^{1}H–^{1}H homonuclear shift correlated (COSY) 2D NMR spectroscopy. The α configurations of **4a**–**d** were indicated by the appearance of the anomeric protons as doublets at δ 6.35, 6.33, 6.59 and 6.40 with coupling constant values of $J_{1,2}$ 1.6, 1.7, 1.7 and 1.7 Hz, respectively. The α configuration at C-1 in the reaction products was finally established by ^{1}H NMR analysis and comparison with the spectroscopic data recorded in literature.[44] The ^{1}H NMR spectra showed singlets at δ 2.21, 2.19, 2.19 and 2.17 corresponding to the acetyl groups, and the ^{13}C NMR spectra showed signals at δ 170.01, 169.98, 170.24, 170.17 (C=O), 20.81, 20.99, 21.12 and 21.10 (Me) of the acetyl groups, respectively. Deacetylation gave the corresponding donors **5a**–**d** in quantitative yields. The ^{1}H NMR spectra of the deacetylated products **5a**–**d** showed the disappearance of the acetyl groups, and the appearance of the hydroxyl groups as broad singlets (D_2O exchangeable) at δ 2.46, 2.38, 2.52, and 2.76, respectively.



Scheme 1. Reagents and conditions: (a) $HgBr_2$, MeCN; (b) NaOMe, MeOH.

Isophthaloyl spacer system in the intramolecular glycosylation.—Treatment of **5d** with isophthaloyl chloride (**6**) in dry toluene and in the presence of a catalytic amount of dry pyridine under argon at room temperature afforded **7a** which is very sensitive to moisture, therefore, it was used for the next step without purification (Scheme 2). In the case of purification of the acid chloride derivative **7a** by flash-column chromatography, the hydrolyzed product **7b** was obtained in 78% yield. The structure of **7b** was confirmed by studying its ^{1}H NMR spectrum, which showed a broad singlet (D_2O exchangeable) at δ 3.04 corresponding to the OH group. For the synthesis of the isophthaloyl spacer connected donor–acceptor system **9**, methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside (**8**)[45,46] was treated with dibutyltin oxide in dry toluene at reflux temperature under azeotropic removal of water, cooled to room temperature, and then followed by addition of compound **7a** and tetrabutylammonium iodide. The reaction was monitored by TLC which gave 77% yield after purification with flash-column chromatography. Compound **9** could also be synthesized in 70% yield by dissolving the 4,6-*O*-unprotected glucoside **8** and **7a** in dry dichloromethane at 0 °C with catalytic amounts of pyridine. Alternatively, compound **9** could be synthesized in 68% yield by adding diethyl azodicarboxylate (DEAD) solution in tetrahydrofuran (THF) to the dissolved mixture of compound **7b**, diol **8** and triphenylphosphine in dry THF at room temperature. Activation of the pyridylthio group in **9** with *N*-iodosuccinimide (NIS, 1.3 equiv) and trimethylsilyl



Scheme 2. (a) Toluene/Py; (b) Method A, Bu_2SnO, Toluene; Method B, CH_2Cl_2/Py; Method C, Ph_3P, THF, DEAD; (c) NIS/TMSOTf, CH_2Cl_2; (d) MeONa, MeOH; (e) Pd/C, H_2; Ac_2O, Py.

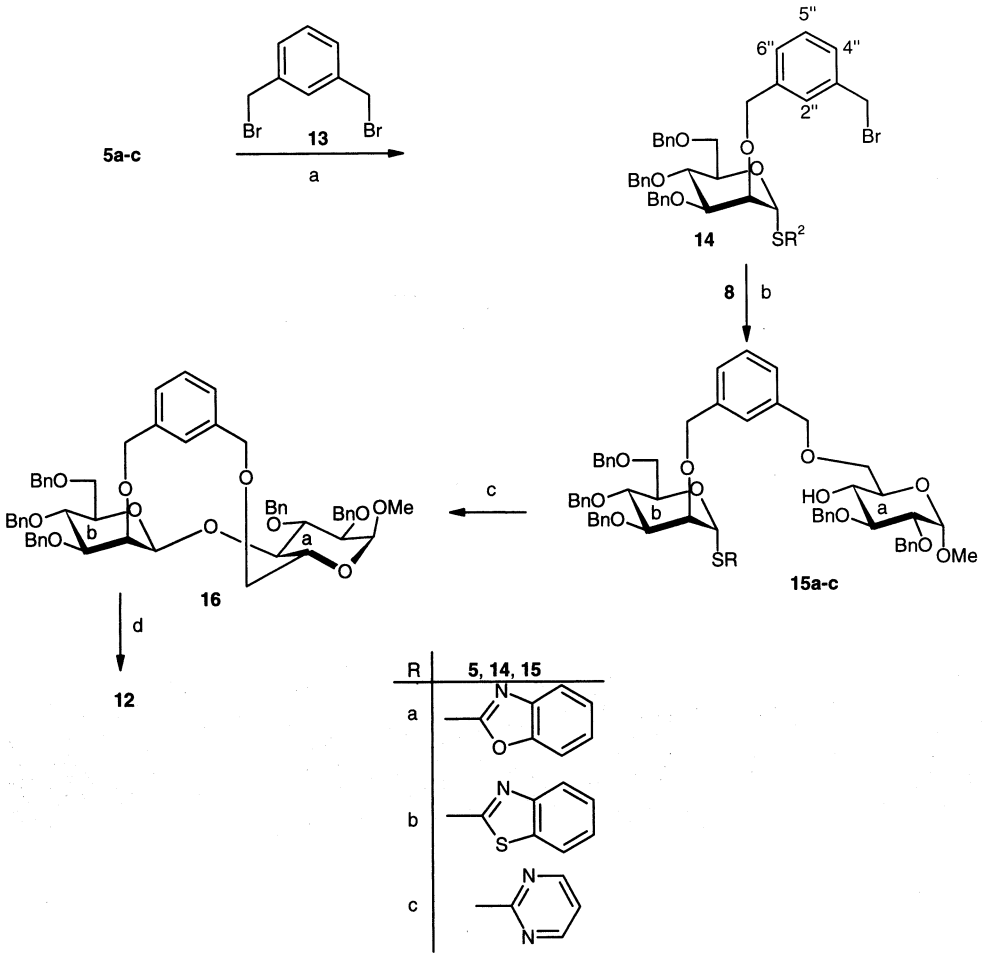
trifluoromethanesulfonate[†,‡] (TMSOTf, 0.1 equiv)[47–50] in dry CH_2Cl_2 at room temperature afforded the desired (1→4)-linked disaccharide **10**, after separation by flash-column chromatography in an α/β ratio of 1:6 (yield 70%). The α and β configuration could be assigned with the help of ^{13}C NMR data of the anomeric carbon. The β anomer showed a signal at δ 101.01 (J_{CH} 158.1 Hz), while the α anomer showed a signal at δ 99.71 (J_{CH} 173.1 Hz). The α and β configuration at C-1 in **10** was established by NMR analysis and comparison with the spectroscopic data recorded in literature.[36] Removal of the isophthaloyl spacer was carried out by treating **10**β with a solution of sodium methoxide in methanol at room temperature to give **11** with 90% yield. Hydrogenolytic *O*-debenzylation of **11** and then *O*-acetylation afforded **12**, which was structurally assigned by homo- and heteronuclear NMR spectra.

m-Xylylene spacer system in the intramolecular glycosylation.—For the investigation of this concept, compounds **5a**–**c** were transformed with α,α′-dibromoxylene (**13**) in the presence of NaH as base and 15-crown-5 as supporting reagent into 2-*O*-linked derivatives **14a**–**c** (Scheme 3). Treatment of the diol **8** with dibutyltin oxide in dry toluene, and then reaction with **14a**–**c** in the presence of tetrabutylammonium iodide (TBAI) afforded the desired 2a,6b-*O*-linked intermediates **15a**–**c** in 78–84% yield. Activation of **15a**–**c** with NIS–TMSOTf afforded **16** in 78% yield (from **15a**, α/β ratio 1:10), 75% yield (from **15b**, α/β ratio 1:9) and 76% yield (from **15c**, α/β ratio 1:10). The α and β configuration could be assigned with the help of ^{13}C NMR data of the anomeric carbon. The β anomer showed a signal at δ 101.09 (J_{CH} 158.3 Hz), while the α anomer showed a signal at δ 99.97 (J_{CH} 174.0 Hz). Hydrogenolytic O-debenzylation of **16** and then O-acetylation afforded again **12**.

Synthesis of the disaccharide glycosyl donor.—Treatment of a solution of **2**[41–43] in acetonitrile with 2,5-dimercapto-1,3,4-thiadiazole (**17**) by the same method as described for **4a**–**d** afforded, after chromatographic purification, **18** in 88% yield (Scheme 4). The protons in the ^1H NMR spectrum of **18** were assigned by ^1H–^1H homonuclear shift correlated (COSY) 2D NMR spectroscopy. The α configuration of **18** was confirmed by the appearance of the anomeric proton as a doublet at δ 6.39 with coupling constant value of $J_{1,2}$ 1.7 Hz. The integration corresponded to two protons due to reaction with the two available mercapto groups. The ^1H NMR spectrum showed a singlet at δ 2.18 (integration

[†] Mercuric, silver, and copper salts, respectively, were also used for the activation of thioglycosides.[49]

[‡] For the activation of a heterocyclic thioglycoside with TMSOTf, see Ref. 50.



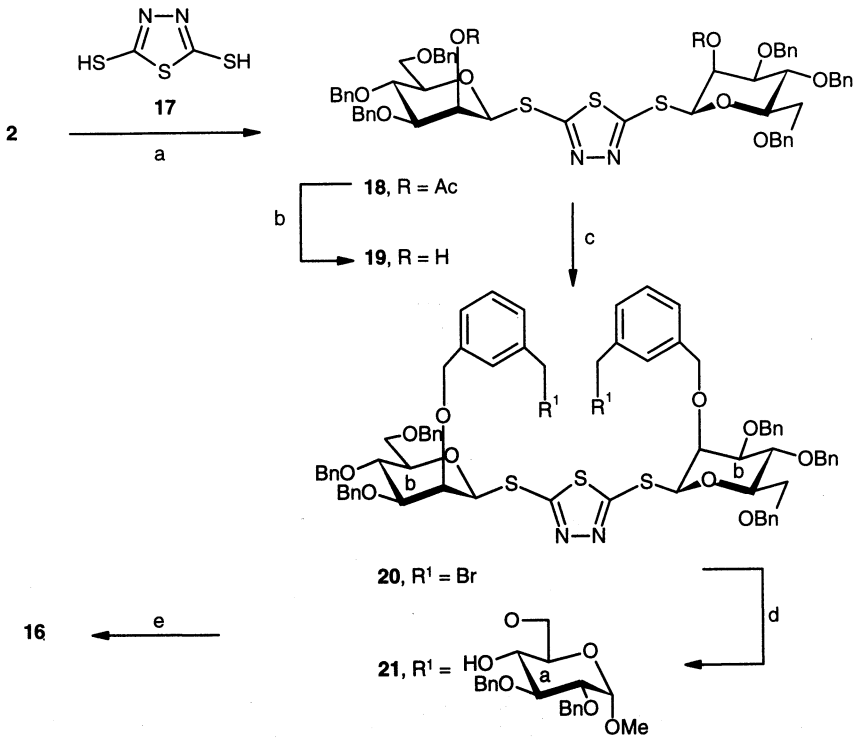
Scheme 3. (a) NaH, 15-Crown-5, CH_2Cl_2; (b) Bu_2SnO, Toluene, TBA; (c) NIS, TMSOTf, CH_2Cl_2; (d) Pd/C, H_2; Ac_2O, Py.

for 6 H) corresponding to the two acetyl groups. Deacetylation gave the corresponding donor derivative **19** in 97% yield. The ^1H NMR spectrum showed the disappearance of the signal of the acetyl group and the appearance of a broad singlet (D_2O exchangeable) at δ 2.79 (integration for 2 H). Compound **19** was transformed with α,α′-dibromoxylene (**13**) (2 equiv), as described for **15a**–**c**, into **20** in 77% yield. Treatment of **8**[44,45] with dibutyltin oxide in dry toluene and then reaction with **20** afforded the bis(2a,6b-O-linked) intermediate **21** in 70% yield. Activation of **21** with NIS–TMSOTf afforded **16** in 72% yield in an α/β ratio of 1:6.

In conclusion, we have developed an efficient and highly regio- and stereoselective protocol for intramolecular β-mannopyranoside synthesis by using 2-thio derivatives of nitrogen heterocycles as the leaving group at the anomeric position and *m*-xylylene and isophthaloyl derivatives, respectively, as rigid spacers linked to the 2-hydroxy group of the mannose residue. The *m*-xylylene spacer proved to be particularly suitable. The method should permit the synthesis of a variety of differently functionalized β-mannopyranoside derivatives which are useful intermediates for various applications.

3. Experimental

General methods.—Acetonitrile, CH_2Cl_2, and pyridine were distilled from CaH_2 and stored over molecular sieves. Tetrahydrofuran (THF) was distilled from sodium–benzophenone before use. Other solvents were purified according to the standard procedures. TLC was performed on plastic plates Silica Gel 60 F_{254} (E. Merck, layer thickness 0.2 mm). The detection was achieved by treatment with a solution of 20 g ammonium molybdate and 0.4 g cerium(IV) sulfate in 400 mL 10% H_2SO_4 or with 15% H_2SO_4 in MeOH and heating at 150 °C. Flash chromatography was carried out on Silica Gel (Baker, 30–60 μm). Optical rotations were determined at 23 °C with a Perkin–Elmer 241/MC polarimeter (1 dm cell). NMR spectra were recorded with Bruker AC 600 DRX instruments, using tetramethylsilane as internal standard. MALDI Mass spectra were recorded on a Kratos Kompact MALDI



Scheme 4. (a) $HgBr_2$, MeCN; (b) MeONa, MeOH; (c) **13**, NaH, 15-Crown-5, CH_2Cl_2; (d) **8**, Bu_2SnO, Toluene; (e) NIS, TMSOTf, CH_2Cl_2.

instrument, using a 2,5-dihydroxybenzoic acid matrix. FAB Mass spectra were recorded on a Finnigan MAT 312/AMD 5000 spectrometer, using a 1:1 (3-nitrobenzyl)alcohol–glycerol matrix.

General procedure for the synthesis of compounds **4a**–**d**.—The thioderivatives **3a**–**d** (4 mmol) and $HgBr_2$ (20 mg) were added to a solution of **2**[41–43] (0.50 g, 1.0 mmol) in dry MeCN (5 mL). The mixture was heated to 60 °C under argon for 3.5–4.0 h, and then concentrated. A solution of the residue in CH_2Cl_2 was washed with 5% aq NaOH (30 mL), water, dried ($MgSO_4$), and concentrated. The residue was purified with flash-column chromatography using 10:1 petroleum ether–EtOAc to give **4a**–**d** in 87–93% yield. Flash-column chromatography using 10:1 petroleum ether–EtOAc to give **4a**–**d** in 87–93% yield.

Benzoxazol-2-yl 2-O-acetyl-3,4,6-tri-O-benzyl-1-thio-α-D-mannopyranoside (**4a**). Yield 89% as an oil; TLC (5:1 petroleum ether–EtOAc): R_f 0.51; $[\alpha]_D$ + 180° (*c* 3.0, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 7.87 (d, 1 H, *J* 6.9 Hz, H-7′), 7.80 (t, 1 H, *J* 7.0 Hz, H-6′), 7.40 (t, 1 H, *J* 6.8 Hz, H-5′), 7.32–7.23 (m, 15 H, 3 Ph), 7.19 (d, 1 H, *J* 6.7 Hz, H-4′), 6.35 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1), 5.64–5.59 (m, 1 H, H-2), 4.72, 4.67 (2 d, 2 H, J_{gem} 11.5 Hz, CH_2Ph), 4.65, 4.58 (2 d, 2 H, J_{gem} 11.9 Hz, CH_2Ph), 4.53, 4.43 (2 d, 2 H, J_{gem} 11.5 Hz, CH_2Ph), 4.11–4.02 (m, 1 H, H-5), 4.08 (t, 1 H, $J_{3,4}$ 9.6 Hz, H-4), 3.89–3.80 (m, 1 H, H-3), 3.84 (dd, 1 H, J_{gem} 11.0, $J_{5,6}$ 3.0 Hz, H-6), 3.71 (dd, 1 H, J_{gem} 11.0, $J_{5,6}$ 3.1 Hz, H-6), 2.21 (s, 3 H, CH_3CO). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ 170.01 (CH_3CO), 161.90, 152.75, 138.00, 137.99, 137.27, 135.78, 128.45, 128.31, 128.20, 127.90, 127.83, 127.75, 127.66, 126.52, 126.37, 126.21, 125.20, 124.71, 124.39, 122.40, 120.99, 117.91 (Ar-carbons), 84.61 (C-1), 78.37 (C-3), 75.30 (CH_2Ph), 74.11 (C-5), 74.02 (C-4), 73.37 (2 CH_2Ph), 72.08, 69.74 (C-2), 68.33 (C-6), 20.81 (CH_3CO). FAB-MS (positive mode, NBOH–NaI-matrix): *m*/*z* 626 [MH^+], 648 [MNa^+]. Anal. Calcd for $C_{36}H_{35}NO_7S$ (625.73): C, 69.10; H, 5.63; N, 2.23. Found: C, 69.00; H, 5.57; N, 2.16.

Benzothiazol-2-yl 2-O-acetyl-3,4,6-tri-O-benzyl-1-thio-α-D-mannopyranoside (**4b**). Yield 89%, mp 90–92 °C from diethyl ether/petroleum ether; TLC (5:1 petroleum ether–EtOAc): R_f 0.55; $[\alpha]_D$ + 166° (*c* 1.4, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 7.91 (d, 1 H, *J* 6.8 Hz, H-7′), 7.73 (t, 1 H, *J* 7.0 Hz, H-6′), 7.42 (t, 1 H, *J* 6.9 Hz, H-5′), 7.33–7.24 (m, 15 H, 3 Ph), 7.17 (d, 1 H, *J* 6.8 Hz, H-4′), 6.33 (d, 1 H, $J_{1,2}$ 1.7 Hz, H-1), 5.66–5.59 (m, 1 H, H-2), 4.75, 4.73 (2 d, 2 H, J_{gem} 11.2 Hz, CH_2Ph), 4.66, 4.57 (2 d, 2 H, J_{gem} 10.7 Hz, CH_2Ph), 4.52, 4.45 (2 d, 2 H, J_{gem} 11.1 Hz, CH_2Ph), 4.13–4.09 (m, 1 H, H-5), 4.06 (t, 1 H, $J_{3,4}$ 9.5 Hz, H-4), 3.90–3.85 (m, 2 H, H-3, H-6), 3.70 (d, 1 H, J_{gem} 10.9 Hz, H-6), 2.19 (s, 3 H, CH_3CO). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ 169.98 (CH_3CO), 161.96, 152.74, 138.07, 137.97, 137.27, 135.78, 128.45, 128.30, 128.18, 127.95, 127.80, 127.73, 127.67, 126.51, 126.36, 126.21, 125.22, 124.78, 124.34, 122.30, 120.94, 117.98 (Ar-car-

bons), 84.80 (C-1), 78.21 (C-3), 75.26 (CH_2Ph), 74.09 (C-5), 73.97 (C-4), 73.32, 72.00 (2 CH_2Ph), 69.71 (C-2), 68.35 (C-6), 20.99 (CH_3CO). FAB-MS (positive mode, NBOH–NaI-matrix): m/z 642 [MH^+], 664 [MNa^+]. Anal. Calcd for $C_{36}H_{35}NO_6S_2$ (641.79): C, 67.37; H, 5.49; N, 2.18. Found: C, 67.17; H, 5.33; N, 2.09.

*Pyrimidin-2-yl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-1-thio-α-*D*-mannopyranoside* (**4c**). Yield 93% as an oil; TLC (5:1 petroleum ether–EtOAc): R_f 0.50; $[\alpha]_D$ +150° (*c* 2.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.53 (t, 1 H, *J* 7.0 Hz, H-5′), 7.34–7.24 (m, 15 H, 3 Ph), 7.16 (d, 1 H, *J* 6.8 Hz, H-6′), 7.00 (d, 1 H, $J_{3,4}$ 6.9 Hz, H-4′), 6.59 (d, 1 H, $J_{1,2}$ 1.7 Hz, H-1), 5.63–5.60 (m, 1 H, H-2), 4.87, 4.73 (2 d, 2 H, J_{gem} 11.2 Hz, CH_2Ph), 4.63, 4.56 (2 d, 2 H, J_{gem} 11.1 Hz, CH_2Ph), 4.51, 4.45 (2 d, 2 H, J_{gem} 12.2 Hz, CH_2Ph), 4.03–3.98 (m, 2 H, H-4, H-5), 3.91 (dd, 1 H, $J_{2,3}$ 9.1, $J_{3,4}$ 3.3 Hz, H-3), 3.83 (dd, 1 H, J_{gem} 11.0, $J_{5,6}$ 3.0 Hz, H-6), 3.67 (dd, 1 H, J_{gem} 11.0, $J_{5,6}$ 3.0 Hz, H-6), 2.19 (s, 3 H, CH_3CO). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ 170.24 (CH_3CO), 157.62, 138.17, 138.15, 137.46, 128.42, 128.29, 128.21, 128.18, 127.87, 127.72, 127.64, 127.47, 117.48 (Ar-carbons), 82.00 (C-1), 78.77 (C-3), 75.27 (CH_2Ph), 74.72 (C-5), 74.13 (C-4), 73.25, 71.85 (2 CH_2Ph), 70.57 (C-2), 68.63 (C-6), 21.12 (CH_3CO). FAB-MS (positive mode, NBOH–NaI-matrix): m/z 587 [MH^+], 609 [MNa^+]. Anal. Calcd for $C_{33}H_{34}N_2O_6S$ (586.70): C, 67.55; H, 5.84; N, 4.77. Found: C, 67.38; H, 5.57; N, 4.57.

*Pyridin-2-yl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-l-thio-α-*D*-mannopyranoside* (**4d**). Yield 93%, mp 67–68 °C from diethyl ether/petroleum ether; TLC (5:1 petroleum ether–EtOAc): R_f 0.54; $[\alpha]_D$ +118° (*c* 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.48 (d, 1 H, *J* 6.9 Hz, H-6′), 7.48 (t, 1 H, *J* 7.0 Hz, H-5′), 7.34–7.29 (m, 15 H, 3 Ph), 7.26 (d, 1 H, *J* 7.1 Hz, H-4′), 7.17 (d, 1 H, *J* 7.0 Hz, H-3′), 6.40 (d, 1 H, $J_{1,2}$ 1.7 Hz, H-1), 5.64–5.60 (m, 1 H, H-2), 4.87, 4.74 (2 d, 2 H, J_{gem} 11.2 Hz, CH_2Ph), 4.63, 4.54 (2 d, 2 H, J_{gem} 11.2 Hz, CH_2Ph), 4.52, 4.43 (2 d, 2 H, J_{gem} 11.9 Hz, CH_2Ph), 4.11–4.07 (m, 1 H, H-5), 4.00 (t, 1 H, $J_{3,4}$ 9.6 Hz, H-4), 3.92 (dd, 1 H, $J_{3,4}$ 9.3, $J_{2,3}$ 3.2 Hz, H-3), 3.83 (dd, 1 H, J_{gem} 11.1, $J_{5,6}$ 3.0 Hz, H-6), 3.68 (dd, 1 H, J_{gem} 11.0, $J_{5,6}$ 3.2 Hz, H-6), 2.17 (s, 3 H, CH_3CO). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ 170.17 (CH_3CO), 155.83, 149.70, 138.29, 138.21, 137.57, 136.64, 128.42, 128.29, 128.21, 128.19, 127.84, 127.71, 127.62, 127.47, 123.47, 123.33, 120.76, 119.43 (Ar-carbons), 82.18 (C-1), 78.80 (C-3), 75.22 (CH_2Ph), 74.30 (C-5), 73.91 (C-4), 73.26, 71.82 (2 CH_2Ph), 70.54 (C-2), 68.83 (C-6), 21.10 (CH_3CO). FAB-MS (positive mode, NBOH–NaI-matrix): m/z 586 [MH^+], 608 [MNa^+]. Anal. Calcd for $C_{34}H_{35}NO_6S$ (585.71): C, 69.72; H, 6.02; N, 2.39. Found: C, 69.60; H, 5.87; N, 2.22.

General procedure for the synthesis of compounds **5a**–**d**.—Compounds **4a**–**d** (1 mmol) were dissolved in dry MeOH (10 mL) and 1 M sodium methoxide in MeOH was added with stirring for 2 h at rt. The reaction mixture was neutralised with Amberlite IR-120. The ion-exchange resin was removed and after evaporation of the solvent under reduced pressure, compounds **5a**–**d** were obtained in quantitative yield. The products are pure enough for the next step.

*Benzoxazol-2-yl 3,4,6-tri-*O*-benzyl-1-thio-α-*D*-mannopyranoside* (**5a**). Yellow oil; TLC (5:1 petroleum ether–EtOAc): R_f 0.44; $[\alpha]_D$ +28° (*c* 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.86 (d, 1 H, *J* 7.0 Hz, H-7′), 7.79 (t, 1 H, *J* 7.0 Hz, H-6′), 7.41 (t, 1 H, *J* 7.2 Hz, H-5′), 7.33–7.24 (m, 15 H, 3 Ph), 7.21 (d, 1 H, *J* 6.7 Hz, H-4′), 6.71 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1), 4.81, 4.60 (2 d, 1 H, J_{gem} 11.5 Hz, CH_2Ph), 4.70–4.66 (m, 2 H, CH_2Ph), 4.50, 4.48 (2 d, 2 H, J_{gem} 10.8 Hz, CH_2Ph), 4.31 (d, 1 H, $J_{2,3}$ 1.7 Hz, H-2), 4.10–4.01 (m, 2 H, H-4, H-5), 3.88–3.83 (m, 1 H, H-3), 3.80 (d, 1 H, J_{gem} 10.9 Hz, H-6), 3.69 (d, 1 H, J_{gem} 10.7 Hz, H-6), 2.38 (br.s, 1 H, OH, D_2O exchangeable). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ 161.88, 152.71, 138.04, 137.90, 137.25, 135.77, 128.43, 128.32, 128.23, 127.90, 127.80, 127.73, 127.66, 126.52, 126.36, 126.20, 125.21, 124.70, 124.40, 122.40, 120.97, 117.90 (Ar-carbons), 83.52 (C-1), 80.40 (C-3), 75.22 (CH_2Ph), 74.71 (C-5), 74.10 (C-4), 73.36, 72.13 (2 CH_2Ph), 70.34 (C-2), 68.66 (C-6). FAB-MS (positive mode, NBOH–NaI-matrix): m/z 584 [MH^+], 606 [MNa^+]. Anal. Calcd for $C_{34}H_{33}NO_6S$ (583.69): C, 69.96; H, 5.69; N, 2.39. Found: C, 69.81; H, 5.48; N, 2.19.

*Benzothiazol-2-yl 3,4,6-tri-*O*-benzyl-1-thio-α-*D*-mannopyranoside* (**5b**). Mp 105–107 °C from diethyl ether/petroleum ether; TLC (5:1 petroleum ether–EtOAc): R_f 0.43; $[\alpha]_D$ +12° (*c* 1.7, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.93 (d, 1 H, *J* 7.0 Hz, H-7′), 7.71 (d, 1 H, *J* 7.2 Hz, H-6′), 7.41 (t, 1 H, *J* 7.1 Hz, H-5′), 7.31–7.22 (m, 15 H, 3 Ph), 7.20 (d, 1 H, *J* 6.9 Hz, H-4′), 6.77 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 4.83, 4.63 (2 d, 2 H, J_{gem} 12.1 Hz, CH_2Ph), 4.71–4.66 (m, 2 H, CH_2Ph), 4.49, 4.41 (2 d, 2 H, J_{gem} 11.0 Hz, CH_2Ph), 4.38 (d, 1 H, $J_{2,3}$ 1.8 Hz, H-2), 4.08–3.99 (m, 2 H, H-4, H-5), 3.85–3.80 (m, 1 H, H-3), 3.78 (d, 1 H, J_{gem} 10.9 Hz, H-6), 3.72 (d, 1 H, J_{gem} 10.9 Hz, H-6), 2.46 (br.s, 1 H, OH, D_2O exchangeable). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ 161.90, 152.70, 138.09, 137.99, 137.28, 135.77, 128.31, 128.24, 128.13, 127.97, 127.82, 127.77, 127.66, 126.52, 126.33, 126.23, 125.20, 124.76, 124.34, 122.30, 120.95, 118.01 (Ar-carbons), 83.55 (C-1), 80.43 (C-3), 75.26 (CH_2Ph), 74.70 (C-5), 74.14 (C-4), 73.38, 72.15 (2 CH_2Ph), 70.37 (C-2), 68.65 (C-6). FAB-MS (positive mode, NBOH–NaI-matrix): m/z 600 [MH^+], 622 [MNa^+]. Anal. Calcd for $C_{34}H_{33}NO_5S_2$ (599.75): C, 68.08; H, 5.54; N, 2.33. Found: C, 67.89; H, 5.55; N, 2.20.

*Pyrimidin-2-yl 3,4,6-tri-*O*-benzyl-l-thio-α-*D*-mannopyranoside* (**5c**). Yellow oil; TLC (5:1 petroleum ether–EtOAc): R_f 0.39; $[\alpha]_D$ +43° (*c* 1.0, $CHCl_3$); ^{1}H

NMR (600 MHz, $CDCl_3$): δ 8.54 (d, 1 H, J 7.1 Hz, H-5′), 7.36–7.25 (m, 15 H, 3 Ph), 7.18 (d, 1 H, J 6.8 Hz, H-6′), 7.03 (d, 1 H, J 6.9 Hz, H-4′), 6.60 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 4.83, 4.61 (2 d, 2 H, J_{gem} 11.2 Hz, CH_2Ph), 4.71–4.67 (m, 2 H, CH_2Ph), 4.53, 4.45 (2 d, 2 H, J_{gem} 10.7 Hz, CH_2Ph), 4.28 (d, 1 H, $J_{2,3}$ 1.9 Hz, H-2), 4.02–3.98 (m, 2 H, H-4, H-5), 3.87 (m, 1 H, H-3), 3.79 (d, 1 H, J_{gem} 10.4 Hz, H-6), 3.67 (d, 1 H, J_{gem} 10.5 Hz, H-6), 2.52 (br.s, 1 H, OH, D_2O exchangeable). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ 157.61, 138.16, 137.56, 128.57, 128.36, 128.26, 128.04, 127.99, 127.95, 127.89, 127.71, 127.52, 117.35 (Ar-carbons), 83.50 (C-1), 80.41 (C-3), 75.21 (CH_2Ph), 74.77 (C-5), 74.07 (C-4), 73.33, 72.10 (2 CH_2Ph), 70.41 (C-2), 68.61 (C-6). FAB-MS (positive mode, NBOH–NaI-matrix): m/z 545 [MH^+], 567 [MNa^+]. Anal. Calcd for $C_{31}H_{32}N_2O_5S$ (544.66): C, 68.36; H, 5.92; N, 5.14. Found: C, 68.11; H, 5.77; N, 4.98.

Pyridin-2-yl 3,4,6-tri-O-*benzyl-1-thio-α*-D-*mannopyranoside* (**5d**). Mp 80–83 °C from diethyl ether/petroleum ether; TLC (5:1 petroleum ether–EtOAc): R_f 0.45; $[\alpha]_D$ +56° (c 2.3, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 8.46 (d, 1 H, J 7.3 Hz, H-6′), 7.35 (t, 1 H, J 7.1 Hz, H-5′), 7.33–7.24 (m, 15 H, 3 Ph), 7.20 (d, 1 H, J 7.0 Hz, H-4′), 7.03 (d, 1 H, J 6.9 Hz, H-3′), 6.32 (d, 1 H, $J_{1,2}$ 1.7 Hz, H-1), 4.84, 4.59 (2 d, 2 H, J_{gem} 10.9 Hz, CH_2Ph), 4.71–4.66 (m, 2 H, CH_2Ph), 4.53, 4.44 (2 d, 2 H, J_{gem} 11.1 Hz, CH_2Ph), 4.28 (t, 1 H, $J_{2,3}$ 1.9 Hz, H-2), 3.97–3.91 (m, 1 H, H-4), 3.87 (t, 1 H, $J_{4,5}$ 5.1 Hz, H-5), 3.77 (dd, 1 H, $J_{3,4}$ 3.5, $J_{2,3}$ 1.9 Hz, H-3), 3.67 (dd, 1 H, J_{gem} 10.7, $J_{5,6}$ 3.2 Hz, H-6), 3.65 (dd, 1 H, J_{gem} 10.5, $J_{5,6}$ 3.1 Hz, H-6), 2.76 (br.s, 1 H, OH, D_2O exchangeable). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ 156.59, 149.65, 138.24, 138.19, 137.60, 136.68, 128.56, 128.34, 128.24, 128.03, 127.98, 127.90, 127.83, 127.68, 127.49, 123.63, 122.11, 120.70 (Ar-carbons), 83.93 (C-1), 80.37 (C-3), 75.13 (CH_2Ph), 74.32 (C-5), 73.69 (C-4), 73.30, 72.08 (2 CH_2Ph), 70.26 (C-2), 68.77 (C-6). FAB-MS (positive mode, NBOH–NaI-matrix): m/z 544 [MH^+], 566 [MNa^+]. Anal. Calcd for $C_{32}H_{33}NO_5S$ (543.67): C, 70.69; H, 6.11; N, 2.57. Found: C, 70.51; H, 5.97; N, 2.46.

Pyridin-2-yl 2-O-*(benzo-1-yl-3-chlorocarbonyl)-3,4,6-tri*-O-*benzyl-1-thio-α*-D-*mannopyranoside* (**7a**).—To a solution of **5d** (0.543 g, 1 mmol) and isophthaloyl chloride (**6**) (0.203 g, 1 mmol) in dry toluene (10 mL), dry pyridine (80 μL) was added. The reaction mixture was stirred at rt under argon for 2.5 h (TLC). The solvent was evaporated under reduced pressure to give **7a** which was very sensitive to the moisture and was used for the next step without purification.

Pyridin-2-yl 2-O-*(benzo-1-yl-3-carboxy)-3,4,6-tri*-O-*benzyl-1-thio-α*-D-*mannopyranoside* (**7b**).—Purification of the acid chloride derivative **7a** with flash-column chromatography using 5:1 petroleum ether–EtOAc, afforded **7b** in 78% yield as an oil; TLC (2:1 petroleum ether–EtOAc): R_f 0.68; $[\alpha]_D$ +18° (c 1.1, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 8.43 (d, 1 H, J 7.2 Hz, H-6′), 7.50–7.48 (m, 1 H, H-5′), 7.45–7.40 (m, 3 H, H-2″, H-4″, H-5″, H-6″), 7.34–7.19 (m, 15 H, 3 Ph), 7.17–7.10 (m, 1 H, H-4′), 7.02–6.98 (m, 1 H, H-3′), 6.32 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 4.82, 4.62 (2 d, 2 H, J_{gem} 12.2 Hz, CH_2Ph), 4.57–4.53 (m, 2 H, CH_2Ph), 4.50, 4.40 (2 d, 2 H, J_{gem} 10.9 Hz, CH_2Ph), 4.29–4.21 (m, 1 H, H-2), 4.12–4.08 (m, 2 H, H-4, H-5), 3.87 (dd, 1 H, $J_{3,4}$ 3.5, $J_{2,3}$ 1.8 Hz, H-3), 3.75 (d, 1 H, J_{gem} 10.1 Hz, H-6), 3.64 (d, 1 H, J_{gem} 10.0 Hz, H-6), 3.04 (br.s, 1 H, OH, D_2O exchangeable). FAB-MS (positive mode, NBOH–NaI-matrix): m/z 692 [MH^+], 714 [MNa^+].

Pyridin-2-yl 3,4,6-tri-O-*benzyl-2*-O-*[3-(methyl-2,3-di*-O-*benzyl-α*-D-*glucopyranosid-6-yloxy)carbonylbenzo-1-yl]-1-thio-α*-D-*mannopyranoside* (**9**)

Method A. Methyl 2,4-di-*O*-benzyl-α-D-glucopyranoside (**8**)[45,46] (0.374 g, 1 mmol) and dibutyltin oxide (0.270 g, 1.1 mmol) in dry toluene (10 mL) was heated under reflux with azeotropic removal of water for 3 h. The reaction mixture was cooled to rt and then **7a** (0.709 g, 1 mmol) and tetrabutylammonium iodide (0.370 g, 1 mmol) were added. Stirring was continued for 5 h (TLC) followed by concentration and the purification with flash-column chromatography using 6:1 toluene–EtOAc to afford **9** as an oil (0.80 g, 77%).

Method B. A solution of the diol **8** (0.374 g, 1 mmol) and **7a** (0.709 g, 1 mmol) in dry CH_2Cl_2 (20 mL) was cooled to 0 °C. Catalytic amounts of dry pyridine were added and stirring was continued at 0 °C for 8 h (TLC). The solvent was removed under reduced pressure and the residue was purified as in method A to give **9** (0.73 g, 70%).

Method C. A solution of the diol **8** (0.374 g, 1 mmol), triphenylphosphine (0.393 g, 1.5 mmol) and **7b** (0.691 g, 1 mmol) in dry THF (15 mL) was stirred at rt. A solution of diethyl azodicarboxylate (DEAD) (0.233 mL, 1.5 mmol) in dry THF (2 mL) was then added. Stirring was continued overnight and the solvent was removed under reduced pressure to give **9** (0.71 g, 68%), after chromatographic purification; TLC (2:1 petroleum ether–EtOAc): R_f 0.47; $[\alpha]_D$ +11° (c 2.0, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 8.44 (d, 1 H, J 7.2 Hz, H-6′), 7.82–7.55 (m, 1 H, H-5′), 7.51–7.42 (m, 3 H, H-2″, H-4″, H-5″, H-6″), 7.33–7.25 (m, 25 H, 5 Ph), 7.21–7.16 (m, 1 H, H-4′), 7.11–7.01 (m, 1 H, H-3′), 6.36–6.32 (m, 1 H, H-1_a), 5.13–5.04 (m, 2 H, H-1_b, H-2_a), 4.83–4.71 (m, 6 H, 3 CH_2Ph), 4.57–4.40 (m, 4 H, 2 CH_2Ph), 4.21–4.15 (m, 2 H, H-2_b, H-3_a), 4.00–3.94 (m, 2 H, H-4_a, H-5_a), 3.90–3.84 (m, 2 H, H-4_b, H-5_b), 3.76–3.68 (m, 1 H, H-3_b), 3.57–3.45 (m, 4 H, H-6_a, H-6_b), 3.37 (s, 3 H, OCH_3). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ 167.11, 166.21 (2 C=O), 156.50, 149.60, 138.26, 138.17, 137.57, 136.80, 136.71, 136.66, 128.51, 128.39, 128.27, 128.23, 127.98, 127.93, 127.56, 127.44, 127.19, 123.77, 123.53, 122.19, 120.80 (Ar-car-

bons), 98.12 (C-1_a), 82.20 (C-1_b), 81.11 (C-3_a), 79.49 (C-2_a), 79.01 (C-3_b), 76.13, 75.56 (2 CH_2Ph), 74.50 (C-5_b), 74.38 (CH_2Ph), 74.00 (C-4_b), 73.21, 71.99 (2 CH_2Ph), 70.44 (C-2_b), 70.11 (C-4_a), 69.27 (C-5_a), 68.79 (C-6_b), 63.51 (C-6_a), 55.22 (OCH_3). MALDI-MS: m/z 1071 [MNa^+]. Anal. Calcd for $C_{61}H_{61}NO_{13}S$ (1048.21): C, 69.89; H, 5.86; N, 1.33. Found: C, 69.67; H, 5.59; N, 1.24.

*Methyl 6,2′-*O*-(1,3-isophthaloyl)-(3,4,6-tri-*O*-benzyl-α,β-*D*-mannopyranosyl)-(1→4)-2,3-di-*O*-benzyl-α-*D*-glucopyranoside* (**10**).—A stirred solution of **9** (0.52 g, 0.5 mmol) and *N*-iodosuccinimide (0.145 g, 0.65 mmol) in dry CH_2Cl_2 (20 mL) under argon was treated at rt with trimethylsilyl trifluoromethanesulfonate (50 μL). The mixture was stirred for 20 min and then neutralised with triethylamine. The solution was concentrated in vacuo and then flash chromatography (toluene → 10:1 toluene–EtOAc) of the residue afforded **10**α (0.046 g, 10%) and **10**β (0.278 g, 60%) as colorless oils.

10α: TLC (5:1 petroleum ether–EtOAc): R_f 0.66; $[\alpha]_D$ +19° (*c* 0.5, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.42 (d, 1 H, *J* 7.1 Hz, H-6′), 7.61–7.55 (m, 1 H, H-5′), 7.50–7.41 (m, 3 H, H-2″, H-4″, H-5″, H-6″), 7.33–7.23 (m, 25 H, 5 Ph), 7.18–7.12 (m, 1 H, H-4′), 7.10–7.01 (m, 1 H, H-3′), 6.40–6.33 (m, 1 H, H-1_a), 5.12–5.06 (m, 2 H, H-1_b, H-2_a), 4.80–4.70 (m, 6 H, 3 CH_2Ph), 4.55–4.41 (m, 4 H, 2 CH_2Ph), 4.27–4.19 (m, 2 H, H-2_b, H-3_a), 4.06–3.97 (m, 2 H, H-4_a, H-5_a), 3.90–3.80 (m, 2 H, H-4_b, H-5_b), 3.73–3.65 (m, 1 H, H-3_b), 3.52–3.43 (m, 4 H, H-6_a, H-6_b), 3.39 (s, 3 H, OCH_3). ^{13}C NMR (150.8 MHz, $CDC1_3$): δ 167.10, 166.15 (2 C=O), 156.50, 149.60, 138.26, 138.17, 136.80, 136.71, 136.66, 128.51, 128.39, 128.27, 128.23, 127.93, 127.56, 127.19, 123.77, 123.53, 122.19 (Ar-carbons), 99.71 (J_{CH} 173.1 Hz, C-1_a), 98.12 (C-1_b), 82.66 (C-3_a), 79.89 (C-3_b, C-4_a), 76.13, 75.56, 74.38, 73.21, 71.99 (5 CH_2Ph), 71.41, 70.98, 70.56 (C-2_b, C-5_a, C-5_b), 70.12 (C-2_a), 69.89 (C-4_b), 69.77, 69.65 (C-6_a, C-6_b), 55.13 (OCH_3). MALDI-MS: m/z 960 [MNa^+]. Anal. Calcd for $C_{56}H_{56}O_{13}$ (937.05): C, 71.71; H, 6.02. Found: C, 71.60; H, 5.89.

10β: TLC (5:1 petroleum ether–EtOAc): R_f 0.53 $[\alpha]_D$ +9° (*c* 0.4, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.36 (d, 1 H, *J* 7.0 Hz, H-6′), 7.70–7.60 (m, 1 H, H-5′), 7.51–7.47 (m, 3 H, H-2″, H-4″, H-5″, H-6″), 7.31–7.24 (m, 25 H, 5 Ph), 7.20–7.15 (m, 1 H, H-4′), 7.12–7.03 (m, 1 H, H-3′), 6.38–6.31 (m, 1 H, H-1_a), 5.14–5.09 (m, 2 H, H-1_b, H-2_a), 4.80–4.70 (m, 6 H, 3 CH_2Ph), 4.52–4.40 (m, 4 H, 2 CH_2Ph), 4.28–4.25 (m, 2 H, H-2_b, H-3_a), 4.03–3.90 (m, 2 H, H-4_a, H-5_a), 3.91–3.82 (m, 2 H, H-4_b, H-5_b), 3.74–3.60 (m, 1 H, H-3_b), 3.47–3.39 (m, 4 H, H-6_a, H-6_b), 3.36 (s, 3 H, OCH_3). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ 167.19, 166.18 (2 C=O), 156.52, 149.60, 138.23, 138.19, 136.80, 136.70, 136.61, 128.50, 128.33, 128.22, 128.20, 127.92, 127.59, 127.14, 123.73, 123.50, 122.16 (Ar-carbons), 101.01 (J_{CH} 158.1 Hz, C-1_b), 97.16 (C-1_a), 85.09 (C-3_b), 81.23 (C-3_a), 76.10, 75.58 (2 CH_2Ph), 74.99 (C-4_b), 74.36, 73.20 (2 CH_2Ph), 72.81 (C-5_b), 72.02 (CH_2Ph), 71.98 (C-5_a), 71.36 (C-2_a), 70.10 (C-2_b, 69.82 (C-4_a), 69.73, 69.61 (C-6_a, C-6_b 55.16 (OCH_3). MALDI-MS: m/z 960 [MNa^+]. Anal. Calcd for $C_{56}H_{56}O_{13}$ (937.05): C, 71.71; H, 6.02. Found: C, 71.58; H, 5.86.

*Methyl (3,4,6-tri-*O*-benzyl-β-*D*-mannopyranosyl)-(1→4)-2,3-di-*O*-benzyl-α-*D*-glucopyranoside* (**11**).—A stirred solution of **10**β (0.234 g, 0.25 mmol) in dry MeOH to (5 mL) was treated with 1 M sodium methoxide (0.10 mL) at rt. The mixture was stirred for further 5 h and then neutralised with Amberlite IR-120. The ion-exchange resin was removed and after evaporation of the solvent in vacuo, **11**β was obtained (0.181 g, 90%); TLC (5:1 petroleum ether–EtOAc): R_f 0.51; $[\alpha]_D$ +33° (*c* 0.3, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.37–7.29 (m, 25 H, 5 Ph), 6.36–6.30 (m, 1 H, H-1_a), 5.13–5.08 (m, 2 H, H-1_b, H-2_a), 4.79–4.68 (m, 6 H, 3 CH_2Ph), 4.50–4.40 (m, 4 H, 2 CH_2Ph), 4.28–4.20 (m, 2 H, H-2_b, H-3_a), 4.05–3.97 (m, 2 H, H-4_a, H-5_a), 3.92–3.80 (m, 2 H, H-4_b, H-5_b), 3.71–3.63 (m, 1 H, H-3_b), 3.51–3.40 (m, 4 H, H-6_a, H-6_b), 3.33 (s, 3 H, OCH_3), 3.13–3.00 (br.s, 2 H, 2 OH, D_2O exchangeable). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ 156.51, 149.64, 138.21, 136.77, 136.70, 136.60, 128.40, 128.29, 128.27, 127.50, 127.13, 123.40, 122.11 (Ar-carbons), 101.00 (J_{CH} 158.0 Hz, C-1_b), 97.10 (C-1_a), 84.98 (C-3_b), 81.31 (C-3_a), 76.17, 75.55 (2 CH_2Ph), 74.88 (C-4_b), 74.34, 73.21 (2 CH_2Ph), 72.78 (C-5_b), 72.12 (CH_2Ph), 72.01 (C-5_a), 71.41 (C-2_a), 70.30 (C-2_b), 70.01 (C-4_a), 69.87, 69.79 (C-6_a, C-6_b,), 55.20 (OCH_3). MALDI-MS: m/z 829 [MNa^+]. Anal. Calcd for $C_{48}H_{54}O_{11}$ (806.94): C, 71.44; H, 6.74. Found: C, 71.31; H, 6.57.

*Methyl (2,3,4,6-tetra-*O*-acetyl-β-*D*-mannopyranosyl)-(1→4)-2,3,6tri-*O*-acetyl-α-*D*-glucopyranoside* (**12**).—A mixture of **11** (0.161 g, 0.2 mmol), and Pd–C (10%, 30 mg) in 1:1 MeOH–EtOAc (8 mL) and formic acid (0.4 mL) was stirred under hydrogen for 24 h. After filtration and concentration in vacuo, the residue was dissolved in 1:1 pyridine–Ac_2O (4 mL), and the mixture was stirred for 20 h. The solution was concentrated in vacuo and coevaporated with toluene; TLC (5:1 petroleum ether–EtOAc): R_f 0.78; $[\alpha]_D$ −44° (*c* 0.2, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.50 (d, 1 H, $J_{3,4}$ 9.6 Hz, H-3_a), 5.13 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1_b), 4.85–4.80 (m, 2 H, H-1_a, H-2_a), 4.48–4.40 (m, 2 H, H-2_b, H-6_a), 4.16 (dd, 1 H, J_{gem} 12.1, $J_{5,6}$ 5.2 Hz, H-6_a), 4.10–4.00 (m, 1 H, H-4_b), 3.94 (dd, $J_{3,4}$ 9.0, $J_{2,3}$ 3.2 Hz, H-3_b), 3.87 (dd, $J_{5,6}$ 4.7, $J_{4,5}$ 1.9 Hz, H-5_a), 3.80–3.77 (m, 1 H, H-5_b), 3.75–3.70 (m, 3 H, H-4_a, H-6_b), 3.39 (s, 3 H, OCH_3), 2.19, 2.14, 2.08, 2.07, 2.04, 2.03, 1.98 (7 s, 21 H, CH_3CO). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ 170.00, 169.70, 169.63, 169.17, 168.90, 168.51, 168.20 (7 CH_3CO), 101.08 (J_{CH} 158.1 Hz, C-1_b), 97.19 (C-1_a), 85.08 (C-3_b), 81.45 (C-3_a), 74.93 (C-4_b), 72.79 (C-5_b), 72.19 (C-5_a), 71.54 (C-2_a), 70.38 (C-2_b), 70.14 (C-4_a),

69.89, 69.70 (C-6_a, C-6_b), 55.13 (OCH_3), 20.78, 20.50, 20.15, 20.12, 19.78, 19.33, 19.17 (7 CH_3CO). MALDI-MS: m/z 673 [MNa^+]. Anal. Calcd for $C_{27}H_{38}O_{18}$ (650.57): C, 49.84; H, 5.88. Found: C, 49.67; H, 5.91.

General procedure for the synthesis of compounds **14a**–**c**.—A solution of α,α′-dibromo-*m*-xylene (0.528 g, 2 mmol) and **5a**–**c** (1 mmol) in dry CH_2Cl_2 (10 mL) was cooled to −15 °C. 15-Crown-5 (220 μL, 1.1 mmol) and NaH (26 mg, 1.1 mmol) were added to the reaction mixture. Stirring was continued for 16 h (TLC), then the solvent was removed under reduced pressure. The residue was purified with flash-column chromatography using 5:1 petroleum ether–EtOAc to give **14a**–**c** in 74–80% yield.

Benzoxazol-2-yl 2-O-*(α-bromo*-m-*xylyl)-3,4,6-tri*-O-*benzyl-1-thio-α*-D-*mannopyranoside* (**14a**). Yield 76% as an oil; TLC (5:1 petroleum ether–EtOAc): R_f 0.60; $[\alpha]_D$ +10° (*c* 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.85 (d, 1 H, *J* 7.2 Hz, H-7′), 7.81 (t, 1 H, *J* 7.0, H-6′), 7.41 (t, 1 H, *J* 7.1 Hz, H-5′), 7.33–7.21 (m, 19 H, 3 Ph, H-2″, H-4″, H-5″, H-6″), 7.18 (d, 1 H, *J* 6.9 Hz, H-4′), 6.59 (d, 1 H, $J_{1,2}$ 1.7 Hz, H-1), 4.92–4.71 (m, 4 H, 2 CH_2Ph), 4.60–4.45 (m, 4 H, 2 CH_2Ph), 4.19–4.12 (m, 3 H, H-2, CH_2), 4.10–3.99 (m, 2 H, H-4, H-5), 3.89–3.70 (m, 1 H, H-3), 3.66–3.51 (m, 2 H, H-6). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ 162.23, 152.79, 138.12, 137.90, 137.47, 137.27, 135.74, 128.45, 128.38, 128.24, 127.99, 127.93, 127.83, 127.80, 127.76, 126.59, 126.57, 126.40, 125.20, 124.41, 124.30, 122.30, 121.39, 117.87 (Ar-carbons), 85.18 (C-1), 78.47 (C-3), 75.61, 75.37 (2 CH_2Ph), 74.35 (C-5), 74.11 (C-4), 73.51, 72.15 (2 CH_2Ph), 67.19 (C-2), 68.51 (C-6), 33.15 (CH_2). MALDI-MS: m/z 788/790 (bromine isotopes) [MNa^+].

Benzothiazol-2-yl 2-O-*(α-bromo*-m-*xylyl)-3,4,6-tri*-O-*benzyl-1-thio-α*-D-*mannopyranoside* (**14b**). Yield 74% as an oil; TLC (5:1 petroleum ether–EtOAc): R_f 0.69; $[\alpha]_D$ +18° (*c* 0.7, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.90 (d, 1 H, *J* 7.1 Hz, H-7′), 7.70 (t, 1 H, *J* 7.0 Hz, H-6′), 7.41 (t, 1 H, *J* 7.1 Hz, H-5′), 7.38–7.22 (m, 19 H, 3 Ph, H-2″, H-4″, H-5″, H-6″), 7.19 (d, 1 H, *J* 7.1 Hz, H-4′), 6.60 (d, 1 H, $J_{1,2}$ 1.7 Hz, H-1), 4.90–4.77 (m, 4 H, 2 CH_2Ph), 4.62–4.43 (m, 4 H, 2 CH_2Ph), 4.20–4.08 (m, 3 H, H-2, CH_2), 3.98–3.89 (m, 2 H, H-4, H-5), 3.81–3.70 (m, 1 H, H-3), 3.61–3.50 (m, 2 H, H-6). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ 161.96, 152.94, 152.70, 138.27, 137.94, 137.31, 135.84, 135.78, 128.45, 128.30, 128.23, 127.92, 127.86, 127.73, 127.61, 126.50, 126.51, 126.38, 126.20, 125.22, 124.77, 124.30, 122.40, 120.90, 119.90 (Ar-carbons), 84.90 (C-1), 78.13 (C-3), 75.19, 75.13 (2 CH_2Ph), 73.98 (C-5), 73.80 (C-4), 73.27, 72.11 (2 CH_2Ph), 69.49 (C-2), 68.20 (C-6), 33.23 (CH_2). MALDI-MS: m/z 804/806 (bromine isotopes) [MNa^+].

Pyrimidin-2-yl 2-O-*(α-bromo*-m-*xylyl)-3,4,6-tri*-O-*benzyl-1-thio-α*-D-*mannopyranoside* (**14c**). Yield 80% as an oil; TLC (5:1 petroleum ether–EtOAc): R_f 0.65; $[\alpha]_D$ +21° (*c* 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.66 (d, 1 H, *J* 7.0, H-6′), 7.40–7.21 (m, 19 H, 3 Ph, H-2″, H-4″, H-5″, H-6″), 7.18 (d, 1 H, *J* 7.1 Hz, H-5′), 7.09 (d, 1 H, *J* 7.1 Hz, H-4′), 6.51 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 4.91–4.78 (m, 4 H, 2 CH_2Ph), 4.61–4.47 (m, 4 H, 2 CH_2Ph), 4.17–4.12 (m, 3 H, H-2, CH_2), 4.10–3.91 (m, 2 H, H-4, H-5), 3.80–3.69 (m, 1 H, H-3), 3.60–3.55 (m, 2 H, H-6). ^{13}C NMR (150.8 MHz, $CDCl_3$):δ 157.60, 139.25, 138.19, 138.15, 137.46, 128.49, 128.34, 128.29, 128.23, 128.19, 127.86, 127.72, 127.60, 127.41, 117.50 (Ar-carbons), 82.17 (C-1), 78.90 (C-3), 75.24, 75.20 (2 CH_2Ph), 74.80 (C-5), 74.11 (C-4), 72.99, 71.90 (2 CH_2Ph), 70.51 (C-2), 68.53 (C-6), 33.20 (CH_2). MALDI-MS: m/z 749/751 (bromine isotopes) [MNa^+].

General procedure for the synthesis of compounds **15a**–**c**.—Methyl 2,4-di-*O*-benzyl-α-D-glucopyranoside (**8**)[45,46] (0.374 g, 1 mmol) and dibutyltin oxide (0.270 g, 1.1 mmol) in dry toluene (10 mL) was refluxed under azeotropic removal of water for 3 h. The reaction mixture was cooled to rt. Compounds **14a**–**c** (1 mmol) and tetrabutylammonium iodide (0.370 g, 1 mmol) were added to the reaction mixture. Stirring was continued for 10 h (TLC). Removal of the solvent under reduced pressure and purification with flash-column chromatography using 6:1 toluene–EtOAc afforded **15a**–**c** as oils in 78–84% yield.

Benzoxazol-2-yl 2-O-*[(methyl-2,3-di*-O-*benzyl-α*-D-*glucopyranosid-6-yloxy)*-m-*xylyl]-3,4,6-tri*-O-*benzyl-l-thio-α*-D-*mannopyranoside* (**15a**).—Yield 81% as an oil; TLC (2:1 petroleum ether–EtOAc): R_f 0.38; $[\alpha]_D$ −43° (*c* 0.4, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.88 (d, 1 H, *J* 6.9 Hz, H-7′), 7.84 (t, 1 H, *J* 7.2 Hz, H-6′), 7.40 (t, 1 H, *J* 6.9 Hz, H-5′), 7.30–7.23 (m, 29 H, 5 Ph, H-2″, H-4″, H-5″, H-6″), 7.21 (d, 1 H, *J* 6.8 Hz, H-4′), 6.39–6.31 (m, 1 H, H-1_a), 5.16–5.04 (m, 2 H, H-1_b, H-2_a), 4.99–4.80 (m, 6 H, 3 CH_2Ph), 4.77–4.63 (m, 4 H, 2 CH_2Ph), 4.58–4.40 (m, 4 H, 2 CH_2Ph), 4.29–4.21 (m, 2 H, H-2_b, H-3_a), 4.09–3.95 (m, 2 H, H-4_a, H-5_a), 3.92–3.83 (m, 2 H, H-4_b, H-5_b), 3.78–3.61 (m, 1 H, H-3_b), 3.55–3.43 (m, 4 H, H-6_a, H-6_b), 3.35 (s, 3 H, OCH_3). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ 162.45, 152.89, 138.32, 138.12, 137.91, 137.40, 137.27, 135.70, 128.65, 128.58, 128.44, 128.29, 127.93, 127.84, 127.80, 127.72, 126.69, 126.58, 126.40, 125.20, 124.41, 124.31, 122.32, 121.39, 117.81 (Ar-carbons), 98.00 (C-1_a), 85.22 (C-1_b), 81.14 (C-3_a), 79.53 (C-2_a), 78.44 (C-3_b), 75.83, 75.77, 75.38 (3 CH_2Ph), 74.42 (C-5_b), 74.19 (C-4_b), 73.66, 73.50, 72.19, 72.13 (4 CH_2Ph), 70.15 (C-4_a), 69.31 (C-5_a), 67.23 (C-2_b), 68.50 (C-6_b), 64.11 (C-6_a), 55.10 (OCH_3). MALDI-MS: m/z 1083 [MNa^+]. Anal. Calcd for $C_{63}H_{65}NO_{12}S$ (1060.26): C, 71.36; H, 6.17; N, 1.32. Found: C, 71.21; H, 6.01; N, 1.11.

Benzothiazol-2-yl 2-O-*[(methyl-2,3-di*-O-*benzyl-α*-D-*glucopyranosid-6-yloxy)*-m-*xylyl]-3,4,6-tri*-O-*benzyl-1-thio-α*-D-*mannopyranoside* (**15b**).—Yield 78% as an oil; TLC (2:1 petroleum ether–EtOAc): R_f 0.41; $[\alpha]_D$ −52°

(c 0.2, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 7.85 (d, 1 H, J 6.9 Hz, H-7′), 7.80 (t, 1 H, J 7.2 Hz, H-6′), 7.38 (t, 1 H, J 6.9 Hz, H-5′), 7.35–7.23 (m, 29 H, 5 Ph, H-2″, H-4″, H-5″, H-6″), 7.17 (d, 1 H, J 6.8 Hz, H-4′), 6.43–6.39 (m, 1 H, H-1_a), 5.15–5.06 (m, 2 H, H-1_b, H-2_a), 4.82–4.99 (m, 6 H, 3 CH_2Ph), 4.74–4.66 (m, 4 H, 2 CH_2Ph), 4.48–4.37 (m, 4 H, 2 CH_2Ph), 4.33–4.20 (m, 2 H, H-2_b, H-3_a), 4.06–3.91 (m, 2 H, H-4_a, H-5_a), 3.90–3.83 (m, 2 H, H-4_b, H-5_b), 3.74–3.60 (m, 1 H, H-3_b), 3.51–3.43 (m, 4 H, H-6_a, H-6_b), 3.34 (s, 3 H, OCH_3). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ 162.07, 152.99, 152.94, 152.73, 138.29, 137.94, 137.31, 135.80, 135.72, 128.47, 128.35, 128.28, 128.23, 127.92, 127.86, 127.73, 127.61, 126.56, 126.50, 126.33, 126.25, 125.21, 124.72, 124.22, 122.45, 120.91, 119.99, (Ar-carbons), 98.00 (C-1_a), 84.94 (C-1_b), 81.20 (C-3_a), 79.55 (C-2_a), 78.19 (C-3_b), 75.44, 75.19, 75.15 (3 CH_2Ph), 73.90 (C-5_b), 73.85 (C-4_b), 73.43, 73.20, 72.17, 72.13 (4 CH_2Ph), 70.20 (C-4_a), 69.50 (C-5_a), 69.46 (C-2_b), 68.22 (C-6_b), 64.18 (C-6_a), 55.16 (OCH_3). MALDI-MS: m/z 1099 [MNa^+]. Anal. Calcd for $C_{63}H_{65}NO_{11}S_2$ (1076.32): C, 70.30; H, 6.08; N, 1.30. Found: C, 70.11; H, 5.88; N, 1.09.

*Pyrimidin-2-yl 2-*O*-[(methyl-2,3-di-*O*-benzyl-α-*D*-glucopyranosid-6-yloxy)-*m*-xylyl]-3,4,6-tri-*O*-benzyl-1-thio-α-*D*-mannopyranoside* (**15c**).—Yield 84% as an oil; TLC (2:1 petroleum ether–EtOAc): R_f 0.40; $[\alpha]_D$ −66° (c 0.1, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 8.50 (d, 1 H, J 7.1 Hz, H-6′), 7.31–7.20 (m, 29 H, 5 Ph, H-2″, H-4″, H-5″, H-6″), 7.14 (d, 1 H, J 7.1 Hz, H-5′), 7.01 (d, 1 H, J 7.2 Hz, H-4′), 6.31–6.27 (m, 1 H, H-1_a), 5.15–5.07 (m, 2 H, H-1_b, H-2_a), 4.96–4.82 (m, 6 H, 3 CH_2Ph), 4.73–4.60 (m, 4 H, 2 CH_2Ph), 4.55–4.45 (m, 4 H, 2 CH_2Ph), 4.27–4.18 (m, 2 H, H-2_b, H-3_a), 4.16–4.10 (m, 2 H, H-4_a, H-5_a), 3.94–3.87 (m, 2 H, H-4_b, H-5_b), 3.72–3.65 (m, 1 H, H-3_b), 3.59–3.50 (m, 4 H, H-6_a, H-6_b), 3.38 (s, 3 H, OCH_3).^{13}C NMR (150.8 MHz, $CDCl_3$): δ 157.73, 157.65, 139.28, 138.77, 138.19, 138.15, 137.46, 128.79, 128.54, 128.44, 128.29, 128.17, 127.88, 127.70, 127.62, 127.41, 117.54 (Ar-carbons), 97.98 (C-1_a), 82.44 (C-1_b), 81.34 (C-3_a), 79.50 (C-2_a), 78.95 (C-3_b), 75.31, 75.24, 75.21 (3 CH_2Ph), 74.85 (C-5_b), 74.18 (C-4_b), 74.00, 73.12, 72.95, 71.93 (4 CH_2Ph), 70.55 (C-2_b), 70.33 (C-2_a), 68.53 (C-6_b), 64.47 (C-6_a), 55.21 (OCH_3). MALDI-MS: m/z 1045 [MNa^+]. Anal. Calcd for $C_{60}H_{65}N_2O_{11}S$ (1022.23): C, 70.49; H, 6.40; N, 2.74. Found: C, 70.30; H, 6.31; N, 2.59.

*Methyl 6,2′-*O*-(m-xylyl)-(3,4,6-tri-*O*-benzyl-α,β-*D*-mannopyranosyl)-(1→4)-2,3-di-*O*-benzyl-α-*D*-glucopyranoside* (**16**).—Trimethylsilyl trifluoromethanesulfonate (50 μL) was added under argon at rt to a solution of **15a**–**c** (1 mmol) and *N*-iodosuccinimide (0.290 g, 1.3 mmol) in dry CH_2Cl_2 (20 mL); the mixture was stirred for 20 min. The solution was neutralised with triethylamine and concentrated in vacuo. Chromatography (toluene→10:1 toluene–EtOAc) of the residue afforded **16** in 78% yield from **15a** (α/β ratio, 1:10), in 75% yield from **15b** (α/β ratio, 1:9), in 76% yield from **15c** (α/β ratio, 1:10), and from **21** in 72% yield (α/β ratio, 1:6).

16α: TLC (5:1 petroleum ether–EtOAc): R_f 0.60; $[\alpha]_D$ +65° (c 0.4, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 7.51–7.23 (m, 29 H, 5 Ph, H-2″, H-4″, H-5″, H-6″), 6.36–6.31 (m, 1 H, H-1_a), 5.12–5.06 (m, 2 H, H-1_b, H-2_a), 4.95–4.86 (m, 6 H, 3 CH_2Ph), 4.76–4.67 (m, 4 H, 2 CH_2Ph), 4.53–4.40 (m, 4 H, 2 CH_2Ph), 4.27–4.21 (m, 2 H, H-2_b, H-3_a), 4.10–3.94 (m, 2 H, H-4_a, H-5_a), 3.93–3.86 (m, 2 H, H-4_b, H-5_b), 3.75–3.60 (m, 1 H, H-3_b), 3.52–3.41 (m, 4 H, H-6_a, H-6_b), 3.34 (s, 3 H, OCH_3). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ 156.54, 149.66, 138.34, 138.19, 136.80, 136.75, 136.65, 128.77, 128.60, 128.57, 128.43, 127.90, 127.51, 127.15, 123.77, 123.50, 122.11 (Ar-carbons), 99.77 (J_{CH} 174.0 Hz, C-1_b), 98.10 (C-1_a), 82.54 (C-3_b), 79.82 (C-3_a, C-4_b), 75.51, 75.39, 75.26, 74.09, 73.19, 73.15, 71.99 (7 CH_2Ph), 71.21, 70.99, 70.63 (C-2_a, C-5_a, C-5_b), 70.14 (C-2_b), 69.92 (C-4_a), 69.71, 69.64 (C-6_a, C-6_b), 55.21 (OCH_3). MALDI-MS: m/z 932 [MNa^+]. Anal. Calcd for $C_{56}H_{60}O_{11}$ (909.08): C, 73.98; H, 6.65. Found: C, 73.83; H, 6.51.

16β: TLC (5:1 petroleum ether–EtOAc): R_f 0.47; $[\alpha]_D$ +77° (c 0.3, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 7.54–7.24 (m, 29 H, 5 Ph, H-2″, H-4″, H-5″, H-6″), 6.36–6.33 (m, 1 H, H-1_a), 5.16–5.06 (m, 2 H, H-1_b, H-2_a), 4.93–4.80 (m, 6 H, 3 CH_2Ph), 4.71–4.60 (m, 4 H, 2 CH_2Ph), 4.48–4.43 (m, 4 H, 2 CH_2Ph), 4.22–4.16 (m, 2 H, H-2_b, H-3_a), 4.00–3.90 (m, 2 H, H-4_a, H-5_a), 3.86–3.77 (m, 2 H, H-4_b, H-5_b), 3.68–3.51 (m, 1 H, H-3_b), 3.46–3.38 (m, 4 H, H-6_a, H-6_b), 3.33 (s, 3 H, OCH_3). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ 156.55, 149.69, 138.39, 138.22, 136.81, 136.85, 136.75, 128.73, 128.60, 128.54, 128.40, 127.90, 127.50, 127.19, 123.77, 123.55, 122.14 (Ar-carbons), 101.09 (J_{CH} 158.3 Hz, C-1_b), 97.10 (C-1_a), 85.12 (C-3_b), 81.31 (C-3_a), 75.50, 75.32, 75.23 (3 CH_2Ph), 74.90 (C-4_b), 74.00, 73.12, 73.10, 72.92 (4 CH_2Ph), 72.89 (C-5_b), 71.93 (C-5_a), 71.56 (C-2_a), 70.10 (C-2_b), 70.00 (C-4_a), 69.72, 69.68 (C-6_a, C-6_b), 55.23 (OCH_3). MALDI-MS: m/z 932 [MNa^+]. Anal. Calcd for $C_{56}H_{60}O_{11}$ (909.08): C, 73.98; H, 6.65. Found: C, 73.79; H, 6.54.

*1,3,4-Thiadiazole-2,5-diyl bis(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-1-thio-α-*D*-mannopyranoside)* (**18**).—2,5-Dimercapto-1,3,4-thiadiazole (**17**) (8 mmol) and $HgBr_2$ (40 mg) was added to a solution of **2**[41,42] (0.50 g, 1.0 mmol) in dry MeCN (10 mL). The mixture was heated to 60 °C under argon for 5 h, and then concentrated. A solution of the residue in CH_2Cl_2 was washed with 5% aq NaOH (50 mL), water, dried ($MgSO_4$), and concentrated. The residue was purified by flash-column chromatography using 10:1 petroleum ether–EtOAc to give **18** in 88% yield as an oi1; TLC (5:1 petroleum ether–EtOAc): R_f 0.41; $[\alpha]_D$ −106° (c 1.0, $CHCl_3$); ^1H NMR

(600 MHz, $CDCl_3$): δ 7.38–7.26 (m, 30 H, 6 Ph), 6.39 (d, 2 H, $J_{1,2}$ 1.7 Hz, H-1), 5.69–5.61 (m, 2 H, H-2,), 4.70–4.43 (m, 12 H, 6 CH_2Ph), 4.18–4.12 (m, 2 H, H-5), 4.00–3.97 (m, 2 H, H-4), 3.94–3.90 (m, 6 H, H-3, H-6), 3.70 (d, 2 H, J_{gem} 11.0 Hz, H-6), 2.18 (s, 6 H, CH_3CO). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ 170.00 (2 CH_3CO), 161.90, 152.70, 138.04, 137.88, 137.34, 135.87, 128.46, 128.31, 128.20, 127.90, 127.75, 127.69, 126.54, 126.39, 124.59, 122.45, 121.19, 117.99 (Ar-carbons), 84.73 (C-1), 78.44 (C-3), 75.39 (CH_2Ph), 74.19 (C-5), 74.15 (C-4), 73.45, 72.28 (2 CH_2Ph), 69.79 (C-2), 68.39 (C-6), 20.84 (CH_3CO). MALDI-MS: m/z 1122 [MNa^+].

1,3,4-Thiadiazole-2,5-diyl bis(3,4,6-tri-O-*benzyl-1-thio-α*-D-*mannopyranoside)* (**19**).—Compound **18** (1.10 g, 1 mmol) was dissolved in dry MeOH (10 mL) and 1 M sodium methoxide in MeOH (0.1 mL) was added with stirring at rt. After 2 h, the reaction mixture was neutralised with Amberlite IR-120. The ion-exchange resin was removed and after evaporation of the solvent under reduced pressure, compound **19** was obtained in quantitative yield as yellow oil. The product was pure enough for the next step; TLC (5:1 petroleum ether–EtOAc): R_f 0.37; $[\alpha]_D$ −87° (*c* 1.0, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 7.38–7.24 (m, 30 H, 6 Ph), 6.79 (d, 2 H, $J_{1,2}$, 1.6 Hz, H-1), 4.84–4.43 (m, 12 H, 6 CH_2Ph), 4.40 (m, 2 H, H-2), 4.15–4.01 (m, 4 H, H-4, H-5), 3.87–3.83 (m, 2 H, H-3), 3.80–3.75 (m, 2 H, H-6), 3.73–3.69 (m, 2 H, H-6), 2.79 (br.s, 2 H, 2 OH, D_2O exchangeable). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ 161.80, 152.70, 138.24, 137.93, 137.25, 135.77, 128.30, 128.25, 127.94, 127.80, 127.71, 126.52, 126.36, 125.21, 124.72, 124.41, 120.90, 117.90. (Ar-carbons), 83.66 (C-1), 80.44 (C-3), 75.32 (CH_2Ph), 74.70 (C-5), 74.16 (C-4), 73.41, 72.19 (2 CH_2Ph), 70.45 (C-2), 68.69 (C-6). MALDI-MS: m/z 1038 [MNa^+].

1,3,4-Thiadiazole-2,5-diyl bis[2-O-*(α-bromo*-m-*xylyl)-3,4,6-tri*-O*benzyl-1-thio-α*-D-*mannopyranoside]* (**20**).—A solution of α,α′-dibromo-*m*-xylene (1.056 g, 4 mmol) and **19** (1.01 g, 1 mmol) in dry CH_2Cl_2 (20 mL) was cooled to −15 °C. 15-Crown-5 (440 μL, 2.2 mmol) and NaH (52 mg, 2.2 mmol) were added to the reaction mixture. Stirring was continued for overnight (TLC), and then the solvent was removed under reduced pressure. The residue was purified with flash-column chromatography using 5:1 petroleum ether–EtOAc to give **20** in 77% yield as an oil; TLC (2:1 petroleum ether–EtOAc): R_f 0.40; $[\alpha]_D$ −77° (*c* 0.3, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 7.37–7.24 (m, 38 H, 6 Ph, H-2″, H-4″, H-5″, H-6″), 6:63 (d, 2 H, $J_{1,2}$ 1.6 Hz, H-1), 4.90–4.43 (m, 20 H, 10 CH_2Ph), 4.23–3.51 (m, 12 H, H-2, H-3, H-4, H-5, H-6). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ 162.45, 152.73, 138.11, 137.92, 137.42, 135.74, 128.45, 128.38, 128.33, 127.92, 127.90, 127.82, 126.59, 126.42, 125.21, 124.30, 122.32, 121.31, 117.80 (Ar-carbons), 85.22 (C-1), 78.55 (C-3), 75.60, 75.33 (2 CH_2Ph), 74.39 (C-5), 74.15 (C-4), 73.50, 72.18 (2 CH_2Ph), 67.23 (C-2), 68.50 (C-6), 33.50 (CH_2). MALDI-MS: m/z 1403/1405 (bromine isotopes) [MNa^+].

1,3,4-Thiadiazole-2,5-diyl bis{[2-O-*(methyl-2,3-di*-O-*benzyl-α*-D-*glucopyranosid-6-yloxy)*-m-*xylyl]-(3,4,6-tri*-O-*benzyl-1-thio-α*-D-*mannopyranoside)}* (**21**).—Methyl 2,4-di-*O*-benzyl-α-D-glucopyranoside (**8**) (0.748 g, 2 mmol) and dibutyltin oxide (0.540 g, 2.2 mmol) in dry toluene (20 mL) was refluxed under azeotropic removal of water for 3 h. The reaction mixture was cooled to rt and then **20** (1.96 g, 1 mmol) and tetrabutylammonium iodide (0.740 g, 2 mmol) were added. Stirring was continued for overnight (TLC). Removal of the solvent under reduced pressure and purification with flash-column chromatography using 6:1 toluene–EtOAc afforded **21** in 72% yield as an oil; TLC (2:1 petroleum ether–EtOAc) R_f 0.30; $[\alpha]_D$ −21° (*c* 0.1, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 7.39–7.23 (m, 38 H, 6 Ph, H-2″, H-4″, H-5″, H-6″), 6.36–6.30 (m, 2 H, H-1_a), 5.13–5.00 (m, 4 H, H-1_b, H-2_a), 4.90–4.80 (m, 12 H, 6 CH_2Ph), 4.70–4.60 (m, 8 H, 4 CH_2Ph), 4.48–4.36 (m, 8 H, 4 CH_2Ph), 4.31–4.20 (m, 4 H, H-2_b, H-3_a), 4.04–3.93 (m, 4 H, H-4_a, H-5_a), 3.83–3.73 (m, 4 H, H-4_b, H-5_b), 3.73–3.60 (m, 2 H, H-3_b), 3.53–3.43 (m, 8 H, H-6_a, H-6_b), 3.38 (s, 6 H, OCH_3). ^{13}C NMR (150.8 MHz, $CDCl_3$): δ 162.45, 152.89, 138.34, 138.11, 137.97, 137.21, 135.73, 128.63, 128.50, 127.94, 127.80, 127.71, 126.79, 126.43, 125.30, 124.53, 124.38, 122.30, 121.43, 117.80 (Ar-carbons), 98.06 (C-1_a), 85.27 (C-1_b), 81.42 (C-3_a), 79.66 (C-2_a), 78.42 (C-3_b), 75.88, 75.70, 75.30 (3 CH_2Ph), 74.45 (C-5_b), 74.33 (C-4_b), 73.60, 73.44, 72.12, 72.10 (4 CH_2Ph), 70.10 (C-4_a), 69.39 (C-5_a), 68.54 (C-6_b), 67.34 (C-$_b$), 64.14 (C-6_a), 55.20 (OCH_3). MALDI-MS: m/z 1990 [MNa^+].

Acknowledgements

This work was supported by the Deutsche Froschungsgemeinschaft and the Fonds der Chemischen Industrie. A.A.-H.A.-R. is grateful for an Alexander von Humboldt-Fellowship. The continued support from the Alexander von Humboldt Stiftung for E.S.H.E.A. is highly appreciated.

References

1. Schmidt, R. R. *Comprehensive Organic Synthesis*; Pergamon: Oxford, 1991; Vol. 6, pp. 33–64.
2. Sinaÿ, P. *Pure Appl. Chem.* **1991**, *63*, 519–528.
3. Garegg, P. J. *Acc. Chem. Res.* **1992**, *25*, 575–580.
4. Toshima, K.; Tatsuta, K. *Chem. Rev.* **1993**, *93*, 1503–1531.
5. Kunz, H.; Wernig, P.; Schultz, M. *Synlett* **1990**, 631–632.
6. Barressi, F.; Hindsgaul, O. *J. Am. Chem. Soc.* **1991**, *113*, 9376–9377.

7. Bols, M. *Tetrahedron* **1993**, *49*, 10049–10060.
8. Ito, Y.; Ogawa, T. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1765–1767.
9. López, J. C.; Gómez, A. M.; Valverde, S.; Fraser-Reid, B. *J. Org. Chem.* **1995**, *60*, 3851–3858.
10. Winterfeld, G. A.; Ito, Y.; Ogawa, T.; Schmidt, R. R. *Eur. J. Org. Chem.* **1999**, 1167–1171.
11. (a) Weingart, R.; Schmidt, R. R. *Tetrahedron Lett.* **2000**, *41*, 8753–8758;
(b) El Ashry, E. S. H.; Schuerch, C. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 1581–1586;
(c) Awad, L. F.; El Ashry, E. S. H.; Schuerch, C. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 1587–1592.
12. Takhi, M.; Abdel-Rahman, A. A.-H.; Schmidt, R. R. *Synlett* **2000**, 427–429.
13. Abdel-Rahman, A. A. -H.; Winterfeld, G. A.; Takhi, M.; Schmidt, R. R. *Eur. J. Org. Chem.*, unpublished result.
14. Jung, K.-H.; Müller, M.; Schmidt, R. R. *Chem. Rev.* **2000**, *100*, 4423–4442.
15. Huchel, U.; Schmidt, R. R. *Tetrahedron Lett.* **1998**, *39*, 7693–7694.
16. Müller, M.; Huchel, U.; Geyer, A.; Schmidt, R. R. *J. Org. Chem.* **1999**, *64*, 6190–6201.
17. Müller, M.; Schmidt, R. R. *Eur. J. Org. Chem.* **2001**, 2055–2066.
18. Khan, S. H.; O'Neill, R. A., Eds. *Modern Methods in Carbohydrate Chemistry*; Harwood Academic: Amsterdam, 1996.
19. Gridley, J. J.; Osborn, H. M. I. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1471–1491.
20. Barresi, F.; Hindsgaul, O. *J. Am. Chem. Soc.* **1991**, *113*, 9376–9377.
21. Barresi, F.; Hindsgaul, O. *Synlett* **1992**, 759–761.
22. Ennis, S. C.; Fairbanks, A. J.; Tennant-Eyles, R. J.; Yates, H. S. *Synlett* **1999**, 1387–1390.
23. Seward, C. M. P.; Cumpstey, I.; Aloui, M.; Ennis, S. C.; Redgrave, A. J.; Fairbanks, A. J. *J. Chem. Soc., Chem. Commun.* **2000**, 1409–1410.
24. (a) Ito, Y.; Ogawa, T. *Angew. Chem.* **1994**, *106*, 1843–1845;
(b) Ito, Y.; Ogawa, T. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1765–1767.
25. Ito, Y.; Ohnishi, Y.; Ogawa, T.; Nakahara, Y. *Synlett* **1998**, 1102–1104.
26. Lergenmüller, M.; Nukada, T.; Kuramochi, K.; Dan, A.; Ogawa, T.; Ito, Y. *Eur. J. Org. Chem.* **1999**, 1367–1376.
27. Dan, A.; Ito, Y.; Ogawa, T. *Tetrahedron Lett.* **1995**, *36*, 7487–7490.
28. Dan, A.; Ito, Y.; Ogawa, T. *J. Org. Chem.* **1995**, *60*, 4680–4681.
29. Ito, Y.; Ogawa, T. *J. Am. Chem. Soc.* **1997**, *119*, 5562–5566.
30. Stork, G.; Kim, G. *J. Am. Chem. Soc.* **1992**, *114*, 1087–1088.
31. Stork, G.; La Clair, J. *J. Am. Chem. Soc.* **1996**, *118*, 247–248.
32. Ziegler, T.; Lemanski, G.; Rakoczy, A. *Tetrahedron Lett.* **1995**, *36*, 8973–8976.
33. (a) Ziegler, T.; Lemanski, G. *Angew. Chem.* **1998**, *110*, 3367–3369;
(b) Ziegler, T.; Lemanski, G. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 3129–3132.
34. Ziegler, T.; Lemanski, G. *Tetrahedron* **2000**, *56*, 563–579.
35. Valverde, S.; Gómez, A. M.; Hernàndez, A.; Herrandón, B.; López, J. C. *J. Chem. Soc., Chem. Commun.* **1995**, 2005–2006.
36. Valverde, S.; Gómez, A. M.; López, J. C.; Herrandón, B. *Tetrahedron Lett.* **1996**, *37*, 1105–1108.
37. Valverde, S.; García, M.; Gómez, A. M.; López, J. C. *Synlett* **2000**, 22–26.
38. Perlin, A. S. *Can J. Chem.* **1963**, *41*, 399–406.
39. Mazurek, M.; Perlin, A. S. *Can. J. Chem.* **1965**, *43*, 1918–1923.
40. Kochetkov, N. K.; Khorlin, A. J.; Bochkov, A. F. *Tetrahedron* **1967**, *23*, 693–707.
41. Franks, N. E.; Montgomery, R. *Carbohydr. Res.* **1968**, *6*, 286–298.
42. Borén, H. B.; Ekborg, G.; Eklind, K.; Garegg, P. J.; Pilotti, Å.; Swahn, C.-G. *Acta Chem. Scand.* **1973**, *27*, 2639–2644.
43. Garegg, P. J.; Maron, L. *Acta Chem. Scand., Ser. B.* **1979**, *33*, 39–41.
44. Zhang, Y.-M.; Mallet, J.-M.; Sinaÿ, P. *Carbohydr. Res.* **1992**, *236*, 73–88.
45. Bell, D. J.; Lorber, J. *J. Chem. Soc.* **1940**, 453–455.
46. Kiss, J.; Taschner, P. *J. Carbohydr. Nucleosides Nucleotides* **1977**, *4*, 101–119.
47. Veeneman, G. H.; van Leeuwen, S. H.; van Boom, J. H. *Tetrahedron Lett.* **1990**, *31*, 1331–1334.
48. Konradsson, P.; Udodon, U. E.; Fraser-Reid, B. *Tetrahedron Lett.* **1990**, *31*, 4313–4316.
49. (a) Ferrier, R. J.; Hay, R. W.; Vethaviyasar, N. *Carbohydr. Res.* **1973**, *27*, 55–61;
(b) Mukaiyama, T.; Nakatsuki, T.; Shoda, S. *Chem. Lett.* **1979**, 487–490;
(c) Hanessian, S.; Bacquet, C.; Lehong, N. *Carbohydr. Res.* **1980**, *80*, C17–C22;
(d) Woodward, R. B.; et al. *J. Am. Chem. Soc.* **1981**, *103*, 3215–3217;
(e) Wuts, P. G. M.; Bigelow, S. S. *J. Org. Chem.* **1983**, *48*, 3489–3493;
(f) Hanessian, S. In *Preparative Carbohydrate Chemistry*; Hanessian, S., Ed.; Marcel Dekker: New York, 1997; pp. 381–388.
50. Chen, Q; Kong, F. *Carbohydr. Res.* **1995**, *272*, 149–157.