Syntheses of Model Oligosaccharides of Biological Significance. 2. Synthesis of a Tetramannoside and of Two Lyxose-Containing Trisaccharides[1]

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The synthesis of two isomeric trisaccharides containing D-mannose and D-lyxose are reported. Methyl 2-*O*-allyl-4,6-*O*-benzylidene-α-D-mannopyranoside was reacted with an α-D-lyxopyranosyl bromide. The disaccharide obtained was glycosylated with an α-D-mannopyranosyl bromide after hydrolysis of the benzylidene group. This sequence led to methyl 3-*O*-α-D-lyxopyranosyl-6-*O*-α-D-mannopyranosyl-α-D-mannopyranoside after deblocking of all hydroxyl groups. When the two glycosyl bromides were added to the methyl mannopyranoside in the reversed order, methyl 6-*O*-α-D-lyxopyranosyl-3-*O*-α-D-mannopyranosyl-α-D-mannopyranoside was obtained. The tetrasaccharide methyl 6-*O*-(3-*O*-α-D-mannopyranosyl-α-D-mannopyranosyl)-3-*O*-α-D-mannopyranosyl-α-D-mannopyranoside was prepared by condensation of two dimannosyl compounds. The use of the allyl, benzyl, 2,2,2-trichloroethyl, and *O*-nitrobenzyl groups for the protection of the anomeric position is discussed.

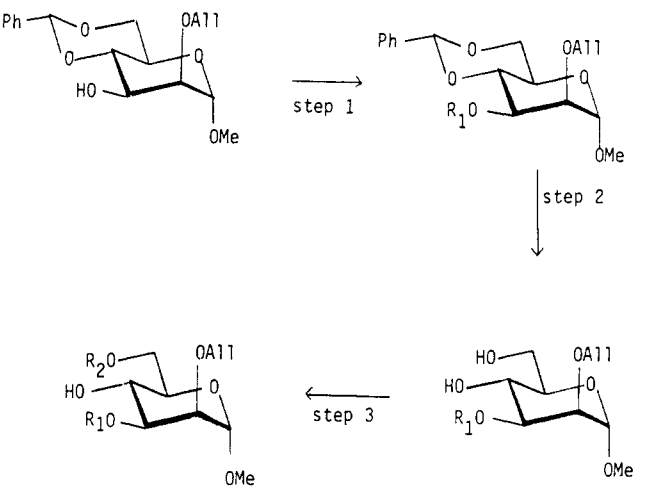
Several classes of carbohydrate structures have been identified in membrane glycoproteins.[2] All oligosaccharides glycosidically N-linked to L-asparagine have a common structural feature consisting of a 3,6-di-*O*-α-D-mannopyranosyl-D-mannopyranosyl moiety attached via a 1,4-β linkage to a chitobiose group. We have reported[1] recently the synthesis of a part of this core structure, methyl 3,6-di-*O*-α-D-mannopyranosyl-α-D-mannopyranoside (1). Our synthesis differs from other published[3] preparations of 1 in that it gives access to a whole class of structurally related oligosaccharides where the C-3 and C-6 substituents of the central mannopyranose are different. We report here the synthesis of the two isomeric trisaccharides 2 and 3 and of the tetrasaccharide 4 (Figure 1). The trisaccharides 2 and 3, which contain D-lyxose, an aldopenose homomorphous to D-mannose, have been used as substrates in a study of the binding specificity of the lectin Concanavalin A.[4] The syntheses of those four oligosaccharides emphasize the efficiency and versatility of this synthetic method.

Results and Discussion

Synthesis and Characterization of the Trisaccharides 2 and 3. Both trisaccharides 2 and 3 are prepared from the same key intermediate, methyl 2-*O*-allyl-4,6-*O*-benzylidene-α-D-mannopyranoside (5)[1] (Scheme I). Reaction of a glycosyl bromide with the free C-3 hydroxyl group of 5 gives a disaccharide (step 1). Hydrolysis of the benzylidene group (step 2) gives a diol, which reacts selectively at the C-6 position as a result of the higher reactivity of the primary hydroxyl group (step 3). Condensation of a glycosyl bromide with an alcohol to form a glycosidic bond (step 1 or step 3) can be effected under various conditions.[5] In our system, the best results were obtained where the condensation was performed in the presence of mercuric bromide and mercuric cyanide, namely by Helferich glycosylation.[6] Glycosylation of the key compound 5, first with a lyxopyranosyl bromide and, after removal of the benzylidene group, with a mannopyranosyl bromide led to structure 2, while consecutive glycosylation of 5 with the two bromides in the reverse order led to structure 3.

The synthesis of methyl 3-*O*-α-D-lyxopyranosyl-6-*O*-α-D-mannopyranosyl-α-D-mannopyranoside (2) has been performed as shown on Scheme II. It involves first the preparation of the disaccharide 10, which was obtained in 82% yield by a mercuric bromide–mercuric cyanide catalyzed condensation of methyl 2-*O*-allyl-4,6-*O*-benzylidene-α-D-mannopyranoside (5) and tri-*O*-acetyl-α-D-lyxopyranosyl bromide (9). The latter, rather unstable compound was prepared immediately before use by reaction[1] of trimethylsilyl bromide with the ortho ester 8, a stable crystalline compound.[7,8] The NMR spectrum of the disaccharide 10 has two doublets in the anomeric re-

Scheme I



R_1, R_2 : glycosyl moieties

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(1) For part I, see F. M. Winnik, J.-R. Brisson, J. P. Carver, and J. J. Krepinsky, *Carbohydr. Res.*, in press.
(2) J. Montreuil, *Adv. Carbohydr. Chem. Biochem.*, **37**, 157 (1980).
(3) T. Ogawa, K. Katano, and M. Matsui, *Carbohydr. Res.*, **64**, C3 (1978); J. Arnap and J. Lonngren, *Acta Chem. Scand., Ser. B*, **B32**, 696 (1978).
(4) A. E. MacKenzie, F. M. Winnik, J. J. Krepinsky, and J. P. Carver, to be submitted for publication in Biochemistry.
(5) For a general review, see A. F. Bochkov and G. E. Zaikov, "Chemistry of the *O*-Glycosidic Bond", Pergamon Press, Oxford, 1979.
(6) B. Helferich and J. Zirner, *Chem. Ber.*, **95**, 2604 (1962).
(7) M. Mazurek and A. S. Perlin, *Can. J. Chem.*, **43**, 1918 (1965).
(8) The use of the ortho ester might appear redundant, since the ortho ester itself is prepared from the bromide. This purification of the bromide via the ortho ester leads to a cleaner and more efficient condensation.

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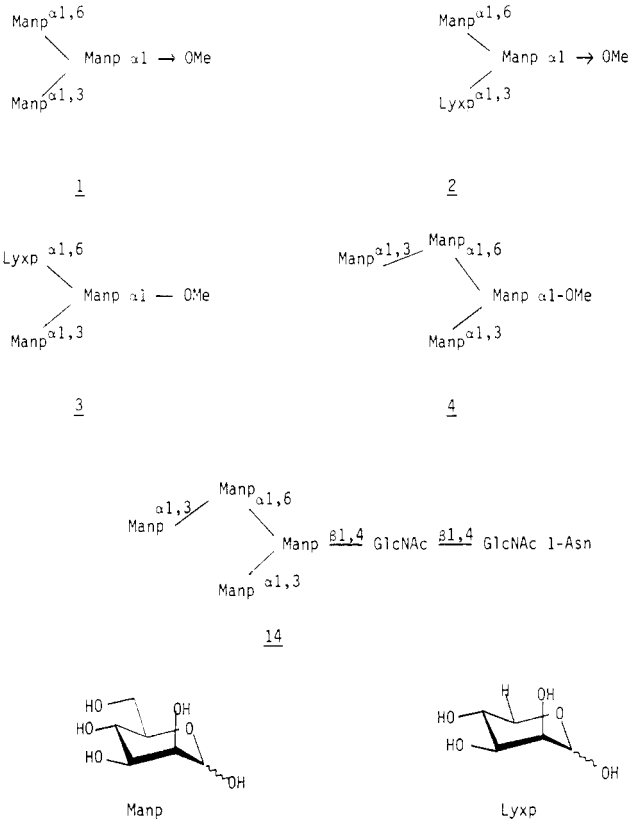
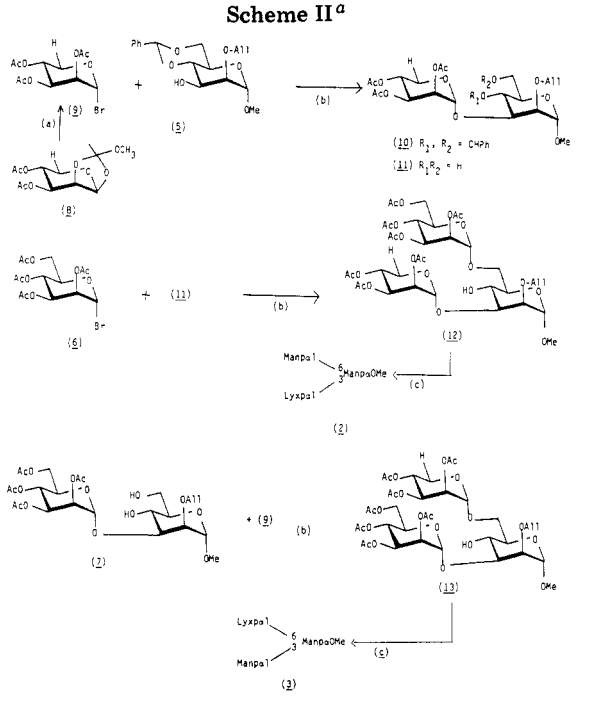


Figure 1.

Scheme II[a]



[a] Reagents: (a) Me_3SiBr, CH_2Cl_2; (b) $HgBr_2$, $Hg(CN)_2$, molecular sieves, CH_3CN; (c) 10% Pd/C, EtOH, AcOH, H_2O, 70%, then MeONa, MeOH. AC = acetyl; All = allyl.

gion: a 1.4-Hz doublet at δ 4.70 assigned to H-1′ and a 2.4-Hz doublet at δ 5.17 assigned to H-1.[9] The presence of three acetyl proton signals at δ 1.99, 2.04, and 2.05 and of a methoxy proton signal at δ 3.37 are in agreement with the proposed structure. The α configuration was assigned to the newly formed glycosidic bond on the basis of mechanistic considerations[10] and by analogy with the synthesis of methyl 2-*O*-allyl-4,6-*O*-benzylidene-3-*O*-(tetra-*O*-acetyl-α-D-mannopyranosyl)-α-D-mannopyranoside.[1] Deprotection of the hydroxyl groups of the disaccharide **10** was effected in three consecutive steps: hydrolysis of the benzylidene group with 60% acetic acid[11] to give **11**, deallylation with palladium on charcoal,[12] Zemplén deacetylation. It led to methyl 3-*O*-α-D-lyxopyranosyl-α-D-mannopyranoside (**11a**).

The final step in the preparation of the trisaccharide **12** involved glycosylation of the diol **11** with 1 equiv of tetra-*O*-acetyl-α-D-mannopyranosyl bromide **6** (Scheme II). Under Helferich conditions, only one product was obtained in 58% yield. Its NMR spectrum in $CDCl_3$ exhibites three resonances in the anomeric region, a 1.4-Hz doublet at δ 4.71, a 1.5-Hz doublet at δ 4.92, and 3.3-Hz doublet at 5.08, assigned to the protons H-1, H-1″, and H-1′, respectively. Seven three-proton singlets between δ 1.98 and 2.15 are assigned to the acetyl protons resonances, and a three-proton singlet at δ 3.38 is assigned to the methoxy proton resonance. A deuterium-exchangeable one-proton doublet at δ 2.95 (J = 12 Hz) is assigned to the C-4 hydroxyl proton. The regioselectivity of the glycosylation could not be inferred from the NMR spectrum of the condensation product. However, we have shown that under identical conditions, reaction of the bromide **6** with the dimannoside methyl 2-*O*-allyl-3-*O*-(tetra-*O*-acetyl-α-D-mannopyranosyl)-α-D-mannopyranoside (**7**) gave only the C-6 glycosylated product.[1] Thus, by analogy, we assigned structure **12** to the condensation product of the bromide **6** and the analogous disaccharide **11**. Standard deprotection of **12** gave methyl 3-*O*-α-D-lyxopyranosyl-6-*O*-α-D-mannopyranosyl-α-D-mannopyranoside (**2**). The NMR spectrum of **2** has three anomeric proton resonances at δ 4.73 (1.7 Hz), 4.91 (1.7 Hz), and 5.02 (1.7 Hz) assigned to H-1, H-1″, and H-1′, respectively.

Methyl 6-*O*-α-D-lyxopyranosyl-3-*O*-α-D-mannopyranosyl-α-D-mannopyranoside (**3**) was synthesized starting from the known dimannoside **7** (Scheme II). The Helferich glycosylation of **7** with 1 equiv of tri-*O*-acetyl-α-D-lyxopyranosyl bromide **9** gave the protected trisaccharide **13** in 59% yield. The hydroxyl groups of **13** were deblocked under standard conditions to give compound **3** characterized by its NMR spectrum (see Experimental Section).

Synthesis of the Tetrasaccharide 4. The oligosaccharide **4** constitutes the tetramannose part of the glycopeptide GP VI (i.e., F) (**14**) isolated from the pronase digest of ovalbumin.[13] This is glycopeptide has the smallest carbohydrate unit among the ovalbumin glycopeptides. It is also the least abundant, since it represents less than 1% dry weight of the total glycopeptide fraction.

(9) The carbon positions of the central mannoside are designated 1–6, the carbon positions of the C-3 substituent are designated 1′–6′, and the carbon positions of the C-6 substituent are designated 1″–6″.

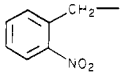
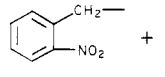
(10) This conclusion is corroborated by the calculation of molecular rotations according to Hudson's isorotation rules (cf. J. Staněk, M. Černý, J. Kocourek, and J. Pacák, "The Monosaccharides", Academic Press, New York, 1963, p 50) of methyl 3-*O*-α-D-lyxopyranosyl-α-D-mannopyranoside (11a; $[\alpha]_D$ +44.7°). Its $[M]_D$ +136° agrees better with the calculated $[M]_D$ for the α anomer (+253°) than for the β anomer (−55°). Similar difference was observed in the case[1] of methyl 3-*O*-α-D-mannopyranosyl-α-D-mannopyranoside (deprotected 7, $[\alpha]_D$ +93.5°): $[M]_D$ found +347.8°; calcd $[M]_D$ (α-anomer) +321.3°, (β-anomer) +21.0°.

(11) R. U. Lemieux, T. Takeda, and B. Y. Chung, *ACS Symp. Ser.* No. 39, 90 (1976).

(12) R. Boss and R. Scheffold, *Angew. Chem., Int. Ed. Engl.*, **15**, 558 (1976).

(13) T. Tai, K. Yamashita, and A. Kobata, *Biochem. Biophys. Res. Commun.*, **78**, 434 (1977); J. Conchie and I. Strachan, *Carbohydr. Res.*, **63**, 193 (1978).

Table I. Protective Group R of the Anomeric Hydroxyl Group

R	preparation[a] method	yield, %	ref	removal method	yield, %	ref
CCl_3CH_2—	17 + CCl_3CH_2OH + $BF_3 \cdot Et_2O$	30[b]	14	Zn/AcOH	45	14
CH_2=CH—CH	18 + CH_2=CH—CH_2OH, HCl (60 °C, N_2)	46	17	Pd/C, AcOH, EtOH, H_2O, N_2	70	12
$PhCH_2$—	18 + $PhCH_2OH$, HCl (60 °C, N_2)	45	18	H_2, Pd/C, EtOH	75	18
	17 +  + $Hf(OAc)_2$ + $CaSO_4$, benzene	28[c]	19	$h\nu$, $\lambda > 320$ nm	high (not given)	19

[a] (17) Penta-*O*-acetyl-D-mannopyranose; (18) D-mannose. [b] Yield based on D-mannose. [c] Reported yield.[19]

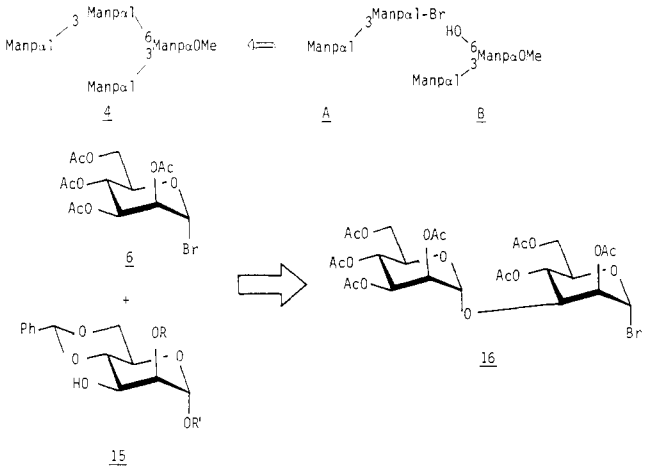
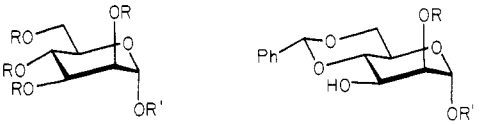


Figure 2.

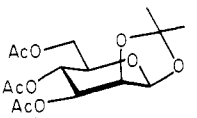
In order to achieve the most efficient synthesis of **4**, we devised a scheme where the oligosaccharide **4** was formed by condensation of two disaccharides: a dimannosyl bromide, A, and a dimannosyl alcohol, B, (Figure 2). We have already prepared a dimannoside of type B, compound **7**, and shown that it undergoes selective glycosylation of the C-6 hydroxyl group with sugar bromides. As a type A compound, 3-*O*-(tetra-*O*-acetyl-α-D-mannopyranosyl)-2,4,6-tri-*O*-acetyl-α-D-mannopyrannosyl bromide (**16**) was selected. **16** can be obtained by condensation of tetra-*O*-acetyl-α-D-mannopyranosyl bromide (**6**) and a monosaccharide such as **15**, where only the C-3 hydroxyl group is free (Figure 2). In this approach one faces a delicate choice for the anomeric protecting group R′—such a group has to remain intact during Helferich glycosylation, and its removal should affect neither an acetate group nor a glycosidic bond.

Since the protection of anomeric hydroxyl groups is a major problem in the synthesis of complex oligosaccharides, a detailed account is given here of the preparation and removal techniques for the acceptable blocking groups (Table I). The 2,2,2-trichloroethyl group has been used as an anomeric protective group in 2-amino-2-deoxypyranosides,[14] furanosides,[15] and pyranosides.[16] We obtained the best yields of 2,2,2-trichloroethyl α-D-mannopyranoside (**19**) by reaction of penta-*O*-acetyl-D-mannopyranose (**17**) with 2,2,2-trichloroethanol in the presence of boron trifluoride etherate and subsequent Zemplén deacetylation of the tetra-*O*-acetyl compound **19a**. We never succeeded in bringing the glycosylation to completion and had to perform a chromatographic separation of **19a** and **17**. Both allyl α-D-mannopyranoside (**20a**) and benzyl α-D-mannopyranoside (**20b**) were prepared in good yields by treating D-mannose with HCl-saturated allyl alcohol and benzyl alcohol, respectively. The reaction was performed at 60 °C, under nitrogen, in order to avoid air oxidation of the reducing sugar–a side reaction that drastically reduces the glycosylation yields.



17, R = R′ = Ac
18, R = R′ = H
19, R = H; R′ = CH_2CCl_3
19a, R = Ac; R′ = CH_2CCl_3
20a, R = H; R′ = CH_2—CH=CH_2
20b, R = H; R′ = CH_2Ph

15a, R = R′ = CH_2CH=CH_2
15b, R = R′ = CH_2Ph
15c, R = CH_2—CH=CH_2; R′ = CH_2Ph
21a, R = H; R′ = CH_2—CH=CH_2
21b, R = H; R′ = CH_2Ph



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The allyl and benzyl α-D-mannopyranosides were converted as follows to a partially protected monosaccharide of the type **15**, the important intermediate in the synthesis of the disaccharide **16**. The C-4 and C-6 hydroxyl groups were protected by formation of a benzylidene group in both **20a** and **20b**, leading to allyl 4,6-*O*-benzylidene-α-D-mannopyranoside (**21a**) and benzyl 4,6-*O*-benzylidene-α-D-mannopyranoside **21b**,[20] respectively. The allyl mannoside **21a** was allylated with allyl bromide under phase-transfer conditions to give **15a**, while the benzyl mannoside **21b** was alkylated with benzyl bromide to give **15b** and with allyl bromide to give **15c**. The regiochemistry of the O-alkylation in **21a** and **21b** was established by NMR spin-decoupling experiments analogous to those reported for the corresponding methyl mannoside.[1] The NMR data (cf. Experimental Section) indicate that upon allylation

(14) R. U. Lemieux and H. Driguez, *J. Am. Chem. Soc.*, **97**, 4069 (1975).
(15) M. Prystasz, L. Kalvoda, and F. Šorm, *Coll. Czech. Chem. Commun.*, **41**, 1426 (1975).
(16) P. A. Risbood, L. A. Reed, III, and L. Goodman, *Carbohydr. Res.*, **88**, 245 (1981).
(17) E. A. Talley, M. D. Vale, and E. Yanovsky, *J. Am. Chem. Soc.*, **67**, 2037 (1945).
(18) P. A. J. Gorin and A. S. Perlin, *Can. J. Chem.*, **39**, 2474 (1961).
(19) U. Zehavi and A. Patchornik, *J. Org. Chem.*, **37**, 2285 (1972).
(20) G. Alfredsson, H. B. Boren, and P. J. Garegg, *Acta Chem. Scand.*, **26**, 3431 (1972).

Table II. ^{1}H NMR Chemical Shifts of the Mono- and Di(methyl orthoacetates) 24 and 25[a]

	H-1	H-2	H-3	H-4	H-5	H-6′	H-6	OCH_3	CH_3
24	5.46 $J_{1,2}$ = 2	4.60 $J_{1,2}$ = 2 $J_{2,3}$ = 4	3.86 $J_{2,3}$ = 4 $J_{3,4}$ = 10	5.29 $J_{3,4} = J_{4,5}$ 10	3.62 m	4.20 $J_{5,6'}$ = 5 $J_{6,6'}$ = 12	4.14 $J_{5,6}$ = 3 $J_{6,6'}$ = 12	3.29	1.75
25	5.50 $J_{1,2}$ = 2	4.62 $J_{1,2}$ = 2 $J_{2,3}$ = 4	5.15 $J_{2,3}$ = 4 $J_{3,4}$ = 10	5.30 $J_{3,4} = J_{4,5}$ 10	3.65 m	4.24 $J_{5,6'}$ = 5 $J_{6,6'}$ = 12	4.15 $J_{5,6}$ = 3 $J_{6,6'}$ = 12	3.29	1.75

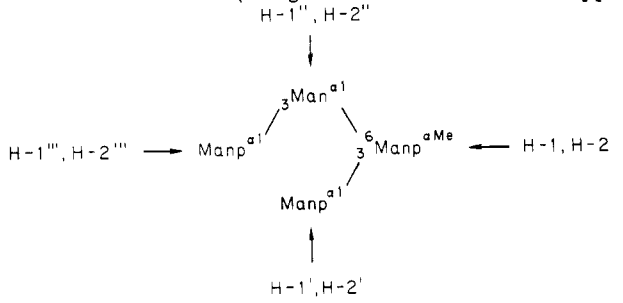
[a] Chemical shifts are in ppm relative to internal Me_4Si in $CDCl_3$ at 24 ± 1 °C; coupling constants are in Hz.

Table III. Chemical Shifts of the Anomeric and C-2 Protons in 1 and 4[a]

	H-1	H-1′	H-1″	H-1‴	H-2	H-2′	H-2″	H-2‴	H-3″
1	4.73[c]	5.10	4.91		4.09	4.06	3.99		3.84
4	4.73	5.10	4.89	5.16	4.09	4.07	4.14	4.07	3.95

[a] Chemical shifts are in ppm relative to internal DSS (using internal acetone at 2.225 ppm) in D_2O at 23 ± 2 °C.

[b]



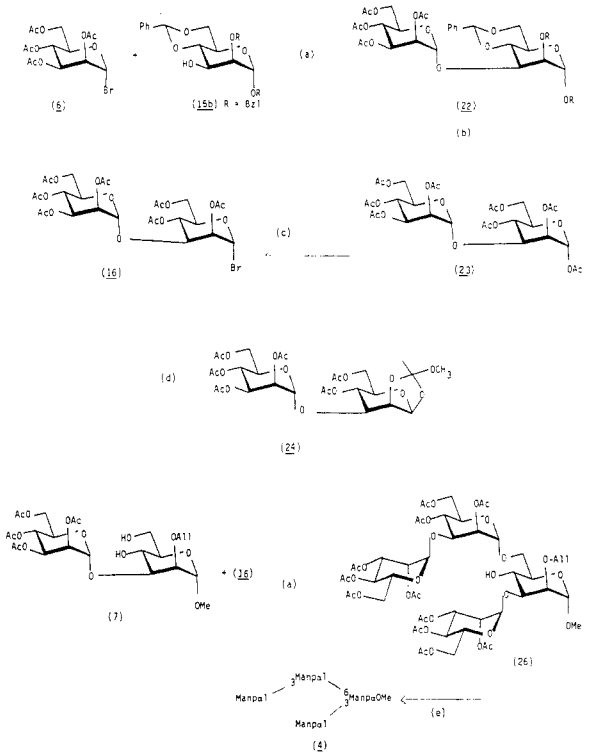
[c] From ref 1.

of the C-2 hydroxyl group in **21a** and **21b** the resonance of H-2 is shifted upfield by 1.17 ppm. This effect, which was observed also in the case of methyl 4,6-*O*-benzylidene-α-D-mannopyranoside,[1] confirms the assignment of structures **15b** and **15c** to the phase-transfer allylation products of **21a** and **21b**.

The disaccharide **16**, the fundamental building block in the synthesis of the target tetrasaccharide, was prepared in four steps from benzyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (**15b**). This compound was favored over **15a** and **15c** for the following reasons.[21] All intermediates with an anomeric benzyl group are crystalline. The C-1 and C-2 benzyl groups as well as the benzylidene group can be hydrogenolyzed in a single, high-yield reaction (vide infra) (Scheme III). Helferich glycosylation of **15b** with tetra-*O*-acetyl-α-D-mannopyranosyl bromide (**6**) gave the disaccharide **22** in 73% yield. The NMR spectrum of **22** shows two doublets characteristic of anomeric protons at δ 4.96 (1.5 Hz) and at δ 5.27 (1.5 Hz), assigned to H-1 and H-1′, respectively. Four three-proton singlets between δ 1.90 and 2.07 are assigned to the acetyl proton resonances. Hydrogenolysis of the benzyl and benzylidene groups in **22** over palladium on carbon gave the reducing disaccharide, which was acetylated to give **23** as an oil. The bromide **16** was obtained by treatment of a cold anhydrous solution of **23** in methylene chloride with a solution of hydrogen bromide in glacial acetic acid.[22]

16 was converted to the crystalline ortho ester **24** which was fully characterized. In the NMR spectrum of **24**, the assignments were made on the basis of spin-decoupling experiments and by comparison with the spectrum of 3,4,6-tri-*O*-acetyl-α-D-mannopyranose-1,2-(methyl ortho-

Scheme III[a]



[a] Reagents: (a) $HgBr_2$, $Hg(CN)_2$, molecular sieves, CH_3CN; (b) H_2, 10% Pd/C, EtOH, then AC_2O-py; (c) AcOH/HBr, CH_2Cl_2; (d) CH_3OH, 2,6-lutidine, $CHCl_3$; (e) 10% Pd/C, EtOH, AcOH, H_2O, 70 °C, then CH_3ONa, CH_3OH. AC = acetyl; All = allyl; Bzl = benzyl.

acetate) (**25**)[1] (Table II). The following resonances are characteristic of the methyl orthoacetate group in **24**: two three-protons singlets at δ 1.75 and 3.29 assigned to the quaternary methyl and methoxy groups, respectively, a one-proton doublet at δ 5.46 (J = 2 Hz) and a one-proton doublet of doublets at δ 4.60 (J = 2 Hz, J = 4 Hz) assigned

(21) We also prepared the condensation products of tetra-*O*-acetyl-α-D-mannopyranosyl bromide with each of the monosaccharides **15a** and **15c**. However, the removal of the allyl group in each disaccharide was accompanied by side reactions and the reducing disaccharides could be isolated in relatively poor yields only.

(22) N. K. Kochetkov, V. I. Torgov, N. N. Malysheva, and A. S. Shashkov, *Tetrahedron*, **36**, 1099 (1980); K. L. Matta, C. F. Piskorz, and J. J. Barlow, *Carbohydr. Res.*, **90**, C1 (1981).

to H-1 and H-2, respectively. The coupling constant $J_{1,2}$ is larger than usual for α-mannopyranose.[23] This effect reflects a slight change in the conformation of the pyranose ring resulting from the introduction of a cis-fused five-membered ring between C-1 and C-2. It is observed also in the spectrum of **25**. The presence of a one-proton doublet at δ 4.98 ($J_{1,2}$ = 1.7 Hz) assigned to H-1 and of six three-protons singlets between δ 1.99 and 2.17 due to the acetyl protons resonances confirms the fact that **24** is indeed a disaccharide. In **25** the resonance of H-3 occurs at δ 5.15 ($J_{2,3}$ = 4 Hz, $J_{3,4}$ = 10 Hz), while in the disaccharide **24** a doublet of doublets at δ 3.86 ($J_{2,3}$ = 4 Hz, $J_{3,4}$ = 10 Hz) is assigned to H-3. The upfield shift of the H-3 resonance in **24** is consistent with the replacement of a C-3 resonance in **24** is consistent with the replacement of a C-3 acetyl group by a glycosidic bond and corroborates the assigned linkage between the two mannopyranosyl units in **24**.

The final step of the sequence leading to the tetrasaccharide **4** was performed successfully by Helferich glycosylation of the dimannoside **7** with the dimannosyl bromide **16** (Scheme II). The latter compound was prepared immediately prior to use either by reaction of the octaacetyl compound **23** with hydrobromic acid (vide supra) or by opening of the ortho ester group in **24** with trimethylsilyl bromide.[8,24] After standard deprotection of all hydroxyl groups, the crude reaction mixture was purified by size-exclusion chromatography on Bio Gel P-2. The compound eluting first was identified as the tetrasaccharide **4** on the basis of its NMR spectrum. Table III presents the chemical shifts of the anomeric and C-2 protons for the structurally related compounds **1** and **4**. There is a remarkable coincidence between the chemical shifts of analogous protons, except for those of the protons H-2″: the presence of a C-3 mannopyranosyl substituent results in a 0.15-ppm downfield shift of the proton H-2″. Likewise the resonance of H-3″ in **4** is shifted downfield compared to H-3″ in **1**. These effects, which can be predicted by shift-increment calculations,[26] are diagnostic of the substitution pattern. A complete analysis of the spectrum of **4** will be reported in a separate communication,[26] together with some additional data concerning NMR spectroscopy of these compounds.

Experimental Section

Melting points were determined on a Fischer-Johns melting-point apparatus and are uncorrected. Optical rotations were measured with a Jasco (Model ORD/UV-5) polarimeter at 26 ± 1 °C. Microanalyses were performed by the Microanalytical Laboratory Ltd., Markham, Ontario. ^{1}H NMR spectra were recorded at 360 MHz with a Nicolet spectrometer at the Toronto Biomedical NMR Centre, University of Toronto. They were obtained at 23 ± 2 °C either in $CDCl_3$ containing 1% Me_4Si as the internal standard or in D_2O (99.996%, Merck Sharp and Dohme) with acetone (0.1%, 2.225 ppm relative to internal DSS) as the internal standard. For a 10 mM solution of sugar in D_2O, 128 transients were accumulated and a pulse angle of 90° was used in all cases. Solutions were concentrated in vacuo with the bath temperature kept below 35 °C. All solvents were distilled before use. Dichloromethane was dried by distillation under dry nitrogen in the presence of P_2O_5 and kept over 4A molecular sieves. Acetonitrile was dried by a 3-h reflux over CaH_2 and subsequent distillation under dry nitrogen onto 4A molecular sieves, the first 15% of the distillate being discarded. Methanol was dried by a 4-reflux over Mg and trace of iodine and subsequent under dry nitrogen onto 3A molecular sieves. $HgBr_2$ was dissolved in hot toluene, dried by azeotropic distillation, and crystallized upon cooling from toluene.

TLC was performed on precoated plates of silica gel 60F, 0.20 mm thick (Merck). For detection, the plates were sprayed with 50% H_2SO_4 and heated for 3–5 min at 130 °C. Gel filtration chromatography was performed on Bio-Gel P-2, 200–400 mesh (Bio Rad), the column effluent being monitored with a Flow Cell Refractive Index detector (Pharmacia). Analytical HPLC was performed with a Beckman HPLC 324 system equipped with a multiple-wavelength detector set at 254 nm and a refractive index detector. An Ultrasphere ODS column Beckman-Altex (250 × 4.6 mm) eluted with 4:6 H_2O/CH_3CN was used as well as a Microporasil-5 column (Waters, 300 × 3.9 mm) eluted with 9.5:0.5 toluene/ethyl acetate. Preparative HPLC was done with a Waters Prep LC/System 500-A equipped with one PrePAK-500/Silica cartridge eluted with 9.5:0.5 toluene–ethyl acetate.

The allyl- and acetyl-substituted carbohydrates were deprotected as follows: the saccharide (1 equiv) was added to a suspension of palladium on carbon (10%, 0.1 equiv) in 2:1:1 ethanol/water/glacial acetic acid. The solution was heated at 75 °C for 17 h under nitrogen. The cold reaction mixture was filtered through a Celite bed. The filtrate was neutralized with $NaHCO_3$ and evaporated. The residue was taken up with CH_2Cl_2 which was washed with water, saturated $NaHCO_3$, and brine. It was dried over $MgSO_4$, filtered, and evaporated to give an amorphous solid. This was dissolved in dry methanol and treated with sodium methoxide (0.05 equiv, 2 M in methanol). After 20 min, the solution was evaporated to dryness. The residue was dissolved in water and desalted with mixed-bed resin (AG501-X8, 20–50 mesh, Bio-Rad). Filtration and lyophilization gave the crude deprotected oligosaccharide.

3,4-Di-*O*-acetyl-β-D-lyxopyranose 1,2-(Methyl orthoacetate) (8). The orthoacetate **8** was prepared in three steps from D-lyxose, as described by Mazurek and Perlin[7] (yield: 43% from D-lyxose): mp 92–93 °C (MeOH), (lit.[7] mp 90 °C); $[\alpha]_D$ −108.5° (*c* 0.39 in $CHCl_3$) (lit.[7] $[\alpha]_D$ −103.1°, *c* 4.0 in $CHCl_3$); TLC (9.75:0.25 $CHCl_3$/MeOH) R_f 0.51; NMR δ 1.73 (s, 3 H, $CHC(OR)_3$), 2.07 (s, 3 H, Ac) 2.13 (s, 3 H, Ac), 3.30 (s, 3 H, OCH_3), 3.66 (dd, 1 H, $J_{5,5}$ = −14 Hz, $J_{4,5'}$ = 2 Hz, H-5′), 4.18 (dd, 1 H, $J_{5,5'}$ = −14 Hz, $J_{4,5}$ = 2 Hz, H–5), 4.61 (dd, 1 H, $J_{1,2}$ = 5 Hz, $J_{2,3}$ = 2.2 Hz, H–2), 5.05–5.10 (m, 1 H, H-4), 5.20 (dd, 1 H, $J_{2,3}$ = 2.2 Hz, $J_{3,4}$ = 7 Hz, H-3), 5.60 (d, 1 H, $J_{1,2}$ = 5 Hz, H-1).

2,3,4-Tri-*O*-acetyl-α-D-lyxopyranosyl Bromide (9). Trimethylsilyl bromide (460 mg, 3.0 mmol) was added dropwise to a solution of **8** (522 mg, 1.8 mmol) in dry CH_2Cl_2 (20 mL). The solution was heated at reflux under nitrogen for 2 h, cooled to room temperature, evaporated, and dried under high vacuum for 1 h. The resulting amorphous solid was used without further purification.

Methyl 2-*O*-Allyl-4,6-*O*-benzylidene-3-*O*-(2,3,4-tri-*O*-acetyl-α-D-lyxopyranosyl)-α-D-mannopyranoside (10). To a solution of methyl 2-*O*-allyl-4,6-*O*-benzylidene-α-D-mannopyranoside (**5**) (500 mg, 1.55 mmol) in dry acetonitrile (15 mL) containing 4A molecular sieves were added sequentially mercuric bromide (640 mg, 1.78 mmol), mercuric cyanide (455 mg, 1.80 mmol), and a solution of **9** [from 522 mg of (**8**) in dry acetonitrile (3 mL)]. The reaction mixture was stirred at room temperature in a closed system for 90 min. Evaporation of the solvent gave an oily residue which was extracted three times with chloroform. The organic extracts were washed twice with saturated aqueous KCl solution and twice with saturated $NaHCO_3$ solution, water, and brine. The dried (Na_2SO_4) organic phase was concentrated, and the condensation product **10** (755 mg, 82%) was crystallized from the residue (45:5 ether/hexane): mp 168–169 °C; TLC (3:2 toluene/ethyl acetate) R_f 0.45; NMR δ 1.99 (s, 3 H, Ac), 2.04 (s, 3 H, Ac), 2.05 (s, 3 H, Ac), 3.37 (s, 3 H, OCH_3), 3.62–3.92 (m, 8 H), 4.10–4.32 (m, 4 H), 4.70 (d, 1 H, $J_{1,2}$ = 1.4 Hz, H-1), 5.17 (d, 1 H $J_{1,2}$ = 2.4 Hz, H-1′), 5.25–5.40 (m, 3 H), 5.60 (s, 1 H, OCH<), 5.95–6.04 (m, 1 H, CH=CH_2), 7.30–7.42 (m, 5 H, Ar).

Methyl 2-*O*-Allyl-3-*O*-(2,3,4-tri-*O*-acetyl-α-D-lyxopyranosyl)-α-D-mannopyranopyranoside (11). A suspension of **10** (300 mg, 0.51 mmol) in 60% aqueous acetic acid (10 mL) was heated at 80 °C for 30 min. The clear solution was cooled

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to room temperature and concentrated to dryness under high vacuum. The residue was taken up with CH_2Cl_2 and washed with water, saturated $NaHCO_3$, and brine. It was dried over Na_2SO_4, filtered, and evaporated to give **11** as an amorphous solid (210 mg, 84%), TLC (1:1 ethyl acetate–toluene) R_f 0.05. **11** was reacted without further purification.

Methyl 3-*O*-α-D-Lyxopyranosyl-α-D-mannopyranoside (11a). Deprotection of **11** as described in the general procedure gave an amorphous solid which was purified on a Bio Gel P-2 column and eluted with degassed, distilled water; mp 150–152 °C; $[\alpha]_D$ +44.7° (*c* 0.29 in water); NMR (D_2O) δ 3.41 (s, 3 H, OCH_3), 3.58–3.83 (m, 9 H), 3.99 (m, 1 H, H-2′), 4.07 (dd, 1 H, $J_{1,2}$ = 1.7 Hz, $J_{2,3}$ = 3 Hz, H-2), 4.74 (d, 1 H, $J_{1,2}$ = 1.7 Hz, H-1), 5.03 (d, 1 H, $J_{1',2'}$ = 3 Hz, H-1′).

Methyl 3-*O*-α-D-Lyxopyranosyl-6-*O*-α-D-mannopyranosyl-α-mannopyranoside (2). To a solution of **11** (620 mg, 1.26 mmol) in dry CH_3CN (20 mL) containing 4A molecular sieves were added sequentially $HgBr_2$ (580 mg, 1.61 mmol), $Hg(CN)_2$ (403 mg, 1.60 mmol), and a solution of **6** [1.60 mmol prepared from **25** (580 mg, 1.60 mmol) and trimethylsilyl bromide (300 mg, 1.96 mmol)[1]] in dry CH_3CN (3 mL). After 30 min, TLC indicated complete disappearance of starting material (1:1 toluene/ethyl acetate). The solvent was evaporated, and the residue was extracted three times with $CHCl_3$. The organic extracts were washed with aqueous saturated KCl, saturated aqueous $NaHCO_3$, water, and brine. The dried (Na_2SO_4) organic layer was evaporated to give **12** as a colorless oil (594 mg, 58%); TLC (1:1 toluene/ethyl acetate) R_f 0.25; NMR ($CDCl_3$) δ 1.98 (s, 3 H, Ac), 2.050 (s, 3 H, Ac), 2.054 (s, 3 H, Ac), 2.07 (s, 3 H, Ac), 2.10 (s, 3 H, Ac), 2.12 (s, 3 H, Ac), 2.15 (s, 3 H, Ac), 2.95 (d, 1 H, *J* = 3.5 Hz, exchangeable with D_2O, OH), 3.38 (s, 3 H, OCH_3), 3.71 (dd, 1 H, $J_{1,2}$ = 1.4 Hz, $J_{2,3}$ = 4 Hz, H-2), 4.71 (d, 1 H, $J_{1,2}$ = 1.4 Hz, H-1), 4.92 (d, 1 H, $J_{1'',2''}$ = 1.5 Hz, H-1″), 5.08 (d, 1 H, $J_{1',2'}$ = 3.3 Hz, H-1′), 5.85–6.0 (m, 1 H, C**H**=CH_2). Deprotection of the hydroxyl groups of **12** in the usual manner gave **2** as an amorphous solid (185 mg, 53%) which was purified on a Bio Gel P-2 column; $[\alpha]_D$ +91.5° (*c* 0.23 in water); NMR δ (D_2O) 3.41 (s, 3 H, OCH_3), 3.59–4.05 (m, 16 H), 4.08 (dd, 1 H, $J_{1,2}$ = 4 Hz, $J_{2,3}$ = 8 Hz, H-2), 4.73 (d, 1 H, $J_{1,2}$ = 1.8 Hz, H-1), 4.91 (d, 1 H, $J_{1'',2''}$ = 1.8 Hz, H-1″), 5.02 (d, 1 H, $J_{1',2'}$ = 4 Hz, H-1′). Anal. Calcd for $C_{18}H_{32}O_{15}$: C, 44.26; H, 6.60. Found: C, 44.34; H, 6.64.

Methyl 6-*O*-α-D-Lyxopyranosyl-3-*O*-α-D-mannopyranosyl-α-D-mannopyranoside (3). To a solution of **7** (500 mg, 0.89 mmol) in dry CH_3CN (20 mL) containing 4A molecular sieves were added sequentially $HgBr_2$ (3.82 mg, 1.06 mmol), $Hg(CN)_2$ (270 mg, 1.06 mmol), and a solution of **9** [prepared from **8** (290 mg, 1.0 mmol) and trimethylsilyl bromide (182 mg, 1.19 mmol)[1]] in dry CH_3CN (3 mL). After 30 min, TLC indicated total disappearance of starting material (1:1 toluene–ethyl acetate). The solvent was evaporated, and the residue was extracted three times with $CHCl_3$. The organic extracts were washed with saturated KCl solution, saturated $NaHCO_3$ solution, water, and brine. The dried (Na_2SO_4) organic layer was evaporated to give **13** as a foamy solid (430 mg, 59%): TLC (1:1 toluene/ethyle acetate) R_f 0.28; NMR ($CDCl_3$) δ 1.98 (s, 3 H, Ac), 2.02 (s, 3 H, Ac), 2.06 (s, 6 H, two Ac), 2.10 (s, 3 H, Ac), 2.12 (s, 3 H, Ac), 2.14 (s, 3 H, Ac), 3.0 (1 H, br s, exchangeable with D_2O, OH), 3.36 (s, 3 H, OCH_3), 3.65–4.25 (m, 12 H), 4.73 (d, 1 H, $J_{1,2}$ = 1.4 Hz, H-1), 4.86 (d, 1 H, $J_{1'',2''}$ = 2.6 Hz, H-1″), 5.15–5.40 (m, 9 H), 5.86–6.0 (m, 1 H, C**H**=CH_2). Deprotection of the hydroxyl groups of **13** as described in the general procedure gave **3** as an amorphous solid (122 mg, 48%) which was purified further on a Bio Gel P-2 column eluted with water; $[\alpha]_D$ +89.6° (*c* 0.23 in water); NMR (D_2O) δ 3.41 (s, 3 H, OCH_3), 3.52–3.90 (m, 15 H), 3.94 (t, 1 H, $J_{1'',2''}$ = $J_{2'',3''}$ = 3 Hz, H-2″), 3.98–4.04 (m, 2 H) 4.06 (dd, 1 H, $J_{1',2'}$ = 1.7 Hz, $J_{2',3'}$ = 3.2 Hz, H-2′), 4.09 (dd, 1 H, $J_{1,2}$ = 1.8 Hz, $J_{2,3}$ = 3 Hz, H-2), 4.73 (d, 1 H, $J_{1,2}$ = 1.8 Hz, H-1) 4.84 (d, 1 H, $J_{1'',2''}$ = 3 Hz, H-1″), 5.11 (d, 1 H, $J_{1',2'}$ = 1.7 Hz, H-1′).

2,2,2-Trichloroethyl Tetra-*O*-acetyl-α-D-mannopyranoside (19a). To a solution of **17** (20.0 g, 53.4 mmol) in dry diethyl ether (50 mL) at 0 °C were added sequentially 2,2,2-trichloroethanol (16 mL, freshly distilled) and $BF_3{\cdot}Et_2O$ (25 mL, distilled before use under reduced pressure). The reaction mixture was kept at 0 °C for 1 h and then at room temperature for 4 h. It was poured over ice (100 g) and diluted with diethyl ether. The organic extracts were washed with water, aqueous $NaHCO_3$, and brine. The dried solution was evaporated to give an oil (21 g) containing **19a** (60% by HPLC) and starting material, **17**. Preparative HPLC separation (98:2 toluene/ethyl acetate) gave pure **19a** (11.2 g, 44%): mp 96–97 °C (ether); $[\alpha]_D$ +45.3° (*c* 0.22 in $CHCl_3$; NMR ($CDCl_3$). Anal. Calcd for $C_8H_{13}O_6Cl_3$: C, 30.84; H, 4.20. Found: C, 30.60; H, 4.09.

2,2,2-Trichloroethyl α-D-Mannopyranoside (19). A solution of **19a** (9.0 g, 1.88 mmol) in anhydrous CH_3O (40 mL) was treated with CH_3ONa (1 mmol, 1 mL, 2 M in CH_3OH). After being kept at room temperature for 30 min, the reaction mixture was concentrated. The residue was dissolved in water (30 mL), desalted with mixed-bed resin, and filtered. Upon concentration of the filtrate, compound **19** crystallized (4.1 g, 70%); 160 °C dec; $[\alpha]_D$ +47.4 (*c* 0.24 in water).

Allyl α-D-Mannopyranoside (20a). D-mannose (**18**) (10.0 g, 55 mmol) was added to allyl alcohol (80 mL) saturated with HCl at 0 °C. The reaction mixture was heated at 60 °C under nitrogen for 4 h and kept at room temperature overnight. The clear solution obtained was neutralized with $NaHCO_3$ filtered over Celite. The filtrate was evaporated to give an oil, and crystallization from acetone gave **20a** (5.6 g, 46%): mp 138–139 °C (lit.[12] mp 98–99 °C) $[\alpha]_D$ +51.6° (*c* 0.23 in water), (lit.[17] $[\alpha]_D$ +99° (in water)); TLC (9:4:2 ethyl acetate–2-propanol/water) R_f 0.32; NMR (D_2O) δ 3.62–3.83 (m, 4 H), 3.89 (dd, 1 H, $J_{6,6'}$ = −12 Hz, $J_{5,6}$ = 2 Hz, H-6), 3.90 (dd, 1 H, $J_{2,3}$ = 3 Hz, H-2), 4.05–4.01 (m, 1 H, CH_2–CH=CH_2), 4.21–4.27 (m, 1 H, CH_2–CH=CH_2), 4.91 (d, 1 H, $J_{1,2}$ = 1.7 Hz, H-1), 5.25–5.40 (m, 2 H, CH_2–CH=CH_2), 5.92–6.04 (m, 1 H, C**H**=CH_2).

Benzyl α-D-Mannopyranoside (20b). D-mannose (**18**) (20.2 g, 0.11 mol) was added to benzyl alcohol (100 mL) saturated with HCl 0 °C. The reaction mixture was heated under nitrogen for 4 h at 60 °C and overnight at room temperature. Addition of diethyl ether (150 mL) to the clear reaction mixture led to the crystallization of **20b** (12.5 g, 42%): mp 130–131 °C, (lit.[18] mp 131–132 °C); TLC (9:4:2 ethyl acetate/2-propanol/water) R_f 0.8; NMR (D_2O) δ 3.64–3.73 (m, 3 H), 3.77 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 10 Hz, H-4), 3.81 (dd, 1 H, $J_{2,3}$ = 3 Hz, $J_{3,4}$ = 10 Hz, H-3), 3.88 (dd, 1 H, $J_{6,6'}$ = −12 Hz, $J_{5,6}$ = 1.5 Hz, H-6), 3.96 (dd, 1 H, $J_{1,2}$ = 1.7 Hz, $J_{2,3}$ = 3 Hz, H-2), 4.59, 4.77 (AB_9, 2 H, *J* = 11 Hz, O**C**H_2Ph), 4.99 (d, 1 H, $J_{1,2}$ = 1.7 Hz, H-1), 7.4–7.5 (m, 5 H, Ar).

Allyl 4,6-*O*-Benzylidene-α-D-mannopyranoside (21a). Finely powdered **20a** (4.0 g, 18.2 mmol) was dissolved in formic acid (25 mL, 98%). As soon as the dissolution was complete, benzaldehyde (25 mL) was added at once, and the reaction mixture was stirred for 15 min. It was then added slowly to a mixture of hexane (150 mL) and aqueous $NaHCO_3$ (60 g in 150 mL of water) and stirred for 30 min. Compound **21a** was separated by filtration and recrystallized from ether (1.4 g, 25%); mp 148–149 °C; $[\alpha]_D$ +68.6° (*c* 0.26 in $CHCl_3$; NMR ($CDCl_3$) δ 2.60 (m, 2 H, exchanges with D_2O, two OH), 3.80–3.97 (m, 3 H), 3.98–4.05 (m, 1 H, O**C**H_2CH=CH_2), 4.08 (m, 1 H, H-2), 4.12 (m, 1 H, H-3), 4.19–4.25 (m, 1 H, O**C**H_2CH=CH_2), 4.26–4.30 (m, 1 H), 4.94 (d, 1 H, $J_{1,2}$ = 1.8 Hz, H-1), 5.20–5.35 (m, 2 H, CH=CH_2), 5.59 (s, 1 H, PhC**H**<), 5.85–5.98 (m, 1 H, C**H**=CH_2), 7.34–7.56 (m, 5 H, Ar). Anal. Calcd for $C_{16}H_{20}{\cdot}H_2O$: C, 58.91; H, 6.75. Found: C, 58.50; H, 6.68.

Benzyl 4,6-*O*-Benzylidene-α-D-mannopyranoside (21b). Compound **21b** was prepared in the same manner as compound **21a**, starting with **20b** (15 g, 0.056 mol), benzaldehyde (150 mL), and formic acid (150 mL, 98%) (yield 28%): mp 155–156 °C (ethanol) (lit.[15] mp 148–151 °C); NMR ($CDCl_3$) δ 2.60 (br s, 2 H, exchangeable with D_2O, two OH), 3.80–3.96 (m, 3 H), 4.10 (dd, 1 H, $J_{1,2}$ = 1.7 Hz, $J_{2,3}$ = 3 Hz, H-2), 4.15 (dd, 1 H, $J_{2,3}$ = 3 Hz, $J_{3,4}$ = 9 Hz, H-3), 4.26–4.29 (m, 1 H), 4.54, 4.76 (AB_9, 2 H, *J* = 12 Hz, OCH_2O), 4.98 (d, 1 H, $J_{1,2}$–1.7 Hz, H-1), 5.59 (s, 1 H, PhC**H**<), 7.30–7.58 (m, 10 H, Ar). Anal. Calcd for $C_{20}H_{22}O_6{\cdot}3.5\ H_2O$: C, 57.00; H, 6.91. Found: C, 57.15, H, 6.29.

Allyl 2-*O*-Allyl-4,6-*O*-benzylidene-α-D-mannopyranoside (15a). A solution of **21a** (500 mg, 1.62 mmol), allyl bromide (350 mg, 1.95 mmol, freshly distilled), and *n*-Bu_4NHSO_4 (110 mg, 0.32 mmol) in CH_2Cl_2 (60 mL) was stirred vigorously with an aqueous NaOH solution (3 mL, 50%) and refluxed for 20 h. The aqueous phase was removed from the cold reaction mixture. The organic layer was washed with water, aqueous saturated $NaHCO_3$ solution, and brine. The dried (Na_2SO_4) solution was evaporated to give an oil which was purified on a silica gel column eluted with 4:1

toluene/ethyl acetate. The second eluting fraction, identified as compound **15a** was crystallized from 9:1 hexane/ethyl acetate (280 mg, 49%); mp 75–76 °C; $[\alpha]_D$ +30.7 (*c* 0.26 in $CHCl_3$); NMR ($CDCl_3$) δ 2.40 (d, 1 H, *J* = 12 Hz, exchanges with D_2O, OH), 3.77 (dd, 1 H, $J_{1,2}$ = 1.7 Hz, $J_{2,3}$ = 3 Hz, H-2), 3.80–3.92 (m, 3 H), 3.96–4.04 (m, 2 H, OCH_2-CH=CH_2), 4.08–4.14 (m, 1 H, H-3), 4.15–4.26 (m, 3 H), 4.92 (d, 1 H, $J_{1,2}$ = 1.7 Hz, H-1), 5.20–5.36 (m, 4 H, CH=CH_2), 5.59 (s, 1 H, PhCH<), 5.85–6.01 (m, 2 H, CH=CH_2), 7.35–7.58 (m, 5 H, Ar). Anal. Calcd for $C_{19}H_{24}O_6$: C, 65.50; H, 6.94. Found: C, 65.21; H, 6.71.

Benzyl 2-*O*-Benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (15b). A solution of **21b** (1.5 g, 4.19 mmol), benzyl bromide (0.93 mg, 0.65 mL, 5.45 mmol), and *n*-Bu_4NHSO_4 (284 mg, 0.84 mmol) in CH_2Cl_2 (120 mL) was stirred vigorously with an aqueous NaOH solution (10 mL, 30%) and heated at reflux for 20 h. The aqueous phase was removed from the cold reaction mixture. The organic layer was washed with water, saturated aqueous $NaHCO_3$ solution, and brine. The dried (Na_2SO_4) solution was evaporated to give an amorphous solid from which **15b** was crystallized with 3:2 hexane/ethyl acetate (970 mg, 51%); $[\alpha]_D$ +39.4° (*c* 0.26 in $CHCl_3$); NMR ($CDCl_3$) δ 2.35 (d, 1 H, *J* = 12 Hz, OH), 3.80–3.96 (m, 4 H, includes a dd at 3.96, $J_{1,2}$ = 1.7 Hz, $J_{2,3}$ = 3 Hz, H-2), 4.11–4.18 (m, 1 H, H-3), 4.22–4.25 (m, 1 H), 4.48, 4.72 (AB_9, 2 H, *J* = 12 Hz, PhCH_2O), 4.65–4.73 (AB_9, 2 H, PhCH_2O), 4.94 (d, 1 H, $J_{1,2}$ = 1.7 Hz, H-1), 5.59 (s, 1 H, PhCH<), 7.34–7.55 (m, 15 H, Ar). Anal. Calcd for $C_{27}H_{28}O_6 \cdot {}^1/_2H_2O$: C, 70.88; H, 6.38. Found: C, 70.95; H, 6.21.

Benzyl 2-*O*-Allyl-4,6-*O*-benzylidene-α-D-mannopyranoside (15c). **15c** was prepared in the same manner as **15a**, starting from **21b** (0.80 g, 2.2 mmol), allyl bromide (0.684 g, 3.8 mmol), *n*-Bu_4NHSO_4 (0.15 g, 0.44 mmol), and NaOH (3 mL, 50%). After chromatography of the crude reaction mixture (silica gel, 4:1 toluene/ethyl acetate), **15c** was crystallized from hexane (480 mg, 54%); mp 93–94 °C; NMR ($CDCl_3$) δ 2.37 (d, 1 H, *J* = 12 Hz, OH), 3.79 (dd, 1 H, $J_{1,2}$ = 1.7 Hz, $J_{2,3}$ = 3 Hz, H-2), 3.81–3.92 (m, 3 H), 4.10–4.25 (m, 4 H), 4.52, 4.76 (AB_9, 2 H, *J* = 12 Hz, PhCH_2O), 4.96 (d, 1 H, $J_{1,2}$ = 1.7 Hz, H-1), 5.18–5.32 (m, 2 H, CH=CH_2), 5.59 (s, 1 H, PhCH<), 5.85–5.96 (m, 1 H, CH=CH_2), 7.30–7.55 (m, 5 H, Ar).

Benzyl 2-*O*-Benzyl-3-*O*-(tetra-*O*-acetyl-α-D-mannopyranosyl)-4,6-*O*-benzylidine-α-D-mannopyranoside (22). To a solution of **15b** (880 mg, 1.96 mmol) in dry CH_3CN (20 mL) containing 4A molecular sieves were added sequentially $HgBr_2$ (846 mg, 2.35 mmol), $Hg(CN)_2$ (592 mg, 2.35 mmol), and a solution of **6** [prepared from **25** (782 mg, 2.16 mmol) and trimethylsilyl bromide (306 mg, 2.0 mmol)] in dry CH_3CN (5 mL). The reaction mixture was stirred at room temperature in a closed system for 30 min or until complete disappearance of starting material (as indicated by TLC, eluent 3:2 toluene/ethyl acetate). Evaporation of the solvent gave a solid residue which was extracted three times with $CHCl_3$. The organic extracts were washed with saturated KCl solution, saturated $NaHCO_3$ solution, water, and brine. The dried (Na_2SO_4) organic layer was concentrated to give **22** as a crystalline solid (1.12 g, 73%): mp 211–212 °C (2:3 hexane/ethyl acetate); $[\alpha]_D$ +6.15°) (*c* 0.22 in $CHCl_3$); NMR ($CDCl_3$) δ 1.90 (s, 3 H, Ac), 1.99 (s, 3 H, Ac), 2.06 (s, 3 H, Ac), 2.07 (s, 3 H, Ac), 3.80 (m, 1 H, H-2), 3.82–3.86 (m, 3 H), 4.00 (dd, 1 H, $J_{5,6'}$ = 2 Hz, $J_{6,6'}$ = −12 Hz, H-6′), 4.16 (dd, 1 H, $J_{5,6'}$ = 5 Hz, $J_{6,6'}$ = −12 Hz, H-6′), 4.22–4.28 (m, 3 H), 4.49, 4.71 (AB_9, 2 H, *J* = 12 Hz, PhCH_2O), 4.76 (m, 2 H, PhCH_2O), 4.96 (d, 1 H, $J_{1,2}$ = 1.7 Hz, H-1), 5.22 (t, 1 H, $J_{3',4'} = J_{4',5'}$ = 10 Hz, H-4′), 5.41 (dd, 1 H, $J_{2',3'}$ = 3.8 Hz, $J_{3',4'}$ = Hz, H-3′), 5.46 (dd, 1 H, $J_{1',2'}$ = 1.7 Hz, $J_{2',3'}$ = 3.8 Hz, H-2′), 5.61 (s, 1 H, PhCH<), 7.25–7.40 (m, 15 H, Ar). Anal. Calcd for $C_{41}H_{46}O_{16}$: C, 61.96; H, 5.83. Found: C, 62.14; H, 5.92.

Tetra-*O*-acetyl-3-*O*-(tetra-*O*-acetyl-α-D-mannopyranosyl)-D-mannopyranose (23). A suspension of **22** (700 mg, 0.90 mmol) and PdC (600 mg, 10%) in ethanol was hydrogenolyzed at atmospheric pressure for 17 h. The reaction mixture was filtered over Celite and washed with methanol. The filtrate was evaporated and immediately treated with a cold mixture of acetic anhydride (20 mL) and pyridine (20 mL). The reaction mixture was kept at 4 °C for 48 h. It was poured over ice, stirred for 30 min, and then extracted three times with chloroform. The organic extracts were washed with water, saturated aqueous $NaHCO_3$ solution, and brine. The dried (Na_2SO_4) solution was concentrated in vacuo to give **23** as an oil (480 mg, 60%): NMR ($CDCl_3$)δ 1.99 (s, 3 H, Ac), 2.06 (s, 3 H, Ac), 2.10 (m, 9 H, three Ac), 2.15 (m, 9 H, three Ac), 3.7–4.3 (m), 5.00–5.05 (m), 5.18–5.4 (m), 5.82 (d, 0.3 H, $J_{1,2}$ = 1.5 Hz, H-1, β acetate), 6.10 (d, 0.7 H, $J_{1,2}$ = 1.8 Hz, H-1, α acetate).

3-*O*-(Tetra-*O*-acetyl-α-D-mannopyranosyl)-2,4,6-tri-*O*-acetyl-α-D-mannopyranosyl Bromide (16). Acetic acid saturated with HBr (4 mL) was added to a solution of **23** (200 mg, 0.30 mmol) in CH_2Cl_2 (20 mL, distilled in situ from P_2O_5 under nitrogen) at 0 °C. The solution was stirred at 0 °C for 6 h. The reaction mixture was poured over ice and extracted with cold CH_2Cl_2. The organic extracts were washed with cold water, cold aqueous saturated $NaHCO_3$, and cold brine. The dried (Na_2SO_4) solution was evaporated in vacuo to give **16** as a white foam (160 mg, 78%) which was used immediately, without further purification.

3-*O*-(Tetra-*O*-acetyl-α-D-mannopyranosyl)-4,6-di-*O*-acetyl-β-D-mannopyranose 1,2-(Methyl orthoacetate) (24). A cold mixture of dry methanol (1.5 mL) and 2,6-lutidine (1.5 mL, freshly distilled from CaH_2) was added to a solution of **16** (160 mg, 0.23 mmol) in dry $CHCl_3$ (15 mL). The solution was stirred in the dark, at room temperature for 17 h. After that time it was diluted with $CHCl_3$ washed with iced water, cold aqueous saturated $NaHCO_3$, and brine. The dried solution was evaporated in vacuo, and toluene (3 mL) was added to facilitate the removal of 2,6-lutidine. Crystallization of the residue with methanol gave **24** (98 mg, 66%): mp 96–97 °C; $[\alpha]_D$ −45.0° (*c* 0.22 in $CHCl_3$); NMR (CDC_3) δ 1.75 (s, 3 H, $CH_3C(OR)_3$), 1.99 (s, 3 H, Ac), 2.06 (s, 3 H, Ac), 2.08 (s, 3 H, Ac), 2.09 (s, 3 H, Ac), 2.14 (s, 3 H, Ac), 2.17 (s, 3 H, Ac), 3.29 (s, 3 H, OCH_3), 3.62 (m, 1 H, H-5), 3.86 (dd, 1 H, $J_{2,3}$ = 4 Hz, $J_{3,4}$ = 9.5 Hz), 4.08–4.34 (m, 6 H), 4.60 (dd, 1 H, $J_{1,2}$ = 2 Hz, $J_{2,3}$ = 4 Hz, H-2), 4.98 (d, 1 H, $J_{1',2'}$ = 1.7 Hz, H-1′), 5.13 (dd, 1 H, $J_{1',2'}$ = 1.7 Hz, $J_{2',3'}$ = 3 Hz, H-2′), 5.29 (t, 1 H, $J_{3,4} = J_{4,5}$ = 9.5 Hz, H-4), 5.34 (m, 1 H, H-3), 5.46 (d, 1 H, $J_{1,2}$ = 2 Hz, H-1). Anal. Calcd for $C_{27}H_{38}O_{18}$: C, 49.84; H, 5.89. Found: C, 50.00; H, 6.00.

Methyl 6-*O*-(3-*O*-α-D-Mannopyranosyl-α-D-mannopyranosyl)-3-*O*-α-D-mannopyranosyl-α-D-mannopyranoside (4). To a solution of **7** (50 mg, 0.087 mmol) in dry CH_3CN (10 mL) containing 4A molecular sieves were added sequentially $HgBr_2$ (25 mg, 0.10 mmol), $Hg(CN)_2$ (36 mg, 0.10 mmol), and a solution of **16** (61 mg, 0.087 mmol) in dry CH_3CN (3 mL). The reaction mixture was stirred for 2 h at room temperature. Evaporation of the solvent gave a solid residue, which was treated three times with chloroform. The organic extracts were washed with saturated KCl solution, saturated sodium bicarbonate solution, water, and brine. Concentration of the dried (Na_2SO_4) organic layer gave a white foam, which by NMR and TLC (1:1 toluene/ethyl acetate) was shown to be the condensation product together with some unreacted starting material. The mixture was deallylated and deacetylated under standard conditions. Chromatography over Bio Gel P-2 eluted with distilled water gave pure **4** (10 mg, 16%, based on **7**): $[\alpha]_D$ +71.3° in water); NMR (D_2O) δ 3.41 (s, 3 H, OCH_3), 3.66 (m, 2 H, H-4′, H-4‴), 3.72–3.92 (m, 16 H), 3.95 (dd, 1 H, *J* = 3.4 Hz, *J* = 9.5 Hz, H-3″), 4.02 (dd, 1 H, *J* = 4 Hz, *J* = 11 Hz, H-6), 4.07 (dd, 2 H, *J* = 1.7 Hz, *J* = 3 Hz, H-2′, H-2‴), 4.09 (dd, 1 H, *J* = 1.7 Hz, *J* = 3 Hz, H-2), 4.14 (dd, 1 H, *J* = 1.7 Hz, 3 Hz, H-2″), 4.73 (d, 1 H, *J* = 1.7 Hz, H-1), 4.89 (d, 1 H, *J* = 1.7 Hz, H-1″), 5.10 (d, 1 H, *J* = 1.7 Hz, H-1′), 5.16 (d, 1 H, *J* = 1.7 Hz, H-1‴).

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