Graphical Abstract

Direct and stereoselective synthesis of β-D-mannosides using 4,6-*O*-benzylidene-protected mannosyl diethyl phosphite as a donor

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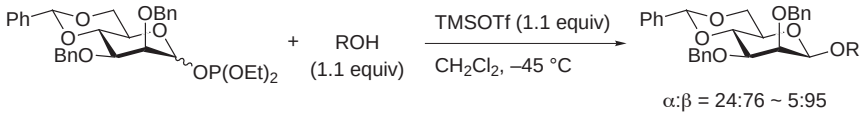

α:β = 24:76 ~ 5:95

Direct and stereoselective synthesis of β-D-mannosides using 4,6-*O*-benzylidene-protected mannosyl diethyl phosphite as a donor

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Abstract—A direct and practical method for the construction of β-mannosidic linkages is described. While β-selectivities in the TMSOTf-promoted glycosidation of 2,3,4,6-tetra-*O*-benzyl-D-mannosyl diethyl phosphite are found to be highly dependent on the reactivity of acceptor alcohols, 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-D-mannosyl diethyl phosphite reacts with a wide range of acceptor alcohols in the presence of TMSOTf in CH_2Cl_2 at –45 °C to give β-mannosides in high yields with good to high β-selectivities.

1. Introduction

The rapidly growing significance of glycosides and oligosaccharides as constituents of biologically important compounds such as antitumor antibiotics and glycoconjugates has created an interest in the rational design and development of stereocontrolled glycosidation reactions.[1] Since the β-D-mannosidic linkage is present in virtually all eukaryotic *N*-linked glycoproteins as part of the core pentasaccharide, an enormous amount of creative endeavor has been devoted to the construction of this linkage.[2] Despite these efforts, the stereoselective synthesis of β-mannosides is recognized as one of the most challenging problems in carbohydrate chemistry, because both the anomeric effect and the steric repulsion between a non-participating group disposed axially at C-2 and an incoming alcohol uniformly favor the formation of α-mannosidic linkages. Departing from the seminal work of Paulsen and Lockhoff on the direct construction of this linkage via an S_N2-type displacement in the presence of insoluble silver silicate,[3] a number of indirect methods involving the epimerization of accessible β-glucosides at C-2,[4] the hexo-2-ulosyl bromide approach,[5] the reductive cleavage of mannosyl anomeric orthoesters,[6] intramolecular aglycon delivery (IAD)[7] using a temporary mixed acetal[8–10] or silyl ether connectors,[11] and intramolecular mannosylation via prearranged glycosides,[12] have been reported.

Although these indirect methods provide reliable access to pure β-mannosides, additional synthetic steps are required for the substrate preparation. Therefore, it is clear that a direct β-mannosylation method would constitute an ideal procedure in terms of efficiency and practicality. In this context, good to high β-selectivities have been achieved using some per-*O*-benzylated mannosyl donors.[13] The use of sulfonates as non-participating protecting groups at O-2 enhances β-selectivity due to a strong dipole effect.[14,15] The locked anomeric configuration method, wherein 1,2-*O*-dibutylstannylene derivatives of mannose are used as glycosyl donors and the roles of the donor and acceptor are reversed, results in complete β-selectivity; however, a significantly long reaction time is required to reach completion.[16] Among the direct methods reported to date, the protocol recently developed by Crich and Sun is a notable landmark in this field, in which the activation of 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-protected mannosyl sulfoxide or thioglycoside at –78 ˚C in dichloromethane with trifluoromethanesulfonic (triflic) anhydride or benzenesulfenyl triflate, respectively, is followed by the addition of acceptor alcohols to provide β-mannosides in high yields and with excellent levels of selectivity.[17] They claimed that the success of the two methods hinges critically on the presence of the 4,6-*O*-benzylidene group, where the α-mannosyl triflate as a common intermediate generated in situ from the donors reacts predominantly via an S_N2-like displacement.[18] Very recently, Crich and Chandrasekera, based on kinetic isotope effects (KIEs) measurements, proposed that the displacement of the α-mannosyl triflate by an acceptor alcohol proceeded with the development of a substantial oxocarbenium ion character.[19] The effectiveness of the intermediate was also recognized by Weingart and Schmidt[20] with the corresponding trichloroacetimidate and by Kim and co-workers[21] with the 2-(hydroxycarbonyl)benzyl 4,6-*O*-benzylidenemannoside.[22]

We have developed glycosyl donors that incorporate various phosphorus-containing leaving groups. The glycosidations constitute mild and efficient methods for the highly stereocontrolled construction of 1,2-*trans*-β- and 1,2-*cis*-α-glycosidic linkages with or without a participat-

Keywords: 4,6-*O*-Benzylidene acetal; Mannosyl diethyl phosphite; β-Selective glycosidation

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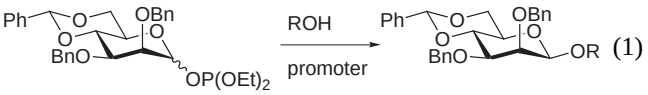
ing group at C-2.[23] The exceptionally high levels of β-selectivity observed with 2,3,4,6-tetra-*O*-benzyl-protected glycosyl diphenyl phosphates,[23a] *N,N,N',N'*-tetramethyl-phosphorodiamidates,[23d] and diethyl phosphites[23e] suggest that these leaving groups would also be promising candidates for the construction of β-mannosidic linkages. In the following discussion, the details of our investigations in this area are presented (Eq. 1).[24,25]

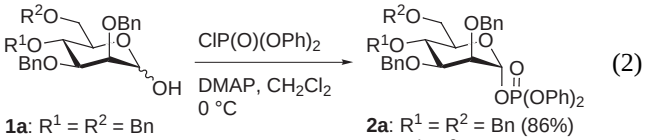


(1)

2. Results and discussion

2.1. Preparation of D-mannosyl donors

2,3,4,6-Tetra-*O*-benzyl-D-mannosyl and 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-D-mannosyl donors were prepared from the corresponding mannoses **1a**[26] and **1b**[27] according to standard procedures. Phosphorylation with diphenyl chlorophosphate under the Sabesan conditions[28] (DMAP, CH_2Cl_2, 0 °C) provided diphenyl phosphates **2a** and **2b** in good yields (Eq. 2). Tetramethylphosphorodiamidates **3a**

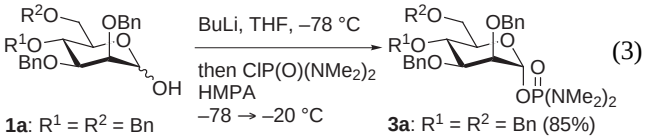


(2)

1a: $R^1 = R^2$ = Bn
1b: R^1, R^2 = CHPh

2a: $R^1 = R^2$ = Bn (86%)
2b: R^1, R^2 = CHPh (82%)

and **3b** were obtained by the condensation of lithium alkoxides derived from **1a** and **1b**, respectively, with bis(dimethylamino)phosphorochloridate in THF–HMPA (Eq. 3).[23d]

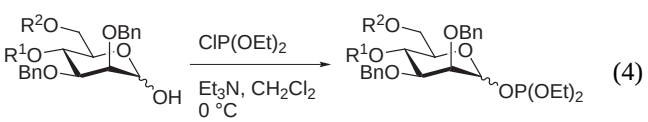


(3)

1a: $R^1 = R^2$ = Bn
1b: R^1, R^2 = CHPh

3a: $R^1 = R^2$ = Bn (85%)
3b: R^1, R^2 = CHPh (97%)

Diethyl phosphites **4a** and **4b** were prepared by the reaction of mannose derivatives with diethyl chlorophosphite and triethylamine at 0 °C (Eq. 4). Donors with an α-configuration were predominantly formed in all cases except for the diethyl phosphites **4a** and **4b**. The obtained mannosyl donors were purified by silica gel column chromatography, and could be stored without decomposition in a freezer (at –30 °C) for several months.



(4)

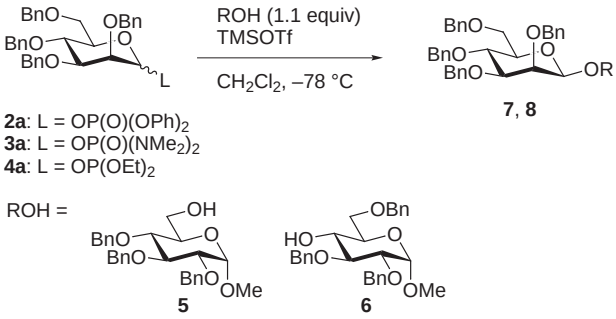
1a: $R^1 = R^2$ = Bn
1b: R^1, R^2 = CHPh

4a: $R^1 = R^2$ = Bn
(73%, α:β = 87:13)
4b: R^1, R^2 = CHPh
(88%, α:β = 93:7)

2.2. Glycosidation of 2,3,4,6-tetra-*O*-benzyl-D-mannosyl donors

At the outset of this study, the glycosidation of 2,3,4,6-tetra-*O*-benzyl-D-mannosyl donors was explored using *O*-6- or *O*-4-unprotected glycosides **5** or **6** (1.1 equiv each) as highly reactive and less reactive acceptor alcohols, respectively (Table 1).[29,30] The addition of a 1.0 M solution of TMSOTf (1.1 equiv) in CH_2Cl_2 to a cooled solution of the donor and acceptor in CH_2Cl_2 afforded a disaccharide and the α:β ratio was assayed by HPLC (Zorbax® Sil column). The TMSOTf-promoted glycosidation of diphenyl phosphate **2a** with **5** in CH_2Cl_2 proceeded at –78 °C within 1 h to give disaccharide **7** in 86% yield with good β-selectivity (α:β = 21:79) (Fig. 1). Almost the same results were obtained when phosphorodiamidate **3a** and diethyl phosphite **4a** were used (entries 2 and 3). However, a limitation of the TMSOTf-promoted glycosidations of 2,3,4,6-tetra-*O*-benzyl-D-mannosyl donors **2a**, **3a** and **4a**

Table 1. TMSOTf-promoted glycosidation of 2,3,4,6-tetra-*O*-benzyl-D-mannosyl donors **2a**, **3a** and **4a**.[a]



Entry	Donor[b]	Acceptor	Time, h	Disaccharide		
					Yield, %	α:β[c]
1	**2a**	**5**	1	**7**	86	21:79
2[d]	**3a**	**5**	1	**7**	91	22:78
3	**4a**	**5**	1	**7**	86	25:75
4	**2a**	**6**	1.5	**8**	75	77:23
5[d]	**3a**	**6**	1.5	**8**	89	80:20
6	**4a**	**6**	1.5	**8**	74	76:24

[a]Donor/acceptor/TMSOTf molar ratio=1.0/1.1/1.1 unless otherwise noted.

[b]The anomeric ratio of the donors: **2a**, 100:0; **3a**, 100:0; **4a**, 87:13.

[c]The ratio was determined by HPLC (column, Zorbax® Sil, 4.6×250 mm; eluent, 13% THF in hexane or 20% ethyl acetate in hexane; flow rate 1.5 or 1.0 mL/min).

[d]The reaction was performed using 2.0 equiv of TMSOTf.

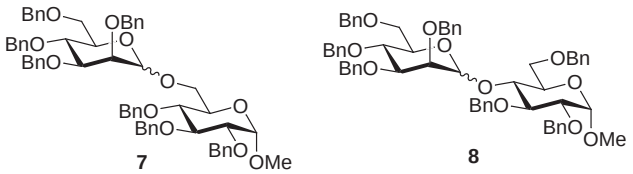


Figure 1. Products of the mannosylation of alcohols **5** and **6** with 2,3,4,6-tetra-*O*-benzyl-D-mannosyl donors.

was encountered with the unreactive *O*-4-unprotected glycoside **6**, the mannosylation of which produced disaccharide **8** favoring the α-mannoside in high yields (entries 4–6).

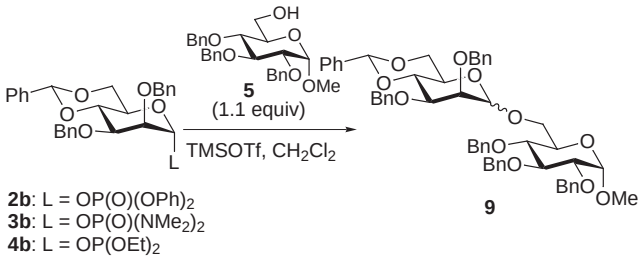
2.3. Glycosidation of 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-D-mannosyl donors

2.3.1. Reaction optimization. Since the glycosidation of the fully benzylated mannosyl donors **2a**–**4a** proved to be an unreliable method for the construction of β-mannosidic linkages, we were prompted to investigate the glycosidation of 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-D-mannosyl donors. Consistent with a general trend that 4,6-*O*-benzylidene-protected glycosyl donors exhibit reduced reactivities,[31] mannosyl donors **2b**–**4b** were activated with TMSOTf in CH_2Cl_2 at a higher temperature than that required for the corresponding per-*O*-benzylated donors **2a**–**4a**, but the reaction with **5** gave disaccharide **9** with an enhanced β-selectivity (Table 2). Although Seeberger and co-workers reported that the use of 4,6-*O*-benzylidene-protected mannosyl phosphate met with failure due to the partial hydrolysis of the cyclic acetal functionality under acidic conditions,[32] mannosylation with diphenyl phosphate **2b** provided disaccharide **9** in 54% yield with an α:β ratio of 10:90 (entry 1). The use of phosphorodiamidate **3b** as a donor gave virtually the same results as those found with **2b** (entries 1 vs 2), although a protracted reaction time was required. On the other hand, the TMSOTf-promoted mannosylation of **5** with diethyl phosphite **4b** in CH_2Cl_2 proceeded to completion at –45 °C within 30 min, affording disaccharide **9** in 83% yield with a similar high level of β-selectivity (entry 3). As a result of these observations, we selected the phosphite method for the β-selective mannosylation in terms of reactivity and product yield.[33]

Promoters other than TMSOTf were screened for their ability to activate the mannosyl diethyl phosphite **4b** (Table 3). Although a previous study from this laboratory demonstrated that the $BF_3{\cdot}OEt_2$-promoted glycosidations of per-*O*-benzyl-protected glycosyl diethyl phosphites exhibited the highest levels of β-selectivities known to date,[23e] the coupling of **4b** with **5** in the presence of $BF_3{\cdot}OEt_2$ gave disaccharide **9** in only 54% yield with an α:β ratio of 40:60 and considerable amounts of mannosyl fluoride **10** (entry 2). It has been well documented in the literature that some Brønsted acids such as TfOH are effective activators of glycosyl phosphites.[23g,23j,25,34] While mannosyl diethyl phosphite **4b** could also be activated by TfOH at –65 °C in CH_2Cl_2, the reaction with **5** afforded no discernible benefits (entry 3). Reactions of glycosyl phosphites have been shown to be promoted by catalytic amounts of TMSOTf;[23f,34a,35] however, the use of 0.2 equiv of TMSOTf resulted in a diminished β-selectivity (α:β = 19:81, entry 4). The reason for the attenuated selectivity in the catalytic reaction is unclear at present.

We next explored the optimal solvent for this reaction (Table 4). Solvents such as toluene and Et_2O were found to be less effective in terms of stereoselectivity (entries 2 and 3). The use of propionitrile gave a complex mixture of products, most likely due to the low anomeric reactivity of the nitrilium ion intermediates that causes a nucleophilic attack by alcohol **5** on a nitrilium carbon (entry 4).[23i] The temperature profile of the reaction of **4b** with **5** in CH_2Cl_2 demonstrated that this reaction performed extremely well

Table 2. TMSOTf-promoted glycosidation of 4,6-*O*-benzylidene-D-mannosyl donors **2b**, **3b** and **4b** with **5**.



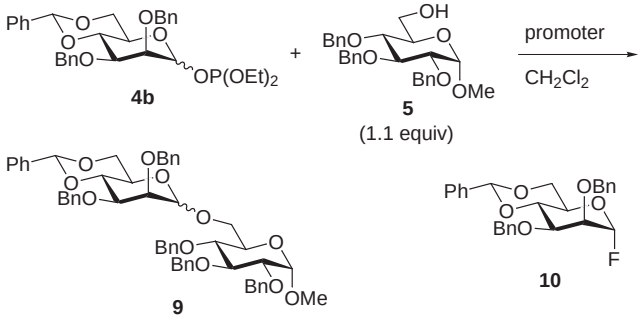
Entry	Donor[a]	TMSOTf equiv	Temp[b] °C	Time h	Yield %	α:β[c]
1	**2b**	1.5	–30	1	54	10:90
2	**3b**	2.0	–30	2	55	12:88
3	**4b**	1.1	–45	0.5	83	10:90

[a]The anomeric ratio of the donors: **2b**, 100:0; **3b**, 100:0; **4b**, 93:7.

[b]Temperature limit for a smooth reaction.

[c]The ratio was determined by HPLC (column, Zorbax® Sil, 4.6×250 mm; eluent, 20% ethyl acetate in hexane; flow rate, 1.0 mL/min; t_R α-mannoside, 21.1 min; t_R β-mannoside, 24.4 min).

Table 3. Effect of promoter in the glycosidation of 4,6-*O*-benzylidene-D-mannosyl diethyl phosphite **4b** with **5**.



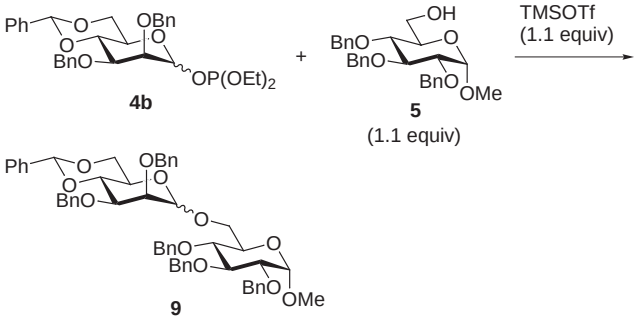
Entry	Promoter	equiv	Temp, °C	Time, h	Yield, %	α:β[a]
1	TMSOTf	1.1	–45	0.5	83	10:90
2	$BF_3{\cdot}OEt_2$	1.1	–45	6	54[b]	40:60
3[c]	TfOH	1.1	–65	6	79	9:91
4	TMSOTf	0.2	–45	1	81	19:81

[a]The ratio was determined by HPLC (column, Zorbax® Sil, 4.6×250 mm; eluent, 20% ethyl acetate in hexane; flow rate, 1.0 mL/min; t_R α-mannoside, 21.1 min; t_R β-mannoside, 24.4 min).

[b]Mannosyl fluoride **10** was obtained in 31% yield.

[c]In the presence of 4-Å molecular sieves (4Å MS).

Table 4. Effect of solvent and temperature in the TMSOTf-promoted glycosidation of 4,6-*O*-benzylidene-D-mannosyl diethyl phosphite **4b** with **5**.

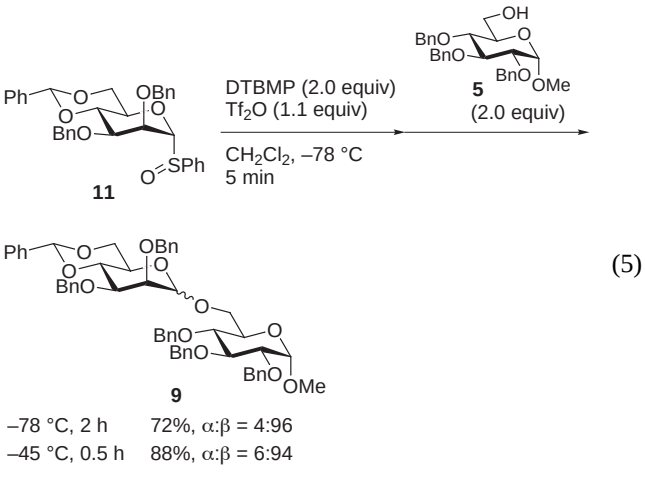


Entry	Solvent	Temp, °C	Time, min	Yield, %	α:β[a]
1	CH_2Cl_2	–45	30	83	10:90
2	toluene	–45	30	86	20:80
3	Et_2O	–45	30	77	22:78
4	EtCN	–45	15	complex mixture	
5	CH_2Cl_2	–23	15	74	11:89
6	CH_2Cl_2	0	15	75	12:88

[a]The ratio was determined by HPLC (column, Zorbax® Sil, 4.6×250 mm; eluent, 20% ethyl acetate in hexane; flow rate, 1.0 mL/min; t_R α-mannoside, 21.1 min; t_R β-mannoside, 24.4 min).

over a wide temperature range; only minor erosion (2%) in β-selectivity was observed (entries 1 vs 5 and 6).

Although it appeared likely that the conditions employed in the coupling of **4b** with **5** could be optimized, the observed β-selectivity (α:β = 10:90) did not match the selectivity (α:β ratio with **5** was 4:96 at –78 ˚C and 6:94 at –45 ˚C) obtained by us using the corresponding sulfoxide **11** (Eq. 5).[17] It is clear that the difference in selectivity between

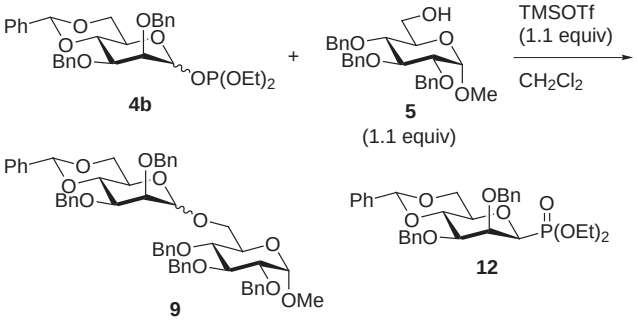


(5)

the two methods cannot be attributed to the reaction temperature used. In this context, it is likely that another factor accounts for the difference in stereoselectivity. Our procedure involves the dropwise addition of TMSOTf to a mixture of **4b** and **5** in CH_2Cl_2. On the other hand, in Crich and Sun's study, the order of addition of reactants was critical for the success of the reaction, since the intermediate triflate should be prepared before the addition of the alcohol.

Thus, we focused on the possibility of improving the β-selectivity by changing the mixing sequence (Table 5). Pretreatment of donor **4b** with TMSOTf in CH_2Cl_2 at –45 °C for 30 min followed by the addition of alcohol **5** was found to increase the α:β ratio to 8:92 (method B, entry 2). This protocol enabled the β-selectivity to be enhanced further by lowering the temperature to –78 ˚C during the addition (entry 3). It is noteworthy that the observed selectivity (α:β = 5:95) is comparable to that obtained by the sulfoxide method. However, the permuted order of addition provided much lower yields of mannoside **9** due to the inevitable formation (ca. 15–20%) of phosphonate **12**.[36,37] Although Schmidt and Weingart employed the "inverse conditions"[38] for the formation of β-mannosides using 4,6-*O*-benzylidene-protected mannosyl trichloroacetimidate,[20] no difference in stereoselectivity was observed under inverse conditions, in which **4b** was added to a mixture of **5** and TMSOTf at –45 °C (method C, entry 4). These results strongly suggest that the problem associated with the phosphite method is that the mannosyl donor **4b** cannot be cleanly converted into the α-mannosyl triflate by treatment with TMSOTf before the addition of an acceptor alcohol. This also means that Crich's optimal protocol is crucial not only for the preferential formation of

Table 5. Effect of mixing sequence of the reactants in the TMSOTf-promoted glycosidation of 4,6-*O*-benzylidene-D-mannosyl diethyl phosphite **4b** with **5**.



Entry	Method[a]	Temp, °C	Time, min	Yield, %	α:β[b]
1	A	–45	30	83	10:90
2	B	–45	30	65[c]	8:92
3	B	–78	120	55[c]	5:95
4	C	–45	30	79	10:90

[a]Method A: A 1 M solution of TMSOTf in CH_2Cl_2 was added to a mixture of donor **4b** and alcohol **5** in CH_2Cl_2 at –45 °C. Method B: After stirring a solution of donor **4b** and TMSOTf in CH_2Cl_2 at –45 °C for 30 min, a solution of alcohol **5** in CH_2Cl_2 was added at the indicated temperature. Method C (inverse conditions): A solution of donor **4b** in CH_2Cl_2 was added to a solution of alcohol **5** and TMSOTf in CH_2Cl_2 at –45 °C.

[b]The ratio was determined by HPLC (column, Zorbax® Sil, 4.6×250 mm; eluent, 20% ethyl acetate in hexane; flow rate, 1.0 mL/min; t_R α-mannoside, 21.1 min; t_R β-mannoside, 24.4 min).

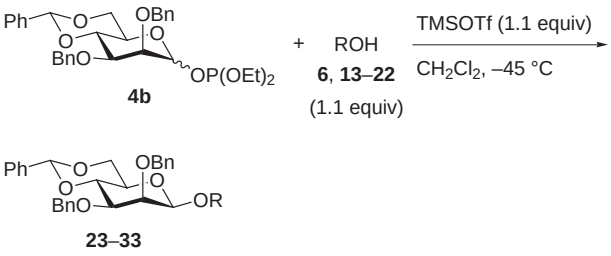
[c]Phosphonate **12** was obtained as a by-product in ca. 15–20% yield.

β-mannosides using Kahne's sulfoxide glycosidation method[39] but also for general use whenever the efficient in situ generation of the α-mannosyl triflate from 4,6-*O*-benzylidene-protected mannosyl donors is possible.

2.3.2. Scope of the TMSOTf-promoted glycosidations of 4,6-*O*-benzylidene-D-mannosyl diethyl phosphite 4b. With the reaction conditions optimized, the scope of the glycosidation reaction of **4b** with a range of acceptor alcohols was then investigated (Fig. 2). The results are compiled in Table 6.

As anticipated from the preceding experiments, the β-selectivities obtained in the reaction of **4b** did not surpass the selectivities observed with the corresponding sulfoxide **11** (entries 2, 4 and 7);[17] however, the TMSOTf-promoted glycosidation in CH_2Cl_2 at –45 ˚C offered a facile and high-yielding route to β-mannosides in all cases, wherein the α:β ratios ranged from 24:76 to 5:95. The mannosylation of less reactive *O*-4-unprotected glycosides **6** and **14**[40] proceeded to completion within 1 h under these conditions (entries 1 and 3), and the glycosidation of **14** led to the preferential formation of β-mannoside **25**β, which corresponds to a constituent of *N*-linked glycoproteins (entry 3). As previously mentioned by Crich, the coupling with 1,2:3,4-di-*O*-isopropylidenegalactose (**15**) exhibited a much lower selectivity (α:β = 24:76, entry 4). Considering that the

Table 6. TMSOTf-promoted glycosidation of 4,6-*O*-benzylidene-D-mannosyl diethyl phosphite **4b** with acceptor alcohols.[a,b]



Entry	ROH	Time, min	Product	Yield, %	α:β[c]
1	**6**	60	**23**	84	11:89
2	**13**	30	**24**	85	11:89
3	**14**	60	**25**	72	17:83
4	**15**	30	**26**	89	24:76
5	**16**	30	**27**	77	15:85[d]
6	**17**	30	**28**	96	5:95
7	**18**	30	**29**	89	11:89
8[e]	**19**	30	**30**	85	14:86[f]
9	**20**	30	**31**	89	16:84
10	**21**	15	**32**	87	15:85
11	**22**	30	**33**	86	17:83

[a]The reaction was carried out on a 0.1 mmol scale.

[b]Donor **4b**/ROH/TMSOTf molar ratio=1.0/1.1/1.1 unless otherwise noted.

[c]The ratio was determined by HPLC (column, Zorbax® Sil, 4.6×250 mm; eluent, 5~17% ethyl acetate in hexane or 5~20% THF in hexane; flow rate, 1.0 mL/min), unless otherwise stated.

[d]Determined by 500 MHz ^{1}H NMR.

[e]The reaction was performed with 2.0 equiv of TMSOTf.

[f]Determined by 126 MHz ^{13}C NMR.

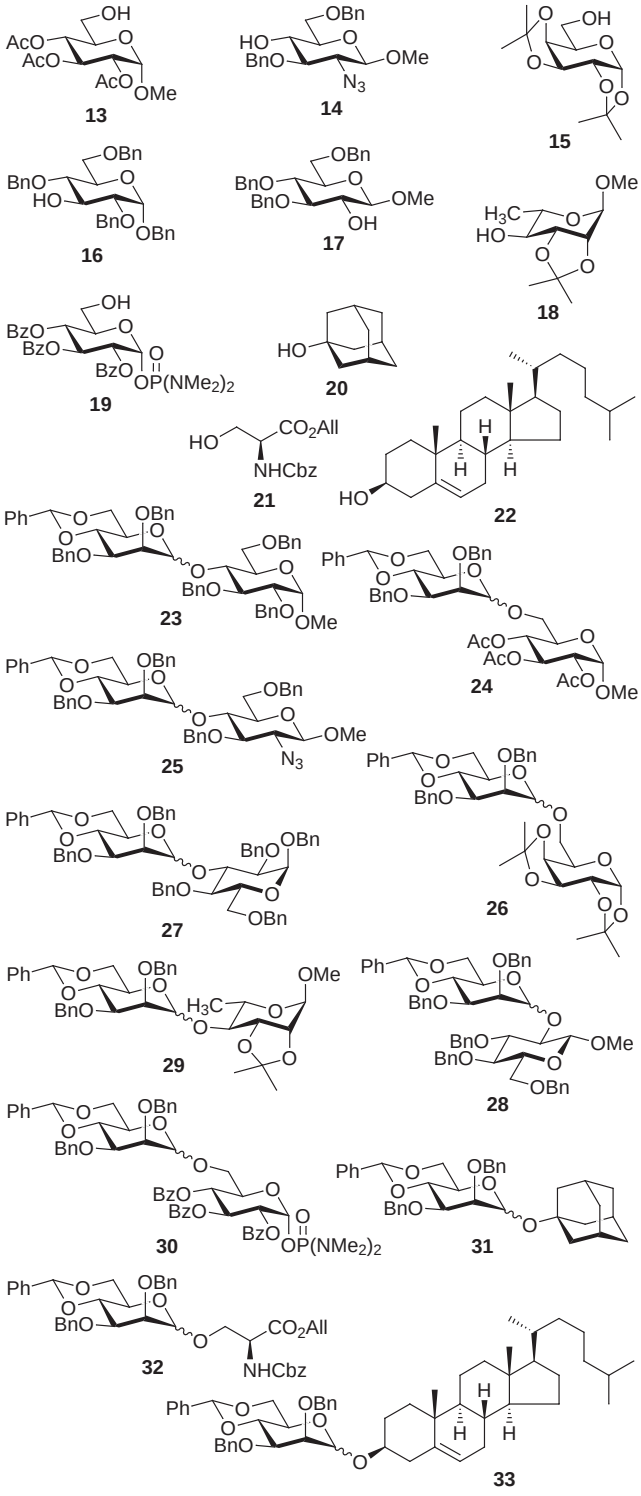


Figure 2. Acceptor alcohols and products in Table 6.

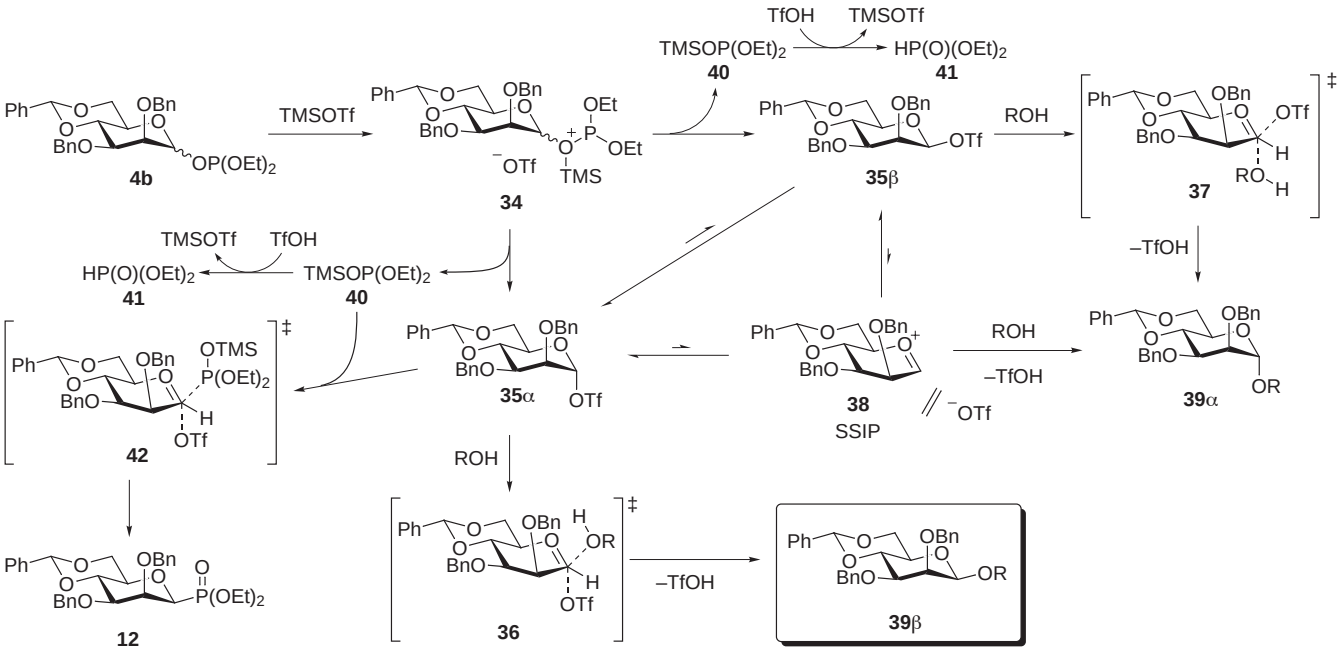
reaction reached completion within 30 min, this stereochemical outcome might be attributed to a sterically mismatched interaction in the transition state leading to the β-linked disaccharide **26**β.[41] The best β-selectivity (α:β = 5:95) was achieved by the mannosylation of the *O*-2-unprotected glucoside **17** (entry 6). It is also noteworthy that chemoselective glycosidation was realized when *O*-6-unprotected glucosyl phosphorodiamidate **19** was used as a disarmed acceptor because **19** was unaffected by such conditions when kept at temperatures below –5 ˚C (entry 8).[34b,42] Crich and co-workers demonstrated that some *tert*-alcohols such as 1-adamantanol (**20**) could be mannosylated upon activation of phenyl thiomannoside with a variety of thiophilic reagents.[17d,f,g] In our system, glycoside **31** with an α:β ratio of 16:84 was obtained from **20** in 89% yield (entry 9). The serine derivative **21** and cholesterol (**22**) could be safely glycosylated under these conditions with good β-selectivities (entries 10 and 11).

2.4. Mechanistic considerations

Crich and Sun proposed, based on NMR experiments, that mannosyl triflate was cleanly generated from 4,6-*O*-benzylidene-D-mannosyl sulfoxide upon treatment with Tf_2O in the presence of 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP) in CD_2Cl_2 at –78 °C within 5 min.[18] As alluded to above, Crich and Chandrasekera, based on the KIEs, proposed that the displacement of the α-mannosyl triflate by an acceptor alcohol proceeded with the development of a substantial oxocarbenium ion character, although the complete set of equilibria between mannosyl triflates, the transient contact ion pair (CIP) and the solvent-separated ion pair (SSIP) lie very heavily toward the α-mannosyl triflate.[19] The possibility that the 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-D-mannosyl triflate is also an intermediate in the phosphite method is suggested by the following: (1) the effectiveness of the triflate as a counterion of the promoter and (2) almost the same β-selectivity as that obtained with the sulfoxide method when premixing the phosphite with TMSOTf prior to addition of the acceptor alcohol. Based on these results, the similar reaction mechanism would be applicable to the phosphite method. While CIP, in which the triflate anion is necessarily closely associated with the face of the oxocarbenium ion, would be a possible intermediate in this reaction, a mechanism involving an "exploded" transition state[19] is outlined in Scheme 1.

Diethyl phosphite **4b** is activated by silylation of the oxygen atom[34a] and the phosphite group is cleaved, to produce an equilibrium mixture of α- and β-mannosyl triflates **35**α and **35**β. The displacement by acceptor alcohols at the anomeric carbon of **35**α and **35**β affords glycosides **39**β and **39**α via triplets **36** and **37**, respectively, along with generation of TfOH. Since the equilibrium between the mannosyl triflates would heavily lie to **35**α on kinetic and thermodynamic grounds, high β-selectivities are observed in the present method. The generation of SSIP (**38**) from **35**α and **35**β results in the formation of α-mannoside **39**α. Trimethylsilyl phosphite **40** is converted to diethyl phosphite (**41**) during the course of the reaction. Since phosphite **40** is less nucleophilic than the acceptor alcohols, high yields can be obtained when the promoter is added to a mixture of donor **4b** and the acceptor alcohol. However, α-mannosyl triflate **35**α reacts with phosphite **40** in the absence of the acceptor alcohol, providing β-mannosyl phosphonate **12** as a by-product.

3. Conclusion



Scheme 1. Potential pathways for the TMSOTf-promoted glycosidation of 4,6-*O*-benzylidene-protected mannosyl diethyl phosphite **4b**.

The effectiveness of the diethyl phosphite group as a leaving group of mannosyl donors has been demonstrated. β-Selectivities in the TMSOTf-promoted glycosidation of 2,3,4,6-tetra-*O*-benzyl-D-mannosyl donors were found to be highly dependent on the reactivity of the acceptor alcohols used. On the other hand, the TMSOTf-promoted glycosidation of 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-D-mannosyl diethyl phosphite with a broad variety of acceptor alcohols in CH_2Cl_2 at –45 ˚C offered a facile and high-yielding route to β-mannosides, wherein the α:β ratios ranged from 24:76 to 5:95. Although the β-selectivities did not surpass those reported by Crich with the sulfoxide or thioglycoside method, the present method has the following advantages in terms of practicality: (1) high product yield can be achieved with approximately equimolar proportions of glycosyl donors and acceptors; (2) the reaction is very clean, allowing very easy isolation of the product, in contrast to the sulfoxide method in which several by-products derived from the sulfinate moiety are produced; and (3) TMSOTf is a stable and inexpensive reagent compared to those used for the activation of thioglycosides. The effectiveness of the triflate as a counterion of the promoter and almost the same β-selectivity as that obtained with the sulfoxide method when the phosphite is premixed with TMSOTf prior to the addition of the acceptor alcohol suggest that the corresponding mannosyl triflate is an intermediate in the present mannosidation method.

4. Experimental

4.1. General

Melting points were determined on a Büchi 535 digital melting point apparatus and were uncorrected. Optical rotations were recorded on a JASCO P-1030 digital polarimeter. Infrared (IR) spectra were recorded on a JASCO FT/IR-5300 spectrophotometer and absorbance bands are reported in wavenumber (cm^{-1}). Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a Bruker ARX500 (500 MHz) spectrometer with tetramethylsilane (δ_H 0.00) as an internal standard. Coupling constants (*J*) are reported in hertz (Hz). Abbreviations of multiplicity are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Data are presented as follows: chemical shift, multiplicity, coupling constants, integration and assignment. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on JEOL AL400 (100 MHz) or Bruker ARX500 (126 MHz) spectrometers with $CDCl_3$ (δ_C 77.0) as an internal standard. Phosphorus nuclear magnetic resonance (^{31}P NMR) spectra were recorded on JEOL EX270 (109 MHz) or Bruker ARX500 (202 MHz) spectrometers with H_3PO_4 (δ_P 0.00) as an external standard. Fast atom bombardment (FAB) mass spectra were obtained on a JEOL JMS HX110 spectrometer in the Center for Instrumental Analysis, Hokkaido University.

Column chromatography was carried out on Kanto silica gel 60 N (40–50 μm or 63–210 μm) or Wakogel C-200 (75–150 μm). Analytical thin layer chromatography (TLC) was carried out on Merck Kieselgel 60 F_{254} plates. Visualization was accomplished with ultraviolet light and anisaldehyde or phosphomolybdic acid stain, followed by heating. HPLC analyses were performed on a JASCO PU-980 and UV-970 (detector, λ = 254 nm). Retention times (t_R) and peak ratios were determined with a Shimadzu Chromatopac C-R6A. Hexane was HPLC grade, and filtered and degassed prior to use.

Reagents and solvents were purified by standard means or used as received unless otherwise noted. Dehydrated stabilizer free THF was purchased from Kanto Chemical Co., Inc. Dichloromethane and propionitrile were distilled from P_2O_5, and redistilled from calcium hydride prior to use. 4-Å molecular sieves was finely ground in mortar and heated in vacuo at 220 °C for 12 h.

All reactions were conducted under an argon atmosphere. Lactols **1a**[26] and **1b**[27] were prepared according to literature procedures.

4.2. Preparation of D-mannosyl donors

4.2.1. 2,3,4,6-Tetra-*O*-benzyl-α-D-mannopyranosyl diphenyl phosphate (2a). Diphenylphosphoryl chloride (0.57 mL, 2.74 mmol) was added to a stirred solution of lactol **1a** (1.14 g, 2.11 mmol) and DMAP (645 mg, 5.28 mmol) in CH_2Cl_2 (15 mL) at 0 °C. After 30 min, the reaction was quenched with crushed ice, followed by stirring at room temperature for 15 min. The mixture was poured into a two-layer mixture of Et_2O (10 mL) and saturated aqueous $NaHCO_3$ (15 mL), and the whole was extracted with AcOEt (25 mL). The organic extract was washed with brine (2×15 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the pale yellow oil (1.74 g), which was purified by column chromatography (silica gel 40 g, 8:1 hexane/AcOEt with 2% Et_3N) to give diphenyl phosphate **2a** (1.41 g, 86%) as a colorless oil: $[\alpha]_D^{23}$ +29.6° (*c* 1.01, $CHCl_3$); IR (film) 3063, 3030, 2905, 2868, 1952, 1877, 1811, 1726, 1591, 1491, 1454, 1364, 1292, 1188, 1103, 1026, 949, 876, 739, 696 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.53 (dd, *J* = 1.5, 11.2 Hz, 1H, H-6a), 3.74 (dd, *J* = 4.1, 11.2 Hz, 1H, H-6b), 3.76 (dd, *J* = 1.9, 3.1 Hz, 1H, H-2), 3.82 (dd, *J* = 3.1, 9.6 Hz, 1H, H-3), 3.85 (ddd, *J* = 1.5, 4.1, 9.8 Hz, 1H, H-5), 4.10 (dd, *J* = 9.6, 9.8 Hz, 1H, H-4), 4.43 (d, *J* = 11.8 Hz, 1H, OC*H*Ph), 4.46 (d, *J* = 12.1 Hz, 1H, OC*H*Ph), 4.48 (d, *J* = 11.8 Hz, 1H, OC*H*Ph), 4.52 (d, *J* = 10.7 Hz, 1H, OC*H*Ph), 4.63 (d, *J* = 12.1 Hz, 1H, OC*H*Ph), 4.69 (s, 2H, OCH_2Ph), 4.85 (d, *J* = 10.7 Hz, 1H, OC*H*Ph), 5.99 (dd, *J* = 1.9, 4.3 (J_{H-P}) Hz, 1H, H-1), 7.13–7.19 (m, 8H, Ar-H), 7.24–7.35 (m, 22H, Ar-H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 68.4, 72.2, 72.7, 73.3, 74.1 (d, J_{C-P} = 9.0 Hz), 74.2, 75.1, 78.8, 97.6 (d, J_{C-P} = 7.0 Hz), 120.0 (d, J_{C-P} = 5.0 Hz), 125.4 (d, J_{C-P} = 6.0 Hz), 127.4, 127.5, 127.60, 127.61, 127.72, 127.75, 127.88, 127.90, 128.21, 128.25, 128.32, 128.34, 129.71, 129.74, 137.5, 138.1, 138.15, 138.20, 150.2, 150.29, 150.34; ^{31}P NMR (202 MHz, $CDCl_3$) δ –13.4; FAB-HRMS *m*/*z* calcd for $C_{46}H_{46}O_9P$ $(M+H)^+$ 773.2879, found 773.2870; Anal. calcd for $C_{46}H_{45}O_9P$: C, 71.49; H, 5.87, found: C, 71.27; H, 5.88.

4.2.2. 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-manno-pyranosyl diphenyl phosphate (2b). Diphenylphosphoryl chloride (0.37 mL, 1.8 mmol) was added to a stirred solution of lactol **1b** (673 mg, 1.5 mmol) and DMAP (367 mg, 3.0 mmol) in CH_2Cl_2 (7 mL) at 0 °C. After 30 min, the reaction was quenched with crushed ice, followed by stirring at room temperature for 15 min. The mixture was poured into a two-layer mixture of Et_2O (7 mL) and saturated aqueous $NaHCO_3$ (10 mL), and the whole was extracted with AcOEt (20 mL). The organic extract was washed with brine (2×10 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the pale yellow oil (1.50 g), which was purified by column chromatography (silica gel 40 g, 4:1 hexane/AcOEt with 2% Et_3N) to give diphenyl phosphate **2b** (838 mg, 82%) as a colorless oil: $[\alpha]_D^{25}$ +30.1° (*c* 2.00, $CHCl_3$); IR (film) 3065, 2868, 1589, 1489, 1454, 1373, 1288, 1188 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.75 (dd, *J* = 10.0, 10.2 Hz, 1H, H-6ax), 3.80 (dd, *J* = 1.5, 3.2 Hz, 1H, H-2), 3.85 (ddd, *J* = 4.7, 9.4, 10.2 Hz, 1H, H-5), 3.90 (dd, *J* = 3.2, 10.1 Hz, 1H, H-3), 4.00 (dd, *J* = 4.7, 10.0 Hz, 1H, H-6eq), 4.25 (dd, *J* = 9.4, 10.1 Hz, 1H, H-4), 4.55 (d, *J* = 12.2 Hz, 1H, OC*H*Ph), 4.67 (d, *J* = 12.0 Hz, 1H, OC*H*Ph), 4.73 (d, *J* = 12.2 Hz, 1H, OC*H*Ph), 4.74 (d, *J* = 12.0 Hz, 1H, OC*H*Ph), 5.57 (s, 1H, C*H*Ph), 5.88 (dd, *J* = 1.5, 6.4 (J_{H-P}) Hz, 1H, H-1), 7.11–7.20 (m, 6H, Ar-H), 7.25–7.37 (m, 17H, Ar-H), 7.46–7.48 (m, 2H, Ar-H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 66.0, 68.0, 73.0, 73.7, 75.0, 75.7 (d, J_{C-P} = 9.8 Hz), 78.0, 98.0 (d, J_{C-P} = 6.3 Hz), 101.4, 119.85 (d, J_{C-P} = 5.0 Hz), 119.91 (d, J_{C-P} = 5.0 Hz), 125.50, 125.53, 125.9, 127.4, 127.5, 127.9, 128.0, 128.1, 128.2, 128.4, 128.8, 129.8, 137.2, 138.1, 150.1 (d, J_{C-P} = 7.5 Hz), 150.2 (d, J_{C-P} = 7.5 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ –13.4; FAB-HRMS *m*/*z* calcd for $C_{39}H_{38}O_9P$ $(M+H)^+$ 681.2254, found 681.2252; Anal. calcd for $C_{39}H_{37}O_9P$: C, 68.82; H, 5.48, found: C, 68.71; H, 5.71.

4.2.3. 2,3,4,6-Tetra-*O*-benzyl-α-D-mannopyranosyl *N,N,N',N'*-tetramethylphosphorodiamidate (3a). Butyllithium in hexane (1.58 M, 1.0 mL, 1.58 mmol) was added to a stirred solution of lactol **1a** (800 mg, 1.48 mmol) in THF (15 mL) at –78 °C. After 15 min, a solution of bis(dimethylamino)phosphorochloridate (0.22 mL, 1.48 mmol) in HMPA (2.0 mL) was added, and the mixture was allowed to warm to –20 °C over 30 min. After stirring at this temperature for 2 h, the reaction was quenched with crushed ice, followed by stirring at 0 °C for 30 min. The mixture was poured into a two-layer mixture of Et_2O (10 mL) and saturated aqueous $NaHCO_3$ (15 mL), and the whole was extracted with AcOEt (50 mL). The organic extract was washed with brine (2×15 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the yellow residue (1.55 g), which was purified by flash column chromatography (silica gel 40 g, 1:3→1:4 hexane/AcOEt) to give diamidate **3a** (850 mg, 85%) as a colorless oil: $[\alpha]_D^{24}$ +24.2° (*c* 1.00, $CHCl_3$); IR (film) 3030, 2895, 1954, 1454, 1306, 1225, 990 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.46 (d, J_{H-P} = 10.1 Hz, 6H, $N(CH_3)_2$), 2.60 (d, J_{H-P} = 10.1 Hz, 6H, $N(CH_3)_2$), 3.72 (dd, *J* = 1.5, 10.9 Hz, 1H, H-6a), 3.80 (dd, *J* = 4.7, 10.9 Hz, 1H, H-6b), 3.81 (dd, *J* = 1.8, 3.1 Hz, 1H, H-2), 3.88 (dd, *J* = 3.1, 9.5 Hz, 1H, H-3), 3.86 (ddd, *J* = 1.5, 4.7, 9.7 Hz, 1H, H-5), 4.05 (dd, *J* = 9.5, 9.7 Hz, 1H, H-4), 4.52 (d, *J* = 12.0 Hz, 1H, OC*H*Ph), 4.55 (d, *J* = 10.6 Hz, 1H, OC*H*Ph), 4.60 (s, 2H, OCH_2Ph), 4.66 (d, *J* = 12.0 Hz, 1H, OC*H*Ph), 4.74 (d, *J* = 12.1 Hz, 1H, OC*H*Ph), 4.78 (d, *J* = 12.1 Hz, 1H, OC*H*Ph), 4.92 (d, *J* = 10.6 Hz, 1H, OC*H*Ph), 5.75 (dd, *J* = 1.8, 8.2 (J_{H-P}) Hz, 1H, H-1), 7.21 (m, 2H, Ar-H), 7.24–7.34 (m, 16H, Ar-H), 7.42 (m, 2H, Ar-H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 36.2 (d, J_{C-P} = 3.9 Hz), 36.4 (d, J_{C-P} = 4.3 Hz), 69.0, 71.8, 72.4, 73.3, 73.6, 74.4, 75.0 (d, J_{C-P} = 6.5 Hz), 75.3, 78.5, 93.3 (d, J_{C-P} = 3.8 Hz), 127.3, 127.51, 127.54, 127.6, 127.7, 127.9, 128.0, 128.08, 128.14, 128.19, 128.25, 137.9, 138.1, 138.21, 138.22; ^{31}P NMR (202 MHz, $CDCl_3$) δ 19.1; FAB-HRMS *m*/*z* calcd for $C_{38}H_{48}N_2O_7P$ $(M+H)^+$ 675.3199, found 675.3189; Anal. calcd for $C_{38}H_{47}N_2O_7P$: C, 67.54; H, 7.16; N, 4.15, found: C, 67.71; H, 7.15; N, 4.29.

4.2.4. 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-manno-pyranosyl *N,N,N',N'*-tetramethylphosphorodiamidate (3b). Butyllithium in hexane (1.59 M, 0.89 mL, 1.42 mmol) was added to a stirred solution of lactol **1b** (606 mg, 1.35 mmol) in THF (10 mL) at –78 °C. After 15 min, a solution of bis(dimethylamino)phosphorochloridate (0.20 mL, 1.35 mmol) in HMPA (1.5 mL) was added, and the mixture was allowed to warm to –20 °C over 30 min. After stirring at this temperature for 2 h, the reaction was quenched with crushed ice, followed by stirring at 0 °C for 30 min. The mixture was poured into a two-layer mixture of Et_2O (5 mL) and saturated aqueous $NaHCO_3$ (10 mL), and the whole was extracted with AcOEt (25 mL). The organic extract was washed with brine (2×10 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the yellow residue (1.12 g), which was purified by column chromatography (silica gel 40 g, 1:3→1:4 hexane/AcOEt) to give diamidate **3b** (731 mg, 97%) as a colorless oil: $[\alpha]_D^{22}$ +31.9° (*c* 1.00, $CHCl_3$); IR (film) 3063, 3032, 1454, 1308, 1218, 993 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.45 (d, J_{H-P} = 10.1 Hz, 6H, $N(CH_3)_2$), 2.62 (d, J_{H-P} = 10.0 Hz, 6H, $N(CH_3)_2$), 3.82 (dd, *J* = 1.5, 3.2 Hz, 1H, H-2), 3.85–3.91 (m, 2H, H-6ax, H-6eq), 3.93 (dd, *J* = 3.2, 9.9 Hz, 1H, H-3), 4.23 (m, 1H, H-5), 4.29 (dd, *J* = 9.5, 9.9 Hz, 1H, H-4), 4.66 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.77 (d, *J* = 12.0 Hz, 1H, OC*H*Ph), 4.81 (d, *J* = 12.0 Hz, 1H, OC*H*Ph), 4.81 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 5.65 (dd, *J* = 1.5, 5.7 (J_{H-P}) Hz, 1H, H-1), 5.66 (s, 1H, C*H*Ph), 7.24–7.43 (m, 13H, Ar-H), 7.52 (m, 2H, Ar-H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 36.1 (d, J_{C-P} = 4.2 Hz), 36.3 (d, J_{C-P} = 4.2 Hz), 65.7, 68.5, 72.8, 73.3, 74.6, 76.7 (d, J_{C-P} = 6.8 Hz), 77.3, 78.5, 94.3 (d, J_{C-P} = 3.9 Hz), 101.3, 125.9, 127.5, 127.6, 127.7, 128.06, 128.13, 128.2, 128.3, 128.7, 137.4, 137.6, 138.2; ^{31}P NMR (202 MHz, $CDCl_3$) δ 18.8; FAB-HRMS *m*/*z* calcd for $C_{31}H_{40}N_2O_7P$ $(M+H)^+$ 583.2573, found 583.2568; Anal. calcd for $C_{31}H_{39}N_2O_7P$: C, 63.91; H, 6.75; N, 4.81, found: C, 63.75; H, 6.81; N, 4.82.

4.2.5. 2,3,4,6-Tetra-*O*-benzyl-D-mannopyranosyl diethyl phosphite (4a). Diethyl chlorophosphite (0.26 mL, 1.81 mmol) was added to a stirred solution of lactol **1a** (0.85 g, 1.57 mmol) and Et_3N (0.44 mL, 3.14 mmol) in CH_2Cl_2 (15 mL) at 0 °C. After 30 min, the reaction was quenched with crushed ice, followed by stirring at room temperature for 15

min. The mixture was poured into a two-layer mixture of Et_2O (10 mL) and saturated aqueous $NaHCO_3$ (15 mL), and the whole was extracted with AcOEt (30 mL). The organic extract was washed with brine (2×15 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the pale yellow oil (1.18 g), which was purified by column chromatography (silica gel 25 g, 8:1 hexane/AcOEt with 2% Et_3N) to give diethyl phosphite **4a** (755 mg, 73%, α:β = 87:13) as a colorless oil. The anomeric α:β ratio of the product was determined by ^{31}P NMR. $[\alpha]_D^{24}$ +36.5° (*c* 1.00, $CHCl_3$); IR (film) 3063, 3030, 1454, 1310, 1207, 1101, 1028, 988 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) (data for α-anomer) δ 1.16–1.19 (m, 6H, 2×OCH_2CH_3), 3.69–3.82 (m, 7H, H-2, H-6a, H-6b, 2×OCH_2CH_3), 3.94–3.96 (m, 2H, H-3, H-5), 4.05 (t, *J* = 9.6 Hz, 1H, H-4), 4.51 (d, *J* = 12.0 Hz, 1H, OC*H*Ph), 4.55 (d, *J* = 10.8 Hz, 1H, OC*H*Ph), 4.61 (d, *J* = 11.8 Hz, 1H, OC*H*Ph), 4.65 (d, *J* = 11.8 Hz, 1H, OC*H*Ph), 4.66 (d, *J* = 12.0 Hz, 1H, OC*H*Ph), 4.73 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.76 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.90 (d, *J* = 10.8 Hz, 1H, OC*H*Ph), 5.56 (dd, *J* = 1.5, 8.2 (J_{H-P}) Hz, 1H, H-1), 7.17 (m, 2H, Ar-H), 7.23–7.39 (m, 18H, Ar-H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 16.67, 16.71, 58.2 (d, J_{C-P} = 9.8 Hz), 58.4 (d, J_{C-P} = 11.9 Hz), 69.0, 72.1, 72.4, 72.8, 73.2, 74.7, 75.4 (d, J_{C-P} = 3.2 Hz), 79.2, 91.9 (d, J_{C-P} = 13.3 Hz, C-1α), 94.6 (d, J_{C-P} = 12.9 Hz, C-1β), 127.3, 127.4, 127.5, 127.57, 127.63, 127.7, 127.8, 128.1, 128.15, 128.18, 138.1, 138.27, 138.30, 138.4; ^{31}P NMR (202 MHz, $CDCl_3$) δ 139.7 (β), 139.8 (α); FAB-HRMS *m*/*z* calcd for $C_{38}H_{46}O_8P$ $(M+H)^+$ 661.2931, found 661.2921; Anal. calcd for $C_{38}H_{45}O_8P$: C, 69.08; H, 6.86, found: C, 68.92; H, 6.83.

4.2.6. 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-D-mannopyranosyl diethyl phosphite (4b). Diethyl chlorophosphite (0.21 mL, 1.47 mmol) was added to a stirred solution of lactol **1b** (576 mg, 1.28 mmol) and Et_3N (0.36 mL, 2.56 mmol) in CH_2Cl_2 (6 mL) at 0 °C. After 20 min, the reaction was quenched with crushed ice, followed by stirring at room temperature for 15 min. The mixture was poured into a two-layer mixture of Et_2O (7 mL) and saturated aqueous $NaHCO_3$ (10 mL), and the whole was extracted with AcOEt (25 mL). The organic extract was washed with brine (2×10 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the pale yellow oil (741 mg), which was purified by column chromatography (silica gel 15 g, 8:1 hexane/AcOEt with 2% Et_3N) to give diethyl phosphite **4b** (644 mg, 88%, α:β = 93:7) as a colorless oil. The anomeric α:β ratio of the product was determined by ^{31}P NMR. $[\alpha]_D^{23}$ +45.7° (*c* 1.01, $CHCl_3$); IR (film) 3065, 3032, 1454, 1242, 1215, 1026, 916 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) (data for α-anomer) δ 1.18–1.27 (m, 6H, 2×OCH_2CH_3), 3.72–3.89 (m, 6H, H-2, H-6ax, 2×OCH_2CH_3), 3.97 (ddd, 1H, *J* = 4.6, 9.6, 10.1 Hz, H-5), 4.01 (dd, *J* = 3.1, 10.0 Hz, 1H, H-3), 4.13 (dd, *J* = 4.6, 10.1 Hz, 1H, H-6eq), 4.27 (dd, *J* = 9.6, 10.0 Hz, 1H, H-4), 4.66 (d, *J* = 12.2 Hz, 1H, OC*H*Ph), 4.75 (d, *J* = 12.2 Hz, 1H, OC*H*Ph), 4.83 (d, *J* = 12.2 Hz, 1H, OC*H*Ph), 4.85 (d, *J* = 12.2 Hz, 1H, OC*H*Ph), 5.45 (dd, *J* = 1.4, 8.2 (J_{H-P}) Hz, 1H, H-1), 5.65 (s, 1H, C*H*Ph), 7.26–7.40 (m, 13H, Ar-H), 7.51 (m, 2H, Ar-H). The β-anomer had an additional signal at 5.62 (s, 1H, PhC*H*). ^{13}C NMR (126 MHz, $CDCl_3$) δ 16.70, 16.74, 16.8, 58.2 (d, J_{C-P} = 10.0 Hz), 58.5 (d, J_{C-P} = 12.1 Hz), 65.0, 68.6, 73.1, 73.4, 75.5, 77.1 (d, J_{C-P} = 3.3 Hz), 79.0, 93.2 (d, J_{C-P} = 13.4 Hz, C-1α), 94.9 (d, J_{C-P} = 13.1 Hz, C-1β), 101.4, 126.0, 127.4, 127.5, 127.7, 128.0, 128.1, 128.2, 128.3, 128.7, 137.6, 137.9, 138.5; ^{31}P NMR (202 MHz, $CDCl_3$) δ 139.0 (β), 139.5 (α); FAB-HRMS *m*/*z* calcd for $C_{31}H_{38}O_8P$ $(M+H)^+$ 569.2304, found 569.2295.

4.3. Glycosidations of 2,3,4,6-tetra-*O*-benzyl-D-mannosyl donors 2a–4a

4.3.1. Typical procedure for glycosidation of 2,3,4,6-tetra-*O*-benzyl-D-mannosyl donors: methyl 2,3,4-tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-D-mannopyranosyl)-α-D-glucopyranoside (7).

TMSOTf in CH_2Cl_2 (1.0 M, 0.11 mL, 0.11 mmol) was added to a stirred solution of diphenyl phosphate **2a** (73.6 mg, 0.10 mmol) and alcohol **5** (51.1 mg, 0.11 mmol) in CH_2Cl_2 (1 mL) at –78 °C. After stirring at this temperature for 1 h, the reaction was quenched with Et_3N (0.15 mL). The reaction mixture was poured into a two-layer mixture of AcOEt (3 mL) and $NaHCO_3$ (6 mL), and the whole was extracted with AcOEt (15 mL). The organic extract was successively washed with saturated aqueous $NaHCO_3$ (6 mL) and brine (2×6 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (100.2 mg), from which an anomeric mixture of the known disaccharide **7**[13i] (84.4 mg, 86%, α:β = 21:79) was obtained as a colorless oil after column chromatography (silica gel 7 g, 5:1 hexane/AcOEt). The anomeric ratio of the disaccharide was determined by HPLC analysis [column, Zorbax® Sil, 4.6×250 mm; eluent, 7:1 hexane/THF; flow rate, 1.5 mL/min; detection, 254 nm; t_R (α-mannoside) = 29.4 min, t_R (β-mannoside) = 31.7 min]. The α- and β-mannosides were separated by flash column chromatography with 5:1 hexane/AcOEt.

4.3.2. Methyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-D-mannopyranosyl)-α-D-glucopyranoside (8). The glycosidation was performed according to the typical procedure (1 mL CH_2Cl_2, –78 °C, 1.5 h) employing diphenyl phosphate **2a** (73.6 mg, 0.10 mmol), alcohol **6** (51.1 mg, 0.11 mmol) and TMSOTf (1.0 M in CH_2Cl_2, 0.11 mL, 0.11 mmol). An anomeric mixture of the known disaccharide **8**[13i] (74.2 mg, 75%, α:β = 77:23) was obtained as a colorless oil from the crude product (107 mg) after column chromatography (silica gel 12 g, 20:1→17:1 toluene/AcOEt). The anomeric ratio of the product was determined by HPLC analysis [eluent, 4:1 hexane/AcOEt; flow rate, 1.0 mL/min; t_R (α-mannoside) = 14.3 min, t_R (β-mannoside) = 26.2 min].

4.4. Glycosidations of 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-D-mannosyl donors 2b–4b

4.4.1. Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-D-mannopyranosyl)-α-D-glucopyranoside (9). The glycosidation was performed according to the typical procedure (1 mL CH_2Cl_2, –45 °C, 30 min) employing diethyl phosphite **4b** (56.9 mg, 0.10 mmol),

alcohol **5** (51.1 mg, 0.11 mmol) and TMSOTf (1.0 M in CH_2Cl_2, 0.11 mL, 0.11 mmol). An anomeric mixture of disaccharide **9**[25b] (73.9 mg, 83%, α:β = 10:90) was obtained as a white solid from the crude product (102 mg) after column chromatography (silica gel 5 g, 4:1 hexane/AcOEt). The anomeric ratio of **9** was determined by HPLC analysis [eluent, 4:1 hexane/AcOEt; flow rate, 1.0 mL/min; t_R (α-mannoside) = 21.1 min, t_R (β-mannoside) = 24.4 min].

Data for 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranosyl fluoride (**10**): $[\alpha]_D^{23}$ +13.0° (*c* 1.06, $CHCl_3$); IR ($CHCl_3$) 3624, 3026, 3016, 2401, 1226, 1205, 792, 719 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.85 (t, *J* = 10.0 Hz, 1H, H-6ax), 3.91–3.98 (m, 3H, H-2, H-3, H-5), 4.26–4.31 (m, 2H, H-4, H-6eq), 4.69 (d, *J* = 12.0 Hz, 1H, OC*H*Ph), 4.71 (d, *J* = 12.0 Hz, 1H, OC*H*Ph), 4.87 (d, *J* = 12.0 Hz, 2H, 2×OC*H*Ph), 5.49 (dd, *J* = 1.4, 49.8 (J_{H-F}) Hz, 1H, H-1), 5.64 (s, 1H, C*H*Ph), 7.29–7.40 (13H, m, Ar-H), 7.50 (2H, m, Ar-H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 66.0 (d, J_{C-F} = 1.8 Hz), 68.1, 73.2, 74.0, 74.9 (d, J_{C-F} = 36.0 Hz), 75.5, 78.1, 101.4, 106.8 (d, J_{C-F} = 222.6 Hz), 125.9, 127.4, 127.5, 127.8, 127.9, 128.0, 128.2, 128.3, 128.7, 137.3, 137.5, 138.2; FAB-HRMS *m*/*z* calcd for $C_{27}H_{28}O_5F$ $(M+H)^+$ 451.1921, found 451.1950.

Data for diethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranosylphosphonate (**12**): $[\alpha]_D^{25}$ –73.0° (*c* 1.33, $CHCl_3$); IR ($CHCl_3$) 3013, 1454, 1369, 1249, 1227, 1097, 1028 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.16 (t, *J* = 7.1 Hz, 3H, OCH_2CH_3), 1.31 (t, *J* = 7.0 Hz, 3H, OCH_2CH_3), 3.41 (ddd, *J* = 5.0, 9.8, 10.5 Hz, 1H, H-5), 3.72 (dd, *J* = 3.0, 9.8 Hz, 1H, H-3), 3.85 (t, *J* = 10.5 Hz, 1H, H-6ax), 3.89 (dd, *J* = 1.1, 15.3 (J_{H-P}) Hz, 1H, H-1), 3.98–4.16 (m, 4H, 2×OCH_2CH_3), 4.27–4.34 (m, 3H, H-2, H-4, H-6eq), 4.75 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.81 (d, *J* = 10.4 Hz, 1H, OC*H*Ph), 4.85 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 5.11 (d, *J* = 10.4 Hz, 1H, OC*H*Ph), 5.65 (s, 1H, C*H*Ph), 7.25–7.38 (m, 11H, Ar-H), 7.47–7.51 (m, 4H, Ar-H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 16.2 (d, J_{C-P} = 5.9 Hz), 16.4 (d, J_{C-P} = 5.8 Hz), 62.3 (d, J_{C-P} = 6.5 Hz), 63.3 (d, J_{C-P} = 6.4 Hz), 68.3, 72.8, 73.8, 73.9, 75.4, 75.5 (d, J_{C-P} = 2.2 Hz), 77.1 (d, J_{C-P} = 173 Hz), 78.85, 79.5 (d, J_{C-P} = 15.8 Hz), 101.5, 126.05, 127.48, 127.51, 127.6, 128.0, 128.2, 128.4, 128.5, 128.9, 137.5, 138.3, 138.4; ^{31}P NMR (109 MHz, $CDCl_3$) δ 17.6; FAB-HRMS *m*/*z* calcd for $C_{31}H_{38}O_8P$ $(M+H)^+$ 569.2304, found 569.2257.

4.4.2. Methyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-D-mannopyranosyl)-α-D-glucopyranoside (23). The glycosidation was performed according to the typical procedure (1 mL CH_2Cl_2, –45 °C, 60 min) employing diethyl phosphite **4b** (56.9 mg, 0.10 mmol), alcohol **6** (51.1 mg, 0.11 mmol) and TMSOTf (1.0 M in CH_2Cl_2, 0.11 mL, 0.11 mmol). An anomeric mixture of the known disaccharide **23**[25b] (75.0 mg, 84%, α:β = 11:89) was obtained as a colorless oil from the crude product (106.8 mg) after column chromatography (silica gel 10 g, 4:1 hexane/AcOEt). The anomeric ratio of **23** was determined by HPLC analysis [eluent, 5:1 hexane/AcOEt; flow rate, 1.0 mL/min; t_R (α-mannoside) = 16.2 min, t_R (β-mannoside) = 30.6 min].

4.4.3. Methyl 2,3,4-tri-*O*-acetyl-6-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-D-mannopyranosyl)-α-D-glucopyranoside (24). The glycosidation was performed according to the typical procedure (1 mL CH_2Cl_2, –45 °C, 30 min) employing diethyl phosphite **4b** (56.9 mg, 0.10 mmol), alcohol **13** (35.2 mg, 0.11 mmol) and TMSOTf (1.0 M in CH_2Cl_2, 0.11 mL, 0.11 mmol). An anomeric mixture of the known disaccharide **24**[17d] (63.7 mg, 85%, α:β = 11:89) was obtained from the crude product (88.7 mg) after column chromatography (silica gel 5 g, 2:1 hexane/AcOEt). The anomeric ratio of **24** was determined by HPLC analysis [eluent, 4:1 hexane/THF; flow rate, 1.0 mL/min; t_R (α-mannoside) = 21.1 min, t_R (β-mannoside) = 26.1 min].

4.4.4. Methyl 2-azido-3,6-di-*O*-benzyl-2-deoxy-4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-D-mannopyranosyl)-β-D-glucopyranoside (25). The glycosidation was performed according to the typical procedure (1 mL CH_2Cl_2, –45 °C, 60 min) employing diethyl phosphite **4b** (56.9 mg, 0.10 mmol), alcohol **14** (43.9 mg, 0.11 mmol) and TMSOTf (1.0 M in CH_2Cl_2, 0.11 mL, 0.11 mmol). An anomeric mixture of disaccharide **25** (59.8 mg, 72%, α:β = 17:83) was obtained as a colorless oil from the crude product (100.5 mg) after flash column chromatography (silica gel 7 g, 30:1 toluene/AcOEt). The anomeric ratio of **25** was determined by HPLC analysis [eluent, 5:1 hexane/AcOEt; flow rate, 1.0 mL/min; t_R (α-mannoside) = 10.3 min, t_R (β-mannoside) = 18.9 min]. The α- and β-mannosides were separated by flash column chromatography with 30:1 toluene/AcOEt. Data for β-anomer (**25**β): $[\alpha]_D^{24}$ –58.2° (*c* 1.00, $CHCl_3$); IR (film) 3030, 2922, 2857, 2110, 1497, 1454, 1366, 1279, 1213, 1092, 1055 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.07 (ddd, *J* = 4.8, 9.6, 10.4 Hz, 1H, H-5′), 3.29 (ddd, *J* = 2.0, 3.4, 9.4 Hz, 1H, H-5), 3.34–3.41 (m, 3H, H-2, H-3, H-3′), 3.49 (t, *J* = 10.4 Hz, 1H, H-6′ax), 3.54 (dd, *J* = 3.4, 11.1 Hz, 1H, H-6a), 3.56 (s, 3H, OCH_3), 3.64 (dd, *J* = 2.0, 11.1 Hz, 1H, H-6b), 3.72 (d, *J* = 3.0 Hz, 1H, H-2′), 3.96 (dd, *J* = 9.0, 9.4 Hz, 1H, H-4), 4.05 (dd, *J* = 4.8, 10.4 Hz, 1H, H-6′eq), 4.09 (t, *J* = 9.6 Hz, 1H, H-4′), 4.13 (d, *J* = 7.5 Hz, 1H, H-1), 4.38 (d, *J* = 12.1 Hz, 1H, OC*H*Ph), 4.48 (s, 1H, H-1′), 4.58 (d, *J* = 12.4 Hz, 1H, OC*H*Ph), 4.63 (d, *J* = 12.1 Hz, 1H, OC*H*Ph), 4.64 (d, *J* = 10.4 Hz, 1H, OC*H*Ph), 4.74 (d, *J* = 12.4 Hz, 1H, OC*H*Ph), 4.79 (d, *J* = 11.9 Hz, 1H, OC*H*Ph), 4.87 (d, *J* = 11.9 Hz, 1H, OC*H*Ph), 5.09 (d, *J* = 10.4 Hz, 1H, OC*H*Ph), 5.51 (s, 1H, C*H*Ph), 7.20–7.41 (m, 23H, Ar-H), 7.47 (m, 2H, Ar-H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 57.1, 65.7, 67.3, 68.3, 68.5, 72.6, 73.6, 74.8, 75.11, 75.13, 77.1, 78.4, 78.7, 81.6, 101.3 (C-1′), 101.4, 102.8 (C-1), 126.1, 127.4, 127.49, 127.54, 127.8, 127.96, 128.01, 128.10, 128.14, 128.30, 128.31, 128.5, 128.8, 137.6, 138.48, 138.53, 138.6; FAB-HRMS *m*/*z* calcd for $C_{48}H_{52}N_3O_{10}$ $(M+H)^+$ 830.3653, found 830.3660. Data for α-anomer (**25**α): $[\alpha]_D^{24}$ –16.0° (*c* 0.30, $CHCl_3$); IR (film) 3032, 2922, 2858, 2110, 1496, 1454, 1363, 1275, 1116, 1064 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.32 (dd, *J* = 9.4, 9.8 Hz, 1H, H-3), 3.38–3.42 (m, 2H, H-2, H-5), 3.57 (s, 3H, OCH_3), 3.72 (dd, *J* = 4.5, 11.0 Hz, 1H, H-6a), 3.76–3.81 (m, 4H, H-4, H-6b, H-2′, H-6′ax), 3.83 (dt, *J* = 3.9, 10.3 Hz, 1H, H-5′), 3.90 (dd, *J* = 3.1, 10.3 Hz, 1H, H-3′), 4.12 (m, 1H, H-6′eq), 4.19 (d, *J* = 7.9 Hz, 1H, H-1), 4.24 (t, *J* = 10.3 Hz, 1H, H-4′), 4.25 (d, *J* = 11.8 Hz, 1H, OC*H*Ph), 4.47 (d, *J* =

11.8 Hz, 1H, OC*H*Ph), 4.54 (d, *J* = 11.4 Hz, 1H, OC*H*Ph), 4.56 (d, *J* = 12.1 Hz, 1H, OC*H*Ph), 4.59 (d, *J* = 12.2 Hz, 1H, OC*H*Ph), 4.63 (d, *J* = 12.1 Hz, 1H, OC*H*Ph), 4.82 (d, *J* = 12.2 Hz, 1H, OC*H*Ph), 4.94 (d, *J* = 11.4 Hz, 1H, OC*H*Ph), 5.26 (d, *J* = 1.2 Hz, 1H, H-1′), 5.61 (s, 1H, C*H*Ph), 7.15 (m, 2H, Ar-H), 7.21–7.37 (m, 21H, Ar-H), 7.50 (m, 2H, Ar-H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 57.1, 65.3, 66.2, 68.6, 69.0, 73.1, 73.4, 73.6, 74.6, 74.7, 76.2, 76.3, 77.7, 79.0, 83.0, 101.2 (C-1′), 101.4, 103.0 (C-1), 126.1, 127.0, 127.46, 127.48, 127.6, 127.7, 127.8, 128.2, 128.3, 128.4, 128.6, 128.8, 137.7, 138.1, 138.2, 138.7; FAB-HRMS *m*/*z* calcd for $C_{48}H_{52}N_3O_{10}$ $(M+H)^+$ 830.3653, found 830.3669.

4.4.5. 6-*O*-(2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-D-mannopyranosyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (26). The glycosidation was performed according to the typical procedure (1 mL CH_2Cl_2, –45 °C, 30 min) employing diethyl phosphite **4b** (56.9 mg, 0.10 mmol), alcohol **15** (28.6 mg, 0.11 mmol) and TMSOTf (1.0 M in CH_2Cl_2, 0.11 mL, 0.11 mmol). An anomeric mixture of the known disaccharide **26**[17d] (61.5 mg, 89%, α:β = 24:76) was obtained as a colorless oil from the crude product (83.0 mg) after column chromatography (silica gel 6 g, 5:1 hexane/AcOEt). The anomeric ratio of **26** was determined by HPLC analysis [eluent, 7:2 hexane/AcOEt; flow rate, 1.0 mL/min; t_R (α-mannoside) = 8.2 min, t_R (β-mannoside) = 11.4 min].

4.4.6. Benzyl 2,4,6-tri-*O*-benzyl-3-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-D-mannopyranosyl)-α-D-glucopyranoside (27). The glycosidation was performed according to the typical procedure (1 mL CH_2Cl_2, –45 °C, 30 min) employing diethyl phosphite **4b** (56.9 mg, 0.10 mmol), alcohol **16** (60.0 mg, 0.11 mmol) and TMSOTf (1.0 M in CH_2Cl_2, 0.11 mL, 0.11 mmol). An anomeric mixture of disaccharide **27** (75.4 mg, 77%, α:β = 15:85) was obtained as a colorless syrup from the crude product (105.9 mg) after column chromatography (silica gel 6 g, 5:1 hexane/AcOEt). The anomeric ratio of the product was determined by ^{1}H NMR [integration of benzylidene proton, β-anomer (5.57 ppm), α-anomer (5.60 ppm)]. The α- and β-mannosides were separated by flash column chromatography with 5:1 hexane/AcOEt. Data for β-anomer (**27**β): $[\alpha]_D^{23}$ +32.5° (*c* 1.01, $CHCl_3$); IR ($CHCl_3$) 3067, 3025, 3015, 2872, 1497, 1454, 1366, 1209, 1090, 791, 671 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.27 (ddd, *J* = 4.9, 9.5, 10.4 Hz, 1H, H-5′), 3.41 (dd, *J* = 3.6, 9.7 Hz, 1H, H-2), 3.45 (dd, *J* = 3.0, 9.9 Hz, 1H, H-3′), 3.56–3.59 (m, 2H, H-4, H-6a), 3.68–3.75 (m, 2H, H-6b, H-6′ax), 3.77 (m, 1H, H-5), 3.81 (d, *J* = 3.0 Hz, 1H, H-2′), 4.14 (dd, *J* = 9.5, 9.9 Hz, 1H, H-4′), 4.17 (dd, *J* = 9.2, 9.7 Hz, 1H, H-3), 4.21 (dd, *J* = 4.9, 10.4 Hz, 1H, H-6′eq), 4.26 (d, *J* = 11.6 Hz, 1H, OC*H*Ph), 4.33 (d, *J* = 10.1 Hz, 1H, OC*H*Ph), 4.37 (d, *J* = 11.6 Hz, 1H, OC*H*Ph), 4.48–4.52 (m, 3H, 3×OC*H*Ph), 4.62–4.67 (m, 3H, 3×OC*H*Ph), 4.84–4.90 (m, 4H, H-1, H-1′, 2×OC*H*Ph), 5.13 (d, *J* = 10.1 Hz, 1H, OC*H*Ph), 5.57 (s, 1H, C*H*Ph), 7.15 (m, 2H, Ar-H), 7.21–7.36 (m, 29H, Ar-H), 7.45–7.49 (m, 4H, Ar-H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 67.3, 68.4, 68.7, 69.2, 70.1, 72.5, 72.6, 73.6, 74.7, 74.9, 75.9, 78.6, 78.8, 80.3, 81.1, 94.9 (C-1′), 101.3, 102.8 (C-1), 126.1, 127.4, 127.47, 127.51, 127.7, 127.9, 127.97, 128.02, 128.05, 128.06, 128.11, 128.25, 128.31, 128.37, 128.39, 128.5, 128.7, 136.9, 137.7, 137.8, 138.0, 138.6, 138.9; FAB-HRMS *m*/*z* calcd for $C_{61}H_{62}O_{11}Na$ $(M+Na)^+$ 993.4190, found 993.4234; Anal. calcd for $C_{61}H_{62}O_{11}$: C, 75.44; H, 6.43, found: C, 75.13; H, 6.55. Data for α-anomer (**27**α): $[\alpha]_D^{24}$ +38.2° (*c* 0.33, $CHCl_3$); IR ($CHCl_3$) 3029, 3007, 2928, 1497, 1454, 1366, 1229, 1071, 1026, 756, 737, 716, 669 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.38 (dd, *J* = 3.7, 9.7 Hz, 1H, H-2), 3.50 (dd, *J* = 1.8, 10.8 Hz, 1H, H-6a), 3.58–3.63 (m, 2H, H-4, H-6b), 3.74–3.81 (m, 3H, H-5, H-2′, H-6′ax), 3.96 (dd, *J* = 3.1, 9.6 Hz, 1H, H-3′), 4.14–4.19 (m, 2H, H-3, H-6′eq), 4.22 (t, *J* = 9.6 Hz, 1H, H-4′), 4.29 (ddd, *J* = 4.7, 9.6, 9.9 Hz, 1H, H-5′), 4.36 (d, *J* = 12.0 Hz, 1H, OC*H*Ph), 4.41–4.49 (m, 5H, 5×OC*H*Ph), 4.53–4.61 (m, 4H, 4×OC*H*Ph), 4.63 (d, *J* = 12.2 Hz, 1H, OC*H*Ph), 4.80 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.82 (d, *J* = 3.7 Hz, 1H, H-1), 5.34 (d, *J* = 1.0 Hz, 1H, H-1′), 5.60 (s, 1H, C*H*Ph), 7.14–7.36 (m, 33H, Ar-H), 7.47 (m, 2H, Ar-H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 64.2, 68.3, 68.8, 69.3, 70.0, 72.6, 73.0, 73.2, 73.6, 74.0, 76.5, 77.5, 77.8, 78.8, 79.2, 95.6 (C-1′), 99.9 (C-1), 101.4, 126.2, 126.8, 127.4, 127.5, 127.6, 127.7, 127.77, 127.83, 127.96, 128.04, 128.1, 128.2, 128.3, 128.36, 128.39, 128.44, 128.5, 128.6, 137.2, 137.7, 137.8, 138.0, 138.1, 138.2, 138.9; FAB-HRMS *m*/*z* calcd for $C_{61}H_{63}O_{11}$ $(M+H)^+$ 971.4371, found 971.4413.

4.4.7. Methyl 3,4,6-tri-*O*-benzyl-2-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-D-mannopyranosyl)-β-D-glucopyranoside (28). The glycosidation was performed according to the typical procedure (1 mL CH_2Cl_2, –45 °C, 30 min) employing diethyl phosphite **4b** (56.9 mg, 0.10 mmol), alcohol **17** (51.2 mg, 0.11 mmol) and TMSOTf (1.0 M in CH_2Cl_2, 0.11 mL, 0.11 mmol). An anomeric mixture of disaccharide **28** (85.6 mg, 96%, α:β = 5:95) was obtained as a colorless syrup from the crude product (105.4 mg) after column chromatography (silica gel 15 g, 20:1→15:1 toluene/AcOEt). The anomeric ratio of **28** was determined by HPLC analysis [eluent, 4:1 hexane/AcOEt; flow rate, 1.0 mL/min; t_R (α-mannoside) = 4.9 min, t_R (β-mannoside) = 26.7 min]. The α- and β-mannosides were separated by column chromatography with 5:1 hexane/AcOEt. Data for β-anomer (**28**β): $[\alpha]_D^{24}$ –27.5° (*c* 1.02, $CHCl_3$); IR (film) 3021, 2976, 2895, 1522, 1424, 1215, 1047, 928, 775, 673 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.25 (ddd, *J* = 4.8, 9.6, 10.3 Hz, 1H, H-5′), 3.37 (dd, *J* = 2.9, 9.6 Hz, 1H, H-3′), 3.48 (m, 1H, H-5), 3.54 (s, 3H, OCH_3), 3.56–3.67 (m, 3H, H-2, H-3, H-4), 3.70–3.77 (m, 3H, H-6a, H-6b, H-2′), 3.92 (t, *J* = 10.3 Hz, 1H, H-6′ax), 4.18 (t, *J* = 9.6 Hz, 1H, H-4′), 4.30 (dd, *J* = 4.8, 10.3 Hz, 1H, H-6′eq), 4.36 (d, *J* = 7.1 Hz, 1H, H-1), 4.45 (d, *J* = 12.1 Hz, 1H, OC*H*Ph), 4.51 (d, *J* = 11.7 Hz, 1H, OC*H*Ph), 4.55–4.60 (m, 3H, 3×OC*H*Ph), 4.64 (d, *J* = 12.1 Hz, 1H, OC*H*Ph), 4.72–4.74 (m, 2H, H-1′, OC*H*Ph), 4.78 (d, *J* = 12.1 Hz, 1H, OC*H*Ph), 4.84 (d, *J* = 12.1 Hz, 1H, OC*H*Ph), 4.85 (d, *J* = 11.7 Hz, 1H, OC*H*Ph), 5.59 (s, 1H, C*H*Ph), 7.14–7.38 (m, 28H, Ar-H), 7.48 (m, 2H, Ar-H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 56.7, 67.4, 68.6, 68.7, 72.5, 73.5, 74.5, 74.78, 74.81, 75.1, 76.4, 78.2, 78.6, 78.7, 80.9, 85.0, 101.3, 102.0 (C-1′), 102.6 (C-1), 126.0, 126.9, 127.3, 127.4, 127.5, 127.6, 127.7, 127.8, 127.9, 128.1, 128.2, 128.3, 128.37, 128.42, 128.7, 137.6, 137.8, 138.1, 138.4, 138.5; FAB-HRMS *m*/*z* calcd for $C_{55}H_{59}O_{11}$

$(M+H)^+$ 895.4057, found 895.4059; Anal. calcd for $C_{55}H_{58}O_{11}$: C, 73.81; H, 6.53, found: C, 73.62; H, 6.54. Data for α-anomer (**28**α): $[\alpha]_D^{24}$ +51.1° (*c* 1.00, $CHCl_3$); IR (film) 3030, 2926, 2865, 1497, 1454, 1368, 1215, 1092, 914, 750, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.40 (s, 3H, OCH_3), 3.42 (ddd, *J* = 1.5, 4.5, 9.4 Hz, 1H, H-5), 3.48 (dd, *J* = 9.1, 9.2 Hz, 1H, H-3), 3.59 (dd, *J* = 7.8, 9.1 Hz, 1H, H-2), 3.60 (dd, *J* = 9.2, 9.4 Hz, 1H, H-4), 3.67 (dd, *J* = 4.5, 9.8 Hz, 1H, H-6a), 3.72 (dd, *J* = 1.5, 9.8 Hz, 1H, H-6b), 3.77 (t, *J* = 10.0 Hz, 1H, H-6′ax), 3.84 (dd, *J* = 1.0, 3.1 Hz, 1H, H-2′), 3.92 (dd, *J* = 3.1, 10.0 Hz, 1H, H-3′), 4.03 (ddd, *J* = 4.8, 9.6, 10.0 Hz, 1H, H-5′), 4.09 (dd, *J* = 4.8, 10.0 Hz, 1H, H-6′eq), 4.13 (d, *J* = 7.8 Hz, 1H, H-1), 4.24 (dd, *J* = 9.6, 10.0 Hz, 1H, H-4′), 4.50 (d, *J* = 10.8 Hz, 1H, OC*H*Ph), 4.53 (d, *J* = 12.3 Hz, 1H, OC*H*Ph), 4.60 (d, *J* = 12.3 Hz, 1H, OC*H*Ph), 4.64 (d, *J* = 12.3 Hz, 1H, OC*H*Ph), 4.70 (d, *J* = 10.7 Hz, 1H, OC*H*Ph), 4.74–4.81 (m, 5H, 5×OC*H*Ph), 5.38 (d, *J* = 1.0 Hz, 1H, H-1′), 5.60 (s, 1H, C*H*Ph), 7.11–7.16 (m, 5H, Ar-H), 7.22–7.43 (m, 25H, Ar-H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 56.7, 64.4, 68.66, 68.70, 72.9, 73.0, 73.5, 74.9, 75.1, 75.7, 75.9, 76.1, 76.9, 78.2, 79.1, 83.2, 98.7 (C-1′), 101.3, 104.3 (C-1), 126.2, 127.4, 127.56, 127.60, 127.62, 127.7, 127.8, 127.9, 128.0, 128.2, 128.3, 128.35, 128.38, 128.6, 137.7, 137.90, 137.94, 138.0, 138.2, 138.6; FAB-HRMS *m*/*z* calcd for $C_{55}H_{59}O_{11}$ $(M+H)^+$ 895.4057, found 895.4064; Anal. calcd for $C_{55}H_{58}O_{11}$: C, 73.81; H, 6.53, found: C, 73.48; H, 6.60.

4.4.8. Methyl 4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-D-mannopyranosyl)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (29). The glycosidation was performed according to the typical procedure (1 mL CH_2Cl_2, –45 °C, 30 min) employing diethyl phosphite **4b** (56.9 mg, 0.10 mmol), alcohol **18** (25.6 mg, 0.11 mmol) and TMSOTf (1.0 M in CH_2Cl_2, 0.11 mL, 0.11 mmol). An anomeric mixture of the known disaccharide **29**[17d] (59.1 mg, 89%, α:β = 11:89) was obtained as a colorless oil from the crude product (79 mg) after column chromatography (silica gel 7 g, 10:1 hexane/AcOEt). The anomeric ratio of **29** was determined by HPLC analysis [eluent, 13:1 hexane/AcOEt; flow rate, 1.0 mL/min; t_R (β-mannoside) = 47.7 min, t_R (α-mannoside) = 51.9 min].

4.4.9. 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-D-mannopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranosyl *N*,*N*,*N*',*N*'-tetramethylphosphorodiamidate (30). The glycosidation was performed according to the typical procedure (1 mL CH_2Cl_2, –45 °C, 30 min) employing diethyl phosphite **4b** (56.9 mg, 0.10 mmol), alcohol **19** (68.9 mg, 0.11 mmol) and TMSOTf (1.0 M in CH_2Cl_2, 0.20 mL, 0.20 mmol). An anomeric mixture of disaccharide **30** (90.0 mg, 85%, α:β = 14:86) was obtained as a colorless syrup from the crude product (101 mg) after column chromatography (silica gel 4 g, 3:4 hexane/AcOEt). The anomeric ratio of the product was determined by ^{13}C NMR [peak height of C-1′, β-anomer (102.7 ppm), α-anomer (99.9 ppm)]. The α- and β-mannosides were separated by flash column chromatography with 10:1 CH_2Cl_2/acetone. Data for β-anomer (**30**β): $[\alpha]_D^{23}$ –5.20° (*c* 1.07, $CHCl_3$); IR ($CHCl_3$) 3016, 1730, 1452, 1278, 1093 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.59 (d, J_{H-P} = 10.1 Hz, 6H, N(CH_3)$_2$), 2.65 (d, J_{H-P} = 10.0 Hz, 6H, N(CH_3)$_2$), 3.27 (ddd, *J* = 4.8, 9.6, 10.2 Hz, 1H, H-5′), 3.60 (dd, *J* = 3.0, 9.9 Hz, 1H, H-3′), 3.68 (dd, *J* = 5.0, 11.6 Hz, 1H, H-6a), 3.86 (dd, *J* = 10.2, 10.4 Hz, 1H, H-6′ax), 4.10 (d, *J* = 3.0 Hz, 1H, H-2′), 4.17 (dd, *J* = 0.9, 11.6 Hz, 1H, H-6b), 4.18 (dd, *J* = 9.6, 9.9 Hz, 1H, H-4′), 4.23 (dd, *J* = 4.8, 10.4 Hz, 1H, H-6′eq), 4.448 (s, 1H, H-1′), 4.453 (ddd, *J* = 0.9, 5.0, 10.0 Hz, 1H, H-5), 4.62 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.71 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.93 (d, *J* = 12.0 Hz, 1H, OC*H*Ph), 4.99 (d, *J* = 12.0 Hz, 1H, OC*H*Ph), 5.35 (ddd, *J* = 3.2, 10.0, 1.6 (J_{H-P}) Hz, 1H, H-2), 5.58 (s, 1H, C*H*Ph), 5.63 (t, *J* = 10.0 Hz, 1H, H-4), 6.13 (dd, *J* = 3.2, 8.1 (J_{H-P}) Hz, 1H, H-1), 6.17 (t, *J* = 10.0 Hz, 1H, H-3), 7.26–7.55 (m, 24H, Ar-H), 7.87 (m, 2H, Ar-H), 7.92–7.96 (m, 4H, Ar-H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 36.4 (d, J_{C-P} = 3.9 Hz), 36.5 (d, J_{C-P} = 3.9 Hz), 67.6, 68.1, 68.3, 68.4, 68.6, 70.0, 70.8, 71.5 (d, J_{C-P} = 6.3 Hz), 72.2, 75.1, 76.2, 77.2, 77.9, 78.4, 92.0 (d, J_{C-P} = 3.3 Hz, C-1), 101.3, 102.7 (C-1′), 126.0, 127.4, 127.5, 128.07, 128.13, 128.2, 128.27, 128.33, 128.34, 128.4, 128.68, 128.74, 128.9, 129.6, 129.7, 129.8, 133.2, 133.3, 133.5, 137.5, 138.3, 138.5, 165.2, 165.4, 165.9; ^{31}P NMR (109 MHz, $CDCl_3$) δ 19.9; FAB-HRMS *m*/*z* calcd for $C_{58}H_{62}N_2O_{15}P$ $(M+H)^+$ 1057.3888, found 1057.3900; Anal. calcd for $C_{58}H_{61}N_2O_{15}P$: C, 65.90; H, 5.82; N, 2.65, found: C, 65.66; H, 5.88; N, 2.72. Data for α-anomer (**30**α): $[\alpha]_D^{24}$ +43.3° (*c* 0.86, $CHCl_3$); IR ($CHCl_3$) 3016, 1730, 1452, 1278, 1093 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.59 (d, J_{H-P} = 10.5 Hz, 6H, N(CH_3)$_2$), 2.66 (d, J_{H-P} = 10.0 Hz, 6H, N(CH_3)$_2$), 3.62 (dd, *J* = 3.5, 11.4 Hz, 1H, H-6a), 3.65 (ddd, *J* = 4.8, 9.5, 10.2 Hz, 1H, H-5′), 3.73–3.78 (m, 2H, H-2′, H-6′ax), 3.88 (dd, *J* = 3.8, 11.4 Hz, 1H, H-6b), 3.96 (dd, *J* = 3.3, 9.9 Hz, 1H, H-3′), 4.00 (dd, *J* = 4.8, 10.1 Hz, 1H, H-6′eq), 4.18 (dd, *J* = 9.5, 9.9 Hz, 1H, H-4′), 4.37 (ddd, *J* = 3.5, 3.8, 9.8 Hz, 1H, H-5), 4.56 (d, *J* = 11.9 Hz, 1H, OC*H*Ph), 4.69 (d, *J* = 12.1 Hz, 1H, OC*H*Ph), 4.76 (d, *J* = 11.9 Hz, 1H, OC*H*Ph), 4.78 (d, *J* = 12.1 Hz, 1H, OC*H*Ph), 4.82 (d, *J* = 1.0 Hz, 1H, H-1′), 5.38 (ddd, *J* = 3.2, 10.0, 1.6 (J_{H-P}) Hz, 1H, H-2), 5.58 (s, 1H, C*H*Ph), 5.67 (dd, *J* = 9.8, 10.0 Hz, 1H, H-4), 6.08 (dd, *J* = 3.2, 7.8 (J_{H-P}) Hz, 1H, H-1), 6.14 (t, *J* = 10.0 Hz, 1H, H-3), 7.26–7.53 (m, 24H, Ar-H), 7.88 (m, 2H, Ar-H), 7.92–7.96 (m, 4H, Ar-H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 36.4 (d, J_{C-P} = 4.0 Hz), 36.5 (d, J_{C-P} = 4.0 Hz), 64.4, 66.1, 68.6, 68.9, 70.0, 70.1, 71.5 (d, J_{C-P} = 6.3 Hz), 73.2, 73.6, 76.3, 76.4, 78.9, 92.1 (d, J_{C-P} = 3.5 Hz, C-1), 99.9 (C-1′), 101.3, 126.2, 127.6, 127.7, 128.00, 128.03, 128.3, 128.35, 128.38, 128.5, 128.7, 129.0, 129.7, 129.8, 129.9, 133.3, 133.36, 133.42, 137.8, 138.1, 138.8; ^{31}P NMR (109 MHz, $CDCl_3$) δ 19.9; FAB-HRMS *m*/*z* calcd for $C_{58}H_{61}N_2O_{15}PNa$ $(M+Na)^+$ 1079.3703, found 1079.3750.

4.4.10. 1-Adamantyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-D-mannopyranoside (31). The glycosidation was performed according to the typical procedure (1 mL CH_2Cl_2, –45 °C, 30 min) employing diethyl phosphite **4b** (56.9 mg, 0.10 mmol), 1-adamantanol (**20**, 16.7 mg, 0.11 mmol) and TMSOTf (1.0 M in CH_2Cl_2, 0.11 mL, 0.11 mmol). An anomeric mixture of the known mannoside **31**[17d] (52.0 mg, 89%, α:β = 16:84) was obtained as a colorless oil from the crude product (69.8 mg) after column chromatography (silica gel 10 g, 9:1 hexane/AcOEt). The anomeric ratio of

31 was determined by HPLC analysis [eluent, 20:1 hexane/AcOEt; flow rate, 1.0 mL/min; t_R (α-mannoside) = 27.4 min, t_R (β-mannoside) = 40.1 min].

4.4.11. Allyl *N*-(benzyloxycarbonyl)-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-D-mannopyranosyl)-L-serinate (32). The glycosidation was performed according to the typical procedure (1 mL CH_2Cl_2, –45 °C, 15 min) employing diethyl phosphite **4b** (56.9 mg, 0.10 mmol), alcohol **21** (30.7 mg, 0.11 mmol) and TMSOTf (1.0 M in CH_2Cl_2, 0.11 mL, 0.11 mmol). An anomeric mixture of mannoside **32** (61.7 mg, 87%, α:β = 15:85) was obtained from the crude product (95.9 mg) after column chromatography (silica gel 7 g, 3:1 hexane/AcOEt). The anomeric ratio of **32** was determined by HPLC analysis [eluent, 5:1 hexane/AcOEt; flow rate, 1.0 mL/min; t_R (α-mannoside) = 24.9 min, t_R (β-mannoside) = 30.0 min]. The α- and β-mannosides were separated by flash column chromatography with 5:1 hexane/AcOEt. Data for β-anomer (**32**β): $[\alpha]_D^{24}$ –35.4° (*c* 1.74, $CHCl_3$); IR ($CHCl_3$) 3020, 2878, 1720, 1508, 1217, 1093 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.28 (ddd, *J* = 4.7, 9.5, 10.3 Hz, 1H, H-5), 3.55 (dd, *J* = 2.9, 9.8 Hz, 1H, H-3), 3.78 (dd, *J* = 2.9, 10.1 Hz, 1H, Ser-β-C*H*), 3.87–3.91 (m, 2H, H-2, H-6ax), 4.18 (dd, *J* = 9.5, 9.8 Hz, 1H, H-4), 4.28 (dd, *J* = 4.7, 10.4 Hz, 1H, H-6eq), 4.34 (dd, *J* = 3.0, 10.1 Hz, 1H, Ser-β-C*H*), 4.40 (s, 1H, H-1), 4.57 (m, 1H, Ser-α-C*H*), 4.60 (d, *J* = 12.4 Hz, 1H, OC*H*Ph), 4.62–4.73 (m, 2H, CH_2CH=CH$_2$), 4.70 (d, *J* = 12.4 Hz, 1H, OC*H*Ph), 4.75 (d, *J* = 12.3 Hz, 1H, OC*H*Ph), 4.87 (d, *J* = 12.3 Hz, 1H, OC*H*Ph), 5.11 (d, *J* = 12.4 Hz, 1H, CO$_2$C*H*Ph), 5.14 (d, *J* = 12.4 Hz, 1H, CO$_2$C*H*Ph), 5.23 (d, *J* = 10.4 Hz, 1H, CH$_2$CH=C*H*), 5.33 (d, *J* = 17.2 Hz, 1H, CH$_2$CH=C*H*), 5.57 (d, *J* = 8.2 Hz, 1H, N*H*), 5.60 (s, 1H, C*H*Ph), 5.88 (m, 1H, CH$_2$C*H*=CH$_2$), 7.22–7.42 (m, 18H, Ar-H), 7.49 (m, 2H, Ar-H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 54.2, 66.4, 67.2, 67.7, 68.4, 69.8, 72.5, 74.5, 75.2, 77.8, 78.5, 101.4, 102.4 (C-1), 118.9, 126.0, 127.5, 127.59, 127.63, 128.16, 128.20, 128.29, 128.32, 128.5, 128.6, 128.9, 131.4, 136.1, 137.5, 138.2, 155.9, 169.5; FAB-HRMS *m/z* calcd for $C_{41}H_{44}NO_{10}$ $(M+H)^+$ 710.2965, found 710.2920. Data for α-anomer (**32**α): $[\alpha]_D^{23}$ +36.0° (*c* 0.61, $CHCl_3$); IR ($CHCl_3$) 3020, 2935, 1722, 1504, 1454, 1238, 1199, 1062 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.70–3.75 (m, 2H, H-2, H-5), 3.84 (t, *J* = 10.1 Hz, 1H, H-6ax), 3.87 (dd, *J* = 3.2, 9.9 Hz, 1H, H-3), 3.88 (dd, *J* = 3.2, 10.2 Hz, 1H, Ser-β-C*H*), 3.93 (dd, *J* = 2.8, 10.2 Hz, 1H, Ser-β-C*H*), 4.21–4.25 (m, 2H, H-4, H-6eq), 4.54 (m, 1H, Ser-α-C*H*), 4.59 (brd, *J* = 4.7 Hz, 2H, CH_2CH=CH$_2$), 4.63 (d, *J* = 12.0 Hz, 1H, OC*H*Ph), 4.68 (d, *J* = 12.3 Hz, 1H, OC*H*Ph), 4.74 (s, 1H, H-1), 4.79 (d, *J* = 12.3 Hz, 1H, OC*H*Ph), 4.84 (d, *J* = 12.0 Hz, 1H, OC*H*Ph), 5.10 (d, *J* = 12.1 Hz, 1H, CO$_2$C*H*Ph), 5.15 (d, *J* = 12.1 Hz, 1H, CO$_2$C*H*Ph), 5.19 (d, *J* = 10.6 Hz, 1H, CH$_2$CH=C*H*), 5.28 (d, *J* = 17.2 Hz, 1H, CH$_2$CH=C*H*), 5.59 (d, *J* = 8.1 Hz, 1H, N*H*), 5.63 (s, 1H, C*H*Ph), 5.83 (m, 1H, CH$_2$C*H*=CH$_2$), 7.25–7.39 (m, 18H, Ar-H), 7.49 (m, 2H, Ar-H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 54.3, 64.7, 66.3, 67.3, 68.3, 68.6, 73.4, 73.7, 76.3, 78.9, 100.1 (C-1), 101.5, 119.1, 126.1, 127.5, 127.6, 127.8, 128.0, 128.1, 128.2, 128.3, 128.4, 128.6, 128.8, 131.3, 136.0, 137.6, 138.0, 138.6, 155.8, 169.5; FAB-HRMS *m/z* calcd for $C_{41}H_{44}NO_{10}$ $(M+H)^+$ 710.2965, found 710.2974.

4.4.12. Cholesteryl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-D-mannopyranoside (33). The glycosidation was performed according to the typical procedure (1 mL CH_2Cl_2, –45 °C, 30 min) employing diethyl phosphite **4b** (56.9 mg, 0.10 mmol), cholesterol (**22**, 42.6 mg, 0.11 mmol) and TMSOTf (1.0 M in CH_2Cl_2, 0.11 mL, 0.11 mmol). An anomeric mixture of mannoside **33** (70.5 mg, 86%, α:β = 17:83) was obtained from the crude product (110.6 mg) after column chromatography (silica gel 8 g, 10:1 hexane/AcOEt). The anomeric ratio of **33** was determined by HPLC analysis [eluent, 20:1 hexane/THF; flow rate, 1.0 mL/min; t_R (α-mannoside) = 8.1 min, t_R (β-mannoside) = 9.1 min]. The α- and β-mannosides were separated by flash column chromatography with 15:1 hexane/AcOEt. Data for β-anomer (**33**β): mp 108.0–109.0 °C (colorless fine needles from MeOH); $[\alpha]_D^{25}$ +49.6° (*c* 1.62, $CHCl_3$); IR ($CHCl_3$) 3018, 2943, 1454, 1381, 1217, 1095 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.68 (s, 3H, H-18), 0.86–1.67 (m, 33H), 1.81–1.87 (m, 2H), 1.96–2.03 (m, 3H), 2.21 (m, 1H, H-4a), 2.29 (m, 1H, H-4b), 3.31 (ddd, *J* = 4.8, 9.4, 10.2 Hz, 1H, H-5′), 3.56 (m, 1H, H-3), 3.58 (dd, *J* = 3.0, 9.7 Hz, 1H, H-3′), 3.87 (d, *J* = 3.0 Hz, 1H, H-2′), 3.92 (dd, *J* = 10.2, 10.4 Hz, 1H, H-6′ax), 4.21 (dd, *J* = 9.4, 9.7 Hz, 1H, H-4′), 4.28 (dd, *J* = 4.8, 10.4 Hz, 1H, H-6′eq), 4.58 (s, 1H, H-1′), 4.59 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.68 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.90 (d, *J* = 12.4 Hz, 1H, OC*H*Ph), 4.99 (d, *J* = 12.4 Hz, 1H, OC*H*Ph), 5.35 (m, 1H, H-6), 5.61 (s, 1H, C*H*Ph), 7.25–7.37 (m, 11H, Ar-H), 7.48–7.50 (m, 4H, Ar-H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 11.8, 18.7, 19.4, 21.0, 22.5, 22.8, 23.8, 24.3, 28.0, 28.2, 29.6, 31.88, 31.94, 35.8, 36.2, 36.8, 37.2, 38.8, 39.5, 39.8, 42.3, 50.2, 56.1, 56.7, 67.5, 68.7, 72.3, 74.7, 76.3, 77.2, 78.1, 78.6, 100.0 (C-1′), 101.4, 122.0, 126.0, 127.4, 127.48, 127.49, 128.0, 128.1, 128.3, 128.7, 128.8, 137.7, 138.4, 138.5, 140.5; FAB-HRMS *m/z* calcd for $C_{54}H_{72}O_6Na$ $(M+Na)^+$ 839.5226, found 839.5244; Anal. calcd for $C_{54}H_{72}O_6$: C, 79.37; H, 8.88, found: C, 79.12; H, 8.86. Data for α-anomer (**33**α): $[\alpha]_D^{23}$ +37.5° (*c* 0.99, $CHCl_3$); IR ($CHCl_3$) 3009, 2939, 1454, 1375, 1099 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.67 (3H, s, H-18), 0.86–1.58 (m, 33H), 1.74–1.84 (m, 3H), 1.95–2.02 (m, 2H), 2.28 (brd, *J* = 7.5 Hz, 2H, H-4a, H-4b), 3.43 (m, 1H, H-3), 3.80 (dd, *J* = 1.3, 3.1 Hz, 1H, H-2′), 3.84–3.91 (m, 2H, H-5′, H-6′ax), 4.00 (dd, *J* = 3.1, 9.9 Hz, 1H, H-3′), 4.22–4.28 (m, 2H, H-4′, H-6′eq), 4.67 (d, *J* = 12.2 Hz, 1H, OC*H*Ph), 4.72 (d, *J* = 12.2 Hz, 1H, OC*H*Ph), 4.84 (d, *J* = 12.2 Hz, 1H, OC*H*Ph), 4.85 (d, *J* = 12.2 Hz, 1H, OC*H*Ph), 4.93 (d, *J* = 1.3 Hz, 1H, H-1′), 5.33 (brd, *J* = 4.1 Hz, 1H, H-6), 5.65 (s, 1H, C*H*Ph), 7.26–7.39 (m, 13H, Ar-H), 7.52 (m, 2H, Ar-H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 11.9, 18.7, 19.3, 21.1, 22.6, 22.8, 23.8, 24.3, 27.5, 28.0, 28.2, 31.87, 31.91, 35.8, 36.2, 36.7, 37.0, 39.5, 39.8, 39.9, 42.3, 50.1, 56.2, 56.8, 64.3, 68.9, 73.2, 73.6, 79.4, 97.3 (C-1′), 101.4, 122.0, 126.0, 127.40, 127.43, 127.7, 128.1, 128.2, 128.3, 128.4, 128.8, 137.8, 138.3, 138.9, 140.5; FAB-HRMS *m/z* calcd for $C_{54}H_{71}O_6$ $(M–H)^+$ 815.5250, found 815.5275.

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