Isopropenyl Glycosides and Congeners as Novel Classes of Glycosyl Donors: Theme and Variations

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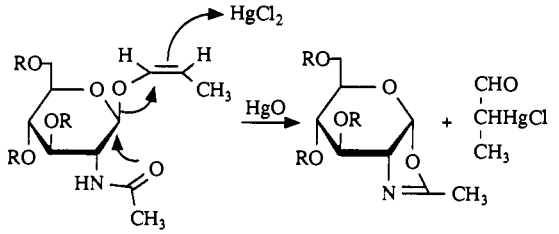
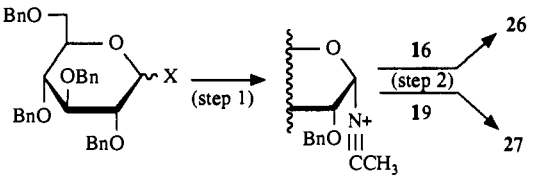
Abstract: Isopropenyl glycosides (i.e., **10** and **11**) have been synthesized in high yields by reacting the corresponding anomeric acetates with the Tebbe reagent. These compounds undergo glycosylation with primary or secondary carbohydrate alcohols in the presence of trimethylsilyl triflate or boron trifluoride etherate, probably via a mixed acetal glycoside intermediate. On the basis of this principle, a quite efficient glycosylation of monosaccharide hemiacetal donors (i.e., **1**, **7**, and **9**) with acceptors bearing an isopropenyl ether function at a primary or secondary position (i.e., **18** and **21**) has been developed. Also investigated were the glycosylating properties of isopropenyl glucosyl and galactosyl carbonates (i.e., **12–15**), easily prepared from the corresponding hemiacetals, toward sugar alcohols. In each case, the β-selective synthesis of disaccharides from donors having nonparticipating groups at C-2 was ensured by the use of acetonitrile, at low temperature, as the solvent.

Simple, efficient, and selective synthesis of oligosaccharides is a central problem in carbohydrate chemistry.[1] The so-called Koenigs–Knorr glycosylation, based on the use[2] of glycosyl halides as glycosyl donors, has by and large been the essential synthesis for a very long period of time. Recently a lot of work has been devoted to the search for a "non-Koenigs–Knorr" activation of the anomeric center. The trichloroacetimidate glycosylation[3]—a useful modification of the imidate procedure[4] —has been frequently used for the practical, selective syntheses of complex oligosaccharides and glycoconjugates. Thioglycosides are also attracting considerable attention along these lines.[5] In the same respect, the glycosylating properties of the alkenyl glycosides have been explored. The pent-4-enyl glycosides[6] are currently used as glycosyl donors. Much less studied is the behavior of the alk-1-enyl glycosides, molecules which should be good candidates for the generation of anomeric oxycarbenium ions.

Vinyl glycopyranosides[7] are known compounds, but prop-1-enyl glycosides are the most common members of the alk-1-enyl family. The widespread use of prop-2-enyl (allyl) ether as a protecting group originates from its easy conversion[8] into a prop-1-enyl ether which, in the presence of various reagents,[8] regenerates the hydroxyl group. It has been shown[9] that the mercury(II) chloride induced cyclization of prop-1-enyl β-glycosides provided a simple and efficient procedure for the preparation of oxazoline derivatives.



Scheme I



leaving group	T (°C)	β : α ratio	product	ref.
X = SEt	+20	4.6 : 1	26	17
X = SEt	+20	2.2 : 1	27	17
X = SC:SOEt	+20	4.8 : 1	26	17
X = SC:SOEt	+20	2.1 : 1	27	17
X = F	0[a]	10 : 1	26	18
X = F	0[a]	3.4 : 1	27	18
X = SEt	-25	25 : 1	26	17
X = SEt	-25	5.4 : 1	27	17
X = OC:NHCCl3	-40	16 : 1	26	19
X = OP:O(OPh)2	-78[b]	32 : 1	26	20
X = OP:O(OPh)2	-78[b]	13 : 1	27	20
X = OC:NHCCl3	-80[b]	19 : 1	27	19

[a] TMS-derivatives of alcohols **16** and **19** were used as acceptors. [b] In propionitrile.

Prop-1-enyl glycosides were thus tested as potential glycosyl donors in intermolecular reactions. Allyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside[10] (**4α**) was isomerized[10] into prop-1-enyl glucoside **5α** with potassium *tert*-butoxide in dimethyl sulfoxide. After experimentation, we found that the *O*-glycosylation reaction of **5α** with methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside[11] (**16**) indeed occurred and was best achieved by the use of trimethylsilyl triflate (TMSOTf) in acetonitrile. Known[12] glucosides **26** were isolated in 65% overall yield after 20 min at 0 °C, with **26β** being the predominant isomer (β:α = 4:1). When the reaction was performed in dichloromethane, the yield dropped to 53% and the α-selectivity was poor (α:β = 1.8:1). The β-selectivity observed in acetonitrile, with a nonparticipating protecting group at C-2 (*O*-benzyl is a classical case), appears

(1) (a) Paulsen, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 155–224. (b) Schmidt, R. R. *Ibid.* **1986**, *25*, 212–235.
(2) (a) Koenigs, W.; Knorr, E. *Ber.* **1901**, *34*, 957–981. (b) Fischer, E.; Armstrong, E. F. *Ibid.* **1901**, *34*, 2885–2900.
(3) Schmidt, R. R.; Michel, J. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 731–732.
(4) Sinaÿ, P. *Pure. Appl. Chem.* **1978**, *50*, 1437–1452.
(5) For short reviews, see: (a) Fügedi, P.; Garegg, P. J.; Löhn, H.; Norberg, T. *Glycoconjugate J.* **1987**, *4*, 97–108. (b) Sinaÿ, P. *Pure Appl. Chem.* **1991**, *63*, 519–528.
(6) Fraser-Reid, B.; Konradsson, P.; Mootoo, D. R.; Udodong, U. E. *J. Chem. Soc., Chem. Commun.* **1988**, 823–825.
(7) (a) Perrine, T. D.; Glaudemans, C. P. J.; Ness, R. U.; Kyle, J.; Fletcher, H. G. *J. Org. Chem.* **1967**, *32*, 664–669. (b) Cottier, L.; Remy, G.; Descotes, G. *Synthesis* **1979**, 711–712. (c) Rollin, P.; Verez-Bencomo, V.; Sinaÿ, P. *Ibid.* **1984**, 134–135. (d) de Raadt, A.; Ferrier, R. J. *J. Chem. Soc., Chem. Commun.* **1987**, 1009–1010.
(8) For a short, recent review, see: Boullanger, P.; Chatelard, P.; Descotes, G.; Kloosterman, M.; van Boom, J. H. *J. Carbohydr. Chem.* **1986**, *5*, 541–559.
(9) (a) Nashed, M. A.; Slife, C. W.; Kiso, M.; Anderson, L. *Carbohydr. Res.* **1977**, *58*, C13–C16. (b) Nashed, M. A. *Ibid.* **1979**, *71*, 299–304. (c) Nashed, M. A.; Slife, C. W.; Kiso, M.; Anderson, L. *Ibid.* **1980**, *82*, 237–252.
(10) (a) Gigg, J.; Gigg, R. *J. Chem. Soc. C* **1966**, 82–86.
(11) (a) Eby, R.; Schuerch, C. *Carbohydr. Res.* **1974**, *34*, 79–90. (b) Liptāk, A.; Jodāl, I.; Nānāsi, P. *Ibid.* **1975**, *44*, 1–11.
(12) Pougny, J.-R.; Jacquinet, J.-C.; Nassr, M.; Duchet, D.; Milat, M.-L.; Sinaÿ, P. *J. Am. Chem. Soc.* **1977**, *99*, 6762–6763.

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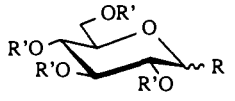
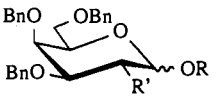
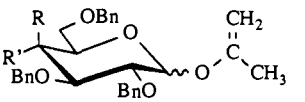
Chart I



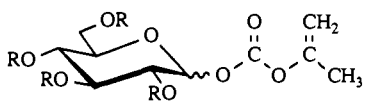
1 R = OH, R' = Bn
2 R = OAc, R' = Bn
3 R = Cl, R' = Bn
4 R = O-CH_2-CH=CH_2, R' = Bn
5 R = O-CH=CH-CH_3, R' = Bn
6 R = OH, R' = Bz



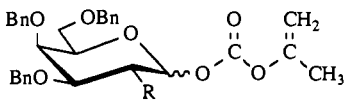
7 R = H, R' = OBn
8 R = Ac, R' = OBn
9 R = H, R' = N_3



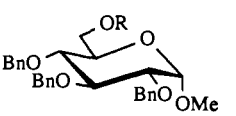
10 R = H, R' = OBn
11 R = OBn, R' = H



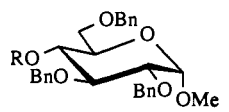
12 R = Bn
13 R = Bz



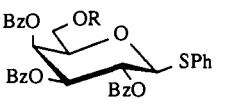
14 R = OBn
15 R = N_3



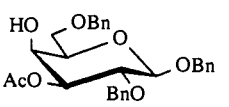
16 R = H
17 R = Ac
18 R = C(=CH_2)-CH_3



19 R = H
20 R = Ac
21 R = C(=CH_2)-CH_3



22 R = H
23 R = $C(CH_3)_2CH_2CCH_3$



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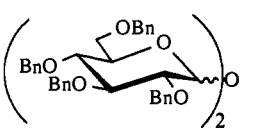

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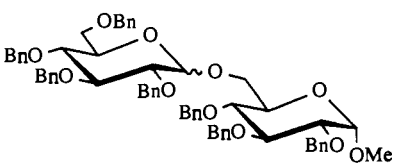
Chart II



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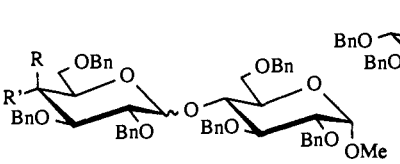
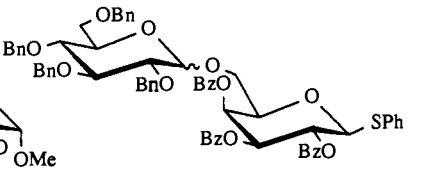


27 R = H, R' = OBn
28 R = OBn, R' = H



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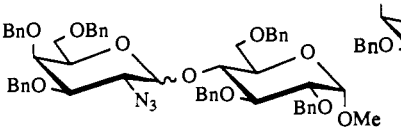

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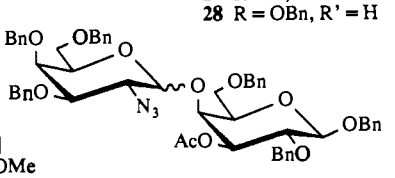

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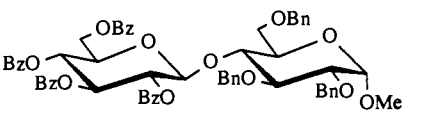

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to be constantly observed in the field and deserves comment.

In 1976, we reported[13] that orthochlorobenzoic acid added regioselectivity to a transient glycosylacetonitrilium ion, finally giving a stable imide. The isolation of this imide in high yield is a demonstration of the formation of a covalent anomeric nitrilium species. Recently, Ratcliffe and Fraser-Reid confirmed[14] this observation, but reinterpreted the anomeric assignments[13,15] of such an imide. The formation of a kinetic α-nitrilium species has also been clearly demonstrated by other groups.[16] When a given glycosyl donor (with a nonparticipating group next to the anomeric center) and glycosyl acceptor couple is employed, the β-selectivity observed in acetonitrile depends on the temperature and appears to be rather unaffected, at a fixed temperature, by the glycosylation procedure used. These results are in accordance with the formation of an α-glycopyranosylacetonitrilium ion (step 1) as the rate-determining step. This is followed by an S_N2 displacement at the anomeric center (step 2), which governs the steric outcome of the reaction. The synthetic utility of the nitrilium procedure has now been well exploited[21] (Scheme I).

Condensation of **5**α with the secondary sugar alcohol, methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside[22] (**19**), in acetonitrile for

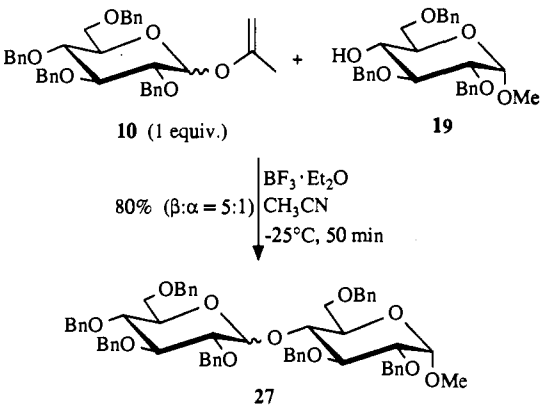
(13) Pougny, J.-R.; Sinaÿ, P. *Tetrahedron Lett.* **1976**, 4073–4076.
(14) Ratcliffe, A. J.; Fraser-Reid, B. *J. Chem. Soc., Perkin Trans. 1* **1990**, 747–750.
(15) Schmidt, R. R.; Michel, J. *J. Carbohydr. Chem.* **1985**, *4*, 141–169.
(16) (a) Lemieux, R. U.; Ratcliffe, R. M. *Can. J. Chem.* **1979**, *57*, 1244–1251. (b) Pavia, A. A.; Ung-Chhun, S. N.; Durand, J.-L. *J. Org. Chem.* **1981**, *46*, 3158–3160. (c) Klemer, A.; Kohla, M. *J. Carbohydr. Chem.* **1988**, *7*, 785–797. (d) Gordon, D. M.; Danishefsky, S. J. *J. Org. Chem.* **1991**, *56*, 3713–3715.
(17) Marra, A.; Mallet, J.-M.; Amatore, C.; Sinaÿ, P. *Synlett* **1990**, 572–574.
(18) Hashimoto, S.; Hayashi, M.; Noyori, R. *Tetrahedron Lett.* **1984**, 1379–1382.
(19) Schmidt, R. R.; Behrendt, M.; Toepfer, A. *Synlett* **1990**, 694–696.
(20) Hashimoto, S.; Honda, T.; Ikegami, S. *J. Chem. Soc., Chem. Commun.* **1989**, 685–687.
(21) For further examples of glycosylation by the nitrilium procedure, see ref 17 and (a) Schmidt, R. R.; Rücker, E. *Tetrahedron Lett.* **1980**, 1421–1424. (b) Murase, T.; Kameyama, K.; Kartha, P. R.; Ishida, H.; Kiso, M.; Hasegawa, A. *J. Carbohydr. Chem.* **1989**, *8*, 265–283, and the following papers in the same series. (c) Marra, A.; Sinaÿ, P. *Carbohydr. Res.* **1990**, *195*, 303–308. (d) Marra, A.; Gauffeny, F. Sinaÿ, P. *Tetrahedron* **1991**, *47*, 5149–5160.

20 min at 0 °C in the presence of TMSOTf gave the known[18] *O*-glucosides **27** in 52% yield, with **27β** again being the major isomer (β:α = 2:1, expected ratio at 0 °C, see above). Also isolated were small amounts of the trehalose derivatives, **25α,α**[23] and **25α,β**,[24] which could not be totally removed from the desired disaccharides.

The Theme: Isopropenyl Glycosides as a Novel Class of Glycosyl Donors. These results encouraged us to explore the alk-1-enyl glycoside approach and to search for necessary improvements. We reasoned that an isopropenyl glycoside might be a more appropriate candidate[25] for effective *O*-glycosylation, inasmuch as the incipient cation formed during the Lewis acid activation would be further stabilized by the methyl group which, in the case of the prop-1-enyl was, in fact, misplaced. Isopropenyl glycosides have been reported[26] as byproducts occurring in syntheses of mixed acetal glycosides and have also been prepared[25] from glycosyl bromides. More complex alk-1-enyl glycoside derivatives have been synthesized[27] in an expeditious manner from the corresponding anomeric esters.

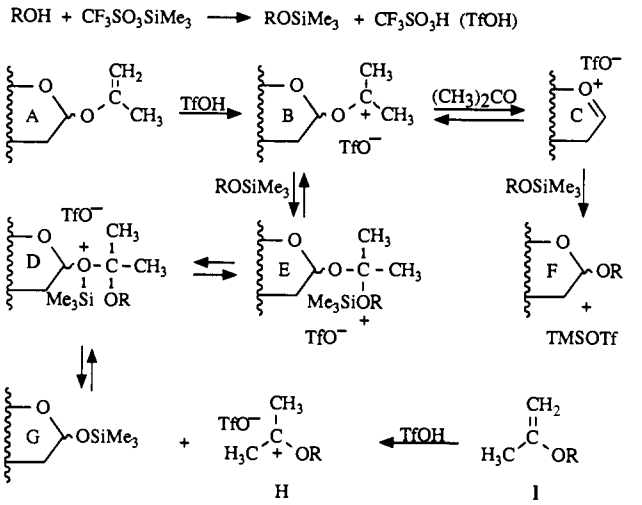
Reaction of 1-*O*-acetyl-2,3,4,6-tetra-*O*-benzyl-D-glucopyranose[28] (**2**) with a solution[29] of Tebbe reagent[30] in toluene gave the isopropenyl glycosides **10** in 87–90% yields. Treatment of **10** (α:β = 4:1) in acetonitrile at −25 °C for 50 min with the acceptor **16** (1 equiv) in the presence of TMSOTf gave the disaccharides **26** (68%) with an expected β-selectivity (β:α = 20:1).

It was also pleasant to learn that condensation of the secondary alcohol **19** with **10** (1.2 equiv) in acetonitrile at −25 °C for 50 min in the presence of $BF_3{\cdot}Et_2O$[31] afforded the disaccharide **27** in good yield (80%, **27β**:**27α** = 5:1). When the same glycosylation



reaction was carried out in dichloromethane[32] instead of acetonitrile, **27** was isolated in limited yield (~45%) and was contaminated by **25**. We did not find significant variations in the stereoselectivity (**27α**:**27β** ≅ 1.5:1) by employing either mainly

Scheme II



α or mainly β isopropenyl derivative **10**. We therefore used anomeric mixtures of glycosyl donors in all of the subsequent condensations.

Condensation of phenyl 2,3,4-tri-*O*-benzoyl-1-thio-β-D-galactopyranoside (**22**) with **10** (1 equiv) in acetonitrile in the presence of TMSOTf at −25 °C for 30 min gave[33] the disaccharides **29** (65%, **29β**:**29α** = 5:1). This exemplifies the possible use of the isopropenyl glycoside procedure for the direct synthesis of thiophenyl disaccharides, useful building blocks for the preparation of complex oligosaccharides.

Next we explored the galactosylation reaction. The isopropenyl galactoside **11** (α:β ≅ 1:1) was first prepared from the corresponding acetate[34] **8** by Tebbe methylenation in 88% yield. It was then submitted to glycosylation with the acceptor **19** under different conditions (see the Experimental Section). The best results were achieved in dichloromethane with TMSOTf as promoter; the disaccharides[35] **28α** and **28β** were isolated in 70% yield and a 4:1 ratio. The α-selectivity in this solvent was significantly better than that observed for the glucosylation of **19** in the same solvent to give **27**. Whether this already reported[35] behavior is mainly due to a steric or electronic influence of the axially oriented *O*-benzyl group at C-4 remains to be established. Conversely, the β-selectivity in acetonitrile was generally poorer.

TMSOTf is known[36] to be a powerful silylating reagent of alcohols in a variety of solvents such as dichloromethane or acetonitrile, trimethylsilylation taking place almost instantaneously. We propose that TMSOTf reacts with the glycosyl acceptor and that the triflic acid generated protonates the enol ether group in A to create an electrophilic species B (Scheme II). B may undergo a kinetic attack by the silylated glycosyl acceptor to give a positively charged, silylated mixed acetal glycoside (E). Intermediate E may either eject acetone through B, leading to the glycosylation step[37] (i.e., F), or after 1,3 *O*→*O* silyl migration collapse into G and H. G may react with the glycosyl oxy-

(22) (a) Küster, J. M.; Dyong, I. *Liebigs, Ann. Chem.* **1975**, 2179–2189. (b) Garegg, P. J.; Hultberg, H.; Wallin, S. *Carbohydr. Res.* **1982**, *108*, 97–101.

(23) Pavia, A. A.; Rocheville, J.-M.; Ung, S. N. *Carbohydr. Res.* **1980**, *79*, 79–89.

(24) Koto, S.; Morishima, N.; Zen, S. *Chem. Lett.* **1976**, 61–64.

(25) Recently de Raadt and Ferrier attempted glycosylations by reacting 1′-substituted vinyl glycosides with methanol in the presence of *N*-bromosuccinimide or bromine–silver perchlorate: de Raadt, A.; Ferrier, R. J. *Carbohydr. Res.* **1991**, *216*, 93–107.

(26) (a) Koto, S.; Inada, S.; Narita, T.; Morishima, N.; Zen, S. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 3665–3666. (b) Tietze, L. F.; Beller, M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 868–869.

(27) Barrett, A. G. M.; Bezuidenhout, B. C. B.; Gasiecki, A. F.; Howell, A. R.; Russell, M. A. *J. Am. Chem. Soc.* **1989**, *111*, 1392–1396.

(28) Lemieux, R. U.; Hendrix, K. B.; Stick, R. V.; James, K. *J. Am. Chem. Soc.* **1975**, *97*, 4056–4062.

(29) See general procedures in the Experimental Section.

(30) Tebbe, F. N.; Parshall, G. W.; Reddy, G. S. *J. Am. Chem. Soc.* **1978**, *100*, 3611–3613.

(31) $BF_3{\cdot}Et_2O$ was found to be superior to TMSOTf in this condensation.

(32) Use of benzene, toluene, or nitromethane did not prove more satisfactory. Unfortunately, the glycosylation does not take place in ether, a solvent which allows a remarkable α-selectivity. See refs 18, 35, and Mukaiyama, T.; Katsurada, M.; Takashima, T. *Chem. Lett.* **1991**, 985–988.

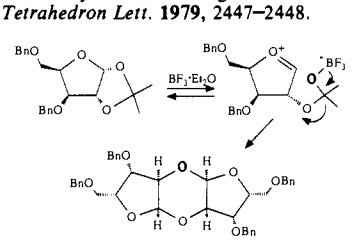
(33) Also isolated was the monosaccharide derivative **23** (5%).

(34) Austin, P. W.; Hardy, F. E.; Buchanan, J. G.; Baddiley, J. *J. Chem. Soc.* **1965**, 1419–1424.

(35) Wegmann, B.; Schmidt, R. R. *J. Carbohydr. Chem.* **1987**, *6*, 357–375.

(36) Olah, G. O.; Husain, A.; Gupta, B. G. B.; Salem, G. F.; Narang, S. C. *J. Org. Chem.* **1981**, *46*, 5212–5214.

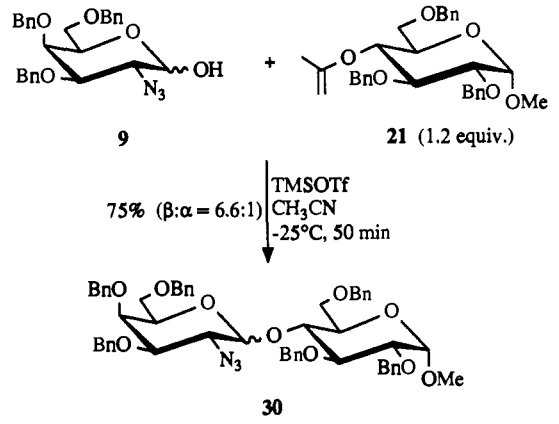
(37) It is interesting to compare this novel glycosylation reaction with the following one discovered by us some time ago: Amvam Zollo, P. H.; Pougny, J.-R.; Sinaÿ, P. *Tetrahedron Lett.* **1979**, 2447–2448.



carbenium ion C to provide the trehaloses. Indeed, trehaloses are formed to a certain extent in this process.

Variation One: The *Reverse* Isopropenyl Approach. According to the proposed mechanism, where a mixed acetal glycoside (E) was a key intermediate, we anticipated that reaction of G with H should result in glycosylation. Acid-sensitive, mixed acetal glycosides have been prepared by Tietze and co-workers from aldehydes,[38] ketones,[39] and enol ethers[40] under kinetic conditions (at −70 °C) and by Lehmann and co-workers[41] under thermodynamic conditions but, surprisingly, their potential for glycosylation reactions has not been investigated.

Thus, the secondary alcohol **19** was converted, via the known[42] acetate **20**, into the enol ether **21** by the Tebbe reagent. Reaction of **21** (1.2 equiv) with 2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-D-galactopyranose[43] (**9**) in the presence of TMSOTf (CH_3CN, −25 °C, 50 min) afforded, in good yield and selectivity (75%, $\beta:\alpha$ = 6.6:1), the disaccharides **30**, which were isolated and characterized.



30

We found that the Tebbe reagent completely destroyed molecules bearing an azido function; thus, the 2-azido-2-deoxy analogue of the isopropenyl galactoside **11** cannot be obtained by the Tebbe procedure. The aforementioned, successful *reverse* condensation nicely circumvented this problem. Compound **21** was also reacted, under the same conditions, with 2,3,4,6-tetra-*O*-benzyl-D-galactopyranose[34] (**7**) to yield **28**β and **28**α (68%) in a 1.1:1 ratio. In dichloromethane (−25 °C, 50 min), the yield obtained from **21** and **7** in the presence of TMSOTf was lower (56%), but the selectivity was improved ($\alpha:\beta$ = 5.4:1). The glucosylation reaction was performed by reacting commercially available 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (**1**) with **21** in dichloromethane (**1** is not soluble in acetonitrile at low temperature) in the presence of TMSOTf at −25 °C for 50 min. The disaccharides **27**α and **28**β were recovered in 68% yield and a 1.5:1 ratio together with the trehalose derivatives **25**α,α and **25**α,β (~18%). Better results were obtained when **18**, prepared from the acetate[42] **17**, was used as acceptor; condensation of **1** (1 equiv) with **18** (CH_2Cl_2, TMSOTf, −25 °C, 50 min) afforded **26** in 81% yield, although without selectivity ($\alpha:\beta$ = 1:1).

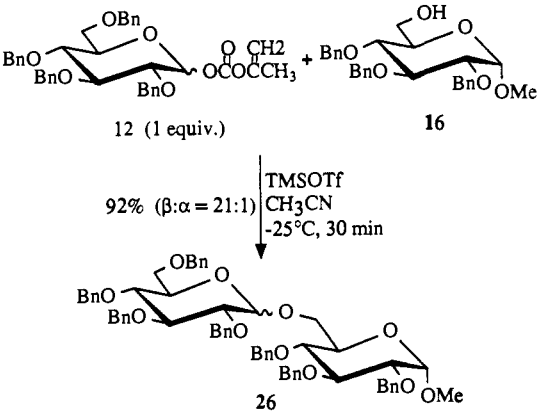
Variation Two: The Isopropenyl Glycosyl Carbonate Route to Disaccharides. To our knowledge, the use of anomeric carbonates as glycosyl donors has been attempted with very limited success.[44] Boursier and Descotes demonstrated[45] that heating ethyl 2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl carbonate with a large excess of simple alcohols (methanol, isopropyl alcohol, benzyl alcohol) gave the expected glycosides, but the reaction failed when a carbohydrate acceptor was employed. Thus, the procedure offers no decisive advantages when compared to historical Fischer glycosylation or transglycosylation reactions. On the basis of our aforementioned results and encouraged by the commercial availability of the isopropenyl chloroformate, we anticipated that the glycosylating properties of the isopropenyl glycosyl carbonates (e.g., **12**) should be of valuable synthetic utility.

Carbonates **12**–**15** were prepared from the corresponding hemiacetal derivatives **1**, **6**,[46] **7**, and **9** in nearly quantitative yields by treatment with isopropenyl chloroformate (1.1 equiv) in dichloromethane in the presence of pyridine at 0 °C for 1 h. Much to our pleasure, condensation of **12** with the primary alcohol **16** (1 equiv) in acetonitrile at −25 °C delivered the disaccharides **26** in 92% yield with a good, and fully expected, β-selectivity. The results achieved with secondary carbohydrate acceptors are summarized in Table I.

Table I. Condensation of Isopropenyl Glycosyl Carbonates with Secondary Alcohols in the Presence of TMSOTf at −25 °C

donor	ROH	solvent	product	yield, %	$\alpha:\beta$ ratio
12	**19**	CH_3CN	**27**	85	1:5.1
13[47]	**19**	CH_3CN	**32**[48]	81	0:1
14[a]	**19**	CH_2Cl_2	**28**	79	4:1
14	**19**	CH_3CN	**28**	80	1:1.6
15	**19**	CH_2Cl_2	**30**	77	2.4:1
15	**19**	CH_3CN	**30**	81	1:5
15	**24**[49]	CH_3CN	**31**	78	1:3.9
15	**24**	CH_3CH_2CN[b]	**31**	78	1:5.5

[a] Use of **14**α or **14**β gave similar yields and selectivities. [b] At −45 °C.



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Compared with the isopropenyl glycoside method and the reverse method, this variation on the theme appears advantageous, inasmuch as it circumvents the manipulation of, and limitations associated with, the Tebbe reagent.

Experimental Section

General Procedures. Melting points were determined with a Büchi Model 510 capillary apparatus and were not corrected. Optical rotations were measured at 20 ± 2 °C with a Perkin-Elmer Model 241 polarimeter. Elemental analyses were performed at the University Pierre et Marie Curie (Paris) and at the Service Central d'Analyse (C.N.R.S., Vernaison). ^1H NMR spectra were recorded with Bruker AC-250 and AM-400 spectrometers for solutions in $CDCl_3$ (internal Me_4Si) unless otherwise stated. Assignments were aided by decoupling and/or COSY-45 experiments. CI (NH_3) mass spectra were obtained with a Nermag R10-10 spectrometer. Reactions were monitored by TLC on silica gel

(38) Tietze, L. F.; Beller, M. *Liebigs Ann. Chem.* **1990**, 587–591.
(39) Tietze, L. F.; Fischer, R.; Lögers, M.; Beller, M. *Carbohydr. Res.* **1989**, *194*, 155–162.
(40) Tietze, L. F.; Lögers, M. *Liebigs Ann. Chem.* **1990**, 261–265.
(41) Blanc-Muesser, M.; Defaye, J.; Lehmann, J. *Carbohydr. Res.* **1982**, *108*, 103–110.
(42) Koto, S.; Morishima, N.; Kawahara, R.; Ishikawa, K.; Zen, S. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 1092–1096.
(43) Grundler, G.; Schmidt, R. R. *Liebigs Ann. Chem.* **1984**, 1826–1847. Recently we prepared **9** by denitration (PhSH, iPr_2EtN, room temperature, 10 min) of the corresponding azido nitrate: Gauffeny, F.; Marra, A.; Shi Shun, L. K.; Sinaÿ, P.; Tabeur, C. *Carbohydr. Res.* **1991**, *219*, 237–240.
(44) For glucosylation of phenols by phenyl or methyl glycosyl carbonates under pyrolytic conditions, see: Ishido, Y.; Inaba, S.; Matsuno, A.; Yoshino, T.; Umezawa, H. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1382–1390.
(45) Boursier, M.; Descotes, G. *C. R. Acad. Sci.* **1989**, *308*, 919–921.
(46) Fiandor, J.; Garcia Lopez, M. T.; De Las Heras, F. G.; Méndez-Castrillön, P. P. *Synthesis* **1985**, 1121–1124.
(47) Obviously donors having benzoyl functions cannot be submitted to the Tebbe reagent.
(48) Dasgupta, F.; Garegg, P. J. *Carbohydr. Res.* **1988**, *117*, C13–C17.
(49) Marecaux, A.; Sinaÿ, P. Manuscript in preparation.

60 F_{254} (Merck) with detection by charring with sulfuric acid. Flash column chromatography[50] was performed on silica gel 60 (40–63 μm, Merck). Preparative TLC was performed on silica gel 60 F_{254} 20 × 20 cm plates (1-mm layer, Merck). The α:β ratios of the disaccharide mixtures were evaluated by ^{1}H NMR spectroscopy (400 MHz, $CDCl_3$). Pure samples of known disaccharide derivatives were isolated by column or thin-layer chromatography; their spectroscopic and physical data were in agreement with those reported in the literature. Tebbe reagent was prepared from titanocene dichloride and trimethylaluminum according to ref 5 and used, without further purification, as an ~0.5 M solution in dry toluene stable for several weeks at room temperature. Isopropenyl chloroformate, now commercially available, was kindly furnished by the Société Nationale des Poudres et Explosifs (Vert le Petit, France).

(*Z*)-Prop-1-enyl 2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranoside (5). A mixture of 4[10] (580 mg, 1 mmol), freshly sublimated potassium *tert*-butoxide (220 mg, 2 mmol), and DMSO (10 mL) was stirred at 100 °C for 4 h and then cooled to room temperature, diluted with Et_2O (100 mL), and washed with water (10 mL). The aqueous phase was extracted with Et_2O (50 mL), and the combined organic phases were dried ($MgSO_4$) and concentrated to dryness. The brown residue was eluted from a column of silica gel with 6:1 hexane–AcOEt (containing 0.5% of Et_3N) to give **5** (500 mg, 86%) contaminated by another product (~5%), presumably the corresponding (*E*) isomer by NMR analysis (selected ^{1}H NMR data, δ 6.13, dq, J_{trans} = 12.5, $J_{H,Me}$ = 2.0 Hz, OCH=): ^{1}H NMR (250 MHz) δ 7.36–7.12 (m, 20 H, 4 Ph), 6.02 (dq, 1 H, J_{cis} = 6.2, $J_{H,Me}$ = 1,6 Hz, OCH=), 5.00 and 4.85 (2 d, 2 H, J = 10.9 Hz, PhCH_2), 4.95 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.84 and 4.66 (2 d, 2 H, J = 12.2 Hz, PhCH_2), 4.80 and 4.48 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.60 and 4.44 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.58 (dq, 1 H, $J_{H,Me}$ = 6.8 Hz, CH_3CH=), 4.05 (dd, 1 H, H-3), 3.80–3.55 (m, 5 H, H-2,4,5,6a,6b), 1.64 (dd, 3 H, Me). Anal. Calcd for $C_{37}H_{40}O_6$: C, 76.53; H, 6.94. Found: C, 76.59; H, 6.84.

Isopropenyl 2,3,4,6-Tetra-*O*-benzyl-α,β-D-glucopyranoside (10). To a cooled (−60 °C), stirred solution of **2**[28] (2.33 g, 4 mmol; α:β ratio of ~4:1) in 5:1 dry THF–pyridine (15 mL) was added an ~0.5 M solution of the Tebbe reagent in dry $PhCH_3$ (3 mL, ~6 mmol). The solution was stirred at room temperature for 15 min and then cooled to 0 °C and treated with 15% aqueous NaOH (1 mL) and then with Et_2O (~30 mL). The blue solid was removed by filtration through Celite, and the solution was concentrated to dryness. The residue was eluted from a column of silica gel with 7:1 hexane–AcOEt (containing 0.5% of Et_3N) to give **10** (2.09 g, 90%) as a syrup: selected ^{1}H NMR data (250 MHz) δ 7.36–7.10 (m, 20 H, 4 Ph), 5.31 (d, 0.8 H, $J_{1,2}$ = 3.5 Hz, H-1α), 4.28 (bd, 0.8 H, J_{gem} = 1.6 Hz, Ha of CH_2=Cα), 4.24 (bd, 0.2 H, J_{gem} = 1.8 Hz, Ha of CH_2=Cβ), 1.89 (bs, 0.6 H, Meβ), 1.86 (bs, 2.4 H, Meα). Anal. Calcd for $C_{37}H_{40}O_6$: C, 76.53; H, 6.94. Found: C, 76.28; H, 6.97.

Mainly **10β** (α:β ratio of ~1:4) was prepared as described above from the corresponding mixture of acetates in 87% yield. This mixture was synthesized, in turn, by treatment of the chloride derivative **30** (obtained from **1** according to ref 52) with 2.5 equiv of CsOAc in dry CH_3CN at room temperature for 48 h (total yield, 75%).

Isopropenyl 2,3,4,6-Tetra-*O*-benzyl-α,β-D-galactopyranoside (11). Treatment of **8**[34] (1.16 g, 2 mmol; α:β ratio of ~1:1) as for the preparation of **3** gave, after identical workup and purification, **11** (1.02 g, 88%): selected ^{1}H NMR data (250 MHz) δ 7.38–7.17 (m, 20 H, 4 Ph), 5.38 (d, 0.5 H, $J_{1,2}$ = 3.5 Hz, H-1α), 4.78 (d, 0.5 H, $J_{1,2}$ = 7.2 Hz, H-1β), 4.25 (bd, 0.5 H, J_{gem} = 1.5 Hz, Ha of CH_2=Cα), 4.20 (bd, 0.5 H, J_{gem} = 1.7 Hz, Ha of CH_2=Cβ), 1.86 (bs, 3 H, Meα,β). Anal. Calcd for $C_{37}H_{40}O_6$: C, 76.53; H, 6.94. Found: C, 76.73; H, 6.82.

Methyl 2,3,6-Tri-*O*-benzyl-4-*O*-isopropenyl-α-D-glucopyranoside (21). Treatment of **20**[42] (506 mg, 1 mmol) as for the preparation of **10** afforded, after column chromatography (4:1 hexane–AcOEt, containing 0.5% of Et_3N), **21** (454 mg, 90%): $[\alpha]_D$ +114° (*c* 0.9, C_6H_6); ^{1}H NMR (250 MHz, C_6D_6) δ 7.34–6.96 (m, 15 H, 3 Ph), 4.78 (s, 2 H, PhCH_2), 4.59 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.78 and 4.34 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.42 (d, 1 H, J_{gem} = 1.7 Hz, Ha of CH_2=C), 4.38 (dd, 1 H, $J_{3,4}$ = 8.7, $J_{4,5}$ = 9.9 Hz, H-4), 4.34 (s, 2 H, PhCH_2), 4.15 (dd, 1 H, $J_{2,3}$ = 9.6 Hz, H-3), 3.95 (dq, 1 H, $J_{Hb,Me}$ = 0.6 Hz, Hb of CH_2=C), 3.88 (ddd, 1 H, $J_{5,6a}$ = 2.3, $J_{5,6b}$ = 4.1 Hz, H-5), 3.59–3.48 (m, 2 H, H-6a,6b), 3.45 (dd, 1 H, H-2), 3.08 (s, 3 H, MeO), 1.66 (d, 3 H, Me). Anal. Calcd for $C_{31}H_{36}O_6$: C, 73.79; H, 7.19. Found: C, 73.80; H, 7.15.

Methyl 2,3,4-Tri-*O*-benzyl-6-*O*-isopropenyl-α-D-glucopyranoside (18). Treatment of **17**[42] (1.01 g, 2 mmol) as for the preparation of **21** gave, after identical workup and purification, **18** (0.91 g, 90%): $[\alpha]_D$ +82° (*c* 0.9, C_6H_6); ^{1}H NMR (250 MHz, C_6D_6) δ 7.26–6.92 (m, 15 H, 3 Ph), 4.94 and 4.72 (2 d, 2 H, J = 11.3 Hz, PhCH_2), 4.83 and 4.50 (2 d, 2 H, J = 11.2 Hz, PhCH_2), 4.54 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.40 and 4.30 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.16 (dd, 1 H, $J_{2,3}$ = 9.6, $J_{3,4}$ = 8.7 Hz, H-3), 3.90–3.75 (m, 5 H, H-5,6a,6b, CH_2=C), 3.68 (dd, 1 H, $J_{4,5}$ = 10.0 Hz, H-4), 3.45 (dd, 1 H, H-2), 3.04 (s, 3 H, MeO), 1.67 (d, 3 H, J = 0.6 Hz, Me). Anal. Calcd for $C_{31}H_{36}O_6$: C, 73.79; H, 7.19. Found: C, 73.67; H, 7.06.

Isopropenyl 2,3,4,6-Tetra-*O*-benzyl-α,β-D-glucopyranosyl Carbonate (12). To a cooled (0 °C), stirred solution of **1** (1.08 g, 2 mmol) and isopropenyl chloroformate (240 μL, 2.2 mmol) in dry CH_2Cl_2 (10 mL) was added pyridine (240 μL, 3 mmol) dropwise. The mixture was stirred at 0 °C for 1 h, warmed to room temperature, and concentrated. The residue was eluted from a column of silica gel with 6:1 hexane–AcOEt to afford **12** (1.19 g, 95%): selected ^{1}H NMR data (250 MHz) δ 7.34–7.12 (m, 20 H, 4 Ph), 6.18 (d, 0.8 H, $J_{1,2}$ = 3.5 Hz, H-1α), 5.50 (d, 0.2 H, $J_{1,2}$ = 7.7 Hz, H-1β), 3.98 (dd, 0.8 H, $J_{2,3}$ = $J_{3,4}$ = 9.2 Hz, H-3α), 3.92 (ddd, 0.8 H, $J_{4,5}$ = 10.0, $J_{5,6a}$ = 2.4, $J_{5,6b}$ = 2.8 Hz, H-5α), 1.97 (bs, 0.6 H, Meβ), 1.95 (bs, 2.4 H, Meα). Anal. Calcd for $C_{38}H_{40}O_8$: C, 73.06; H, 6.45. Found: C, 72.89; H, 6.48.

Isopropenyl 2,3,4,6-Tetra-*O*-benzyl-α-(and β)-D-galactopyranosyl Carbonate (14α and 14β). Treatement of **7**[34] (1.01 g, 2 mmol) as for the preparation of **12** gave, after column chromatography (20:1 CCl_4–THF), first **14α** (0.75 g, 60%): $[\alpha]_D$ +56° (*c* 0.7, $CHCl_3$); ^{1}H NMR (250 MHz) δ 7.38–7.24 (m, 20 H, 4 Ph), 6.22 (d, 1 H, $J_{1,2}$ = 3.7 Hz, H-1), 4.95 and 4.56 (2 d, 2 H, J = 11.3 Hz, PhCH_2), 4.84 and 4.74 (2 d, 2 H, J = 11.8 Hz, PhCH_2), 4.80 (d, 1 H, J_{gem} = 1.5 Hz, Ha of CH_2=C), 4.74 (s, 2 H, PhCH_2), 4.69 (dq, 1 H, $J_{Hb,Me}$ = 0.7 Hz, Hb of CH_2=C), 4.48 and 4.40 (2 d, 2 H, J = 11.8 Hz, PhCH_2), 4.18 (dd, 1 H, $J_{2,3}$ = 10.1 Hz, H-2), 4.09 (ddd, 1 H, $J_{4,5}$ ≅ 0.6, $J_{5,6a}$ = $J_{5,6b}$ = 6.5 Hz, H-5), 4.04 (dd, 1 H, $J_{3,4}$ = 2.8 Hz, H-4), 3.93 (dd, 1 H, H-3), 3.56–3.53 (m, 2 H, H-6a,6b), 1.93 (d, 3 H, Me). Anal. Calcd for $C_{38}H_{40}O_8$: C, 73.06; H, 6.45. Found: C, 72.93; H, 6.54.

14β eluted second (0.41 g, 33%): $[\alpha]_D$ +12° (*c* 1.6, $CHCl_3$); ^{1}H NMR (250 MHz) δ 7.36–7.26 (m, 20 H, 4 Ph), 5.48 (d, 1 H, $J_{1,2}$ = 8.0 Hz, H-1), 4.96 and 4.61 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.84 and 4.79 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.80 (d, 1 H, J_{gem} = 1.5 Hz, Ha of CH_2=C), 4.73 (s, 2 H, PhCH_2), 4.72 (dq, 1 H, $J_{Hb,Me}$ = 0.7 Hz, Hb of CH_2=C), 4.46 and 4.40 (2 d, 2 H, J = 11.8 Hz, PhCH_2), 3.98 (dd, 1 H, $J_{2,3}$ = 9.8 Hz, H-2), 3.98 (dd, 1 H, $J_{3,4}$ = 2.6, $J_{4,5}$ ≅ 0.6 Hz, H-4), 3.73–3.58 (m, 4 H, H-3,5,6a,6b), 1.95 (d, 3 H, Me). Anal. Found: C, 73.34; H, 6.44.

Isopropenyl 2-Azido-3,4,6-tri-*O*-benzyl-2-deoxy-α-(and β)-D-galactopyranosyl Carbonate (15α and 15β). Treatment of **9**[39] (0.95 g, 2 mmol) as for the preparation of **12** gave, after column chromatography (4:1 hexane–AcOEt), **15α** and **15β** as an ~1:1 mixture (1.01 g, 90%). Pure samples were obtained by preparative TLC using the same eluent. Compound **15α**: $[\alpha]_D$ +65° (*c* 1.1, $CHCl_3$); ^{1}H NMR (250 MHz) δ 7.42–7.24 (m, 15 H, 3 Ph), 6.10 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1), 4.88 and 4.54 (2 d, 2 H, J = 11.2 Hz, PhCH_2), 4.85 (d, 1 H, J_{gem} = 1.6 Hz, Ha of CH_2=C), 4.76 and 4.72 (2 d, 2 H, J = 11.4 Hz, PhCH_2), 4.72 (dq, 1 H, $J_{Hb,Me}$ = 0.7 Hz, Hb of CH_2=C), 4.48 and 4.40 (2 d, 2 H, J = 11.7 Hz, PhCH_2), 4.16 (dd, 1 H, $J_{2,3}$ = 10.5 Hz, H-2), 4.10–4.05 (m, 2 H, H-4,5), 3.94 (dd, 1 H, $J_{3,4}$ = 2.5 Hz, H-3), 3.66 (dd, 1 H, $J_{5,6a}$ = 8.0, $J_{6a,6b}$ = 9.2 Hz, H-6a), 3.55 (dd, 1 H, $J_{5,6b}$ = 6.0 Hz, H-6b), 1.98 (d, 3 H, Me). Anal. Calcd for $C_{31}H_{33}N_3O_7$: C, 66.54; H, 5.94. Found: C, 66.47; H, 5.92.

Compound **15β**: $[\alpha]_D$ +8° (*c* 0.8, $CHCl_3$); ^{1}H NMR (250 MHz) δ 7.40–7.24 (m, 15 H, 3 Ph), 5.24 (d, 1 H, $J_{1,2}$ = 8.5 Hz, H-1), 4.89 and 4.57 (2 d, 2 H, J = 11.4 Hz, PhCH_2), 4.85 (d, 1 H, J_{gem} = 1.6 Hz, Ha of CH_2=C), 4.73 and 4.65 (2 d, 2 H, J = 11.6 Hz, PhCH_2), 4.72 (dq, 1 H, $J_{Hb,Me}$ = 0.7 Hz, Hb of CH_2=C), 4.46 and 4.40 (2 d, 2 H, J = 11.7 Hz, PhCH_2), 3.98 (dd, 1 H, $J_{2,3}$ = 10.2 Hz, H-2), 3.98 (dd, 1 H, $J_{3,4}$ = 2.7, $J_{4,5}$ ≅ 0.5 Hz, H-4), 3.69–3.55 (m, 3 H, H-5,6a,6b), 3.46 (dd, 1 H, H-3), 1.96 (d, 3 H, Me). Anal. Found: C, 66.38; H, 5.98.

Isopropenyl 2,3,4,6-Tetra-*O*-benzoyl-α-D-glucopyranosyl Carbonate (13α). Treatment of **6**[46] (1.19 g, 2 mmol) as for the preparation of **12** gave, after column chromatography (3:1 hexane–AcOEt), **13α** together with its β-anomer (1.29 g, 95%) as a white solid. Crystallization (Et_2O–hexane) of the mixture afforded pure **13α** (0.88 g, 65%): mp 168–170 °C; $[\alpha]_D$ +81° (*c* 0.9, $CHCl_3$); ^{1}H NMR (250 MHz) δ 8.08–7.85 and 7.60–7.26 (2 m, 20 H, 4 Ph), 6.50 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1), 6.22 (dd, 1 H, $J_{2,3}$ = 10.3, $J_{3,4}$ = 9.7 Hz, H-3), 5.80 (dd, 1 H, $J_{4,5}$ = 10.0 Hz, H-4), 5.57 (dd, 1 H, H-2), 4.78 (d, 1 H, J_{gem} = 1.8 Hz, Ha of CH_2=C), 4.68 (dq, 1 H, $J_{Hb,Me}$ = 0.7 Hz, Hb of CH_2=C), 4.64–4.58 (m, 2 H, H-5,6a), 4.50–4.44 (m, 1 H, H-6b), 1.89 (d, 3 H, Me). Anal. Calcd for $C_{38}H_{32}O_{12}$: C, 67.06; H, 4.74. Found: C, 66.87; H, 4.69.

Phenyl 2,3,4-Tri-*O*-benzoyl-1-thio-β-D-galactopyranoside (22). A mixture of commercially available phenyl 1-thio-β-D-galactopyranoside (1.09 g, 4 mmol), trityl chloride (1.67 g, 6 mmol), Et_3N (1.67 mL, 12 mmol), 4-DMAP (50 mg, 0.4 mmol), and DMF (20 mL) was stirred at

(50) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.
(51) Chou, T. S.; Huang, S.-B.; Hsu, W.-H. *J. Chin. Chem. Soc. (Taipei)* **1983**, *30*, 277–279; *Chem. Abstr.* **1984**, *100*, 85865p.
(52) Iversen, T.; Bundle, D. R. *Carbohydr. Res.* **1982**, *103*, 29–40.

70 °C for 6 h and then concentrated, diluted with CH_2Cl_2, washed with H_2O and saturated aqueous NH_4Cl, dried ($MgSO_4$), and concentrated. The residue was treated overnight at room temperature with solution of benzoyl chloride (1.40 mL, 12 mmol) and pyridine (0.97 mL, 12 mmol) in CH_3CN (20 mL). Then the mixture was concentrated to dryness, dissolved in MeOH (50 mL), and treated with TsOH (~50 mg) at room temperature. After 2 h, the solution was neutralized with Et_3N and concentrated. The residue was eluted from a column of silica gel with 2:1 hexane–AcOEt to give **22** (1.10 g, 47%): $[\alpha]_D$ +131° (*c* 1, $CHCl_3$); ^1H NMR (250 MHz) δ 8.02–7.19 (m, 20 H, 4 Ph), 5.83 (dd, 1 H, $J_{3,4}$ = 3.3, $J_{4,5} \cong$ 0.6 Hz, H-4), 5.79 (dd, 1 H, $J_{1,2} = J_{2,3}$ = 10.0 Hz, H-2), 5.58 (dd, 1 H, H-3), 5.02 (d, 1 H, H-1), 4.10 (ddd, 1 H, $J_{5,6a} = J_{5,6b}$ = 7.0 Hz, H-5), 3.86 (dd, 1 H, $J_{6a,6b}$ = 11.8 Hz, H-6a), 3.63 (dd, 1 H, H-6b). Upon addition[53] of trichloroacetyl isocyanate to the sample, the expected downfield shifts of H-6a and H-6b were observed: δ 8.44 (s, 1 H, NH), 8.00–7.20 (m, 20 H, 4 Ph), 5.92 (dd, 1 H, $J_{3,4}$ = 3.3, $J_{4,5} \cong$ 0.6 Hz, H-4), 5.73 (dd, 1 H, $J_{1,2} = J_{2,3}$ = 10.0 Hz, H-2), 5.55 (dd, 1 H, H-3), 5.02 (d, 1 H, H-1), 4.56–4.31 (m, 3 H, H-5,6a,6b). Anal. Calcd for $C_{33}H_{28}O_8S$: C, 67.80; H, 4.83. Found: C, 67.89; H, 4.95.

Methyl 2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-(and β)-D-glucopyranosyl)-α-D-glucopyranoside (26α and 26β). (a) To a cooled (0 °C), stirred mixture of **5** (116 mg, 0.2 mmol), **16**[11] (93 mg, 0.2 mmol), activated 4-Å powdered molecular sieves (0.20 g), and dry CH_3CN (2 mL) was added TMSOTf (36 μL, 0.2 mmol). Stirring was continued for an additional 20 min at 0 °C, and then the mixture was neutralized with Et_3N, diluted with CH_2Cl_2, filtered through Celite, and concentrated. The residue was eluted from a column of silica gel with 15:1 $PhCh_3$–AcOEt to give known[12] **26α** together with **26β** (128 mg, 65%) in a 1:4 ratio. When the same glycosylation reaction was performed in CH_2Cl_2 instead of CH_3CN, a 1.8:1 mixture of **26α** and **26β** (55%) was recovered.

(b) To a cooled (−25 °C), stirred mixture of **10** (116 mg, 0.2 mmol), **16**[11] (93 mg, 0.2 mmol), activated 4-Å powdered molecular sieves (0.20 g), and dry CH_3CN (2 mL) was added TMSOTf (36 μL, 0.2 mmol). Stirring was continued for an additional 50 min at −25 °C, and then the mixture was neutralized with Et_3N, diluted with CH_2Cl_2, filtered through Celite, and concentrated. The residue was eluted from a column of silica gel with 5:1 hexane–AcOEt to give **26α** together with **26β** (134 mg, 68%) in a 1:20 ratio. Repetition of the reaction in the presence of CH_2Cl_2 instead of CH_3CN gave a mixture of **26α** and **26β** (70%) in a 1:1.3 ratio.

(c) Glycosylation of **1** with **18** (1 equiv) carried out as described in preparation b (1 equiv of TMSOTf, CH_2Cl_2, −25 °C, 50 min) afforded **26α** and **26β** (81%) in a 1:1 ratio. The lack of solubility of **1** in CH_3CN at low temperature did not allow reaction in this solvent.

(d) Glycosylation of **12** with **16**[11] (1 equiv) performed as reported in preparation b (1 equiv of TMSOTf, CH_3CN, −25 °C, 30 min) yielded **26α** and **26β** (92%) in a 1:21 ratio.

Methyl 2,3,6-Tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-(and β)-D-glucopyranosyl)-α-D-glucopyranoside (27α and 27β). (a) Glycosylation of **5** (1.2 equiv) with **19**[22] carried out as described for the synthesis of **26** (preparation a) gave, after identical workup and purification, known[18] **27α** and **27β** (52%) in a 1:2 ratio together with the trehalose derivatives[23,24] **25α,α** and **25α,β** (~8%) in an ~1:1 ratio. By further purification (preparative TLC, 20:1 $CHCl_3$–Et_2O), only **27β** and **25α,β** could be fractionated. Use of BF_3·Et_2O instead of TMSOTf led to poor yields of disaccharides.

(b) Glycosylation of **10** (1 equiv) with **19**[22] performed as described for the synthesis of **26** (preparation b) but using BF_3·Et_2O (1 equiv) instead of TMSOTf gave, after identical workup and purification, **27α** and **27β** (80%) in a 1:5 ratio. Use of CH_2CL_2 as solvent led to poor yields of disaccharides (<50%).

(c) Glycosylation of **1** with **21** (1 equiv) carried out as described for the synthesis of **26** (preparation c) afforded, after column chromatography with 15:1 $PhCH_3$–AcOEt, **27α** and **27β** (68%) in a 1.5:1 ratio together with **25α,α** and **25α,β** (~18%) in an ~1:1 ratio. The lack of solubility of **1** in CH_3CN at low temperature did not allow reaction in this solvent.

(d) Glycosylation of **12** (1.2 equiv) with **19**[31] performed as reported for the synthesis of **26** (preparation d) yielded **27α** and **27β** (85%) in a 1:5.1 ratio.

Phenyl 2,3,4-Tri-*O*-benzoyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-(and β)-D-glucopyranosyl)-1-thio-β-D-galactopyranoside (29α and 29β). To a cooled (−25°C), stirred mixture of **10** (116 mg, 0.2 mmol), **22** (116 mg, 0.2 mmol), activated 4-Å powdered molecular sieves (0.20 g), and dry CH_3CN (2 mL) was added TMSOTf (36 μL, 0.2 mmol). Stirring was continued for an additional 30 min, and then the mixture was neutralized with Et_3N, diluted with CH_2Cl_2, filtered through Celite, and concentrated. The residue was eluted from a column of silica gel with 3:1 hexane–AcOEt to give **29α** first, together with **29β** (144 mg, 65%) in a 1:5 ratio by ^1H NMR analysis. Pure samples were obtained by preparative TLC using the same eluent. Compound **29α**: $[\alpha]_D$ +107° (*c* 1, $CHCl_3$); ^1H NMR (400 MHz) δ 8.04–8.01, 7.94–7.91, 7.81–7.78, 7.67–7.55, and 7.49–7.15 (5 m, 40 H, 8 Ph), 5.96 (dd, 1 H, $J_{3,4}$ = 3.2, $J_{4,5} \cong$ 0.5 Hz, H-4), 5.76 (dd, 1 H, $J_{1,2}$ = 10.0, $J_{2,3}$ = 9.8 Hz, H-2), 5.59 (dd, 1 H, H-3), 5.01 (d, 1 H, H-1), 4.99 and 4.84 (2 d, 2 H, *J* = 11.0 Hz, PhCH_2), 4.87 and 4.53 (2 d, 2 H, *J* = 11.0 Hz, PhCH_2), 4.76 (d, 1 H, $J_{1',2'}$ = 3.5 Hz, H-1'), 4.73 and 4.69 (2 d, 2 H, *J* = 11.0 Hz, PhCH_2), 4.62 and 4.47 (2 d, 2 H, *J* = 12.2 Hz, PhCH_2), 4.31 (ddd, 1 H, $J_{5,6a}$ = 6.5, $J_{5,6b}$ = 5.0 Hz, H-5), 4.00 (dd, 1 H, $J_{2',3'}$ = 9.6, $J_{3',4'}$ = 9.4 Hz, H-3'), 3.99 (ddd, 1 H, $J_{4',5'}$ = 9.8, $J_{5',6'a}$ = 3.5, $J_{5',6'b}$ = 1.8 Hz, H-5'), 3.94 (dd, 1 H, $J_{6a,6b}$ = 10.5 Hz, H-6a), 3.78 (dd, 1 H, $J_{6'a,6'b}$ = 10.8 Hz, H-6'a), 3.71 (dd, 1 H, H-6'b), 3.68 (dd, 1 H, H-4'), 3.65 (dd, 1 H, H-6b), 3.58 (dd, 1 H, H-2'). Anal. Calcd for $C_{67}H_{62}O_{13}S$: C, 72.68; H, 5.64. Found: C, 72.50; H, 5.57.

Compound **29β**: $[\alpha]_D$ +81° (*c* 0.8, $CHCl_3$); ^1H NMR (400 MHz) δ 8.02–7.99, 7.89–7.85, 7.81–7.78, 7.66–7.55, and 7.48–7.16 (5 m, 40 H, 8 Ph), 5.95 (dd, 1 H, $J_{3,4}$ = 3.2, $J_{4,5} \cong$ 0.5 Hz, H-4), 5.75 (dd, 1 H, $J_{1,2}$ = 10.0, $J_{2,3}$ = 9.8 Hz, H-2), 5.56 (dd, 1 H, H-3), 5.03 (d, 1 H, H-1), 5.03 and 4.78 (2 d, 2 H, *J* = 11.0 Hz, PhCH_2), 4.98 and 4.83 (2 d, 2 H, *J* = 11.0 Hz, PhCH_2), 4.84 and 4.55 (2 d, 2 H, *J* = 10.8 Hz, PhCH_2), 4.57 and 4.49 (2 d, 2 H, *J* = 12.0 Hz, PhCH_2), 4.47 (d, 1 H, $J_{1',2'}$ = 7.6 Hz, H-1'), 4.29 (ddd, 1 H, $J_{5,6a}$ = 4.2, $J_{5,6b}$ = 7.4 Hz, H-5), 4.06 (dd, 1 H, $J_{6a,6b}$ = 11.0 Hz, H-6a), 3.92 (dd, 1 H, H-6b), 3.71 (dd, 1 H, $J_{5',6'a}$ = 2.0, $J_{6'a,6'b}$ = 10.8 Hz, H-6'a), 3.69–3.60 (m, 3 H, H-3',4',6'b), 3.51 (dd, 1 H, $J_{2',3'}$ = 9.0 Hz, H-2'), 3.45 (ddd, 1 H, $J_{4',5'}$ = 9.2, $J_{5'6'b}$ = 4.5 Hz, H-5'). Anal. Found: C, 72.32; H, 5.62.

An uncharacterized product eluted second, presumably phenyl 2,3,4-tri-*O*-benzoyl-6-*O*-[(2-methyl-4-oxo)-2-pentyl]-1-thio-β-D-galactopyranoside (**23**, 5%): ^1H NMR (250 MHz) δ 7.98–7.16 (m, 20 H, 4 Ph), 5.96 (dd, 1 H, $J_{3,4}$ = 3.2, $J_{4,5} \cong$ 0.6 Hz, H-4), 5.71 (dd, 1 H, $J_{1,2}$ = 10.0, $J_{2,3}$ = 9.8 Hz, H-2), 5.55 (dd, 1 H, H-3), 5.01 (d, 1 H, H-1), 4.10 (ddd, 1 H, $J_{5,6a}$ = 5.8, $J_{5,6b}$ = 7.8 Hz, H-5), 3.64 (dd, 1 H, $J_{6a,6b}$ = 9.0 Hz, H-6a), 3.51 (dd, 1 H, H-6b), 2.51 (s, 2 H, CH_2CO), 2.12 (s, 3 H, CH_3CO), 1.21 and 1.10 (2 s, 6 H, 2 Me); CI (NH_3) mass spectrum, *m/z* 700 $(M + NH_4)^+$.

Methyl 2,3,6-Tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-(and β)-D-galactopyranosyl)-α-D-glucopyranoside (28α and 28β). (a) To a cooled (−25 °C), stirred mixture of **11** (140 mg, 0.24 mmol), **19**[22] (93 mg, 0.2 mmol), activated 4-Å powdered molecular sieves (0.20 g), and dry CH_2Cl_2 (2 mL) was added TMSOTf (43 μL, 0.24 mmol). The mixture was stirred at −25 °C for 50 min and then neutralized with Et_3N, diluted with CH_2Cl_2, filtered through Celite, and concentrated. The residue was eluted from a column of silica gel with 12:1 $PhCH_3$–AcOEt to afford known[35] **28α** together with **28β** (138 mg, 70%) in a 4:1 ratio. An analytical sample of **28β** was obtained by preparative TLC (20:1 $CHCl_3$–Et_2O): $[\alpha]_D$ +10° (*c* 1, $CHCl_3$); selected ^1H NMR data (400 MHz) δ 4.60 (d, 1 H, $J_{1,2}$ = 3.7 Hz, H-1), 4.35 (d, 1 H, $J_{1',2'}$ = 7.8 Hz, H-1'), 3.79 (dd, 1 H, $J_{2',3'}$ = 9.6 Hz, H-2'), 3.52 (dd, 1 H, $J_{2,3}$ = 9.5 Hz, H-2), 3.42 (s, 3 H, MeO). Anal. Calcd for $C_{62}H_{66}O_{11}$: C, 75.43; H, 6.74. Found: C, 75.18; H, 6.86. Repetition of the reaction in the presence of CH_3CN instead of CH_2Cl_2 gave a mixture of **28α** and **28β** (68%) in a 1:1.6 ratio. Use of BF_3·Et_2O, instead of TMSOTf, in CH_2Cl_2 and in CH_3CN gave the two disaccharides in 58% (α:β = 2:1) and 74% yields (α:β = 1:2.4), respectively, after further purification by preparative TLC (20:1 $CHCl_3$–Et_2O) in order to remove the small amounts of 1,1'-galactopyranosylgalactopyranoside derivatives.[23]

(b) Glycosylation of **7** with **21** (1.2 equiv) as described in preparation a (TMSOTf, CH_2Cl_2, −25 °C, 50 min) afforded **28α** and **28β** in 56% yield and a 5.4:1 ratio. When CH_3CN was used as solvent, 68% of a 1:1.1 mixture of **28α** and **28β** was recovered.

(c) Glycosylation of **14α** (1.2 equiv) with **19**[22] as described in preparation a (TMSOTf, CH_2Cl_2, −25 °C, 50 min) gave **28α** and **28β** in 79% yield and a 4:1 ratio. Use of the β-anomer **14β** as glycosyl donor gave similar results. When CH_3CN was used as solvent, 80% of a 1:1.6 mixture of **28α** and **28β** was isolated.

Methyl 4-*O*-(2-Azido-3,4,6-tri-*O*-benzyl-2-deoxy-α-(and β)-D-galactopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (30α and 30β). (a) To a cooled (−25 °C), stirred mixture of 9[39] (47 mg, 0.1 mmol), **21** (60 mg, 0.12 mmol), activated 4-Å powdered molecular sieves (0.10 g), and dry CH_3CN (1 mL) was added TMSOTf (22 μL, 0.12 mmol). The mixture was stirred at −25 °C for 50 min and then neutralized with Et_3N, diluted with CH_2Cl_2, filtered through Celite, and concentrated. The residue was eluted from a column of silica gel with 3:1 hexane–AcOEt to afford **30α** together with **30β** (69 mg, 75%) in a 1:6.6 ratio. Further column chromatography (15:1 $PhCH_3$–AcOEt) gave, first, **30α**: $[\alpha]_D$ +48° (*c* 0.7, $CHCl_3$); ^1H NMR (400 MHz) δ 7.45–7.24 (m, 30 H, 6 Ph), 5.75 (d, 1 H, $J_{1',2'}$ = 2.6 Hz, H-1'), 5.11 and 4.91 (2 d, 2 H, *J* = 10.6 Hz, PhCH_2), 4.85 and 4.53 (2 d, 2 H, *J* = 11.5 Hz, PhCH_2), 4.79 and

(53) Goodlett, V. W. *Anal. Chem.* **1965**, *37*, 431–432.

4.66 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.71 and 4.64 (2 d, 2 H, J = 11.2 Hz, PhCH_2), 4.63 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.60 and 4.47 (2 d, 2 H, J = 12 Hz, PhCH_2), 4.33 and 4.27 (2 d, 2 H, J = 11.6 Hz, PhCH_2), 4.10 (dd, 1 H, $J_{2,3}$ = 9.5, $J_{3,4}$ = 8.2 Hz, H-3), 4.01 (dd, 1 H, H-4'), 3.90–3.81 (m, 5 H, H-2',3'5',4,5), 3.72–3.66 (m, 2 H, H-6a,6b), 3.59 (dd, 1 H, H-2), 3.51 (dd, 1 H, $J_{5',6'a}$ = 7.8, $J_{6'a,6'b}$ = 9.0 Hz, H-6'a), 3.43 (s, 3 H, MeO), 3.43 (dd, 1 H, $J_{5',6'b}$ = 5.5 Hz, H-6'b). Anal. Calcd for $C_{55}H_{59}N_3O_{10}$: C, 71.64; H, 6.45. Found: C, 71.57; H, 6.56.

30β eluted second: $[\alpha]_D$ −7° (c 1, $CHCl_3$); ^{1}H NMR (400 MHz) δ 7.43–7.15 (m, 30 H, 6 Ph), 5.00 and 4.79 (2 d, 2 H, J = 10.8 Hz, PhCH_2), 4.92 and 4.55 (2 d, 2 H, J = 11.2 Hz, PhCH_2), 4.84 and 4.66 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.72 and 4.65 (2 d, 2 H, J = 11.8 Hz, PhCH_2), 4.71 and 4.48 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.62 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1), 4.37 and 4.26 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.18 (d, 1 H, $J_{1',2'}$ = 8.0 Hz, H-1'), 3.98 (dd, 1 H, $J_{5,6a}$ = 3.0, $J_{6a,6b}$ = 10.8 Hz, H-6a), 3.96 (dd, 1 H, $J_{3,4}$ = 9.0, $J_{4,5}$ = 9.5 Hz, H-4), 3.90 (dd, 1 H, $J_{3',4'}$ = 2.6, $J_{4',5'} \cong$ 0.3 Hz, H-4'), 3.89 (dd, 1 H, $J_{2,3}$ = 9.2 Hz, H-3), 3.81 (ddd, 1 H, $J_{5,6b}$ = 1.4 Hz, H-5), 3.78 (dd, 1 H, $J_{2',3'}$ = 10.2 Hz, H-2'), 3.74 (dd, 1 H, H-6b), 3.53 (dd, 1 H, H-2), 3.52 (dd, 1 H, $J_{5',6'a}$ = 8.2, $J_{6'a,6'b}$ = 9.2 Hz, H-6'a), 3.42 (s, 3 H, MeO), 3.34 (dd, 1 H, $J_{5',6'b}$ = 5.0 Hz, H-6'b), 3.25 (ddd, 1 H, H-5'), 3.17 (dd, 1 H, H-3'). Anal. Found: C, 71.55; H, 6.46. When CH_2Cl_2 was used as solvent, 55% of a 3.7:1 mixture of **30α** and **30β** was isolated.

(b) Glycosylation of **15** (1.2 equiv) with **19**[22] as described in preparation a (TMSOTf, CH_3CN, −25 °C, 2 h) afforded **30α** and **30β** in 81% yield and a 1:5 ratio. When CH_2Cl_2 was used as solvent (reaction time, 6 h), 77% of a 2.4:1 mixture of **30α** and **30β** was recovered.

Benzyl 3-*O*-Acetyl-4-*O*-(2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-α-(and β)-D-galactopyranosyl)-2,6-di-*O*-benzyl-β-D-galactopyranoside (31α and 31β). To a cooled (−25 °C), stirred mixture of **15** (67 mg, 0.12 mmol), **24**[49] (49 mg, 0.1 mmol), activated 4-Å powdered molecular sieves (0.10 g), and dry CH_3CN (1 mL) was added TMSOTf (22 μL, 0.12 mmol). The mixture was stirred at −25 °C for 1.5 h and then neutralized with Et_3N, diluted with CH_2Cl_2, filtered through Celite, and concentrated. The residue was eluted from a column of silica gel with $PhCH_3$–AcOEt (from 19:1 to 9:1) to give, first, **31α** (15 mg, 16%): $[\alpha]_D$ +64° (c 1.3, $CHCl_3$); ^{1}H NMR (400 MHz) δ 7.49–7.26 (m, 30 H, 6 Ph), 5.00 and 4.69 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.99 (dd, 1 H, $J_{2,3}$ = 10.4, $J_{3,4}$ = 3.2 Hz, H-3), 4.95 (d, 1 H, $J_{1',2'}$ = 3.6 Hz, H-1'), 4.93 and 4.57 (2 d, 2 H, J = 11.2 Hz, PhCH_2), 4.91 and 4.62 (2 d, 2 H, J = 11.6 Hz,-PhCH_2), 4.83 and 4.76 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.58 (d, 1 H, $J_{1,2}$ = 7.8 Hz, H-1), 4.57 (s, 2 H, PhCH_2), 4.43 and 4.39 (2 d, 2 H, J = 11.6 Hz, PhCH_2), 4.29 (ddd, 1 H, $J_{4',5'} \cong$ 1.0, $J_{5',6'a}$ = 9.0, $J_{5',6'b}$ = 4.4 Hz, H-5'), 4.19 (dd, 1 H, $J_{3',4'}$ = 2.4 Hz, H-4'), 4.17 (dd, 1 H, $J_{4,5} \cong$ 0.4 Hz, H-4), 4.02 (dd, 1 H, $J_{2',3'}$ = 10.8 Hz, H-3'), 3.97 (ddd, 1 H, $J_{5,6a}$ = $J_{5,6b}$ = 7.0 Hz, H-5), 3.91 (dd, 1 H, H-2'), 3.75–3.68 (m, 4 H, H-2,6a,6'a,6b), 3.43 (dd, 1 H, $J_{6'a,6'b}$ = 8.4 Hz, H-6'b), 1.91 (s, 3 H, Ac). Anal. Calcd for $C_{56}H_{59}N_3O_{11}\cdot 1H_2O$: C, 69.48; H, 6.35. Found: C, 69.56; H, 6.24.

31β eluted second (59 mg, 62%): $[\alpha]_D$ −16° (c 1, $CHCl_3$); ^{1}H NMR (400 MHz) δ 7.42–7.25 (m, 30 H, 6 Ph), 5.03 and 4.72 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.94 and 4.56 (2 d, 2 H, J = 11.6 Hz, PhCH_2), 4.93 and 4.68 (2 d, 2 H, J = 11.4 Hz, PhCH_2), 4.91 (dd, 1 H, $J_{2,3}$ = 10.2, $J_{3,4}$ = 3.2 Hz, H-3), 4.74 and 4.72 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.61 and 4.52 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.57 (d, 1 H, $J_{1,2}$ = 7.8 Hz, H-1), 4.35 (s, 2 H, PhCH_2), 4.15 (d, 1 H, $J_{1',2'}$ = 8.0 Hz, H-1'), 4.14 (dd, 1 H, $J_{4,5} \cong$ 0.5 Hz, H-4), 4.01 (dd, 1 H, H-2), 3.92 (dd, 1 H, $J_{2',3'}$ = 10.4 Hz, H-2'), 3.89 (dd, 1 H, $J_{3',4'}$ = 2.8, $J_{4',5'} \cong$ 0.5 Hz, H-4'), 3.81 (dd, 1 H, $J_{5,6a}$ = 4.6, $J_{6a,6b}$ = 10.2 Hz, H-6a), 3.76–3.70 (m, 2 H, H-5,6b), 3.56 (dd, 1 H, $J_{5',6'a}$ = 7.8, $J_{6'a,6'b}$ = 8.2 Hz, H-6'a), 3.44 (ddd, 1 H, $J_{5',6'b}$ = 5.2 Hz, H-5'), 3.37 (dd, 1 H, H-6'b), 3.21 (dd, 1 H, H-3'), 2.06 (s, 3 H, Ac). Anal. Calcd for $C_{56}H_{59}N_3O_{11}$: C, 70.79; H, 6.26. Found: C, 70.70; H, 6.38. When the glycosylation reaction was performed at −45 °C (3 h), using CH_3CH_2CN as solvent, **31α** and **31β** were isolated in 12% and 66% yields, respectively.

Methyl 4-*O*-(2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (32). Glycosylation of **13α** (1.2 equiv) with **19**[22] as for the preparation of **31** (TMSOTf, CH_3CN, −25 °C, 4 h) gave, after column chromatography (2.5:1 hexane–AcOEt), **32** in 81% yield: $[\alpha]_D$ −3° (c 1, $CHCl_3$) [lit.[48] $[\alpha]_D$ −3° (c 1.65, $CHCL_3$)]. The ^{1}H NMR (400 MHz) spectrum fully confirmed the structure.

Registry No. 1, 38768-81-9; **2**, 80300-30-7; **3**, 67068-83-1; 4, 6207-45-0; **5**, 139684-64-3; **6**, 88962-62-3; **7**, 53081-25-7; **α-8**, 3964-13-4; **β-8**, 3866-62-4; **9**, 79781-69-4; **α-10**, 139684-66-5; **β-10**, 139684-67-6; **α-11**, 139684-65-4; **β-11**, 139686-51-4; **α-12**, 139608-01-8; **β-12**, 139608-02-9; **α-13**, 139608-03-0; **β-13**, 139608-04-1; **α-14**, 139608-05-2; **β-14**, 139608-06-3; **α-15**, 139608-07-4; **β-15**, 139608-08-5; **16**, 53008-65-4; **17**, 82231-38-7; **18**, 139608-09-6; **19**, 19488-48-3; **20**, 82231-37-6; **21**, 139608-10-9; **22**, 139608-11-0; **23**, 139608-12-1; **24**, 139630-81-2; **α,α-25**, 58781-26-3; **α,β-25**, 58781-27-4; **α-26**, 55094-26-3; **β-26**, 56632-57-6; **α-27**, 64694-18-4; **β-27**, 77117-44-3; **α-28**, 114817-97-9; **β-28**, 114817-98-0; **α-29**, 139608-13-2; **β-29**, 139608-14-3; **α-30**, 139608-15-4; **β-30**, 139608-16-5; **α-31**, 139608-17-6; **β-31**, 139608-18-7; **32**, 118579-76-3; isopropenyl chloroformate, 57933-83-2; phenyl 1-thio-β-D-galactopyranoside, 16758-34-2; Tebbe reagent, 67719-69-1.