The Chemistry of Isopropenyl Glycopyranosides. Transglycosylations and Other Reactions

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Received January 30, 1996[⊗]

Various anomerically pure isopropenyl α- and β-glycopyranosides have been synthesized and shown to undergo synthetically useful transglycosylation reactions with a variety of primary and secondary carbohydrate alcohols. Although stable when stored, isopropenyl glycosides are readily activated as glycosyl donors by a variety of electrophiles, including *N*-iodosuccinimide/triflic acid, trimethylsilyl triflate, and triflic anhydride. Under conditions that retard formation of the glycosyl cation, the reactivity of isopropenyl glycosides is diverted away from transglycosylation and toward electrophilic addition across the vinyl ether double bond.

Introduction

Oligosaccharides and glycoconjugates play important roles in cellular development, adhesion, communication, migration, infection, and disease.[1,2] Work aimed at the preparation and study of these compounds has resulted in the development of a variety of new glycosylating agents.[2,3] Among those more recently introduced are thioglycosides,[4−6] glycosyl trichloroacetimidates,[7] glycosyl fluorides,[8−10] *n*-pentenyl glycosides,[11] glycosyl sulfoxides[12] and sulfones,[13] selenoglycosides,[14] and glycosyl phosphites.[15] We and others have introduced the use of isopropenyl[16,17] and other vinyl glycosides[18] as glycosyl donors.

At the beginning of our work, we envisioned that isopropenyl glycosides would be activated as glycosyl donors by electrophiles in a manner similar to that already observed by Fraser-Reid and co-workers with *n*-pentenyl glycosides.[11] In fact, the expectation was that conjugation of the electrophilic double bond with the glycosidic oxygen would make isopropenyl glycosides even more reactive than *n*-pentenyl glycosides. The mechanism of activation was expected to involve initial capture of the electrophile (E^+) by the vinyl ether double bond of **1** leading to the formation of cation **2** or **3** (Scheme 1). Collapse of **2** or **3** to form glycosyl oxocarbenium cation **5** and acetone derivative **4** would be followed by nucleophilic attack on **5** to generate glycoside **7**. If the isopropenyl glycoside contained an ester protecting group at C-2, neighboring-group participation would lead to the formation of a resonance-stabilized dioxocarbenium ion **6**, which would then undergo nucleophilic attack to generate exclusively the 1,2-*trans*-glycoside (e.g., β-glucoside) **7**β. An alternative reaction would involve direct nucleophilic attack on **2** or **3** to generate the addition product **8**.

We describe here the stereoselective synthesis of a variety of isopropenyl α- and β-glycopyranosides and the use of these compounds as glycosyl donors for oligosaccharide synthesis. The effects of varying the promoter, glycosyl donor, and glycosyl acceptor have been studied. It turns out that isopropenyl glycosides are poised delicately between two manifolds of reactivity. Solvent, promoter, and protecting groups on the glycosyl donor can direct the reactivity of isopropenyl glycosides toward either transglycosylation or electrophilic addition.

Results and Discussion

Synthesis of Isopropenyl Glycopyranosides. Reaction of bis(acetonyl)mercury[19] with glycopyranosyl halides **9a**−**f** resulted in *O*-glycosylation[20] and produced the corresponding isopropenyl β-glycopyranosides **10a**−**f**

[⊗] Abstract published in *Advance ACS Abstracts,* July 1, 1996.

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S0022-3263(96)00190-9 CCC: $12.00

Scheme 1

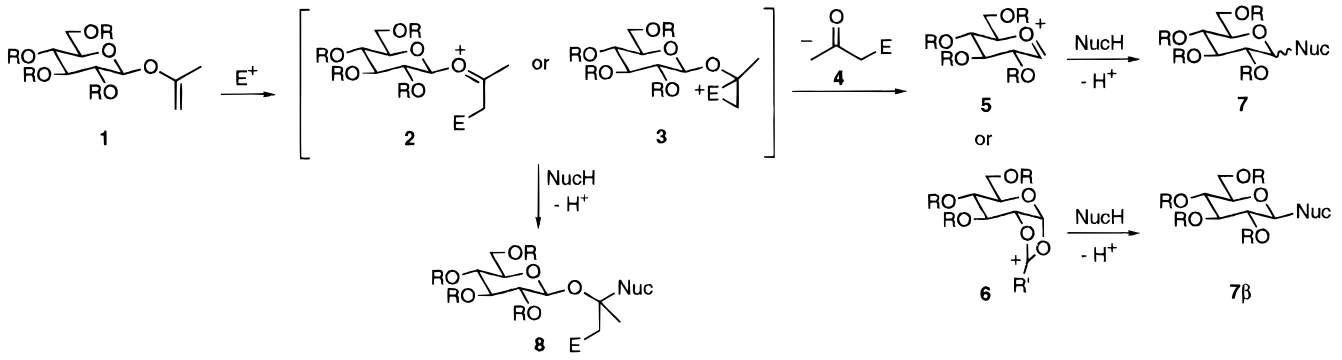
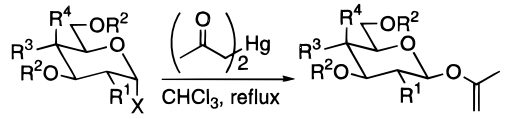
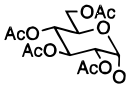


Table 1. Synthesis of Isopropenyl β-D-Glycopyranosides



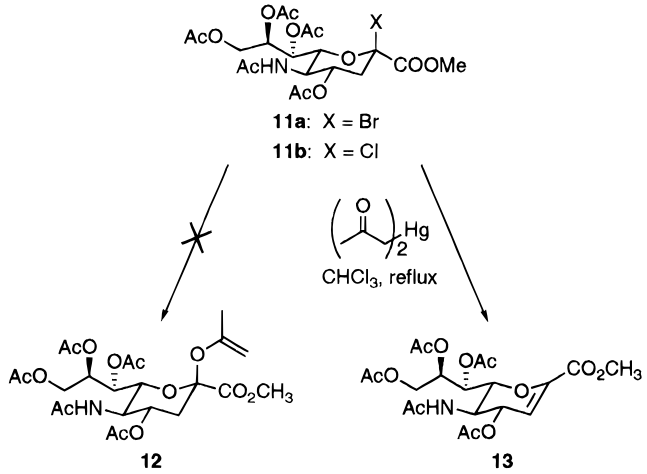
9a-f **10a-f**

reaction	R^1	R^2	R^3	R^4	X	yield, %
9a → 10a	AcO	Ac	AcO	H	Br	62
9b → 10b	PivO[a]	Piv	PivO	H	Br	72
9c → 10c	PivO	Piv	H	PivO	Br	64
9d → 10d	BnO	Bn	BnO	H	Cl	85
9e → 10e	AcO	Ac		H	Br	60
9f → 10f	PhthN	Ac	AcO	H	Br[b]	43

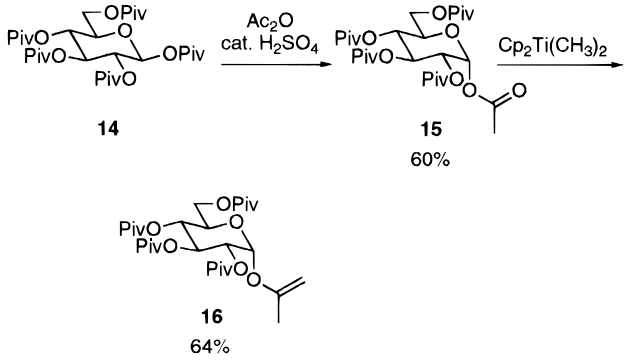
in generally good yield (Table 1). The reaction was successful with ester or ether protecting groups, a glycosyl chloride or bromide, and derivatives of both a disaccharide and an amino sugar. In all cases, the β-glycoside was produced as a single diastereomer.[21] Attempts to prepare isopropenyl sialoside **12** by a similar reaction of either sialosyl bromide **11a**[22] or sialosyl chloride **11b**[23] with bis(acetonyl)mercury failed. Instead, elimination led to the formation of glycal **13**[24] (Scheme 2). Such elimination is a common problem in the synthesis of sialosides.

Isopropenyl 2,3,4,6-tetra-*O*-pivaloyl-α-D-glucopyranoside (**16**) was prepared stereoselectively as outlined in Scheme 3.[25] Acid-catalyzed exchange of the anomeric pivaloyloxy group of penta-*O*-pivaloyl-β-D-glucopyranose (**14**)[26] led to the formation of **15** as the only anomer. Regioselective methylidenation of **15** by dimethyltitanocene[27] generated **16** as the only product. It appears that the regioselectivity exhibited by dimethyltitanocene results from both a steric preference for acetate rather than pivaloate esters as well as an electronic preference

Scheme 2



Scheme 3



for an anomeric acyloxy group rather than other, less electrophilic acyloxy groups. The reaction of penta-*O*-acetyl-α-D-glucopyranose with dimethyltitanocene exhibits some regioselectivity, generating the isopropenyl glucoside and a mixture of the other, regioisomeric monoisopropenyl ethers in a 1.3:1.0 ratio, as determined by ^{1}H NMR.

Isopropenyl glycosides are stable and are readily purified by column chromatography on silica gel. Isopropenyl β-glycosides bearing ester protecting groups have shown no decomposition, as determined by change in melting point or ^{1}H NMR spectrum, even after being stored for over two years at room temperature.

Transglycosylations: The Effect of Promoter. To investigate the ability of various electrophiles to promote transglycosylation by isopropenyl glycosides, the coupling

(21) It is unclear whether the stereoselective formation of **10a**−**f** is due to neighboring-group participation or a concerted mechanism with a cyclic transition state in which mercury coordinates the departing halide and delivers the enolate nucleophile from the opposite face of the pyranose ring. The reaction of **9c** with inversion suggests a concerted mechanism, but reaction of **9f** (α:β = 1:1) to give exclusively β glycoside might suggest neighboring-group participation. The unusually low yield of **10f**, however, leaves open the possibility that only the α anomer of **9f** reacted successfully to give **10f** and that it did so by a concerted mechanism.

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Scheme 4

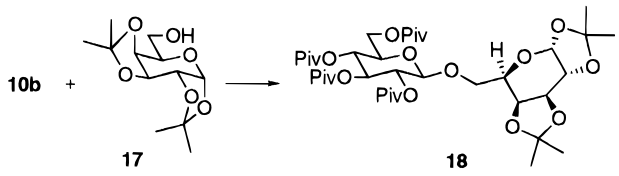


Table 2. Ability of Various Electrophiles To Promote Transglycosylation of 17 by 10b (Scheme 4)

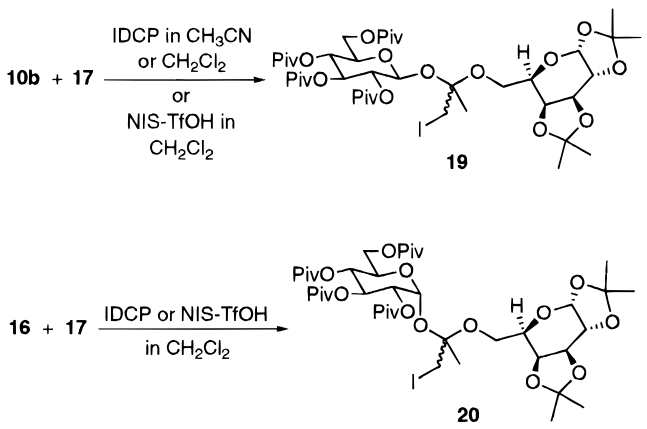
promoter	solvent	yield[a]
NIS/triflic acid	CH_3CN	70%
trimethylsilyl triflate	CH_3CN	69%
triflic anhydride	CH_3CN	65%
silver triflate	CH_3CN	24% (24h)
DMTST	CH_2Cl_2	48%
triflic acid	CH_3CN	no reaction
trimethylsilyl iodide	CH_3CN	no reaction
NIS or NBS	CH_3CN	no reaction
N-(phenylselenyl)phthalimide	CH_3CN	no reaction
$Cp_2Zr(OTf)_2(THF)$	CH_2Cl_2	no reaction
$Hg(CN)_2/HgBr_2$	CH_2Cl_2	no reaction
$CuBr_2/nBu_4NBr$	1:5 DMF−CH_2Cl_2	no reaction

[a] Reaction of 0.077 mmol of **17** and 0.155 mmol of **10b** in 2 mL of solvent at 0 °C.

of **10b** with glycosyl acceptor **17** was used as a representative reaction (Scheme 4). Trimethylsilyl triflate (TMSOTf),[17,28] *N*-iodosuccinimide/triflic acid (NIS/TfOH),[29] and triflic anhydride (Tf_2O)[30] all led to the formation of disaccharide **18** in good yield (Table 2). Reactions were carried out at 0 °C, in acetonitrile, and were complete within 2−5 min. Silver triflate (AgOTf)[31] promoted the reaction **10b** and **17** to form **18** in low yield, but only after prolonged reaction time. When triflic acid (TfOH) alone was tested as promoter, **10b** failed to react with **17** or the trimethylsilyl ether of **17**,[32] and **10b** was recovered unchanged. Thus, TMSOTf does not promote reaction of **10b** and **17** by silylating the glycosyl acceptor and generating TfOH.[17] Furthermore, neither NIS/TfOH, TMSOTf, Tf_2O, nor AgOTf activate isopropenyl glycosides toward transglycosylation simply by acting as a source of TfOH. Silylating agents, such as trimethylsilyl iodide (TMSI), that are less electrophilic than TMSOTf also failed to promote reaction of **10b**. Dimethyl(methylthio)-sulfonium triflate (DMTST)[6] promoted rapid coupling of **17** and **10b**, but the yield of **17** was lower than that obtained with NIS/TfOH, TMSOTf, or Tf_2O. Interestingly, DMTST is the only promoter that led exclusively to the formation of disaccharide from **10b** when dichloromethane was used as the solvent (see Addition Reactions: The Effect of Solvent).

We and others[20] have observed transglycosylation when isopropenyl glycosides were reacted with NIS or *N*-bromosuccinimide (NBS) in protic solvents, such as methanol or water. In 99:1 acetonitrile−water, isopropenyl glycosides hydrolyze readily in the presence of NIS or NBS. In the absence of acidic protons or excess nucleophile, however, NIS and NBS are not electrophilic enough to promote transglycosylation by isopropenyl

Scheme 5



glycosides. Neither NIS nor NBS promoted the coupling of **10b** and **17**. Despite precedent for their activities as promoters of transglycosylation, *N*-(phenylselenyl)phthalimide,[33] $Zr(Cp_2)(OTf)_2THF$,[10] mercuric cyanide/mercuric bromide,[34] and cupric bromide/tetra-*n*-butylammonium bromide (TBAB),[35] also failed to promote the transglycosylation of **17** by **10b**. Each left only unreacted starting materials after 19−48 h.

When iodonium dicollidine perchlorate (IDCP)[36] was examined as promoter,[11] **10b** and **17** reacted but failed to produce **18**. Instead, electrophilic addition formed **19** as a 1:1 mixture of diastereomers (Scheme 5).[37] Mixed iodoacetonide **19** was produced whether the reaction was run in dichloromethane or acetonitrile (see Addition Reactions: The Effect of Solvent). Similarly, reaction of **16** and **17** with IDCP produced **20** as the only dimeric species (Scheme 5).

Addition Reactions: The Effect of Solvent. All of the preceding, successful transglycosylation reactions, except the one with DMTST as promoter, used acetonitrile as solvent. However, when the same reactions were performed in a less polar solvent, electrophilic addition across the isopropenyl ether occurred, as when IDCP was the promoter (Scheme 5). Reaction of **10b** and **17** with NIS/TfOH in dichloromethane led to the formation of **19** in 41% yield (Table 3). No disaccharide product **17** was observed. Likewise, reaction of **16** and **17** in dichloromethane, with NIS/TfOH as promoter, gave **20** as the sole product (Scheme 5). When **10b** and **17** were reacted with TMSOTf in dichloromethane, a mixture of disaccharide **18** and the mixed acetonide **21** was obtained (Scheme 6).

It was not obvious, initially, whether the favorable influence of acetonitrile on disaccharide formation was

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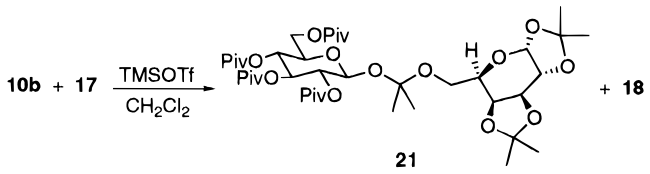
Table 3. Effect of Solvent on the Distribution of Products Formed by the Reaction of 10b and 17[a]

promoter	solvent	18	19
IDCP	CH_3CN[b]	–	53%
	CH_2Cl_2[b]	–	53%
NIS/TfOH	CH_3CN[c]	70%	–
	CH_2Cl_2[b]	–	41%
	4:1 ether:CH_2Cl_2[c]	36%	–
	4:1 *dry* ether:CH_2Cl_2[c]	31%	25%
	50 mM *t*BuOH in CH_2Cl_2[c]	75%	–

[a] Reaction of 0.077 mmol of **17** and 0.077−0.155 mmol of **10b** in 2 mL of solvent at 0 °C. The quantity of glycosyl donor **10b** affected the yields but not the identities of products formed. [b] 0.077 mmol of **10b**. [c] 0.155 mmol of **10b**.

Scheme 6



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the result of a bulk solvent (dielectric constant) effect or the result of specific complexation (and thereby stabilization) of the glycosyl oxocarbenium ion **5** or **6** (Scheme 1) by acetonitrile. Specific complexation of glycosyl cations, leading to the formation of *N*-glycosylnitrilium ions, is known to be responsible for the stereochemical outcome of some glycosylation reactions performed in nitrile solvents.[17,38] Insight into the present system came from the observation that trace quantities of water in nonpolar solvents, like dichloromethane or diethyl ether, led to improved selectivity for the formation of disaccharide. For example, in a 4:1 mixture of incompletely dried diethyl ether and dichloromethane, reaction of **10b** and **17** with NIS/TfOH as promoter gave **18** as the sole dimeric product. However, when the same reaction was run using scrupulously dried diethyl ether, a 6:5 mixture of **18** and **19** was produced (Table 3).

The effect of trace water could be mimicked by deliberate introduction of another protic solvent, *tert*-butyl alcohol, into the reaction mixture. When **10b** and **17** were reacted with NIS/TfOH in dichloromethane containing one mole equivalent (~50 mM) of *tert*-butyl alcohol, **18** was produced in 75% yield (Table 3). Further experiments demonstrated that the yield of **18** was not particularly sensitive to the concentration (25−100 mM) or absolute quantity (0.5−2.0 equivalents) of *tert*-butyl alcohol present. To our knowledge, this is the first example of improving the yield of a transglycosylation reaction by adding a protic solvent.

The results obtained with various solvents and promoters suggest that subtle energetic effects steer the reactivity of isopropenyl glycopyranosides toward transglycosylation or electrophilic addition. Factors that favor cation formation (strong electrophile, polar solvent) lead to outright addition of the electrophile to the isopropenyl glycoside, followed by formation of the glycosyl cation and then disaccharide. Factors that retard cation formation (weak electrophile, nonpolar solvent) cause nucleophile-assisted electrophilic addition across the vinyl ether double bond to become kinetically dominant. It appears that trace protic species, such as water or *tert*-butyl alcohol, favor glycosyl cation formation by specific solvation,[39] not by covalent complex formation.[40] Ironically, hydrolysis of unprotected isopropenyl glycopyranosides in completely aqueous solution proceeds by electrophilic addition of water across the vinyl ether double bond, not by formation of the glycosyl oxocarbenium intermediate.[25]

To investigate the possibility that mixed glycosyl ketals **19-21** were mechanistic intermediates in the formation of disaccharide **18**,[41] iodoacetonide **19** was subjected to reaction conditions in which **10b** and **17** form disaccharide. Exposure of **19** to NIS/TfOH in acetonitrile caused immediate conversion of **19** to 2,3,4,6-tetra-*O*-pivaloyl-D-glucopyranose and **17**, which were recovered quantitatively. By comparison, disaccharide **18** was stable when subjected to the same reaction conditions and was recovered quantitatively.

Effect of the Glycosyl Acceptor. To determine the effect of the glycosyl acceptor on the outcome of transglycosylation reactions, **10b** was reacted with various glycosyl acceptors, using TMSOTf or NIS/TfOH as promoter (Table 4). Yields of β-glycosides were good, except for that from the reaction of the sterically hindered glycosyl acceptor **28**.

The glycosylations of pent-4-enyl 2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**24**) and phenyl 2,3,4-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (**30**)[42] are significant since no self-coupling of either **24** or **30** was detected by TLC or ^{1}H NMR. Both **24** and **30** are less reactive toward the promoters used than **10b**, despite the fact that **10b** bears electronically "disarming"[43] ester protecting groups and compounds **24** and **30** bear electronically "arming" ethereal protecting groups.[44] We have recently used the selective activation of **10b** in the presence of **24** or **30** to prepare trisaccharides via two successive glycosylations performed in one reaction vessel.[16,45]

Effects of Various Glycosyl Donors. To determine the effects of the glycosyl donor on transglycosylation reactions, various glycosyl donors were reacted with **17** as a representative glycosyl acceptor. When **10b** (Scheme 4) was replaced by its α anomer, **16**, reaction with **17** gave β-disaccharide **18** as a single diastereomer, in yields similar to those obtained from **10b**. Thus, it appears that

(38) (a) Pougny, J.-R.; Sinaÿ, P. *Tetrahedron Lett.* **1976**, 4073−4076. (b) Lemieux, R. U.; Ratcliffe, R. M. *Can. J. Chem.* **1979**, *57*, 1244−1251. (c) Schmidt, R. R.; Behrendt, M.; Toepfer, A. *Synlett* **1990**, 694−696. (d) Pavia, A. A.; Ung-Chhun, S. N.; Durand, J. L. *J. Org. Chem.* **1981**, *46*, 3158−3160. (e) Ratcliffe, A.; Fraser-Reid, B. *J. Chem. Soc., Perkin Trans. 1* **1990**, 747−750.

(39) The effect of trace quantities of protic solvents is too dramatic to be due simply to the change in bulk dielectric constant.

(40) Specific (covalent) complexation of the glycosyl cation intermediate would have led to the enhanced formation of hydrolysis product or *tert*-butyl glycoside, not the observed disaccharide.

(41) For intramolecular glycosyl delivery via acetal rearrangement, see: (a) Ito, Y.; Ogawa, T. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1765−1767. For intramolecular glycosyl delivery via orthoester rearrangement, see: (b) Reference 28. (c) Gass, J.; Strobl, M.; Loibner, A.; Kosma, P.; Zähringer, U. *Carbohydr. Res.* **1993**, *244*, 69−84. (d) Sznaidman, M. L.; Johnson, S. C.; Crasto, C.; Hecht, S. M. *J. Org. Chem.* **1995**, *60*, 3942−3943.

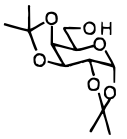
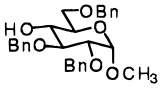
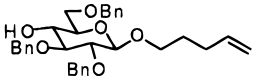
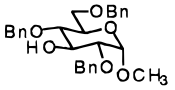
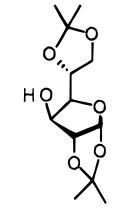
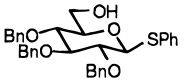
(42) (a) Anderson, L.; Pfaffli, P. J.; Hixson, S. *Carbohydr. Res.* **1972**, *23*, 195−206. (b) Kovãc, P.; Lerner, L. *Carbohydr. Res.* **1988**, *184*, 87−112.

(43) For discussions of electronically armed and disarmed glycosyl donors, see (a) Mootoo, D. R.; Konradsson, P.; Udodong, U.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1988**, *110*, 5583−5584. (b) Friesen, R. W.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1989**, *111*, 6656−6660. (c) Halcomb, R. L.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1989**, *111*, 6661−6666. (d) Veeneman, G. H.; van Boom, J. H. *Tetrahedron Lett.* **1990**, *31*, 275−278.

(44) A similar result based on the differential reactivity of seleno- and thioglycosides has been reported: Mehta, S.; Pinto, B. M. *Tetrahedron Lett.* **1991**, *32*, 4435−4438.

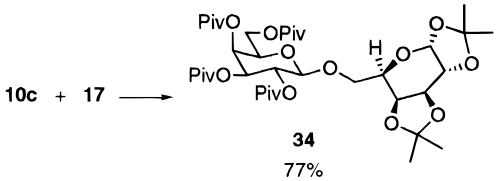
(45) Castro, A. Ph.D. Dissertation, University of Delaware, 1995.

Table 4. β-Glycosylation of Various Glycosyl Acceptors by 10b[a]

promoter	glycosyl acceptor	disaccharide	yield, %
NIS/TfOH	 **17**	**18**	70
TMSOTf	 **22**	**23**	69
TMSOTf	 **24**	**25**	70
TMSOTf	 **26**	**27**	74
TMSOTf	 **28**	**29**	23
TMSOTf	 **30**	**31**	65
NIS/TfOH	$HO(CH_2)_{10}OAc$ **32**	**33**	64

[a] Reaction of 1 equiv of glycosyl acceptor and 1.5−3.0 equiv of **10b** in 2 mL of solvent at 0 °C.

Scheme 7



both **10b** and **16** generate the same glycosyl cation intermediate. Because **10b** is more conveniently prepared and exhibits greater shelf life than **16**, we chose early on to use **10b** as a glycosyl donor over **16**.

Isopropenyl galactopyranoside **10c** behaved similar to **10b**. It and **17** reacted with TMSOTf in acetonitrile to give disaccharide **34** in 77% yield (Scheme 7). Acetylated glucopyranoside **10a** also behaved similar to **10b**, except that the transglycosylation reactions of **10a** proceeded with yields lower than those of **10b**, presumably because of complications due to orthoester formation.[46]

Tetra-*O*-benzyl glucopyranoside **10d** was investigated as an isopropenyl glycoside bearing nonparticipating[47] ethereal protecting groups. When **10d** and **17** were reacted with IDCP in dichloromethane, a 1.2:1.0 mixture of disaccharide **35**[48] and its β anomer was obtained in 64% overall yield (Scheme 8). Despite the relatively weak electrophile and nonpolar solvent, disaccharide formation occurred instead of addition across the isopropenyl ether (see Addition Reactions: The Effect of Solvent). Apparently, the relatively electron-releasing ethereal protecting groups lower the energy barrier to glycosyl cation formation from **10d** relative to that from the ester-protected glycosides, **10a**−**c** and **16**.

Scheme 8

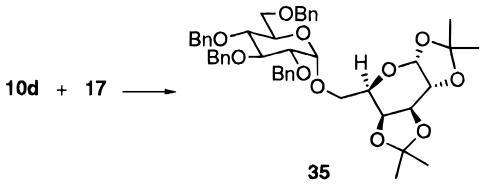


Table 5. Effects of Temperature and Solvent on the Stereoselective Coupling of 10d and 17 (Scheme 8)[a]

solvent	temperature, °C	yield, %	α:β
dichloromethane[b]	rt	64	1.2:1.0
acetonitrile[c]	rt	70	1.0:1.7
diethyl ether	35	96	5:1
	rt	84	7:1
	0	95	6:1
	−30	90	2.5:1.0
	−78	50	1:3
diisopropyl ether	rt	85	3.5:1.0

[a] Unless specified otherwise, reactions were conducted with 0.10 mmol of **10d**, 0.11 mmol of **17**, and 0.10 mmol of TMSOTf as promoter. [b] Reaction of 0.059 mmol of **10d**, 0.053 mmol of **17**, and 0.064 mmol of IDCP. [c] Reaction of 0.16 mmol of **10d**, 0.077 mmol of **17**, and 0.093 mmol of TMSOTf .

When **10d** and **17** were reacted with TMSOTf at room temperature in diethyl ether,[49] a 7:1 mixture of **35** and its β anomer was produced in 84% yield. Interestingly, the stereoselectivity for formation of α product decreased upon both increasing and reducing the temperature of the reaction (Table 5). When **10d** and **17** were reacted in the presence of excess DMTST and TBAB,[50,51] **10d** could be seen by TLC to react almost instantaneously and generate the corresponding glycosyl bromide *in situ*. Slower reaction (69 h) of the equilibrating mixture of α and β glycosyl bromides led to the formation of **35** in 53% yield as a 9.3:1.0 mixture of α and β anomers.

Finally, the use of an isopropenyl glycoside as an aminoglycosyl donor was investigated. Reaction of **10f** and **17** with TMSOTf as promoter, either in acetonitrile at 0 °C or in dichloromethane at −25 °C, generated the corresponding β disaccharide, **36**,[52] in 40% yield as the only dimeric product.

(46) Kunz, H.; Harreus, A. *Liebigs Ann. Chem.* **1982**, 41−48.
(47) Paulsen, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 155−173.
(48) Thiem, J.; Kreuzer, M. *Carbohydr. Res.* **1986**, *149*, 347−361.
(49) The use of ether as solvent is known to promote the formation of 1,2-*cis*-disaccharides: (a) Igarashi, K.; Irisawa, J.; Honma, T. *Carbohydr. Res.* **1975**, *39*, 213−225. (b) Reference 8. (c) Hashimoto, S.; Hayashi, M.; Noyori, R. *Tetrahedron Lett.* **1984**, *25*, 1379−1382. (d) Mukaiyama, T.; Katsurada, M.; Takashima, T. *Chem. Lett.* **1991**, 985−988.
(50) Tetraalkylammonium bromide salts promote the equilibration of α-glycosyl bromides to the more reactive β-glycosyl bromides, leading to stereoselective α-glycoside formation in dichloromethane: Lemieux, R. U.; Hendriks, K. B.; Stick, R. V.; James, K. *J. Am. Chem. Soc.* **1975**, *97*, 4056−4062.
(51) DMTST and TBAB have been used to promote the stereoselective formation of 1,2-*cis*-disaccharides, using thioglycosides as glycosyl donors. See reference 5.
(52) Ogawa, T.; Ito, Y. *Carbohydr. Res.* **1990**, *202*, 165−175.

Conclusion

In conclusion, isopropenyl glycopyranosides are stable upon storage and yet are readily activated as glycosyl donors by a variety of electrophiles. Transglycosylation reactions proceed in good yield and seem to be fairly general with respect to both the glycosyl residue being transferred and the nature of the carbohydrate glycosyl acceptor. A novel electronic effect of solvent, protecting groups, and promoter was discovered and found to influence the products formed. Factors which favor the formation of the glycosyl oxocarbenium cation (strong electrophile, polar solvent, electron-releasing protecting groups on the glycosyl donor) lead to transglycosylation. Factors which retard the formation of the glycosyl cation (weak electrophile, nonpolar solvent, electron-withdrawing protecting groups on the glycosyl donor) lead to addition across the isopropenyl ether double bond.

Experimental Section

General Procedures. Acetonitrile, chloroform, and dichloromethane were purified by distillation from CaH_2 under argon. Diethyl ether and tetrahydrofuran were purified by distillation from sodium/benzophenone under argon. TMSOTf, Tf_2O, TfOH, TESOTf, and tBuOH were distilled under argon prior to use. DMTST[53] and IDCP[36] were prepared as previously described. Column chromatography was performed on silica gel 60 (230−400 mesh).

^1H and ^{13}C NMR spectra (250 and 62.9 MHz, respectively) were recorded at ambient temperature with samples in $CDCl_3$. Liquid secondary ion mass spectroscopy (LSIMS) was performed using Cs^+(20 eV) as the ionizing beam and *m*-nitrobenzyl alcohol or glycerol as the matrix. In some cases, LiCl or NaI was added to the matrix to enhance the relative intensity of the quasi-molecular ions. Of the alkali metal cations examined, Na was found to enhance the relative intensity of the quasi-molecular ion more than Li, K, or Cs. The relative intensity of the quasi-molecular ion was found to be insensitive to the counterion (F, Cl, Br, I) present in the matrix additive.

Bis(acetonyl)mercury.[19] 2-Methoxypropene (11.5 mL) was added dropwise from an addition funnel to a stirred suspension of yellow mercuric oxide (10.82 g) and mercuric acetate (0.40 g) in 6 mL of methanol and 3 mL of distilled water, at 0 °C. After 30 min at room temperature, the initially orange mixture had turned gray. The mixture was filtered through a fine (4−5.5 μm) fritted funnel. On cooling to 0 °C, the mercurial compound precipitated as a gray solid (16.2 g, 86%): mp 66−67 °C; ^1H NMR δ 2.46 (s, 2H), 2.15 (s, 3H).

Isopropenyl 2,3,4,6-Tetra-*O*-pivaloyl-β-D-glucopyranoside (10b). 2,3,4,6-Tetra-*O*-pivaloyl-α-D-glucopyranosyl bromide (**9b**)[46] (1.0 g) in chloroform (10 mL) was added to bis(acetonyl)mercury (1.1 g) in chloroform (20 mL). The mixture was heated at reflux for 27 h, cooled and then washed with 10% potassium thiocyanate, 1 M sodium bicarbonate, and water. The organic layer was dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography (12:1 hexane−ethyl acetate) afforded **10b** (0.69 g, 72%) as a white solid: mp 120−123 °C; ^1H NMR δ 5.35 (t, J = 9.5 Hz, 1H), 5.14 (dd, J = 8.0, 9.6 Hz, 1H), 5.08 (t, J = 9.6 Hz, 1H), 4.91 (d, J = 8.0 Hz, 1H), 4.19 (dd, J = 1.8, 12.2 Hz, 1H), 4.13 (d, J = 2.0 Hz, 1H), 4.06 (br s, 1H), 4.02 (dd, J = 6.8, 12.2 Hz, 1H), 3.80 (ddd, J = 1.8, 6.8, 10.0 Hz, 1H), 1.76 (s, 3H), 1.18, 1.14, 1.13 and 1.10 (4 s, 9H each); ^{13}C NMR δ 178.0, 177.2, 176.6, 176.4, 158.1, 97.6, 86.9, 72.8, 72.3, 70.9, 68.3, 62.4, 38.9, 38.8, 27.2, 27.1, 20.3; IR (KBr) 2973, 1745, 1481, 1280, 1143, 1085 cm$^{-1;}$ LSIMS *m*/*z* 563.4 (M + Li^+), 499.3. Anal. Calcd for $C_{29}H_{48}O_{10}$: C, 62.57; H, 8.69. Found: C, 62.53; H, 8.75.

Isopropenyl 2,3,4,6-Tetra-*O*-pivaloyl-β-D-galactopyranoside (10c). As described for the synthesis of **10b**, 2,3,4,6-tetra-*O*-pivaloyl-α-D-galactopyranosyl bromide (**9c**) (1.83 g) was reacted with bis(acetonyl)mercury (1.99 g) for 48 h. Chromatography (8:1 hexane−ethyl acetate) afforded **10c** (1.12 g, 64%) as a white solid: mp 126−127 °C; ^1H NMR δ 5.42 (d, J = 3.1 Hz, 1H), 5.35 (dd, J = 8.0, 10.4 Hz, 1H), 5.13 (dd, J = 3.3, 10.5 Hz, 1H), 4.92 (d, J = 8.0 Hz, 1H), 4.18−4.02 (m, 6H), 1.79 (s, 3H), 1.25, 1.16, 1.14 and 1.10 (4 s, 9H each); IR (KBr) 2980,-1741, 1481, 1280, 1146, 1082 cm^{-1}; LSIMS *m*/*z* 563.4 (M + Li^+), 499.5. Anal. Calcd for $C_{29}H_{48}O_{10}$: C, 62.57; H, 8.69. Found: C, 62.57; H, 8.69.

Isopropenyl 2,3,4,6-Tetra-*O*-benzyl-β-D-glucopyranoside (10d). According to the procedure described for the preparation of **10b**, 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl chloride (**9d**)[54] (2.48 g) was reacted with bis(acetonyl)mercury (2.8 g). After 24 h, TLC (diethyl ether−hexane 1:1) showed disappearance of starting material (R_f 0.68) and appearance of product (R_f 0.72). Chromatography (9:1 hexane−ethyl acetate, containing 1% Et_3N) afforded **10d** (2.19 g, 85%) as a waxy solid: mp 61−64 °C; ^1H NMR δ 7.32−7.12 (m, 20H), 4.91 (d, J = 10.9 Hz, 2H), 4.84−4.70 (m, 4H), 4.61−4.49 (m, 3H), 4.23 (d, J = 1.8 Hz, 1H), 4.08 (br s, 1H), 3.77−3.52 (m, 6H), 1.87 (s, 3H); IR (film) 2906, 2863, 1644, 1497, 1454 , 1385, 1265, 1072 cm^{-1}; LSIMS *m*/*z* 603.3 (M + Na^+).

Isopropenyl Hepta-*O*-acetyl-β-D-maltopyranoside (10e). As described for the synthesis of **10b**, hepta-*O*-acetyl-α-D-maltopyranosyl bromide (**9e**)[55] (1.0 g) was reacted with bis-(acetonyl)mercury (0.90 g) for 68 h. Chromatography (2:1 hexane−ethyl acetate) afforded **10e** (0.58 g, 60%) as a white solid: mp 181−182 °C; ^1H NMR δ 5.39 (d, J = 4.1 Hz, 1H), 5.34 (t, J = 10.4 Hz, 1H), 5.27 (t, J = 8.7 Hz, 1H), 5.02 (t, J = 9.8 Hz, 1H), 4.93 (m, 2H), 4.84 (dd, J = 4.0, 10.5 Hz, 1H), 4.41 (dd, J = 2.7, 11.9 Hz, 1H), 4.25−4.19 (m, 2H), 4.14 (d, J = 2.0 Hz, 1H), 4.09−3.93 (m, 4H), 3.79 (m, 1H), 2.10, 2.08, 2.03, 2.01, 1.99 and 1.98 (6 s, 21H), 1.76 (s, 3H).

Isopropenyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (10f). According to the procedure described for the preparation of **10b**, 3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-D-glucopyranosyl bromide (**9f**)[56] (0.69 g) was reacted with bis(acetonyl)mercury (0.87 g). After 1 h, TLC (chloroform−methanol 19:1) showed disappearance of starting material (R_f 0.62) and appearance of product (R_f 0.54). Chromatography (3:1 hexane−ethyl acetate) afforded **10f** (0.30 g, 45%) as a pale yellow solid: mp 182−184 °C; ^1H NMR δ 7.85 (dd, J = 3.0, 5.5 Hz, 2H), 7.73 (dd, J = 3.0, 5.5 Hz, 2H), 5.83 (dd, J = 9.0, 10.6 Hz, 1H), 5.78 (d, J = 8.5 Hz, 1H), 5.17 (dd, J = 9.1, 10.1 Hz, 1H), 4.45 (dd, J= 8.6, 10.7 Hz, 1H), 4.31 (dd, J = 5.5, 12.3 Hz, 1H), 4.17−4.09 (m, 2H), 4.05 (br s, 1H), 3.94 (ddd, J = 2.3, 5.4, 10.2 Hz, 1H), 2.08, 2.02 and 1.86 (3 s, 3H each), 1.64 (s, 3H); IR (KBr) 3488, 1754, 1714, 1390, 1047 cm^{-1}; LSIMS *m*/*z* 498.2 (M + Na^+).

1-*O*-Acetyl-2,3,4,6-Tetra-*O*-pivaloyl-α-D-glucopyranose (15). To a stirred solution of 10.14 g of **14**[26] in 120 mL of acetic anhydride was added dropwise 7 mL of concentrated sulfuric acid. After 1 h, the mixture was poured onto ice and extracted with chloroform. The organic layer was washed with saturated $NaHCO_3$ and water, dried over anhydrous $MgSO_4$, and evaporated under reduced pressure. Recrystallization of the crude product from ethanol yielded 5.64 g (60%) of **15**: mp 144−145 °C; ^1H NMR δ 6.34 (d, J = 3.9 Hz, 1H), 5.53 (t, J = 9.8 Hz, 1H), 5.17 (t, J = 9.8 Hz, 1H), 5.05 (dd, J = 3.9, 10.0 Hz, 1H), 4.16−4.04 (m, 3H), 2.15 (s, 3H), 1.22−1.10 (m, 36H); IR (film) 2974, 1745, 1550, 1279, 1138, 1009 cm^{-1}; LSIMS *m*/*z* 581 (M + Na^+) 499, 397, 295, 211, 126, 109. Anal. Calcd for $C_{28}H_{46}O_{11}$: C, 60.20; H, 8.30. Found: C, 60.33; H, 8.30 .

Isopropenyl 2,3,4,6-Tetra-*O*-pivaloyl-α-D-glucopyranoside (16). To 2.03 g of **15** was added 22 mL of a 0.5 M solution of dimethyltitanocene[27] in toluene. The reaction was protected

(53) Ravenscroft, M.; Roberts, R. M. G.; Tillet, J. G. *J. Chem. Soc., Perkin Trans. 2* **1982**, 1569−1572.

(54) (a) Iversen, T.; Bundle, D. R. *Carbohydr. Res.* **1982**, *103*, 29−40. (b) Austin, P. W.; Hardy, F. E.; Buchanan, J. G.; Baddiley, J. *J. Chem. Soc.* **1964**, 2128−2137.

(55) Brauns, D. H. *J. Am. Chem. Soc.* **1929**, *51*, 1820−1831.

(56) Lemieux, R. U.; Takeda, T.; Chung, B. In *Synthetic Methods for Carbohydrates*; El Khadem, H. S., Ed.; American Chemical Society: Washington, DC, 1976; pp 91−115.

from light and heated at 65 °C for 15 h. The orange solution was diluted with petroleum ether, filtered, and evaporated under reduced pressure. Chromatography of the orange residue (acetone−petroleum ether 2:98) afforded 1.30 g (64%) of **16**: mp 104−105 °C; ^{1}H NMR δ 5.61 (t, J = 9.8 Hz, 1H), 5.50 (d, J = 3.8 Hz, 1H), 5.10 (t, J = 9.8 Hz, 1H), 4.85 (dd, J = 3.8, 10.0 Hz, 1H), 4.30 (d, J = 2.0, 1H), 4.14−3.97 (m, 4H), 1.82 (s, 3H), 1.18−1.10 (m, 36H); IR (film) 2973, 1743, 1643, 1550, 1460, 1140, 1051, 760 cm^{-1}; LSIMS m/z 579 (M + Na$^+$), 499, 397, 295, 211, 127, 109. Anal. Calcd for $C_{29}H_{48}O_{10}$: C, 62.57; H, 8.69. Found: C, 62.66; H, 8.96.

General Procedure for Glycosylation Reactions. Glycosyl acceptor, glycosyl donor (1−2 equiv), and activated, powdered 4-Å molecular sieves were combined in 2 mL of dry solvent and stirred for 30 min at room temperature. The mixture was cooled to 0 °C, and promoter was added. Within 5 min, reaction was complete as judged by TLC. The reaction mixture was neutralized with Et_3N (∼0.2 mL per 0.077 mmol of glycosyl acceptor), diluted with ethyl acetate (10 mL), filtered, and transferred to a separatory funnel. The organic layer was washed with 10% sodium thiosulfate (if NIS was used in the promoter mixture), 1 M sodium bicarbonate, distilled water, and brine. It was then dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. Chromatography gave the desired disaccharide as a pure compound. Excess glycosyl donor could be recovered as 2,3,4,6-tetra-*O*-pivaloylglucose.

1,2:3,4-Di-*O*-isopropylidene-6-*O*-(2,3,4,6-tetra-*O*-pivaloyl-*β*-D-glucopyranosyl)-α-D-galactopyranose (18). According to the general glycosylation procedure, **10b** (86 mg) and **17** (20 mg) were reacted in acetonitrile with NIS (17.3 mg) and TfOH (18 μL). Chromatography (0.8% methanol in 1,2-dichloroethane) afforded **18** (70%) as a syrup: ^{1}H NMR δ 5.45 (d, J = 4.9 Hz, 1H), 5.28 (t, J = 9.5 Hz, 1H), 5.09 (t, J = 9.5 Hz, 1H), 5.02 (dd, J = 7.9, 9.5 Hz, 1H), 4.56 (d, J = 7.9 Hz, 1H), 4.55 (dd, J = 2.4, 7.9 Hz, 1H), 4.25 (dd, J = 2.3, 5.0 Hz, 1H), 4.18 (dd, J = 1.8, 8.0 Hz, 1H), 4.17 (dd, J = 1.8, 12 Hz, 1H), 4.05 (dd, J = 5.4, 12.2 Hz, 1H), 3.99 (dd, J = 4.6, 10.2 Hz, 1H), 3.89 (m, 1H), 3.70 (m, 1H), 3.59 (dd, J = 6.4, 10.3 Hz, 1H), 1.47 (s, 3H), 1.40 (s, 3H), 1.29 (s, 6H), 1.20, 1.14, 1.12 and 1.08 (4 s, 9H each); ^{13}C NMR δ 178.1, 177.2, 176.6, 176.4, 109.2, 108.5, 101.2, 96.2, 72.3, 71.2, 71.1, 70.6, 70.5, 68.7, 68.2, 67.1, 62.0, 38.9, 38.7, 27.12, 27.05, 26.1, 25.9, 25.0, 24.3; IR (film) 2974, 2874, 1744, 1481, 1461, 1398, 1370, 1280, 1139, 1070 cm^{-1}; LSIMS m/z 765 (M + Li$^+$), 499. Anal. Calcd for $C_{38}H_{62}O_{15}$: C, 60.14; H, 8.23. Found: C, 59.90; H, 8.33.

Reaction of **10b** and **17** as above, except using TMSOTf (18 μL) or Tf_2O (15 μL) as promoter, yielded **18** (69 or 65%, respectively). Reaction of **10b** and **17** as above, except using 1 mol equiv of tBuOH (∼50 mM) in dichloromethane as solvent, gave **18** (75%). The use of DMTST (40 mg) as promoter and dichloromethane as solvent generated **18** (48%). Reaction of **10b** and **17** in acetonitrile, using AgOTf (19.8 mg) as promoter, required stirring for 24 h at room temperature to go to completion and yielded **18** (24%).

6-*O*-[2-Iodo-1-methyl-1-(2,3,4,6-tetra-*O*-pivaloyl-*β*-D-glucopyranosyloxy)ethyl]-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (19). According to the general glycosylation procedure, **10b** (43 mg) and **17** (20 mg) were reacted in dichloromethane with IDCP (0.077 mmol) as promoter. Column chromatography (12% ethyl acetate in hexane) afforded **19** (53%) as a waxy solid that was an approximately 1:1 mixture of epimers at the newly formed acetal center: mp 65−68 °C; ^{1}H NMR δ 5.50 (m, 1H), 5.29 (m, 1H), 5.16−4.95 (m, 3H), 4.64 (m, 1H), 4.36−4.20 (m, 3H), 3.97−3.21 (m, 7H), 1.61, 1.58, 1.56, 1.54, 1.53, 1.48, 1.41 and 1.33 (8 s, 15H), 1.21, 1.19, 1.131, 1.127 and 1.08 (5 s, 36H); ^{13}C NMR δ 179.3, 178.1, 178.0, 177.1, 176.6, 176.5, 109.7, 109.5, 108.8, 108.7, 101.3, 101.0, 96.4, 96.3, 94.2, 93.3, 73.0, 72.8, 72.7, 72.5, 71.6, 70.9, 70.8, 70.6, 70.3, 68.7, 68.1, 66.8, 66.2, 65.9, 62.6, 62.5, 62.4, 61.8, 60.5, 38.9, 38.7, 27.3, 27.2, 27.12, 27.05, 26.1, 26.03, 25.98, 25.3, 24.9, 24.72, 24.65, 24.3, 23.2, 13.6, 9.8; IR (film) 2976, 2874, 1744 , 1481, 1461, 1398, 1383, 1370, 1280, 1141, 1073 cm^{-1}; LSIMS m/z 965.4 (M + Na$^+$), 499.3. Anal. Calcd for $C_{41}H_{67}O_{16}I$: C, 52.23; H, 7.16; I, 13.46. Found: C, 52.13; H, 7.20; I, 13.46.

Reaction of **10b** and **17** as above, except using NIS (17.3 mg) and TfOH (18 μL) as promoter, yielded **19** (41%). Reaction of **10b** and **17** as above, except using CH_3CN as solvent, gave **19** (53%). Reaction of 0.155 mmol of each of **10b** and **17** as above, except using NIS (35 mg) and TfOH (15 μL) as promoter and 2.5 mL of 4:1 diethyl ether−dichloromethane as solvent, generated **19** (25%) and **18** (31%).

6-*O*-[2-Iodo-1-methyl-1-(2,3,4,6-tetra-*O*-pivaloyl-α-D-glucopyranosyloxy)ethyl]-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (20). According to the general glycosylation procedure, **16** (43 mg) and **17** (20 mg) were reacted in dichloromethane with NIS (17.3 mg) and TfOH (18 μL). TLC (hexane−ethyl acetate 2:1) showed disappearance of **10b** (R_f 0.87) and **17** (R_f 0.26) and appearance of product (R_f 0.85). Chromatography (10% ethyl acetate in hexane) afforded **19** (50%) as a waxy solid that was an approximately 1:1 mixture of epimers at the newly formed acetal center: mp 54−58 °C; ^{1}H NMR δ 5.57−5.49 (m, 2H), 5.45 (d, J = 5.0 Hz, 1H), 5.11 (dd, J = 9.6, 10.0 Hz, 1H), 4.91 and 4.87 (2 d, J = 3.9 Hz, 1H), 4.56 (dd, J = 2.1, 8.0 Hz, 1H), 4.31−4.12 (m, 3H), 4.07−3.99 (m, 2H), 3.90 (m, 1H), 3.66−3.25 (m, 4H), 1.63, 1.52, 1.40, 1.31, 1.30 (5 s, 3H each), 1.20, 1.15, 1.13 and 1.10 (4 s, 9H each); ^{13}C NMR δ 178.2, 177.6, 177.1, 176.4, 109.2, 108.6, 101.1, 96.3, 90.1, 70.9, 70.7, 70.0, 68.3, 66.8, 62.4, 62.1, 38.8, 30.8, 29.7, 27.4, 27.3, 27.2, 27.1, 26.2, 26.0, 25.0, 24.4, 23.1, 11.0; IR (film) 2973, 1743, 1480, 1398, 1280, 1139, 1072 cm^{-1}; LSIMS m/z 949.5 (M + Li$^+$), 499.4 ($C_{26}H_{43}O_9$)$^+$. Anal. Calcd for $C_{41}H_{67}O_{16}I$: C, 52.23; H, 7.16; I, 13.46. Found: C, 52.29; H, 7.40; I, 13.13.

1,2:3,4-Di-*O*-isopropylidene-6-*O*-[1-methyl-1-(2,3,4,6-tetra-*O*-pivaloyl-*β*-D-glucopyranosyloxy)ethyl]-α-D-galactopyranose (21). According to the general glycosylation procedure, **10b** (86 mg) and **17** (20 mg) were reacted in dichloromethane with TMSOTf (18 μL) as promoter. TLC (hexane−ethyl acetate 2:1) showed disappearance of starting materials and appearance of two products (R_f 0.84 and R_f 0.81). Chromatography (0.8% methanol in 1,2-dichloroethane) afforded **21** (32%) as a white waxy solid: mp 73−75 °C: ^{1}H NMR δ 5.49 (d, J = 5.0 Hz, 1H), 5.28 (ddd, J = 1.8, 7.5, 9.1 Hz, 1H), 5.08−4.96 (m, 3H), 4.62 (dd, J = 2.3, 8.0 Hz, 1H), 4.30 (dd, J = 2.3, 5.0 Hz, 1H), 4.29 (dd, J = 1.7, 7.8 Hz, 1H), 4.20 (dd, J = 1.7, 12.1 Hz, 1H), 3.91 (dd, J = 6.7, 12.1 Hz, 1H), 3.87 (m, 1H), 3.68 (ddd, J = 1.7, 6.8, 10.1 Hz, 1H), 3.60−3.56 (m, 2H), 1.53 and 1.52 (2 s, 6 H), 1.43 and 1.32 (2 s, 6H each), 1.18, 1.13, 1.12 and 1.08 (4 s, 9H each); ^{13}C NMR δ 178, 177, 176, 109.5, 108.6, 102.2, 96.4, 93.8, 73.1, 72.5, 71.2, 70.9, 70.8, 69.0, 66.6, 62.6, 60.3, 38.8, 38.7, 28.3, 27.3, 27.23, 27.20, 27.1, 26.2, 25.1, 24.9, 24.7; IR (film) 2975, 2875, 1744, 1481, 1461, 1398, 1383, 1371, 1280, 1141, 1073 cm^{-1}; LSIMS m/z 839.5 (M + Na$^+$), 801.5, 499.3. Anal. Calcd for $C_{41}H_{68}O_{16}$: C, 60.28; H, 8.39. Found: C, 60.24; H, 8.05.

Methyl 2,3,6-Tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-pivaloyl-*β*-D-glucopyranosyl)-α-D-glucopyranoside (23). According to the general glycosylation procedure, **10b** (129 mg) and **22**[57] (36 mg) were reacted in acetonitrile with TMSOTf (21 μL). TLC (hexane−ethyl acetate 2:1) showed disappearance of **10b** and **22** (R_f 0.59) and appearance of product (R_f 0.76). Chromatography (9% ethyl acetate in hexanes) afforded 51.6 mg (69%) of **23** as a syrup: ^{1}H NMR δ 7.45, 7.36 and 7.22 (3 m, 15H), 4.96 (d, J = 11.3 Hz, 1H), 4.85−4.78 (m, 4H), 4.72−4.53 (m, 5H), 4.28 (d, J = 12.1 Hz, 1H), 4.05 (dd, J = 1.7, 12.0 Hz, 1H), 3.99 (m, 1H), 3.89−3.69 (m, 4H), 3.57−3.47 (m, 2H), 3.34 (s, 3H), 3.24 (m, 1H), 1.18, 1.15, 1.12 and 1.07 (4 s, 9H each); IR (film) 2970, 2873, 1745, 1480, 1455, 1398, 1367, 1281, 1139, 1046 cm^{-1}; LSIMS m/z 969.2 (M + Li$^+$), 499.2. Anal. Calcd for $C_{54}H_{74}O_{15}$: C, 67.34; H, 7.74. Found: C, 67.27; H, 8.09.

Pent-4-enyl 2,3,6-Tri-*O*-benzyl-*β*-D-glucopyranoside (24). Pent-4-enyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside[58] (0.74 g) was reacted with sodium cyanoborohydride and HCl in THF.[57] TLC (hexane−ethyl acetate 2:1) showed disappearance of starting material (R_f 0.88) and formation of

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product (R_f 0.63). After aqueous workup, chromatography afforded **24** as a yellow syrup (76%): ^{1}H NMR δ 7.36−7.26 (m, 15H), 5.81(ddt, J = 6.7, 10.2, 17.0 Hz, 1H), 5.05−4.90 (m, 4H), 4.71 (d, J = 11.5 Hz, 2H), 4.58−4.55 (m, 2H), 4.40 (d, J = 7.3 Hz, 1H), 3.94 (dt, J = 6.4, 9.5 Hz, 1H), 3.78−3.41 (m, 7H), 2.51 (d, J = 1.9 Hz, 1H), 2.15 (m, 2H), 1.74 (m, 2H); IR (film) 3445, 2913, 2871, 1496, 1454, 1364, 1063 cm^{-1}; LSIMS m/z 541.2 (M + Na$^+$), 433.1. Anal. Calcd for $C_{32}H_{38}O_6$: C, 74.11; H, 7.38. Found: C, 73.88; H, 7.35.

Pent-4-enyl 2,3,6-Tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-pivaloyl-*β*-D-glucopyranosyl)-*β*-D-glucopyranoside (25). According to the general glycosylation procedure, **10b** (86 mg) and **24** (40 mg) were reacted in acetonitrile with TMSOTf (16 μL). TLC (hexane−ethyl acetate 7:2) showed disappearance of **10b** (R_f 0.74) and **23** (R_f 0.40) and appearance of product (R_f 0.67). Chromatography (15% ethyl acetate in hexane) afforded 54.9 mg (70%) of **25** as a syrup: ^{1}H NMR δ 7.46−7.23 (m, 15H), 5.81 (ddt, J = 6.7, 10.2, 17.0 Hz, 1H), 5.05−4.79 (m, 10H), 4.69−4.63 (m, 4H), 4.38 (d, J = 12.1 Hz, 1H), 4.29 (dd, J = 7.9, 10.0 Hz, 1H), 4.07−3.92 (m, 2H), 3.82−3.67 (m, 2H), 3.48 (t, J = 9.0 Hz, 1H), 3.31−3.21 (m, 3H), 2.15 (m, 2H), 1.74 (m, 2H), 1.18, 1.16, 1.14 and 1.10 (4 s, 9H each); IR (film) 2972, 2873, 1745, 1480, 1454 , 1397, 1367, 1280, 1138, 1050 cm^{-1}; LSIMS m/z 1023.1 (M + Li$^+$), 499.3. Anal. Calcd for $C_{58}H_{80}O_{15}$: C, 68.48; H, 7.93. Found: C, 68.50; H, 7.72.

Methyl 2,4,6-Tri-*O*-benzyl-3-*O*-(2,3,4,6-tetra-*O*-pivaloyl-*β*-D-glucopyranosyl)-α-D-glucopyranoside (27). According to the general glycosylation procedure, **10b** (129 mg) and **26**[59] (36 mg) were reacted in acetonitrile with TMSOTf (21 μL). TLC (hexane−ethyl acetate 2:1) showed disappearance of **10b** and **26** (R_f 0.57) and appearance of product (R_f 0.80). Chromatography (0.8% methanol in 1,2-dichloroethane) afforded 54.9 mg (74%) of **27** as a syrup: ^{1}H NMR δ 7.42, 7.30 and 7.25 (3 m, 15H), 5.34−5.26 (m, 2H), 5.14−5.05 (m, 2H), 4.99 (d, J = 11.2 Hz, 1H), 4.70−4.33 (m, 8H), 4.09 (m, 2H), 3.67−3.50 (m, 5H), 3.27 (s, 3H), 1.21, 1.15, 1.14 and 1.13 (4 s, 9H each); IR (film) 2972, 2873, 1745, 1480, 1455, 1398, 1368, 1280, 1140, 1052 cm^{-1}; LSIMS m/z 985.7 (M + Na$^+$), 499.3. Anal. Calcd for $C_{54}H_{74}O_{15}$: C, 67.34; H, 7.74. Found: C, 67.02; H, 7.44.

1,2:5,6-Di-*O*-isopropylidene-3-*O*-(2,3,4,6-tetra-*O*-pivaloyl-*β*-D-glucopyranosyl)-α-D-glucofuranoside (29). According to the general glycosylation procedure, **10b** (86 mg) and **28** (20 mg) were reacted in acetonitrile with TMSOTf (18 μL). TLC (hexane−ethyl acetate 2:1) showed disappearance of **10b** and **28** (R_f 0.30) and appearance of product (R_f 0.82). Chromatography (0.8% methanol in 1,2-dichloroethane) afforded 13.5 mg (23%) of **29** as a white solid: mp 156−158 °C; ^{1}H NMR δ 5.94 (d, J = 3.7 Hz, 1H), 5.27 (t, J = 9.4 Hz, 1H), 5.09 (t, J = 9.7 Hz, 1H), 5.01 (dd, J = 8.1, 9.4 Hz, 1H), 4.57 (d, J = 7.9 Hz, 1H), 4.53 (d, J = 3.7 Hz, 1H), 4.20−3.93 (m, 5H), 3.75−3.62 (m, 3H), 1.44 (s, 3H), 1.30 (s, 6H), 1.29 (s, 3H), 1.20, 1.125, 1.120 and 1.08 (4 s, 9H each); IR (KBr) 2970, 2933, 1743, 1481, 1458, 1383, 1282, 1140, 1035 cm^{-1}; LSIMS m/z 781.6 (M + Na$^+$), 499.3. Anal. Calcd for $C_{38}H_{62}O_{15}$: C, 60.14; H, 8.23. Found: C, 59.80; H, 8.08.

Phenyl 2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-pivaloyl-*β*-D-glucopyranosyl)-1-thio-*β*-D-glucopyranoside (31). According to the general glycosylation procedure, **10b** (31 mg) and **30**[42] (13 mg) were reacted in 1 mL of acetonitrile with TMSOTf (11 μL). TLC (hexane−ethyl acetate 4:1) showed disappearance of **10b** (R_f 0.75) and **30** (R_f 0.31) and appearance of product (R_f 0.56). Chromatography (12.5% ethyl acetate in hexane) afforded 25 mg (65%) of **31** as a syrup: ^{1}H NMR δ 7.54−7.21 (m, 20H), 5.13 (t, J = 9.3 Hz, 1H), 5.02 (dd, J = 9.4, 9.7 Hz, 1H), 4.93 (dd, J = 8, 9.4 Hz, 1H), 4.90−4.69 (m, 6H), 4.55 (d, J = 10.9 Hz, 1H), 4.44 (d, J = 8.0 Hz, 1H), 4.21 (dd, J = 1.4, 12.2 Hz, 1H), 3.98−3.90 (m, 2H), 3.79−3.64 (m, 2H), 3.47−3.27 (m, 4H), 1.20, 1.16, 1.10 and 1.08 (4 s, 9H each); IR (film) 2904 , 2874, 1747, 1499, 1439, 1359, 1151, 1078 cm^{-1}; LSIMS m/z 1062.6 (M + Na$^+$). Anal. Calcd for $C_{59}H_{76}O_{14}S$: C, 68.05; H, 7.36; S, 3.08. Found: C, 68.01; H, 8.01; S, 2.94.

10-Acetoxydecyl 2,3,4,6-Tetra-*O*-pivaloyl-*β*-D-glucopyranoside (33). According to the general glycosylation procedure, **10b** (103 mg) and **32** (20 mg) were reacted in 2.5 mL of acetonitrile with NIS (42 mg) and TfOH (16 μL). TLC (hexane−ethyl acetate 6:2) showed disappearance of **10b** (R_f 0.83) and **32** (R_f 0.34) and appearance of product (R_f 0.76). Chromatography (5% ethyl acetate in hexane) afforded 42 mg (64%) of **33** as a clear oil: ^{1}H NMR δ 5.28 (t, J = 9.4 Hz, 1H), 5.06 (dd, J = 9.5, 9.9 Hz, 1H), 4.98 (dd, J = 8.0, 9.6 Hz, 1H), 4.46 (d, J = 8.0 Hz, 1H), 4.19 (dd, J = 1.9, 12.1 Hz, 1H), 4.02 (dd, J = 5.8, 12.1 Hz, 1H), 4.02 (t, J = 6.7 Hz, 2H), 3.79 (dt, J = 6.5, 9.4 Hz, 1H), 3.69 (ddd, J = 1.9, 5.8, 10.0 Hz, 1H), 3.40 (dt, J = 6.8, 9.4 Hz, 1H), 2.02 (s, 3H), 1.58−1.49 (m, 4H), 1.22 (br s, 12H), 1.19 (s, 9H), 1.123 and 1.121 (2s, 18H), 1.08 (s, 9H); IR (film) 2969, 2857, 1741, 1480, 1461, 1397, 1356, 1280, 1143, 1038 cm^{-1}; LSIMS m/z 737.3 (M + Na$^+$), 499.3. Anal. Calcd for $C_{38}H_{66}O_{12}$: C, 63.84; H, 9.30. Found: C, 64.06; H, 9.22.

1,2:3,4-Di-*O*-isopropylidene-6-*O*-(2,3,4,6-tetra-*O*-pivaloyl-*β*-D-galactopyranosyl)-α-D-galactopyranose (34). According to the general glycosylation procedure, **10c** (86 mg) and **17** (20 mg) were reacted in acetonitrile with TMSOTf (18 μL). TLC (hexane−ethyl acetate 2:1) showed disappearance of **10c** (R_f 0.86) and **17** (R_f 0.26) and appearance of product (R_f 0.80). Chromatography (0.8% methanol in 1,2-dichloroethane) afforded **34** (77%) as a syrup: ^{1}H NMR δ 5.45 (d, J = 4.9 Hz, 1H), 5.38 (d, J = 3.1 Hz, 1H), 5.21 (dd, J = 8.1, 10.2 Hz, 1H), 5.07 (dd, J = 2.5, 10.4 Hz, 1H), 4.56 (d, J = 7.7 Hz, 1H), 4.55 (dd, J = 3.3, 7.8 Hz, 1H), 4.26-4.10 (m, 3H'), 4.02−3.92 (m, 4H), 3.62 (dd, J = 6.4, 10.0 Hz, 1H), 1.47 (s, 3H), 1.40 (s, 3H), 1.30 (s, 3H), 1.29 (s, 3H), 1.24, 1.15, 1.14 and 1.08 (4 s, 9H each); IR (film) 2977, 2874, 1790, 1481, 1461, 1398, 1382, 1370, 1280, 1140, 1072 cm^{-1}.

1,2:3,4-Di-*O*-isopropylidene-6-*O*-(2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl)-α-D-galactopyranose (35).[48] According to the general glycosylation procedure, **10d** (34 mg) and **17** (13.8 mg) were reacted in dichloromethane with IDCP (0.064 mmol). TLC (diethyl ether−hexane 1:1) showed disappearance of **10d** (R_f 0.94) and **17** (R_f 0.30) and formation of product (R_f 0.62). Chromatography (15% ethyl acetate in hexane) afforded 29.3 mg (64%) of a 1.2:1.0 mixture of **35** and its β anomer. The ratio of anomers was determined by integration of the NMR signals for the anomeric protons of the α (δ 5.50, d, J = 5.0 Hz) and β (δ 5.55, d, J = 5.0 Hz) anomers.

Reaction of **10d** (89 mg) and **17** (20 mg) as above, except with acetonitrile as solvent and TMSOTf (18 μL) as promoter, yielded 42 mg (70%) of a 1.0:1.7 mixture of **35** and its β anomer. Reaction of **10d** (58 mg) and **17** (28 mg) at various temperatures in diethyl or diisopropyl ether with TMSOTf (20 μL) as promoter gave **35** and its β anomer in various yields and anomeric ratios (Table 5). Reaction of **10d** (89 mg), **17** (20 mg), and TBAB (124 mg) in acetonitrile with DMTST (40 mg) for 69 h at rt gave 31.6 mg (53%) of a 9.3:1.0 mixture of **35** and its β anomer.

1,2:3,4-Di-*O*-isopropylidene-6-*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl)-α-D-galactopyranose (36).[52] According to the general glycosylation procedure, **10f** (38 mg) and **17** (10.5 mg) were reacted in 1 mL of acetonitrile at 0 °C with TMSOTf (15 μL). Within 5 min, TLC (hexane−ethyl acetate 1:1) showed disappearance of **10f** (R_f 0.63) and **17** (R_f 0.46) and appearance of product (R_f 0.48). Chromatography (33% ethyl acetate in hexane) afforded **36** (40%) as a yellow solid: mp 205−207 °C.

Reaction of **10f** and **17** as above, except performing the reaction at −25 °C and using 1 mL of CH_2Cl_2 as solvent, gave 10.8 mg (40%) of purified **36**.

Acknowledgment. This work has been supported, in part, by the National Science Foundation (CHE 90-19078), the Petroleum Research Fund (ACS-PRF 25395-G1), and the University of Delaware Research Foundation. We thank Dr. Gordon Nicol and Adam Bratis for LSIMS data, Dr. Fred Askham for providing Zr(Cp$_2$)(OTf)$_2$THF, Dr. Subramanium Sabesan for providing **11b**, Robert Meagley for providing **32**, and Janeen Argyros for preparing **30**.

JO960190P

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