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Stereoselective Synthesis of 2-Deoxy-β-glycosides From Glycal Precursors. 2. Stereochemistry of Glycosidation Reactions of 2-Thiophenyl- and 2-Selenophenyl-α-D-*gluco*-pyranosyl Donors

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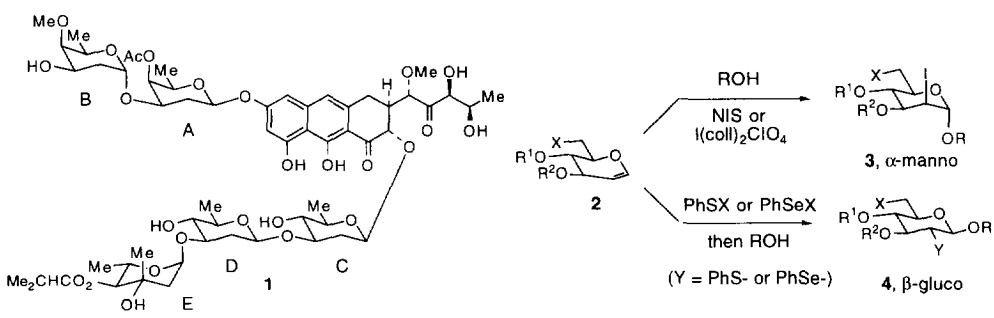
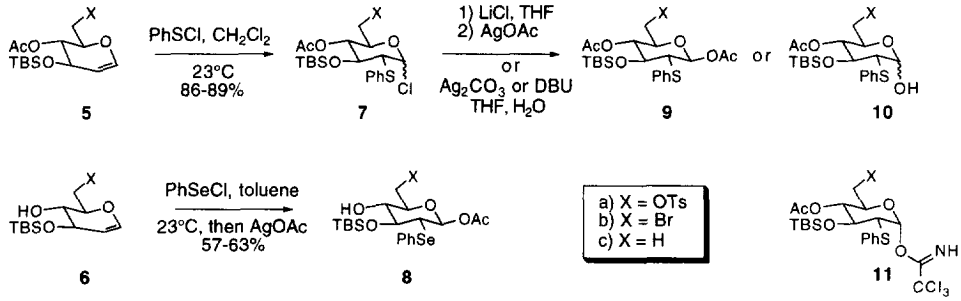
Abstract: *We have demonstrated that 4-O-acetyl-6-bromo-3-O-(tert-butyldimethylsilyl)-2-deoxy-2-thiophenyl-1-trichloroacetimido-α-D-glucopyranose* ***11b*** *is the most efficient and selective donor for use in the synthesis of 2-deoxy-β-glycosides of the series of glycosyl donors examined. Unlike the 2-selenophenyl substituted donors* ***8*** *which proved to be configurationally unstable under standard TMS-OTf promoted glycosylation conditions, giving rise to α-manno glycosides* ***14***, ***17*** *and* ***20*** *from β-gluco donors* ***8***, *the 2-thiophenyl substituted donors* ***9*** *and* ***11*** *appeared to be completely configurationally stable (at C(2)). The main problem with imidates* ***11*** *is that the stereoselectivity of their reactions with alcohols is substrate dependent, with best selectivity for the desired β-glycosides* ***35*** *and* ***42*** *being obtained with the least sterically hindered alcohols. The fact that the α-glycosides* ***36*** *and* ***43*** *comprise up to 20-50% of the product in glycosidation reactions of hindered secondary alcohols supports the thesis that the reaction stereoselectivity is not governed by the intermediacy of episulfonium ions (****47*** *and* ***47'****), but rather that substitution reactions of oxonium ions* ***46*** *and its conformationally inverted isomer* ***46'*** *play a dominant role.*

2-Deoxy-β-glycosides are important structural components of many natural products, including the aureolic acids,[1,2] the calicheamicins,[3,4] cardiac glycosides,[5] the angucycline antibiotics[6] (e.g., landomycin A[7]), and others.[8,9] Methods for the synthesis of 2-deoxy-β-glycosides have been reviewed.[10-12] In connection with our work on the synthesis of olivomycin A (**1**),[12-17] we decided to pursue a strategy in which both the β- and α-2-deoxyglycosides would be constructed from glycal precursors.[10,18] This would facilitate the synthesis of aureolic acid di- and trisaccharide analogs designed to probe the nature of the interactions of the aureolic acid oligosaccharides with DNA.[19-24] In this connection, we were particularly attracted to the methodology extensively developed by Thiem,[10] Danishefsky[18] and Horton[25] for the synthesis of 2-iodo-α-D-mannosides **3** via the electrophilic substitution reactions of glycals and alcohols with NIS or $I(coll)_2ClO_4$, and the procedures reported by Ogawa,[26] Franck,[27,28] Schmidt[29] and Beau[30] for the synthesis of 2-thiophenyl or 2-selenophenyl-β-D-glucosides **4** via the reactions of glycals **2** with electrophilic sulfur (PhSOR;[26] arylbis(arylthio)sulfonium salts;[28] PhSCl[29]) or selenium (PhSeCl)[30] reagents. An additional attractive feature to this methodology is that



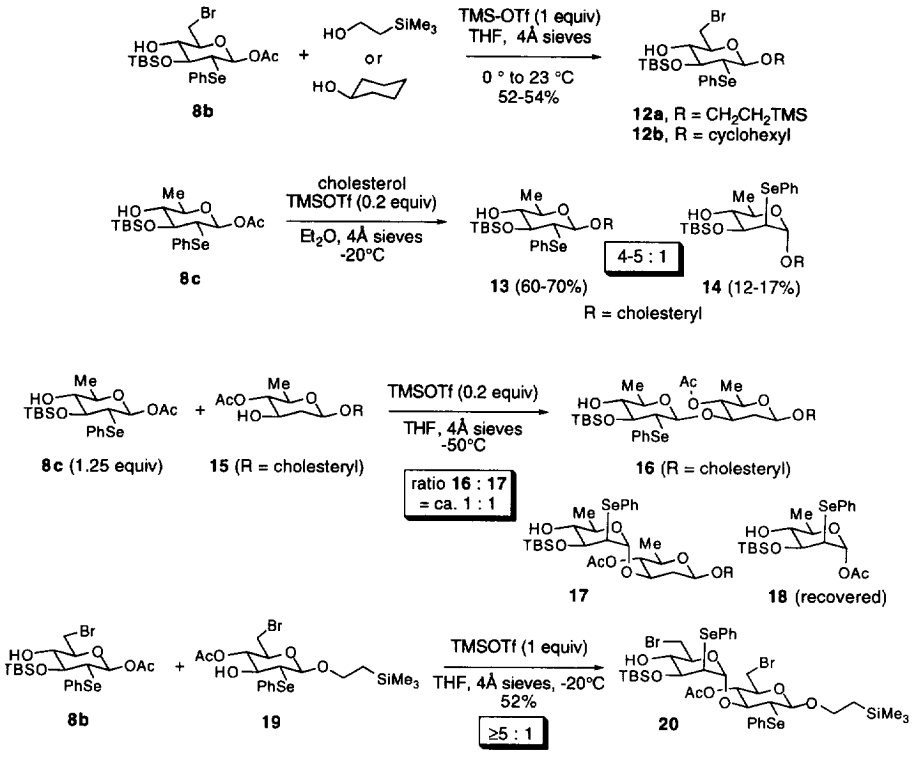
the heteroatom substituents at C(2) of **3** and **4** should stabilize the resulting glycosides with respect to acid catalyzed hydrolysis (an important consideration in the projected synthesis of **1**).[12,31,32]

In the preceding paper we described our studies of the stereochemistry of the reactions of glycals with PhSCl and PhSeCl.[33] We observed that the reactions of glycals **5** and **6** with PhSCl and PhSeCl gave excellent selectivity (≥10 : 1, *gluco* : *manno*) for adducts **7** and **8** only when the C(6)-X substituent is strongly electron withdrawing (e.g., X = OBn, -OTs, -Br, but not X = H). Selectivity in the PhSCl additions was also maximized when the C(4) substitute is an acetate derivative (as in **5**), whereas the best selectivity in the PhSeCl additions was obtained with substrates containing C(4)-OH groups (e.g., **6**). We report herein the results of our studies of the glycosidation reactions of **8**, **9** and **11**, resulting in the identification of trichloroacetimidate **11b** as the most efficient and selective donor for use in the synthesis of 2-deoxy-β-glycosides that we have studied to date.



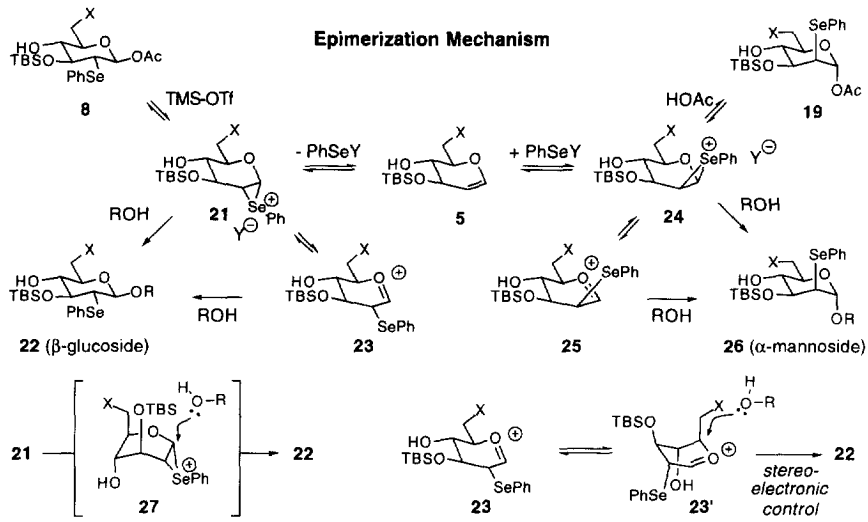
RESULTS AND DISCUSSION

Glycosylation Reactions of 2-Selenophenyl-β-D-*gluco*-pyranosyl Acetates. Prior to the initiation of our work, Beau had reported a reasonably selective protocol for the synthesis of 2-deoxy-β-glycosides via glycosidation reactions of 2-selenophenyl substituted glycosyl acetates.[30] We therefore anticipated that the seleno acetate donors **8** would give excellent results in glycosylation reactions leading to the C-D disaccharide unit of olivomycin A. Initial experiments performed with **8b** as the donor and either β-trimethylsilylethanol or cyclohexanol as the acceptor provided the expected β-glycosides **12a** and **12b** with excellent selectivity, albeit in modest yield (52-54%). Based on these encouraging preliminary results, glycosidation reactions with a series of more structurally complex acceptors were performed. Treatment of cholesterol with glycosyl donor **8c**[30,33] and 0.2 equiv. of TMS-OTf in Et_2O at -20 °C provided the β-glycoside **13** in 60-70% yield. However, a significant amount of the α-manno glycoside **14** was also obtained (12-17%), suggesting that equilibration of the activated donor had occurred, presumably at the stage of an episelenonium ion. Episelenonium ion equilibration can also be inferred from the data reported by Beau,[30] as well as in related studies by Ogawa[34] and Sinaÿ.[35] However, since Beau had suppressed C(2)-epimerization of the donors by using TMS-OTf in ethereal solvents, and because he had reported excellent results in the glycosidations of glycoside acceptors containing relatively hindered hydroxyl groups, we continued our survey of the suitability of donors **8** for use in the olivomycin synthesis. Accordingly, the coupling of donor **8c** (1.25 equiv.) and acceptor **15** (prepared in three steps from **13** : (i) Bu_3SnH, AIBN; (ii) Ac_2O, pyridine; (iii) TBAF, 1% HOAc, THF, 62% overall) in the presence of 0.2 equiv. of TMS-OTf in THF at -50°C provided a ca. 1 : 1 mixture of **16** and **17**, the latter containing an α-manno linkage between the two monosaccharide units. Interestingly, the excess donor **8c** used in this experiment was recovered as the α-manno acetate **18**. The most significant problem of C(2)-SePh isomerization occurred in couplings with acceptors such as **19** which have very hindered alcohols (in this case flanked by two equatorial substituents): the glycosidation of **19** with donor **8b** provided the α-manno disaccharide **20** as the major product (≥5 : 1 selectivity) in 52% yield. All attempts to suppress the equilibration



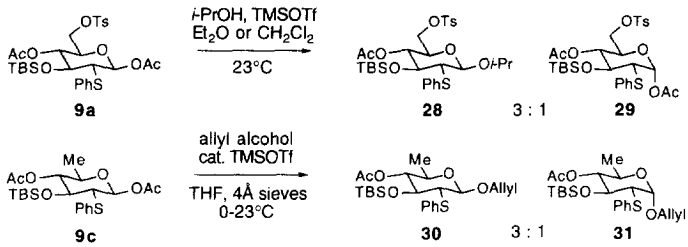
pathway (e.g., by acylating the free hydroxyl in donors **8a** and **8b**; use of lower reaction temperatures) were unsuccessful.[36]

It is clear from these results that donors such as **8** are poorly suited for use in the synthesis of complex glycosides such as those that occur in the aureolic acid trisaccharide units. Nevertheless, these data are quite interesting in that they provide insight into the glycosidation-equilibration pathway. Activation of **8** with TMS-OTf leads either to episelenonium ion **21** or the corresponding oxonium ion **23** by loss of the anomeric acetate. Our data show that as long as the nucleophile is relatively unhindered (e.g., a primary alcohol), the β-glucoside **22** is obtained with good selectivity. However, as the nucleophile becomes increasingly hindered, selectivity for the β-glucoside **22** decreases at the expense of increased production of the α-mannoside **26**. This can be rationalized by noting that the transition state for substitution of **21** by the alcohol acceptor must be boat-like (see **27**), since the conversion of **21** → **22** involves formal diequatorial opening of the episelenonium ion.[37-40] If, on the other hand, the reaction proceeds by way of oxonium ion intermediates (e.g., **23** ⇔ **23'**), then the β-selectivity observed in the glycosidations of **8** can be rationalized if one assumes that the reactive conformation of the oxonium ion is the $^3H_4$ half-chair **23'**, as opposed to the $^4H_3$ half-chair **23**, in which case the new C-O bond develops anti to the α-C-Se bond (i.e., Felkin-Anh mode of addition).[41,42] This pathway (via **23'**) also benefits from the development of an anomeric effect in the transition state. In either event, it would be expected that transition states for substitutions via either **27** or **23'** would be increasingly destabilized as the steric requirements of the alcohol acceptors (ROH) increase. Thus, the rate of the gluco substitution pathway should slow with increased steric demands of ROH, allowing competitive, reversible deselenenylation of **21** (or **23/23'**) to dominate, thereby providing the epimeric episelenonium ion **24** or the corresponding oxonium ion **25**, either of which should undergo smooth substitution to give the α-mannoside **26**. The transition states for



substitution of **24** and **25** will be chair-like.[37-40] Moreover, axial addition of ROH to oxonium ion **25** will benefit from the development of an anomeric effect in the transition state, with additional stereoelectronic control (Felkin) deriving from interactions of the the developing C-O bond with the anti $\sigma^*_{C\text{-}Se}$ orbital.

Glycosylation Reactions of 2-Thiophenyl-β-D-*gluco*-pyranosyl Acetates. Having determined that the 2-selenophenyl substituted donors were not suitable for our purposes, we turned our attention to the use of the analogous 2-thiophenyl substituted glycosyl acetates **9a** and **9c**.[33] However, initial experiments, summarized below, indicated that these donors were not sufficiently reactive or stereoselective. For example, reactions with even simple alcohol acceptors like allyl alcohol and isopropanol required temperatures between 0 °C and room temperature, and even then the reaction of **9a** with excess isopropanol did not go to completion; α-gluco acetate **29** was recovered. In the case of the reaction of **9c** with allyl alcohol, a 3 : 1 mixture of the β- and α-glucosides **30** and **31** was obtained. Fortunately, no evidence of epimerization of the C(2)-SPh unit was observed.

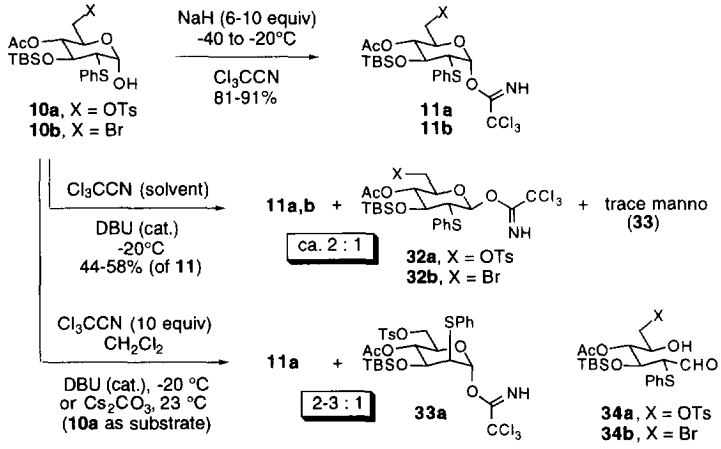


These unpromising results prompted us to continue searching for a suitable activating group strategy for use with 2-thiophenyl glycosyl donors.

Glycosylation Reactions of 2-Thiophenyl-α-D-*gluco*-pyranosyl Trichloroacetimidates. Glycosyl trichloroacetimidates are one of the most versatile and synthetically useful classes of glycosylating agents currently available.[43,44] They are highly reactive when activated by an appropriate protic or Lewis acid catalyst, and in many cases their glycosylation reactions are rapid even at -78°C. These considerations, together with the fact that Schmidt[29] had already demonstrated that 2-thiophenyl glycosyl trichloroacetimidates were

useful for the synthesis of 2-deoxy-β-glycosides, prompted us to turn to these derivatives for our work on the olivomycin C-D disaccharide.[15]

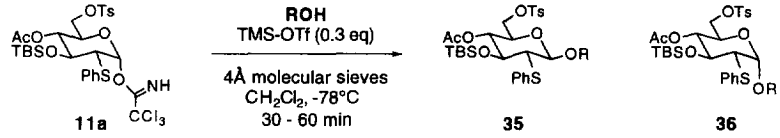
Synthesis of trichloroacetimidates **11a** and **11b** was more challenging than we anticipated. Use of Schmidt's standard conditions with pyranose **10a**[33] (e.g., excess NaH, CCl_3CN, CH_2Cl_2) resulted in an intractable mixture of products. When milder bases such as DBU[45] (catalytic) or Cs_2CO_3[46] were used in experiments with **10a** and Cl_3CCN (10 equiv.), cleaner mixtures of products was obtained. However, the product contained substantial amounts (25-30%) of the α-manno imidate **33a** resulting from base catalyzed epimerization of C(2) of **10a** (presumably by way of the hydroxy aldehyde tautomer **34a**). The epimerization was suppressed to a large extent when the reaction with DBU was performed in trichloroacetonitrile as solvent, in which case only 5-8% of **33a,b** was observed. However, under these conditions the desired α-gluco imidates **11a** and **11b** were obtained as the major products of ca. 2 : 1 mixtures with the β-gluco isomers **32a** and **32b**, respectively. When the latter mixtures were purified by chromatography over silica gel, the β-gluco imidates **32a** and **32b** selectively hydrolyzed, thereby allowing the desired α-imidates **11a** and **11b** to be obtained in 44-58% yield (up to 25% of lactols **10a** and **10b** were recovered). Better still, competitive formation of **32** and **33** was almost completely suppressed when the reactions were performed with excess NaH (6 - 10 equiv.) in trichloroacetonitrile (as solvent) at -40 °C to -20 °C. Under these conditions, imidates **11a** and **11b** were obtained in 81-91% yield following chromatographic purification.

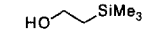
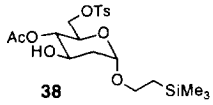
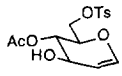
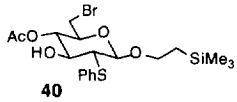
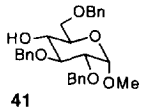


Results of glycosylation reactions of various alcohol acceptors with the 6-tosyl trichloroacetimidate derivative **11a** are summarized in Table 1. As expected,[29] this donor proved to be highly reactive and reactions with all acceptors were complete within a 1 h period at -78°C. Best results were obtained when the glycosidations were performed by using TMS-OTf (typically 0.3 equiv.) as the Lewis acidic activating agent, in the presence of activated 4 Å molecular sieves. Successful glycosylations have also been achieved in several cases by using $BF_3{\bullet}Et_2O$[16] and triflic acid (TfOH)[47] as the catalysts.

As the data summarized in Table 1 clearly indicate, the stereoselectivity of these reactions is highly dependent on the structure of the alcohol acceptor, with selectivity decreasing with increasing steric demand of the glycosyl acceptor. When trimethylsilylethanol (**37**), a representative primary alcohol, was used, the stereoselectivity was excellent (20 : 1) in favor of the desired β-glucoside **35a**. However, the glycosidations of all secondary alcohol acceptors examined gave much lower selectivity, ranging from 8 : 1 for the reaction with **38**, to 3-5 : 1 with **39** and **40**, to 1 : 1 in the glycosidation of the relatively unreactive methyl 2,3,6-tri-O-benzyl-α-D-glucopyranoside (**41**).[48] In all cases, the minor products were α-glucosides; products with axial C(2)-SPh

Table 1. Glycosylation Reactions of 4-O-Acetyl-3-O-(*tert*-butyldimethylsilyl)-2-deoxy-2-thiophenyl-6-O-*p*-toluenesulfonyl-1-trichloroacetimido-α-D-glucopyranose (11a)



Entry	ROH	Equiv. ROH	Yield[a]	Ratio 35 : 36 (β/α Selectivity)
1	 **37**	2.0	80%	20 : 1
2	 **38**	1.2	95%	8 : 1
3	 **39**	1.5	91%	4-5 : 1
4	 **40**	1.2	89%	3 : 1
5	 **41**	2.0	75%	1 : 1

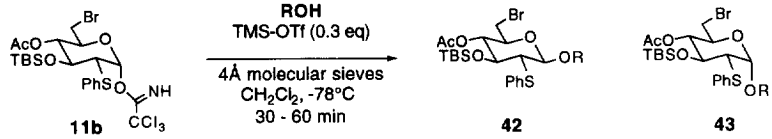
(a) Yield of glycosides **35** and **36** isolated by chromatography.
(b) Selectivity determined by ^{1}H NMR analysis of the crude reaction mixture.

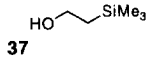
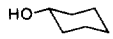
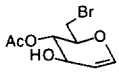
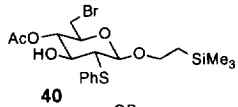
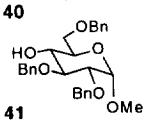
groups (e.g., *manno* configuration) were not observed in any cases. This indicates that the thiophenyl donors are configurationally stable at C(2), unlike the C(2)-selenophenyl derivatives discussed earlier.[49]

Much better stereochemical control was achieved in glycosidation reactions with the 6-bromo trichloroacetimidate derivative **11b** (Table 2). Selectivity was 20-50 : 1 for reactions of **11b** with simple primary and secondary alcohols (entries 1-4), while the reactions with glycal **44** and the 3-hydroxy glucopyranose derivative **40** resulted in 9-10 : 1 selectivity favoring the desired β-glycoside **42** (compare entries 4 and 5 of Table 2, with entries 3 and 4 of Table 1). Even the reaction of **11b** with the relatively unreactive 4-hydroxy glucopyranose derivative **41** provided a 3 : 1 mixture of **42f** and **43f**, which is considerably improved relative to the 1 : 1 mixture obtained in the reaction of **41** with **11a** (compare entry 6, Table 2, with entry 5, Table 1).

Two of the most striking features about the data summarized in Tables 1 and 2 are that mixtures of β- and α-glucosides were obtained in nearly all cases, and that the stereoselectivity clearly depends on the steric requirements of the alcohol acceptor: the best selectivity is consistently obtained with the least hindered alcohols. At the outset, we expected that substitution of the activated trichloroacetimidate donors **45a,b**, either by way of a direct S_N2 pathway or via the substitution of a tightly solvated trichloroacetamide-oxonium ion pair, would provide the targeted β-glucoside products **35** (X = OTs) or **42** (X = Br) with high selectivity.[29,43,44]

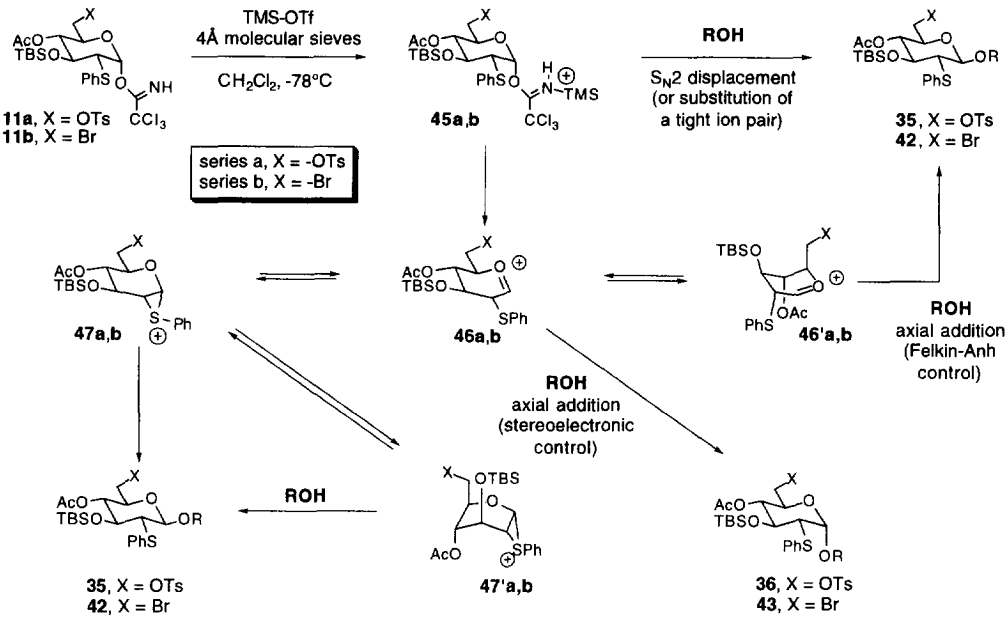
Table 2. Glycosylation Reactions of 4-O-Acetyl-6-bromo-3-O-(*tert*-butyldimethylsilyl)-2,6-dideoxy-2-thiophenyl-1-trichloroacetimido-α-D-glucopyranose (11b)



Entry	ROH	Equiv. ROH	Yield[a]	Ratio 42 : 43 (β/α Selectivity)[b]
1	 **37**	2.0	99%	50 : 1
2		4.0	96%	22 : 1
3		2.0	96%	50 : 1
4	 **44**	1.2	85%	9 : 1
5	 **40**	1.2	93%	10 : 1
6	 **41**	2.0	75%	3 : 1

(a) Yield of glycosides **42** and **43** isolated by chromatography.
(b) Selectivity determined by ^{1}H NMR analysis of the crude reaction mixture.

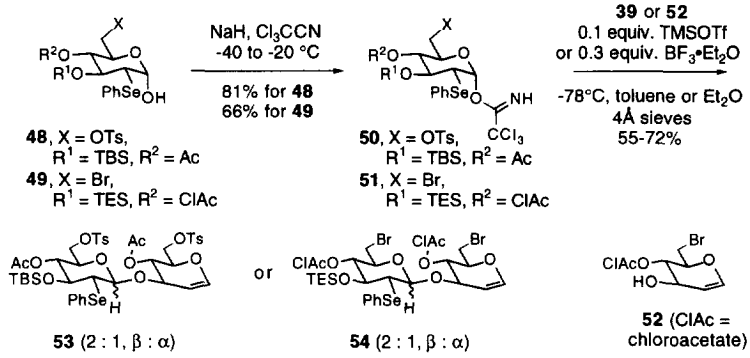
Further, it was expected that if the trichloroacetimidate leaving group were to disassociate completely prior to the substitution event, the resulting oxonium ion **46a,b** would be stabilized by formation of episulfonium ion **47a,b**, which the literature implied should serve as an efficient precursor to the desired β-glucosides.[26,28,50] Clearly, however, the α-gluco products **36** and **43**, which in several cases comprised 20-50% of the total product mixture, can not arise by way of such intermediates.[49] Moreover, computational studies by Liotta suggest that oxonium ions (e.g., **46a,b**) and not episulfonium ions actually may be the reactive intermediates in glycosylations of 2-thioalkyl substituted pyranosides.[51] While we can not rule out the possibility that the β-glycoside products arise by way of episulfonium ions **47a,b**, we note that this pathway faces an intrinsic kinetic barrier since the direct diequatorial substitution of **47a,b** must proceed by way of a boat-like transition state, or via the boat-like conformation **47'**.[37-40] In either event, one would expect that the rate of this pathway should decrease as the steric demands of the nucleophile increase, thereby permitting formation of the α-glycosides **36** (X = OTs) and **43** (X = Br) via stereoelectronically controlled axial substitution of oxonium ion **46a,b** to become increasingly competitive. Given that **46a,b** must be invoked to explain the formation of the α-glycosides **36** and **43**, it is interesting to speculate that the β-glycosides could also be generated by substitution of an oxonium ion intermediate. In this case, the most likely candidate is the conformationally inverted oxonium ion **46'** which should undergo stereoelectronically favored axial addition of the alcohol acceptors.



This pathway should benefit from the development of an anomeric effect in the transition state. In addition, Felkin-Anh type stabilization[42] of the developing C-O bond by overlap with the σ* orbital of the adjacent C-S bond should also play a favorable role in this transition state. As in the substitutions of the conformationally inverted episulfonium ion **47'**, one would expect that the rate of substitution of **46'** would diminish with increased steric demands of the alcohol acceptor. Finally, the diminished selectivity of the reactions of imidate **11a** compared to **11b** can be rationalized in terms of the equilibrating pair of oxonium ions **46** and **46'**: the greater inductive effect of the tosylate compared to a bromine substituent will destabilize **46a** to a larger extent than **46b**, and hence **46a** should be less stereodifferentiating in its reactions with nucleophiles.

We did not include trichloroacetimidate **11c** in the detailed investigations reported here, since the results of a coworker indicated that this reagent is very acid sensitive and is quite difficult to prepare and handle.[52] Moreover, **11c** is significantly more reactive than either **11a** or **11b**, and in side-by-side comparisons **11c** gave lower yields of glycosidation products.[16,52]

Glycosylation Reactions 2-Selenophenyl-α-D-*gluco*-pyranosyl Trichloroacetimidates. Given the success summarized above for the glycosylation reactions of the 2-thiophenyl substituted trichloroacetimidates **11a** and **11b**, and given that the 2-selenophenyl glycosyl acetate donors **8b** and **8c** were much more reactive than the analogous 2-thiophenyl glycosyl acetates **9a** and **9c**, we became interested in the possibility that 2-selenophenyl trichloroacetates **50** and **51** might be excellent glycosidation reagents. In the event, trichloroacetimidates **50** and **51** were prepared in 66-81% yield from lactols **48** and **49**, which in turn were synthesized by addition of PhSeCl to the corresponding glycals followed by hydrolysis of the intermediate 2-selenophenyl glycosyl chlorides with Na_2CO_3 in aqueous THF.[12,33] Imidates **50** and **51** proved to be highly reactive glycosylating agents, giving essentially complete reaction with glycal acceptors **39** or **52** within 5-10 minutes at -78°C using TMS-OTf as the catalyst. Although disaccharides with α-manno configuration in the unit deriving from **50** and **51** were not detected, indicating that the equilibration pathway noted for the reactions of the 2-selenophenyl glycosyl donors had been suppressed, 2 : 1 mixtures of the β- and α-gluco disaccharides



53 and **54** were observed in all cases. Similar results were also obtained when $BF_3•Et_2O$ was used as the Lewis acid activator. Accordingly, we concluded that **50** and **51** are not superior to imidates **11a** and **11b** as glycosylating agents (c.f., Tables 1 and 2).

Summary. We have demonstrated that the 2-thiophenyl-6-bromo substituted glycosyl trichloroacetimidate **11b** is the most efficient and selective donor for use in the synthesis of 2-deoxy-β-glycosides of the series of glycosyl donors examined. Unlike the 2-selenophenyl substituted donors **8** which proved to be configurationally unstable under standard TMS-OTf promoted glycosylation conditions, the 2-thiophenyl substituted donors **9** and **11** appeared to be completely configurationally stable (at C(2)). The main problem with imidates **11** is that the stereoselectivity of their reactions with alcohols is substrate dependent, with best selectivity for the desired β-glycosides **35** and **42** being obtained with the least sterically hindered alcohols. The fact that the α-glycosides **36** and **43** comprise up to 20-50% of the product in glycosidation reactions of hindered secondary alcohols supports the thesis that the reaction stereoselectivity is not governed by the intermediacy of episulfonium ions (**47**), but rather that substitution reactions of oxonium ion **46** and its conformationally inverted isomer **46'** play a dominant role. While this methodology has proven useful for the synthesis of functionalized precursors of the olivomycin C-D-E trisaccharide, both in solution[15,16] and solid phase reactions,[17] we continue to search for improved glycosidation protocols useful for the highly stereocontrolled synthesis of 2-deoxy-β-glycosides. Our continuing efforts along these lines will be reported in due course.

Experimental Section[53]

2-(Trimethylsilyl)ethyl 6-Bromo-3-O-(*tert*-butyldimethylsilyl)-2,6-dideoxy-2-phenylseleno-β-D-glucopyranoside (12a). To a stirred, 0 °C mixture of **8b**[33] (133 mg, 0.247 mmol), 2-(trimethylsilyl)ethanol (32 mg, 0.27 mmol) and powdered 4 Å molecular sieves (120 mg) in THF (2.5 mL) was added TMSOTf (52 μL, 1 equiv.). The mixture was allowed to warm to ambient temperature over 1.5 h. The mixture was treated with saturated $NaHCO_3$ solution, diluted with EtOAc, and filtered through Celite. The filtrate was washed with saturated $NaHCO_3$ solution, dried over Na_2SO_4, and concentrated. Purification of the crude residue by chromatography on silica gel (eluting with EtOAc-hexanes, 1: 19) gave 77 mg (52%) of **12a**: $[\alpha]_D^{28}$ +35.5° (c 2.3, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.62-7.60 (m, 2 H), 7.29-7.20 (m, 3 H), 4.38 (d, J = 8.8 Hz, 1 H, H-1), 3.91-3.84 (m, 1 H), 3.77-3.72 (m, 1 H), 3.59-3.34 (overlapping signals, 3 H), 3.06 (dd, J = 10.4, 8.8 Hz, 1 H, H-2), 2.20 (broad s, 1 H, OH), 0.94 (s, 9 H), 0.27 (s, 3 H), 0.18 (s, 3 H), 0.02 (s, 9 H); IR ($CHCl_3$) 3614, 3059, 3002, 1471 cm^{-1}; HRMS calcd for $C_{19}H_{32}O_4Si_2SeBr$ (M-$C_4H_9^+$) m/e 539.0213; found 539.0231.

Cyclohexyl 6-Bromo-3-O-(*tert*-butyldimethylsilyl)-2,6-dideoxy-2-phenylseleno-β-D-gluco-

pyranoside (12b). β-Glycoside **12b** (43 mg) was prepared in 54% yield from **8b**[33] (75 mg, 0.15 mmol) and cyclohexanol (15 mg, 0.15 mmol) in the presence of TMSOTf (15 μL) and 4Å molecular sieves (30 mg) using the procedure described for the synthesis of **12a**: $[\alpha]_D^{28}$ +45.4° (c 2.2, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.61-7.52 (m, 2 H), 7.20-7.14 (m, 3 H), 4.59 (d, *J* = 9.1 Hz, H-1), 3.76 (dd, *J* = 11.2, 1.3 Hz, 1 H), 3.67-3.58 (m, 1 H), 3.55-3.50 (m, 2 H), 3.42 (m, 1 H), 3.13 (dd, *J* = 10.5, 9.1 Hz, H-2), 2.16-1.01 (overlapping signals for aliphatic ring Hs, 10 H), 0.93 (s, 9 H), 0.21 (s, 3 H), 0.15 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.0, 130.6, 128.6, 126.8, 102.4, 78.1, 75.1, 74.1, 52.9, 33.3, 32.8, 31.3, 26.2, 25.6, 25.5, 23.9, 23.8, 18.5, -3.5, -3.6; IR ($CDCl_3$) 3621, 3060, 2940, 2861 cm^{-1}; HRMS calcd for $C_{20}H_{30}O_4SiSeBr$ ($M-C_4H_9^+$) m/e 521.0286, found 521.0271.

2-(Trimethylsilyl)ethyl 4-O-(4-O-Acetyl-3-O-(*tert*-butyldimethylsilyl)-6-bromo-2,6-dideoxy-2-selenophenyl-α-D-mannopyranosyl)-6-bromo-2,6-dideoxy-2-selenophenyl-α-D-glucopyranose (20). To a stirred, -20 °C mixture of **8b**[33] (52 mg, 0.097 mmol), **19**[54] (42 mg, 0.081 mmol) and powdered 4 Å molecular sieves (32 mg) in THF (1 mL) was added TMSOTf (16 μL, 1 equiv). The mixture was stirred for 2 h at -20°C, then treated with saturated $NaHCO_3$ solution, diluted with EtOAc, and filtered through Celite. The filtrate was washed with saturated $NaHCO_3$ solution, dried over Na_2SO_4, and concentrated in vacuo. ^1H NMR analysis showed disaccharide **20** to be the major component (≥5 : 1) of the crude product mixture. Chromatography of the crude residue on silica gel (eluting with EtOAc-hexanes, 1: 19 then 1 : 9) gave 42 mg (52%) of **20** as a colorless wax: $[\alpha]_D^{28}$ +31.3° (c 2.2, $CHCl_3$); ^1H NMR (400 MHz, C_6D_6) δ 7.79-7.76 (m, 2 H), 7.71-7.69 (m, 2 H), 7.07-6.94 (m, 6 H), 5.57 (d, *J* = 1.2 Hz, H-1'), 4.97 (m, H-4), 4.80 (dt, *J* = 9.2, 2.5 Hz, H-5'), 4.41 (dd, *J* = 8.8, 4.0 Hz, H-3'), 4.24 (d, *J* = 8.4 Hz, H-1), 4.12 (dt, *J* = 9.2, 6.4 Hz, 1 H), 3.94 (dt, *J* = 9.2, 6.4 Hz, 1 H), 3.86 (dd, *J* = 4.4, 1.6 Hz, H-2'), 3.79 (m, 2 H), 3.69 (dd, *J* = 11.2, 6.0 Hz, 1 H), 3.12 (dt, *J* = 10.4, 8.8 Hz, H 2), 3.10-3.05 (m, 3 H), 1.70 (d, *J* = 3.6 Hz, -OH), 1.55 (s, 3 H), 1.00-0.85 (m, 2 H), 0.04 (s, 3 H), 0.02 (s, 3 H), 0.03 (s, 9 H); IR ($CHCl_3$) 3680, 3025, 3000, 1750 cm^{-1}.

4-O-Acetyl-3-O-(*tert*-butyldimethylsilyl)-2-deoxy-2-thiophenyl-6-O-*p*-toluenesulfonyl-1-trichloroacetimido-α-D-glucopyranose (11a). To a vigorously stirred solution of pyranose **10a**[12] (500 mg, 0.91 mmol) in freshly distilled trichloroacetonitrile (10 mL) was added NaH (150 mg, 7.7 equiv) portionwise. The mixture was allowed to warm to -20 °C over a 1 h period. The mixture was then stored in a -20°C freezer overnight. Saturated aqueous $NaHCO_3$ was then added to the cold mixture, and the aqueous phase was separated and extracted with CH_2Cl_2. The organic phase was washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. Chromatographic purification of the crude product (silica gel, 7 : 1 EtOAc-hexanes with 1% Et_3N) provided 554 mg (91%) of the α-D-imidate **11a**: R_f 0.36 (2 : 8 EtOAc-hexanes); $[\alpha]_D^{20}$ +44.9° (c 2.7, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.67 (s, 1 H, NH), 7.74 (d, *J* = 8.4 Hz, 2 H), 7.44-7.41 (m, 2 H), 7.32-7.20 (m, 5 H), 6.31 (d, *J* = 3.5 Hz, 1 H), 5.01 (t, *J* = 9.0 Hz, 1 H), 4.20-3.95 (m, 4 H), 3.47 (dd, *J* = 10.1, 3.5 Hz, 1 H), 2.42 (s, 3 H), 2.10 (s, 3 H), 0.87 (s, 9 H), 0.16 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 160.4, 144.9, 134.8, 132.5, 131.3, 129.7, 129.1, 128.1, 127.2, 95.8, 91.0, 72.3, 70.7, 70.6, 68.0, 55.7, 25.9, 21.6, 21.3, 18.1, -3.6, -4.2; IR ($CDCl_3$) 3358, 3079, 2978, 2903, 2872, 1770, 1750, 1663, 1605 cm^{-1}; HRMS calcd for $C_{25}H_{29}O_8S_2SiCl_3N$ (M^+-t-Bu), 668.0172, found, 668.0156.

Characteristic ^1H NMR data for the β-gluco imidate **32a**: δ 8.53 (s, NH), 6.38 (d, *J* = 8.6 Hz, H-1).

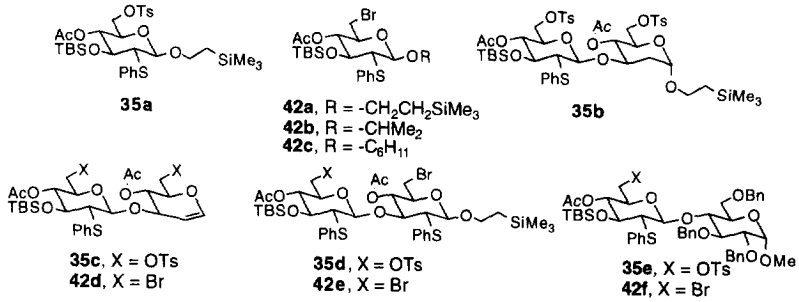
Characteristic ^1H NMR data for the α-manno imidate **33a**: δ 8.52 (s, NH), 6.22 (d, *J* = 1.9 Hz, H-1), 4.40 (dd, *J* = 9.0, 3.3 Hz, H-3), 3.74 (dd, *J* = 3.3, 1.9 Hz, H-2).

4-O-Acetyl-6-bromo-3-O-(*tert*-butyldimethyl)silyl-2,6-dideoxy-2-thiophenyl-1-trichloroacetimido-α-D-glucopyranose (11b): A solution of the lactol **10b**[33] (3.20g, 6.51 mmol) in freshly distilled trichloroacetonitrile (95 mL) was cooled to -40°C and treated with dry NaH powder (1.22 g, 50.8 mmol), portionwise. The mixture was left to warm to -20°C over 1h afterwhich the reaction was sealed with parafilm and placed in the freezer at -20°C for 16 - 23h. The resulting yellow solution was placed in a -20°C bath and ice added in small portions. The mixture was stirred at this temperature for 30 min, then was poured into staurated aqueous $NaHCO_3$ and extracted with CH_2Cl_2 (3 x). The combined organic phases were washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. The crude residue was chromatographed on silica gel using 15% EtOAc/hexanes containing 2% triethylamine to give the α-imidate **10b** (4.12 g, 99% yield):

R_f 0.51 (25% EtOAc-hexanes); $[\alpha]_D^{20}$ +12.5 (c 3.6, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.72 (s, 1 H, NH), 7.48-7.44 (m, 1 H), 7.31-7.21 (m, 4 H), 6.41 (d, J = 3.2 Hz, 1 H), 5.02 (dd, J = 10.1, 9.8 Hz, 1 H), 4.16 (dd, J = 10.7, 8.8 Hz, 1 H), 4.10 (br ddd, J = 9.9, 6.9, 2.8 Hz, 1 H), 3.41 (dd, J = 10.7, 3.1 Hz, 1 H), 3.38 (dd, J = 11.3, 2.8 Hz, 1 H), 3.30 (dd, J = 11.3, 6.6 Hz, 1 H), 2.16 (s, 3 H), 0.88 (s, 9 H), 0.18 (s, 3 H), 0.12 (s, 3 H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 169.6, 160.4, 134.9, 133.0, 131.5, 129.2, 129.1, 128.3, 127.3, 95.9, 74.7, 72.5, 70.7, 55.8, 31.1, 25.9, 25.8, 25.6, 21.4, 18.1, -3.5, -4.1; IR (film) 3370-3260, 2960, 2930, 2900, 2860, 1750, 1680 cm^{-1}; HRMS calcd for $C_{18}H_{22}NSiSBrCl_3O_5$ (M^+-t-Bu), 575.9237; found, 575.9281.

Characteristic ^1H NMR data for the α-manno imidate **33b**: δ 8.62 (s, NH), 6.35 (d, J = 1.6 Hz, H-1), 4.42 (dd, J = 9.0, 3.3 Hz, H-3).

General Procedure for Glycosidation Reactions of Imidates 11a and 11b. Activated 4Å molecular sieves (ca. 40 mg/mL of CH_2Cl_2) were added to a 23°C solution of the imidate (1 equiv) and the acceptor (1.2 - 2.0 equiv) in CH_2Cl_2 (freshly distilled from P_2O_5), and the resulting mixture stirred for 15 - 20 min. The reaction mixture was then cooled to -78 °C and TMSOTf (0.3 equiv) was then added in one portion. When the reactions were complete according to TLC analysis (typically within 30 min to 1 h), they were quenched with triethylamine (3 equiv.) and diluted successively with saturated aqueous $NaHCO_3$ and CH_2Cl_2. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 x). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give the crude product that was purified by flash column chromatography. In all cases the product glycoside α : β ratio was calculated by integration of the appropriate, well resolved signals of the crude anomeric mixtures.



2-(Trimethylsilyl)ethyl 4-O-Acetyl-3-O-(*tert*-butyldimethylsilyl)-2-deoxy-2-thiophenyl-6-O-*p*-toluenesulfonyl-α,β-D-glucopyranose (35a) was obtained in 80% yield (137 mg) from **11a** (178 mg, 0.25 mmol) and 2-(trimethylsilyl)ethanol (57 mg, 0.49 mmol) as a 20 : 1 (β : α) mixture of **35a** and **36a**: R_f 0.29 (20% EtOAc-hexanes); $[\alpha]_D^{20}$ -8.3° (c 3.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 8.1 Hz, 2 H), 7.47 - 7.43 (m, 2 H), 7.34 (d, J = 8.1 Hz, 2 H), 7.27 - 7.17 (m, 3 H), 4.74 (dd, J = 9.7 Hz, 1 H, H-4), 4.33 (d, J = 8.6 Hz, 1 H, H-1), 4.01 (d, J = 5.1, 2 H), 3.78 - 3.74 (m, 1 H), 3.72 (dd, J = 9.9, 8.6 Hz, 1 H), 3.63 - 3.57 (m, 1 H), 3.49 - 3.40 (m, 1 H), 3.03 (dd, J = 9.9, 8.6 Hz, 1 H, H-2), 2.44 (s, 3 H), 2.09 (s, 3 H), 0.84 (s, 9 H), 0.83 - 0.72 (m, 2 H), 0.18 (s, 3 H), 0.06 (s, 3 H), -0.09 (s, 9 H); IR ($CHCl_3$) 3059, 2955, 2930, 2860, 1745, 1597 cm^{-1}; HRMS calcd for $C_{28}H_{41}O_8Si_2S_2$ (M^+-t-Bu), m/e 625.1782; found 625.1763.

2-(Trimethylsilyl)ethyl 4-O-Acetyl-3-O-(4-O-acetyl-2-deoxy-3-O-(*tert*-butyldimethylsilyl)-2-thiophenyl-6-O-*p*-toluenesulfonyl-α,β-D-glucopyranosyl)-2-deoxy-6-O-*p*-toluenesulfonyl-α-D-*arabino*-hexopyranose (35b) was prepared in 95% yield as an inseparable 8 : 1 (β : α) mixture of **35b** and **36b** from imidate **11a** (314 mg, 0.43 mmol) and acceptor **38**[15] (247 mg, 0.53 mmol): R_f = 0.45 (30% EtOAc in hexanes); ^1H NMR data for β-isomer **35b**, (400 MHz, $CDCl_3$) δ 7.78 (d, J = 8.3 Hz, 2 H), 7.76 (d, J = 8.4 Hz, 2 H), 7.37 (d, J = 8.3 Hz, 1 H), 7.35 - 7.11 (m, 7 H), 4.78 (dd, J = 9.7, 8.3 Hz, 1 H, H-4′), 4.74 (br s, 1 H), 4.57 (dd, J = 9.7, 9.1 Hz, 1 H, H-4), 4.35 (d, J = 8.9 Hz, 1 H, H-1′), 4.07 - 3.95 (m, 5 H), 3.91 - 3.35 (m, 1 H), 3.03 (dd, J = 10.1, 8.9 Hz, 1 H, H-2′), 2.46 (s, 3 H), 2.43 (s, 3 H), 2.12 - 2.03 (s, 3 H), 1.92 (s, 3 H), 1.43 - 1.33 (m, 1 H), 0.98 - 0.83 (m, 2 H), 0.78 (s, 9 H), 0.13 (s, 3 H), 0.07 (s, 3 H), 0.02 (s, 9 H); partial ^1H NMR data for the α-anomer **36b**, δ 4.91 (d, J = 3.5 Hz, 1 H), 3.88 (dd, J = 9.7, 9.1 Hz, 1 H, H-4), 3.10 (dd, J = 10.7, 3.1 Hz, 1 H, H-2′); IR

(obtained on the mixture; $CDCl_3$) 3050, 2950, 2858, 1742, 1596 cm^{-1}. *Anal.* Calc'd for $C_{41}H_{54}O_{15}S_3Si$: C, 54.96; H, 6.67. Found C, 55.06; H, 6.69.

4-O-Acetyl-3-O-(4-O-acetyl-3-O-(*tert*-butyldimethylsilyl)-2-deoxy-2-thiophenyl-6-O-*p*-toluenesulfonyl-α,β-D-glucopyranosyl)-2-deoxy-6-O-*p*-toluenesulfonyl-D-*arabino*-hex-1-enitol (35c) was prepared in 91% yield (169 mg) as an inseparable 5 : 1 (β : α) mixture of **35c** and **36c** from imidate **11a** (148 mg, 0.20 mmol) and acceptor **39**[15] (105 mg, 0.3 mmol). ^1H NMR resonances (400 MHz, $CDCl_3$) assigned to the β-anomer **35c**: δ 7.76 (d, *J* = 8.1 Hz, 2 H), 7.72 (d, *J* = 8.3 Hz, 2 H), 7.36 - 7.29 (m, 6 H), 7.22 (t, *J* = 7.3 Hz, 2 H), 7.20 - 7.12 (m, 1 H), 6.13 (dd, *J* = 6.2, 0.8 Hz, 1 H, H-1), 5.02 (m, 1 H, H-4), 4.92 (dd, *J* = 9.7, 8.3 Hz, 1 H, H-3), 3.62 (m, 1 H), 3.00 (dd, *J* = 10.2, 8.1 Hz, 1 H, H-2′), 2.44 (s, 3 H), 2.43 (s, 3 H), 2.08 (s, 3 H), 2.01 (s, 3 H), 0.82 (s, 9 H), 0.16 (s, 3 H), 0.05 (s, 3 H); ^1H NMR resonances assigned to α-anomer **36c**, δ 7.83 (d, *J* = 8.1 Hz, 2 H), 6.27 (dd, *J* = 6.5, 1.1 Hz, 1 H, H-1), 5.08 m, 1 H, H-4), 4.89 (m, H 2), 4.80 (dd, *J* = 9.9, 8.9 Hz, 1 H), 3.14 (dd, *J* = 10.5, 3.2 Hz, H-2′); IR (obtained on mixture, $CDCl_3$) 3066-3000, 2959, 2921, 2851, 1732, 1645, 1593 cm^{-1}. *Anal.* Calcd for $C_{42}H_{54}O_{14}S_3Si$: C, 55.61; H, 5.98. Found: C, 55.79, H, 5.98.

2-(Trimethylsilyl)ethyl 4-O-Acetyl-3-O-(4-O-acetyl-3-O-(*tert*-butyldimethylsilyl)-2-deoxy-2-thiophenyl-6-O-*p*-toluenesulfonyl-α,β-D-glucopyranosyl)-6-bromo-2,6-dideoxy-2-thiophenyl-β-D-glucopyranose (35d) was prepared in 89% yield (42 mg) as an inseparable 3 : 1 mixture of **35d** and **36d** from the coupling of imidate **11a** (33 mg, 0.045 mmol) and acceptor **40**[55] (26 mg, 0.054 mmol): R_f 0.48 (25% EtOAc-hexanes). ^1H NMR (500 MHz, $CDCl_3$) data for the β-anomer **35d** (obtained on the mixture): δ 7.84 - 7.78 (d, *J* = 8.4 Hz, 2 H), 7.48 (m, 2 H), 7.40 - 7.22 (m, 7 H), 7.22 - 7.17 (d, *J* = 4.2 Hz, 2 H), 7.14 - 7.08 (t, *J* = 7.4 Hz, 1 H), 5.22 (d, *J* = 8.8 Hz, 1 H, H-1′), 4.82 - 4.76 (dd, *J* = 9.9, 8.4 Hz, 1 H), 4.76 - 4.71 (dd, *J* = 9.9, 8.5 Hz, 1 H), 4.45 - 4.43 (d, *J* = 8.5 Hz, 1 H, H-1), 3.92 - 3.76 (m, 5 H), 3.55 - 3.45 (m, 3 H), 3.40 - 3.34 (dd, *J* = 11.1, 2.6 Hz, 1 H), 3.30 - 3.24 (dd, *J* = 11.1, 8.3 Hz, 1 H), 3.16 - 3.10 (dd, *J* = 10.0, 9.0 Hz, 1 H), 3.10 - 3.04 (dd, *J* = 10.0, 8.6 Hz, 1 H), 3.04 - 2.99 (m, 1 H), 2.44 - 2.43 (s, 3 H), 2.07 - 2.05 (s, 3 H), 2.05 - 2.02 (s, 3 H), 0.97 (m, 2 H), 0.82 - 0.76 (s, 9 H), 0.14 - 0.13 (s, 3 H), 0.04 - 0.02 (s, 3 H), 0.01 - -0.04 (s, 9 H); Partial ^1H NMR data for the α-anomer **36d** (obtained on the mixture): δ 7.78 (d, *J* = 8.1 Hz, 2 H), 7.52 (d, *J* = 6.7 Hz, 2 H), 7.36 - 7.26 (m, 8 H), 7.26 - 7.20(t, *J* = 7.7 Hz, 1 H), 5.41 (d, *J* = 3.2 Hz, 1 H, H-1′), 5.05 - 4.95 (dd overlapping for H-4 and H-4′, *J* = 10.8, 9.0 Hz and *J* = 10.6, 9.5 Hz, 2 H), 4.89 - 8.83 (m, 1 H), 4.33 (d, *J* = 8.4 Hz, 1 H, H-1), 3.92 - 3.87 (dd, *J* = 10.0, 8.4 Hz, 1 H), 3.50 - 3.38 (m, 3 H), 3.28 - 3.22 (dd, *J* = 10.9, 3.5 Hz, 1 H), 3.13 -3.07, (dd, *J* = 10.0, 8.3 Hz, 1 H); ^{13}C NMR (400 MHz, $CDCl_3$; obtained on mixture) δ 170.0 169.9, 153.3, 145.2, 136.2, 133.5, 133.3, 132.9, 129.9, 129.0, 128.7, 128.5, 128.1, 128.0, 127.6, 127.5, 126.0, 125.7, 103.5, 103.0, 102.6, 101.9, 76.2, 73.2, 73.0, 72.8, 72.0, 71.6, 68.3, 67.6, 55.8, 55.7, 55.1, 53.1, 31.4, 25.8, 25.78, 21.3, 20.9, 18.0, -1.4, -1.5, -3.6, -4.1; IR ($CHCl_3$) 3005, 2955, 2932, 2859, 1746, 1599, 1584 cm^{-1}; FAB MS (NaOAc and 3-nitrobenzyl alcohol matrix) 1063 (M^+ + Na) for $C_{46}H_{65}{}^{79}BrO_{12}S_3Si_2$ and 1065 (M^+ + Na) for $C_{46}H_{65}{}^{81}BrO_{12}S_3Si_2$. *Anal.* Calcd for $C_{46}H_{65}BrO_{12}S_3Si_2$: C, 53.01; H, 6.29. Found: C, 53.23; H, 6.53.

Methyl 4-O-(4-O-Acetyl-3-O-(*tert*-butyldimethylsilyl)-2-deoxy-2-thiophenyl-6-O-*p*-toluenesulfonyl-α,β-D-glucopyranosyl)-2,3,6-tri-O-benzyl-α-D-glucopyranose (35e) was prepared in 75% yield as a 1 : 1 mixture (β : α) of **35e** and **36e** via the coupling of imidate **11a** (45 mg, 0.06 mmol) and acceptor **41**[48] (58 mg, 0.13 mmol). Data for **35e**: R_f 0.57 (25% EtOAc-hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 7.76 - 7.71 (m, 2 H), 7.46 - 7.33 (m, 5 H), 7.33 - 7.24 (m, 11 H), 7.24 - 7.10 (m, 6 H), 4.78 - 4.66 (m, 4 H), 4.62 - 4.56 (br t, *J* = 11.4 Hz, 2 H), 4.55 - 4.52 (d, *J* = 3.5 Hz, 1 H), 4.40 - 4.36 (d, *J* = 12.3 Hz, 1 H), 4.24 - 4.18 (d, *J* = 9.8 Hz, 1 H), 4.16 - 4.11 (dd, *J* = 10.7, 2.6 Hz, 1 H), 3.92 - 3.86 (m, 2 H), 3.85 - 3.80 (dd, *J* = 10.6, 5.3 Hz, 1 H), 3.62 - 3.25 (m, 5 H), 2.97 - 2.91 (dd, *J* = 10.2, 8.8 Hz, 1 H), 2.38 (s, 3 H), 2.12 (s, 3 H), 0.82 (s, 9 H), 0.16 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 170.3, 144.8, 139.3, 138.3, 137.8, 136.3, 129.9, 129.6, 128.7, 128.5, 128.3, 128.0, 127.99, 127.9, 127.88, 127.8, 127.1, 126.1, 102.1, 98.1, 80.2, 79.0, 75.3, 74.8, 73.8, 73.6, 73.5, 72.6, 70.9, 69.3, 69.0, 68.1, 57.1, 55.1, 25.8, 21.6, 21.4, 18.1, -3.5, -3.97; IR ($CHCl_3$) 3059, 2932, 2861, 1742, 1599, 1584 cm^{-1}; FAB MS (NaOAc and 3-nitrobenzyl alcohol matrix) 1051 (M^+ + Na) for $C_{55}H_{68}O_{13}S_2Si$. *Anal.* Calcd for $C_{55}H_{68}O_{13}S_2Si$: C, 64.18; H, 6.66. Found: C, 64.18; H, 6.81.

Partial ^{1}H NMR data for α-anomer **36e**: δ 5.75 (d, *J* = 3.5 Hz, 1 H), 5.05 (s, 1 H), 4.85 (dd, *J* = 9.8, 9.1 Hz, 1 H), 3.96 (dd, *J* = 10.4, 8.8, Hz, 1 H), 3.65 (dd, *J* = 10.1, 8.5 Hz, 1 H), 3.59 (dd, *J* = 9.4, 3.5 Hz, 1 H), 3.43 (s, 3 H), 3.16 (dd, *J* = 10.4, 3.5 Hz, 1 H).

2-(Trimethylsilyl)ethyl 4-O-Acetyl-6-bromo-3-O-(*tert*-butyldimethylsilyl)-2,6-dideoxy-2-thiophenyl-α,β-D-glucopyranose (**42a**) was prepared in 99% yield from the reaction of imidate **11b** (136 mg, 0.21 mmol) and 2-(trimethylsilyl)ethanol (50 mg, 4.3 mmol) as a 50 : 1 (β : α) mixture of **42a** and **43a**. Data for **42a**: R_f 0.51 (10% EtOAc-hexanes); ^{1}H NMR ($CDCl_3$) δ 7.71 - 7.46 (m, 2 H), 7.29 - 7.18 (m, 3 H), 4.79 - 4.45 (dd, *J* = 9.3, 8.3 Hz, 1 H), 4.42 - 4.37 (d, *J* = 8.4 Hz, 1 H), 3.94 - 3.86 (m, 1 H), 3.78 - 3.72 (dd, *J* = 9.3, 8.1 Hz, 1 H), 3.58 - 3.50 (m, 2 H), 3.39 - 3.36 (m, 2 H), 3.14 - 3.08 (dd, *J* = 9.9, 9.8 Hz, 1 H), 2.14 (s, 3 H), 0.86 (s, 9 H), 0.86 - 0.78 (m, 2 H), 0.20 (s, 3 H), 0.09 (s, 3 H), -0.03 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 170.1, 136.2, 131.4, 128.6, 126.7, 103.2, 75.3, 74.2, 73.3, 67.6, 56.8, 31.9, 25.9, 21.6, 18.2, 17.9, -1.5, -3.4, -4.0; IR ($CHCl_3$) 3054, 2957, 2932, 2888, 2861, 1746, 1584 cm^{-1}; FAB HRMS (NaOAc and 3-nitrobenzyl alcohol matrix) 613.1461 (M^+ + Na) for $C_{25}H_{43}{}^{79}BrO_5SSi_2$ and 615.1455 (M^+ + Na) for $C_{25}H_{43}{}^{81}BrO_5SSi_2$. *Anal.* Calcd for $C_{25}H_{43}BrO_5SSi_2$: C, 50.74; H, 7.32; Found: C, 50.98; H, 7.48.

Isopropyl 4-O-Acetyl-6-bromo-3-O-(*tert*-butyldimethylsilyl)-2,6-dideoxy-2-thiophenyl-α,β-D-glucopyranose (**42b**) was prepared in 96% yield from bromo imidate **11b** (94 mg, 0.15 mmol) and freshly distilled isopropanol (35 mg, 0.60 mmol) as a 22 : 1 (β : α) mixture of glycosides **42b** and **43b**. Data for **42b**: R_f = 0.64 (20% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 - 7.43 (dd, *J* = 8.3, 1.2 Hz, 2 H), 7.27 - 7.21 (m, 2 H), 7.19 - 7.14 (m, 1 H), 4.83 - 4.77 (dd, *J* = 9.5, 8.4 Hz, 1 H, H-4), 4.51 - 4.46 (d, *J* = 8.8 Hz, 1 H, H-1), 3.98 - 3.88 (m, 1 H), 3.75 - 3.68 (dd, *J* = 10.0, 8.3 Hz, 1 H), 3.56 - 3.49 (m, 1 H), 3.37 - 3.33 (d, *J* = 6.3 Hz, 2 H), 3.19 - 3.13 (dd, *J* = 10.0, 8.6 Hz, 1 H, H-2), 2.13 (s, 3 H), 2.16 (d, *J* = 6.3 Hz, 3 H), 1.01 (d, *J* = 6.0 Hz, 3 H), 0.84 (s, 3 H), 0.19 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 170.1, 130.5, 128.5, 126.2, 102.6, 75.3, 74.0, 73.2, 72.9, 57.1, 31.8, 25.9, 25.8, 23.2, 21.6, 18.2, -3.5, -4.1; IR ($CHCl_3$) 3061, 3044, 3009, 2974, 2959, 2932, 2886, 2859, 1740, 1584 cm^{-1}; FAB HRMS (NaOAc and 3-nitrobenzyl alcohol matrix) 555.1198 (M^+ + Na) for $C_{23}H_{37}{}^{79}BrO_5SSi$ and 557.1185 (M^+ + Na) for $C_{23}H_{37}{}^{81}BrO_5SSi$. *Anal.* Calcd for $C_{23}H_{37}BrO_5SSi$: C, 51.77; H, 6.99. Found: C, 52.03; H, 7.12.

Cyclohexyl 4-O-Acetyl-6-bromo-3-O-(*tert*-butyldimethylsilyl)-2,6-dideoxy-2-thiophenyl-α,β-D-glucopyranose(42c) was prepared in 96% yield from bromo imidate **11b** (115 mg 0.18 mmol) and cyclohexanol (36 mg, 0.36 mmol) as a 50: 1 (β : α) mixture of glycosides **42c** and **43c**. Data for **42c**: R_f = 0.72 (20% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 - 7.43 (d, *J* = 8.4, 1.1 Hz, 2 H), 7.28 - 7.21 (m, 2 H), 7.18 - 7.13 (m, 1 H), 4.84 - 4.78 (dd, *J* = 9.5, 8.1 Hz, 1 H), 4.55 - 4.50 (d, *J* = 8.8 Hz, 1 H), 3.75 - 3.69 (dd, *J* = 9.5, 8.3 Hz, 1 H), 3.68 - 3.60 (m, 1 H), 3.56 - 3.49 (m, 1 H), 3.38 - 3.34 (m, 2 H), 3.22 - 3.16 (dd, *J* = 9.9, 8.8 Hz, 1 H), 2.13 (s, 3 H), 1.92 - 1.82 (m, 1 H), 1.70 - 1.54 (m, 3 H), 1.48 - 1.10 (m, 6 H), 0.83 (s, 9 H), 0.18 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 170.1, 136.2, 130.1, 128.5, 126.1, 102.4, 78.2, 75.4, 74.0, 73.2, 57.0, 33.2, 31.9, 31.3, 25.9, 25.6, 23.7, 23.6, 21.6, 18.2, -3.4, -4.0; IR ($CHCl_3$) 3040, 3009, 2936, 2859, 1742, 1584, 1522 cm^{-1}; FAB HRMS (NaOAc and 3-nitrobenzyl alcohol matrix) 595.1515 (M^+ + Na) for $C_{26}H_{41}{}^{79}BrO_5SSi$ and 597.1509 (M^+ + Na) for $C_{26}H_{41}{}^{81}BrO_5SSi$. *Anal.* Calcd for $C_{26}H_{41}BrO_5SSi$: C, 54.44; H, 7.20. Found: C, 54.47; H, 7.42.

4-O-Acetyl-3-O-(4-O-acetyl-6-bromo-3-O-(*tert*-butyldimethylsilyl)-2,6-dideoxy-2-thiophenyl-α,β-D-glucopyranosyl)-6-bromo-2,6-dideoxy-D-*arabino*-hex-1-enitol (**42d**) was prepared in 85% yield from the reaction of bromo imidate **11b** (2.17 g, 3.41 mmol) and glycal acceptor **44**[56] (1.02 g, 4.09 mmol) as a 9 : 1 mixture of disaccharides **42d** and **43d**. This mixture was separated by preparative HPLC [20% EtOAc-hexanes; t_R (**43d**) 12 min; t_R (**42d**) 13 min)] giving the β-anomer **42d** in 76% yield and the α-anomer **43d** in 9% yield. Data for **42d**: R_f = 0.59 (25% EtOAc in hexanes); $[\alpha]_D^{29}$ -8.6 (c 1.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43-7.38 (m, 2 H), 7.39-7.15 (m, 3 H), 6.41-6.37 (dd, *J* = 6.9, 0.8 Hz, 1 H), 5.27 - 5.23 (m, 1 H), 4.85 - 4.78 (dd, *J* = 9.7, 8.4 Hz, 1 H), 4.74 - 4.69 (m, 1 H), 4.66 - 4.62 (d, *J* = 8.8 Hz, 1 H), 4.36 - 4.30 (m, 1 H), 4.05 - 4.00 (m, 1 H), 3.75 - 3.68 (dd, *J* = 10.2, 8.2 Hz, 1 H), 3.61 - 3.54 (m, 1 H), 3.51 - 3.44 (dd, *J* = 11.6, 9.4 Hz, 1 H), 2.13 (s, 3 H), 2.06 (s, 3 H), 0.82 (s, 9 H), 0.18 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 170.0,

169.6, 144.2, 135.5, 130.2, 128.8, 126.5, 102.4, 97.6, 75.4, 75.1, 74.0, 73.1, 69.1, 56.8, 31.6, 29.6, 25.8, 21.5, 21.0, 18.2, -3.5, -4.1; IR ($CHCl_3$) 3041, 3030, 3009, 2958, 2931, 2887, 1743, 1651 cm^{-1}; FAB MS (NaOAc and 3-nitrobenzyl alcohol matrix) 745 (M^+ + Na) for $C_{28}H_{40}{}^{79}Br_2O_8SSi$ and 747 (M^+ + Na) for $C_{28}H_{40}{}^{81}Br_2O_8SSi$. *Anal.* Calcd for $C_{28}H_{44}Br_2O_8SSi$: C, 46.41; H, 5.56. Found: C, 45.85; H, 5.41.

Partial ^1H NMR data ($CDCl_3$, 500 MHz) for α-anomer **43d**: δ 6.49 - 6.45 (dd, *J* = 6.3, 1.3 Hz, 1 H, H-1), 5.30 (t, *J* = 5.0 Hz, 1 H, H-2), 5.18 (d, *J* = 3.1 Hz, 1 H, H-1′), 5.13 - 5.08 (ddd, *J* = 6.3, 3.8, 0.5 Hz, 1 H, H-4), 4.88 - 4.81 (dd, *J* = 9.9, 8.5 Hz, 1 H, H-4′), 4.04 - 3.97 (dd, *J* = 10.7, 8.8 Hz, 1 H, H-3′), 3.27 - 3.22 (dd, *J* = 10.7, 3.2 Hz, 1 H, H-2′).

2-(Trimethylsilyl)ethyl 4-O-Acetyl-3-O-(4-O-acetyl-6-bromo-3-O-(*tert*-butyldimethylsilyl)-2,6-dideoxy-2-thiophenyl-α,β-D-glucopyranosyl)-6-bromo-2,6-dideoxy-2-thiophenyl-β-D-glucopyranose (**42e**) was prepared in 93% yield from the reaction of bromo imidate **11b** (72 mg, 0.12 mmol) and acceptor **40**[55] (65 mg, 0.14 mmol) as a 10 : 1 (β : α) mixture of the disaccharides **42e** and **43e**. Data for **42e**: R_f = 0.59 (15% EtOAc-hexanes); $[\alpha]_D^{27}$ 44.8 (c 0.65, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.50 (dd, *J* = 6.9, 2.5 Hz, 2 H), 7.28 - 7.10 (m, 8 H), 5.24 (d, *J* = 8.8 Hz, 1 H), 4.77 - 4.70 (dd, *J* = 9.7, 8.3 Hz, 1 H), 4.66 - 4.58 (dd, *J* = 9.7, 8.6 Hz, 1 H), 4.22(d, *J* = 8.6 Hz, 1 H), 3.91 - 3.82 (m, 2 H), 3.76 - 3.70 (dd, *J* = 10.2, 8.1 Hz, 1 H), 3.61 - 3.47 (m, 3 H), 3.43 - 3.37 (m, 2 H), 3.32 - 3.37(m, 2 H), 3.16 - 3.10 (dd, *J* = 8.7, 7.8 Hz, 1 H), 2.94 - 2.87 (dd, *J* = 10.3, 8.6 Hz, 1 H), 2.13 (s, 3 H), 2.12 (s, 3 H), 0.94 - 0.84 (m, 2 H), 0.80 (s, 9 H), 0.14 (s, 3 H), 0.05 (s, 3 H), -0.03 (s, 9 H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 170.1, 169.6, 136.3, 133.1, 129.2, 129.1, 128.7, 128.6, 127.5, 125.8, 103.5, 102.6, 75.6, 74.1, 73.4, 73.2, 72.2, 67.5, 56.0, 55.0, 31.7, 31.5, 25.9, 25.6, 21.5, 21.1, 18.2, 18.1, -1.5, -3.5, -4.1; IR ($CHCl_3$) 3046, 2968, 2428, 1747 cm^{-1}; FAB MS (NaOAc and 3-nitrobenzyl alcohol matrix) 971 (M^+ + Na) for $C_{39}H_{58}{}^{79}Br_2O_9SSi_2$ and 973 (M^+ + Na) for $C_{39}H_{58}{}^{81}Br_2O_9S_2Si$. *Anal.* Calcd for $C_{39}H_{58}Br_2O_9S_2Si_2$: C, 49.26; H, 6.15. Found: C, 49.34; H, 6.22.

Partial ^1H NMR data (500 MHz, $CDCl_3$) for α-anomer **43e**: δ 5.33 (d, *J* = 3.2 Hz, 1 H, H-1′), 4.90 (t, *J* = 8.8 Hz, 1 H), 4.88 (t, 9.1 Hz, 1 H), 4.39 (d, *J* = 8.8 Hz, 1 H, H-1), 5.19 (dd, *J* = 8.9, 9.7 Hz, 1 H), 4.05 (dd, *J* = 10.8, 8.8 Hz, 1 H), 3.94 (dd, *J* = 10.7, 3.6 Hz, 1 H, H-2′), 3.19 (dd, *J* = 10.0, 8.9 Hz, 1 H, H-1).

Methyl 4-O-(4-O-Acetyl-6-bromo-3-O-(*tert*-butyldimethylsilyl)-2,6-dideoxy-2-thiophenyl-α,β-D-glucopyranosyl)-2,3,6-tri-O-benzyl-α-D-glucopyranose (**42f**) was prepared in 87% yield as a 3 : 1 mixture of **42f** and **43f** from bromo imidate **11b** (96 mg, 0.16 mmol) and acceptor **41**[48] (144 mg, 0.31 mmol). Data for **42f**: R_f = 0.37 (25% EtOAc in hexanes); ^1H NMR (500 MMz, $CDCl_3$) δ 7.46 - 7.39 (m, 6 H), 7.37 - 7.24 (m, 11 H), 7.23 - 7.12 (m, 4 H), 4.88 - 4.81 (d, *J* = 11.3 Hz, 1 H), 4.82 - 4.66 (m, 3 H), 4.62 - 4.56 (d, *J* = 12.0 Hz, 1 H), 4.56 - 4.52 (d, *J* = 3.9 Hz, 1 H), 4.45 - 4.40 (d, *J* = 12.0 Hz, 1 H), 4.30 - 4.25 (d, *J* = 8.8 Hz, 1 H), 4.20 - 4.15 (dd, *J* = 10.7, 2.6 Hz, 1 H), 4.05 - 3.99 (dd, *J* = 9.9, 9.2 Hz, 1 H), 3.44 - 3.38 (dd, *J* = 10.0, 8.3 Hz, 1 H), 3.36 - 3.31 (br overlapping m, 4 H), 3.28 - 3.21 (m, 2 H), 3.14 - 3.08 (m, 1 H), 3.06 - 3.00 (dd, *J* = 10.0, 9.2 Hz, 1 H), 2.15 - 2.12 (s, 3 H), 0.86 - 0.82 (s, 9 H), 0.19 - 0.16 (s, 3 H), 0.09 - 0.06 (s, 3 H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 170.0, 139.5, 138.0, 136.3, 129.6, 128.62, 128.56, 128.5, 128.3, 128.1, 128.0, 127.9, 127.7, 127.2, 126.2, 102.0, 98.2, 80.1, 78.9, 75.3, 75.1, 75.0, 73.6, 73.4, 72.8, 69.4, 68.2, 63.6, 57.2, 55.1, 31.1, 25.8, 24.5, 21.6, 18.1, -3.4, -4.0; IR ($CHCl_3$) 3065, 3032, 3009, 2953, 2932, 2901, 2861, 1740, 1584 cm^{-1}; FAB MS (NaOAc and 3-nitrobenzyl alcohol matrix) 959 (M^+ + Na) for $C_{48}H_{61}{}^{79}BrO_{10}SiS$ and 961 (M^+ + Na) for $C_{48}H_{61}{}^{81}BrO_{10}SSi$. *Anal.* Calcd for $C_{48}H_{61}BrO_{10}SSi$: C, 61.46; H, 6.55; Found: C, 60.95; H, 6.69.

Partial ^1H NMR data (500 MMz, $CDCl_3$) for α-anomer **43f**: δ 5.87 - 5.84 (d, *J* = 3.2 Hz, 1 H), 5.41 - 5.38 (d, *J* = 3.5 Hz, 1 H), 5.23 - 5.17 (dd, *J* = 10.1, 9.1, 1 H), 5.15 - 5.10 (t, *J* = 8.2 Hz, 1 H), 4.96 - 4.89 (t, *J* = 10 0 Hz, 1 H), 4.35 - 4.30 (t, *J* = 8.7 Hz, 1 H), 3.24 (dd, *J* = 9.8, 3.5 Hz, 1 H, H-2).

6-Bromo-3-O-(6-bromo-4-O-chloroacetyl-2,6-dideoxy-2-phenylselenyl-3-O-triethylsilyl-β-D-glucopyranosyl)-4-O-chloroacetyl-2,6-dideoxy-D-*arabino*-hex-1-enitol (**54β**) was prepared in 55% yield from the reaction of bromo imidate **51** (53.8 mg, 75 μmol) and glycal acceptor **52** (25.7 mg, 90 μmol) as an inseparable 2 : 1 mixture of β– and α-disaccharides in toluene at -78°C using 0.3 equiv of BF_3•Et_2O as catalyst: R_f 0.61 (30% EtOAc in hexanes); IR (film) 2957, 2914, 2878, 1766, 1650, 1579, 1479, 1413, 1310, 1248, 1162, 1133, 1057, 1010, 916, 804 cm^{-1}. Data for β-anomer **54β**: ^1H NMR (400 MHz, $CDCl_3$) δ 7.57 - 7.51 (m, 2 H), 7.28 - 7.25 (m, 3 H), 6.42 - 6.38 (d, *J* = 6.3 Hz, 1 H), 5.41 - 5.39 (m, 1 H), 4.91 - 4.84 (dd, *J* = 9.6, 8.3 Hz,

1 H), 4.79 - 4.75 (ddd, J = 6.0, 4.4, 1.3 Hz, 1 H), 4.75 - 4.70 (d, J = 9.1 Hz, 1 H, H-1), 4.39 - 4.31 (m, 1 H), 4.11 (s, 2 H), 4.07 (s, 2 H), 3.84 - 3.78 (dd, J = 10.4, 8.2 Hz, 1 H, H-3), 3.66 -3.61 (m, 1 H), 3.54 - 3.30 (m, 4 H), 3.18 - 3.12 (dd, J = 10.2, 9.3 Hz, 1 H, H-2), 0.97 - 0.91 (t, J = 7.9 Hz, 9 H), 0.65 (q, J = 7.9 Hz, 6 H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 166.3, 166.2, 144.2, 133.2, 129.0, 127.5, 102.9, 97.8, 76.55, 74.9, 73.4, 70.8, 69.9, 52.8, 40.7, 31.2, 29.2, 6.9, 5.1; Partial data for α-anomer **54α**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.48 - 6.44 (dd, J = 6.3, 1.1 Hz, 1 H), 5.28 - 5.25 (d, J = 3.2 Hz, 1 H, H-1), 5.14 - 5.10 (dd, J = 6.3, 3.5 Hz, 1 H), 4.94 - 4.88(dd, J = 10.8, 8.8 Hz, 1 H), 4.27 - 4.22 (m, 1 H), 4.17 (s, 2 H), 4.13 (s, 2 H), 4.04 - 4.00 (m, 1 H), 3.22 - 3.17 (dd, J = 10.8, 3.3 Hz, 1 H, H-2), 0.94 - 0.88 (t, J = 8.4 Hz, 9 H), 0.68 (q, J = 8.4 Hz, 6 H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 166.3, 166.2, 144.4, 132.1, 129.2, 127.2, 101.2, 100.3, 75.1, 73.3, 72.6, 70.5, 52.1, 40.8, 31.4, 29.4.

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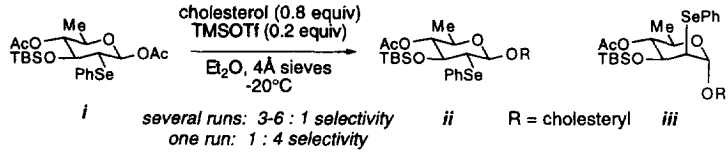
(36) For example, use of the acetate derivative of **8c** (e.g., *i*)as a donor in the reaction with cholesterol gave non-reproducible results. In several experiments, the β-glucoside *ii* was obtained with selectivity of 3-6 : 1, however in one case the α-mannoside *iii* predominated (4 : 1 selectivity). This reflects the dependence of these glycosidations on subtle variations in reaction conditions.



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(49) Control experiments established that glycosides **35d** and **42a,b,d,e** are stable under the reaction conditions (0.3 equiv. TMSOTf, CH_2Cl_2, 4Å sieves, -78°C; ≥98% recovery).
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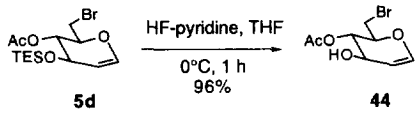
(53) For general experimental details, see: Roush, W. R.; Lin, X.-F. *J. Am. Chem. Soc.* **1995**, *117*, 2236. Unless otherwise noted, all compounds purified by chromatography are sufficiently pure (>95% by ^1H NMR analysis) for use in subsequent reactions.
(54) Alcohol **19** was prepared in 77% overall yield from **12a** by sequential acylation (Ac_2O, pyridine, CH_2Cl_2) and removal of the TBS protecting group (Et_3N-HF, CH_3CN, 23°C, 24 h).
(55) Acceptor **40** was prepared by desilylation of **42a** (Et_3N-HF, CH_3CN, 23°C, 36-48 h, 83% yield).
(56) Acceptor **44** was prepared by desilylation of glycal **5d** (HF-pyridine, THF, 0 °C, 96% yield).



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