on silica gel, eluting with ethyl acetate/hexane (90:10) to give pure *cis*-**2b** as a thick paste [^{1}H NMR (acetone-d_6) δ 1.08–1.55 (m, 2 H, norbornyl), 3.30–3.61 (m, 4 H, norbornyl), 4.06 (ddd, 2 H, $-CH_2O-$, J_{HH} = 11.9 Hz, J_{HH} = 11.8 Hz, J_{PH} = 7.1 Hz), 4.27 (ddd, 2 H, $-CH_2O-$, J_{HH} = 11.9 Hz, J_{HH} = 2.5 Hz, J_{PH} = 25.2 Hz), 6.23 (t, 2 H, vinyl, J_{HH} = 1.6 Hz), 7.47–7.87 (m, 9 H, aryl); ^{31}P NMR (acetone-d_6) δ 18.08; IR (thin film) 2960–2850, 1400, 1255 (s, P=O), 1100–1020, 795, 700–660 cm^{-1}] and pure *trans*-**2b** as a colorless crystalline solid: mp 131–136 °C; ^{1}H NMR (C_6D_6) δ 1.00 (dt, 1 H, norbornyl bridge, J_{HH} = 8.3 Hz, J_{HH} = 1.4 Hz), 1.20 (dt, 1 H, norbornyl bridge, J_{HH} = 8.3 Hz, J_{HH} = 1.9 Hz), 2.18 (m, 2 H, norbornyl), 2.42 (m, 2 H, norbornyl), 3.70 (ddd, 2 H, $-CH_2O-$, J_{HH} = 12.3 Hz, J_{HH} = 3.8 Hz, J_{PH} = 20.5 Hz), 4.25 (ddd, 2 H, $-CH_2O-$, J_{HH} = 12.3 Hz, J_{HH} = 12.3 Hz, J_{PH} = 8.4 Hz), 5.59 (t, 2 H, vinyl), 6.69–7.07 (m, 3 H, aryl), 8.04–8.09 (m, 2 H, aryl); ^{31}P NMR (acetone-d_6) δ 22.90; IR (KBr) 3050, 2990, 2965 (s), 2940, 2900, 2870, 1595, 1568, 1494, 1475, 1453, 1439, 1382, 1339, 1268, 1254, 1230 (s, P=O), 1177, 1137 (s), 1057 (s), 1020, 1000, 982, 968, 906, 860 (s), 840, 825, 806 (s), 746, 730, 711, 693 (s), 593, 546, 498, 457, 430 cm^{-1}.

5,6-(*endo*,*endo*-2',3'-Bicyclo[2.2.1]hept-5'-eno)-2-oxo-2-(*N*,*N*-dimethylamino)-1,3,2-dioxaphosphepane, 2c. Hexamethylphosphorous triamide (10.0 mL, 42.8 mmol) was slowly added to a stirred solution of 5-norbornene-*endo*,*endo*-2,3-dimethanol (6.72 mg, 42.8 mmol) in anhydrous ethyl acetate (200 mL) under dry nitrogen atmosphere. The reaction mixture was allowed to reflux overnight and then cooled to 0 °C. A solution of *tert*-butyl hydroperoxide (14.3 mL of a 3 M solution in 2,2,4-trimethylpentane, 42.8 mmol) was slowly added and the reaction mixture allowed to stir at 0 °C for 15 min. The reaction mixture was allowed to warm to room temperature and stirred for 1 h. The solvents were removed from the reaction mixture by rotary evaporation to leave 14.9 g of a yellow solid. A 2.00-g sample of the crude product was chromatographed by a gravity column (2.5 × 60 cm) on silica gel, eluting with ethyl acetate, to give 580 mg (41.5% yield) **2c** as a mixture of diastereomers. Anal. Calcd for $C_{11}H_{18}NO_3P$: C, 54.27; H, 7.46; N. 5.76; P, 12.73. Found: C, 54.15; H, 7.56; P, 12.01. The diastereomers were separated by preparative HPLC on silica gel eluting with ethyl acetate to give pure *cis*-**2c** as a colorless oil [^{1}H NMR (acetone-d_6) δ 1.41–1.50 (m, 2 H, norbornyl), 2.59 (d, 6 H, NMe_2, J_{PH} = 7.0 Hz), 2.75–2.85 (m, 4 H, norbornyl), 3.60 (ddd, 2 H, $-CH_2O-$, J_{HH} = 11.9 Hz, J_{HH} = 11.4 Hz, J_{PH} = 3.1 Hz), 41.3 (ddd, 2 H, $-CH_2O-$, J_{HH} = 11.9 Hz, J_{HH} = 2.7 Hz, J_{PH} = 23.7 Hz), 6.15 (t, 2 H, vinyl); ^{31}P NMR (acetone-d_6) δ 13.79 ppm; IR (thin film) 2960–2860, 1455, 1376, 1245 (s, P=O), 1175, 1090, 1040 (s), 1015, 1000, 940 (s), 817, 789, 740, 717 cm^{-1}] and pure *trans*-**2c** as a colorless crystalline solid: mp 137.5 °C; ^{1}H NMR (acetone-d_6) δ 1.41–1.53 (m, 2 H, norbornyl), 2.60 (d, 6 H, NMe_2, J_{PH} = 10.0 Hz), 2.71–2.87 (m, 4 H, norbornyl), 3.83 (ddd, 2 H, $-CH_2O-$, J_{HH} = 12.3 Hz, J_{HH} = 10.0 Hz, J_{PH} = 10.0 Hz), 3.97 (ddd, 2 H, $-CH_2O-$, J_{HH} = 12.3 Hz, J_{HH} = 4.1 Hz, J_{PH} = 21.5 Hz), 6.15 (t, 2 H, vinyl); ^{31}P NMR (acetone-d_6) δ 18.61 ppm; IR (KBr) 2970, 2935, 2900, 1474, 1456, 1386, 1333, 1302, 1276, 1228 (s, P=O), 1172, 1050 (s), 985 (s), 963 (s), 857, 839, 812, 750, 736, 710, 555, 476 cm^{-1}.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the National Science Foundation (Grant No. CHE-8603849) for support of this work. We thank Mr. Bruce Hovanes (University of Alabama in Huntsville) for technical assistance in obtaining the low-temperature NMR spectra.

Redox Glycosidation: Stereoselective Syntheses of 1 → 6 Linked Disaccharides via Thionoester Intermediates

Anthony G. M. Barrett* and Albert C. Lee

Department of Chemistry, Colorado State University, Fort Collins, Colorado 80523

Received November 12, 1991 (Revised Manuscript Received February 14, 1992)

Perbenzyl derivatives of the disaccharides benzyl 6-*O*-(α(and β)-D-glucopyranosyl)-α-D-galactopyranoside and benzyl 6-*O*-(α(and β)-D-mannopyranosyl)-α-D-galactopyranoside were each prepared in a stereoselective manner by acylation, thionation, and reductive desulfurization. The use of 2,4-bis(4-phenoxyphenyl)-1,3,2,4-dithiadiphosphetane 2,4-disulfide (**4b**) as a mild thionation reagent for esters and lactones is also described.

Introduction

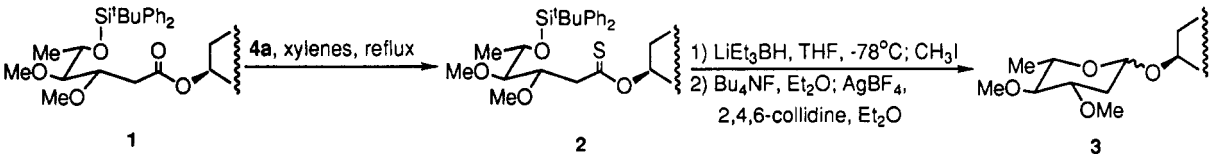
The efficient synthesis of oligosaccharides is a highly desirable objective, the key to which relies upon the efficient stereoselective formation of the glycosidic bond. Virtually all oligosaccharide syntheses rely heavily upon the Koenigs–Knorr alkylation chemistry or modern variations of this theme.[1] Recently, our laboratory[2] presented a novel approach for assembling glycosidic bonds using redox glycosidation. This strategy establishes the anomeric C–O bond by acylation, not alkylation as in the Koenigs–Knorr reaction. Tebbe methylenylation, desilylation, and iodoetherification reveals the glycosidic linkage. The application of redox glycosidation was recently demonstrated in a highly stereoselective synthesis of sucrose.[3] While this method is of potential use for the synthesis of ketose-based oligosaccharides, it is totally inappropriate for the more common aldose-based systems. We have reported a potential solution to this problem by way of thionoester intermediates.[4] In this case, aldonic ester thionation using Lawesson's reagent **4a**,[5] reductive *S*-methylation, and cyclization of the resultant monothioacetal gave the corresponding glycoside. The process is exemplified by the transformation in Scheme I.

As an extension of this methodology, we report in this paper the syntheses of several 1→6 linked disaccharides by the stereoselective acylation of a protected D-galactose derivative, thionation, and reductive desulfurization. Furthermore, we report the use of 2,4-bis(4-phenoxy-

(1) Schmidt, R. R. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Winterfeldt, E., Eds.; Pergamon Press: Oxford, 1991; Vol. 6, pp 33–64.
(2) Barrett, A. G. M.; Bezuidenhoudt, B. C. B.; Gasiecki, A. F.; Howell, A. R.; Russell, M. A. *J. Am. Chem. Soc.* **1989**, *111*, 1392.
(3) Barrett, A. G. M.; Bezuidenhoudt, B. C. B.; Melcher, L. M. *J. Org. Chem.* **1990**, *55*, 5196.
(4) Barrett, A. G. M.; Bezuidenhoudt, B. C. B.; Howell, A. R.; Lee, A. C.; Russell, M. A. *J. Org. Chem.* **1989**, *54*, 2275.
(5) Pedersen, B. S.; Scheibye, S.; Lawesson, S.-O. *Bull. Soc. Chim. Belg.* **1978**, *87*, 293.

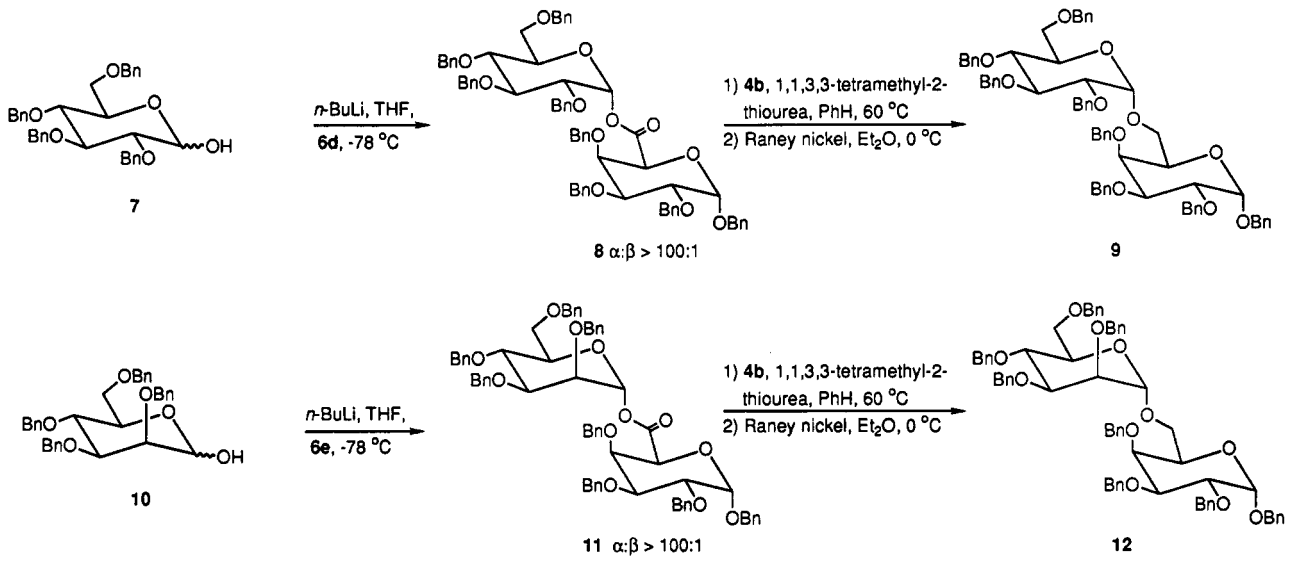
0022-3263/92/1957-2818$03.00/0

Scheme I



1 2 3

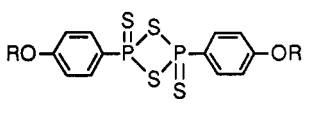
Scheme II



7 8 α:β > 100:1 9

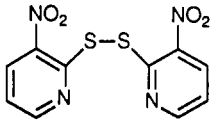
10 11 α:β > 100:1 12

phenyl)-1,3,2,4-dithiadiphosphetane 2,4-disulfide (**4b**)[6] as a mild thionation reagent for esters and lactones.

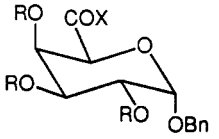


4

a R=CH$_3$
b R=Ph

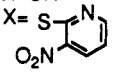


5



6

a R=H, X=OBn
b R=Bn, X=OBn
c R=Bn, X=OH
d R=Bn, X=



e R=Bn, X=OC$_6$H$_4$-4-NO$_2$

Results and Discussion

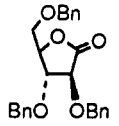
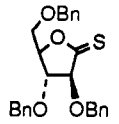
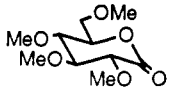
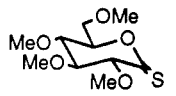
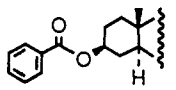
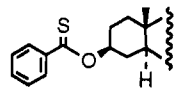
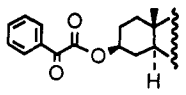
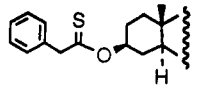
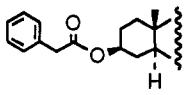
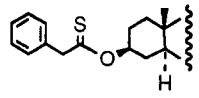
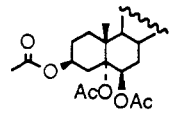
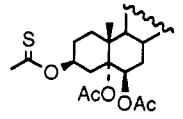
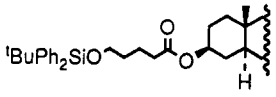
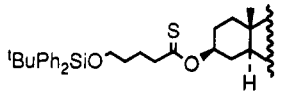
The masked glycosyl acceptor **6c** was prepared in three steps from galacturonic acid by Fischer glycosidation with concomitant benzyl ester formation, perbenzylation of the resultant triol, and saponification. The galacturonic acid **6c** was either used directly for β-selective esterification or converted into the 2-(acylthio)-3-nitropyridine ester **6d** or *p*-nitrophenol ester **6e** derivatives for α-selective esterification.[7]

α-Selective esterification of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (**7**)[8] was accomplished by sequential reaction with *n*-butyllithium and the thioester **6d** at −78 °C in THF for 168 h to provide **8** (79%, α:β > 100:1) (Scheme II). In a similar fashion, 2,3,4,6-tetra-*O*-benzyl-D-mannopyranose (**10**)[9] was stereoselectively converted into the α-ester **11** (71%, α:β > 100:1) by transesterification using **6e** for 36 h. In this process the 4-nitrophenyl ester **6e** was found to be more reactive toward the lithium alkoxide of **10** than the thioester **6d**. In both examples, much to our delight, esters **8** and **11** were formed only as the desired α anomers. The stereochemistry of the glucopyranosyl ester was determined by examining the ^{1}H NMR spectrum (δ 6.35, d, $J_{H1,H2}$ = 3.4 Hz).[10] Pyranoside rings generally form the $^4C_1$ chair conformation, and with both gluco- and galactopyranosides the H2 proton is axial and thus coupling constants based on the Karplus relation between H1 and H2 are therefore indicative of the anomeric configuration. In the case with α anomers, a small $J_{H1,H2}$ (2–4 Hz) is observed by virtue of the gauche relationship between H1 and H2. The anti alignment of H1 and H2 in the β anomer would result in a large $J_{H1,H2}$ (7–9 Hz). Since the equatorial mannose H2 proton is gauche to H1 in both the α and the β anomers of the mannopyranosyl configuration, the stereochemistry of ester **11** was determined by ^{13}C NMR chemical shifts, TLC, and optical rotation data of similar structures.[11]

The Schmidt trichloroacetimidate[12] protocol was applied for the synthesis of the β-esters **14** and **17** (Scheme III). The β-esters **14** and **17** were formed from benzyl 2,3,4-tri-*O*-benzyl-α-D-galacturonic acid **6c** and the known trichloroacetimidates **13**[13] and **16**.[14] The reaction with tri-

(6) Lajoie, G.; Lepine, F.; Maziak, L.; Belleau, B. *Tetrahedron Lett.* **1983**, *24*, 3815.
(7) Barrett, A. G. M.; Bezuidenhoudt, B. C. B. *Heterocycles* **1989**, *28*, 209.
(8) Schmidt, O. T.; Auer, T.; Schmadel, H. *Chem. Ber.* **1960**, *93*, 556.
(9) Koto, S.; Morishima, N.; Miyata, Y.; Zen, S. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 2639.
(10) Bush, C. A. *Bull. Magn. Reson.* **1988**, *10*, 73.
(11) Schmidt, R. R.; Moering, U.; Reichrath, M. *Chem. Ber.* **1982**, *115*, 39. Jansson, P. E.; Kenne, L.; Ottosson, H. *J. Chem. Soc., Perkin Trans. I* **1990**, 2011.
(12) Schmidt, R. R. *Pure Appl. Chem.* **1989**, *61*, 1257.
(13) Schmidt, R. R.; Michel, J. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 731.

Table I. Thionation of Various Esters and Lactones by the Belleau Reagent 4b[a]

entry	substrate (ref)	product (ref)	solvent	time (h)	temp (°C)	yield (%)
1	 **19**	 **20** (17)	C_6H_6	4	70	82
2	 **21** (18)	 **22**	C_6H_6	12	70	80
3	 **23** (19)	 **24**	$CHCl_3$	12	60	42
4	 **25** (20)	 **26** (21)	DME	12	85	82
5	 **27**	 **28** (22)	$CHCl_3$	36	60	87
6	 **29** (22)	 **28** (22)	C_6H_6	18	70	87
7	 **30** (23)	 **31**	C_6H_6	12	70	67
8	 **32** (4)	 **33** (4)	$CHCl_3$	12	60	88

[a] The esters and thionoesters in entries –48 were derivatives of 5α-cholestane.

chloroacetimidate **13** required 7 days at –78 °C for completion. However, when the process was catalyzed with BF_3·OEt_2 at –78 °C, the esterification of **16** was complete within 12 h. Under these specific reaction conditions, the esters **14** and **17** with the desired β-anomeric centers were the only products observed. The stereochemistry of ester **14** was again determined by examining the ^1H NMR spectrum (δ 5.70, d, $J_{H1,H2}$ = 8.1 Hz). The anomeric configuration of the ester **17** was determined from the ^{13}C NMR (δ 92.4). This appeared downfield from that observed in the α-anomer **11** (δ 92.3).

Thionation of the esters **8**, **11**, **14**, and **17** was next examined. However, much to our disappointment, reaction of these esters with the Lawesson's reagent (**4a**), at the elevated temperatures needed for thionation, resulted in the formation of complex untractable mixtures. The drastic conditions for thionation are necessary for two reasons. Firstly Lawesson's reagent (**4a**) is not particularly soluble in cold organic solvents. Secondly esters are considerably less nucleophilic than amides which are more readily thionated. A more soluble analogue of Lawesson's reagent, 2,4-bis(4-phenoxyphenyl)-1,3,2,4-dithiadiphosphetane 2,4-disulfide (**4b**),[15] was employed to avoid such drastic conditions. Reagent **4b** was first reported by Belleau and co-workers for the preparation of thiopeptides from peptides.[6] Additionally, **4b** was particularly useful for the regioselective monothionation of several oligopeptides by reaction in THF solution at 23 °C. Recently, Nicolaou and co-workers[16] reported higher efficiency in the

(14) Schmidt, R. R.; Michel, J.; Roos, M. *Liebigs Ann. Chem.* **1984**, 1343.

(15) The solubilities of **4a** and **4b** in $CHCl_3$ at reflux were 21 g L^{-1} and 117 g L^{-1} and in toluene at reflux were 14 g L^{-1} and 82 g L^{-1}, respectively.

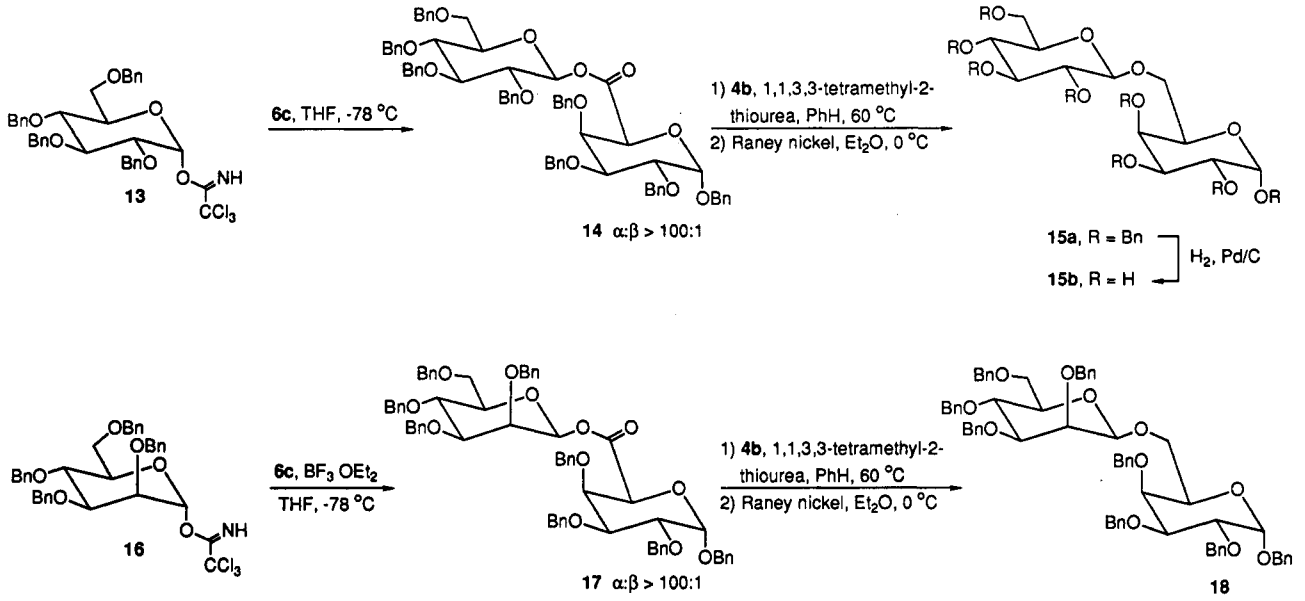
(16) Nicolaou, K. C.; McGarry, D. G.; Somers, P. K.; Kim, B. H.; Ogilvie, W. W.; Yiannikouros, G.; Prasad, C. V. C.; Veale, C. A.; Hark, R. R. *J. Am. Chem. Soc.* **1990**, *112*, 6263.

(17) Prey, V.; Kondler, P. *Monatsh. Chem.* **1958**, *89*, 505.

(18) Rabinsohn, Y.; Fletcher, H. G., Jr. *J. Org. Chem.* **1967**, *32*, 3452.

(19) Moeller, P. *Liebigs Ann. Chem.* **1972**, *755*, 191.

Scheme III



use of Belleau's reagent (**4b**) over Lawesson's (**4a**) in the thionation of a lactone system.

A series of model thionations were undertaken in order to fully define the utility of **4b**. Esters and lactones were smoothly thionated using reagent **4b** in benzene, chloroform, or DME solution at 60–85 °C to provide the corresponding thionoesters and thionolactones (Table I). In entries 2 and 3, 1,1,3,3-tetramethyl-2-thiourea[16] was added to buffer the reaction mixtures. It is clear from Table I that the thionation reaction works well for γ- and δ-lactones as well as both aromatic and aliphatic esters. In addition, the stability of benzyl, methyl, and *tert*-butyldiphenylsilyl ethers is noteworthy. Entry 5 shows the reductive thionation of a benzoyl formate ester. It is interesting to note that the ester thionation was accompanied by ketone deoxygenation and the product was identical with the thionoester from entry 6. This unexpected result is currently under further investigation. Ester thionation using reagent **4b** is also regioselective. Entry 7 shows that the procedure may be used to selectively thionate an equatorial acetate substituent in the presence of two axial acetate groups. Such selectivity should be of considerable use in synthesis.

This useful thionation protocol was thus applied to the treatment of the galacturonic esters **8**, **11**, **14**, and **17** with the Belleau reagent **4b** in C_6H_6 at 60 °C to produce the corresponding thionoesters which were, without further purification, subjected to reductive desulfurization over a suspension of Raney nickel in diethyl ether at 0 °C. This resulted in the formation of the desired disaccharides **9**,[24] **12**, **15a**[24] and **18**, all in excellent yields. Isolation of the thionoester intermediates was difficult since impurities tended to coelute on attempted purification by flash chromatography. Furthermore, the overall yields of the thionation and reduction steps are much better without isolation of the thionoesters intermediates.

The stereochemical assignments of the resultant disaccharides were based on the differences in chemical shifts of the anomeric carbons. For perbenzylated disaccharides **9** and **15a**, the ^{13}C NMR data are in agreement with the respective literature values.[24] Furthermore, disaccharide **15a** was subjected to catalytic hydrogenation to reveal the debenzylated disaccharide **15b**.[25] Analytical data for **15b** are in agreement with reported literature values.[25] In the mannoside examples **12** and **18**, the ^{13}C NMR signal of the C-1 α anomer also appears upfield of the β anomer. This is consistent with the trend reported for various other mannosides of similar structure.[11]

In conclusion, the results reported here demonstrate the efficacy of redox glycosidation in the stereoselective formation of glycoside bonds by acylation, thionation, and reductive desulfurization. The anomeric stereochemistry is efficiently controlled via diastereoselective α- or β-esterification.

Experimental Section

General Procedures. All reactions were carried out under dry N_2 at room temperature unless noted otherwise. Low-temperature reactions were recorded as bath temperatures. Microanalyses were determined by G.D. Searle & Co., Skokie, IL.

Column chromatography was performed on E. Merck silica gel 60, 230–400-mesh ASTM, and analytical thin-layer chromatography was performed on E. Merck precoated silica gel 60 F_{254} plates. Hexane refers to redistilled ACS reagent with a boiling range of 35–60 °C. The following solvents were purified by redistillation under nitrogen: CH_2Cl_2 (from CaH_2), Et_2O (from Ph_2CO–Na), $CHCl_3$ (from P_2O_5), THF (from Ph_2CO–Na), DME (from Ph_2CO–Na), and C_6H_6 (from Ph_2CO–Na).

Benzyl (Benzyl 2,3,4-tri-*O*-benzyl-α-D-galactopyranosid)uronate (6b). D-Galacturonic acid (4.4 g, 21 mmol), $TsOH{\cdot}H_2O$ (1.5 g, 8 mmol), and $PhCH_2OH$ (8.0 mL) were heated at 60 °C for 24 h. Cooling and direct filtration through silica (eluant $CHCl_3$/MeOH 20:1) gave crude **6a**. This was dissolved in CH_2Cl_2 (30 mL), and to this were added $PhCH_2Br$ (15.8 g, 92 mmol) and Ag_2O (9.5 g, 41 mmol). After being heated to reflux for 24 h, the reaction mixture was filtered through Celite and concentrated. The residual oil was purified by chromatography (eluant hexane/Et_2O 3:2) to yield **6b** (5.6 g, 41%) as a slightly yellow oil: TLC R_f 0.31 (silica; hexane/Et_2O 3:2); $[\alpha]_D$ +37.7° (c 1.54, $CHCl_3$); IR ($CHCl_3$) 3030, 1763, 1605, 1496, 1454, 1345, 1271, 1208, 1105, 1067, 1027, 909 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40–7.15 (m, 25 H), 5.04 (d, 1 H, J = 3.6 Hz), 5.13, 4.94 (AB q, 2 H, J = 12 Hz), 4.87 (app t, 2 H, J = 11.6 Hz), 4.74 (d, 1 H, J = 12 Hz), 4.73 (d, 1 H, J = 12 Hz), 4.68, 4.61 (AB q, 2 H, J = 12.4

(20) Windaus, A.; Uibrig, C. *Ber.* **1914**, *47*, 2384.
(21) Achmatowicz, S.; Barton, D. H. R.; Magnus, P. D.; Poulton, G. A.; West, P. J. *J. Chem. Soc., Perkin Trans. I* **1973**, 1567.
(22) Ellis, J.; Schibeci, R. A. *Aust. J. Chem.* **1974**, *27*, 429.
(23) Rowland, A. T.; Nace, H. R. *J. Am. Chem. Soc.* **1960**, *82*, 2833.
(24) Gent, P. A.; Gigg, R. *J. Chem. Soc., Perkin Trans. I* **1974**, 1446.
(25) Mortier, C. U.; Varela, O.; De Lederkremer, R. M. *Carbohydr. Res.* **1989**, *189*, 79.

Hz), 4.55 (d, 1 H, J = 12 Hz), 4.46 (d, 1 H, J = 11.6 Hz), 4.38 (d,1 H, J = 1.2 Hz), 4.29 (app t, 1 H, J = 2.4 Hz), 4.10 (dd, 1 H, J = 10, 3.6 Hz), 4.04 (dd, 1 H, J = 10, 2.8 Hz); ^{13}C NMR (76 MHz, $CDCl_3$) δ 168.5, 138.5, 138.4, 138.3, 137.1, 135.1, 128.6, 128.5, 128.4, 128.35, 128.29, 128.1, 127.9, 127.8, 127.65, 127.62, 127.52, 127.40, 127.37, 96.9, 78.4, 76.6, 75.8, 74.5, 73.31, 73.27, 70.8, 69.9, 66.9; MS (FAB) m/z 667 (M + Na^+), 645 (M + H^+), 551, 537, 445, 403, 321, 271, 253, 223; HRMS calcd for $C_{41}H_{40}O_7$ (M + Na^+) 667.2672, found (M + Na^+) 667.2665. Anal. Calcd for $C_{41}H_{40}O_7$: C, 76.38; H, 6.25. Found: C, 76.67; H, 6.31.

Benzyl 2,3,4-Tri-*O*-benzyl-α-D-galactopyranosiduronic Acid (6c). To a solution of ester **6b** (1.24 g, 1.9 mmol) in THF (50 mL) were added $LiOH·H_2O$ (0.31 g, 7.3 mmol) and Aliquat 336 (200 mg) in H_2O (35 mL). After being stirred for 4 h, the reaction mixture was poured over ice–water (100 mL), acidified with H_3PO_4, and extracted with EtOAc (6 × 100 mL). The organic layers were combined, dried ($MgSO_4$), and concentrated. The resultant oil was recrystallized from hexane/CCl_4 to give **6c** (0.63 g, 59%) as fine white needles: mp 108–110 °C; TLC R_f 0.28 (silica; EtOAc); $[\alpha]_D$ +86.1° (c 1.32, $CHCl_3$); IR (CCl_4) 3018, 1735, 1454, 1348, 1215, 1104, 1102, 1024, 757 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.38 (bs, 1 H), 7.39–7.22 (m, 20 H), 5.00 (d, 1 H, J = 1.5 Hz), 4.93 (d, 1 H, J = 11.1 Hz), 4.87 (d, 1 H, J = 11.7), 4.78 (d, 1 H, J = 11.9 Hz), 4.77 (d, 1 H, J = 11.7 Hz), 4.71 (d, 1 H, J = 12.4 Hz), 4.62 (d, 1 H, J = 11.4 Hz), 4.60 (d, 1 H, J = 11.1 Hz), 4.58 (d, 1 H, J = 11.8 Hz), 4.37 (d, 1 H, J = 1.2 Hz), 4.33 (m, 1 H), 4.04 (m, 2 H); ^{13}C NMR (76 MHz, $CDCl_3$) δ 171.4, 138.3, 138.2, 137.9, 136.8, 128.44, 128.36, 128.3, 128.1, 128.01, 127.94, 127.8, 127.7, 127.59, 127.57, 127.4, 97.0, 77.9, 76.2, 75.6, 75.1, 73.4, 73.3, 70.7, 70.2; MS (EI) m/z 553 (M – H^+), 463, 355, 253, 223, 181, 91, 65. Anal. Calcd for $C_{34}H_{34}O_7$: C, 73.63; H, 6.18. Found: C, 73.72; H, 6.24.

3-Nitropyridyl 2-(Benzyl 2,3,4-tri-*O*-benzyl-α-D-galactopyranosid)thiouronate (6d). A suspension of acid **6c** (800 mg, 1.4 mmol), bis(3-nitro-2-pyridyl) disulfide (**5**) (556 mg, 1.8 mmol) and Ph_3P (473 mg, 1.8 mmol) in CH_2Cl_2 (30 mL) was stirred under argon overnight. The mixture was filtered through a pad of Celite, rinsed with CH_2Cl_2, and concentrated. The residue was dissolved in $CHCl_3$ and chromatographed (eluant hexane/EtOAc 2:1) to yield **6d** (0.98 g, 98%) as a yellow syrup: TLC R_f 0.33 (silica; hexane/EtOAc 2:1); $[\alpha]_D$ +11.7° (c 1.42, $CHCl_3$); IR (CCl_4) 2872, 1706, 1531, 1454, 1354, 1124, 1060, 1026, 913 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.81 (dd, 1 H, J = 4.7, 1.5 Hz), 8.25 (dd, 1 H, J = 7.2, 1.5 Hz), 7.49–7.20 (m, 21 H), 5.11 (d, 1 H, J = 3.7 Hz), 4.802 (d, 1 H, J = 11.9 Hz), 4.799 (d, 1 H, J = 10.4 Hz), 4.78 (d, 1 H, J = 12.2 Hz), 4.72 (d, 1 H, J = 11.6 Hz), 4.70 (d, 1 H, J = 11.3 Hz), 4.66 (d, 1 H, J = 12.2 Hz), 4.58 (d, 1 H, J = 10.9 Hz), 4.55 (d, 1 H, J = 11.9 Hz), 4.46 (d, 1 H, J = 1.3 Hz), 4.33 (m, 1 H), 4.12 (dd, 1 H, J = 10.0, 3.7 Hz), 3.97 (dd, 1 H, J = 10.0, 2.8 Hz); ^{13}C NMR (76 MHz, $CDCl_3$) δ 195.3, 152.6, 149.7, 146.2, 138.4, 138.3, 138.2, 136.6, 132.9, 128.51, 128.46, 128.32, 128.27, 128.14, 128.06, 127.98, 127.8, 127.6, 127.5, 127.43, 127.36, 124.1, 96.7, 78.2, 77.4, 76.2, 76.0, 75.1, 73.4, 73.2, 70.0; MS (FAB) m/z 693 ($M^{+\cdot}$), 677, 660, 552, 417, 337, 247, 181; HRMS (FAB) calcd for $C_{39}H_{37}N_2SO_8$ ($M^{+\cdot}$) 693.2270, found ($M^{+\cdot}$) 693.2189.

4-Nitrophenyl (Benzyl 2,3,4-tri-*O*-benzyl-α-D-galactopyranosid)uronate (6e). Acid **6c** (0.40 g, 0.72 mmol), p-nitrophenol (0.12 g, 0.86 mmol), DCC (0.18 g, 0.86 mmol), and 4-pyrrolidinopyridine (1 crystal) in CH_2Cl_2 (2 mL) were stirred overnight under an atmosphere of argon. Following removal of the urea by filtration, the filtrate was washed with aqueous $NaHCO_3$ and H_2O. The aqueous layer was back extracted with Et_2O, and the organic layers were combined, dried ($MgSO_4$), and concentrated. The residue was separated by chromatography (eluant hexane/Et_2O 4:1) to give **6e** (0.25 g, 52%) as a yellow oil: TLC R_f 0.29 (silica; hexane/Et_2O 3:2); $[\alpha]_D$ +32.0° (c 2.35, $CHCl_3$); IR (CCl_4) 2915, 1791, 1759, 1593, 1525, 1347, 1129, 1104, 1067, 1027 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (d, 2 H, J = 9 Hz), 7.44–7.22 (m, 20 H), 6.96 (d, 2 H, J = 9 Hz), 5.14–5.11 (m, 2 H), 4.94 (d, 1 H, J = 11.6 Hz), 4.82 (d, 1 H, J = 12.2 Hz), 4.74 (d, 1 H, J = 12.3 Hz), 4.75–4.66 (m, 2 H), 4.60 (d, 1 H, J = 11.9 Hz), 4.60 (d, 1 H, J = 1.6 Hz), 4.59 (d, 1 H, J = 11.5 Hz), 4.45 (m, 1 H), 4.15 (m, 2 H); ^{13}C NMR (76 MHz, $CDCl_3$) δ 166.6, 154.7, 145.5, 138.4, 138.2, 137.1, 128.9, 128.4, 128.34, 128.30, 128.0, 127.9, 127.74, 127.67, 127.5, 126.0, 125.1, 122.2, 97.3, 78.2, 77.3, 75.8, 75.2, 73.7, 73.4, 71.2, 70.5; MS (FAB) m/z 674 (M – H^+), 653, 582, 547, 476, 415; HRMS calcd for $C_{40}H_{36}NO_9$ (M – H^+) 674.2390, found (M – H^+) 674.2402.

2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl (Benzyl 2,3,4-tri-*O*-benzyl-α-D-galactopyranosid)uronate (8). n-BuLi (115 μL, 1.88 M in hexanes) was added to a solution of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (**7**)[8] (114 mg, 0.21 mmol) in THF (400 μL) at −78 °C. After 45 min of stirring, a solution of thioester **6d** (287 mg, 0.41 mmol) in THF (300 μL) was added. The mixture was stirred for 7 days at −78 °C and then quenched with pH 7 phosphate buffer and extracted with Et_2O (5 × 10 mL). The Et_2O layers were combined, dried ($MgSO_4$), concentrated, and separated by chromatography (eluant hexane/Et_2O 7:3) to give ester **8** (179 mg, 79%) as a clear, colorless oil: TLC R_f 0.42 (silica; hexane/EtOAc 4:1); $[\alpha]_D$ +70.4° (c 0.61, $CHCl_3$); IR ($CHCl_3$) 3030, 2869, 1732, 1496, 1454, 1360, 1207, 1102, 1027 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37–7.14 (m, 40 H), 6.35 (d, 1 H, J = 3.4 Hz), 5.02 (d, 1 H, J = 2.7 Hz), 4.92–4.44 (m, 16 H), 4.38 (d, 1 H, J = 1.2 Hz), 4.29 (m, 1 H), 4.06 (m, 2 H), 3.88–3.56 (m, 6 H); ^{13}C NMR (76 MHz, $CDCl_3$) δ 167.3, 138.8, 138.6, 138.4, 138.3, 138.0, 137.7, 137.4, 137.0, 128.42, 128.36, 128.28, 128.26, 127.98, 127.93, 127.88, 127.83, 127.8, 127.64, 127.59, 127.5, 127.4, 127.04, 126.97, 96.6, 91.4, 81.6, 78.4, 78.0, 77.0, 76.9, 75.8, 75.5, 75.3, 74.5, 73.5, 73.3, 73.04, 72.95, 70.6, 69.8, 67.8; MS (FAB) m/z 1099 (M + Na^+), 1075, 897, 643, 551, 537, 415, 271. Anal. Calcd for $C_{68}H_{68}O_{12}$: C, 75.82; H, 6.36. Found: C, 75.68; H, 6.44.

2,3,4,6-Tetra-*O*-benzyl-α-D-mannopyranosyl (Benzyl 2,3,4-tri-*O*-benzyl-α-D-galactopyranosid)uronate (11). 2,3,4,6-Tetra-*O*-benzyl-D-mannopyranose (**10**)[9] (45 mg, 0.08 mmol) was dissolved in THF (200 μL) and cooled to −78 °C under an atmosphere of argon. n-BuLi (150 μL, 1.6 M in hexanes) was added and, after 30 min, ester **6e** (66 mg, 0.10 mmol) in THF (200 μL) then added. After 36 h, the mixture was quenched with pH 7 phosphate buffer (5 mL) and extracted with EtOAc (3 × 15 mL). The organic layers were combined, dried ($MgSO_4$), and concentrated. Chromatography (hexane/EtOAc 4:1) yielded **11** (61 mg, 71%) as a clear, colorless oil: TLC R_f 0.34 (silica; hexane/Et_2O 3:2); $[\alpha]_D$ +62.5° (c 2.60, $CHCl_3$); IR (CCl_4) 3031, 1730, 1454, 1264, 1099, 1027 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.15 (m, 40 H), 6.29 (d, 1 H, J = 2.0 Hz), 5.01 (d, 1 H, J = 2.4 Hz), 4.97 (d, 1 H, J = 12 Hz), 4.88 (app t, 2 H, J = 11.6 Hz), 4.74 (d, 1 H, J = 12 Hz), 4.69 (d, 1 H, J = 12 Hz), 4.67 (d, 2 H, J = 12.4 Hz), 4.61 (d, 1 H, J = 12.44 Hz), 4.59 (d, 1 H, J = 12 Hz), 4.58–4.49 (m, 4 H), 4.37–4.27 (m, 4 H), 4.13–4.08 (m, 2 H), 4.03 (m, 2 H), 3.77–3.71 (m, 3 H), 3.63–3.61 (m, 1 H), 3.52 (app t, 1 H, J = 2.4 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 138.5, 138.4, 138.1, 138.0, 137.6, 136.9, 128.3, 128.27, 128.23, 128.17, 128.04, 128.0, 127.9, 127.8, 127.77, 127.70, 127.63, 127.6, 127.54, 127.5, 127.36, 127.29, 127.25, 126.5, 96.6, 92.3, 78.9, 78.1, 77.4, 75.8, 75.3, 74.7, 74.4, 74.0, 73.4, 73.5, 73.2, 72.4, 71.6, 70.6, 69.9, 68.5; MS (FAB) m/z 1099 (M + Na^+), 1075, 733, 674, 643, 551, 537, 523, 415, 271. Anal. Calcd for $C_{68}H_{68}O_{12}$: C, 75.82; H, 6.36. Found: C, 75.93; H, 6.38.

2,3,4,6-Tetra-*O*-benzyl-β-D-glucopyranosyl (Benzyl 2,3,4-tri-*O*-benzyl-α-D-galactopyranosid)uronate (14). Benzyl 2,3,4-tri-*O*-benzyl-D-galactopyranosiduronic acid (**6c**) (100 mg, 0.18 mmol) was dissolved in THF (500 μL) and cooled to −78 °C, and trichloroacetimidate **13**[13] (132 mg, 0.19 mmol) in THF (500 μL) was added. The mixture was stirred for 7 days, quenched with pH 7 phosphate buffer (5 mL), and extracted with Et_2O (4 × 10 mL). The extracts were dried ($MgSO_4$) and concentrated. Chromatography of the residue (eluant hexane/Et_2O 7:3) gave **14** (164 mg, 85%) as a white solid: mp 126–127 °C; TLC R_f 0.29 (silica; hexane/Et_2O 3:2); $[\alpha]_D$ +37.1° (c 0.48, $CHCl_3$); IR ($CHCl_3$) 3030, 2870, 1730, 1496, 1359, 1070, 1027 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38–7.10 (m, 40 H), 5.70 (d, 1 H, J = 8.1 Hz), 5.01 (d, 1 H, J = 2.8 Hz), 4.88–4.53 (m, 13 H), 4.49 (d, 1 H, J = 2.0 Hz), 4.29–4.22 (m, 3 H), 4.08–4.01 (m, 3 H), 3.78–3.33 (m, 6 H); ^{13}C NMR (76 MHz, $CDCl_3$) δ 167.2, 138.60, 138.56, 138.4, 138.0, 137.8, 137.0, 128.33, 128.26, 127.95, 127.90, 127.8, 127.7, 127.61, 127.58, 127.48, 127.36, 127.25, 96.7, 94.3, 84.8, 80.3, 77.7, 77.1, 76.4, 75.8, 75.7, 75.4, 74.9, 74.8, 73.3, 73.2, 72.9, 70.6, 69.8, 67.9; MS (FAB) m/z 1099 (M + Na^+), 1075, 1009, 667, 577, 545, 415; HRMS (FAB) calcd for $C_{68}H_{68}O_{12}$ (M + Na^+) 1099.4608, found (M + Na^+) 1099.4674. Anal. Calcd for $C_{68}H_{68}O_{12}$: C, 75.82; H, 6.36. Found: C, 75.66; H, 6.46.

2,3,4,6-Tetra-*O*-benzyl-β-D-mannopyranosyl (Benzyl 2,3,4-tri-*O*-benzyl-α-D-galactopyranosid)uronate (17). Acid

6c (0.45 g, 0.81 mmol) in THF (1.6 mL) was cooled to −78 °C and trichloroacetimidate **16**[14] (0.59 g, 0.86 mmol) in THF (2.0 mL) and $BF_3{\cdot}OEt_2$ (100 μL) was added sequentially. The mixture was stirred for 12 h, quenched with pH 7 phosphate buffer (5 mL), and extracted with Et_2O (5 × 20 mL). The combined Et_2O layers were dried ($MgSO_4$) and concentrated. Chromatography of the residue (eluant hexane/Et_2O 4:1) gave ester **17** (0.78 g, 84%) as a clear, colorless oil: TLC R_f 0.34 (silica; hexane/Et_2O 3:2); $[\alpha]_D$ +54.8° (*c* 1.12, $CHCl_3$); IR (CCl_4) 3031, 1731, 1454, 1262, 1099, 1026 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.39–7.15 (m, 40 H), 6.28 (d, 1 H, *J* = 2.0 Hz), 5.01 (d, 1 H, *J* = 1.8 Hz), 4.96 (d, 1 H, *J* = 12 Hz), 4.89 (d, 1 H, *J* = 11.6 Hz), 4.86 (d, 1 H, *J* = 10.4 Hz), 4.73 (d, 1 H, *J* = 11.6 Hz), 4.69 (d, 1 H, *J* = 11.9 Hz) 4.67 (d, 2 H, *J* = 11.9 Hz), 4.61 (d, 1 H, *J* = 12.3 Hz), 4.58 (d, 1 H, *J* = 13 Hz), 4.57 (d, 1 H, *J* = 12.9 Hz), 4.54 (d, 1 H, *J* = 14.8), 4.50 (d, 1 H, *J* = 12 Hz), 4.38–4.27 (m, 4 H), 4.14–4.02 (m, 4 H), 3.79–3.71 (m, 3 H), 3.63–3.52 (m, 2 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 138.5, 138.4, 138.14, 138.05, 137.6, 137.0, 128.3, 128.22, 128.16, 128.0, 127.8, 127.7, 127.6, 126.5, 127.44, 127.37, 127.3, 127.2, 126.5, 96.7, 92.4, 79.0, 78.1, 77.3, 75.9, 75.3, 74.7, 74.4, 74.1, 73.54, 73.46, 73.2, 72.4, 71.7, 70.6, 70.0, 68.5; MS (FAB) *m/z* 1099 (M + Na^+), 1076, 998, 643, 523, 431, 361. Anal. Calcd for $C_{68}H_{68}O_{12}$: C, 75.82; H, 6.36. Found: C, 76.19; H, 6.41.

Benzyl 2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-α-D-galactopyranoside (9). Ester **8** (20 mg, 0.019 mmol) and thionating agent **4b** (40 mg, 0.076 mmol) in PhH (200 μL) were heated to 60 °C for 36 h under an atmosphere of argon. Upon cooling, the mixture was transferred to a suspension of W-2 Raney nickel (1 g) in Et_2O (5 mL) and stirred at 0 °C for 12 h and the mixture was carefully filtered to remove the metal. The filtrate was concentrated, dissolved in $CHCl_3$, and chromatographed (eluant hexane/Et_2O 7:3) to yield the disaccharide **9** (16 mg, 81%) as a white solid: mp 109–111 °C (hexane/CCl_4) (lit.[24] mp 112–113.5 °C); TLC R_f 0.37 (silica; hexane/Et_2O 3:2); $[\alpha]_D$ +61.1° (*c* 1.0, $CHCl_3$) (lit.[24] $[\alpha]_D$ +62.3° *c* 0.8, $CHCl_3$); IR ($CHCl_3$) 3030, 2907, 1496, 1454, 1133, 1097, 1047, 1028 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40–7.10 (m, 40 H), 4.95–4.37 (m, 18 H), 4.04–3.55 (m, 12 H); ^{13}C NMR (76 MHz, $CDCl_3$) δ 138.9, 138.7, 138.6, 138.4, 138.3, 137.9, 137.2, 128.4, 128.3, 128.2, 128.02, 127.95, 127.8, 127.6, 127.5, 97.2, 95.4, 82.1, 79.8, 79.2, 77.7, 75.6, 75.0, 74.5, 73.5, 73.4, 73.3, 73.1, 70.3, 69.6, 68.7, 68.4, 67.3 (lit.[24] α-glucopyranoside δ 97.0, α-galactopyranoside δ 95.3); MS (FAB) *m/z* 1085 (M + Na^+), 1061, 969, 953, 937, 863, 847, 739, 674, 629, 523, 415, 271; HRMS calcd for $C_{68}H_{70}O_{11}$ (M + Na^+) 1085.4816, found 1085.4808. Anal. Calcd for $C_{68}H_{70}O_{11}$: C, 76.81; H, 6.64. Found: C, 76.92; H, 6.70.

Benzyl 2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-α-D-galactopyranoside (12). Ester **11** (42 mg, 0.039 mmol), thionating agent **4b** (20 mg, 0.20 mmol), and 1,1,3,3-tetramethyl-2-thiourea (10 mg, 0.076 mmol) in PhH (300 μL) was warmed to 60 °C under an atmosphere of argon for 24 h. Upon cooling, the reaction mixture was dissolved in Et_2O (0.5 mL) and transferred to a stirring suspension of W-2 Raney nickel (1 g) in Et_2O (5 mL) at 0 °C. After 6 h, the metal was carefully filtered off, and filtrate was concentrated, and the residue was dissolved in $CHCl_3$ and chromatographed (eluant hexane/Et_2O 4:1) to yield the disaccharide **16** (31 mg, 74%) as a clear, colorless oil: TLC R_f 0.39 (silica; hexane/Et_2O 3:2); $[\alpha]_D$ +8.3° (*c* 1.14, $CHCl_3$); IR (CCl_4) 3030, 2916, 1496, 1454, 1359, 1208, 1098, 1028 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40–7.14 (m, 40 H), 4.92–4.43 (m, 19 H), 4.08–3.64 (m, 10 H), 3.36 (m, 1 H); ^{13}C NMR (76 MHz, $CDCl_3$) δ 138.9, 138.6, 138.5, 138.4, 137.1, 128.4, 128.3, 128.1, 128.0, 127.8, 127.7, 127.6, 127.5, 127.4, 97.7, 95.4, 80.0, 79.2, 75.2, 75.1, 74.9, 74.6, 73.5, 73.3, 73.0, 72.5, 72.2, 72.0, 69.1, 68.6, 66.2; MS (FAB) *m/z* 1085 (M + Na^+), 1061, 953, 863, 795, 715, 653, 595, 523, 431. Anal. Calcd for $C_{68}H_{70}O_{11}$: C, 76.81; H, 6.64. Found: C, 77.12; H, 6.72.

Benzyl 2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)-α-D-galactopyranoside (15a). Thionation and subsequent Raney nickel reduction of ester **14** (41 mg, 0.038 mmol) as for ester **11** gave disaccharide **15** (29 mg, 72%) as a white solid: mp 109–111 °C (hexane/EtOAc) (lit.[24] mp 115.5–117.5 °C); TLC R_f 0.37 (silica; hexane/Et_2O 3:2); $[\alpha]_D$ +38.3° (*c* 1.38, $CHCl_3$) (lit.[24] $[\alpha]_D$ +33.5° (*c* 0.8, $CHCl_3$)); IR (CCl_4) 3029, 2908, 1496, 1452, 1356, 1208, 1069 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40–7.18 (m, 40 H), 4.95 (d, 1 H, *J* = 1.0 Hz), 4.95–4.43 (m, 16 H), 4.39 (d, 1 H, *J* = 7.7 Hz), 4.06–3.39 (m, 12 H); ^{13}C NMR (76 MHz, $CDCl_3$) δ 138.9, 138.6, 138.4, 138.13, 138.07, 137.3, 128.3, 128.24, 128.19, 127.96, 127.88, 127.82, 127.77, 127.73, 127.60, 127.53, 127.46, 127.40, 103.6, 95.9, 84.6, 82.3, 82.1, 79.1, 77.7, 76.4, 75.6, 75.4, 74.9, 74.7, 74.6, 73.4, 73.3, 73.2, 73.1, 69.9, 68.9, 68.8 (lit.[24] β-glucopyranoside δ 103.5, α-galactopyranoside δ 95.8); MS (FAB) *m/z* 1062 ($M^{+\cdot}$), 969, 863, 739, 629, 523, 431, 415, 325, 307. Anal. Calcd for $C_{68}H_{70}O_{11}$: C, 76.81; H, 6.64. Found: C, 76.68; H, 6.66.

Benzyl 2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-mannopyranosyl)-α-D-galactopyranoside (18). Thionation and Raney nickel reduction of ester **17** (38 mg, 0.035 mmol) as for ester **11** gave the disaccharide **18** as a clear, colorless oil (29 mg, 77%): TLC R_f 0.21 (silica; hexane/Et_2O 3:2); $[\alpha]_D$ +100.0° (*c* 1.38, $CHCl_3$); IR (CCl_4) 3030, 2868, 1496, 1454, 1362, 1207, 1101, 1027 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40–7.15 (m, 40 H), 5.00–4.41 (m, 17 H includes 4.93 (d, 1 H, *J* = 1.1 Hz), 4.85 (d, 1 H, *J* = 2.4 Hz)), 4.08–3.88 (m, 8 H), 3.77 (app d, 2 H, *J* = 3.4 Hz), 3.64 (m, 1 H), 3.52 (dd, 1 H, *J* = 9.3, 3.0 Hz), 3.44 (m, 1 H); ^{13}C NMR (76 MHz, $CDCl_3$) δ 138.80, 138.75, 138.5, 138.4, 138.1, 137.2, 128.9, 128.3, 128.20, 128.16, 128.05, 127.98, 127.9, 127.8, 127.74, 127.69, 127.5, 127.4, 127.3, 102.0, 95.8, 82.1, 79.0, 76.4, 75.8, 75.5, 75.1, 74.8, 74.6, 74.5, 74.0, 73.4, 73.3, 73.1, 71.5, 70.3, 69.5, 68.6; MS (FAB) *m/z* 1085 (M + Na^+), 1062, 629, 523, 431; HRMS (FAB) calcd for $C_{68}H_{70}O_{11}$ (M + Na^+) 1085.4816; found (M + Na^+) 1085.4862. Anal. Calcd for $C_{68}H_{70}O_{11}$: C, 76.81; H, 6.64. Found: C, 76.67; H, 6.65.

6-*O*-(β-D-Glucopyranosyl)-D-galactopyranose (15b). Perbenzylated disaccharide **15a** (100 mg, 0.094 mmol) was added as a solution in EtOH/Et_2O (5:3, 16 mL) to a stirred suspension of activated 10% Pd on carbon (300 mg) in EtOH (5 mL). The reaction mixture was stirred for 6 h under an atmosphere of H_2 and then purged with argon and filtered through Celite. The filtrate was concentrated and chromatographed ($CHCl_3$/MeOH/H_2O 12:6:1) to give **15b** as a clear colorless syrup (22 mg, 68%): TLC R_f 0.31 (silica, EtOAc/*i*-PrOH/H_2O 3:3:2); $[\alpha]_D$ +15.2° (*c* 1.1, H_2O) (lit.[25] $[\alpha]_D$ +14.5° (*c* 1, H_2O)); ^{13}C NMR (76 MHz, D_2O) δ 103.4, 97.3, 93.2, 76.7, 76.5, 74.6, 73.9, 73.5, 72.6, 70.4, 70.3, 70.2, 70.0, 69.8, 69.6, 69.1, 61.5 (lit.[25] β-glucopyranoside δ 103.5, β-galactopyranose δ 97.3, α-galactopyranose δ 93.2).

Thiophthalide (20). Phthalide (**19**) (50 mg, 0.37 mmol), **4b** (216 mg, 0.41 mmol), and dry benzene (0.4 mL) were heated with stirring at 70 °C for 4 h. After cooling, the reaction mixture was chromatographed (eluant hexane/Et_2O 3:2) to give the thionolactone **20** (46 mg, 82%) as a yellow solid: mp 110–111 °C (sealed tube, hexane/Et_2O) (lit.[17] mp 108–109 °C). Anal. Calcd for C_8H_6OS: C, 63.97; H, 4.03. Found: C, 63.67; H, 4.17.

2,3,5-Tri-*O*-benzyl-D-arabino-1,4-thiolactone (22). 2,3,5-Tri-*O*-benzyl-D-arabino-1,4-lactone (**21**)[18] (138 mg, 0.33 mmol), 1,1,3,3-tetramethyl-2-thiourea (78 mg, 0.59 mmol), **4b** (266 mg, 0.50 mmol), and benzene (1 mL) were heated to 70 °C. After 4 h, an additional amount of **4b** (200 mg, 0.38 mmol) was added and heating was continued for 12 h. The mixture was cooled and chromatographed (eluant hexane/Et_2O 4:1) to give thionolactone **22** (115 mg, 80%) as a white solid: mp 78–80 °C (hexane/Et_2O): TLC R_f 0.56 (silica; hexane/Et_2O 3:2); $[\alpha]_D$ +25.6° (*c* 0.23, $CHCl_3$); IR (CCl_4) 3031, 2870, 1584, 1319, 1205, 1129, 1104, 1028, 730 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40–7.21 (m, 15 H), 5.05, 4.75 (AB q, 2 H, *J* = 11.4 Hz), 4.69, (m, 1 H), 4.61–4.43 (m, 5 H), 4.28 (t, 1 H *J* = 6.6 Hz), 3.69 (dd, 1 H, *J* = 11.9, 2.2 Hz), 3.58 (dd, 1 H, *J* = 11.9, 3.5 Hz); ^{13}C NMR (76 MHz, $CDCl_3$) δ 218.2, 137.4, 137.0, 128.5, 128.4, 128.13, 128.1, 127.9, 127.8, 88.7, 87.0, 80.3, 73.5, 72.8, 72.6, 67.9; MS (FAB) *m/z* 435 (M + H^+), 329, 307, 289, 286, 181, 176; HRMS (FAB) calcd for $C_{26}H_{26}O_4S$ (M + H^+) 435.1630, found (M + H^+) 435.1643. Anal. Calcd for $C_{26}H_{26}O_4S$: C, 71.86; H, 6.03. Found: C, 71.46; H, 6.05.

2,3,4,6-Tetra-*O*-methyl-D-glucono-1,5-thiolactone (24). Thionation of 2,3,4,6-tetra-*O*-methyl-D-glucono-1,5-lactone (**23**)[19] (135 mg, 0.61 mmol) as for **21** and chromatography (eluant hexane/Et_2O 3:2) gave **24** (61 mg, 42%) as a viscous colorless syrup: TLC R_f 0.34 (silica; hexane/Et_2O 3:2); $[\alpha]_D$ +270.8° (*c* 0.26, $CHCl_3$); IR ($CHCl_3$) 2933, 1455, 1380, 1283, 1176, 1106, 1044, 974 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.77–4.73 (ddd, 1 H, *J* = 9.8, 4.5, 2.1 Hz), 4.35 (dd, 1 H, *J* = 3.0, 0.6 Hz), 3.79 (dd, 1 H, *J* = 11.3, 2.1), 3.71 (dd, 1 H, *J* = 11.3, 4.6), 3.60 (dd, 1 H, *J* = 3.4, 2.8 Hz), 3.52 (s + m, 4 H), 3.49 (s, 3 H), 3.46 (s, 3 H), 3.44 (s, 3 H); ^{13}C NMR (76 MHz, $CDCl_3$) δ 214.9, 85.4, 82.3, 80.1, 78.1, 70.8,

59.4, 58.3, 57.8, 57.5; MS (FAB) m/z 250 ($M^{+\cdot}$), 218, 173, 162, 145, 102, 88, 71, 45; HRMS (EI) calcd for $C_{10}H_{18}O_5S$ ($M^{+\cdot}$) 250.0875, found ($M^{+\cdot}$) 250.0882.

5α-Cholestan-3β-yl Thiobenzoate (26). Cholestan-3β-yl benzoate (**25**)[20] (144 mg, 0.29 mmol), **4b** (360 mg), and DME (1 mL) were warmed to 70 °C for 0.5 h. Since **4b** was not entirely in solution, additional DME (1.0 mL) was added and the mixture was heated to reflux. After 12 h, additional **4b** (180 mg, 0.34 mmol) was added and reflux continued for 24 h. Cooling and chromatography (silica; eluant hexanes) gave **26** (121 mg, 82%) as a yellow solid: mp 139–141 °C (Et_2O) (lit.[21] mp 141–142 °C); $[\alpha]_D$ +4.0° (c 1.5, $CHCl_3$) (lit.[21] $[\alpha]_D$ +3.0° (c 1.0, $CHCl_3$).

5α-Cholestan-3β-yl Phenylglyoxylate (27). Cholestanol (2.0 g, 5.1 mmol), benzoyl formic acid (0.8 g, 5.1 mmol), DCC (1.3 g, 6.3 mmol), and 4-pyrrolidinylpyridine (74 mg, 0.5 mmol) were dissolved in CH_2Cl_2 (30 mL) and stirred overnight. The reaction mixture was filtered through Celite, concentrated, and chromotographed (hexane) to give **27** (1.73 g, 65%) as a white solid: mp 103–105 °C; TLC R_f 0.51 (hexane/Et_2O 9:1); $[\alpha]_D$ + 23.2° (c 1.14, $CHCl_3$); IR ($CHCl_3$) 2933, 2866, 1728, 1691, 1450, 1202, 1176, 990, 681 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.00–7.97 (m, 2 H), 7.65 (ttt, 1 H, J = 7.4, 2.0, 1.3 Hz), 7.50 (m, 2 H), 5.03 (m, 1 H), 2.00–1.00 (m, 31 H), 0.91 (d, 3 H, J = 6.5 Hz), 0.88 (d, 3 H, J = 1.3 Hz), 0.86 (d, 3 H, J = 1.3 Hz), 0.84 (s, 3 H), 0.65 (s, 3 H); ^{13}C NMR (76 MHz, $CDCl_3$) δ 186.7, 163.6, 134.7, 132.6, 129.9, 128.8, 76.4, 56.4, 56.3, 54.2, 44.7, 42.6, 44.0, 39.5, 36.7, 36.2, 35.8, 35.5, 33.8, 32.0, 28.6, 28.2, 28.0, 27.3, 24.2, 23.8, 22.8, 22.5, 21.2, 18.7, 12.2, 12.1; MS (EI) m/z 518 (M − $2H^+$), 476, 458, 405, 371, 316, 245, 215, 149, 105, 95, 81, 55; HRMS (EI) calcd for $C_{35}H_{52}O_3$ (M − $2H^+$) 518.3759, found (M − $2H^+$) 518.3749. Anal. Calcd for $C_{35}H_{52}O_3$: C, 80.72; H, 10.06. Found: C, 80.74; H, 10.27.

5α-Cholestan-3β-yl 2-Phenylthioacetate (28, Entry 5). Cholestan-3β-yl phenylglyoxylate (**27**) (51 mg, 0.10 mmol), **4b** (108 mg, 0.20 mmol), and $CHCl_3$ (300 μL) were warmed to reflux for 36 h. After cooling, the reaction mixture was chromatographed (eluant hexanes) to yield **28** (45 mg, 87%) as a white solid: mp 116–117 °C (sealed tube, hexane/Et_2O) (lit.[22] mp 105–106 °C); $[\alpha]_D$ +30.1° (c 1.1, $CHCl_3$) (lit.[22] $[\alpha]_D$ +31° (c 1.0, $CHCl_3$)); IR ($CHCl_3$) 3029, 2936, 2867, 1493, 1453, 1378, 1334, 1301, 1277, 1205, 1184, 1122, 1074, 1001, 730, 689; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34–7.21 (m, 5 H), 5.31 (m, 1 H), 3.99 (s, 2 H), 1.98–0.91 (m, 31 H), 0.89 (d, 3 H, J = 6.4 Hz), 0.87 (d, 3 H, J = 0.7 Hz), 0.85 (d, 3 H, J = 0.7 Hz), 0.84 (s, 3 H), 0.64 (s, 3 H); ^{13}C NMR (76 MHz, $CDCl_3$) δ 219.9, 136.3, 129.0, 128.4, 126.9, 81.7, 56.4, 56.3, 54.2, 44.5, 42.6, 40.0, 39.5, 36.6, 36.2, 35.8, 35.5, 32.8, 32.0, 28.6, 28.2, 28.0, 26.5, 24.2, 23.8, 22.8, 22.6, 21.2, 18.7, 12.3, 12.1; MS (EI) m/z 522 ($M^{+\cdot}$), 463, 371, 316, 257, 215, 149, 95, 57; HRMS (EI) calcd for $C_{35}H_{54}OS$ ($M^{+\cdot}$) 522.3895, found ($M^{+\cdot}$) 522.3873. Anal. Calcd for $C_{35}H_{54}OS$: C, 80.47; H, 10.42. Found: C, 80.60; H, 10.63.

5α-Cholestan-3β-yl 2-Phenylthioacetate (28, Entry 6). Cholestan-3β-yl 2-phenylacetate (**29**)[22] (134 mg, 0.26 mmol), **4b** (236 mg, 0.44 mmol), and $CHCl_3$ (1 mL) were warmed to reflux for 18 h. Upon cooling, the reaction mixture was chromatographed (eluant hexanes) to yield **28** (118 mg, 87%) as a white solid: mp 93–94 °C (hexane/Et_2O); $[\alpha]_D$ +30.3° (c 0.51, $CHCl_3$).

5α,6β-Diacetoxy-3β-cholestanyl Thioacetate (31). Triester **30**[23] (123 mg, 0.23 mmol), **4b** (165 mg, 0.31 mmol), and C_6H_6 (1.4 mL) were stirred at 25 °C for 3 h and warmed to reflux overnight. After cooling, the mixture was directly chromatographed (eluant hexane/Et_2O 4:1) to yield monothioester **31** (86 mg, 87%) as a white solid: mp 62–4 °C (hexane); TLC R_f 0.59 (silica; hexane/Et_2O 3:2); $[\alpha]_D$ −101.3° (c 0.95, $CHCl_3$); IR (CCl_4) 2950, 2869, 1744, 1583, 1488, 1365, 1280, 1250, 1120, 1034, 929, cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.94 (app t, 1 H, J = 2.6 Hz), 5.48 (m, 1 H), 2.90 (ddd, 1 H, J = 13.5, 5.0, 1.9 Hz), 2.51 (s, 3 H), 2.09 (s, 3 H), 2.07 (s, 3 H), 2.05–1.25 (m, 17 H), 1.24 (s, 3 H), 1.20–0.88 (m, 5 H), 0.92 (d, 3 H, J = 6.5 Hz), 0.86 (d, 6 H, J = 6.6 Hz), 0.67 (s, 3 H); ^{13}C NMR (76 MHz, $CDCl_3$) δ 218.8, 169.4, 169.3, 86.7, 77.4, 69.6, 56.1, 55.9, 45.4, 42.7, 39.9, 39.8, 39.5, 36.1, 35.7, 34.9, 31.9, 31.3, 30.2, 29.6, 28.1, 28.0, 25.4, 24.0, 23.7, 22.5, 22.1, 21.3, 21.1, 18.7, 17.2, 12.2; MS (EI) m/z 523 (M − C_2H_3O), 504, 488, 442, 428, 385, 367, 325, 159, 95. Anal. Calcd for $C_{33}H_{55}O_5S$: C, 70.30; H, 9.83. Found: C, 70.53; H, 9.85.

3β-Cholestanyl 5-(*tert*-Butyldiphenylsiloxy)thionovalerate (33). Ester **32** (120 mg, 0.17 mmol), **4b** (160 mg, 0.30 mmol), and $CHCl_3$ were heated to reflux for 6 h. Upon cooling, the reaction mixture was chromatographed (eluant hexanes) to yield **33**[4,26] as a clear, colorless syrup (108 mg, 88%).

Acknowledgment. We thank the National Institutes of Health (GM-40949) for support of this program and G.D. Searle & Company for support and for providing microanalyses.

Supplementary Material Available: ^1H and ^{13}C NMR spectra of compounds **6d**, **6e**, and **14** and ^{13}C NMR spectra of compounds **9**, **12**, **15a**, and **18** (10 pages). Ordering information is given on any current masthead page.

(26) Barrett, A. G. M.; Howell, A. R. Unpublished data.