Regioselective Acylation of Hexopyranosides with Pivaloyl Chloride

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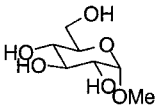
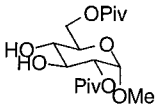
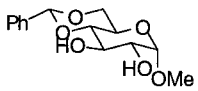
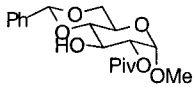
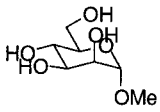
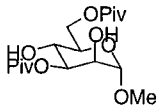
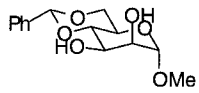
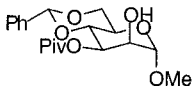
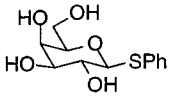
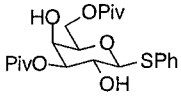
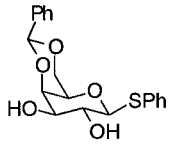
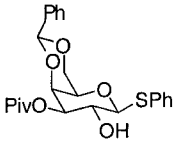
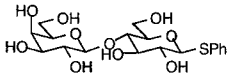
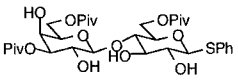
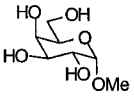
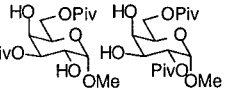
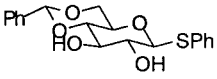
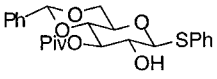
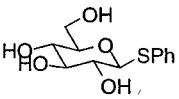
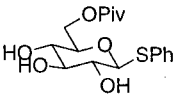
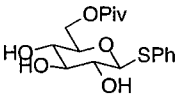
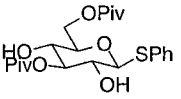
Received February 18, 1998

Selective acylation of carbohydrates is one of the most valuable reactions in carbohydrate synthesis.[1] The most widely studied is selective benzoylation. A number of benzoylating reagents, such as benzoyl cyanide,[2] benzoyl imidazole,[3] and 1-(benzoyloxy)benzotriazole[4] in addition to benzoyl chloride,[5] have been examined. More recently, activation through partial stannylation of carbohydrate with $(Bu_3Sn)_2O$ or Bu_2SnO followed by electrophilic attack with benzoyl chloride[6] has been used. However, the selectivity of benzoylation has not always been high, and the separation of various regioisomers of benzoylated carbohydrate derivatives, often by chromatography, can be tedious. Selective acylation of carbohydrates with pivaloyl chloride to give the corresponding pivaloyl ester has been used, however, mainly as a selective method of esterifying the primary hydroxy group in the presence of secondary hydroxy groups.[7] There have been few systematic studies in the selective pivaloylation of secondary hydroxy groups in various mono- or oligosaccharides. Treatment of methyl α-D-glucopyranoside (**1**) in ether with pivaloyl chloride and pyridine at 4 °C gave almost exclusively the 2,6-di-*O*-pivalate (**2**) (Table 1).[8] Similarly, methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (**3**) gave the corresponding 2-*O*-pivalate **4** as the major product. It thus appears that the 2-OH is the most reactive among all the secondary hydroxy functions in α-D-glucopyranosides. As far as we are aware, no investigation of pivaloylation of other monosaccharides has been reported.[9] Because the pivaloyl esters are usually crystalline compounds and easily characterized by ^{1}H NMR spectroscopy, we became interested in the selective esterification of other hexopyranosides.

Results and Discussion

We found that the use of pivaloyl chloride in pyridine is very effective in the selective acylation of carbohydrates under mild conditions. As reported previously with ether as the solvent, **1** was converted selectively to **2** in 83% yield, and **3** to **4** in 79% yield. On the other hand, treatment of methyl α-D-mannopyranoside (**5**) with pivaloyl chloride in pyridine gave selectively methyl 3,6-di-*O*-pivaloyl-α-D-mannopyranoside (**6**) in 91% isolated yield as a crystalline solid. Similarly, methyl 4,6-*O*-benzylidene-α-D-mannopyranoside (**7**) was regioselectively converted to methyl 3-*O*-pivaloyl-4,6-*O*-benzylidene-α-D-mannopyranoside (**8**) in 89% yield. The higher reactivity of the 3-OH group in mannopyranosides is not unexpected since the 2-OH is in the sterically hindered axial

Table 1. Selective Acylation of Carbohydrates with Pivaloyl Chloride in Pyridine at 0 °C

Entry	Substrate	Product	Isolated Yield (%)
1	 **1**	 **2**	83
2	 **3**	 **4**	79
3	 **5**	 **6**	91
4	 **7**	 **8**	89
5	 **9**	 **10**	78
6	 **11**	 **12**	75
7	 **13**	 **14**	73
8	 **15**	 **16** **17**	88 (1:1)
9	 **18**	 **19**	79
10	 **20**	 **21**	77
11	 **21**	 **22**	74

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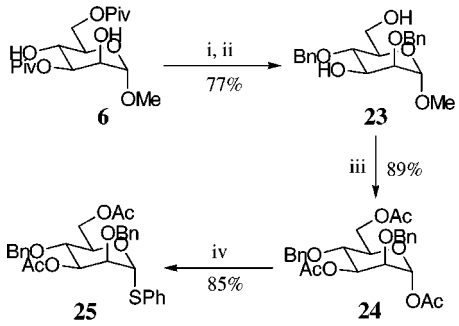
S0022-3263(98)00294-1 CCC: $15.00
Published on Web 07/31/1998

position, and the 4-OH is generally known to be the least reactive. On the other hand, treatment of phenyl 1-thio-β-D-galactopyranoside (**9**) with pivalolyl chloride in pyridine at 0 °C gave the 3,6-di-*O*-pivalate **10** in 78% yield. The selective acylation of 3-OH persisted in the reaction of phenyl 4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside (**11**) under the same conditions. The 3-*O*-pivalate **12** was obtained in 75% yield. The greater reactivity of the 3-OH in the galactopyranosides is more difficult to explain. It may be caused by the lower reactivity of the 2-OH which is due to the presence of the β-substituent at the anomeric position or the enhanced reactivity of the 3-OH due to the presence of the adjacent axial function at the 4-position. It is likely that the latter explanation is more plausible.[10] When the thiophenyl lactose pyranoside **13** was treated with pivaloyl chloride in pyridine, the 3′,6′,6-tri-*O*-pivalate **14** was obtained in 73% yield. It is the 3′-OH with the adjacent axial function (at 4′-OH) rather than the 3-OH that has been esterified selectively after the primary hydroxyl groups. This is in agreement with the observation that methyl α-D-galactopyranoside (**15**) gave a 1:1 mixture of 3,6-di-*O*-pivalate **16** and 2,6-di-*O*-pivalate **17** in 88% yield under the same pivaloylation conditions. It may be due to the similar reactivities of the 2- and 3-OH which are both adjacent to an axial function at 1- and 4-positions. Finally, it should be noted that it is not possible to selectively pivaloylate the primary 6-OH over one of the secondary hydroxyl groups in compouds **1**, **5**, **9**, **13**, and **15**. This suggests that the reactivity of a secondary hydroxyl group with an adjacent axial function is as high as that of the primary 6-OH group toward pivaloylation.[10]

In the absence of the adjacent axial alkoxy group as in the case of the phenyl 1-thio-β-D-glucopyranoside **20**, the compound can be selectively pivaloylated to afford the 6-*O*-pivaloyl-β-D-glucopyranoside **21** in 77% yield together with 10% of the 3,6-di-*O*-pivaloyl-β-D-glucopyranoside **22**. Furthermore, compound **22** can be obtained in high yield (entry 11) from **21** under the same reaction conditions. This tends to suggest that in the absence of an adjacent axial function, the secondary 3-OH may be more reactive than the secondary 2-OH toward pivaloylation. Similarly, high selectivity was observed on the pivaloylation of phenyl 4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (**18**) which gave the 3-*O*-pivalate **19** in 79% yield.

These partially protected carbohydrates are very useful intermediates for oligosaccharide synthesis. For example, the mannose di-*O*-pivalate derivative **6** can be used readily as a precursor for the synthesis of polymannans (Scheme 1).[11] Compound **6** was easily benzylated with benzyl imidate under acidic conditions,[12] and the pivaloyl groups can be readily removed with KOH in CH_3OH to give the 3,6-diol **23** which can serve as the glycosyl acceptor in the synthesis of 3,6-branched polymannans.[11a] Alternatively, compound **23** can undergo acetolysis with

Scheme 1[a]



[a] Reagents and conditions: (i) 4.0 equiv of benzyl 2,2,2-trichloroacetimidate, 0.05 equiv of CF_3SO_3H, 4:1 cyclohexane/CH_2Cl_2, rt, 4 h; (ii) KOH, CH_3OH, reflux for 3 h; (iii) CH_3COOH, $(CH_3CO)_2O$, catalytic H_2SO_4, 4 h; (iv) 1.2 equiv of thiophenol, 0.8 equiv of $Me_3SiOSO_2CF_3$, 4 Å molecular sieves, CH_2Cl_2, 2 h.

acetic anhydride/acetic acid with sulfuric acid as a catalyst to give the 1,3,6-tri-*O*-acetate **24**.[11b] The anomeric acetate group in **24** can be exchanged with thiophenol under acidic conditions to give the phenyl 3,6-di-*O*-acetyl-2,4-di-*O*-benzyl-1-thio-α-D-mannopyranoside **25** which is an important glycosyl donor frequently used in the synthesis of branched high mannans.

Experimental Section

General. ^1H and ^{13}C NMR spectra were recorded at 500 and 125 MHz, respectively, and the chemical shifts are reported in parts per million on the δ scale relative to internal TMS. The site of pivaloylation is determined by 2D COSY ^1H NMR spectroscopy. Melting points are uncorrected. Solvents and reagents were used as received from commercial sources. Analytical thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F-254 polyester-backed plates (250 μm thick). Benzylidene acetals were prepared according to the known procedure.[13]

General Procedure for the Pivaloylation. To a stirred solution of the carbohydrate compound (10 mmol) in pyridine (15 mL) at 0 °C was slowly added pivaloyl chloride (20−50 mmol). The reaction was monitored by TLC, and the addition of pivaloyl chloride was stopped when the starting material or the intermediate disappeared. The reaction mixture was then diluted with ethyl acetate and washed with a dilute HCl solution, a saturated $NaHCO_3$ solution, and then brine. The organic phase was dried over anhydrous $MgSO_4$ and evaporated to dryness. The crude product was subject to flash column chromatography (E. Merck silica gel 60, 230−400 mesh ASTM) using hexanes and ethyl acetate (2:1, v/v) as an eluant to afford the pure product. It can also be crystallized from the 10:1 (v/v) mixture of hexanes and ethyl acetate with a slightly lower yield.

Methyl 2,6-di-*O*-pivaloyl-α-D-glucopyranoside (2):[8] colorless crystals; mp 84−85 °C (lit.[8] mp 82−84 °C); $[\alpha]^{20}_D$ +87.7° (*c* 1.03, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 4.89 (1H, d, 3.7 Hz, *H*-1), 4.60 (1H, dd, 3.7 and 10.0 Hz, *H*-2), 4.52 (1H, dd, 4.4 and 12.2 Hz, *H*-6a), 4.25 (1H, dd, 2.0 and 12.2 Hz, *H*-6b), 3.98 (1H, dd, 9.5 and 9.5 Hz, *H*-3), 3.76 (1H, ddd, 2.2, 4.1, and 10.1 Hz, *H*-5), 3.37 (3H, s, OCH_3), 3.34 (1H, dd, 9.5 and 9.5 Hz, *H*-4), 3.06 [1H, s (br), O*H*], 2.41 [1H, s (br), O*H*], 1.24 [9H, s, COC(CH_3)$_3$]; ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.4, 178.3, 96.9, 72.9, 71.2, 70.4, 69.4, 62.8, 55.3, 38.8, 38.7, 27.0, 26.9.

Methyl 4,6-*O*-benzylidene-2-*O*-pivaloyl-α-D-glucopyranoside (4):[8] colorless crystals; mp 150−152 °C (lit.[8] mp 149−151 °C); $[\alpha]^{20}_D$ +105° (*c* 1.00, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.50−7.37 (5H, m, Ar-*H*), 5.56 (1H, s, PhC*H*), 4.94 (1H, d, 3.7 Hz, *H*-1), 4.74 (1H, dd, 3.7 and 9.5 Hz, *H*-2), 4.30 (1H, dd, 4.6 and 10.3 Hz, H-6a), 4.20 (1H, dd, 9.5 and 9.5 Hz, *H*-3), 3.86 (1H, ddd, 4.6, 9.9, and 10.0 Hz, *H*-5), 3.77 (1H, dd, 10.0 and 10.3 Hz,

(10) The origin of the selectivity is not clear. Since pivaloyl chloride is relatively bulky, it is likely that the reagent would approach the hydroxyl group from the side and not from the top or bottom of the ring system. The reaction is therefore more subject to steric hindrance of the adjacent equatorial substituents.

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H-6b), 3.57 (1H, dd, 9.4 and 9.4 Hz, *H*-4), 3.39 (3H, s, OCH_3), 2.31 [1H, s (br), C_3-O*H*], 1.24 [9H, s, COC(CH_3)$_3$]; ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.2, 137.0, 129.3, 128.3, 126.3, 102.0, 97.6, 81.3, 73.4, 68.9, 68.8, 62.0, 55.6, 38.9, 27.0.

Methyl 3,6-di-*O*-pivaloyl-α-D-mannopyranoside (6): colorless crystals; R_f = 0.28 (2:1 hexanes/EtOAc); mp 93−94 °C; $[\alpha]^{20}_D$ +56.3° (*c* 0.71, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.04−5.01 (1H, m, *H*-3), 4.70 (1H, d, 1.7 Hz, *H*-1), 4.41−4.35 (2H, m, *H*-6a, *H*-6b), 3.98 [1H, s (br), *H*-2], 3.81−3.75 (2H, m, *H*-4, *H*-5), 3.38 (3H, s, OCH_3), 2.62 (1H, d, 2.2 Hz, C_4-O*H*), 1.86 (1H, d, 2.9 Hz, C_2-O*H*), 1.23 [9H, s, COC(CH_3)$_3$], 1.22 [9H, s, COC(CH_3)$_3$]; ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.9, 178.8, 100.4, 74.2, 70.9, 69.4, 66.3, 63.2, 54.9, 39.0, 38.7, 27.2, 27.1; FAB HRMS calcd for $C_{17}H_{31}O_8$ (M + H^+) 363.2019, found 363.2018. Anal. Calcd for $C_{17}H_{30}O_8$: C, 56.34; H, 8.34. Found: C, 56.72; H, 8.34.

Methyl 4,6-*O*-benzylidene-3-*O*-pivaloyl-α-D-mannopyranoside (8): colorless crystals; R_f = 0.27 (2:1 hexanes/EtOAc); mp 98−100 °C; $[\alpha]^{20}_D$ +28.9° (*c* 0.58, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44−7.32 (5H, m, Ar-*H*), 5.57 (1H, s, PhC*H*), 5.33 (1H, dd, 3.4 and 10.3 Hz, *H*-3), 4.76 (1H, d, 1.7 Hz, *H*-1), 4.30 (1H, dd, 4.2 and 9.8 Hz, *H*-6a), 4.13 (1H, dd, 1.5 and 3.2 Hz, *H*-2), 4.10 (1H, dd, 9.3 and 10.3 Hz, *H*-4), 3.92 (1H, ddd, 4.4, 9.3, and 10.3 Hz, *H*-5), 3.85 (1H, dd, 10.0 and 10.3 Hz, *H*-6b), 3.41 (3H, s, OCH_3), 2.04 [1H, s (br), C_2-O*H*], 1.23 [9H, s, COC(CH_3)$_3$]; ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.2, 137.3, 128.8, 128.2, 125.9, 101.4, 101.3, 76.3, 70.4, 70.0, 68.9, 63.6, 55.1, 39.0, 27.2; FAB HRMS calcd for $C_{19}H_{27}O_7$ (M + H^+) 367.1757, found 367.1755. Anal. Calcd for $C_{19}H_{26}O_7$: C, 62.27; H, 7.16. Found: C, 62.24; H, 7.25.

Phenyl 3,6-di-*O*-pivaloyl-1-thio-β-D-galactopyranoside (10): colorless cryatals; R_f = 0.38 (2:1 hexanes/EtOAc); mp 107−108 °C; $[\alpha]^{20}_D$ +11.5° (*c* 0.75, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57−7.31 (5H, m, Ar-*H*), 4.88 (1H, dd, 3.2 and 9.5 Hz, *H*-3), 4.61 (1H, d, 9.8 Hz, *H*-1), 4.35 (1H, dd, 5.5 and 11.6 Hz, *H*-6a), 4.28 (1H, dd, 6.8 and 11.6 Hz, *H*-6b), 4.01 [1H, s (br), *H*-4], 3.88 [1H, dd (br), 9.5 and 9.8 Hz, *H*-2], 3.80 [1H, dd (br), 6.1 and 6.1 Hz, *H*-5], 2.37 [1H, s (br), C_2-O*H*], 2.06 [1H, s (br), C_4-O*H*], 1.25 [9H, s, COC(CH_3)$_3$], 1.20 [9H, s, COC(CH_3)$_3$]; ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.4, 178.0, 132.4, 132.3, 129.1, 128.1, 89.6, 76.2, 75.6, 67.6 (2C), 62.8, 39.1, 38.8, 27.2, 27.1; FAB HRMS calcd for $C_{22}H_{33}O_7S$ (M + H^+) 441.1947, found 441.1949. Anal. Calcd for $C_{22}H_{32}O_7S$: C, 59.97; H, 7.33. Found: C, 59.77; H, 7.54.

Phenyl 4,6-*O*-benzylidene-3-*O*-pivaloyl-1-thio-β-D-galactopyranoside (12): colorless cryatals; R_f = 0.36 (2:1 hexanes/EtOAc); mp 178−179 °C; $[\alpha]^{20}_D$ +46.7° (*c* 0.61, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67−7.20 (10H, m, Ar-*H*), 5.50 (1H, s, PhC*H*), 4.86 (1H, dd, 3.5 and 9.6 Hz, *H*-3), 4.60 (1H, d, 9.5 Hz, *H*-1), 4.40−4.37 (2H, m, *H*-4, *H*-6a), 4.05−4.01 (2H, m, *H*-6b, *H*-2), 3.61 [1H, s (br), *H*-5], 2.29 (1H, d, 2.7 Hz, C_2-O*H*), 1.19 [9H, s, COC(CH_3)$_3$]; ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.4, 137.8, 133.0, 131.1, 129.0, 128.9, 128.1, 128.0, 126.1, 100.5, 88.0, 74.6, 73.4, 69.9, 69.2, 65.9, 39.0, 27.0; FAB HRMS calcd for $C_{24}H_{29}O_6S$ (M + H^+) 445.1685, found 445.1686. Anal. Calcd for $C_{24}H_{28}O_6S$: C, 64.84; H, 6.35. Found: C, 64.90; H, 6.29.

Phenyl 4-(3′,6′-di-*O*-pivaloyl-β-D-galactopyranosyl)-6-*O*-pivaloyl-1-thio-β-D-glucopyranoside (14): colorless crystals; R_f = 0.40 (1:2 hexanes/EtOAc); mp 101−103 °C; $[\alpha]^{20}_D$ +10.8° (*c* 0.58, CH_3OH); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57−7.27 (5H, m, Ar-*H*), 4.83 (1H, dd, 3.3 and 10.1 Hz, *H*-3 Gal), 4.67 (1H, dd, 1.5 and 12.0 Hz, *H*-6a Glc), 4.58 (1H, d, 9.8 Hz, *H*-1 Glc), 4.38 (1H, dd, 4.9 and 11.9 Hz, *H*-6a Gal), 4.35 (1H, d, 7.6 Hz, *H*-1 Gal), 4.23 (1H, dd, 7.3 and 11.7 Hz, *H*-6b Gal), 4.21 (1H, d, 1.5 Hz, C_3-O*H* Glc), 4.12 (1H, dd, 5.9 and 12.3 Hz, *H*-6b Glc), 3.99 [1H, dd (br), 4.2 and 4.4 Hz, *H*-4 Gal], 3.92 (1H, ddd, 3.9, 7.8, and 10.3 Hz, *H*-2 Gal), 3.82 [1H, dd (br), 4.9 and 7.6 Hz, *H*-5 Gal], 3.64 (1H, ddd, 1.2, 8.6, and 8.8 Hz, *H*-3 Glc), 3.55 (1H, ddd, 1.5, 6.1, and 10.0 Hz, *H*-5 Glc), 3.39 (1H, ddd, 1.7, 8.8, and 9.8 Hz, *H*-2 Glc), 3.32 [1H, s (br), C_2-O*H* Gal], 3.31 (1H, dd, 8.4 and 9.8 Hz, *H*-4 Glc), 2.79 [1H, s (br), C_2-O*H* Glc], 2.42 [1H, s (br), C_4-O*H* Gal], 1.25 [9H, s, COC(CH_3)$_3$], 1.20 [9H, s, COC(CH_3)$_3$], 1.19 [9H, s, COC(CH_3)$_3$]; ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.8, 178.5, 178.0, 132.5, 132.2, 128.9, 128.0, 104.3, 87.2, 80.9, 77.3, 76.1, 74.2, 73.1, 71.6, 69.0, 67.2, 63.4, 62.8, 39.0, 38.9, 38.8, 27.2, 27.1, 27.0; FAB HRMS calcd for $C_{33}H_{50}O_{13}SNa$ (M + Na^+) 709.2870, found 709.2868. Anal. Calcd for $C_{33}H_{50}O_{13}S\cdot 2H_2O$: C, 54.82; H, 7.53. Found: C, 55.16; H, 7.68.

Mixture of methyl 3,6-di-*O*-pivaloyl-α-D-galactopyranoside (16) and methyl 2,6-di-*O*-pivaloyl-α-D-galactopyranoside (17): colorless foam; R_f = 0.30 (2:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.05 (1H, dd, 3.2 and 10.3 Hz), 4.93 (1H, dd, 3.7 and 10.0 Hz), 4.89 (1H, d, 3.7 Hz), 4.84 (1H, d, 3.9 Hz), 4.43 (1H, dd, 6.3 and 11.5 Hz), 4.33 (1H, dd, 5.4 and 11.5 Hz), 4.24 (1H, dd, 7.1 and 11.5 Hz), 4.20 (1H, dd, 6.6 and 11.5 Hz), 4.04−3.95 (5H, m), 3.92 [1H, dd (br), 3.2 and 3.4 Hz], 3.45 (3H, s, OCH_3), 3.37 (3H, s, OCH_3), 2.70 (1H, d, 3.7 Hz, O*H*), 2.56 (1H, d, 6.8 Hz, O*H*), 2.06 (1H, d, 1.9 Hz, O*H*), 1.88 (1H, d, 11.2 Hz, O*H*), 1.26 [9H, s, COC(CH_3)$_3$], 1.24 [9H, s, COC(CH_3)$_3$], 1.22 [9H, s, COC(CH_3)$_3$], 1.21 [9H, s, COC(CH_3)$_3$]; ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.0, 178.7, 178.4, 178.3, 99.6, 97.4, 72.7, 71.4, 69.4, 68.3, 68.2, 68.0, 67.6, 67.3, 63.1, 63.0, 55.4 (2C), 39.0, 38.9, 38.8 (2C), 27.1 (2C), 27.0 (2C).

Phenyl 4,6-*O*-benzylidene-3-*O*-pivaloyl-1-thio-β-D-glucopyranoside (19): colorless cryatals; R_f = 0.51 (2:1 hexanes/EtOAc); mp 131−132 °C; $[\alpha]^{20}_D$ −71.2° (*c* 0.68, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56−7.33 (10H, m, Ar-*H*), 5.52 (1H, s, PhC*H*), 5.19 (1H, dd, 9.1 and 9.5 Hz, *H*-3), 4.71 (1H, d, 9.8 Hz, *H*-1), 4.40 (1H, dd, 5.0 and 10.6 Hz, *H*-6a), 3.79 (1H, dd, 10.3 and 10.3 Hz, *H*-6b), 3.66 (1H, dd, 9.5 and 9.5 Hz, *H*-4), 3.59−3.54 (2H, m, *H*-2, *H*-5), 2.88 (1H, d, 2.9 Hz, C_2-O*H*), 1.22 [9H, s, COC(CH_3)$_3$]; ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.9, 136.9, 133.0, 131.6, 129.1, 128.9, 128.4, 128.2, 125.9, 101.1, 89.6, 78.2, 75.0, 71.9, 70.7, 68.5, 39.0, 27.1; FAB HRMS calcd for $C_{24}H_{29}O_6S$ (M + H^+) 445.1685, found 445.1686. Anal. Calcd for $C_{24}H_{28}O_6S$: C, 64.84; H, 6.35. Found: C, 64.83; H, 6.60.

Phenyl 6-*O*-pivaloyl-1-thio-β-D-glucopyranoside (21): colorless foam; R_f = 0.20 (1:3 hexanes/EtOAc); $[\alpha]^{20}_D$ −32.5° (*c* 0.75, CH_3OH); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50−7.18 (5H, m, Ar-*H*), 4.58 (1H, d, 9.8 Hz, *H*-1), 4.48 [s (br), H_2O], 4.43 (1H, dd, 1.8 and 12.1 Hz, *H*-6a), 4.14 (1H, dd, 6.9 and 12.1 Hz, *H*-6b), 3.56 (1H, dd, 8.8 and 9.0 Hz, *H*-3), 3.51 (1H, ddd, 1.8, 7.2, and 9.7 Hz, *H*-5), 3.37 (1H, dd, 9.3 and 9.3 Hz, *H*-2), 3.33 (1H, dd, 9.5 and 9.5 Hz, *H*-4), 1.16 [9H, s, COC(CH_3)$_3$]; ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.1, 132.8, 131.8, 128.9, 127.6, 87.6, 77.7, 77.6, 71.9, 70.1, 64.0, 38.8, 27.1; FAB HRMS calcd for $C_{17}H_{25}O_6S$ (M + H^+) 357.1372, found 357.1370. Anal. Calcd for $C_{17}H_{24}O_6S\cdot H_2O$: C, 54.53; H, 7.00. Found: C, 54.89; H, 6.70.

Phenyl 3,6-di-*O*-pivaloyl-1-thio-β-D-glucopyranoside (22): colorless cryatals; R_f = 0.36 (2:1 hexanes/EtOAc); mp 70−71 °C; $[\alpha]^{20}_D$ −34.8° (*c* 0.56, CH_3OH); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59−7.29 (5H, m, Ar-*H*), 4.89 (1H, dd, 9.2 and 9.2 Hz, *H*-3), 4.58 (1H, d, 9.8 Hz, *H*-1), 4.43 (1H, dd, 2.3 and 12.1 Hz, *H*-6a), 4.34 (1H, dd, 5.5 and 12.1 Hz, *H*-6b), 3.59 (1H, ddd, 2.3, 5.5, and 9.8 Hz, *H*-5), 3.46 (1H, dd, 9.4 and 9.4 Hz, *H*-2), 3.44 (1H, dd, 9.5 and 9.5 Hz, *H*-4), 3.02 [1H, s (br), O*H*], 2.58 [1H, s (br), O*H*], 1.24 [9H, s, COC(CH_3)$_3$], 1.22 [9H, s, COC(CH_3)$_3$]; ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.3, 178.8, 132.8, 131.7, 129.0, 128.2, 88.4, 79.0, 78.5, 70.4, 69.2, 63.4, 39.1, 38.9, 27.2, 27.1; FAB HRMS calcd for $C_{22}H_{33}O_7S$ (M + H^+) 441.1947, found 441.1949. Anal. Calcd for $C_{22}H_{32}O_7S\cdot 0.75H_2O$: C, 58.19; H, 7.44. Found: C, 58.31; H, 7.27.

Methyl 2,4-di-*O*-benzyl-α-D-mannopyranoside (23):[11a] colorless syrup; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38−7.25 (10H, m, Ar-*H*), 4.91 (1H, d, 11.2 Hz, PhCH_2), 4.75 (1H, d, 1.7 Hz, *H*-1), 4.72 (1H, d, 11.7 Hz, PhCH_2), 4.66 (1H, d, 11.2 Hz, PhCH_2), 4.60 (1H, d, 11.7 Hz, PhCH_2), 3.98 (1H, dd, 3.9 and 9.0 Hz, *H*-3), 3.86 (1H, dd, 2.9 and 11.7 Hz, *H*-6a), 3.79 (1H, dd, 4.4 and 11.7 Hz, *H*-6b), 3.73 (1H, dd, 1.7 and 3.7 Hz, *H*-2), 3.67 (1H, dd, 9.5 and 9.5 Hz, *H*-4), 3.59 (1H, ddd, 2.9, 4.4, and 9.8 Hz, *H*-5), 3.31 (3H, s, OCH_3), 2.27 [1H, s (br), C_2-O*H*], 1.93 [1H, s (br), C_6-O*H*]; ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.3, 137.6, 128.6, 128.5, 128.1, 128.0, 127.8, 127.7, 98.1, 78.3, 76.5, 74.9, 73.1, 71.7, 71.1, 62.3, 54.8.

1,3,6-Tri-*O*-acetyl-2,4-di-*O*-benzyl-α-D-mannopyranose (24):[11a] colorless syrup; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.25 (10H, m, Ar-*H*), 6.15 (1H, d, 2.2 Hz, *H*-1), 5.19 (1H, dd, 3.4 and 9.3 Hz, *H*-3), 4.71 (1H, d, 12.2 Hz, PhCH_2), 4.69 (1H, d, 11.2 Hz, PhCH_2), 4.57 (1H, d, 11.2 Hz, PhCH_2), 4.53 (1H, d, 12.2 Hz, PhCH_2), 4.31 (1H, dd, 2.2 and 12.2 Hz, *H*-6a), 4.27 (1H, dd, 4.4 and 12.2 Hz, *H*-6b), 3.99 (1H, dd, 9.5 and 9.8 Hz, *H*-4), 3.93 (1H, ddd, 2.2, 4.4, and 9.8 Hz, *H*-5), 3.84 (1H, dd, 2.2 and 3.4 Hz, *H*-2), 2.08 (3H, s, COCH_3), 2.05 (3H, s, COCH_3), 1.96 (3H, s, COCH_3).

Phenyl 3,6-di-*O*-acetyl-2,4-di-*O*-benzyl-1-thio-α-D-mannopyranoside (25): colorless foam; R_f = 0.42 (2:1 hexanes/EtOAc); $[\alpha]^{20}_D$ +64.9° (*c* 0.50, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47−7.25 (15H, m, Ar-*H*), 5.54 (1H, d, 2.0 Hz, *H*-1), 5.20 (1H,

dd, 3.3 and 9.4 Hz, *H*-3), 4.71 (1H, d, 11.0 Hz, C*H*$_2$Ph), 4.67 (1H, d, 12.2 Hz, C*H*$_2$Ph), 4.58 (1H, d, 11.2 Hz, C*H*$_2$Ph), 4.48 (1H, d, 12.2 Hz, C*H*$_2$Ph), 4.38 (1H, ddd, 3.2, 4.7, and 9.8 Hz, *H*-5), 4.34−4.28 (2H, m, *H*-6a, *H*-6b), 4.11 (1H, dd, 2.0 and 3.2 Hz, *H*-2), 3.98 (1H, dd, 9.5 and 9.5 Hz, *H*-4), 2.02 (3H, s, COC*H*$_3$), 1.98 (3H, s, COC*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.6, 170.0, 137.7, 137.4, 133.7, 131.8, 129.0, 128.5, 128.4, 127.9 (2C), 127.8, 127.7, 127.6, 85.1, 76.9, 74.7, 73.8, 73.5, 72.2, 70.6, 63.3, 20.9, 20.8; FAB HRMS calcd for $C_{24}H_{27}O_7$ ($MH^+ - C_6H_6S$) 427.1757, found 427.1756. Anal. Calcd for $C_{30}H_{32}O_7S$: C, 67.14; H, 6.01. Found: C, 66.93; H, 5.91.

Acknowledgment. We thank the Natural Sciences and Engineering Research Council of Canada and FCAR of Quebec for financial support.

JO980294V