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Selectivity Switch in the Catalytic Functionalization of Nonprotected Carbohydrates: Selective Synthesis in the Presence of Anomeric and Structurally Similar Carbohydrates under Mild Conditions

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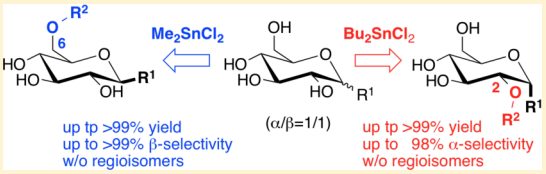
Supporting Information

ABSTRACT: A catalytic process for the chemo- and regioselective functionalization of nonprotected carbohydrates has been developed. This novel process allows selective thiocarbonylation, acylation, and sulfonylation of a particular hydroxy group in a particular carbohydrate in the simultaneous presence of structurally similar carbohydrates such as anomers. In addition, the chemoselectivity can be switched by regulating only the length of the alkyl chain in the organotin catalyst.



INTRODUCTION

Carbohydrates including oligosaccharides and glycoconjugates have been known to play crucial roles in various physiologic and pathologic events such as cell adhesion, fertilization, and cancer cell metastases.[1] With the aim to gain insight into the mechanism of these events and to develop new medicines, the development of efficient routes and comprehensive procedures for the high purity synthesis of such carbohydrates is indispensable. In the past years, various methods for stereo- and regioselective synthesis of carbohydrates have been developed.[2] However, these methods do not necessarily afford high stereo- and regioselectivity to all the substrates, and subsequent separation of anomers by simple methods such as silica gel column chromatography and recrystallization is generally very difficult as anomers often have similar polarity and solubility properties. In addition, special instrument techniques such as high-performance liquid chromatography (HPLC) are unsuitable for the fast separation of a large quantity of anomers. Therefore, effort-consuming derivatization of anomers with multistep protection−deprotection sequences has been often attempted for separation of anomers. To resolve such problems, enzymatic method for the separation of an anomeric mixture of carbohydrates and structurally similar carbohydrates has been developed in the last few decades.[3] For example, Gotor and co-workers reported the separation method of an anomeric mixture of α- and β-D-nucleosides through regioselective lipase-catalyzed acylation.[3d] More recently, Prasad and co-workers reported the separation method of a mixture of furanosyl and pyranosyl nucleosides through chemo- and regioselective lipase-catalyzed acylation.[3e] These catalyses are useful techniques for the separation with protection (acyl) group in a minimum number of steps. However, the resulting functionalized nucleosides and carbohydrates are usually not the ideal precursors for further functionalization. To the best of our knowledge, on the other hand, a nonenzymatic method has not been reported to date. Herein, we present research to facilitate chemical functionalization and separation of carbohydrates utilizing the high molecular recognition ability of organotin catalysts.

RESULTS AND DISCUSSION

In the last a few years, we have investigated a catalytic method for the regioselective introduction of useful functional groups into nonprotected carbohydrates.[2j,4] In these results, we found that Me_2SnCl_2-catalyzed reaction at C(6)-OH of methyl β-D-glucopyranoside was much faster than Bu_2SnCl_2 (or Oc_2SnCl_2)-catalyzed reaction. On the other hand, Bu_2SnCl_2 (or Oc_2SnCl_2)-catalyzed reaction at C(2)-OH of methyl α-D-glucopyranoside was faster than Me_2SnCl_2-catalyzed reaction. Therefore, we expect that a particular carbohydrate can be selectively functionalized (= extracted) among structurally similar carbohydrates by regulating the length of the alkyl chain in the organotin catalyst.

First of all, we investigated the chemo- and regioselective thiocarbonylation of methyl D-glucopyranosides with various organotin catalysts (10 mol %) in entries 1−16 in Table 1. Treatment of a mixture of methyl α-D-glucopyranoside and methyl β-D-glucopyranoside (1.0 equiv) with phenyl chlorothionoformate (1.3 equiv) as an electrophile, 1,2,2,6,6-pentamethylpiperidine (PEMP, 1.5 equiv), and tetrabutylammonium iodide (TBAI, 10 mol %) in the absence of organotin catalysts in THF at 20 °C gave no products (entry 1). In the presence of Me_2SnCl_2, methyl β-D-glucopyranoside was selectively converted into methyl 6-*O*-phenoxythiocarbonyl-β-D-glucopyranoside **1b** without formation of its regioisomers (entry 2; 93% yield and 79% chemoselectivity). On the other hand, Bu_2SnCl_2 favored selective formation of methyl 2-*O*-phenoxythiocarbonyl-α-D-glucopyranoside **1a** without formation of its regioisomers (entry 3; 80% yield and 95% chemoselectivity). High selectivities to **1a** were also afforded

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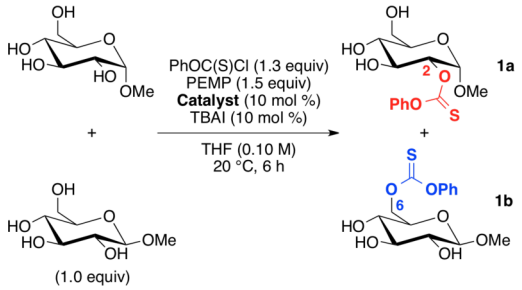
Table 1. Scope of a Catalyst in Chemo- and Regioselective Thiocarbonylation



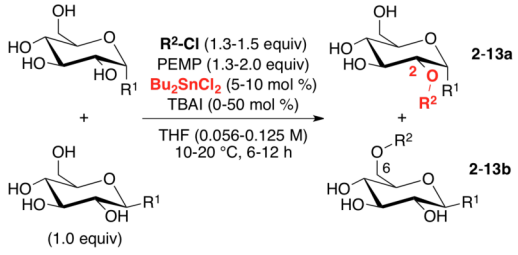
entry	catalyst	yield of **1a**[a] (%)	yield of **1b**[a] (%)	ratio[a] (**1a**/**1b**)
1	none	0	0	nd
2	Me_2SnCl_2	24	93	21:79
3	Bu_2SnCl_2	80	4	95:5
4	*t*-Bu_2SnCl_2	0	0	nd
5	Oc_2SnCl_2[b]	81	9	90:10
6	Dd_2SnCl_2[c]	64	10	87:13
7	Ph_2SnCl_2	0	0	nd
8	Me_2SnBr_2	26	91	22:78
9	Me_2SnO	29	38	43:57
10	Me_2SnS	24	90	21:79
11	Bu_2SnBr_2	53	2	96:4
12	$Bu_2Sn(OAc)_2$	46	13	78:22
13	$Bu_2Sn(OTf)_2$	38	13	75:25
14	$Bu_2Sn(OMe)_2$	66	13	89:11
15	Bu_2SnO	21	0	>99:<1
16	Bu_2SnS	61	4	94:6
17[d]	Me_2SnCl_2	20	97	17:83
18[e]	Me_2SnCl_2	15	87	14:86
19[f]	Me_2SnCl_2	17	78	18:82
20[g]	Me_2SnCl_2	10	74	12:88
21[d]	Bu_2SnCl_2	73	4	95:5
22[e]	Bu_2SnCl_2	32	11	74:26
23[h]	Bu_2SnCl_2	50	9	86:14
24[i]	Bu_2SnCl_2	74	7	91:9
25[j]	Me_2SnCl_2	2	91	2:98
26[j]	Bu_2SnCl_2	>99	3	97:3

[a]The yield and ratio were calculated by ^{1}H NMR after isolation of mixture of **1a** and **1b**. [b]Oc = *n*-octyl. [c]Dd = *n*-dodecyl. [d]Without TBAI. [e]3,5-Lutidine was added instead of TBAI. [f]3,5-Diphenylpyridine was added instead of TBAI. [g]DMAP was added instead of TBAI. [h]TMAI was added instead of TBAI. [i]TBABr was added instead of TBAI. [j]Under optimized conditions (see the Experimental Section).

with Oc_2SnCl_2 and Dd_2SnCl_2 (entries 5 and 6), whereas *t*-Bu_2SnCl_2 and Ph_2SnCl_2 were completely ineffective (entries 4 and 7). Dimethyltin and dibutyltin derivatives were also employed as catalysts in the titled reaction. Unlike Me_2SnO (entry 9), Me_2SnBr_2 and Me_2SnS afforded the desired product **1b** in 90−91% yields with 78−79% chemoselectivities (entries 8 and 10). On the other hand, organotin catalysts containing a butyl group furnished **1a** with yields up to 66% and chemoselectivities up to >99% (entries 11−16). Next, we investigated a screening of additive reagent instead of TBAI. In the case of Me_2SnCl_2 without TBAI, the catalysis gave better yield and chemoselectivity (entry 17; 97% yield and 83% chemoselectivity). Addition of 3,5-lutidine (10 mol %) instead of TBAI improved the chemoselectivity (entry 18; 87% yield and 86% chemoselectivity). However, addition of the other pyridine derivatives such as DMAP or ammonium salts did not bring a superior result (entries 19 and 20). On the other hand, Bu_2SnCl_2-catalyzed reaction without TBAI gave slightly lower yield (entry 21; 73% yield and 95% chemoselectivity). Additionally, addition of the other pyridine derivatives such as DMAP or ammonium salts also did not give better results (entries 22−24). Finally after a series of optimization studies, we found that the selective thiocarbonylation at C(6)-OH of methyl *β*-D-glucopyranoside in the presence of methyl *α*-D-glucopyranoside (1.0 equiv), Me_2SnCl_2 (10 mol %), 3,5-lutidine (10 mol %), and PEMP (1.5 equiv) in THF at 20 °C with slow addition of phenyl chlorothionoformate (1.3 equiv) proceeded efficiently in 91% yield and 98% chemoselectivity without formation of its regioisomers (entry 25). On the other hand, selective thiocarbonylation at C(2)-OH of methyl *α*-D-glucopyranoside in the presence of methyl *β*-D-glucopyranoside (1.0 equiv), Bu_2SnCl_2 (10 mol %), TBAI (50 mol %),[4] PEMP (1.3 equiv), and phenyl chlorothionoformate (1.3 equiv) in THF at 20 °C proceeded efficiently in >99% yield and 97% chemoselectivity without formation of its regioisomers (entry 26).

Once optimized conditions were identified, we next performed the Bu_2SnCl_2-catalyzed chemo- and regioselective functionalization with respect to both the substituent R^1 at C(1)-position of D-glucopyranosides and several kinds of electrophiles (Table 2). Substrates with *O*-alkyl or *O*-aryl

Table 2. Chemo- and Regioselective Functionalization Catalyzed by Bu_2SnCl_2



entry	R^1/R^2	products	yield[a] (**a**/**b**, %)	ratio[a] (**a**/**b**)
1	OOc/PhOC(S)	**2a**, **2b**	96:4	96:4
2	OPh/PhOC(S)	**3a**, **3b**	92:2	98:2
3	OPNP[b]/PhOC(S)	**4a**, **4b**	92:2	98:2
4	SEt/PhOC(S)	**5a**, **5b**	92:9	91:9
5	OMe/(4-Tol)OC(S)	**6a**, **6b**	95:6	94:6
6	OMe/(2-Naph)OC(S)	**7a**, **7b**	>99:2	98:2
7	OMe/(4-Cl-Ph)OC(S)	**8a**, **8b**	>99:5	95:5
8	OMe/(4-F-Ph)OC(S)	**9a**, **9b**	>99:3	97:3
9	OMe/$Me_2NC(S)$	**10a**, **10b**	0:0	nd
10	OMe/Bz	**11a**, **11b**	>99:8	93:7
11	OMe/*i*-PrC(O)	**12a**, **12b**	96:11	90:10
12	OMe/(3,5-CF_3)-$PhSO_2$	**13a**, **13b**	97:14	87:13

[a]The yield and ratio were calculated by ^{1}H NMR after isolation of mixture of **2**−**13a** and **2**−**13b**. [b]PNP = *p*-nitrophenyl.

substituents R^1 at the C(1)-position were readily thiocarbonylated at C(2)-OH of *α*-D-glucopyranosides with 92−96% yields and 96−98% chemoselectivities (entries 1−3). Ethyl *β*-D-thioglucopyranoside,[5] a useful glycosyl donor, was converted under the same reaction conditions to the corresponding thiocarbonate **5a** with 92% yield and 91% chemoselectivity (entry 4). The use of chlorothionoformates R^2-Cl containing an electron-donating or electron-withdrawing group as an electro-

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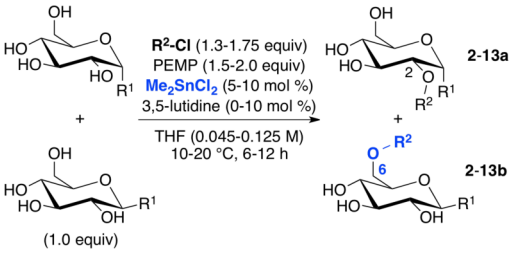
phile resulted in strong reactivities and high selectivities at C(2)-OH, whereas dimethylthiocarbamoyl chloride did not show reactivity for this reaction (entries 5−9). Remarkably, the protocol herein described can be applied for the chemo- and regioselective introduction of acyl protection groups as well as sulfonyl functionalities serving as a good leaving group for the subsequent nucleophilic substitution reactions (entries 10−12). In these catalytic reactions, the corresponding regioisomers were not observed.

On the other hand, the results for the Me_2SnCl_2-catalyzed chemo- and regioselective functionalization with respect to both the substituent R^1 at C(1)-position of D-glucopyranosides and several kinds of electrophiles R^2-Cl are shown in Table 3.

Table 3. Chemo- and Regioselective Functionalization Catalyzed by Me_2SnCl_2



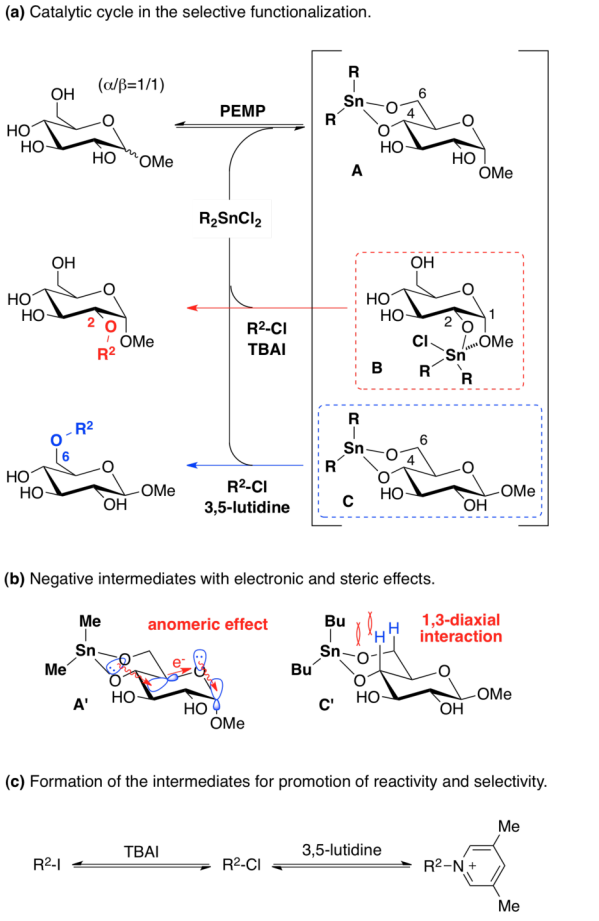
entry	R^1/R^2	products	yield[a] (a/b, %)	ratio[a] (a/b)
1	OOc/PhOC(S)	**2a**, **2b**	12:85	12:88
2	OPh/PhOC(S)	**3a**, **3b**	14:68	17:83
3	OPNP[b]/PhOC(S)	**4a**, **4b**	18:68	21:79
4	SEt/PhOC(S)	**5a**, **5b**	5:79	6:94
5	OMe/(4-Tol)OC(S)	**6a**, **6b**	6:91	6:94
6	OMe/(2-Naph)OC(S)	**7a**, **7b**	3:80	4:96
7	OMe/(4-Cl-Ph)OC(S)	**8a**, **8b**	4:82	4:96
8	OMe/(4-F-Ph)OC(S)	**9a**, **9b**	6:90	6:94
9	OMe/Me_2NC(S)	**10a**, **10b**	0:0	nd
10	OMe/Bz	**11a**, **11b**	7:97	7:93
11	OMe/*i*-PrC(O)	**12a**, **12b**	<1:>99	<1:>99
12	OMe/(3,5-CF_3)-$PhSO_2$	**13a**, **13b**	<1:>99	<1:>99

[a]The yield and ratio were calculated by ^{1}H NMR after isolation of mixture of **2**−**13a** and **2**-**13b**. [b]PNP = *p*-nitrophenyl.

In the screening of the R^1 substituent, selective thiocarbonylation at C(6)-OH of *β*-D-glucopyranosides proceeded in 68−85% yields and 79−94% chemoselectivities without formation of its regioisomers (entries 1−4). Similarly, the catalytic thiocarbonylation with various chlorothionoformates R^2-Cl as electrophiles proceeded in high yields and excellent selectivities (entries 5−8). As in the case of Bu_2SnCl_2, dimethylthiocarbamoyl chloride was not effective under the reaction conditions of the present study (entry 9). Again, this protocol can be further applied for chemo- and regioselective acylation and sulfonylation with 92−>99% yields and 93−>99% chemoselectivities (entries 10−12).

The mechanism explaining the chemo- and regioselectivities in the catalytic functionalization of D-glucopyranosides can be rationalized as follows (Scheme 1a).[6] Organotin catalysts coordinate reversibly to *cis*-1,2- or 1,3-diol moieties after moving freely among diol moieties. As the coordination of metal ions may increase the acidity of hydroxy groups, even a weak base such as PEMP is sufficient to induce deprotonation of both hydroxy groups leading to five- or six-membered ring

Scheme 1. Plausible Mechanism of the Chemo- and Regioselective Functionalization



intermediates **A**, **B**, or **C** whose subsequent irreversible functionalization proceeds much more rapidly at the less hindered hydroxy group. In the case of the use of organotin catalysts containing long alkyl groups such as Bu_2SnCl_2 and Oc_2SnCl_2, the catalytic functionalization proceeds with high chemo- and regioselectivities at C(2)-OH of *α*-D-glucopyranosides via kinetically stabilized intermediate **B** as the other intermediates **A** and **C** are unstabilized by the 1,3-diaxial interaction such as **C′** between the alkyl group R and axial-H at C(4)- and C(6)-positions (Scheme 1b). Additionally, comparatively more reactive electrophiles R^2-I, generated from R^1-Cl and TBAI, accelerate the reaction (Scheme 1c).

In the case of the use of Me_2SnCl_2, the catalytic functionalization proceeds selectively at the less hindered hydroxy group, C(6)-OH, of *β*-D-glucopyranosides through the intermediate **C**. Additionally, a bulky pyridinium intermediate, generated from R^1-Cl and 3,5-lutidine (Scheme 1c), yielded 6-*O*-functionalized-*β*-D-glucopyranosides with higher selectivities. On the other hand, the reaction at C(2)-OH of *α*-D-glucopyranosides with the intermediate formation of **B** is considerably slower than that involving the formation of the intermediate **C** because of steric hindrance around C(2)-OH of *α*-D-glucopyranosides. Furthermore, we investigated a comparison of potential reactivities of C(6)-OH in *α*-D-Glc with C(6)-OH in *β*-D-Glc under standard acylation conditions (Figure 1). As a result, we could not find a dominant difference between the reactivities of C(6)-OH in *β*-D-Glc and C(6)-OH in *α*-D-Glc. This shows that Me_2SnCl_2 clearly controls chemo-

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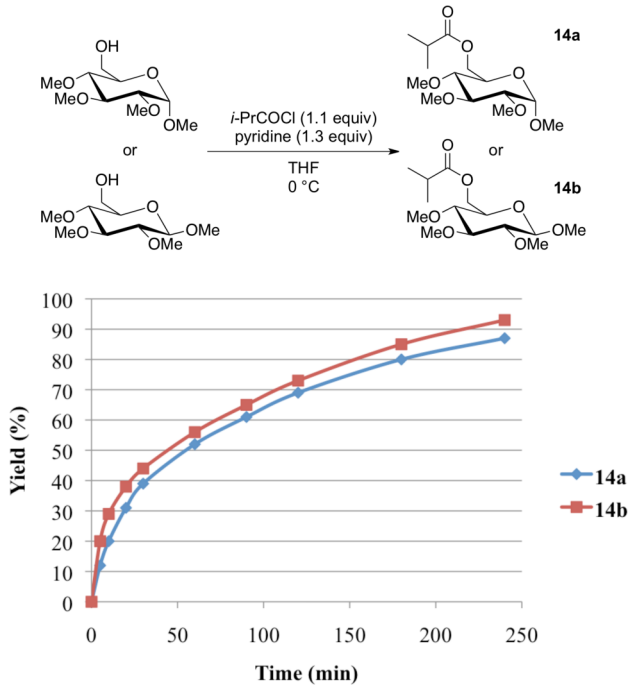
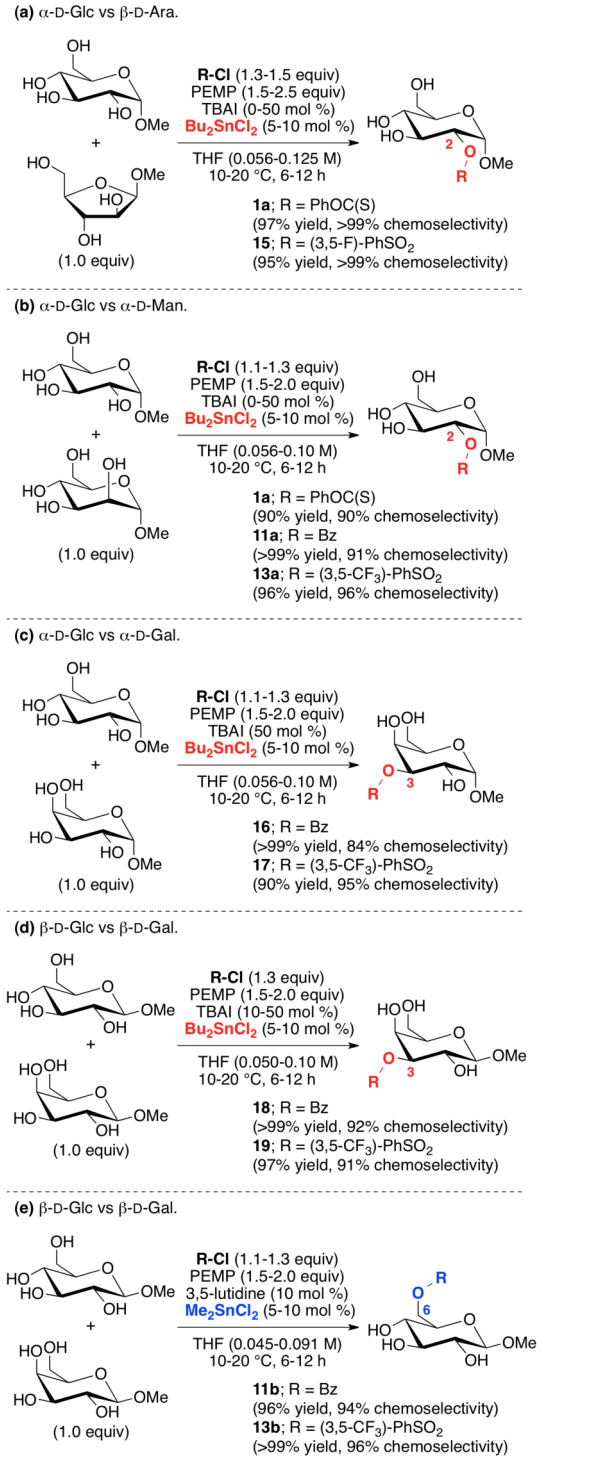


Figure 1. Comparison of the reactivities of C(6)-OH in glucopyranosides.

selectivity under catalytic conditions, and we consequently suppose that nucleophilicity (reactivity) of C(6)-OH in β-D-Glc is weakened because of a decline of the electron density of C(6)-OH in β-D-Glc in the intermediates **A** by a long-range stereoelectronic effect (anomeric effect) as shown **A′** in Scheme 1b.[7,8] However, it is still unclear.

As shown in Scheme 2, the protocol can be applied to the chemo- and regioselective functionalization in the presence of structurally similar carbohydrates.[9] In the case of thiocarbonylation with Bu_2SnCl_2 in the simultaneous presence of a pyranoside and furanoside containing *cis*-1,2-diol moieties (for example, α-D-Glc vs α-D-Ara), C(2)-OH of α-D-Glc was thiocarbonated with 97% yield and >99% chemoselectivity without formation of its regioisomers. Additionally, the catalytic sulfonylation afforded the corresponding sulfonate **15** in high yield with excellent selectivities (Scheme 2 (a)). Bu_2SnCl_2-catalyzed thiocarbonylation, acylation, and sulfonylation were effectively carried out in the presence of α-D-Glc and α-D-Man. Thus, in these reactions, α-D-Glc was converted to 2-*O*-thiocarbonate **1a**, 2-*O*-benzoate **11a**, and 2-*O*-sulfonate **13a**, respectively, in 90−>99% yields with 90−96% chemoselectivities (Scheme 2 (b)). Remarkably, these functionalizations selectively proceeded at C(3)-OH of D-Gals in the presence of D-Glcs (Scheme 2 (c) and (d)). Taking into consideration the above results, the most suitable 1,2-diol moieties in common carbohydrates that coordinate tightly and reversibly to Bu_2SnCl_2 are C(3)- and C(4)-OHs of D-Gals. We suppose that the most effective factor determining the coordination is the *O*−*Sn*−*O* binding angle. As shown in Scheme 2e, Me_2SnCl_2-catalyzed functionalization in the simultaneous presence of β-D-Glc and β-D-Gal proceeded at C(6)-OH of β-D-Glc with 96−>99% yields and 94−96% chemoselectivities without formation of its regioisomers.

Scheme 2. Chemo- and Regioselective Functionalization Among Structurally Similar Carbohydrates



CONCLUSION

A catalytic process for the chemo- and regioselective functionalization of nonprotected carbohydrates in the presence of the stereoisomers has been developed. The present method with Bu_2SnCl_2 enables direct functionalization at C(2)-OH of methyl α-D-glucopyranoside in the presence of methyl β-D-glucopyranoside in >99% yield with 97% chemoselectivity without formation of its regioisomers. On the other hand, Me_2SnCl_2 leads to direct functionalization at C(6)-OH of

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methyl β-D-glucopyranoside in the presence of methyl α-D-glucopyranoside in 91% yield and 98% chemoselectivity without formation of its regioisomers. The chemo- and regioselectivities of functionalization are found to be intrinsic to the carbohydrates based on the affinity of metal ion with diol moieties in carbohydrates and the stereorelationship among hydroxy groups, respectively. In addition, the method can be applied to chemo- and regioselective functionalization in the presence of the structurally similar carbohydrates, thereby providing a novel and helpful strategy to efficiently separate inseparable carbohydrates. Additional efforts for extending these methods to more complex polyols including oligosaccharides and glycoconjugates, and mechanistic investigations are underway in our laboratories.

EXPERIMENTAL SECTION

General Methods. NMR spectra were recorded at 400, 100, and 376 MHz for ^{1}H, ^{13}C, and ^{19}F acquisitions, respectively. Chemical shifts are reported in ppm with a solvent resonance as an internal standard (^{1}H NMR: tetramethylsilane, acetone, chloroform, or pyridine as internal standards, indicating 0, 2.05, 7.26, or 8.71, respectively; ^{13}C NMR: acetone, methanol, chloroform, or pyridine as internal standards, indicating 0, 29.8, 77.0, or 135.5, respectively). ^{19}F NMR: $CFCl_3$ as internal standard, indicating 0 ppm). Data is reported as follows: s = singlet, br = broad, d = doublet, t = triplet, q = quartet, m = multiplet; coupling constants in Hz; integration. Assignments were based on analysis of coupling constants and COSY spectra. Mass spectra were recorded with fast atom bombardment (FAB) and a double-focusing magnetic sector mass analyzer for MS and HRMS measurements. All screenings of chemo- and regioselective functionalization were carried out in oven-dried screw-cap vials fitted with a septum.

General Procedure for the Chemo- and Regioselective Functionalization of Anomeric Mixture of Glucopyranoside Catalyzed by Bu_2SnCl_2 (Entry 26 in Table 1). After a mixture of methyl α-D-glucopyranoside (194.2 mg, 1.0 mmol), methyl β-D-glucopyranoside (194.2 mg, 1.0 mmol), and dibutyltin dichloride (30.4 mg, 0.10 mmol) in THF (8 mL) was stirred in a vial at room temperature for 10 min, tetrabutylammonium iodide (184.7 mg, 0.50 mmol), phenyl chlorothionoformate (0.175 mL, 1.3 mmol), and 1,2,2,6,6-pentamethylpiperidine (0.235 mL, 1.3 mmol) were added to the suspension at 20 °C. After being stirred vigorously for 6 h at the same temperature, the reaction mixture was quenched with saturated aqueous NH_4Cl and subsequently extracted with ethyl acetate. The organic layer was washed with water and brine, dried over $MgSO_4$, filtrated, and concentrated in vacuo (water bath temperature: <20 °C). The residue was purified by SiO_2 column chromatography (hexane/ethyl acetate = 3:1−0:1) to give a mixture of methyl 2-*O*-phenoxythiocarbonyl-α-D-glucopyranoside **1a** (330.9 mg, >99%) and methyl 6-*O*-phenoxythiocarbonyl-β-D-glucopyranoside **1b** (10.2 mg, 3%).

*Methyl 2-O-Phenoxythiocarbonyl-α-D-glucopyranoside (**1a**, Entry 26, Table 1).*[4,10] Major product **1a**: 330.9 mg, >99% yield. Minor product **1b**: 10.2 mg, 3% yield. White solid: R_f = 0.27 (MeOH/$CHCl_3$, 10:90); mp 130−132 °C; $[\alpha]^{26}_D$ = +96.4 (*c* 1.02, CH_3OH). ^{1}H NMR (400 MHz, C_5D_5N) δ 7.35−7.30 (m, 2H, PhH), 7.21−7.11 (m, 3H, PhH), 5.88 (dd, *J* = 9.9, 3.4 Hz, 1H, *H*-2), 5.58 (d, *J* = 3.4 Hz, 1H, *H*-1), 4.86 (t, *J* = 9.2 Hz, 1H, *H*-3), 4.51−4.48 (m, 1H, *H*-6a), 4.42−4.25 (m, 3H, *H*-5 and *H*-6b), 3.42 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, C_5D_5N) δ 196.0, 154.0, 129.9 (2C), 126.8, 122.4 (2C), 96.8, 84.5, 74.3, 72.1, 71.8, 62.3, 54.9; IR (solid) 3323, 2900, 1489, 1269, 1221, 1204, 1043, 1016 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 331 (M + H^+, 20), 307 (25), 289 (15), 177 (5), 154 (100), 136 (70), 107 (20), 77 (20); HRMS (FAB) calcd for $C_{14}H_{19}O_7S$ (M + H^+) 331.0846, found 331.0855. Anal. Calcd for $C_{14}H_{18}O_7S$: C, 50.90; H, 5.49. Found: C, 50.61; H, 5.33.

*Octyl 2-O-Phenoxythiocarbonyl-α-D-glucopyranoside (**2a**, Entry 1, Table 2).*[4] Major product **2a**: 409.4 mg, 96% yield. Minor product **2b**: 17.1 mg, 4% yield. White solid: R_f = 0.40 (MeOH/$CHCl_3$, 10:90); mp 100−102 °C; $[\alpha]^{26}_D$ = +125.5 (*c* 1.00, CH_3OH); ^{1}H NMR (400 MHz, C_5D_5N) δ 7.60−7.37 (m, 2H, PhH), 7.27−7.18 (m, 3H, PhH), 5.89 (dd, *J* = 9.8, 3.7 Hz, 1H, *H*-2), 5.78 (d, *J* = 3.7 Hz, 1H, *H*-1), 5.22 (br s, 3H, OH), 4.95−4.90 (m, 1H, *H*-3), 4.58−4.54 (m, 1H, *H*-6a), 4.45−4.38 (m, 3H, *H*-4, *H*-5 and *H*-6b), 4.00−3.93 (m, 1H, $OCH_2(CH_2)_6CH_3$), 3.59−3.52 (m, 1H, $OCH_2(CH_2)_6CH_3$), 1.70−1.50 (m, 2H, $OCH_2CH_2(CH_2)_5CH_3$), 1.45−1.25 (m, 2H, $OCH_2CH_2CH_2(CH_2)_4CH_3$), 1.25−1.00 (m, 8H, $OCH_2CH_2CH_2(CH_2)_4CH_3$), 0.82 (t, *J* = 6.8 Hz, 3H, $OCH_2(CH_2)_6CH_3$); ^{13}C NMR (100 MHz, C_5D_5N) δ 195.9, 153.9, 129.9 (2C), 126.8, 122.3 (2C), 95.5, 84.4, 74.3, 72.0, 71.8, 68.1, 62.3, 31.9, 29.7, 29.5, 29.4, 26.3, 22.8, 14.1; IR (solid) 3447, 2926, 1489, 1342, 1283, 1204, 1049, 1020 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 429 (M + H^+, 30), 307 (25), 299 (30), 281 (30), 275 (15), 145 (100), 77 (40), 57 (45); HRMS (FAB) calcd for $C_{21}H_{33}O_7S$ (M + H^+) 429.1942, found 429.1960. Anal. Calcd for $C_{21}H_{32}O_7S$: C, 58.86; H, 7.53. Found: C, 58.65; H, 7.43.

*Phenyl 2-O-Phenoxythiocarbonyl-α-D-glucopyranoside (**3a**, Entry 2, Table 2).*[4] Major product **3a**: 374.6 mg, 92% yield. Minor product **3b**: 7.6 mg, 2% yield. White solid: R_f = 0.35 (MeOH/$CHCl_3$, 10:90); mp 204−206 °C; $[\alpha]^{26}_D$ = +157.3 (*c* 1.00, CH_3OH); ^{1}H NMR (400 MHz, C_5D_5N) δ 8.20 (br s, 1H, OH), 7.84 (br s, 1H, OH), 7.50−7.26 (m, 6H, PhH), 7.25−7.17 (m, 1H, PhH), 7.15−7.00 (m, 3H, PhH), 6.49 (d, *J* = 3.4 Hz, 1H, *H*-1), 6.49 (br s, 1H, OH), 6.04 (dd, *J* = 10.0, 3.4 Hz, 1H, *H*-2), 5.10 (t, *J* = 9.2 Hz, 1H, *H*-3), 4.60−4.30 (m, 4H, *H*-4, *H*-5 and *H*-6); ^{13}C NMR (100 MHz, C_5D_5N) δ 195.9, 157.6, 153.9, 130.0 (2C), 129.9 (2C), 126.9, 123.1, 122.3 (2C), 117.7 (2C), 95.3, 83.8, 75.3, 72.0, 71.4, 61.9; IR (solid) 3412, 2941, 1492, 1261, 1217, 1176, 1099, 1022 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 393 (M + H^+, 25), 354 (5), 307 (25), 289 (15), 154 (100), 136 (70), 107 (20), 77 (20); HRMS (FAB) calcd for $C_{19}H_{21}O_7S$ (M + H^+) 393.1003, found 393.1015. Anal. Calcd for $C_{19}H_{20}O_7S$: C, 58.15; H, 5.14. Found: C, 57.87; H, 5.26.

*4-Nitrophenyl 2-O-Phenoxythiocarbonyl-α-D-glucopyranoside (**4a**, Entry 3, Table 2).*[4] Major product **4a**: 404.1 mg, 92% yield. Minor product **4b**: 8.2 mg, 2% yield. White solid: R_f = 0.35 (MeOH/$CHCl_3$, 10:90); mp 180−182 °C; $[\alpha]^{22}_D$ = +221.6 (*c* 1.00, CH_3OH); ^{1}H NMR (400 MHz, C_5D_5N) δ 8.18 (d, *J* = 9.0 Hz, 2H, 4-NO_2-PhH), 7.37−7.33 (m, 4H, 4-NO_2-PhH and PhH), 7.25−7.14 (m, 3H, PhH), 6.61 (d, *J* = 3.2 Hz, 1H, *H*-1), 6.12 (dd, *J* = 9.9, 3.2 Hz, 1H, *H*-2), 5.31 (br s, 3H, OH), 5.09 (t, *J* = 9.3 Hz, 1H, *H*-3), 4.57−4.34 (m, 4H, *H*-4, *H*-5 and *H*-6); ^{13}C NMR (100 MHz, C_5D_5N) δ 195.9, 161.9, 154.0, 150.0, 130.0 (2C), 127.0, 126.0 (2C), 122.3 (2C), 117.2 (2C), 95.0, 83.3, 76.0, 71.9, 71.2, 61.8; IR (solid) 3385, 2928, 2361, 1593, 1516, 1344, 1244, 1213, 1020 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 438 (M + H^+, 5), 307 (35), 289 (20), 154 (100), 136 (65), 107 (20), 77 (20); HRMS (FAB) Calcd for $C_{19}H_{20}NO_9S$ (M + H^+) 438.0853, found 438.0867. Anal. Calcd for $C_{19}H_{19}NO_9S$: C, 52.17; H, 4.38; N, 3.20. Found: C, 51.77; H, 4.23; N, 2.98.

*Ethyl 2-O-Phenoxythiocarbonyl-α-D-thioglucopyranoside (**5a**, Entry 4, Table 2).*[4] Major product **5a**: 331.1 mg, 92% yield. Minor product **5b**: 32.8 mg, 9% yield. White solid: R_f = 0.32 (MeOH/$CHCl_3$, 10:90); mp 165−167 °C; $[\alpha]^{28}_D$ = +193.4 (*c* 1.09, CH_3OH); ^{1}H NMR (400 MHz, C_5D_5N) δ 8.14 (br s, 1H, OH), 7.76 (br s, 1H, OH), 7.37 (t, *J* = 7.8 Hz, 2H, PhH), 7.30−7.10 (m, 3H), 6.40 (d, *J* = 5.6 Hz, 1H, *H*-1), 6.00 (dd, *J* = 9.9, 5.6 Hz, 1H, *H*-2), 5.11 (br s, 1H, OH), 4.78 (t, *J* = 9.5 Hz, 1H, *H*-3), 4.80−4.70 (m, 1H, *H*-5), 4.54 (dd, *J* = 12.0, 2.1 Hz, 1H, *H*-6a), 4.45 (dd, *J* = 12.0, 5.1 Hz, 1H, *H*-6b), 4.39 (t, *J* = 9.4 Hz, 1H, *H*-4), 2.78−2.62 (m, 2H, SCH_2CH_3), 1.23 (t, *J* = 7.5 Hz, 3H, SCH_2CH_3); ^{13}C NMR (100 MHz, C_5D_5N) δ 195.4, 153.9, 129.9 (2C), 126.9, 122.3 (2C), 83.7, 83.1, 74.8, 72.9, 71.8, 62.2, 24.3, 15.0; IR (solid) 3356, 2918, 1487, 1288, 1215, 1103, 1043, 1015 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 361 (M + H^+, 5), 307 (25), 289 (15), 154 (100), 136 (70), 107 (20), 77 (20); HRMS (FAB) calcd for $C_{15}H_{21}O_6S_2$ (M + H^+) 361.0774, found 361.0797. Anal. Calcd for $C_{15}H_{20}O_6S_2$: C, 49.98; H, 5.59. Found: C, 49.73; H, 5.70.

*Methyl 2-O-(4-Tolyloxy)thiocarbonyl-α-D-glucopyranoside (**6a**, Entry 5, Table 2).*[4] Major product **6a**: 327.4 mg, 95% yield. Minor product **6b**: 20.9 mg, 6% yield. White solid: R_f = 0.35 (MeOH/$CHCl_3$,

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10:90); mp 148−150 °C; $[\alpha]^{26}_{D}$ = +8.4 (*c* 1.00, CH_3OH); ^1H NMR (400 MHz, C_5D_5N) δ 7.06 (d, *J* = 8.1 Hz, 2H, 4-CH_3-Ph*H*), 7.01 (d, *J* = 8.1 Hz, 2H, 4-CH_3-Ph*H*), 5.92 (dd, *J* = 10.0, 3.7 Hz, 1H, *H*-2), 5.62 (d, *J* = 3.7 Hz, 1H, *H*-1), 4.89 (dd, *J* = 10.0, 8.7 Hz, 1H, *H*-3), 4.52 (dd, *J* = 12.0, 2.2 Hz, 1H, *H*-6a), 4.44−4.37 (m, 2H, *H*-4 and *H*-6b), 4.33−4.28 (m, 1H, *H*-5), 3.45 (s, 3H, OCH_3), 2.12 (s, 3H, 4-CH_3-Ph); ^{13}C NMR (100 MHz, C_5D_5N) δ 196.2, 151.8, 136.4, 130.3 (2C), 121.9 (2C), 96.7, 84.4, 74.2, 72.1, 71.8, 62.2, 54.8, 20.6; IR (solid) 3385, 2907, 1504, 1271, 1219, 1192, 1038, 1015 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 345 (M + H^+, 15), 291 (40), 235 (15), 177 (20), 145 (80), 99 (100), 91 (95), 71 (85); HRMS (FAB) calcd for $C_{15}H_{21}O_7S$ (M + H^+) 345.1014, found 345.1003. Anal. Calcd for $C_{15}H_{20}O_7S$: C, 52.31; H, 5.85. Found: C, 52.52; H, 5.72.

*Methyl 2-O-(2-Naphthoxy)thiocarbonyl-α-D-glucopyranoside (**7a**, Entry 6, Table 2).*[4] Major product **7a**: 381.4 mg, >99% yield. Minor product **7b**: 7.8 mg, 2% yield. White solid: R_f = 0.35 (MeOH/$CHCl_3$, 10:90); mp 142−144 °C; $[\alpha]^{19}_{D}$ = +88.6 (*c* 1.02, CH_3OH); ^1H NMR (400 MHz, C_5D_5N) δ 7.89−7.80 (m, 3H, Naph*H*), 7.59−7.56 (m, 1H, Naph*H*), 7.50−7.44 (m, 2H, Naph*H*), 7.32 (dd, *J* = 8.9, 2.3 Hz, 1H, Naph*H*), 6.27 (br s, 3H, O*H*), 5.95 (dd, *J* = 9.9, 3.7 Hz, 1H, *H*-2), 5.66 (d, *J* = 3.7 Hz, 1H, *H*-1), 4.93 (t, *J* = 9.3 Hz, 1H, *H*-3), 4.54 (dd, *J* = 11.8, 2.1 Hz, 1H, *H*-6a), 4.46−4.40 (m, 2H, *H*-4 and *H*-6b), 4.35−4.30 (m, 1H, *H*-5), 3.50 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, C_5D_5N) δ 196.0, 151.5, 134.1, 132.1, 129.9, 128.2, 128.1, 127.1, 126.5, 121.8, 119.4, 96.8, 84.6, 74.3, 72.1, 71.8, 62.2, 54.9; IR (solid) 3348, 2907, 1508, 1265, 1227, 1193, 1030, 1015 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 381 (M + H^+, 20), 307 (25), 242 (55), 154 (100), 136 (70), 117 (20), 77 (20); HRMS (FAB) calcd for $C_{18}H_{21}O_7S$ (M + H^+) 381.1003, found 381.0999. Anal. Calcd for $C_{18}H_{20}O_7S$: C, 56.83; H, 5.30. Found: C, 56.54; H, 5.24.

*Methyl 2-O-(4-Chlorophenoxy)thiocarbonyl-α-D-glucopyranoside (**8a**, Entry 7, Table 2).*[4] Major product **8a**: 364.2 mg, >99% yield. Minor product **8b**: 19.2 mg, 5% yield. White solid: R_f = 0.30 (MeOH/$CHCl_3$, 10:90); mp 133−134 °C; $[\alpha]^{19}_{D}$ = +100.5 (*c* 1.05, CH_3OH); ^1H NMR (400 MHz, C_5D_5N) δ 7.37 (d, *J* = 8.8 Hz, 2H, 4-Cl-Ph*H*), 7.24 (br s, 3H, O*H*), 7.08 (d, *J* = 8.8 Hz, 2H, 4-Cl-Ph*H*), 5.87 (dd, *J* = 9.8, 3.7 Hz, 1H, *H*-2), 5.59 (d, *J* = 3.7 Hz, 1H, *H*-1), 4.87 (t, *J* = 9.3 Hz, 1H, *H*-3), 4.52 (dd, *J* = 11.7, 2.2 Hz, 1H, *H*-6a), 4.42 (t, *J* = 5.1 Hz, 1H, *H*-4), 4.38 (d, *J* = 11.7 Hz, 1H, *H*-6b), 4.32−4.27 (m, 1H, *H*-5), 3.45 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, C_5D_5N) δ 195.5, 152.3, 131.9, 129.9 (2C), 124.0 (2C), 96.6, 84.6, 74.2, 72.0, 71.7, 62.2, 54.8; IR (solid) 3443, 2936, 1487, 1281, 1206, 1146, 1042, 1013 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 365 (M + H^+, 10), 307 (25), 289 (10), 242 (10), 154 (100), 136 (75), 107 (25); HRMS (FAB) calcd for $C_{14}H_{18}ClO_7S$ (M + H^+) 365.0456, found 365.0475. Anal. Calcd for $C_{14}H_{17}ClO_7S$: C, 46.09; H, 4.70. Found: C, 46.05; H, 4.60.

*Methyl 2-O-(4-Fluorophenoxy)thiocarbonyl-α-D-glucopyranoside (**9a**, Entry 8, Table 2).*[4] Major product **9a**: 360.5 mg, >99% yield. Minor product **9b**: 11.1 mg, 3% yield. White solid: R_f = 0.30 (MeOH/$CHCl_3$, 10:90); mp 125−127 °C; $[\alpha]^{25}_{D}$ = +0.6 (*c* 1.00, CH_3OH); ^1H NMR (400 MHz, C_5D_5N) δ 7.14−7.06 (m, 4H, 4-F-Ph*H*), 5.86 (dd, *J* = 9.9, 3.7 Hz, 1H, *H*-2), 5.57 (d, *J* = 3.7 Hz, 1H, *H*-1), 5.23 (br s, 3H, O*H*), 4.85 (t, *J* = 9.2 Hz, 1H, *H*-3), 4.50 (dd, *J* = 11.8, 2.1 Hz, 1H, *H*-6a), 4.42−4.34 (m, 2H, *H*-4 and *H*-6b), 4.30−4.25 (m, 1H, *H*-5), 3.43 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, C_5D_5N) δ 196.0, 160.9 (d, *J* = 244.1 Hz), 150.1, 124.1 (d, *J* = 8.3 Hz, 2C), 116.4 (d, *J* = 24.0 Hz, 2C), 96.7, 84.6, 74.3, 72.1, 71.8, 62.2, 54.9; IR (solid) 3368, 2936, 1503, 1271, 1210, 1190, 1042, 1013 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 349 (M + H^+, 5), 281 (10), 207 (10), 154 (35), 136 (40), 107 (35), 77 (40), 55 (100); HRMS (FAB) Calcd for $C_{14}H_{18}FO_7S$ (M + H^+) 349.0752, found 349.0741. Anal. Calcd for $C_{14}H_{17}FO_7S$: C, 48.27; H, 4.92. Found: C, 48.36; H, 4.98.

*Methyl 2-O-Benzoyl-α-D-glucopyranoside (**11a**, Entry 10, Table 2).*[11,12] Major product **11a**: 303.3 mg, >99% yield. Minor product **11b**: 22.8 mg, 8% yield. White solid: R_f = 0.47 (MeOH/$CHCl_3$, 10:90); mp 168−170 °C (lit.[12] mp 174−175 °C); $[\alpha]^{19}_{D}$ = +151.7 (*c* 1.03, CH_3OH) [lit.[11a] $[\alpha]^{25}_{D}$ = +156.0 (*c* 2.09, EtOAc)]; ^1H NMR (400 MHz, $(CD_3)_2CO$) δ 8.07 (dd, *J* = 8.0, 1.2 Hz, 2H, Ph*H*), 7.66 (t, *J* = 8.0 Hz, 1H, Ph*H*), 7.53 (t, *J* = 8.0 Hz, 2H, Ph*H*), 4.96 (d, *J* = 3.7 Hz, 1H, *H*-1), 4.83 (dd, *J* = 9.8, 3.7 Hz, 1H, *H*-2), 4.63 (br s, 1H, O*H*), 4.42 (br s, 1H, O*H*), 4.05 (t, *J* = 9.3 Hz, 1H, *H*-3), 3.90−3.80 (m, 1H, *H*-6a), 3.80−3.60 (m, 3H, *H*-5, *H*-6b and O*H*), 3.60−3.50 (t, *J* = 9.3 Hz, 1H, *H*-4), 3.35 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 166.6, 134.0, 131.1, 130.4 (2C), 129.3 (2C), 97.9, 75.2, 73.2, 72.2, 71.9, 62.5, 55.1; IR (solid) 3347, 2920, 1705, 1333, 1294, 1256, 1119, 1030 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 299 (M + H^+, 20), 267 (20), 154 (100), 136 (70), 107 (20), 105 (25), 77 (15); HRMS (FAB) calcd for $C_{14}H_{19}O_7$ (M + H^+) 299.1125, found 299.1159. Anal. Calcd for $C_{14}H_{18}O_7$: C, 56.37; H, 6.08. Found: C, 56.49; H, 6.05.

*Methyl 2-O-Isobutyryl-α-D-glucopyranoside (**12a**, Entry 11, Table 2).* Major product **12a**: 253.7 mg, 96% yield. Minor product **12b**: 29.0 mg, 11% yield. White solid: R_f = 0.35 (MeOH/$CHCl_3$, 10:90); mp 92−93 °C; $[\alpha]^{25}_{D}$ = +146.7 (*c* 1.00, CH_3OH); ^1H NMR (400 MHz, C_5D_5N) δ 5.37 (dd, *J* = 10.0, 3.7 Hz, 1H, *H*-2), 5.29 (d, *J* = 3.7 Hz, 1H, *H*-1), 4.99 (br s, 2H, O*H*), 4.75−4.65 (m, 1H, *H*-3), 4.50 (d, *J* = 11.7 Hz, 1H, *H*-6a), 4.36 (d, *J* = 11.7 Hz, 1H, *H*-6b), 4.30−4.20 (m, 2H, *H*-4 and *H*-5), 3.43 (s, 3H, OCH_3), 2.64 (sept, *J* = 7.0 Hz, 1H, OCOC*H*$(CH_3)_2$), 1.18 (d, *J* = 7.0 Hz, 3H, OCOCH$(CH_3)_2$), 1.16 (d, *J* = 7.0 Hz, 3H, OCOCH$(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.4, 97.2, 73.0, 71.6, 71.0, 70.0, 61.3, 55.3, 33.8, 19.0, 18.8; IR (solid) 3296, 2916, 1715, 1196, 1155, 1107, 1038, 1009 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 265 (M + H^+, 40), 233 (80), 154 (100), 137 (70), 136 (70), 107 (20), 89 (15), 77 (15); HRMS (FAB) calcd for $C_{11}H_{21}O_7$ (M + H^+) 265.1282, found 265.1319. Anal. Calcd for $C_{11}H_{20}O_7$: C, 49.99; H, 7.63. Found: C, 49.93; H, 7.85.

*Methyl 2-O-[3,5-Bis(trifluoromethyl)benzenesulfonyl]-α-D-glucopyranoside (**13a**, Entry 12, Table 2).*[2j] Major product **13a**: 455.9 mg, 97% yield. Minor product **13b**: 68.1 mg, 14% yield. White solid: R_f = 0.31 (MeOH/$CHCl_3$, 10:90); mp 108−109 °C; $[\alpha]^{17}_{D}$ = +79.5 (*c* 1.29, CH_3OH); ^1H NMR (400 MHz, $(CD_3)_2CO$) δ 8.55 (s, 2H, 3,5-CF_3-Ph*H*), 8.47 (s, 1H, 3,5-CF_3-Ph*H*), 4.88 (d, *J* = 3.7 Hz, 1H, *H*-1), 4.66 (br s, 1H, O*H*), 4.45 (br s, 1H, O*H*), 4.37 (dd, *J* = 9.8, 3.7 Hz, 1H, *H*-2), 3.79 (t, *J* = 9.3 Hz, 1H, *H*-3), 3.85−3.72 (m, 2H, *H*-6a and O*H*), 3.65 (dd, *J* = 11.7, 5.1 Hz, 1H, *H*-6b), 3.54−3.50 (m, 1H, *H*-5), 3.36 (t, *J* = 9.3 Hz, 1H, *H*-4), 3.36 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 140.4, 133.0 (q, *J* = 34.8 Hz, 2C), 129.7 (q, *J* = 3.3 Hz, 2C), 128.4 (sept, *J* = 3.3 Hz), 123.6 (q, *J* = 272.3 Hz, 2C), 98.2, 82.5, 73.1, 71.8, 71.6, 62.1, 55.2; ^{19}F NMR (376 MHz, $(CD_3)_2CO$) δ −62.4 (s, 6F); IR (solid) 3377, 2932, 1381, 1362, 1279, 1179, 1134, 974 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 471 (M + H^+, 10), 421 (35), 361 (30), 277 (30), 213 (35), 154 (25), 145 (100), 127 (70); HRMS (FAB) calcd for $C_{15}H_{17}F_6O_8S$ (M + H^+) 471.0543, found 471.0559. Anal. Calcd for $C_{15}H_{16}F_6O_8S$: C, 38.30; H, 3.43. Found: C, 38.29; H, 3.14.

General Procedure for the Chemo- and Regioselective Functionalization of Anomeric Mixture of Glucopyranoside Catalyzed by Me_2SnCl_2 (Entry 25, Table 1). After a mixture of methyl α-D-glucopyranoside (194.2 mg, 1.0 mmol), methyl β-D-glucopyranoside (194.2 mg, 1.0 mmol), and dimethyltin dichloride (22.0 mg, 0.10 mmol) in THF (6 mL) was stirred in a vial at room temperature for 10 min, 3,5-lutidine (0.0114 mL, 0.10 mmol) and 1,2,2,6,6-pentamethylpiperidine (0.271 mL, 1.5 mmol) were added to the suspension at 20 °C. Then, phenyl chlorothionoformate (0.175 mL, 1.3 mmol) in THF (2 mL) was flowed over 2 h at 20 °C. After being stirred vigorously for 6 h at 20 °C, the reaction mixture was quenched with saturated aqueous NH_4Cl and subsequently extracted with ethyl acetate. The organic layer was washed with water and brine, dried over $MgSO_4$, filtrated, and concentrated in vacuo (water bath temperature: <20 °C). The residue was purified by SiO_2 column chromatography (hexane/ethyl acetate = 3:1−0:1) to give a mixture of methyl 2-*O*-phenoxythiocarbonyl-α-D-glucopyranoside **1a** (6.2 mg, 2%) and methyl 6-*O*-phenoxythiocarbonyl-β-D-glucopyranoside **1b** (301.7 mg, 91%).

*Methyl 6-O-Phenoxythiocarbonyl-β-D-glucopyranoside (**1b**, Entry 25, Table 1).*[4,10] Major product **1b**: 301.7 mg, 91% yield. Minor product **1a**: 6.2 mg, 2% yield. White solid: R_f = 0.27 (MeOH/$CHCl_3$, 10:90); mp 143−144 °C; $[\alpha]^{25}_{D}$ = −14.0 (*c* 1.00, CH_3OH); ^1H NMR (400 MHz, C_5D_5N) δ 7.38 (t, *J* = 7.8 Hz, 2H, Ph*H*), 7.25−7.18 (m, 3H, Ph*H*), 5.41 (d, *J* = 11.5 Hz, 1H, *H*-6a), 5.20 (d, *J* = 11.5 Hz, 1H, *H*-6b), 4.76 (d, *J* = 7.6 Hz, 1H, *H*-1), 4.30−4.10 (m, 3H, *H*-3,

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H-4 and *H*-5), 4.05 (t, *J* = 8.3 Hz, 1H, *H*-2), 3.63 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, C_5D_5N) δ 195.6, 153.9, 129.9 (2C), 126.8, 122.3 (2C), 105.6, 78.1, 74.8, 74.6, 71.1, 56.8; IR (solid) 3424, 2920, 1489, 1263, 1207, 1159, 1098, 1016 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 331 (M + H^+, 30), 307 (20), 289 (15), 177 (5), 154 (100), 136 (70), 107 (20), 77 (25); HRMS (FAB) calcd for $C_{14}H_{19}O_7S$ (M + H^+) 331.0846, found 331.0845. Anal. Calcd for $C_{14}H_{18}O_7S$: C, 50.90; H, 5.49. Found: C, 50.83; H, 5.37.

*Octyl 6-O-Phenoxythiocarbonyl-β-D-glucopyranoside (**2b**, Entry 1, Table 3).* Major product **2b**: 364.4 mg, 85% yield. Minor product **2a**: 49.7 mg, 12% yield. White solid: R_f = 0.40 ($MeOH/CHCl_3$, 10:90); mp 85−86 °C; $[\alpha]^{24}_D$ = −12.3 (*c* 1.03, CH_3OH); ^1H NMR (400 MHz, C_5D_5N) δ 7.67 (br s, 1H, O*H*), 7.55−7.30 (m, 2H, Ph*H*), 7.41 (br s, 1H, O*H*), 7.30−7.15 (m, 3H, Ph*H*), 5.44 (d, *J* = 11.2 Hz, 1H, *H*-6a), 5.22 (dd, *J* = 11.2, 5.0 Hz, 1H, *H*-6b), 4.99 (br s, 1H, O*H*), 4.88 (d, *J* = 7.8 Hz, 1H, *H*-1), 4.30−4.00 (m, 5H, *H*-2, *H*-3, *H*-4, *H*-5 and $OCH_2(CH_2)_6CH_3$), 3.71 (dt, *J* = 16.1, 6.8 Hz, 1H, $OCH_2(CH_2)_6CH_3$), 1.75−1.60 (m, 2H, $OCH_2CH_2(CH_2)_5CH_3$), 1.40−1.25 (m, 2H, $OCH_2CH_2CH_2(CH_2)_4CH_3$), 1.25−1.05 (m, 8H, $OCH_2CH_2CH_2(CH_2)_4CH_3$), 0.82 (t, *J* = 7.0 Hz, 3H, $OCH_2(CH_2)_6CH_3$); ^{13}C NMR (100 MHz, C_5D_5N) δ 195.7, 154.0, 129.9 (2C), 126.8, 122.4 (2C), 104.8, 78.2, 75.0, 74.8, 74.7, 71.3, 70.0, 31.9, 30.2, 29.6, 29.4, 26.3, 22.8, 14.2; IR (solid) 3414, 2924, 1491, 1375, 1290, 1200, 1082, 1020 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 429 (M + H^+, 20), 299 (90), 281 (25), 154 (40), 145 (100), 127 (65), 85 (95), 57 (65); HRMS (FAB) calcd for $C_{21}H_{33}O_7S$ (M + H^+) 429.1942, found 429.1960. Anal. Calcd for $C_{21}H_{32}O_7S$: C, 58.86; H, 7.53. Found: C, 58.86; H, 7.78.

*Phenyl 6-O-Phenoxythiocarbonyl-β-D-glucopyranoside (**3b**, Entry 2, Table 3).* Major product **3b**: 266.7 mg, 68% yield. Minor product **3a**: 54.6 mg, 14% yield. White solid: R_f = 0.35 ($MeOH/CHCl_3$, 10:90); mp 140−141 °C; $[\alpha]^{26}_D$ = −65.5 (*c* 1.06, CH_3OH); ^1H NMR (400 MHz, C_5D_5N) δ 8.00−7.80 (m, 2H, Ph*H* and O*H*), 7.65 (br s, 1H, O*H*), 7.50−7.30 (m, 5H, Ph*H*), 7.30−7.10 (m, 3H, Ph*H*), 7.04 (t, *J* = 7.1 Hz, 1H, Ph*H*), 6.60 (d, *J* = 7.1 Hz, 1H, *H*-1), 5.39 (d, *J* = 11.5 Hz, 1H, *H*-6a), 5.25 (dd, *J* = 11.5, 5.9 Hz, 1H, *H*-6b), 5.02 (br s, 1H, O*H*), 4.50−4.20 (m, 4H, *H*-2, *H*-3, *H*-4 and *H*-5); ^{13}C NMR (100 MHz, C_5D_5N) δ 195.6, 158.6, 154.0, 129.9 (4C), 126.8, 122.5, 122.4 (2C), 117.0 (2), 102.2, 78.1, 74.8, 74.7, 74.4, 71.0; IR (solid) 3389, 2887, 1489, 1279, 1221, 1196, 1070, 1016 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 393 (M + H^+, 10), 307 (20), 299 (10), 289 (15), 154 (100), 136 (70), 107 (20), 77 (20); HRMS (FAB) Calcd for $C_{19}H_{21}O_7S$ (M + H^+) 393.1003, found 393.1015. Anal. Calcd for $C_{19}H_{20}O_7S$: C, 58.15; H, 5.14. Found: C, 57.89; H, 5.31.

*4-Nitrophenyl 6-O-Phenoxythiocarbonyl-β-D-glucopyranoside (**4b**, Entry 3, Table 3).* Major product **4b**: 299.3 mg, 68% yield. Minor product **4a**: 79.5 mg, 18% yield. White solid: R_f = 0.35 ($MeOH/CHCl_3$, 10:90); mp 66−69 °C; $[\alpha]^{25}_D$ = −111.4 (*c* 1.05, CH_3OH); ^1H NMR (400 MHz, C_5D_5N) δ 8.24 (d, *J* = 9.0 Hz, 2H, 4-NO_2-Ph*H*), 8.09 (br s, 1H, O*H*), 7.58 (br s, 1H, O*H*), 7.45−7.27 (m, 4H, 4-NO_2-Ph*H* and Ph*H*), 7.27−7.10 (m, 3H, Ph*H*), 5.81 (d, *J* = 7.3 Hz, 1H, *H*-1), 5.44 (dd, *J* = 11.5 Hz, *H*-6a), 5.26 (dd, *J* = 11.5, 5.8 Hz, 1H, *H*-6b), 5.03 (br s, 1H, O*H*), 4.60−4.47 (m, 1H, *H*-5), 4.47−4.20 (m, 3H, *H*-2, *H*-3 and *H*-4); ^{13}C NMR (100 MHz, C_5D_5N) δ 195.6, 163.0, 154.0, 142.7, 130.0 (2C), 126.8, 126.1 (2C), 122.3 (2C), 116.8 (2C), 101.5, 78.0, 75.1, 74.5, 74.3, 70.8; IR (solid) 3366, 2895, 1591, 1514, 1344, 1240, 1198, 1016 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 438 (M + H^+, 5), 307 (30), 289 (15), 154 (100), 136 (75), 107 (20), 77 (15); HRMS (FAB) Calcd for $C_{19}H_{20}NO_9S$ (M + H^+) 438.0853, found 438.0841. Anal. Calcd for $C_{19}H_{19}NO_9S$: C, 51.89; H, 4.38; N, 3.08. Found: C, 51.77; H, 4.23; N, 2.98.

*Ethyl 6-O-Phenoxythiocarbonyl-β-D-thioglucopyranoside (**5b**, Entry 4, Table 3).* Major product **5b**: 284.2 mg, 79% yield. Minor product **5a**: 18.1 mg, 5% yield. White solid: R_f = 0.32 ($MeOH/CHCl_3$, 10:90); mp 89−90 °C; $[\alpha]^{26}_D$ = −31.3 (*c* 1.01, CH_3OH); ^1H NMR (400 MHz, C_5D_5N) δ 7.38 (t, *J* = 7.8 Hz, 2H, Ph*H*), 7.30−7.10 (m, 3H), 5.41 (dd, *J* = 11.5, 1.5 Hz, 1H, *H*-6a), 5.17 (dd, *J* = 11.5, 5.9 Hz, 1H, *H*-6b), 5.02 (d, *J* = 9.8 Hz, 1H, *H*-1), 4.30−4.10 (m, 3H, *H*-3, *H*-4 and *H*-5), 4.05 (t, *J* = 9.2 Hz, 1H, *H*-2), 3.00−2.73 (m, 2H, SCH_2CH_3), 1.29 (t, *J* = 7.5 Hz, 3H, SCH_2CH_3); ^{13}C NMR (100 MHz, C_5D_5N) δ 195.6, 153.9, 129.9 (2C), 126.8, 122.3 (2C), 87.0, 79.8, 78.4, 74.9, 74.2, 71.1 24.3, 15.4; IR (solid) 3347, 2926, 1489, 1283, 1198, 1101, 1072, 1018 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 361 (M + H^+, 5), 307 (30), 289 (15), 154 (100), 136 (70), 107 (20), 77 (15); HRMS (FAB) calcd for $C_{15}H_{21}O_6S_2$ (M + H^+) 361.0774, found 361.0812. Anal. Calcd for $C_{15}H_{20}O_6S_2$: C, 49.98; H, 5.59. Found: C, 49.68; H, 5.87.

*Methyl 6-O-(4-Tolyloxy)thiocarbonyl-β-D-glucopyranoside (**6b**, Entry 5, Table 3).* Major product **6b**: 315.3 mg, 91% yield. Minor product **6a**: 20.1 mg, 6% yield. White solid: R_f = 0.35 ($MeOH/CHCl_3$, 10:90); mp 64−66 °C; $[\alpha]^{25}_D$ = −14.8 (*c* 1.05, CH_3OH); ^1H NMR (400 MHz, C_5D_5N) δ 7.69 (br s, 1H, O*H*), 7.47 (br s, 1H, O*H*), 7.12 (d, *J* = 8.5 Hz, 2H, Ph*H*), 7.07 (d, *J* = 8.5 Hz, 2H, Ph*H*), 5.42 (d, *J* = 11.5 Hz, 1H, *H*-6a), 5.22 (dd, *J* = 11.5, 5.2 Hz, 1H, *H*-6b), 5.01 (br s, 1H, O*H*), 4.76 (d, *J* = 7.8 Hz, 1H, *H*-1), 4.30−4.15 (m, 2H, *H*-3, *H*-4 and *H*-5), 4.05 (t, *J* = 8.3 Hz, 1H, *H*-2), 3.64 (s, 3H, OCH_3), 2.15 (s, 3H, 4-CH_3-Ph); ^{13}C NMR (100 MHz, C_5D_5N) δ 195.9, 151.9, 136.4, 130.4 (2C), 122.0 (2C), 105.7, 78.2, 74.9, 74.7, 74.6, 71.2, 56.8, 20.6; IR (solid) 3368, 2918, 1506, 1285, 1219, 1190, 1034, 1015 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 345 (M + H^+, 5), 307 (35), 289 (20), 165 (5), 154 (100), 136 (70), 107 (20), 77 (20); HRMS (FAB) calcd for $C_{15}H_{21}O_7S$ (M + H^+) 345.1014, found 345.1017. Anal. Calcd for $C_{15}H_{20}O_7S$: C, 52.31; H, 5.85. Found: C, 52.22; H, 5.98.

*Methyl 6-O-(2-Naphthoxy)thiocarbonyl-β-D-glucopyranoside (**7b**, Entry 6, Table 3).* Major product **7b**: 302.8 mg, 80% yield. Minor product **7a**: 12.6 mg, 3% yield. White solid: R_f = 0.35 ($MeOH/CHCl_3$, 10:90); mp 114−116 °C; $[\alpha]^{27}_D$ = −14.8 (*c* 1.22, CH_3OH); ^1H NMR (400 MHz, C_5D_5N) δ 7.89 (d, *J* = 8.8 Hz, 1H, Naph*H*), 7.90−7.80 (m, 2H, Naph*H*), 7.63 (d, *J* = 2.4 Hz, 1H, Naph*H*), 7.60−7.40 (m, 2H, Naph*H*), 7.37 (dd, *J* = 8.8, 2.4 Hz, 1H, Naph*H*), 5.46 (d, *J* = 11.0 Hz, 1H, *H*-6a), 5.28 (dd, *J* = 11.0, 2.4 Hz, 1H, *H*-6b), 4.79 (d, *J* = 7.8 Hz, 1H, *H*-1), 4.35−4.15 (m, 3H, *H*-3, *H*-4 and *H*-5), 4.08 (t, *J* = 8.3 Hz, 1H, *H*-2), 3.66 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, C_5D_5N) δ 195.8, 151.5, 134.1, 132.1, 129.9, 128.2, 128.1, 127.1, 126.5, 121.9, 119.4, 105.7, 78.2, 74.9, 74.8, 74.7, 71.2, 56.8; IR (solid) 3352, 2913, 1510, 1448, 1290, 1103, 1080, 1034 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 381 (M + H^+, 20), 307 (25), 289 (25), 154 (100), 136 (70), 117 (25), 77 (30); HRMS (FAB) calcd for $C_{18}H_{21}O_7S$ (M + H^+) 381.1003, found 381.1020.

*Methyl 6-O-(4-Chlorophenoxy)thiocarbonyl-β-D-glucopyranoside (**8b**, Entry 7, Table 3).* Major product **8b**: 298.5 mg, 82% yield. Minor product **8a**: 12.4 mg, 4% yield. White solid: R_f = 0.30 ($MeOH/CHCl_3$, 10:90); mp 136−138 °C; $[\alpha]^{25}_D$ = −13.6 (*c* 1.08, CH_3OH); ^1H NMR (400 MHz, C_5D_5N) δ 7.71 (br s, 1H, O*H*), 7.50 (br s, 2H, O*H*), 7.40 (d, *J* = 9.0 Hz, 2H, 4-Cl-Ph*H*), 7.13 (d, *J* = 9.0 Hz, 2H, 4-Cl-Ph*H*), 5.39 (dd, *J* = 11.5 Hz, 1H, *H*-6a), 5.19 (d, *J* = 11.5, 4.5 Hz, 1H, *H*-6b), 4.76 (d, *J* = 7.6 Hz, 1H, *H*-1), 4.30−4.22 (m, 1H, *H*-3), 4.22−4.13 (m, 2H, *H*-4 and *H*-5), 4.10−4.00 (m, 1H, *H*-2), 3.64 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, C_5D_5N) δ 195.3, 152.4, 131.9, 130.0 (2C), 124.1 (2C), 105.7, 79.7, 78.1, 74.9, 74.7, 71.2, 56.9; IR (solid) 3374, 2922, 1485, 1285, 1196, 1084, 1032, 1011 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 365 (M + H^+, 10), 307 (25), 289 (20), 221 (10), 154 (100), 136 (75), 107 (30); HRMS (FAB) calcd for $C_{14}H_{18}ClO_7S$ (M + H^+) 365.0456, found 365.0488. Anal. Calcd for $C_{14}H_{17}ClO_7S$: C, 46.09; H, 4.70. Found: C, 46.01; H, 4.38.

*Methyl 6-O-(4-Fluorophenoxy)thiocarbonyl-β-D-glucopyranoside (**9b**, Entry 8, Table 3).* Major product **9b**: 311.8 mg, 90% yield. Minor product **9a**: 19.9 mg, 6% yield. White solid: R_f = 0.30 ($MeOH/CHCl_3$, 10:90); mp 57−59 °C; $[\alpha]_D^{23}$ = −14.6 (*c* 1.04, CH_3OH); ^1H NMR (400 MHz, C_5D_5N) δ 8.58 (br s, 1H, O*H*), 7.16 (d, *J* = 6.1 Hz, 4H, 4-F-Ph*H*), 5.40 (d, *J* = 11.2 Hz, 1H, *H*-6a), 5.20 (dd, *J* = 11.2, 5.3 Hz, 1H, *H*-6b), 4.76 (d, *J* = 7.6 Hz, 1H, *H*-1), 4.30−4.10 (m, 3H, *H*-3, *H*-4 and *H*-5), 4.05 (t, *J* = 8.3 Hz, 1H, *H*-2), 3.64 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, C_5D_5N) δ 195.7, 160.8 (d, *J* = 244.1 Hz), 150.1, 124.1 (d, *J* = 8.3 Hz, 2C), 116.5 (d, *J* = 24.0 Hz, 2C), 105.7, 78.1, 74.8 (2C), 74.6, 71.1, 56.8; IR (solid) 3362, 2903, 1501, 1283, 1213, 1184, 1082, 1011 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 349 (M + H^+, 25), 317 (25), 307 (15), 237 (20), 154 (100), 137 (55), 85 (35), 77 (20); HRMS (FAB) calcd for $C_{14}H_{18}FO_7S$ (M + H^+) 349.0752, found

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349.0791. Anal. Calcd for $C_{14}H_{17}FO_7S$: C, 48.27; H, 4.92. Found: C, 48.04; H, 4.95.

*Methyl 6-O-Benzoyl-β-D-glucopyranoside (**11b**, Entry 10, Table 3).*[11b,12] Major product **11b**: 286.7 mg, 97% yield. Minor product **11a**: 21.6 mg, 7% yield. White solid: R_f = 0.47 ($MeOH/CHCl_3$, 10:90); mp 129−131 °C (lit.[12] mp 131−132 °C); $[\alpha]^{25}_D$ = −17.8 (*c* 1.03, CH_3OH) [lit.[12] $[\alpha]^{27}_D$ = −24.2 (*c* 1.40, H_2O)]; ^1H NMR (400 MHz, $(CD_3)_2CO$) δ 8.10−8.00 (m, 2H, PhH), 7.70−7.60 (m, 1H, PhH), 7.60−7.45 (m, 2H, PhH), 4.68 (dd, *J* = 11.7, 2.2 Hz, 1H, H-6a), 4.48 (br s, 1H, OH), 4.46 (dd, *J* = 11.7, 5.9 Hz, 1H, H-6b), 4.37 (br s, 1H, OH), 4.31 (br s, 1H, OH), 4.25 (d, *J* = 7.8 Hz, 1H, H-1), 3.70−3.60 (m, 1H, H-5), 3.55−3.40 (m, 3H, H-3 and H-4), 3.43 (s, 3H, OCH_3), 3.23 (t, *J* = 7.2 Hz, 1H, H-2); ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 166.7, 133.9, 131.2, 130.2 (2C), 129.4 (2C), 105.1, 77.8, 74.8, 74.8, 71.4, 65.0, 56.6; IR (solid) 3399, 2878, 1713, 1271, 1072, 1045, 1016, 974 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 299 (M + H^+, 20), 267 (10), 154 (100), 136 (70), 107 (25), 105 (20), 77 (20); HRMS (FAB) calcd for $C_{14}H_{19}O_7$ (M + H^+) 299.1125, found 299.1154. Anal. Calcd for $C_{14}H_{18}O_7$: C, 56.37; H, 6.08. Found: C, 56.23; H, 6.06.

*Methyl 6-O-Isobutyryl-β-D-glucopyranoside (**12b**, Entry 11, Table 3).* Major product **12b**: 243.4 mg, 92% yield. Minor product **12a**: 1.0 mg, <1% yield. White solid: R_f = 0.35 ($MeOH/CHCl_3$, 10:90); mp 101−102 °C; $[\alpha]^{26}_D$ = −17.2 (*c* 1.01, CH_3OH); ^1H NMR (400 MHz, C_5D_5N) δ 6.86 (br s, 3H, OH), 4.98 (d, *J* = 11.5 Hz, 1H, H-6a), 4.81 (dd, *J* = 11.5, 5.9 Hz, 1H, H-6b), 4.70 (d, *J* = 7.8 Hz, 1H, H-1), 4.23 (t, *J* = 8.7 Hz, 1H, H-4), 4.10−3.95 (m, 3H, H-2, H-3 and H-5), 3.63 (s, 3H, OCH_3), 2.57 (sept, *J* = 6.8 Hz, 1H, $OCOCH(CH_3)_2$), 1.12 (d, *J* = 6.8 Hz, 3H, $OCOCH(CH_3)_2$), 1.10 (d, *J* = 6.8 Hz, 3H, $OCOCH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.7, 103.5, 76.1, 73.9, 73.4, 70.3, 63.5, 57.0, 33.9, 19.0, 18.9. IR (solid) 3412, 2907, 1717, 1192, 1161, 1098, 1049, 1003 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 265 (M + H^+, 15), 233 (20), 154 (100), 137 (60), 136 (65), 107 (15), 89 (15), 77 (10); HRMS (FAB) Calcd for $C_{11}H_{21}O_7$ (M + H^+) 265.1282, found 265.1281. Anal. Calcd for $C_{11}H_{20}O_7$: C, 49.99; H, 7.63. Found: C, 49.72; H, 7.65.

*Methyl 6-O-[3,5-Bis(trifluoromethyl)benzenesulfonyl]-β-D-glucopyranoside (**13b**, Entry 12, Table 3).* Major product **13b**: 472.9 mg, >99% yield. Minor product **13a**: 1.9 mg, <1% yield. White solid: R_f = 0.31 ($MeOH/CHCl_3$, 10:90); mp 136−138 °C; $[\alpha]^{17}_D$ = −13.0 (*c* 1.15, CH_3OH); ^1H NMR (400 MHz, $(CD_3)_2CO$) δ 8.51 (s, 3H, 3,5-CF_3-PhH), 4.58 (dd, *J* = 11.0, 1.3 Hz, 1H, H-6a), 4.46 (dd, *J* = 11.0, 5.4 Hz, 1H, H-6b), 4.44 (br s, 1H, OH), 4.32 (br s, 1H, OH), 4.29 (br s, 1H, OH), 4.11 (d, *J* = 7.6 Hz, 1H, H-1), 3.60−3.45 (m, 1H, H-5), 3.40−3.20 (m, 2H, H-3 and H-4), 3.30 (s, 3H, OCH_3), 3.04 (t, *J* = 8.2 Hz, 1H, H-2); ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 140.0, 133.4 (q, *J* = 34.8 Hz, 2C), 129.3 (q, *J* = 3.3 Hz, 2C), 128.6 (sept, *J* = 3.3 Hz), 123.6 (q, *J* = 272.3 Hz, 2C), 104.9, 77.5, 74.4, 74.1, 72.2, 70.4, 56.7; ^{19}F NMR (376 MHz, $(CD_3)_2CO$) δ −62.3 (m, 6F); IR (solid) 3376, 2922, 1607, 1466, 1362, 1281, 1179, 976 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 471 (M + H^+, 15), 451 (10), 421 (55), 277 (30), 213 (60), 154 (100), 145 (40), 136 (95); HRMS (FAB) calcd for $C_{15}H_{17}F_6O_8S$ (M + H^+) 471.0543, found 471.0559. Anal. Calcd for $C_{15}H_{16}F_6O_8S$: C, 38.30; H, 3.43. Found: C, 38.01; H, 3.25.

Kinetics Experiment (Figure 1). To a solution of 1,2,3,4-*O*-tetramethyl-α- or β-D-glucopyranoside[13] (118.1 mg, 0.50 mmol) in THF (5 mL) in a vial was added pyridine (0.053 mL, 0.13 mmol) and isobutyryl chloride (0.50 mL, 1.1 mmol) at 0 °C. Then, after stirring vigorously for 5−240 min at 0 °C, the reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with ethyl acetate. The organic layer was washed with water and brine, dried over $MgSO_4$, filtrated, and concentrated in vacuo. The residue was purified by SiO_2 column chromatography (*n*-hexane/ethyl acetate = 9:1−1:1) to give 1,2,3,4-*O*-tetramethyl-6-*O*-isobutyryl-α- or β-D-glucopyranoside **14a** or **14b**, respectively.

*1,2,3,4-O-Tetramethyl-6-O-isobutyryl-α-D-glucopyranoside (**14a**, Figure 1).* Colorless oil: R_f = 0.52 (EtOAc/*n*-hexane, 50:50); $[\alpha]^{24}_D$ = +125.0 (*c* 1.07, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 4.81 (d, *J* = 3.7 Hz, 1H, H-1), 4.31 (dd, *J* = 11.8, 2.3 Hz, 1H, H-6a), 4.25 (dd, *J* = 11.8, 5.0 Hz, 1H, H-6b), 3.71 (ddd, *J* = 10.3, 5.0, 2.3 Hz, 1H, H-5), 3.63 (s, 3H, OCH_3), 3.53 (s, 3H, OCH_3), 3.53 (dd, *J* = 9.5, 8.9 Hz, 1H, H-3), 3.52 (s, 3H, OCH_3), 3.41 (s, 3H, OCH_3), 3.20 (dd, *J* = 9.5, 3.7 Hz, 1H, H-2), 3.08 (dd, *J* = 10.3, 8.9 Hz, 1H, H-4), 2.61 (sept, *J* = 7.1 Hz, 1H, $OCOCH(CH_3)_2$), 1.20 (d, *J* = 7.1 Hz, 3H, $OCOCH(CH_3)_2$), 1.19 (d, *J* = 7.1 Hz, 3H, $OCOCH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 97.2, 83.4, 81.6, 79.7, 68.6, 62.8, 60.8, 60.4, 58.9, 55.0, 33.8, 19.0, 18.8; IR (oil) 2934, 1734, 1470, 1387, 1190, 1155, 1098, 1043 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 307 (M + H^+, 20), 305 (20), 275 (70), 243 (90), 155 (80), 127 (50), 101 (100), 71 (85); HRMS (FAB) calcd for $C_{14}H_{27}O_7$ (M + H^+) 307.1757, found 307.1757.

*1,2,3,4-O-Tetramethyl-6-O-isobutyryl-β-D-glucopyranoside (**14b**, Figure 1).* Colorless oil: R_f = 0.58 (EtOAc/*n*-hexane, 50:50); $[\alpha]^{26}_D$ = −13.1 (*c* 1.10, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 4.34 (dd, *J* = 11.8, 2.2 Hz, 1H, H-6a), 4.21 (dd, *J* = 11.8, 5.6 Hz, 1H, H-6b), 4.16 (d, *J* = 7.8 Hz, 1H, H-1), 3.63 (s, 3H, OCH_3), 3.57 (s, 3H, OCH_3), 3.52 (s, 3H, OCH_3), 3.52 (s, 3H, OCH_3), 3.39 (ddd, *J* = 9.5, 5.6, 2.2 Hz, 1H, H-5), 3.19 (dd, *J* = 9.0, 8.8 Hz, 1H, H-3), 3.10 (dd, *J* = 9.5, 9.0 Hz, 1H, H-4), 3.00 (dd, *J* = 8.8, 7.8 Hz, 1H, H-2), 2.60 (sept, *J* = 7.1 Hz, 1H, $OCOCH(CH_3)_2$), 1.19 (d, *J* = 7.1 Hz, 3H, $OCOCH(CH_3)_2$), 1.18 (d, *J* = 7.1 Hz, 3H, $OCOCH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 104.1, 86.5, 83.6, 79.6, 72.8, 63.0, 60.8, 60.4, 60.4, 56.9, 33.9, 19.1, 18.8; IR (oil) 2936, 1736, 1470, 1387, 1192, 1150, 1109, 1076 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 307 (M + H^+, 20), 305 (25), 275 (75), 243 (90), 155 (80), 127 (45), 101 (100), 71 (75); HRMS (FAB) calcd for $C_{14}H_{27}O_7$ (M + H^+) 307.1757, found 307.1768.

General Procedure for the Chemo- and Regioselective Functionalization of Structurally Similar Carbohydrates Catalyzed by Bu_2SnCl_2 (Scheme 2 (a)). After the mixture of methyl α-D-glucopyranoside (194.2 mg, 1.0 mmol), methyl β-D-arabinofuranoside (164.2 mg, 1.0 mmol), and dibutyltin dichloride (30.4 mg, 0.10 mmol) in THF (8 mL) was stirred in a vial at room temperature for 10 min, tetrabutylammonium iodide (184.7 mg, 0.50 mmol), phenyl chlorothionoformate (0.175 mL, 1.3 mmol), and 1,2,2,6,6-pentamethylpiperidine (0.271 mL, 1.5 mmol) were added to the suspension at 20 °C. After being stirred vigorously for 6 h at 20 °C, the reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with ethyl acetate. The organic layer was washed with water and brine, dried over $MgSO_4$, filtrated, and concentrated in vacuo (water bath temperature: <20 °C). The residue was purified by SiO_2 column chromatography (*n*-hexane/ethyl acetate = 3:1−0:1) to give a mixture of methyl 2-*O*-phenoxythiocarbonyl-α-D-glucopyranoside **1a** (320.4 mg, 97% yield) as a white solid.

*Methyl 2-O-(3,5-Difluorobenzenesulfonyl)-α-D-glucopyranoside (**15**, Scheme 2 (a)).*[2j] Yield of **15**: 352.5 mg, 95%; white solid; R_f = 0.27 ($MeOH/CHCl_3$, 10:90); mp 38−40 °C; $[\alpha]^{21}_D$ = +94.4 (*c* 1.13, CH_3OH); ^1H NMR (400 MHz, $(CD_3)_2CO$) δ 7.70−7.60 (m, 2H, 3,5-F-PhH), 7.55−7.45 (m, 1H, 3,5-F-PhH), 4.82 (d, *J* = 3.7 Hz, 1H, H-1), 4.67 (br s, 1H, OH), 4.48 (br s, 1H, OH), 4.28 (dd, *J* = 9.6, 3.7 Hz, 1H, H-2), 3.90−3.60 (m, 4H, H-3, H-6 and OH), 3.60−3.50 (m, 1H, H-5), 3.39 (t, *J* = 9.3 Hz, 1H, H-4), 3.34 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 163.6 (d, *J* = 252.4 Hz), 163.5 (d, *J* = 252.4 Hz), 140.8 (t, *J* = 9.1 Hz), 112.6 (d, *J* = 19.9 Hz), 112.5 (d, *J* = 19.9 Hz), 110.2 (t, *J* = 25.7 Hz), 98.1, 82.2, 73.0, 71.7, 71.6, 62.1, 55.2; ^{19}F NMR (376 MHz, $(CD_3)_2CO$) δ −106.4 to −106.5 (m, 2F). IR (solid) 3377, 2928, 1607, 1443, 1371, 1300, 1179, 962 cm^{-1}; MS (FAB) *m*/*z* (rel intensity) 371 (M + H^+, 10), 339 (20), 307 (20), 289 (15), 261 (5), 154 (100), 145 (30), 137 (90); HRMS (FAB) calcd for $C_{13}H_{17}F_2O_8S$ (M + H^+) 371.0607, found 371.0629. Anal. Calcd for $C_{13}H_{16}F_2O_8S$: C, 42.16; H, 4.35. Found: C, 42.37; H, 4.11.

*Methyl 3-O-Benzoyl-α-D-galactopyranoside (**16**, Scheme 2 (c)).*[11b] Major product **16**: 297.9 mg, >99% yield. Minor product **11a**: 56.7 mg, 19% yield. White solid: R_f = 0.30 ($MeOH/CHCl_3$, 10:90). Mp 55−57 °C. $[\alpha]^{27}_D$ = +190.1 (*c* 1.20, CH_3OH); ^1H NMR (400 MHz, $(CD_3)_2CO$) δ 8.08 (dd, *J* = 8.4, 1.3 Hz, 2H, PhH), 7.63 (tt, *J* = 7.4, 1.3 Hz, 1H, PhH), 7.50 (t, *J* = 7.7 Hz, 2H, PhH), 5.22 (dd, *J* = 10.3, 3.2 Hz, 1H, H-3), 4.80 (d, *J* = 3.9 Hz, 1H, H-1), 4.44 (br s, 1H, OH), 4.33−4.15 (m, 2H, H-2 and H-4), 3.89 (t, *J* = 5.7 Hz, 1H, H-5), 3.89 (br s, 1H, OH), 3.85−3.65 (m, 3H, H-6 and OH), 3.42 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 166.7, 133.7, 131.5, 130.4 (2C), 129.1 (2C), 101.2, 75.5, 71.6, 68.5, 67.5, 62.2, 55.4; IR

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(solid) 3385, 2932, 1697, 1315, 1273, 1119, 1053, 970 cm^{-1}; MS (FAB) *m/z* (rel intensity) 299 (M + H^+, 5), 289 (15), 154 (100), 136 (90), 107 (15), 105 (10), 77 (10); HRMS (FAB) calcd for $C_{14}H_{19}O_7$ (M + H^+) 299.1125, found 299.1154.

*Methyl 3-O-[3,5-Bis(trifluoromethyl)benzenesulfonyl]-α-D-galactopyranoside (**17**, Scheme 2 (c)).* Major product **17**: 425.3 mg, 90% yield. Minor product **13a**: 22.4 mg, 5% yield. White solid: R_f = 0.41 ($MeOH/CHCl_3$, 10:90); mp 134−135 °C; $[\alpha]^{28}_D$ = +128.8 (*c* 1.01, CH_3OH); ^1H NMR (400 MHz, $(CD_3)_2CO$) δ 8.54 (s, 2H, 3,5-CF_3-PhH), 8.44 (s, 1H, 3,5-CF_3-PhH), 4.78 (dd, *J* = 10.3, 3.2 Hz, 1H, *H*-3), 4.69 (d, *J* = 3.9 Hz, 1H, *H*-1), 4.66 (d, *J* = 5.1 Hz, 1H, OH), 4.30 (t, *J* = 4.0 Hz, 1H, *H*-4), 4.03 (ddd, *J* = 10.3, 3.9, 2.9 Hz, 1H, *H*-2), 3.95−3.65 (m, 5H, *H*-5, H-6 and OH), 3.31 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 141.1, 133.0 (q, *J* = 34.8 Hz, 2C), 129.5 (q, *J* = 3.3 Hz, 2C), 128.2 (sept, *J* = 3.3 Hz), 123.6 (q, *J* = 272.3 Hz, 2C), 101.0, 85.2, 71.4, 69.4, 67.3, 61.9, 55.3; ^{19}F NMR (376 MHz, $(CD_3)_2CO$) δ −62.3 (s, 6F); IR (solid) 3385, 2940, 1366, 1292, 1175, 1130, 1045, 962 cm^{-1}; MS (FAB) *m/z* (rel intensity) 471 (M + H^+, 30), 439 (75), 349 (40), 277 (20), 213 (20), 154 (85), 137 (100), 85 (40); HRMS (FAB) calcd for $C_{15}H_{17}F_6O_8S$ (M + H^+) 471.0543, found 471.0547.

*Methyl 3-O-Benzoyl-β-D-galactopyranoside (**18**, Scheme 2 (d)).*[11b,14] Major product **18**: 298.4 mg, >99% yield. Minor product **11b**: 26.9 mg, 9% yield. White solid: R_f = 0.30 ($MeOH/CHCl_3$, 10:90); mp 123−125 °C (lit.[14] mp 120−121 °C); $[\alpha]^{27}_D$ = +52.4 (*c* 1.18, CH_3OH) [lit.[14] $[\alpha]_D$ = +57.0 (*c* 1.00, C_2H_5OH)]; ^1H NMR (400 MHz, $(CD_3)_2CO$) δ 8.08 (d, *J* = 7.6 Hz, 2H, PhH), 7.63 (t, *J* = 7.6 Hz, 1H, PhH), 7.51 (t, *J* = 7.6 Hz, 2H, PhH), 4.99 (dd, *J* = 10.0, 2.7 Hz, 1H, *H*-3), 4.46 (br s, 1H, OH), 4.33 (d, *J* = 7.6 Hz, 1H, *H*-1), 4.31 (br s, 1H, OH), 4.24 (s, 1H, *H*-4), 3.97 (t, *J* = 8.8 Hz, 1H, *H*-2), 3.90−3.65 (m, 3H, *H*-6 and OH), 3.50 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 166.5, 133.7, 131.5, 130.4 (2C), 129.2 (2C), 105.6, 78.1, 75.7, 69.5, 67.7, 62.0, 56.7; IR (solid) 3393, 2936, 1705, 1450, 1273, 1117, 1067, 1026 cm^{-1}; MS (FAB) *m/z* (rel intensity) 299 (M + H^+, 30), 267 (55), 154 (100), 136 (65), 107 (25), 105 (95), 77 (25); HRMS (FAB) calcd for $C_{14}H_{19}O_7$ (M + H^+) 299.1125, found 299.1153.

*Methyl 3-O-[3,5-Bis(trifluoromethyl)benzenesulfonyl]-β-D-galactopyranoside (**19**, Scheme 2 (d)).*[2j] Major product **19**: 458.8 mg, 97% yield. Minor product **13b**: 45.4 mg, 10% yield. White solid: R_f = 0.34 ($MeOH/CHCl_3$, 10:90); mp 144−146 °C; $[\alpha]^{21}_D$ = +37.4 (*c* 1.10, CH_3OH); ^1H NMR (400 MHz, $(CD_3)_2CO$) δ 8.53 (s, 2H, 3,5-CF_3-PhH), 8.45 (s, 1H, 3,5-CF_3-PhH), 4.64 (dd, *J* = 9.9 Hz, 1H, *H*-3), 4.58 (s, 1H, OH), 4.57 (s, 1H, OH), 4.30−4.20 (m, 1H, *H*-4), 4.14 (d, *J* = 7.6 Hz, 1H, *H*-1), 4.00−3.90 (m, 1H, *H*-5), 3.85−3.65 (m, 3H, *H*-2, *H*-6a and OH), 3.61 (dd, *J* = 11.7, 5.9 Hz, 1H, *H*-6b), 3.39 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 140.8, 132.8 (q, *J* = 34.8 Hz, 2C), 129.6 (q, *J* = 3.9 Hz, 2C), 128.2 (sept, *J* = 3.9 Hz), 123.6 (q, *J* = 272.2 Hz, 2C), 105.0, 86.7, 75.1, 69.4, 68.7, 61.7, 56.8; ^{19}F NMR (376 MHz, $(CD_3)_2CO$) δ −62.4 (s, 6F); IR (solid) 3445, 2922, 1358, 1277, 1198, 1134, 1074, 961 cm^{-1}; MS (FAB) *m/z* (rel intensity) 471 (M + H^+, 15), 439 (35), 349 (20), 277 (15), 213 (15), 154 (100), 136 (85), 77 (35); HRMS (FAB) calcd for $C_{15}H_{17}F_6O_8S$ (M + H^+) 471.0556, found 471.0562. Anal. Calcd for $C_{15}H_{16}F_6O_8S$: C, 38.30; H, 3.43. Found: C, 38.57; H, 3.03.

*Methyl 3-O-Phenoxythiocarbonyl-α-D-mannopyranoside (**20**, Scheme 2 (b)).*[4] Major product **1a**: 312.4 mg, 95% yield. Minor product **20**: 34.7 mg, 10% yield. White solid: R_f = 0.29 ($MeOH/CHCl_3$, 10:90); mp 65−70 °C; $[\alpha]^{14}_D$ = +29.9 (*c* 1.40, CH_3OH); ^1H NMR (400 MHz, C_5D_5N) δ 7.77 (br s, 3H, OH), 7.32 (t, *J* = 7.8 Hz, 2H, PhH), 7.22−7.18 (m, 1H, PhH), 6.97 (d, *J* = 8.3 Hz, 2H, PhH), 6.37−6.33 (m, 1H, *H*-3), 5.25 (br s, 1H, *H*-1), 5.14 (t, *J* = 9.6 Hz, 1H, *H*-4), 5.08 (d, *J* = 1.5 Hz, 1H, *H*-2), 4.56 (d, *J* = 11.7 Hz, 1H, *H*-6a), 4.46 (dd, *J* = 11.7, 5.3 Hz, 1H, *H*-6b), 4.39−4.33 (m, 1H, *H*-5), 3.44 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, C_5D_5N) δ 195.5, 153.9, 129.8 (2), 126.7, 122.3 (2), 102.7, 87.7, 75.5, 68.0, 65.4, 62.5, 54.6; IR (solid) 3354, 2928, 1489, 1271, 1190, 1128, 1057, 1016 cm^{-1}; MS (FAB) *m/z* (rel intensity) 331 (M + H^+, 15), 307 (20), 289 (20), 154 (100), 136 (75), 107 (30), 77 (45), 65 (15); HRMS (FAB) calcd for $C_{14}H_{19}O_7S$ (M + H^+) 331.0846, found 331.0869. Anal. Calcd for $C_{14}H_{18}O_7S$: C, 50.90; H, 5.49. Found: C, 50.63; H, 5.33.

*Methyl 3-O-Benzoyl-α-D-mannopyranoside (**21**, Scheme 2 (b)).*[11b] Major product **11a**: 296.2 mg, >99% yield. Minor product **21**: 29.3 mg, 10% yield. White solid: R_f = 0.31 ($MeOH/CHCl_3$, 10:90); mp 33−34 °C (high moisture absorption); $[\alpha]^{27}_D$ = +17.5 (*c* 0.90, CH_3OH); ^1H NMR (400 MHz, $(CD_3)_2CO$) δ 8.08 (d, *J* = 7.6 Hz, 2H, PhH), 7.63 (t, *J* = 7.6 Hz, 1H, PhH), 7.50 (t, *J* = 7.6 Hz, 2H, PhH), 5.23 (dd, *J* = 9.8, 3.2 Hz, 1H, *H*-3), 4.70 (s, 1H, *H*-1), 4.60−4.45 (m, 2H, OH), 4.23−4.10 (m, 2H, *H*-2 and *H*-4), 3.88 (ddd, *J* = 11.5, 6.0, 2.8 Hz, 1H, *H*-6a), 3.77 (dd, *J* = 11.5, 6.3 Hz, 1H, *H*-6b), 3.70−3.55 (m, 2H, *H*-5, OH), 3.40 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 166.5, 133.7, 131.6, 130.5 (2C), 129.1 (2C), 102.3, 76.7, 74.4, 69.5, 65.8, 62.8, 54.8; IR (solid) 3385, 2932, 1697, 1315, 1273, 1119, 1053, 970 cm^{-1}; MS (FAB) *m/z* (rel intensity) 299 (M + H^+, 40), 267 (30), 154 (100), 136 (90), 107 (25), 105 (60), 77 (25); HRMS (FAB) calcd for $C_{14}H_{19}O_7$ (M + H^+) 299.1125, found 299.1128.

*Methyl 3-O-[3,5-Bis(trifluoromethyl)benzenesulfonyl]-α-D-mannopyranoside (**22**, Scheme 2 (b)).*[2j] Major product **13a**: 450.9 mg, 96% yield. Minor product **22**: 18.8 mg, 4% yield. White solid: R_f = 0.36 ($MeOH/CHCl_3$, 10:90); mp 48−50 °C; $[\alpha]^{21}_D$ = +15.6 (*c* 1.01, CH_3OH); ^1H NMR (400 MHz, $(CD_3)_2CO$) δ 8.51 (s, 2H, 3,5-CF_3-PhH), 8.46 (s, 1H, 3,5-CF_3-PhH), 4.70 (d, *J* = 9.8, 3.2 Hz, 1H, *H*-3), 4.67 (d, *J* = 2.0 Hz, 1H, *H*-1), 4.09 (dd, *J* = 3.2, 2.0 Hz, 1H, *H*-2), 3.97 (t, *J* = 9.8 Hz, 1H, *H*-4), 3.75 (dd, *J* = 12.0, 2.8 Hz, 1H, *H*-6a), 3.65 (dd, *J* = 12.0, 4.9 Hz, 1H, *H*-6b), 3.60−3.20 (m, 4H, *H*-5 and OH), 3.33 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 140.9, 133.4 (q, *J* = 34.8 Hz, 2C), 129.5 (q, *J* = 3.3 Hz, 2C), 128.3 (sept, *J* = 3.3 Hz), 123.6 (q, *J* = 272.3 Hz, 2C), 102.1, 86.3, 74.3, 70.4, 65.4, 62.2, 54.9; ^{19}F NMR (376 MHz, $(CD_3)_2CO$) δ −62.3 (s, 6F); IR (solid) 3389, 2940, 1362, 1279, 1179, 1132, 1057, 961 cm^{-1}; MS (FAB) *m/z* (rel intensity) 471 (M + H^+, 10), 451 (5), 439 (40), 421 (45), 277 (25), 213 (50), 154 (100), 136 (95); HRMS (FAB) calcd for $C_{15}H_{17}F_6O_8S$ (M + H^+) 471.0543, found 471.0556. Anal. Calcd for $C_{15}H_{16}F_6O_8S$: C, 38.30; H, 3.43. Found: C, 38.01; H, 3.43.

General Procedure for the Chemo- and Regioselective Functionalization of Structurally Similar Carbohydrates Catalyzed by Me_2SnCl_2 (Scheme 2 (e)). After the mixture of methyl β-D-glucopyranoside (194.2 mg, 1.0 mmol), methyl β-D-galactopyranoside (194.2 mg, 1.0 mmol), and dimethyltin dichloride (22.0 mg, 0.10 mmol) in THF (9 mL) was stirred in a vial at room temperature for 10 min, 3,5-lutidine (0.0114 mL, 0.10 mmol) and 1,2,2,6,6-pentamethylpiperidine (0.271 mL, 1.5 mmol) were added to the suspension at 20 °C. Then, benzoyl chloride (0.128 mL, 1.1 mmol) in THF (2 mL) was flowed over 2 h at 20 °C. Then, after being stirred vigorously for 6 h at 20 °C, the reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with ethyl acetate. The organic layer was washed with water and brine, dried over $MgSO_4$, filtrated, and concentrated in vacuo. The residue was purified by SiO_2 column chromatography (*n*-hexane/ethyl acetate = 3:1−0:1) to give a mixture of methyl 6-*O*-benzoyl-β-D-glucopyranoside **11b** (284.4 mg, 96%) and methyl 3-*O*-benzoyl-β-D-galactopyranoside **18** (18.2 mg, 6%).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of spectra for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) For examples, see: (a) Feizi, T. *Nature* **1985**, *314*, 53−57. (b) Gabius, H.-J.; Gabius, S. *Lectins and Cancer*; Springer-Verlag: New York, 1991. (c) Crocker, P. R.; Feizi, T. *Curr. Opin. Struct. Biol.* **1996**, *6*, 679−691. (d) Kansas, G. S. *Blood* **1996**, *88*, 3259−3287. (e) Liedtke, S.; Geyer, H.; Wuhrer, M.; Geyer, R.; Frank, G.; Gerardy-Schahn, R.; Zahringer, U.; Schachner, M. *Glycobiology* **2001**, *11*, 373−384. (f) Brodesser, S.; Sawatzki, P.; Kolter, T. *Eur. J. Org. Chem.* **2003**, *11*, 2021−2034. (g) Almkvist, J.; Karlsson, A. *Glycoconjugate J.* **2004**, *19*, 575−581.

(2) For examples of the stereo- and regioselective synthesis, see: (a) Oshima, K.; Aoyama, Y. *J. Am. Chem. Soc.* **1999**, *121*, 2315−2316. (b) Herzner, H.; Reipen, T.; Schultz, M.; Kunz, H. *Chem. Rev.* **2000**, *100*, 4495−4538. (c) Martinelli, M. J.; Vaidyanathan, R.; Pawlak, J. M.; Nayyar, N. K.; Dhokte, U. P.; Doecke, C. W.; Zollars, L. M.; Moher, E. D.; Khau, V. V.; Košmrlj, B. *J. Am. Chem. Soc.* **2002**, *124*, 3578−3585. (d) Wang, C.-C.; Lee, J.-C.; Luo, S.-Y.; Kulkarni, S. S.; Huang, Y.-W.; Lee, C.-C.; Chang, K.-L.; Hung, S.-C. *Nature* **2007**, *446*, 896−899. (e) Kawabata, T.; Muramatsu, W.; Nishio, T.; Shibata, T.; Schedel, H. *J. Am. Chem. Soc.* **2007**, *129*, 12890−12895. (f) Lee, D.; Taylor, M. S. *J. Am. Chem. Soc.* **2011**, *133*, 3724−3727. (g) Hsu, C.-H.; Hung, S.-C.; Wu, C.-Y.; Wong, C.-H. *Angew. Chem., Int. Ed.* **2011**, *50*, 11872−11923. (h) Jordan, P. A.; Miller, S. J. *Angew. Chem., Int. Ed.* **2012**, *51*, 2907−2911. (i) Lee, D.; Williamson, C. L.; Chan, L.; Taylor, M. S. *J. Am. Chem. Soc.* **2012**, *134*, 8260−8267. (j) Muramatsu, W. *J. Org. Chem.* **2012**, *77*, 8083−8091. (k) Lee, D.; Taylor, M. S. *Synthesis* **2012**, *44*, 3421−3431.

(3) For examples, see: (a) VanDraanen, N. A.; Koszalka, G. W. *Nucleosides Nucleotides* **1994**, *13*, 1679−1693. (b) Damkjaer, D. L.; Petersen, M.; Wengel, J. *Nucleosides Nucleotides* **1994**, *13*, 1801−1807. (c) García, J.; Fernández, S.; Ferrero, M.; Sanghvi, Y. S.; Gotor, V. *Org. Lett.* **2004**, *6*, 3759−3762. (d) García, J.; Díaz-Rodríguez, A.; Fernández, S.; Sanghvi, Y. S.; Ferrero, M.; Gotor, V. *J. Org. Chem.* **2006**, *71*, 9765−9771. (e) Maity, J.; Shakya, G.; Singh, S. K.; Ravikumar, V. T.; Parmar, V. S.; Prasad, A. K. *J. Org. Chem.* **2008**, *73*, 5629−5632. (f) Singh, S. K.; Sharma, V. K.; Bohra, K.; Olsen, C. E.; Prasad, A. K. *J. Org. Chem.* **2011**, *76*, 7556−7562.

(4) The use of a tetrabutylammonium iodide promotes the thiocarbonylation with activation of chlorothionoformates, see: Muramatsu, W.; Tanigawa, S.; Takemoto, Y.; Yoshimatsu, H.; Onomura, O. *Chem.—Eur. J.* **2012**, *18*, 4850−4853.

(5) Vic, G.; Hastings, J. J.; Howarth, O. W.; Crout, D. H. G. *Tetrahedron: Asymmetry* **1996**, *7*, 709−720.

(6) Investigations of the coordination and effect of Sn reagent including ^{119}Sn NMR analysis on the regioselectivity of dialkylstannylene acetal-mediated reactions have been reported. However, their ^{119}Sn NMR analyses were carried out at high temperature or after dialkylstannylene acetals were prepared. For examples, see: (a) Grindley, T. B.; Thangarasa, R. *Can. J. Chem.* **1990**, *68*, 1007−1019. (b) Grindley, T. B.; Thangarasa, R. *J. Am. Chem. Soc.* **1990**, *112*, 1364−1373. (c) Grindley, R.; Thangarasa, T. B.; Bakshi, P. K.; Cameron, T. S. *Can. J. Chem.* **1992**, *70*, 197−204. (d) Kong, X.; Grindley, T. B. *Can. J. Chem.* **1994**, *72*, 2396−2404. (e) Kong, X.; Grindley, T. B. *Can. J. Chem.* **1994**, *72*, 2405−2415. (f) Reference 5a. In our case of the use of R_2SnCl_2, on the other hand, we have not observed a peak of dialkylstannylene acetals so far under our best reaction conditions.

(7) Long-range stereoelectronic controlled reaction of carbohydrates in the presence of stereoisomers has been a few reported. For example, see: (a) Miljkovic, M.; Yeagley, D.; Deslongchamps, P.; Dory, Y. L. *J. Org. Chem.* **1997**, *62*, 7597−7604. (b) Magaud, D.; Dolmazon, R.; Anker, D.; Doutheau, A.; Dory, Y. L.; Deslongchamps, P. *Org. Lett.* **2000**, *2*, 2275−2277. (c) Zeng, Y.; Wang, Z.; Whitfield, D.; Huang, X. *J. Org. Chem.* **2008**, *73*, 7952−7962.

(8) We have not found reasonable data about the influences of anomeric effects so far in the screening of anomeric substituent (entries 1−4 of Table 3) due to the different solubilities of each carbohydrates in THF.

(9) All data of a minor product **20**−**22** in each reaction are shown in the Experimental Section and Supporting Information.

(10) Haque, M. E.; Kitauchi, T.; Kanemitsu, K.; Tsuda, Y. *Chem. Pharm. Bull.* **1987**, *35*, 1016−1029.

(11) (a) Ho, W. M.; Wang, H. N. C. *Tetrahedron* **1995**, *51*, 7373−7388. (b) Tsuda, Y.; Haque, M. E.; Yoshimoto, K. *Chem. Pharm. Bull.* **1983**, *31*, 1612−1624.

(12) Bollenback, G. N.; Parrish, F. W. *Carbohydr. Res.* **1971**, *17*, 431−438.

(13) (a) Haworth, W. N.; Hirst, E. L.; Miller, E. J. *J. Chem. Soc.* **1927**, 2436−2443. (b) Bernet, B.; Vasella, A. *Helv. Chim. Acta* **1979**, *62*, 1990−2016. (c) Martín, A.; Salazar, J. A.; Suárez, E. *J. Org. Chem.* **1996**, *61*, 3999−4006. (d) Pinilla, I. M.; Martínez, M. B.; Galbis, J. A. *Carbohydr. Res.* **2003**, *338*, 549−555. (e) Boultadakis-Arapinis, M.; Lemoine, P.; Turcaud, S.; Micouin, L.; Lecourt, T. *J. Am. Chem. Soc.* **2010**, *132*, 15477−15479.

(14) Marra, A.; Sinay, P. *Carbohydr. Res.* **1990**, *195*, 303−308.