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Preparations and reactions of acylated and partially acylated glycosyl fluorides

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ABSTRACT

Partial acylation of glycosyl fluorides in the *galacto* (**2** and **3**) and *gluco* series (**8–10**) is readily achieved. Attempts to further alkylate these acyl derivatives failed. Treatment of **2** with Lewis acid, however, provided a facile route to the 1,4-anhydro derivative **5**. Lewis acid-mediated glycosylation of 2-acetamido-3,4,6-tri-*O*-acetyl-α-D-glucopyranosyl fluoride **11** led to the simple glycosides and thioglycosides **12–16**. Similarly, in the *galacto* series (**17**) an advantageous route to the β-galactosidase inhibitor **19** could be elaborated.

INTRODUCTION

The particular stability of glycosyl fluorides has long been recognized, and many of them have been prepared by various routes[1–5]. However, few reports have discussed the less successful attempts for their application in glycosylation reactions[1]. Based on Mukaiyama's seminal papers[6,7] some other groups started to elaborate the synthetic potential of Lewis acid-catalyzed glycosylations employing glycosyl fluorides[8–11]. Considerable knowledge of this approach to glycosides has now accumulated[4,5,12,13] and the glycosyl fluoride route indeed constitutes a valuable alternative approach.

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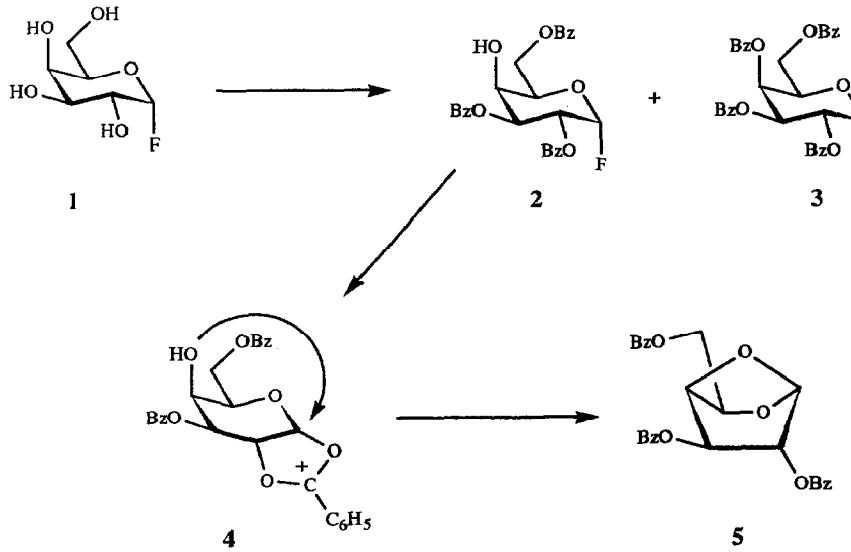
Acylated and alkylated glucosyl fluorides have enjoyed increasing applications in glycosylation reactions. In connection with our finding of an improved direct access to alkylated glycosyl fluorides[14] we attempted the generation of selectively mixed alkylated-acylated glycosyl fluorides as precursors ideally suited for oligosaccharide synthesis.

RESULTS AND DISCUSSION

In keeping with the previously observed comparison between methyl glycosides and glycosyl fluorides, the preparation of regioselectively acylated derivatives was considered possible. In the stoichiometric acylation of methyl α-D-galactopyranoside the free 4-OH compound may be readily obtained[15], and corresponding observations were made with L-fucose derivatives[16,17]. Thus, low-termperature treatment of α-D-galactopyranosyl fluoride[18] (**1**) with three equivalents of benzoyl chloride afforded the nicely crystalline 2,3,6-tribenzoate **2** in > 70% yield. An excess of benzoyl chloride gave the syrupy compound (**3**, 64%) and only a minor amount (17%) of the tribenzoate **2** was isolated after column chromatography.

Attempts to benzylate and alkylate **2** by treatment with the corresponding alkyl bromides and silver oxide at room temperature were not successful, and elevated temperatures (60–70°C) led to uncontrolled partial alkylations, deacylations and rearrangements. Thus, as reported earlier[14], the alkylation procedure may have limitations. However, it was of interest to test an oligomerization reaction of **2** directed towards (1–4)-β-D-galactans (cf. ref 19) by Lewis acid catalysis. Reaction with either titanium tetrafluoride in acetonitrile or boron trifluoride etherate in

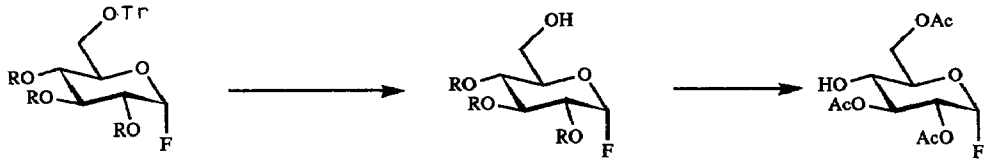


Scheme 1.

dichloromethane for 2 h at room temperature resulted in complete conversion of **2**. After washing the well crystallized 1,4-anhydro derivative **5** could be separated from some oligosaccharide material and isolated in ~ 50% yield. The small NMR coupling constants observed in the ^{1}H NMR spectrum indicate the stable camphor framework of **5** which displays the bridged $^{1,4}B$ conformation[20].

The formation of **5** evidently involves intramolecular nucleophilic attack of the axial 4-OH group on the Lewis acid-activated glycosyl fluoride directly or, as indicated in Scheme 1, on the 1,2-benzoxonium intermediate **4**. This derivative was previously reported, being formed by reaction of 1,2,3,6-tetra-*O*-benzoyl-4-*O*-methylsulfonyl-α-D-glucopyranose with sodium azide. This did not lead to the expected 4-azide, but gave **5** by rearrangement and attack of the anomeric benzoate function on the 4-carbenium intermediate (refs 20, 21).

Tritylation of α-D-glucopyranosyl fluoride[22] and subsequent acylation gave the benzoate **6** or the acetate **7** which upont detritylation led to the 6-OH compounds **8** (ref 23) or **9**, respectively. The benzoate **8** was earlier employed for the first synthesis of gentiobiose[23]. As previously reported for other partially acetylated derivatives, attempted column-chromatographic purification resulted in acetyl migrations[24,25].



6 : R = Bz

7 : R = Ac

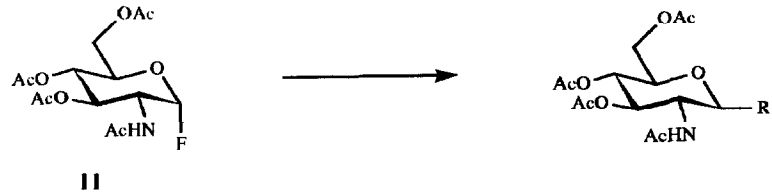
8 : R = Bz

9 : R = Ac

10

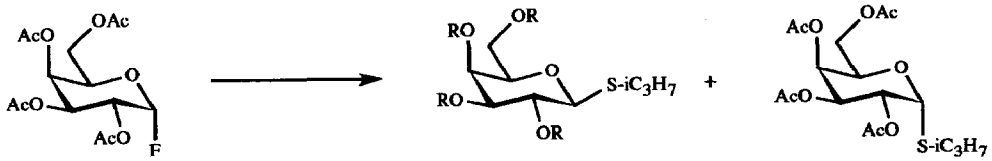
Similarly, the crystalline acetate **9**, in the presence of very minor amounts of base, underwent acetyl migration to give the syrupy 4-OH isomer **10**. As observed with the galactose derivatives, a mild and selective alkylation of these glucopyranosyl fluorides could not be accomplished. Although the direct alkylation[14] constitutes a convenient and rapid approach to activated species, partially acylated-alkylated glycosyl fluorides have to be prepared by classical multistep approaches.

In glycosylation reactions 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl fluoride[26] (**11**) displays a markedly decreased reactivity as compared to other glycosyl fluorides. Under Lewis-acid catalysis, only very reactive aglycons such as methanol, benzyl alcohol, and 2-propanethiol give glycosides. Thus for, no sugar derivative has been employed to produce the corresponding glycosides. With titanium tetrafluoride in acetonitrile at room temperature, the methyl α- and β-glycosides **12** and **13** (ref 27) were obtained in 71% yield in 11 : 98 ratio. Under similar conditions, the crystalline benzyl β-glycoside[28] **14** was isolated as the sole product. 2-Propanethiol, a highly reactive nucleophile, reacted rapidly at room



11

	R
12	α - OCH_3
13	β - OCH_3
14	β - $OCH_2C_6H_5$
15	α - S-iC_3H_7
16	β - S-iC_3H_7



17

18 : R = Ac

19 : R = H

20

temperature in dichloromethane with boron trifluoride as catalyst giving an $\alpha:\beta$ ratio (**15**:**16**) of 30:70. At elevated temperature and in acetonitrile with titanium tetrafluoride, only the β-glycoside **16** was isolated. In the latter case it may be assumed that the oxazolinium intermediate is formed first and then undergoes *trans*-opening by the nucleophile. This would imply an alternative stabilization of the oxocarbenium intermediate at room temperature, by participation of the 6-acetoxy group, to account for the 30% of α anomer formed.

In another experiment, crystalline 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl fluoride[29] (**17**) was treated with the good nucleophile 2-propanethiol in the presence of titanium tetrafluoride at 0°C in acEtOnitrile. After 10 min predominantly the β-glycoside[30] **18** was formed ($\alpha:\beta$ ratio, **20**:**18** of 11:89). More drastic conditions with boron trifluoride etherate in dichloromethane at room temperature gave mainly the α anomer **20** ($\alpha:\beta$ ratio, 20:18 of 78:22). Obviously, the

reaction conditions could be adapted to give the desired anomer; further optimizations should be possible. Subsequent deacetylation of **18** gave the crystalline isopropyl 1-thio-β-D-galactopyranoside[31] (**19**). This derivative ("IPTG") is used as a gratuitous inducer of β-galactosidase synthesis in *Escherichia coli*[32] and is required in considerable quantities by the pharmaceutical industry.

EXPERIMENTAL

General methods.—All reactions were monitored by TLC on Silica Gel 60 F_{254} (Merck). Detection was by UV absorption and/or spraying with 10% H_2SO_4 in EtOH and subsequent charring. Column chromatography was performed on Silica Gel 60 (70–230 mesh, Merck). Melting points were taken on a Reichert heating-table microscope. Optical rotations were measured with Perkin–Elmer polarimeter 241 at 20°C and 589 nm (Na D-line) and are given as [α]. ^1H (300 MHz) and ^{13}C NMR (75.46 MHz) spectra were recorded on a Bruker WM 300 instrument.

2,3,6-Tri-O-benzoyl-α-D-galactopyranosyl fluoride (**2**) *and 2,3,4,6-tetra-O-benzoyl-α-D-galactopyranosyl fluoride* (**3**).—*(a)* α-D-Galactopyranosyl fluoride[18] (**1**, 2.0 g, 11.0 mmol) dissolved in anhyd pyridine (30 mL) was cooled and treated with BzCl (5 mL) under stirring at room temperature. The mixture was poured into ice–water, twice extracted with EtOAc, washed with water three times, dried ($MgSO_4$) and evaporated. Following evaporation of toluene from the residue, the product was separated by column chromatography on silica gel (15:1 toluene–EtOAc).

Yield of **2**: 290 mg (17%); mp 157°C; [α] + 66.6° (*c* 0.95, $CHCl_3$), ^1H NMR (C_6D_6): δ 2.36 (d, 1 H, OH-4), 4.02 (m, 1 H, H-4), 4.18 (ddd ≈ bt, 1 H, H-5), 4.52 (m, 2 H, H-6a,6b), 5.94 (dd, 1 H, H-3), 5.96 (dd, 1 H, H-1), 6.11 (ddd, 1 H, H-2), 6.81–7.31 and 8.05–8.13 (m, 15 H, aryl-H); $J_{1,2}$ 2.7, $J_{1,F}$ 54.2, $J_{2,F}$ 23.8, $J_{2,3}$ 10.9, $J_{3,4}$ 3.0, $J_{4,5}$ 0.5, $J_{4,OH-4}$ 4.5, $J_{5,6a}$ 5.5, $J_{5,6b}$ 6.4 Hz. Anal. Calcd. for $C_{27}H_{23}FO_8$ (494.5): C, 65.58; H, 4.69. Found: C, 65.25; H, 4.55.

Yield of **3**: 4.2 g (64%); colorless syrup; [α] +119.2° (*c* 1.06, $CHCl_3$). ^1H NMR (C_6D_6): δ 4.26 (dd, 1 H, H-6b), 4.32 (ddd ≈ bt, 1 H, H-5), 4.62 (dd, 1 H, H-6a), 6.00 (dd, 1 H, H-1), 6.10 (ddd, 1 H, H-2), 6.17 (dd, 1 H, H-4), 6.26 (dd, 1 H, H-3), 6.70–7.22 and 7.78–8.17 (m, 20 H, aryl-H); $J_{1,2}$ 2.7; $J_{1,F}$ 54.0, $J_{2,F}$ 23.8, $J_{2,3}$ 10.8, $J_{3,4}$ 3.1, $J_{4,5}$ 1.0, $J_{5,6a}$ 6.1, $J_{5.6b}$ 5.7, $J_{6a,6b}$ 10.8 Hz. Anal. Calcd for $C_{34}H_{27}FO_9$ (598.6): C, 68.22; H, 4.55. Found: C, 68.50; H, 4.70.

(b) Compound **1** (1 mol equiv) and a stoichiometric amount of BzCl (3.1 mol equiv) were treated in anhyd pyridine at 0°C and worked up as under *(a)*. The tribenzoate **2** was obtained virtually quantitatively along with minor, polar side-products. Purification was by spontaneous crystallization of **2** from EtOAc–petroleum ether in 73% yield.

1,4-Anhydro-2,3,6-tri-O-benzoyl-β-D-galactopyranose (**5**).—To a solution of **2** (470 mg, 0.95 mmol) in anhyd CH_2Cl_2 (10 mL) was added pulverized 3A molecular sieves and $BF_3 \cdot OEt_2$ (0.36 mL, 2.96 mmol). After stirring for 2 h at room

temperature the starting material had disappeared (TLC, 4:1 toluene–EtOAc). The mixture was filtered via a pad of silica gel, poured into ice–water, and extracted with EtOAc. The extract was washed three times with water, dried ($MgSO_4$) and evaporated. Separation of **5** from some more polar components was effected by chromatography (8:1 hexane–EtOAc). Compound **5** crystallized as long colorless needles from EtOAc–hexane. Yield: 212 mg (47%); mp 137–138°C; [α] +177.5 (*c* 0.4, $CHCl_3$) [lit.[20] mp 141–143°C, [α] +117 ($CHCl_3$)]. ^{1}H NMR (C_6D_6): δ 3.79 (dd ≈ t, H-5), 4.11 (m, 1 H, H-6b), 4.18 (dd, 1 H, H-6a), 4.53 (d, 1 H, H-4), 5.06 (d, 2 H, H-3) 5.11 (ddd, 1 H, H-2), 5.84 (d, 1 H, H-1), 6.98–7.14 and 8.07–8.16 (m, 15 H, aryl-H); $J_{1,2}$ 2.5, $J_{2,3}$ 1.3, $J_{2,4}$ 1.4, $J_{3,4}$ 0, $J_{4,5}$ 0, $J_{5,6a}$ 5.6, $J_{5,6b}$ 6.2, $J_{6a,6b}$ 11.6 Hz. ^{13}C NMR ($CDCl_3$): δ 63.8 (C-6),73.5, 77.0, 81.1, 81.6 (C-2,3,4,5), 128.4–129.8 (18 aryl-C), 165.7, 165.8, 166.0 (3 *C*=O).

*2,3,4-Tri-*O*-acetyl-6-*O*-triphenylmethyl-α-*D*-glucopyranosyl fluoride*[23] (**7**).—^{1}H NMR ($CDCl_3$):δ 1.73, 2.02, 2.12 (each s, each 3 H, OAc), 3.03 (dd, 1 H, H-6b), 3.38 (dd, 1 H, H-6a), 4.10 (ddd, 1 H, H-5), 5.04 (ddd, 1 H, H-2), 5.35 (dd ~ t, 1 H, H-4), 5.45 (dd ~ t, 1 H, H-3), 5.85 (dd, 1 H, H-1), 7.20–7.47 (m, 15 H, aryl-H); $J_{1,2}$ 2.7, $J_{1,F}$ 53.4, $J_{2,F}$ 24.4, $J_{2,3}$ 10.1, $J_{3,4}$ 9.7, $J_{4,5}$ 10.1, $J_{5,6a}$ 2.1, $J_{5,6b}$ 3.8, $J_{6a,6b}$ 10.9 Hz.

*2,3,4-Tri-*O*-acetyl-α-*D*-glucopyranosyl fluoride* (**9**) *and 2,3,6-tri-*O*-acetyl-α-*D*-glucopyranosyl fluoride* (**10**).—(*a*) Compound **7** (1.8 g, 3.27 mmol)[23] was dissolved in AcOH (10 mL) at 10°C and shaken with HBr in AcOH (33%, 0.8 mL) for 1 min. Following filtration over a pad of silica gel the solution was poured onto ice–water, extracted twice with CH_2Cl_2, dried ($MgSO_4$), and evaporated. The yellow raw material was separated from triphenyl-methanol by chromatography (4:1 toluene–EtOAc). Yield of **9**: 620 mg (62%); mp 93°C; [α] + 90.6° (*c* 1.55, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 2.05, 2.09, 2.11 (each s, each 3 H, OAc), 3.62 (dd, 1 H, H-6b), 3.79 (dd, 1 H, H-6a), 4.00 (ddd, 1 H, H-5), 4.94 (ddd, 1 H, H-2), 5.14 (dd ~ t, 1 H, H-4), 5.56 (dd ~ t, 1 H, H-3), 5.79 (dd, 1 H, H-1); $J_{1,2}$ 2.7, $J_{1,F}$ 53.2, $J_{2,F}$ 24.2, $J_{2,3}$ 10.2, $J_{3,4}$ 9.9, $J_{4,5}$ 10.1, $J_{5,6a}$ 2.2, $J_{5,6b}$ 3.6, $J_{6a,6b}$ 13.1 Hz. Anal. Calcd for $C_{12}H_{17}FO_8$ (308.3): C, 46.76; H, 5.56. Found: C, 46.52; H, 5.21.

(b) Purification of the yellow crude product of *(a)* by chromatography on silica gel with 4:1 toluene–EtOAc plus 3% Et_3N afforded compound **10**; yield 665 mg (66%) as a colorless syrup; [α] + 67.1° (*c* 1.42, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 2.11, 2.12, 2.14 (each s, each 3 H, OAc), 3.63 (dd ~ t, 1 H, H-4), 4.04 (ddd, 1 H, H-5), 4.34 (dd, 1 H, H-6b), 4.50 (dd, 1 H, H-6a), 4.90 (ddd, 1 H, H-2), 5.35 (dd ~ t, 1 H, H-3), 5.72 (dd, 1 H, H-1); $J_{1,2}$ 2.9 $J_{1,F}$ 53.1, $J_{2,F}$ 24.2, $J_{2,3}$ 10.2, $J_{3,4}$ 9.7, $J_{4,5}$ 10.2, $J_{5,6a}$ 4.0, $J_{5,6b}$ 2.2, $J_{6a,6b}$ 12.6 Hz. Anal. Calcd for $C_{12}H_{17}FO_8$ (308.3): C, 46.76; H, 5.56. Found: C, 46.88; H, 5.69.

*Methyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-* (**12**) *and -β-*D*-glucopyranoside* (**13**).—The glycosyl fluoride[26] **11** (152 mg, 0.44 mmol) dissolved in anhyd MeCN (5 mL) was stirred with pulverized 3A molecular sieves for 30 min and then treated with MeOH (0.2 mL, 6 mmol) and TiF_4 (270 mg, 2.2 mmol) for 12 h at room temperature. The solution was filtered (silica gel), evaporated and the crude

product purified by chromatography (1 : 1 toluene–EtOAc); yield of **12** plus **13**: 112 mg (73%). The anomeric mixture contained **12** and **13** in 11 : 89 ratio by integration of the OCH_3 or NHAc signals in the ^1H NMR-spectrum. The β anomer was obtained crystalline; mp 161°C; $[\alpha]$ −14.8° (*c* 0.72, MeOH), [lit.[27] mp 163°C, $[\alpha]$ −22° (*c* 1.0, MeOH)].

Benzyl 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranoside (**14**).—Compound **11** (90 mg, 0.26 mmol) and benzyl alcohol (56 μL, 0.52 mmol) in anhyd MeCN (3 mL) were treated with TiF_4 (160 mg, 1.3 mmol) for 3 h at room temperature. Work-up was as in the previous preparation. The crude product was freed from excessive benzyl alcohol by chromatography (1 : 1 hexane–EtOAc) and the product crystallized from EtOAc–hexane; yield 83 mg (74%); mp 163°C; $[\alpha]$ −50.8° (*c* 1.07, $CHCl_3$), [lit.[28] mp 164–165°C, $[\alpha]$ −54.4° $CHCl_3$)]. ^1H NMR ($CDCl_3$): δ 1.92, 2.01, 2.02, 2.11 (each s, each 3 H, OAc, NAc), 3.68 (ddd, 1 H, H-5), 3.98 (ddd, 1 H, H-2), 4.17 (dd, 1 H, H-6b), 4.28 (dd, 1 H, H-6a), 4.64 (d, 1 H, H-1), 4.90 (AB, 2 H, C_6H_5–CH_2), 5.09 (dd ~ t, 1 H, H-4), 5.21 (dd, 1 H, H-3), 5.53 (d, 1 H, NH), 7.28–7.38 (m, 5 H, aryl-H); $J_{1,2}$ 8.4, $J_{2,3}$ 10.5, $J_{2,NH}$ 8.8, $J_{3,4}$ 9.4, $J_{4,5}$ 10.0, $J_{5,6a}$ 4.8, $J_{5,6b}$ 2.6, $J_{6a,6b}$ 12.4 Hz.

Isopropyl 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-1-thio-α- (**15**) *and -β-D-glucopyranoside* (**16**).—*(a)* Compound **11** (200 mg, 0.57 mmol) and 2-propanethiol (160 μL, 1.72 mmol) dissolved in anhyd MeCN (5 mL) were treated with TiF_4 (355 mg, 2.9 mmol) for 3 h at 0°C. Work-up as for **14** and chromatography (1 : 1 toluene–EtOAc) gave the pure, crystalline β anomer **16**; yield 144 mg (62%).

(b) Compound **11** (117 mg, 0.33 mmol) and 2-propanethiol (95 μL, 1.0 mmol) dissolved in anhyd CH_2Cl_2 (5 mL) were treated with $BF_3 \cdot OEt_2$ (0.21 mL, 1.73 mmol) for 4 h at room temperature. Following filtration over silica gel the mixture was poured onto ice–water, neutralized with $NaHCO_3$ and extracted with EtOAc. The organic layer was washed three times with water, dried ($MgSO_4$), evaporated, and the crude product (**15** : **16** ratio of 30 : 70, according to ^1H NMR) separated by chromatography (1 : 1 toluene–EtOAc); yield of anomeric mixture: 90 mg (66%).

Compound **15** had: mp 97°C; $[\alpha]$ +128.4° (*c* 0.95 $CHCl_3$). ^1H NMR ($CDCl_3$): δ 1.31, 1.33, (each d, each 3 H, CH_3), 1.96, 2.03, 2.04, 2.09 (each s, each 3 H, OAc, NAc), 3.07 [sept. 1 H, $CH(CH_3)_2$], 4.08 (dd, 1 H, H-6b), 4.27 (dd, 1 H, H-6a), 4.39 (ddd, 1 H, H-5), 4.52 (ddd, 1 H, H-2), 5.03 (dd, 1 H, H-3), 5.12 (dd ~ t, 1 H, H-4), 5.47 (d, 1 H, H-1), 5.69 (d, 1 H, NH); $J_{1,2}$ 5.5, $J_{2,3}$ 10.9, $J_{2,NH}$ 9.1, $J_{3,4}$ 9.5, $J_{4,5}$ 9.8, $J_{5,6a}$ 4.5, $J_{5,6b}$ 2.4, $J_{6a,6b}$ 12.4, $J_{CH,CH3}$ 6.8 Hz. Anal. Calcd for $C_{17}H_{27}NO_8S$ (405.4): C, 50.36; H, 6.71; N, 3.45. Found: C, 50.02; H, 6.61; N, 2.98.

Compound **16** had: mp 207°C; $[\alpha]$ −32.4° (*c* 1.14, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 1.29, 1.30 (each d, each 3 H, CH_3), 1.96, 2.03, 2.04, 2.07 (each s, each 3 H, OAc, NAc), 3.19 [sept, 1 H, $CH(CH_3)_2$], 3.71 (ddd, 1 H, H-5), 4.01 (ddd ~ q, 1 H, H-2), 4.13 (dd, 1 H, H-6b), 4.23 (dd, 1 H, H-6a), 4.77 (d, 1 H, H-1), 5.08 (dd ~ t, 1 H, H-4), 5.25 (dd ~ t, 1 H, H-3), 5.74 (d, 1 H, NH); $J_{1,2}$ 10.4, $J_{2,3}$ 10.1, $J_{2,NH}$ 9.2, $J_{3,4}$ 9.7, $J_{4,5}$ 10.0, $J_{5,6a}$ 5.4, $J_{5,6b}$ 2.4, $J_{6a,6b}$ 12.4, $J_{CH,CH3}$ 6.9 Hz. Anal. Calcd for $C_{17}H_{27}NO_8S$ (405.4): C, 50.36; H, 6.71; N, 3.45. Found: C, 50.12; H, 6.74; N, 3.29.

Isopropyl 2,3,4,6-tetra-O-acetyl-1-thio-α- (**20**) *and -β-D-galactopyranoside* (**18**).—*(a)* Compound **17** (1.35 g, 3.85 mmol) and 2-propanethiol (1 mL, 10.8 mmol) dissolved in dry CH_2Cl_2 (20 mL) were treated with $BF_3 \cdot OEt_2$ (2.34 mL, 19.3 mmol) for 10 min at room temperature. The mixture was poured into ice–water, extracted with EtOAc, ashed with water three times, dried ($MgSO_4$), and evaporated to give a mixture 1.38 g (88%) of **18** and **20** in 22:78 ratio (^{1}H NMR).

(b) Compound **17** (448 mg, 1.28 mmol) and 2-propanethiol (0.38 mL, 3.9 mmol) in dry MeCN (15 mL) were treated with TiF_4 (800 mg, 6.4 mmol) for 15 min at 0°C. Work-up as for **14** gave 426 mg (82%) of a mixture of **18** and **20** in 89:11 ratio (^{1}H NMR). The anomers were separated by chromatography (6:1 toluene–EtOAc).

Compound **18** was a colorless syrup; [α] −10.9° (*c* 2.11, $CHCl_3$) [lit.[30] syrup, [α] −14.2° (*c* 1.0, $CHCl_3$)]. ^{1}H NMR ($CDCl_3$): δ 1.31, 1.32 (each d, each 3 H, CH_3), 1.99, 2.04, 2.06, 2.16 (each s, each 3 H, OAc), 3.19 [sept., 1 H, C*H*$(CH_3)_2$], 3.93 (ddd, 1 H, H-5), 4.11 (dd, 1 H, H-6b), 4.18 (dd, 1 H, H-6a), 4.59 (d, 1 H, H-1), 5.06 (dd, 1 H, H-3), 5.22 (t, 1 H, H-2), 5.44 (dd, 1 H, H-4); $J_{1,2}$ 10.0, $J_{2,3}$ 10.0, $J_{3,4}$ 3.3, $J_{4,5}$ 1.0, $J_{5,6a}$ 7.0, $J_{5,6b}$ 6.5, $J_{6a,6b}$ 11.3, $J_{CH,CH3}$ 7.7 Hz.

Compound **20** had mp 80°C; [α] + 193.2° (*c* 1.91, $CHCl_3$). ^{1}H NMR ($CDCl_3$):δ 1.29, 1.31 (each d, each 3 H, CH_3), 1.99, 2.04, 2.07, 2.18 (each s, each 3 H, OAc), 3.00 [sept., 1 H, C*H*$(CH_3)_2$], 4.11 (m, 2H, H-6a,6b), 4.63 (ddd ~ t, 1 H, H-5), 5.19 (dd, 1 H, H-3), 5.26 (dd, 1 H, H-2), 5.45 (dd, 1 H, H-4), 5.82 (d, 1 H, H-1); $J_{1,2}$ 5.3, $J_{2,3}$ 11.1, $J_{3,4}$ 3.1, $J_{4,5}$ 1.2, $J_{5,6a}$ 6.5, $J_{5,6b}$ 6.5, $J_{CH,CH3}$ 7.7 Hz. Anal. Calcd for $C_{17}H_{26}O_9S$ (406.5): C, 50.24; H, 6.45. Found: C, 50.27; H, 6.55.

Isopropyl 1-thio-β-D-galactopyranoside (**19**).—Compound **18** (1.07 g, 2.63 mmol) dissolved in dry MeOH (30 mL) was treated with 1% methanolic NaOMe (2 mL) for 1 h at room temperature. The solution was neutralized with ion-exchange resin (Amberlite IR 120, H^+), evaporated, and the crude product crystallized from EtOH–ether to give 450 mg (72%) of **19**; mp 107.5°C; [α] −28.6 (*c* 0.82, H_2O), [lit.[31] mp 109.5°C, [α] −31.4° (H_2O)].

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