JOC*Article*

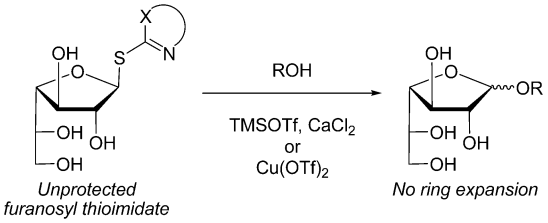
First *O*-Glycosylation from Unprotected 1-Thioimidoyl Hexofuranosides Assisted by Divalent Cations

Ronan Euzen, Jean-Paul Guégan, Vincent Ferrières,* and Daniel Plusquellec

Sciences Chimiques de Rennes, Ecole Nationale Supérieure de Chimie de Rennes, CNRS, Avenue du Général Leclerc, F-35700 Rennes, France

vincent.ferrieres@ensc-rennes.fr

Received April 10, 2007



The preparation of *O*-hexofuranosides was accomplished from unprotected 1-thioimidoyl furanosides as donors. The present methodology was first used for the synthesis of octyl galactofuranoside and further extended to D-galactofuranose-containing disaccharides. Within this study, we emphasized the need for additional complexing cations to maintain the furanose ring in its initial size. After experimentation, calcium ion was first used concomitantly with trimethylsilyl trifluoromethanesulfonate, the latter being able to activate the thioimidate and the former being likely to inhibit ring expansion. Moreover, an improvement was performed by using copper(II) trifluoromethanesulfonate which could then meet the requirements as both promoter and complexing agent.

Introduction

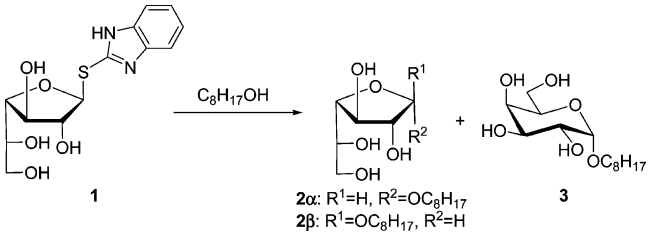
Many natural oligosaccharides and polysaccharides are structurally based on hexoses in a pyranose configuration. This explains why the wide majority of the related publications both in glycobiology and in glycochemistry deal with the study and the synthesis of hexopyranoconjugates.[1−5] However, it is also well-established that only some microorganisms, and not mammals, are able to biosynthesize and metabolize membrane components and other bioconjugates that are built up with hexoses in a thermodynamically less stable furanose form. In this context, we[6−8] and other teams[9−15] have contributed to the development of chemical methodologies specially dedicated to the preparation of hexofuranose-containing oligosaccharides as potential pharmacophores devoted to innovative therapies.[16,17]

Glycosylation strategies generally require functional arrangements on both glycosyl donor and acceptor. The appropriate choice of protecting groups allows at the same time (i) modulation of the reactivity of both partners and (ii) diastereocontrol of the coupling reactions.[2] With nonparticipating groups, control of the stereochemistry of the newly formed glycosidic bond is more delicate and the glycosylation reactions evolve according to many parameters, among them solvent, temperature, and also anomeric and steric effects. Anomeric mixtures of pyranosides, notably in gluco and galacto series, are thus

(1) Toshima, K.; Tatsuta, K. *Chem. Rev.* **1993**, *93*, 1503−1531.
(2) Demchenko, A. *Lett. Org. Chem.* **2005**, *2*, 580−589.
(3) Pellissier, H. *Tetrahedron* **2005**, *61*, 2947−2993.
(4) Gabius, H.-J.; Siebert, H.-C.; André, S.; Jiménez-Barbero, J.; Rüdiger, H. *ChemBioChem* **2004**, *5*, 740−764.
(5) Dwek, R. A. *Chem. Rev.* **1996**, *96*, 683−720.
(6) Gelin, M.; Ferrières, V.; Plusquellec, D. *Eur. J. Org. Chem.* **2000**, 1423−1431.
(7) Ferrières, V.; Roussel, M.; Gelin, M.; Plusquellec, D. *J. Carbohydr. Chem.* **2001**, *20*, 855−865.
(8) Gelin, M.; Ferrières, V.; Lefeuvre, M.; Plusquellec, D. *Eur. J. Org. Chem.* **2003**, 1285−1293.
(9) Bai, Y.; Lowary, T. L. *J. Org. Chem.* **2006**, *71*, 9672−9680.
(10) Bai, Y.; Lowary, T. L. *J. Org. Chem.* **2006**, *71*, 9658−9671.
(11) Bohn, M. L.; Colombo, M. I.; Stortz, C. A.; Ruveda, E. A. *Carbohydr. Res.* **2006**, *341*, 1096−1104.
(12) Gandolfi-Donadio, L.; Gola, G.; de Lederkremer, R. M.; Gallo-Rodriguez, C. *Carbohydr. Res.* **2006**, *341*, 2487−2497.
(13) Lee, Y. J.; Lee, B. Y.; Jeon, H. B.; Kim, K. S. *Org. Lett.* **2006**, *8*, 3971−3974.
(14) Zhang, G.; Fu, M.; Ning, J. *Tetrahedron: Asymmetry* **2005**, *16*, 733−738.
(15) Zhang, G.; Fu, M.; Ning, J. *Carbohydr. Res.* **2005**, *340*, 155−159.
(16) Joe, M.; Sun, D.; Taha, H.; Completo, G. C.; Croudace, J. E.; Lammas, D. A.; Besra, G. S.; Lowary, T. L. *J. Am. Chem. Soc.* **2006**, *128*, 5059−5072.
(17) Mennink-Kersten, M. A. S. H.; Ruegebrink, D.; Wasei, N.; Melchers, W. J. G.; Verweij, P. E. *J. Clin. Microbiol.* **2006**, *44*, 1711−1718.

10.1021/jo070741j CCC: $37.00
Published on Web 06/28/2007

TABLE 1. Glycosylation of 1-Octanol by Remote Activation of Thioimidate 1



1 **2α**: R^1=H, R^2=OC_8H_{17} **2β**: R^1=OC_8H_{17}, R^2=H **3**

entry	$C_8H_{17}OH$ (equiv)	solvent	promoter (equiv)	additive (equiv)	time (h)	yield (%)	**2**/**3**[c]	**2**α/**2**β[c]
1	2	DMF	TMSOTf (0.1)		2	18	100:0	1:1.3
2[a]	10	DMF	TMSOTf (0.02)		2	38	100:0	1:1.4
3[b]	10	DMF	TMSOTf (0.1)		2	41	100:0	1:1.5
4	10	THF	TMSOTf (0.1)		2	33	100:0	1:1
5	10	THF	TMSOTf (0.5)		2	52	79:21	1:1
6	10	THF	TMSOTf (1.0)		2	79	73:27	1:4.9
7	20	THF	TMSOTf (0.1)		2	28	100:0	1:1
8	20	THF	TMSOTf (0.5)		2	53	89:11	1:1.1
9	20	THF	TMSOTf (1.0)		2	98	88:12	1:3.7
10	20	THF	TMSOTf (1.0)	$CaCl_2$ (1.0)	2	65	97:3	1:5.6
11	20	THF	$Cu(OTf)_2$ (0.1)		24	38	100:0	1:0.6
12	20	THF	$Cu(OTf)_2$ (1.0)		2	47	100:0	1:1.2
13	20	THF	$Cu(OTf)_2$ (1.0)		24	65	100:0	1:5.1
14	20	THF	$Cu(OTf)_2$ (2.0)		24	43	100:0	1:6.2

[a] Donor **1** was added over 12 min. [b] Donor **1** was added over 1 h. [c] Ratios were calculated by ^{1}H NMR from integrations corresponding to the anomeric protons.

obtained. In the field of hexofuranosides, the conformational flexibility of the five-membered ring plays a stronger role than those observed with the pyranose counterparts,[18] so that diastereoselectivity of the coupling is generally highly influenced by steric hindrance.[8] While benzyl ethers are often used as a nonparticipating protecting group, a free hydroxyl could also be regarded as nonstereodirecting function. Such an approach was initiated by Ferrier[19] and nicely complemented through recent research.[20−23] Thioglycosides and 2-thiopyridinyl derivatives were first proposed as unprotected pyranosyl donors which led to the desired alkyl pyranosides under activation assisted by mercuric salts. A few years later, Hanessian extended this strategy and developed the MOP technology (3-methoxy-2-pyridyloxyl glycosides) as well as the remote activation process.[24] The main advantages of this strategy rely on (i) the absence of protecting group manipulations at the end of a synthetic scheme, which is highly desirable for charged targets and the removal of undesired side products such as orthoesters, and (ii) a greater reactivity of the glycosyl donors.

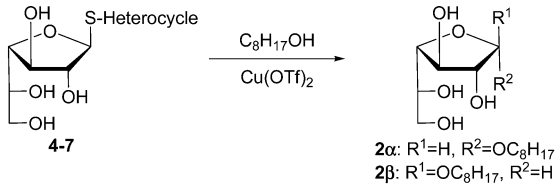
Considering our interest in the chemistry of glycofuranoconjugates,[25−27] we have recently performed the synthesis of hexofuranosyl 1-phosphates in only one step by remote activation of various 1-thioimidoyl furanosides directly by phosphoric acid and concluded that the corresponding 2-benzimidazolyl 1-thio-D-galacto-, D-fuco-, D-gluco-, and D-mannofuranosides were the most appropriated donors under these conditions.[26] Herein, we report on the direct access to *O*-furanosides from free thioimidates, alcohols and underline how divalent cations efficiently contribute to keep the glycoside in its initial five-membered ring configuration.

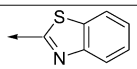
Results and Discussion

On the assumption that 2-benzimidazolyl thiofuranosides are suitable donors in the formation of anomeric furanosyl phosphates, our study began with the galactofuranosylation of 1-octanol with donor **1**[26] (Table 1). In order to mimic the conditions of the previous phosphorylation, the hard Lewis acid such trimethylsilyl trifluoromethansulfonate (TMSOTf) was first studied as a promoter in *N*,*N*-dimethylformamide (DMF). After 2 h at room temperature, an anomeric mixture of the target furanoside **2** was obtained in a low 18% yield but without any formation of the more stable pyranoside **3** (entry 1). This moderate yield was ascribed to degradation of the thioimidoyl donor. To overcome this side reaction, the reactions were performed either by using only 0.02 molar equiv of the Lewis acid or by increasing the amount of the aliphatic acceptor, and by slow adding of **1** (entries 2 and 3). Nevertheless, the latter precaution was no more required by substituting DMF by the less polar tetrahydrofuran (THF) (entry 4). It is rather likely that such new conditions modulate the dissociation of activated species thus limiting degradation processes. Subsequent improved glycosidic couplings were obtained by concomitantly increasing amounts of 1-octanol and TMSOTf (entries 5−9), so that conversion of donor **1** to the desired galactoside was interestingly performed in a near quantitative yield (entry 9). These modifications also impacted, first, the stability of the desired furanosides **2**α,β, since they were contaminated by octyl

(18) Kirby, A. J. *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*; Springer-Verlag: Berlin, Heidelberg, New York, 1983.
(19) Ferrier, R. J.; Furneaux, R. H. *Carbohydr. Res.* **1976**, *52*, 63−68.
(20) Hanessian, S.; Bacquet, C.; Lehong, N. *Carbohydr. Res.* **1980**, *80*, C17−C22.
(21) Ferrières, V.; Blanchard, S.; Fischer, D.; Plusquellec, D. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 3515−3518.
(22) Demchenko, A. V.; Malysheva, N. N.; De Meo, C. *Org. Lett.* **2003**, *5*, 455−458.
(23) Demchenko, A. V.; Pornsuriyasak, P.; De Meo, C.; Malysheva, N. N. *Angew. Chem., Int. Ed.* **2004**, *43*, 3069−3072.
(24) Hanessian, S.; Lou, B. *Chem. Rev.* **2000**, *100*, 4443−4463.
(25) Euzen, R.; Ferrières, V.; Plusquellec, D. *Carbohydr. Res.* **2006**, *341*, 2759−2768.
(26) Euzen, R.; Ferrières, V.; Plusquellec, D. *J. Org. Chem.* **2005**, *70*, 847−855.
(27) Euzen, R.; Lopez, G.; Nugier-Chauvin, C.; Ferrières, V.; Plusquellec, D.; Rémond, C.; O'Donohue, M. *Eur. J. Org. Chem.* **2005**, 4860−4869.

TABLE 2. Glycosylation of 1-Octanol by Remote Activation of Thioimidates 4−7



Entry	Donor	Heterocycle	$Cu(OTf)_2$ (equiv.)	Time (h)	Yield (%)	2α/2β
1	**4**		1.0	24	50	1:4.7
2	**5**		0.1	24	22	1:0.5
3	**5**		1.0	2	49	1:1.1
4	**5**		1.0	24	54	1:4.6
5	**6**		0.1	24	46	1:0.6
6	**6**		1.0	2	48	1:1.5
7	**6**		1.0	24	48	1:6.7
8	**7**		0.1	24	24	1:0.7
9	**7**		1.0	2	58	1:3.2
10	**7**		1.0	24	71	1:4.7

α-D-galactopyranoside (**3**) until 27% (entry 6), and second, the diastereoselectivity of the furanosylation. Indeed, a more acidic media resulted in an increased amount of the most stable 1,2-*trans*-furanoside **2***β* as shown by the **2**α/**2***β* ratio which started from 1:1 to attain 1:4.9 or 1:3.7 (entries 4−6 and 7−9, respectively).

Although conversion was thus ensured in THF in the presence of 1 molar equiv of TMSOTf, the limitation of our approach seemed to rely on the production of the unwanted pyranoside **3**. Nevertheless, in order to avoid its formation, we hypothesized that free hydroxyl could interact with alkaline earth or metal cations to inhibit the undesired ring expansion. Indeed, additives such as calcium or barium chloride have already shown their potential in a revisited Fischer glycosylation reaction from unprotected reducing monosaccharides.[28,29] The resulting specificity of this approach toward the hexofuranosides was connected with reversible complexation phenomena that are likely to stabilize substrates, intermediates, and/or products in a furanose configuration. As expected, the presence of calcium cations in the reaction media allowed significant decrease of galactopyranoside **3** (entry 10). This experiment also strengthened better affinity of calcium for the 1,2-*trans*-furanoside since **2***β* represented 85% of the resulting anomeric mixture of galactofuranosides (**2**α/**2***β*, 1:5.6).

Subsequent improvement brought us to also consider the ability of metal and rare earth cations which have acidic properties and exhibit higher solubility in THF than calcium chloride. Among silver, ytterbium, zinc, scandium, tin, and copper triflates, the last three Lewis acids showed the desired smooth activation of thioimidate **1** and the more interesting results were observed with copper(II) triflate. The set of experiments (entries 11−14), led with metallic promoter, allowed us to show that glycosidation of donor **1**, characterized by a *β* configuration, first proceeded with inversion of configuration (entry 11, **2**α/**2***β*, 1:0.6) and that anomerization occurred with increased reaction times and/or acidity. Consequently, one can hypothesized that copper(II) was not only involved as a mild activating agent but also presented the expected coordination properties required to fully inhibit the ring expansion as a side reaction. In order to explain this phenomenon, we hypothesized that both calcium and copper were likely to interact with either the starting furanosyl thioimidate or the resulted *O*-furanoside or with both compounds. More precisely, we assumed that free OH-5 of the furanosidic derivatives was involved in such a bond. Owing to heterogeneity of the reaction media, complexation was qualitatively studied by NMR using calcium chloride or copper(II) triflate as source of divalent cation and octyl *β*-D-galactofuranoside (**2***β*) as a complexing agent in deuterated dimethylformamide. Thus, the most relevant results were obtained with cupric ions by proton decoupled ^{13}C NMR. Indeed, a selective and apparent disappearance of C-5 and C-6 signals was observed when 1 molar equiv concentration of Cu^{2+} ions was used. This was attributed to the broadening of the corresponding signals which is indicative for a metal interaction with O-5 and O-6. These results are in good agreement with those demonstrating complexation of cupric ions by pyrimidine nucleotides and nucleosides.[30] In our study, the ^{13}C NMR spectrum therefore confirmed the assumption according to which the aforementioned preservation of the five-membered ring of the starting furanosyl thioimidate donor during *O*-glycosylation reaction is assisted by copper(II) ions.

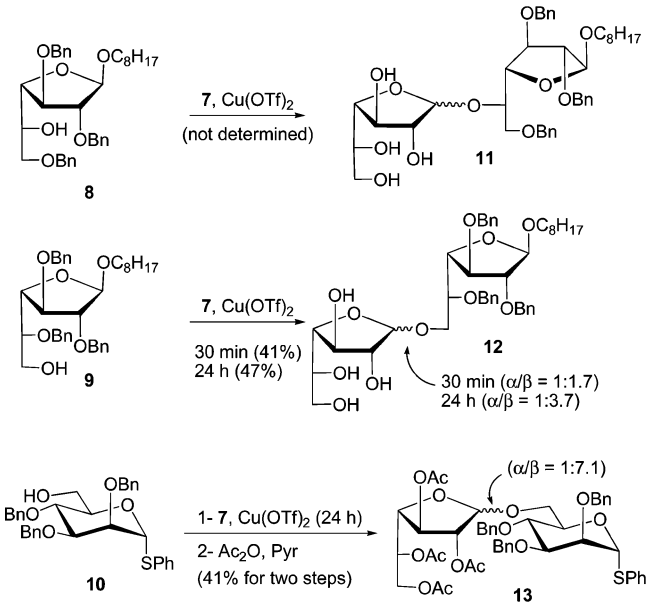
Having an efficient method in hand, we further studied the reactivity of known benzothiazolyl, pyridinyl, thiazolinyl, and pyrimidinyl galactofuranosides **4**, **5**, **6**, and **7**,[26] respectively, in order to highlight the scope of the remote activation of unprotected thioimidoyl furanosides. Each of these donors was studied under conditions similar to those previously used with donor **1** (Table 2). Whatever the nature of the aglycon, it is

(28) Bertho, J.-N.; Ferrières, V.; Plusquellec, D. *Chem. Commun.* **1995**, 1391−1393.

(29) Ferrières, V.; Bertho, J.-N.; Plusquellec, D. *Tetrahedron Lett.* **1995**, *36*, 2749−2752.

(30) Kotowycz, G. *Can. J. Chem.* **1974**, *52*, 924−929.

SCHEME 1. Synthesis of Galactofuranose-Containing Disaccharides 10 and 11



important to emphasize the total conservation of the size of the initial five-membered ring thanks to the presence of copper ions. Moreover, **2**α, formed under kinetic conditions, smoothly anomerized to afford **2**β, so that the best selectivity toward the 1,2-*trans* furanoside was observed from the thiazolinyl derivative **6** (entry 7, **2**α/**2**β = 1:6.7) even if this donor allowed the synthesis of **2** in a moderate 48% yield. Nevertheless, the desired galactoside **2** was synthesized and isolated in an excellent 71% yield starting from the pyrimidinyl furanoside **7** (entry 10). This result prompted us to prefer donor **7** for subsequent glycosylation of furanosidic or pyranosidic acceptors **8**,[31] **9**,[26] and **10**[32] (Scheme 1). Under these optimal conditions, no coupling could be performed between **7** and **8** since fast degradation of the donor was observed. Nevertheless, compounds **9** and **10** were smoothly glycosylated so that the desired galactofuranose-containing disaccharides **12** and **13** were isolated in 41−47% and 41% yield, respectively. Although yields are quite similar, it is interesting to note that the resulting diastereocontrol of the reaction slightly depended on the ring size of the saccharidic acceptor as α/β ratio was 1:3.7 for the furano−furano coupling but reached 1:7.1 for the furano−pyrano one.

Conclusions

In conclusion, we present herein the first *O*-glycosidation performed from unprotected furanosyl donors and neutral acceptors. Our approach, which required the preservation of the initial size of five-membered rings, rested on the remote activation of free thioimidoyl furanosides by an appropriate Lewis acid and on the complexation of furanosidic reactants and/or products. Two versatile solutions were developed. They involved either the combination of TMSOTf and calcium chloride or the use of only copper(II) triflate to realize the targeted glycosylation reactions. Under such experimental conditions, the desired D-galactofuranosides were synthesized with limited or no ring expansion toward the most stable pyranosides.

Experimental Section

Synthesis of Octyl D-Galactofuranoside (2) in the Presence of Calcium Chloride (Procedure A). To a solution of donor **1** (59.3 mg, 0.167 mmol) in dry THF (0.5 mL) were successively added *n*-octanol (530 μL, 3.35 mmol), calcium chloride (18.6 mg, 0.167 mmol), and TMSOTf (32 μL, 0.167 mmol). The resulting suspension was stirred for 2 h at rt before being quenched by the addition of a few drops of triethylamine. After fitration and concentration under reduced pressure, the target furanoside was chemically purified. The first step consisted of acetylation using pyridine (1 mL) and acetic anhydride (1 mL). The media was kept for 24 h at rt, concentrated, codistilled with toluene, and purified by chromatography (light petroleum/EtOAc, 4:1). Deacetylation was further performed under standard conditions: the resulting product reacted overnight in a 0.1 M solution of sodium methylate in methanol (1 mL). The solution was further neutralized using resin IR-120 (H^+-form), filtered, and concentrated to afford a mixture of **2** and **3** in a 65% yield (31.7 mg). NMR spectra were in good accordance with those previously described.[33,34]

Synthesis of Octyl D-Galactofuranoside (2) in the Presence of Copper(II) Triflate (Procedure B). To a solution of donor **7** (50 mg, 0.18 mmol) in anhyd THF (1 mL) were successively added octanol (575 μL, 3.6 mmol) and copper(II) triflate (66 mg, 0.18 mmol). The reaction was stirred for 24 h at rt, quenched by addition of triethylamine, and finally diluted with methanol (5 mL). After filtration of the residual salts, washing with methanol, and concentration under reduce pressure, the target galactoside **2** was purified as previously described and isolated in 71% yield (25 mg, **2**α/**2**β = 1:4.7)

Octyl α,β-D-Galactofuranosyl-(1,6)-2,3,5-tri-*O*-benzyl-β-D-galactofuranoside (12). Compound **12** was synthesized according to a procedure similar to that described for **2** in procedure B starting from **7** (35 mg, 0.13 mmol), acceptor **9**[25] (1.42 g, 2.52 mmol), and copper(II) triflate (46.2 mg, 0.13 mmol). Chromatography eluting with CH_2Cl_2−MeOH (19:1) gave the desired disaccharide **12** (43 mg, 47%, α/β = 1:3.7): R_f 0.2 (CH_2Cl_2/MeOH, 19:1); ^{1}H NMR (400 MHz, CD_3OD) and ^{13}C NMR (400 MHz, CD_3OD) for the β-anomer **12**β were similar to those previously described;[25] ^{1}H NMR (400 MHz, CD_3OD) data for **12**α δ 7.36−7.23 (m, 15 H, C_6H_5), 5.00 (s, 1 H, H-1a), 4.84 (d, 1 H, J = 4.6 Hz, H-1b), 4.73−4.32 (m, 6 H, OC*H*$_2$Ph), 4.12 (dd, 1 H, J = 7.4, 7.1 Hz, H-3b), 4.10 (dd, 1 H, J = 6.9, 3.6, H-4a), 4.00 (dd, 1 H, J = 10.4, 6.4, H-6a), 3.99−3.94 (m, 3 H, H-2a, H-3a, H-2b), 3.81 (ddd, 1 H, J = 10.4, 6.4, 6.1 Hz, H-5a), 3.73 (dd, 1 H, J = 7.1, 5.1 Hz, H-4b), 3.66 (dt, 1 H, J = 9.6, 6.4 Hz, OC*H*$_2$CH$_2$), 3.65−3.57 (m, 3 H, H-6′a, H-5b, H-6b), 3.54 (dd, 1 H, J = 10.9, 6.1 Hz, H-6′b), 3.39 (dt, 1 H, J = 9.6, 6.4 Hz, OC*H*$_2$CH$_2$), 1.61−1.54 (m, 2 H, OCH$_2$C*H*$_2$), 1.39−1.25 [m, 10 H, (CH$_2$)$_5$], 0.89 (t, 3 H, J = 7.1 Hz, CH$_3$); ^{13}C NMR (400 MHz, CD_3OD) δ 139.6, 139.2, 139.1 (C_{ipso}), 129.7, 129.4, 129.3, 128.9, 128.8 (C_6H_5), 107.4 (C-1a), 103.1 (C-1b), 89.3 (C-2a), 84.1 (C-3a), 83.4 (C-4b), 82.2 (C-4a), 78.9 (C-2b), 77.8 (C-5a), 76.1 (C-3b), 74.3 (O*C*H$_2$Ph), 74.1 (C-5b), 73.0, 72.9 (O*C*H$_2$Ph), 69.1 (C-6a), 64.1 (C-6b), 68.6 (O*C*H$_2$CH$_2$), 33.0, 30.6, 30.5, 27.4, 23,8 [(CH$_2$)$_6$], 14.5 (CH$_3$); HRMS calcd for $C_{41}H_{56}NaO_{11}$ [M + Na]$^+$ 747.3720, found 747.3721.

Phenyl 2,3,5,6-Tetra-*O*-acetyl-α,β-D-galactofuranosyl-(1,6)-2,3,4-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (13). Disaccharide **13** was synthesized according to a procedure similar to that previously described for **2** starting from **7** (48 mg, 0.17 mmol),

(31) Pathak, A. K.; Pathak, V.; Seitz, L.; Maddry, J. A.; Gurcha, S. S.; Besra, G. S.; Suling, W. J.; Reynolds, R. C. *Bioorg. Med. Chem.* **2001**, *9*, 3129−3143.

(32) Martín-Lomas, M.; Khiar, N.; García, S.; Koessler, J. L.; Nieto, P. M.; Rademacher, T. W. *Chem. Eur. J.* **2000**, *6*, 3608−3621.

(33) Ferrières, V.; Bertho, J.-N.; Plusquellec, D. *Carbohydr. Res.* **1998**, *311*, 25−35.

(34) Ferrières, V.; Gelin, M.; Boulch, R.; Toupet, L.; Plusquellec, D. *Carbohydr. Res.* **1998**, *314*, 79−83.

acceptor **10** (1.89 g, 3.50 mmol), and copper(II) triflate (61.5 mg, 0.17 mmol). Chromatography eluting with CH_2Cl_2−MeOH (19:1) gave the a crude oil (R_f 0.2) which was diluted in pyridine (570 μL, 6.99 mmol) and anhydride acetic (650 μL, 6,92 mmol). After being stirred at rt for 48 h, the reaction medium was concentrated and codistilled with toluene. The resulting mixture was finally purified by flash chromatography eluting with light petroleum−EtOAc (4:1 → 3:2). An anomeric mixture (α/β = 1:7.1) of the target furanose-containing disaccharide **13** was thus obtained in 41% yield (60 mg, 0.07 mmol): R_f 0.1 (light petroleum−EtOAc, 4:1); ^{1}H NMR (400 MHz, CD_3OD) data for **13**α δ 7.42−7.18 (m, 20 H, C_6H_5), 5.51 (dd, 1 H, J = 7.5, 7.1 Hz, H-3b), 5.41 (d, 1 H, J = 1.6 Hz, H-1a), 5.17 (d, 1 H, J = 4.4 Hz, H-1b), 5.05−5.00 (m, 2 H, H-2b, H-5b), 4.89−4.85, 4.65−4.52 (2 m, 6 H, OC*H*$_2$Ph), 4.27−4.17 (m, 2 H, H-5a, H-6′b), 4.04 (dd, 1 H, J = 7.1, 4.9 Hz, H-4b), 4.00 (dd, 1 H, J = 12.0, 6.0 Hz, H-6′b), 3.93 (dd, 1 H, J = 11.1, 4.2 Hz, H-6a), 3.92−3.89 (m, 2 H, H-2a, H-4a), 3.75 (dd, 1 H, J = 9.3, 3.1 Hz, H-3a), 3.61 (dd, 1 H, J = 11.1, 1.5 Hz, H-6′a), 2.01, 1.94, 1.86, 1.78 (4 s, 12 H, CH_3CO); ^{13}C NMR (400 MHz, CD_3OD) δ 170.5, 170.4, 169.9 (CO), 138.3, 138.2, 137.9 (C_{ipso} OCH_2Ph), 134.0 (C_{ipso} SPh), 132.8, 129.2, 128.5, 128.2, 128.1, 128.0, 127.9, 127.8 (C_6H_5), 99.9 (C-1b), 85.8 (C-1a), 80.1 (C-3a), 77.7 (C-4b), 76.4 (C-2a), 76.2 (C-2b), 75.1 (C-4a), 73.5 (C-3b), 72.6 (C-5a), 70.3 (C-5b), 67.2 (C-6a), 62.2 (C-6b), 20.9, 20.8, 20.6, 20.5 (CH_3); ^{1}H NMR (400 MHz, CD_3OD) data for **13**β δ 7.44−7.16 (m, 20 H, C_6H_5), 5.49 (d, 1 H, J = 1.6 Hz, H-1a), 5.31 (dd, 1 H, J = 7.5, 3.8 Hz, H-5b), 5.03 (d, 1 H, J = 1.6 Hz, H-2b), 4.99 (s, 1 H, H-1b), 4.89−4.85, 4.68−4.51 (2 m, 6 H, OC*H*$_2$Ph), 4.84 (dd, 1 H, J = 5.5, 1.6 Hz, H-3b), 4.26 (dd, 1 H, J = 5.5, 3.5 Hz, H-4b), 4.22 (dd, 1 H, J = 11.9, 3.8 Hz, H-6b), 4.21−4.18 (m, 1 H, H-5a), 4.08 (dd, 1 H, J = 11.9, 7.5 Hz, H-6′b), 3.93−3.92 (m, 1 H, H-2a), 3.90 (dd, 1 H, J = 9.7, 9.1 Hz, H-4a), 3.85 (dd, 1 H, J = 10.8, 1.5 Hz, H-6a), 3.77 (dd, 1 H, J = 9.1, 2.9 Hz, H-3a), 3.70 (dd, 1 H, J = 10.8, 6.0, H-6′a), 2.03, 2.00, 1.92, 1.87 (4 s, 12 H, CH_3CO); ^{13}C NMR (400 MHz, CD_3OD) δ 170.5, 170.2, 170.1, 169.5 (CO), 138.4, 138.1, 137.8 (C_{ipso} OCH_2Ph), 134.3 (C_{ipso} SPh),131.8, 129.1, 128.5, 128.0, 127.9, 127.8, 127.6 (C_6H_5), 105.4 (C-1b), 85.8 (C-1a), 82.2 (C-3a or C-3b, C-4b), 81.2 (C-2b), 80.1 (C-3a or C-3b), 74.9 (C-4a), 76.2 (C-2a), 72.4 (C-5a), 69.4 (C-5b), 66.7 (C-6a), 63.1 (C-6b), 20.9, 20.8, 20.6 (CH_3); HRMS calcd for $C_{47}H_{52}NaO_{14}S$ $[M + Na]^+$ 895.2976, found 895.2976.

Acknowledgment. We are grateful to the French Ministry of Education, Research and Technology for a grant to R.E.

Supporting Information Available: 1D- and 2D-correlational NMR, ^{1}H−^{1}H, and ^{1}H−^{13}C spectra for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

JO070741J