JOC*Note*

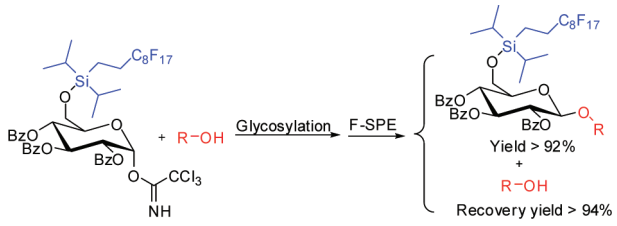
Synthesis and Applications of a Light-Fluorous Glycosyl Donor

Fa Zhang,[†] Wei Zhang,[‡] Yan Zhang,[†] Dennis P. Curran,[§] and Gang Liu*[,†]

Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, P. R. China, Department of Chemistry, University of Massachusetts-Boston, Boston, Massachusetts 02125, and Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260

gangliu27@yahoo.com

Received January 15, 2009



A new method using a light-fluorous glycosyl donor and an orthogonal tagging strategy to synthesize oligosaccharides and glycoconjugates has been developed. The glycosyl donor orthogonally protected with a C_8F_{17}-silyl tag and benzoyl groups was reacted with excess amounts of glycosyl acceptor. Fluorous solid-phase extraction separated the glycosylated product and unreacted glycosyl acceptor. This new protocol has high reaction efficiency and easy separation, which was demonstrated in the synthesis of an unprotected trisaccharide and an *O*-glycosylated serine in this paper.

Carbohydrates play a pivotal role in many biological processes, such as cell adhesion, inflammation, immune response, and tumor metastasis.[1] Low glycosylation efficiency and difficulty of product purification are two major issues in glycochemistry. Numerous chemical and enzymatic glycosylation methods have been developed.[2] However, the separation of oligosaccharides from deletion sequences still heavily relies on chromatographic methods. In recent years, synthesis of oligosaccharides on solid support[3] or soluble support (PEG)[4] has been extensively studied. These methods usually have the drawbacks of reduced reactivity, incapability of removing anchored unreacted intermediates and byproducts, and difficulty of structure characterization.

Fluorous chemistry has been widely used in biphasic catalysis, combinatorial and parallel synthesis of small molecules, and separation of biomolecules.[5] Since the Curran group first reported the utility of heavy-fluorous tagged glucal for the synthesis of a disaccharide,[6n] more heavy-fluorous tags[6] and new light-fluorous tags[7] have been developed for oligosaccharide synthesis. Most of these reports focused on fluorous-tagged glycosyl acceptors for the synthesis of oligosaccharides. Tagged glycosyl donors could have broader applications than acceptor for the synthesis of oligosaccharides as well as other glycoconjugates, but to date the effort on fluorous glycosyl donors is limited to heavy-fluorous tag.[6n] The synthesis and separation for heavy-fluorous tagged compounds rely on highly fluorinated solvents, which are expensive and persistent. Very recently, Pohl's group reported the use of a light-fluorous glycosyl donor in the synthesis of a monosaccharide.[7c] We herein introduce the synthesis of oligosaccharides and glycosylated amino acid by using a light-fluorous glycosyl donor and an orthogonal tagging strategy.

In our current work, a glycosyl donor is attached to a fluorous tag, and the tagged donor is reacted with a nonfluorous glycosyl acceptor. The acceptor is used in excess amount to consume the fluorous donor (Scheme 1). After each glycosylation, the desired fluorous product is easily isolated by fluorous solid-

[†] Institute of Materia Medica.
[‡] University of Massachusetts-Boston.
[§] University of Pittsburgh.

(1) (a) Rudd, P. M.; Elliott, T.; Cresswell, P.; Wilson, I. A.; Dwek, R. A. *Science* **2001**, *291*, 2370. (b) Dwek, R. A. *Chem. Rev.* **1996**, *96*, 683. (c) Varki, A. *Glycobiology* **1993**, *3*, 97.

(2) (a) Sears, P.; Wong, C.-H. *Science* **2001**, *291*, 2344. (b) Koeller, K. M.; Wong, C.-H. *Chem. Rev.* **2000**, *100*, 4465.

(3) (a) Seeberger, P. H. *Chem. Soc. Rev.* **2008**, *37*, 19. (b) Plante, O. J.; Palmacci, E. R.; Seeberger, P. H. *Science* **2001**, *291*, 1523. (c) Seeberger, P. H.; Haase, W.-C. *Chem. Rev.* **2000**, *100*, 4349, and references therein.

(4) (a) Ando, H.; Manabe, S.; Nakahara, Y.; Ito, Y. *Angew. Chem., Int. Ed.* **2001**, *40*, 4725. (b) Eichler, E.; Yan, F.; Sealy, J.; Whitfield, D. M. *Tetrahedron* **2001**, *57*, 6679. (c) Ando, H.; Manabe, S.; Nakahara, Y.; Ito, Y *J. Am. Chem. Soc.* **2001**, *123*, 3848, and references therein.

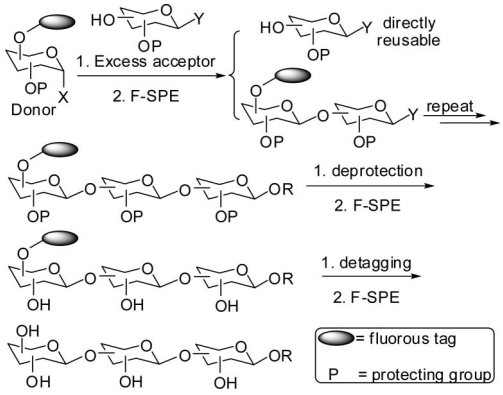
(5) (a) Curran, D. P. *Science* **2008**, *321*, 1645. (b) Zhang, W.; Cai, C. *Chem. Commun.* **2008**, 5686. (c) Zhang, W. *Chem. Rev.* **2004**, *104*, 2531, and references therein.

(6) (a) Mizuno, M.; Kitazawa, S; Goto, K *J. Fluorine Chem.* **2008**, *129*, 955. (b) Goto, K.; Mizuno, M. *Tetrahedron Lett.* **2007**, *48*, 5605. (c) Mizuno, M.; Matsumoto, H.; Goto, K.; Hamasaki, K. *Tetrahedron Lett.* **2006**, *47*, 8831. (d) Mizuno, M.; Goto, K.; Miura, T.; Inazu, T. *QSAR Comb. Sci.* **2006**, *25*, 742. (e) Goto, K.; Miura, T.; Mizuno, M. *Tetrahedron Lett.* **2005**, *46*, 8293. (f) Miura, T.; Tsujino, S.; Satoh, A.; Goto, K.; Mizuno, M.; Noguchi, M.; Kajimoto, T.; Node, M.; Murakami, Y.; Imai, N.; Inazu, T. *Tetrahedron* **2005**, *61*, 6518. (g) Miura, T.; Satoh, A.; Goto, K.; Murakami, Y.; Imai, N.; Inazu, T. *Tetrahedron: Asymmetry* **2005**, *16*, 3. (h) Goto, K.; Miura, T.; Mizuno, M.; Takaki, H.; Imai, N.; Murakami, Y.; Inazu, T. *Synlett* **2004**, 2221. (i) Goto, K.; Miura, T.; Hosaka, D.; Matsumoto, H.; Mizuno, M.; Ishida, H.-K.; Inazu, T. *Tetrahedron* **2004**, *60*, 8845. (j) Miura, T.; Goto, K.; Waragai, H.; Matsumoto, H.; Hirose, Y.; Ohmae, M.; Ishida, H.-K.; Satoh, A.; Inazu, T. *J. Org. Chem.* **2004**, *69*, 5348. (k) Miura, T.; Inazu, T. *Tetrahedron Lett.* **2003**, *44*, 1819. (l) Miura, T.; Goto, K.; Hosaka, D.; Inazu, T. *Angew. Chem., Int. Ed.* **2003**, *42*, 2047. (m) Miura, T.; Hirose, Y.; Ohmae, M.; Inazu, T. *Org. Lett.* **2001**, *3*, 3947. (n) Curran, D. P.; Ferritto, R.; Hua, Y. *Tetrahedron Lett.* **1998**, *39*, 4937.

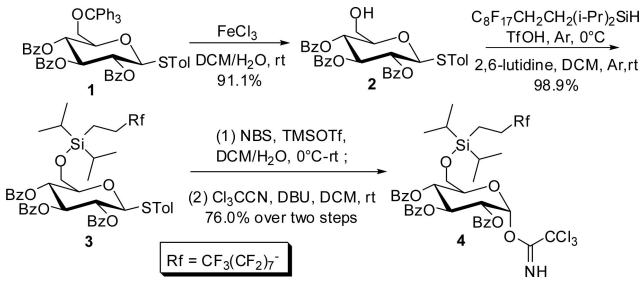
(7) (a) Ko, K.-S.; Park, G.; Yu, Y.; Pohl, N. L. *Org. Lett.* **2008**, *10*, 5381. (b) Tojino, M.; Mizuno, M. *Tetrahedron Lett.* **2008**, *49*, 5920. (c) Park, G.; Ko, K.-S.; Zakharova, A.; Pohl, N. L. *J. Fluorine Chem.* **2008**, *129*, 978. (d) Jaipuri, F. A.; Pohl, N. L. *Org. Biomol. Chem.* **2008**, *6*, 2686. (e) Pohl, N. L. *ACS Symp. Ser.* **2008**, *990*, 272. (f) Chen, G.-S.; Pohl, N. L. *Org. Lett.* **2008**, *10*, 785. (g) Jaipuri, F. A.; Collet, B. Y. M.; Pohl, N. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 1707. (h) Kojima, M.; Nakamura, Y.; Takeuchi, S. *Tetrahedron Lett.* **2007**, *48*, 4431. (i) Carrel, F. R.; Geyer, K.; Codée, J. D. C.; Seeberger, P. H. *Org. Lett.* **2007**, *9*, 2285. (j) Manzoni, L.; Castelli, R. *Org. Lett.* **2006**, *8*, 955. (k) Kasuya, M. C. Z.; Ito, A.; Cusi, R.; Sato, T.; Hatanaka, K. *Chem. Lett.* **2005**, *34*, 856. (l) Manzoni, L.; Castelli, R. *Org. Lett.* **2004**, *6*, 4195. (m) Jing, Y.; Huang, X. *Tetrahedron Lett.* **2004**, *45*, 4615. (n) Kasuya, M. C. Z.; Cusi, R.; Ishihara, O.; Miyagawa, A.; Hashimoto, K.; Sato, T.; Hatanaka, K. *Biochem. Biophys. Res. Commun.* **2004**, *316*, 599. (o) Manzoni, L. *Chem. Commun.* **2003**, 2930.

10.1021/jo9000993 CCC: $40.75
Published on Web 02/13/2009

SCHEME 1. Glycosylation with a Light-Fluorous Glycosyl Donor



SCHEME 2. Synthesis of Light-Fluorous Glycosyl Donor



phase extraction (F-SPE),[8] and the excess glycosyl acceptor can be recovered and recycled. Once the glycosylation sequence is completed, all nonfluorous protecting groups on the fluorous product are selectively removed. The deprotected fluorous compound is separated by F-SPE. In the last step, the desired oligosaccharide or glycoconjugate is obtained by removal of the fluorous tag followed by F-SPE separation again. This method takes the advantage of a light-fluorous glycosyl donor and the orthogonal tagging strategy. A temporary protecting group is unnecessary at the glycosylation position of all acceptors, so the method has potential for the synthesis of oligosaccharides as well as other glycoconjugates. In addition, F-SPE replaces the time-demanding preparative HPLC to simplify the purification.

In this note, we demonstrate the method of glycosylation using a light-fluorous gylcosyl donor protected with a fluorous TIPS group[9] and nonfluorous benzoyl groups. The fluorous protecting group is stable to the reaction conditions required for glycosylations and acyl-deprotections, while the detagging could be achieved with weak acid.

The known thioglycoside **1** (Scheme 2) with trityl and benzoyl protection was synthesized.[10] The temporary trityl group was then removed with $FeCl_3$.[11] The F-silyl group was subsequently attached to the primary hydroxyl group of **2** to give the intermediate **3**. The thioglycoside **3** was then converted into trichloroacetimidate **4** in two steps.[12]

For quick investigation of the glycosylation reactions, intermediate **2** was glycosylated with fluorous trichloroacetimidate

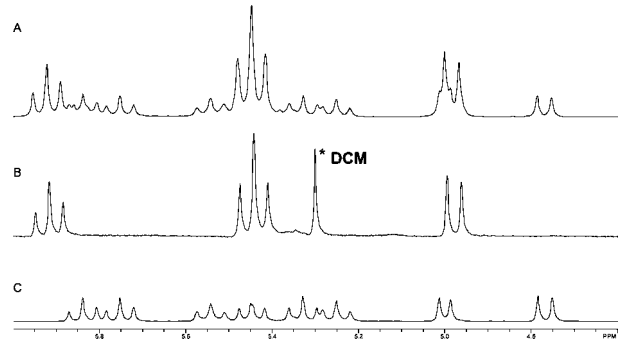
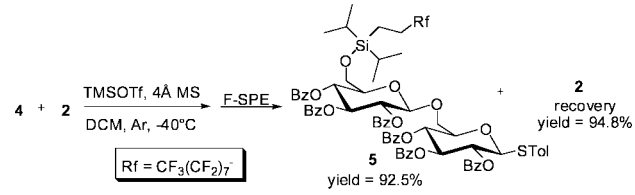


FIGURE 1. ^{1}H NMR spectrum of (A) crude product, (B) organic fraction (**2**), and (C) fluorous fraction (**5**) after glycosylation of **2** with **4**.

SCHEME 3. Disaccharide Synthesis with Tagged Glycosyl Donor



4 (Scheme 3). The reaction was carried out in anhydrous DCM at −40 °C in the presence of a catalytic amount of TMSOTf as activator. ^{1}H NMR spectrum of the crude product confirmed the clean and efficient conversion (Figure 1A). No obvious formation of hydrolyzed byproduct or silyl migrated byproduct was observed. After a quick F-SPE,[13] the products from the organic fraction and the fluorous fraction were analyzed by ^{1}H NMR spectroscopy. Comparison of Figure 1B and C with A of the crude product indicates that compounds **2** and **5** were completely separated. The anticipated disaccharide **5** was obtained in 92.5% yield, and the unreacted compound **2** was recovered in 94.8% yield.

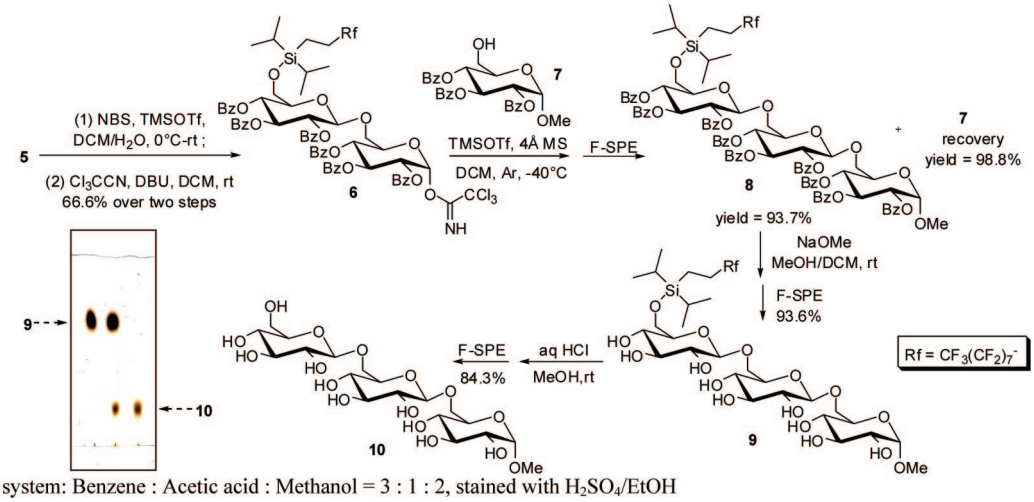
Compound **5** was further converted into trichloroacetimidate **6** (Scheme 4) following the procedure described above and then purified by silica gel chromatography. After one more cycle of glycosylation and F-SPE, the protected trisaccharide **8** was obtained in 93.7% yield. All of the Bz groups of **8** were removed by treatment with 0.02 M NaOMe in MeOH/DCM, which gave intermediate **9** after another F-SPE separation. Finally, the fluorous tag was removed with 0.02 M HCl in MeOH/H_2O. After F-SPE and lyophilization, the final unprotected trisaccharide **10** was obtained as a white powder. The high purity (99.9%, HPLC-ELSD) of the trisaccharide **10** with 10 free hydroxyl groups was confirmed by TLC and NMR analyses.

We further extended the utility of fluorous glycosyl donor for glycosylation with a typical amino acid (Scheme 5). Fmoc-L-Ser-OMe **11** was reacted with glycosyl donor **4** under the previous glycosylation conditions. After F-SPE, the glycosylated compound **12** was obtained in 96.6% yield. Fmoc-L-Ser-OMe was recovered in 95.0% yield. Both the glycosylation and the F-SPE separation were still efficient. All of these F-SPE separations were performed with one F-SPE cartridge containing 2 g of fluorous silica gel.

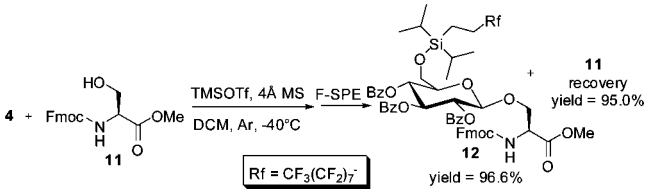
(8) Zhang, W.; Curran, D. P. *Tetrahedron* **2006**, *62*, 11837.
(9) (a) Carrel, F. R.; Seeberger, P. H. *J. Org. Chem.* **2008**, *73*, 2058. (b) Zhang, W.; Luo, Z.; Chen, C. H.-T.; Curran, D. P. *J. Am. Chem. Soc.* **2002**, *124*, 10443. (c) Palmacci, E. R.; Hewitt, M. C.; Seeberger, P. H. *Angew. Chem., Int. Ed.* **2001**, *40*, 4433.
(10) France, R. R.; Compton, R. G.; Davis, B. G.; Fairbanks, A. J.; Rees, N. V.; Wadhawan, J. D. *Org. Biomol. Chem.* **2004**, *2*, 2195.
(11) Ding, X.; Wang, W.; Kong, F. *Carbohydr. Res.* **1997**, *303*, 445.
(12) Yu, H.; Ensley, H. E. *Tetrahedron Lett.* **2003**, *44*, 9363.

(13) **General F-SPE Procedure.** The crude product was loaded onto the column using DMF/H_2O (90:10). MeOH/H_2O (80:20) was used for loading of **10**. Nonfluorous compounds were eluted using MeOH/H_2O (80:20), whereas the fluorinated compound was collected using pure MeOH. The F-SPE cartridge was regenerated with acetone.

SCHEME 4. Synthesis of Unprotected Trisaccharide



SCHEME 5. Synthesis of Glycosylated Fmoc-L-Ser-OMe



In summary, we report the light-fluorous glycosyl donor and its application for the synthesis of oligosaccharides and a glycosylated amino acid. Orthogonal protecting groups including C_8F_{17}-silyl and benzoyl groups were employed. Glycosylation with fluorous trichloroacetimidate gave clean and complete conversion. No fluorous solvent was needed during the synthesis and separation. The fluorous glycosyl donor avoids the use of a temporary protecting group on the acceptor. Unprotected trisaccharide with high purity was obtained after F-SPE, avoiding the use of time-demanding preparative HPLC. The fluorous glycosyl donor was also successfully used for the synthesis of an *O*-glycosylated amino acid. The facile F-SPE separation provides the basis of a potential automatic synthesis procedure. Further applications of this light-fluorous glycosyl donor for synthesis of oligosaccharides, glycoconjugates, and glycosylated natural products are now in progress.

Experimental Section

***p*-Methylphenyl 2,3,4-Tri-*O*-benzoyl-6-*O*-(2,3,4-tri-*O*-benzoyl-6-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-decyl)diisopropylsilyl-*β*-D-glucopyranoside)-1-thio-*β*-D-glucopyranoside (5).** Glycosyl donor **4** (260.0 mg, 0.217 mmol) and glycosyl acceptor **2** (390.0 mg, 0.652 mmol) were coevaporated two times with toluene, dried under vacuum for 2 h, and dissolved in anhydrous DCM (4.7 mL) with powdered 4 Å molecular sieves (200 mg). The solution was cooled to −40 °C, and TMSOTf (43 μL of freshly prepared 0.5 M solution in DCM, 0.022 mmol) was added dropwise. After 30 min, the reaction was quenched by addition of saturated aqueous $NaHCO_3$ (20 mL). The mixture was filtered and extracted three times with DCM (50 mL × 3). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was separated with F-SPE. Concentration of the fluorous fraction provided the disaccharide **5** (328.1 mg, 0.201 mmol, 92.5%) as a white foam. The nonfluorous fraction was extracted with DCM (50 mL × 3) after removal of MeOH and further purified by flash chromatography (petroleum ether/ethyl acetate, 4:1 v/v) on silica gel to give recovered **2** (246.6 mg, 0.412 mmol, 94.8%). $[\alpha]^{20}_D$ +4.4 (*c* 1.4, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94−7.90 (m, 6H), 7.86−7.82 (m, 4H), 7.73 (d, J = 7.2 Hz, 2H), 7.55−7.21 (m, 20H), 7.17 (d, J = 7.8 Hz, 2H), 5.83 (t, J = 9.6 Hz, 1H), 5.75 (t, J = 9.6 Hz, 1H), 5.54 (t, J = 9.6 Hz, 1H), 5.45 (t, J = 9.9 Hz, 1H), 5.33 (t, J = 9.6 Hz, 1H), 5.25 (t, J = 9.6 Hz, 1H), 5.00 (d, J = 7.8 Hz, 1H), 4.76 (d, J = 9.9 Hz, 1H), 3.99−3.79 (m, 6H), 2.36 (s, 3H), 2.11−2.05 (m, 2H), 1.05−0.90 (m, 2H), 0.96 (d, J = 5.1 Hz, 12H), 0.81−0.75 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.8, 165.7, 165.3, 165.2, 165.0, 164.9, 138.9, 134.0, 133.4, 133.3, 133.3, 133.2, 133.1, 129.9, 129.8, 129.8, 129.7, 129.4, 129.3, 129.1, 129.0, 128.9, 128.7, 128.4, 128.3, 128.2, 128.2, 127.6, 101.1, 86.0, 78.6, 75.1, 74.1, 73.3, 72.0, 70.5, 69.5, 69.3, 68.1, 62.7, 25.2 (m), 21.2, 17.3, 17.3, 17.3, 12.3, 12.2, −0.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.13 (3F), −116.73 (2F), −122.24 (6F), −123.06 (2F), −123.36 (2F), −126.46 (2F); HRMS (ESI) calcd for $C_{77}H_{69}O_{16}F_{17}NaSiS$ $[M + Na]^+$ 1655.3696, found 1655.3622.

2,3,4-Tri-*O*-benzoyl-6-*O*-(2,3,4-tri-*O*-benzoyl-6-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-decyl)diisopropylsilyl-*β*-D-glucopyranosyl)-α-D-glucopyranosyl Trichloroacetimidate (6). Disaccharide **5** (313.5 mg, 0.192 mmol) was dissolved in DCM/H_2O (5.9 mL, 100:1 v/v) and cooled to 0 °C. The solution was treated with NBS (34.2 mg, 0.192 mmol) and TMSOTf (38 μL of freshly prepared 0.5 M solution in DCM, 0.019 mmol). After completion, saturated aqueous $NaHCO_3$ (20 mL) was added, and the mixture was extracted with DCM (50 mL × 3). The combined organic layer was washed with brine (50 mL), dried over Na_2SO_4, and concentrated. The residue was purified by flash chromatography (Petroleum ether/ethyl acetate, 6:1 v/v) on silica gel. The resulting syrup was dissolved in anhydrous DCM (2 mL) and cooled to 0 °C. To the resulting solution were added trichloroacetonitrile (115.5 μL, 1.152 mmol) and 1,8-dizaabicyclo [5.4.0] undec-7-ene (DBU) (14.4 μL, 0.096 mmol). After stirring for 30 min, the solvent was evaporated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/ethyl acetate, 7:1 v/v, 0.1% Et_3N) on silica gel to give **6** (213.6 mg, 66.6% over two steps) as a white foam. $[\alpha]^{20}_D$ +12.3 (*c* 1.4, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.30 (s, 1H), 8.03−7.78 (m, 12H), 7.51−7.24 (m, 18H), 6.67 (d, J = 3.0 Hz, 1H), 6.17 (t, J = 9.6 Hz, 1H), 5.84 (t, J = 9.6 Hz, 1H), 5.54−5.34 (m, 4H), 4.94 (d, J = 7.8 Hz, 1H), 4.44 (dd, J = 9.6, 5.7 Hz, 1H), 4.10 (m, 1H), 3.86−3.77 (m, 4H), 2.11−1.95 (m, 2H), 1.00−0.90 (m,14H), 0.81−0.75 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.8, 165.6, 165.2, 165.1, 165.0, 165.0, 160.2, 133.4, 133.4, 133.2, 133.2, 133.1, 133.0, 130.0, 129.9, 129.9, 129.9, 129.8, 129.7, 129.7, 129.5, 129.1, 129.0, 129.0, 128.7, 128.4, 128.3, 128.2, 128.2, 100.9, 92.9, 75.1, 73.2, 72.0, 71.9, 70.7, 70.1, 69.4, 68.7, 67.3, 62.7, 25.2 (m), 17.3, 17.3, 17.2, 12.2, 12.2, −0.3; ^{19}F NMR

(376 MHz, $CDCl_3$) δ −81.13 (3F), −116.73 (2F), −122.25 (6F), −123.06 (2F), −123.39 (2F), −126.46 (2F).

Methyl 2,3,4-Tri-*O*-benzoyl-6-*O*-(2,3,4-Tri-*O*-benzoyl-6-*O*-(2,3,4-tri-*O*-benzoyl-6-(3,3,4,4,5,5,6,6,7,7,8,8,8,9,9,10,10, 10-heptadecafluorodecyl)diisopropylsilyl-*β*-D-glucopyranosyl)-*β*-D-glucopyranosyl)-α-D-glucopyranoside (8). The reaction was repeated with **6** (149.5 mg, 0.089 mmol) and **7** (135.9 mg, 0.268 mmol) as for the dimeric glucose reported above. F-SPE provided trisaccharide **8** (168.9 mg, 0.084 mmol, 93.7%) as light yellow syrup. The unreacted **7** (89.5 mg, 98.8%) was recovered by flash chromatography (petroleum ether/ethyl acetate, 3:1 v/v) on silica gel. $[\alpha]^{20}_D$ +13.2 (*c* 1.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99−7.74 (m, 18H), 7.54−7.13 (m, 27H), 6.08 (t, J = 9.6 Hz, 1H), 5.98 (t, J = 9.6 Hz, 1H), 5.76 (t, J = 9.6 Hz, 1H), 5.56 (t, J = 9.6 Hz, 1H), 5.44 (t, J = 9.9 Hz, 1H), 5.40 (t, J = 9.9 Hz, 1H), 5.37 (t, J = 9.9 Hz, 1H), 5.23 (t, J = 9.6 Hz, 1H), 5.13 (dd, J = 9.9, 3.6 Hz, 1H), 5.10 (d, J = 3.6 Hz, 1H), 5.02 (d, J = 8.1 Hz, 1H), 4.69 (d, J = 7.8 Hz, 1H), 4.00−3.78 (m, 8H), 3.47 (dd, J = 12.0, 6.0 Hz, 1H), 3.17 (s, 3H), 2.11−2.02 (m, 2H), 1.00−0.94 (m, 14H), 0.88−0.75 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.8, 165.7, 165.6, 165.3, 165.2, 165.1, 165.0, 165.0, 133.4, 133.3, 133.2, 133.2, 133.1, 133.0, 133.0, 132.9, 129.9, 129.8, 129.7, 129.6, 129.5, 129.5, 129.3, 129.2, 129.1, 129.1, 129.0, 128.9, 128.7, 128.4, 128.4, 128.3, 128.2, 128.1, 101.2, 101.1, 96.7, 74.9, 74.5, 73.0, 72.8, 72.2, 72.0, 71.9, 70.3, 69.8, 69.7, 69.1, 68.6, 68.1, 67.9, 62.6, 55.2, 25.0 (m), 17.4, 17.3, 17.3, 17.2, 12.2, 12.2, −0.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.13 (3F), −116.73 (2F), −122.25 (6F), −123.06 (2F), −123.38 (2F), −126.46 (2F); HRMS (ESI) calcd for $C_{98}H_{87}O_{25}F_{17}NaSi$ $[M + Na]^+$ 2037.4926, found 2037.4886.

Methyl 6-*O*-(6-*O*-(6-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-decyl)diisopropylsilyl-*β*-D-glucopyranosyl)-*β*-D-glucopyranosyl)-α-D-glucopyranoside (9). To a solution of trisaccharide **8** (92.8 mg, 0.046 mmol) in MeOH/DCM (1.2 mL, 5:1 v/v) was added 0.5 M NaOMe solution in MeOH (46 μL, 0.023 mmol). The reaction mixture was stirred at room temperature for 12 h. Then solid NH_4Cl (2.1 mg, 0.04 mmol) was added for neutralization. After filtration through celite, the solution was concentrated under reduced pressure and purified by F-SPE. Evaporation of fluorous fraction gave **9** (46.5 mg, 0.043 mmol, 93.6%) as a white foam. $[\alpha]^{20}_D$ +6.8 (*c* 1.0, CH_3OH); ^{1}H NMR (300 MHz, CD_3OD) δ 4.60 (d, J = 3.9 Hz, 1H), 4.36 (d, J = 7.8 Hz, 1H), 4.28 (d, J = 7.8 Hz, 1H), 4.10−4.05 (m, 2H), 3.99 (d, J = 10.2 Hz, 1H), 3.83 (dd, J = 10.8, 4.8 Hz, 1H), 3.74−3.65 (m, 3H), 3.56 (t, J = 9.3 Hz, 1H), 3.41−3.11 (m, 10H), 3.36 (s, 3H), 2.23−2.11 (m, 2H), 1.15−0.95 (m, 14H), 0.88−0.82 (m, 2H); ^{13}C NMR (125 MHz, CD_3OD) δ 104.9, 104.8, 101.3, 78.1, 78.0, 77.3, 75.2, 75.0, 74.9, 73.4, 72.6, 71.7, 71.4, 71.2, 70.3, 69.5, 64.2, 55.8, 26.5 (m), 18.0, 17.9, 13.6, 13.6, 0.8; ^{19}F NMR (376 MHz, CD_3OD) δ −78.80 (3F), −113.73 (2F), −119.14 (2F), −119.30 (4F), −120.15 (2F), −120.43 (2F), −123.69 (2F); HRMS (ESI) calcd for $C_{35}H_{51}O_{16}F_{17}NaSi$ $[M + Na]^+$ 1101.2567, found 1101.2587.

Methyl 6-*O*-(6-*O*-*β*-D-Glucopyranosyl)-*β*-D-gluco-pyranosyl-α-D-glucopyranoside (10). Twelve molar HCl (30 μL) was dissolved in 18 mL of MeOH. Part of the resulting solution (905 μL) was added to trisaccharide **9** (19.5 mg, 0.018 mmol). The reaction mixture was stirred at room temperature for 5 h. After purification by F-SPE, the organic fraction was concentrated under reduced pressure to remove most of MeOH and filtered through celite. Freeze-drying of the resulting solution gave aim product **10** (7.9 mg, 0.015 mmol, 84.3%) as a white powder. $[\alpha]^{20}_D$ +20.0 (*c* 0.7, H_2O); ^{1}H NMR (500 MHz, D_2O) δ 4.81 (d, J = 4.5 Hz, 1H), 4.52 (t, J = 8.5 Hz, 2H), 4.22 (d, J = 11.5 Hz, 1H), 4.19 (dd, J = 12.0, 1.0 Hz, 1H), 3.95−3.87 (m, 3H), 3.81 (dd, J = 9.5, 3.0 Hz, 1H), 3.74 (dd, J = 12.5, 5.5 Hz, 1H), 3.68 (t, J = 9.5 Hz, 1H), 3.65−3.62 (m, 1H), 3.58 (dd, J = 9.5 Hz, 4.0 Hz, 1H), 3.53−3.39 (m, 6H), 3.44 (s, 3H), 3.36−3.30 (m, 2H); ^{13}C NMR (125 MHz, D_2O) δ 105.7, 105.6, 102.2, 78.8, 78.5, 78.4, 77.8, 76.0, 75.9, 75.8, 74.0, 73.4, 72.5, 72.3, 72.2, 71.5, 71.4, 63.6, 58.1; HRMS (ESI) calcd for $C_{19}H_{34}O_{16}Na$ $[M + Na]^+$ 541.1739, found 541.1750.

Acknowledgment. This research was financially supported by the National Natural Science Foundation of China (no. 90713045).

Supporting Information Available: HPLC chromatogram of compound **10**. Detailed experimental procedures and compound characterization data for compounds **1**−**4**, **7**, **11**, and **12**. ^{1}H and ^{13}C NMR spectra for all described compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO9000993