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Synthesis and Applications of a Light-Fluorous Glycosyl Donor

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Abstract

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 support³ or soluble support (PEG)⁴ has been extensively studied. These methods usually have the drawbacks of reduced reactivity,

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

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,^{6a} more heavy-fluorous tags⁶ and new light-fluorous tags⁷ 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.^{6a} 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-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 glycosyl donor protected with a fluorous TIPS group⁹ 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 FeCl₃.¹¹ 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 **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. ¹H 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 ¹H 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 fluororous tag was removed with 0.02 M HCl in MeOH/H₂O. 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 fluororous 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 fluororous silica gel.

In summary, we report the light-fluororous glycosyl donor and its application for the synthesis of oligosaccharides and a glycosylated amino acid. Orthogonal protecting groups including C₈F₁₇-silyl and benzoyl groups were employed. Glycosylation with fluororous trichloroacetimidate gave clean and complete conversion. No fluororous solvent was needed during the synthesis and separation. The fluororous 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 fluororous 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-fluororous 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-heptafluoro-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 μ L 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 NaHCO₃ (20 mL). The mixture was filtered and extracted three times with DCM (50 mL $\times$ 3). The combined organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The residue was separated with F-SPE. Concentration of the fluororous fraction provided the disaccharide **5** (328.1 mg, 0.201 mmol, 92.5%) as a white foam. The nonfluororous fraction was extracted with DCM (50 mL $\times$ 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%). [α]_D²⁰ +4.4 (*c* 1.4, CHCl₃); ¹H NMR (300 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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; ¹⁹F NMR (376 MHz, CDCl₃) δ -81.13 (3F), -116.73 (2F), -122.24 (6F), -123.06 (2F), -123.36 (2F), -126.46 (2F); HRMS (ESI) calcd for C₇₇H₆₉O₁₆F₁₇NaSiS [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/H₂O (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 μ L of freshly prepared 0.5 M solution in DCM, 0.019 mmol). After completion, saturated aqueous NaHCO₃ (20 mL) was added, and the mixture was extracted with DCM (50 mL $\times$ 3). The combined organic layer was washed with brine (50 mL), dried over Na₂SO₄, 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 μ L, 1.152 mmol) and 1,8-diazaabicyclo [5.4.0] undec-7-ene (DBU) (14.4 μ L, 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% Et₃N) on silica gel to give **6** (213.6 mg, 66.6% over two steps) as a white foam. $[\alpha]_D^{20}$ +12.3 (*c* 1.4, CHCl₃); ¹H NMR (300 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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; ¹⁹F NMR (376 MHz, CDCl₃) 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-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-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. $[\alpha]_D^{20}$ +13.2 (*c* 1.8, CHCl₃); ¹H NMR (300 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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; ¹⁹F NMR (376 MHz, CDCl₃) δ –81.13 (3F), –116.73 (2F), –122.25 (6F), –123.06 (2F), –123.38 (2F), –126.46 (2F); HRMS (ESI) calcd for C₉₈H₈₇O₂₅F₁₇NaSi [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 μ L, 0.023 mmol). The reaction mixture was stirred at room temperature for 12 h. Then solid NH₄Cl (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 fluororous fraction gave **9** (46.5 mg, 0.043 mmol, 93.6%) as a white foam. $[\alpha]_D^{20} +6.8$ (c 1.0, CH₃OH); ¹H NMR (300 MHz, CD₃OD) 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); ¹³C NMR (125 MHz, CD₃OD) 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; ¹⁹F NMR (376 MHz, CD₃OD) 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 C₃₅H₅₁O₁₆F₁₇NaSi [M + Na]⁺ 1101.2567, found 1101.2587.

Methyl 6-O-(6-O- β -D-Glucopyranosyl)- β -D-glucopyranosyl- α -D-glucopyranoside (**10**)

Twelve molar HCl (30 μ L) was dissolved in 18 mL of MeOH. Part of the resulting solution (905 μ L) 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. $[\alpha]_D^{20} +20.0$ (c 0.7, H₂O); ¹H NMR (500 MHz, D₂O) 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); ¹³C NMR (125 MHz, D₂O) 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 C₁₉H₃₄O₁₆Na [M + Na]⁺ 541.1739, found 541.1750.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. a Rudd PM, Elliott T, Cresswell P, Wilson IA, Dwek RA. Science 2001;291:2370. [PubMed: 11269318] b Dwek RA. Chem. Rev 1996;96:683. [PubMed: 11848770] c Varki A. Glycobiology 1993;3:97. [PubMed: 8490246]
2. a Sears P, Wong C-H. Science 2001;291:2344. [PubMed: 11269314] b Koeller KM, Wong C-H. Chem. Rev 2000;100:4465. [PubMed: 11749355]
3. a Seeberger PH. Chem. Soc. Rev 2008;37:19. [PubMed: 18197330] b Plante OJ, Palmacci ER, Seeberger PH. Science 2001;291:1523. [PubMed: 11222853] c Seeberger PH, Haase W-C. Chem. Rev 2000;100:4349. [PubMed: 11749351] 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 DM. Tetrahedron 2001;57:6679. c Ando H, Manabe S, Nakahara Y, Ito Y. J. Am. Chem. Soc 2001;123:3848. [PubMed: 11457129] and references therein
5. a Curran DP. Science 2008;321:1645. [PubMed: 18801990] b Zhang W, Cai C. Chem. Commun 2008:5686. c Zhang W. Chem. Rev 2004;104:2531. [PubMed: 15137799] 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. [PubMed: 15287781] 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. [PubMed: 11720576] n Curran DP, Ferritto R, Hua Y. *Tetrahedron Lett* 1998;39:4937.
7. a Ko K-S, Park G, Yu Y, Pohl NL. *Org. Lett* 2008;10:5381. b Tojino M, Mizuno M. *Tetrahedron Lett* 2008;49:5920. c Park G, Ko K-S, Zakharova A, Pohl NL. *J. Fluorine Chem* 2008;129:978. d Jaipuri FA, Pohl NL. *Org. Biomol. Chem* 2008;6:2686. [PubMed: 18633525] e Pohl NL. *ACS Symp. Ser* 2008;990:272. f Chen G-S, Pohl NL. *Org. Lett* 2008;10:785. [PubMed: 18247626] g Jaipuri FA, Collet BYM, Pohl NL. *Angew. Chem., Int. Ed* 2008;47:1707. h Kojima M, Nakamura Y, Takeuchi S. *Tetrahedron Lett* 2007;48:4431. i Carrel FR, Geyer K, Codée JDC, Seeberger PH. *Org. Lett* 2007;9:2285. [PubMed: 17489597] j Manzoni L, Castelli R. *Org. Lett* 2006;8:955. [PubMed: 16494483] k Kasuya MCZ, Ito A, Cusi R, Sato T, Hatanaka K. *Chem. Lett* 2005;34:856. l Manzoni L, Castelli R. *Org. Lett* 2004;6:4195. [PubMed: 15524441] m Jing Y, Huang X. *Tetrahedron Lett* 2004;45:4615. n Kasuya MCZ, Cusi R, Ishihara O, Miyagawa A, Hashimoto K, Sato T, Hatanaka K. *Biochem. Biophys. Res. Commun* 2004;316:599. [PubMed: 15033442] o Manzoni L. *Chem. Commun* 2003:2930.
8. Zhang W, Curran DP. *Tetrahedron* 2006;62:11837. [PubMed: 18509513]
9. a Carrel FR, Seeberger PH. *J. Org. Chem* 2008;73:2058. [PubMed: 17956118] b Zhang W, Luo Z, Chen CH-T, Curran DP. *J. Am. Chem. Soc* 2002;124:10443. [PubMed: 12197746] c Palmacci ER, Hewitt MC, Seeberger PH. *Angew. Chem., Int. Ed* 2001;40:4433.
10. France RR, Compton RG, Davis BG, Fairbanks AJ, Rees NV, Wadhawan JD. *Org. Biomol. Chem* 2004;2:2195. [PubMed: 15280955]
11. Ding X, Wang W, Kong F. *Carbohydr. Res* 1997;303:445.
12. Yu H, Ensley HE. *Tetrahedron Lett* 2003;44:9363.
13. General F-SPE Procedure. The crude product was loaded onto the column using DMF/H₂O (90:10). MeOH/H₂O (80:20) was used for loading of **10**. Nonfluorous compounds were eluted using MeOH/H₂O (80:20), whereas the fluorinated compound was collected using pure MeOH. The F-SPE cartridge was regenerated with acetone.

SCHEME 1.
Glycosylation with a Light-Fluorous Glycosyl Donor

SCHEME 2.
Synthesis of Light-Fluorous Glycosyl Donor

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

SCHEME 3.
Disaccharide Synthesis with Tagged Glycosyl Donor

*TLC solvent system: Benzene : Acetic acid : Methanol = 3 : 1 : 2, stained with H₂SO₄/EtOH

SCHEME 4.
Synthesis of Unprotected Trisaccharide

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