phosphomolybdic acid (PMA) in ethanol. Flash chromatography was performed on EM 230–400-mesh silica gel 60.

***B*-[2-(Trimethylsilyl)ethynyl]-9-borabicyclo[3.3.1]nonane (2).** To a solution of 3.5 mL (25.0 mmol) of (trimethylsilyl)-acetylene in THF (40 mL) at −78 °C was added 10.4 mL (26.0 mmol) of 2.5 N *n*-butyllithium in hexane dropwise over a 10-min period. The solution was stirred at −78 °C for an additional 15 min to ensure complete generation of the acetylenic anion before 25.0 mL (25.0 mmol) of a 1.0 M solution of *B*-methoxy-9-borabicyclo[3.3.1]nonane in hexane was added. The reaction mixture was stirred at −78 °C for 1.5 h. Boron trifluoride etherate (4.0 mL, 33 mmol) was then added, and the reaction mixture was stirred at −78 °C for an additional 15 min before being allowed to warm to room temperature. The volatiles were evaporated under vacuum to afford a white solid and 25 mL of pentane was added. The suspension was stirred for a few minutes and allowed to settle, and the supernatant liquid was carefully decanted via a double-ended needle to a second flask. The remaining solid was then washed with pentane (2 × 10 mL), and the extracts were combined. The pentane solution was then cooled to −78 °C to precipitate the product. The mother liquor was removed, and the crystals were dried (vacuum) to afford 6.52 g (90%) of *B*-[2-(trimethylsilyl)ethynyl]-9-borabicyclo[3.3.1]nonane·THF complex (**2**) as a white crystalline material (extremely hygroscopic): ^{11}B NMR (THF-d_8) δ −9.06 (s); ^{29}Si NMR (THF-d_8) δ −22.67 (s); ^{13}C NMR (THF-d_8) δ 103.5, 31.93, 26.19, 0.787; ^{1}H NMR (THF-d_8) δ 0.60 (s, −Si(CH_3)$_3$, 9 H), 1.29 (br, 2 H), 1.92 (m, 2 H), 2.11 (m, 4 H), 2.29 (m, 10 H), 4.14 (m, 4); IR (CCl_4) 2187 cm^{-1} (C≡C).

1-(Trimethylsilyl)-1-decyn-3-ol (5). The following procedure is representative. To the *B*-[2-(trimethylsilyl)ethynyl]-9-borabicyclo[3.3.1]nonane·THF complex (2.4 g, 8.3 mmol) in pentane (25 mL) at 25 °C was added 1-octanal (1.3 mL, 8.3 mmol). A slight yellow color immediately developed. After 40 min TLC revealed the disappearance of the starting aldehyde and the appearance of a new spot. The solvent was removed under positive nitrogen pressure, resulting in a yellow solid. To the solid was added ether (30 mL) and 336 μL (8.3 mmol) of methanol. The resulting solution was colled to 0 °C, and 0.5 mL (8.3 mmol) of ethanolamine was added dropwise. A white precipitate was instantly formed. The solution was stirred overnight to ensure complete cleavage of the borinate ester. The reaction mixture was then centrifuged and the clear supernatant liquid separated. The precipitate was washed with pentane (2 × 10 mL), and the phases were combined, washed with water (2 × 25 mL) and dried ($MgSO_4$). Concentration and purification of the resulting oil by flash chromatography on silica gel using hexane/ethyl acetate (19:1) afforded 1.71 g (91%) of **5** as a clear liquid: ^{1}H NMR ($CDCl_3$) δ 0.16 (s, −Si(CH_3)$_3$, 9 H), 1.13 (t, 3 H), 2.23–1.35 (m, 13 H), 4.25 (m, 1 H); IR (neat) 3550–3150 (br), 2967, 2925 (s), 2868, 2190, 1470, 1251 (s), 848 (vs) cm^{-1}.

5-Phenyl-1-(trimethylsilyl)-1-pentyn-3-ol (6). From 1.0 mL (7.6 mmol) of hydrocinnamaldehyde there was obtained, after purification by flash chromatography on silica gel using hexane/ethyl acetate (19:1), 1.57 g (89%) of **6** as a pale yellow liquid: ^{13}C NMR ($CDCl_3$) δ 141.2, 128.4, 128.3, 125.4, 106.6, 89.6, 61.9, 39.1, 31.3, −0.181; ^{1}H NMR ($CDCl_3$) δ 0.16 (s, −Si(CH_3)$_3$, 9 H), 2.00 (m, 2 H), 2.42 (br, −O*H*, 1 H), 2.78 (t, 2 H), 4.34 (t, 1 H), 7.26 (m, 5 H); IR (neat) 3600–3250 (br), 3027, 2960, 2945, 2865, 2188, 1495, 1455, 1253 (s), 1048, 848 (vs), 760, 701 cm^{-1}.

4,4-Dimethyl-1-(trimethylsilyl)-1-pentyn-3-ol (7). From 795 μL (7.3 mmol) of trimethylacetaldehyde there was obtained, after purification by flash chromatography on silica gel using hexane/ethyl acetate (19:1), 1.25 g (93%) of **7** as a clear liquid: ^{13}C NMR ($CDCl_3$) δ 105.6, 90.1, 71.7, 35.7, 25.2, −0.139; ^{1}H NMR ($CDCl_3$) δ 0.102 (s, −Si(CH_3)$_3$, 9 H), 0.919 (s, 9 H), 1.67 (s, −O*H*, 1 H), 3.92 (d, 1 H); IR (neat) 3600–3180 (br), 2975 (s), 2963, 2901, 2875, 2187, 1481, 1460, 1365, 1253 (s), 1065, 1008 (s), 882, 858 (s), 845 (vs), 712 cm^{-1}.

(3*S*,4*R*)-4-Methoxy-4-methyl-1-(trimethylsilyl)-1-octyn-3-ol (8) and (3*R*,4*R*)-4-Methoxy-4-methyl-1-(trimethylsilyl)-1-octyn-3-ol (9). From 1.06 g (7.3 mmol) of (2*R*)-2-methyl-2-methoxyhexanal there was obtained, after purification by flash chromatography on silica gel using hexane/ethyl acetate (19:1), 900 mg (51%) of **8** as a clear liquid: ^{13}C NMR ($CDCl_3$) δ 104.3, 90.7, 78.6, 67.5, 49.7, 33.7, 25.5, 23.3, 19.0, 13.9, −0.307; ^{1}H NMR ($CDCl_3$) δ 0.145 (s, −Si(CH_3)$_3$, 9 H), 0.895 (t, 3 H), 1.19 (s, 3 H), 1.30 (m, 4 H), 1.66 (m, 2 H), 2.48 (d, −O*H*, *J* = 5.0 Hz, 1 H), 3.24 (s, 3 H), 4.28 (d, *J* = 4.9 Hz, 1 H); IR (neat) 3600–3120 (br), 2958 (s), 2940, 2186, 1465, 1375, 1250 (s), 1069 (s), 845 (vs), 760 cm^{-1}.

A second product, **9** (180 mg, 10%), eluted as a clear liquid: ^{13}C NMR ($CDCl_3$) δ 103.6, 90.7, 79.5, 67.2, 49.7, 33.6, 24.9, 23.1, 17.6, 13.9, −0.298; ^{1}H NMR ($CDCl_3$) δ 0.146 (s, −Si(CH_3)$_3$, 9 H), 0.890 (t, 3 H), 1.22 (s, 3 H), 1.26 (m, 4 H), 2.47 (br, −O*H*, 1 H), 3.21 (s, 3 H) 4.33 (s, 1 H); IR (neat) 3600–3120 (br), 2960 (vs), 2941 (vs), 2871, 2186, 1465, 1375, 1251 (s), 1065, 1055, 845 (vs), 760 cm^{-1}.

1-[2-(Trimethylsilyl)-1-ethynyl]cyclohexanol (10). From 907 μL (9.0 mmol) of cyclohexanone there was obtained, after purification by flash chromatography on silica gel using hexane/ethyl acetate (19:1), 1.56 g (88%) of **10** as a white crystalline material, mp 72–73 °C: ^{13}C NMR ($CDCl_3$) δ 109.6, 88.4, 68.7, 39.9, 25.2, 23.3, −0.010; ^{1}H NMR ($CDCl_3$) δ 0.138 (s, −Si(CH_3)$_3$, 9 H), 1.21 (m, 2 H), 1.53 (m, 4 H), 1.65 (m, 2 H), 1.85 (m, 2 H), 2.05 (s, −O*H*, 1 H); IR (KBr) 3400–3250 (br), 2937 (s), 2902, 2861, 2166, 1450, 1348, 1285, 1251 (s), 1169, 1075 (s), 975 (s), 866 (vs), 840 (vs), 760, 699 cm^{-1}.

1-(Trimethylsilyl)-3-methyl-1-nonyn-3-ol (11). From 1.41 mL (9.0 mmol) of 2-octanone there was obtained, after purification by flash chromatography on silica gel using hexane/chloroform/methanol (20:5:1), 1.56 g (88%) of **11** as a pale yellow liquid: ^{13}C NMR ($CDCl_3$) δ 109.8, 87.2, 68.4, 43.5, 31.6, 29.7, 29.3, 24.5, 22.5, 14.0, −0.059; ^{1}H NMR ($CDCl_3$) δ 0.129 (s, −Si(CH_3)$_3$, 9 H), 0.862 (m, 3 H), 1.29 (m, 6 H), 1.43 (s, 3 H), 1.45 (m, 2 H), 1.60 (m, 2 H), 2.02 (br, −O*H*, 1 H); IR (neat) 3550–3220 (br), 2975 (s), 2941 (s), 2865, 2179, 1470, 1258 (s), 939, 865 (s), 845 (vs), 765 cm^{-1}.

(3*R*,4*R*)-4-Methoxy-4-methyl-1-octyn-3-ol (12). A solution of 40 mg (0.17 mmol) of **9** in 1.4 mL (1.4 mmol) of a 1.0 M solution of tetrabutylammonium fluoride in THF was stirred at rt for 3 h. The reaction was diluted with 5 mL of water and extracted with ethyl acetate (3 × 5 mL), and the organic layer was dried ($MgSO_4$). Concentration and purification of the resulting oil by flash chromatography on silica gel using hexane/ethyl acetate (19:1) afforded 21 mg (75%) of **12** as an oil: ^{13}C NMR ($CDCl_3$) δ 82.2, 79.3, 74.1, 66.9, 49.8, 33.6, 25.2, 23.2, 17.8, 14.0.

Registry No. **2**, 140149-83-3; **5**, 140149-76-4; **6**, 140149-77-5; **7**, 71321-14-7; **8**, 140149-78-6; **9**, 140149-79-7; **10**, 17962-22-0; **11**, 140149-80-0; **12**, 140149-81-1; (trimethylsilyl)acetylene, 1066-54-2; *B*-methoxy-9-borabicyclo[3.3.1]nonane, 38050-71-4; 1-octanal, 124-13-0; hydrocinnamaldehyde, 104-53-0; trimethylacetaldehyde, 630-19-3; (2*R*)-2-methyl-2-methoxyhexanal, 140149-82-2; cyclohexanone, 108-94-1; 2-octanone, 111-13-7.

Supplementary Material Available: IR and ^{1}H and ^{13}C NMR spectra of the (trimethylsilyl)ethynyl alcohols reported in this study (22 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Efficient Chemical Synthesis of GDP-fucose

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Sugar nucleotide-dependent glycosyltransferases are a class of enzymes with great potential for oligosaccharide synthesis. Several preparative-scale syntheses of saccharides have been demonstrated based on glycosyltransferases with in situ regeneration of sugar nucleotides.[1] As part of our interest in the field of enzymatic oligo-

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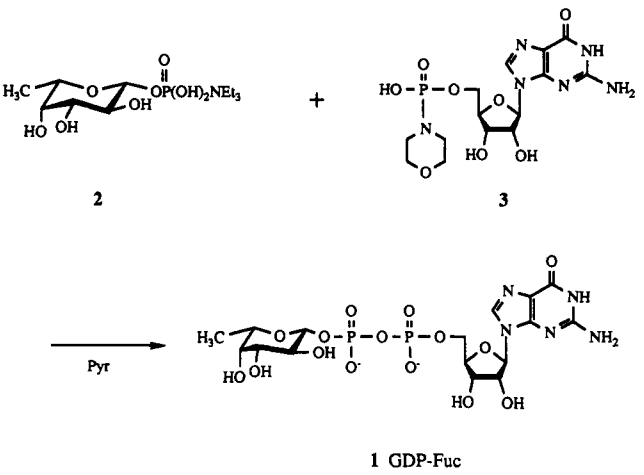
Scheme I. Preparation of GDP-Fuc



2 3

1 GDP-Fuc

saccharide synthesis, we here report two efficient procedures for the synthesis of guanosine 5′-diphospho-β-L-fucose (GDP-Fuc, 1)—a donor substrate for fucosyltransferases.[2]

Unlike other sugar nucleotides, the enzymatic preparation[3-5] of GDP-fucose has not been established on a large scale, and as such, several groups[6-8] have reported the chemical synthesis of this novel sugar nucleotide. The most common synthesis of GDP-Fuc relies on the coupling of fucose 1-phosphate (Fuc-1-P) (2) and an activated guanosine 5′-monophosphate (GMP) such as GMP-morpholidate (3)[9] (Scheme I). Since Fuc-1-P is relatively unstable compared to other glycosyl 1-phosphates, it is difficult to control the stereochemistry during the introduction of the phosphate group.[10]

We used two different procedures for the synthesis of Fuc-1-P: one started with benzoylated fucosyl bromide 6 and dibenzyl phosphate or tetrabutylammonium dihydrogen phosphate (Scheme II) and and the other involved the use of a trivalent phosphitylating reagent on a suitably protected fucose derivative 9 (Scheme II).

Employing benzoyl group instead of acetyl for the protection of the hydroxyl groups of fucose was expected to stabilize the fucose derivative and improve the stereoselectivity of the glycosylation reaction. In fact, the glycosylation of 6 with dibenzyl phosphate in the presence of silver carbonate[11] proceeded very smoothly and gave a glycosyl phosphate derivative[12] 7 in 95% yield as a sole product. As expected, 7 was stable enough ($t_{1/2}$ > 3 H) to be purified on silica gel chromatography compared to the corresponding acetyl derivative 11 ($t_{1/2}$ < 10 min).[7] When the purified 7 was left overnight at room temperature, some decomposition and anomerization were observed. On the other hand, the unpurified 7 was stable enough to store for 1 week at room temperature. It should be noted that the purified 7 was used for the next step immediately. Deprotection of the benzyl and the benzoyl groups from 7 was performed in accord with the reported procedure[7] to give 2 in 82% yield. A direct phosphorylation of 6 with tetrabutylammonium dihydrogen phosphate followed by deprotection gave 2 with some contamination of the α anomer.

The second method involves the use of a very effective trivalent phosphitylating reagent, dibenzyl *N,N*-diethylphosphoroamidite (DDP).[13,14] Readily available 2,3,4-tri-*O*-acetyl-L-fucose (9) from 8 either chemically[15] or enzymatically[16] was phosphitylated with DDP in the presence of triazole. It is worth noting that this phosphitylating reaction of an anomeric mixture (α:β = 1:1) of 9 gave a thermodynamically unstable β-phosphitylated L-fucose (10) as a major product (α:β = 1:10). Compound 10 was purified by silica gel chromatography and oxidized by hydrogen peroxide to give the unstable glycosyl phosphate 11. Deprotection of 11 was carried out in a similar manner as that of 7 to give 2 as a mixture (α:β = 1:10) in 78% yield.

The coupling reaction of anomerically pure fucose 1-phosphate (2) and GMP-morpholidate (3) was carried out according to the literature procedure[6,7] to give GDP-Fuc. We found that during the column purification of GDP-Fuc elution with NH_4HCO_3 would not cause the decomposition of GDP-Fuc as reported previously[7] with the use of LiCl.

In summary, the methods demonstrated here provide new routes to fucose 1-phosphate. The use of benzoyl protecting groups improve the stability and stereoselectivity during the synthesis. The phosphitylating reagent is easily prepared[13] and can be stored for a long period of time. It should be applicable to the synthesis of other sugar 1-phosphates on large scales. The synthesized GDP-Fuc has been used for the enzymatic synthesis of fucosylated oligosaccharides.[17]

Experimental Section

Dibenzylphosphoryl 2,3,4-Tri-*O*-benzoyl-β-L-fucopyranoside (7). Benzoyl chloride (21.4 g, 152.3 mmol; 17.7 mL) was added dropwise to a cooled solution of L-fucose (4) (5.0 g, 30.5

(1) (a) Wong, C.-H.; Haynie, S. L.; Whitesides, G. M. *J. Org. Chem.* **1982**, *47*, 5416. (b) Auge, C.; Mathieu, C.; Merienne, C. *Carbohydr. Res.* **1986**, *151*, 147. (c) Ichikawa, Y.; Shen, G.-J.; Wong, C.-H. *J. Am. Chem. Soc.* **1991**, *113*, 4698. (d) Ichikawa, Y.; Liu, J. L.-C.; Shen, G.-J.; Wong, C.-H. *J. Am. Chem. Soc.* **1991**, *113*, 6300. (e) Gygax, D.; Spies, P.; Winkler, T.; Pfaar, V. *Tetrahedron* **1991**, *47*, 5119.

(2) Beyer, A. T.; Sadler, J. E.; Rearick, J. I.; Paulson, J. C.; Hill, H. L. *Adv. Enzymol.* **1981**, *52*, 24.

(3) (a) Ginsburg, V. *J. Biol. Chem.* **1960**, *235*, 2196. (b) Yamamoto, K.; Maruyama, T.; Kumagai, H.; Tochikura, T.; Seno, T. *Agric. Biol. Chem.* **1984**, *48*, 823.

(4) (a) Ishihara, H.; Massaro, D. J.; Heath, E. C. *J. Biol. Chem.* **1968**, *243*, 1103. (b) Ishihara, H.; Heath, E. C. *J. Biol. Chem.* **1968**, *243*, 1110. (c) Schachter, H.; Ishihara, H.; Heath, E. C. *Methods Enzymol.* **1972**, *28*, 285. (d) Richard, W. L.; Serif, G. S. *Biochim. Biophys. Acta* **1977**, *484*, 353. (e) Kilker, R. D.; Shuey, D. K.; Serif, G. S. *Biochim. Biophys. Acta* **1979**, *570*, 271. (f) Butler, W.; Serif, G. S. *Biochim. Biophys. Acta* **1985**, *829*, 238.

(5) Stangier, P.; Thiem, *J. Enzymes in Carbohydrate Synthesis*; Bednarski, M. D., Simon, E. S., Eds.; ACS Symposium Series 466; American Chemical Society: Washington, DC, 1991; p 63. For other chemical and enzymatic syntheses of sugar nucleotides see: Toone, E. J.; Simon, E. S.; Whitesides, G. M. *J. Org. Chem.* **1991**, *56*, 5603 and references cited therein.

(6) Nunez, H. A.; O'Connor, J. V.; Rosevear, P. R.; Barker, R. *Can. J. Chem.* **1981**, *59*, 2086.

(7) Gokhale, V. B.; Hindsgaul, O.; Palcic, M. M. *Can. J. Chem.* **1990**, *68*, 1063.

(8) Schimidt, R. R.; Wegmann, B.; Jung, K.-H. *Liebigs Ann. Chem.* **1991**, *191*, 121.

(9) (a) Kochetkov, N. K.; Shibaev, V. N. *Adv. Carbohydr. Chem. Biochem.* **1973**, *28*, 307. (b) Moffat, J. G. *Methods Enzymol.* **1966**, *8*, 136. (c) Roseman, S.; Distler, J. J.; Moffat, J. G.; Khorana, H. G. *J. Am. Chem. Soc.* **1961**, *83*, 659.

(10) Pale, P.; Whitesides, G. M. *J. Org. Chem.* **1991**, *56*, 4547.

(11) Linshort, T. K.; Thiem, J. *Carbohydr. Res.* **1991**, *209*, 119.

(12) Very recently, another GDP-fucose synthesis was reported. Veeneman, G. H.; Broxterman, H. J. G.; van der Marel, G. A.; van Boom, J. H. *Tetrahedron Lett.* **1991**, *32*, 6175.

(13) Pederson, R. L.; Esker, J.; Wong, C.-H. *Tetrahedron* **1991**, *47*, 2643. DDP was described previously but not characterized: de Bont, H. B. A.; Veeneman, G. H.; van Boom, J. H.; Liskamp, R. M. J. *Recl. Trav. Chim. Pays-Bas* **1987**, *106*, 641; Houben Weyl, *Methoden der Organischen Chemie*, Georg Thieme Verlag: Stuttgart, 1964; Vol. 12/2, p 96.

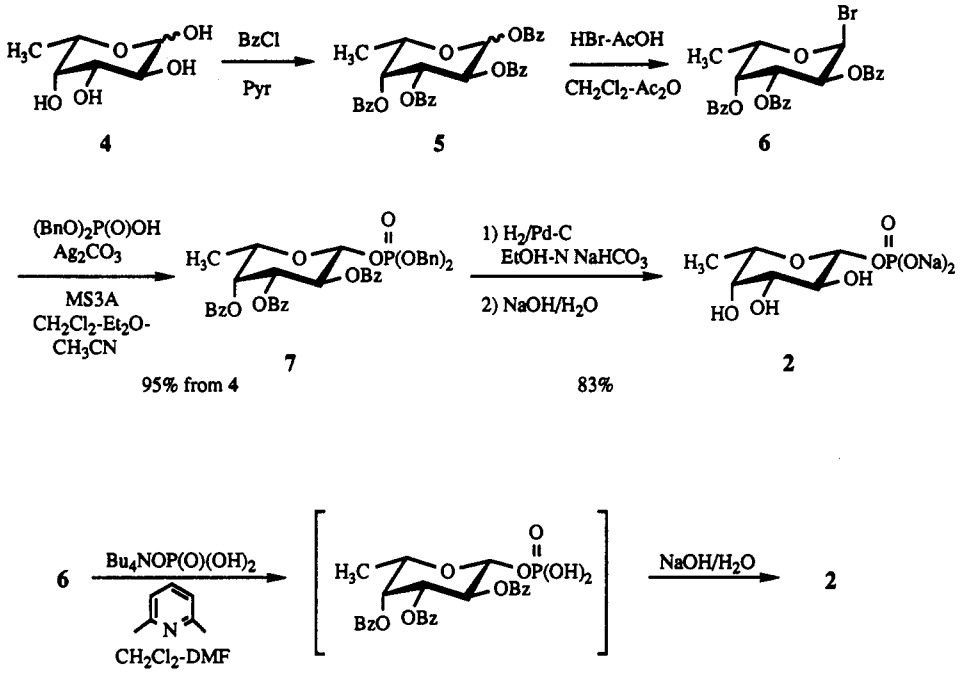
(14) Another trivalent phosphorylating reagent used for the synthesis of α-fucosyl 1-phosphate: Westerduin, P.; Veeneman, G. H.; Marugg, J. E.; van der Marel, G. A.; van Boom, J. H. *Tetrahedron Lett.* **1986**, *27*, 1211.

(15) Helferich, B.; Portz, W. *Chem. Ber.* **1953**, *86*, 604.

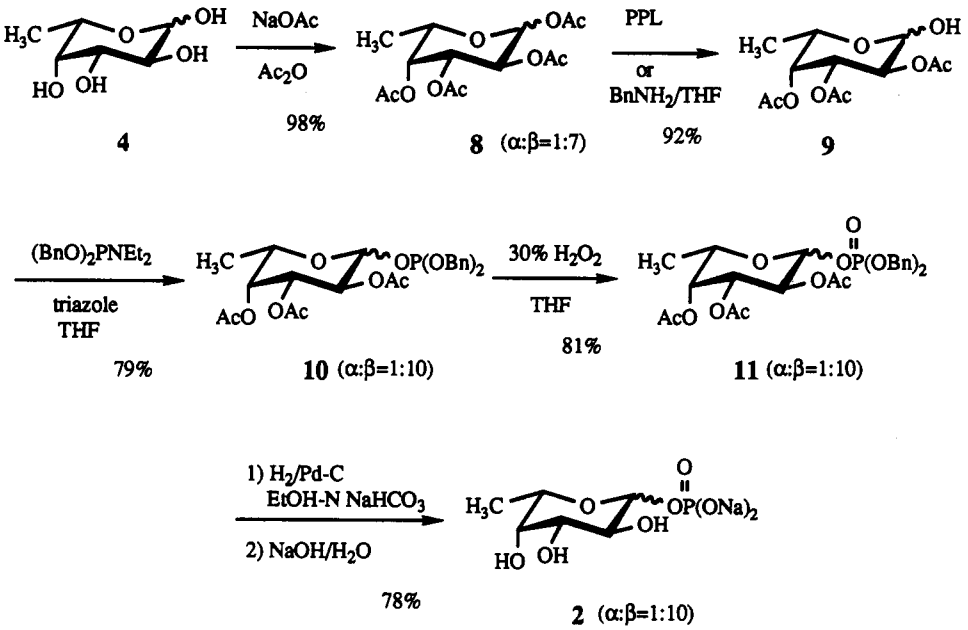
(16) Hennen, W. J.; Sweers, H. M.; Wang, Y.-F.; Wong, C.-H. *J. Org. Chem.* **1988**, *53*, 4943.

(17) Dumas, D. P.; Ichikawa, Y.; Wong, C.-H.; Lowe, J. B.; Nair, R. P. *BioMed. Chem. Lett.* **1991**, *1*, 425.

Scheme II. Fuc-1-P Preparation Using Glycosylation Reaction



Scheme III. Fuc-1-P Preparation Using Trivalent Phosphitylating Reagent



mmol) in pyridine (100 mL) at 0–5 °C, and the mixture was stirred for 3 h at room temperature. The mixture was poured onto ice–water and extracted with EtOAc. The extracts were successively washed with ice-cold dilute HCl, aqueous $NaHCO_3$, and brine, dried over anhydrous $MgSO_4$, and concentrated to give 1,2,3,4-tetra-*O*-benzoyl-L-fucopyranose (**5**). This was used for the next step without further purification.

To a cooled solution of **5** (2.0 g, 3.44 mmol) in CH_2Cl_2 (20 mL) and Ac_2O (2 mL) was added dropwise 30% HBr–AcOH (8 mL) at 0–5 °C, and the mixture was stirred for 2 h at room temperature. The mixture was poured onto ice–water and extracted with EtOAc. The extracts were successively washed with water, aqueous $NaHCO_3$, and brine, dried over anhydrous $MgSO_4$, and concentrated to give 2,3,4-tri-*O*-benzoyl-α-L-fucopyranosyl bromide (**6**). This was used for the next step without further purification: ^1H NMR ($CDCl_3$) δ 1.36 (3 H, d, *J* 6.51 Hz, 6-CH_3), 4.69 (1 H, br q, *J* 6.56 Hz, H-5), 5.62 (1 H, dd, *J* 3.91, 10.5 Hz, H-2), 5.84 (1 H, dd, *J* 0.97, 3.33 Hz, H-4), 6.01 (1 H, dd, *J* 3.36, 10.50 Hz, H-3), 6.94 (1 H, d, *J* 3.92 Hz, H-1); ^{13}C NMR ($CDCl_3$) δ 15.8, 68.8, 69.2, 70.4, 70.8, 89.4, 165.4, 165.6, 165.7.

Ag_2CO_3 (1.90 g, 6.89 mmol) was added in one portion to a cooled mixture of **6**, dibenzyl phosphate (2.88 g, 10.3 mmol), and MS 3A (6 g) in CH_2Cl_2–Et_2O–CH_3CN[11] (20 mL each) in a round-bottom flask lapped with aluminum foil to shut out light. The mixture was stirred for 10 h at room temperature and filtered through Celite, and the filtrate was concentrated. The residue was chromatographed on silica gel, with toluene–EtOAc (2.5:1), to give **7** (2.4 g, 95%) as a single product: ^1H NMR ($CDCl_3$) δ 1.35 (1 H, d, *J* 6.35 Hz, 6-CH_3), 4.225 (1 H, br dt, *J* 5.71, 6.70 Hz, H-5), 4.77 (1 H, dd, *J* 7.07, 11.65 Hz, benzylic), 4.86 (1 H, dd, *J* 6.50, 1.63 Hz, benzylic), 5.11 (1 H, dd, *J* 7.51, 11.71 Hz, benzylic), 5.14 (1 H, dd, *J* 7.27, 11.70 Hz, benzylic), 5.58 (1 H, dd, *J* 3.48, 10.44 Hz, H-3), 5.69 (1 H, dd, *J* 7.37, 7.89 Hz, H-1), 5.76 (1 H, dd, 0.88, 3.44 Hz, H-4), 5.90 (1 H, dd, *J* 8.03, 10.45 Hz, H-2); ^{13}C NMR ($CDCl_3$) δ 16.12, 69.31, 69.35, 69.54, 69.58, 69.64, 69.70, 70.57, 70.83, 71.70, 96.97, 97.00, 127.28, 129.06, 129.67, 129.72, 129.77, 129.93, 133.27, 133.41, 133.51, 165.24, 165.45, 165.79; HRMS calcd for $C_{41}H_{37}O_{11}PCs$ (M + Cs^+) 869.1128, found 869.1138.

β-L-Fucose 1-Phosphate (2). Compound **7** (2.32 g, 3.15 mmol) was hydrogenated over 5% Pd/C (400 mg) in EtOH (60 mL) and

1 N $NaHCO_3$ (15 mL) under a hydrogen atmosphere for 10 h at room temperature. The catalyst was filtered off through Celite, and the filtrate was concentrated. To a cooled mixture of the residue in water (20 mL) was added dropwise 1 N NaOH (20 mL) at 0–5 °C, and the mixture was stirred for 3 h at room temperature. The mixture was carefully neutralized by the addition of cold 1 N AcOH to pH 7.5, and the insoluble material was filtered off with Celite. The filtrate was diluted to 250 mL, applied to a column of Dowex 1-X8 [HCO_2^-] (2 × 15 cm), and eluted with stepwise gradient of NH_4HCO_3, water (200 mL), 0.1 M NH_4HCO_3 (200 mL), 0.2 M NH_4HCO_3 (200 mL), and 0.3 M NH_4HCO_3 (200 mL). A trace amount of fucose was eluted out with water, and the desired **2** was eluted out between 0.2–0.3 M NH_4HCO_3. After removal of salt (NH_4HCO_3) by addition of Dowex 50W-X8 [H^+] into a solution of the residue, the resin was filtered off, and the filtrate was passed through a column of Dowex 50W-X8 [Na^+] (1 × 15 cm) with water. The appropriate fractions were pooled and lyophilized to give **2** (700 mg, 83%) concomitant with a small amount of NH_4HCO_3. The ^1H and ^{13}C NMR spectra were in good agreement with those reported.[6]

Preparation of 2 from 6 via Reaction of Tetrabutylammonium Dihydrogen Phosphate. A solution of tetrabutylammonium dihydrogen phosphate (1.29 g, 3.79 mmol) and 2,6-lutidine (814 mg, 7.6 mmol; 885 μL) in CH_2Cl_2 (5 mL) was added in one portion to a cooled solution of **6** (freshly prepared from **5** (2.0 g, 3.4 mmol) with HBr–AcOH (10 mL) in CH_2Cl_2 (30 mL) and Ac_2O (1 mL)) in CH_2Cl_2 (30 mL) at 0–5 °C, and the reaction mixture was stirred for 5 min at room temperature then cooled with an ice bath to 0–5 °C. To the cooled mixture was added water (20 mL) and 1 M NaOH (20 mL), and the reaction mixture was stirred for 5 h at room temperature. The mixture was neutralized with cold 1 M AcOH to pH 7.5. The organic phase was separated with a separatory funnel, and the aqueous layer contained fucose 1-phosphate. The products were purified as described for the preparation of **2** from **7** to give **2** in ~40% yield ($\alpha:\beta$ = 1:1 judged by ^1H NMR spectrum).

2,3,4-Tri-*O*-acetyl-L-fucose (9). A mixture of L-fucose (**4**) (3.0 g, 18.2 mmol) and anhydrous NaOAc (50 mg, 0.61 mmol) in Ac_2O (20 mL) was stirred for 2 h at room temperature and then heated for 2 h at 100 °C. After being cooled, the mixture was poured onto ice–water, stirred for 2 h, and extracted with $CHCl_3$. The extracts were successively washed with water, aqueous $NaHCO_3$, and water, dried over anhydrous $MgSO_4$, and concentrated. The residual syrup was chromatographed on silica gel, with toluene–EtOAc (10:1), to give 1,2,3,4-tetra-*O*-acetyl-L-fucose (**8**) (5.92 g, 98%) as a mixture of α and β (1:7 judged by ^1H NMR spectrum) anomers, H-1β 5.68 (8.29 Hz), H-1α 6.36 (2.19 Hz).

Chemical Method. A solution of **8** (3.0 g, 9.0 mmol) and $BnNH_2$[14] (1.45 g, 13.5 mmol; 1.47 mL) in THF (35 mL) was stirred for 1 day at room temperature. The mixture was diluted with $CHCl_3$ and successively washed with ice-cold dilute HCl, aqueous $NaHCO_3$, and water, dried over anhydrous $MgSO_4$, and concentrated. The residual syrup was chromatographed on silica gel, with toluene–EtOAc (1:1), to give **9** (2.40 g, 92%). Its ^1H NMR spectral data was in good agreement with that reported.[16]

Enzymatic Method.[16] A suspension of **8** (2.5 g, 7.5 mmol) and lipase (5.6 g) in 13% (v/v) DMF/phosphate buffer (50 mM, pH 7) was stirred for 5 days at room temperature, at which time the pH was adjusted by the addition of 1 N NaOH. The mixture was filtered, and the filtrate was extracted with EtOAc. The extracts were washed with water, dried over anhydrous $MgSO_4$, and concentrated. The residual syrup was chromatographed on silica gel, with toluene–EtOAc (1:1), to give **9** (1.1 g, 48%) as a mixture of α and β (1:1 judged by ^1H NMR) anomers. The yield could be higher as the reaction was incomplete and the byproduct obtained was mainly the unreacted starting material.

Dibenzylphosphoryl 2,3,4-Tri-*O*-acetyl-L-fucoside (11). Dibenzyl *N,N*-diethylphosphoamidate[12] (2.7 g, 8.5 mmol) was added dropwise to a solution of **9** (1.0 g, 3.4 mmol) and 1,2,4,-triazole (1.0 g, 14.5 mmol) in THF (50 mL) under nitrogen atmosphere, and the mixture was stirred for 1 h at room temperature. Ether (50 mL) was added to the mixture, and the organic phase was successively washed with ice-cold dilute HCl, aqueous $NaHCO_3$, and water, dried over anhydrous $MgSO_4$, and concentrated. The residual syrup was chromatographed on silica gel, with hexane–EtOAc (4:1), to give **10** (1.43 g, 79%) as a mixture of α and β (1:10) anomers. β anomer: ^1H NMR ($CDCl_3$) δ 1.22 (3 H, d, *J* 6.50 Hz, 6-CH_3), 1.91, 1.99, 2.19 (3 H each, s, 3 × OAc), 3.85 (1 H, dq, *J* 1.00, 6.50 Hz, H-5), 4.82–4.96 (4 H, m, benzylic protons), 5.02–5.08 (2 H, m, H-2,3), 5.25 (1 H, dd, *J* 0.50, 3.50 Hz, H-4), 5.32 (1 H, dd, *J* 8.00, 10.50 Hz, H-1); H-1 for α anomer δ 5.82 (dd, *J* = 4.83, 8.62 Hz).

To a cooled solution of **10** (500 mg, 0.9 mmol) in THF (50 mL) was added 30% H_2O_2 (7 mL) in one portion, and the mixture was allowed to warm to room temperature and stirred for 1.5 h at room temperature. The mixture was diluted with ether and washed with ice-cold aqueous $Na_2S_2O_3$, aqueous $NaHCO_3$, and water, dried over anhydrous $MgSO_4$, and concentrated to give **11** (420 mg, 81%) as a mixture of α and β (1:10) anomers. This was used for the next step without further purification. The ^1H NMR spectrum of the β anomer was in good agreement with that reported:[8] ^1H NMR ($CDCl_3$) δ 1.22 (3 H, d, *J* 7.5 Hz, 6-CH_3), 1.91, 1.99, 2.19 (3 H each, s, 3 × OAc), 3.90 (1 H, dq, *J* 6.50, 7.50 Hz, H-5), 5.00–5.03 (m, H-3, benzylic), 5.03–5.12 (m, benzylic), 5.26 (1 H, dd, *J* 1.00, 3.50 Hz, H-4), 5.27–5.33 (2 H, m, H-1,2); H-1 for α anomer δ 5.93 (dd, *J* = 3.68, 5.51 Hz); HRMS calcd for $C_{26}H_{31}O_{11}PCs$ (M + Cs^+) 683.0658, found 683.0658.

L-Fucose 1-Phosphate (2). Compound **11** (5.0 g, 9.1 mmol) was treated in the same manner as that for the preparation of **2** from **7** to give **2** (2.61 g) as a mixture of α and β anomers with some contamination of NH_4HCO_3 (78% yield) (1:10 judged by ^1H NMR, H-1α 5.33 (q); H-1β 4.86 (t). The ^1H and ^{13}C NMR data of the β anomer were in good agreement with those reported.[6]

GDP-fucose (1). GDP-Fuc was prepared following the procedure of Gokhale et al.[7] with some modifications. Anomerically pure compound **2** was first converted to its triethylammonium salt by passing through a column of Dowex 50W-X-8 [Et_3NH^+] form with water and lyophilized.[7] The lyophilized L-fucose 1-phosphate triethylammonium salt (300 mg, 0.83 mmol) and guanosine 5′-monophosphomorphalidate (600 mg, 0.83 mmol) were separately dried by coevaporating with pyridine twice. They were then combined in pyridine (20 mL), and the mixture was stirred for 5 days at room temperature and concentrated. The residual syrup was diluted to 50 mL with water and applied to a column of Dowex 1-X8 [HCO_2^-] (3 × 25 cm) and eluted with a gradient of NH_4HCO_3 (0–1 M NH_4HCO_3). The GDP-Fuc-containing fractions were pooled and lyophilized, and the product was further purified with a column of Sephadex G-25 (superfine) (3 × 65 cm) twice with water. The appropriate fractions were pooled and lyophilized. A solution of the lyophilized product in water was passed through a column of Dowex 50 W-X8 [Na^+] form with water. The fractions were pooled and lyophilized to give **1** (~300 mg) concomitant with a small amount of GMP (judged by ^1H NMR). The ^1H NMR spectral data were in good agreement with those reported.[6,7]

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Supplementary Material Available: ^1H-NMR spectra of compounds **2**, **7** and **11** (3 pages). Ordering information is given on any current masthead page.

Electrolytic Reactions of Fluoro Organic Compounds. 11.[1] Anodic Preparation and Synthetic Applications of β-Trifluoromethylated *O,S*-Acetals

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Introduction

Fluoro organic compounds, particularly partially fluorinated compounds, have attracted much interest in many

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