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Note

Synthesis of 2-chloro-4-nitrophenyl α-L-fucopyranoside: a substrate for α-L-fucosidase (AFU)

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Abstract

An effective method to prepare the substrate of α-L-fucosidase (AFU) is described. Ethyl 1-thiofucoside with a free 2-OH group was used as the glycosyl donor, and there was found no self-condensed side product. The use of the HF·pyridine reagent to remove the silyl protecting group in the last step afforded a target molecule of high purity.

Keywords: α-L-Fucosidase; Hepatocellular carcinoma; Glycosylation

Glycosidases are involved in the metabolism of a wide range of biologically essential oligo- and polysaccharides.[1] What attracts chemists is how to control the biological processes of the glycosidases through suitable substrates or potent inhibitors.[2] α-L-Fucosidase (AFU), which is one type of hydrolyase, is found widely distributed in many organisms. Recent research has demonstrated that AFU in blood serum plays an important role in diagnosing hepatocellular carcinoma (HCC).[3–6] In 1992, Kasai and coworkers first reported the synthesis of 2-chloro-4-nitrophenyl α-L-fucopyranoside (NCP α-L-fucopyranoside) as a substrate for AFU.[7] In a collaborative project, we needed to prepare pure NCP α-L-fucopyranoside for enzyme kinetic studies. When we tried the above-mentioned method for the making of NCP α-L-fucopyranoside, we found that it was technically challenging, and we got only a moderate yield of an α,β mixture of product, with the α anomer predominating. This prompted us to look for a new way to synthesize the target compound efficiently. We present herein a method to prepare NCP α-L-fucopyranoside in good overall yield and with complete stereoselectivity.

The synthetic route is as shown in Scheme 1. As known, an α-glycosidic bond is best formed using a glycosyl donor with a nonparticipating group on C-2.[8] Following this idea, fully benzylated 1-thiofucopyranoside **1**[9] and commercially available 2-chloro-4-nitrophenol was condensed in anhydrous CH_2Cl_2 in the presence of TMSOTf to afford 2-chloro-4-nitrophenyl 2,3,4-tri-*O*-benzyl-α-L-fucopyranoside (**2**) in 71% yield. However, hydrogenation of compound **2** with 20% $Pd(OH)_2$-on-charcoal under an H_2 atmosphere (1 atm) for 10 h, yielded 2-chloro-4-aminophenyl 2,3,4-tri-*O*-benzyl-α-L-fucopyranoside (**3**, 77%), based on MALDITOF-MS and ^{1}H NMR spectral analysis. We found no debenzylated product under these hydrogenation conditions. ^{1}H NMR spectra of compounds **2** and **3** showed that the chemical shifts of the aromatic protons moved from downfield (δ 8.29, 8.08, 7.30) to upfield (δ 6.99, 6.48, 6.72, respectively). We then turned our attention to the silyl-protected fucopyranosyl donors. Silylation of ethyl 1-thio-β-L-fucopyranoside with *tert*-

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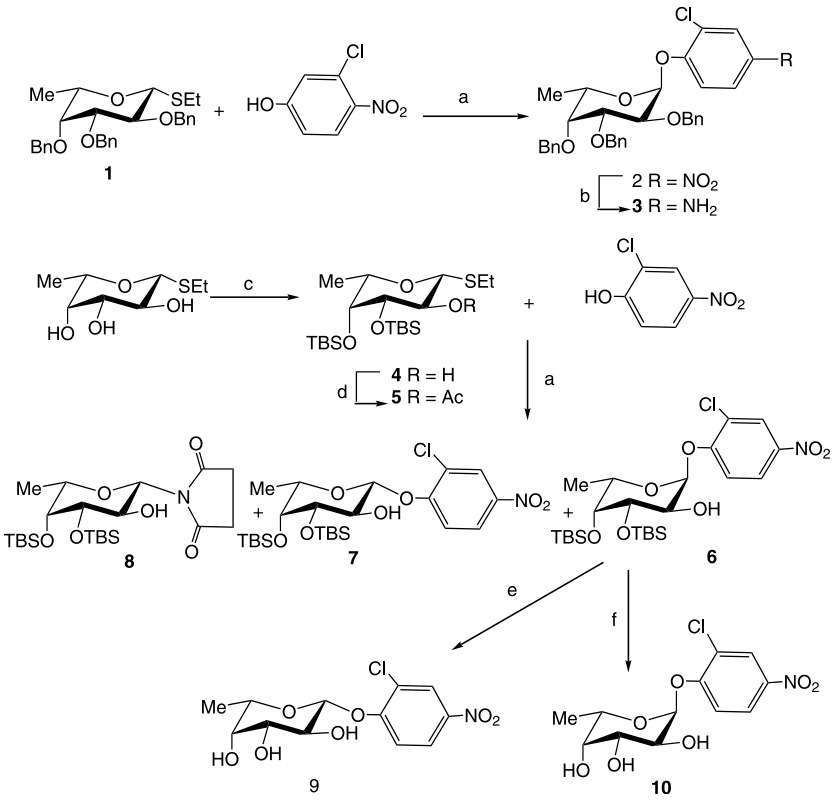

Scheme 1. Reagents and conditions: (a) NIS, TMSOTf, CH_2Cl_2; 71% for **2**; 61% for **6**; 8% for **7**; 26% for **8**; (b) H_2, $Pd(OH)_2$/C, MeOH–EtOAc; 77% for **3**; (c) TBDMSCl, imidazol, DMF, 78% for **4**; (d) Ac_2O, Py; 20% for **5**; (e) TBAF, THF; 73% for **9**; (f) HF·pyridine, CH_3CN; 68% from **10**.

butylchlorodimethylsilane (TBSCl, 3.0 equiv) and imidazole (6.0 equiv) in dry DMF surprisingly afforded 3,4-di-*O*-disilylated thiofucopyranoside (**4**). The correct position of the TBSs on **4** was further confirmed by a downfield shift of H-2 (δ 5.34 ppm, J 9.4 Hz) in the ^{1}H NMR spectra of its acetylated derivative **5**. It should be noted that the complete acetylation of compound **4**, even with acetic anhydride in pyridine in the presence of DMAP, was very difficult. Only about 20% of **4** was converted to **5** at 60 °C for 20 h. We ascribed this to the steric hindrance to OH-2 caused by adjacent β-thioethyl and bulky TBS groups. Although we could not gain a fully silylated donor,[10] we thought that compound **4** might be a good donor extended from our former project on 1,2-anhydrosugars.[11] Coupling of disilylated 1-thiofucopyranoside **4** and 2-chloro-4-nitrophenol in anhydrous CH_2Cl_2 with 1.1 equiv of NIS and a catalytic amount of TMSOTf (5% equiv) under standard glycosylation conditions afforded 2-chloro-4-nitrophenyl 3,4-di-*O*-*tert*-butyldimethylsilyl-α-L-fucopyranoside (**6**) as the major component (61% of isolated yield), accompanied with 8% of isomer 2-chloro-4-nitrophenyl 3,4-di-*O*-*tert*-butyldimethylsilyl-β-L-fucopyranoside (**7**) and 26% of *N*-(3,4-di-*O*-*tert*-butyldimethylsilyl-β-L-fucopyranosyl)succinimide (**8**). Chemical shifts of H-1s (δ 5.52, J 2.6 Hz of **6**; δ 5.05, J 7.3 Hz of **7**) in the ^{1}H NMR spectra confirmed the structure assignments. As for byproduct **8**, we rationalized that it was generated from the condensation of intermediates, i.e., 1,2-anhydro-3,4-di-*O*-*tert*-butyldimethylsilyl-α-L-fucopyranose and deiodinated NIS. Removal of TBS from compound **6** with TBAF in THF afforded 2-chloro-4-nitrophenyl β-L-fucopyranoside (**9**) in a high yield. The chemical shift of H-1 for **9** appears at δ 4.80 in the ^{1}H NMR spectrum ($J_{1,2}$ 7.6 Hz), which confirms β-bond formation. HCl (gas, 3% w/v), AcOH and $BF_3 \cdot Et_2O$ were also tried, but none of these reagents gave satisfactory results. Finally, the HF·pyridine complex[12] was found to be the best neutral reagent to thoroughly deprotect TBS from **9** to smoothly give the desired 2-chloro-4-nitrophenyl α-L-fucopyranoside (**10**, 68%). The α-linkage shown in the ^{1}H NMR spectrum (δ 5.71 ppm, J 3.1 Hz, H-1) and the MALDITOF-MS ($[M+Na]^+$: 342.3) of compound **10** confirmed the correct structure of the target molecule.

In summary, we have described a method for preparing of pure AFU substrate, 2-chloro-4-nitrophenyl α-L-fucopyranoside, using a partially silylated 1-thiofucopyranoside as donor. The HF·pyridine complex was shown to be the best reagent to remove TBS-protecting groups in this case. Large-scale preparation of compound **10** can be performed by this method.

1. Experimental

1.1. General methods

Optical rotations were determined at 20 °C with a Perkin–Elmer Model 241-Mc automatic polarimeter. ^{1}H and ^{13}C NMR spectra were recorded with ARX 400 spectrometers for solutions in $CDCl_3$. Chemical shifts are given in δ-units (ppm) downfield from internal Me_4Si. Mass spectra were measured using MALTITOF-MS with dihydroxybenzoic acid (DHB) as matrix. Thin-layer chromatography (TLC) was performed on silica gel HF_{254} with detection by charring with 30% (v/v) H_2SO_4 in MeOH or in some cases by a UV lamp.

1.2. 2-Chloro-4-nitrophenyl 2,3,4-tri-*O*-benzyl-α-L-fucopyranoside (2)

To a solution of compound **1** (500 mg, 1.05 mmol) and 2-chloro-4-nitrophenol (200 mg, 1.16 mmol) in anhyd CH_2Cl_2 (3 mL) was added NIS (260 mg, 1.16 mmol) and TMSOTf (10 μL, 0.05 mmol) under an N_2 atmosphere at −42 °C. The mixture was stirred for 30 min under these conditions, neutralized with Et_3N, and concentrated. The residue was subjected to a silica gel column with 10:1 petroleum ether–EtOAc as the eluent to afford syrupy **2** (439 mg, 71%): $[\alpha]_D^{20}$ +113° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.23 (d, 3 H, $J_{5,6}$ 6.5 Hz, H-6), 3.67–3.73 (m, 1 H, H-5), 4.11–4.17 (m, 2 H, H-3, H-4), 4.41–4.47 (m, 3 H, H-2, PhCH_2), 4.45 (d, 1 H, *J* 11.6 Hz, one proton of PhCH_2), 4.61–4.69 (m, 3 H, three protons of PhCH_2), 5.70 (d, 1 H, $J_{1,2}$ 1.3 Hz, H-1), 7.23–7.35 (m, 16 H, *Ph* and *Ar*), 8.08 (dd, 1 H, *J* 2.7, 9.2 Hz, *Ar*), 8.29 (d, 1 H, *J* 2.7 Hz, *Ar*). Anal. Calcd for $C_{33}H_{32}ClNO_7$: C, 67.17; H, 5.47. Found: C, 67.42; H, 5.39.

1.3. 2-Chloro-4-aminophenyl 2,3,4-tri-*O*-benzyl-α-L-fucopyranoside (3)

To a solution of compound **2** (415 mg, 0.71 mmol) in 2:1 MeOH–EtOAc (6 mL) was added $Pd(OH)_2$/C (40 mg). The mixture was stirred under an H_2 flow (80 mL/min) for 10 h at room temperature, at the end of which time TLC showed disappearance of the starting material. The mixture was filtered, and the filtrate was concentrated and purified on a silica gel column using 3:1 petroleum ether–EtOAc as a eluent to give **3** (306 mg, 77%) as a syrup: $[\alpha]_D^{20}$ +75° (*c* 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.24 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6), 3.50–3.56 (br s, 2 H, NH_2), 3.69–3.73 (m, 1 H, H-5), 4.06 (dd, 1 H, *J* 3.6, 7.4 Hz, H-3), 4.25 (dd, 1 H, *J* 3.8, 7.4 Hz, H-2), 4.36 (dd, 1 H, *J* 1.2, 3.6 Hz, H-4), 4.42, 4.49, 4.54, 4.58, 4.61, 4.71 (6 d, 6 H, PhCH_2), 5.51 (d, 1 H, *J* 3.8 Hz, H-1), 6.48 (dd, 1 H, *J* 2.7, 8.6 Hz, *Ar*), 6.72 (d, 1 H, *J* 2.7 Hz, *Ar*), 6.99 (d, 1 H, 8.6 Hz, *Ar*), 7.23–7.40 (m, 15 H, *Ph*). Anal. Calcd for $C_{33}H_{34}ClNO_5$: C, 70.77; H, 6.12. Found: C, 70.40; H, 6.09.

1.4. Ethyl 3,4-di-*O*-*tert*-butyldimethylsilyl-1-thio-β-L-fucopyranoside (4)

Compound **1** (1.04 g, 5 mmol) was dissolved in *N*,*N*-dimethylformamide (DMF, 5 mL). To the solution was added imidazole (2.04 g, 30 mmol) and TBSCl (2.26 g, 15 mmol) at 0 °C. The mixture was stirred at 0 °C for 30 min, then it was heated to 40 °C, and stirred for another 12 h, diluted with water (50 mL) and extracted with EtOAc (3 × 50 mL). The organic phase was dried over anhyd Na_2SO_4 and concentrated. Purification of the residue on a silica gel column (20:1 petroleum ether–EtOAc) gave **4** (2.08 g, 78%) as a syrup: $[\alpha]_D^{20}$ +25° (*c* 2, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 0.09, 0.14, 0.17 (3 s, 12 H, 2 (CH_3)$_2$Si), 0.92, 0.94 (2 s, 18 H, 2 (CH_3)$_3$C), 1.23 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6), 1.28 (t, 3 H, *J* 7.4 Hz, CH_3CH$_2$S), 2.60–2.75 (m, 2 H, CH$_3$CH_2S), 3.44 (dd, 1 H, $J_{2,3}$ 9.1, $J_{3,4}$ 2.7 Hz, H-3), 3.56 (q, 1 H, $J_{5,6}$ 6.4 Hz, H-5), 3.64 (t, 1 H, $J_{1,2} = J_{2,3} = 9.1$ Hz, H-2), 3.78 (d, 1 H, $J_{3,4}$ 2.7 Hz, H-4), 4.22 (d, 1 H, $J_{1,2}$ 9.1 Hz, H-1). Anal. Calcd for $C_{20}H_{44}O_4SSi_2$: C, 54.99; H, 10.15. Found: C, 55.26; H, 10.41.

1.5. Ethyl 2-*O*-acetyl-3,4-di-*O*-*tert*-butyldimethylsilyl-1-thio-β-L-fucopyranoside (5)

A mixture of compound **4** (22 mg, 0.05 mmol), py (2 mL) and Ac_2O (1 mL) was stirred at 60 °C for 10 h, then evaporated with toluene to dryness under reduced pressure. Column chromatography (20:1 petroleum ether–EtOAc) of the residue afforded recovered **4** and syrupy product **5** (5 mg, 20%): ^{1}H NMR ($CDCl_3$): δ 0.09, 0.14, 0.18 (3 s, 12 H, 2 (CH_3)$_2$Si), 0.92, 0.93 (2 s, 18 H, 2 (CH_3)$_3$C), 1.23 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6), 1.28 (t, 3 H, *J* 7.4 Hz, CH_3CH$_2$S), 2.61–2.74 (m, 2 H, CH$_3$CH_2S), 3.46 (dd, 1 H, $J_{1,2}$ 9.4, $J_{2,3}$ 2.7 Hz, H-3), 3.55 (q, 1 H, $J_{5,6}$ 6.4 Hz, H-5), 3.77 (d, 1 H, $J_{3,4}$ 2.7 Hz, H-4), 4.23 (d, 1 H, $J_{1,2}$ 9.4 Hz, H-1), 5.34 (t, 1 H, $J_{1,2} = J_{2,3} = 9.4$ Hz, H-2). Anal. Calcd for $C_{22}H_{46}O_5SSi_2$: C, 55.18; H, 9.68. Found: C, 55.53; H, 9.49.

1.6. 2-Chloro-4-nitro-phenyl 3,4-di-*O*-*tert*-butyldimethylsilyl-α-L-fucopyranoside (6), 2-chloro-4-nitrophenyl 3,4-di-*O*-*tert*-butyldimethylsilyl-β-L-fucopyranoside (7) and *N*-(3,4-di-*O*-*tert*-butyldimethylsilyl-β-L-fucopyranosyl)succinimide (8)

Compound **4** (2.0 g, 3.73 mmol) and 2-chloro-4-nitrophenol (712 mg, 4.1 mmol) were placed in a pre-dried in a flask under vacuum at 60 °C. The mixture was dissolved in anhyd CH_2Cl_2 (10 mL), followed by the addition of NIS (923 mg, 4.01 mmol) and TMSOTf (30

μL, 0.19 mmol) under an N_2 atmosphere at −42 °C. The mixture was then stirred for 30 min under these conditions, neutralized with Et_3N, and concentrated to dryness. The residue was purified on a silica gel column using 30:1–20:1 petroleum ether–EtOAc as the eluent to afford syrupy **6** (1.25 g, 61%), **7** (163 mg, 8%), and **8** (528 mg, 26%).

1.6.1. Compound 6. $[\alpha]_D^{20}$ −131° (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.02, 0.11, 0.12, 0.17 (4 s, 12 H, $(CH_3)_2Si$), 0.85, 0.96 (2 s, 18 H, $(CH_3)_3CSi$), 1.18 (d, 3 H, $J_{5,6}$ 6.5 Hz, H-6), 3.92 (br s, 1 H, H-4), 3.97 (q, 1 H, $J_{5,6}$ 6.5 Hz, H-5), 4.11–4.13 (m, 2 H, H-2, H-3), 5.52 (d, 1 H, $J_{1,2}$ 2.6 Hz, H-1), 7.30 (d, 1 H, *J* 9.2 Hz, *Ar*), 8.13 (dd, 1 H, *J* 9.2, 2.7 Hz, *Ar*), 8.30 (d, 1 H, *J* 2.7 Hz, *Ar*). Anal. Calcd for $C_{24}H_{42}ClNO_7Si_2$: C, 52.58; H, 7.72. Found: C, 52.71; H, 7.59.

1.6.2. Compound 7. $[\alpha]_D^{20}$ −53° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.11, 0.12, 0.18, 0.21 (4 s, 12 H, $(CH_3)_2Si$), 0.87, 0.96 (2 s, 18 H, $(CH_3)_3CSi$), 1.28 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6), 3.58–3.63 (dd, 1 H, $J_{2,3}$ 7.3, $J_{3,4}$ 2.5 Hz, H-3), 3.78 (q, 1 H, $J_{5,6}$ 6.4 Hz, H-5), 3.87 (d, 1 H, $J_{3,4}$ 2.5 Hz, H-4), 4.01 (t, 1 H, $J_{1,2} = J_{2,3} = 7.3$ Hz, H-2), 5.05 (d, 1 H, $J_{1,2}$ 7.3 Hz, H-1), 7.11 (d, 1 H, *J* 9.2 Hz, *Ar*), 8.11 (dd, 1 H, *J* 2.7, 9.2 Hz, *Ar*), 8.85 (d, 1 H, *J* 2.7 Hz, *Ar*). MALDITOF-MS Calcd for $C_{24}H_{42}ClNNaO_7Si_2$ $[M+Na]^+$: 570.22. Found: 570 $[M+Na]^+$.

1.6.3. Compound 8. $[\alpha]_D^{20}$ −46° (*c* 4, $CHCl_3$); ^1H NMR ($CDCl_3$): δ −0.02, 0.08, 0.10, 0.15 (4 s, 12 H, $(CH_3)_2Si$), 0.79, 0.94 (2 s, 18 H, $(CH_3)_3CSi$), 1.13 (d, 3 H, *J* 6.4 Hz, H-6), 2.62–2.74 (m, 4 H, $-CH_2CH_2-$), 3.89 (d, 1 H, *J* 2.8 Hz, H-4), 4.15 (dd, 1 H, *J* 7.4, 9.1 Hz, H-2), 4.24 (q, 1 H, *J* 6.4 Hz, H-5), 4.45 (dd, 1 H, *J* 2.8, 9.1 Hz, H-3), 5.87 (d, 1 H, *J* 7.4 Hz, H-1). MALDITOF-MS Calcd for $C_{22}H_{43}NNaO_6Si_2$ $[M+Na]^+$: 496.26. Found: 496 $[M+Na]^+$.

1.7. 2-Chloro-4-nitrophenyl β-L-fucopyranoside (9)

To a solution of compound **6** (150 mg, 0.274 mmol) in THF (1 mL) was added TBAF (260 mg, 0.82 mmol). The mixture was stirred at rt for 1 h, then evaporated to dryness. Column chromatography (1:20 petroleum ether–EtOAc) of the residue gave **9** (64 mg, 73%) as a syrup: $[\alpha]_D^{20}$ −66° (*c* 0.1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.13 (d, 3 H, *J* 6.6 Hz, H-6), 3.74–3.83 (m, 2 H, H-4, H-5), 3.95 (dd, 1 H, *J* 3.6, 9.6 Hz, H-3), 4.33 (dd, 1 H, *J* 7.6, 9.6 Hz, H-2), 4.80 (d, 1 H, *J* 7.6 Hz, H-1), 7.31 (d, 1 H, *J* 9.2 Hz, *Ar*), 8.08 (dd, 1 H, *J* 2.6, 9.2 Hz, *Ar*), 8.85 (d, 1 H, *J* 2.6 Hz, *Ar*). MALDITOF-MS Calcd for $C_{12}H_{14}ClNNaO_7$ $[M+Na]^+$: 342. Found: 342 $[M+Na]^+$.

1.8. 2-Chloro-4-nitrophenyl α-L-fucopyranoside (10)

Compound **6** (1.0 g, 1.54 mmol) was dissolved in py (4 mL) and MeCN (15 mL). To the solution was added HF·Py (15 mL, 70%), and the mixture was stirred at 0 °C for 20 h, at the end of which time TLC indicated the completion of the reaction. The mixture was evaporated to dryness under reduced pressure. Purification of the residue on a silica gel column using EtOAc as eluent afforded **10** (335 mg, 68%) as a white solid: $[\alpha]_D^{20}$ −153° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.31 (d, 3 H, $J_{5,6}$ 6.6 Hz, H-6), 3.94 (br s, 1 H, H-4), 4.01–4.10 (m, 3 H, H-2, H-3, H-5), 5.71 (d, 1 H, $J_{1,2}$ 3.1 Hz, H-1), 7.40 (d, 1 H, *J* 9.2 Hz, *Ar*), 8.18 (dd, 1 H, *J* 9.2, 2.7 Hz, *Ar*), 8.32 (d, 1 H, *J* 2.7 Hz, *Ar*); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 16.11, 68.25, 68.96, 71.15, 71.34, 98.86, 115.48, 124.06, 124.25, 126.00, 142.58, 157.14. MALDITOF-MS Calcd for $C_{12}H_{14}ClNNaO_7$ $[M+Na]^+$: 342.05. Found: 342.3 $[M+Na]^+$. Anal. Calcd for $C_{12}H_{14}ClNO_7$: C, 45.08; H, 4.41. Found: C, 44.81; H, 4.57.

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References

1. Elbein, A. D. *Annu. Rev. Biochem.* **1987**, *56*, 497–534.
2. (a) Legler, G. *Adv. Carbohydr. Chem. Biochem.* **1990**, *48*, 319–384;
   (b) Winchester, B.; Fleet, G. W. J. *Glycobiology* **1992**, *2*, 199–210;
   (c) Asano, N.; Nash, R. J.; Molyneux, R. J.; Fleet, G. W. J. *Tetrahedron: Asymmetry* **2000**, *11*, 1645–1680;
   (d) Sinnott, M. L. *Chem. Rev.* **1990**, *90*, 1171–1202;
   (e) Behr, J. B.; Chevrier, C.; Defoin, A.; Tarnus, C.; Streith, J. *Tetrahedron* **2003**, *59*, 543–553.
3. Deugnier, Y.; David, V.; Brissot, P.; Mabo, P.; Delamaire, D.; Messner, M.; Bourel, M.; Legall, J. Y. *Hepatology* **1984**, *4*, 889–892.
4. Marotta, F.; Chui, D. H.; Safran, P. *Dig. Dis. Sci.* **1991**, *36*, 993–997.
5. Giardina, M. G.; Matarazzo, M.; Varriale, A.; Morante, R.; Napoli, A.; Martino, R. *Cancer* **1992**, *70*, 1044–1047.
6. Takahashi, H.; Saibara, T.; Iwamura, S.; Tomita, A.; Maeda, T.; Onishi, S.; Yamamoto, Y.; Enzan, H. *Hepatology* **1994**, *19*, 1414–1417.
7. Kasai, K.; Okada, K.; Yamatsugu, N. *Jpn. Pat. Appl.* 92-353689, 15 December, 1992; Jpn. Kokai Tokkyo Koho, JP 06179690, 1994; *Chem. Abstr.* **1995**, *122*, 133678.
8. (a) Lay, L.; Windmuller, R.; Reinhardt, S.; Schmidt, R. R. *Carbohydr. Res.* **1997**, *303*, 39–49;
   (b) Geyer, A.; Reinhardt, S.; Bendas, G.; Rothe, U.;

Schmidt, R. R. *J. Am. Chem. Soc.* **1995**, *119*, 11707–11708.
9. Lönn, H. *Carbohydr. Res.* **1985**, *139*, 105–113.
10. Boons, G.-J.; Hale, K. J. *Organic Synthesis with Carbohydrates*; Blackwell Science Inc: Oxford, 2000; pp 38–40.
11. (a) Du, Y.; Kong, F. *J. Carbohydr. Chem.* **1995**, *14*, 341–352;
(b) Du, Y.; Kong, F. *Tetrahedron Lett.* **1995**, *36*, 427–430;
(c) Du, Y.; Kong, F. *Carbohydr. Res.* **1995**, *275*, 413–420.
12. Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; 3rd ed.; Wiley: New York, 1991; p 134.