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Practical synthesis of D-[1-^{13}C]mannose, L-[1-^{13}C] and L-[6-^{13}C]fucose

Ken-ichi Sato,* Shoji Akai, Hiroki Youda, Masaru Kojima, Mayumi Sakuma, Shu-ichirou Inaba and Kyota Kurosawa

Laboratory of Organic Chemistry, Faculty of Engineering, Kanagawa University, 3-27-1, Rokkakubashi, Kanagawa-ku, Yokohama 221-8686, Japan

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Abstract—The chemical synthesis of ^{13}C-labeled mannose and fucose is important for the preparation of molecular probes used in the conformational study of the oligosaccharide portions of glycoproteins. A new method for the synthesis of the title [1-^{13}C]-labeled compounds via the corresponding olefin compounds, which are in turn derived from D-mannitol or L-arabinose by efficient introduction of ^{13}C, by the Wittig reaction using $Ph_3P^{13}CH_3I$ and *n*-BuLi, is described. The introduction of $^{13}CH_3I$ to produce the [1-^{13}C]- and [6-^{13}C]-labeled compounds was accomplished in 62%, 56%, and 71% yields, respectively. All mannose and fucose protons, from H-1 to H-6, were observed by the HMQC-TOCSY technique using 1:1 mixtures of [1-^{13}C]- and [6-^{13}C]-labeled compounds.

1. Introduction

Sialyl glycoconjugates are important cell surface components, active in a variety of intercellular recognition events. Therefore, the study of the conformation and dynamics of these sialyl oligosaccharides and their analogues is necessary in order to gain insight into how these cell surface oligosaccharides intact with the corresponding receptor molecules. However, although the conformational properties[1–3] of low molecular weight sialyl oligosaccharide analogues have been reported by many research groups, the conformation and dynamics of sialyl oligosaccharides and their analogues attached to glycoproteins have not yet been fully analyzed. To address this problem, ^{13}C-labeled sialic acid (NeuAc) has been utilized for the conformational analysis of sialyl oligosaccharides on artificial membrane surfaces[4] and by TRNOE experiments.[4] Recently, a novel NMR technique, HSQC-TOCSY-NOESY-TOCSY, for observation of all protons of glycoprotein NeuAc, H-3 to H-9, even with only a single ^{13}C-labeled atom (3-position), has been reported.[2] However, since combined multipulse techniques generally suffer from low sensitivity, we have synthesized minimally labeled [3,9-^{13}C]NeuAc for convenient observation of all protons of NeuAc from H-3 to H-9 by the HMQC-HOHAHA technique. We have also synthesized [3-^{13}C]- and [9-^{13}C]-labeled NeuAc and demonstrated that identical results are obtained by NMR for [3,9-^{13}C]NeuAc as for 1:1 mixtures of [3-^{13}C] and [9-^{13}C]NeuAc.[5a] This efficient method for preparation of minimally ^{13}C-labeled compounds has enabled us to prepare practical amounts of important ^{13}C-labeled monosaccharides, such as NeuAc, KDN, galactose, mannose, mannosamine, and fucose for use in the preparation of cell surface sialyl and KDN oligosaccharides. Labeled oligosaccharides are necessary for the study of the interactions between these oligosaccharides and the corresponding receptor molecules. We previously reported[5] a practical synthesis of minimally ^{13}C-labeled NeuAc, KDN, and galactose monosaccharides.

In this letter, the practical syntheses of D-[1-^{13}C]-mannose, L-[1-^{13}C]fucose, and L-[6-^{13}C]fucose are described. ^{13}C is preferably introduced at the last stage, thereby preserving as much labeled compound as possible, in a strategy analogous to that reported previously. As a ^{13}C source, commercially available $^{13}CH_3I$ was used and the introduction of ^{13}C was performed by extension of either the terminal head or end of the precursor with labeled reagents derived from $^{13}CH_3I$. D-[6-^{13}C]Mannose has already been synthesized

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* Corresponding author. Tel.: +81 45 481 5661x3853; fax: +81 45 413 9770; e-mail: satouk01@kanagawa-u.ac.jp

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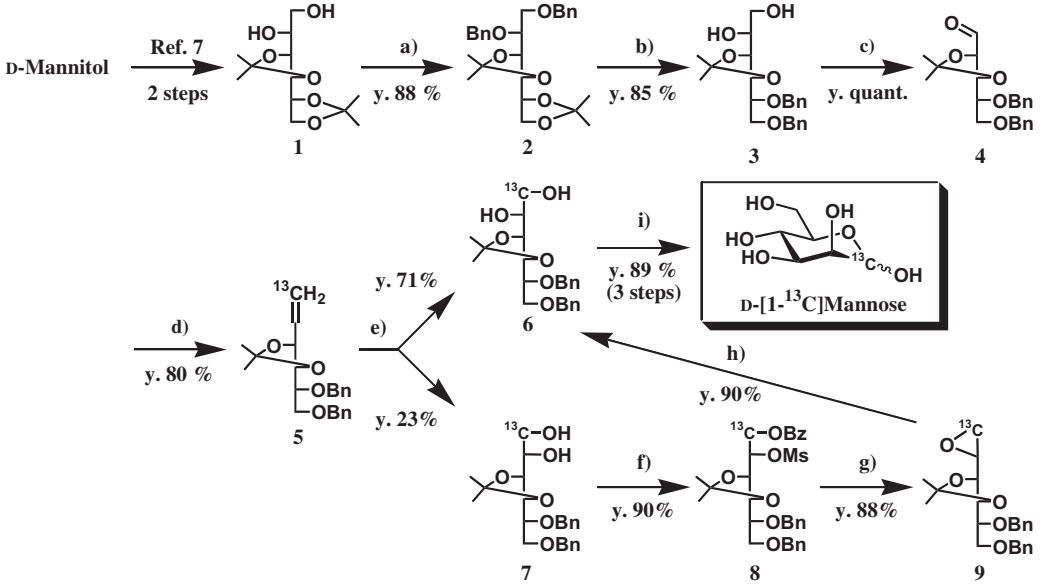
efficiently in previous studies.[5] The synthesis of L-[6-^{13}C]fucose was achieved using a similar procedure to that for the unlabeled compound.[6] The labeling effect of a 1:1 mixture of these monosaccharides by the HMQC-TOCSY technique was also examined.

2. Synthesis of D-[1-^{13}C]mannose from D-mannitol

D-[1-^{13}C]Mannose was synthesized from D-mannitol as follows (Scheme 1). 1,2:3,4-Di-*O*-isopropylidene-D-mannitol (**1**) was synthesized by Inch's method.[7] Compound **1** was treated with sodium hydride (2.5 equiv) and benzyl bromide (2.2 equiv) in DMF at 0 °C to give the syrupy benzyl derivative **2**[10] in 88% yield, which was purified on a column of silica gel (ethyl acetate/hexane = 1:8). Compound **2** was then treated with 90% aqueous acetic acid at room temperature (rt) for 11 h to give the partially hydrolyzed syrupy derivative **3**[10] in 85% yield. The structure of **3** was confirmed by preparation of the corresponding 1,2-di-*O*-acetyl derivative. Compound **3** was then treated with sodium metaperiodate (2.0 equiv) in methanol until disappearance of **3** to give the corresponding syrupy degradation product, 4,5-di-*O*-benzyl-2,3-*O*-isopropylidene-D-arabinose (**4**) [^{1}H NMR (500 MHz, $CDCl_3$): δ 9.68 ppm, doublet, J = 1.7 Hz, –CHO] quantitatively. After azeotropic removal of water from **4** with toluene, the Wittig reaction of **4** with $Ph_3P^{13}CH_3I$ (1.0 equiv) and *n*-BuLi in hexane (2.44 M, 1.0 equiv) in dry THF at −30 °C gave the syrupy *arabino*-hex-1-[1-^{13}C]enitol (**5**),[10] which was purified on a column of silica gel (ethyl acetate/hexane = 1:8) in 80% yield. The ^{13}C-labeled phosphonium salt $Ph_3P^{13}CH_3I$ was conveniently synthesized using $^{13}CH_3I$ and PPh_3 in toluene in almost quantitative yield. Oxidation of **5** with 4-methylmorphorine *N*-oxide (NMO, 2.0 equiv) and OsO_4 (*t*-BuOH solution, 0.01 equiv) in *t*-BuOH at rt for 5 h gave a mixture of the syrupy diol compounds **6**[10] and **7**, which were purified on a column of silica gel (ethyl acetate/hexane = 2:3), in 71% and 23% yields, respectively. Another effort to obtain the 2,3,4,5-tetra-*O*-benzyl derivative of **4** from D-arabinose was also made, but the oxidation products of the corresponding enitol derivative of **5** could not be separated.

For the transformation to mannose, selective oxidation of the primary OH of the D-mannitol derivative **6** with trichloroisocyanuric acid (TCCA, 1.1 equiv) and 2,2,6,6-tetramethyl-1-piperidinyloxy radical[8] (TEMPO, 0.01 equiv) in CH_2Cl_2 at 0 °C for 2 h gave the corresponding aldehyde derivative in good yield. The aldehyde derivative was then treated with 10% Pd–C and H_2 in EtOH, followed by acid hydrolysis with Dowex H^+ in H_2O at 50 °C to give the required D-[1-^{13}C]mannose. The yield of D-[1-^{13}C]mannose from **6** (three steps) was 89%. The structure of ^{13}C-labeled D-[1-^{13}C]-mannose was confirmed by comparison of the NMR data with that of non-labeled mannose. NMR data for the non-labeled and the ^{13}C-labeled mannose are shown in Figure 1. The undesired D-glucitol derivative **7** can be converted into **6** as follows: compound **7** was treated with benzoyl chloride (1.1 equiv) in pyridine at 0 °C until disappearance of the starting material, followed by mesylation with methanesulfonyl chloride (2.0 equiv) to give the corresponding syrupy derivative **8**,[10] followed by separation on a column of silica gel (ethyl acetate/hexane = 1:4), in 90% yield. Compound **8** was then treated with a solution of KOH (3.0 equiv) in MeOH for 3 h at rt to give the syrupy 1,2-epoxy derivative **9**,[10] which was purified on a column of silica gel (ethyl acetate/hexane = 1:3), in 88% yield. The epoxy derivative **9** was hydrolyzed with 1 M KOH in DMSO at 70 °C for 6 h to give **6**, which was purified



Scheme 1. Reagents and conditions: (a) BnBr, NaH/DMF; (b) 90% AcOH aq, (c) $NaIO_4$/MeOH–H_2O; (d) $Ph_3P^{13}CH_3I$, *n*-BuLi/THF; (e) OsO_4, NMO/*t*-BuOH–H_2O; (f) BzCl, Py then MsCl; (g) KOH/MeOH; (h) 1 M KOH/DMSO; (i) i. TEMPO, TCCA/CH_2Cl_2, ii. 10% Pd–C, H_2/EtOH, iii. Dowex H^+/H_2O.

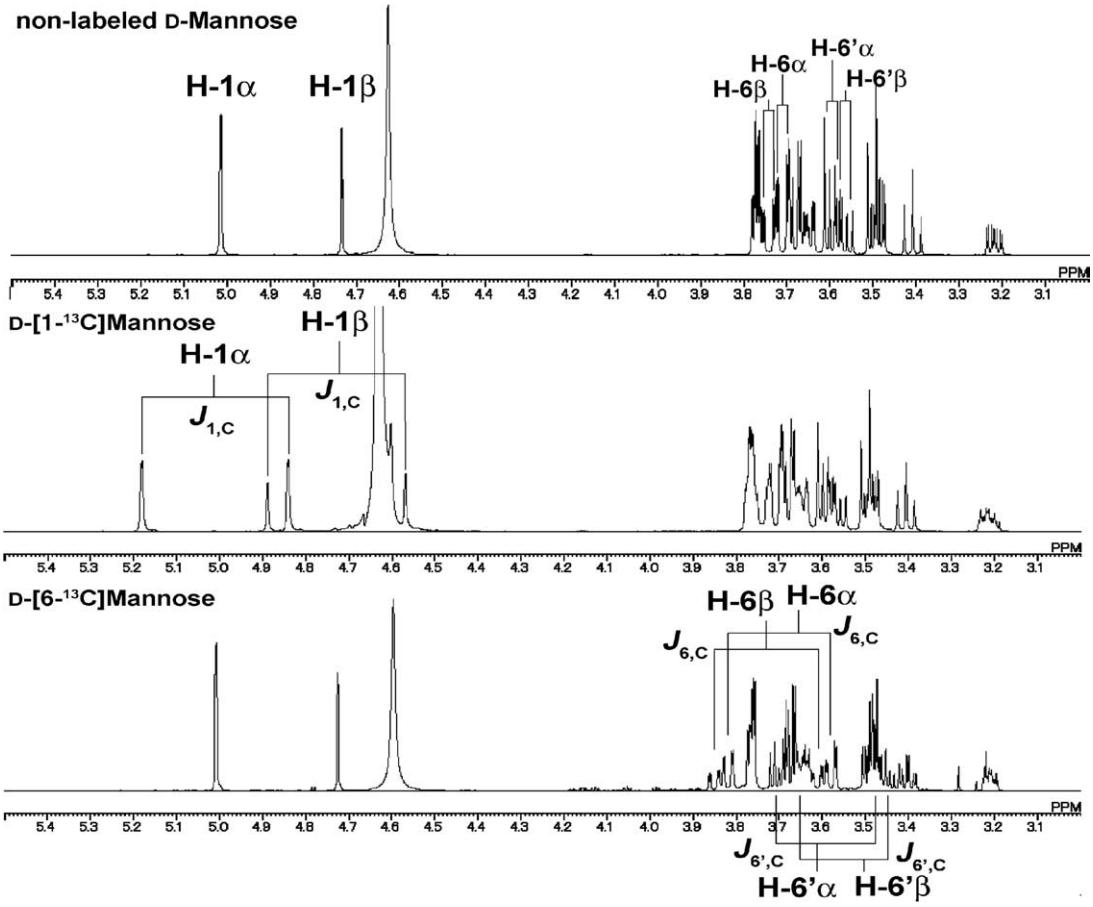


Figure 1. ^{1}H NMR spectra of non-labeled and ^{13}C-labeled D-mannoses.

on a column of silica gel (ethyl acetate/hexane = 1:3), in 90% yield. These procedures result in 62% utilization of $^{13}CH_3I$ in this D-[1-^{13}C]mannose synthesis.

3. Synthesis of D-[6-^{13}C]mannose from D-mannose

We have already reported a convenient chemoenzymatic synthesis of [3,9-^{13}C]-labeled NeuAc and KDN using D-[6-^{13}C]mannose.[5a] In that work, D-[6-^{13}C]mannose was synthesized via the benzyl 2,3-*O*-isopropylidene-α-D-mannofuranoside for use as an intermediate in labeled KDN syntheses. The utilization of $^{13}CH_3I$ in the synthesis of D-[6-^{13}C]mannose from D-mannose was 54%. NMR data for each ^{13}C-labeled mannose are given in Ref. 6. HMQC-TOCSY spectra of the 1:1 mixture of methyl α-D-[1-^{13}C] and [6-^{13}C]mannopyranoside is shown in Figure 2. It is easy to analyze the chemical shifts and *J* values of all protons using this technique.

4. Synthesis of L-[1-^{13}C]fucose from L-arabinose

This compound was synthesized from L-arabinose as shown in Scheme 2. The reaction of L-arabinose and ethane thiol (4.0 equiv) in 12 M HCl at 0 °C gave the corresponding diethyl dithioacetal **10**[10] in 87% yield. Reduction of **10** with Raney Ni in 70% aq ethanol solution under reflux conditions gave the deoxy derivative **11**[10] in 83% yield. Compound **11** was treated with triphenylmethyl chloride (1.2 equiv) in pyridine at 55 °C for 1 h to give the trityl derivative **12**[10] in 90% yield. To a solution of **12** and NaH (3.3 equiv) in DMF, benzyl bromide (3.3 equiv) was added dropwise at 0 °C and quenched with NaOMe in methanol to give **13**[10] in 95% yield. Compound **13** was then hydrolyzed in 90% aq acetic acid at 50 °C for 30 min to give the syrupy compound **14**[10] [purified on a column of silica gel, (ethyl acetate/hexane = 1:5)] in 95% yield. The primary hydroxyl group of the product was then selectively oxidized with TCCA (1.2 equiv) and TEMPO (0.01 equiv) in CH_2Cl_2 at 0 °C to give the syrupy 5-deoxy-L-*lyxo* derivative **15**[10] [purified on a column of silica gel, (ethyl acetate/hexane = 1:5)] quantitatively. Wittig reaction of **15** with $Ph_3P^{13}CH_3I$ (1.0 equiv) and *n*-BuLi in hexane (2.44 M, 1.0 equiv) in dry THF at −20 °C gave the syrupy L-*lyxo*-hex-1-[1-^{13}C]enitol (**16**)[10] [purified on a column of silica gel, (ethyl acetate/hexane = 1:12)] in 71% yield. Oxidation of **16** with NMO (2.0 equiv) and OsO_4 (*t*-BuOH solution, 0.01 equiv) in *t*-BuOH/H_2O (1:1) at 0 °C until the disappearance of **16** gave a mixture of the syrupy diol compounds **17**[10] and **18**,[10] which were purified on a column of silica gel (ethyl acetate/hexane = 1:2), in 9% and 88% yields, respectively. For transformation into fucose, the primary OH of 6-deoxy-L-galactitol derivative **17** was selectivity oxidized with TCCA (1.1 equiv) and TEMPO[8] (0.01 equiv) in CH_2Cl_2 at 0 °C for 30 min to give the corresponding

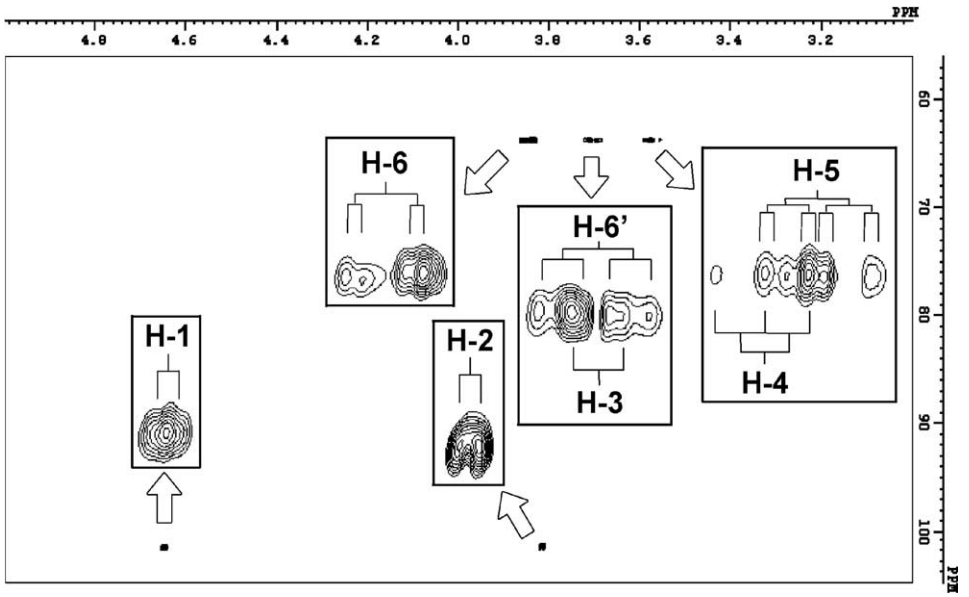
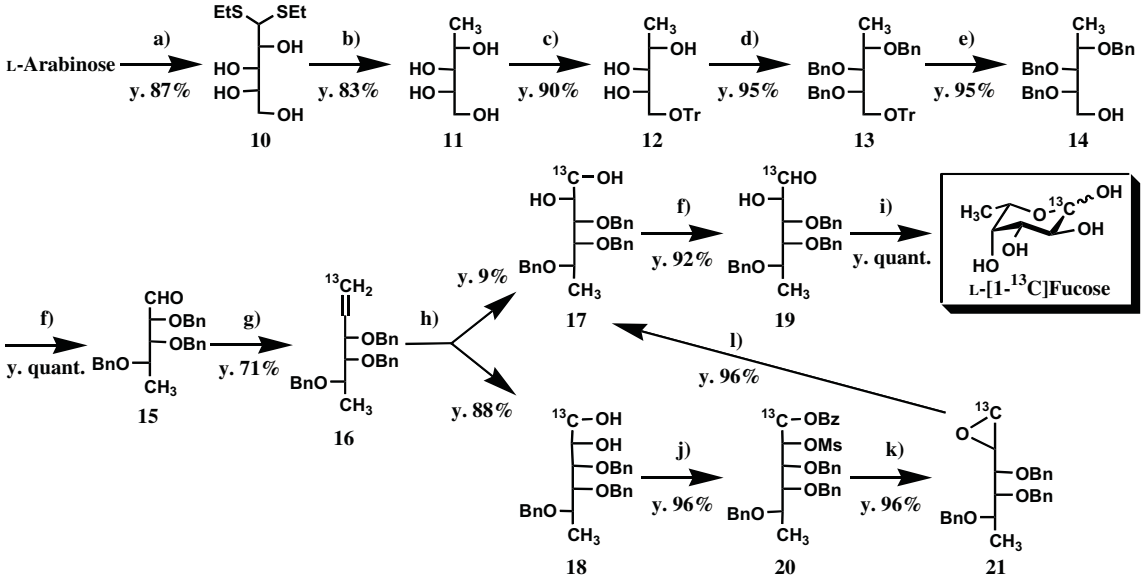


Figure 2. HMQC-TOCSY spectra of a 1:1 mixture of methyl α-D-[1-^{13}C] and [6-^{13}C]mannopyranoside.



Scheme 2. Reagents and conditions: (a) EtSH, 12 M HCl; (b) Raney Ni/70% EtOH aq; (c) TrCl, Py; (d) NaH, BnBr/DMF; (e) 90% AcOH aq; (f) TEMPO, TCCA/CH_2Cl_2; (g) $Ph_3P^{13}CH_3I$, *n*-BuLi/THF; (h) OsO_4, NMO/*t*-BuOH–H_2O; (i) 10% Pd–C, H_2/EtOH–H_2O; (j) BzCl, Py then MsCl; (k) 1 M KOH/MeOH; (l) 1 M KOH/DMSO.

syrupy aldehyde derivative **19**[10] [IR: $\nu_{C=O}$ 1671 cm^{-1}, purified on a column of silica gel (ethyl acetate/hexane = 1:2)] in 92% yield. The product **19** was then treated with Pd–C/H_2 at rt to give ^{13}C-labeled L-fucose quantitatively. The structure of L-[1-^{13}C]fucose was confirmed by comparison of the NMR data with those of non-labeled fucose. The NMR data for non-labeled fucose and the ^{13}C-labeled fucose are shown in Figure 3. The undesired L-talitol derivative **18** was transformed into **20**[10] [purified on a column of silica gel, (acetone/toluene = 1:20)] by reaction with benzoyl chloride (1.2 equiv) in pyridine at 0 °C, followed by mesylation with methanesulfonyl chloride (1.5 equiv) in 96% yield. Compound **20** was then treated with KOH in MeOH (1.0 M, 3.0 equiv) at 40 °C and the reaction was monitored by TLC (acetone/toluene = 1:20) to give the syrupy 1,2-epoxy derivative **21**[10] [purified on a column of silica gel, (ethyl acetate/hexane = 1:10)] in 96% yield. The epoxy derivative **21** was then hydrolyzed with 1 M KOH in DMSO at 70 °C to give **17** in 96% yield. This method results in 56% utilization of $^{13}CH_3I$ in the preparation of L-[1-^{13}C]fucose.

5. Synthesis of L-[6-^{13}C]fucose from D-mannose

L-[6-^{13}C]Fucose was prepared according to the method described by Petit et al. (Scheme 3). Therefore, here we

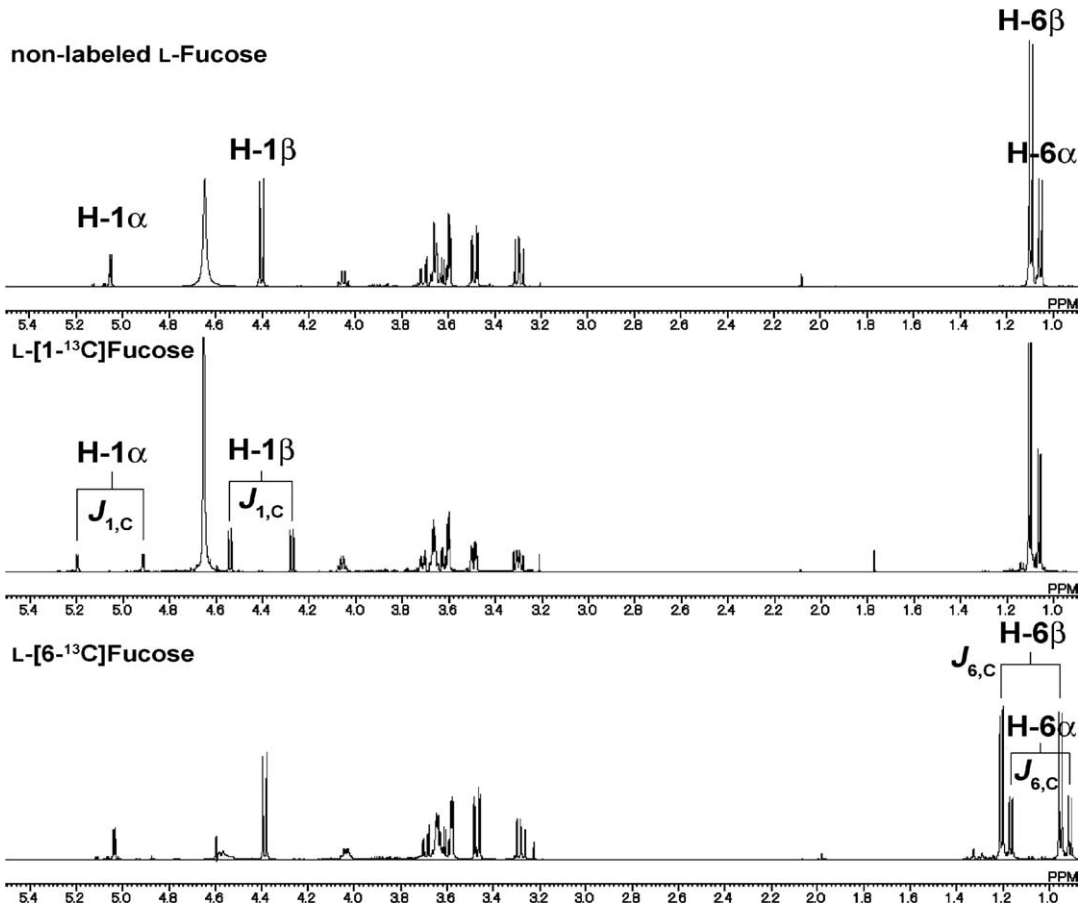
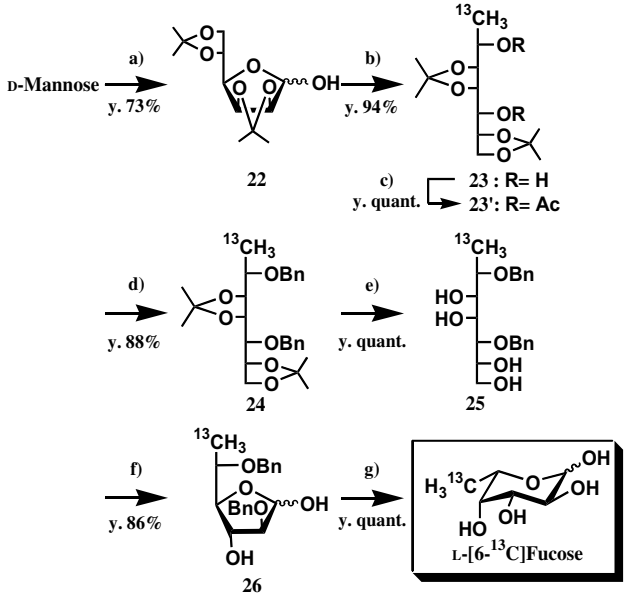


Figure 3. ^{1}H NMR spectra of non-labeled and ^{13}C-labeled L-fucoses.



Scheme 3. Reagents and conditions: (a) $(CH_3)_2C(OCH_3)_2$, *p*-TsOH/acetone; (b) $^{13}CH_3Li$/THF; (c) Ac_2O, Py; (d) NaH, BnBr/DMF; (e) 70% AcOH aq; (f) $NaIO_4$/MeOH–H_2O; (g) 10% $Pd(OH)_2$–C, H_2/EtOH.

only briefly describe the synthesis of the ^{13}C-labeled compound from D-mannose. D-Mannose was treated with dimethoxypropane in the presence of a catalytic amount of *p*-toluenesulfonic acid in acetone to give the di-*O*-isopropylidene derivative **22** in 73% yield. A reaction mixture of **22** and $^{13}CH_3Li$ (1.14 M in THF, 3.0 equiv, prepared from $^{13}CH_3I$ and lithium quantitatively) in THF was stirred at −50 °C and the temperature was allowed to rise to 0 °C gradually within 5 h and then to rt for another 2 h under argon to give the corresponding syrupy ^{13}C-labeled heptitol derivative **23**[10] [purified on a column of silica gel, (acetone/toluene = 1:4)] in 94% yield. The structure of **23** was confirmed using NMR by preparation of the acetyl derivative **23′**.[10] Compound **23** was treated with NaH (3.0 equiv) and benzyl bromide (2.5 equiv) in DMF at 0 °C and the temperature was allowed to rise to rt to give the syrupy di-*O*-benzyl derivative **24** [purified on a column of silica gel, (ethyl acetate/hexane = 1:9)] in 88% yield. Compound **24** was treated in 70% aq acetic acid solution at 50 °C to give the de-isopropylidene derivative **25**[10] quantitatively. The product of **25** was treated with an aq $NaIO_4$ solution in MeOH at 0 °C to give a syrupy mixture of 2,5-di-*O*-benzyl-L-[6-^{13}C]fucofuranose (α and β) **26**[10] [purified on a column of silica gel, (ethyl acetate/hexane = 1:1)] in 86% yield. Finally, catalytic reduction of **26** with 10% $Pd(OH)_2$–C/H_2 in EtOH at 35 °C gave the desired L-[6-^{13}C]fucose quantitatively. The structure of L-[6-^{13}C]fucose was confirmed by comparison of the NMR data with those for the non-labeled fucose. This method results in 71%

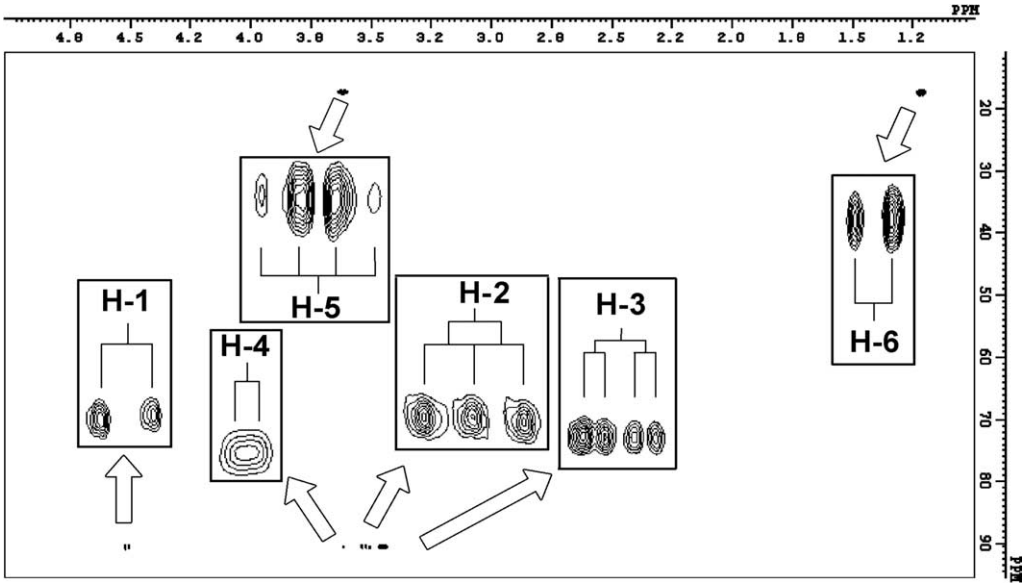


Figure 4. HMQC-TOCSY spectra of a 1:1 mixture of phenyl 1-thio-β-L-[1-^{13}C] and [6-^{13}C]fucopyranoside.

utilization of $^{13}CH_3I$ in this synthesis of L-[6-^{13}C]fucose. The NMR data for non-labeled fucose and the ^{13}C-labeled fucose are shown in Figure 3. NMR data for each ^{13}C-labeled fucose are given in Ref. 9. The HMQC-TOCSY spectra of the 1:1 mixture of phenyl 1-thio-β-L-[1-^{13}C] and [6-^{13}C]fucopyranoside is shown in Figure 4. Using this technique enabled us to determine the chemical shifts and *J* values of all protons.

As described above, a practical synthesis of minimally ^{13}C-labeled D-mannose and L-fucose should facilitate studies on the conformational properties and dynamic behavior of oligosaccharides that contain mannose and fucose. This short and efficient ^{13}C-labeling method should also be applicable for ^{14}C-labeling, facilitating the preparation of labeled oligosaccharides for reaction with the corresponding receptor molecules in order to determine the interaction mechanisms.

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9. ^{1}H and ^{13}C NMR data of ^{13}C-labeled mannose and fucose.
D-[*1-^{13}C*]*mannose*: ^{1}H NMR (500 MHz, D_2O): δ 5.03 (1H, dd, $J_{1,2}$ = 1.4 Hz, $J_{1,C}$ = 170.4 Hz, H-1α), 4.75 (1H, dd, $J_{1,2}$ = 1.0 Hz, $J_{1,C}$ = 160.5 Hz, H-1β), 3.78 (1H, dd, $J_{2,3}$ = 3.3 Hz, H-2β), 3.78 (1H, dd, $J_{2,3}$ = 3.3 Hz, H-2α), 3.76 (1H, dd, $J_{6,5}$ = 2.3 Hz, $J_{6,6'}$ = 12.3 Hz, H-6β), 3.73 (1H, dd, $J_{6,5}$ = 2.1 Hz, $J_{6,6'}$ = 12.0 Hz, H-6α), 3.70 (1H, dd, $J_{3,4}$ = 9.9 Hz, H-3α), 3.67 (1H, dddd, $J_{5,4}$ = 9.7 Hz, $J_{5,6'}$ = 5.9 Hz, $J_{5,C}$ = 1.3 Hz, H-5), 3.61 (1H, dd, H-6′α), 3.58 (1H, dd, $J_{6',5}$ = 6.3 Hz, H-6′β), 3.51 (1H, dd, H-4α), 3.51 (1H, dd, $J_{3,4}$ = 9.7 Hz, H-3β), 3.42 (1H, dd, $J_{4,5}$ = 9.7 Hz, H-4β), 3.23 (1H, dddd, $J_{5,C}$ = 2.1 Hz, H-5β); ^{13}C NMR (125 MHz, D_2O): δ 94.02 (C-1α), 93.66 (C-1β).
D-[*6-^{13}C*]*mannose*: ^{1}H NMR (500 MHz, D_2O): δ 5.06 (1H, dd, $J_{1,2}$ = 1.7 Hz, H-1α), 4.75 (1H, dd, $J_{1,2}$ = 0.9 Hz, H-1β), 3.82 (1H, dd, $J_{2,3}$ = 3.3 Hz, H-2β), 3.81 (1H, dd, $J_{2,3}$ = 3.4 Hz, H-2α), 3.78 (1H, dd, $J_{6,5}$ = 2.2 Hz, $J_{6,6'}$ = 12.2 Hz, $J_{6,C}$ = 144.3 Hz, H-6β), 3.73 (1H, dd, $J_{6,5}$ = 2.2 Hz, $J_{6,6'}$ = 12.2 Hz, $J_{6,C}$ = 144.0 Hz, H-6α), 3.73 (1H, dd, $J_{3,4}$ = 9.6 Hz, H-3α), 3.70 (1H, ddd, $J_{5,4}$ = 10.0 Hz, $J_{5,6'}$ = 5.8 Hz, H-5α), 3.64 (1H, ddd, $J_{6',C}$ = 143.0 Hz, H-6′α), 3.60 (1H, ddd, $J_{6',5}$ = 6.0 Hz, $J_{6',C}$ = 120.8 Hz, H-

6′β), 3.54 (1H, ddd, $J_{4,C}$ = 3.6 Hz, H-4α), 3.52 (1H, dd, $J_{3,4}$ = 9.8 Hz, H-3β), 3.46 (1H, ddd, $J_{4,5}$ = 9.7 Hz, $J_{4,C}$ = 3.6 Hz, H-4β), 3.26 (1H, dddd, $J_{5,C}$ = 2.2 Hz, H-5β); ^{13}C NMR (125 MHz, D_2O): δ 62.01 (C-6β), 62.00 (C-6α).

L-[*1-^{13}C]fucose*: ^{1}H NMR (600 MHz, D_2O): δ 5.05 (1H, dd, $J_{1,2}$ = 4.0 Hz, $J_{1,C}$ = 168.9 Hz, H-1α), 4.40 (1H, d, $J_{1,2}$ = 7.9 Hz, $J_{1,C}$ = 160.5 Hz, H-1β), 4.05 (1H, q, $J_{5,6}$ = 6.5 Hz, H-5a), 3.71 (1H, dd, $J_{3,2}$ = 10.3 Hz, $J_{3,4}$ = 3.3 Hz, H-3α), 3.66 (1H, d, H-4α), 3.66 (1H, dq, $J_{5,6}$ = 6.5 Hz, $J_{5,C}$ = 2.4 Hz, H-5β), 3.62 (1H, dd, H-2α), 3.60 (1H, d, $J_{4,3}$ = 3.4 Hz, H-4β), 3.49 (1H, ddd, $J_{3,2}$ = 10.0 Hz, $J_{3,C}$ = 1.2 Hz, H-3β), 3.30 (1H, ddd, $J_{2,C}$ = 7.9 Hz, H-2β), 1.10 (3H, d, H-6β), 1.06 (3H, d, H-6α); ^{13}C NMR (150 MHz, D_2O): δ 96.24 (C-1β), 92.22 (C-1α).

L-[*6-^{13}C]fucose*: ^{1}H NMR (500 MHz, D_2O): δ 5.08 (1H, d, $J_{1,2}$ = 3.7 Hz, H-1α), 4.44 (1H, d, $J_{1,2}$ = 7.9 Hz, H-1β), 4.09 (1H, dq, $J_{5,6}$ = 6.7 Hz, $J_{5,C}$ = 3.1 Hz, H-5α), 3.75 (1H, dd, $J_{3,2}$ = 10.4 Hz, $J_{3,4}$ = 3.4 Hz, H-3α), 3.69 (1H, dq, $J_{5,6}$ = 6.7 Hz, $J_{5,C}$ = 3.3 Hz, H-5β), 3.66 (1H, d, H-4α), 3.65 (1H, dd, H-2α), 3.63 (1H, d, $J_{4,3}$ = 3.7 Hz, H-4β), 3.52 (1H, dd, $J_{3,2}$ = 10.1 Hz, H-3β), 3.34 (1H, dd, H-2β), 1.13 (3H, dd, $J_{6,C}$ = 127.6 Hz, H-6β), 1.09 (3H, dd, $J_{6,C}$ = 127.3 Hz, H-6α); ^{13}C NMR (125 MHz, D_2O): δ 15.63 (C-6α), 16.76 (C-6β).

10. Physical data ($[\alpha]_D$ and mp) of synthesized compounds. Compound **2**: $[\alpha]_D^{26}$ +8.9 (*c* 1.1, $CHCl_3$); compound **3**: $[\alpha]_D^{26}$ −18.3 (*c* 1.0, $CHCl_3$); compound **5**: $[\alpha]_D^{26}$ +1.9 (*c* 1.0, $CHCl_3$); compound **6**: $[\alpha]_D^{26}$ −19.4 (*c* 1.2, $CHCl_3$); compound **7**: $[\alpha]_D^{26}$ −9.2 (*c* 1.1, $CHCl_3$); compound **8**: $[\alpha]_D^{26}$ −17.1 (*c* 1.1, $CHCl_3$); compound **9**: $[\alpha]_D^{26}$ −1.3 (*c* 1.3, $CHCl_3$); compound **10**: mp 127.0–128.7 °C, (recrystallized from ethanol); compound **11**: mp 131.5–132.3 °C, (recrystallized from ethanol–hexane); compound **12**: mp 89.8–90.7 °C, (recrystallized from ethanol–hexane); compound **13**: mp 94.3–95.2 °C, (recrystallized from ethyl acetate–hexane); compound **14**: $[\alpha]_D^{26}$ +11.6 (*c* 1.1, CH_3OH); compound **15**: $[\alpha]_D^{25}$ +24.3 (*c* 1.0, $CHCl_3$); compound **16**: $[\alpha]_D^{25}$ +26.6 (*c* 1.0, CH_3OH); compound **17**: $[\alpha]_D^{27}$ −15.8 (*c* 1.0, $CHCl_3$); mp 75.0–76.0 °C, (recrystallized from ethyl acetate–hexane); compound **18**: $[\alpha]_D^{24}$ −10.7 (*c* 0.8, $CHCl_3$); compound **20**: $[\alpha]_D^{26}$ −36.0 (*c* 1.1, $CHCl_3$); mp 78.9–81.2 °C, (recrystallized from ethyl acetate–hexane); compound **21**: $[\alpha]_D^{25}$ +18.3 (*c* 1.0, $CHCl_3$); compound **23**: $[\alpha]_D^{28}$ +64.2 (*c* 0.3, $CHCl_3$); compound **23′**: $[\alpha]_D^{28}$ −11.3 (*c* 1.0, $CHCl_3$); mp 73.5–75.0 °C, (recrystallized from ethanol–hexane); compound **24**: $[\alpha]_D^{26}$ −2.5 (*c* 1.1, $CHCl_3$); compound **25**: $[\alpha]_D^{24}$ +26.7 (*c* 1.1, $CHCl_3$); mp 99.5–101 °C, (recrystallized from ethanol–hexane); compound **26**: $[\alpha]_D^{22}$ +13.9 (*c* 0.6, $CHCl_3$).