Supporting information

Controlling the Lectin Recognition of Glycopolymer by Distance Arrangement of Sugar Blocks

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1.Materials

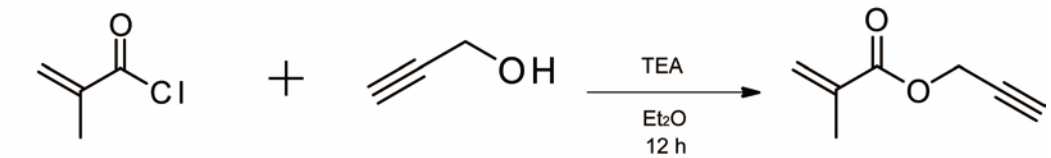
N,*N*'-diisopropylethylamine (DIPEA, 98%), methacryloyl chloride (80.0%), and chlorotrimethylsilane (98%) were purchased from Tokyo Chemical Industry (Tokyo, Japan). Triethylamine (99.0%), 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU, 97%), 2,2'-azobis isobutyronitrile (AIBN, 95%), acetic acid (99.7%), *D*(+)-Mannose (Mannose・H_2O), and deuterium oxide (D_2O, 99.8%) were purchased from Wako Pure Chemical Industries (Osaka, Japan). Magnesium sulfate ($MgSO_4$, 95.0%), sodium azide (NaN_3, 97.0%) were purchased from Kanto Chemical (Tokyo, Japan). Propargyl alcohol (99%), silver chloride (99.999%), tetrabutylammonium fluoride (TBAF) trihydrate (97.0%), 4-cyano-4-(phenylcarbonothioylthio)pentanoic acid (CPADB, 97%), and copper(I) bromide (CuBr, 99.999%) were purchased from Sigma Aldrich (St. Louis, USA). Triethylene glycol monoethyl ether monomethacrylate (TEG-MA) was purchased from Polyscience, Inc (Warrington, USA). Concanavalin A - fluorescein isothiocyanate (ConA-FITC) was purchased from COSMO BIO (Tokyo, Japan). Peanut agglutinin - fluorescein isothiocyanate (PNA-FITC) was purchased from Seikagaku Bio Business (Tokyo, Japan). Rabit blood was purchased from Nippon Bio-test Laboratories Inc (Saitama, Japan). Tris[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]amine (TBTA) was synthesized according to the procedure reported.[1]

2. Characterization

^1H NMR spectra were recorded on a JEOL-ECP400 spectrometer (JEOL, Japan) using $CDCl_3$, $(CD_3)_2CO$, d_7-DMF, d6-DMSO or D_2O as a solvent. Size exclusion chromatography (SEC) with organic solvent was performed on a HLC-8320 GPC equipped with TSKgel Super AW (4000, 3000 and 2500) columns (TOSOH, Japan). The SEC analyses were performed by injecting 20 μL of a polymer solution (2 mg/mL) in DMAc buffer with 10 mM LiBr or DMF buffer with 10 mM LiBr. All the samples for SEC were previously filtered through a 0.45 μm filter. The buffer solution was also used as the eluent at a flow rate of 0.5 mL/min. Dynamic light scattering (DLS) was performed on a ZETASIZER NANO-ZS (Malvern, UK). The DLS analyses were performed by using a 1 mL disposable cell of a polymer solution (0.5 mg/mL) in 10mM PBS(+) buffer. All the samples for DLS were previously filtered through a 0.45 μm filter. Fluorescent quenching measurement was performed on a JASCO FP-6500 (JASCO, Japan). The fluorescence quenching measurement analyses were performed by using a 1 mL disposable cell of a ConA-FITC solution (0.033 mM) in 10mM PBS(+) buffer and polymer solution (0.1 mM : sugar concentration) in 10mM PBS(+) buffer. The hemagglutination was measured by microtiter plate reader (Varioskan Flash, Thermo Fisher Scientific).

3. Synthesis

Synthesis of Propargyl methacrylate (Pr-MA)



Methacryloyl chloride Propargyl alcohol Propargyl methacrylate

Propargyl alcohol (1 eq, 257 mmol, 15.0 mL) and triethylamine (TEA; 1.3 eq, 333 mmol, 46.6 mL) were stirred with 120 mL of diethyl ether (Et_2O) in an ice bath for 10 min. Methacryloyl chloride (1.5 eq, 386 mmol, 30.1 mL) dissolved in another 120 mL of Et_2O was added dropwise over 40 min using a dropping funnel. Ice bath was removed and after stirring for 12 h at room temperature, the solution was filtered and concentrated under reduced pressure with an evaporator. The

crude product was purified by distillation at 1.2 kPa at 65°C to yield colorless oil (yield: 10.8 g, 34%).

^{1}H-NMR ($CDCl_3$, δ in ppm): 6.18 (ddd, J = 1.4, 2.3 Hz, trans C**H**$_2$=CH, 1H), 5.63 (ddd, J = 1.4, 2.7 Hz, cis C**H**$_2$=CH, 1H), 4.76 (d, J = 2.8 Hz, -C**H**$_2$-C≡CH, 2H), 2.48 (t, J = 2.6 Hz, CH$_2$=C**H**, 3H), 1.97 (t, J = 1.4 Hz, -CH$_2$-C-C**H**$_3$, 3H).

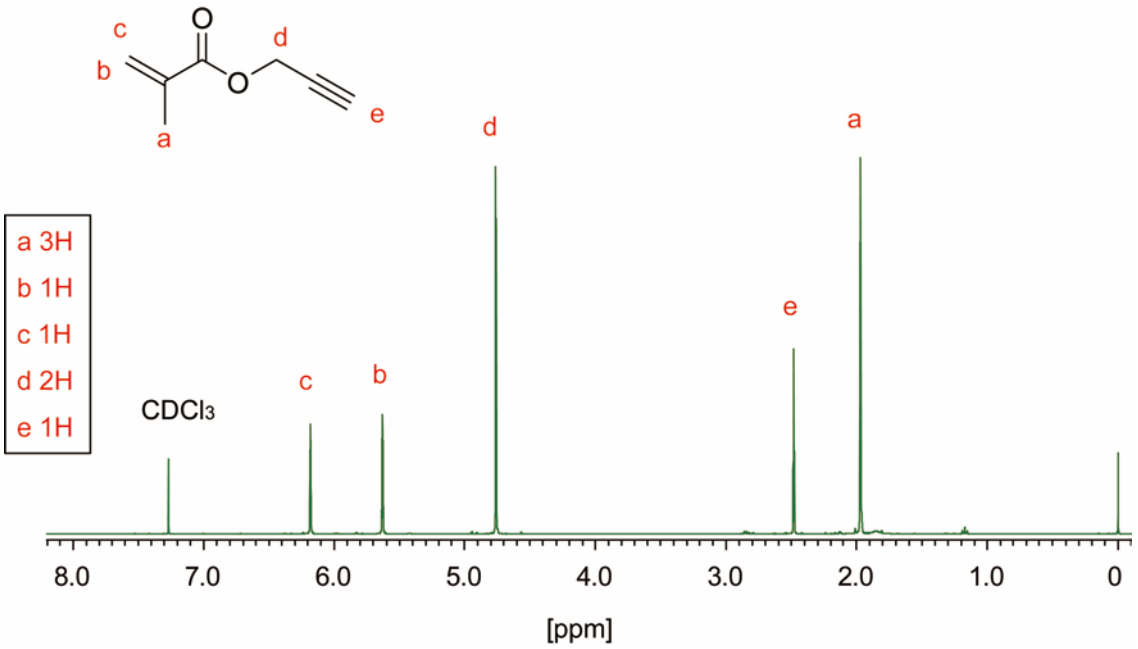
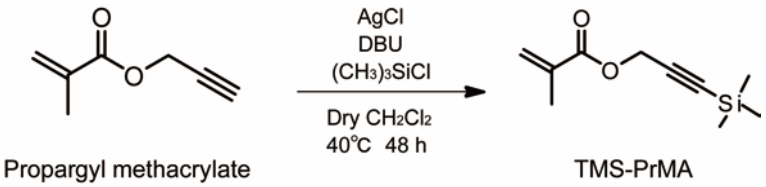


Figure S1. ^{1}H NMR spectrum of Pr-MA.

Synthesis of Trimethylsilyl propargyl methacrylate (TMS-PrMA)



Pr-MA (1 eq, 86.7 mmol, 10.8 g), silver (I) chloride (AgCl) (0.1 eq, 8.7 mmol, 1.2 g) and 1,8-diazabicyclo [5.4.0] undec-7-ene 1.3 eq, 110.8 mmol, 16.8 g) were dissolved in 119 mL of anhydrous CH_2Cl_2 with a condenser, and the solution was stirred with a magnetic stirrer for 15 min. Chlorotrimethylsilyl (2 eq, 175.4 mmol, 19.1 g) was added and stirred at 40°C for 48 h. The reaction mixture was diluted with 200 mL of hexane, and washed 4 times with saturated $NaHCO_3$aq, and 3 times with pure water. The organic layer was dried with anhydrous $MgSO_4$ and filtered off. The solution was evaporated under vacuum to yield colorless oil (yield : 10.2 g, 60%).

^{1}H NMR ($CDCl_3$, δ in ppm): 6.18 (ddd, J = 1.4, 2.4 Hz, trans C**H**$_2$=CH, 1H), 5.68 (ddd, J = 1.4, 2.7 Hz, cis C**H**$_2$=CH, 1H), 4.76 (s, -C**H**$_2$-C≡CH, 2H), 1.97 (t, J = 1.4 Hz, -CH$_2$-C-C**H**$_3$, 3H), 0.19 (s, Si(C**H**$_3$)$_3$, 9H).

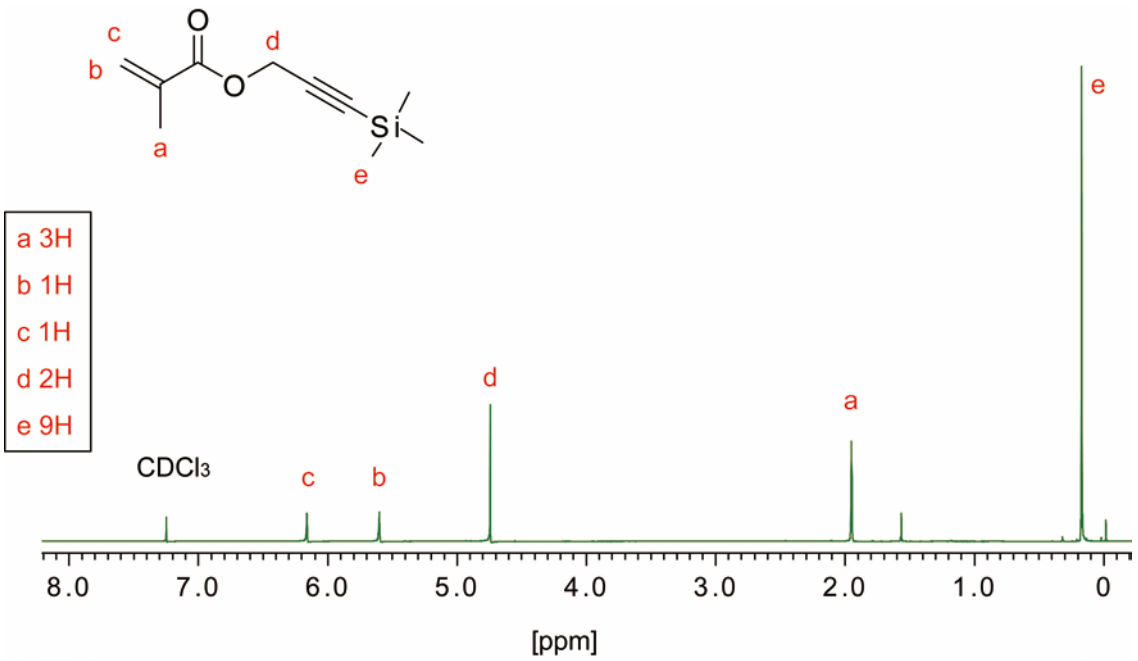
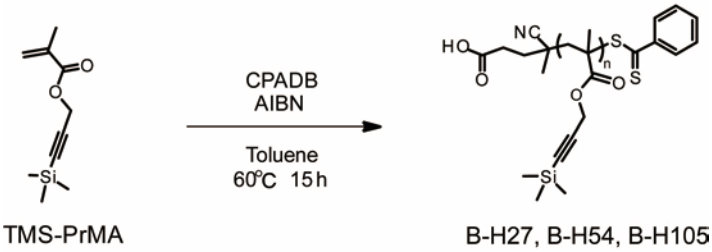


Figure S2. ^{1}H NMR spectrum of TMS-PrMA.

Synthesis of Poly(TMS-PrMA)$_n$ (B-H27, B-H54, B-H105)



TMS-PrMA (4.0 mmol, 786.0 mg), 4-cyano-4-(phenylcarbonothioylthio) pentanoic acid (CPADB) (**B-H27** : 0.160 mmol, 22.4 mg, **B-H54** : 0.080 mmol, 11.2 mg, **B-H105** : 0.040 mmol, 5.6 mg) and azobisisobutyronitrile (AIBN) (**B-H27** : 0.032 mmol, 5.3 mg, **B-H54** : 0.016 mmol, 2.7 mg, **B-H105** : 0.008 mmol, 1.3 mg) were dissolved in 1 mL toluene with a glass tube. The reaction mixture was degassed by three freeze-pump-thaw cycles, and sealed with a gas burner. The polymerization was conducted at 60 °C for 15 h. The reaction mixture was diluted in 1 mL of acetone, and precipitated in a mixed solution of 30 mL MeOH, 3 mL water and 0.1 mL 1 M HCl_{aq}. The polymer solution was separated by centrifugation for 20 min. The obtained precipitate was dissolved in acetone and dried again under vacuum (yields : 481.0 mg, 62% (**B-H27)**, 626.0 mg, 80% (**B-H54)**, 588.0 mg, 75% (**B-H105**)).

(Figure S3-1,2)

^{1}H NMR ($CDCl_3$, δ in ppm): 7.91 (brs, -C**H**-CH-C-), 7.46 (brs, -C**H**-CH-CH-C-), 7.19 (brs, -CH-C**H**-C-), 4.65 (brs, -C**H**$_2$-C≡C-, 2H), 1.91 (brs, -C-C**H**$_2$-C-, 2H), 1.11 (brs, -CH$_2$-C-C**H**$_3$), 0.94 (brs, -CH$_2$-C-C**H**$_3$, 3H), 0.20 (brs, Si(C**H**$_3$)$_3$, 9H).

(Figure S3-3)

^{1}H NMR ($(CD_3)_2NCDO$, δ in ppm): 7.23 (brs, -C**H**-C**H**-C**H**-C-), 4.79 (brs, -C**H**$_2$-C≡C-, 2H), 1.98 (brs, -C-C**H**$_2$-C-, 2H), 1.16 (brs, -CH$_2$-C-C**H**$_3$), 0.99 (brs, -CH$_2$-C-C**H**$_3$, 3H), 0.24 (brs, Si(C**H**$_3$)$_3$, 9H).

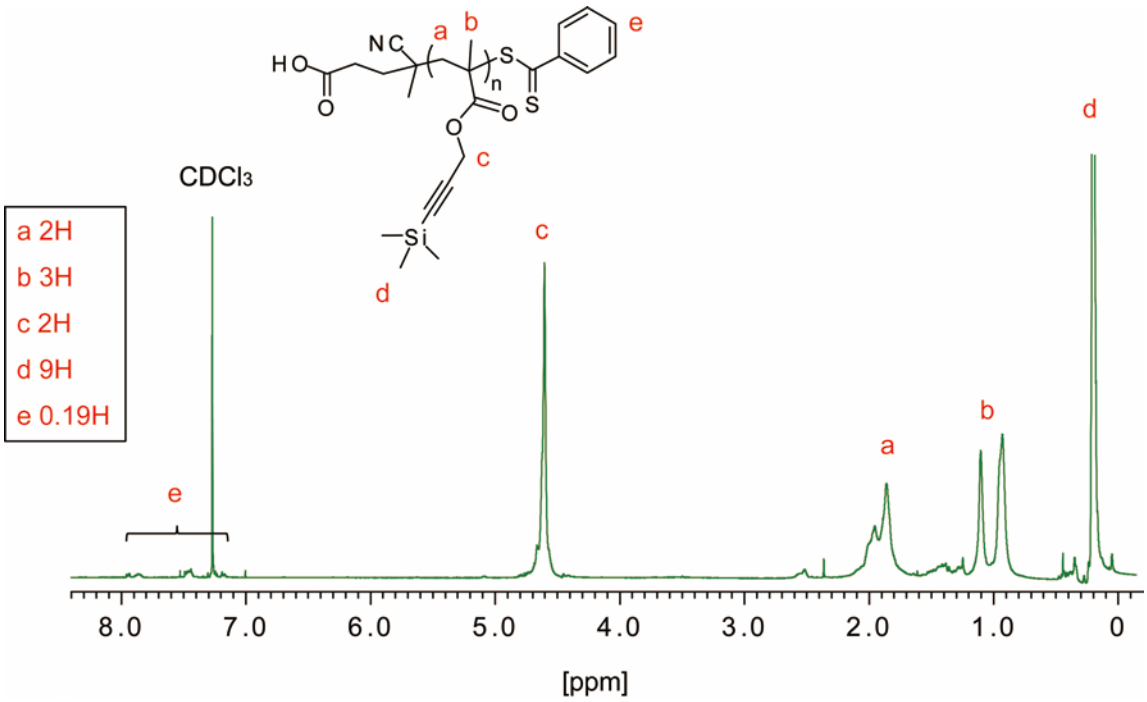


Figure S3-1. ^{1}H NMR spectrum of Poly(TMS-PrMA)$_{27}$ (**B-H27**).

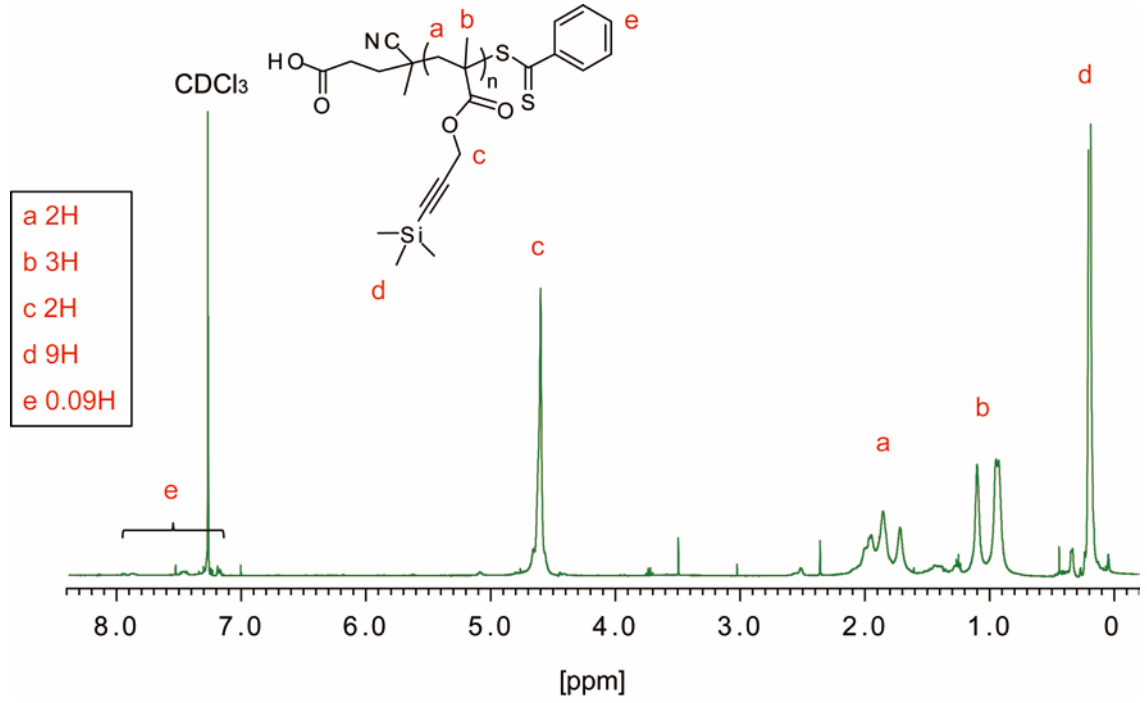


Figure S3-2. ^{1}H NMR spectrum of Poly(TMS-PrMA)$_{54}$ (**B-H54**).

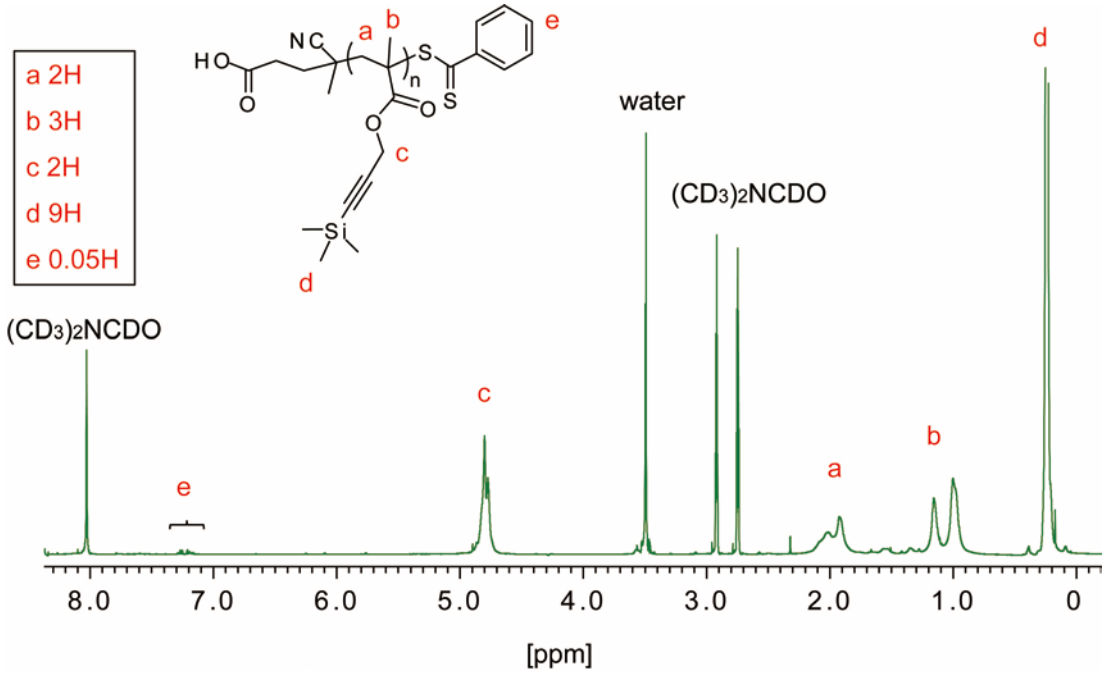
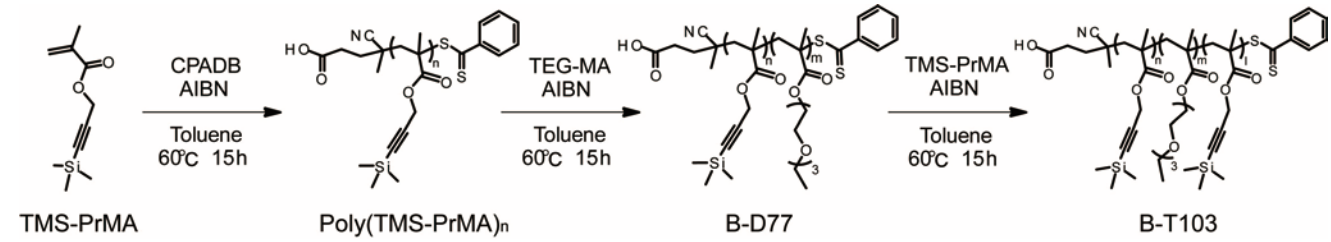


Figure S3-3. ^{1}H NMR spectrum of Poly(TMS-PrMA)$_{105}$ (**B-H105**).

Synthesis of [(TMS-PrMA)$_n$-*b*-(TEG-MA)$_m$-*b*-(TMS-PrMA)$_l$] (B-D77, B-T103)



TMS-PrMA (25 eq, 2.0 mmol, 393.0 mg), CPADB (1 eq, 0.080 mmol, 22.4 mg) and AIBN (0.2 eq, 0.016 mmol, 2.7 mg) were dissolved in 1mL toluene with a glass tube, and the reaction mixture was degassed by three freeze-pump-thaw cycles. The tube was sealed with a gas burner, and reacted with an oil bath at 60 ℃ for 15 h. The conversion was measured by ^{1}H NMR. The reaction mixture was diluted with 1 mL acetone, and precipitated in a mixed solution of 30 mL MeOH, 3mL water and 0.1 mL 1M HCl_{aq}. The polymer solution was separated by centrifugation for 20 min. The obtained precipitate was dissolved in acetone and dried again under vacuum. The obtained product (1 eq, 0.053 mmol, 339.0 mg), TEG-MA (50 eq, 2.65 mmol, 652.7 mg) and AIBN (0.2 eq, 0.011 mmol, 1.8 mg) were placed in a glass tube with 1 mL of toluene, where the obtained product was used as macro-RAFT reagent. Reaction and analysis were carried out under the same conditions. The compound (**B-D77**) was purified by dialysis (MWCO: 3500) against acetone where the solvent was changed 4 times every 4 h, and dried under vacuum (yield : 881.0 mg, 89%). **B-D77** was used as macro-RAFT, and tri-block copolymer was prepared. **B-D77** (1 eq, 0.015 mmol, 265.5 mg), TMS-PrMA (40 eq, 0.600 mmol, 117.8 mg) and AIBN (0.2 eq, 0.003 mmol, 0.5 mg) were dissolved in 1 mL of toluene with a glass tube, and the tri-blockcopolymer (**B-T103**) was obtained by the same procedure as the diblock copolymer (yield : 339.0 mg, 82%).

(Figure S4-1)

^{1}H-NMR ($(CD_3)_2CO$, δ in ppm): 4.72 (brs, -C**H**$_2$-C≡C-, 2H), 4.14 (brs, -C**H**$_2$-CH_2-O-, 3H), 3.75 (brs, -C-O-CH_2-C**H**$_2$-O-, 3H), 3.66 (brs, -O-C**H**$_2$-C**H**$_2$-O-, 6H), 3.64 (brs, -C**H**$_2$-CH_2-O-CH_2-CH_3, 3H), 3.58 (brs, -CH_2-C**H**$_2$-O-CH_2-CH_3, 3H), 3.52 (brs, -C**H**$_2$-CH_3, 3H), 1.91 (brs, -C-C**H**$_2$-C-, 5H), 1.19 (brs, -CH_2-C**H**$_3$, 4.5H), 1.17 (brs, -CH_2-C-C**H**$_3$), 0.97 (brs, -CH_2-C-C**H**$_3$, 7.5H), 0.23 (brs, Si(C**H**$_3$)$_3$, 9H).

(Figure S4-2)

^{1}H NMR ($(CD_3)_2CO$, δ in ppm): 4.72 (brs, -C**H**$_2$-C≡C-, 2H), 4.14 (brs, -C**H**$_2$-CH_2-O-, 1.6H), 3.75 (brs, -C-O-CH_2-C**H**$_2$-O-, 1.6H), 3.66 (brs, -O-C**H**$_2$-C**H**$_2$-O-, 3.2H), 3.64 (brs, -C**H**$_2$-CH_2-O-CH_2-CH_3, 1.6H), 3.59 (brs, -CH_2-C**H**$_2$-O-CH_2-CH_3, 1.6H), 3.53 (brs, -C**H**$_2$-CH_3, 1.6H), 1.91 (brs, -C-C**H**$_2$-C-, 3.6H), 1.19 (brs, -CH_2-C**H**$_3$, 2.4H), 1.17 (brs, -CH_2-C-C**H**$_3$), 0.98 (brs, -CH_2-C-C**H**$_3$, 5.4H), 0.23 (brs, Si(C**H**$_3$)$_3$, 9H).

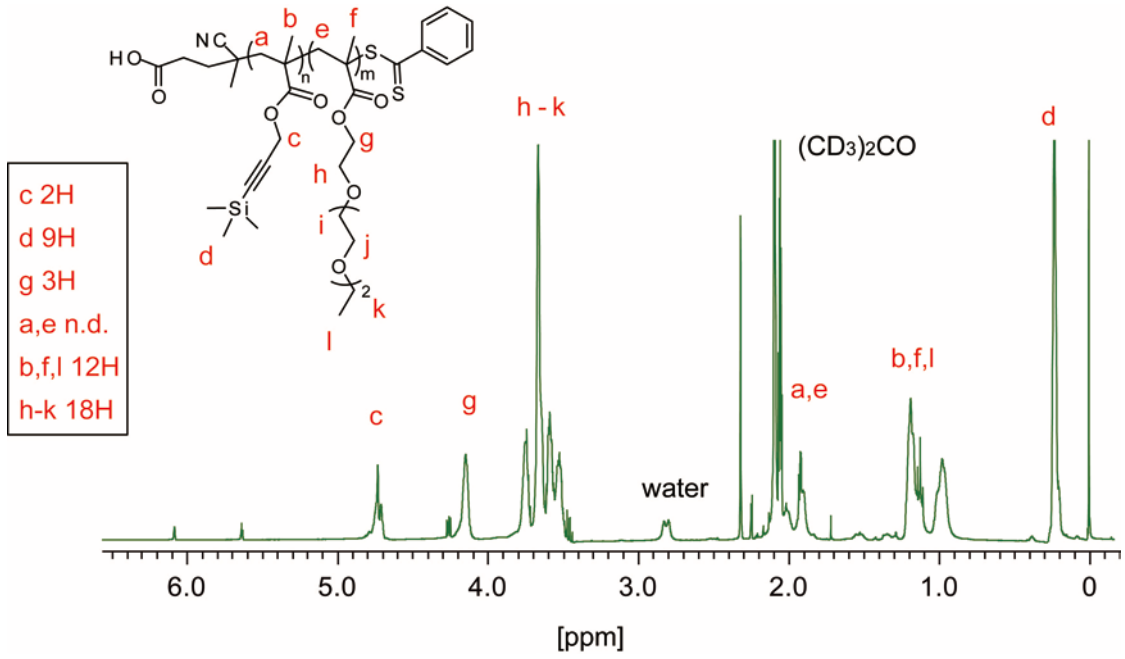


Figure S4-1. ^{1}H NMR spectrum of [(TMS-PrMA)$_{31}$-*b*-(TEG-MA)$_{46}$] (**B-D77**).

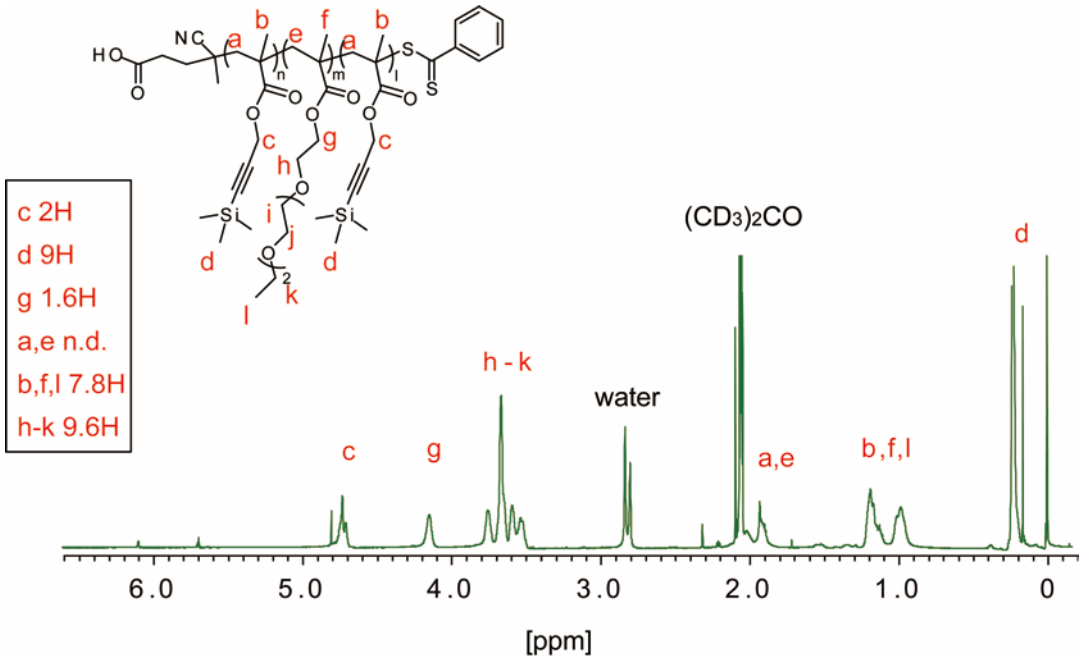
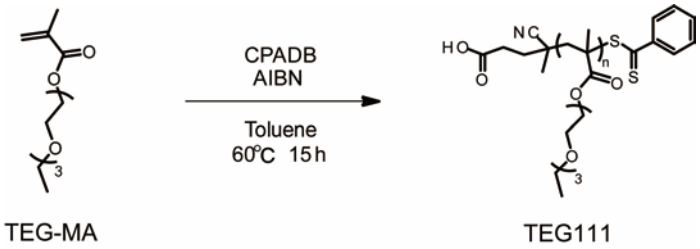


Figure S4-2. ^{1}H NMR spectrum of [(TMS-PrMA)$_{31}$-*b*-(TEG-MA)$_{46}$-*b*-(TMS-PrMA)$_{26}$] (**B-T103**).

Synthesis of Poly(TEG-MA)$_n$ (TEG111)



TEG-MA (100 eq, 8.0 mmol, 1970.4 mg), CPADB (1 eq, 0.080 mmol, 22.4 mg) and AIBN (0.2 eq, 0.016 mmol, 2.7 mg) were dissolved in 1 mL toluene with a glass tube, and the reaction mixture was degassed by three freeze-pump-thaw cycles. The glass tube was sealed with a gas burner, and the polymerization was performed at 60°C for 15 h. The conversion was measured by ^{1}H NMR. The product was purified by dialysis (MWCO 3500) against acetone exchanging 4 times every 4h, and dried under vacuum (yield : 1637.0 mg, 82%).

^{1}H-NMR ($(CD_3)_2CO$, δ in ppm): 7.90 (brs, -C**H**-CH-C-), 7.60 (brs, -C**H**-CH-CH-C-), 7.46 (brs, -CH-C**H**-C-), 4.11 (brs, -C**H**$_2$-CH$_2$-O-, 2H), 3.71 (brs, -C-O-CH$_2$-C**H**$_2$-O-, 2H), 3.62 (brs, -O-C**H**$_2$-C**H**$_2$-O-, 4H), 3.55 (brs, -C**H**$_2$-CH$_2$-O-CH$_2$-CH$_3$, 2H), 3.49 (brs, -CH$_2$-C**H**$_2$-O-CH$_2$-CH$_3$, 2H), 3.48 (brs, -C**H**$_2$-CH$_3$, 2H), 1.91 (brs, -C-C**H**$_2$-C-, 2H), 1.19 (brs, -CH$_2$-C**H**$_3$, 3H), 1.15 (brs, -CH$_2$-C-C**H**$_3$), 0.93 (brs, -CH$_2$-C-C**H**$_3$, 3H).

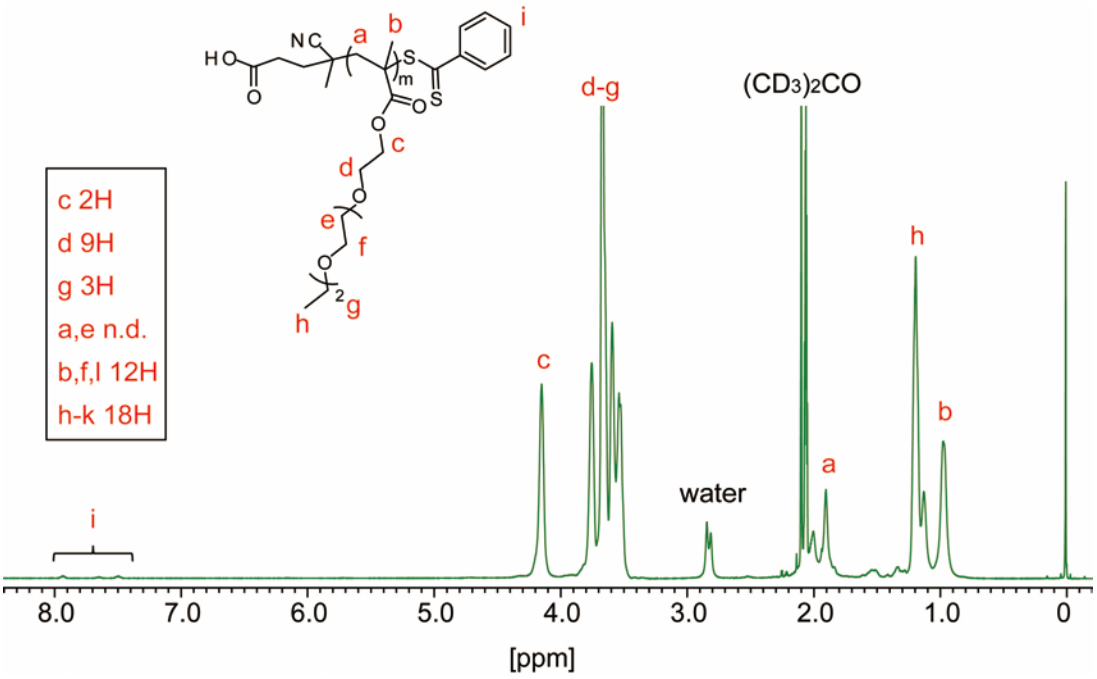


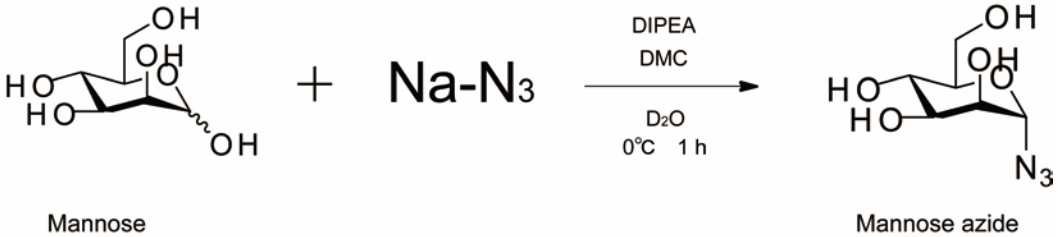
Figure S5. ^{1}H NMR spectrum of **TEG111**.

Table S1. The results of polymerization of of polymer backbones.

	1st block (Pr-MA) (mer)[a]	2nd block (TEG-MA) (mer)[a]	3rd block (Pr-MA) (mer)[a]	$M_{n,NMR}$ (g mol^{-1})	$M_{n,GPC}$ (gmol^{-1})[b]	M_w / M_n
B-H27	27	---	---	5600	3200	1.41
B-H54	54	---	---	10900	7800	1.34
B-H105	105	---	---	20900	20700	1.42
B-D77	31	46	---	17700	12500	1.67
B-T103	31	46	26	22800	15600	1.67
TEG111	---	111	---	27600	15600	1.36

[a]. Determined by ^{1}H NMR. b. Calculated by pullulan standard.

Synthesis of mannose azide



Mannose Mannose azide

Mannose・H_2O (1 eq, 2.8 mmol, 500 mg), Na_2O_3 (10 eq, 28.0 mmol, 1810 mg) and *N*,*N*-diisopropylethylamine (DIPEA; 9 eq, 25.0 mmol, 4.31 mL) were dissolved in 11 mL of D_2O in an ice bath. The solution was added to 2-chloro-1,3-

dimethylimidazolinium chloride (DMC; 3 eq, 8.3 mmol, 1410 mg) and stirred at 0 °C for 1 h. The completion of the reaction was confirmed by ^{1}H NMR where the anomer position peak became one. The solvent was removed under reduced pressure, dissolved in EtOH and filtered. The solution was removed under reduced pressure. The compound was dissolved in 50 mL of H_2O, and washed with CH_2Cl_2. The water layer was stirred with cation exchange resin for 3h. The solution was filtered, distilled, dissolved with EtOH and evaporated. The product was dissolved in water, and lyophilized for 3 days (yield : 392.0 mg, 69%).

^{1}H NMR ($(CD_3)_2SO$, δ in ppm): 5.32 (dd, J = 1.8 Hz, -C**H**-N_3, 1H), 3.77 (d, J = 10.1 Hz, -C**H**$_2$-OH), 3.73 (dd, J = 2.3, 3.2 Hz, -C**H**$_2$-OH, 2H), 3.65 (t, J = 6.4 Hz, -CH-C**H**-CH_2-, 1H), 3.60 (m, -C**H**-CH-CH-N_3, 1H), 3.52 (dd, J = 4.1, 9.6 Hz, -C**H**-CH-CH_2-, 1H), 3.49 (t, J = 5.3 Hz, -CH-C**H**-CH-N_3, 1H).

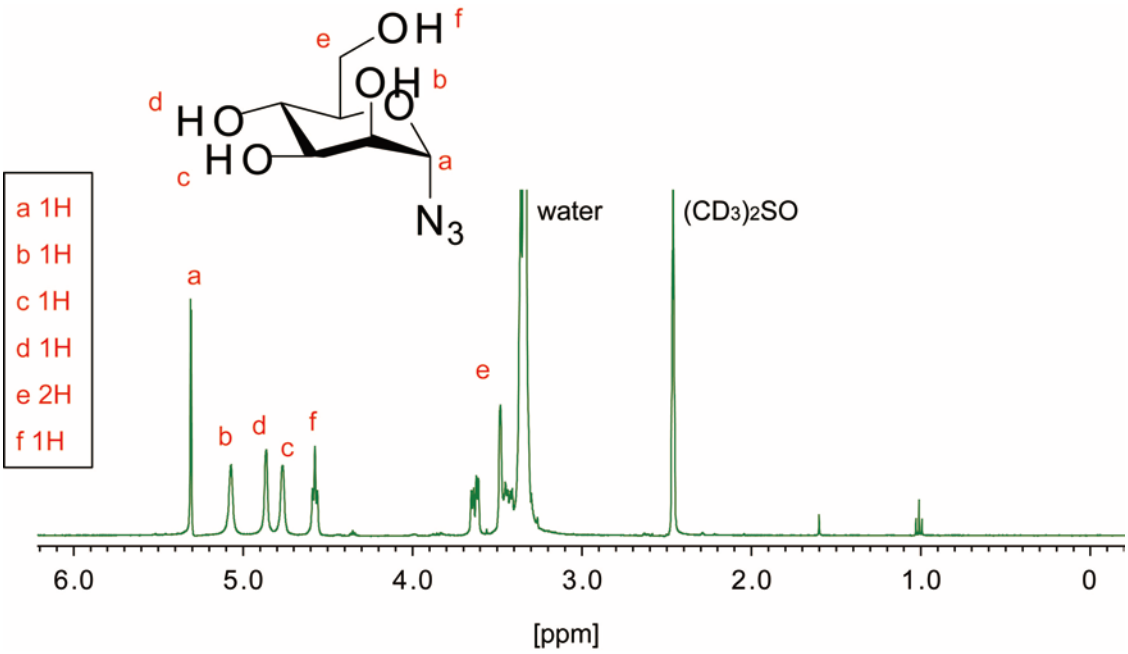
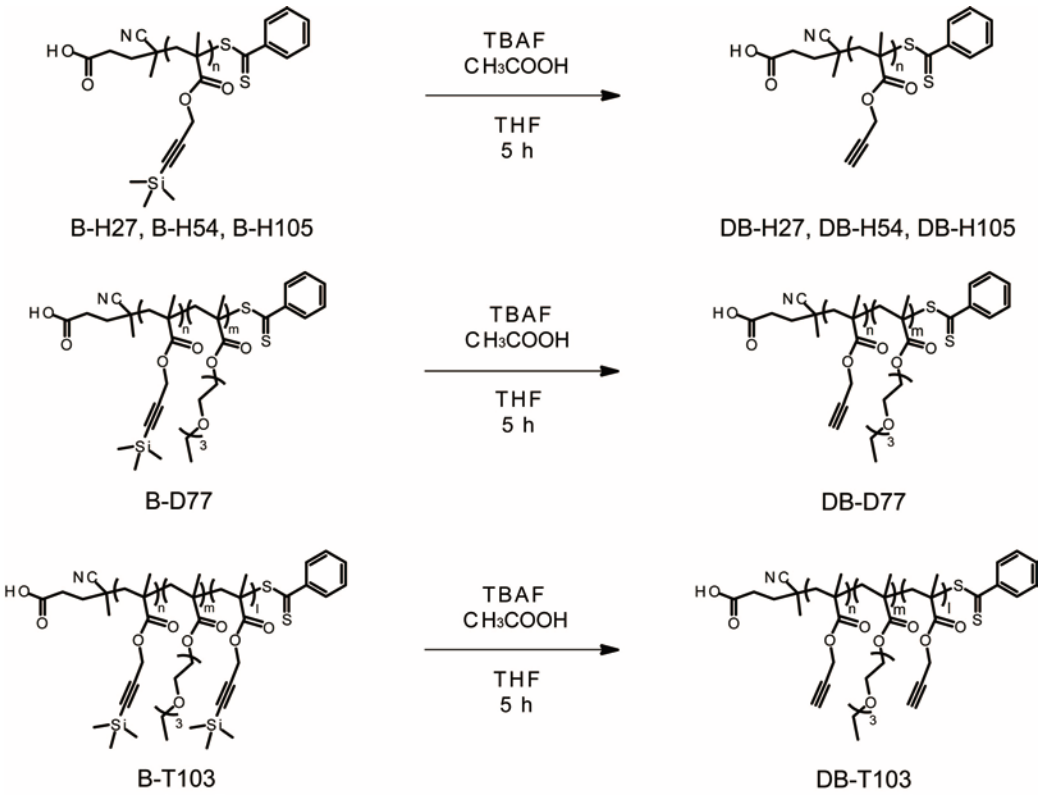


Figure S6. ^{1}H NMR spectrum of mannose azide.

Deprotection of polymer (DB-H27, DB-H54, DB-H105, DB-D77, DB-T103)



Polymer backbone, tetra-n-butylammonium fluoride (TBAF; 1.5 eq) and CH_3COOH (1.5 eq) were dissolved in 1 mL of dehydrated tetrahydrofuran (THF) with 1 equivalent of the TMS protecting group, and stirred at room temperature for 5 h. The solution was poured into a teflon-made round flask, and concentrated under reduced pressure. The reaction mixture was dissolved in DMSO, and purified by dialysis (MWCO 3500) with DMSO 3 times every 4 h, 1 M HCl_{aq} at pH4 2 times and water. The obtained product was lyophilized to yield solid compounds (yields : 47% (**DB-H27)**, 29% (**DB-H54)**, 70% (**DB-H105**), 71% (**DB-D77)**, 80% (**DB-T103**)).

(Figure S7-1,2,3)

^{1}H NMR ($(CD_3)_2NCDO$, δ in ppm): 4.78 (brs, -C**H**$_2$-C≡CH, 2H), 1.98 (brs, -C-C**H**$_2$-C-, 2H), 1.12 (brs, -CH_2-C-C**H**$_3$), 0.97 (brs, -CH_2-C-C**H**$_3$, 3H).

(Figure S7-4)

^{1}H NMR ($CDCl_3$, δ in ppm): 4.62 (brs, -C**H**$_2$-C≡CH, 2H), 4.09 (brs, -C**H**$_2$-CH_2-O-, 3H), 3.66 (brs, -C-O-CH_2-C**H**$_2$-O-, -O-C**H**$_2$-C**H**$_2$-O-, -C**H**$_2$-CH_2-O-CH_2-CH_3, 12H), 3.61 (brs, -CH_2-C**H**$_2$-O-CH_2-CH_3, 3H), 3.54 (brs, -C**H**$_2$-CH_3, 3H), 2.52 (brs, -C≡C**H**, 1H), 1.90 (brs, -C-C**H**$_2$-C-, 2H), 1.12 (brs, -CH_2-C**H**$_3$, 4.5H), 1.07 (brs, -CH_2-C-C**H**$_3$), 0.92 (brs, -CH_2-C-C**H**$_3$, 7.5H).

(Figure S7-5)

^{1}H NMR ($CDCl_3$, δ in ppm): 4.62 (brs, -C**H**$_2$-C≡CH, 2H), 4.09 (brs, -C**H**$_2$-CH_2-O-, 1.6H), 3.66 (brs, -C-O-CH_2-C**H**$_2$-O-, -O-C**H**$_2$-C**H**$_2$-O-, -C**H**$_2$-CH_2-O-CH_2-CH_3, 6.4H), 3.61 (brs, -CH_2-C**H**$_2$-O-CH_2-CH_3, 1.6H), 3.54 (brs, -C**H**$_2$-CH_3, 1.6H), 2.52 (brs, -C≡C**H**, 1H), 1.90 (brs, -C-C**H**$_2$-C-, 2H), 1.12 (brs, -CH_2-C**H**$_3$, 2.4H), 1.07 (brs, -CH_2-C-C**H**$_3$), 0.92 (brs, -CH_2-

C-C**H**$_3$, 5.4H).

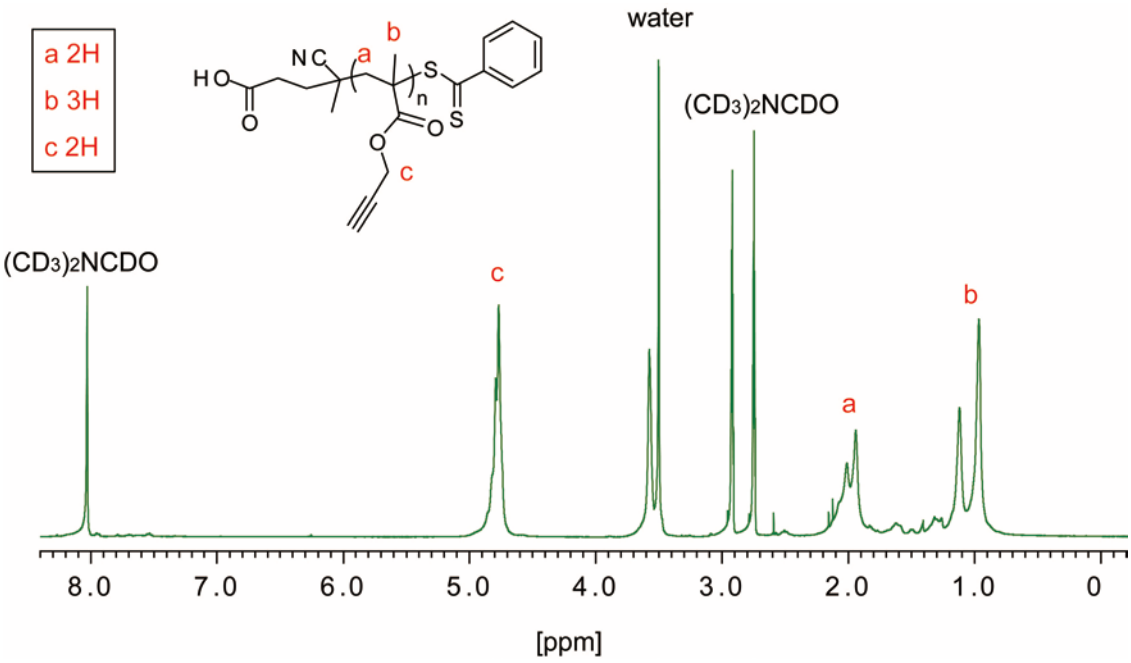


Figure S7-1. ^{1}HNMR spectrum of deprotected **B-H27**.

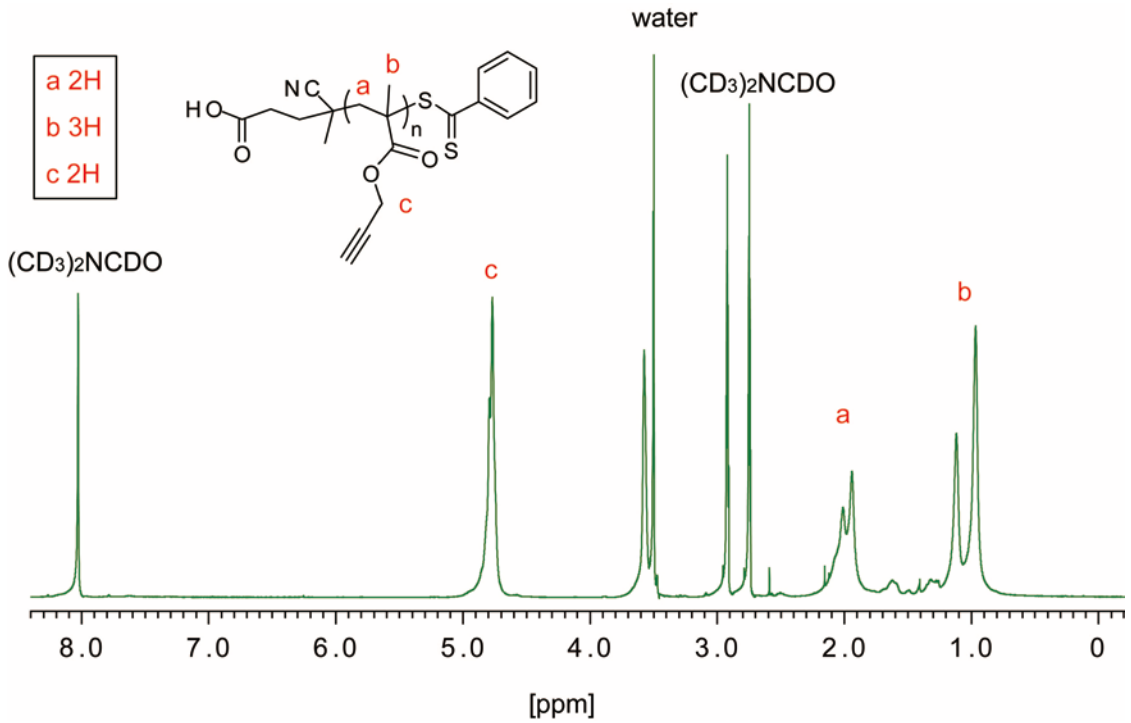


Figure S7-2. ^{1}HNMR spectrum of deprotected **B-H54**.

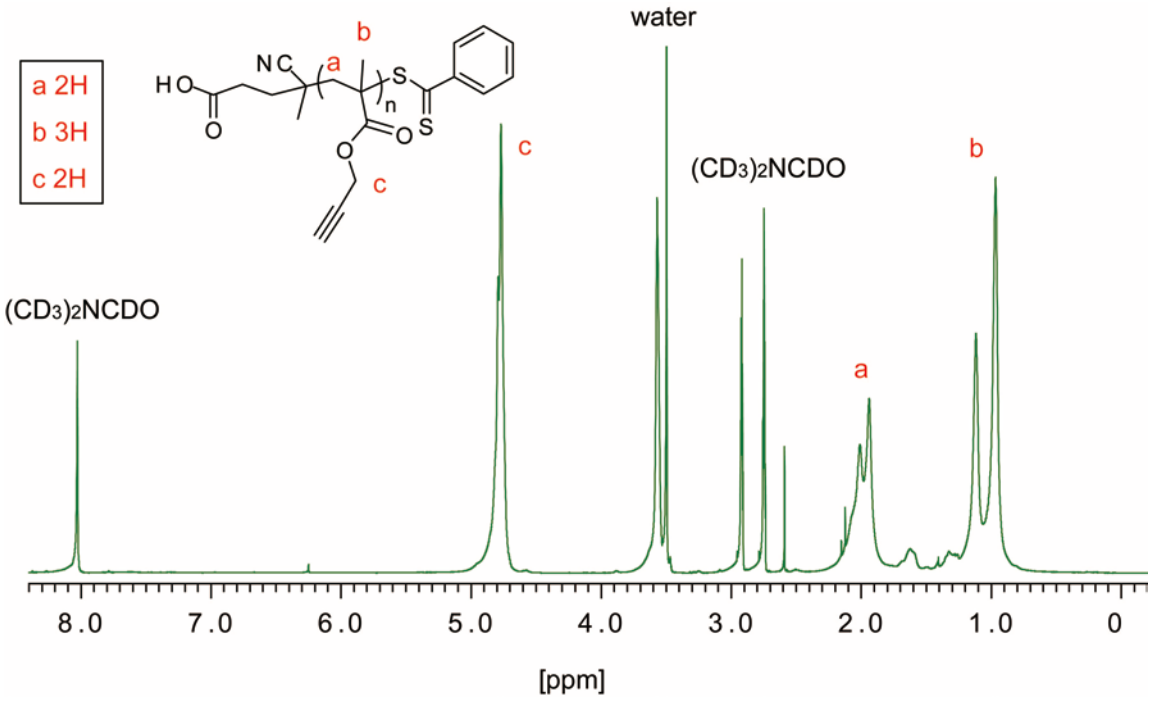


Figure S7-3. [1]HNMR spectrum of deprotected **B-H105**.

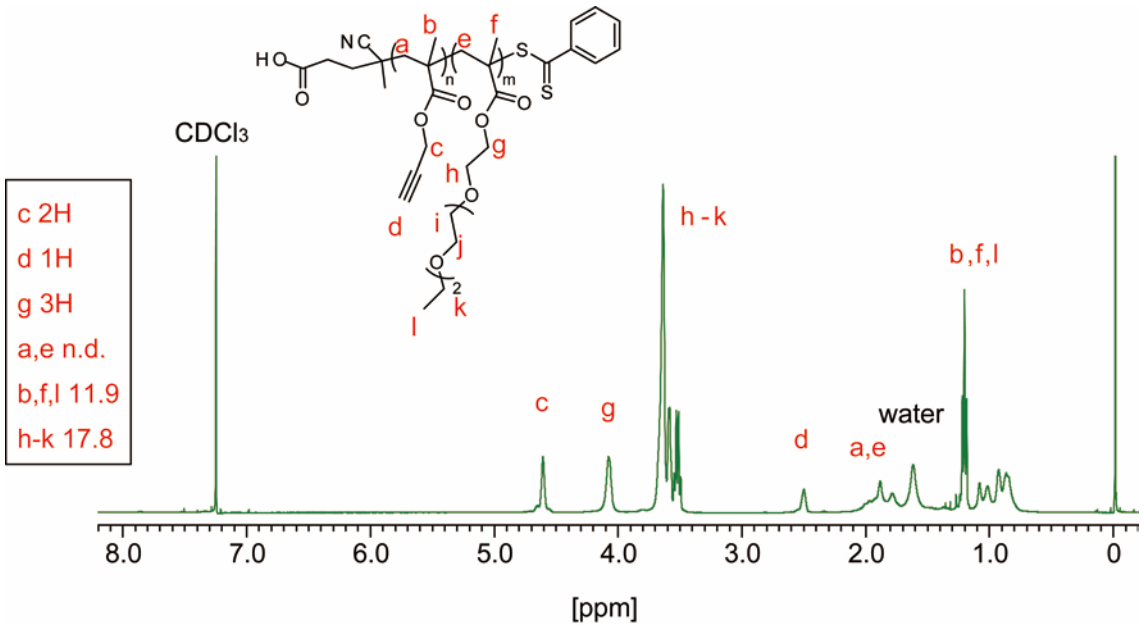


Figure S7-4. [1]HNMR spectrum of deprotected **B -D77**.

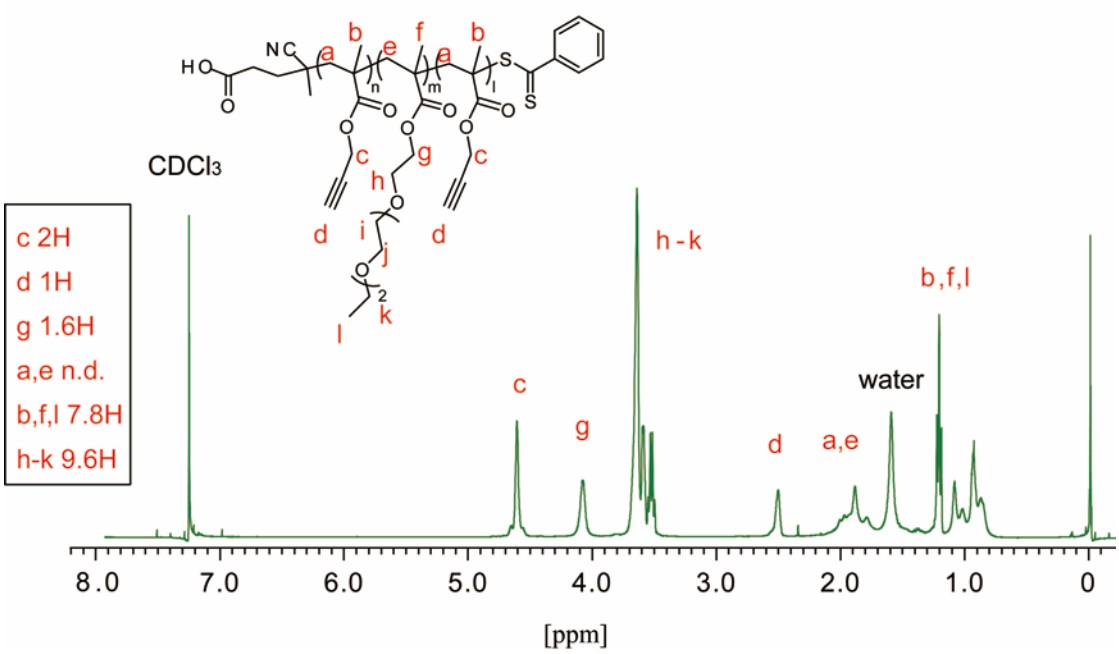
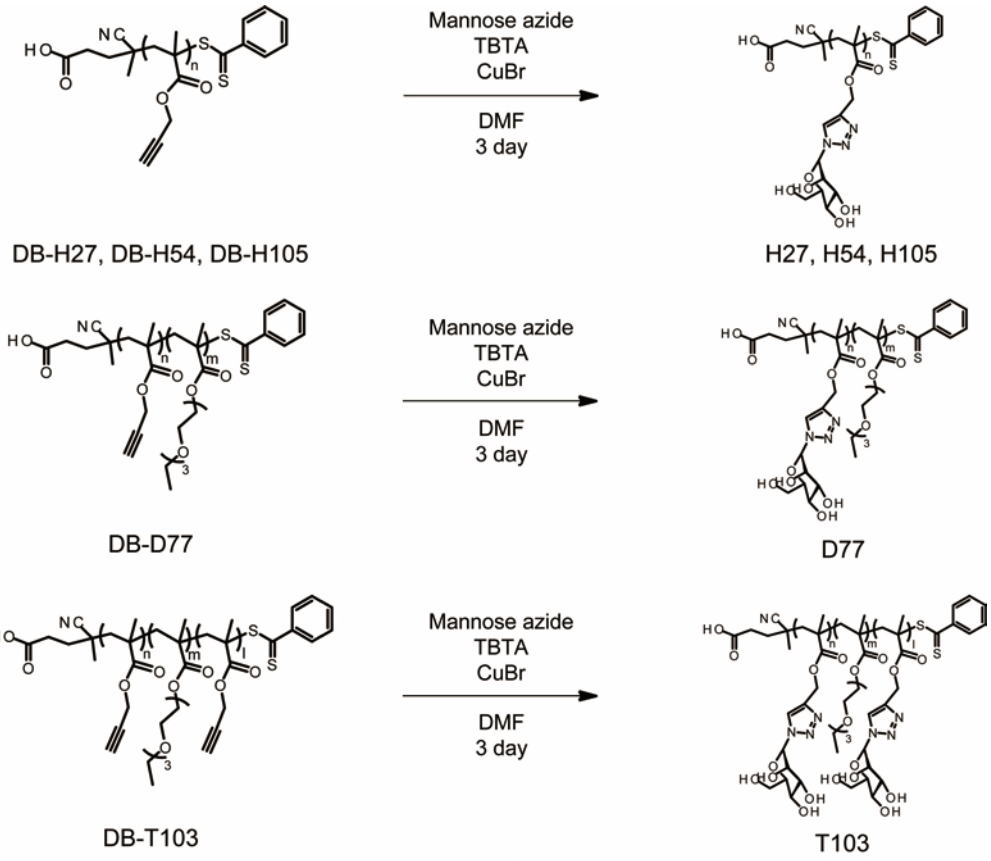


Figure S7-5. [1]HNMR spectrum of deprotected **B -T103**.

Mannose-introduced by click chemistry (H27, H54, H103, D77, T103)



The molar ratio for click chemistry is described in Table S2. Mannose azide, tris[(1-benzyl-1H-1, 2, 3-triazol-4-yl) methyl] amine (TBTA) and triethylamine (TEA) were dissolved in 1 mL of DMF. The solution was bubbled with N_2 for 15 min. CuBr was added to the solution and bubbled with N_2 for 5 min. The solution was reacted in a glove box for 3 days.

The product was purified by dialysis against DMSO with 1M HCl_{aq} at pH 4, and the solution was exchanged 3 times every 4 h. Then, the product was purified by dialysis against water. The product was obtained by lyophilization (yields : 71% (**H27)**, 81% (**H54)**, 93% (**H105**), 89% (**D77)**, 88% (**T103**)).

(Figure S8-1,2,3)

^{1}H NMR ($(CD_3)_2SO$, δ in ppm): 8.32 (brs, -C-C**H**-N-, 1H), 5.98 (brs, -N-C**H**-O-, 1H), 5.08 (brs, -O-C**H**$_2$-C-, 2H), 0.80 (brs, -CH_2-C-C**H**$_3$), 0.54 (brs, -CH_2-C-C**H**$_3$, 3H).

(Figure S8-4)

^{1}H NMR ($(CD_3)_2SO$, δ in ppm): 8.46 (brs, -C-C**H**-N-), 8.31 (brs, -C-C**H**-N-, 0.91H), 5.98 (brs, -N-C**H**-O-, 0.91H), 5.06 (brs, -O-C**H**$_2$-C-, 2H), 4.01 (brs, -C**H**$_2$-CH_2-O-, 3H), 1.11 (brs, -CH_2-C**H**$_3$, 4.5H), 0.95 (brs, -CH_2-C-C**H**$_3$), 0.78 (brs, -CH_2-C-C**H**$_3$, 7.5H).

(Figure S8-5)

^{1}H NMR ($(CD_3)_2SO$, δ in ppm): 8.46 (brs, -C-C**H**-N-), 8.32 (brs, -C-C**H**-N-, 0.83H), 5.98 (brs, -N-C**H**-O-, 0.83H), 5.07 (brs, -O-C**H**$_2$-C-, 2H), 4.02 (brs, -C**H**$_2$-CH_2-O-, 1.6H), 1.11 (brs, -CH_2-C**H**$_3$, 2.4H), 0.95 (brs, -CH_2-C-C**H**$_3$), 0.79 (brs, -CH_2-C-C**H**$_3$, 5.4H).

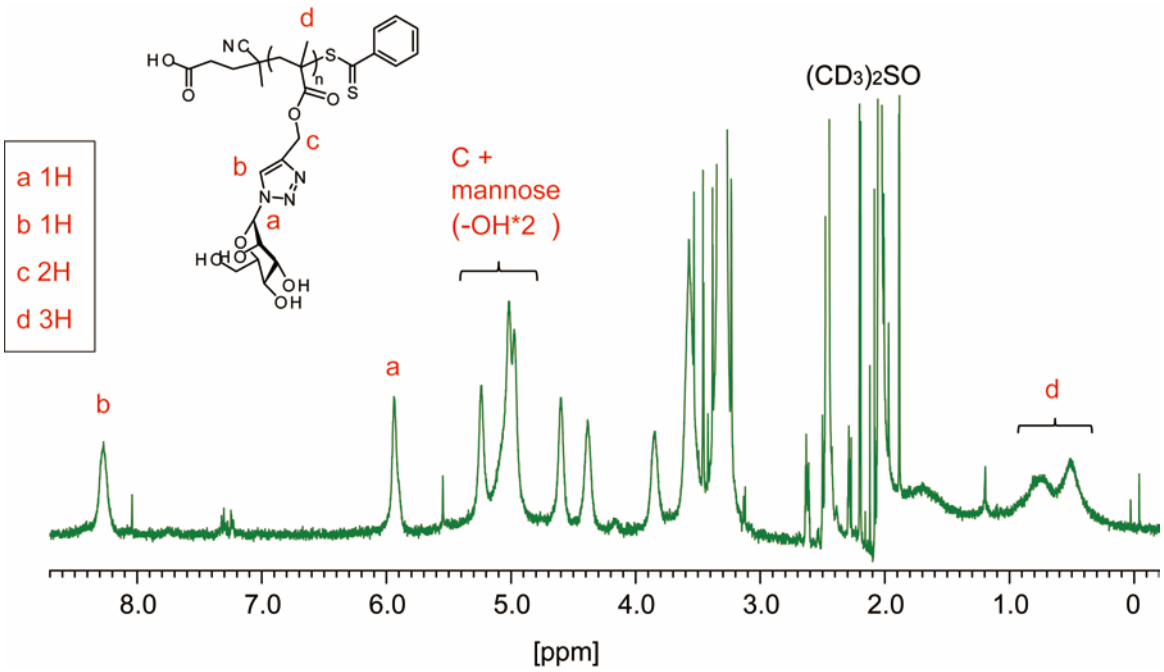


Figure S8-1. ^{1}H NMR spectrum of **H27.**

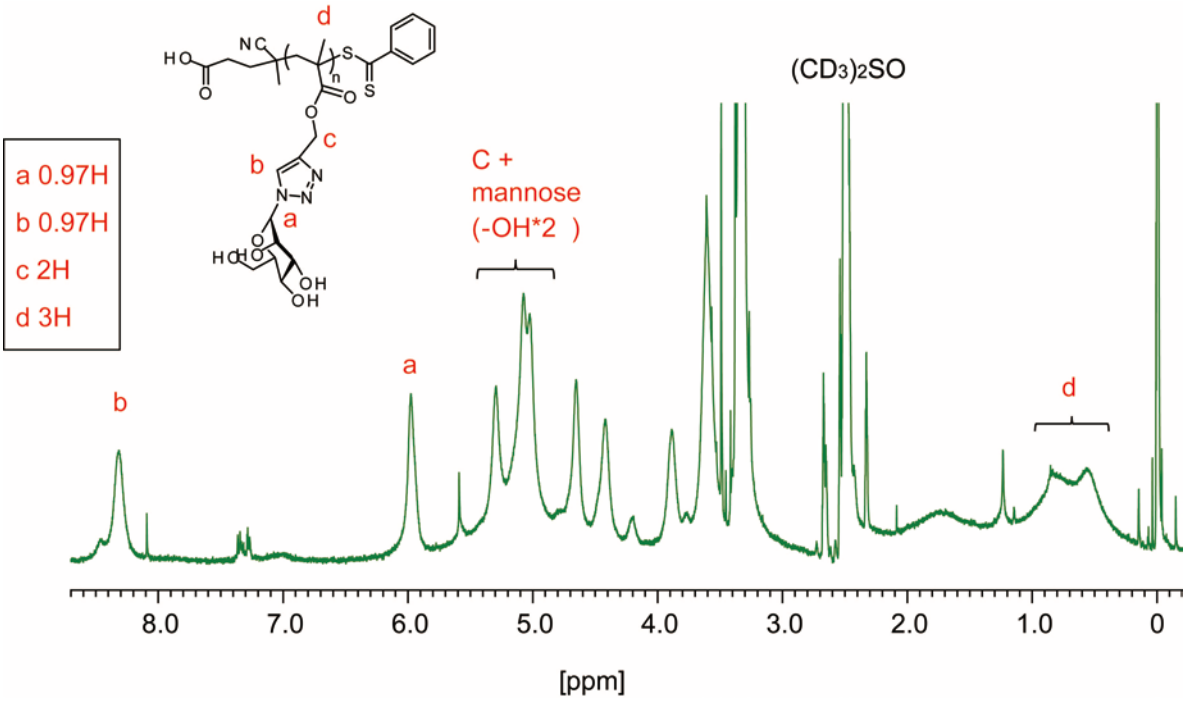


Figure S8-2. ^{1}H NMR spectrum of **H54.**

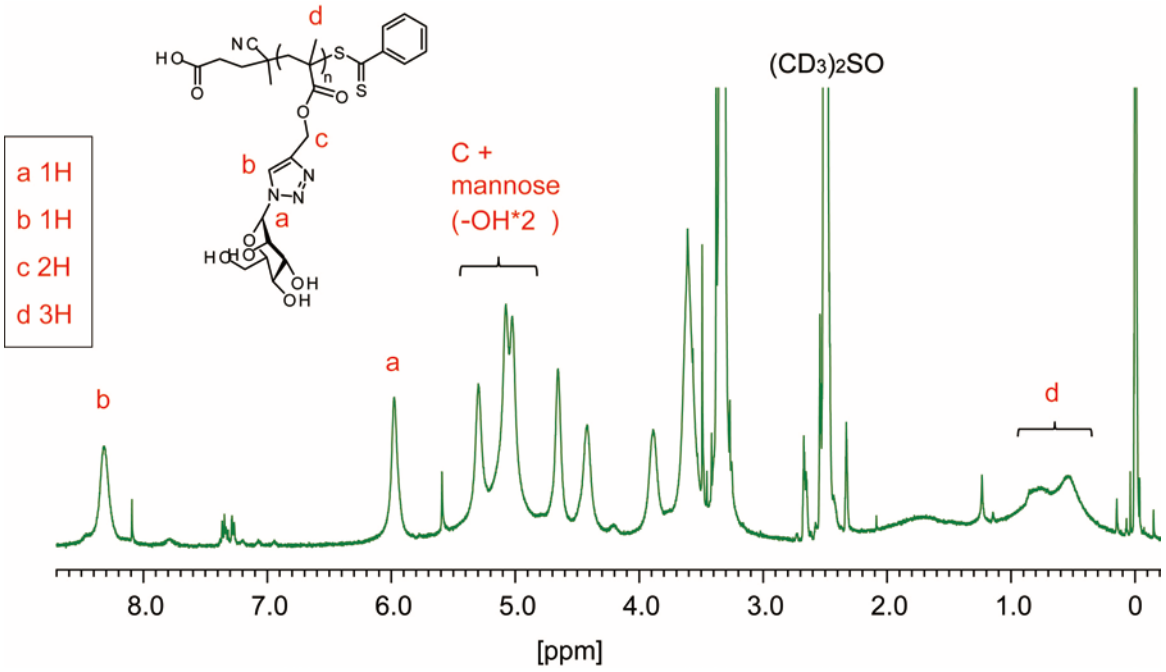


Figure S8-3. ^{1}H NMR spectrum of **H103.**

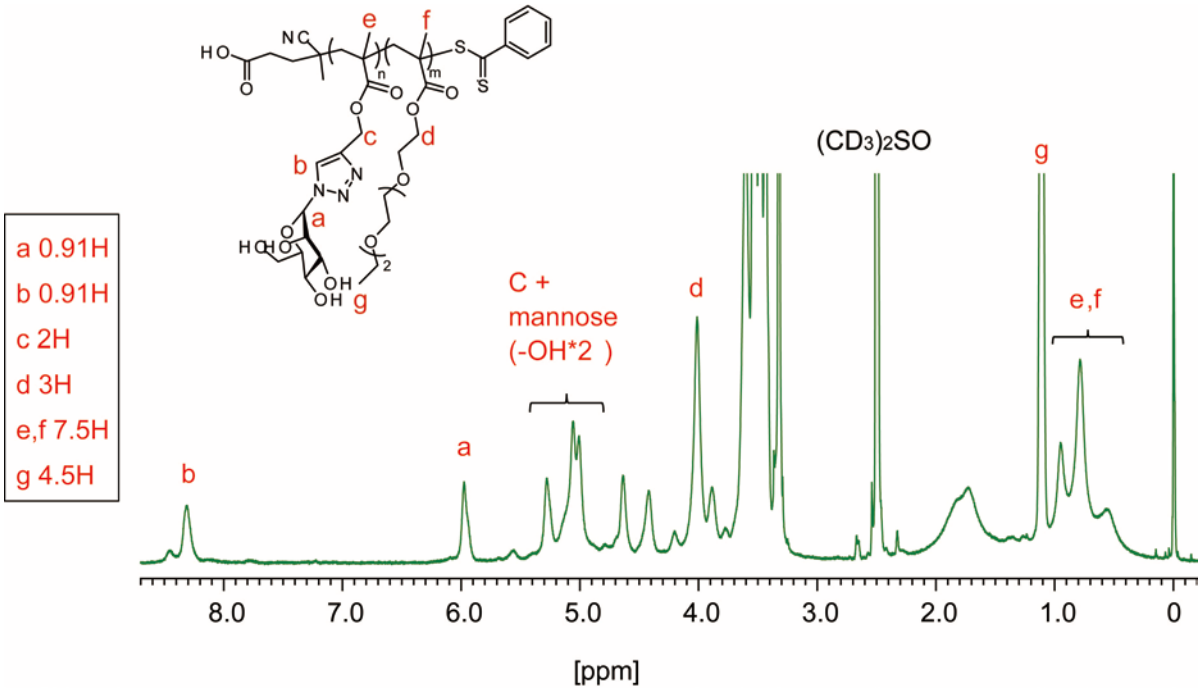


Figure S8-4. ^{1}H NMR spectrum of **D77.**

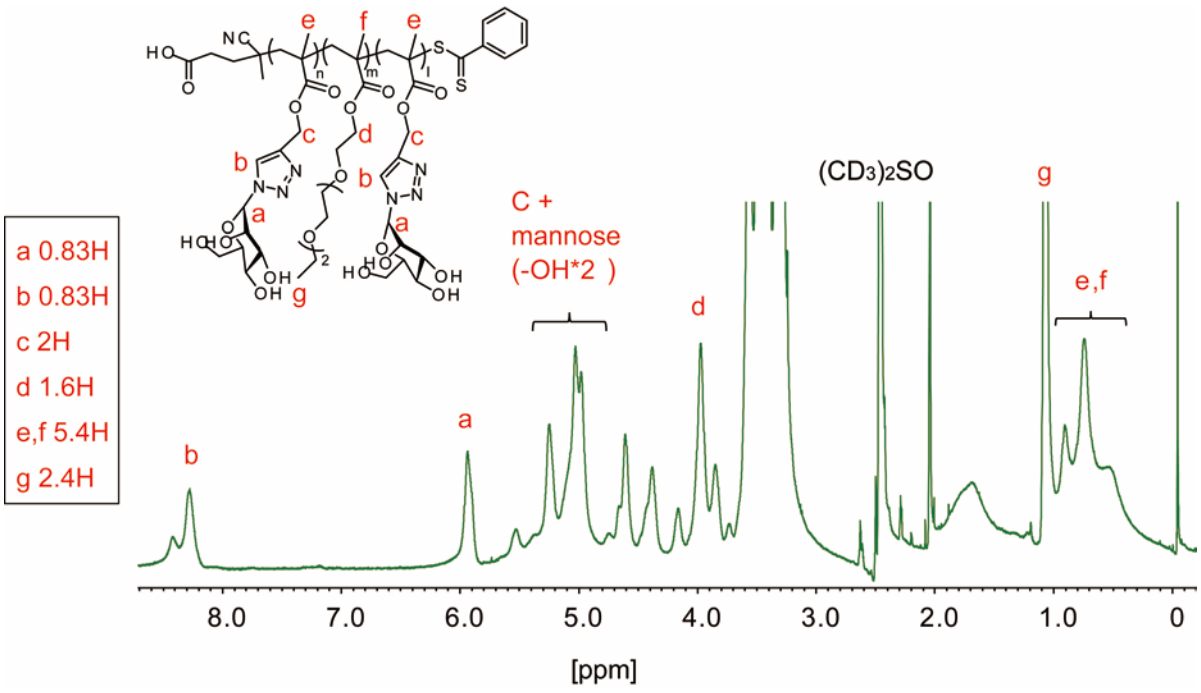


Figure S8-5. ^{1}H NMR spectrum of **T103.**

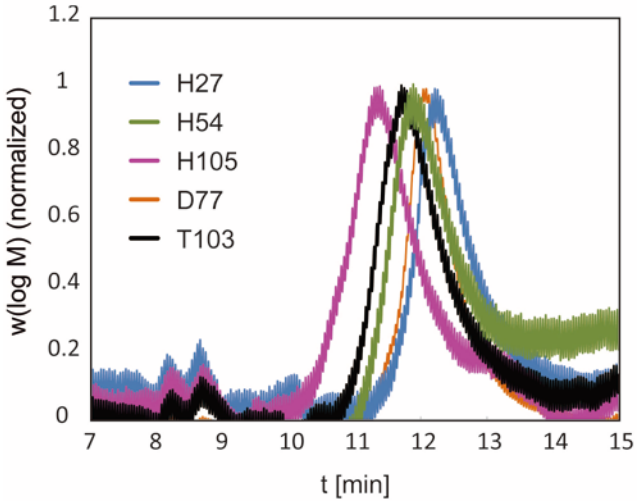


Figure S8-6. GPC traces of **H27**, **H54**, **H105**, **D77** and **T103**

Table S2 Reaction conditions of polymers for sugar introduction by click chemistry.

	Alkine (mM ; 1 eq)	Mannnose azide (eq)	CuBr (eq)	TBTA (eq)	TEA (eq)	Sugar introduction (%)[a]
H27	0.05	3	0.6	0.6	0.36	100
H54	0.05	3	0.6	0.6	0.36	97
H105	0.05	3	0.6	0.6	0.36	100
D77	0.14	9	0.6	0.6	0.36	91
T103	0.14	9	0.6	0.6	0.36	83

[a]. Determined by ^{1}H NMR.

4. Evaluation of affinity of glycopolymer to lectin

4-1 Fluorescence quenching measurement

FITC-ConA (0.026 mL, Mw 1.04 × 10^5, 2.0 mg / mL) was dissolved in phosphate buffered saline PBS (+) (15 mL, 1 mM) to prepare a 0.033 μM FITC-ConA solution. 1.66 mg of **H27** and **H105** were respectively dissolved in 50 mL of PBS (+) to prepare glycopolymer solution with a sugar side chain of 0.1 mM. 1.71 mg of **H54** was dissolved in 50 mL of PBS (+) to prepare glycopolymer solution with a sugar side chain of 0.1 mM. 3.75 mg of **D77** was dissolved in 50 mL of PBS (+) to prepare glycopolymer solution with a sugar side chain of 0.1 mM. 2.99 mg of **T103** was dissolved in 50 mL of PBS (+) to prepare glycopolymer solution with sugar side chain of 0.1 mM. 2.91 mg of **TEG111** was dissolved in 50 mL of PBS (+) to prepare solution of 2.1 μM with the same polymer concentration as **T103**. 1.80 mg of mannose · H_2O (Man) was dissolved in 100 mL of PBS (+) to prepare 0.1 mM solution. 1 mL of the FITC-ConA solution prepared in disposable cell (1 mL) was placed and set in a fluorescent spectrometer. The fluorescence at 515 nm was recorded with varying the sugar concentration using the excitation wavelength at 490 nm. The fluorescence intensity of the FITC-ConA solution was first measured as the 0th measurement. The aliquots of glycopolymer was added every 5 min. The injection volumes were 1μl (1st and 2nd rounds), 2 μl (3rd and 4th rounds), 3μl (5th and 6th rounds), 5 μl (7th to 9th rounds), 10 μl (10th to 14th rounds), 20 μl (15th to 17th rounds), 50 μl (18th to 21st rounds) and 100 μl (22nd round), respectively. The fluorescent quenching without protein-sugar interaction was measured by the addition of PBS(+) as a blank, and the quenching effect by PBS(+) was subtracted. The value obtained after blank subsractin was taken as the fluorescence intensity change ΔF (F_o-F_n). **TEG111** solution and monomeric Man solution were measured by the same operation. Fluorescence measurement with FITC-PNA solution with **T103** was performed by the same operation.

Evaluation of interaction between glycopolymer and FITC-ConA

The association constants were estimated by the following Langmuir isotherm.

$$\frac{\Delta F}{\Delta F_{max}} = \frac{C}{1/K_a + C}$$

(ΔF_{max} : maximum fluorescence intensity change, K_a : binding constants, C : sugar concentration) Plots, fitting curves and R2 for fitting were shown below (Figure S9-1).

ΔF of FITC-ConA didn't increase in the control experiment using **TEG111**, suggesting inertness to fluorescence change (Figure S9-2). .

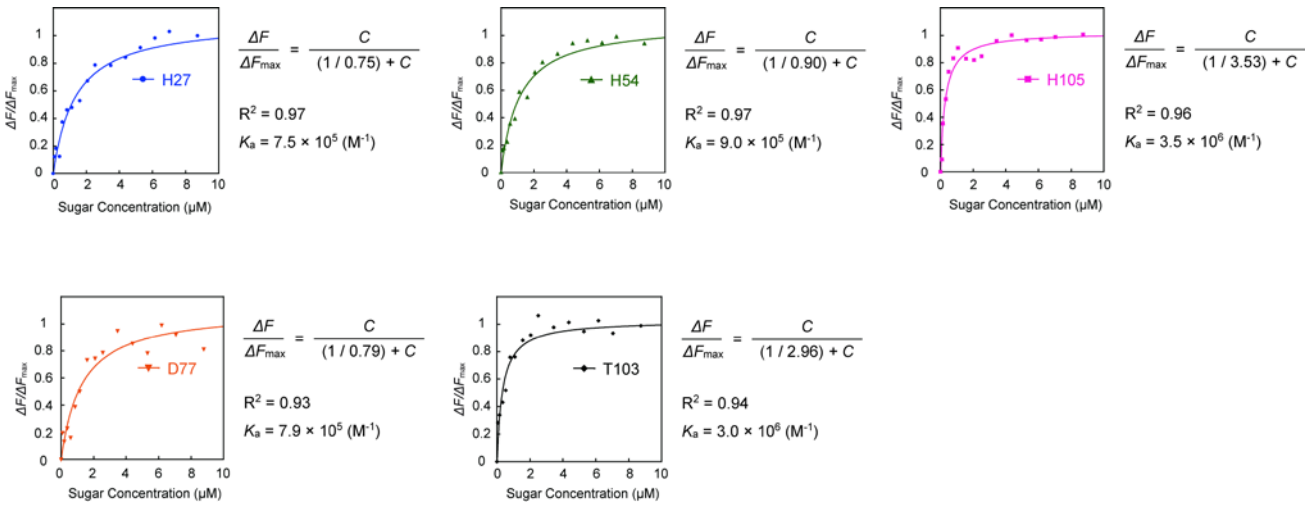


Figure S9-1. Fluorescence quenching measurements (FITC-ConA) by addition of glycopolymers (**H27**, **H54**, **H105**, **D77**

and **T103**).

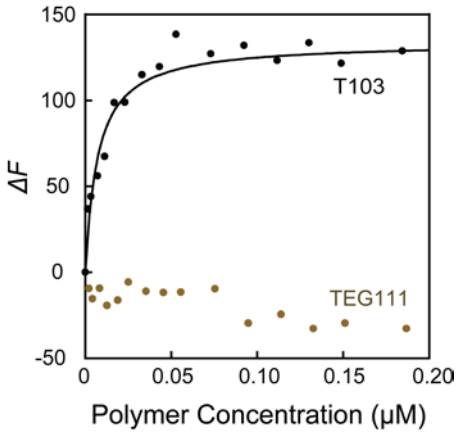


Figure S9-2. Fluorescence quenching measurement (FITC-ConA) by addition of **TEG111**

4-2 Hemagglutination inhibition assay[2]

Blood preparation

Rabbit blood was pelleted by centrifugation (2000 rcf × 5 min), and the layer of white blood cells and plasma proteins was removed by pipette. The blood was then diluted to 1 mL with PBS buffer, the solution was centrifuged and upper layer was removed by pipette. This process was repeated 3 times. The purified blood was diluted to 0.5 v/v% with PBS buffer.

ConA concentration titration of hemagglutination

Rabbit blood solutions were incubated with the ConA solutions at each concentration to determine the ConA concentration required for hemagglutination. Serial two fold dilutions were made in the wells of a 96 well V-bottomed plate. The two fold dilutions were made by adding 100 µL of ConA solution 1.0 mg/mL to the first well, then 50 µL of PBS buffer to the 2nd - 10th well (n = 3). 50 µL was then transferred from the 1st well to the 2nd well. The 2nd well was mixed and 50 µL was transferred to the 3rd well. This procedure was repeated until the 10th well two fold serial dilutions through all wells of interest. To each well 50 µL of the blood solution was added and incubated for 2 hours at room temperature. Precipitation of red blood cells was confirmed at the bottom of the well, and the amount of Con A required for hemagglutination was determined as hemagglutinin units. 4 Hemagglutinin unit was used for measuring the minimum inhibition concentration of hemagglutination.

Measurement of minimum inhibition concentration of the hemagglutination by glycopolymers

Starting with a concentration of 1.0 mg/mL, serial two fold dilutions of the each glycopolymer (**H27**, **H105**, **T103**, **TEG111**, and monomeric mannose) were made as described above (25 mL solution in 1st ~ 10th well). The glycopolymer solutions were incubated with 25 mL of the Con A solution for 1 hours at room temperature. Then, 50 mL of the blood solution was added and incubated for 2 hours at room temperature. Precipitation of red blood cells was confirmed at the bottom of the well, and the minimum concentration causing inhibition was determined by naked eyes. The degree of precipitation of the red blood cells was confirmed by the absorbance at 540 nm using a microtiter plater reader (Thermo Fisher Scientific).

Result of hemagglutination assay.

As a result, the minimum sugar concentration causing hemagglutination inhibition of **H27**, **H105** and **T103** was 3.0 × 10^{-3}, 1.9 × 10^{-4} and 2.1 × 10^{-4} (M, sugar concentration), respectively. No inhibition was observed in **TEG111** and

monomeric mannose.

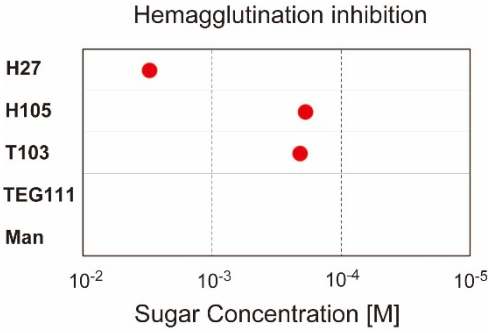


Figure S10. Hemagglutination inhibition assay.

5. Size measurement of glycopolymer in the solution

Each glycopolymer (**H27**, **H54**, **H105**, **D77**, and **T103**) was dissolved in PBS (+) to prepare 0.5 mg/mL solution, respectively. 1 mL of the glycopolymer solution prepared in disposable cell (1 mL) was placed and set in a DLS instrument (Malvern). The solution temperature was set at 20℃, and the solute model was set to polystyrene.

6. Theoretical assumption of the molecular length of glycopolymer

The molecular length of glycopolymers in solution was assumed based on the theoretical values (R) of the distances between the molecular chain terminals. Assuming the approximation of rotational isomeric state in the hindered rotation chain,[3] the average ⟨R⟩ of the ideal chain R is given by

$$\langle R \rangle = C^{0.5} N^{0.5} b$$

(C : characteristic ratio of monomer (styrene model : 10), N : C − C bond number of backborn, b : C − C bond length (0.154 nm))

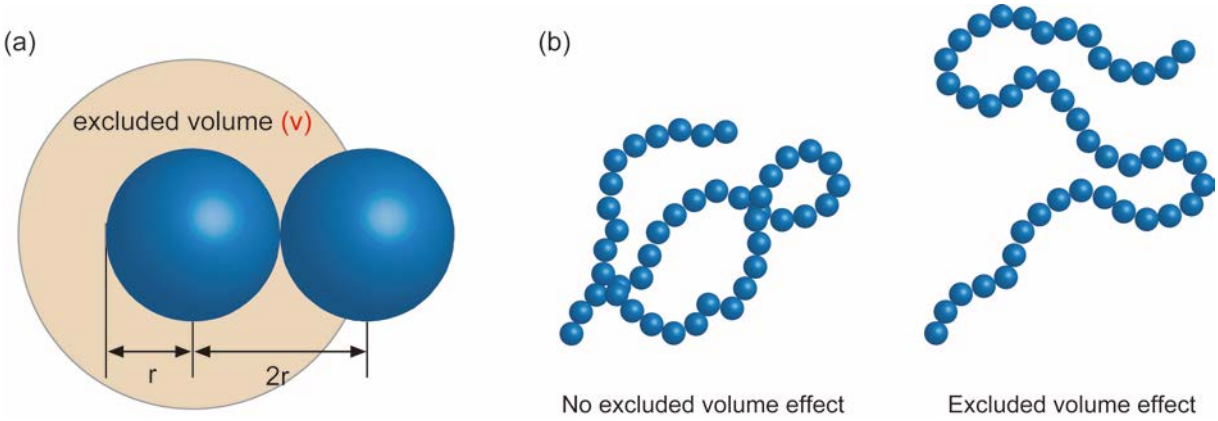


Figure S11-1. (a) Schematic diagram of the excluded volume per segment. (b) Expansion behavior of ideal chain and real chain in consideration of excluded volume effect.

Since polymers have the actual volume, the excluded volume was taken into consideration. The excluded volume is inaccessible volume of a long polymer chain that is occupied by another part of the same molecule. *R* was calculated by assuming the hard sphere model.[4] In the hard sphere model, the excluded volume was calculated assuming that a long polymer segment is composed of hard spheres. The segment radius (*r*) was defined as a half of C-C bond in the polymer backbone (Figure S11-1a). The excluded volume (*v*) of one segment is given by

$$v = \frac{4\pi}{3}(2r)$$

(r : Segment radius ($2r = b = 0.154$))

The statistical distribution $W_0(R)$ of the ideal chain R is expressed by

$$W_0(R) = 4\pi R^2 \left(\frac{3}{2\pi\langle R^2\rangle}\right)^{3/2} exp\left(-\frac{3R^2}{2\langle R^2\rangle}\right)$$

$p(R)$ is defined as probability that no polymer segment is present in the exclusion volume on the on the assumption of $R^3 >> v$ and $N >> 1$.

$$p(R) = exp\left(-\frac{N^2 v}{2R^3}\right)$$

Based on $p(R)$ and $W_0(R)$, the statistical distribution $W(R)$ of R in consideration of the excluded volume effect was estimated as follows:

$$W(R) = p(R)\ W_0(R)$$

$$W(R) = 4\pi \left(\frac{3}{2\pi\langle R^2\rangle}\right)^{3/2} exp\left[-\frac{N^2 v}{2R^3} - \frac{3R^2}{2\langle R^2\rangle}\right] R^2$$

The vertex of the distribution (R') of R was used as polymer length in the manuscript. R' of **H27**, **H54**, **H103**, **D77**, and **T103** are 3.7, 5.5, 8.0, 6.7, and 8.0 nm, respectively (Figure S11-2). The distance between binding site of ConA was 6.5 nm (Ref 17 and 18 in the manuscript). The glycopolymer theoretically formed two site binding with ConA, in the case of the glycopolymer with sugar blocks at both ends and R'over 6.5 nm. The two-site binding was confirmed by a marked increase in K_a.

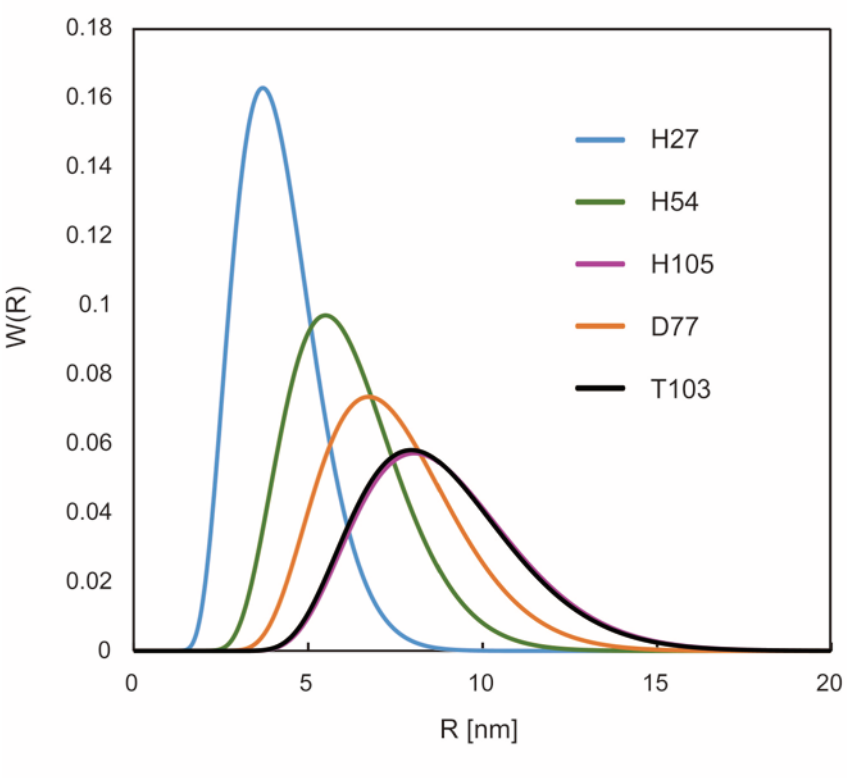


Figure S11-2. The statistical distribution W(*R*) of glycopolymers on the assumption of the excluded volume effect.

Reference:

1. M. Nagao, Y. Kurebayashi, H. Seto, T. Tanaka, T. Takahashi, T. Suzuki, Y. Hoshino and Y. Miura, *Polym. J.*, 2016, **48**, 745–749.
2. M. L. Wolfenden and M. J. Cloninger, *J. Am. Chem. Soc.*, 2005, **127**, 12168-12169.
3. C. M. Guttman and E. A. DiMarzio, *Macromolecules*, 1982, **15**, 525–531.
4. Polymer Properties Database, http://polymerdatabase.com/polymer%20physics/Excluded%20Volume.html, (accessed November 2017).