Supporting Information

Fructose-sensitive thermal transition behaviour of boronic ester-bearing telechelic poly(2-isopropyl-2-oxazoline)

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Experimental Section

Materials and measurements

All commercially available reagents were reagent grade and used without further purification. Tetrahydrofuran (THF) and acetonitrile were distilled before each use. Analytical SEC was performed on a JASCO HPLC equipped with HF-403HQ and HF-404HQ columns (Shodex, Tokyo, Japan) using THF as the eluent. Recycling preparative size-exclusion chromatography (SEC) was carried out on a LC-9201 (JAI, Tokyo, Japan) instrument equipped with JAIGEL-1H, JAIGEL-2H, and JAIGEL-3H columns, using $CHCl_3$ as the eluent. ^{1}H NMR spectra were measured using a Bruker DPX 400 (400 MHz) spectrometer in CD_2Cl_2. MALDI-TOF-MS measurements were performed on a Bruker model LRF20 using dithranol (1,8,9-trihydroxyanthracene) as the matrix. Transmittance spectra were measured using a V-660 (JASCO, Tokyo, Japan) spectrophotometer equipped with a thermostatic cell holder coupled with a controller (ETCS-761, JASCO, Tokyo, Japan).

Determination of thermal transition temperature

The transmittance of the solution at 800 nm was measured using a V-660 spectrophotometer equipped with a thermostatic cell holder coupled with a controller (ETCS-761, JASCO). The heating rate of the sample cells was adjusted to 2.0 °C/min. The cloud-point temperature was taken as the temperature at which the transmittance reached 50% in the resulting transmittance versus temperature curves.

Synthesis

The synthesis of **B-PiPrOx-B** is outlined in Scheme 1. **2**, **3** and **4** were synthesized according to literature procedures.[1-3]

Synthesis of 2. 4-Hydroxymethylphenyl boronic acid (**1**, 5 g, 32.9 mmol), pinacol (5.83 g, 49.4 mmol), and sodium sulfate (5 g, 35.2 mmol) were added to a 250 mL flask with 35 mL of dry THF under N_2 atmosphere and stirred for 5 h at room temperature. Then, the mixture solution was filtered, and the filtrate was evaporated. The residue was dissolved in CH_2Cl_2 (100 mL) and washed with brine. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residue was chromatographed on silica gel using ethyl acetate/hexane (1:1) as the eluent and evaporated as a transparent liquid. (6.08 g, 76%). ^{1}H NMR (400 MHz, CD_2Cl_2, 25 ℃) δ (ppm): 7.76-7.74 (d, 2H; benzene peak adjacent to boron), 7.36–7.34 (d, 2H; benzene peak adjacent to methyl hydroxy), 4.67 (s, 2H; CH_2 in methyl hydroxy), 2.47–2.26 (broad s, 1H; OH), 1.34 (s, 12H; CH_3 in pinacol).

Synthesis of 3. Tetrabromomethane (5.67 g, 17.1 mmol) and **2** (2 g, 8.54 mmol) were placed in a 100 mL flask with 40 mL dry THF under N_2 atmosphere and stirred for 30 min. Triphenylphosphine (4.49 g, 17.1 mmol) was added to the mixture solution under N_2 atmosphere at 0 ℃ and stirred for 4 h at room temperature. Then, the mixture solution was concentrated under reduced pressure. The residue was dissolved in ethyl acetate (200 mL) and washed with brine. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residue was chromatographed on silica gel using hexane/CH_2Cl_2 (1:1) as the eluent to give **3** as a white solid (2.10 g, 83%). ^{1}H NMR (400 MHz, CD_2Cl_2, 25 ℃) δ (ppm): 7.74–7.72 (d, 2H), 7.41–7.39 (d, 2H), 4.51 (s, 2H), 1.32 (s, 12H).

Synthesis of 4. To a solution of **3** (2 g, 6.76 mmol) in dimethoxymethane (25 mL) in a 100 mL flask, methylamine (1.05 g, 33.8 mmol) was added, and the mixture solution was stirred for 5 h at room temperature. Then, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in ethyl acetate (200 mL) and washed with brine. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to give **4** as a yellow liquid (1.45 g, 87%). ^{1}H NMR (400 MHz, CD_2Cl_2, 25 ℃) δ (ppm): 7.79–7.77 (d, 2H), 7.33–7.31 (d, 2H), 3.77 (s, 2H), 2.45 (s, 3H), 1.34 (s, 12H).

B-PiPrOx-B. A Schlenk flask was heated to remove inner moisture, degassed under high vacuum, and backfilled with N_2; this process was repeated three times. A solution of **3** (0.754 g, 2.55 mmol) as an initiator in acetonitrile (3 mL), 2-isopropyl-2-oxazoline (**PiPrOx**) (9.50 g, 10.0 mL, 84.0 mmol), and acetonitrile (12 mL) were added to the Schlenk flask. The mixture solution was stirred at 40 ℃ under N_2 atmosphere and monitored by analytical SEC and MALDI-TOF-MS. After confirming that the target molecular weight has been reached, a solution of **4** (0.948 g, 3.84 mmol) as a terminator in acetonitrile (3 mL) was added to the reaction mixture, which was further stirred at 70 ℃ for 48 h to introduce phenylboronic acid at the polymer terminal. The aqueous solution of the polymer was poured into dichloromethane, and the mixture was washed with brine. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residue was recovered by freeze-drying to afford **B-PiPrOx-B** as yellow powder (6.27 g, 62%). ^{1}H NMR (400 MHz, CD_2Cl_2, 25 ℃) δ (ppm): 8.13–6.86 (strong broad m, 8H; benzene peak), 4.63–4.52 (broad d, 2 H; C-CH_2-N beside the benzene), 4.24–3.87 (broad s, 2 H; N-CH_2-C beside the benzene), 3.82–3.11 (broad s, 132 H; -CH_2-CH_2- on the polymer backbone), 2.98–2.51 (broad d, 33H; -CH_2- on the polymer side chain), 2.48–2.23 (broad d, 3H; -N-CH_3), 1.31 (s, 26H; CH_3 in pinacol), 1.26–0.83 (broad s, 198H; -CH_2- on the polymer side chain).

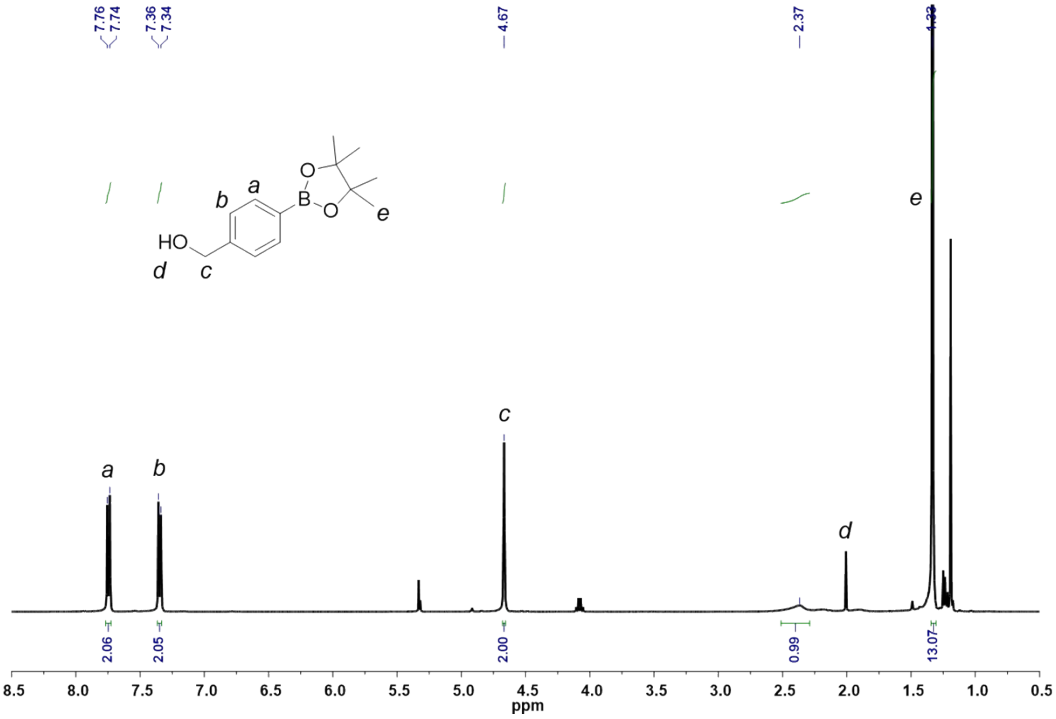

Figure S1. [1]H NMR spectrum of **2**.

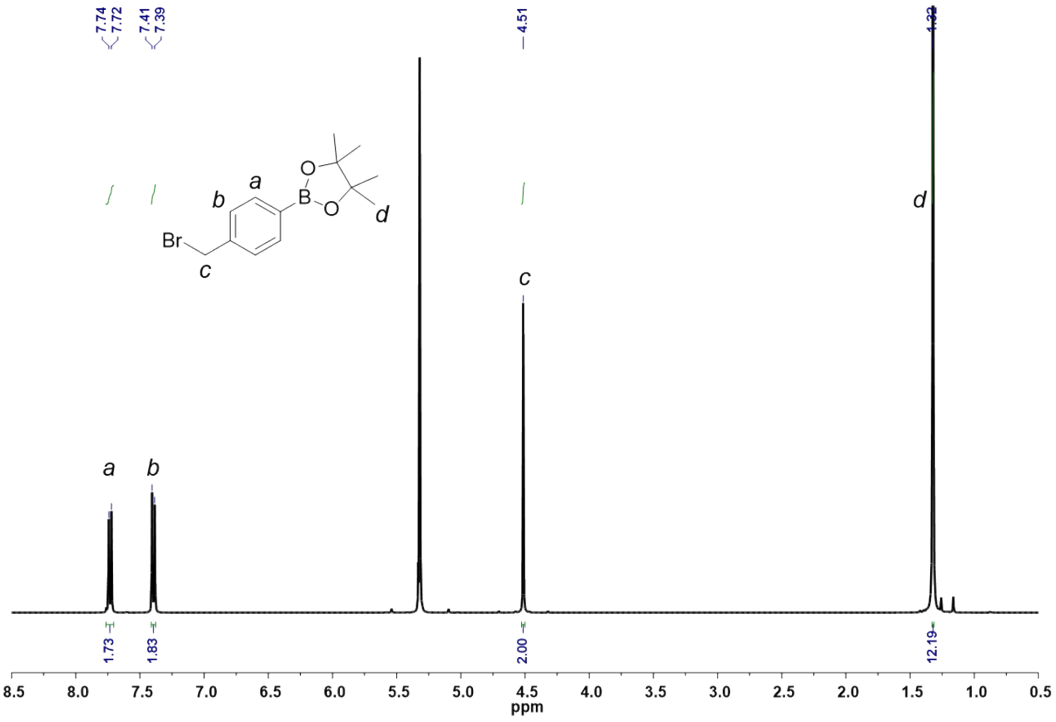

Figure S2. [1]H NMR spectrum of **3**.

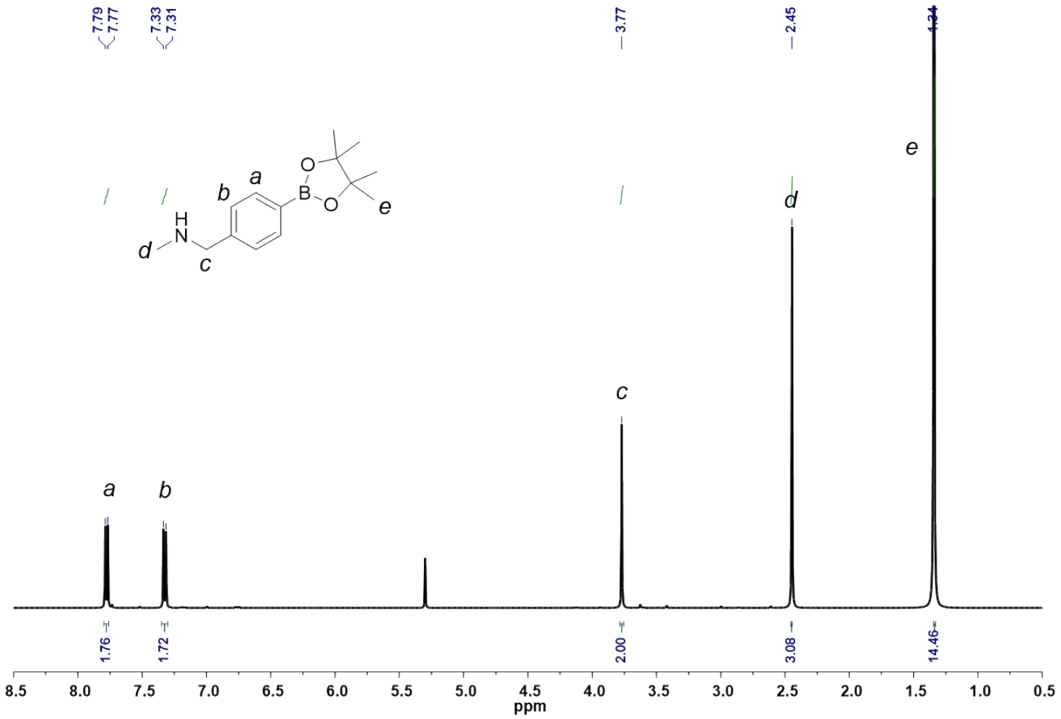

Figure S3. [1]H NMR spectrum of **4**.

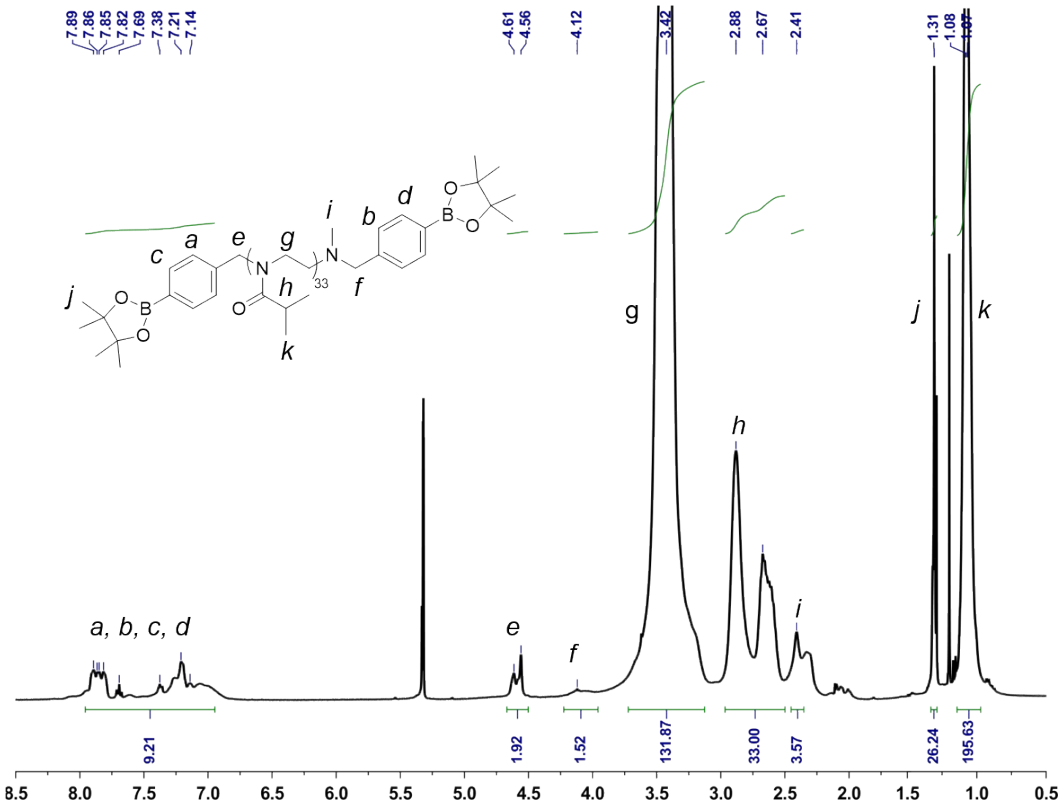

Figure S4. [1]H spectrum of **B-PiPrOx-B**.

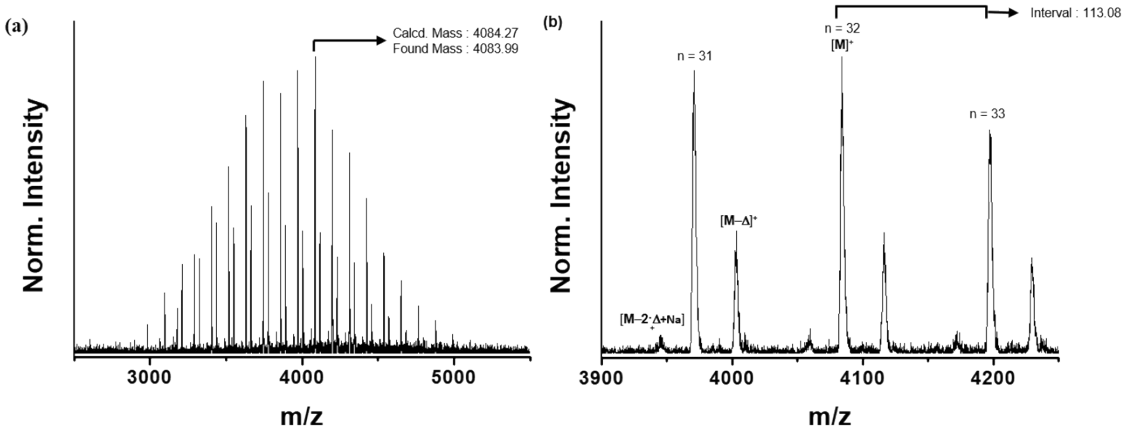

Figure S5. (a) MALDI-TOF-MS profile of **B-PiPrOx-B**. (b) Magnified section of the spectra for 31, 32, and 33 repeating units of **B-PiPrOx-B**. Δ represents the value between MS peaks in molecular weight of pinacol ester.

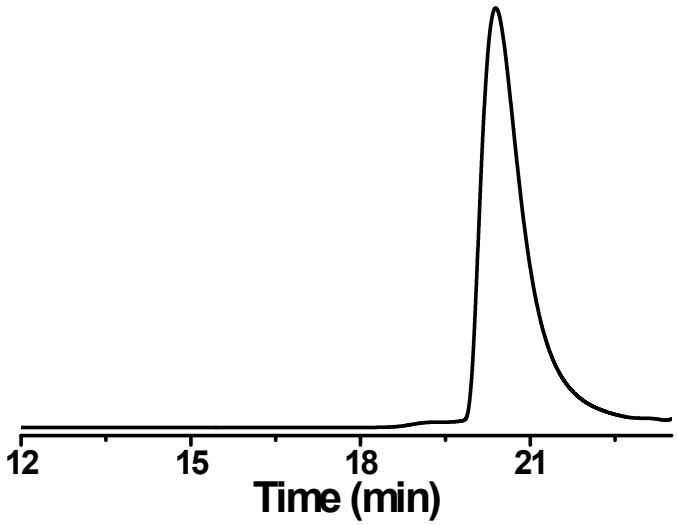

Figure S6. SEC traces of **B-PiPrOx-B**.

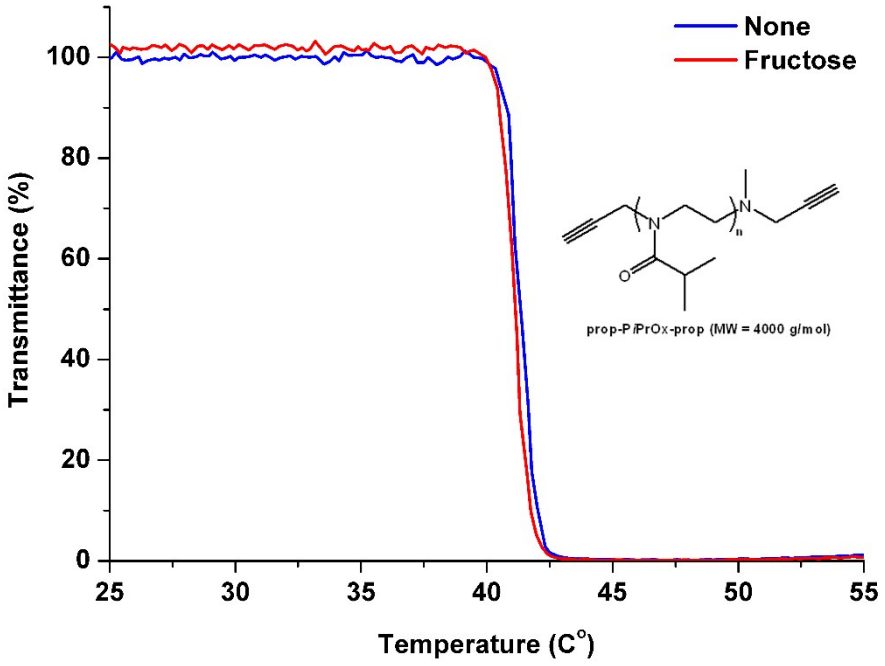

Figure S7. Temperature-dependent transmittance changes of **Prop-P*i*PrOx-Prop** (4.0 g/L) with fructose (50 mM)

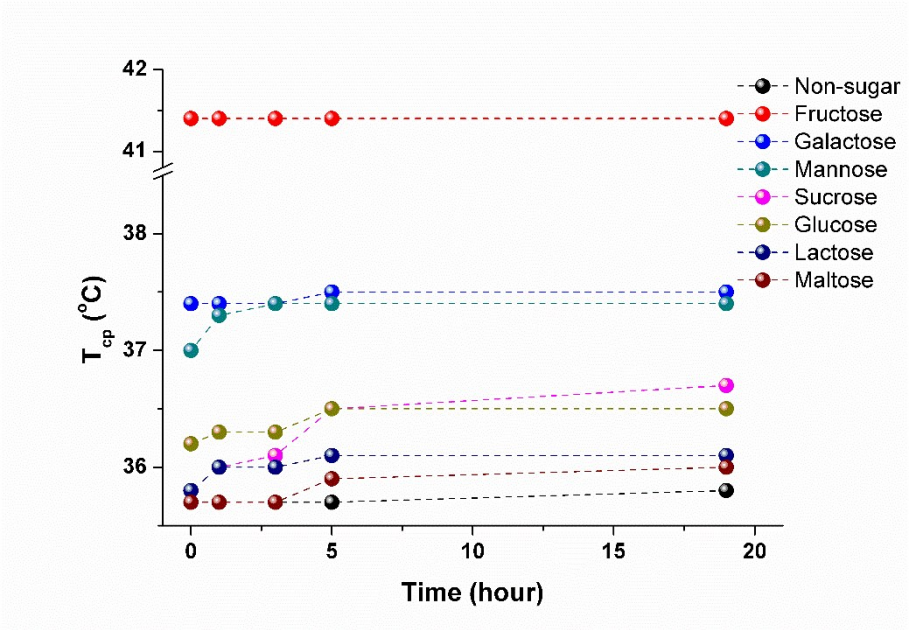

Figure S8. Time-dependent thermal transition temperature of **B-PiPrOx-B** after addition of various sugars up to 19 h.

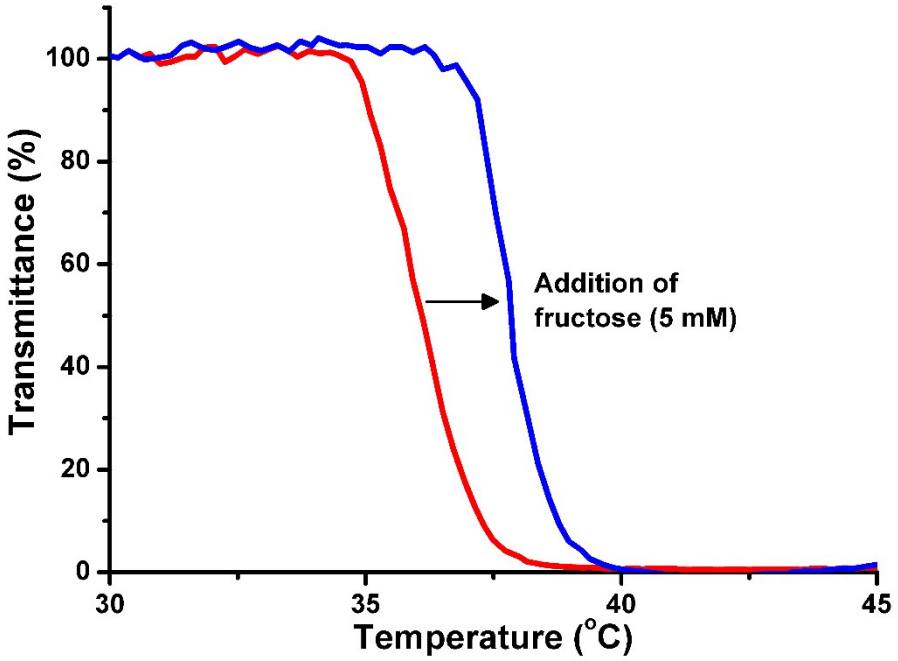

Figure S9. Temperature-dependent transmittance changes of **B-P*i*PrOx-B** in pH 7.4 PBS solutions containing 5 mM glucose before (red line) and after (blue line) the addition of 5 mM fructose.

References

1. K. E. Broaders, S. Grandhe and J. M. Frechet, *J. Am. Chem. Soc.*, 2011, **133**, 756-758.
2. V. Aucagne, J. Berná, J. D. Crowley, S. M. Goldup, K. D. Hänni, D. A. Leigh, P. J. Lusby, V. E. Ronaldson, A. M. Slawin and A. Viterisi, *J. Am. Chem. Soc.*, 2007, **129**, 11950-11963.
3. M. Gravel, K. A. Thompson, M. Zak, C. Bérubé and D. G. Hall, *J. Org. Chem.*, 2002, **67**, 3-15.