

Sugar complexation to silicone-boronic acids

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Electronic Supplementary Information

Materials and Methods

4-Vinylphenylboronic acid (95%), dimethyl-L-tartrate (99%), platinum(0)-1,3-divinyl-1,1,3,3-tetramethyldisiloxane complex (Karstedt's catalyst, solution in xylenes 2% Pt), tris(hydroxymethyl)aminomethane (99.9%), D-(+)-glucose (99.5%), and D-(-)-fructose (98%) were obtained from Sigma-Aldrich. 1,1,1,3,3,5,5-Heptamethyltrisiloxane was obtained from Fluorchem. Pentamethyldisiloxane, bis(trimethylsiloxy)methylsilane, and hydride-terminated polydimethylsiloxane ($\text{HMe}_2\text{Si}(\text{OSiMe}_2)_n\text{OSiMe}_2\text{H}$ where $n = 8, 14, \text{ and } 67$, respectively) were obtained from Gelest. The solvents (Caledon Laboratories) dichloromethane and toluene were dried over activated alumina prior to use.

IR analysis was performed using a Thermo Scientific Nicolet 6700 FTIR infrared spectrometer. NMR spectra were recorded on a Bruker Avance 600 MHz nuclear magnetic resonance spectrometer using deuterated solvents (chloroform- d , acetone- d_6 or DMSO- d_6). High-resolution mass spectrometry was performed using a Waters Quattro Ultima Global quadrupole time-of-flight mass spectrometer with electrospray ionization mode.

Synthesis

Synthesis of dimethyl-L-tartrate-protected 4-vinylphenylboronic acid **6**

Molecular sieves ($4\text{\AA}$, approximately 1 g) and a magnetic stir-bar were placed in a 50 mL round-bottomed flask and dried in an oven at $100\text{ }^\circ\text{C}$ for 20 h. The dry flask was purged with nitrogen, and then 25 mL dry dichloromethane were added followed by 4-vinylphenylboronic acid (500 mg, 3.38 mmol) and dimethyl-L-tartrate (602 mg, 3.38 mmol). The reaction mixture consisted of a suspension of a white solid in colorless, clear solvent. The mixture was stirred at room temperature under nitrogen atmosphere for 3 h, after which it appeared as an opaque, colorless mixture. Following removal of molecular sieves via filtration and rinsing with dichloromethane, the volatiles were removed *in vacuo* to afford the product as a colorless, opaque waxy solid. Yield: 826 mg (84 %). ^1H NMR (600 MHz, CDCl_3): $\delta = 7.83$ (d, $J = 8.0$ Hz, 2H), 7.42 (d, $J =$

8.0 Hz, 2H), 6.72 (dd, $J = 11.0, 17.1$, 1H), 5.82 (d, $J = 17.6$ Hz, 1H), 5.31 (d, $J = 11.0$ Hz, 1H), 5.08 (s, 2H), 3.84 (s, 6H). ^{13}C NMR (150.92 MHz, CDCl_3): $\delta = 170.05, 141.41, 136.88, 136.14, 135.76, 125.91, 115.76, 78.08, 53.25$. MS (ES-positive mode): m/z [$\text{M} + \text{H}^+$] calculated = 291.1040; [$\text{M} + \text{H}^+$] found = 291.1023.

Hydrosilylation of **6**: General Procedure Using Pentamethyldisiloxane (PMDS-derivative)

Freshly prepared (within 12 h) TPVPBA (102 mg, 0.35 mmol) was added to a 50 mL round-bottomed flask containing a magnetic stir bar. After addition of 4 mL dry toluene to the reaction flask, pentamethyldisiloxane (82 μL , 0.42 mmol) was added using an automatic pipette. At that point, the reaction mixture was a clear, colorless solution. Karstedt's catalyst (10 μL , 2% solution in xylenes) was added to the reaction, causing the solution to immediately turn bright yellow. The reaction was stirred at room temperature for 1 additional h, during which time the yellow color faded considerably. The reaction was then stirred with activated carbon (~1 g) for 20 h prior to filtration through a short (2 cm) column of Celite, eluting with hexanes. The volatile solvents as well as excess pentamethyldisiloxane were removed in vacuo and under a stream of nitrogen, giving the product as a clear, colorless oil. Yield: 133 mg (87 %); ratio of products (terminal: internal) was 10:7.

Terminal Isomer: **7t** (62%): ^1H NMR (600 MHz, CDCl_3): $\delta = 7.79$ (d, $J = 8.0$ Hz, 2H), 7.24 (d, $J = 8.0$ Hz, 2H), 5.07 (s, 2H), 3.83 (s, 6H), 2.65 (m, 2H), 0.87 (m, 2H), 0.07 to -0.03 (m, 15H).

Internal Isomer **7i** (38%): ^1H NMR (600 MHz, CDCl_3): $\delta = 7.75$ (d, $J = 8.0$ Hz, 2H), 7.10 (d, $J = 8.0$ Hz, 2H), 5.06 (s, 2H), 3.83 (s, 6H), 2.19 (m, 1H), 1.35 (d, $J = 6.7$ Hz, 3H), 0.07 to -0.03 (m, 15H).

Mixture: ^{13}C NMR (150.92 MHz, CDCl_3): $\delta = 172.10, 170.19, 170.13, 150.54, 150.13, 135.63, 135.25, 127.72, 127.19, 78.05, 78.02, 72.16, 53.34, 53.19, 32.33, 29.96, 20.35, 14.28, 2.19, 2.05, 1.81, 1.21, 0.50, -0.20, -1.21$. ^{29}Si NMR (119.22 MHz, CDCl_3): $\delta = 8.13, 7.66, 6.98, 5.22$. ^{11}B NMR (192.55 MHz, CDCl_3): $\delta = 32.66$. MS (ES-positive mode): m/z [$\text{M} + \text{Na}^+$] calculated = 461.1599; [$\text{M} + \text{Na}^+$] found = 461.1598.

1,1,1,3,3,5,5-Heptamethyltrisiloxane derivative: Following the same general procedure, TPVPBA (102 mg, 0.35 mmol) and 1,1,1,3,3,5,5-heptamethyltrisiloxane (115 μL , 0.42 mmol) were combined with 10 μL of Karstedt's catalyst solution ($\sim 9 \times 10^{-4}$ mmol Pt) in dry toluene. The reaction was stirred for 1 h before activated carbon (~1 g) was added. Purification using the above described extraction afforded the product as a clear, slightly yellow oil. Yield: 106 mg (59 %). Ratio of products (terminal : internal) was 10:7.

Terminal Isomer: **8t** (58): ^1H NMR (600 MHz, CDCl_3): $\delta = 7.78$ (d, $J = 8.0$ Hz, 2H), 7.23 (d, $J = 8.1$ Hz, 2H), 5.07 (s, 2H), 3.83 (s, 6H), 2.67 (m, 2H), 0.89 (m, 2H), 0.3 to -0.1 (m, 21H).

Internal Isomer: **8i** (42): ^1H NMR (600 MHz, CDCl_3): $\delta = 7.74$ (d, $J = 8.0$ Hz, 2H), 7.11 (d, $J = 7.9$ Hz, 2H), 5.06 (s, 2H), 3.83 (s, 6H), 2.22 (m, 1H), 1.36 (m, 3H), 0.3 to -0.1 (m, 21H).

Mixture: ^{13}C NMR (150.92 MHz, CDCl_3): δ = 170.15, 170.09, 150.42, 150.06, 135.59, 135.25, 127.66, 127.17, 78.00, 72.10, 53.34, 53.17, 32.25, 29.85, 29.33, 20.19, 15.49, 14.27, 1.98, 1.96, 1.45, 1.32, 0.31, -0.29, -1.29. ^{29}Si NMR (119.22 MHz, CDCl_3): δ = 7.84, 7.25, 7.12, 6.89, -20.67. ^{11}B NMR (192.55 MHz, CDCl_3): δ = 32.69. MS (ES-positive mode): m/z [$\text{M} + \text{Na}^+$] calculated = 535.1787; [$\text{M} + \text{Na}^+$] found = 535.1780.

Bis(trimethylsiloxy)methylsilane derivative: Following the general procedure, TPVPBA (102 mg, 0.35 mmol) and bis(trimethylsiloxy)methylsilane (114 μL , 0.42 mmol) were combined with 10 μL of Karstedt's catalyst solution ($\sim 9 \times 10^{-4}$ mmol Pt) in dry toluene. The reaction was stirred overnight (approximately 17 h) before activated carbon (~ 1 g) was added. Purification using the above described extraction afforded the product as clear, slightly yellow oil. Yield: 86 mg (48 %). Ratio of products (terminal : internal) was 5:2.

Terminal Isomer: **9t** (72%): ^1H NMR (600 MHz, CDCl_3): δ = 7.78 (d, J = 7.9 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 5.07 (s, 2H), 3.83 (s, 6H), 2.64 (m, 2H), 0.80 (m, 2H), 0.2 to -0.1 (m, 21H).

Internal Isomer: **9i** (28%): ^1H NMR (600 MHz, CDCl_3): δ = 7.73 (d, J = 8.1 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 5.07 (s, 2H), 3.83 (s, 6H), 2.12 (m, 1H), 1.32 (d, J = 7.4 Hz, 3H), 0.2 to -0.1 (m, 21H).

Mixture: ^{13}C NMR (150.92 MHz, CDCl_3): δ = 172.11, 170.20, 170.15, 150.21, 150.12, 149.12, 135.65, 135.22, 127.78, 127.72, 127.48, 78.07, 78.02, 73.28, 72.15, 53.38, 53.21, 31.80, 29.81, 29.39, 19.72, 15.55, 14.48, 14.44, 2.08, 1.96, 1.77, -0.10, -2.20. ^{29}Si NMR (119.22 MHz, CDCl_3): δ = 9.58, 9.35, 7.97, 7.81, -22.68. ^{11}B NMR (192.55 MHz, CDCl_3): δ = 32.44. MS (ES-positive mode): m/z [$\text{M} + \text{Na}^+$] calculated = 535.1787; [$\text{M} + \text{Na}^+$] found = 535.1786.

($\text{HMe}_2\text{SiO}(\text{Me}_2\text{SiO})_9\text{SiMe}_2\text{H}$ -Derivative: Approximate molecular weight determined by ^1H NMR end group analysis (ratio of terminal to internal SiMe_2 groups) ≈ 730 g/mol. Following the general procedure, TPVPBA (100 mg, 0.34 mmol) and DMS-H03 (140 μL , 0.17 mmol) were combined with 10 μL of Karstedt's catalyst solution ($\sim 9 \times 10^{-4}$ mmol Pt) in dry toluene. The reaction was stirred for 3 h before activated carbon was added. After stirring with activated carbon (~ 1 g) for 20 h, the mixture was gravity filtered using 125 mm $\varnothing$ Whatman filter paper and rinsed with hexanes. After removal of solvents, the product was isolated as a clear, colorless oil. Yield: 120 mg (54 %). Ratio of products (terminal : internal) was 2:1. Note that it is not possible to quantify polymers with α,ω -diterminal vs diinternal vs internal/terminal end groups.

Terminal Isomer: **10t** (66%): ^1H NMR (600 MHz, acetone- d_6): δ = 7.76 (d, J = 7.9 Hz, 2H), 7.32 (d, J = 7.8 Hz, 2H), 5.18 (s, 2H), 3.81 (s, 6H), 2.75 (m, 2H), 0.98 (m, 2H), 0.2-0.0 (m, 60H).

Internal Isomer: **10i** (33%): ^1H NMR (600 MHz, CDCl_3): δ = 7.73 (d, J = 8.0 Hz, 2H), 7.22 (d, J = 7.9 Hz, 2H), 5.17 (s, 2H), 3.81 (s, 6H), 2.33 (q, J = 7.5 Hz, 1H), 1.42 (d, J = 7.5 Hz, 3H), 0.2-0.0 (m, 60H).

Mixture: ^{13}C NMR (150.92 MHz, acetone- d_6): δ = 170.73, 150.99, 150.70, 136.17, 135.85, 135.26, 128.51, 128.04, 127.93, 127.54, 78.73, 73.42, 53.16, 52.63, 32.74, 30.41, 20.97, 20.85, 14.65, 1.56, 1.47, 0.47, -1.53.

(HMe₂SiO(Me₂SiO)₁₆SiMe₂H-Derivative: Approximate molecular weight determined by ^1H NMR by end group analysis $\approx$ 1170 g/mol. Following the general procedure, TPVPBA (100 mg, 0.34 mmol) and DMS-H11 (220 μL , 0.17 mmol) were combined with 10 μL of Karstedt's catalyst solution ($\sim 9 \times 10^{-4}$ mmol Pt) in dry toluene. The reaction was stirred for 3 h before activated carbon ($\sim$ 1 g) was added. After stirring with activated carbon for 20 h, the mixture was gravity filtered using 125 mm $\varnothing$ Whatman filter paper and rinsed with hexanes. After removal of solvents, the product was isolated as a clear, colorless oil. Yield: 217 mg (73 %). Ratio of products (terminal : internal) was 5:4.

Terminal Isomer: **11t** (56%): ^1H NMR (600 MHz, acetone- d_6): δ = 7.76 (d, J = 7.9 Hz, 2H), 7.32 (d, J = 7.9 Hz, 2H), 5.18 (s, 2H), 3.81 (s, 6H), 2.75 (m, 2H), 0.98 (m, 2H), 0.2 to 0.0 (m, 112H).

Internal Isomer: **11i** (44%): ^1H NMR (600 MHz, CDCl₃): δ = 7.73 (d, J = 8.0 Hz, 2H), 7.22 (d, J = 7.9 Hz, 2H), 5.17 (s, 2H), 3.81 (s, 6H), 2.33 (q, J = 7.4 Hz, 1H), 1.43 (d, J = 7.5 Hz, 3H), 0.2 to 0.0 (m, 112H).

Mixture: ^{13}C NMR (150.92 MHz, acetone- d_6): δ = 170.73, 150.70, 136.17, 135.85, 135.26, 128.50, 128.04, 127.93, 127.54, 78.73, 73.42, 53.15, 52.63, 32.74, 30.41, 20.85, 14.66, 1.72, 1.56, 1.47, 1.23, 0.47, -1.09, -1.53.

(HMe₂SiO(Me₂SiO)₈₀SiMe₂H-Derivative: Approximate molecular weight determined by end group analysis using ^1H NMR $\approx$ 5100 g/mol. Following the general procedure, TPVPBA (68 mg, 0.23 mmol) and DMS-H03 (598 μL , 0.11 mmol) were combined with 10 μL of Karstedt's catalyst solution ($\sim 9 \times 10^{-4}$ mmol Pt) in dry toluene. The reaction was stirred for 3 h before activated carbon was added. After stirring with activated carbon ($\sim$ 1 g) for 20 h, the mixture was gravity filtered using 125 mm $\varnothing$ Whatman filter paper and rinsed with hexanes. After removal of solvents, the product was isolated as a clear, colorless oil. Yield: 475 mg (76 %). Ratio of products (terminal : internal) was 5:4.

Terminal Isomer: **12t** (56%): ^1H NMR (600 MHz, CDCl₃): δ = 7.78 (d, J = 8.0 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 5.07 (s, 2H), 3.83 (s, 6H), 2.66 (m, 2H), 1.36 (d, J = 7.4 Hz, 2.6H), 0.89 (m, 2H), 0.2 to -0.1 (m, 443H).

Internal Isomer: **12i** (46%): ^1H NMR (600 MHz, CDCl₃): δ = 7.74 (d, J = 8.0 Hz, 2H), 7.11 (d, J = 8.0 Hz, 2H), 5.06 (s, 2H), 3.83 (s, 6H), 2.22 (m, 1H), 1.36 (d, J = 7.4 Hz, 3H), 0.2 to -0.1 (m, 443H).

Mixture: ^{13}C NMR (150.92 MHz, CDCl_3): δ = 170.22, 170.17, 150.47, 150.13, 135.68, 135.34, 127.74, 127.24, 78.09, 72.16, 53.21, 32.33, 29.94, 20.26, 14.33, 1.50, 1.42, 1.26, 1.09, 1.01, 0.38, -1.19, -1.28, -1.85.

Sugar Binding: NMR Experiment

Boronic acid deprotection

Samples were prepared in standard-sized NMR tubes (Table 1). Phosphate-buffered saline (50 mM) was prepared in Milli-q water and the pH was adjusted using a 1.0M solution of sodium hydroxide. Samples were inverted several times to facilitate mixing prior to obtaining NMR spectra. Spectra were obtained after 5 min, 3.5 h, and 18 h from time of mixing. Sample 1 was used as a reference spectrum for the tartrate-bound silicone boronic ester, and was measured only once.

Table 1: Conditions used to optimize tartrate hydrolysis of **7**

Sample #	DMSO- d_6 (mL)	PMDS-deriv. (μL)	PBS buffer (μL)	H ₂ O (μL)	pH
1	0.6	20	-	-	-
2	0.6	20	-	20	-
3	0.6	30	20	-	4.5
4	0.6	30	20	-	7.4
5	0.6	30	20	-	8.0
6	0.6	30	20	-	9.0

Binding to fructose and glucose

Two NMR-scale samples were prepared with the same composition. To a standard-sized NMR tube was added DMSO- d_6 (0.6 mL), and Milli-q water (20 μL), phosphate-buffered saline (20 μL , 50 mM, pH 7.4). The mixture was inverted multiple times to facilitate mixing. To one sample was added pentamethyldisiloxane silicone-boronic ester derivative **7** (20 μL , approx. 0.035 mmol) and glucose in DMSO- d_6 (32 μL , 1.67 M, 0.053 mmol). To the other was added **7** (30 μL , 0.052 mmol) and fructose in DMSO- d_6 (52 μL 1.55 M, 0.080 mmol). Both samples were inverted several times prior to obtaining NMR spectra.

Table 2: Chemical shifts of aromatic peaks arising from sugar complexation to silicone-boronic acid **7** (^1H -NMR) (terminal isomer).

Contents	H ^a (ppm)	H ^b (ppm)	H ^{a'} (ppm)	H ^{b'} (ppm)
No Sugar	7.68	7.15	-	-
D-Glucose	7.67	7.15	-	-
D-Fructose	7.67	7.14	7.57	7.20

Binding to fructose in the presence of Tris

Tris buffer (100 mM, pH 7.4) was prepared by dissolving 303 mg (2.5 mmol) tris(hydroxymethyl)aminomethane in 10 mL D₂O. The pH of the solution was adjusted to 7.4 using 2.0 M HCl (in D₂O), then diluted to 25 mL with D₂O. A sample was prepared containing pentamethyldisiloxane silicone-boronic ester derivative **7** (20 mg, 0.046 mmol) and fructose (8 mg, 0.046 mmol) dissolved in DMSO-*d*₆ (1 mL). Aliquots of 100, 200, 300, and 460 µL were added to the same sample, and ¹H-NMR spectra were measured after each aliquot. Peak data and relative integration values within the aromatic region are summarized in Table 3.

Table 3: Binding of silicone-boronic acid **7** to fructose in the presence of Tris

Tris added (µL)	Tris Molarity (mM)	Relative Integration of all Aromatic Signals			
		H ^a (int + term) ~7.59 ppm	H ^b (int + term) ~7.06 ppm	H ^{a'} (int + term) ~7.52 ppm	H ^{b'} (int + term) ~6.82 ppm
0	0	2.00	2.07	-	-
100	8	2.00	2.05	-	-
200	14	2.00	1.90	1.63	1.88
300	20	2.00	1.80	4.13	5.14
460	28	2.00	2.12	8.42	9.50

Improved solubility of boronic acid-modified silicones in the presence of both fructose and Tris

Samples were prepared in standard-sized NMR tubes. Samples were prepared such that the molar ratio of **7** : sugar : Tris was 1:2:2. For example, a sample contained 20 mg **7**, 12 mg glucose, and 8 mg Tris. Each sample also contained one molar equivalent of tertiary-butanol as an internal standard, and samples were suspended/dissolved in 0.8 mL D₂O. Table 6 summarizes the contents of each sample. ¹H NMR spectra were obtained and the relative integration of the entire aromatic region was compared to the signal arising from *t*-BuOH (calibrated to 9H) (Table 4).

Table 4: Solubility of **11** in water (*t*-BuOH internal reference)

Sugar	Tris	Relative integration*
None	No	0.34
None	Yes	0.12
Glucose	No	0.15
Glucose	Yes	0.28
Fructose	No	0.34
Fructose	Yes	0.43

* against *t*-BuOH (tBu peak integrates for 9H).

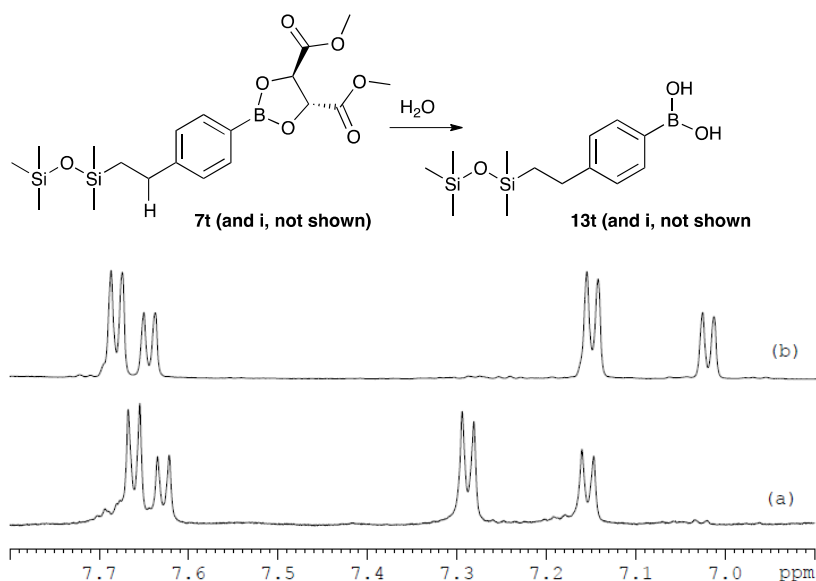


Figure 1S: ¹H NMR spectra showing hydrolysis of tartrate from silicone-boronic acids **7t,i** to **13t,i** in the presence of PBS buffer pH 7.4.

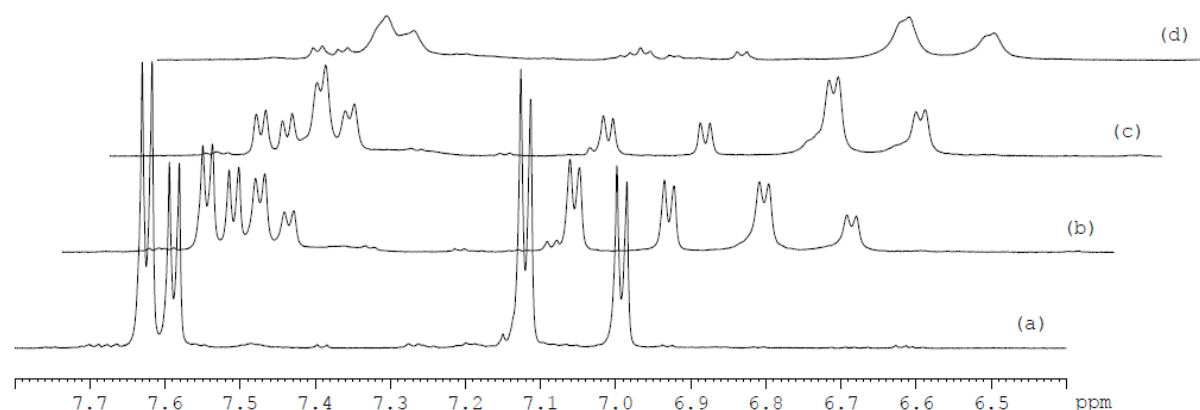


Figure 2S: Addition of tris(hydroxymethyl)aminomethane solution (50 mM in D₂O) improved complexation of **7** to fructose. Amount of Tris added (a) 100 μL; (b) 200 μL; (c) 300 μL; (d) 460 μL.

Rheology

Bolaamphiphilic silicone-boronic acids were hydrolyzed by pipetting the neat compound (as an oil) onto distilled water (approx. 75mL) in a 15cm-diameter glass Petri dish. The resulting rubbery film was lifted from the water and placed into a vial. The procedure was repeated until 175-200mg of each sample was collected.

Samples were analyzed using an Ares Rheometer (TA Instruments) using the program TA Orchestra for data acquisition. Samples were punched into discs (diameter 9.5 mm) and placed in between two parallel plates and compressed to the diameter of the plates (14 mm), giving good contact between the bottom

plate, sample, and top plate. The total distance between plates varied between 1-2 mm depending on sample size. The first measurements performed were the dynamic strain-sweep test between 0.1-100% strain at a constant frequency of 1 Hz. The dynamic strain-sweep test was performed to determine the linear viscoelastic region of the sample. The strain for the linear region (unique for each formulation) was used in subsequent dynamic frequency-sweep tests. A dynamic frequency-sweep test was performed to determine how the modulus of the elastomer changed with respect to frequency, while being independent of strain. All frequency-sweep measurements were performed at a frequency range between 1-100 rad/s. All tests were performed at 23-24 °C (Figure 3).

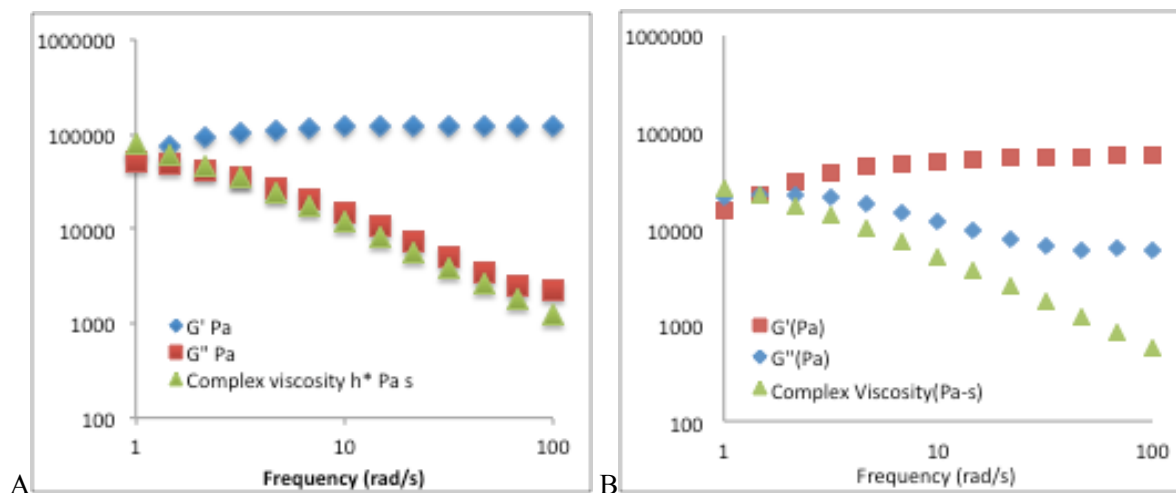


Figure 3S: Complex viscosities of A: **17** (i.e., **11** after hydrolysis of tartrate ester) and B: **18** (i.e., **12** after hydrolysis of tartrate ester).

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PURPOSES

tri- **1** and tetracoordinate **2**
1,2- or 1,3-diol sites **3**, which are particularly are present **4**.
4-Vinylphenylboronic acid **5** is
Dimethyl-L-tartrate boronic ester **6** was f

Product ^a
7 di
8 linear tri
9 brachedtri
10 bola 9
11 bola 15
12 bola 68

The boronic acid products after hydrolysis (**Error! Reference source not found.**) are compounds **13**, **14**, **15**, **16**, **17** and **18**.