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Highly selective recognition of monosaccharide based on two-component system in aqueous solution

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ABSTRACT

A highly selective switch for D-fructose was formed by water-soluble conjugated polymer PP-*S*-BINOL and tetraboronic acid functionalized benzyl viologen ToBV. The two-component system showed a high selectivity and sensitivity only for D-fructose in familiar D-monosaccharides. The high selectivity of the sensing system for D-fructose may be depended on stable pyranose ester form of D-fructose with ToBV. A desirable linear response of the sensing system to low concentrations of D-fructose (<10.0 mM) was observed with 0.9936 linear dependent coefficient at pH 7.4.

1. Introduction

D-Monosaccharides are the most widespread nature saccharides and play important roles in life processes.[1] Owing to their wide usages and special bioactivities, it is indispensable to develop efficient method for detection of D-monosaccharides in aqueous solution.[2] Among various analytical methods, the detection based on fluorescence is the most promising because it can offer the advantages of high sensitivity, real-time analysis, remote detection capabilities, and multiple sensing modes.[3] Regrettably, despite the progress achieved in fluorescence-based recognition systems for monosaccharides, no methods for D-monosaccharides with obviously high selectivity in aqueous solution have been reported.[4] Although a few monosaccharide sensing systems based on fluorescence with passable selectivity have been developed, the significant drawbacks of the systems are lower sensitivity and restricted detection media (only in organic or organic/water mixed solvents).[5] Due to most D-monosaccharides with only one kind of functional group (hydroxyl), the highly selective recognition of D-monosaccharide is rather difficult for the method based on fluorescence.[6] Therefore, how to design and obtain highly selective and water-soluble sensing system of D-monosaccharide is a challenge for chemists, biologists, and medical scientists.[6b,7]

Fortunately, boronic acid functionalized benzyl viologens for sensing D-monosaccharides have been reported by Singaram and co-workers.[8] However, it is a pity that there are high sensitivities and not obvious selectivity for D-monosaccharides. Given the importance of fructose to the food and beverage industry, developing a promising detection system for D-fructose is urgent.[6b,7a,b] Herein, we now introduce a new strategy for highly selective recognition of D-fructose in aqueous solution. The sensing system is comprised of water-soluble anionic polymer (PP-*S*-BINOL) and tetraboronic acid functionalized benzyl viologen (ToBV). (Scheme 1 and Scheme 2) Anionic conjugated polymer PP-*S*-BINOL is optic signal report section and its fluorescence is modulated by electron transfer from PP-*S*-BINOL to ToBV. Cationic viologen ToBV acts as both quencher and receptor in the system. The electrostatic interaction between PP-*S*-BINOL and ToBV through forming ground-state complex will lead to a decrease in the fluorescence intensities of PP-*S*-BINOL. The different binding capabilities between D-monosaccharides and ToBV by forming reversible boronates can weaken the interaction of ToBV with PP-*S*-BINOL, which will result in the fluorescence recovery of PP-*S*-BINOL at different degree. Due to stronger binding action of ToBV with D-fructose and architectural space position of boronic acid on ToBV, the recognition system is worth to expect with high selectivity and sensitivity for D-fructose.

2. Results and discussion

2.1. Synthesis

Polymer PP-*S*-BINOL was synthesized by six steps from the commercially available *p*-hydroquinone and (*S*)-2,2′-dimethoxy-

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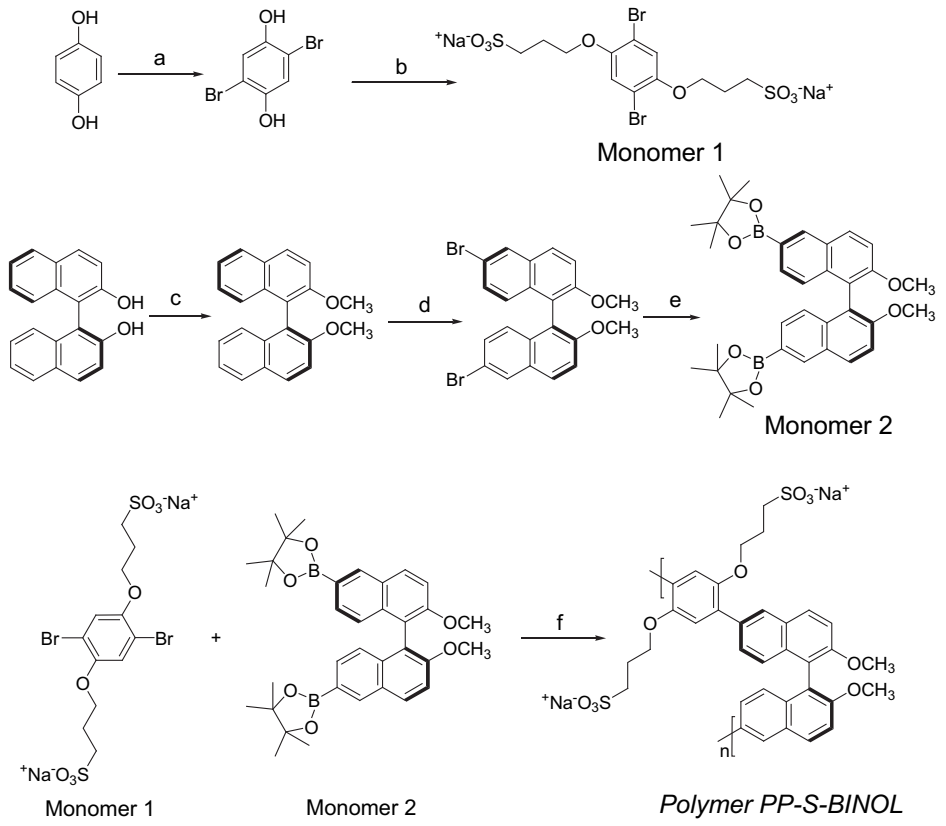
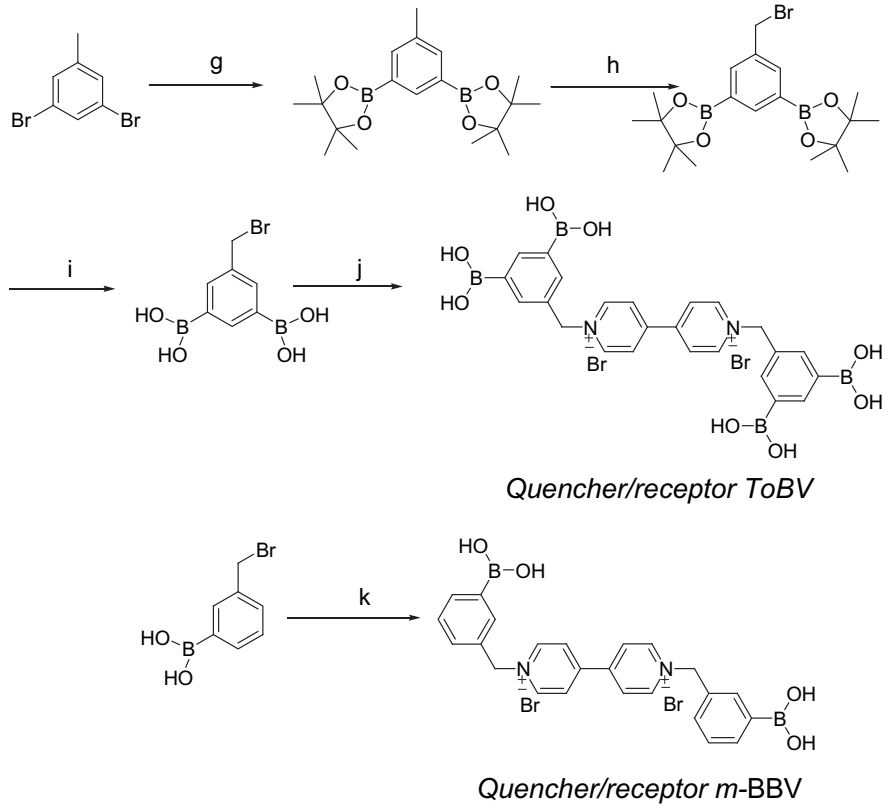


Scheme 1. (a) CH_3COOH, Br_2, room temperature 24 h, 45.8%; (b) 1,3-propanesultone, NaOH, dioxane/H_2O, N_2, room temperature 12 h, then 80–100 °C 3 h, 68.4%; (c) CH_3I, K_2CO_3, acetone, reflux 36 h, N_2, 89.2%; (d) Br_2, CH_2Cl_2, 0 °C, 5 h, 92.3%; (e) bis(pinacolato)diboron, Pd(dppf)Cl_2, KOAc, DMSO, 80 °C 6 h, N_2, 51.4%; (f) Pd(PPh_3)$_4$, 1,4-dibromo-2,5-bis (3-sulfonatopropoxy)benzene, Na_2CO_3, DMF/H_2O, 80 °C 48 h, N_2, 51.6%.



Scheme 2. (g) Bis(pinacolato)diboron, Pd(dppf)Cl_2, KOAc, DMSO, 80 °C 6 h, N_2, 82.3%; (h) NBS, benzoyl peroxide, CCl_4, reflux 7 h, N_2, 74.5%; (i) sodium periodate, hydrochloric acid, THF/H_2O, 48 h, room temperature, 38.6%; (j) 4,4′-bipyridine, DMF, 80 °C 48 h, 47.8%; (k) 4,4′-bipyridine, DMF, 70 °C 48 h, 76.4%.

l,l′-dinaphthyl (*S*-BINOL).[9] Water-soluble monomer **1**, 1,4-dibromo-2,5-bis(3-sulfonatopropoxy)benzene, was obtained by bromination of *p*-hydroquinone and then reaction with 1,3-propanesultone in strong alkali solution. Monomer **2**, (*S*)-2,2′-dimethoxy-6,6′-bis (4,4,5,5-tetramethyl-1,3,2-dioxaborolane)1,1′-naphthalene, was prepared through etherification, bromination, and then boronic acid esterification under Pd(dppf)Cl_2 catalysis. Lastly, the interaction of the monomer **1** and monomer **2** gave polymer PP-*S*-BINOL through Suzuki coupling reaction in 51.6%.

Quencher/receptor To*B*V was synthesized by four steps from the commercially available 1,3-dibromo-5-methylbenzene.[10] Firstly, the C–B coupling reaction between 1,3-dibromo-5-methylbenzene and bis(pinacolato)diboron gave 3,5-bis-(4,4,5,5-tetramethyl-1,3,2-dioxaboro-lane)toluene. Then 5-(bromomethyl)phenyl-1,3-diboronic acid was obtained by bromination of NBS and deesterification of sodium periodate. Lastly, *N*,*N*′-4,4′-bis(benzyl-3,5-diboronic acid)-bipyridinium dibromide (To*B*V) was synthesized by quaternization of commercially available 4,4′-dipyridyl and 5-(bromomethyl)phenyl-1,3-diboronic acid in 47.8%. (Scheme 2).

2.2. Fluorescence studies

Firstly, the quenching interaction of PP-*S*-BINOL and To*B*V was investigated by fluorescence spectra in detail. The fluorescent titration experiments showed that the fluorescence of PP-*S*-BINOL can be effectively quenched by To*B*V in pH 7.4 buffer solution (Fig. 1). Obviously, ground-state complex between PP-*S*-BINOL and To*B*V was formed by electron transfer from PP-*S*-BINOL to To*B*V, resulting in a great reduction of PP-*S*-BINOL fluorescence intensities. At lower concentrations of To*B*V, the Stern–Volmer plot was linear and the static quenching constant (K_{SV}) was 2.37×10^4 M^{-1}. At higher concentrations of To*B*V, the Stern–Volmer plot was curved upward, which indicated a large sphere static quenching had been produced by the electrostatic interaction between PP-*S*-BINOL and To*B*V. The effectively quenching action between fluorescence dye and quencher through forming a complex was very helpful for developing highly sensitive sensing systems of saccharides.

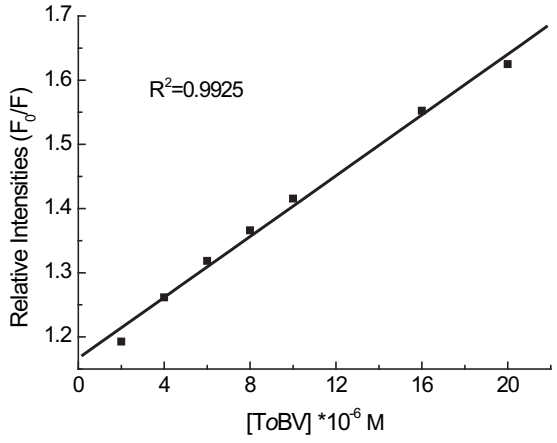


Fig. 1. Stern–Volmer plot of PP-*S*-BINOL (2.84×10^{-3} g/L) quenched by low concentration of To*B*V, measured in phosphate buffer solution pH 7.4 (λ_{ex}=320 nm; λ_{em}=425 nm).

Next, the selectivity of the two-component sensing system for D-monosaccharides was determined in an aqueous solution at pH 7.4 (Fig. 2). As expected, we found the To*B*V/PP-*S*-BINOL sensing system embodied dramatically high selectivity only for D-fructose in seven common D-monosaccharides. The rather large fluorescence recovery of PP-*S*-BINOL was observed by adding D-fructose to the sensing system. However, respectively introducing other D-monosaccharides to the sensing system, no obvious fluorescence changes of To*B*V/PP-*S*-BINOL system were observed. To the best of our knowledge, the selectivity of the sensing system for D-fructose was the highest ever recorded and the response ratio for D-fructose/D-glucose was about 85-fold increase in the present of 10 mM D-monosaccharides. The high selectivity of the sensing system for D-fructose may result from the *meta*-position of boronic acid groups in the same benzyl ring of To*B*V, which can provide suited binding space for the pyranose form of fructose. This supposed binding way was imitated by Chem3D (see Fig. S1). To confirm our guess, another sensing system of *N*,*N*′-4,4′-bis(benzyl-2-boronic acid)bipyridinium dibromide (*m*-BBV, Scheme 2) with PP-*S*-BINOL was composed to determine D-monosaccharides in pH 7.4 buffer solution (see Figs. S2 and S3). We found the fluorescence of PP-*S*-BINOL can be quenched by *m*-BBV in pH 7.4 buffer solution. However, though the fluorescent recoveries of PP-*S*-BINOL were all observed with the addition of any D-monosaccharides, no obvious differences of fluorescent changes were observed, which indicated the *m*-BBV/PP-*S*-BINOL two-component system did not have obvious selectivity for D-monosaccharides. From the titration curves, it is believed that 1:2 boronate complex between To*B*V and D-fructose was formed.[8d] Due to no considering the interaction of PP-*S*-BINOL and To*B*V, the binding constants of the system to monosaccharides were roughly calculated. The results showed that the binding order of the sensing system to monosaccharides was D-fructose>D-galactose>D-ribose≈D-xylose≈D-arabinose>D-mannitose≈D-glucose.[8]

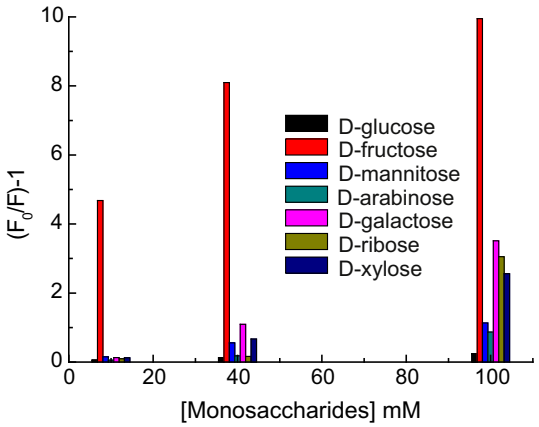


Fig. 2. The binding characteristics of PP-*S*-BINOL (2.84×10^{-3} g/L) and To*B*V (0.674 g/L, 1.0×10^{-3} M) with different D-monosaccharides in pH 7.4 phosphate buffer solutions (λ_{ex}=320 nm; λ_{em}=425 nm). The concentrations of monosaccharides were 10.0 mM, 40.0 mM, and 100.0 mM, respectively.

The sensitivity of the sensing system to D-fructose was investigated by fluorescence spectra in pH 7.4 buffer solution (Fig. 3). Upon introducing D-fructose to the sensing system, an apparent recovery of the fluorescence was observed by forming negatively charged borate ester between To*B*V and D-fructose. The fluorescence recovery of PP-*S*-BINOL was dependent on the D-fructose concentration. The 11-fold increase of fluorescence intensity was observed by adding 100 mM D-fructose to PP-*S*-BINOL/To*B*V sensing system. Remarkably, we investigated a desirable linear response to low concentrations of D-fructose (<10.0 mM) at pH 7.4 (see Fig. S4). Additionally, the desirable linear response of the sensing system to D-fructose was no obvious influence in the present of other D-monosaccharides (see Figs. S5 and S6). It is well known that the linear response of sensing system to D-fructose was important for practical detection in food safety field.

Lastly, the ground-state complex (PP-*S*-BINOL/To*B*V) formation and the return to the uncomplex (PP-*S*-BINOL) led to the color changes of solutions under 365 nm UV–vis light (see Fig. S7). The

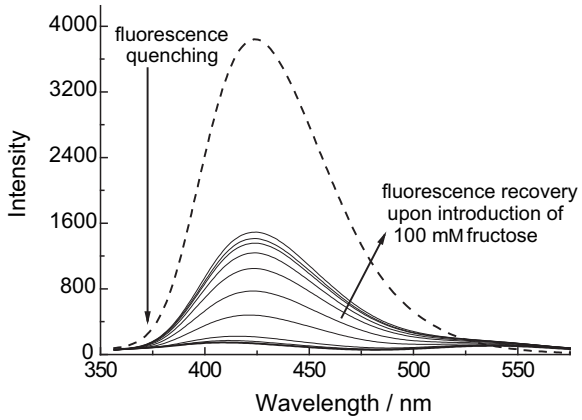


Fig. 3. Characteristic fluorescence response by introduction of quencher followed by fructose to PP-*S*-BINOL solution (2.84×10^{-3} g/L) at pH 7.4. The concentration of T*o*BV was 0.674 g/L (1.0×10^{-3} M) and final fructose concentration was 100 mM (λ_{ex}=320 nm; λ_{em}=425 nm). The dashed line indicates unquenched fluorescence, the bold line indicates fluorescence after introduction of quencher T*o*BV.

blue solution of PP-*S*-BINOL turned into black solution with the addition of T*o*BV, revealing the ground-state complex formation (low-fluorescence). With the increase of D-fructose in the sensing system, the quenched black solution gradually changed to darkblue solution, which demonstrated the complex was less stable and had been largely dissociated with a considerable recovery of the original PP-*S*-BINOL.

3. Conclusions

We developed a highly selective and sensitive D-fructose sensing system based on water-soluble PP-*S*-BINOL and tetraboronic acid functionalized benzyl viologen T*o*BV. The high selectivity of the sensing system for D-fructose may depend on stable pyranose ester form of D-fructose and suitable boronic acid position of T*o*BV. The response ratio for D-fructose/D-glucose was about 85-fold increase in the present of 10 mM D-monosaccharides, respectively. Remarkably, a desirable linear response of the sensing system to low concentration of D-fructose (<10.0 mM) was observed at pH 7.4. We believe that these results can offer a new strategy for developing highly selective monosaccharides sensors. Further studies of PP-*S*-BINOL/T*o*BV sensing system for D-monosaccharides are currently underway.

4. Experimental

4.1. General procedures

Unless otherwise stated, all chemical reagents were obtained from commercial suppliers and used without further purification. Solvents used were purified and dried by standard methods prior to use. *p*-Hydroquinone, 1,3-propanesultone, 1,3-dibromo-5-methylbenzene, $Pd(PPh_3)_4$, $Pd(dppf)Cl_2$, bis-(pinacolato)diboron, and (*S*)-2,2′-dihydroxy-l,l′-di-naphthyl were purchased from Aldrich (Steinheim, Germany). *N*,*N*′-4,4′-Bis(benzyl-2-boronic acid)bipyridinium dibromide (*m*-BBV) was synthesized according to previously reported literature.[10d] pH measurements were carried out on a Mettler Toledo MP 220 pH meter, ^{1}H NMR and ^{13}C NMR were measured on a Bruker ARX400 spectrometer with chemical shifts reported as parts per million (TMS as an internal standard). ^{11}B NMR spectra were recorded on a Bruker at 80 MHz and were reported in ppm with respect to $BF_3\cdot OEt_2$ (δ=0). Elemental analyses were performed on a Vario EL elemental analysis instrument (Elementar Co.). High-resolution mass spectra (HRMS) were acquired on an Agilent 6510 Q-TOF LC/MS instrument (Agilent Technologies, Palo Alto, CA) equipped with an electrospray ionization (ESI) source.

4.2. Fluorescent measurements for quenching and sensing studies of D-monosaccharides

All experiments of water were pure water. All of the working solutions were buffered at pH 7.4±0.1 using a phosphate (the mixture system of Na_2HPO_4 (0.2 M, 61.0 mL) and NaH_2PO_4 (0.2 M, 39.0 mL)) buffer solution. The stock solution (2.84 g/L, 1.0 mL) of PP-*S*-BINOL was diluted in 1.0 L measuring flask with pH 7.4 buffer solution to afford the working solution (2.84×10^{-3} g/L). The stock solution (0.04 M) of T*o*BV was prepared by 0.2694 g T*o*BV in 10 mL measuring flask. The stock solutions of monosaccharides were 1.0 M in 10 mL measuring flask. The standard stock solutions of lower concentration were prepared by suitable dilution of the stock solutions with pH 7.4 buffer solution.

All spectra analysis studies were carried out at pH=7.4 buffer solution and the working solutions were placed in a quartz cuvette with 1 cm path. The total volume of working solution was 2 mL. The studies of fluorescence quenching and sensing monosaccharides used titration experiments and the volume added did not exceed 3% of the total. After the mixture solution was shaken for 30 s, the new spectra were measured. Fluorescence spectra were acquired with a Hitachi F-4500 fluorescence spectrophotometer, the excitation and emission slit widths were 5 nm and 10 nm, respectively. The excitation wavelength was set in 320 nm according to experimental requirements. All of the experiments were performed at barometric pressure and room temperature. Stern–Volmer static quenching constants were calculated by fitting the data to $F_0/F=1+K_{sv}[Q]$, where F_0 was the initial unquenched fluorescence intensity, F was the fluorescence intensity in the presence of quencher, K_{SV} was the static quenching constant, [Q] is the quencher concentration.

4.3. Synthesis

4.3.1. 2,5-Dibromobenzene-1,4-diol. A solution of 32.0 g (0.2 mol) Br_2 in 30 mL glacial acetic acid was generally added by dropping funnel to a solution of 11.0 g (0.1 mol) *p*-hydroquinone in 60 mL glacial acetic acid. The mixture was stirred for 24 h at room temperature. The mixture solution was added 1 L water and the resulting brown solid was filtered. The crude products were purified by recrystallization twice from water to yield product as white needles (12.27 g, yield 45.8%), mp 177–178 °C (lit. 177 °C).

4.3.2. 1,4-Dibromo-2,5-bis(3-sulfonatopropoxy)benzene. A solution of 6.35 g (20.0 mmol) 2,5-dibromobenzene-1,4-diol, 2.0 g (50.0 mmol) sodium hydroxide, and 200 mL water in a Erlenmeyer flask was stirred under nitrogen. Then, a solution of 6.1 g (50.0 mmol) 1,3-propanesultone in 40 mL dioxane was added to the former solution at once. The resulting mixture was then stirred at room temperature overnight, during which time a thick pink slurry formed. The reaction mixture was then stirred at 80–100 °C for another 30 min and then cooled in a water/ice bath. The suspension obtained was vacuum filtered, and the retained solid was washed with cold water followed by acetone. The crude products were purified by recrystallization twice from water to yield product as white powder (7.61 g, yield 68.4%). ^{1}H NMR (D_2O, 400 MHz) δ 7.16 (s, 1H), 4.03 (dd, *J*=6.0, 6.0 Hz, 4H), 3.05 (dd, *J*=4.4, 5.6 Hz, 4H), 2.21 (m, 4H); ^{13}C NMR (D_2O, 100 MHz) δ 24.24, 47.91, 68.97, 111.03, 119.19, 149.42. Element Analysis for $C_{12}H_{14}Br_2Na_2O_8S_2$ (Mol. wt: 556.15) calcd: C 25.92; H 2.54; Br 28.73; S 11.53, found: C 25.89; H

2.57; Br 28.69; S 11.58; HRMS-ESI for $C_{12}H_{14}Br_2Na_2O_8S_2$ (*m*/*z*) 533.51 [M-23].

4.3.3. (S)-2,2′-Dimethoxy-l,l′-dinaphthyl. A suspension of 25.0 g (8.7 mmol) (*S*)-2,2′-di-hydroxy-l,l′-dinaphthyl in 800 mL of acetone was heated and stirred with maximum rotation to give a homogeneous solution. To this solution stirred under N_2 was added 40.0 g (29.0 mmol) K_2CO_3 and 60.0 g (0.42 mol) CH_3I, and the mixture was refluxed for 24 h. An additional 20.0 g (0.14 mol) portion of CH_3I was added, and the mixture was refluxed for an additional 12 h. The solvent was evaporated to leave a volume of 150 mL, which was cooled to 25 °C, and 900 mL water was added to the stirred suspension. The solid was collected, washed with water, and dried under vacuum to give crude product. The crude product was dissolved in 100 mL CH_2Cl_2 and heated. The solution was poured into 500 mL petroleum ether and appeared as a precipitate. The precipitate was filtered off and dried in vacuo to give desired product as a white powder that was used without further purification in the next reaction. Mp 224–225 °C (24.48 g, yield 89.2%).

4.3.4. (S)-6,6′-Dibromo-2,2′-dimethoxy-1,1′-binaphthyl. (*S*)-2,2′-Dimethoxy-1,1′-binaphthyl 9.4 g (30.0 mmol) was dissolved in 500 mL CH_2Cl_2 and stirred at 0 °C. 3.36 mL (66.0 mmol) Bromine was added in one portion with stirring and a stream of nitrogen was bubbled through the solution to remove the evolving HBr. The reaction mixture was stirred for 5 h while the flask was allowed to warm to room temperature. During this procedure, the product precipitates as a white solid and was filtered off and dried in vacuo to give desired product (9.52 g, 92.3%) as a white powder.

4.3.5. (S)-2,2′-Dimethoxy-6,6′-bis-(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)-1,1′-naphtha-lene. A mixture with 9.44 g (20.0 mmol) (*S*)-6,6′-dibromo-2,2′-dimethoxy-1,1′-binaphthyl, 11.18 g (44.0 mmol) bis(pinacolato)diboron, 0.58 g (8 mol %) $Pd(dppf)Cl_2$, and 11.78 g (0.12 mol) potassium acetate in 60 mL DMSO was stirred at 80 °C for 6 h under a nitrogen atmosphere. The reaction mixture was cooled to room temperature, poured into the 200 mL ice water, filtrated, and then purified by column chromatography on silica gel with ethyl acetate/petroleum ether (1/15) as the eluant to afford a white power (5.82 g, 51.4%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.42 (s, 2H), 8.05 (d, *J*=9.2 Hz, 2H), 7.58 (d, *J*=8.8 Hz, 2H), 7.45 (d, *J*=8.8 Hz, 2H), 7.10 (d, *J*=8.8 Hz, 2H), 3.76 (s, 6H), 1.38 (s, 24H); ^{13}C NMR (DMSOd_6, 100 MHz) δ 24.89, 56.71, 83.70, 113.94, 119.31, 124.32, 128.60, 130.34, 130.85, 135.73, 136.52, 155.94; HRMS-ESI for $C_{34}H_{40}B_2O_6$ (*m*/*z*) 567.40 [M+1], 566.24 [M], 565.16 [M−1].

4.3.6. PP-S-BINOL. To 100 mL three-neck flask, equipped with mechanical stirrer was added 3.336 g (6.0 mmol) 1,4-dibromo-2,5-bis(3-sulfonatopropoxy)benzene, 3.396 g (6.0 mmol) 2,2′-dimethoxy-6,6′-bis-(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)-1,1′-naphthalene, 60 mL dried DMF, and 0.224g (0.18 mol) $Pd(PPh_3)_4$ under nitrogen. The mixture was stirred under nitrogen for 30 min, and then 20 mL aqueous solution with 3.816 g (36.0 mmol) sodium carbonate was generally added by dropping funnel. The reaction was heated at 80 °C for 48 h. The reaction turned black as Pd(0) particles were liberated. The tan-violet filtrate was collected, precipitated into 1 L of acetone, and redissolved in deionized water. The polymer was dialyzed using a membrane with a 3500 cutoff for 3 days. The final product, a dark yellow polymer, was obtained after dried in vacuo at 110 °C for 24 h (2.21 g, 51.6%). ^{1}H NMR (DMSOd_6, 400 MHz) δ 8.22 (s, 2H), 8.15 (d, *J*=7.6 Hz, 2H), 7.64 (d, *J*=7.6 Hz, 2H), 7.55 (d, *J*=7.6 Hz, 2H), 7.16 (s, 2H), 7.04 (d, *J*=7.2 Hz, 2H), 4.12 (broad, 4H), 3.77 (s, 6H), 2.58 (broad, 4H), 1.97 (broad, 4H); ^{13}C NMR (DMSOd_6, 100 MHz) δ 25.82, 48.47, 56.74, 68.32, 114.82, 116.23, 118.64, 129.11, 129.87, 130.26, 132.80, 133.35, 150.24, 153.20, 155.25. Element Analysis for $C_{34}H_{30}Na_2O_{10}S_2$ (Mol. wt monomeric unit: 708.72) calcd: C 57.62; H 4.27; S 9.04; Na 6.49, found: C 57.58; H 4.31; S 9.09; Na 6.55.

4.3.7. 3,5-Bis-(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)toluene. A mixture of 10.0 g (0.04 mol) 1,3-dibromo-5-methylbenzene, 22.4 g (0.088 mol) diborane pinacol ester, 1.5 g (2.0 mmol) $Pd(dppf)Cl_2$, 23.52 g (0.24 mmol) KOAc, and 80 mL DMSO was heated to 80 °C for 4 h. After the mixture was cooled, 500 mL water was added, and the mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and the solvent was removed by vacuum distillation. The crude product was purified by column chromatography on silica gel with ethyl acetate/petroleum ether (1/20) as the eluant to afford a white power (11.32 g, 82.3%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.09 (s, 1H), 7.73 (s, 2H), 2.35 (s, 3H), 1.33 (s, 24H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.09, 24.89, 83.77, 136.32, 138.42; HRMS-ESI for $C_{19}H_{30}B_2O_4$ (*m*/*z*) 345 [M+1], 344 [M], 189 [M−155].

4.3.8. 3,5-Bis-(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)-1-bromoemethylbenzene. A mixture of 10.32 g (30.0 mmol) 3,5-bis-(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)-toluene, 6.23 g (35.0 mmol) NBS, 0.35g (1.4 mmol) benzoyl peroxide, and 250 mL CCl_4 was refluxed for 7 h under N_2 atmosphere. The resulting solution was filtered while it was cooled to room temperature. The filtrate was washed with saturated sodium hyposulfite solution (3×100 mL) then brine (2×100 mL), dried over Na_2SO_4, and concentrated by vacuum distillation to afford yellow-white precipitate. The precipitate was recrystallized with CCl_4 to give white solid (9.46 g, 74.5%).

4.3.9. 5-(Bromomethyl)phenyl-1,3-diboronic acid. A mixture of 8.46 g (20.0 mmol) 3,5-bis-(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)-1-bromoemethylbenzene, 12.84 g (60.0 mmol) sodium periodate, and 50 mL THF/H_2O (4/1) was stirred until homogeneous at room temperature, and then 2 N HCl (0.2 mL) was added. After 48 h, the reaction mixture was extracted with ethyl acetate (3×50 mL), and the combined organic extracts were washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. The crude product was recrystallized for two times with CCl_4 to give white solid (1.99 g, 38.6%).

4.3.10. N,N′-4,4′-Bis(benzyl-3,5-diboronic acid)-bipyridinium dibromide (ToBV). To a solution of 1.94 g (7.5 mmol) 5-(bromomethyl) phenyl-1,3-diboronic acid in 20 mL DMF was added 0.585 g (3.75 mmol) 4,4′-dipyridyl, and the reaction mixture was stirred at 80 °C for 48 h under nitrogen. The orange precipitate was collected by filtration, washed with DMF, acetone, then ether and dried under a stream of nitrogen to yield ToBV (1.21 g, 47.8%). ^{1}H NMR (D_2O, 400 MHz) δ 9.50 (d, *J*=10.0 Hz, 4H), 8.76 (d, *J*=7.2 Hz, 4H), 8.07 (s, 6H), 5.95 (s, 4H); ^{13}C NMR (D_2O, 100 MHz) δ 64.52, 99.98, 127.67, 132.52, 136.58, 146.12, 149.68, 151.44; ^{11}B NMR (80 MHz, D_2O) δ 25.4; HRMS-ESI for $C_{24}H_{24}B_2Br_2N_2O_4$ (*m*/*z*) HRMS-ESI (*m*/*z*) 513.24 [M-2Br].

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Supplementary data

^{1}H NMR, ^{13}C NMR, and ESI-MS of compounds and fluorescent spectroscopy (PDF). Supplementary data related to this article can be found online at doi:10.1016/j.tet.2011.03.025. These data include MOL files and InChIKeys of the most important compounds described in this article.

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