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Enantioselective Recognition of Mandelic Acid by a 3,6-Dithiophen-2-yl-9*H*-carbazole-Based Chiral Fluorescent Bisboronic Acid Sensor

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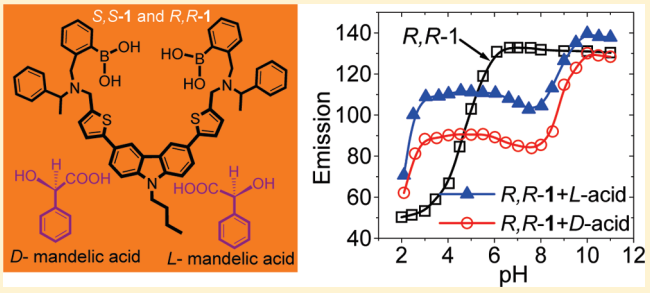
Supporting Information

ABSTRACT: We have prepared chiral fluorescent bisboronic acid sensors with 3,6-dithiophen-2-yl-9*H*-carbazole as the fluorophore. The thiophene moiety was used to extend the π-conjugation framework of the fluorophore in order to red-shift the fluorescence emission and, at the same time, to enhance the novel process where the fluorophore serves as the electron donor of the photoinduced electron transfer process (d-PET) of the boronic acid sensors; i.e., the background fluorescence of the sensor **1** at acidic pH is weaker compared to that at neutral or basic pH, in stark contrast to the typical a-PET boronic acid sensors (where the fluorophore serves as the electron acceptor of the photoinduced electron transfer process). The benefit of the d-PET boronic acid sensors is that the recognition of the hydroxylic acids can be achieved at acidic pH. We found that the thiophene moiety is an efficient π-conjugation linker and electron donor; as a result, the d-PET contrast ratio of the sensors upon variation of the pH is improved 10-fold when compared to the previously reported d-PET sensors without the thiophene moiety. Enantioselective recognition of tartaric acid was achieved at acid pH, and the enantioselectivity (total response $K_D I_F^D / K_L I_F^L$) is 3.3. The fluorescence enhancement (I_F^{Sample}/I_F^{Blank}) of sensor **1** upon binding with tartaric acid is 3.5-fold at pH 3.0. With the fluorescent bisboronic acid sensor **1**, enantioselective recognition of mandelic acid was achieved for the first time. To the best of our knowledge, this is the first time that the mandelic acid has been enantioselectively recognized using a chiral fluorescent boronic acid sensor. Chiral *mono*boronic acid sensor **2** and bisboronic acid sensor **3** without the thiophene moiety failed to enantioselectively recognize mandelic acid. Our findings with the thiophene-incorporated boronic acid sensors will be important for the design of d-PET fluorescent sensors for the enantioselective recognition of α-hydroxylic acids such as mandelic acid, given that it is currently a challenge to recognize these analytes with boronic acid fluorescent molecular sensors.



1. INTRODUCTION

Fluorescent boronic acid sensors have attracted considerable attention for the recognition of biologically significant chemical species, ranging from glucose,[1−18] to cations such as Cu^{2+} or anions such as F^-,[19−22] to disaccharides or oligosaccharides,[15b] and more recently to ginseng glycosides, etc.[23−26] Most of these molecular boronic acid sensors are based on the formation of a borate ester of the sensors with polyhydroxyl analytes.[1,2] Furthermore, photoinduced electron transfer (PET) is the most popular sensing mechanism used in the construction of fluorescent boronic acid sensors, more specifically, a-PET sensors; i.e., the fluorophore serves as the electron acceptor of the PET process.[1,2] These boronic acid sensors show strong background emission at acidic pH; thus, the fluorescence relay at acidic pH upon binding with analytes is poor, and the recognition can only be studied at neutral or basic pH. However, some analytes require the recognition to be carried out at acidic pH in order to achieve high binding constants, such as tartaric or mandelic acid.[27] However, it should be pointed out that for sensors that are not sensitive to variation in pH of the media, such limitations do not exist.

We have been interested in fluorescent boronic acid sensors for a while[27] and have devised boronic acid sensors based on a new fluorescence relay mechanism, the d-PET effect; i.e., the fluorophore acts as the electron donor of the PET process.[27f,g] d-PET sensors give weak background fluorescence emission at acidic pH but stronger emission in neutral and basic pH; at acidic pH, the protonated N atom (fluorescence switching center) and the boronic acid moiety are stronger electron acceptors than that at neutral/basic pH. As a result, the PET quenching effect is more significant and thus the fluorescence of the sensor is diminished. This behavior is in contrast to that observed with the normal a-PET sensors. Thus, the fluorescence relay in the acidic pH

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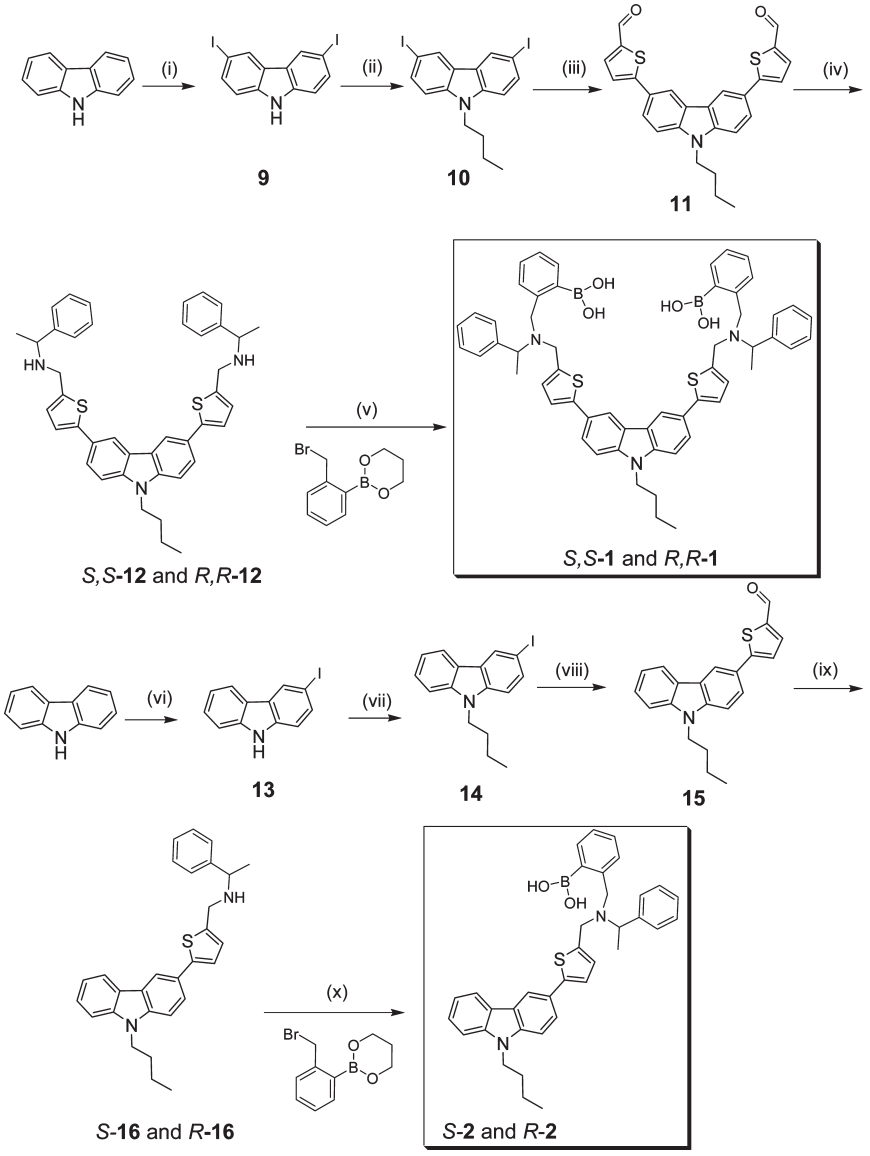
Scheme 1. Synthesis of the 3,6-Dithiophen-2-yl-9*H*-carbazole Based Boronic Acid Sensor 1 and the Monoboronic Acid Sensor 2



Reagents and conditions: (i) KI, KIO_3, CH_3COOH, reflux, 10 min, 42.1%; (ii) NaH, DMF, *n*-C_4H_9Br, rt 1 h, 85.0%; (iii) THF, K_2CO_3, $Pd(PPh_3)_4$, 5-formylthiophene-2-boronic acid, N_2 atmosphere, reflux, 10 h, 62.4%; (iv) *R*- and *S*-1-phenylethanamine, DCM, ethanol, reflux, 8 h, then $NaBH_4$, rt 1 h, 79.4% (*S*,*S*-**12**), 64.6% (*R*,*R*-**12**); (v) acetonitrile, DCM, K_2CO_3, 2-(2-bromomethylphenyl)-1,3,2-dioxaborinane, reflux, 10 h, 27.5% (*S*,*S*-**1**), 31.2% (*R*,*R*-**1**); (vi) KI, KIO_3, CH_3COOH, reflux, 10 min, 40.0%; (vii) NaH, DMF, *n*-C_4H_9Br, rt 1 h, 90.2%; (viii) THF, K_2CO_3, $Pd(PPh_3)_4$, 5-formylthiophene-2-boronic acid, N_2 atmosphere, reflux, 10 h, 52.0%; (ix) *R*- and *S*-1-phenylethanamine, DCM, ethanol, reflux, 8 h, then $NaBH_4$, rt 1 h, 71.2% (*S*-**16**), 78.4% (*R*-**16**); (x) acetonitrile, DCM, K_2CO_3, 2-(2-bromomethylphenyl)-1,3,2-dioxaborinane, reflux, 10 h, 42.0% (*S*-**2**), 44.5% (*R*-**2**).

region upon binding with analytes is improved compared to that of the normal a-PET sensors.[27b] Typical a-PET boronic acid sensors cannot recognize tartaric acid at acidic pH due to the strong background emission of the sensors.[27b]

However, we noticed some limitations for the development of the d-PET boronic acid sensors. (1) Currently the d-PET boronic acid sensors are limited to those with carbazole as the fluorophore (a chromophore with strong electron-donating ability), which show excitation and emission in the UV region.[27g] Unfortunately, we found that extension of the π-conjugation of the carbazole with ethynylene moiety, a typical strategy for extension the emission wavelength of fluorophores, does not always retain the d-PET effect.[27f,g] For example, in some cases the ethynylene linker changes the receptors from a d-PET to an a-PET system;[27g] therefore, an alternative strategy, other than the acetylide approach, to extend the π-conjugation framework of the fluorophore has to be developed to red-shift the emission wavelength of the sensors. The C=C double bond is not an ideal candidate, since the fluorescence emission of a fluorophore is often quenched by cis−trans isomerization of C=C double bonds. (2) The contrast ratio, or the PET efficiency, of the d-PET boronic acid sensors is usually poor.[27f,g] The typical fluorescence variation of the d-PET boronic acid sensors is much less than the normal a-PET boronic acid sensors.[27b] Therefore, we propose that it will be helpful to use a fluorophore with stronger electron-donating ability to achieve a higher contrast

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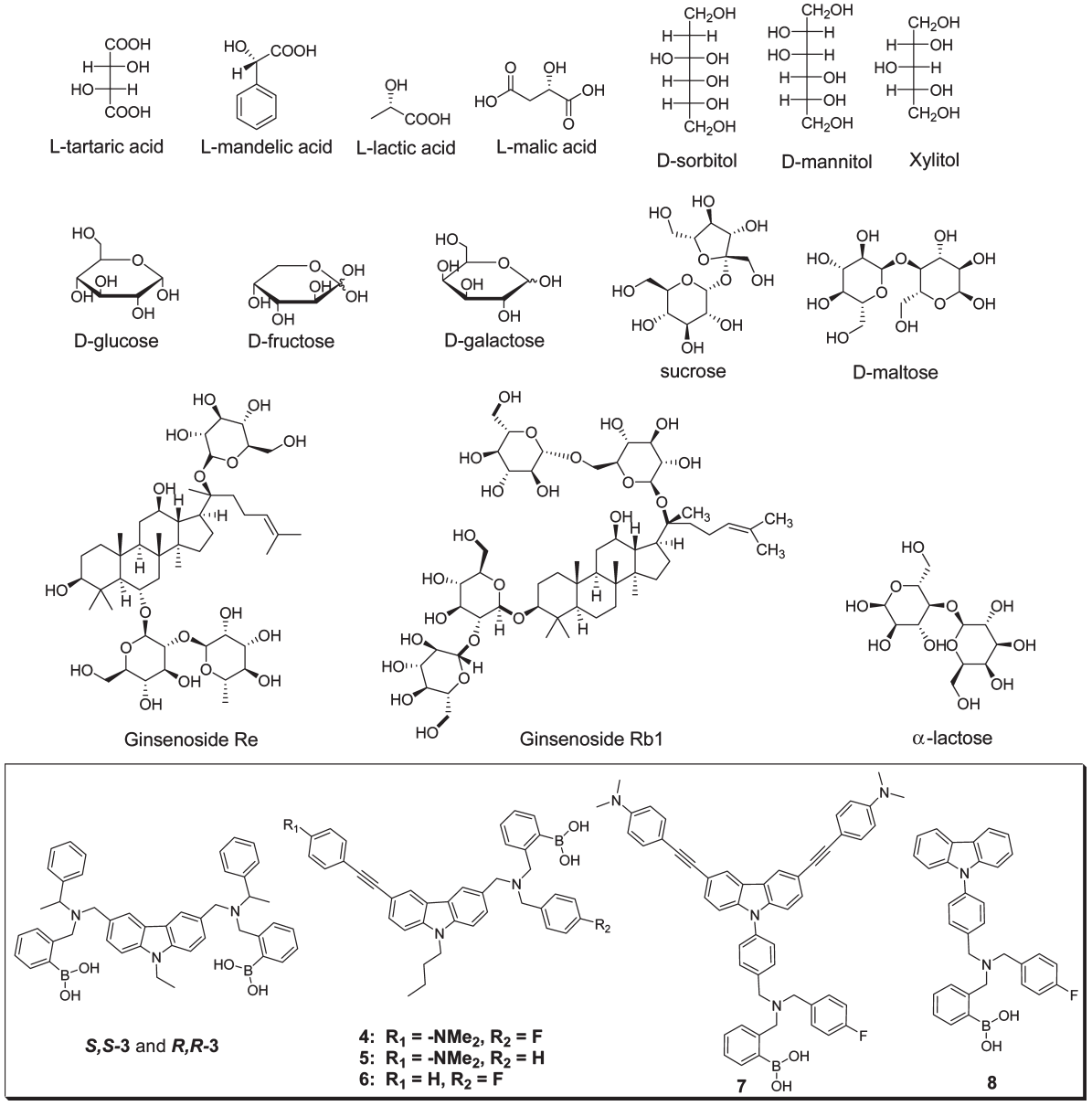
Scheme 2. Analytes Used in the Enantioselective Recognitions with the Sensors 1 and 2 and the Known d-PET Fluorescent Boronic Acid Sensors 3−8



ratio. (3) It is still a challenge to enantioselectively recognize mandelic acid with fluorescent boronic acid sensors. The enantioselective recognition of mandelic acid has been achieved with sensors based on the hydrogen-bonding motif, but the recognition has to be performed in nonprotic organic solvents.[28−35] Also, although a chiral boronic acid sensor for the enantioselective recognition of mandelic acid has been reported, the chirogenic center is limited to a constrained cyclic chiral amine and the sensor is without any fluorophore; thus, a three-component displacement assay was used for the signal relay.[36] Previously, we reported a fluorescent chiral boronic acid sensor (with boronic acid binding site and an extra hydroxyl group as a potential hydrogen-bonding site) for the enantioselective recognition of mandelic acid, but that sensor was only effective in nonprotic organic solvents.[37] To the best of our knowledge, no *fluorescent* chiral boronic acid sensors have been reported to date for the enantioselective recognition of mandelic acid.[38] Enantioselective recognition of mandelic acid is more important than recognition of tartaric acid, because the single α-hydroxyl carboxylic acid structure of mandelic acid is a more general structural motif than the bis α-hydroxyl carboxylic acid structure of tartaric acid.

In order to address the aforementioned challenges and inspired by the application of the thiophene moiety as a π-conjugation linker and strong electron donor in material chemistry, in particular dye-sensitized solar cells[39−42] and fluorescent molecular sensors,[43−59] etc., we devised the boronic acid sensor **1** with 3,6-dithiophen-2-yl-9*H*-carbazole as the fluorophore and monoboronic acid sensor **2** was prepared as a model sensor (Scheme 1). Emission in the visible region was observed for the chiral boronic acid sensors. We found that the PET contrast ratio of the d-PET sensors is up to 3.0, which is 10-fold that of

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our previously reported d-PET sensors without the thiophene moiety.[27f] Various analytes were tested with the boronic acid sensors (Scheme 2). Enantioselective recognition of tartaric acid was observed. More interestingly, enantioselective fluorescent recognition of D- and L-mandelic acid was observed with the bisboronic acid sensor **1**. To the best of our knowledge, this is the first time that mandelic acid, with a mono-α-hydroxylic acid unit, has been enantioselectively recognized by a fluorescent boronic acid sensor. We believe that our findings with the thiophene incorporated boronic acid sensors will be useful for design of new d-PET fluorescent sensors with improved fluorescence transduction efficiency and for the enantioselective recognition of mandelic acid and other α-hydroxylic acids in aqueous solution.

2. RESULTS AND DISCUSSION

2.1. Design and Synthesis of the Thiophen-2-yl-9*H*-carbazole-Based Boronic Acid Sensors. In order to improve the PET efficiency or the contrast ratio of the d-PET boronic acid sensors (usually smaller than the normal a-PET sensors) and at the same time to optimize the fluorescence properties of the d-PET fluorophore, such as the excitation and emission wavelength, thiophene units are used to extend the π-conjugation of the carbazole and to enhance the electron-donating ability of the fluorophore (sensor **1** and **2**, Scheme 1). Thiophene has been widely used in material chemistry, such as with optoelectrics, as a conjugation linker and electron donor. However, the application of thiophene moiety in fluorescent molecular sensors is also reported.[43−59] However, only one thiophene-containing boronic acid sensor was reported.[59]

Carbazole was used as the fluorophore core and the scaffold of the chiral sensors (Scheme 1). First the carbazole core was iodated and then 2-formyl-5-thiopheneboronic acid was attached to the carbazole by Pd(0)-catalyzed Suzuki cross-coupling. The chirogenic center was introduced by reductive amination with α-benzylamine. The boronic acid moieties were attached by alkylation with 2-(2-bromomethylphenyl)-1,3,2-dioxaborinane (Scheme 1).[27b,f] The monoboronic acid sensor **2** was also prepared and used for comparison in the binding studies. The chiral sensors were obtained in moderate to satisfying yields. The previously reported carbazole-based bisboronic acid sensor **3** was used in the binding studies as a model compound.[27f]

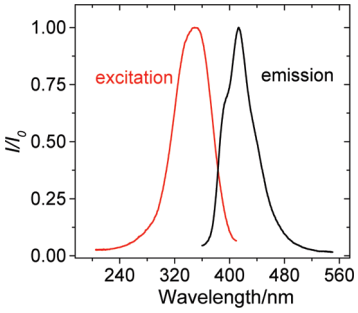

Figure 1. Normalized excitation and emission spectra of *S*,*S*-**1**: λ_{ex} = 349 nm, λ_{em} = 413 nm, 5.0×10^{-7} mol dm^{-3} of sensor in methanol/water mixed solvent (3:1, v/v), pH = 7.0, and 20 °C.

2.2. Fluorescence of the Sensors and the d-PET Effect. The fluorescence excitation and emission spectra of sensor **1** were investigated, with the excitation and emission maxima located at 349 and 413 nm, respectively (Figure 1). These values are red-shifted by 38 nm compared to sensor **3** based on the unsubstituted carbazole fluorophore (Scheme 2).[27f] The emission wavelength of sensor **1** (413 nm) is similar to the boronic acid sensors based on phenylethynylated carbazole fluorophore.[27h] This result indicates that the thiophene moiety is an efficient π-conjugation linker suitable for red-shifting the emission wavelength of the carbazole fluorophore. The enantiomers of **2**, i.e., *R*-**2** and *S*-**2**, were prepared, and blue-shifted excitation and emission wavelengths (340 nm/396 nm) were observed for sensor **2** compared to sensor **1** (Supporting Information). We attribute the blue-shifted excitation/emission of sensor **2** to its smaller π-conjugation framework.

The photophysical properties of the sensors are summarized in Table 1. The fluorescence quantum yields of the sensors at basic pH are higher than that at acidic pH. This is in agreement with the expectation for d-PET boronic acid sensors;[27f−h] thus, we propose that these sensors will demonstrate the d-PET effect, which is in contrast to the normal a-PET fluorescent boronic acid sensors.

2.3. Improved Enantioselective Recognition of Tartaric Acid. The emission intensity−pH profile of sensor **1** was investigated (Figure 2). The emission of *S*,*S*-**1** at acidic pH is weaker than that at neutral and basic pH, which is a clear indication of the d-PET effect.[27f−h] A similar result was also observed for *R*,*R*-**1** (Figure 2b). In the presence of D- or L-tartaric acid, the emission of the sensors was enhanced, particularly at acidic pH. An enantioselective fluorescence response was observed, e.g. for *S*,*S*-**1**, the fluorescence enhancement is 5-fold in the presence of L-tartaric acid, vs 3-fold enhancement in the presence of D-tartaric acid. With *R*,*R*-**1**, the profiles are reversed (Figure 2b). The contrast ratio of the PET effect,[27g] that is, the ratio of the emission intensity of the sensor at neutral pH vs the emission intensity at acidic pH is ca. 3.0, which is 10-fold greater than the d-PET effect of boronic acid sensor **3** based on the carbazole fluorophore (without a thiophene moiety).[27f] Furthermore, the fluorescence enhancement in the presence of tartaric acid is ca. 5.0-fold, which is substantially improved compared to the previous d-PET sensor **3** (Scheme 2). We attribute the improved d-PET effect (contrast ratio) to the strong electron-donating ability of the thiophene moiety.

In order to prove the enantioselective recognition of tartaric acid using sensor **1**, binding isotherms were obtained (Figure 3).

Table 1. Photophysical Parameters of the Chiral *R*,*R*-1 and *R*-2

					Φ		
sensors	ε^a (M^{-1} cm^{-1})	λ_{abs} (nm)	λ_{em} (nm)	Stokes shift (nm)	pH 3.0[b]	pH 7.0[b]	pH 3.0 + L-acid[c]
R,*R*-**1**	5.04×10^4	322	412	90	0.024	0.062	0.069
R-**2**	3.74×10^4	303	396	93	0.032	0.076	0.048

[a] In methanol/water mixed solvent (3:1, v/v), pH 7.0. Concentrations of the sensors are 3.3×10^{-6} mol dm^{-3}. [b] Fluorescence quantum yields, with quinine sulfate as the standard (Φ = 0.54 in 0.05 M H_2SO_4). *c*(L-tartaric acid) = 0.01 mol dm^{-3}. [c] The fluorescence quantum yield of the sensors in the presence of L-tartaric acid at pH 3.0.

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The enantioselective recognition of tartaric acid with sensor **1** was unambiguously proven by the "mirror" profile of the fluorescence response of *R,R*-**1** and *S,S*-**1** to the two enantiomers of the tartaric acid. For example, *S,S*-**1** gives higher fluorescence response to L-tartaric acid at several pH values (pH 3.0, 5.6, 7.0), whereas *R,R*-**1** gives stronger response to D-tartaric acid (Figure 3). Enantioselective recognition of tartaric acid was observed over a wide pH range. At pH 3.0, the fluorescence enhancement upon binding with tartaric acid is up to 3.5-fold, which is a 3-fold improvement from the previously reported d-PET sensor **3** (Scheme 2).[27f] Similar results were observed for the recognition of tartaric acid at pH 5.6 and 7.0 (Figure 3). The binding constants of the sensors toward tartaric acid were determined (Table 2). The binding constant of *S,S*-**1** with D-tartaric acid is $(5.32 \pm 0.26) \times 10^4\ M^{-1}$, while for L-tartaric acid, the binding constant is $(1.35 \pm 0.04) \times 10^5\ M^{-1}$. Thus, the enantioselectivity of the binding constant is $K_D/K_L = 1:2.5$. With *R,R*-**1**, the enantioselectivity was reversed and $K_D/K_L = 2.5:1$ (Table 2).

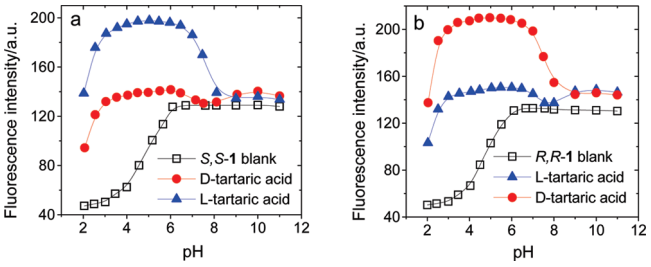

Figure 2. Fluorescence intensity−pH profile of (a) *S,S*-**1** and (b) *R,R*-**1** in the presence of D- and L-tartaric acid, with 5.0×10^{-7} mol dm^{-3} of sensor in methanol/water mixed solvent (3:1, v/v). $\lambda_{ex} = 325$ nm, $\lambda_{em} = 410$ nm, c(D- and L-tartaric acid) = 0.01 mol dm^{-3}, 20 °C.

For the monoboronic acid sensor **2** (Figure 4), however, the emission intensity−pH profile is different from the bisboronic acid sensor **1**. For example, the fluorescence enhancement at acidic pH in the presence of tartaric acid is much smaller than that of the bisboronic sensor **1** (Figure 2). Moreover, the fluorescence decreased at neutral pH in the presence of tartaric acid, whereas the bisboronic acid sensor **1** does not give significant response. Furthermore, negligible enantioselectivity was observed for the pH titrations of sensor **2** in the presence of tartaric acid, which was further corroborated by the determination of the binding constants at pH 7.0 (Figure 5).

Note that the binding constants of the monoboronic acid sensor **2** with tartaric acid are in the range of $1.0 \times 10^3\ M^{-1}$ (Table 2), which are much smaller than that of the bisboronic acid sensor **1** with tartaric acid. On the basis of these observations, we conclude that the binding stoichiometry of the bisboronic acid sensor **1** with tartaric acid is primarily 1:1; i.e., cyclic binding complexes were formed between sensor **1** and the tartaric acid.[27a,b,f]

Since the binding pocket of the bisboronic acid sensor **1** is larger than the previously reported carbazole-based sensor **3**,[27f] the binding of the sensor **1** with disaccharides and glycosylated steroids (ginsenosides) was investigated (Figure 6). No pH titration was carried out because the disaccharides are unstable in acidic solutions). For sensor **1** in the presence of sucrose and ginsenosides **Re** and **Rb1**, a decrease in fluorescence was observed, which is similar to the recently reported sensor for ginsenosides.[23] For example, the binding constants of a porphyrin receptor for ginsenosides **Rb1** and **Re** are 2500 and 3900 M^{-1}, respectively.[23] The binding constants of *R,R*-**1** for ginsenosides **Rb1** and **Re** are 4260 and 4170 M^{-1}, respectively, which are similar to those of the porphyrin receptor. The binding constants of *S,S*-**1** for ginsenoside **Re** are 7980 M^{-1}, which is 2-fold that of the porphyrin receptor. Furthermore, the binding constants of *S,S*-**1** for ginsenoside **Rb1** is 17 800 M^{-1}, which is 7-fold higher than that of the porphyrin receptor.

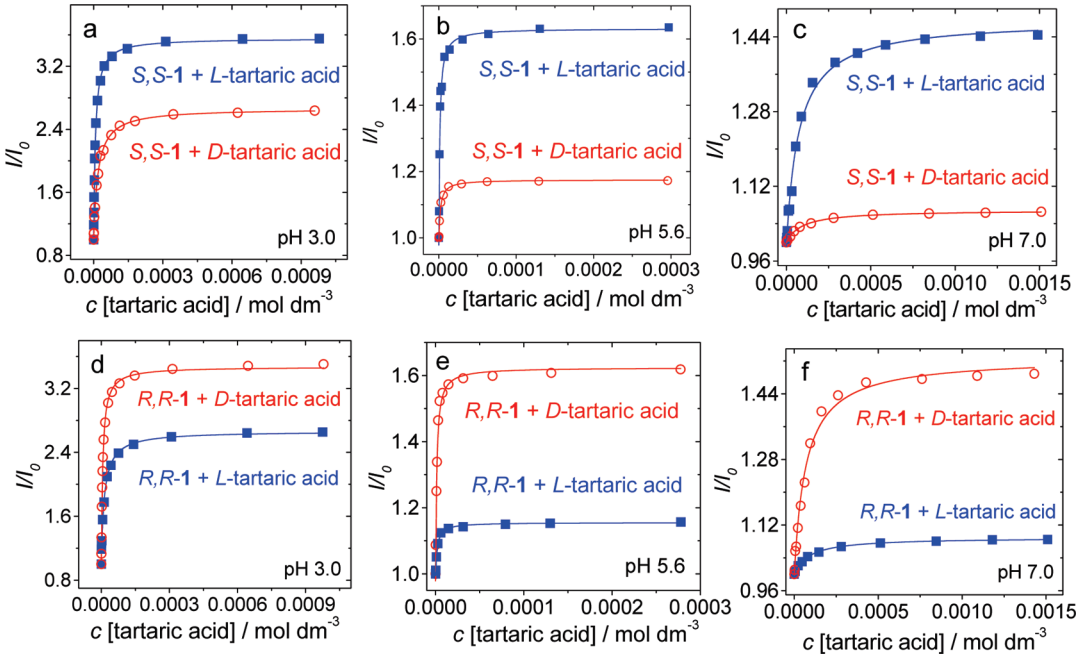

Figure 3. Relative fluorescence intensity of *S,S*-**1** and *R,R*-**1** vs concentration of D- and L-tartaric acid: (a) *S,S*-**1**, pH = 3.0, (b) *S,S*-**1**, pH = 5.6, (c) *S,S*-**1**, pH = 7.0, (d) *R,R*-**1**, pH = 3.0, (e) *R,R*-**1**, pH = 5.6, and (f) *R,R*-**1**, pH = 7.0. $\lambda_{ex} = 325$ nm, $\lambda_{em} = 410$ nm, 5.0×10^{-7} mol dm^{-3} of sensor in MeOH/H_2O mixed solvent (3:1, v/v), 20 °C.

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Table 2. Stability Constants K (1:1), Fluorescence Response (I/I_0) on Binding, and Enantioselectivity (K_S:K_R) of Sensors 1 and 2[a]

		K		I/I_0		
analytes	pH	*S,S*-**1**	*R,R*-**1**	*S,S*-**1**	*R,R*-**1**	K_S/K_R
D-tartaric acid	3.0	$(5.32 \pm 0.26) \times 10^4$	$(1.63 \pm 0.06) \times 10^5$	2.64	3.50	1:3.1
	5.6	$(5.19 \pm 0.78) \times 10^5$	$(8.11 \pm 0.88) \times 10^5$	1.17	1.62	1:1.6
	7.0	$(1.08 \pm 0.06) \times 10^4$	$(1.44 \pm 0.16) \times 10^5$	1.07	1.49	1:1.3
L-tartaric acid	3.0	$(1.35 \pm 0.04) \times 10^5$	$(6.59 \pm 0.62) \times 10^4$	3.55	2.65	2.0:1
	5.6	$(8.30 \pm 1.07) \times 10^5$	$(5.48 \pm 0.62) \times 10^5$	1.63	1.16	1.5:1
	7.0	$(1.36 \pm 0.12) \times 10^4$	$(1.09 \pm 0.05) \times 10^4$	1.44	1.08	1.2:1
D-mandelic acid[b]	3.0	$(1.38 \pm 0.21) \times 10^3$	$(2.11 \pm 0.41) \times 10^3$	2.09	1.78	1:1.5
	7.4	$(2.36 \pm 0.22) \times 10^3$	$(1.38 \pm 0.25) \times 10^3$	0.80	0.69	1.7:1
L-mandelic acid[b]	3.0	$(2.24 \pm 0.51) \times 10^3$	$(1.11 \pm 0.22) \times 10^3$	1.78	2.04	2.0:1
	7.4	$(1.51 \pm 0.27) \times 10^3$	$(2.68 \pm 0.20) \times 10^3$	0.70	0.80	1:1.8
L-malic acid[b]	4.0	$(4.92 \pm 0.34) \times 10^3$	$(6.76 \pm 0.40) \times 10^3$	1.91	2.21	1:1.4
L-lactic acid[b]	4.0	$(2.27 \pm 0.29) \times 10^3$	$(3.17 \pm 0.56) \times 10^3$	2.05	2.13	1:1.4
D-lactic acid[b]	4.0	$(2.75 \pm 0.49) \times 10^3$	$(2.41 \pm 0.40) \times 10^3$	2.15	2.06	1.1:1
D-glucose	7.4	$(2.13 \pm 0.30) \times 10^3$	$(3.17 \pm 0.68) \times 10^2$	0.92	0.91	6.7:1
D-fructose	7.4	$(1.46 \pm 0.44) \times 10^3$	$(1.26 \pm 0.14) \times 10^3$	0.90	0.93	1.2:1
D-galactose	7.4	$(7.71 \pm 0.15) \times 10^2$	$(5.61 \pm 0.88) \times 10^2$	0.88	0.89	1.4:1
sucrose	7.4	$(1.13 \pm 0.25) \times 10^4$	$(2.49 \pm 0.56) \times 10^3$	0.88	0.76	4.5:1
α-lactose	7.4	$(9.67 \pm 2.48) \times 10^4$	$(2.36 \pm 0.12) \times 10^4$	0.92	0.94	4.1:1
maltose	7.4	$(6.89 \pm 1.57) \times 10^3$	$(1.53 \pm 0.54) \times 10^3$	0.93	0.90	4.5:1
ginsenoside **Re**	7.4	$(7.98 \pm 1.61) \times 10^3$	$(4.17 \pm 0.39) \times 10^3$	0.83	0.86	1.9:1
Ginsenoside **Rb1**	7.4	$(1.78 \pm 0.40) \times 10^4$	$(4.26 \pm 0.52) \times 10^3$	0.87	0.90	4.2:1
D-sorbitol	7.4	$(1.92 \pm 0.35) \times 10^3$	$(3.06 \pm 0.35) \times 10^3$	0.89	0.92	1:1.6
D-mannitol	7.4	$(9.70 \pm 1.23) \times 10^2$	$(1.14 \pm 0.19) \times 10^3$	0.87	0.85	1:1.2
xylitol	7.4	$(1.10 \pm 0.17) \times 10^3$	$(1.98 \pm 0.37) \times 10^3$	0.90	0.93	1:1.8
analytes	pH	*S*-**2**	*R*-**2**	*S,S*-**1**	*R,R*-**1**	K_S/K_R
D-mandelic acid	7.0	$(6.57 \pm 0.72) \times 10^2$	$(8.18 \pm 0.54) \times 10^2$	0.60	0.56	1:1.3
L-mandelic acid	7.0	$(8.68 \pm 0.58) \times 10^2$	$(6.24 \pm 0.58) \times 10^2$	0.57	0.60	1.4:1
L-tartaric acid	7.0	$(1.39 \pm 0.12) \times 10^3$	$(1.12 \pm 0.12) \times 10^3$	0.44	0.39	1.2:1
D-tartaric acid	7.0	$(1.01 \pm 0.12) \times 10^3$	$(1.45 \pm 0.11) \times 10^3$	0.39	0.45	1:1.4

[a] Binding studies were conducted in MeOH/H_2O mixed solvent (3:1, v/v). Constants determined by fitting a 1:1 binding model to I/I_0. $r^2 = 0.99$ in most cases. I_0 is the fluorescence intensity of sensors without analytes and I is the maximum fluorescence response of sensors with analytes. [b] Constants determined by fitting a 1:2 binding model to I/I_0.

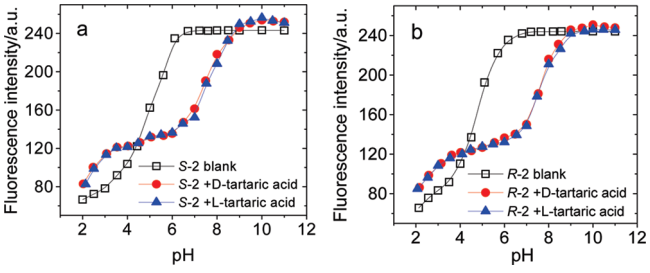

Figure 4. Fluorescence intensity−pH profile of the monoboronic acid sensor (a) *S*-**2** and (b) *R*-**2** in the presence of D/L-tartaric acid and 5.0×10^{-7} mol dm^{-3} of sensor in methanol/water mixed solvent (3:1, v/v). $\lambda_{ex} = 325$ nm, $\lambda_{em} = 396$ nm, c(D/L-tartaric acid) = 0.01 mol dm^{-3}, 20 °C.

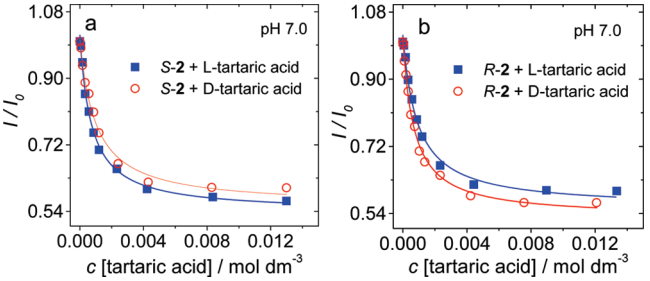

Figure 5. Relative fluorescence intensity of (a) *S*-**2** and (b) *R*-**2** vs concentration of D- and L-tartaric acid. pH = 7.0. $\lambda_{ex} = 325$ nm, $\lambda_{em} = 396$ nm, 5.0×10^{-7} mol dm^{-3} of sensor in MeOH/H_2O mixed solvent (3:1, v/v), 20 °C.

2.4. Enantioselective Recognition of Mandelic Acid with Fluorescent Boronic Acid Sensor. Previously, enantioselective recognition of tartaric acid with bisboronic acid sensors was achieved.[27a,b,f,h] However, it is still a challenge to enantioselectively recognize mandelic acid, in which a single α-hydroxyl carboxylic acid unit is present.[36] Hydrogen-bonding-based enantioselective fluorescent sensors are available for recognition of mandelic acid,

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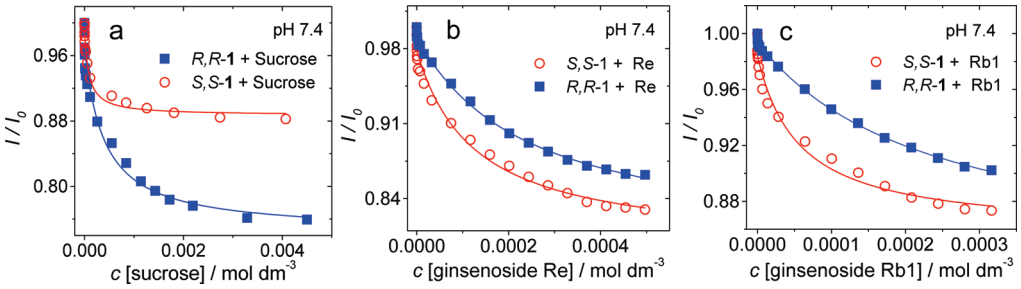

Figure 6. Relative fluorescence intensity of *R,R*-**1** and *S,S*-**1** vs concentration of (a) sucrose, (b) ginsenoside **Re**, and (c) ginsenoside **Rb1**. pH = 7.4. λ_{ex} = 325 nm, λ_{em} = 410 nm, 5.0 × 10^{-7} mol dm^{-3} of sensor in MeOH/H_2O mixed solvent (3:1, v/v), 20 °C.

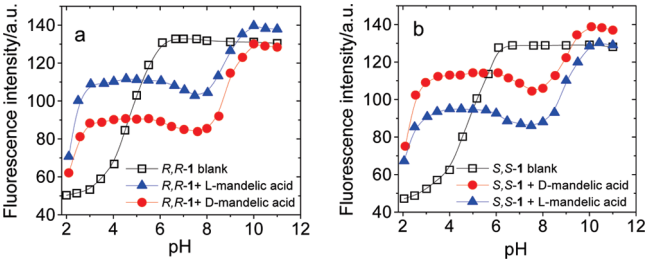

Figure 7. Fluorescence intensity−pH profile of (a) *R,R*-**1** and (b) *S,S*-**1** in the presence of D/L-mandelic acid, with 5.0 × 10^{-7} mol dm^{-3} of sensor in methanol/water mixed solvent (3:1, v/v). λ_{ex} = 325 nm, λ_{em} = 410 nm, *c*(D/L-mandelic acid) = 0.01 mol dm^{-3}, 20 °C.

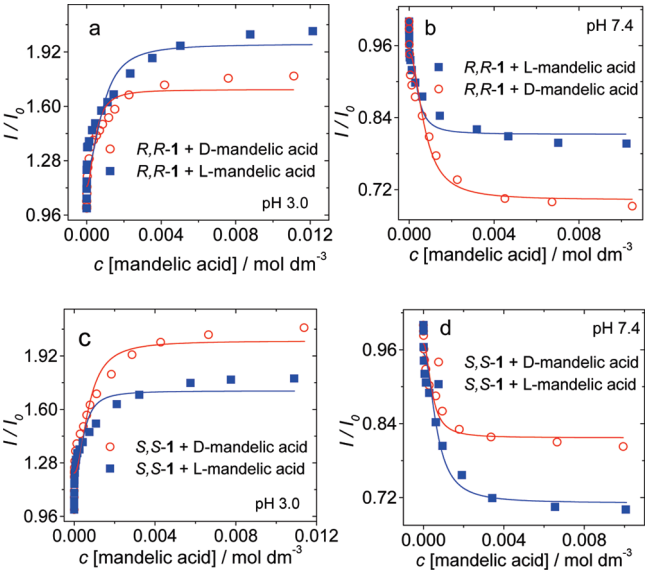

Figure 8. Relative fluorescence intensity of *R,R*-**1** and *S,S*-**1** vs concentration of D- and L-mandelic acid: (a) *R,R*-**1**, pH = 3.0, (b) *R,R*-**1**, pH = 7.4, (c) *S,S*-**1**, pH = 3.0, (d) *S,S*-**1**, pH = 7.4. λ_{ex} = 325 nm, λ_{em} = 410 nm, 5.0 × 10^{-7} mol dm^{-3} of sensor **1** in methanol/water mixed solvent (3:1, v/v), 20 °C.

but the recognition has to be performed in nonprotic organic solvents, not aqueous solution.[28−31]

The interaction of sensor **1** with D- or L-mandelic acid was investigated (Figure 7). To our surprise, the pH titration of sensor **1** in the presence of D- and L-mandelic acid indicated enantioselective recognition. For example, the fluorescence

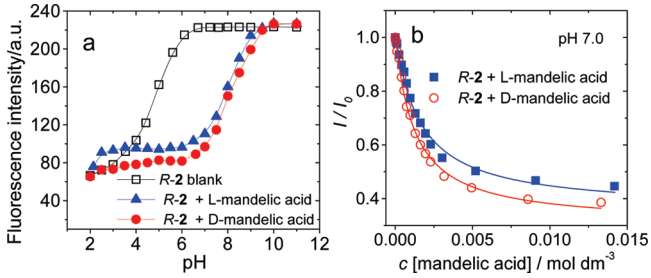

Figure 9. Recognition of mandelic acid with *R*-**2**. (a) Fluorescence intensity−pH profile of *R*-**2** in the presence of D/L-mandelic acid. *c*(D/L-mandelic acid) = 0.01 mol dm^{-3}. (b) Binding isotherms of *S*-**2** vs concentration of D- and L-mandelic acid. pH = 7.0, 5.0 × 10^{-7} mol dm^{-3} of sensor in methanol/water mixed solvent (3:1, v/v), λ_{ex} = 325 nm, λ_{em} = 396 nm, 20 °C.

response of *R,R*-**1** toward L-mandelic acid is more significant than that with D-mandelic acid (Figure 7a). With *S,S*-**1**, the profile is reversed (Figure 7b). Enantioselective response toward mandelic acid was also found at pH 6−8.

The enantioselective recognition of mandelic acid with sensor **1** was further confirmed by binding studies at pH 3.0 and 7.4 (Figure 8). For example, the *R,R*-**1** produces an enhanced response to L-mandelic acid over D-mandelic acid (Figure 8a). The binding constants for D- and L-mandelic acid are (2.11 ± 0.41) × 10^3 and (1.11 ± 0.22) × 10^3 M^{-1}, respectively (K_D/K_L = 1.9:1). With *S,S*-**1**, the profile reversed (Figure 8c), with an enhanced response to D-mandelic acid, and the binding constants are (2.24 ± 0.51) × 10^3 and (1.38 ± 0.21) × 10^3 M^{-1} for L- and D-mandelic acid, respectively (K_D/K_L = 1:1.6).

This is the first time that the enantioselective recognition of mandelic acid with the fluorescent bisboronic acid sensor is achieved. To date most chiral boronic acid sensors cannot enantioselectively recognize mandelic acid. The only successful example is a boronic acid sensor with a constrained chiral amine chirogenic center (no fluorophore can be readily incorporated into the sensor; thus, the binding was studied using a displacement strategy, monitored by UV−vis absorption).[36] In order to reveal the mechanism of the enantioselective recognition of mandelic acid with sensor **1**, we performed NMR NOE experiments of mixed solutions of sensor **1** with mandelic acid, but no useful information could be derived. Also, the monoboronic acid sensor **2** failed to show significant enantioselectivity toward D- and L-mandelic acid (Figure 9).

In order to probe the recognition of α-hydroxyl carboxylic acid further, we investigated D- and L-lactic acid with sensor **1**, but no significant enantioselectivity was observed (Figure 10 and

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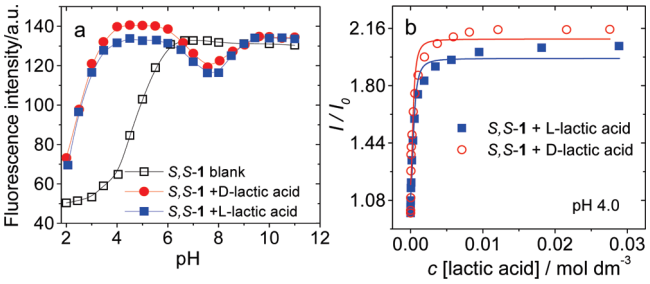

Figure 10. (a) Fluorescence intensity−pH profile of *S*,*S*-**1** in the presence of L/D-lactic acid. (b) The binding isotherms of *S*,*S*-**1** with L- and D-lactic acid and 5.0×10^{-7} mol dm^{-3} of sensor in methanol/water mixed solvent (3:1, v/v). pH = 4.0. λ_{ex} = 325 nm, λ_{em} = 410 nm, *c* (L/D-lactic acid) = 0.01 mol dm^{-3}, 20 °C.

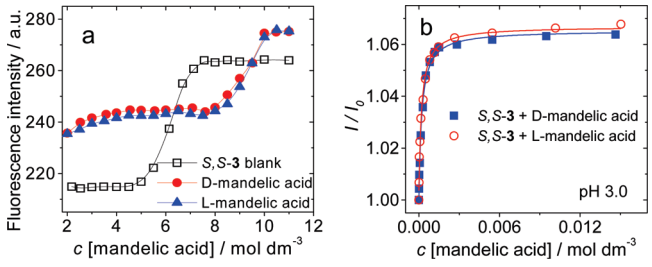

Figure 11. (a) Fluorescence intensity−pH profile of *S*,*S*-**3** in the presence of D/L-mandelic acid. (b) Relative fluorescence intensity of *S*,*S*-**3** vs concentration of D- and L-mandelic acid, with 1.0×10^{-6} mol dm^{-3} of sensor in methanol/water mixed solvent (3:1, v/v). pH = 3.0, λ_{ex} = 307 nm, λ_{em} = 375 nm, *c*(D/L-mandelic acid) = 0.01 mol dm^{-3}, 20 °C.

Table 2). The binding constants of *S*,*S*-**1** with L- and D-lactic acid are (2.27 ± 0.29) × 10^3 and (2.75 ± 0.49) × 10^3 M^{-1}, respectively (Figure 10b). Enantioselectivity was found for the *R*,*R*-**1** with L- and D-lactic acid (Supporting Information). Enantioselectivity was observed for the recognition of malic acid with sensor **1** (Table 2). The recognition of saccharides, such as glucose, fructose, and galactose, was also carried out with sensor **1**, and enantioselectivity was found (Table 2). We noticed that the enantioselectivity for recognition of small analytes is not significant, which is probably due to the minor steric hindrance imparted by the chirogenic center of sensor **1**. Using a more bulky chiral amine for preparation of the boronic acid sensor may improve the enantioselectivity.

We also studied the recognition of mandelic acid with the previously reported bisboronic acid sensor **3** (Scheme 2),[27f] which does not contain the thiophene moiety (Figure 11). No enantioselectivity was observed; i.e., the *S*,*S*-**3** gives similar response to the L- and D-mandelic acid. Thus, the thiophene moiety contained in sensor **1** is crucial for the enantioselective recognition of mandelic acid.

2.5. Conclusions. In conclusion, we have prepared chiral fluorescent bisboronic acid sensor **1** with 3,6-dithiophen-2-yl-9*H*-carbazole as the fluorophore, and monoboronic acid sensor **2** was prepared as a model sensor. The thiophene moiety was used to extend the π-conjugation framework of the fluorophore to impart long fluorescence emission wavelength and, at the same time, to enhance the novel d-PET effect. We found that the thiophene moiety is efficient as a π-conjugation linker and the PET contrast ratio of the sensor upon variation of pH is 3, ca. 10-fold superior to the previous d-PET sensor without the thiophene moiety. With the bisboronic acid sensor **1**, enantioselective recognition of D- and L-mandelic acid was observed for the first time, whereas the monoboronic acid sensor **2** and the bisboronic acid sensor **3** without the thiophene moiety failed to display enantioselectivity toward the recognition of mandelic acid. To the best of our knowledge, this is the first time that mandelic acid has been enantioselectively recognized with a fluorescent boronic acid sensor. We believe that our findings with the thiophene-containing boronic acid sensors will be useful for the design and development of fluorescent chemosensors for the enantioselective recognition of α-hydroxylic acids such as mandelic acid.

3. EXPERIMENTAL SECTION

3.1. Synthesis of 3,6-Diiodocarbazole (9). Carbazole (16.7 g, 0.1 mol) was dissolved in boiling glacial acetic acid (300 mL), and KI (22.0 g, 0.13 mol) was added. The solution was cooled, ground potassium iodate (32 g, 0.15 mol) was added, and the mixture was then boiled until it acquired a clear straw-colored tint (10 min). The hot solution was decanted from the undissolved potassium iodate, and it was allowed to cool to 45 °C. The faintly brown plates were rapidly filtered off and recrystallized from alcohol, the solution being allowed to cool to 45 °C and filtered, yielding 17.6 g of white solid (42.1%): ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 8.30 (s, 2H), 7.66 (d, 2H, *J* = 8.4 Hz), 7.18 (d, 2H, *J* = 7.6 Hz); TOF MS EI+ calcd for $C_{12}H_7I_2N$ 418.8668, found 418.8664.

3.2. 9-Butyl-3,6-diiodocarbazole (10). NaH (60 wt % in mineral oil, 0.51 g, 0.13 mol) and *n*-C_4H_9Br (2.72 g, 0.02 mmol) were added to a solution of **9** (4.19 g, 0.01 mol) in dry DMF (5 mL). The mixture was stirred at room temperature until the reaction was complete, as monitored by TLC. The solvents were removed under reduced pressure. The residue was taken up with dichloromethane (DCM) and washed with water. The organic layer was dried over Na_2SO_4. After the solvent was removed under reduced pressure, the residue was purified by column chromatography (silica gel, DCM/petroleum ether, 1/1, v/v) to yield 4.0 g of white solid (85.0%): ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 8.34 (s, 2H), 7.70 (d, 2H, *J* = 7.2 Hz), 7.17 (d, 2H, *J* = 8.4 Hz), 4.22 (t, 2H, *J* = 7.2 Hz), 1.77−1.84 (m, 2H), 1.30−1.40 (m, 2H), 0.91 (t, 3H, *J* = 7.2 Hz); TOF MS EI+ calcd for $C_{16}H_{15}I_2N$ 474.9294, found 474.9297.

3.3. 5-[9-Butyl-3-(5-formylthiophen-2-yl)carbazol-6-yl]-thiophene-2-carbaldehyde (11). To a deaerated solution of **10** (0.54 g, 1.14 mmol) in THF (4 mL) were successively added a solution of K_2CO_3 (276.0 mg, 2.0 mmol) in water (1.0 mL), $Pd(PPh_3)_4$ (52.7 mg, 0.046 mmol), and 5-formylthiophene-2-boronic acid (443.4 mg, 2.84 mmol). The reaction mixture was refluxed under N_2 for 10 h. The solvents were removed under reduced pressure. The residue was taken up with DCM and washed with water. The organic layer was dried over Na_2SO_4. After the solvent was removed, the residue was purified by column chromatography (silica gel, DCM/MeOH, 50/1, v/v), yielding 315.2 mg of yellow solid (62.4%): ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 9.88 (s, 2H), 8.35 (s, 2H), 7.75−7.78 (m, 4H), 7.39−7.45 (m, 4H), 4.26 (t, 2H, *J* = 6.8 Hz), 1.82−1.89 (m, 2H), 1.34−1.43 (m, 2H), 0.93 (t, 3H, *J* = 7.2 Hz); TOF MS EI+ calcd for $C_{26}H_{21}NO_2S_2$ 443.1014, found 443.1017.

3.4. *S*,*S*-12. To a solution of **11** (120.0 mg, 0.27 mmol) in DCM (2 mL) and ethanol (3 mL) was added (*S*)-1-phenylethanamine (131.2 mg, 1.10 mmol). The reaction mixture was refluxed under nitrogen for 8 h. After the solution was cooled to room temperature, $NaBH_4$ (111.0 mg, 3 mmol) was added in several portions to the stirred solution and the stirring was continued for 1 h. The resulting mixture was evaporated to dryness. The residue was purified by column chromatography (silica gel, DCM/MeOH, 20/1, v/v), yielding 140.0 mg of light green oil (79.4%): ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 8.30 (s, 2H), 7.68

(d, 1H, J = 7.6 Hz), 7.24−7.42 (m, 12H), 7.16 (d, 2H, J = 3.6 Hz), 6.85 (s, 2H), 4.26 (t, 2H, J = 6.8 Hz), 3.92 (q, 2H, J = 6.4 Hz), 380−3.89 (m, 4H), 1.80−1.89 (m, 2H), 1.35−1.43 (m, 8H), 0.93 (t, 3H, J = 7.2 Hz); TOF MS ES+ calcd for $C_{42}H_{43}N_3S_2$ ($[M + H]^+$) 654.2977, found 654.2971.

3.5. *R,R*-12. The compound was prepared with the same method as *S,S*-**12**: 64.6% yield; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 8.27 (s, 2H), 7.68 (d, 1H, J = 8.4 Hz), 7.24−7.43 (m, 12H), 7.16 (d, 2H, J = 3.2 Hz), 6.87 (s, 2H), 4.23 (t, 2H, J = 7.2 Hz), 3.94 (q, 2H, J = 6.4 Hz), 3.79−3.90 (m, 4H), 1.80−1.87 (m, 2H), 1.34−1.45 (m, 8H), 0.92 (t, 3H, J = 7.2 Hz); TOF MS ES+ calcd for $C_{42}H_{43}N_3S_2$ ($[M + H]^+$) 654.2977, found 654.2949.

3.6. *S,S*-1. *S,S*-**12** (140.0 mg, 0.21 mmol), 2-(2-bromomethylphenyl)-1,3,2-dioxaborinane (218.5 mg, 0.86 mmol), and K_2CO_3 (173.9 mg, 1.26 mmol) were mixed in dry MeCN (3.0 mL) and DCM (1 mL) and then the mixture was refluxed for 10 h under N_2. The reaction mixture was cooled to room temperature, diluted HCl was added, and then the mixture was stirred for a further 1 h. The solvent was removed under vacuum, and DCM was added to take up the residue. The organic layer was washed with water and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by column chromatography (silica gel, DCM/MeOH, 30/1, v/v), yielding 53.2 mg of light yellow powder (27.5%): $[\alpha]_D^{20} = -36.1° \pm 0.8°$ (c = 0.30 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 8.34 (s, 2H), 7.88 (d, 2H, J = 6.8 Hz), 7.71 (d, 2H, J = 8.8 Hz), 7.19−7.43 (m, 20H), 6.79 (s, 2H), 4.31 (t, 2H, J = 7.2 Hz), 4.21 (d, 2H, J = 6.8 Hz), 3.66−4.01 (m, 8H), 1.85−1.93 (m, 2H), 1.64 (d, 6H, J = 6.8 Hz), 1.36−1.46 (m, 2H), 0.95 (t, 3H, J = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3/CD_3OD$) δ 145.6, 141.4, 140.4, 139.7, 137.2, 136.2, 134.7, 131.4, 130.0, 129.1, 128.9, 128.4, 127.7, 127.2, 125.8, 124.4, 123.2, 121.5, 117.8, 109.2, 58.6, 56.2, 53.4, 47.5, 43.0 31.2, 20.5, 17.7, 13.8; TOF MS ES+ calcd for $C_{56}H_{57}B_2N_3O_4S_2$ ($[M + 2MeOH - 2H_2O + 2H]^{2+}$) 475.7223, found 475.7225.

3.7. *R,R*-1. This compound was prepared with the same method as *S,S*-**1**: 31.2% yield; $[\alpha]_D^{20} = +34.8° \pm 1.0°$ (c = 0.30 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 8.34 (s, 2H), 7.89 (d, 2H, J = 8.4 Hz), 7.71 (d, 2H, J = 8.8 Hz), 7.19−7.43 (m, 20H), 6.80 (s, 2H), 4.30 (t, 2H, J = 6.8 Hz), 4.21 (d, 2H, J = 5.6 Hz), 3.66−4.01 (m, 8H), 1.84−1.92 (m, 2H), 1.64 (d, 6H, J = 6.4 Hz), 1.38−1.46 (m, 2H), 0.94 (t, 3H, J = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3/CD_3OD$) δ 149.60, 144.3, 135.2, 133.9, 133.1, 132.9, 132.3, 131.6, 131.1, 129.7, 128.3, 127.0, 125.4, 121.7, 113.1, 62.6, 60.1, 51.4, 46.9, 35.1, 33.5, 24.4, 21.5, 17.7; TOF MS ES+ calcd for $C_{56}H_{57}B_2N_3O_4S_2$ ($[M + 2MeOH - 2H_2O + 2H]^{2+}$) 475.7223, found 475.7233.

3.8. 3-Iodocarbazole (13). Carbazole (16.7 g, 0.1 mol) was dissolved in boiling glacial acetic acid (260 mL), and potassium iodide (11.0 g, 0.066 mol) was added. The solution was cooled, finely powdered potassium iodate (16.0 g, 0.075 mol) added, and the mixture then boiled until it acquired a clear straw-colored tint (10 min). The hot solution was decanted from the undissolved potassium iodate and allowed to cool slowly to 45 °C. The precipitate were rapidly filtered off and recrystallized from alcohol, the solution being allowed to cool to 45 °C and filtered, yielding 11.7 g of white solid (40.0%): ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 8.38 (s, 1H), 8.00 (d, 1H, J = 8.0 Hz), 7.64 (d, 1H, J = 8.0 Hz), 7.40−7.46 (m, 2H), 7.20−7.24 (m, 2H); TOF MS EI+ calcd for $C_{12}H_8NI$ 292.9702, found 292.9707.

3.9. 9-Butyl-3-iodocarbazole (14). NaH (60 wt % in mineral oil; 0.17 g, 4.25 mmol) and *n*-C_4H_9Br (0.59 g, 4.35 mmol) were added to a solution of compound **13** (0.85 g, 2.9 mmol) in DMF (5 mL). The mixture was stirred at room temperature until the reaction was complete, as monitored by TLC. The mixture was poured into water (100 mL) and the precipitate collected by filtration and purified by column chromatography (silica gel, DCM/petroleum ether, 1/1, v/v), yielding 0.91 g of white solid (90.2%): ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 8.40 (s, 1H), 8.03 (d, 1H, J = 7.2 Hz), 7.69 (d, 1H, J = 8.0 Hz), 7.47 (t, 1H, J = 8.0 Hz), 7.39 (d, 1H, J = 8.0 Hz), 7.18−7.26 (m, 2H), 4.25 (t, 2H, J = 7.2 Hz), 1.80−1.87 (m, 2H), 1.33−1.43 (m, 2H), 0.93 (t, 3H, J = 7.2 Hz); TOF MS EI+ calcd for $C_{16}H_{16}NI$ 349.0328, found 349.0331.

3.10. 5-(9-Butylcarbazol-6-yl)thiophene-2-carbaldehyde (15). To a degassed solution of **14** (0.80 g, 2.29 mmol) in THF (5 mL) were successively added a solution of K_2CO_3 (0.55 g, 4.0 mmol) in water (2 mL), $Pd(PPh_3)_4$ (52.9 mg, 0.046 mmol), and 5-formylthiophene-2-boronic acid (536.0 mg, 3.44 mmol). The reaction mixture was refluxed under N_2 for 6 h. The solvents were removed under reduced pressure. The residue was taken up with DCM and washed with water. The organic layer was dried over Na_2SO_4. After the solvent was removed, the residue was purified by column chromatography (silica gel, DCM), yielding 396.7 mg of yellow solid (52.0%): ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 9.89 (s, 1H), 8.40 (s, 1H), 8.13 (d, 1H, J = 8.0 Hz), 7.56−7.79 (m, 2H), 7.49 (t, 1H, J = 7.2 Hz), 7.42−7.46 (m, 3H), 7.28 (d, 1H, J = 7.6 Hz), 4.31 (t, 2H, J = 7.2 Hz), 1.84−1.92 (m, 2H), 1.36−1.46 (m, 2H), 0.94 (t, 3H, J = 7.2 Hz); TOF MS EI+ calcd for $C_{21}H_{19}NOS$ 333.1187, found 333.1193.

3.11. *R*-16. To a solution of **15** (100.0 mg, 0.30 mmol) in DCM (3 mL) and ethanol (3 mL) was added (*R*)-1-phenylethanamine (72.7 mg, 0.60 mmol). The reaction mixture was refluxed under nitrogen for 8 h. After the solution was cooled to room temperature, $NaBH_4$ (111.0 mg, 3 mmol) was added in several portions to the stirred solution and the stirring was continued for 1 h. The mixture was evaporated to dryness. The residual was purified by column chromatography (silica gel, DCM/MeOH, 15/1, v/v), yielding 103.0 mg of yellow oil (78.4%): ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 8.28 (s, 1H), 8.10 (d, 1H, J = 7.6 Hz), 7.67 (d, 1H, J = 8.4 Hz), 7.44 (d, 1H, J = 8.0 Hz),7.34−7.40 (m, 6H), 7.21−7.28 (m, 2H), 7.14 (s, 1H), 6.82 (s, 1H), 4.26 (t, 2H, J = 7.2 Hz), 3.90 (q, 1H, J = 6.4 Hz), 3.78−3.88 (m, 2H), 1.81−1.88 (m, 2H), 1.36−1.44 (m, 5H), 0.92 (t, 3H, J = 7.2 Hz); TOF MS ES+ calcd for $C_{29}H_{31}N_2S$ ($[M + H]^+$) 439.2208, found 439.2217.

3.12. *S*-16. To a solution of **15** (130.0 mg, 0.39 mmol) in DCM (3 mL) and ethanol (3 mL) was added (*S*)-1-phenylethanamine (94.3 mg, 0.78 mmol). The reaction mixture was refluxed under nitrogen for 8 h. After the solution was cooled to room temperature, $NaBH_4$ (144.3 mg, 3.9 mmol) was added in several portions to the stirred solution and the stirring was continued for 1 h. The resulting mixture was evaporated to dryness. The residue was purified by column chromatography (silica gel, DCM/MeOH, 15/1, v/v), yielding 121.6 mg of yellow oil (71.2%): ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 8.26 (s, 1H), 8.09 (d, 1H, J = 7.6 Hz), 7.67 (d, 1H, J = 8.0 Hz), 7.44 (d, 1H, J = 8.0 Hz),7.14−7.48 (m, 9H), 6.82 (s, 1H), 4.25 (t, 2H, J = 7.2 Hz), 3.95 (q, 1H, J = 6.4 Hz), 3.79−3.91 (m, 2H), 1.82−1.86 (m, 2H), 1.46 (d, 3H, J = 6.4 Hz), 1.34−1.42 (m, 2H), 0.92 (t, 3H, J = 7.2 Hz); TOF MS ES+ calcd for $C_{29}H_{31}N_2S$ ($[M + H]^+$) 439.2208, found 439.2216.

3.13. *S*-2. *S*-**16** (120.0 mg, 0.27 mmol), 2-(2-bromomethylphenyl)-1,3,2-dioxaborinane (138.0 mg, 0.54 mmol), and K_2CO_3 (111.8 mg, 0.81 mmol) were mixed in dry MeCN (3.0 mL) and DCM (1 mL), and then the mixture was refluxed for 10 h under N_2. The reaction mixture was cooled to room temperature and diluted HCl was added, and then the mixture was stirred for a further 1 h. The solvent was removed under reduced pressure, and DCM was added to take up the residue. The organic layer was washed with water and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by column chromatography (silica gel, DCM/MeOH, 30/1, v/v), yielding 64.7 mg of light yellow powder (42.0%): $[\alpha]_D^{20} = -44.2° \pm 0.6°$ (c = 0.30 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 8.30 (s, 1H), 8.14 (d, 1H, J = 7.6 Hz), 7.88 (s, 1H), 7.70 (d, 1H, J = 8.4 Hz), 7.16−7.50 (m, 13H), 6.78 (s, 1H), 4.30 (t, 2H, J = 7.2 Hz), 4.19 (d, 1H, J = 6.8 Hz), 3.96 (d, 1H, J = 8.4), 3.64−3.87 (m, 3H), 1.83−1.90 (m, 2H), 1.62 (d, 3H, J = 6.8 Hz), 1.36−1.45 (m, 2H), 0.93 (t, 3H, J = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3/CD_3OD$) δ 145.8, 141.4, 140.9, 140.0, 139.7, 137.0, 136.3, 131.4, 130.0, 129.0, 128.9, 128.4, 127.7, 127.2, 125.9,

125.5, 124.0, 123.2, 122.7, 121.4, 120.5, 119.0, 117.6,109.0, 108.9, 58.6, 56.2, 47.5, 42.9, 31.1, 20.5, 17.8, 13.9; TOF MS ES+ calcd for $C_{36}H_{37}BN_2O_2S$ ($[M + H]^+$) 573.2747, found 573.2749.

3.14. *R*-2. This compound was prepared with a similar method as *S*-**2** in 44.5% yield: $[\alpha]_D^{20} = +43.3° \pm 0.8°$ ($c = 0.30$ in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 8.29 (s, 1H), 8.12 (d, 1H, $J = 7.6$ Hz), 7.88 (s, 1H), 7.68 (d, 1H, $J = 8.4$ Hz), 7.15−7.48 (m, 13H), 6.76 (s, 1H), 4.25 (t, 2H, $J = 6.8$ Hz), 4.18 (d, 1H, $J = 6.8$ Hz), 3.63−3.97 (m, 4H), 1.80−1.87 (m, 2H), 1.60 (d, 3H, $J = 6.0$ Hz), 1.33−1.42 (m, 2H), 0.91 (t, 3H, $J = 7.2$ Hz); ^{13}C NMR (100 MHz, $CDCl_3/CD_3OD$) δ 145.9, 141.4, 140.9, 140.0, 139.7, 137.0, 136.4, 131.5, 130.0, 129.1, 129.0, 128.4, 127.7, 127.3, 126.0, 125.5, 124.1, 123.2, 122.8, 121.4, 120.6, 119.0, 117.7, 109.0, 108.9, 58.7, 56.3, 47.5, 42.9, 31.2, 20.6, 17.7, 13.9; TOF MS ES+ calcd for $C_{36}H_{37}BN_2O_2S$ ($[M + H]^+$) 573.2747, found 573.2732.

■ ASSOCIATED CONTENT

Supporting Information. General experimental methods, ^{1}H and ^{13}C NMR data of the compounds, and the photophysical data of the boronic acid sensors. This material is available free of charge via the Internet at http://pubs.acs.org.

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