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Enantioselective Fluorescent Sensors: A Tale of BINOL

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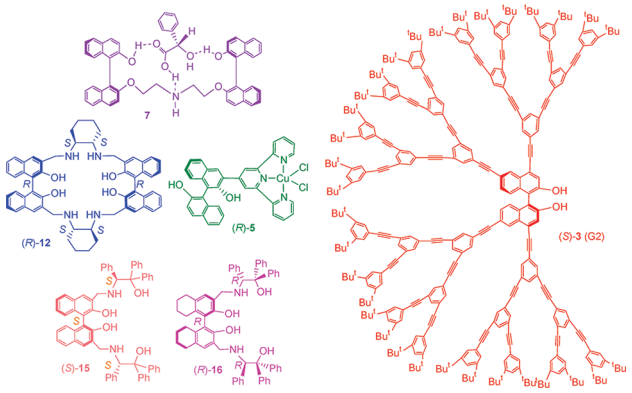
CONSPECTUS



The development of automated, high-throughput organic synthesis and screening techniques has created an urgent demand for methods that rapidly determine the enantiomeric composition of chiral compounds. Enantioselective fluorescent sensors offer the potential for real-time, high-sensitivity techniques for determining enantiomeric data in high-throughput chiral assays. In this Account, we describe a range of fluorescent sensors derived from 1,1′-bi-2-naphthol (BINOL), a readily available biaryl compound with axial chirality.

We show that BINOL can be used to construct structurally diverse, chiral fluorescent sensors to carry out highly enantioselective, sensitive recognition of chiral amino alcohols, α-hydroxycarboxylic acids, and amino acid derivatives. For example, we prepared an (*S*)-BINOL derivative whose 3,3′-positions are attached to two chiral amino alcohol units, each having two phenyl substituents. This compound shows a fluorescence enhancement of 950-fold in the presence of (*S*)-mandelic acid but very little change in the presence of (*R*)-mandelic acid. It also allows the enantiomers of this α-hydroxycarboxylic acid to be visually discriminated by an enantioselective precipitation process.

A structurally similar (*S*)-BINOL–amino alcohol molecule, but with three rather than two phenyl substitutents in each of the two amino alcohol units, was found to exhibit generally enantioselective fluorescence responses toward structurally diverse α-hydroxycarboxylic acids. We further prepared a pseudoenantiomeric analogue of this compound from (*R*)-H_8BINOL, which has the opposite chiral configuration at both the biaryl center as well as the pendant amino alcohols. These two compounds have opposite enantioselectivity in the recognition of a chiral substrate, with distinctly different fluorescence emission wavelengths. By mixing them together, we developed a pseudoenantiomeric sensor pair to facilitate chiral assays. Using this pseudoenantiomeric sensor pair allows both the concentration and the enantiomeric composition of a substrate to be determined in a single fluorescence measurement.

We synthesized another compound by ligating a terpyridine unit to BINOL and found that coordination of a Cu(II) ion to the terpyridine unit almost completely quenched its fluorescence. Displacement of the Cu^{2+} ion from this complex by chiral amino alcohols leads to enantioselective fluorescence enhancement. This BINOL–terpyridine–Cu(II) complex also exhibits enantioselective gel collapsing in the presence of chiral amino alcohols, providing a new visual chiral discrimination method.

When a series of light-absorbing conjugated units are attached to the BINOL structure, the resulting multiarmed dendritic molecules show greatly amplified fluorescence responses. Thus, the light harvesting effect of dendrimers can be used to greatly increase the sensitivity of the fluorescent sensors.

The progress described here demonstrates that highly enantioselective and sensitive fluorescent sensors can be obtained through a systematic investigation of the structure–property relation between the sensors and the substrates. These sensors show great potential for the development of rapid assays of chiral organic compounds.

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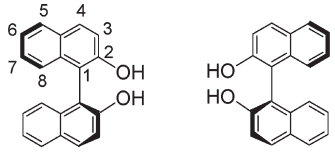
1. Introduction

The inherently high sensitivity of the fluorescence technique has attracted enormous activity for the study of molecule-based fluorescent sensors, and these sensors can provide multiple signaling modes such as quenching, enhancement, excimer/exciplex formation, lifetime, and anisotropy for substrate analysis. Applications of fluorescent sensors or labels in the detection of protons, metal cations, anions and neutral molecules and in biological investigations have been extensively investigated.[1−7] In recent years, the development of fluorescent sensors for the enantioselective recognition of chiral organic molecules has also received increasing attention.[8] These sensors can potentially provide a real-time technique to determine the enantiomeric composition of chiral organic compounds which could greatly facilitate the high throughput screening of chiral catalysts and reagents and allow rapid assay of chiral molecules. References 9−21 list a number of selected publications by other researchers in this area.

1,1′-Binaphthyls represent a class of important chiral molecules that have found extensive application in molecular recognition, asymmetric synthesis, and materials.[22−30] In our laboratory, we have chosen 1,1′-bi-2-naphthol (BINOL) as the starting material to build fluorescent sensors for the recognition of a variety of chiral organic molecules. A BINOL molecule has the following unique features: (1) It has a stable chiral configuration with both of its pure enantiomers, (*R*)- and (*S*)-BINOL, commercially available. (2) The structure of a BINOL molecule is highly tunable since functional groups can be specifically introduced to the 2-, 3-, 4-, 5- and 6-positions of the enantiomerically pure BINOL. (3) The fluorescent properties of BINOL can be systematically varied by structural modification. We have studied the use of the BINOL-based fluorescent sensors for the recognition of amines, amino alcohols, α-hydroxycarboxylic acids and amino acid derivatives, and have achieved both high enantioselectivity and sensitivity in a number of cases. Herein, these studies are discussed. For the selected work of other researchers on the fluorescence of 1,1′-binaphthyl-based molecules in chiral recognition, see refs 9−14.

2. Fluorescent Recognition of Amino Alcohols

2.1. Using Dendritic BINOLs for Signal Amplification. In 1992, Iwanek and Mattay reported that the fluorescence of BINOL can be quenched by chiral amines with small enantioselectivity.[31] The fluorescence quenching followed the Stern−Volmer equation, and the ratios of the Stern−Volmer constants (K_{SV}) between (*S*)-BINOL and (*R*)-BINOL in the presence of the optically active amines were ca. 0.89−1.16 in acetonitrile. The fluorescence quenching of BINOL by the amines was probably due to the formation of the excited hydrogen-bonded complexes and the excited state proton transfer complexes.



(*S*)-BINOL (*R*)-BINOL

We studied the use of dendritic structures to amplify the fluorescent response of BINOL for the detection of amino alcohols. Dendrimers with light absorbing branching units and a built-in energy gradient are found to exhibit light harvesting effect because of an efficient intramolecular energy transfer.[32] We envisioned that attaching dendritic light absorbing groups to a BINOL core unit should significantly increase its fluorescence signal. If fluorescence quenching occurs upon the interaction of the BINOL core hydroxyl groups with an amine molecule, the fluorescence intensity change should be much greater for the

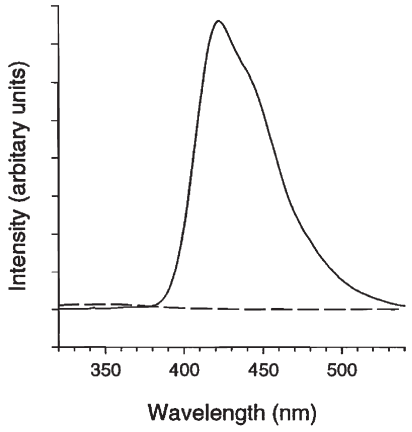


FIGURE 1. Comparison of the fluorescence spectrum of (*S*)-**3** (λ_{exc} = 310 nm) (solid line) with that of (*S*)-BINOL (λ_{exc} = 280 nm) (dashed line) (each at 4.0×10^{-8} M in 1:4 benzene/hexane).

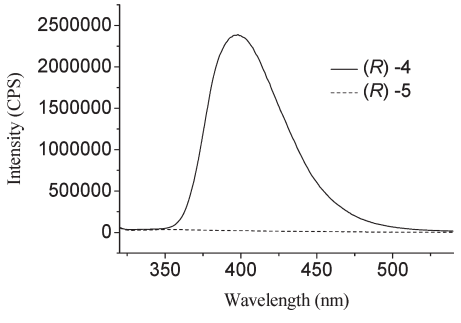
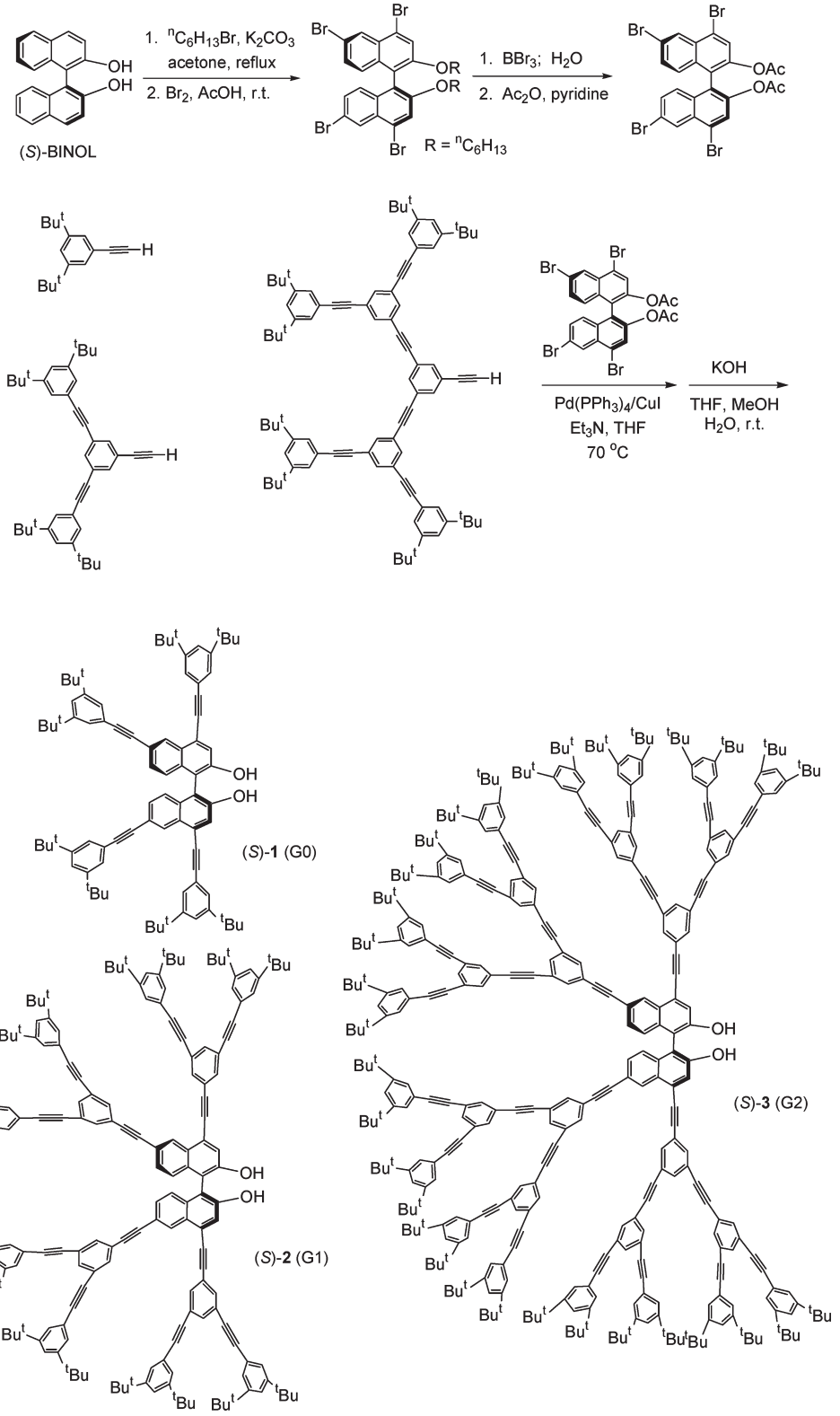


FIGURE 2. Fluorescence spectra of (*R*)-**4** and (*R*)-**5** (each at 5.0×10^{-7} M in 2:3 CH_2Cl_2/*n*-hexane).

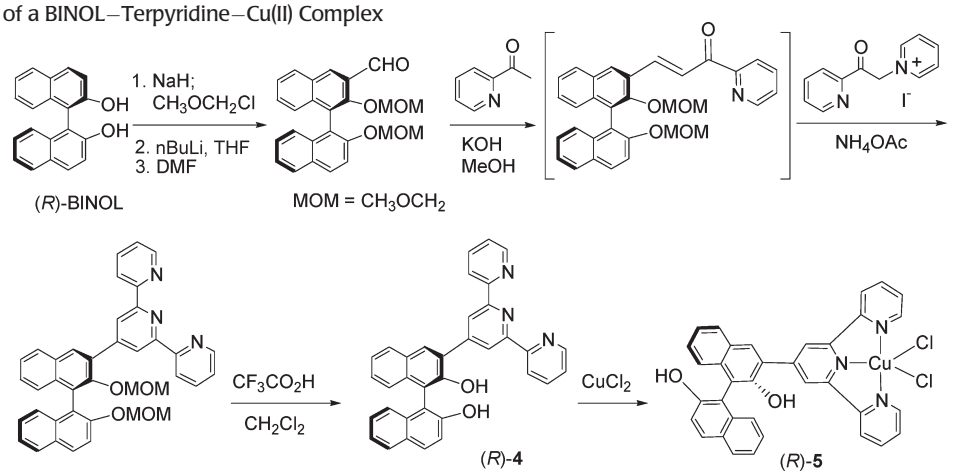
SCHEME 1. Synthesis of the BINOL-Based Dendrimers



dendritic sensor than the small molecule. Thus, the dendritic structure should amplify the fluorescent sensitivity of the sensor.

Scheme 1 shows the synthesis of (*S*)-**1**, (*S*)-**2**, and (*S*)-**3** as generation 0–2 (G0–G2) dendrimers from the Sonogashira coupling of the phenylene-ethynylene-based dendrons with

SCHEME 2. Synthesis of a BINOL–Terpyridine–Cu(II) Complex



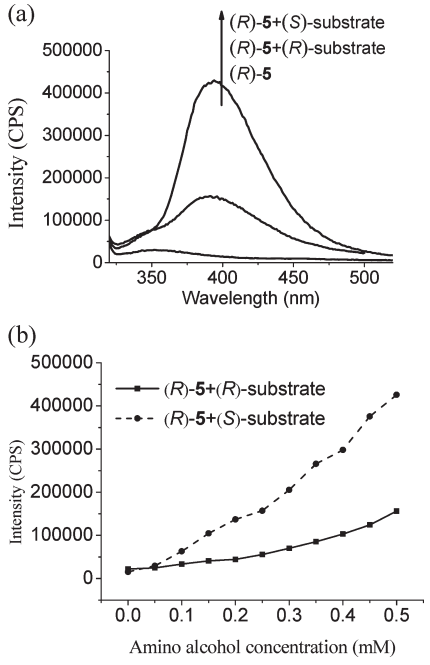


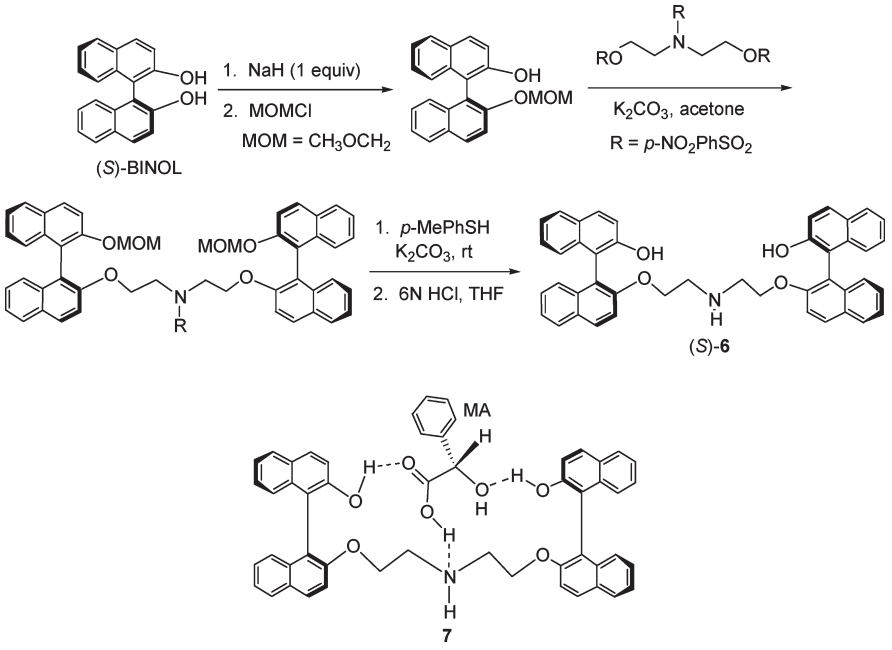
FIGURE 3. (a) Fluorescence spectra of (*R*)-**5** (5.0×10^{-7} M in 2:3 CH_2Cl_2/*n*-hexane) in the presence of (*R*)- and (*S*)-phenylglycinol (5.0×10^{-4} M) ($\lambda_{exc} = 289$ nm). (b) Fluorescence responses of (*R*)-**5** (5.0×10^{-7} M in 2:3 CH_2Cl_2/*n*-hexane) toward (*R*)- and (*S*)-phenylglycinol at $\lambda_{emi} = 396$ nm.

the 4,4′,6,6′-tetrabrominated BINOL acetate.[33] The fluorescence intensity increases greatly from (*S*)-BINOL to (*S*)-**1**, (*S*)-**2**, and (*S*)-**3** as the dendritic branches increase. As shown in Figure 1, at 4.0×10^{-8} M, BINOL is barely emissive while the G2 dendrimer (*S*)-**3** exhibits an intense emission maximum at 422 nm. This greatly enhanced emission is attributed to an efficient energy migration from the periphery light absorbing diphenylacetylene units ($\lambda_{max} = 310$ nm) of (*S*)-**3** to its core of more extended conjugation. The light harvesting effect of these dendrimers makes (*S*)-**3** a much more sensitive fluorescent sensor than BINOL when treated with amino alcohol quenchers. A small enantioselectivity was also observed in the fluorescent quenching by the (*S*)- and (*R*)-amino alcohols including valinol, leucinol, and phenylalaninol with $K_{SV}^{S}/K_{SV}^{R} = 1.10-1.27$.[34,35a] When the core hydroxyl groups of (*S*)-**3** were methylated, no significant fluorescence quenching by an amino alcohol was observed. The BINOL-based dendrimers with phenylene dendrons were also prepared which exhibited the same light harvesting effect as (*S*)-**1**–(*S*)-**3**.[35b]

2.2. A Fluorescence Enhancement Sensor for Amino Alcohols and Enantioselective Gel Collapsing. As described above, the fluorescence of BINOL and its derivatives is generally quenched by amines and amino alcohols. In order to prepare a fluorescent sensor that could exhibit fluorescence *enhancement* in the presence of amino alcohols, the BINOL-terpyridine compound (*R*)-**4** was obtained (Scheme 2).[36] The fluorescence of (*R*)-**4** at $\lambda = 396$ nm ($\lambda_{exc} = 289$ nm) was almost completely quenched upon coordination with a Cu(II) ion to form (*R*)-**5** probably due to a ligand to metal energy or electron transfer process (Figure 2).

When (*R*)-**5** was treated with (*S*)-phenylglycinol, its fluorescence signal at $\lambda = 396$ nm was greatly enhanced (Figure 3). This indicates that the excess amino alcohol molecules might compete with the terpyridine ligand of (*R*)-**5** to displace the Cu(II) from (*R*)-**5** and restore the emission of (*R*)-**4**. The fluorescence enhancement of (*R*)-**5** was much weaker in the presence of the enantiomer (*R*)-phenylglycinol. This enantioselective fluorescent response could be attributed to a more favorable equilibrium for the reaction of (*R*)-**5** with the (*S*)-amino alcohol than with the (*R*)-one, giving $I_S/I_0 = 24$ and ef = 2.8 (Figure 3a). Figure 3b shows the fluorescence enhancement of (*R*)-**5** in the presence of (*R*)- and (*S*)-phenylglycinol at various concentrations. When (*R*)-**5**

SCHEME 3. Synthesis of a Monoamine-Linked BisBINOL Sensor



was treated with other chiral amino alcohols including prolinol, valinol, phenylalaninol, leucinol, and 1-amino-2-propanol, significant enantioselective fluorescent enhancements were also observed.

(*R*)-**5** (15 mg) was not completely soluble in $CHCl_3$ (0.40 mL) at 3.75% (w/v, g/mL) (5.74×10^{-2} M) but formed a green suspension. Upon sonication for 1 min and then standing at room temperature for 30 s, the suspension of (*R*)-**5** turned into an opaque green and unmovable gel. When this gel was treated with a solution of (*S*)-phenylglycinol (0.10 equiv) in $CHCl_3$ (0.1 mL), after sonication for 2 min, the gel collapsed. However, under the same conditions when the gel of (*R*)-**5** was treated with (*R*)-phenylglycinol, the gel remained stable. This enantioselective gel collapsing provides a new means to visually recognize the two enantiomers of phenylglycinol. It also demonstrates that in the gel of (*R*)-**5** there should be a cooperative effect between the molecules through intermolecular interactions which allows the use of only a small amount of (*S*)-amino alcohol (0.1 equiv) to cause the gel to collapse. Similar enantioselective gel collapsing was observed when the gel of (*R*)-**5** was treated with (*R*)- and (*S*)-1-amino-2-propanol.

3. Sensors for the Recognition of α-Hydroxycarboxylic Acids

3.1. A Monoamine-Linked BisBINOL Sensor. α-Hydroxycarboxylic acids are biologically important and synthetically versatile compounds. We designed and synthesized the bisBINOL compound (*S*)-**6** for the recognition of α-hydroxycarboxylic acids (Scheme 3).[37] Structure **7** shows a proposed interaction between (*S*)-**6** and (*S*)-mandelic acid (MA). The nitrogen atom in (*S*)-**6** is incorporated to quench the fluorescence of the two BINOL units it links. Upon binding with the acid proton of MA as shown in **7**, the basicity of the nitrogen will be neutralized and the fluorescence of the BINOL unit in (*S*)-**6** should be restored, giving fluorescence enhancement. The chirality of the bisBINOL unit in (*S*)-**6** and the three point hydrogen bonding shown in **7** should make the interactions of (*S*)-**6** with the two enantiomers of MA different, generating enantioselective fluorescent response.

Figure 4 gives the fluorescence spectra of (*S*)-**6** (9.5×10^{-5} M) in the presence of (*R*)- and (*S*)-MA in benzene in which 2% dimethoxyethylene (DME) was added to improve the solubility of MA. It shows that (*S*)-MA (5.0×10^{-3} M) enhances the fluorescence of (*S*)-**6** more than (*R*)-MA with $I_S/I_0 = 2.87$ and the enantiomeric fluorescence enhancement ratio ef $[=(I_S - I_0)/(I_R - I_0)] = 2.49$. This is attributed to the stronger binding of (*S*)-**6** with (*S*)-MA than with (*R*)-MA.

In order to enhance the fluorescence sensitivity of (*S*)-**6**, (*R*)-**8** and (*R*)-**9** were prepared as the two dendritic derivatives of (*S*)-**6**.[38] As we have shown in the study of the dendrimers (*S*)-**1**–(*S*)-**3**, the light harvesting effect of the polyaromatic branching units in (*R*)-**8** and (*R*)-**9** should increase the fluorescence of the BINOL units which could then be quenched by the central nitrogen atom. Upon interaction with a chirality-matched α-hydroxycarboxylic

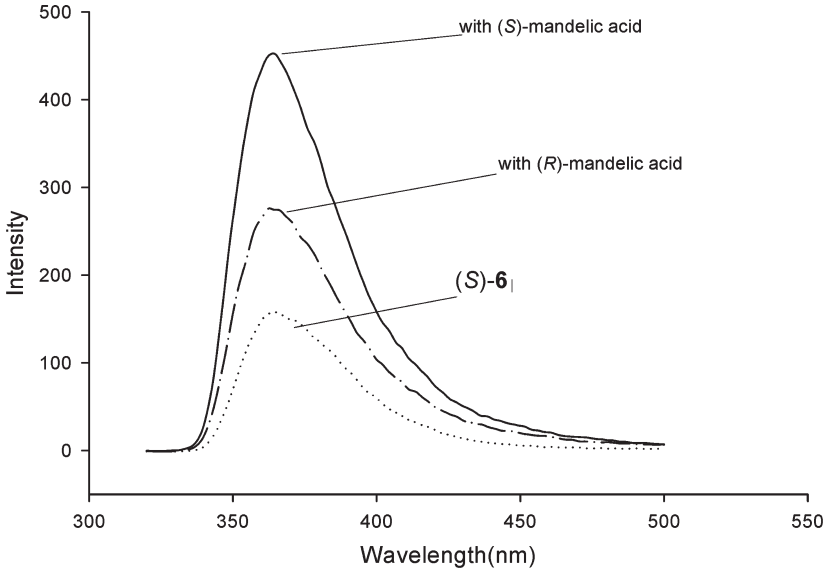


FIGURE 4. Fluorescence spectra of (*S*)-**6** with and without MA ($\lambda_{exc} = 310$ nm).

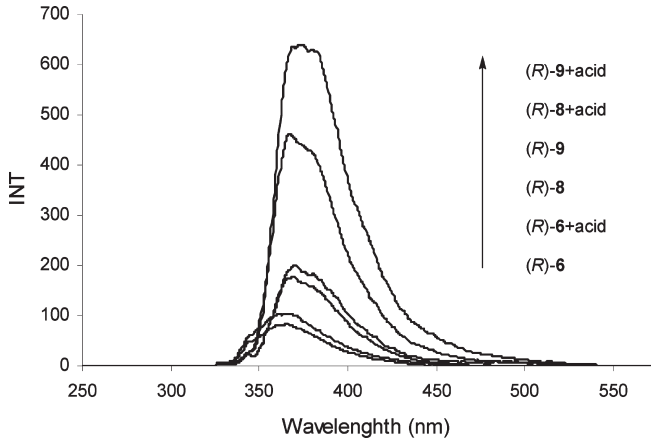
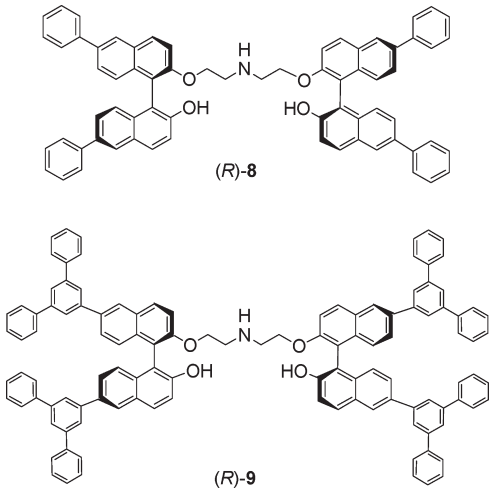


FIGURE 5. Fluorescence spectra of (*R*)-**6**, (*R*)-**8**, and (*R*)-**9** (each at 3.1×10^{-6} M in benzene/0.1% DME) with/without (*R*)-MA (1.0×10^{-3} M).

acid, the fluorescence enhancement of (*R*)-**8** and (*R*)-**9** should be greater than that of (*R*)- or (*S*)-**6**.

Figure 5 gives the fluorescence spectra of (*R*)-**6**, (*R*)-**8**, and (*R*)-**9** with and without (*R*)-MA. It shows that in the presence of the chirality-matched (*R*)-MA at a sensor concentration significantly lower than that in Figure 4, the fluorescence enhancement of (*R*)-**8** is 14 times that of (*R*)-**6** and the fluorescence enhancement of (*R*)-**9** is 22 times that of (*R*)-**6**. Thus, these dendritic derivatives are much more sensitive fluorescent sensors than the core. The enantioselectivities of (*R*)-**8** and (*R*)-**9** are close to that of the core.

3.2. BisBINOL-Based Macrocyclic Sensors. In order to improve the enantioselectivity of the BINOL-based fluorescent sensor for the recognition of α-hydroxycarboxylic acids, two bisBINOL-based macrocyclic compounds (*S*)-**11**[39,40] and

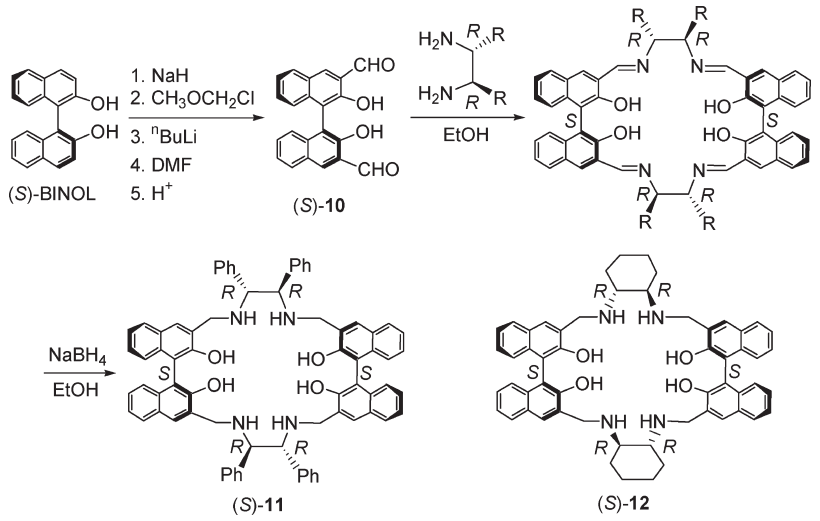


(*S*)-**12**[41] were prepared from (*S*)-BINOL. As shown in Scheme 4, the synthesis involved a four component condensation of a chiral diamine with the 3,3′-diformylBINOL (*S*)-**10** followed by reduction.

The macrocycle (*S*)-**11**, made of (*R,R*)-1,2-diphenylethylenediamine, gave dual emissions at $\lambda_{emi} = 365$ and 424 nm (Figure 6).[40] The long wavelength signal was assigned to be the excimer emission and the short wavelength one to be the monomer emission. As shown in Figure 6, when (*S*)-**11** was treated with (*S*)-MA, there is a large fluorescence enhancement at the excimer emission with $I_S/I_0 = 2.9$. In the presence of (*R*)-MA, the fluorescence enhancement at the excimer emission was much smaller which led to ef = 12. Thus, the enantioselectivity of (*S*)-**11** is much greater than that of the acyclic bisBINOL compound (*S*)-**6**.

Very different fluorescence responses were observed when (*S*)-**12**, made of (*R,R*)-cyclohexane-1,2-diamine, was treated with

SCHEME 4. Synthesis of the BisBINOL-Based Macrocycles (*S*)-**11** and (*S*)-**12**



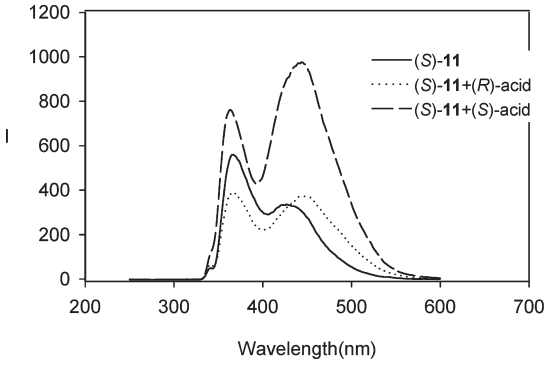


FIGURE 6. Fluorescence spectra of (*S*)-**11** (1.0×10^{-4} M in benzene/2% DME) with/without (*R*)- and (*S*)-MA (2.0×10^{-2} M) ($\lambda_{exc} = 340$ nm).

MA.[41] As shown in Figure 7a, in the presence of (*S*)-MA, the fluorescence of (*S*)-**12** was greatly enhanced with the major enhancement (20-fold) observed at the monomer emission. (*R*)-MA only generated a very small fluorescence enhancement with the enantioselectivity ef = 46. Figure 7b shows the fluorescence enhancement of (*S*)-**12** at various concentrations of MA.

A two stage fluorescence enhancement mechanism was proposed to account for the high fluorescence sensitivity and enantioselectivity of (*S*)-**12** toward MA. In the first stage, (*S*)-**12** includes (*S*)-MA inside its chiral cavity to form a 1:1 complex. A large upfield shift ($\delta\Delta = \sim 1.1$) for the ^{1}H NMR signal of the α-proton of (*S*)-MA was observed for the 1:1 complex. Although the structural rigidity of such a 1:1 complex should make it a much stronger fluorophore, the multiple nitrogen atoms in (*S*)-**12** should still quench its fluorescence. In the second stage, an excess amount of (*S*)-MA interacts with the 1:1 complex and protonates the remaining nitrogen atoms to cause the observed large fluorescence enhancement. The much greater

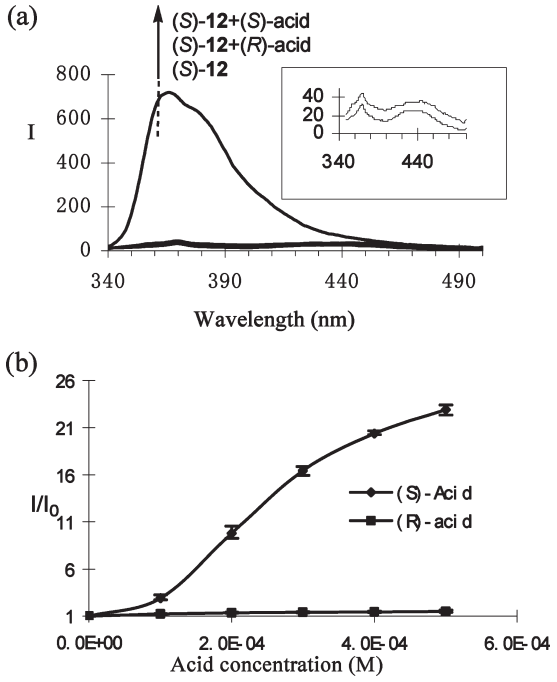


FIGURE 7. (a) Fluorescence spectra of (*S*)-**12** (1.0×10^{-5} M in benzene/0.05% DME) with/without (*R*)- and (*S*)-MA (5.0×10^{-4} M) ($\lambda_{exc} = 332$ nm). (b) Fluorescence enhancement of (*S*)-**12** (1.0×10^{-5} M in benzene/0.05% DME) versus concentration of (*R*)- and (*S*)-MA ($\lambda_{exc} = 332$ nm).

fluorescent sensitivity and enantioselectivity of (*S*)-**12** than (*S*)-**11** are attributed to their structural differences. The single crystal X-ray structures of (*S*)-**11** and (*R*)-**12** are given in Figure 8. It shows that the structure of (*S*)-**11** is more like a tube with both ends open so that small guest molecules can easily fall through. However, the structure of (*R*)-**12** is more like a bucket with a closed bottom which allows it to form a stable and structurally rigid 1:1 complex with the chirality-matched (*S*)-MA.

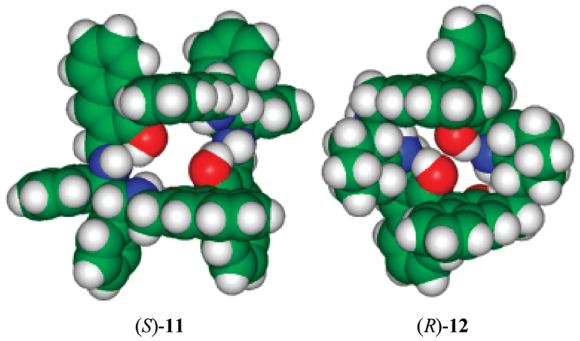
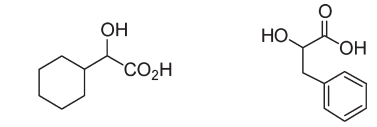


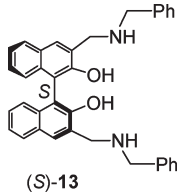
FIGURE 8. Space-filling models for the X-ray structures of (*S*)-**11** and (*R*)-**12**.

The interaction of (*R*)-**12** with the enantiomers of other α-hydroxycarboxylic acids was studied. When (*R*)-**12** (1.0×10^{-5} M in benzene/0.4% DME) was treated with (*R*)-hexahydromandelic acid (4.0×10^{-3} M), an even greater fluorescence enhancement was observed with $I_R/I_0 = 80$. The enantioselectivity was also very high with ef $[(I_R - I_0)/(I_S - I_0)] = 64$. This indicates that the sterically more bulky hexahydromandelic acid might lead to the formation of a more structurally rigid complex with the sensor than MA, giving the greater fluorescence response and higher enantioselectivity. However, when (*R*)-**12** [1.0×10^{-5} M (benzene/1% DME) was treated with the structurally more flexible phenyllactic acid (8.0×10^{-3} M), both the fluorescence enhancement ($I_R/I_0 = 6$) and the enantioselectivity (ef = 3) were significantly lower.



hexahydromandelic acid phenyllactic acid

3.3. MonoBINOL-Based Sensors. The acyclic monoBINOL (*S*)-**13** was prepared which contains only half of the structural units of the macrocycles (*S*)-**11** and (*S*)-**12**.[42] This compound gave dual emission at $\lambda_{em} = 360$, 430 nm (Figure 9 inset). When (*S*)-**13** was treated with (*R*)-MA, its fluorescence intensity was increased to 30-fold ($I_R/I_0 = 30$) with the enantioselectivity ef = 4.2 (Figure 9). The enantioselectivty of (*S*)-**13** is the opposite of (*S*)-**11** and (*S*)-**12** which indicates their very different steric interactions with the enantiomers of MA.



(*S*)-**13**

Additional hydroxyl groups were introduced to (*S*)-**13** to increase its binding with α-hydroxycarboxylic acids in order

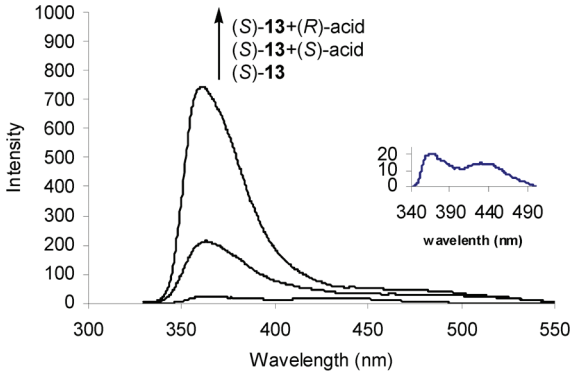


FIGURE 9. Fluorescence spectra of (*S*)-**13** (1.0×10^{-4} M in benzene/2% DME) with/without (*R*)- and (*S*)-MA (2.0×10^{-2} M) ($\lambda_{exc} = 320$ nm).

FIGURE 10. Images of (*S*)-**14** (5.0×10^{-4} M in benzene/0.4% v DME) with (*R*)- and (*S*)-MA (4.0×10^{-3} M).

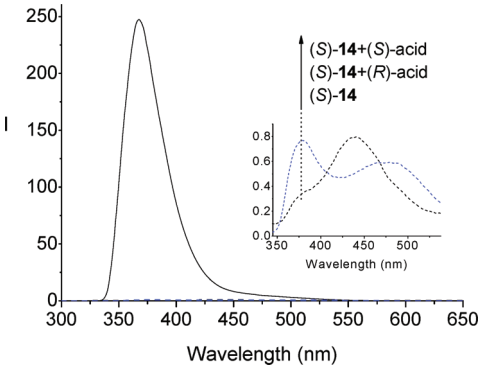
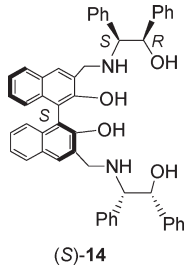


FIGURE 11. Fluorescence spectra of (*S*)-**14** (5.0×10^{-4} M in benzene/0.4% v DME) with (*R*)- and (*S*)-MA (4.0×10^{-3} M) ($\lambda_{exc} = 341$ nm).

to improve its enantioselectivity. From the reductive amination of (*S*)-**10** with (1*R*,2*S*)-2-amino-1,2-diphenylethanol, (*S*)-**14** was obtained.[43] As shown in Figure 10, when (*S*)-**14** was treated with (*S*)-MA ($\geq 3.0 \times 10^{-3}$ M) in benzene (0.4% DME), a white precipitate was produced but (*R*)-MA (3.0×10^{-3}–8.0×10^{-3} M) could not give a precipitate. This enantioselective precipitation allows the two

enantiomers of the α-hydroxycarboxylic acid to be discriminated visually.



(*S*)-**14**

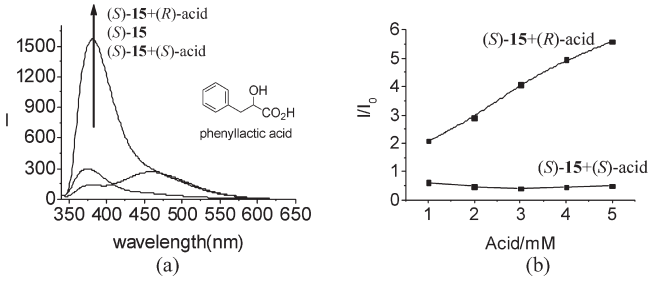


FIGURE 12. (a) Fluorescence spectra of (*S*)-**15** (2.0×10^{-4} M in benzene/0.4%v DME) with (*R*)- and (*S*)-phenyllactic acid (5.0×10^{-3} M). (b) Fluorescence enhancement of (*S*)-**15** with varying concentrations of (*R*)- and (*S*)-phenyllactic acid at $\lambda_{em.} = 382$ nm ($\lambda_{exc} = 334$ nm).

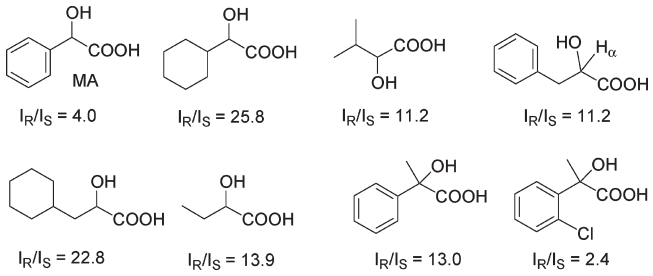


FIGURE 13. Fluorescent enantioselectivity of (*S*)-**15** toward various chiral α-hydroxycarboxylic acids.

The fluorescence spectra of (*S*)-**14** in the presence of (*R*)- and (*S*)-MA were obtained. As shown in Figure 11, the white suspension of (*S*)-**14**+(*S*)-MA gave a dramatically increased fluorescence signal at 367 nm with up to 950-fold enhancement, but the solution of (*S*)-**14**+(*R*)-MA showed a much smaller change with ef as high as 485. The white precipitate of (*S*)-**14**+(*S*)-MA was dissolved in $CDCl_3$, and its ^1H NMR spectrum showed a sensor/substrate ratio of 1:4. The solid state induced large fluorescence enhancement of (*S*)-**14**+(*S*)-MA is attributed to the isolation of the fluorophore by complexing with the chirality matched chiral acid and the greatly increased structural rigidity in the solid state. (*S*)-**14** also showed enantioselective precipitation and enantioselective fluorescent enhacement in the presence of hexahydromandelic acid, but its enantioselective fluorescent response toward other α-hydroxycarboxylic acid such as phenyllactic acid was much lower.

Through the study of a number of derivatives of (*S*)-**14** containing various substituents on the 3,3′-amino alcohol units, we found that (*S*)-**15** containing three phenyl substituents on each of its amino alcohol units is a generally enantioselective fluorescent sensor for structurally diverse α-hydroxycarboxylic acids though it did not form precipitate with the acids.[44] As shown in Figure 12, while (*S*)-phenyllactic acid quenches the fluorescence of (*S*)-**15** at the monomer emission, (*R*)-phenyllactic acid greatly enhances it. Because of these opposite effects of the two enantiomers of the chiral acids on the fluorescence signal of (*S*)-**15** at the monomer emission, I_R/I_S instead of ef is used to represent the enantioselectivity which is 11.2. Figure 13 summarizes the I_R/I_S values when (*S*)-**15** was used to interact with a variety of α-hydroxycarboxylic acids under the same conditions.

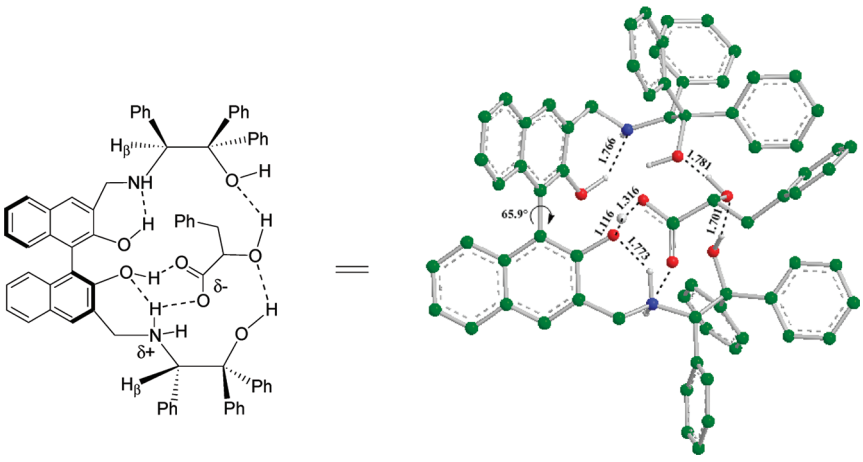


FIGURE 14. Calculated structure of the proposed 1:1 complex of (*S*)-**15**+(*R*)-phenyllactic acid.

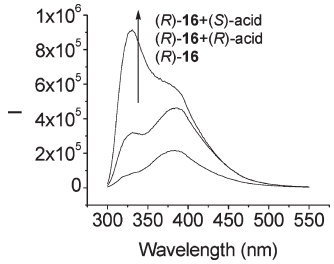


FIGURE 15. Fluorescence spectra of (*R*)-**16** (1.0×10^{-4} M in CH_2Cl_2) with/without (*R*)- and (*S*)-MA (4.0×10^{-3} M).

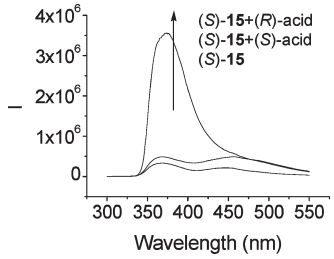


FIGURE 16. Fluorescence spectra of (*S*)-**15** (1.0×10^{-4} M in CH_2Cl_2) with/without MA (4.0×10^{-3} M).

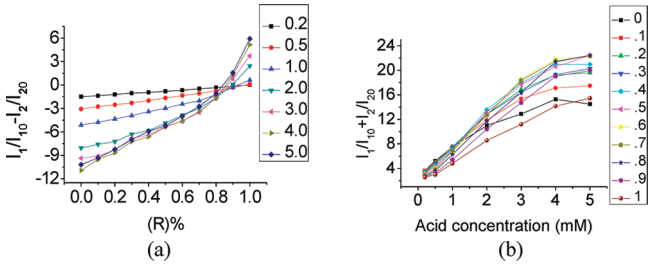
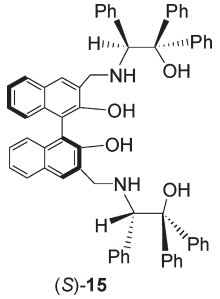


FIGURE 17. (a) Plot of $(I_1/I_{10} - I_2/I_{20})$ versus [(*R*)-Acid]% at varying MA concentrations (mM). (b) Plot of $(I_1/I_{10} + I_2/I_{20})$ versus MA concentration at varying [(*R*)-acid]%. ($\lambda_{exc} = 290$ nm).

These data demonstrate that (*S*)-**15** can be used to determine the enantiomeric composition of various types of α-hydroxycarboxylic acids.



(*S*)-**15**

A computational study of the 1:1 complexes of (*S*)-**15** and (*R*)-phenyllactic acid using the Gaussian 03 program with the density functional theory method of B3LYP was conducted. As shown in Figure 14, there are strong acid–base interactions between the amine nitrogen of (*S*)-**15** and the carboxylic acid group. The α-hydroxy group of the acid could also form hydrogen bonds with each of the hydroxyl groups of the amino alcohol units in (*S*)-**15**. The structural rigidity of this 1:1 complex and its further interaction with additional chiral acid molecules should have contributed to the observed enantioselective fluorescent response.

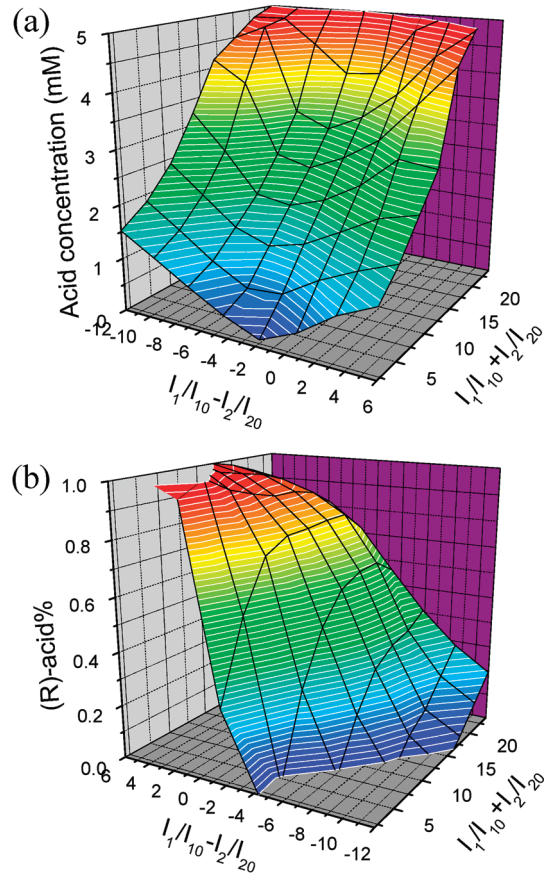
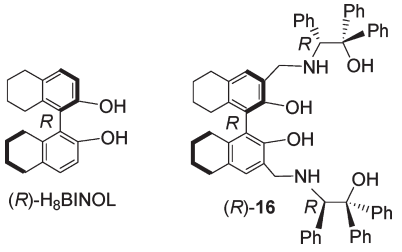


FIGURE 18. (a) 3D plot of $(I_1/I_{10} - I_2/I_{20})$ and $(I_1/I_{10} + I_2/I_{20})$ versus the MA concentration (mM). (b) 3D plot of $(I_1/I_{10} - I_2/I_{20})$ and $(I_1/I_{10} + I_2/I_{20})$ versus [(*R*)-acid]%.

3.4. Using Pseudoenantiomeric Sensor Pair for Chiral Assay. Because the fluorescence of a chiral sensor is strongly influenced by both the concentration and the enantiomeric composition of the substrate, these two parameters need to be determined separately. We have developed a strategy to use a pseudoenantiomeric sensor pair to determine both the concentration and the enantiomeric composition of an α-hydroxycarboxylic acid by a single fluorescence measurement.

The H_8BINOL-amino alcohol (*R*)-**16** was synthesized from the partially hydrogenated BINOL (*R*)-H_8BINOL for use with (*S*)-**15** as a pseudoenantiomeric sensor.[45] These two compounds have opposite chiral configuration at both the axially chiral biaryl centers and the amino alcohol units with distinctly different

emission wavelengths. (*S*)-**15** has more extended conjugation than (*R*)-**16**, and thus, it emits at a much longer wavelength (λ_1 = 374 nm) than (*R*)-**16**. Figure 15 gives the fluorescence spectra of (*R*)-**16** in the presence of (*R*)- and (*S*)-MA in CH_2Cl_2. It shows that (*S*)-MA greatly enhances the fluorescence of (*R*)-**16** at λ_2 = 330 nm but (*R*)-MA causes a much smaller fluorescence enhancement. It is found that I_S/I_0 = 11.7 and ef = 3.6.



As described in section 3.3, (*S*)-**15** exhibits generally enantioselective fluorescent responses toward α-hydroxycarboxylic acids in benzene solution. Because of the reduced conjugation of (*R*)-**16** versus (*S*)-**15**, benzene interferes with the fluorescence spectrum of (*R*)-**16** and is not a suitable solvent for this pseudoenantiomeric pair. Thus, the interaction of (*S*)-**15** with MA in CH_2Cl_2 was studied which also gave highly enantioselective fluorescent responses. As shown in Figure 16, (*R*)-MA greatly enhances the fluorescence of (*S*)-**15** at λ_1 = 374 nm in CH_2Cl_2 similar to that observed in benzene, but (*S*)-MA causes a very small fluorescence enhancement which is different from that observed in benzene where a slight quenching at the short wavelength signal was observed. Figure 16 gives I_R/I_0 = 11.4 and ef [= $(I_R - I_0)/(I_S - I_0)$] = 26.0.

Because of the distinctly different fluorescent responding wavelengths between (*S*)-**15** and (*R*)-**16**, a 1:1 mixture of this pseudoenantiomeric pair in CH_2Cl_2 (each at 1.0×10^{-4} M) was used to interact with MA of varying concentrations and enantiomeric compositions. It is proposed that the fluorescence intensity difference at λ_1 and λ_2 could be used to determine the enantiomeric composition of the substrate and the sum of the fluorescence intensity at these two wavelengths could be used to determine the total concentration of the substrate. In Figure 17a, the fluorescence intensity difference at λ_1 (374 nm) and λ_2 (330 nm), that is $(I_1/I_{10} - I_2/I_{20})$ (I_1 and I_2: fluorescence intensity at λ_1 and λ_2 in the presence of the acid. I_{10} and I_{20}: fluorescence intensity in the absence of the acid), is plotted against the enantiomeric composition [(*R*)-acid]% at various acid concentrations. In Figure 17b, the fluorescence intensity sum at λ_1 (374 nm) and λ_2 (330 nm), that is $(I_1/I_{10} + I_2/I_{20})$, is plotted against the acid concentration at various enantiomeric compositions.

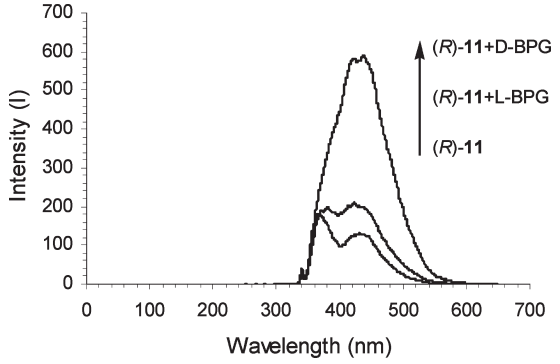


FIGURE 19. Fluorescence spectra of (*R*)-**11** (1.0×10^{-4} M in benzene/2% DME) with/without D- and L-BPG (4.0×10^{-3} M) (λ_{exc} = 340 nm).

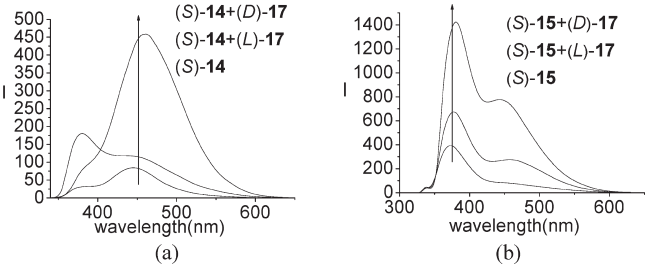


FIGURE 21. (a) Fluorescence spectra of (*S*)-**14** (5.0×10^{-4} M in benzene/2.5%DME) with (*D*)- and (*L*)-**17** (2.0×10^{-3} M) (λ_{exc}= 341 nm). (b) Fluorescence spectra of (*S*)-**15** (2.0×10^{-4} M in benzene/2.5%DME) with (*L*)- and (*D*)-**17** (1.0×10^{-3} M) (λ_{exc} = 334 nm).

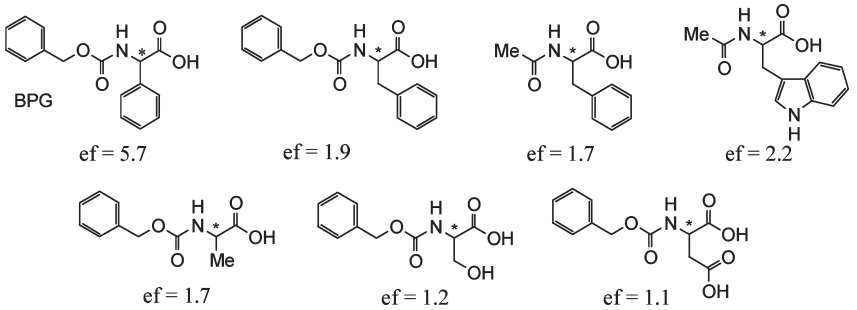
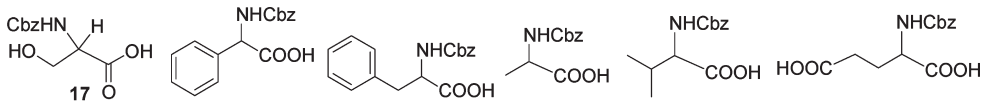


FIGURE 20. Enantioselectivity of (*R*)-**11** in the fluorescent recognition of various amino acid derivatives.



(*S*)-**14**: I_D/I_0 =	6.0	2.8	16.2	9.0	6.5	16.0
ef =	12.5	10.9	5.0	6.3	9.3	2.8
(*S*)-**15**: I_D/I_0 =	3.8	4.8	3.6	4.5	2.4	7.8 (I_L/I_0)
ef =	3.5	10.8	13.0	5.3(I_D/I_L)	2.7(I_D/I_L)	2.1

FIGURE 22. Fluorescent sensitivity and enantioselectivity in the recognition of amino acid derivatives.

Using the data of Figure 17, the 3D graphs of the acid concentration and the enantiomeric composition versus the sum and difference of the pseudoenantiomeric sensor pair at λ_1 and λ_2 were obtained (Figure 18). These 3D graphs demonstrate that both the acid concentration and the enantiomeric composition of an MA sample can be determined by a single fluorescence measurement of the sample in the presence of the pseudoenantiomeric sensor pair.

4. Sensors for the Recognition of α-Amino Acid Derivatives

4.1. Using BisBINOL Macrocycle-Based Sensors. The macrocycles **11** and **12** were also used for the recognition of N-protected amino acids. As shown in Figure 19, when (*R*)-**11** was treated with *N*-benzyloxycarbonylphenyl glycine (BPG), the D-BPG increases the long wavelength emission of (*R*)-**11** much greater than L-BPG with I_D/I_0 = 4.3 and ef =5.7.[40b,46] The fluorescence enhancement of (*R*)-**11** was also found to be linear with the enantiomeric composition of the acid. ^{1}H NMR study indicates that (*R*)-**11** could form a 1:4 complex with BPG in the ground state probably by protonation of the four nitrogen atoms of the macrocycle with the acid. Although the interaction of (*R*)-**11** with BPG showed good enantioselectivity, much smaller enantioselectivity was observed when (*R*)-**11** was used to interact with other amino acid derivatives as shown in Figure 20. (*R*)-**12** also gave good enantioselectivity in the recognition of BPG with ef up to 7.[41b]

4.2. Using MonoBINOL-Based Sensors. The interaction of the monoBINOL (*R*)-**13** with BPG was studied.[42] It was found that the fluorescence intensity of (*R*)-**13** (1.0×10^{-4} M in benzene/2% DME) increased over 11.5-fold in the presence of D-BPG (4.0×10^{-3} M) and 6.1-fold in the presence of L-BPG. Thus, the enantioselectivity (ef = 2.0) was lower than those of the macrocycles (*R*)-**11** and (*R*)-**12**.

The interactions of (*S*)-**14** and (*S*)-**15** with N-protected amino acids were studied. When (*S*)-**14** was treated with the enantiomers of the N-protected serine **17** (see Figure 22), highly enantioselective fluorescent responses were observed.[47] As shown in Figure 21a, at the long wavelength emission of (*S*)-**14**, the fluorescent sensitivity I_D/I_0 was found to be 6.0 and the enantioselectivity ef to be 12.5. When (*S*)-**15** was used to interact with **17**, the enantioselective fluorescent enhancement at the monomer emission of (*S*)-**15** was observed with I_D/I_0 = 3.8 and ef = 3.5 (Figure 21b). Figure 22 shows that compounds (*S*)-**14** and (*S*)-**15** have exhibited quite high fluorescent sensitivity and enantioselectivity for a number of amino acid derivatives.

5. Summary

The unique structure of BINOL has been used to construct enantioselective fluorescent sensors. Various types of functional groups have been attached to the enantiomerically pure BINOL to build chiral macrocycles, dendrimers, and a variety of acyclic compounds. It has been demonstrated that the conjugated dendritic units can be used to amplify the fluorescence response of the BINOL-based sensors to generate highly sensitive sensors. Incorporation of a metal ion (Cu^{2+}) and its subsequent enantioselective displacement by chiral amino alcohols can convert a fluorescent quench sensor to a fluorescent enhancement sensor. Highly sensitive and enantioselective fluorescent sensors for the recognition of α-hydroxycarboxylic acids and amino acid derivatives have been obtained by incorporating amine and amino alcohol units into the BINOL structure. The research on the BINOL-based molecules has demonstrated that it is possible to develop enantioselective and sensitive fluorescent sensors for the chiral assay of organic molecules by designing and systematically modifying the structure of the chiral molecular receptors.

BIOGRAPHICAL INFORMATION

Lin Pu was born in 1965 in Xuyong, Sichuan Province, China. He received his B.S. degree in chemistry from Sichuan University in 1984. He then obtained the Doering Fellowship (CGP) to undertake graduate study in the department of chemistry at University of California San Diego in 1985. Under the supervision of Professor Joseph M. O'Connor, he obtained his Ph.D. degree in 1990. As a postdoctoral fellow, he worked with Professor Henry Taube at Stanford University from January 1991 to November 1992, and

with Professor Robert Grubbs at the California Institute of Technology from November 1992 to August 1994. In the fall of 1994, he was appointed as an assistant professor at North Dakota State University. He then moved to University of Virginia as an associate professor in the department of chemistry in 1997 and as a professor in 2003. The research projects in his laboratory focus on the design and synthesis of novel chiral molecules and macromolecules for applications in areas such as enantioselective fluorescent sensors, asymmetric catalysis, and electrical and optical materials.

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FOOTNOTES

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REFERENCES

1 McDonagh, C.; Burke, C. S.; MacCraith, B. D. Optical Chemical Sensors. *Chem. Rev.* **2008**, *108*, 400–422.

2 Borisov, S. M.; Wolfbeis, O. S. Optical Biosensors. *Chem. Rev.* **2008**, *108*, 423–461.

3 Johnson, K. S.; Needoba, J. A.; Riser, S. C.; Showers, W. J. Chemical Sensor Networks for the Aquatic Environment. *Chem. Rev.* **2007**, *107*, 623–640.

4 Jelinek, R.; Kolusheva, S. Carbohydrate Biosensors. *Chem. Rev.* **2004**, *104*, 5987–6015.

5 (a) Nolan, E. M.; Lippard, S. J. Small-Molecule Fluorescent Sensors for Investigating Zinc Metalloneurochemistry. *Acc. Chem. Res.* **2009**, *42*, 193–203. (b) Morawetz, H. On the Versatility of Fluorescence Techniques in Polymer Research. *J. Polym. Sci., Part A: Polym. Chem.* **1999**, *37*, 1725–1735.

6 Thompson, R. B. *Fluorescence Sensors and Biosensors*; CRC: Boca Raton, FL, 2005.

7 de Silva, A. P.; Gunaratne, H. Q. N.; Gunnlaugsson, T.; Huxley, A. J. M.; McCoy, C. P.; Rademacher, J. T.; Rice, T. E. Signaling Recognition Events with Fluorescent Sensors and Switches. *Chem. Rev.* **1997**, *97*, 1515–1566.

8 Pu, L. Fluorescence of Organic Molecules in Chiral Recognition. *Chem. Rev.* **2004**, *104*, 1687–1716.

9 (a) Irie, M.; Yorozu, T.; Hayashi, K. Steric Effect on Fluorescence Quenching of 1,1′-Binaphthyl by Chiral Amines. *J. Am. Chem. Soc.* **1978**, *100*, 2236–2237. (b) Yorozu, T.; Hayashi, K.; Irie, M. Chiral Discrimination in Fluorescence Quenching. *J. Am. Chem. Soc.* **1981**, *103*, 5480–5484.

10 James, T. D.; Sandanayake, K. R. A. S.; Shinkai, S. Chiral Discrimination of Monosaccharides Using a Fluorescent Molecular Sensor. *Nature* **1995**, *374*, 345–347.

11 Avnir, D.; Wellner, E.; Ottolenghi, M. Photophysical Recognition of Chiral Surfaces. *J. Am. Chem. Soc.* **1989**, *111*, 2001–2003.

12 (a) Parker, K. S.; Townshend, A.; Bale, S. J. Simultaneous Determination of the Concentrations of Each Enantiomer of 1-Phenylethylamine Using Their Quenching of the Fluorescence of Two Chiral Fluorophores. *Anal. Commun.* **1996**, *33*, 265–267. (b) Wang, D.; Liu, T.-J.; Zhang, W.-C.; Slaven, W. T., IV; Li, C.-J. Enantiomeric Discrimination of Chiral Amines with New Fluorescent Chemosensors. *J. Chem. Soc., Chem. Commun.* **1998**, 1747–1748. (c) Murakoshi, K.; Azechi, T.; Hosokawa, H.; Wada, Y.; Yanagida, S. Chiroselective Electron Transfer at Enantiomer-Capped ZnO Nanocrystalline Surfaces. *J. Electroanal. Chem.* **1999**, *473*, 117–124.

13 (a) Beer, G.; Rurack, K.; Daub, J. Chiral Discrimination with a Fluorescent Boron-Dipyrromethene dye. *J. Chem. Soc., Chem. Commun.* **2001**, 1138–1139. (b) He, X.; Cui, X.; Li, M.; Lin, L.; Liu, X.; Feng, X. Highly Enantioselective Fluorescent sensor for Chiral Recognition of Amino Acid Derivatives. *Tetrahedron Lett.* **2009**, *50*, 5853–5856.

14 Lee, S. J.; Lin, W. —B. A Chiral Molecular Square with Metallo-Corners for Enantioselective Sensing. *J. Am. Chem. Soc.* **2002**, *124*, 4554–4555.

15 Grady, T.; Harris, S. J.; Smyth, M. R.; Diamond, D.; Hailey, P. Determination of the Enantiomeric Composition of Chiral Amines based on the Quenching of the Fluorescence of a Chiral Calixarene. *Anal. Chem.* **1996**, *68*, 3775–3782.

16 Pagliari, S.; Corradini, R.; Galaverna, G.; Sforza, S.; Dossena, A.; Marchelli, R. Enantioselective Sensing of Amino Acids by Copper(II) Complexes of Phenylalanine-Based Fluorescent Beta-Cyclodextrins. *Tetrahedron Lett.* **2000**, *41*, 3691–3695.

17 Abe, Y.; Fukui, S.; Koshiji, Y.; Kobayashi, M.; Shoji, T.; Sugata, S.; Nishizawa, H.; Suzuki, H.; Iwata, K. Enantioselective Binding Sites on Bovine Serum Albumin to Dansyl Amino Acids. *Biochim. Biophys. Acta* **1999**, *1433*, 188–197.

18 Mei, X. F.; Wolf, C. Determination of Enantiomeric Excess and Concentration of Unprotected Amino Acids, Amines, Amino Alcohols, and Carboxylic Acids by Competitive Binding Assays with a Chiral Scandium Complex. *J. Am. Chem. Soc.* **2006**, *128*, 13326–13327.

19 Heo, J.; Mirkin, C. A. Pseudo-Allosteric Recognition of Mandelic Acid with an Enantioselective Coordination Complex. *Angew. Chem., Int. Ed.* **2006**, *45*, 941–944.

20 Zhu, L.; Zhong, Z. L.; Anslyn, E. V. Guidelines in Implementing Enantioselective Indicator-Displacement Assays for Alpha-Hydroxycarboxylates and Diols. *J. Am. Chem. Soc.* **2005**, *127*, 4260–4269.

21 (a) Dai, Z. H.; Xu, X. D.; Canary, J. W. Rigidified Tripodal Chiral Ligands in the Asymmetric Recognition of Amino Compounds. *Chirality* **2005**, *17*, S227–S233. (b) Reetz, M. T.; Sostmann, S. 2,15-Dihydroxy-hexahelicene (HELIXOL): Synthesis and Use as an Enantioselective Fluorescent Sensor. *Tetrahedron* **2001**, *57*, 2515–2520.

22 (a) Cram, D. J.; Cram, J. M. Host-Guest Chemistry. *Science* **1974**, *183*, 803–809. (b) Cram, D. J. Molecular Container Compounds. *Nature* **1992**, *356*, 29–36.

23 Dietrich, B.; Lehn, J.-M.; Simon, J. Chiral Macrobicyclic and Macrotricyclic Ligands. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 406–407.

24 Noyori, R.; Takaya, H. BINAP—An Efficient Chiral Element for Asymmetric Catalysis. *Acc. Chem. Res.* **1990**, *23*, 345–350.

25 Rosini, C.; Franzini, L.; Raffaelli, A.; Salvadori, P. Synthesis and Applications of Binaphthylic C_2 Symmetry Deriavtives as Chiral Auxiliaries in Enantioselective Reactions. *Synthesis* **1992**, 503–517.

26 Whitesell, J. K. C_2 Symmetry and Asymmetric Induction. *Chem. Rev.* **1989**, *89*, 1581–1590.

27 Bringmann, G.; Walter, R.; Weirich, R. The Directed Synthesis of Biaryl Compounds — Modern Concepts and Strategies. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 977–991.

28 (a) Pu, L. 1,1′-Binaphthyl Dimers, Oligomers, and Polymers: Molecular Recognition, Asymmetric Catalysis, and New Materials. *Chem. Rev.* **1998**, *98*, 2405–2494. (b) Pu, L. *1,1′-Binaphthyl-Based Chiral Materials: Our Journey*; Imperial College Press: 2009.

29 (a) Chen, Y.; Yekta, S.; Yudin, A. K. Modified BINOL Ligands in Asymmetric Catalysis. *Chem. Rev.* **2003**, *103*, 3155–3211. (b) Kočovský, P.; Vyskočil, S.; Smrčina, M. Non-symmetrically Substituted 1,1′-Binaphthyls in Enantioselective Catalysis. *Chem. Rev.* **2003**, *103*, 3213–3245.

30 (a) Park, J.-W.; Ediger, M. D.; Green, M. M. Chiral Studies in Amorphous Solids: The Effect of the Polymeric Glassy State on the Racemization Kinetics of Bridged Paddled Binaphthyls. *J. Am. Chem. Soc.* **2001**, *123*, 49–56. (b) Yang, S. Y.; Schultz, G.; Green, M. M.; Morawetz, H. Clustering of Poly(methacrylic acid) around Appended Binaphthyl Labels As Reflected by the Disruption of γ-Cyclodextrin Complexation and Racemization Kinetics. *Macromolecules* **1999**, *32*, 2577–2584.

31 Iwanek, W.; Mattay, J. Ground-State and Excited-State Association — Chiral recognition between 2,2′-Dihydroxy-1,1′-binaphthyl and Amines. *J. Photochem. Photobiol., A* **1992**, *67*, 209–226.

32 Devadoss, C.; Bharathi, P.; Moore, J. S. Energy Transfer in Dendritic Macromolecules: Molecular Size Effects and the Role of an Energy Gradient. *J. Am. Chem. Soc.* **1996**, *118*, 9635–9644.

33 Hu, Q. -S.; Pugh, V.; Sabat, M.; Pu, L. Structurally Rigid and Optically Active Dendrimers. *J. Org. Chem.* **1999**, *64*, 7528–7536.

34 Pugh, V.; Hu, Q.-S.; Pu, L. The First Dendrimer-Based Enantioselective Fluorescent Sensor for the Recognition of Chiral Amino Alcohols. *Angew. Chem., Int. Ed.* **2000**, *39*, 3638–3641.

35 (a) Pugh, V.; Hu, Q.-S.; Zuo, X.-B.; Lewis, F. D.; Pu, L. Optically Active BINOL Core-Based Phenyleneethynylene Dendrimers for the Enantioselective Fluorescent Recognition of Amino Alcohols. *J. Org. Chem.* **2001**, *66*, 6136–6140. (b) Gong, L. Z.; Hu, Q. S.; Pu, L. Optically Active Dendrimers with a Binaphthyl Core and Phenylene Dendrons: Light Harvesting and Enantioselective Fluorescent Sensing. *J. Org. Chem.* **2001**, *66*, 2358–2367.

36 Chen, X.; Huang, Z.; Chen, S.-Y.; Li, K.; Yu, X.-Q.; Pu, L. Enantioselective Gel Collapsing: A New Means of Visual Chiral Sensing. *J. Am. Chem. Soc.* **2010**, *132*, 7297–7299.

37 Lin, J.; Hu, Q.-S.; Xu, M. H.; Pu, L. A Practical Enantioselective Fluorescent Sensor for Mandelic Acid. *J. Am. Chem. Soc.* **2002**, *124*, 2088–2089.

38 Xu, M.-H.; Lin, J.; Hu, Q.-S.; Pu, L. Fluorescent Sensors for the Enantioselective Recognition of Mandelic Acid: Signal Amplification by Dendritic Branching. *J. Am. Chem. Soc.* **2002**, *124*, 14239–14246.

39 Brunner, H.; Schiessling, H. Dialdehyde plus Diamine — Polymer or Macrocycle. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 125–126.

40 (a) Lin, J.; Zhang, H.-C.; Pu, L. Bisbinaphthyl Macrocycle-Based Highly Enantioselective Fluorescent Sensors for Alpha-Hydroxycarboxylic Acids. *Org. Lett.* **2002**,

4, 3297–3300. (b) Li, Z.-B.; Lin, J.; Zhang, H.-C.; Sabat, M.; Hyacinth, M.; Pu, L. Macrocyclic Bisbinaphthyl Fluorophores and Their Acyclic Analogues: Signal Amplification and Chiral Recognition. *J. Org. Chem.* **2004**, *69*, 6284–6293.

41 (a) Li, Z.-B.; Lin, J.; Pu, L. A Cyclohexyl-1,2-diamine-derived Bis(binaphthyl) Macrocycle: Enhanced Sensitivity and Enantioselectivity in the Fluorescent Recognition of Mandelic Acid. *Angew. Chem., Int. Ed.* **2005**, *44*, 1690–1693. (b) Li, Z.-B.; Lin, J.; Sabat, M.; Hyacinth, M.; Pu, L. Enantioselective Fluorescent Recognition of Chiral Acids by Cyclohexane-1,2-diamine-based Bisbinaphthyl Molecules. *J. Org. Chem.* **2007**, *72*, 4905–4916.

42 Lin, J.; Rajaram, A. R.; Pu, L. Enantioselective Fluorescent Recognition of Chiral Acids by 3- and 3,3′-Aminomethyl Substituted BINOLs. *Tetrahedron* **2004**, *60*, 11277–11281.

43 Liu, H.-L.; Hou, X.-L.; Pu, L. Enantioselective Precipitation and Solid-State Fluorescence Enhancement in the Recognition of alpha-Hydroxycarboxylic Acids. *Angew. Chem., Int. Ed.* **2009**, *48*, 382–385.

44 Liu, H.-L.; Peng, Q.; Wu, Y.-D.; Chen, D.; Hou, X.-L.; Sabat, M.; Pu, L. Highly Enantioselective Recognition of Structurally Diverse alpha-Hydroxycarboxylic Acids using a Fluorescent Sensor. *Angew. Chem., Int. Ed.* **2010**, *49*, 602–606.

45 Yu, S.; Pu, L. Pseudoenantiomeric Fluorescent Sensors in a Chiral Assay. *J. Am. Chem. Soc.* **2010**, *132*, 17698–17700.

46 Lin, J.; Li, Z.-B.; Zhang, H.-C.; Pu, L. Highly Enantioselective Fluorescent Recognition of Alpha-Amino Acid Derivatives. *Tetrahedron Lett.* **2004**, *45*, 103–106.

47 Liu, H. L.; Hou, X.-L.; Pu, L. Highly Enantioselective Fluorescent Recognition of Serine and Other Amino Acid Derivatives. *Org. Lett.* **2010**, *12*, 4172–4175.