Enantiomeric discrimination of chiral amines with new fluorescent chemosensors

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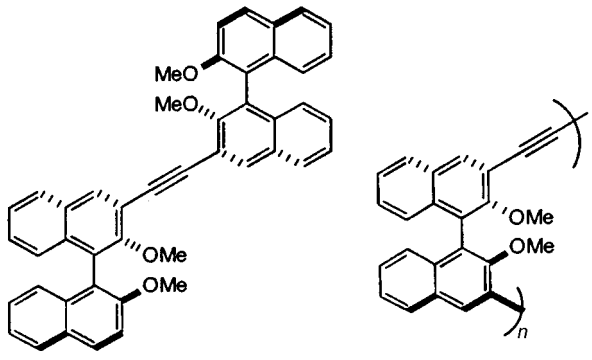
Fluorescent chiral sensors for the enantiomeric recognition of chiral amines have been developed.

Molecular recognition is a fundamental property of various natural systems and has attracted a significant amount of research interest recently.[1] Such recognition plays a key role in biosynthesis and protein folding. Enantiomeric recognition is a characteristic of many enzymatically catalyzed reactions generating optically active biological molecules and is the basis of asymmetric synthesis.[2] Because chiral amines and related compounds are the basic building blocks of biological systems, the study of enantiomeric recognition of these compounds is of particular significance.[3] Such studies, besides providing an understanding of the functions of natural living processes, also provide useful information for the understanding and design of asymmetric catalysis systems, new pharmaceutical agents[4] and separation materials.[5] Optical sensors have been of great interest in the last decade due to their often simple design and ease of handling. These sensors are increasingly important for biological and environmental analysis[6] as well as for pharmaceutical applications.[7] A promising technique is based on fluorescent probes due to their very sensitive detection ability.[8] These sensors are based on the large changes in their fluorescent properties during interaction with analytes. Recently, Shinkai's group developed a fluorescent molecular sensor that can discriminate D- and L-monosaccharides through their fluorescence response to the binding of guest species.[9] Binding of each enantiomer of the monosaccharides alters the fluorescence intensity to differing degrees, enabling them to be distinguished. More recently, Still and co-workers described small organic fluorescent sensors that detect the presence of unlabeled tripeptides in a sequence-selective manner.[10] Here we report the enantiomeric discrimination of chiral amines using designed receptors that act as sensors by changing fluorescence intensity during host–guest interactions.[11]



1 **2**

The chiral hosts used in our study are dimeric (**1**) and oligomeric (**2**) binaphthol-derivatives that we have previously developed.[12] For the chiral guest amines, we chose D- and L-α-phenylethylamines (**3**), as well as D- and L-phenylalanine methyl esters (**4**). The ^{1}H NMR studies were carried out in a $CDCl_3$ solution of chiral dimer (−)-**1** and D- or L-phenylethylamine (**3**) (host : guest = 1 : 1). Differences in chemical shifts of D- and L-**3** were observed: $\Delta\delta$(D−L) = 0.04 ppm (12 Hz) at δ 1.37 due to methyl-H, 0.04 ppm (12 Hz) at δ 4.2 due to CH of **3**, and 0.01 ppm (3 Hz) at δ 3.7 due to methoxy-H of the host **1**. The results indicated clearly that the complexation of chiral host **1** and the guest chiral amine, as well as enantio discriminations, occurred in $CDCl_3$ solution.

The fluorescence study was carried out in MeCN with the measurements performed on a Hitachi 850 Fluorescent Spectrometer. The experimental procedure is as follows: a solution of the host in MeCN (c 1.4 × 10^{-5} mol ml^{-1}) was titrated with a solution of the chiral amine in MeCN. The fluorescence intensity was measured and the quantum yields determined.[12] The fluorescence quantum yield of the chiral host was assigned as ϕ_0. Upon addition of the chiral guest, the fluorescence quantum yield ϕ of the solution was measured at various concentrations. ϕ/ϕ_0 was plotted against the concentration of the guest. Because most amines do not have a fluorescence chromaphore, an emission wavelength (λ_{em}) at 410 nm, the typical emission of a naphthalene ring, was used to measure the change in fluorescence intensity. Thus, changes in this wavelength can be attributed to the interaction of the guest chiral amines with the chiral host due to host–guest complexation.

It was found that the interaction of the two enantiomers of chiral amines did not have a substantial effect on the emission wavelength. On the other hand, a strong change in fluorescence response intensity was observed with the use of different enantiomers. As illustrated from the plots (Figs. 1 and 2), the dimer and oligomer hosts have different responses to the concentration changes of the guest molecules. When α-phenylethylamine was used as the chiral guest, the following observations were made: at a concentration of (10–15) × 10^{-5} mol dm^{-3}, $[\phi/\phi_0]_L/[\phi/\phi_0]_D$ has a value of 1.13 for the dimeric host and a value of 1.37 for the oligomeric host; whereas at a concentration of (2–5) × 10^{-5} mol dm^{-3}, the $[\phi/\phi_0]_L/[\phi/\phi_0]_D$ values changed to 0.81 for the dimeric and 1.07 for the oligomeric hosts respectively. Thus, in the case of the dimeric host, a change in the concentration of α-phenylethylamine from (10–15) to (2–5) × 10^{-5} mol dm^{-3} reversed the fluorescence

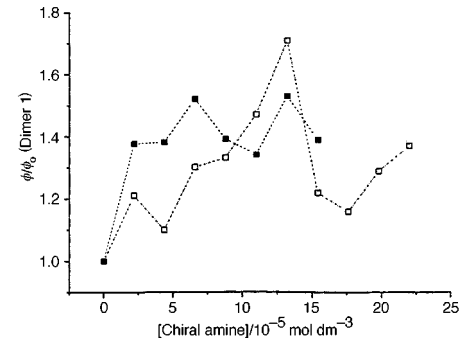


Fig. 1 ϕ/ϕ_0 ratio of fluorescent quantum yield of D- and L-α-phenylethylamine with dimer **1** as the host: (■) D-α-phenylethylamine and (□) D-α-phenylethylamine

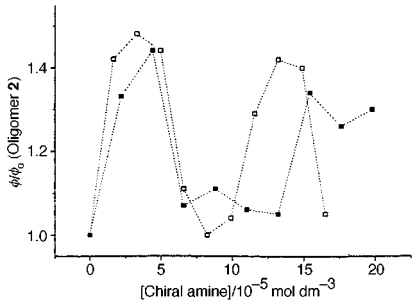


Fig. 2 ϕ/ϕ_0 ratio of fluorescent quantum yield of D- and L-α-phenylethylamine with oligomer **2** as the host: (■) D-α-phenylethylamine and (□) D-α-phenylethylamine

response of the two enantiomers. Such a reversed fluorescence response was also observed during the measurement of phenylalanine methyl ester (Figs. 3 and 4). At a concentration of (7–9) $\times$ 10^{-5} mol dm^{-3}, the $[\phi/\phi_0]_L/[\phi/\phi_0]_D$ has a value of 1.19 for the dimeric host and a vlaue of 1.10 for the oligomeric host; whereas at a concentration of (2–4) $\times$ 10^{-5} mol dm^{-3}, the $[\phi/\phi_0]_L/[\phi/\phi_0]_D$ values changed to 0.97 for the dimeric and 0.98 for the oligomer hosts. Interestingly, the strongest reversal of fluorescence properties for the two enantiomers with the dimeric host was observed at a concentration of 5 $\times$ 10^{-5} mol dm^{-3}, in which the $[\phi/\phi_0]_L/[\phi/\phi_0]_D$ value was measured at 0.86. However, the fluorescence response of the oligomeric host appears relatively constant under the different concentrations of phenylalanine methyl ester. At a concentration of 5 $\times$ 10^{-5} mol dm^{-3}, the $[\phi/\phi_0]_L/[\phi/\phi_0]_D$ value of the oligomeric host was measured at 0.96. As the structure of the hosts has been characterized as having a helical concave structure,[12] we suspect that the chiral amines would clathrate into the chiral host through a π–π interaction between the naphthyl moiety of the host and the phenyl group of the aromatic amine and hydrogen bond. The enantio discrimination could stem from the chiral naphthyl moiety and the main chain chirality of the oligomers. The multiple interacting points and chiral units of the hosts may play different roles during chiral discrimination, which could explain the aberrant response of fluorescence on the concentration of the chiral guest. In conclusion, we have developed two fluorescence sensors for the chiral recognition of chiral amines. The recognition was confirmed by ^{1}H NMR measurement. The fluorescence response of the chiral sensor was found to be markedly influenced by the concentration of chiral amines. Currently, we are developing more selective systems to discrimination among chiral amines on the basis of the present investigation.

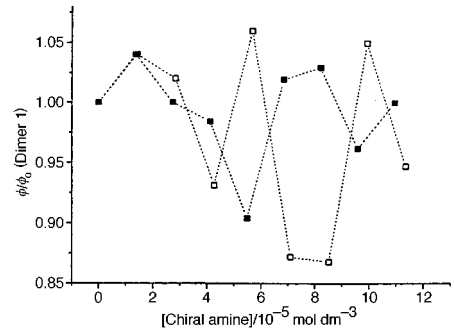


Fig. 3 ϕ/ϕ_0 ratio of fluorescent quantum yield of D- and L-phenylalanine methyl ester with dimer **1** as the host: (□) D-phenylalanine methyl ester and (■) I-α-phenylalanine methyl ester

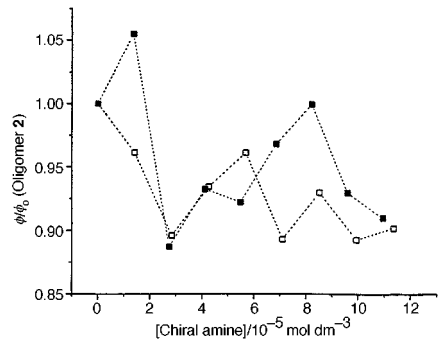


Fig. 4 ϕ/ϕ_0 ratio of fluorescent quantum yield of D- and L-phenylalanine methyl ester with oligomer **1** as the host: (□) D-phenylalanine methyl ester and (■) L-phenylalanine methyl ester

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Notes and References

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1 For recent treatises on molecular recognition, see *Inclusion Phenomena and Molecular Recognition*, ed. J. L. Atwood, Plenum, New York, 1990; *Molecular Recognition Mechanisms*, ed. M. Delaage, VCH, New York, 1991; *Molecular Structure and Life: Molecular Recognition of Nucleic Acids*, ed. Y. Kyogoku and Y. Nishimura, Japan Scientific Society Press, Tokyo, 1992; *Principles of Molecular Recognition*, ed. A. D. Buckingham, A. C. Legon and S. M. Roberts, Blackie Academic and Professional, London 1993; S. M. Roberts, *Molecular Recognition: Chemical and Biochemical Problems II*, CRC Press, Boca Raton, 1992; J. M. Lehn, *Supramolecular Chemistry*, VCH, Weinheim, 1995.

2 For recent treatises, see *Supramolecular Chemistry I—Directed Synthesis and Molecular Recognition, Topics in Current Chemistry*, ed. W. Weber, vol. 165, Springer-Verlag, Berlin, 1993; R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, Wiley, New York 1994; J. Seyden-Penne, *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*, Wiley, New York, 1995; G. Procter, *Asymmetric Synthesis*, Oxford University Press, Oxford, 1996; *Catalytic Asymmetric Synthesis*, ed. I. Ojima, VCH, New York, 1993.

3 For an excellent up-to-date review, see X. X. Zhang, J. S. Bradshaw and R. M. Izatt, *Chem. Rev*., 1997, **97**, 3313.

4 For a recent treatise, see *The Design of Drugs to Macromolecular Targets*, ed. C. R. Beddell, Wiley, Chichester, 1992.

5 For recent monograph, see *Chromatographic Separations Based on Molecular Recognition*, ed. K. Jinno, VCH, Weinheim, 1996.

6 For examples, see M. A. Mortellaro and D. G. Nocera, *J. Am. Chem. Soc.*, 1996, **118**, 7414.

7 For a recent monograph, see M. C. Trans, *Biosensors (Sensor Physics and Technology)*, Chapman & Hall, London, 1993; B. R. Eggins, *Biosensors: An Introduction*, Wiley, Chichester, 1996; D. Buerk, *Biosensors: Theory and Applications*, Technomic, Lancaster, 1993.

8 For representitative examples, see T. W. Bell, Z. Hou, Y. Luo, M. G. B. Drew, E. Chapoteau, B. P. Czech and A. Kumar, *Science*, 1995, **269**, 671; Q. Zhou and T. M. Swager, *J. Am. Chem. Soc.*, 1995, **117**, 7017 and refs. cited therein; R. Dagani, *C & EN*, 1995, July 17, 63; For a recent monograph, see *Fluorescent Chemosensors for Ion and Molecular Recognition*, ed. A. W. Czarnik, *ACS Symp. Ser.* 538, American Chemical Society, Washington, DC, 1993.

9 T. D. James, K. R. A. S. Sandanayake and S. Shinkai, *Nature*, 1995, **374**, 345.

10 C. T. Chen, H. Wagner and W. C. Still, *Science*, 1998, **279**, 851.

11 Previously, Irie and co-workers observed a significant difference in the fluorescence quenching rate duing the study of the interaction between simple binaphthyl and chiral amines, see M. Irie, T. Yorozu and K. Hayashi, *J. Am. Chem. Soc.*, 1978, **100**, 2236; T. Yorozu, K. Hayashi and M. J. Irie, *J. Am. Chem. Soc.*, 1981, **103**, 5480.

12 C. J. Li, D. Wang and W. T. Slaven IV, *Tetrahedron Lett.*, 1996, **37**, 4459; C. J. Li, W. T. Slaven IV, V. T. John and S. Banerjee, *Chem. Commun.* 1997, 1569; D. Wang, T. J. Liu, C. J. Li and W. T. Slaven IV, *Polym. Bull.*, 1997, **39**, 265; T. J. Liu, D. Wang, F. L. Bai, C. J. Li and W. T. Slaven IV, *Chin. J. Polym. Sci.*, 1998, **18**, 234.

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