Thiourea-based molecular clips for fluorescent discrimination of isomeric dicarboxylates†

Zhi-hua Lin, Li-xia Xie, Yong-gang Zhao, Chun-ying Duan* and Jing-ping Qu*

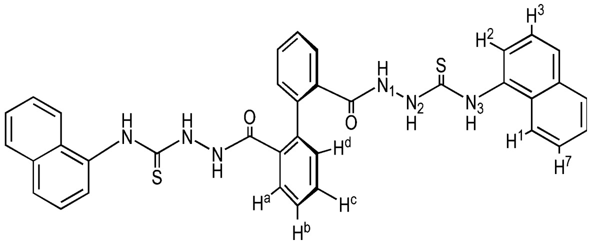
Received 14th June 2007, Accepted 18th September 2007
First published as an Advance Article on the web 1st October 2007
DOI: 10.1039/b708983j

A new clip-like receptor, which comprises two thiourea-based binding groups and two naphthalene units, has been designed and synthesized as a fluorescent chemosensor for distinguishing *o*-phthalate from two other isomers of dicarboxylates. Upon the addition of these three ions, the emission intensity at 420 nm (excitation at 340 nm) decreases drastically through PET. When excited at 380 nm, a new emission band at 460 nm appears and develops gradually upon the addition of the *o*-phthalate ion and the fluorescent intensity increases markedly over time, but the presence of *m*-phthalate or *p*-phthalate do not cause this kind of change. It suggests a guest-induced "off–on" conformational switching signaling transduction. The presence of the *o*-phthalate anion induces a special conformation with two naphthalene units positioned close enough to exhibit a new emission.

Introduction

The development of synthetic receptors able to bind polyanions selectively in a detectable fashion to an observer *via* changes in electrochemical response or in fluorescence intensity constitutes an important yet difficult task facing supramolecular chemists,[1,2] since these species are not only strongly solvated in protic media but also characterized by multiple charges and complex shapes. While several elegant receptor systems for the selective bindng of dicarboxylate anions based on the use of two guanidium-like units,[3] bis-urea and bisthiourea units,[4,5] as well as the clever use of amidopyridine[6] hydrogen bonding subunits within well-defined structural arrays have been reported,[7–9] differentiation of geometric isomers (such as *ortho*/*meta*/*para* dicarboxylates) is, in general, a difficult task, because of their rather similar chemical and physical properties *e.g.* charge density and structural complexity.[9,10]

In this paper, we address the problem of discriminating *o*-phthalate from *m*-phthalate and *p*-phthalate isomers by using a conformational switching fluorescent chemosensor (**SN**). The clip-like receptor contains two thiourea-based binding groups and two naphthalene units serving as the fluorescent read-out (Scheme 1). It is well known that urea and thiourea derivatives are attractive in the construction of neutral hydrogen bonding receptors.[11] The relative acidic thiourea NH protons with a strong hydrogen-bond donor capability, can establish multipoint, often cooperative, hydrogen bonds with complementary acceptor groups in a specific and predictable manner.[12] In the presence of a specific anion as the conformational template, the hydrogen bonds between the thiourea groups and the anion induce the clip-like receptor to display a *cis*-conformation with two naphthalene lumophores close enough, from which an excimer fluorescence is formed.[13,14]



Scheme 1 Chemical structure of **SN**.

It is clear that the three isomers of dicarboxylates might induce the molecular clips into different conformations, and different fluorescence is expected.

Results and discussion

Compound **SN** was obtained by the reaction of isothiocyanatomethyl naphthylene with a biphenyl derivative in good yield. The fluorescence spectrum of **SN** in a CH_3CN solution (Fig. 1) shows a strong emission band at 420 nm attributing to the naphthyl-thiourea group (excitation at 340 nm).[10,15] Upon addition

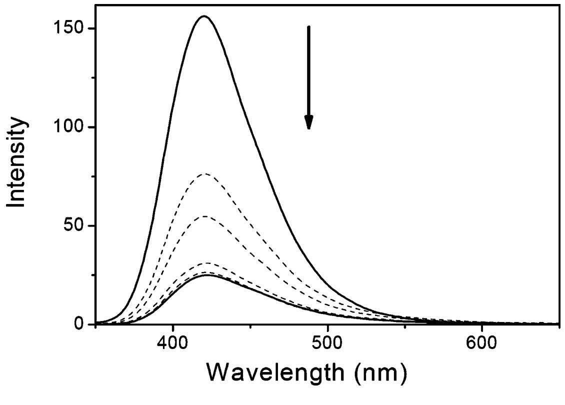


Fig. 1 Emission spectra of **SN** (1×10^{-4}M) upon addition of *o*-phthalate as its TBA salt in CH_3CN. Excitation wavelength is 340 nm.

State Key Laboratory of Fine Chemicals, Dalian University of Technology, Dalian, 116012, China. E-mail: cyduan@dlut.edu.cn

† Electronic supplementary information (ESI) available: Experimental procedures and characterization data, fluorescence and absorption spectra of **SN**. See DOI: 10.1039/b708983j

of a *o*-phthalate ion in the form of tetrabutylammonium (TBA) salt, the emission intensity decreases drastically, and no significant shift of the wavelength is found when excited at 340 nm. The observed fluorescent quenching could be attributed to the typical guest-induced PET process.[16] Upon coordination of the anion with the sensor, the hydrogen bonds between the anion and thiourea (TU) cause a decrease in the oxidation potential of the thiourea receptor, which triggers the PET from thiourea to coordinate to the relatively electron deficient naphthalene fluorophore, leading to the enhancement of a PET effect, thus causing the fluorescence to be "switched-off".

Upon the addition of *m*- or *p*-phthalate ions, the intensity of the emission band at 420 nm decreases similarly. The luminescent titrations with the three isomeric phthalates suggest the formation of 1 : 1 stoichiometry host–guest interacted species with the association constants calculated as $\log K = 5.14 \pm 0.02$, 5.65 ± 0.02 and 5.67 ± 0.03, for the *o*-, *p*-, and *m*-phthalate anions, respectively (Fig. S1†). When excited at 380 nm, a new emission band at 460 nm appears and develops gradually upon the addition of a *o*-phthalate ion, whereas, no obvious emission is found with the free **SN** receptor being excited at the same wavelength (Fig. 2). And upon the addition of *m*-phthalate or *p*-phthalate to the CH_3CN solution of **SN**, no new emission band appears (Fig. 3); even the excitation wavelength varies from 340 to 500 nm, indicating that no new luminescence species are obtained. Such a selectivity suggests that the observed process is an anion-binding rather than a deprotonation process, since the three isomers have similar abilities of deprotonation.

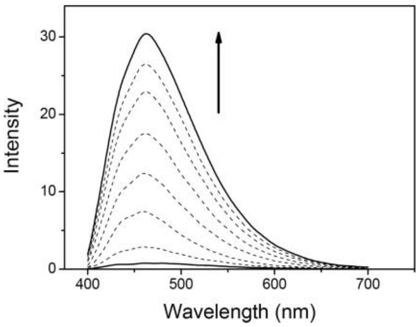


Fig. 2 Emission spectra of **SN** (1×10^{-4} M) upon addition of *o*-phthalate as its TBA salt in CH_3CN. Excitation wavelength is 380 nm.

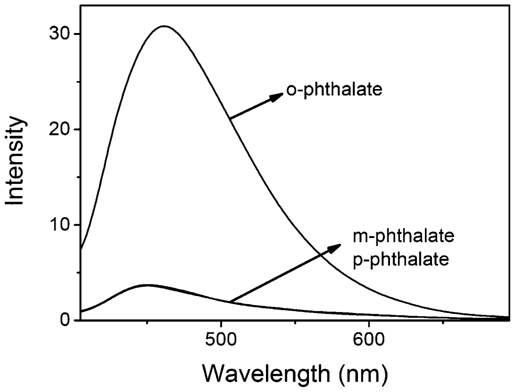


Fig. 3 Fluorescence spectra of **SN** (1×10^{-4} M) in the presence of 60 equiv. mole ratio of phthalate ions as TBA salts in MeCN. Excitation wavelength is 380 nm.

Generally, such a new emission band could be assigned either to the emission of an excited naphthyl dimer, or to a dimer of an excited naphthyl with a second naphthyl in its ground state that are attributed to the anion-induced mutual interactions between naphthalene moieties,[13,17] or to the emission of the biphenyl moiety in the anion-induced restricted conformation.[18] The excitation spectrum of the emission recorded at 460 nm is quite different from that recorded at 420 nm (Fig. 4), and the excitation at 340 nm does not induce any obvious emission at 460 nm, suggesting that the new broad excitation band at 380 nm is the origin of the emission band at 460 nm.[19] Such a result demonstrates that the new emission band at 460 nm should not be assigned to the dimer of an excited naphthyl with a second naphthyl in its ground state. Further investigation exhibits that the fluorescent intensity at 460 nm is observed to increase markedly over time (Fig. 5). Such a time-dependent behavior demonstrates that the new emission should not be originated from the emission of the biphenyl moiety in the anion-induced restricted conformation.[20,21] Thus, the new emission can be assigned to the emission of an excited naphthyl dimer, in which the UV–vis irradiation may favor the stableness of the excited naphthyl dimer. It also seems that a photoreaction is taking place, and that the new band is due to some photoproduct. Since the *o*-dicarboxylate anion itself exhibits significant absorption, UV–vis titration (Fig. S2†) could not give enough useful information.

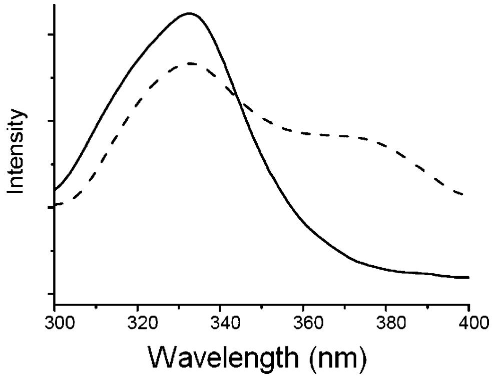


Fig. 4 Excitation spectra with the emission recorded at 420 nm (solid) and 460 nm (dash), respectively.

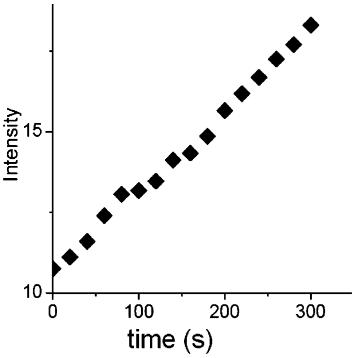


Fig. 5 The plot of emission intensity against time in the presence of a 5 molar ratio of *o*-phthalate, irradiated at 380 nm at 20 seconds intervals.

Although no appropriate explanation would account satisfactorily for such fluorescent responding behavior, which has never been observed before, the receptor **SN** has high selectivity to the *o*-phthalate ion over the other two isomers of dicarboxylates. It is suggested that when receptor **SN** binds with *m*-phthalate or *p*-phthalate, the two branches cannot compact together and the two naphthalene units cannot overlap efficiently, and, as a consequence, no excimer fluorescence is observed ("off" state), despite that the twist conformation of the phenyl rings makes the geometrical conformation of **SN** suitable for binding to different phthalates. The tweezer-like *o*-phthalate anion induces the two branches of **SN** to point in the same direction by H-bonding, with the two naphthalene units being close enough to exhibit a new emission. Compared with similar receptors that have been reported,[5] the presence of torsional groups rather than foldaway ones make the receptor **SN** only fit one isomer and high selectivity is achieved (Fig. 6).

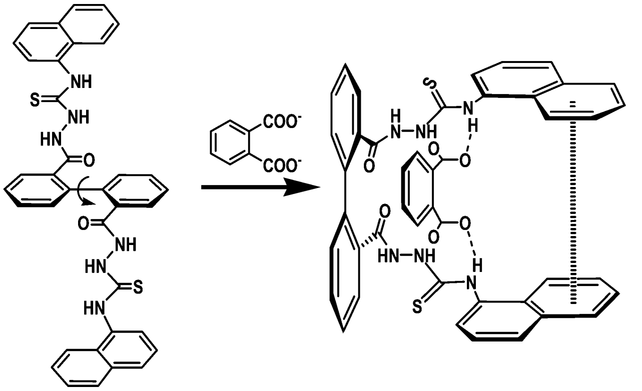


Fig. 6 Structure proposal of the complex formed between **SN** and the *o*-phthalate anion with the twist conformation induced by the anion.

To further investigate the anion binding properties of the receptor **SN**, ^{1}H NMR spectra changes by the addition of the *o*-phthalate as a TBA salt to acetonitrile-d_3 solution were measured. As shown in Fig. 7, in the presence of *o*-phthalate, the signals of the H_{N2} and H_{N3} protons are broad and downfield from 8.02 to 8.76 ppm, which may be attributed to the net deshielding that is induced by hydrogen-bonding between the thiourea subunit and the anion.[22] The signals of H_1 and H_2 shift downfield from 7.66 to 7.72 ppm, and from 7.26 to 7.35 ppm, respectively. These deshielding effects may be created from the partial positive charge of these protons that come from the nearness of the carboxyl group of the guest and the protons, and the probable participation of these protons in the formation of additional hydrogen bonds. The presence of the *o*-phthalate anion also makes the signal of H_d shift upfield from 7.90 to 7.85 ppm and all other protons in the naphthalene rings exhibit small but significant upfield shift, due to the presence of anions enhancing the electron density on these naphthalene rings.[23] From a mechanistic point of view, in the free outspread conformation of **SN**, H_d has the potential to form intramolecular H-bonds with the C=O group of the other arm, whereas the presence of *o*-phthalate could induce the two branches to form a *cis* conformation, and the H-bonding is destroyed with the signal of H_d exhibiting upfield shift. At the same time, the formation of hydrogen bonds between the anions and the thiourea groups causes significant downfield shifts of these imine protons as well as the protons of the naphthalene rings that are close to the thiourea group, with the two naphthalene lumophores close enough to exhibit naphthyl dimer fluorescence.

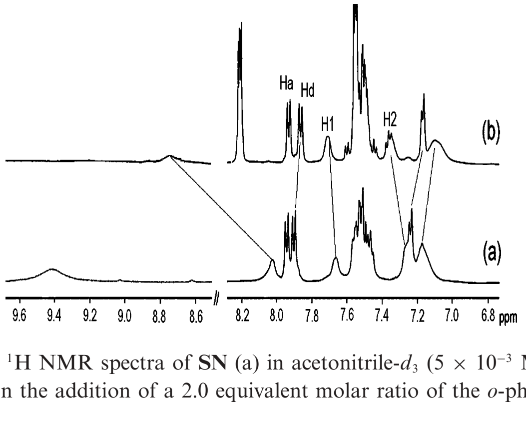


Fig. 7 ^{1}H NMR spectra of **SN** (a) in acetonitrile-d_3 (5×10^{-3} M) and (b) upon the addition of a 2.0 equivalent molar ratio of the *o*-phthalate anion.

Two dimensional NMR studies have been also carried out to give more information about the anion binding properties of the receptor **SN**. As shown in Fig. 8, in the presence of the *o*-phthalate anion, NOESY experiments show that the H_a and H_d of **SN** correlate with the protons of the anion, indicating the formation of a complex between **SN** and the *o*-phthalate anion. In addition, no obvious signal shows the nearness between the protons of the naphthalene rings and the anion. With all this information, a structure proposal as shown in Fig. 6 can be acceptable.

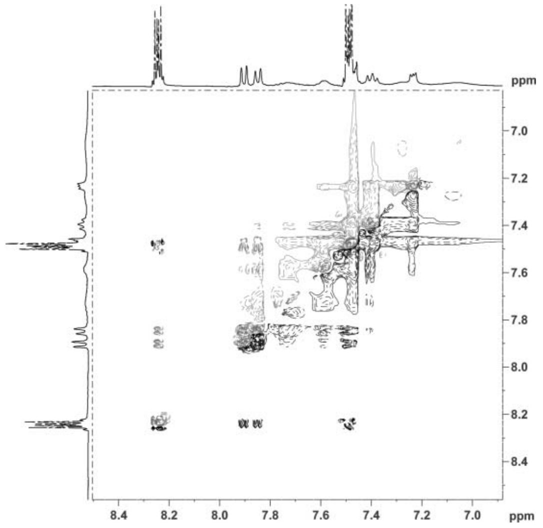


Fig. 8 ^{1}H NOESY NMR spectra of **SN** in acetonitrile-d_3 (5×10^{-3} M) upon the addition of a 2.0 equivalent molar ratio of the *o*-phthalate anion.

Conclusions

In summary, a new clip-like receptor, which comprises two thiourea-based binding groups and two naphthalene units, has been described as a fluorescent chemosensor to distinguish *o*-phthalate from two other isomers of dicarboxylates through fluorescent response in an "off–on" manner. The presence of torsional groups rather than foldaway ones makes the receptor **SN** exhibit high selectivity by fitting the conformation of one isomer well. Such fluorescent responding behavior has never been observed before, and no appropriate explanation would account satisfactorily for it. We are now going on with our investigation of the system and expect that more results will be obtained in the future.

Experimental section

Materials and measurements

Biphenyl-2,2′-dicarbohydrazide was prepared according to a procedure reported in the literature.[24] Elemental analyses (C, H, and N) were carried out on a Perkin-Elmer 240 analyzer. UV–vis spectra were obtained on a Shimadzu 3100 spectrophotometer in CH_3CN at room temperature. Fluorescence spectra were recorded on an AMINCO Bowman Series 2 Luminescence spectrometer. Both excitation and emission slit widths were 3 nm. Stock solutions (0.10 M) of the tetrabutylammonium salts were prepared in MeCN. Fluorescence titration experiments were performed with 0.10 mM solution of **SN** in MeCN and varying concentrations of the tetrabutylammonium salts in MeCN. ^1H NMR spectra were measured on a Bruker DRX-500 NMR spectrometer. ^1H COSY NMR spectra and ^{13}C NMR spectra were measured on a Varian INOVA spectrometer. Mass spectra were recorded on a HP1100LC/MSD spectrometer. IR spectra were recorded in KBr or neat on a Nicolet-20DXB spectrophotometer.

Preparation of SN

A solution of biphenyl-2,2′-dicarbohydrazide (0.270 g, 1 mmol) and 1-naphthylisocyanate (0.407 g, 2.2 mmol) in 25 mL EtOH was refluxed with stirring for 1 hour and then evaporated to 5 mL. After cooling to room temperature, an ivory-white precipitate formed (0.46 g, 72%), which was collected by filtration, and washed with EtOH and ether. ^1H NMR (500 MHz, CD_3CN), δ(ppm): 9.41 (br, $2H_{N1}$), 8.02 (br, 4H, $2H_{N2}$, $2H_{N3}$), 7.94 (d, $2H_a$, $J = 8.1$), 7.89 (d, $2H_d$, $J = 8.3$), 7.66 (br, $2H_1$), 7.53 (m, 8H, $2H_b$, $2H_c$, $2H_5$, $2H_6$), 7.26 (br, $2H_2$), 7.24 (m, 2H, $2H_7$), 7.17 (br, 4H, $2H_3$, $2H_4$). ^{13}C NMR (100 MHz, CD_3CN), δ(ppm): 184.31, 169.85, 139.32, 134.40, 133.24, 130.90, 130.80, 130.18, 128.39, 128.34, 128.26, 128.15, 126.90, 126.75, 126.58, 123.36. Anal. calcd for $C_{36}H_{28}N_6S_2O_2$: C, 67.5; H, 4.4; N, 13.1%. Found: C, 67.4; H, 4.5; N, 13.2%. IR (KBr):, 3222 ($\nu_{N–H}$), 1671 ($\nu_{C=O}$), 1596, 1508, 1397 ($\nu_{C–N}$), 1340, 1229 ($\nu_{N–N}$), 1091 ($\nu_{C=S}$), 774 ($\nu_{C–H}$) cm^{-1}. MS m/z: 641.1 ($[M - H^+]$), 663.2 ($[M - Na^+]$).

Acknowledgements

This work was supported by the National Natural Science Foundation of China and the Education Ministry of China. The authors thank the referees for their helpful suggestions.

Notes and references

1 A. Bianchi, K. Bowman-James and E. García-España, ed. *Supramolecular Chemistry of Anions*, Wiley-VCH, New York, 1997.

2 F. P. Schmidtchen and M. Berger, *Chem. Rev.*, 1997, **97**, 1609; P. D. Beer and P. A. Gale, *Angew. Chem., Int. Ed.*, 2001, **40**, 486; R. Martínez-Máñez and F. Sancenón, *Chem. Rev.*, 2003, **103**, 4419.

3 J. Raker and T. E. Glass, *J. Org. Chem.*, 2002, **67**, 6113.

4 E. Fan, S. A. Van Arman, S. Kincaid and A. D. Hamilton, *J. Am. Chem. Soc.*, 1993, **115**, 369; T. R. Kelly and M. H. Kim, *J. Am. Chem. Soc.*, 1994, **116**, 7072; J. M. Benito, M. Gómez-García, J. L. J. Blanco, C. O. Mellet and J. M. G. Fernández, *J. Org. Chem.*, 2001, **66**, 1366; S.-Y. Liu, L. Fang, Y.-B. He, W.-H. Chan, K.-T. Yeung, Y.-K. Cheng and R.-H. Yang, *Org. Lett.*, 2005, **7**, 5825; T. Gunnlaugsson, P. A. Davis, E. J. O'Brient and M. Glynn, *Org. Lett.*, 2002, **4**, 2449.

5 M. H. Mei and S. K. Wu, *New J. Chem.*, 2001, **25**, 471; Y.-P. Yen and K.-W. Ho, *Tetrahedron Lett.*, 2006, **47**, 1193.

6 F. Garcia-Tellado, S. Goswami, S. K. Chang, S. J. Geib and A. D. Hamilton, *J. Am. Chem. Soc.*, 1990, **112**, 7393; M. S. Goodman, A. D. Hamilton and J. Weiss, *J. Am. Chem. Soc.*, 1995, **117**, 8447; T. Moriuchi, K. Yoshida and T. Hirao, *Org. Lett.*, 2003, **5**, 4285.

7 J. L. Sessler, A. Andrievsky and L. Vincent, *J. Am. Chem. Soc.*, 1997, **119**, 9385; M. Boiocchi, M. Bonizzoni, L. Fabbrizzi, G. Piovani and A. Taglietti, *Angew. Chem., Int. Ed.*, 2004, **43**, 3847; K. Kacprzak and J. Gawronski, *Chem. Commun.*, 2003, 1532; B. R. Linton, M. S. Goodman, E. Fan, S. A. van Arman and A. D. Hamilton, *J. Org. Chem.*, 2001, **66**, 7313; M. H. Filby, T. D. Humphries, D. R. Turner, R. Kataky, J. Kruusma and J. W. Steed, *Chem. Commun.*, 2006, 156.

8 J. V. Hernández, A. I. Oliva, L. Simón, F. M. Muñiz, A. A. Mateos and J. R. Morán, *J. Org. Chem.*, 2003, **68**, 7513; S. K. Kim, B.-G. Kang, H. S. Koh, Y. J. Yoon, S. J. Jung, B. Jeong, K.-D. Lee and J. Yoon, *Org. Lett.*, 2004, **6**, 4655.

9 F. Sancenón, R. Martínez-Máñez, M. A. Miranda, M.-J. Seguí and J. Soto, *Angew. Chem., Int. Ed.*, 2003, **42**, 647; Y.-P. Yen and K.-W. Ho, *Tetrahedron Lett.*, 2006, **47**, 7357.

10 A. M. Costero, M. Colera, P. Gaviña and S. Gil, *Chem. Commun.*, 2006, 761.

11 B. P. Hay, T. K. Firman and B. A. Moyer, *J. Am. Chem. Soc.*, 2005, **127**, 1810; D. H. Lee, H. Y. Lee, K. H. Lee and J.-I. Hong, *Chem. Commun.*, 2001, 1188.

12 F.-Y. Wu, Z. Li, Z.-C. Wen, N. Zhou, Y.-F. Zhao and Y.-B. Jiang, *Org. Lett.*, 2002, **4**, 3203.

13 F. M. Winnik, *Chem. Rev.*, 1993, **93**, 587.

14 A. M. Costero, J. Sanchis, S. Gil, V. Sanz and J. A. G. Williams, *J. Mater. Chem.*, 2005, **15**, 2848; A. C. Benniston, A. Harriman and P. V. Patel, *Eur. J. Org. Chem.*, 2005, 4680.

15 K. Suzuki, H. Tanabe, S. Tobita and H. Shizuka, *J. Phys. Chem. A*, 1997, **101**, 4496.

16 T. Gunnlaugsson, A. P. Davis and M. Glynn, *Chem. Commun.*, 2001, 2556.

17 S. K. Kim, J. H. Bok, R. A. Bartsch, J. Y. Lee and J. S. Kim, *Org. Lett.*, 2005, **7**, 4839; J.-S. Wu, J.-H. Zhou, P.-F. Wang, X.-H. Zhang and S.-K. Wu, *Org. Lett.*, 2005, **7**, 2133; M. T. Albelda, E. Garcia-Espana, L. Gil, J. C. Lima, C. Lodeiro, J. Seixas de Melo, M. J. Melo, A. J. Parola, F. Pina and C. Soriano, *J. Phys. Chem. B*, 2003, **107**, 6573; S. Nishizawa, Y. Kato and N. Teramae, *J. Am. Chem. Soc.*, 1999, **121**, 9463; H. K. Cho, D. H. Lee and J.-I. Hong, *Chem. Commun.*, 2005, 1690; J.-S. Yang, C.-S. Lin and C.-Y. Hwang, *Org. Lett.*, 2001, **3**, 889.

18 D. H. Lee, J. H. Im, J.-H. Lee and J.-I. Hong, *Tetrahedron Lett.*, 2002, **43**, 9637.

19 The excitation band at 340 nm is just attributed to the emission band centered at 420 nm. Since the separation of 40 nm between the two emission bands is too small, the tail of the emission band centered at 420 nm has a significant contribution to that at 460 nm.

20 H. Bouas-Laurent, A. Casellan, J.-P. Desvergne and R. Lapouyade, *Chem. Soc. Rev.*, 2000, **29**, 43; H. Bouas-Laurent, A. Castellan, J.-P. Desvergne and R. Lapouyade, *Chem. Soc. Rev.*, 2001, **30**, 248.

21 K. J. Wallace, W. J. Belcher, D. R. Turner, K. F. Syed and J. W. Steed, *J. Am. Chem. Soc.*, 2003, **125**, 9699; Y. Bai, B.-G. Zhang, J. Xu, C.-Y. Duan, D.-B. Dang, D.-J. Liu and Q.-J. Meng, *New J. Chem.*, 2005, **29**, 777.

22 A. B. Descalzo, K. Rurack, H. Weisshoff, R. Martínez-Máñez, M. D. Marcos, P. Amorós, K. Hoffmann and J. Soto, *J. Am. Chem. Soc.*, 2005, **127**, 184; F. Hibbert and J. Emsley, *Adv. Phys. Org. Chem.*, 1990, **26**, 255 and references therein.

23 M. Boiocchi, L. Del Boca, D. E. Gomez, L. Fabbrizzi, M. Licchelli and E. Monzani, *J. Am. Chem. Soc.*, 2004, **126**, 16507.

24 L. Kalb and O. Grob, *Ber*, 1926, **69**, 736; R. Labriola, *J. Org. Chem.*, 1940, **5**, 329.