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Tuning the photoinduced electron transfer in near-infrared heptamethine cyanine dyes

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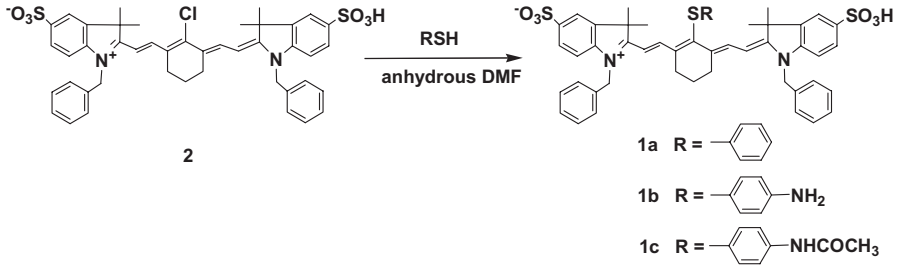
Abstract—An efficient photoinduced electron transfer (PET) system in near-infrared region was described. The PET in heptamethine cyanine dyes was tuned by changing the electron-donating ability of the substituent at the central position of the polymehine chain. 4-Aminophenylthio-substitution led to an efficient PET and the lowest fluorescence quantum yield. The acetylation, protonation or transition metal cation coordination of the amino group could recover fluorescence greatly via suppressing the PET.

Fluorescent sensors via the photoinduced electron transfer (PET) strategy have been of great interest due to their various prospective applications.[1] However, most of these PET systems work effectively in UV–visible region, few of them in near-infrared (NIR) region. An inspection of the Weller equation[2] regarding intramolecular PET processes clearly shows that it is difficult to find a PET system when the HOMO–LUMO energy gap is very small as the case of NIR fluorescent dyes.[3] An additional problem for NIR sensing schemes is that the ultrafast radiationless deactivation of the excited state is very efficient in these dyes, which can be an obstacle to use them as sensors.[4]

Recently heptamethine cyanine dyes employed as fluorescence labels and sensors in vivo[5] have attracted immense interest because their spectra reach the NIR region where biological matrix exhibits the least absorption and auto-fluorescence background.[6] Patonay and co-workers have developed heptamethine cyanine dyes with a rigid chloro cyclohexenyl ring in the methine chain (like dye **2** in Scheme 1), which can increase the photostability and fluorescence quantum yield.[7,8] This structure also provides the dye with a reactive chloro-group for chemical substitution at the central position.[9] By this substitution many heptamethine cyanine dyes as biosensors and fluorescent probes were obtained.[6,7,10,11] But few of them were employed as PET sensors for the above mentioned reasons.

Here we report three heptamethine cyanine dyes with thio-substituents in the central position in which PET can be tuned by changing the electron-donating ability of the substituent. The thioether bond was used as the



Scheme 1. Synthesis of the heptamethine cyanine dyes.

Keywords: Heptamethine cyanine dyes; Fluorescence sensors; Near-infrared; Photoinduced electron transfer.
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spacer, which was seldom found. The PET in dye **1b** could be inhibited when proton, zinc or iron ion was added to the system and the fluorescence was observed to recover.

The synthesis of dyes **1a–c** was outlined in Scheme 1 according to a similar method.[12,13] Dye **2** was stirred with thiophenols in anhydrous DMF under argon at room temperature in the dark for 1 h. The green products **1a–c** were purified on C18-RP column using methanol–water mixture as the eluent and characterized by spectroscopic data.[14]

The maximum absorption and emission wavelengths (λ_{max}) of **1a–c** had a small red shift compared with their parent dye **2** (Table 1). Dye **1b** was found to have a lower fluorescence quantum yield ($\Phi_f = 0.0065$) than the others. But, after acetylation of the amino group the quenched fluorescence recovers completely (**1c**, $\Phi_f = 0.036$, close to **1a**, $\Phi_f = 0.038$).

When a high-energy amino group was introduced into the *para* position of the thiophenyl, the substituent moiety in **1b** had a sufficiently high HOMO energy level to transfer an electron to the HOMO of the excited fluorophore. The ΔG_{PET} value of **1b** calculated from its potentials according to Weller equation[2,3] was found to be the smallest among all dyes. It means that **1b** has the strongest thermodynamic force to perform an efficient PET process. But after acetylation of the amino group, the HOMO energy level of the moiety in **1c** decreased and was close to that in **1a**, so that PET process was inhibited and the fluorescence recovered. The weaker fluorescence of dye **1a** and **1c** than their parent dye **2** might also be attributed to the weak electron-donating capability of thiophenol group, which led to a weak PET process. In our previous work, the attachment of a carboxymethyl mercapto group, a electron-withdrawing group, in the position caused a stronger fluorescence ($\Phi_f = 0.096$).[12] The relationship between molecule structure and orbital energy level was concluded in Figure 1.

Table 1. Photophysical characteristics of dyes in water at 1×10^{-6} M

Dye	λ_{ab} (nm)	λ_{em} (nm)	ε ($\times10^5$)[a]	Φ_f[b]	$E_{ox}-E_{re}$ (eV)[c]	ΔG_{PET} (eV)
1a	794	817	2.3	0.038	1.242	−0.380
1b	795	820	0.9	0.0065	1.212	−0.408
1c	798	823	1.6	0.036	1.225	−0.389
2	783	803	2.0	0.065	1.260	−0.384

[a] Molar extinction coefficients are in cm^{-1} M and in the maximum of the highest peak.
[b] The fluorescence quantum yields were determined in reference to IR-125 in DMSO ($\Phi_f = 0.13$).[15]
[c] E_{ox} and E_{re}, the oxidative and reductive, respectively, were detected by cyclic voltammetry.

According to the mechanism of PET, the HOMO energy level of the amine will decrease after the amine being protonated or bound by cation.[16] However, PET process can generally occur when the HOMO–LUMO gap of the fluorophore is relatively large like fluorescence sensors in UV–visible region. It is difficult to achieve effective PET as the HOMO–LUMO gap is small according to the Weller equation regarding PET processes, for the energy introduced into the NIR system by excitation is too small to reduce the fluorophore and oxidize the donor via intramolecular electron transfer. So, it seems efficient PET is less likely for NIR dyes.[3]

Fortunately, the fluorescence off-on switching based on PET mechanism had been observed in the new dyes. The fluorescence of dye **1b** in aqueous solution became stronger with the increase of HCl concentration (Fig. 2). The inverse trend was observed in the cases of dye **1a**, **1c** and **2**, for cyanine dyes can generally be decolourized by light and acid.[17] These results indicated that the PET was inhibited after the protonation of the amine.

It is well known that heavy and transition metal cations possess intrinsic properties that they can usually quench the emission of organic lumophores.[18] And cyanine dyes have been used as sensors for transition metal ions such as Fe(III), Co(II) and Cu(III) based on Förster type quenching.[19,20] This kind of fluorescence quenching was also observed in the cases of dye **1a** and dye **1c** when zinc (II) was added. However, dye **1b** (Fig. 3) exhibited a fluorescence enhancement effect with the increase of concentration of $ZnSO_4$. Similar results were obtained when $ZnSO_4$ was displaced by $FeCl_3$, $Al_2(SO_4)_3$, $Ce(NO_3)_3$.

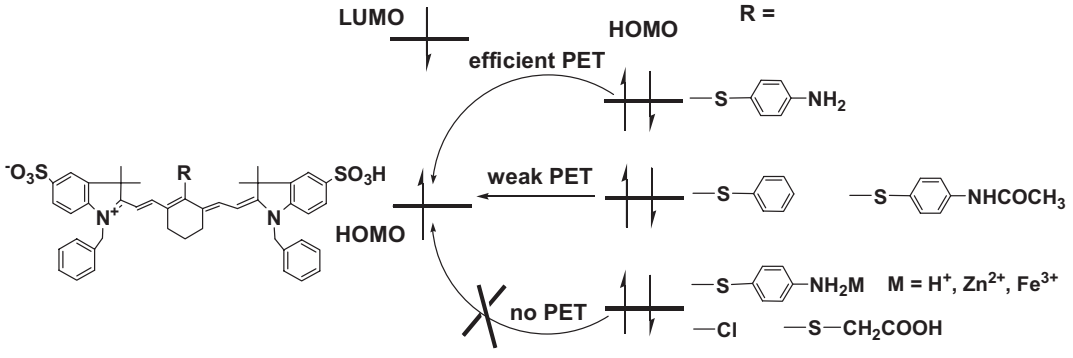

Figure 1. Structure and molecule orbital diagrams of the heptamethine cyanine dyes.

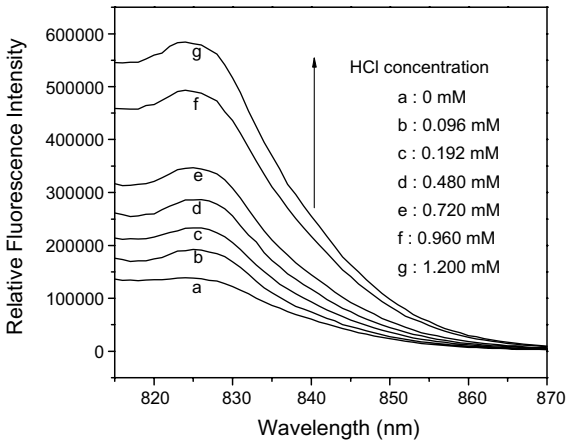

Figure 2. Emission spectra of dye **1b** at 1×10^{-6} M in water with different concentrations of HCl. (λ_{ex} = 795 nm).

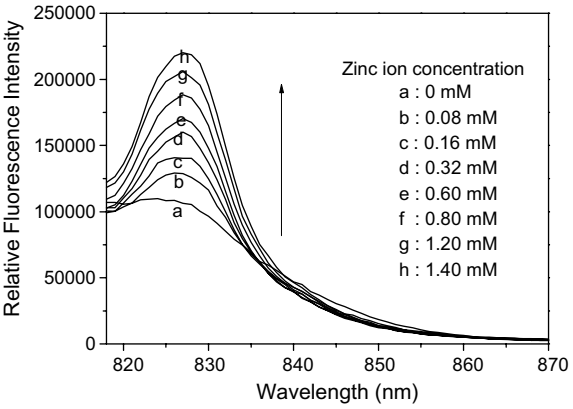

Figure 3. Emission spectra of dye **1b** at 1×10^{-6} M in aqueous buffer (hexamethylene amine-HCl, pH = 7.04) with different concentrations $ZnSO_4$. (λ_{ex} = 795 nm).

So it can be concluded that both the protonation and transition metal cation coordination of the amino group in **1b** can also lead to the decrease of the HOMO energy level of the substituent (Fig. 1) and recover fluorescence.[21,22] This result suggests that it is feasible to design NIR fluorescence cation probe based on this kind of heptamethine cyanine dyes.

In conclusion, PET in long wavelength region occurs when 4-amino-phenyl-thio group is introduced at the central position of heptamethine cyanine dyes. The PET can be suppressed by the acetylation of the amino, and the fluorescence recovers. The protonation and metal cation coordination of the amino-group can also modulate the PET to low efficiency and enhance fluorescent greatly. This can be useful for the designing of new NIR fluorescent sensors for proton or metal ions.

Acknowledgements

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Supplementary data

Synthetic details and other spectroscopy data can be available in the online version. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tetlet.2005.04.089.

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