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ORIGINAL ARTICLE

Cis/*trans* Fluorescent Recognition by Naphthalimide Dyes ⊂ CB [7] Assembly

Junyong Li[1] · Xiaomin Gu[1] · Xiaosheng Yuan[1] · Qiqi Qiu[1] · Jie Sun[1] · Haibo Wang[2]

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Abstract A novel method to recognize *cis*/*trans* isomers was studied here. The naphthalimide dye as guest could bind with host cucurbit [7]uril (CB [7]) and 1:1 naphthalimide dye ⊂ CB [7] assembly was formed. Moreover, this assembly was used as a fluorescent probe to recognized Fumaric acid (FA) and maleic acid (MA) via fluorescence titration. Two carboxyls in MA are in the same side, they could form stable interaction with the assembly and the fluorescence intensity decreased obviously when naphthalimide dye ⊂ CB [7] was titrated by MA (nearly quenched in 1.5 equiv). But two carboxyls in FA are in opposite sides, the interaction between FA and the assembly was weak and not stable, and the fluorescence intensity changed inconspicuously when the assembly was titrated by FA.

Keywords *Cis*/*trans* recognition · CB [7] · Naphthalimide dye · Fluorescent titration

Introduction

Cis/*trans* isomerism is an important stereoisomerism in compounds, usually because there are rotation limit factors in molecules and various groups in different space arrangement [1]. *Cis*/*trans* isomerism commonly exist in pesticides, drugs and food additives etc. Although *cis*/*trans* isomers have the same molecule formula, but they often show different physical property and biological activity. *Trans*-perillartine is a kind of sweeteners which is 2000 times sweeter than sucrose [2], it has been widely applied in beverage, cigarette and food, but its *cis* isomer tastes not sweet absolutely. *Cis* tamoxifen and *trans* tamoxifen showed completely opposite functions, the *trans* isomer is a kind of anti-estrogen [3], but the *cis* isomer is an estrogen stimulant. Fumaric acid (FA) is a general food additive, but its isomer maleic acid (MA) has strong poisonousnesss, and its residual in food is limited. At present, the assay and recognition of *cis*/*trans* isomers are mainly manipulated by LC-ESIMS/MS [4], PLS and ultraviolet spectrophotometry [5], IR, and HPLC etc., while to explore some new detecting methods is also necessary.

As the third class of macrocycles after cycledextrins and calixarenes [6], CBs are synthetic products by glycoluril and formaldehyde in acid catalyzed condition [7]. CB [6] synthesis was first reported in 1905 [8] and named by Mock [9] in 1981. Then other four new family members (CB [5], CB [7], CB [8], and CB [10].CB [5]) had been found by Kim [10] and Day [11]. CBs have hydrophobic inner cavity and ion–dipole carbonyl oxygens regions [12]. Various protonated alkyl amines and arylamines were included by CBs through hydrophobic interaction inside the non-polar inner cavity and ion–dipole interaction with the carbonyl portals [10, 13]. Some fluorescent dyes with chain amine unit could bind with CBs in those methods too. The inclusion of fluorescent dyes into macrocycles could affect their photophysical properties and potentially lead to new applications [6]. When the hemicyanine dye was included by CB [6], about 270 times

✉ Jie Sun
sunjie5516@126.com

✉ Haibo Wang
wanghaibo@njtech.edu.cn

[1] College of Food Science and Light Industry, Nanjing Tech University, No. 30 PuZhu south road, Pukou district, Nanjing 211816, China

[2] College of Chemistry and Molecular Engineering, Nanjing Tech University, No. 30 PuZhu south road, Pukou district, Nanjing 211816, China

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of fluorescence enhancement was observed [14]. There were completely opposite fluorescence behaviors when acridine dyes bound with CB [7] and CB [8], enhancement and quenching, respectively [6, 15, 16]. The stability of c*is*-styryl dye could be effectively enhanced when the dye was inside the cavity of CBs [17]. Based on the binding behaviors between fluorescent dyes and CBs, CBs was considered suitable to remove dyes from waste water [18]. Moreover, fluorescent dye ⊂ CBs could be used as a probe to detected volatile hydrocarbons in aqueous solution, the conducted hydrocarbon gas would displace the dye and came into the host cavity, result in fluorescent decrease [13]. In this paper, we constructed a 1:1 naphthalimide dye ⊂ CB [7] assembly to recognized FA and MA, carboxyls in FA or MA could interact with carbonyls in CB [7], which would lead to π…π interaction between the double bond in FA or MA and the naphthalene ring. Therefore, when the 1:1 assembly was titrated by different concentration of FA and MA, fluorescence intensity changes happened.

Experimental Section

Materials and Methods

CB [7] was prepared according to previous literature procedures [19]. 4-bromo-1,8-naphthalic anhydride was recrystallized from dichloromethane. Other reagents were commercially available and used without further purification.

Absorption spectra was measured on a Agilent Cary60 UV-Vis spectrophotometer. Fluorescent titration were measured in a conventional rectangular quartz cell (10 × 10 × 45 mm^3) with the excitation and emission slits at a width of 3 nm and 5 nm on a Horiba Fluoro Max-4 Fluorescence Spectrophotometer. The excitation wavelength of N-butyl-4[(4′-aminobutyl)amino]-1,8-naphthalimide (**1**) and N-butyl-4[(6′-aminobutyl)amino]-1,8-naphthalimide (**2**) are both 260 nm. ^{1}H NMR spectra were recorded on a Brüker AM 400 spectrometer with tetramethyl silane (TMS) as internal reference.

Synthesis of N-butyl-4-bromo-1,8-naphthalimide

4-bromo-1,8-naphthalic anhydride 2.77 g (10.0 mmol) and *n*-butylamine 0.73 g (10.0 mmol) were dissolved in ethanol. The mixture was refluxed for 10 h and cooled, the precipitate was collected by vacuum filtration to give 2.50 g product (75 %) and used without further purification. M.P. 93–94 °C; ^{1}H NMR (400 MHz, Chloroform-d^6, δ,ppm): 8.67 (dd, J = 7.3 Hz,J = 1.1 Hz,1H), 8.58 (dd,J = 8.6 Hz,J = 1.1 Hz, 1H), 8.42 (d,J = 7.8 Hz, 1H), 8.05 (d,J = 7.9 Hz,1H), 7.86 (dd, J = 8.5 Hz,J = 7.3 Hz,1H), 4.18 (m,2H), 1.70 (m,2H), 1.45 (m, 2H), 0.98 (t,J = 7.3 Hz,3H).

*Synthesis of N-butyl-4[(4'-aminobutyl)amino] -1,8-naphthalimide (**1**)*

N-butyl-4[(4′-aminobutyl)amino]-1,8-naphthalimide was synthesized according to the literature procedures [20]. N-butyl-4-bromo-1,8-naphthalimide 1.0 g (2.87 mmol) and 1,4-butanediamine 0.5 g (5.68 mmol) was dissolved in 30 ml acetonitrile, the mixture was refluxed for 3 days and then poured into water and the solid was collected by vacuum filtration as a yellow solid. The crude product purified by silica gel column chromatography using ethyl acetate/petroleum ether (2/1) as eluant to give 0.4 g (42 %) **1** as a yellow solid. M.P. 91–93 °C; ^{1}H NMR(400 MHz, DMSO-d^6, δ,ppm): 8.72 (m,1H), 8.45 (d, J = 7.1 Hz,1H), 8.28 (d,J = 8.5 Hz,1H), 7.70 (dd,J = 8.4 Hz, J = 7.3 Hz,1H), 6.82 (d,J = 8.7 Hz,1H), 4.02 (m,2H), 3.44 (t, J = 5.9 Hz,5H), 2.84 (t, J = 7.4 Hz,2H), 1.74 (q, J = 7.2 Hz, 2H), 1.65 (dd,J = 14.6 Hz,J = 6.3 Hz,2H), 1.58 (d,J = 5.9 Hz, 2H), 1.34 (m,2H), 0.92 (t, J = 7.3 Hz,3H).

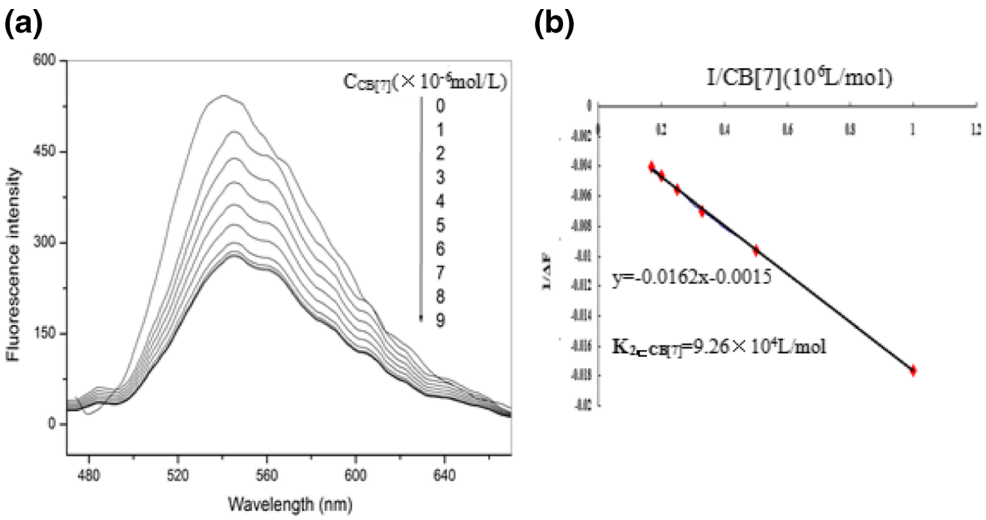

Fig. 1 **a** Fluorescence titration curves of **1** by CB [7]; **b** Inclusion constant of **1** ⊂ CB [7]

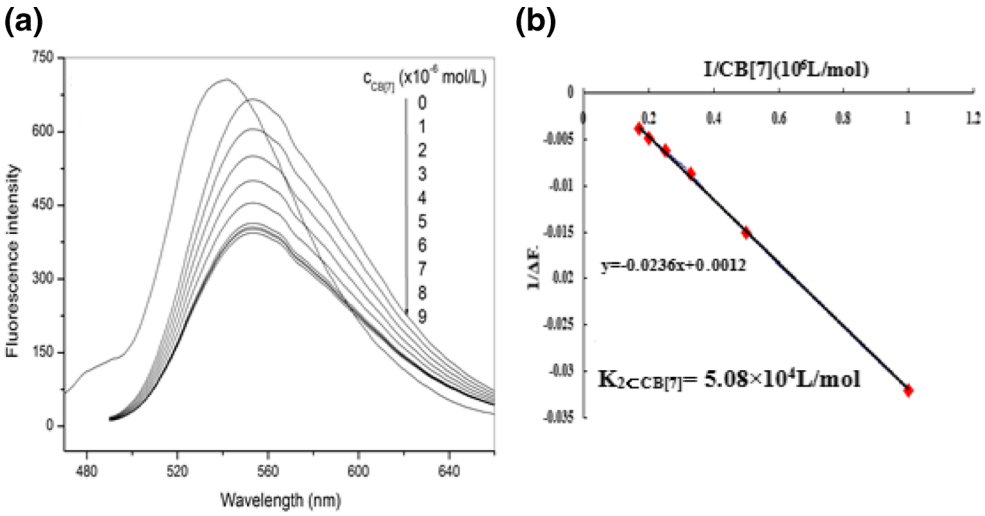

Fig. 2 **a** Fluorescence titration curves of **2** by CB [7]; **b** Inclusion constant of **2** ⊂ CB [7]

*Synthesis of N-butyl-4[(6'-aminobutyl)amino] -1,8-naphthalimide (**2**)*

N-butyl-4-bromo-1,8-naphthalimide 0.8 g (2.29 mmol) and 1, 6-hexanediamine (0.5 g 4.31 mmol) was dissolved in 30 ml acetonitrile, the mixture was refluxed for 3 days and then poured into water and the solid was collected by vacuum filtration as a yellow/orange solid. The crude product purified by silica gel column chromatography using ethyl acetate/ petroleum ether (2/1) as eluant to give 0.4 g (49 %) **2** as a red solid. M.P. 60–62 °C; ^{1}H NMR(400 MHz, DMSO-d^6, δ,ppm): 8.80 (dd, J = 8.6 Hz, J = 1.2 Hz,1H), 8.48 (dt,J = 7.2 Hz,J = 2.2 Hz,1H), 8.31 (d,J = 8.5 Hz,1H), 7.72 (m,1H), 6.82 (d,J = 8.6 Hz, 1H), 4.06 (t, J = 7.4 Hz,2H), 3.49 (d,J = 14.2 Hz,5H), 2.83 (q, J = 8.0 Hz,2H), 1.76 (m,2H), 1.62 (q,J = 8.5 Hz, J = 8.0 Hz,4H), 1.40 (m,6H), 0.97 (t,J = 7.3 Hz,3H).

Results and Discussion

Formation of 1/2 ⊂ CB [7] Assembly

In order to quantitatively estimate the binding behaviors of **1**/**2** with CB [7], fluorescent titration was performed. **1** (concentration is 6 × 10^{-6} mol/L) was titrated by different concentration of CB [7] solution, and its fluorescence curves and inclusion constant were obtained, respectively (Fig. 1). When CB [7] was added, the emission spectrum red shift from 541 nm to 545 nm, and the fluorescence intensity was declined. When the concentration of CB [7] solution was equal to **1**, fluorescence intensity decreased to its minimum. Continually increased the concentration of CB [7], the fluorescence intensity was keeping the same, which proved **1** and CB [7] formed 1:1 host-guest complex.

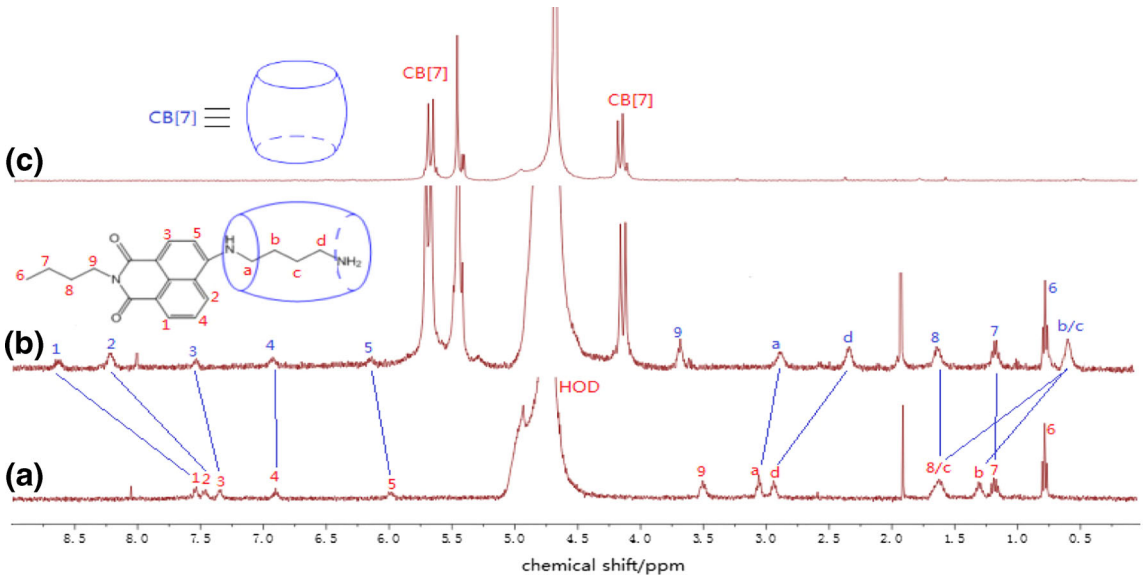

Fig. 3 ^{1}H NMR spectra in D_2O: **a** **1**, **b** **1** ⊂ CB [7](5 mM) and **c** CB [7]

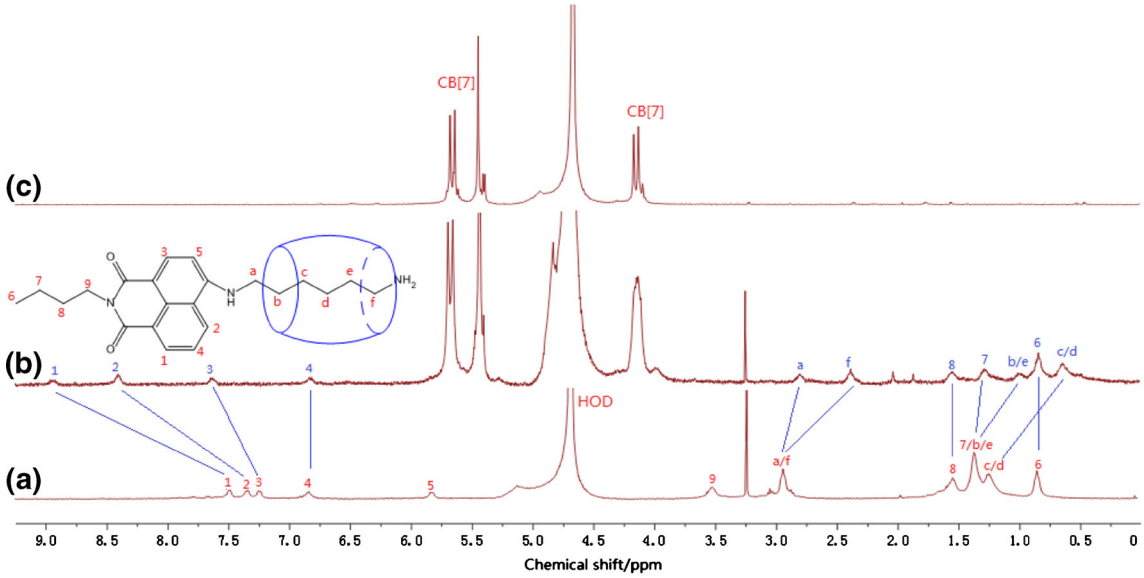

Fig. 4 ^{1}H NMR spectra in D_2O: **a 2**, **b 2** ⊂ CB [7](7.5 mM) and **c** CB [7]

Used the numerical value of 1/ΔF (ΔF = F-F_0) and 1/CB [7] drawing could get a straight line, and the ratio of linear intercept and slope is the inclusion constant. Where F is the fluorescence intensity when different concentration of CB [7] formed host-guest complex with naphthalimide dye, F_0 is the fluorescence intensity of guest solution.

The K_1⊂$_{CB}$ [7] was estimated to be 9.26×10^4 L/mol. In the same way, the fluorescence titration curves and inclusion constant of **2** ⊂ CB [7] had been gotten (Fig. 2), 1:1 host-guest complex was formed too, the inclusion constant was K_2⊂$_{CB}$ [7] = 5.08×10^4 L/mol.

^{1}H NMR Characterization of the 1/2 ⊂ CB [7]

CBs' negative regions and cavity could bind with the alkyl amine structure in **1** and **2**, and the complex of **1**/**2** ⊂ CB [7] had been characterised by ^{1}H NMR spectroscopy. The peaks of the protons of **1** exhibit great upfield shifted (Δδ = −0.16, −0.73, −1.04, and −0.75 ppm for protons of a, b, c and d, respectively) compared to free guest as a consequence of inclusion-induced shielding effects, as show in Fig. 3. At the same time, the peaks of protons in naphthalene shifted downfield as the deshielding effect. Protons of CB [7] had no obvious NMR changes. The peaks of the protons of 2 shifted upfield (Δδ = −0.18, −0.40, −0.64, −0.59 ppm for protons of a, b and c, d and e, f, respectively) compared to free guest were shown in Fig. 4. The peaks of protons in naphthalene had shift downfield too. These phenomena provided convincing evidence for the formation of an inclusion complex between the alkyl diamine structure in guests **1**/**2** and CB [7].

Fluorescent Recognition of MA and FA by 1/2 ⊂ CB [7]

A concentration is 6×10^{-6} mol/L solution of **1** ⊂ CB [7] was titrated by different concentration (0 ~ 9×10^{-6} mol/L) of FA and MA, fluorescence spectra had been measured and

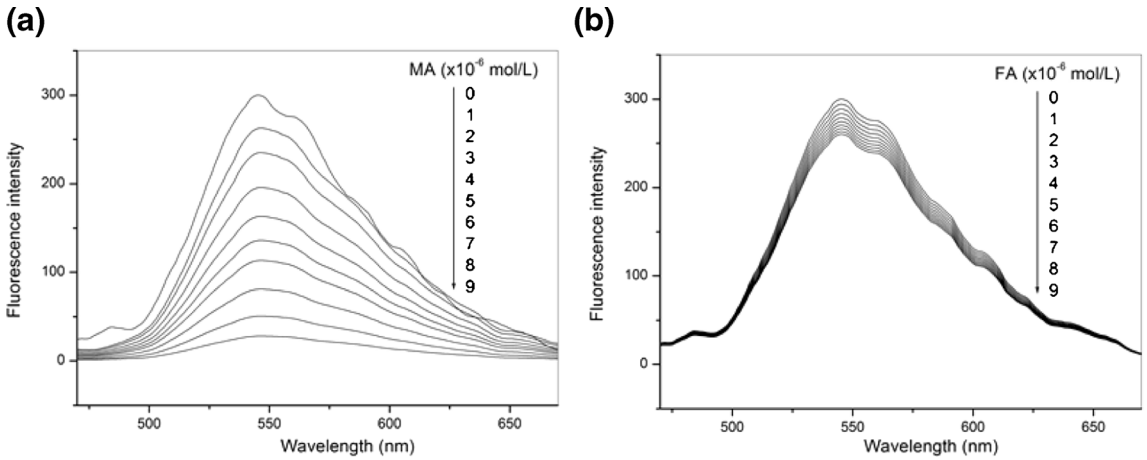

Fig. 5 Fluorescence spectra of **1** ⊂ CB [7] titrated by different concentration of MA (**a**) and FA (**b**)

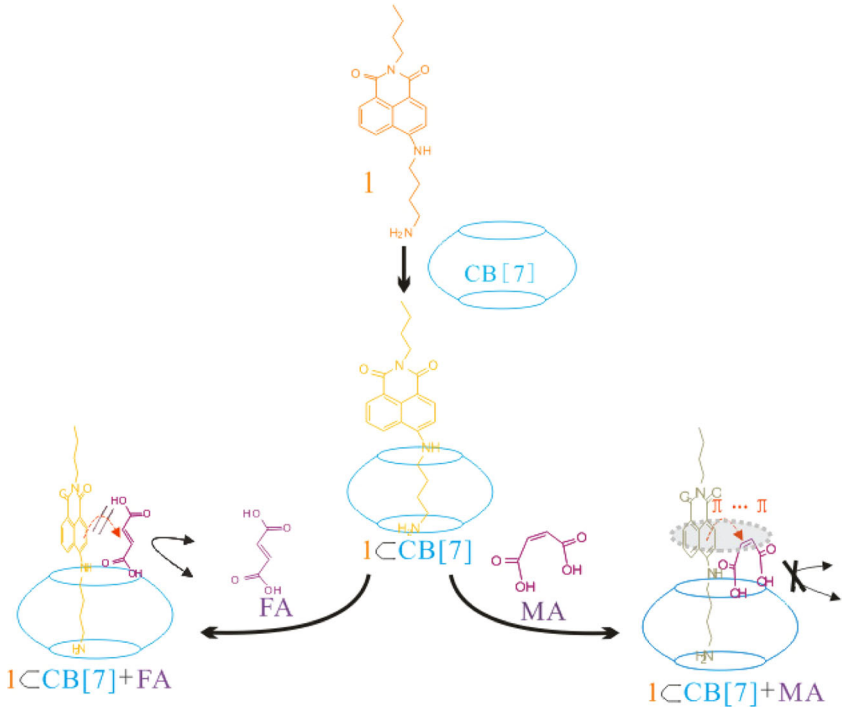

Fig. 6 **1** ⊂ CB [7] assembly interact with FA and MA

recorded. Emission wavelength had little red shift (from 545 nm to 547 nm) when MA been added (Fig. 5), fluorescence intensity became weaker and weaker with the concentration of MA increased. But the fluorescence intensity changed little when **1** ⊂ CB [7] titrated by different concentration of FA. So we could draw a conclusion that MA interacted with **1** ⊂ CB [7] complex in some ways but FA was not.

While the interaction mechanism was not same to Nau.'s [13], because if **1**/**2** was replaced by FA or MA, fluorescence intensity of solution would increase. Compared the size of CB [7] cavity (portal diameter about 5.4 Å) to MA (length 5.7 Å, width 4.1 Å) and FA (length 7.1 Å, width 3.1 Å), both of FA and MA could hardly enter into the host cavity which already contained an alkyl amine chain, so the interaction maybe happen in the carbonyl region of CB [7], we had provided a probable mechanism of naphthalimide dye ⊂ CB [7] assembly interact with FA and MA in Fig. 6.

When **1** and **2** bound with CB [7], electron transmitted to naphthalene was stopped by the host cavity, electron density of naphthalene reduced and the fluorescence intensity decreased. When MA was added, two carboxyls in MA could

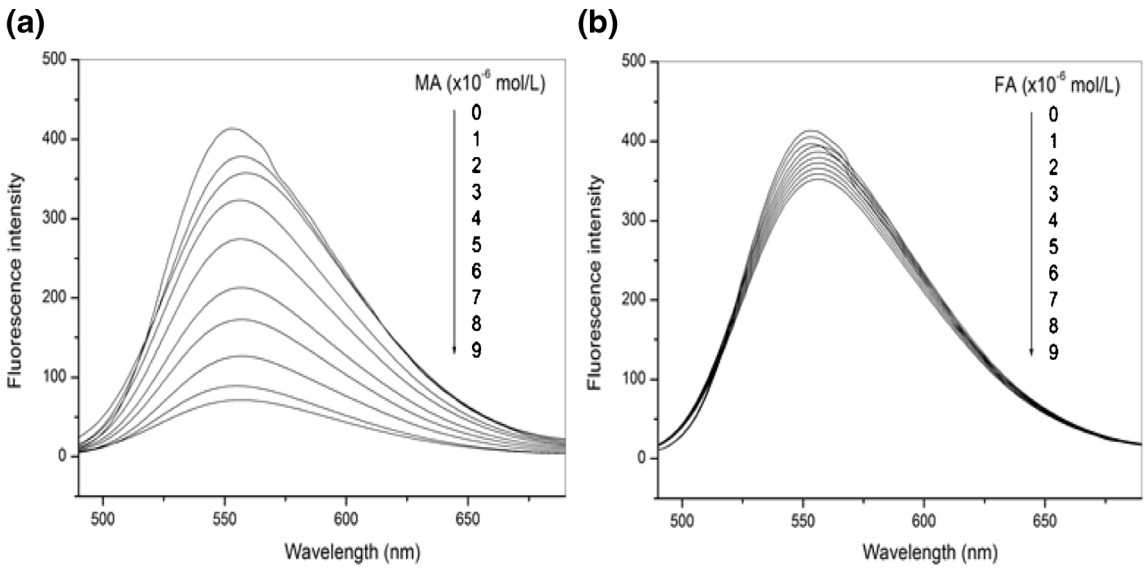

Fig. 7 Fluorescence spectra of **2** ⊂ CB [7] titrated by different concentration of MA (**a**) and FA (**b**)

form hydrogen bond with the carbonyls of CB [7], at the same time, the double bond would parallel to the naphthalene, π…π interaction could be formed, the strong electron-withdrawing capacity of carboxyl connected to the double bond might reduce naphthalene electron density further, so the fluorescence intensity became lower and nearly quenched when 1.5 equivalent of MA was added. Due to the two carboxyls in FA are in opposite sides, only one carboxyl group could form hydrogen bond with carbonyls of CB [7], the FA molecule would swing freely and could not form stable π…π interaction with naphthalene, so the fluorescence intensity changed inconspicuously.

In the same way, **2** ⊂ CB [7] titrated by different concentration of MA and FA were showed in Fig. 7, it showed that MA was interacted with **2** ⊂ CB [7] while FA was not too.

Conclusion

In summary, naphthalimide dye **1** and **2** had been prepared. We constructed 1:1 naphthalimide dye ⊂ CB [7] assembly, estimated the 1:1 assembly by fluorescent titration and verified their inclusion behavior through ^{1}H NMR. This 1:1 assembly was used as fluorescent probe to recognized MA and FA, when it was titrated by MA, fluorescence changed greatly, when it was titrated by FA, fluorescence almost kept the same. In other words, we recognized FA and MA by fluorescent titration successfully, and a novel method of *cis*/*trans* isomers recognition was offered by us.

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