Tetrahedron Letters xxx (2013) xxx–xxx

Contents lists available at SciVerse ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Rational design of fluorescent viscosity sensors by the principle of photoinduced electron transfer

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ARTICLE INFO

Article history:
Received 12 December 2012
Revised 31 January 2013
Accepted 19 February 2013
Available online xxxx

Keywords:
Fluorescent viscosity sensors
Photoinduced electron transfer
4-Aminonaphthalimide
Exciplex formation

ABSTRACT

To establish a new strategy for the development of fluorescent viscosity sensors by the principle of photoinduced electron transfer, three 4-aminonaphthalimide based D-$(CH_2)_2$-A molecules were designed and synthesized. The effects of solvent polarity and viscosity on the fluorescence spectra of these compounds were investigated. These compounds exhibit viscosity-sensitive fluorescence spectra in ethylene glycol–glycerol mixtures. A mechanism about exciplex formation was proposed to explain their viscosity sensitivity.

Introduction

Viscosity is an important physicochemical parameter which determines the diffusion rates of solutes in solvents. Changes in the local microviscosity of biological systems have been linked to many diseases and disorders.[1] The demands of the quantitative measurements of viscosity on a microscopic scale, where traditional mechanical methods met with difficulties, led to the development of fluorescent viscosity sensors.

Fluorescent viscosity sensors are functional molecules whose fluorescence properties are dependent upon the viscosity of the local environments.[1–14] The most reported fluorescent viscosity sensors are molecular rotors, such as *p*-dialkylaminobenzylidenemalononitriles,[2] and their carboxy dilogs,[1,3–6] 4-*p*-dimethylaminostyrylpyridinium salts,[7,8] etc. They usually have a D-π-A structure with an electron donor and an electron acceptor being linked together by a single bond or single double alternative bonds. The internal rotations of the single bonds linking the different parts are associated with the nonradiative pathways of the excited states and are influenced by the changes of the viscosity of the medium.[15,16] Benefit from high sensitivity, fast response and good spatial resolution, these kind of fluorescent viscosity sensors were widely used in biochemical research.[17–27] Their wide applications stimulated the development of new fluorescent viscosity sensors. However, the mechanism of the effects of solvent viscosity on the fluorescence properties of molecular rotors is complicated. The relationship between molecular structure and viscosity sensitivity was not well established. It is difficult to develop new fluorescent viscosity sensors with diverse sensitivity and emission wavelengths to meet the needs of different applications. Strategies for the rational design of fluorescent viscosity sensors are severely desired.

We focused our efforts on the establishment of a rational strategy to develop fluorescent viscosity sensors by the principle of photoinduced electron transfer (PET). Photoinduced electron transfer is one of the most employed principles in the design of fluorescent sensors.[28] The typical structure of an intramolecular PET system is that an electron donor and an electron acceptor are linked together by a flexible chain. In the ground state, there are no electronic interactions between the donor and the acceptor moieties. In the excited state, electron transfer from the donor moiety to the acceptor moiety may quench the fluorescence from the fluorophore. Electron transfer efficiency will be strongly influenced by the steric nature of the flexible chain linking the donor and acceptor moieties. This is because the steric nature of the flexible chain determines the distance between the donor and the acceptor moieties and their relative orientations, and therefore, determines the distance the electron must travel in the electron transfer process and the extent of the orbital interactions between the donor and acceptor moieties.[29,30] Viscosity may influence the conformational motions of the flexible chain in the electron transfer process, and thus, affect electron transfer efficiency. Therefore, it is reasonable to suppose that viscosity sensors can be developed based on the principle of photoinduced electron transfer. However, PET fluorescent viscosity sensors were rarely reported.

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http://dx.doi.org/10.1016/j.tetlet.2013.02.111

Please cite this article in press as: Wu, Z.; et al. *Tetrahedron Lett.* (2013), http://dx.doi.org/10.1016/j.tetlet.2013.02.111

In order to develop PET fluorescent viscosity sensors, three D-$(CH_2)_2$-A molecules (**1**–**3**, Fig. 1) with *N*-alkyl anilines as electron donors and 4-aminonaphthalimides as electron acceptors were designed and synthesized. 4-Aminonaphthalimide was chosen as the fluorophore for its excellent photophysical properties, such as high fluorescence efficiency, long emission wavelengths and good photostability.[31–33] The chain length of the alkyl substituent on the N atom of the aniline moiety was purposely altered to investigate the effect of substituent on viscosity sensitivity. Compound **A** which has no aniline moieties connected was used as a reference to determine the electron transfer efficiency.[31]

Results and discussion

The synthesis procedures of **1**–**3** are shown in Scheme 1. *N*-Butyl-4-bromo-1,8-naphthalimide (**4**) was refluxed with *N*-methyl-2-aminoethanol in 2-methoxyethanol with triethylamine as catalyst to give *N*-butyl-4-(*N*-methyl-2-hydroxyethylamino)-1,8-naphthalimide (**5**). Compound **5** was treated with phosphorous tribromide in dichloromethane to get *N*-butyl-4-(*N*-methy-2-bromoethylamino)-1,8-naphthalimide (**6**). The bromine atom of **6** was substituted by *N*-alkyl anilines to give **1**–**3**.

Firstly, we examined the photophysical properties of **1**–**3** in solvents with different polarity. The absorption spectra of **1**–**3** in various solvents (Supplementary data, Table S1, Figs. S1–S5) indicate that there are no appreciable interactions between the aniline and the 4-aminonaphthalimide moieties on the ground state. The absorption maxima of **1**–**3** are about 20 nm shorter than those of **A** in the solvents tested. This can be attributed to the steric interaction between the 4-amino group and the 5-H atom of the naphthalene ring, which prevents the 4-amino group from conjugating well with the naphthalene ring.

Figure 2 displays the fluorescence efficiency of **A** and **1**–**3** in solvents with different polarity (see also Supplementary data, Table S1). The fluorescence efficiency of **A** decreases progressively with the increase of solvent polarity, indicating an intramolecular charge transfer (ICT) character.[31] Compared to that of **A**, the fluorescence of **1**–**3** is extensively quenched both in nonpolar and polar solvents, which indicates that efficient electron transfer takes place in these compounds. With the increase of solvent polarity, the fluorescence intensity of **1**–**3** decreases steeply. In moderate polar solvents, such as tetrahydrofuran, the fluorescence of these compounds is almost fully quenched.

Figure 3 shows the emission maxima of **A** and **1**–**3** in solvents with different polarity. The emission maximum of **A** increases linearly with the increase of solvent polarity. This is also a character of an ICT emission. Interestingly, in nonpolar solvents, **1**–**3** exhibit much longer emission maxima than those of **A**. For example, in tol-

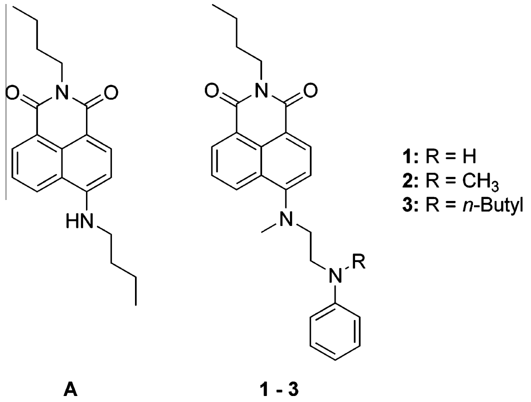
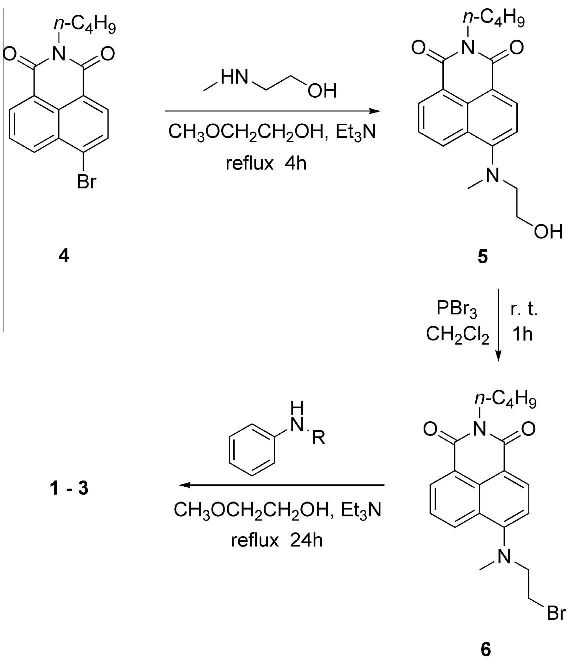


Figure 1. Structures of **A** and **1**–**3**.



Scheme 1. Synthesis procedures of **1**–**3**.

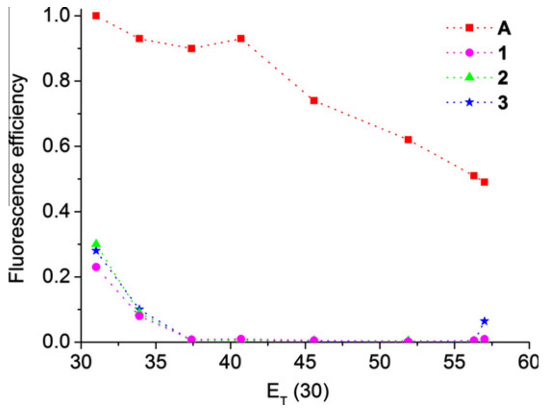


Figure 2. Fluorescence efficiency of **A** and **1**–**3** in solvents with different polarity. Solvents, from left to right are hexane, toluene, tetrahydrofuran, dichloromethane, acetonitrile, ethanol, ethylene glycol, and glycerol.

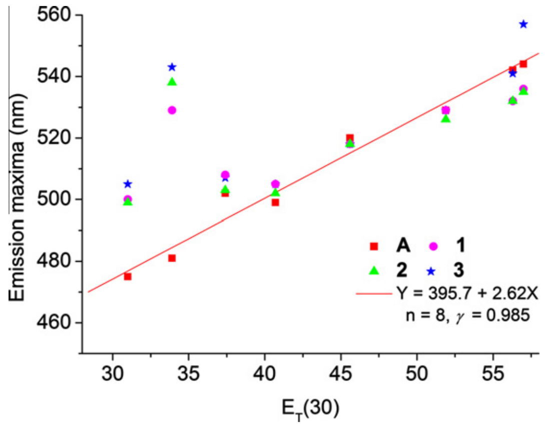


Figure 3. Emission maxima of **A** and **1**–**3** in solvents with different polarity. The straight line is the linear fitness of the emission maxima of **A** to the solvent polarity parameter, E_T (30). Solvents, from left to right are hexane, toluene, tetrahydrofuran, dichloromethane, acetonitrile, ethanol, ethylene glycol, and glycerol.

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uene, the maximal emission wavelength of **3** (543 nm) is about 60 nm longer than that of **A** (481 nm). This phenomenon indicates that an excited state with much larger charge separation character than that of an ICT state is formed. The emission maxima of **1**–**3** shift to red when the solvent changes from hexane to toluene. In solvents more polar than toluene, this long-wavelength emission is quenched, and **1**–**3** exhibit emission maxima similar to those of **A**. Some representative fluorescence spectra of **1**–**3** are shown in Figure 4 (see also Supplementary data, Figs. S6–S8).

Then, we investigated the fluorescence spectra of **1**–**3** in ethylene glycol–glycerol mixtures with varied viscosity. The fluorescence intensity of **1** and **2** (Supplementary data, Figs. S9 and S10) is weakly sensitive to solvent viscosity. The fluorescence intensity of **3** increases about 10-fold when solvent viscosity increases from 50 to 1000 cP (Fig. 5, see also Supplementary data, Fig. S12). As shown in the inset of Figure 5, the fluorescence intensity of **3** is linearly related to solvent viscosity, which can be described well by Förster–Hoffmann equation (Eq. 1):[34]

$$\log I = C + x\log\eta \tag{1}$$

where I = fluorescent emission intensity; η = solvent viscosity; x = dye-dependent constant; C = concentration and temperature constant. The slope x, an indicator of viscosity sensitivity, is 0.8 for **3**. This value is higher than most of the reported fluorescent viscosity sensors, where the slope $x \leqslant 0.66$.[3–6] These phenomena indicate that substituent effects have great influence on the viscosity sensitivity of this kind of fluorescent viscosity sensors and that higher viscosity sensitivity than that of molecular rotors can be obtained in PET fluorescent viscosity sensors.

Finally, we proposed a mechanism of exciplex formation to explain the fluorescence properties of these compounds, which is shown in Scheme 2. Exciplexes are intermediates of photoinduced electron transfer, and are characterized by partial charge separation and large dipole moments.[29] We suppose that, when 4-aminonaphthalimide is photoexcited, an ICT state is formed with the 4-N atom partially positively charged.[31] The N atom of the aniline moiety gives its lone-pair electrons to the positively charged N atom of 4-aminonaphthalimide to form a charge-transfer exciplex. When this exciplex is formed, the fluorescence from the ICT state is quenched and an emission from the exciplex appears. Due to the extended charge separation of the exciplex relative to that of the ICT state, exciplex formation leads to the decrease of the fluorescence intensity and the red-shift of the emission wavelengths.[29] The broad and long-wavelength emissions of these compounds in nonpolar solvents give support in this suggestion. The decrease of the fluorescence intensity and the red-shift of the emission maxima of these compounds with the increase of solvent polarity can be accounted for by assuming that the extent of the charge separation of this exciplex increases with the increase of solvent polarity.[35–37] In polar solvents, this exciplex may separate to ion pairs, and the fluorescence of **1**–**3** is fully quenched. This exciplex may also be considered as a three-electron N–N σ bond formed between these two N atoms with both of them partially positively charged.[16,38]

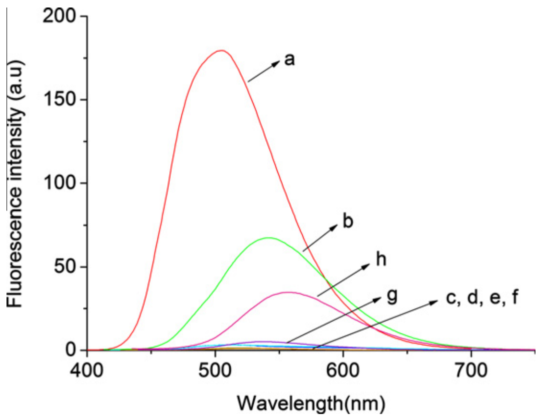


Figure 4. The fluorescence spectra of **3** in different solvents: (a) hexane; (b) toluene; (c) tetrahydrofuran; (d) dichloromethane; (e) acetonitrile; (f) ethanol; (g) ethylene glycol; and (h) glycerol. [**3**] = 1 × 10^{-5} M. All the spectra were recorded at 20 °C and excited at the maximal absorption wavelengths.

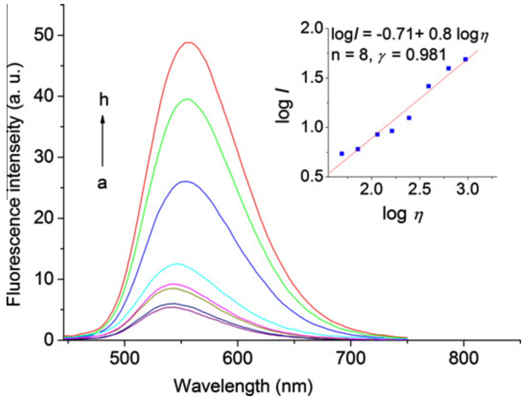
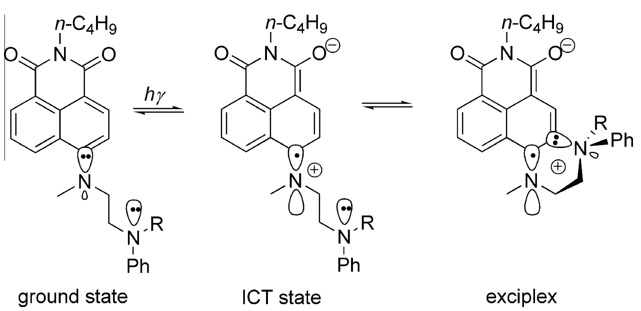


Figure 5. Fluorescence emission spectra of **3** in ethylene glycol/glycerol (v/v) mixtures: (a) 7:3; (b) 6:4; (c) 5:5; (d) 4:6; (e) 3:7; (f) 2:8; (g) 1:9; and (h) glycerol only. [**3**] = 4 × 10^{-5} M, All the spectra were recorded at 20 °C and λ_{ex} = 435 nm. The inset shows the linear relationship of log$I$ and logη.



Scheme 2. The proposed mechanism of exciplex formation.

We suppose that orbital overlapping between the N atom of the 4-amino group and the N atom of the aniline moiety is necessary for this exciplex formation. On the ground state, the most stable conformation of the flexible chain is an extended conformation and the two N atoms are far from each other. On the excited state, a conformational change from an extended conformation to a folded conformation is required for orbital overlap between these two N atoms. The increase of the solvent viscosity hinders this conformational change and prevents the formation of this exciplex, which leads to the resuming of the fluorescence from the ICT state and the increase of the total fluorescence intensity. This is the reason why **1**–**3** are sensitive to solvent viscosity.

The relationship between viscosity sensitivity and the chain length of the alkyl substituent on the aniline moiety can also be accounted for by this mechanism. Increasing the length or volume of the substituent on the donor moiety increases the activation energy of the bond rotations of the flexible chain, so that the conformational changes in the electron transfer process are more easily affected by the changes in solvent viscosity. It is reasonable to suppose that the viscosity sensitivity of these kind of fluorescent viscosity sensors can be finely tuned by simply altering the length or volume of the substituent on the donor moiety.

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Conclusions

In conclusion, a new strategy for the rational design of fluorescent viscosity sensors was established, by which, three 4-aminonaphthalimide based PET fluorescent viscosity sensors (**1**–**3**) were developed. Among these compounds, **3** exhibits higher viscosity sensitivity than most of the reported fluorescent viscosity sensors. The clear-cut relationship between substituent and viscosity sensitivity indicates the potential use of this strategy in the rational design of fluorescent viscosity sensors. More sensitive PET fluorescent viscosity sensors are expected to be developed by this strategy.

Acknowledgment

We are grateful to the National Science & Technology Pillar Program of China (2011BAE31B01).

Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2013.02.111.

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