Tetrahedron Letters 52 (2011) 4843–4847

Contents lists available at ScienceDirect

Tetrahedron Letters

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

Synthesis, luminescence properties, and theoretical insights of *N*-alkyl-or *N*,*N*-dialkyl-pyrene-1-carboxamide

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ARTICLE INFO

Article history:
Received 2 June 2011
Revised 28 June 2011
Accepted 6 July 2011
Available online 22 July 2011

Keywords:
Pyrene
Pyrenecarboxamide
Fluorescent
Fluorescence quantum yield
DFT theory

ABSTRACT

We report the synthesis and photophysical properties of *N*-alkyl- or *N*,*N*-dialkyl-pyrene-1-carboxamide. These derivatives, as well as pyrene, exhibited blue emission. *N*-Alkyl-type derivatives exhibited strong fluorescence emission ($\Phi_{fl} = 0.61$ in EtOH) in both nonpolar and polar solvents. On the other hand, *N*,*N*-dialkyl-type derivatives showed weak fluorescence emission ($\Phi_{fl} < 0.01$) due to vibrational deactivation. However, in highly viscous solvents such as glycerin, the quantum efficiencies of *N*-alkyl-type ($\Phi_{fl} = 0.91$) and *N*,*N*-dialkyl-type ($\Phi_{fl} = 0.082$) derivatives were increased. We also investigated the fluorescence mechanism of these compounds using time-dependent density-functional theory (TD-DFT). From these results, we find that highly fluorescent pyrene-1-carboxamide derivatives can be designed by introducing an appropriate functional group at the nitrogen atom of the amide. Thus, *N*,*N*-dialkyl-type pyrene-1-carboxamide has considerable potential for use in applications such as environmental response sensors and probes.

Pyrene, a well-known chromophore, has a singlet excited state with a rather high fluorescence quantum yield and long lifetime.[1] In addition, it exhibits various unique photophysical properties. In particular, its fluorescence is sensitive to the polarity of the surrounding medium, and it can form fluorescent excimers in aggregate states; these properties are quite helpful in studying the local structures or mobilities of multimolecular systems.[2–5] Therefore, pyrene and its derivatives have been widely used as fluorescence probes.[6–13]

Recently, pyrene has also been used as a fluorescence label in investigations of polypeptides, DNA oligomers, and duplexes in terms of their distances,[14,15] electric field effects,[16,17] and conformational dependence[18] of their electron transfer rates. In these investigations, pyrene and its derivatives have usually been attached to target molecules through alkyl spacer linkages because the fluorescence of pyrene changes owing to its constituent polar functional groups.[14–19] For example, chromophores having a carbonyl group often lose their fluorescence owing to intersystem crossing from the lowest n–π* singlet state to the triplet state.[20,21] In a manner similar to pyrene, formylpyrene also has weak fluorescence because of intersystem crossing.[22] In contrast, pyrenes having a carboxylic acid group and ester group exhibit strong fluorescence. Therefore, these compounds have been used as probes and as sensitizers, respectively.[23–25] However, unlike in the case of these pyrene carbonyl derivatives, there have been few mechanistic investigations of highly luminescent pyrene carboxamides, and little is known of their design. For example, pyrene-1-carboxanilide exhibited weak fluorescent emission ($\Phi_{fl} = 0.0013$).[26] In previous studies,[27–29] aromatic anilide derivatives such as benzanilide[27,28] and naphthanilide[29] were reported to exhibit weak fluorescence. This phenomenon can be attributed to the formation of twisted intramolecular charge transfer (TICT) states in benzanilide and naphthanilide. An anilide group can reduce the luminescence of a chromophore. However, from a synthetic viewpoint, carboxamides can be easily prepared and applied to the modification of substrates, such as artificial polymers, biomacromolecules, and other surfaces. Therefore, from analytical and materials science viewpoints, it is very important to design highly luminescent pyrene carboxamides.[30] Toward this end, we focused on *N*-alkyl- and *N*,*N*-dialkyl-pyrene-1-carboxamides. Previously, *N*-alkyl-type derivatives were used as fluorescence labels without any explanation of why their use is preferred.[31–33]

In this study, we synthesized *N*-alkyl- and *N*,*N*-dialkyl-pyrene-1-carboxamides (Scheme 1). Our objectives were to investigate how these functional groups affect the photoluminescence properties of pyrene and to synthesize highly fluorescent derivatives of pyrene-1-carboxamides. We expected these *N*-alkyl substituted carboxamide derivatives to exhibit fluorescence because, unlike anilide-type derivatives, they do not form TICT species, owing to the flexibility of the substituted alkyl chain. Moreover, to the best of our knowledge (see Supplementary data), this is the first report that details the photophysical properties of *N*,*N*-dialkyl-type derivatives.

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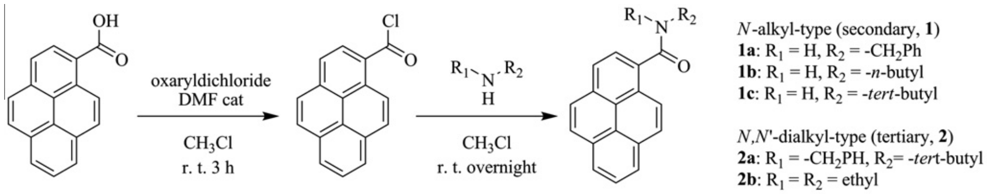
doi:10.1016/j.tetlet.2011.07.020



Scheme 1. Synthesis of *N*-alkyl type (secondary amide, **1**) and *N,N*-dialkyl-type (tertiary amide, **2**) pyrene-1-carboxamide derivatives.

N-Alkyl-type (secondary, **1**) and *N,N*-dialkyl-type (tertiary, **2**) pyrene-1-carboxamide derivatives were prepared from pyrene-1-carboxylic acid chloride and the corresponding amines with good yields. Their structures were confirmed by ^{1}H NMR, ^{13}C NMR, FT-IR, and mass spectrometry as well as by elemental analysis.

In the case of *N,N*-dialkyl-type (tertiary) derivatives, it was speculated that *cis* and *trans* conformations may exist. In photophysical investigations, mixing these conformations is unsuitable because it then becomes difficult to determine which conformation generates given spectra and parameters. Therefore, because it appears difficult to synthesize *N,N*-dialkyl-type derivatives with a fixed *trans* structure, we synthesized **2a** with the objective of producing *N,N*-dialkyl-type derivatives with a fixed *cis* structure via the introduction of a bulky substituent onto the nitrogen atom. On the other hand, *N*-alkyl-type (secondary) derivatives are considered to have a *trans* conformation based on the large size difference between the hydrogen and the alkyl substituents.

The UV–vis absorption spectra (Fig. 1a), fluorescence spectra (Fig. 1b), absolute quantum yields (Φ_{fl}), and fluorescence lifetimes (τ) of **1a** and **2a** were obtained in a deaerated ethanol solution. In this study, we performed the fluorescence measurements of **1a** and **2a** in dilute solution ($<10^{-5}$ M); therefore, excimer emissions were not observed. The spectroscopic parameters of the pyrene derivatives are summarized in Table 1. As shown in Figure 1a, the wavelengths of the absorption maxima (λ_{abs}) were similar (337–339 nm). As compared to the λ_{abs} value of other pyrene-1-carbonyl derivatives such as 1-formylpyrene (359 nm)[22] and benzyl-1-pyrenoate (350 nm),[25] those of pyrene-1-carboxamides **1a** and **2a** were blue-shifted by ca. 10–20 nm. The molar absorption coefficients (ε) of **1a** and **2a** at the maxima did not differ significantly from each other.

As shown in Figure 1b, the fluorescence spectra and emission wavelength (λ_{em}) of **1a** and **2a** were also similar. In the fluorescence spectrum of the tertiary carboxamide **2a**, a vibronic fine structure was observed. The absolute fluorescence quantum yield of the *N,N*-dialkyl-type compound **2a** was very low (Φ_{fl} <0.01). However, that of the *N*-alkyl type compound **1a** was high ($\Phi_{\text{fl}} = 0.61$). The fluorescence quantum yield of **1a** was higher than that of pyrene ($\Phi_{\text{fl}} = 0.39$) measured in our laboratory under the same conditions.[34] Similar results were obtained for the other *N*-alkyl-type compounds **1b** and **1c**, indicating that *N*-alkyl-type carboxamide groups can enhance the fluorescent performance of pyrene dyes (see Supplementary data).

In order to examine the fluorescence mechanism in greater detail, the electronic structure and the singlet and triplet energies of **1a** and **2a** in the ground state were investigated by the time-dependent density-functional theory (TD-DFT) method at the B3LYP/6-31G level of theory. Compounds **1a** and **2a** each have a large dihedral angle between the pyrene and the carbonyl group (41.3° and 56.8°, respectively). In contrast, other pyrene-1-carbonyl compounds have a planar structure (Chart 1). This structure results in weaker stabilizing interactions between the p-orbitals on the pyrene and those on the carbonyl group, which probably caused the blue-shift in the UV–vis absorption and fluorescence wavelength relative to other pyrene-1-carbonyl compounds.

From Chart 1b and c, *N,N*-dialkyl-type **2a** was expected to have two conformations. The results of DFT calculations indicated that the *cis* structure is much more stable than the *trans* structure in the ground state (by ca. 40.2 kcal/mol). The results of ^{1}H NMR spectroscopy suggested the same. *N,N*-Dialkyl-type **2b** contained a symmetric amine and showed split peaks for the protons on the two carbons adjacent to the nitrogen. *N,N*-Dialkyl-type **2a**, however, contained an asymmetric amine and did not show split peaks for the protons on the tertiary butyl group and the benzyl position (see Supplementary data).

As shown in Table 2, HOMO–LUMO transitions in $S_0 \rightarrow S_1$ had the highest oscillator strengths, and these transitions were assigned as π–π^* transitions in both **1a** and **2a**. Moreover, all triplet states near S_1 were also assigned as π–π^* transitions. From these results and

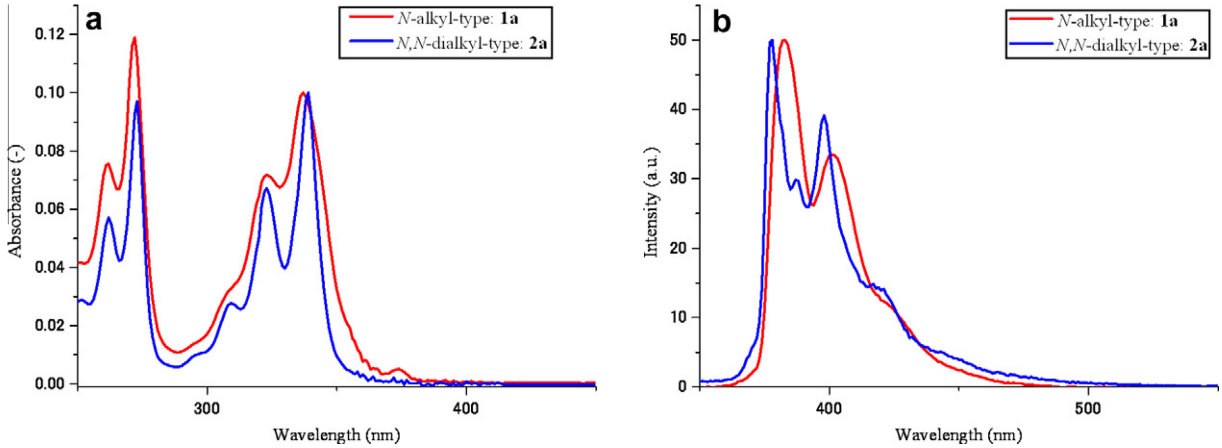


Figure 1. Normalized (a) UV–vis absorption and (b) fluorescence spectra of **1a** and **2a** (ethanol solvent, $\lambda_{\text{ex}} = \lambda_{\text{abs}}$, room temperature).

Table 1
Spectroscopic parameters of compounds **1a** and **2a** (ethanol, room temperature)

Entry	λ_{abs} (nm)	ε (M^{-1} cm^{-1})	λ_{em} (nm)	τ (ns)	Φ_{fl}	k_r[a] (S^{-1})	k_{nr}[b] (S^{-1})
1a	337	30,800	383, 401	27.1	0.61	2.3×10^7	1.4×10^7
2a	339	30,600	378, 387, 398, 420	2.9	0.0076	2.8×10^6	3.2×10^8

[a] $k_r = \Phi_{fl}/\tau$.
[b] $k_n = (1 - \Phi_{fl})/\tau$.

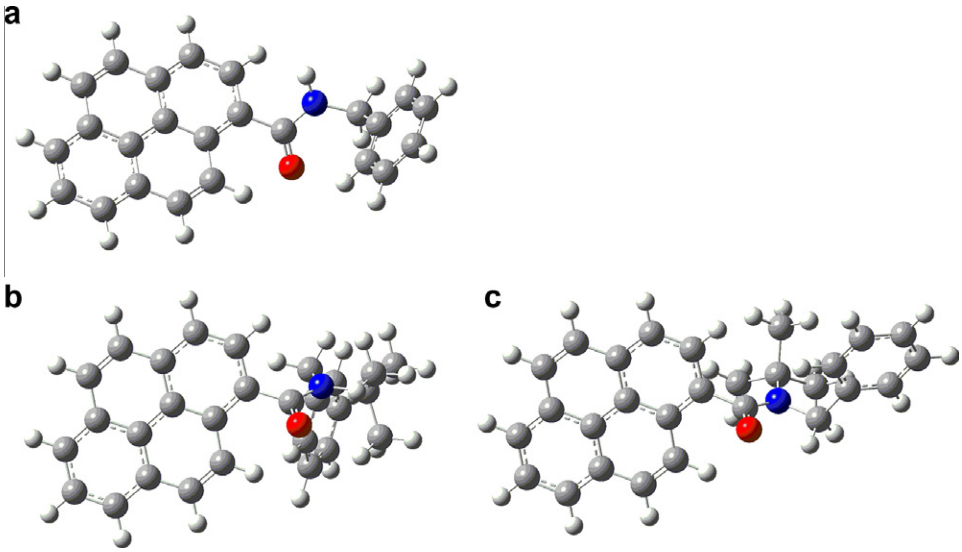


Chart 1. Optimized structures of (a) **1a**, (b) *cis* structure of **2a** and (c) *trans* structure of **2a**.

Table 2
Excitation wavelength, oscillator strength, orbital, and contribution calculated for **1a** and **2a** using TD-DFT (B3LYP/6-31G (d))

Entry	State	Transition wavelength (nm)	Oscillator strength	Main transition orbital	Contribution
1a	T_1	602	–	HOMO–LUMO	0.94
	S_1	370	0.754	HOMO–LUMO	0.98
	T_2	365	–	HOMO−1–LUMO	0.63
				HOMO–LUMO+1	0.37
2a	T_1	599	–	HOMO–LUMO	0.94
	S_1	365	0.737	HOMO–LUMO	1
	T_2	364	–	HOMO−1–LUMO	0.39
				HOMO–LUMO+1	0.55

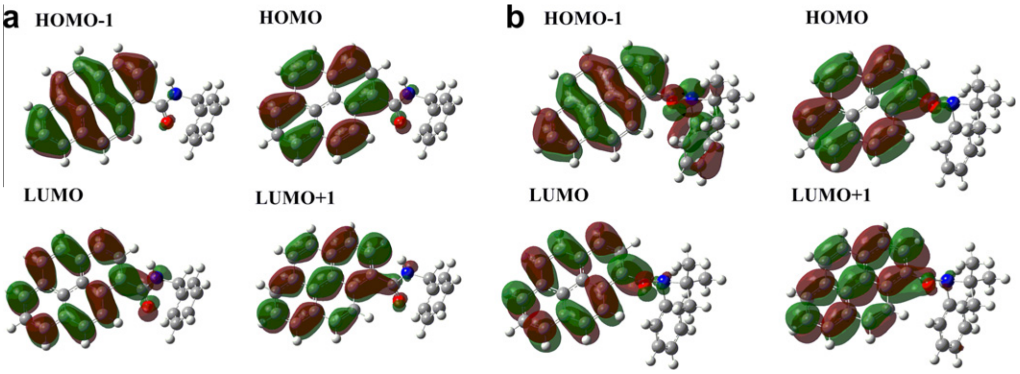


Chart 2. Frontier orbitals of (a) **1a** and (b) **2a**.

El-Sayed's rule,[35] it is suggested that the intersystem crossing process was inefficiently quenched in both **1a** and **2a**, while that quenching was often observed in formylpyrene (Chart 2).[22]

In order to evaluate the solvent dependence of the UV–vis absorption and fluorescence spectra of **1a** and **2a**, they were measured in several polar solvents (acetonitrile and ethanol), non-polar

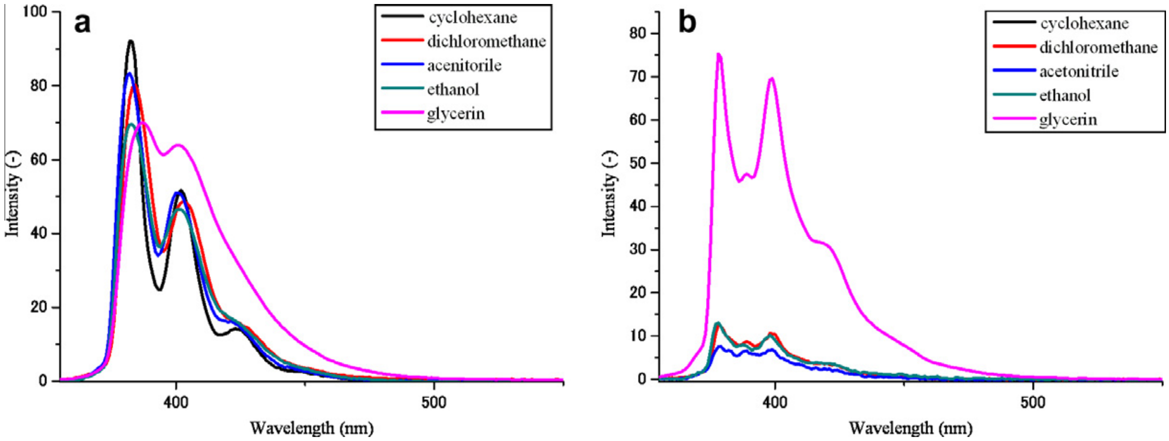


Figure 2. Fluorescence spectra of (a) **1a** and (b) **2a** in various solvents (ε = 10,000, ethanol solvent, $\lambda_{ex} = \lambda_{abs}$, room temperature).

solvents (cyclohexane and dichloromethane), and a high-viscosity solvent (glycerin)[30] (Fig. 2).

N-Alkyl-type 1

As shown in Figure 2a, the shape of the *N*-alkyl-type **1a** fluorescence spectra exhibited no dependence on the polarity of the solvent. Although solvent-sensitive changes in the vibronic structure, one of the advantageous features of pyrene, were not observed, compound **1a** showed strong emission in all solvents, especially viscous glycerin media (Φ_{fl} = 0.91), as well as a stable emission color. The fact that **1a** shows a similar wavelength in both the absorption and the fluorescence emissions, along with the higher fluorescence quantum yields as compared to those of pyrene, indicates that such compounds are useful as fluorescence probes, labels, and other luminescence materials.

N,*N*-Dialkyl-type 2

Tertiary (*N*,*N*-dialkyl-type) **2a** was observed to have weak fluorescence emission in almost all solvents, similar to the results obtained for ethanol (Φ_{fl} <0.01). However, in glycerin (highly viscous media), relatively strong fluorescence was observed (Φ_{fl} = 0.082). This is because the viscosity of glycerin prevented molecular vibrations. Considering these results along with the TD-DFT calculations and the already reported TICT mechanism, it can be inferred that the high non-radiative constant (k_{nr}) was mainly derived from a vibrational deactivation process and not from an intersystem crossing process or by the generation of charge separation species. Thus, because **2a** potentially possesses fluorescence emitting ability, the fluorescence of **2a** can be controlled by adjusting its vibrational relaxation.

In conclusion, the photophysical properties of two types of pyrene-1-carboxamide derivatives (*N*-alkyl-type **1** and *N*,*N*-dialkyl-type **2**) and theoretical insights into these compounds have been discussed. *N*-Alkyl-type **1a** showed strong fluorescence emission (EtOH: Φ_{fl} = 0.61) in all solvents with almost no changes in the UV–vis and in fluorescence spectra. *N*,*N*-Dialkyl-type **2a** showed weak emission (Φ_{fl} <0.01) in almost all solvents. However, in highly viscous media (glycerin), strong fluorescence was observed (Φ_{fl} = 0.082) because of the suppression of molecular vibrations. Owing to the excellent and stable emission properties of **1a**, *N*-alkyl-type **1** can be used as a fluorescence probe and label material. *N*,*N*-Dialkyl-type **2** can be used as a fluorescence environmental response sensor material because of its unique on–off emission. Moreover, such compounds have many analogs, and therefore, it is expected that new functions and applications of such compounds will be proposed. We are currently investigating whether other fluorophores such as naphthalene, anthracene, and polycyclic aromatic hydrocarbons can exhibit the same effects when *N*-alkyl-type or *N*,*N*-dialkyl-type amide groups are incorporated into them.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.07.020.

References and notes

1. Montalti, M.; Credi, A.; Prodi, L.; Gandolfi, M. T. *Handbook of Photochemistry*, 3rd ed; Taylor & Francis, **2006**.
2. Kalyanasundaram, K.; Thomas, J. K. *J. Am. Chem. Soc.* **1977**, *99*(7), 2039–2044.
3. Winnik, F. M. *Chem. Rev.* **1993**, *93*, 587–614.
4. Karpovic, D. S.; Blanchard, G. J. *Langmuir* **1996**, *12*, 5522–5524.
5. Galla, H.-J.; Hartmann, W.; Theilen, U.; Sackmann, E. *Membr. Biol.* **1979**, *48*, 215–236.
6. Saito, Y.; Shinohara, Y.; Ishioroshi, S.; Suzuki, A.; Tanaka, M.; Saito, I. *Tetrahedron Lett.* **2011**, *52*, 2359–2361.
7. Saito, Y.; Suzuki, A.; Imai, K.; Nemoto, N.; Saito, I. *Tetrahedron Lett.* **2010**, *51*, 2606–2609.
8. Fujimoto, K.; Yamada, S.; Inouye, M. *Chem. Commun.* **2009**, 7164–7166.
9. (a) Sumi, K.; Konishi, G. *Molecules* **2010**, *15*, 7582–7592; (b) Uchimura, M.; Watanabe, Y.; Araoka, F.; Watanabe, J.; Takezoe, H.; Konishi, G. *Adv. Mater.* **2010**, *22*, 4473–4478; (c) Watanabe, Y.; Uchimura, M.; Araoka, F.; Konishi, G.; Watanabe, J.; Takezoe, H. *Appl. Phys. Express* **2009**, *2*, 102501.
10. (a) Maeda, H.; Maeda, T.; Mizuno, K.; Fujimoto, K.; Shimzu, H.; Inouye, M. *Chem. Eur. J.* **2006**, *12*, 824–831; (b) Fujimoto, K.; Shimizu, H.; Frusyo, M.; Akiyama, S.; Ishida, M.; Furukawa, U.; Yokoo, T.; Inouye, M. *Tetrahedron* **2009**, *45*, 9357–9361; (c) Shimizu, H.; Fujimoto, K.; Furusyo, M.; Maeda, H.; Nanai, Y.; Mizuno, K.; Inouye, M. *J. Org. Chem.* **2007**, *72*, 1530–1533.
11. Yang, Y.; Gou, X.; Blecha, J.; Cao, H. *Tetrahedron Lett.* **2010**, *51*, 3422–3425.
12. Kumar, M.; Kumar, R.; Bhalla, V. *Tetrahedron Lett.* **2010**, *51*, 5559–5562.
13. (a) Jung, J. H.; Lee, M. H.; Kim, H. J.; Jung, H. S.; Lee, S. Y.; Shin, N. R.; No, K.; Kim, J. S. *Tetrahedron Lett.* **2009**, *50*, 2013–2016; (b) Diring, S.; Ziessel, R. *Tetrahedron Lett.* **2009**, *50*, 1203–1208; (c) Fukuda, M.; Nakamura, M.; Takada, T.; Yamana, K. *Tetrahedron Lett.* **2010**, *51*, 1732–1735; (d) Hirano, T.; Osaki, T.; Fuji, S.; Komatsu, D.; Azumaya, I.; Tanatani, A.; Kagechika, H. *Tetrahedron Lett.* **2009**, *50*, 488–491.
14. Isied, S. S.; Ogawa, M. Y.; Wishart, J. F. *Chem. Rev.* **1992**, *92*, 381–394.
15. Sisido, M.; Hoshino, S.; Kusano, H.; Kuragaki, M.; Makino, M.; Sasaki, H.; Smith, T. A.; Ghiggino, K. P. *J. Phys. Chem. B* **2001**, *105*, 10407–10415.
16. Piotrowiak, P. *Chem. Soc. Rev.* **1999**, *28*, 143–150.
17. Fox, M. A.; Galoppini, E. *J. Am. Chem. Soc.* **1997**, *119*(23), 5277–5285.
18. Manoharan, M.; Tivel, K. L.; Zhao, M.; Nafisi, K.; Netzel, T. L. *J. Phys. Chem.* **1995**, *99*, 17461–17472.
19. Karuppannan, S.; Chambron, J.-C. *Chem. Asian J.* **2011**, *6*, 964–984.
20. Herkstroeter, W. G.; Lamola, A. A.; Hammond, G. S. *J. Am. Chem. Soc.* **1964**, *86*, 4537–4540.
21. Boldridge, D. W.; Justus, B. L.; Scott, G. W. *J. Chem. Phys.* **1984**, *80*, 3179–3184.
22. Kumar, C. V.; Chattopadhyay, S. K.; Das, P. K. *Photochem. Photobiol.* **1983**, *38*, 141–152.
23. Nucci, N. V.; Zelent, B.; Vanderkooi, J. M. *J. Fluoresc.* **2007**, *18*, 41–49.
24. Tulock, J. J.; Blanchard, G. J. *J. Phys. Chem. B* **1998**, *102*, 7148–7155.

25. Costta, S. M. B.; Macanita, A. L.; Prieto, M. J. *J. Photochem.* **1979**, *11*, 109–119.
26. Pyrene-1-carboxanilide was prepared by the reaction of pyrene-1-carboxylic acid chloride and aniline. In the measurement of absolute fluorescence quantum yield of pyrene-1-carboxanilide, the conditions were the follow; ε = 10,000, $\lambda_{ex} = \lambda_{abs}$ (337 nm), ethanol solvent temperature.
27. Azumaya, I.; Kagechika, H.; Fujiwara, Y.; Itoh, M.; Yamaguchi, K.; Shudo, K. *J. Am. Chem. Soc. A* **1991**, *113*, 2833–2838.
28. Lewis, F. D.; Long, T. M. *J. Phys. Chem. A* **1998**, *102*, 5327–5332.
29. Heldt, J. *J. Photochem. Photobiol., A* **1991**, *60*, 183–191.
30. Morozumi, T.; Anada, T.; Nakamura, H. *J. Phys. Chem. B* **2001**, *105*, 2923–2931.
31. Okamoto, A.; Ichiba, T.; Saito, I. *J. Am. Chem. Soc.* **2004**, *126*, 8364–8365.
32. Yao, C.; Kraatz, H.-B.; Steer, R. P. *Photochem. Photobiol. Sci.* **2005**, *4*, 191–199.
33. Siegmund, K.; Daublain, P.; Wang, Q.; Trifonov, A.; Fiebig, T.; Lewis, F. D. *J. Phys. Chem. B* **2009**, *113*, 16276–16284.
34. In the measurement of absolute fluorescence quantum yield of pyrene, the conditions were the follow; ε = 10,000, $\lambda_{ex} = \lambda_{abs}$ (330 nm), ethanol solvent, room temperature.
35. Lower, S. K.; El-Sayed, M. A. *Chem. Rev.* **1966**, *66*, 199–241.