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Synthesis and spectroscopic properties of the first phthalocyanine–nucleobase conjugates

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Abstract—The adenine-containing zinc(II) phthalocyanines **3**, **4a**, and **4b** have been prepared by standard *O*-alkylation of the tetrahydroxy analogue **1**. These macrocycles exhibit rather strong intermolecular interactions resulting in a poor solubility in organic solvents and unusual spectral properties that are highly solvent-dependent. Self-assembly of the tetra-adenine phthalocyanine **3** and the thymine-containing 9,10-anthraquinone **6** through the Watson–Crick base-pairing interactions has also been demonstrated by fluorescence quenching experiments. © 2000 Elsevier Science Ltd. All rights reserved.

Phthalocyanine, which was first developed as a pigment, has found widespread applications in materials science. To name a few, this compound and its substituted analogues can be used as semiconductors, photoconductors, electrochromic displays, optical recording materials, and gas sensors.[1] Apart from their important contributions in materials science, this class of functional dyes also has potential applications in the treatment of a range of cancers, infectious diseases,[2] and eye and neurodegenerative diseases;[3] most of them are related to the photocytotoxic effects of these compounds. For the medical applications, it is desirable that the macrocycles can be substituted with biocompatible moieties which can not only enhance the solubility of these compounds in biological media, but also promote cellular recognition and maintain the photoactivity of the phthalocyanine core by preventing its self-association.[4] To date, phthalocyanines conjugated with biological molecules are rare and only a few examples containing monosaccharides,[5] amino acids,[6] and antibodies[7] have been described. Although porphyrin–nucleobase and nucleoside conjugates have been studied extensively owing to their potential applications in molecular recognition, energy- and electron-transfer processes, and antiviral and anticancer therapies,[8] to our knowledge, analogous conjugates based on the structurally related phthalocyanine have not been reported. In this paper, we describe the first phthalocyanine–nucleobase conjugates including their synthesis and spectroscopic properties.

Treatment of tetrahydroxyphthalocyanine **1** (as a mixture of constitutional isomers)[9] with an excess of 9-(2-bromoethyl)adenine **2a** and K_2CO_3 led to the formation of adenine-containing phthalocyanine **3** (Scheme 1). The compound has poor solubility in most organic solvents and purification could only be achieved by column chromatography using DMF as eluent. The unsymmetrical analogues **4a** and **4b** were also prepared by treating **1** with an equiv. of (bromoalkyl)adenine **2a** or **2b**, followed by the addition of excess 1-bromopentane (Scheme 1). Due to the presence of three pentyloxy substituents, these unsymmetrical phthalocyanines are slightly soluble in $CHCl_3$, CH_2Cl_2 and toluene, but their solubility in MeOH, EtOH and water is still limited. Interestingly, the solubility of these compounds in $CHCl_3$ or CH_2Cl_2 is greatly increased by the addition of a small amount of MeOH. All these observations suggest that the intermolecular interactions of these adenine–phthalocyanine conjugates are substantial, and apart from the π–π interactions, intermolecular hydrogen bonding and/or axial coordination of the zinc(II) center with adenine[10] may also play a significant role.

All the new compounds were characterized with a range of spectroscopic methods.[11] The absorption spectrum of **3** in DMF showed strong Q and B band absorptions at 682 and 354 nm, respectively, indicating that **3** exists mainly as a monomeric species in DMF. Upon addition of $CHCl_3$, the intensity of these two bands decreased, while a new signal at 630 nm emerged which can be

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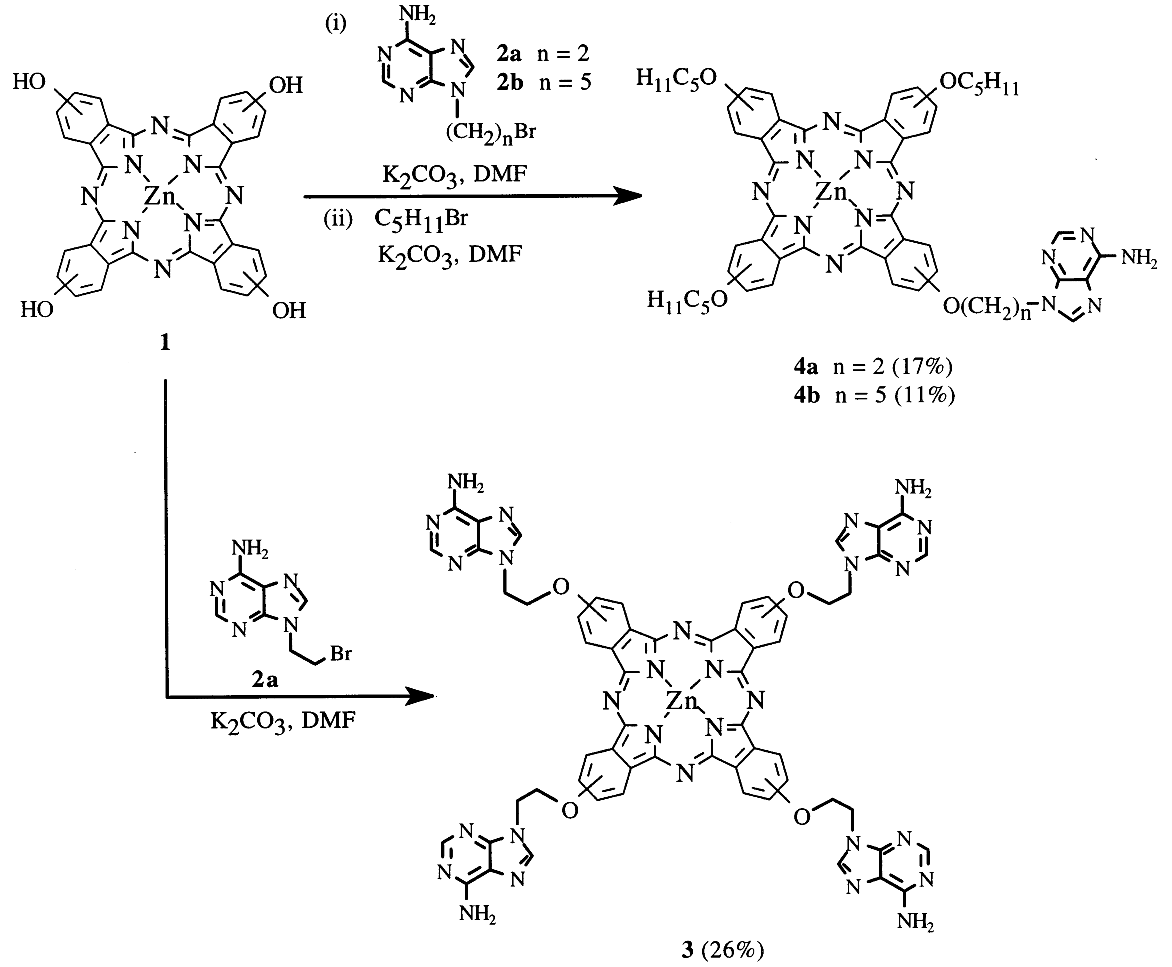
ascribed to an aggregated species.[12] These results showed that $CHCl_3$, being a poor solvent for **3**, induces molecular aggregation of this compound. This was corroborated with a decrease in fluorescence intensity ($\lambda_{ex} = 615$ nm, $\lambda_{em} = 686$ nm) with increasing $CHCl_3$ content.[13]



Scheme 1.

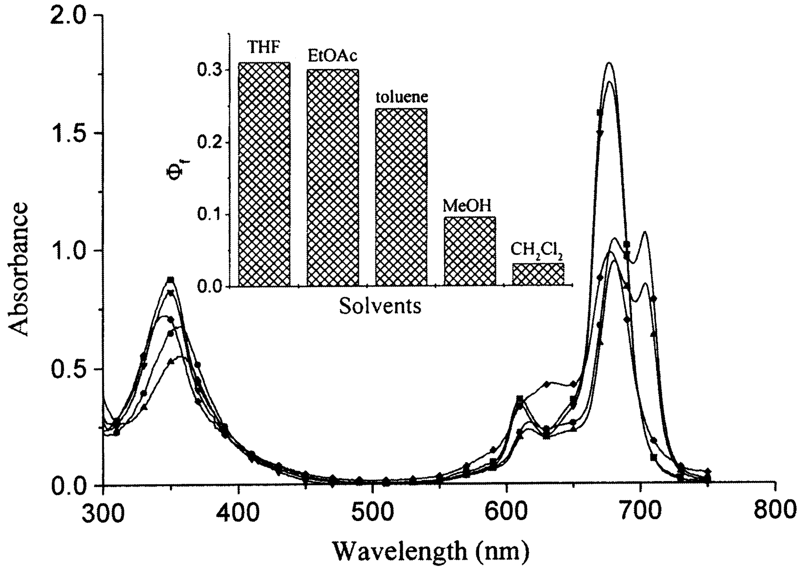


Figure 1. Absorption spectra and fluorescence quantum yields (inset) of **4a** in THF (■), EtOAc (▼), toluene (▲), MeOH (◆), or CH_2Cl_2 (●) (1.0×10^{-5} mol dm^{-3}).

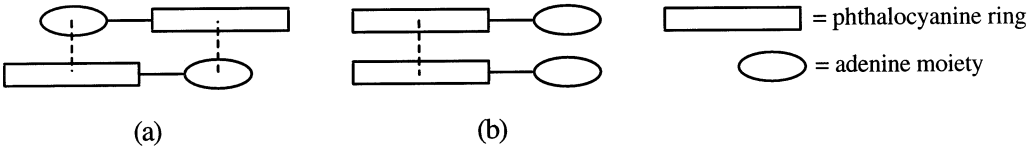


Figure 2. Schematic diagrams of (a) a head-to-tail or slipped face-to-face dimer of **4a** and (b) a normal face-to-face dimer of **4a**.

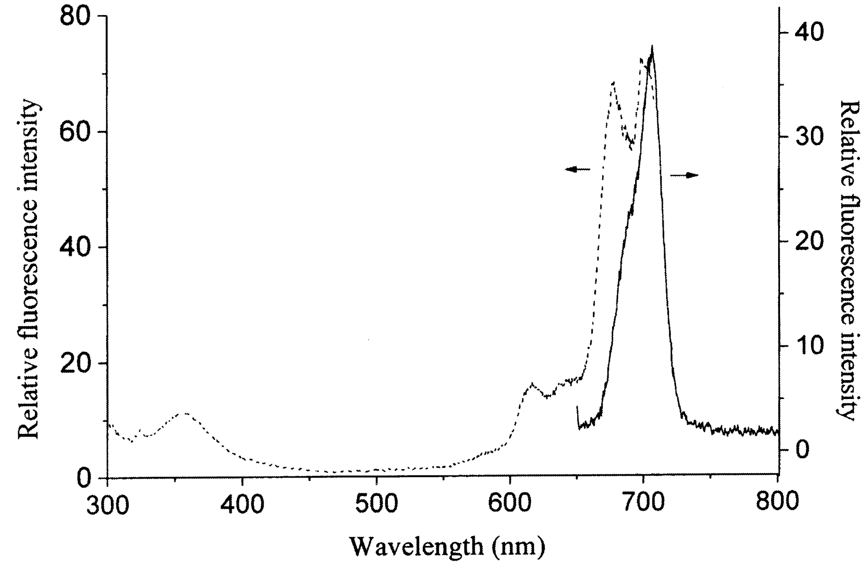


Figure 3. Fluorescence (solid line, excited at 610 nm) and excitation (dash, monitored at 710 nm) spectra of **4a** in toluene (5.0×10^{-6} mol dm^{-3}).

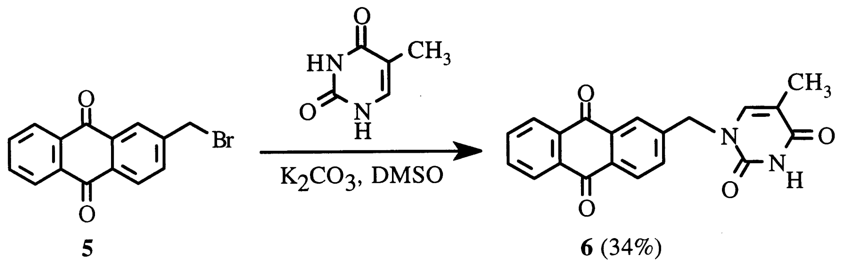
The UV–vis spectrum of **4a** is also solvent-dependent. As shown in Fig. 1, the spectra recorded in relatively polar solvents such as THF and ethyl acetate show a single Q band at 677 nm, which is characteristic of monomeric species. In CH_2Cl_2 or toluene, the Q band is split and slightly red-shifted. The two Q band absorptions were found to follow the Beer–Lambert law in CH_2Cl_2 (from 6.3×10^{-6} to 1.0×10^{-4} mol dm^{-3}). In MeOH, the spectrum displays a rather weak Q band at 677 nm and the band attributable to the aggregated species at 633 nm, suggesting that **4a** exhibits a rather high aggregation tendency under these conditions.

According to the molecular exciton model,[12c,14] the red-shifted Q bands observed for **4a** in CH_2Cl_2 and toluene may be attributed to a head-to-tail dimer (Fig. 2a), or a so-called J-aggregate, while the blue-shifted Q band observed in MeOH is due to a face-to-face dimer (Fig. 2b), or a so-called H-aggregate, which is commonly seen in many phthalocyanine systems.[12] The appearance of additional Q band at longer wavelength was also found for zinc(II) phthalocyanines with four 3-pentyloxy[15] or 2-ferrocenylethoxy moieties.[16] This band, however, is of a different nature with that observed in this case. For these macrocycles, the relative intensity of the 'normal' Q band and the red-shifted Q band decreases with decreasing concentration of phthalocyanine which is in contrast to the present case in which both Q bands for **4a** strictly follow the Beer–Lambert law.

Methanol thus appears to play a crucial role in controlling the mode of aggregation of **4a**. This solvent also has a great influence on the spectral properties of **4a** in CH_2Cl_2. Upon addition of a small amount of MeOH (up to 4%), the split Q band coalesced and intensified, and the fluorescence quantum yield increased from 0.03 to 0.30, showing that MeOH is very effective on disrupting molecular association of **4a** in CH_2Cl_2.

As shown in the inset of Fig. 1, the fluorescence quantum yield of **4a** also depends on the solvent. The values observed in THF and ethyl acetate (ca. 0.30) are typical for monomeric zinc(II) phthalocyanines,[17] while those measured in CH_2Cl_2, toluene or MeOH are significantly lower due to the formation of some kinds of dimers. Fig. 3 shows the fluorescence and excitation spectra of **4a** in toluene. It can be seen that the excitation spectrum closely resembles the absorption spectrum, showing that the two absorption bands in the red region belong to the same species (i.e. the slipped face-to-face dimer), which is emissive. It is worth noting that dimeric and aggregated phthalocyanines are normally not fluorescent due to an efficient internal conversion, and to our knowledge only one exception has been reported so far.[18]

The assignment of a slipped face-to-face dimer for the red-shifted Q bands of **4a** was further supported by the spectral features of **4b**. The absorption spectra of **4b** in various solvents such as THF, $CHCl_3$, toluene, CH_2Cl_2,



Scheme 2.

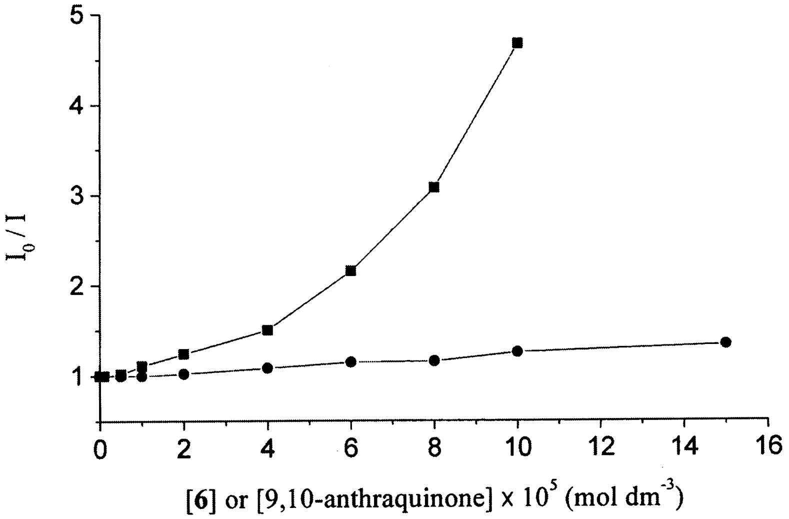


Figure 4. Stern–Volmer plots for the fluorescence quenching of **3** in DMF/THF (9:1) (3.0×10^{-6} mol dm^{-3}) by **6** (■) or 9,10-anthraquinone (●).

or MeOH showed only a single Q band at ca. 680 nm. Although the absorption intensity as well as the fluorescence quantum yield was solvent-dependent, split and red-shifted dimeric bands were not observed. This might arise from the larger separation between the phthalocyanine core and the adenine moiety in **4b** compared with **4a**, which hinders the formation of a stable cofacial dimer such as the one shown in Fig. 2(a).

To investigate the base-pairing effects of these adenine-containing phthalocyanines, the fluorescence quencher **6**, which contains a thymine moiety, was prepared by standard nucleophilic substitution of **5** with thymine (Scheme 2). Fig. 4 shows the Stern–Volmer plots for the fluorescence quenching of **3** with **6** and unsubstituted 9,10-anthraquinone. It can be seen that the fluorescence quenching is much faster when a thymine moiety is linked to the quencher, suggesting that the Watson–Crick base-pairing interactions between the adenine and thymine moieties are present. Such non-covalent interactions have been found to be important in the construction of supramolecular systems of porphyrin-nucleobase conjugates in which photo-induced electron- and energy-transfer processes occur readily.[8b,19] Under similar conditions, fluorescence quenching of **4a** and **4b** was found to be slow and the rate virtually did not depend whether or not a thymine moiety is linked to the quencher, suggesting that the two-point adenine–thymine interactions are rather weak in these mono-adenine systems.

In summary, we have reported the first nucleobase-containing phthalocyanines **3**, **4a**, and **4b**. Due to the presence of adenine substituent, these compounds possess strong intermolecular interactions which result in a poor solubility in common organic solvents and unusual spectral features.

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References

1. *Phthalocyanines—Properties and Applications*; Leznoff, C. C.; Lever, A. B. P., Eds.; VCH: New York, 1989, Vol. 1; 1993, Vols. 2 and 3; 1996, Vol. 4.
2. (a) Rouhi, A. M. *Chem. Eng. News* **1998**, November 2, 22. (b) Ali, H.; van Lier, J. E. *Chem. Rev.* **1999**, *99*, 2379.

3. (a) Rivellese, M. J.; Baumal, C. R. *Ophthal. Surg. Lasers* **1999**, *30*, 653. (b) Priola, S. A.; Raines, A.; Caughey, W. S. *Science* **2000**, *287*, 1503.
4. (a) Dhami, S.; Phillips, D. *J. Photochem. Photobiol. A: Chem.* **1996**, *100*, 77. (b) Lang, K.; Kubát, P.; Mosinger, J.; Wagnerová, D. M. *J. Photochem. Photobiol. A: Chem.* **1998**, *119*, 47.
5. Maillard, P.; Guerquin-Kern, J.-L.; Momenteau, M.; Gaspard, S. *J. Am. Chem. Soc.* **1989**, *111*, 9125.
6. (a) Dong, R. A.; Qiu, Y.; Song, X. Q.; Chen, D. W. *Chin. Chem. Lett.* **1996**, *7*, 399. (b) Dong, R.; Qiu, Y.; Tian, S.; Wang, S.; Song, X. *Sci. China (Ser. B)* **1998**, *41*, 45. (c) Drechsler, U.; Pfaff, M.; Hanack, M. *Eur. J. Org. Chem.* **1999**, 3441.
7. Carcenac, M.; Larroque, C.; Langlois, R.; van Lier, J. E.; Artus, J. C.; Pelegrin, A. *Photochem. Photobiol.* **1999**, *70*, 930.
8. See, for example: (a) Cornia, M.; Binacchi, S.; Del Soldato, T.; Zanardi, F.; Casiraghi, G. *J. Org. Chem.* **1995**, *60*, 4964 and references cited therein. (b) Sessler, J. L.; Wang, B.; Harriman, A. *J. Am. Chem. Soc.* **1995**, *117*, 704 and references cited therein. (c) Sirish, M.; Maiya, B. G. *J. Porphyrins Phthalocyanines* **1998**, *2*, 327. (d) Solladié, N.; Gross, M. *Tetrahedron Lett.* **1999**, *40*, 3359.
9. Leznoff, C. C.; Hu, M.; McArthur, C. R.; Qin, Y.; van Lier, J. E. *Can. J. Chem.* **1994**, *72*, 1990.
10. Axial coordination of zinc(II) porphyrins with an adenine moiety via the N1 site has been reported previously: Ogoshi, H.; Hatakeyama, H.; Kotani, J.; Kawashima, A.; Kuroda, Y. *J. Am. Chem. Soc.* **1991**, *113*, 8181.
11. Selected data for **3**: MS (MALDI-TOF) an isotopic cluster peaking at m/z 1284.80 (M^+); UV–vis (DMF) [λ_{max} nm ($\log \varepsilon$)] 354 (4.97), 613 (4.18), 682 (5.23). For **4a**: ^{1}H NMR ($CDCl_3/CD_3OD$) δ 6.7–8.5 (several br s, 14 H), 3.8–4.5 (br s, 8 H), 0.7–2.0 (several br s, 29 H); HRMS (FAB) m/z calcd for $C_{54}H_{54}N_{13}O_4Zn$ (MH^+) 1012.3707, found 1012.3706; UV–vis (THF) [λ_{max} nm ($\log \varepsilon$)] 350 (4.94), 610 (4.56), 677 (5.25). For **4b**: ^{1}H NMR ($CDCl_3/CD_3OD$) δ 6.7–8.5 (several br s, 14 H), 3.9–4.3 (br s, 8 H), 0.8–2.0 (several br s, 35 H); HRMS (LSI) m/z calcd for $C_{57}H_{60}N_{13}O_4Zn$ (MH^+) 1054.4177, found 1054.4276; UV–vis ($CHCl_3$) [λ_{max} nm ($\log \varepsilon$)] 350 (4.97), 615 (4.66), 682 (5.21). For **6**: ^{1}H NMR ($CDCl_3$) δ 8.47 (br s, 1 H), 8.30–8.35 (m, 3 H), 8.20 (d, $J = 1.5$ Hz, 1 H), 7.81–7.86 (m, 2 H), 7.75 (dd, $J = 8.1$, 1.8 Hz, 1 H), 7.05 (d, $J = 1.2$ Hz, 1 H), 5.05 (s, 2 H), 1.92 (s, 3 H); MS (EI) m/z 334 (M^+); Anal. Calcd for $C_{19}H_{14}N_2O_4$: C, 68.26; H, 4.22; N, 8.38. Found: C, 68.09; H, 4.13; N, 8.43.
12. (a) Yang, Y.-C.; Ward, J. R.; Seiders, R. P. *Inorg. Chem.* **1985**, *24*, 1765. (b) Schutte, W. J.; Sluyters-Rehbach, M.; Sluyters, J. H. *J. Phys. Chem.* **1993**, *97*, 6069. (c) Osburn, E. J.; Chau, L.-K.; Chen, S.-Y.; Collins, N.; O'Brien, D. F.; Armstrong, N. R. *Langmuir* **1996**, *12*, 4784.
13. Aggregation of phthalocyanines usually reduces the fluorescence emission, see for example: (a) Vacus, J.; Simon, J. *Adv. Mater.* **1995**, *7*, 797. (b) Kobayashi, N.; Higashi, R.; Ishii, K.; Hatsusaka, K.; Ohta, K. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 1263. (c) Li, X.-y.; He, X.; Ng, A. C. H.; Wu, C.; Ng, D. K. P. *Macromolecules* **2000**, *33*, 2119.
14. (a) Katayose, M.; Tai, S.; Kamijima, K.; Hagiwara, H.; Hayashi, N. *J. Chem. Soc.*, *Perkin Trans. 2* **1992**, 403. (b) Chau, L.-K.; England, C. D.; Chen, S.; Armstrong, N. R. *J. Phys. Chem.* **1993**, *97*, 2699. (c) Kroon, J. M.; Koehorst, R. B. M.; van Dijk, M.; Sanders, G. M.; Sudhölter, E. J. R. *J. Mater. Chem.* **1997**, *7*, 615.
15. Kasuga, K.; Asano, K.; Lin, L.; Sugimori, T.; Handa, M.; Abe, K.; Kikkawa, T.; Fujiwara, T. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 1859.
16. Poon, K.-W.; Yan, Y.; Li, X.-y.; Ng, D. K. P. *Organometallics* **1999**, *18*, 3528.
17. Ferraudi, G. In *Phthalocyanines—Properties and Applications*; Leznoff, C. C.; Lever, A. B. P., Eds.; VCH: New York, 1989; Vol. 1, pp. 291–340.
18. A fluorescent dimer of zinc(II) tetrasulfonated phthalocyanine has been reported recently which may also adopt a slipped face-to-face or tilted conformation in MeCN/water: Kaneko, Y.; Arai, T.; Tokumaru, K.; Matsunaga, D.; Sakuragi, H. *Chem. Lett.* **1996**, 345.
19. Berg, A.; Shuali, Z.; Asano-Someda, M.; Levanon, H.; Fuhs, M.; Möbius, K.; Wang, R.; Brown, C.; Sessler, J. L. *J. Am. Chem. Soc.* **1999**, *121*, 7433.