DOI: 10.1002/ejoc.200800317

Self-Assembled Azaphthalocyanine Dimers with Higher Fluorescence and Singlet Oxygen Quantum Yields than the Corresponding Monomers

Veronika Novakova,[a] Petr Zimcik,*[a] Kamil Kopecky,[a] Miroslav Miletin,[a] Jiří Kuneš,[b] and Kamil Lang[c]

Keywords: Aggregation / Electron transfer / Fluorescence / Phthalocyanines / Singlet oxygen

In this work, we describe diethylamino-substituted metal azaphthalocyanines that form self-assembled J-dimers in noncoordinating solvents. The dimers are formed by the coordination of the free electron pair of one diethylamino group with the central metal of the adjacent molecule. The addition of pyridine leads to monomerization and considerable quenching of fluorescence and singlet oxygen formation as a result of intramolecular photoinduced singlet electron transfer (PET). PET is efficiently inhibited in dimers; therefore, dimers have higher fluorescence and singlet oxygen quantum yields than the corresponding monomers.

Introduction

Phthalocyanines (Pc), the structural analogues of porphyrins, have been the subject of intense research activity due to their possible usage in fields such as catalytic chemistry, nonlinear optics and photochemistry, and they also have potential medical applications (e.g., photodynamic therapy, treatment of age-related macular degeneration).[1] The organization of molecular components through supramolecular assembly is a useful technique to obtain species with specific properties and morphology.[2] The structure of self-assembled molecular aggregates can be classified as H- or J-type according to the alignment of the transition dipole moments of the interacting monomeric units, either cofacial or edge-to-edge, respectively.[3] Despite many reports on the aggregation phenomena of Pc compounds,[4] very few of them have been focused on photophysical properties of dimers and higher aggregates. The majority of described Pc aggregates are nonfluorescent and nonphotosensitizing species of the H-type. Aggregation is often a disadvantage for the photosensitizing applications of Pc and other porphyrinoids, because the dynamics of excited aggregates becomes faster due to new nonradiative energy relaxation channels.[5] Only few assembled Pc structures exhibit fluorescence, mostly with less fluorescence quantum yields (Φ_F) than respective monomers.[6–11] The formation of singlet oxygen by Pc aggregates has not been reported yet.

We formulated the structure–photophysical activity relationship in an azaphthalocyanine (AzaPc) series of the tetrapyrazinoporphyrazine type.[12] The Φ_F and singlet oxygen quantum yields (Φ_Δ) markedly decreased upon the introduction of nitrogen heteroatoms connecting peripheral chains with the AzaPc moiety[12,13] or upon the addition of peripheral aliphatic tertiary amino groups. These changes indicate a contribution of a competitive nonradiative process.[14] The presence of amino groups leads to the quenching of structurally similar excited Pc[15,16] as a result of photoinduced electron transfer (PET) between the nitrogen donating atoms and the Pc moiety.

Herein, we describe the properties of self-assembled AzaPc dimers. The unique structural arrangement combined with intramolecular PET switches on fluorescence at longer wavelengths and strong singlet oxygen production.

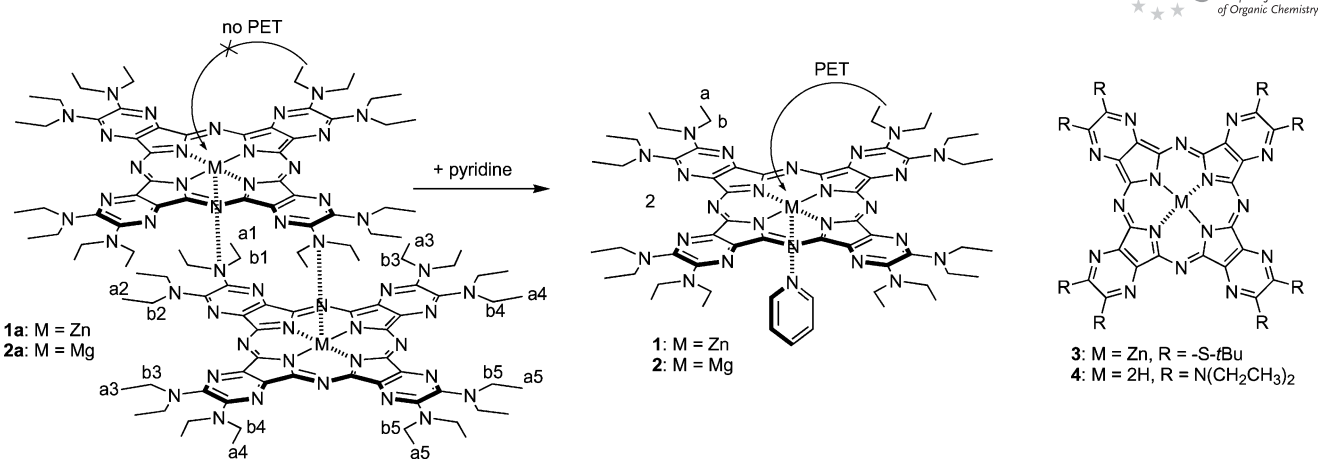
Results and Discussion

Zinc AzaPc **1**, its metal-free derivative **4** and AzaPc **3** (Scheme 1) were synthesized and purified following the procedures developed recently.[17,18] Magnesium AzaPc **2** was prepared by tetramerization of 5,6-bis(diethylamino)pyrazine-2,3-dicarbonitrile by using magnesium butoxide (see Supporting Information).

In coordinating solvents like pyridine, THF, or DMF, the absorption spectra of **1** and **2** were typical for monomeric AzaPc. The Beer law was obeyed up to the maximum concentration used for the measurements (1×10^{-4} M). In non-

[a] Department of Pharmaceutical Chemistry and Drug Control, Faculty of Pharmacy in Hradec Kralove, Charles University in Prague,
Heyrovskeho 1203, 50005 Hradec Kralove, Czech Republic
Fax: +420-49-5067167
E-mail: petr.zimcik@faf.cuni.cz
[b] Department of Inorganic and Organic Chemistry, Faculty of Pharmacy in Hradec Kralove, Charles University in Prague, Heyrovskeho 1203, 50005 Hradec Kralove, Czech Republic
[c] Institute of Inorganic Chemistry, v.v.i., Academy of Sciences of the Czech Republic,
25068 Řež, Czech Republic

Supporting information for this article is available on the WWW under http://www.eurjoc.org/ or from the author.



Scheme 1. Structures of AzaPc dimers (**1a** and **2a**) and monomers (**1** and **2**) in toluene; model AzaPc **3** and **4**; PET is inhibited within the dimer.

coordinating solvents, such as toluene, $CHCl_3$ and CH_2Cl_2, the spectra gained a broad and flat character with two resolved maxima at about 636 and 700 nm (Figure 1a). Such spectral features are typical for Pc and AzaPc dimers or aggregates.[17,19] Aggregation is caused by π–π stacking of planar macrocycles and aggregates usually "dissolve" upon dilution of a solution. In contrast, the J-dimers formed by coordinating the central metal by the peripheral substituents of the adjacent macrocycle are very stable.[6,20] Dimers **1a** and **2a** were unusually stable because no spectral changes were observed upon dilution of a 1×10^{-4} M solution to 3×10^{-8} M. Titration of a toluene solution with pyridine led to the reappearance of the intensive Q bands at 658 nm belonging to monomer AzaPc. Well-defined isosbestic points suggest the equilibrium of only two species in a solution, namely, monomer and J-type dimer of the proposed structure (Scheme 1). The presence of possible oligomers was not confirmed by any analytical method (NMR, UV/Vis). Their presence may be, however, possible, but only under the conditions that they are NMR silent and have the same absorption spectrum as the dimers.

The corresponding model compound **3** and metal-free derivative **4** stayed monomeric also in noncoordinating solvents. Small spectral changes were observed only at high concentrations and indicate some contribution of H aggregates.

The structure of the J-dimers was confirmed by ^1H NMR spectroscopy (Figure 2, see also Supporting Information, Figures S1, S2). The structural investigation of monomeric **1** and **2** was performed in [D_5]pyridine. The ^1H NMR spectra show one signal for all peripheral diethylamino groups due to the symmetrical structure of the studied molecules (Figure 2b). The spectra became more complicated in [D_8]toluene (or $CDCl_3$), which is indicative of the presence of isomeric structures with a reduced symmetry (Figure 2a). The multiplet at ca. 4.25 ppm with the intensity corresponding to one diethylamino group per one AzaPc molecule can be attributed to the b1 methylene groups of diethylamine, which is coordinated to the central Zn atom of the adjacent AzaPc molecule (Scheme 1). The

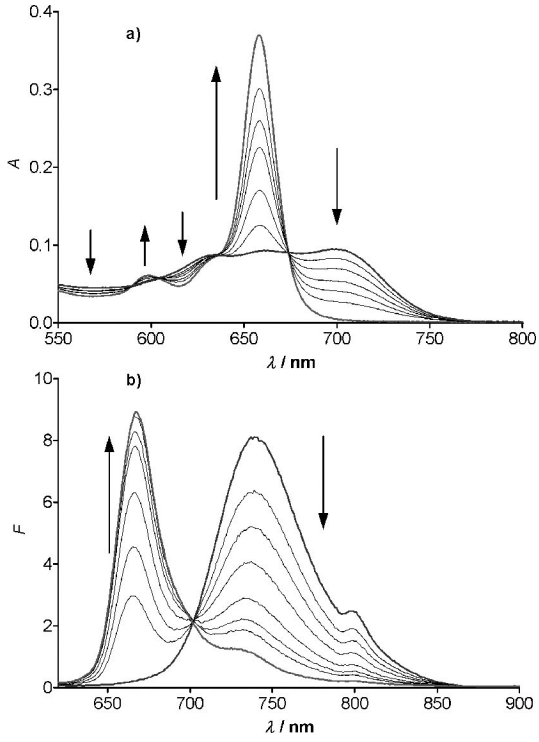


Figure 1. Absorption (a) and fluorescence emission (b) spectra of **1a** (1.0×10^{-6} M) in toluene. The arrows indicate the spectral changes induced by increasing the concentration of pyridine from 0 to 4.5×10^{-2} M. The excitation wavelength is at 605 nm (isosbestic point).

multiplet character is caused by overlapped quadruplets of two possible dimer isomers – parallel and oblique[20] (Supporting Information, Figure S3). The triplet at δ = 1.70 ppm was assigned to the a1 and a2 methyl groups on the basis of the homonuclear decoupling experiment. Furthermore, irradiation of the methyl hydrogen atoms at δ = 1.70 ppm removed the splitting of the multiplet of the b1 methylene group at δ = 4.25 ppm with the appearance of two singlet signals in a ca. 2:3 ratio. The attribution of these signals to the parallel and oblique isomers is still in ques-

tion. In summary, the ^{1}H NMR spectroscopic results indicate that a free electron pair of one diethylamino group coordinates with the central metal of the adjacent molecule to form closely stacked J-type dimers **1a** and **2a**, in which the AzaPc moieties are shifted with respect to each other (Scheme 1). In accordance with the dimerization model, the ^{1}H NMR spectra of **3** and **4** were quite similar in both [D_5]-pyridine and [D_8]toluene, because coordination bonding is not possible.

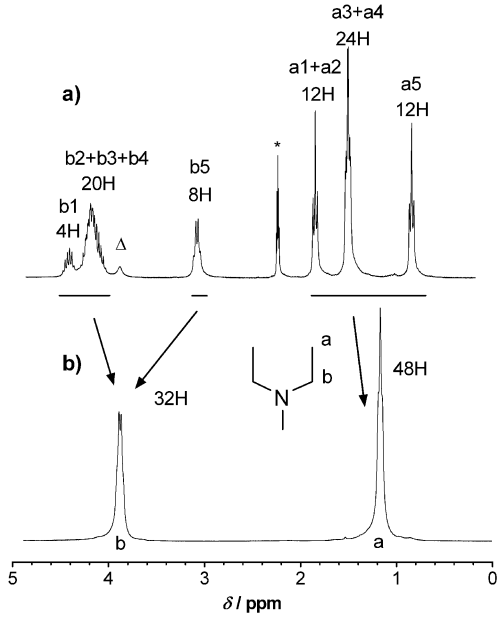


Figure 2. ^{1}H NMR spectra of (a) **1a** in [D_8]toluene and (b) **1** in [D_5]pyridine. The symbols (*) and (Δ) indicate residuals of nondeuterated toluene and water, respectively. Labelling of protons is in Scheme 1.

Derivative **3** in pyridine and toluene showed fluorescence properties typical for the monomeric AzaPc moiety, that is, high Φ_F and emission maxima at 660 nm. The Φ_F values are affected minimally by the solvent (Table 1) and a small decrease in Φ_F in toluene can be explained by a minor contribution of nonfluorescent H aggregates. Though **1** and **2** were monomeric in pyridine, they had no fluorescence. These observations can be attributed to the quenching of the excited singlet states by the eight diethylamino substituents as a result of effective intramolecular PET. Contrary to most Pc dimers, both **1a** and **2a** showed fluorescence. The fluorescence band at 738 nm can be assigned to emission of **1a** and **2a**, because of good correlation between fluorescence excitation and absorption spectra (Supporting Information, Figure S4). In order to corroborate the proposed model, we carried out stepwise titration of a toluene solution of **1a** with pyridine (Figure 1b). The emission intensity at 738 nm (dimer) decreased with a concomitant increase in emission at 665 nm as a result of an increasing contribution of monomer **1**. Dimer **2a** needed higher pyridine concentrations to induce monomerization, which is indicative of stronger coordination between the central Mg atom and the diethylamino groups within the dimer.

Table 1. Quantum yields and lifetimes of the studied AzaPc molecules.

	Pyridine (monomer)	Toluene/pyridine (monomer)[c]	Toluene (dimer, except for **3**)
Φ_Δ[a]			
1 or **1a**	0.020	0.070	0.29
2 or **2a**	0.013	0.019	0.10
3	0.65	0.68	0.50
Φ_F[a]			
1 or **1a**	n.d.[b]	0.0041	0.0071
2 or **2a**	n.d.[b]	0.0052	0.0099
3	0.30	0.25	0.24
τ_F /ns			
1 or **1a**	n.d.[b]	0.13	0.62 (37.6%), 0.92 (62.4%)
2 or **2a**	n.d.[b]	0.08	0.83 (32.6%), 1.44 (67.4%)
3	2.49	–	2.61

[a] Mean of three independent measurements, estimated error ±15%. No changes in absorption spectra were observed during the measurements. [b] Not detected. [c] Pyridine 1% (v/v) for **1**, 15% (v/v) for **2**.

As mentioned above, the fluorescence emission of monomers **1** and **2** was completely quenched in pure pyridine. As the thermodynamic feasibility of PET decreases in nonpolar solvents,[21] the monomer emission is partially restored in toluene with a small amount of pyridine (Figure 1b) that induces complete monomerization. The Φ_F values of dimers **1a** and **2a** (Table 1) were, surprisingly, almost double than those of the corresponding monomers, which indicates that competitive PET is further suppressed after the formation of the dimer.

The fluorescence properties are complemented by the fluorescence lifetime analysis. The lifetime of **3** is only slightly affected by the solvent. The formation of dimers **1a** and **2a** is accompanied by a considerable decrease in the lifetimes. These results are in line with the general behavior of aggregate structures expressed also by the low Φ_F values. The fluorescence curves were best fit by two exponentials, which might indicate an equilibrium of at least two structurally different arrangements of the AzaPc moieties within the dimers. Monomers **1** and **2** formed in the presence of small amounts of pyridine have very short lifetimes of 130 and 80 ps, respectively, as a result of effective PET.

Singlet oxygen quantum yields (Φ_Δ) were determined by the comparative method[22] with ZnPc as a reference (Table 1). Model compound **3** with no PET showed high quantum yields in all solvents. In accordance with the fluorescence behaviour, the Φ_Δ values of monomers **1** and **2** were very low in pyridine because of efficient PET, and they were slightly higher in toluene/pyridine because of partial suppression of PET in a nonpolar environment. However, dimers **1a** and **2a** in pure toluene had about one order of magnitude larger Φ_Δ values than those of the corresponding monomers in pure pyridine. The Φ_Δ value of **1a** is even in the range typical for sensitizers used in clinical practice for photodynamic therapy (PDT).[23] These results document that the stacking of **1** and **2** inhibits PET, which leads to a large increase in the singlet oxygen productivity.

Conclusions

We described the formation of self-assembled AzaPc J-dimers that efficiently produce both fluorescence and singlet oxygen. Furthermore, they exhibit much higher Φ_F and Φ_Δ values than those of the corresponding monomers as a consequence of the inhibition of competitive PET. To the best of our knowledge, this is the first example of AzaPc or Pc aggregates that are efficient producers of singlet oxygen. Building of stable supramolecular constructs with suitable spectral, photophysical and photochemical properties opens new possibilities for the use of these dimers in applications connected with the production of singlet oxygen, for example, PDT or photocatalysis. The shift in the excitation wavelength closer to the red spectral region and the high Φ_Δ value can be taken into account in the design of novel photosensitizers for PDT. In addition, switching on fluorescence emission at higher wavelengths can be well suited for detection purposes.

Supporting Information (see footnote on the first page of this article): Synthesis of compound **2**; NMR spectra of dimer **2a** and **4**; description of fluorescence and singlet oxygen measurements; additional UV/Vis and fluorescence spectra of monomers and dimers.

Acknowledgments

This work was supported by a Research Project of the Ministry of Education, Youth and Sports of the Czech Republic (MSM0021620822).

[1] K. M. Kadish, K. M. Smith, R. Guilard (Eds.), *The Porphyrin Handbook*, Elsevier, USA, **2003**, vol. 19.
[2] K. Ogawa, Y. Kobuke, *J. Photochem. Photobiol. C: Photochem. Rev.* **2006**, *7*, 1–16.
[3] M. Kasha, H. R. Rawls, M. A. El-Bayoumi, *Pure Appl. Chem.* **1965**, *11*, 371.
[4] A. W. Snow in *The Porphyrin Handbook* (Eds.: K. M. Kadish, K. M. Smith, R. Guilard), Elsevier, USA, **2003**, vol. 17, pp. 129–176.
[5] K. Lang, J. Mosinger, D. M. Wagnerová, *Coord. Chem. Rev.* **2004**, *248*, 321–350.
[6] X. Huang, F. Q. Zhao, Z. Y. Li, L. Huang, Y. W. Tang, F. S. Zhang, C. H. Tung, *Chem. Lett.* **2007**, *36*, 108–109.
[7] X. Y. Li, D. K. P. Ng, *Tetrahedron Lett.* **2001**, *42*, 305–309.
[8] N. M. Speirs, W. J. Ebenezer, A. C. Jones, *Photochem. Photobiol.* **2002**, *76*, 247–251.
[9] C. Farren, S. FitzGerald, A. Beeby, M. R. Bryce, *Chem. Commun.* **2002**, 572–573.
[10] S. FitzGerald, C. Farren, C. F. Stanley, A. Beeby, M. R. Bryce, *Photochem. Photobiol. Sci.* **2002**, *1*, 581–587.
[11] L. Oddos-Marcel, F. Madeore, A. Bock, D. Neher, A. Ferencz, H. Rengel, G. Wagner, C. Kryschi, H. P. Trommsdorff, *J. Phys. Chem.* **1996**, *100*, 11850–11856.
[12] P. Zimcik, M. Miletin, M. Kostka, J. Schwarz, Z. Musil, K. Kopecky, *J. Photochem. Photobiol. A: Chem.* **2004**, *163*, 21–28.
[13] P. Zimcik, M. Miletin, Z. Musil, K. Kopecky, D. Slajsova, *Dyes Pigm.* **2008**, *77*, 281–287.
[14] P. Zimcik, M. Miletin, Z. Musil, K. Kopecky, L. Kubza, D. Brault, *J. Photochem. Photobiol. A: Chem.* **2006**, *183*, 59–69.
[15] M. E. Daraio, A. Völker, P. F. Aramendía, E. San Román, *Langmuir* **1996**, *12*, 2932–2938.
[16] P. C. Lo, J. D. Huang, D. Y. Y. Cheng, E. Y. M. Chan, W. P. Fong, W. H. Ko, D. K. P. Ng, *Chem. Eur. J.* **2004**, *10*, 4831–4838.
[17] M. Kostka, P. Zimcik, M. Miletin, P. Klemera, K. Kopecky, Z. Musil, *J. Photochem. Photobiol. A: Chem.* **2006**, *178*, 16–25.
[18] P. Petrik, P. Zimcik, K. Kopecky, Z. Musil, M. Miletin, V. Loukotova, *J. Porphyrins Phthalocyanines* **2007**, *11*, 487–495.
[19] M. T. M. Choi, P. P. S. Li, D. K. P. Ng, *Tetrahedron* **2000**, *56*, 3881–3887.
[20] K. Kameyama, M. Morisue, A. Satake, Y. Kobuke, *Angew. Chem. Int. Ed.* **2005**, *44*, 4763–4766.
[21] L. Fajari, P. Fors, K. Lang, S. Nonell, F. R. Trull, *J. Photochem. Photobiol. A: Chem.* **1996**, *93*, 119–128.
[22] Z. Musil, P. Zimcik, M. Miletin, K. Kopecky, M. Link, P. Petrik, J. Schwarz, *J. Porphyrins Phthalocyanines* **2006**, *10*, 122–131.
[23] R. W. Redmond, J. N. Gamlin, *Photochem. Photobiol.* **1999**, *70*, 391–475.

Received: March 26, 2008
Published Online: May 20, 2008

