

Photosensitizing Properties of Diazaporphyrin Derivatives for Singlet Oxygen Generation

Hideyuki Shinmori,* Fumiaki Kodaira, Seiichi Matsugo, Shigeki Kawabata,[†] and Atsuhiko Osuka^{††}
 Graduate School of Medical and Engineering Science, University of Yamanashi, 4-3-11 Takeda, Kofu, Yamanashi 400-8511
[†]Faculty of Engineering, Toyama Prefectural University, 5180 Kurokawa, Kosugi-machi, Toyama 939-0398
^{††}Department of Chemistry, Graduate School of Science, Kyoto University, Sakyo-ku, Kyoto 606-8502

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Diazaporphyrin derivatives (H₂DAP and ZnDAP) are shown to possess photosensitizing ability of the singlet oxygen generation in toluene with quantum yields of 0.92 and 0.84 for H₂DAP and ZnDAP, respectively.

Photodynamic therapy (PDT) has been shown to be a particularly effective treatment for certain types of tumors.¹ This therapy is performed with photosensitizers that generate the reactive oxygen species such as the singlet oxygen in the presence of light and oxygen.^{1,2} In the PDT studied, many novel porphyrin-based photosensitizers have been explored.^{3,4} Photosensitized Type II reactions can occur through energy transfer from the triplet excited state of a sensitizer to the oxygen to produce the singlet oxygen. In the clinical level, however, a lot of problems on PDT are pointed out, including the selectivity to cancer cell, the light penetration of the biological tissue, and the efficiency for the production of the singlet oxygen etc. Recently, a new class of porphyrin-like photosensitizer⁵ in which one or more of the pyrrolic nitrogens are replaced with other heteroatoms have been synthesized and their physical properties and the singlet oxygen generation have been investigated. But these core-modified porphyrins do not show the strong red light absorption, which is one of the most desirable properties for the photosensitizers since the red light penetrates the tissue more deeply with minimal light loss to biological cells. In this connection, replacement of one or more of the bridging carbons at *meso* positions of the porphyrin ring with nitrogen atoms leads to azaporphyrins,⁶⁻¹⁰ which, the formal hybrid of phthalocyanine and porphyrin, are an interesting chromophore because of red-shifted and intensified Q-bands compared with those of porphyrins.^{7c}

In this paper, we report the photosensitizing properties for singlet oxygen generation from diazaporphyrins bearing two nitrogen atoms at 5-, 15-positions (H₂DAP and ZnDAP shown in Figure 1). Figure 2 shows the absorption spectra of H₂DAP and ZnDAP.^{8a,11} In the case of H₂DAP, the Q-bands appear at 545 and 625 nm with molecular coefficients of 3.8×10^4 and $7.3 \times 10^4 \text{ M}^{-1} \text{ cm}^{-1}$, respectively, in toluene. On the basis of this spectrum, the S₁-state energy of H₂DAP is quite similar to that of octaethylporphyrin (OEP). Substantially intensified Q-bands can be regarded as a favorable feature for PDT therapy. The absorption spectrum of ZnDAP shows a very intense Q-band at 589 nm ($\epsilon = 1.4 \times 10^5 \text{ M}^{-1} \text{ cm}^{-1}$), suggesting that the red light is well absorbed by this sensitizer.

The singlet oxygen generation profiles were studied by means of photooxidation of 1,3-diphenylisobenzofuran (DPBF) using a halogen lamp attached to light filter.¹² The photoirradiation (470–610 nm) of a H₂DAP or ZnDAP solution containing DPBF caused obvious absorption spectral changes associated with the degradation of DPBF, which was monitored by absorp-

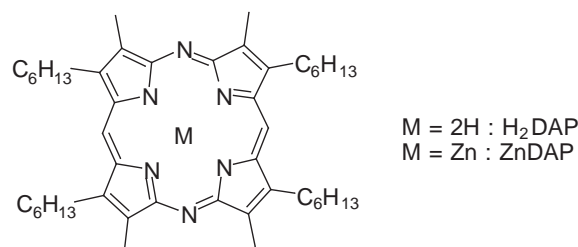


Figure 1. Structures of diazaporphyrins.

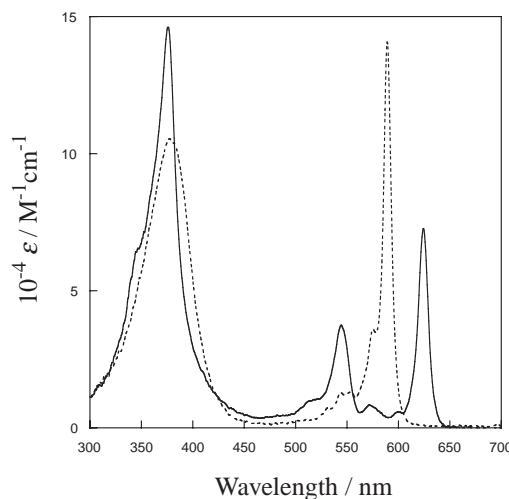


Figure 2. Absorption spectra of H₂DAP (solid line) and ZnDAP (dotted line) in toluene.

ance decrease at 417 nm (λ_{max} of DPBF). The absorption spectral features of H₂DAP or ZnDAP were not affected significantly by the photoirradiation, indicating high stability under these illuminating conditions. Plots of the absorbance changes at 417 nm against photoirradiation time are shown in Figure 3 to compare with OEP derivatives and phthalocyanine (Pc). It is clear that H₂DAP and ZnDAP are more effective than Pc, OEP, and ZnOEP, hence indicating that H₂DAP and ZnDAP are more efficient sensitizers for the singlet oxygen. Based on these results, the quantum yields of singlet oxygen formation (ϕ_{Δ}) in toluene were determined by comparing to DPBF decomposition of a standard compound, namely, *meso*-tetraphenylporphyrin ($\phi_{\Delta s} = 0.73$).^{12b} It is interesting to note that Pc which can be regarded as a tetraazaporphyrin derivative was a poorer photosensitizer with $\phi_{\Delta} = 0.16$. While the quantum yield of ZnDAP ($\phi_{\Delta} = 0.84$) was similar to that of ZnOEP ($\phi_{\Delta} = 0.84$), H₂DAP exhibited much higher quantum yield ($\phi_{\Delta} = 0.92$) than the observed value for OEP ($\phi_{\Delta} = 0.51$). The observed high quantum

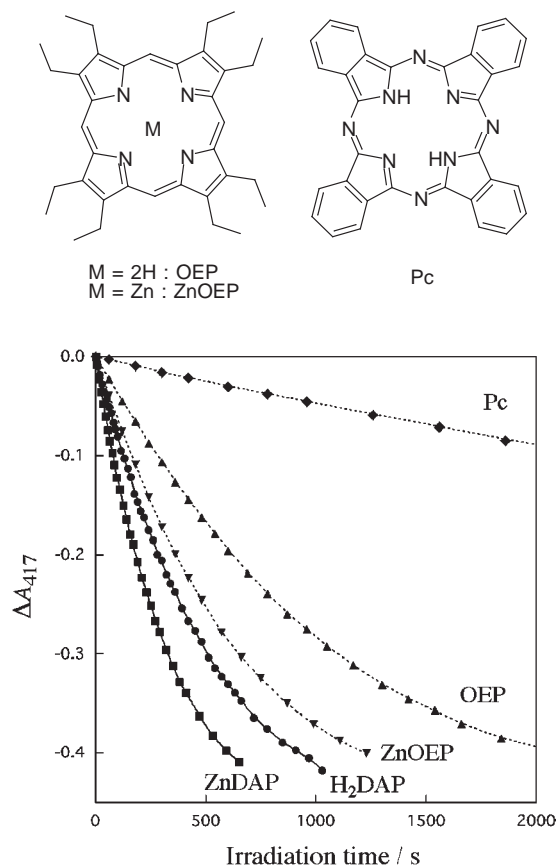


Figure 3. Photooxidation of DPBF with diazaporphyrins, OEP derivatives and Pc in toluene; $[H_2DAP] = [ZnDAP] = [OEP] = [ZnOEP] = [Pc] = 1.0 \times 10^{-6} M$, $[DPBF] = 2.0 \times 10^{-5} M$.

yields of H_2DAP and $ZnDAP$ are comparable to that of the Photofrin[®] ($\phi_{\Delta} = 0.89$),^{3b} which has been proved its efficacy in the treatment of patients worldwide on the PDT. To confirm the singlet oxygen generation, its emission around 1270 nm was detected¹³ by means of high sensitive near infrared detection system, which comprised of a spectroscope, a photon counter, and a multichannel detector (NIR-PII from Hamamatsu Photonics Co.) attached to a second harmonic generated YAG laser (532 nm) for the excitation. Indeed, emission band was observed at 1275 nm from both H_2DAP and $ZnDAP$, suggesting the production of singlet oxygen due to the energy transfer through the triplet states of the photosensitizers. The emission intensity at 1275 nm for H_2DAP was 1.3 times as large as that of $ZnDAP$, indicating that H_2DAP was more suitable for the singlet oxygen generation.

In summary, the diazaporphyrins H_2DAP and $ZnDAP$ have been shown to be very effective photosensitizers for the single oxygen generation. This may be arising from effective absorption of low energy light in the visible region. Further development of this approach and more extensive biological studies will be reported elsewhere.

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