π-Extended Porphyrin-based Photosensitizers for Singlet Oxygen Generation

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In photodynamic therapy (PDT) for cancer, singlet oxygen ($^1O_2$) destroys tumor vasculature, directly kills tumor tissue and cells, and induces an immune response.[1-3] The use of near-infrared (NIR) light in PDT is an effective therapeutic approach due to its good tissue penetration and radiation safety. Porphyrins have a low extinction coefficient in the absorption spectrum above 600 nm. Therefore, for deep tissue PDT, various derivatives with a porphyrin core structure have been synthesized to access energy in the NIR region and produce $^1O_2$.[4] We already reported a π-extended porphyrin-based photosensitizer, **rTPA** (Figure 1), which can efficiently use NIR light and produce $^1O_2$.[5] In this study, novel **rTPA** derivatives are developed and further explored based on an original **rTPA** as the core structure to invent more efficient and promising compounds for PDT.

The **rTPA** derivatives exhibited similar absorption spectra to the original **rTPA**, indicating that the π-conjugated structure or the hydrocarbon chains do not significantly affect the intrinsic photophysical properties of rTPA. Among them, **rTPA-NH$_2$** showed a slightly generation of $^1O_2$. Meanwhile, the absorption intensity of **rTPA-OH** decreased during photoexcitation, which may be due to the aggregation caused by the interaction of the hydroxy groups and the zinc atom in **rTPA-OH**. Next, we labeled GFP-expressing PCI55 cells with the derivatives. In the CLM observations, the fluorescence in the 500-540 nm range showed the emission from GFP, and 690-740 nm showed the emission from **rTPA** or an **rTPA** derivative, demonstrating the localization of **rTPA** or its derivatives on the periphery of cells.

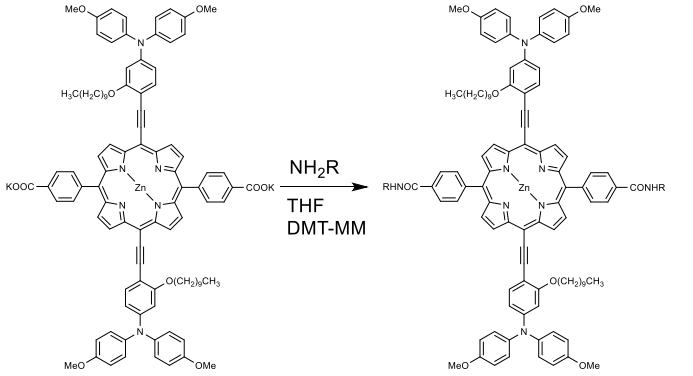

Figure 1. The structure of **rTPA** and the reaction scheme to prepare **rTPA** derivatives.

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