

Synthesis and Spectral Properties of *gem*-Dimethyl Chlorin Photosensitizers

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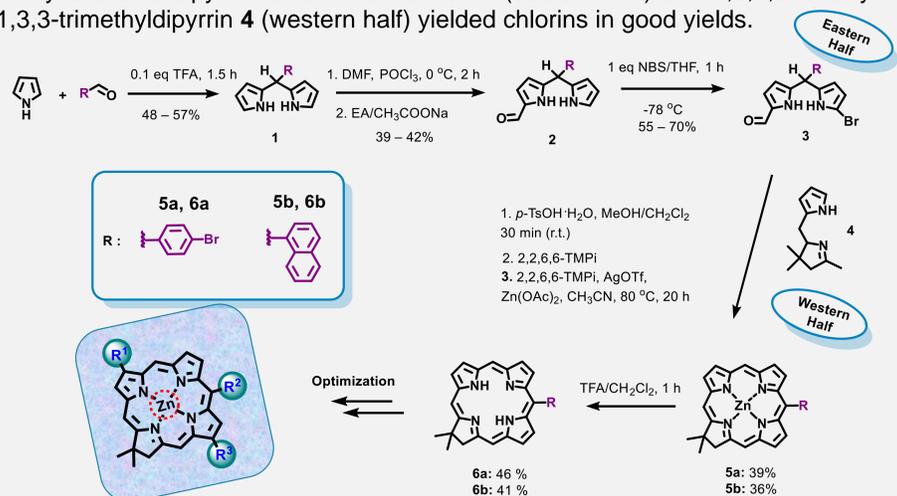
Introduction

Photodynamic therapy (PDT) is a developing non-invasive targeted therapy which involves systemic or topical administration of a drug, photosensitizer (PS), which after irradiation of a specific wavelength of light reacts with the coexisting molecular oxygen. As a result, highly reactive singlet oxygen (1O_2) and other reactive oxygen species (ROS) can be formed leading to specific apoptotic or necrotic cell death of the cancer cells.¹ Therefore, the generation of singlet oxygen is an important requirement of any potential PS in PDT.

Herein, we present two zinc(II)dihydroporphyrins (chlorins) and their free base counterparts (Scheme 1), which bear a *gem*-dimethyl group, attributing resistance to oxidation. These compounds have potential use as anticancer or antimicrobial agents as they generate singlet oxygen in good yields, steady state (Figure 1 and 2) and time-resolved spectroscopy (Figure 3) have been performed and Table 1 summarizes the photophysical properties of the chlorins in polar solvents (ethanol and methanol).²

Results / Synthesis

Scheme 1. Synthesis of the chlorins **5a-b** and **6a-b**. Synthesis was performed following a method reported by Lindsey and co-workers.³ A [2+2] condensation of 1-formyl-9-bromo-dipyrromethane derivatives **3** (eastern half) and 2,3,4,5-tetrahydro-1,3,3-trimethyldipyririn **4** (western half) yielded chlorins in good yields.



Results / Spectral properties

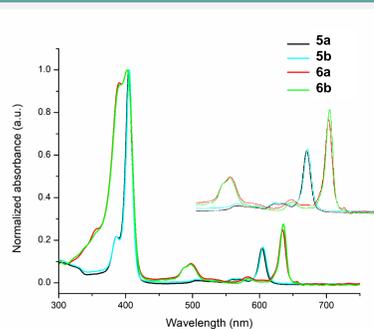


Figure 1. UV-Vis absorption spectra of the chlorins in ethanol. Spectra are normalized at the maximum of the B bands, with an inset showing the Q-bands between ca. 450 – 700 nm.

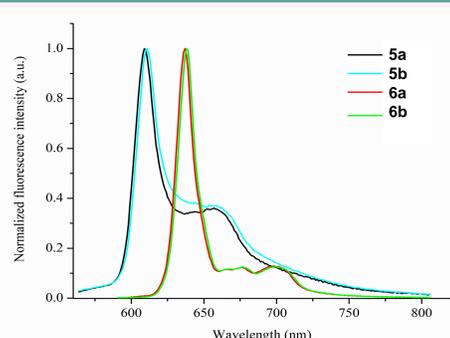


Figure 2. Normalized fluorescence emission spectra of the chlorins in ethanol.

Results / Spectral properties

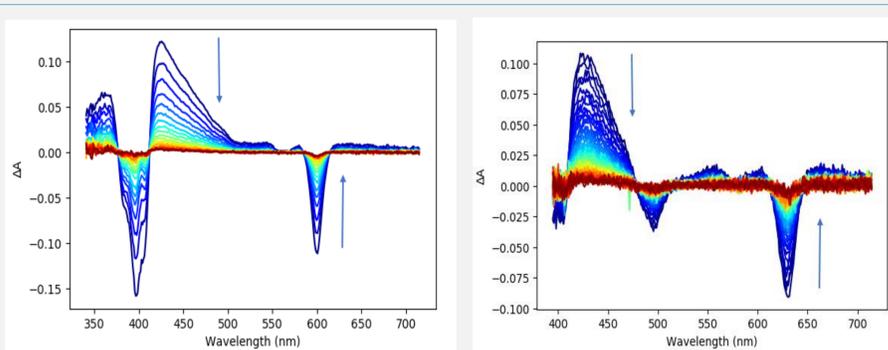


Figure 3. TA spectra of **5a** in methanol (ambient conditions; incremental time 40 ns; 604 nm λ_{exc}) on the left; TA spectra of **6a** in methanol (oxygen free conditions; incremental time 3000 ns; 637 nm λ_{exc}) on the right (arrows from blue to red color show the decay from the maximum intensity in the successive steps respectively).

Table 1. Photophysical properties of the chlorins.

Chlorin	λ_{em} (nm)	τ_s^a (ns)	τ_T^b (ns)	τ_T^c (μ s)	Φ_{isc}^d	Φ_f^e	Φ_{Δ}^f
5a *	609	0.9	200	27	0.80	0.03	0.58
5a **	609	0.9	202	26	0.94	0.04	0.90
5b *	611	1.5	210	28	0.78	0.05	0.55
5b **	611	1.5	210	30	0.88	0.08	0.85
6a *	637	5	160	47	0.78	0.07	0.40
6a **	637	5	170	70	0.80	0.08	0.70
6b *	637	7	150	50	0.70	0.10	0.38
6b **	638	7	166	64	0.75	0.14	0.60

* MeOH; ** EtOH; ^a singlet state lifetime in air (equilibrated); ^b triplet state lifetime in air (equilibrated); ^c triplet state lifetime in oxygen free solution; ^d triplet state quantum yield; ^e fluorescence quantum yield; ^f singlet oxygen quantum yield.

Summary / Conclusion

- ✓ Chlorins are potential PSs candidates themselves or they can act as building blocks for PSs.
- ✓ Both zinc(II) chlorins (**5a-b**) exhibit high triplet state yields ($\Phi_{isc} = 0.70$ – 0.90) and excellent singlet oxygen quantum yields in methanol and ethanol ($\Phi_{\Delta} = 0.60$ – 0.85). In comparison the free base analogues (**6a-b**) exhibited suitable singlet oxygen quantum yields ($\Phi_{\Delta} = 0.40$ – 0.70).
- ✓ Future work includes the optimization of the photophysical properties of the chlorins and enhancing the water solubility through modification of the periphery with a variety of substituents.
- ✓ Additionally, *in vitro* evaluation will be employed in future.

References

[1] A. Wiehe, J. M. O'Brien, M. O. Senge, *Photochem. Photobiol. Sci.* **2019**, 18, 11, 2565-2612; [2] Z. Melissari, H. C. Sample, B. Twamley, R. M. Williams, M. O. Senge, *ChemPhotoChem* **2020**, 4, 601–611; [3] (a) M. Ptaszek, B. E. McDowell, M. Taniguchi, H. Kim, J. S. Lindsey, *Tetrahedron* **2007**, 63, 18, 3826-3839; (b) O. Mass, M. Ptaszek, M. Taniguchi, J. R. Diers, H. L. Kee, D. F. Bocian, D. Holten, J. S. Lindsey, *J. Org. Chem.* **2009**, 74, 15, 5276-5289.

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