Synthesis and photophysical studies of a chlorin sterically designed to prevent self-aggregation

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INTRODUCTION

Chlorins are obtained by reduction of one double bond at the β position of the porphyrin ring (Figure 1).

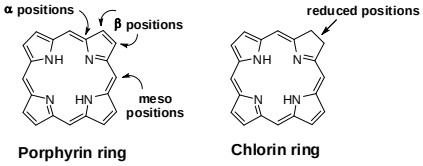
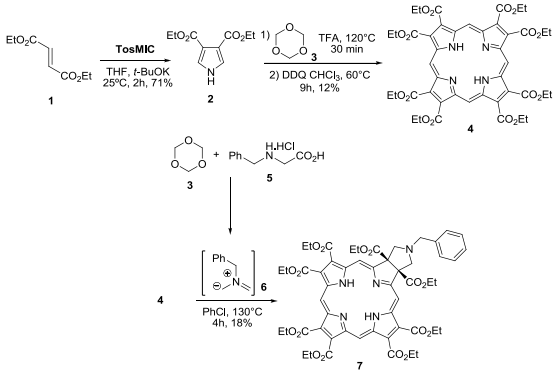


Figure 1. Porphyrin and chlorin core structures.

The chlorins exhibit a strong absorption band around 660 nm, which suggests use in photodynamic therapy (PDT).[1] Due to the extended conjugated core structure, they often suffer self-aggregation, which is a negative point for application in PDT. In this work, we have prepared a new chlorin derivative which is self-prevented from aggregation, by a 1,3-dipolar cycloaddition between a very activated porphyrin (dipolarophile) and a benzyl azomethine ylide.[2] We have also performed some preliminary photophysical studies in order to evaluate its ability to act as a photosensitizer in PDT.

RESULTS AND DISCUSSION

Our approach started from pyrrole **2**, prepared from diethyl fumarate (**1**) and *p*-toluenesulfonylmethyl isocyanide (TosMIC) in 71% yield (Scheme 1). Compound **2** was used as the building block in the synthesis of porphyrin **4**, utilizing trioxane (**3**) and TFA (Scheme 1). A 1,3-dipolar cycloaddition reaction was then performed with porphyrin **4**, using benzyl azomethine ylide **6**, generated *in situ* from trioxane (**3**) and *N*-benzylglycine hydrochloride (**5**). Chlorin **7** was obtained in 18% yield after purification by preparative TLC. Aggregation studies were carried out using two different techniques: UV-Vis and ^{1}H NMR. Measurements were performed in different concentrations using chloroform as solvent. In the NMR studies, the range of concentrations was much higher than for the UV-Vis analysis, and even in that case, chlorin **7** exhibited no aggregation (Figure 2).



Scheme 1. Synthesis of chlorin **7**.

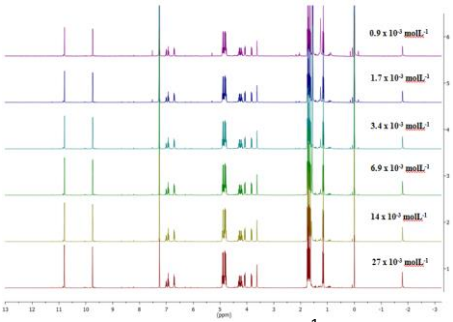


Figure 2. Aggregation studies by ^{1}H NMR in $CDCl_3$.

Other measurements such as singlet oxygen production, fluorescence yield, and photo degradation studies were also performed, providing good results as demonstrated in our recent publication in *Dyes and Pigments*.[2]

CONCLUSION

We conclude that chlorin **7** is a good candidate for PDT studies, due to its low-aggregation character and very good photophysical properties for PDT studies.

ACKNOWLEDGEMENTS

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[2] de Assis, F. F.; de Souza, J. M.; Assis, B. H. K.; Brocksom, T. J.; de Oliveira, K. T. *Dyes and Pigments* **2013**, *98*, 153.