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). 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. 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 1H 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).

Figure 2. Aggregation studies by 1H NMR in CDCl3.

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.

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.

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