



Original Research Article

Photosensitization of phthalocyanine for singlet oxygen generation in photodynamic therapy applications

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KEYWORDS

Phthalocyanine

Photosensitizer

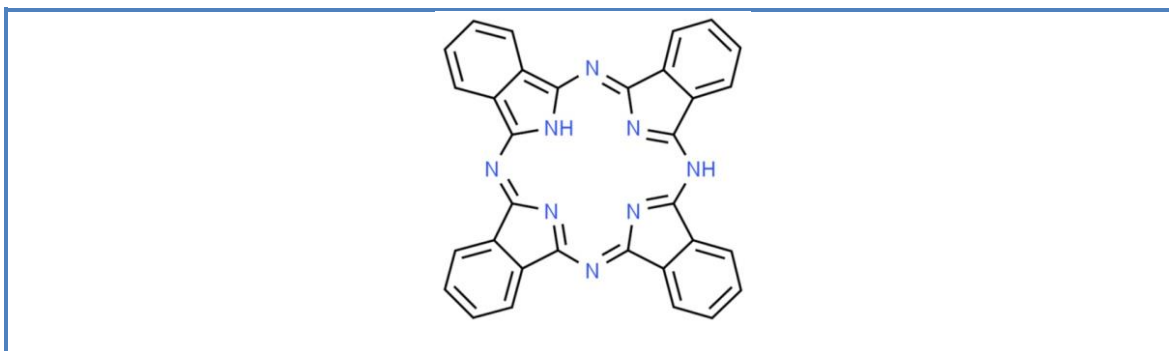
Singlet molecular oxygen

Density functional theory

ABSTRACT

In this work, phthalocyanine and its OCH₃ derivatives were investigated to see their photosensitization characteristics for producing singlet molecular oxygen, which is important in photodynamic therapy type-II. All structures were first optimized to achieve the minimized energy 3D models. Subsequently, they were prepared for the photosensitization investigations. All the experiments were conducted based on the density functional theory calculations. The energy absorption and emission observed between the occupied and unoccupied molecular orbitals based on the required energy for excitation and the corresponding energy of emission. The results indicated that the OCH₃ models could be expected to be safer than the original phthalocyanin by their required energy at longer wavelengths. The ratio of singlet molecular oxygen generation was found to be 1:1 for each of the OCH₃ derivatives.

Graphical Abstract



Introduction

Photosensitization might occur for the materials called photosensitizers (PS), which

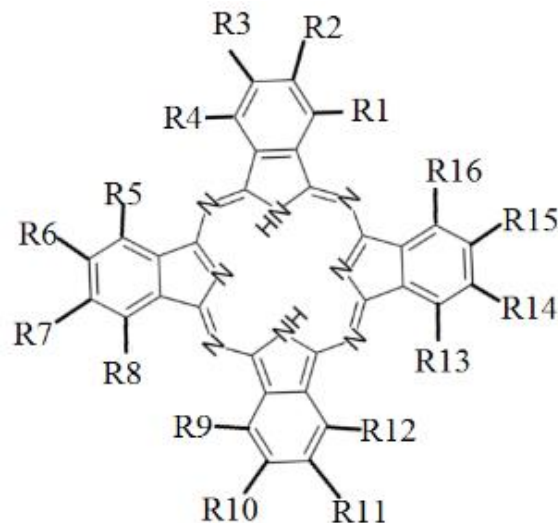
could be excited by absorption of energy from the extra light source [1]. In this case, the absorbed energy pushes the electrons of a lower state in ground mode to an upper state in an excited mode (PS→PS*) [1]. The PS materials could also store the absorbed energy as a new source of energy, in which the energy could be released by relaxing from excited mode of PS to the ground mode of PS by stopping the extra source. This procedure of energy transferring could be employed in the novel photodynamic therapy (PDT) of cancer cells [2]. Briefly, the excited PS could be considered as a resource to supply required energy to convert normal triplet molecular oxygen ($^3\text{O}_2$) with lower energy to activated singlet one ($^1\text{O}_2$) with higher energy as an oxidant agent to kill the cancer cells in the PDT type-II [3]. Consequently, evaluating the ability of PS materials to generate enough $^1\text{O}_2$ counterparts is an important task for using PS in the PDT systems [4]. Phthalocyanine, which is a natural material, has been proposed earlier as a proper PS material for PDT [5]. However, extra works indicated that further characterization are still required for original phthalocyanine or its derivatives to be employed in PDT [6]. By the importance of PDT, other materials have been also examined to see their PS capability for PDT as indicated for example by the work of Russo and co-workers [7]. Further looking inside the literature shows that the methylene blue and pentamethincyanin could be also seen as PS materials for PDT processes [8–10]. For example, porphyrin and porphyrazine are seen as important PS materials for PDT applications [11–14].

In the current work, we have studied the photosensitization of metal-free

phthalocyanine (Pc) in the original model and its OCH₃ (OMe) functionalized derivatives for the purpose of PS applications in PDT. Quantum chemical density functional theory (DFT) computational procedures have been employed to achieve the purpose of this work. In addition to structural optimization to achieve the minimized-energy structures, the $^1\text{O}_2$ generation efficiency for PDT type-II has been examined by the magnitude of transferred energies from excited mode to ground mode in various Pc molecules of this work.

Computational Details

Density functional theory (DFT) calculations [15–19] were carried out using the B3LYP functional and the 3-21G* basis set to obtain the optimized structures (Chart 1) by the Gaussian program [20–24]. Subsequently, molecular orbital properties including the energy levels of highest occupied and lowest unoccupied molecular orbitals (HOMO and LUMO) have been evaluated for the optimized structures at the same theoretical level. Furthermore, absorption and emission energies have been calculated for the optimized structures to see the required absorption wavelength and the amount of released energy of emission. It is important to note that the energy of 0.98 eV is required for $^3\text{O}_2 \rightarrow ^1\text{O}_2$ conversion; therefore, the amount of emission energy is a crucial factor to reach this task. It is worth to note that the computational studies are always very much helpful for predictions and interpretations of the research achievements, in which the important characteristics of PS structures have been investigated in this work.

**Chart 1.** Models of phthalocyanines

Pc	R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11	R12	R13	R14	R15	R16
1	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H
2	OMe	H	H	H	OMe	H	H	H	H	H	H	OMe	H	H	H	OMe
3	OMe	H	H	H	OMe	H	H	H	OMe	H	H	H	OMe	H	H	H
4	H	H	H	OMe	OMe	H	H	H	H	H	H	OMe	OMe	H	H	OMe
5	H	H	H	OMe	H	H	H	OMe	H	H	H	OMe	OMe	H	H	H
6	H	OMe	H	H	H	OMe	H	H	H	H	OMe	H	H	H	OMe	H
7	H	H	OMe	H	H	OMe	H	H	H	H	OMe	H	H	OMe	H	H
8	H	OMe	H	H	H	OMe	H	H	H	H	OMe	H	H	OMe	H	H

Table 1. HOMO and LUMO for Pc models

Pc	1	2	3	4	5	6	7	8
LUMO /eV	-2.99	-2.84	-2.84	-2.85	-2.85	-2.84	-2.88	-2.86
HOMO /eV	-5.24	-4.96	-4.96	-4.95	-4.96	-4.99	-4.99	-4.99

Results and Discussion

Structures

First, we have optimized the 3D models of investigated phthalocyanines (Pc) based on the DFT methods. It is important to note that the structural optimization is crucial to have minimized-energy systems for computational studies. Therefore, it was conducted at the first step of calculations of this work. The structures

of this work include the original Pc and seven of its OMe-functionalized models. All molecular structures of eight models have been reached to the minimized energy point by the energy convergency versus geometries. By the geometrical optimization processes, the 3D models have been prepared for the further investigations of electronic transitions during absorption/emission processes. For any computational jobs, geometry optimization is indeed located in the first step.

Table 2. Absorption and Emission properties

Pc	E (eV) S ₀ →S ₁	λ (nm) S ₀ →S ₁	E (eV) T ₁ →S ₀	No. ¹ O ₂
1	2.02	614	1.05	1.07
2	1.86	667	0.99	1.01
3	1.86	667	0.99	1.01
4	1.85	669	0.99	1.01
5	1.86	667	0.99	1.01
6	1.90	652	0.97	0.99
7	1.87	661	0.97	0.99
8	1.89	657	0.97	0.99

Absorption/Emission

One of the important characters of photosensitizers is to absorb and to emit energy through specific wavelengths. According to the therapeutical window, the range of 650-800 nm is good enough for the purpose of photodynamic therapy. In this point, the absorbed wavelength of original Pc is 614 nm, in which it was increased up to ~660 nm in the OMe-functionalized models. Since the wavelength and energy has a reversed relationship, longer wavelength means lower energy, in which it is safer to be utilized for living systems. The required energy to excite the photosensitizer from ground state (S₀) to the excited state (S₁) is 2.02 eV for the original Pc and the range of between 1.85 and 1.90 eV for the OMe-functionalized models. On the other hand, the largest magnitude of emission energy is for the larger absorbed energy of original Pc. For the functionalized models, the emission energy is again decreased to ~1 eV. The required energy for ³O₂→¹O₂ conversion is 0.98 eV, in which all the functionalized models could produce the singlet molecular oxygen with a ratio of 1:1 for the purpose. As a concluding remark, the OMe-functionalized models could be seen very much better for photosensitization, because they require lower absorption energy for excitation and they emit

required amount of energy for ³O₂→¹O₂ conversion. It is worth mentioning that the T₁ state is a semi-stable state in which the system first relaxes from S₁ to T₁ and then it emits energy from T₁ to S₀ in the phosphorescence process. This emitted energy is used for ³O₂→¹O₂ conversion, which is an important point for the photodynamic therapy type-II.

Conclusion

The evaluated energy values of the absorption and emission for the phthalocyanine and its OMe-derivatives demonstrated that the OMe models could be safer for living systems, in which their absorption energy are taken place at the longer wavelengths in comparison with that of the original model. Moreover, their emission energies indicated that the 1:1 ratio is available for each model to produce singlet molecular oxygen. Interestingly, based on the positions of additional OMe, the amount of production of singlet molecular oxygens are slightly different among the OMe models.

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