

Synthesis and photodynamic potential of tetra- and octa-triethyleneoxysulfonyl substituted zinc phthalocyanines

Devrim Atilla^a, Nil Saydan^b, Mahmut Durmuş^{a,e}, Ayşe Gül Gürek^a, Tania Khan^c,
Angelika Rück^d, Heinrich Walt^c, Tebello Nyokong^e, Vefa Ahsen^{a,f,*}

^a Gebze Institute of Technology, Department of Chemistry, PO Box 141, Gebze 41400, Turkey

^b Gebze Institute of Technology, Department of Biology, PO Box 141, Gebze 41400, Turkey

^c University Hospital Zurich, Frauenklinikstrasse 10, CH-8091 Zurich, Switzerland

^d Institut for Lasertechnologies in Medicine and Metrology (ILM), Helmholtzstrasse 12, D-89081 Ulm, Germany

^e Department of Chemistry, Rhodes University, Grahamstown 6140, South Africa

^f TUBITAK-Marmara Research Center, Materials Research Institute, PO Box 21, Gebze 41470, Turkey

Received 22 June 2006; received in revised form 31 July 2006; accepted 28 August 2006

Available online 1 September 2006

Abstract

Synthesis of the water soluble zinc phthalocyanines (**3**, **4**) obtained from the phthalonitriles substituted with oligo(ethyleneoxy)thia groups are described. The new compounds have been characterized by elemental analysis, IR, ¹H and ¹³C NMR spectroscopy, including HSQC, HMBC and COSY bidimensional correlation techniques, electronic spectroscopy and mass spectra. The aggregation behaviour of the phthalocyanine compounds (**3**, **4**) was investigated using UV–vis spectroscopy in dimethylsulphoxide. Photochemical and photophysical measurements were conducted on oligo(ethyleneoxy)thia appended zinc phthalocyanines. General trends are described for quantum yields of photodegradation, fluorescence yields, triplet lifetimes and triplet quantum yields as well as singlet oxygen quantum yields of these compounds. The phototoxicity against cancer cells of the new compounds was investigated during several *in vitro* experiments. The dye-sensitized photooxidation of 1,3-diphenylisobenzofurane via ¹O₂ was studied in dimethylsulphoxide.

© 2006 Elsevier B.V. All rights reserved.

Keywords: Phthalocyanine; Quantum yields; Singlet oxygen; Photodynamic therapy; Phototoxicity

1. Introduction

For photodynamic therapy (PDT), a combination of a photosensitizing drug and light in the presence of molecular oxygen is used to obtain a therapeutic effect, and has been proposed as an alternative treatment to complement conventional protocols in the management of malignant tumours and many other non-oncologic diseases [1]. The use of photosensitizing agents for inactivation of several cancer cells has been widely studied [2].

The first photosensitizers were hematoporphyrin derivatives and have already been described in detail in several articles [3]. Second generation photosensitizers such as phthalocyanines

(Pcs) have also been introduced for PDT in research and clinical trials [4]. Due to their high molar absorption coefficient in the red part of the spectrum, photostability, and long lifetimes of the photoexcited triplet states, Pcs are known to be useful photosensitizers [5,6]. Altering the peripheral substitution of the macrocyclic ring is one way of tailoring the solubility properties of the Pc material. The aggregation properties of Pcs are very important for the development of new photosensitizers [7]. The introduction of either long chains or bulky substituents to the periphery of the macrocycle should prevent the aggregation [8].

Recently, zinc Pcs have found applications as photosensitizers in PDT since diamagnetic central metals, such as Zn or Mg enhance phototoxicity of Pc's [9–12]. Thiol-derivatized metallophthalocyanine (MPc) complexes show rich spectroscopic and photochemical properties. For example, they are known to absorb at longer wavelengths (>700 nm) [13–16] than other MPc complexes. Therefore these complexes have a very useful feature

* Corresponding author at: Gebze Institute of Technology, Department of Chemistry, PO Box 141, Gebze 41400, Turkey. Tel.: +90 262 605 31 06; fax: +90 262 605 31 01.

E-mail address: ahsen@gyte.edu.tr (V. Ahsen).

for applications in optoelectronics, near-IR devices and PDT. The phototoxicity of Pcs is dependent on various factors such as subcellular localization (e.g. different partitioning in different compartments of cell membranes), physico-chemical structure, concentration, incubation time, exposure time, light energy and properties of cell lines [17].

In this work water soluble tetra and octa-triethyleneoxy-sulfonyl substituted zinc Pcs (**3**, **4**) were synthesized. Aggregation behavior, photophysical (triplet state lifetimes and quantum yields, and fluorescence quantum yields) and photochemical (singlet oxygen and photodegradation quantum yields) properties, biological effects and possible phototoxicity of the Pc compounds were investigated. Since PDT activity is mainly based on singlet oxygen, its production was determined by the dye-sensitized photooxidation of 1,3-diphenylisobenzofuran (DPBF), a specific scavenger of this toxic species [18]. Studies of the photostability of MPcs during photosensitized reactions is also of immense importance.

2. Experimental

2.1. Materials and equipment

4(4,7,10-Trioxaundecan-1-sulfonyl) phthalonitrile (**1**) and 4,5-bis(4,7,10-trioxaundecan-1-sulfonyl) phthalonitrile (**2**) were prepared according to published procedures [19]. All other reagents and solvents were reagent-grade quality, were obtained from commercial suppliers, and were dried before use, as described by Perrin and Armarego [20].

Elemental analyses were obtained from Carlo Erba 1106 Instrument. Infrared spectra in KBr pellets were recorded on a Bio-Rad FTS 175C FT-IR spectrophotometer. Absorption spectra in UV–vis region were recorded with an Shimadzu 2001 UV Pc spectrophotometer and Varian 500 UV–vis–NIR spectrophotometer. Fluorescence excitation and emission spectra, were recorded on a Varian Eclipse spectrofluorometer using 1 cm pathlength cuvettes at room temperature. Electrospray full scan spectra, in the range of m/z 50–2000 amu or m/z 2000–3000 amu, were obtained by infusion through fused silica tubing at 2–10 $\mu\text{l min}^{-1}$. The solutions were analyzed in a positive mode. The LCQ calibration (m/z 50–2000) was achieved according to the standard calibration procedure from the manufacturer (mixture of caffeine, MRFA and Ultramark 1621). An ES-Tuning Mix solution (Agilent) was used to calibrate the spectrometer between 2000 and 3000 amu. The temperature of the heated capillary of the LCQ was set to the range of 180–200 °C, the ion spray voltage was in the range of 1–7 kV with an injection time of 5–200 ms. ^1H and ^{13}C NMR spectra were recorded in DMSO- d_6 solutions on a Bruker and Varian 500 MHz spectrometers using TMS as an internal reference.

Photo-irradiations were done using a General electric Quartz line lamp (300 W). A 600 nm glass cut off filter (Schott) and a water filter were used to filter off ultraviolet and infrared radiations, respectively. An interference filter (Intor, 670 nm with a band width of 20 nm) was additionally placed in the light path before the sample. Light intensities were measured with a POWER MAX5100 (molelectron detector incorporated) power

meter. Triplet absorption and decay kinetics were recorded on a laser flash photolysis system, the excitation pulses were produced by a Quanta-Ray Nd: YAG laser providing 400 mJ, 90 ns pulses of laser light at 10 Hz, pumping a Lambda-Physik FL3002 dye (Pyridine 1 dye in methanol). Single pulse energy was 2 mJ. The analyzing beam source was from a Thermo Oriel xenon arc lamp, and a photomultiplier tube was used as a detector. Signals were recorded with a two-channel digital real-time oscilloscope (Tektronix TDS 360); the kinetic curves were averaged over 16 laser pulses.

2.2. Synthesis

2.2.1. Tetrakis(4,7,10-trioxaundecan-1-sulfonyl) phthalocyaninato zinc (**3**)

A mixture of **1** (0.50 g, 1.63 mmol), anhydrous $\text{Zn}(\text{O}_2\text{CMe})_2$ (30.00 mg, 0.50 mmol), 0.07 ml (0.45 mmol) 1,8-diazabicyclo-[5.4.0]-undec-7-ene (DBU) and dried 1-hexanol (5 ml) were heated to reflux for 18 h under argon in a round-bottomed flask. The resulting green suspension was cooled and the crude product was precipitated by addition of hexane. The crude green product was purified by column chromatography (silica gel, CH_2Cl_2 :MeOH 15:1). Yield: 174 mg (% 33). $\text{C}_{60}\text{H}_{72}\text{N}_8\text{O}_{12}\text{S}_4\text{Zn}$ (1290); Found C, 56.85; H, 5.26; N, 8.53; requires C, 56.12; H, 5.65; N, 8.72; IR (KBr): ν_{max} (cm^{-1}) 3055, 2926–2854(CH_2 , CH_3), 1600 (C=N), 1350 (C–N), 1281 (C–O–C), 1200, 1160–1090. MS (ES–MS), m/z (%): 1291(1 0 0) [$M+H$] $^+$. ^1H and ^{13}C NMR chemical shifts are given in Tables 1 and 2, respectively.

2.2.2. Octakis(4,7,10-trioxaundecan-1-sulfonyl) phthalocyaninato zinc (**4**)

A mixture of **2** (0.75 g, 1.55 mmol), anhydrous $\text{Zn}(\text{O}_2\text{CMe})_2$ (30.00 mg, 0.50 mmol), 0.07 ml (0.45 mmol) DBU and dried 1-hexanol (6 ml) were heated to reflux for 18 h under argon in a round-bottomed flask. The resulting green suspension was cooled and the crude product was precipitated by addition of hexane. After that **4** was isolated and purified by the same procedure as for **3**. Yield: 108 mg (% 18). $\text{C}_{88}\text{H}_{128}\text{N}_8\text{O}_{24}\text{S}_8\text{Zn}$ (2002); Found C, 53.00; H, 6.43; N, 5.18; requires C, 52.92; H, 6.46; N, 5.61; IR (KBr): ν_{max} (cm^{-1}) 3055, 2920–2840(CH_2 , CH_3), 1600 ($\text{C}_{\text{ar}}=\text{N}$), 1530, 1350 (C–N), 1290 (C–O–C), 1250, 1200, 1140–1070. MS (ES–MS), m/z (%): 2003(1 0 0) [$M+H$] $^+$,

Table 1
 ^1H chemical shifts (ppm) for compounds **3** and **4** in DMSO- d_6

Proton	3	4
H ₃	8.81 (s)	9.10 (s)
H _{3'}	8.88 (d)	9.10 (s)
H _{4'}	8.04 (d)	–
H ₅	3.72 (t)	3.66 (t)
H ₆	4.02 (t)	3.98 (t)
H ₇	3.78 (t)	3.74 (t)
H ₈	3.68 (t)	3.62 (t)
H ₉	3.58 (t)	3.51 (t)
H ₁₀	3.44 (t)	3.35 (t)
H ₁₁	3.20 (s)	3.12 (s)

Download English Version:

<https://daneshyari.com/en/article/28363>

Download Persian Version:

<https://daneshyari.com/article/28363>

[Daneshyari.com](https://daneshyari.com)