



Tetrapyrizinoporphyrazines with different number of peripheral pyridyl rings: Synthesis, photophysical and photochemical properties

Petr Zimcik*, Miroslav Miletin, Veronika Novakova, Kamil Kopecky, Zuzana Dvorakova

Department of Pharmaceutical Chemistry and Drug Control, Faculty of Pharmacy, Charles University, Heyrovského 1203, Hradec Kralove 50005, Czech Republic

ARTICLE INFO

Article history:

Received 10 June 2008

Received in revised form 17 July 2008

Accepted 19 July 2008

Available online 31 August 2008

Keywords:

Singlet oxygen

Fluorescence

Phthalocyanine

Tetrapyrizinoporphyrazine

Pyridyl

ABSTRACT

Zinc tetrapyrizinoporphyrazines comprising different numbers of pyridin-2-yl and *tert*-butylsulfanyl substituents were prepared by the statistical condensation of two precursors – 5,6-bis(*tert*-butylsulfanyl)pyrazine-2,3-dicarbonitrile (A) and 5,6-dipyridin-2-yl-pyrazine-2,3-dicarbonitrile (B). The ensuing zinc tetrapyrizinoporphyrazines were chromatographically separated on silica column and characterized. Adjacent (AABB) and opposite (ABAB) isomers were not separated. The prepared zinc tetrapyrizinoporphyrazines did not differ in their Q-band position but the B-band position was shifted hypsochromically for compounds bearing more pyridyl units; in addition, a weak band at 450–520 nm decreased with increasing number of pyridyl substituents. Singlet oxygen quantum yields (Φ_{Δ} in the range 0.69–0.53) decreased with increasing number of pyridyl units on the macrocyclic core, while fluorescence quantum yields showed the reverse tendency (Φ_F in the range 0.22–0.26).

© 2008 Elsevier Ltd. All rights reserved.

1. Introduction

Phthalocyanine (Pc) dyes have attracted much attention over a number of years [1]. Aza analogues of Pc, namely azaphthalocyanines (AzaPc), can be used in similar applications as their parent macrocycles [2]. Recently, we have investigated several tetrapyrizinoporphyrazines, a type of AzaPc, for their possible use in photodynamic therapy (PDT) [3–5]. This kind of medical treatment is based on production of cytotoxic species after illumination of a photosensitizer (e.g. porphyrins, chlorins, Pc) [6–8]. Photosensitizer absorbs the light and efficiently transfers the energy to ground state triplet oxygen forming highly reactive singlet oxygen that destroys the target tissues.

Peripheral pyridyls have been already used as substituents on Pc or AzaPc in relation to different applications. Tetrapyrizinoporphyrazines (TPyzPA) with eight pyridyl moieties have been investigated for their remarkable electron-deficient properties in electrochemistry both free and quarternized which allowed water solubility [9–12]. The same compounds have also been investigated for their non-linear optical properties [13]. Pyridyl moieties are also excellent substrates for metal-binding and can be used as ligands attached to Pc core [14]. Pyridyls bound to Pc

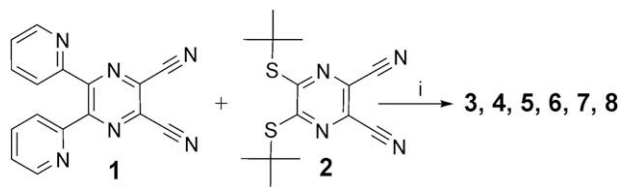
macrocycle through oxygen bridge have been tested as substituents also in photodynamic application [15–17].

As it has been shown previously, peripheral substituents influence substantially the properties of AzaPc macrocycle. They may increase or, on the other hand, significantly decrease the production of singlet oxygen which is important for photodynamic action of AzaPc [18]. For example, alkylsulfanyl substituents were shown to belong among the most suitable for compounds in PDT. In presented work, we synthesized and studied photochemical and photophysical properties of TPyzPA derivatives bearing different number of pyridyl and *tert*-butylsulfanyl substituents. *Tert*-butylsulfanyl, in addition to the best influence on photodynamic properties, have also very good aggregation-inhibiting properties [19]. Aggregation is a common undesirable property of planar Pc, AzaPc and other porphyrinoid macrocycles and causes decrease of singlet oxygen and fluorescence quantum yields because the dynamics of excited aggregates become faster due to new non-radiative energy relaxation channels [20].

2. Experimental

All organic solvents used for the synthesis were of analytical grade. Anhydrous dimethylformamide (DMF) was purchased from Acros, 1,3-diphenylisobenzofuran (DPBF) from Aldrich. Zinc phthalocyanine (ZnPc) was obtained from Eastman Organic Chemicals (New York, USA). All chemicals were used as received except for zinc acetate dihydrate (Lachema, Czech Republic)

* Corresponding author. Tel.: +420 49 5067257; fax: +420 49 5067167.
E-mail address: petr.zimcik@faf.cuni.cz (P. Zimcik).



Scheme 1. Statistical condensation of compounds **1** and **2**. Reaction conditions: (i) anhydr. DMF, zinc acetate, 160 °C, 2 h.

which was dried at 78 °C under reduced pressure (13 mbar) for 5 h. TLC was performed on Merck aluminium sheets with silica gel 60 F₂₅₄. Merck Kieselgel 60 (0.040–0.063 mm) was used for column chromatography. Melting points were measured on Electrothermal IA9200 Series Digital Melting point Apparatus (Electrothermal Engineering Ltd., Southend-on-Sea, Essex, Great Britain) and are uncorrected. Infrared spectra were measured in KBr pellets on IR-Spectrometer Nicolet Impact 400. ¹H and ¹³C NMR spectra were recorded on Varian Mercury-Vx BB 300 (299.95 MHz – ¹H and 75.43 MHz – ¹³C). Chemical shifts reported are given relative to Si(CH₃)₄. UV–vis spectra were recorded on spectrophotometer UV-2401PC, Shimadzu Europa GmbH (Duisburg, Germany). MALDI-TOF mass spectra were recorded in positive reflectron mode on a mass spectrometer Voyager-DE STR (Applied Biosystems, Framingham, MA, USA). For each sample, 0.5 μl of the mixture was spotted onto the target plate, air-dried and covered with 0.5 μl of matrix solution consisting of 10 mg of α-cyano-4-hydroxycinnamic acid in 100 μl of 50% ACN in 0.1% trifluoroacetic acid. The instrument was calibrated externally with a five-point calibration using Peptide Calibration Mix1 (LaserBio Labs, Sophia-Antipolis, France).

Compound **2** was prepared according to previously published method [19]. Compound **1** was prepared according to literature [21]

with the small modification in eluent used for column chromatography purification (chloroform:acetone, 15:1 instead of published acetone).

2.1. Statistical condensation of compounds **1** and **2**

A mixture of **1** (569 mg, 2 mmol), **2** (613 mg, 2 mol) and anhydrous zinc acetate (2.56 g, 14 mmol) in anhydrous DMF was stirred on preheated oil bath at 160 °C for 2 h. The mixture was poured into distilled water and green precipitate was separated by filtration, washed with water and methanol and air-dried. The crude mixture was separated by column chromatography on silica using step gradient starting from chloroform:THF:pyridine, 100:6:1.5. The first eluted compound was symmetrical **3**. This compound showed the same characteristics as the standard already prepared in our laboratory by simple tetramerization of **2** [19]. The second green fraction contained compound **4** that was eluted using increased polarity of the mobile phase (chloroform:pyridine, 16:1). Further increase of eluent polarity to chloroform:pyridine, 6:1 led to isolation of isomers **5** and **6** as one fraction followed by compound **7**. Symmetrical **8** was not isolated from the column but prepared in a separate reaction according to published procedure [22]. Each fraction containing unsymmetrical TPyzPA was further purified as mentioned below.

2.2. [2,3,9,10,16,17-Hexakis(tert-butylsulfanyl)-23,24-bis(pyridin-2-yl)-1,4,8,11,15,18,22,25-(octaaza)phtalocyaninato] zinc (II) (**4**)

The fraction with this compound was purified by preparative TLC on silica using toluene:pyridine, 7:1 as eluent (*R_f* 0.23). The spot was scrapped from the plate and product was extracted with pyridine, filtered and evaporated. The compound was isolated in minimal amount. MS (MALDI-TOF) *m/z* 1267 [M + H]⁺; 1211 [M-56 + H]⁺. UV–vis (pyridine) λ (nm) 657; 596; 385.

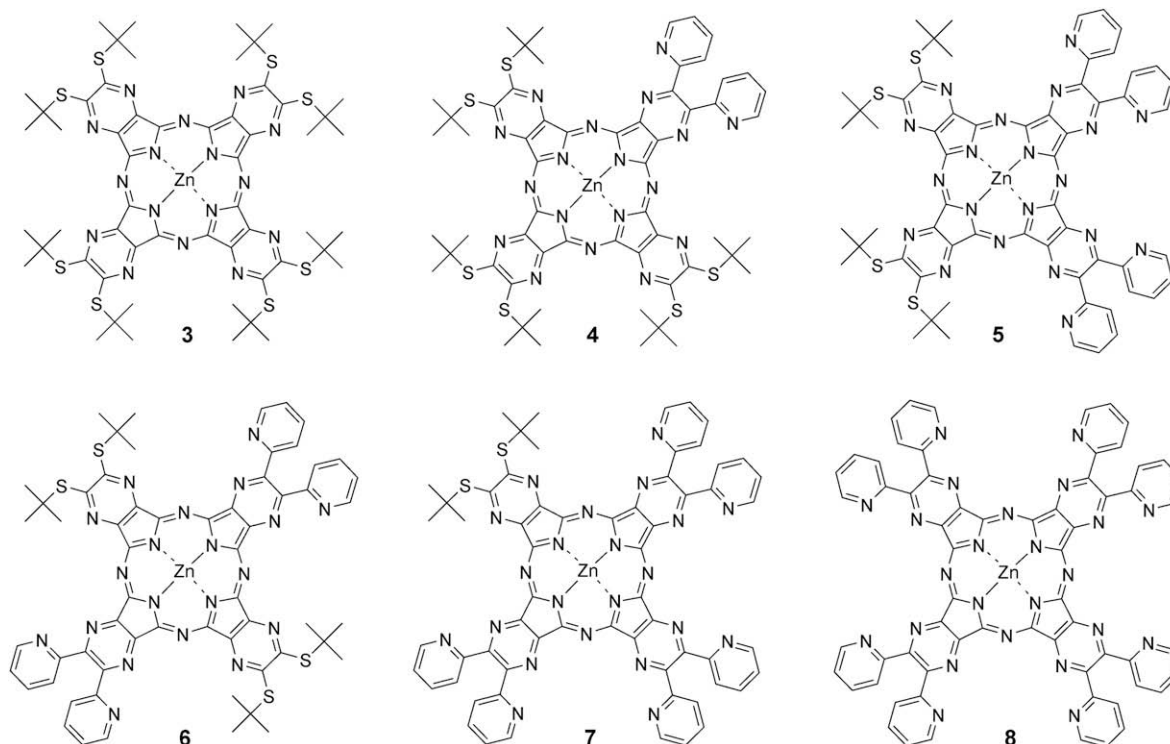


Fig. 1. Products of statistical condensation: compounds **3–8**.

Download English Version:

<https://daneshyari.com/en/article/177763>

Download Persian Version:

<https://daneshyari.com/article/177763>

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