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Synthesis and characterization of a new tetracationic phthalocyanine

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Abstract

Metal-free **3** and metallophthalocyanines **4**, **5** (N=Co, Zn) with four, peripheral 4-pyridylmethyloxy groups were synthesized by cyclotetramerization of 4-(4-pyridylmethyloxy)-phthalonitrile (**2**). The zinc derivative **5** was converted into the water-soluble quaternized product **6** by its reaction with methyl iodide. The new compounds were characterized by elemental analysis, IR, NMR and their mass and electronic spectra.

Keywords: Phthalocyanine; Quaternized product; Water soluble; Cyclotetramerization

1. Introduction

Phthalocyanines (pcs) have been one of the most extensively studied classes of organic functional materials because of their aromatic 18-π electron system which is closely related to that of the naturally occurring porphyrin ring. Phthalocyanines are highly stable and versatile aromatic macrocyclic compounds, capable of including more than 70 metallic and non-metallic ions in the ring cavity. The optical and electronic properties of the phthalocyanine (pc) macrocycle make it suitable for a wide range of applications. Some technological applications of these macrocycles have been intensively investigated, such as electrophotography, photovoltaic and solar cells, semiconductor devices, molecular electronics, Langmuir–Blodgett films, electrochromic display devices, low-dimensional conductors and synthetic metals, gas sensors, liquid crystals, nonlinear optics, optical disks, and electrocatalytic agents [1,2]. However, their insolubility in common organic solvents causes difficulties for many applications. Because of this reason, one of the important aims of research on the chemistry of phthalocyanines is to enhance their solubility in various solvents. Whereas peripheral substitution with bulky or long-chain hydrophobic moieties leads to pc derivatives soluble in apolar solvents [3–14]; on the contrary, amino, sulfo or carboxyl groups result in water-soluble products, atleast within certain pH ranges [10–17]. Quaternized aza groups are especially useful to achieve solubility within a wide pH range of aqueous solutions [8,18–22].

In the last few years, phthalocyanines have also been intensively studied as photosensitizers for photodynamic cancer therapy [23–29,19]. For this application the most important property of these tetrapyrrol rings is their solubility in water over a wide pH range. Especially, cationic water-soluble phthalocyanines have some advantages over porphyrins in PDT because of their strong absorbance at long wavelengths of the visible spectrum as well as their high yield triplet states with long lifetimes [30]. Cationic phthalocyanines also represent a large and expanding class of compounds which have applications in biology, catalysis and materials.

The synthesis of tetrakis-(3-pyridyloxy)phthalocyanines and tetracationic derivative of zinc phthalocyanine has been reported [31]. Recently, our group has also reported the synthesis of an octacationic porphyrazine by quaternization of the pyridyl- and dimethylaminoethyl-donors [32,33].

This paper describes the preparation of novel phthalocyanine compounds which carry 4-pyridylmethyloxy groups or *N*-methyl-4-pyridylmethyloxy substituents on the periphery. The latter group was designed to achieve solubility in water.

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2. Experimental

IR spectra were recorded on a Perkin Elmer Spectrum One FT-IR (ATR sampling spectra accessory) spectrophotometer, electronic spectra on a Unicam UV2 spectrophotometer. ^{1}H NMR spectra were recorded on Bruker 250 MHz using TMS as internal standard. Mass spectra were performed on Varian 711 mass spectrometer. All reagents and solvents were of reagent grade quality obtained from commercial suppliers. The homogeneity of the products was tested in each step by TLC. The solvents were stored over molecular sieves. 4-Nitrophthalonitrile (**1**) was prepared according to reported procedures [34].

*2.1. Synthesis of 4-(4-pyridylmethyloxy)phthalonitrile (**2**)*

4-Hydroxymethylpyridine (1.091 g, 0.01 mol) was dissolved in 40 cm^3 of dry DMF at 30 °C under nitrogen and **1** (0.865 g, 5 mmol) was added. After stirring for 10 min finely ground anhydrous K_2CO_3 (6.9 g, 0.05 mol) was added and the reaction mixture was stirred at 30 °C for 60 h under nitrogen. Then the mixture was poured into 150 cm^3 of ice-water. The resulting solid was collected by filtration and washed with water until the washings were neutral. After drying *in vacuo* at 100 °C, the crude product was recrystallised from ether–hexane. The compound was soluble in acetone, methanol, THF, CH_2Cl_2 and ethyl acetate. Yield: 0.69 g (59%); mp: 137 °C. (Found: C, 56.63; H, 4.46; N, 8.69 $C_{14}H_9N_3O$. Calcd.: C, 56.17; H, 4.09; N, 8.73%.) ^{1}H NMR ($CDCl_3$, δ, 250 MHz): 8.67 (m, 2H), 7.75 (d, 1H), 7.34 (m, 2H), 7.33 (d, 1H), 7.27 (m, 1H), 5.18 (s, 2H); IR (KBr), ν_{max} (cm^{-1}): 3106 (CH aromatic), 2917 (CH, aliphatic), 2238 (C≡N), 1595 (C=N), 1625, 1497 (C=C), 1191, 1114 (C–O–C).

*2.2. 2,9,16,23-Tetra(4-pyridylmethyloxy) phthalocyanine (**3**)*

A solution of **2** (0.150 g, 0.637 mmol) and catalytic amount of DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) in 2.5 cm^3 of 1-hexanol was heated and stirred at 160 °C in a sealed glass tube (10 × 75 mm) for 24 h under nitrogen. After cooling to room temperature, the reaction mixture was precipitated by the addition of 20 cm^3 of methanol and green precipitate was filtered off. It was treated with boiling ethanol, dichloromethane, ethyl acetate, and carbon tetrachloride several times to dissolve the unreacted starting materials and decomposition products and dried *in vacuo*. Yield: 0.042 g (28%). (Found: C, 72.27; H, 3.98; N, 17.41 $C_{56}H_{38}N_{12}O_4$. Calcd.: C, 71.33; H, 4.06; N, 17.82%.) FAB-MS [*m/z*] (%): 944.14 (34) $[M+H]^+$. IR (KBr), ν_{max} (cm^{-1}): 3110 (CH, aromatic), 2978 (CH, aliphatic), 1625, 1497 (C=C), 1268, 1114 (C–O–C), 3285 (NH). UV–vis (DMSO): λ (log ε) = 344 (4.1), 674 (4.21), 705 (4.15) nm.

*2.3. 2,9,16,23-Tetra(4-pyridylmethyloxy) phthalocyaninato cobalt(II) (**4**)*

A mixture of **2** (0.150 g, 0.637 mmol), anhydrous $CoCl_2$ (0.0206 g, 0.159 mmol) and catalytic amount of pyridine in 2.5 cm^3 of 1-hexanol was heated and stirred at 160 °C in a sealed glass tube (10 × 75 mm) for 24 h under nitrogen. After cooling to room temperature, the resulting green suspension was precipitated by the addition of methanol and the solid was filtered off. It was treated with boiling ethanol, dichloromethane, ethyl acetate, and carbon tetrachloride several times to dissolve the unreacted starting materials and decomposition products and dried *in vacuo*. Yield: 0.048 g (30.2%). (Found: C, 67.38; H, 3.45; N, 16.95 $C_{56}H_{36}N_{12}O_4Co$. Calcd.: C, 67.27; H, 3.63; N, 16.81%.) FAB-MS [*m/z*] (%): 999.27 (62) $[M]^+$, 909.15 (62) $[M-(-CH_2-C_5H_4N)+H)]^+$, 908.21 (99.37) $[M-(-CH_2-C_5H_4N)]^+$, 817.09 (69) $[M-2(-CH_2-C_5H_4N)+H]^+$, 816.08 (12) $[M-2(-CH_2-C_5H_4N)]^+$. IR (KBr), ν_{max} (cm^{-1}): 3057 (CH, aromatic), 2953 (CH, aliphatic), 1548, 1497 (C=C), 1242, 1114 (C–O–C). UV–vis (DMSO): λ (log ε) = 332 (4.4), 668 (4.39) nm.

*2.4. 2,9,16,23-Tetra(4-pyridylmethyloxy) phthalocyaninato zinc(II) (**5**)*

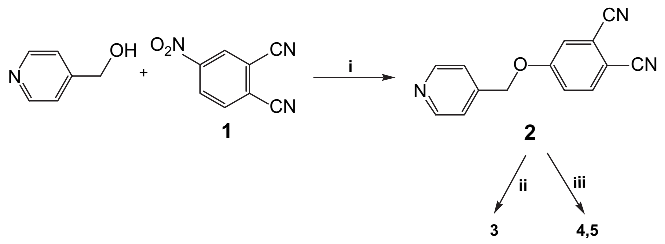
Compound **5** was prepared and purified following the procedure described for **4**, starting from 0.100 g **2** (0.425 mmol), 1.5 cm^3 1-hexanol, 0.0195 g anhydrous $Zn(CH_3COO)_2$ (0.106 mmol) and catalytic amount of DBU. Yield: 0.040 g (37%). (Found: C, 66.95; H, 4.01; N, 16.51 $C_{56}H_{36}N_{12}O_4Zn$. Calcd.: C, 66.84; H, 3.61; N, 16.70%.) FAB-MS [*m/z*] (%): 1006.32 (52.8) $[M]^+$. IR (KBr), ν_{max} (cm^{-1}): 3057 (CH, aromatic), 2953 (CH, aliphatic), 1574, 1497 (C=C), 1242, 1114 (C–O–C). UV–vis (DMSO): λ (log ε) = 357 (4.16), 614 (3.86), 682 (4.43) nm.

*2.5. 2,9,16,23-Tetra[4-(N-methyl)pyridylmethyloxy] phthalocyaninato zinc(II)tetraiodide (**6**)*

A mixture of 0.020 g **5** (20 μmol), 0.0567 g methyl iodide (0.04 mmol) and 5 cm^3 DMSO was stirred for 48 h at room temperature. The solid was resuspended in methanol and filtered. The product was washed successively with ethanol, acetone, diethyl ether, and chloroform. Yield: 0.0123 g (58%). (Found: H, 46.02; N, 3.22; N, 10.25 $C_{60}H_{48}N_{12}O_4I_4Zn$. Calcd.: C, 45.78; H, 3.07; N, 10.68%.) FAB-MS [*m/z*] (%): 1576.62 (100) $[M+2]^+$, 639.11 (21) $[M-4(-CH_2-C_5H_4N-CH_3I)+1]^+$, 638.29 (14.5) $[M-4(-CH_2-C_5H_4N-CH_3I)]^+$. IR (KBr), ν_{max} (cm^{-1}): 3055 (CH, aromatic), 2927 (CH, aliphatic), 1548, 1497 (C=C), 1248, 1114 (C–O–C). UV–vis (H_2O): λ (log ε) = 337 (4.58), 632 (4.45) nm.

3. Results and discussion

The synthetic procedure, as outlined in Scheme 1, started with the synthesis the phthalonitrile derivative, namely 4-(4-pyridylmethyloxy)phthalonitrile (**2**). It was obtained by base-catalyzed nucleophilic aromatic nitro displacement of 4-nitrophthalonitrile (**1**) with the –OH function of 4-hydroxymethylpyridine (Scheme 1). The reaction was carried out at 30 °C in anhydrous DMF with K_2CO_3 as a base. This reaction has been effectively used in the preparation of variety of ether



Scheme 1. Synthesis of pcs. (i) K_2CO_3, DMF, 30 °C; (ii) DBU, 1-hexanol, 24 h; (iii) metal salts, 24 h.

or thioether-substituted phthalonitrile derivatives [11,35,36]. Cyclotetramerization of **2** with anhydrous metal salts ($CoCl_2$, $Zn(CH_3COO)_2$) and a *N*-donor base (pyridine or DBU) at 160 °C in 1-hexanol led to the formation of metallophthalocyanines (Fig. 1). The synthesis of metal-free phthalocyanine **3** was accomplished in hexanol in the presence of a strong base (DBU) at reflux temperature (Fig. 1). Methylation of the pyridyl groups on the periphery of the zinc phthalocyanine **5** resulted in the tetracationic derivative **6** (Fig. 2). As a natural consequence of the single substituent on each benzo group, the phthalocyanines **3–6** are all a mixture of four constitutional isomers (Figs. 1 and 2) [37,38]. All phthalocyanine compounds were purified by treatment successively with various boiling solvents such as ethanol, dichloromethane, ethyl acetate, and carbon tetrachloride. A common feature of phthalocyanines **3–5**, in contrast to the analogous compounds with bulky moieties, is their insolubility in the common solvents. The phthalocyanines **3–5** are soluble to certain extent, only in high boiling polar solvents such as DMF and DMSO. Since phthalocyanines with bulky peripheral substituents are known to be soluble in common organic solvents, the solubility behaviour of **3–5** is exceptional. However, such unexpected evidences been have also reported for phthalocyanines carrying four 13-membered tetrathiamacrocycles which were also insoluble in common organic solvents [39]. The tetracationic phthalocyanine **6** is also relatively soluble in water.

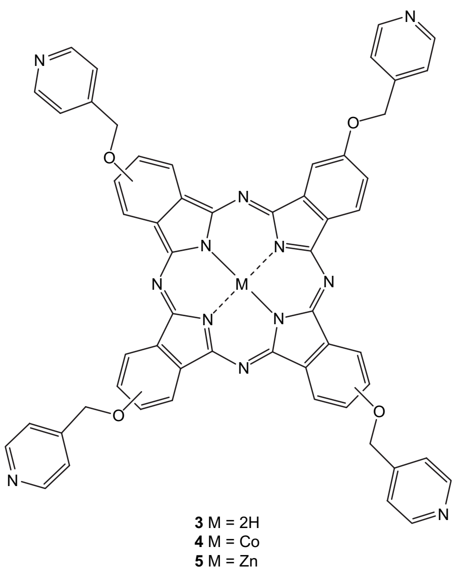


Fig. 1. Phthalocyanines (**3–5**).

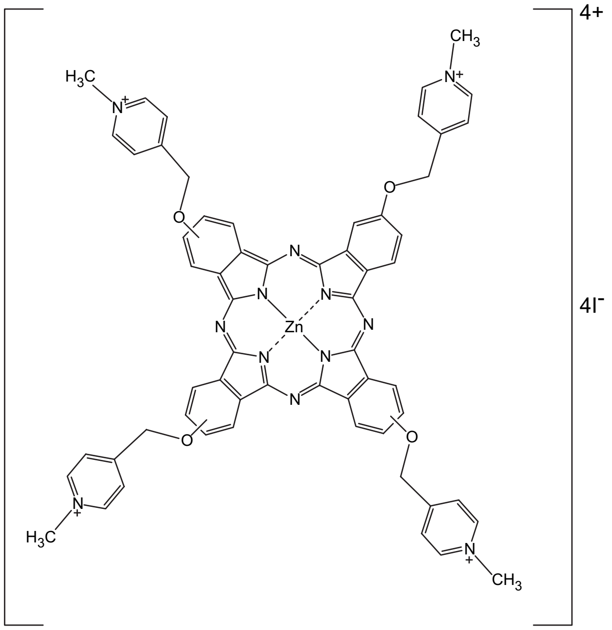


Fig. 2. Quaternized phthalocyanine **6**.

All new compounds were characterized by spectral data and their elemental analyses. Spectral data on the synthesized compounds are consistent with the assigned formulations. In the IR spectrum of **2**, stretching vibrations of pyridine C=N, nitrile (C≡N), aliphatic and aromatic CH groups were observed at 1595, 2238, 2917, and 3106 cm^{-1}, respectively. In addition, comparison of the IR spectrum of **2** and 4-nitrophthalonitrile (**1**) gave support for the proposed structure. They indicated the formation of **2** by the disappearance of the NO_2 band of 4-nitrophthalonitrile at 1548 cm^{-1} and the appearance of new absorptions at 1191–1114 cm^{-1} belonging to ether group [11]. In the ^1H NMR spectrum of **2** ($CDCl_3$), the aromatic protons appear in the range at 7.27–8.67 ppm and the aliphatic protons as singlet at 5.18 ppm. Cyclotetramerization of the dinitrile **2** was confirmed by disappearance of the sharp CN vibration at 2238 cm^{-1} after pc formation. The IR spectra of the phthalocyanines **3–6** are very similar, with the exception of the metal-free **3** showing an NH stretching band peak at 3285 cm^{-1} due to the inner core. No major change in the IR spectra was found after quaternization.

The UV–vis spectra of the phthalocyanines in DMSO showed the typical pattern, mainly $\pi-\pi^*$ transition of the tetrapyrrole units, which are located in the central core of the phthalocyanine: intense Q-absorption band in the visible region of around 668–705 nm. In the ultraviolet region of around 360 nm the characteristic Soret or B band was also observed. The characteristic Q-band absorption of metallophthalocyanines with D_{4h} symmetry is observed as a single band of high intensity in the visible region. The aggregation of pc units in metallophthalocyanines is clearly observed by following the changes occurring in the Q-band region. In the spectra of **4** and

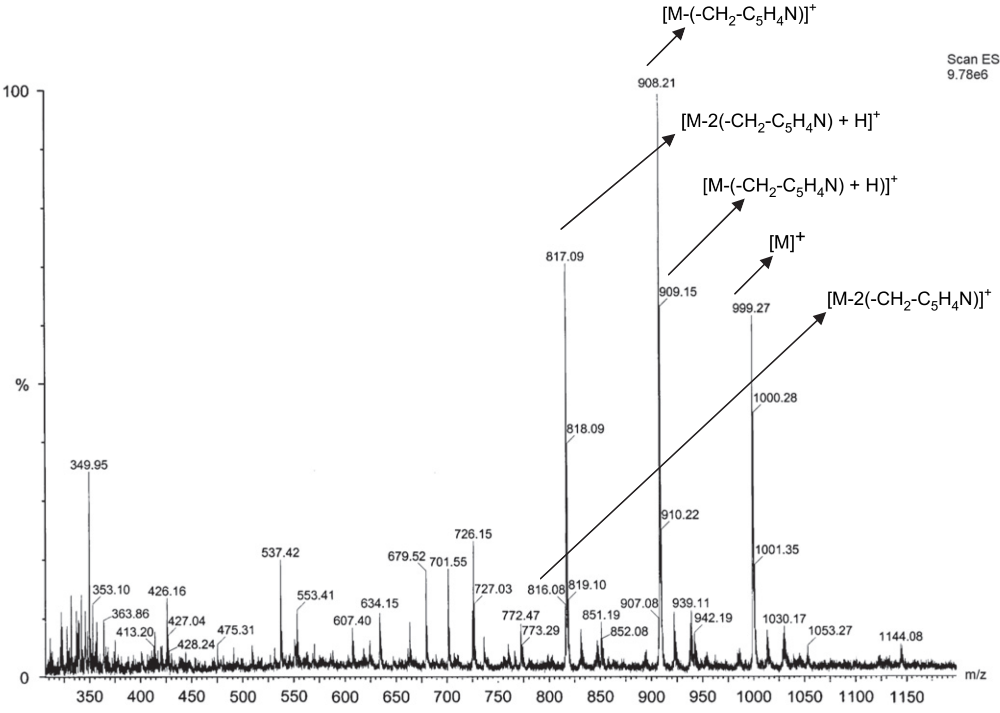


Fig. 3. FAB-MS spectrum of **4**.

5 in DMSO, there is an intense band around 668–682 nm corresponding to monomeric species and a shoulder around 620 nm indicating aggregated ones [13,14,40]. The spectrum of compound **3** is somewhat different with a split Q band (673 and 705 nm) indicating the lower symmetry (D_{2h}) of the metal-free derivative [3,4,13,14]. For the water-soluble quarternarized pc **6** the appearance of the spectra is *vice versa*; *i.e.*, the longer wavelength absorption is less intense and appears as a shoulder while that of the absorption of the aggregated species at 630 nm is the main peak as a result of solvent effect [21].

Also, FAB-MS gave data consistent with the proposed structures of compound **3**–**6**. We observed the molecular ion peaks at $m/z = 944.14$ and 1006.32 for compounds **3** and **5**, respectively. The mass spectrum of the cobalt phthalocyanine **4** supported its structure with a molecular ion peak at $m/z = 999.27$. In addition to the $[M]^+$ peak, the other fragment ions such as $[M-(-CH_2-C_5H_4N)+1)]^+$, $[M-(-CH_2-C_5H_4N)]^+$, $[M-2(-CH_2-C_5H_4N)+1]^+$, $[M-2(-CH_2-C_5H_4N)]^+$, have been observed at 909.15, 908.21, 817.09, 816.08, respectively. The molecular ion $[M]^+$ and the other fragment ions of compound **4** are shown in Fig. 3, together with the corresponding leaving groups.

In the case of **6**, molecular ion peak $[M+2]^+$ appeared at $m/z = 1576.62$. In addition to this peak, the other fragment ions such as $[M-4(-CH_2-C_5H_4N-CH_3I)+1]^+$, $[M-4(-CH_2-C_5H_4N-CH_3I)]^+$ have been also observed at 639.11, 638.29, respectively.

In conclusion, metal-free and metallophthalocyanines containing four 4-(4-pyridylmethyloxy) groups on the periphery have been synthesized. Pyridyl groups on the periphery of the zinc phthalocyanine have been quaternized to prepare tetracationic derivative. By extension from the interest in the pyridyl phthalocyanines, the new macrocycles are liable to find many applications, as is the case with interactions of similar tetracationic or octacationic tetrapyrrol rings with DNA.

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