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Dyes and Pigments 64 (2005) 63–71

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Synthesis of novel cationic amphiphilic phthalocyanine derivatives for next generation photosensitizer using photodynamic therapy of cancer

Keiichi Sakamoto[a,*], Taku Kato[a], Eiko Ohno-Okumura[b], Masaki Watanabe[a], Michael J. Cook[c]

[a] *Department of Applied Molecular Chemistry, College of Industrial Technology, Nihon University, 1-2-1 Izumi-cho, Narashino-shi, Chiba-ken 275-8575, Japan*

[b] *Research Institute of Chemical Science, Technology and Education, 8-37-1 Narashinodai, Funabashi-shi, Chiba-ken 274-0063, Japan*

[c] *School of Chemical Sciences and Pharmacy, University of East Anglia, Norwich NR4 7TJ, UK*

Received 14 January 2004; received in revised form 6 April 2004; accepted 12 April 2004
Available online 2 July 2004

Abstract

Phthalocyanine derivatives have attracted attention in the photodynamic therapy of cancer. The preparation of cationic amphiphilic zinc phthalocyanine derivatives is described. Novel amphiphilic non-peripheral substituted zinc phthalocyanine derivative is performed by quaternation. Amphiphilic zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine will be a useful photosensitizer for photodynamic therapy of cancer.

Keywords: Amphiphilic; Phthalocyanine derivatives; Quaternation; Photodynamic therapy

1. Introduction

Phthalocyanine derivatives are important commercial pigments and dyes for a number of years, and their chemical and heat stabilities are well known. In the last decade, phthalocyanine derivatives have been utilized in important functional chromophores as molecular electronics, optoelectronics, photonics, etc. [1]. Moreover, phthalocyanine derivatives have also attracted attention in the photodynamic therapy of cancer (PDT) [2], because they show strong absorption of far-red region between 600 and 850 nm wavelength, which has a greater penetration of tissue [3], and photo-sensitization of singlet oxygen [4].

In general, unsubstituted phthalocyanine derivatives are known to be insoluble or lower soluble in common organic solvents. Insolubility or lower solubility of unsubstituted phthalocyanine derivatives has problems to utilize in many fields including PDT. Insolubility or lower solubility in common organic solvents is improved to introduce substituents such as alkyl groups onto the ring system. Alkyl group substituted phthalocyanine derivatives become soluble in common organic solvents, and are lipophilic. Lipophilic phthalocyanine derivatives are reported to have a higher tumor affinity [5].

Whereas, introduction of hydrophilic groups into substituted phthalocyanine derivatives was performed in order to be soluble in aqueous media, water solubility of phthalocyanine derivatives has a strong influence on the bioavailability and in vivo distribution. Synthesized water-soluble phthalocyanine derivatives possess sulfo-, carboxy- and phosphono-substituents, which are used in compounds that have been synthesized for use in tumor treatment [6–14].

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[*] Corresponding author. Tel.: +81-47-474-2572; fax: +81-47-474-2579.
E-mail address: k5saka@cit.nihon-u.ac.jp (K. Sakamoto).

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doi:10.1016/j.dyepig.2004.04.004

Phthalocyanine analogs in which one or more of benzenoid rings are replaced by pyridine rings are interesting compounds because quaternation of the pyridine nitrogen is expected to confer solubility in aqueous media [15]. Tetrapyridoporphyrazines containing four pyridinoid rings in place of four benzenoid ones were first synthesized by Linstead and his co-workers [16]. Tetramethylated tetrapyridoporphyrazines by quaternation were reported to become soluble in water [17,18], and then these compounds were studied for PDT [19].

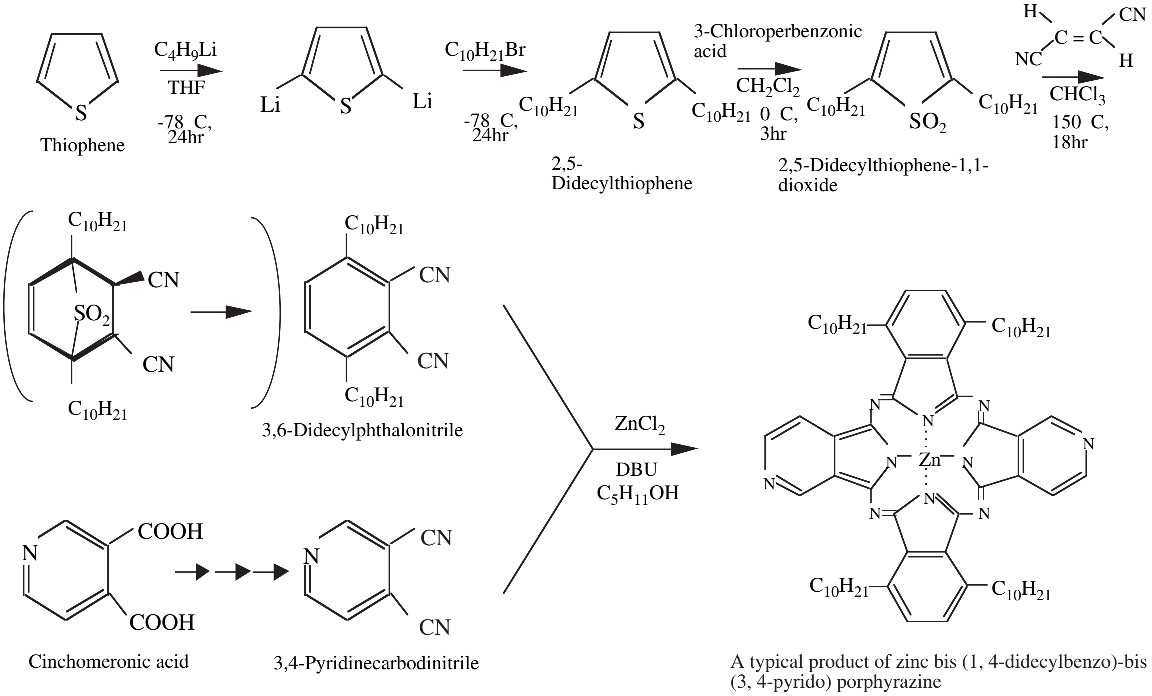
The authors reported a fundamental study on PDT by measuring for the triplet state lifetime of non-peripheral substituted phthalocyanine derivatives [20]. We synthesized to use non-peripheral substituted phthalocyanine derivative, zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine, which possesses two didecylbenzenoid and two pyridinoid moieties in the molecule [15]. Zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine exhibits solubility in organic solvents and is expected to have a higher tumor affinity than water-soluble phthalocyanines such as tetrasulfophthalocyanines. And then, quaternation of the pyridine nitrogen in zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine is expected to confer solubility in an aqueous media [17,18], and to have bioavailability and in vivo distribution. The amphiphilic phthalocyanine derivatives are considered the best compound for a new generation of photosensitizers for PDT [4,5,14,19]. Thus, the quaternation of zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine will provide amphiphilic phthalocyanine derivatives.

2. Results and discussion

2.1. Preparation of phthalocyanine analogs and its regioisomers

Zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine was synthesized by cross cyclotetramerization (Scheme 1). Cross cyclotetramerization of 3,6-didecylphthalodinitrile and 3,4-dicyanopyridine was performed for 1:1 mole ratio in the presence of 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU) as a catalyst, anhydrous zinc(II)chloride in pentanol at 137 °C for 4 h to produce 84% yield of zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine [15]. Synthesized zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine is a mixture of five regioisomers, which are at different locations of pyridinoid rings [15] (Fig. 1).

The regioisomers of zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine was separated with thin layer chromatography (TLC) (Merk Silica gel 60 F_{254} on aluminum sheet, eluent:toluene–pyridine, 7:3) into four green- to blue-colored fractions. These fractions were numbered 1, 2, 3 and 4, according to the R_f values, and the R_f values were 0.95, 0.91, 0.75 and 0.65, respectively. Each fraction was recovered by scraping from the TLC plate, dissolved in pyridine, the solution filtered, and the solvent removed. The four fractions have different proton nuclear magnetic resonance (^{1}H NMR), ultraviolet–visible (UV–vis) and fluorescent spectra. The four fractions separated by TLC have been attributed to four of five possible regioisomers of the



Scheme 1. Reagents and conditions: (i) anhydrous $ZnCl_2$, DBU, $C_5H_{11}OH$, 4 h.

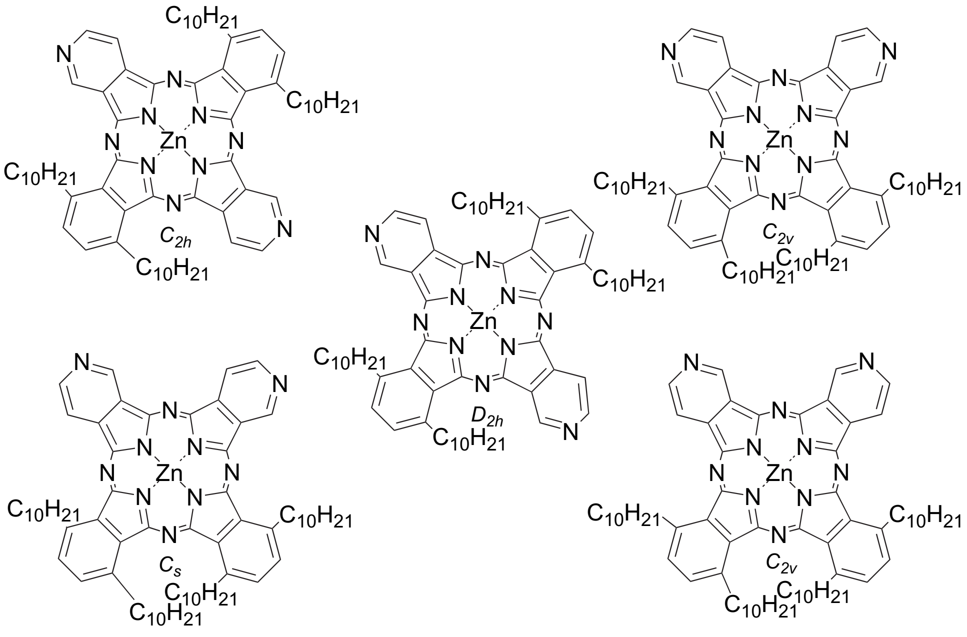


Fig. 1. Regioisomers of zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine.

zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine. The total amounts of fractions 1–4 are 26.1, 17.4, 17.4 and 39.1%, respectively [15]. Two types of C_{2v} isomers in fraction 4 were not able to be isolated [15]. The UV–vis spectra of the four fractions show the typical shape for phthalocyanine analogs. The strongest peaks around 700 nm are assigned as the Q band, which could be attributed to the allowed $\pi-\pi^*$ transition of phthalocyanine ring. The assignment of the Q band from each fraction was carried out on the theory of the relationship between symmetry and the Q band [21–24]. The Q band splits into two peaks of the highest isomer symmetry [24] (Fig. 2). The symmetry of regioisomers of zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine was decreased in the order C_{2h}, C_{2h}, C_{2v} and C_s (fractions 2, 1, 4 and 3), respectively.

2.2. Quaternation of phthalocyanine analogs

Zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine was reacted with quaternizing agents such as monochloroacetic acid (MCAA), diethyl sulfate (DES) and dimethyl sulfate (DMS) in *N*,*N*-dimethylformamide (DMF) as solvent at 140 °C (Scheme 2). Yields of products were 23%, 17% and 28% for MCAA, DES and DMS as quaternizing agents, respectively. After reaction with quaternizing agents, zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazines were identified through spectroscopic techniques such as ^{1}H NMR, infrared (IR) and UV–vis spectra. When MCAA or DMS was employed as the quaternizing agent, it is confirmed that *N*-CH_2COOH or *N*-CH_3 bond was obtained on the pyridinoid rings in zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine, while as DES was used, we verified quaternation was not achieved but sulfonation occurred [18]. The shapes of UV–vis spectra of pyridine solution changed after quaternation. It is thought that interactions between molecules are complicated, when DES and DMS were used as quaternizing agents. Then the quaternized products give rise to easy aggregation in aqueous media.

After reaction with quaternizing agents, all compounds gave the water solubility, and got amphiphilic property (Table 1).

Zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine is readily soluble in pyridine with strongest absorption at 687 nm (log ϵ_{max} 4.81). The Q band absorption of the compound quaternized with DMS showed 739 nm and shifted by 56 nm to longer wavelength in comparison with compounds reacted with MCAA and DES. After reaction with MCAA, DES and DMS, all compounds are very soluble in water; they show strongest absorptions in the Q band at 715, 731 and 747 nm, respectively (Fig. 3).

Cyclic voltammetry was carried out with a BAS CV-50W voltammetric analyzer at room temperature in acetonitrile containing a 0.01 mol dm^{-3} solution of tetrabutylammonium perchlorate (TBAP). Cyclic voltammograms (CV) were recorded by scanning the potential at the rate of 50 mV s^{-1}.

The important parameters of a CV are the reduction and oxidation potentials for irreversible peaks, and the midpoint potential for a reversible couple, E_{mid} (Table 2). The reduction and oxidation potentials of zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine

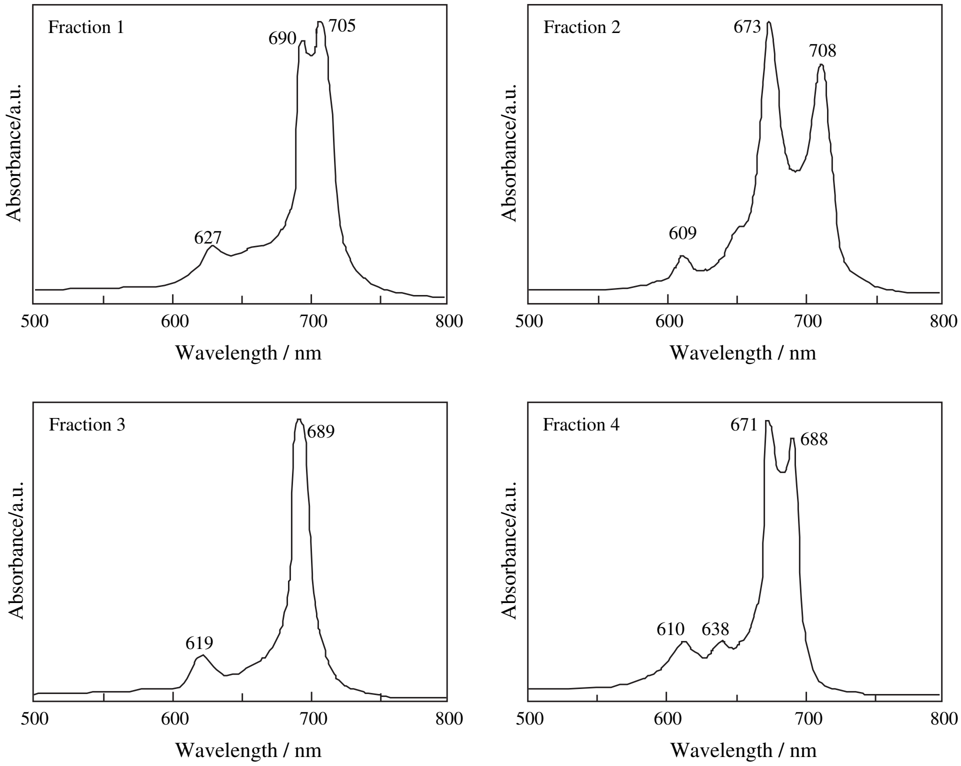


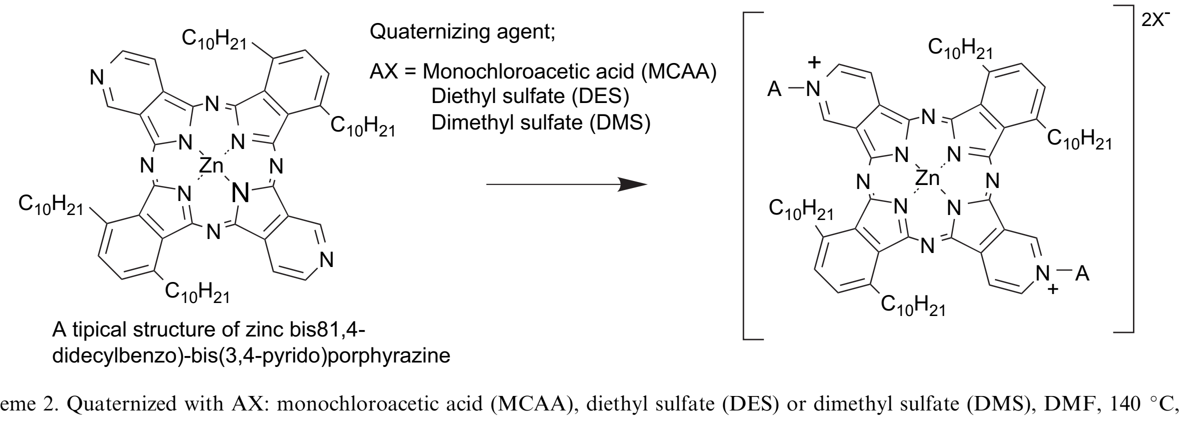
Fig. 2. UV–vis spectra of each regioisomer in zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine.

are sorted into six irreversible peaks. The irreversible peaks are attributed to the oxidation of the central metal and the reversible couples represent the redox of the phthalocyanine ring.

Shapes of CVs were changed before and after the reaction. The redox potentials of zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine have six irreversible peaks. The redox potentials of quaternized compounds were different from each other. The CVs of compounds quaternized with MCAA, DMS showed three anodic peaks and two cathodic peaks, while DES had four anodic peaks and two cathodic peaks. It is thought that no effect on quaternation takes place for redox properties of phthalocyanine analogs, because redox potentials were not changed.

2.3. Quaternation of regioisomers

The separated regioisomers of zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine were quaternized with DMS. Yields of products were 11%, 9%, 15% and 11% for fractions 1, 2, 3 and 4, respectively. Quaternized regioisomers were also identified through spectroscopic techniques such as ^{1}H NMR, IR, UV–vis and fluorescence spectra.



Scheme 2. Quaternized with AX: monochloroacetic acid (MCAA), diethyl sulfate (DES) or dimethyl sulfate (DMS), DMF, 140 °C, 2 h.

Table 1
Solubilities of zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine, and quaternized compounds with monochloroacetic acid (MCAA), diethyl sulfate (DES) and dimethyl sulfate (DMS) in solvents

Compound	Toluene	Chloroform	Pyridine	Water
Zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido) porphyrazine before quaternization	○	○	○	×
Quaternized with MCAA	○	○	○	○
Quaternized with DES	○	○	○	○
Quaternized with DMS	○	○	○	○

○: soluble, ×: insoluble.

In comparison with UV–vis spectra of before and after the quaternation of regioisomers with DMS, the Q band absorption of quaternized regioisomer was split into two or more. Then after quaternation, the Q band absorptions were moved to longer wavelength (Fig. 4).

In general, fluorescence spectra are measured as mirror images of excitation spectra. Excitation spectra show the same profile of absorption bands. Fluorescence spectra show longer wavelength than absorption and excitation spectra.

For quaternized products except for fractions 1 and 4, fluorescence spectra showed longer wavelength than their own absorption spectra.

In fractions 1 and 4, the degree of overlaps between absorption and fluorescence spectra was determined. These phenomena result from re-absorption or re-emission of fluorescence.

Accordingly, fluorescence spectra of fractions 1 and 4 showed shorter wavelength than the longest wavelength of absorption bands.

The CVs of fractions 1–3 have one pair of reversible oxidation potential and four irreversible peaks. Fraction 4 has one pair of reversible oxidation and three irreversible reduction waves. The reduction and oxidation of metal phthalocyanine derivatives are due to the interaction between the phthalocyanine ring and the central metal.

The porphyrazine ring in the molecules of metal phthalocyanine derivatives or analogs is influenced by the π electrons about the closed system. Although the π electron system of zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine and fractions 1–4 consist of one porphyrazine, two pyridinoids and two didecyl substituted phenylene rings, the locations of these rings except for porphyrazine are different from each regioisomer.

The irreversible peaks are attributed to the oxidation of the central metal and the reversible couples represent the redox of the phthalocyanine ring.

Substituents and pyridinoid rings influenced the π electron environment in the fractions 1–4 of zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine. It is thought that the effect of pyridinoid rings gives rise to changes of the electron density of the metal phthalocyanine derivative. The difference of reduction and oxidation peaks between fractions 1–4 is attributed to the effect of the variation of the interaction between the central metal and the alkylbenzoporphyrazine. And then, the difference of CV between zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine and fractions 1–4 is also the effect of the interaction, since zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazines is a mixture of its regioisomers (Fig. 5).

The ΔE values are the anodic peak to cathodic peak separation located in the oxidation potential region. The ΔE values are around 100 mV and the redox processes are the same for regioisomers, except for fraction 4. This means that the electron process of regioisomers between fractions 1–3 involve approximately one electron transfer. The ΔE values of fraction 4 show different behavior in comparison to the others. It is thought that the different behavior for fraction 4 is attributable to the mixture of two types of C_{2v} isomers. The redox potentials of fraction 4 are based on the interaction between two types of C_{2v} position isomers. No observation on the reversible couple

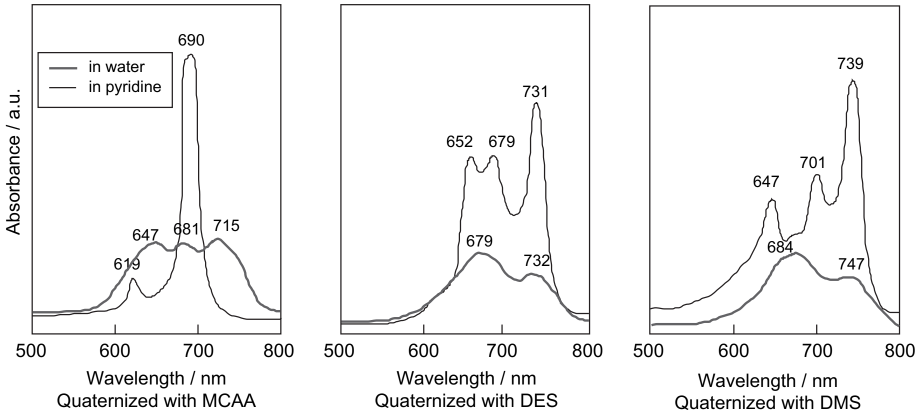


Fig. 3. UV–vis spectra of zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine quaternized with monochloroacetic acid (MCAA), diethyl sulfate (DES) and dimethyl sulfate (DMS). The UV–vis spectra of each quaternized compound was measured in pyridine solution or water.

Table 2
Redox potentials of zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine derivative and its quaternized compound with monochloroacetic acid (MCAA), diethyl sulfate (DES) and dimethyl sulfate (DMS) in *N*,*N*-dimethylformamide solution containing tetrabutylammonium perchlorate

Compound	Potential (V vs. Ag/AgCl)						
	Reduction				Oxidation		
Zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine	-0.97^{a}	-0.71^{a}	-0.45^{a}	-0.15^{a}	0.37^{a}	0.93^{a}	
Quaternized with monochloroacetic acid (MCAA)	-0.95^{a}	-0.45^{a}	-0.14^{a}		0.45^{a}	0.97^{a}	
Quaternized with diethyl sulfate (DES)	-0.95^{a}	−0.89	-0.65^{a}	-0.19^{a}	0.50^{a}	1.01^{a}	
ΔE^{b}		0.13					
Quaternized with dimethyl sulfate (DMS)	−0.78	-0.58^{a}	-0.14^{a}		0.31^{a}	0.50^{a}	1.13^{a}
ΔE^{b}	0.10						

Potentials of reversible wave are midpoint potentials of anodic and cathodic peaks for each couple, E_{mid}.
[a] Irreversible peak.
[b] The anodic peak to cathodic peak separation for reversible couple.

in zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazines resulted in the interaction between the regioisomers.

The redox potentials of quaternized regioisomers were varied. After quaternation of regioisomers, the shapes of CVs appeared clearly. It is thought that electron transfer ability of regioisomers have been increased remarkably by the acquisition of cation groups. The CVs showed two anodic and two cathodic peaks, two anodic and three cathodic peaks, two anodic and two cathodic peaks, and one anodic and five cathodic peaks for fractions 1, 2, 3 and 4, respectively. Fractions 1 and 4 have a reversible couple in a reduction potential region at −0.24 and −0.57 V vs. Ag/AgCl, respectively. For quaternized regioisomers, some of the redox potentials are recognized before the reaction.

Consequently, it suggested that the photoelectron transfer ability is kept unchanged regardless of the quaternation.

3. Experimental

3.1. Equipments

UV–vis spectra were measured on a Shimadzu UV-2400PC spectrometer. Each sample was prepared

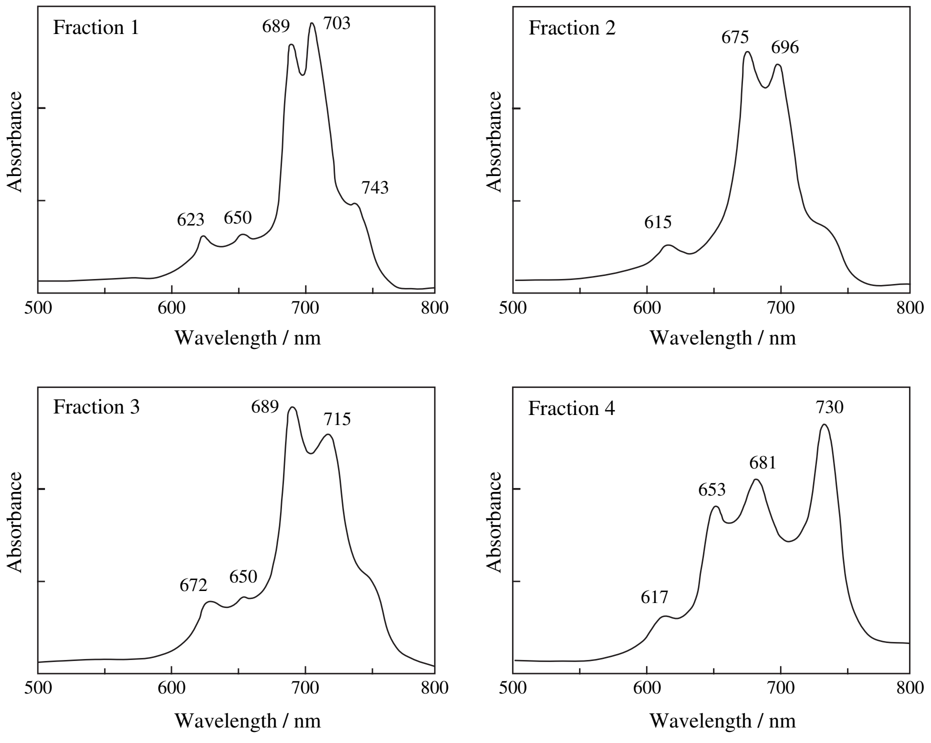


Fig. 4. UV–vis spectra of each regioisomer in zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine quaternized with dimethyl sulfate (DMS). The UV–vis spectra of each quaternized isomer was measured in pyridine solution.

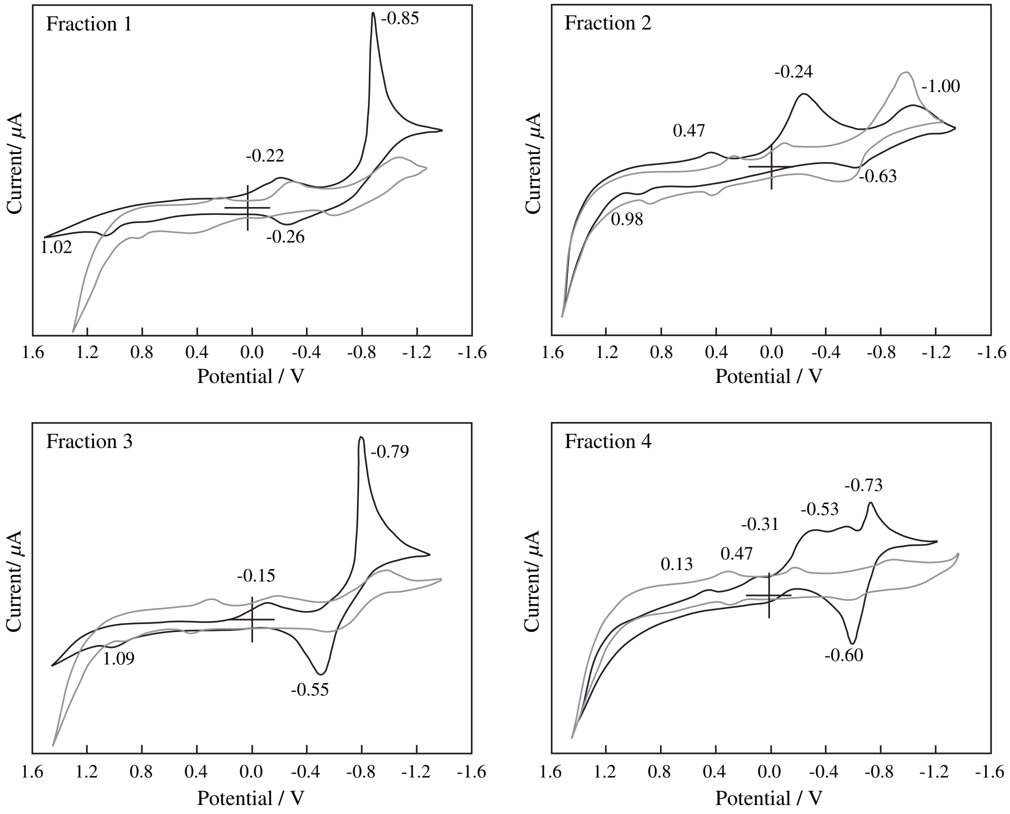


Fig. 5. Cyclic voltammograms of each regioisomer in zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine quaternized with dimethyl sulfate (DMS). Black line, after quaternation with DMS; gray line, before quaternation.

in toluene at 5.0×10^{-5} mol dm^{-3}, except for the toluene-insoluble sample (the insoluble sample was prepared in pyridine at 2.6×10^{-5} mol dm^{-3}). Fluorescent spectra were recorded in DMF on a Hitachi F-4500 fluorescence spectrometer by using a solid sample holder, which was also used for a solution in order to minimize the effect of an internal light filter.

IR spectra were recorded on a Shimadzu FTIR-8100A spectrometer. The ^{1}H NMR spectra were measured at 400 MHz on a Bruker Avance 400S in benzene-d_6 (C_6H_6-d_6) or dimethyl sulfoxide (DMSO-d_6) using tetramethylsilane (TMS) as an internal standard.

Elemental analysis was carried out using Perkin Elmer 2400CHN equipment. Samples for elemental analysis were purified by repeated sublimation. The equipment was calibrated with copper phthalocyanine before elemental analysis for phthalocyanine compounds was measured.

CV was carried out with a BAS CV-50W voltammetric analyzer at room temperature in acetonitrile containing a 0.01 mol dm^{-3} solution of TBAP. CVs were recorded by scanning the potential at the rate of 50 mV s^{-1}. The working and counter electrodes were platinum wires, and the reference electrode was a silver/silver chloride (Ag/AgCl) saturated sodium chloride electrode. The area of the working electrode was 2.0×10^{-2} cm^2.

3.2. Synthesis

3.2.1. Zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine

The quaternation of zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine is shown in Scheme 1.

Compounds 3,6-didecylphthalodinitrile and 3,4-dicyanopyridine were prepared from thiophene and cinchomeronic acid, respectively [15].

Zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine is synthesized by cross cyclotetramerization of 3,6-didecylphthalodinitrile and 3,4-dicyanopyridine [15]: a mixture of 3,6-didecylphthalodinitrile and 3,4-dicyanopyridine for 1 (0.12 g, 0.29 mmol):1 (0.04 g, 0.29 mmol) mole ratio was dissolved in pentanol (7 cm^3) and anhydrous zinc(II)chloride (0.05 g) was added. The mixture was heated at 137 °C for 4 h in the presence of DBU as a catalyst. After cooling, the reaction mixture was dissolved in toluene (50 cm^3) and the solution filtered. The solvent was removed by evaporation. The products were separated and purified by TLC (eluent:toluene). Blue solid (0.18 g; yield 84%). ^{1}H NMR (δ 400 MHz, C_6H_6-d_6/ppm) 0.9 (m, 12H, CH_3), 1.61–2.61 (m, 64H, CH_2), 4.18–4.36 (m, 8H, α-CH_2), 7.45 (m, 4H, arom), 8.26 (m, 6H, Py); IR (ν KBr/cm^{-1}) 2970 (ν_{C-H}), 1600 (ν_{C-C}), 1500 (ν_{C-C}), 1470 (ν_{C-C}), 1450 (ν_{C-C}), 1210

(δ_{C-H}), 1090 (δ_{C-H}), 720 (δ_{C-H}); UV–vis [λ_{max} toluene/nm (log ϵ_{max})] 686 (4.814), 636, 617. Anal Calcd. for $C_{70}H_{94}N_{10}Zn$: C, 73.68; H, 8.30; N, 12.28. Found: C, 73.67; H, 8.30; N, 12.28.

3.2.2. Isomer separation of zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine

The regioisomers of zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine was separated with TLC (Merk Silica gel 60 F_{254} on aluminum sheet, eluent: toluene–pyridine, 7:3) into four green- to blue-colored fractions. These fractions were numbered from 1, 2, 3 and 4, according to the R_f values, and the R_f values were 0.95, 0.91, 0.75 and 0.65, respectively. Each fraction was recovered by scraping from the TLC plate, dissolved in pyridine, the solution filtered, and the solvent removed.

3.2.3. Quaternation of zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine

Quaternized zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine is performed as follows: zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine (0.17 g, 0.15 mmol) was reacted with quaternizing agents such as MCAA (0.57 g, 6 mmol), DES (0.1 g, 0.6 mmol) and DMS (0.2 g, 1.5 mmol), respectively, in DMF as solvent at 140 °C for 2 h. The reaction mixture was dissolved in acetone (20 cm^3), cooled to room temperature and the solution filtered. The solvent was removed. The products were purified by TLC (eluent:THF–toluene, 8:2). Each product was recovered by scraping from the TLC plate, dissolved in pyridine, the solution filtered, and the solvent removed.

(a) Product with MCAA: dark blue solid (32 mg; yield 23%). ^{1}H NMR (δ 400 MHz, DMSO-d_6/ppm) 0.85 (m, 12H, CH_3), 1.19–1.71 (m, 48H, γ-CH_2), 1.79–2.12 (m, 8H, β-CH_2), 2.27–2.68 (m, 8H, β-CH_2), 4.15 (m, 4H, α-CH_2), 4.39 (m, 4H, α-CH_2), 6.19 (s, 2H, CH_2), 7.37 (m, 4H, arm), 8.32 (m, 6H, Py); IR (ν KBr/cm^{-1}) 3050 (ν_{C-H}), 2980 (ν_{C-H}), 1730 (ν_{C-O}), 1620 (ν_{C-C}), 1400 (ν_{C-C}), 1210 (δ_{C-H}), 1080 (δ_{C-H}), 790 (δ_{C-H}), 690 (δ_{C-H}); UV–vis (λ_{max} toluene/nm) 686: (λ_{max} pyridine/nm) 690: (λ_{max} water/nm) 681. Anal Calcd. for $C_{74}H_{100}N_{10}O_4Zn$: C, 45.05; H, 2.52; N, 17.50. Found: C, 45.02; H, 2.49; N, 17.48.

(b) Product with DES: blue solid (37 mg, yield 17%). ^{1}H NMR (δ 400 MHz, DMSO-d_6/ppm) 0.86 (m, 12H, CH_3), 1.02–1.70 (m, 48H, γ-CH_2), 1.88–2.11 (m, 8H, β-CH_2), 2.30–2.68 (m, 8H, β-CH_3), 4.11 (m, 4H, α-CH_2), 4.25 (m, 4H, α-CH_2), 7.38 (m, 4H, arom), 8.18 (m, 4H, Py); IR (ν KBr/cm^{-1}) 3050 (ν_{C-H}), 2960 (ν_{C-H}), 1500 (ν_{C-C}), 1450 (ν_{C-C}), 1400 (ν_{C-C}), 1340 (ν_{S-O}), 1180 (ν_{S-O}), 1250 (δ_{C-H}), 920 (δ_{C-H}), 760 (δ_{C-H}), 590 (δ_{C-S}); UV–vis (λ_{max} toluene/nm) 687: (λ_{max} pyridine/nm) 731: (λ_{max} water/nm) 679. Anal Calcd. for $C_{70}H_{98}N_{10}S_2O_6Zn$: C, 37.11; H, 1.78; N, 18.54. Found: C, 37.10; H, 1.78; N, 18.49.

(c) Product with DMS: dark blue solid (53 mg, yield 28%). ^{1}H NMR (δ 400 MHz, DMSO-d_6/ppm) 0.88 (m, 12H, CH_3), 1.14–1.72 (m, 48H, γ-CH_2), 1.82–2.17 (m, 8H, β-CH_2), 2.29–2.62 (m, 8H, β-CH_2), 4.06 (s, 6H, CH_3), 4.27 (m, 4H, α-CH_2), 4.51 (m, 4H, α-CH_2), 7.34 (m, 4H, arom), 8.23 (m, 6H, Py); IR (ν KBr/cm^{-1}) 3060 (ν_{C-H}), 2980 (ν_{C-H}), 1500 (ν_{C-C}), 1450 (ν_{C-C}), 1400 (ν_{C-C}), 1250 (δ_{C-H}), 1100 (δ_{C-H}), 950 (δ_{C-H}), 830 (δ_{C-H}), 660 (δ_{C-H}); UV–vis (λ_{max} toluene/nm) 739: (λ_{max} pyridine/nm) 739: (λ_{max} water/nm) 684. Anal Calcd. for $C_{72}H_{100}N_{10}Zn$: C, 49.03; H, 3.09; N, 21.43. Found: C, 49.03; H, 3.08; N, 21.40.

3.2.4. Quaternation of regioisomers of zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine

Quaternized regioisomers of zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine: regioisomers of zinc bis(1,4-didecylbenzo)-bis(3,4-pyrido)porphyrazine (0.4 mg, 0.35 μmol) was reacted with quaternizing agent as DMS (0.5 mg, 3.5 μmol) in DMF as solvent at 140 °C for 2 h. The products were purified with TLC (eluent:THF–toluene, 8:2). Each product was recovered by scraping from the TLC plate, dissolved in pyridine, the solution filtered, and the solvent removed.

(a) Fraction 1 with DMS: dark blue solid (0.053 mg, yield 13%). ^{1}H NMR (δ 400 MHz, DMSO-d_6/ppm) 0.86 (t, 12H, CH_3), 1.15–1.70 (m, 48H, γ-CH_2), 1.82–2.12 (m, 8H, β-CH_2), 2.19–2.49 (m, 8H, β-CH_2), 3.67 (s, 6H, CH_3), 3.92 (t, 4H, α-CH_2), 4.19 (t, 4H, α-CH_2), 7.37 (m, 4H, arom), 8.20 (m, 6H, Py); IR (ν KBr/cm^{-1}) 3070 (ν_{C-H}), 2980 (ν_{C-H}), 1500 (ν_{C-C}), 1400 (ν_{C-C}), 1250 (δ_{C-H}), 1100 (δ_{C-H}), 950 (δ_{C-H}), 820 (δ_{C-H}), 660 (δ_{C-H}); UV–vis (λ_{max} toluene/nm) 680: (λ_{max} pyridine/nm) 703: (λ_{max} water/nm) 690; fluorescence (F_{max} pyridine/nm) 687: (F_{max} water/nm) 695. Anal Calcd. for $C_{72}H_{100}N_{10}Zn$: C, 49.03; H, 3.09; N, 21.43. Found: C, 49.00; H, 3.01; N, 21.33.

(b) Fraction 2 with DMS: dark blue solid (0.065 mg, yield 15%). ^{1}H NMR (δ 400 MHz, DMSO-d_6/ppm) 0.87 (t, 12H, CH_3), 1.16–1.73 (m, 48H, γ-CH_2), 1.73–2.10 (m, 8H, β-CH_2), 2.10–2.55 (m, 8H, β-CH_2), 3.90 (s, 6H, CH_3), 3.99 (t, 4H, α-CH_2), 4.17 (t, 4H, α-CH_2), 7.23 (m, 4H, arom), 8.25 (m, 6H, Py); IR (ν KBr/cm^{-1}) 3070 (ν_{C-H}), 2980 (ν_{C-H}), 1500 (ν_{C-C}), 1400 (ν_{C-C}), 1250 (δ_{C-H}), 1100 (δ_{C-H}), 980 (δ_{C-H}), 830 (δ_{C-H}), 660 (δ_{C-H}); UV–vis (λ_{max} toluene/nm) 689: (λ_{max} pyridine/nm) 675: (λ_{max} water/nm) 686; fluorescence (F_{max} pyridine/nm) 684: (F_{max} water/nm) 690. Anal Calcd. for $C_{72}H_{100}N_{10}Zn$: C, 49.03; H, 3.09; N, 21.43. Found: C, 48.99; H, 2.98; N, 21.22.

(c) Fraction 3 with DMS: dark blue solid (0.055 mg, yield 11%). ^{1}H NMR (δ 400 MHz, DMSO-d_6/ppm) 0.85 (m, 12H, CH_3), 1.09–1.63 (m, 48H, γ-CH_2), 1.70–2.11 (m, 8H, β-CH_2), 2.11–2.42 (m, 8H, β-CH_2), 3.86 (s, 6H, CH_3), 3.97 (t, 4H, α-CH_2), 4.21 (t, 4H, α-CH_2), 7.23–7.33 (m, 4H, arom), 8.21 (m, 6H, Py); IR (ν KBr/

cm^{-1}) 3080 (ν_{C-H}), 2970 (ν_{C-H}), 1500 (ν_{C-C}), 1400 (ν_{C-C}), 1250 (δ_{C-H}), 1100 (δ_{C-H}), 950 (δ_{C-H}), 830 (δ_{C-H}), 660 (δ_{C-H}); UV–vis (λ_{max} toluene/nm) 681: (λ_{max} pyridine/nm) 689: (λ_{max} water/nm) 689; fluorescence (F_{max} pyridine/nm) 690: (F_{max} water/nm) 698. Anal Calcd. for $C_{72}H_{100}N_{10}Zn$: C, 49.03; H, 3.09; N, 21.43. Found: C, 49.03; H, 3.03; N, 21.40.

(d) Fraction 4 with DMS: dark blue solid (0.078 mg, yield 19%). ^{1}H NMR (δ 400 MHz, DMSO-d_6/ppm) 0.87 (t, 12H, CH_3), 1.20–1.63 (m, 48H, γ-CH_2), 1.71–2.17 (m, 8H, β-CH_2), 2.17–2.47 (m, 8H, β-CH_2), 3.85 (s, 6H, CH_3), 4.09 (t, 4H, α-CH_2), 4.27 (t, 4H, α-CH_2), 7.21–7.36 (m, 4H, arom), 8.22 (m, 6H, Py); IR (ν KBr/cm^{-1}) 3070 (ν_{C-H}), 2980 (ν_{C-H}), 1500 (ν_{C-C}), 1400 (ν_{C-C}), 1250 (δ_{C-H}), 1100 (δ_{C-H}), 950 (δ_{C-H}), 830 (δ_{C-H}), 660 (δ_{C-H}); UV–vis (λ_{max} toluene/nm) 677: (λ_{max} pyridine/nm) 730: (λ_{max} water/nm) 673; fluorescence (F_{max} pyridine/nm) 686: (F_{max} water/nm) 687. Anal Calcd. for $C_{72}H_{100}N_{10}Zn$: C, 49.03; H, 3.09; N, 21.43. Found: C, 49.02; H, 3.08; N, 21.43.

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