Synthesis of Amphiphilic Porphyrins

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Synopsis. A water soluble surfactant porphyrin 5,10,15-tris(1-methylpyridinium-4-yl)-20-[4-(octadecyloxy)phenyl]-21*H*, 23*H*-porphine triiodide and its metal complexes have been synthesized and characterized.

Recently, several surfactant porphyrins have been reported in relation to the simulation of the intricate functions of chlorophylls in photosynthetic membranes.[1-3]

We report here the synthesis of 5,10,15-tris(1-methylpyridinium-4-yl)-20-[4-(octadecyloxy)phenyl]-21*H*,23*H*-porphine triiodide and its metal complexes which are amphiphilic.

Experimental

*Preparation of 5,10,15-Tris(4-pyridyl)-20-[4-(octadecyloxy)-phenyl]-21*H, *23*H*-porphine (Abbreviated as H_2TPyStPP).* A starting compound, *p*-(octadecyloxy)benzaldehyde, was prepared in the following manner according to the literature method.[4] *p*-Hydroxybenzaldehyde (48.8 g, 0.4 mol) and octadecyl iodide (243.2 g, 1.7 mol) in cyclohexane (320 cm³) were heated under reflux for 3 h. The reaction mixture was cooled to room temperature and extracted with diethyl ether (300 cm³). The ether was evaporated and the residue was distilled under high vacuum (250 °C, 0.03 Pa) to give the product (25.6 g, 17.1%).

p-(Octadecyloxy) benzaldehyde (21.2 g, 0.057 mol), 4-pyridinecarbaldehyde (18.2 g, 0.17 mol), and pyrrole (15.2 g, 0.23 mol) in propionic acid (1000 cm³) were heated under reflux for 2 h. Propionic acid was removed by distillation to give a mixture of porphyrins having one to three octadecyloxyphenyl and three to one pyridyl groups. Tetrakis(octadecyloxyphenyl)- and tetrapyridylporphine were not produced. The crude mixture was dissolved in chloroform and chromatographed on alumina columns (Merck 70—230 mesh, grade 2—3, 5 cm × 50 cm) with chloroform as an eluent. Mono-, bis-, and tris(octadecyloxyphenyl) porphyrins eluted first and the other by-products tended to be adsorbed on alumina. Similar procedures were repeated three times and the mixture of the three porphyrins was obtained. When the mixture was again chromatographed using half the flow rate of chloroform, three bands were separated and the slowest elute was the solution of the target compound. Chloroform was evaporated to give the mono(octadecyloxyphenyl) porphyrin. Yield 6.5 g (12.8% based on *p*-(octadecyloxyphenyl)benzaldehyde). Found C, 79.21; H, 7.45; N, 10.67%. Calcd for $C_{59}H_{63}N_7 \cdot 1/2H_2O$: C, 79.16; H, 7.21; N, 10.95%. Vis ($CHCl_3$) 418 (ε 369000), 483 (sh), 514 (17500), 550 (6910), 580 (5490), and 646 nm (3100).

Preparation of [Zn(TPyStPP)]. H_2TPyStPP (0.5 g, 0.56 mmol) and $Zn(CH_3COO)_2 \cdot 2H_2O$ (0.25 g, 1.1 mmol) in acetic acid (50 cm³) were heated under reflux for 1 h. Acetic acid was removed by distillation to give a solid product. The zinc porphyrin was isolated by using alumina column (Merck, 70—230 mesh, grade 2—3, 2 cm × 30 cm) chromatography with a mixture of chloroform and methanol (8 : 2) as an eluent. Yield 0.48 g (90%). Found: C, 74.77; H, 6.63; N, 10.25%. Calcd for $C_{59}H_{61}N_7OZn$: C, 74.63; H, 6.48; N, 10.33%. Vis (DMSO) 317 (ε 19200), 406 (sh), 428 (512000), 516 (sh), 560 (20600), and 599 nm (7380).

Preparation of [Co(TPyStPP)] and [Mn(OH)(TPyStPP)]. The cobalt and manganese complexes were prepared from H_2TPyStPP and $Co(CH_3COO)_2 \cdot 4H_2O$ or $Mn(CH_3COO)_2 \cdot 4H_2O$ by similar procedures to those for the preparation of the zinc porphyrin. In the case of the cobalt complex, tetrahydrofuran was used as an eluent of the chromatography. [Co(TPyStPP)]: Yield 85%. Found: C, 73.11; H, 6.59; N, 9.51%. Calcd for $C_{59}H_{61}CoN_7O \cdot 3/2H_2O$: C, 73.05;H, 6.65; N, 10.11%. Vis ($CHCl_3$–CH_3OH (1 : 1)) 328 (ε14800), 432 (141000), 546 (8970), and 592 nm (sh).

[*Mn(OH)(TPyStPP)*]: Yield 85%. Found: C, 74.08; H, 6.56; N, 10.00%. Calcd for $C_{59}H_{62}MnN_7O_2$: C, 74.12; H, 6.54; N, 10.25%. Vis (DMSO) 372 (ε 41900), 394 (44000), 463 (143000), 512 (7140), 565 (12200), 600 (8170), and 762 nm (1140).

Preparation of [Mg(TPyStPP)]. The magnesium complex was prepared according to the method of Eschenmoser.[5] The preparation was carried out in nitrogen atmosphere. Magnesium turnings (1.5 g, 62 mmol) and ethyl iodide (5 cm³, 62 mmol) were treated in diethyl ether (80 cm³) to give ethyl Grignard (C_2H_5MgI) reagent. 3,5-Di-*t*-butyl-4-hydroxytoluene (1.5 g, 11 mmol) was treated with the Grignard solution (8 cm³, 5.8 mmol), and H_2TPyStPP (0.5 g, 0.56 mmol) in dichloromethane (40 cm³) was added dropwise to the reaction mixture in 30 min. The solution was kept for 16 h at room temperature and water (500 cm³) was added. After the mixture was well shaken in a separatory funnel, the dichloromethane layer was separated. Dichloromethane was removed and the residue was dried *in vacuo*. The magnesium porphyrin was isolated by alumina column chromatography using $CHCl_3$–CH_2OH (8 : 2) as an eluent. Yield 0.36 g (70% based on H_2TPyStPP). Found: C, 77.54; H, 6.80; N, 10.48%. Calcd for $C_{59}H_{61}N_7MgO \cdot 1/2H_2O$: C, 77.24; H, 6.81; N, 10.69%. Vis (DMF) 314 (ε 21200), 404 (sh), 425 (570000), 520 (sh), and 563 nm (20100).

N-Methylation of [Mg(TPyStPP)]. [Mg(TPyStPP)] (0.5 g, 0.54 mmol) and methyl iodide (7.8 g, 55 mmol) in mixed solvents of chloroform, methanol, and tetrahydrofuran (1 : 1 : 1) (300 cm³) were heated under reflux in nitrogen atmosphere for 5 h. The solvents were removed by distillation and the solid product was dried *in vacuo*. The *N*-methylated porphyrin was purified by column chromatography using alumina (Merck, 70—230 mesh, grade 4) columns and $CHCl_3$–CH_3OH (8 : 2) as an eluent. Yield 0.73 g (90%). Found: C, 49.72; H, 5.22; N, 6.37%. Calcd for $C_{62}H_{70}I_3MgN_7O \cdot 9H_2O$: C, 49.76; H, 5.93; N, 6.55%. Vis ($CHCl_3$–CH_3OH (1 : 1)) 328 (ε 14800), 432 (141000), 546 (8970), and 592 nm (sh).

N-Methylation of H_2TPyStPP and [M(TPyStPP)] (M=Zn, Co, and Mn). The porphyrins were treated with methyl iodide in mixed solvents of chloroform, methanol, and tetrahydrofuran (1 : 1 : 1) in a similar manner to the *N*-methylation of magnesium porphyrin. In the case of the cobalt

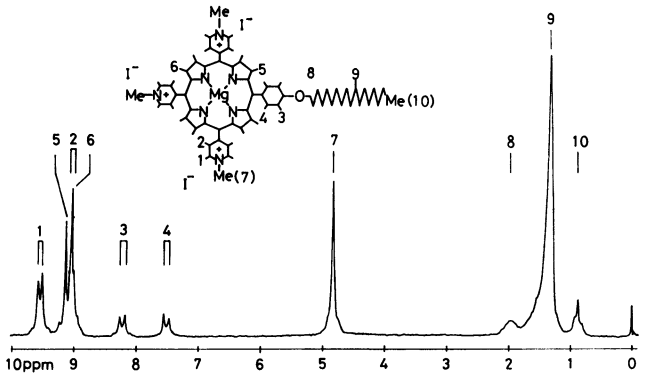

Fig. 1. ^{1}H-NMR Spectrum of 5,10,15-tris(1-methylpyridinium-4-yl)-20-[4-(octadecyloxy)phenyl]porphinatomagnesium(II) triiodide (dimethyl sulfoxide-d_6 solution, TMS internal reference, 100 MHz).

complex, a mixture of chloroform, methanol, and pyridine was used as an eluent.

5,10,15-Tris(1-methylpyridinium-4-yl)-20-[4-(octadecy)loxyphenyl]-21H,23H-porphine Triiodide (Abbreviated as $H_2TMePyStPPI_3$): Yield 50%. Found :C, 56.67; H, 5.66; N, 7.47%. Calcd for $C_{62}H_{72}I_3N_7O$: C, 56.76; H, 5.53; N, 7.18%. Vis (DMSO) 422 (ε 230000), 515 (15000), 552 (6800), 584 (5200), and 645 nm (3100).

[Zn(TMePyStPP)]I_3: Yield 80%. Found: C, 50.60; H, 5.06; N, 6.21%. Calcd for $C_{62}H_{70}I_3N_7OZn\cdot 6H_2O$: C, 50.20; H, 5.57; N, 6.61%. Vis (H_2O) 437 (ε 127000), 568 (16200), and 614 nm (9160).

[Co(TMePyStPP)]I_3: Yield 85%. Found: C, 54.67; H, 5.15; N, 7.19%. Calcd for $C_{62}H_{70}CoI_3N_7O$: C, 54.40; H, 5.15; N, 7.16%. Vis (H_2O) 332 (ε 12700), 439 (58700), 554 (8920), and 610 nm (sh).

[Mn(OH)(TMePyStPP)]I_3: Yield 50%. Found: C, 52.77; H, 5.20; N, 6.73%. Calcd for $C_{62}H_{71}I_3MnN_7O_2\cdot 2H_2O$: C, 52.52; H, 5.33; N, 6.91%. Vis (H_2O) 400 (ε 44700), 464 (111000), 563 (12900), 680 (1920), and 774 nm (1970).

Results and Discussion

All the *N*-methylated porphyrins are soluble in polar organic solvents such as *N,N*-dimethylformamide, dimethyl sulfoxide, tetrahydrofuran, methanol, chloroform, *etc.* They are soluble also in water due to the hydrophilic 1-methylpyridinium-4-yl groups forming presumably normal micelle colloid solutions. In a preliminary experiment to check the colloid formation in water, loss of porphyrins was not observed after passing the solution through a Sephadex G-50 column, indicating that they dissolve in water as high molecular weight aggregates. Because of the water solubility, they can be readily incorporated into pre-formed vesicles of phospholipids by immersing them in aqueous solutions of the porphyrins to give interesting asymmetrical vesicles[6] which are convenient systems for the study of the role of electron mediators in the photo-induced electron transport *via* the lipid membranes.[7–10]

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