COMMUNICATIONS

- New or improved synthetic methods
- Key intermediates
- with full experimental and analytical data

An Improved Synthesis of Surfactant Porphyrins

Yohmei OKUNO*, William E. FORD, Melvin CALVIN

Laboratory of Chemical Biodynamics, Lawrence Berkeley Laboratory, University of California, Berkeley, California 94720, U.S.A.

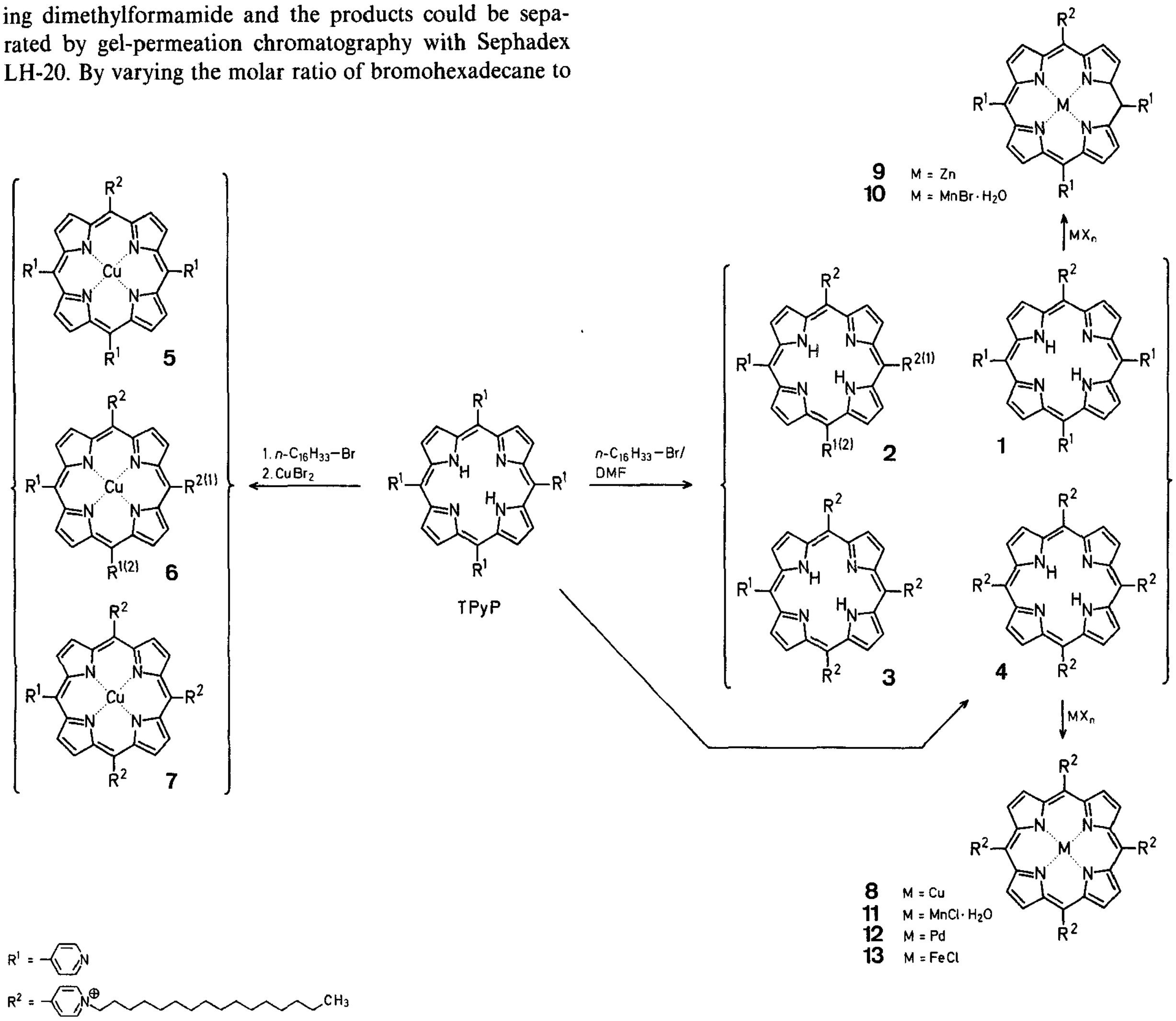
Considerable effort has recently been directed towards finding chemical processes that are capable of conversion and storage of light energy. One approach to this involves the photolysis of water by means of dye-sensitized electron-transfer reactions, as in photosynthesis. Surfactant porphyrins seem to be promising for such reactions across artificial photosynthetic membranes. Preparation of some surface-active porphyrins has been reported[1,2]. However, there remained some difficulties in yields and degree of alkylation. We now report the improved preparation and purification of surfactant porphyrins derived from the partial quaternization of *meso*-tetra(4-pyridyl)-porphyrin (TPyP), and the partial esterification of *meso*-tetra(4-carboxyphenyl)-porphyrin (TCPP).

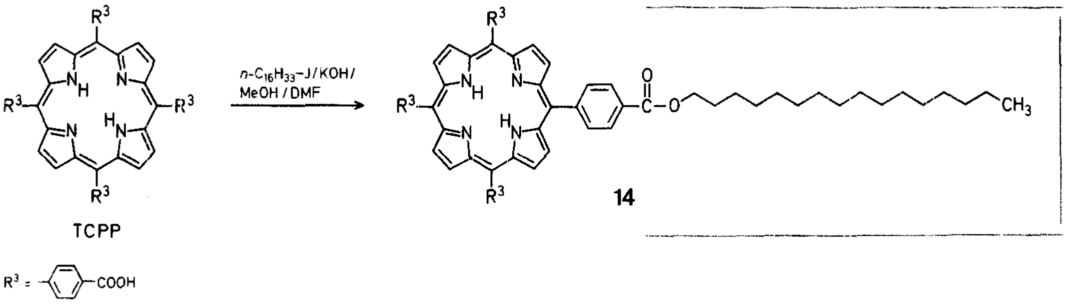
The quaternization of TPyP proceeded smoothly in refluxing dimethylformamide and the products could be separated by gel-permeation chromatography with Sephadex LH-20. By varying the molar ratio of bromohexadecane to TPyP, and the reaction time, the relative proportions of the mono-, di-, tri-, and tetraquaternized porphyrins (designated **1**, **2**, **3**, and **4**) can be adjusted. The tetra-derivative (**4**) was obtained with 83% yield by using a forty-fold excess of bromohexadecane. The porphyrins (**1–4**) were converted to their metal chelates (**9–13**) by reacting them with the metal salts. Alternatively, the metallocomplexes (**5–8**) could be obtained by reacting the metal salts with mixture of **1–4** in dimethylformamide, then separating by chromatography on alumina and Sephadex LH-20.

The mono-hexadecyl ester of TCPP (**14**) was prepared by reaction of TCPP with 1 equiv of potassium hydroxide in methanol and excess 1-iodohexadecane.

Thus cationic and anionic surfactant porphyrins can be prepared from commercially available synthetic porphyrins.

The photochemical properties of these porphyrins in aqueous media will be published elsewhere.





Mono-, Di-, Tri-, and Tetraquaternized Porphyrins (1, 2, 3, 4):

A solution of TPyP (306 mg, 0.49 mmol) and 1-bromohexadecane (2.1 g, 6.8 mmol) in dimethylformamide (300 ml) is refluxed for 4 h under nitrogen. The solvent is removed and the residue is washed with ether (3 × 25 ml) to remove the excess bromide. The solid mixture is dissolved in methanol (~6 ml) and the unreacted TPyP (negligible) is filtered off. The filtrate is evaporated and the product is purified by repeated gel filtrations over Sephadex LH-20 using methanol as eluent as shown below. After one pass through a short column (1.8 × 24 cm), the first treatment with a 4 × 50 cm column gives three fractions: A, B and C. Fraction A which moves fastest is a mixture of 3 and 4; it is gel-filtrated again to give two new fractions: D and E. Each of the fractions B, D, and E which contain predominantly **2**, **3**, and **4**, respectively, is once again gel-filtrated individually using the same conditions. Fraction C is mainly the mono-derivative **1**. Fractions B, C, D, and E are further purified by precipitations from methanol/ether and from ethanol/ether, and are then dried overnight at 50 °C in vacuo over phosphorus pentoxide.

Monoquaternized Porphyrin **1**; yield: 68 mg (15%) of violet solid.

$C_{56}H_{59}BrN_8 \cdot H_2O$	calc.	C 71.34	H 6.84	N 11.89
(942.1)	found	71.62	6.43	11.85

Vis. (ethanol/DMF, 1/1): λ_{max} = 417 (log ε = 5.43), 512 (4.26), 548 (3.80), 588 (3.77), 644 nm (3.38).

Vis. (methanol): λ_{max} = 415 (log ε = 5.37), 512 (4.24), 548 (3.81), 591 (3.76), 645 nm (3.34).

Diquaternized Porphyrin **2**; yield: 157 mg (25%) of a violet solid; mixture of two isomers.

$C_{72}H_{92}Br_2N_8 \cdot 2H_2O$	calc.	C 68.30	H 7.58	N 8.85
(1265.4)	found	67.88	7.30	8.73

Vis. (ethanol/DMF, 1/1): λ_{max} = 421 (log ε = 5.38), 514 (4.20), 551 (3.84), 589 (3.76), 646 nm (3.32).

Triquaternized Porphyrin **3**; yield: 177 mg (23%) of a violet solid.

$C_{88}H_{125}Br_3N_8 \cdot 3H_2O$	calc.	C 66.46	H 8.24	N 7.05
(1588.8)	found	66.15	8.10	6.95

Vis. (ethanol/DMF, 1/1): λ_{max} = 424 (log ε = 5.36), 516 (4.20), 553 (3.85), 590 (3.78), 647 nm (3.28).

Tetraquaternized Porphyrin **4**; yield: 78 mg (8%) of a violet solid; m.p. >260 °C.

$C_{104}H_{158}Br_4N_8 \cdot 3H_2O$	calc.	C 65.89	H 8.66	N 5.91
(1894.2)	found	65.83	8.34	6.08

Vis. (ethanol/DMF, 1/1): λ_{max} = 425 (log ε = 5.36), 516 (4.23), 553 (3.87), 590 (3.82), 646 nm (3.26).

Vis. (methanol): λ_{max} = 426 (log ε = 5.35), 517 (4.29), 557 (4.06), 593 (3.99), 647 nm (3.65).

*5,10,15,20-Tetrakis[1-hexadecylpyridinium-4-yl]-21*H*,23*H*-porphine Tetrabromide* (tetraquaternized porphyrin 4) may be obtained in 83% yield in the same manner using a 40 fold molar excess of 1-bromohexadecane (2 h at reflux temperature).

5,10,15,20-Tetrakis[1-hexadecylpyridinium-4-yl]-21*H*,23*H*-porphine-copper Tetraperchlorate (8):

The tetraquaternized porphyrin **4** (25 mg, 13 μmol) and copper(II) bromide (6 mg, 27 μmol) are added to boiling methanol (100 ml). [The reaction may be monitored spectrophotometrically.] After 1 h, methanol is evaporated and the residue washed with water (3 × 15 ml). The crude product (20 mg, 78%) is purified by column chromatography over alumina (Woelm, neutral, activity I; 1.8 × 18 cm) using chloroform/methanol (80/20) as eluent and by gel filtration (1.8 × 24 cm) using methanol. The solvent is removed, the residual product dissolved in methanol (~3 ml), and then precipitated as the perchlorate **8** by addition of an equal volume of aqueous 0.1 molar sodium perchlorate solution. The resultant solid red product is isolated by suction, washed with water, and dried overnight over phosphorus pentoxide in vacuo at 50 °C; yield: 21 mg (79%).

$C_{104}H_{156}N_8O_{16}Cl_4Cu$	calc.	C 63.09	H 7.96	N 5.66
(1979.8)	found	62.92	7.88	5.63

Vis. (methanol): λ_{max} = 428 (ε, ratios, 100), 549 (5.1), 585 nm (sh, 1.6).

Copper Complexes 5, 6, and 7:

A solution of TPyP (101 mg, 0.16 mmol) and 1-bromohexadecane (502 mg, 1.6 mmol) in dimethylformamide (100 ml) is refluxed under nitrogen for 2 h, and then evaporated to dryness. The residue is washed with ether (3 × 15 ml) and dissolved in methanol (~10 ml), and the unreacted TPyP is filtered off. The filtrate is diluted with methanol (100 ml) and copper(II) bromide (21 mg, 94 μmol) is added. The mixture is refluxed for 1 h and then evaporated. The residue is washed with water (3 × 15 ml) and column-chromatographed on alumina (Woelm, neutral, activity I; 1.8 × 18 cm) using chloroform/methanol (85/15) as eluent to give three fractions. Each fraction is gel-chromatographed on Sephadex LH-20. The solvent is evaporated and the residue dissolved in methanol and precipitated again as the perchlorate (**5**, **6**, **7**) by the addition of an equal volume of aqueous 0.1 molar sodium perchlorate solution. The resultant solid product is isolated by suction, washed with water, and dried overnight over phosphorus pentoxide in vacuo at 50 °C.

Copper Complex **5**; yield: 45 mg (27%) of a red solid.

$C_{56}H_{57}ClCuN_8O_4$	calc.	C 66.92	H 5.72	N 11.15
(1005.1)	found	66.68	5.76	10.92

Vis. (methanol): λ_{max} = 414 (log ε = 5.37), 543 (4.23), 584 nm (3.54).

Copper Complex **6**; yield: 29 mg (13%) of a red solid; mixture of two isomers.

$C_{72}H_{90}Cl_2CuN_8O_8 \cdot H_2O$	calc.	C 64.15	H 6.88	N 8.31
(1330.0)	found	64.02	7.10	7.70

Vis. (methanol): λ_{max} = 418 (ε, ratios, 100), 544 (8.3), 583 nm (2.4).

Copper Complex **7**; yield: 9 mg (3.3%) of a red solid.

$C_{88}H_{123}Cl_3CuN_8O_{12}$	calc.	C 63.87	H 7.49	N 6.77
(1654.9)	found	63.88	7.44	7.09

Vis. (methanol): λ_{max} = 422 (ε, ratios, 100), 545 (9.5), 580 nm (sh, 3.3).

5-(1-Hexadecylpyridinium-4-yl)-10,15,20-tris[4-pyridyl]-21*H*,23*H*-porphine-zinc Perchlorate Semihydrate (9):

5-(1-Hexadecylpyridinium-4-yl)-10,15,20-tris[4-pyridyl]-21*H*,23*H*-porphine bromide (**1**; 50 mg, 53 μmol) and zinc acetate dihydrate (16 mg, 73 μmol) are added to acetic acid (40 ml), the mixture is refluxed for 9 min, and then evaporated to dryness in vacuo at 40 °C. The residue is taken up in chloroform (~3 ml) and column-chromatographed on alumina (Woelm, neutral, activity I; 1.8 × 14.5 cm) using chloroform/methanol (95/5) as eluent followed by gel filtration on Sephadex LH-20 (1.8 × 24.5 cm) using chloroform/methanol (50/50) as eluent. The solvent is evaporated, the residual product dissolved in methanol (~6 ml), and an equal volume of aqueous 0.1 molar sodium perchlorate solution is added. The precipitate is isolated by suction, washed with water and methanol, and dried over phosphorus pentoxide in vacuo at 50 °C; yield: 40 mg (74%).

$C_{56}H_{57}ClN_8O_4Zn \cdot 1/2\,H_2O$	calc.	C 66.20	H 5.76	N 11.03
(1016.0)	found	66.44	5.77	10.89

Vis. (methanol): λ_{max}=423 (log ε=5.37), 559 (4.26), 606 nm (3.79).

Chloro-(5,10,15,20-tetrakis[1-hexadecylpyridinium-4-yl]-21*H*,23*H*-porphine)-manganese Tetraperchlorate Trihydrate (11):
Manganese(II) chloride tetrahydrate (10 mg, 51 μmol) is added to a solution of 5,10,15,20-tetrakis[1-hexadecylpyridinium-4-yl]-21*H*,23*H*-porphine tetrabromide (4; 49 mg, 26 μmol) in dimethylformamide (100 ml). The mixture is refluxed for 35 min and then evaporated to dryness. The product is column-chromatographed on alumina (Woelm, neutral, activity I; 1.8 × 13 cm) using chloroform/methanol (80/20) as eluent. The resultant product is dissolved in methanol (~3 ml), and **11** is precipitated by adding an equal volume of aqueous 0.1 molar sodium perchlorate solution. The precipitate is isolated by suction, washed with water, and dried in vacuo over phosphorus pentoxide at 50 °C; yield: 16 mg (30%).

$C_{104}H_{156}Cl_5MnN_8O_{16}(H_2)\cdot$	calc.	C 60.62	H 7.92	N 5.44
$2H_2O$ (2060.7)	found	60.38	7.52	5.45

Vis. (methanol): λ_{max}=463 (ε, ratios, 100), 571 (8.8), 615 (sh, 3.0), 680 (sh, 0.9), 768 nm (0.8).

Bromo-(5-[1-hexadecylpyridinium-4-yl]-10,15,20-tris[4-pyridyl]-21*H*,23*H*-porphine)-manganese Perchlorate Trihydrate (10):
A procedure analogous to that for **11** is employed using the monoquaternized porphyrin **1** (86 mg, 91 μmol) and manganese(II) acetate tetrahydrate (119 mg, 0.49 mmol) in acid (100 ml); yield: 69 mg (67%).

$C_{56}H_{37}BrClMnN_8O_4\cdot$	calc.	C 59.50	H 5.61	N 9.91
(H_2O) 2 H_2O (1130.5)	found	59.35	5.26	9.79

Vis. (methanol): λ_{max}=463 (log ε=5.07), 560 (4.07), 590 (sh, 3.77), 682 (3.07), 773 nm (3.07).

5,10,15,20-Tetrakis[1-hexadecylpyridinium-4-yl]-21*H*,23*H*-porphine-palladium Tetraperchlorate (12):
Palladium(II) chloride dihydrate (6.2 mg, 29 μmol) is added to a solution of 5,10,15,20-tetrakis[1-hexadecylpyridinium-4-yl]-21*H*,23*H*-porphine tetrabromide (4; 52 mg, 28 μmol) in dimethylformamide (100 ml). The mixture is refluxed under nitrogen for 1 h and then evaporated to dryness. The residue is column-chromatographed on alumina (Woelm, neutral, activity I; 1.8 × 15 cm). The main fraction is eluted with chloroform/methanol (90/10) and then chloroform/methanol (80/20) and further purified by gel filtration on Sephadex LH-20 (1.8 × 26 cm) using methanol/chloroform (90/10). The solvent is evaporated to give the bromide salt (32 mg, 58%). This salt is dissolved in methanol (~3 ml), and an equal volume of aqueous 0.1 molar sodium perchlorate solution is added. The precipitated perchlorate is isolated by suction, washed with water, and dried in vacuo over phosphorus pentoxide to give **12** as a brown solid; yield: 22 mg (40%).

$C_{104}H_{156}Cl_4N_8O_{16}Pd$	calc.	C 61.76	H 7.77	N 5.54
(2022.7)	found	61.52	7.72	5.47

Vis. (methanol): λ_{max}=420 (ε, ratios, 100), 525 (10), 560 nm (4.9).

Chloro-(5,10,15,20-tetrakis[1-hexadecylpyridinium-4-yl]-21*H*,23*H*-porphine)-iron Tetraperchlorate (13):
Iron(III) chloride (3.9 mg, 24 μmol) is added to a solution of 5,10,15,20-tetrakis[1-hexadecylpyridinium-4-yl]-21*H*,23*H*-porphine tetrabromide (4; 25 mg, 13 μmol) in dimethylformamide (100 ml) under nitrogen. The mixture is heated at 120 °C for 2 h and is then refluxed for an additional 2 h. The solvent is evaporated, the residue washed with water (2 × 15 ml) and with acetone (2 × 15 ml), and is column-chromatographed twice on alumina (Woelm, neutral, activity I; 1.8 × 13 cm) using chloroform/methanol (95/5) as eluent. The eluate is evaporated, the residue dissolved in methanol (~2 ml), and an equal volume of aqueous 0.1 molar sodium perchlorate solution is added. The precipitated iron complex is isolated by suction, washed with water, and dried in vacuo over phosphorus pentoxide at 50 °C; yield: 5 mg (19%).

$C_{104}H_{156}Cl_5FeN_8O_{16}$	calc.	C 62.22	H 7.83	N 5.58
(2007.6)	found	62.15	7.80	5.59

Vis. (methanol): λ_{max}=414 (ε, ratios, 100), 441 (sh, 75), 572 (10), 630 nm (3.1).

10-(4-Hexadecyloxycarbonylphenyl)-5,15,20-tris[4-carboxyphenyl]-21*H*,23*H*-porphine Trihydrate (14):
5,10,15,20-Tetrakis[4-carboxyphenyl]-21*H*,23*H*-porphine (TCPP; 220 mg, 0.27 mmol) is dissolved in dimethylformamide (200 ml), potassium hydroxide (22 mg, ~0.4 mmol) and 1-iodohexadecane (310 mg, 0.87 mmol) are added, and the mixture is refluxed under nitrogen for 2 h. The solvent is then evaporated and the residual product is purified by column chromatography on silica gel (Bio-Rad, Bio-Sil HA) using methanol/chloroform/triethylamine (30/70/1, by volume) as eluent. Compound **14** is obtained as a violet solid; yield: 0.033 mg (12%); m.p. >285 °C.

$C_{64}H_{62}N_4O_8\cdot 3H_2O$	calc.	C 71.89	H 6.41	N 5.24
(1069.3)	found	71.97	6.89	5.09

I.R. (KBr): ν=1722, 1691 cm^{-1}.

Vis. (ethanol/DMF, 1/1): λ_{max}=418 (log ε=5.57), 513 (4.18), 549 (3.90), 591 (3.65), 648 nm (3.60).

Vis. (methanol): λ_{max}=416 (log ε=5.65), 513 (4.26), 551 (3.93), 591 (3.69), 646 nm (3.55).

This work was supported by the Division of Chemical Sciences, Office of Basic Energy Sciences, Department of Energy under contract W-7405-Eng-48.

Received: July 19, 1979
(Revised form: November 26, 1979)

---

* Present address: Faculty of Pharmaceutical Sciences, Hokkaido University, Sapporo, Japan 060.

** Address for correspondence.

[1] J. H. Fuhrhop, M. Baccouche, *Justus Liebigs Ann. Chem.* **1976**, 2058.

[2] T. Yamamura, *Chem. Lett.* **1977**, 773.

0039-7881/80/0732-0539 $ 03.00