Pergamon

Tetrahedron 57 (2001) 2103–2108

TETRAHEDRON

The first isolation of unsubstituted porphyrinogen and unsubstituted 21-oxaporphyrinogen by the '3+1' approach from 2,5-bis(hydroxymethyl)pyrrole and tripyrrane derivatives

Shozo Taniguchi,[a,*] Hikaru Hasegawa,[b] Shoko Yanagiya,[b] Yusuke Tabeta,[b] Yoshiharu Nakano[c] and Masahiko Takahashi[a]

[a]*Department of Materials Science, Faculty of Engineering, Ibaraki University, Hitachi, Ibaraki 316-8511, Japan*
[b]*Department of Chemistry and Material Engineering, Ibaraki National College of Technology, Hitachinaka, Ibaraki 312-8508, Japan*
[c]*Department of Natural Material Science, Faculty of Science, Ibaraki University, Mito, Ibaraki 310-8512, Japan*

Received 20 November 2000; accepted 11 January 2001

Abstract—The treatment of 2,5-bis(hydroxymethyl)pyrrole or 2,5-bis(hydroxymethyl)furan with pyrrole in the presence of hydrochloric acid gave tripyrrane and 2,5-bis(2-pyrrolylmethyl)furan in 58–61% yield, which afforded the simplest porphyrinogen (hexahydroporphine) and 21-oxaporphyrinogen by the '3+1' approach in 14 and 11% yields, respectively. 21-Oxaporphyrinogen has been shown to adopt a 1,2-alternated conformation in the solid state by X-ray crystallography.

1. Introduction

'Porphine' and its precursor 'porphyrinogen' are often cited in guidebooks of chemistry and biology. Although porphine is the most basic compound in the porphyrin chemistry and it has been more than 60 years since its first synthesis,[1] its preparation is still one of the most difficult processes in organic synthesis.[2] In the previous letter,[3] we described a route to porphine using the '3+1' condensation of 2,5-bis(hydroxymethyl)pyrrole (**1**) with newly acquired tripyrrane (**3**) in 31% yield. This approach has been adopted by Sakata et al. for the synthesis of a squared π-conjugated porphyrin tetramer.[4]

In general, the precursor porphyrinogen is readily oxidized into the corresponding porphyrin with oxidizing agents such as chloranil. However, the simplest porphyrinogen (**5**), to the best of our knowledge, has not been isolated yet. Fully *meso*-substituted porphyrinogens are stable, and the octamethyl derivative was isolated back in 1886 by Baeyer.[5] Although the chemistry of fully *meso*-substituted porphyrinogens has been extensively studied by Sessler et al.[6] and Floriani et al.[7] in recent years, that of β-substituted and *meso*-unsubstituted porphyrinogens has remained unexplored since Fischer and Baumler's first isolation in 1929.[8]

In 1979, Kämmerer et al.[9] reported a route to the methylene bridged trimer of phenols by the condensation of 2,6-bis-(hydroxymethyl)-4-substituted phenols with excess 4-substituted phenols in the presence of hydrochloric acid. The trimers were then converted to calix[4]arenes using acid-catalyzed '3+1' condensation with 2,6-bis(halogenomethyl)-4-substituted phenols. The structural similarity of the calix[4]arenes to *meso*-unsubstituted porphyrinogens prompted us to apply this methodology to the synthesis of **5** and its furan analog **6**, and the results will be described with full experimental details in this paper.

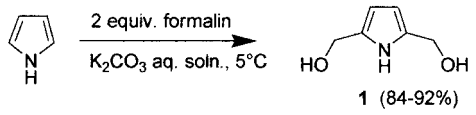
2. Results and discussion

2.1. Formation of 2,5-bis(hydroxymethyl)pyrrole (1)

2-(Hydroxymethyl)pyrrole is a quite attractive compound for preparing porphyrinogen (**5**). In fact, Longo et al. obtained porphine (8–10%), an oxidation product of **5**, in a reaction of the 2-(hydroxymethyl)pyrrole over a period of 10 days in chromatographed ethylbenzene at 100°C.[10] However, the compound is very hard to handle and to store for a long period of time because of the occurrence of self-condensation. 2-(Hydroxymethyl)pyrrole was obtained from pyrrole by two steps, formylation of pyrrole followed by reduction of the resulting pyrrolecarboxaldehyde.[11] An attempt to obtain 2-(hydroxymethyl)pyrrole by a direct method was unsuccessful. In aqueous solution, under the conditions of equimolar pyrrole and formalin, only pyrrole and **1** were detected by MS measurement without the desired compound.

Keywords: tripyrrane; porphyrinogen; porphyrin; 21-oxaporphyrinogen; '3+1' type condensation.
* Corresponding author. Tel.: +81-29-271-2981; fax: +81-29-271-2992; e-mail: taniguti@chem.ibaraki-ct.ac.jp

0040–4020/01/$ - see front matter
PII: S0040-4020(01)00059-X



Scheme 1. Synthesis of 2,5-bis(hydroxymethyl)pyrrole.

We then examined preparation of **1** from pyrrole under various conditions of condensation according to the literature.[12] Acid-catalyzed condensation by hydrochloric acid or acetic acid afforded a black polymer or intractable tar. Homogeneous, base-catalyzed condensation in ethanol or ethanol–water afforded linear and cyclic oligomers. Usually, but not always, pyrrole at a high concentration in formalin solution tends to condense readily to tar or a polymer. As pyrrole slowly dissolves into aqueous solution with the progress of the reaction, the heterogeneous conditions seems to be well suited to this work-up process, in which water plays a vital role to control the reaction. Since we needed to obtain **1** in sufficiently large quantity, we did not examine a high-dilution technique in a homogeneous solution.

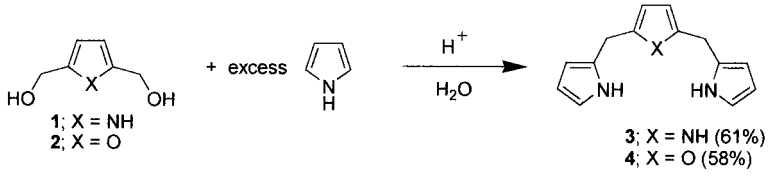
At a temperature above 50°C, condensation of pyrrole with 2 equiv. of formalin in a K_2CO_3 solution afforded yellow tar, which solidified to a black polymer within 2 days upon exposure to the atmosphere. At room temperature, condensation under the same condition afforded **1** (<30%) with tacky liquid. In this case, it was very difficult to separate **1** from oligomers in the purification process. A technique of column chromatography on silica gel was not effective in this separation. The problem of oligomerization was solved by vigorously stirring the heterogeneous solution in a refrigerator below 5°C for 7 days (Scheme 1). The upper layer of pyrrole disappeared within 3 days. After the reaction had been completed, water was quickly removed to dryness at a temperature below 50°C in vacuo (3–4 Torr) with a rotary evaporator. The compound **1** is stable even at 50°C in an alkaline solution under reduced pressure. Acetone was added to the resulting white tacky solid, and K_2CO_3 was filtered off. The acetone solution was kept over Na_2SO_4 overnight to achieve complete dryness. Allowing the solution to stand for more than one day, the work-up process became difficult because of self-condensation. The crude product was obtained by removing the solvent. Washing the white solid formed in a freezer with a minimum amount of cooled acetone afforded white precipitates in 84–92% yield, and these can be used without further purification for the next step. An attempt to purify of **1** by vacuum distillation was unsuccessful because of decomposition.

2,5-Bis(hydroxymethyl)furan (**2**) was obtained by acid-pyrolysis of sugar followed by reduction of the resulting 3-(hydroxymethyl)furancarboxaldehyde, according to the literature.[13,14]

2.2. Formation of tripyrrane (3) and 2,5-bis (2-pyrrolylmethyl)furan (4)

As described above, pyrrolic alcohols readily condense with pyrrole to oligomers and polymers in the presence of acid above room temperature. By analogy of the methylene-bridged trimer of phenols from 2,6-bis(hydroxymethyl)-4-substituted phenols and excess phenols,[9] we applied the methodology to a pyrrole system instead of phenols (Scheme 2).

Due to the lability and high reactivity of **1**, it afforded only intractable tar above room temperature in the presence of acid. In alcoholic solution, the condensation products were a mixture of a dimer and a trimer. The dimer, dipyrrolylmethane, was already isolated[15] by column chromatography on silica gel in a basic medium.[16] We found that the dimer



Scheme 2. Direct synthesis of tripyrrane analogs.

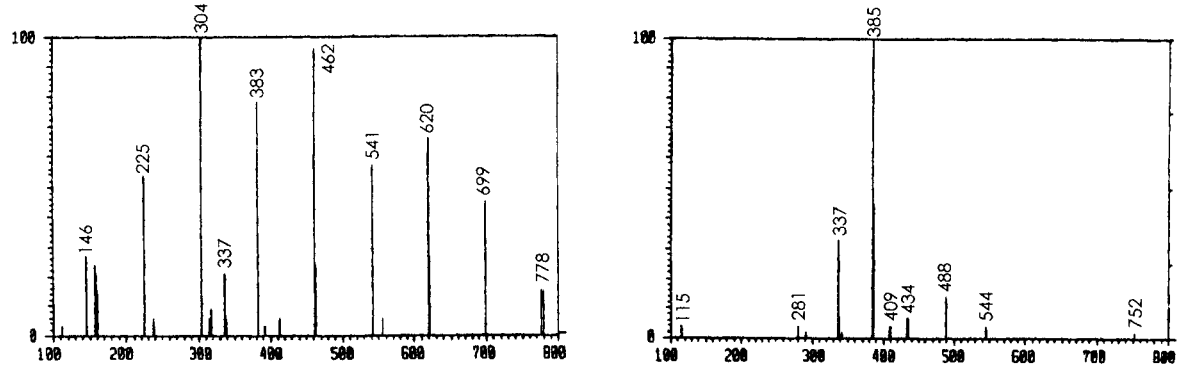
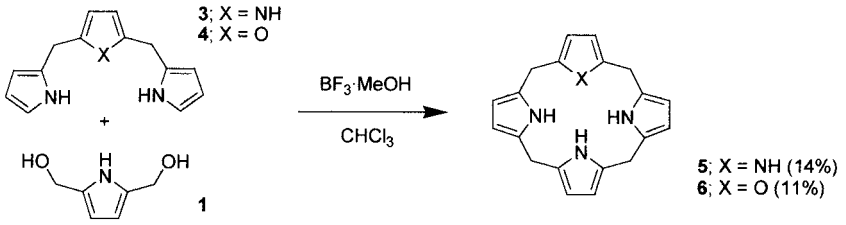


Figure 1. The FDMS spectra of the distillation residue (TFA-catalyzed) of **3** (left) and **4** (right). The peaks of **3** at *m/z* 146, 225, 304, 383, 462, 541, 620, 699 and 778 show linear dimer to decamer, and cyclic trimer and tetramer are observed at *m/z* 237 and 316, respectively. The peak of **4** at *m/z* 385 corresponds to linear pentamer (pyrrole 3, furan 2).



Scheme 3. Porphyrinogen synthesis by '3+1' condensation.

could be easily purified by distillation at 107–112°C/0.1 Torr. The trifluoroacetic acid-catalyzed condensation of **1** with excess pyrrole was found to be quite effective, but always accompanied by a small amount of the dimer. Finally, we found that hydrochloric acid-catalyzed condensation in water at low temperature gave **3** in the best yield (61%). These results mean that water is the best solvent and it prefers a polar-protic solvent in this condensation.

Although the acid-catalyzed condensation of 1,3-bis-(hydroxymethyl)benzene or 2,6-bis(hydroxymethyl)pyridine with excess pyrrole was unsuccessful, 2,5-bis(2-pyrrolylmethyl)furan (**4**) (58%) was obtained upon reflux for 1 h from **2** and pyrrole in a similar manner. The distillate was pale yellow viscous liquid with greenish fluorescence and quickly solidified. Vacuum distillation of **3** (TFA-catalyzed) and **4** left a small amount of residue, in each case. The FDMS spectra of the residues are shown in Fig. 1. A linear dimer to decamer and the cyclic trimer and tetramer seem to exist in the residue of **3**. In contrast to **3**, a linear pentamer (pyrrole 3, furan 2) was observed as the main peak in the residue of **4**. These observation and the reaction temperature indicate that **3** is more labile than **4**.

2.3. Formation of porphyrinogen (5) and 21-oxaporphyrinogen (6)

Recently, we recorded a good yield (31%) on porphine synthesis in 1 mM condition.[3] In order to demonstrate the usefulness of the newly acquired unsubstituted tripyrrane analogs, the synthesis of **5** by the '3+1' method was carried out in the concentration of a 10 mM scale (Scheme 3). As porphyrinogen is easily oxidized to porphyrin and is very difficult to handle, except for calixpyrroles,[17] we examined the condensation in a 10-fold higher concentration as compared to porphine synthesis. Thus, **5** was isolated for the first time in 14% yield. In the ^{1}H NMR spectra of **5** in $CDCl_3$ at room temperature, *meso*-methylene protons appeared at δ 3.82 as a sharp singlet, and pyrrolic protons appeared in an ordinary field (δ 7.38). This fact suggest that the conformational inversion of the unsubstituted porphyrinogen **5** occurs rapidly in a chloroform solution at room temperature. An attempt to collect X-ray diffraction data was unsuccessful because of the unsuitable single crystals from diethyl ether solution. In spite of an unstable compound, the difference of reactivity between the sp^3 carbons (*meso*-positions) and the sp^2 carbons (β-positions) in **5** is of particular interest. Methylation of **5** with excess CH_3I in the presence of $AlCl_3$ afforded a reaction mixture of mono- to octamethyl porphyrinogens. However, the isolated products were so slight that we could not determine the reaction positions.

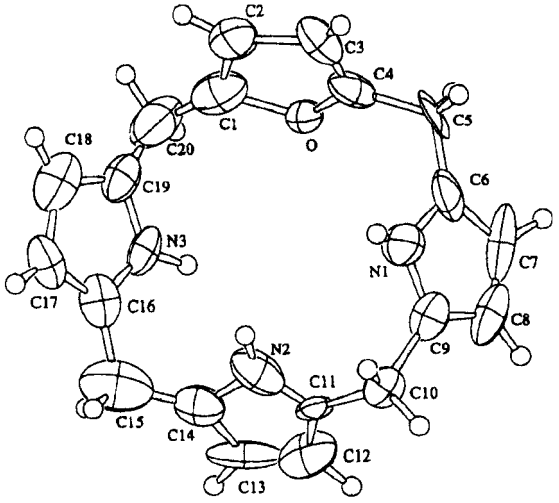


Figure 2. View of the molecular structure of **6**. Thermal ellipsoids are scaled to the 50% probability level. The compound adopts a 1,2-alternated conformation in the solid state. Dihedral angles between least-squares planes: O plane–N1 plane, 68.8°; N1 plane–N2 plane, 70.7°; N2 plane–N3 plane, 72.0°; O plane–N2 plane, 2.4°; N1 plane–N3 plane, 2.4°.

A sample of **4** was treated in the same manner as that of **3**, affording **6** (11% yield). In the ^{1}H NMR spectra of 6 in $CDCl_3$ at room temperature, *meso*-methylene protons connected with a pyrrole ring and connected with a furan ring appeared at δ 3.79 and δ 3.86 as a sharp singlet, respectively. This fact also suggests that the conformational inversion of the unsubstituted 21-oxaporphyrinogen **6** occurs rapidly in a chloroform solution at room temperature. The structure of **6** in the solid state was confirmed by X-ray analysis as shown in Fig. 2. The results of analysis revealed that **6** adopts a 1,2-alternated conformation[18] and that rings of the opposite side is approximately parallel to each other. Sessler et al. reported that in the solid state *meso*-octamethylcalix[4]pyrrole and *meso*-tetraspirocyclohexylcalix[4]pyrrole adopt a 1,3-alternated conformation,[17,19] but β-octabromo-*meso*-octamethylcalix[4]pyrrole adopts a flattened 1,2-alternated conformation.[20] Recently, Uno et al. reported that fully β-substituted, *meso*-unsubstituted porphyrinogen containing 2-propanol in the solid state also adopts an ideal 1,2-alternate structure in the solid state.[21]

The condensation of **2** with **3** seems to be another route to **6**. In fact, the reaction afforded a very small amount of **6**. It could be detect only on TLC but not isolated. An attempt to obtain 21-oxaporphine by oxidation of **6** was carried out. After the reaction had been completed, chloranil was directly added to the solution, which was refluxed for 30 min and concentrated. The FDMS spectrum is shown

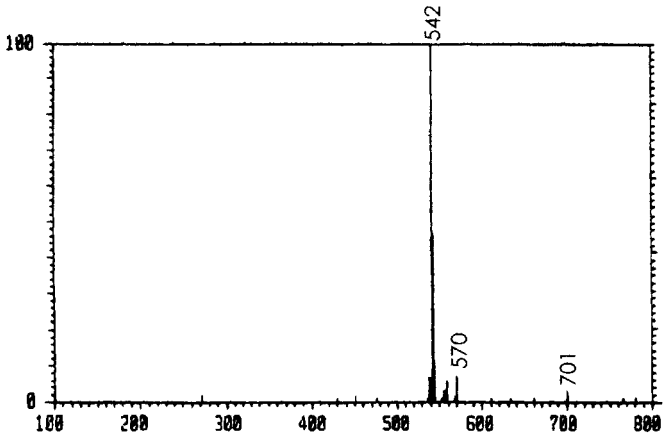


Figure 3. FDMS spectrum of the oxidation mixture of one-pot synthesis: reaction of **4** with **6**.

in Fig. 3. No peak corresponding to 21-oxaporphine (311 *m/z*) was observed, and the intense peak at *m/z* 542 was tentatively assigned to the product of Diels–Alder reaction of **4** with **6**.

3. Conclusions

The most basic unsubstituted porphyrinogen and unsubstituted 21-oxaporphyrinogen were isolated for the first time in the yield of 14 and 11%, respectively, by new building blocks, 2,5-bis(hydroxymethyl)pyrrole and tripyrranes. 21-Oxaporphyrinogen adopts a 1,2-altenated conformation in the solid state. This new synthesis of tripyrranes would contribute to the chemistry of porphyrins, core-modified porphyrins and expanded porphyrins.

4. Experimental

4.1. General

Melting points were determined with a SHIBATA 5227-01 and are uncorrected. IR spectra (JASCO FTIR-230) and ^{1}H NMR spectra (HITACHI R-1900 and JEOL GSX 400) were recorded routinely. Mass spectra were taken on a HITACHI M-70 or a JEOL JMS DX-300. FDMS was taken on a HITACHI M-2000 equipped with a carbon emitter (acetone) at the HITACHI CHEMICAL. X-ray diffraction data were collected on a RIGAKU AFC7R diffractometer with graphite monochromated Mo Kα. The structure was typically solved by direct methods (SIR92). Elemental analyses were performed with a YANACO CHN-CODER MT-5. HPLC-analyses were performed on a HITACHI 655A-12 connected to a HITACHI 655A UV-monitor. As columns, GASKUROKOGYO Inertsils (ODS-2, 100×4 mm^2 or ODS, 150×4 mm^2) were used with eluent, acetonitrile/water 50:50. TLC was measured on KODAK CHROMAGRAM sheet, #13181 silica gel.

Pyrrole and acetone were distilled before use. All other chemicals were purchased in reagent quality and used as received. All processes and reactions were carried out under argon with shielding from light. 2,5-Bis(hydroxymethyl)furan (**2**) was prepared according to the literature methods by two steps from sugar.[13,14]

4.1.1. 2,5-Bis(hydroxymethyl)pyrrole (1). We improved the reported method[12] as follows. An aqueous solution (200 mL) of potassium carbonate (62 g, 485 mmol) was degassed by bubbling with argon for 30 min below 5°C, then 35% formalin (41.6 g, 485 mmol) was added. To the cooled solution, pyrrole (16.4 g, 240 mmol) was immediately added, then the solution was vigorously stirred for 5–7 days in a refrigerator at 5°C. The upper layer of pyrrole disappeared in 2–3 days. The solution was evaporated to dryness below 50°C under reduced pressure. Fresh acetone (500 mL) was added to the resulting white viscous slurry. The precipitated potassium carbonate was filtered off and washed with acetone (2×300 mL), and the combined organic solution was refrigerated overnight over Na_2SO_4 (300 g). Evaporation of the solvent under reduced pressure below 30°C left a colorless viscous oil, which sometimes solidified during vacuum drying. A few milligrams of the desired powders was added to the oil, then the oil was cooled at −20°C in a freezer for 2 days, yielding a tacky white solid. This solid was washed with efficiently cooled acetone (20 mL) or 2-propanol (20 mL), giving a white solid, which was collected by filtration to give **1** (25.6–28.0 g, 84–92%). Can be stored for over five years at −20°C in a freezer, mp 115–116°C (dec., acetone, lit.[12] 117–118°C). TLC: R_f=0.38 (silica gel, ethanol). HPLC: R_t=0.74 min (Inertsil ODS-2, 100×4 mm^2, CH_3CN/H_2O 50:50, 1 mL/min). ^{1}H NMR (90 MHz, acetone-d_6): δ 3.79 (br, 2H, OH), 4.48 (s, 4H, CH_2), 5.84 (s, 2H, 3-H), 9.70 (br, 1H, NH). Ms: *m/z* 127 (M^+, 54), 110 (46), 96 (14), 80 (100), 53 (14). FTIR (KBr, cm^{-1}) 3304, 3250, 2938, 2869, 1425, 1203, 1027, 775. Anal. calcd for $C_6H_9NO_2$: C, 56.68; H, 7.13; N, 11.02. Found: C, 56.85; H, 7.21; N, 10.90.

4.1.2. 2,5-Bis(2-pyrrolylmethyl)pyrrole (tripyrrane) (3). Pyrrole (26.4 g, 394 mmol) was added to a stirred solution of **1** (5.0 g, 39 mmol) in water (700 mL) below 5°C under argon with shielding from light. After 30 min, concentrated hydrochloric acid (0.5 mL, 6 mmol) was added to the efficiently stirred solution. The solution immediately changed to a white emulsion. After 30 min, the mixture was neutralized with aqueous $NaHCO_3$, water and excess pyrrole were removed in vacuo (3–4 Torr) with a rotary evaporator, the residue was extracted with Et_2O or CH_2Cl_2 (3×300 mL), and the extract was subjected to distillation to

give **3** (5.4 g, 61%). Instead of the distillation, the separation by column chromatography (300×20 mm^2) on silica gel using CH_2Cl_2 as an eluent afforded **3** in 41% yield. Must be stored in a freezer. A colorless solid, mp 97–98°C (bp 186–194°C/0.1 Torr). TLC: R_f=0.90 (silica gel, CH_2Cl_2). HPLC: R_t=5.15 min (Inertsil ODS, 150×4 mm^2). ^1H NMR (90 MHz, $CDCl_3$): δ 3.74 (s, 4H, 5,10-H), 5.86 (d, 2H, J= 2.4 Hz, 7-, 8-H), 5.93 (m, 2H, 3-, 12-H), 6.07 (m, 2H, 2-, 13-H), 6.50 (m, 2H, 1-, 14-H), 7.36 (br, 1H, 16-NH), 7.64 (br, 2H, 15-, 17-NH). Ms: *m/z* 225 (M^+, 100), 158 (52), 145 (71), 80 (74). FTIR (KBr, cm^{-1}): 3415, 3338, 3085, 2898, 1097, 1026, 808, 800, 733, 725. Anal. calcd for $C_{14}H_{15}N_3$: C, 74.64; H, 6.71; N, 18.65. Found: C, 74.69; H, 6.52; N, 18.82.

4.1.3. 2,5-Bis(2-pyrrolylmethyl)furan (4). Pyrrole (7.0 g, 104 mmol) was added to a stirred solution of **2** (1.28 g, 10 mmol) in water (400 mL) at room temperature under argon with shielding from light. After 20 min, concentrated hydrochloric acid (0.2 mL, 2 mmol) was added to the efficiently stirred solution, and then the aqueous solution was refluxed for 30 min. The mixture was cooled and neutralized with aqueous $NaHCO_3$, water and excess pyrrole were removed in vacuo (3–4 Torr) with a rotary evaporator, the residue was extracted with CH_2Cl_2 (3×200 mL), and the extract was subjected to distillation to give **4** (1.3 g, 58%). A pale yellow solid, mp 84–85°C (bp 158–160°C/0.1 Torr). TLC: R_f=0.95 (silica gel, CH_2Cl_2). HPLC: R_t=3.46 min (Inertsil ODS-2, 100×4 mm^2). ^1H NMR (90 MHz, $CDCl_3$): δ 3.95 (s, 4H, CH_2), 5.95 (s, 2H, 3-, 4-H), 6.00 (m, 2H, 3′-H), 6.13 (m, 2H, 4′-H), 6.65 (m, 2H, 5′-H), 8.00 (br, 2H, NH). Ms: *m/z* 226 (M^+, 100), 159 (49), 146 (78), 80 (47). FTIR (KBr, cm^{-1}): 3376, 3351, 3336, 3129, 3105, 2886, 2830, 1563, 1182, 1113, 1013, 802, 719, 708. Anal. calcd for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24; N, 12.38. Found: C, 74.03; H, 6.31; N, 12.40.

4.1.4. Porphyrinogen (hexahydroporphine) (5). Compound **3** (0.45 g, 2 mmol) was added to the stirred solvent of chloroform (200 mL) previously degassed by bubbling with argon at room temperature in a dark room. A solution of **1** (0.254 g, 2 mmol) in methanol (5 mL) was added to the stirred solution. After 20 min, 20% $BF_3{\cdot}CH_3OH$–methanol solution (227 μL, 0.4 mmol) was added with a micropipette, and then the reaction mixture was stirred for 1 h. Further stirring for 1 h was continued at 50°C. Evaporation of the solvent in vacuo left a viscous colorless oil. This oil was dissolved in dichloromethane (10 mL), column chromatographed (300×20 mm^2) on silica gel using CH_2Cl_2 as an eluent, and concentrated in vacuo to afford a colorless solid. Recrystallization from acetone (5 mL) at −20°C afforded **5** (86 mg, 14%). Attempt to collect the X-ray diffraction data was not successful because of unsuitable condition of single crystals from diethyl ether solution. Colorless needles, mp 185°C (dec., acetone). TLC: R_f= 0.76 (silica gel, CH_2Cl_2). HPLC: R_t=7.83 min (Inertsil ODS, 150×4 mm^2). ^1H NMR (90 MHz, $CDCl_3$): δ 3.82 (s, 8H, CH_2), 5.87 (d, 8H, J=2.4 Hz, aromatic-H), 7.38 (br, 4H, NH). Ms: *m/z* 316 (M^+, 100), 171 (20), 158 (40), 145 (10), 124 (12). FTIR (KBr, cm^{-1}): 3372, 3311, 3097, 3084, 2892, 2882, 1413, 1302, 1039, 817, 806, 764, 753, 640. Anal. calcd for $C_{20}H_{20}N_4$: C, 75.92; H, 6.37; N, 17.71. Found: C, 76.02; H, 6.52; N, 17.54.

4.1.5. 21-Oxaporphyrinogen (21-oxa-hexahydroporphine) (6). A sample of **4** (0.452 g, 2 mmol) was treated identically as for **5**, affording 72 mg (11%) of colorless needles. The single crystals were prepared in diethyl ether. Mp 157°C (dec., acetone). TLC: R_f=0.87 (silica gel, CH_2Cl_2). HPLC: R_t=6.02 min (Inertsil ODS-2, 100×4 mm^2). ^1H NMR (90 MHz, $CDCl_3$): δ 3.79 (s, 4H, 10-, 15-H), 3.86 (s, 4H, 5-, 20-H), 5.83 (s, 2H, 12-, 13-H), 5.86 (s, 2H, 8-, 17-H), 5.93 (s, 2H, 7-, 18-H), 5.97 (s, 2H, 2-, 3-H), 7.42 (br, 2H, 22-, 24-NH), 7.52 (br, 1H, 23-NH). Ms: *m/z* 317 (M^+, 100), 172 (22), 160 (48), 157 (32), 146 (23). FTIR (KBr, cm^{-1}): 3350, 3337, 3128, 3105, 1563, 1182, 1113, 1091, 1028, 1012, 803, 765, 744, 738, 715, 566. Anal. calcd for $C_{20}H_{19}N_3O$: C, 75.69; H, 6.03; N, 13.24. Found: C, 75.46; H, 6.36; N, 13.03.

4.1.6. X-Ray structure of 21-oxaporphyrinogen (6). Colorless crystals were grown slowly in a diethyl ether solution in a refrigerator at 5°C. The crystals were quickly moved from a vial to a microscope slide in a steam of argon. Under the microscope, a colorless plate (0.50×0.35×0.10 mm^3) was selected and mounted on a glass fiber using Aronalpha®, and then coated with the bonding agent. A total of 2694 reflections were collected in the θ range 3–30° of which 2470 were unique (R_{int}=0.035). The structure was solved by direct method and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. The least-squares refinement converged normally with residuals of R (based on F)=0.042, wR (based on F^2)=0.044, and GOF=1.44 based upon $I>3\sigma(I)$. Crystal data for $C_{20}H_{19}N_3O$: trigonal, space group=R3 (#146), Z=8, a=20.225(4) Å, c=10.762(6) Å, V=3812(2) $Å^3$, ρ_{calc}=1.106 g cm^{-3}, F(000)=1344. Atomic coordinates, bond lengths and angles, and thermal parameters for **6** have been deposited at the Cambridge Crystallographic Data Center (CCDC).

Acknowledgements

We thank the Hitachi Chemical, for the FDMS measurement. We also thank Dr Shouichi SATOH for helpful discussion of X-ray structural analysis.

References

1. Fischer, H.; Gleim, W. *Justus Liebigs Ann. Chem.* **1935**, *521*, 157.
2. Neya, S.; Yodo, H.; Funasaki, N. *J. Heterocycl. Chem.* **1993**, *30*, 549.
3. Taniguchi, S.; Hasegawa, H.; Nishimura, M.; Takahashi, M. *Synlett* **1999**, 73.
4. Sugiura, K.; Fujimoto, Y.; Sakata, Y. *Chem. Commun.* **2000**, 1105.
5. Baeyer, A. *Chem. Ber.* **1886**, *19*, 2184.
6. For example,Miyaji, H.; Anzenbacher Jr, P.; Sessler, J. L.; Bleasdale, E. R.; Gale, P. A. *Chem. Commun.* **1999**, 1723. Gale, P. A.; Sessler, J. L.; Král, V. *Chem. Commun.* **1998**, 1 (and references cited therein).
7. For example, Bonomo, L.; Solari, E.; Scopelliti, R.; Floriani, C.; Re, N. *J. Am. Chem. Soc.* **2000**, *122*, 5312. Floriani, C. *Chem. Commun.* **1996**, 1257 (and references cited therein).
8. Fischer, H.; Baumler, R. *Ann.* **1929**, *468*, 58.

9. Happel, G.; Mathiasch, B.; Kämmerer, H. *Makromol. Chem.* **1975**, *176*, 3317. Böhmer, V.; Chim, P.; Kämmerer, H. *Makromol. Chem.* **1979**, *180*, 2503.
10. Longo, F. R.; Thorne, E. J.; Adler, A. D.; Dym, S. *J. Heterocycl. Chem.* **1975**, *12*, 1305.
11. Silverstein, R. M.; Ryskiewicz, E. E.; Chaikin, S. W. *J. Am. Chem. Soc.* **1954**, *76*, 4485.
12. Tschelinzew, W. W.; Maxorow, B. W. *Chem. Zentr.* **1923**, *1*, 1505.
13. Harris, J. F.; Saeman, J. F. *Forest Products J.* **1960**, *2*, 125.
14. Ziegler, G. R. *J. Am. Chem. Soc.* **1969**, *91*, 446.
15. Wang, Q. M.; Bruce, D. W. *Synlett* **1995**, 1267.
16. Lee, C.-H.; Lindsey, J. S. *Tetrahedron* **1994**, *50*, 11427.
17. Gale, P. A.; Sessler, J. L.; Král, V.; Lynch, V. *J. Am. Chem. Soc.* **1996**, *118*, 5140.
18. Gutsche, D. D. *Acc. Chem. Res.* **1983**, *16*, 161.
19. Gale, P. A.; Sessler, J. L.; Král, V. *Chem. Commun.* **1996**, 1257.
20. Gale, P. A.; Sessler, J. L.; Allen, W. E.; Tvermos, N. A.; Lynch, V. *Chem. Commun.* **1997**, 665.
21. Uno, H.; Inoue, T.; Fumoto, Y.; Shiro, M.; Ono, N. *J. Am. Chem. Soc.* **2000**, *122*, 6773.