Synthesis and Nucleic Acid-Binding Properties of Water-Soluble Porphyrins Appending Platinum(II) Complexes

Hiroki MUNAKATA,* Toshiki KANZAKI, Shigeo NAKAGAWA, Hiroyasu IMAI, and Yoshio UEMORI

Faculty of Pharmaceutical Sciences, Hokuriku University, Ho-3, Kanagawa-machi, Kanazawa 920–1181, Japan.
Received July 27, 2001; accepted September 17, 2001

We synthesized two water-soluble porphyrins appending platinum(II) complexes [α,β-(4a) and α,α-(4b) 5,15-bis(2-*trans*-[PtCl(NH_3)$_2$]*N*-2-aminoethylaminocarbonylphenyl) 2,3,7,8,12,13,17,18-octamethylporphyrin] and studied their reactions with a variety of nucleic acids [disodium adenosine-5′-monophosphate (AMP), disodium guanosine-5′-monophosphate (GMP), disodium thymidine-5′-monophosphate (TMP), disodium cytidine-5′-monophosphate (CMP), synthetic polymer poly(dG)–poly(dC), poly(dA)–poly(dT)] by ^{1}H-NMR, UV–vis and FAB-MS spectroscopies. Based on the denaturation experiments of synthetic nucleic acid polymers, we conclude that the presence of the porphyrins (5.6 μM) does not cause significant changes in the melting temperature of poly(dA)–poly(dT) (28 μM) (ΔT=1 °C) and shows reannealing. On the other hand, gradual melting of poly(dG)–poly(dC) (28 μM) occurs at a low temperature (ΔT=−27 °C) in the presence of the porphyrins (5.6 μM), and the solutions do not show reannealing phenomena. The results of UV–vis and ^{1}H-NMR experiments revealed that the porphyrins bind to guanine bases and that the porphyrins bind to GMP more strongly than to the other nucleotides. The binding modes between the porphyrins and synthetic nucleic acids are affected more by the coordination of the nucleobase [poly(dG)–poly(dC)] to the Pt(II) in the porphyrins than by Coulomb and hydrophobic interactions.

Key words porphyrin; platinum complex; nucleic acid

There has been considerable interest in understanding the binding of the antitumor drug *cis*-dichlorodiammine platinum(II) (CDDP) and its analogs to their putative target DNA in cancer cells.[1)] Platinum complexes can bind rapidly to nucleic acids (including DNA) in aqueous solution and therefore are useful as a functional group to design artificial receptors for DNA. The anti-cancer activity of CDDP arises from its ability to damage DNA by forming a major adduct with intrastrand d(GpG) and d(ApG) crosslinks.[2)] These crosslinks of CDDP to d(GpG) and d(ApG) bend and unwind the duplex, and then the altered structure attracts high-mobility-group (HMG) domain proteins.[3)] This binding of HMG-domain proteins to CDDP-modified DNA has been postulated to mediate the antitumor properties of the drugs.[4)]

Studies on the binding of cationic porphyrins to DNA have been of great significance to those working in cancer research and gene technology.[5)] Some cationic porphyrins bearing quaternary ammonium salt units such as ammonium or pyridinium groups can act as binders for DNA. Several researchers have investigated how cationic porphyrins bind to DNA in groove or outside binding on the basis of Coulomb and/or hydrophobic interactions.[5a,c,6)] We designed and synthesized two water-soluble porphyrins appending platinum(II) complexes and studied their reactions with a variety of DNA and nucleic acids. In the porphyrins, cationic groups of the appended platinum(II) complex solubilize the porphyrins to water and provide coordination ability for binding to DNA. Furthermore, because the cationic porphyrins can also bind to DNA, the platinum(II) complexes appended by the porphyrins are expected to function additively with the porphyrins and then bind strongly to DNA.

This report describes the synthesis of two derivatives of 5,15-bis(*o*-substituted phenyl)porphyrin appending two chlorodiammineplatinum(II) complexes at the ortho position of the two phenyl rings of the porphyrin (see **4a** and **4b** in Fig. 1). We then studied their reactions with a variety of nucleic acids [disodium adenosine-5′-monophosphate (AMP), disodium guanosine-5′-monophosphate (GMP), disodium thymine-5′-monophosphate (TMP), disodium cytidine-5′-monophosphate (CMP), synthetic polymer poly(dG)–poly(dC), poly(dA)–poly(dT)] using ^{1}H-NMR, UV–vis or FAB-MS spectroscopies.

Results and Discussion

Syntheses and Characterization of Water-Soluble Porphyrins Appending Platinum(II) Complexes or Quaternary Ammonium Groups Syntheses of the water-soluble porphyrins with two platinum(II) complexes are outlined in Fig. 1. Condensation of (tetramethyldipyrryl)methane[7)] with *o*-phthalaldehydic acid gave porphyrinogen **1** in a good yield. Oxidation of the porphyrinogen to porphyrin **2** was accomplished by using *o*-chloranil. Because of the limited solubility of **2**, the chromatographic separation of the two atropisomers could not be accomplished; it was achieved after deriving to aminoethylcarbamides **3a** and **3b**. Compound **3b** was hydorolyzed with hydrochloric acid (6 M), and a treatment of the hydrolyzed product with 1,5-diaminopentane gave strapped porphyrin **8** (Fig. 2), where the 1,5-diaminopentane group is found to be strapping over the porphyrin,[8)] judging from the ^{1}H-NMR data. The formation of the strapped porphyrin indicates that **3b** is assigned to be the α,α-isomer.[9)] The expected polarity of the porphyrins, which is that **3b** is more polar than **3a**, also agrees with the order of the *Rf* values of TLC (see Experimental section). We used *trans*-[PtCl(NH_3)$_2$(*N*,*N*-dimethylformamide (DMF))]NO_3 as the appending platinum(II) complexes to **3a** and **3b**. The counter ions of the porphyrins appending platinum(II) complexes (**4a**, **b**) were exchanged from nitrates to chlorides by passing them through an ion-exchange column in the Cl^- form.

For comparison, we prepared two cationic porphyrins bearing two quaternary ammonium salts α,β-(**7a**) and α,α-(**7b**) 5,15-bis((*o*-*N*,*N*,*N*-trimetylammoniummethylamido)-

* To whom correspondence should be addressed. e-mail: h-munakata@hokuriku-u.ac.jp

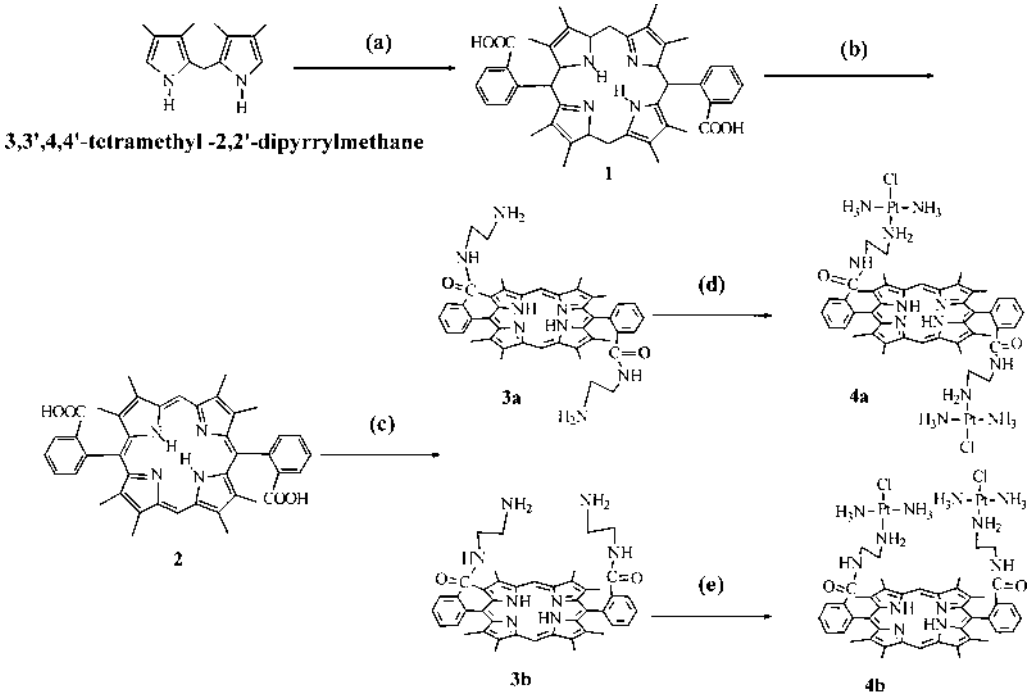

Fig. 1. Synthetic Route of Porphyrins Appending Platinum(II) Complexes

(a) *o*-Phthalaldehyde, *p*-toluenesulfonic acid, methanol; (b) (i) *o*-chloranil, tetrahydrofuran, (ii) triethylamine, methanol; (c) (i) oxalyl chloride, dichloromethane, (ii) ethylenediamine, dichloromethane, (iii) silicagel column chlomatography; (d), (e) (i) *trans*-[PtCl(DMF)$(NH_3)_2$], DMF, (ii) anion-excange regin.

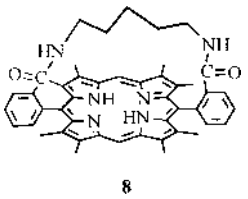

Fig. 2. Structure of Strapped Porphyrin

phenyl)-2,3,7,8,12,13,17,18-octamethylporphyrin (Fig. 3) from **5a** and **5b**, respectively. The precursors (**6a**, **b**) prepared from **5a** and **5b** with *N*-dimethylglycine were methylated by methyl iodide to give **7a** and **7b**, respectively.

Some water-soluble porphyrins have a tendency to form intermolecular aggregates in aqueous solution.[10] The binding of the porphyrins to nucleic acids is often complicated by the aggregation. UV–vis spectroscopy is a prominent and simple tool that allows one to gain information on the aggregates. It has been reported that porphyrin aggregates generally have large $W_{1/2}$ (band width at half-height peak) of the Soret band and that the aggregates are more stable in water than in several organic solvents, such as DMF, dimethyl sulfoxide (DMSO), MeCN or MeOH.[10] The spectral data for the Soret band of the porphyrins **4a**, **4b**, **7a** and **7b** in aqueous solution are given in Tables 1 and 2. The UV–vis spectral changes of **4a** at various concentrations in H_2O are shown in Fig. 4. The spectra for these porphyrins in the concentration range from 0.17 to 10 μM do not obey Beer's law in H_2O at 25 °C (Table 2). Figure 5 represents the UV–vis spectra of **4a** in H_2O, MeOH and DMF. Each porphyrin has a Soret band with a large $W_{1/2}$ in H_2O, while in DMF each has a Soret band with small $W_{1/2}$ as shown in Table 3. These results suggest that the synthesized water-soluble porphyrins were dimerized or aggregated in H_2O. We also examined the temperature dependence of the absorption spectrum for **4a** in aqueous solution (20 mM NaCl) (Fig. 6). Temperature rising caused spectral changes with a blue shift of the Soret band, and these spectral changes were reversible. The $W_{1/2}$ of a Soret band in this condition (20—60 °C, 20 mM NaCl) has a large $W_{1/2}$ compared with the value of the porphyrins in DMF (monomer form). These results suggest that the synthesized water-soluble porphyrins were also dimerized or aggregated in 20 mM NaCl at the temperature range from 20 to 60 °C.

Melting and Reannealing Behavior of Synthetic Nucleic Acid Polymers We studied the interactions between porphyrins and synthetic nucleic acid polymers by measuring the melting temperatures and observing the reannealing behavior. The reannealing phenomenon is what occurs when a warmed solution containing denaturated duplexes is slowly cooled to room temperature and the UV–vis spectrum of the solution becomes the same as it was before denaturation. Before measuring the melting temperatures of the synthetic nucleic acid polymer, the solutions containing the porphyrins must be equilibrated at 20 °C. Figure 7 represents the time-courses of the UV–vis spectra for the solution containing **4a** and poly(dG)–poly(dC) in 20 mM NaCl at 20 °C. The Soret maximum at 425 nm of **4a** shows a basochromic shift to 440 nm just after the mixing of **4a** with poly(dG)–poly(dC). Subsequently, a blue hyperchromic shift of the Soret maximum occurs gradually, and the spectrum reaches a steady state after 15 h. The first changes were observed in the cases of **4b** or **7a**, whereas the second change was not observed in **7a**. Since such a gradual change in UV–vis spectra has been accompanied by outside, groove, and/or intercalative binding, the binding interactions of **4a** and **4b** with poly(dG)–poly(dC) may be different from that of **7a**.

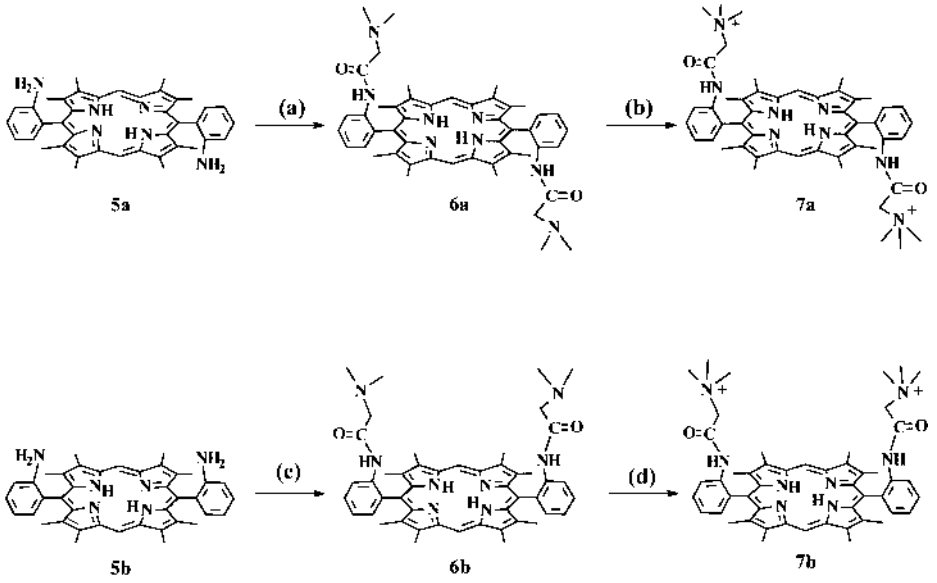

Fig. 3. Synthetic Route of Porphyrins Appending Platinum(II) Complexes

(a), (c) (i) *N*,*N*-dimethylaminoacetic acid, oxalyl chloride, dichloromethane, (ii) dichloromethane, (iii) silica-gel column chlomatography; (b), (d) (i) iodomethane, dimethylformamide, (ii) ainion excange regin.

Table 1. UV–Vis Spectral Data for Porphyrins

Prophyrins	λ_{max}, nm (log ε)[a)]	$W_{1/2}$
4a[b)]	408.5 (5.03)	40
4b[b)]	405.5 (4.98)	48
7a[c)]	404.0 (5.20)	39
7b[c)]	402.0 (4.99)	63

a) ε (M^{-1} cm^{-1}). *b*) Concentration of porphyrins is 8 μM at 25 °C. *c*) Concentration of porphyrins is 5 μM at 25 °C.

Table 2. UV–Vis Spectral Data for Porphyrins[a)]

Porphyrins	Conc./μM	λ_{max}, nm (log ε)[b)]	
4a	0.17	410 (sh)	423.5 (4.90)
	0.35	410.5 (4.88)	420 (sh)
	0.50	410.0 (4.89)	420 (sh)
	1.0	409.0 (4.81)	
	5.0	409.0 (4.93)	
	10	409.0 (5.00)	
4b	0.17	410 (sh)	423.0 (5.09)
	0.35	408.5 (4.93)	
	0.50	408.5 (4.87)	
	1.0	407.0 (4.81)	
	5.2	404.0 (4.88)	
	10	401.0 (4.91)	
7a	0.5	406.0 (5.01)	427.0 (5.14)
	1.0	404.0 (5.10)	
	2.1	403.0 (5.17)	
	7.0	402.5 (5.23)	
7b	0.5		427.0 (4.88)
	1.0		426.5 (5.07)
	2.1		426.5 (5.11)
	7.0		426.5 (5.23)

a) In aqueous solution at 25 °C. *b*) ε (M^{-1} cm^{-1}).

The melting temperatures for poly(dA)–poly(dT) in the presence of **4a**, **4b** and **7a** are listed in Table 4. The melting curves for poly(dG)–poly(dC) in the presence of **4a**, **4b** and **7a** are also shown in Fig. 8. The presence of the porphyrins

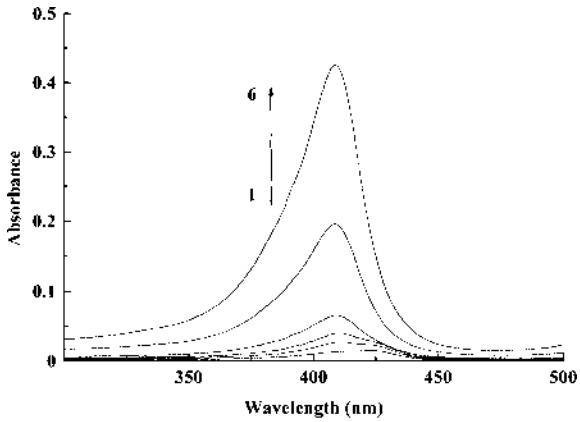

Fig. 4. Spectral Changes of **4a** at Various Concentrations in H_2O

1, 2, 3, 4, 5 and 6 are the spectra at 0.17, 0.35, 0.50, 1.0, 2.7 and 5.0 μM, respectively.

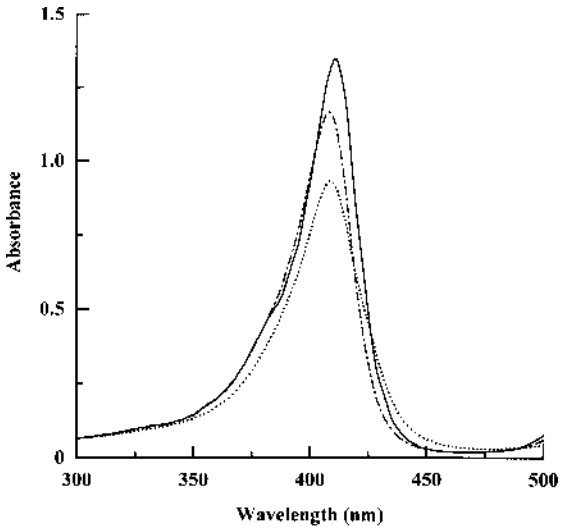

Fig. 5. UV–Vis Spectra of **4a** (8 μM) in DMF (——), MeOH (— · —), and H_2O (------) at 25 °C

Table 3. UV–Vis Spectral Data for Porphyrins in Various Solvents[a)]

Solvent	**4a**[b)]		**4b**[b)]		**7a**[c)]		**7b**[c)]	
	λ_{max} (nm)	$W_{1/2}$ (nm)	λ_{max} (nm)	$W_{1/2}$ (nm)	λ_{max} (nm)	$W_{1/2}$ (nm)	λ_{max} (nm)	$W_{1/2}$ (nm)
H_2O	40.8.5	38	406.0	52	403.0	33	400.0	51
MeOH	408.5	32	408.0	32	403.0	35	403.5	36
DMF	411.0	28	411.0	28	409.5	31	409.0	32

a) At 25 °C. *b*) Porphyrin concentration is 8 μM. *c*) Porphyrin concentration is 6 μM.

Table 4. Melting Temperatures (°C)[a)] of Poly(dA)–Poly(dT)[b)] in the Presence of Porphyrins

N/P[c)]	**7a**	**4a**	**4b**
10[d)]	61	55	*f*)
5[e)]	58	57	56

a) The estimated errors in melting temperatures were ±1 °C. *b*) Concentration of poly(dA)–poly(dT) is 28 μM in H_2O (NaCl=20 mM). The melting temperature in the absence of porphyrin is 56 °C. *c*) Ratio of poly(dA)–poly(dT) concentration (in base pairs) to porphyrin concentration. *d*) Concentrations of porphyrins are 2.8 μM. *e*) Concentrations of porphyrins are 5.6 μM. *f*) Melting temperature was not determined.

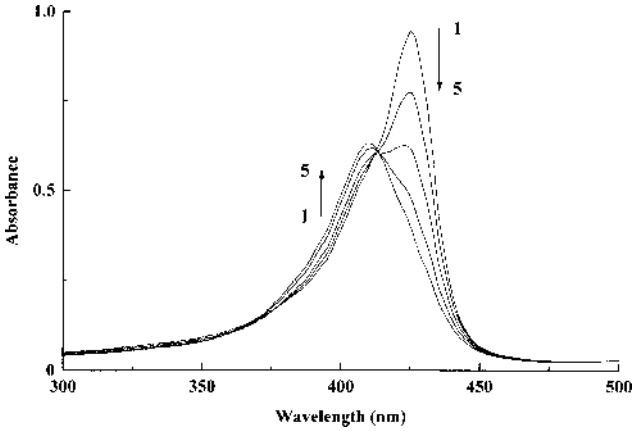

Fig. 6. Spectral Changes of **4a** (8 μM) at Various Temperatures in H_2O (20 mM NaCl)

1, 2, 3, 4 and 5 are the spectra at 20, 30, 40, 50 and 60 °C, respectively.

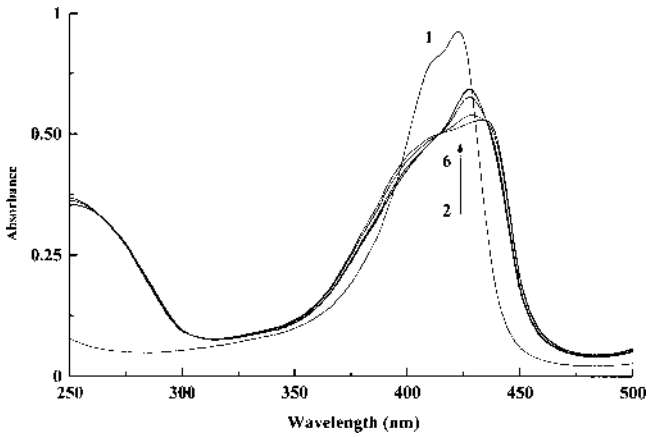

Fig. 7. Time-Dependent UV–Vis Spectra of the Reaction between **4a** (5.6 μM) and Poly(dG)–Poly(dC) (28 μM) at 20 °C in 20 mM NaCl

1 is the spectrum of **4a**. 2, 3, 4, 5, and 6 are the spectra at 0, 2, 8, 16, and 20 h, respectively, after mixing of **4a** with Poly(dG)–poly(dC).

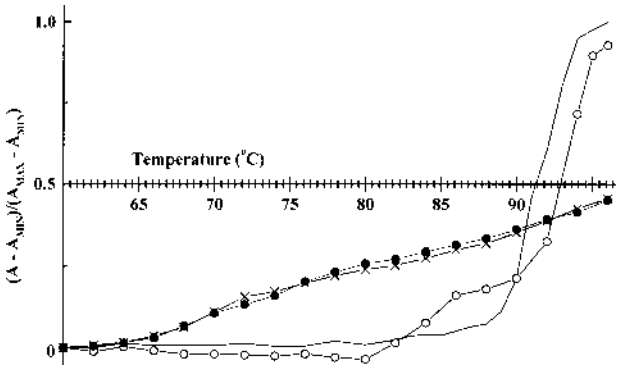

Fig. 8. Melting Profiles at 260 nm of Poly(dG)–Poly(dC) (28 μM in Base Pair Concentration) in the Presence of Porphyrins (5.6 μM) in 20 mM NaCl at 260 nm

A is the observed absorbance, A_{MIN} is the absorbance of duplex poly(dG)–poly(dC) and A_{MAX} is the absorbance of denaturated duplex poly(dG)–poly(dC). Porphyrin: (——) non, (—●—) **4a**, (—×—) **4b**, (—○—) **7a**.

did not cause a significant change in the melting temperature of poly(dA)–poly(dT), and reannealing was observed with and without the porphyrins. Since groove or outside binding should not affect the melting temperature or UV–vis spectral behavior,[6)] the binding of **7a** to both poly(dA)–poly(dT) and poly(dG)–poly(dC) will be in these binding modes. Further, the binding modes of **4a** and **4b** with poly(dA)–poly(dT) will be similar to that of **7a**, and these binding modes are affected by Coulomb and hydrophobic interaction. Contrary to this, gradual melting of poly(dG)–poly(dC) occurs at low temperatures (*ca.* 65 °C) in the presence of **4a** and **4b**, and these solutions do not show reannealing. The destabilization of the poly(dG)–poly(dC) by **4a** and **4b**, together with the spectral changes of the solution at 20 °C (Fig. 7), suggests that the binding mode for **4a**, **4b** to poly(dG)–poly(dC) should be different from that for **7a** to poly(dG)–poly(dC). To explore the binding mode of **4a** and **4b** to poly(dG)–poly(dC) polymers, we measured the UV–vis spectra of the porphyrins with four nucleotides (GMP, AMP, CMP, TMP).

Reactions of Porphyrins with Nucleotides The time-course of the reaction between **4a** and GMP is shown in Fig. 9. As in the case of **4a** with poly(dG)–poly(dC), the spectral changes consist of two steps. By adding GMP to the solution containing **4a**, a change of the first step occurs immediately (the spectral change between spectrum 0 and 1 in Fig. 9). After the first step, a gradual change is observed as the second step over a period of 10 h (the spectral changes between spectrum 1 and 7 in Fig. 9). The first step is also observed in all cases of the porphyrins with the four nucleotides. The spectral change in the first step will be due to the dissociation of a porphyrin dimmer to monomers[11)] and subsequently to

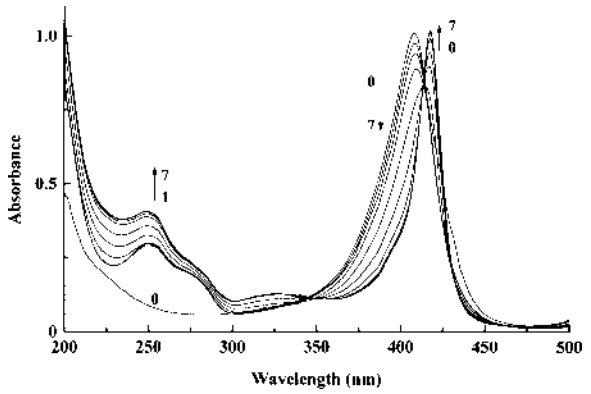

Fig. 9. Time-Dependent UV–Vis Spectra of the Reaction between **4a** (7.8 μM) and GMP (19 μM) at 40 °C in 10% MeOH

0 is the spectrum of **4a**. 1, 2, 3, 4, 5, 6, and 7 are the spectra at 0, 2, 4, 6, 8, 10, and 12 h, respectively, after mixing of **4a** with GMP.

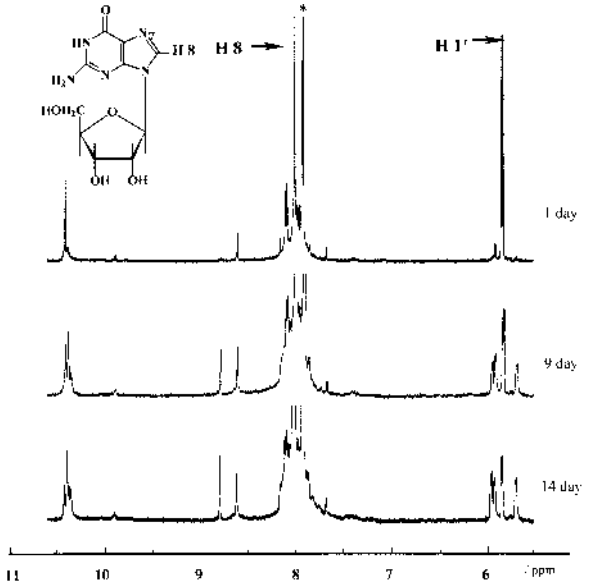

Fig. 10. ^{1}H-NMR Spectra of the Mixture of **4a** (7.5 μM) and Guanosine (15 μM) at 27 °C in 1 : 1 Mixtures between D_2O and DMF-d_7 (1 : 1)

The signal marked with an asterisk is due to the solvent.

the association of the porphyrin monomer with GMP.[6e] The second step is not observed in any other combination of the porphyrins with the nucleotides except for **4a** with poly(dG)–poly(dC). Since a gradual change similar to the second step has been reported in the case of CDDP with GMP,[12] we propose that the second step is due to coordination of GMP to Pt in **4a**.

To determine the binding mode of **4a** with poly(dG)–poly(dC) or GMP, we measured ^{1}H-NMR spectra of **4a** and guanosine in DMF-d_7–D_2O mixed solvent (Fig. 10). Since the solubility of GMP in DMF–D_2O is low and the mixing of the DMF-d_7–D_2O solution containing GMP with the porphyrin gave precipitation, we used guanosine instead of GMP. The solution containing guanosine (15 mM) was added to a porphyrin solution (7.5 mM) dissolved in DMF-d_7 : D_2O= 1 : 1, and the reaction was monitored by using ^{1}H-NMR at 27 °C. The spectral changes occurred over a period of 14 d. A day after from the mixing of **4a** with guanosine, new signals

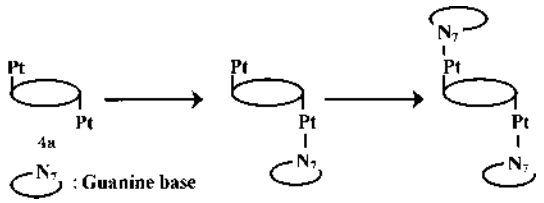

Fig. 11. Possible Structures of the Guanine Base Adducts **4a**

for H-8 and H-1′ protons for guanosine appeared at 8.63 and 5.93 ppm, respectively. Subsequently, the signals were converted to 8.79 ppm for H-8 and to 5.70 and 5.97 ppm for H-1′, respectively. These changes can be explained by successive binding of two guanosine molecules to **4a** and not by non-bonding association of guanosine with **4a**, as observed for many aromatic compounds with porphyrins, for the following reasons: (1) The association reaction of aromatic compounds with porphyrins reaches to equilibrium within a few minutes,[13] but the observed changes are continued over a period of 14 d, and (2) the proton signals for the aromatic compounds shift to a high field by the ring current upon association,[14] but the H-8 proton signal for guanosine shifts to a low field.

FAB-MS spectra provide information on the products formed in the solution. The spectrum for the DMF solution containing **4a** and guanosine shows peaks at m/z=1852 and 1656, which correspond to the formation of a bis-guanosine adduct to **4a** (=2 guanosine+**4a**−2Cl) and a mono-guanosine adduct to **4a** (=guanosine+**4a**−Cl), respectively. This result also supports the successive binding of two guanosine molecules to **4a**. The binding site of guanosine to **4a** is tentatively assignable to N-7, in analogy with the reaction of *trans*-[$Pt(NH_3)_2Cl_2$] with guanosine,[12] and a proposed structure is shown in Fig. 11. The spectrum for the solution containing **4a** and adenosine does not show any peak corresponding to a mono- or bis-adenosine adduct to **4a**. These results indicate that guanosine coordinates to Pt(II) but adenosine does not coordinate and that formation of the coordination bond can be detected by the FAB-MS spectra. On the other hand the FAB-MS spectrum for the solution containing **4b** and guanosine shows a peak corresponding to mono-guanosine adduct of **4b** (=guanosine+**4b**−Cl, FAB-MS m/z: 1565 [M^+]) but does not show a peak corresponding to bis guanosine adduct. This is unexpected from the UV–vis spectrum of **4b** and GMP where the second step change observed for the case of **4a** was not detected. However, the FAB-MS spectrum demonstrates the formation of the mono-guanosine adduct. From these results, it is clear that **4a** reacts with two guanosine molecules successively and **4b** reacts with one guanosine molecule.

Binding Modes of Porphyrins with Synthetic Nucleic Acid Polymer In conclusion, we wish to note the following significant findings of this investigation. The UV–vis spectral changes of the second step observed for **4a** with GMP can be explained by the selective binding of the appended platinum(II) complexes to two guanine bases. For the case of **4b** with GMP, the lack of the spectral changes of the second step may be due to the fact that **4b** binds only one guanine base, as exemplified by the binding of **4b** with guanosine. Furthermore, it is reasonable to speculate that the two appended

platinum(II) complexes in the porphyrins react with guanine bases in poly(dG)–poly(dC) as in the case of the CDDP.[1,15] Finally, the destabilization of poly(dG)–poly(dC) by **4a** and **4b**, suggests that the binding mode for **4a**, **4b** to poly(dG)–poly(dC) should be different from that for **7a** to poly(dG)–poly(dC). It has been reported that coordination of CDDP to adjacent guanosines destabilizes the double helix.[16] The gradual melting of poly(dG)–poly(dC) in the presence of **4a** or **4b** can also be explained by the selective binding of the appended platinum(II) complexes with guanine bases in the duplex. The binding modes between the porphyrins and synthetic nucleic acids are affected more by coordination of the nucleobase (poly(dG)–poly(dC)) to the Pt(II) in the porphyrins than by Coulombic interaction between cations to the porphyrins and anions on nucleic acids and/or by hydrophobic interaction between the porphyrin ring and the nucleobase.

Experimental

Measurements of UV–vis spectra and the DNA denaturation experiments were carried out on a Hitachi U-3000 spectrophotometer with a temperature controller Hakke F423 or on a Shimadzu UV-2500PC with a temperature controlled cell holder Shimadzu TCC-240A. ^{1}H-NMR spectra were measured on a JEOL JNM-GSX-400 (400 MHz) spectrometer with tetramethylsilane (TMS) as the internal standard and chemical shifts were expressed in δ value. Signal multiplicities are represented by s (singlet), d (doublet), t (triplet), dd (double doublet), and m (multiplet). FAB-MS spectra were measured on a JEOL JMS-SX-102A mass spectrometer using magic bullet as matrix. IR spectra were recorded on a Perkin-Elmer Spectrum 2000 spectrophotometer. Elemental analyses were performed on a Perkin-Elmer 240C elemental analyzer.

All chemicals were purchased commercially and were used as received without further purification unless otherwise noted. Silica gel (Wakogel C-200 Wako Pure Chemicals Industries, Ltd.) was used for column chromatography. Precoated silica gel plates (Merck Kieselgel 60F_{254}) or reversed phase silica gel plates (Merck Kieselgel RP-8 F_{254}) with a layer thickness of 0.25 mm were used for TLC to determine *Rf* values. Distilled water was purchased from CAMBEX Company. Synthetic nucleic acids polymers, poly(dG)–poly(dC), and poly(dA)–poly(dT) were purchased from Sigma and were used without further purification. Ethyenediamine was used after distillation. (3,3,4′,4′-tetramethyl-2,2′-dipyrryl) methane,[7e] 5,15-(2-amino)-diphenyloctamethylporphyrin (**5a**, **b**)[9] were prepared according to the literature. *trans*-[PtCl$(NH_3)_2$(DMF)]NO_3 was prepared according to the publish method.[17]

UV–Vis Analysis To obtain the time-course of the UV–vis spectra of the solution containing porphyrin and synthetic nucleic acid polymer in 20 mM NaCl at 20 °C, the sample solution was prepared by adding a solution of porphyrin to a solution of synthetic nucleic acid polymer in a cuvette (the pathlength is 1 cm) *via* a micro syringe. The sample solution to measure the melting curves was prepared by a similar method for the measurements of the time-course of the UV–vis spectra. The sample solution containing 5 μM (in base pair) synthetic nucleic acid polymer in 20 mM NaCl was used after standing the solution at 20 °C over 15 h.

Synthetic Nucleic Acid Polymer Denaturation Experiments The melting curves of both free synthetic nucleic acid polymers (poly(dA)–poly(dT) and poly(dG)–poly(dC)) and their reactants with porphyrins in 20 mM NaCl (pH 7) were obtained by measuring the hypochromicity of polymers at 260 nm as a function of temperature. The temperature was scanned from 20 to 99 °C at a speed of 1 °C per min. The melting temperature (T_m) was taken as the mid-point of the hyperchromic transition.

Method for Studying the Interactions between Porphyrin Appending Platinum(II) Complexes and Nucleotides During incubation of a mixture of porphyrin and nucleotide in 10% methanol aqueous solution at 40±0.1 °C, UV–vis spectra were measured.

Synthesis of 5,15-Bis(*o*-carboxyphenyl)-2,3,7,8,12,13,17,18-octamethylporphyrin (2) A solution of (3,3,4′,4′-tetramethyl-2,2′-dipyrryl)methane (3.10 g, 15.3 mmol), *o*-phthalaldehydic acid (2.40 g, 16.0 mmol), and *p*-toluensulfonic acid monohydrate (1.00 g, 5.26 mmol) in methanol (200 ml) was allowed to stand at 20 °C for 5 h. The brown solid was recovered by filtration and was washed with methanol.

The crude porphyrinogen **1** (6.5 g, 9.7 mmol) was dissolved in tetrahydrofuran (200 ml) and *o*-chloranil (13.0 g, 52.9 mmol) in tetrahydofurane (50 ml) was added to the solution. The solution was stirred at room temperature for 8 h. The purple solid was recovered by filtration and the solid was redissolved in methanol (100 ml). To the methanol solution, triethylamine (60 ml) was added to precipitate the porphyrin. The product was collected by filtration and was washed with methanol (yield, 5.30 g, 52.2%).

Syntheses of α,β- and α,α-5,15-Bis((*o*-aminoethylaminocarbonyl)-phenyl)-2,3,7,8,12,13,17,18-octamethylporphyrin (3a, b) Compound **2** (1.00 g, 1.51 mmol) was dissolved in dichloromethane (20 ml) and was cooled to 5 °C. Oxalyl chloride (3.0 ml, 37 mmol) was carefully added to the solution with cooling and the reaction mixture was stirred for 2 h. The solvent and excess oxalyl chloride was removed *in vacuo.* The residue was then redissolved in a small amount of dichloromethane, and the solvent was again removed *in vacuo.* The residue in dichloromethane (30 ml) was added drop wise to a solution of ethylenediamine (1.0 g, 16.7 mmol) in dichloromethane (20 ml) under N_2. After the addition was completed (*ca.* 2 h), the mixture was stirred for 8 h at 0 °C, then the solution was poured into water. The product was extracted with dichloromethane (3×200 ml). The organic layer was washed with water, 2% aqueous sodium bicarbonate, and water, in turn. The organic layer was dried over anhydrous sodium sulfate. Evaporation of the solvent gave a purple residue which was chromatographed on a silica-gel column (dichloromethane, 3ϕ×50 cm). Elution with 10% methanol in dichloromethane gave the α,β-isomer **3a** first. The α,α-isomer **3b** was eluted with 25% methanol in dichloromethane. From 1.0 g of a mixture of **3a** and **3b** was isolated 598 mg (53.1%) of **3a** and 348 mg (30.9%) of **3b**.

α,β-Isomer **3a**: *Rf* value=0.51 ($CHCl_3$: CH_3OH=5 : 1). ^{1}H-NMR ($CDCl_3$) δ: −2.40 (2H, s, pyrrole-N<u>H</u>), 0.54 (4H, br, –C<u>H</u>$_2$–NH_2), 2.16 (4H, m, –CO–NH–C<u>H</u>$_2$–), 2.49 (12H, s, 2, 8, 12, 18-CH_3), 3.54 (12H, s, 3, 7, 13, 17-CH_3), 5.20 (2H, br, –CH_2–N<u>H</u>$_2$), 7.82 (2H, t, ph-H), 7.94 (2H, t, ph-H), 8.02 (2H, d, ph-H), 8.39 (2H, d, ph-H), 10.26 (2H, s, 10, 20-H). IR (KBr) cm^{-1}: 694 (pyrrole-NH), 2962, 2926, 1160, 1137 (pyrrole–CH_3), 1650 (–CONH–), 3401 (–NH_2). *Anal.* Calcd for $C_{46}H_{50}N_8O_2\cdot H_2O\cdot 1/3CHCl_3$: N, 13.97; C, 69.33; H, 6.57. Found: N, 13.74; C, 69.38; H, 6.62. FAB-MS *m*/*z*: 746 [Calcd for $C_{46}H_{50}N_8O_2$ 746 M^+].

α,α-Isomer **3b**: *Rf* value=0.22 ($CHCl_3$: CH_3OH=5 : 1). ^{1}H-NMR ($CDCl_3$) δ: −2.46 (2H, s, pyrrole-N<u>H</u>), 0.38 (4H, br, –C<u>H</u>$_2$–NH_2), 2.24 (4H, br, –CO–NH–C<u>H</u>$_2$–), 2.49 (12H, s, 2, 8, 12, 18-CH_3), 3.53 (12H, s, 3, 7, 13, 17-CH_3), 5.23 (2H, br, –CH_2–N<u>H</u>$_2$), 7.82 (2H, t, ph-H), 7.94 (2H, t, ph-H), 8.04 (2H, d, ph-H), 8.33 (2H, d, ph-H), 10.26 (2H, s, 10,20-H). IR (KBr) cm^{-1}: 694 (pyrrole-NH), 2955, 2926, 1161, 1137 (pyrrole–CH_3), 1644 (–CONH–), 3401 (–NH_2). *Anal.* Calcd for $C_{46}H_{50}N_8O_2\cdot CHCl_3\cdot 4H_2O$: N, 11.94; C, 60.16; 6.34. Found: N, 12.58; C, 60.18; H, 6.12. FAB-MS *m*/*z*: 746 [Calcd for $C_{46}H_{50}N_8O_2$ 746 M^+].

Synthesis of α,β-5,15-Bis(2-*trans*-[PtCl$(NH_3)_2$]*N*-2-aminoethylaminocarbonylphenyl)2,3,7,8,12,13,17,18-octamethylporphyrin (4a) *trans*-[PtCl$(NH_3)_2$(DMF)]NO_3 was prepeared *in situ* by reacting *trans*-[$PtCl_2(NH_3)_2$] (48.5 mg, 0.0162 mmol) with 0.97 eq of $AgNO_3$ (26.6 mg, 0.0157 mmol) in DMF (10 ml) solution for 24 h at room temperature. The α,β-isomer **3a** (50.0 mg, 0.0670 mmol) was dissolved in DMF (10 ml) and was cooled to −18 °C. The *trans*-[PtCl$(NH_3)_2$(DMF)]NO_3 solution was added to the porphyrin solution below −18 °C and the reaction mixture was stirred for 3 d at room temperature. The solution was then evaporated to dryness under high vacuum. The residue was dissolved in methanol (20 ml), and the solution was kept overnight at 4 °C. The solid was filtered off, then washed with diethyl ether (5 ml), chloroform (5 ml), and methanol (5 ml), in turn. The resultant solid was dissolved in methanol and chromatographed on a cation-exchange resin column (amberlist A-21 chloride form: 2ϕ×25 cm) to exchange the counter ion to Cl^-. The column was eluted with methanol. The eluate was evaporated to dryness and the residue was crystallized from methanol/diethyl ether, and dried *in vacuo* to afford the α,β-isomer **4a** (47.6 mg, 52.9%).

Rf value=0.64 (n-C_4H_9OH : $(CH_3)_2CO$: H_2O : NH_4OH=5 : 3 : 1 : 1) RP-8. ^{1}H-NMR (DMF-d_7) δ: −2.25 (2H, s, pyrrole-N<u>H</u>), 2.53 (12H, s, 2, 8, 12, 18-CH_3), 2.75 (4H, br, –C<u>H</u>$_2$–NH_2), 2.90 (4H, br, –CO–NH–C<u>H</u>$_2$–), 3.56 (12H, s, 3, 7, 13, 17-CH_3), 4.04 (12H, br, Pt-NH_3), 5.84 (4H, br, –CH_2–N<u>H</u>$_2$), 7.87—7.98 (6H, m, ph-H), 8.36 (2H, d, ph-H), 8.90 (2H, br, –CO–N<u>H</u>–), 10.27 (2H, s, 10,20-H). IR (KBr) cm^{-1}: 695 (pyrrole-NH), 2970, 2926, 1161, 1137 (pyrrole–CH_3), 1642 (–CONH–), 3401 (–NH_2), 327 (Pt-Cl), 3250 (Pt-NH_3). *Anal.* Calcd for $C_{46}H_{62}Cl_2N_{12}O_2Pt_2\cdot(Cl_2)\cdot CHCl_3$: N, 11.46; C, 38.50; H, 4.33. Found: N, 11.39;C, 38.91; H, 4.50. FAB-MS *m*/*z*: 1275 [Calcd for $C_{46}H_{62}Cl_2N_{12}O_2Pt_2$ 1275 M^+]. UV–visible spectrum $\lambda_{max}^{H_2O}$ nm (log ε); 408.5 (5.06), 512.0 (3.95), 547.0 (3.70), 571.5 (3.79), 620.5 (3.34).

Synthesis of α,α-5,15-Bis(2-*trans*-[PtCl(NH$_3$)$_2$]*N*-2-aminoethylaminocarbonylphenyl)-2,3,7,8,12,13,17,18-octamethylporphyrin (4b) This porphyrin was prepared by a similar procedure to that of the α,β-isomer (**4a**) from **3b** (50.0 mg, 0.670 mmol) and *trans*-[PtCl(NH$_3$)$_2$(DMF)]NO$_3$ (prepared *in situ* from 48.5 mg, 0.160 mmol of *trans*-[PtCl$_2$(NH$_3$)$_2$] and AgNO$_3$) in 10 ml of DMF. Yield 21.9 mg (24.3%).

Rf value=0.50 (*n*-C$_4$H$_9$OH : (CH$_3$)$_2$CO : H$_2$O : NH$_4$OH=5 : 3 : 1 : 1) RP-8. ^{1}H-NMR (DMF-d_7) δ: −2.26 (2H, s, pyrrole-NH), 2.53 (12H, s, 2,8,12,18-CH$_3$), 2.79 (4H, br, –CH$_2$–NH$_2$), 2.95 (4H, br, –CO–NH–CH$_2$–), 3.58 (12H, s, 3,7,13,17-CH$_3$), 3.88 (12H, br, Pt-NH$_3$), 5.53 (4H, br, –CH$_2$–NH$_2$), 7.97 (2H, t, ph-H), 8.19 (2H, d, ph-H), 8.25 (2H, d, ph-H), 8.51 (2H, br, –CO–NH–), 10.30 (2H, s, 10,20-H). IR (KBr) cm^{-1}: 695 (pyrrole-NH), 2955, 2926, 1161, 1137 (pyrrole–CH$_3$), 1642 (–CONH–), 3400 (–NH$_2$), 327 (Pt-Cl), 3249 (Pt-NH$_3$). *Anal.* Calcd for C$_{46}$H$_{62}$Cl$_2$N$_{12}$O$_2$Pt$_2$·(Cl$_2$)·2CHCl$_3$: N, 10.60; C, 36.36; H,4.07. Found: N, 11.25; C, 35.89; H, 4.41. FAB-MS *m*/*z*: 1275 [Calcd for C$_{46}$H$_{62}$Cl$_2$N$_{12}$O$_2$Pt$_2$ 1275 M$^+$]. UV–visible spectrum $\lambda_{max}^{H_2O}$ nm (log ε); 406.0 (4.91), 514.0 (3.95), 547.5 (3.49), 575.0 (3.63), 622.5 (3.00).

Synthesis of α,β-5,15-Bis((*o*-*N*,*N*-dimetylaminomethylamido)phenyl)-2,3,7,8,12,13,17,18-octamethylporphyrin (6a) *N*,*N*-dimethylglycine hydrochloride (940 mg, 6.76 mmol) was dissolved in dichloromethane (5 ml) and cooled to 5 °C. Oxalyl chloride (3.0 ml, 37 mmol) was carefully added to the solution below 10 °C and the reaction mixture was stirred for 2 h. The solvent and excess oxalyl chloride were removed *in vacuo.* The residue of acid chloride was then redissolved in a small amount of dichloromethane, and the solvent was again removed *in vacuo.* The residue was dissolved in dichloromethane (30 ml) and the solution was added slowly to dichloromethane (50 ml) containing aminoporphyrin **5a** (1.00 g, 1.65 mmol), and the reaction mixture was stirred at 0 °C. After the addition was complete (*ca.* 2 h), triethylamine (4 ml) was added to the solution, and the mixture was stirred for 8 h at 0 °C. Then the solution was poured into water and was extracted with dichloromethane (3×200 ml). The organic layer was washed with water, 2% aqueous sodium bicarbonate, and water, in turn. The organic layer was dried over anhydrous sodium sulfate. Evaporation of the solvent gave a purple residue which was chromatographed on a silica-gel column (3φ×50 cm) eluted with 10% diethyl ether in chloroform, yielding **6a**, 570 mg (44.3%).

α,β-Isomer **6a**: *Rf* value=0.78 (CHCl$_3$: C$_6$H$_6$: C$_2$H$_5$OH=20 : 20 : 1). ^{1}H-NMR (CDCl$_3$) δ: −2.51 (2H, s, pyrrole-NH), 1.33 (4H, s, –NH–CO–CH$_2$–), 2.11 (12H, s, N-(CH$_3$)$_2$), 2.35 (12H, s, 2, 8, 12, 18-CH$_3$), 3.34 (12H, s, 3, 7, 13, 17-CH$_3$), 7.33 (2H, t, ph-H), 7.65 (2H, t, ph-H), 7.72 (2H, d, ph-H), 8.61 (2H, d, ph-H), 8.85 (2H, br, –NH–CO–), 10.01 (2H, s, 10,20-H). IR (KBr) cm^{-1}: 693 (pyrrole-NH), 2963, 2926, 1160, 1136 (pyrrole–CH$_3$), 3273, 1688 (–CONH–). *Anal.* Calcd for C$_{48}$H$_{54}$N$_8$O$_2$·1/2(C$_2$H$_5$)$_2$O: N, 13.80; C, 73.95; H, 7.32. Found: N, 13.84; C, 73.53; H, 7.07. FAB-MS *m*/*z*: 775 [Calcd for C$_{48}$H$_{54}$N$_8$O$_2$ 775 M$^+$].

Synthesis of α,α-5,15-Bis((*o*-*N*,*N*-dimetylaminomethylamido)phenyl)-2,3,7,8,12,13,17,18-octamethylporphyrin (6b) This porphyrin was prepared from **5b** (1.00 g, 1.65 mmol) by a similar procedure to that of the corresponding α,β-isomer (**6a**), yielding 370 mg (28.8%).

Rf value=0.55 (CHCl$_3$: C$_6$H$_6$: C$_2$H$_5$OH=20 : 20 : 1). ^{1}H-NMR (CDCl$_3$) δ: −2.25 (2H, s, pyrrole-NH), 1.61 (12H, s, N-(CH$_3$)$_2$), 2.99 (4H, s, –NH–CO–CH$_2$–), 2.62 (12H, s, 2, 8, 12, 18-CH$_3$), 3.61 (12H, s, 3, 7, 13, 17-CH$_3$), 7.63 (2H, t, ph-H), 7.93 (2H, t, ph-H), 8.06 (2H, d, ph-H), 8.83 (2H, d, ph-H), 9.10 (2H, br, –NH–CO–), 10.28 (2H, s, 10,20-H). IR (KBr) cm^{-1}: 693 (pyrrole-NH), 2962, 2924, 1160, 1136 (pyrrole–CH$_3$), 3217, 1689 (–CONH–). *Anal.* Calcd for C$_{48}$H$_{54}$N$_8$O$_2$·1/2H$_2$O: N, 14.29; C, 73.54; 7.07. Found: N, 14.07; C, 73.53; H, 7.12.

Synthesis of α,β-5,15-Bis((*o*-*N*,*N*,*N*-trimetylammoniummethylamido)-phenyl)-2,3,7,8,12,13,17,18-octamethylporphyrin (7a) Iodomethan (0.20 ml, 3.2 mmol) was added to a DMF solution (20 ml) containing **6a** (105 mg, 0.136 mmole) at room temperature and the solution was stirred for 3 h. Ether (20 ml) was added to the reactant to produce a solid. After filteration, the resultant solid was dissolved in methanol and chromatographed on a caion-exchange resin column (Amberlist A-21: 2φ×25 cm) to exchange the counter ion to Cl$^-$. The column was eluted with methanol. The eluate was evaporated to dryness and was recrystallized from methanol/acetone, yielding 107 mg (90.0%).

Rf value=0.52 RP-8 (H$_2$O : CH$_3$COOH : CH$_3$OH : C$_5$H$_5$N=2 : 2 : 1 : 1). ^{1}H-NMR (CD$_3$OD) δ: 2.24 (18H, s, N-(CH$_3$)$_3$), 2.47 (12H, s, 2, 8, 12, 18-CH$_3$), 3.09 (4H, s, –NH–CO–CH$_2$–), 3.44 (12H, s, 3, 7, 13, 17-CH$_3$), 7.66 (2H, t, ph-H), 7.82 (2H, t, ph-H), 7.98 (2H, d, ph-H), 8.08 (2H, d, ph-H), 10.24 (2H, s, 10,20-H). IR (KBr) cm^{-1}: 693 (pyrrole-NH), 2963, 2926, 1160, 1136 (pyrrole–CH$_3$) 3276, 1686 (–CONH–), 3413 (N$^+$−CH$_3$). *Anal.* Calcd for C$_{50}$H$_{60}$N$_8$O$_2$·(Cl$_2$)·2H$_2$O·CH$_3$OH: N, 11.87; C, 64.89; H, 7.06. Found: N, 11.72; C, 64.92; H, 7.06. FAB-MS *m*/*z*: 803 [Calcd for C$_{50}$H$_{60}$N$_8$O$_2$ 804 (M−H)$^+$]. UV–visible spectrum $\lambda_{max}^{H_2O}$ nm (log ε): 403.0 (5.18), 507.0 (3.95), 545.0 (3.69), 565.5, (3.79), 616.5 (3.29).

Synthesis of α,α-5,15-Bis((*o*-*N*,*N*,*N*-trimetylammoiummethylamido)-phenyl)-2,3,7,8,12,13,17,18-octamethylporphyrin (7b) This porphyrin was prepared from **6b** (105 mg, 0.136 mmol), by a similar procedure to that of the corresponding α,β-isomer (**7a**), yielding 77.4 mg (65.3%).

Rf value=0.37 RP-8 (H$_2$O : CH$_3$COOH : CH$_3$OH : C$_5$H$_5$N=2 : 2 : 1 : 1). ^{1}H-NMR (CD$_3$OD) δ: 2.55 (12H, s, 2, 8, 12, 18-CH$_3$), 2.66 (18H, s, N-(CH$_3$)$_3$), 3.30 (4H, m, –NH–CO–CH$_2$–), 3.54 (12H, s, 3, 7, 13, 17-CH$_3$), 7.70 (2H, t, ph-H), 7.90—7.95 (4H, m, ph-H), 8.28 (2H, d, ph-H), 10.31 (2H, s, 10,20-H). IR (KBr) cm^{-1}: 693 (pyrrole-NH), 2962, 2926, 1160, 1135 (pyrrole–CH$_3$), 3238, 1695 (–CONH–), 3410 (N$^+$−CH$_3$). *Anal.* Calcd for C$_{50}$H$_{60}$N$_8$O$_2$·5H$_2$O: N, 11.60; C, 62.16; 7.30. Found: N, 11.59; C, 62.62; H, 6.95. FAB-MS *m*/*z*: 803 [Calcd for C$_{50}$H$_{60}$N$_8$O$_2$ 804 (M−H)$^+$]. UV–visible spectrum $\lambda_{max}^{H_2O}$ nm (log ε): 400.0 (4.93), 511.5 (3.76), 547.0 (3.47), 573.5 (3.59), 621.0 (3.00)

Synthesis of α,α-5,15-Bis((*o*-pentaneaminocarbonyl)phenyl)-2,3,7,8,12,13,17,18-octamethylporphyrin (8) A mixture of **3b** (1.00 g, 1.51 mmol) and 6 M HCl (100 ml) was heated at 60 °C with stirring for 8 h. The solution was cooled, diluted with water (100 ml), and neutralized with 5 M aqueous ammonia (*ca.* 90 ml). The precipitate was recoverd by filtration and the solid was washed with water, and dried *in vacuo* to afford the hydrolyzed product. The product was dissolved in dichloromethane (20 ml) and was cooled to 5 °C. Oxalyl chloride (3.0 ml, 37 mmol) was carefully added below 10 °C and the reaction mixture was stirred for 2 h. The solvent and excess oxalyl chloride was removed *in vacuo.* The residue was then redissolved in a small amount of dichloromethane, and the solvent was again removed *in vacuo.* The resultant acid chloride of porphyrin in dichloromethane (30 ml) was added to dichloromethane solution (20 ml) containing 1,5-diaminopentane (0.20 g, 0.20 mmol) and the mixture was stirred for 12 h at 0 °C. Then the solution was poured into water and was extracted with dichloromethane (3×200 ml). The organic layer was washed with water, 2% aqueous sodium bicarbonate, and water, in turn. The organic layer was dried over anhydrous sodium sulfate. Evaporation of the solvent gave a purple solid which was chromatographed on a silica-gel column (3φ×50 cm) eluted with chloroform. The main brown fraction was collected to yield 550 mg of **8** (50.0%).

Strapped Porphyrin **8**: ^{1}H-NMR (CDCl$_3$) δ: −4.7—−4.5 (4H, m, –CH$_2$–CH$_2$–NHCO–), −2.28 (2H, s, pyrrole-NH), −1.40—−1.34 (4H, m, –CH$_2$–NHCO–), −1.53 (2H, m, –CH$_2$–CH$_2$–CH$_2$–NHCO–), 2.52 (12H, s, 2, 8, 12, 18-CH$_3$), 3.55 (12H, s, 3, 7, 13, 17-CH$_3$), 7.86—7.97 (6H, m, ph-H), 8.63—8.65 (2H, m, ph-H), 10.21 (2H, s, 10,20-H). *Anal.* Calcd for C$_{47}$H$_{48}$N$_6$O$_2$·CHCl$_3$·H$_2$O: N, 9.70; C, 66.85; 5.93. Found: N, 9.39; C, 66.85; H, 5.80. FAB-MS *m*/*z*: 729 [Calcd for C$_{47}$H$_{48}$N$_6$O$_2$ 729 M$^+$].

References

1) Lippert B. (ed.), "Cisplatin," Verlog Helvetica chimica acta, Zurich, 1999, pp. 73—157.
2) Eckstein F., Lilley D. M. J. (ed.), "Nucleic acids And Molecular Biology," Springer, Heidelberg, 1990, pp. 9—38.
3) Zlatanova J., Yaneva J., Leuba S. H., *FASEB J.*, **12**, 791—799 (1998).
4) *a*) Zamble D. B., Lippard S. J., *Trends Biochem. Sci*., **20**, 435—439 (1995); *b*) Zhai X., Beckmann H., Janzen, H.-M., Essigmann J. M., *Biochemistry*, **37**, 16307—16315 (1998).
5) *a*) Fiel R. J., Howard J. C., Mark E. H., Gupta N. G., *Nucleic Acid Res*., **6**, 3093—3118 (1979); *b*) Carvlin M. J., Mark E., Fiel R., *ibid*., **11**, 6121—6139 (1983); *c*) Marzilli L. G., Pethö G., Lin M., Kim M. S., Dixon D. W., *J. Am. Chem. Soc*., **114**, 7575—7577 (1992); *d*) Mukundan N. E., Pethö G., Dixon D. W., Kim M. S., Marzilli L. G., *Inorg. Chem*., **33**, 4676—4687 (1994); *e*) Ishikawa Y., Yamashita A., Uno T., *Chem. Pharm. Bull*., **49**, 287—293 (2001).
6) *a*) Revew: Marzilli L. G., *New J. Chem*., **14**, 409—420 (1990), and references cited therein; *b*) Pasternack R. F., Gibbs E. J., Villafranca J. J., *Biochemistry*, **22**, 2406—2414 (1983); *c*) Ward B., Skorobogaty A., Dabriwiak J. C., *ibid*., **25**, 7827—7833 (1986); *d*) Sari M. A., Battioni J. P., Dupré D., Mansuy D., Le Pecq J. B., *ibid*., **29**, 4205—4215 (1990); *e*) Pasternack R. F., Bustamante C., Collings P. J., Giannetto A., Gibbs E. J., *ibid*., **115**, 5395—5399 (1993); *f*) Pethö G., Elliott N. B., Kim M. S., Lin M., Dixon D. W., Marzilli L. G., *J. Chem. Soc*., *Chem. Commun*., **1993**, 1547—1548; *g*) Kuroda R., Tanaka H., *ibid*., **1994**, 1575—1576; *h*) McKinnie R. E., Choli J., Bell J. W., Gibbs E. J., Pastanack R. F., *J. Inorg. Biochem*., **32**, 207—224 (1988).
7) *a*) Dorphin D. (ed.), "The porphyrins," Vol. I, Chapter 4, Academic

Press, New York , 1979, pp. 107—234; *b*) Wang C.-B., Chang C. K., *Synthesis*, **1979**, 548—549; *c*) Bllock E., W. Johnson A., Kay I. T., Markham E., Shaw K. B., *J. Chem. Soc*., **1958**, 1430—1440; *d*) Johnson A. W., Kay I. T., Markham E., Price R., Shaw K. B., *ibid*., **1959**, 3416—3424; *e*) Crazy P. S., Nicol A. W., *Aust. J. Chem*., **11**, 1835—1845 (1965).

8) Uemori Y., Miyakawa H., Kyuno E., *Inorg. Chem*., **27**, 377—382 (1988).
9) Gunter M. J., Lewis N. M., *J. Org. Chem*., **46**, 4792—4795, (1981).
10) Ren-Hua J., Aoki S., Shima K., *J. Chem. Soc*., *Faraday Trans*., **1997**, 3945—3953.
11) Kubát P., Lang K., Anzenbacher P., Jr., Jursíková K., Král V., Ehrenberg B., *J. Chem. Soc*., *Perkin Trans. 1*, **2000**, 933—941.
12) Mansy S., Rosenberg B., Thomson A. J., *J. Am. Chem. Soc*., **95**, 1633—1640 (1973).
13) Pasternack R. F., Brigandi R. A., Abrams M. J., Williams A. P., Gibbs E. J., *Inorg. Chem*., **29**, 4483—4486 (1990).
14) Kadish K. M., Smith K. M., Guilard R. (ed.), "The Porphyrin Handbook," Vol. 5/NMR and ESR, Academic press, San Diego, 2000.
15) Lippert B., (ed.), "Cisplatin," Verlog Helvetica chimica acta, Zurich, 1999, pp. 159—245.
16) Sherman S. E., Lippard S. J., *Chem. Rev*., **87**, 1153 (1987), and references cited therein.
17) Rauter H., Domenico R. D., Menta E., Olivia A., Qu Y., Farrell N., *Inorg. Chem*., **36**, 3919—3927 (1997).