CHEMISTRY LETTERS, pp. 51-54, 1990.

Novel 1:1 Complex of Rhodium(III)porphyrins with Nucleobases

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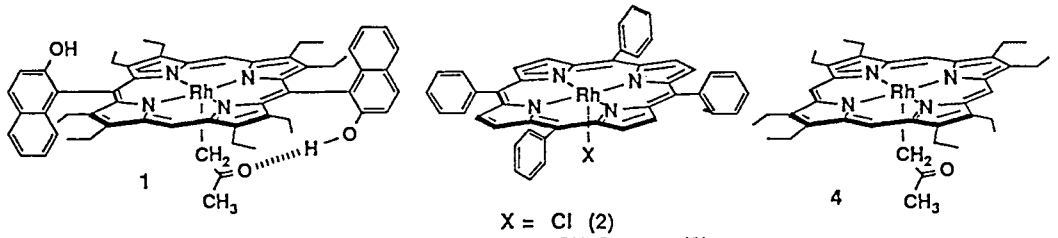
Axial ligation behaviors of nucleobases to Rh(III)porphyrins were investigated. Except the case of TPP•Rh(III) — 1-methylthymine system, tight 1:1 complexations were observed between Rh(III)-porphyrins and nucleobases and their binding constants were determined by spectroscopic titration.

Since R. J. Fiel and co-workers reported that *meso*-tetra(4-*N*-methylpyridyl)-porphine, TMPyP, intercalates in calf thymus DNA,[1] the interaction between TMPyP and DNA has been intensively investigated by several groups.[2] Through these investigations, it has been established that TMPyP and its Ni(II) derivative selectively intercalate into G-C rich region of DNA[2a] and free base TMPyP induces the conformational change of DNA from the Z-form to the B-form.[3] In contrast with the results obtained for these flat porphyrins, metalloporphyrins, which have axial ligands, such as TMPyP{Mn(III), Fe(III) and Co(III)} complexes show no such intercalation behavior but bind to the A-T rich region of the minor grooves in a manner of which detailed mechanism is not still clarified.[2a] Thus, it should be noted that, in spite of importance of the coordination interaction in the porphyrin chemistry, the possibility of *direct axial coordination* of a nucleobase to a metal center of porphyrin is still remained as a question.

Recently, in the course of our investigation of the molecular recognition in metalloporphyrins, we found that rhodium(III) complex of 5,15-*trans*-bis(2-hydroxy-1-naphthyl)octaethylporphyrin(**1**) showed strong binding affinity for amino acid, where



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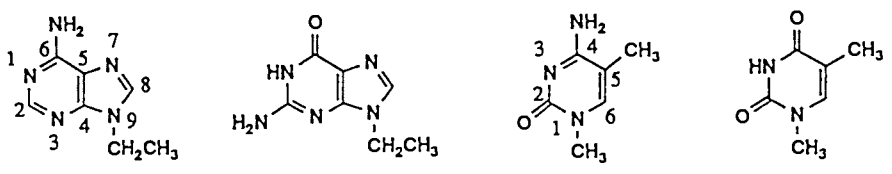

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the two-point fixation of amino acids was achieved through the coordination of the amino group on Rh(III) and the hydrogen bond between the carboxyl group and hydroxy group of *meso*-naphthyl unit in **1**.[4] The observed strong binding ability of Rh(III)porphyrins toward amino acids leads us to the investigation on the new interaction mode of Rh(III)porphyrin with nucleobases, including the direct coordination of nucleobase to the metal center, which is expected to open new aspect of both porphyrin and nucleotide chemistry. As the first example on this line of investigations, we herein report novel complex formation between nucleobase derivatives (**5 - 8**) and various types of Rh(III)porphyrins (**1 - 4**).[5] The results obtained here show the most of nucleobases strongly coordinate to the Rh(III) metal center of porphyrin and their association equilibrium constants(K_{ass}) are as large as those for amino acids.[4]

The complex formation of Rh(III)porphyrins with nucleobases in CH_2Cl_2 was easily monitored by spectroscopic titration. The typical example of the titration was shown in Fig. 1. On addition of nucleobase, the red shift and decrease of intensity of Soret band at 420 nm with the tight isosbestic point was generally observed and the plot of the absorption intensity vs. the concentration of nucleobase showed the typical saturation behavior. The association constants for Rh(III)porphyrin – nucleobases were determined from this type of plots (Table 1),[6] though the reliable K_{ass} value could not be obtained in the following two cases,; a) the system of TPP•Rh(III)•Cl (**2**) and nucleobases (**5 - 7**), where the association constants are too large to determine the K_{ass} values by the present method (see Fig. 1b) and only their lowest limits were estimated, b) the system of TPP•Rh(III) complexes (**2 - 3**) and 1-methylthymine (**8**), which showed no appreciable spectral change on addition of **8**. The observed coordination behaviors are very suggestive in consideration of the structures of the present porphyrin-nucleobase complexes, i.e., the extremely large association constants between chloride complex,**2**, and **5 - 7** compared with those for acetone complex,**3**, indicates that the present complex formation is mainly dominated by the electrophilicity of the Rh(III) metal center. Similar enhanced binding in the chloride complex of Rh(III)porphyrin was observed in amino acid recognition.[4]

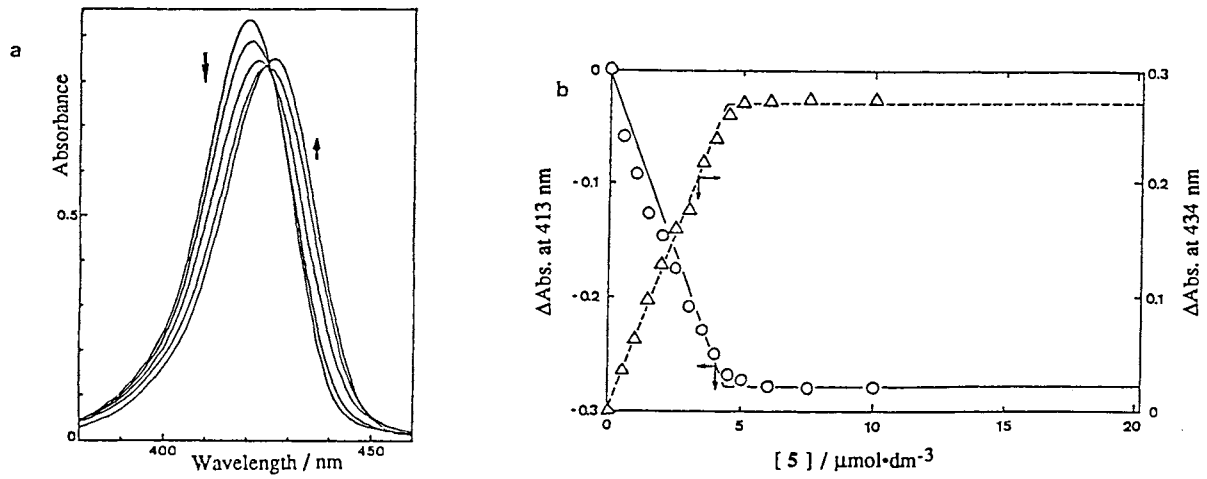

Fig.1. (a) Absorption spectra of **2** on addition of **5**; [**2**]=4.0 μmol•dm^{-3}, [**5**]=0, 0.5, 2.0, 3.5, 10 μmol•dm^{-3} in CH_2Cl_2. (b) Titration curve. Theoretical lines were drawn at $K_{ass}=10^{10}$ dm^3•mol^{-1} in CH_2Cl_2.

Table 1. Association Constants (K_{ass}) between Rh(III)Porphyrins and Nucleobase Derivatives[a)]

	2	3	4	1
EtAde(5)	$>10^7$	$(2.8\pm0.4)\times10^5$	$(2.5\pm1.0)\times10^6$	$(1.5\pm0.4)\times10^5$
EtGua(6)	$>10^7$	$(2.1\pm0.5)\times10^4$	$(1.2\pm0.5)\times10^5$	$(1.4\pm0.6)\times10^5$
diMeCyt(7)	$>10^7$	$(8.6\pm1.5)\times10^4$	$(2.3\pm0.4)\times10^6$	$(2.8\pm0.4)\times10^5$
MeThy(8)	b	b	$(1.5\pm0.5)\times10^5$	$(1.7\pm0.8)\times10^5$

a) K_{ass}: $dm^3 \cdot mol^{-1}$. Determined by UV-VIS titration in CH_2Cl_2.
b) The values of K_{ass} could not be determined due to their small spectral change.

Based on these observations, the most possible coordination sites of present nucleobase derivatives are expected to be the most basic positions of nucleobases. Thus, the positions N1 (pK_b=4.20) in **5**, N7 (pK_b=3.3) in **6** and N3 (pK_b=4.58) in **7** are the most probable candidates of the present coordination sites.[7)] In order to confirm this proposal, ^{1}H-NMR spectra of these complexes are measured. The ^{1}H-NMR spectra of the 1:1 complex of **2** and **5** are shown in Fig. 2 as the typical example.[8)] As is expected, the largest upfield shift due to the diamagnetic ring current effect of porphyrin is observed for H2 of **5** ($\Delta\delta$=-7.9 ppm) and relatively small upfield shifts are observed for H8 and ethyl protons ($\Delta\delta$=-1.0 for H8, -1.0 for CH_2 and -0.7 ppm for CH_3).[9)] Similar upfield shifts are also found in ^{1}H-NMR spectra of **2•6** and **2•7** pairs.[10)] Furthermore, assuming that each nucleobase coordinates at the above mentioned position perpendicularly toward the porphyrin plane, these observed upfield shifts show the fairly good agreement with those estimated from the isoshielding map of porphyrin.[11)] These results clearly indicate the complex formation of Rh(III)porphyrin with nucleobases (**5 - 7**) *via the coordination on the Rh(III) metal center*, not via a stacking interaction. It, however, should be noted at same time that the both structures of porphyrins and nucleobases also affect the present complex formation. For example, the OEP complex, **4**, generally shows larger association constants for **5 - 7** than those of the TPP complex, **3**, by factors of 5-30, which suggests the existence of steric hindrance of phenyl groups in **3**.[12)] Another example of the structural effect is observed for the complexation of the guanine

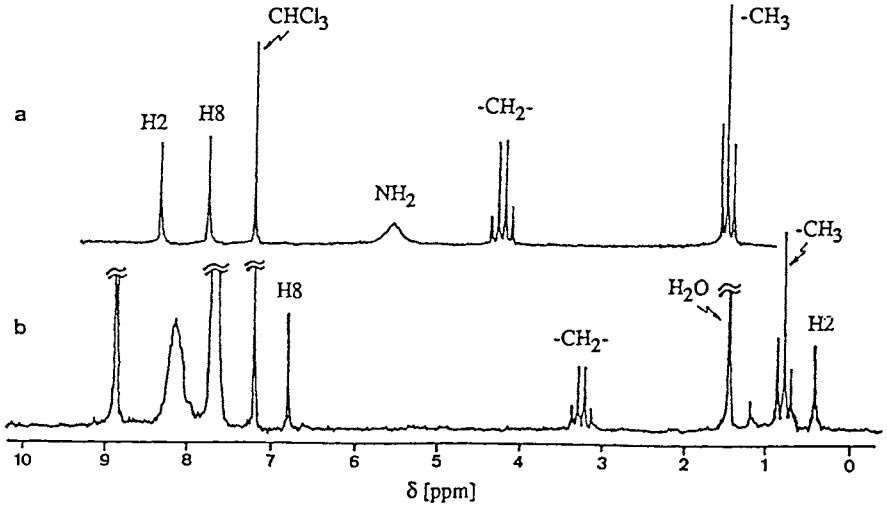

Fig.2. ^{1}H-NMR(90 MHz) spectra of (a) **5** in $CDCl_3$ and (b) recrystallized **2•5** complex in $CDCl_3$.

derivative, **6**, which shows the smallest association constants among **5** - **7** for all porphyrin molecules examined here (**3** - **4**). This relatively weak complexation of **6** appears to reflect the steric hindrance of the oxygen atom at the C6 position which faces toward the plane of porphyrins on coordination at the N7 position of **6**. Although, in the case of bis-naphthylporphyrin, **1**, the enhanced complex formation by a hydrogen bond as observed in the amino acid recognition[4] is expected, the clear evidences for such hydrogen bonding could not be obtained in the present nucleobase recognition.

Finally, a particular attention should be paid to the results for the thymine derivative, **8**. Since thymine is known to be rather weak acidic compound (pKa=9.94), the weak complex formation of **8** with present porphyrin complex is basically expected. In spite of this expectation, **8** showed relatively tight complex formation with **1** and **4**, though the thymine adducts of TPP-type complexes, **2** and **3**, could not be confirmed both by the spectroscopic titration due to their too small spectral change and by the NMR measurement due to very low solubility of **8**. Although the origin of these complexation phenomena of **8** which has no basic position is not clear at the present stage, these complexes are very interesting from structural and electronical viewpoints.

Further investigations on the interaction between Rh(III)porphyrins and nucleotides,nucleosides and DNA or RNA are now under way in our laboratory.

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8) The complex of **2** with **8** is so stable that the crystalline 1:1 complex could be isolated.
9) The assignments of two aromatic protons in the **2•5** complex were confirmed by the similar experiment using 8-bromo-9-ethyladenine where the signal at 6.75 ppm disappeared.
10) The upfield shifts for **6** and **7** are as follows ; $\Delta\delta$ (ppm), **6**: -7.4 (H8), -1.5 (CH_2 of ethyl group), -1.0 (CH_3 of ethyl group), **7**: -9.9 (NH_2), -0.8 (CH_3 at N1), -2.4 (CH_3 at C5), -2.3 (H6).
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(Received September 18, 1989)