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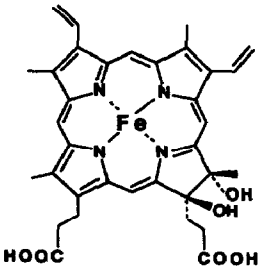
The First Observation of Dynamic Ruffling Inversion of an Iron(III) Dihydroxychlorin Complex by Proton NMR Spectroscopy

Shinji Ozawa, Yoshihito Watanabe, and Isao Morishima*

Division of Molecular Engineering, Graduate School of Engineering, Kyoto University, Kyoto 606-01, Japan

Abstract: As models for the iron chlorin prosthetic groups (1 and 2), solution behaviors (ruffling in solution) of iron(III) complexes of *cis*-dihydroxyoctaethylchlorin (3) and *trans*-octaethylchlorin (4) have been examined by variable-temperature proton NMR spectroscopy.

While many heme enzymes contain iron porphyrin (protoheme IX), iron chlorin complexes are also utilized as prosthetic groups of a variety of heme enzymes.[1] For instance, cytochrome *d* contains heme *d* prosthetic group[2] which has been proposed to be dihydroxychlorin (**1**), derived by reductive dihydroxylation of pyrrole ring C of protoheme IX.[3] A similar structure bearing γ-spirolactone and hydroxy groups (**2**) has been postulated[4] for the prosthetic group of HPII (one of two catalases isolated from *Escherichia Coli*).



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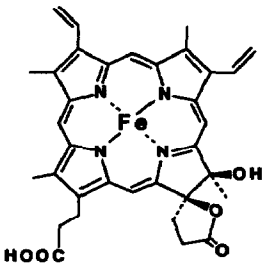

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One of the significant structural properties of metallo-chlorin complexes is the loss of planarity (ruffling) of the macrocycles with concomitant increase in macrocycle flexibility.[5,6] Although the relevance of the macrocycle ruffling in solution to enzymic functions is still obscure, the ruffling deformation is suggested to be important for reactivities in *nickel* hydroporphyrin complexes.[5a,7] Furthermore, in the case of F430 of methanogenic bacteria,[8] the biological activity is lost upon modification of the macrocycle to strongly ruffled 12,13-diepimer.[9] On the other hand, the solution behaviors (ruffling in solution) of *iron* chlorin complexes have never been examined in spite of the fact that *iron* chlorins are utilized as prosthetic groups of heme enzymes such as cytochrome *d* and HPII. It is thus very important to examine the ruffling behavior of *iron dihydroxychlorin* in solution as a model for the iron chlorin prosthetic groups, **1** and **2**.

We report here the first observation of dynamic ruffling inversion of chloro-iron(III) *cis*-dihydroxyoctaethylchlorin (*c*-DHOECFe^{III}Cl, **3**)[10] by employing variable-temperature proton NMR spectroscopy. Further, the ruffling behavior of **3** in solution is shown to be distinctive from that of chloro-iron(III) *trans*-octaethylchlorin (*t*-OECFe^{III}Cl, **4**).

Proton NMR spectra of **3** and **4** in dichloromethane-d_2 at 23 °C exhibit well-defined hyperfine-shifted NMR resonances as shown in Figure 1.[11] The meso proton signals (15, 20- and 5, 10-positions) of **3** are observed in the upfield region at –50.5 and –91.5 ppm, respectively (Figure 1a). The resonances of the methylene protons bound to the pyrrole rings of **3** exhibit multiple splittings in the range of 40-60 ppm, and the pyrroline methylene proton resonances are observed at 10-20 ppm, respectively. The NMR spectral features of **4** are similar to those of **3**, except for their meso proton resonances (Figure 1b). The meso proton resonances of 15, 20- and 5, 10-positions of **4** split into four lines, observed at –46.3, –56.3 and –82.4, –92.5 ppm, respectively. Since **4** exhibits only 16 and 2 lines of the methylene and the pyrroline proton resonances (Figure 1b), respectively, **4** is expected to be a well-defined single species as well as **3**. Thus, the splitting of the meso proton signals of **4** implies that the *t*-OEC macrocycle of **4** is ruffled in solution to make four meso protons non-equivalent (in the ruffling conformation, the opposite pyrrole rings are counterrotated, thus the meso carbon atoms are alternately displaced above and below the mean macrocycle plane).[12] The *c*-DHOEC macrocycle of **3** would also be ruffled, but the meso proton resonances are averaged on the NMR time scale at 23 °C.

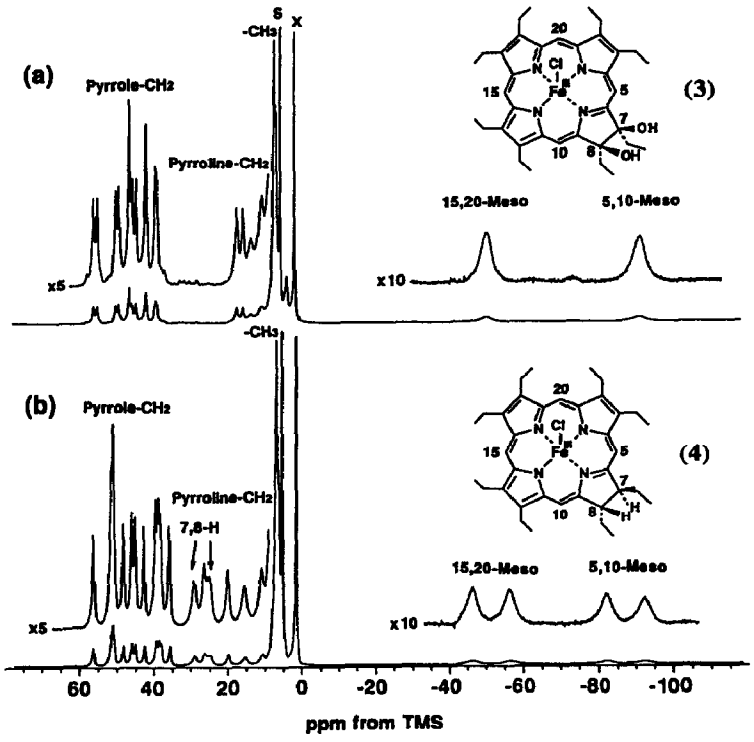

Figure 1. Proton NMR spectra of *c*-DHOECFe^{III}Cl, **3** (a) and *t*-OECFe^{III}Cl, **4** (b) in dichloromethane-d_2 at 23 °C.

To gain further insight into the ruffling behavior of **3**, variable-temperature proton NMR measurements have been performed in the range from 23 to –80 °C. When the temperature was lowered, two meso proton resonances of **3** were broadened and then separated into four lines below –70 °C, as shown in Figure 2. This process is completely reversible and independent of concentration. Further, the electronic absorption spectrum of **3** in dichloromethane (λ_{max}, nm: 378, 469, 602, 688, and 755) did not show any significant change when the solution was cooled down to –100 °C. These observations demonstrate that the unusual NMR spectral behavior of **3** is hardly due to the equilibrium between monomer and dimer complexes nor the motion of the iron atom through the macrocycle hole (*porphyrin inversion*) as observed in iron(III) porphyrin complexes,[15] but rather results from dynamic ruffling inversion of the *c*-DHOEC macrocycle. Thus, the ruffling inversion of the *c*-DHOEC macrocycle of **3** is fast enough to make two meso protons equivalent on the NMR time scale at ambient temperature, and the inversion slowed down to exhibit four NMR resonances of the meso protons when the temperature was lowered. This is the first example of the dynamic ruffling inversion of iron chlorin complexes.[16]

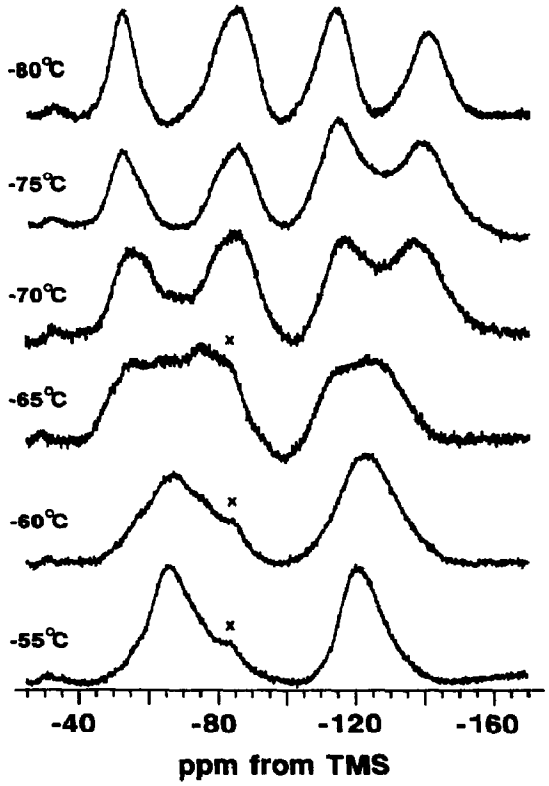

Figure 2. Temperature dependence of the meso proton resonances of **3** in the temperature range from –55 to –80 °C (dichloromethane-d_2).

The activation parameters of the inversion barrier of **3** are estimated to be $\Delta H^{\ddagger} \sim 15$ kcal mol^{-1} and $\Delta S^{\ddagger} \sim 30$ cal mol^{-1} by the line shape fitting of calculated[17] and observed NMR spectra at different five temperatures. In contrast to **3**, the dynamic ruffling inversion of **4** is not detectable under the conditions in this study,[18] implying that the ruffling of **4** in solution is quite different from that of **3**. These observations suggest that the structure of the substituents on the pyrroline ring would largely affect the solution behavior (ruffling in solution) of the iron chlorin complexes.[19]

In conclusion, the macrocycles of **3** and **4** are ruffled in solution, established by their proton NMR spectra. Furthermore, the ruffling behavior of **3** in solution is shown to be different from that of **4** by the observation of the dynamic ruffling inversion of **3**. Detailed studies of redox and ligand binding properties of **3** and **4** are under investigation.

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8. F430 is the nickel hydrocorphinoid prosthetic group of methyl coenzyme M reductase.[9]
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10. Abbreviations: *c*-DHOEC, *cis*-7,8-dihydroxy-2,3,7,8,12,13,17,18-octaethylporphyrin (*cis*-dihydroxyoctaethylchlorin); *t*-OEC, *trans*-7,8-dihydro-2,3,7,8,12,13,17,18-octaethylporphyrin (*trans*-octaethylchlorin); *ttt*-OEiBC, *trans-trans-trans*-2,3,7,8-tetrahydro-2,3,7,8,12,13,17,18-octaethylporphyrin (*trans-trans-trans*-octaethylisobacteriochlorin).
11. Proton NMR spectra at 300 MHz were recorded on a Nicolet NT-300 spectrometer equipped with a 1280 computer system. Proton chemical shifts are referenced to Me_4Si internal standard, and downfield shifts are given a positive sign. Sample concentrations are ~3 mM.
12. It was suggested that the appearance of four meso proton resonances of the *t*-OEC complex (**4**) could be caused by removal of the macrocycle C_2 axis upon formation of the five-coordinated complex.[13] However, the corresponding octaethylisobacteriochlorin complex (*ttt*-OEiBC) is not the case, i.e., the 10, 20-meso proton resonance of the complex does not split.[14] Therefore, the splitting of the meso proton signals of **4** should result from the ruffling deformation of the macrocycle.
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16. The splittings of the meso proton signals of **3** are also observed in both chloroform-*d* and toluene-d_8 (the coalescence temperatures are –65 and –75 °C, respectively).
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18. The meso proton resonances of **4** remain four lines in the temperature range from –80 to 80 °C.
19. Attempts to synthesize the *trans*-DHOEC derivative, which is more suitable to be compared with the *cis*-DHOEC, have been unsuccessful at this time.

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