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Resonance Raman studies of dioxygen binding to *ortho*-substituted tetraphenyl- and tetranaphthyl-porphyrinatoiron(II) derivatives with a covalently linked axial imidazole

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Resonance Raman spectra with 457.9 nm laser excitation have been recorded for the deoxy and oxy complexes of *ortho*-substituted tetraphenyl- and tetranaphthyl-porphyrinatoiron(II) derivatives with a covalently linked proximal imidazole. The intramolecular imidazole co-ordination gives high-spin iron(II) states in the deoxy forms of these complexes, which are revealed by the appearances of the indicative ν_8 bands of the porphyrin ring at 367–375 cm^{-1}. Their Fe–N (imidazole) stretching modes were directly detected at 201–223 cm^{-1}, and are discussed in relation to the Fe–N (imidazole) bond strength and the geometry of the imidazole co-ordination. As a result, a significant tilting of the imidazole ring plane from the Fe–N (imidazole) vector is proposed for the double-side encumbered derivatives. The dioxygenation was monitored by the upshift of the porphyrin skeletal band (ν_4). The dioxygen adducts of the double-side encumbered porphyrins showed high iron–dioxygen stretching frequencies (579 and 580 cm^{-1}) relative to those of oxyhemoproteins and other dioxygenated porphyrinatoiron(II) complexes generally observed in the range 568–573 cm^{-1}. These high frequencies are considered to reflect the decreased Fe–O–O angle induced by the narrow ester-linked cavity. For complexes of 5,10,15,20-tetrakis(*o*-pivalamidophenyl)porphyrinatoiron(II) with a covalently attached imidazolyl group at the β-pyrrole position the ν(Fe–N_ε) and ν(Fe–O_2) frequencies were found to be fairly similar to those of the same complexes with externally added imidazole ligands. This indicates that the covalent linkage between the imidazole and the porphyrin periphery is flexible and long enough to allow the formation of stable O_2-adduct species.

In natural hemoproteins the two axial ligands of the heme prosthetic group are significantly involved in their biological functions. The proximal histidine (E7) co-ordinated to the protoheme in hemoglobin plays a crucial role in regulation of the O_2-binding affinity, and is a trigger for the allosteric phenomena observed in the dioxygenation process. To get an insight into the electronic structure of the hemes, several synthetic porphyrinatoiron(II) complexes with an intramolecular co-ordinated axial base have been prepared.[1–5] More recently, we have synthesized a series of *ortho*-substituted tetraphenyl- and tetranaphthyl-porphyrinatoiron(II) derivatives **1**–**4**, in which an N-alkylated imidazole is covalently linked to the porphyrin periphery.[6–8] It has been found that these iron(II) complexes can reversibly bind dioxygen in toluene at ambient temperature. In particular, the double-side encumbered models, **1** and **2**, could not form an unfavorable μ-oxo porphyrin dimer, producing a kinetically stable O_2-adduct species. These four compounds, differing in the structure of substituents on the porphyrin macrocycle, exhibited varied O_2-binding affinities and kinetics. Consequently, the steric and electronic effects of the substituent structure on the iron–ligand bonding are of current interest to us and resonance Raman (RR) spectroscopy has been employed as the probe. It is known that Soret excitation of the synthetic hemes normally gives rich RR spectra consisting of totally symmetric vibrations of the porphyrin core; some of them have been identified and found to be sensitive to the axial ligation.[9–11] Especially, the low-frequency (<600 cm^{-1}) vibration associated with motions of the iron atom can be clearly detected with this technique. We report here the RR spectra of **1**–**4** and their dioxygen adducts. The observed iron–imidazole (Fe–N_ε) and –dioxygen (Fe–O_2) stretching frequencies are discussed in terms of the bond strength and geometry.

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Experimental

The corresponding bromides of compounds **1**–**4**, {5-[2-(5-imidazol-1-ylvaleryloxy)-6-(pivaloyloxy)phenyl]-10,15,20-tris-[2,6-bis(pivaloyloxy)phenyl]porphyrinato}iron(III) bromide, {2-[(8-imidazol-1-yl)octanoyloxymethyl]-5,10,15,20-tetrakis-(2-pivaloyloxynaphthyl)porphyrinato}iron(III) bromide, {2-[(8-imidazol-1-yl)octanoyloxymethyl]-5,10,15,20-tetrakis(*o*-pivalamidophenyl)porphyrinato}iron(III) bromide, and {2-[8-(2-methylimidazol-1-yl)octanoyloxymethyl]-5,10,15,20-tetrakis(*o*-pivalamidophenyl)porphyrinato}iron(III) bromide, were synthesized as previously described.[6–8] Dichloromethane (special grade for fluorescence analysis, Kanto Chemical Co., Tokyo) was used without further treatment. The $^{18}O_2$ (>99% ^{18}O) gas was obtained from Isotec Inc. (USA).

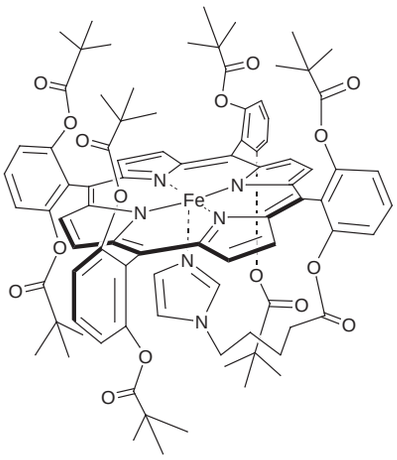
Reduction of the iron(III) bromides in CH_2Cl_2 with aqueous $Na_2S_2O_4$ under anaerobic conditions afforded the iron(II) complexes (deoxy form). After the formation of the deoxy complex had been confirmed by the UV/VIS absorption spectrum,[6–8] the CH_2Cl_2 layer (*ca.* 1 mmol dm^{-3}) was transferred to a rubber-septum quartz cell (2 mm thickness) for Raman spectroscopic measurement. Dioxygenation was then achieved by bubbling oxygen gas into the solution for 1 min.

Resonance Raman spectra were obtained with excitation of the 457.9 nm line of a NEC GLG2162 Ar^+ ion laser in a back-scattering geometry at 25 °C, using a JASCO NRS-2000 laser Raman spectrometer equipped with a CCD multichannel detector. The spectrometer was calibrated with indene.

Results and Discussion

Deoxy complexes

Low-frequency RR spectra of the iron(II) complexes **1**–**4** under argon, namely the deoxy form, are shown in Fig. 1. Complexes **1**, **2** and **3** gave a band at 222, 223 and 222 cm^{-1}, respectively,



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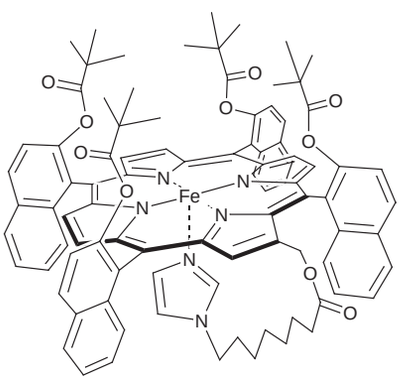

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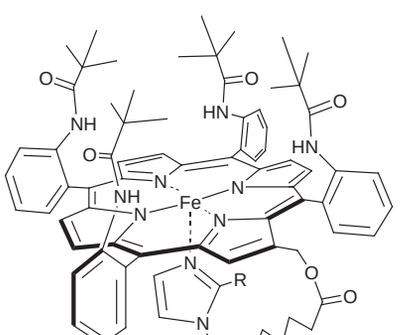

R = H **3**
R = CH_3 **4**

whereas **4**, an analog of **3** with a C2-methylated imidazole, gave an overlapped band at 201 cm^{-1}. Similar bands were reported for five-co-ordinated [5,10,15,20-tetrakis(*o*-pivalamidophenyl)-porphyrinato]iron(II) complexes **5** with externally added imidazole ligands, which have been assigned to the iron–imidazole stretching mode.[12] Accordingly, the bands at 201–223 cm^{-1} observed here are assigned to the $\nu(Fe–N_\varepsilon)$ frequencies for the intramolecular five-co-ordinated complexes **1**–**4**.

The $\nu(Fe–N_\varepsilon)$ frequency of complex **3** at 222 cm^{-1} is close to that of **5** complexed with 1-methylimidazole (mim) at 225 cm^{-1}, and the same is true for **4** at 201 cm^{-1} and **5** complexed with 1,2-dimethylimidazole (dmim) at 200 cm^{-1}. This indicates that the covalent linkage between the imidazole and the porphyrin periphery is flexible and long enough to allow intramolecular iron–imidazole co-ordination. Compared with **3**, complex **4** shows an ≈20 cm^{-1} reduced $\nu(Fe–N_\varepsilon)$ frequency. Assuming a diatomic oscillator model and an identical force constant for the $Fe–N_\varepsilon$ stretching vibration, the frequency shift is calculated

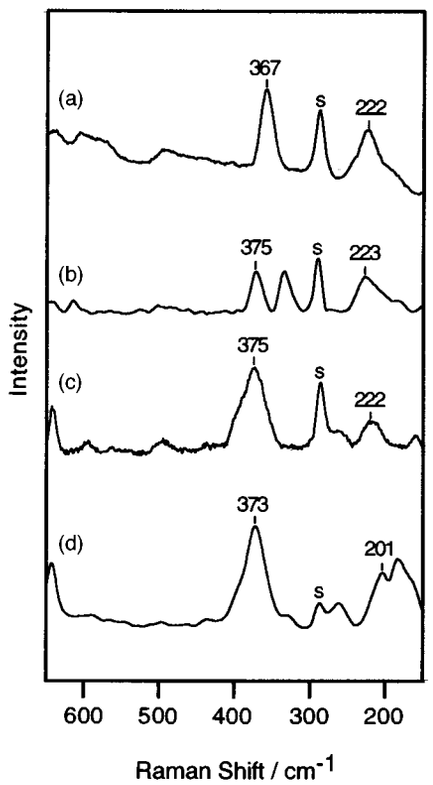

Fig. 1 Low-frequency RR spectra of the deoxy complexes **1** (a), **2** (b), **3** (c) and **4** (d) in CH_2Cl_2 with 457.9 nm excitation. Laser power, 60 mW; accumulation time, 60 s; three scans; sample concentration, 1 mmol dm^{-3}; s denotes solvent bands

as ≈6 cm^{-1} when replacing the imidazole moiety with methylimidazole. Thus the observed larger shift represents a weakened Fe–N (imidazole) bond in **4** caused by the steric hindrance of the 2-methyl group on the imidazole ring.

Interestingly, the $\nu(Fe–N_\varepsilon)$ frequencies of complexes **1** and **2** are almost the same as that of **3**. The double-sided porphyrins are expected to have a weak Fe–N (imidazole) bond due to the steric hindrance of the rear-side substituents. An infrared spectroscopic study of **1** and **2** showed a significant high ν(CO) at 1979 cm^{-1} relative to those of single-face hindered derivatives, *e.g.* 1969 cm^{-1} for **5** bonded to mim and CO.[6,8] This is presumably caused by the low π-back donation from the central iron to the bound CO, due to the weak *trans*-imidazole co-ordination. The O_2- and CO-binding kinetic parameters also supported this assumption.[6,8] Nevertheless, the stretching frequency is generally determined by both the bond strength and structure factors including the geometry of the bond. Studies of the carbon monoxide complexes of hemoproteins, for example, demonstrated that ν(Fe–C) increased according to the inclination of the Fe–C–O bond angle.[13] This has been attributed to the reduction of the effective mass of CO for the Fe–CO stretching vibration as the Fe–C–O angle decreases.[14] Results of molecular simulations‡ of **1** and **2** showed that the imidazole ring plane is significantly tilted from the Fe–N (imidazole) vector with an angle (ψ) of *ca.* 150–160°, while this angle is almost 180° for **3**. The inclination of the imidazole ring, normally resulting in a weakened Fe–N (imidazole) bond, may also lead to a lowering of the effective mass of the imidazole moiety. Such opposite effects on the stretching frequency probably produce a higher value than the expected one. Therefore, the observed $\nu(Fe–N_\varepsilon)$ frequencies of **1** and **2** could be interpreted as corresponding to the tilted geometry of the imidazole ring.

‡ The ESFF forcefield simulation was performed using an Insight II system (Molecular Simulation Inc.). The structure was generated by alternative minimizations and annealing dynamic calculations.

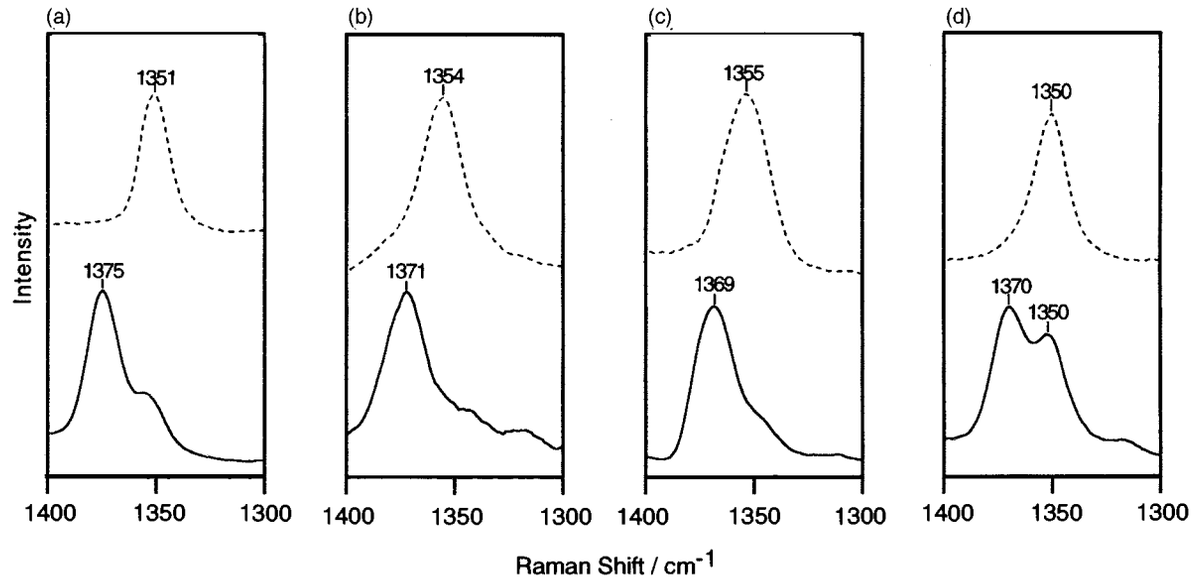

Fig. 2 The RR spectra in the 1200–1400 cm^{-1} region of the deoxy (dotted line) and oxy (solid line) complexes **1** (a), **2** (b), **3** (c) and **4** (d) in CH_2Cl_2 with 457.9 nm excitation. Measurement conditions for the deoxy complexes as in Fig. 1. Conditions for the oxy complexes: laser power, 5 mW; accumulation time, 360 s; three scans

Furthermore, several porphyrin skeletal modes have been identified for hemoproteins and some synthetic hemes, the frequencies of which are sensitive to the spin state.[11] Systematic studies on tetraphenylporphyrinatoiron(II) derivatives showed that the observation of a band at 365–370 or 380–390 cm^{-1} is indicative of high-spin five-co-ordination or low-spin six-co-ordination, respectively.[15] This band has been assigned to a deformation mode of the porphyrin ring (ν_8).[16] The appearance of a ν_8 band at 367–375 cm^{-1} for all the complexes **1**–**4** under argon clearly showed the formation of the high-spin five-co-ordination states (Fig. 1).

Dioxygen adducts

The high-frequency region of the RR spectra of tetraphenylporphyrinatometal derivatives exhibits a strong band at 1340–1390 cm^{-1}, which has been assigned to ν_4, a deformed pyrrole-ring breathing-like mode.[17] The ν_4 frequency depends on the electron density in the π^* antibonding orbital of the porphyrin core,[18] and hence is sensitive to the axial ligation state of the central iron. It was found that ν_4 bands of complexes **1**–**4** at 1350–1355 cm^{-1} under argon, which correspond to the five-co-ordinated high-spin state, shifted immediately to 1369–1375 cm^{-1} after exposure to dioxygen (Fig. 2). This observation indicates the formation of six-co-ordinated low-spin species, namely the oxy form. In the spectra of the dioxygenated complexes **1**–**4**, however, the deoxy signals still remain probably due to photodissociation of the bound O_2 during the measurement.

Fig. 3 shows the low-frequency RR spectra of $^{16}O_2$ and $^{18}O_2$ adducts of complex **1**. A band at 579 cm^{-1} in the spectrum of the $^{16}O_2$ adduct shifted to 557 cm^{-1} upon $^{18}O_2$ substitution. This is indicated by the difference spectrum in which the strong porphyrin bands at 385 cm^{-1} are completely cancelled. Consequently, the Fe–O_2 stretching mode of the oxy complex of **1** is identified at 579 cm^{-1}. The low-frequency RR spectra of the dioxygen adducts of **2**, **3** and **4** are shown in Fig. 4, where the ν(Fe–O_2) vibrations appear at 580, 566 and 565 cm^{-1}, respectively.

Comparison of these frequencies with the O_2-binding affinities [$P_{\frac{1}{2}}(O_2)$] of the iron(II) complexes **1**, **2**, **3** and **4** which have been determined as 13, 18, 0.29 and 38 Torr (Torr ≈ 133 Pa) (25 °C, toluene), respectively,[6–8] shows that the ν(Fe–O_2) frequency lacks a straightforward relation with $P_{\frac{1}{2}}(O_2)$. In particular, the ν(Fe–O_2) frequencies for **3** (566 cm^{-1}) and **4** (565 cm^{-1}) are nearly identical, while the O_2-binding affinity of **3** is 135 times higher than that of **4**. Such a lack of correlation is consistent with previous results for **5** and imidazole-appended hemes.[12,14]

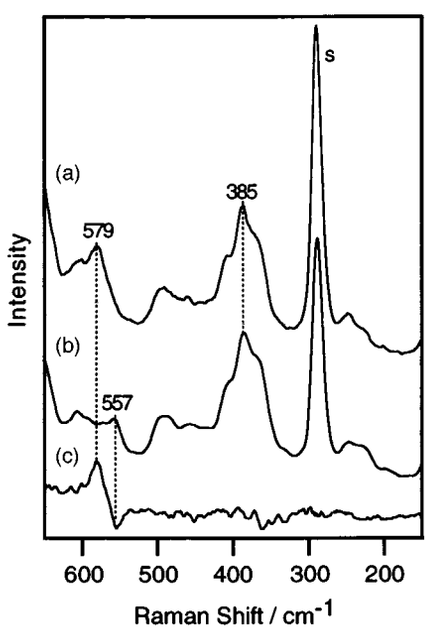

Fig. 3 Low-frequency RR spectra of $^{16}O_2$ (a) and $^{18}O_2$ (b) adducts of complex **1**, and the difference spectrum (c). Laser power, 5 mW; accumulation time, 360 s; three scans; sample concentration, 1 mmol dm^{-3}; s denotes solvent bands

The ν(Fe–O_2) frequencies for the dioxygen adducts of complexes **3** and **4** are very close to those of **5** with mim and dmim,[12] which were both reported as 568 cm^{-1}. Combining the results of the ν(Fe–N_ε) and ν(Fe–O_2) vibrations, it can be concluded that the intramolecular complexes **3** and **4** have similar iron–ligand bonding characters to those of the corresponding intermolecular ones, respectively.

It is noteworthy that the ν(Fe–O_2) frequencies for the oxy forms of complexes **1** and **2** are appreciably high compared to those of oxyhemoproteins[19] and other dioxygenated porphyrinatoiron(II) complexes[11,12,14] generally observed in the range 568–573 cm^{-1}. The high frequency probably has its origin in the

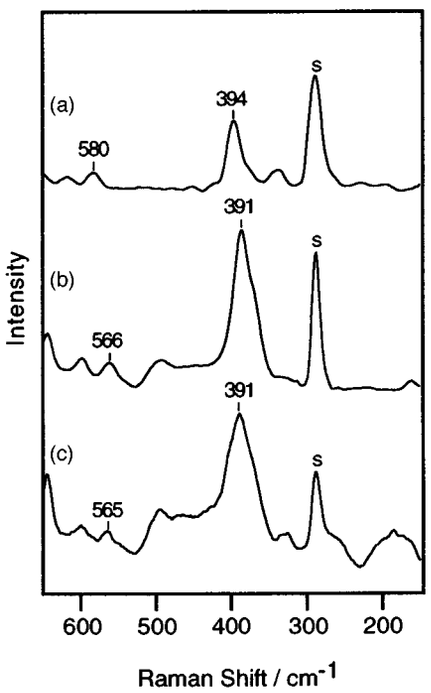

Fig. 4 Low-frequency RR spectra of the dioxygen adducts of complexes **2** (a), **3** (b) and **4** (c). Conditions as in Fig. 3

molecular structure. In complexes **1** and **2** the cavity surrounding the bound dioxygen is composed of four pivaloyloxy substituents rather than the pivalamido groups in most model compounds. A study on the CO adducts of capped hemes showed that the amide-linked cavity results in an increased Fe–CO stretching frequency, which has been ascribed to the increased Fe→CO back bonding caused by the polar interaction between the terminal O atom of bound CO and the amide NH groups.[20] Accordingly, an ester-linked cavity lacking such interaction is expected to lead to a relatively low Fe–CO stretching frequency. Since the situations for Fe→CO and Fe→O_2 back bonding are similar, it seems difficult to interpret the high Fe–O_2 stretching frequency observed for the oxy forms of complexes of **1** and **2** from the viewpoint of a polar interaction.

On the other hand, O_2-binding kinetic results suggested that this ester-linked cavity provides a narrower space for dioxygen binding than that of the amide-linked one, resulting in the low O_2-association rate constant.[8,21] If this is the case, the four pivaloyloxy groups may induce deformation of the Fe–O–O bond. An inverse relationship between the ν(Fe–O_2) frequency and the Fe–O–O angle has previously been pointed out based on theoretical calculations.[22] In a recent study on the oxymyoglobin mutants, Kitagawa and co-workers[19] also revealed that a 9° decrease in the Fe–O–O angle corresponds to a 6 cm^{-1} increase in the Fe–O_2 stretching frequency. We thus consider that the high ν(Fe–O_2) frequency observed for **1** and **2** presumably reflects a decreased Fe–O–O angle which is caused by the steric hindrance in the ester-linked cavity.

In conclusion, the double-side encumbered complexes **1** and **2** were found to exhibit unique ν(Fe–N_ε) and ν(Fe–O_2) vibrations, which are interpreted in terms of the bond geometry. We are currently attempting to prepare crystals of these porphyrinato-iron and -zinc complexes to get more detailed information about the structures.

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