Binding and Kinetics of 1-Methylimidazol on Fe(III)-Protoporphyrin(IX)dimethylester and Fe(III)-Tetraphenylporphyrin in Chloroform

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NMR, Kinetics, Ferriporphyrins

Nuclear magnetic line widths data have been used to determine the rate of solvent exchange between the coordination sphere of Fe(III)-protoporphyrin(IX)dimethylester or Fe(III)-tetraphenylporphyrin and the bulk phase of 1-methylimidazol/chloroform. At temperatures below 322 K both porphyrins are in the low-spin state and separate PMR absorption caused by the methyl protons of two 1-methylimidazol molecules complexed in fifth and sixth position of ferri-porphyrins is detected. At \( T > 320 \) K an accelerated exchange of these ligands was observed and the underlying kinetic parameters have been extracted. It was found that this exchange takes place when the paramagnetic species is in its low-spin state. For \( 240 \) K \( \leq T \leq 290 \) K dynamic line broadening of bulk phase 1-methylimidazol indicates occurrence of chemical exchange attributed to 1-methylimidazol interacting with ferri-porphyrin in addition to the strongly bound axial ligands.

Introduction

The biological function of metal porphyrins acting as prosthetic groups in many proteins, rests largely upon their ability to exchange ligands coordinated to the metal ion in axial position\(^1\). In view of their possible relevance for the function in heme-proteins the specific interaction of axial ligand substitution reactions of ferri- and ferro-porphyrins has been the subject of several investigations recently\(^2\)\(-\)\(^6\).

Here we report preliminary results of a study dealing with the affinity of Fe(III)-protoporphyrin(IX)dimethylester (\(=\)Fe(III)-PPD) and Fe(III)-tetraphenylporphyrin (\(=\)Fe(III)-TPP) towards the nitrogenous base 1-methylimidazol (\(=\)CH\(_3\)-Im) in deuterochloroform.

Abbreviations:

PMR: Proton magnetic resonance,
Fe(III)-PPD: Ferrprotoporphyrin(IX) dimethyl-ester,
Fe(III)-TPP: Ferritetraphenylporphyrin,
CH\(_3\)-Im: 1-Methylimidazol.

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Experimental

A Varian XL-100-15 high resolution spectrometer operating at 100 MHz has been used for the PMR measurements. Reproducibility of line widths was \( \pm 2 \) Hz. Magnetic susceptibilities where measured as described elsewhere\(^7\). Tetramethylsilane was chosen as an inert marker for the PMR susceptibility measurements. The diamagnetic contribution to the susceptibilities was taken from the literature\(^8\); for Fe(III)-TPP a value of \( \chi^M = 4.6 \cdot 10^{-6} \) has been estimated.

Results and Discussion

The spin-spin relaxation rates \( 1/T_2 \) derived from experimental line widths of bulk phase CH\(_3\)-Im in solutions of Fe(III)-PPD or Fe(III)-TPP in CH\(_3\)-Im/CDCl\(_3\) are presented in a semilogarithmic plot in Figs. 1 and 2. At temperatures \( T \leq 300 \) K separate PMR signals appear for the protons of coordinated CH\(_3\)-Im. These PMR absorptions have been assigned to methyl protons of two complexed molecules of CH\(_3\)-Im by comparison of their intensities with corresponding PMR signals of the methyl groups attached to Fe(III)-PPD or the pyrrol protons of Fe(III)-TPP. In Fig. 1 the PMR relaxation behavior of the two complexed CH\(_3\)-Im ligands in solutions of (CH\(_3\)-Im)\(_2\)-Fe(III)-PPD in CH\(_3\)-Im/
Fig. 1. Spin-spin relaxation rates \(1/T_2\) of Fe(III)-protoporphyrin(IX)dimethylester in 1-methylimidazol/chloroform (18.2 \(\mu\)M Fe(III)-PPD; 1.2 mM CH\(_3\)-Im).

- **O**: 2-H of bulk phase CH\(_3\)-Im (left scale),
- **X**: methyl protons of bulk phase CH\(_3\)-Im (left scale),
- **•**: methyl protons of complexed CH\(_3\)-Im (right scale).

Fig. 2. Spin-spin relaxation rates \(1/T_2\) of bulk phase 1-methylimidazol (2-H) in solutions of Fe(III)-tetraphenylporphyrin in 1-methylimidazol/chloroform (7.5 \(\mu\)M Fe(III)-TPP; 0.6 mM CH\(_3\)-Im).

CDC\(_3\) is included. The deviations from linearity of \(\lg (T_2-1)\) immediately demonstrates chemical exchange between coordinated and non-coordinated CH\(_3\)-Im.

The changes of line width observed are attributed to jumps of nuclei from the bulk phase (site A) to the coordination sphere (site M) and may be obtained by rigorous solution of the corresponding Bloch equation\(^9\). For a system, as the one under consideration, in which the metal complex is highly diluted, i.e., the concentration of non-coordinated species \(c_A\) is much higher than the concentration \(c_M\) of coordinated molecules, the relaxation times in the limit of 'slow exchange' is given as\(^9\),

\[
\frac{1}{T_2} - \frac{1}{T_{2A}} = x_M \frac{1}{\tau_M}
\]

The limiting case of 'slow exchange' is defined as in Ref.\(^9\). The symbols in Eq. (1) have the following meaning: \(T_2\) is the observed relaxation time; \(T_{2A}\) corresponds to the line width of nuclei in environment A (bulk phase); \(x_M\) gives the molar ratio of coordinated species and \(\tau_M\) symbolizes the mean lifetime of the nuclei under consideration in the coordination sphere of the metal complex. The negative slopes where Eq. (1) holds are indicated in Fig. 1 by 'A' and 'B'.

The kinetic parameters \(\tau_M\), \(\Delta H^+\), and \(\Delta S^+\) which are collected in Table I where determined by fitting the data in Figs. 1 and 2 to Eq. (1). The temperature dependence of \(\tau_M\) was taken as:

\[
\tau_M = \left(\frac{h}{kT}\right) \cdot \exp\left[\frac{\Delta H^+/RT - \Delta S^+/R}\right]
\]

In general \(\tau_M\) has to be considered as a weighted average for the particles in the coordination sphere of low- and/or high-spin ferri-porphyrins [\(cf.\] ref. 5], viz.,

\[
\tau_M^{-1} = x_H \cdot \tau_H^{-1} + x_L \cdot \tau_L^{-1}
\]
Table I. Kinetic and thermodynamic parameters for the exchange of 1-methylimidazol between the coordination sphere of Fe(III)-protoporphyrin(IX)dimethyl ester [Fe(III)-PPD] or Fe(III)-tetraphenylporphyrin [Fe(III)-TPP] and the bulk phase in solution of 1-methylimidazol/chloroform, as extracted from PMR line broadening of the noncoordinated species.

<table>
<thead>
<tr>
<th></th>
<th>( \tau_M ) [ms]</th>
<th>( \Delta H^+ ) [kJ mol(^{-1})]</th>
<th>( \Delta S^+ ) [J mol(^{-1})K(^{-1})]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fe(III)-TPP</td>
<td>1 ± 0.5 (322 K)</td>
<td>68 ± 7 (322 K)</td>
<td>21 ± 2 (322 K)</td>
</tr>
<tr>
<td>Fe(III)-PPD</td>
<td>2.5 ± 1.2 (322 K)</td>
<td>115 ± 12 (322 K)</td>
<td>160 ± 20 (322 K)</td>
</tr>
<tr>
<td></td>
<td>3.5 ± 1.8 (256 K)</td>
<td>50 ± 5 (256 K)</td>
<td>0 ± 8 (256 K)</td>
</tr>
</tbody>
</table>

where \( x_H \), \( x_L \) represent the mole ratios of the species in high- and low-spin electron configuration and \( \tau_H^{-1} \), \( \tau_L^{-1} \) stand for the corresponding exchange rates.

Considering region 'B' \((T \approx 322 \text{ K})\) it seems reasonable to assume, \( \tau_M = \tau_L \), for the two systems in the present investigation, i.e., the experimentally determined values of \( \tau_M \) exclusively reflect the exchange of CH\(_3\)-Im between the low-spin Fe(III)-porphyrin complex and the bulk phase. This behavior which differs from corresponding results\(^6\) of ferri-porphyrins in pyridine/CDCl\(_3\) is supported by the following two experimental facts:

i) The values of the effective magnetic moments of iron shown in Fig. 3 imply: \( x_H \ll x_L \).

ii) The mean lifetime \( \tau_L \) obtained from dynamic line broadening of the methyl protons of complexed species reveals: \( \tau_M \approx \tau_L \) (cf. Table II). By comparison of the data in Table I with the results reported in ref.\(^3\), one finds that this is also true for (CH\(_3\)-Im)\(_2\)-Fe(III)-TPP.

From i) and ii) it follows, \( x_L \cdot \tau_L^{-1} \gg x_H \cdot \tau_H^{-1} \), yielding, \( \tau_M \approx \tau_L \).

Table II. Kinetic and thermodynamic parameters related to line broadening of the methyl protons of complexed 1-methylimidazol in low-spin bis(1-methylimidazol)-Fe(III)-protoporphyrin(IX)dimethyl ester dissolved in 1-methylimidazol/chloroform.

<table>
<thead>
<tr>
<th></th>
<th>( \tau_L ) [ms]</th>
<th>( \Delta H^+ ) [kJ mol(^{-1})]</th>
<th>( \Delta S^+ ) [J mol(^{-1})K(^{-1})]</th>
</tr>
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<tr>
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<tr>
<td>11</td>
<td>± 4.5 (298 K)</td>
<td>115 ± 12 (298 K)</td>
<td>160 ± 20 (298 K)</td>
</tr>
<tr>
<td>2.5</td>
<td>± 1.2 (322 K)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A second region of dynamic line broadening exists at lower temperatures \((T \approx 256 \text{ K})\) marked 'A' in Fig. 1. This exchange of CH\(_3\)-Im from the coordination sphere of ferri-porphyrins (which is of less importance for Fe(III)-TPP – cf. Fig. 2) is given by an interaction of additional CH\(_3\)-Im molecules with ferri-porphyrins besides the two ligands bound in fifth and sixth position which are characterized by their separate PMR absorption. This is seen in Fig. 1 where the PMR line widths for the 'strongly' bound molecules in fifth and sixth position decrease with increasing temperatures in the range marked by 'A', whereas the bulk phase CH\(_3\)-Im already experiences a PMR exchange broadening. This may be understood by assuming that the probability of finding a bulk phase CH\(_3\)-Im molecule in the nearest neighborhood of \((\text{CH}_3\text{-Im})_2\)-Fe(III)-PPD is higher than the probability of finding it elsewhere distributed in the bulk phase solution; i.e., there are additional molecules of CH\(_3\)-Im interacting 'weakly' with Fe(III)-PPD. This agrees with analogous results found for Fe(III)-PPD in pyridine/CDCl\(_3\)\(^6\).

So far, we neither know the number of these additionally 'complexed' species nor the kind of specific interaction responsible for their existence. The kinetic parameters extracted from the line widths data in Fig. 1 (range 'A'), which are listed in Table I, have been obtained with a rather arbitrary 'coordination number' of two. Any other number changes the values of the mean lifetime, whereas \( \Delta H^+ \) and \( \Delta S^+ \) are more or less independent to such variations. It is interesting to note that the entropy of activation
for this exchange process is practically zero (cf. Table I). Further investigations are necessary to
analyse the specific properties of these 'complexed' species.

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