Small Reorganization Energy for Ligand-Centered Electron-Transfer Reduction of Compound I to Compound II in a Heme Model Study

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Supporting Information

ABSTRACT: The electron-transfer (ET) processes from electron-donor substrates to oxoiron(IV) porphyrin π-cation-radical species (Cpd I) are key steps in their oxygenation reactions. Here, we have evaluated the rate constants of the outer-sphere ET reduction of Cpd I model complexes of meso-tetramesitylporphyrin (1) and 2,7,12,17-tetramesityl-3,8,13,18-tetramethylporphyrin (2) in light of the Marcus theory of ET to determine the ET reorganization energies (λ). The λ values of the ligand-centered ET reduction of Cpd I model complexes are much smaller than those of the metal-centered ET reduction of various oxoiron(IV) complexes. Moreover, the λ value of 1 is larger than that of 2, resulting from the difference in the nature of the a_1u/a_2u porphyrin π-cation-radical orbitals.

Oxoiron(IV) porphyrin π-cation-radical species, referred to as compound I (Cpd I), are pivotal reaction intermediates in many biological reactions catalyzed by heme enzymes such as peroxidases, catalases, and cytochromes P450. Because Cpd I is reduced to an oxoiron(IV) porphyrin species referred to as compound II (Cpd II), or a ferric heme complex in their biological reactions, the chemical reactions of Cpd I accompany electron-transfer (ET) processes from substrates to Cpd I. The reaction mechanisms of Cpd I with various substrates have so far been extensively studied by using heme enzymes and their synthetic model compounds. The ET processes are key to gaining an understanding of the reactivity and selectivity of Cpd I. The N-demethylation reactions of Cpd I of horseradish peroxidase (HRP) with N,N-dimethylaminilines were studied previously to discuss the ET pathways in hydrogen-atom transfer from organic substrates to Cpd I. However, outer-sphere ET processes from one-electron donor to Cpd I and analogues have yet to be scrutinized in light of the Marcus theory of ET to determine the reorganization energy (λ) of outer-sphere ET.

We report herein the ligand-centered outer-sphere ET from various one-electron donors to Cpd I model complexes, evaluating the ET rate constants in light of the Marcus theory of outer-sphere ET to determine the λ values, which can be compared with metal-centered outer-sphere ET reactions of oxoiron(IV) species. The difference in the λ values depending on the types of orbitals of the porphyrin π-cation radicals has also been clarified. To the best of our knowledge, this is the first time for clarification on how the ligand-centered versus metal-centered ET controls the ET reactivity of Cpd I and II.

We prepared structurally different Cpd I model complexes (Figure 1) of meso-tetramesitylporphyrin (1) and 2,7,12,17-tetramesityl-3,8,13,18-tetramethylporphyrin (2). 1 and 2 have the bulky mesityl group at the meso position and the pyrrole β position, respectively. The overall structure of 2 resembles that of a protoheme (Figure 1), the prosthetic groups of most heme enzymes, rather than that of 1. The redox potentials of Cpd I of 1 and 2 were reported to be almost the same, and the reported E1/2 value is calibrated to be 0.974 V versus saturated calomel electrode (SCE). We examined the reactions of Cpd I of 1 and 2 with one-electron donors, such as triphenylamine derivatives and 1,1′-diacetylferrocene, by using a low-temperature rapid-mixing stopped-flow technique. Cpd I model complexes of 1 and 2 were prepared by premixing ferric nitrate complexes of 1 and 2 with 5 equiv of m-chloroperoxybenzoic acid in dichloromethane at −20 °C, respectively. After Cpd I (∼10 s) was generated, the reaction mixture was rapidly mixed with the solution of the reductant.

Figure 2 shows the absorption spectral change after rapid mixing of 1 with tris-p-tolylamine in dichloromethane at −20 °C. The peaks at 504, 549, and 672 nm appear after rapid mixing. A comparison with authentic spectra indicates that the peaks at 504, 549, and 672 nm result from the ferric porphyrin

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complex, Cpd II and tris-p-tolylamine π-cation radical, respectively (Figure S1). The intensity of the peak at 549 nm increased for 0.090 s after mixing but then decreased (Figure 2a, inset). On the other hand, the intensities of the peaks at 504 and 672 nm increased in the reaction. Finally, the absorption spectral changes for the reactions with tris-p-tolylamine derivatives other than tris-p-bromophenylamine were similar to those with tris-p-tolylamine (Figures S6–S8). The reactions of Cpd I with tris-p-bromophenylamine stopped in the middle of the reaction because of the endergonic ET process, even when a large excess (~500 equiv) of tris-p-bromophenylamine was present (Figure S9). In addition, the time courses for the reactions with tris-p-tolylamine, tris-p-bromophenylamine, and 1,1′-diacetylferrocene were similar to those with tris-p-tolylamine (Figures S6–S8). The reduction rate constant for Cpd I linearly depends on the concentration of tris-p-tolylamine, providing apparent reduction rate constants for Cpd II (eq 2)

\[ k_{eq} = \frac{Z}{\Delta G_{et}^0} \frac{1}{T} \]  

where \( Z \) is the collision frequency, taken as 1 s\(^{-1}\) (refer to Table 1). The second-order rate constants of ET from one-electron reductants to Cpd I of 1 and 2 in light of the Marcus theory of outer-sphere ET (eq 1):

\[ k_{et} = Z \exp(-\lambda/4)(1 + \Delta G_{et}/\lambda)^2/k_BT \]  

where \( Z \) is the collision frequency, taken as 1 × 10\(^{11}\) M\(^{-1}\) s\(^{-1}\), \( \lambda \) is the reorganization energy of ET, \( k_B \) is the Boltzmann constant, and \( T \) is the absolute temperature. From the fitting of the rate constants, the reorganization energy (\( \lambda \)) values of ET from triphenylamines to Cpd I model complexes of 1 and 2 were estimated to be 1.44 and 1.21 eV, respectively.

Table 1. Redox Potentials and ET Rate Constants of Triphenylamine Derivatives and 1,1′-Diacetylferrocene

<table>
<thead>
<tr>
<th>Triphenylamine Derivative</th>
<th>( E_{1/2} ) (V vs SCE)</th>
<th>( k_{eq} ) (M(^{-1}) s(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>OCH(_3) OCH(_3) Br</td>
<td>0.800</td>
<td>6.11 × 10(^7)</td>
</tr>
<tr>
<td>CH(_3) CH(_3) CH(_3)</td>
<td>0.829</td>
<td>1.54 × 10(^7)</td>
</tr>
<tr>
<td>OCH(_3) H H</td>
<td>0.860</td>
<td>6.43 × 10(^7)</td>
</tr>
<tr>
<td>CH(_3) H Br</td>
<td>0.964</td>
<td>1.43 × 10(^7)</td>
</tr>
<tr>
<td>OCH(_3) Br Br</td>
<td>0.968</td>
<td>8.45 × 10(^7)</td>
</tr>
<tr>
<td>H H H H</td>
<td>1.020</td>
<td>5.07 × 10(^7)</td>
</tr>
<tr>
<td>Br Br Br</td>
<td>1.172</td>
<td>3.34 × 10(^7)</td>
</tr>
<tr>
<td>Ferrocene</td>
<td>0.974</td>
<td>4.94 × 10(^7)</td>
</tr>
</tbody>
</table>

\( E_{1/2} \) of ferrocene was 0.484 V versus SCE. The reported \( E_{1/2} \) value (0.92 V) was calibrated using the reported \( E_{1/2} \) (0.76 V) for 4-methoxytriphenylamine.
The estimated $\lambda$ values of Cpd I model complexes of 1 and 2 are smaller than those (1.6–1.8 eV) of one-electron-reduction processes of Cpd II model complexes of myoglobin and HRP.\textsuperscript{12,17–19} These $\lambda$ values are also much smaller than those (2.05–2.74 eV) of ET of nonheme oxoiron(IV) complexes.\textsuperscript{12,20–22} The small $\lambda$ values for Cpd I may result from the site of the ET reaction, which is on the porphyrin ligand moiety. Previous studies showed that the $\lambda$ values for metal-centered redox processes are significantly larger than those for porphyrin ligand-centered redox processes because the metal-centered ET process induces the change of the oxidation state of the metal ion, which results in changes of the charge and ionic radius of the metal ion and enforces the structural change around the metal ion with the redox process.\textsuperscript{22}

The $\lambda$ value for 2 is smaller than that for 1. The difference in the $\lambda$ values can be interpreted with the nature of the porphyrin \(\pi\)-cation-radical orbitals of these Cpd I species. Previously, we showed that the porphyrin $\pi$-radical electron of Cpd I of 1 is in the \(a_{2u}\) orbital, whereas that of 2 is in the \(a_{1u}\) orbital.\textsuperscript{19,20} The porphyrin $\pi$-radical electron in the \(a_{1u}\) orbital of 1 delocalized not only in the porphyrin ligand but also in the iron oxo moiety (\(\sim5\%\)) because of the orbital interaction between the \(a_{2u}\) orbital and the Fe 4p\(_{z}\)–O 2p\(_{z}\) antibonding orbital (Figure 4). On the other hand, the porphyrin $\pi$-radical electron in the \(a_{1u}\) orbital of 2 mainly delocalized in the porphyrin ligand because of the absence of suitable orbital interaction with oxoiron orbitals (i.e., mismatch of the orbital symmetry). Therefore, the ET process of Cpd I of 2 shows the porphyrin ligand-centered character with no metal-centered character. Consequently, as discussed above, the $\lambda$ value of the Cpd I of 1 becomes larger than that of 2. In addition, the flexibility of the porphyrin ligand also affects the $\lambda$ values. The absence of the substituent at the meso position in 2 makes the porphyrin ligand flexible, giving the smaller $\lambda$ value. The similarity of the $\lambda$ values suggests that the contribution of the protein moiety of HRP to the reorganization energy for the ET reaction process of Cpd I would be small because participation of the protein moiety is expected to increase the $\lambda$ value.

The reorganization energies for the ET exchange processes of Cpd I model complexes of 1 and 2 were also estimated from density functional theory (DFT) calculations. Details of the DFT calculations are described in the Supporting Information. The calculated $\lambda$ value (1.15 eV) for the ET reduction process of 1 is larger than that (1.05 eV) of 2 (Table S1), which agrees well with the experimental results in Figure 3. The geometric analysis, which can disclose the flexibility difference between two porphyrin systems, indicates that the ET reduction of the Cpd I of 1 resulted in a larger structural change, showing a higher root-mean-square-deviation (RMSD) value of 0.262 Å, whereas that of 2 presented a smaller structural change with a lower RMSD value of 0.107 Å (Table S2). The larger is the structural change during the ET process, the higher the reorganization energy (vide supra). Thus, the results from both electronic and geometric analyses support a higher reorganization energy (\(\lambda\), a lower ET reactivity) for Cpd I of 1 compared to that of 2.

In conclusion, we report the $\lambda$ values for the outer-sphere ET reductions of Cpd I to Cpd II in heme model complexes. The estimated $\lambda$ values for Cpd I model complexes are much smaller than those for nonheme oxoiron(IV) complexes. This is due to the fact that the site of the reduction is the porphyrin ligand in the heme system, and thus the $\lambda$ value is modulated by the nature of the \(a_{1g}/a_{2u}\) porphyrin $\pi$-cation-radical orbital. Understanding the $\lambda$ values for the ligand-centered ET of Cpd I provides quantitative insight into the difference in the redox reactivity between Cpds I and II.

### ASSOCIATED CONTENT

#### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.inorgchem.9b01051.

Experimental and computational details, Scheme S1, Figures S1–S11, and Tables S1 and S2 (PDF)

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Notes
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