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Biomimic O₂ Activation Hydroxylates a meso-Carbon of the Porphyrin Ring Regioselectively under Mild Condition

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The reaction site of the Co(II) porphyrin created by an amide group and coordinating 1,2-dimethylimidazole at the fifth site activated an O₂ molecule, and then hydroxylated the meso-carbon of the ligand. The biomimic O₂ activation under mild condition is described.

Proximal and distal histidine residues provide the coordination environment for stable O₂ fixation at the heme site of hemoglobin (Hb) and myoglobin (Mb), while proximal and distal-polar residues create a reaction environment for O–O bond activation at the heme sites of some metalloenzymes such as cytochrome c peroxidase (CcP), cytochrome P450 (CYPs), and heme oxygenase (HO) (Fig. 1). HO activates O₂ at the active site, and then hydroxylates the meso-carbon of heme, yielding hydroxy heme in the initial step (Fig. 1c). For activation of the O–O bond at the active sites, the so-called “push–pull” mechanism has been proposed. This is a cooperative effect by electron donation from the proximal residue at the fifth site (push effect) and associations from distal-polar residues to the coordinating substrate (pull effect).

Although various porphyrin complexes that mimic the microenvironments have been designed and synthesized, model complexes that activate O₂ molecules under mild conditions are still rare. As an important example, Chang and co-workers have shown that their complex [Co II(npca-por)] (H₂npca-por = naphthoic acid porphyrin), having a carboxyl group that interacts with O₂ bound at the metal center, activates O₂ and then oxidizes itself to the oxaporphyrin cation. Because this reaction did not need coordination of a proximal base, the O₂ activation of this system would be caused by the carboxyl group (pull effect).

We have recently designed a new porphyrin ligand, amtpp, that has an amide group at the ortho-position of a phenyl group of tetraphenylporphyrin (TPP) to mimic the microenvironment created by a distal-polar residue observed in the heme-containing metallocproteins. In a recent report, we have shown that [CoII(amtpp)] (1) converted to new Co(III) complexes bearing an acyclic pentapyrrole-type ligand, lpp, under air in the presence of nitrogen bases (Scheme 1). The structure of lpp is shown in this Scheme.

Scheme 1 Conversion of 1 to [Co III(lpp)(1-Melm)] by reaction with O₂ in the presence of 1-Melm.

We have continued studies on the conversion reaction by using other types of nitrogen bases. Through this work, we have found...
that treatment of 1 with 1,2-dimethylimidazole (1,2-Me2Im) under air yielded a new Co(III) complex 2 bearing a porphodimethene-type ligand, ampord, whose structure is illustrated in Scheme 2. We report herein the new conversion reaction from 1 to 2 by “push–pull” O2 activation, which mimics the initial step of the catalytic reaction by HO.

A chloroform solution of 1 led to a dramatic color change from red to brown in a few hours by addition of 1,2-Me2Im. Diffusion of n-hexane into the solution afforded single crystals of [CoIII(ampord)(OH)(1,2-Me2Im)] (2) in 32% yield after a few days. As byproduct, [Co(amtpp)(1,2-Me2Im)2]Cl was isolated in 28% yield (Scheme S1 in ESI†).

We confirmed that OH– at the Co(III) center and a hydroxyl group at the meso-carbon of 2 come from O2 molecules by 18O2-labeling experiments. Fig. 3 shows the electrospray ionization–time of flight (ESI–TOF) mass spectrum charts of 2 obtained by reaction of 1 with 16O2 or 18O2 in the presence of 1,2-Me2Im. Complex 2 obtained under 18O2 showed an isotope cluster at m/z 844.2, assigned to [H+·OH·2-Me2Im]+, while 2 obtained under 16O2 showed the corresponding isotope cluster at m/z 848.3. The isotope shift clearly shows that both of the OH– and hydroxyl groups in 2 originate from the O2 molecules.

When the reaction was carried out in tetrahydrofuran containing 2,000 equiv of H218O under 16O2, 18O was not incorporated into the obtained 2 (Fig. S12 in the ESI†), showing that the water molecule is not a source of the OH– and hydroxyl group in 2. This result is consistent with the above isotope-labeling experimental results.

Scott and co-workers have reported that porphyrins that have two carboxyl groups near two different meso-carbon atoms that are located in the trans position converted to porphodimethene-type compounds by chemical or electrochemical oxidation.7 The metal ions are not necessary in this conversion system. We characterized the electrochemical behavior of 1 in the presence of 1,2-Me2Im using cyclic voltammetry (CV). The oxidation wave was observed at 1063 mV (vs. SCE), which is extremely positive compared with those of Scott’s compounds (286–516 mV). Moreover, in contrast to the case of Scott’s treatment, 2 did not yield Co(III)-ampord-type compounds (page 18 in the ESI†), whereas 2,3-dichloro-5,6-dicyano-1,4-benzoquinone in MeOH did not yield Co(III)-ampord-type compounds (page 18 in the ESI†).
showing that the formation of 2 from 1 is not the result of the simple oxidation of the amptpp framework by O₂ molecules without O–O bond activation.

The nitrogen base 1,2-Me₂Im has a stronger electron-donating ability than other nitrogen bases that yielded Co(III)-lpp-type complexes by treatment with 1 (Fig. S22 in the ESI†). To examine whether or not the conversion of 1 to 2 is due to the strong electron-donating ability of the axial ligand, we studied the reaction of 1 with 1,5-dicyclohexylimidazole (1,5-Cy₂Im), which has a similar strong electron-donating ability compared with that of 1,2-Me₂Im. Single-crystal X-ray analysis and elemental analysis clearly showed that the reaction product is not a Co(III)-ammp-type complex, but [Co₃(II)-lpp](1,5-Cy₂Im)] (3) (page 5 and Figs. S3-S5 in the ESI†). This result means that the formation of 2 in this system is not due to stronger electron donation from the axial ligand, but would likely be due to the steric effect of the methyl groups of 1,2-Me₂Im.

To obtain insight into the steric effects of the 1,2-Me₂Im on the reactivity of 1 toward O₂, structures of [Co₃(II)-amtp](B) (B = 1-MeIm and 1,2-Me₂Im) were estimated by density functional theory (DFT) calculations at the B3LYP/6-31G* level. Their optimized structures are shown in Fig. S29. For 1-MeIm, although the phenyl group in the position trans to the benzamide bends down slightly, the conjugating porphyrin framework including four meso-carbon atoms remains planar. In contrast, for 1,2-Me₂Im, the porphyrin framework significantly deviates from planarity because of the steric repulsion from the methyl group of 1,2-Me₂Im in the 2-position. The two cis-meso-carbon atoms bend down from the porphyrin plane, while the trans-meso-carbon site bends up from the plane. Selective hydroxylation at the trans-meso-carbon atom induced by 1,2-Me₂Im in this system would be due to the approach of the trans-meso-carbon atom to the activated O₂ species, and the separation of the cis-meso-carbon atom from the activated O₂ species. It is likely that terminal oxygen of the activated O₂ molecule is a source of hydroxyl group which was introduced to the meso-carbon, and the residual oxygen would be the source of OH- for Instrumental Analysis in Shizuoka University for support in obtaining the elemental analysis data.

Notes and references
