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Activation of Water at Active-site Cavity of Zinc Phthalocyanine with Tris(pentafluorophenyl)borane

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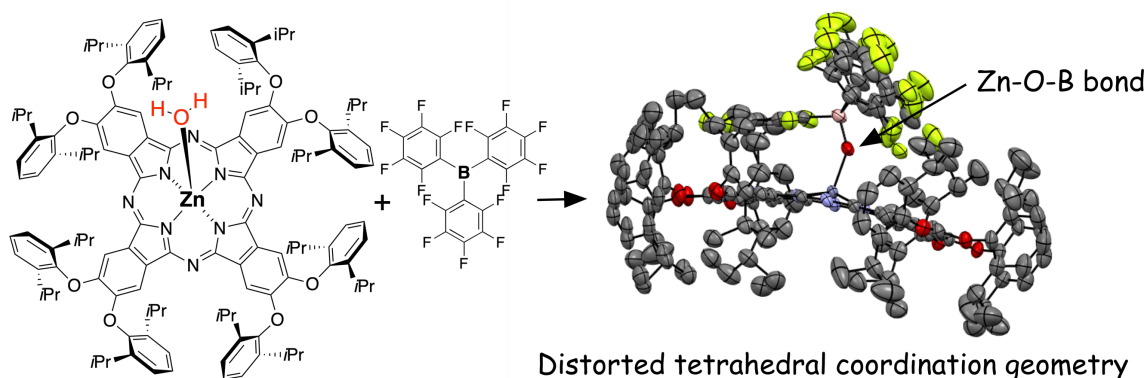
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Keywords: Phthalocyanines, Zn ion, Lewis Acid, Acid-base reaction, Single crystal X-ray structural analysis

Graphical Abstract



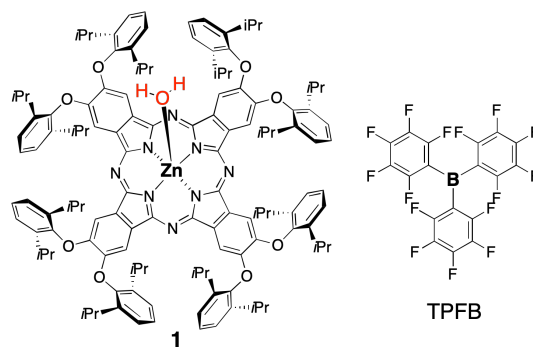
Key Topics: Water activation

TOC Text: Coordination of tris(pentafluorophenyl)borane with water bounded with zinc phthalocyanine results in the dissociation of water, and the dissociated proton from water moves to one nitrogen atom of the phthalocyanine ring through the intramolecular proton transfer.

Abstract: Activation of water bound with Zn^{2+} has attracted much attention as an artificial model of natural enzymes. Despite many attempts, water activation accompanied with a change in the coordination geometry of Zn^{2+} in complexes remains a challenge. In this study, we discover a new structure that is composed of partially protonated zinc phthalocyanine (ZnPc), hydroxide ion, and tris(pentafluorophenyl)borane (TPFB). The coordination of TPFB with water bounded with ZnPc results in the dissociation of water, and the dissociated proton from water moves to one nitrogen atom of the phthalocyanine ring through the intramolecular proton transfer. On the basis of this reaction, the coordination geometry transforms from a five-coordinated to a distorted tetrahedral species. The Zn^{2+} -bound hydroxide nucleophile in the ZnPc-TPFB complex attacks amide of ϵ -caprolactam to produce hydrolyzed 6-aminohexanoic acid in toluene.

Zinc ion (Zn^{2+}) is an essential element for enzymatic activities such as *carbonic anhydrase*, *carboxypeptidase*, *alkaline phosphatase*, β -*lactamase*, and *alcohol*

dehydrogenase.^[1,2] Since Zn^{2+} contains a filled *d* orbital, the Zn^{2+} ion in biological systems does not participate in redox reactions and works as a Lewis acid to accept an electron pair of donor groups of amino acids in proteins and exogenous water. Furthermore, the ligand-field stabilization energy for the Zn^{2+} ion is zero in all metal coordination geometries. The equally accessible coordination geometries of Zn^{2+} can alter reactivity to catalyze chemical transformations accompanied by changes in the geometries. The lack of redox activity, high electron affinity, and flexibility of coordination geometry give Zn^{2+} an important role in catalyzing specific acid-base reactions in biological media. In the active site of *carbonic anhydrase*, the Zn^{2+} ion is coordinated by three imidazole units in peptide and one exchangeable water molecule in a tetrahedral arrangement.^[1] The coordination of Zn^{2+} with neutral imidazole units decreases the pK_a value of the bounded water by about three units as compared with free water, thus creating an optically positioned OH^- nucleophile that makes attacking the carbonyl carbon atom of substrates possible. Artificial models of natural zinc metalloenzymes have been designed to reproduce the molecular recognition and acid-base properties of natural enzymes.^[3] Although the model compounds have exhibited significantly lower catalytic activities than natural enzymes, these models could elucidate the intrinsic chemical roles of Zn^{2+} . In this study, we found a change in the coordination geometries of zinc phthalocyanine (ZnPc) complexes caused by the activation of water molecules bounded to the central Zn^{2+} of ZnPc.



ZnPcs have been widely studied as photosensitizers for the photochemical production of $^1\Delta_g \text{O}_2$ from O_2 ^[4-6] as well as for the dye-sensitized solar cells^[7,8]; however, there have been no reports on the reactivity of water molecules bounded to the central Zn^{2+} in ZnPcs so far. The axial coordination of donor solvents such as acetone and water was confirmed by the single-crystal X-ray structural characterization of two ZnPcs having bulky peripheral substituents.^[9,10] Bench et al. reported the stable ligation of two acetone

molecules with Zn^{2+} in ZnPc bearing bulky perfluoro(isopropyl) units at the peripheral positions of the phthalocyanine ring.^[9] McKeown et al. succeeded in preparing crystalline nanoporous materials composed of steric-crowded zinc 2,3,9,10,16,17,23,24-octa(2,6-diisopropylphenoxy)phthalocyanine **1** with the axial water molecules.^[10] The introduction of bulky substituents around these ZnPcs could prevent the formation of densely packed cofacial aggregates among ZnPcs and create nanoscopic cavities above and below the phthalocyanine plane. The O atom of solvent molecules was coordinated with Zn^{2+} within the cavities of ZnPcs.

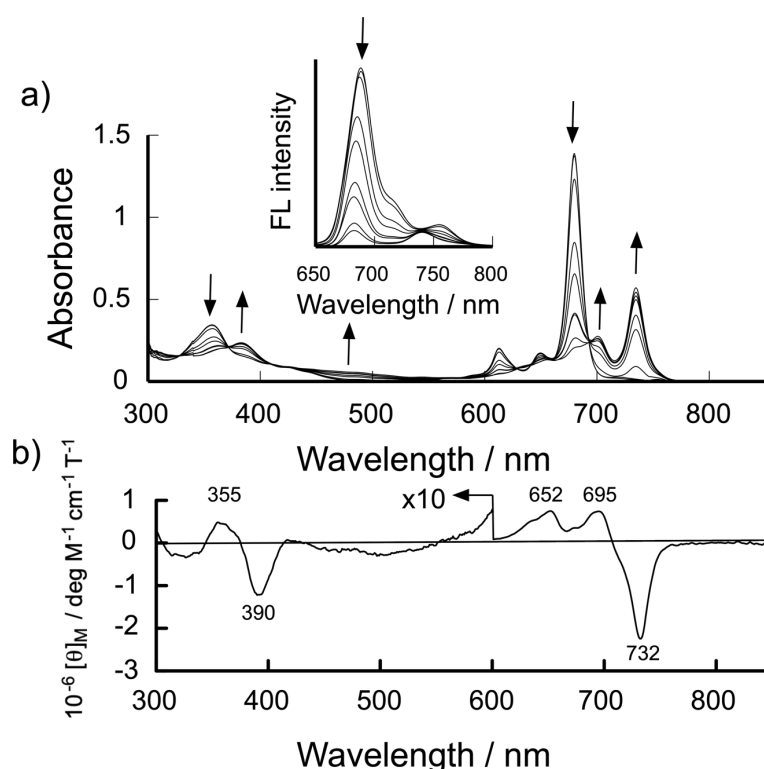


Figure 1. a) Absorption and fluorescence (inset) spectral changes of **1** ($[1] = 5.0 \mu\text{M}$) by titration with TPFB ($[TPFB] = 0-9.0 \mu\text{M}$) in toluene at room temperature. b) MCD spectra of the mixed toluene solution of **1** ($[1] = 5.0 \mu\text{M}$) with TPFB ($[TPFB] = 7.5 \mu\text{M}$).

First, we checked the reactivity of water bounded to **1** with the addition of tris(pentafluorophenyl)borane (TPFB). TPFB has been used as a strong Lewis acidic cocatalyst in various reactions.^[11-13] Here, TPFB was chosen as the additional receptor for electron pairing with O atom in the coordinated water. Figure 1a shows the UV-Vis absorption and fluorescence spectral changes of **1** in toluene due to the addition of TPFB. The gradual addition of TPFB to the **1** solution generated an isosbestic spectral change (Figure 1a), and caused a decrease in the Q band at 680 nm together with a rise of a new

absorption band at 735 nm. The fluorescence at 688 nm was quenched by the addition of TPFB as shown in the inset of Figure 1a. In contrast, a metal free Pc and cobalt (II) complex having the same peripheral units showed no spectral changes in the same concentration range of TPFB (Figure S1). TPFB can also interact with nitrogen (N) atoms through the formation of a strong B-N bond^[14,15], however, the eight N atoms in the Pc ring do not form a bond with TPFB. These spectral changes suggest the interaction of water bounded to the ZnPc core in **1** with TPFB. While single Faraday *A*-term signals of magnetic circular dichroism (MCD) for **1** were observed at 675 and 685 nm in correspondence with the Q band position (Figure S2)^[16], these signals disappeared and a new trough was observed at 732 nm by the addition of TPFB (Figure 1b). Since the peak position at the trough in the MCD spectrum almost agrees with that of the new absorption peak, the observed MCD signal of **1** with TPFB is assigned to be a Faraday *B* term. This indicates a break in the degeneracy of the LUMO and LUMO+1 energy levels.

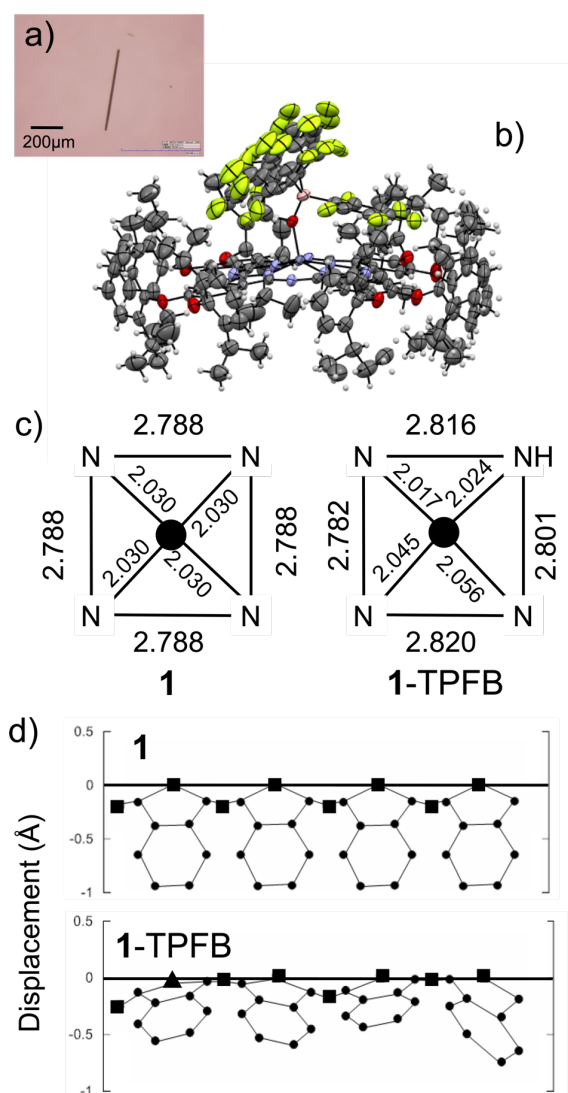


Figure 2. a) Needle crystal of **1**-TPFB complex formed by slow diffusion of n-hexane into a CHCl_3 solution. b) Molecular structures of **1**-TPFB complex with thermal ellipsoid set at 50% probability level. c) Bond lengths (Å) for **1** and **1**-TPFB complex. d) Derivations from planarity made of 4N or 3N-plain for C and N atoms of **1** and **1**-TPFB complex. ●, ■, and ▲ indicate C, N, and NH, respectively.

To obtain the direct structural information on the complex of **1** with TPFB, we conducted a single-crystal X-ray structural analysis. McKeown et al. succeeded in obtaining large cubic crystals of **1** through a slow crystallization with the diffusion of acetone into a CHCl_3 solution of **1**.^[10] However, the UV-Vis absorption spectrum of **1** with TPFB returned to that of only **1** during the diffusion of acetone, suggesting the dissociation of complex by acetone. We changed poor solvent from acetone to n-hexane for the crystal growth of **1** with TPFB. Large crystals with a cubic morphology were

obtained by the crystallization from a CHCl_3 solution of **1** by diffusing n-hexane, and the molecular packing arrangement of **1** in the single crystal [$Pn3n$ space group with 12 molecules of **1** in the unit cell ($a = 3.76$ nm)] agreed with the reported structure.^[10] The presence of an axial O atom coordinated with the central Zn in the cone-shaped phthalocyanine core of **1** was also confirmed (Figure S3). The crystal morphology was changed from a cube to a needle by the addition of TPFB, implying the formation of a different molecular packing arrangement (Figure 2a). The crystal structure is monoclinic and belongs to the $P2_1/n$ space group with four molecules in the unit cell ($a = 2.44$ nm, $b = 1.64$ nm, $c = 3.84$ nm, $\beta = 96.5^\circ$) (Figure S4).

The X-ray structure of the **1**-TPFB complex reveals the attachment of the B atom in TPFB to the O atom coordinated with the Zn of **1**, indicating the formation of a Zn-O-B bond (Figure 2b)^[17]. Interestingly, the dissociated proton from water moves to one N atom of the inside four N atoms of the phthalocyanine ring and the OH^- nucleophile is produced on the basis of this intramolecular proton transfer. Figure 2c shows the distances of Zn-N bonds in the **1**-TPFB complex. Whereas the distances of the Zn-N bonds in **1** are completely the same (2.030 Å), the four Zn-N distances in the **1**-TPFB complex are different and the position of Zn^{2+} atom in the Pc ring approaches to the N atom at the upper left. Moreover, the change in Zn-N bond lengths due to TPFB leads to the skeletal deformation of the Pc ring as shown in Figure 2d.^[18] ^1H NMR spectral analysis of the **1**-TPFB complex in toluene- d_8 was carried out at room temperature to obtain the structural information (Figure S5). All proton resonances in the aromatic region and -CH in isopropyl units shifted upfield compared with **1**, revealing the shielding effect of TPFB on the Pc ring. The appearance of a broad signal around -1.2 ppm supported the protonation of an internal N atom in the Pc ring as observed in the single-crystal X-ray structural analysis. The proton signal corresponding to - CH_3 in the peripheral isopropyl units was split into two peaks at 1.2 and 1.4 ppm for the **1**-TPFB complex. One pentafluorobenzene unit in the TPFB for the crystal structure of the **1**-TPFB complex was located near several peripheral isopropyl units lying out of plain of the Pc ring. The hydrogen bonding between the fluoride of TPFB and protons of the isopropyl units may result in the creation of two different proton resonances. Thus, the metal coordination geometry of **1** transforms from a five-coordinated specie to a distorted tetrahedral specie with the Zn^{2+} ion coordinating with three N atoms in the Pc ring and one O atom by bonding of TPFB with an axial water molecule. The observed geometry of the **1**-TPFB

complex resembles the binding geometry in the active center of natural zinc metalloenzymes. As far as we know, this is the first report on the dynamic transformation of metal coordination geometries in ZnPcs.

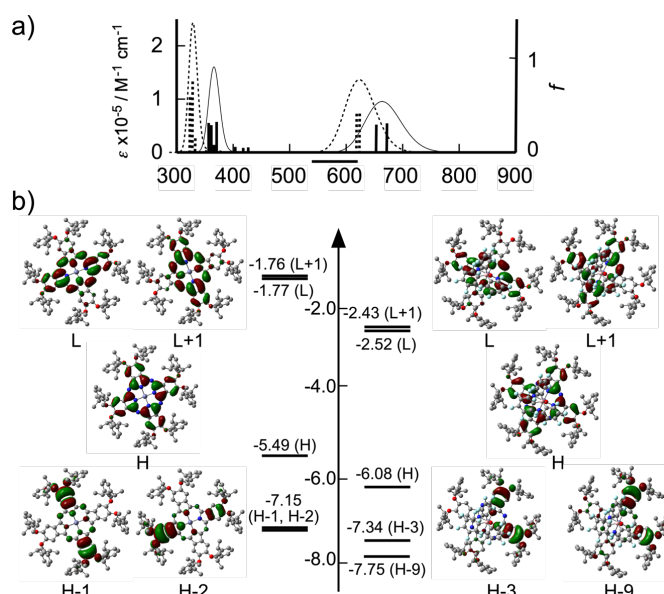


Figure 3. a) Calculated UV-Vis absorption spectra of **1** (dashed line) and **1-TPFB** complex (solid line). b) Calculated energy diagrams and selected molecular orbitals of **1** (left) and **1-TPFB** complex (right).

Table 1 Calculated transition energies, oscillator strengths f , and configurations of **1-TPFB** complex.

Energy / eV (nm)	f	Configurations (Main percentage contribution)
1.84 (672)	0.38	H→L (94%)
1.89 (654)	0.36	H→L+1(91%)
3.35 (370)	0.40	H-3→L (39%), H-4→L (35%)
3.39 (366)	0.35	H-4→L+1 (38%), H-1→L (22%)
3.42 (363)	0.38	H-9→L (22%), H-4→L+1 (16%)

Density functional theory (DFT) calculations at the CAM-B3LYP/6-31G* level (Gaussian 16^[19]) were carried out for the **1** and **1-TPFB** complex using the results of the single-crystal X-ray diffraction analysis to enhance our understanding of the spectroscopic data. The trends in the absorption spectral differences between the **1** and **1-TPFB** complex calculated by time-dependence DFT were in fair agreement with the trends in the absorption spectral change of the experiment (Figure 3a). The calculated Q bands of **1** were red-shifted and splitted into two peaks due to bonding with the TPFB. In Table 1, the configurations for each calculated peak are summarized so as to clarify the origin of the spectral features. The split Q bands in the **1-TPFB** complex can be assigned

to the HOMO→LUMO and HOMO→LUMO+1 transitions of the macrocycles. The Faraday *B* term observed in the MCD spectrum of the **1**-TPFB complex also supports the splitting of the degenerated LUMO and LUMO+1 energy levels of **1** by bonding with TPFB.^[16] The absorption band at 370 nm (HOMO-3→LUMO HOMO-4→LUMO) is assignable to the Soret band. Figure 3b shows a calculated energy diagram of the **1** and **1**-TPFB complex and the frontier orbitals of HOMO-1 (HOMO-3 and HOMO-4 for **1**-TPFB complex), HOMO, LUMO, and LUMO+1. Both of the calculated energy levels of HOMO and LUMO for the **1**-TPFB complex were lower than those for **1**, and the calculated HOMO-LUMO band gap of the **1**-TPFB complex was narrower than that of **1**. Therefore, it is inferred that the coordination of TPFB with the O atom on ZnPc caused both the HOMO and LUMO energy levels to stabilize, which lead to a narrowing of the HOMO-LUMO band gap as well as the degeneracy breaking of the LUMO and LUMO+1 energy levels. Whereas the HOMO frontier orbitals of **1** are located homogeneously over the Pc ring, the HOMO and LUMO+1 orbitals in the **1**-TPFB complex delocalize at the side of the three coordinated N atoms in the distorted tetrahedral geometry.

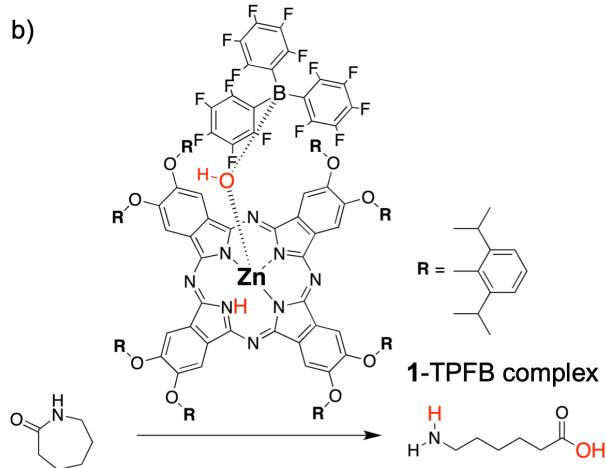
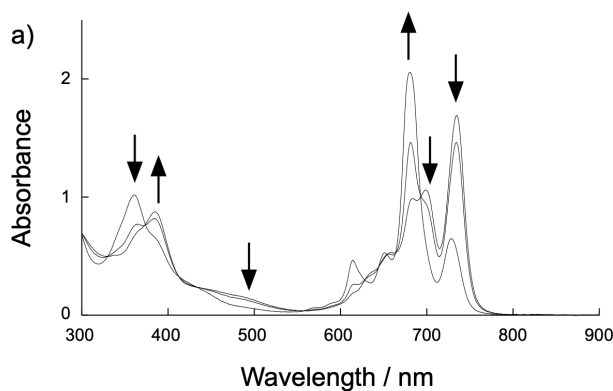


Figure 4. a) UV-Vis absorption spectral change of **1**-TPFB complex by the addition of ϵ -caprolactam. [**1**] = 5.0 μ M; [TPFB] = 5.0 μ M, [ϵ -caprolactam] = 0, 5.0, and 20.0 μ M. b) Reaction scheme for hydrolysis of ϵ -caprolactam by **1**-TPFB complex.

We investigated the reactivity of Zn^{2+} -bound OH^- nucleophile generated by the activation of water molecule. Figure 4a shows the absorption spectral change of the **1**-TPFB complex in toluene with increasing the concentrations of ϵ -caprolactam at room temperature. When an ϵ -caprolactam solution was admixed with the toluene solution of the **1**-TPFB complex^[20], a sharp Q band peak appeared at 680 nm (Figure 4a), and hydrolyzed 6-aminohexanoic acid was formed as confirmed by electrospray ionization time-of-flight mass (ESI-TOF-MS) spectroscopic analysis. In contrast, the absorption spectral change and the formation of 6-aminohexanoic acid were observed for the mixed solution of **1** and ϵ -caprolactam without TPFB. This result suggests that the coordinated OH^- in the **1**-TPFB complex can attack to the carbonyl carbon atom of ϵ -caprolactam while changing the metal coordination geometry of ZnPc (Figure 4b).

In summary, our results provide a new approach to causing the tetrahedral geometry of ZnPc to be distorted as observed at the active-sites in natural enzymes. According to a single-crystal X-ray structural analysis of the **1**-TPFB complex, the central Zn^{2+} coordinated with three N atoms in the Pc ring and one OH^- within the cavity of **1**, and a proton dissociated from water was transferred to the remaining N atom in the inside of the Pc ring simultaneously. We found that the hydrolysis of amide in cyclic ϵ -caprolactam was caused by the amide being attacked by a Zn^{2+} -bound OH^- nucleophile in the **1**-TPFB complex in toluene. The flexibility of the coordination geometry in ZnPc can open new reactions on the basis of the activation of water molecules within the hydrophobic cavity around ZnPc. Studies are in progress on the design of the hydrophobic cavity in water-soluble ZnPc to create high local concentrations of OH^- as nucleophiles under neutral aqueous conditions.

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[20] ϵ -Caprolactam (61 μg , 0.54 μmol) was added to the mixed toluene solution (1.5 ml) of **1** (1.0 mg, 0.54 μmol) and TPFB (410 μg , 0.80 μmol) at room temperature. After 5 min, the ESI-TOF mass spectrum of the mixed solution diluted with acetonitrile was obtained to monitor the hydrolysis of ϵ -caprolactam (the peak at $m/z = 132.1019$ corresponding to 6-aminohexanoic acid).