Novel Phosphate–Phosphate Bond Formation Mediated upon Cobalt(III) Complex Systems

Yasuhiro Funahashi, Atsuro Yoneda, Chiyoe Taki, Miwa Kosuge, Tomohiro Ozawa, Koichiro Jitsukawa, and Hideki Masuda*

Department of Applied Chemistry, Graduate School of Engineering, Nagoya Institute of Technology, Gokiso-cho, Showa-ku, Nagoya 466-8555

(Received July 4, 2005; CL-050858)

In an aqueous solution (pH 3) containing active charcoal as a solid phase, reaction of $[Co^{III}(tpa)(CO_3)]^+$(**1**) (tpa = tris(2-pyridylmethyl)amine) and 2 equiv. of an active phosphate ester, disodium 4-nitrophenylphosphate (NPP), at 60 °C gave $[Co^{III}(tpa)(PO_4)]$ (**2**) (8% yield) and $[\{Co^{III}(tpa)\}_2(\mu\text{-}P_2O_7)]^{2+}$ (**3**) (51% yield) as isolated products. The X-ray crystal structure of main product **3** revealed that an NPP-derived diphosphate bridged to the dinuclear Co(III) centers. The diphosphate formation was not detected without active charcoal or under neutral pH condition.

There has been much effort of biomimetic model studies[1a–1c] for understanding the role of metal ions accelerating hydrolysis of phosphate esters in phosphatase. In spite of the biological importance, there are few examples of the phosphate–phosphate bond formation assisted by metal ions.[1d] In this report, we describe a novel phosphate–phosphate bond formation mediated on a Co(III) complex system in the presence of a phosphate ester in an acidic aqueous solution containing active charcoal as a solid phase.

The Co(III) carbonato complex, $[Co^{III}(tpa)(CO_3)]^+$ (**1**)[2,3] (tpa = tris(2-pyridylmethyl)amine) and 2 equiv. of disodium 4-nitrophenylphosphate (NPP) were mixed in water at pH 3. To the mixed solution was added an approximate amount of active charcoal,[4] which was then stirred for 7 h at 60 °C. After that, the solution pH was neutralized and the products were purified by column chromatography with cation-exchange resin, giving $[Co^{III}(tpa)(PO_4)]$ (**2**) (8% yield) and $[\{Co^{III}(tpa)\}_2(\mu\text{-}P_2O_7)]^{2+}$ (**3**) (51% yield).[3–6]

Recrystallization of neutral complex **2** and the perchlorate salt of **3** in methanol/diethylether gave both red crystals for **2** and **3**·$(ClO_4)_2$. The structures of these Co(III) complexes were determined by X-ray diffraction analyses as shown in Figures 1a and 1b for complexes **2** and **3**, respectively. In the molecular structure of **2**, bidentate phosphate and tetradentate tpa ligands are coordinated to the mononuclear Co(III) ion (Figure 1a). The Co–phosphate bond distances in **2** (Co–O(1) = 1.898(3) and Co–O(2) = 1.911(4) Å) are significantly shorter than those in $[Co^{III}(en)_2(PO_4)]$ (en = ethylenediamine) (Co–O = 1.927(4)–1.948(3) Å),[8] implying that the aromatic pyridine ligands of tpa may induce a higher affinity of the phosphate to the Co(III) center than aliphatic amine ligands of en. Surprisingly, the molecular structure of **3** clearly showed that a diphosphate-bridged dimer complex has been formed as a result of a novel reaction involving phosphate bond formation (Figure 1b). The diphosphate molecule coordinates with each Co(III) center as a bidentate ligand. The unit cell contains two independent structures of **3**. The tendency of Co–phosphate bond distances in mononuclear Co(III) complexes can be adapted for those in

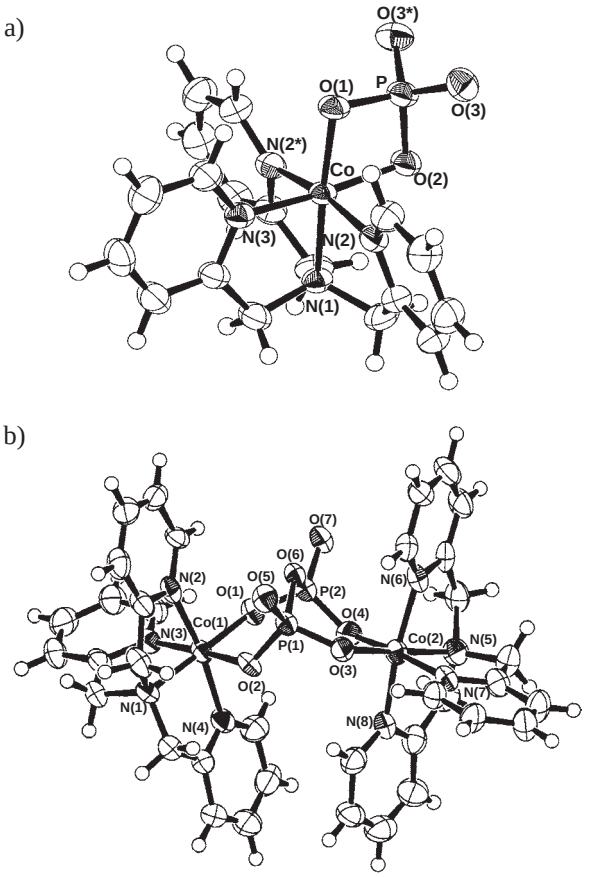

Figure 1. Molecular structures of a) **2** and b) **3** with thermal ellipsoids drawn at the 50% probability.

dinuclear Co(III) complexes. In the molecular structures of **3**, the bond distances between Co(III) ion and diphosphate oxygen atoms (Co(1)–O(1) = 1.895(5) and 1.900(5), Co(1)–O(2) = 1.901(4) and 1.918(4), Co(2)–O(3) = 1.909(5) and 1.912(5), and Co(2)–O(4) = 1.915(4) and 1.904(4) Å) are remarkably shorter than those of dinuclear Co(III)–monophosphate complexes with aliphatic ligands, $\{[Co^{III}(en)_2(\mu\text{-}O_3POC_6H_5)]_2\}^{2+}$ (Co–O = 1.922(5)–1.956(5) Å),[9a] $[\{Co^{III}([9]aneN_3)\}_2(OH)_2(\mu\text{-}O_2P(OCH_3)_2)]^{3+}$ ([9]aneN3 = 1,4,7-triazacyclononane) (Co–O = 1.935(6) Å),[9b] and $[\{Co^{III}(trpn)\}_2(\mu\text{-}PO_4)]^{3+}$ (trpn = tris(aminopropyl)amine (Co–O = 1.950(6)–1.980(9) Å),[9c] and are equal to those of a dinuclear Co(III)–monophosphate complex with aromatic pyridine ligands (Co–O = 1.890(5)–1.904(5) Å for $[Co^{III}_2(bpmp)(\mu\text{-}O_3POC_6H_5)(H_2O)(OH)]^{2+}$ (bpmp = 2,6-bis[{bis(2-pyridylmethyl)amino}methyl]-4-methylphenolate).[9d] The weaker electron-donating aromatic ligands like tpa than those of aliphatic amine ligands may increase a

Lewis acidity and affinity of the Co(III) center for the diphosphate ligand, stabilizing the dimer structure of **3**. In the molecular structures of **3**, π–π stacking interactions were also observed between two tpa-derived pyridine rings with an average intramolecular distance of 3.84 Å. Such an intermolecular interaction between ligands would promote dimerization of Co(III) complexes in the formation of **3**.

In order to investigate the reaction requirements for the phosphate bond formation carried out on the Co(III)–tpa complex system,[3,4] the reaction products were quantified under partly changing the conditions. First, the reaction was stopped at an adequate time, and the time course of accumulation of main product **3** was estimated. The yields of **3** changed to 6% after 1 h, 26% after 3 h, and 46% after 5 h, respectively. The formation of product **3** was completely saturated in 5 h. The formation of this Co(III) diphosphate complex **3** was so slow, because Co(III) complex is substitutionally inert. Secondary, an increase of pH values causes the yield of **3** to decrease in the order; 51% yield (pH 3) >20% yield (pH 5) ≈0% yield (pH 7). The yield of **3** at pH 7 is essentially negligible. Generally, neutral pH is suitable for hydrolysis of phosphate compounds catalyzed by Co(III) complexes.[10] Such an acidic condition (pH 3) in this reaction is supposed to prevent OH^- formation and hydrolysis of diphosphate. The reaction of **1** and Na_3PO_4 under the same conditions in presence of active charcoal[3,4] produces monophosphate complex **2** (42% yield) with no yield of diphosphate complex **3**. Therefore, the active phosphate ester, NPP, is required for the diphosphate formation. Finally, in the absence of active charcoal, increase of $H_2PO_4^-$ as only one product for hydrolysis of NPP was detected by using ^{31}P NMR under the acidic conditions (pH 3). In this case, the Co(III)–phosphate complexes **2** and **3** were not detected (≈0% yield). These facts indicate that the additional active charcoal is essential for the phosphate bond formation on the Co(III)–tpa complex system. When traced by ^{31}P NMR spectra, about 30% of 1 equiv. of NPP was adsorbed by the active charcoal, and addition of $[Co^{III}(tpa)(CO_3)]^+$(**1**) decreased the residual NPP in the solution until less than about 20%, indicating that the cation **1** and the NPP anion were simultaneously adsorbed on the active charcoal. Accumulation rate of diphosphate product **3** was independent on the NPP concentration, and not changed in both of 1 equiv. and 2 equiv. of NPP used, suggesting that concentrations of the reactants were kept proportional and constant on the active charcoal.

Taking account of the above experimental results, we can describe the following essential factors for formation of dicobalt(III) diphosphate complex **3**: i) a part of NPP must be hydrolyzed, ii) the reaction intermediate is possibly a dinuclear complex or a pair of two Co(III) complexes, and iii) in the intermediate complexes, an inorganic phosphate is supposed to have attacked the active NPP with elimination of a good leaving group, *p*-nitrophenol. The mechanisms ii) and iii) were postulated on the basis of the molecular structure of the major product **3**, which contains essential information about prior reaction intermediate, because such cobalt(III) complexes are substitutionally inert. Further studies for the reaction between dicobalt(III) monophosphate complex and NPP are in progress.

References and Notes

1 a) N. H. Williams, B. Takasaki, M. Wall, and J. Chin, *Acc. Chem. Res.*, **32**, 485 (1999). b) E. Kimura, *Curr. Opin. Chem. Biol.*, **4**, 207 (2000). c) G. Parkin, *Chem. Rev.*, **104**, 699 (2004). d) A. Vieyra, J. R. Meyer-Fernandes, and O. B. H. Gama, *Arch. Biochem. Biophys.*, **238**, 574 (1985).

2 **1**: The ligand tpa was synthesized by the reported procedure.[7] **1** was prepared by reaction of $Na_3[Co^{III}(CO_3)_3]$ and tpa in EtOH/H_2O (1/1) at 40 °C overnight. The reaction mixture was purified by the column chromatography, and recrystallization in CH_3OH gave pure products as pale-red powder (25% yield). Elemental Anal. Calcd for **1**·Cl·1.5H_2O ($C_{19}H_{21}N_4O_{4.5}ClCo$): C, 48.37; H, 4.49; N, 11.88%. Found: C, 48.14; H, 4.60; N, 11.54%.

3 Chromatographic purification of products was carried out using Sp-Sephadex C25 cation-exchange resin.

4 Reaction of **1** and NPP with active charcoal at pH 3 in water: To a 50 mL solution of **1**·Cl·1.5H_2O (0.19 g, 0.40 mmol) was added a 10 mL solution of disodium 4-nitrophenylphosphate (NPP) (0.30 g, 0.81 mmol). The mixed solution was adjusted to pH 3 with small amount of 0.1 M (1 M = 1 mol dm^{-3}) NaOH solution. After heating to 60 °C, a catalytic amount of active charcoal (0.10 g) was added to the mixture, which was stirred at 60 °C for 7 h.

5 **2**: ^{1}H NMR (D_2O, DSS) δ/ppm 4.99 (d, J = 15.6 Hz, 2H), 5.07 (s, 2H), 5.32 (d, J = 15.6 Hz, 2H), 7.23 (d, J = 7.9 Hz, 1H), 7.52 (dd, $J = J'$ = 6.5 Hz, 2H), 7.61 (dd, $J = J'$ = 7.8 Hz, 1H), 7.63 (d, J = 7.9 Hz, 2H), 7.84 (dd, $J = J'$ = 7.2 Hz, 1H), 8.01 (dd, $J = J'$ = 7.3 Hz, 2H), 8.58 (broad, 2H), 8.89 (broad, 1H); ^{31}P NMR (D_2O, Na_3PO_4) δ/ppm = 18 (s); ESI mass: m/z = 445.2 amu for $[\mathbf{2} + H^+]^+$.

6 **3**: ^{1}H NMR (D_2O, DSS) δ 4.58 (d, J = 15.2 Hz, 2H), 4.69 (d, J = 15.4 Hz, 2H), 4.98 (s, 2H), 4.99 (s, 2H), 5.33 (d, J = 15.2 Hz, 2H), 5.43 (d, J = 15.2 Hz, 2H), 7.07 (d, J = 8.2 Hz, 2H), 7.08 (dd, $J = J'$ = 7.8 Hz, 2H), 7.41 (d, J = 6.7 Hz, 2H), 7.49 (d, J = 7.7 Hz, 2H), 7.58 (dd, $J = J'$ = 6.4 Hz, 2H), 7.71 (d, J = 7.8 Hz, 2H), 7.76 (dd, $J = J'$ = 7.3 Hz, 2H), 8.09 (dd, $J = J'$ = 7.7 Hz, 2H), 8.36 (d, J = 4.8 Hz, 2H), 8.61 (d, J = 5.2 Hz, 2H), 8.64 (d, J = 5.3 Hz, 2H); ^{31}P NMR (D_2O, Na_3PO_4) δ/ppm = 11 (s); ESI mass: m/z = 436.2 amu for $[\{Co^{III}(tpa)\}_2(\mu\text{-}P_2O_7)]^{2+}$ (**3**).

7 Z. Tyeklár, R. R. Jacobson, N. Wei, N. N. Murthy, J. Zubieta, and K. D. Karlin, *J. Am. Chem. Soc.*, **115**, 2677 (1993).

8 B. Anderson, R. M. Milburn, J. M. Harrowfield, G. B. Robertson, and A. M. Sargeson, *J. Am. Chem. Soc.*, **99**, 2652 (1977).

9 a) D. R. Jones, L. F. Lindoy, A. M. Sargeson, and M. R. Snow, *Inorg. Chem.*, **21**, 4155 (1982). b) D. Wahnon, A.-M. Lebuis, and J. Chin, *Angew. Chem., Int. Ed. Engl.*, **34**, 2412 (1995). c) J. A. Connolly, M. Banaszczyk, R. C. Hynes, and J. Chin, *Inorg. Chem.*, **33**, 665 (1994). d) J. S. Seo, N.-D. Sung, R. C. Hynes, and J. Chin, *Inorg. Chem.*, **35**, 7472 (1996).

10 J. Chin, M. Banaszczyk, V. Jubian, and X. Zou, *J. Am. Chem. Soc.*, **111**, 186 (1989).

11 X-ray crystal structure analyses: The diffraction data were collected on a Rigaku R-AXIS-IV imaging plate area detector using a graphite monochromated Mo Kα radiation at room temperature. Crystal data of **2**·2CH_3OH·2H_2O ($C_{20}H_{30}N_4O_8PCo$): orthorhombic, space group *Pnma*, a = 15.468(2) Å, b = 15.406(2) Å, c = 9.831(3) Å, V = 2342 Å^3, Z = 4, μ = 8.54 cm^{-1}, D_{calcd} = 1.543 g/cm^3. For **3**·$(ClO_4)_2$·2.5CH_3OH·2.5H_2O ($C_{77}H_{102}N_{16}O_{40}P_4Cl_4Co_4$): triclinic, space group $P\bar{1}$, a = 17.574(4) Å, b = 22.035(2) Å, c = 14.205(2) Å, α = 92.24(1)°, β = 103.48(1)°, γ = 110.82(1)°, V = 4996 Å^3, Z = 4, μ = 9.19 cm^{-1}, D_{calcd} = 1.591 g/cm^3. Full-matrix least-squares refinement on F converged to R = 0.048, R_w = 0.064 based on 1568 independent reflections ($I > 3\sigma(I)$) and 173 variables for **2**·2CH_3OH·2H_2O and R = 0.074, R_w = 0.107 based on 9740 independent reflections ($I > 3\sigma(I)$) and 1307 variables for **3**·$(ClO_4)_2$·2.5CH_3OH·2.5H_2O. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication Nos. CCDC-164882(2) and CCDC-164883(3).

Published on the web (Advance View) September 3, 2005; DOI 10.1246/cl.2005.1332