Electronic Supporting Information

Mechanistic Insight into Hydroxamate Transfer Reaction

Mimicking the Inhibition of Zinc-Containing Enzymes

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Experimental Section

Materials. All chemicals obtained from Aldrich Chemical Co. were the best available purity and used without further purification unless otherwise indicated. The solvents acetonitrile (CH$_3$CN) and diethyl ether (Et$_2$O) were passed through solvent purification columns (JC Meyer Solvent Systems) prior to use. The $N,N'$-di-tert-butyl-2,11-diaza[3.3][2,6]-pyridinophane (TBDAP) ligand was prepared by reacting 2,6-bis(chloromethyl)pyridine with 2,6-bis[$(N$-tert-butylamino)methyl]-pyridine at 80 °C as reported previously.$^{S1}$ [Co(TBDAP)(NO$_3$)(H$_2$O)](NO$_3$) and [Co(TBDAP)(CH$_3$C(=NO)O)](NO$_3$)(H$_2$O) (2-NO$_3$·H$_2$O) were prepared according to literature method.$^{S2}$ Human matrix metalloproteinase-9 (MMP-9) full-length protein and 4-aminophenylmercuric acetate (APMA) were purchased from Abcam (Cambridge, UK) and used without further purification. Two peptides, PLGMWSR and HH, were obtained from Anygen Co. Ltd. (Gwangju, Korea).

Instrumentation. UV-vis spectra were recorded on a Hewlett Packard 8454 diode array spectrophotometer equipped with a UNISOKU Scientific Instruments for low-temperature experiments or with a circulating water bath. Electrospray ionization mass (ESI-MS) spectra were collected on a Waters (Milford, MA, USA) Acquity SQD quadrupole Mass instrument, by infusing samples directly into the source using a manual method. The spray voltage was set at 2.5 kV and the capillary temperature at 80 °C. Infrared spectra were recorded on a Thermo Scientific Nicolet iS10 FT-IR spectrometer equipped with a diamond attenuated total reflectance (ATR) accessory. $^1$H NMR spectra were measured with Bruker AVANCE III-400 spectrometer at CCRF in DGIST. The crystallographic analysis was conducted with a SMART APEX II CCD equipped with a Mo X-ray tube at CCRF in DGIST. Mass spectrometric analyses for analyzing %inhibition against MMP-9 were performed by an Agilent 6530 Accurate Mass Quadrupole Time-of-Flight (Q-TOF) mass
spectrometer (Agilent Technologies, Santa Clara, USA) equipped with the ESI source, operating in the positive ion mode. The capillary voltage, drying gas flow, and the gas temperature were set to 5.8 kV, 12 L/min, and 300 °C, respectively. The fragmentor voltage was set to 170 V.

**Synthesis of [Co(TBDAP)(CH$_3$C(-NHO)O)](NO$_3$) (1-NO$_3$).** 1 was prepared by reacting [Co(TBDAP)(NO$_3$)(H$_2$O)](NO$_3$) (0.0278 g, 0.050 mmol) and acetohydroxamic acid (0.0038 g, 0.050 mmol) with 2 equiv of TEA in CH$_3$CN (10 mL). The mixture was stirred for 6 h at ambient temperature, resulting that the color was changed from pink to orange. The resulting solution was dried in a vacuo and then, washed with Et$_2$O (40 mL). X-ray crystallographically suitable crystals were obtained by slow diffusion of Et$_2$O into a solution of the complex in CH$_3$CN. Crystalline yield: 94% (0.0257 g). UV-vis in CH$_3$CN: $\lambda_{\text{max}}$ ($\varepsilon$) = 361 nm (1900 M$^{-1}$ cm$^{-1}$), 468 nm (100 M$^{-1}$ cm$^{-1}$). ESI-MS in CH$_3$CN (see Figure S1): $m/z$ 485.33 for [Co(TBDAP)(CH$_3$C(-NHO)O)]$^+$. FT-IR (ATR) (see Figure S2): 3207 cm$^{-1}$ (w, N-H). $\mu_{\text{eff}}$ = 4.41 B.M. Anal. Calcd for C$_{24}$H$_{36}$CoN$_6$O$_5$: C, 52.65; H, 6.63; N, 15.35. Found: C, 52.12; H, 6.53; N, 15.33.

**Synthesis of [Zn(Me$_3$-TACN)(NO$_3$)](NO$_3$)(H$_2$O) (3-NO$_3$$\cdot$H$_2$O).** 3 was synthesized according to a modified literature method.$^{53}$ 3 was prepared by reacting Zn(NO$_3$)$_2$·6H$_2$O (0.348 g, 1.17 mmol) and Me$_3$-TACN (0.200 g, 1.17 mmol) in ethanol (15 mL). The mixture was gently heated with stirring for 6 h, giving a colorless solution. Et$_2$O (40 mL) was added to the resulting solution to yield a white powder, which was collected by filtration, washed with Et$_2$O, and dried in a vacuo. The colorless crystals were obtained by slow diffusion of Et$_2$O into a solution of the complex in CH$_3$CN. Crystalline yield: 58%
(0.2570 g). ESI-MS in CH$_3$CN (see Figure S9): $m/z$ 297.2 for [Zn(Me$_3$-TACN)(NO$_3$)]$^+$. Anal. Calcd for C$_9$H$_{23}$N$_5$O$_7$Zn: C, 28.54; H, 6.12; N, 18.49. Found: C, 28.62; H, 6.17; N, 18.70.

**Synthesis of [Zn(Me$_3$-TACN)(CH$_3$C(-NHO)O)(CH$_3$OH)](BPh$_4$) (4-CH$_3$OH-BPh$_4$).** 4 was synthesized by reacting 3 (0.0189 g, 0.050 mmol) and acetohydroxamic acid (0.0152 g, 0.20 mmol) with 8 equiv of TEA in CH$_3$CN (10 mL). The mixture was stirred for 6 h, giving a colorless solution. Et$_2$O (40 mL) was added to the resulting solution to yield a white powder, which was collected by filtration, washed with Et$_2$O, and dried in a vacuo. X-ray crystallographically suitable crystals of 4-CH$_3$OH-BPh$_4$ were obtained by slow diffusion of Et$_2$O into a CH$_3$OH solution of the white product in the presence of NaBPh$_4$ (0.0170 g). Crystalline yield: 32% (0.0107 g). ESI-MS in CH$_3$CN (see Figure S10): $m/z$ 309.4 for [Zn(Me$_3$-TACN)(CH$_3$C(-NHO)O)]$^+$. Anal. Calcd for C$_{36}$H$_{49}$BN$_4$O$_3$Zn: C, 65.31; H, 7.46; N, 8.46. Found: C, 65.14; H, 7.15; N, 8.55.

**Synthesis of [Co(TBDAP)(CH$_3$C(-NHO)O)](NO$_3$)(ClO$_4$)(H$_2$O) (5-NO$_3$·ClO$_4$·H$_2$O).** 5 was prepared by adding 1 equiv of HClO$_4$ to the solution of 2 (0.0282 g, 0.050 mmol) in CH$_3$CN (1.5 mL), resulting in the generation of a pale green solution at –40 °C. Et$_2$O (40 mL) was added to the resulting solution to yield a pale green powder, which was washed with Et$_2$O, and dried in a vacuo. Pale green powder dissolves in CH$_3$CN at –40 °C. The solid was recrystallized from slow diffusion Et$_2$O to give 5 at –40 °C. Yield: 40% (0.0133 g). UV-vis in CH$_3$CN (see Figure S12a): $\lambda_{\text{max}}$ ($\varepsilon$) = 310 nm (3200 M$^{-1}$ cm$^{-1}$), 420 nm (190 M$^{-1}$ cm$^{-1}$), 820 nm (240 M$^{-1}$ cm$^{-1}$). ESI-MS in CH$_3$CN (see Figure S12b): $m/z$ 242.73 for
[Co(TBDAP)(CH₃C(-NHO)O)]²⁺. Anal. Calcd for C₂₄H₃₈ClCoN₆O₁₀: C, 43.35; H, 5.76; N, 12.64. Found: C, 43.13; H, 5.37; N, 12.87.

**Synthesis of [Co(TBDAP)(C₆H₅C(-NHO)O)(NO₃)(H₂O) (6-NO₃⋅H₂O).** 6 was prepared by reacting [Co(TBDAP)(NO₃)(H₂O)][NO₃] (0.0278 g, 0.050 mmol) and benzohydroxamic acid (0.0069 g, 0.050 mmol) with 2 equiv of TEA in CH₃CN (10 mL). The mixture was stirred for 6 h at ambient temperature, resulting that the color was changed from pink to orange. The resulting solution was dried in a vacuo and then, washed with Et₂O (40 mL). Yield: 91% (0.0286 g). UV-vis in CH₃CN (see Figure S15): λ_max (ε) = 355 nm (2300 M⁻¹ cm⁻¹). ESI-MS in CH₃CN (see Figure S15): m/z 547.1 for [Co(TBDAP)(C₆H₅C(-NHO)O)]⁺. Anal. Calcd for C₂₀H₄₀CoN₆O₆: C, 55.50; H, 6.42; N, 13.39. Found: C, 55.4; H, 6.21; N, 13.4.

**Magnetic Moment Measurement.** The effective magnetic moments were determined by the ¹H NMR Evans method at 25 °C.⁴⁻⁶ A WILMAD® coaxial insert (sealed capillary) tube containing the blank acetonitrile-d₃ solvent (with 1.0 % TMS) only was inserted into the normal NMR tube containing the complexes dissolved in acetonitrile-d₃ (with 0.03 % TMS). The chemical shift of the TMS peak (and/or solvent peak) in the presence of the paramagnetic metal complexes was compared to that of the TMS peak (and/or solvent peak) in the inner coaxial insert tube. The effective magnetic moments were calculated using the equation, \( \mu_{\text{eff}} = 0.0618(\Delta \nu T/2fM)^{1/2} \), where \( f \) is the oscillator frequency (MHz) of the superconducting spectrometer, \( T \) is the absolute temperature, \( M \) is the molar concentration of the metal ion, and \( \Delta \nu \) is the difference in frequency (Hz) between the two reference signals.⁶
**X-ray Crystallography.** Single crystals of 1-NO₃ and 4-CH₃OH-BPh₄ were picked from solutions by a nylon loop (Hampton Research Co.) on a hand made copper plate mounted inside a liquid N₂ Dewar vessel at ca. −40 °C and mounted on a goniometer head in a N₂ cryostream. Data collections were carried out on a Bruker SMART APEX II CCD diffractometer equipped with a monochromator in the Mo Kα (λ = 0.71073 Å) incident beam. The CCD data were integrated and scaled using the Bruker-SAINT software package, and the structure was solved and refined using SHEXTL V 6.12.³⁷ Hydrogen atoms were located in the calculated positions except H1 for 1 and 4 and H2 for 4, which were found from the Fourier difference map. All non-hydrogen atoms were refined with anisotropic thermal parameters. The crystallographic data with the selected bond distances and angles for 1-NO₃ and 4-CH₃OH-BPh₄ are listed in Tables S1 and S2. Crystal data for 1-NO₃: C₂₄H₃₆CoN₆O₅, triclinic, P̅1, Z = 2, a = 10.7961(4), b = 11.0539(5), c = 13.2535(6) Å, α = 92.008(2), β = 113.595(2), γ = 110.629(2)°, V = 1327.60(10) Å³, µ = 0.691 mm⁻¹, ρcalcd = 1.370 g/cm³, R₁ = 0.0371, wR₂ = 0.0810 for 5211 unique reflections, 345 variables. The hydrogen bonding interaction is found between hydroxamate N-H of 1 and nitrate anion (N5⁻…O4 2.994(3) Å, N5-H1A⁻…O4 163(3)°). Crystal data for 4-CH₃OH-BPh₄: C₃₆H₄₉BN₄O₃Zn, triclinic, P̅1, Z = 2, a = 11.260(18), b = 11.588(19), c = 14.33(2) Å, α = 69.62(6), β = 75.44(3), γ = 80.18(7)°, V = 1689.5(5) Å³, µ = 0.768 mm⁻¹, ρcalcd = 1.302 g/cm³, R₁ = 0.0448, wR₂ = 0.1129 for 8332 unique reflections, 415 variables. CCDC-1847955 for 1-NO₃ and CCDC-1864483 for 4-CH₃OH-BPh₄ contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif (or from the Cambridge Crystallographic Data
Reactivity Studies. All reactions were performed in a 1-cm UV cuvette by monitoring UV-vis spectral changes of reaction solutions, and rate constants were determined by fitting the changes in absorbance at 356 nm for the decay of 1. Reactions were run at least in triplicate, and the data reported represent the average of these reactions. The crystal of 1 (0.25 mM) was used in reactivity studies. After the completion of reactions, pseudo-first-order fitting of the kinetic data allowed us to determine $k_{\text{obs}}$ values.

Cyclic voltammetry. Electrochemical measurements were performed on a CHI600E electrochemical analyzer in a CH$_3$CN containing $n$-Bu$_4$NPF$_6$ (TBAPF$_6$, 0.10 M) as a supporting electrolyte at 298 K. A conventional three-electrode cell was used with a platinum working electrode (surface area of 0.3 mm$^2$), a platinum wire as a counter electrode and an Ag/AgNO$_3$ (0.010 M) electrode as a reference electrode. The platinum working electrode (BAS) was routinely polished with BAS polishing alumina suspension and rinsed with acetone and acetonitrile before use. The measured potentials were recorded with respect to an Ag/AgNO$_3$ (0.010 M) reference electrode. All potentials (vs. Ag/Ag$^+$) were converted to values vs. SCE by using the potential of ferrocene in the same conditions. All electrochemical measurements were carried out under N$_2$ atmosphere.

Equilibrium constant. The expression used for determination of $K_{\text{eq}}$ was derived according to a literature method.$^{88}$ The equation of equilibrium is provided below. The $K_{\text{eq}}$ values of $5.9 \times 10^{-2}$ and $4.4 \times 10^{-2}$ are determined from the slope of the linear plot $(\alpha^{-1}-1)^{-1}$ against $[1]_0/\alpha[3]_0-1$ and $[6]_0/\alpha[3]_0-1$, respectively (see Figure S4 and S18).
Theoretical calculations. DFT calculations were performed to obtain mechanistic insights into the hydroxamate transfer reaction. M06/[Lanl2dz(Co,Zn),6-31G*] (method 1) was used for geometry optimization, whereas M06(SCRF,acetonitrile)/def2-TZVP (method 2) was used for energy evaluations.\textsuperscript{S9-S12} Free energy corrections were obtained from frequency calculations with method 2. The quartet spin state of the system was examined. Gaussian 09 was used for DFT calculations.\textsuperscript{S13}

Inhibition against MMP-9. The peptide, PLGMWSR, was chosen as a substrate of MMP-9.\textsuperscript{S14,S15} The concentration of the substrate was determined by measuring the absorbance of the solution at 280 nm (\(\varepsilon = 5690 \text{ M}^{-1}\text{cm}^{-1}\)).\textsuperscript{S16} MMP-9 (44 nM) was activated by incubation with APMA (1 mM) in 50 mM tris [tris = tris(hydroxymethyl)aminomethane], pH 7.4, 100 mM NaCl, and 10 mM CaCl\(_2\) at 37 °C for 2 h with constant agitation.\textsuperscript{S17} The activated MMP-9 (20 nM) was preincubated with or without an inhibitor [acetohydroxamic acid, benzohydroxamic acid, 1, 2, and 6] (10 mM) in the buffered solution for 15 min at room temperature with constant agitation followed by addition of the substrate (1 mM). Due to the limited solubility of 6 in H\(_2\)O, DMSO was used as a vehicle for testing its inhibitory
activity, compared to 1. The reaction mixtures were incubated at room temperature for 8 or 12 h without agitation and diluted by 1,000 fold with H$_2$O before injection into the mass spectrometer. All measurements were conducted with HH (10 µM; H, histidine) as an internal standard (vide infra). The percentage of inhibition against MMP-9 by each molecule was calculated by analyzing the amount of the substrate from the samples, relative to that of the control treated with the equal volume of H$_2$O or DMSO (vehicle).

**Internal standard calibration.** The concentration of HH was determined by measuring the absorbance of the solution at 210 nm (ε = 13180 M$^{-1}$cm$^{-1}$). Different concentrations of PLGMWSR (0.5 – 12.5 µM) were prepared in the buffered solution (0.5 mM tris, pH 7.4, 1 mM NaCl, and 0.1 mM CaCl$_2$) with or without DMSO (0.1% v/v) and diluted by 10 fold with H$_2$O. The resulting solutions were injected to the mass spectrometer with the internal standard, HH (10 µM) to construct calibration plots (Figure S13). The calibration equation was derived by linear regression of the signal intensity ratio between the substrate and the internal standard.

**Docking studies.** Docking of 1 with the catalytic domain of MMP-9 obtained from the previously reported X-ray crystal structure (PDB 4H3X) was determined by AutoDock Vina. The X-ray crystal structure of 1 was converted to the PDB format by Mercury software. The structural files of the protein were generated by AutoDock Tools and imported into PyRx to run AutoDock Vina. A grid map was set to contain the active site of the protein. The exhaustiveness was set to 1024. The resultant poses of 1 with the catalytic domain of MMP-9 were visualized using Pymol.

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Table S1. Crystal Data and Structural Refinements for 1-NO₃ and 4-CH₃OH-BPh₄

|                          | 1-NO₃                      | 4-CH₃OH-BPh₄               |
|--------------------------|-----------------------------|----------------------------|
| Empirical formula        | C₂₄H₃₆CoN₆O₅               | C₃₆H₄₀BN₄O₅Zn             |
| Formula weight           | 547.52                     | 661.97                     |
| Temperature (K)          | 143(2)                     | 153(2)                     |
| Wavelength (Å)           | 0.71073                    | 0.71073                    |
| Crystal system/space group | triclinic, P1              | triclinic, P1              |
| Unit cell dimensions     |                             |                            |
|  a (Å)                   | 10.7961(4)                 | 11.260(18)                 |
|  b (Å)                   | 11.0539(5)                 | 11.588(19)                 |
|  c (Å)                   | 13.2535(6)                 | 14.33(2)                   |
|  α (°)                   | 92.008(2)                  | 69.62(6)                   |
|  β (°)                   | 113.595(2)                 | 75.44(3)                   |
|  γ (°)                   | 110.629(2)                 | 80.18(7)                   |
| Volume (Å³)              | 1327.60(10)                | 1689.5                     |
| Z                        | 2                           | 2                          |
| Calculated density (g/cm³) | 1.370                      | 1.302                      |
| Absorption coefficient (mm⁻¹) | 0.691                    | 0.768                      |
| Reflections collected    | 34141                       | 50708                      |
| Independent reflections [R(int)] | 5211 [0.0486]            | 8332 [0.0990]              |
| Refinement method        | Full-matrix least-squares on F² | Full-matrix least-squares on F² |
| Data/restraints/parameters | 5211/0/345                | 8332/0/415                |
| Goodness-of-fit on F²    | 1.047                       | 0.825                      |
| Final R indices [I > 2sigma(I)] | R₁ = 0.0371, wR₂ = 0.0810 | R₁ = 0.0448, wR₂ = 0.1129 |
| R indices (all data)     | R₁ = 0.0519, wR₂ = 0.0909  | R₁ = 0.0820, wR₂ = 0.1364  |
Table S2. Selected Bond Distances (Å) and Angles (°) for 1-NO₃ and 4-CH₃OH-BPh₄

| Bond Distances (Å) | 1-NO₃                        | 4-CH₃OH-BPh₄                        |
|--------------------|------------------------------|------------------------------------|
| Co-O1              | 2.090(2)                     | Zn-O1                              |
| Co-O2              | 1.978(2)                     | Zn-O2                              |
| Co-N1              | 2.056(2)                     | Zn-O3                              |
| Co-N2              | 2.366(2)                     | Zn-N2                              |
| Co-N3              | 2.055(2)                     | Zn-N3                              |
| Co-N4              | 2.350(2)                     | Zn-N4                              |
| O1-C23             | 1.268(3)                     | O1-C1                              |
| N5-C23             | 1.295(3)                     | N1-C1                              |
| O2-N5              | 1.363(2)                     | O2-N1                              |

| Bond Angles (°)    | 1-NO₃                        | 4-CH₃OH-BPh₄                        |
|--------------------|------------------------------|------------------------------------|
| O1-Co-O2           | 79.78(6)                     | O1-Zn-O2                           |
| N1-Co-N2           | 75.04(7)                     | O1-Zn-O3                           |
| N1-Co-N3           | 87.30(7)                     | O2-Zn-O3                           |
| N1-Co-N4           | 78.65(7)                     | N2-Zn-N3                           |
| N2-Co-N3           | 78.32(7)                     | N2-Zn-N4                           |
| N2-Co-N4           | 143.39(6)                    | N3-Zn-N4                           |
| N3-Co-N4           | 75.42(7)                     | O3-Zn-N2                           |
| O2-Co-N1           | 175.09(7)                    | O2-Zn-N2                           |
| O1-Co-N1           | 96.57(7)                     | O1-Zn-N2                           |
| O2-Co-N2           | 102.56(7)                    | O3-Zn-N3                           |
| O1-Co-N2           | 104.08(6)                    | O2-Zn-N3                           |
| O2-Co-N3           | 96.45(7)                     | O1-Zn-N3                           |
| O1-Co-N3           | 175.86(7)                    | O3-Zn-N4                           |
| O2-Co-N4           | 105.33(6)                    | O2-Zn-N4                           |
| O1-Co-N4           | 103.82(6)                    | O1-Zn-N4                           |
| C23-O1-Co          | 109.57(14)                   | C1-O1-Zn                           |
| N5-C23-O1          | 120.9(2)                     | N1-C1-O1                           |
| C23-N5-O2          | 119.0(2)                     | C1-N1-O2                           |
| N5-O2-Co           | 110.67(13)                   | N1-O2-Zn                           |

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Scheme S1. (a) Schematic drawings of the structures of 1 – 6 used in this study. (b) Reaction scheme depicting an intermolecular hydroxamate transfer between metal complexes (L = TBDAP; L’ = Me₃-TACN).
**Figure S1.** ESI-MS spectrum of [Co$^{II}$.(TBDAP)(CH$_3$C(-NHO)))(NO$_3$)](NO$_3$) (1-NO$_3$) in CH$_3$CN. Mass peak at m/z 485.3 corresponds to [Co$^{II}$.(TBDAP)(CH$_3$C(-NHO))]+ (calcd m/z 485.2). Inset shows the observed (upper) and calculated (lower) isotope distribution patterns of the peak at m/z 485.3.
Figure S2. FT-IR (ATR) spectra of (a) 1-NO₃ (red line): 3207 cm⁻¹ (w, N-H), and (b) 2-NO₃·H₂O (blue line): 1523 cm⁻¹ (w, C=N).
**Figure S3.** X-ray crystal structure of the $[\text{Zn}^{\text{II}}(\text{Me}_3\text{-TACN})(\text{CH}_3\text{C(-NHO)}\text{O})(\text{CH}_3\text{OH})](\text{BPh}_4)$ (4-CH$_3$OH-BPh$_4$) with thermal ellipsoids drawn at the 30% probability level (black C, cyan H, blue N, green Zn, red O). All hydrogen atoms except H1 and H2 are omitted for clarity. H1 and H2 were found in the Fourier difference map.
Figure S4. Plot of $(\alpha^{-1})^{-1}$ vs $[1]/[\alpha [3]]^{-1}$ to determine the equilibrium constant ($K_{eq}$) between 1 and 3 in CH$_3$CN/H$_2$O (99:1) at 25 °C.
Figure S5. (a) UV-vis spectral changes of 2 (0.5 mM) upon addition of 40 equiv of 3 at -10 °C. Inset shows the time course of the absorbance at 790 nm. (b) ESI-MS spectrum taken after the completion of the reaction. Mass peaks at \( m/z \) 297.2, 356.3, and 484.3 are assigned to [Zn\textsuperscript{II}(Me\textsubscript{3}-TACN)(NO\textsubscript{3})]\textsuperscript{+} (calcd \( m/z \) 297.1), [Zn\textsuperscript{II}(Me\textsubscript{2}-TACN)(CH\textsubscript{3}CN)(NO\textsubscript{3})(H\textsubscript{2}O)]\textsuperscript{+} (calcd \( m/z \) 356.1), and [Co\textsuperscript{III}(TBDAP)(CH\textsubscript{3}C(=NO)O)]\textsuperscript{+} (calcd \( m/z \) 484.2), respectively.
Figure S6. (a) UV-vis spectral change of 2 (0.5 mM) upon addition of 0.5 equiv of ascorbic acid in the presence of 40 equiv of 3 in CH$_3$CN:H$_2$O (99:1) at -10 ºC. Inset shows the time course of the absorbance at 356 nm. (b) ESI-MS spectrum taken after the completion of the reaction. Mass peaks at m/z 297.2, 309.2, 356.3, and 485.3 correspond to [Zn$^{ll}$(Me$_3$-TACN)(NO$_3$)]$^+$ (calcd m/z 297.1), [Zn$^{ll}$(Me$_3$-TACN)(CH$_3$C(-NHO)O)]$^+$ (calcd m/z 309.1), [Zn$^{ll}$(Me$_3$-TACN)(CH$_3$CN)(NO$_3$)(H$_2$O)]$^+$ (calcd m/z 356.1), and [Co$^{ll}$(TBDAP)(CH$_3$C(-NHO)O)]$^+$ (calcd m/z 485.2), respectively.
Figure S7. Cyclic voltammograms of (a) 1 (3.0 mM) and (b) 2 (3.0 mM) in CH$_3$CN containing TBAPF$_6$ (0.10 M) with a Pt working electrode at ambient temperature. Scan rate was 0.1 V s$^{-1}$. All electrochemical measurements were performed under N$_2$ atmosphere.
**Figure S8.** Cyclic voltammograms of (a) 2 (3.0 mM) and (b) 2 (3.0 mM) in the presence of 1 equiv of HClO₄ in CH₃CN containing TBAPF₆ (0.10 M) with a Pt working electrode at ambient temperature. Scan rate was 0.1 V s⁻¹. All electrochemical measurements were performed under N₂ atmosphere.
Figure S9. ESI-MS spectrum of 3 in CH$_3$CN. Mass peak at $m/z$ 297.2 corresponds to [Zn$^{II}$(Me$_3$-TACN)(NO$_3$)]$^+$ (calcd $m/z$ 297.1). Inset shows the observed (upper) and calculated (lower) isotope distribution patterns of the peak at $m/z$ 297.2.
Figure S10. ESI-MS spectrum of 4 in CH$_3$CN. Mass peak at $m/z$ 309.4 corresponds to $[\text{Zn}^{II}(\text{Me}_3\text{-TACN})(\text{CH}_3\text{C(-NHO)O})]^+$ (calcd $m/z$ 309.1). Inset shows the observed (upper) and calculated (lower) isotope distribution patterns of the peak at $m/z$ 309.4.
Figure S11. UV-vis absorption spectra of 2 (0.5 mM) in the absence of HClO₄ (black) and in the presence of 1 equiv of HClO₄ (red) in CH₃CN at –40 °C.
Figure S12. (a) UV-vis absorption spectrum of isolated [Co^{III}(TBDAP)(CH$_3$C(-NHO)O)]$_2^{2+}$ (5) (2 mM) at -40 °C in CH$_3$CN. (b) ESI-MS spectrum of 5 in CH$_3$CN. ESI-MS peaks at $m/z$ 226.2 and 242.7 are assigned to [Co^{I}(TBDAP)(CH$_3$CN)]$_2^{2+}$ (calcd. $m/z$ 226.1) and [Co^{III}(TBDAP)(CH$_3$C(-NHO)O)]$_2^{2+}$ (calcd. $m/z$ 242.6), respectively. Inset shows the observed (upper) and calculated (lower) isotope distribution patterns of the peak at $m/z$ 242.7.
Figure S13. Calibration curve for the signal intensity ratio (substrate/standard) as a function of [substrate] (a) without or (b) with DMSO. Different concentrations of the substrate (PLGMWSR; 0.05 – 1.25 µM) with the internal standard (HH; 10 µM) were measured by MS.
Figure S14. UV-vis spectral change of 1 in 50 mM tris [tris = tris(hydroxymethyl)aminomethane], pH 7.4, 100 mM NaCl, and 10 mM CaCl₂ at room temperature. The stability test of 1 was performed in a 0.2 cm quartz cuvette. Inset shows the time course of the absorption band at 340 nm. The absorption band at 340 nm remain intact over 24 h.
Figure S15. (a) UV-vis absorption spectrum of 6 (0.25 mM) at 25 °C in CH$_3$CN. (b) ESI-MS spectrum of 6 in CH$_3$CN. ESI-MS peak at $m/z$ 547.1 is assigned to [Co$^{II}$(TBDAP)(C$_6$H$_5$C(-NHO)O)]$^+$ (calcd $m/z$ 547.2). Inset shows the observed (upper) and calculated (lower) isotope distribution patterns of the peak at $m/z$ 547.1.
Figure S16. Reaction of 6 with 3. (a) UV-vis spectral change during the reaction of 6 (0.25 mM) with 3 (10 mM) in CH$_3$CN/H$_2$O (99:1) at –10 °C. Inset shows the time course of the absorption band at 355 nm. (b) ESI-MS spectra obtained for the reaction of 6 (0.25 mM) with 3 (25 mM) before (lower) and after (upper) the reaction. The peaks at m/z 371.1 and 547.1 are assigned to [Zn$^{II}$Me$_3$-TACN(C$_6$H$_5$C(-NHO)O)]$^+$ (calcd m/z 371.1) and [Co$^{II}$TBDAP(C$_6$H$_5$C(-NHO)O)]$^+$ (calcd m/z 547.2), respectively.
Figure S17. Plot of $k_{\text{obs}}$ against the concentration of 3 obtained in the reaction of 6 with 3 at $-10 \, ^\circ\text{C}$ to determine a second-order rate constant.
Figure S18. Plot of \((\alpha^{-1} - 1)^{-1}\) vs \([6]_0/\alpha[3]_0 - 1\) to determine the equilibrium constant \((K_{eq})\) between 6 and 3 in CH\(_3\)CN/H\(_2\)O (99:1) at 25 °C.
Figure S19. UV-vis spectral change for the reaction 1 with 3 depending on concentration of the acetic acid in CH$_3$CN/H$_2$O (99:1) at 25 °C. Inset shows the decrease of the absorbance of 1 with increasing concentration of the acetic acid.
Figure S20. ESI-MS spectra taken after the completion of reaction of 1 with 3 (a) in the absence of acetic acid; (b) in the presence of acetic acid in CH$_3$CN/H$_2$O (99:1) at 298 K. The peak with asterisk is [n-Bu$_4$N]$^+$ as an internal standard. ESI-MS peaks at $m/z$ 294.0, 297.0, 309.0, 470.1 and 485.0 are assigned to [Zn$^{II}$ (Me$_3$-TACN)(CH$_3$COO)]$^+$ (calcd $m/z$ 294.1), [Zn$^{II}$ (Me$_3$-TACN)(NO$_3$)]$^+$ (calcd $m/z$ 297.1), [Zn$^{II}$ (Me$_3$-TACN)(CH$_3$C(-NHO)O)]$^+$ (calcd $m/z$ 309.1), [Co$^{II}$ (TBDAP)(CH$_3$COO)]$^+$ (calcd $m/z$ 470.2) and [Co$^{II}$ (TBDAP)(CH$_3$C(-NHO)O)]$^+$ (calcd $m/z$ 485.2), respectively. Compared to internal standard, the relative intensity of 1 and 4 changed from 20% and 23% to 7% and 48%, respectively.
Figure S21. DFT-calculated free energy profile (in kcal/mol) for the hydroxamate transfer reaction. In this particular mechanism, two water molecules are involved.
### XYZ coordinates of DFT optimized geometries

| Atom | x    | y    | z    |
|------|------|------|------|
| C    | 1.862702 | 0.925525 | 3.536432 |
| O    | 1.106765 | -0.956481 | 4.101842 |
| C    | 5.519361 | 0.515865 | 3.623864 |
| H    | 4.818028 | 0.461866 | 2.780420 |
| H    | 6.301906 | -0.236100 | 3.461955 |
| C    | 6.017309 | 1.493964 | 3.618080 |
| C    | 4.330546 | -1.241952 | 4.861399 |
| H    | 2.372716 | -1.559378 | 5.724476 |
| H    | 5.215743 | -1.890356 | 4.835134 |
| C    | 3.762129 | -1.422139 | 3.944955 |
| C    | -0.619055 | 0.292613 | 0.999002 |
| H    | -0.468323 | 0.737247 | 0.006281 |
| N    | -1.378629 | -0.490083 | 0.879418 |
| C    | 0.322149 | -0.172516 | 1.307658 |
| N    | 2.147663 | -1.435760 | 2.189738 |
| C    | 1.250724 | -0.148056 | 0.705395 |
| C    | -0.665554 | 2.390589 | 6.080811 |
| H    | -1.544966 | 3.921874 | 5.943526 |
| C    | 2.695772 | 4.524848 | 1.343272 |
| C    | 2.237905 | 0.570538 | 0.602659 |
| C    | 4.397560 | 4.344283 | 3.132629 |
| C    | 5.286539 | 4.717452 | 3.638257 |
| C    | 3.870245 | 0.334432 | 6.118635 |
| H    | 6.016240 | 1.363544 | 6.300862 |
| H    | 6.668861 | -0.260250 | 5.912521 |
| C    | 5.337351 | -0.052426 | 7.050502 |
| N    | 1.421230 | -1.815037 | 3.238054 |
| N    | 0.041529 | 1.974494 | 5.147572 |
| N    | 0.063266 | 2.133858 | 5.341548 |
| C    | 2.667071 | 2.741775 | 2.968392 |
| C    | 3.621663 | 1.195678 | 5.075450 |
| C    | -1.110993 | 1.314103 | 2.023630 |
| C    | 0.103225 | -3.249668 | 3.358209 |
| C    | 1.362201 | -3.854741 | 2.506522 |
| C    | -0.057266 | -3.326967 | 3.448068 |
| C    | 1.464305 | -3.665500 | 4.276707 |
| C    | 1.595280 | 1.761040 | 6.348042 |
| C    | 1.022725 | 2.309203 | 4.983947 |
| C    | 1.482324 | 2.160696 | 4.864632 |
| C    | -0.143860 | 3.056453 | 7.347917 |
| C    | -0.627090 | 3.482335 | 8.224893 |
| C    | -0.017144 | 2.738997 | 4.981885 |
| C    | -0.363067 | 3.110663 | 3.560660 |
| C    | -1.143687 | 3.337958 | 3.488510 |
| C    | 0.143106 | 0.648948 | 3.363959 |
| C    | 0.812561 | 2.804003 | 1.446992 |
| C    | 0.221627 | 3.599416 | 0.959936 |
| C    | 1.039075 | 2.050030 | 0.863263 |
| C    | 2.110497 | 3.389807 | 1.944079 |
| C    | 3.875714 | 4.996551 | 2.019434 |
| C    | 4.369952 | 5.883141 | 1.627424 |
| C    | 4.375605 | 3.216245 | 2.909450 |
| C    | 4.058664 | 2.571163 | 4.932527 |
| C    | 5.126225 | 2.693919 | 5.156171 |
| C    | 3.538888 | 3.177767 | 5.693515 |
| C    | 2.883945 | 0.979322 | 6.346240 |
| C    | 3.486005 | 1.275081 | 7.222941 |
| C    | 2.649026 | -0.086653 | 6.455787 |
| C    | 2.246886 | 0.206849 | 4.937781 |
| C    | -1.720793 | 0.573525 | 3.211123 |
| C    | -0.989222 | -0.098083 | 3.691060 |
| C    | -2.563338 | -0.035920 | 2.860295 |
| O    | 2.255972 | 1.237004 | 3.316571 |
| O    | 5.902430 | 0.558016 | 3.562766 |
| O    | 5.281932 | 0.752538 | 2.667151 |
| O    | 6.662299 | -0.194950 | 3.314643 |
| O    | 6.446061 | 1.479961 | 3.806695 |
| O    | 4.505016 | -1.340604 | 2.634390 |
| O    | 3.819929 | -1.797056 | 4.985706 |
| O    | 5.351669 | -2.035292 | 3.453499 |
| O    | 3.995314 | -1.278791 | 3.294509 |
| O    | 0.919168 | 1.919313 | -0.33892 |
| O    | 0.916306 | 0.645975 | 0.168059 |
| O    | 0.753369 | 0.656246 | 0.792611 |
| O    | 2.347242 | -1.039427 | 1.396751 |
| O    | 2.950023 | 0.214957 | 1.003222 |
| O    | -0.364037 | 3.120740 | 6.095061 |
| O    | -1.199978 | 3.815531 | 6.038598 |
| O    | 3.330033 | 5.198808 | 2.171894 |
| Element | X     | Y     | Z    |
|---------|-------|-------|------|
| H       | 3.368554 | 6.400663 | 4.75046 |
| H       | 3.548960 | 7.414432 | 5.106548 |
| C       | 3.5799161 | 4.047123 | 5.889163 |
| H       | 4.913337 | 2.808799 | 5.640940 |
| H       | 5.079999 | 2.981740 | 6.201705 |
| C       | 3.399924 | 2.657526 | 6.411020 |
| C       | 3.574080 | 0.452156 | 5.538418 |
| C       | 2.964756 | 0.352295 | 6.563233 |
| N       | 5.702169 | 1.258174 | 4.462524 |
| C       | 8.258719 | 0.083542 | 0.914189 |
| Zn      | 3.499103 | -0.123973 | 0.16340 |
| N       | 3.741973 | -0.485999 | -1.695565 |
| H       | 6.182875 | 0.652423 | -0.568694 |
| C       | 5.346212 | -0.207219 | 0.203212 |
| C       | 4.492101 | 0.576213 | -2.421034 |
| C       | 4.011221 | 1.530030 | -1.639171 |
| C       | 4.399146 | 0.445595 | -3.511994 |
| C       | 5.967128 | 0.619986 | -2.048135 |
| C       | 6.507451 | -0.235101 | -2.469073 |
| C       | 6.420518 | 1.508298 | -2.508203 |
| C       | 4.464947 | -2.706047 | -0.789892 |
| C       | 5.314423 | -2.940245 | -0.276117 |
| C       | 4.896733 | -3.676681 | -1.828705 |
| C       | 5.805626 | 2.005586 | -0.131535 |
| C       | 5.661406 | 0.203847 | 0.962573 |
| C       | 5.829739 | 2.733599 | -0.461258 |
| C       | 7.555118 | 2.289752 | -0.554910 |
| C       | 5.410985 | -2.832440 | 1.444182 |
| C       | 4.421415 | -2.897553 | 1.998866 |
| C       | 6.093466 | -2.351206 | 2.135494 |
| C       | 5.8731995 | -3.844944 | 1.229484 |
| C       | 7.677170 | -1.788964 | -3.361384 |
| C       | 7.642439 | -2.063733 | -1.397096 |
| C       | 7.429097 | -2.465408 | 0.154951 |
| C       | 7.187738 | -0.353263 | -0.131856 |
| C       | 7.377770 | -0.170960 | 0.395403 |
| C       | 8.143156 | -0.196750 | -0.658061 |

--- Int2 ---

| Element | X     | Y     | Z    |
|---------|-------|-------|------|
| Co      | 2.902044 | 2.025897 | 3.298113 |
| O       | 2.689662 | -1.910421 | 1.154250 |
| Zn      | 5.997007 | 0.641678 | 4.656433 |
| H       | 5.837935 | 1.159382 | 3.697520 |
| H       | 6.752975 | -0.137766 | 4.496334 |
| C       | 4.939374 | 1.257609 | 5.599008 |
| C       | 4.319535 | -0.089723 | 4.519314 |
| C       | 3.419234 | -1.651299 | 4.438959 |
| C       | 5.130853 | -1.826300 | 4.109966 |
| C       | 4.171159 | -0.666656 | 3.155043 |
| C       | 2.047157 | 3.209791 | -0.175596 |
| C       | 2.870774 | 3.868439 | -0.483909 |
| C     | 3.727535 | -0.419068 | 1.902139 |
| C     | -0.777044 | 1.486100 | 0.812561 |
| C     | -0.684466 | 2.257852 | 0.304967 |
| C     | -0.292073 | 0.724717 | 3.605452 |
| N     | 0.183703  | 0.956101 | 0.910246 |
| N     | 1.446793  | -1.502827 | 0.835113 |
| O     | 1.928297  | -0.482212 | 0.110994 |
| H     | -0.262130 | 2.329473 | 6.606869 |
| H     | -1.17008 | 2.858867 | 6.980003 |
| C     | 2.163508  | 5.738146 | 2.559375 |
| C     | 0.530698  | 0.519319 | 2.229911 |
| C     | 4.137387  | 0.503755 | 3.750250 |
| H     | 5.064122  | 2.568767 | 4.257771 |
| C     | 6.112524  | 0.206901 | 3.426672 |
| H     | 6.470047  | 0.106226 | 4.936455 |
| C     | 6.970666  | -0.143545 | 3.740074 |
| H     | 5.832309  | -0.610550 | 5.002409 |
| C     | 1.196441  | -1.413252 | 2.150137 |
| N     | 1.299473  | 1.683136 | 4.962045 |
| N     | -0.066624 | 2.779959 | 2.813973 |
| N     | 2.517014  | 3.449202 | 3.055457 |
| N     | 3.824277  | 1.267948 | 4.125748 |
| C     | -1.240714 | 2.064854 | 2.151143 |
| C     | 0.679662  | -2.640741 | 2.825596 |
| H     | 0.567619  | -3.499930 | 2.156771 |
| C     | 1.498771  | 3.637701 | 0.976330 |
| C     | 1.748734  | 4.417544 | 2.530924 |
| C     | 3.396914  | 0.604310 | 3.116146 |
| C     | 3.756178  | 7.068203 | 3.124745 |
| C     | 3.643395  | 3.739484 | 3.716330 |
| C     | 4.212880  | 2.634245 | 4.564915 |
| C     | 5.300177  | 2.739677 | 4.669960 |
| C     | 3.817898  | 2.300839 | 5.578169 |
| C     | 2.511799  | 0.485260 | 5.304687 |
| C     | 4.116268  | 0.453128 | 6.993894 |
| C     | 3.172656  | -0.547225 | 4.978662 |
| C     | 4.972402  | 0.589254 | 3.381980 |
| C     | -1.684964 | 0.915614 | 3.054345 |
| H     | -0.859844 | 0.227698 | 3.276689 |
| H     | -2.480373 | 0.350370 | 2.550450 |
| C     | -2.110958 | 1.261662 | 4.003705 |
| C     | -2.421232 | 3.001377 | 1.892895 |
| C     | -2.830451 | 3.443874 | 2.809160 |
| C     | -2.338060 | 2.429006 | 1.435500 |
| C     | -2.174283 | 3.814741 | 1.199136 |
| Zn    | 1.265422  | -2.357493 | 0.357795 |
| N     | 2.389284  | -0.803636 | 1.877103 |
| N     | 2.714678  | -0.702621 | -0.405757 |
| N     | 3.496437  | 1.088410 | -1.914446 |
| N     | 4.369135  | -1.699678 | -1.914490 |
| C     | 2.786212  | 0.759834 | -4.285633 |
| C     | 1.767901  | 1.154509 | -4.150277 |
| C     | 3.074224  | 0.979874 | -5.327214 |
| C     | 3.739684  | 1.467979 | -3.329970 |
