Supplementary Material (ESI) for Chemical Communications


*Supporting Information*

# Rapid Phosphorus Triester Hydrolysis Catalyzed by Bimetallic Tetrabenzimidazole Complexes

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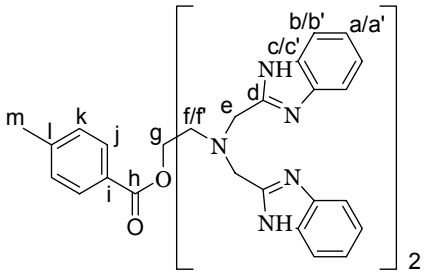
### *Syntheses and Characterization Data*

**General Information.** All reactions were performed in air unless stated otherwise. Ligand **[1]L**, [1] 2-[*bis*-(1H-benzoimidazol-2-ylmethyl)-amino]-ethanol (**[3]L**), *bis*-(1H-benzoimidazol-2-ylmethyl)-methyl-amine (**[4]L**)[2] and 4-nitrophenyl-diphenylphosphate[3] (PNPDPP) were prepared and purified as described in published procedures. 4-Ethylmorpholine and *p*-toluoyl chloride were purchased from Sigma-Aldrich and used as received. *N,N,N′,N′*-Tetramethylethylenediamine (TMEDA) was purchased from TCI and distilled over sodium metal under $N_2$ prior to use. Tetrahydrofuran (THF) was passed through a column of activated alumina and sparged with $N_2$ prior to use. The water used in hydrolysis experiments was doubly distilled and deionized (18 MΩ $cm^{-1}$) prior to use. $CuCl_2{\cdot}2H_2O$, $CoCl_2{\cdot}6H_2O$, and *N,N*-dimethylformamide (DMF) were purchased from commercial suppliers (Sigma-Aldrich, Baker) and used as received. $ZnCl_2$ was dried over $Me_3SiCl$ and was handled in a drybox. All pH measurements were determined at 20 ºC using a Corning 320 pH Meter. UV-Visible absorption spectra were obtained at 21 ± 1 ºC using an Agilent 8453 spectrometer. Infrared spectra were recorded using a Mattson Satellite FTIR spectrometer. NMR spectra were measured using 400 and 500 MHz Varian spectrometers. Chemical shifts (δ) for $^1$H NMR spectra are given relative to residual protium in the deuterated solvent at 2.50 for $d_6$-methyl sulfoxide ([$d_6$]DMSO). Combustion analysis was performed by Galbraith Laboratories. Mass spectrometry was performed using an Applied




Biosystems ATP Q-Star Pulsar I instrument.

**Synthesis of [2]L.** THF (50 mL) was added to a mixture of **1a** (1.00 g, 1.64 mmol) and $K_2CO_3$ (2.26 g, 16.4 mmol) in a 200 mL round-bottomed flask. To the pale pink suspension was added *p*-toluoyl chloride (0.220 mL, 1.64 mmol), and the mixture was stirred at 55 ºC for 5 days. Filtration of the mixture gave a clear orange-pink solution. Evaporation of the volatiles afforded the crude product as a solid. The solid was crystallized from acetone (20 mL) at -15 ºC to yield analytically pure product as pale orange-pink crystals (0.78 g, 65%). m.p. 169 ºC. $^1$H and $^{13}$C NMR assignments (drawing above) were determined using 2D-HMQC and COSY experiments. $^1$H NMR ([$d_6$]DMSO): δ 12.64 (br s, $\omega_{1/2}$ = 43.42 Hz, ca. 3 to 4H, N-*H*), 7.55 (d, 2H, J = 8.0 Hz, j), 7.46 (br s, 8H, b/b'), 7.14 (m, 8H, a/a'), 7.11 (d, 2H, J = 8.0 Hz, k), 5.32 (pent, 1H, J = 5.5 Hz, g), 4.10 (m, 8H, e), 3.01 (dd, 2H, J = 14.0, 5.0, f/f'), 2.89 (dd, 2H, J = 14.0, 6.5, f/f'), 2.34 (s, 3H, m). $^{13}$C NMR ([$d_6$]DMSO): δ 165.6 (h), 152.2 (d), 143.4 (i), 143.1 (br, c/c'), 134.2 (br, c/c'), 129.2 (j), 129.0 (k), 127.0 (l), 121.9 (br, a/a'), 121.3 (br, a/a'), 118.5 (br, b/b'),

111.3 (br, b/b'), 70.5 (g), 55.4 (f), 51.9 (e), 21.2 (m). IR (KBr): 3247 (m), 3055 (s), 2967 (s), 2905 (s), 2847 (s), 2783 (m), 1702 (s, carbonyl), 1653 (w), 1623 (w), 1611 (m), 1591 (w), 1577 (w), 1540 (w), 1507 (w), 1489 (w), 1457 (s), 1436 (s), 1378 (w), 1356 (m), 1338 (m), 1310 (m), 1271 (s), 1244 (m), 1226 (m), 1209 (w), 1180 (m), 1121 (w), 1106 (s), 1053 (m), 1026 (m), 998 (m), 979 (w), 928 (w), 875 (w), 846 (w), 835 (w), 788 (w), 767 (m), 745 (s), 692 (w), 473 (w) $cm^{-1}$. Anal. Calcd. (found) for $C_{44.6}H_{46.8}N_{10}O_{3.6}$ ($^2$**L**·$(H_2O)$·$(EtOH)_{0.8}$): C, 68.35 (68.06); H, 6.02 (6.04); N, 17.87 (18.11). HRMS ($ESI^-$) calcd. for $C_{43}H_{39}N_{10}O_2$ 727.3257 ($[M - H]^-$), found 727.3242.

**Synthesis of $^1$LZn$_2$Cl$_4$ ($^1$L·Zn$_2$).** Ethanol (5 mL) was added to $^1$**L** (0.10 g, 0.16 mmol) to form a clear colorless solution. Then an ethanol solution (1 mL) of $ZnCl_2$ (0.045 g, 0.33 mmol) was added to the solution to form a cloudy mixture. Upon mild heating the solution became clear. Filtration of the solution followed by cooling to -15 °C yielded the product as colorless crystals after 2 days (0.12 g, 86%). $^1$H NMR ([$d_6$]DMSO): δ 13.67 (br s, $\omega_{1/2}$ = 54.0 Hz, 4H), 8.46 (br s, $\omega_{1/2}$ = 46.4 Hz, 4H), 7.61 (br s, $\omega_{1/2}$ = 21.5 Hz, 4H), 7.34 (br s, $\omega_{1/2}$ = 20.7 Hz, 8H), 4.42 (br s, $\omega_{1/2}$ = 113.5 Hz, 1H), 4.28 (br s, $\omega_{1/2}$ = 30.4 Hz, 8H), 2.95 (br s, $\omega_{1/2}$ = 33.5 Hz, 2H), 2.66 (br s, $\omega_{1/2}$ = 28.8 Hz, 2H) . $^1$H NMR ([$d_6$]DMSO, 98 ºC): δ 7.91 (br s, $\omega_{1/2}$ = 78.1 Hz, 8H), 7.29 (m, 8H), 4.29 (s, 9H), 3.01 (dd, J = 13.7, 3.1 Hz, 2H), 2.72 (dd, J = 13.5, 8.8 Hz, 2H), N-H protons are not observed. Attempts to obtain reportable $^{13}$C NMR spectroscopic data in common solvents failed, apparently due to the broadness of the resonances. IR: 3503 (m), 3422 (m), 3332 (m), 3292 (m), 3182 (m), 3113 (m), 3060 (m), 2969 (m), 2914 (m), 2783 (m), 1624 (w), 1594 (w), 1541 (w), 1492 (m), 1474 (s), 1445 (s), 1388 (m), 1343 (w), 1315 (w), 1278 (m), 1220 (w), 1081 (w), 1046 (m), 1005 (m), 974 (m), 957 (w), 915 (w), 876 (w), 850 (m), 765 (s), 748 (s), 618 (w), 576 (w), 551 (w), 503 (w), 437 (w), 428 (w) $cm^{-1}$. HRMS ($ESI^-$) calcd. for $C_{35}H_{33}Cl_4N_{10}OZn_2$ 877.0176 ($[M–H]^-$), found 877.0181. Anal. Calcd. (found) for $C_{37}H_{44}Cl_4N_{10}O_4Zn_2$ ($^1$**L**$Zn_2Cl_4$·$(H_2O)_2$·(EtOH)): C, 46.03 (45.86); H, 4.59 (4.76); N, 14.51 (14.26).

**Formation of metal derivatives of $^1$L.** The other metal-containing derivatives of $^1$**L** were prepared analogously to $^1$**L·Zn$_2$** with the substitution of $ZnCl_2$ by the appropriate metal dichlorides.

**Synthesis of $^2$LZn$_2$Cl$_4$ ($^2$L·Zn$_2$).** The ligand $^2$**L** (0.071 g, 0.10 mmol) was dissolved in warm ethanol (15 mL). To this solution was added an ethanol (1 mL) solution of $ZnCl_2$ (0.027 g, 0.19 mmol) to form a cloudy solution. The solution was heated to ca. 70 ºC and filtered while hot. Cooling of the solution to -15 °C yielded the product as colorless crystals after 2 days (0.054 g, 55%). $^1$H NMR ([$d_6$]DMSO): δ 13.52 (br s, $\omega_{1/2}$ = 19.3 Hz, 4H), 8.42 (br s, $\omega_{1/2}$ = 34.9 Hz, 4H), 7.91 (br s, $\omega_{1/2}$ = 31.3 Hz, 2H), 7.58 (br s, $\omega_{1/2}$ = 19.4 Hz, 4H) 7.32 (br s, $\omega_{1/2}$ = 23.3 Hz, 10H), 5.86 (br s, $\omega_{1/2}$ = 22.6 Hz, 1H), 4.21 (br s, $\omega_{1/2}$ = 23.5 Hz, 8H), 3.10 (br s, $\omega_{1/2}$ = 14.8 Hz, 4H), 2.39 (br s, $\omega_{1/2}$ = 3.6 Hz, 3H). IR: 3496 (m), 3364 (m), 3197 (s), 3146 (m), 3064 (m), 2923 (w), 1706 (s, carbonyl), 1690 (m), 1654 (w), 1610 (m), 1559 (w), 1540 (w), 1507 (w), 1491 (m), 1472 (s), 1455 (s), 1388 (m), 1340 (m), 1313 (m), 1278 (s), 1179 (w), 1108 (m, br), 1048 (w), 1020 (w), 1005 (w), 976 (w), 845 (w), 744 (s), 694 (w)

$cm^{-1}$. HRMS ($ESI^-$) calcd. for $C_{43}H_{39}Cl_4N_{10}O_2Zn_2$ 995.0594 ($[M–H]^-$), found 995.0599. Anal. Calcd. (found) for $C_{43}H_{46}Cl_4N_{10}O_5Zn_2$ ($^2$**L**$Zn_2Cl_4\cdot(H_2O)_3$): C, 48.93 (48.84); H, 4.39 (4.54); N, 13.27 (13.22).

**Formation of metal derivatives of $^2$L.** The other metal-containing derivatives of $^2$**L** were prepared analogously to $^2$**L·Zn$_2$** with the substitution of $ZnCl_2$ by the appropriate metal dichlorides.

### *Phosphorous Ester Hydrolyses*

**General procedure for PNPDPP hydrolysis studies.** To a 1 cm cuvette was added 3.000 mL of a 4-ethylmorpholine buffer solution (67.3 mM, 30% EtOH) with a pH of 8.70. To this was added the bimetallic catalyst (0.505 μmol in 40.4 μL DMF) and then PNPDPP (0.505 μmol in 1.000 mL of 50% EtOH). Assuming a final volume of 4.040 mL, the initial concentrations of the reactants are: [PNPDPP] = [catalyst] = 0.125 mM, [metal] = 0.250 mM, [buffer] = 50 mM. The cuvette was then capped and shaken. The rate of hydrolysis was monitored at 401 nm (ε(*p*-nitrophenolate ion, pH 8.70) = 1.9 x $10^4$ $cm^{-1}M^{-1}$) for at least 3 half lives. A pseudo-first-order rate constant was determined from each reaction from a linear plot of $\ln(A_e-A_t)$ versus time (where $A_e$ is the equilibrium absorbance at 401 nm). All reported data and standard deviations were determined by averaging at least three separate runs. Statistically identical results were obtained for runs using isolated (crystalline) catalysts and mixtures prepared *in situ* by mixing ligand and metal salts together in EtOH. For entries 2-5 and 20-25 in Table 1 the general procedure was followed except the [metal] = [catalyst] = 0.250 mM.

**Effect of [catalyst] on PNPDPP hydrolysis rate.** The rate of PNPDPP hydrolysis catalyzed by $^1$**L·Zn$_2$** and $^2$**L·Zn$_2$** was studied as a function of catalyst concentration. The reactions were monitored as described above. Reactions were run using nine different catalyst concentrations that varied between 1.25 x $10^{-4}$ M and 1.25 x $10^{-5}$ M. By plotting the negative log of the concentration of catalyst versus the negative log of the resulting rate constant, the order dependence on catalyst was determined from the slope of the resulting line. The order dependence on catalyst was found to be approximately first order (1.27 for $^1$**L·Zn$_2$** and 1.07 $^2$**L·Zn$_2$**) for both systems. These data are shown in Figure S1.

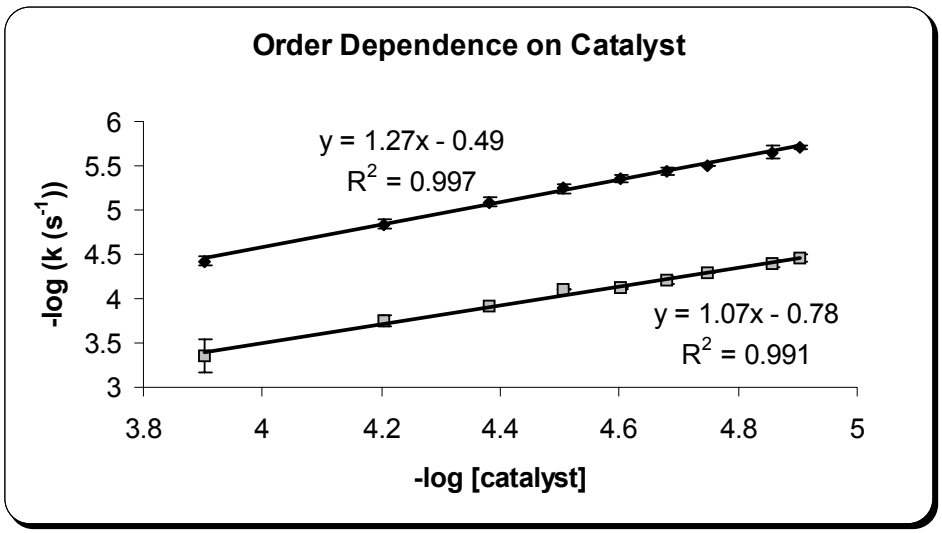


**Figure S1.** Determination of reaction order of catalysts $^{1}$**L·Zn$_2$** (diamonds) and $^{2}$**L·Zn$_2$** (squares) for the hydrolysis of PNPDPP. Data are corrected for the non-catalyzed, background rate of hydrolysis.

**Determination of ε(*p*-nitrophenolate ion).** To a 100 mL volumetric flask containing 50 mM *N*-ethylmorpholine buffer (pH 8.7, 65/35 $H_2O$/EtOH), 10 μL aliquots of 0.1 M *p*-nitrophenol in EtOH were added. The absorbance was monitored after each aliquot was added and the solution shaked. The results are depicted below in Figure S2. A molar absorbtivity of 1.6 x $10^4$ $cm^{-1}M^{-1}$ was obtained.

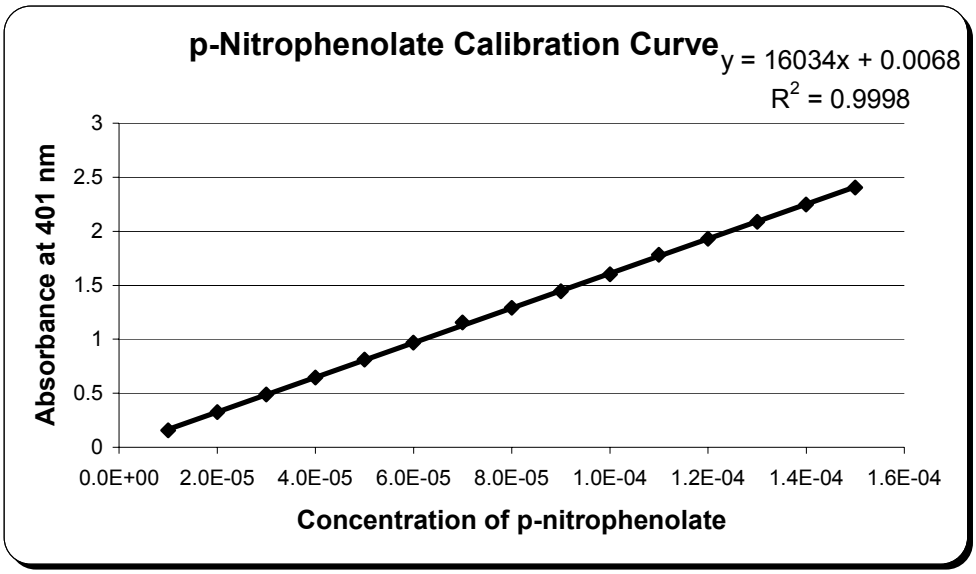



**Figure S2.** Determination of molar absorptivity at 401 nm for *p*-nitrophenolate ion using a Beer-Lambert plot. Experiment performed at ambient temperature using a 1.00 cm path length.

### *X-ray Crystallography*

Table S1 lists a summary of crystal data and collection parameters for all crystallographically characterized compounds. Additional data are presented as crystallogaphic information files which have been submitted to the Cambridge Crystallographic Database (CCDC 290488, 290489).

*General Procedure.* A crystal of appropriate size was mounted on a glass fiber using hydrocarbon oil (Paratone-N), transferred to a Siemens SMART diffractometer/CCD area detector, centered in the beam (Mo-K$\alpha$; $\lambda$ = 0.71073 Å; graphite monochromator), and cooled to -125 ± 10 ºC by a nitrogen low-temperature apparatus. Preliminary orientation matrix and cell constants were determined by collection of 60 frames, followed by spot integration and least-squares refinement. A minimum of a hemisphere of data was collected using 0.3˚ $\omega$ scans. The raw data were integrated and the unit cell parameters refined using SAINT. Data analysis was performed using XPREP. Absorption correction was applied using SADABS. The data were corrected for Lorentz and polarization effects, but no correction for crystal decay was applied. Structure solutions and refinements were performed (SHELXTL-Plus V5.1) on F-squared.[4] Notable details of each data collection and refinement are described below.

**Structure of $^{1}L(ZnCl_2)_2{\cdot}2EtOH{\cdot}2H_2O$ ($^{1}L{\cdot}Zn_2{\cdot}2EtOH{\cdot}2H_2O$).** Crystals that were suitable for X-ray diffraction studies were grown from aqueous EtOH at ambient temperature. Preliminary data indicated a triclinic unit cell. Choice of the centric space group was confirmed by the successful solution and refinement of the structure. The asymmetric unit contains one molecule of $^{1}L(ZnCl_2)_2$, two EtOH, and two water molecules. All non-H atoms were refined anisotropically. Hydrogens were placed in idealized positions and were included in structure factor calculations but were not refined. The hydrogen atoms of the water molecules were not included in the model.

**Structure of $^{2}L(ZnCl_2)_2{\cdot}2EtOH$ ($^{2}L{\cdot}Zn_2{\cdot}2EtOH$).** Crystals that were suitable for X-ray diffraction studies were grown from warm EtOH. Preliminary data indicated a primitive monoclinic cell. Systematic absences indicated space group $P2_1/c$ (#14). This was confirmed by the successful solution and refinement of the structure. The asymmetric unit contains one molecule of $^{2}L(ZnCl_2)_2$ and two co-crystallized EtOH molecules. All non-H atoms were refined anisotropically. Hydrogens (except hydroxy hydrogens) were placed in idealized positions and were included in structure factor calculations but were not refined. The torsion angles of the hydroxy hydrogens of the co-crystallized EtOH molecules were optimized.

**Table S1.** Crystallographic Data and Collection Parameters

| compound | **$^{1}$L·Zn$_2$·2EtOH·2H$_2$O** | **$^{2}$L·Zn$_2$·2EtOH** |
|---|---|---|
| formula | $C_{39}H_{50}Cl_4N_{10}O_5Zn_2$ | $C_{47}H_{52}Cl_4N_{10}O_4Zn_2$ |
| formula wt (g·mol$^{-1}$) | 1011.43 | 1093.53 |
| space group | P-1 (#2) | P2(1)/c (#14) |
| temp (K) | 152 | 147 |
| a (Å) | 12.3747(4) | 17.5457(4) |
| b (Å) | 13.7692(5) | 12.8691(4) |
| c (Å) | 14.0177(5) | 23.3783(8) |
| $\alpha$ (deg) | 93.140(1) | 90 |
| $\beta$ (deg) | 111.015(1) | 104.362(1) |
| $\gamma$ (deg) | 93.478(1) | 90 |
| $Z$ | 2 | 4 |
| V (Å$^3$) | 2218.0(1) | 5113.9(3) |
| $d_{calc}$ (g·cm$^{-3}$) | 1.514 | 1.420 |
| θ range (deg) | 1.77-27.48 | 1.90-27.88 |
| $\mu$ (mm$^{-1}$) | 1.376 | 1.199 |
| $T_{min}$, $T_{max}$ | 0.683, 0.725 | 0.646, 0.795 |
| crystal size (mm) | 0.30 x 0.25 x 0.25 | 0.4 x 0.3 x 0.2 |
| reflections collected | 17620 | 40729 |
| data/restraints/parameters | 10150/0/541 | 12192/0/606 |
| R1 (for $F_o>4\sigma F_o$) | 0.0799 | 0.0676 |
| R1, wR2 (all data) | 0.1170, 0.2252 | 0.1317, 0.1766 |
| GOF | 1.021 | 1.020 |
| largest peak, hole (e·Å$^{-3}$) | 1.328, -0.786 | 1.047, -0.415 |

### *Catalyst composition studies by NMR spectroscopy*

**General procedure for NMR-titrations.** 750 µL of a 25 mM solution of ligand (**$^{1}$L** or **$^{2}$L**) in [$d_6$]DMSO was placed into an NMR tube. To this solution were added aliquots of a solution containing 25 mM ligand and 500 mM $ZnCl_2$. The NMR tube was shaken after each aliquot. NMR spectra were taken on a Varian 500 MHz instrument at 20 $^{o}$C. Selected spectra are shown below for titrations involving **$^{1}$L** (Figure S3) and **$^{2}$L** (Figure S4).

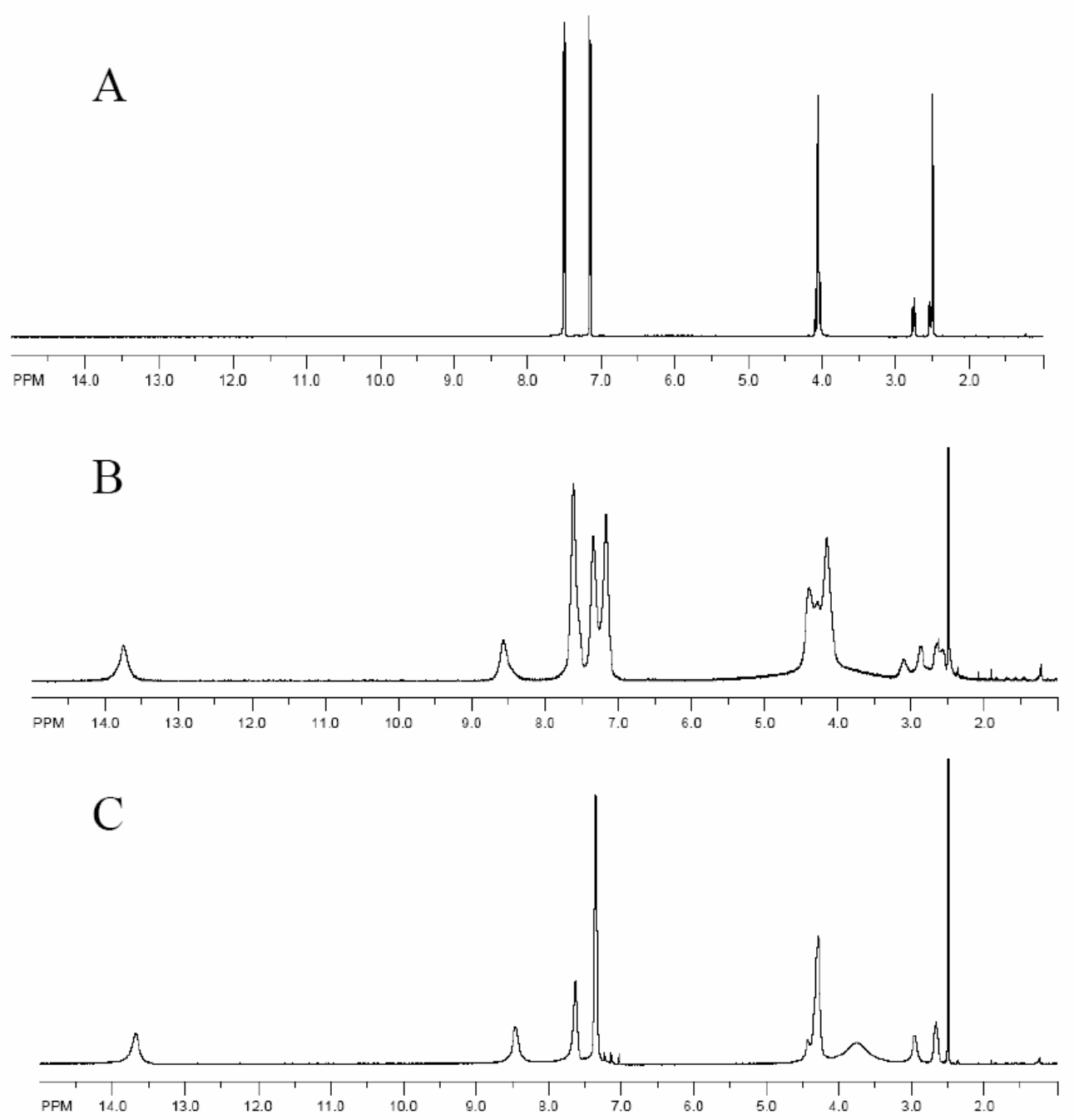



**Figure S3.** 500 MHz $^{1}$H-NMR spectra for a [$D_6$]DMSO solution of **$^{1}$L** with varying amounts (**A:** 0 equiv; **B:** 1.0 equiv; **C:** 2.0 equiv) of $ZnCl_2$ added. The sharp resonance observed at δ 2.5 ppm is from [$d_5$]DMSO.

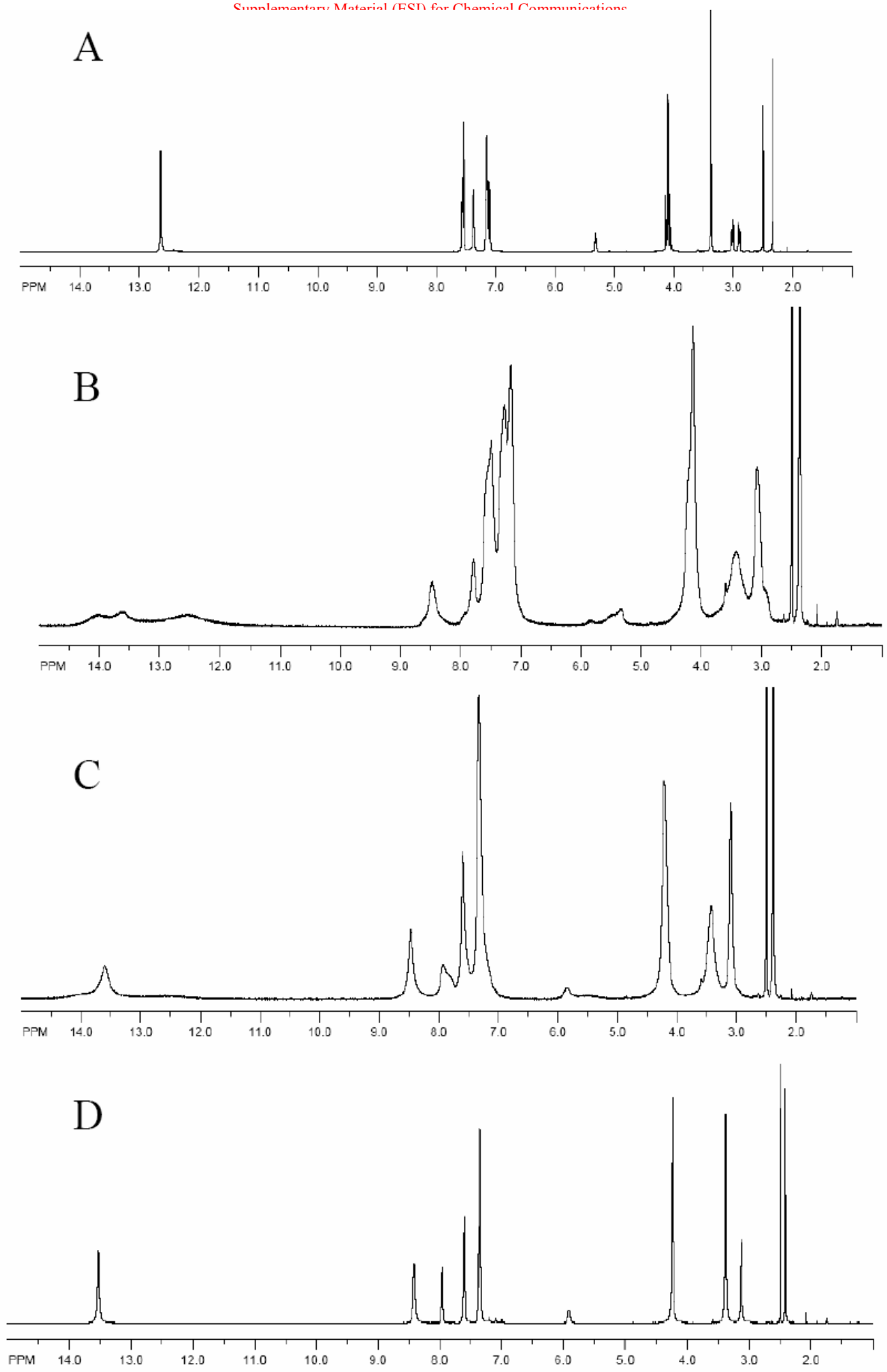



**Figure S4.** 500 MHz $^{1}$H-NMR spectra for a [$D_6$]DMSO solution of **$^{2}$L** with varying amounts (**A:** 0 equiv; **B:** 1.0 equiv; **C:** 2.0 equiv; **D:** 2.4 equiv) of $ZnCl_2$ added. The sharp resonance observed at δ 2.5 ppm is from [$d_5$]DMSO.

### *Catalyst composition studies by UV-visible absorption spectroscopy*

**Titration of $^1$L solutions with $CuCl_2$.** A 3.13 mM solution of $^1$L was prepared from 50.0 μL of a 0.3125 M solution of $^1$L in DMF, 0.5 mL DMF (to help solubilze the ligand), and enough 35% (by volume) $EtOH_{(aq)}$ to form 5.000 mL of solution. A second solution containing 3.13 mM $^1$L and 0.399 M $CuCl_2$ was made in an analogous manner. Aliquots of this second solution were added to the ligand solution and a UV-Visible absorption spectrum was taken after each aliquot was added and the solution shaken. Data for this titration at 675 nm ($\lambda_{max}$ for the complex) are depicted in Figure S5. These data are corrected for the expected background absorbance of free, uncomplexed $CuCl_2$. Data were acquired at 20 ºC and with a 1 cm path length.

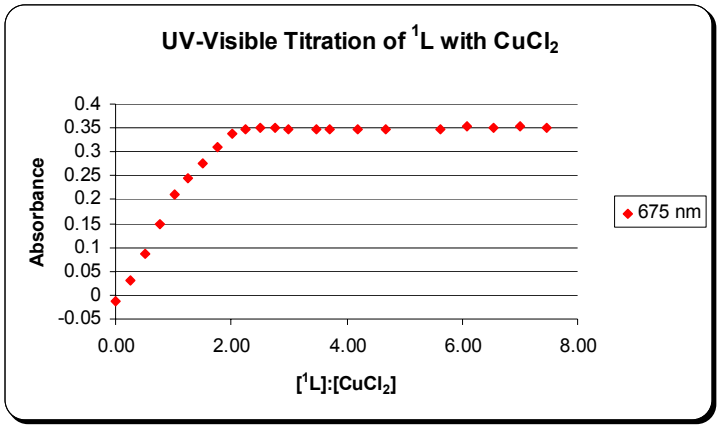



**Figure S5.** Absorption at 675 nm ($\lambda_{max}$ for complex) for the titration of a 3.13 mM $^1$L solution (mixture of $H_2O$, EtOH, DMF) with a solution containing 3.13 mM $^1$L and 399 mM $CuCl_2$.

**Titration of $^1$L solutions with $CoCl_2$.** A 3.13 mM solution of $^1$L in DMF was titrated with a DMF solution containing 3.13 mM $^1$L and 240 mM $CoCl_2$. An absorption spectrum was recorded taken after each aliquot was added and the solution shaken. The results of this titration at 556 nm ($\lambda_{max}$ for the complex) are shown in Figure S6. Data were acquired at 20 ºC and with a 0.1 cm path length.

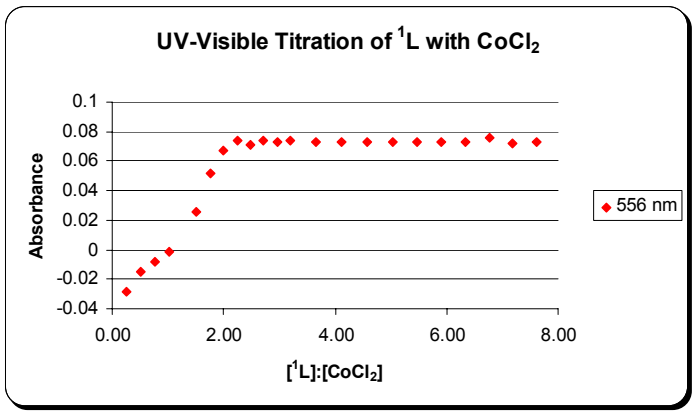



**Figure S6.** Absorption at 556 nm ($\lambda_{max}$ for complex) for the titration of a 3.13 mM $^1$L solution (in DMF) with a DMF solution containing 3.13 mM $^1$L and 240 mM $CoCl_2$.

### *References*


1 V. McKee, M. Zvagulis, J. V. Dagdgian, M. G. Patch, C. A. Reed, *J. Am. Chem. Soc.* **1984**, *106*, 4765-4772.

2 Y. Nishida, K, Takahashi, *J. Chem. Soc., Dalton Trans*. **1988**, *3*, 691-699.

3 W. M. Gluick, Jr., D. H. Geske, *J. Am. Chem. Soc.* **1966**, *88*, 2928-2934.

4 G. M. Sheldrick, *A Program for Crystal Structure Determination*: Version 5.1, Bruker AXS: Madison WI, 1998.