Synthesis of a Pentadentate, Polypyrazine Ligand and its Application in Cobalt-Catalyzed Hydrogen Production

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Materials and Methods. Unless otherwise noted, all synthetic manipulations were carried out using standard Schlenk techniques or in an MBraun glovebox under nitrogen atmosphere. Tetrahydrofuran and diethyl ether were dried with a Pure Process Technology solvent purification system. Acetonitrile was distilled over CaH₂ and stored over molecular sieves before use. Co(CH₃CN)₂(OTf)₂¹ and Co(bpy)₃(PF₆)₂² were prepared as previously described and stored in the glove box. Compounds 2-ethylpyrazine, 2-chloropyrazine, and 2,6-dichloropyrazine were purchased from Oakwood Chemicals. Water was purified with a Barnstead NANOpure Diamond system. All other chemicals were reagent or ACS grade, purchased from commercial vendors, and used without further purification. ¹H and ¹³C NMR spectra were obtained using a Bruker spectrometer operating at 500 MHz (¹H) or 125 MHz (¹³C). Spectra were calibrated to residual protiated solvent peaks; chemical shifts are reported in ppm. High-resolution electrospray ionization mass spectra (HR-ESI-MS) were obtained with a Waters SYNAPT HDMS Q-TOF mass spectrometer and elemental analyses of carbon, hydrogen, and nitrogen were conducted by Atlantic Microlab, Inc., Atlanta, Georgia.

Electrochemical Measurements. Electrochemistry was performed with a Bioanalytical Systems, Inc. (BASi) Epsilon potentiostat. Cyclic voltammetry studies employed a three-electrode cell equipped with a glassy carbon disc (3 mm dia.) working electrode, a platinum wire counter electrode, and a Ag/AgCl (3.0 M NaCl) aqueous reference or a silver wire quasi-reference electrode for nonaqueous experiments. Nonaqueous electrochemistry was conducted in anhydrous acetonitrile containing 0.1 M Bu₄NPF₆ electrolyte and was referenced using ferrocene as an internal standard.

Small volume controlled potential electrolyses were performed under inert atmosphere in the glovebox using a thin-layer electrochemical cell from Pine Research Instrumentation with a gold "honeycomb" working electrode, silver wire quasi-reference electrode, and platinum wire counter electrode. The electroactive volume was calibrated with a known 1-electron redox couple, $Co(bpy)_3(PF_6)_2$ at a concentration of 1 mM, in anhydrous $CH_3CN / 0.1$ M Bu_4NPF_6 . A potential beyond the Co(II/I) reduction was applied until the reduction was complete (150 s) and 1.2 x 10^{-3} coulombs had passed. The Co(II/I) couple of **1-Co** was investigated in the same manner and the accumulated charge following complete reduction was also 1.2×10^{-3} C.

Controlled potential electrolyses (CPE) in aqueous pH 7 potassium phosphate buffer were conducted in two compartment H-cells with a Hg pool working electrode. Constant stirring was maintained during CPE experiments. Evolved H₂ during electrolysis was quantified by gas chromatographic analysis of headspace gases using a custom Agilent 7890B Gas Chromatograph (column, Agilent PorapakQ 6 ft, 1/8 OD) and TCD detector. Integrated gas

peaks were quantified versus a calibration curve generated from known concentrations of H₂ gas. Values are plotted against the theoretical (assuming 100% Faradaic efficiency) hydrogen volume based on the accumulated charge passed during electrolysis.

X-ray Crystallography. A single crystal was coated with Paratone-N hydrocarbon oil and mounted on a Kapton loop. The temperature was maintained at 100 K with an Oxford Cryostream during data collection. Samples were irradiated with Cu-K α radiation with λ = 1.54178 Å using a MicroSTAR-H X8 APEX II diffractometer equipped with a microfocus rotating anode and APEX-II detector. The Bruker APEX2 v. 2009.1 software package was used to integrate raw data which were corrected for Lorentz and polarization effects.³ A semi-empirical absorption correction (SADABS) was applied.⁴ Space groups were identified based on systematic absences, E-statistics, and successive refinement of the structures. The structures were solved using direct methods and refined by least-squares refinement on F² and standard difference Fourier techniques using SHELXL.⁵ Thermal parameters for all non-hydrogen atoms were refined anisotropically, and hydrogen atoms were included at ideal positions.

Synthetic Procedures.

2,6-bis(1,1-di(pyrazin-2-yl)ethyl)pyrazine, (PZ5Me₂, 1)

Under nitrogen atmosphere, 50 mL of anhydrous tetrahydrofuran was added to 1,1'dipyrazyl(ethane) (3.8 g, 20.4 mmol) in an oven-dried 2-neck round bottom flask equipped with stir bar and reflux condenser. The reaction vessel was then cooled to -78 °C using a dry ice/acetone bath. A 2.0 M solution of LDA (1 eq, 20.4 mmol, 10.2 mL) was added *via* syringe to the stirred solution before allowing it to warm slowly to room temperature. Next, 2,6dichloropyrazine (0.33 eq, 1.01 g, 6.8 mmol) was added to the red reaction mixture and set to reflux at 85 °C for 2 days. After cooling to room temperature, the unreacted LDA was quenched with ice, and organics were extracted with diethyl ether (1X), then dichloromethane (2X). The extract was dried over anhydrous sodium sulfate, and the solvent was subsequently removed by rotary evaporation. Purification was achieved by silica gel chromatography to give a white powder (2.06 g) in 68% yield. ¹H NMR (CDCl₃, 500 MHz): δ 8.48 (6H, m), 8.43 (4H, br), 8.30 (4H, br s), 2.25 (6H, s). ¹³C NMR (CDCl₃, 125 MHz): δ 159.43 (s), 157.91 (s), 145.10 (s), 143.45 (s), 142.68 (s), 142.05 (s), 56.30 (s), 25.84 (s). HR-ESI-MS (M⁺) m/z calc. [**1** + H⁺], 449.1945, found, 449.1946.

[(PZ5Me₂)Co(OH₂)](OTf)₂, (1-Co)

To a 20 mL scintillation vial was added 0.1 g (0.223 mmol) of PZ5Me₂ (**1**) along with 1 equivalent of Co(CH₃CN)₂(OTf)₂ (0.098 g, 0.223 mmol), which was stored inside of a glove box. Then, 5 mL of a 9:1 acetone:H₂O mixture was added to the vial and the reaction was stirred overnight at room temperature under N₂. The reaction mixture was taken to dryness and re-dissolved in acetone. Ether diffusion affords a pure yellow precipitate in 76% yield (0.140 g). X-ray quality crystals (golden shards) of the complex were grown from slow evaporation of a concentrated acetonitrile solution. Elem. Anal. calc. for $C_{26}H_{22}CoF_6N_{10}O_7S_2$: C, 37.92; H, 2.69; N, 17.01. Found: C, 37.94; H, 2.94; N, 16.99. HR-ESI-MS (M⁺) m/z calc. [(PZ5Me₂)Co(OTf)⁺], 656.0719, found, 656.0714; m/z calc. [(PZ5Me₂)Co²⁺], 253.5597, found, 253.5596.

PZ5Me₂ (1) – ¹H NMR (500 MHz, CDCl₃)



PZ5Me₂ (1) – ¹³C NMR (125 MHz, CDCl₃)



Scheme 1. Line Drawings of Cobalt Complexes with Related PY5Me₂-type Ligands and Pyrazine-Substituted Derivatives, including **1-Co**.



Table 1. Selected Bond Distances of Cobalt Complexes with Related PY5Me₂-type Ligands and Pyrazine-Substituted Derivatives (illustrated in Scheme 1 above).

Complex	Co-N _{ax}	Co-O	avg Co-N _{eq}
1-Co , $[(PZ5Me_2)Co(OH_2)](OTf)_2$ (this work)	2.103(5)	2.010(4)	2.127(5)
[(PY5Me ₂)Co(OH ₂)](OTf) ₂ ref 6	2.103	2.055	2.139
$[(CF_3PY5Me_2)Co(OH_2)](OTf)_2$ ref 6	2.132	2.050	2.129
[(ax-PY4PZMe ₂)Co(OH ₂)](OTf) ₂ ref 7	2.105	2.034	2.142
[(eq-PY4PZMe ₂)Co(OH ₂)](OTf) ₂ ref 7	2.099	2.032	2.127
[(PY3PZ2Me ₂)Co(OH ₂)](OTf) ₂ ref 7	2.094	2.016	2.113

Empirical Formula	$C_{32}H_{31}CoF_6N_{13}O_7S_2$	
Formula Weight	946.75 g/mol	
Т (К)	100(2)	
λ (Å)	1.54178	
Crystal System	Monoclinic	
Space Group	P2(1)/c	
a (Å)	13.9091(7)	
b (Å)	18.0464(9)	
c (Å)	16.7575(8)	
α (°)	90	
β (°)	113.296(2)	
γ (°)	90	
V (Å ³)	3863.4(3)	
Z	4	
$ ho_{calc}$ (g/cm ³)	1.628	
μ (mm ⁻¹)	5.343	
F(000)	1932	
θ range for data collectn	3.46 to 68.33°	
Index ranges	$-11 \le h \le 16, -21 \le k \le 20,$	
	-20 ≤ l ≤ 16	
Reflections collected	30862	
Independent reflections	6876 [R(int) = 0.0653]	
Completeness to θ = 67.00°	98.0%	
Max. and min. transmission	0.4000 and 0.3604	
data/restr/params	6876 / 0 / 563	
GOF on F ²	1.154	
Final R indices $[I > 2\sigma(I)]$	R1 = 0.0671, wR2 = 0.1820	
R indices (all data)	R1 = 0.0747, wR2 = 0.1854	
Largest diff. peak and hole (e Å ⁻³)	0.797 and -0.587	



Figure S1. Cyclic voltammograms of free ligand, PZ5Me₂ (1 mM concentration), in 0.1 M Bu_4NPF_6 CH₃CN with the ferrocene peak included as the internal reference, scan rate = 100 mV/s. The background is shown in black under the same conditions.



Figure S2. Cyclic voltammograms of 1 mM [(PZ5Me₂)Co(OH₂)](OTf)₂ in 0.1 M Bu_4NPF_6 CH₃CN referenced to ferrocene, scan rates = 50 to 1000 mV/s.



Figure S3. Scan rate dependence of cyclic voltammograms shown in Figure S2. **A)** Reductive peak current of Co(II/I) couple versus the square root of scan rate. **B)** Reductive peak current of last reduction versus square root of scan rate.



Figure S4. Scan rate dependence of cyclic voltammograms shown in Figure S2. **A)** Oxidative peak current of most negative redox couple versus the square root of scan rate. **B)** Oxidative peak current of most negative redox couple versus scan rate.



Figure S5. Cyclic voltammograms of 2 mM [(PZ5Me₂)Co(CH₃CN)](OTf)₂ in 0.1 M Bu₄NPF₆ CH₃CN referenced to ferrocene, scan rates = 50 to 1000 mV/s, with glassy carbon working electrode (3 mm dia.). This solution was prepared by metalating **1** with Co(CH₃CN)₂(OTf)₂ in anhydrous CH₃CN and using the crude reaction mixture to form the indicated solution for cyclic voltammetry. HR-ESI-MS (M⁺) m/z calc. [(PZ5Me₂)Co(CH₃CN)²⁺], 274.0730, found, 274.0729. Further characterization was not performed.



Figure S6. $E_{1/2}$ of Co(II/I) couple versus pH for 1 mM **1-Co** in 25 mM KHP buffer, glassy carbon disc (3 mm dia.). A slope of 60 mV/pH unit is observed from cyclic voltammograms shown in Figure 3 of the manuscript.



Figure S7. A) Scan rate dependent cyclic voltammograms of 1 mM **1-Co** in 0.025 M pH 7 KHP buffer with 0.1 M KNO₃, scan rates from 10 to 1000 mV/s, glassy carbon disc working electrode. **B)** Oxidative peak current of first wave plotted versus the square root of scan rate.



Figure S8. Cyclic voltammograms of 1 mM **1-Co** in 25 mM KHP buffer at **A)** pH 3 (red) and **B)** pH 7 (blue) with glassy carbon working electrode, v = 50 mV/s. Successive cycles are shown with the second cycle displayed as a dashed line. The background at each pH is shown in black.



Figure S9. Cyclic voltammograms of 1 mM **1-Co** in 0.1 M pH 2.5 phosphate buffer showing 10 successive, overlaying cycles with a glassy carbon working electrode, v = 100 mV/s. A background CV is shown in black under the same conditions.



Figure S10. Current vs time plot corresponding to evolved H₂ measurement in Figure 4B with (red line) and without (black line) 10 μ M catalyst **1-Co** in 1 M pH 7 phosphate buffer at an applied potential of -1.3 V vs NHE with a Hg pool electrode (A = 12.57 cm²).



Figure S11. Current (A) and charge (B) vs time plots from controlled potential electrolyses with (red line) and without (black line) 10 μ M catalyst **1-Co** in 1 M pH 7 phosphate buffer at an applied potential of -1.4 V vs NHE with a Hg pool electrode (A = 12.57 cm²).



Figure S12. A series of 60-second controlled potential electrolyses at different applied potentials (vs NHE) of 38 μ M **1-Co** in 1 M pH 7 phosphate buffer with Hg pool working electrode. The accumulated charge (in Coulombs) is plotted versus time.



Figure S13. A) Charge build-up versus applied potential, and B) charge build-up versus overpotential for water reduction at pH 7, from controlled potential electrolyses in Figure S11. The thermodynamic potential for H_2O reduction at pH 7 was taken to be -0.414 V vs NHE.



Figure S14. Cyclic voltammograms as different catalyst concentrations of **1-Co** in pH 7 phosphate buffer with a Hg pool working electrode (A = 12.57 cm^2), scan rate = 100 mV/s. A background scan is shown in black.



Figure S15. A) Cyclic voltammograms as different catalyst concentrations of **1-Co** in pH 7 KHP buffer with a glassy carbon working electrode, scan rate = 100 mV/s. The background is shown in black under the same conditions. B) Catalytic current at -0.95 V versus catalyst concentration.

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