Supplementary Information for

Coordination Chemistry of a Model for the GP Cofactor in the Hmd Hydrogenase: Hydrogen-Bonding and Catalysis

by

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General considerations. Unless otherwise indicated, reactions were conducted using standard Schlenk techniques (N_2) at room temperature with stirring. cmhpH_2 was synthesized according to a modification of the literature preparation (given below).[1] The proposed structure was confirmed by ^{1}H NMR. Attempts to prepare cmhpH_2 by the method of Shaw *et al.* were unsuccessful.[2] 2-hydroxypyridine, pyrazole, Et_3N, picolinic acid, 2-pyridylacetic acid hydrochloride, and $AgPF_6$ were purchased from Aldrich. DL-1-phenylethanol was obtained from Alfa-Aesar. Electrospray ionization-mass spectra (ESI-MS) were acquired using a Micromass Quattro QHQ quadrupole-hexapole-quadrupole instrument. ^{1}H NMR was acquired on Varian UNITY INOVATM 500NB and UNITY 500 NB instruments. Elemental analyses were performed by the School of Chemical Sciences Microanalysis Laboratory utilizing a Model CE 440 CHN Analyzer.

cmhpH_2. A solution of 10 mL (79 mmol) ethyl 3-aminocrotonate in 20 mL Et_2O was purged with HCl at 0 ^{o}C. Upon formation of an off-white precipitate, the addition of HCl was stopped. A second 10-mL portion (79 mmol) of ethyl 3-aminocrotonate in 20 mL Et_2O was added, and the combined slurry was thoroughly stirred for 5 min. Ether was removed by vacuum to give a cloudy yellow oil, which was heated at 120 ^{o}C. Crystals formed (presumably NH_4Cl) and the oil thickened. The residue was washed with 40 mL water and 40 mL Et_2O, leaving ~7.6 g of an off-white solid. This solid residue was extracted into a solution of 1.65 g (41 mmol) NaOH in 50 mL of H_2O. The solution was neutralized to pH7 by the addition of HCl, whereupon a colorless precipitate formed. The precipitate was collected by filtration and washed with 30 mL EtOH, leaving white crystals. Yield: 3.52 g (21 mmol) (26%). ^{1}H NMR (500 MHz, DMSO): 2.04 (s, 3H, 4-C*H*$_3$), 3.14 (s, 2H, CO_2CH_2), 5.73 (s, 1H, aryl-C*H*), 5.86 (s, 1H, aryl-C*H*), 12.18 (s, 1H, O*H*) exchanged in D_2O.

Cp*IrCl(cmhpH) (1). A colorless solution of 0.1091 g (0.65 mmol) of cmhpH_2 and 91 μL (0.65 mmol) of Et_3N in 3 mL of MeCN was transferred to an orange solution of 0.260 g (0.32 mmol) of $(Cp^*IrCl_2)_2$ in 2 mL of MeCN. The reaction solution became yellow and a yellow precipitate appeared upon stirring 1 h. The bright yellow powder was collected by filtration and washed with 5 mL cold MeCN and 5 mL Et_2O. Yield: 300 mg (0.57 mmol) (87 %). ^{1}H NMR (500 MHz, CD_2Cl_2): δ1.58 (s, 15 H, Cp*), 2.39 (s, 3H, 4-C*H*$_3$), 3.64 (q, 2H, CO_2CH_2), 6.71 (s, 1H, aryl-C*H*), 6.79 (s, 1H, aryl-C*H*), 9.46 (s, 1H, O*H*) exchanged in D_2O. Anal. Calcd for $C_{18}H_{23}ClIrNO_3$ (found): C, 40.86 (40.64); H, 4.38 (4.27); N, 2.65 (2.80).

Cp*RhCl(cmhpH) (2). This compound was prepared similarly to **1**. Orange powder. Yield: 80%. ^{1}H NMR (500 MHz, CD_2Cl_2): δ1.60 (s, 15 H, Cp*), 2.39 (s, 3H, 4-CH_3), 3.67 (q, 2H, CO_2CH_2), 6.68 (s, 1H, aryl-CH), 6.78 (s, 1H, aryl-CH), 9.83 (s, 1H, O*H*) exchanged in D_2O. Anal. Calcd for $C_{18}H_{23}ClNO_3Rh$ (found): C, 49.16 (48.96); H, 5.27

(5.27); N, 3.19 (3.37). Single crystals of **2** suitable for X-ray diffraction were obtained by diffusion of Et_2O into a concentrated solution of **2** in MeOH.

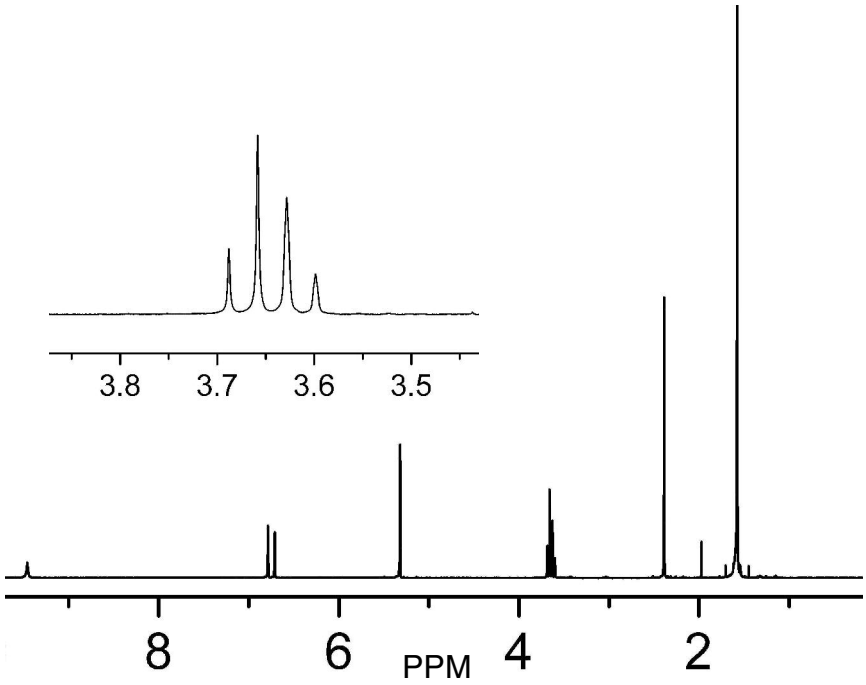

Figure 1. ^{1}H NMR spectrum of Cp*IrCl(cmhpH) in CD_2Cl_2 solution (inset: Methylene signals showing bound chelate ring).

Cp*IrCl(paa), (3) paaH = 2-pyridylacetic acid. A mixture of 199 mg (0.25 mmol) of $(Cp^*IrCl_2)_2$, 86.8 mg (0.50 mmol) of paaH·HCl, and 69.1 mg (0.50 mmol) K_2CO_3 was stirred in 10 mL of 1:1 MeOH:H_2O for 45 min. by which time the orange color disappeared. Upon concentrating the solution to 2 mL, a yellow precipitate appeared. The solid was collected by filtration and washed with 5 mL Et_2O. Yield: 191 mg (0.383 mmol, 77 %). ^{1}H NMR (500 MHz, CD_2Cl_2): δ1.58 (s, 15 H, Cp*), 3.61 (d, 1H, 14.7 Hz, $CO_2CH\mathit{H}$), 3.77 (d, 1H, 14.7 Hz, $CO_2C\mathit{H}H$), 7.31 (d of t, 1H, 0.8 Hz, 6 Hz, NCHC*H*), 7.35 (d, 1H, 8 Hz, NCC*H*), 7.76 (d of t, 1H, 2 Hz, 8 Hz, NCCC*H*), 8.69 (d of d, 1H, 1 Hz, 6 Hz, NC*H*). Anal. Calcd for $C_{17}H_{21}ClIrNO_2$ (found): C, 40.92 (40.78); H, 4.24 (3.92); N, 2.81 (2.79).

Cp*IrCl(pa), (4) (paH = picolinic acid). A mixture of 79.7 mg (0.10 mmol) of $(Cp^*IrCl_2)_2$, 24.6 mg (0.10 mmol) of paH, and 27.6 mg (0.10 mmol) K_2CO_3 was stirred in 8 mL of 1:1 MeOH:H_2O for 45 min. (until orange color disappeared). The solution was concentrated to 2 mL under vacuum with formation of a yellow precipitate. The solid was collected by filtration and washed with 5 mL Et_2O. Yield: 74 mg (0.153 mmol, 76 % yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ1.70 (s, 15 H, Cp*), 7.55 (d of t, 1H, 1.5 Hz, 5.5 Hz, NCHC*H*), 7.94 (d of t, 1H, 1.4 Hz, 8 Hz, NCCC*H*), 8.13 (d of d, 1H, 0.7 Hz, 8 Hz, NCC*H*), 8.69 (d of d, 1H, 0.6 Hz, 5 Hz, NC*H*). Anal. Calcd for $C_{16}H_{19}ClIrNO_2$ (found): C, 39.62 (39.40); H, 3.95 (3.81); N, 2.89 (2.84).

General Procedure for Treatment of Cp*RhCl(cmhpH), Cp*IrCl(cmhpH), Cp*IrCl(paa), and Cp*IrCl(pa) with $AgPF_6$ in D_2O. 10 mg (0.023 mmol) Cp*RhCl(cmhpH) was dissolved 0.7 mL D_2O in an NMR tube. ^1H NMR was obtained. 6.3 mg (0.025 mmol) $AgPF_6$ was added and a white precipitate formed immediately. ^1H NMR was obtained.

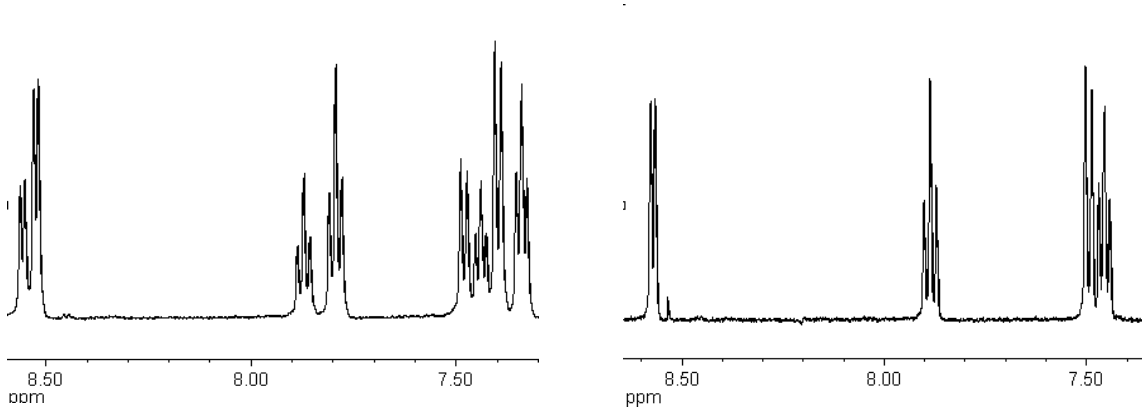

Figure 2. (left) ^1H NMR spectrum of Cp*IrCl(paa) in D_2O solution before (right) and after (left) addition of $AgPF_6$.

[Cp*Rh(MeCN)(cmhpH)][PF_6]. A solution of 114 mg (0.45 mmol) of $AgPF_6$ in 8 mL MeCN was added to a mixture of 200 mg (0.45 mmol) **2** in 3 mL MeCN. A white precipitate formed immediately. The orange solution was filtered and solvent removed by vacuum. Orange microcrystals were obtained by recrystallization from 2 mL MeCN and 10 mL of a 1:1 Et_2O: hexanes mixture. Solid was dried by vacuum. Yield: 222 mg (0.38 mmol) (85%). ^1H NMR (500 MHz, CD_3CN): δ1.625 (s, 15 H, Cp*), 1.737 (s, 3H, CH_3CN) exchanged with CD_3CN, 2.324 (s, 3H, 4-CH_3), 3.53 (d, broad, 2H, CO_2CH_2), 6.737 (s, 1H, aryl-CH), 6.797 (s, 1H, aryl-CH). ESI-MS: m/z = 445.3 ([Cp*Rh(MeCN)(cmhpH)]$^+$), 404.3([Cp*Rh(cmhpH)]$^+$), 401.3([Cp*Rh(MeCN)(cmhpH-CO_2)]$^+$), 360.3([Cp*Rh(cmhpH-CO_2)]$^+$).

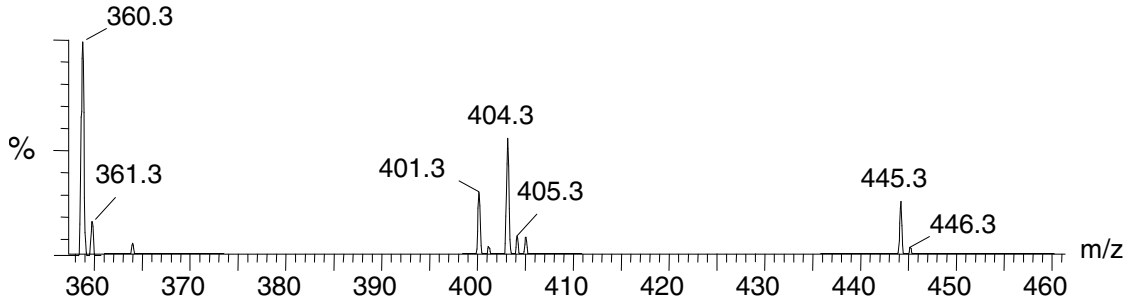

Figure 3. ESI-MS of Cp* Rh(MeCN)(cmhpH) in MeCN solution showing signals due to fragmentation by loss of CO_2 and MeCN.

Cp*Rh(hp)(cmhpH)·1.5 MeCN (5). A solution of 19.3 mg (0.20 mmol) of 2-hydroxypyridine and 28 µL (0.20 mmol) of Et_3N in 5 mL of CH_2Cl_2 was transferred to an orange solution of 90 mg (0.20 mmol) of **2** in 3 mL CH_2Cl_2. The solution darkened and was stirred 10 min. Et_3NHCl was removed by extraction with water 3 x 3 mL (under

vigorous mixing all products dissolve in water layer). The organic phase was evaporated, and the product was extracted into 1 mL MeCN, and this extract was diluted with 10 mL of a 1:1 Et_2O/hexanes and stored at -20 ^{O}C for 24 h. Solvent was decanted from the red crystals (some of which were suited for X-ray diffraction). Yield: 50.3 mg (0.20 mmol, 50 %). ^{1}H NMR (500 MHz, CD_2Cl_2): δ1.46 (s, 15 H, Cp*), 2.16 (s, 3H, 4-CH_3), 3.50 (d, 1H, 15 Hz, CO_2CH*H*), 3.55 (d, 1H, 15 Hz, CO_2C*H*H), 6.30 (s, 1H, cmhpH-aryl-CH), 6.34 (s, 1H, cmhpH-aryl-CH), 6.61 (d of t, 1H, 6 Hz, 1 Hz, hp-NCC*H*), 6.68 (d, 1H, 8 Hz, hp-NCOC*H*), 7.461 (d of t, 1H, 7 Hz, 2 Hz, hp-NCOCC*H*), 8.32 (d, 1H, 5 Hz, hp-NC*H*) 17.1 (s, 1H, O*H*···O; this signal disappeared upon addition of D_2O).

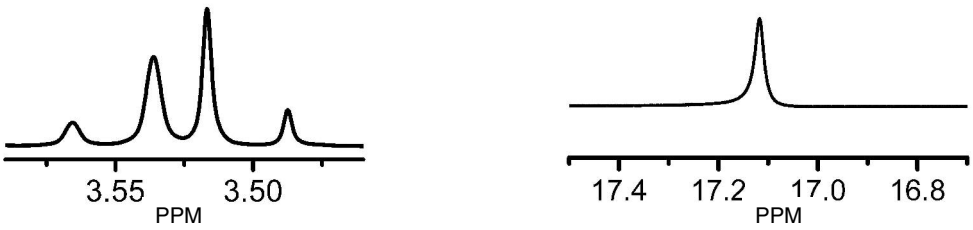

Figure 4. From the ^{1}H NMR spectrum of Cp*Rh(hp)(cmhpH) in CD_2Cl_2 solution: methylene signals (left) and shared proton between 2-hp and cmhpH (right).

Cp*Rh($C_3H_3N_2$)(cmhpH) (6). A solution of 8.5 mg (0.128 mmol) of pyrazole and 18 µL (0.128 mmol) of Et_3N in 5 mL of CH_2Cl_2 was transferred to an orange solution of 56.4 mg (0.128 mmol) of **2** in 5 mL CH_2Cl_2. After stirring for 30 min. the solution was extracted three times with 5 mL water. Solvent was removed by vacuum, and the product was extracted into ~1mL CH_2Cl_2. The product precipitated from solution upon addition of 10 mL 1:1 Et_2O/hexanes. Yield: 28 mg (0.059 mmol, 46 %). ^{1}H NMR (500 MHz, CD_2Cl_2): δ1.52 (s, 15 H, Cp*), 2.12 (s, 3H, 4-CH_3), 3.32 (d, 1H, 14 Hz, CO_2CH*H*), 3.55 (d, 1H, 14 Hz, CO_2C*H*H), 6.07 (s, 1H, cmhpH-aryl-C*H*), 6.15 (d, 1H, 1 Hz, cmhpH-aryl-C*H*), 6.39 (q, 1H, 2Hz, pyrazolate-CC*H*C), 7.61 (d, 1H, 1 Hz, pyrazolate-NC*H*), 7.67 (s, 1H, pyrazolate-NC*H*), 16.3 (s, 1H, O*H*···O; this signal disappeared upon addition of D_2O).

Dehydrogenation of 1-Phenylethanol. In a typical procedure, a mixture of 3.4 mg (0.0060 mmol) of Cp*IrCl(cmhpH) in 725 µL (6.00 mmol) DL-1-phenylethanol was heated by oil bath at 130 ^{o}C. After 2 h, 50 µL of reaction mixture was removed, diluted with $CDCl_3$ and the ratio of PhCOMe/PhCHOHMe was analyzed by ^{1}H NMR spectroscopy.

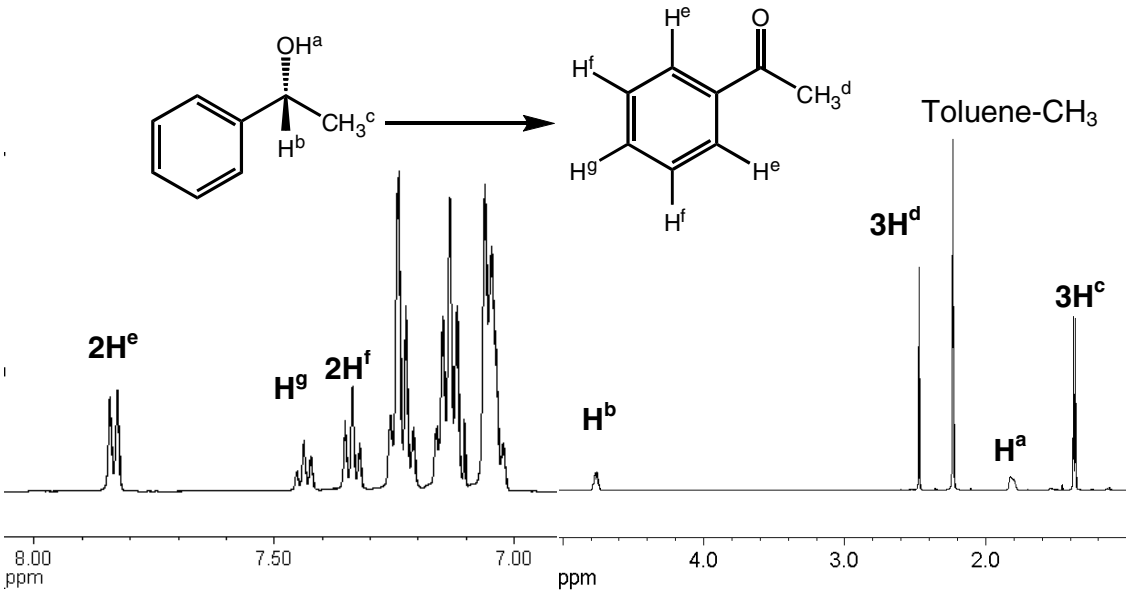

Figure 5. Illustrative ^{1}H NMR spectrum of products from dehydrogenation of 1-phenylethanol ($CDCl_3$ solution).

1. Collie, J. N. *J. Chem. Soc.* **1897**, *71*, 299-311
2. Ahmed, S.; Lofthouse, R.; Shaw, G. *J. Chem. Soc.* **1976**, *71*, 1969-1975