Supplementary Information for

β-Turn-Structure-Assembled Palladium Complexes by Complexation-Induced Self-Organization of Ferrocene-Dipeptide Conjugates

Toshiyuki Moriuchi,* Takashi Fujiwara, and Toshikazu Hirao*

Department of Applied Chemistry, Graduate School of Engineering, Osaka University, Yamada-oka, Suita, Osaka 565-0871, Japan

hirao@chem.eng.osaka-u.ac.jp

General Methods.

All reagents and solvents were purchased from commercial sources and were further purified by the standard methods, if necessary. Melting points were determined on a Yanagimoto Micromelting Point Apparatus and were uncorrected. Infrared spectra were obtained with a JASCO FT/IR-480 Plus spectrometer. ^{1}H NMR spectra were recorded on a JEOL JNM-ECP 400 (400 MHz) spectrometer with tetramethylsilane as an internal standard. Mass spectra were run on a JEOL JMS-700 mass spectrometer.

Dipeptide derivatives were prepared according to the method reported in a previous paper by coupling of Boc-Ala-Pro-OH with 4-aminopyridine using EDCI (Moriuchi, T.; Yoshida, K.; Hirao, T. *Organometallics* **2001**, *20*, 3101-3105.). (Chlorocarbonyl)ferrocene was prepared according to the literature method (Knobloch, F. W.; Rauscher, W. H. *J. Polymer Sci.* **1961**, *54*, 651-656.).

General Procedure for Synthesis of Ferrocenes 1 and 2 Bearing One Heterochoral Dipeptide Chain.

To a stirred solution of Boc-Ala-Pro-NHPy (544 mg, 1.50 mmol) in methanol (15 mL) was added 30 mL of 1.0 M HCl/diethyl ether under argon at room temperature, and the mixture was stirred for 10 h. The solvent was removed in vacuo and the resulting residue was washed three times with anhydrous diethyl ether to give H-Ala-Pro-NHPy hydrochloric acid. To a stirred mixture of the thus-obtained H-Ala-Pro-NHPy hydrochloric acid, 4-dimethylaminopyridine (12.0 mg, 0.098 mmol) and triethylamine (1.0 mL, 7.2 mmol) in dichloromethane (30 mL) was dropwise added the solution of (chlorocarbonyl)ferrocene (437 mg, 1.76 mmol) in dichloromethane (10 mL) under argon at 0 °C. The mixture was stirred at 0 °C for 1 h and then at room temperature for 11 h. The resulting mixture was diluted with dichloromethane, washed with saturated $NaHCO_3$ aqueous solution and brine, and then dried over Na_2SO_4. The solvent was evaporated in vacuo and the residue was chromatographed on alumina column eluting with 5% methanol/95% ethyl acetate. The ferrocene **1** or **2** was isolated by recrystallization from dichloromethane-hexane.

1: yield 66%; mp 235-237 °C (decomp.); IR (CH_2Cl_2, 2.0 x 10^{-2} M) 3442, 3310, 3033, 2982, 1697, 1684, 1653, 1636, 1589, 1516 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 2.0 x 10^{-2} M) δ 9.15 (s, 1H), 8.53 (d, 2H, J = 6.5 Hz), 7.85 (d, 2H, J = 6.5 Hz), 6.23 (d, 1H, J = 5.8 Hz), 4.78-4.76 (m, 1H), 4.70-4.69 (m, 1H), 4.66-4.58 (m, 2H), 4.38-4.34 (m, 2H), 4.17-4.07 (m, 6H), 3.63-3.56 (m, 1H), 2.49-2.43 (m, 1H), 2.22-2.06 (m, 3H), 1.45 (d, 3H, J = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 2.0 x 10^{-2} M) 172.8, 172.4, 170.6, 150.5, 145.2, 114.5, 73.6, 71.1, 71.0, 69.8, 68.9, 67.5, 61.5, 47.9, 47.3, 29.2, 24.4, 16.2 ppm; FAB-MS *m/z* 474 (M^+); Anal. Calcd. for $C_{24}H_{26}N_4O_3Fe \bullet 0.25H_2O$: C, 60.20; H, 5.58; N, 11.70. Found: C, 60.30; H, 5.62; N, 11.55.

2: yield 45%; mp 235-237 °C (decomp.); IR (CH_2Cl_2, 2.0 x 10^{-2} M) 3442, 3310, 3033, 2982, 1697, 1684, 1653, 1636, 1589, 1516 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 2.0 x 10^{-2} M) δ 9.15 (s, 1H), 8.53 (d, 2H, J = 6.5 Hz), 7.85 (d, 2H, J = 6.5 Hz), 6.23 (d, 1H, J =

5.8 Hz), 4.78-4.76 (m, 1H), 4.70-4.69 (m, 1H), 4.66-4.58 (m, 2H), 4.38-4.34 (m, 2H), 4.17-4.07 (m, 6H), 3.63-3.56 (m, 1H), 2.49-2.43 (m, 1H), 2.22-2.06 (m, 3H), 1.45 (d, 3H, J = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 2.0 x 10^{-2} M) 172.8, 172.4, 170.6, 150.5, 145.2, 114.5, 73.6, 71.1, 71.0, 69.8, 68.9, 67.5, 61.5, 47.9, 47.3, 29.2, 24.4, 16.2 ppm; FAB-MS *m/z* 474 (M^+); Anal. Calcd. for $C_{24}H_{26}N_4O_3Fe \bullet 0.25H_2O$: C, 60.20; H, 5.58; N, 11.70. Found: C, 60.15; H, 5.58; N, 11.76.

General Procedure for Preparation of Palladium Complexes 3 and 4

To a stirred solution of the ferrocene-dipeptide conjugate **1** or **2** (75.9 mg, 1.60 mmol) in acetonitrile (35 mL) was dropwise added the solution of $[Pd(MeCN)_4](BF_4)_2$ (17.7 mg, 0.40 mmol) in acetonitrile (5 mL) under argon at room temperature. The mixture was stirred at room temperature for 12 h. After evaporation of the solution, the palladium complex **3** or **4** was quatitatively isolated, respectively, by recrystallization from acetonitrile-ether.

3: mp 232-235 °C (uncorrected); IR (CH_3CN, 1.0 x 10^{-3} M) 3385, 3277, 3095, 2995, 1700, 1661, 1653, 1628, 1616, 1588, 1521 cm^{-1}; ^{1}H NMR (400 MHz, CD_3CN, 1.0 x 10^{-3} M) δ9.52 (s, 1H), 8.70 (d, 2H, J = 7.3 Hz), 8.20 (d, 2H, J = 7.3 Hz), 6.98 (d, 1H, J = 4.8 Hz), 4.77-4.76 (m, 1H), 4.68-4.66 (m, 1H), 4.50-4.41 (m, 2H), 4.38-4.37 (m, 1H), 4.35-4.33 (m, 1H), 3.94-3.86 (m, 6H), 3.68-3.62 (m, 1H), 2.31-2.22 (m, 1H), 2.06-1.97 (m, 3H), 1.37 (d, 3H, J = 7.0 Hz); ^{13}C NMR (100 MHz, CD_3CN, 0.1 x 10^{-2} M) 173.9, 173.7, 173.2, 152.3, 150.1, 117.8, 75.0, 72.1, 71.8, 70.5, 70.2, 68.9, 62.7, 49.6, 48.3, 30.6, 25.4, 15.8 ppm; FAB-MS *m/z* 2089 ($(M\text{-}BF_4)^+$); Anal. Calcd. for $C_{96}H_{104}N_{16}O_{12}B_2F_8Fe_4Pd$: C, 52.96; H, 4.81; N, 10.29. Found: C, 52.89; H, 5.07; N, 10.46.

4: mp 232-235 °C (uncorrected); IR (CH_3CN, 1.0 x 10^{-3} M) 3385, 3277, 3095, 2995, 1700, 1661, 1653, 1628, 1616, 1588, 1521 cm^{-1}; ^{1}H NMR (400 MHz, CD_3CN, 1.0 x 10^{-3} M) δ9.52 (s, 1H), 8.70 (d, 2H, J = 7.3 Hz), 8.20 (d, 2H, J = 7.3 Hz), 6.98 (d, 1H, J = 4.8 Hz), 4.77-4.76 (m, 1H), 4.68-4.66 (m, 1H), 4.50-4.41 (m, 2H), 4.38-4.37 (m, 1H), 4.35-4.33 (m, 1H), 3.94-3.86 (m, 6H), 3.68-3.62 (m, 1H), 2.31-2.22 (m, 1H), 2.06-1.97 (m,

3H), 1.37 (d, 3H, J = 7.0 Hz); ^{13}C NMR (100 MHz, CD_3CN, 0.1 x 10^{-2} M) 173.9, 173.7, 173.2, 152.3, 150.1, 117.8, 75.0, 72.1, 71.8, 70.5, 70.2, 68.9, 62.7, 49.6, 48.3, 30.6, 25.4, 15.8 ppm; FAB-MS *m/z* 2089 ($(M\text{-}BF_4)^+$); Anal. Calcd. for $C_{96}H_{104}N_{16}O_{12}B_2F_8Fe_4Pd$: C, 52.96; H, 4.81; N, 10.29. Found: C, 52.69; H, 5.03; N, 10.62.

Proton Magnetic Resonance Nuclear Overhauser Effect Measurements.

A sample was prepared under argon. Nuclear Overhauser effect experiments were performed with 2 second irradiation of a freeze-pump-thaw degassed 2.0 x 10^{-2} M solution ($CDCl_3$) for **1** and 1.0 x 10^{-3} M solution (CD_3CN) for **3**. The 400 MHz ^{1}H NMR spectra were recorded at 25 °C. Nuclear Overhauser enhancements were obtained by saturation of the desired resonance. Irradiation of the pyridyl proton at the 2-position of **1** enhanced the Cp protons (Figure S1) and irradiation of the pyridyl proton at the 3-position enhanced the Cp protons (Figure S2). Irradiation of the pyridyl proton at the 2-position of **3** enhanced the Cp protons (Figure S3) and irradiation of the pyridyl proton at the 3-position enhanced the Cp protons (Figure S4).

CD Measurements.

CD spectra were recorded using a JASCO J-720 spectropolarimeter in an deaerated acetonitrile solution with the concentration 1.0 x 10^{-4} M for **1** and **2**, and 0.25 x 10^{-4} M for **3** and **4** under argon at 25 °C (Figure S5).

Electrochemical Experiments.

The cyclic voltammetry was performed on a BAS CV-50W voltammetry analyzer in a deaerated acetonitrile solution ([**1** or **2**] = 5.0 x 10^{-4} M and [**3** or **4**] = 1.25 x 10^{-4} M) containing 0.1 M Bu_4NBF_4 as a supporting electrolyte at 298 K with a three-electrode system consisting of a platinum working electrode (BAS), a platinum auxiliary electrode (BAS), and an Ag/Ag^+ (0.01 M) reference electrode (BAS) at 100 mV/s scan rate. Redox potentials are given vs Fc/Fc^+.

X-ray Structure Analysis.

All measurements for **1**-**4** were made on a Rigaku RAXIS-RAPID Imaging Plate diffractometer with graphite monochromated Mo Kα radiation. The structures of **1**-**4** were solved by direct methods and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. In the case of **1** and **2**, the H atoms involved in hydrogen bonding were located in electron density maps and the remainder of the H atoms were placed in idealized positions and allowed to ride with the C atoms to which each was bonded. The H atoms of **3** and **4** were placed in idealized positions and allowed to ride with the C atoms to which each was bonded. Crystallographic details are given in Table S1. Hydrogen bonds and selected torsion angles are listed in Table S2 and S3, respectively. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-674718 for **1**, CCDC-674719 for **2**, CCDC-674720 for **3**, and CCDC-674721 for **4**. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

Table S1. Crystallographic Data for **1-4**

	1	**2**	**3**	**4**
formula	$C_{24}H_{26}N_4O_3Fe \bullet CH_2Cl_2$	$C_{24}H_{26}N_4O_3Fe \bullet CH_2Cl_2$	$C_{96}H_{104}N_{16}O_{12}B_2F_8Fe_4Pd$	$C_{96}H_{104}N_{16}O_{12}B_2F_8Fe_4Pd$
formula weight	559.27	559.27	2177.37	2177.37
crystal system	monoclinic	monoclinic	monoclinic	monoclinic
space group	$P2_1$ (No. 4)	$P2_1$ (No. 4)	$P2_1$ (No. 4)	$P2_1$ (No. 4)
a, Å	10.2028(4)	10.2083(6)	14.6365(1)	14.7270(5)
b, Å	9.6738(4)	9.6645(8)	24.1369(2)	23.8008(8)
c, Å	12.9507(8)	12.949(1)	16.8830(1)	16.7659(5)
β, deg	93.389(2)	93.298(1)	107.4305(8)	107.4267(9)
V, Å^3	1276.0(1)	1275.4(2)	5690.53(7)	5606.9(3)
Z	2	2	2	2
D_{calcd}, g cm^{-3}	1.456	1.456	1.271	1.290
μ(Mo Kα), cm^{-1}	8.34	8.34	7.24	7.35
T, °C	4	4	4	4
λ(Mo Kα), Å	0.71069	0.71069	0.71069	0.71075
Flack parameter	0.01(2)	0.01(2)	-0.01(2)	0.021(17)
$R1$ [a]	0.046	0.051	0.084	0.070
$wR2$ [b]	0.125	0.146	0.239	0.225

[a] $R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. [b] $wR2 = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$.

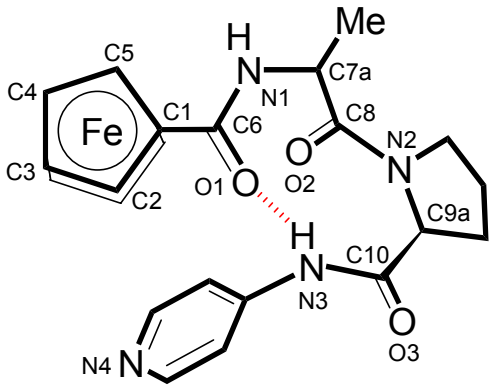

Table S2. Hydrogen Bonds for **1-4**

crystal	type [a]	donor	acceptor	D • • • A (Å)	D–H • • • A (°)
1	intra	N(3)	O(1)	3.038(3)	157(1)
2	intra	N(3)	O(1)	3.039(3)	159(2)
3	intra	N(3A)	O(1A)	2.947(8)	150.3
	intra	N(3B)	O(1B)	2.989(9)	156.5
	intra	N(3C)	O(1C)	2.862(11)	151.5
	intra	N(3D)	O(1D)	2.899(8)	150.7
	inter	N(1C)	O(2D)[1) b]	2.819(13)	147.9
	inter	N(1D)	O(2B)[2) b]	2.993(8)	170.5
	inter	N(1C)[3) b]	O(2D)	2.819(13)	147.9
	inter	N(1D)[4) b]	O(2B)	2.993(8)	170.5
4	intra	N(3A)	O(1A)	2.992(6)	153.0
	intra	N(3B)	O(1B)	2.995(7)	157.3
	intra	N(3C)	O(1C)	2.820(9)	153.5
	intra	N(3D)	O(1D)	2.896(6)	152.6
	inter	N(1C)	O(2D)[1) b]	2.797(12)	147.7
	inter	N(1D)	O(2B)[2) b]	3.013(6)	168.9
	inter	N(1C)[3) b]	O(2D)	2.797(12)	147.7
	inter	N(1D)[4) b]	O(2B)	3.013(6)	168.9

[a] inter: intermolecular, intra: intramolecular. [b] Each molecule is connected to four neighboring molecules through hydrogen bonds.

Table S3. Torsion Angles (deg) for **1-4**

	angle [a]	**1**	**2**	**3**	**4**
ϕ_{A2}	C(6A)-N(1A)-C(7AA)-C(8A)	-57.0(3)	57.6(4)	-55.8(7)	56.3(6)
ψ_{A2}	N(1A)-C(7AA)-C(8A)-N(2A)	125.7(3)	-126.5(3)	129.2(6)	-129.2(5)
ω_{A2}	C(7AA)-C(8A)-N(2A)-C(9AA)	176.0(3)	-176.2(3)	175.7(7)	-176.8(5)
ϕ_{A3}	C(8A)-N(2A)-C(9AA)-C(10A)	68.9(4)	-68.3(4)	60.4(9)	-55.5(7)
ψ_{A3}	N(2A)-C(9AA)-C(10A)-N(3A)	16.8(4)	-16.8(5)	21.3(9)	-25.7(7)
ϕ_{B2}	C(6B)-N(1B)-C(7BA)-C(8B)			-56.3(8)	57.5(7)
ψ_{B2}	N(1B)-C(7BA)-C(8B)-N(2B)			134.6(6)	-134.7(5)
ω_{B2}	C(7BA)-C(8B)-N(2B)-C(9BA)			176.5(6)	-177.0(4)
ϕ_{B3}	C(8B)-N(2B)-C(9BA)-C(10B)			75.1(9)	-74.8(7)
ψ_{B3}	N(2B)-C(9BA)-C(10B)-N(3B)			5.5(11)	-6.0(9)
ϕ_{C2}	C(6C)-N(1C)-C(7CA)-C(8C)			48.1(17)	-48.4(14)
ψ_{C2}	N(1C)-C(7CA)-C(8C)-N(2C)			45(2)	-44.2(17)
ω_{C2}	C(7CA)-C(8C)-N(2C)-C(9CA)			175.7(15)	-177.3(11)
ϕ_{C3}	C(8C)-N(2C)-C(9CA)-C(10C)			69.4(18)	-68.9(13)
ψ_{C3}	N(2C)-C(9CA)-C(10C)-N(3C)			11.4(15)	-11.4(11)
ϕ_{D2}	C(6D)-N(1D)-C(7DA)-C(8D)			-54.7(9)	55.1(7)
ψ_{D2}	N(1D)-C(7DA)-C(8D)-N(2D)			132.0(6)	-131.4(5)
ω_{D2}	C(7DA)-C(8D)-N(2D)-C(9DA)			173.1(5)	-174.7(4)
ϕ_{D3}	C(8D)-N(2D)-C(9DA)-C(10D)			72.7(9)	-69.6(7)
ψ_{D3}	N(2D)-C(9DA)-C(10D)-N(3D)			9.0(12)	-13.2(10)

[a] Symbol used for torsion angles in peptides (IUPAC–IUB Commission on Biochemical Nomenclature).

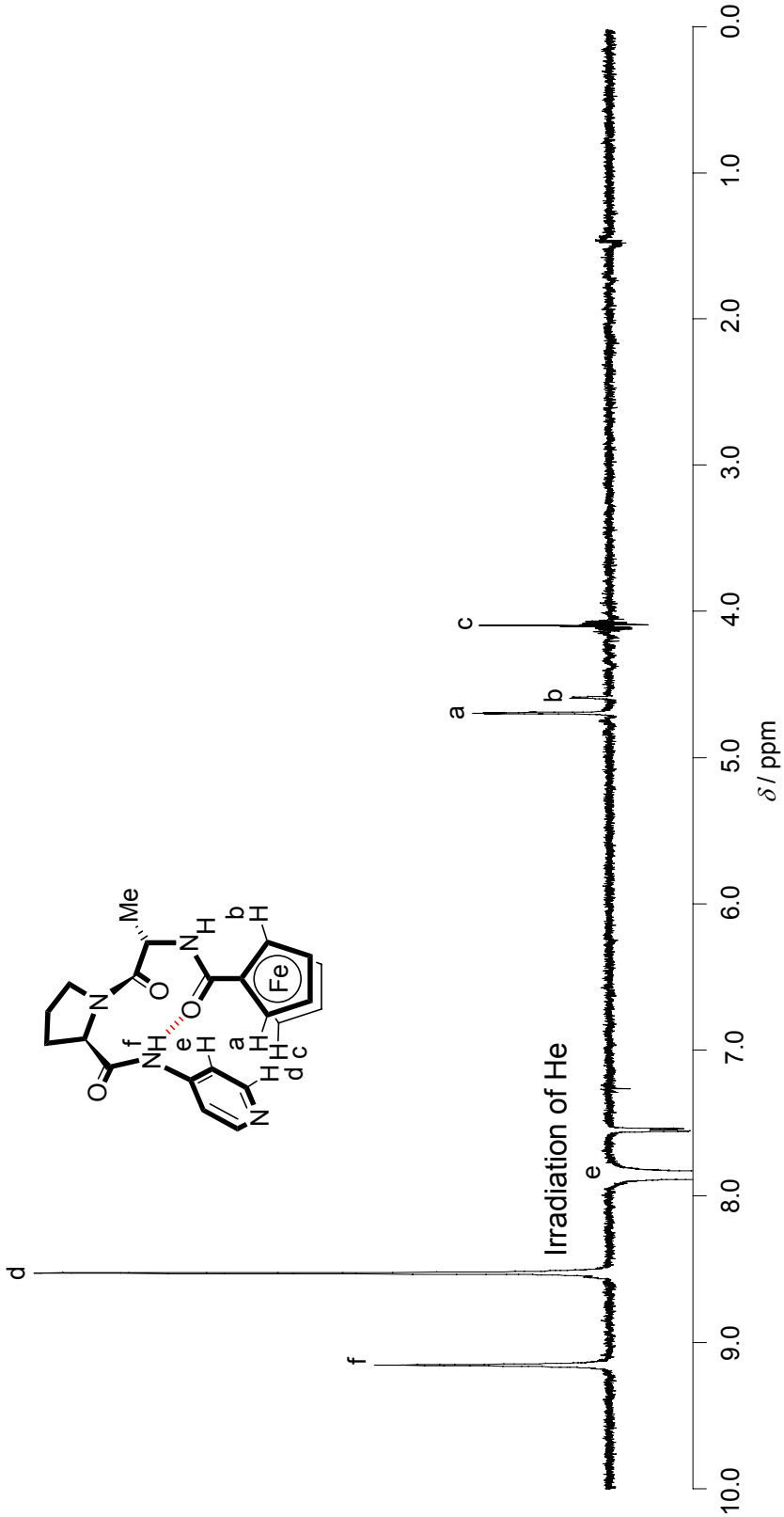

Figure S1. 400 MHz ^{1}H NMR difference NOE experiment performed at 25 °C with 2 second irradiation of a freeze-pump-thaw degassed 2.0 x 10^{-2} M solution of **1** in $CDCl_3$.

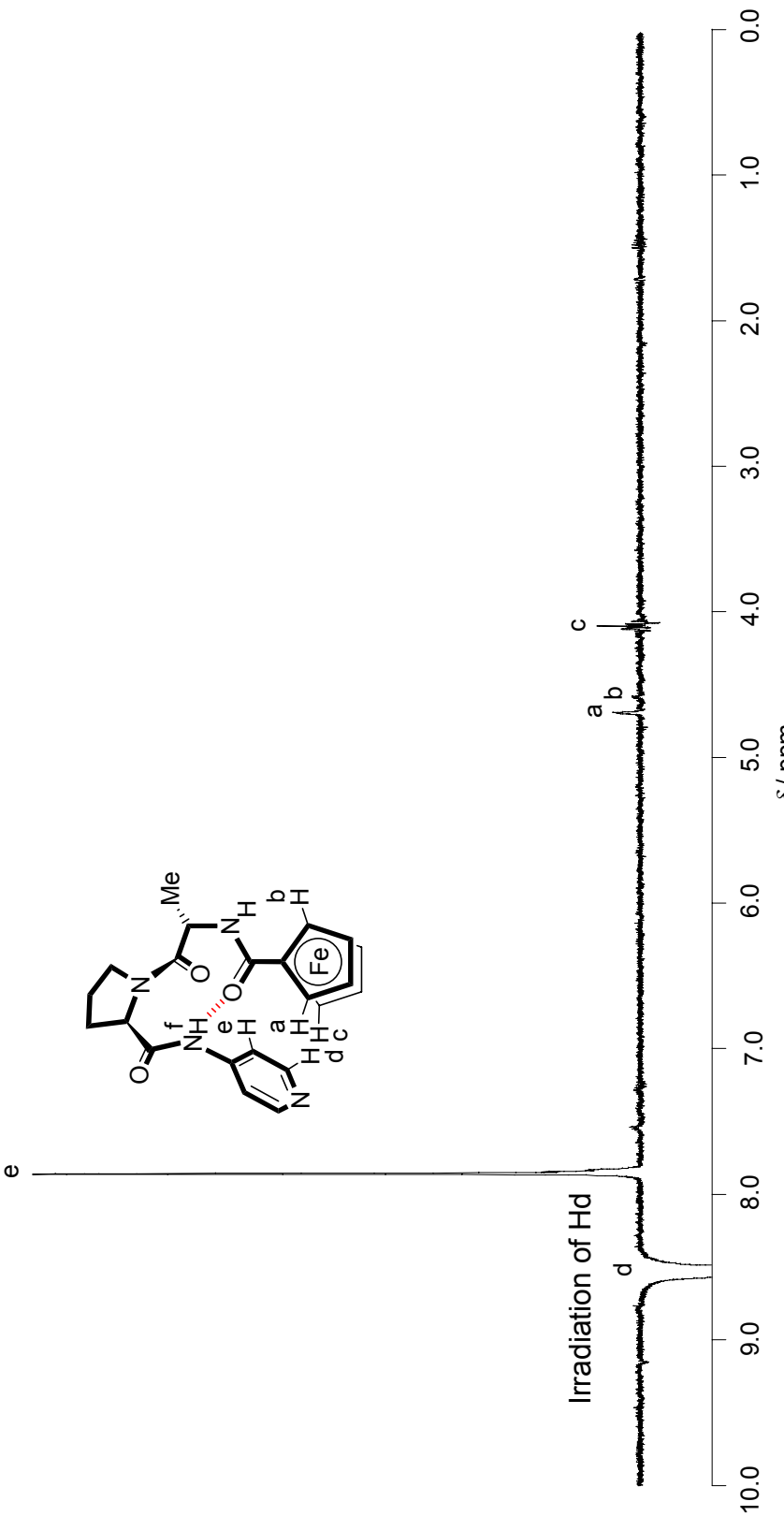

Figure S2. 400 MHz ^{1}H NMR difference NOE experiment performed at 25 °C with 2 second irradiation of a freeze-pump-thaw degassed 2.0 x 10^{-2} M solution of **1** in $CDCl_3$.

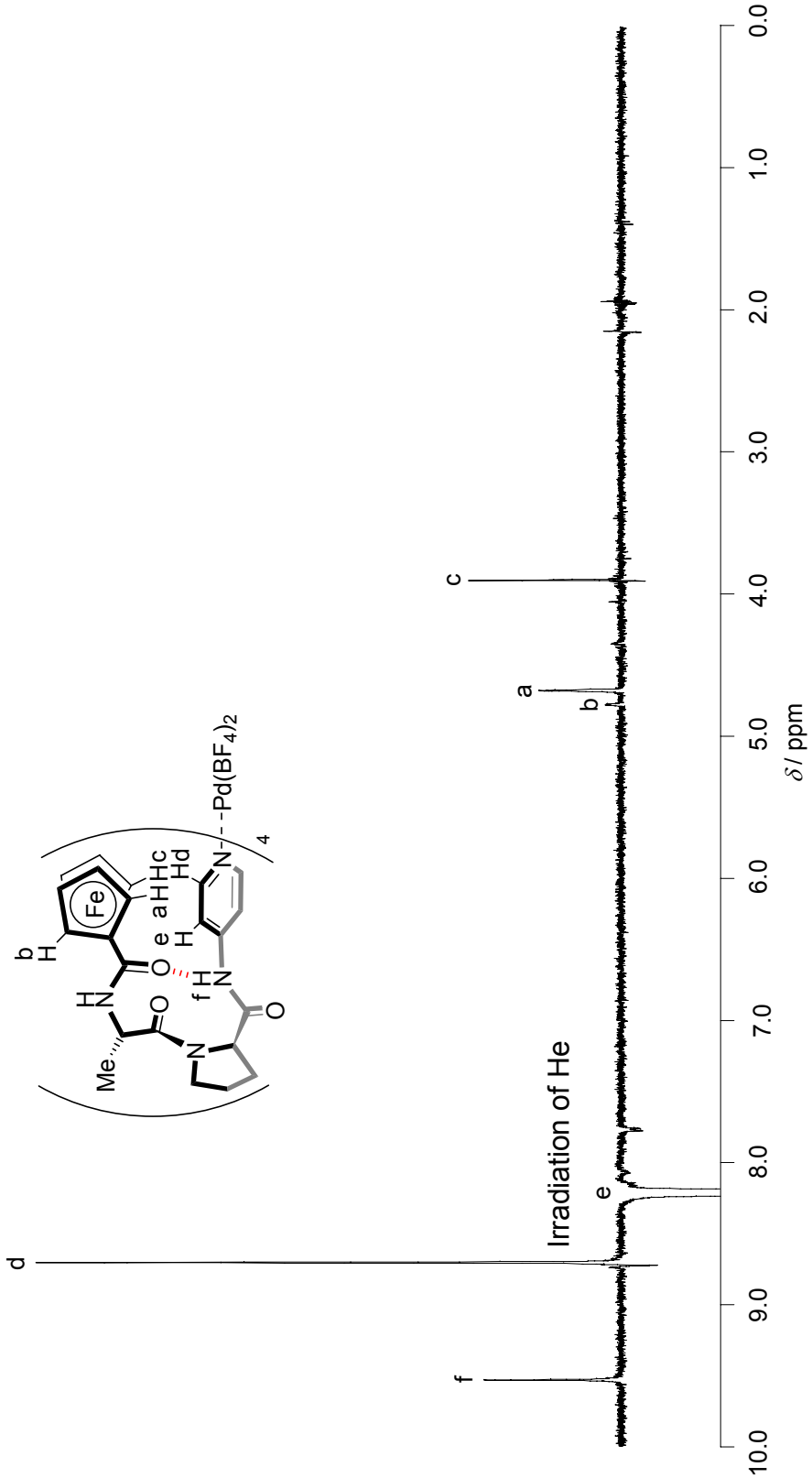

Figure S3. 400 MHz ^{1}H NMR difference NOE experiment performed at 25 °C with 2 second irradiation of a freeze-pump-thaw degassed 1.0 x 10^{-3} M solution of **3** in $CDCl_3$.

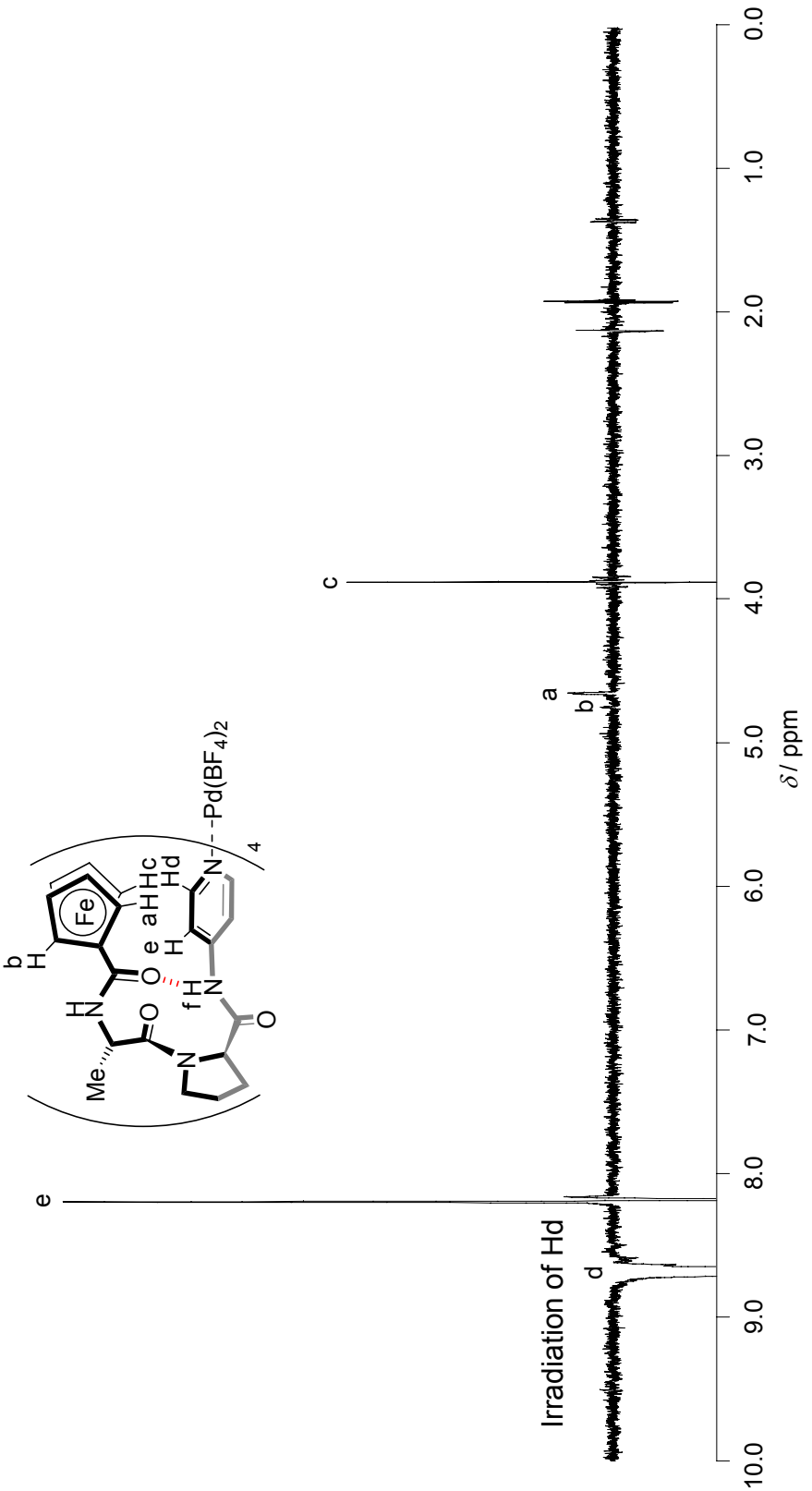

Figure S4. 400 MHz ^{1}H NMR difference NOE experiment performed at 25 °C with 2 second irradiation of a freeze-pump-thaw degassed 1.0 x 10^{-3} M solution of **3** in $CDCl_3$.

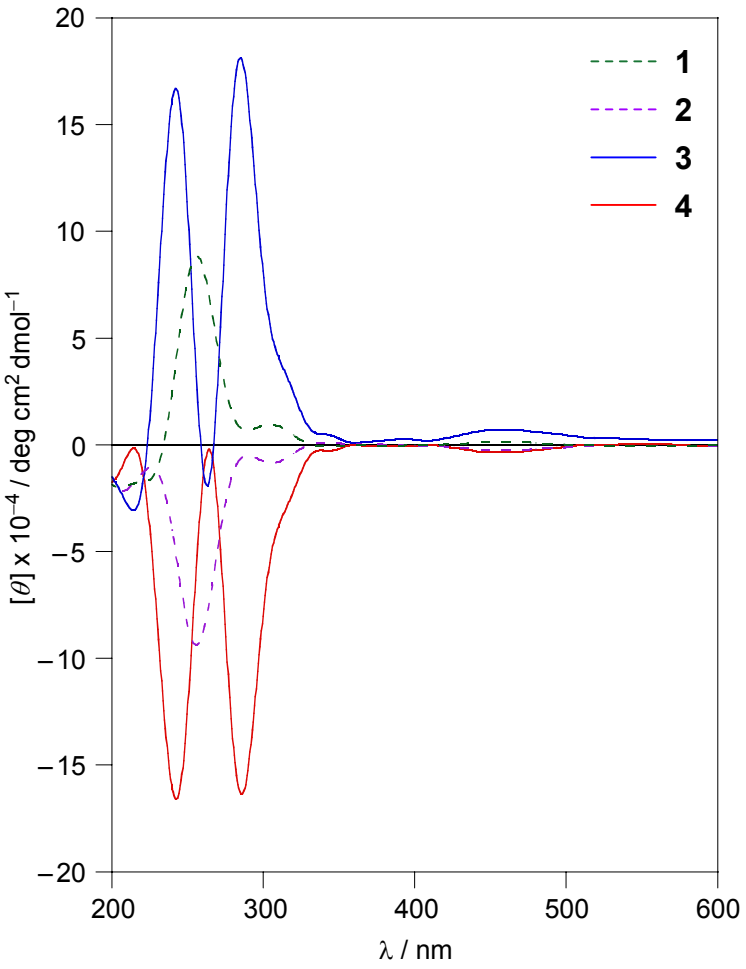

Figure S5. CD spectra of **1**-**4** in acetonitrile (**1** and **2**, 1.0 x 10^{-4} M; **3** and **4**, 0.25 x 10^{-4} M).