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Supplementary Information

Functionalized Rhodium Intercalators for DNA Recognition

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Synthesis of Ligands. *4-carboxaldehyde-1,10-phenanthroline (1).* This compound was prepared using a variation of the procedure described in reference 28 such that 4-methyl-1,10-phenanthroline (8.2 g, 42.2 mmole) was used as a starting material. The product was isolated by filtering the hot reaction through celite. The celite was washed with 100 mL of absolute ethanol, and the ethanol wash was combined with the filtrate. This solvent was removed by rotary evaporation. The residue was dissolved in water, and after adjusting the pH to 7 with aqueous Na_2CO_3, the solution was extracted with chloroform. The chloroform was dried over anhydrous sodium sulfate and after filtering, the solvent was removed by rotary evaporation to yield a yellow solid. Yield = 70%, ^{1}H NMR ($CDCl_3$, ppm) 7.80 (1H, dd), 8.10 (2H, m), 8.40 (1H, d), 9.1 (1H, d), 9.3 (1H, d), 9.55 (1H, d), 10.65 (1H, s)

4-carboaldoxime-1,10-phenanthroline (2) This compound was prepared using a variation of the procedure described in reference 28 such that compound **1** was used as a starting material. The desired product was isolated by collecting the precipitate that is formed during the reaction. The precipitate is dissolved in 100 mL H_2O. The solution is filtered and then the solvent is removed by rotary evaporation to yield a white solid. Yield = 65%. ^{1}H NMR (DMSO-d_6, ppm) 8.20 (1H, dd), 8.40 (2H, m), 8.85 (1H, d), 9.05 (1H, d), 9.15 (1H, s), 9.20 (1H, d), 9.30 (1H, d), 12.75 (1H, s); ^{13}C NMR (D_2O, ppm) 122.7, 124.0, 125.2, 125.8, 126.7, 128.6, 135.6, 137.0, 139.7, 143.6, 145.6, 145.9, 147.8.

4-(aminomethyl)-1,10-phenanthroline (3) This compound was prepared using a variation of the procedure described in reference 28 such that compound **2** (3.0 g, 13.5 mmole) was used as a starting material. Yield = 71 %. ^{1}H NMR: (D_2O(pH 3), ppm) 4.75 (2H, s), 8.8 (1H, d), 7.95 (1H, d), 8.1 (2H, m), 8.8 (1H, d), 9.0 (1H, d), 9.1 (1H, d); ^{13}C NMR (D_2O, ppm): 40.0, 124, 124.5, 125, 126, 126.5, 129, 135, 137, 142, 144, 147, 151.

4-guanidylmethyl-1,10-phenanthroline (4). **3** (0.5 g, 2.1 mmole) was dissolved in 100 mL of water. $ZnCl_2$ (285 mg, 2.1 mmol) was added, and the pH of the reaction mixture was raised to pH 6.0 by addition of aqueous Na_2CO_3 (1.0 M). 2-methyl-2-thiopseudourea hydrogen sulfate (1.15 g, 4.14 mmole) was added and the reaction mixture was heated to reflux for 5 days under nitrogen. The reaction was purified by column chromatography (silica; 88% $CHCl_3$/10% ethanol/2% conc. HCl). Yield = 63%. ^{1}H NMR (D_2O, ppm) 4.5 (2H, s), 8.5 (2H, m), 8.0 (1H, d), 7.65 (1H, d), 7.5 (1H, m), 7.35 (1H, d), 7.15 (1H, d); ^{13}C NMR (D_2O, ppm) 41.0, 121.6, 122.1, 125.8, 126.3, 127.7, 128.4, 135.2, 136.2, 140.4, 145.4, 148.2, 154.1, 161.4 C14H14N5 calc. 252.3; Found FABMS m/z 253 (M^+)

4-(2-Hydroxyethyl)-4'-methyl-2,2'-bipyridine (5). This compound was prepared using a variation of the procedure described in reference 18 such that paraformaldehyde was added a solution of lithiated 4,4'-dimethyl-2,2'-bipyridine. The paraformaldehyde (3.0 g, 99 mmole) was dried under vacuum for 3 hours and added to the lithiated bipyridine against a strong flow of argon. After one hour, the low-temperature bath was removed and the reaction was stirred overnight under a slow flow of argon. The reaction turned bright yellow. A solution of saturated NaCl (120 mL) was added and the reaction was extracted with CH_2Cl_2 (2 x150 mL). The solution was dried over anhydrous Na_2SO_4 and the solvent was removed to yield an oily mixture, which was purified by column chromatography (silica; 19:1 CH_2Cl_2:Methanol). The product was recovered as a yellow oil. Yield = 42.5%. ^{1}H NMR ($CDCl_3$, ppm) 2.45 (1H, s), 2.96 (2H, t), 3.98 (2H, t), 7.13

(1H, d), 7.19 (1H, d), 8.20 (1H, s), 8.23 (1H, s), 8.49 (1H, d), 8.56 (1H, d); ^{13}C NMR ($CDCl_3$, ppm) 21.60 , 39.02 , 62.55, 122.18 , 122.65, 124.98, 125.15, 148.80 , 149.13, 149.45, 149.70, 156.20, 156.40.

4-(2-Bromoethyl)-4'-methyl-2,2'-bipyridine· 2HBr (6). This compound was prepared using a variation of the procedure described in reference 18 such that **5** (4.5 g, 21.3 mmole) was refluxed in 48% HBr (60 mL) for 8 hours. The solvent was removed under vacuum and the resulting dark brown powder was dissolved in 200 mL ethanol with warming. The product was precipitated by addition of ether (500 mL). The brown sticky solid was filtered and washed with ether. Yield = 69.5 %. ^1H NMR (D_2O, ppm) 2.4 (3H, s), 3.2 (2H, t), 3.65 (2H, t), 7.45 (1H, d), 7.6 (1H, d), 8.0 (1H, s), 8.15 (1H, s), 8.45 (1H, d), 8.55 (1H, d); ^{13}C NMR (D_2O, ppm) 22, 32, 37, 123, 125, 127, 127.2, 143, 145, 145.1, 147, 154, 159

4-(2-Phthalimidoethyl)-4'-methyl-2,2'-bipyridine (7). This compound was prepared using a variation of the procedure described in reference 18 such that **6** (4.5 g, 10.4 mmole) was dissolved in 0.2 M NaOH (350 mL). The solution was extracted with $CHCl_3$ (2 x 350 mL). The extracts were washed with water (350 mL) and dried over anhydrous Na_2SO_4. The volume of the solution was reduced to 25 mL on a rotary evaporator. Evaporation to dryness has to be avoided because of product decomposition. DMF (110 mL) and potassium phthalimide (3.2 g, 17.2 mmole) were added. The mixture was heated at 50 ^oC for 12 hours, colled to room temperature, and 400 mL of water were added. The solution was extracted with $CHCl_3$ (2 x 400 mL).he combined organic layers were washed with 0.2 M NaOH (400 mL), water (400 mL), and dried over anhydrous Na_2SO_4. The mixture was purified by column chromatography on silica. The first product which was eluted off with 9:1 toluene: ethyl acetate (Rf = 0.47) was an elimination product; 4-vinyl-4'-methyl-2,2'-bipyridine (Yield = 40%, Rf = 0.47) ^1H NMR ($CDCl_3$) 2.5 (3H,s), 5.55 (1H, d), 6.05 (1H, d), 6.8 (1H, dd), 7.15 (1H, d), 7.3 (1H, d), 8.25 (1H, s), 8.4 (1H, s), 8.55 (1H, d), 8.65 (1H, d) ^{13}C NMR ($CDCl_3$, ppm) 21.6,

34.5, 38.5, 122, 122.4, 123.7, 124.4, 125.1, 132.3, 134.4, 148.3, 148.5, 149.3, 149.7, 156.0, 168.4. The solvent was changed to 2:1 toluene: ethyl acetate and the desired product was collected as a pure white powder. Yield = 11.0 %. ^{1}H NMR ($CDCl_3$) 2.45 (3H, s), 3.1 (2H, t), 4.05 (2H, t), 7.2 (1H, d), 7.3 (1H, d), 7.8 (2H, m), 7.9 (2H, m), 8.30 (1H, s), 8.4 (1H, s), 8.6 (1H, d), 8.65 (1H, d). ^{13}C NMR ($CDCl_3$, ppm) 21.6, 34.5, 38.5, 122, 122.4, 123.7, 124.4, 125.1, 132.3, 134.4, 148.3, 148.5, 149.3, 149.7, 156.0, 168.4

4-(2-aminoethyl)-4'-methyl-2,2'-bipyridine (8). This compound was prepared using a variation of the procedure described in reference 18 such that **7** (1.0 g, 2.86 mmole) was used as a starting material. ^{1}H NMR ($CDCl_3$, ppm) 2.44 (3H, s), 2.80 (2H, t), 3.10 (2H, t), 7.2 (2H, m), 8.23 (1H, s), 8.24 (1H, s), 8.56 (1H, d), 8.6 (1H, d); ^{13}C NMR ($CDCl_3$, ppm): 21.6, 38.8, 42.5, 122, 122.5, 124.7, 125.2, 149.3, 149.6, 149.8, 152, 156, 156.2

4-(2-guanidylethyl)-4'-methyl-2,2'-bipyridine (9). **8** (0.6 g, 1.70 mmole) and zinc (II) acetate were dissolved in 50 mL water. 2-methyl-2-thiopseudourea hydrogen sulfate (4.1 g, 14.3 mmole) was added, and the pH of the solution was adjusted to 7.5 by the addition of an aqueous solution of Na_2CO_3 (1.0 M). The reaction was heated to reflux under a nitrogen atmosphere for 5 days, and purified by column chromatography on silica. The unreacted 2-methyl-2-thiopseudourea was eluted with 78% $CHCl_3$/18% ethanol/ 4% conc. HCl. The solvent was changed to 78% $CHCl_3$/18% methanol/ 4% conc. HCl to elute the guanidylethylbipyridine ligand. This ligand is unstable when stored dry. Therefore, the ligand was stored in acidified water (pH 2, HCl). ^{1}H NMR (D_2O, ppm) 2.45 (3H, s), 2.95 (2H, t), 3.35 (2H, t), 7.55 (1H, d), 7.65 (1H, d), 8.05 (1H, s), 8.15 (1H, s), 8.45 (1H, d), 8.55 (1H, d); ^{13}C NMR (D_2O, ppm) 22.0, 36.0, 40.1, 123, 123.5, 128, 129, 144, 147, 149, 154, 157, 159, 163 $C_{14}H_{18}N_5$ calc. 256.33 Found m/z 256 (M+)

4-[2-(1,3-dioxolan-2-yl)ethyl]-4'-methyl-2,2'-bipyridine (10). This compound was prepared using a variation of the procedure described in reference 18 such that 2-

bromomethyl-1,3-dioxolane was added to the lithiated 4,4'-dimethyl-2,2'-bipyridine solution. The crude reaction product was used without further purification.

*4-(2-Formylethyl)-4'-methyl-2,2'-bipyridine (**11**).* This compound was prepared using a variation of the procedure described in reference 18. The crude reaction product was used without further purification.

*4-(2-carboxylethyl)-4'-methyl-2,2'-bipyridine (**12**).* This compound was prepared using a variation of the procedure described in reference 18.

*4-(2-amidoethyl)-4'-methyl-2,2'-bipyridine (**13**).* **12** (542 mg, 2.27 mmole) was dissolved in 50 mL of methanol and 2 mL of concentrated H_2SO_4 and heated to reflux for 5 hours. The reaction was cooled to room temperature and neutralized with a saturated Na_2CO_3 solution. The solvent was removed under vacuum and the residue was dissolved in 100 mL 50/50 CH_2Cl_2/H_2O. The mixture was extracted with CH_2Cl_2 (2 x 50 mL) and the combined organic extracts were dried over anhydrous Na_2SO_4. The solvent was removed under vacuum to yield the methyl ester. The solid was redissolved in 25 mL methanol saturated with ammonia and stirred in a sealed flask at 55 ^oC for 12 hours. The product was purified purified by column chromatography on silica (20:1 CH_2Cl_2/methanol). Yield = 71%. ^1H NMR ($CDCl_3$, ppm) 2.4 (3H, s), 2.6 (2H, t), 3.0 (2H, t), 5.5 (2H, m), 7.1 (1H, d), 7.15 (1H, d), 8.2 (1H, s), 8.22 (1H, s), 8.5 (1H, d), 8.55 (1H, d).

*4-(3-Hydroxypropyl)-4'-methyl-2,2'-bipyridine (**14**).* This compound was prepared using a variation of the procedure described in reference 18 such that crude **11** was used as a starting material. Yield = 35%. ^1H NMR ($CDCl_3$, ppm) 1.95 (2H, m), 2.43 (3H, s), 2.80 (2H, t), 3.67 (2H, t), 7.1 (2H, m), 8.2 (2H, m), 8.51 (1H, d), 8.55 (1H, d); ^{13}C NMR ($CDCl_3$, ppm): 21.62, 31.98, 33.43, 61.96, 121.84, 122.57, 124.41, 125.13, 148.71, 149.24, 149.49, 152.45, 156.35, 156.49.

*4-(3-Bromopropyl)-4'-methyl-2,2'-bipyridine · 2HBr (**15**).* This compound was prepared using a variation of the procedure described in reference 18 such that **14** was

used as a starting material. refluxed in a 48% solution of HBr (60 mL) for 8 hours. After the reaction was complete, the solvent was removed by rotary evaporation. The resulting light brown powder was dissolved in 200 mL of warm ethanol. Addition of diethyl ether (500 mL) precipitated a powder which was collected on a frit and washed with diethyl ether. Yield = 88%. ^{1}H NMR (D_2O, ppm) 2.2 (1H, m), 2.56 (3H, s), 2.94 (1H, t), 3.42 (2H, t), 7.64 (1H, d), 7.69 (1H, d), 8.12 (1H, s), 8.17 (1H, s), 8.55 (1H, d), 8.58 (1H, d); ^{13}C NMR (D_2O, ppm): 21.87, 32.40, 33.61, 33.83, 124.35, 125.24, 127.78, 128.30, 144.16, 146.59, 146.69, 146.73, 158.56, 158.95.

4-(3-Phthalimidopropyl)-4'-methyl-2,2'-bipyridine ***(16)***. This compound was prepared using a variation of the procedure described in reference 18 such that compound **15** was used as a starting material. **15** (6.87 g, 15.2 mmole) was dissolved in 0.2 M NaOH (350 mL). This solution was extracted with $CHCl_3$ (2 x 350 mL). The combined $CHCl_3$ extracts were washed with water (350 mL) and dried over anhydrous Na_2SO_4. The solvent volume was reduced to 25 mL by rotary evaporation. Evaporation of the solvent was not achieved due to product decomposition. DMF (110 mL) and potassium phthalimide (3.2 g, 17.2 mmole) were added. The mixture was kept at 50 ^{o}C for 12 hours. The reaction was cooled and 400 mL water were added. The solution was extracted with $CHCl_3$ (2 x 400 mL). The combined organic extracts were washed with 0.2 M NaOH (400 mL) and water (400 mL), and dried over anhydrous Na_2SO_4. The mixture was purified by column chromatography on silica. (2:1 toluene: ethyl acetate). Yield = 70% ^{1}H NMR ($CDCl_3$, ppm) 2.09 (2H, m), 2.44 (3H, s), 2.80 (2H, t), 3.79 (2H, t), 7.12 (1H, d), 7.17 (1H, d), 7.7 (2H, m), 7.85 (2H, m), 8.18 (1H, s), 8.22 (1H, s), 8.53 (2H, m); ^{13}C NMR ($CDCl_3$, ppm): 21.59, 29.37, 33.15, 38.00, 121.52, 122.39, 123.63, 124.12, 125.07, 132.39, 134.35, 148, 149.33, 149.54, 152, 157, 169.

4-(3-aminopropyl)-4'-methyl-2,2'-bipyridine ***(17)***. This compound was prepared using a variation of the procedure described in reference 18. A quantitative yield was obtained.^{1}H NMR ($CDCl_3$, ppm) 1.85 (2H, m), 2.44 (3H, s), 2.75 (4H, m), 7.15 (2H, m),

8.23 (2H, s), 8.56 (2H, m); ^{13}C NMR ($CDCl_3$, ppm): 21.55, 33.14, 34.48, 41.98, 121.58, 122.38, 124.23, 125.04, 148.50, 149.27, 149.42, 152.51, 156.30, 156.51.

4-[3-guanidylpropyl]-4'-methyl-2,2'-bipyridine (18). **17** (630 mg, 2.80 mmole) was dissolved in 50 mL 4:1 H_2O/DMSO and 2-methyl-2-thiopseudourea hydrogen sulfate (3.2 g, 11.2 mmole) and zinc acetate (630 mg, 2.80 mmole) were added. The pH of the solution was adjusted to 7.5 by addition of aqueous Na_2CO_3 (1.0 M). The reaction was heated to reflux under nitrogen for 5 days. The reaction was purified by column chromatography on silica. The unreacted 2-methyl-2-thiopseudourea was eluted with 78% $CHCl_3$/18% ethanol/ 4% conc. HCl and then the solvent was switched to 78% $CHCl_3$/18% methanol/ 4% conc. HCl to elute the guanidylpropyl ligand. This ligand is unstable when stored dry. Therefore, the ligand was stored in acidified water (pH 2, HCl). Yield = 28% ^1H NMR (D_2O (pH 3), ppm) 1.75 (2H, t), 2.45 (3H, s), 2.75 (2H, t), 2.95 (2H, t), 7.8 (2H, m), 8.1 (2H, m), 8.55 (1H, d), 8.57 (1H, d) $C_{15}H_{20}N_5$ calc. 270.33 m/z 270 (M+)