Supporting information: Wood *et al*

Stereochemically stable double helicate dinuclear complexes of bis(dipyrromethene)s: a chiroptical study

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Supporting Information

Experimental

General: All nuclear magnetic resonance experiments were conducted using either a Bruker AC250, or a Bruker Avance 500 spectrometer, as indicated. All ^{1}H NMR chemical shifts are reported using tetramethylsilane as an internal reference (0.00 ppm), ^{13}C NMR chemical shifts are reported using the solvent residual as an internal reference; $CDCl_3$ (77.23 ppm), acetone-d_6 (29.92 ppm), DMSO-d_6 (39.51 ppm). All ultraviolet-visible spectra were recorded using a Varian-Cary Bio 100 spectrophotometer. All circular dichroism data was recorded using a Jasco 500 Spectropolarimeter. All melting points were determined through use of a Fisher-John melting point apparatus, and are reported uncorrected. Chromatography was performed using 230-400 mesh Silicycle ultra pure silica. With the exclusion of solvents, chemicals used in the preparations were received from suppliers and used without further purification. Dry, deoxygenated dichloromethane was obtained from an Innovative Technology solvent purification system. The syntheses of zinc(II) di[bis(3-ethyl-2,2′,4,4′-tetramethyldipyrromethene)] (**2**) (Zhang, Y.; Wang, Z.; Yan, C.; Li, G.; Ma, J. *Tetrahedron Lett*. **2000**, *41*, 7717-7721), benzyl 3,5-dimethyl-4-(methyl propionate)-1H-pyrrole-2-carboxylate (**3**) (Johnson, A. W.; Markham, E.; Price, R.; Shaw, K. B. *J. Chem. Soc*. **1958**, 4254-4257) and 2,2′,4,4′-tetramethyl-5,5′-diformyl-3,3′-dipyrromethane (**6**) (Zhang, Y.; Ma, J. S. *Org. Prep. Proced. Int*. **2001**, *33*, 81-86) have been reported previously.

Benzyl 3,5-dimethyl-4-propionic acid-pyrrole-2-carboxylate (**4**)

A solution of lithium hydroxide monohydrate (2.0 g, 48 mmol) in a 1:1 (v/v) tetrahydrofuran:water solution (190 mL) was added to a solution of benzyl 4-(2′-methoxycarbonylethyl)-3,5-dimethylpyrrole-2-carboxylate (**3**) (15 g, 48 mmol) dissolved in a 1:1 (v/v) tetrahydrofuran:water solution (60 mL) contained in a 500 mL round bottom flask with stirring. This mixture was stirred at room temperature for 24 hours. The reaction mixture was washed with dichloromethane (2 x 30 mL). The aqueous layer was acidified with 5% (v/v) aqueous solution of hydrochloric acid, resulting in the precipitation of a white solid. The product was collected by suction filtration to give a white powder. (13 g, 93%)

mp: 126-127ºC; ^{1}H NMR: δ(500 MHz, acetone-d_6): 2.23 (3H, s, ArCH_3), 2.29 (3H, s, ArCH_3), 2.42 (2H, t, J = 7.5 Hz, C(O)CH_2CH$_2$), 2.69 (2H, t, J = 7.5 Hz, ArCH_2CH$_2$), 5.25 (2H, s, CH_2Ph), 7.29-7.43 (5H, m, ArH), 10.3 (1H, br s, NH); ^{13}C NMR: δ(126 MHz, acetone-d_6): 10.9, 11.3, 20.3, 35.4, 65.5, 117.3, 121.0, 127.9, 128.7, 128.9, 129.3, 131.7, 138.3, 161.6, 174.7; EI-HRMS calcd 301.1314 for $C_{17}H_{19}NO_4$; Found 301.1312.

Benzyl 3,5-Dimethyl-4-[(*S*)-2-(1-phenyl-ethylcarbamoyl)-ethyl]-1H-pyrrole-2-carboxylate (**5a**)

Under dry conditions and using nitrogen gas as an inert atmosphere benzyl 3,5-dimethyl-4-propionic acid-pyrrole-2-carboxylate (**4**) (2.0 g, 6.6 mmol) was dissolved in dry, deoxygenated dichloromethane (50 mL) in a dry two-neck 250 mL round bottom flask with stirring. To this was added 4-(*N*,*N*-dimethylamino)pyridine (DMAP) (0.81g, 6.6 mmol). The resulting solution was cooled to 0°C by suspension in an ice bath. At this lowered temperature (*S*)-(-)-α-methylbenzylamine (0.86 mL, 0.82 g, 6.7 mmol) was added slowly dropwise by syringe. This solution was stirred for 30 seconds until a light pink solid began to form. At this time additional dry dichloromethane (20 mL) was added, followed by *O*-benzotriazol-1-yl-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate (HBTU) (2.5 g, 6.6 mmol). The reaction was allowed to warm to room temperature and stirred for two days. The reaction was then filtered, concentrated, washed with 5% (w/vol) aqueous hydrochloric acid solution (2 x 50 mL), washed with brine (20 mL) and concentrated by rotary evaporation. Chromatographic separation on silica using 30% (v/v) ethyl acetate/hexanes as the eluent gave the product as a white solid. (2.6 g, 99%) Sol: chloroform, methanol, tetrahydrofuran, dimethylsulfoxide; Sp. Sol: dichloromethane, acetone, ethyl acetate, ethanol; Insol: water, diethyl ether, hexanes.
mp: 200-203ºC; ^{1}H NMR: δ(500 MHz, $CDCl_3$): 1.41 (3H, d, J = 6.7 Hz, CHCH_3), 2.09 (3H, s, ArCH_3), 2.23-2.29 (5H, m, ArCH_3 + C(O)CH_2CH$_2$), 2.72 (2H, t, J = 6.9 Hz, ArCH_2CH$_2$), 5.04-5.09 (1H, m, CHCH$_3$), 5.30 (2H, s, CH_2Ph), 5.42 (1H, br d, J = 7.6 Hz, amide NH), 7.14-7.41 (10H, m, ArH), 8.44 (1H, br s, NH); ^{13}C NMR: δ(126 MHz, $CDCl_3$): 11.0, 11.3, 20.4, 22.8, 36.9, 47.9, 64.6, 115.9, 120.6, 126.3, 126.8, 127.1, 128.1, 128.2, 128.6, 128.9, 131.6, 137.6, 161.0, 171.2; EI-HRMS calcd 404.2100 for $C_{25}H_{28}N_2O_3$; Found 404.2093.

Benzyl 3,5-Dimethyl-4-[(*R*)-2-(1-phenyl-ethylcarbamoyl)-ethyl]-1H-pyrrole-2-carboxylate (**5b**)

Following the procedure used for the preparation of (**5a**), benzyl 3,5-dimethyl-4-propionic acid-1H-pyrrole-2-carboxylate (**4**) (2.0g, 6.6 mmol) was dissolved in dry, deoxygenated dichloromethane (50 mL) in a dry two-neck 250 mL round bottom flask with stirring. To this was added DMAP (0.81 g, 6.6 mmol). The resulting solution was cooled to 0°C by suspension in an ice bath. At this lowered temperature (*R*)-(+)-α-methylbenzylamine (0.86 mL, 0.82 g, 6.7 mmol) was added slowly dropwise by syringe. This solution was stirred for 30 seconds until a light pink solid began to form. At this time additional dry dichloromethane (20 mL) was added, followed by HBTU (2.5 g, 6.6 mmol) and then stirring was maintained. The reaction was stirred, eventually warming to room temperature, for two days. The work-up and purification were the same as for (**5a**). The product is a white solid. (2.6 g, 97%) Sol: chloroform, methanol, tetrahydrofuran, dimethylsulfoxide; Sp. Sol: dichloromethane, acetone, ethyl acetate, ethanol; Insol: water, diethyl ether, hexanes.
mp: 201-203ºC; ^{1}H NMR: δ(500 MHz, $CDCl_3$): 1.41 (3H, d, J = 6.7 Hz, CHCH_3), 2.09 (3H, s, ArCH_3), 2.24-2.32 (5H, m, ArCH_3 + C(O)CH_2CH$_2$), 2.72 (2H, t, J = 7.1 Hz, ArCH_2CH$_2$), 5.05-5.08 (1H, m, CHCH$_3$), 5.30 (2H, s, CH_2Ph), 5.44 (1H, br d, J = 7.6 Hz,

amide N*H*), 7.14-7.41 (10H, m, Ar*H*), 8.46 (1H, br s, N*H*); ^{13}C NMR: δ(125 MHz, $CDCl_3$): 10.9, 11.3, 20.4, 22.7, 36.9, 47.9, 64.6, 115.8, 120.5, 126.3, 126.8, 127.0, 128.1, 128.2, 128.5, 128.8, 131.6, 137.5, 160.9, 171.2; EI-HRMS calcd 404.2100 for $C_{25}H_{28}N_2O_3$; Found 404.2091.

Bis{3-[(*S*)-2-(1-phenyl-ethylcarbamoyl)-ethyl]-2,2′,4,4′-tetramethyldipyrromethene} hydrobromide salt (**7a**)

To a mixture of benzyl 3,5-dimethyl-4-[(*S*)-2-(1-phenyl-ethylcarbamoyl)-ethyl]-1H-pyrrole-2-carboxylate (**5a**) (0.50 g, 1.24 mmol) dissolved in tetrahydrofuran (25 mL) in a 100 mL round bottom flask was added a catalytic amount of 10 mol % palladium on activated carbon (0.011 g). Hydrogenolysis of the benzyl ester was achieved using an enclosed hydrogenation apparatus. After purging the mixture with hydrogen gas, the reaction was allowed to stir for sixteen hours. The mixture was then filtered through a plug of Celite® to remove the catalyst. The filtrate was collected in a 100 mL round bottom flask and diluted with methanol (5 mL). At this time 2,2′,4,4′-tetramethyl-5,5′-diformyl-3,3′-dipyrromethane (**6**) (0.16 g, 0.62 mmol) was added, followed by the addition of 48% (w/v) hydrobromic acid (0.40 mL). The reaction quickly changed from a light brown suspension to a very dark red homogenous solution. The reaction was stirred for twenty minutes, then washed with water (50 mL), dried with anhydrous sodium sulfate, filtered and concentrated to a dark red liquid by rotary evaporation. To this dark red liquid was added just enough chloroform to form a homogenous solution and then diethyl ether was added to precipitate the product as a dark orange powder, which was collected by filtration and rinsed with more diethyl ether. (0.36 g, 63%) Sol: methanol, dimethylsulfoxide; Sp. Sol: chloroform, dichloromethane, tetrahydrofuran, ethanol, acetone, ethyl acetate; Insol: water, diethyl ether, hexanes.
mp: >250ºC (dec.); $\lambda_{max}(CH_2Cl_2)$: 506 nm, 462 nm; $\varepsilon_{506}(CH_2Cl_2)$: 1.72×10^6 $Lmol^{-1}dm^{-1}$; $[\Theta]_{503}(CH_2Cl_2)$ = +28884 deg cm^2dmol^{-1}; ^{1}H NMR: δ(500 MHz, DMSO-D_6): 1.28 (6H, d, *J* = 7.2 Hz, CHC*H*$_3$), 2.11 (6H, s, ArC*H*$_3$), 2.27 (6H, s, ArC*H*$_3$), 2.31-2.35 (10H, m, ArC*H*$_3$ + C(O)C*H*$_2$CH$_2$), 2.44 (6H, s, ArC*H*$_3$), 2.50 (6H, s, ArC*H*$_3$), 2.63-2.74 (4H, m, ArC*H*$_2$CH$_2$), 3.73 (2H, s, ArC*H*$_2$Ar), 4.83-4.89 (2H, m, C*H*CH$_3$), 7.14-7.25 (10H, m, Ar*H*), 7.37 (2H, s, vinylic *H*), 8.28 (2H, br d, *J* = 7.5 Hz, amide N*H*), 12.29 (2H, br s, N*H*), 12.31 (2H, br s, N*H*); ^{13}C NMR: δ(126 MHz, DMSO-D_6): 9.9, 10.1, 12.7, 12.8, 19.7, 18.7, 22.4, 34.9, 47.7, 120.6, 125.1, 125.8, 126.4, 126.6, 128.1, 142.3, 144.7, 150.2, 152.1, 170.3; ESI+ calcd 922.3 for $C_{49}H_{60}N_6O_2Br_2$; Found 763.2 (M – 2HBr).

Bis{3-[(*R*)-2-(1-phenyl-ethylcarbamoyl)-ethyl]-2,2′,4,4′-tetramethyldipyrromethene} hydrobromide salt (**7b**)

Following the procedure used for the preparation of (**7a**), to a mixture of benzyl 3,5-dimethyl-4-[(*R*)-2-(1-phenyl-ethylcarbamoyl)-ethyl]-1H-pyrrole-2-carboxylate (**5b**) (0.50 g, 1.24 mmol) dissolved in tetrahydrofuran (25 mL) in a 100 mL round bottom flask was added a catalytic amount of 10 mol % palladium on activated carbon (0.011 g). Hydrogenolysis of the benzyl ester was achieved using an enclosed hydrogenation apparatus. After purging the mixture with hydrogen gas, the reaction was allowed to stir for sixteen hours. The mixture was then filtered through a plug of Celite® to remove the

catalyst. The filtrate was collected in a 100 mL round bottom flask and diluted with methanol (5 mL). At this time 2,2′,4,4′-tetramethyl-5,5′-diformyl-3,3′-dipyrromethane (**8**) (0.16 g, 0.62 mmol) was added, followed by the addition of 48% (w/v) hydrobromic acid (0.40 mL). The reaction quickly turned from a light brown suspension to a very dark red homogenous solution. The reaction was stirred for twenty minutes, then washed with water (50 mL), dried with anhydrous sodium sulfate, filtered and concentrated to a dark red liquid by rotary evaporation. To this dark red liquid was added just enough chloroform to form a homogenous solution and then diethyl ether was added to precipitate the product as a dark orange powder, which was collected by filtration and rinsed with more diethyl ether. (0.40 g, 70%) Sol: methanol, dimethylsulfoxide; Sp. Sol: chloroform, dichloromethane, tetrahydrofuran, ethanol, acetone, ethyl acetate; Insol: water, diethyl ether, hexanes.
mp: >250ºC (dec.); $\lambda_{max}(CH_2Cl_2)$: 506 nm, 463 nm; $\varepsilon_{506}(CH_2Cl_2)$: $1.72x10^6$ $Lmol^{-1}dm^{-1}$; $[\Theta]_{509}(CH_2Cl_2)$ = -21271 deg cm^2dmol^{-1}; ^1H NMR: δ(250 MHz, DMSO-D_6): 1.28 (6H, d, *J* = 6.6 Hz, CHC*H*$_3$), 2.24 (6H, s, ArC*H*$_3$), 2.29 (6H, s, ArC*H*$_3$), 2.32 (4H, t, *J* = 7.1 Hz, C(O)C*H*$_2$CH$_2$), 2.43 (6H, s, ArC*H*$_3$), 2.49 (6H, s, ArC*H*$_3$), 2.61-2.72 (4H, m, ArC*H*$_2$CH$_2$), 3.71 (2H, s, ArC*H*$_2$Ar), 4.96-5.07 (1H, m, C*H*CH$_3$), 7.13-7.16 (10H, m, Ar*H*), 7.34 (2H, s, vinylic *H*), 8.28 (2H, br d, *J* = 8.3 Hz, amide N*H*), 12.35 (2H, br s, N*H*), 12.37 (2H, br s, N*H*); ^{13}C NMR: δ(126 MHz, DMSO-D_6): 9.8, 10.0, 12.8, 12.9, 18.7, 19.6, 22.4, 34.9, 47.6, 120.8, 125.1, 125.8, 126.1, 126.4, 126.9, 128.1, 128.2, 142.3, 144.6, 152.0, 155.0, 170.2; ESI+ calcd 922.3 for $C_{49}H_{60}N_6O_2Br_2$; Found 763.5 (M – 2HBr).

Zinc(II) Di(bis{3-[(*S*)-2-(1-phenyl-ethylcarbamoyl)-ethyl]- 2,2′,4,4′-tetramethyldipyrromethene}) (**8a**)

To a solution of bis{3-[(*S*)-2-(1-phenyl-ethylcarbamoyl)-ethyl]- 2,2′,4,4′-tetramethyldipyrromethene} hydrobromide salt (**7a**) (0.10 g, 0.11 mmol) in chloroform (5 mL) in a 50 mL round bottom flask was added a solution of zinc acetate dihydrate (0.12 g, 0.54 mmol) and sodium acetate trihydrate (0.074 g, 0.54 mmol) in methanol (5 mL). The mixture was stirred for twenty minutes. The resulting dark purple solution was washed with distilled water (2 x 30 mL), dried with sodium sulfate, filtered and the solvent was removed by rotary evaporation. A minimal amount of dichloromethane was added, followed by hexanes to precipitate the product as a fuscia-coloured powder. (0.023 g, 25%) Sol: chloroform, dichloromethane; Sp. Sol: methanol, ethanol, acetone, tetrahydrofuran, ethyl acetate; Insol: water, diethyl ether, hexanes.
mp: >250ºC (dec.); $\lambda_{max}(CH_2Cl_2)$: 478 nm, 526 nm; λ_{max}(95:5 CH_3OH:$CHCl_3$): 475 nm, 525 nm; $\varepsilon_{527}(CH_2Cl_2)$: $1.96x10^7$ $Lmol^{-1}dm^{-1}$; ε_{525}(95:5 CH_3OH:$CHCl_3$): 2.50 $x10^6$ $Lmol^{-1}dm^{-1}$; $[\Theta_{478}(CH_2Cl_2)$ = -55007 deg cm^2dmol^{-1}, $[\Theta]_{521}$ = +222103 deg cm^2dmol^{-1}, $[\Theta]_{539}$ = -234056 deg cm^2dmol^{-1}; $[\Theta]_{476}$(95:5 CH_3OH:$CHCl_3$) = -98.10 deg cm^2dmol^{-1}, $[\Theta]_{521}$ = +271.37 deg cm^2dmol^{-1}, $[\Theta]_{537}$ = -201.00 deg cm^2dmol^{-1}; ^1H NMR: δ(250 MHz, $CDCl_3$): 1.37-1.39 (24H, m , CHC*H*$_3$ + ArC*H*$_3$), 1.93 (12H, d, *J* = 5.5 Hz, ArC*H*$_3$), 2.13 (12H, d, *J* = 3.3 Hz, ArC*H*$_3$), 2.20 (12H, s, ArC*H*$_3$), 2.26-2.32 (8H, m, C(O)C*H*$_2$CH$_2$), 2.65-2.71 (8H, m, ArC*H*$_2$CH$_2$), 3.41 (4H, br s, ArC*H*$_2$Ar), 5.00-5.11 (4H, m, C*H*CH$_3$), 5.55-5.66 (4H, m, amide N*H*), 6.87 (4H, d, *J* = 2.3 Hz, vinylic *H*), 7.16-7.28 (20H, m, Ar*H*); ^{13}C NMR: δ(126 MHz, $CDCl_3$): 10.1, 10.2, 15.3, 15.3, 22.2, 37.7, 48.8, 48.9, 121.0, 125.5,

126.3, 126.4, 127.4, 128.8, 135.4, 135.8, 137.1, 137.4, 143.4, 155.1, 158.3, 171.8; APCI+ calcd 1652.8 for $C_{98}H_{112}N_{12}O_4Zn_2$; Found 1653.5.

Zinc(II) Di(bis{3-[(*R*)-2-(1-phenyl-ethylcarbamoyl)-ethyl]- 2,2′4,4′-tetramethyldipyrromethene}) (**8b**)

Following the procedure used for the preparation of (**8a**), to a solution of bis{3-[(*R*)-2-(1-phenyl-ethylcarbamoyl)-ethyl]- 2,2′,4,4′-tetramethyldipyrromethene} hydrobromide salt (**7b**) (0.10 g, 0.11 mmol) in chloroform (5 mL) in a 50 mL round bottom flask was added a solution of zinc acetate dihydrate (0.12 g, 0.54 mmol) and sodium acetate trihydrate (0.074 g, 0.54 mmol) in methanol (5 mL). The mixture was stirred for twenty minutes. The resulting dark purple solution was washed with distilled water (2 x 30 mL), dried with sodium sulfate, filtered and the solvent was removed by rotary evaporation. A minimal amount of dichloromethane was added, followed by hexanes to precipitate the product as a fuscia-coloured powder. (0.029 g, 32%) Sol: chloroform, dichloromethane; Sp. Sol: methanol, ethanol, acetone, tetrahydrofuran, ethyl acetate; Insol: water, diethyl ether, hexanes.
mp: >250ºC (dec.); $\lambda_{max}(CH_2Cl_2)$: 478 nm, 527 nm; λ_{max}(95:5 CH_3OH:$CHCl_3$): 476 nm, 524 nm; $\varepsilon_{527}(CH_2Cl_2)$: $1.96x10^7$ $Lmol^{-1}dm^{-1}$; ε_{524}(95:5 CH_3OH:$CHCl_3$): 2.19 $x10^6$ $Lmol^{-1}dm^{-1}$; $[\Theta]_{512}(CH_2Cl_2)$ = +53086 deg cm^2dmol^{-1}, $[\Theta]_{542}$ = -43793 deg cm^2dmol^{-1}; $[\Theta]_{474}$(95:5 CH_3OH:$CHCl_3$) = +71.99 deg cm^2dmol^{-1}, $[\Theta]_{524}$ = -215.56 deg cm^2dmol^{-1}, $[\Theta]_{538}$ = +137.49 deg cm^2dmol^{-1}; ^{1}H NMR: δ(250 MHz, $CDCl_3$): 1.37-1.39 (24H, m , CHC*H*$_3$ + ArC*H*$_3$), 1.93 (12H, d, *J* = 5.3 Hz, ArC*H*$_3$), 2.13 (12H, d, *J* = 3.0 Hz, ArC*H*$_3$), 2.20 (12H, s, ArC*H*$_3$), 2.26-2.31 (8H, m, C(O)C*H*$_2$CH$_2$), 2.65-2.71 (8H, m, ArC*H*$_2$CH$_2$), 3.41 (4H, br s, ArC*H*$_2$Ar), 5.00-5.11 (4H, m, C*H*CH$_3$), 5.54-5.65 (4H, m, amide N*H*), 6.87 (4H, d, *J* = 2.3 Hz, vinylic *H*), 7.19-7.29 (20H, m, Ar*H*); ^{13}C NMR: δ(126 MHz, $CDCl_3$): 10.1, 10.2, 15.3, 15.3, 21.1, 22.2, 37.7, 48.8, 48.9, 121.0, 125.5, 126.3, 126.4, 127.4, 128.8, 135.4, 135.8, 137.1, 137.4, 143.4, 155.1, 158.3, 171.8; APCI+ calcd 1652.8 for $C_{98}H_{112}N_{12}O_4Zn_2$; Found 1652.4.

<u>HPLC Analysis of compounds **2**, **8a** and **8b**.</u>
(**2**)
HPLC: eluent: methanol; flow rate: 0.5 mL/min; column: CHIRALPAK IA (25 cm x 0.46 cm i.d.)

(**8a**)
HPLC: eluent: methanol; flow rate: 1 mL/min; column: CHIRALCEL OD (25 cm x 0.46 cm i.d.)

(**8b**)
HPLC: eluent: methanol; flow rate: 1 mL/min; column: CHIRALCEL OD (25 cm x 0.46 cm i.d.)