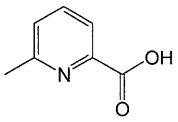
SUPPLEMENTARY MATERIAL

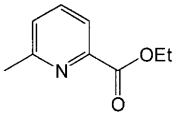
All reagents were purchased at the highest quality available and used as received unless stated otherwise. All starting materials were co-evaporated from either toluene or pyridine to remove excess water unless otherwise stated. Thin-layer chromatography (TLC) was performed on Select Scientific Flexible TLC plates (Alumina B, F-254, 200 μ) or Analtech silica plates (250 μ, with fluorescent indicator). Column chromatography was performed with, for alumina, Selecto Scientific Aluminum Oxide, Basic (20–90 μ) or Natland International Corp. silica (200–400 mesh). All solvents were dried over the appropriate solvent (usually CaH_2). All reactions were carried out under an inert atmosphere of argon (Ar) or nitrogen (N_2).

6-Methyl-pivalic acid



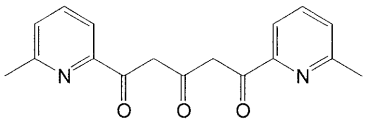
This procedure was adopted from Dancanale and Mantanari. (37). $NaClO_2$ (8.0 g, 70 mmol) in H_2O (70 ml) was added dropwise over 2 h to a stirred mixture of 6-methyl-2-pyridine carboxaldehyde (6.1 g, 50 mmol) in acetonitrile (50 ml) and NaH_2PO_4 (1.6 g, 13 mmol) in H_2O (20 ml) and 30% H_2O_2 (5.89 g) keeping the temperature of the solution at 10°C. Oxygen evolution was monitored by an oil bubbler. Oxygen evolution ceased after 4 h. $NaSO_3$ (0.5 g, 4.8 mmol) was added. The mixture was acidified with 10% HCl (aq.). The solvents were removed *in vacuo* and the resulting white solid was extracted with methanol. The methanol fractions were collected and dried to give white powder 6-methyl-pivalic acid (6.85 g, 50 mmol, ~100%). TLC: R_f 0.0 (5% MeOH/CH_2Cl_2 on basic alumina). ^{1}H NMR (300 MHz, $CDCl_3$, in p.p.m. relative to TMS): δ 8.0185 (d, J = 7.5 Hz, 1 H), 7.811 (t, J = 7.5 Hz, 1 H), 7.408 (d, J = 7.4 Hz, 1 H), 2.603 (s, 3 H); ^{13}C NMR (300 MHz, $CDCl_3$, in p.p.m. relative to TMS): δ 164.5, 157.5, 145.6, 138.8, 127.6, 121.1, 23.6. HR-MS (FAB / 3 NBA-Gly-TFA Matrix) calculated for $C_7H_8NO_2$: *m/z* 138.0555, found 138.0553.

Ethyl-(6-methyl)-picolonate



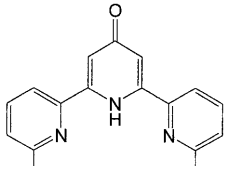
Under N_2 gas, a slurry of 6-methyl-2-pyridine-carboxylate (5.55 g, 40.5 mmol) was made in ethanol (50 ml). $SOCl_2$ (5 ml, 8.19 g, 68.8 mol) was added to the slurry at <0°C. The slurry was heated to reflux overnight during which the solid dissolved and the solution turned brown. The solution was taken to dryness *in vacuo* to yield a brown liquid dissolved in $CHCl_3$ extracted with 10% $NaCO_3$ until neutral, and then an extraction with concentrated NaCl was performed. The organic layers were combined, dried over $MgSO_4$ and evaporated to dryness to yield pure ethyl-(6-methyl)-picolonate (6.73 g, 40.5 mmol, ~100%). TLC, R_f 0.75 (5% MeOH/CH_2Cl_2 on basic alumina). ^{1}H NMR (300 MHz, $CHCl_3$, in p.p.m. relative to TMS): δ 7.832 (d, J = 7.8 Hz, 1 H), 7.613 (t, J = 7.8 Hz, 1H), 7.230 (d, J = 7.5 Hz, 1H), 4.372 (q, J = 7.2 Hz, 2H, CH_2), 2.556 (s, 3H), 1.330 (t, J = 7.2 Hz, 3H). ^{13}C NMR (300 MHz, $CDCl_3$, in p.p.m. relative to TMS) δ 165.2, 158.8, 147.6, 136.8, 126.5, 122.1, 61.6, 24.5, 14.1. HR-MS (FAB 3-NBA Matrix) calculated for $C_9H_{12}NO_2$ (M+H)$^+$: *m/z* 166.0868, found 166.0868.

6,6′-Dimethyl-dipyridiyl-trione



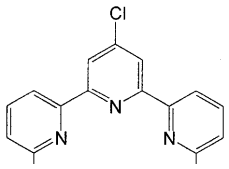
This procedure was adopted from Constable and Ward (38). THF (27 ml) was added under Ar gas to NaH (1.13 g, 47.1 mmol) and the mixture was refluxed. A mixture of ethyl, 6-methyl-2-pyridine-carboxylate (6.63 g, 40.2 mmol), acetone (0.9648 ml, 13.4 mmol) and THF (27 ml) was added over 4 h to the refluxing NaH/THF mixture. The solution was refluxed for an additional 2 h following the addition of the reagents. The THF was removed *in vacuo* and the brownish paste was treated with H_2O (50 ml). The brownish-orange solution was filtered through Celite 545. Addition of 5% acetic acid to pH 7 produced a yellow solid that was collected, washed with H_2O and dried. Recrystallization from 95% ethanol afforded thin needle-like crystals of orange-yellow product (2.38 g, 40%). TLC: R_f 0.68 (5% MeOH/CH_2Cl_2 on basic alumina). ^{1}H NMR (300 MHz, $CDCl_3$, in p.p.m. relative to TMS): δ 8.25 (m, 2 H); 8.13 (m, 2H); 7.60 (m, 2H); 3.1–3.0 (m, 10 H). ^{13}C NMR (300 MHz, $CDCl_3$, in p.p.m. relative to $CDCl_3$): δ 195.5, 171.4, 158.4, 150.6, 136.9, 125.9, 118.5, 98.6, 48.0, 24.6. HR-MS (FAB 3-NBA Matrix) calculated for $C_{17}H_{17}N_2O_3$ (M+H)$^+$: *m/z* 297.1239, found 297.1248. LR-MS 297.1 (M+H)$^+$.

4′-Hydroxy-6,6′-dimethyl-2,2′:6,2″-terpyridine



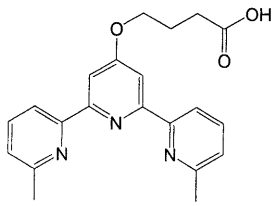
This procedure was adopted from Constable and Ward (38). 6,6′-Dimethyl-dipyridiyl-trione (7.9 g, 267 mmol) was dissolved in 100% EtOH (200 ml) and NH_4OAc (15.6 g, 202 mmol) was added to afford a clear solution. The solution was heated to reflux for 6 h. The reaction was then concentrated to one-third its original volume, and a white precipitate formed. The precipitate was collected by vacuum filtration and washed with Et_2O three times (3 × 20 ml). The precipitate was then recrystallized from ethanol to yield a white crystalline solid 4′-hydroxy-6,6′-dimethyl-2,2′:6,2″-terpyridine (5.56 g, 20 mmol, 76%). R_f 0.70 (5% MeOH/CH_2Cl_2 on basic alumina). ^{1}H NMR (300 MHz, $CDCl_3$, in p.p.m. relative to TMS); (two tautomers in solution): δ 7.76 (m, 4 H), 7.26 (m, 4 H), 2.70 (m, 2 H). ^{13}C NMR (300 MHz, $CDCl_3$, relative to $CDCl_3$): δ 174.4, 158.4, 147.3, 144.5, 137.7, 124.8, 117.4, 112.8, 24.4. HR-FAB-MS (FAB, Triglycerol matrix): calculated for $C_{17}H_{16}CN_3O$ (M+H)$^+$; *m/z* 278.1293, found 278.1292. LR-MS 296.0 (M+H)$^+$.

4′-Chloro-6,6′-dimethyl-2,2′:6,2″-terpyridine



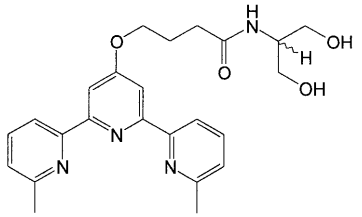
This procedure was adopted from Constable and Ward (38). A mixture of 2,6-bis(6′-methyl-2′-pyridyl)-4-pyridone (1.04 g, 3.76 mmol) and PCl_5 (2.14 g, 10.3 mmol) in $POCl_3$ (50 ml) was refluxed for 12 h. A white solid precipitated in the brown solution. The $POCl_3$ was removed *in vacuo* and the residue treated with H_2O (50 ml). The strongly acidic solution was made basic with KOH (aq.), causing a white suspension. This mixture was extracted with $CHCl_3$ (3 × 30 ml). The organic extracts were combined, dried over $MgSO_4$ and the chloroform was removed *in vacuo*. The brown solid was recrystallized in MeOH with charcoal decolorization to yield a white precipitate. This was collected, washed with diethyl ether, and recrystallized from ethanol to yield white needles of product (0.37 g, 33%). TLC: R_f 0.83 (5% MeOH/CH_2Cl_2 on basic alumina). ^{1}H NMR (300 MHz, $CDCl_3$, in p.p.m. relative to TMS): δ 8.481 (s, 2 H), 8.378 (d, J = 8.1 Hz, 2 H), 7.734 (t, J = 7.8 Hz, 2 H), 7.206 (d, J = 7.2 Hz, 2 H), 2.649 (s, 6 H). ^{13}C NMR (300 MHz, $CDCl_3$, relative to $CDCl_3$): δ 158.0, 156.9, 154.4, 146.1, 137.1, 123.8, 120.9, 118.4, 24.5. HR-MS (FAB, Triglycerol matrix): calculated for $C_{17}H_{15}ClN_3$ $(M+H)^+$; *m/z* 296.0954, found 296.09065. LR-MS 296.0 $(M+H)^+$.

4′-(3′-Carboxypropoxy)-6,6′-dimethyl-2,2′:6,2″-terpyridine



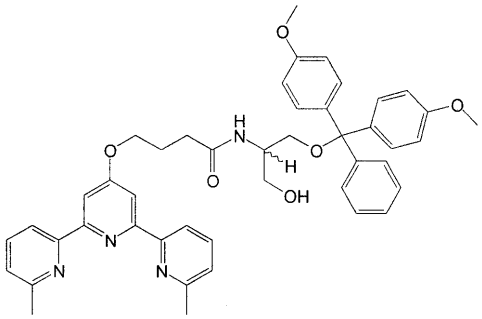
KOH and 4-hydroxybutyric acid were dried on a vacuum line overnight. KOH (8.00 g, 143 mmol) was added to a flame-dried RBF. DMSO (anhydrous, 50 ml) was added to the flask via cannula. Under a blanket of Ar the RBF was placed in an Ar-filled glove bag. 4-Hydroxybutyric acid (3.61 g, 28.7 mmol) was added. The solution was allowed to stir for 30 min. 4′-Chloro-6,6′-dimethyl-2,2′:6,2″-terpyridine (1.70 g, 5.70 mmol) was added. The reaction was heated to 60°C and allowed to stir slowly for 24 h. The crude reaction mixture was poured over ice and 1 vol distilled water was added. The pH was adjusted to pH 6.0 by the addition of 2 M HCl. The precipitate was then dissolved in 5% MeOH/CH_2Cl_2 and chromatographed on a basic alumina column with a gradient elution with 5–10% MeOH/CH_2Cl_2. The column solvent was removed to yield a white precipitate 4′-(3′-carboxypropoxy)-6,6′-dimethyl-2,2′:6,2″-terpyridine (1.82 g, 5.00 mmol, 88% yield). TLC: R_f 0.00 (5% methanol/CH_2Cl_2 on basic alumina). ^{1}H NMR (300 MHz, $CDCl_3$, in p.p.m. relative to TMS): δ 9.65 (s, 1 H); 8.23 (d, J = 6.9 Hz, 2 H), 7.83 (s, 2 H), 7.54 (t, J = 6.9 Hz, 2 H); 7.03 (d, J = 7.0 Hz, 2 H), 4.12 (t, J = 8.0 Hz, 2H), 2.52 (s, 3H), 2.47 (m, 2H), 2.08 (tt, J = 8.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, in p.p.m. relative to $CDCl_3$): δ 175.0, 166.6, 157.3, 156.6, 154.8, 137.3, 123.1, 118.4, 107.0, 66.7, 39.7, 30.4, 24.1. HR-FAB-MS calculated for $C_{21}H_{22}N_3O_3$ $(M+H)^+$: *m/z* 364.1661, found 364.1662.

Serinol-dimethyl-terpy



4′-(3′-Carboxypropoxy)-6,6′-dimethyl-2,2′:6,2″-terpyridine, (1.00 g, 2.75 mmol) was co-evaporated from toluene three times to remove any trace water. Anhydrous DMF (15 ml) was introduced via a cannula. EDC-HCl (0.63 g, 3.30 mmol) was introduced to the reaction mixture in an argon atmosphere in a glove bag. The reaction mixture was allowed to stir for 30 min. Serinol (0.38 g, 4.1 mmol) was co-evaporated from toluene three times and then introduced to the reaction under the argon blanket. The mixture was allowed to stir for 12 h at room temperature. The reaction was allowed to proceed at room temperature overnight. The reaction was deemed (>90%) complete by TLC (10% methanol/CH_2Cl_2 on basic alumina) after 20 h of reaction. Almost no starting material remained and a new product had been formed: (R_f 0.08, 10% methanol/CH_2Cl_2 on basic alumina). The solvent was removed by rotary evaporation. The resulting precipitate was subject to chromatography with a short (3 cm tall, 5 cm wide) basic alumina column (10% methanol/CH_2Cl_2 as the eluent). The column solvent was removed to yield a white precipitate serinol-dimethyl-terpy (0.87 g, 2.0 mmol, ~73% yield), and this precipitate was used without further purification. TLC: R_f 0.08 (10% methanol/CH_2Cl_2 on basic alumina).

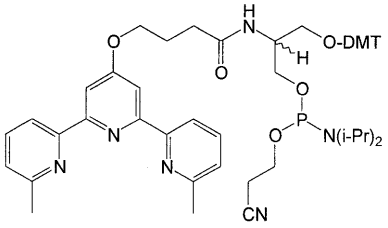
Serinol-(O-DMT)-dimethyl-terpy



Serinol-dimethyl-terpy (0.50 g, 1.15 mmol) was co-evaporated from pyridine three times and then dissolved in freshly distilled (over CaH_2) pyridine (5 ml). (0.43 g, 1.26 mmol) of DMT-Cl was introduced to the reaction mixture under a blanket of Ar. The reaction mixture turned to a deep orange and was allowed to stir overnight. After 12 h, the reaction was considered complete by TLC (steady-state distribution of products and reactants achieved). One volume of cold distilled H_2O was introduced and the reaction mixture was extracted three times with diethyl ether. The organic layers were extracted once with 1 vol of saturated NaCl and then combined dried over $MgSO_4$. The organic solvent was removed by rotary evaporation. The precipitate was then redissolved in fresh CH_2Cl_2 and subject to chromatography on a basic alumina

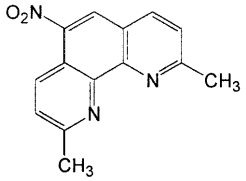
column. A gradient elution profile was used that entailed a gradient of methanol 0–2% in CH_2Cl_2. The product containing fractions were collected and dried to yield pure Serinol-(O-DMT)-dimethyl-terpy in a 62% yield (0.52 g, 0.71 mmol). TLC: R_f 0.49 (5% methanol/CH_2Cl_2 on basic alumina). ^{1}H NMR (300 MHz, $CDCl_3$, in p.p.m. relative to TMS) δ 9.65 (s, 1 H); 8.37 (d, *J* = 7.0 Hz, 2 H), 7.99 (s, 2 H), 7.70 (t, *J* = 7.0 Hz, 2 H); 7.38 (d, *J* = 7.0 Hz, 2 H); 7.3–7.1 (m, 9 H); 6.79 (d, *J* = 8.7 Hz, 4 H); 6.09 (d, *J* = 7.8 Hz); 4.2–4.1 (m, 3 H); 3.85–3.65 (m, 8 H); 3.55 (s, 1 H); 3.29 (m, 2 H); 2.62 (s, 6 H); 2.40 (t, *J* = 6.8 Hz, 2 H); 2.14 (tt, *J* = 6.9, 6.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, in p.p.m. relative to $CDCl_3$): δ 172.4, 166.8, 158.4, 157.4, 155.4, 157.0, 144.5, 135.6, 129.8, 127.9, 127.8, 126.8, 123.3, 118.3, 119.4, 114.6, 107.1, 86.3, 77.4, 63.3, 63.0, 55.1, 51.1, 32.9, 24.9, 24.5. HR-FAB-MS calculated for $C_{45}H_{47}N_4O_6$ $(M+H)^+$: *m/z* 739.3496, found 739.3496.

Serinol-(O-DMT)-dimethyl-terpy phosphoramidite building block



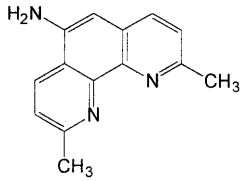
Serinol-(O-DMT)-dimethyl-terpy (0.50 g, 0.67 mmol) was dried down one time from a 5:1 CH_2Cl_2:Py mix and then further dried down twice from pyridine. The product was placed on a vacuum overnight. Freshly distilled (over CaH_2) CH_2Cl_2 was added (5 ml) under a blanket of Ar gas. The solution was cooled in an ice bath while stirring. Two equivalents of freshly distilled (over CaH_2) triethylamine (0.19 ml, 1.3 mmol) were added. The solution was allowed to stir for 5 min. Three equivalents of 2-cyanoethyl *N*,*N*-diisopropylchlorophosphoramidite (0.44 ml, 2.0 mmol) were added dropwise via a syringe. The solution was allowed to stir while warming to room temperature. The reaction was complete by TLC (5% MeOH/CH_2Cl_2 v/v) in 10 min with just a trace of starting material remaining. The reaction was allowed to proceed for 1 h. The CH_2Cl_2 was removed by a stream of Ar gas. The crude reaction was chromatographed on basic alumina twice using a gradient elution of (0–1% methanol: CH_2Cl_2) to give pure product Serinol-(O-DMT)-dimethyl-terpy phosphoramidite building block in a 76% yield (0.48 g, 0.51 mmol). R_f 0.58, 2% methanol/CH_2Cl_2 on basic alumina. ^{31}P NMR (75 MHz, acetone-d_6, referenced to TMP) δ 145.9, 145.7 (two diastereomers). HR-FAB on $C_{54}H_{64}N_6O_7P$ ($[M+H]^+$): expected 939.4574, found 939.4574.

5′-nitro-neocuproine



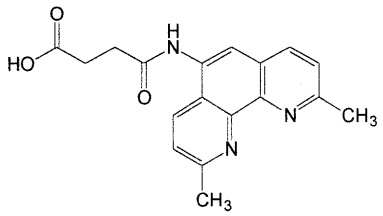
This procedure was adopted from Gallager *et al.* (8). Neocuproine (4.0 g, 19 mmol) was dissolved in 50 ml of concentrated H_2SO_4. Fuming HNO_3 (18.4 ml) was added. The reaction was then brought to reflux and maintained for 5 h. The reaction was allowed to cool to room temperature (~30 min). Solid NaOH was added slowly until a neutral pH was obtained. The cloudy solution was extracted with $CHCl_3$ three times. The organic layers were combined and dried over $MgSO_4$. TLC (50% EtOAc/hexanes) on basic alumina demonstrated consumption of all of the starting material. The solvent was removed by rotary evaporation to yield crude 5-nitro-neocouproine (brown powder, 5.0 g). The product was used without further purification. R_f 0.56 (50% EtOAc/hexanes on basic alumina). HR-MS FAB ($[M+H]^+$): *m/z* calculated for $C_{14}H_{12}N_3O_2$: 254.0930; found 254.0929.

5′-amino-neocuproine



This procedure was adopted from Lecompte *et al.* (35). To a suspension of 132 ml of EtOH and crude 5′-nitro-neocuproine (5.0 g, ~19.5 mmol), 0.88 g of Pd/C (5% Pd content, 50% water) was added. Then a solution of 90 ml EtOH and (4.37 ml, 140 mmol) hydrazine was added dropwise. The resulting black suspension was heated to reflux for 5 h and then allowed to cool to room temperature. The reaction mixture was filtered through Celite 545, and concentrated to dryness. A bilayer of CH_2Cl_2 and water was added to the yellow-green precipitate. After extraction the organic layer was dried over $MgSO_4$ and the solvent was removed by rotary evaporation. The resulting precipitate was chromatographed on a basic alumina column with a gradient elution of 0–5% methanol in CH_2Cl_2 to give pure 5′-amino-neocuproine (yellow powder, 1.31 g, 5.07 mmol) in a 26% yield over the first two steps. R_f 0.70 (2% methanol/CH_2Cl_2 on basic alumina). ^{1}H NMR (300 MHz, $CDCl_3$, relative to TMS): δ 8.37 (d, *J* = 8.4 Hz, 1 H); 8.00 (d, *J* = 8.4 Hz, 1 H); 7.54 (d, *J* = 8.4 Hz, 1 H); 7.52 (d, *J* = 8.4 Hz, 1 H); 6.99 (s, 1 H); 4.8 (s, 2 H); 3.06 (s, 3 H); 3.04 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$, in p.p.m. relative to $CDCl_3$): δ 158.4, 154.9, 145.3, 140.6, 139.4, 133.6, 129.7, 127.6, 123.3, 122.1, 119.9, 104.4, 25.1, 24.9. HR-MS FAB ($[M+H]^+$): *m/z* calculated for $C_{14}H_{14}N_3$: 224.1188; found 224.1188.

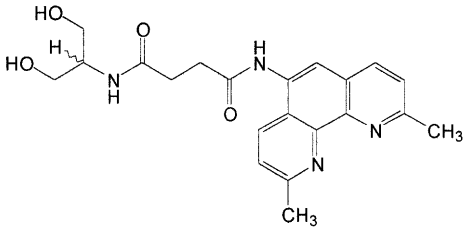
5′-amino-succinate-neocuproine



5′-Amino-neocuproine (1.31 g, 5.07 mmol) was dissolved in 40 ml of freshly distilled (over CaH_2) pyridine to yield a yellow solution. Succinic anhydride (0.71 g, 7.1 mmol) and *N*,*N*-dimethyl-4-aminopyridine (DMAP) (spatula tip full) were added to the solution in a glove bag under an Ar atmosphere. The reaction was then heated to 35°C and allowed to react overnight. The reaction was deemed complete (>95%) by TLC

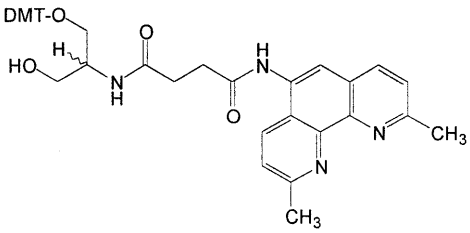
(2% methanol/CH_2Cl_2 on basic alumina) after 16 h. The pyridine was removed by rotary evaporation and the off-yellow solid was recrystallized from as solution of 5% methanol/CH_2Cl_2 to give pure 5′-amino-succinate-neocuproine (1.46 g, 3.0 mmol) in a 59% yield. R_f 0.00 (2% methanol/CH_2Cl_2 on basic alumina). ^{1}H NMR [300 MHz, DMSO-d_6, in p.p.m. relative to $CD_2HS(O)CD_3$]: δ 10.11 (s, 1H); 8.49 (d, J = 8.4 Hz, 1H); 8.28 (d, J = 8.4 Hz, 1H); 8.00 (s, 1H); 7.63 (d, J = 8.4 Hz, 1H); 7.57 (d, J = 8.4 Hz, 1H); 2.8–2.7 (m, 8 H, 2H); 2.6 (t, J = 6.3 Hz, 2H). ^{13}C NMR (75 MHz, DMSO-d_6, in p.p.m. relative to DMSO-d_6): δ 174.1, 171.8, 158.4, 157.2, 144.6, 143.0, 136.0, 132.1, 131.5, 126.2, 123.4, 122.9, 119.3, 31.4, 28.7, 21.2, 21.1. HR-MS FAB ([M+H]$^+$): *m/z* calculated for $C_{18}H_{18}N_3O_3$: 324.1348; found 324.1347.

Serinol-neocuproine



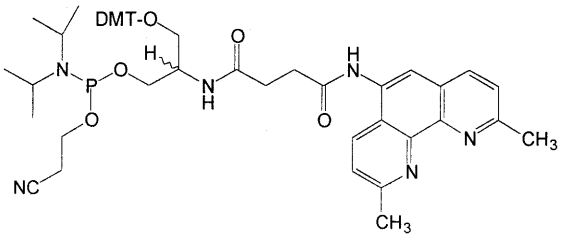
5′-Amino-succinate-neocuproine (1.46 g, 3.00 mmol) was co-evaporated with toluene three times to remove any water and was then dissolved in 30 ml of anhydrous DMF. EDC-HCl (0.70 g, 3.6 mmol) and DMAP (spatula tip full) were added and the solution was allowed to stir for 30 min. Then serinol (0.33 g, 3.6 mmol) was added to the solution under an inert atmosphere of Ar in a glove bag. The reaction was allowed to proceed at room temperature overnight. The reaction was deemed complete (>90%) by TLC (5% methanol/CH_2Cl_2 on basic alumina) after 20 h of reaction. Almost no starting material remained and a new product had been formed; with R_f 0.05 (5% methanol/CH_2Cl_2 on basic alumina). The solvent was removed by rotary evaporation. The resulting precipitate was used without further purification.

Serinol-(O-DMT)-neocuproine



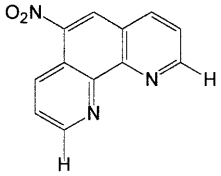
Serinol–neocuproine (~3.00 mmol) was co-evaporated with pyridine three times to remove any water and then dissolved in 10 ml of freshly distilled pyridine (over CaH_2). DMT-Cl (1.16 g, 3.6 mmol) was added to the solution under an inert atmosphere of Ar in a glove bag. The solution was allowed to stir at room temperature for 18 h. The solvent was removed by rotary evaporation and a bilayer of CH_2Cl_2 and water was added. After extraction, the water layer was further extracted with 1 vol of CH_2Cl_2. The organic layers were collected, dried over $MgSO_4$, and the solvent was removed. The orange precipitate was dissolved in CH_2Cl_2 and chromatographed twice on a basic alumina column with a gradient elution of 0–1% methanol-CH_2Cl_2. The column solvent was removed to yield pure Serinol-(O-DMT)-neocuproine (0.84 g, 1.2 mmol) in a 40% yield over two steps. TLC: R_f 0.40 (2% methanol/CH_2Cl_2 on basic alumina). ^{1}H NMR (300 MHz, $CDCl_3$, in p.p.m. relative to TMS): δ 10.11 (s, 1 H); 8.45 (d, J = 8.4 Hz, 1 H); 8.17 (s, 1 H); 7.81 (d, J = 8.4 Hz, 1 H); 7.4–7.05 (m, 11 H); 7.95 (d, 1 H); 7.75 (d, J = 7.75 Hz, 4H); 4.19 (m, 1 H); 3.8–3.6 (m, 8 H); 3.27 (m, 2 H); 2.8–2.6 (m, 8 H). ^{13}C NMR (75 MHz, $CDCl_3$, in p.p.m. relative to $CDCl_3$): δ 172.5, 172.4, 158.5, 158.3, 154.9, 145.3, 144.4, 140.6, 139.4, 135.6, 133.6, 129.9, 129.7, 127.9, 127.6, 126.9, 123.3, 122.1, 119.9, 113.2, 104.4, 85.5, 63.2, 62.8, 55.2, 51.3, 31.6, 29.6, 30.0. HR-MS FAB ([M+H]$^+$): *m/z* calculated for $C_{42}H_{43}N_4O_6$: 699.3183; found 699.3182.

Serinol-(O-DMT)-neocuproine phosphoramidite



Serinol-(O-DMT)-neocuproine (0.20 g, 0.29 mmol) was dried down once from a 5:1 CH_2Cl_2:Py mix and then further dried down twice from pyridine. The product was placed on a vacuum overnight. Freshly distilled (over CaH_2) CH_2Cl_2 was added (5 ml) under a blanket of Ar gas. The solution was cooled in an ice bath while stirring. Two equivalents of freshly distilled (over CaH_2) triethylamine (0.08 ml, 0.6 mmol) were added. The solution was allowed to stir for 5 min. Three equivalents of 2-cyanoethyl *N,N*-diisopropylchlorophosphoramidite (0.20 ml, 0.9 mmol) were added dropwise via a syringe. The solution was allowed to stir while warming to room temperature. The reaction was complete by TLC (5% MeOH/CH_2Cl_2 v/v) in 10 min with just a trace of starting material. The reaction was allowed to proceed for 1 h. The CH_2Cl_2 was removed by a stream of Ar gas. The crude reaction was chromatographed on basic alumina twice using a gradient elution of (0–1% methanol: CH_2Cl_2) to give pure product [serinol-(O-DMT)-neocuproine phosphoramidite] in a 82% yield (0.21 g, 0.24 mmol). R_f 0.55 (2% methanol/CH_2Cl_2 on basic alumina). ^{31}P NMR (75 MHz, acetone-d_6, in p.p.m. relative to TMP) δ 145.4, 145.7 (two diastereomers). HR-FAB on $C_{51}H_{60}N_6O_7P$ ([M+H]$^+$): expected 899.4261, found 899.4261.

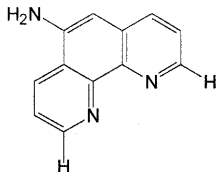
5′-Nitro-phenanthroline



This procedure was adopted from Smith and Cagles' nitration (36). 1,10-Phenanthroline (*o*-phen) (24.0 g, 133 mmol) was dissolved in 125 ml of H_2SO_4 (30% SO_3) and allowed to stir in a RBF for 10 min. 65 ml of concentrated HNO_3 was added dropwise to the stirring solution. The temperature of the addition reached 120°C. The reaction mixture was then heated

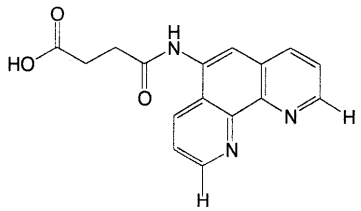
to 150°C for 30 min and stirring was maintained. The reaction was poured over crushed ice. NaOH (35%) was added slowly until the solution was neutral to litmus. A yellow precipitate formed. The product was filtered and washed with 2 vol ice-chilled distilled water. The product (5′-nitro-phenanthroline; 13.7 g, 60.8 mmol, 46% yield), was dried under vacuum for 24 h. R_f 0.23 (2% methanol/CH_2Cl_2 on basic alumina). ^{1}H NMR (300 MHz, $CDCl_3$, in p.p.m. relative to TMS): δ 9.24 (dd, J = 5.4, 1.8 Hz, 1 H); 9.23 (dd, J = 5.2, 1.8 Hz, 1 H); 8.90 (dd, J = 7.8, 1.8 Hz, 1 H); 8.55 (s, 1 H); 8.33 (dd, J = 8.1, 1.8 Hz, 1 H); 7.72 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, in p.p.m. relative to $CDCl_3$): δ 153.4, 151.3, 147.4, 145.9, 144.0, 137.7, 132.3, 125.4, 125.2, 124.3, 124.2, 120.8. HR-MS FAB ([M+H]$^+$): *m/z* calculated for $C_{12}H_8N_3O_2$: 226.0617; found 226.0616.

5′-Amino-phenanthroline



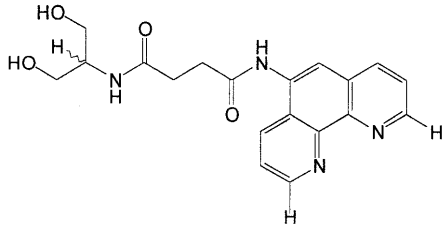
This procedure was adopted from Lecompte *et al.* (35). 5-Nitro-phenanthroline (13.7 g, 60.8 mmol), was suspended in 415 ml of EtOH (100%). Pd/C (2.75 g; 5% Pd content, 50% water) was added to yield a black suspension that was stirred for 10 min. A solution of hydrazine (13.7 ml, 440 mmol) in 280 ml EtOH was added dropwise. The resulting suspension was brought to reflux and maintained for 5 h. The solution was allowed to cool to room temperature, and was filtered through Celite 545. The yellow filtrate was concentrated to a volume of ~100 ml. Then 800 ml of distilled water was added and the solution was allowed to stand overnight. A yellow precipitate formed which was filtered and dried on a vacuum line overnight. The product, a yellow solid, 5′amino-phenanthroline (10.1 g, 51.7 mmol) was formed in an 85% yield. R_f 0.32 (5% methanol/CH_2Cl_2 on basic alumina). ^{1}H NMR (300 MHz, DMSO-d_6, in p.p.m. relative to CD_2HSOCD_3): δ 9.06 (dd, J = 5.6, 1.8 Hz, 1 H); 8.74 (dd, J = 8.0, 1.8 Hz, 1 H); 8.68 (dd, J = 5.6, 1.8 Hz, 1 H); 8.14 (dd, J = 8.0, 1.8 Hz, 1 H); 7.73 (dd, J = 7.8, 5.6 Hz, 1 H); 7.47 (dd, J = 8.0, 5.3 Hz, 1 H); 6.91 (s, 1 H); 6.24 [s (br), 2 H, NH_2]. ^{13}C NMR (75 MHz, DMSO-d_6, in p.p.m. relative to DMSO-d_6): δ 149.2, 146.0, 144.6, 140.3, 132.6, 130.8, 130.5, 123.1, 122.0, 122.0, 121.7, 101.7. HR-MS FAB ([M+H]$^+$): *m/z* calculated for $C_{12}H_{10}N_3$: 196.0875, found 196.0875.

5′-Amino-succinate-phenanthroline



5′-Amino-phenanthroline (2.0 g, 10.2 mmol) was co-evaporated from pyridine three times and dissolved in 40 ml freshly distilled (over CaH_2) pyridine to yield a yellow solution. Succinic anhydride (1.43 g, 14.3 mmol) and DMAP (spatula tip full) were added to the solution in a glove bag under an Ar atmosphere. The reaction was then allowed to react overnight at room temperature. The reaction was deemed complete (>95%) by TLC (5% methanol/CH_2Cl_2 on basic alumina) after 25 h of reaction. The insoluble precipitate was filtered and washed with 3 vol of ice-cold pyridine. This product, 5′-amino-succinate-phenanthroline (2.17 g, 7.34 mmol), was formed in a 72% yield. R_f 0.00 (2% methanol/CH_2Cl_2 on basic alumina). ^{1}H NMR [300 MHz, DMSO-d_6, in p.p.m. relative to $CD_2HC(O)CD_3$]: δ 10.20 (s, 1 H); 9.11 (dd, J = 3.0, 1.5 Hz, 1 H); 9.02 (dd, J = 2.7, 1.5 Hz, 1 H); 8.64 (dd, J = 8.1, 1.5 Hz, 1 H); 8.45 (dd, J = 8.0, 1.5 Hz, 1 H); 8.15 (s, 1 H); 7.81 (dd, J = 8.1, 3.0 Hz, 1 H); 7.74 (dd, J = 8.1, 3.0 Hz, 1 H); 2.75 (t, J = 6.9 Hz, 2 H); 2.53 (t, J = 7.0 Hz, 2 H). ^{13}C NMR (75 MHz, DMSO-d_6, in p.p.m. relative to DMSO-d_6): δ 174.0, 171.4, 149.9, 149.3, 145.8, 135.8, 131.8, 128.1, 123.6, 122.8, 120.0, 30.4, 29.0. HR-MS FAB ([M+H]$^+$): *m/z* calculated for $C_{16}H_{14}N_3O_3$: 296.1035, found 296.1035.

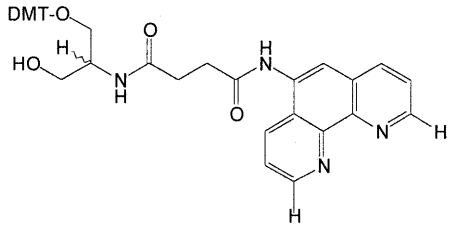
Serinol–phenanthroline



5′-Amino-succinate-phenanthroline (2.00 g, 6.77 mmol) was co-evaporated with toluene three times to remove any water and was then dissolved in 40 ml of anhydrous DMF. EDC-HCl (1.55 g, 8.1 mmol) and DMAP (spatula tip full) were added and the solution was allowed to stir for 30 min. Then serinol (0.74 g, 8.1 mmol) was added to the solution under an inert atmosphere of Ar in the glove bag. The reaction was allowed to proceed at room temperature overnight. The reaction was deemed complete (>95%) by TLC (60% methanol/H_2O on basic alumina) after 12 h of reaction. Almost no starting material remained and a new product had formed. The insoluble precipitate was filtered and washed with 3 vol ice-cold ethanol. This product serinol–phenanthroline was formed in a 60% yield (1.49 g, 4.06 mmol) and was used without further purification. R_f 0.71 (60% methanol/H_2O on basic alumina). ^{1}H NMR (300 MHz, DMSO-d_6, in p.p.m. relative to TMS): δ 11.14 (s, 1 H); 9.09 (d, J = 3.3 Hz, 1 H); 8.99 (d, J = 3.0 Hz, 1 H,); 8.77 (d, J = 8.4 Hz, 1 H); 8.36 (d, J = 8.4 Hz, 1 H); 8.28 (s, 1 H); 7.78 (dd, J = 8.4, 3.0 Hz, 1 H); 7.70 (dd, J = 8.4, 3.0 Hz, 1 H); 3.6–3.4 (m, 1 H); 2.96 (m, 1 H); 2.67 (m, 1 H); 2.49 (m, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6, in p.p.m. relative to TMS): 175.1, 172.7, 150.0, 149.7, 148.7, 148.6, 135.7, 129.5, 128.4, 120.8, 119.9, 119.5, 117.8, 109.8, 65.1, 54.1, 30.3, 29.6. HR-MS FAB ([M+H]$^+$): *m/z* calculated for $C_{19}H_{21}N_4O_4$: 369.1563; found 369.1563.

Serinol-(O-DMT)-phenanthroline

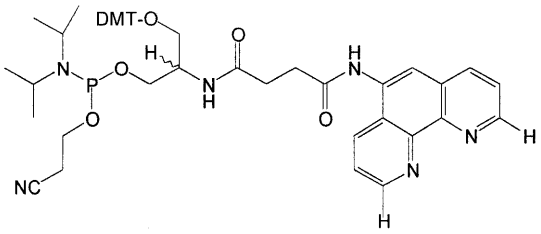
Serinol–phenanthroline (0.94 g, 2.54 mmol) was co-evaporated with pyridine three times to remove any water and then dissolved in 10 ml of freshly distilled pyridine (over CaH_2). DMT-Cl (0.82 g, 2.54 mmol) was added to the solution under an inert atmosphere of Ar in a glove bag. The solution was allowed to stir at room temperature for 18 h. The solvent was removed by rotary evaporation and a bilayer of CH_2Cl_2 and water was added. After extraction, the water layer was further extracted with 1 vol CH_2Cl_2. The organic layers were



collected, dried over $MgSO_4$, and the solvent was removed. The orange precipitate was dissolved in CH_2Cl_2 and chromatographed twice on a basic alumina column with a gradient elution of 0–2% methanol-CH_2Cl_2. The column solvent was removed to yield pure serinol-(O-DMT)-phenanthroline, a white foam, in a 64% yield (1.09 g, 1.6 mmol). R_f 0.36 (5% methanol/CH_2Cl_2 on basic alumina). ^{1}H NMR (300 MHz, $CDCl_3$, in p.p.m. relative to TMS): δ 9.89 (s, 1 H); 8.97 (d, J = 6.0 Hz, 1 H); 8.92 (d, J = 6.0 Hz, 1 H); 8.61 (d, J = 6.5 Hz, 1 H); 8.14 (s, 1 H); 7.93 (d, J = 6.7 Hz, 1 H); 7.5–7.0 (m, 9 H); 6.94 (d, J = 7.0 Hz, 1 H); 6.75 (m, 4 H); 4.20 (m, 1 H); 3.9–3.6 (m, 10 H); 3.43 (m, 1 H); 3.30 (m, 2 H); 3.01 (m, 1 H); 2.55 (m, 2 H); 2.76 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, in p.p.m. relative to $CDCl_3$): δ 173.4, 173.1, 159.5, 144.4, 144.1, 143.5, 143.0, 142.2, 136.2, 136.1, 129.5, 129.4, 129.0, 128.4, 128.4, 126.0, 122.5, 122.4, 122.3, 117.8, 114.6, 109.8, 88.8, 66.7, 65.4, 56.0, 52.5, 30.3, 29.6. HR-MS FAB ([M+H]$^+$): *m/z* calculated for $C_{40}H_{39}N_4O_6$: 671.2870; found 671.2869.

Serinol-(O-DMT)-phenanthroline phosphoramidite

Serinol-(O-DMT)-phenanthroline (0.53 g, 0.79 mmol) was dried down once from a 5:1 CH_2Cl_2:Py mix and then further



dried down twice from pyridine. The product was placed on a vacuum overnight. Freshly distilled (over CaH_2) CH_2Cl_2 was added (5 ml) under a blanket of Ar gas. The solution was cooled in an ice bath while stirring. Two equivalents of freshly distilled (over CaH_2) triethylamine (0.22 ml, 1.6 mmol) was added. The solution was allowed to stir for 5 min. Three equivalents of 2-cyanoethyl *N*,*N*-diisopropylchlorophosphoramidite (0.53 ml, 2.4 mmol) were added dropwise via a syringe. The solution was allowed to stir while warming to room temperature. The reaction was complete by TLC (5% MeOH/CH_2Cl_2 v/v) in 10 min with just a trace of starting material. The reaction was allowed to proceed for 1 h. The CH_2Cl_2 was removed by a stream of Ar gas. The crude reaction was chromatographed on basic alumina twice using a gradient elution of (0–1% methanol: CH_2Cl_2) to give pure product [Serinol-(O-DMT)-phenanthroline phosphoramidite] in a 73% yield (0.50 g, 0.58 mmol). R_f 0.36 (2% methanol/CH_2Cl_2 on basic alumina). ^{31}P NMR (75 MHz, acetone-d_6, in p.p.m. relative to TMP) δ 145.6, 145.8 (two diastereomers). HR-FAB on $C_{49}H_{56}N_6O_7P$ ([M+H]$^+$): expected 871.3948, found 871.3948.