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DNA-based Asymmetric Organometallic Catalysis in Water

Supporting Information

Jens Oelerich and Gerard Roelfes*

General Remarks.

Salmon testes DNA, compounds **L1**, **L2**, **6** and **7** were obtained from Sigma Aldrich and used without further purifications. Sulfone **6f**^[1], β -keto sulfones **8a,c,g**^[2, 3], ligands **L4**, **L5a-c** and **L6**^[4-6] and copper complexes of ligand **L2** and **L3**^[7] **L4** and **L5**^[8] were synthesized following published procedures. ¹H-NMR, and ¹³C-NMR spectra were recorded on a Varian 400 (400 and 100 MHz). Chemical shifts (δ) are denoted in ppm using residual solvent peaks as internal standard ($\delta_H=7.26$ and $\delta_C=77.0$ for CDCl₃). For all diazo compounds no C¹³ signal of the carbon bound to the diazo function was observed, which is in agreement with literature.^[2] High resolution mass spectra (HRMS) were recorded on an Orbitrap XL (Thermo Fisher Scientific; ESI pos. mode). Enantiomeric excess determinations were performed by HPLC analysis (Chiracel-ADH or Chiralpak-ASH) using UV-detection (Shimadzu SCL-10Avp). Flash chromatography was performed using silica gel 60 Å (Merck, 200-400 mesh) or a Grace Reveleris® Flash System (40 μ m silica column).

Representative procedure for the asymmetric cyclopropanation of **1** catalyzed by DNA/Cu-complex

Salmon testes DNA (1.5 mg/ml) was dissolved in 10 mM solution of MOPS buffer pH 6.5 (2.25 mM in base pairs) 24 hours before use. The DNA solution and buffer were deoxygenated by bubbling a stream of nitrogen through the solution for at least 4 hours and then was transferred into a glove box (O₂ <20ppm). To reach a final concentration of 1.0 mM of substrate **1**, 0.3 mM of copper complex and 1.5 mM of DNA base pairs; 100 μ l of a 22.5 mM solution of previously formed copper complex in DMF was added to 2.350 ml of buffer in a 15 ml plastic tube. Then, 5 ml of st-DNA solution was slowly added and the solution was mixed by continuous inversion at room temperature. After incubation for 16 hours, 50 μ l of a 150 mM solution of **1** in DMF was added to start the catalytic reaction. After 3 days the product was extracted with EtOAc (3 x 7,5 mL). After drying (Na₂SO₄) and evaporation of the solvent the crude product was analyzed by HPLC, using methyl phenyl sulfone as external standard.

Analysis of side reaction

Figure S1: ¹H-NMR of the aqueous phase in d₆-DMSO

Figure S2: Mass analysis of the organic phase by DART (Direct Analysis in Real time) ionization technique (negative and positive mode)

Synthesis protocols and analytic data

Scheme S1: General synthesis of diazo substrates 1a-g

General procedure 1: Synthesis of β -keto-sulfones **14**:

Under inert atmosphere sulfone **12** (5 mmol) was dissolved in dry THF (50 ml). n-Butyllithium in hexane (1.6 M, 10 mmol, 6.25 ml) was added drop wise at 0 °C and the mixture was stirred for additional 10 min. To this strong yellow suspension ester, **13** (6.0 mmol) in 2 ml THF was added in two portions. The mixture discolored and was stirred at 0 °C for 30 min. The reaction was quenched with saturated aqueous NH₄Cl solution (50 ml) and extracted with Et₂O (50ml) and CH₂Cl₂ (50ml x 2). The combined organic layers were washed with brine (50ml), dried over Na₂SO₄ and the solvent was evaporated.

1-(phenylsulfonyl)hexan-2-one (**8b**).

Synthesized using general procedure 1 starting from (1.562 g, 10 mmol) **6a**. Purified by column chromatography (SiO₂, 20% EtOAc:heptane), to afford the product as a white solid. Yield: 1.38 g (5.74 mmol, 57%) of **8b**. mp = 75 – 76 °C. ¹H NMR (400 MHz, CDCl₃) δ = 7.91 – 7.81 (m, 2H), 7.67 (t, *J*=6.8, 1H), 7.56 (dd, *J*=7.9, 7.9, 2H), 4.14 (s, 2H), 2.68 (t, *J*=7.2, 2H), 1.58 – 1.44 (m, 2H), 1.28 (tq, *J*=7.3, 7.3, 2H), 0.88 (t, *J*=7.3, 3H). ¹³C NMR (101

MHz, CDCl₃) δ = 198.17, 138.69, 134.19, 129.26, 128.20, 66.71, 44.08, 25.10, 21.88, 13.70. HRMS calcd for C₁₂H₁₇O₃S⁺ [M+H⁺]: 241.08929, found 241.08918.

1-(phenylsulfonyl)hexan-2-one (8d).

Synthesized using general procedure 1 starting from (500 mg, 3.2 mmol) **6a**. Purified by column chromatography (SiO₂, 20% EtOAc:heptane), to afford the product as a white solid. Yield: 478 mg (1.89 mmol, 59%) of **8d**. mp = 32 – 34 °C. ¹H NMR (400 MHz, CDCl₃) δ = 7.92 – 7.83 (m, 2H), 7.69 (t, *J*=7.5, 1H), 7.58 (dd, *J*=7.9, 7.9, 2H), 5.84 – 5.64 (m, 1H), 5.09 – 4.90 (m, 2H), 4.14 (s, 2H), 2.71 (t, *J*=7.2, 2H), 2.14 – 1.94 (m, 2H), 1.70–1.64 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ = 197.98, 138.70, 137.50, 134.28, 129.33, 128.27, 115.56, 66.91, 43.58, 32.62, 22.16. HRMS calcd for C₁₃H₁₇O₃S⁺ [M+H⁺]: 253.08984, found 253.08929.

5-methyl-1-(phenylsulfonyl)hex-5-en-2-one (8e).

Synthesized using general procedure 1 starting from (915 mg, 5.86 mmol) **6a**. Purified by column chromatography (SiO₂, 20% EtOAc:heptane), to afford the product as a colorless oil. Yield: 992 mg (3.93 mmol, 67%) of **8e**. ¹H NMR (400 MHz, CDCl₃) δ = 7.88 (d, *J*=7.4, 2H), 7.68 (t, *J*=7.5, 1H), 7.57 (dd, *J*=7.9, 7.9, 2H), 4.75 – 4.72 (m, 1H), 4.66 – 4.63 (m, 1H), 4.16 (s, 2H), 2.85 (t, *J*=7.4, 2H), 2.26 (t, *J*=7.4, 2H), 1.71 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ = 197.50, 143.45, 138.64, 134.24, 129.29, 128.22, 110.67, 66.78, 42.49, 30.76, 22.52. HRMS calcd for C₁₃H₁₇O₃S⁺ [M+H⁺]: 253.08984, found 253.08929.

1-(pyridin-2-ylsulfonyl)hex-5-en-2-one (8f).

6f (0.786 g, 5 mmol) was dissolved in 50 ml dry THF and cooled to -78°C. *n*-Butyllithium (6.25 ml, 1.6 mM solution in hexane, 10.00 mmol) was added drop wise at -78°C over 20 min and stirred for another 20 min. To this solution **7f** (0.599 g, 5.25 mmol) in 1.5 ml THF was added drop wise at -78°C over 20 min and stirred for another 20 min. Then the reaction mixture was allowed to warm to room temperature over 30 min and was quenched with saturated aqueous NH₄Cl solution (50 ml). The aqueous phase was extracted with ether (3 x 30 ml) and the combined organic layers were washed with brine (50 ml), dried over Na₂SO₄ and evaporated. The residue was purified by column chromatography (SiO₂, 50% EtOAc:heptane) to afford the product as an orange oil. Yield: 778 mg (3.25 mmol, 65%) of **8f**. ¹H NMR (400 MHz, CDCl₃) δ = 8.72 (d, *J*=4.7, 1H), 8.05 (d, *J*=7.8, 1H), 7.97 (td, *J*=7.7, 1.6, 1H), 7.57 (ddd, *J*=7.5, 4.7, 0.8, 1H), 5.74 (ddt, *J*=16.8, 10.2, 6.5, 1H), 5.06 – 4.89 (m, 2H), 4.48 (s, 2H), 2.79 (t, *J*=7.2, 2H), 2.30 (t, *J*=7.0, 2H). ¹³C NMR (101 MHz, CDCl₃) δ = 197.39, 156.60, 150.09, 138.28, 136.03, 127.69, 122.12, 115.76, 62.26, 43.30, 27.00. HRMS calcd for C₁₁H₁₄NO₃S⁺ [M+H⁺]: 240.06889, found 240.06878.

General procedure 2: Synthesis of diazo compounds **1**:

Under inert atmosphere β -keto sulfone **8** (3.0 mmol) was dissolved in CH_3CN (25 ml) and triethylamine (450 mg, 4.50 mmol) was added at 0°C . Then freshly prepared 4-methylbenzenesulfonyl azide (592 mg, 3.60 mmol) was added drop wise while stirring. The reaction mixture was allowed to warm to room temperature while stirring for 3 h. Then the mixture was washed with saturated NH_4Cl (10 ml) and the aqueous layer was extracted with ether (3 x 10 ml). The combined organic phases were washed with 10% KOH (5 ml), saturated NaHCO_3 (5 ml), and saturated NaCl (5 ml), dried over anhydrous MgSO_4 and concentrated in vacuo at room temperature until ~1ml solvent is left. The product was purified by column chromatography.

Note: For all diazo compounds no C^{13} signal of the carbon bound to the diazo function was observed, which is in agreement with literature.^[2]

1-diazo-1-(phenylsulfonyl)hex-5-en-2-one (1a).

Synthesized using general procedure 2 starting from (2g, 8.39 mmol) **8a**. Purified by column chromatography (SiO_2 , 10% EtOAc :heptane), to afford the product as a yellow solid. Yield: 2.04 g (7.33 mmol, 87%) of **1a**. mp = $38 - 40^\circ\text{C}$. ^1H NMR (400 MHz, CDCl_3) δ = 7.97 (d, $J=7.3$, 2H), 7.67 (t, $J=7.4$, 1H), 7.58 (dd, $J=7.4$, 7.3, 2H), 5.81 – 5.58 (m, 1H), 5.03 – 4.84 (m, 2H), 2.64 (t, $J=7.3$, 2H), 2.33 – 2.21 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ = 187.57, 141.98, 135.94, 134.13, 129.46, 127.23, 115.85, 38.20, 27.49. HRMS calcd for $\text{C}_{12}\text{H}_{13}\text{N}_2\text{O}_3\text{S}^+$ [$\text{M}+\text{H}^+$]: 265.06414, found 265.06372.

1-diazo-1-(phenylsulfonyl)hexan-2-one (1b).

Synthesized using general procedure 2 starting from (481mg, 2.00 mmol) **8b**. Purified by column chromatography (SiO_2 , 10% EtOAc :heptane), to afford the product as a yellow oil. Yield: 394 mg (1.48 mmol, 74%) of **1b**. mp = $34 - 35^\circ\text{C}$. ^1H NMR (400 MHz, CDCl_3) δ = 7.96 (dd, $J=5.3$, 3.4, 2H), 7.65 (ddd, $J=6.7$, 3.9, 1.2, 1H), 7.56 (dd, $J=10.5$, 4.8, 2H), 2.52 (t, $J=7.4$, 2H), 1.55 – 1.46 (m, 1H), 1.30 – 1.19 (m, 1H), 0.82 (t, $J=7.3$, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ = 188.39, 141.95, 134.06, 129.37, 127.23, 38.76, 25.64, 21.96, 13.58. HRMS calcd for $\text{C}_{12}\text{H}_{15}\text{N}_2\text{O}_3\text{S}^+$ [$\text{M}+\text{H}^+$]: 267.07979, found 267.07966.

1-diazo-1-(phenylsulfonyl)hex-5-en-2-one (1c).

Synthesized using general procedure 2 starting from (675 mg, 2.68 mmol) **8c**. Purified by column chromatography (SiO_2 , 10% EtOAc :heptane), to afford the product as a yellow solid. Yield: 564 mg (2.03 mmol, 76%) of **1c**. mp = $40 - 41^\circ\text{C}$. ^1H NMR (400 MHz, CDCl_3) δ = 8.12 (d, $J=8.0$, 1H), 7.55 (t, $J=7.5$, 1H), 7.46 – 7.33 (m, 2H), 5.62 (m, 1H),

4.97 – 4.82 (m, 2H), 2.61 (s, 3H), 2.54 (t, $J=7.3$, 2H), 2.23 (q, $J=7.2$, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ = 188.02, 139.50, 137.43, 135.93, 134.19, 133.10, 130.16, 126.73, 115.74, 38.06, 27.47, 20.07. HRMS calcd for $\text{C}^{13}\text{H}^{14}\text{N}^2\text{O}^3\text{SNa}^+ [\text{M}+\text{Na}^+]$: 301.06173, found 301.06177

1-diazo-1-(phenylsulfonyl)hex-5-en-2-one (1d).

Synthesized using general procedure 2 starting from (400 mg, 1.59 mmol) **8d**. Purified by column chromatography (SiO_2 , 10% EtOAc:heptane), to afford the product as a yellow oil. Yield: 231 mg (0.83 mmol, 53%) of **1b**. ^1H NMR (400 MHz, CDCl_3) δ = 8.04 – 7.91 (m, 2H), 7.67 (dd, $J=10.6$, 4.3, 1H), 7.58 (dd, $J=10.5$, 4.8, 2H), 5.75 – 5.57 (m, 1H), 5.00 – 4.88 (m, 2H), 2.54 (t, $J=7.3$, 2H), 2.01 (q, $J=7.1$, 2H), 1.67 (dd, $J=14.6$, 7.3, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ = 188.47, 142.25, 137.58, 134.35, 129.68, 127.55, 115.82, 38.46, 32.94, 22.84. HRMS calcd for $\text{C}_{13}\text{H}_{15}\text{N}_2\text{O}_3\text{S}^+ [\text{M}+\text{H}^+]$: 279.08034 found 279.07979.

1-diazo-5-methyl-1-(phenylsulfonyl)hex-5-en-2-one (1e).

Synthesized using general procedure 2 starting from (505mg, 2.00 mmol) **8e**. Purified by column chromatography (SiO_2 , 10% EtOAc:heptane), to afford the product as a yellow oil. Yield: 440 mg (1.58 mmol, 79%) of **1f**. ^1H NMR (400 MHz, CDCl_3) δ = 8.00 – 7.94 (m, 2H), 7.70 – 7.63 (m, 1H), 7.62 – 7.55 (m, 2H), 4.70 – 4.67 (m, 1H), 4.56 – 4.53 (m, 1H), 2.73 – 2.63 (m, 2H), 2.24 (t, $J=7.6$, 2H), 1.65 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ = 187.78, 143.44, 141.98, 134.13, 129.47, 127.25, 110.62, 37.31, 31.09, 22.46. HRMS calcd for $\text{C}^{13}\text{H}^{14}\text{N}^2\text{O}^3\text{SNa}^+ [\text{M}+\text{Na}^+]$: 301.06173, found 301.06177.

1-diazo-1-(pyridin-2-ylsulfonyl)hex-5-en-2-one (1f).

Synthesized using general procedure 2 starting from (400mg, 1.67 mmol) **8f**. Purified by column chromatography (SiO_2 , 20% EtOAc:heptane), to afford the product as a yellow oil. Yield: 201 mg (0.76 mmol, 48%) of **1d**. ^1H NMR (400 MHz, CDCl_3) δ = 8.75-8.69 (m, 1H), 8.10 (dd, $J=7.9$, 1.0, 1H), 7.99 (dd, $J=7.8$, 1.7, 1H), 7.58 (ddd, $J=7.6$, 4.7, 1.1, 1H), 5.74 (dd, $J=17.0$, 10.3, 1H), 5.04 – 4.88 (m, 2H), 2.80 (t, $J=7.3$, 2H), 2.33 (dt, $J=13.7$, 6.9, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ = 188.65, 159.03, 150.66, 138.61, 136.50, 128.00, 121.84, 115.91, 38.55, 27.90. HRMS calcd for $\text{C}_{11}\text{H}_{12}\text{N}_3\text{O}_3\text{S}^+ [\text{M}+\text{H}^+]$: 266.05939, found 266.05968.

1-diazo-1-tosylhex-5-en-2-one (1g).

Synthesized using general procedure 2 starting from (600mg, 2.38 mmol) **8g**. Purified by column chromatography (SiO_2 , 10% EtOAc:heptane), to afford the product as a yellow oil. Yield: 431 mg (1.55 mmol, 69%) of **1e**. ^1H NMR (400 MHz, CDCl_3) δ = 7.85 (d, $J=8.4$, 2H), 7.37 (d, $J=8.0$, 2H), 5.78-5.68 (m, 1H), 5.06 – 4.86 (m, 2H), 2.65

(t, $J=7.4$, 2H), 2.46 (s, 3H), 2.39 – 2.19 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ = 188.02, 145.64, 139.42, 136.29, 130.31, 127.57, 116.09, 38.45, 27.77, 21.90. HRMS calcd for $\text{C}_{13}\text{H}_{14}\text{N}_2\text{O}_3\text{SNa}^+$ [$\text{M}+\text{Na}^+$]: 301.06173, found 301.06233.

General procedure 3: Synthesis of racemic cyclopropanation products **2**:

Under inert atmosphere diazo compound **1** (0.4 mmol) was dissolved in dry CH_2Cl_2 (8 ml) to give a yellow solution. $\text{Rh}_2(\text{OAc})_4$ (2 mol%, 8.00 μmol) was added and the reaction monitored by TLC. After full conversion (~1 h) the solution was filtered over a small batch of SiO_2 to remove the rhodium catalyst. The column was washed with CH_2Cl_2 (8 ml) and the solvent evaporated under reduced pressure to afford the crude product.

1-(phenylsulfonyl)bicyclo[3.1.0]hexan-2-one (2a).

Synthesized using general procedure 3. starting from (100 mg, 0.378 mmol) **1a**. Purified by flash chromatography (SiO_2 , gradient EtOAc:pentane), to afford the product as a white solid. Yield: 51mg (0.216 mmol, 57%) of **2a**. mp=98-99°C. ^1H NMR (400 MHz, CDCl_3) δ = 8.02 (d, $J=7.9$, 2H), 7.69 – 7.58 (m, 1H), 7.58 – 7.44 (m, 2H), 3.02 (m, 1H), 2.32 – 2.11 (m, 4H), 2.06 – 1.93 (m, 1H), 1.52 (dd, $J=5.5$, 3.7, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ = 203.35, 139.47, 133.75, 128.91, 128.81, 53.18, 33.67, 31.09, 20.49, 20.31 HRMS calcd for $\text{C}_{12}\text{H}_{13}\text{O}_3\text{S}^+$ [$\text{M}+\text{H}^+$]: 237.05799, found 237.05840.

5-methyl-1-(phenylsulfonyl)bicyclo[3.1.0]hexan-2-one (2e).

Synthesized using general procedure 3 starting from (111 mg, 0.400 mmol) **1e**. Purified by flash chromatography (SiO_2 , gradient EtOAc:pentane), to afford the product as a white solid. Yield: 78 mg (3.12 mmol, 78%) of **2e**. mp=129-130. ^1H NMR (400 MHz, CDCl_3) δ = 8.08 – 7.95 (m, 2H), 7.61 (t, $J=7.4$, 1H), 7.52 (dd, $J=7.9$, 7.3, 2H), 2.28 (d, $J=5.0$, 1H), 2.17 – 1.90 (m, 4H), 1.79 (s, 3H), 1.67 (d, $J=5.1$, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ = 203.92, 140.32, 133.58, 128.89, 128.71, 56.94, 42.24, 33.00, 28.47, 26.17, 18.35. HRMS calcd for $\text{C}_{13}\text{H}_{15}\text{O}_3\text{S}^+$ [$\text{M}+\text{H}^+$]: 251.07364, found 251.07401.

1-(pyridin-2-ylsulfonyl)bicyclo[3.1.0]hexan-2-one (2f).

Diazo compound **1f** (0.4 mmol) was dissolved in deoxygenated H_2O (40 ml) under inert atmosphere to give a yellow solution. $\text{Cu}(\text{NO}_3)_2(\text{H}_2\text{O})_2$ (25 mol%, 0.1 mmol) was added and the reaction monitored by TLC. After full conversion was reached (~18 h), the reaction mixture was extracted with CH_2Cl_2 (3 x 20ml), the combined organic phases were washed with brine (20 ml) and dried (Na_2SO_4). Then the solvent was evaporated under reduced pressure to afford the crude product, which was purified by flash chromatography (SiO_2 , gradient EtOAc:pentane), to afford the product as a colorless oil. Yield: 61 mg (2.72 mmol, 68%) of **2f**. ^1H NMR (400 MHz, CDCl_3) δ =

8.70 – 8.63 (m, 1H), 8.22 (t, $J=7.9$, 1H), 7.96 (td, $J=7.8$, 1.7, 1H), 7.51 (dd, $J=7.6$, 4.7, 1H), 3.05 (dt, $J=8.7$, 5.4, 1H), 2.45 (dd, $J=8.6$, 5.7, 1H), 2.35 – 2.15 (m, 3H), 2.05 (ddd, $J=11.5$, 8.4, 5.5, 1H), 1.67 (t, $J=5.7$, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ = 203.59, 157.31, 149.81, 137.95, 127.26, 123.55, 50.62, 33.42, 30.63, 20.27, 20.17. HRMS calcd for $\text{C}_{11}\text{H}_{12}\text{NO}_3\text{S}^+$ $[\text{M}+\text{H}^+]$: 238.05324, found 238.05445.

1-tosylbicyclo[3.1.0]hexan-2-one (2g).

Synthesized using general procedure 3 starting from (111 mg, 0.400 mmol) **1g**. Purified by flash chromatography (SiO_2 , gradient EtOAc:pentane), to afford the product as a white solid. Yield: 80 mg (3.20 mmol, 80%) of **2g**. mp=123-124. ^1H NMR (400 MHz, CDCl_3) δ = 7.92 (d, $J=8.2$, 2H), 7.34 (d, $J=8.1$, 2H), 3.09 – 2.95 (m, 1H), 2.44 (s, 3H), 2.33 – 2.10 (m, 4H), 2.01 (dd, $J=7.0$, 4.6, 1H), 1.51 (t, $J=5.4$, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ = 203.48, 144.67, 136.44, 129.46, 128.70, 53.15, 33.57, 31.00, 21.55, 20.30, 20.20. HRMS calcd for $\text{C}_{13}\text{H}_{15}\text{O}_3\text{S}^+$ $[\text{M}+\text{H}^+]$: 251.07364, found 251.07359.

General procedure 4: Synthesis of dppz derivatives L5d,e:

The phenanthroline derivative **L3** (6.5 mmol) and potassium bromide (7.5 g, 63.0 mmol) were combined and stirred. Sulfuric acid (30 ml, 540 mmol) was added drop wise over 15 min at 0°C . After an additional 15 min nitric acid (15 ml, 245 mmol) was added drop wise at 0°C . The resulting mixture was heated at 80°C for 4 h and then cooled to 0°C . The cold acidic mixture was carefully poured out on ice (~300g). Subsequently, 5% NaOH solution was added slowly under vigorous stirring until the pH reached 3. Then the mixture was extracted with CH_2Cl_2 (3 x 300 ml). The organic phase was dried over MgSO_4 and the solvent was evaporated.

Benzene-1,2-diamine (409 mg, 3.78 mmol) was dissolved in ethanol (50 ml). To the stirred solution the crude yellow solid (~1.5 g, 6.3 mmol) was added at room temperature and the mixture was stirred while heating under reflux overnight. Then the ethanol was evaporated and the residue dissolved in 100 ml of CH_2Cl_2 . The product was extracted with 0.1 M HCl solution (3 x 100ml). The combined aqueous phases were basified to pH 10 with 1 M NaOH and the precipitate was filtered off and dried. The crude product was purified by recrystallization from CH_2Cl_2 .

1,2,7,8-tetramethyldipyrido[3,2-a:2',3'-c]phenazine (L5d).

Synthesized using general procedure 4 starting from (1.0 g, 3.93 mmol) 3,4,7,8-tetramethyl-1,10-phenanthroline hydrate. Yield: 376 mg (1.11 mmol, 28%) of **L3c**. mp = decomposition > 250°C, ^1H NMR (400 MHz, CDCl_3) δ = 8.90 (s, 2H), 8.23 (dd, J =6.4, 3.4, 2H), 7.83 (dd, J =6.4, 3.4, 2H), 3.23 (s, 6H), 2.55 (s, 6H). ^{13}C NMR (101 MHz, CDCl_3) δ = 152.17, 148.22, 147.13, 144.26, 139.12, 133.52, 129.80, 129.03, 124.99, 20.32, 18.12. HRMS calcd for $\text{C}_{22}\text{H}_{19}\text{N}_4^+$ [$\text{M}+\text{H}^+$]: 339.16042, found 339.15967.

1,8-dimethyldipyrido[3,2-a:2',3'-c]phenazine (L5e).

Synthesized using general procedure 4 starting from (1.35 g, 6.5 mmol) 4,7-dimethyl-1,10-phenanthroline. Yield: 129 mg (0.416 mmol, 11%) of **L3b**. mp = decomposition > 265°C, ^1H NMR (400 MHz, CDCl_3) δ = 9.02 (d, J =4.6, 2H), δ = 8.21 (dd, J =6.4, 3.4, 2H), 7.82 (dd, J =6.5, 3.4, 2H), 7.49 (d, J =4.6, 2H), 3.32 (s, 6H). ^{13}C NMR (101 MHz, CDCl_3) δ = 150.83, 149.79, 149.38, 143.96, 139.59, 130.05, 129.16, 127.93, 125.93, 26.44. HRMS calcd for $\text{C}_{20}\text{H}_{15}\text{N}_4^+$ [$\text{M}+\text{H}^+$]: 311.12912, found 311.12918.

General procedure 5: Synthesis of Copper complexes $\text{Cu}(\text{L5})(\text{NO}_3)_2$:

$\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$ (73.5 mg, 0.30 mmol) and dppz derivative **L5** (0.27 mmol) were dissolved in a minimum amount of ethanol. **L5** was added drop wise to the stirred copper solution and stirring was continued for 1 h at room temperature. The solid was filtered off and washed with ethanol and diethyl ether.

$\text{Cu}(\text{L5d})(\text{NO}_3)_2$

Synthesized using general procedure 5 starting from (200 mg, 0.591 mmol) **L5d**. Yield: 264 mg (0.485 mmol, 82%) of **Cu-L5d**. Elemental analysis (calcd %) for $\text{C}_{22}\text{H}_{18}\text{CuN}_6\text{O}_6 \cdot 1\text{H}_2\text{O}$: C, 48.57; H, 3.71; N, 15.45; found: C, 49.01; H, 3.31; N, 15.73. ESI-MS positive mode, calcd for $\text{C}_{22}\text{H}_{18}\text{CuN}_5\text{O}_3$ [$\text{M}-\text{NO}_3$] $^+$: 463.1, found 463.0.

$\text{Cu}(\text{L5e})(\text{NO}_3)_2$

Synthesized using general procedure 5 starting from (20 mg, 0.064 mmol) **L5e**. Yield: 24 mg (0.047 mmol, 72%) of **Cu-L5e**. Elemental analysis (calcd %) for $\text{C}_{20}\text{H}_{14}\text{CuN}_6\text{O}_6 \cdot 0.5\text{H}_2\text{O}$: C, 47.39; H, 2.98; N, 16.58; found: C, 47.12; H, 2.71; N, 16.08. ESI-MS positive mode, calcd for $\text{C}_{20}\text{H}_{14}\text{CuN}_5\text{O}_3$ [$\text{M}-\text{NO}_3$] $^+$: 435.0, found 435.0.

HPLC traces for cyclopropanation products 2

Standard is methyl phenyl sulfone

Analysis Report

<Sample Information>

Sample Name : JOC-210-9
Sample ID : JOC-210-9
Data Filename : JOC-210-9.lcd
Method Filename : ADH 90_10 45 min fl 0.5 -analyze_phen.lcm
Batch Filename : 20120113.lcb
Vial # : 1-38
Injection Volume : 5 uL
Date Acquired : 1/14/2012 3:23:11 PM
Date Processed : 1/14/2012 4:05:24 PM
Sample Type : Unknown
Level : 1
Acquired by : System Administrator
Processed by : System Administrator

<Chromatogram>

mAU

Peak Table

Name	Ret. Time	Area	Height
substrate	12.753	532688	33838
DMF	13.689	21685018	933548
standard	18.136	25570881	1115760
product enantiomer 1	33.720	7133715	185641
product enantiomer 2	37.771	654800	15769
		55577101	2284556

(1R,5R)-2a: 83% ee

Racemate:

Analysis Report

<Sample Information>

Sample Name : JOC-phen-prod
Sample ID : JOC-phen-prod
Data Filename : JOC-phen-prod.lcd
Method Filename : ADH 90_10 45 min fl 0.5 -analyze_phen.lcm
Batch Filename : 20120821.lcb
Vial # : 1-40
Injection Volume : 5 uL
Date Acquired : 8/20/2012 7:10:36 PM
Date Processed : 8/20/2012 7:55:41 PM
Sample Type : Unknown
Level : 1
Acquired by : System Administrator
Processed by : System Administrator

<Chromatogram>

mAU

2f: 52% ee

<Sample Information>

Sample Name : JOC-208-09
Sample ID : JOC-208-09
Data Filename : 20111220-JOC-208-09-ASH.lcd
Method Filename : ASH 90_10 60 min fl 0.5 -analyze_pyr.lcm
Batch Filename : 20111221.lcb
Vial # : 1-58
Injection Volume : 10 uL
Date Acquired : 12/21/2011 7:06:11 PM
Date Processed : 12/21/2011 8:06:15 PM
Sample Type : Unknown
Level : 1
Acquired by : System Administrator
Processed by : System Administrator

<Chromatogram>

Peak Table

PDA Ch1 210nm				
Name	Ret. Time	Area	Height	
substrate	16.285	16451121	578378	
DMF	22.694	14581447	421970	
standard	23.915	52112381	1058683	
product enantiomer 1	50.356	2713286	31449	
product enantiomer 2	54.592	886882	9262	
		86745116	2099742	

Racemate:

Analysis Report

<Sample Information>

Sample Name : JOC-pyr-prod
Sample ID : JOC-pyr-prod
Data Filename : JOC-pyr-prod.lcd
Method Filename : ASH 90_10 60 min fl 0.5 -analyze_pyr.lcm
Batch Filename : 20120821.lcb
Vial # : 1-41
Injection Volume : 5 uL
Date Acquired : 8/20/2012 8:26:19 PM
Date Processed : 8/20/2012 9:26:22 PM
Sample Type : Unknown
Level : 1
Acquired by : System Administrator
Processed by : System Administrator

<Chromatogram>

Analysis Report

<Sample Information>

Sample Name : JOC-208-08
Sample ID : JOC-208-08
Data Filename : 20111220-JOC-208-08-ADH-92-8.lcd
Method Filename : ADH 92_08 45 min fl 0.5 -analyze_tol.lcm
Batch Filename : 20111221.lcb
Vial # : 1-57
Injection Volume : 10 uL
Date Acquired : 12/21/2011 5:50:20 PM
Date Processed : 12/21/2011 6:35:24 PM
Sample Type : Unknown
Level : 1
Acquired by : System Administrator
Processed by : System Administrator

<Chromatogram>

Peak Table

Name	Ret. Time	Area	Height
substrate	13.882	20441483	1022868
DMF	15.480	31551431	995259
standard	20.387	44506506	1412151
product enantiomer 1	37.582	4981536	109821
product enantiomer 2	39.760	1135560	23951
		102616517	3564050

Racemate:

Analysis Report

<Sample Information>

Sample Name : JOC-o-tol-prod
Sample ID : JOC-o-tol-prod
Data Filename : JOC-o-tol-prod.lcd
Method Filename : ADH 92_08 45 min fl 0.5 -analyze_tol.lcm
Batch Filename : 20120821.lcb
Vial # : 1-42
Injection Volume : 5 uL
Date Acquired : 8/20/2012 9:56:58 PM
Date Processed : 8/20/2012 10:42:01 PM
Sample Type : Unknown
Level : 1
Acquired by : System Administrator
Processed by : System Administrator

<Chromatogram>

(1R,5R)-2g: 64% ee

SHIMADZU LabSolutions Analysis Report

<Sample Information>

Sample Name : JOC-208-10
Sample ID : JOC-208-10
Data Filename : 20111220-JOC-208-10.lcd
Method Filename : ADH 90_10 45 min fl 0.5 -analyze_b-Me.lcm
Batch Filename : 20111219-b.lcb
Vial # : 1-59
Injection Volume : 10 uL
Date Acquired : 12/20/2011 10:45:12 PM
Date Processed : 12/20/2011 11:30:16 PM
Sample Type : Unknown
Level : 1
Acquired by : System Administrator
Processed by : System Administrator

<Chromatogram>

mAU

Peak Table

Name	Ret. Time	Area	Height
substrate	12.123	5712158	311249
DMF	13.449	59265495	1529792
standard	18.116	42120970	1439740
product enantiomer 1	29.083	4560370	95420
product enantiomer 2	35.988	3282561	77730
		114941553	3453931

2e: 16% ee

Racemate:

SHIMADZU LabSolutions Analysis Report

<Sample Information>

Sample Name : JOC-b-Me-prod
Sample ID : JOC-b-Me-prod
Data Filename : JOC-b-Me-prod.lcd
Method Filename : ADH 90_10 45 min fl 0.5 -analyze_b-Me.lcm
Batch Filename : 20120821.lcb
Vial # : 1-43
Injection Volume : 5 uL
Date Acquired : 8/20/2012 11:12:39 PM
Date Processed : 8/20/2012 11:57:42 PM
Sample Type : Unknown
Level : 1
Acquired by : System Administrator
Processed by : System Administrator

<Chromatogram>

mAU

NMR spectra for all described compounds

^1H NMR of **8b**

^{13}C NMR of **8b**

^1H NMR of **8d**

^{13}C NMR of **8d**

^1H NMR of **8e**

^{13}C NMR of **8e**

^1H NMR of 8f

^{13}C NMR of 8f

^1H NMR of **1a**

^{13}C NMR of **1a**

^1H NMR of **1b**

^{13}C NMR of **1b**

^1H NMR of **1c**

^{13}C NMR of **1c**

^1H NMR of **1d**

^{13}C NMR of **1d**

^1H NMR of **1e**

^{13}C NMR of **1e**

^1H NMR of **1f**

^{13}C NMR of **1f**

^1H NMR of **1g**

^{13}C NMR of **1g**

^1H NMR of **2a**

^{13}C NMR of **2a**

^1H NMR of **2e**

^{13}C NMR of **2e**

^1H NMR of **2f**

^{13}C NMR of **2f**

^1H NMR of **2g**

^{13}C NMR of **2g**

^1H NMR of **L5d**

^{13}C NMR of **L5d**

^1H NMR of **L5e**

^{13}C NMR of **L5e**

- [1] P. H. Bos, B. Macia, M. A. Fernandez-Ibanez, A. J. Minnaard, B. L. Feringa, *Org. Biomol. Chem.* **2010**, *8*, 47-49.
- [2] M. Honma, T. Sawada, Y. Fujisawa, M. Utsugi, H. Watanabe, A. Umino, T. Matsumura, T. Hagihara, M. Takano, M. Nakada, *J. Am. Chem. Soc.* **2003**, *125*, 2860-2861.
- [3] H. Takeda, M. Nakada, *Tetrahedron-Asymmetry* **2006**, *17*, 2896-2906.
- [4] D. S. Beaudoin, S. O. Obare, *Tetrahedron Lett.* **2008**, *49*, 6054-6057
- [5] K. L. Reddy, Y. H. K. Reddy, S. Satyanarayana, *Nucleosides Nucleotides Nucleic Acids* **2009**, *28*, 953-968
- [6] A. Greguric, I. D. Greguric, T. W. Hambley, J. R. Aldrich-Wright, J. G. Collins, *J. Chem. Soc., Dalton Trans.* **2002**, 849-855.
- [7] G. Roelfes, A. J. Boersma, B. L. Feringa, *Chem Commun.* **2006**, 635-637.
- [8] M. Navarro, E. J. Cisneros-Fajardo, A. Sierralta, M. Fernandez-Mestre, P. Silva, D. Arrieché, E. Marchan, *J. Biol. Inorg. Chem.* **2003**, *8*, 401-408.