

**A Reagent based DOS strategy via Evans chiral auxiliary: Highly stereoselective Michael reaction towards optically active quinolizidinones, piperidinones and pyrrolidinones**

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## Experimental Section

**General Methods.** Air and moisture sensitive reactions were carried out in oven-dried glassware sealed with rubber septa under a positive pressure of dry argon. Similarly sensitive liquids and solutions were transferred via syringe. Reactions were stirred using teflon-coated magnetic stir bars. Elevated temperatures were maintained using thermostat-controlled silicon oil baths. Organic solutions were concentrated using a rotary evaporator with a desktop vacuum pump. Tetrahydrofuran, diethyl ether, dioxane, benzene, and toluene were distilled from sodium and benzophenone prior to use. Dichloromethane was distilled from CaH<sub>2</sub> prior to use. Analytical TLC was performed with 0.25 mm silica gel G plates with a 254 nm fluorescent indicator. The TLC plates were visualized by ultraviolet light and treatment with phosphomolybdic acid stain followed by gentle heating. Purification of products was accomplished by flash chromatography on silica gel and the purified compounds showed a single spot by analytical TLC. The diastereomeric ratio and the regioisomeric ratio were determined by <sup>1</sup>H NMR of crude reaction mixtures. Data for <sup>1</sup>H-NMR spectra are reported as follows: chemical shift (ppm, referenced to TMS; s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, ddd = doublet of doublet of doublets, m = multiplet), coupling constant (Hz), and integration. Data for <sup>13</sup>C-NMR spectra are reported in terms of chemical shift (ppm) relative to residual solvent peak (CDCl<sub>3</sub>: 77.0 ppm).

### General procedures for the TiCl<sub>4</sub> catalyzed Michael reaction

To an oven dried three-necked flask was added imide **1**, **10-14** (1.00 mmol) in anh. THF (5.0 mL) under argon. To the resulting solution was added sodium hexamethyldisilylazide (1M NaHMDS in THF, 1.00 mmol) at -78°C and stirred at same temperature for 30 min. After which trimethylsilyl chloride (TMSCl) (1.5 eq.) was added and stirred at rt for 3-4 h. The above solution was cooled to 0 °C, then β-nitrostyrene (1.20 mmol) and titanium tetrachloride (TiCl<sub>4</sub>) (0.057 g, 0.3 mmol) were added to it. After stirring at that temperature for 4 h, the solution was poured into cooled water. The mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (20 mL x 4). The combined extracts were dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (hexane/ethyl acetate = 80/20) to afford pure product.

**2.** Imide **1** (2g, 6.4 mmol) in THF (30 mL), NaHMDS, (1M in THF, 6.4mL, 6.4 mmol) at  $-78^{\circ}\text{C}$ . After stirring at  $-78^{\circ}\text{C}$  for 0.5 h, TMSCl, (1.3mL, 9.6 mmol) was added and stirred at rt for 4h. Again cooled to  $0^{\circ}\text{C}$ , nitrostyrene (0.95g, 6.4 mmol) and titanium tetrachloride (0.364 g, 1.92 mmol) were added to it. The final compound **2** was obtained as off-white solid (2.1g, 4.5 mmol), with 72% yield.  $R_f = 0.6$  (PE/AcOEt = 70:30).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.04 (dd,  $J_1 = 13.2$  Hz,  $J_2 = 3.2$  Hz, 1H), 2.48 (dd,  $J_1 = 13.6$  Hz,  $J_2 = 2.8$  Hz, 1H), 3.96 (m, 3H), 4.27 (dd,  $J_1 = 12.4$  Hz &  $J_2 = 4$  Hz, 1H), 4.39 (m, 2H), 5.76 (d,  $J = 11.6$  Hz, 1H), 6.83 (m, 2H), 7.13 (t, 1H), 7.21-7.29 (m, 3H), 7.36 (t,  $J = 7.6$  Hz, 1H), 7.43 (d, 2H,  $J = 7.2$  Hz), 7.61 (dd,  $J_1 = 8$  Hz &  $J_2 = 5.2$  Hz, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  35.6, 47.3, 50.4, 54.1, 65.3, 78.3, 115.9 ( $J = 21.7$  Hz), 126.7, 127.8, 128.1, 129, 131, 134.7, 138.3, 152.4, 160.7, 163.16, 170.6. HRMS (ESI): calcd for  $\text{C}_{26}\text{H}_{23}\text{FN}_2\text{O}_5$ : 462.4696; found: 462.4693.

**15.** Imide **1** (3g, 9.6 mmol) in THF (40.0 mL), was added NaHMDS (1M, 9.6 mL, 9.6 mmol) at  $-78^{\circ}\text{C}$ . After stirring at  $-78^{\circ}\text{C}$  for 30 min TMSCl (1.96 mL, 14.4 mmol) was added and stirred at rt for 4 h. Then (E)-1-methoxy-4-(2-nitrovinyl) benzene (2.06 g, 11.5 mmol) and titanium tetrachloride (0.32 mL, 2.88 mmol) were added to it and stirred at rt for 4h. The final compound **15** was obtained as yellow solid (2.6g, 5.27 mmol), with 55% Yield.  $R_f = 0.4$  (PE/AcOEt = 7:3).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.14 (m, 1H), 2.59 (dd,  $J_1 = 13.6$  Hz,  $J_2 = 3.6$  Hz, 1H), 3.77 (s, 3H), 4.01 (m, 2H), 4.23 (dd,  $J_1 = 12.4$  Hz,  $J_2 = 4$  Hz, 1H), 4.4 (m, 2H), 5.72 (d,  $J = 11.6$  Hz, 1H), 6.86 (m, 2H), 7.10 (t,  $J = 8.4$  Hz, 2H), 7.2 (m, 2H), 7.34 (d,  $J = 8.4$  Hz, 2H), 7.6 (dd,  $J_1 = 8.8$  Hz,  $J_2 = 5.2$  Hz, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ): 172.1, 153.3, 138.6, 129.3, 129.1, 128.3, 128.1, 127.9, 127.6, 127.3, 127.1, 79.2, 65.7, 56.1, 51.1, 48.9, 36.8 HRMS (ESI): calcd for  $\text{C}_{13}\text{H}_{18}\text{NaO}_2$ : 229.1199; found: 229.1193.

**16.** Imide **1** (312 mg, 1 mmol) in THF (5.0 mL), was added NaHMDS (1M, 0.312 mL, 1 mmol) at  $-78^{\circ}\text{C}$ . After stirring at  $-78^{\circ}\text{C}$  for 30 min TMSCl (0.20 mL, 1.5 mmol) was added and stirred at rt for 4 h. Then the reaction mixture was cooled to  $0^{\circ}\text{C}$  and (E)-1-chloro-2-(2-nitrovinyl) benzene (0.22 g, 1.2 mmol) and titanium tetrachloride (0.057 g, 0.30 mmol) were added to it and stirred at rt for 4h. The final compound **16** was obtained as white solid.  $R_f = 0.11$  (PE/AcOEt = 100:1).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  0.62-0.65 (m, 2H), 0.91-0.97 (m, 2H), 1.04 (s, 3H), 1.13 (s, 3H), 1.53-1.60 (m, 1H), 2.13 (dm,  $J = 16.7$  Hz, 1H), 2.33 (ddd,  $J = 16.7, 4.4, 2.0$  Hz, 1H), 5.33-5.35 (m, 1H), 5.68-5.71 (m, 1H), 5.90 (d,  $J = 15.3$  Hz, 1H), 5.99-6.02 (m, 1H), 6.41 (dd,  $J =$

15.3, 9.9 Hz, 1H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.6, 14.3, 22.9, 28.6, 40.9, 46.9, 85.5, 118.3, 128.8, 136.3, 153.9, 166.6. HRMS (ESI): calcd for  $\text{C}_{26}\text{H}_{22}\text{ClFN}_2\text{O}_5$ : 496.9147; found: 496.9138.

**17.** Imide **1** (1.5g, 4.8 mmol) in THF (25.0 mL), was added NaHMDS (1M, 4.8mL, 4.8 mmol) at  $-78^\circ\text{C}$ . After stirring at  $-78^\circ\text{C}$  for 30 min, TMSCl (0.98 mL, 7.2 mmol) was added and stirred at rt for 4 h. Then 1-methoxy-3-[2-nitrovinyl]benzene (1.03 g, 5.76 mmol) and titanium tetrachloride (0.15 mL, 1.4 mmol) were added to it and stirred at rt for 4h. The final compound **17** was obtained as yellow color solid (860mg, 1.7 mmol), with 36% Yield.  $R_f = 0.4$  (PE/AcOEt = 7:3).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.156 (dd,  $J_1 = 14.0$  Hz,  $J_2 = 8.8$  Hz, 1H), 2.54 (dd,  $J_1 = 13.6$  Hz,  $J_2 = 3.8$ , 1H), 3.9 (m, 2H), 4.28 (dd,  $J_1 = 12.8$  Hz,  $J_2 = 4.0$ , 1H), 4.35-4.54 (m, 3H), 5.76 (d,  $J = 11.6$  Hz, 1H), 6.80-6.85 (m, 3H), 6.96-7.02 (m, 2H), 7.1 (t,  $J = 8.4$  Hz, 1H), 7.1-7.29 (m, 4H), 7.60 (dd,  $J_1 = 8.8$  Hz,  $J_2 = 5.6$  Hz, 2H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  36.8, 47.7, 50.9, 55.03, 65.43, 78.81, 127.2, 128.7, 129.07, 129.41, 137.4, 154.86, 171.09. HRMS (ESI): calcd for  $\text{C}_{27}\text{H}_{25}\text{FN}_2\text{O}_6$  492.4956; found: 492.4952.

**18.** Imide **12** (2.5g, 7.35 mmol) in THF (20 mL), was added NaHMDS (1M in THF, 7.3 mL, 7.36 mmol) was added at  $-78^\circ\text{C}$  and stirred at same temperature for 30 min. Then TMSCl (1.5 mL, 11.01 mmol) was added and stirred at rt for 4 h. Then 1-methoxy-4-[2-nitrovinyl]benzene (1.58 g, 8.81 mmol) and titanium tetrachloride (0.24 mL, 2.2 mmol) were added to it. The final compound **18** was obtained as brown color solid (1.85g, 3.56 mmol), with 48% yield.  $R_f = 0.2$  (PE/AcOEt = 7:3).  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  2.6 (m, 2H), 2.7 (m, 1H), 3.75 (s, 3H), 4.05 (m, 1H), 4.5 (m, 2H), 4.86 (t,  $J = 11.2$  Hz, 1H), 5.84 (d,  $J = 10.8$ , 1H), 6.77 (d,  $J = 8.0$  Hz, 2H), 6.87 (m, 2H), 7.05-7.15 (m, 4H), 7.3 (t,  $J = 7.6$  Hz, 1H), 7.70-7.8 (m, 3H), 8.09 (d,  $J = 8.0$  Hz, 1H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  37.1, 47, 55, 66, 78, 113, 120, 126.8, 127.3, 128.7, 129.9, 130.1, 134.5, 139.6, 160.8, 170.7 HRMS (ESI): calcd for  $\text{C}_{27}\text{H}_{25}\text{N}_3\text{O}_8$ : 519.5027; found: 519.5021.

**19.** Imide **12** (7g, 20.6 mmol) in THF (20 mL), was added NaHMDS (1M, 20.5 mL, 20.6 mmol) was added at  $-78^\circ\text{C}$  and stirred at same temperature for 30 min. Then TMSCl (4.2 mL, 31 mmol) was added and stirred at rt for 4 h. Then (E)-(2-nitrovinyl)benzene (3.69 g, 24.72 mmol) and titanium tetrachloride (0.68 mL, 6.18 mmol) were added to it. The final compound **19** was obtained as brown color solid (6.9g, 14 mmol), with 68% yield.  $R_f = 0.6$  (PE/AcOEt = 7:3).  $^1\text{H}$

NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  2.45 (dd,  $J_1 = 13.2$  Hz,  $J_2 = 3.0$ , 1H), 3.0 ( $J_1 = 13.5$  Hz,  $J_2 = 2.8$ , 1H), 3.95 (m, 2H), 4.35-4.4 (m, 2H), 4.6 (m, 1H), 5.0 (m, 1H), 6.0 (d,  $J = 11.6$ , 1H), 6.95 (m, 2H), 7.2-7.35 (m, 6H), 7.6 (t,  $J = 8.2$  Hz, 1H), 7.75 (t,  $J = 8.0$  Hz, 1H), 7.9 (d,  $J = 8.0$ , 1H), 8.0 (d,  $J = 8.0$ , 1H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):  $\delta$  36.9, 37.1, 37.4, 54.94, 66.02, 78.8, 122.55, 127.5, 128.2, 129.18, 133.3, 138.12, 151.00, 152.55. HRMS (ESI): calcd for C<sub>26</sub>H<sub>23</sub>N<sub>3</sub>O<sub>7</sub>: 489.4767; found: 489.4763.

**20.** Imide **10** (2.6 g, 11.1 mmol) in THF (30 mL), was added NaHMDS (1M, 11.1 mL, 11.1 mmol) was added at  $-78$  °C and stirred at same temperature for 30 min. Then TMSCl (2.27 mL, 16.7 mmol) was added and stirred at rt for 4 h. Then (E)-(2-nitrovinyl)benzene (1.9 g, 13.3 mmol) and titanium tetrachloride (0.367mL, 3.33 mmol) were added to it. The final compound **20** was obtained as yellow solid (3.3g, 8.7 mmol), with 78% yield.  $R_f = 0.3$  (PE/AcOEt = 7:3). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  1.3 (d,  $J = 6.8$  Hz, 3H), 2.01 (m, 1H), 2.60 (dd,  $J_1 = 13.2$  Hz,  $J_2 = 3.6$ , 1H), 3.93-4.01 (m, 2H), 4.11 (t,  $J = 8.8$  Hz, 1H), 4.5 (m, 2H), 4.62-4.8 (m, 2H), 6.95 (d,  $J = 6.0$  Hz, 2H), 7.225-7.34 (m, 8H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):  $\delta$  15.1, 36.9, 40.4, 46.6, 65.8, 127.2, 128.8, 129.3, 135.0, 137.8, 152.9, 174.8 HRMS (ESI): calcd for C<sub>21</sub>H<sub>22</sub>N<sub>2</sub>O<sub>5</sub>: 382.4098; found: 382.4098.

**21.** Imide **11** (1.6 g, 4.2 mmol) in THF (20 mL), was added NaHMDS (1M, 4.2 mL, 4.2 mmol) was added at  $-78$  °C and stirred at same temperature for 30 min. Then TMSCl (0.8 mL, 6.3 mmol) was added and stirred at rt for 4 h. Then (E)-(2-nitrovinyl)benzene (0.76 g, 504 mmol) and titanium tetrachloride (0.13 mL, 1.26 mmol) were added to it. The final compound **21** was obtained as off-white solid (1.8 g, 3.4 mmol), with 81% yield..  $R_f = 0.3$  (PE/AcOEt = 7:3). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  2.48 (dd,  $J_1 = 13.6$  Hz,  $J_2 = 3.2$ , 1H), 2.79 (dd,  $J_1 = 13.2$  Hz,  $J_2 = 10.4$ , 1H), 3.95-4.25 (m, 5H), 4.56 (m, 1H), 5.76, (d,  $J = 11.6$  Hz, 1H), 6.8 (m, 2H), 7.04 (d,  $J = 8.0$ , 2H), 7.15-7.5 (m, 12H). <sup>13</sup>C NMR (101 MHz, DMSO):  $\delta$  35.6, 47.4, 54.3, 66.1, 78.2, 122.0, 128.7, 129.6, 131.8, 137.5, 153.0, 171.2. Calcd for C<sub>26</sub>H<sub>23</sub>BrN<sub>2</sub>O<sub>5</sub> 523.3752; found: 523.3748.

**23.** Imide **14** (3 g, 10.15 mmol) in THF (30 mL), was added NaHMDS (1M, 10 mL, 10.1 mmol) was added at  $-78$  °C and stirred at same temperature for 30 min. TMSCl (2 mL, 15.3 mmol) was

then added and the reaction mixture was stirred at rt for 4 h. Then (E)-(2-nitrovinyl)benzene (1.81 g, 12.2 mmol) and titanium tetrachloride (0.33 mL, 3.04 mmol) were added to it. The final compound **23** was obtained as fluffy white solid (2.2g, 4.2 mmol), with 41% yield.  $R_f = 0.5$  (PE/AcOEt = 7:3).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.07 (m, 1H), 2.49 (dd,  $J_1 = 13.2$  &  $J_2, 3.2$  Hz, 1H), 3.94 (m, 2H), 4.27 (dd,  $J_1 = 12$  Hz,  $J_2 = 4$  Hz, 1H), 4.38-4.57 (m, 3H), 5.76 (d,  $J = 11.2$  Hz, 1H), 7.21-7.48 (m, 10H), 7.63 (m, 2H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  36.8, 47.8, 49.9, 55.04, 55.27, 65.5, 78.7, 113.7, 114.0, 120.5, 128.8, 129.2, 130.4, 130.8, 138.8, 152.9, 160.0, 161.2, 164.0, 171.08. HRMS (ESI): calcd for  $\text{C}_{26}\text{H}_{24}\text{N}_2\text{O}_5$ : 444.4792; found: 444.4785.

### General procedure for the formation of quinolizidinones and unsaturated quinolizodinones

Nitro adduct **2** or **18** (1.00 mmol) and appropriate cyclic imines (1- 2 eq) were taken in water (1- 3 mL) under argon in a sealed vessel. The resulting mixture was heated at 70°C for 16-30 h. After which it was cooled to rt. The mixture was extracted with  $\text{CH}_2\text{Cl}_2$  (10 mL x 3). The combined extracts were dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (pet. ether/ethyl acetate = 70/30) to afford pure product.

**25.** Nitro adduct **2** (250 mg, 0.54 mmol) and 3, 4-dihydroisoquinoline (78 mg, 0.59 mmol) were taken in water (3.0 mL) under argon in a sealed vessel. The resulting mixture was heated at 70°C for 16h. Final compound **25** was purified by silica gel column chromatography (pet. ether/ethyl acetate = 85/15) to afford 60 mg of pure product in 32% yield.  $R_f = 0.5$  (PE/AcOEt = 7:3).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 2.8 (m, 1H), 3.05 (m, 1H), 3.15 (d,  $J = \text{Hz}$ , 1H), 4.05 (d,  $J = \text{Hz}$ , 1H), 5.0 (m, 1H), 5.4 (d,  $J = 1\text{H}$ ), 5.56 (d,  $J = \text{Hz}$ , 1H), 6.92-7.3 (m, 14H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  14.1, 22.6, 28.14, 31.9, 39.04, 50.2, 51.8, 56.9, 94.7, 115.0, 126.5, 128.4, 131.18, 139.2, 172.0. HRMS (ESI): calcd for  $\text{C}_{25}\text{H}_{20}\text{FNO}$ : 369.1308; found: 369.4300.

**30.** Nitro adduct **18** (0.25g, 0.48 mmol) and 3,4-dihydroisoquinoline (80 mg, 0.6 mmol) were taken in water (2.4 mL) under argon in a sealed vessel. The resulting mixture was heated at 70°C for 16h. Final compound **30** was purified by silica gel column chromatography (pet. ether/ethyl acetate = 80/20) to afford 80 mg of pure product (35%).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 2.95 (m, 2H), 3.85 (s, 3H), 4.2 (m, 2H), 4.82 (m, 2H), 5.05 (d,  $J = 10.41\text{H}$ ), 5.5 (s, 1H), 5.68 (s, 1H), 6.62 (s, 1H), 6.72 (d,  $J = 7.2$  Hz, 1H), 6.82 (d,  $J_1 = 8\text{Hz}$ ,  $J_2 = 2$  Hz, 1H), 7.01 (brs, 2H), 7.2-7.45 (m,

7H), 8.05 (brs, 1H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  28.6, 29.6, 46.7, 55.2, 58.6, 75.5, 89.4, 113.7, 119.5, 126.9, 128.5, 129.6, 130.3, 133.4, 136.6, 160.0, 167.4. HRMS (ESI): calcd for  $\text{C}_{26}\text{H}_{23}\text{N}_3\text{O}_6$ : 473.4773; found: 473.4773.

**26.** Nitro adduct **2** (0.1 g, 0.26 mmol) and 3,4-dihydroisoquinoline (45 mg, 0.35 mmol) were taken in water (2.0 mL) under argon in a sealed vessel. The resulting mixture was heated at 70°C for 20 h. Final compound **26** was purified by silica gel column chromatography (pet. ether/ethyl acetate = 80/20) to afford pure 42 mg of product.  $R_f$  = 0.65 (PE/AcOEt = 7:3).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 2.95 (t,  $J$  = 4.6 Hz, 2H), 3.8-4.0 (m, 3H), 4.05 (m, 1H), 5.95 (d,  $J$  = 4.4 Hz, 1H), 6.92 (t,  $J$  = 8.0 Hz, 2H), 7.15-7.35 (m, 8H), 7.65 (d,  $J$  = 8.0 Hz, 1H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  14.1, 22.6, 29.3, 31.9, 39.0, 45.6, 54.2, 105.5, 115.7, 124.2, 127, 128.06, 129.1, 129.9, 130, 134.6, 135.3, 142.17, 160.6, 163.06, 169. HRMS (ESI): calcd for  $\text{C}_{25}\text{H}_{20}\text{FNO}$ : 369.4308; found: 369.4315.

**32.** Nitro adduct **19** (0.1 g, 0.21 mmol) and 3,4-dihydroisoquinoline (45 mg, 0.35 mmol) were taken in water (1.05 mL) under argon in a sealed vessel. The resulting mixture was heated at 70°C for 20 h. Final compound **32** was purified by silica gel column chromatography (pet. ether/ethyl acetate = 80/20) to afford pure 36 mg of product.  $R_f$  = 0.65 (PE/AcOEt = 7:3).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 2.92-2.93 (m, 2H), 3.88-3.91 (m, 1H), 4.19-4.2.7 (m, 2H), 4.44-4.49 (m, 1H), 5.85 (s, 1H), 6.95-6.99 (m, 1H), 7.06-7.14 (m, 2H), 7.21-7.31 (m, 8H), 7.59 (d,  $J$  = 7.6 Hz, 1H), 7.83 (d, 8 Hz, 1H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  21.0, 29.3, 39.1, 45.5, 58.3, 60.3, 106.6, 124.2, 125.5, 127.2, 128.6, 129.9, 134.7, 142.1, 149.4, 167.7 HRMS (ESI): calcd for  $\text{C}_{25}\text{H}_{20}\text{N}_2\text{O}_3$ : 396.1474; found: 396.1501.

**33.** Nitro adduct **18** (0.1 g, 0.21 mmol) and 3,4-dihydroisoquinoline (45 mg, 0.35 mmol) were taken in water (0.36 mL) under argon in a sealed vessel. The resulting mixture was heated at 70°C for 20 h. Final compound **32** was purified by silica gel column chromatography (pet. ether/ethyl acetate = 80/20) to afford pure 36 mg of product.  $R_f$  = 0.65 (PE/AcOEt = 7:3).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 2.92-2.94 (m, 2H), 3.75 (s, 1H), 3.78-3.82 (m, 1H), 4.21-4.2.8 (m, 2H), 4.52-4.59 (m, 1H), 5.86 (s, 1H), 6.81-6.90 (m, 3H), 7.06-7.18 (m, 2H), 7.21-7.31 (m, 7H), 7.59 (d,  $J$  = 7.8 Hz, 1H), 7.83 (d, 8 Hz, 1H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  22.7, 31.6, 43.5,

57.7, 120.4, 124.3, 125.4, 125.7, 127.1, 127.8, 128.2, 129.7, 129.9, 133.6, 134.9, 135.7, 143.2, 168.6 HRMS (ESI): calcd for C<sub>26</sub>H<sub>22</sub>N<sub>2</sub>O<sub>4</sub>: 426.4639; found: 426.5645.

### General procedure for the synthesis of piperidinones

Nitro adduct **2** (1.00 mmol), ammonium acetate (5 eq) and appropriate aldehydes (1.5 mmol) were taken in ethanol (5.4 mL) under argon. The resulting mixture was heated in a sealed vessel and refluxed for 10h. After which it was cooled to rt. The mixture was diluted with water and extracted with CH<sub>2</sub>Cl<sub>2</sub> (10 mL x 3). The combined extracts were dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (pet. ether/ethyl acetate = 1/1) to afford pure product.

**24.** Nitro adduct **2** (0.25g, 0.54 mmol), ammonium acetate (0.21 g, 2.7 mmol) and p-anisaldehyde (0.10 mL, 0.81 mmol) were taken in ethanol (5.4 mL) under argon in a sealed vessel. The resulting mixture was heated under reflux for 10h. Final compound **24** was purified by silica gel column chromatography (pet. ether/ ethyl acetate = 50/50) to afford pure product as a off-white solid (130 mg, 57%). R<sub>f</sub> = 0.11 (PE/AcOEt = 1:1). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): 3.81 (s, 3H), 3.85 (m, 2H), 5.2 (m, 2H), 5.95 (s, 1H), 6.92-7.05 (m, 7H), 7.2-7.4 (m, 5H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>): δ 52.3, 53.5, 55.3, 60.1, 92.3, 115.4, 127.5, 129.01, 130.4, 132.7, 135.2, 160.8, 170.4 HRMS (ESI): calcd for C<sub>24</sub>H<sub>21</sub>FN<sub>2</sub>O<sub>4</sub>: 420.4329; found: 420.4322.

**27.** Nitro adduct **2** (0.25 g, 0.54 mmol), ammonium acetate (0.21 g, 2.71 mmol) and m-fluorobenzaldehyde (0.09 mL, 0.81 mmol) were taken in ethanol (5.4 mL) under argon in a sealed vessel. The resulting mixture was heated under reflux for 10h. Final compound **27** was purified by silica gel column chromatography (pet. ether/ ethyl acetate =70/30) to afford pure product as a off-white solid (140 mg, 63%) (R<sub>f</sub> = 0.4 (PE/AcOEt = 1:1). <sup>1</sup>H NMR (400 MHz, DMSO-D<sub>6</sub>): 4.06 (t, *J* = 11.2 Hz, 1H), 4.15 (d, *J* = 12.4 Hz, 1H), 5.27 (d, *J* = 9.6 Hz, 1H), 5.7 (t, *J* = 10.8 Hz, 1H), 6.9 (t, *J* = 8.8 Hz, 2H), 7.1-7.25 (m, 9H), 7.45 (m, 2H), 8.47 (s, 1H). <sup>13</sup>C NMR (101 MHz, DMSO-D<sub>6</sub>): δ 50.31, 52.3, 59.1, 91.5, 114.2, 115.8, 116, 124.05, 127.9, 130.6, 131.2, 134.5, 140.1, 150.6, 160.9, 163.3, 169.6, calcd for C<sub>23</sub>H<sub>18</sub>F<sub>2</sub>N<sub>2</sub>O<sub>3</sub>: 408.3974; found: 408.3969

**28.** Nitro adduct **2** (0.25 g, 0.54 mmol), ammonium acetate (0.21 g, 2.71 mmol) and 3,4-dichlorobenzaldehyde (0.14 mL, 0.81 mmol) were taken in ethanol (5.4 mL) under argon in a

sealed vessel. The resulting mixture was heated under reflux for 10h. Final compound **28** was purified by silica gel column chromatography (pet. ether/ ethyl acetate =75 /25) to afford pure product as a white solid (0.21 g, 84%). ( $R_f = 0.2$  (PE/AcOEt = 7:3).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ): 3.87-3.92 (m, 2H), 5.10 (t,  $J = 10.2$  Hz, 1H), 5.23 (d,  $J = 9.9$  Hz, 1H), 5.98 (s, 1H), 6.9-7.02 (m, 6H), 7.2-7.26 (m, 4H). 7.5-7.55 (m, 2H)  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  52.04, 53.28, 59.5, 91.9, 115.5, 115.7, 126.3, 127.5, 128.7, 130.4, 131.61, 132.2, 134.6, 135.8, 160.8, 163.2, 170.5 calcd for  $\text{C}_{23}\text{H}_{17}\text{Cl}_2\text{FN}_2\text{O}_3$ : 459.2971; found: 459.2974.

**29.** Nitro adduct **2** (0.25 g, 0.54 mmol), ammonium acetate (0.21 g, 2.71 mmol) and 3-ethoxybenzaldehyde (0.13 g, 0.88 mmol) were taken in ethanol (5.4 mL) under argon in a sealed vessel. The resulting mixture was heated under reflux for 10h. Final compound **29** was purified by silica gel column chromatography (pet. ether/ ethyl acetate =75 /25) to afford pure product as a brown color solid (160 mg, 69%). ( $R_f = 0.2$  (PE/AcOEt = 7:3).  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}D_6$ ): 1.35 (t,  $J = 6.8$  Hz, 3H), 4.05 (q, 2H), 4.09 (d,  $J = 6.8$  Hz, 1H), 4.16 (d,  $J = 12.4$  Hz, 1H), 5.12 (d,  $J = 10$  Hz, 1H), 5.69 (t,  $J = 10.8$  Hz, 1H), 6.93-6.99 (m, 4H), 7.09-7.19 (m, 8H), 7.29 (t,  $J = 8$  Hz, 1H), 8.38 (s, 1H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  14.7, 52.2, 53.4, 60.5, 63.6, 92.2, 113.1, 115.5, 115.8, 118.7, 127.5, 128.4, 129.03, 130.4, 132.7, 135.2, 137.1, 159.74, 170.3 calcd for  $\text{C}_{25}\text{H}_{23}\text{FN}_2\text{O}_4$ : 434.4595; found: 434.4592.

**31.** Nitro adduct **2** (0.25 g, 0.54 mmol), ammonium acetate (0.21 g, 2.71 mmol) and 4-(trifluoromethoxy)benzaldehyde (0.09 g, 0.81 mmol) were taken in ethanol (5.4 mL) under argon in a sealed vessel. The resulting mixture was heated under reflux for 10h. Final compound **31** was purified by silica gel column chromatography (pet. ether/ ethyl acetate =70 /30) to afford pure product as a brown color solid (121 mg, 47%). ( $R_f = 0.2$  (PE/AcOEt = 7:3).  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}D_6$ ): 4.08 (t,  $J = 12.0$  Hz, 1H), 4.15 (d,  $J = 11.6$  Hz, 1H), 5.3 (d,  $J = 10$  Hz, 1H), 5.75 (t,  $J = 10.8$  Hz, 1H), 6.97 (t,  $J = 8.8$  Hz, 2H), 7.1-7.19 (m, 7H), 7.45 (d,  $J = 8.4$  Hz, 2H), 7.6 (d,  $J = 8.4$  Hz, 2H), 8.4 (s, 1H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  52.1, 53.3, 59.8, 92.1, 115.5, 119.0, 120.9, 127.5, 128.1, 129, 130.4, 130.5, 132.4, 134.9, 137.2, 150.2, 160.7, 163.2, 170.5 calcd for  $\text{C}_{24}\text{H}_{18}\text{F}_4\text{N}_2\text{O}_4$ : 474.4043; found: 474.4044.

**37.** Nitro adduct **2** (0.29 g, 0.63 mmol), ammonium acetate (0.24 g, 3.13 mmol) and 3-bromobenzaldehyde (0.11 g, 0.94 mmol) were taken in ethanol (6 mL) under argon in a sealed

vessel. The resulting mixture was heated under reflux for 10h. Final compound **31** was purified by silica gel column chromatography (pet. ether/ ethyl acetate =70 /30) to afford pure product as a brown color solid (152 mg, 54%). ( $R_f = 0.3$  (PE/AcOEt = 7:3).  $^1\text{H}$  NMR (400 MHz, DMSO- $\text{D}_6$ ): 4.03-4.09 (m, 1H), 4.15 (d,  $J = 12$  Hz, 1H), 5.23 (d,  $J = 12$  Hz, 1H), 5.75-5.80 (m, 1H), 6.96-7.0 (m, 2H), 7.10-7.19 (m, 7H), 7.35-7.38 (m, 2H), 7.58-7.61 (m, 1H), 7.86 (d,  $J = 8$ Hz, 1H), 8.44 (s, 1H). Calcd for  $\text{C}_{23}\text{H}_{18}\text{BrFN}_2\text{O}_3$ : 469.3030; found: 469.3457.

### General procedure for the synthesis of pyrrolidinones

Appropriate nitro adduct (1.00 mmol), was hydrogenated with Pd-C w/w (10%) in Ethanol (6-7 mL). The resulting mixture was stirred under hydrogenation at 40 psi at rt for 2h. After completion of reaction by TLC, the reaction mixture was filtered through celite-545 bed and concentrated under reduced pressure to get crude product. The crude product was purified by silica gel (100-200mesh) using 20-50% ethyl acetate in pet ether as eluent pure products.

**34.** Nitro adduct **2** (300 mg, 0.64 mmol) was hydrogenated with 10% Pd/C (30 mg) and ethanol (6.4 mL). The final compound **33** was obtained 110 mg of as off-white solid (68%). ( $R_f = 0.25$  (PE/AcOEt = 1:1).  $^1\text{H}$  NMR (400 MHz, DMSO- $\text{D}_6$ ): 3.59-3.7 (m, 2H), 3.98 (m, 2H), 6.85-6.93 (m, 6H), 7.06 (m, 3H), 8.15 (brs, 1H).  $^{13}\text{C}$  NMR (75 MHz, DMSO- $\text{D}_6$ ):  $\delta$  44.8, 45.3, 51.8, 114.4, 126.2, 127.5, 128.4, 131.1, 132.8, 139.1, 159.0, 175.2, calcd for  $\text{C}_{16}\text{H}_{14}\text{FNO}$ : 255.2869; found: 255.2859.

**35.** Nitro adduct **15** (300 mg, 0.6 mmol) was hydrogenated with 10% Pd/C (30 mg) and ethanol (6 mL). The final compound **34** was obtained 80 mg of as brown color solid (47%). ( $R_f = 0.23$  (PE/AcOEt = 1:1).  $^1\text{H}$  NMR (400 MHz, DMSO- $\text{D}_6$ ): 3.48-3.56 (m, 2H), 3.7 (s, 3H), 3.82 (m, 2H), 6.85 (d,  $J = 8.4$  Hz, 2H), 7.08-7.18 (m, 4H), 7.26 (d,  $J = 8.4$  Hz, 2H), 9.8 (brs, 1H).  $^{13}\text{C}$  NMR (75 MHz, DMSO- $\text{D}_6$ ):  $\delta$  43.5, 52.2, 54.2, 54.9, 113.9, 114.7, 128.3, 129.3, 130.2, 131.19, 134.4, 158.2, 159.8, 162.7, 169.1. calcd for  $\text{C}_{17}\text{H}_{16}\text{FNO}_2$ : 285.3128; found: 285.3128.

**36.** Nitro adduct **23** (300 mg, 0.6 mmol) was hydrogenated with 10% Pd/C (30 mg) and ethanol (6.7 mL). The final compound **35** was obtained 120 mg of as brown color solid (84%). ( $R_f = 0.15$  (PE/AcOEt = 1:1).  $^1\text{H}$  NMR (400 MHz, DMSO- $\text{D}_6$ ): 3.5-3.65 (m, 2H), 3.86 (m, 2H), 7.15 (d,  $J = 6.8$  Hz, 2H), 7.22 (t,  $J = 7.6$  Hz, 2H), 7.29 (t,  $J = 7.2$  Hz, 4H), 7.34 (d,  $J = 7.6$  Hz, 2H). 9.8

(brs, 1H).  $^{13}\text{C}$  NMR (75 MHz, DMSO- $\text{D}_6$ ):  $\delta$  44.1, 52.9, 54.1, 126.9, 127.0, 128.0, 128.5, 138.4, 139.7, 169. calcd for  $\text{C}_{16}\text{H}_{15}\text{NO}$ : 237.2964; found: 237.2962.

### General procedure for the catalytic asymmetric Michael reaction.

**22.** 0.2 equivalent of  $\text{Cu}(\text{OTf})_2$  (mg, mmol) was taken in an oven dried schlenk vial and was purged with argon thrice. Dry THF (3mL) was added to it followed by addition of 0.2 eq. of 4,4'-(isopropyl)-substituted isopropylidene-bridged 2,2'-bis-1,3'-oxazoline ligand (mg, mmol) and the reaction mixture was stirred at  $-20^\circ\text{C}$  for 4h, during which the reaction mixture turned thick green from light blue. This indicates the formation of the desired catalyst Cu-4,4'-(isopropyl)-substituted isopropylidene-bridged 2,2'-bis-1,3'-oxazoline.

Simultaneously to an oven dried three-necked flask was added imide **13** (1.00 mmol) in anh. THF (5.0 mL) under argon. To the resulting solution was added sodium hexamethyldisilylazide (1M NaHMDS in THF, 1.00 mmol) at  $-78^\circ\text{C}$  and stirred at same temperature for 30 min. After which trimethylsilyl chloride (TMSCl) (1.5 eq.) was added and was further stirred at rt for 3-4 h. It was then cooled to  $-20^\circ\text{C}$ , followed by addition of Cu-bis-isopropylloxazolidinone catalyst (0.057 g, 0.3 mmol). They were stirred for 0.5h at that temperature and  $\alpha$ -nitrostyrene (mg, mmol) was added to the reaction mixture and was stirred for ~24h. After stirring at that temperature for 4 h, the solution was poured into cooled water. The mixture was extracted with  $\text{CH}_2\text{Cl}_2$  (10 mL x 4). The combined extracts were dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (hexane/ethyl acetate = 90/10) to afford pure product in 50% yield.  $^1\text{H}$  NMR (400 MHz, DMSO- $\text{D}_6$ ):  $\delta$  3.14 (dd,  $J_1 = 13.2$  Hz,  $J_2 = 3.2$  Hz, 1H), 3.48 (dd,  $J_1 = 13.6$  Hz,  $J_2 = 2.8$  Hz, 1H), 4.27-4.34 (m, 4H), 4.39-4.45 (m, 1H), 5.76 (d,  $J = 11.6$  Hz, 1H), 6.83-6.85 (m, 1H), 7.21-7.29 (m, 7H), 7.63-7.66 (d,  $J = 8$  Hz, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  38.6, 45.3, 54.4, 56.1, 65.3, 78.3, 117.9 ( $J = 21.7$  Hz), 127.7, 128.8, 129.1, 130.1, 131, 134.7, 138.3, 153.4, 161.7, 163.16, 172.6. HRMS (ESI): calcd for  $\text{C}_{19}\text{H}_{17}\text{FN}_2\text{O}_5$ : 372.3471; found: 372.3462.