C-H Bond Functionalization via Hydride Transfer: Direct Coupling of Unactivated Alkynes and sp^3 C-H Bonds Catalyzed by Platinum Tetraiodide

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Supporting Information

Part A. Key to Abbreviated Terms:

n-BuLi – *n*-Butyl lithium
$CDCl_3$ – Chloroform (deuterated)
DCM – Dichloromethane
DMF – Dimethylformamide
DMSO – Dimethylsulfoxide
Fmoc-Cl – 9-Fluorenylmethyl Chloroformate
HMPA – Hexamethylphosphoramide
MeOH – Methanol
MsCl – Methanesulfonyl chloride

TBAF – Tetrabutylammonium fluoride
TCB – 1,2,4,5-Tetrachlorobenzene
TEA – Triethylamine
TFA – Trifluoroacetic acid
THF – Tetrahydrofuran

Part B. General Considerations

General

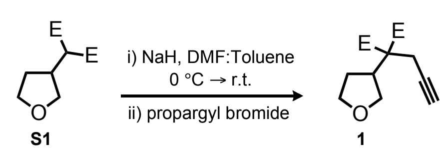
All manipulations of air and/or water sensitive compounds were performed using standard Schlenk techniques. Argon was purified by passage through Drierite. Nuclear Magnetic Resonance spectra were recorded at 300 K on Bruker 300, 400 or 500 Fourier transform NMR spectrometers. ^{1}H NMR spectra recorded in $CDCl_3$ solutions were referenced to TMS (0.00 ppm). Spectra recorded in CD_3OD, DMSO-*d*6, and C_6D_6 solutions were referenced to the solvent residual peaks (3.31 ppm, 2.50 ppm, and 7.16 ppm, respectively). ^{13}C NMR spectra recorded in $CDCl_3$, CD_3OD and DMSO-*d*6 were referenced to the residual solvent peak (77.16 ppm, 49.00 ppm, and 39.52, respectively). Many of the carbamate compounds were found to exist in rotameric forms. As such, NMR spectra were recorded at elevated temperatures in order produce clearer spectra. Flash chromatography was performed on SILICYCLE silica gel (230-400 mesh). Mass spectra were recorded on a JEOL LCmate (Ionization mode: APCI+). Reactions were monitored by GC or TLC analysis using hexanes/ethyl acetate and hexanes/diethyl ether mixtures as the eluent and visualized using permanganate stain and/or cerric ammonium molybdate stain and/or UV light.

Materials

Chloroform-d_1 was purchased from Cambridge Isotope Laboratories and stored over 4Å molecular sieves. Methanol-d_4 was purchased from Cambridge Isotope Laboratories in ampules and used as received. DMSO-d_6 was purchased from Aldrich in ampules and used as received. $PtCl_2$, $PtBr_2$, PtI_2, K_2PtCl_4 and $PtCl_4$, were purchased from Strem and stored in a glovebox under argon atmosphere. PtI_4 was purchased from Alfa Aesar and was stored in a glovebox under argon atmosphere. Acetonitrile was purified by passage through a solvent purification system.

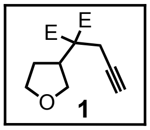
Part C. Synthesis of Starting Materials:

Synthesis of 1.



S1 → **1**

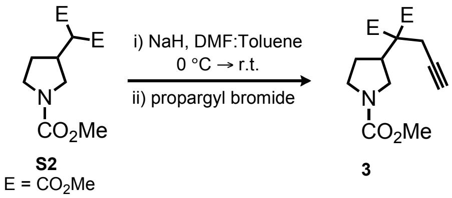
E = CO_2Me

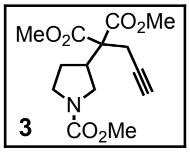


1

Dry 95% NaH (1.85g, 77.0 mmol) was weighed into a flame dried flask equipped with a magnetic stir bar. The flask was sealed under Ar with a piercible septa cap. Toluene (32 mL) and DMF (32 mL) were added and the suspension was cooled to 0 °C in an ice bath. To this suspension was added **S1**[1] (13 g, 64 mmol) slowly. Upon complete addition, the reaction was warmed to room temperature and stirred for 30 minutes, which lead to the formation of a heavy white precipitate. Propargyl bromide (11.5 g, 96.5 mmol) was then added neat to the slurry. The reaction was monitored by TLC (25% EtOAc:Hex). Upon complete consumption of the starting material, the reaction was quenched slowly with water. The reaction was then diluted with water (200 mL) and extracted with 50% Et_2O:Hex. The organic layer was then washed twice with water, once with brine, and dried over $MgSO_4$. The suspension was filtered and the filtrate was concentrated *in vacuo*. The residue was then chromatographed on silica gel, eluting with 20% EtOAc:Hex, to afford a white solid (5.52g, 72%). **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 1.86-1.77 (m, 1H); 2.12-2.04 (m, 2H); 2.85 (d, *J* = 2.8 Hz, 2H); 3.12 (apparent quint, *J* = 7.6 Hz, 1H); 3.65 (apparent quart, *J* = 8.4 Hz, 1H); 3.75 (s, 3H); 3.76 (s, 3H); 3.85-3.80 (m, 2H); 3.94 (t, *J* = 8.4 Hz, 1H); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 24.3, 27.7, 41.8, 52.76, 52.78, 58.7, 67.8, 69.3, 71.8, 78.7, 169.8, 170.1. **MS (LR-APCI):** calculated for $C_{12}H_{16}O_5$ 240.1, measured 241.1. **IR (NaCl):** 3277, 2950, 2859, 1729, 1437, 1271, 1225, 1191, 1064 cm^{-1}.

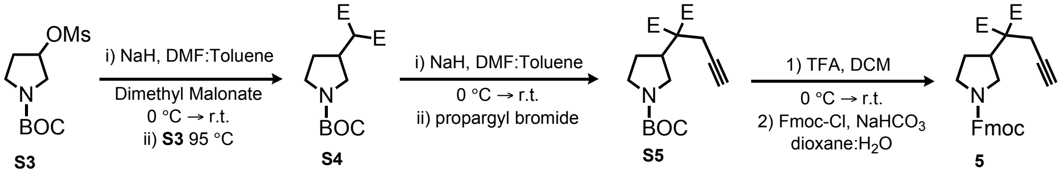
Synthesis of 3.

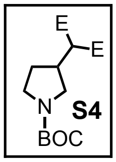




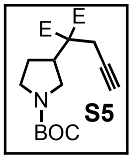
Compound **3** was prepared from **S2**[1] (4.56 g, 17.6 mmol) according to the procedure above used for compound **1**, to afford a clear oil, which solidified upon standing (5.18 g, 99%). **^{1}H NMR ($CDCl_3$, 300 MHz)** δ 1.74 (apparent quint, *J* = 10.2 Hz, 1H); 2.08 (s, 1H); 2.15-2.08 (m, 1H); 2.86 (d, *J* = 2.7 Hz, 2H); 3.11-2.99 (m, 1H); 3.32-3.20 (m, 2H); 3.52 (apparent quint, *J* = 9.6 Hz, 1H); 3.68 (s, 3H); 3.81-3.68 (m, 7H); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 24.2, 26.6, 27.4, 40.5, 41.2, 45.2, 45.5, 47.0, 47.4, 52.3, 52.8, 58.1, 72.0, 78.3, 155.3, 169.7. **MS (LR-APCI):** calculated for $C_{14}H_{19}NO_6$ 297.1, measured 298.1. **IR (NaCl):** 3290, 2955, 2891, 2366, 2340, 1742, 1701, 1454, 1397, 1280, 1242, 1207, 1131, 1102 cm^{-1}.

Synthesis of 5.



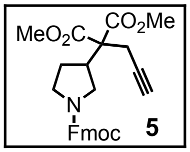


Prepared according to the procedure described above for compound **S2**, employing mesylate **S3**[2] (6.0 g, 22.6 mmol), to afford diester **S4** as a colorless oil (5.4 g, 80%). **^{1}H NMR (CDCl$_3$, 400 MHz)** δ 1.45 (s, 9H); 1.70-1.59 (m, 1H); 2.15-2.0 (m, 1H); 2.81 (bs, 1H); 3.02 (apparent quint, *J* = 9.2 Hz, 1H); 3.22-3.35 (m, 1H); 3.33 (d, *J* = 10.0 Hz, 1H); 3.61-3.50 (bm, 1H); 3.64 (apparent quart, *J* = 7.6 Hz, 1H); 3.75 (s, 6H). **MS (LR-APCI):** calculated for $C_{14}H_{23}NO_6$ 301.1, measured 302.2.



S5

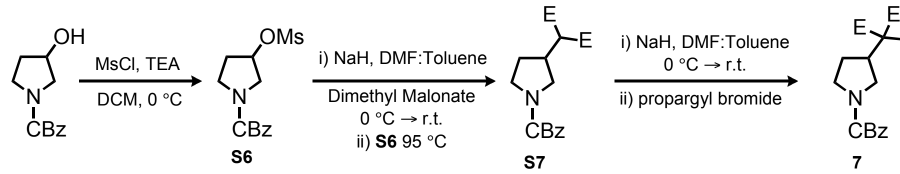
Compound **S5** was prepared according to the procedure described above for compound **1**, employing diester **S4** (4.32 g, 14.3 mmol), to afford a golden oil (4.87 g, 99%). **^{1}H NMR (CDCl$_3$, 400 MHz)** δ 1.45 (s, 9H); 1.82-1.77 (m, 1H); 2.01 (s, 1H); 2.12-2.09 (m, 1H); 2.86 (s, 2H); 3.03 (apparent quint, *J* = 8.8 Hz, 1H); 3.28-3.20 (m, 2H); 3.45 (t, *J* = 9.6 Hz, 1H); 3.67 (t, *J* = 8.8 Hz, 1H); 3.74 (s, 6H); **^{13}C NMR (CDCl$_3$, 100 MHz)** δ 24.4, 27.4, 28.8, 41.6, 45.5, 47.4, 52.6, 58.8, 71.8, 79.0, 79.4, 154.6, 169.9. **MS (LR-APCI):** calculated for $C_{17}H_{25}NO_6$ 339.1, measured 340.5.

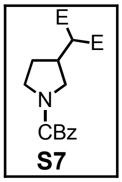


5

To a solution of BOC-protected amine **S5** (3.8 g, 11.2 mmol) in DCM (50 mL) at 0 °C was added TFA (10 mL). The reaction was allowed to warm to room temperature. After 2 hours, the reaction was carefully quenched with $NaHCO_3$ (aq. sat.) to reach neutral pH. The solution was then extracted with DCM. The organic extracts were combined and washed with brine and dried over $MgSO_4$. The solution was filtered and the filtrate was concentrated to give a residue, which was used directly in the next step without further purification. The resulting orange oil was dissolved in 1,4-dioxane (30 mL) and water (70 mL). Solid $NaHCO_3$ (1.45 g, 17.2 mmol) was then added to the solution, followed by Fmoc-Cl (3.35 g, 12.9 mmol) in 1,4-dioxane (5 mL). The mixture was stirred overnight at room temperature. The 1,4-dioxane was then removed *in vacuo* and the aqueous solution was extracted with EtOAc, washed with brine, dried over $MgSO_4$, filtered and concentrated. The resulting oil was chromatographed on silica gel, eluting with 25% EtOAc:Hex to afford a golden oil (2.98 g, 75% over two steps). **^{1}H NMR (CDCl$_3$, 400 MHz)** δ 1.81 (apparent sept, *J* = 10.8 Hz, 1H); 2.07 (d, *J* = 12.0 Hz, 1H); 2.22-2.02 (m, 1H); 2.89 (s, 2H); 3.08 (sept, *J* = 9.2 Hz, 1H); 3.41-3.26 (m, 2H); 3.57 (apparent quint, *J* = 9.2 Hz, 1H); 3.86-3.74 (m, 7H); 4.27-4.21 (m, 1H); 4.39-4.30 (m, 2H); 7.30 (t, *J* = 7.6 Hz, 2H); 7.38 (t, *J* = 7.6 Hz, 2H); 7.60 (d, *J* = 4.8 Hz, 2H); 7.75 (d, *J* = 7.2 Hz, 2H); **^{13}C NMR (CDCl$_3$, 100 MHz)** δ 24.2, 24.3, 26.7, 27.5, 40.6, 41.4, 45.4, 45.6, 47.2, 47.4, 47.5, 52.9, 58.2, 67.2, 67.3, 72.1, 78.4, 120.0, 125.1, 125.2, 127.0, 127.7, 141.3, 144.2, 154.7, 169.6. **MS (LR-APCI):** calculated for $C_{27}H_{27}NO_6$ 461.1, measured 462.3. **IR (NaCl):** 3283, 2945, 2882, 1729, 1695, 1420, 1231, 1202, 1122 cm^{-1}.

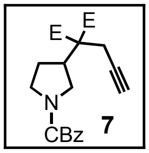
Synthesis of 7.





S7

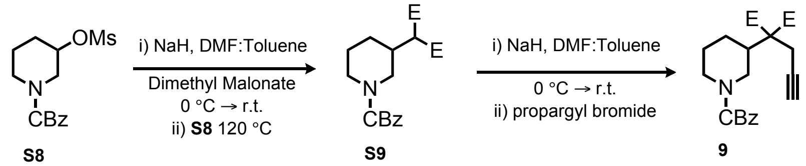
Dry 95% NaH (1.09 g, 45.4 mmol) was weighed into a flame dried flask equipped with a magnetic stir bar. The flask was sealed under Ar with a piercible septum cap. Toluene (23 mL) and DMF (23 mL) were added and the suspension was cooled to 0 °C in an ice bath. To this suspension was added neat dimethyl malonate (5.17 mL, 39.1 mmol) slowly. Upon complete addition, the mixture was warmed to room temperature and stirred for 30 minutes, which led to the formation of a heavy white precipitate. The slurry was then cooled to 0 °C and mesylate **S6**[3] (6.0 g, 22.6 mmol) was added in one portion. After complete addition of the mesylate, the reaction was warmed to 95 °C and monitored by TLC (50% EtOAc:Hex). Upon complete consumption of the mesylate, the mixture was cooled to room temperature and treated slowly with water. The mixture was then diluted with water (100 mL) and extracted with 50% Et_2O:Hex. The organic layer was then washed twice with water, once with brine and finally dried with $MgSO_4$. The suspension was filtered and concentrated *in vacuo*. The residue was then chromatographed on silica gel, eluting with 25% EtOAc:Hex, to afford a colorless oil (5.4 g, 80%). **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 1.64 (apparent sext, *J* = 9.2 Hz, 1H); 2.09-2.03 (m, 1H); 2.83 (apparent quint, *J* = 7.6 Hz, 1H); 3.10 (apparent quart, *J* = 10.8 Hz, 1H); 3.41-3.31 (m, 2H); 3.60-3.52 (m, 1H); 3.73 (bs, 4H); 3.74 (s, 3H); 5.12 (s, 2H); 7.36-7.30 (m, 5H); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 29.1, 29.9, 37.5, 38.3, 45.1, 45.5, 49.4, 49.9, 52.7, 54.5, 66.8, 127.9, 128.0, 128.5, 136.9, 154.7, 168.5. **MS (LR-APCI):** calculated for $C_{17}H_{21}NO_6$ 335.1, measured 336.3.

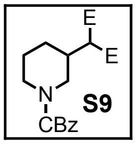


7

Substrate **7** was prepared from **S7** (4.79 g, 14.3 mmol) according to the procedure above used for **1**, to afford a colorless oil (4.21g, 79%). **^{1}H NMR ($CDCl_3$, 400 MHz, 350 K)** δ 1.80 (apparent quint, *J* = 10.8 Hz, 1H); 2.01 (t, *J* = 2.4 Hz, 1H); 2.15-2.08 (m, 1H); 2.85 (d, *J* = 2.4 Hz, 2H); 3.03 (apparent quint, *J* = 8.4 Hz, 1H); 3.36-3.28 (m, 2H); 3.56-3.51 (m, 1H); 3.69 (s, 3H); 3.72 (s, 3H); 3.79-3.72 (m, 1H); 5.12 (s, 2H); 7.35-7.24 (m, 5H); **^{13}C NMR ($CDCl_3$, 100 MHz, 350 K)** δ 24.3, 27.2, 41.4, 45.5, 47.6, 52.5, 58.6, 66.8, 71.9, 78.8, 127.89, 127.93, 128.5, 137.4, 154.8, 169.6. **MS (LR-APCI):** calculated for $C_{20}H_{23}NO_6$ 373.1, measured 374.6. **IR (NaCl):** 3294, 2950, 2876, 1729, 1707, 1414, 1363, 1236, 1208, 1128 cm^{-1}.

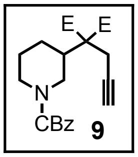
Synthesis of 9.





S9

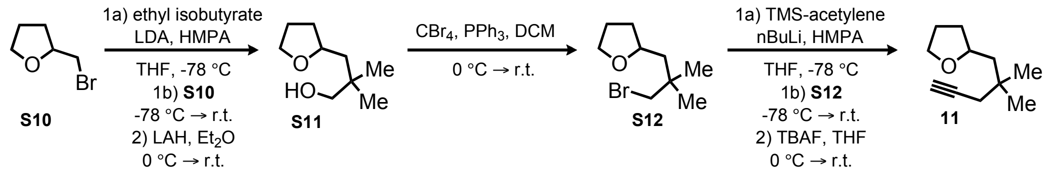
Compound **S9** was prepared according to the procedure described above for compound **S7**, employing mesylate **S8**[4] (6.27 g, 20 mmol), to afford a colorless oil (3.84 g, 55%). **^{1}H NMR ($CDCl_3$, 400 MHz, 350 K)** δ 1.38-1.29 (m, 1H); 1.54-1.46 (m, 1H); 1.69-1.65 (m, 1H); 1.84-1.81 (m, 1H); 2.32-2.25 (m, 1H); 3.00-2.88 (m, 2H); 3.29 (d, *J* = 8.8 Hz, 1H); 3.72-3.66 (m, 6H); 3.89 (d, *J* = 13.2 Hz, 1H); 3.97 (d, *J* = 12.8 Hz, 1H); 5.15-5.08 (m, 2H); 7.33-7.28 (m, 5H); **^{13}C NMR ($CDCl_3$, 100 MHz, 350 K)** δ 24.4, 28.4, 35.9, 44.7, 47.8, 52.3, 54.7, 67.2, 127.9, 128.0, 128.5, 137.2, 155.4, 168.3, 168.5. **MS (LR-APCI):** calculated for $C_{18}H_{23}NO_6$ 349.1, measured 350.3.

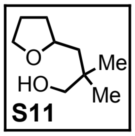


9

Compound **9** was prepared according to the procedure described above for substrate **1**, employing diester **S9** (2.34 g, 6.7 mmol), to afford a golden oil (2.12 g, 81%). **^{1}H NMR (CDCl$_3$, 400 MHz, 350 K)** δ 1.33-1.25 (m, 1H); 1.56-1.47 (m, 1H); 1.71-1.67 (m, 1H); 1.98-1.95 (m, 2H); 2.39-2.33 (m, 1H); 2.69-2.61 (m, 2H); 2.83 (s, 2H); 3.69 (s, 6H); 4.15 (d, *J* = 12.4 Hz, 1H); 4.40 (d, *J* = 12.8 Hz, 1H); 5.12 (apparent quart, *J* = 12.4 Hz, 2H); 7.34-7.26 (m, 5H); **^{13}C NMR (CDCl$_3$, 100 MHz, 350 K)** δ 23.1, 25.6, 26.6, 40.0, 44.7, 46.6, 52.3, 59.6, 67.1, 71.7, 79.1, 127.8, 128.4, 137.2, 155.2, 169.7. **MS (LR-APCI):** calculated for $C_{21}H_{25}NO_6$ 387.1, measured 388.3. **IR (NaCl):** 3283, 2950, 2847, 2360, 1729, 1689, 1437, 1277, 1231, 1150 cm^{-1}.

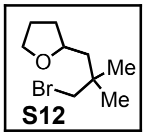
Synthesis of 11.





S11

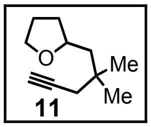
To a solution of diisopropylamine (10.2 mL, 72 mmol) in THF (59 mL) at -78 °C was added *n*-BuLi (1.6 M in THF, 42 mL, 66 mmol) slowly. The mixture was stirred at -78 °C for 20 minutes, followed by 30 minutes at 0 °C. Ethyl isobutyrate (8.0 mL, 60 mmol) in THF (18 mL) was then added slowly to the stirred solution. After 10 minutes, HMPA (11.5 mL, 66 mmol) was added and the mixture stirred at 0 °C for 30 minutes. Commercially available bromide **S10** (8.72g, 66 mmol) was then added neat and the reaction was monitored by TLC (20% Et_2O:Hex), while it warmed to room temperature. Upon complete consumption of the bromide, the reaction was quenched with water, extracted with EtOAc and dried over $MgSO_4$. The resulting solution was concentrated *in vacuo* to afford a yellow oil, which was used directly in the next step. The oil was dissolved in Et_2O (30 mL) and added dropwise to a suspension of LAH (4.56 g, 120 mmol) in Et_2O (200 mL) at 0 °C. The reaction was then allowed to warm to room temperature, while being monitored by TLC (20% Et_2O:Hex). Upon complete consumption of the starting material, the reaction was quenched with water (5 mL), then 10% NaOH (aq.) (5 mL) and finally a second portion of water (15 mL). The precipitate was filtered and the filtrate was concentrated *in vacuo*. The residue was vaccum distilled (b.p. 49-52 °C) to afford a colorless liquid (8.19 g, 89% over two steps). **^{1}H NMR (CDCl$_3$, 400 MHz)** δ 0.89 (s, 3H); 0.93 (s, 3H); 1.46-1.39 (m, 2H); 1.58-1.47 (m, 1H); 1.91-1.85 (m, 2H); 2.01-1.96 (m, 1H); 3.27 (apparent dd, *J* = 11.5 Hz, *J* = 6.4 Hz, 1H); 3.35 (apparent dd, *J* = 11.4 Hz, *J* = 7.6 Hz, 1H); 3.80-3.74 (m, 1H); 3.98-3.86 (m, 3H); **^{13}C NMR (CDCl$_3$, 100 MHz)** δ 23.1, 25.6, 28.0, 33.0, 35.3, 46.4, 68.1, 71.6, 76.2. **MS (LR-APCI):** calculated for $C_9H_{18}O_2$ 158.1, measured 159.0.



S12

A solution of alcohol **S11** (8.14 g, 51.5 mmol) in DCM (200 mL) was cooled to 0 °C. To the resulting solution was added CBr_4 (20.5 g, 61.8 mmol), followed by portionwise addition of PPh_3 (13.52 g, 51.5 mmol).

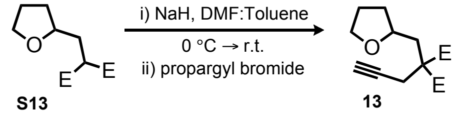
The reaction mixture was stirred at 0 °C for 30 minutes, after which it was warmed to room temperature. After stirring overnight, significant starting material remained, so additional CBr_4 (3.42, 10 mmol) and PPh_3 (2.70g, 10 mmol) were added. After an additional 12 hours, all of the starting material was consumed, as determined by TLC (20% Et_2O:Hex). Half of the solvent was removed *in vacuo* and hexanes was then added. The resulting precipitate was filtered through celite and the filtrate was concentrated *in vacuo*. The residue was dissolved in a minimal amount of DCM. This solution was treated with hexanes and the resulting precipitate was filtered through celite. The solution was concentrated and the residue was chromatographed on silica gel, eluting with 10% Et_2O:Hex to afford a colorless liquid (10.5 g, 92%), which was stored in a refrigerator at 0° C. **^{1}H NMR ($CDCl_3$, 300 MHz)** δ 1.09 (s, 3H); 1.10 (s, 3H); 1.34 (apparent dd, *J* = 12.1 Hz, *J* = 9 Hz, 1H); 1.66 (apparent quart, *J* = 7.2 Hz, 2H); 1.79 (apparent dd, *J* = 12.3 Hz, *J* = 6.6 Hz, 1H); 2.07-1.85 (m, 2H); 3.52-3.42 (m, 4H); 4.05-3.95 (m, 1H); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 26.7, 27.1, 29.9, 34.1, 35.0, 39.7, 47.1, 78.7, 80.1. **MS (LR-APCI):** calculated for $C_9H_{17}OBr$ 220.0, 222.0 measured 221.0, 223.0.

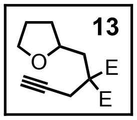


11

To an oven dried flask was added TMS-acetylene (740 mg, 7.5 mmol) followed by THF (10 mL). The solution was sealed under Ar and cooled to -78 °C. *n*-BuLi (1.6M in THF, 4.5 mL, 7.5 mmol) was then added slowly and the reaction mixture was stirred for 30 minutes. Neat HMPA (1.3 mL, 7.5 mmol) was then added to the solution, which was stirred for 5 minutes. This solution was then transferred via cannula to a solution of bromide **S12** (1.1 g, 5 mmol) in THF (7 mL) at -78 °C. The reaction was allowed to warm to room temperature slowly over one hour and was then stirred overnight. The reaction was quenched with NH_4Cl (aq. sat.) (50 mL), extracted with Et_2O, washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The resulting residue was dissolved in THF (10 mL) and cooled to 0 °C. To the solution was added TBAF (1 M in THF, 5 mL, 5 mmol). The reaction mixture was then warmed to room temperature and after 3 hours the reaction was concentrated *in vacuo.* The resulting residue was chromatographed on silica gel, eluting with 1% Et_2O:Hex. The product was found to be slightly volatile under full vacuum of the hi-vacuum pump (~3 torr). After careful evaporation of the solvent on a rotary evaporator, the clear liquid was dried on a vacuum line under full vacuum for one minute, affording a colorless liquid (535 mg, 64% over two steps). **^{1}H NMR ($CDCl_3$, 300 MHz)** δ 1.08 (s, 3H); 1.09 (s, 3H); 1.34 (apparent dd, *J* = 12.3 Hz, *J* = 9.0 Hz, 1H); 1.71-1.53 (m, 4H); 1.76 (apparent dd, *J* = 12.0 Hz, *J* = 6.6 Hz, 1H); 1.94 (t, *J* = 2.7 Hz, 1H); 2.26-2.20 (m, 2H); 3.42 (d, *J* = 8.1 Hz, 1H); 3.51 (d, *J* = 8.1 Hz, 1H); 4.04-3.94 (m, 1H); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 18.6, 25.4, 26.7, 27.1, 35.5, 39.7, 47.1, 68.5, 79.0, 80.1, 84.5. **MS (LR-APCI):** calculated for $C_{11}H_{18}O$ 166.1, measured 167.0. **IR (NaCl):** 3294, 2950, 2870, 1724, 1460, 1363, 1076 cm^{-1}.

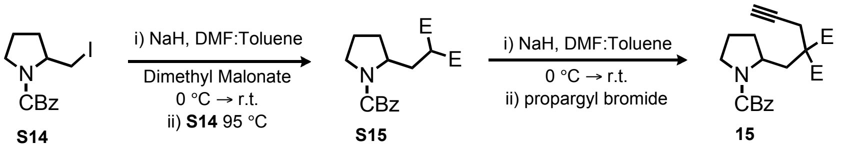
Synthesis of 13.

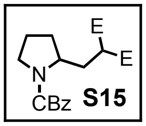



13

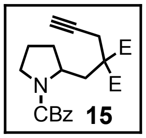
Compound **13** was prepared from **S13**[5] (4.16 g, 19.3 mmol) according to the procedure above used for compound **1**, to afford a clear oil (4.58 g, 95%). **^{1}H NMR (CDCl$_3$, 400 MHz)** δ 1.59-1.52 (m, 1H); 1.92-1.80 (m, 2H); 2.07-2.00 (m, 2H); 2.33-2.21 (m, 2H); 2.90 (apparent dd, *J* = 17.6 Hz, *J* = 2.4 Hz, 1H); 3.04 (apparent dd, *J* = 17.2 Hz, *J* = 2.8 Hz, 1H); 3.77-3.64 (m, 2H); 3.73 (s, 3H); 3.74 (s, 3H); 3.98-3.91 (m, 1H); **^{13}C NMR (CDCl$_3$, 100 MHz)** δ 22.8, 25.3, 32.1, 37.7, 52.5, 52.7, 55.5, 67.6, 71.4, 74.6, 79.1, 170.5, 170.6. **MS (LR-APCI):** calculated for $C_{13}H_{18}O_5$ 254.1, measured 255.1. **IR (NaCl):** 3277, 2956, 2870, 1741, 1437, 1288, 1208, 1082 cm^{-1}.

Synthesis of 15.



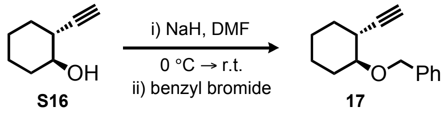

S15

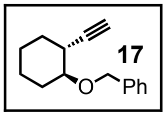
To an oven dried flask was added dry 95% NaH (1.00 g, 39.9 mmol), followed by DMF (20 mL) and toluene (20 mL). The suspension was cooled to 0 °C and dimethyl malonate (4.56 mL, 39.9 mmol) was added slowly. Upon complete addition, the reaction mixture was warmed to room temperature and a heavy precipitate formed. After stirring at room temperature for 30 minutes, iodide **S14**[6] (6.88 g, 19.95 mmol) was added and the reaction mixture was heated to 95 °C and stirred overnight. The reaction mixture was cooled to room temperature and diluted with water (150 mL). The resulting solution was extracted with EtOAc. The organic layer was washed twice with water, then brine and dried over MgSO$_4$, filtered and concentrated *in vacuo*. The resulting residue was chromatographed on silica gel, eluting with 20% EtOAc:Hex, to afford a colorless oil (4.21 g, 60%). **^{1}H NMR (CDCl$_3$, 400 MHz)** δ 1.64 (br s, 1H); 1.94-1.85 (br m, 3H); 2.20-2.02 (m, 2H); 3.38-3.32 (m, 1H); 3.51-3.40 (m, 1H); 3.74-3.62 (m, 7H); 4.06-4.00 (m, 1H); 5.23-5.00 (m, 2H); 7.36-7.29 (m, 5H); **^{13}C NMR (CDCl$_3$, 100 MHz)** δ 22.8, 23.7, 30.6, 31.1, 33.9, 34.0, 46.2, 46.5, 49.0, 49.2, 52.5, 55.3, 56.0, 66.7, 66.9, 127.8, 127.9, 128.1, 128.4, 136.7, 136.8, 155.0, 155.5, 169.4, 169.7, 169.9. **MS (LR-APCI):** calculated for $C_{18}H_{23}NO_6$ 349.1, measured 350.6.


15

Prepared from **S15** (2.8 g, 8.0 mmol) following the procedure described above for compound **13** to afford a golden oil (3.88 g, 87%) which solidified upon standing. **^{1}H NMR (CDCl$_3$, 300 MHz)** 1.69-1.63 (br m, 1H); 1.92-1.84 (m, 4H); 2.21-2.18 (br m, 1H); 2.44 (apparent dd, *J* = 10.8 Hz, *J* = 3.9 Hz, 1H); 2.88-2.81 (br m, 1H); 3.16-2.93 (m, 1H); 3.31-3.27 (m, 1H); 3.48-3.40 (br m, 1H); 3.73-3.62 (m, 6H): 4.03-3.95 (br m, 1H); 5.24-5.02 (m, 2H); 7.39-7.29 (m, 5H); **^{13}C NMR (CDCl$_3$, 100 MHz)** δ 22.7, 23.5, 31.1, 31.3, 36.3, 45.4, 45.8, 52.8, 53.3, 53.7, 55.7, 66.6, 66.9, 71.7, 79.1, 127.7, 127.8, 128.4, 136.8, 154.8, 170.2, 170.5; **MS (LR-APCI):** calculated for $C_{21}H_{25}NO_6$ 387.1, measured 388.2. **IR (NaCl):** 3283, 2956, 2876, 1735, 1695, 1437, 1408, 1288, 1214, 1093 cm^{-1}.

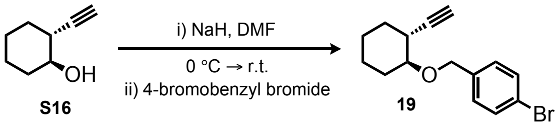
Synthesis of 17.

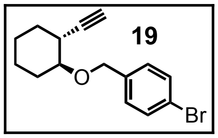




Dry 95% NaH (360 mg, 15 mmol) was added to a flame dried flask equipped with a magnetic stir bar. The flask was sealed under Ar and DMF (40 mL) was added. The suspension was then cooled to 0 °C and alcohol **S16**[7] (1.24 g, 10 mmol) was added neat. The reaction mixture was warmed to room temperature and stirred for 30 minutes. Benzyl bromide (1.82 g, 10.5 mmol) was then added and the reaction stirred overnight. The reaction was quenched with water and extracted with Et_2O. The organic portion was washed with water and brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was chromatographed on silica gel, eluting with 1 to 2% Et_2O:Hex, to afford a colorless oil (1.91g, 88%). **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 1.50-1.27 (m, 4H); 1.72-1.63 (m, 2H); 2.03-1.99 (m, 2H); 2.09 (d, J = 2.4 Hz, 1H); 2.53-2.49 (m, 1H); 3.39 (apparent dt, J = 8.0 Hz, J = 3.6 Hz, 1H); 4.65 (s, 2H); 7.27-7.22 (m, 1H); 7.34-7.30 (m, 2H); 7.40-7.34 (m, 2H); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 23.3, 24.0, 30.2, 30.4, 35.0, 69.5, 71.3, 79.3, 86.8, 127.5, 127.7, 128.4, 139.0. **MS (LR-APCI):** calculated for $C_{15}H_{18}O$ 214.1, measured 215.0. **IR (NaCl):** 3284, 3065, 3034, 2926, 2875, 2359, 2340, 2103, 1593, 1486, 1441, 1283, 1254, 1229, 1109, 1020 cm^{-1}.

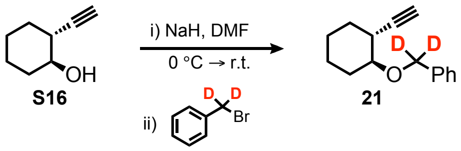
Synthesis of 19.

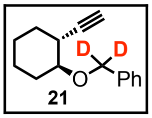




Prepared according to the procedure described above for **17**, employing 4-bromobenzyl bromide in place of benzyl bromide to afford a colorless oil (854 mg, 50%). **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 1.35-1.22 (m, 3H); 1.50-1.41 (m, 1H); 1.73-1.63 (m, 2H); 2.03-1.96 (m, 2H); 2.10 (d, J = 2.4 Hz, 1H); 2.51-2.45 (m, 1H); 3.35 (apparent dt, J = 8.4 Hz, J = 3.6 Hz, 1H); 4.60 (s, 2H); 7.26 (d, J = 8.4 Hz, 2H); 7.45 (d, J = 8.4 Hz, 2H); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 23.3, 24.0, 30.3, 30.6, 35.1, 69.5, 70.5, 79.6, 86.7, 121.3, 129.4, 131.4, 138.0. **MS (LR-APCI):** calculated for $C_{15}H_{17}BrO$ 292.0, 294.0, measured 293.1, 295.1.

Synthesis of 21.

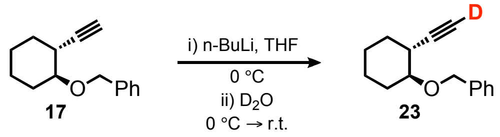


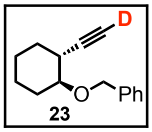


21

Prepared according to the procedure described above for **17**, employing α,α-dideuterobenzyl bromide in place of benzyl bromide to afford a colorless oil (1.91g, 88%).**^{1}H NMR ($CDCl_3$, 400 MHz)** δ 1.50-1.25 (m, 4H); 1.71-1.62 (m, 2H); 2.03-1.96 (m, 2H); 2.09 (d, *J* = 2.4 Hz, 1H); 2.53-2.47 (m, 1H); 3.38 (td, *J* = 8.0 Hz, *J* = 3.6 Hz, 1H); 7.27 (t, *J* = 8.2 Hz, 1H); 7.32 (t, *J* = 8.2 Hz, 2H); 7.38 (d, *J* = 8.2 Hz, 2H); **^{2}H NMR ($CDCl_3$, 400 MHz)** δ 4.54 (s); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 23.2, 24.0, 30.2, 30.4, 35.0, 69.4, 79.2, 86.8, 127.5, 127.7, 128.3, 138.9. **MS (LR-APCI):** calculated for $C_{15}H_{16}D_2O$ 216.3, measured 217.2. **IR (NaCl):** 3300, 2936, 2863, 2356, 2344, 2116, 2062, 1495, 1441, 1368, 1242, 1106, 1061, 1020 cm^{-1}.

Synthesis of 23.





23

To a solution of **17** (321 mg, 1.5 mmol) in Et_2O (7.5 mL) at -30 °C was added nBuLi (1.6M in THF, 1.03 mL, 1.65 mmol). The reaction stirred for 20 minutes, after which D_2O (2 mL) was added and the organic layer was separated, dried over $MgSO_4$ and concentrated *in vacuo* to afford a colorless oil (300mg, 93%), which was pure by ^{1}H NMR. **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 1.56-1.30 (m, 4H); 1.76-1.64 (m, 2H); 2.09-2.00 (m, 2H); 2.55 (td, *J* = 11 Hz, *J* = 5.2 Hz, 1H); 3.43 (td, *J* = 10.8 Hz, *J* = 4.4 Hz, 1H); 4.69 (s, 2H); 7.44-7.28 (m, 5H); **^{2}H NMR ($CDCl_3$, 400 MHz)** δ 2.01 (bs); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 23.3, 24.0, 30.2, 30.4, 35.0, 71.3, 79.2, 86.4, 127.5, 127.7, 128.3, 139.0. **MS (LR-APCI):** calculated for $C_{15}H_{17}DO$ 215.3, measured 216.1. **IR (NaCl):** 2936, 2860, 2591, 2356, 2347, 1495, 1451, 1356, 1090, 1061cm^{-1}.

Part D. General Hydroalkylation Procedure:

The described hydroalkylation reaction was typically setup in a glovebox under an argon atmosphere according to the procedure described below. The reaction may also be conducted on the benchtop, however the isolated yields were slightly lower in comparison to reactions setup in the glovebox. As a representative example, substrate **3** produced the desired product **4** in 67% yield when setup according to the glovebox procedure; 51% was obtained on the benchtop.

Glovebox Procedure:

In an argon filled glovebox, an oven dried heavy walled pressure vessel (cat. # CG-1880 Chemglass) was charged with PtI_4 (5 mol%, 15.8 mg) followed by dry MeCN (6 mL). A stock solution (3 mL) of the desired substrate in MeCN (0.15 M), was added to the suspension of catalyst. The tube was then equipped with a magnetic stir bar and sealed with a Teflon screw-cap fitted with a rubber O-ring. The vessel was then removed from the glovebox and placed in a silicon oil bath preheated to 120 °C. Upon completion of the reaction, as determined by TLC and/or GC, the solvent was removed *in vacuo* and the residue was chromatographed on silica gel to afford the desired product.

Benchtop Procedure:

Into an oven dried 8 mL glass vial (cat. # 66010-426 VWR) was weighed PtI_4 (5 mol%, 10.6 mg, 0.015 mmol) and the appropriate substrate (0.3 mmol). An oven dried magnetic stir bar was then added to the vial and the mixture was sealed with an open top screw-cap (cat. # 66012-598 VWR) fitted with a piercible PTFE Silicone-lined septum (cat. # 66010-774 VWR). The vial was evacuated and backfilled with argon three times. Dry MeCN (6 mL) was then syringed into the vial. The septum-cap was exchanged under argon flow for a solid Teflon lined screw-cap (cat. # cat. # 66012-372 VWR). The vial was then placed in a reaction block preheated to 120 °C. Upon completion of the reaction, as determined by TLC and/or GC, the solvent was removed *in vacuo* and the residue was chromatographed on silica gel to afford the desired product.

Part E. Catalyst Screen

Table S1: The Effect of Various Metal Salts and Complexes on Substrate **1**

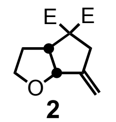
entry	catalyst	cat. loading	product **2** (%)	recovered SM **1** (%)
1	$AlCl_3$	10 mol%	0	99
2	CuCl	10 mol%	trace	98
3	$CuCl_2$	10 mol%	trace	98
4	$HgCl_2$	10 mol%	0	70
5	$HfCl_4$	10 mol%	0	96
6	$InCl_3$	10 mol%	0	97
7	$PdCl_2$	10 mol%	0	0
8	$RhCl_3$	10 mol%	0	0
9	$RuCl_3$	10 mol%	0	61
10	$RuCl_3$ + AgOTf	10 mol%	0	78
11	AuCl	10 mol%	1	97
12	AuCl[a]	5 mol%	0	99
13	AuCl[c]	5 mol%	0	99
14	$AuCl_3$	10 mol%	2	85
15	$AuCl_3$[a]	5 mol%	trace	73
16	$AuCl_3$[c]	5 mol%	trace	82
17	$KAuCl_4$	10 mol%	0	99
18	$Au(PPh_3)Cl$ + $AgSbF_6$	10 mol%	0	99
19	$Au(PPh_3)Cl$ + $AgSbF_6$[a]	5 mol%	8	25

20	Au(PPh$_3$)Cl + AgSbF$_6^{b}$	5 mol%	trace	33
21	Au(PPh$_3$)Cl + AgSbF$_6^{c}$	5 mol%	3	0
22	Au(PPh$_3$)Cl + AgSbF$_6^{d}$	5 mol%	8	30
23	Au(PPh$_3$)Cl + AgSbF$_6^{d}$	5 mol%	8	30
24	Au(PPh$_3$)Cl + AgNTf$_2^{a}$	5 mol%	9	90
25	Au(PPh$_3$)Cl + AgNTf$_2^{c}$	5 mol%	trace	98
26	Au(IPr)Cl + AgSbF$_6$	10 mol%	2	97
27	{[Au(PPh$_3$)]$_3$O}BF$_4$	10 mol%	0	99
28	[AuCl]$_2$(dppm) + AgSbF$_6$	10 mol%	2	98
29	Au((*p*-CF$_3$Ph)$_3$P)Cl + AgSbF$_6$	10 mol%	0	99
30	*cis*-PtCl$_4$(NH$_3$)$_2$	10 mol%	11	76
31	*trans*-PtCl$_4$(NH$_3$)$_2$	10 mol%	14	70
32	*trans*-PtCl$_4$(NH$_3$)$_2$ + AgOTf	10 mol%	6	92
33	K$_2$PtCl$_4$	10 mol%	11	44
34	K$_2$PtCl$_4$ + AgOTf	10 mol%	25	34
35	(COD)PtMe$_2$	10 mol%	1	0
36	(bipy)PtCl$_2$	10 mol%	1	99
37	(bipy)PtCl$_2$ + AgOTf	10 mol%	14	78
38	(MeCN)$_2$PdCl$_2$	10 mol%	0	0
39	(2-pyridine carboxylato)AuCl$_2$	10 mol%	2	87
40	[PtCl$_2$(ethylene)]$_2$	10 mol%	52	0
41	[PtCl$_2$(ethylene)]$_2$	5 mol%	33	17
42	[PtCl$_2$(ethylene)]$_2$ + AgOTf	10 mol%	29	0
43	[PtCl$_2$(ethylene)]$_2$ + AgOTf	5 mol%	30	18
44	PtCl$_2$(DMSO)$_2$	10 mol%	28	29
45	PtCl$_2$(DMSO)$_2$ + AgOTf	10 mol%	15	24
46	(COD)PtCl$_2$	10 mol%	0	100
47	(COD)PtCl$_2$ + AgOTf	10 mol%	2	1
48	Pt(CN)$_2$	10 mol%	0	100
49	(MeCN)$_2$PtCl$_2$	10 mol%	32	37
50	(MeCN)$_2$PtCl$_2$ + AgOTf	10 mol%	12	55
51	Pt(acac)$_2$	10 mol%	0	100
52	PtCl$_2$	10 mol%	37	0
53	PtCl$_2$	5 mol%	23	58
54	PtCl$_2$ + AgOTf	10 mol%	11	50
55	PtCl$_4$	10 mol%	24	38
56	PtCl$_4$ + AgOTf	10 mol%	11	73
57	PtBr$_2$	5 mol%	43	6
58	PtI$_2$	5 mol%	69	2
59	PtI$_4$	10 mol%	75	0
60	**PtI$_4$**	**5 mol%**	**86**	**0**

All reactions were setup in a glovebox under argon atmosphere in MeCN at 0.05 M relative to substrate **1** and heated in a reaction block at 120 °C. Yields were determined by GC and ^{1}H-NMR relative to tetrachlorobenzene, which was used as an internal standard. ^{a}Reaction conducted in DCE (0.05 M) at 120 °C. ^{b}Reaction conducted in DCE (0.05M) at 80 °C. ^{c}Reaction conducted in PhMe (0.05 M) at 120 °C. ^{d}Reaction conducted in PhMe (0.05 M) at 80 °C.

Part F. Hydroalkylation Product Data:

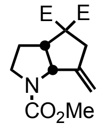
Product 2.



2

Product **2** was eluted with 10% EtOAc:Hex, as a colorless oil. **^{1}H NMR (CDCl$_3$, 400 MHz)** δ 1.59-1.46 (m, 1H); 2.04-1.94 (m, 1H); 2.63 (d, *J* = 16.0 Hz, 1H); 3.19 (apparent dt, *J* = 15.6 Hz, *J* = 1.2 Hz, 1H); 3.45 (apparent quart, *J* = 8.0 Hz, 1H); 3.68-3.61 (m, 1H); 3.71 (s, 3H); 3.74 (s, 3H); 3.91 (apparent dt, *J* = 8.0 Hz, *J* = 3.6 Hz, 1H); 4.71 (d, *J* = 7.2 Hz, 1H); 5.11 (s, 1H); 5.19 (d, *J* = 1.2 Hz, 1H); **^{13}C NMR (CDCl$_3$, 100 MHz)** δ 29.9, 38.0, 48.0, 52.7, 53.0, 62.0, 68.6, 84.7, 113.3, 147.0, 170.2, 171.9. **MS (LR-APCI):** calculated for $C_{12}H_{16}O_5$ 240.1, measured 241.1. **IR (NaCl):** 2955, 2853, 2363, 2340, 1732, 1432, 1277, 1248, 1216, 1163, 1058, 1033 cm^{-1}.

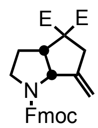
Product 4.



4

Product **4** was eluted with 20% EtOAc:Hex, as a colorless oil. **^{1}H NMR (CDCl$_3$, 400 MHz, 350K)** δ 1.60 (apparent quint, *J* = 9.6 Hz, 1H); 1.97-1.89 (m, 1H); 2.77 (d, *J* = 17.2 Hz, 1H); 3.26 (d, *J* = 17.2 Hz, 1H); 3.35 (apparent quart, *J* = 8.4 Hz, 1H); 3.49-3.43 (m, 2H); 3.74-3.72 (m, 9H); 4.82 (d, *J* = 7.2 Hz, 1H); 5.08 (s, 1H); 5.37 (s, 1H); **^{13}C NMR (CDCl$_3$, 100 MHz, 350K)** δ 26.7, 38.0, 46.6, 47.8, 52.2, 52.4, 52.8, 60.7, 64.3, 112.5, 147.4, 155.9, 169.9, 171.7. **MS (LR-APCI):** calculated for $C_{14}H_{19}NO_6$ 297.1, measured 298.5. **IR (NaCl):** 2985, 2950, 2876, 1729, 1707, 1449, 1380, 1277, 1248 cm^{-1}.

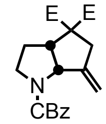
Product 6.



6

Product **6** was eluted with 25% EtOAc:Hex, as a colorless oil. **^{1}H NMR (CDCl$_3$, 400 MHz, 350 K)** δ 1.65-1.54 (m, 1H); 2.00-1.85 (m, 1H); 2.78-2.74 (m, 1H); 3.40-3.27 (m, 2H); 3.55-3.47 (m, 2H); 3.74 (s, 6H); 4.23 (t, *J* = 6.4 Hz, 1H); 4.48-4.38 (m, 2H); 5.49-4.74 (br m, 3H); **^{13}C NMR (CDCl$_3$, 100 MHz, 350 K)** δ 26.7, 38.0, 46.7, 47.8, 52.5, 52.8, 60.6, 64.4, 67.3, 112.8, 120.0, 125.1, 127.1, 127.7, 141.6, 144.4, 147.0, 155.4, 169.9, 171.7. **MS (LR-APCI):** calculated for $C_{27}H_{27}NO_6$ 461.1, measured 462.4. **IR (NaCl):** 3472, 2956, 2893, 2240, 1741, 1701, 1454, 1351, 1271, 1087 cm^{-1}.

Product 8.

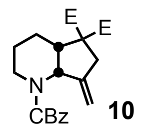


8

Product **8** was eluted with 25% EtOAc:Hex, as a colorless oil. **^{1}H NMR (CDCl$_3$, 400 MHz, 350 K)** δ 1.58 (apparent quint, *J* = 9.6 Hz, 1H); 1.91-1.90 (m, 1H); 2.74 (d, *J* = 17.2 Hz, 1H); 3.24 (d, *J* = 17.2 Hz, 1H); 3.33

(apparent quart, *J* = 8.4 Hz, 1H); 3.51-3.44 (m, 2H); 3.72 (s, 6H); 4.84 (d, *J* = 6.4 Hz, 1H); 5.04 (s, 1H); 5.18-5.10 (m, 2H); 5.32 (bs, 1H); 7.35-7.26 (m, 5H); **^{13}C NMR ($CDCl_3$, 100 MHz, 350 K)** δ 26.7, 38.1, 46.7, 47.9, 52.4, 52.8, 60.7, 64.3, 67.1, 112.7, 128.0, 128.1, 128.5, 137.1, 147.2, 155.3, 169.9, 171.7. **MS (LR-APCI):** calculated for $C_{20}H_{23}NO_6$ 373.1, measured 374.4. **IR (NaCl):** 2951, 2860, 2356, 2344, 1732, 1698, 1429, 1248, 1207, 1159, 1096 cm^{-1}.

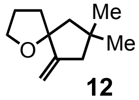
Product 10.



10

Product **10** was eluted with 20% EtOAc:Hex, as a colorless oil. **^{1}H NMR ($CDCl_3$, 300 MHz, 350 K)** δ 1.11-1.02 (m, 1H); 1.46-1.39 (m, 2H); 1.62-1.58 (m, 1H); 2.88-2.69 (m, 3H); 3.31 (apparent dd, *J* = 18.0 Hz, *J* = 2.1 Hz, 1H); 3.70 (s, 6H); 4.03-4.00 (m, 1H); 4.75 (d, *J* = 2.4 Hz, 1H); 5.02 (d, *J* = 2.1 Hz, 1H); 5.17 (s, 2H); 5.28 (bs, 1H); 7.33-7.25 (m, 5H); **^{13}C NMR ($CDCl_3$, 75 MHz, 350 K)** δ 22.6, 24.3, 35.3, 39.3, 42.0, 52.5, 52.8, 58.4, 60.3, 67.3, 107.8, 127.8, 128.0, 128.5, 137.3, 143.4, 156.0, 169.7, 171.8. **MS (LR-APCI):** calculated for $C_{21}H_{25}NO_6$ 387.1, measured 387.7. **IR (NaCl):** 2945, 2853, 1735, 1701, 1431, 1254, 1156, 1093 cm^{-1}.

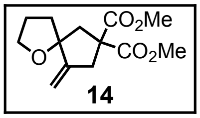
Product 12.



12

Product **12** was eluted with 1% Et_2O:Hex, as a colorless oil. **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 1.14 (s, 6H); 1.63-1.55 (m, 1H); 1.80-1.68 (m, 3H); 1.93-1.87 (m, 2H); 2.34-2.27 (m, 1H); 2.51-2.44 (m, 1H); 3.50 (d, *J* = 8.4 Hz, 1H); 3.57 (d, *J* = 8.4 Hz, 1H); 4.94 (t, *J* = 2.4 Hz, 1H); 5.06 (t, *J* = 2.4 Hz, 1H); **^{13}C NMR ($CDCl_3$, 75 MHz)** δ 21.7, 26.9, 27.5, 30.8, 40.1, 40.6, 50.8, 79.5, 90.0, 105.9, 156.7. **MS (LR-APCI):** calculated for $C_{11}H_{18}O$ 166.1, measured 167.2. **IR (NaCl):** 2955, 2872, 2356, 2331, 1460, 1365, 1273, 1058 cm^{-1}.

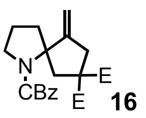
Product 14.



14

Product **14** was eluted with 20% Et_2O:Hex, as a colorless oil. **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 2.01-1.83 (m, 4H); 2.41 (d, *J* = 13.6 Hz, 1H); 2.57 (d, *J* = 13.6 Hz, 1H); 2.87 (apparent dt, *J* = 16.8 Hz, *J* = 2.4 Hz, 1H); 3.26 (d, *J* = 16.8 Hz, 1H); 3.72 (s, 3H); 3.73 (s, 3H); 3.89-3.78 (m, 2H); 5.00 (t, *J* = 2.0 Hz, 1H); 5.04 (t, *J* = 2.4 Hz, 1H); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 26.0, 35.6, 39.2, 45.9, 53.0, 56.7, 67.6, 88.2, 107.6, 151.8, 171.9, 172.6. **MS (LR-APCI):** calculated for $C_{13}H_{18}O_5$ 254.1, measured 255.1. **IR (NaCl):** 2958, 2866, 2359, 2337, 1732, 1432, 1254, 1204, 1169, 1087, 1058 cm^{-1}.

Product 16.

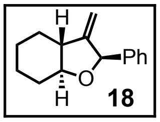


16

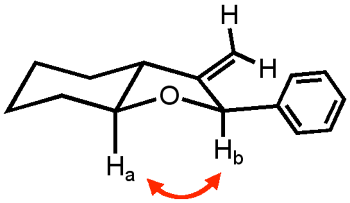
Product **16** was eluted with 20% EtOAc:Hex, as a colorless oil. **^{1}H NMR (DMSO-d_6, 300 MHz, 350 K)** 1.91-1.74 (m, 4H); 2.33 (d, *J* = 13.2 Hz, 1H); 3.05-2.99 (br m, 3H); 3.48 (t, *J* = 6.0 Hz, 2H); 3.68-3.64 (m, 6H); 4.83 (t, *J* = 2.4 Hz, 1H); 4.89 (s, 1H); 5.02 (s, 2H); 7.35-7.29 (m, 5H); **^{13}C**

NMR (DMSO-d_6, 75 MHz, 350 K) δ 23.1, 44.0, 48.4, 53.45, 53.49, 57.7, 66.6, 70.3, 106.5, 128.2, 128.4, 129.1, 137.9, 153.9, 154.2, 171.6, 172.4; **MS (LR-APCI):** calculated for $C_{21}H_{25}NO_6$ 387.1, measured 388.1.

Product 18.

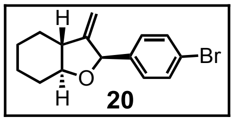


Product **18** was eluted with 1% Et_2O:Hex, as a colorless oil. **^{1}H NMR ($CDCl_3$, 300 MHz)** δ 1.40-1.18 (m, 3H); 1.56 (apparent dq, J = 11.5 Hz, J = 3.6 Hz, 1H, overlapped with water); 1.93-1.80 (m, 2H); 2.14-2.05 (m, 2H); 2.25-2.20 (m, 1H); 3.27 (apparent dt, J = 10.8 Hz, J = 3.6 Hz, 1H: H_a); 4.85-4.82 (m, 2H); 5.27 (d, J = 2.1 Hz, 1H: H_b); 7.36-7.27 (m, 5H); **^{1}H NMR (C_6D_6, 300 MHz)** δ 1.10-0.80 (m, 3H); 1.58-1.43 (m, 3H); 1.76-1.73 (m, 1H); 1.90-1.84 (m, 1H); 2.18-2.13 (m, 1H); 3.14 (apparent dt, J = 10.8 Hz, J = 3.6 Hz, 1H); 4.73 (apparent t, J = 2.7 Hz, 1H); 4.80 (apparent t, J = 2.4, 1H); 7.23-7.17 (m, 3H, overlapped with residual solvent peak); 7.45 (d, J = 7.2 Hz, 2H); **^{13}C NMR ($CDCl_3$, 75 MHz)** δ 24.4, 25.4, 26.5, 31.8, 50.0, 83.4, 83.7, 103.6, 126.8, 127.8, 128.5, 142.4, 155.0. **MS (LR-APCI):** calculated for $C_{15}H_{18}O$ 214.1, measured 215.2. **IR (NaCl):** 3070, 3027, 2936, 2853, 2359, 2334, 1726, 1672, 1444, 1273, 1064, 1007 cm^{-1}.



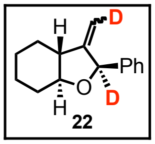
nOe signal observed for H_a and H_b.

Product 20.



Product **20** was eluted with 1% Et_2O:Hex, as a colorless oil. **^{1}H NMR ($CDCl_3$, 300 MHz)** δ 1.40-1.16 (m, 3H); 1.62-1.50 (m, 1H, overlapped with water); 1.83-1.81 (m, 1H); 1.93-1.90 (m, 1H); 2.09-2.02 (m, 2H); 2.25-2.20 (m, 1H); 3.25 (apparent dt, J = 10.8 Hz, J = 3.9 Hz, 1H); 4.81 (apparent t, J = 2.4 Hz, 1H); 4.85 (t, J = 2.4 Hz, 1H); 5.22 (d, J = 1.8 Hz, 1H); 7.25 (d, J = 8.1 Hz, 2H, overlaps with $CHCl_3$); 7.45 (d, J = 8.1 Hz, 2H); **^{13}C NMR ($CDCl_3$, 75 MHz)** δ 24.2, 25.2, 26.2, 31.6, 49.7, 82.7, 83.4, 103.8, 121.6, 128.3, 131.5, 141.4, 154.5. **MS (LR-APCI):** calculated for $C_{15}H_{17}BrO$ 292.0, 294.0, measured 293.0, 295.0. **IR (NaCl):** 2929, 2856, 2359, 2347, 1717, 1593, 1489, 1451, 1400, 1277, 1074, 1011cm^{-1}.

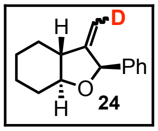
Product 22.



Product **22** was eluted with 1% Et_2O:Hex, as a colorless oil. **^{1}H NMR (C_6D_6, 300 MHz)** δ 1.02-0.93 (m, 3H); 1.56-1.43 (m, 3H); 1.76-1.73 (m, 1H); 1.96-1.89 (m, 1H); 2.18-2.14 (m, 1H); 3.14 (apparent dt, J = 10.8 Hz, J = 3.6 Hz, 1H); 4.72 (apparent d, J = 2.7 Hz, 0.56 H); 4.78 (apparent t, J =

2.7, 0.40 H); 7.21-7.16 (m, 3H, overlapped with residual solvent peak); 7.44 (d, *J* = 7.2 Hz, 2H); **^{2}H NMR (C_6D_6, 300 MHz)** δ 4.73, 4.79, 5.25; **MS (LR-APCI):** calculated for $C_{15}H_{16}D_2O$ 216.15, measured 217.11.

Product 24.



24

Product **24** was eluted with 1% Et_2O:Hex, as a colorless oil. **^{1}H NMR (C_6D_6, 300 MHz)** δ 0.98-0.89 (m, 3H); 1.54-1.39 (m, 3H); 1.72-1.69 (m, 1H); 1.90-1.84 (m, 1H); 2.13-2.07 (m, 1H); 3.09 (apparent dt, *J* = 10.8 Hz, *J* = 3.6 Hz, 1H); 4.68 (m, 0.61 H); 4.78 (m, 0.77 H); 5.25 (d, *J* = 1.8 Hz, 1H); 7.18-7.04 (m, 3H, overlapped with residual solvent peak); 7.44 (d, *J* = 7.2 Hz, 2H); **^{2}H NMR (C_6D_6, 300 MHz)** δ 4.73, 4.79; **MS (LR-APCI):** calculated for $C_{15}H_{17}DO$ 215.14, measured 215.11.

Part G. Kinetic Profile Measurements:

Due to the air sensitivity of the reaction mixture it was determined that only 3 aliquots could be removed from a single reaction without poisoning the reaction mixture with air. As such, four parallel reactions were setup in an argon filled glovebox in oven dried 8 mL glass vials (cat. # 66010-426 VWR). The catalyst (5 mol%, 0.0075 mmol) was weighed into the vial. A MeCN stock solution 1 mL (0.15 M in substrate, 0.15 M in TCB) of substrate **1** was then added to the vial, followed by 2 mL of MeCN. An oven dried magnetic stir bar was then added to the vial and the mixture was sealed with an open top screw-cap (cat. # 66012-598 VWR) fitted with a piercible PTFE Silicone-lined septum (cat. # 66010-774 VWR).

The reactions were then placed in a reaction block preheated to 120 °C. From the first reaction, 3 aliquots were removed at 1 minute intervals. The next set of 3 aliquots were taken from reaction 2 and this process was repeated until 3 aliquots had been removed from each vial at 1 minute intervals, covering a period of 12 minutes. This procedure was repeated twice and the data from each trial was averaged. The yield of the product was then determined by GC analysis of the aliquots by integration relative to the internal standard. Due to the slow rate of the $PtCl_2$ catalyzed reaction, a single aliquot was removed from each of six reactions at 15 minute intervals.

Part H. References:

1) Pastine, S. J. et al. *Org. Lett.* **2005**, *7*, 5429.
2) Bernard, G. et al. *Syn. Comm.* **2008**, *38*, 517.
3) Sanchez, J. P. et al. *J. Med. Chem.* **1992**, *35*, 1764.
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5) Descours, D. et al. *Helv. Chem. Acta,* **1991**, *74*, 1757.
6) Anderson, G. T. et al. *J. Org. Chem.,* **1996**, *61*, 125.
7) Jones, G. B. et al.; *J. Org. Chem.* **2002**, *67*, 5727.