Supporting Information

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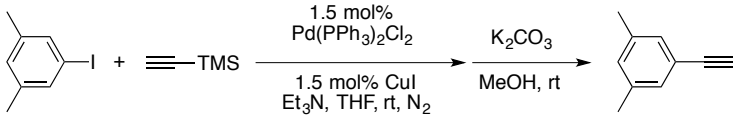
I. General experimental

All solvents were dried appropriately if used in the reaction. VANOL and VAPOL were prepared according to literature procedures and were determined to be at least 99% optical purity.[1] Phenols were sublimed or recrystallized and stored in a dry desiccator. Solid aldehydes were either used as purchased from Aldrich or sublimed before use. Liquid aldehydes were distilled before use. Preparation of phenols **P-42**[2], **P-43**[3], ligands (*S*)-**L2**[4] and (*S*)-**L3**[4] have been previously reported.

Melting points were determined on a Thomas Hoover capillary melting point apparatus and were uncorrected. IR spectra were taken on a Galaxy series FTIR-3000 spectrometer. ^{1}H NMR and ^{13}C NMR were recorded on a Varian Inova-300 MHz, Varian UnityPlus-500 MHz or Varian Inova-600 MHz instrument in $CDCl_3$ unless otherwise noted. $CHCl_3$ was used as the internal standard for both ^{1}H NMR (δ = 7.24) and ^{13}C NMR (δ = 77.0). HR-MS was performed in the department of Biochemistry at Michigan State University. Analytical thin-layer chromatography (TLC) was performed on silica gel plates with F-254 indicator. Visualization was by short wave (254 nm) and long wave (365 nm) ultraviolet light, by staining with phosphomolybdic acid in ethanol or with the aid of Iodine vapor. Column chromatography was performed with silica gel 60 (230 – 450 mesh). HPLC analyses were carried out using a Varian Prostar 210 Solvent Delivery Module with a Prostar 330 PDA Detector and a Prostar Workstation. Optical rotations were obtained on a Perkin-Elmer 341 polarimeter at a wavelength of 589 nm (sodium D line) using a 1.0-decimeter cell with a total volume of 1.0 mL. Specific rotations are reported in degrees per decimeter at 20 °C.

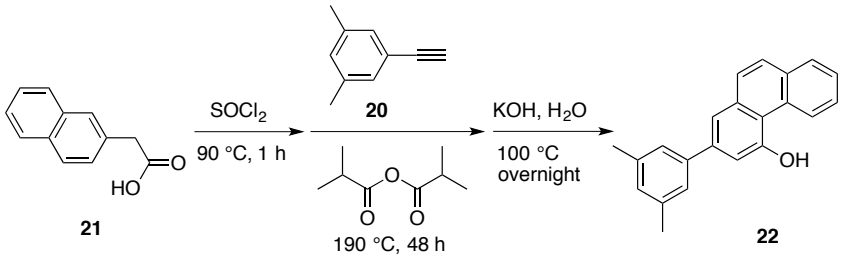
II. Preparation of chiral ligand L-5—L-9

*Preparation of (S)-**L-5**:*



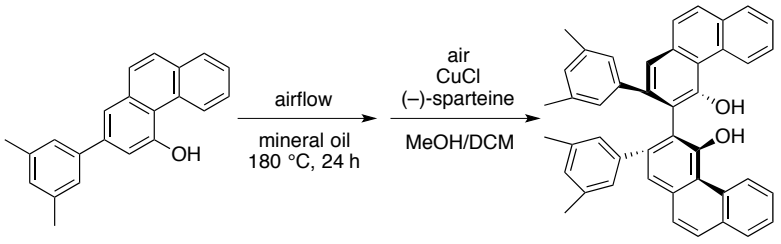
19 **20**

*1-Ethynyl-3,5-dimethylbenzene **20**:* To a 1 L flame-dried flask filled with argon was added 1-iodo-3,5-dimethylbenzene **19** (69.6 g, 300 mmol), $Pd(PPh_3)_2Cl_2$ (3.16 g, 4.50 mol) and CuI (855 mg, 4.5 mmol), dry THF (450 mL) and Et_3N (168 mL, 1.20 mol) under argon. The reaction mixture was stirred at room temperature for 5 minutes and then trimethylsilyl acetylene (47 mL, 333 mmol) was added slowly. The reaction mixture was stirred at room temperature overnight. After removal of the solvent by rotary evaporation, the residue was treated with $NaHCO_3$ (sat. aq. 800 mL) and Et_2O (600 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (300 mL × 2). The combined organic layer was washed with H_2O (300 mL × 2), dried over $MgSO_4$, filtered through Celite and concentrated to dryness. The crude product was roughly purified by passing through a short column (50 mm × 150 mm, neutral Al_2O_3, hexanes as eluent) to give a yellow oil. The oil was then taken up in MeOH (900 mL) and treated with K_2CO_3 (124 g, 900 mmol). The reaction mixture was stirred at room temperature overnight. To the resulting reaction mixture was added H_2O (2.4 L) and this mixture was extracted with Et_2O (500 mL × 3). The organic layer was dried over $MgSO_4$, filtered through Celite and concentrated to dryness. Purification of the crude product by column chromatography on silica gel (50 mm × 200 mm, hexanes) gave **20** as a yellow oil (34.2 g, 263 mmol, 88%). R_f = 0.21 (hexanes). Spectral data for **20**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.28 (s, 6H), 2.99 (s, 1H), 6.97(s, 1H), 7.11 (s, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.04, 76.34, 83.99, 121.69, 129.78, 130.67, 137.87; IR (thin film) 3295s, 2921s, 2108m, 1601s, 1456s, 1264s cm^{-1}; mass spectrum, *m/z* (% rel intensity) 130 M^+ (91), 115 (100), 102 (10), 89 (12). These spectral data match those previously reported for this compound.[5]



2-(3,5-dimethylphenyl)phenanthren-4-ol ***22***: A single-neck 500 mL round bottom flask equipped with a condenser was charged with 2-naphthaleneacetic acid **21** (11.2 g, 60.0 mmol), and $SOCl_2$ (16 mL, 219 mmol). The top of the condenser was vented to a bubbler and then into a beaker filled with NaOH (sat. aq.) to trap acidic gases. The mixture was heated to reflux for 1 h in a 90 °C oil bath, and then all of the volatiles were carefully removed by swirling it under high vacuum (1 mm Hg) for 1 h with a 2nd liquid N_2 trap to protect the pump. To the flask containing the acyl chloride was added 1-ethynyl-3,5-dimethylbenzene **20** (8.58 g, 66.0 mmol) and $(i\text{-PrCO})_2O$ (20 mL, 120 mmol) under N_2. The mixture was stirred at 190 °C for 48 h with a gentle nitrogen flow across the top of the condenser. The brown reaction mixture was cooled down to below 100 °C (*ca.* 60 °C, oil bath temperature) and a solution of KOH (20 g, 357 mmol) in H_2O (80 mL) was then added slowly. This two-phase mixture was stirred at 100 °C overnight. The mixture was cooled to room temperature and ethyl acetate (200 mL) was added and the mixture stirred for 10 min before the organic layer was separated. The aqueous layer was extracted twice with ethyl acetate (100 mL × 2) and the combined organic layer was washed with brine (100 mL), dried over $MgSO_4$, filtered through Celite and concentrated to dryness. Purification of the crude product by column chromatography on silica gel (50 mm x 250 mm, CH_2Cl_2:hexanes 1:3 to 1:1 to 2:1) gave **22** as a yellow solid (10.1 g, 33.8 mmol, 56%). Mp 140-142 °C; R_f = 0.18 (1:1 CH_2Cl_2/hexane). Spectral data for **22**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.41 (s, 6H), 5.64 (s, 1H), 7.03 (s, 1H), 7.20 (d, 1H, *J* = 1.5 Hz), 7.34 (s, 2H), 7.55-7.59 (m, 1H), 7.63-7.66 (m, 1H), 7.70 (d, 1H, *J* = 1.5 Hz), 7.73 (s, 2H), 7.87 (dd, 1H, *J* = 8.0, 1.0 Hz), 9.61 (d, 1H, *J* = 9.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.44, 112.35, 118.45, 119.88, 125.15, 125.93, 126.62, 127.27, 128.24, 128.32, 128.41, 129.29, 130.19, 132.57, 135.26, 138.42, 139.46, 140.08, 154.49; IR (thin film) 3517s, 2921m, 1597s,

1458s, 1279m, 1229s cm^{-1}; HRMS (ESI–) *m/z* calculated for $C_{22}H_{17}O$ ($M\text{-}H^+$) 297.1279, found 297.1281.



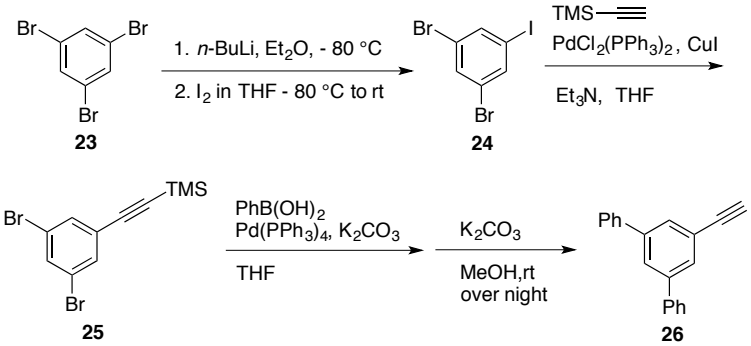
22 (*S*)-***L-5***

General procedure for oxidative phenol-coupling illustrated for racemic ***L-5*****:**[1] To a 100 mL flame-dried three neck round bottom flask equipped with a cooling condenser was added 2-(3,5-dimethylphenyl)phenanthren-4-ol **22** (9.37 g, 31.4 mmol) and mineral oil (45 mL). Airflow was introduced from one side neck via a needle located one inch above the mixture. The airflow rate was about one bubble per second. The mixture was stirred at 180 °C for 24 h. After cooling down to room temperature, CH_2Cl_2 (50 mL) and hexanes (50 mL) were added to the flask and the mixture was stirred until all large chunks had been broken up. The suspension was cooled in a freezer (–20 °C) and then filtered through filter paper. The yellow powder was washed with chilled CH_2Cl_2/hexanes and dried under vacuum to afford the product as a yellow solid (5.00 g). Purification of the product remaining in the mother liquor by column chromatography on silica gel (50 mm x 250 mm, CH_2Cl_2:hexanes 1:2) gave racemic **L-5** as an off-white solid (2.46 g). The total yield is 80% (7.46 g, 12.6 mmol).

*General procedure for de-racemization illustrated for (S)-****L-5***:[6] The original procedure involves sonification to presumably facilitate reaction. However, it was later found that the deracemization of VAPOL gives the same result whether or not sonification is employed.[7] The following procedure follows the original report: To a 500 mL round bottom flask was added (–)-sparteine (6.56 g, 28 mmol), CuCl (1.35 mg, 13.6 mmol) and MeOH (210 mL) under an atmosphere of air. The reaction mixture was sonicated in a water bath for 60 minutes with exposure to air. The flask was then sealed with a septum and purged with argon, which was introduced by a needle under the surface for 60 minutes. At the same time, to a 2 L flame-dried round bottom flask was added racemic **L-5** (4.75 g, 8.00 mmol) and CH_2Cl_2 (840 mL). The

resulting solution was purged with argon for 60 minutes under the surface. The green Cu(II)-(–)-sparteine solution was then transferred via cannula to the solution of racemic **L-5** under argon and then the combined mixture was sonicated for 15 minutes and then allowed to stir at room temperature overnight with an argon balloon attached to the flask which was covered with aluminum foil. The reaction was quenched by slow addition of $NaHCO_3$ (sat. aq.100 mL), H_2O (400 mL) and most of the organic solvent was removed under reduced pressure. The residue was then extracted with CH_2Cl_2 (200 mL × 3). The combined organic layer was dried over $MgSO_4$, filtered through Celite and concentrated to dryness. The crude product was purified by column chromatography (silica gel, 30 mm × 250 mm, CH_2Cl_2/hexanes 2:5) to afford *(S)*-**L-5** as a yellow solid (4.27 g, 7.19 mmol, 90%). The optical purity was determined to be >99% *ee* by HPLC analysis (Pirkle D-Phenylglycine column, 75:25 hexane/*i*PrOH at 254 nm, flow-rate: 2.0 mL/min). Retention times: R_t = 9.68 min for (*R*)-**L-5** (minor) and R_t = 13.08 min for *(S)*-**L-5** (major). Mp 135-137 °C; R_f = 0.19 (1:2 CH_2Cl_2/hexanes). Spectral data for **L-5**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.99 (s, 12H), 6.42 (s, 4H), 6.51 (s, 2H), 6.71 (s, 2H), 7.46 (s, 2H), 7.60-7.64 (m, 2H), 7.65-7.69 (m, 4H), 7.80 (d, 2H, *J* = 8.5 Hz), 7.92 (dd, 2H, *J* = 8.5, 1.5 Hz), 9.73 (d, 2H, *J* = 8.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.10, 116.15, 117.96, 122.94, 126.22, 126.76, 126.92, 126.93, 128.36, 128.40, 128.80, 129.11, 130.36, 132.79, 135.17, 136.76, 139.77, 141.88, 153.43; IR (thin film) 3482br s, 2917m, 1559s, 1456s, 1223s cm^{-1}; HRMS (ESI–) *m/z* calculated for $C_{44}H_{33}O_2$ (M-H$^+$) 593.2481, found 593.2498. $[\alpha]_D^{20}$ = +3.9 (c 1.0, CH_2Cl_2) on >99% *ee (S)*-**L-5** (HPLC).

*Prepαration of (R)-**L-6**:*

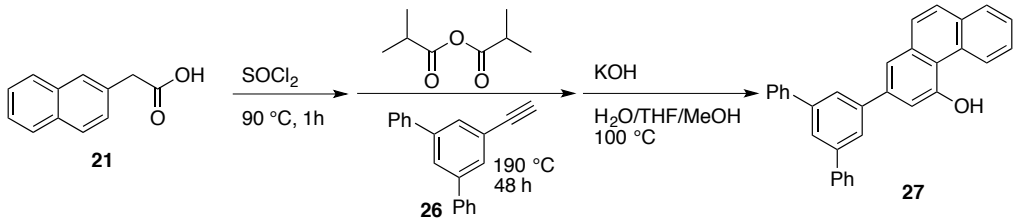


*1,3-dibromo-5-iodobenzene **24**[8]:* To a flame-dried 1 L round bottom flask was added 1,3,5-tribromobenzene **23** (25.2 g, 80.0 mmol, 1.00 equiv) and dry Et_2O (620 mL). The solution was

pre-cooled to – 78°C. Then *n*-BuLi (2.5 M in hexanes, 33 mL, 1.03 equiv) was added via syringe pump in 1.2 h. The reaction mixture was stirred at – 78°C for another 30 min. Then a solution of I_2 (21.3 g in 46 mL THF, 84.0 mmol, 1.05 equiv) was quickly added to the mixture. After it was slowly warmed up to room temperature by removal of the cold bath (about 2 h), a solution of $Na_2S_2O_3$ (8.5 g) in 160 mL H_2O was added to the reaction flask and the resulting mixture was stirred for 20 min. The organic layer was separated and the aqueous layer was extracted with Et_2O (150 mL × 2). The combined organic layer was washed with H_2O (100 mL × 2) and brine (100 mL), dried over Na_2SO_4, filtered and concentrated to afford a greenish solid (27.6 g, 76.3 mmol) in a crude yield of 95%, which was directly used in the next step without further purification. mp 120-121 °C (Lit.[8] 118 °C). R_f = 0.59 (hexane). Spectral data for **24**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (t, 1H, *J* = 1.8 Hz), 7.78 (d, 2H, *J* = 1.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 94.42, 123.37, 133.64, 138.51. These spectral data match those previously reported for this compound.[9]

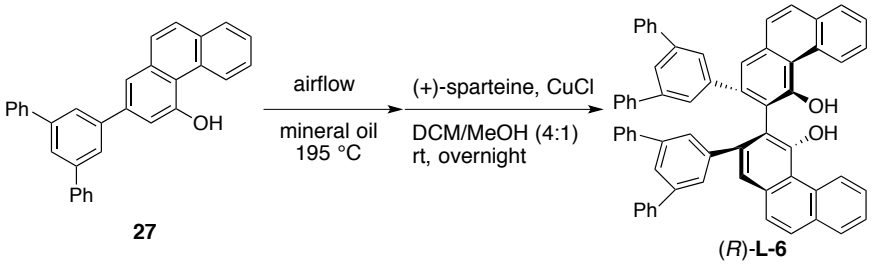
1,3-Dibromo-5-(trimethylsilylethynyl)benzene ***25***: To a 250 mL flame-dried round bottom flask filled with nitrogen was added 1,3-dibromo-5-iodobenzene **24** (27.5 g, 76.0 mmol, 1.00 equiv), $PdCl_2(PPh_3)_2$ (801 mg, 1.14 mmol, 1.5 mol %), CuI (218 mg, 1.14 mmol, 1.5 mol %), dry THF (115 mL) and Et_3N (43 mL) under nitrogen. The reaction mixture was stirred at room temperature for 5 min and then trimethylsilyl acetylene (11.3 mL, 79.8 mmol, 1.05 mmol) was added slowly. The reaction mixture was stirred at room temperature for 27 h. After removal of the solvent by rotary evaporation, the residue was treated with $NaHCO_3$ (sat. aq. 450 mL) and Et_2O (450 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (150 mL × 3). The combined organic layer was washed with H_2O (300 mL × 2), dried over Na_2SO_4, filtered through Celite and concentrated to dryness. The crude product was purified by passing through a short column (50 mm × 150 mm, neutral Al_2O_3, hexanes as eluent) to give **25** as a light orange oil (24.6 g, 74.1 mmol) in 98% yield. R_f = 0.53 (hexane). Spectral data for **25**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.24 (s, 9H), 7.51 (d, 2H, *J* = 1.7 Hz), 7.58 (t, 1H, *J* = 1.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 0.25, 97.55, 101.68, 122.48, 126.51, 133.31, 134.13. These spectral data match those previously reported for this compound.[10]

1-(Ethynyl)-3,5-diphenylbenzene ***26****:* This compound was prepared using a procedure that has been reported for a related compound.[11] To a solution of **25** (4.99 g, 15.0 mmol, 1.00 equiv) in THF (100 mL) were added $Pd(PPh_3)_4$ (2.60 g, 2.25 mmol), K_2CO_3 (20.7 g, 150 mmol) and $PhB(OH)_2$ (5.49 g, 45.0 mmol). After the mixture was stirred at 65 °C under nitrogen for 48 h, it was treated with NH_4Cl (sat. aq. 65 mL) and then subjected to rotary evaporation to remove the organic solvent. Then 30 mL H_2O was added to the residue and it was extracted with Et_2O (100 mL × 3), dried over Na_2SO_4, filtered and concentrated to give an orange residue, which was passed through a short column (silica gel, 30 mm × 150 mm, hexanes) to give a yellow oil. The oil was then dissolved in MeOH (35 mL) and treated with K_2CO_3 (4.81 g, 34.8 mmol). The reaction mixture was stirred at room temperature for 25 h. To the resulting reaction mixture was added H_2O (95 mL) and this mixture was extracted with Et_2O (60 mL × 3). The organic layer was dried over $MgSO_4$, filtered through Celite and concentrated to dryness. Purification of the crude product by column chromatography on silica gel (40 mm × 200 mm, hexanes/EtOAc 10:1) gave **26** as a white solid (2.71 g, 10.7 mmol, 92%). mp 103-105 °C; R_f = 0.41 (1:10 EtOAc/hexanes). Spectral data for **26**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.12 (s, 1H), 7.35-7.40 (m, 2H), 7.42-7.48 (m, 4H), 7.59-7.64 (m, 4H), 7.69 (d, 2H, *J* = 1.7 Hz), 7.77 (t, 1H, *J* = 1.7 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 77.33, 83.58, 122.98, 126.68, 127.19, 127.79, 128.88, 129.66, 140.19, 142.00. IR (thin film) 3291(s), 3036(w), 1591(m), 1497(m) cm^{-1}; HRMS (EI+) calcd for $C_{20}H_{14}$ *m/z* 254.1096 ([M]$^+$), meas 254.1088.



2-(3,5-diphenylphenyl)phenanthren-4-ol ***27****:* The procedure for the preparation of 2-(3,5-dimethylphenyl)phenanthren-4-ol **22** was followed with 2-naphthaleneacetic acid **21** (1.44 g, 7.70 mmol, 1.00 equiv), $SOCl_2$ (2.0 mL, 28 mmol, 3.6 equiv), 1-(Ethynyl)-3,5-diphenylbenzene **26** (2.56 g, 10.1 mmol, 1.3 equiv), (*i*-PrCO)$_2$O (2.6 mL, 15.7 mmol, 2.0 equiv), KOH (2.6 g, 46 mmol,

6.0 equiv) and 10 mL H_2O. The difference was that in the last step THF (4.0 mL) and MeOH (7.0 mL) were added to the mixture in addition to a solution of KOH in H_2O to improve the solubility of the intermediate. Upon completion, the reaction mixture was subjected to rotary evaporation to remove the organic solvents. Then EtOAc (20 mL) was added to the residue and it was stirred for 10 min at room temperature. The organic layer was separated and the aqueous layer was extracted with EtOAc (15 mL × 3). The combined organic layer was washed with brine (5 mL), dried over $MgSO_4$, filtered through Celite and concentrated to dryness. Purification of the crude product by column chromatography on silica gel (50 mm x 200 mm, CH_2Cl_2/hexanes 1:2 to 1:1 to 2:1) gave the product **27** as a light brown solid, which was recrystallized from CH_2Cl_2/hexane 2:1 (20 mL) to give **27** as an off-white solid (1.40 g, 3.31 mmol) in a yield of 43%. The mother liquor was concentrated to dryness and recrystallized from CH_2Cl_2/hexane 2:1 (3.5 mL) to give a second crop (247 mg, 0.58 mmol) in a yield of 7.6%. This was repeated one more time to give a third crop (118 mg, 0.28 mmol) in a yield of 3.6%. The total yield was 54%. mp 198-199 °C; R_f = 0.25 (1:1 CH_2Cl_2/hexane). Spectral data for **27**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.74 (s, 1H), 7.28 (d, 1H, *J* = 1.8 Hz), 7.39-7.43 (m, 2H), 7.48-7.52 (m, 4H), 7.58-7.62 (m, 1H), 7.65-7.69 (m, 1H), 7.71-7.75 (m, 4H), 7.76 (s, 2H), 7.80-7.83 (m, 2H), 7.88-7.91 (m, 3H), 9.65 (d, 1H, *J* = 8.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 112.31, 118.73, 120.05, 125.19, 125.49, 126.07, 126.70, 127.22, 127.37, 127.63, 128.28, 128.46, 128.53, 128.89, 130.13, 132.63, 135.31, 139.02, 141.05, 141.17, 142.48, 154.69; IR (thin film) 3532(m), 3058(w), 1595(s), 1570(s), 1385(m), 1227(m) cm^{-1}; HRMS (ESI–) *m/z* calculated for $C_{32}H_{21}O$ ($M\text{-}H^+$) 421.1592, found 421.1590.

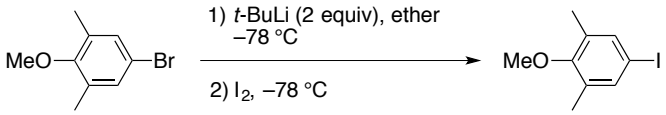


*Rac-**L-6***: The general procedure for oxidative phenol-coupling illustrated for racemic **L-5** was followed with 2-(3,5-diphenylphenyl)phenanthren-4-ol **27** (1.69 g, 4.0 mmol, 1.0 equiv) and 5 mL mineral oil at 195 °C with a reaction time of 12 h. Upon completion, the crude product was

purified by column chromatography on silica gel (50 mm x 200 mm, CH_2Cl_2/hexanes 1:2 to 1:1 to 2:1) to afford (±)-***L*-6** as an off-white solid (843 mg, 1.00 mmol) in a yield of 50%.

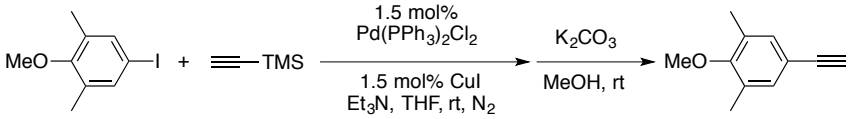
(R)-***L*-6**: To a 25 mL round bottom flask was added (+)-sparteine (170.6 mg, 0.728 mmol, 3.40 equiv), CuCl (36 mg, 0.36 mmol, 1.7 equiv) and MeOH (6.5 mL) under an atmosphere of air. The reaction mixture was stirred for 60 minutes with exposure to air. The flask was then sealed with a septum and purged with nitrogen, which was introduced by a needle under the surface for 60 minutes. At the same time, to a 100 mL flame-dried round bottom flask was added racemic **L-6** (180.4 mg, 0.214 mmol, 1.00 equiv) and CH_2Cl_2 (26 mL). The resulting solution was purged with nitrogen for 45 minutes under the surface. The green Cu(II)-(+)-sparteine solution was then transferred via cannula to the solution of racemic **L-6** under nitrogen and then the combined mixture was stirred at room temperature for 42 h with an nitrogen balloon attached to the flask which was covered with aluminum foil. The reaction was quenched by slow addition of $NaHCO_3$ (sat. aq. 4.2 mL) and H_2O (4.2 mL) and most of the organic solvent was removed under reduced pressure. The residue was then extracted with CH_2Cl_2 (10 mL × 3). The combined organic layer was dried over $MgSO_4$, filtered through Celite and concentrated to dryness. The crude product was purified by column chromatography (silica gel, 25 mm × 200 mm, CH_2Cl_2/hexanes 1:2) to afford *(R)*-**L-6** as a off-white solid (119 mg, 0.141 mmol) in a yield of 66%. The optical purity was determined to be >99% *ee* by HPLC analysis (Chiralpak AD column, hexanes/2-propanol 90:10, 222 nm, flow 1 mL/min). Retention times: R_t = 6.29 min for (*S*)-**L-6** (minor enantiomer) and R_t = 11.31 min for (*R*)-**L-6** (major enantiomer). Mp 203-206 °C; R_f = 0.24 (1:2 CH_2Cl_2/hexane). Spectral data for **L-6**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.82-6.92 (m, 10H), 6.94-7.02 (m, 8H), 7.04-7.09 (m, 4H), 7.10 (d, 4H, *J* = 1.7 Hz), 7.47 (t, 2H, *J* = 1.7 Hz), 7.64 (s, 2H), 7.71-7.79 (m, 6H), 7.90 (d, 2H, *J* = 8.8 Hz), 8.02-8.06 (m, 2H), 9.88 (dd, 2H, *J* = 8.3, 1.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 116.37, 118.62, 123.48, 124.60, 126.52, 126.65, 126.89, 127.03, 127.07, 127.33, 128.41, 128.48, 129.00, 129.67, 130.19, 133.00, 135.61, 140.33, 140.46, 141.12, 141.49, 154.08; IR (thin film) 3480(m), 3056(w), 1593(s) cm^{-1}; HRMS (ESI–) *m/z* calculated for $C_{64}H_{41}O_2$ (M-H$^+$) 841.3107, found 841.3112. $[\alpha]_D^{20}$= +357.5 (c 0.2, EtOAc) on >99% *ee* material.

*Preparation of (S)-**L-7**:*



28 **29**

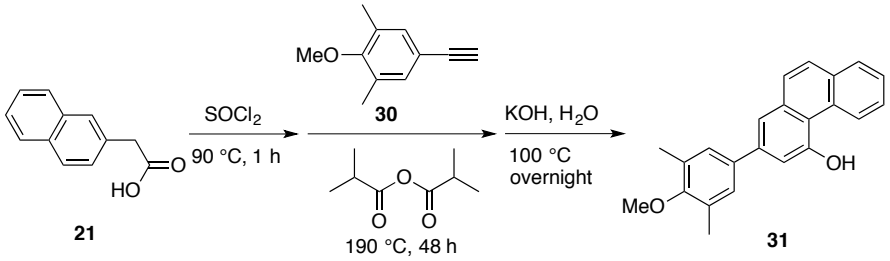
*5-iodo-2-methoxy-1,3-dimethylbenzene **29***: To a 1 L flame-dried flask filled with argon was added commercially available 5-bromo-2-methoxy-1,3-dimethylbenzene **28** (21.5 g, 100 mmol) and dry Et_2O (250 mL). The mixture was stirred until the bromide was dissolved at room temperature and then the flask was submerged into a –78 ºC bath, followed by slow addition of *t*-BuLi (118 mL, 200 mmol, 1.7 M in hexanes) and then the solution was stirred at –78 ºC for 1h. At the same time, in a flame-dried 250 mL flask iodine (27.9 g, 110 mmol) was dissolved in dry Et_2O (150 mL). The iodine solution was then cooled to –78 ºC and transferred to the aryllithium solution via cannula under argon. The mixture was warmed up gradually to room temperature and stirred for an additional 2 h. The reaction was quenched by pouring the reaction mixture slowly into a $Na_2S_2O_3$ solution (aq. 5%, 200 mL) and stirred for 20 minutes. The organic layer was separated and the aqueous layer was extracted with Et_2O (100 mL × 3). The combined organic layer was washed with H_2O (100 mL × 2) and NaCl (aq. Sat.), dried over $MgSO_4$ and filtered through Celite. Removal of the solvent by rotary evaporation afforded the crude product as a yellow oil in 100% yield. The ^{1}H NMR spectrum of the unpurified product was clean, and it was used in the next step without purification. Spectral data for **29**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.21 (s, 6H), 3.68 (s, 3H), 7.32 (s, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 15.67, 59.69, 87.55, 133.47, 137.49, 157.01. These spectral data match those previously reported for this compound.[12]



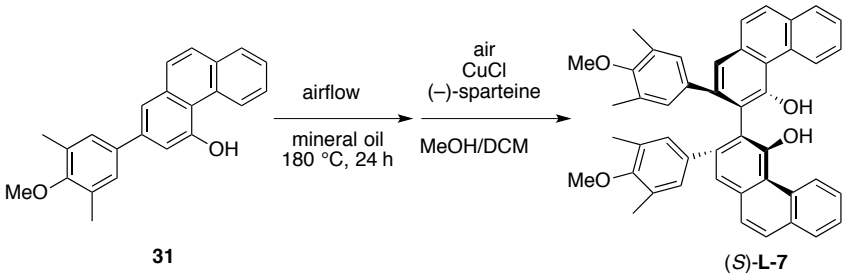
29 **30**

*5-ethynyl-2-methoxy-1,3-dimethylbenzene **30***: The reaction of 5-iodo-2-methoxy-1,3-dimethylbenzene **29** (26.2 g, 100 mmol) and trimethylsilyl acetylene (16.0 mL, 110 mmol) was performed according to the procedure for the preparation of 1-ethynyl-3,5-dimethylbenzene **20**. Purification of the crude product by column chromatography on silica gel (50 mm × 150 mm,

CH_2Cl_2:hexanes 1:5) gave the product **30** as a yellow oil (15.1 g, 94.4 mmol, 94%). R_f = 0.14 (1:5 CH_2Cl_2:hexanes). Spectral data for **30**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.24 (s, 6H), 2.96 (s, 1H), 3.70 (s, 3H), 7.15 (s, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 15.89, 59.70, 75.94, 83.63, 117.26, 131.11, 132.65, 157.66; IR (thin film) 3291s, 2946s, 2107m, 1482s, 1304s, 1227s, 1140s cm^{-1}; mass spectrum, *m/z* (% rel intensity) 160 M^+ (100), 145 (70), 128 (6), 115 (45). These spectral data match those previously reported for this compound.[13]



*2-(4-methoxy-3,5-dimethylphenyl)phenanthren-4-ol **31***: The reaction of 2-naphthaleneacetic acid **21** (7.44 g, 40.0 mmol), $SOCl_2$ (10.5 mL, 144 mmol), 5-ethynyl-2-methoxy-1,3-dimethylbenzene **30** (6.4 g, 40.0 mmol) and (*i*-PrCO)$_2$O (13.3 mL, 80.0 mmol) was performed according to the procedure for the preparation of 2-(3,5-dimethylphenyl)phenanthren-4-ol **22**. Purification of the crude product by column chromatography on silica gel (50 mm x 250 mm, CH_2Cl_2:hexanes 1:1 to 2:1 to 1:0) gave **31** as an off-white solid (4.64 g, 14.1 mmol, 35%). Mp 164-165 °C; R_f = 0.31 (CH_2Cl_2). Spectral data for **31**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.38 (s, 6H), 3.79 (s, 3H), 5.76 (s, 1H), 7.15 (d, 1H, *J* = 1.5 Hz), 7.36 (s, 2H), 7.54-7.58 (m, 1H), 7.62-7.66 (m, 2H), 7.72 (d, 2H, *J* = 1.0 Hz), 7.86 (dd, 1H, *J* = 8.0, 1.5 Hz), 9.61 (dd, 1H, *J* = 8.5, 0.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 16.31, 59.85, 112.22, 118.32, 119.55, 125.87, 126.60, 127.25, 127.71, 128.23, 128.30, 128.41, 130.25, 131.28, 132.55, 135.26, 135.76, 139.02, 154.60, 156.77; IR (thin film) 3341br s, 2934s, 1487s, 1381s, 1265s, 1226s, 1159s cm^{-1}; HRMS (ESI–) *m/z* calculated for $C_{23}H_{19}O_2$ (M-H$^+$) 327.1385, found 327.1391.



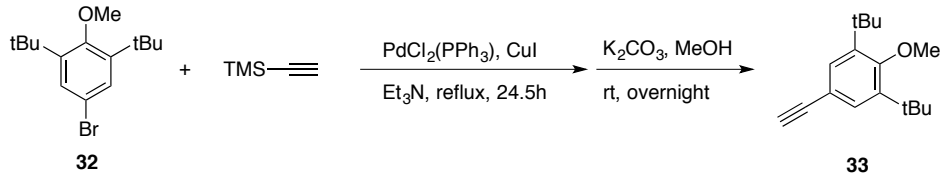
31 (*S*)-**L-7**

*Rac-**L-7***: The general procedure for oxidative phenol-coupling illustrated for **L-5** was followed with 2-(4-methoxy-3,5-dimethylphenyl)phenanthren-4-ol **31** (3.05 g, 9.30 mmol) and 14 mL mineral oil. The mixture was stirred at 180 °C for 24 h. After cooling down to room temperature, CH_2Cl_2 (10 mL) and hexanes (30 mL) were added to the flask and the mixture was stirred until all large chunks had been broken up. The suspension was cooled in a freezer (–20 °C) and then filtered through filter paper. The yellow powder was washed with chilled CH_2Cl_2/hexanes and dried under vacuum. Purification of the product remaining in the mother liquor by column chromatography on silica gel (30 mm × 200 mm, CH_2Cl_2:hexanes 2:1) and then washing with CH_2Cl_2/hexanes gave additional product as a yellow solid. The total yield of the two parts was 60% (1.84 g, 2.81 mmol).

*(S)-**L-7***: The general procedure for the de-racemization of (*S*)-**L-5** was followed with racemic **L-7** (3.25 g, 4.97 mmol), CuCl (837 mg, 8.45 mmol) and (–)-sparteine (4.08 g, 17.4 mmol). The crude product was purified by column chromatography on silica gel (30 mm × 250 mm, CH_2Cl_2/hexanes 2:1) to afford *(S)*-**L-7** as an off-white solid (3.10 g, 4.74 mmol, 95%). The optical purity was determined to be >99% *ee* by HPLC analysis (Pirkle D-Phenylglycine column, 75:25 hexane/*i*PrOH at 254 nm, flow-rate: 2.0 mL/min). Retention times: R_t = 15.13 min for (*R*)-**L-7** (minor) and R_t = 21.73 min for *(S)*-**L-7** (major). Mp 158-160 °C; R_f = 0.20 (2:1 CH_2Cl_2/hexanes). Spectral data for **L-7**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.93 (s, 12H), 3.60 (s, 6H), 6.40 (s, 4H), 6.51 (s, 2H), 7.34 (s, 2H), 7.62 (t, 2H, *J* = 7.5 Hz), 7.65-7.68 (m, 4H), 7.81 (d, 2H, *J* = 9.0 Hz), 7.93 (d, 2H, *J* = 7.5 Hz), 9.72 (d, 2H, *J* = 8.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 15.89, 59.67, 116.14, 117.88, 122.84, 126.23, 126.91, 126.93, 128.38, 128.77, 129.16, 129.38, 129.66, 130.33, 132.79, 135.19, 135.36, 141.33, 153.43, 156.10; IR (thin film) 3482br s, 2932s, 1487s, 1372s, 1244s,

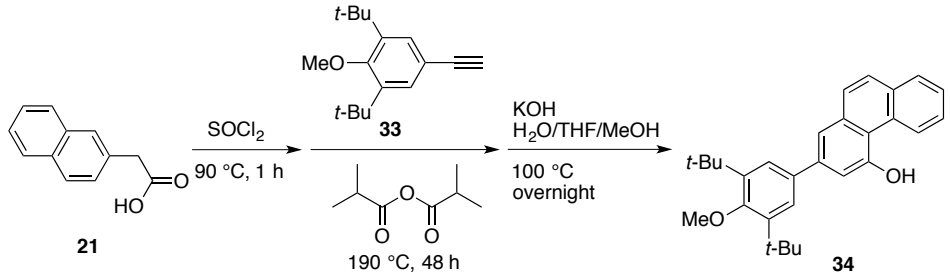
1225s,1130s cm^{-1}; HRMS (ESI–) *m/z* calculated for $C_{46}H_{37}O_4$ ($M\text{-}H^+$) 653.2692, found 653.2712. $[\alpha]_D^{20}$ = –16.5 (c 1.0, CH_2Cl_2) on >99% *ee (S)*-**L-7** (HPLC).

*Preparation of (R)-**L-8**:*

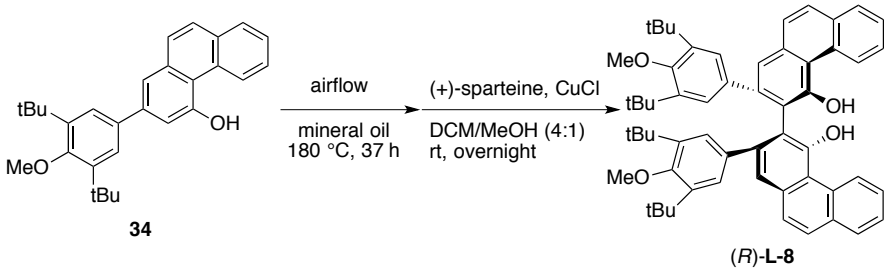


*1,3-di-tert-butyl-5-ethynyl-2-methoxybenzene **33***: The first step was carried out with an adaptation of a procedure reported for a related compound.[14] To a 500 mL round bottom flask filled with nitrogen was added 5-bromo-1,3-di-*tert*-butyl-2-methoxybenzene **32**[15] (31.5 g, 105 mmol, 1.00 equiv), $Pd(PPh_3)_2Cl_2$ (1.48 g, 2 mol, 2 mol %), CuI (400 mg, 2 mmol, 2 mol %) and dry Et_3N (210 mL) under nitrogen. The flask was then sealed with a septum and purged for 10 minutes with nitrogen, which was introduced by a needle under the surface. Then trimethylsilyl acetylene (26.9 mL, 180 mmol, 1.80 equiv) was added slowly to the flask. After the mixture was refluxed (oil bath: 100 °C) for 24.5 h under nitrogen atmosphere, the solvent was removed by reduced pressure. The residue was dissolved in Et_2O (600 mL) and treated with $NaHCO_3$ (600 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (200 mL × 3). The combined organic layer was washed with H_2O (200 mL), dried over Na_2SO_4, filtered and concentrated to give a black oil. The crude product was roughly purified by passing through a short column (50 mm × 150 mm, neutral Al_2O_3, hexanes as eluent) to give a yellow oil. This oil was then dissolved in MeOH (300 mL) and treated with K_2CO_3 (43.5 g, 315 mmol). The reaction mixture was stirred at room temperature for 14 h. To the resulting reaction mixture was added H_2O (800 mL) and this mixture was extracted with Et_2O (500 mL × 3). The combined organic layer was dried over Na_2SO_4, filtered and concentrated to dryness. Purification of the crude product by column chromatography on silica gel (50 mm × 200 mm, hexanes) gave **33** as a light yellow oil (24.4 g, 99.8 mmol, 95%). R_f = 0.16 (hexanes). Spectral data for **33**: ^1H NMR ($CDCl_3$, 500 MHz) δ 1.40 (s, 18H), 2.98 (s, 1H), 3.66 (s, 3H), 7.37 (s, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ

31.90, 35.72, 64.37, 75.49, 84.52, 116.24, 130.60, 144.04, 160.47. These spectral data match those previously reported for this compound.[16]



2-(3,5-di-tert-butyl-4-methoxyphenyl)phenanthren-4-ol ***34***: The procedure for the preparation of 2-(3,5-dimethylphenyl)phenanthren-4-ol **22** was followed with 2-naphthaleneacetic acid **21** (16.8 g, 90.3 mmol, 1.00 equiv), $SOCl_2$ (23.8 mL, 325 mmol, 3.60 equiv), 1,3-di-tert-butyl-5-ethynyl-2-methoxybenzene **33** (24.4g, 99.8 mmol, 1.10 equiv) and $(i\text{-PrCO})_2O$ (30.2 mL, 181 mmol, 2.00 equiv). The difference was that in the last step THF (75 mL) and MeOH (75 mL) were added to the mixture in addition to a solution of KOH (33.0 g, 588 mmol, 6.50 equiv) in H_2O (130 mL) to improve the solubility of the intermediate. Purification of the crude product by column chromatography on silica gel (50 mm x 250 mm, CH_2Cl_2/hexanes 1:3 to 1:1) gave **34** as a light yellow solid (14.84 g, 36.0 mmol) in a yield of 40%. mp 202-203 °C; R_f = 0.21 (1:1 CH_2Cl_2/hexanes). Spectral data for **34**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.50 (s, 18H), 3.75 (s, 3H), 5.69 (s, 1H), 7.18 (d, 1H, *J* = 2.0 Hz), 7.55-7.59 (m, 3H), 7.62-7.67 (m, 2H), 7.74 (d, 2H, *J* = 1.0 Hz), 7.87 (dd, 1H, *J* = 8.0, 1.5 Hz), 9.61 (d, 1H, *J* = 8.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 32.18, 35.99, 64.34, 112.41, 118.21, 119.69, 125.60, 125.86, 126.61, 127.27, 128.24, 128.32, 128.39, 130.26, 132.55, 134.37, 135.30, 139.99, 144.15, 154.52, 159.57; IR (thin film) 3521br m, 2961s, 1420s, 1227s cm^{-1}; HRMS (ESI–) *m/z* calculated for $C_{29}H_{31}O_2$ ($M\text{-}H^+$) 411.2324, found 411.2312.

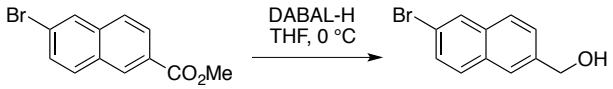


*Rac-**L-8***: The general procedure for oxidative phenol-coupling illustrated for **L-5** was followed with 2-(3,5-di-tert-butyl-4-methoxyphenyl)phenanthren-4-ol **34** (14.3 g, 34.7 mmol) and mineral oil (55 mL). The mixture was stirred at 180 °C for 37 h. After cooling down to room temperature, hexanes (83 mL) were added to the flask and the mixture was stirred until all large chunks had been broken up. The suspension was cooled in a freezer (–20 °C) overnight and then filtered through filter paper. The yellow powder was washed with chilled hexanes and dried under vacuum to afford racemic **L-8** as an orange solid (10.3 g, 12.5 mmol) in a yield of 72%.

*(R)-**L-8***: Sonification was not employed in this procedure for deracemization. To a 100 mL round bottom flask was added CuCl (1.77 g, 17.9 mmol, 1.70 equiv), (+)-sparteine (8.61 g, 36.8 mmol, 3.5 equiv) and MeOH (60 mL) under an atmosphere of air. The mixture was stirred under air for 45 min. Then the flask was sealed with a septum and purged for 60 min with nitrogen, which was introduced by a needle under the surface of the solution. At the same time, to a flame-dried 1 L round bottom flask was added *rac*-**L-8** (8.65 g, 10.5 mmol, 1.00 equiv) and dry CH_2Cl_2 (240 mL). The resulting solution was purged with nitrogen for 60 min. The green Cu(II)-(+)-sparteine suspension was then transferred via cannula to the solution of *rac*-**L-8** under nitrogen and the combined mixture was stirred at room temperature for 16 h with a nitrogen balloon attached to the flask which was covered with aluminum foil. The reaction was quenched by slow addition of 125 mL $NaHCO_3$ (aq. Sat.) and 400 mL H_2O. Most of the organic solvent was removed by rotary evaporation. The residue was then extracted with CH_2Cl_2 (300 mL × 3). Then combined organic layer was dried with Na_2SO_4, filtered and concentrated to dryness. The crude product was purified by column chromatography (silica gel, 55 × 230 mm, hexane: CH_2Cl_2 3:1) to afford *(R)*-**L-8** as a light pink foamy solid (8.65 g, 10.5 mmol) in 100% isolated yield. The optical purity was determined to be 97.9% *ee* by HPLC analysis (Pirkle D-Phenylglycine column, 75:25 hexane/iPrOH at 254 nm, flow-rate: 2.0 mL/min). Retention times: R_t = 10.75 min (major enantiomer, *(R)*-**L-8**) and R_t = 21.60 min (minor enantiomer, (*S*)-**L-8**). To enhance the optical purity, 13 mL of a mixture of hexane/CH_2Cl_2 (40:3) was added to the product and it was heated untill a clear solution was obtained. After the solution was kept at room temperature for 2 h, a fine powder formed which made the solution slightly cloudy. The mixture was filtered through a filter

paper and the original flask was rinsed with hexane (5 mL × 2). The rinse was also filtered. The combined filtrate was kept at room temperature for 1 h. It turned cloudy again. The above filtration procedure was repeated untill the new filtrate did not turn cloudy after it was kept at room temperature for 1 h. The clear filtrate was concentrated to dryness to afford the product as a light yellow foamy solid (8.30 g, 10.1 mmol) in a yield of 96% with an optical purity of >99% *ee* determined by HPLC analysis (Pirkle D-Phenylglycine column, 75:25 hexane/*i*PrOH at 254 nm, flow-rate: 2.0 mL/min). Retention times: R_t = 11.22 min for (*R*)-**L-8** (major) and R_t = 22.90 min for *(S)*-**L-8** (minor). mp 150-153 °C; R_f = 0.23 (hexane: CH_2Cl_2 3:1). Spectral data for **L-8**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.07 (s, 36H), 3.20 (s, 6H), 6.16 (s, 2H), 7.14 (s, 4H), 7.48-7.55 (m, 4H), 7.71-7.79 (m, 6H), 7.82-7.87 (m, 2H), 9.33-9.38 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 31.74, 35.46, 63.78, 116.54, 118.38, 122.27, 125.99, 126.57, 126.80, 127.04, 128.14, 128.59, 129.00, 130.17, 132.54, 133.59, 135.34, 140.81, 142.83, 153.19, 158.84; IR (thin film) 3486(br s), 2961(s), 1412(s), 1225(s), 1115(m) cm^{-1}; HRMS (ESI–) *m/z* calculated for $C_{58}H_{62}O_4$ 822.4648, found 822.4680. $[\alpha]_D^{20}$ = +239.5 (c 1.0, CH_2Cl_2) on >99% *ee* material.

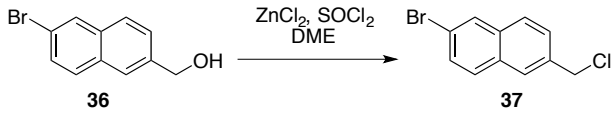
*Preparation of (S)-**L-9**:*



35 **36**

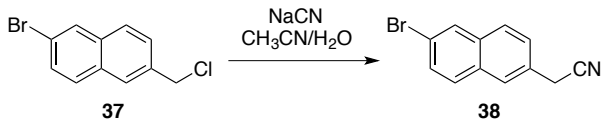
*(6-bromonaphthalen-2-yl)methanol **36***:[15] To a flame-dried round bottom flask was added methyl 6-bromo-2-naphthoate **35** (31.8 g, 120 mmol) and dry THF (300 mL) under argon. The solution was cooled to 0 °C and DIBAL-H (1 M in heptane, 252 mL, 252 mmol) was added dropwise to the mixture. The mixture was warmed up to room temperature and stirred overnight. The resulting mixture was poured slowly into HCl (4N aq. 200 mL) at 0 °C. The mixture was stirred for 30 min and the organic layer was separated. The organic layer was washed with HCl (4N aq. 48 mL), $NaHCO_3$ (5% aq. 240 mL), and brine (240 mL). The organic layer was dried over $MgSO_4$, filtered through Celite and concentrated to dryness. EtOAc (20 mL) and hexanes (160 mL) were added to the product. Filtration by filter paper and drying under vacuum gave **36** as a white solid (27.0 g, 114 mmol, 95%). Mp 150-151 °C (lit.[15] 152-153 °C). Spectral data for **36**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.75 (t, 1H, *J* = 0.5 Hz), 4.83 (d, 2H, *J* = 5.5 Hz), 7.48 (dd, 1H *J* = 8.5,

1.5 Hz), 7.53 (dd, 1H, *J* = 8.5, 2.0 Hz), 7.68 (d, 1H, *J* = 8.5 Hz), 7.73 (d, 1H, *J* = 8.5 Hz), 7.77 (s, 1H), 7.98 (d, 1H, *J* = 2.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 65.25, 119.83, 125.28, 126.16, 127.42, 129.52, 129.59, 129.78, 131.80, 133.98, 138.85; IR (thin film) 3276s, 1591s, 1269s, 1129s, 1013s cm^{-1}; mass spectrum, *m/z* (% rel intensity) 238 M^+ (32, ^{81}Br), 236 M^+ (35, ^{79}Br), 209 (9, ^{81}Br), 207 (12, ^{79}Br), 157 (7), 139 (20), 128 (100). These spectral data match those previously reported for this compound.[17]



36 **37**

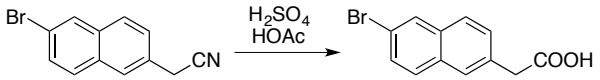
*2-bromo-6-(chloromethyl)naphthalene **37***:[17] To a 250 mL round bottom flask was added (6-bromonaphthalen-2-yl)methanol **36** (1.90, 8.00 mmol), $ZnCl_2$ (27.2 mg, 0.20 mmol) and DME (20 mL). The reaction mixture was cooled to 0 °C and $SOCl_2$ (1.17 mL, 16 mmol) was added dropwise. The resulting mixture was stirred at 0 °C for 3 h, and then at room temperature overnight. The solvent was removed by rotary evaporation. Hexanes (25 mL) were added to the crude product. Filtration by filter paper and drying under vacuum gave **37** as a white solid (2.00 g, 7.80 mmol, 98%). Mp 118-119 °C (lit.[15] 130-131 °C). Spectral data for **37**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.71 (s, 2H), 7.51 (dd, 1H, *J* = 8.5, 2.0 Hz), 7.55 (dd, 1H, *J* = 8.5, 2.0 Hz), 7.68 (d, 1H, *J* = 8.5 Hz), 7.74 (d, 1H, *J* = 8.5 Hz), 7.78 (s, 1H), 7.99 (d, 1H, *J* = 2.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 46.27, 120.54, 127.32, 127.43, 127.79, 129.59, 129.82, 129.90, 131.59, 134.13, 135.35; IR (thin film) 1576s, 1456s cm^{-1}; mass spectrum, *m/z* (% rel intensity) 256 M^+ (23, ^{81}Br and ^{35}Cl or ^{79}Br and ^{37}Cl), 254 M^+ (18, ^{79}Br and ^{35}Cl), 221 (66, ^{81}Br), 219 (69, ^{79}Br), 139 (64), 111 (22). These spectral data match those previously reported for this compound.[17]



37 **38**

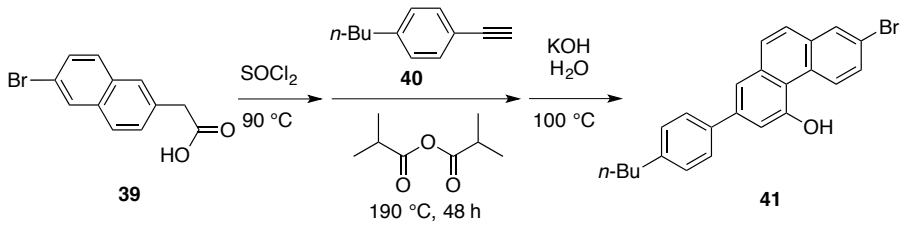
*2-(6-bromonaphthalen-2-yl)acetonitrile **38***:[17] To a 500 mL round bottom flask was added 2-bromo-6-(chloromethyl)naphthalene **37** (27.1 g, 106 mmol), NaCN (6.76 g, 138 mmol), CH_3CN (275 mL) and H_2O (33 mL) The mixture was refluxed overnight. After cooling to room temperature, H_2O (240 mL) was added to the flask. The organic solvent was removed by rotary

evaporation and H_2O (320 mL) was added. Methylene chloride (500 mL) was added to the mixture. The organic layer was separated, dried over $MgSO_4$, filtered through Celite and concentrated to dryness. The crude product was washed with CH_2Cl_2/hexanes (1:25). Filtration by filter paper and drying under vacuum gave **38** as a light yellow solid (25.6 g, 104 mmol, 98%). Mp 117-118 °C (lit.[15] 118-119 °C). Spectral data for **38**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.88 (s, 2H), 7.39 (dd, 1H, *J* = 8.5, 2.0 Hz), 7.58 (dd, 1H, *J* = 9.0, 2.0 Hz), 7.69 (d, 1H, *J* = 9.0 Hz), 7.76 (d, 1H, *J* = 9.0 Hz), 7.79 (s, 1H), 7.99 (d, 1H, *J* = 1.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 23.82, 117.50, 120.58, 126.53, 126.84, 127.78, 128.16, 129.35, 129.84, 130.26, 131.77, 133.77; IR (thin film) 1558s, 1456s cm^{-1}. These spectral data match those previously reported for this compound.[17]



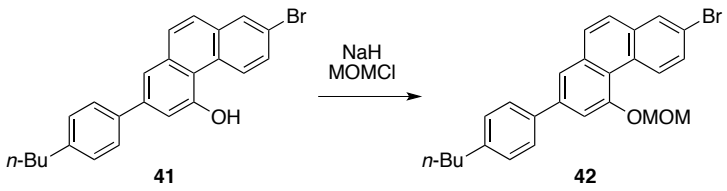
38 **39**

*2-(6-bromonaphthalen-2-yl)acetic acid **39***:[17] To a 500 mL round bottom flask was added 2-(6-bromonaphthalen-2-yl)acetonitrile **38** (21.1 g, 86 mmol), H_2O (85 mL), acetic acid (115 mL) and H_2SO_4 (80 mL). The mixture was stirred at 110 °C for 24 h. After cooling to room temperature, the mixture was poured into ice H_2O (750 mL). The crude product was filtered by filter paper and washed with H_2O (200 mL). The solid was dissolved in acetone, dried over $MgSO_4$, filtered through Celite and concentrated to dryness. Drying under vacuum gave **39** as a tan solid (22.7 g, 86 mmol, 100%). Mp 177-179 °C (lit.[17] 178-180 °C). Spectral data for **39**: ^{1}H NMR (DMSO-d*6*, 500 MHz) δ 3.74 (s, 2H), 7.47 (dd, 1H, *J* = 8.5, 1.5 Hz), 7.61 (dd, 1H, *J* = 8.5, 2.0 Hz), 7.80 (s, 1H), 7.85 (dd, 2H, *J* = 9.0, 6.0 Hz), 8.17 (d, 1H, *J* = 2.0 Hz), 12.39 (s, 1H); ^{13}C NMR (DMSO-d*6*, 125 MHz) δ 40.66, 118.70, 126.85, 127.72, 129.01, 129.15, 129.32, 129.68, 131.40, 132.98, 133.49, 172.43. These spectral data match those previously reported for this compound.[17]



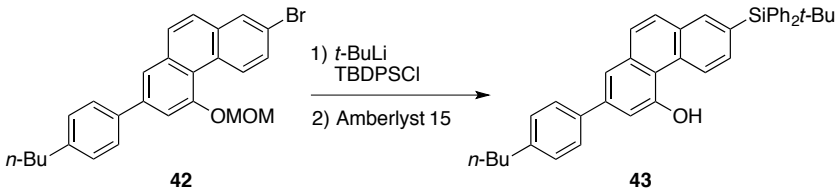
39 **41**

*7-bromo-2-(4-butylphenyl)phenanthren-4-ol **39***: The procedure for the preparation of 2-(3,5-dimethylphenyl)phenanthren-4-ol **22** was followed with 2-(6-bromonaphthalen-2-yl)acetic acid **39** (6.63 g, 25.0 mmol), $SOCl_2$ (6.7 mL, 92 mmol), 1-butyl-4-ethynylbenzene **40** (5.0 g, 31.6 mmol) and $(i\text{-PrCO})_2O$ (8.4 mL, 50.7 mmol). Purification of the crude product by column chromatography on silica gel (50 mm x 250 mm, CH_2Cl_2/hexanes 1:3 to 1:1 to 2:1) gave **41** as a yellow solid (5.36 g, 13.2 mmol, 53%). Mp 140-142 °C; R_f = 0.31 (2:1 CH_2Cl_2/hexanes). Spectral data for **41**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.95 (t, 3H, *J* = 7.5 Hz), 1.35-1.44 (m, 2H), 1.61-1.68 (m, 2H), 2.67 (t, 2H, *J* = 7.5 Hz), 5.68 (s, 1H), 7.20 (d, 1H, *J* = 1.5 Hz), 7.29 (d, 2H, *J* = 8.0 Hz), 7.60-7.62 (m, 3H), 7.70 (dd, 2H, *J* = 9.0, 2.0 Hz), 7.73 (d, 1H, *J* = 9.0 Hz), 7.99 (d, 1H, *J* = 2.0 Hz), 9.48 (d, 1H, *J* = 9.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.95, 22.40, 33.60, 35.33, 112.50, 118.04, 119.80, 119.87, 127.04, 127.16, 128.52, 128.84, 129.04, 129.57, 130.23, 130.29, 134.15, 135.14, 137.19, 139.65, 142.75, 154.39; IR (thin film) 3517s, 2926s, 1559s, 1458s, 1390s, 1231s cm^{-1}; HRMS (ESI–) *m/z* calculated for $C_{20}H_{12}{}^{79}BrO$ (M-H$^+$) 403.0698, found 403.0684.



*7-bromo-2-(4-butylphenyl)-4-(methoxymethoxy)phenanthrene **42***: To a flame-dried 250 mL round bottom flask was added 7-bromo-2-(4-butylphenyl)phenanthren-4-ol **41** (10.1 g, 24.9 mmol) and dry THF (80 mL) under N_2. The resulting solution was cooled to 0 °C and NaH (1.10 g, 60% in mineral oil, 27.5 mmol) was added. The resulting mixture was stirred at 0 °C for 1 h. MOMCl (2.1 mL, 27.8 mmol) was then added to the mixture at 0 °C. The mixture was warmed up to room temperature and stirred for additional 24 h. NH_4Cl (sat. aq. 20 mL) was added to the mixture and the organic solvent was removed by rotary evaporation. The two phase residue was extracted with CH_2Cl_2 (30 mL × 3). The combined organic layer was washed with brine (20 mL), dried over $MgSO_4$, filtered through Celite and concentrated to dryness. Purification of the crude product by column chromatography on silica gel (30 mm x 250 mm, CH_2Cl_2:hexanes 1:3) gave **42** as a light yellow solid (10.7 g, 23.8 mmol, 96%). Mp 84-85 °C; R_f = 0.31 (1:2 CH_2Cl_2/hexanes). Spectral

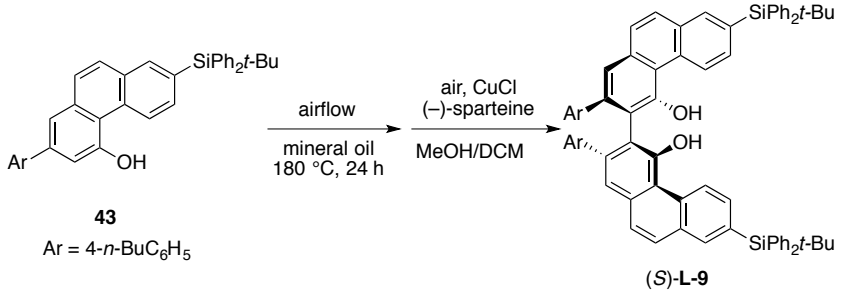
data for **42**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.95 (t, 3H, *J* = 7.5 Hz), 1.35-1.44 (m, 2H), 1.61-1.68 (m, 2H), 2.67 (t, 2H, *J* = 8.0 Hz), 3.61 (s, 3H), 5.56 (s, 2H), 7.30 (d, 2H, *J* = 8.5 Hz), 7.61-7.67 (m, 4H), 7.70 (dd, 1H, *J* = 9.0, 2.5 Hz), 7.74-7.76 (m, 2H), 8.00 (d, 1H, *J* = 2.5 Hz), 9.51 (d, 1H, *J* = 9.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.96, 22.39, 33.64, 35.34, 56.56, 95.27, 111.57, 119.74, 119.86, 120.57, 127.02, 127.21, 128.69, 128.75, 129.01, 129.51, 130.10, 130.36, 134.41, 134.75, 137.65, 139.81, 142.67, 156.42; IR (thin film) 2955s, 2928s, 2857m, 1455s, 1154s, 1046s cm^{-1}; mass spectrum, *m/z* (% rel intensity) 450 M^+ (8, ^{81}Br), 448 M^+ (7, ^{79}Br), 418 (9, ^{81}Br), 416 (7, ^{79}Br), 337 (7), 281 (37), 252 (25), 131 (25). Anal calcd for $C_{26}H_{25}BrO_2$: C, 69.49; H, 5.61. Found: C, 69.45; H, 5.45.



42 **43**

7-(tert-butyldiphenylsilyl)-2-(4-butylphenyl)phenanthren-4-ol ***43***: The following procedure was adapted from one for a related compound:[18] To a 250 mL flame-dried round bottom flask was added 7-bromo-2-(4-butylphenyl)-4-(methoxymethoxy)phenanthrene **42** (2.87 g, 6.39 mmol) and dry THF (65 mL) under N_2. The resulting solution was cooled to –78 °C and *t*-BuLi (1.7 M in pentane, 7.7 mL, 13.1 mmol) was added dropwise. The resulting mixture was stirred at –78 °C for 1 h. TBDPSCl (1.8 mL, 7.06 mmol) was then added to the mixture at –78 °C. The mixture was warmed up to room temperature and stirred for an additional 24 h. $NaHCO_3$ (sat. aq. 5 mL) was added to the mixture. The reaction mixture was partitioned between Et_2O (60 mL) and $NaHCO_3$ (sat. aq. 60 mL). The organic layer was washed with brine (30 mL), dried over $MgSO_4$, filtered through Celite and concentrated to dryness. The product was partially purified by column chromatography on silica gel (30 mm x 250 mm, CH_2Cl_2:hexanes 1:3). The partially purified product was dissolved in a mixture of THF and MeOH (130 mL, 1:1) and Amberlyst 15 (1.6 g) was added. The mixture was stirred at 65 ºC for 15 h under N_2 in a balloon. After cooling down to room temperature, the mixture was filtered through filter paper and concentrated to dryness. Purification of the crude product by column chromatography on silica gel (30 mm x 300 mm,

CH_2Cl_2:hexanes 1:2) gave **43** as a white solid in 48% yield over two steps (1.73 g, 3.07 mmol). Mp 176-178 °C; R_f = 0.26 (1:1 CH_2Cl_2/hexanes). Spectral data for **43**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.95 (t, 3H, *J* = 7.5 Hz),1.24 (s, 9H), 1.37-1.42 (m, 2H), 1.61-1.68 (m, 2H), 2.67 (t, 2H, *J* = 7.5 Hz), 5.74 (s, 1H), 7.20 (d, 1H, *J* = 2.0 Hz), 7.29 (d, 2H, *J* = 8.0 Hz), 7.34-7.38 (m, 4H), 7.39-7.44 (m, 2H), 7.62-7.66 (m, 8H), 7.69-7.71 (m, 2H), 7.87 (dd, 1H, *J* = 8.5, 2.0 Hz), 8.06 (d, 1H, *J* = 1.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.95, 18.92, 22.39, 28.92, 33.61, 35.33, 112.07, 118.21, 119.60, 127.04, 127.16, 127.70, 128.70, 129.00, 129.20, 130.68, 131.70, 132.34, 134.05, 134.91, 135.62, 136.64, 137.37, 137.47, 139.46, 142.61, 154.83 (1 sp^2 C not located); IR (thin film) 3526(br, m), 2930(s), 2857(s), 1653(s), 1558(s), 1458(s) cm^{-1}; HRMS (ESI–) *m/z* calculated for $C_{40}H_{39}OSi$ ($M\text{-}H^+$) 563.2770, found 563.2784.



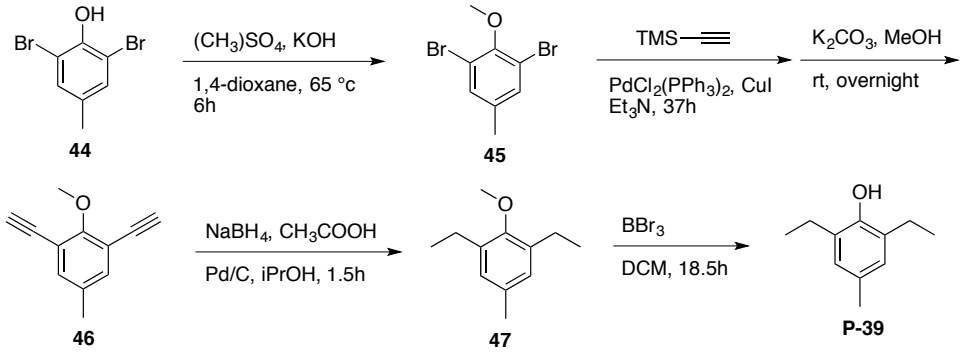
*Rac-**L-9***: The general procedure for oxidative phenol-coupling illustrated for **L-5** was followed with 7-(tert-butyldiphenylsilyl)-2-(4-butylphenyl)phenanthren-4-ol **43** (1.46 g, 2.58 mmol). The mixture was stirred at 180 °C for 24 h. Purification by column chromatography on silica gel (30 mm × 250 mm, CH2Cl2/hexanes 1:4) gave racemic **L-9** as an off-white solid (812 mg, 0.72 mmol, 56% yield).

*(S)-**L-9***: The general procedure for de-racemization illustrated for (*S*)-**L-5** was followed with racemic **L-9** (563 mg, 0.50 mmol) with CuCl (84 mg, 0.85 mmol), (–)-sparteine (0.41 g, 1.75 mmol), dry CH_2Cl_2 (60 mL) and MeOH (15 mL). The crude product was purified by column chromatography on silica gel (30 mm × 200 mm, CH_2Cl_2/hexanes 1:3) to afford (*S*)-**L-9** as an off-white solid (486 mg, 0.43 mmol, 86%). The optical purity was determined to be >99% *ee* by HPLC analysis (Pirkle D-Phenylglycine column, 75:25 hexane/*i*PrOH at 254 nm, flow-rate: 2.0 mL/min). Retention times: R_t = 1.91 min for (*R*)-**L-9** (minor) and R_t = 2.21 min for (*S*)-**L-9** (major). mp 165-167 °C; R_f = 0.19 (1:3 CH2Cl2/hexanes). Spectral data for **L-9**: ^{1}H NMR (CDCl3, 500

MHz) δ 0.88 (t, 6H, *J* = 7.5 Hz), 1.21-1.30 (m, 22H), 1.45-1.52 (m, 4H), 2.46 (t, 4H, *J* = 7.5 Hz), 6.52 (s, 2H), 6.59 (d, 4H, *J* = 8.0 Hz), 6.76 (d, 4H, *J* = 8.0 Hz), 7.35-7.45 (m, 14H), 7.64-7.67 (m, 10H), 7.73 (d, 2H, *J* = 8.5 Hz), 7.91 (dd, 2H, *J* = 8.5, 1.5 Hz), 8.11 (s, 2H), 9.67 (d, 2H, *J* = 8.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.89, 18.93, 22.20, 28.92, 33.47, 35.12, 115.92, 117.84, 123.15, 126.94, 127.59, 127.64, 127.73, 128.67, 129.25, 129.55, 130.84, 131.92, 132.93, 134.40, 134.82, 135.60, 136.63, 137.02, 137.65, 141.52, 141.88, 153.56; IR (thin film) 3490(s), 2930(s), 2857(s), 1558(s), 1456(s), 1105(s) cm-1; HRMS (ESI+) *m/z* calculated for $C_{80}H_{78}O_2Si_2Na$ ($M+Na^+$) 1149.5438, found 1149.5453. $[\alpha]_D^{20}$ = +85.3 (c 1.0, CH_2Cl_2) on >99% *ee (S)*-**L-9** (HPLC).

III. Preparation of phenols

*Preparation of phenol **P-39**:*



*2,6-Dibromo-4-methylanisole **45***: This compound was prepared using a procedure reported for related compounds.[19] To a solution of 2,6-dibromo-4-methylphenol **44** (3.99 g, 15.0 mmol, 1.00 equiv) in 1,4-dioxane (15 mL) at 65 °C was added crushed commercial KOH (3.00 g, 53.5 mmol, 3.57 equiv). Then $(CH_3)_2SO_4$ (1.43 mL, 15.1 mmol, 1.01 equiv) was added slowly to the orange reaction mixture over about 2 h. The resulting mixture was stirred for another 4 h at 65 °C. After it was cooled to rt, the reaction mixture was filtered. The filtrate was concentrated by rotary evaporation and then subjected to vacuum to remove 1,4-dioxane. Purification by column chromatography on silica gel (35 × 160 mm, hexanes as eluent) gave the product **45** as a colorless liquid (3.23 g, 11.5 mmol) in 77% yield. R_f = 0.26 (hexanes). Spectral data for **45**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.25 (t, 3H, *J* = 0.6 Hz), 3.83 (s, 3H), 7.29 (q, 2H, *J* = 0.6 Hz); ^{13}C NMR

(125 MHz, $CDCl_3$) δ 20.20, 60.59, 117.60, 133.08, 136.53, 151.84. These spectral data match those previously reported for this compound.[20]

1,3-diethynyl-2-methoxy-5-methylbenzene ***46***: The first step was carried out with an adaptation of a procedure reported for a related compound.[14] To a flame-dried 50 mL round bottom flask was added 2,6-dibromo-4-methylanisole **45** (2.24g, 8.00 mmol, 1.00 equiv), $Pd(PPh_3)_2Cl_2$ (225 mg, 0.320 mmol, 0.0400 equiv) and CuI (61 mg, 0.32 mmol, 0.040 equiv) and dry NEt_3 (16 mL). Then the flask was sealed with a septum and purged for 5 min with nitrogen, which was introduced by a needle under the surface of the solution. Then trimethylsilylacetylene (3.90 mL, 27.4 mmol, 3.42 equiv) was added to the flask via syringe. The mixture was refluxed for 37 h under a nitrogen atmosphere. After removal of the solvent, the residue was dissolved in 60 mL Et_2O, followed by the addition of $NaHCO_3$ (sat. aq. 60 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (20 mL x 3). The combined organic layer was washed with 20 mL H_2O, 10 mL brine, dried with Na_2SO_4, filtered and concentrated to give a brown oil. It was roughly purified by passing through a short column (35 mm x 120 mm, neutral Al_2O_3, CH_2Cl_2 as eluent) to give the partially purified product as a yellow liquid, which was dissolved in 45 mL MeOH and treated with K_2CO_3 (6.30g, 45.6 mmol). The reaction mixture was stirred at room temperature overnight to give complete conversion. To the mixture was added 60 mL H_2O and the mixture was extracted with Et_2O (40 mL x 3). The combined organic layer was dried with Na_2SO_4, filtered and concentrated to give the crude product as a light yellow liquid. Purification by silica gel chromatography (30 × 160 mm, hexane: EtOAc 20:1) afforded the product **46** (1.28 g, 7.52 mmol) as a light yellow liquid in 94% overall yield from **45**. R_f = 0.32 (hexane: EtOAc 5:1). Spectral data for **46**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.24 (s, 3H), 3.25 (s, 2H), 4.00 (s, 3H), 7.24 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.20, 61.36, 79.37, 81.42, 115.96, 133.00, 135.19, 161.01. IR (thin film) 3289(w), 2955(w) cm^{-1}; HRMS (EI+) calcd for $C_{12}H_{10}O$ *m/z* 170.0732 ($[M]^+$), meas 170.0744.

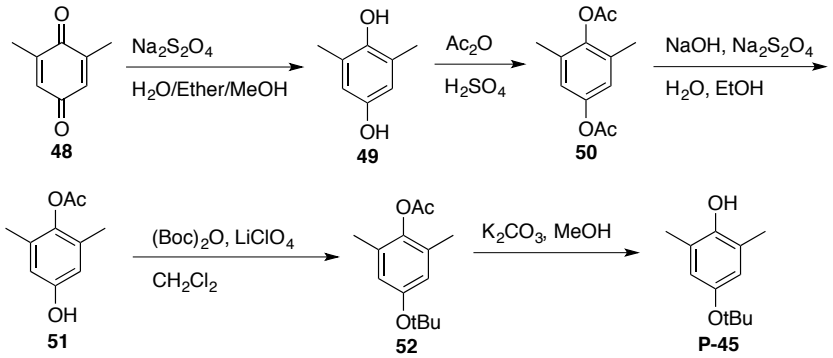
1,3-diethyl-2-methoxy-5-methylbenzene ***47***: This compound was prepared using a procedure reported for related compounds.[21] To a 250 mL round bottom flask was added 1,3-diethynyl-2-methoxy-5-methylbenzene **46** (946 mg, 5.56 mmol, 1.00 equiv), Pd/C (594 mg, 10

mol%), iPrOH (55 mL) and acetic acid (1.27 mL, 22.2 mmol, 3.99 equiv). The flask was put into a room temperature water bath before the addition of powdered $NaBH_4$ (1.68 g, 44.5 mmol, 8.00 equiv). Then the water bath was removed. After the reaction mixture was stirred at room temperature open to air for 90 min, 15 mL 0.1 M HCl was carefully added to the pre-cooled mixture at 0 °C. It was stirred until bubbles ceased coming out of solution. Then the pH of the solution was adjusted to 10 with aqueous NaOH. The mixture was filtered through a Celite pad and the Celite pad was washed with Et_2O (20 mL x 3). The filtrate was washed with H_2O (20 mL x 2). The organic layer was separated. The combined aqueous layer was subjected to rotary evaporation to remove iPrOH. Then it was extracted with Et_2O (40 mL x 3). The combined organic layer was dried with Na_2SO_4, filtered and concentrated to give a yellow oil. Purification by column chromatography (35 × 160 mm, hexanes: EtOAc 40:1) gave the product **47** as a colorless oil (798 mg, 4.47 mmol) in 80% yield. R_f = 0.22 (hexanes: EtOAc 40:1). Spectral data for **47**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.23 (t, 6H, *J* = 7.5 Hz), 2.28 (s, 3H), 2.64 (q, 4H, *J* = 7.5 Hz), 3.71 (s, 3H), 6.86 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.03, 20.91, 22.63, 61.19, 127.58, 133.36, 136.60, 153.88. IR (thin film) 2965(s), 2930(s), 1478(m), 1217(m), 1017(m) cm^{-1}; HRMS (EI+) calcd for $C_{12}H_{18}O$ *m/z* 178.1358 ($[M]^+$), meas 178.1361.

2,6-diethyl-4-methylphenol ***P-39***: To a 100 mL round bottom flask was added 1,3-diethyl-2-methoxy-5-methylbenzene **47** (798 mg, 4.47 mmol, 1.00 equiv) and dry CH_2Cl_2 (30 mL). The solution was pre-cooled to 0 °C, followed by the addition of BBr_3 (1M in CH_2Cl_2, 9.0 mL, 9.0 mmol, 2.0 equiv). After the reaction mixture was stirred at room temperature for 18.5 h, 45 mL H_2O was added to the flask. The organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (25 mL x 3). The combined organic layer was dried with Na_2SO_4, filtered and concentrated to give a gray brown solid. Purification by column chromatography (25 × 180 mm, hexanes: EtOAc 16:1) gave product **P-39** as white solid (524 mg, 3.19 mmol) in a yield of 71%; mp 47-48 °C; R_f = 0.28 (hexanes: EtOAc 10:1). Spectral data for **P-39**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.22 (t, 6H, *J* = 7.5 Hz), 2.24 (s, 3H), 2.58 (q, 4H, *J* = 7.5 Hz), 4.46 (s, 1H), 6.79 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.07, 20.61, 23.04, 127.28, 128.99, 129.52, 148.87. IR (thin film)

3351(br, s), 2959(w), 1464(m) cm^{-1}; HRMS (ESI–) *m/z* calculated for $C_{11}H_{15}O$ ($M\text{-}H^+$) 163.1123, found 163.1120.

*Preparation of phenol **P-45**:*



*2,6-Dimethyl-1,4-benzenediol **49***[22]: $Na_2S_2O_4$ (20.9 g, 120 mmol, 4.00 equiv) was dissolved in 145 mL H_2O in a 500 mL round bottom flask filled with nitrogen. A solution of 2,6-dimethylbenzoquinone **48** (4.08 g, 30.0 mmol, 1.00 equiv) in a mixture of 65 mL ether and 40 mL MeOH was poured into the aqueous solution with stirring. Then a balloon filled with nitrogen was attached to the flask through a septum. After the reaction mixture was stirred at room temperature for 1h, the organic layer was separated and the aqueous layer was extracted with ether (60 mL x 4). The combined organic layer was washed with 50 mL H_2O and 25 mL brine, dried over Na_2SO_4, filtered and concentrated to afford the product as an off-white solid (3.77g, 27.3 mmol) in 91% yield. It was used without further purification; mp 150-151 °C (Lit.[19] 145-148 °C); R_f = 0.11 (hexanes: EtOAc 4:1). Spectral data for **49**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.18 (s, 6H), 4.19 (s, 1H), 4.23 (brs, 1H), 6.46 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.06, 115.00, 124.36, 146.08, 148.62.

*2,6-Dimethylphenylene-1,4-diacetate **50***: This compound was prepared using a procedure reported for a related compound.[23] To a oven-dried 50 mL round bottom flask filled with nitrogen was added 2,6-dimethyl-1,4-benzenediol **49** (3.77g, 27.2 mmol, 1.00 equiv), acetic anhydride (8.20 mL, 86.7 mmol, 3.19 equiv) and two drops of H_2SO_4 (conc.). After the solution was stirred at room temperature for 1.7 h, it was poured into 100 mL H_2O and the mixture was stirred for 10 min to produce a white precipitate. The mixture was then filtered and the precipitate was washed with

H_2O several times and dried under vacuum to give the product **50** as a white solid (5.85 g, 26.3 mmol) in a 97% yield; mp 90-92 °C (Lit.[24] 91-93 °C). R_f = 0.27 (hexanes: EtOAc 3:1). Spectral data for **50**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.12 (s, 6H), 2.25 (s, 3H), 2.31 (s, 3H), 6.78 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.44, 20.42, 21.09, 121.28, 131.42, 145.68, 147.75, 168.70, 169.59. IR (thin film) 1759(s), 1370(m), 1215(s), 1169(s) cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{15}O_4$ *m/z* 223.0970 ($[M+H]^+$), meas 223.0969.

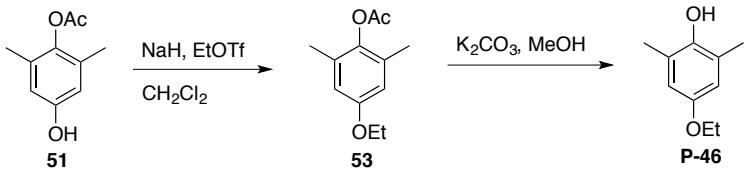
*4-hydroxy-2,6-dimethylphenyl acetate **51***: This compound was prepared using a procedure reported for a related compound.[25a] To a 250 mL round bottom flask filled with nitrogen was added 2,6-dimethylphenylene-1,4-diacetate **50** (5.83 g, 26.2 mmol, 1.00 equiv) and EtOH (87 mL). A solution of NaOH (1.05 g, 26.2 mmol, 1.0 equiv) and $Na_2S_2O_4$ (1.15 g, 6.6 mmol, 0.25 equiv) in 8.7 mL H_2O was slowly added to the flask. After the mixture was stirred at room temperature for 40 min, 44 mL 1M HCl was added to the flask. The mixture was subjected to rotary evaporation to remove EtOH, during which the reaction mixture became cloudy. The residue was dissolved in 250 mL EtOAc. The organic layer was separated and washed with NH_4Cl (aq. Sat. 25 mL), dried with Na_2SO_4, filtered and concentrated to give a yellow solid. It was crystallized from hexanes/EtOAc (8:1) to give an additional quantity of the product as white crystals (2.20 g, 12.2 mmol). The mother liquor was purified by column chromatography (silica gel, 40 × 200 mm, hexane:EtOAc 6:1➔5:1➔3:1) to give the product **51** as a white solid (1.65 g, 9.20 mmol). The combined yield was 82%. Mp 108-110 °C (Lit. [22b] 105-106 °C); R_f = 0.18 (hexanes: EtOAc 3:1). Spectral data for **51**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.04 (s, 6H), 2.31 (s, 3H), 5.78 (brs, 1H), 6.38 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.24, 20.43, 115.16, 130.80, 141.41, 153.19, 170.26. The ^{1}H NMR data match those previously reported for this compound.[25b]

*4-(tert-butoxy)-2,6-dimethylphenyl acetate **52***: This compound was prepared using a procedure reported for a related compound.[26] To a flame-dried 25 mL round bottom flask filled with nitrogen was added 4-hydroxy-2,6-dimethylphenyl acetate **51** (361 mg, 2.00 mmol, 1.00 equiv), $Mg(ClO_4)_2$ (45 mg, 0.20 mmol, 0.10 equiv) and dry CH_2Cl_2 (3 mL), followed by the addition of $(Boc)_2O$ (1.53 g, 7.00 mmol, 3.50 equiv). Then the flask was connected to a condenser with a nitrogen balloon attached on top of the condenser through a septum. The mixture was stirred at

40 °C for 24 h. Then another portion of $(Boc)_2O$ (300 mg, 1.37 mmol) was added to the reaction flask. The reaction mixture was stirred for another 23 h. The solvent was removed by slowly maintaining a nitrogen flow into the flask. The crude product was purified by column chromatography (silica gel, 25 × 200 mm, hexanes➔hexane:EtOAc 5:1) to give the product **52** as a colorless oil (444 mg, 1.88 mmol) in a yield of 94%. R_f = 0.43 (hexanes: EtOAc 5:1). Spectral data for **52**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.31 (s, 9H), 2.08 (s, 6H), 2.29 (s, 3H), 6.66 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.43, 20.41, 28.83, 78.17, 123.77, 130.23, 143.97, 152.57, 168.85. IR (thin film) 2978(s), 1761(s), 1482(s), 1368(s), 1217(s), 1167(s) cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{21}O_3$ *m/z* 237.1491 ($[M+H]^+$), meas 237.1494.

4-(tert-butoxy)-2,6-dimethylphenol ***P-45***: This compound was prepared using a procedure reported for a related compound.[27] To a 25 mL round bottom flask filled with nitrogen was added 4-(tert-butoxy)-2,6-dimethylphenyl acetate **52** (444 mg, 1.88 mmol, 1.00 equiv), K_2CO_3 (390 mg, 2.82 mmol, 1.50 equiv) and MeOH (9 mL). After the mixture was stirred at room temperature for 21 h, 15 mL H_2O was added to the reaction flask. The pH of the solution was adjusted to 3-4 with 2N HCl. The mixture was concentrated to about 15 mL and extracted with Et_2O (40 mL × 3). The combined organic layers were dried with Na_2SO_4, filtered and concentrated to afford a yellow solid, which was purified by column chromatography (silica gel, 30 × 200 mm, hexane:EtOAc 5:1) to give the product **P-45** as an off-white solid (351 mg, 1.81 mmol) in a yield of 96%. It was recrystallized from 1 mL hexanes to give the first crop as white needles (270 mg, 1.39 mmol) in a yield of 74%. The second crop (39 mg, 0.20 mmol) was obtained from the residue. The combined yield was 85%. Mp 81-82 °C; R_f = 0.40 (hexanes: EtOAc 3:1). Spectral data for **P-45**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.27 (s, 9H), 2.18 (s, 6H), 4.37 (s, 1H), 6.60 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.07, 28.77, 77.65, 123.06, 124.35, 147.76, 148.22. IR (thin film) 3407(s), 2978(m), 1485(s), 1167(m), 1138(m) cm^{-1}; HRMS (ESI–) *m/z* calculated for $C_{12}H_{17}O_2$ ($M\text{-}H^+$) 193.1229, found 193.1227.

*Preparation of phenol **P-46**:*

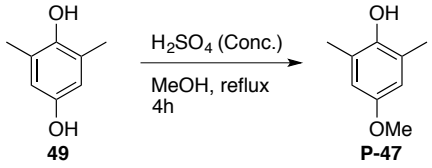


*4-(Ethoxy)-2,6-dimethylphenyl acetate **53***: This compound was prepared using a procedure reported for a related compound.[28] To a 100 mL flame dried round bottom flask filled with nitrogen was added the 4-hydroxy-2,6-dimethylphenyl acetate **51** (541 mg, 3.00 mmol, 1.00 equiv) and dry CH_2Cl_2 (15 mL), followed by the addition of NaH (134 mg, 60% in mineral oil, 3.35 mmol. 1.10 equiv) with stirring. At the end of hydrogen evolution, EtOTf (0.47 mL, 3.63 mmol, 1.21 equiv) was added to the reaction flask. After the reaction mixture was stirred at room temperature for 7 h, NH_4Cl (aq. sat. 8 mL) was added to the mixture. The organic layer was separated and the aqueous layer was extracted with EtOAc (10 mL x 3). The combined organic layer was dried over Na_2SO_4, filtered and concentrated to give a yellow oil with some precipitate in it. The crude product was purified by column chromatography (silica gel, 25 × 200 mm, hexane:EtOAc 10:1) to give the product **53** as a colorless oil (562 mg, 2.70 mmol) in a yield of 90%. R_f = 0.37 (hexanes/EtOAc 10:1). Spectral data for **53**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.36 (t, 3H, *J* = 7.0 Hz), 2.10 (s, 6H), 2.30 (s, 3H), 3.96 (q, 2H, *J* = 7.0 Hz), 6.57 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.88, 16.56, 20.43, 63.53, 114.16, 130.87, 141.68, 156.29, 169.26. IR (thin film) 2980(w), 2928(w), 1759(s), 1221(s), 1183(s) cm^{-1}; HRMS (ESI+) calcd for $C_{12}H_{17}O_3$ *m/z* 209.1178 ($[M+H]^+$), meas 209.1180.

*4-Ethoxy-2,6-dimethylphenol **P-46***: To a 25 mL round bottom flask filled with nitrogen was added the 4-(ethoxy)-2,6-dimethylphenyl acetate **53** (560 mg, 2.69 mmol, 1.00 equiv) and EtOH (6 mL). Then a solution of KOH (377 mg, 6.72 mmol, 2.50 equiv) in H_2O (6 mL) was added to the mixture. After the mixture was stirred at room temperature for 2 h, the pH of the solution was adjusted to ~3 with 2 M HCl. It was then concentrated to approximately 10 mL and extracted with EtOAc (20 mL x 3). The combined organic layer was dried over Na_2SO_4, filtered and concentrated to give a brown oil, which was loaded onto a silica gel column (25 × 200 mm, hexane:EtOAc 10:1) and eluted to afford **P-46** as a light brown solid (364 mg, 2.19 mmol) in a yield of 81%. Mp 43-44

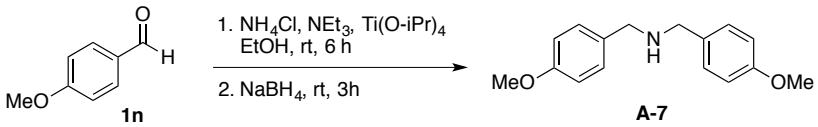
°C; R_f = 0.29 (hexanes: EtOAc 3:1). Spectral data for **P-46**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.36 (t, 3H, *J* = 7.0 Hz), 2.21 (s, 6H), 3.94 (q, 2H, *J* = 7.0 Hz), 4.26 (brs, 1H), 6.54 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.96, 16.24, 63.85, 114.54, 124.05, 146.02, 152.24. IR (thin film) 3449(s), 2978(m), 2923(w), 1491(s), 1196(s), 1059(s) cm^{-1}; HRMS (ESI–) calcd for $C_{10}H_{13}O_2$ *m/z* 165.0916 ($[M-H]^+$), meas 165.0915.

*Preparation of phenol **P-47**:*



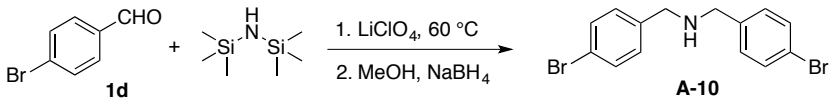
*4-methoxy-2,6-dimethylphenol **P-47***[29]: To a 100 mL oven dried round bottom flask was added the 2,6-dimethyl-1,4-benzenediol **49** (4.61 g, 33.4 mmol, 1.00 equiv), MeOH (30 mL) and H_2SO_4 (conc., 12 mL). The mixture was refluxed for 4 h (oil bath: 100 °C). The mixture was then cooled to room temperature and poured into a 250 mL beaker containing 100 g ice. After the ice melted, the mixture was extracted with Et_2O (100 mL x 4). The combined organic layer was dried over Na_2SO_4, filtered and concentrated to give a brown oil. The crude product was purified by column chromatography (silica gel, 35 × 200 mm, hexane:EtOAc 8:1 to 6:1 to 5:1) and recrystallization from hexanes (43 mL) to afford white needles (3.24 g, 21.3 mmol) in a yield of 64%. Mp 75-76 °C; R_f = 0.45 (hexanes: EtOAc 3:1). Spectral data for **P-47**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.21 (s, 6H), 3.72 (s, 3H), 4.21 (s, 1H), 6.53 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.25, 55.65, 113.77, 124.08, 146.10, 152.99. The ^{1}H NMR data match those previously reported for this compound.[29]

IV. Preparation of amines A-7—A-12



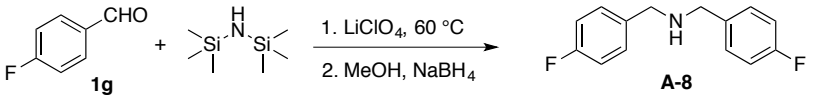
*Bis-(4-methoxybenzyl)amine **A-7***[30]: To a flame-dried 25 mL round bottom flask filled with N_2 was added NH_4Cl (214 mg, 4.00 mmol, 2.00 equiv), absolute ethanol (4 mL), dry NEt_3 (0.56 mL,

4.0 mmol, 2.0 equiv) and 4-methoxybenzaldehyde **1n** (272 mg, 0.250 mL, 2.00 mmol, 1.00 equiv). Then the vacuum adapter was quickly replaced with a septum to which a N_2 balloon was attached *via* a needle. Then Ti(O-*i*-Pr)$_4$ (1.14 g, 1.20 mL, 4.00 mmol, 2.00 equiv) was added dropwise via syringe. The resulting mixture was stirred at rt for 6 hours. $NaBH_4$ (114 mg, 3.00 mmol, 1.50 equiv) was added in one portion. The reaction mixture was stirred at rt for another 3 hours. After it was poured into *aq* ammonia (2M, 5 mL), the mixture was filtered and washed well with EtOAc (20 mL). The aqueous layer was separated and extracted with EtOAc (2 × 10 mL). The combined organic extracts were dried ($MgSO_4$) and filtered. The filtrate was concentrated and the product was purified by column chromatography (silica gel, 25 × 200 mm, hexane:EtOAc 4:1 to 1:1). The product **A-7** was obtained as a pale yellow oil (177 mg, 0.689 mmol, 69%); R_f = 0.05 (hexane:EtOAc 1:1). Spectral data for **A-7**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.70 (brs, 1H), 3.72 (s, 4H), 3.78 (s, 6H), 6.87 (d, 4H, *J* = 8.5 Hz), 7.25 (d, 4H, *J* = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.05, 54.80, 113.35, 128.90, 132.14, 158.21; MS (EI) 257.1 M^+ (10.88), 121.0 (100). The ^{1}H NMR data match those previously reported for this compound.[30]

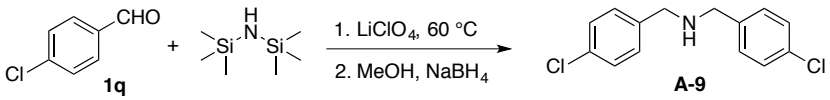


Bis-(4-bromobenzyl)amine ***A-10***[31]: To a flame dried 50 mL round bottom flask filled with N_2 was added 4-bromobenzaldehyde **1d** (925 mg, 5.00 mmol, 1.0 equiv), $LiClO_4$ (532 mg, 5.00 mmol, 1.00 equiv) and hexamethyldisilazane (HMDS, 2.20 mL, 10.0 mmol, 2.00 equiv). The mixture was stirred at 60 °C for 2 hours. After it was cooled to 0 °C, MeOH (10 mL) was added. Then $NaBH_4$ (568 mg, 15.0 mmol, 3.00 equiv) was added in three portions. After it was stirred at 0 °C for 10 min, the reaction mixture was stirred at rt overnight. Then the volatiles were removed, and *aq* sat $NaHCO_3$ (10 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$) and filtered. The filtrate was concentrated. The crude product was dissolved in CH_2Cl_2 (10 mL) and *aq* HCl (6M, ~5 mL) was added dropwise until pH ~1. The resulting white precipitate was collected by filtration and suspended in EtOAc (20 mL). Then Na_2CO_3 (aq. sat. ~10 mL) was added. The aqueous layer was separated and extracted with EtOAc (2 × 20 mL). The combined organic extracts were

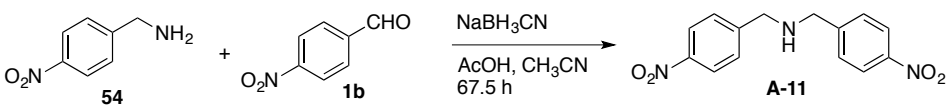
dried ($MgSO_4$) and filtered. The filtrate was concentrated and the product was purified by column chromatography (silica gel, 25 × 200 mm, Hexane:EtOAc 3:1). The product **A-10** was obtained as a colorless oil (536 mg, 1.51 mmol, 60%); R_f = 0.30 (hexane:EtOAc). Spectral data for **A-10**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.60 (brs, 1H), 3.70 (s, 4H), 7.20 (d, 4H, *J* = 8.0 Hz), 7.43 (d, 4H, *J* = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.27, 120.69, 129.73, 131.40, 139.07. The ^{1}H NMR data match those previously reported for this compound.[31]



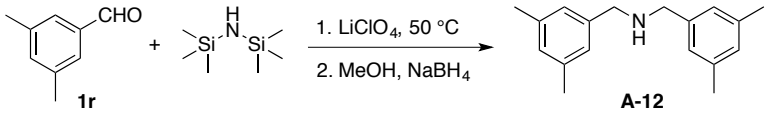
*Bis-(4-fluorobenzyl)amine **A-8**[31]:* The procedure for the preparation of **A-10** was followed with 4-fluorobenzaldehyde **1g** (620 mg, 5.00 mmol, 1.00 equiv). The filtrate was concentrated and the product purified by column chromatography (silica gel, 25 × 200 mm, hexane:EtOAc 3:1), affording the product **A-8** as a colorless oil (400 mg, 1.72 mmol, 69%); R_f = 0.30 (hexane:EtOAc 1:1). Spectral data for **A-8**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.60 (brs, 1H), 3.72 (s, 4H), 6.96-7.14 (m, 4H), 7.26-7.50 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.34, 115.14 (*J* = 21.1 Hz), 129.60 (*J* = 7.8 Hz), 135.91 (*J* = 3.1 Hz), 161.92 (*J* = 243.0 Hz). The ^{1}H NMR data match previously reported for this compound.[30]



*Bis-(4-chlorobenzyl)amine **A-9**[31]*: The procedure for the preparation of **A-10** was followed with 4-chlorobenzaldehyde **1q** (703 mg, 5.00 mmol, 1.00 equiv). The product **A-9** was obtained as a colorless oil (410 mg, 1.54 mmol, 61.7%); R_f = 0.30 (Hexane:EtOAc 1:1). Spectral data for **A-9**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.60 (brs, 1H), 3.70 (s, 4H), 7.20-7.40 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.36, 128.58, 129.50, 132.72, 138.67. The ^{1}H NMR data match those previously reported for this compound.[31]



Bis-(4-nitrobenzyl)amine ***A-11***[32]: To an oven-dried 25 mL round bottom flask was added 4-nitrobenzaldehyde **1b** (453 mg, 3.00 mmol, 1.00 equiv) and a solution of 4-nitrobenzylamine **54** (456 mg, 3.00 mmol, 1.00 equiv) in CH_3CN (12 mL). After the mixture was stirred at room temperature for 1.5 h, $NaBH_3CN$ (566 mg, 9.00 mmol, 3.00 equiv) was added to the flask. After 20 min, acetic acid (0.86 mL, 15 mmol, 5.0 equiv) was added to the mixture. It was then stirred at room temperature for 67.5 h. The reaction mixture was diluted with CH_2Cl_2 (6 mL), washed with NaOH (1.0 M, 12 mL x 2), dried with Na_2SO_4, filtered and concentrated to dryness. The crude product was purified by column chromatography (silica gel, 30 × 200 mm, hexane/EtOAc 1:1) and recrystallized from hexane/EtOAc (1:1) to give a yellow crystalline solid (302 mg, 1.05 mmol) in a yield of 35%. Mp 90-91 °C (Lit. 90 °C); R_f = 0.13 (hexanes: EtOAc 1:1). Spectral data for **A-11**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.76 (brs, 1H), 3.91 (s, 4H), 7.52 (d, 4H, *J* = 8.5 Hz), 8.18 (d, 4H, *J* = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.41, 123.71, 128.61, 147.18, 147.43. The ^{1}H NMR data match previously reported for this compound.[32]



Bis-(3,5-dimethylbenzyl)amine ***A-12***[31]: The procedure for the preparation of **A-10** was followed with 3,5-dimethylbenzaldehyde **1r** (295 mg, 2.20 mmol, 1.00 equiv), bis(trimethylsilyl)amine (1.2 mL, 5.73 mmol, 2.60 equiv), $LiClO_4$ (234 mg, 2.20 mmol, 1.00 equiv), $NaBH_4$ (250 mg, 6.60 mmol, 3.00 equiv) and MeOH (5.5 mL). The difference was that the reaction temperature for the first step was 50 °C instead of 60 °C. The product **A-12** was obtained as a colorless oil (171 mg, 0.675 mmol, 61%); R_f = 0.19 (Hexane:EtOAc 5:1). Spectral data for **A-12**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.56 (brs, 1H), 2.34 (s, 12H), 3.77 (s, 4H), 6.92 (s, 2H), 6.99 (s, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.21, 53.28, 125.93, 128.46, 137.81, 140.21. The ^{1}H NMR data match previously reported for this compound.[32]

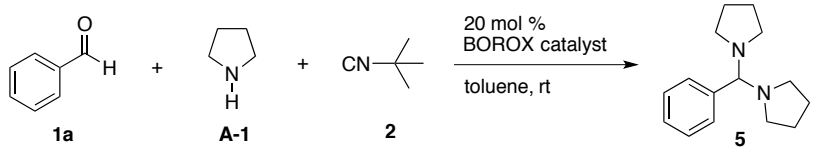
V. General procedure A for optimization of the Ugi-3CR (Table 1-3)

A 25 mL Schlenk flask equipped with a stir bar was flame dried, cooled to rt under N_2 and charged with 20 mol% ligand (0.050 mmol, 0.20 equiv), 40 mol% phenol (0.10 mmol, 0.40 equiv),

dry toluene (1.5 mL), 60 mol% H_2O (27 mg, 2.7 μL, 0.15 mmol, 0.60 equiv), and 60 mol% BH_3•SMe_2 (2M, 75 μL, 0.15 mmol, 0.60 equiv). The Teflon valve on the Schlenk flask was then closed, and the mixture heated at 100 ° C for 1 h. After the flask was cooled to rt, the valve was carefully opened to gradually apply high vacuum (0.1 mm Hg) and the solvent and volatiles were removed. Then the flask was heated at 100 °C under high vacuum for 30 min. Dry reaction solvent (1 mL) was added to dissolve the residue in the flask after it was cooled to room temperature. To the resulting solution was added amine **A** (0.5 mmol, 2.0 equiv) under a N_2 stream, followed by the addition of benzaldehyde **1a** (26 μL, 0.25 mmol, 1.0 equiv) and then *t*-butyl isocyanide **2** (45 μL, 0.38 mmol, 1.5 equiv). The Teflon valve was then closed, and the resulting mixture was stirred at room temperature for a specified time 24-46 h. Upon completion, the reaction mixture was directly loaded onto a silica gel column (20 × 160 mm, hexanes:EtOAc 15:1) to afford the corresponding product **3**. The optical purity was determined by HPLC analysis (Pirkle Covalent (*R*,*R*) WHELK-O1 column or Chiralpak AD column).

VI. Attempted Ugi reaction with amines A-1 and A-6 (Table 1)

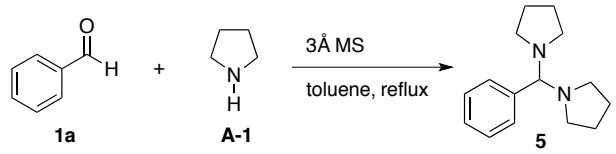
*Attempted Ugi reaction with pyrrolidine **A-1**:*



1a **A-1** **2** **5**

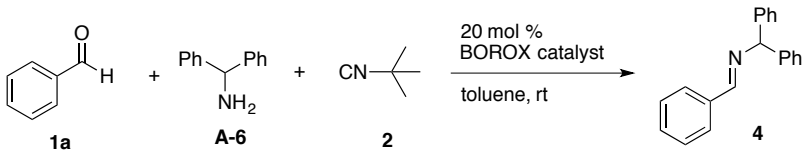
The general procedure A described in **Part V** was followed with (*S*)-VAPOL ligand (27 mg, 0.050 mmol), phenol **P-11** (9.6 mg, 0.10 mmol), pyrrolidine **A-1** (42 μL, 0.51 mmol, 2.0 equiv) and d_8-toluene (1 mL) as the reaction solvent. After the reaction mixture was stirred at room temperature for 19 h, the crude NMR spectrum showed that the aminal **5** was formed in 50% yield (average of two runs) with the aid of Ph_3CH as an internal standard. Aminal **5** was the only major species present in the crude reaction mixture other than the starting materials. The assignment of this major species as the aminal **5** was made based on the ^1H NMR data of **5** that was prepared separately as described below.

*Separate preparation of aminal **5** from benzaldehyde **1a** and prolidine **A-1**:*



*α,α-Bis(pyrrolidinyl)toluene **5***: An oven-dried 50 mL round bottom flask charged with 3Å powdered molecular sieves (3.0 g) and equipped with a magnetic stir bar was flame dried under high vacuum and cooled down under nitrogen. To the flask was then added 9.0 mL of dry toluene, pyrrolidine **A-1** (0.82 mL, 10 mmol, 2.0 equiv) and benzaldehyde **3a** (0.51 mL, 5.0 mmol, 1.0 equiv). After the mixture was heated to reflux for 16 h in an 80 °C oil bath, it was cooled to room temperature and filtered through a Celite pad. The pad was washed with dry CH_2Cl_2 (3 mL). The combined filtrate was concentrated to dryness to give **5** as a light yellow oil (980 mg, 4.25 mmol) in 85% yield. The crude product contains a very small amount of benzaldehyde **3a** and pyrrolidine **A-1**. Spectral data for **5**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.60-1.69 (m, 8H), 2.41-2.50 (m, 8H), 3.89 (s, 1H), 7.23-7.33 (m, 5H); ^{1}H NMR (500 MHz, d_8-toluene) δ 1.50-1.64 (m, 8H), 2.43-2.60 (m, 8H), 3.89 (s, 1H), 7.17-7.31 (m, 5H). The ^{1}H NMR data ($CDCl_3$) match those reported for this compound.[33]

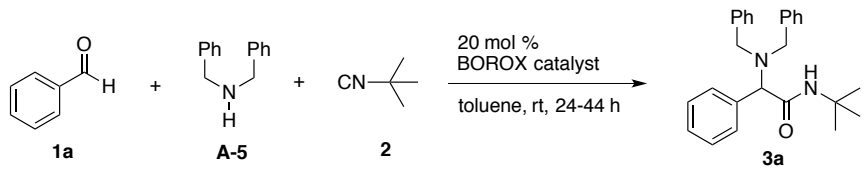
*Attempted Ugi reaction with pyrrolidine **A-6**:*



The general procedure A described in **Part V** was followed with (*S*)-VAPOL ligand (27 mg, 0.050 mmol), phenol **P-11** (9.6 mg, 0.10 mmol), benzhydrylamine **A-6** (88 μL, 0.51 mmol, 2.0 equiv) and toluene (1 mL) as the reaction solvent. The crude NMR spectrum was taken after the reaction mixture had been stirred at room temperature for 18 h and for 89 h. In both cases, the crude NMR spectrum showed 100% formation of imine **4**[34] with the aid of Ph_3CH as an internal standard.

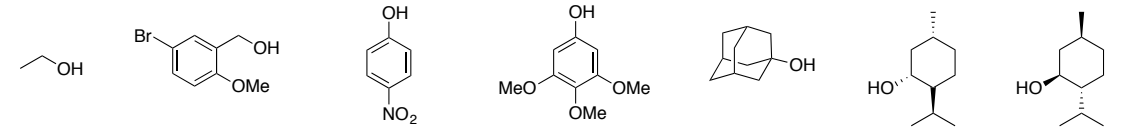
VII. Screen of phenols P-1—P-46 with general procedure A

*Screen of phenols **P-1—P-38** with (S)-VAPOL catalyst in toluene with general procedure A:*

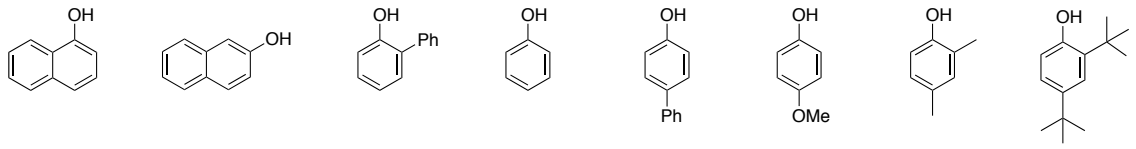


1a **A-5** **2** **3a**

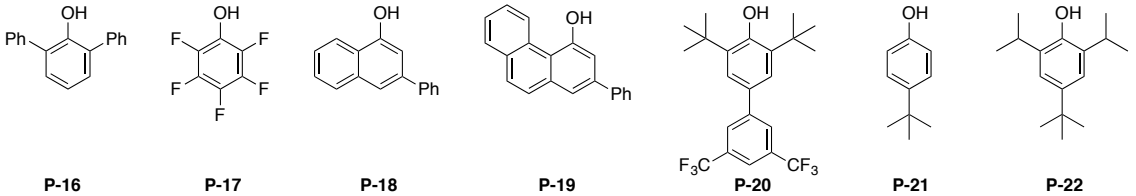
The general procedure A described in **Part V** was followed with (*S*)-VAPOL ligand (27 mg, 0.050 mmol), phenol **P-1**—**P-38** (0.10 mmol) and toluene (1 mL) as the reaction solvent. The results are shown below.



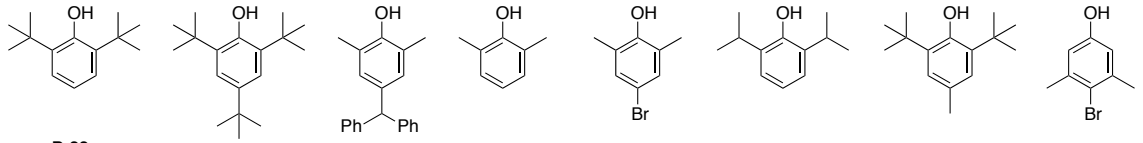
P-1 % yield: trace % ee: —
P-2 % yield: trace % ee: —
P-3 % yield: 64 % ee: 13
P-4 % yield: 76 % ee: 14
P-5 % yield: 86 % ee: 15
P-6 % yield: 91 % ee: 16
P-7 % yield: 73 % ee: 17



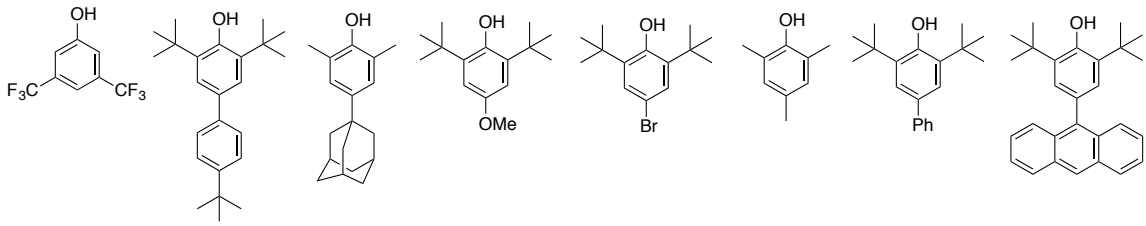
P-8 % yield: 56 % ee: 17
P-9 % yield: 71 % ee: 17
P-10 % yield: 76 % ee: 17
P-11 % yield: 76 % ee: 18
P-12 % yield: 70 % ee: 18
P-13 % yield: 75 % ee: 18
P-14 % yield: 82 % ee: 19
P-15 % yield: 76 % ee: 19



P-16 % yield: 87 % ee: 19
P-17 % yield: 65 % ee: 19
P-18 % yield: 77 % ee: 19
P-19 % yield: 70 % ee: 19
P-20 % yield: 42 % ee: 20
P-21 % yield: 89 % ee: 22
P-22 % yield: 76 % ee: 24

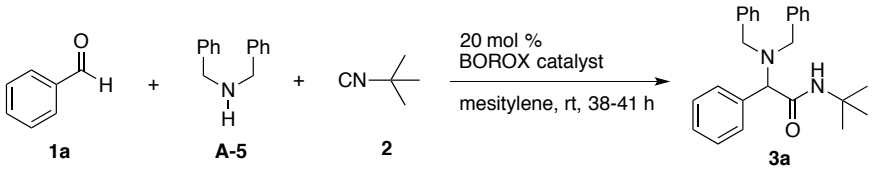


P-23 % yield: 69 % ee: 24
P-24 % yield: 48 % ee: 24
P-25 % yield: 80 % ee: 25
P-26 % yield: 70 % ee: 26
P-27 % yield: 92 % ee: 26
P-28 % yield: 82 % ee: 26
P-29 % yield: 50 % ee: 26
P-30 % yield: 83 % ee: 27



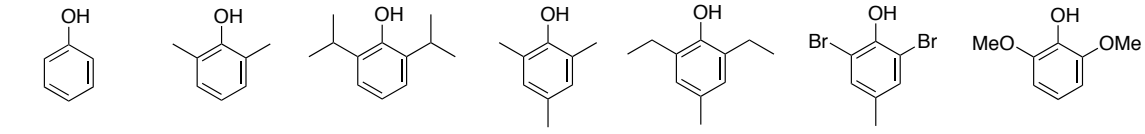
P-31 % yield: 77 % ee: 31
P-32 % yield: 59 % ee: 33
P-33 % yield: 76 % ee: 35
P-34 % yield: 68 % ee: 36
P-35 % yield: 60 % ee: 36
P-36 % yield: 72 % ee: 40
P-37 % yield: 73 % ee: 40
P-38 % yield: 73 % ee: 40

*Screen of phenols **P-11**, **P-26**, **P-28**, **P-36**, **P-39** and **P-40—P-47** with catalyst prepared from (S)-**L-8** in mesitylene with general procedure A:*

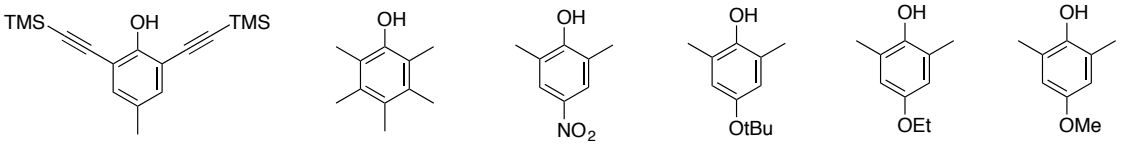


1a **A-5** **2** **3a**

The general procedure A described in **Part V** was followed with (*S*)-**L-8** ligand (41.5 mg, 0.0504 mmol), with the appropriate phenol (0.10 mmol) and mesitylene (1 mL) as the reaction solvent. The results are shown below.

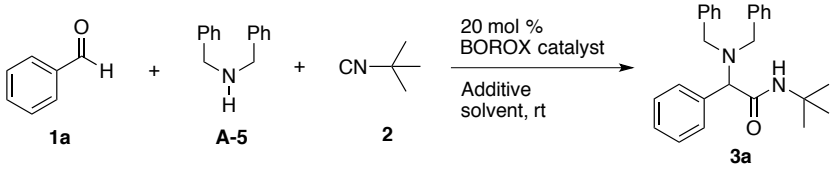


P-11 % yield: 72 % ee: 34 | **P-26** % yield: 94 % ee: 66 | **P-28** % yield: 72 % ee: 36 | **P-36** % yield: 89 % ee: 74 | **P-39** % yield: 95 % ee: 64 | **P-40** % yield: 54 % ee: 10 | **P-41** % yield: 35 % ee: 34



P-42 % yield: 28 % ee: 26 | **P-43** % yield: 81 % ee: 69 | **P-44** % yield: 76 % ee: 17 | **P-45** % yield: 90 % ee: 67 | **P-46** % yield: 87 % ee: 76 | **P-47** % yield: 88 % ee: 80

VIII. Effects of different additives



1a **A-5** **2** **3a**

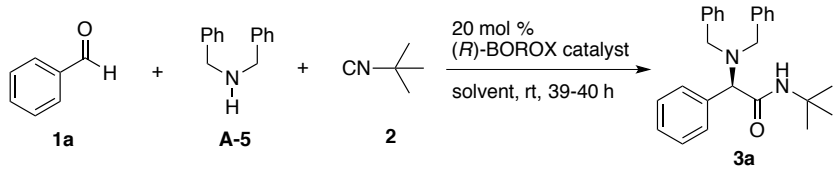
The general procedure A described in **Part V** was followed with (*R*)-**L-8** ligand (41.5 mg, 0.0504 mmol), phenol **P-36** (14 mg, 0.10 mmol) and 1 mL reaction solvent. The additive was added to the pre-catalyst solution right before the addition of dibenzylamine **A-5**. The results are shown in **Table 1** and entry 1-6 are plotted in **Part XVIII** in **Charts 2** & **3**.

Table 1. The effects of different additives on the three-component Ugi reaction.

Entry	Solvent	Additive/Amount	Time (h)	%Yield[b]	*er*
1	toluene	none	39	94[c]	85:15
2	d_8-toluene	H_2O/100 mol %	91	8.6	59:41
3	d_8-toluene	H_2O/50 mol %	91	17.3	61:39
4[a]	d_8-toluene	H_2O/20 mol %	88	78	24:76
5	d_8-toluene	4Å MS/13 mg	18.3	83	85:15
6	d_8-toluene	4Å MS/6 mg	18.3	80	85:15
7	mesitylene	none	39	89[c]	87:13
8	mesitylene	5Å MS/13 mg	39	80[c]	87:13
9	mesitylene	$Mg(ClO_4)_2$/20 mol %	39	15[c]	65:35

[a] Catalyst was generated from (*S*)-**L-8**; The additive was added after the addition of benzaldehyde **3a**. [b] ^{1}HNMR yield with Ph_3CH as an internal standard. [c] Isolated yield after chromatography on silica gel.

IX. Screen of different solvents with general procedure A



1a **A-5** **2** **3a**

The general procedure A described in **Part V** was followed with (*R*)-**L-8** ligand (41.5 mg, 0.0504 mmol), phenol **P-36** (14 mg, 0.10 mmol) and 1 mL reaction solvent with a reaction time of 39-40 h. The results are shown in **Table 2**. The reaction carried out in those less polar solvents gave good aymmetric inductions. The reaction carried out in THF and CH_3CN gave lower yield and low inductions. This was supportive of the proposed mechanism involving ion pairs. The electrostatic interactions between the anionic catalyst and cationic intermediate would be expected to decrease in polar solvents, resulting in a loose ion pair and a loss in stereoselectivity.

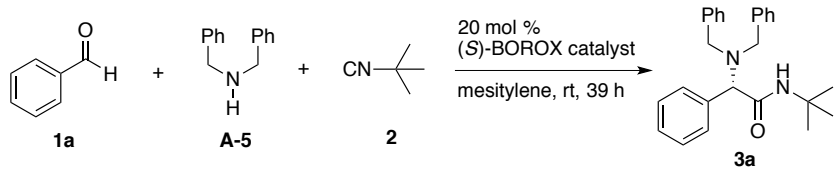
Table 2. Solvent effect on the three-component Ugi reaction.

Entry	Solvent	%Yield[b]	*er*
1	toluene	94	85:15
2	m-xylene	92	86:14
3	mesitylene	91	88:12
4[a]	1,3,5-triisopropyl benzene	90	13:87
5	CCl_4	90	86:14

6	THF	77	54:46
7	CH_3CN	26	64:36

[a] Catalyst was generated from (*S*)-**L-8** (97% *ee*). [b] Isolated yield after chromatography on silica gel.

X. Effects of concentration and amine stoichiometry on the Ugi-3CR.



1a **A-5** **2** **3a**

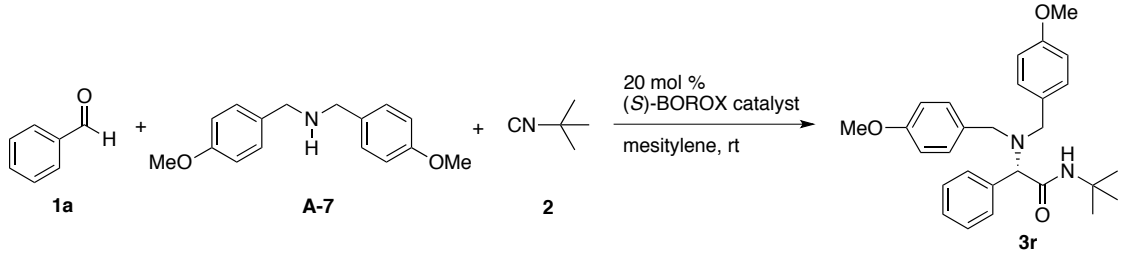
The general procedure A described in **Part V** was followed with (*S*)-**L-8** ligand (41.5 mg, 0.0504 mmol), phenol **P-36** (14 mg, 0.10 mmol), amine **A-5** (0.05-0.1 mL) and mesitylene (0.45-5.0 mL) as the reaction solvent with a reaction time of 39 h. The results are shown in **Table 3**.

Table 3. Ugi-3CR with different concentrations and equivalents of amine.

Entry[a]	Amine equivalents	Concentration (M)	%Yield[b]	*er*
1	2.00	0.05	53	77:23
2	2.00	0.1	89	86:14
3	2.00	0.2	92	87:13
4	2.00	0.4	93	87:13
5	1.20	0.2	86	86:14
6	1.02	0.2	75	84:16

[a] (*S*)-**L-8** was 97% *ee*. [b] Isolated yield after chromatography on silica gel.

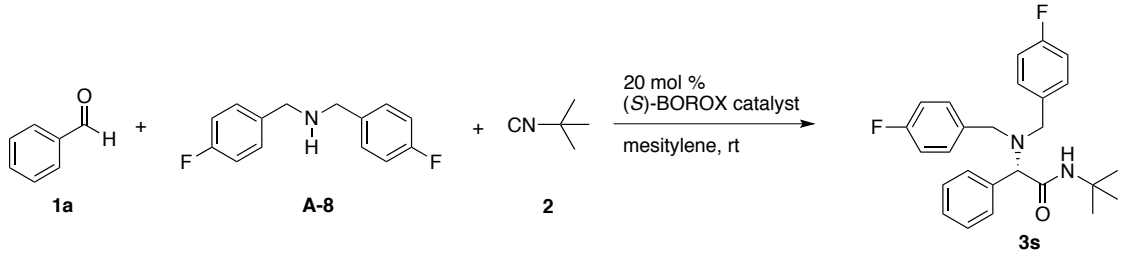
XI. Screen of amines A-7—A-12 with general procedure A (Part V) and B (Part XII).



1a **A-7** **2** **3r**

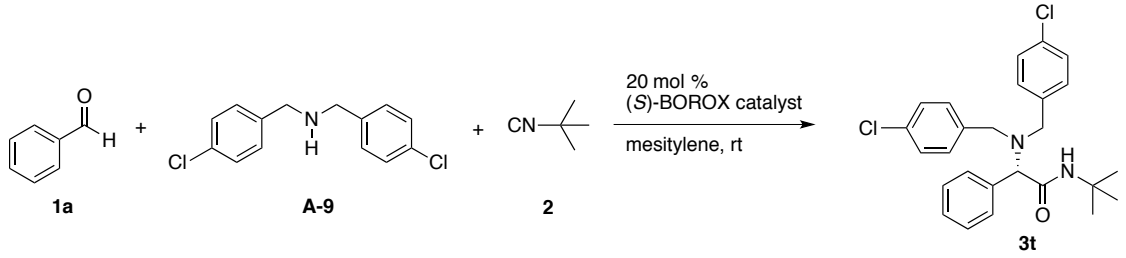
(S)-2-(bis(4-methoxybenzyl)amino)-N-(tert-butyl)-2-phenylacetamide ***3r***: The general procedure A described in **Part V** was followed with ligand (*S*)-**L-8** (41.5 mg, 0.0504 mmol), phenol **P-36** (14 mg, 0.10 mmol), amine **A-7** (98 mg, 0.50 mmol) and mesitylene (1 mL) with a reaction time of 39 h. After purification by column chromatography (silica gel, 20 × 160 mm, hexane:EtOAc 9:1), the product **3r** was obtained as a yellow semi-solid (105 mg, 0.23 mmol, 92%). The optical

purity was determined to be 85:15 *er* by HPLC analysis (Chiralpak AD column, hexanes/2-propanol 90:10, 222 nm, flow 1 mL). Retention times: R_t = 7.04 min (major enantiomer) and R_t = 20.04 min (minor enantiomer). A reaction that was run according to general procedure B (described in **Part XII**) with (*R*)-**L-8** and phenol **P-47** for 24 h at room temperature afforded the product **3r** in 91% yield with 12:88 er. R_f = 0.30 (hexane:EtOAc 4:1). Spectral data for **3r**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.40 (s, 9H), 3.26 (d, 2H, *J* = 13.5 Hz), 3.76 (s, 6H), 3.81 (d, 2H, *J* = 13.5 Hz), 4.30 (s, 1H), 6.90 (d, 4H, *J* = 9.0 Hz), 7.18 (brs, 1H), 7.25 (d, 4H, *J* = 8.5 Hz), 7.28-7.42 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.78, 50.84, 53.58, 55.20, 67.95, 113.87, 127.55, 128.00, 129.69, 130.29, 130.68, 134.60, 158.78, 170.77; MS (EI) 346 (M^+-100, 32.94), 121 (100); IR (thin film) 3348(w), 2963(w), 1680(s), 1512(s) cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{35}N_2O_3$ *m/z* 447.2648 ($[M+H]^+$), meas 447.2631. $[\alpha]_D^{20}$ = +19.8 (c 1.0, CH_2Cl_2) on 85:15 *er* material.



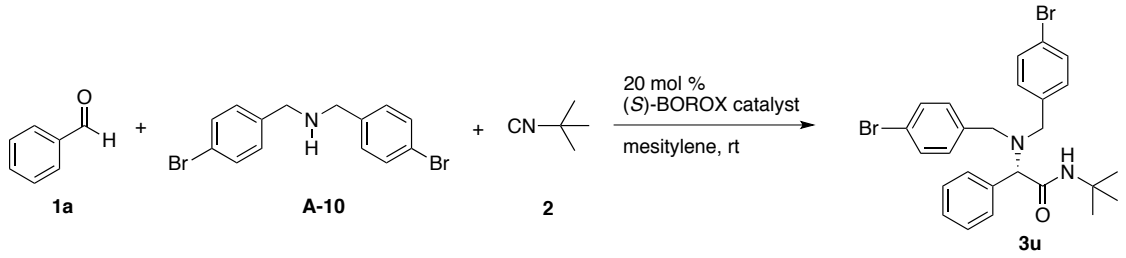
(S)-2-(bis(4-fluorobenzyl)amino)-N-(tert-butyl)-2-phenylacetamide ***3s***: The general procedure A described in **Part V** was followed with ligand (*S*)-**L-8** (41.5 mg, 0.05 mmol), phenol **P-36** (14 mg, 0.10 mmol), amine **A-8** (119 mg, 0.51 mmol) and mesitylene (1 mL) as the solvent with a reaction time of 39 h. After purification by column chromatography (silica gel, 18 × 200 mm, hexane:EtOAc 15:1), the product **3s** was obtained as a yellow foamy-solid (95.2 mg, 0.225 mmol, 88%). The optical purity was determined to be 86:14 *er* by HPLC analysis (Chiralpak AD column, hexanes/2-propanol 98:2, 222 nm, flow 1 mL). Retention times: R_t = 10.25 min (major enantiomer) and R_t = 27.23 min (minor enantiomer); mp 105-107 °C; A reaction that was run according to general procedure B (described in **Part XII**) with (*R*)-**L-8** and phenol **P-47** for 24 h at room temperature afforded the product **3s** in 85% yield with 10:90 er. R_f = 0.40 (hexane:EtOAc 4:1). Spectral data for **3s**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.38 (s, 9H), 3.38 (d, 2H, *J* = 14.0 Hz), 3.74 (d, 2H, *J* = 14.0 Hz), 4.20 (s, 1H), 6.66 (brs, 1H), 6.96-7.20 (m, 4H), 7.20-7.38 (m, 9H); ^{13}C

NMR (125 MHz, $CDCl_3$) δ 28.79, 51.12, 53.70, 68.28, 115.34 (*J* = 21.13 Hz), 127.85, 128.26, 129.90, 130.06 (*J* = 7.75 Hz), 134.46 (*J* = 3.3 Hz), 135.03, 162.03 (*J* = 244.6 Hz), 170.50; IR (thin film) 3339(w), 2968(w), 1684(s), 1508(s) cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{29}F_2N_2O$ *m/z* 423.2248 ($[M+H]^+$), meas 423.2268. $[\alpha]_D^{20}$ = +29.8 (c 1.0, CH_2Cl_2) on 86:14 *er* material.



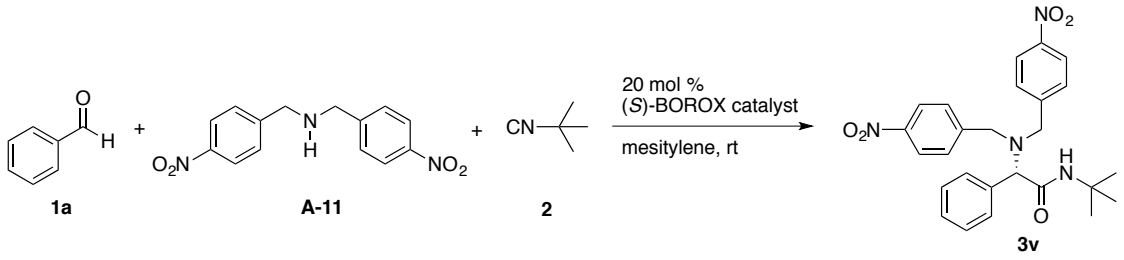
1a **A-9** **2** **3t**

(S)-2-(bis(4-chlorobenzyl)amino)-N-(tert-butyl)-2-phenylacetamide ***3t***: The general procedure A described in **Part V** was followed with ligand (*S*)-**L-8** (41.5 mg, 0.05 mmol), phenol **P-36** (14 mg, 0.10 mmol), amine **A-9** (135 mg, 0.51 mmol) and mesitylene (1 mL) as the solvent with a reaction time of 39 h. After purification by column chromatography (silica gel, 20 × 200 mm, hexane:EtOAc 15:1), the product **3t** was obtained as a white foamy-solid (105 mg, 0.23 mmol, 90%). The optical purity was determined to be 85:15 *er* by HPLC analysis (Chiralpak AD column, hexanes/2-propanol 98:2, 222 nm, flow 1 mL). Retention times: R_t = 9.35 min (major enantiomer) and R_t = 36.82 min (minor enantiomer); mp 105-106 °C, A reaction that was run according to general procedure B (described in **Part XII**) with (*R*)-**L-8** and phenol **P-47** for 24 h at room temperature afforded the product **3t** in 80% yield with 12:88 er. R_f = 0.50 (hexane:EtOAc 4:1). Spectral data for **3t**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.40 (s, 9H), 3.44 (d, 2H, *J* = 14.1 Hz), 3.78 (d, 2H, *J* = 14.1 Hz), 4.23 (s, 1H), 6.60 (brs, 1H), 7.22-7.46 (m, 13H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.75, 51.17, 53.77, 68.16, 127.90, 128.28, 128.64, 129.78, 129.82, 132.96, 134.91, 137.20, 170.41; IR (thin film) 3337(w), 2966(w), 1668(s), 1491(s) cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{29}{}^{35}Cl_2N_2O$ *m/z* 455.1657 ($[M+H]^+$), meas 455.1680. $[\alpha]_D^{20}$ = +30.8 (c 1.0, CH_2Cl_2) on 85:15 *er* material.



1a **A-10** **2** **3u**

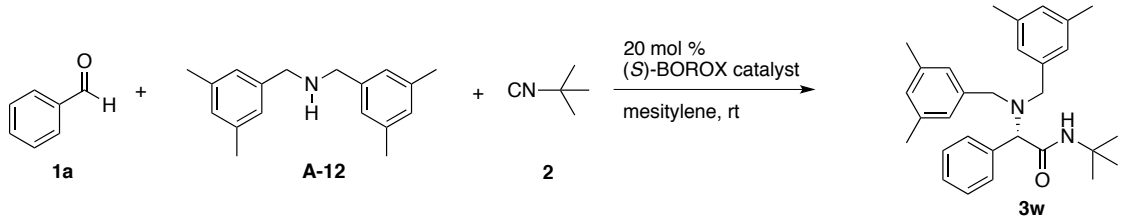
(S)-2-(bis(4-bromobenzyl)amino)-N-(tert-butyl)-2-phenylacetamide ***3u***: The general procedure A described in **Part V** was followed with ligand (*S*)-**L-8** (41.5 mg, 0.05 mmol), phenol **P-36** (14 mg, 0.10 mmol), amine **A-10** (178 mg, 0.50 mmol) and mesitylene (1 mL) as the solvent with a reaction time of 37 h. After purification by column chromatography (silica gel, 20 × 200 mm, hexane:EtOAc 15:1), the product **3u** was obtained as a white foamy-solid (119 mg, 0.219 mmol, 86%). The optical purity was determined to be 83:17 *ee* by HPLC analysis (Chiralpak AD column, hexanes/2-propanol 98:2, 222 nm, flow 1 mL); Retention times: R_t = 9.87 min (major enantiomer) and R_t = 45.29 min (minor enantiomer). Mp 108-109 °C; A reaction that was run according to general procedure B (described in **Part XII**) with (*R*)-**L-8** and phenol **P-47** for 24 h at room temperature afforded the product **3u** in 79% yield with 13:87 er. R_f = 0.50 (hexane:EtOAc 4:1); Spectral data for **3u**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.40 (s, 9H), 3.41 (d, 2H, *J* = 14.5 Hz), 3.74 (d, 2H, 14.0 Hz), 4.20 (s, 1H), 6.50 (brs, 1H), 7.14-7.24 (m, 4H), 7.26-7.40 (m, 5H), 7.42-7.52 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.50, 50.94, 53.61, 67.98, 120.79, 127.66, 128.04, 129.48, 129.94, 131.33, 134.77, 137.51, 179.10; IR (thin film) 3337(w), 2966(w), 1669(s), 1487(s) cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{29}{}^{79}Br_2N_2O$ *m/z* 543.0647 ([M+H]$^+$), meas 543.0645. $[\alpha]_D^{20}$ = +27.1 (c 1.0, CH_2Cl_2) on 83:17 *er* material.



1a **A-11** **2** **3v**

(S)-2-(bis(4-nitrobenzyl)amino)-N-(tert-butyl)-2-phenylacetamide ***3v***: The general procedure A described in **Part V** was followed with ligand (*S*)-**L-8** (41.5 mg, 0.05 mmol), phenol **P-36** (14

mg, 0.10 mmol), amine **A-11** (144 mg, 0.50 mmol) and mesitylene (1 mL) as the solvent with a reaction time of 37 h. After purification by column chromatography (silica gel, 20 × 200 mm, hexane:EtOAc 3:1), the product **3v** was obtained as a yellow oil (26 mg, 0.055 mmol, 22%). The optical purity was determined to be 67:33 *er* by HPLC analysis (Pirkle Covalent (*R*,*R*) WHELK-O1 column, hexanes/2-propanol 90:10, 222 nm, flow 1 mL); Retention times: R_t = 51.63 min (major enantiomer) and R_t = 65.73 min (minor enantiomer). A reaction that was run according to general procedure B (described in **Part XII**) with (*R*)-**L-8** and phenol **P-47** for 24 h at room temperature afforded the product **3v** in 22% ^{1}H NMR yield with 27:73 er. R_f = 0.18 (hexane:EtOAc 3:1); Spectral data for **3v**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.37 (s, 9H), 3.73 (d, 2H, *J* = 14.8 Hz), 3.98 (d, 2H, *J* = 14.8 Hz), 4.16 (s, 1H), 5.73 (s, 1H), 7.30-7.40 (m, 5H), 7.47 (d, 4H, *J* = 9.0 Hz), 8.16 (d, 4H, *J* = 9.0 Hz); Unfortunately, the product as obtained was contaminated with some impurities. Thus, a clean ^{13}C NMR could not be obtained. HRMS (ESI) calcd for $C_{26}H_{29}N_4O_5$ *m/z* 477.2138 ($[M+H]^+$), meas 477.2134.

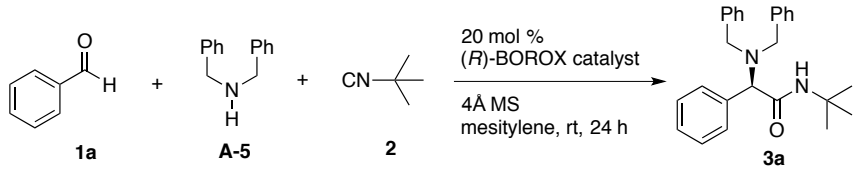


(S)-2-(bis(3,5-dimethylbenzyl)amino)-N-(tert-butyl)-2-phenylacetamide ***3w***: The general procedure A described in **Part V** was followed with ligand (*S*)-**L-8** (41.5 mg, 0.05 mmol), phenol **P-36** (14 mg, 0.10 mmol), amine **A-12** (130 mg, 0.51 mmol) and mesitylene (1 mL) as the solvent with a reaction time of 39 h. After purification by column chromatography (silica gel, 20 × 200 mm, hexane:EtOAc 15:1), the product **3w** was obtained as a yellow oil (74 mg, 0.167 mmol, 65%). The optical purity was determined to be 61:39 *er* by HPLC analysis (Pirkle Covalent (*R*,*R*) WHELK-O1 column, hexanes/2-propanol 95:5, 222 nm, flow 0.7 mL); Retention times: R_t = 39.43 min (major enantiomer) and R_t = 58.69 min (minor enantiomer). R_f = 0.17 (hexane:EtOAc 10:1); Spectral data for **3w**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (s, 9H), 2.31 (s, 12H), 3.14 (d, 2H, *J* = 14.0 Hz), 3.75 (d, 2H, 14.0 Hz), 4.32 (s, 1H), 6.90 (s, 2H), 6.94 (s, 4H), 7.22-7.28 (m, 2H), 7.29-7.34 (m,

1H), 7.35-7.40 (m, 2H), 7.59 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.30, 28.80, 50.78, 54.59, 68.02, 126.49, 127.52, 127.96, 128.80, 130.58, 134.13, 137.92, 138.71, 170.81; IR (thin film) 3343(w), 2963(m), 2919 (m), 1684(s), 1507(s), 1453 (s) cm^{-1}; HRMS (ESI) calcd for $C_{30}H_{39}N_2O$ *m/z* 443.3062 ($[M+H]^+$), meas 443.3058. $[\alpha]_D^{20}$ = +5.2 (c 1.0, CH_2Cl_2) on 61:39 *er* material.

XII. Formation of α-amino amides 3a—3q with General Procedure B (Table 4)

*General procedure B for the catalytic asymmetric Ugi reaction – Illustrated for the synthesis of (R)-N-(tert-butyl)-2-(dibenzylamino)-2-(phenyl)acetamide **3a** (Table 4, entry 1):*



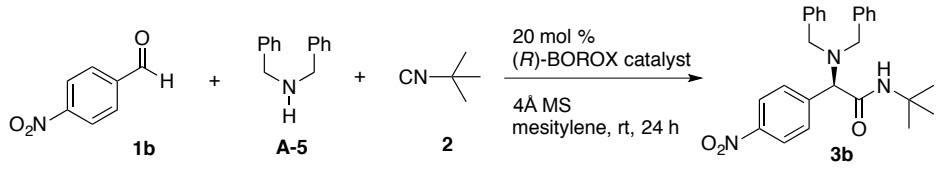
1a **A-5** **2** **3a**

Preparation of catalyst stock solution: A 25 mL Schlenk flask equipped with a stir bar was flame dried, cooled to rt under N_2 and charged with (*R*)-**L-8** (128 mg, 0.156 mmol), **P-47** (49 mg, 0.32 mmol), H_2O (8.3 mg, 8.3 µL, 0.46 mmol), dry toluene (4.6 mL) and BH_3•SMe_2 (2M, 232.5 µL, 0.465 mmol). The Teflon valve on the Schlenk flask was then closed, and the mixture heated at 100 ° C for 1 h. After the flask was cooled to rt, the valve was carefully opened to gradually apply high vacuum (0.1 mm Hg) and the solvent and volatiles were removed. Then the flask was heated at 100 °C under high vacuum for 30 min. Dry mesitylene (3.04 mL) was added to dissolve the residue in the flask after it was cooled to room temperature.

*Catalytic asymmetric Ugi reaction with benzaldehyde **1a**:* A 25 mL Schlenk flask charged with 4Å powdered molecular sieves (13 mg) and equipped with a magnetic stir bar was flame dried under high vacuum and cooled down under nitrogen. To the flask was then added 1.0 mL of the catalyst stock solution (20 mol% catalyst, 0.05 mmol) via a plastic syringe fitted with a metallic needle. To the resulting solution was added dibenzylamine **A-5** (0.10 mL, 0.52 mmol, 2.0 equiv) under a N_2 stream, followed by the addition of benzaldehyde **1a** (26.0 µL, 0.255 mmol, 1.00 equiv) and then *t*-butyl isocyanide (45 µL, 0.39 mmol, 1.5 equiv). The Teflon valve was then closed, and the resulting mixture was stirred at rt for 24 h. Upon completion, 8 µL H_2O was added to the reaction flask. After the mixture was stirred vigorously at room temperature for another 5

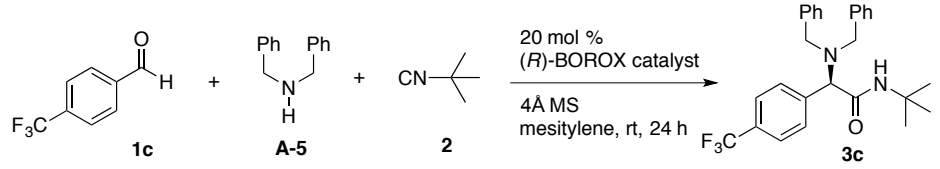
min, it was directly loaded onto a silica gel column (20 mm x 160 mm) with a pipette. Purification by column chromatography (1st column, 20 × 160 mm, hexanes:EtOAc 15:1; 2nd column, 20 × 160 mm, hexanes/CH_2Cl_2 1:1 as eluent untill all the phenol **P-47** came out, then EtOAc/hexanes 1:5 as eluent) gave product **3a** as a white solid (85 mg, 0.22 mmol) in 86% yield. The optical purity was determined to be 91:9 *er* by HPLC analysis (Pirkle Covalent (*R*,*R*) WHELK-O1 column, hexanes/2-propanol 90:10, 222 nm, flow 1 mL/min). Retention times: R_t = 12.77 min (minor enantiomer) and R_t = 16.45 min (major enantiomer). The product **3a** (85 mg, 0.22 mmol) was recrystallized from hexanes/EtOAc (15:1, 0.8 mL) at room temperature to give colorless crystals of **3a** (60.5 mg, 0.157 mmol) with >99.5:0.5 er and in 71% recovery. A reaction that was run at 40 °C for 7 h afforded the product **3a** in 87% NMR yield with 86:14 er. A reaction that was run at 0 °C for 66 h afforded the product **3a** (74 mg, 0.19 mmol) in 75% isolated yield with 92:8 er. mp 136-137 °C; R_f = 0.40 (hexane: EtOAc 4:1). Spectral data for **3a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.38 (s, 9H), 3.33 (d, 2H, *J* = 14.0 Hz), 3.81 (d, 2H, *J* = 14.0 Hz), 4.28 (s, 1H), 7.10 (brs, 1H), 7.20-7.42 (m, 15H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.81, 50.97, 54.55, 68.14, 127.27, 127.67, 128.09, 128.53, 128.61, 130.31, 134.55, 138.79, 170.65; MS (EI) 386 (M, 0.23), 314 (M-72, 1.30), 286 (M-100, 89.80), 91 (M-295, 100); IR (thin film) 3343(w), 2966(w), 1684(s) cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{31}N_2O$ *m/z* 387.2431 ($[M+H]^+$), meas 387.2461. $[\alpha]_D^{20}$ = – 34.5° (*c* 1.0, CH_2Cl_2) on >99.5:0.5 *er* material.

*Recovery of the ligand (R)-**L-8**:* The fractions containing the ligand (*R*)-**L-8** obtained from the purification of **3a** were combined and concentrated to dryness to give an orange foamy solid (49 mg), the ^{1}H NMR spectrum of which showed that the ligand was contaminated with a small amount of impurities that were not identified. This solid was purified by column chromatography on silica gel (20 × 150 mm, hexanes:EtOAc 30:1) to give *(R)-**L-8*** as an off-white foamy solid (37 mg, 0.045 mmol) in 90% recovery with > 99% *ee*. If the fractions containing the ligand are allowed to stay at room temperature for several days before purification, a decrease in the *ee* of the recovered *(R)-**L-8*** can be observed.



1b **A-5** **2** **3b**

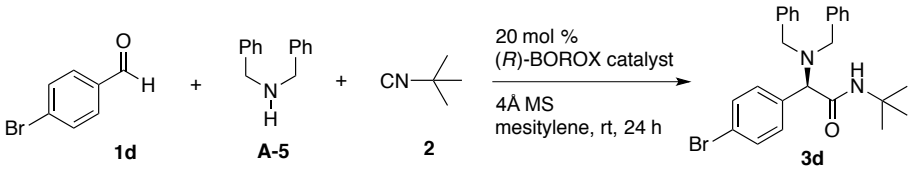
*(R)-N-(tert-butyl)-2-(dibenzylamino)-2-(4-nitrophenyl)acetamide **3b**:* The general procedure B for the catalytic asymmetric Ugi reaction described in **Part XII** was followed with 4-nitrobenzaldehyde **1b** (38.5 mg, 0.255 mmol, 1.00 equiv) with a reaction time of 24 h. The crude product was purified by column chromatography on silica gel (1st column, 20 × 160 mm, hexanes:EtOAc 15:1**;** 2nd column, 20 × 160 mm EtOAc/hexanes 1:8 as eluent) to afford the product **3b** as a yellow oil (91 mg, 0.21 mmol) in a yield of 83%. The optical purity was determined to be 93:7 *er* by HPLC analysis (Pirkle Covalent (*R*,*R*) WHELK-O1 column, hexanes/2-propanol 90:10, 222 nm, flow 1 mL). Retention times: R_t = 23.87 min (minor enantiomer) and R_t = 31.55 min (major enantiomer); A reaction that was run at 0 °C for 66 h afforded the product **3a** in 51% NMR yield with 92:8 er. R_f = 0.17 (hexane: EtOAc 8:1). Spectral data for **3b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (s, 9H), 3.27 (d, 2H, *J* = 14.0 Hz), 3.85 (d, 2H, *J* = 14.0 Hz), 4.39 (s, 1H), 7.09 (brs, 1H), 7.26-7.41 (m, 10H), 7.46 (d, 2H, *J* = 9.0 Hz), 8.23 (d, 2H, *J* = 9.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.76, 51.29, 54.69, 67.17, 123.12, 127.65, 128.43, 128.75, 131.22, 137.99, 141.91, 147.40, 169.24; IR (thin film) 3351(w), 2969(w), 1680(s), 1520(s), 1348(s) cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{30}N_3O_3$ *m/z* 432.2287 ($[M+H]^+$), meas 432.2283. $[\alpha]_D^{20}$ = – 92.3° (*c* 1.0, CH_2Cl_2) on 93:7 *er* material.



1c **A-5** **2** **3c**

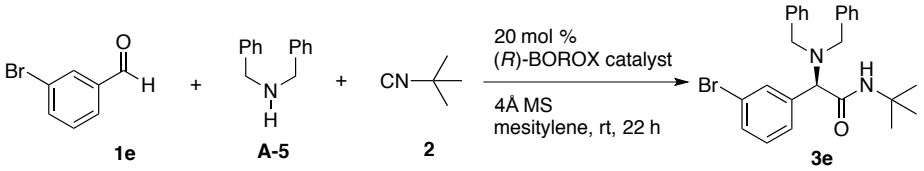
*(R)-N-(tert-butyl)-2-(dibenzylamino)-2-(4-trifluoromethylphenyl)acetamide **3c**:* The general procedure B for the catalytic asymmetric Ugi reaction described in **Part XII** was followed with *4-trifluoromethyl*benzaldehyde **1c** (35 μL, 0.256 mmol, 1.00 equiv) with a reaction time of 24 h. The crude product was purified by column chromatography on silica gel (20 × 160 mm, hexanes:EtOAc 15:1) to give pure product **3c** as a off-white semi-solid (91.6 mg, 0.202 mmol) in

a yield of 79% along with fractions containing a mixture of **3c** and phenol **P-47**. This mixture was loaded onto a silica gel column (20 × 160 mm, hexanes:EtOAc 15:1) and eluted to give additional product **3c** (7.40 mg, 0.016 mmol) in a yield of 6%. The combined yield of **3c** was 85%. The optical purity was determined to be 91:9 *er* by HPLC analysis (Pirkle Covalent (*R*,*R*) WHELK-O1 column, hexanes/2-propanol 90:10, 222 nm, flow 1 mL). Retention times: R_t = 9.70 min (minor enantiomer) and R_t = 13.94 min (major enantiomer); R_f = 0.43 (hexanes: EtOAc 3:1). Spectral data for **3c**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.40 (s, 9H), 3.28 (d, 2H, *J* = 14.0 Hz), 3.83 (d, 2H, *J* = 14.0 Hz), 4.34 (s, 1H), 7.10 (brs, 1H), 7.25-7.37 (m, 10H), 7.39 (d, 2H, *J* = 8.0 Hz), 7.63 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.81, 51.19, 54.69, 67.61, 124.15 (q, *J* = 271.8 Hz), 125.00 (q, *J* = 3.8 Hz), 127.53, 128.52, 128.70, 129.92 (q, *J* = 32.4 Hz), 130.73, 138.35, 138.44, 169.81; IR (thin film) 3343(w), 2969(w), 1682(s), 1325(s) cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{30}F_3N_2O$ *m/z* 455.2310 ([M+H]$^+$), meas 455.2311. $[\alpha]_D^{20}$ = – 33.8° (*c* 1.0, CH_2Cl_2) on 91:9 *er* material.

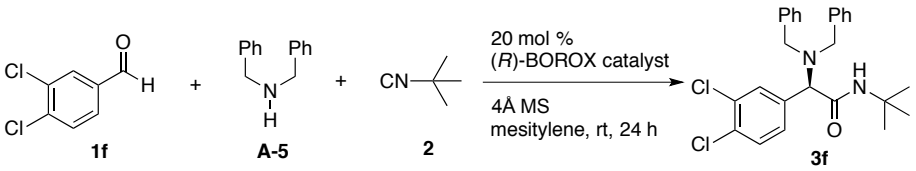


(R)-N-(tert-butyl)-2-(dibenzylamino)-2-(4-bromophenyl)acetamide ***3d****:* The general procedure B for the catalytic asymmetric Ugi reaction described in **Part XII** was followed with 4-bromobenzaldehyde **1d** (47.1 mg, 0.255 mmol, 1.00 equiv) with a reaction time of 24 h. The crude product was purified on silica gel according to the standard procedure (1st column, 20 × 160 mm, hexanes:EtOAc 15:1; 2nd column, 20 × 160 mm, hexanes/CH_2Cl_2 1:1 as eluent untill all the phenol **P-47** came out, then EtOAc/hexanes 1:5 as eluent) to afford the product **3d** as a colorless oil (100.5 mg, 0.216 mmol) in a yield of 85%. The optical purity was determined to be 93:7 *er* by HPLC analysis (Pirkle Covalent (*R*,*R*) WHELK-O1 column, hexanes/2-propanol 90:10, 222 nm, flow 1 mL). Retention times: R_t = 14.82 min (minor enantiomer) and R_t = 22.53 min (major enantiomer); R_f = 0.14 (hexane: EtOAc 15:1). A reaction that was run at 0 °C for 48 h afforded the product **3d** (77.2 mg, 0.166 mmol) in a yield of 65% with 95:5 er. Spectral data for **3d**: ^{1}H NMR

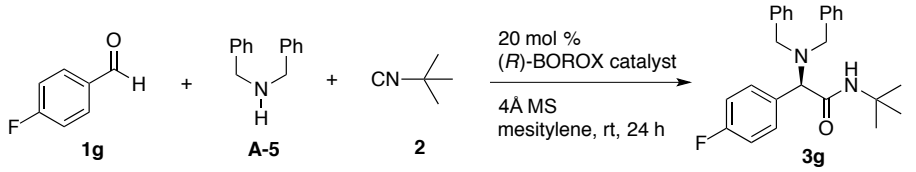
(500 MHz, $CDCl_3$) δ 1.39 (s, 9H), 3.27 (d, 2H, *J* = 14.0 Hz), 3.80 (d, 2H, *J* = 14.0 Hz), 4.25 (s, 1H), 7.11 (brs, 1H), 7.13-7.17 (m, 2H), 7.24-7.29 (m, 2H), 7.29-7.37 (m, 8H), 7.47-7.52 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.79, 51.07, 54.54, 67.37, 121.85, 127.43, 128.52, 128.64, 131.22, 132.04, 133.29, 138.46, 170.06; IR (thin film) 3345(w), 2967(w), 1684(s), 1507(s), 1453(m), 698(m) cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{30}{}^{79}BrN_2O$ *m/z* 465.1542 ($[M+H]^+$), meas 465.1540. $[\alpha]_D^{20}$ = – 68.3° (*c* 1.0, CH_2Cl_2) on 95:5 *er* material.



(R)-N-(tert-butyl)-2-(dibenzylamino)-2-(3-bromophenyl)acetamide ***3e****:* The general procedure B for the catalytic asymmetric Ugi reaction described in **Part XII** was followed with 3-bromobenzaldehyde **1e** (47.2 mg, 0.255 mmol, 1.00 equiv) with a reaction time of 22 h. The crude product was purified on silica gel according to the standard procedure (1st column, 20 × 160 mm, hexanes:EtOAc 15:1; 2nd column, 20 × 180 mm, hexanes/CH_2Cl_2 1:1 as eluent untill all the phenol **P-47** came out, then EtOAc/hexanes 1:5 as eluent) to afford the product **3e** as a colorless oil (98 mg, 0.21 mmol) in a yield of 82%. The optical purity was determined to be 93:7 *er* by HPLC analysis (Pirkle Covalent (*R*,*R*) WHELK-O1 column, hexanes/2-propanol 90:10, 222 nm, flow 1 mL). Retention times: R_t = 13.57 min (minor enantiomer) and R_t = 17.64 min (major enantiomer); A reaction that was run at 0 °C for 66 h at 0.4 M afforded the product **3e** (78.0 mg, 0.168 mmol) in a yield of 66% with 92:8 *er*. R_f = 0.28 (hexane: EtOAc 8:1). Spectral data for **3e**: ^1H NMR (500 MHz, $CDCl_3$) δ 1.41 (s, 9H), 3.30 (d, 2H, *J* = 13.5 Hz), 3.82 (d, 2H, *J* = 13.5 Hz), 4.23 (s, 1H), 7.11 (brs, 1H), 7.20-7.39 (m, 12H), 7.41 (s, 1H), 7.46 (d, 1H, *J* = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.79, 51.09, 54.59, 67.49, 122.23, 127.45, 128.55, 128.65, 129.00, 129.59, 130.83, 133.30, 136.62, 138.41, 169.86; IR (thin film) 3345(w), 2967(w), 1682(s), 1506(s), 1453(s) cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{30}{}^{79}BrN_2O$ *m/z* 465.1542 ($[M+H]^+$), meas 465.1536. $[\alpha]_D^{20}$ = – 43.1° (*c* 1.0, CH_2Cl_2) on 93:7 *er* material.

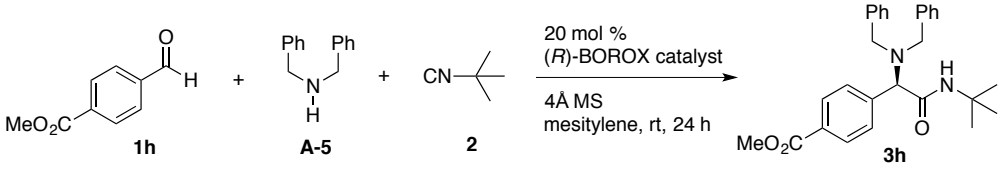


(R)-N-(tert-butyl)-2-(dibenzylamino)-2-(3,4-dichlorolphenyl)acetamide ***3f****:* The general procedure B for the catalytic asymmetric Ugi reaction described in **Part XII** was followed with 3-bromobenzaldehyde **1f** (44.5 mg, 0.255 mmol, 1.00 equiv) with a reaction time of 24 h. The crude product was purified on silica gel according to the standard procedure (1st column, 20 × 160 mm, hexanes:EtOAc 15:1; 2nd column, 20 × 180 mm, hexanes/CH_2Cl_2 1:1 as eluent untill all the phenol **P-47** came out, then EtOAc/hexanes 1:5 as eluent) to afford the product **3f** as a colorless semi-solid (98.7 mg, 0.217 mmol) in a yield of 85%. The optical purity was determined to be 94:6 *er* by HPLC analysis (Pirkle Covalent (*R*,*R*) WHELK-O1 column, hexanes/2-propanol 90:10, 222 nm, flow 1 mL). Retention times: R_t = 12.31 min (minor enantiomer) and R_t = 17.81 min (major enantiomer); R_f = 0.18 (hexane: EtOAc 10:1). A reaction that was run at 0 °C for 66 h afforded the product **3f** with 95:5 er in a yield of 54% as determined by ^{1}HNMR with the aid of an internal standard (Ph_3CH). Spectral data for **3f**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39 (s, 9H), 3.28 (d, 2H, *J* = 13.5 Hz), 3.80 (d, 2H, *J* = 13.5 Hz), 4.23 (s, 1H), 7.05 (brs, 1H), 7.11 (dd, 1H, *J* = 8.3 Hz, 1.8 Hz), 7.25-7.39 (m, 11H) 7.43 (d, 1H, *J* = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.80, 51.19, 54.67, 67.02, 127.56, 128.52, 128.72, 129.71, 129.98, 131.93, 132.25, 132.28, 134.57, 138.25, 169.52; IR (thin film) 3349(w), 2969(w), 1682(s), 1509(s), 733(m), 698(m) cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{29}{}^{35}Cl_2N_2O$ *m/z* 455.1657 ($[M+H]^+$), meas 455.1658. $[\alpha]_D^{20}$ = – 65.6° (*c* 1.0, CH_2Cl_2) on 94:6 *er* material.



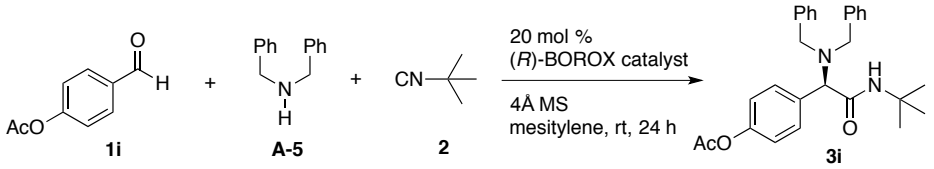
(R)-N-(tert-butyl)-2-(dibenzylamino)-2-(4-fluorophenyl)acetamide ***3g****:* The general procedure B for the catalytic asymmetric Ugi reaction described in **Part XII** was followed with 4-fluorobenzaldehyde **1g** (31.7 mg, 28 μL, 0.255 mmol, 1.00 equiv) with a reaction time of 24 h.

The crude product was purified on silica gel according to the standard procedure (1st column, 20 × 160 mm, hexanes:EtOAc 15:1; 2nd column, 20 × 150 mm, hexanes/CH_2Cl_2 1:1 as eluent untill all the phenol **P-47** came out, then EtOAc/hexanes 1:5 as eluent) to afford the product **3g** as a colorless oil (89.7 mg, 0.22 mmol) in a yield of 87%. The optical purity was determined to be 91:9 *er* by HPLC analysis (Pirkle Covalent (*R*,*R*) WHELK-O1 column, hexanes/2-propanol 90:10, 222 nm, flow 1 mL). Retention times: R_t = 11.97 min (minor enantiomer) and R_t = 15.26 min (major enantiomer); A reaction that was run at 0 °C for 67 h afforded the product **3g** (63.9 mg, 0.158 mmol) in a yield of 62% with 94:6 er. R_f = 0.19 (hexanes: EtOAc 10:1). Spectral data for **3g**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39 (s, 9H), 3.29 (d, 2H, *J* = 13.8 Hz), 3.80 (d, 2H, *J* = 13.8 Hz), 4.27 (s, 1H), 7.02-7.09 (m, 2H), 7.12 (brs, 1H), 7.21-7.28 (m, 4H), 7.29-7.37 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.77, 51.01, 54.52, 67.22, 114.97 (d, *J* = 21.0 Hz), 127.38, 128.50, 128.60, 129.95 (d, *J* = 3.0 Hz), 131.98 (d, *J* = 7.9 Hz), 138.53, 162.28 (d, *J* = 245.8 Hz), 170.39; IR (thin film) 3345(w), 2967(w), 1682(s), 1509(s), 1227(s) cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{30}FN_2O$ *m/z* 405.2342 ($[M+H]^+$), meas 405.2341. $[\alpha]_D^{20}$ = –21.0 ° (*c* 1.0, CH_2Cl_2) on 94:6 *er* material.

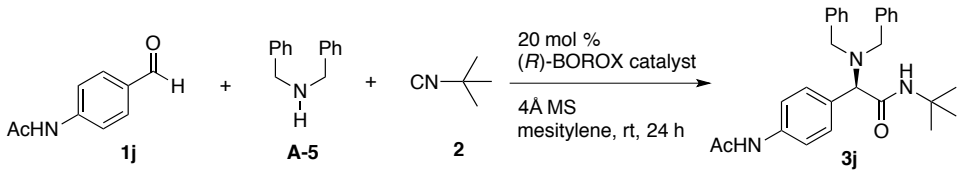


*Methyl (R)-4-(2-(tert-butylamino)-1-(dibenzylamino)-2-oxoethyl)benzoate **3h**:* The general procedure B for the catalytic asymmetric Ugi reaction described in **Part XII** was followed with methyl-4-formylbenzoate **1h** (42.0 mg, 0.255 mmol, 1.00 equiv) with a reaction time of 24 h. The crude product was purified by column chromatography on silica gel (20 × 160 mm, hexanes:EtOAc 15:1➔7.5:1➔5:1) to afford the product **3h** as a colorless semisolid (90.7 mg, 0.204 mmol) in a yield of 80%. The optical purity was determined to be 93:7 *er* by HPLC analysis (Pirkle Covalent (*R*,*R*) WHELK-O1 column, hexanes/2-propanol 75:25, 222 nm, flow 2 mL). Retention times: R_t = 7.84 min (minor enantiomer) and R_t = 11.73 min (major enantiomer); A reaction that was run at 0 °C for 67 h afforded the product **3g** (70 mg, 0.157 mmol) in a yield of 62% with 93:7 er. R_f = 0.34 (hexanes: EtOAc 3:1). Spectral data for **3h**: ^{1}H NMR (500 MHz,

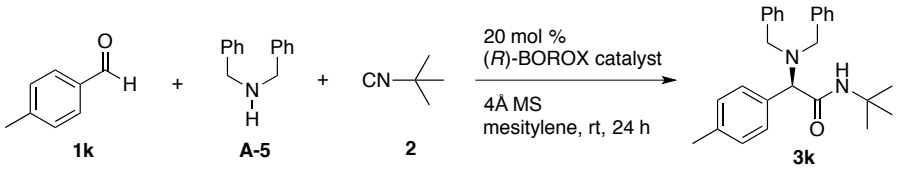
$CDCl_3$) δ 1.39 (s, 9H), 3.28 (d, 2H, *J* = 13.8 Hz), 3.82 (d, 2H, *J* = 13.8 Hz), 3.91 (s, 3H), 4.33 (s, 1H), 7.07 (brs, 1H), 7.24-7.28 (m, 2H), 7.29-7.38 (m, 10H), 8.02-8.06 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.77, 51.11, 52.12, 54.56, 67.62, 127.45, 128.52, 128.63, 129.30, 129.44, 130.34, 138.35, 139.65, 166.90, 169.95; IR (thin film) 3370(w), 2963(w), 1725(s), 1680(s), 1281(s), 1111(m) cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{33}N_2O_3$ *m/z* 445.2491 ($[M+H]^+$), meas 445.2486. $[\alpha]_D^{20}$ = – 64.3° (*c* 1.0, CH_2Cl_2) on 93:7 *er* material.



(R)-4-(2-(tert-butylamino)-1-(dibenzylamino)-2-oxoethyl)phenyl acetate ***3i****:* The general procedure B for the catalytic asymmetric Ugi reaction described in **Part XII** was followed with 4-acetoxybenzaldehyde **1i** (42.0 mg, 0.255 mmol, 1.00 equiv) with a reaction time of 24 h. The crude product was purified by column chromatography on silica gel (1st column, 20 × 160 mm, hexanes:EtOAc 15:1➔7.5:1➔5:1; 2nd column, 2nd column, 20 × 150 mm, hexanes:EtOAc 4:1) to afford the product **3i** as a yellow viscous oil (98.6 mg, 0.22 mmol) in a yield of 86%. The optical purity was determined to be 85:15 *er* by HPLC analysis (Pirkle Covalent (*R,R*) WHELK-O1 column, hexanes/2-propanol 75:25, 222 nm, flow 2 mL). Retention times: R_t = 10.49 min (minor enantiomer) and R_t = 13.12 min (major enantiomer); R_f = 0.31 (hexanes: EtOAc 3:1). Spectral data for **3i**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39 (s, 9H), 2.29 (s, 3H), 3.35 (d, 2H, *J* = 13.8 Hz), 3.81 (d, 2H, *J* = 13.8 Hz), 4.28 (s, 1H), 7.06 (brs, 1H), 7.08-7.12 (m, 2H), 7.23-7.30 (m, 4H), 7.31-7.35 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.17, 28.80, 51.03, 54.50, 67.36, 121.13, 127.33, 128.56, 128.58, 131.30, 131.95, 138.70, 150.20, 169.26, 170.38; IR (thin film) 3374(w), 2965(w), 1763(s), 1680(s), 1505(s), 1202(s) cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{33}N_2O_3$ *m/z* 445.2491 ($[M+H]^+$), meas 445.2490. $[\alpha]_D^{20}$ = – 31.6° (*c* 1.0, CH_2Cl_2) on 85:15 *er* material.



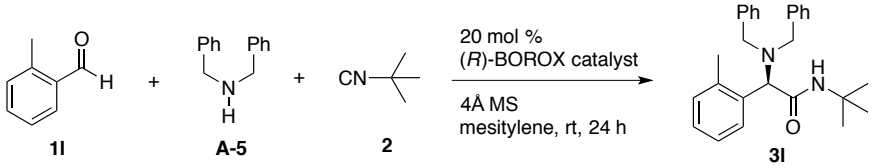
(R)-2-(4-Acetamidophenyl)-N-(tert-butyl)-2-(dibenzylamino)acetamide ***3j****:* The general procedure B for the catalytic asymmetric Ugi reaction described in **Part XII** was followed with 4-acetaminobenzaldehyde **1j** (41.6 mg, 0.255 mmol, 1.00 equiv) with a reaction time of 24 h. The crude product was purified by column chromatography on silica gel (20 × 160 mm, hexanes:EtOAc 3:1➔1:1) to afford the product **3j** as a white solid (87.0 mg, 0.196 mmol) in a yield of 77%. The optical purity was determined to be 85:15 *er* by HPLC analysis (Pirkle Covalent (*R*,*R*) WHELK-O1 column, hexanes/2-propanol 75:25, 254 nm, flow 2 mL). Retention times: R_t = 15.33 min (minor enantiomer) and R_t = 18.83 min (major enantiomer); The product was extracted with Et_2O to give **3j** as an off-white foamy solid with 96:14 *er* in 47% recovery. This material contains a very small amount of impurities. The precipitate that remained after the extraction was pure *rac*-**3j**. R_f = 0.12 (hexanes: EtOAc 1:1). Spectral data for (±)-**3j**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.40 (s, 9H), 2.04(s, 3H), 3.19 (d, 2H, *J* = 13.9 Hz), 3.78 (d, 2H, *J* = 13.9 Hz), 4.23 (s, 1H), 7.05 (d, 2H, *J* = 7.5 Hz), 7.24-7.36 (m, 12H), 7.55 (s, 1H), 8.27 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.20, 28.81, 51.01, 54.60, 67.65, 119.85, 127.38, 128.55, 128.63, 129.14, 130.83, 137.72, 138.57, 168.62, 171.09; IR (thin film) 3312(m), 2969(w), 1663(s), 1514(s) cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{34}N_3O_2$ *m/z* 444.2651 ($[M+H]^+$), meas 444.2654.



1k **A-5** **2** **3k**

(R)-N-(tert-butyl)-2-(dibenzylamino)-2-(4-methyl)acetamide ***3k****:* The general procedure B for the catalytic asymmetric Ugi reaction described in **Part XII** was followed with p-tolualdehyde **1k** (30.6 mg, 30 μL, 0.255 mmol, 1.00 equiv) with a reaction time of 24 h. The crude product was purified on silica gel according to the standard procedure (1st column, 20 × 160 mm, hexanes:EtOAc 15:1; 2nd column, 20 × 150 mm, hexanes/CH_2Cl_2 1:1 as eluent untill all the phenol **P-47** came out, then EtOAc/hexanes 1:5 as eluent) to afford the product **3k** as a colorless semi-solid (85.7 mg, 0.214 mmol) in a yield of 84%. The optical purity was determined to be 91:9 *er* by HPLC analysis (Pirkle Covalent (*R*,*R*) WHELK-O1 column, hexanes/2-propanol 90:10, 222 nm,

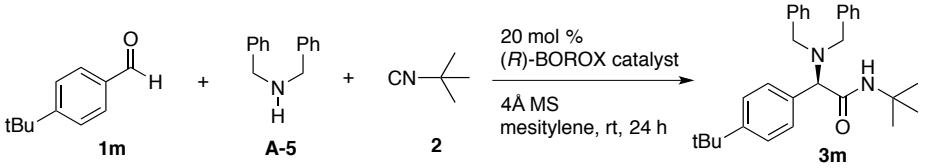
flow 1 mL). Retention times: R_t = 15.61 min (minor enantiomer) and R_t = 23.03 min (major enantiomer); R_f = 0.12 (hexanes: EtOAc 10:1). The product **3k** (85.7 mg, 0.214 mmol) was recrystallized from hexanes (0.5 mL) at room temperature to give colorless crystals of **3k** (40.5 mg, 0.101 mmol) with 99.4:0.6 er and in 47% recovery. A reaction that was run at 0 °C for 66 h afforded the product **3k** in 80% NMR yield with 92:8 er. Spectral data for **3k**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.41 (s, 9H), 2.36 (s, 3H), 3.37 (d, 2H, *J* = 14.0 Hz), 3.84 (d, 2H, *J* = 14.0 Hz), 4.28 (s, 1H), 7.09 (brs, 1H), 7.19 (s, 4H), 7.24-7.30 (m, 2H) 7.32-7.37 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.11, 28.79, 50.87, 54.50, 67.92, 127.20, 128.47, 128.59, 128.78, 130.17, 131.48, 137.28, 138.87, 170.79; IR (thin film) 3347(w), 2967(w), 1684(s), 1507(s), 1453(m) cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{33}N_2O$ *m/z* 401.2593 ([M+H]$^+$), meas 401.2587. $[\alpha]_D^{20}$ = – 40.7° (*c* 1.0, CH_2Cl_2) on 91:9 *er* material.



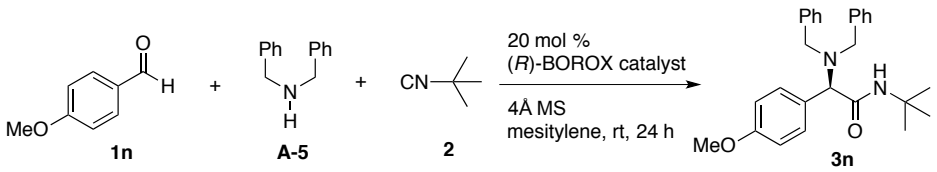
1l **A-5** **2** **3l**

*(R)-N-(tert-butyl)-2-(dibenzylamino)-2-(2-methyl)acetamide **3l**:* The general procedure B for the catalytic asymmetric Ugi reaction described in **Part XII** was followed with o-tolualdehyde **1l** (30.6 mg, 30 μL, 0.255 mmol, 1.00 equiv) with a reaction time of 24 h. The crude product was purified on silica gel according to the standard procedure (1st column, 20 × 160 mm, hexanes:EtOAc 15:1; 2nd column, 20 × 150 mm, hexanes/CH_2Cl_2 1:1 as eluent untill all the phenol **P-47** came out, then EtOAc/hexanes 1:5 as eluent) to afford the product **3l** as a white solid (77.5 mg, 0.193 mmol) in a yield of 76%. The optical purity was determined to be 78:22 *er* by HPLC analysis (Pirkle Covalent (*R*,*R*) WHELK-O1 column, hexanes/2-propanol 90:10, 222 nm, flow 1 mL). Retention times: R_t = 6.91 min (minor enantiomer) and R_t = 13.34 min (major enantiomer). The product (71.4 mg, 0.178 mmol) was recrystallized from 0.9 mL hexanes/EtOAc 20:1 at – 10°C to give a white solid (40 mg, 0.010 mmol) with > 99:1 *er* in 56% recovery. mp 104-105 °C. R_f = 0.16 (hexanes: EtOAc 10:1). Spectral data for **3l**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.35 (s, 9H), 2.22 (s, 3H), 3.74 (d, 2H, *J* = 14.0 Hz), 3.83 (d, 2H, *J* = 14.0 Hz), 4.37 (s, 1H), 6.31 (brs, 1H), 7.15

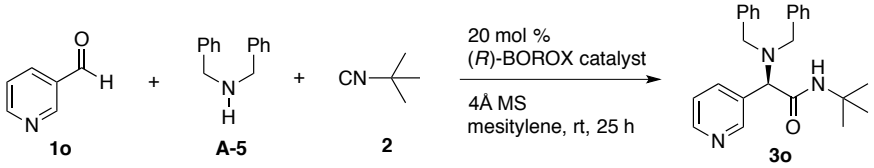
(s, 3H), 7.19-7.25 (m, 6H) 7.26-7.31 (m, 4H), 7.39-7.45 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.87, 28.71, 51.07, 54.53, 65.93, 125.81, 127.03, 127.70, 128.22, 128.75, 129.04, 130.91, 135.52, 138.10, 138.99, 171.66; IR (thin film) 3337(w), 2967(w), 1671(s), 1509(s), 1453(s) cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{33}N_2O$ *m/z* 401.2593 ($[M+H]^+$), meas 401.2589. $[\alpha]_D^{20}$ = –20.1° (*c* 1.0, CH_2Cl_2) on >99:1 *er* material.



*(R)-N-(tert-butyl)-2-(dibenzylamino)-2-(4-tert-butyl)acetamide **3m**:* The general procedure B for the catalytic asymmetric Ugi reaction described in **Part XII** was followed with tert-butylbenzaldehyde **1m** (41.3 mg, 42.6 μL, 0.255 mmol, 1.00 equiv) with a reaction time of 24 h. The crude product was purified by column chromatography on silica gel (1st column, 20 × 160 mm, hexanes:EtOAc 15:1; 2nd column, 20 × 150 mm, hexanes/CH_2Cl_2 1:1 as eluent untill all the phenol **P-47** came out, then EtOAc/hexanes 1:5 as eluent) to afford the product **3m** as a white solid (93.7 mg, 0.212 mmol) in a yield of 83%. The optical purity was determined to be 84:16 *er* by HPLC analysis (Pirkle Covalent (*R*,*R*) WHELK-O1 column, hexanes/2-propanol 90:10, 222 nm, flow 1 mL). Retention times: R_t = 10.99 min (minor enantiomer) and R_t = 16.16 min (major enantiomer); mp 48-51 °C. R_f = 0.52 (hexanes: EtOAc 3:1). Spectral data for **3m**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.31 (s, 9H), 1.39 (s, 9H), 3.37 (d, 2H, *J* = 14.0 Hz), 3.81 (d, 2H, *J* = 14.0 Hz), 4.25 (s, 1H), 7.10 (brs, 1H), 7.17-7.22 (m, 2H) 7.22-7.29 (m, 2H), 7.30-7.40 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.83, 31.33, 34.50, 50.93, 54.64, 67.99, 125.01, 127.21, 128.49, 128.63, 129.96, 131.42, 139.02, 150.41, 170.89; IR (thin film) 3341(w), 2965(s), 1682(s), 1507(s) cm^{-1}; HRMS (ESI) calcd for $C_{30}H_{39}N_2O$ *m/z* 443.3062 ($[M+H]^+$), meas 443.3063. $[\alpha]_D^{20}$ = – 40.9° (*c* 1.0, CH_2Cl_2) on 84:16 *er* material.

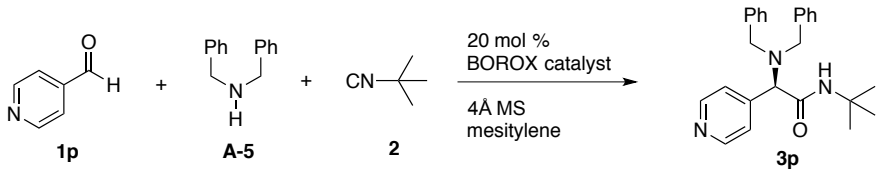


*(R)-N-(tert-butyl)-2-(dibenzylamino)-2-(4-methoxy)acetamide **3n**:* The general procedure B for the catalytic asymmetric Ugi reaction described in **Part XII** was followed with 4-anisaldehyde **1n** (34.7 mg, 31.0 μL, 0.255 mmol, 1.00 equiv) with a reaction time of 24 h. The crude product was purified by column chromatography on silica gel (20 × 160 mm, hexanes:EtOAc 10:1) to afford the product **3n** as a semi-solid (74.4 mg, 0.179 mmol) in a yield of 70%. The optical purity was determined to be 89:11 *er* by HPLC analysis (Pirkle Covalent (*R*,*R*) WHELK-O1 column, hexanes/2-propanol 75:25, 222 nm, flow 2 mL). Retention times: R_t = 5.91 min (minor enantiomer) and R_t = 8.80 min (major enantiomer); R_f = 0.34 (hexanes: EtOAc 3:1). A reaction that was run at 0 °C for 66 h afforded the product **3n** (54.2 mg, 0.130 mmol) in a yield of 51% with 92:8 er. Spectral data for **3n**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39 (s, 9H), 3.32 (d, 2H, *J* = 14.0 Hz), 3.799 (d, 2H, *J* = 14.0 Hz), 3.802 (s, 3H), 4.24 (s, 1H), 6.87-6.93(m, 2H), 7.11 (brs, 1H), 7.17-7.22 (m, 2H), 7.22-7.28 (m, 2H), 7.30-7.35 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.81, 50.90, 54.54, 55.23, 67.61, 113.54, 126.58, 127.24, 128.52, 128.60, 131.45, 138.89, 159.08, 170.88; IR (thin film) 3355(m), 2963(w), 1680(s), 1510(s), 1248(s) cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{33}N_2O_2$ *m/z* 417.2542 ([M+H]$^+$), meas 417.2548. $[\alpha]_D^{20}$ = – 46.4° (*c* 1.0, CH_2Cl_2) on 92:8 *er* material.

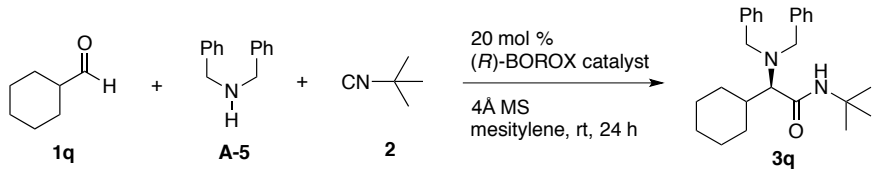


(R)-N-(*tert*-butyl)-2-(dibenzylamino)-2-(55yridine-3-yl)*acetamide **3o**:* The general procedure B for the catalytic asymmetric Ugi reaction described in **Part XII** was followed with 3-pyridinecarboxaldehyde **1o** (27.3 mg, 24.0 μL, 0.255 mmol, 1.00 equiv) with a reaction time of 25 h. The crude product was purified by column chromatography on silica gel (20 × 160 mm, hexanes:EtOAc 15:1➔5:1➔1:1) to afford the product **3o** as a solid (79.0 mg, 0.204 mmol) in a yield of 80%. The optical purity was determined to be 90:10 *er* by HPLC analysis (Chiralpak AD column, hexanes/2-propanol 90:10, 222 nm, flow 1 mL). Retention times: R_t = 6.97 min (minor enantiomer) and R_t = 10.93 min (major enantiomer). The product (79.0 mg, 0.204 mmol) was crystallized from a mixture of hexanes/EtOAc (8:1) at room temperature to give 48 mg of **3a** as

colorless crystals in >99:1 er and 61% recovery. mp 123-124 °C. R_f = 0.29 (hexanes: EtOAc 1:2). Spectral data for **3o**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.40 (s, 9H), 3.22 (d, 2H, *J* = 13.7 Hz), 3.83 (d, 2H, *J* = 13.7 Hz), 4.34 (s, 1H), 7.21 (brs, 1H), 7.25-7.30 (m, 2H) 7.30-7.38 (m, 9H), 7.65-7.70 (m, 1H), 8.48 (s, 1H), 8.57 (d, 1H, *J* = 4.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.77, 51.17, 54.63, 65.40, 123.12, 127.61, 128.48, 128.76, 129.75, 138.09, 138.43, 148.60, 151.08, 169.46; IR (thin film) 3349(w), 2969(w), 1680(s) cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{30}N_3O$ *m/z* 388.2389 ([M+H]$^+$), meas 388.2384. $[\alpha]_D^{20}$ = –17.1° (*c* 1.0, CH_2Cl_2) on >99:1 *er* material.



(R)-N-(*tert*-butyl)-2-(dibenzylamino)-2-(56yridine-4-yl)*acetamide **3p**:* The general procedure B for the catalytic asymmetric Ugi reaction described in **Part XII** was followed with 4-pyridinecarboxaldehyde **1p** (27.3 mg, 24.0 μL, 0.255 mmol, 1.00 equiv) except that the reaction time is 70 h. The crude product was purified by column chromatography on silica gel (20 × 160 mm, hexanes:EtOAc 3:1➔1:1) to afford the product **3p** as a semi-solid (65.2 mg, 0.168 mmol) in a yield of 66%. The optical purity was determined to be 89:11 *er* by HPLC analysis (Chiralpak AD column, hexanes/2-propanol 95:5, 222 nm, flow 0.7 mL). Retention times: R_t = 18.38 min (minor enantiomer) and R_t = 22.86 min (major enantiomer). R_f = 0.30 (hexanes/EtOAc 1:2). Spectral data for **3p**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.40 (s, 9H), 3.26 (d, 2H, *J* = 13.8 Hz), 3.82 (d, 2H, *J* = 13.8 Hz), 4.27 (s, 1H), 7.07 (brs, 1H), 7.20-7.22 (m, 2H), 7.25-7.30 (m, 2H), 7.30-7.38 (m, 8H), 8.59-8.64 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.75, 51.24, 54.61, 66.74, 125.41, 127.60, 128.44, 128.73, 138.04, 143.18, 149.42, 169.10; IR (thin film) 3341(w), 3258(w), 3031(w), 2967(w), 1680(s) cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{30}N_3O$ *m/z* 388.2389 ([M+H]$^+$), meas 388.2382. $[\alpha]_D^{20}$ = –11.9° (*c* 1.0, CH_2Cl_2) on >89:11 *er* material.



(R)-N-(tert-butyl)-2-cyclohexyl-2-(dibenzylamino)acetamide ***3q****:* The general procedure B for the catalytic asymmetric Ugi reaction described in **Part XII** was followed with cyclohexanecarboxaldehyde **1q** (28.7 mg, 31.0 μL, 0.256 mmol, 1.00 equiv) with a reaction time of 24 h. The crude product was purified by column chromatography on silica gel (20 × 160 mm, hexanes:EtOAc 15:1) to afford the product **3q** as an off-white solid (45.1 mg, 0.115 mmol) in a yield of 45%. A second run gave **3q** (49.2 mg, 0.125 mmol) in 49% isolated yield. The optical purity was determined to be 50.5:49.5 *er* by HPLC analysis (Pirkle Covalent (*R*,*R*) WHELK-O1 column, hexanes/2-propanol 90:10, 222 nm, flow 1 mL). Retention times: R_t = 4.59 min (minor enantiomer) and R_t = 5.06 min (major enantiomer). mp 97-100 °C. R_f = 0.25 (hexanes/EtOAc 10:1). Spectral data for **3q**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.67-0.79 (m, 1H), 0.80-0.92 (m, 1H), 1.01-1.14 (m, 1H), 1.14-1.31 (m, 2H), 1.37 (s, 9H), 1.53-1.67 (m, 3H), 1.72 (d, 1H, *J* = 13.3 Hz), 1.90-2.01 (m, 1H), 2.27 (d, 1H, *J* = 13.3 Hz), 2.46 (d, 1H, *J* = 10.3 Hz), 3.45 (d, 2H, *J* = 14.5 Hz), 4.06 (d, 2H, *J* = 14.5 Hz), 5.02 (s, 1H), 7.22 (t, 2H, *J* = 7.5 Hz), 7.31 (t, 4H, *J* = 7.5 Hz), 7.40 (d, 4H, *J* = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.97, 26.00, 26.62, 28.98, 29.83, 30.53, 36.14, 51.49, 54.37, 68.75, 126.82, 128.30, 128.37, 140.16, 170.17; IR (thin film) 3430(w), 2926(s), 2851(s), 1676(s), 1503(s), 1453(s) cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{37}N_2O$ *m/z* 393.2906 ($[M+H]^+$), meas 393.2904.

XIII. Formation of α-amino amides with different isocyanides

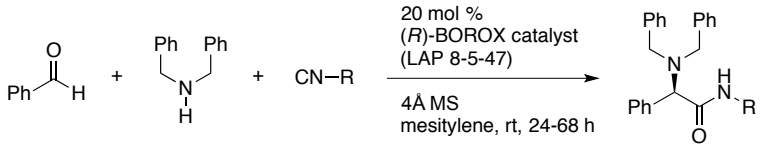
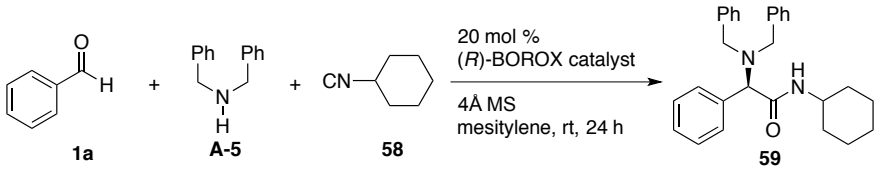


Table 4. Ugi-3CR with different isocyanides.

Entry	R	Time (h)	%Yield[a]	*er*
1	*t*-Bu	24	86	90:10
2	1,1,3,3-tetramethylbutyl	68	55	87:13
3	Cy	24	75	67:33
4	*n*-Bu	39	48	52:48
5	Bn	29	46	51:49

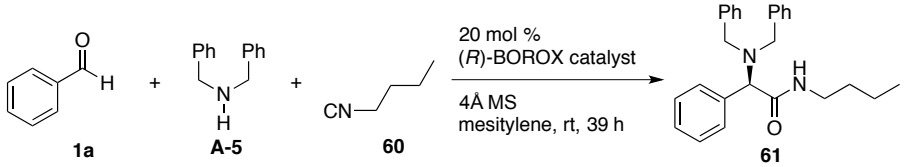
6	2,6-diMeC_6H_3	44	29	85:15
7	4-$MeOC_6H_4$	24	65	88:12

[a] Isolated yield after chromatography on silica gel.



1a **A-5** **58** **59**

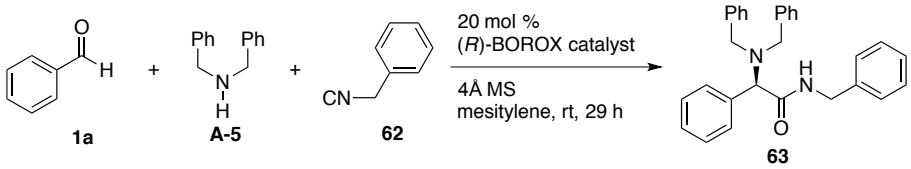
*(R)-N-cyclohexyl-2-(dibenzylamino)-2-phenylacetamide **59**:* The general procedure B for the catalytic asymmetric Ugi reaction described in **Part XII** was followed with isocyanide **58** (47.5 μL, 0.382 mmol, 1.50 equiv) with a reaction time of 24 h. The crude product was purified by column chromatography on silica gel (20 × 160 mm, hexanes:EtOAc 15:1) to afford the product **59** as a white solid (78.8 mg, 0.191 mmol) in a yield of 75%. The optical purity was determined to be 67:33 *er* by HPLC analysis (CHIRALCEL OD-H column, hexanes/2-propanol 98:2, 222 nm, flow 1 mL). Retention times: R_t = 8.00 min (minor enantiomer) and R_t = 9.18 min (major enantiomer); mp 129-132 °C. R_f = 0.33 (hexanes: EtOAc 3:1). Spectral data for **59**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.12-1.30 (m, 3H), 1.32-1.46 (m, 2H), 1.57-1.77 (m, 3H), 1.85-2.01 (m, 2H), 3.35 (d, 2H, *J* = 14.0 Hz), 3.82 (d, 2H, *J* = 14.0 Hz), 4.35 (s, 1H), 7.06 (d, 1H, *J* = 8.4 Hz), 7.23-7.39 (m, 15H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.67,24.73, 25.55, 33.02, 33.35, 47.81, 54.50, 67.72, 127.26, 127.74, 128.13, 128.52, 128.64, 130.16, 134.71, 138.73, 170.28; IR (thin film) 3318(w), 2930(s), 2853(m), 1663(s), 1506(s), 1453(m) cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{33}N_2O$ *m/z* 413.2593 ([M+H]$^+$), meas 413.2591. $[\alpha]_D^{20}$ = – 5.8° (*c* 1.0, CH_2Cl_2) on 67:33 *er* material.



1a **A-5** **60** **61**

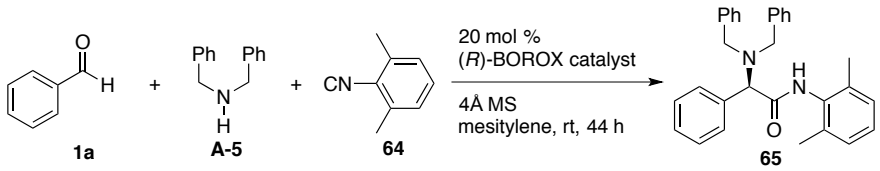
*(R)-N-butyl-2-(dibenzylamino)-2-phenylacetamide **61**:* The general procedure B for the catalytic asymmetric Ugi reaction described in **Part XII** was followed with isocyanide **60** (40 μL, 0.38 mmol, 1.5 equiv) with a reaction time of 39 h. The crude product was purified by column chromatography on silica gel (20 × 160 mm, hexanes:EtOAc 15:1 to 5:1) to afford the product **61**

as an off-white solid (47.3 mg, 0.122 mmol) in a yield of 48%. The optical purity was determined to be 52:48 *er* by HPLC analysis (Pirkle Covalent (*R*,*R*) WHELK-O1 column, hexanes/2-propanol 90:10, 222 nm, flow 1 mL). Retention times: R_t = 30.04 min (major enantiomer) and R_t = 33.40 min (minor enantiomer); mp 83-85 °C. R_f = 0.26 (hexanes: EtOAc 3:1). Spectral data for **61**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.93 (t, 3H, *J* = 7.3 Hz), 1.31-1.41 (m, 2H), 1.53 (pentet, 2H, *J* = 7.3 Hz), 3.26-3.42 (m, 2H), 3.34 (d, 2H, *J* = 13.5 Hz), 3.84 (d, 2H, *J* = 13.5 Hz), 4.39 (s, 1H), 7.14 (br, t, 1H, *J* = 5.8 Hz), 7.22-7.42 (m, 15H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.70, 20.08, 31.73, 38.91, 54.48, 67.66, 127.27, 127.76, 128.13, 128.53, 128.58, 130.18, 134.39, 138.62, 171.25; IR (thin film) 3310(m), 2957(m), 2930(m), 1655(s), 1495(m), 1453(m) cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{31}N_2O$ *m/z* 387.2436 ([M+H]$^+$), meas 387.2433.



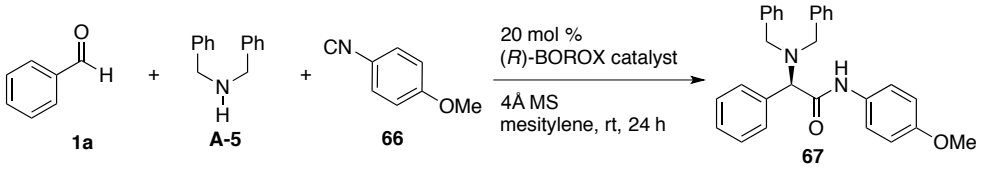
1a A-5 62 63

(R)-N-benzyl-2-(dibenzylamino)-2-phenylacetamide ***63****:* The general procedure B for the catalytic asymmetric Ugi reaction described in **Part XII** was followed with isocyanide **62** (47 μL, 0.39 mmol, 1.5 equiv) with a reaction time of 29 h. The crude product was purified by column chromatography on silica gel (20 × 160 mm, hexanes:EtOAc 6:1) to afford the product **63** as a light yellow solid (49.4 mg, 0.117 mmol) in a yield of 46%. The optical purity was determined to be 51:49 *er* by HPLC analysis (Pirkle Covalent (*R*,*R*) WHELK-O1 column, hexanes/2-propanol 85:15, 222 nm, flow 1 mL). Retention times: R_t = 34.61 min (major enantiomer) and R_t = 39.08 min (minor enantiomer); mp 104-105 °C. R_f = 0.11 (hexanes: EtOAc 6:1). Spectral data for **63**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.33 (d, 2H, *J* = 14.0 Hz), 3.86 (d, 2H, *J* = 14.0 Hz), 4.48 (s, 1H), 4.51 (dd, 1H, *J* = 14.5 Hz, *J* = 6.0 Hz), 4.61 (dd, 1H, *J* = 14.5 Hz, *J* = 6.0 Hz), 7.24-7.45 (m, 20H), 7.52 (t, 1H, *J* = 5.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 43.47, 54.51, 67.66, 127.29, 127.52, 127.76, 127.88, 128.19, 128.53, 128.68, 128.73, 130.29, 134.06, 138.25, 138.43, 171.31; IR (thin film) 3310(m), 3029(m), 1662(s), 1495(m), 1453(m) cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{29}N_2O$ *m/z* 421.2280 ([M+H]$^+$), meas 421.2278.



1a A-5 64 65

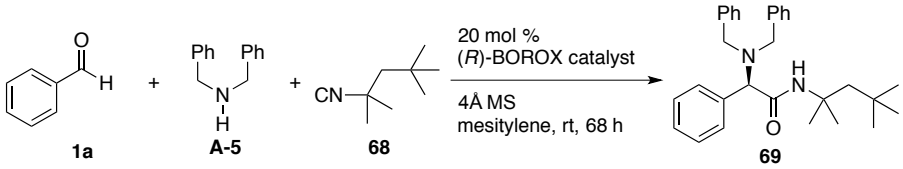
(R)-2-(dibenzylamino)-N-(2,6-dimethylphenyl)-2-phenylacetamide ***65****:* The general procedure B for the catalytic asymmetric Ugi reaction described in **Part XII** was followed with isocyanide **64** (50 mg, 0.38 mmol, 1.5 equiv) with a reaction time of 44 h. The crude product was purified by column chromatography on silica gel (20 × 160 mm, hexanes:EtOAc 6:1) to afford a mixture of phenol **P-47** and the product **65** which contained the product **65** (32 mg, 0.074 mmol) in a yield of 29%. The optical purity was determined to be 85:15 *er* by HPLC analysis (Pirkle Covalent (*R*,*R*) WHELK-O1 column, hexanes/2-propanol 75:25, 222 nm, flow 2 mL). Retention times: R_t = 4.84 min (major enantiomer) and R_t = 10.60 min (minor enantiomer); R_f = 0.16 (hexanes: EtOAc 6:1). Spectral data for **65**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.17 (s, 1H), 3.34 (d, 2H, *J* = 14.0 Hz), 4.02 (d, 2H, *J* = 14.0 Hz), 4.67 (s, 1H), 7.05-7.12 (m, 3H), 7.25-7.30 (m, 2H), 7.32-7.45 (m, 13H), 8.83 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.76, 54.59, 67.74, 127.17, 127.54, 128.00, 128.22, 128.29, 128.70, 128.73, 130.68, 133.45, 133.92, 135.38, 138.11, 169.71; HRMS (ESI) calcd for $C_{30}H_{31}N_2O$ *m/z* 435.2436 ($[M+H]^+$), meas 435.2435.



1a A-5 66 67

(R)-2-(dibenzylamino)-N-(4-methoxyphenyl)-2-phenylacetamide ***67****:* The general procedure B for the catalytic asymmetric Ugi reaction described in **Part XII** was followed with isocyanide **66** (51 mg, 0.38 mmol, 1.5 equiv) with a reaction time of 24 h. The crude product was purified by column chromatography on silica gel (20 × 160 mm, hexanes:EtOAc 6:1) to afford the product **67** as a yellow solid (72.2 mg, 0.165 mmol) in a yield of 65%. The optical purity was determined to be 88:12 *er* by HPLC analysis (Pirkle Covalent (*R*,*R*) WHELK-O1 column, hexanes/2-propanol 75:25, 222 nm, flow 2 mL). Retention times: R_t = 14.25 min (major enantiomer) and R_t = 30.58 min (minor enantiomer); mp 54-55 °C. R_f = 0.13 (hexanes: EtOAc 6:1). Spectral data for **67**: ^{1}H

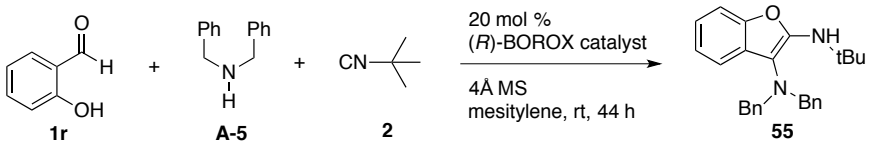
NMR (500 MHz, $CDCl_3$) δ 3.33 (d, 2H, *J* = 14.0 Hz), 3.79 (s, 3H), 3.95 (d, 2H, *J* = 14.0 Hz), 4.57 (s, 1H), 6.87-6.92 (m, 2H), 7.26-7.46 (m, 15H), 7.50-7.55 (m, 2H), 9.30 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 54.67, 55.48, 68.17, 114.22, 120.83, 127.50, 128.03, 128.24, 128.63, 128.74, 130.59, 131.06, 133.25, 138.21, 156.22, 169.31; IR (thin film) 3322(w), 3029(w), 1682(m), 1514(s), 1246(m) cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{29}N_2O_2$ *m/z* 437.2229 ($[M+H]^+$), meas 437.2227. $[\alpha]_D^{20}$ = + 67.4° (*c* 1.0, CH_2Cl_2) on 88:12 *er* material.



1a **A-5** **68** **69**

(R)-2-(dibenzylamino)-2-phenyl-N-(2,4,4-trimethylpentan-2-yl)acetamide ***69****:* The general procedure B for the catalytic asymmetric Ugi reaction described in **Part XII** was followed with isocyanide **68** (67 μL, 0.38 mmol, 1.5 equiv) with a reaction time of 68 h. The crude product was purified by column chromatography on silica gel (20 × 160 mm, hexanes:EtOAc 15:1) to afford the product **69** as a colorless semi-solid (62.2 mg, 0.141 mmol) in a yield of 55%. The optical purity was determined to be 87:13 *er* by HPLC analysis (Pirkle Covalent (*R,R*) WHELK-O1 column, hexanes/2-propanol 90:10, 222 nm, flow 1 mL). Retention times: R_t = 9.78 min (minor enantiomer) and R_t = 11.13 min (major enantiomer); R_f = 0.25 (hexanes: EtOAc 6:1). Spectral data for **69**: ^1H NMR (500 MHz, $CDCl_3$) δ 0.94 (s, 9H), 1.43 (s, 3H), 1.48 (s, 3H), 1.64 (d, 1H, *J* = 15.3 Hz), 1.94 (d, 1H, *J* = 15.3 Hz), 3.25 (d, 2H, *J* = 13.5 Hz), 3.86 (d, 2H, *J* = 13.5 Hz), 4.30 (s, 1H), 7.23-7.42 (m, 16H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 29.27, 29.38, 31.42, 31.49, 51.28, 54.46, 54.91, 68.02, 127.31, 127.63, 128.02, 128.55, 128.63, 130.63, 133.86, 138.55, 170.28; IR (thin film) 3351(w), 2955(m), 1684(s), 1507(s), 1453(w) cm^{-1}; HRMS (ESI) calcd for $C_{30}H_{39}N_2O$ *m/z* 443.3062 ($[M+H]^+$), meas 443.3060. $[\alpha]_D^{20}$ = – 15.2° (*c* 1.0, CH_2Cl_2) on 87:13 *er* material.

XIV. Intramolecular interception of the nitrilium cation



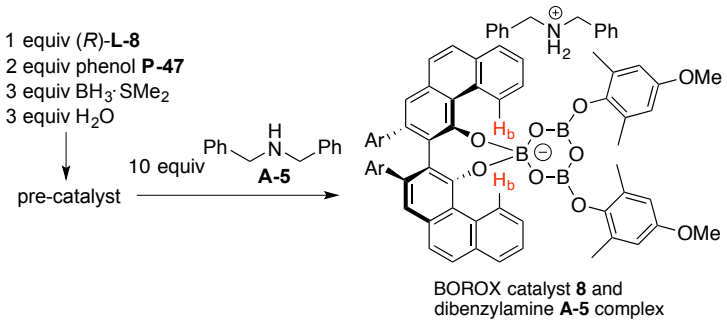
1r **A-5** **2** **55**

N^3,N^3-dibenzyl-N^2-(tert-butyl)benzofuran-2,3-diamine: The general procedure B for the catalytic asymmetric Ugi reaction described in **Part XII** was followed with salicylaldehyde **1r** (31.1 mg, 27.0 μL, 0.255 mmol, 1.00 equiv) with a reaction time of 44 h. The crude product was purified by column chromatography on silica gel (20 × 160 mm, hexanes:EtOAc 20:1) to afford the product **55** as an yellow solid (21.5 mg, 0.0559 mmol) in a yield of 22%. The product was assigned as **55** on the basis of its ^{1}H and ^{13}C NMR spectra. A reaction that was run at 0 °C for 66 h afforded the product **55** (20 mg, 0.052 mmol) in a yield of 20%. R_f = 0.24 (hexanes/EtOAc 20:1). Spectral data for **55**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.06 (s, 9H), 3.80 (s, 1H), 4.16 (s, 4H), 6.96-7.02 (m, 1H), 7.12 (t, 1H, *J* = 7.5 Hz), 7.18-7.30 (m, 11H), 7.40-7.44 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 29.99, 52.33, 58.60, 106.83, 110.38, 117.01, 119.44, 122.08, 127.07, 127.69, 128.21, 129.11, 139.60, 149.26, 155.28.

XV. NMR study of BOROX catalyst formation

Preparation of pre-catalyst stock solution: A flame-dried 25 mL Schlenk flask equipped with a stir bar was cooled to rt under N_2 and charged with (*R*)-**L-8** (91.6 mg, 0.111 mmol), **P-47** (35.0 mg, 0.229 mmol), H_2O (5.9 mg, 5.9 μL, 0.33 mmol), dry toluene (3.3 mL) and BH_3•SMe_2 (2M, 165 μL, 0.33 mmol). The Teflon valve on the Schlenk flask was then closed, and the mixture heated at 100 ° C for 1 h. After the flask was cooled to rt, the valve was carefully opened to gradually apply high vacuum (0.1 mm Hg) and the solvent and volatiles were removed. Then the flask was heated at 100 °C under high vacuum for 30 min. The resulting mixture was dissolved in dry d_8-toluene (1.04 mL) after it was cooled to room temperature.

*Catalyst formation with 1.0 equivalent of dibenzylamine **A-5**:*



BOROX catalyst **8** and dibenzylamine **A-5** complex

To an oven-dried quartz NMR tube filled with nitrogen was added Ph_3CH (10.4 mg, 0.0426 mmol) as an internal standard, the pre-catalyst stock solution (0.49 mL, 0.05 mmol (*R*)-**L-8**) and 0.21 mL d_8-toluene. The tube was sealed with a rubber cap. The ^1H NMR and ^{11}B NMR spectra of the pre-catalyst were taken at this point. To this NMR tube was added 1.0 equivalent dibenzylamine **A-5** (10 μL, 0.05 mmol) under a N_2 stream applied via a needle through the rubber cap. The ^1H NMR and ^{11}B NMR spectra of the mixture were taken at different time points. The bay proton (H_b) region of the ^1H NMR spectra and the ^{11}B NMR spectra are shown in **Figure 1** and **Figure 2**. The integration of the methine proton in Ph_3CH was set to 1.00.

A DMAP-BOROX complex[35] has been previously synthesized and fully characterized by our group. Its structure was elucidated by X-ray diffraction analysis. The most distinctive absorption in the ^1H NMR spectrum for this DMAP-BOROX complex is the bay-region peak at 10.4 ppm. The ^{11}B NMR spectrum of the complex shows a sharp peak at 5.7 ppm for the tetra-coordinated boron in the structure. Both of these two distinctive absorptions were observed for the Ugi-3CR system. After the addition of 1 equiv of the amine **A-5** to the pre-catalyst solution, the ^1H NMR spectrum showed a peak around 10.6 ppm and the ^{11}B NMR spectrum revealed a sharp peak at 5.9 ppm. These results are indicative of the formation of the amine **A-5**-BOROX complex. The absorption for the bay proton of the free ligand (*R*)-**L-8** in the ^1H NMR spectrum appears at 9.6 ppm in d_8-toluene. It might shift to 9.8 ppm depending on the composition of reaction mixture or on any equilibrium that the ligand may be involved in (**Figure 3**, c and d).

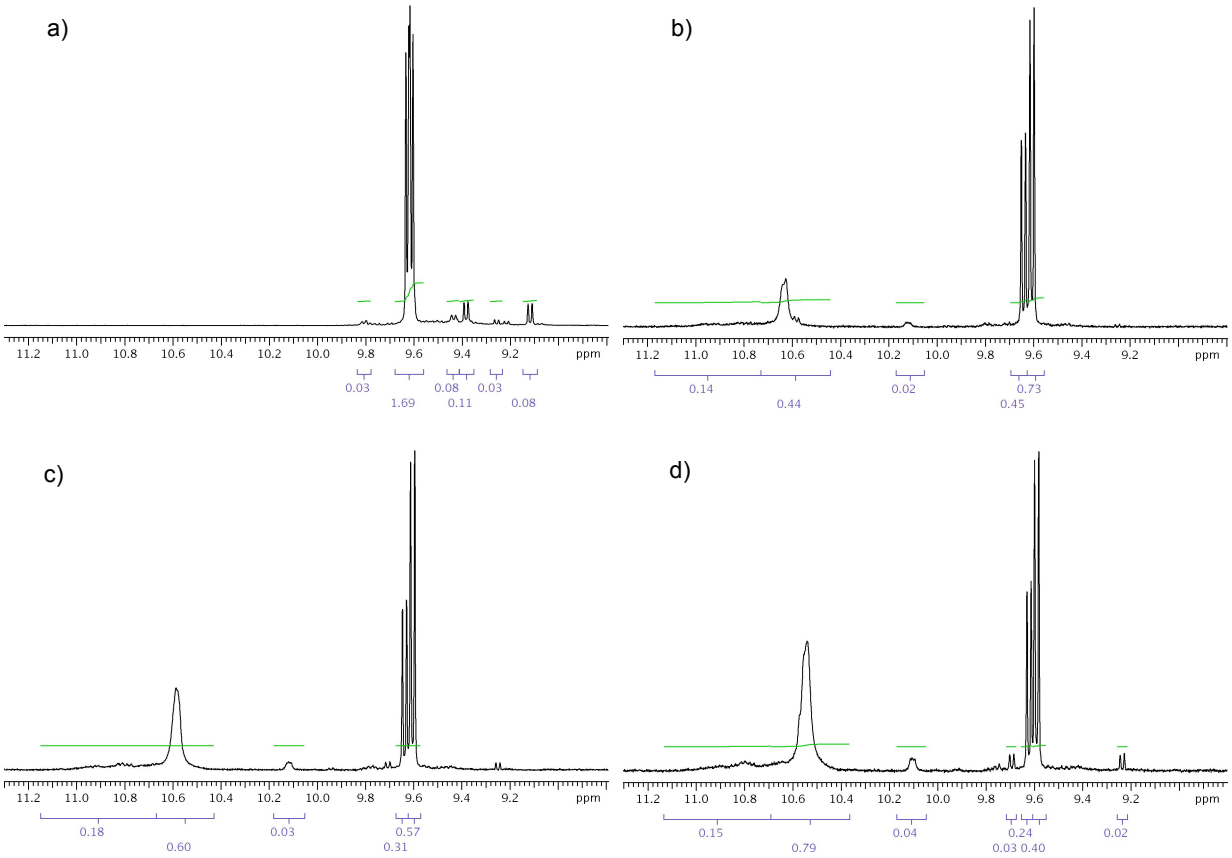
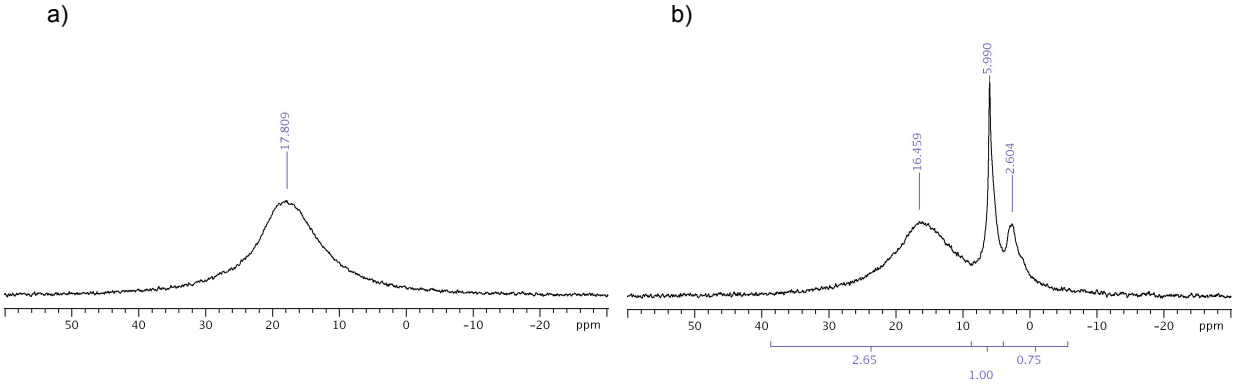


Figure 1. ^{1}H NMR spectra of the pre-catalyst and catalyst (bay proton region)
[a)] Pre-catalyst; [b)] 1 h after the addition of 1 equiv dibenzylamine; [c)] 2 h after the addition of dibenzylamine; [d)] 6 h after the addition of dibenzylamine (The integrations are based on the methine proton in Ph_3CH, which was set to 1.00.)



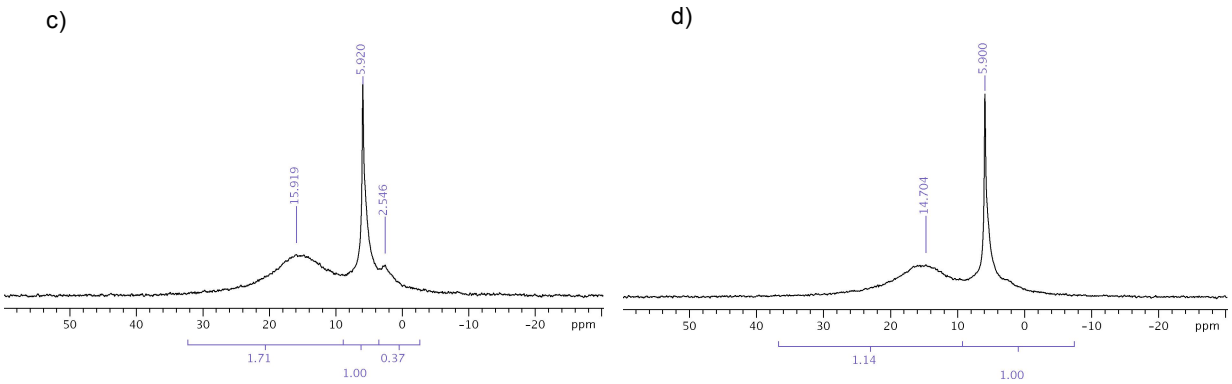
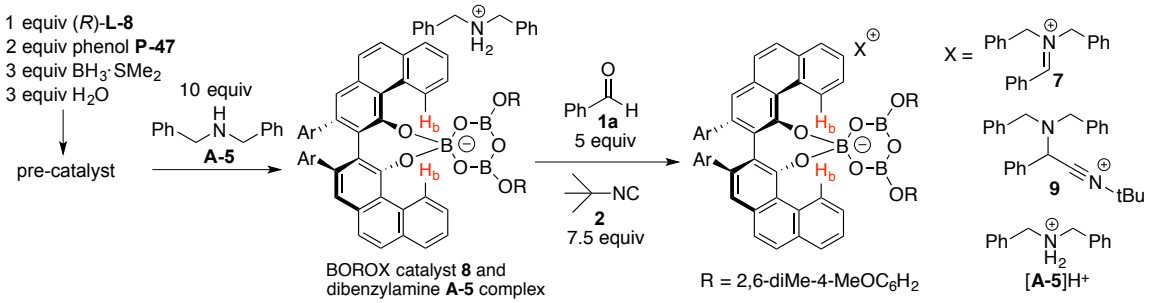


Figure 2. ^{11}B NMR spectra of the pre-catalyst and catalyst
[a] Pre-catalyst; [b] 30 min after the addition of 1 equiv dibenzylamine; [c] 2 h after the addition of dibenzylamine; [d] 3.5 h after the addition of dibenzylamine

*Catalyst formation with 10.0 equivalent of dibenzylamine **A-5***:



To an oven-dried quartz NMR tube filled with nitrogen was added Ph_3CH (11.7 mg, 0.0479 mmol) as an internal standard, the pre-catalyst stock solution (0.49 mL, 0.05 mmol (*R*)-**L-8**) and 0.21 mL d_8-toluene. The tube was sealed with a rubber cap. The ^{1}H NMR and ^{11}B NMR spectra of the pre-catalyst were taken at this point. To this NMR tube was added 10.0 equivalent dibenzylamine **A-5** (0.1 mL, 0.5 mmol) under a N_2 stream applied via a needle through the rubber cap. The ^{1}H NMR and ^{11}B NMR spectra of the mixture were taken immediately. Then benzaldehyde **3a** (26 μL, 0.255 mmol) was added to the mixture. After the spectra were taken, *t*-butyl isocyanide **2** (45 μL, 0.39 mmol, 1.5 equiv) was added to the NMR tube. The ^{11}B NMR spectra and the bay proton region of the ^{1}H NMR spectra are shown below. The integration of the methine proton in Ph_3CH was set to 1.00.

After the addition of 10 equiv of the amine **A-5** to the pre-catalyst solution, a peak around 10.8 ppm in the ^{1}HNMR spectrum and a sharp peak at 5.7 ppm in the ^{11}BNMR spectrum were

indicative of the formation of the **A-5**-BOROX complex. After the addition of 5 equiv benzaldehyde, three broad absorptions around 10.8 ppm were observed. This is not surprising since the protonated amine **A-5**, iminium **7** and nitrilium **9** could all pair up with the BOROX anion. These different ion pairs are in equilibrium in the reaction mixture, resulting in slightly different absorptions in the bay-region in ^{1}HNMR spectrum.

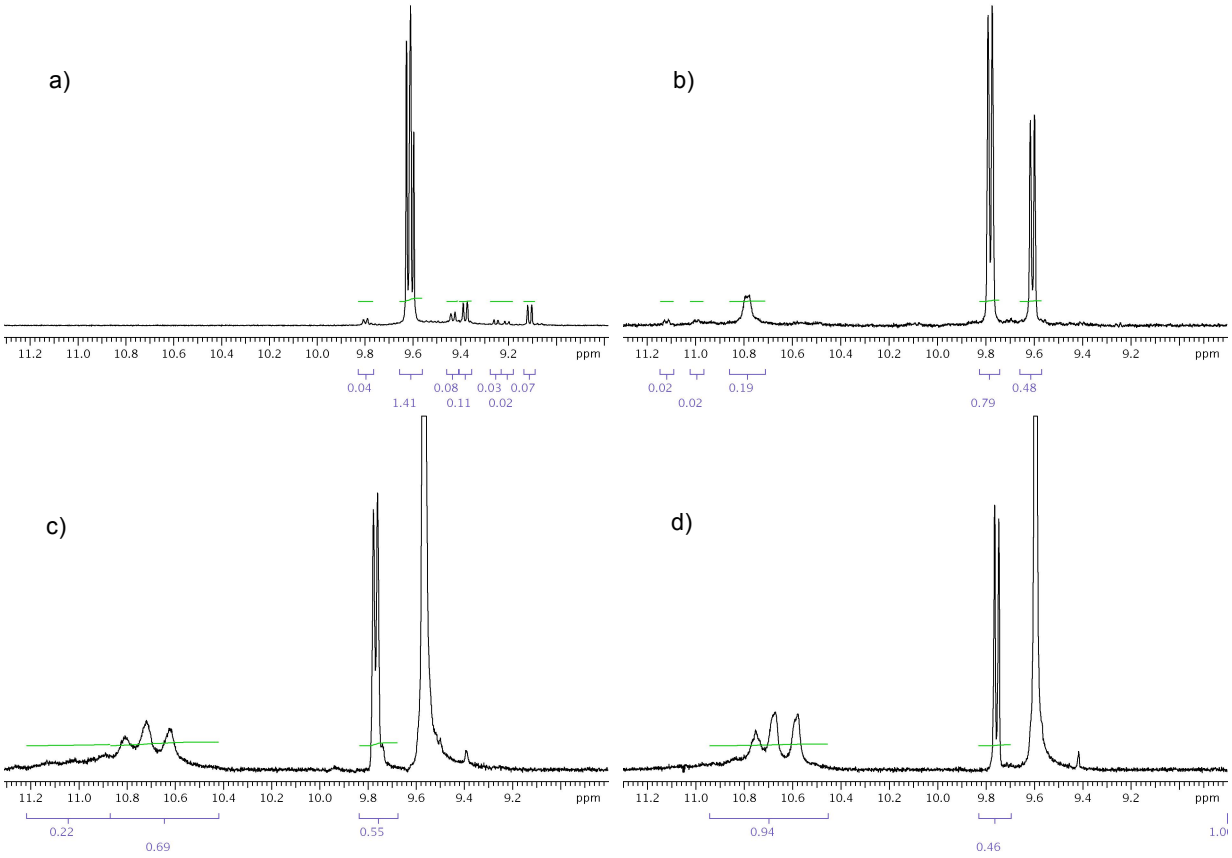


Figure 3. ^{1}H NMR spectra of the pre-catalyst and catalyst (bay proton region)
[a)] Pre-catalyst; [b)] After the addition of 10 equiv dibenzylamine **A-5**; [c)] After the addition of 5 equiv benzaldehyde **3a**; [d)] After the addition of 7.5 equiv isocyanide **2**

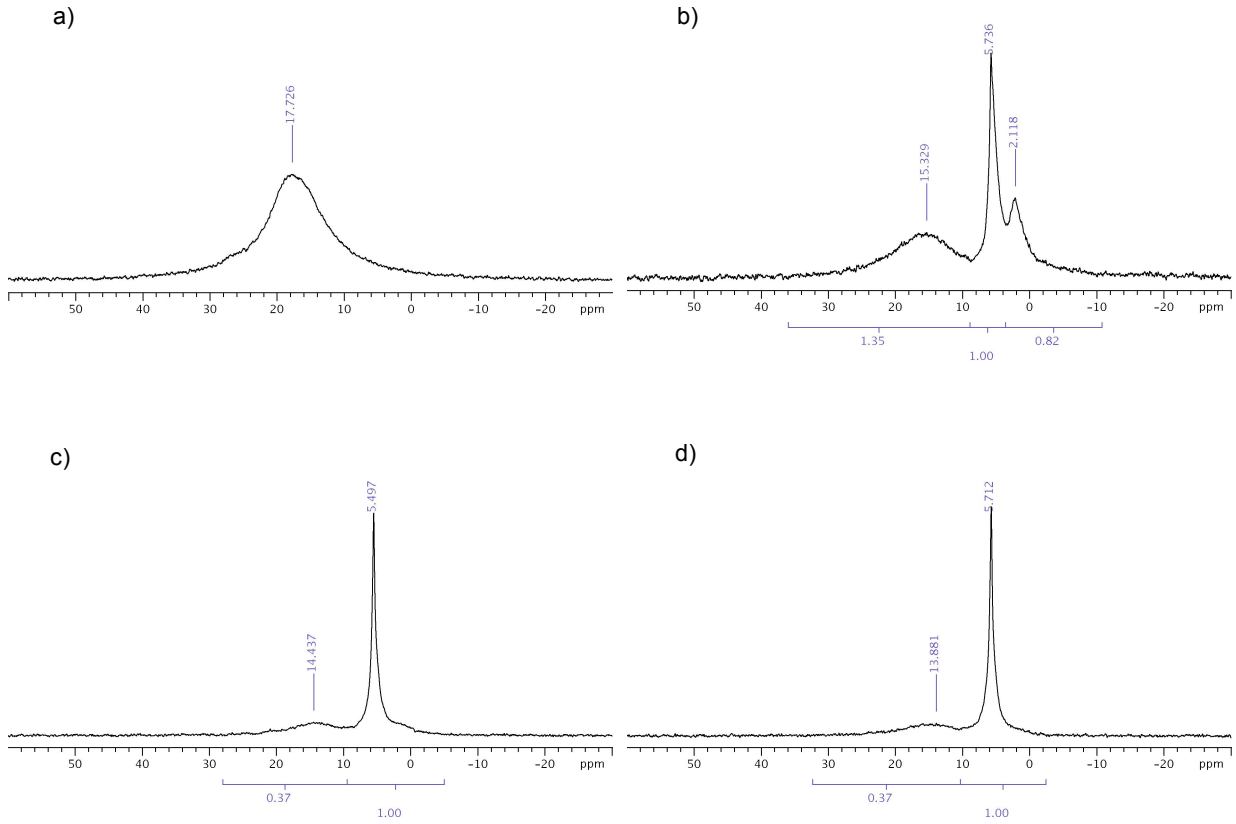
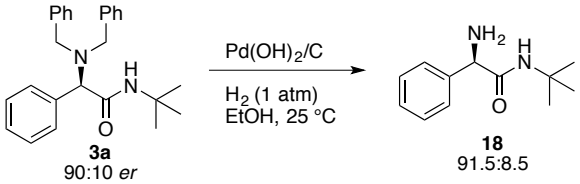


Figure 4. ^{11}B NMR spectra of the pre-catalyst and catalyst
a) Pre-catalyst; [b] After the addition of 10 equiv dibenzylamine **A-5**; [c] After the addition of 5 equiv benzaldehyde **3a**; [d] After the addition of 7.5 equiv isocyanide **2**

XVI. Determination of the absolute configuration of the Ugi product 3a

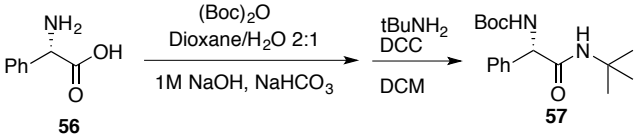
*Removal of the benzyl groups of **3a** (Scheme 4):*



*(R)-2-amino-N-(tert-butyl)-2-phenylacetamide **18***: To a flame-dried 25 mL round bottom flask filled with nitrogen was added **3a** (70.0 mg, 0.181 mmol, 90:10 *er*), $Pd(OH)_2$ (20.0 mg, 0.028 mmol) ($Pd(OH)_2$ on carbon 20%, moisture ≤ 50%). The flask was sealed with a rubber septum and a needle connected to a vacuum line was used to apply vacuum in the flask through the septum. The vacuum was applied for a few seconds. Then the vacuum was stopped and a

hydrogen balloon was connected to the flask by a needle through the septum. This process was repeated four times. Then 5.0 mL EtOH was added to the flask via a needle through the septum. The suspension was stirred at room temperature under hydrogen for 18 hours and then filtered through a pad of Celite. The filter cake was washed with MeOH (5 mL) and DCM (5 mL × 3). The combined filtrate was concentrated to give a light yellow oil. Purification of the crude product by column chromatography on silica gel (20 mm × 160 mm, CH_2Cl_2/MeOH 20:1) gave the product **18** as a colorless oil (33.4 mg, 0.162 mmol, 90%). The optical purity was determined to be 91.5:8.5 *er* by HPLC analysis (Chiralpak AS column, hexanes/2-propanol 85:15, 222 nm, flow 1 mL). Retention times: R_t = 8.55 min (minor enantiomer) and R_t = 13.56 min (major enantiomer). The retention times appear to be dependent on the concentration of the sample. R_f = 0.28 (CH_2Cl_2/MeOH 12:1). Spectral data for **18**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.31 (s, 9H), 1.83 (brs, 2H), 4.36 (s, 1H), 6.92 (brs, 1H), 7.22-7.28 (m, 1H) 7.28-7.36 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.64, 50.69, 60.27, 126.79, 127.76, 128.74, 141.54, 172.04; IR (thin film) 3310(m), 2969(m), 1653(s), 1522(m) cm^{-1}; HRMS (ESI+) calcd for $C_{12}H_{19}N_2O$ *m/z* 207.1497 ([M+H]$^+$), meas 207.1498. $[\alpha]_D^{20}$ = –23.1° (*c* 1.0, CH_2Cl_2) on >91.5:8.5 *er* material.

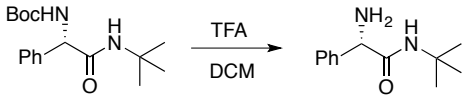
*Preparation of (S)-2-amino-N-(tert-butyl)-2-phenylacetamide **18** from L-(+)-α-phenylglycine:*



56 **57**

*tert-Butyl (S)-(2-(tert-butylamino)-2-oxo-1-phenylethyl)carbamate **57***: To a 100 mL round bottom flask was added L-(+)-α-phenylglycine **56** (756 mg, 5.00 mmol, 1.00 equiv), a mixture of dioxane/water (2:1, 10 mL) and 1M NaOH (5 mL). After the mixture was cooled in an ice-bath for 5 min, $(Boc)_2O$ (1.64 g, 7.50 mmol, 1.50 equiv) and $NaHCO_3$ (420 mg, 5.00 mmol, 1.00 equiv) were added to the flask. The mixture was stirred at room temperature for 18 h. Then EtOAc (30 mL) was added to the reaction mixture and then it was cooled in an ice bath for 5 min. The pH of the mixture was adjusted to 2-3 with 1M HCl. The organic layer was separated and the aqueous layer was extracted with EtOAc (20 mL x 3). The combined organic layer was dried over Na_2SO_4,

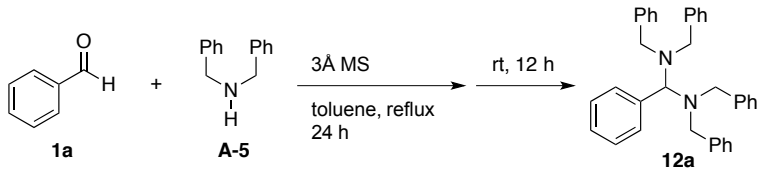
filtered and concentrated to dryness. The residue was transferred to a 50 mL round bottom flask and dissolved in CH_2Cl_2 (15 mL). After the solution was cooled to 0 °C, *N,N'*-dicyclohexylcarbodiimide (1.05 g, 5.09 mmol, 1.02 equiv) was added to the flask, followed by the addition of *tert*-butylamine (0.51 mL, 4.9 mmol, 0.98 equiv). The reaction mixture was warmed up to room temperature and stirred for 18 h. Then the white precipitate that formed in the reaction was removed by filtration through a Celite pad. The pad was washed with CH_2Cl_2 (5 mL x 4). The combined filtrate was concentrated and the product was purified by column chromatography on silica gel (30 mm × 160 mm, hexanes/EtOAc 5:1) to give the product **57** as a white solid (774 mg, 2.53 mmol) in a 51% yield over two steps. mp 144-146 °C. R_f = 0.24 (hexanes/EtOAc 3:1). Spectral data for **57**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.26 (s, 9H), 1.38 (s, 9H), 4.99 (brs, 1H), 5.45 (brs, 1H), 5.81 (brs, 1H), 7.25-7.36 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.26, 28.52, 51.64, 58.71, 79.81, 127.12, 128.13, 128.92, 138.95, 155.15, 169.11; IR (thin film) 3360(w), 3283(m), 2975(w), 1692(s), 1645(s), 1364(m) cm^{-1}; HRMS (ESI+) calcd for $C_{17}H_{27}N_2O_3$ *m/z* 307.2022 ([M+H]$^+$), meas 307.2018. $[\alpha]_D^{20}$ = + 102.5° (*c* 1.0, CH_2Cl_2).



57 **18**

*(S)-2-amino-N-(tert-butyl)-2-phenylacetamide **18***: To an oven-dried 10 mL round bottom flask was added tert-butyl (*S*)-(2-(*tert*-butylamino)-2-oxo-1-phenylethyl)carbamate **57** (92.0 mg, 0.300 mmol, 1.00 equiv), dry CH_2Cl_2 (0.80 mL) and trifluoroacetic acid (0.82 mL). After the mixture was stirred at room temperature for 3 h, it was concentrated and diluted with 1 mL H_2O. The pH of the mixture was adjusted to ~10 with sat. aq. $NaHCO_3$ (*ca*. 35 mL). Then the mixture was extracted with CH_2Cl_2 (30 mL x 3). The combined organic layer was dried over Na_2SO_4, filtered and concentrated to give **18** as a colorless oil (62 mg, 0.30 mmol, 100%). $[\alpha]_D^{20}$ = +27.1° (*c* 1.0, CH_2Cl_2) on >99:1 *er* (by HPLC) material.

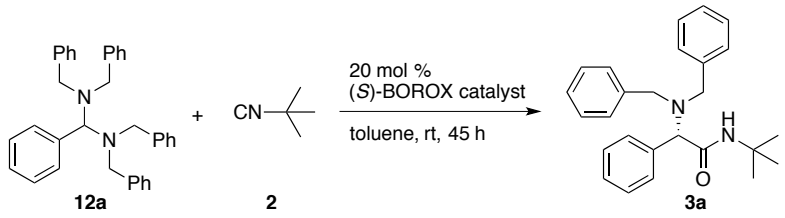
XVII. Preparation of the aminal 12a and conversion of 12a to amino amide 3a



1a **A-5** **12a**

*α,α-Bis(N,N-dibenzylamino)toluene **12a***: An oven-dried 100 mL round bottom flask charged with 3Å powdered molecular sieves (10.0 g) and equipped with a magnetic stir bar was flame dried under high vacuum and cooled down under nitrogen. To the flask was then added 9.0 mL of dry toluene, dibenzylamine **A-5** (0.60 mL, 3.0 mmol, 1.0 equiv) and benzaldehyde **3a** (0.46 mL, 4.5 mmol, 1.5 equiv). After the mixture was heated to reflux for 24 h in an 80 °C oil bath, it was cooled to room temperature and stirred for another 12 h. The mixture was filtered through a Celite pad. The pad was washed with dry CH_2Cl_2 (3 mL). The combined filtrate was concentrated to dryness to give a light yellow viscous oil. After this oil was kept at room temperature for 7 days, a solid separated from the oil, which was filtered off and washed with hexanes to give **12a** as colorless crystals (434 mg, 0.899 mmol) in 30% yield. Mp 142-144 °C (Lit.[33] 138-140 °C); Spectral data for **12a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.54 (d, 4H, *J* = 14.0 Hz), 3.96 (d, 4H, *J* = 14.0 Hz), 4.47 (s, 1H), 7.13-7.22 (m, 20H), 7.30-7.36 (m, 1H), 7.37-7.42 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.67, 79.64, 126.53, 127.67, 127.74, 128.04, 129.09, 129.69, 135.09, 139.47; HRMS (ESI) calcd for $C_{35}H_{35}N_2$ *m/z* 483.2800 ($[M+H]^+$), meas 483.2803. The ^{1}H NMR data match those reported for this compound.[33]

*Conversion of **12a** to amino amide **3a**:*



12a **2** **3a**

The pre-catalyst was prepared according to general procedure A described in **Part V** with (*S*)-VAPOL ligand (16.2 mg, 0.0301 mmol), phenol **P-36** (8.5 mg, 0.62 mmol), $BH_3{\cdot}SMe_2$ (2M, 60 μL, 0.12 mmol), H_2O (1.7 mg, 1.7 μL, 0.94 mmol) and dry toluene (1.2 mL). After the pre-catalyst

was cooled to room temperature, dry solvent (0.5 mL) was added to the flask to dissolve the pre-catalyst, followed by the addition of the aminal **12a** (72.4 mg, 0.150 mmol, 1.00 equiv). The mixture was stirred for 10 min at room temperature. Then *tert*-butyl isocyanide **2** (25 μL, 0.22 mmol, 1.5 equiv) was added to the reaction flask and the resulting mixture was stirred at room temperature for 45 h. The crude product was purified by column chromatography on silica gel (20 mm × 160 mm, hexanes/EtOAc 15:1). The results are shown in **Table 5**. One of the components for the successful convertion of ***12a to amino amide 3a***, H_2O, was not added to the reaction mixture, because the reaction is shut down by H_2O according to our previous study (**Part VIII**) and this may well be due to hydrolysis of the catalyst. The product **3a** was obtained, however, only in a very low yield. Perhaps there was some hydroxyl source in the pre-catalyst.

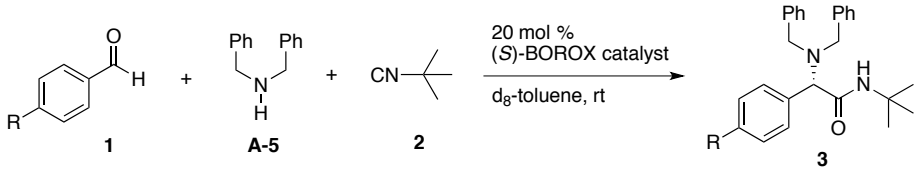
Table 5. Conversion of aminal **12a** to amino amide **3a**.

Entry	Solvent	%Yield	*er*
1[a]	toluene	27	74:26
2[b]	DCM	< 7	68:32

[a] The reaction mixture was directly loaded onto the silica gel column. [b] The reaction product was concentrated to dryness and then purified by chromatography on silica gel.

XVIII. ^{1}H NMR study of the catalytic asymmetric Ugi-3CR

Ugi-3CR with different aldehydes:



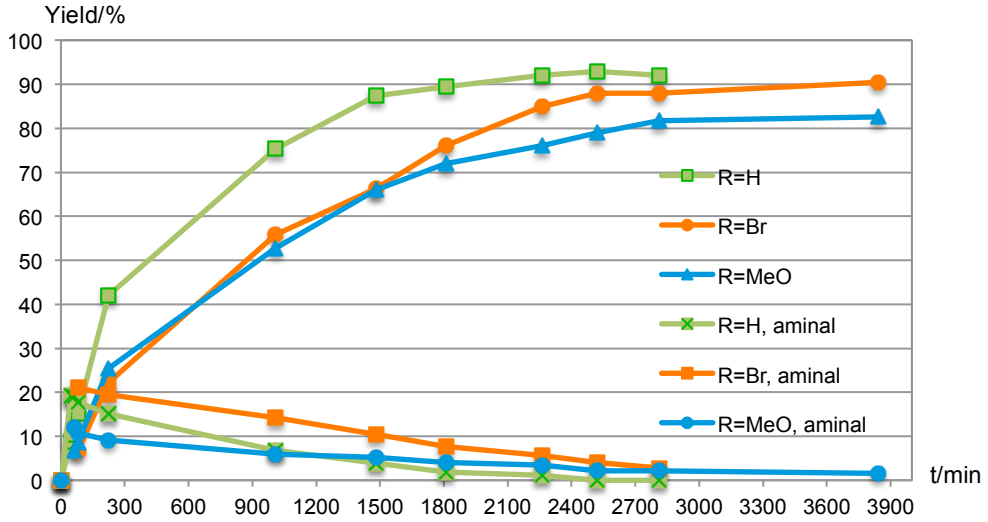
Preparation of pre-catalyst stock solution: A 25 mL Schlenk flask equipped with a stir bar was flame dried, cooled to rt under N_2 and charged with (*S*)-**L-8** (145.3 mg, 0.1765 mmol), **P-36** (49 mg, 0.36 mmol), H_2O (9.5 mg, 9.5 μL, 0.53 mmol), dry toluene (5.3 mL) and BH_3•SMe_2 (2M, 262.5 μL, 0.525 mmol). The Teflon valve on the Schlenk flask was then closed, and the mixture heated at 100 ° C for 1 h. After the flask was cooled to rt, the valve was carefully opened to gradually apply high vacuum (0.1 mm Hg) and the solvent and volatiles were removed. Then the

flask was heated at 100 °C under high vacuum for 30 min. Dry mesitylene (3.5 mL) was added to dissolve the residue in the flask after it was cooled to room temperature.

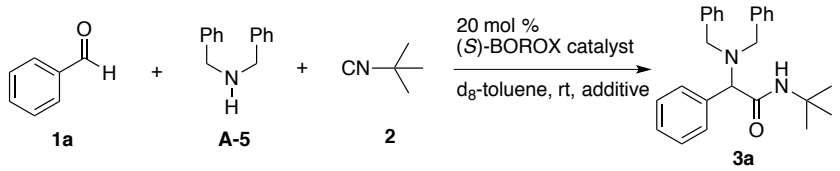
*^{1}H NMR study of the Ugi-3CR with aldehyde **1a**, **1d** and **1n**:* A 25 mL Schlenk flask equipped with a magnetic stir bar was flame dried under high vacuum and cooled to 25 °C under nitrogen. To the flask was then added Ph_3CH as an internal standard and the pre-catalyst stock solution (1.0 mL, 0.050 mmol (*S*)-**L-8**) via a plastic syringe fitted with a metallic needle. To the resulting solution was added dibenzylamine **A-5** (0.10 mL, 0.52 mmol, 2.0 equiv) under a N_2 stream, followed by the addition of benzaldehyde **1a** (26.0 μL, 0.255 mmol, 1.00 equiv) and then *t*-butyl isocyanide (45 μL, 0.39 mmol, 1.5 equiv). Then to an oven-dried NMR tube filled with nitrogen was added 0.7 mL of the reaction mixture and the tube was sealed with a rubber cap. The ^{1}H NMR spectrum was taken at certain intervals. The NMR yields of **3a** at different time points were determined by comparing the methine proton of Ph_3CH and the methine proton of **3a**.

This procedure was repeated with aldehyde **1d** (47.1 mg, 0.255 mmol, 1.00 equiv) and **1n** (34.7 mg, 31.0 μL, 0.255 mmol, 1.00 equiv). The combined results are presented in **Chart 1**. In each case, there is an intitial build-up of aminal **12** and then it slowly disappears as the product grows in and is gone at the end of the reaction. The rates of the reaction with *para*-methoxylbenzaldehyde **1n** and *para*-bromobenzaldehyde **1d** are essentially the same and both are slower than benzaldehyde **1a**.

Chart 1. ^{1}H NMR study of the Ugi-3CR with aldehydes **1a**, **1d** and **1n**



Ugi-3CR with different amounts of 4Å MS or H_2O as an additive:



The general procedure A described in **Part V** was followed with (*S*)-**L-8** ligand (41.5 mg, 0.0504 mmol), phenol **P-36** (14 mg, 0.10 mmol) and 1 mL d_8-toluene as the reaction solvent. A certain amount of 4Å MS was added to the pre-catalyst solution right before the addition of dibenzylamine **A-5**. In the case of H_2O as an additive, it was added right after the addition of benzaldehyde **1a**, followed by the addition of *tert*-butyl isocyanide **2**. The results are shown in **Chart 2** and **Chart 3**.

As shown in **Chart 2**, 4Å MS does have some effect in bringing the reaction to the ultimate yield at a slightly shorter time. However, too much sieves will diminish the yield, which is revealed by the reaction with 60 mg 4Å MS. The sieves have essentially no effect on the asymmetric induction. (see **Part VIII**).

The results shown in **Chart 3** reveals that the addition of H_2O will slow down the reaction and diminish the ultimate yield. It was also found that the reaction with H_2O as an additive gives lower asymmetric induction than the one without H_2O (**Part VIII**).

Chart 2. ^{1}H NMR study of the Ugi-3CR with different amounts of 4Å MS

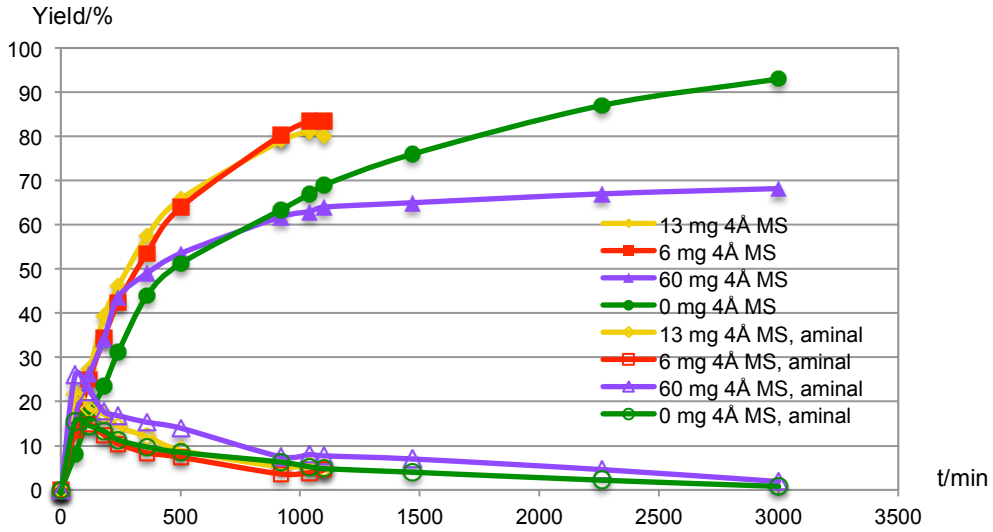
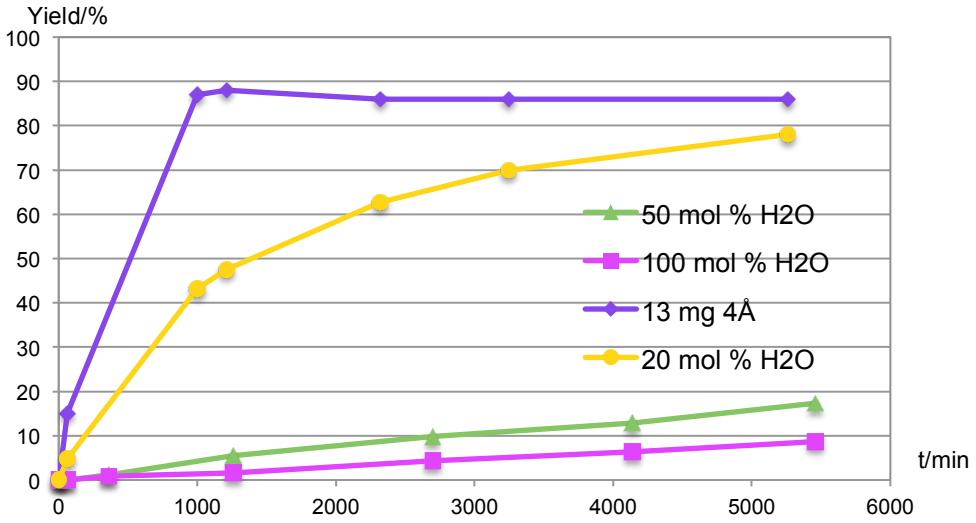
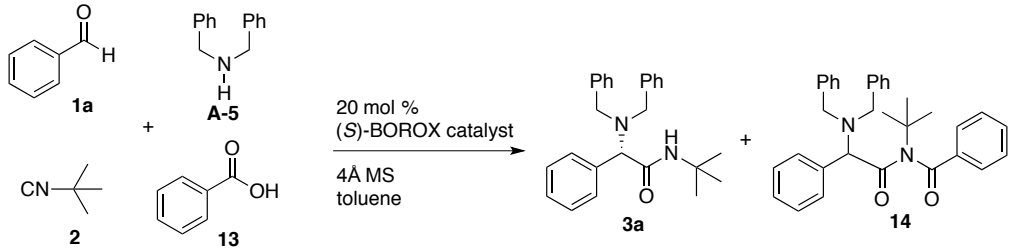


Chart 3. ^{1}H NMR study of the Ugi-3CR with 4Å MS and H_2O



XIX. Effect of PhCOOH on the Ugi-3CR



The pre-catalyst was prepared according to the general procedure A described in **Part V** with (*S*)-VAPOL ligand (27 mg, 0.050 mmol) and phenol **P-36** (14 mg, 0.10 mmol). Dry toluene (1 mL) was added to the flask to dissolve the pre-catalyst, followed by the addition of dibenzylamine **A-5** (0.10 mL, 0.52 mmol, 2.0 equiv) and a certain amount of benzoic acid **13**. This mixture was stirred at 60 °C for 0.5 h. After it was cooled to room temperature, benzaldehyde **1a** (26.0 μL, 0.255 mmol, 1.00 equiv) and *tert*-butyl isocyanide **2** (45 μL, 0.38 mmol, 1.5 equiv) were added in sequence. The reaction mixture was stirred at room temperature for 36-42 h and the crude product was purified by column chromatography on silica gel (20 x 160 mm, hexanes/EtOAc 15:1). The results are shown in **Table 6**.

Table 6. Ugi-3CR with PhCOOH as an additive.

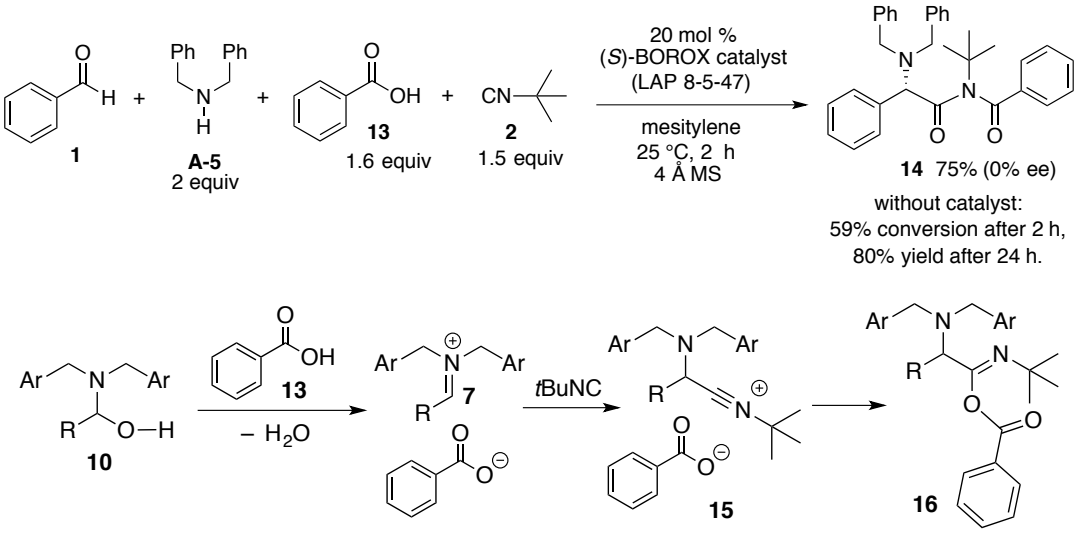
Entry	Time (h)	PhCOOH (mol %)	Ratio of **3a:14**	**3a**[a] %Yield/*er*	**14** %Yield/*er*
1	36	0	1:0	72/70:30	nd

2	39	20	1:0.27	78[b]/65:35	21[b]/nd
3[c]	42	100	1:0.60	60[b]/nd	36[b]/52:48
4[c,d]	42	100	1:0.88	nd	nd

[a] Isolated yield after chromatography on silica gel. [b] NMR yield with the aid of Ph_3CH. [c] 100 mg 4 Å MS was added before the addition of benzaldehyde **3a** [d] The mixture of pre-catalyst, dibenzylamine and PhCOOH was stirred at rt for 5 min instead of at 60 °C for 0.5 h

XX. Four-component Ugi reaction

A four-component version of this reaction with the optimal BOROX catalyst (LAP 8-5-47) was attempted with benzoic acid (shown below). The carboxylic acid component is known to accelerate the 4-component Ugi reaction and this was observed in the present case as well where the reaction was complete in 2 h to give the amino imide **14** in 75% yield but the product was racemic. One possible explanation involves the protonation of the hemi-aminal **10** by benzoic acid to give the iminium ion **7** and then upon addition of the isonitrile, the non-chiral ion pair **15**. Subsequent combining of the ions gives **16** and then an O to N acyl migration would produce **14.**



*N-(tert-butyl)-N-(2-(dibenzylamino)-2-phenylacetyl)benzamide **14***: The pre-catalyst was prepared according to the general procedure A (**Part V**) with (*S*)-**L-8** (41.5 mg, 0.050 mmol), **P-36** (14.0 mg, 0.10 mmol), H_2O (2.7 mg, 2.7 µL, 0.15 mmol), dry toluene (1.5 mL) and BH_3•SMe_2 (2M, 75 µL, 0.15 mmol). After the pre-catalyst was cooled to room temperature, 4 Å MS (250 mg) was added to the flask, followed by the addition of dry toluene (0.5 mL) to dissolve the pre-catalyst.

Then dibenzylamine **A-5** (0.1 mL, 0.5 mmol, 2 equiv) and benzoic acid **13** (50 mg, 0.41 mmol, 1.6 equiv) were added to the solution, followed by addition of another portion of toluene (0.5 mL). After the mixture was stirred for 5 min at room temperature, benzaldehyde **3a** (26.0 μL, 0.255 mmol, 1.00 equiv) and *tert*-butyl isocyanide **2** (45 μL, 0.38 mmol, 1.5 equiv) were added in sequence. After the mixture was stirred at room temperature for 2 h, the crude ^{1}H NMR spectrum showed that the reaction was complete and that the ratio of **14:3a** was about 16:1. Then the reaction mixture was directly loaded onto a silica gel column (20 x 160 mm, hexanes/EtOAc 15:1) to afford a mixture of the product **14** and phenol **P-36**. The yield of product **14** was calculated to be 75% with the aid of Ph_3CH as an internal standard. The optical purity was determined to be 50.1:49.9 *er* by HPLC analysis (Chiralpak AD column, hexanes/2-propanol 98:2, 222 nm, flow 1 mL). Retention times: R_t = 4.91 min and R_t = 12.49 min. Spectral data for **14**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.56 (s, 9H), 3.75 (d, 2H, *J* = 14.5 Hz), 3.84 (d, 2H, *J* = 14.5 Hz), 4.18 (s, 1H), 6.92-7.06 (m, 4H), 7.10-7.29 (m, 16H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.61, 54.59, 59.44, 66.95, 126.63, 127.58, 127.98, 128.03, 128.20, 128.49, 129.48, 129.86, 133.47, 135.21, 136.72, 140.22, 171.54, 174.82; HRMS (ESI+) calcd for $C_{33}H_{35}N_2O_2$ *m/z* 491.2699 ($[M+H]^+$), meas 496.2696.

XXI. Reference

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