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Supporting Information

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Pd^{II}-Catalyzed Enantioselective Activation of sp^2 and sp^3 C-H Bonds Using *mono*-Protected Amino Acids as Chiral Ligands

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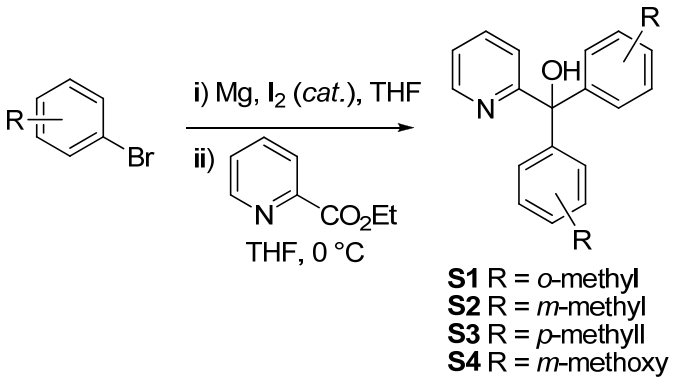
General Information: Unless otherwise noted all commercial materials were used without further purification. Solvents were obtained from Acros or Sigma-Aldrich and used directly without further purification. Infrared spectra were recorded on a Perkin Elmer FT-IR Spectrometer. Nuclear magnetic resonance (NMR) spectra were recorded with Varian Inova-400, Bruker DRX-500. ^1H and ^{13}C chemical shifts are reported in ppm downfield of tetramethylsilane and referenced to residual solvent peak ($CHCl_3$ = 7.26) unless otherwise noted. Multiplicities are reported using the following abbreviations: s =

singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad resonance. Optical rotations were measured using a 2 mL cell with a 1 dm path length on a Perkin Elmer polarimeter at 589 nm. High resolution mass spectra for new compounds were recorded at Mass Spectrometry Facilities, The Scripps Research Institute (TSRI). Enantiomeric excesses (ees) were determined on a Hitachi LaChrow Elite HPLC system using commercially available chiral columns. X-ray diffraction was recorded at X-Ray Facility, The Scripps Research Institute (TSRI).

All amino acids (**7a-7c, 7e, 7g-7h** and **8**-1**6**) were purchased from Bachem or EMD except **3-5** and **S6-S11** which were purchased from Acros. **6** was synthesized according to the method of Burgess.[1] **21** was prepared from a lithium salt of 2-ethylpyridine reacted with the corresponding alkyl bromide.[2] **2** was prepared according to the literature procedure.[3]

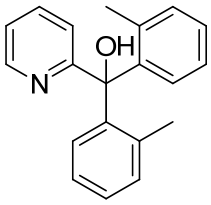
Experimental Procedures:

General Procedure for Grignard Formation and Carboxylate Addition: Preparation of Compound S1-S4 [4]



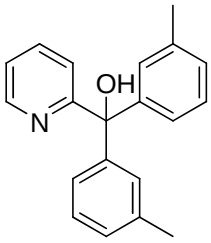
Magnesium (1.17 g, 48.13 mmol) was placed in a 250 mL, oven-dried flask under a nitrogen atmosphere. Anhydrous THF (80 mL) and iodine (*cat.* 40 mg) were added. The reaction mixture was heated at reflux until the purple iodine color disappeared. To this was added dropwise 2-bromotoluene (5.27 mL, 43.75 mmol) in THF (40 mL) via pressure-equalizing addition funnel. The reaction mixture was heated at reflux for about 3 h until a cloudy gray color formed. The resulting Grignard reagent was then cooled to 0 ^{o}C and treated with methyl picolinate (2.05 mL, 17.50 mmol) in THF (40 mL). The mixture was allowed to warm to room temperature and stir overnight. The reaction mixture was quenched by *aqueous* NH_4Cl and extracted with Et_2O. The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. The residue was purified by flash chromatography with ethyl acetate/hexanes as the solvent.

Bis(2-methylphenyl)-2-pyridylmethanol S1



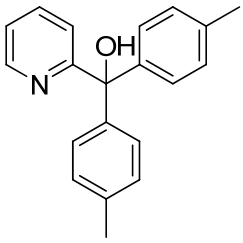
The title compound **S1** was prepared according to the general procedure and was purified by flash chromatography (hexanes : ethyl acetate = 15 : 1). **S1** was obtained as a white solid (3.85 g, 76%).[1]H NMR (400 MHz, $CDCl_3$): δ 8.65 (dd, *J* = 0.8, 4.0 Hz, 1 H), 7.60 (dt, *J* = 1.6, 8.0 Hz, 1 H), 7.26-7.23 (m, 1 H), 7.20-7.15 (m, 4 H), 7.00-6.96 (m, 2 H), 6.90 (d, *J* = 8.0 Hz, 1 H), 6.59 (d, *J* = 8.0 Hz, 2 H), 6.21 (s, 1 H), 2.20 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.4, 147.9, 144.0, 139.1, 136.5, 132.8, 128.6, 127.7, 125.1, 123.8, 122.5, 83.3, 22.4; HRMS (ESI) *m/z*: 290.1546 ($M+H^+$); calc. for $C_{20}H_{20}NO$: 290.1539.

Bis(3-methylphenyl)-2-pyridylmethanol S2



The title compound **S2** was prepared according to the general procedure and was purified by flash chromatography (hexanes : ethyl acetate = 15 : 1). **S2** was obtained as a white solid (5.12 g, 92%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.56 (d, *J* = 4.4 Hz, 1 H), 7.60 (dt, *J* = 7.6, 1.6 Hz, 1 H), 7.21-7.11 (m, 6 H), 7.07 (d, *J* = 7.6 Hz, 2 H), 7.01 (d, *J* = 8.0 Hz, 2 H), 6.26 (s, 1 H), 2.29 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.5, 147.8, 146.3, 137.7, 136.5, 128.9, 128.2, 127.9, 125.5, 123.1, 122.5, 81.0, 21.8; HRMS (ESI) *m/z*: 290.1535 ($M+H^+$); calc. for $C_{20}H_{20}NO$: 290.1539.

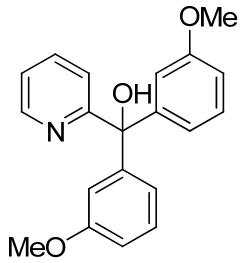
Bis(4-methylphenyl)-2-pyridylmethanol S3



The title compound **S3** was prepared according to the general procedure and was purified by flash chromatography (hexanes : ethyl acetate = 20 : 1 to 15 : 1). **S3** was obtained as a white solid (5.32 g, 90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57 (d, *J* = 4.4 Hz, 1 H), 7.59 (dt, *J* = 1.6, 8.0 Hz, 1 H), 7.21 (d, *J* = 8.4 Hz, 4 H), 7.19-7.15 (m, 2 H), 7.12 (d, *J* = 8.0 Hz, 4 H), 6.25 (s, 1 H), 2.34 (s, 6 H); ^{13}C NMR (100

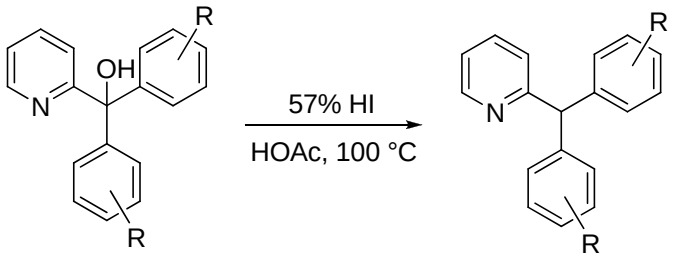
MHz, $CDCl_3$): δ 163.8, 147.9, 143.6, 137.0, 136.5, 128.8, 128.3, 123.0, 122.4, 80.8, 21.3; HRMS (ESI) *m/z*: 290.1538 ($M+H^+$); calc. for $C_{20}H_{20}NO$: 290.1539.

Bis(3-methoxylphenyl)-2-pyridylmethanol S4



The title compound **S4** was prepared according to the general procedure and was purified by flash chromatography (hexanes : ethyl acetate = 5 : 1). **S4** was obtained as a white solid (2.93 g, 81%). ^1H NMR (400 MHz, $CDCl_3$): δ 8.59-8.57 (m, 1 H), 7.53 (dt, *J* = 1.6, 8.0 Hz, 1 H), 7.2-7.19 (m, 3 H), 7.13 (dt, *J* = 0.8, 8.0 Hz, 1 H), 6.93 (t, *J* = 2.0 Hz, 2 H), 6.82 (d, *J* = 2.0 Hz, 2 H), 6.80 (d, *J* = 2.0 Hz, 2 H), 6.27 (s, 1 H), 3.75 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.2, 159.5, 147.9, 147.7, 136.6, 129.0, 123.0, 122.6, 120.9, 114.1, 112.9, 80.9, 55.4, 55.3; HRMS (ESI) *m/z*: 322.1439 ($M+H^+$); calc. for $C_{20}H_{20}NO_3$: 322.1438.

General Procedure for the Reduction of S1-S3 with HI: Preparation of Compound 1, 17 and 20. [5]

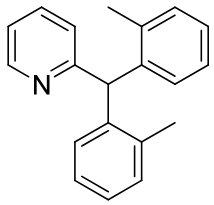


S1 R = *o*-methyl
S2 R = *m*-methyl
S3 R = *p*-methyl

1 R = *o*-methyl
17 R = *m*-methyl
20 R = *p*-methyl

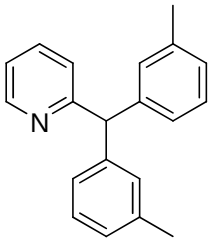
A mixture of **S1** (300 mg, 1.04 mmol), *aqueous* 57% HI (0.8 mL), and HOAc (4 mL) was heated to 100 ^oC for 4 hours. The resulting mixture was then cooled to 0 ^oC, basified to pH 9 with *aqueous* NaOH, diluted with ethyl acetate and washed successively with *aqueous* $NaHSO_3$ and brine. The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. The residue was purified by flash chromatography with ethyl acetate/hexanes as the solvent.

Bis(2-methylphenyl)-2-pyridylmethanol (1)



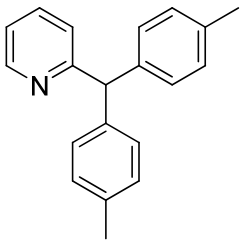
The title compound **S1** was prepared according to the general procedure and was purified by flash chromatography (hexanes : ethyl acetate = 8 : 1). **1** was obtained as a white solid (259 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.62-8.60 (m, 1 H), 7.58 (dt, *J* = 2.0, 7.6 Hz, 1 H), 7.16-7.13 (m, 5 H), 7.09(dt, *J* = 2.0, 7.2 Hz, 2 H), 6.90 (d, *J* = 8.0 Hz, 1 H), 6.71 (d, *J* = 7.2 Hz, 2 H), 5.90 (s, 1 H), 2.20 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.0, 150.0, 141.1, 137.0, 136.5, 130.7, 129.2, 126.8, 126.1, 124.1, 121.5, 53.6, 19.9; HRMS (ESI) *m/z*: 274.1600 ($M+H^+$); calc. for $C_{20}H_{20}N$: 274.1590.

Bis(3-methylphenyl)-2-pyridylmethanol (17)



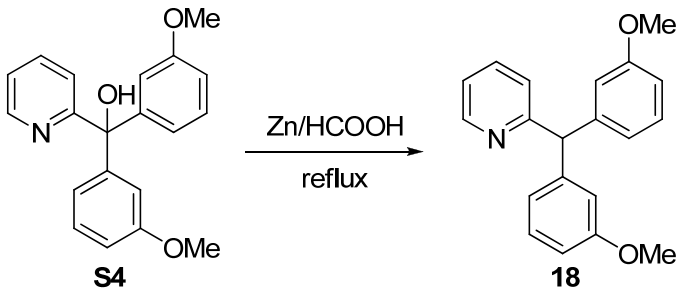
The title compound **S2** was prepared according to the general procedure and was purified by flash chromatography (hexanes : ethyl acetate = 8 : 1). **17** was obtained as a white solid (1.36 g, 93%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.62-8.60 (m, 1 H), 7.60 (dt, *J* = 2.0, 7.6 Hz, 1 H), 7.20 (t, *J* = 7.6 Hz, 2 H), 7.15-7.09 (m, 2 H), 7.07 (d, *J* = 7.6 Hz, 2 H), 7.02 (s, 2 H), 6.97 (d, *J* = 7.6 Hz, 2 H), 5.65 (s, 1 H), 2.31 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.6, 149.6, 142.8, 138.1, 136.5, 130.3, 128.4, 127.4, 126.6, 123.8, 121.5, 59.5, 21.7; HRMS (ESI) *m/z*: 274.1589 ($M+H^+$); calc. for $C_{20}H_{20}N$: 274.1590.

Bis(4-methylphenyl)-2-pyridylmethanol (20)



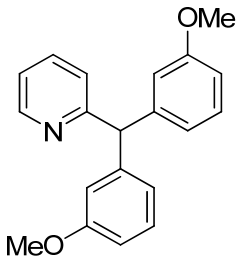
The title compound **S3** was prepared according to the general procedure and was purified by flash chromatography (hexanes : ethyl acetate = 15 : 1 to 10 : 1). **20** was obtained as a yellow oil (1.68 g, 93%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.63 (dd, *J* = 5.2, 2.0 Hz, 1 H), 7.60 (dt, *J* = 2.0, 7.6 Hz, 1 H), 7.16-7.10 (m, 2 H), 7.15 (d, *J* = 8.4 Hz, 4 H), 7.11(d, *J* = 8.4 Hz, 4 H), 5.68 (s, 1 H), 2.36 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.8, 149.7, 140.2, 136.5, 136.1, 129.4, 129.3, 123.8, 121.5, 58.8, 21.2; HRMS (ESI) *m/z*: 274.1594 ($M+H^+$); calc. for $C_{20}H_{20}N$: 274.1590.

Preparation of Bis(3-methoxylphenyl)-2-pyridylmethane (18) [6]



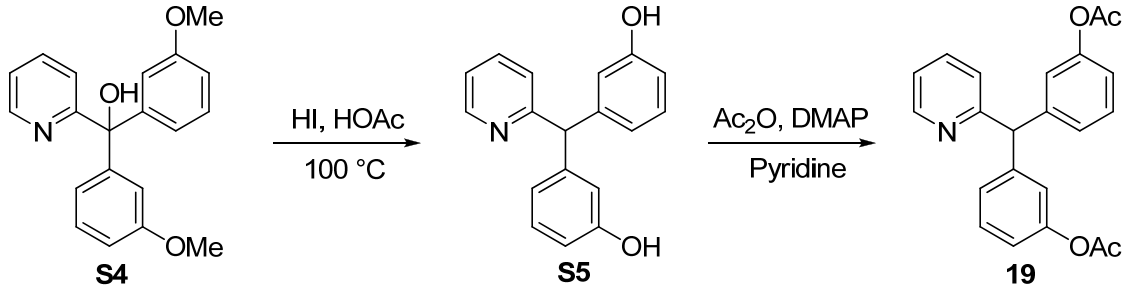
S4 **18**

Zinc (3.36 g, 51.7 mmol) was added to a solution of **S4** (1.663 g, 5.17 mmol) in formic acid (15 mL). The mixture was vigorously stirred under reflux for 16 h and then filtered. The filter cake was washed with formic acid and the filtrate concentrated under reduced pressure. The residue was taken up in water and the pH adjusted to 9 with aqueous NaOH. The solution was extracted with ethyl acetate, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (hexanes : ethyl acetate = 5: 1 to 2: 1) to give **18** (967 mg, 61%) as a yellow oil.



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.58 (d, *J* = 5.2 Hz, 1 H), 7.57 (dt, *J* = 2.0, 10.4 Hz, 1 H), 7.25-7.06 (m, 4 H), 6.76-6.72 (m, 6 H), 5.63 (s, 1 H), 3.72 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.1, 159.8, 149.7, 144.2, 136.6, 129.5, 123.8, 122.0, 121.6, 115.6, 111.8, 59.5, 55.3; HRMS (ESI) *m/z*: 306.1492 ($M+H^+$); calc. for $C_{20}H_{20}NO_2$: 306.1488.

Preparation of Bis(3-acetoxylphenyl)-2-pyridylmethane 19



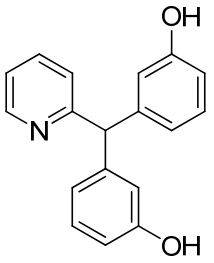
S4 **S5** **19**

Bis(3-hydroxylphenyl)-2-pyridylmethane was prepared according to the general procedure as described for the preparation of **1** and was purified by flash chromatography (hexanes : ethyl acetate = 1 : 3) to give **S5** as a white solid (1.50 g, 89%).

To a solution of bis(3-hydroxylphenyl)-2-pyridylmethane (1.50 g, 5.41 mmol) and DMAP (150 mg) in dry pyridine (mL) was added Ac_2O (1.5 mL, 16.23 mmol) dropwise under N_2 at 0 ^oC. The reaction mixture was allowed to warm to rt and stir overnight after which the solvent was evaporated under reduced pressure and the resulting residue was diluted with ethyl acetate, washed successively with

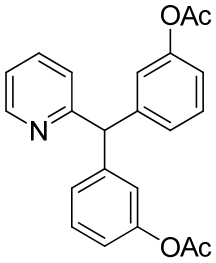
saturated $NaHCO_3$ and brine. The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. The residue was purified by flash chromatography (hexanes : ethyl acetate = 3 : 1) to give **19** (1.88 g, 96%) as a white solid.

Bis(3-hydroxylphenyl)-2-pyridylmethane S5



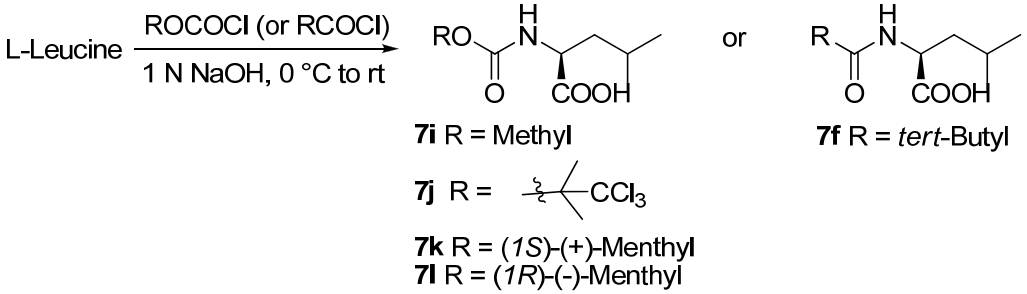
^{1}H NMR (400 MHz, DMSO-d_6): δ 9.22 (s, 2 H), 8.48 (d, J = 3.6 Hz, 1 H), 7.68 (dt, J = 1.6, 7.6 Hz, 1 H), 7.20-7.15 (m, 2 H), 7.04-7.00 (m, 2 H), 6.55-6.54 (m, 6 H), 5.42 (s, 1 H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.2, 157.8, 149.7, 145.0, 137.2, 129.7, 124.1, 122.2, 120.4, 116.7, 113.9, 58.7; HRMS (ESI) *m/z*: 278.1179 ($M+H^+$); calc. for $C_{18}H_{16}NO_2$: 278.1175.

Bis(3-acetoxylphenyl)-2-pyridylmethane (19)



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.56 (dd, J = 1.6, 4.4 Hz, 1 H), 7.56 (dt, J = 1.6, 7.6 Hz, 1 H), 7.28 (t, J = 8.0 Hz, 2 H), 7.11-7.08 (m, 2 H), 7.04 (d, J = 8.0 Hz, 2 H), 6.98 (dd, J = 1.6, 8.0 Hz, 2 H), 6.90 (s, 2 H), 5.67 (s, 1 H), 2.20 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.5, 162.1, 150.9, 149.8, 144.1, 136.9, 129.5, 126.9, 124.0, 122.6, 121.9, 120.2, 58.8, 21.3; HRMS (ESI) *m/z*: 362.1394 ($M+H^+$); calc. for $C_{22}H_{20}NO_4$: 362.1387.

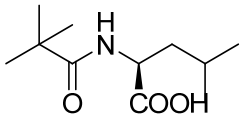
General Procedure for the Preparation of L-leucine Derived Chiral Ligands [7]



To a magnetically stirred solution at 0 °C of L-leucine (5 g, 38.12 mmol) and 1 N NaOH (100 mL) was added methyl chloroformate (3.84 mL, 49.55 mmol) in portions over 0.5 h. The reaction mixture was allowed to warm to rt and stir overnight, and then was extracted with ether. The aqueous phase was

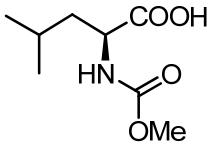
cooled to 0 °C, adjusted to pH 1 by the addition of HCl and then extracted with ethyl acetate. The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The residue was purified by flash chromatography (methanol : dichloromethane = 1:15) to give **7i** (6.06 g, 84%) as a yellow liquid.

***N*-Pivalyl-L-leucine 7f**



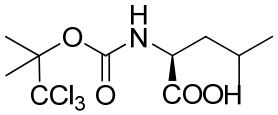
The title compound **7f** was prepared according to the general procedure and was purified by recrystallization from ethyl acetate/hexanes. **7f** was obtained as a white solid (6.06 g, 91%). $[\alpha]_D^{20}$ = -15.19 (*c* 1.31, ethyl acetate);[9] ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.43 (br, 1 H), 6.26 (d, *J* = 8.4 Hz, 1 H), 4.53-4.48 (m, 1 H), 1.60-1.49 (m, 3 H), 1.09 (s, 9 H), 0.82 (d, *J* = 6.0 Hz, 3 H), 0.81 (d, *J* = 5.6 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.3, 176.4, 50.9, 41.3, 38.8, 27.4, 25.0, 22.9, 22.1; IR (neat) 2956, 1724, 1618, 1545, 1209 cm^{-1}; HRMS (ESI) *m/z*: 216.1592 ($M+H^+$); calc. for $C_{11}H_{22}NO_3$: 216.1594.

***N*-Methoxycarbonyl-L-leucine 7i**



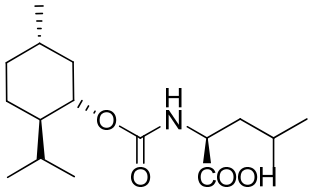
$[\alpha]_D^{20}$ = -18.21 (*c* 1.06, $CHCl_3$);[8] ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.46 (d, *J* = 6.8 Hz, 1 H), 4.03-3.99 (m, 1 H), 3.60 (s, 3 H), 1.71-1.69 (m, 1 H), 1.59-1.51 (m, 2 H), 0.94 (d, *J* = 5.2 Hz, 3 H), 0.91 (d, *J* = 5.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.8, 157.1, 52.6, 52.5, 41.4, 24.8, 23.0, 21.7; IR (neat) 2958, 1701, 1541, 1230 cm^{-1}; HRMS (ESI) *m/z*: 190.1068 ($M+H^+$); calc. for $C_8H_{16}NO_4$: 190.1074.

***N*-[2,2,2-trichloro-1,1-dimethylethoxycarbonyl]-L-leucine 7j**



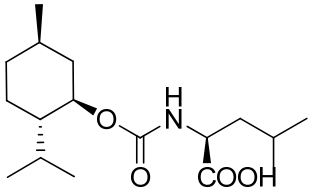
The title compound **7j**was prepared according to the general procedure and was purified by recrystallization from ethyl acetate/hexanes. **7j** was obtained as a white solid (6.13 g, 87%). $[\alpha]_D^{20}$ = -5.47 (*c* 1.28, $CHCl_3$); ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.64 and 7.25 (d, *J* = 8.0 Hz, 1 H), 4.02-3.99 (m, 1 H), 1.90, 1.88 and 1.85 (s, 6 H), 1.69-1.66 (m, 1 H), 1.52 (m, 2 H), 0.94 (d, *J* = 7.0 Hz, 6 H), 0.95 (d, *J* = 6.5 Hz, 3 H), 0.92 (d, *J* = 6.5 Hz, 3 H), 0.79 (d, *J* = 6.5 Hz, 3 H); IR (neat) 2953, 1719, 1541, 1223 cm^{-1}; HRMS (ESI) *m/z*: 334.0382 ($M+H^+$); calc. for $C_{11}H_{19}Cl_3NO_4$: 334.0374.

***N*-[(+)-Menthoxylcarbonyl]-L-leucine 7k**



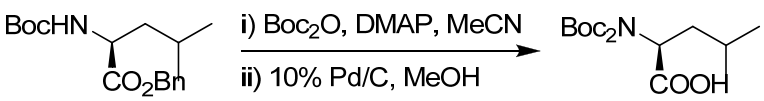
The title compound **7k**was prepared according to the general procedure and was purified by flash chromatography (dichloromethane : methanol = 15 : 1). **7k** was obtained as a white foam (2.13 g, 85%). $[\alpha]_D^{20}$ = 39.58 (*c* 0.95, $CHCl_3$); ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.33 (d, *J* = 8.0 Hz, 1 H), 4.48 (dt, *J* = 4.0, 11.0 Hz, 1 H), 4.04-4.01 (m, 1 H), 1.95-1.93 (m, 2 H), 1.71-1.66 (m, 3 H), 1.59-1.56 (m, 1 H), 1.52-1.48 (m, 2 H), 1.37-1.32 (m, 1 H), 1.10-1.04 (m, 1 H), 1.01-0.99 (m, 1 H), 0.94 (d, *J* = 6.5 Hz, 3 H), 0.93 (d, *J* = 6.5 Hz, 3 H), 0.92 (d, *J* = 7.5 Hz, 3 H), 0.90 (d, *J* = 6.5 Hz, 3 H), 0.79 (d, *J* = 7.0 Hz, 3 H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 175.2, 156.9, 73.9, 52.8, 47.9, 42.2, 34.7, 31.8, 26.6, 25.2, 24.0, 23.6, 22.7, 21.9, 21.3, 17.1; IR (neat) 2958, 1717, 1541, 1228 cm^{-1}; HRMS (ESI) *m/z*: 314.2329 ($M+H^+$); calc. for $C_{17}H_{32}NO_4$: 314.2326.

***N*-[(-)-Menthoxylcarbonyl]-L-leucine 7l**



The title compound **7l** was prepared according to the general procedure and was purified by flash chromatography (dichloromethane : methanol = 15 : 1). **7l** was obtained as a white foam (4.31 g, 91%). $[\alpha]_D^{20}$ = -54.19 (*c* 1.36, $CHCl_3$); ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.29 (d, *J* = 8.5 Hz, 1 H), 4.47 (dt, *J* = 4.0, 11.0 Hz, 1 H), 4.00-3.99 (m, 1 H), 2.04-2.01 (m, 1 H), 1.95-1.92 (m, 1 H), 1.71-1.66 (m, 3 H), 1.59-1.58 (m, 1 H), 1.53-1.47 (m, 2 H), 1.37-1.31 (m, 1 H), 1.12-1.04 (m, 1 H), 1.00-0.97 (m, 1 H), 0.94 (d, *J* = 7.0 Hz, 6 H), 0.92 (d, *J* = 7.0 Hz, 3 H), 0.91 (d, *J* = 6.0 Hz, 3 H), 0.79 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 175.0, 156.7, 73.5, 52.7, 47.6, 41.8, 34.4, 31.5, 26.1, 24.9, 23.6, 23.4, 22.5, 21.7, 21.1, 16.8; IR (neat) 2958, 1717, 1541, 1228 cm^{-1}; HRMS (ESI) *m/z*: 314.2329 ($M+H^+$); calc. for $C_{17}H_{32}NO_4$: 314.2326.

Preparation of *N*,*N*-Di-*tert*-butoxycarbonyl-L-leucine 7d

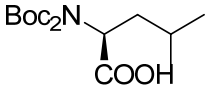


To a stirred solution of BocLeu-OBn (8.09 g, 25.17 mmol) and DMAP (615 mg, 5.03 mmol,) in dry CH_3CN (90 ml) was added $(Boc)_2O$ (6.04 g, 27.69 mmol) at rt. The mixture was stirred for 2 h, after which TLC showed that some starting material still remained. Another portion of $(Boc)_2O$ (3.02 g, 13.84 mmol) was added and the mixture was additionally stirred overnight. The solvent was evaporated,

and the resulting residue was purified by flash chromatography to afford Boc_2Leu-OBn (10.83 g, 98% yield) as an oil.

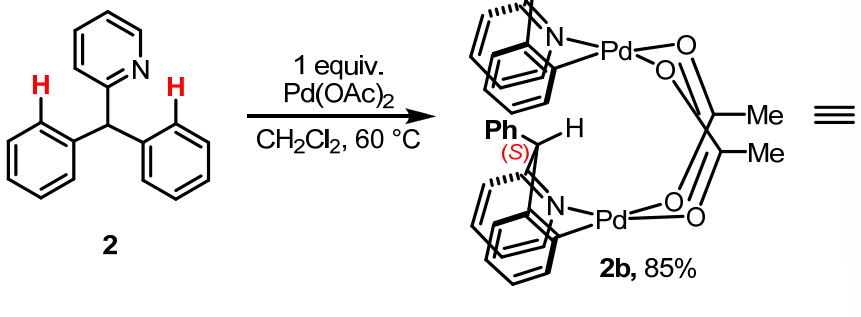
To a mixture containing Boc_2Leu-OBn (6.46 g, 15.33 mmol) and 10% palladium on activated carbon (323 mg) in methanol (100 mL) was added a balloon of hydrogen, and the flask was evacuated and flushed with hydrogen from the balloon several times. After stirring at rt overnight, the hydrogen was removed and the mixture was filtered through a plug of Celite 545. The plug was rinsed with methanol (150 mL), and the combined filtrates were concentrated under reduced pressure. The residue was recrystalized from ethyl acetate/hexanes to give **7d** (4.83 g, 95%) as a white solid.

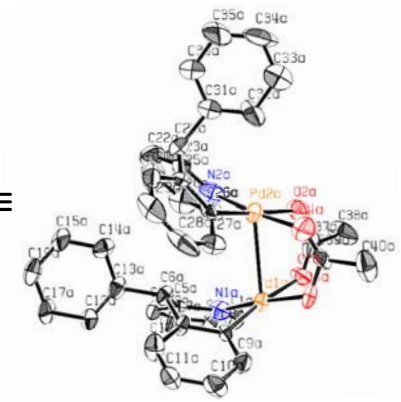
***N,N*-Di-*tert*-butoxycarbonyl L-leucine 7d**



$[\alpha]_D^{20}$ = -26.31 (*c* 1.25, CH_2Cl_2);[10] ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.24 (br, 1 H), 4.91 (dd, J = 5.2, 9.2 Hz, 1 H), 1.82-1.75 (m, 2 H), 1.57-1.53 (m, 1 H), 1.42 (s, 18 H), 0.86 (d, *J* = 6.8 Hz, 3 H), 0.85 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.0, 152.1, 83.3, 56.5, 38.6, 28.0, 25.2, 23.3, 21.9; IR (neat) 2361, 1735, 1712, 1699, 1366, 1129 cm^{-1}; HRMS (ESI) *m/z*: 354.1887 ($M+Na^+$); calc. for $C_{16}H_{29}NNaO_6$: 354.1887.

Synthesis of the Acetato-bridged Dinuclear Cyclopalladated Complex 2b:





$Pd(OAc)_2$ (471.5 mg, 2.1 mmol, 1.0 equiv) and **2** (515.2 mg, 2.1 mmol, 1.0 equiv) were combined in CH_2Cl_2 (30 mL). The reaction was stirred at 60 °C for 24 h, and then was filtered through celite to remove the palladium black and washed thoroughly with dichloromethane. The solvent was removed under reduced pressure. Hexanes was added to the resulting yellow solid, and this suspension was sonicated for 5 minutes. The yellow precipitate was collected by vacuum filtration, washed with hexanes, and dried under vacuum to afford **2b** (730 mg, 85%) as a yellow powder. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.82 (m, 2 H), 8.10 (t, *J* = 5.0 Hz, 2 H), 7.96 (d, *J* = 7.5 Hz, 2 H), 7.51-7.45 (m, 4 H), 7.32-7.30 (m, 6 H), 7.27-7.18 (m, 6 H), 7.02 (t, 2 H), 6.91 (t, *J* = 5.5 Hz, 2 H), 5.85 (s, 2 H), 1.74 (s, 6 H); ESI-MS *m/z*: 819.05 ($M+H^+$).

X-ray crystal structure data for 2b:

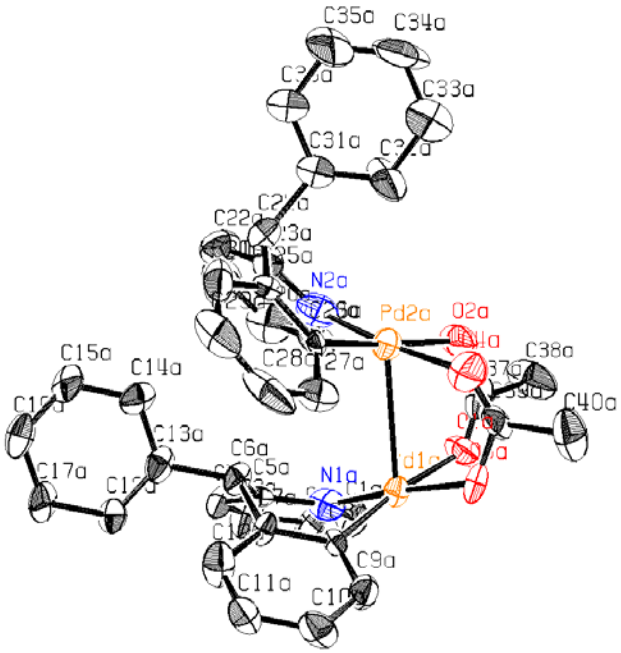
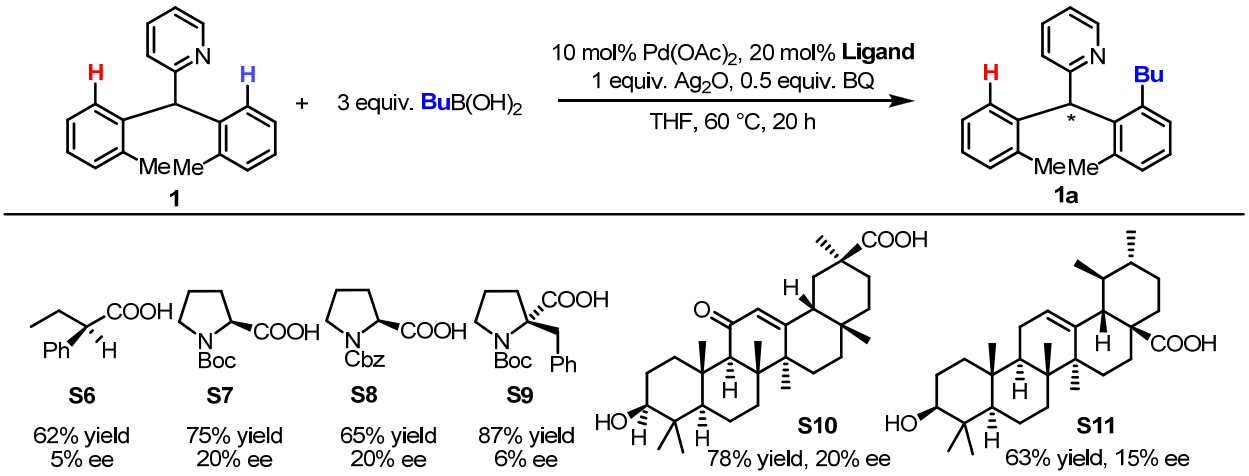


Table S1. Crystal data and structure refinement for **2b**.

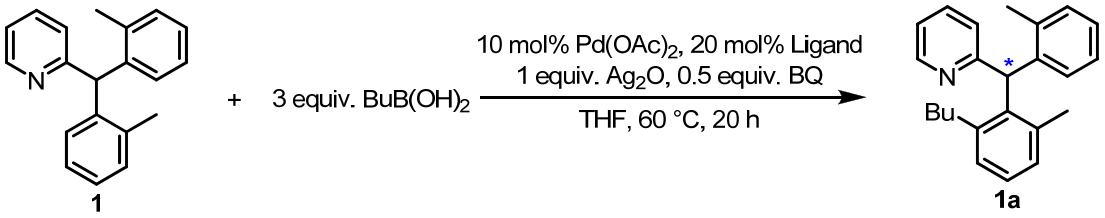
X-ray ID	**2b**	
Empirical formula	C41H34N2O4Pd2·CH2Cl2	
Formula weight	904.42	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	orthorhombic	
Space group	$Pna2_1$ (No. 33, C_{2v}^9)	
Unit cell dimensions	a = 47.632 (10) Å	α= 90°.
	b = 11.154(2) Å	β= 113.995(5)°.
	c = 14.125(3) Å	γ = 90°.
Volume	7505(3) $Å^3$	
Z	8	
Density (calculated)	1.601 Mg/m^3	
Absorption coefficient	1.145 mm^{-1}	
F(000)	3632	
Crystal size	0.22 x 0.18 x 0.03 mm^3	
Crystal color/habit	yellow plate-like	
Theta range for data collection	1.68 to 25.00°.	
Index ranges	-56<=h<=56, -13<=k<=13, -16<=l<=16	

Reflections collected	53475
Independent reflections	13227 [R(int) = 0.0502]
Completeness to theta = 25.00°	100 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9665 and 0.7868
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	13227 / 10 / 715
Goodness-of-fit on F^2	1.055
Final R indices [I>2sigma(I)]	R1 = 0.0646, wR2 = 0.1514
R indices (all data)	R1 = 0.0878, wR2 = 0.1660
Absolute structure parameter	0.55(6)
Extinction coefficient	0.00000(2)
Largest diff. peak and hole	1.330 and -1.107 e.Å^{-3}

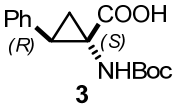
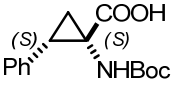
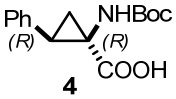
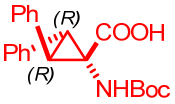
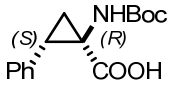
Preliminary Results Obtained with Chiral Carboxylic Acids



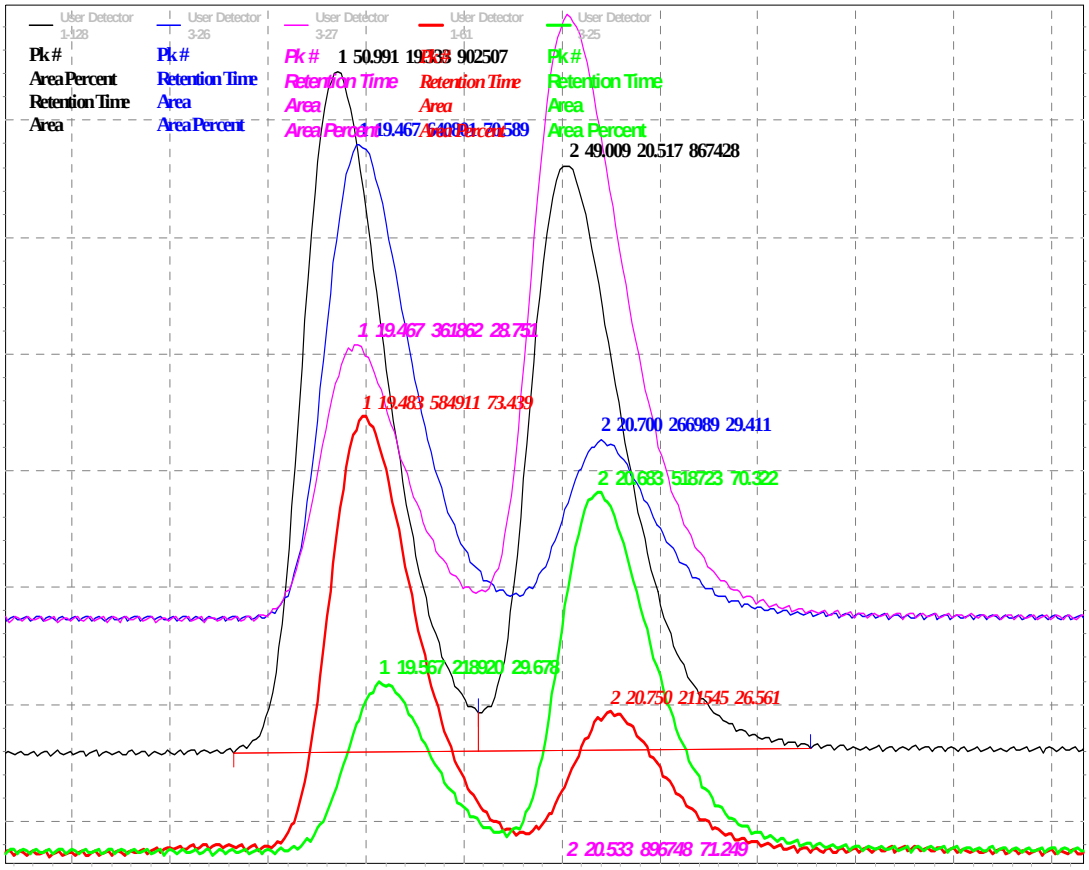
Influence of Ligand Structures on Enantioselectivity



1 1a

Entry	Ligand	Yield (%)[a]	Ee (%)[b]	Entry	Ligand	Yield (%)[a]	Ee (%)[b]
1	 **3**	46	46	4	 **S12**	69	41
2	 **4**	71	-41[c]	5	 **6**	58	2
3	 **5**	63	-42[c]				

[a]Isolated yields. [b]Enantiomeric excess (ee) was determined by chiral HPLC.[c]Opposite enantiomer was obtained.



Area % report for entry 1 (red line):

User detector results

Retention Time	Area	Area %	Height	Height %
19.483	584911	73.44	18603	75.54
20.750	211545	26.56	6023	24.46
Totals	796456	100.00	24626	100.00

Area % report for entry 2 (green line):

User detector results

Retention Time	Area	Area %	Height	Height %
19.567	218920	29.68	7171	31.97
20.683	518723	70.32	15258	68.03
Totals	737643	100.00	22429	100.00

Area% report for entry 3 (pink line):

User detector results

Retention Time	Area	Area %	Height	Height %
19.467	361862	28.75	11804	31.40
20.533	896748	71.25	25787	68.60
Totals	1258610	100.00	37591	100.00

Area% report for entry 4 (blue line):

User detector results

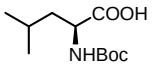
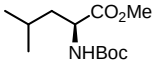
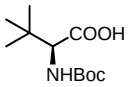
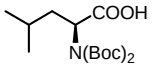
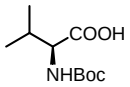
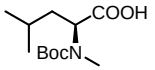
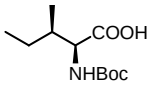
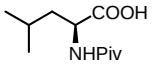
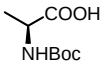
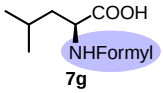
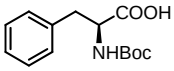
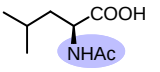
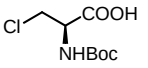
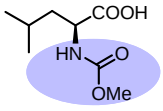
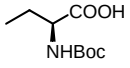
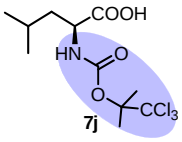
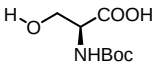
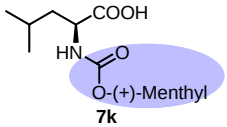
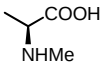
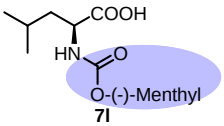
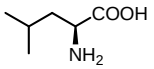
Retention Time	Area	Area %	Height	Height %
19.467	640801	70.59	20324	72.71
20.700	266989	29.41	7627	27.29
Totals	907790	100.00	27951	100.00

Area% report for entry 5 (black line):

User detector results

Retention Time	Area	Area %	Height	Height %
19.333	902507	50.99	29169	53.82
20.517	867428	49.01	25027	46.18
Totals	1769935	100.00	54196	100.00

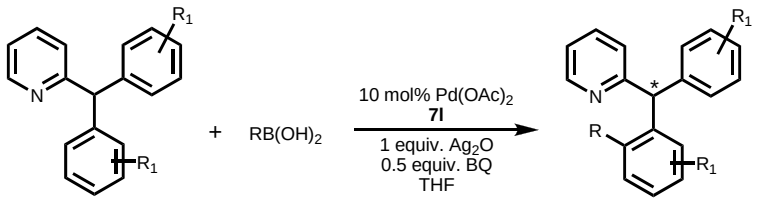
Optimization of Chiral Ligands for Butylation of Prochiral sp^2 C-H Bonds

Entry	Ligand	Yield (%)[b]	Ee (%)[c]	Entry	Ligand	Yield (%)[a]	Ee (%)[c]
1	 **7a**	63	90	12	 **7c**	86	0
2	 **8**	60	52	13	 **7d**	74	7
3	 **9**	69	70	14	 **7e**	63	6[d]
4	 **10**	85	72	15	 **7f**	58	7
5	 **11**	60	80	16	 **7g**	53	6
6	 **12**	66	81	17	 **7h**	74	80
7	 **13**	83	83	18	 **7i**	88	79
8	 **14**	47	85	19	 **7j**	89	85
9	 **15**	65	88	20	 **7k**	87	85
10	 **16**	nr	\	21	 **7l**	91	87
11	 **7b**	nr	\				

[a]All reactions were performed with **1** (0.2 mmol) and BuB(OH)2 (0.6 mmol) in the presence of $Pd(OAc)_2$ (10 mol%), chiral lignad (20 mol%), BQ (0.5 equv.), and Ag_2O (1.0 equiv.) in 2 mL of anhydrous THF at 60 °C for 20 h. [b]Yields were based on isolated products. [c]Enantiomeric excesses (ees) were determined by chiral HPLC. [d]Opposite enantiomer was obtained.

(**Table 1**)

General Procedure for the Enantioselective Alkylation of sp^2 C-H Bonds with Boronic Acids



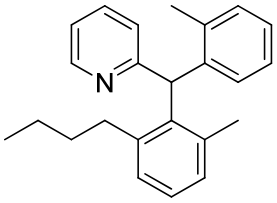
Entry	Substrate	R_1	R	*T* (°C)	**7l** (mol%)	Time (h)	Yield (%)[a]	ee (%)[b]
1	**1**	*o*-Me	*n*-Butyl	60	20	20	91	87
2	**1**	*o*-Me	*n*-Butyl	50	20	20	50	95
3	**1**	*o*-Me	*n*-Butyl	60	10	20	96	88
4	**2**	H	*n*-Butyl	80	20	20	47	79
5	**2**	H	*n*-Butyl	80	10	20	56	74
6	**1**	*o*-Me	Ethyl	60	10	20	81	84
7	**1**	*o*-Me	Cyclopropyl	60	10	20	61	89
8[c]	**17**	*m*-Me	*n*-Butyl	60	10	40	58	84
9[c]	**18**	*m*-OMe	*n*-Butyl	80	10	20	55	54
10[c]	**19**	*m*-OAc	*n*-Butyl	80	10	20	43	72
11	**20**	*p*-Me	*n*-Butyl	80	10	20	61	78

[a]Isolated yields. [b]Ees were determined by chiral HPLC. [c]Alkylation occured only at the less hindered position.

(**Table 2**)

In a 20 mL tube, the substrate (0.2 mmol, 1 equiv.), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol, 10 mol%), boronic acid (0.6 mmol, 3 equiv.), Ag_2O (46.3 mg, 0.2 mmol, 1 equiv.), benzoquinone (10.8 mg, 0.1 mmol, 0.5 equiv.) and **7l** (equivalent as described in Table 2) were dissolved in 2 mL of anhydrous THF under atmospheric air. The tube was sealed with a Teflon lined cap, and the reaction mixture was stirred at desired temperature and time as shown in Table 2. The reaction mixture was filtered through a pad of Celite, and the Celite was washed with 20 mL of CH_2Cl_2. The filtrate was concentrated under vacuum. The residue was purified by column chromatography to give the alkylated product and enantiomeric excesses (ees) were determined on a Hitachi LaChrow Elite HPLC system using commercially available chiral columns as described below.

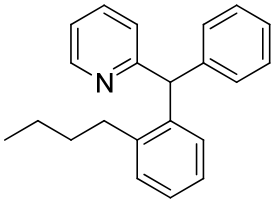
(2-Butyl-6-methylphenyl)(2-pyridyl)(*o*-tolyl)methane 1a



(Table 2, entry 2): The title compound **1a** was prepared according to the general procedure and was purified by flash chromatography (hexanes : ethyl acetate = 15 : 1). **2** was obtained as a white solid (32.9 mg, 50%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.59 (d, *J* = 4.0 Hz, 1 H), 7.53 (t, *J* = 7.6 Hz, 1 H), 7.21-7.10 (m, 6 H), 7.01 (d, *J* = 7.2 Hz, 1 H), 6.93 (d, *J* = 7.6 Hz, 1 H), 6.85 (d, *J* = 7.6 Hz, 1 H), 6.12 (s, 1 H), 2.51-2.44 (m, 2 H), 2.15 (s, 3 H), 1.94 (s, 3 H), 1.28-1.14 (m, 4 H), 0.75 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.6, 149.5, 142.5, 139.5, 139.1, 137.9, 137.5, 136.3, 130.5, 129.5, 129.4,

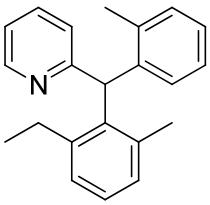
128.5, 127.0, 126.8, 126.2, 123.6, 120.9, 52.3, 52.3, 34.7, 33.2, 23.1, 22.4, 20.0, 14.0; HRMS (ESI) *m/z*: 330.2223 ($M+H^+$); calc. for $C_{24}H_{28}N$: 330.2216; $[\alpha]_D^{20}$ = -86.60 (*c* 0.50, $CHCl_3$); HPLC chiralcel OD-H then OD column (0.25% isopropanol in hexanes, 1 mL/min) t_r 17.983 min (major), 19.433 min (minor): 95% ee.

(2-Butylphenyl)phenyl-2-pyridylmethane 2g



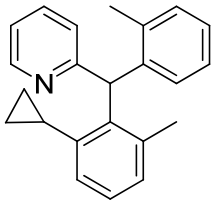
(Table 2, entry 4): The title compound **2g** was prepared according to the general procedure and was purified by flash chromatography (hexanes : ethyl acetate = 15 : 1). **2g** was obtained as a white solid (28.3 mg, 47%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.60 (dd, *J* = 0.8, 4.8 Hz, 1 H), 7.57 (dt, *J* = 2.0, 7.6 Hz, 1 H), 7.30-7.23 (m, 2 H), 7.21-7.18 (m, 3 H), 7.17-7.06 (m, 4 H), 6.98 (d, *J* = 8.0 Hz, 1 H), 6.87 (d, *J* = 7.6 Hz, 1 H), 5.96 (s, 1 H), 2.60-2.56 (m, 2 H), 1.46-1.40 (m, 2 H), 1.33-1.26 (m, 2 H), 0.84 (t, *J* = 7.6 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.5, 149.7, 143.0, 141.5, 140.6, 136.5, 129.8, 129.7, 129.6, 128.5, 126.7, 126.5, 125.9, 124.1, 121.4, 77.5, 77.2, 76.8, 55.5, 33.3, 32.7, 22.9, 14.1; HRMS (ESI) *m/z*: 302.1908 ($M+H^+$); calc. for $C_{22}H_{24}N$: 302.1903; $[\alpha]_D^{20}$ = 3.27 (*c* 0.52, $CHCl_3$); HPLC chiralcel OD then AD column (5% isopropanol in hexanes, 1 mL/min) t_r 9.273 min (major), 7.545 min (minor): 79% ee.

(2-Ethyl-6-methylphenyl)(2-pyridyl)(*o*-tolyl)methane 1b



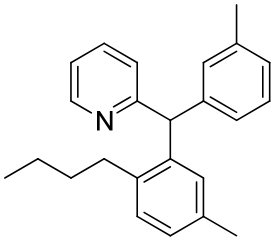
(Table 2, entry 6): The title compound **1b** was prepared according to the general procedure and was purified by flash chromatography (hexanes : ethyl acetate = 15 : 1). **1b** was obtained as a white solid (48.8 mg, 81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.58 (dd, *J* = 0.8, 4.8 Hz, 1 H), 7.53 (dt, *J* = 2.0, 7.6 Hz, 1 H), 7.22-7.16 (m, 3 H), 7.16-7.14 (m, 3 H), 7.01 (d, *J* = 7.6 Hz, 1 H), 6.92 (d, *J* = 8.0 Hz, 1 H), 6.83 (d, *J* = 7.6 Hz, 1 H), 6.11 (s, 1 H), 2.57-2.42 (m, 2 H), 2.14 (s, 3 H), 1.94 (s, 3 H), 0.88 (t, *J* = 7.6 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.5, 149.5, 143.6, 139.4, 139.0, 137.8, 137.5, 136.3, 130.5, 129.5, 129.4, 127.6, 127.1, 126.8, 126.2, 123.6, 121.0, 52.2, 27.5, 22.4, 20.0, 14.8; HRMS (ESI) *m/z*: 302.1910 ($M+H^+$); calc. for $C_{22}H_{24}N$: 302.1903. $[\alpha]_D^{20}$ = -99.31 (*c* 0.72, $CHCl_3$); HPLC chiralcel OD-H then OD column (0.25% isopropanol in hexanes, 1 mL/min) t_r 22.000 min (major), 25.767 min (minor): 84% ee.

(2-Cyclopropyl-6-methylphenyl)(2-pyridyl)(*o*-tolyl)methane 1c



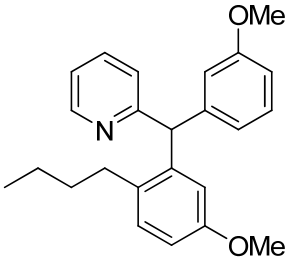
(Table 2, entry 7): The title compound **1c** was prepared according to the general procedure and was purified by flash chromatography (hexanes : ethyl acetate = 15 : 1). **1c** was obtained as a white solid (38.2 mg, 61%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57 (dd, *J* = 1.2, 4.8 Hz, 1 H), 7.52 (dt, *J* = 2.0, 7.6 Hz, 1 H), 7.21-7.09 (m, 5 H), 6.99 (d, *J* = 7.6 Hz, 1 H), 6.94 (t, *J* = 8.8 Hz, 2 H), 6.85 (d, *J* = 7.6 Hz, 1 H), 6.51 (s, 1 H), 2.15 (s, 3 H), 1.86 (s, 3 H), 1.71-1.67 (m, 1 H), 0.73-0.70 (m, 1 H), 0.61-0.52 (m, 2 H), 0.46-0.44 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.7, 149.5, 142.1, 141.1, 139.6, 137.7, 136.3, 130.5, 129.9, 129.4, 127.0, 126.7, 126.2, 125.0, 123.6, 121.0, 52.5, 22.3, 20.1, 15.4, 7.4, 7.3; HRMS (ESI) *m/z*: 314.1900 ($M+H^+$); calc. for $C_{23}H_{24}N$: 314.1903; $[\alpha]_D^{20}$ = -77.27 (*c* 0.44, $CHCl_3$); HPLC chiralcel AD then AD column (0.3% isopropanol in hexanes, 1 mL/min) t_r 16.117 min (major), 21.950 min (minor): 89% ee.

(2-Butyl-5-methylphenyl)(2-pyridyl)(*m*-tolyl)methane 17a



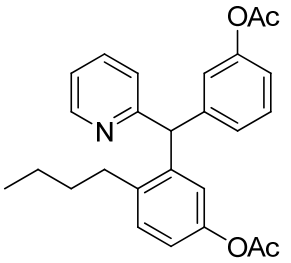
(Table 2, entry 8): The title compound **17a** was prepared according to the general procedure and was purified by flash chromatography (hexanes : ethyl acetate = 15 : 1). **17a** was obtained as a yellow liquid (38.2 mg, 58%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.60 (dd, *J* = 1.2, 4.8 Hz, 1 H), 7.58 (dt, *J* = 2.0, 7.6 Hz, 1 H), 7.17 (t, *J* = 7.6 Hz, 1 H), 7.14-7.10 (m, 2 H), 7.08-6.99 (m, 3 H), 6.91 (s, 1 H), 6.86 (d, *J* = 7.6 Hz, 1 H), 6.71 (s, 1 H), 5.89 (s, 1 H), 2.56-2.52 (m, 2 H), 2.29 (s, 3 H), 2.22 (s, 3 H), 1.45-1.39 (m, 2 H), 1.33-1.28 (m, 2 H), 0.85 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.8, 149.7, 142.9, 140.4, 138.4, 138.0, 136.3, 135.1, 130.4, 129.6, 128.3, 127.5, 127.3, 126.8, 124.0, 121.3, 77.5, 77.2, 76.9, 55.6, 33.5, 32.4, 22.9, 21.7, 21.4, 14.1; HRMS (ESI) *m/z*: 330.2228 ($M+H^+$); calc. for $C_{24}H_{28}N$: 330.2216; $[\alpha]_D^{20}$ = 6.41 (*c* 0.39, $CHCl_3$); HPLC chiralcel OD then AD column (5% isopropanol in hexanes, 1 mL/min) t_r 7.840 min (major), 10.713 min (minor): 84% ee.

(2-Butyl-5-methoxylphenyl)(*m*-methoxylphenyl)-2-pyridylmethane 18a



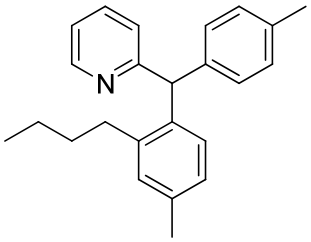
(Table 2, entry 9): The title compound **18a** was prepared according to the general procedure and was purified by flash chromatography (hexanes : ethyl acetate = 8 : 1 to 5 : 1). **18a** was obtained as a yellow liquid (39.8 mg, 55%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.59 (d, *J* = 4.8 Hz, 1 H), 7.57 (dt, *J* = 1.6, 7.6 Hz, 1 H), 7.20 (t, *J* = 8.0 Hz, 1 H), 7.11 (d, *J* = 8.4 Hz, 2 H), 7.01 (d, *J* = 8.0 Hz, 1 H), 6.77-6.64 (m, 4 H), 6.48 (d, *J* = 2.0 Hz, 1 H), 5.88 (s, 1 H), 3.73 (s, 3 H), 3.67 (s, 3 H), 2.51 (t, *J* = 8.8 Hz, 2 H), 1.44-1.38 (m, 2 H), 1.32-1.26 (m, 2 H), 0.84 (t, *J* = 7.6 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.3, 159.8, 157.6, 149.7, 144.4, 141.7, 136.5, 133.8, 130.5, 129.5, 124.0, 122.2, 121.5, 116.4, 116.4, 115.8, 111.6, 111.3, 77.5, 77.2, 76.9, 55.7, 55.7, 55.3, 55.2, 55.2, 33.5, 31.9, 22.9, 14.1; HRMS (ESI) *m/z*: 362.2116 ($M+H^+$); calc. for $C_{24}H_{28}NO_2$: 362.2114; $[\alpha]_D^{20}$ = 1.98 (*c* 0.81, $CHCl_3$); HPLC chiralcel OD then AD column (5% isopropanol in hexanes, 1 mL/min) t_r 14.293 min (major), 24.733 min (minor): 54% ee.

(3-Acetoxyl-6-butylphenyl)(*m*-acetoxylphenyl)-2-pyridylmethane 19a



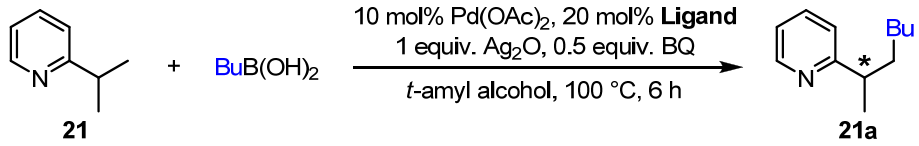
(Table 2, entry 10): The title compound **19a** was prepared according to the general procedure and was purified by flash chromatography (hexanes : ethyl acetate = 3 : 1). **19a** was obtained as a white solid (35.9 mg, 43%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.60-8.59 (m, 1 H), 7.60 (dt, *J* = 2.0, 8.0 Hz, 1 H), 7.29 (t, *J* = 8.0 Hz, 1 H), 7.19 (d, *J* = 8.5 Hz, 1 H), 7.16 (m, 1 H), 7.01 (d, *J* = 8.0 Hz, 1 H), 7.00- 6.98 (m, 1 H), 6.95-6.93 (m, 2 H), 6.77 (t, *J* = 2.0 Hz, 1 H), 6.61 (d, *J* = 2.5 Hz, 1 H), 5.91 (s, 1 H), 2.57-2.53 (m, 2 H), 2.24 (s, 3 H), 2.21 (s, 3 H), 1.44-1.41 (m, 2 H), 1.33-1.28 (m, 2 H), 0.85 (t, *J* = 7.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.9, 169.6, 162.6, 151.2, 150.1, 149.0, 144.5, 141.8, 139.2, 137.0, 130.8, 129.7, 127.3, 124.3, 122.9, 122.8, 122.0, 120.3, 55.4, 33.4, 32.5, 30.1, 23.1, 21.5, 14.3; HRMS (ESI) *m/z*: 418.2019 ($M+H^+$); calc. for $C_{26}H_{28}NO_4$: 418.2013; $[\alpha]_D^{20}$ = -2.38 (*c* 0.21, $CHCl_3$); HPLC chiralcel OD then AD column (6% isopropanol in hexanes, 1 mL/min) t_r 17.300 min (major), 20.033 min (minor): 72% ee.

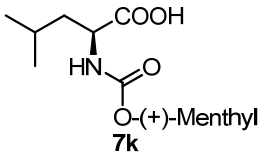
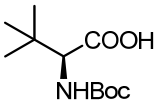
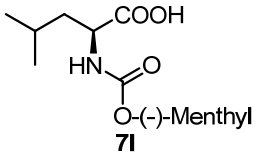
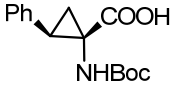
(2-Butyl-4-methylphenyl)(2-pyridyl)(*p*-tolyl)methane 20a



(Table 2, entry 11): The title compound **20a** was prepared according to the general procedure and was purified by flash chromatography (hexanes : ethyl acetate = 15 : 1). **20a** was obtained as a yellow oil (40.2 mg, 61%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.60-8.58 (m, 1 H), 7.56 (dt, *J* = 1.6, 6.4 Hz, 1 H), 7.12-7.10 (m, 2 H), 7.08 (s, 1 H), 7.00 (d, *J* = 6.8 Hz, 2 H), 6.97 (d, *J* = 6.8 Hz, 2 H), 6.91 (dd, *J* = 6.4, 1.2 Hz, 1 H), 6.79 (d, *J* = 6.0 Hz, 1 H), 5.87 (s, 1 H), 2.57-2.53 (m, 2 H), 2.32 (s, 3 H), 2.30 (s, 3 H), 1.47-1.41 (m, 2 H), 1.34-1.27 (m, 2 H), 0.86 (t, *J* = 6.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.3, 149.9, 141.5, 140.4, 138.1, 136.5, 136.3, 136.1, 130.7, 129.9, 129.7, 129.4, 126.8, 124.2, 121.5, 55.1, 33.7, 33.0, 23.2, 21.4, 14.3; HRMS (ESI) *m/z*: 330.2225 ($M+H^+$); calc. for $C_{24}H_{28}N$: 330.2216; $[\alpha]_D^{20}$ = 8.18 (*c* 0.33, $CHCl_3$); HPLC chiralcel OD then AD column (0.5% isopropanol in hexanes, 1 mL/min) t_r 15.420 min (major), 21.293 min (minor): 78% ee.

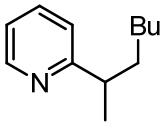
Enantioselective Butylation of Prochiral sp^3 C-H Bonds with Butylboronic Acid



Entry	Ligand	Yield (%)*	Ee (%)†	Entry	Ligand	Yield (%)*	Ee (%)†
1	 **7k**	35	15	3	 **8**	43	21
2	 **7l**	34	14	4	 **3**	38	37

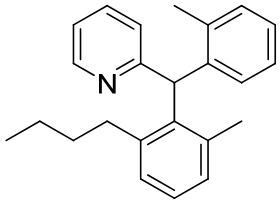
*Isolated yields. †Enantiomeric excess (ee) was determined by chiral HPLC.

2-(Heptane-2-yl)pyridine 21a

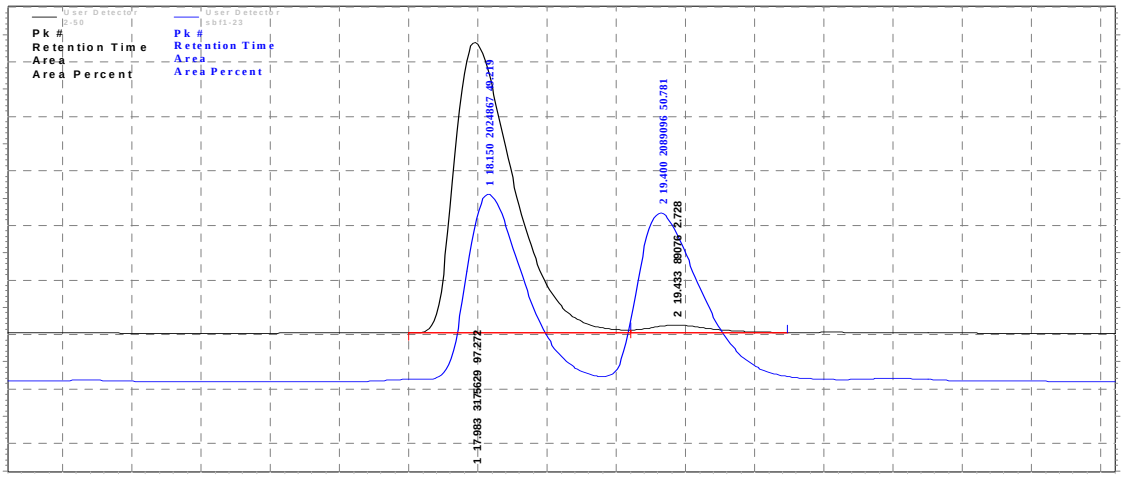


(Entry 4): In a 20 mL tube, **21** (24.2 mg, 0.2 mmol, 1 equiv), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol, 0.1 eq), boronic acid (0.6 mmol, 3 equiv), Ag_2O (46.3 mg, 0.2 mmol, 1 equiv), benzoquinone (10.8 mg, 0.1 mmol, 0.5 equiv) and **3** (11.1 mg, 0.04 mmol, 0.2 eq) were dissolved in 2 mL of anhydrous *t*-amyl alcohol under atmospheric air. The tube was sealed with a Teflon lined cap, and the reaction mixture was stirred at 100 ^oC for 6 h. The reaction mixture was filtered through a pad of Celite, and the Celite was washed with 20 mL of CH_2Cl_2. The filtrate was concentrated under vacuum. The residue was purified by PTLC (hexanes : ethyl acetate = 9 : 1) to give **21a** as a yellow oil (13.5 mg, 38%). NMR spectra were consistent with that previously reported.[11] HPLC chiralcel OD-H then OD column (1% isopropanol in hexane, 1 mL/min) t_r 8.733 min (major), 9.387 min (minor): 37% ee.

Chiral HPLC Data:



HPLC chiralcel OD-H then OD (0.25% isopropanol in hexanes, 1 mL/min), 95% ee.



Area% report for enantioselective (black line):

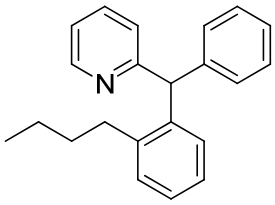
User detector results:

Retention Time	Area	Area %	Height	Height %
17.983	3175629	97.27	106548	97.40
19.433	89076	2.73	2844	2.60
Totals	3264705	100.00	109392	100.00

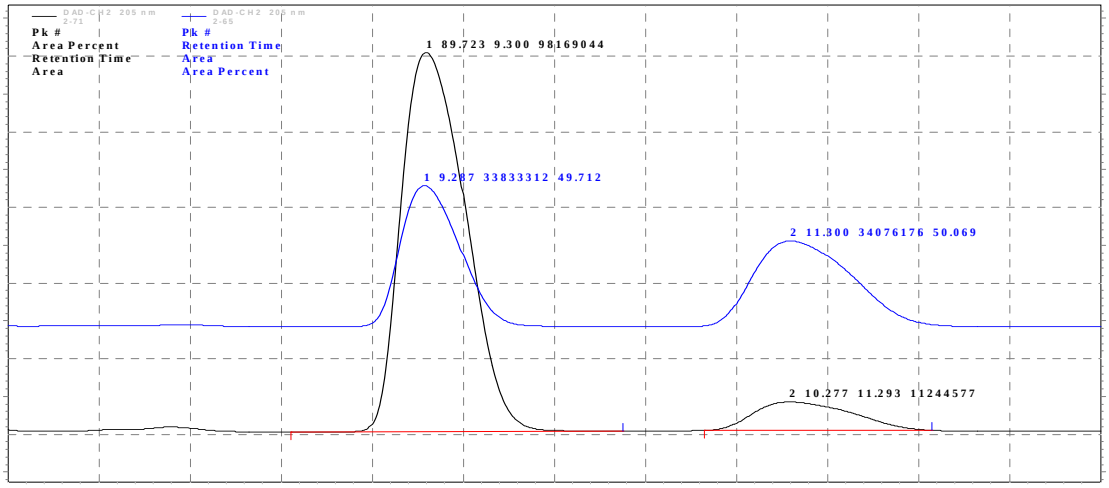
Area% Report for Racemic (blue line):

User detector results:

Retention Time	Area	Area %	Height	Height %
18.150	2024867	49.22	68689	52.65
19.400	2089096	50.78	61769	47.35
Totals	4113963	100.00	130458	100.00



HPLC chiralcel OD then AD (5% isopropanol in hexanes, 1 mL/min), 79% ee.



Area% Report for Enantioselective (black line):

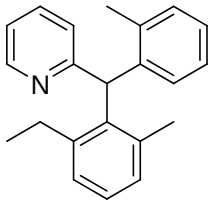
DAD-CH2 205 nm results

Retention Time	Area	Area %	Height	Height %
9.300	98169044	89.72	4011913	93.02
11.293	11244577	10.28	301264	6.98
Totals	109413621	100.00	4313177	100.00

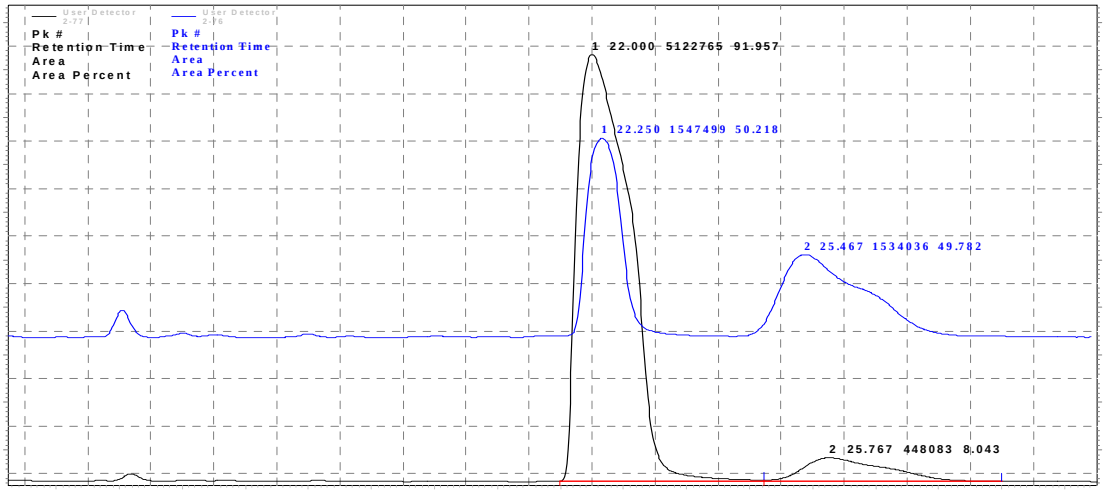
Area% Report for Racemic (blue line):

DAD-CH2 205 nm results

Retention Time	Area	Area %	Height	Height %
9.287	3315047	49.94	147783	62.58
11.300	3323577	50.06	88374	37.42
Totals	6638624	100.00	236157	100.00



HPLC chiralcel OD-H then OD (0.25% isopropanol in hexanes, 1 mL/min), 84% ee.



Area% report for enantioselective (black line):

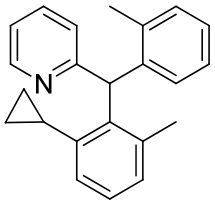
User detector results:

Retention Time	Area	Area %	Height	Height %
22.000	5122765	91.96	89812	94.76
25.767	448083	8.04	4963	5.24
Totals	5570848	100.00	94775	100.00

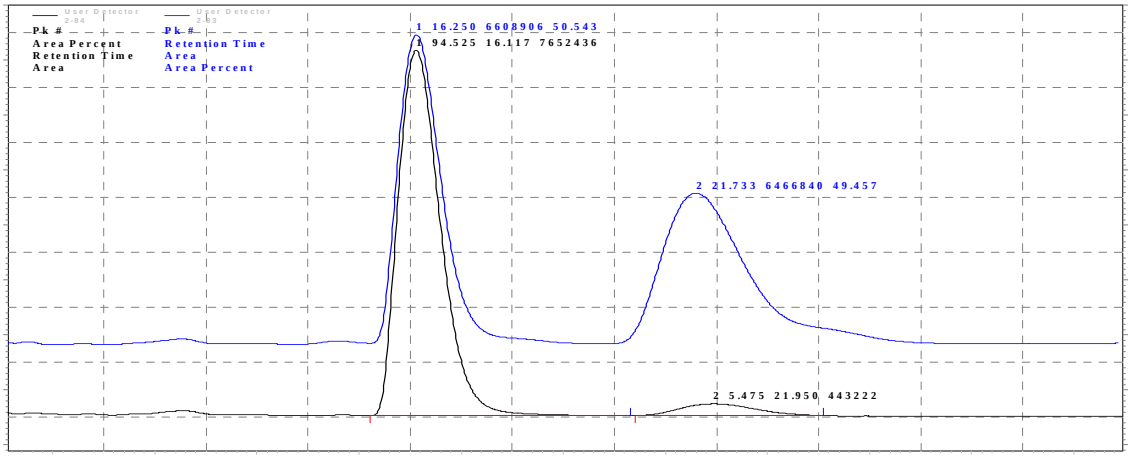
Area% report for racemic (blue line):

User detector results:

Retention Time	Area	Area %	Height	Height %
22.250	1547499	50.22	41535	70.80
25.467	1534036	49.78	17134	29.20
Totals	3081535	100.00	58669	100.00



HPLC chiralcel AD then AD (0.3% isopropanol in hexanes, 1 mL/min), 89% ee



Area% report for enantioselective (black line):

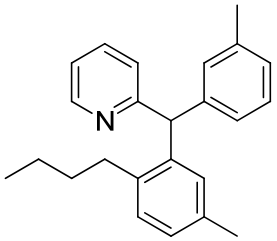
User detector results:

Retention Time	Area	Area %	Height	Height %
16.117	7652436	94.53	133085	96.84
21.950	443222	5.47	4349	3.16
Totals	8095658	100.00	137434	100.00

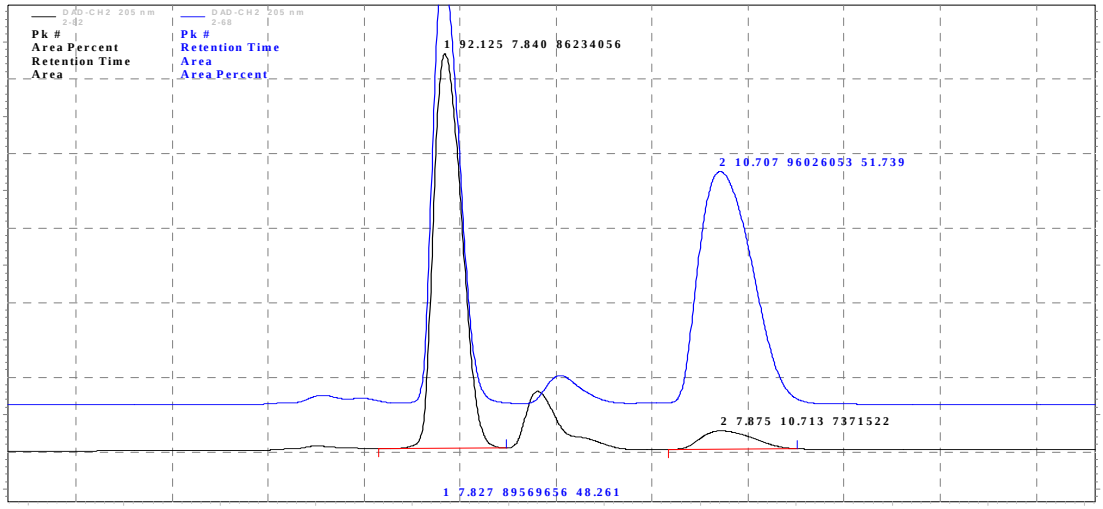
Area% report for racemic (blue line):

User detector results:

Retention Time	Area	Area %	Height	Height %
16.250	6608906	50.54	112129	67.15
21.733	6466840	49.46	54864	32.85
Totals	13075746	100.00	166993	100.00



HPLC chiralcel OD then AD (5% isopropanol in hexane, 1 mL/min), 84% ee



Area% report for enantioselective (black line):

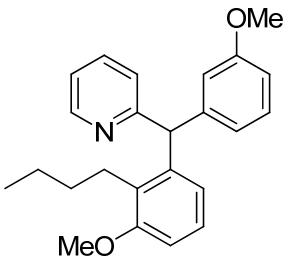
DAD-CH2 205 nm results

Retention Time	Area	Area %	Height	Height %
7.840	86234056	92.12	4232729	95.56
10.713	7371522	7.88	196813	4.44
Totals	93605578	100.00	4429542	100.00

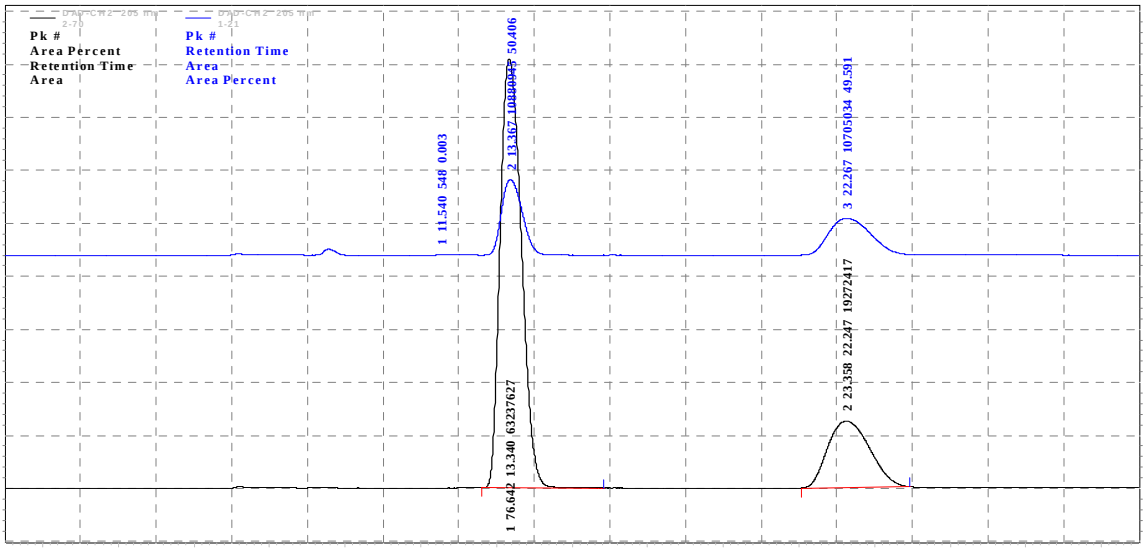
Area% report for racemic (blue line):

DAD-CH2 205 nm results

Retention Time	Area	Area %	Height	Height %
7.827	89569656	48.26	4583817	64.81
10.707	96026053	51.74	2489062	35.19
Totals	185595709	100.00	7072879	100.00



HPLC chiralcel OD then AD (5% isopropanol in hexane, 1 mL/min), 54% ee



Area% report for enantioselective (black line):

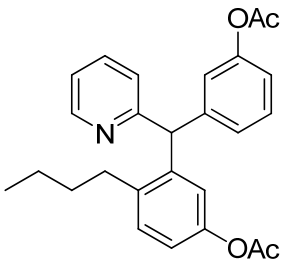
DAD-CH2 205 nm results

Retention Time	Area	Area %	Height	Height %
13.340	63237627	76.64	1619666	86.61
22.247	19272417	23.36	250295	13.39
Totals	82510044	100.00	1869961	100.00

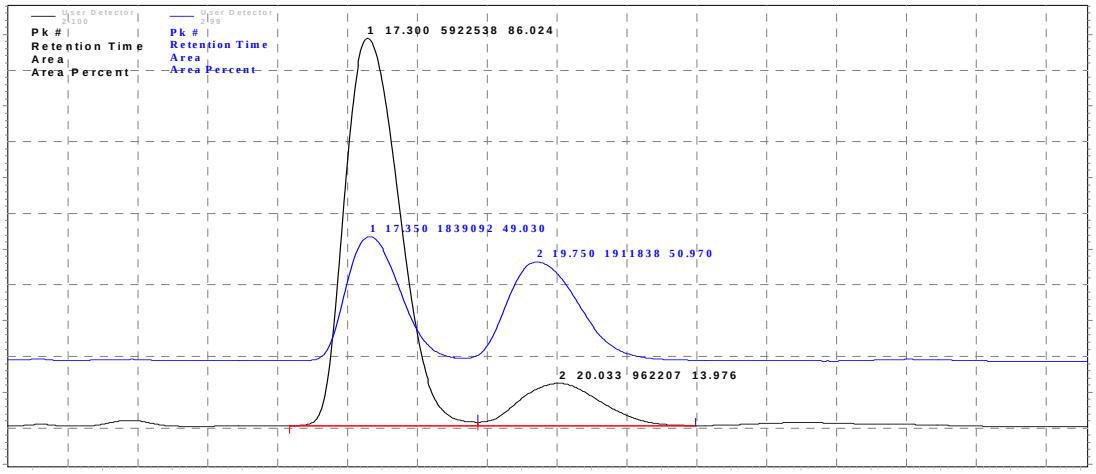
Area% report for racemic (blue line):

DAD-CH2 205 nm results

Retention Time	Area	Area %	Height	Height %
13.367	10880945	50.41	286617	67.31
22.267	10705034	49.59	139102	32.67
Totals	21586527	100.00	425822	100.00



HPLC chiralcel OD then AD (6% isopropanol in hexanes, 1 mL/min), 72% ee



Area% report for enantioselective (black line):

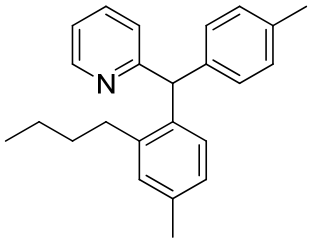
User detector results:

Retention Time	Area	Area %	Height	Height %
17.300	5922538	86.02	108320	90.12
20.033	962207	13.98	11880	9.88
Totals	6884745	100.00	120200	100.00

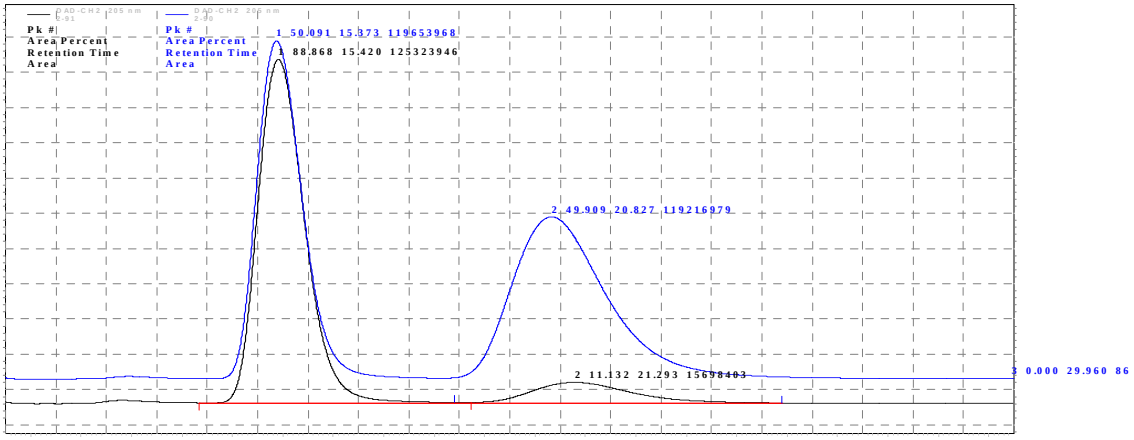
Area% report for racemic (blue line):

User detector results:

Retention Time	Area	Area %	Height	Height %
17.350	1839092	49.03	34444	55.88
19.750	1911838	50.97	27198	44.12
Totals	3750930	100.00	61642	100.00



HPLC chiralcel OD then AD (0.5% isopropanol in hexanes, 1 mL/min), 78% ee



Area% report for enantioselective (black line):

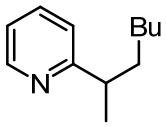
DAD-CH2 205 nm results

Retention Time	Area	Area %	Height	Height %
15.420	125323946	88.87	1946476	94.35
21.293	15698403	11.13	116504	5.65
Totals	141022401	100.00	2062980	100.00

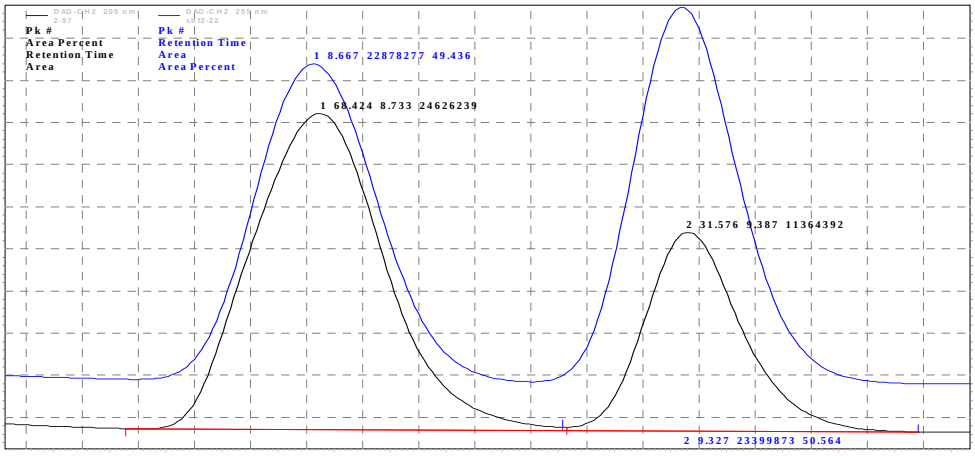
Area% report for racemic (blue line):

DAD-CH2 205 nm results

Retention Time	Area	Area %	Height	Height %
15.373	9046483	51.10	148247	68.26
20.827	8655610	48.90	68930	31.74
Totals	17702093	100.00	217177	100.00



HPLC chiralcel OD-H then OD (1% isopropanol in hexane, 1 mL/min), 37% ee



Area% report for enantioselective (black line):

DAD-CH2 205 nm results

Retention Time	Area	Area %	Height	Height %
8.733	24626239	68.42	1498695	61.38
9.387	11364392	31.58	942950	38.62
Totals	35990631	100.00	2441645	100.00

Area% report for racemic (blue line):

DAD-CH2 205 nm results

Retention Time	Area	Area %	Height	Height %
8.667	22878277	49.44	1499785	45.76
9.327	23399873	50.56	1777587	54.24
Totals	46278150	100.00	3277372	100.00

References and notes:

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