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Supporting Information

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Rh-Catalyzed Asymmetric Hydrogenation of a-Aryl Imino Esters: An Efficient Enantioselective Synthesis of Arylglycine Derivatives

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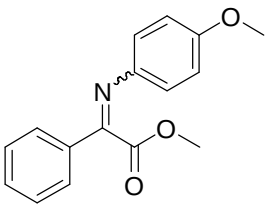
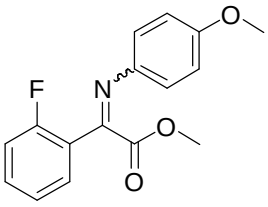
General Methods. All reactions and manipulations were performed in a nitrogen-filled glove box or under nitrogen using Schlenk techniques unless otherwise noted. Column chromatography was performed using Sorbent silica gel 60 Å (230×450 mesh). ^{1}H NMR and ^{13}C NMR spectral data were recorded on Bruker DPX-300, CDPX-300, AMX-360 and DRX-400 MHz spectrometers. Chemical shifts were reported in ppm upfield to tetramethylsilane with solvent resonance as the internal standard. MS spectra were recorded on a KRATOS mass spectrometer MS 9/50 for LR-APCI and HR-APCI.

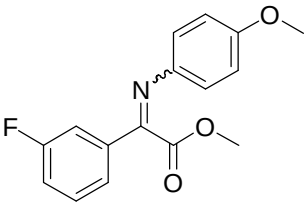
General Procedure for the Preparation of a-Imino Esters.[1] *p*-Anisidine (1.05 equiv), the appropriate a-keto esters (1 equiv) and toluene-4-sulfonic acid (0.05 equiv) were dissolved in benzene (40-100 mL) in a round bottle flask. The flask was equipped with a reflux condenser and a Dean-Stark trap. The mixture was heated to reflux for 1-3 days after which the solvent was removed in *vacuo*. The imine products were purified by column chromatography using 5:1 hexanes and ethyl acetate as eluent. The product was further purified by recrystallization if necessary. The ratio of geometric isomers was determined by ^{l}H NMR spectrometry.



(4-Methoxy-phenylimino)-phenyl-acetic acid methyl ester (1a).[2] 92:8 mixture of geometric isomers. ^{1}H NMR (400 MHz, $CDCl_3$): major isomer d 7.87-7.85 (m, 2H), 7.50-7.44 (m, 3H), 6.98 (d, *J* = 4.6 Hz, 2H), 6.89 (d, *J* = 4.6 Hz, 2H), 3.81 (s, 3H), 3.70 (s, 3H); minor isomer d 7.31-7.21 (m, 5H), 6.74-6.72 (m, 4H), 3.95 (s, 3H), 3.74 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): d 166.0, 159.1, 157.3, 143.1, 134.0, 131.5, 128.6, 127.8, 121.1, 114.1, 55.3, 51.9, resonances of the minor isomer are obscured.

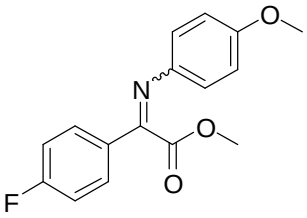


(2-Fluoro-phenyl)-(4-methoxy-phenylimino)-acetic acid methyl ester (1b). 54:46 mixture of geometric isomers. ^{1}H NMR (360 MHz, $CDCl_3$): major isomer d 7.50-7.43 (m, 1H), 7.26-7.22 (m, 1H), 7.07-7.02 (m, 2H), 6.95 (d, *J* = 7.2 Hz, 2H), 6.88 (d, *J* = 7.2 Hz, 2H), 3.79 (s, 3H), 3.67 (s, 3H); minor isomer d 8.02-7.97 (m, 1H), 7.35-7.28 (m, 1H), 7.12-7.08 (m, 2H), 6.78 (d, *J* = 10.8 Hz, 2H), 6.71 (d, *J* = 10.8 Hz, 2H), 3.94 (s, 3H), 3.71 (s, 3H); ^{13}C NMR (90 MHz, $CDCl_3$): d 165.0 (d, *J* = 88 Hz), 162.8, 160.6 (d, *J* = 96 Hz), 158.3, 157.9, 157.5, 154.6, 153.8, 142.7, 141.1, 133.2 (d, *J* = 9.0 Hz), 131.4 (d, *J* = 8.1 Hz), 130.1 (d, *J* = 3.6 Hz), 129.9 (d, *J* = 1.8 Hz), 124.6 (d, *J* = 3.6 Hz), 124.0 (d, *J* = 3.6 Hz), 123.3, 123.2, 122.8, 121.8 (d, *J* = 17.1 Hz), 121.1, 116.0 (d, *J* = 21.6 Hz), 115.7 (d, *J* = 23.4 Hz), 113.9 (d, *J* = 27 Hz), 55.3, 55.2, 53.3, 52.2; APCI-HRMS Calcd. for $C_{16}H_{14}NO_3FNa$ [M+Na^+]: 310.0855, found 310.0835.

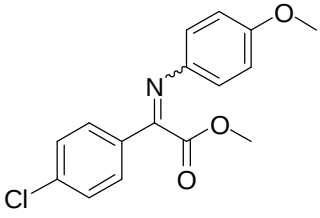


(3-Fluoro-phenyl)-(4-methoxy-phenylimino)-acetic acid methyl ester (1c). 93:7 mixture of geometric isomers. ^{1}H NMR (360 MHz, $CDCl_3$): major isomer d 7.66-7.63 (m, 1H), 7.61-7.58 (m, 1H), 7.46-7.40 (m, 1H), 7.24-7.17 (m,

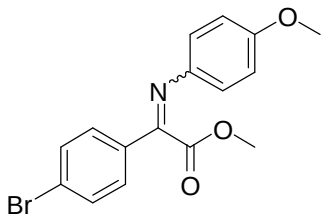
1H), 6.99 (d, *J* = 9.0 Hz, 2H), 6.90 (d, *J* = 9.0 Hz, 2H), 3.82 (s, 3H), 3.71 (s, 3H); minor isomer d 3.96 (s, 3H), 3.75 (s, 3H), aromatic resonance are obscured by the major isomer; ^{13}C NMR (90 MHz, $CDCl_3$): d 165.7, 162.9 (d, *J* = 246 Hz), 157.6, 157.5 (d, *J* = 2.7 Hz), 142.6, 136.3 (d, *J* = 7.2 Hz), 130.2 (d, *J* = 8.1 Hz), 123.6 (d, *J* = 2.7 Hz), 121.2, 118.4 (d, *J* = 20.7), 114.5, 114.2 (d, *J* = 2.7 Hz), 55.4, 52.1, resonance of the minor isomer are obscured; APCI-HRMS Calcd. for $C_{16}H_{14}NO_3FNa$ [M+Na$^+$]: 310.0855, found 310.0851.



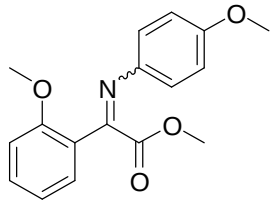
(4-Fluoro-phenyl)-(4-methoxy-phenylimino)-acetic acid methyl ester (1d). 93:7 mixture of geometric isomers. ^{1}H NMR (300 MHz, $CDCl_3$): major isomer d 7.89-7.84 (m, 2H), 7.19-7.12 (m, 2H), 6.96 (d, *J* = 9.0 Hz, 2H), 6.89 (d, *J* = 9.0 Hz, 2H), 3.81 (s, 3H), 3.70 (s, 3H); minor isomer d 8.13-8.07 (m, 1H), 3.96 (s, 3H), 3.76 (s, 3H), the other aromatic resonance are obscured by the major isomer; ^{13}C NMR (75 MHz, $CDCl_3$): d 166.4, 165.9, 160.4 (d, *J* = 407.6 Hz), 157.4, 142.9, 133.0 (d, *J* = 10.1 Hz), 130.4 (d, *J* = 3.1 Hz), 130.0 (d, *J* = 8.8 Hz), 123.0, 121.1, 116.3 (d, *J* = 22.1 Hz), 115.8 (d, *J* = 21.9 Hz), 114.2, 114.0, 55.4, 55.3, 52.0, some of the resonance are obscured; APCI-HRMS Calcd. for $C_{16}H_{14}NO_3FNa$ [M+Na$^+$]: 310.0855, found 310.0848.



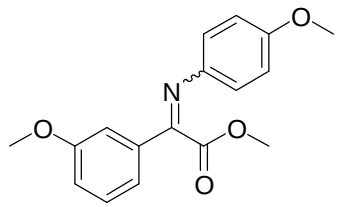
(4-Chloro-phenyl)-(4-methoxy-phenylimino)-acetic acid methyl ester (1e). 92:8 mixture of geometric isomers. ^{1}H NMR (300 MHz, $CDCl_3$): major isomer d 8.33 (d, *J* = 8.7 Hz, 2H), 7.95 (d, *J* = 8.7 Hz, 2H), 7.49 (d, *J* = 9.1 Hz, 2H), 7.41 (d, *J* = 9.0 Hz, 2H), 4.32 (s, 3H), 4.21 (s, 3H); minor isomer d 4.47 (s, 3H), 4.26 (s, 3H), aromatic resonance are obscured by the major isomer; ^{13}C NMR (75 MHz, $CDCl_3$): d 165.7, 165.1, 157.6, 157.54, 157.47, 157.1, 142.7, 140.9, 137.6, 135.6, 132.6, 131.3, 130.5, 129.0, 128.9, 128.6, 123.1, 121.1, 114.2, 114.0, 55.3, 55.2, 53.2, 52.1; APCI-HRMS Calcd. for $C_{16}H_{14}NO_3NaCl$ [M+Na$^+$]: 326.0560, found 326.0537.



(4-Bromo-phenyl)-(4-methoxy-phenylimino)-acetic acid methyl ester (1f). 90:10 mixture of geometric isomers. ^{1}H NMR (300 MHz, $CDCl_3$): major isomer d 7.74 (d, *J* = 8.7 Hz, 2H), 7.60 (d, *J* = 8.8 Hz, 2H), 6.97 (d, *J* = 8.8 Hz, 2H), 6.89 (d, *J* = 9.0 Hz, 2H), 3.81 (s, 3H), 3.70 (s, 3H); minor isomer d 7.95-7.89 (m, 2H), 7.72-7.63 (m, 2H), 7.48-7.40 (m, 2H), 7.15-7.05 (m, 2H), 3.95 (s, 3H), 3.75 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): d 165.7, 157.7, 157.5, 142.7, 133.0, 132.2, 131.9, 131.5, 131.4, 130.7, 129.2, 126.2, 123.1, 121.1, 114.2, 114.0, 55.3, 55.2, 52.8, 52.0, some resonance of the minor isomer are obscured; APCI-HRMS Calcd. for $C_{16}H_{14}NO_3Na$ [M+Na^+]: 370.0055, found 370.0021.

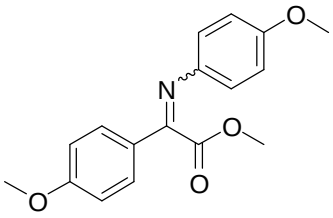


(2-Methoxy-phenyl)-(4-methoxy-phenylimino)-acetic acid methyl ester (1g). 52:48 mixture of geometric isomers. ^{1}H NMR (300 MHz, $CDCl_3$): major isomer d 7.91-7.86 (m, 1H), 7.34-7.28 (m, 1H), 7.10-7.04 (m, 1H), 6.98-6.80 (m, 1H), 6.76 (d, *J* = 7.4 Hz, 2H), 6.69 (d, *J* = 7.4 Hz, 2H), 3.92 (s, 3H), 3.73 (s, 3H), 3.72 (s, 3H); minor isomer d 7.49-7.42 (m, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 3.62 (s, 3H), the other aromatic resonance are obscured by the major isomer; ^{13}C NMR (75 MHz, $CDCl_3$): d 165.9, 165.5, 158.3, 157.5, 157.45, 157.43, 157.1, 143.5, 141.8, 136.4, 132.8, 130.9, 130.2, 129.7, 125.0, 123.2, 122.7, 121.4, 121.0, 120.5, 114.0, 113.6, 111.6, 111.0, 56.1, 55.5, 55.4, 55.2, 53.1, 51.7; APCI-HRMS Calcd. for $C_{17}H_{17}NO_4Na$ [M+Na^+]: 322.1055, found 322.1036.

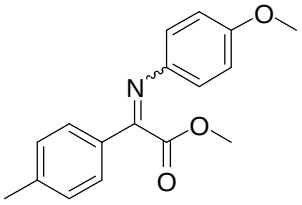


(3-Methoxy-phenyl)-(4-methoxy-phenylimino)-acetic acid (1h). 88:12 mixture of geometric isomers. ^{1}H NMR (300 MHz, $CDCl_3$): major isomer d

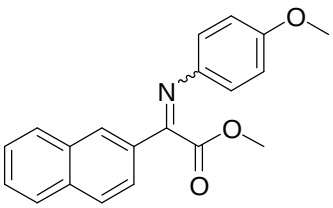
7.49-7.46 (m, 1H), 7.33-7.27 (m, 2H), 7.04-6.96 (m, 1H), 6.94 (d, *J* = 8.9 Hz, 2H), 6.83 (d, *J* = 8.9 Hz, 2H), 3.79 (s, 3H), 3.73 (s, 3H), 3.63 (s, 3H), minor resonance are obscured by the major isomer; ^{13}C NMR (75 MHz, $CDCl_3$): major isomer d 165.8, 159.7, 158.8, 157.2, 142.8, 135.2, 129.5, 121.0, 120.5, 117.9, 114.0, 111.6, 55.2, 55.1, 51.8, resonance of the minor isomer are obscured by the major isomer; APCI-HRMS Calcd. for $C_{17}H_{17}NO_4Na$ [M+Na^+]: 322.1055, found 322.1045.



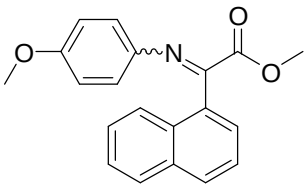
(4-Methoxy-phenyl)-(4-methoxy-phenylimino)-acetic acid methyl ester (1i). 92:8 mixture of geometric isomers. ^{1}H NMR (300 MHz, $CDCl_3$): major isomer d 7.80 (d, *J* = 8.9 Hz, 2H), 6.97-6.91 (m, 4H), 6.87 (d, *J* = 9.0 Hz, 2H), 3.86 (s, 3H), 3.80 (s, 3H), 3.67 (s, 3H); minor isomer d 3.94 (s, 3H), 3.78 (s, 3H), 3.75 (s, 3H), aromatic resonance are obscured by the major isomer; ^{13}C NMR (75 MHz, $CDCl_3$): d 166.2, 162.3, 158.6, 157.1, 143.4, 129.6, 126.8, 121.1, 114.12, 114.06, 55.42, 55.37, 51.9, resonance of the minor isomer are obscured; APCI-HRMS Calcd. for $C_{17}H_{18}NO_4$ [M+H^+]: 300.1236, found 300.1218.



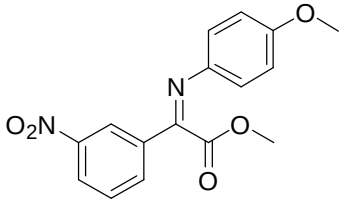
(4-Methoxy-phenylimino)-(4-methyl-cyclohexa-1,5-dienyl)-acetic acid methyl ester (1j). 87:13mixture of geometric isomers. ^{1}H NMR (300 MHz, $CDCl_3$): major isomer d 7.92 (d, *J* = 8.2 Hz, 2H), 7.43 (d, *J* = 8.1 Hz, 2H), 7.13 (d, *J* = 8.9 Hz, 2H), 7.04 (d, *J* = 8.9 Hz, 2H), 3.97 (s, 3H), 3.85 (s, 3H), 2.58 (s, 3H); minor isomer d 4.11 (s, 3H), 3.91 (s, 3H), 2.49 (s, 3H), aromatic resonance are obscured by the major isomer; ^{13}C NMR (75 MHz, $CDCl_3$): d 166.2, 159.1, 157.2, 143.2, 142.1, 131.4, 129.4, 127.7, 121.1, 114.1, 55.3, 51.9, 21.5, resonance of the minor isomer are obscured; APCI-HRMS Calcd. for $C_{17}H_{17}NO_3Na$ [M+Na^+]: 306.1106, found 306.1076.



(4-Methoxy-phenylimino)-naphthalen-2-yl-acetic acid methyl ester (1k). 94:6 mixture of geometric isomers. ^{1}H NMR (300 MHz, $CDCl_3$): major isomer d 8.24-8.15 (m, 2H), 7.97-7.86 (m, 3H), 7.62-7.50 (m, 2H), 7.08 (d, *J* = 8.9 Hz, 2H), 6.94 (d, *J* = 8.9 Hz, 2H), 3.82 (s, 3H), 3.77 (s, 3H); minor isomer d 3.98 (s, 3H), 3.72 (s, 3H), aromatic resonance of the minor isomer are obscured; ^{13}C NMR (75 MHz, $CDCl_3$): d 166.1, 159.0, 157.3, 143.1, 134.8, 132.7, 131.5, 129.2, 129.0, 128.5, 127.72, 127.70, 126.6, 123.6, 121.2, 114.1, 55.3, 52.0, resonance of the minor isomer are obscured; APCI-HRMS Calcd. for $C_{20}H_{17}NO_3Na$ [M+Na$^+$]: 342.1106, found 342.1078.

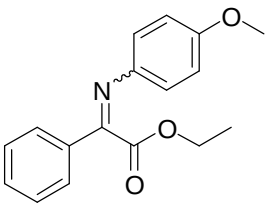


(4-Methoxy-phenylimino)-naphthalen-1-yl-acetic acid methyl ester (1l). 77:23 mixture of geometric isomers. ^{1}H NMR (300 MHz, $CDCl_3$): major isomer d 7.88-7.82 (m, 2H), 7.50-7.37 (m, 3H), 7.29-7.24 (m, 2H), 6.75 (d, *J* = 9.0 Hz, 2H), 6.56 (d, *J* = 9.0 Hz, 2H), 3.90 (s, 3H), 3.63 (s, 3H); minor isomer 7.06 (d, *J* = 8.9 Hz, 2H), 6.93 (d, *J* = 8.9 Hz, 2H), 3.83 (s, 3H), 3.67 (s, 3H), the other aromatic resonance are obscured by the major isomer; ^{13}C NMR (75 MHz, $CDCl_3$): d 165.8, 165.5, 160.2, 158.4, 157.8, 157.4, 143.2, 140.8, 133.9, 133.1, 132.5, 131.9, 131.4, 130.7, 130.4, 129.5, 128.6, 128.5, 128.3, 127.5, 126.9, 126.6, 126.3, 126.2, 125.2, 125.0, 124.6, 124.5, 123.5, 120.9, 114.1, 113.5, 55.3, 55.0, 53.2, 52.0; APCI-HRMS Calcd. for $C_{20}H_{17}NO_3Na$ [M+Na$^+$]: 342.1106, found 342.1113.

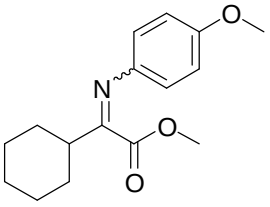


(4-Methoxy-phenylimino)-(3-nitro-phenyl)-acetic acid methyl ester (1m). 95:5 mixture of geometric isomers. ^{1}H NMR (300 MHz, $CDCl_3$): major isomer d 8.72 (t, *J* = 2.0 Hz, 1H), 8.36-8.32 (m, 1H), 8.21-8.12 (m, 1H), 7.64 (t, *J* = 8.0 Hz, 1H), 7.0 (d, *J* = 8.9 Hz, 2H), 6.9 (d, *J* = 8.9 Hz, 2H), 3.82 (s, 3H), 3.75 (s, 3H);

minor isomer d 8.92-8.91 (m, 1H), 8.57-8.50 (m, 1H), 8.45-8.39 (m, 1H), 7.64 (t, *J* = 8.0 Hz), 4.03 (s, 3H), 3.98 (s, 3H), some of the resonance are obscured; ^{13}C NMR (75 MHz, $CDCl_3$): d 165.3, 158.0, 155.8, 148.5, 142.1, 135.9, 133.3, 129.7, 125.7, 122.7, 121.4, 114.3, 55.4, 52.4, resonance of minor isomer are obscured. APCI-HRMS Calcd. for $C_{16}H_{15}N_2O_5$ [M+H$^+$]: 315.0981, found 315.0995.



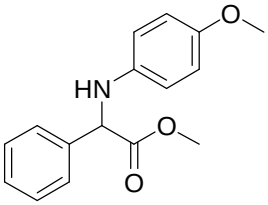
(4-Methoxy-phenylimino)-phenyl-acetic acid ethyl ester (1n).[1] 93:7 mixture of geometric isomers. ^{1}H NMR (300 MHz, $CDCl_3$): major isomer d 7.87-7.84 (m, 2H), 7.45-7.42 (m, 3H), 6.94 (d, *J* = 9.0 Hz, 2H), 6.84 (d, *J* = 9.0, 2H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.76 (s, 3H), 1.05 (t, *J* = 7.1 Hz, 3H); minor isomer d 4.43 (q, *J* = 7.2 Hz, 2H), 3.73 (s, 3H), 1.40 (t, *J* = 7.1, 3H), aromatic resonance are obscured; ^{13}C NMR (75 MHz, $CDCl_3$): d 165.4, 159.5, 157.2, 143.2, 134.0, 131.4, 128.6, 127.7, 121.1, 114.0, 61.3, 55.3, 13.8, some resonance of the minor isomer are obscured.



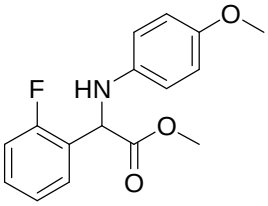
Cyclohexyl-(4-methoxy-phenylimino)-acetic acid methyl ester (1o). 81:19 mixture of geometric isomers. ^{1}H NMR (300 MHz, $CDCl_3$): major isomer d 6.89-6.69 (m, 4H), 3.76 (s, 3H), 3.53 (s, 3H), 2.68-2.50 (m, 1H), 2.05-1.90 (m, 2H), 1.90-1.72 (m, 2H), 1.72-1.65 (m, 2H), 1.60-1.20 (m, 4H); minor isomer 3.84 (s, 3H), 3.80 (s, 3H), the other resonance are obscured by the major isomer; ^{13}C NMR (75 MHz, $CDCl_3$): d 168.3, 167.7, 166.4, 165.3, 156.8, 156.5, 143.4, 141.7, 120.6, 120.0, 114.1, 113.9, 55.32, 55.28, 52.4, 51.5, 44.6, 41.0, 29.4, 27.4, 25.82, 25.77, 25.5, 25.4; APCI-HRMS Calcd. for $C_{16}H_{21}NO_3Na$ [M+Na$^+$]: 298.1419, found 298.1404.

General Procedure for Asymmetric Hydrogenation of a-Imino Esters. $Rh(cod)_2BF_4$ (40.6 mg, 0.1mmol) and (*S,S,R,R*)-TangPhos (28.6 mg, 0.1 mmol) were dissolved in 2 mL degassed dichloromethane in a Schlenk tube under N_2. After stirring at room

temperature for 1 h, 10 mL degassed hexanes was added to the solution to precipitate the catalyst which was filtered under nitrogen to give the complex as an orange solid. The complex (52.0 mg, 88.9% yield) was stored in a nitrogen filled glovebox for further usage. The complex (11.7 mg, 0.02 mmol) was dissolved in degassed dichloromethane (10 mL) in a glovebox and divided equally among 10 vials. To each of the vial, a-imino ester substrate (0.2 mmol, S/C = 100) was then added to the catalyst solution and the resulting mixture was transferred to an autoclave which was charged with H_2 (50 atm). The hydrogenation was performed at 50 °C for 24 h. After carefully releasing the hydrogen gas, the solvent was removed under reduced pressure. The crude product was purified through a silica gel plug (eluting with a mixture of Hexanes : EtOAc = 10:1) to afford corresponding aryglycines. The enantiomeric excess was determined by chiral HPLC under conditions in the following.

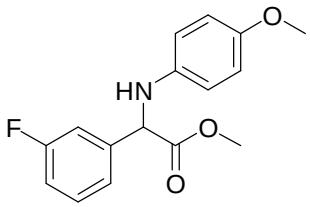


(4-Methoxy-phenylamino)-phenyl-acetic acid methyl ester (2a).[3] 95% *ee*. Enantiomeric excess was determined by HPLC, Chiralcel OJ-H column, IPA:Hex:CH_3CN = 30: 70:1, 1.0 mL/min, t_{major} = 22.8 min, t_{minor} = 27.6 min. $[\alpha]^{24}_D$ = -80.1° (c =0.20, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): d 7.53-7.46 (m, 2H), 7.38-7.28 (m, 3H), 6.73 (d, *J* = 8.9 Hz, 2H), 6.54 (d, *J* = 8.9 Hz, 2H), 5.02 (s, 1H), 4.95-4.50 (b, 1H), 3.73 (s, 3H), 3.71 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): d 172.5, 152.5, 140.1, 137.7, 128.8, 128.2, 127.2, 114.8, 114.7, 61.6, 55.6, 52.7.

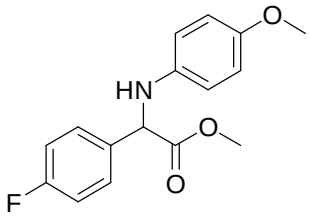


(2-Fluoro-phenyl)-(4-methoxy-phenylamino)-acetic acid methyl ester (2b). 91% *ee*. Enantiomeric excess was determined by HPLC using a Chiralcel OJ-H column, IPA:Hex = 30:70, 1.0 mL/min, t_{major} = 28.4 min, t_{minor} = 35.0 min. $[\alpha]^{24}_D$ = -109.0° (c = 0.61, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): d 7.47-7.41 (m, 1H), 7.33-7.26 (m, 1H), 7.15-7.07 (m, 2H), 6.74 (d, *J* = 8.9 Hz, 2H), 6.58 (d, *J* = 8.9 Hz, 2H), 5.39 (s,

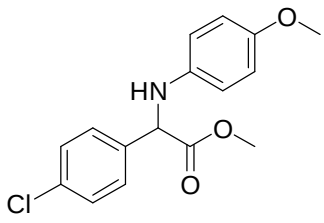
1H), 5.00-4.55 (b, 1H), 3.74 (s, 3H), 3.71 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): d 172.0, 160.8 (d, *J* = 247.5 Hz), 152.7, 139.8, 129.8 (d, *J* = 7.5 Hz), 128.2 (d, *J* = 3.5 Hz), 125.3 (d, *J* = 13.7 Hz), 124.6 (d, *J* = 3.5 Hz), 115.8 (d, *J* = 21.7 Hz), 114.8, 55.6, 54.6 (d, *J* = 3.2 Hz), 52.9; APCI-HRMS Calcd. for $C_{16}H_{17}NO_3F$ [M+H$^+$]: 290.1192, found 290.1197.



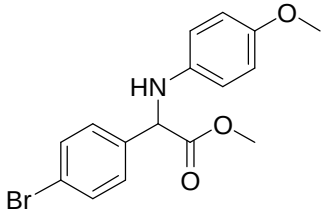
(3-Fluoro-phenyl)-(4-methoxy-phenylamino)-acetic acid methyl ester (2c). 94% *ee*. Enantiomeric excess was determined by HPLC using a Chiralcel OJ-H column, IPA:Hex = 30:70, 1.0 mL/min, t_{major} = 31.8 min, t_{minor} = 35.3 min. $[\alpha]^{24}_D$ = -65.8° (c = 0.24, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): d 7.37-7.19 (m, 3H), 7.06-6.97 (m, 1H), 6.73 (d, *J* = 8.9 Hz, 2H), 6.51 (d, *J* = 8.9 Hz, 2H), 5.01 (s, 1H), 4.80-4.65 (b, 1H), 3.74 (s, 3H), 3.71 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): d 171.9, 163.0 (d, *J* = 246.2 Hz), 152.6, 140.5 (d, *J* = 6.7 Hz), 139.8, 130.3 (d, *J* = 8.1 Hz), 122.9 (d, *J* = 2.1 Hz), 115.3 (d, *J* = 20.4 Hz), 114.9, 114.7, 114.3 (d, *J* = 22.4 Hz), 61.2 (d, *J* = 1.7 Hz), 55.7, 52.9; APCI-HRMS Calcd. for $C_{16}H_{17}NO_3F$ [M+H$^+$]: 290.1192, found 290.1170.



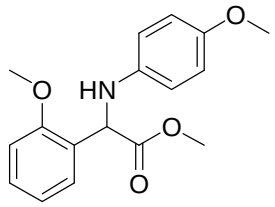
(4-Fluoro-phenyl)-(4-methoxy-phenylamino)-acetic acid methyl ester (2d). 93% *ee*. Enantiomeric excess was determined by HPLC using a Chiralpak AS column, IPA:Hex = 20:80, 1.0 ml/min, t_{minor} = 12.3 min, t_{major} = 15.0 min. $[\alpha]^{24}_D$ = -70.4° (c = 1.69, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): d 7.53-7.44 (m, 2H), 7.12-7.02 (m, 2H), 6.75 (d, *J* = 8.9 Hz, 2H), 6.54 (d, *J* = 9.0 Hz, 2H), 5.02 (d, *J* = 5.9 Hz, 1H), 4.78-4.68 (b, 1H), 3.74 (s, 3H), 3.72 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): d 172.3, 162.6 (d, *J* = 245.6 Hz), 152.6, 139.9, 133.5 (d, *J* = 3.2 Hz), 128.9 (d, *J* = 8.1 Hz), 115.8 (d, *J* = 21.5 Hz), 114.8, 114.7, 60.9, 55.6, 52.7; APCI-HRMS Calcd. for $C_{16}H_{17}NO_3F$ [M+H$^+$]: 290.1192, found 290.1214.



(4-Chloro-phenyl)-(4-methoxy-phenylamino)-acetic acid methyl ester (2e).[4] 92% *ee*. Enantiomeric excess was determined by HPLC using a Chiralcel OJ-H column, IPA:Hex = 10:90, 1.0 mL/min, t_{minor} = 40.3 min, t_{major} = 43.9 min. $[\alpha]^{24}_{D}$ = -111.5° (c = 0.91, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): d 7.45 (d, *J* = 8.5 Hz, 2H), 7.32 (d, *J* = 8.6 Hz, 2H), 6.72 (d, *J* = 9.0 Hz, 2H), 6.50 (d, *J* = 8.9 Hz, 2H), 4.99 (s, 1H), 4.85-4.65 (b, 1H), 3.73 (s, 3H), 3.71 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): d 172.0, 152.6, 139.8, 136.4, 134.1, 129.0, 128.6, 114.9, 114.8, 61.0, 55.7, 52.9.

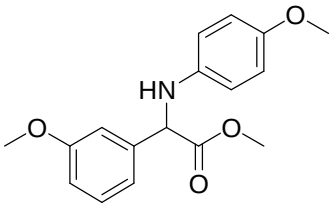


(4-Bromo-phenyl)-(4-methoxy-phenylamino)-acetic acid methyl ester (2f).[5] 92% *ee*. Enantiomeric excess was determined by HPLC using a Chiralcel OJ-H column, IPA:Hex = 10: 90, 1.0 mL/min, t_{minor} = 43.5 min, t_{major} = 47.6 min. $[\alpha]^{24}_{D}$ = -120.5° (c = 0.51, $CHCl_3$) ^{1}H NMR (300 MHz, $CDCl_3$): d 7.48 (d, *J* = 8.6 Hz, 2H), 7.38 (d, *J* = 8.5 Hz, 2H), 6.72 (d, *J* = 9.0 Hz, 2H), 6.50 (d, *J* = 9.0 Hz, 2H), 4.97 (s, 1H), 4.80-4.60 (b, 1H), 3.73 (s, 3H), 3.71 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): d 171.9, 152.6, 139.7, 136.9, 132.0, 129.0, 122.2, 114.9, 114.7, 61.0, 55.7, 52.9.

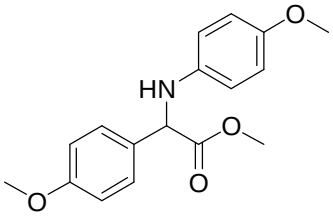


(2-Methoxy-phenyl)-(4-methoxy-phenylamino)-acetic acid methyl ester (2g). 95% *ee*. Enantiomeric excess was determined by HPLC using a Chiralcel OJ-H column, IPA:Hex = 30:70, 1.0 mL/min, t_{major} = 46.6 min, t_{minor} = 60.5 min. $[\alpha]^{24}_{D}$ = -111.6° (c = 0.36, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): d 7.40-7.26 (m, 2H), 6.99-6.92 (m, 2H), 6.75 (d, *J* = 6.7 Hz, 2H), 6.64 (d, *J* = 6.7 Hz, 2H), 5.47 (s, 1H), 4.70-4.55 (b, 1H), 3.93 (s, 3H), 3.73 (s, 3H), 3.72 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): d

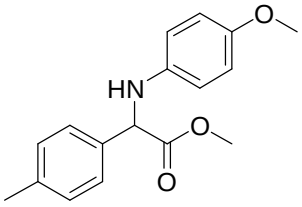
173.0, 157.1, 152.5, 140.6, 129.4, 128.1, 126.5, 121.0, 115.0, 114.7, 111.1, 55.8, 55.7, 55.6, 52.5; APCI-HRMS Calcd. for $C_{17}H_{20}NO_4$ [M+H$^+$]: 302.1392, found 302.1378.



(3-Methoxy-phenyl)-(4-methoxy-phenylamino)-acetic acid methyl ester (2h).[3] 93% *ee*. Enantiomeric excess was determined by HPLC using a Chiralcel OJ-H column, IPA:Hex = 30:70, 1.0 mL/min, t_{major} = 45.9 min, t_{minor} = 57.5 min. $[\alpha]^{24}_D$ = -80.3° (c = 0.90, $CHCl_3$).^{1}H NMR (300 MHz, $CDCl_3$): d 7.31-7.24 (m, 1H), 7.10-7.03 (m, 2H), 6.87-6.83 (m, 1H), 6.73 (d, *J* = 9.0 Hz, 2H), 6.54 (d, *J* = 9.0 Hz, 2H), 4.98 (s, 1H), 4.75-4.58 (b, 1H), 3.80 (s, 3H), 3.73 (s, 3H), 3.71 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): d 172.4, 160.0, 152.5, 140.2, 139.4, 129.8, 119.6, 114.8, 114.7, 113.7, 112.8, 61.6, 55.7, 55.2, 52.7.

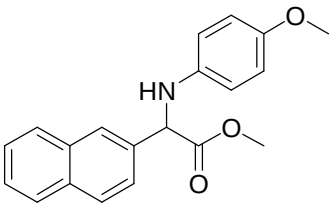


(4-Methoxy-phenyl)-(4-methoxy-phenylamino)-acetic acid methyl ester (2i).[3] 93% *ee*. Enantiomeric excess was determined by HPLC using a Chiralcel OJ-H column, IPA:Hex = 30:70, 1.0 mL/min, t_{major} = 48.4 min, t_{minor} = 58.8 min. $[\alpha]^{24}_D$ = -94.6° (c = 0.59, $CHCl_3$)^{1}H NMR (400 MHz, $CDCl_3$): d 7.41 (d, *J* = 8.7 Hz, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 6.74 (d, *J* = 9.0 Hz, 2H), 6.55 (d, *J* = 9.0 Hz, 2H), 4.99 (s, 1H), 3.80 (s, 3H), 3.73 (s, 3H), 3.72 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): d 172.8, 159.5, 152.4, 140.2, 129.7, 128.4, 114.8, 114.7, 114.2, 61.0, 55.6, 55.2, 52.6.

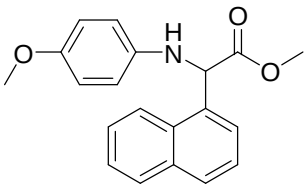


(4-Methoxy-phenylamino)-*p*-tolyl-acetic acid methyl ester (2j).[3] 93% *ee*. Enantiomeric excess was determined by HPLC using a Chiralcel OJ-H column, IPA:Hex:CH_3CN = 30:70:1, 1.0 mL/min, t_{minor} = 18.5 min, t_{major} = 20.8 min. $[\alpha]^{24}_D$ = -86.1° (c = 0.46, $CHCl_3$).^{1}H NMR (360 MHz, $CDCl_3$): d 7.41 (d, *J* = 9.0 Hz, 2H),

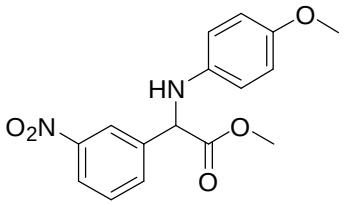
7.19 (d, *J* = 9.0 Hz, 2H), 6.76 (d, *J* = 9.0 Hz, 2H), 6.57 (d, *J* = 9.0 Hz, 2H), 5.03 (s, 1H), 4.74-4.62 (b, 1H), 3.74 (s, 3H), 3.71 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (90 MHz, $CDCl_3$): d 172.7, 152.4, 140.2, 138.0, 134.7, 129.5, 127.1, 114.8, 114.7, 61.3, 55.6, 52.6, 21.1.



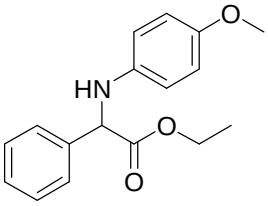
(4-Methoxy-phenylamino)-naphthalen-2-yl-acetic acid methyl ester (2k).[4] 90% *ee*. Enantiomeric excess was determined by HPLC using a Chiralcel OD-H column, IPA:Hex = 10:90, 1.0 mL/min, t_{major} = 12.8 min, t_{minor} = 14.1 min. $[\alpha]^{24}_D$ = -74.7° (c = 0.10, $CHCl_3$).^{1}H NMR (300 MHz, $CDCl_3$): d 7.98-7.95 (m, 1H), 7.87-7.80 (m, 3H), 7.64-7.58 (m, 1H), 7.52-7.45 (m, 2H), 6.72 (d, *J* = 9.0 Hz, 2H), 6.58 (d, *J* = 9.0 Hz, 2H), 5.19 (s, 1H), 5.00-4.70 (b, 1H), 3.73 (s, 3H), 3.69 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): d 172.5, 152.5, 140.1, 135.3, 133.3, 133.2, 128.7, 128.0, 127.7, 126.5, 126.3, 126.2, 124.9, 114.82, 114.80, 61.8, 55.6, 52.8.



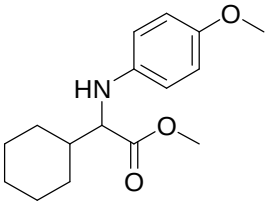
(4-Methoxy-phenylamino)-naphthalen-1-yl-acetic acid methyl ester (2l). 91% *ee*. Enantiomeric excess was determined by HPLC using a Chiralcel OD-H column, IPA:Hex = 30:70, 1.0 mL/min, t_{major} = 7.5 min, t_{minor} = 9.2 min. $[\alpha]^{24}_D$ = -105.2° (c = 0.07, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): d 8.32 (d, *J* = 8.6 Hz, 1H), 7.94-7.88 (m, 1H), 7.85 (d, *J* = 8.2 Hz, 1H), 7.69-7.51 (m, 3H), 7.49-7.42 (m, 1H), 6.73 (d, *J* = 8.6 Hz, 2H), 6.57 (d, *J* = 8.6 Hz, 2H), 5.80 (s, 1H), 4.80-4.65 (b, 1H), 3.72 (s, 3H), 3.70 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): d 172.9, 152.5, 140.4, 134.1, 133.5, 131.3, 129.0, 128.9, 126.6, 125.9, 125.5, 125.0, 123.3, 114.8, 114.5, 58.3, 55.6, 52.7; APCI-HRMS Calcd. for $C_{20}H_{20}NO_3$ [M+H$^+$]: 322.1443, found 322.1447.



(4-Methoxy-phenylamino)-(3-nitro-phenyl)-acetic acid methyl ester (2m). 93% *ee*. Enantiomeric excess was determined by HPLC using a Chiralcel OJ-H column, IPA:Hex:CH_3CN = 30:70:1, 1.0 mL/min, t_{major} = 65.7 min, t_{minor} = 46.5 min. $[\alpha]^{24}_D$ = -65.1° (c = 0.27, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): d 8.40 (t, *J* = 1.9 Hz, 1H), 8.15 (d, *J* = 4.0 Hz, 1H), 7.86 (d, *J* = 8 Hz, 1H), 6.72 (d, *J* = 6.8 Hz, 2H), 6.49 (d, *J* = 6.8 Hz, 2H), 5.12 (s, 1H), 4.85 (b, 1H), 3.75 (s, 3H), 3.69 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): d 171.1, 152.8, 148.6, 140.3, 139.3, 133.3, 129.8, 123.3, 122.4, 114.9, 114.8, 60.9, 55.6, 53.2. APCI-HRMS Calcd. for $C_{16}H_{17}N_2O_5$ [M+H$^+$]: 317.1137, found 317.1139.



(4-Methoxy-phenylamino)-phenyl-acetic acid ethyl ester (2n).[1] 84% *ee*. Enantiomeric excess was determined by HPLC using a Chiralcel OJ-H column, IPA:Hex = 30:70, 1.0 mL/min, t_{major} = 23.7 min, t_{minor} = 27.4 min. $[\alpha]^{25}_D$ = -10.2° (c = 0.14, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): d 7.53-7.46 (m, 2H), 7.40-7.28 (m, 3H), 6.73 (d, *J* = 6.0 Hz, 2H), 6.54 (d, *J* = 6.0 Hz, 2H), 5.01 (s, 1H), 4.88-4.58 (b, 1H), 4.30-4.06 (m, 2H), 3.71 (s, 3H), 1.21 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): d 172.0, 152.4, 140.2, 137.8, 128.8, 128.1, 127.2, 114.8, 114.7, 61.7, 55.7, 14.0.



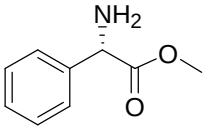
Cyclohexyl-(4-methoxy-phenylamino)-acetic acid methyl ester (2o). 94% *ee*. Enantiomeric excess was determined by HPLC using a Chiralpak AS column, IPA/Hex = 10:90, 1.0 mL/min, t_{major} = 5.7 min, t_{minor} = 6.8 min. $[\alpha]^{24}_D$ = 30.9° (c = 0.12, $CHCl_3$).^{1}H NMR (300 MHz, $CDCl_3$): d 6.76 (d, *J* = 8.9 Hz, 2H), 6.60 (d, *J* = 8.6

Hz, 2H), 3.88-3.75 (m, 2H), 3.73 (s, 3H), 3.68 (s, 3H), 1.95-1.60 (m, 6H), 1.50-1.05 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): d 174.5, 152.6, 141.5, 115.1, 114.8, 63.3, 55.6, 51.7, 41.3, 29.6, 29.2, 26.1, 26.0; APCI-HRMS Calcd. for $C_{16}H_{24}NO_3$ [M+H$^+$]: 278.1756, found 278.1729.

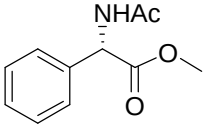
Procedure for the hydrogenation of 1a with low catalyst loadings: In a nitrogen filled glove box, to the 1 mL CH_2Cl_2 solution of $Rh(cod)_2BF_4$ (4.1 mg, 0.01 mmol) was added the 1 mL CH_2Cl_2 solution of TangPhos (2.9 mg, 0.01 mmol). The resulting solution was stirred in a closed vial to prevent solvent evaporation for 30 min. To a 20 mL vial containing substrate **1a** (1.08 g, 4 mmol) was added different amount of the catalyst solution made above (1.6 mL for S/C = 500; 0.8 mL for S/C = 1000). To the reaction vial was added another 5 mL of CH_2Cl_2 and the vial was put into an autoclave which was charged with H_2 (50 atm). The hydrogenation was performed at 50 °C for 24 h. After carefully releasing the hydrogen gas, the solvent was removed under reduced pressure. The crude product was purified through a silica gel column (eluting with a mixture of Hexanes : EtOAc = 10:1) to afford **2a**. The enantiomeric excess was determined by chiral HPLC.

When 0.2 mol% catalyst was used (S/C = 500), >99% conversion was observed from the crude ^{1}HNMR and 93% *ee* was obtained. When 0.1 mol% catalyst (S/C = 1000) was used, >85% conversion was observed from the crude ^{1}HNMR and 82% **2a** was isolated by column. The *ee* was 91% from this S/C = 1000 experiment.

General procedure for the removal of *p*-methoxyphenyl group of 2a:[6] To a CH_3CN (5 mL) solution of (*S*)-**2a** (150 mg, 0.55 mmol, 1 eq) at 0 °C was added a H_2O (1.5 mL) solution of cerium ammonium nitrate (CAN, 667 mg, 1.21 mmol, 2.2 eq). The resulting dark solution was stirred at 0 °C for 30 min before treated with 2N HCl to pH = 1. The aqueous phase was washed with EtOAc (15 mL × 3) and brought to basic by saturated $NaHCO_3$. The resulting suspension was then extracted with CH_2Cl_2 (15 mL × 3). The combined organic phase was dried over anhydrous Na_2SO_4. Phenylglycine methyl ester (78.0 mg, 86% yield) was obtained by removal of the solvent under vacuum. The enantiomeric excess was determined by chiral HPLC after derivatization with Ac_2O in CH_2Cl_2.



(*S*)-Phenylglycine methyl ester. $[\alpha]^{24}_{D}$ = 202.3° (c = 0.49, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): d 7.41-7.28 (m, 5H), 4.62 (s, 1H), 3.71 (s, 3H), 1.98-1.72 (b, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): d 174.4, 140.2, 128.7, 128.0, 126.7, 58.7, 52.3.



(*S*)-Acetyl phenylglycine methyl ester. ^1H NMR (300 MHz, $CDCl_3$): d 7.37-7.30 (m, 5H), 6.60-6.42 (b, 1H), 5.59 (d, *J* = 7.3 Hz, 1H), 3.73 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): d 171.5, 169.3, 136.5, 129.0, 128.5, 127.2, 56.4, 52.8, 23.0.

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