Enantioselective Mannich Reactions Using the Practical Proline Mimetic *N*-(*p*-dodecylphenylsulfonyl)-2-Pyrrolidinecarboxamide

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Electronic Supplementary Information: Experimental

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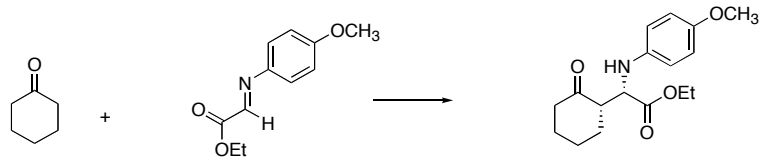
General. Infrared spectra were recorded neat unless otherwise indicated and are reported in cm^{-1}. ^1H NMR spectra were recorded in deuterated solvents and are reported in ppm relative to tetramethylsilane and referenced internally to the residually protonated solvent. ^{13}C NMR spectra were recorded in deuterated solvents and are reported in ppm relative to tetramethylsilane and referenced internally to the residually protonated solvent. Chiral HPLC was performed with chiral columns (chirapak AD, OD, OJ columns, (Daicel Chemical Ind., Ltd.)).

Routine monitoring of reactions was performed using silica gel, aluminum-backed TLC plates. Flash chromatography was performed with the indicated eluents on 230-400 mesh silica gel.

All solvents and commercially available reagents were either purified via literature procedures or used without further purification.

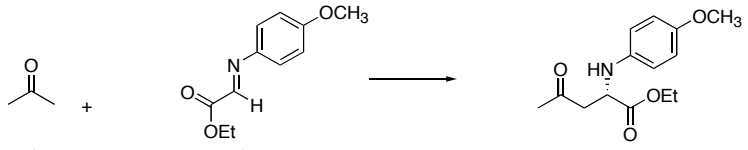
General procedure for Mannich reaction with iminoester 6 in DCE (20 mol% catalyst): To a solution of iminoester **6**[1] (0.125 mmol) and the corresponding ketone (0.625 mmol, 5 equiv.) in appropriate solvent (DCE, 2-Me-THF or DMF) was added sulfonamide **3** (10.6 mg, 0.025 mmol) and water (0.125 mmol, 2.3 mg, 1 equiv.) at 4ºC or room temperature. After stirring at same temperature for the denoted time, the reaction was loaded directly onto silica gel and was purified by chromatography, eluting with 10-30% EtOAc / hexanes, to give the corresponding Mannich product.

Large-scale preparation of Mannich product 7: To a solution of iminoester **6** (20.7 g, 100 mmol) and cyclohexanone **5** (49.0 g, 51.7 mL, 500 mmol, 5 equiv.) was added sulfonamide **3** (6.33 g, 15 mmol) and water (1.8 g, 1.8 mL, 100 mmol) at rt. After stirring at same temperature for 18 h, the reaction mixture was filtered, and the solid filtrate **3** (3.24 g, 7.68 mmol) was kept. The mother liquor was diluted with hexanes (50 mL) and filtered through silica gel pad (MTBE –20% MeOH / CH_2Cl_2) to give Mannich product **7** (24.7 g, 81 mmol – 81% yield, 97% ee, >20:1 dr) and recovered catalyst **3** (2.58 g, 6.11 mmol, 92% overall recovery).



5 **6** **7**

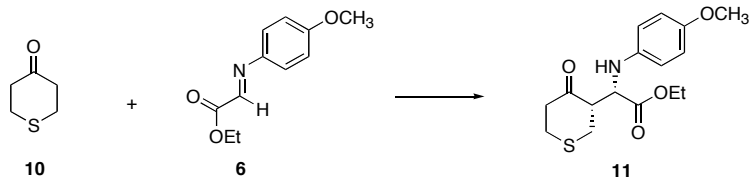
(2S, 1'S)-Ethyl-2-(*p*-methoxyphenylamino)-2-(2'-oxocyclohex-1'-yl)acetate 7:[1] (*In DCE:* time 16 h, 35.6 mg, 93%, 96% ee, >20:1 dr; *In 2-Me-THF:* time 16 h, 85%, 98% ee, >20:1 dr); $[\alpha]_D^{23}$ = -41.3° (c=1.4, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 6.80 (d, *J* = 9.2 Hz, 2H), 6.75 (d, *J* = 9.2 Hz, 2H), 4.25 (br s, 1H), 4.21-4.14 (m, 2H), 3.92 (br s, 1H), 3.77(s, 3H), 2.83 (dt, *J* = 12.4, 5.2 Hz, 1H), 1.58-2.51 (m, 8H), 1.25 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.1, 173.5, 153.1, 141.1, 116.1, 114.8, 61.1, 58.1, 55.7, 53.4, 41.9, 29.6, 26.9, 24.8, 14.2; HPLC: Daicel Chiralpak AD. Hexanes-*i*-PrOH, 92:8, 1 mL min^{-1}, 254 nm: t_R (major) = 25.2 min; t_R (minor) = 23.5 min.



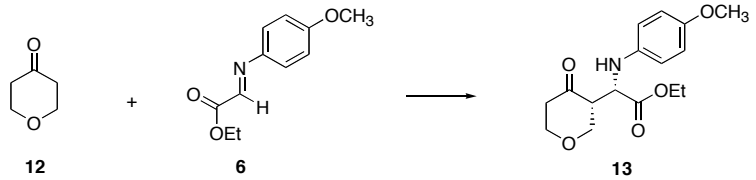
8 **6** **9**

(2S)-Ethyl-2-(*p*-methoxyphenylamino)-4-oxo-pentanoate 9:[1] (*In DCE:* time 4 d, 20.6 mg, 62%, 92% ee); $[\alpha]_D^{23}$ = -13.7° (c=1.1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 6.80 (d, *J* = 9.2 Hz, 2H), 6.67 (d, *J* = 9.2 Hz, 2H), 4.36 (t, *J* = 5.6 Hz, 1H), 4.20 (q, *J* = 6.8 Hz, 2H), 3.77(s, 3H), 2.99 (d, *J* = 5.6 Hz, 2H), 2.21 (s, 3H), 1.26 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.9, 173.0, 153.1, 140.5, 115.8, 114.9, 61.5, 55.7,

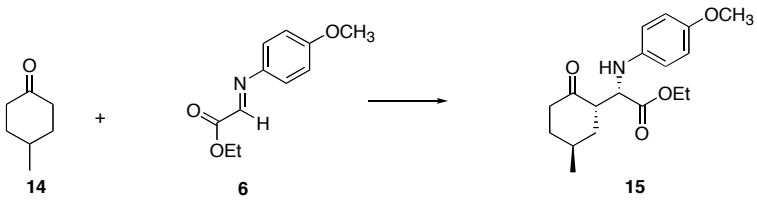
54.3, 45.8, 30.4, 14.1; HPLC: Daicel Chiralpak AD. Hexanes-*i*-PrOH, 92:8, 1 mL min^{-1}, 254 nm: t_R (major) = 32.5 min; t_R (minor) = 28.5 min.



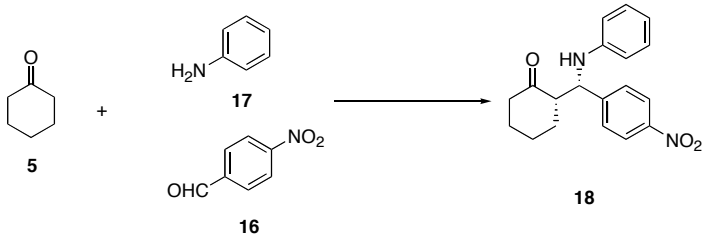
(2*S*, 3*S*)-Ethyl-2-(*p*-methoxyphenylamino)-2-(4'-oxotetrahydrothiopyran-3'-yl)acetate 11:[2] (*In DCE:* time 48 h, 32.7 mg, 81%, 99% ee, 1.3:1 dr; *In DMF:* time 48 h, 31.7 mg, 79%, 99% ee, >20:1 dr); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.80 (d, *J* = 8.8 Hz, 2H), 6.75 (d, *J* = 8.8 Hz, 2H), 4.39 (d, *J* = 6.8 Hz, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 3.94 (br s, 1H), 3.77(s, 3H), 2.70-3.20 (m, 7H), 1.23 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.8, 172.8, 153.4, 140.7, 116.3, 114.9, 61.4, 58.3, 56.1, 55.7, 43.8, 32.6, 30.3, 14.1; HPLC: Daicel Chiralpak AD. Hexanes-*i*-PrOH, 90:10, 1.0 mL min^{-1}, 254 nm: t_R (major) = 35.6 min; t_R (minor) = 30.1 min.



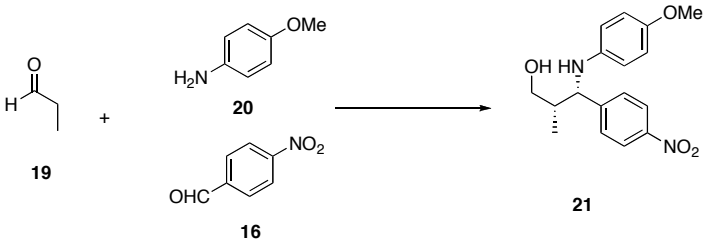
(2*S*, 3*S*)- Ethyl-2-(*p*-methoxyphenylamino)-2-(4'-oxotetrahydropyran-3'-yl)acetate 13:[3] (*In DMF:* time 72 h, 34.2 mg, 89%, 91% ee, >20:1 dr); $[\alpha]_D^{23}$ = -30.1° (c=2.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.80 (d, *J* = 8.8 Hz, 2H), 6.73 (d, *J* = 8.8 Hz, 2H), 4.28 (d, *J* = 6.0 Hz, 1H), 3.89-4.22 (m, 7H), 3.76 (s, 3H), 2.93 (q, *J* = 6.0 Hz, 1H), 2.59-2.63 (m, 2H), 1.24 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.9, 172.6, 153.4, 140.7, 116.2, 114.8, 69.6, 68.1, 61.5, 56.6, 55.7, 54.5, 42.1, 14.1; HPLC: Daicel Chiralpak OD. Hexanes-*i*-PrOH, 95:5, 1.0 mL min^{-1}, 254 nm: t_R (major) = 30.8 min; t_R (minor) = 37.0 min.



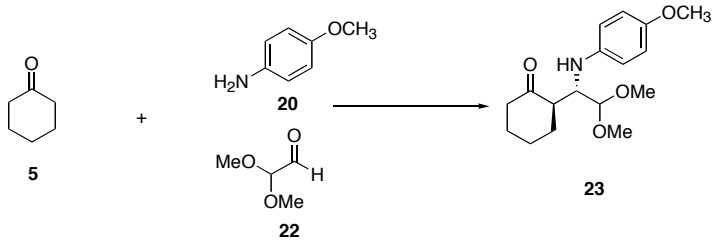
(2S, 1'S)-Ethyl-2-(*p*-methoxyphenylamino)-2-(2'-oxo-5'-methylcyclohex-1'-yl)acetate 15:[4] (*In DMF:* time 72 h, 35.1 mg, 88%, 99% ee, 2.4:1 dr); $[\alpha]_D^{23}$ = -10.4° (c=3.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, major isomer) δ 6.81-6.75 (m, 4H), 4.25 (d, *J* = 4.8 Hz, 1H), 4.13-4.20 (m, 2H), 3.91 (br s, 1H), 3.75 (s, 3H), 2.86-2.92 (m, 1H), 2.41-2.49 (m, 2H), 1.98-2.18 (m, 3H), 1.42-1.69 (m, 2H), 1.24 (t, *J* = 7.2 Hz, 3H), 1.06 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, major isomer) δ 210.0, 173.5, 153.1, 141.2, 116.1, 114.8, 61.2, 58.1, 55.7, 52.5, 41.1, 37.5, 34.8, 31.7, 21.5, 14.2; HPLC: Daicel Chiralpak AD. Hexanes-*i*-PrOH, 80:20, 0.4 mL min^{-1}, 254 nm: t_R (major) = 28.5 min; t_R (minor) = 32.3 min.



2-[1'-(*p*-Nitrophenyl)-1'-*N*-phenylamino]methylcyclohexanone 18:[5] To a vial containing the *p*-nitrobenzaldehyde **16** (37.8 mg, 0.25 mmol) and aniline **17** (25.6 mg, 0.275 mmol) in DCE (0.12 mL) was added cyclohexanone **5** (123 mg, 0.129 mL, 1.25 mmol, 5 equiv.) and sulfonamide **3** (21.1 mg, 0.05 mmol) at rt. After stirring at same temperature for 48 h, reaction was loaded directly onto silica gel and was purified by chromatography, eluting with 5-20% EtOAc / hexanes, to give the product **18** (49.2 mg, 0.152 mmol, 60%, 96% ee, 5:1 dr) as yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 8.8 Hz, 2H), 7.58 (d, J = 8.8 Hz, 2H), 7.11 (t, J = 8.4 Hz, 2H), 6.71 (t, J = 7.2 Hz, 1H), 6.52 (d, J = 8.0 Hz, 2H), 4.88 (br s, 1H), 4.61 (br s, 1H), 2.86-2.89 (m, 1H), 2.32-2.49 (m, 2H), 1.60-2.09 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, major isomer) δ 210.6, 149.5, 147.2, 146.6, 129.2, 128.6, 123.7, 118.4, 114.1, 57.3, 56.2, 42.5, 29.1, 27.1, 25.0; HPLC: Daicel Chiralpak AD. Hexanes-*i*-PrOH, 80:20, 1.0 mL min^{-1}, 254 nm: t_R (major) = 18.9 min; t_R (minor) = 14.2 min.



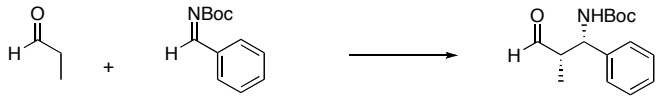
(2S, 3S)-2-Methyl-3-(*p*-methoxyphenylamino)-3-(4-nitrophenyl)propan-1-ol 21:[2] To a vial containing the *p*-nitrobenzaldehyde **16** (37.8 mg, 0.25 mmol) and *p*-anisidine **20** (34.0 mg, 0.275 mmol) in DCE (0.16 mL) was added propionaldehyde **19** (72.5 mg, 0.09 mL, 1.25 mmol, 5 equiv.) and sulfonamide **3** (10.6 mg, 0.025 mmol) at rt. After stirring at same temperature for 48 h, reaction was cooled to 0 ºC followed by addition of MeOH (0.1 mL) and $NaBH_4$ (95 mg, 2.5 mmol). After stirring at 0 ºC for 30 min, the reaction mixture was added ether (5 mL) and sat. aq. NH_4Cl solution (2 mL). The organic layer was washed with sat. aq. NH_4Cl solution (2 mL). The dried (Na_2SO_4) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10-30% EtOAc/Hexanes, to give **21** (58.5 mg, 0.86 mmol, 75%, 99% ee, 5:1 dr) as yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 8.8 Hz, 2H), 7.53 (d, J = 8.8 Hz, 2H), 6.70 (t, J = 9.2 Hz, 2H), 6.71 (d, J = 7.6 Hz, 1H), 4.68 (br s, 1H), 3.70 (s, 3H), 3.66-3.71 (m, 2H), 2.21-2.27 (m, 1H), 0.93 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.6, 150.5, 147.0, 140.9, 128.0, 123.7, 114.86, 114.79, 65.7, 60.6, 55.7, 41.4, 11.7; HPLC: Daicel Chiralpak OD. Hexanes-*i*-PrOH, 90:10, 1.0 mL min^{-1}, 254 nm: t_R (major) = 31.8 min; t_R (minor) = 34.9 min.



(1'*S*, 2*R*)-2-(2', 2'-dimethoxy-1'-(4''-methoxyphenylamino)ethyl)cyclohexanone 23:[6] To a solution of glyoxal dimethyl acetal **22** (60% aq. solution, 26 mg, 0.038 mL, 0.25 mmol) in DCE (0.13 mL) was added *p*-anisidine **20** (46.1 mg, 0.375 mmol) at rt. After stirring at same temperature for 2 h, cyclohexanone **5** (73.5

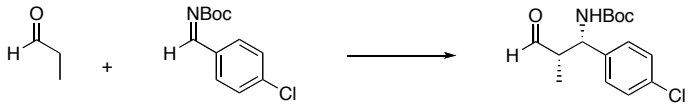
mg, 0.078 mL, 0.75 mmol) and sulfonamide **3** (21.1 mg, 0.05 mmol) were added to the reaction mixture at rt. After stirring at same temperature for 72 h, reaction was loaded directly onto silica gel and was purified by chromatography, eluting with 10-25% EtOAc / hexanes, to give the product **23** (36.9 mg, 0.120 mmol, 48%, 20% ee, 10:1 dr) as yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.75 (d, J = 8.8 Hz, 2H), 6.60 (d, J = 8.8 Hz, 2H), 4.59 (d, J = 6.4 Hz, 1H), 4.14 (br s, 1H), 3.75 (s, 3H), 3.51-3.57 (m, 1H), 3.39 (s, 3H), 3.35 (s, 3H), 2.85-2.89 (m, 1H), 2.31-2.41 (m, 2H), 1.62-2.08 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.6, 151.6, 142.6, 114.8, 114.1, 106.6, 58.2, 55.8, 55.4, 55.3, 51.5, 42.8, 31.5, 27.5, 25.0; HPLC: Daicel Chiralpak OJ. Hexanes-*i*-PrOH, 90:10, 1.0 mL min^{-1}, 254 nm: t_R (major) = 16.5 min; t_R (minor) = 11.6 min.

General procedure for Mannich reaction with *N*-Boc-protected imine in CH_2Cl_2 (20 mol% catalyst): To a solution of *N*-Boc-protected imine[7] (0.125 mmol) and propionaldehyde **19** (14.5 mg, 0.018 mL, 0.25 mmol, 2 equiv.) in CH_2Cl_2 (0.107 mL) was added sulfonamide **3** (10.6 mg, 0.025 mmol) at room temperature. After stirring at same temperature, the reaction was loaded directly onto silica gel and was purified by chromatography, eluting with 10-30% EtOAc / hexanes, to give the corresponding Mannich product.



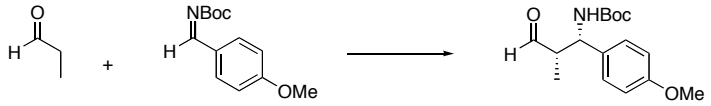
19 **24** **25**

***syn-tert*-Butyl 2-formyl-1-phenylpropylcarbamate 25:**[8] (time 13 h, 23.4 mg, 71%, 99% ee, 19:1 dr); $[\alpha]_D^{23}$ = -5.5° (c=0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1H), 7.26-7.41 (m, 5H), 5.16-5.21 (m, 2H), 2.89 (br s, 1H), 1.44-1.47 (m, 9H), 1.09 (d, J = 3.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.0, 155.1, 128.8, 127.7, 126.7, 125.8, 80.1, 54.7, 51.6, 28.3, 9.3; HPLC: Daicel Chiralpak AD. Hexanes-*i*-PrOH, 90:10, 1.0 mL min^{-1}, 220 nm: t_R (major) = 14.9 min; t_R (minor) = 11.4 min.



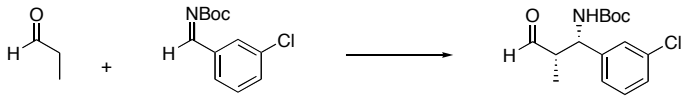
19 **26** **27**

***syn-tert*-Butyl 2-formyl-1-(4-chlorophenyl)propylcarbamate 27:**[9] (time 24 h, 20.2 mg, 54%, 99% ee, >20:1 dr); $[\alpha]_D^{23}$ = -4.7° (c=0.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.71 (s, 1H), 7.35 (d, J = 8.4 Hz, 2H), 7.22 (d, J = 8.4 Hz, 2H), 5.17 (br s, 1H), 2.87 (br s, 1H), 1.43 (br s, 9H), 1.09 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.7, 155.0, 138.2, 133.5, 128.9, 128.1, 80.3, 54.2, 51.2, 28.3, 9.35; HPLC: Daicel Chiralpak AD. Hexanes-*i*-PrOH, 90:10, 1 mL min^{-1}, 235 nm: t_R (major) = 18.3 min; t_R (minor) = 12.0 min.



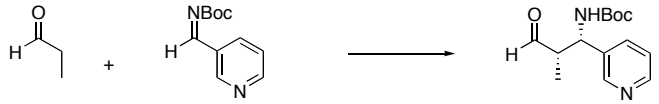
19 **28** **29**

***syn-tert*-Butyl 2-formyl-1-(4-methoxyphenyl)propylcarbamate 29**:[9] (time 24 h, 20.5 mg, 56%, 90% ee, >20:1 dr); $[\alpha]_D^{23}$ = -10.3° (c=0.72, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.72 (s, 1H), 7.19 (d, J = 8.8 Hz, 2H), 6.90 (d, J = 8.8 Hz, 2H), 5.10 (br s, 1H), 3.82 (s, 3H), 2.87 (br s, 1H), 1.44 (br s, 9H), 1.10 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.3, 159.0, 155.1, 131.7, 127.9, 114.1, 80.2, 55.3, 54.4, 51.6, 28.3, 9.61; HPLC: Daicel Chiralpak AD. Hexanes-*i*-PrOH, 95:5, 0.8 mL min^{-1}, 235 nm: t_R (major) = 43.3 min; t_R (minor) = 32.7 min.



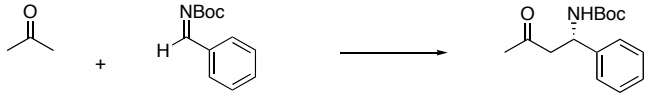
19 **30** **31**

***syn-tert*-Butyl 2-formyl-1-(3-chlorophenyl)propylcarbamate 31**: (colorless oil, time 36 h, 14.1 mg, 38%, 99% ee, >20:1 dr); $[\alpha]_D^{23}$ = -8.3° (c=0.9, $CHCl_3$); IR (neat) 3330, 2982, 2927, 1718, 1702, 1511, 1478, 1451, 1391, 1364, 1391, 1364, 1250, 1162, 1081, 868, 776, 700, 683cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (s, 1H), 7.28-7.42 (m, 3H), 7.17 (d, *J* = 7.2 Hz, 1H), 5.16-5.19 (m, 2H), 2.88 (br s, 1H), 1.44 (br s, 9H), 1.10 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.5, 155.0, 142.3, 134.7, 130.0, 127.9, 126.9, 124.9, 80.4, 54.1, 51.3, 28.3, 9.15; HRMS (ES+) calcd. for $C_{15}H_{20}NO_3NaCl$ (M+Na), 320.1016 found 320.1029; HPLC: Daicel Chiralpak AD. Hexanes-*i*-PrOH, 90:10, 1 mL min^{-1}, 254 nm: t_R (major) = 12.3 min; t_R (minor) = 9.84 min.



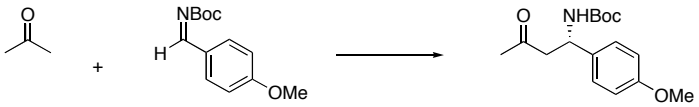
19 **32** **33**

***syn-tert*-Butyl 2-formyl-1-(3-pyridinyl)propylcarbamate 33**: (colorless oil, time 13 h, 19.2 mg, 58%, 99% ee, 15:1 dr); $[\alpha]_D^{23}$ = -15.3° (c=1.2, $CHCl_3$); IR (neat) 3325, 3221, 2976, 2933, 1718, 1702, 1522, 1364, 1277, 1157, 923, 879, 710cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.72 (s, 1H), 8.57 (d, *J* = 10.0 Hz, 2H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.29-7.32 (m, 1H), 5.38 (br s, 1H), 5.23 (br s, 1H), 2.93 (br s, 1H), 1.46 (br s, 9H), 1.13 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.4, 155.0, 149.0, 148.5, 135.4, 134.6, 123.5, 80.4, 52.7, 51.0, 28.3, 9.43; HRMS (EI+) calcd. for $C_{16}H_{23}NO_4$ (M+H), 265.1552 found 265.1542; HPLC: Daicel Chiralpak AD. Hexanes-*i*-PrOH, 90:10, 1.0 mL min^{-1}, 254 nm: t_R (major) = 36.2 min; t_R (minor) = 24.4 min.



8 **26** **34**

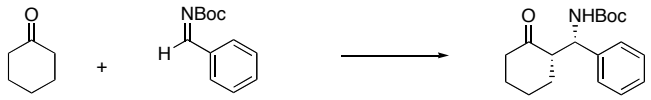
***tert*-Butyl ((1S)-3-oxo-1-phenylbutyl)carbamate 34**:[10] To a solution of *N*-Boc-protected imine **26** (25.6 mg, 0.125 mmol) in acetone **8** (0.125 mL) was added sulfonamide **3** (10.6 mg, 0.025 mmol) at room temperature. After stirring at same temperature for 36 h, the reaction was loaded directly onto silica gel and was purified by chromatography, eluting with 5-30% EtOAc / hexanes, to give the Mannich product **34** (16.3 mg, 0.062 mmol, 50%, 87% ee) as a white solid. $[\alpha]_D^{23}$ = -23.8° (c=0.9, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24-7.38 (m, 5H), 5.34 (br s, 1H), 5.07-5.14 (m, 1H), 3.06 (dd, *J* = 16.8, 6.0 Hz, 1H), 2.94 (dd, *J* = 16.8, 6.0 Hz, 1H), 2.11 (s, 3H), 1.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.4, 155.1, 141.5, 128.7, 127.4, 126.2, 79.9, 51.4, 49.4, 30.6, 28.4; HPLC: Daicel Chiralpak AD. Hexanes-*i*-PrOH, 90:10, 1.0 mL min^{-1}, 207 nm: t_R (major) = 11.7 min; t_R (minor) = 10.4 min.



8 **28** **35**

***tert*-Butyl ((1S)-3-oxo-1-(4-methoxyphenyl)butyl)carbamate 35:** To a solution of *N*-Boc-protected imine **28** (29.4 mg, 0.125 mmol) in acetone **8** (0.125 mL) was added sulfonamide **3** (10.6 mg, 0.025 mmol) at room temperature. After stirring at same temperature for 36 h, the reaction was loaded directly onto silica gel and was purified by chromatography, eluting with 5-40% EtOAc / hexanes, to give the Mannich product **35** (15.4 mg, 0.053 mmol, 42%, 91% ee) as a white solid. Mp: 107-108 ºC; $[\alpha]_D^{23}$ = -22.2° (c=0.7, $CHCl_3$); IR (neat) 3385, 2976, 2933, 2834, 1718, 1685, 1615, 1516, 1359, 1250, 1168, 1108, 1026, 879, 830 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 5.32 (br s, 1H), 5.04 (br s, 1H), 3.80(s, 3H), 3.02-3.06 (m, 1H), 2.91 (dd, *J* = 16.0, 6.4 Hz, 1H), 2.11 (s, 3H), 1.47 (br s, 9H); ^{13}C NMR (100

MHz, $CDCl_3$) δ 207.1, 158.8, 155.1, 133.6, 127.5, 114.0, 79.7, 55.3, 50.6, 49.5, 30.6, 28.4; HRMS (CI+) calcd. for $C_{16}H_{23}NO_4$ (M+), 293.1627 found 293.1632; HPLC: Daicel Chiralpak AD. Hexanes-*i*-PrOH, 90:10, 1.0 mL min^{-1}, 235 nm: t_R (major) = 14.7 min; t_R (minor) = 12.5 min.



5 **26** **36**

***syn-tert*-Butyl (2-oxocyclohexyl)(phenyl)methylcarbamate 36:**[2] To a solution of *N*-Boc-protected imine **26** (25.6 mg, 0.125 mmol) in cyclohexanone **5** (0.125 mL) was added sulfonamide **3** (10.6 mg, 0.025 mmol) at room temperature. After stirring at same temperature for 48 h, the reaction was loaded directly onto silica gel and was purified by chromatography, eluting with 5-20% EtOAc / hexanes, to give the Mannich product **36** (17.4 mg, 0.057 mmol, 46%, 99% ee, >20:1 dr) as a white solid. Mp: 163-164 ºC; $[\alpha]_D^{23}$ = +70° (c=0.5, $CHCl_3$); IR (neat) 3385, 2971, 2922, 281, 1702, 1680, 1516, 1288, 1249, 749, 700cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.23-7.36 (m, 5H), 5.77 (br s, 1H), 4.91 (dd, *J* = 9.2, 3.2 Hz, 1H), 2.85-2.88 (m, 1H), 1.65-2.41 (m, 8H), 1.43 (br s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.6, 155.3, 140.7, 128.3, 128.1, 127.2, 79.4, 55.3, 42.4, 30.7, 28.4, 27.0, 24.6; HRMS (CI+) calcd. for $C_{18}H_{26}NO_3$ (M+1), 304.1913 found 304.1899; HPLC: Daicel Chiralpak AD. Hexanes-*i*-PrOH, 90:10, 1.0 mL min^{-1}, 220 nm: t_R (major) = 12.8 min; t_R (minor) = 9.58 min.

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