Supporting Information
for
Enantioselective Hydrogenation of Tetrasubstituted Olefins of Cyclic -(Acylamino)Acrylates

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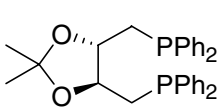
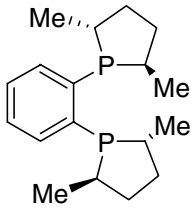
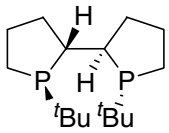
1. Structures of employed chiral ligands



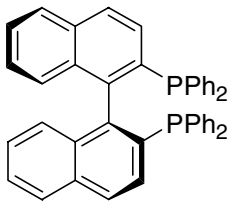
(*S*,*S*)-DIOP



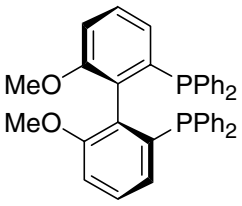
(*R*,*R*)-Me-DuPhos



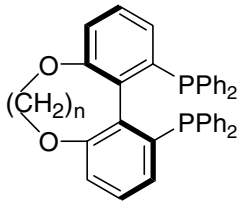
(*S*,*S*,*R*,*R*)-TangPhos



(*S*)-BINAP

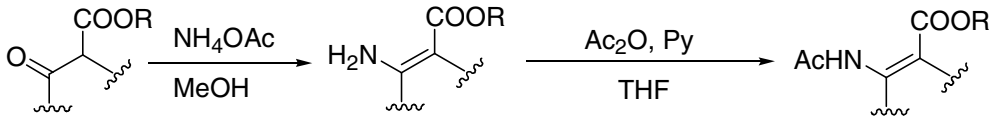


(*S*)-BIPHEP



(*S*)-Cn-TunaPhos
n = 1-6

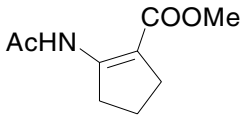
2. General procedures for the synthesis of -(acylamino) acrylates



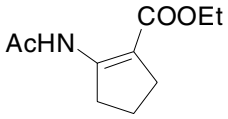
A B

A mixture of -keto ester A (100 mmol) and ammonium acetate (38.5 g, 500 mmol) in MeOH (250 mL) was stirred at room temperature until the starting material totally disappeared. The whole reaction mixture was then concentrated. The residue was re-dissolved in CH_2Cl_2 (200 mL). The resulting solid was filtered and washed with ample CH_2Cl_2. The combined CH_2Cl_2 was washed with water and brine, and then dried over sodium sulfate. The solution was concentrated under vacuum to give enamine B, which was used directly for the next step without further purifications.

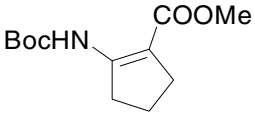
A mixture of enamine B (100 mmol), pyridine (18.2 mL, 225 mmol), and acetic anhydride (55 mL, 582 mmol) in THF (100 mL) was heated at reflux overnight. The mixture was concentrated under vacuum. The residue was treated with EtOAc (300 mL) and 1N HCl (200 mL). The aqueous layer was discarded. The organic phase was washed sequentially with 1N HCl (100 mL), water (100 mL), and brine. After dried over anhydrous sodium sulfate, the solution was concentrated and the residue was distilled under vacuum or recrystallized to give pure -(acylamino)acrylate product in 50-70% yield. (For the synthesis of 2-*tert*-butoxycarbonylamino-cyclopent-1-enecarboxylic acid methyl ester, Boc_2O was used instead of Ac_2O)



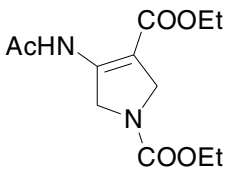
2-Acetylamino-cyclopent-1-enecarboxylic acid methyl ester (**5**): ^{1}H NMR ($CDCl_3$) 400 MHz 10.29 (s, 1H), 3.73 (s, 3H), 3.17 (m, 2H), 2.47 (m, 2H), 2.13 (s, 3H), 1.87 (m, 2H); ^{13}C NMR ($CDCl_3$) 100 MHz 168.7, 155.7, 107.3, 51.5, 34.5, 28.5, 25.1, 21.5; MS (ESI): 184 (M^++1); HRMS calcd for $C_9H_{14}NO_3$ 184.0974; found 184. 0960.



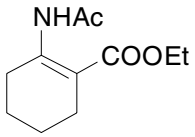
2-Acetylamino-cyclopent-1-enecarboxylic acid ethyl ester (**4**): ^{1}H NMR ($CDCl_3$) 360 MHz 10.29 (s, 1H), 4.17 (q, 7.1 Hz, 2H), 3.14 (m, 2H), 2.44 (m, 2H), 2.09 (s, 3H), 1.84 (m, 2H), 1.27 (t, 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$) 90 MHz 168.8, 168.3, 155.4, 107.6, 60.2, 34.5, 28.6, 25.0, 21.4, 14.7; MS (ESI): 198 (M^++1); HRMS calcd for $C_{10}H_{16}NO_3$ 198.1130; found 198.1137.



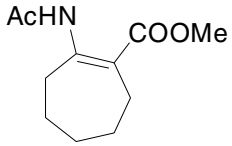
2-*tert*-Butoxycarbonylamino-cyclopent-1-enecarboxylic acid methyl ester (**6**):^{1}H NMR ($CDCl_3$) 300 MHz 9.54 (s, 1H), 3.73 (s, 3H), 3.08 (t, 7.7 Hz, 2H), 2.49 (m, 2H), 1.87 (m, 2H), 1.47 (s, 9H); ^{13}C NMR ($CDCl_3$) 75 MHz 168.5, 156.2, 152.3, 105.2, 81.4, 51.3, 34.0, 28.9, 28.5, 21.4; MS (ESI): 242 (M^++1); HRMS calcd for $C_{12}H_{20}NO_4$ 242.1392; found 242.1382.



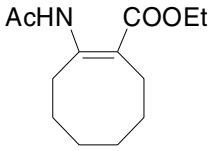
4-Acetylamino-2,5-dihydro-pyrrole-1,3-dicarboxylic acid diethyl ester (**7**):^{1}H NMR ($CDCl_3$) 360 MHz 10.09 (s, 1H), 4.83 (m, 2H), 4.16 (m, 6H), 2.14 (s, 3H), 1.28 (m, 6H); ^{13}C NMR ($CDCl_3$) 90 MHz 168.4, 168.1, 165.8, 165.7, 154.9, 154.7, 148.1, 147.8, 102.5, 102.3, 61.5, 60.7, 53.6, 53.2, 49.3, 48.9, 24.3, 15.0, 14.5, 14.4 (two conformers); MS (ESI): 271 (M^++1); HRMS calcd for $C_{12}H_{19}N_2O_5$ 271.1294; found 271.1315.



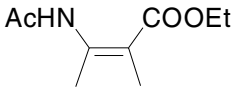
2-Acetylamino-cyclohex-1-enecarboxylic acid ethyl ester (**8**): ^{1}H NMR ($CDCl_3$) 360 MHz 11.56 (s, 1H), 4.15 (q, 7.1 Hz, 2H), 2.94 (m, 2H), 2.28 (m, 2H), 2.08 (s, 3H), 1.57 (m, 4H), 1.27 (t, 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$) 90 MHz 170.1, 168.8, 152.4, 104.5, 60.3, 28.6, 25.6, 24.3, 22.0, 21.9, 14.4; MS (ESI): 212 (M^++1); HRMS calcd for $C_{11}H_{18}NO_3$ 212.1287; found 212.1299.



2-Acetylamino-cyclohept-1-enecarboxylic acid methyl ester (**9**): ^{1}H NMR ($CDCl_3$) 300 MHz 11.1 (s, 1H), 3.67 (s, 3H), 3.01 (m, 2H), 2.46 (m, 2H), 2.06 (s, 3H), 1.71 (m, 2H), 1.60 (m, 2H), 1.42 (m, 2H); ^{13}C NMR ($CDCl_3$) 75 MHz 170.4, 169.6, 158.6, 112.3, 51.9, 32.2, 30.2, 26.8, 26.2, 25.8, 24.8; MS (ESI): 212 (M^++1); HRMS calcd for $C_{11}H_{18}NO_3$ 212.1287; found 212.1284.



2-Acetylamino-cyclooct-1-enecarboxylic acid ethyl ester (**10**): ^{1}H NMR ($CDCl_3$) 360 MHz 11.71 (s, 1H), 4.l7 (q, 7.1 Hz, 2H), 3.04 (m, 2H), 2.44 (m, 2H), 2.10 (s, 3H), 1.76 (m, 2H), 1.46 (m, 6H), 1.28 (t, 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$) 90 MHz 170.2, 168.5, 155.1, 107.7, 60.4, 30.2, 29.1, 27.6, 26.9, 26.5, 25.9, 25.4, 14.4; MS (ESI): 240 (M^++1); HRMS calcd for $C_{13}H_{22}NO_3$ 240.1600; found 240. 1597.

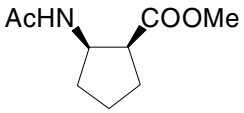


3-Acetylamino-2-methyl-but-2-enoic acid ethyl ester (**11**): ^{1}H NMR ($CDCl_3$) 400 MHz 11.70 (s, 1H), 4.18 (q, 7.1 Hz, 2H), 2.40 (s, 3H), 2.10 (s, 3H), 1.82 (s, 3H), 1.30 (t, 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$) 100 MHz 170.6, 169.4, 150.8, 103.5, 60.8, 25.9, 17.8, 14.7, 13.0; MS (ESI): 186 (M^++1); HRMS calcd for $C_9H_{16}NO_3$ 186.1130; found 186.1142.

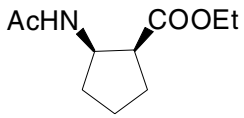
3. General hydrogenation method

Ru(COD)(methallyl)$_2$ (3.2 mg, 10 mol) and C3-TunaPhos (5.9 mg, 10 mol) were dissolved in degassed dichloromethane (0.5 mL) in a Schlenk tube under N_2. The solution was cooled down to 0^{o}C and HBF_4.Me_2O (2.5 L, 2.7 mg, 20 mol) was slowly added. The resulting solution was then allowed to warm to rt and stirred for 0.5 h. The mixture was evaporated under vacuum, and the residue was dissolved in degassed dried MeOH or EtOH (3 mL), and the solution was directly used for hydrogenation. To the catalyst solution was added substrate (0.2 mmol). The resulting mixture was transferred into an autoclave and charged with 50 atm of H_2 pressure. The autoclave was stirred at rt for 18 h.

The reaction solution was then evaporated and the residue was passed through a short silica gel plug to remove the catalyst. The resulting hydrogenation product was then directly analyzed by chiral GC (chiralselect 1000 or gamma dex 225) to determine the enantiomeric excess.

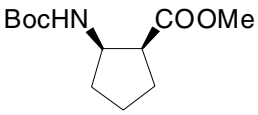


cis-2-Acetylamino-cyclopentanecarboxylic acid methyl ester (**5a**): >99% ee; $[\ ]^{20}_D$ = +99.1^o (c = 1.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$) 400 MHz 6.16 (s, 1H), 4.47 (m, 1H), 3.66 (s, 3H), 2.99 (m, 1H), 1.97 (m, 3H), 1.93 (s, 3H), 1.80 (m, 1H), 1.64 (m, 2H); ^{13}C NMR ($CDCl_3$) 90 MHz 175.6, 170.1, 52.5, 52.1, 46.7, 32.3, 28.6, 23.8, 22.6; MS (ESI): 186 (M^++1); HRMS calcd for $C_9H_{16}NO_3$ 186.1130; found 186. 1133. Chiral GC conditions: chiralselect 1000, 1 mL/min, 150^{o}C isothermal, 22.9 min (1*R*, 2*S*), 23.3 (1*S*, 2*R*).

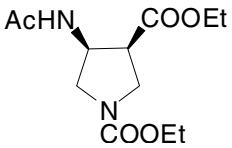


cis-2-Acetylamino-cyclopentanecarboxylic acid ethyl ester (**4a**): 99% ee; $[\ ]^{20}_D$ = +85.9^o (c = 0.9, $CHCl_3$); ^{1}H NMR (CDCl3) 360 MHz 6.14 (s, 1H), 4.45 (m, 1H), 4.09 (q, 7.1 Hz, 2H), 2.95 (m, 1H), 1.93 (m, 3H), 1.91 (s, 3H), 1.77 (m, 1H), 1.61 (m, 2H), 1.22 (t, 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$) 100 MHz 175.1, 170.0, 60.9, 52.4, 46.8, 32.3, 28.6, 23.7, 22.6, 14.6; MS (ESI): 200 (M^++1); HRMS calcd for $C_{10}H_{18}NO_3$ 200.1287;

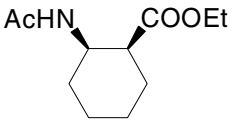
found 200.1306. Chiral GC conditions: chiralselect 1000, 1 mL/min, 160°C isothermal, 24.5 min (1*R*, 2*S*), 25.4 (1*S*, 2*R*).



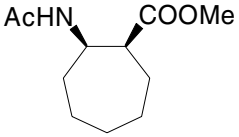
cis-(1*S*, 2*R*)-2-*tert*-Butoxycarbonylamino-cyclopentanecarboxylic acid ethyl ester (**6a**): 98% ee; $[\ ]^{20}_{D} = +77.1^{o}$ (c = 1.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$) 400 MHz 4.93 (s, 1H), 4.22 (m, 1H), 3.68 (s, 3H), 3.01 (dd, 7.4 Hz, 15.0 Hz, 1H), 1.95 (m, 3H), 1.83 (m, 1H), 1.63 (m, 2H), 1.43 (s, 9H); ^{13}C NMR ($CDCl_3$) 100 MHz 175.2, 155.7, 79.6, 54.2, 52.0, 47.2, 32.6, 28.7, 28.1, 22.6; MS (ESI): 244 (M^++1); HRMS calcd for $C_{12}H_{22}NO_4$ 244.1549; found 244.1544. Chiral GC conditions: gama dex 225, 1 mL/min, 140°C isothermal, 42.4 min (1*R*, 2*S*), 43.1 (1*S*, 2*R*).



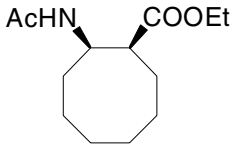
cis-4-Acetylamino-pyrrolidine-1,3-dicarboxylic acid diethyl ester (**7a**): 95% ee; $[\ ]^{20}_{D} = +12.6^{o}$ (c = 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$) 360 MHz 6.43 (b, 1H), 4.74 (m, 1H), 4.11 (m, 4H), 3.60-3.85 (m, 3H), 3.37 (m, 1H), 3.18 (m, 1H), 1.94 (s, 3H), 1.21 (m, 6H); ^{13}C NMR ($CDCl_3$) 90 MHz 171.7, 170.1, 155.2, 61.5, 51.0, 50.6, 50.0, 49.5, 47.4, 47.0, 46.3, 45.2, 23.3, 14.8, 14.2 (two conformers); MS (ESI): 273 (M^++1); HRMS calcd for $C_{12}H_{21}N_2O_5$ 273.1450; found 273.1441. Chiral GC conditions: chiralselect 1000, 1 mL/min, 120°C isothermal, 31.7 min (3*S*, 4*R*), 33.2 min (3*R*, 4*S*).



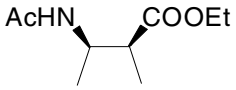
cis-2-Acetylamino-cyclohexanecarboxylic acid ethyl ester (**8a**): 92% ee; $[\ ]^{20}_{D} = +50.0^{o}$ (c = 2.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$) 400 MHz 6.45 (b, 1H), 4.12 (m, 3H), 2.75 (m, 1H), 2.05 (m, 1H), 1.94 (s, 3H), 1.64 (m, 4H), 1.46 (m, 2H), 1.25 (t, 7.1 Hz, 3H), 1.24 (m, 1H); ^{13}C NMR ($CDCl_3$) 100 MHz 174.6, 169.5, 60.8, 48.1, 44.7, 29.7, 27.6, 24.5, 24.0, 22.7, 14.6; MS (ESI): 214 (M^++1); HRMS calcd for $C_{11}H_{20}NO_3$ 214.1443; found 214.1461. Chiral GC conditions: chiralselect 1000, 1 mL/min, 140°C isothermal, 44.7 min (1*R*, 2*S*), 47.4 (1*S*, 2*R*).



cis-2-Acetylamino-cycloheptanecarboxylic acid methyl ester (**9a**): 80% ee; [ ]$^{20}_{D}$ = +43.6^{o} (c = 1.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$) 360 MHz 6.19 (b, 1H), 4.21 (m, 1H), 3.67 (s, 3H), 2.87 (m, 1H), 1.91 (m, 4H), 1.78 (m, 3H), 1.40-1.70 (m, 6H); ^{13}C NMR ($CDCl_3$) 90 MHz 175.3, 168.9, 51.7, 50.9, 47.7, 32.7, 27.3, 27.1, 25.2, 24.7, 23.7; MS (ESI): 214 (M^++1); HRMS calcd for $C_{11}H_{20}NO_3$ 214.1443; found 214.1443. Chiral GC conditions: chiralselect 1000, 1 mL/min, 160^{o}C isothermal, 32.2 min (1*R*, 2*S*), 32.9 (1*S*, 2*R*).

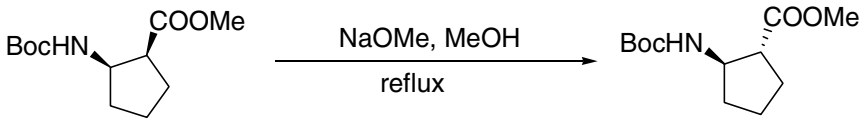


cis-2-Acetylamino-cyclooctanecarboxylic acid ethyl ester (**10a**): 44% ee; [ ]$^{20}_{D}$ = -17.9^{o} (c = 1.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$) 400 MHz 6.06 (d, 8.0 Hz, 1H), 4.43 (m, 1H), 4.15 (q, 7.1 Hz, 2H), 2.83 (m, 1H), 1.93 (m, 4H), 1.52-1.90 (m, 11H), 1.27 (t, 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$) 100 MHz 175.2, 169.2, 61.0, 48.8, 47.1, 31.7, 27.5, 26.8, 26.2, 25.6, 25.0, 23.9, 14.6; MS (ESI): 242 (M^++1); HRMS calcd for $C_{13}H_{24}NO_3$ 242.1756; found 242.1765. Chiral GC conditions: chiralselect 1000, 1 mL/min, 180^{o}C isothermal, 38.8 (large), 39.5 (small).



3-Acetylamino-2-methyl-butyric acid ethyl ester (**11a**): 72% ee; [ ]$^{20}_{D}$ = +23.6^{o} (c = 0.25, $CHCl_3$); ^{1}H NMR ($CDCl_3$) 400 MHz 6.05 (b, 1H), 4.64 (m, 3H), 2.66 (m, 1H), 1.99 (s, 3H), 1.30 (t, 7.1 Hz, 3H), 1.19 (d, 7.2 Hz, 3H), 1.14 (d, 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) 100 MHz 174.7, 169.5, 61.0, 47.4, 44.3, 24.0, 16.9, 14.6, 14.1; MS (ESI): 188 (M^++1); HRMS calcd for C9H18NO3 188.1287; found 188.1280. Chiral GC conditions: chiralselect 1000, 1 mL/min, 140^{o}C isothermal, 15.0 min (2*R*, 3*S*), 16.0 (2*S*, 3*R*).

4. Preparation of *trans*-(1*R*, 2*R*)-2-*tert*-butoxycarbonylamino-cyclopentanecarboxylic acid methyl ester and determination of absolute configuration of hydrogenation product



98% ee

6a **6b**

To a solution of *cis*-(1*S*, 2*R*)-2-*tert*-butoxycarbonylamino-cyclopentanecarboxylic acid ethyl ester **6a** (36 mg, 0.15 mmol, 98% ee) in dried MeOH (2 mL) was added NaOMe (40 mg, 0.75 mmol). The mixture was heated at reflux until the starting material disappeared according to TLC (24 h). After evaporation of the solvent, the residue was directly passed through a silica gel plug to give white crystalline product **6b** (29 mg, 80% yield): [ ]$^{20}_{D}$ = -40^{o} (c = 0.25, $CHCl_3$); ^{1}H NMR ($CDCl_3$) 400 MHz 4.60 (s, 1H), 4.11

(m, 1H), 3.70 (s, 3H), 2.60 (m, 1H), 2.14 (m, 1H), 1.60-2.10 (m, 5H), 1.45 (s, 9H); MS (ESI): 244 (M^++1); HRMS calcd for $C_{12}H_{22}NO_4$ 244.1549; found 244.1549. The NMR data is consistent with the reported data.[1] The (-) sign of optical rotation of the *trans* product proved its absolute configuration as (1*R*, 2*R*) and thus proved the absolute configuration of the *cis* hydrogenation product **6a** as (1*S*, 2*R*).

Reference:

1. Nöteberg, D.; Brånalt, J.; Kvarnström, I.; Classon, B.; Samuelsson, B.; Nillroth, U.; Danielson, U. H.; Karlén, A.; Hallberg, A. *Tetrahedron* **1997**, *53*, 7975.