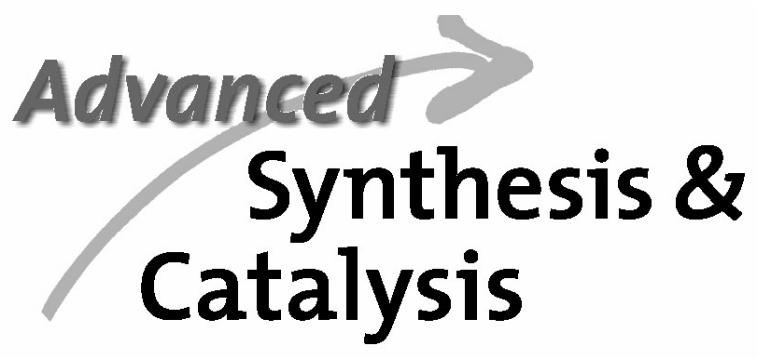

Supporting Information

Highly Efficient Copper(I) Iodide-Tolyl-BINAP-Catalyzed Asymmetric Conjugate Addition of Methylmagnesium Bromide to a,b-Unsaturated Esters

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Supporting Information

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General Methods

Experiments involving moisture and/or air sensitive components were performed in oven-dried glassware under a positive pressure of nitrogen using freshly distilled solvents. Commercial grade solvents and reagents were used without further purification with the following exceptions: *t*-BuOMe was distilled from calcium hydride. Dichloromethane was distilled from calcium hydride. Diethyl Ether was distilled from sodium. Hexane, ethyl acetate were fractionally distilled.

Copper (I) iodide, enoates **4a** and **4b** were purchased from Aldrich or Acros. (*R or S*)-BINAP (**L1**), (*R or S*)-Tol-BINAP (**L2**) and (*R*)-xylyl-BINAP (**L3**) were purchased from Strem. Unsaturated esters (***E***)-**2**, (***Z***)-**2**, and **4c-f** were prepared from the corresponding aldehydes, using Horner-Emmons reaction or Wittig-Horner reaction.[1] Grignard reagent (MeMgBr, 3 M in diethyl ether) was purchased from Aldrich.

Analytical thin layer chromatography (TLC) was performed using Merck 60 F254 precoated silica gel plate (0.2 mm thickness). Subsequent to elution, plates were visualized using UV radiation (254 nm) on Spectroline Model ENF-24061/F 254 nm. Further visualization was possible by staining with basic solution of potassium permanganate or acidic solution of ceric molybdate.

Flash chromatography was performed using Merck silica gel 60 with freshly distilled solvents. Columns were typically packed as slurry and equilibrated with the appropriate solvent system prior to use.

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1. Apella, D. H.; Moritani, Y.; Shintani, R.; Ferreira, E. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9473-9474.

Infrared spectra were recorded on a Bio-Rad FTS 165 FTIR spectrometer. The oil samples were examined under neat conditons.

High Resolution Mass Spectrometry (**HRMS**) spectra were obtained using Finnigan MAT95XP GC/HRMS (Thermo Electron Corporation).

Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded on a Bruker Avance DPX 300 and Bruker AMX 400 spectrophotometer ($CDCl_3$ as solvent). Chemical shifts for ^{1}H NMR spectra are reported as δ in units of parts per million (ppm) downfield from TMS (δ 0.0) and relative to the signal of chloroform-*d* (δ 7.260, singlet) as the internal standard. Multiplicities were given as: s (singlet); d (doublet); t (triplet); q (quartet); dd (doublets of doublet); ddd (doublets of doublets of doublet); dddd (doublets of doublets of doublets of doublet); dt (doublets of triplet); or m (multiplets). The number of protons (n) for a given resonance is indicated by nH. Coupling constants are reported as a *J* value in Hz. Carbon nuclear magnetic resonance spectra (^{13}C NMR) are reported as δ in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform-*d* (δ 77.03, triplet). The proportion of diastereomers and geometric isomers was determined from the integration of ^{1}H NMR and ^{13}C NMR spectra.

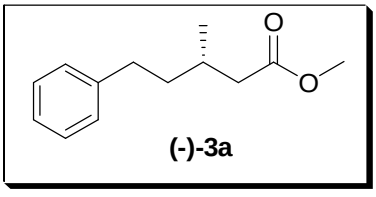
Enantioselectivities were determined by capillary GC analysis (Chiraldex G-TA column (30 m x 0.25 mm)), using the flame ionization detector or HPLC analysis employing a Daicel Chiracel ODH or OJ column at 25 ^{o}C. Optical rotations were measured in $CHCl_3$ on a *Schmidt + Haensdch* polarimeter (Polartronic MH8) with a 10 cm cell (*c* given in g/100 mL). Absolute configurations of the products were determined by comparison with known compounds.

General Procedure for the Enantioselective Conjugate Addition

In a round bottom flask equipped with septum and stirring bar, (*S*)-Tol-BINAP (5.1 mg, 0.0075 mmol) and CuI (0.95 mg, 0.005 mmol) were dissolved in *t*-BuOMe (1.0 mL) and stirred under nitrogen at room temperature until a bright yellow suspension was observed. Alternatively, (*S*)-Tol-BINAP and CuI were stirred in CH_2Cl_2 (1.0 mL) for 15 minutes, concentrated *in vacuo* and then stirred in *t*-BuOMe (1.0 mL) till the same bright yellow suspension was observed. The mixture was then cooled to -20 ^oC and MeMgBr (Aldrich, 3.0 M solution in Et_2O, 1.25 mmol) was added carefully into the reaction mixture. After stirring for 15 minutes, a solution of unsaturated ester (0.25 mmol) in *t*-BuOMe (0.30 mL) was added dropwise over 1 hour via syringe pump. After vigorous stirring at -20 ^oC for another 1.5 hours, MeOH (0.5 mL) and saturated NH_4Cl solution (2 mL) were sequentially added at -20 ^oC, and the mixture was warmed to room temperature. The aqueous layer was extracted with diethyl ether (5 mL x 3) and the combined organic extracts were dried over anhydrous magnesium sulphate, filtered and carefully concentrated *in vacuo*. The residual crude product was purified by flash chromatography (1: 99 Et_2O/Pentane) to afford the desired product as colorless oil.

Racemic 1,4-addition products were obtained by reaction of the enoates with MeMgBr (5.0 eq, 3M in diethyl ether) and CuI (0.05 mol %) at -20 ^oC in diethyl ether.

Characterization of CA Products:



(-)-3a

(-)-Methyl 3-methyl-5-phenylpentanoate

(Table 1, entry 6): colorless oil, 74% yield, 98% *ee*, $[\alpha]_D^{25}$ = - 15.4 (*c* = 1.7, $CHCl_3$); lit. $[\alpha]_D^{20}$ = - 16.9 (*c* = 1.4, $CHCl_3$)[1];

FTIR (KBr, neat): *?* 1737 (C=O);

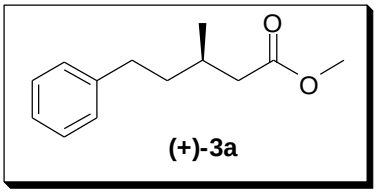
^{1}H NMR (300 MHz, $CDCl_3$): *d* 7.18-7.30 (m, 5H), 3.66 (s, 3H), 2.53-2.72 (m, 2H), 2.36 (dd, *J* = 14.7 and 6.1 Hz, 1H), 2.20 (dd, *J* = 14.7 and 8.0 Hz, 1H), 2.08-1.96 (m, 1H), 1.72-1.45 (m, 2H), 1.01 (d, *J* = 6.6 Hz, 3H);

^{13}C NMR (75.4 MHz, $CDCl_3$): *d* 173.5 (C), 142.3 (C), 128.4(CH), 128.3 (CH), 125.7(CH), 51.4 (CH_3), 41.5 (CH_2), 38.5 (CH_2), 33.3 (CH_2), 30.1 (CH), 19.6 (CH_3);

HRMS (EI) calcd. for $C_{13}H_{18}O_2$ 206.1307, $[M]^+$ found 206.1302;

The enantiomeric excess was determined by chiral HPLC analysis, employing a Dacicel Chiralcel ODH column (Hexane : *i*-propanol 99.2 : 0.8, 1 mL/min): t_1 = 6.90 min (major), t_2 = 7.80 (minor).

[1] López, F.; Harutyunyan, S. R.; Minnaard, A. J.; Feringa, B. L. *Angew. Chem., Int. Ed.* **2005** *44*, 2752-2756.



(+)-3a

(+)-Methyl 3-methyl-5-phenylpentanoate

(Table 2, entry 7): colorless oil, 76% yield, 98% *ee*, $[\alpha]_D^{25}$ = + 15.0 (*c* = 1.2, $CHCl_3$);

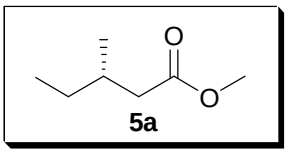
FTIR (KBr, neat): *?* 1737 (C=O);

^{1}H NMR (300 MHz, $CDCl_3$): *d* 7.18-7.30 (m, 5H), 3.66 (s, 3H), 2.53-2.72 (m, 2H), 2.36 (dd, *J* = 14.7 and 6.1 Hz, 1H), 2.20 (dd, *J* = 14.7 and 8.0 Hz, 1H), 2.08-1.96 (m, 1H), 1.72-1.45 (m, 2H), 1.01 (d, *J* = 6.6 Hz, 3H);

^{13}C NMR (75.4 MHz, $CDCl_3$): *d* 173.5 (C), 142.3 (C), 128.4(CH), 128.3 (CH), 125.7(CH), 51.4 (CH_3), 41.5 (CH_2), 38.5 (CH_2), 33.3 (CH_2), 30.1 (CH), 19.6 (CH_3);

HRMS (EI) calcd. for $C_{13}H_{18}O_2$ 206.1307, found $[M]^+$ 206.1302;

The enantiomeric excess was determined by chiral HPLC analysis, employing a Dacicel Chiralcel ODH column (Hexane : *i*-propanol 99.2 : 0.8, 1 mL/min): t_1 = 6.60 min (minor), t_2 = 7.37 (major).



5a

(*S*)-(+)-Methyl 3-methylpentanoate

(Table 2, entry 1): colorless oil, 67% yield, 96% *ee*, $[\alpha]_D^{25}$ = + 5.6 (*c* = 1.2, $CHCl_3$), lit.[2] for (*S*); enantiomer $[\alpha]_D^{20}$ = + 5.9 (*c* = 1.0, $CHCl_3$);

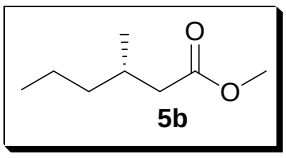
FTIR (KBr, neat): *?* 1734 (C=O);

^{1}H NMR (400 MHz, $CDCl_3$): *d* 3.65 (s, 3H), 2.30 (dd, *J* = 14.8, 6.0 Hz, 1H), 2.09 (dd, *J* = 14.8, 8.4 Hz, 1H), 1.87-1.85 (m, 1H), 1.34-1.32 (m, 1H), 1.24-1.17 (m, 1H), 0.91 (d, *J* = 6.4 Hz, 3H), 0.87 (t, *J* = 7.6 Hz, 3H);

^{13}C NMR (75.4 MHz, $CDCl_3$): *d* 173.9 (C), 51.3 (CH_3), 41.3, 31.9 (CH), 29.3 (CH_2), 19.3 (CH_2), 11.3 (CH_3);

HRMS (EI) calcd. for $C_7H_{14}O_2$ 130.0994, found $[M]^+$ 130.0983;

The enantiomeric excess determined by chiral GC analysis, employing a Chiraldex G-TA column (30 m x 0.25 mm), 60 ºC, retention times (min): t_1 = 11.14 min (minor) , t_2 = 11.90 min (major).



5b

(*S*)-(-)-Methyl 3-methylhexanoate

(Table 2, entry 2): colorless oil, 79% yield, 96% *ee*, $[\alpha]_D^{25}$ = -2.3 (*c* = 1.3, $CHCl_3$), lit.[2] for (*S*) enantiomer: $[\alpha]_D^{25}$ = -2.1 (*c* = 0.9, $CHCl_3$);

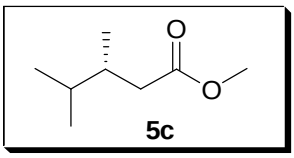
FTIR (KBr, neat): *?* 1737 (C=O);

^{1}H NMR (400 MHz, $CDCl_3$): *d* 3.66 (s, 3H), 2.30 (dd, *J* = 14.6, 6.0 Hz, 1H), 2.10 (dd, *J* = 14.6, 8.0 Hz, 1H), 1.95-1.96 (m, 1H), 1.35-1.21 (m, 4H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.89 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): *d* 173.9 (C), 51.4 (CH_3), 41.7 (CH_2), 39.0 (CH_2), 30.1 (CH), 20.0 (CH_2), 19.7 (CH_3), 14.2 (CH_3);

HRMS (EI) calcd. for $C_8H_{16}O_2$ 144.1150, found $[M]^+$ 144.1143;

The enantiomeric excess was determined by chiral GC analysis, employing a Chiraldex G-TA column (30 m x 0.25 mm), 60 ºC, retention times (min): t_1 = 18.21 min (minor) , t_2 = 19.16 min (major).



5c

(*S*)-(-)-Methyl 3,4-dimethylpentanoate

(Table 2, entry 3): colorless oil, 80% yield, 99% *ee*, colorless oil, $[\alpha]_D^{25}$ = + 3.8 (*c* = 1.4, $CHCl_3$), lit.[3] for (*S*) enantiomer: $[\alpha]_D^{22}$ = + 2.1 (*c* = 2.2, EtOH).

FTIR (KBr, neat): *?* 1737 (C=O);

^{1}H NMR (400 MHz, $CDCl_3$): *d* 3.66 (s, 3H), 2.35 (dd, *J* = 14.7, 5.2 Hz, 1H), 2.07 (dd, *J* = 14.7, 9.2 Hz, 1H), 1.90-1.85 (m, 1H), 1.62-1.55 (m, 1H), 0.88 (d, *J* = 6.8 Hz, 3H), 0.86 (d, *J* = 6.8 Hz, 3H), 0.84 (d, *J* = 6.0 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): *d*174.1 (C), 51.3 (CH_3), 39.0 (CH_2), 35.9 (CH), 32.0 (CH), 19.8 (CH_3), 18.2 (CH_3), 15.8 (CH_3);

HRMS (EI) calcd. for $C_8H_{16}O_2$ 144.1150, found $[M]^+$ 144.1137;

The enantiomeric excess determined by chiral GC analysis, employing a Chiraldex G-TA column (30 m x 0.25 mm), 60 ºC, retention times (min): t_1 = 16.75 min (minor) , t_2 = 17.69 min (major).

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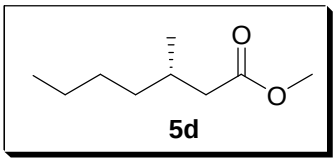
3. Enders, D.; Rendenbach, B. E. M. *Tetrahedron* **1986** *42*, 2235-2242.



5d

(*S*)-(-)-Methyl-3-methylheptanoate

(Table 2, entry 5): colorless oil, 81% yield, 97% *ee*, colorless oil, $[\alpha]_D^{25}$ = -3.4 (*c* = 1.2, $CHCl_3$), lit. for (*S*) enantiomer: $[a]_D^{20}$ = - 3.9 (*c* = 1.5, $CHCl_3$).

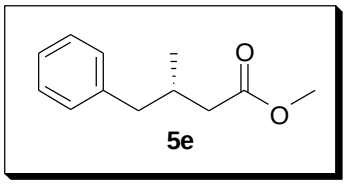
FTIR (KBr, neat):*?* 1738 (C=O);

^{1}H NMR (400 MHz, $CDCl_3$): *d* 3.65 (s, 3H), 2.30 (dd, *J* = 14.6, 6.0 Hz, 1H), 2.10 (dd, *J* = 14.6, 7.8Hz, 1H), 1.96-1.92 (m, 1H), 1.28-1.16 (m, 6H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.88-0.85 (m, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): *d*173.9 (C), 51.3 (CH_3), 41.7 (CH_2), 36.4 (CH_2), 30.3 (CH), 29.1 (CH_2), 22.8 (CH_2), 19.7 (CH_3), 14.0 (CH_3);

HRMS (EI) calcd. for $C_9H_{18}O_2$ 158.1307, found $[M]^+$ 158.1304;

The enantiomeric excess determined by chiral GC analysis, employing a Chiraldex G-TA column (30 m x 0.25 mm), 60 ºC, retention times (min): t_1 = 33.01 min (minor) , t_2 = 34.93 min (major).



5e

(*S*)-(+)-Methyl 3-methyl-4-phenylbutanoate

(Table 2, entries 9-10): colorless oil, 83% yield, 95% *ee*, $[\alpha]_D^{25}$ = + 2.8 (*c* = 1.1, $CHCl_3$).

FTIR (KBr, neat): *?* 1737 (C=O);

^{1}H NMR (300 MHz, $CDCl_3$): *d* 7.14-7.30 (m, 5H), 3.64 (s, 3H), 2.62 (dd, *J* = 13.3, 6.5 Hz, 1H), 2.50 (dd, *J* = 13.3, 7.0 Hz, 1H), 2.37-2.22 (m, 2H), 2.17-2.10 (m, 1H), 0.94 (d, *J* = 6.5 Hz, 3H);

^{13}C NMR (75.4 MHz, $CDCl_3$): *d* 173.5 (C), 140.2 (C), 129.2 (CH), 128.2 (CH), 126.0 (CH), 51.4 (CH_3), 43.0 (CH_2), 40.9 (CH_2), 32.3 (CH), 19.7 (CH_3);

HRMS (EI) calcd. for $C_{12}H_{16}O_2$ 192.1150, found $[M]^+$ 192.1137;

The enantiomeric excess was determined by HPLC analysis, employing a Daicel Chiracel ODH column (Hexane : *i*-propanol 99.5 : 0.5, 0.5 mL/min): t_1 = 17.06 min (major) , t_2 = 22.11 (minor).