Cu(I) Tol-BINAP-Catalyzed Enantioselective Michael Reactions of Grignard reagents and Unsaturated Esters

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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) salts (CuI, CuCl, CuBr, CuBrSMe₂, Cu(OTf).Tol, ethyl crotonate (**4a**) and **4g** 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 Stream. Unsaturated esters (*E*)-**2**, (*Z*)-**2**, **4c**, **4d**, (*E*)-**4e**, (*Z*)-**4e**, and **4g** were prepared from the corresponding aldehydes, via Horner-Emmons reaction or Wittig-Horner reaction using well established protocols, and had identical properties (NMR) to those previously reported.

Grignard reagents were purchased from Aldrich (EtMgBr, MeMgBr) or prepared from the corresponding alkyl bromides and magnesium turnings in Et₂O following standard procedures. Grignard reagents were titrated using *s*BuOH and catalytic amounts of 1,10-phenanthroline.

All reactions were conducted under nitrogen atmosphere using standard Schlenk techniques. Racemic 1,4-addition products were obtained by reaction of the enoates with the corresponding RMgX reagents (-20 °C, Et₂O) and CuI (100 mol%).

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

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

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.

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

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

Proton nuclear magnetic resonance spectra (^1H NMR) were recorded on a Bruker Avance DPX 300 and Bruker AMX 400 spectrophotometer (CDCl_3 as solvent). Chemical shifts for ^1H NMR spectra 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 7.2600, singlet). 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 $n\text{H}$. 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 ^1H NMR and ^{13}C NMR spectra.

Enantioselectivities were determined by capillary GC analysis (Chiraldex G-TA column (30 m x 0.25 mm)), using flame ionization detector or HPLC analysis employing a Daicel Chiracel ODH or OJ column at 25 $^\circ\text{C}$ (in comparison with racemic (1,4)-addition products). 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 configuration of the products was determined by comparison with compounds previously published.

Table I: Additions of EtMgBr to 2: Ligand effect^a

entry	Catalyst	yield (%) ^b	ee (%) ^c
1	1 mol% CuCl + 1.2 mol% L2	86	75
2	1 mol% CuBr + 1.2 mol% L2	83	70
3	1 mol% CuBr SMe ₂ + 1.2 mol% L2	85	78
4	1 mol% CuI + 1.2 mol% L2	85	82
5	1 mol% (CuOTf)Tol _{0.5} + 1.2 mol% L2	83	34
6	1 mol% CuI + 1.2 mol% L1	85	55
7	0.5 mol% 1a	85	57
8	1 mol% CuI + 1.4 mol% L2	86	90
9	1 mol% CuI + 1.5 mol% L2	88	93
10	1 mol% CuI + 2.0 mol% L2	89	93
11	0.5 mol% 1a + 0.5 mol% L2	87	93
12	1 mol% CuI + 1.5 mol% L1	85	85
13	1 mol% CuI + 1.5mol% L3	83	80
14	0.5 mol% 1a + 1mol% Ph ₃ P	85	53
15	0.5 mol% 1a + 1mol% Cy ₃ P	88	83
16	0.5 mol% 1a + 0.5 mol% dppe	86	65

^a All reactions were performed with **2** (0.5 mmol), EtMgBr (2.0 mmol, 3M in ether) in *t*-BuOMe (1 mL) at -40 °C unless otherwise stated. ^b Isolated yield. ^c Determined by HPLC analysis employing a Daicel Chiracel ODH column

Figure 1 The relationship of ee with the ratio of (*R*)-Tol-BINAP : CuI

^a All reactions were performed with **2** (0.5 mmol), EtMgBr (2.0 mmol, 3M in ether) in *t*-BuOMe (1 mL) at -40 °C.

Preparation and characterization of Cu-complexes **1a**.

A solution of **(R)-Tol-BINAP** (67.9 mg, 0.1 mmol) and CuI (19.0 mg, 0.1 mmol) in *t*-BuOMe (10 mL) in a Schlenk tube was stirred at room temperature (RT) for 1 h. The solvent was removed under vacuum and the resulting orange crude residue was washed with cold pentane (3 x 2 mL) to afford **1a** as an light orange powder (86.0 mg, 99% yield, $R_f = 0.35$ (25% Ethyl acetate / Hexane)).

FTIR (KBr, neat): ν 3032, 2960, 2918, 2860, 1597, 1498, 1396, 1261, 1093, 1020, 806, 744;

^1H NMR (300 MHz, CDCl_3): δ 8.00 (m, 8H), 7.43-7.48 (m, 8H), 7.26-7.30 (m, 10H), 7.22-7.23 (m, 8H), 7.26-7.01-7.06 (m, 12H), 6.82 (d, $J = 8.4$ Hz, 4H), 6.23 (d, $J = 7.5$ Hz, 4H), 2.29 (s, 12H), 1.90 (s, 12H);

^{13}C NMR (75.4 MHz, CDCl_3): δ 140.8, 139.0, 138.7, 135.6, 133.3, 133.1, 132.3, 129.8, 128.2, 128.0, 127.8, 127.4, 126.3, 126.0, 21.4, 21.0 .

^{31}P NMR (MHz, CDCl_3): δ -6.5 .

HRMS calcd. For $\text{C}_{96}\text{H}_{81}\text{Cu}_2\text{I}_1\text{P}_4$ [$\text{M}^+ - \text{I} + \text{H}$] 1610.2925, found 1610.2877;

General Procedure for the Enantioselective Conjugate Addition

In a Schlenk tube equipped with septum and stirring bar, (*R*)-Tol-BINAP (5.1 mg, 0.0075 mmol) and CuI (0.95 mg, 0.005 mmol) was dissolved in *t*-BuOMe (1.0 mL) and stirred under nitrogen at room temperature until yellow suspension was observed. The mixture was then cooled to -40 °C and EtMgBr (Aldrich, 3.0 M solution in Et₂O, 2.5 mmol) was added. After stirring for 5 min, a solution of unsaturated ester (0.5 mmol) in *t*-BuOMe (0.25 mL) was added dropwise over 1h by syringe pump. After stirring at -40 °C for 2 to 3 hours, MeOH (0.5 mL) and NH₄Cl (1 M, 2 mL) were sequentially added, and the mixture was warmed to room temperature (RT). After extracted with Et₂O (5 mL x 3), the combined organic phases were dried and concentrated to a yellow oil which was purified by flash chromatograph (1 : 99 Et₂O/pentane) to yield desired product.

Racemic 1,4-addition products were obtained by the reaction of the enoates with the corresponding Grignard reagents (-20 °C, Et₂O) and CuI (100 mol%).

NOTES:

· GC analysis was carried out on a sample obtained after aqueous extraction with Et₂O, which has been passed through a short plug of silica gel.

Characterization of CA products:

(+)-Methyl 3-phenethylpentanoate, $R_f = 0.72$ (EA/Hexane = 1/4);

(Table 3, entry 6): colorless oil, 86% yield, 94% ee, $[\alpha]_D^{22} = +7.7$ ($c = 2.5$), lit.²: $[\alpha]_D^{20} = +7.7$;

FTIR (KBr, neat): ν 1737 (C=O);

^1H NMR (300 MHz, CDCl_3): δ 7.16-7.30 (m, 5H), 3.66 (s, 3H), 2.60 (t, $J = 8.2$ Hz, 2H), 2.31 (d, $J = 6.8$ Hz, 2H), 1.84-1.93 (m, 1H), 1.57-1.66 (m, 2H), 1.38-1.47 (m, 2H), 0.90 (t, $J = 7.4$ Hz, 3H);

^{13}C NMR (75.4 MHz, CDCl_3): δ 173.8 (C), 142.5 (C), 128.3 (CH), 125.7 (CH), 51.4 (CH_3), 38.5 (CH_2), 36.3 (CH), 35.4 (CH_2), 33.0 (CH_2), 26.2 (CH_2), 10.7 (CH_3);

HRMS calcd. For $\text{C}_{14}\text{H}_{20}\text{O}_2$ 220.1463, found 220.1457;

The enantiomeric excess was determined by HPLC analysis employing a Daicel Chiralcel ODH column (Hexane : *i*-propanol 99.2 : 0.8, 1 mL/min): $t_1 = 6.22$ min (minor) , $t_2 = 7.29$ min (major).

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

(-)-Methyl 3-phenethylpentanoate, $R_f = 0.72$ (EA/Hexane = 1/4);

(Figure 1): colorless oil, 86% yield, 94% ee, $[\alpha]_D^{22} = -5.4$ ($c = 1.0$);

The enantiomeric excess was determined by HPLC analysis employing a Daicel Chiracel ODH column (Hexane : *i*-propanol 99.2 : 0.8, 1 mL/min): $t_1 = 6.27$ min (major) , $t_2 = 7.21$ min (minor).

(+)-Methyl 3-phenethylhexanoate, $R_f = 0.70$ (EA/Hexane = 1/4);

(Table 2, entry 2): colorless oil, 90% yield, 92% ee, $[\alpha]_D^{22} = +5.1$ ($c = 3.7$);

FTIR (KBr, neat): ν 1735 (C=O);

^1H NMR (300 MHz, CDCl_3): δ 7.15-7.29 (m, 5H), 3.65 (s, 3H), 2.60 (t, $J = 8.2$ Hz, 2H), 2.31 (d, $J = 6.8$ Hz, 2H), 1.92-1.96 (m, 1H), 1.55-1.66 (m, 2H), 1.29-1.38 (m, 4H), 0.89 (t, $J = 6.9$ Hz, 3H);

^{13}C NMR (75.4 MHz, CDCl_3): δ 173.8 (C), 142.5 (C), 128.5 (CH), 125.7 (CH), 51.4 (CH_3), 38.9 (CH_2), 36.1 (CH_2), 35.9 (CH_2), 34.7 (CH), 33.0 (CH_2), 19.6 (CH_2), 14.3 (CH_3);

HRMS calcd. For $\text{C}_{15}\text{H}_{22}\text{O}_2$ 234.1620, found 234.1607;

The enantiomeric excess was determined by HPLC analysis employing a Daicel Chiracel ODH column (Hexane : *i*-propanol 99.2 : 0.8, 1 mL/min): $t_1 = 5.85$ min (minor) , $t_2 = 6.66$ min (major).

(+)-Methyl 4-methyl-3-phenethylpentanoate, $R_f = 0.71$ (EA/Hexane = 1/4);

(Table 2, entry 3): colorless oil, 89% yield, 91% ee, $[\alpha]_D^{23} = +6.2$ ($c = 1.0$);

FTIR (KBr, neat): ν 1737 (C=O);

^1H NMR (300 MHz, CDCl_3): δ 7.16-7.30 (m, 5H), 3.66 (s, 3H), 2.59 (t, $J = 8.2$ Hz, 2H), 2.35 (dd, $J = 15.0$ and 6.1 Hz, 1H), 2.23 (dd, $J = 15.0$ and 7.3 Hz, 1H), 1.65-1.88 (m, 2H), 1.48-1.63 (m, 2H), 0.87 (t, $J = 6.9$ Hz, 6H);

^{13}C NMR (75.4 MHz, CDCl_3): δ 174.3 (C), 142.6 (C), 128.3 (CH), 125.7 (CH), 51.5 (CH_3), 40.7 (CH), 35.9 (CH_2), 33.7 (CH_2), 33.3 (CH_2), 29.9 (CH), 19.3 (CH_3), 18.5 (CH_3);

HRMS calcd. For $\text{C}_{15}\text{H}_{22}\text{O}_2$ 234.1620, found 234.1606;

The enantiomeric excess was determined by HPLC analysis employing a Daicel Chiracel ODH column (Hexane : *i*-propanol 99.2 : 0.8, 1 mL/min): $t_1 = 5.61$ min (minor) , $t_2 = 6.48$ min (major).

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.788	MM	0.3507	7329.60889	348.29385	50.5233
2	6.561	MM	0.3024	7177.77246	395.65884	49.4767

Totals : 1.45074e4 743.95270

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.606	MM	0.1875	34.25201	3.04520	4.5175
2	6.475	MM	0.2348	723.95917	51.39585	95.4825

Totals : 758.21118 54.44105

(+)-Methyl 3-phenethylheptanoate $R_f = 0.71$ (EA/Hexane = 1/4)

(Table 2, entry 4), colorless oil, 90% yield, 92% ee, $[\alpha]_D^{24} = +6.2$ ($c = 2.2$);

FTIR (KBr, neat): ν 1735 (C=O);

^1H NMR (300 MHz, CDCl_3): δ 7.18-7.32 (m, 5H), 3.68 (s, 3H), 2.62 (t, $J = 8.2$ Hz, 2H), 2.33 (d, $J = 6.8$ Hz, 2H), 1.91-1.97 (m, 1H), 1.54-1.69 (m, 2H), 1.31-1.41 (m, 4H), 0.95 (t, $J = 7.2$ Hz, 3H);

^{13}C NMR (75.4 MHz, CDCl_3): δ 173.9 (C), 142.5 (C), 128.3 (CH), 125.7 (CH), 51.4 (CH_3), 38.9 (CH_2), 35.8 (CH_2), 34.8 (CH), 33.4 (CH_2), 33.0 (CH_2), 28.7 (CH_2), 22.9 (CH_2), 14.0 (CH_3);

HRMS calcd. For $\text{C}_{16}\text{H}_{24}\text{O}_2$ 248.1776, found 248.1767;

The enantiomeric excess was determined by HPLC analysis employing a Daicel Chiracel ODH column (Hexane : *i*-propanol 99.2 : 0.8, 1 mL/min): $t_1 = 5.55$ min (minor) , $t_2 = 6.29$ min (major).

(+)-Methyl 3-phenethylpentanoate, $R_f = 0.72$ (EA/Hexane = 1/4);

(Table 2, entry 5): colorless oil, 86% yield, 90% ee, $[\alpha]_D^{20} = +4.6$ ($c = 1.0$);

FTIR (KBr, neat): ν 1737 (C=O);

^1H NMR (300 MHz, CDCl_3): δ 7.16-7.28 (m, 5H), 3.66 (s, 3H), 2.61 (t, $J = 8.2$ Hz, 2H), 2.29 (d, $J = 6.8$ Hz, 2H), 1.86 (m, 1H), 1.61 (m, 2H), 1.39 (m, 2H), 0.88 (t, $J = 6.8$ Hz, 3H);

^{13}C NMR (75.4 MHz, CDCl_3): δ 173.8 (C), 142.5 (C), 128.3 (CH), 125.7 (CH), 51.4 (CH_3), 38.9 (CH_2), 35.8 (CH_2), 34.9 (CH), 33.7 (CH_2), 33.0 (CH_2), 32.0 (CH_2), 26.1 (CH_2), 22.6 (CH_2), 14.0 (CH_3);

HRMS calcd. For $\text{C}_{17}\text{H}_{26}\text{O}_2$ 262.1933, found 262.1961;

The enantiomeric excess was determined by HPLC analysis employing a Daicel Chiracel ODH column (Hexane : *i*-propanol 99.2 : 0.8, 1 mL/min): $t_1 = 5.42$ min (minor) , $t_2 = 6.34$ min (major).

(+)-Methyl 3-phenethylpentanoate, $R_f = 0.71$ (EA/Hexane = 1/4);

(Table 2, entry 6): colorless oil, 89% yield, 92% ee, $[\alpha]_D^{24} = +3.7$ ($c = 2.2$);

FTIR (KBr, neat): ν 1737 (C=O);

^1H NMR (300 MHz, CDCl_3): δ 7.18-7.32 (m, 5H), 3.68 (s, 3H), 2.63 (t, $J = 8.2$ Hz, 2H), 2.33 (d, $J = 6.8$ Hz, 2H), 1.93-1.95 (m, 1H), 1.60-1.69 (m, 2H), 1.29 (m, 12H), 0.91 (t, $J = 6.9$ Hz, 3H);

^{13}C NMR (75.4 MHz, CDCl_3): δ 173.8 (C), 142.5 (C), 128.3 (CH), 125.7 (CH), 51.4 (CH_3), 38.9 (CH_2), 35.8 (CH_2), 34.9 (CH), 33.8 (CH_2), 33.0 (CH_2), 31.9 (CH_2), 29.8 (CH_2), 29.3 (CH_2), 26.5 (CH_2), 22.7 (CH_2), 14.1 (CH_3);

HRMS calcd. For $\text{C}_{19}\text{H}_{30}\text{O}_2$ 290.2246, found 290.2240;

The enantiomeric excess was determined by HPLC analysis employing a Daicel Chiracel ODH column (Hexane : *i*-propanol 99.2 : 0.8, 1 mL/min): $t_1 = 5.39$ min (minor) , $t_2 = 6.12$ (major).

(+)-Methyl 3-phenethylhept-6-enoate

(Table 1, entry 7): colorless oil, 90% yield, 94% ee, $[\alpha]_D^{20} = +7.9$ ($c = 0.9$);

FTIR (KBr, neat): ν 1737(C=O);

^1H NMR (300 MHz, CDCl_3): δ 7.14-7.29 (m, 5H), 5.74-5.83 (m, 1H), 4.92-5.03 (m, 2H), 3.65 (s, 3H), 2.60 (t, $J = 8.2$ Hz, 2H), 2.34 (d, $J = 6.8$ Hz, 2H), 2.06 (dd, $J = 14.4$ and 7.8 Hz, 1H), 1.91-2.00 (m, 1H), 1.60-1.67 (m, 2H), 1.40-1.50 (dt, $J = 14.8$ and 7.1 Hz, 2H);

^{13}C NMR (75.4 MHz, CDCl_3): δ 173.6 (C), 142.4 (C), 138.5 (CH), 128.3 (CH), 128.3 (CH), 125.8(CH), 114.6(CH₂), 51.5 (CH₃), 38.7 (CH₂), 35.7 (CH₂), 34.4 (CH), 33.0 (CH₂), 33.0 (CH₂), 30.8 (CH₂);

HRMS calcd. For $\text{C}_{16}\text{H}_{22}\text{O}_2$ 246.1620, found 246.1615;

The enantiomeric excess was determined by chiral HPLC analysis, Chiralcel OJ (Hexane : *i*-propanol 99.7 : 0.3, 1 mL/min): $t_1 = 36.88$ min (minor), $t_2 = 39.02$ (major).

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	37.212	MM	1.7513	1.15063e4	109.50121	49.7854
2	40.631	MM	2.2132	1.16055e4	87.39587	50.2146

Totals : 2.31118e4 196.89709

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	36.880	MM	1.1507	2015.00085	29.18636	2.8347
2	39.020	MM	3.4062	6.90684e4	337.95486	97.1653

Totals : 7.10834e4 367.14123

(-)-Methyl 5-methyl-3-phenethylhexanoate

(Table 2, entry 8): colorless oil, 91% yield, 86% ee, $[\alpha]_D^{20} = +7.0$ ($c = 1.0$);

FTIR (KBr, neat): ν 1737 (C=O);

^1H NMR (300 MHz, CDCl_3): δ 7.16-7.30 (m, 5H), 3.65 (s, 3H), 2.60 (t, $J = 8.2$ Hz, 1H), 2.31 (d, $J = 6.6$ Hz, 2H), 1.95-2.04 (m, 1H), 1.57-1.68 (m, 3H), 1.12-1.30 (m, 2H), 0.88 (d, $J = 6.6$ Hz, 6H);

^{13}C NMR (75.4 MHz, CDCl_3): δ 173.8 (C), 142.5 (C), 128.3 (CH), 125.7 (CH), 51.4 (CH_3), 43.6 (CH_2), 39.1 (CH_2), 36.1 (CH_2), 32.8 (CH_2), 32.7 (CH), 25.3 (CH), 22.8 (CH_3), 22.7 (CH_3);

HRMS calcd. For $\text{C}_{16}\text{H}_{24}\text{O}_2$ 248.1776, found 248.1760;

The enantiomeric excess was determined by chiral HPLC analysis, Chiralcel OJ (Hexane : *i*-propanol 99.5 : 0.5, 1 mL/min): $t_1 = 13.86$ min (minor), $t_2 = 16.60$ (major).

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

(Table 2, entry 9): colorless oil, 20% yield, 99% ee, $[\alpha]_D^{20} = +7.5$ ($c = 1.7$);

FTIR (KBr, neat): ν 1737 (C=O);

^1H NMR (300 MHz, CDCl_3): δ 7.18–7.30 (m, 3H), 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), 1.97 (m, 1H), 1.72–1.45 (m, 2H), 1.01 (d, $J = 6.6$ Hz, 3H);

^{13}C NMR (75.4 MHz, CDCl_3): δ 173.5 (C), 142.3 (C), 128.3 (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 calcd. For $\text{C}_{13}\text{H}_{18}\text{O}_2$ 206.1307, found 206.1292;

The enantiomeric excess was determined by chiral HPLC analysis, Chiralcel OD-H (Hexane : *i*-propanol 99.2 : 0.8, 1 mL/min): $t_1 = 6.80$ min (minor), $t_2 = 7.58$ (major).

(S)-(+)-Ethyl 3-methylpentanoate

(Table 3, entry 1): colorless oil, 83% yield, 74% ee, $[\alpha]_D^{25} = +7.2$ ($c = 0.6$), lit.² for (S); enantiomer $[\alpha]_D^{25} = +10.0$ ($c = 0.6$);

FTIR (KBr, neat): ν 1732 (C=O);

^1H NMR (300 MHz, CDCl_3): δ 4.09 (q, $J = 7.1$ Hz, 2H), 2.26 (dd, $J = 14.6$ and 6.1 Hz, 1H), 2.05 (dd, $J = 14.6$ and 8.1 Hz, 1H), 1.79-1.90 (m, 1H), 1.29-1.38 (m, 2H), 1.22 (t, $J = 7.1$ Hz, 3H), 0.83-0.90 (m, 6H);

^{13}C NMR (75.4 MHz, CDCl_3): δ 173.4, 60.0, 41.5, 31.9, 29.3, 19.2, 14.2, 11.2;

HRMS calcd. For $\text{C}_8\text{H}_{16}\text{O}_2$ 144.1150, found 144.1155;

The enantiomeric excess determined by chiral GC analysis, Chiraldex G-TA column (30 m x 0.25 mm), 60°C, retention times (min): $t_1 = 16.29$ min (minor) , $t_2 = 18.25$ min (major).

(S)-(-)-Methyl 3-ethylhexanoate

(Table 3, entry 2): colorless oil, 85% yield, 87% ee, $[\alpha]_D^{25} = -2.6$ ($c = 1.3$), lit.³ for (S) enantiomer: $[\alpha]_D^{25} = -2.1$;

FTIR (KBr, neat): ν 1732 (C=O);

¹H NMR (400 MHz, CDCl₃): δ 3.64 (s, 3H), 2.22 (d, $J = 7.2$ Hz, 2H), 1.76-1.83 (m, 1H), 1.20-1.41 (m, 6H), 0.80-0.95 (m, 6H);

¹³C NMR (100.0 MHz, CDCl₃): δ 174.1 (C), 51.3 (CH₃), 38.6 (CH₂), 36.2 (CH), 35.7 (CH₂), 26.3 (CH₂), 19.7 (CH₂), 14.3 (CH₃), 10.7 (CH₃);

HRMS calcd. For C₉H₁₈O₂ 158.1307, found 158.1301;

The enantiomeric excess was determined by chiral GC analysis, Chiraldex G-TA column (30 m x 0.25 mm), 60°C, retention times (min): $t_1 = 34.67$ min (major), $t_2 = 36.30$ (minor).

3. Schuppan, J.; Minnaard, A. J.; Feringa, B. L. *Chem. Commun.* **2004**, 7, 792-793.

(R)-(-)-Methyl 3-ethyl-4-methylpentanoate

(Table 3, entry 3): colorless oil, 90% yield, 95% ee, colorless oil, $[\alpha]_D^{25} = -3.8$ ($c = 1.4$), lit.² for (*S*) enantiomer: $[\alpha]_D^{25} = +4.4$.

FTIR (KBr, neat): ν 1732 (C=O);

^1H NMR (300 MHz, CDCl_3): δ 3.66 (s, 3H), 2.28 (dd, $J = 15.1$ and 5.9 Hz, 1H), 2.15 (dd, $J = 15.1$ and 7.4 Hz, 1H), 1.66-1.78 (m, 2H), 1.17-1.44 (m, 2H), 0.80-0.90 (m, 9H);

^{13}C NMR (75.4 MHz, CDCl_3): δ 174.7, 51.4, 42.5, 35.6, 29.4, 23.7, 19.4, 18.5, 11.7.

HRMS calcd. For $\text{C}_9\text{H}_{18}\text{O}_2$ 158.1307, found 158.1301;

The enantiomeric excess determined by chiral GC analysis, Chiraldex G-TA column (30 m x 0.25 mm), 60°C, retention times (min): $t_1 = 31.80$ min (major), $t_2 = 33.87$ (minor).

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	31.981	MM	0.5169	11.56110	3.72756e-1	49.99784
2	33.875	MM	0.5530	11.56210	3.48463e-1	50.00216

Totals : 23.12320 7.21219e-1

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	31.797	MM	0.5710	1212.80188	35.39690	97.34052
2	33.872	MM	0.5475	33.13549	1.00877	2.65948

Totals : 1245.93737 36.40567

(S)-(+)-Methyl 3-ethyl-4-methylpentanoate

colorless oil, 75% yield, 56% ee, colorless oil, $[\alpha]_D^{25} = +3.9$ ($c = 1.8$), lit. for (*S*)² enantiomer: $[\alpha]_D^{25} = +4.4$.

The enantiomeric excess determined by chiral GC analysis, Chiraldex G-TA column (30 m x 0.25 mm), 60°C, retention times (min): $t_1 = 31.69$ min (major) , $t_2 = 33.32$ (minor).

(-)-Methyl 3-hydroxy-2,2-dimethyl-5-phenylpentanoate $R_f = 0.70$ (EA/Hexane = 1/4)

(Table 3, entry 7): colorless oil, 85% yield, 94% ee, colorless oil, $[\alpha]_D^{25} = -5.9$ ($c = 1.6$).

FTIR (KBr, neat): ν 1735 (C=O);

^1H NMR (400 MHz, CDCl_3): δ 7.17-7.30 (m, 5H), 3.63 (s, 3H, OCH_3), 2.67 (dd, $J = 13.6$ and 6.8 Hz, 1H), 2.54 (dd, $J = 13.5$ and 5.5 Hz), 2.14-2.17 (m, 2H), 2.10-2.12 (m, 1H), 1.22-1.42 (m, 2H), 0.95 (t, $J = 6.8$ Hz, 3H);

^{13}C NMR (100.0 MHz, CDCl_3): δ 173.8 (C), 140.1 (C), 129.3 (CH), 128.3 (CH), 126.0 (CH), 51.4 (CH_3), 40.0 (CH_2), 38.5 (CH), 37.9 (CH_2), 26.2 (CH_2), 11.0 (CH_3);

HRMS calcd. For $\text{C}_{13}\text{H}_{18}\text{O}_2$ 206.1307, found 158.1296;

The enantiomeric excess was determined by HPLC analysis employing a Daicel Chiracel ODH column (Hexane : *i*-propanol 99.2 : 0.8, 1 mL/min): $t_1 = 6.23\text{min}$ (minor) , $t_2 = 7.79$ (major).

(-)-Methyl 3-((benzyloxy)methyl)pentanoate

(Table 3, entry 8): colorless oil, 83% yield, 73% ee, $[\alpha]_D^{25} = -6.0$ ($c = 1.0$);

FTIR (KBr, neat): ν 1732 (C=O);

^1H NMR (300 MHz, CDCl_3): δ 7.32 (m, 5H), 4.49 (s, 2H), 3.63 (s, 3H), 3.45 (dd, $J = 9.3$ and 5.0 Hz, 1H), 3.35 (dd, $J = 9.2$ and 6.7 Hz, 1H), 2.43 (dd, $J = 15.4$ and 7.3 Hz, 1H), 2.30 (dd, $J = 15.3$ and 6.3 Hz, 1H), 2.08-2.14 (m, 1H), 1.23-1.48 (m, 2H), 0.90 (t, $J = 7.5$ Hz, 3H);

^{13}C NMR (75.4 MHz, CDCl_3): δ 173.8 (C), 138.6 (C), 128.3 (CH), 127.5 (CH), 127.4 (CH), 73.0 (CH_2), 72.5 (CH_2), 51.4 (CH_3), 37.3 (CH), 36.5 (CH_2), 24.2 (CH_2), 11.2 (CH_3);

HRMS calcd. For $\text{C}_{14}\text{H}_{20}\text{O}_3$ 236.1412, found 236.1398;

The enantiomeric excess was determined by HPLC analysis employing a Daicel Chiracel ODH column (Hexane : *i*-propanol 99.2 : 0.8, 1 mL/min): $t_1 = 7.65$ min (minor) , $t_2 = 8.21$ (major).

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.575	MM	0.1832	117.32305	10.67636	48.9933
2	8.130	MM	0.1971	122.14453	10.32942	51.0067
Totals :				239.46758	21.00578

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.651	MM	0.1548	1.00751	1.08453e-1	14.1781
2	8.214	MM	0.2029	6.09858	5.00834e-1	85.8219
Totals :				7.10609	6.09287e-1

The enantiomeric excess was determined by HPLC analysis employing a Daicel Chiracel ODH column (Hexane : *i*-propanol 99.2 : 0.8, 1 mL/min): t₁ = 7.95 min (major) , t₂ = 8.49 (minor).

(S)-(+)-Methyl 3-phenylpentanoate

(Table 3, entry 10): 90% yield, 93% ee, colorless oil, $[\alpha]_D^{25} = +15.5$ ($c = 0.4$), lit.² for : (S) enantiomer: $[\alpha]_D^{25} = +18.7$.

FTIR (KBr, neat): ν 1737 cm^{-1}

^1H NMR (300 MHz, CDCl_3): δ 7.09-7.22 (m, 5H), 3.51 (s, 3H), 2.88-2.98 (m, 1H), 2.46-2.63 (m, 2H), 1.51-1.68 (m, 2H), 0.75 (t, $J = 7.4$ Hz, 3H);

^{13}C NMR (75.4 MHz, CDCl_3): δ 173.0 (C), 143.9 (C), 128.4 (CH), 127.5 (CH), 126.4 (CH), 51.4 (CH_3), 43.8 (CH), 41.3 (CH_2), 29.1 (CH_2), 11.9 (CH_3);

HRMS calcd. For $\text{C}_{12}\text{H}_{16}\text{O}_2$ 192.1150, found 192.1136;

The enantiomeric excess was determined by chiral GC analysis, Chiraldex G-TA column (30 m x 0.25 mm), 90°C, $t_1 = 72.00$ min (minor), $t_2 = 74.65$ (major).

(R)-(-)-Methyl 3-phenylpentanoate

80% yield, 74% ee, colorless oil, $[\alpha]_D^{25} = +15.5$ ($c = 0.4$)

(+)-Methyl 3-(furan-2-yl)pentanoate

(Table 3, entry 12): colorless oil, 80% yield, 85% ee, $[\alpha]_D^{20} = +14.2$ ($c = 0.4$), lit.² $[\alpha]_D^{20} = +1.7$;

FTIR (KBr, neat): ν 1737 (C=O);

^1H NMR (300 MHz, CDCl_3): δ 7.31 (s, 1H), 6.27 (m, 1H), 6.03 (d, $J = 3.0$ Hz, 1H), 3.64 (s, 3H), 3.12-3.21 (m, 1H), 2.53-2.69 (m, 2H), 1.60-1.72 (m, 2H), 0.83 (t, $J = 7.3$ Hz, 3H);

^{13}C NMR (75.4 MHz, CDCl_3): δ 172.7 (C), 157.08 (C), 141.1 (CH), 109.9 (CH), 105.2 (CH), 51.6 (CH_3), 38.4 (CH_2), 37.0 (CH), 26.7 (CH_2), 11.4 (CH_3);

HRMS calcd. For $\text{C}_{10}\text{H}_{14}\text{O}_3$ 182.0943, found 182.0937;

The enantiomeric excess was determined by chiral GC analysis, Chiraldex GTA column (30 m x 0.25 mm), 90°C, retention times (min): $t_1 = 26.01$ min (minor), $t_2 = 26.96$ (major).

Figure 2 The crystal-structure of Cu dimer complex 1a

Figure 3 The spacefill of Cu dimer complex 1a