ChemInform Abstract: Copper-Catalyzed Regio- and Enantioselective Synthesis of Chiral Enol Acetates and β-Substituted Aldehydes.

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SUPPORTING INFORMATION

Copper-Catalyzed Regio- and Enantioselective Synthesis of Chiral Enol Acetates and β-Substituted Aldehydes.

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General Procedures:

Chromatography: Merck silica gel type 9385 230-400 mesh, TLC: Merck silica gel 60, 0.25 mm. Components were visualized by UV and cerium/molibdenum staining. Progress and conversion of the reaction were determined by GC-MS (GC, HP6890: MS HP5973) with an HP1 or HP5 column (Agilent Technologies, Palo Alto, CA). Mass spectra were recorded on a AEI-MS-902 mass spectrometer (EI+) or a LTQ Orbitrap XL (ESI+). ^{1}H- and ^{13}C-NMR were recorded on a Varian AMX400 (400 and 100.59 MHz, respectively) or a Varian VXR300 (300 and 75 MHz, respectively) using $CDCl_3$ as solvent. Chemical shift values are reported in ppm with the solvent resonance as the internal standard ($CHCl_3$: δ 7.26 for ^{1}H, δ 77.0 for ^{13}C). Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), and integration. Carbon assignments are based on APT ^{13}C-NMR experiments. Optical rotations were measured on a *Schmidt + Haensch* polarimeter (Polartronic MH8) with a 10 cm cell (*c* given in g/100 mL). Enantioselectivities were determined by HPLC analysis using a Shimadzu LC-10AD*VP* HPLC equipped with a Shimadzu SPD-M10A*VP* diode array detector or by capillary GC analysis (HP 6890, Chiraldex G-TA column (30 m x 0.25 mm)) using flame ionization detector.

All reactions were carried out under a nitrogen atmosphere using oven dried glassware and using standard Schlenk techniques. CH_2Cl_2 was dried and distilled over calcium hydride. Acetyl chloride, α,β-unsaturated aldehydes (**1**) and all copper-salts (CuI, CuTC, CuBr·SMe2) were purchased from Aldrich, and used without further purification. Grignard reagents were purchased from Aldrich (MeMgBr, EtMgBr, *n*-HexMgBr, *i*-BuMgBr). Grignard reagents were titrated using *s*-BuOH and catalytic amounts of 1,10-phenanthroline. Phosphoramidite ligands **L1-L3**,[1] **L4-L5**,[2] **L6**[3], **L7**,[4] **L8**,[5] **L9**,[6] **L10**[7] were prepared as reported in the literature.

Racemic products were synthesized by reaction of the α,β-unsaturated aldehydes (**1**) with acetyl chloride and $ZnCl_2$ and the corresponding Grignard reagent at –78°C in CH_2Cl_2 in the presence of CuI (10 mol%) and PPh_3 (12 mol%).

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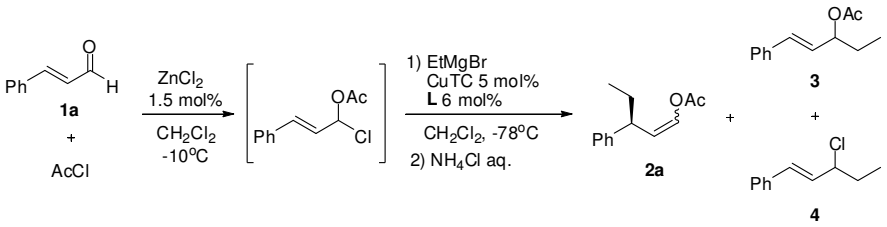
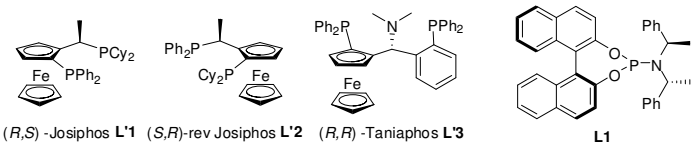
[7] Alexakis, A.; Burton, J.; Vastra, J.; Benhaim, C.; Fournioux, X.; van den Heuvel, A.; Levêque, J.-M.; Mazé, F.; Rosset, S. *Eur. J. Org. Chem.* **2000**, 4011 – 4028.

Table S1. Some copper sources, ligands and conditions tried in the optimization process



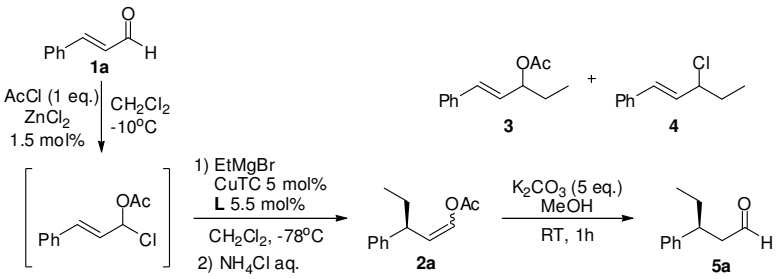
entry[a]	L	**2a** (%)[b]	**3** (%)[b]	**4** (%)[b]	*Z*/*E*	**2a** *ee* (%)[f]
1	**L'1**	12	35	10	1:2	*Z*: rac. *E*: rac.
2	**L'2**	24	32	14	1:2	*Z*: 42 *E*: 25
3	**L'3**	24	26	16	1:3	*Z*: rac. *E*: 4
4	**L1**[c]	57	19	12	4:1	*Z*: 56 *E*: 78
5	**L1**[d]	59	17	13	4:1	*Z*: 53 *E*: 51
6	**L1**[e]	64	14	6	3:1	*Z*: 57 *E*: 56

[a]EtMgBr added dropwise during 5 minutes. [b]Isolated yield. [c]CuTC:**L4** 5:5.5. [d]CuTC:**L4** 5:7.5. [e]CuTC:**L4** 5:10.[f]Determined by HPLC analysis.



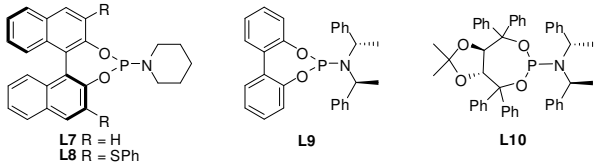
(*R*,*S*) -Josiphos **L'1** (*S*,*R*)-rev Josiphos **L'2** (*R*,*R*) -Taniaphos **L'3** **L1**

Table S2. Screening of different phosphoramidites.[a]



entry	L	**2a** (%)[b]	**3** (%)[b]	**4** (%)[b]	*Z*/*E*[c]	**2a** *ee* (%)[d]	**5a** *ee* (%)[e]
1	**L7**	73	4	3	1.5:1	*Z*: 54 *E*: 55	55
2	**L8**	78	9	2	3:1	*Z*: -59 *E*: -75	-64[f]
3	**L9**	52	10	7	4.5:1	*Z*: 38 *E*: 77	45
4	**L10**	53	12	-	3:1	*Z*: -6 *E*: -2	-5[f]

[a]Reactions run on a 0.5 mmol scale adding 1.2 eq. of EtMgBr diluted with CH_2Cl_2 (0.7 mL) over 1h. [b]Isolated yield. [c]Determined from the ^{1}H NMR spectrum. [d]Determined by chiral HPLC. [e]Determined by chiral GC. [f]Negative *ee* value indicates that the opposite enantiomer was formed.



L7 R = H
L8 R = SPh
L9
L10

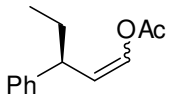
General procedure for the synthesis of enol acetates 2 and transformation to the β-substituted aldehydes 5.

Copper thiophene carboxylate (CuTC) (0.025 mmol, 4.75 mg) and ligand **L1** (0.0275 mmol, 14.84 mg) were charged in a Schlenk tube equipped with septum and stirring bar. CH_2Cl_2 (2 mL) was added and the solution was stirred under nitrogen at room temperature for 30 min. In the meantime, the corresponding α,β-unsaturated aldehyde (0.5 mmol) was added dropwise to a solution of acetyl chloride (0.5 mmol, 38 μL) and freshly fused $ZnCl_2$ (0.0075 mmol, 1 mg) in CH_2Cl_2 (1 mL) at -10°C. Then, the resulting solution was added to the catalyst solution which was previously cooled to -78°C. After 5 min. at this temperature the corresponding Grignard reagent (solution in Et_2O, 0.6 mmol) was diluted with CH_2Cl_2 (0.7 mL) and was added dropwise over 6 hours using a syringe pump. Once the addition was complete, the mixture was stirred other four hours at -78°C. The reaction was quenched with aqueous saturated NH_4Cl (2 mL) and the mixture was warmed up to room temperature. The mixture was diluted with Et_2O and the layers were separated. The aqueous layer was extracted with Et_2O (3 x 5 mL) and the combined organic layers were dried with anhydrous Na_2SO_4, filtered and the solvent was evaporated *in vacuo*. At this point GC analysis was carried out to determine the b:l ratio. The crude product was purified by flash chromatography on silica gel using different mixtures of Pentane:Et_2O as eluents.

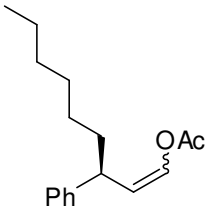
Hydrolysis of the enol acetate was then performed using the following procedure: enol acetate **2** was dissolved in MeOH (10 mL) and K_2CO_3 (5 eq.) was added. The mixture was stirred at room temperature during one hour. Then the solvent was removed *in vacuo*, water (5 mL) was added and the mixture was extracted with Et_2O (3 x 5 mL). The combined organic layers were dried with anhydrous Na_2SO_4, filtered and the solvent was evaporated *in vacuo* to afford the corresponding aldehyde **5**.

One-pot process for the synthesis of β-substituted aldehydes 5.

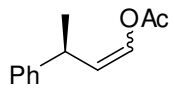
After the reaction was complete, it was quenched with MeOH (5 mL) and was warmed up to room temperature. Then K_2CO_3 (5 eq.) was added and the mixture was stirred for one hour. Same work-up gave rise to the aldehyde **5**.



(*S*)-3-phenylpent-1-enyl acetate (2a): Colorless oil obtained as a 13:1 mixture of *Z* (major) and *E* (minor) isomers in 89% yield after column chromatography using a mixture of Pentane:Et_2O 40:1 as eluent. For the *Z* isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.29 (m, 2H), 7.26-7.19 (m, 3H), 7.11 (d, *J* = 6.4, 1H), 5.04 (dd, *J* = 9.8, 6.4, 1H), 3.73 (q, *J* = 8.3, 1H), 2.16 (s, 3H), 1.82-1.65 (m, 2H), 0.90 (t, *J* = 7.3, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 144.8, 133.9, 128.7, 127.5, 126.4, 117.7, 43.0, 29.6, 21.0, 12.3. HRMS (ESI+, *m/z*): calcd for $C_{13}H_{16}O_2Na$ $[M+Na]^+$: 227.10425; found: 227.10400.
Ee was determined by chiral HPLC analysis, Chiralpak OJ-H column, Heptane/*i*-PrOH 95:5, retention times: 12.6 (*Z*, minor enantiomer), 14.0 (*E*, major enantiomer), 16.4 (*E*, minor enantiomer), and 20.4 (*Z*, major enantiomer) min. [*Z* isomer: 91% ee; *E* isomer: 92% ee].

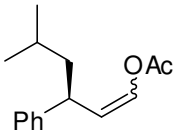


(*S*)-3-phenylnon-1-enyl acetate (2b): Colorless oil obtained as a 10:1 mixture of *Z* (major) and *E* (minor) isomers in 88% yield after column chromatography using a mixture of Pentane:Et_2O 50:1 as eluent. For the *Z* isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.29 (m, 2H), 7.25-7.19 (m, 3H), 7.10 (d, *J* = 6.4, 1H), 5.04 (dd, *J* = 9.8, 6.4, 1H), 3.73 (q, *J* = 8.2, 1H), 2.16 (s, 3H), 1.79-1.61 (m, 2H), 1.37-1.19 (m, 8H), 0.89 (t, *J* = 6.6, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 145.0, 133.7, 128.7, 127.5, 126.4, 118.0, 41.2, 36.7, 32.0, 29.4, 27.6, 22.9, 21.0, 14.3. HRMS (ESI+, *m/z*): calcd for $C_{17}H_{24}O_2Na$ $[M+Na]^+$: 283.16685; found: 283.16528.
Ee was determined by transformation into the aldehyde **5b** following the general procedure (94% *ee*, *vide infra*).



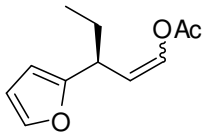
(*S*)-3-phenylbut-1-enyl acetate (2c): Colorless oil obtained as a 7:1 mixture of *Z* (major) and *E* (minor) isomers in 66% yield after column chromatography using a mixture of Pentane:Et_2O 40:1 as eluent. For the *Z* isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.22 (m, 5H), 7.07 (d, *J* = 6.3, 1H), 5.06 (dd, *J* = 9.5, 6.3, 1H), 4.03 (quint, *J* = 7.6, 1H), 2.17 (s, 3H), 1.39 (d, *J* = 7.2, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 145.8, 133.1, 128.7, 127.0, 126.4, 119.1, 35.2, 22.0, 21.0. HRMS (ESI+, *m/z*): calcd for $C_{12}H_{14}O_2Na$ $[M+Na]^+$: 213.08860; found: 213.08682.

Ee was determined by chiral HPLC analysis, Chiralpak OJ-H column, Heptane/*i*-PrOH 95:5, retention times: 13.5 (*Z*, minor enantiomer), 15.2 (*E*, minor enantiomer), 17.4 (*Z*, major enantiomer), and 19.8 (*E*, major enantiomer) min. [*Z* isomer: 83% ee; *E* isomer: 4% ee].



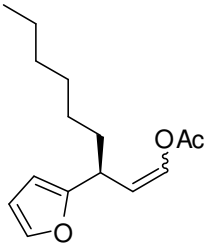
(*S*)-5-methyl-3-phenylhex-1-enyl acetate (2d): Colorless oil obtained as a 12:1 mixture of *Z* (major) and *E* (minor) isomers in 85% yield after column chromatography using a mixture of Pentane:Et_2O 50:1 as eluent. For the *Z* isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.30 (m, 2H), 7.26-7.19 (m, 3H), 7.09 (d, *J* = 6.4, 1H), 5.02 (dd, *J* = 9.8, 6.4, 1H), 3.94 (q, *J* = 7.9, 1H), 2.17 (s, 3H), 1.63-1.49 (m, 3H), 0.95 (d, *J* = 6.5, 3H), 0.93 (d, *J* = 6.6, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 145.1, 133.7, 128.7, 127.5, 126.4, 118.1, 46.1, 39.1, 25.9, 23.2, 22.4, 21.0. HRMS (ESI+, *m/z*): calcd for $C_{15}H_{20}O_2Na$ $[M+Na]^+$: 255.1356; found: 255.1353.

Ee was determined by chiral HPLC analysis, Chiralpak OJ-H column, Heptane/*i*-PrOH 99:1, retention times: 12.5 (*Z*, minor enantiomer), 14.5 (*E*, minor enantiomer), 16.2 (*Z*, major enantiomer), and 18.3 (*E*, major enantiomer) min. [*Z* isomer: 49% ee; *E* isomer: 45% ee].



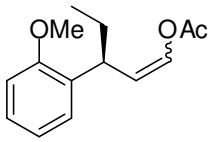
(*S*)-3-(furan-2-yl)pent-1-enyl acetate (2e): In this case the corresponding chloroacetate was formed at -78°C during 5 minutes. Colorless oil obtained as a 18:1 mixture of *Z* (major) and *E* (minor) isomers in 75% yield after column chromatography using a mixture of Pentane:Et_2O 40:1 as eluent. For the *Z* isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (br s, 1H), 7.16 (d, *J* = 6.4, 1H), 6.29 (br s, 1H), 6.02 (br s, 1H), 4.96 (dd, *J* = 9.7, 6.4, 1H), 3.85 (q, *J* = 8.1, 1H), 2.16 (s, 3H), 1.91-1.81 (m, 1H), 1.66- 1.55 (m, 1H), 0.90 (t, *J* = 7.5, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 157.3, 146.9, 134.8, 114.4, 110.2, 104.7, 36.6, 27.2, 21.0, 11.7. HRMS (ESI+, *m/z*): calcd for $C_{11}H_{14}O_3Na$ $[M+Na]^+$: 217.0835; found: 217.0828.

Ee was determined by transformation into the aldehyde **5e** following the general procedure (90% *ee*, *vide infra*).



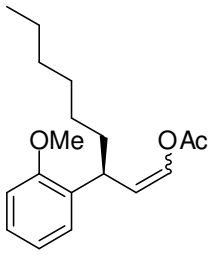
(*S*)-3-(furan-2-yl)non-1-enyl acetate (2f): In this case the corresponding chloroacetate was formed at -78°C during 5 minutes. Colorless oil obtained as a 17:1 mixture of *Z* (major) and *E* (minor) isomers in 69% yield after column chromatography using a mixture of Pentane:Et_2O 40:1 as eluent. For the *Z* isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (br s, 1H), 7.14 (d, *J* = 6.4, 1H), 6.28 (br s, 1H), 6.01 (br s, 1H), 4.96 (dd, *J* = 9.9, 6.4, 1H), 3.85 (q, *J* = 8.1, 1H), 2.15 (s, 3H), 1.85-1.75 (m, 1H), 1.60- 1.52 (m, 1H), 1.33-1.21 (m, 8H), 0.88 (t, *J* = 6.9, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 157.5, 141.2, 134.6, 114.7, 110.2, 104.5, 34.9, 34.1, 31.9, 29.3, 27.1, 22.9, 21.0, 14.3. HRMS (ESI+, *m/z*): calcd for $C_{15}H_{22}O_3Na$ $[M+Na]^+$: 273.1461; found: 273.1454.

Ee was determined by transformation into the aldehyde **5f** following the general procedure (90% *ee*, *vide infra*).



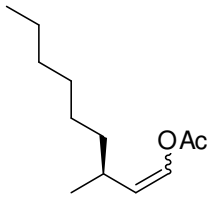
(*S*)-3-(2-methoxyphenyl)pent-1-enyl acetate (2g): In this case the corresponding chloroacetate was formed at -78°C during 5 minutes. Colorless oil obtained as a 16:1 mixture of *Z* (major) and *E* (minor) isomers in 77% yield after column chromatography using a mixture of Pentane:Et_2O 30:1 as eluent. For the *Z* isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20-7.17 (m, 2H), 7.06 (d, *J* = 6.4, 1H), 6.92 (t, *J* = 7.4, 1H), 6.87 (d, *J* = 8.3, 1H), 5.15 (dd, *J* = 9.8, 6.4, 1H), 4.09 (q, *J* = 8.2, 1H), 3.83 (s, 3H), 2.14 (s, 3H), 1.80-1.62 (m, 2H), 0.88 (t, *J* = 7.4, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 157.3, 133.8, 133.0, 128.2, 127.3, 120.8, 117.4, 111.0, 55.6, 37.1, 28.5, 21.0, 12.4. HRMS (ESI+, *m/z*): calcd for $C_{14}H_{18}O_3Na$ $[M+Na]^+$: 257.11482; found: 257.11298.

Ee was determined by transformation into the aldehyde **5g** following the general procedure (91% *ee*, *vide infra*).

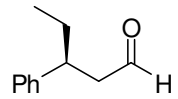


(*S*)-3-(2-methoxyphenyl)non-1-enyl acetate (2h): In this case the corresponding chloroacetate was formed at -78°C during 5 minutes. Colorless oil obtained as a 20:1 mixture of *Z* (major) and *E* (minor) isomers in 81% yield after column chromatography using a mixture of Pentane:Et_2O 50:1 as eluent. For the *Z* isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19-7.16 (m, 2H), 7.03 (d, *J* = 6.4, 1H), 6.91 (t, *J* = 7.4, 1H), 6.86 (d, *J* = 8.5, 1H), 5.14 (dd, *J* = 9.7, 6.4, 1H), 4.17 (q, *J* = 8.2, 1H), 3.83 (s, 3H), 2.14 (s, 3H), 1.76-1.54 (m, 2H), 1.34-1.21 (m, 8H), 0.88 (t, *J* = 6.6, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 157.2, 133.6, 133.3, 128.1, 127.2, 120.8, 117.7, 111.1, 55.7, 35.6, 35.3, 32.0, 29.4, 27.7, 22.9, 21.0, 14.3. HRMS (ESI+, *m/z*): calcd for $C_{18}H_{26}O_3Na$ $[M+Na]^+$: 313.17742; found: 313.17734 .

Ee was determined by transformation into the aldehyde **5h** following the general procedure (93% *ee*, *vide infra*).

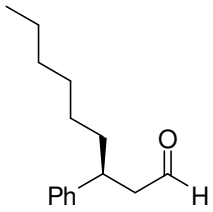


(*S*)-3-methylnon-1-enyl acetate (2i): Colorless oil obtained as a 2:1 mixture of *Z* (major) and *E* (minor) isomers in 86% yield after column chromatography using a mixture of Pentane:Et_2O 80:1 as eluent. For the *Z* isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96 (d, *J* = 6.4, 1H), 4.65 (dd, *J* = 9.6, 6.4, 1H), 2.68-2.60 (m, 1H), 2.12 (s, 3H), 1.30-1.20 (m, 10H), 0.96 (d, *J* = 6.6, 3H), 0.87 (t, *J* = 6.7, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 133.1, 120.6, 37.4, 32.7, 32.1, 29.6, 27.5, 22.9, 21.2, 21.0, 14.3. For the *E* isomer: ^{1}H NMR (400 MHz, $CDCL_3$) δ 7.05 (d, *J* = 12.5, 1H), 5.28 (dd, *J* = 12.5, 8.7, 1H), 2.15-2.07 (m, 1H), 2.09 (s, 3H), 1.30-1.20 (m, 10H), 0.99 (d, *J* = 6.7, 3H), 0.87 (t, *J* = 6.7, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.5, 134.6, 121.0, 37.4, 32.0, 29.7, 29.5, 27.4, 22.9, 21.2, 21.0, 14.3. HRMS (ESI+, *m/z*): calcd for $C_{12}H_{22}O_2Na$ $[M+Na]^+$: 221.15120; found: 221.15100. *Ee* was determined by transformation into the aldehyde **5i** following the general procedure (92% *ee*, *vide infra*).

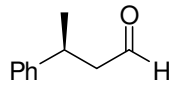


(*S*)-3-phenylpentanal (5a): Colorless oil obtained in 89% yield; 92% *ee*. The physical data were identical in all respects to those previously reported.[8] *Ee* was determined by chiral GC analysis, Chiraldex G-TA column (30 m x 0.25 mm), (90°C isotherm), retention times: 40.4 (major enantiomer) and 41.9 min. $[\alpha]_D^{20}$ = +11.5 (*c* = 1.0, $CHCl_3$).

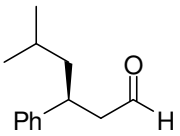
[8] Bräse, S.; Höfener, S. *Angew. Chem., Int. Ed.* **2005**, *44*, 7879-7881.



(*S*)-3-phenylnonanal (5b): Colorless oil obtained in 88% yield; 94% *ee*. The physical data were identical in all respects to those previously reported for the racemic compound.[9] *Ee* was determined by chiral GC analysis, Chiraldex G-TA column (30 m x 0.25 mm), (110°C isotherm), retention times: 46.9 (major enantiomer) and 47.2 min. $[\alpha]_D^{20}$ = +10.8 (*c* = 1.0, $CHCl_3$).



(*S*)-3-phenylbutanal (5c): Colorless oil obtained in 66% yield; 72% *ee*. The physical data were identical in all respects to those previously reported.[10] *Ee* was determined by chiral GC analysis, Chiraldex G-TA column (30 m x 0.25 mm), (110°C isotherm), retention times: 46.9 (major enantiomer) and 47.2 min. $[\alpha]_D^{20}$ = +18.4 (*c* = 0.25, $CHCl_3$).



(*S*)-5-methyl-3-phenylhexanal (5d): Colorless oil obtained in 80% yield; 48% *ee*. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.65 (t, *J* = 2.1, 1H), 7.33-7.29 (m, 2H), 7.23-7.18 (m, 3H), 3.33-3.25 (m, 1H), 2.71 (ddd, *J* = 16.5, 7.7, 2.1, 1H), 2.65 (ddd, *J* = 16.5, 6.8, 2.2, 1H), 1.63 (ddd, *J* = 13.1, 10.1, 4.6, 1H), 1.47- 1.32 (m, 2H), 0.91 (d, *J* = 6.3, 3H), 0.85 (d, *J* = 6.5, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.0, 143.9, 128.6, 127.5, 126.5, 51.1, 45.8, 37.9, 25.2, 23.3, 21.7. HRMS (ESI+, *m/z*): calcd for $C_{13}H_{18}ONa$ $[M+Na]^+$: 213.1250; found: 213.1243.

Ee was determined by chiral GC analysis, Chiraldex G-TA column (30 m x 0.25 mm), (90°C isotherm), retention times: 45.5 (major enantiomer) and 45.9 min. $[\alpha]_D^{20}$ = +5.4 (*c* = 1.0, $CHCl_3$).

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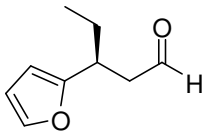
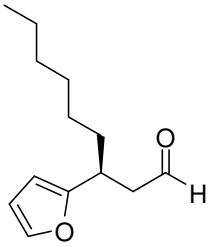
[9] Marshall, J. A.; Herold, M.; Eidam, H. S.; Eidam, P. *Org. Lett.* **2006**, *8*, 5505-5508.
[10] Bull, S. D.; Davies, S. G.; Nicholson, R. L.; Sanganee H. J.; Smith.; A. D. *Org. Biomol. Chem.* **2003***, 1,* 2886 - 2899.



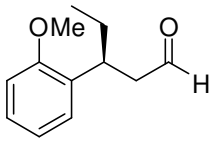
(*S*)-3-(furan-2-yl)pentanal (5e): Pale yellow oil obtained in 68% yield; 90% *ee*. ^{1}H NMR (400 MHz, $CDCl_3$) δ ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.71 (t, *J* = 1.6, 1H), 7.30 (br s, 1H), 6.26 (br s, 1H), 6.02 (d, *J* = 1.9, 1H), 3.22 (quint., *J* = 7.1, 1H), 2.74 (ddd, *J* = 16.6, 7.7, 1.8, 1H), 2.63 (ddd, *J* = 16.6, 6.4, 1.3, 1H), 1.73-1.62 (m, 2H), 0.86 (t, *J* = 7.3, 3H). HRMS (ESI+, *m/z*): calcd for $C_9H_{13}O_2$ $[M+H]^+$: 153.09101; found: 153.08955.

Ee was determined by chiral GC analysis, Chiraldex G-TA column (30 m x 0.25 mm), (90°C isotherm), retention times: 13.8 (major enantiomer) and 14.9 min. $[\alpha]_D^{20}$ = +30.4 (*c* = 0.5, $CHCl_3$).

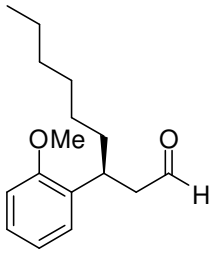


(*S*)-3-(furan-2-yl)nonanal (5f): Pale yellow oil obtained in 63% yield; 90% *ee*. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.71 (t, *J* = 2.0, 1H), 7.31 (d, *J* = 1.0, 1H), 6.27 (dd, *J* = 3.1, 1.8, 1H), 6.02 (d, *J* = 3.1, 1H), 3.33- 3.24 (m, 1H), 2.74 (ddd, *J* = 16.7, 7.8, 2.1, 1H), 2.64 (ddd, *J* = 16.7, 6.3, 1.9, 1H), 1.73-1.54 (m, 2H), 1.35-1.15 (m, 8H), 0.86 (t, *J* = 6.8, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.2, 154.9, 141.4, 109.8, 105.3, 47.7, 39.1, 33.5, 31.7, 29.1, 27.2, 22.6, 14.0. HRMS (ESI+, *m/z*): calcd for $C_{13}H_{21}O_2$ $[M+H]^+$: 209.15361; found: 209.15322.

Ee was determined by chiral GC analysis, Chiraldex G-TA column (30 m x 0.25 mm), (110°C isotherm), retention times: 32.7 (major enantiomer) and 34.4 min. $[\alpha]_D^{20}$ = +4.8 (*c* = 0.92, $CHCl_3$).

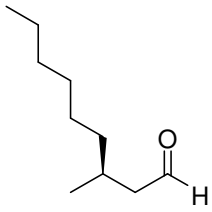


(*S*)-3-(2-methoxyphenyl)pentanal (5g): Colorless oil obtained in 77% yield; 91% *ee*. The physical data were identical in all respects to those previously reported.[8] *Ee* was determined by chiral GC analysis, Chiraldex G-TA column (30 m x 0.25 mm), (110°C isotherm), retention times: 33.4 (major enantiomer) and 34.7 min. $[\alpha]_D^{20}$ = -19.3 (*c* = 2.7, $CHCl_3$).



(*S*)-3-(2-methoxyphenyl)nonanal (5h): Colorless oil obtained in 79% yield; 93% *ee*. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (t, *J* = 2.0, 1H), 7.19 (t, *J* = 7.7, 1H), 7.14 (d, *J* = 7.4, 1H), 6.92 (t, *J* = 7.4, 1H), 6.86 (d, *J* = 8.1, 1H), 3.81 (s, 3H), 3.66-3.57 (m, 1H), 6.86 (dd, *J* = 7.1, 2.0, 2H), 1.76-1.52 (m, 2H), 1.35-1.10 (m, 8H), 0.85 (t, *J* = 6.4, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.3, 157.4, 132.0, 128.0, 127.6, 120.9, 110.9, 55.5, 49.8, 35.1, 33.5, 31.9, 29.5, 27.5, 22.8, 14.3. HRMS (ESI+, *m/z*): calcd for $C_{16}H_{25}O_2$ $[M+H]^+$: 249.18491; found: 249.18463.

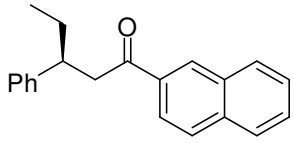
Ee was determined by chiral HPLC analysis, Chiralpak AD-H column, Heptane/*i*-PrOH 99.5:0.5, retention times: 12.2 (major enantiomer) and 12.8 min. $[\alpha]_D^{20}$ = -2.2 (*c* = 0.93, $CHCl_3$).



(*S*)-3-methylnonanal (5i): Colorless oil obtained in 81% yield; 92% *ee*. The physical data were identical in all respects to those previously reported for the racemic compound.[9] *Ee* was determined by chiral GC analysis, Chiraldex G-TA column (30 m x 0.25 mm), (60°C isotherm), retention times: 39.6 (major enantiomer) and 39.9 min. $[\alpha]_D^{20}$ = -18.4 (*c* = 1.95, $CHCl_3$).

General procedure for the synthesis of aryl ketone 6.[11]

To a solution of 2-bromonaphtalene (0.3 mmol, 62 mg) in anhydrous dimethylsulfoxide (0.6 mL) was added the enol acetate **2a** (0.6 mmol, 122 mg), tributyltin methoxide (0.6 mmol, 0.17 mL) followed by $PdCl_2[(o\text{-Tol})_3P]_2$ (0.015 mmol, 12 mg). The mixture was heated under nitrogen at 100°C for 16 hours and then cooled to room temperature. The mixture was diluted with EtOAc (10 mL) and a solution of aqueous KF 4M (5 mL) was added. The mixture was vigorously stirred over 1 hour and the filtered through celite. The organic layer was washed with water (3 x 5 mL) and dried with anhydrous Na_2SO_4. The solvent was evaporated *in vacuo* and the product was purified by column chromatography on silica gel (Pentane : Et_2O 50:1).



(*S*)-1-(naphthalen-2-yl)-3-phenylpentan-1-one (6): Colorless oil obtained in 71% yield; 91% *ee*. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 1H), 8.00 (d, *J* = 8.6, 1H), 7.95 (d, *J* = 8.0, 1H), 7.87 (d, *J* = 8.6, 2H), 7.60 (t, *J* = 7.9, 1H), 7.55 (t, *J* = 7.4, 1H), 7.34-7.28 (m, 5H), 3.42 (t, *J* = 6.9, 2H), 3.38-3.29 (m, 1H), 1.92-1.82 (m, 1H), 1.77-1.66 (m, 1H), 0.86 (t, *J* = 7.4, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.4, 145.0, 135.7, 134.8, 132.7, 129.9,

[11] Jean, M.; Renault, J.; Uriac, P.; Capet, M.; van de Weghe, P. *Org. Lett.* **2007**, *9*, 3623-3625.

129.8, 128.7, 128.6, 128.0, 127.9, 127.0, 126.5, 124.2, 46.0, 43.4, 29.5, 12.4. HRMS (APCI+, *m/z*): calcd for $C_{21}H_{21}O$ $[M+H]^+$: 289.1587; found: 289.1568.

Ee was determined by chiral HPLC analysis, Chiralpak AD-H column, Heptane/*i*-PrOH 95:5, retention times: 14.4 (major enantiomer) and 18.2 min. $[\alpha]_D^{20}$ = -23.3 (*c* = 1.2, $CHCl_3$).