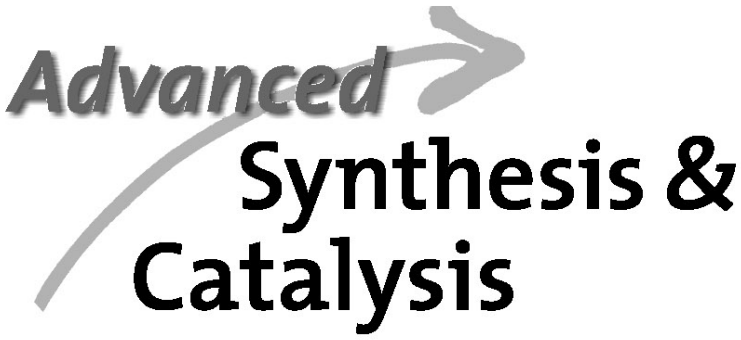

Supporting Information

Supporting Information for

Highly Enantioselective Copper-Phosphoramidite-Catalyzed Conjugate Addition of Dialkylzinc Reagents to Acyclic a,b-Unsaturated Imides.

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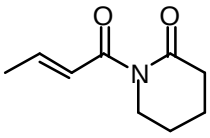
General Methods. All reactions were conducted in flame-dried glassware with magnetic stirring under an atmosphere of argon. Toluene and THF were distilled from sodium/benzophenone ketyl and stored under argon. Analytical TLC were performed on Alugram SIL G/UV254 silica gel sheets (Macherey-Nagel) with detection by 0.5% phosphomolybdic acid solution in 95% EtOH. Silica gel 60 (Macherey-Nagel 230-400 mesh) was used for flash chromatography. Solvents for extraction and chromatography were HPLC grade.

^{1}H NMR spectra were recorded on a Bruker AC-200 spectrometer. Chemical shifts are reported in ppm downfield from tetramethylsilane with the solvent resonance as the internal standard (deuterochloroform: δ **7.26**). ^{13}C NMR spectra were recorded on a Bruker AC-200 (50 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm downfield from tetramethylsilane with the solvent resonance as the internal standard (deuterochloroform: δ **77.7**). Analytical high performance liquid chromatography (HPLC) was performed on a Waters 600E equipped with a Varian Prostar 325 detector.

General procedure for the synthesis of acyl chlorides.

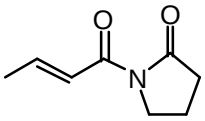
The appropriate carboxylic acid (20.0 mmol) was dissolved in toluene (10 ml) and freshly distilled $SOCl_2$ (30.0 mmol) was added dropwise. The mixture was refluxed overnight, then cooled to rt and evaporated to dryness. The acyl chloride was then dissolved in CH_2Cl_2 (10 ml) and added to the appropriate deprotonated amide.

Typical procedure for the synthesis of *N*-crotonoyl derivatives.



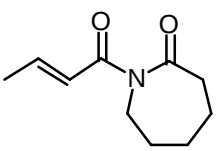
(*E*)-1-But-2-enoylpiperidin-2-one (5a).

A solution of δ-valerolactam (4.73 g, 47.77 mmol) in anhydrous CH_2Cl_2 (10 ml) was added under an argon atmosphere to a suspension of NaH (1.26 g, 52.55 mmol, previously washed with anhydrous hexanes) in CH_2Cl_2 (230 ml). The suspension was stirred at room temperature for 30 min and then cooled to 4°C. Crotonoyl chloride was then added dropwise (5 ml, 71.65 mmol) and the mixture was stirred for 16h and then quenched with water (100 ml). The aqueous phase was extracted with CH_2Cl_2 (3 x 50 ml) and the combined organic phases were washed with H_2O (2 x 50 ml) and brine (2 x 50 ml), dried over $MgSO_4$ and concentrated under a vacuum. The purification of the crude reaction mixture by flash cromatography (hexanes containing 50% AcOEt as the eluant, R_f=0.4) afforded pure compound **3.15** (60% yield). ^{1}H NMR (200 MHz, $CDCl_3$) δ: 6.50-6.99 (m, 2H), 3.45-3.68 (m, 2H), 2.29-2.50 (m, 2H), 1.60-1.83 (m, 7H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 174.0, 169.7, 143.1, 122.7, 44.7, 35.2, 22.8, 21.0, 18.6.



(*E*)-1-But-2-enoylpyrrolidin-2-one (5b).[1]

Following the typical procedure, a solution of 2-pyrrolidinone (1.0 g, 11.74 mmol), dissolved in CH_2Cl_2 (20 ml), was added to a suspension of NaH (309.84 mg, 12.91 mmol) in CH_2Cl_2 (30 ml) followed by crotonoyl chloride (3.22 ml, 45.00 mmol). The reaction was quenched after 3.5h and the crude reaction mixture purified by flash chromatography (hexanes: AcOEt=7:3, R_f=0.31), to give a yellow liquid (70% yield). ^{1}H NMR (200 MHz, $CDCl_3$) δ: 6.72-7.14 (m, 2H), 3.62 (ddd, 2H, *J*=7.0, 6.9 and 3.3 Hz), 2.40 (ddd, 2H, *J*=7.9, 7.8 and 2.7 Hz), 1.79-1.94 (m, 2H), 1.68-1.77 (m, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 175.8, 166.1, 145.6, 123.8, 45.9, 34.1, 18.6, 17.4.

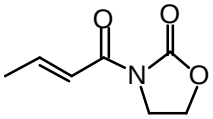


(*E*)-1-But-2-enoylazepan-2-one (5c).

Following the typical procedure, a solution of 2-azepanone (3.39 g, 30.00 mmol), dissolved in CH_2Cl_2 (50 ml), was added to a suspension

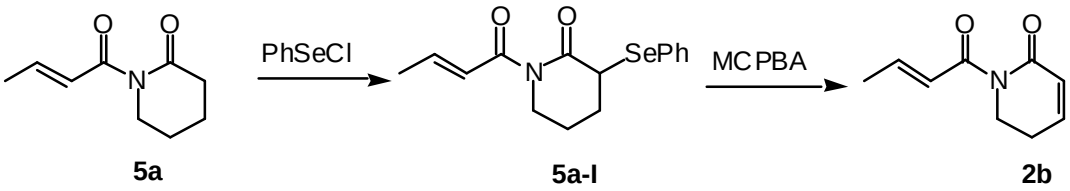
[1] a) Soloshonok, V. A.; Cai, C.; Hruby, V. J. *J. Org. Chem.* **2000**, *65*, 6688; b) Guerin, D. J.; Miller, S. J. *J. Am. Chem. Soc*. **2002**, *124*, 2134.

of NaH (792 mg, 33 mmol) in CH_2Cl_2 (150 ml) followed by crotonoyl chloride (3.22 ml, 45 mmol). The reaction was quenched after 3.5h and the crude reaction mixture purified by flash chromatography (hexanes: AcOEt=7:3, R_f=0.31), to give a yellow liquid (54% yield). ^{1}H NMR (200 MHz, $CDCl_3$) δ: 6.58-6.91 (m, 2H), 6.38-6.55 (m, 1H), 3.52-3.72 (m, 2H), 2.36-2.57 (m, 2H), 1.59-1.69 (m, 3H), 1.36-1.58 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 178.1, 168.7, 142.9, 122.5, 43.6, 39.5, 29.3, 28.8, 23.8, 18.3.



(*E*)-1-But-2-enoyloxazolidin-2-one (5d).[1]

Following the typical procedure, a solution of 2-oxazolidinone (1.04 g, 12 mmol), dissolved in CH_2Cl_2 (30 ml), was added to a suspension of NaH (316.8 mg, 13.2 mmol) in CH_2Cl_2 (20 ml) followed by crotonoyl chloride (1.29 ml, 18 mmol). The reaction was quenched after 3.5h and the crude reaction mixture purified by flash chromatography (hexanes: AcOEt=6:4, R_f=0.26), to give a white solid (m.p.=32-37°C), whose spectral values matched literature values.



Scheme 1.

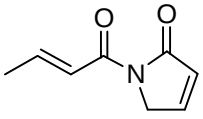
1-(*E*-Crotonoyl)-3-Phenylselenil-2-piperidinone (5a-I). (Scheme 1)

A solution of LHMDS (3.3 ml, 0.0033 moli) in anhydrous THF (14 ml), was added dropwise to a solution of (*E*)-1-but-2-enoylpiperidin-2-one **5a** (0.5 g, 0.00299 moli) in anhydrous THF (14 ml) at –78°C. After 1h a solution of PhSeCl (0.630 g, 0.0033 mol) in THF (14 ml) was added to the mixture at the same temperature. After 2h the reaction mixture was poured into a 1.0 N solution of HCl (10 ml) and the aqueous phase extracted with AcOEt. The organic phase was dried over $MgSO_4$ and evaporated under reduced pressure. The crude product was purified by flash chromatography using hexanes containing 30% AcOEt as the eluant (R_f=0.48), obtaining pure compound **5a-I** (46% yield).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.53-7.66 (m, 2H), 7.16-7.36 (m, 3H), 6.91 (dq, 1H, *J*=15.1 e 6.9 Hz), 6.43 (dq, 1H, *J*=15.1 and 1.7 Hz), 3.92-4.11 (m, 1H), 3.73-3.89 (m, 1H), 3.44-3.61 (m, 1H), 1.86-2.32 (m, 4H), 1.81 (dd, 3H, *J*=6.9 and 1.6 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 173.2, 169.8, 143.2, 135.6, 129.6 (2C), 128.9, 126.0, 45.2, 44.8, 29.2, 21.1, 18.7.

(*E*)-1-But-2-enoyl-5,6-dihydro-2-pyridin-2(1*H*)-one (2b). (Scheme 1)

A solution of MCPBA (351.26 mg, 2.03 mmol) in CH_2Cl_2 (5 ml) was added to a solution of **5a-I** (437 mg, 1.357 mmol) in CH_2Cl_2 (10 ml) cooled to 0°C. The mixture was allowed to warm to rt and stirred for 16h and then poured into a saturated aqueous solution of $NaHCO_3$. The organic solution was dried over $MgSO_4$ and evaporated under a reduced pressure. The crude reaction mixture was subjected to flash chromatography (hexanes:AcOEt=6:4, R_f=0.3) to give **2b** as a yellow liquid (41%yield). ^{1}H NMR (200 MHz, $CDCl_3$) δ: 6.66-7.05 (m, 3H), 5.91 (dq, 1H, *J*=9.7 and 1.2 Hz), 3.88 (t, 2H, *J*=6.5 Hz), 2.31-2.43 (m, 2H), 1.84 (dd, 3H, *J*=6.7 and 1.2 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 169.1, 166.1, 146.0, 143.8, 126.7, 126.1, 41.9, 25.2, 18.8.



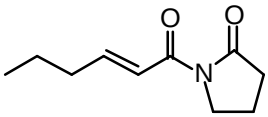
(*E*)-1-But-2-enoyl-1-*H*-pyrrol-2(5*H*)-one (2a).

A solution of BuLi (1.6M in hexanes, 1.63 ml, 2.6 mmol). was added dropwise to a cooled solution of pirrolidin-3-en-2-one[2] (179.28 mg, 2.16 mmol) in anhydrous THF (36 ml) to 0°C. After 80 min a solution of crotonoyl chloride (0.176 ml, 2.46 mmol) in THF (12 ml) was added to 0°C. The solution was maintained at 0°C for 30 min and then stirred at room temperature for 1h. The reaction was quenched by adding a saturated aqueous solution of NH_4Cl (15 ml) and the solvent was removed under reduced pressure. The residue was extracted with $CHCl_3$ (20 ml), washed with water and dried over $MgSO_4$. After filtration and evaporation, the crude product was purified by flash chromatography (hexanes:AcOEt=7:3, R_f=0.22) to give pure compound **2a** (30% yield) as a white solid (m.p.=48-54°C, dec.). ^{1}H NMR (200 MHz, $CDCl_3$) δ: 6.99-7.46 (m, 3H), 6.19 (ddd, 1H,

[2] Rassu, G.; Casiraghi, G.; Spanu, P.; Pinna, L. *Tetrahedron: Asymmetry*, **1992**, *3*, 1035.

J=6.17, 1.8 and 1.6 Hz), 4.48 (t, 2H, *J*=1.8 Hz), 1.98 (dd, 3H, *J*=6.4 and 0.9 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 170.5, 165.3, 147.5, 146.8, 128.1, 123.6, 51.3, 19.0.

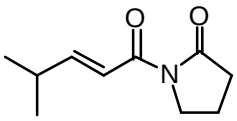
(*E*)-1-Hex-2-enoylpyrrolidin-2-one (7a).



Following the typical procedure, a solution of 2-pyrrolidinone (1.24 g, 14.6 mmol) in CH_2Cl_2 (10 ml), was added to a suspension of NaH (642.4 mg, 16.06 mmol) in CH_2Cl_2 (30 ml) followed by and the crude reaction mixture was subjected to flash chromatography (hexanes: AcOEt=6:4, R_f=0.33) to give **7a**, as a liquid (58% yield).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 6.82-7.12 (m, 2H), 3.59-3.78 (m, 2H), 2.36-2.55 (m, 2H), 2.00-2.19 (m, 2H), 1.78-2.00 (m, 2H), 1.23-1.48 (m, 2H), 0.68-0.92 (m, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 175.8, 166.3, 150.5, 122.6, 45.9, 34.8, 34.2, 21.7, 17.4, 13.9.

(*E*)-1-(4-Methylpent-2-enoyl)pyrrolidin-2-one (7b).

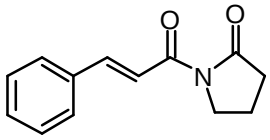


Following the typical procedure, a solution of 2-pyrrolidinone (1.42 g, 16.7 mmol), dissolved in CH_2Cl_2 (10 ml), was added to a suspension of NaH (734.8 mg, 18.37 mmol) in CH_2Cl_2 (30 ml) followed by 4-methyl-2-pentenoic chloride (2.37 g, 20 mmol). The reaction was quenched after 18h and the crude reaction mixture was subjected to flash chromatography (hexanes: AcOEt=6:4, R_f=0.30), to give **7b**, as a liquid (62% yield).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 6.88-7.00 (m, 1H), 6.70 (dd, 1H, *J*=15.5 and 6.3 Hz), 3.57 (t, 2H, *J*=7.2 Hz), 2.15-2.39 (m, 3H), 1.68-1.87 (m, 2H), 0.80 (d, 6H, *J*=6.7 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 175.5, 166.3, 156.2, 119.7, 45.7, 33.9, 31.3, 21.4 (2C), 17.2.

General procedure for the synthesis of substituted *N*-cinnamoyl 2-pyrrolidinones (7c-j).

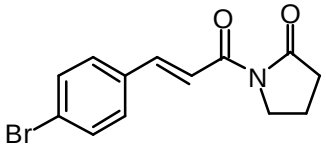
A solution of 2-pyrrolidinone (1.0 g, 11.74 mmol), dissolved in anhydrous CH_2Cl_2 (20 ml), was added ander an argon atmosphere to a suspension of NaH (309.84 mg, 12.91 mmol, previously washed with hexanes) in anhydrous CH_2Cl_2 (30 ml). The suspension was stirred at room temperature for 30 min and then cooled to 4°C. The appropriate cinnamoyl chloride (17.61 mmol) was added dropwise, the reaction was monitored by TLC and quenched with water after 3.5-5h. The aqueous phase was extracted twice with CH_2Cl_2 and the combined organic phases were washed twice with H_2O and brine, dried over $MgSO_4$ and concentrated under a vacuum.



(*E*)-1-[(3-Phenyl)acryloyl]pyrrolidin-2-one (7c).

The crude reaction mixture was purified by flash cromatography using as eluant hexanes: AcOEt=7:3 (R_f=0.31) to give **7c** as a solid (70% yield). m.p.=95-98°C.

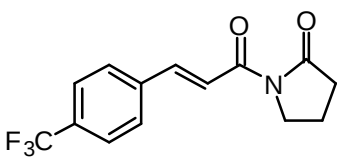
^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.89 (d, 1H, *J*=15.7 Hz), 7.74 (d, 1H, *J*=15.8 Hz), 7.49-7.58 (m, 2H), 7.25-7.35 (m, 3H), 2.80 (t, 2H, *J*=3.8 Hz), 2.52 (t, 2H, *J*=8.0 Hz), 1.83-2.01 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 176.0, 166.4, 145.6, 135.1, 130.7, 129.1, 128.8, 119.4, 46.1, 34.2, 17.4.



(*E*)-1-[3-(4-Bromophenyl)acryloyl]pyrrolidin-2-one (7d).

The crude reaction mixture was recrystallized from hexanes: AcOEt to give **7d** as a yellow solid (45% yield). m.p.=194°C.

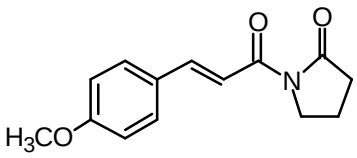
^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.90 (d, 1H, *J*=15.8 Hz), 7.71 (d, 1H, *J*=15.7 Hz), 7.37-7.57 (m, 4H), 3.90 (t, 2H, *J*=7.0 Hz), 2.65 (t, 2H, *J*=8.0 Hz), 1.97-2.15 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 176.4, 166.7, 144.6, 134.4, 132.7, 130.5, 125.2, 120.2, 46.5, 34.6, 17.8.



(*E*)-1-[3-(4-Trifluoromethylphenyl)acryloyl]pyrrolidin-2-one (7e).

The crude reaction mixture was recrystallized from hexanes: AcOEt to give **7e** as a yellow solid (40% yield). m.p.=135-137°C.

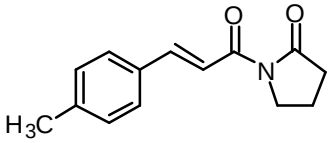
^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.90 (d, 1H, *J*=15.8 Hz), 7.75 (d, 1H, *J*=15.8 Hz), 7.54-7.70 (m, 4H), 3.90 (t, 2H, *J*=7.0 Hz), 2.64 (t, 2H, *J*=8.1 Hz), 1.90-2.14 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 176.4, 166.3, 143.8, 138.8, 129.1 (2C), 126.3, 126.2, 122.1, 46.4, 34.5, 17.7.



(*E*)-1-[3-(4-Methoxyphenyl)acryloyl]pyrrolidin-2-one (7f).

The crude reaction mixture was purified by recrystallization from hexanes:AcOEt (R_f=0.31) to give **7f** as a yellow solid (1.0g, 37% yield). m.p.=147-149°C.

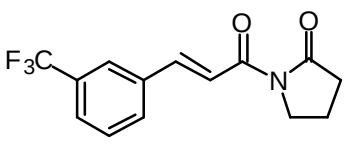
^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.76 (s, 2H), 7.46-7.55 (m, 2H), 6.79-6.90 (m, 2H), 3.85 (t, 2H, *J*=7.0 Hz), 3.76 (s, 3H), 2.59 (t, 2H, *J*=8.0 Hz), 1.89-2.07 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 176.1, 166.9, 161.9, 145.7, 130.7, 128.0, 116.7, 114.7, 55.8, 46.4, 34.5, 17.6.



(*E*)-1-[3-(4-Methylphenyl)acryloyl]pyrrolidin-2-one (7g).

The crude reaction mixture was purified by flash cromatography using as the eluant hexanes:AcOEt=7:3 (R_f=0.18) to give **7g**, as a solid (19% yield). m.p.=119-122°C.

^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.90 (d, 1H, *J*=15.7), 7.79 (d, 1H, *J*=15.7), 7.46-7.55 (m, 2H), 7.13-7.23 (m, 2H), 3.90 (t, 2H, *J*=7.2 Hz), 2.64 (t, 2H, *J*=8.0 Hz), 2.36 (s, 3H), 1.96-2.14 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 176.3, 167.1, 146.2, 141.4, 132.7, 130.1, 129.1, 118.5, 46.5, 34.6, 22.1, 17.8.

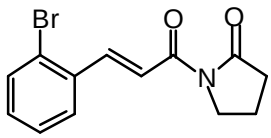


(*E*)-1-[3-(3-Trifluoromethylphenyl)acryloyl]pyrrolidin-2-one (7h).

The crude reaction mixture was purified by flash cromatography using as the eluant hexanes:AcOEt=6:4 (R_f=0.19) to give **7h** as a white solid (70% yield). m.p.=94-98°C.

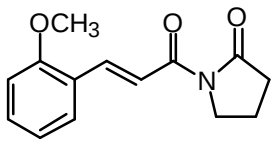
^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.90 (d, 1H, *J*=15.8 Hz), 7.73-7.85 (m, 3H), 7.70 (d, 1H, *J*=15.8 Hz), 7.77-7.81 (m, 2H), 3.90 (t, 2H, *J*=7.1 Hz), 2.60 (t, 2H, *J*=7.9 Hz), 1.99-2.16

(m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 176.4, 166.4, 144.0, 136.2, 131.9, 129.9, 127.2, 125.7, 121.5, 46.4, 34.5, 17.8.



(*E*)-1-[3-(2-Bromophenyl)acryloyl]pyrrolidin-2-one (7i).
The crude reaction mixture was purified by flash cromatography using as the eluant hexanes:AcOEt=6:4 (R_f=0.28) to give **7i** as a solid (56% yield). m.p.=99-102°C.

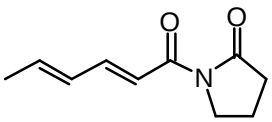
^{1}H NMR (200 MHz, $CDCl_3$) δ: 8.10 (d, 1H, *J*=15.7 Hz), 7.80 (d, 1H, *J*=15.7 Hz), 7.66-7.76 (m, 1H), 7.53-7.62 (m, 1H), 7.15-7.36 (m, 2H), 3.91 (t, 2H, *J*=7.2 Hz), 2.64 (t, 2H, *J*=8.0 Hz), 1.98-2.15 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 176.4, 166.35, 144.2, 135.4, 133.9, 131.8, 128.8, 128.2, 126.2, 122.3, 46.5, 34.5, 17.8.



(*E*)-1-[3-(2-Methoxyphenyl)acryloyl]pyrrolidin-2-one (7j).
The crude reaction mixture was purified by flash cromatography using as the eluant hexanes:AcOEt=6:4 (R_f=0.21) to give **7j** as a white solid (58% yield). m.p.=102-103°C.

^{1}H NMR (200 MHz, $CDCl_3$) δ: 8.10 (d, 1H, *J*=15.9 Hz), 7.90 (d, 1H, *J*=15.9 Hz), 7.51-7.59 (m, 1H), 7.20-7.31 (m, 1H), 6.76-6.93 (m, 2H), 3.75-3.85 (m, 5H), 2.53 (t, 2H, *J*=8.1 Hz), 1.84-2.03 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 176.1, 167.1, 158.9, 140.9, 132.1, 129.4, 124.2, 121.0, 119.7, 111.5, 55.9, 46.3, 34.4, 17.6.

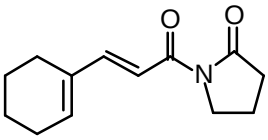
Synthesis of b-alkenyl derivatives.



1-[(2*E*,4*E*)-hexadienoyl]pyrrolidin-2-one (7k).

Following the typical procedure used for crotonoyl derivatives, a solution of 2-pyrrolidinone (1.0 g, 11.74 mmol), dissolved in CH_2Cl_2 (20 ml), was added to a suspension of NaH (309.84 mg, 12.91 mmol) in CH_2Cl_2 (30 ml) followed by hexadienoyl chloride (2.09 g, 17.61 mmol). The reaction was quenched after 2.5h and the crude reaction mixture was recrystallized from hexanes: AcOEt, to give a yellow solid (36% yield). m.p.=95-111°C.

^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.38 (dd, 1H, *J*=15.1 e 9.8 Hz), 7.18 (d, 1H, *J*=15.1 Hz), 6.05-6.37 (m, 2H), 3.82 (t, 2H, *J*=7.1 Hz), 2.57 (t, 2H, *J*=8.0 Hz), 1.90-2.08 (m, 2H), 1.82 (d, 3H, *J*=5.7 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 176.2, 172.5, 146.7, 140.9, 131.2, 120.4, 46.4, 34.6, 19.4, 17.8.



1-[(2*E*)-3-(1-Cyclohexenyl)-2-propenoyl]pyrrolidin-2-one (7l).

Following the general procedure, a solution of 2-pyrrolidinone (270 mg, 3.18 mmol), dissolved in CH_2Cl_2 (15 ml), was added to a suspension of NaH (140 mg, 3.267 mmol) in CH_2Cl_2 (20 ml) and (E)-3-cycloehexenyl acryloyl chloride.[3] The reaction was quenched after 18h and the crude reaction mixture was subjected to flash chromatography (hexanes:AcOEt=6:4, R_f=0.27) to give a **7l** as a solid (51% yield). m.p.=76-79°C.

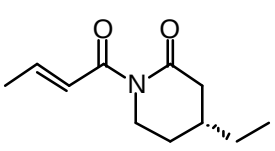
^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.40 (d, 1H, *J*=15.5 Hz), 7.10 (d, 1H, *J*=15.5 Hz), 6.19 (m, 1H), 3.84 (t, 2H, *J*=7.0 Hz), 2.58 (t, 2H, *J*=7.9 Hz), 2.13-2.25 (m, 4H), 1.92-2.09 (m, 2H), 1.52-1.73 (m, 4H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 176.1, 167.5, 149.7, 140.3, 116.2 (2C), 46.4, 34.6, 27.2, 24.9, 22.6 (2C), 17.7.

[3]) Chackalamannil, S.; Davies, R. J.; Wang, Y.; Asberom, T.; Doller, D.; Wong, J.; Leone, D. *J. Org. Chem.* **1999**, *64*, 1932. b) Tanikaga, R.; Nozaki, Y.; Tamura, T.; Kaji, A. *Synthesis*, **1983**, 134.

General procedure for the copper-phosphoramidite catalyzed conjugate addition of dialkylzinc reagents to a,b-unsaturated imides:

A flame-dried Schlenk flask was charged with $Cu(OTf)_2$ (2.5 mg, 0.0069 mmol) and (*R,S,S*)-**1** (7.5 mg, 0.00128 mmol) in anhydrous toluene (1.0 ml) and it was stirred at room temperature for 40 min. The colorless solution was cooled to –78 °C and subsequently, a solution of the *N*-acyl pyrrolidinone (0.46 mmol, dissolved in the minimal amount of toluene or CH_2Cl_2) and the organometallic reagent (0.69-1.38 mmol), were added under an Ar atmosphere. The reaction was monitored by TLC analysis, quenched with saturated aqueous NH_4Cl and extracted several times with Et_2O. The combined organic phases were dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product that was purified by flash chromatography.

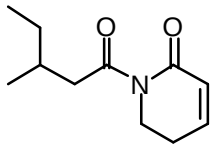
Results of the addition to (*E*)-1-but-2-enoyl-5,6-dihydropyridin-2(1*H*)-one (2b).
Following the general procedure, imide **2b** (42 mg, 0.254 mmol) in anhydrous toluene (0.2 ml) was added to a stirred solution containing $Cu(OTf)_2$ (1.38 mg, 0.00381 mmol) and (*R,S,S*)-**1** (4.1 mg, 0.0076 mmol) in toluene (0.5 ml). The resulting solution was cooled to -78°C and additioned of Et_2Zn (0.381 mmol, 0.346 ml of a 1.1 M solution in toluene). The reaction was quenched after 5h at 0°C and the usual work-up afforded a crude reaction mixture containing the regioisomers **4b** (R_f>) e **3b** (R_f<) in a 75:25 ratio, purified by flash cromatography using hexanes containing 40% of AcOEt as the eluant (R_f=0.55 and 0.47, respectively) to give compound **4b** (24% yield) and compound **3b** (56% yield).



(2'*E*, 4*R*)-1-(2-butenoyl)-4-ethyl-piperidin-2-one (4b): ^1H NMR (200 MHz, $CDCl_3$) δ: 6.98 (dq, 1H, *J*=15.2 and 6.7 Hz), 6.75 (dq, 1H, *J*=15.1 and 1.2 Hz), 3.95 (ddd, 1H, *J*=13.3, 4.7 and 4.6 Hz), 3.47 (ddd, 1H, *J*=13.5, 10.9 and 4.3 Hz), 2.67 (ddd, 1H, *J*=16.8, 5.2 and 1.9 Hz), 2.18 (dd, 1H, *J*=16.9 and 10.5 Hz), 1.95-2.09 (m, 1H), 1.90 (dd, 3H, *J*=6.7 and 1.3 Hz), 1.68-1.85 (m, 1H), 1.17-1.54 (m, 3H), 0.93 (t, 3H, *J*=7.3 Hz). ^{13}C

NMR (50 MHz, $CDCl_3$) δ: 174.2, 170.2, 143.7, 127.1, 44.4, 41.8, 35.1, 29.3, 29.1, 18.9, 17.8.

The enantiomeric excess of compound **4b** (70%) was determined by chiral HPLC (Daicel Chiralcel OB-H) (hexanes/IPA=98:2): t_R 25.4 (minor), t_R 27.1 (major).

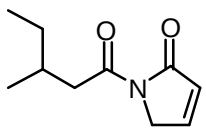


1-(3-Methylpentanoyl)-5,6-dihydropyridin-2(1*H*)-one (3b): ^{1}H NMR (200 MHz, $CDCl_3$) δ: 6.88 (dt, 1H, *J*=9.6 and 4.3 Hz), 5.98 (dt, 1H, *J*=9.7 and 1.8 Hz), 3.96 (dt, 2H, *J*=6.8 and 2.4 Hz), 2.96 (dd, 1H, *J*=16.2 and 5.8 Hz), 2.72 (dd, 1H, *J*=16.2 and 7.9 Hz), 2.34-2.47 (m, 2H), 1.85-2.07 (m, 1H), 1.07-1.52 (m, 2H), 0.84-0.99 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 176.8, 170.2, 145.6, 126.8, 46.7, 41.7, 32.3, 30.2, 25.5, 20.1, 12.1.

The enantiomeric exess of compound **3b** (48%) was determned by chiral HPLC (Daicel Chiralpak AD-H) (hexanes/IPA=98:2, flow:0.8 ml): t_R 11.0 (minor), t_R 11.4 (major).

Addition to (*E*)-1-but-2-enoyl-1*H*-pyrrol-2(5*H*)-one (2a).

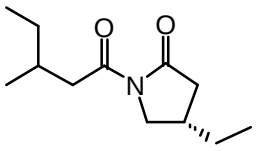
Following the general procedure, a solution of imide **2a** (90.6 mg, 0.6 mmol) dissolved in anhydrous toluene (0.5 ml) was added to a stirred solution containing $Cu(OTf)_2$ (3.24 mg, 0.009 mmol) and (*R*,*S*,*S*)-**1** (9.72 mg, 0.018 mmol) in toluene (1.0 ml). The resulting solution was cooled to -78°C and Et_2Zn (1.2 eq, 1.2 mmol, 1.1 ml of a 1.1 M solution in toluene) was added. The reaction was quenched after 3h at 0°C and the usual work-up afforded a crude reaction mixture containing the regioisomers **3a-I** (R_f>) e **3a** (R_f<) in a 20:80 ratio, purified by flash cromatography using hexanes containing 20% of AcOEt as the eluant (R_f=0.57 e 0.37, respectively), obtaining compound **3a-I** (6% yield) and pure compound **3a** (72% yield), as a yellow liquid.



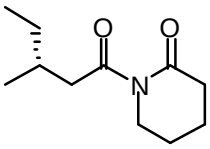
1-(3-Methylpentanoyl)-pyrrol-2(5*H*)-one (3a): ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.34 (ddd, 1H, *J*=5.9, 2.0 and 1.9 Hz), 6.20 (ddd, 1H, *J*=5.9, 1.9 and 1.8 Hz), 4.45 (dd, 2H, *J*=1.9 and 1.8 Hz), 3.00 (dd, 1H, *J*=15.9 and 5.8 Hz), 2.81 (dd, 1H, *J*=16.0 and 7.9 Hz), 1.93-2.16 (m, 1H), 1.18-1.59 (m, 2H), 0.89-1.02 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 173.6, 170.5, 147.2, 128.5, 51.4, 43.7, 31.7, 30.1, 20.0, 12.0.

The enantiomeric excess of compound **3a** (76%) was determined by chiral HPLC (AD-H) (hexanes/IPA=95:5, flow= 0.8 ml/min): t_R 19.6 (minor), t_R 21.4 (major).

The same reaction was repeated in accordance with the general procedure using $AlEt_3$ and compound **3a** was obtained with a 12% *ee*.



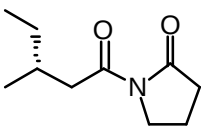
1-(3-Methylpentanoyl)-4-ethylpyrrolidin-2-one (3a-I): ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.88-4.01 (m, 1H), 3.30-3.40 (m, 1H), 2.60-2.98 (m, 3H), 2.12-2.37 (m, 2H), 1.83-2.08 (m, 1H), 1.09-1.56 (m, 4H), 0.84-0.99 (m, 9H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 175.5, 174.7, 51.4, 44.3, 40.7, 32.9, 31.8, 30.2, 27.8, 20.0, 12.3, 12.1.



1-(3-Methylpentanoyl)piperidin-2-one (6a).

Following the general procedure, a solution of the imide **5a** (50.1 mg, 0.3 mmol) in toluene (0.2 ml) was added to a stirred solution of $Cu(OTf)_2$ (1.63 mg, 0.0045 mmol) and (*R*,*S*,*S*)-**1** (4.86 mg, 0.009 mmol) in toluene (0.5 ml). The resulting solution was cooled to -78°C and additioned of Et_2Zn (0.45 mmol, 0.41 ml of a 1.1 M solution in toluene). The reaction was quenched after 6h at 0°C and the usual work-up afforded a crude reaction mixture which was purified by flash cromatography using hexanes containing 40% AcOEt as the eluant, to give 33 mg of pure compound **3.16** (56% yield). ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.58-3.82 (m, 2H), 2.92 (dd, 1H, *J*=16.3 and 5.7 Hz), 2.68 (dd, 1H, *J*=16.3 and 7.8 Hz), 2.45-2.59 (m, 2H), 1.87-2.05 (m, 1H), 1.64-1.86 (m, 4H), 1.06-1.48 (m, 2H), 0.81-0.97 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 174.2, 170.2, 47.1, 44.5, 35.6, 32.1, 30.3, 30.1, 23.1, 21.0, 20.0.

The enantiomeric excess of compound **6a** (56%) was determined by chiral HPLC (Daicel Chiralpack AD-H) (hexanes/IPA=95:5, flow= 0.8 ml/min): t_R 10.0 (minor), t_R 10.3 (major).



(*3R*)-1-(3-Methylpentanoyl)pyrrolidin-2-one (6b).

Following the general procedure, a solution of the imide **5b** (61.6 mg, 0.4 mmol) in toluene (0.2 ml) was added to a stirred solution of $Cu(OTf)_2$ (2.17 mg, 0.006 mmol) and (*R*,*S*,*S*)-**1** (6.48 mg, 0.012 mmol) in toluene (0.5 ml). The resulting solution was cooled to -78°C and additioned of Et_2Zn

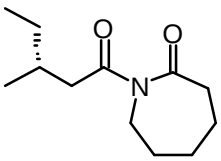
(0.6 mmol, 0.541 ml of a 1.1 M solution in toluene). The reaction was quenched after 2.5h at 0°C and the usual work-up afforded a crude reaction mixture which was purified by flash cromatography using hexanes containing 30% AcOEt as the eluant, (R_f=0.38) to give 55 mg of pure compound **6b** (75% yield). ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.79 (t, 2H, *J*=7.1 Hz), 2.89 (dd, 1H, *J*=16.2 and 5.8 Hz), 2.69 (dd, 1H, *J*=16.1 and 7.9), 2.58 (t, 2H, *J*=8.2 Hz), 1.85-2.13 (m, 3H), 1.09-1.50 (m, 2H), 0.80-0.96 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 176.0, 174.2, 46.2, 44.2, 34.5, 31.6, 30.1, 20.0, 17.8, 12.1.

The enantiomeric excess of compound **6b** (87%) was determined by chiral HPLC (AD-H) (hexanes/IPA=96:4): t_R 17.2 (minor), t_R 18.7 (major).

Addition of Et_3Al to imide 5b:

Following the general procedure, a solution of the imide **5b** (61.6 mg, 0.4 mmol) in toluene (0.2 ml) was added to a stirred solution of $Cu(OTf)_2$ (2.17 mg, 0.006 mmol) and (*R*,*S*,*S*)-**1** (6.48 mg, 0.012 mmol) in toluene (0.5 ml). The resulting solution was cooled to -78°C and additioned of Et_3Al (1.2 mmol, 0.63 ml of a 1.9 M solution in toluene). The reaction was quenched after 3h at 0°C and the usual work-up afforded a crude reaction mixture (78 mg) which was not subjected to further purification.

The enantiomeric excess of compound **6b** (30%) was determined by chiral HPLC (AD-H) (hexanes/IPA=96:4): t_R 17.2 (major), t_R 18.7 (minor).

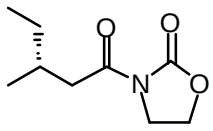


1-(3-Methylpentanoyl)azepan-2-one (6c).

Following the general procedure, a solution of the imide **5c** (72.4 mg, 0.4 mmol) in toluene (0.2 ml) was added to a stirred solution of $Cu(OTf)_2$ (2.17 mg, 0.006 mmol) and (*R*,*S*,*S*)-**1** (6.48 mg, 0.012 mmol) in toluene (0.5 ml). The resulting solution was cooled to -78°C and additioned of Et_2Zn (0.6 mmol, 0.541 ml of a 1.1 M solution in toluene). The reaction was quenched after 6h at 0°C and the usual work-up afforded a crude reaction mixture which was subjected to flash cromatography using hexanes containing 30% AcOEt as the eluant, (R_f=0.4) to give 55 mg of pure compound **3.17** (65% yield). ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.80-3.96 (m, 2H), 2.88 (dd, 1H, *J*=15.9 and 5.8 Hz), 2.63 (dd, 1H, *J*=16.0 and 7.9 Hz), 2.66-2.77 (m, 2H), 1.83-2.06 (m, 1H), 1.55-1.82 (m, 6H), 1.07-1.50 (m, 2H), 0.82-0.93 (m,

6H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 178.4, 176.5, 46.6, 44.0, 40.6, 32.3, 30.1, 29.9, 29.3, 24.4, 20.0, 12.1.

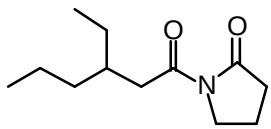
The enantiomeric excess of compound **6c** (30%) was determined by chiral HPLC (AD-H) (hexanes/IPA=94:6): t_R 12.9 (minor), t_R 14.2 (major).



(3*R*)-1-(3-Methylpentanoyl)oxazolidin-2-one (6d).[4]

Following the general procedure, a solution of the imide **5d** (77.54 mg, 0.5 mmol) in toluene (0.5 ml) was added to a stirred solution of $Cu(OTf)_2$ (2.71 mg, 0.0075 mmol) and (*R*,*S*,*S*)-**1** (8.1 mg, 0.015 mmol) in toluene (1.0 ml). The resulting solution was cooled to -78°C and additioned with Et_2Zn (0.75 mmol, 0.68 ml of a 1.1 M solution in toluene). The reaction was quenched after 4h at 0°C and the usual work-up afforded a crude reaction mixture which was purified by preparative TLC using hexanes containing 40% AcOEt as the eluant, (R_f=0.34) to give 57 mg of pure compound **6d** (60% of yield). $[\alpha]^{20}_D$=-8.4 (c=0.45, $CHCl_3$). The measured optical rotatory power was compared to those reported in literature[5] and corrisponded to absolute configuration *R*.

The enantiomeric excess of compound **6d** (65%) was determined by chiral HPLC (AD-H) (hexanes/IPA=93:7, flow: 0.8 ml/min): t_R 25.0 (major), t_R 26.0 (minor).

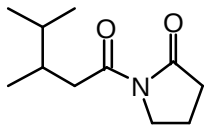


1-(3-Ethylhexenoyl)pyrrolidin-2-one (8).

Following the general procedure, a solution of the imide **7a** (90.5 mg, 0.5 mmol) in toluene (0.5 ml) was added to a stirred solution of $Cu(OTf)_2$ (2.71 mg, 0.0075 mmol) and (*R*,*S*,*S*)-**1** (8.1 mg, 0.015 mmol) in toluene (1.0 ml). The resulting solution was cooled to -78°C and additioned of Et_2Zn (1.5 mmol, 1.36 ml of a 1.1 M solution in toluene). The reaction was quenched after 3h at 0°C and the usual work-up afforded a crude reaction mixture which was purified by flash chromatography using hexanes containing 40% AcOEt as the eluant (R_f=0.47), to give 84 mg of pure compound **8** (80% yield), as an oil.

^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.80 (t, 2H, *J*=7.0 Hz), 2.83 (d, 2H, *J*=6.7 Hz), 2.58 (t, 2H, *J*=7.8 Hz), 1.78-2.10 (m, 3H), 1.13-1.48 (m, 6H), 0.80-0.95 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 175.8, 174.9, 46.2, 41.6, 36.3, 34.4, 30.3, 26.8, 20.4, 17.7, 15.0, 11.4.

The enantiomeric excess of compound **8** (84%) was determined by chiral HPLC (AD-H) (hexanes/IPA=97:3, flow: 1.0 ml/min): t_R 10.3 (minor), t_R 9.3 (major).

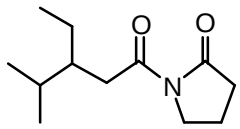


1-(3,4-Dimethylpentanoyl)pyrrolidin-2-one (9).

Following the general procedure, a solution of the imide **5b** (77.0 mg, 0.5 mmol) in toluene (0.5 ml) was added to a stirred solution of $Cu(OTf)_2$ (2.71 mg, 0.0075 mmol) and (*R*,*S*,*S*)-**1** (8.1 mg, 0.015 mmol) in toluene (1.0 ml). The resulting solution was cooled to -78°C and *i*Pr_2Zn (1.5 mmol, 0.5 ml of a solution 3.0 M in toluene) was added. The reaction was quenched after 3h at 0°C and the usual work-up afforded a crude reaction mixture which was purified by preparative TLC using hexanes containing 30% AcOEt as the eluant, (R_f=0.33) to give 76 mg of pure compound **9** (78% yield), as an oil. $[\alpha]^{20}_D$=+73.4 (c=1.7, $CHCl_3$).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.78 (t, 2H, *J*=7.1 Hz), 2.90 (dd, 1H, *J*=16.1 and 4.8 Hz), 2.50-2.75 (m, 3H), 1.84-2.09 (m, 3H), 1.50-1.70 (m, 1H), 0.77-0.92 (m, 9H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 175.9, 175.0, 46.2, 41.9, 35.4, 34.5, 32.8, 20.6, 18.8, 17.8, 16.3.

The enantiomeric excess of compound **9** (60%) was determined by chiral HPLC (AD-H) (hexanes/IPA=99:1, flow: 1.0 ml/min): t_R 11.1 (minor), t_R 13.5 (major).



1-(3-Ethyl-4-methylpentanoyl)pirrolidin-2-one (10).

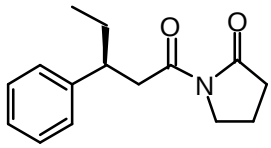
Following the general procedure, a solution of the imide **7b** (90.0 mg, 0.5 mmol) in toluene (0.5 ml) was added to a stirred solution of $Cu(OTf)_2$ (2.71 mg, 0.0075 mmol) and (*R*,*S*,*S*)-**1** (8.1 mg, 0.015 mmol) in toluene (1.0 ml). The resulting solution was cooled to -78°C and additioned of Et_2Zn (1.5 mmol, 1.36 ml of a 1.1 M solution in toluene). The reaction was quenched after 3h at 0°C and the usual work-up afforded a crude reaction mixture which was was purified by flash chromatography using hexanes containing 40% AcOEt as the eluant (R_f=0.26), to give 79 mg of pure compound **10** (75% yield). $[\alpha]^{20}_D$=-8.16 (c=0.5, $CHCl_3$).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.77 (t, 2H, *J*=7.1 Hz), 2.87 (dd, 1H, *J*=16.7 and 5.8 Hz), 2.73 (dd, 1H, *J*=16.7 and 7.0 Hz), 2.56 (t, 2H, *J*=8.0 Hz), 1.89-2.09 (m, 2H), 1.59-1.88 (m,

[4] Hird, A.; Hoveyda, A. H. *Angew. Chem. Int. Ed*. **2003**, *42*, 1276.

2H), 1.06-1.49 (m, 2H), 0.71-0.91 (m, 9H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 175.6, 175.1, 46.0, 41.4, 34.2, 30.0, 29.6, 23.9, 19.7, 19.0, 17.5, 12.2.

The enantiomeric excess of compound **10** (95%) was determined by chiral HPLC (AD-H) (hexanes/IPA=97:3, flow: 1.0 ml/min): t_R 14.1 (minor), t_R 12.8 (major).

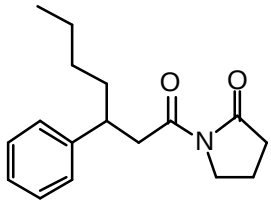


(3*S*)-1-(3-Phenylpentanoyl)pyrrolidin-2-one (11).

Following the general procedure, a solution of the imide **7c** (107.5 mg, 0.4 mmol) in toluene (0.5 ml) was added to a stirred solution of $Cu(OTf)_2$ (2.71 mg, 0.0075 mmol) and (*R*,*S*,*S*)-**1** (8.1 mg, 0.015 mmol) in toluene (1.0 ml). The resulting solution was cooled to -78°C and additioned of Et_2Zn (1.5 mmol, 1.36 ml of a 1.1 M solution in toluene). The reaction was quenched after 3h at 0°C and the usual work-up afforded a crude reaction mixture which was subjected to flash chromatography using hexanes containing 30% AcOEt as the eluant (R_f=0.28) to give pure **11**.

^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.10-7.36 (m, 5H), 3.59-3.82 (m, 2H), 3.30-3.47 (m, 1H), 3.03-3.27 (m, 2H), 2.47-2.60 (m, 2H), 1.84-2.04 (m, 2H), 1.58-1.83 (m, 2H), 0.82 (t, 3H, *J*=7.3 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 175.9, 173.6, 144.9, 128.8, 128.3, 126.7, 46.0, 43.8, 43.7, 34.3, 29.8, 17.7, 12.7.

The enantiomeric excess of compound **11** (99.9%) was determined by chiral HPLC (AD-H) (hexanes/IPA=95:5): t_R 13.6 (minor), t_R 11.1 (major).

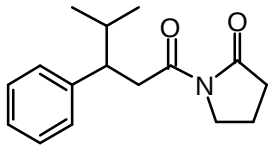


1-(3-Phenyheptanoyl)pyrrolidin-2-one (12).

Following the general procedure, a solution of the imide **7c** (107.5 mg, 0.5 mmol) in toluene (0.5 ml) was added to a stirred solution of $Cu(OTf)_2$ (2.71 mg, 0.0075 mmol) and (*R*,*S*,*S*)-**1** (8.1 mg, 0.015 mmol) in toluene (1.0 ml). The resulting solution was cooled to -78°C and additioned of Bu_2Zn (1.5 mmol, 1.5 ml of a 1.0 M solution in heptane). The reaction was quenched after 6h at 0°C (95% conversion) and the usual work-up afforded a crude reaction mixture which was purified by flash cromatography using hexanes containing 30% AcOEt as the eluant, (R_f=0.33) to give 88 mg of pure compound **12** (62% yield), as an oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.11-7.37 (m, 5H), 3.58-3.81 (m, 2H), 3.08-3.45 (m, 3H), 2.48-2.60 (m, 2H), 1.83-2.08 (m, 2H), 1.53-1.80 (m, 2H), 0.98-

1.41 (m, 4H), 0.83 (t, 3H, *J*=6.7 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 176.0, 173.7, 145.5, 128.9, 128.4, 126.8, 46.1, 44.3, 42.1, 36.8, 34.4, 30.3, 23.3, 17.8, 14.6.

The enantiomeric excess of compound **12** (85%) was determined by chiral HPLC (AD-H) (hexanes/IPA=95:5): t_R 8.31 (minor), t_R 10.1 (major).

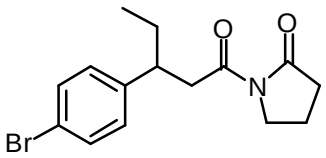


1-(3-Phenyl-4-methylpentanoyl)pyrrolidin-2-one (13).

Following the general procedure, a solution of the imide **7c** (107.0 mg, 0.5 mmol) in toluene (0.5 ml) was added to a stirred solution of $Cu(OTf)_2$ (2.71 mg, 0.0075 mmol) and (*R*,*S*,*S*)-**1** (8.1 mg, 0.015 mmol) in toluene (1.0 ml). The resulting solution was cooled to -78°C and additioned of *i*Pr_2Zn (1.5 mmol, 0.5 ml of a 3.0 M solution in toluene). The reaction was quenched after 4h at 0°C and the usual work-up afforded a crude reaction mixture which was purified by preparative TLC using hexanes containing 30% AcOEt as the eluant, (R_f=0.30) to give 97 mg of pure compound **13** (75% yield), as an oil. $[\alpha]^{20}_D$=-23.3 (c=0.7, $CHCl_3$).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.08-7.32 (m, 5H), 3.38-3.72 (m, 3H), 3.2 (dd, 1H, *J*=16.5 e 4.6 Hz), 2.89-3.05 (m, 1H), 2.43-2.58 (m, 2H), 1.75-2.02 (m, 3H), 0.9 (d, 3H, *J*=6.6 Hz), 0.7 (d, 3H, *J*=6.7 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 175.9, 174.4, 144.0, 129.0, 128.5, 126.7, 48.9, 46.1, 40.9, 34.3, 33.7, 21.4, 21.2, 17.7.

The enantiomeric excess of compound **13** (81%) was determined by chiral HPLC (AD-H) (hexanes/IPA=99:1, flow: 1.0 ml/min): t_R 15.9 (minor), t_R 19.3 (major).



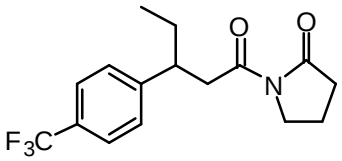
1-[3-(4-Bromophenyl)pentanoyl]pyrrolidin-2-one (14).

Following the general procedure, a solution of the imide **7d** (147.0 mg, 0.5 mmol) in toluene (0.5 ml) was added to a stirred solution of $Cu(OTf)_2$ (2.71 mg, 0.0075 mmol) and (*R*,*S*,*S*)-**1** (8.1 mg, 0.015 mmol) in toluene (1.0 ml). The resulting solution was cooled to -78°C and additioned of Et_2Zn (1.5 mmol, 1.36 ml of a 1.1 M solution in toluene). The reaction was quenched after 3h at -15°C and the usual work-up afforded a crude reaction mixture which was purified by flash cromatography using hexanes containing 30% AcOEt as the eluant, (R_f=0.25) to give 133 mg of pure compound **14** (82% yield).

$[\alpha]^{20}_D$=-37.0 (c=0.7, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.32-7.43 (m, 2H), 7.02-7.13 (m, 2H), 3.56-3.79 (m, 2H), 3.22-3.41 (m, 1H), 3.12-3.19 (m, 1H), 2.69-3.11 (m, 1H), 2.55

(t, 2H, *J*=8.3 Hz), 1.86-2.04 (m, 2H), 1.42-1.84 (m, 2H), 0.80 (t, 3H, *J*=7.3 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 176.0, 173.3, 144.1, 131.2, 130.2, 120.5, 46.0, 43.8, 43.2, 34.3, 29.8, 17.7, 12.6.

The enantiomeric excess of compound **14** (>99%) was determined by chiral HPLC (AD-H) (hexanes/IPA=97:3, flow: 1.0 ml/min): t_R 17.8 (minor), t_R 16.2 (major).

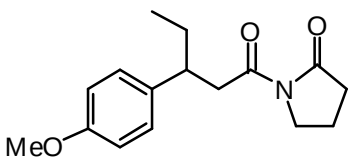


1-[3-(4-Trifluoromethylphenyl)pentanoyl]pyrrolidin-2-one (15).

Following the general procedure, a solution of the imide **7e** (141.5 mg, 0.5 mmol) in toluene (0.5 ml) was added to a stirred solution of $Cu(OTf)_2$ (2.71 mg, 0.0075 mmol) and (*R*,*S*,*S*)-**1** (8.1 mg, 0.015 mmol) in toluene (1.0 ml). The resulting solution was cooled to -78°C and additioned of Et_2Zn (1.5 mmol, 1.36 ml of a 1.1 M solution in toluene). The reaction was quenched after 2h at -30°C and the usual work-up afforded a crude reaction mixture which was purified by flash cromatography using hexanes containing 30% AcOEt as the eluant (R_f=0.24) to give 131 mg of pure compound **15** (84% yield). $[\alpha]^{20}_D$=-33.4 (c=1.0, $CHCl_3$).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 6.90-7.49 (m, 4H), 3.44-3.63 (m, 1H), 3.17-3.36 (m, 1H), 2.98-3.16 (m, 2H), 2.31-2.48 (m, 2H), 1.70-1.89 (m, 2H), 1.42-1.68 (m, 3H), 0.68 (t, 3H, *J*=7.3 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 176.1, 173.2, 149.4, 129.3, 128.8, 125.8, 125.7, 46.0, 43.7, 43.5, 34.3, 29.8, 17.7, 12.6.

The enantiomeric excess of compound **15** (>99%) was determined by chiral HPLC (AD-H) (hexanes/IPA=97:3, flow: 1.0 ml/min): t_R 15.0 (minor), t_R 13.1 (major).

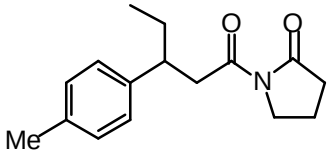


1-[3-(4-Methoxyphenyl)pentanoyl]pyrrolidin-2-one (16).

Following the general procedure, a solution of the imide **7f** (122.5 mg, 0.5 mmol) in toluene (0.5 ml) was added to a stirred solution of $Cu(OTf)_2$ (2.71 mg, 0.0075 mmol) and (*R*,*S*,*S*)-**1** (8.1 mg, 0.015 mmol) in toluene (1.0 ml). The resulting solution was cooled to -78°C and additioned of Et_2Zn (1.5 mmol, 1.36 ml of a 1.1 M solution in toluene). The reaction was quenched after 4h at 0°C and the usual work-up afforded a crude reaction mixture (120 mg, 83% yield) which was subjected to flash chromatography using hexanes containing 30% as the eluant (R_f=0.34) to give 102 mg of pure **16** (74% yield). $[\alpha]^{20}_D$=-

26.1 (c=0.7, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.07-7.18 (m, 2H), 6.76-6.88 (m, 2H), 3.78 (s, 3H), 3.68 (dt, 2H, *J*=7.4 e 2.4 Hz), 3.23-3.42 (m, 1H), 2.95-3.21 (m, 2H), 2.54 (dt, 2H, *J*=8.8 and 1.7 Hz), 1.85-2.05 (m, 2H), 1.47-1.80 (m, 2H), 0.77 (t, 3H, *J*=7.4 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 176.0, 173.8, 158.5, 137.1, 129.3, 114.2, 55.8, 46.1, 44.1, 43.0, 34.4, 30.3, 17.8, 12.8.

The enantiomeric excess of compound **16** (94%) was determined by chiral HPLC (AD-H) (hexanes/IPA=95:5, flow: 1.0 ml/min): t_R 19.6 (major), t_R 23.3 (minor).

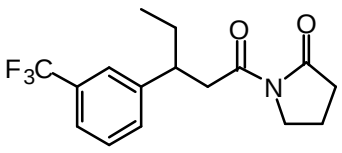


1-[3-(4-Methylphenyl)pentanoyl]pyrrolidin-2-one (17).

Following the general procedure, a solution of the imide **7g** (114.5 mg, 0.5 mmol) in toluene (0.5 ml) was added to a stirred solution of $Cu(OTf)_2$ (2.71 mg, 0.0075 mmol) and (*R*,*S*,*S*)-**1** (8.1 mg, 0.015 mmol) in toluene (1.0 ml). The resulting solution was cooled to -78°C and additioned of Et_2Zn (1.5 mmol, 1.36 ml of a 1.1 M solution in toluene). The reaction was quenched after 4h at 0°C and the usual work-up afforded a crude reaction mixture which was purified by flash cromatography using hexanes containing 30% AcOEt as the eluant, (R_f=0.34) to give 114 mg of pure compound **17** as a pale yellow oil (88% yield). $[\alpha]^{20}_D$=-21.9 (c=1.0, $CHCl_3$).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.04-7.15 (m, 4H), 3.6 (dt, 2H, *J*=7.4 e 2.4 Hz), 3.23-3.40 (m, 1H), 2.96-3.22 (m, 2H), 2.42-2.64 (m, 2H), 2.30 (s, 3H), 1.81-2.03 (m, 2H), 1.51-1.80 (m, 2H), 0.79 (t, 3H, *J*=7.3 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 175.8, 173.7, 141.9, 136.1, 129.4, 128.1, 46.0, 43.9, 43.2, 34.3, 29.8, 21.6, 17.7, 12.6.

The enantiomeric excess of compound **17** (94%) was determined by chiral HPLC (AD-H) (hexanes/IPA=97:3, flow: 1.0 ml/min): t_R 12.9 (minor), t_R 11.7 (major).



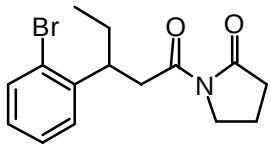
1-[3-(3-Trifluoromethylphenyl)pentanoyl]pyrrolidin-2-one (18).

Following the general procedure, a solution of the imide **7h** (141.6 mg, 0.5 mmol) in toluene (0.5 ml) was added to a stirred solution of $Cu(OTf)_2$ (2.71 mg, 0.0075 mmol) and (*R*,*S*,*S*)-**1** (8.1 mg, 0.015 mmol) in toluene (1.0 ml). The resulting solution was cooled to -78°C and additioned of Et_2Zn (1.5 mmol, 1.36 ml of a 1.1 M solution in toluene). The reaction was quenched after 4h at 0°C and the usual work-up afforded a crude reaction mixture which was purified by

preparative TLC using hexanes containing 40% AcOEt as the eluant, (R_f=0.26) to give 86 mg of pure compound **18** as a semisolid (55% yield). $[\alpha]^{20}_D$=-27.6 (c=0.7, $CHCl_3$).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.37-7.53 (m, 4H), 3.60-3.76 (m, 2H), 3.31-3.47 (m, 1H), 3.13-3.29 (m, 2H), 2.47-2.58 (m, 2H), 1.85-2.02 (m, 2H), 1.62-1.82 (m, 2H), 0.82 (t, 3H, *J*=7.3 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 175.9, 173.0, 131.9, 129.5, 129.3, 128.7, 125.8, 125.0, 123.7, 45.9, 43.6, 34.1, 30.3, 29.7, 17.6, 12.5.

The enantiomeric excess of compound **18** (94%) was determined by chiral HPLC (AD-H) (hexanes/IPA=95:5, flow: 1.0 ml/min): t_R 7.4 (minor), t_R 8.8 (major).

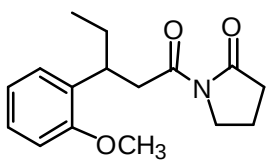


1-[3-(2-Bromophenyl)pentanoyl]pyrrolidin-2-one (19).

Following the general procedure, a solution of the imide **7i** (147.0 mg, 0.5 mmol) in toluene (0.5 ml) was added to a stirred solution of $Cu(OTf)_2$ (2.71 mg, 0.0075 mmol) and (*R*,*S*,*S*)-**1** (8.1 mg, 0.015 mmol) in toluene (1.0 ml). The resulting solution was cooled to -78°C and additioned of Et_2Zn (1.5 mmol, 1.36 ml of a 1.1 M solution in toluene). The reaction was quenched after 4h at 0°C and the usual work-up afforded a crude reaction mixture which was purified by preparative TLC using hexanes containing 40% AcOEt as the eluant, (R_f=0.26) to give 127 mg of pure compound **19** (78% yield).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.50-7.59 (m, 1H), 7.10-7.34 (m, 3H), 3.75-3.86 (m, 1H), 3.70 (t, 2H, *J*=7.2 Hz), 3.38 (dd, 1H, *J*=16.4 e 6.0 Hz), 3.18 (dd, 1H, *J*=16.4 e 8.5 Hz), 2.49-2.61 (m, 2H), 1.86-2.04 (m, 2H), 1.58-1.85 (m, 2H), 0.87 (t, 3H, *J*=7.3 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 175.8, 172.9, 133.3, 129.5, 128.7, 128.3, 128.0, 125.7, 45.9, 43.1, 41.4, 34.1, 29.5, 17.6, 12.1.

The enantiomeric excess of compound **19** (80%) was determined by chiral HPLC (AD-H) (hexanes/IPA=95:5, flow: 1.0 ml/min): t_R 10.0 (minor), t_R 10.9 (major).

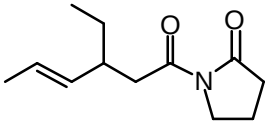


1-[3-(2-Methoxyphenyl)pentanoyl]pyrrolidin-2-one (20).

Following the general procedure, a solution of the imide **7j** (122.5 mg, 0.5 mmol) in toluene (0.5 ml) was added to a stirred solution of $Cu(OTf)_2$ (2.71 mg, 0.0075 mmol) and (*R*,*S*,*S*)-**1** (8.1 mg, 0.015 mmol) in toluene (1.0 ml). The resulting solution was cooled to -78°C and additioned of Et_2Zn (1.5 mmol, 1.36 ml of a 1.1 M solution in toluene). The reaction was quenched after 4h at 0°C and the usual work-up afforded a crude reaction mixture which was purified by

preparative TLC using hexanes containing 40% AcOEt as the eluant, (R_f=0.29) to give 61 mg of pure compound **20** (44% yield). $[\alpha]^{20}_D$=-29.4 (c=0.7, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.09-7.37 (m, 2H), 6.82-7.00 (m, 2H), 3.84 (s, 3H), 3.71 (t, 2H, *J*=7.2 Hz), 3.45-3.66 (m, 1H), 3.28-3.57 (m, 2H), 2.55 (t, 2H, *J*=7.7 Hz), 1.85-2.04 (m, 2H), 1.66-1.84 (m, 2H), 0.86 (t, 3H, *J*=7.3 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 175.9, 158.2, 133.0, 129.6, 128.8, 127.6, 121.1, 111.3, 55.9, 46.0, 42.4, 34.3, 30.3, 28.4, 17.7, 12.6.

The enantiomeric excess of compound **20** (87%) was determined by chiral HPLC (AD-H) (hexanes/IPA=97:3, flow: 1.0 ml/min): t_R 16.4 (minor), t_R 18.0 (major).

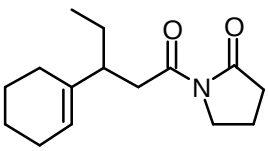


1-(3-Ethyl-4-hexenoyl)pyrrolidin-2-one (21).

Following the general procedure, a solution of the imide **7k** (179 mg, 1.0 mmol) in toluene (0.5 ml) was added to a stirred solution of $Cu(OTf)_2$ (5.42 mg, 0.0015 mmol) and (*R*,*S*,*S*)-**1** (16.2 mg, 0.03 mmol) in toluene (1.0 ml). The resulting solution was cooled to -78°C and additioned of Et_2Zn (3.0 mmol, 2.72 ml of a 1.1 M solution in toluene). The reaction was quenched after 16h at rt (75% conversion) and the usual work-up afforded a crude reaction mixture which was purified by preparative TLC using hexanes containing 30% AcOEt as the eluant, (R_f=0.26) to give 33 mg of compound **21** (16% yield).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 5.10-5.65 (m, 2H), 3.78 (t, 2H, *J*=7.1 Hz), 2.92 (dd, 2H, *J*=7.8 and 1.8 Hz), 2.59 (t, 2H, *J*=8.0 Hz), 2.36-2.53 (m, 1H), 1.92-2.14 (m, 2H), 1.63 (d, 3H, *J*=6.0 Hz), 1.20-1.50 (m, 2H), 0.79-0.96 (m, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 174.2, 171.9, 134.6, 126.1, 46.2, 42.9, 41.2, 34.6, 28.6, 18.6, 17.9, 12.4.

The enantiomeric excess of compound **21** (96%) was determined by chiral HPLC (AD-H) (hexanes/IPA=95:5, flow: 1.0 ml/min): t_R 67.9 (minor), t_R 57.5 (major).

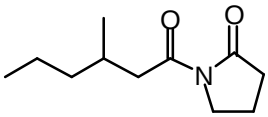


1-(3-Cyclohexenylpentanoyl)pyrrolidin-2-one (22).

Following the general procedure, a solution of the imide **7l** (109.6 mg, 0.5 mmol) in toluene (0.5 ml) was added to a stirred solution of $Cu(OTf)_2$ (2.71 mg, 0.0075 mmol) and (*R*,*S*,*S*)-**1** (8.1 mg, 0.015 mmol) in toluene (1.0 ml). The resulting solution was cooled to -78°C and additioned of Et_2Zn (1.5 mmol, 1.36 ml of a 1.1 M solution in toluene). The reaction was quenched after 48h at rt (38% conversion) and the usual work-up afforded a crude reaction

mixture which was purified by preparative TLC using hexanes containing 30% AcOEt as the eluant, to give compound **22** (7% yield).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 5.36-5.44 (m, 1H), 3.77 (t, 2H, *J*=7.0 Hz), 2.91-2.99 (m, 2H), 2.59 (t, 2H, *J*=8.0 Hz), 2.35-2.47 (m, 1H), 1.19-2.11 (m, 12H), 0.81 (t, 3H, *J*=7.3 Hz).

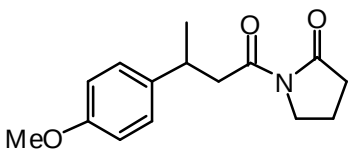


1-(3-Methylhexenoyl)pyrrolidin-2-one (23).

Following the general procedure, a solution of the imide **7a** (90.5 mg, 0.5 mmol) in toluene (0.5 ml) was added to a stirred solution of $Cu(OTf)_2$ (2.71 mg, 0.0075 mmol) and (*R*,*S*,*S*)-**1** (8.1 mg, 0.015 mmol) in toluene (1.0 ml). The resulting solution was cooled to -78°C and additioned of Me_3Al (1.5 mmol, 0.75 ml of a 2.0 M solution in toluene). The reaction was quenched after 5h at 0°C and the usual work-up afforded a crude reaction mixture which was purified by flash chromatography using hexanes containing 40% AcOEt as the eluant (R_f=0.42), to give 69 mg of pure compound **8** (70% yield).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.77 (t, 2H, *J*=7.1 Hz), 2.86 (dd, 1H, *J*=16.1 and 5.7 Hz), 2.66 (dd, 1H, *J*=16.2 and 7.8 Hz), 12.55 (t, 2H, *J*=8.2 Hz), 1.89-2.10 (m, 2H), 1.08-1.40 (m, 4H), 0.78-0.94 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 175.8, 174.4, 46.1, 44.4, 39.7, 34.4, 29.7, 20.6, 20.3, 17.7, 14.7.

The enantiomeric excess of compound **23** (36%) was determined by chiral HPLC (OD-H) (hexanes/IPA=98:2, flow: 1.0 ml/min): t_R 38.4 (minor), t_R 41.0 (major).



1-[3-(4-Methoxyphenyl)butanoyl]pyrrolidin-2-one (24).

Following the general procedure, a solution of the imide **7f** (122.5 mg, 0.5 mmol) in toluene (0.5 ml) was added to a stirred solution of $Cu(OTf)_2$ (2.71 mg, 0.0075 mmol) and (*R*,*S*,*S*)-**1** (8.1 mg, 0.015 mmol) in toluene (1.0 ml). The resulting solution was cooled to -78°C and additioned of Me_3Al (1.5 mmol, 0.75 ml of a 2.0 M solution in toluene). The reaction was quenched after 4h at 0°C and the usual work-up afforded a crude reaction mixture which was subjected to flash chromatography using hexanes containing 40% as the eluant (R_f=0.23) to give 85 mg of pure **24** (65% yield).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.07-7.23 (m, 2H), 6.74-6.86 (m, 2H), 3.59-3.85 (m, 2H), 3.75 (s, 3H), 3.18-3.41 (m, 2H), 2.96-3.15 (m, 1H), 2.46-2.59 (m, 2H), 1.81-2.07 (m, 2H), 1.27 (d, 3H, *J*=6.6 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 175.9, 173.6, 158.5, 138.9, 128.5, 114.3, 55.8, 46.0, 45.6, 35.4, 34.3, 22.8, 17.7.

The enantiomeric excess of compound **25** (20%) was determined by chiral HPLC (AD-H) (hexanes/IPA=92:8, flow: 0.8ml/min): t_R 32.8 (major), t_R 20.7 (minor).

Conversion to the corresponding carboxylic acids of crotonic and cinnamic adducts: Determination of the absolute sense of induction.

The absolute configuration was determined through conversion to **3-methylpentanoic acid** (**3.15a**) which is a known compound:[5]

A solution of **6b** (0.2 mmol) in MeOH (2.0 ml) containing concentrated HCl (0.08 ml), was refluxed for 12h and then (0.1 g) in H_2O (0.2 ml) was added and refluxed again for 5h. After quenching with HCl 10% and extraction of ther acqueous phase with CH_2Cl_2 and AcOEt, the collected organic phases were dried and evaporated under reduced pressure to give a crude reaction mixture (14.1 mg) whith spectral data corresponded to those reported in literature. The measured optical rotatory power ($[\alpha]^{20}_D$=-1.18 (c=0.5, MeOH) was compared to those reported on literature and corrisponded to absolute configuration *R*.

The absolute configuration was determined on **3-phenylpentanoic acid**:[6] a solution of **11** (0.5 mmol) in MeOH (5 ml) containing concentrated HCl (0.2 ml)) was refluxed for 12h and then KOH (0.25 g) in H_2O (1.0 ml) was added and refluxed again for 5h. After quenching with HCl 10% and extraction of the acqueous phase with CH_2Cl_2 and AcOEt, the collected organic phases were dried and evaporated under reduced pressure to give a crude reaction mixture which was subjected to flash cromatography (CH_2Cl_2:MeOH=9.5:5) to give 36 mg of the pure acid. The measured optical rotatory power ($[\alpha]^{20}_D$=+20 (c=0.5, C_6H_6) was compared to that reported in literature which corresponded to absolute configuration *S*.

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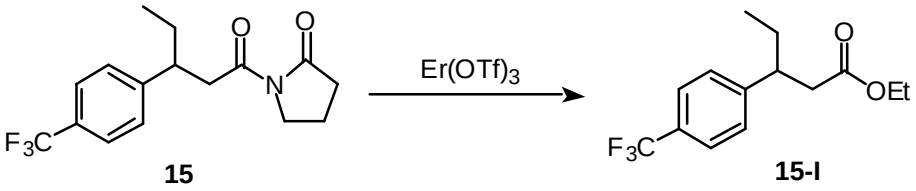
[5] (a) Tomioka, K.; Suenaga, T.; Koga, K. *Tetrahedron Lett.* **1986**, *27*, 369. (b) Meyers, A. I.; Kamata, K. *J. Am. Chem. Soc.* **1976**, 2290.

[6] Meyers, A. I.; Smith, R. K.; Whitten, C. E. *J. Org. Chem.* **1979**, *44*, 2250.

$Er(OTf)_3$-catalyzed conversion to ethyl esters.[7]

Scheme 2.



15 **15-I**

Ethyl 3-*p*-trifluoromethylphenil-pentanoate (15-I).

To a solution of **15** (60 mg, 0.19 mmol) in EtOH (1.5 ml) was added $Er(OTf)_3$ and the reaction was stirred at 4°C for 36h. The solution was then diluted with Et_2O and filtered through SiO_2 eluting with Et_2O and concentrated under reduce pressure to give **15-I** as a liquid (50 mg, 96% yield). ^1H NMR (200 MHz, $CDCl_3$) δ: 7.35-7.47 (m, 2H), 7.11-7.22 (m, 2H), 3.80 (q, 2H, *J*=7.1 Hz), 2.87-3.05 (m, 1H), 2.50 (dd, 1H, *J*=15.2 and 6.7 Hz), 2.40 (dd, 1H, *J*=15.2 and 8.7 Hz), 1.40-1.71 (m, 2H), 1.00 (t, 3H, *J*=7.1 Hz), 0.67 (t, 3H, *J*=7.3 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 172.7, 148.7, 128.6 (2C), 126.0 (2C), 61.0, 44.4, 41.7, 29.7, 14.7, 12.5.

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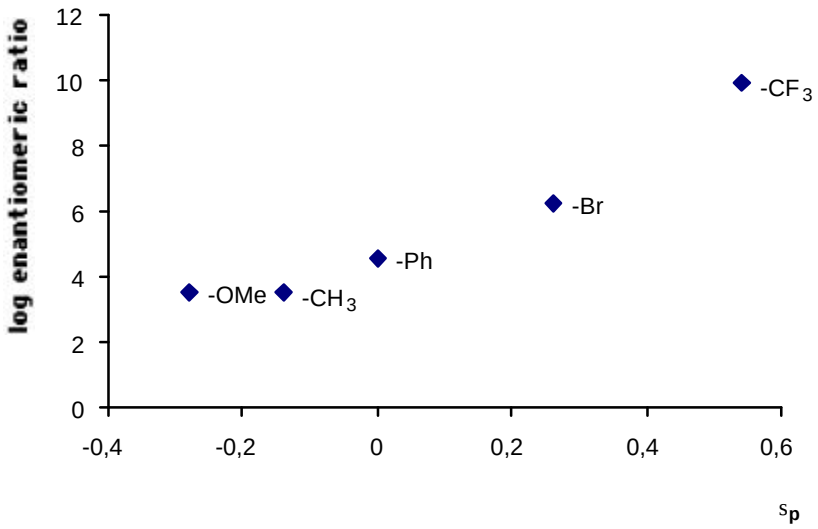
[7] Vanderwal, C.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2004**, *126*, 14724.

Hammett Plot of log enantiomeric ratio *vs* sigma-*p* substituent values.



-R	***ee*%**
-OMe	94.2
-Me	94.3
-H	98.0
-Br	99.6
$-CF_3$	99.9