Suppoting information for

Lewis acid enabled copper catalysed asymmetric synthesis of chiral β-substituted amides

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1. General experimental information

All reactions using oxygen- and/or moisture-sensitive materials were carried out with anhydrous solvents (*vide infra*) under a nitrogen atmosphere using oven-dried glassware and standard Schlenk techniques. Reactions were monitored by ^{1}H NMR. Purification of the products was performed by column chromatography using Merck 60 Å 230-400 mesh silica gel. Components were visualized by UV and $KMnO_4$ staining. NMR data was collected on Varian VXR400 (^{1}H at 400.0 MHz; ^{13}C at 100.58 MHz) equipped with a 5 mm *z*-gradient broadband probe. Chemical shifts are reported in parts per million (ppm) relative to residual solvent peak ($CDCl_3$, ^{1}H: 7.26 ppm; ^{13}C: 77.16 ppm; D_2O, ^{1}H: 4.79 ppm). Coupling constants are reported in Hertz. Multiplicity is reported with the usual abbreviations (s: singlet, br s: broad singlet, d: doublet, dd: doublet of doublets, t: triplet, tdt: triplet doublet of triplets, tqt: triplet quartet of triplets, ttq: triplet triplet of quartets, q: quartet, quint: quintet, sex: sextet, hept: heptet, m: multiplet, if an apparent multiplicity is observed the actual multiplicity will be noted in brackets). Variable-temperature NMR spectra were acquired on a Bruker Avance III spectrometer paired with an Ascend 400 MHz magnet and BBFO dual-resonance probe. All temperatures were calibrated prior to acquisition with an external pure MeOH reference. ^{1}H TOCSY and ROESY experiments were carried out with 9.6 kHz and 4.54 kHz spinlocking fields, and the ROESY mix time was set to 400 ms. ^{1}H-^{19}F HOESY experiments utilized a mix time of 350 ms. ^{1}H-^{13}C HSQCED spectra were recorded with the $^{1}J_{CH}$ constant set to 145 Hz while the ^{1}H-^{13}C and ^{1}H-^{29}Si HMBC spectra were recorded with a $^{n}J_{XH}$ constant set to 8 Hz and 10 Hz, respectively. 1D ^{19}F spectra were acquired with inverse-gated ^{1}H decoupling. 1D ^{31}P spectra were acquired with ^{1}H decoupling during the relaxation delay and acquisition time and thus are non-quantitative. Exact mass spectra were recorded on a LTQ Orbitrap XL apparatus with ESI ionization. Enantiomeric excess (*ee*) were determined by chiral HPLC analysis using a Shimadzu LC-10AD*VP* HPLC equipped with a Shimadzu SPD-M10A*VP* diode array detector.

2. Chemicals

Unless otherwise indicated, reagents and substrates were purchased from commercial sources and used as received. Solvents not required to be dry were purchased as technical grade and used as received. Dry solvents were freshly collected from a dry solvent purification system prior to use. Inert atmosphere experiments were performed with standard Schlenk techniques with dried (P_2O_5) nitrogen gas. Grignard reagents were purchased from Sigma-Aldrich (EtMgBr, MeMgBr, PhMgBr (3.0 M in Et_2O), *i*ButMgBr, *i*PentMgBr, HexMgBr, cyclopentylMgBr (2.0 M in Et_2O). All other Grignard reagents were prepared from the corresponding alkyl bromides and Mg activated with I_2 in Et_2O: phenylethylMgBr (2.6 M in Et_2O), pent-4-en-1-ylMgBr (1.7 M in Et_2O) and (4-chlorobutyl)MgBr (1.3 M in Et_2O). All Grignard reagents were titrated by NMR before use. Unless otherwise noted enamides substrates were prepared following the literature methods (*vide infra*). Chiral ligands (**L1-L4**) were purchased from Sigma Aldrich and Solvias. All reported compounds were characterized by ^1H and ^{13}C NMR and compared with literature data. All new compounds were fully characterized by ^1H and ^{13}C NMR and HRMS techniques.

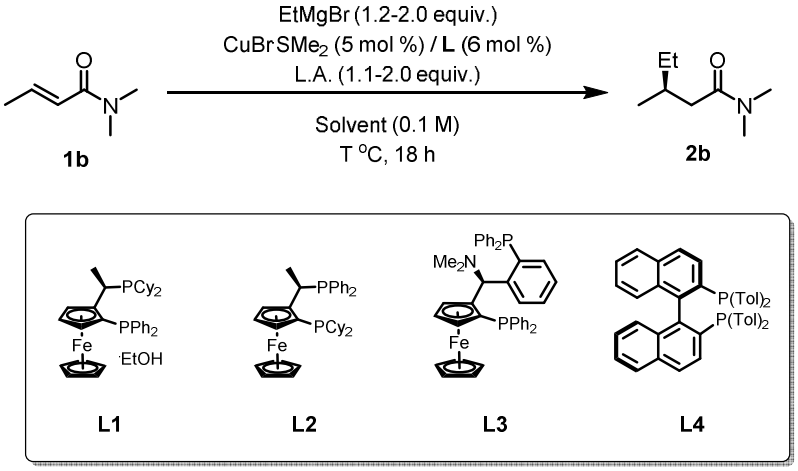
3. Determination of absolute configuration

The absolute configuration was determined by comparison of the optical rotation for the compounds **2b** ($[\alpha]_D^{20}$ = + 10.4 (*c* 1.4, $CHCl_3$), *S*-configuration) and the ester derived from **2m** ($[\alpha]_D^{20}$ = + 16.1 (*c* 1.43, $CHCl_3$), *S*-configuration) with reported data (K. Biswas and S. Woodward, *Tetrahedron: Asymmetry*, **2008**, *19*, 1702; $[\alpha]_D^{20}$ = - 5.6 (*c* 1.5, $CHCl_3$), *R*-configuration) and (C.-J. Hou, W.-L. Gou, X.-P. Hu, J. Deng and Z. Zheng. *Tetrahedron: Asymmetry*, **2011**, *22*, 195-199; $[\alpha]_D^{20}$ = + 7.8 (*c* 1.18, $CHCl_3$), *S*-configuration), respectively. The absolute configurations of other compounds were assigned by analogy.

4. Optimization of reaction conditions for enantioselective conjugate addition to enamides

Optimisation studies were carried out with two enamide substrates **1a** and **1b.**

Table S1. Screening of chiral ligands, solvents, LA for copper 1,4-addition of EtMgBr to acyclic α,β-unsaturated amide **1b**.

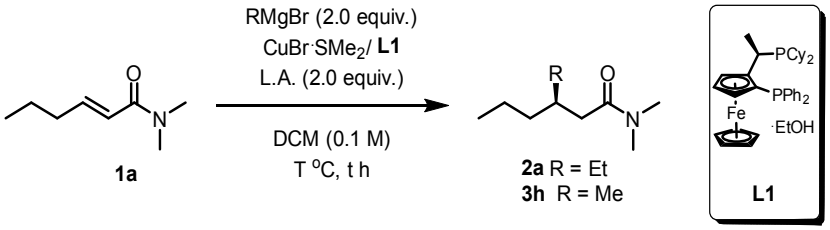


Entry	L	LA	Solvent	T[°C]	Yield [%][a]	*ee* [%][b]
1	**L2**	-	Et_2O	–78	9[c,d]	-
2	-	$BF_3{\cdot}Et_2O$	Et_2O	–78	0[c,e]	-
3	**L2**	$BF_3{\cdot}Et_2O$	Et_2O	–78	45[e]	33
4	**L2**	$BF_3{\cdot}Et_2O$	MTBE	–78	39[f]	23
5	**L2**	$BF_3{\cdot}Et_2O$	DCM	–78	62[f]	24
6	**L1**	$BF_3{\cdot}Et_2O$	DCM	–78	57[f]	90
7	**L3**	$BF_3{\cdot}Et_2O$	DCM	–78	40[f]	84
8	**L4**	$BF_3{\cdot}Et_2O$	DCM	–78	45[f]	65
9	**L1**	TMSOTf	DCM	–78	60[g]	94
10	**L1**	$BF_3{\cdot}Et_2O$ / TMSOTf	DCM	–78	66[g]	92

11	**L1**	TMSCl	DCM	−78	<7[c,h]	-
12	**L1**	$BF_3{\cdot}Et_2O$	DCM	−78	79[g]	94
13	**L1**	$BF_3{\cdot}Et_2O$	DCM	−60	57[g]	92

Reaction conditions: 0.2 mmol of **1b** in 2 mL of solvent, $CuBr{\cdot}SMe_2$ (5 mol%), ligand **L1** (6 mol%), LA (1.1-2.0 equiv.), EtMgBr (3.0 M in Et_2O, 1.1-2.0 equiv.), T (°C), 18 h. [a] Yield of isolated **2b**. [b] Enantiomeric excesses were determined by HPLC on a chiral stationary phase. [c] This value is related to the conversion. [d] 1.5 equiv. of EtMgBr were used in this case. [e] 1.1 equiv. of $BF_3{\cdot}Et_2O$ and 1.2 equiv. of EtMgBr were used in this case. [f] 1.1 equiv. of $BF_3{\cdot}Et_2O$ and 2.0 equiv. of EtMgBr were used in this case. [g] 2.0 equiv. of LA and 2.0 equiv. of EtMgBr were used in this case. [h] 2.0 equiv. of TMSCl and 1.5 equiv. of EtMgBr were used in this case.

Table S2. Optimization data for the Cu- conjugate addition of EtMgBr and MeMgBr to enamide **1a**



Entry	**1a** [mmol]	**L1/Cu** [mol%]	**RMgBr**	**LA**	T[°C]	t[h]	Yield [%][a]	*ee* [%][b]
1	0.2	-	EtMgBr	-	−78	3	0[c]	-
2	0.2	5[d]	EtMgBr	-	−78	1	0[c]	-
3	0.2	5	EtMgBr	-	−78	1	0[c]	-
4	0.2	-	EtMgBr	-	0	5	97[c]	-
5	0.2	5[d]	EtMgBr	-	0	5	42[c]	-
6	0.2	5	EtMgBr	-	0	5	61	*rac.*
7	0.2	-	EtMgBr	-	−50	18	12[c]	-
8	0.2	5	EtMgBr	-	−50	18	20[c]	*5*
9	0.2	-	EtMgBr	$BF_3{\cdot}Et_2O$	−78	1	0[c]	-
10	0.2	-	EtMgBr	TMSOTf	−78	1	50[c]	-
11	0.2	5	EtMgBr	$BF_3{\cdot}Et_2O$	−78	18	73	97

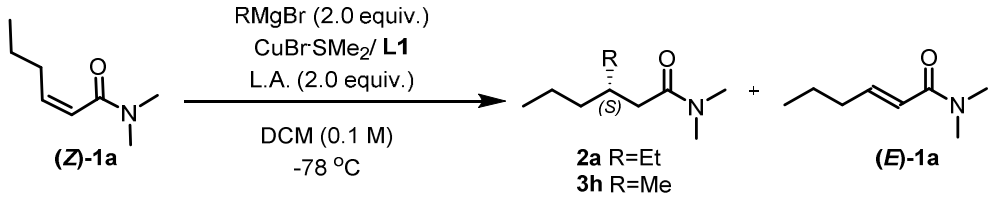
12	0.2	5	EtMgBr	TMSOTf	−78	18	92	92
13	0.2	5	MeMgBr	$BF_3{\cdot}Et_2O$	−78	18	50	99
14	0.2	5	MeMgBr	TMSOTf	−78	18	77	99
15	0.2	5	EtMgBr	$BF_3{\cdot}Et_2O$	−78	18	69[e]	96
16	0.2	100	EtMgBr	-	−30	18	4[c,f]	64
17	0.2	5	MeMgBr	TMSOTf	−50	18	93	99
18	0.2	5	EtMgBr	TMSOTf	25	18	79	76
19	0.2	10	EtMgBr	TMSOTf	0	2	92	93
20	0.5	1	MeMgBr	TMSOTf	0	2	80	95
21	0.2	5	EtMgBr	$BF_3{\cdot}Et_2O$	−78	18	78[g]	96
22	1.0	1	EtMgBr	$BF_3{\cdot}Et_2O$	−78	18	78	98
23	71.0	5	MeMgBr	TMSOTf	0	2	93	96
24	1.0	5	EtMgBr	$BF_3{\cdot}Et_2O$	−78	18	89	96

Reaction conditions: 0.2 mmol of **1a** in 2 mL of DCM, $CuBr{\cdot}SMe_2$ (5 mol%), ligand **L1** (6 mol%), LA (2.0 equiv.), RMgBr (3.0 M in Et_2O, 2.0 equiv.), T (°C), t (h). [a] Yield of isolated **2a**. [b] Enantiomeric excesses were determined by HPLC on a chiral stationary phase. [c] This value is related to the conversion. [d] Without ligand **L1**. [e] $CuBr{\cdot}SMe_2$ (5 mol%) and ligand **L1** (6 mol%) in 2 mL of DCM for 20 min. $BF_3{\cdot}Et_2O$ (2.0 equiv.) was added at −78 °C. After 20 min., **1a** (0.2 mmol) was added at −78 °C. After 20 min., EtMgBr (3.0 M in Et_2O, 2.0 equiv.) was added. [f] With stoichiometric amount of Cu(I)/**L1** complex. [g] With recovered Cu(I)/**L1** complex.

5. (E)/(Z)-Isomerization experiments

A set of experiments was carried out for addition of EtMgBr and MeMgBr to (*E*)-**1a** and (*Z*)-**1a** in the presence of either $BF_3{\cdot}Et_2O$ or TMSOTf at −78 °C (Table S3). The **(*Z*)/(*E*)** ratio of **1a** in the resulting crude mixture was determined by ^1H NMR. No isomerization product to the more stable (*E*)-**1a** was obtained using TMSOTf (entries 3, 9, 11, 13, 16 and 20) or with a little conversion up to 2.5% in the presence of $BF_3{\cdot}Et_2O$ (entries 2, 8, 10, 12, 14 and 18). CA products with opposite absolute configuration were obtained from (*E*)-**1a** and (*Z*)-**1a** using chiral catalyst of the same configuration.

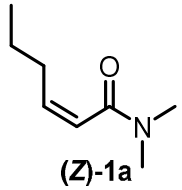
Table S3. Cu- CA of EtMgBr and MeMgBr to (E)- or (Z)-**1a**.



Entry	**1a**	**L1/Cu** [mol%]	**LA**	**RMgBr**	(*Z*):(*E*):**2a**[a] (*Z*):(*E*):**3h**[a]	*ee* [%][b]	Conf **2a** or **3h**
1	***Z***	5	-	-	100:0:-	-	-
2	***Z***	-	$BF_3{\cdot}Et_2O$	-	100:0:-	-	-
3	***Z***	-	TMSOTf	-	100:0:-	-	-
4	***Z***	-	-	MeMgBr	100:0:0	-	-
5	***Z***	-	-	EtMgBr	100:0:0	-	-
6	***Z***	5	-	MeMgBr	100:0:0	-	-
7	***Z***	5	-	EtMgBr	100:0:0	-	-
8	***Z***	-	$BF_3{\cdot}Et_2O$	MeMgBr	100:0:0	-	-
9	***Z***	-	TMSOTf	MeMgBr	100:0:0	-	-
10	***Z***	-	$BF_3{\cdot}Et_2O$	EtMgBr	100:0:0	-	-
11	***Z***	-	TMSOTf	EtMgBr	98:0:2	-	-
12	***Z***	5	$BF_3{\cdot}Et_2O$	-	97.5:2.5:-	-	-
13	***Z***	5	TMSOTf	-	100:0:-	-	-
14	***Z***	5	$BF_3{\cdot}Et_2O$	MeMgBr	75.8:1.6:22.6	99	**(*S*)-3h**
15	***E***[c]	5	$BF_3{\cdot}Et_2O$	MeMgBr	-:35:65	99	**(*R*)-3h**
16	***Z***	5	TMSOTf	MeMgBr	93:0:7	46	**(*S*)-3h**
17	***E***[c]	5	TMSOTf	MeMgBr	-:8:92	99	**(*R*)-3h**
18	***Z***	5	$BF_3{\cdot}Et_2O$	EtMgBr	37.4:1.6:61	96	**(*S*)-2a**
19	***E***[c]	5	$BF_3{\cdot}Et_2O$	EtMgBr	-:6:94	97	**(*R*)-2a**
20	***Z***	5	TMSOTf	EtMgBr	70:0:30	33	**(*S*)-2a**
21	***E***[c]	5	TMSOTf	EtMgBr	-:6:94	92	**(*R*)-2a**

Reaction conditions: 0.16 mmol of (*Z*)-**1a** in 1.6 mL of DCM, $CuBr{\cdot}SMe_2$ (5 mol%), ligand **L1** (6 mol%), LA (2.0 equiv.), RMgBr (3.0 M in Et_2O, 2.0 equiv.), −78 °C. [a] The ratio between (*Z*)-**1a**:(*E*)-**1a**:**2a** or (*Z*)-**1a**:(*E*)-**1a**:**3a** was determined by ^{1}H-NMR. [b] Enantiomeric excesses were determined by HPLC on a chiral stationary phase. [c] 0.2 mmol of (*E*)-**1a** were used in this case.

(*Z*)-*N*,*N*-Dimethylhex-2-enamide (1a)



To a solution of *N*,*N*-dimethylacetamide (465 μL, 5 mmol) in dry THF (15 mL) cooled to −78 °C, a 1.0 M solution of LDA in THF (4.5 mmol, 4.5 mL) was slowly added and the mixture was stirred for 30 minutes at −78 °C. Then, TMSCl (571 μL, 4.5 mmol) was added and the mixture was stirred for 1 h at 0 °C and, afterwards, cooled down again to −78 °C. A 1.0 M solution of LDA in THF (4.5 mmol, 4.5 mL) was slowly added and the reaction mixture was stirred for 30 minutes at −78 °C. Finally, butyraldehyde (405 μL, 4.5 mmol) was added and the mixture was stirred overnight at −78 °C. The reaction was quenched by addition of MeOH (1.0 mL) and 1.0 M HCl aqueous solution (10 mL), stirred at room temperature for 45 minutes and extracted with Et_2O (15 mL × 3). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (SiO_2, pentane:Et_2O 1:1) to afford product **1a** as a colorless oil [39% yield].

^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.95 (dt, *J* = 11.7, 1.3 Hz, 1H, C*H*=CH), 5.89 (dt, *J* = 11.7, 7.3 Hz, 1H, CH=C*H*), 3.00 (s, 6H, N(C*H*$_3$)$_2$), 2.31 (dq, *J* = 7.3, 1.3 Hz, 2H, C*H*$_2$CH=CH), 1.44 (sext (tq), *J* = 7.3 Hz, 2H, $CH_2CH_2CH_3$), 0.92 (t, *J* = 7.3 Hz, 3H,CH_2CH_3).

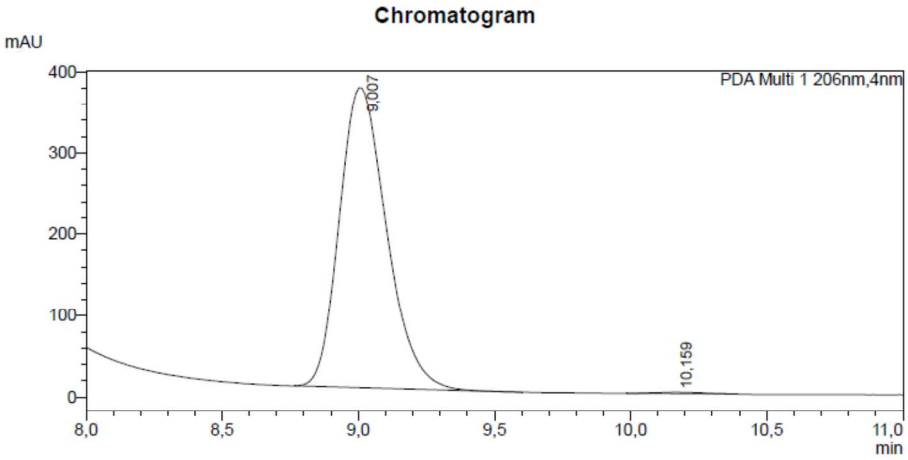
^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.0, 141.0, 122.0, 37.6, 35.1, 31.3, 22.3, 13.8.

Chiral HPLCs of the products from (*Z*)/(*E*) isomerization experiments of (*Z*)-1a

With (*Z*)-1a, catalyst, LA and MeMgBr:

HPLC: Chiracel-OBH, *n*-heptane/*i*-PrOH 90:10, 0.5 mL/min, 40 °C, detection at 206 nm. Retention time (min): 9.0 (major) and 10.1 (minor).

*a) With (Z)-**1a**, **L1**-CuBr, BF_3·Et_2O and MeMgBr:* (*S*)-**3h** [99% ee].

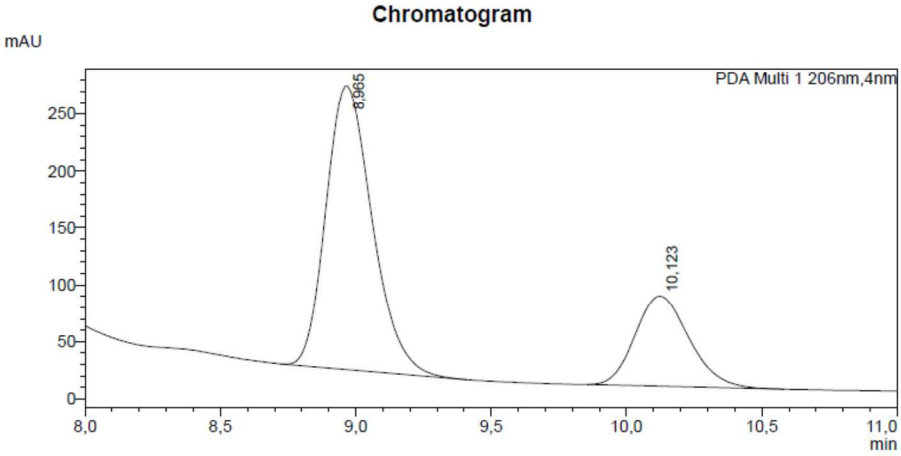


Peak Table

PDA Ch1 206nm

Peak#	Ret. Time	Area	Height	Conc.
1	9,007	4444014	368946	99,599
2	10,159	17895	1603	0,401
Total		4461909	370549	

b) *With (Z)-**1a**, **L1**-CuBr, TMSOTf and MeMgBr:* (*S*)-**3h** [46% *ee*].

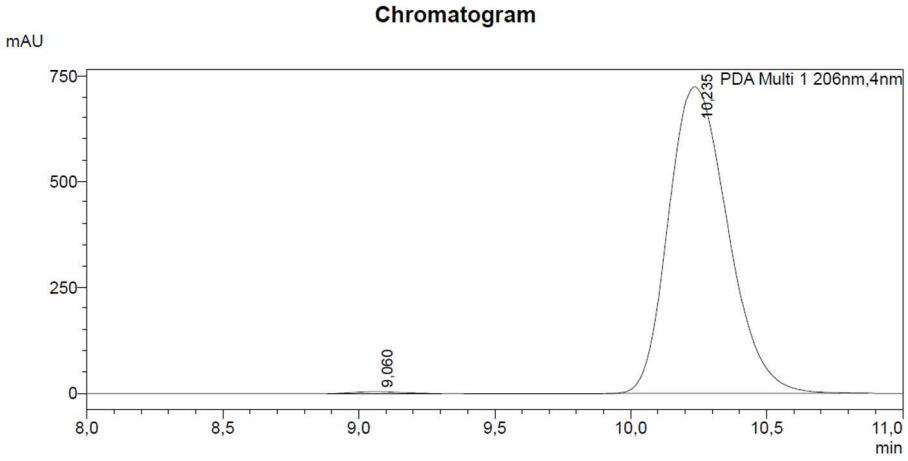


Peak Table

PDA Ch1 206nm

Peak#	Ret. Time	Area	Height	Conc.
1	8,965	2962641	248982	73,087
2	10,123	1090954	79054	26,913
Total		4053595	328036	

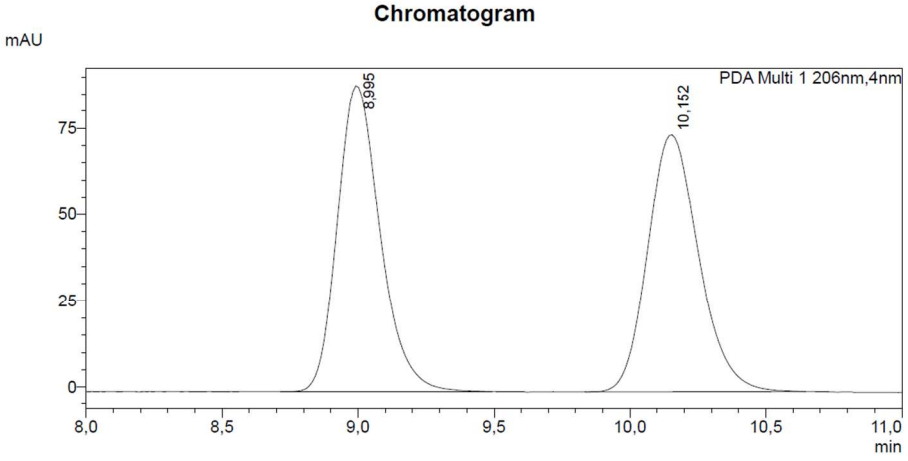
c) *With (E)-**1a**, **L1**-CuBr, BF_3·Et_2O and MeMgBr:* (*R*)-**3h** [99% *ee*].



Peak Table

PDA Ch1 206nm

Peak#	Ret. Time	Area	Height	Conc.
1	9,060	47641	4345	0,432
2	10,235	10974951	724084	99,568
Total		11022592	728429	



Peak Table

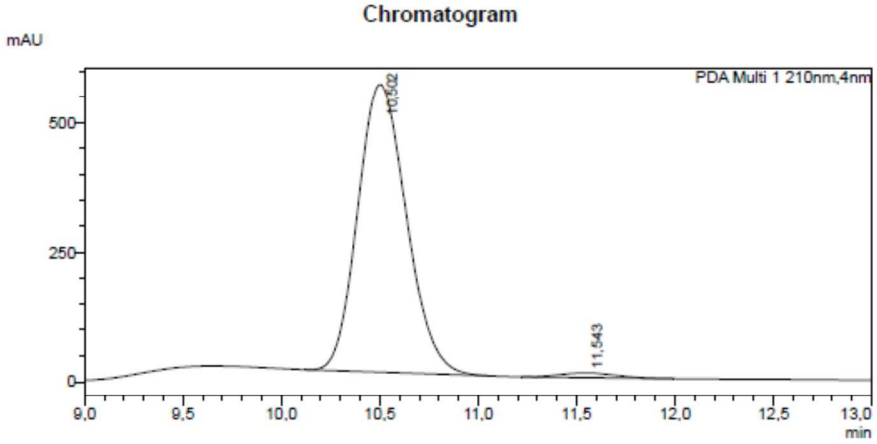
PDA Ch1 206nm

Peak#	Ret. Time	Area	Height	Conc.
1	8,995	972588	88794	49,971
2	10,152	973703	74508	50,029
Total		1946291	163302	

With (*Z*)-1a, catalyst, LA and EtMgBr:

HPLC: Chiracel-OBH, *n*-heptane/*i*-PrOH 95:5, 0.5 mL/min, 40 °C, detection at 210 nm. Retention time (min): 10.5 (major) and 11.5 (minor).

*a) With (Z)-**1a**, **L1**-CuBr, $BF_3{\cdot}Et_2O$ and EtMgBr:* (*S*)-**2a** [96% ee].

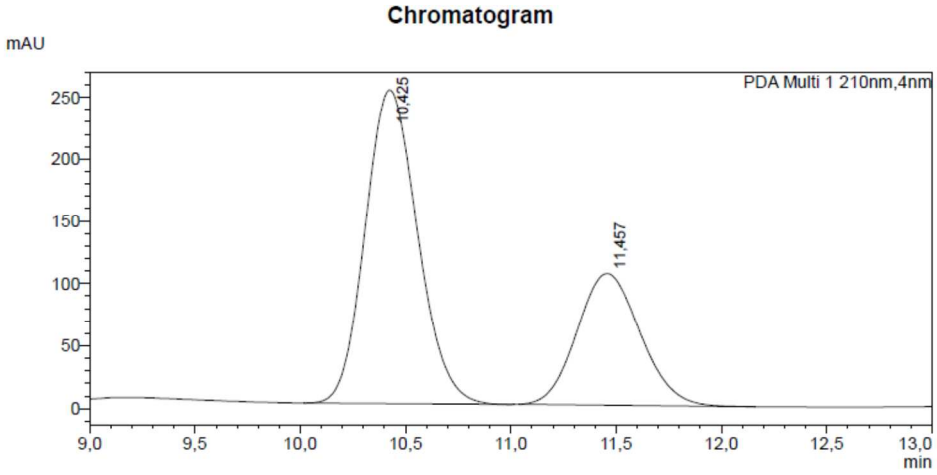


Peak Table

PDA Ch1 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	10,502	9561513	555580	98,228
2	11,543	172532	8964	1,772
Total		9734045	564544	

*b) With (Z)-**1a**, catalyst, TMSOTf and EtMgBr:* (S)-**2a** [33% ee].

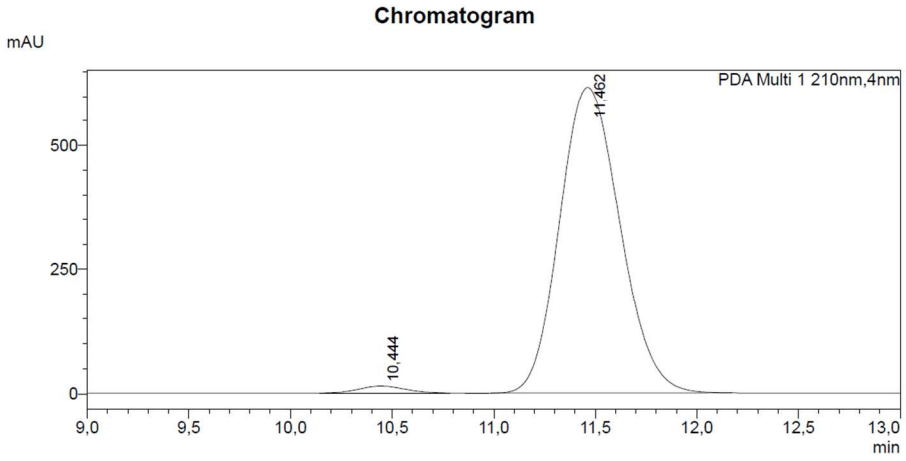


Peak Table

PDA Ch1 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	10,425	4358835	252026	66,473
2	11,457	2198443	105316	33,527
Total		6557277	357342	

*c) With (E)-**1a**, **L1**-CuBr, BF_3·Et_2O and EtMgBr:* (*R*)-**2a** [97% ee].



Peak Table

PDA Ch1 210nm

Peak#	Ret. Time	Area	Height	Conc.
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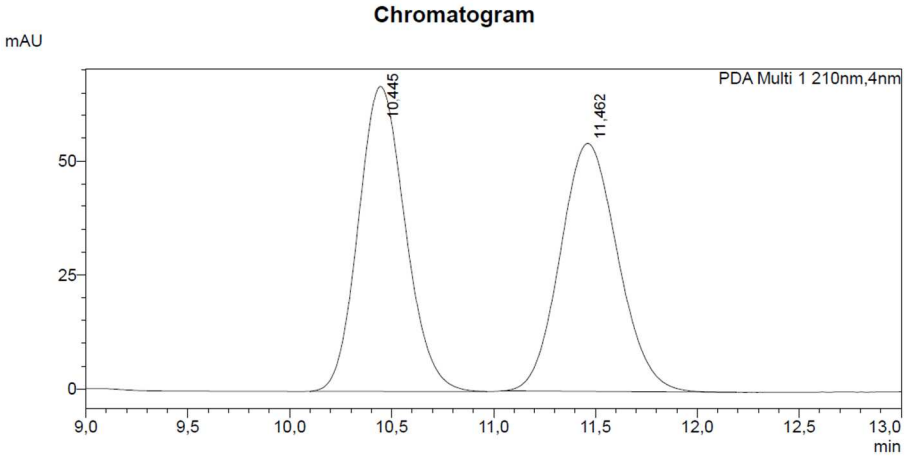
2	11,462	12717057	616670	98,320
Total		12934322	630581	



Peak Table

PDA Ch1 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	10,445	1068987	66946	50,040
2	11,462	1067275	54327	49,960
Total		2136262	121273	

6. NMR spectroscopy based mechanistic studies

Transmetallated species 8

Transmetallated species **8**, which initiates the catalytic cycle (see Figure 3, main manuscript), were prepared by addition of MeMgBr to **L1**-CuBr complex and analyzed by ^{1}H and ^{31}P NMR spectroscopy. A 3 M MeMgBr solution in Et_2O (20 μL, 0.06 mmol) was added to a solution of **L1**-CuBr complex (11 mg, 0.015 mmol) in CD_2Cl_2 (0.6 mL) in a dry NMR tube at −78 °C and the resulting mixture was immediately measured by NMR spectroscopy at −80 °C. Two different transmetallated species (**A** and **B**, Figures S1 and S2) were detected. Both species present methyl moieties coupled with both phosphines with the same pattern in the ^{1}H-^{31}P HMBC spectrum (Figure S3). For both species the integration indicates that only 1 methyl group is bound to the copper (based on the 1:1 ratio measured by comparison of the Me signal with signals from the ferrocene). For these reasons both the species are assumed to be the two possible diastereoisomers of the tetrahedral alkylcuprate **10**[1] (species **B**: -0.28 ppm, dd, Cu*Me* in ^{1}H NMR; 14.8 (d, *J*=155.5 Hz), -18.0 (d, *J*=155.5 Hz) in ^{31}P NMR and species **A**: -0.37 ppm, dd, Cu*Me* in ^{1}H NMR; 7.5 (d, *J*=144.3 Hz), -26.4 (d, *J*=144.3 Hz) in ^{31}P NMR.

[1] The transmetallated species 8 was also formed in our previous work (see ref. 22 in the main manuscript).At that time our understanding was that species **A** and **B** are structurally different. However, based on the additional data in this work we have redefined the structure of species **8** and propose that both species **A** and **B** are diastereoisomers of the transmetallated species **8**. Their catalytic activity is identical as well.

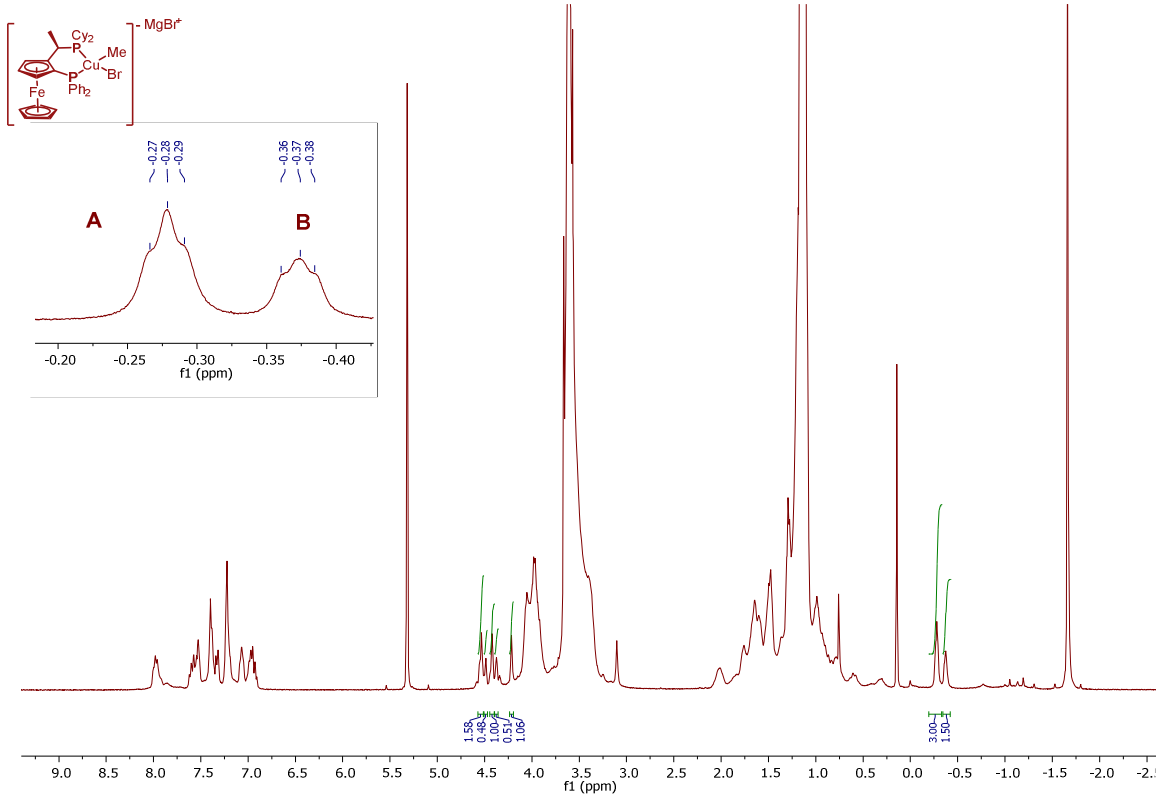


Figure S1: ^{1}H NMR spectrum of the transmetallated species **8**.

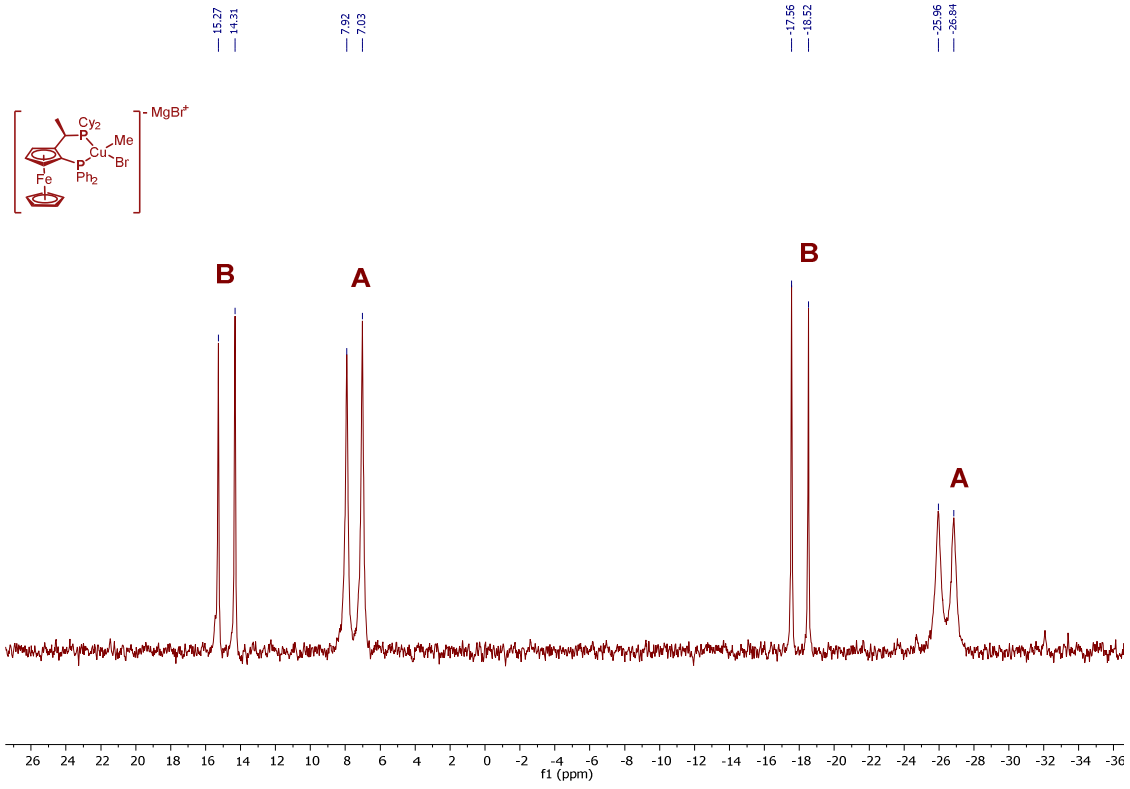


Figure S2: ^{31}P NMR spectrum of the transmetallated species **8**.

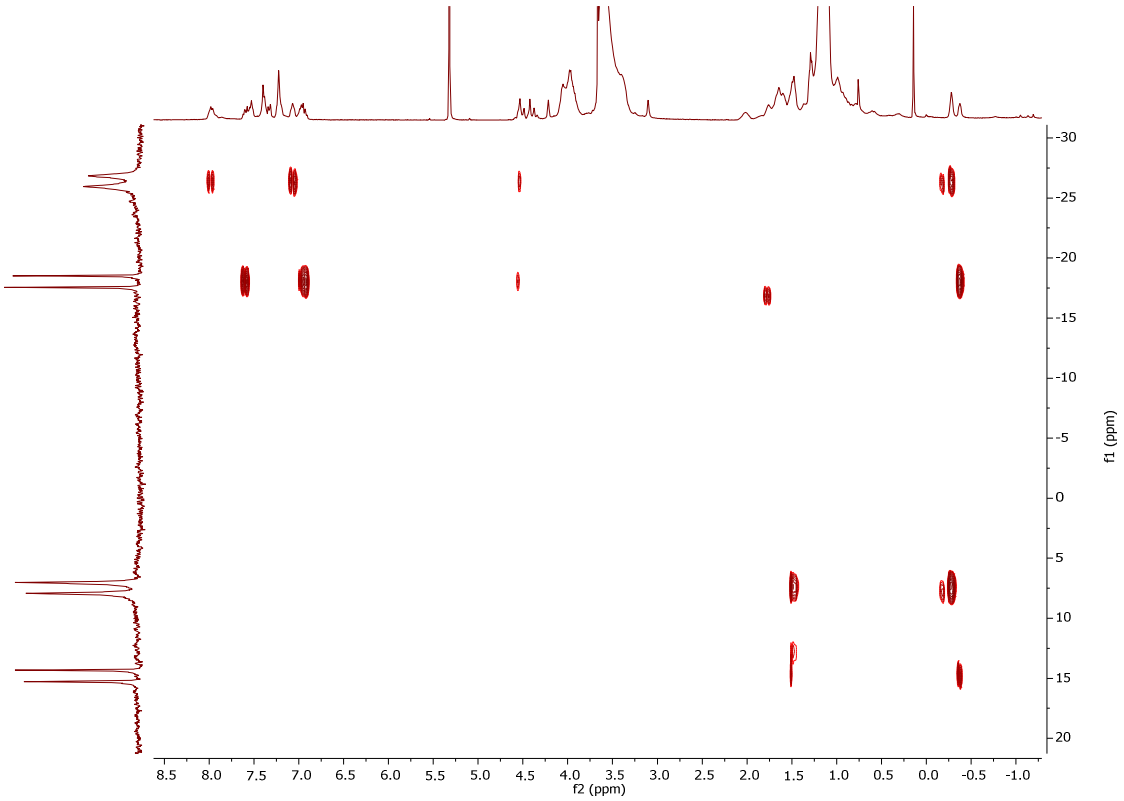


Figure S3: ^{1}H-^{31}P HMBC spectrum of the transmetallated species **8**. Similar pattern of coupling with the phosphines is observed for both species.

Stability of L1-CuBr and transmetallated species 8 towards Lewis acids

With the aim to investigate the interactions between Lewis acids, **L1**-CuBr and transmetalated species **8** a set of experiments was carried out. **L1**-CuBr complex (5.9 mg, 0.08 mmol) was dissolved in CD_2Cl_2 (0.6 mL) in a dry NMR tube under a N_2 atmosphere and cooled down to −78 °C. TMSOTf (15 µL, 0.08 mmol) or $BF_3{\cdot}Et_2O$ (10 µL, 0.08 mmol) was added to the complex and the resulting mixture was measured by ^{1}H and ^{31}P NMR spectroscopy at −60 °C. **L1**-CuBr complex (doublets, see top panels in Fig. S4) disappeared in both cases and unidentified phosphine species were formed: (singlets at 27.1 and 4.4 ppm; with TMSOTf left column, panel (c) of Fig. S4) , and singlets at 31.9, 0.5 and -0.3 ppm; with $BF_3{\cdot}Et_2O$ (right column, panel (d) of ,Fig. S4) spectrum **D**, figure S4). Observing phosphorus signals as singlets instead of

the initial doublets indicates detachment of, at least, one of the phosphine moieties of the **L1**-CuBr complex. Formation of new **L1**-CuBr complex with monodentate instead of bidentate coordination cannot be excluded either. After cooling down again to −78 °C, a 3 M MeMgBr solution in Et_2O (67 µL, 0.2 mmol) was added and the mixture was measured by ^{1}H and ^{31}P NMR spectra NMR spectroscopy at −60 °C. Importantly the transmetallated **L1**-CuBr species **8** was observed in both cases, , although in the case of TMSOTf only isomer **A** (left column, panel (e) of Fig. S4) and in the case of $BF_3{\cdot}Et_2O$ only isomer **B** among other signals (right column, panel (f) of Fig. S4).

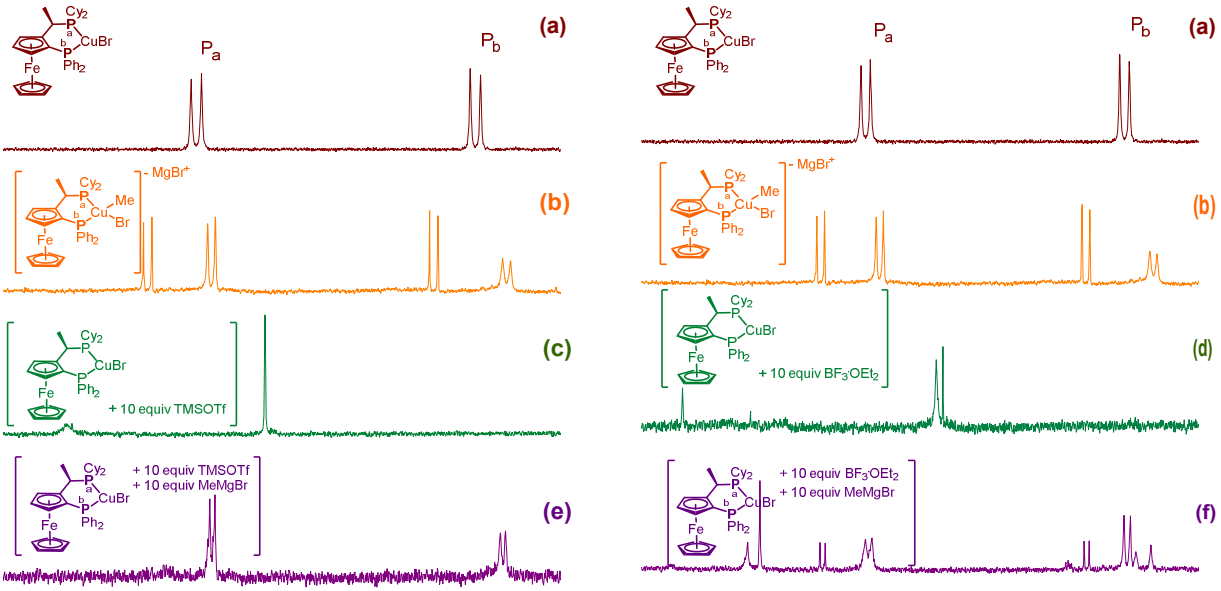


Figure S4: ^{31}P NMR spectra of combinations of **L1**-CuBr, MeMgBr and LA. Left column: from top to bottom the panels show the spectra of (a) the **L1**-CuBr complex, (b) the transmetallated species **8** (with **A** and **B** diastereoisomers), (c) **L1**-CuBr after adding 10 equiv. of TMSOTf, (e) the result of adding 10 equiv. of MeMgBr to (c) leading to the formation of species **A**. Right column: same as left column, but using $BF_3{\cdot}Et_2O$ instead of TMSOTf. (a) the **L1**-CuBr complex, (b) the transmetallated species **8** (with **A** and **B** diastereoisomers), (d) **L1**-CuBr after adding 10 equiv. of $BF_3{\cdot}Et_2O$, (f) the result of adding 10 equiv. of MeMgBr to (d) leading to the formation of species **A** and **L1**-CuBr together with decomposed complex peaks from (d).

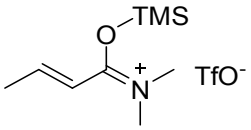
Similarly, the addition of TMSOTf or $BF_3{\cdot}Et_2O$ to the transmetallated species **8** (panels (b) in Fig. S4) does not change the structure of the complex and the same NMR spectra were obtained (not depicted).

Lewis acid-enamide binding

In order to determine the activation mode of enamide **1b** in the presence of a Lewis acid , a set of experiments was carried out. Complexes of enamide/TMSOTf, enamide/$BF_3 \cdot Et_2O$ and enamide/MeMgBr were prepared separately and analysed by NMR spectroscopy.

TMS-amide complex

TMSOTf (16 μL, 0.088 mmol) was added to a solution of enamide **1b** (10 mg, 0.088 mmol) in CD_2Cl_2 (0.6 mL) in a dry NMR tube at −78 °C under N_2 atmosphere, leading to instantaneous formation of a new species which was immediately measured by NMR spectroscopy at −80 °C. Two enamide complexes were observed and characterized as TMS-enamide complex (assigned in Figure S5) and protonated enamide.[2] The formation of an iminium-type complex, placing the silyl moiety on the oxygen atom, was suggested by the deshielded NMe_2 groups in the new iminum moiety (up to 0.5 ppm downfield) and confirmed by a ^1H-^1H ROESY experiment (Figure S6) NMR spectroscopy also confirmed s-*trans* conformation. Full characterization was carried out by ^1H-^{13}C-HSQCED (Figure S7), ^1H-^{13}C-HMBC (Figure S8) and ^1H-^{29}Si-HMBC (figure S9).



^1H NMR (CD_2Cl_2, 400 MHz):δ 6.81 (dq, *J* = 15.5, 6.9 Hz, 1H), 6.41 (dd, *J* = 15.5, 1.5 Hz, 1H), 3.37 (s, 3H), 3.25 (s, 3H), 2.05-2.00 (m, 3H), 0.36 (s, 9H)

^{13}C NMR (CD_2Cl_2, 100 MHz): δ 167.2, 152.5, 117.7, 40.4, 38.8, 19.4, 0.2.

^{29}Si NMR (CD_2Cl_2, 79.5 MHz): δ 38.4.

^{19}F NMR (CD_2Cl_2, 376.6 MHz): δ -79.17.

[2] Water derived from the enamide substrates partially hydrolizes TMSOTf resulting in formation of TfOH, which can protonate the enamide

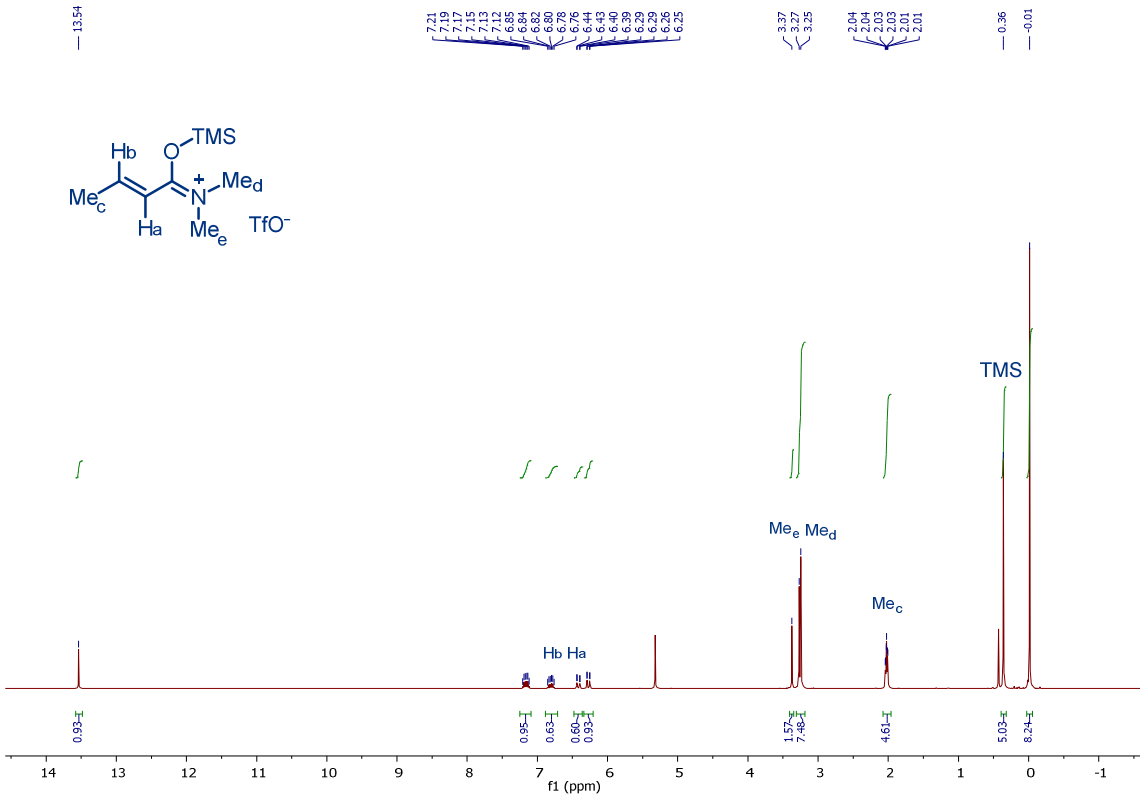


Figure S5: ^{1}H NMR spectrum of the equimolar mixture of enamide **1b** and TMSOTf.

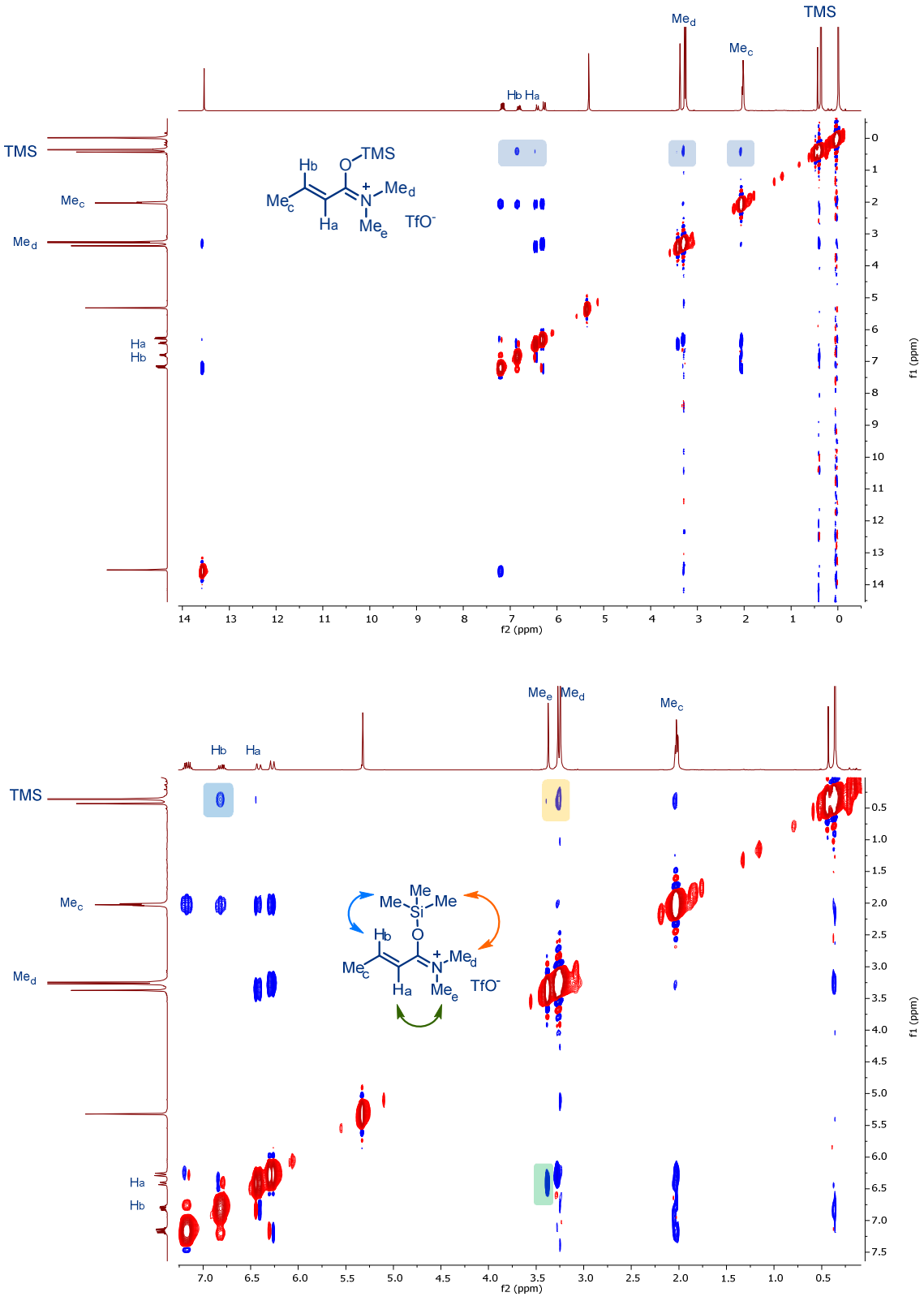


Figure S6: ^{1}H-^{1}H-ROESY spectrum of the equimolar mixture of enamide **1b** and TMSOTf and expansion. Cross-peaks between the TMS moiety and both Hb (blue) and one of the NMe groups (orange) and between the other NMe group and Ha (green) confirmed the O-silylation and the s-*trans* conformation.

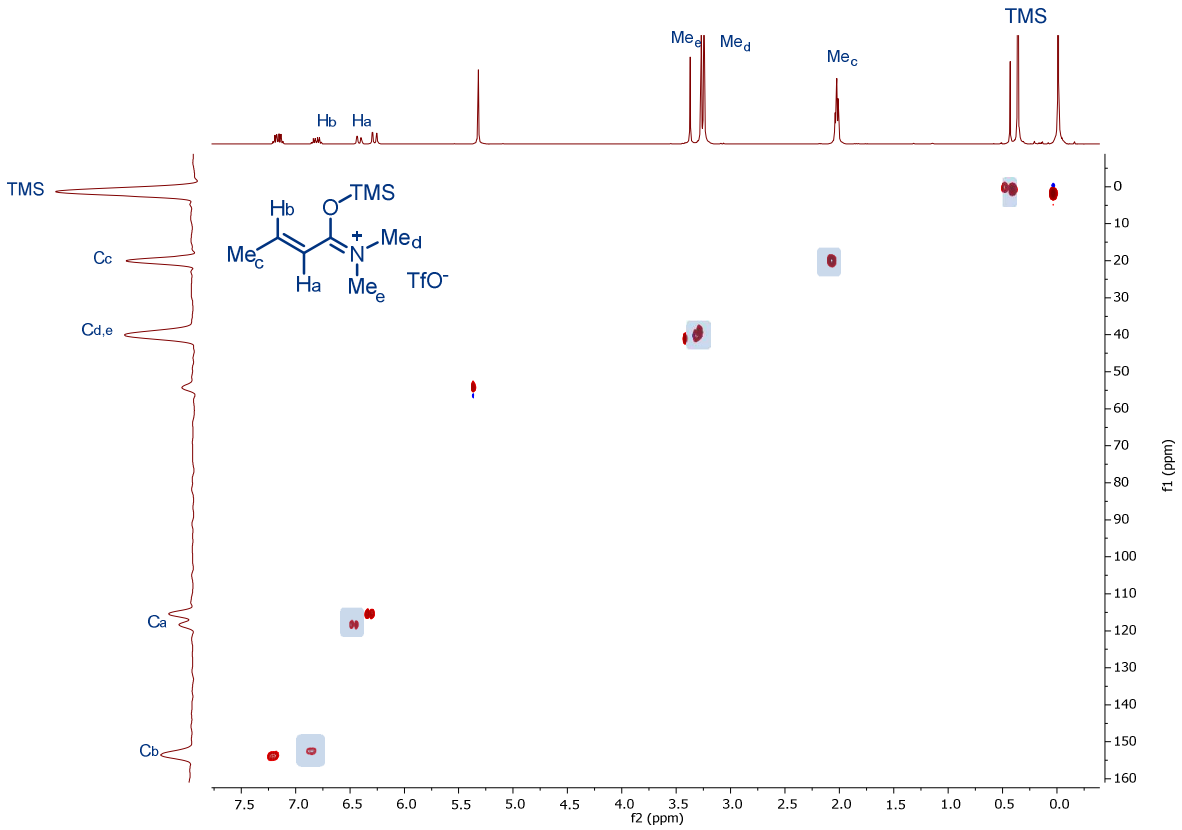


Figure S7: ^{1}H-^{13}C-HSQCED spectrum of the equimolar mixture of enamide **1b** and TMSOTf. TMS-enamide complex cross-peaks are highlighted.

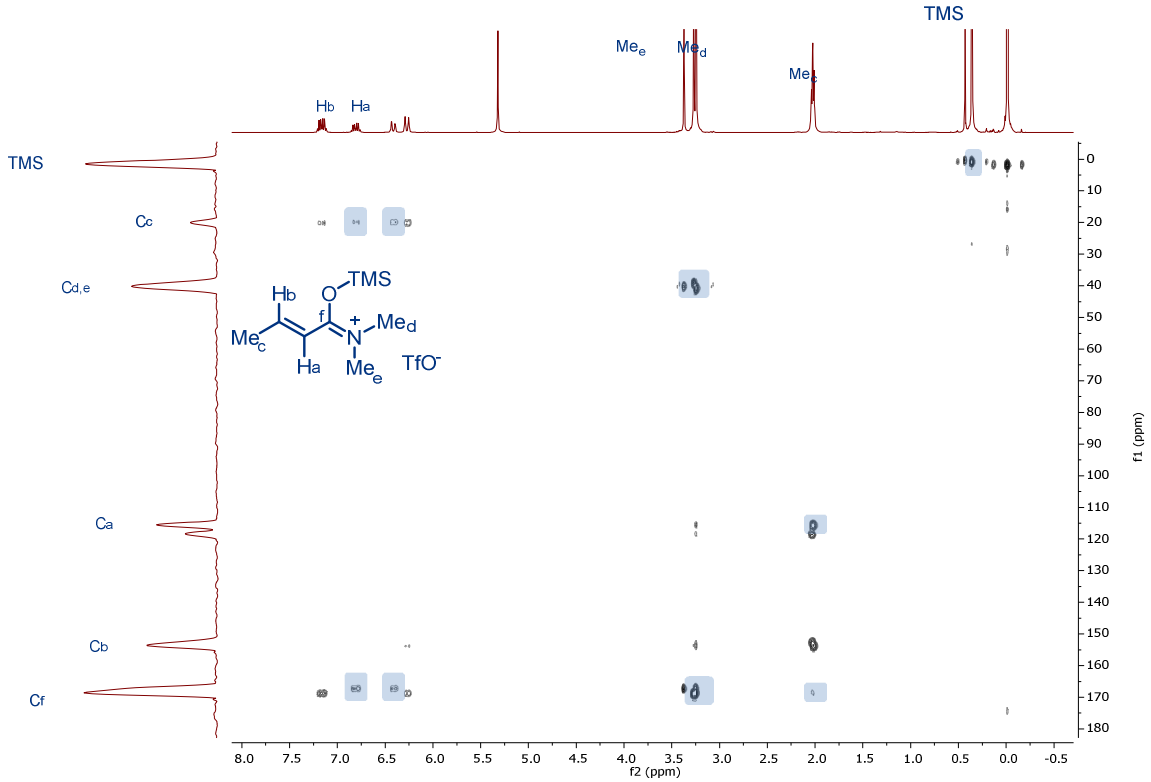


Figure S8: ^{1}H-^{13}C-HMBC spectrum of the equimolar mixture of enamide **1b** and TMSOTf. TMS-enamide complex cross-peaks are highlighted.

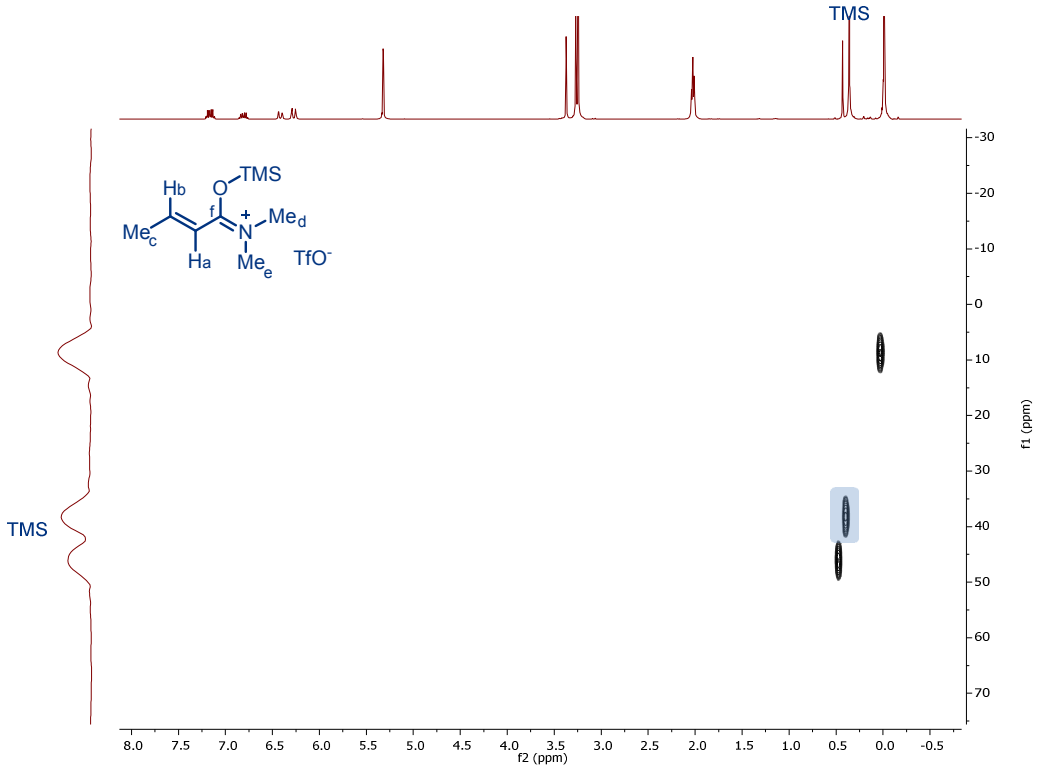
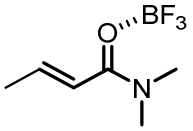


Figure S9: ^{1}H-^{29}Si-HMBC spectrum of the equimolar mixture of enamide **1b** and TMSOTf. TMS-enamide complex cross-peaks are highlighted.

BF_3-amide complex

$BF_3 \cdot Et_2O$ (10 μL, 0.08 mmol) was added to a solution of amide **1b** (9 mg, 0.08 mmol) in CD_2Cl_2 (0.6 mL) in a dry NMR tube at −78 °C. Instantaneous formation of a new species at −80 °C was measured by NMR spectroscopy. In analogy with the experiment above two new enamide species were detected using ^{1}H NMR (Fig. S10).[3] Formation of an enamide-BF_3 complex was confirmed by ^{1}H-^{19}F-HOESY spectra (Figure S11) and fully characterized by ^{11}B-NMR (Figure S12), ^{19}F-NMR (Figure S13), ^{1}H-^{13}C-HSQCED (Figure S14), and ^{1}H-^{13}C-HMBC (Figure S15).



^{1}H NMR (CD_2Cl_2, 400 MHz):δ 13.55 (s, 1H), 6.78 (dq, *J* = 13.6, 6.8 Hz, 1H), 6.23 (d, *J* = 15.9, 1H), 3.30 (s, 3H), 3.22 (s, 3H), 2.00 (d, *J* = 6.8 Hz, 3H) (Major species).

^{13}C NMR (CD_2Cl_2, 100 MHz): δ 169.7, 149.0, 117.6, 41.0, 38.7, 19.9, 14.6 (Major species).

^{11}B NMR (CD_2Cl_2, 100 MHz): δ -0.26, -0.74, -1.22, -1.28.

^{19}F NMR (CD_2Cl_2, 100 MHz): δ -146.82 (^{19}F-^{10}B), -146.88 (^{19}F-^{11}B).

[3] A few other acidic proton peaks were detected as well due to the water present in the substrate.

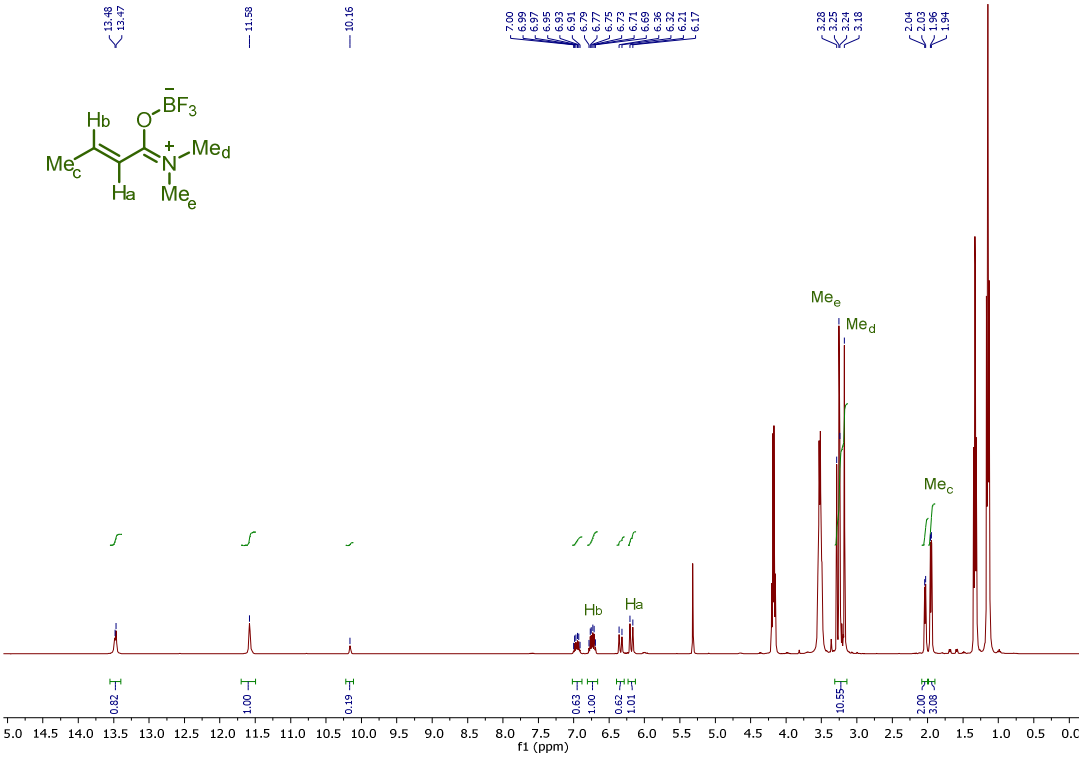


Figure S10: ^{1}H NMR spectrum of the equimolar mixture of enamide **1b** and $BF_3 \cdot Et_2O$.

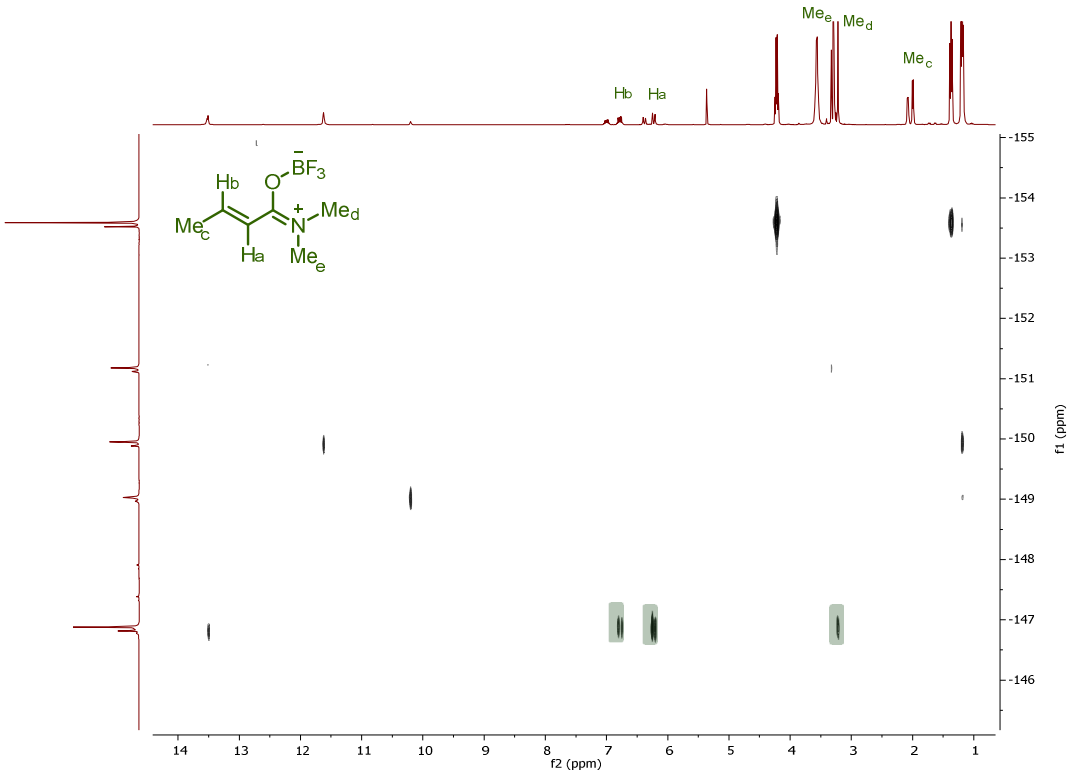


Figure S11: ^{1}H-^{19}F-HOESY spectrum of the equimolar mixture of enamide **1b** and $BF_3 \cdot Et_2O$. Cross-peak with the enamide moieties (green) and ^{19}F signal at -147 ppm confirmed the formation of a complex. BF_3-enamide complex cross-peaks are highlighted.

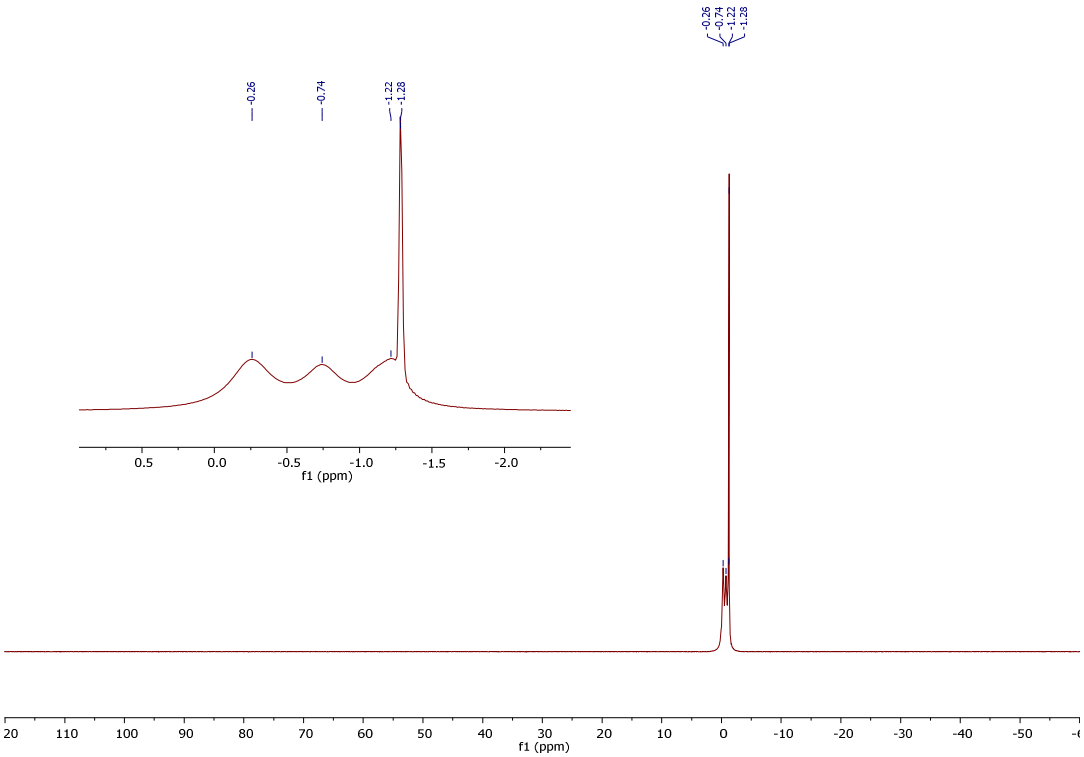


Figure S12: ^{11}B-NMR spectrum of the equimolar mixture of enamide **1b** and $BF_3 \cdot Et_2O$.

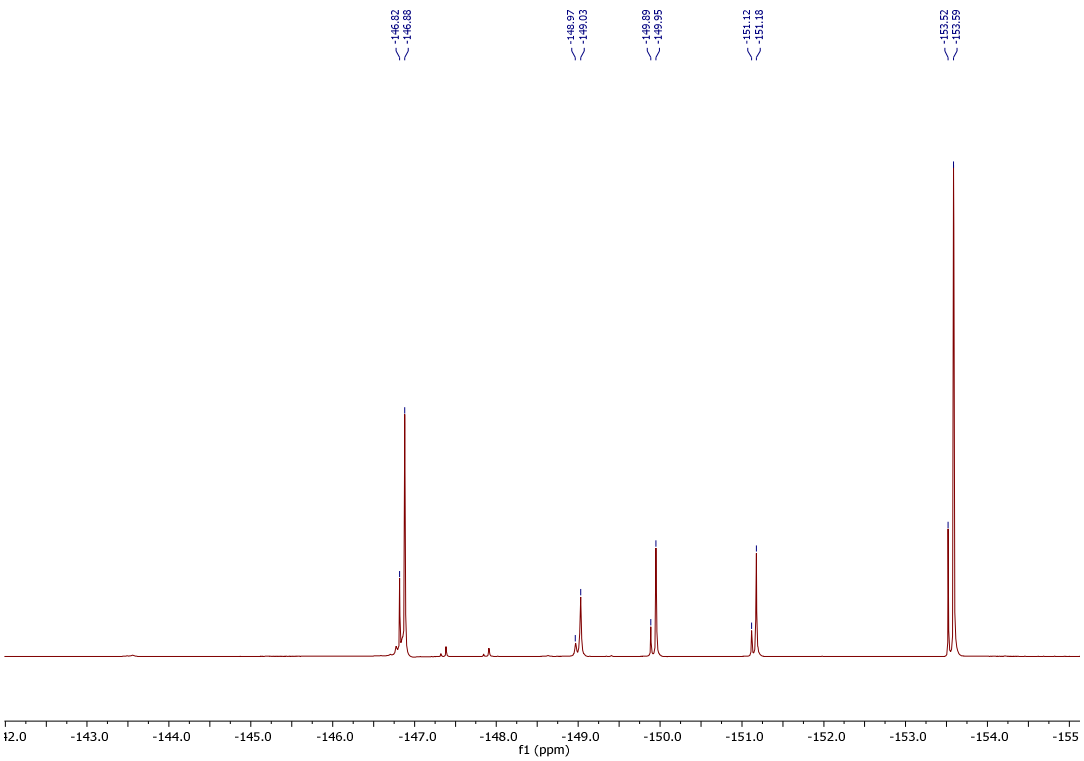


Figure S13: ^{19}F-NMR spectrum of the equimolar mixture of enamide **1b** and $BF_3 \cdot Et_2O$.

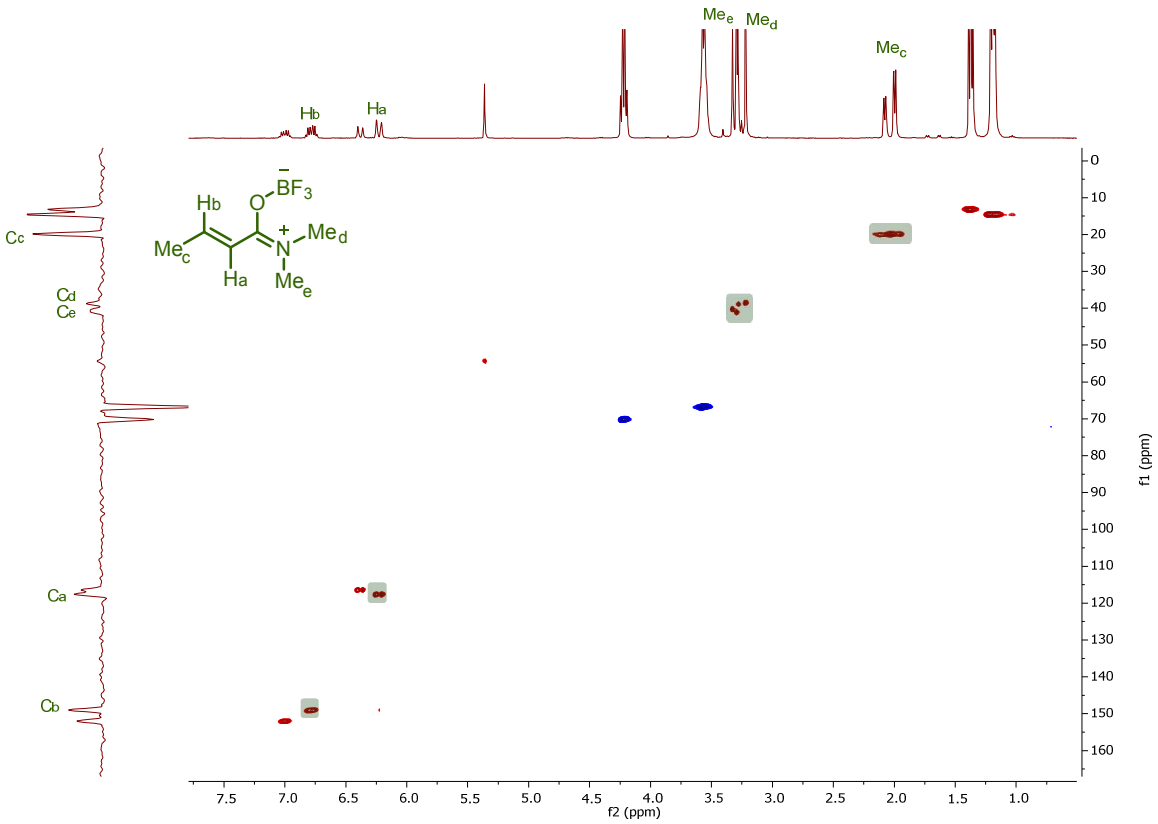


Figure S14: ^{1}H-^{13}C-HSQCED spectrum of the equimolar mixture of enamide **1b** and $BF_3 \cdot Et_2O$. BF_3-enamide complex cross-peaks are highlighted.

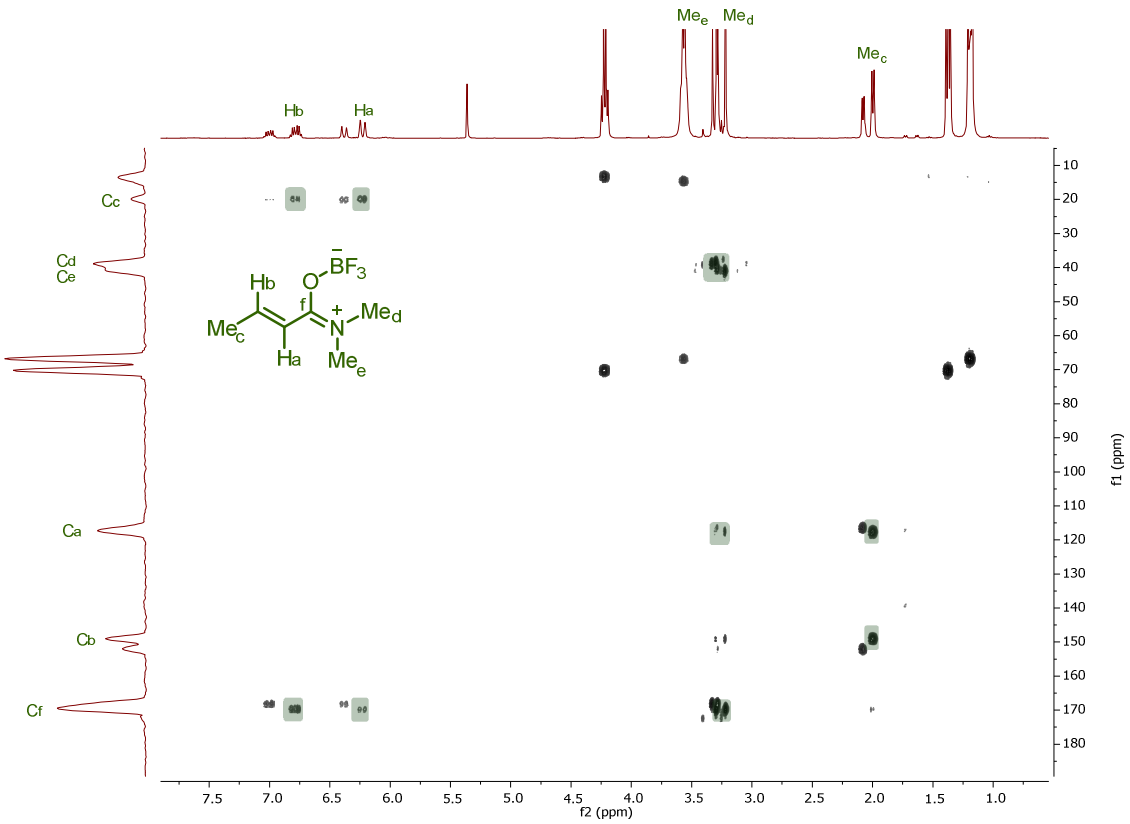


Figure S15: ^{1}H-^{13}C-HMBC spectrum of the equimolar mixture of enamide **1b** and $BF_3 \cdot Et_2O$. BF_3-enamide complex cross-peaks are highlighted.

MeMgBr-amide complex

A 3 M MeMgBr solution in Et_2O (54 µL, 0.2 mmol) was added to a solution of amide **1b** (6 mg, 0.05 mmol) in CD_2Cl_2 (0.6 mL) in a dry NMR tube at −78 °C Instantaneous formation of a new species at −80 °C attributed to MeMgBr/enamide complex was measured by NMR spectroscopy. Only this species was observed in this experiment.

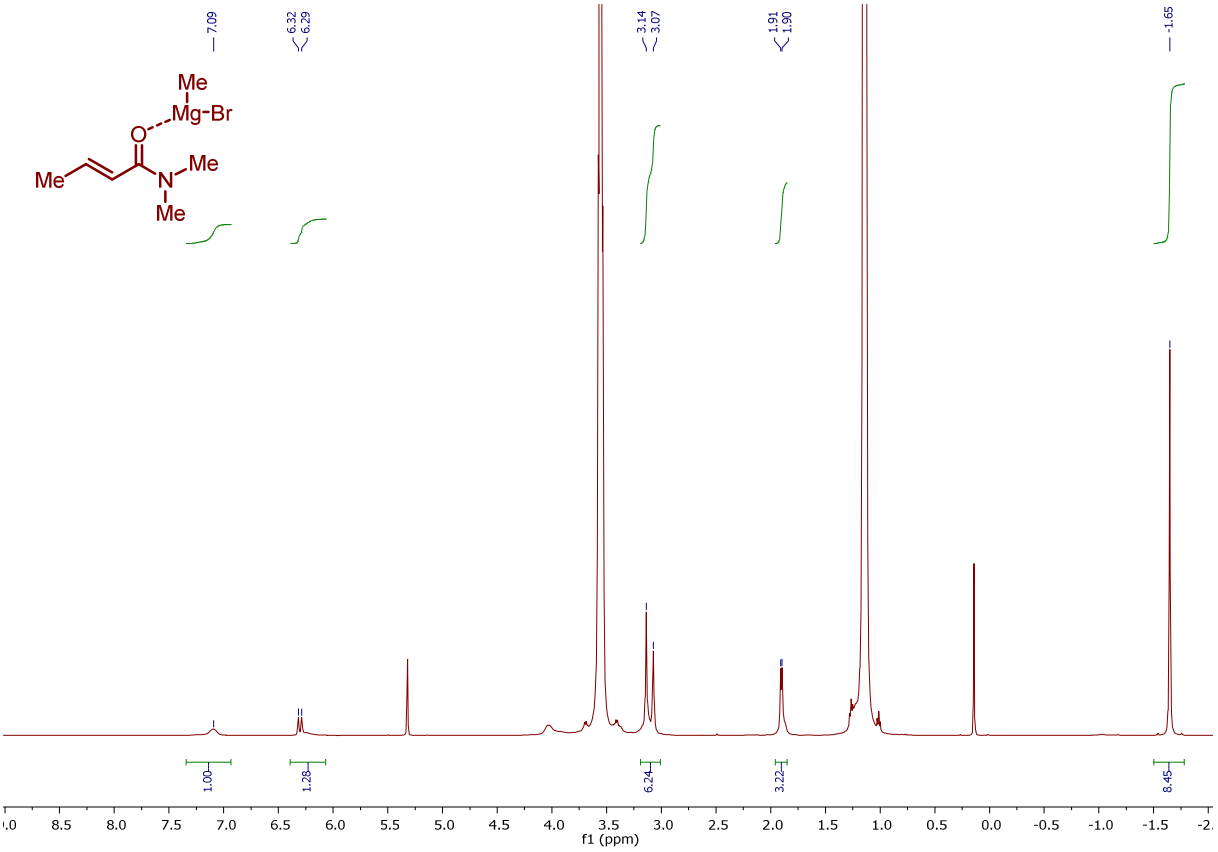


Figure S16: ^{1}H NMR spectrum of the mixture of enamide **1b** and MeMgBr.

Reaction media before the completion of the ACA reaction

In order to determine if any of the species discussed above are present in the reaction media a set of reactions was carried out in the presence of TMSOTf or $BF_3{\cdot}Et_2O$ in CD_2Cl_2 either directly in the NMR tubes or in dry Schlenk flasks at −78 °C and then measured at −80 °C (Figure S17, only the reaction media in the presence of TMSOTf are shown). In a flame-dried Schlenk tube equipped with septum and magnetic stirring bar, CuBr-(R,S_{Fe})-**L1** complex (5.53 mg, 0.0075 mmol, 5 mol%) and amide **1b** (17 mg, 0.15 mmol) were dissolved in CD_2Cl_2 (1.5 mL) and stirred under nitrogen atmosphere. After stirring at room temperature for 5 minutes, the reaction mixture was cooled to −60 °C and TMSOTf (52 µL, 0.30 mmol) was added. After 15 minutes, MeMgBr (100 µL, 0.30 mmol, 3.0 M in Et_2O) was added. Then the mixture was transferred to a NMR tube cooled to −78 °C and then measured by NMR spectroscopy at −80 °C.

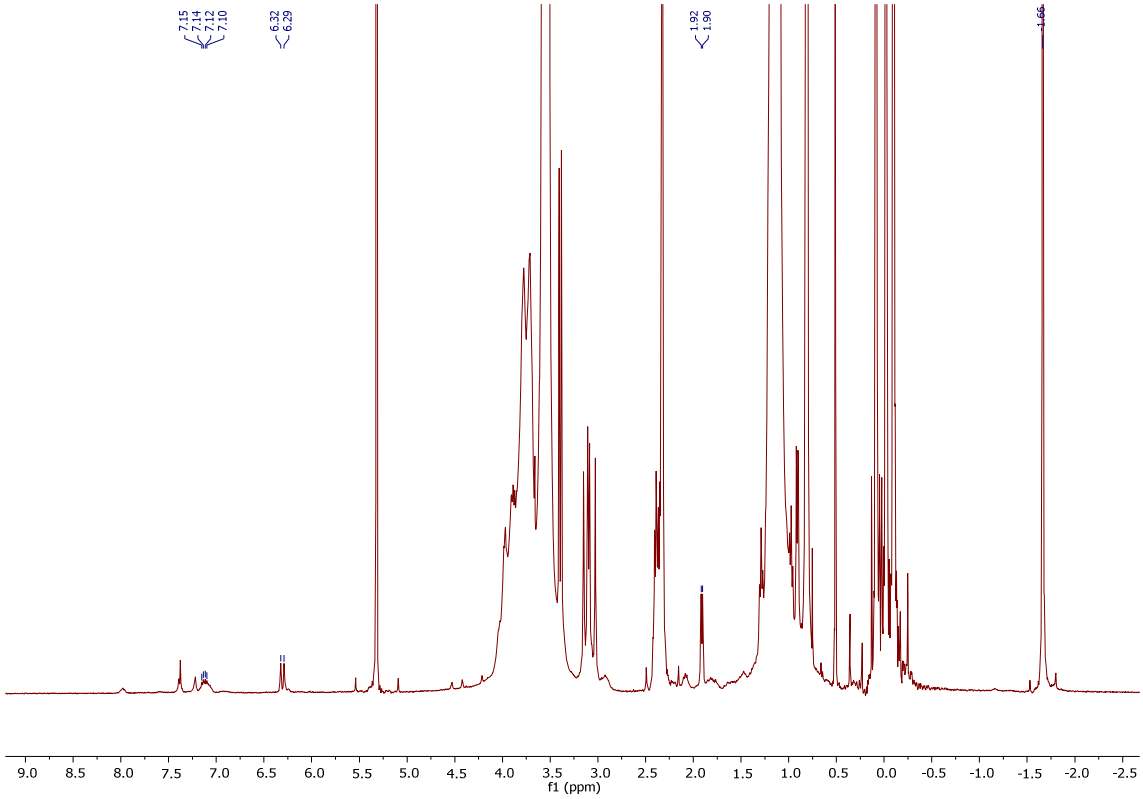


Figure S17: ^{1}H NMR spectrum of the reaction media in the reaction of enamide **1b** with MeMgBr in the presence of **L1**-CuBr complex and TMSOTf in CD_2Cl_2.

Regardless of the LA used, the only species observed in the reaction media correspondeds to the complex derived from the interaction between the enamide and MeMgBr (Figure 3f in the main text). The same complex was also detected when MeMgBr was added to the preformed TMSOTf-enamide or $BF_3{\cdot}Et_2O$-enamide complexes preformed in the absence of other reaction intermediates. These results suggest that MeMgBr replaces the Lewis acid and forms a more stable complex with the enamide.

Transmetallation of the Lewis acid by MeMgBr

Transmetallation of the Lewis acid by MeMgBr was also studied by NMR spectroscopy. An equimolar mixture of MeMgBr solution in Et_2O (33 μL, 0.1 mmol) and $BF_3{\cdot}Et_2O$ (12 μL, 0.1 mmol) in CD_2Cl_2 (0.6 mL) was prepared in a dry NMR tube under N_2 atmosphere at −78 °C and measured by NMR

spectroscopy at −80 °C. Formation of Me_4BMgBr (-0.74 ppm, q, J=3.7 Hz in ^1H NMR, -19.8 ppm, m, J=3.7 Hz in ^{11}B NMR) was immediately detected at −80 °C (Figures S18 and S19).

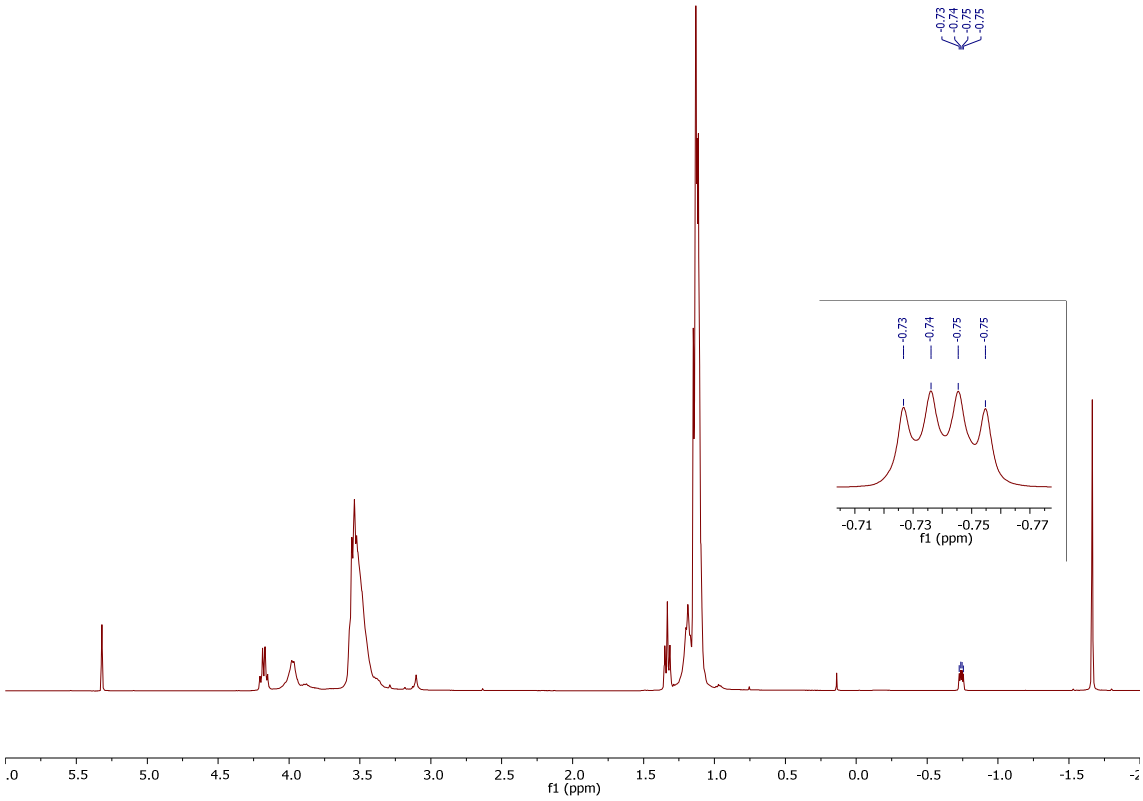


Figure S18: ^1H NMR spectrum of the equimolar mixture of MeMgBr and $BF_3{\cdot}Et_2O$ in CD_2Cl_2.

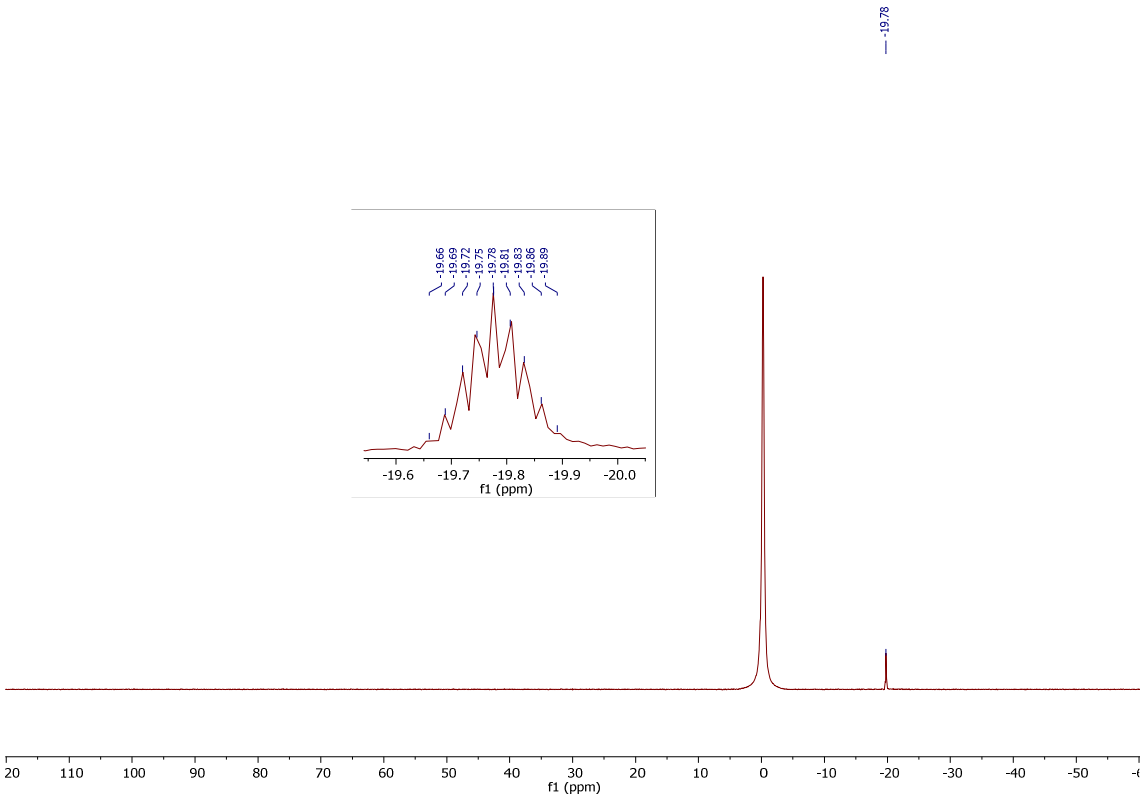


Figure S19: ^{11}B NMR spectrum of the equimolar mixture of MeMgBr and $BF_3{\cdot}Et_2O$ in CD_2Cl_2.

Likewise, formation of tetramethylsilane was detected by ^1H NMR at −60 °C when MeMgBr (solution 3 M in Et_2O, 33 µL, 0.1 mmol) was added to a solution containing TMSOTf (18 µL, 0.1 mmol) in CD_2Cl_2 (0.6 mL). Formation of Me_4Si (-0.08 ppm in ^1H NMR) was immediately detected at −60 °C (figure S20).

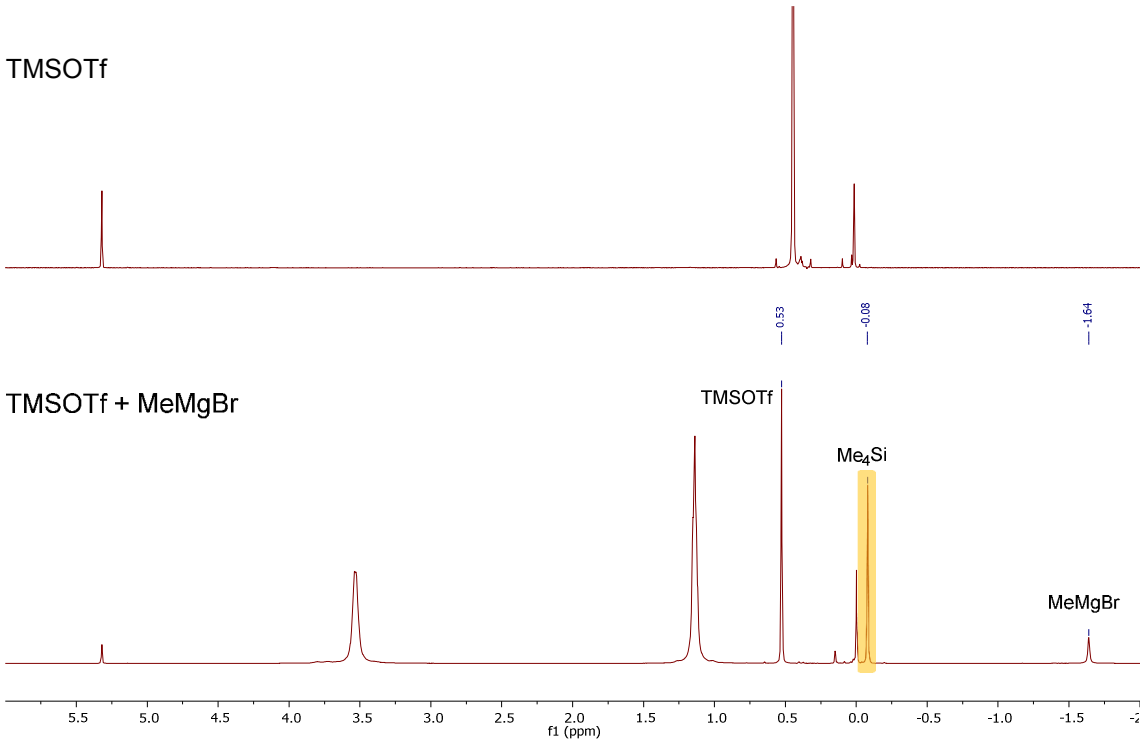


Figure S20: ^{1}H NMR spectrum of TMSOTf (top) and the equimolar mixture of MeMgBr and TMSOTf in CD_2Cl_2 (bottom). Appearance of a new peak of Me_4Si was immediately detected (highlighted).

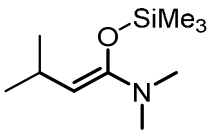
Nature of enolates formed as an end product copper ACA reactions

The structure of the final product of the reaction, namely the enolates, was determined by analysis of the reaction crude before quench in CD_2Cl_2.

Catalytic ACA in the presence of TMSOTf (silyl enolate formation)

In a flame-dried Schlenk tube equipped with septum and magnetic stirring bar, CuBr-(R,S_{Fe})-**L1** complex (5.53 mg, 0.0075 mmol, 5 mol%) and amide **1b** (17 mg, 0.15 mmol) were dissolved in CD_2Cl_2 (1.5 mL) and stirred under nitrogen atmosphere. After stirring at room temperature for 5 min., the reaction mixture was cooled to −60 °C and TMSOTf (52 μL, 0.30 mmol) was added. After 15 min., MeMgBr (100 μL, 0.30 mmol, 3.0 M in Et_2O) was added. After stirring at −60 °C for 18 h, the mixture was transferred to a

NMR tube followed by measurement at −80 °C. The final product in the reaction mixture was identified as a TMS-enolate (Figure S21), based on a TOCSY experiment. (Z)-configuration was assigned to the enolate, based on series of 1D ROESY experiments (Figure S23). Full characterization by ^{1}H-^{13}C-HSQCED (Figure S24), ^{1}H-^{13}C-HMBC (Figure S25) and ^{1}H-^{29}Si-HMBC (figure S26) was carried out.



^{1}H NMR (CD_2Cl_2, 400 MHz):δ 3.39 (d, *J* = 9.4 Hz, 1H), 2.42-2.32 (m, 1H), 2.33 (s, 6H), 0.81 (d, *J* = 6.7 Hz, 6H), 0.08 (s, 9H).

^{13}C NMR (CD_2Cl_2, 100 MHz): δ 152.1, 95.7, 40.4, 25.3, 24.5, -0.4.

^{29}Si NMR (CD_2Cl_2, 79.5 MHz): δ 19.3.

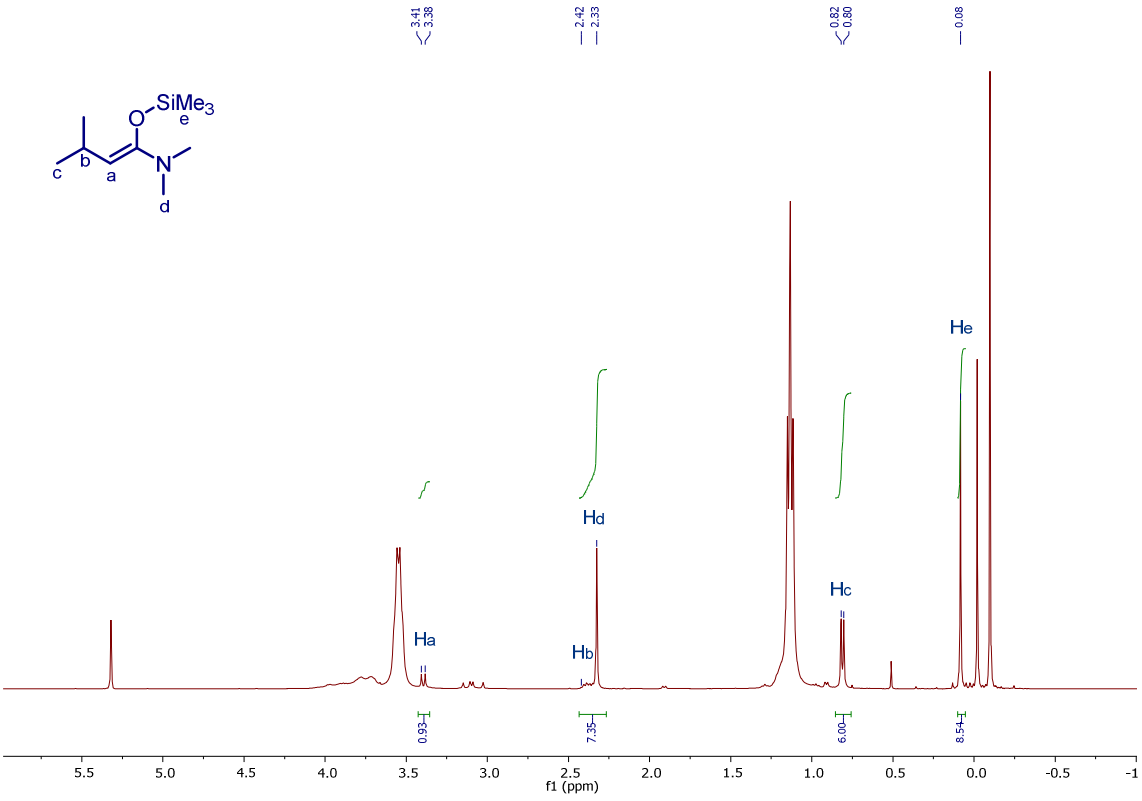


Figure S21: ^{1}H NMR spectrum of the crude of the reaction in the presence of TMSOTf.

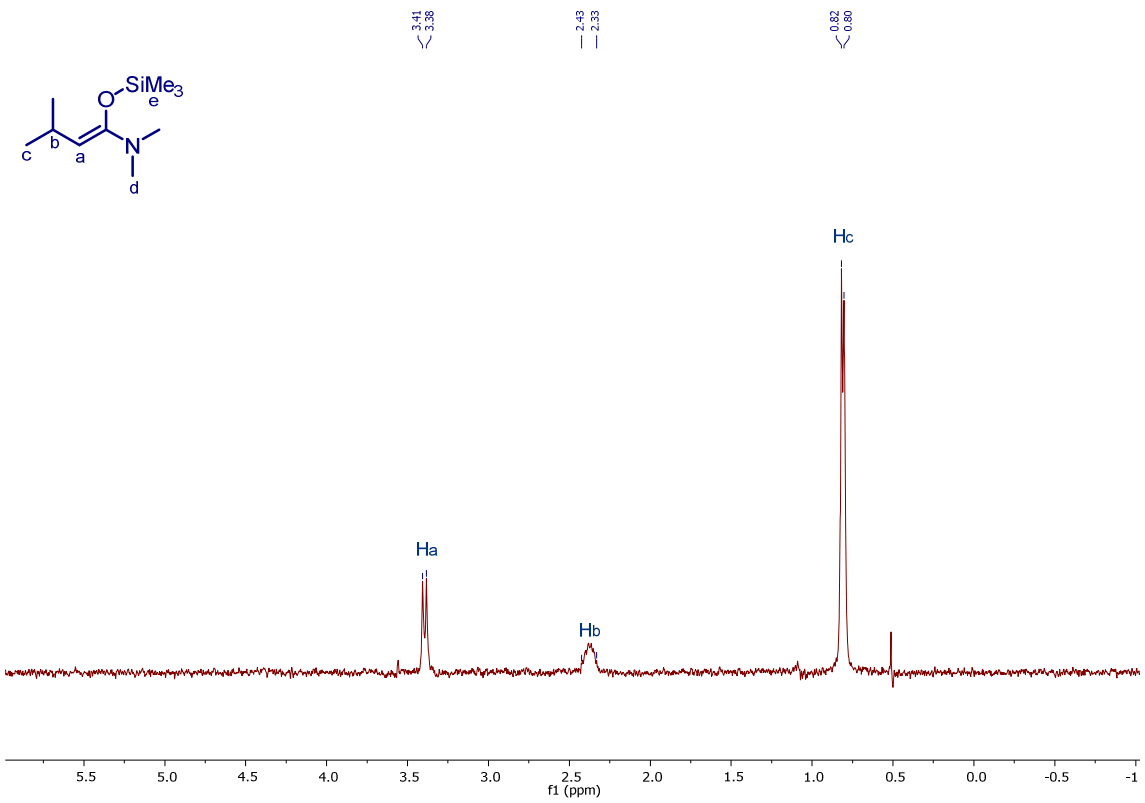


Figure S22: TOCSY experiment (irradiating nucleus Ha) of the crude of the reaction in the presence of TMSOTf.

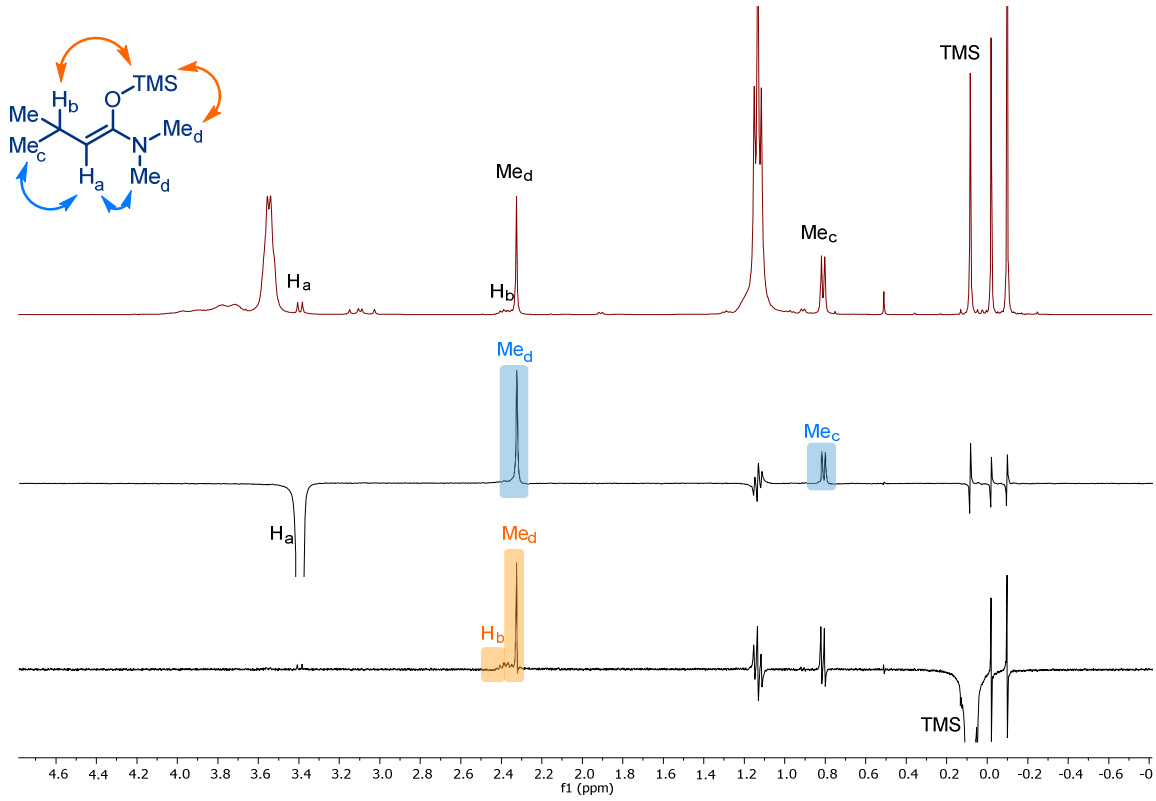


Figure S23: 1D ROESY experiments of the crude of the reaction in the presence of TMSOTf. Z-enolate configuration was determined by observation of NOE between the TMS moiety and Hb (orange) and between Ha and NMe moiety and *gem*-dimethyl moiety (Me c, blue).

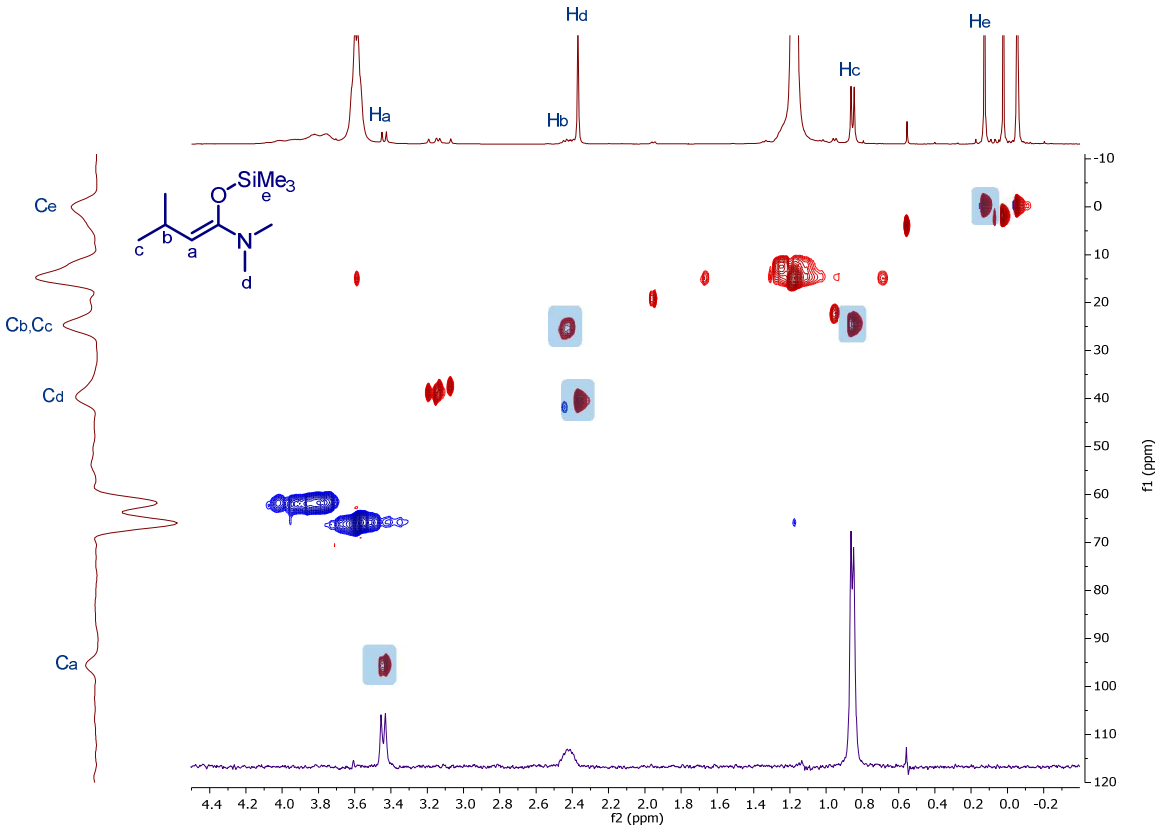


Figure S24: ^{1}H-^{13}C-HSQCED spectrum of the crude of the reaction in the presence of TMSOTf. TMS-enolate peaks are highlighted.

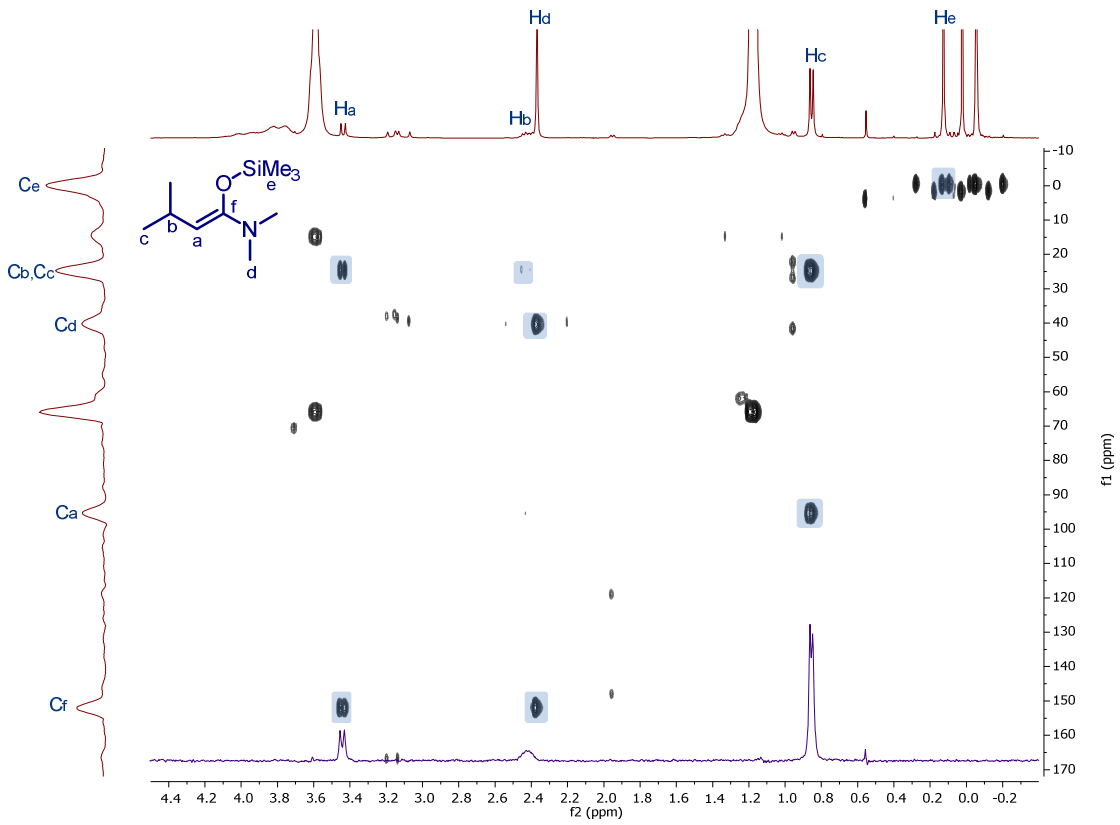


Figure S25: ^{1}H-^{13}C-HMBC spectrum of the crude of the reaction in the presence of TMSOTf. TMS-enolate peaks are highlighted.

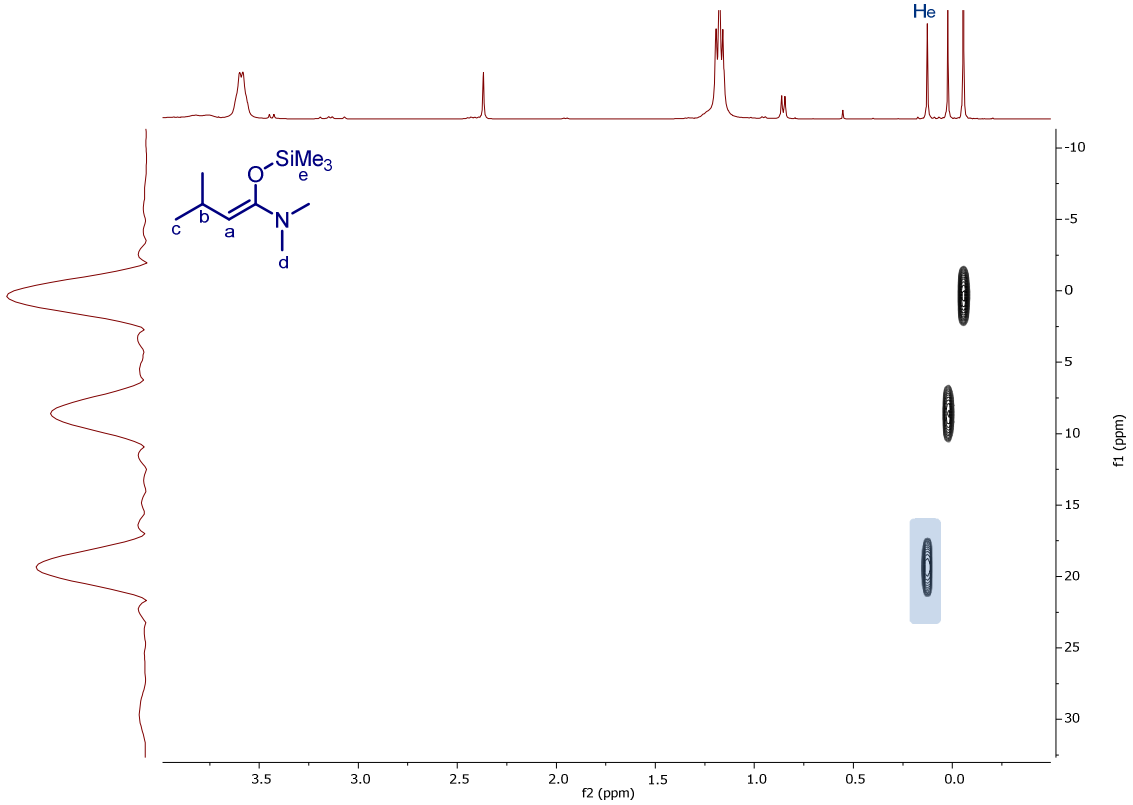
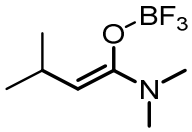


Figure S26: ^{1}H-^{29}Si-HMBC spectrum of the crude of the reaction in the presence of TMSOTf. TMS-enolate peaks are highlighted.

Catalytic ACA in the presence of BF_3·Et_2O (boron enolate formation)

In a flame-dried Schlenk tube equipped with septum and magnetic stirring bar, CuBr-(R,S_{Fe})-**L1** complex (5.53 mg, 0.0075 mmol, 5 mol%) and amide **1b** (17 mg, 0.15 mmol) were dissolved in CD_2Cl_2 (1.5 mL) and stirred under nitrogen atmosphere. After stirring at room temperature for 5 min., the reaction mixture was cooled to −60 °C and BF_3·Et_2O (37 µL, 0.30 mmol) was added. After 15 min., MeMgBr (100 µL, 0.30 mmol, 3.0 M in Et_2O) was added. After stirring at −60 °C for 18 h, the mixture was transferred to a NMR tube, cooled and measured by NMR spectroscopy at −80 °C. A BF_3-enolate structure was assigned based on ^{1}H NMR (Figure S27). Enolate proton (Ha) was detected in the crude and with a TOCSY

experiment (Figure S28) Ha, Hb, Hc protons were assigned. Full characterization of the enolate was done by ^{1}H-^{13}C-HSQCED (Figure S29) and ^{1}H-^{13}C-HMBC (Figure S30) experiments.



^{1}H NMR (CD_2Cl_2, 400 MHz):δ 4.78 (d, J = 10.3 Hz, 1H), 2.66 (s, 6H), 2.50-2.42 (m, 1H), 0.89 (d, J = 6.6 Hz, 6H).

^{13}C NMR (CD_2Cl_2, 100 MHz): δ 132.7, 111.6, 44.5, 25.5, 22.7.

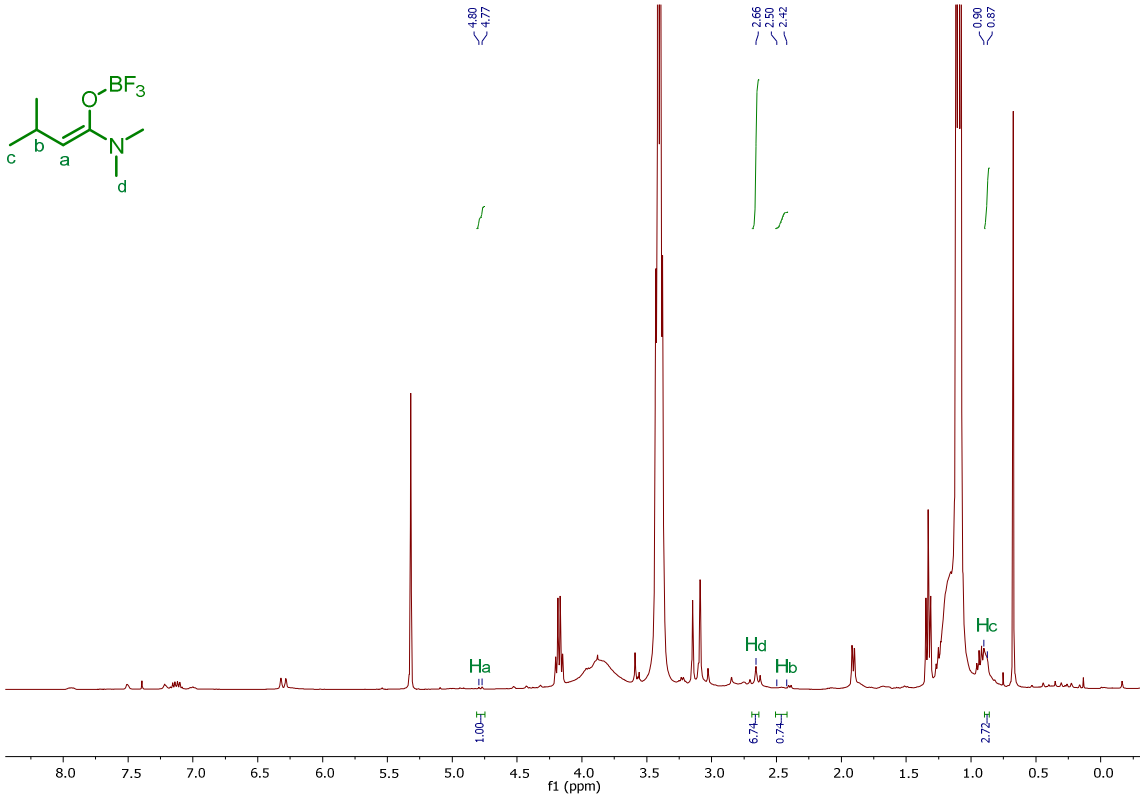


Figure S27: ^{1}H NMR spectrum of the crude of the reaction in the presence of $BF_3 \cdot Et_2O$.

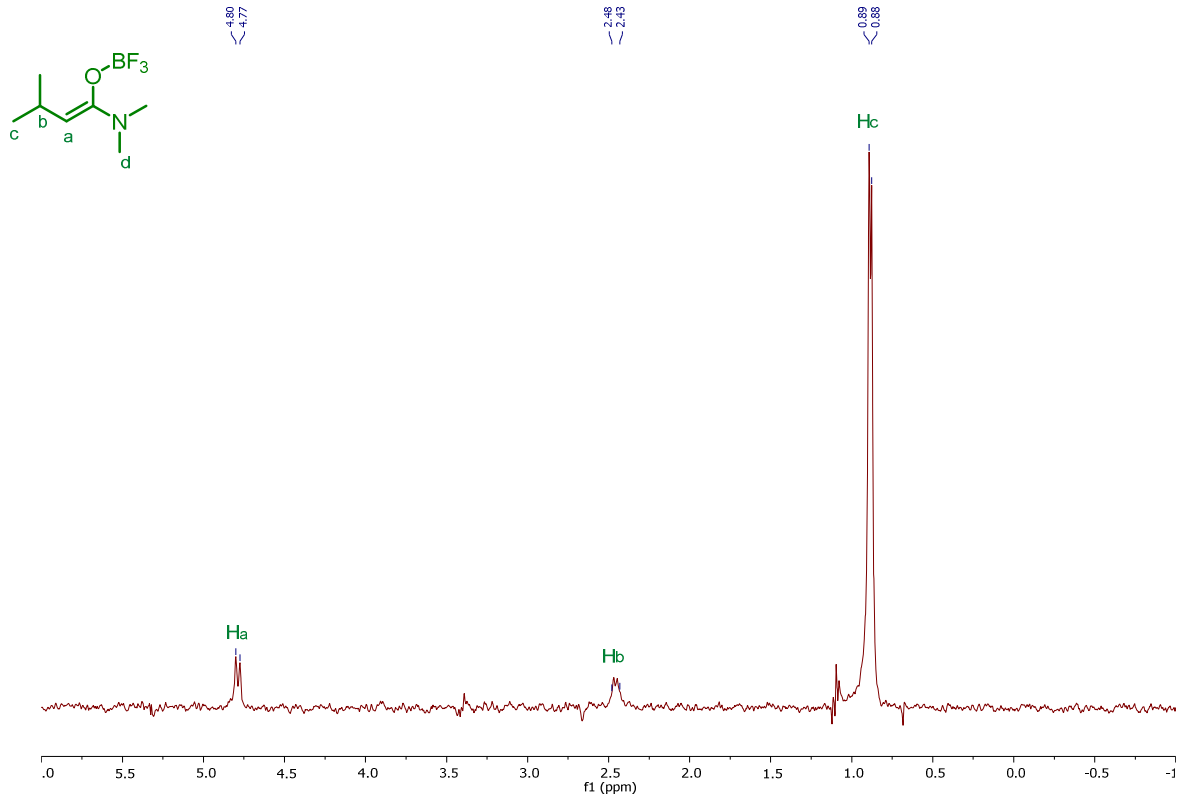


Figure S28: TOCSY experiment (irradiating nucleus Ha) of the crude of the reaction in the presence of $BF_3 \cdot Et_2O$.

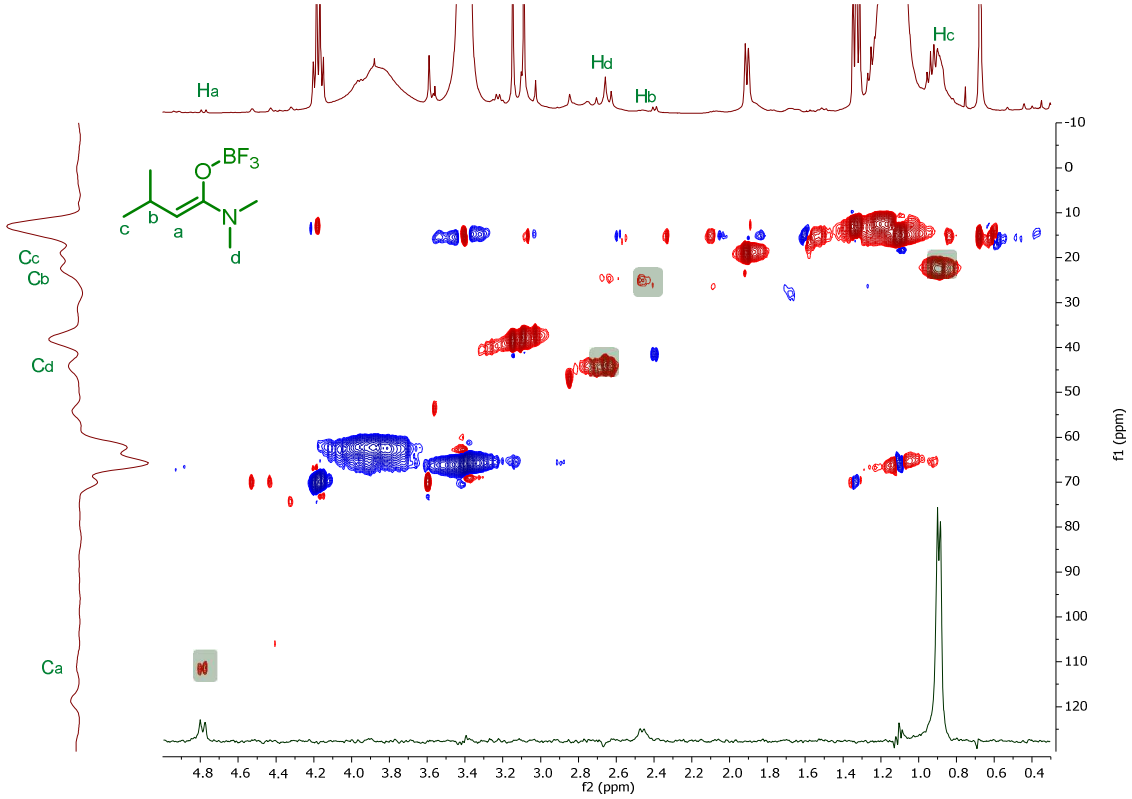


Figure S29: ^{1}H-^{13}C-HSQCED spectrum of the crude of the reaction in the presence of $BF_3 \cdot Et_2O$. BF_3-enolate peaks are highlighted.

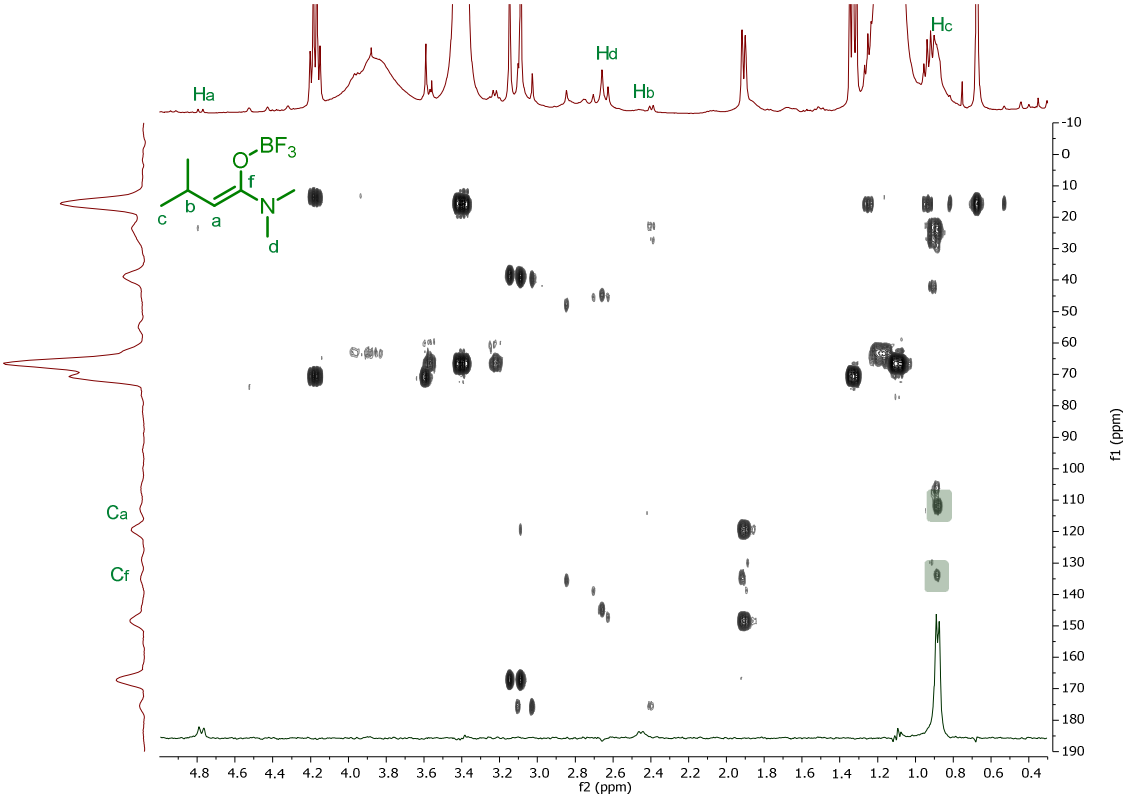


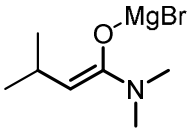
Figure S30: ^{1}H-^{13}C-HMBC spectrum of the crude of the reaction in the presence of $BF_3 \cdot Et_2O$. BF_3-enolate peaks are highlighted.

However, the configuration of the enolate could not be determined by HOESY experiments since no clear cross-peak ^{1}H-^{19}F wase observed. To prove that the enolate we observed in this case is not a magnesium enolate we have prepared Mg-enolate independently in the absence of LA and fully characterize it by NMR spectroscopy.

CA in the absence of Lewis acid (magnesium enolate formation)

A 3 M MeMgBr solution in Et_2O (67 µL, 0.2 mmol) was added to a solution of amide **1a** (12 mg, 0.10 mmol) in CD_2Cl_2 (0.6 mL) in a dry NMR tube under N_2 atmosphere. After 18 h the mixture was measured by NMR spectroscopy at −80 °C. A Mg-enolate structure was assigned based on ^{1}H NMR (Figure S31). Enolate proton (Ha) was detected in the crude and a TOCSY experiment (figure S32) was carried out to

assign the spin system (Ha, Hb, Hc). Full characterization by ^{1}H-^{13}C-HSQCED (Figure S33) and ^{1}H-^{13}C-HMBC (Figure S34) was carried out.



^{1}H NMR (CD_2Cl_2, 400 MHz):δ 3.97 (d, J = 8.7 Hz, 1H), 2.41 (s, 6H), 2.38-2.27 (m, 1H), 0.84 (d, J = 6.6 Hz, 6H).

^{13}C NMR (CD_2Cl_2, 100 MHz): δ 129.7, 110.0, 40.4, 26.9, 24.1.

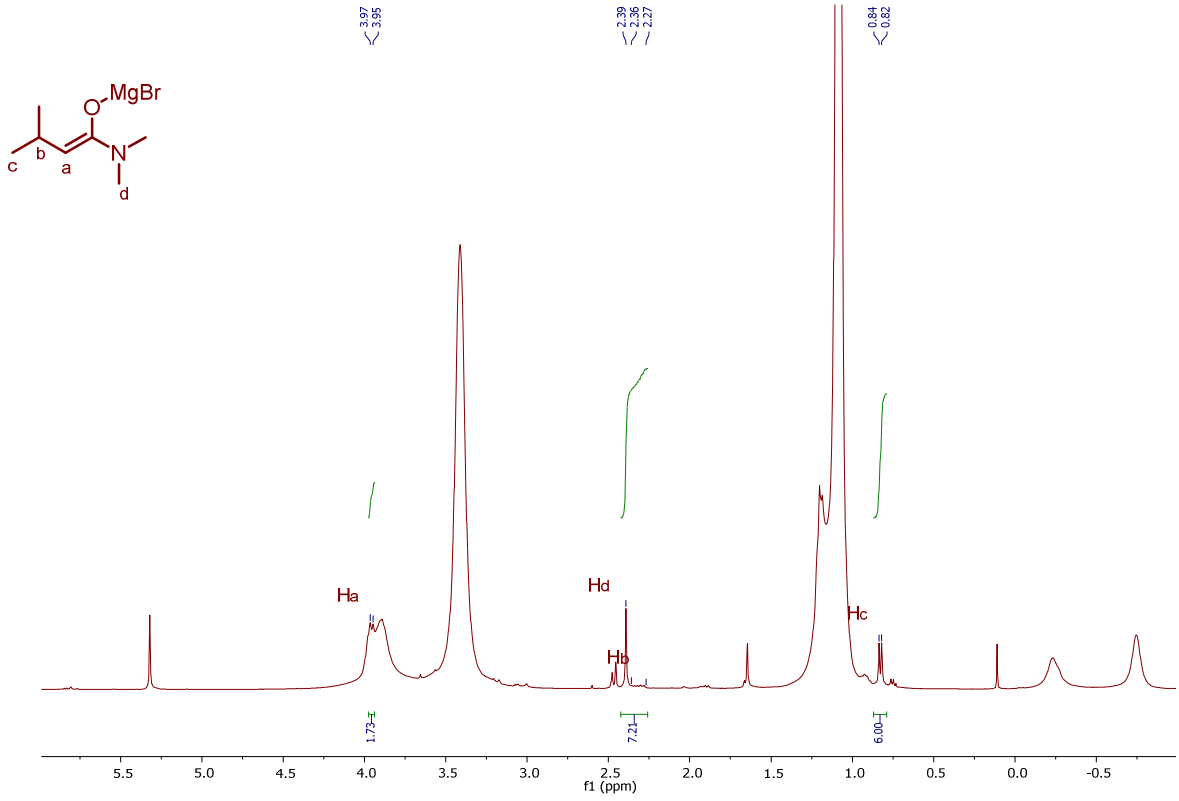


Figure S31: ^{1}H NMR spectrum of the crude of the reaction in the absence of Lewis acid.

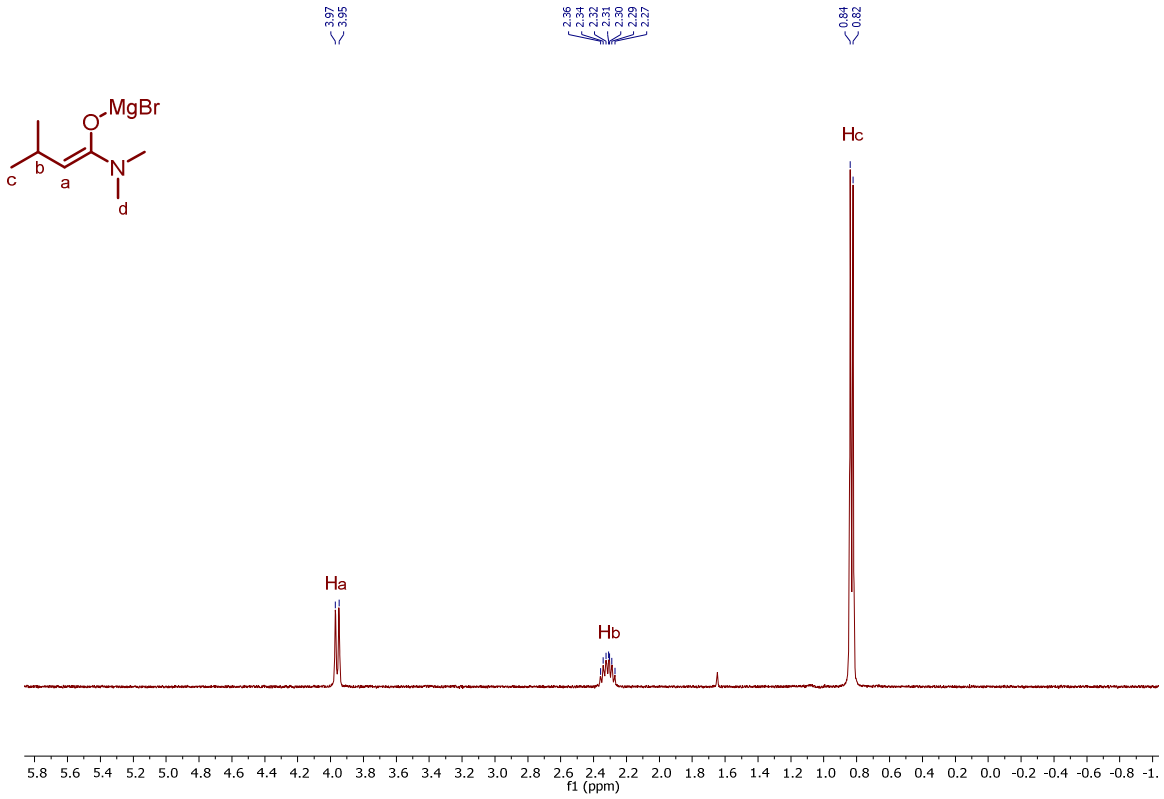


Figure S32: TOCSY experiment (irradiating nucleus Ha) of the crude of the reaction in the absence of Lewis acid.

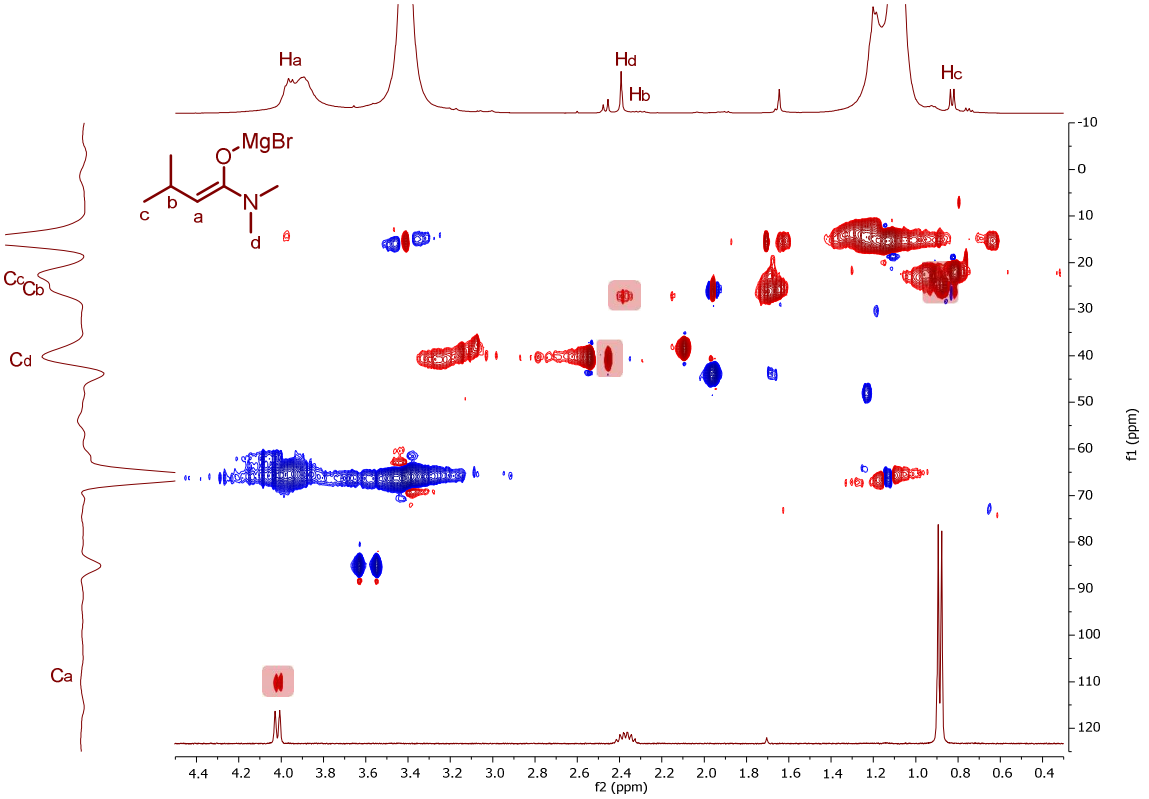


Figure S33: ^{1}H-^{13}C-HSQCED spectrum of the crude of the reaction in the absence of Lewis acid. Mg-enolate peaks are highlighted.

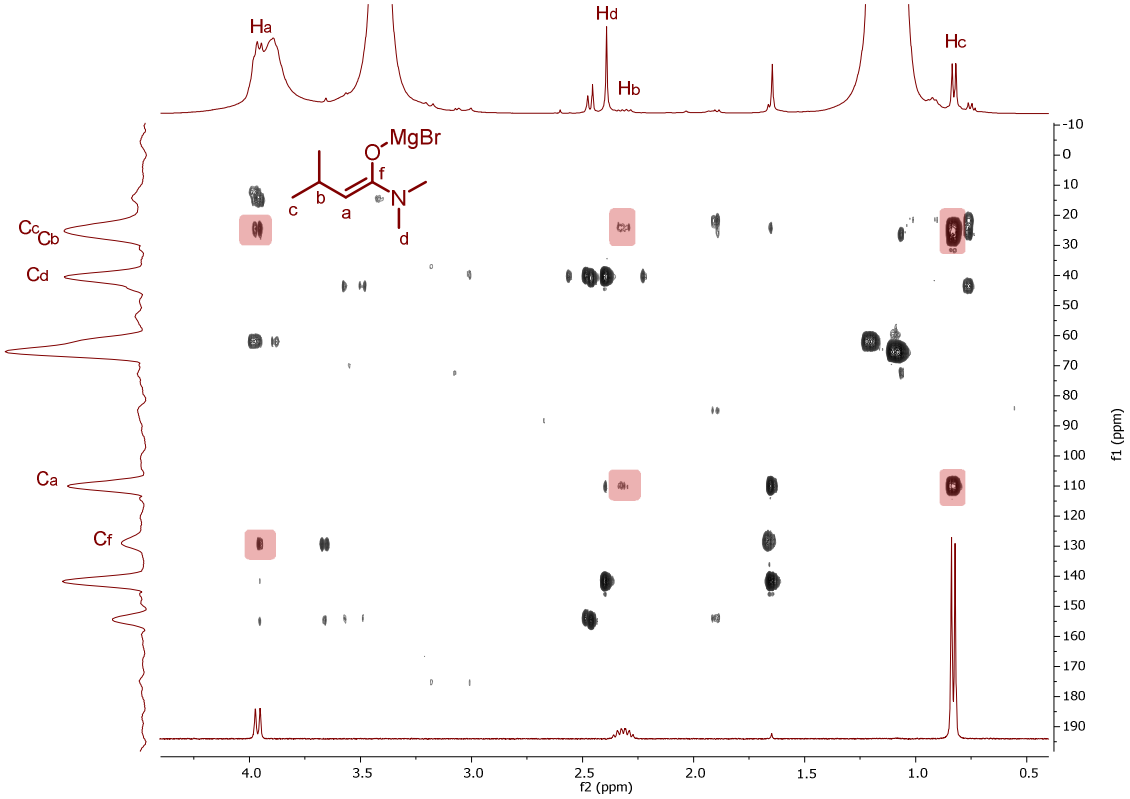


Figure S34: ^{1}H-^{13}C-HMBC spectrum of the crude of the reaction in the absence of Lewis acid. Mg-enolate peaks are highlighted.

This set of experiments shows that three different enolates, namely TMS-enolate (in the presence of TMSOTf), BF3-enolate (in the presence of $BF_3 \cdot Et_2O$) and Mg-enolate (in the absence of Lewis acid).are formed in the reaction mixture, depending on the reaction components

7. Synthesis of enamides: procedures and characterization of products

α,β-Unsaturated amides **1a-x** were prepared from the corresponding acyl chloride (Method 2:[1] RCOCl, amine; Method 3:[1] RCOCl, amine, NEt_3), from the corresponding carboxylic acid (Method 1:[1] (i) RCO_2H, $SOCl_2$, cat. DMF (ii) amine, NEt_3), from the corresponding alkenes (Method 6)[2], and from other derivative compounds (Method 4[3], Method 5[4,5]). **1a-1b**, **1f-j**, **1l-m, 1o, 1q-s**, **1v** are known compounds.

Method 1

To a cold 0 °C solution of the corresponding carboxylic acid (5 mmol) in DCM (4 mL) was added thionyl chloride (6 mmol) and dry DMF (14 μL). The solution was then stirred at room temperature for 2 h and concentrated under reduced pressure to remove residual thionyl chloride. The resulting residue was re-dissolved in DCM (4 mL), cooled at 0 °C and the corresponding amine (8 mmol) was added. Dry triethylamine (6.6 mmol) was added and stirring was continued at ambient temperature (3 h). The solvent was removed under reduced pressure and DCM (14 mL) was added. The organic phase was washed with dilute hydrochloric acid (2.0 M, 2 mL × 2), water (3 mL × 2), and brine (4 mL), and dried over $MgSO_4$. After removal of the solvent, the corresponding enamides were obtained.

Method 2

A solution of acyl chloride (0.96 mL, 10 mmol) in 6.3 mL dry Et_2O was cooled to 0 °C in an ice-bath. Anhydrous dimethylamine (2.0 M in THF, 10 mL, 20 mmol) was added for over 5 min and the reaction mixture was allowed to warm to room temperature (12 h). The solvents were evaporated under reduced pressure. Product **1b** was obtained after purification by column chromatography.

Method 3

To a cold 0 °C solution of the corresponding acyl chloride (5 mmol) in DCM (4 mL) was added the corresponding amine (8 mmol). Dry triethylamine (6.6 mmol) was added and stirring was continued at ambient temperature (3 h). The solvent was removed under reduced pressure and DCM (14 mL) was added. The organic phase was washed with dilute hydrochloric acid (2.0 M, 2 mL × 2), water (3 mL × 2), and brine (4 mL), and dried over $MgSO_4$. After removal of the solvent, the corresponding enamides were obtained.

Method 4

A solution of *N*-methyl-4-methylbenzenesulfonamide (1.85 g, 10 mmol) in anhydrous THF (20 mL) cooled at 0 °C was added under nitrogen a solution of *n*-BuLi (1.6 M in hexanes, 6.9 mL, 11 mmol) and the resulting mixture was stirred for 15 min. Subsequently, crotonyl chloride (1.0 mL, 11 mmol) dissolved in anhydrous THF (5 mL) was added and the mixture was left to warm to room temperature during 2 h. Saturated aqueous NH_4Cl solution was added and the mixture was extracted with DCM (14 mL). The organic phase was washed with dilute hydrochloric acid (2.0 M, 2 mL × 2), water (3 mL × 2), and brine (4 mL), and dried over $MgSO_4$. After removal of the solvent, product **1g** were obtained.

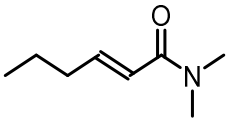
Method 5

LDA (1.0 M in THF/hexane, 6.4 mL, 6.4 mmol) was added to a solution of 1-methyl-2-piperidinone (0.66 mL, 5.8 mmol) in 4 mL of THF under nitrogen at −50 °C. After it was stirred at −50 °C for 45 min, the anion solution was transferred into a solution of phenylselenenyl chloride (1.22 g, 6.4 mmol) in 4 mL of THF at −78 °C under nitrogen. The reaction mixture was stirred at −78 °C for 7 h and quenched with water. Then, it was extracted with DCM. The organic layer was then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The crude mixture was purified by column chromatography on silica gel (SiO_2, pentane:Et_2O 1:2) to afford 1-Methyl-3-(phenylseleno)-2-piperidinone (65% yield) as a colorless oil. Then, a solution of MCPBA (77%, 0.84 g, 3.8 mmol) in anhydrous DCM (10 mL) was added to a solution of 1-methyl-3-(phenylseleno)-2-piperidinone (0.67 g, 2.5 mmol) in anhydrous DCM (10 mL) cooled at 0 °C. The mixture was allowed to rise to room temperature, and stirring was continued for 3 h. Saturated aqueous $NaHCO_3$ was added, and the aqueous layer was extracted with DCM. The organic layer was then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The crude mixture was purified by column chromatography on silica gel (SiO_2, Et_2O) to afford the corresponding enamide **1j** (89% yield).

Method 6

The corresponding alkene (7.5 mmol) and *N*,*N*-dimethylacrylamide (5 mmol) were added simultaneously to a stirred solution of 5 mol% of second generation Grubbs catalyst in DCM (20 mL) at room temperature. The reaction was refluxed under nitrogen for 16 h. The solvent and the remaining *N*,*N*-dimethylacrylamide were removed under reduced pressure and the corresponding enamide was purified by column chromatography.

(*E*)-*N*,*N*-Dimethylhex-2-enamide (1a)[1]

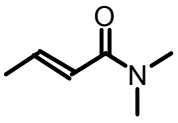


1a

The product **1a** was synthesized following Method 1 and obtained as a colorless oil in 86 % yield.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.86 (dt, *J* = 15.1, 7.0 Hz, 1H, C*H*=CH), 6.24 (dt, *J* = 15.1, 1.3 Hz, 1H, CH=C*H*), 3.07 (s, 3H, NCH_3), 2.99 (s, 3H, NCH_3), 2.18 (q, *J* = 7.1 Hz, 2H, CH_2CH), 1.48 (sex (qt), *J* = 7.4 Hz, 2H, CH_2CH$_3$), 0.93 (t, *J* = 7.4 Hz, 3H, CH$_2$CH_3).

(*E*)-*N*,*N*-Dimethylbut-2-enamide (1b)[1]

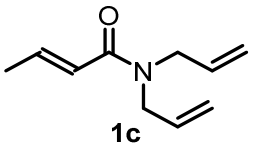


1b

The product **1b** was synthesized following Method 2 and obtained as a colorless liquid after column chromatography (SiO_2, Et_2O) in 90 % yield.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.87 (dq, *J* = 15.0, 6.9 Hz, 1H, C*H*=CH), 6.27 (dq, *J* = 15.0, 1.7 Hz, 1H, CH=C*H*), 3.06 (s, 3H, NCH_3), 2.99 (s, 3H, NCH_3), 1.87 (dd, *J* = 6.9, 1.7 Hz, 3H, CH_3CH).

***(E)*-*N*,*N*-Diallylbut-2-enamide (1c)**



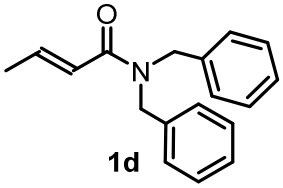
The product **1c** was synthesized following Method 3 and obtained after column chromatography (SiO_2, pentane:Et_2O 2:1) as a colorless oil in 85% of yield.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.93 (dq, *J* = 14.9, 6.9 Hz, 1H, CH_3CH=), 6.16 (dq, *J* = 14.9, 1.7 Hz, 1H, COC*H*=), 5.78 (ddt, *J* = 17.1, 10.3, 5.3 Hz, 2H, NCH_2CH=), 5.21-5.10 (m, 4H, CH=CH_2), 4.01 (d, *J* = 5.7 Hz, 2H, NCH_2), 3.91 (d, *J* = 4.1 Hz, 2H, NCH_2), 1.86 (dd, *J* = 6.9, 1.7 Hz, 3H, CHCH_3).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.7, 142.1, 133.4, 133.1, 121.8, 117.2, 116.7, 49.1, 48.4, 18.3.

HRMS (ESI+, m/Z): calcd for $C_{10}H_{16}NO$ $[M+H]^+$: 166.12264, found: 166.12242.

***(E)*-*N*,*N*-Dibenzyllbut-2-enamide (1d)**



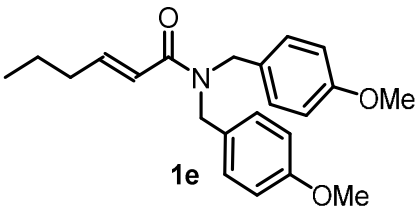
The product **1d** was synthesized following Method 3 and obtained after column chromatography (SiO_2, pentane:Et_2O 2:1) as a colorless oil in 85% of yield.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.39-7.17 (m, 10H, CH_{Ar}), 7.08 (dq, *J* = 14.9, 6.9 Hz, 1H, CH_3CH=), 6.30 (dq, *J* = 14.9, 1.6 Hz, 1H, COC*H*=), 4.64 (s, 2H, NCH_2), 4.51 (s, 2H, NCH_2), 1.87 (dd, *J* = 6.9, 1.6 Hz, 3H, CHCH_3).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.4, 143.1, 137.5, 136.9, 129.0, 128.7, 128.4, 127.7, 127.5, 126.6, 121.7, 49.9, 48.5, 18.4.

HRMS (ESI+, m/Z): calcd for $C_{18}H_{20}NO$ $[M+H]^+$: 266.15394, found: 266.15408.

***(E)*-*N*,*N*-Bis(4-methoxybenzyl)hex-2-enamide (1e)**



1e

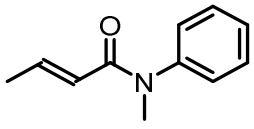
The product **1e** was synthesized following Method 1 and obtained after column chromatography (SiO_2, pentane:Et_2O 2:1) as a pale yellow oil in 91% of yield.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.19 (d, *J* = 8.5 Hz, 2H, C*H*$_{Ar}$), 7.09 (d, *J* = 8.5 Hz, 2H, C*H*$_{Ar}$), 7.04 (dt, *J* = 15.0, 7.1 Hz, 1H, CH_2CH=), 6.89 (d, *J* = 8.5 Hz, 2H, C*H*$_{Ar}$), 6.84 (d, *J* = 8.5 Hz, 2H, C*H*$_{Ar}$), 6.27 (dt, *J* = 15.0, 1.4 Hz, 1H, COC*H*=), 4.54 (s, 2H, NC*H*$_2$), 4.42 (s, 2H, NC*H*$_2$), 3.81 (s, 3H, OC*H*$_3$), 3.80 (s, 3H, OC*H*$_3$), 2.16 (qd, *J* = 7.6, 1.5 Hz, 2H, CHC*H*$_2$), 1.46 (sex (qt), *J* = 7.4 Hz, 2H, CH_3CH_2), 0.90 (t, *J* = 7.4 Hz, 3H, CH_2CH_3).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.2, 159.1, 158.9, 147.6, 129.8, 129.7, 128.7, 127.9, 120.4, 114.3, 113.9, 55.4, 55.3, 49.1, 47.6, 34.6, 21.7, 13.8.

HRMS (ESI+, m/Z): calcd for $C_{22}H_{28}NO_3$ $[M+H]^+$: 354.20637, found: 354.20663.

***(E)*-*N*-Methyl-*N*-phenylbut-2-enamide (1f)**[6]

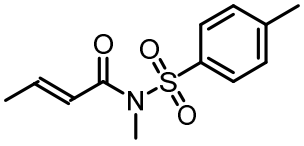


1f

The product **1f** was synthesized following Method 3 and obtained after column chromatography (SiO_2, pentane:Et_2O 2:1) as a colorless oil in 24% of yield.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38 (t, *J* = 7.4 Hz, 2H, C*H*$_{Ar}$), 7.30 (t, *J* = 7.4 Hz, 1H, C*H*$_{Ar}$), 7.15 (d, *J* = 7.4 Hz, 2H, C*H*$_{Ar}$), 6.90 (dq, *J* = 15.1, 6.9 Hz, 1H, CH_3C*H*=), 5.73 (d, *J* = 15.1 Hz, 1H, COC*H*=), 3.30 (s, 3H, NC*H*$_3$), 1.70 (dd, *J* = 6.9, 1.5 Hz, 3H, CHC*H*$_3$).

***(E)*-*N*-Methyl-*N*-tosylbut-2-enamide (1g)**[3]

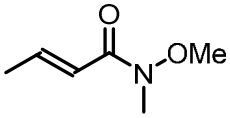


1g

The product **1g** was synthesized following Method 4 and obtained as a colorless oil in 97% of yield.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.74 (d, *J* = 8.0 Hz, 2H, C*H*$_{Ar}$), 7.33 (d, *J* = 8.0 Hz, 2H, C*H*$_{Ar}$), 6.96 (dq, *J* = 15.0, 6.8 Hz, 1H, CH_3C*H*=), 6.80 (dd, *J* = 15.0, 1.5 Hz, 1H, COC*H*=), 3.27 (s, 3H, NC*H*$_3$), 2.43 (s, 3H, PhC*H*$_3$), 1.90 (dd, *J* = 6.8, 1.5 Hz, 3H, CHC*H*$_3$).

***(E)*-*N*-Methyl-*N*-methoxybut-2-enamide (1h)**[7]

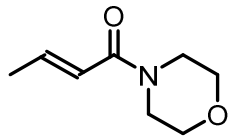


1h

The product **1h** was synthesized following Method 3 and obtained after column chromatography (pentane:Et_2O 1:1) as a colorless oil in 70% of yield. *Note: In this case N-methoxy-methylamine hydrochloride (8 mmol) and dry triethylamine (10 mmol) were used.*

^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.98 (dq, *J* = 15.4, 6.9 Hz, 1H, CH_3C*H*=), 6.42 (dq, *J* = 15.4, 1.7 Hz, 1H, COC*H*=), 3.70 (s, 3H, OC*H*$_3$), 3.23 (s, 3H, NC*H*$_3$), 1.91 (dd, *J* = 6.9, 1.7 Hz, 3H, CHC*H*$_3$).

***(E)*-1-(4-Morpholinyl)-2-buten-1-one (1i)**[8]



1i

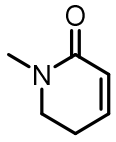
The product **1i** was synthesized following Method 3 and obtained after column chromatography (SiO_2, Et_2O) as a colorless oil in 92% of yield.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.82 (dq, *J* = 15.0, 6.9 Hz, 1H, CH_3CH=), 6.16 (dq, *J* = 15.0, 1.7 Hz, 1H, COC*H*=), 3.61-3.50 (m, 8H, CH_2), 1.81 (dd, *J* = 6.9, 1.7 Hz, 3H, $CHCH_3$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 165.6, 142.1, 121.0, 66.8, 46.1, 42.2, 18.2.

HRMS (ESI+, m/Z): calcd for $C_8H_{14}NO_2$ $[M+H]^+$: 156.10191, found: 156.10190.

5,6-Dihydro-1-methyl-2(*1*H)-pyridinone (1j)[9]

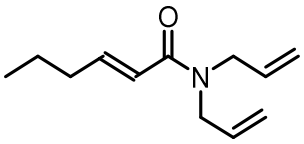


1j

The product **1j** was synthesized following Method 5 and obtained as a colorless oil in 58% of total yield.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.48 (dt, *J* = 9.7, 4.2 Hz, 1H, CH_2CH=), 5.86 (dt, *J* = 9.7, 1.9 Hz, 1H, COC*H*=), 3.36 (t, *J* = 7.2 Hz, 2H, NCH_2), 2.93 (s, 3H, NCH_3), 2.34 (tdd, *J* = 7.2, 4.2, 1.9 Hz, 2H, CH_2CH=).

***(E)*-*N*,*N*-Diallyl-hex-2-enamide (1k)**



1k

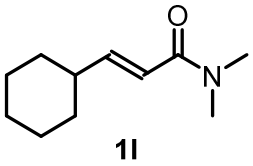
The product **1k** was synthesized following Method 1 and obtained as a colorless oil in 63% of yield.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.93 (dt, *J* = 15.1, 7.0 Hz, 1H, C*H*=CH), 6.14 (dd, *J* = 15.1, 1.5 Hz, 1H, CH=C*H*), 5.84-5.74 (m, 2H, 2 C*H*=CH_2), 5.22-5.11 (m, 4H, 2CH=CH_2), 4.02 (d, *J* = 5.3 Hz, 2H, CH_2CH), 3.92 (d, *J* = 4.6 Hz, 2H, CH_2CH), 2.17 (qd, *J* = 7.3, 1.5 Hz, 2H, C$H_2$$CH_2$), 1.47 (dq, *J* = 14.7, 7.3 Hz, 2H, C$H_2$$CH_3$), 0.92 (t, *J* = 7.3 Hz, 3H, CH_2CH_3).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.9, 147.1, 133.5, 133.2, 120.4, 117.4, 116.8, 49.2, 48.5, 34.7, 21.7, 13.8.

HRMS (ESI+, m/Z): calcd for $C_{12}H_{20}NO$ $[M+H]^+$: 194.15394, found: 194.15402.

(*E*)-*N*,*N*-Dimethyl-3-cyclohexyl-prop-2-enamide (1l)[10]



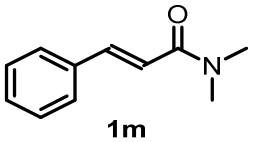
1l

The product **1l** was synthesized following Method 6 and obtained as a colorless liquid after column chromatography (SiO_2, Et_2O) in 14% yield.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.82 (dd, *J* = 15.2, 7.0 Hz, 1H, C*H*=CH), 6.17 (dd, *J* = 15.2, 1.2 Hz, 1H, CH=C*H*), 3.06 (s, 3H, NCH_3), 2.99 (s, 3H, NCH_3), 2.16-2.08 (m, 1H, C*H*), 1.76-1.64 (m, 5H, CH_2), 133-1.09 (m, 5H, CH_2).

HRMS (ESI+, m/Z): calcd for $C_{11}H_{20}NO$ $[M+H]^+$: 182.15394, found: 182.15371.

(*E*)-*N*,*N*-Dimethyl-3-phenyl-prop-2-enamide (1m)[11]

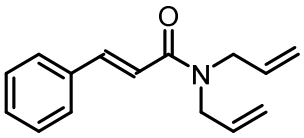


1m

The product **1m** was synthesized following Method 1 and obtained as a white powder in 82 % yield.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.67 (d, *J* = 15.4 Hz, 1H, C*H*=CH), 7.54-7.52 (m, 2H, CH_{Ar}), 7.39-7.32 (m, 3H, CH_{Ar}), 6.89 (d, *J* = 15.4 Hz, 1H, CH=C*H*), 3.17 (s, 3H, NCH_3), 3.07 (s, 3H, NCH_3).

***(E)*-*N*,*N*-Diallyl-3-phenyl-prop-2-enamide (1n)**



1n

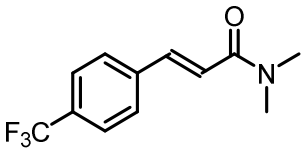
The product **1n** was synthesized following Method 1 and obtained as a colorless oil in 90% of yield.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.72 (d, *J* = 15.4 Hz, 1H, C*H*=CH), 7.50-7.48 (m, 2H, CH_{Ar}), 7.37-7.30 (m, 3H, CH_{Ar}), 6.78 (d, *J* = 15.4 Hz, 1H, CH=C*H*), 5.89-5.78 (m, 2H, 2C*H*=CH_2), 5.25-5.15 (m, 4H, 2CH=CH_2), 4.09 (d, *J* = 5.8 Hz, 2H, CH_2CH), 4.02 (d, *J* = 4.1 Hz, 2H, CH_2CH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.7, 143.0, 135.4, 133.3, 133.3, 129.6, 128.8, 127.9, 117.7, 117.5, 116.9, 49.3, 48.8.

HRMS (ESI+, m/Z): calcd for $C_{15}H_{18}NO$ $[M+H]^+$: 228.13838, found: 228.13829.

***(E)*-*N*,*N*-Dimethyl-3-(4-(trifluoromethyl)phenyl)-prop-2-enamide (1o)**[12]

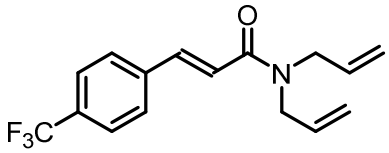


1o

The product **1o** was synthesized following Method 1 and obtained as a white solid in 87% of yield.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.67 (d, *J* = 15.4 Hz, 1H, C*H*=CH), 7.62 (s, 4H, CH_{Ar}), 6.96 (d, *J* = 15.5 Hz, 1H, CH=C*H*), 3.19 (s, 3H, NCH_3), 3.09 (s, 3H, NCH_3).

***(E)*-*N*,*N*-Diallyl-3-(4-(trifluoromethyl)phenyl)-prop-2-enamide (1p)**



1p

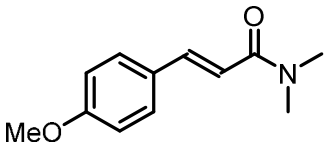
The product **1p** was synthesized following Method 1 and obtained as a colorless oil in 69% of yield.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.73 (d, *J* = 15.4 Hz, 1H, C*H*=CH), 7.61 (d, *J* = 8.6 Hz, 2H, CH_{Ar}), 7.59 (d, *J* = 8.6 Hz, 2H, CH_{Ar}), 6.84 (d, *J* = 15.4 Hz, 1H, CH=C*H*), 5.91-5.78 (m, 2H, 2C*H*=CH_2), 5.29-5.17 (m, 4H, 2CH=CH_2), 4.11 (d, *J* = 6.1 Hz, 2H, CH_2CH), 4.04 (d, *J* = 4.7 Hz, 2H, CH_2CH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.2, 141.3, 138.9 (q, *J* = 1.3 Hz), 133.2, 1^{31}.3 (q, *J* = 32.7 Hz), 128.1, 125.9 (q, *J* = 3.8 Hz), 124.0 (q, *J* = 272.3 Hz), 120.3, 117.8, 117.1, 49.4, 49.0.

HRMS (ESI+, m/Z): calcd for $C_{16}H_{17}F_3NO$ $[M+H]^+$: 296.12568, found: 296.12584.

***(E)*-*N*,*N*-Dimethyl-3-(4-methoxyphenyl)-prop-2-enamide (1q)**[4,5]

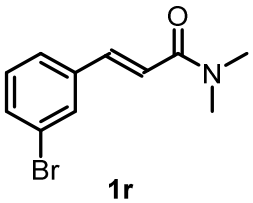


1q

The product **1q** was synthesized following Method 1 and obtained as a white solid in 79% of yield.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.63 (d, *J* = 15.4 Hz, 1H, C*H*=CH), 7.48 (d, *J* = 8.7 Hz, 2H, CH_{Ar}), 6.89 (d, *J* = 8.7 Hz, 2H, CH_{Ar}), 6.76 (d, *J* = 15.4 Hz, 1H, CH=C*H*), 3.83 (s, 3H, OCH_3), 3.16 (s, 3H, NCH_3), 3.06 (s, 3H, NCH_3).

***(E)*-*N*,*N*-Dimethyl-3-(3-bromophenyl)-prop-2-enamide (1r)**[13]



1r

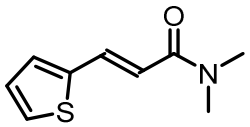
The product **1r** was synthesized following Method 1 and obtained as a white solid in 79% of yield.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.67 (t, *J* = 1.5 Hz, 1H, CH_{Ar}), 7.58 (d, *J* = 15.5 Hz, 1H, C*H*=CH), 7.47 (d, *J* = 7.8 Hz, 1H, CH_{Ar}), 7.42 (d, *J* = 7.8 Hz, 1H, CH_{Ar}), 7.23 (d, *J* = 7.8 Hz, 1H, CH_{Ar}), 6.88 (d, *J* = 15.5 Hz, 1H, CH=C*H*), 3.18 (s, 3H, NCH_3), 3.08 (s, 3H, NCH_3).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.3, 140.8, 137.6, 132.4, 130.4, 130.2, 126.8, 123.0, 119.0, 37.5, 36.1.

HRMS (ESI+, m/Z): calcd for $C_{11}H_{13}BrNO$ $[M+H]^+$: 254.01750, found: 254.01757.

***(E)*-*N*,*N*-Dimethyl-3-(thiophen-2-yl)-prop-2-enamide (1s)**[4,5]

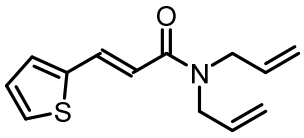


1s

The product **1s** was synthesized following Method 1 and obtained as a brown solid in 77% of yield.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.79 (d, *J* = 15.1 Hz, 1H, C*H*=CH), 7.31 (d, *J* = 5.1 Hz, 1H, CH_{Ar}), 7.21 (d, *J* = 3.6 Hz, 1H, CH_{Ar}), 7.03 (dd, *J* = 5.1, 3.6 Hz, 1H, CH_{Ar}), 6.69 (d, *J* = 15.1 Hz, 1H, CH=C*H*), 3.14 (s, 3H, NCH_3), 3.07 (s, 3H, NCH_3).

***(E)*-*N*,*N*-Diallyl-3-(thiophen-2-yl)-prop-2-enamide (1t)**



1t

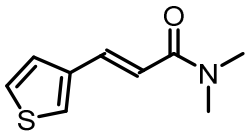
The product **1t** was synthesized following Method 1 and obtained as a colorless oil in 88% of yield.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.83 (d, *J* = 15.1 Hz, 1H, C*H*=CH), 7.31 (d, *J* = 5.0 Hz, 1H, CH_{Ar}), 7.21 (d, *J* = 3.5 Hz, 1H, CH_{Ar}), 7.03 (dd, *J* = 5.0, 3.5 Hz, 1H, CH_{Ar}), 6.58 (d, *J* = 15.1 Hz, 1H, CH=C*H*), 5.90-5.78 (m, 2H, 2 C*H*=CH_2), 5.27-5.15 (m, 4H, 2 CH=CH_2), 4.09 (d, *J* = 5.9 Hz, 2H, CH_2CH), 4.00 (d, *J* = 3.8 Hz, 2H, CH_2CH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.4, 140.6, 135.8, 133.4, 133.3, 130.3, 128.1, 127.3, 117.5, 117.0, 116.5, 49.4, 48.9.

HRMS (ESI+, m/Z): calcd for $C_{13}H_{16}NOS$ $[M+H]^+$: 234.09471, found: 234.09476.

***(E)*-*N*,*N*-Dimethyl-3-(thiophen-3-yl)-prop-2-enamide (1u)**



1u

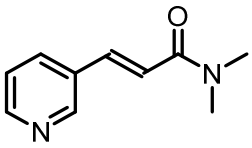
The product **1u** was synthesized following Method 1 and obtained as a brown solid in 72% of yield.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.66 (d, *J* = 15.4 Hz, 1H, C*H*=CH), 7.45 (dd, *J* = 2.8, 1.2 Hz, 1H, CH_{Ar}), 7.32 (dd, *J* = 5.1, 2.8 Hz, 1H, C$H_{Ar)}$, 7.30 (dd, *J* = 5.1, 1.2 Hz, 1H, C$H_{Ar)}$, 6.72 (d, *J* = 15.4 Hz, 1H, CH=C*H*), 3.13 (s, 3H, NCH_3), 3.08 (s, 3H, NCH_3).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.9, 138.4, 136.1, 126.9, 126.7, 125.2, 117.1, 37.4, 36.1.

HRMS (ESI+, m/Z): calcd for $C_9H_{12}NOS$ $[M+H]^+$: 182.06341, found: 182.06333.

***(E)*-*N*,*N*-Dimethyl-3-(3-piridinyl)-prop-2-enamide (1v)**[14]

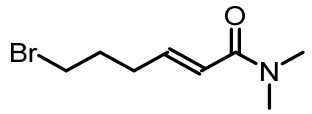


1v

The product **1v** was synthesized following Method 1 and obtained after column (SiO_2, EtOAc) as a white solid in 69% of yield. *Note: In this case the reaction was quenched with saturated Na_2CO_3 solution and the aqueous layer was extracted with DCM. The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure.*

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.70 (d, *J* = 1.9 Hz, 1H, CH_{Ar}), 8.51 (dd, *J* = 4.7, 1.4 Hz, 1H, CH_{Ar}), 7.77 (dt, *J* = 7.9, 1.9 Hz, 1H, CH_{Ar}), 7.59 (d, *J* = 15.5, 1.2 Hz, 1H, PyC*H*), 7.25 (dd, *J* = 7.9, 4.7 Hz, 1H, CH_{Ar}), 6.92 (d, *J* = 15.5 Hz, 1H, COC*H*), 3.13 (s, 3H, NCH_3), 3.02 (s, 3H, NCH_3).

***(E)*-*N*,*N*-Dimethyl-6-bromo-hex-2-enamide (1w)**



1w

The product **1w** was synthesized following Method 6 and obtained as a colorless oil.

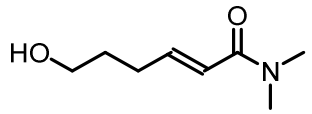
Note: In this case after purification by column chromatography (SiO_2, EtOAc) a mixture of 90% title amide and 10% chloro-substituted amide was obtained. The mixture (1.5 mmol) was dissolved in CH_2Br_2 (10 mL) and added to a stirred solution of tetraethylammonium bromide (3.15 g, 15 mmol) in CH_2Br_2 (20 mL). The flask was fitted with a condenser and heated at 80 °C under nitrogen for 16 h. The reaction mixture was condensed under reduced pressure and Et_2O was added. The mixture was filtered and the filtrate was condensed under reduced pressure. The residue was purified by column chromatography on silica gel (SiO_2, EtOAc) to afford the title amide (21% yield) as a colorless oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.81 (dt, *J* = 15.0, 7.2 Hz, 1H, CH_2CH=), 6.32 (dt, *J* = 15.0, 1.4 Hz, 1H, COC*H*=), 3.42 (t, *J* = 6.5 Hz, 2H, $BrCH_2$), 3.08 (s, 3H, NCH_3), 3.00 (s, 3H, NCH_3), 2.38 (qd, *J* = 7.2, 1.5 Hz, 2H, CH_2CH=), 2.01 (quint, *J* = 6.6 Hz, 2H, $BrCH_2CH_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.5, 143.5, 121.7, 37.3, 35.7, 32.9, 31.0, 30.6.

HRMS (ESI+, m/Z): calcd for $C_8H_{15}BrNO$ $[M+H]^+$: 220.03315, found: 220.03144

***(E)*-*N*,*N*-Dimethyl-6-hydroxy-hex-2-enamide (1x)**



1x

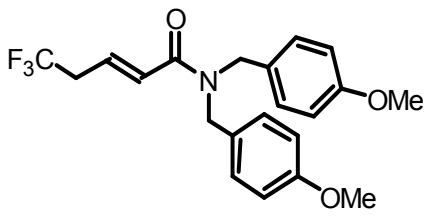
The product **1x** was synthesized following Method 6 and obtained after column chromatography (SiO_2, Et_2O:MeOH 20:1) as a colorless oil 15% of yield.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.87 (dt, *J* = 15.1, 7.0 Hz, 1H, CH_2CH=), 6.28 (dt, *J* = 15.1, 1.5 Hz, 1H, $COCH$=), 3.67 (t, *J* = 6.4 Hz, 2H, $OHCH_2$), 3.07 (s, 3H, NCH_3), 2.99 (s, 3H, NCH_3), 2.31 (qd, *J* = 7.2, 1.5 Hz, 2H, CH_2CH=), 1.73 (quint, *J* = 6.6 Hz, 2H, $OHCH_2CH_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.0, 145.8, 120.4, 61.5, 37.4, 35.7, 31.2, 28.8.

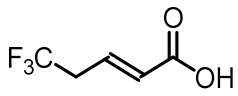
HRMS (ESI+, m/Z): calcd for $C_8H_{16}NO_2$ $[M+H]^+$: 158.11756, found: 158.11764.

(*E*)-*N*,*N*-Bis(4-methoxybenzyl)hex-2-enamide (1y)



1y

Amide **1y** was synthesized from the corresponding carboxylic acid: (*E*)-5,5,5-trifluoropent-2-enoic acid, which was not commercially available and it was prepared by cross metathesis: Allyl trifluoromethane (437 mg, 3.97 mmol) was condensed at 0 °C in a pressure proof flask and dissolved in toluene (2.5 mL). Then, Hoveyda-Grubbs II catalyst (50 mg, 0.079 mmol) and acrylic acid (545 μL, 4.94 mmol) were added, pressure tube was carefully closed and warmed up to 80 °C while stirring overnight. Then, flask was cooled down to room temperature and carefully opened, and solvent was evaporated in vacuo. The crude mixture was purified by column chromatography on silica gel (SiO_2, pentane:Et_2O 10:1) to afford the acid (257 mg, 42% yield) as a yellowish oil and it was fully characterized:



^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.94 (dt, *J* = 15.6, 7.2 Hz, 1H, CH=$CHCH_2$), 6.07 (d, *J* = 15.8 Hz, 1H, CH=$CH$$CH_2$), 3.04 (qdd, *J* = 10.3, 7.3, 1.3 Hz, 2H, CH_2).

^{19}F NMR ($CDCl_3$, 377 MHz): δ -65.4 (t, *J* = 10.3 Hz).

^{13}C NMR ($CDCl_3$, 101 MHz): δ 170.7, 137.9 (q, *J* = 3.6 Hz), 127.0, 125.1 (q, *J* = 276.9 Hz), 36.9 (q, *J* = 30.8 Hz).

HRMS (ESI+, m/Z): calcd for $C_5H_4F_3O_2$ $[M-H]^-$: 153.01689, found: 153.01712.

Then, the product **1y** was synthesized following Method 1 and obtained after column chromatography (SiO_2, pentane:Et_2O 2:1) as a pale yellow oil in 16 % of yield.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.19 (d, *J* = 8.3 Hz, 2H, C*H*$_{Ar}$), 7.07 (d, *J* = 8.4 Hz, 2H, C*H*$_{Ar}$), 6.91-6.84 (m, 5H, C*H*$_{Ar}$, CH_2C*H*=), 6.50 (dt, *J* = 15.2 Hz, 1H, COC*H*=), 4.55 (s, 2H, NC*H*$_2$), 4.42 (s, 2H, NC*H*$_2$), 3.82 (s, 3H, OC*H*$_3$), 3.80 (s, 3H, OC*H*$_3$), 3.02-2.92 (m, 1H, C*H*$_2$).

^{19}F NMR ($CDCl_3$, 377 MHz): δ -65.5 (t, *J* = 10.5 Hz).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 165.8, 159.4, 159.2, 133.3 (q, *J* = 3.5 Hz), 130.0, 129.2, 128.2, 127.9, 127.2, 125.4 (q, *J* = 276.8 Hz), 114.5, 114.1, 55.44, 55.39, 49.3, 47.9, 37.1 (q, *J* = 30.4 Hz).

HRMS (ESI+, m/Z): calcd for $C_{21}H_{23}F_3NO_3$ $[M+H]^+$: 394.16245, found: 394.16197.

8. Cu- asymmetric conjugate addition (ACA) of Grignard reagents to enamides

General procedure

In a flame-dried Schlenk tube equipped with septum and magnetic stirring bar, CuBr·SMe_2 and ligand (*R*,*S*$_{Fe}$)-**L1** were dissolved in DCM (final concentration of enamide substrate is 0.1M) and stirred under nitrogen atmosphere for 20 min. The substrate was added at once. After stirring for 5 min. at RT the reaction mixture was cooled down (see the details per substrate), followed by addition of LA. After 20 min., RMgBr was added by hand in about 1 min. After stirring for 18 h, the reaction was quenched with MeOH followed by addition of saturated aqueous NH_4Cl solution and warming up to RT. The reaction mixture was extracted with DCM (10 mL × 3). Combined organic phases were dried over $MgSO_4$, filtered and solvents were evaporated on a rotary evaporator. The crude was purified by flash chromatography on silica gel.

Note 1: The procedures for ACA differ in LA, the reaction temperature and mode of addition. The details are given per product. The reactions were carried out either using 0.1 or 0.2 mmol of an enamide substrate.

Note 2: DCM was found to be the most optimal solvent while presence of even traces of THF is detrimental for the reaction conversion and enantioselectivity. On the other hand Cu salts other than CuBr can be used as well as long as the halide in the Grignard reagent used is a bromide (RMgBr)

Note 3: Grignard reagents must be used either in Et2O or tBuOMe. THF even in a small quantities must be avoided. Copper catalysed conjugate addition of THF solution of iPrMgBr for instance led to racemic product while Et2O solution afforded product wih 76% ee

Procedure for the preparative (10 g) scale copper ACA using 5 mol% of chiral catalyst and the recovery of the chiral catalyst (L1-CuBr)

The reaction on a preparative scale (Table S2, entry 23) was carried out for the synthesis of the product **3h** using the general procedure described above. The reaction was carried out using **1a** (10 g, 71mmol), $CuBr{\cdot}SMe_2$ (727.9 mg, 3.54 mmol, 5 mol%), ligand **L1** (2721.2 mg, 4.25 mmol, 6 mol%), TMSOTf (25.6 mL, 141.6 mmol), MeMgBr (141.6 mmol, 3.0 M in Et_2O), 708 mL of DCM at 0 ^oC, for a total reaction time of 2h. Product **3h** was obtained as a colorless oil [93% yield, 96% *ee*] after column chromatography (SiO_2, pentane:Et_2O 1:1).

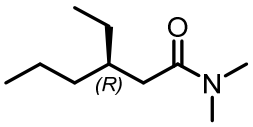
The chiral catalyst was recovered in this reaction in the form of a Cu-complex (**L1**-CuBr**).** The reaction mixture was loaded on a column with silica. Using a pentane:Et_2O ratio of 1:1 the **L1**-CuBr eluted first, followed by CA product **3h**. Catalyst **L1**-CuBr was obtained as a yellow-orange solid in 80% of yield and reused for another ACA reaction (Table S2, entry 21) with similar performance.

General procedure for the synthesis of racemic products

Racemic products were synthesized in a flame-dried Schlenk tube equipped with septum and magnetic stirring bar by mixing the corresponding enamide substrate (0.1 M in DCM) with 2 equiv. of corresponding Grignard reagents and 1.1 equiv. of TMSOTf at −10 °C for 2 h. The quenching and isolation procedure is the same as described above.

Specific experimental details and product characterisation

***(R)*-*N*,*N*-Dimethyl-3-ethyl-hexanamide (2a)**



2a

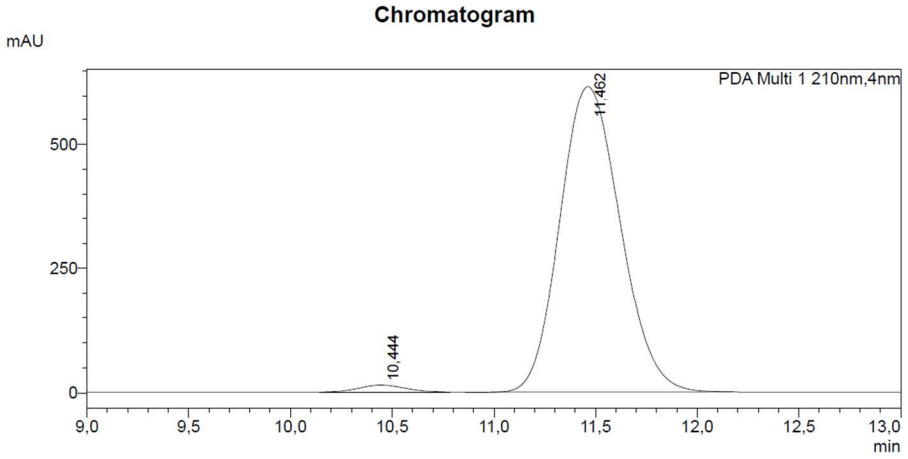
The reaction was performed with 0.2 mmol **1a**, $CuBr{\cdot}SMe_2$ (2.06 mg, 0.01 mmol, 5 mol%), ligand **L1** (7.68 mg, 0.012 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (50 μL, 0.4 mmol), EtMgBr (0.4 mmol, 3.0 M in Et_2O), 2.0 mL of DCM at −78 °C. Product **2a** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 1:1) [73% yield, 97% *ee*]. *Note: When the reaction was carried out at 0 °C using 10mol% of the catalyst and 2 equiv. of TMSOTf the product **2a** was obtained in 92% yield and 93% ee (Table S2, entry 19).*

^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.00 (s, 3H, NC*H*$_3$), 2.93 (s, 3H, NC*H*$_3$), 2.21 (dd, *J* = 15.1, 7.1 Hz, 1H, C*H*HCO), 2.20 (dd, *J* = 15.1, 6.7 Hz, 1H, CH*H*CO), 1.91-1.81 (m, 1H, C*H*CH_2), 1.36-1.21 (m, 5H, C*H*$_2CH_3$, CH_2C*H*$_2CH_3$), 1.24-1.18 (m, 1H, CH*H*CH_3), 0.87 (d, *J* = 7.0 Hz, 3H, C*H*$_3$CH), 0.85 (t, *J* = 7.5 Hz, 3H, C*H*$_3CH_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.1, 37.8, 37.6, 36.1, 35.9, 35.5, 26.4, 19.9, 14.5, 11.0.

HRMS (ESI+, m/Z): calcd for $C_{10}H_{22}NO$ $[M+H]^+$: 172.16959, found: 172.16962.

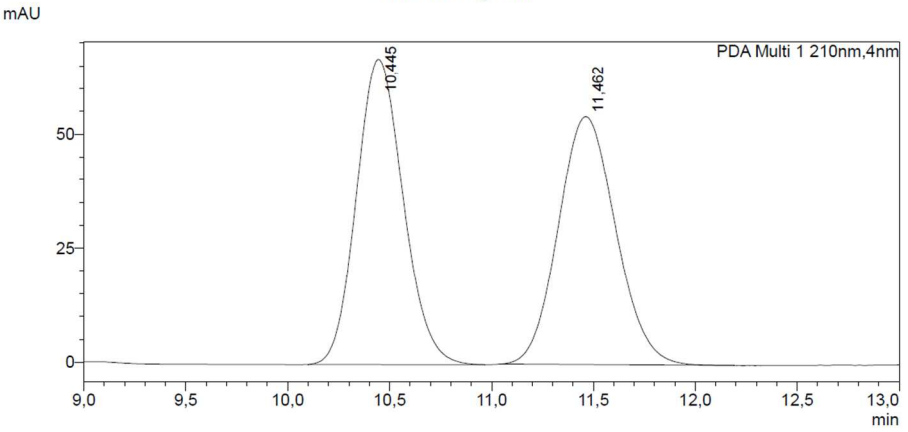
HPLC: Chiracel-OBH, *n*-heptane/*i*-PrOH 95:5, 0.5 mL/min, 40 °C, detection at 210 nm. Retention time (min): 10.4 (minor) and 11.5 (major).



Peak Table

PDA Ch1 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	10,444	217265	13911	1,680
2	11,462	12717057	616670	98,320
Total		12934322	630581	

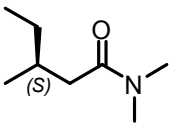


Peak Table

PDA Ch1 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	10,445	1068987	66946	50,040
2	11,462	1067275	54327	49,960
Total		2136262	121273	

***(S)*-*N*,*N*-Dimethyl-3-methyl-pentanamide (2b)**[1]

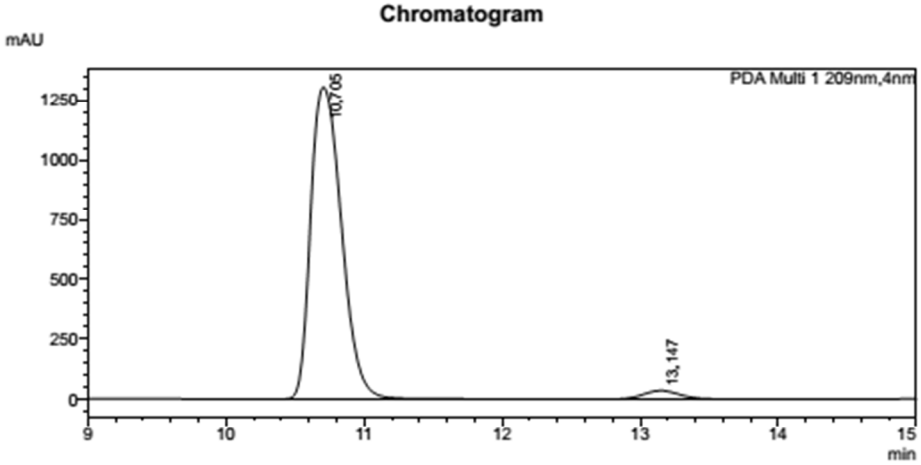


2b

The reaction was performed with 0.2 mmol **1b**, $CuBr{\cdot}SMe_2$ (2.06 mg, 0.01 mmol, 5 mol%), ligand **L1** (7.68 mg, 0.012 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (50 μL, 0.4 mmol), EtMgBr (0.4 mmol, 3.0 M in Et_2O), 2.0 mL of DCM at −78 °C. Product **2b** was obtained as a colorless oil after column chromatography (SiO_2, Et_2O) [79% yield, 94% *ee*].

^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.00 (s, 3H, NC*H*$_3$), 2.94 (s, 3H, NC*H*$_3$), 2.30 (dd, *J* = 14.7, 5.9 Hz, 1H, C*H*HCO), 2.11 (dd, *J* = 14.7, 8.1 Hz, 1H, CH*H*CO), 1.98-1.86 (m, 1H, C*H*CH$_2$), 1.44-1.34 (m, 1H, C*H*HCH$_3$), 1.24-1.14 (m, 1H, CH*H*CH$_3$), 0.92 (d, *J* = 6.7 Hz, 3H, C*H*$_3$CH), 0.89 (t, *J* = 7.3 Hz, 3H, C*H*$_3$CH$_2$).

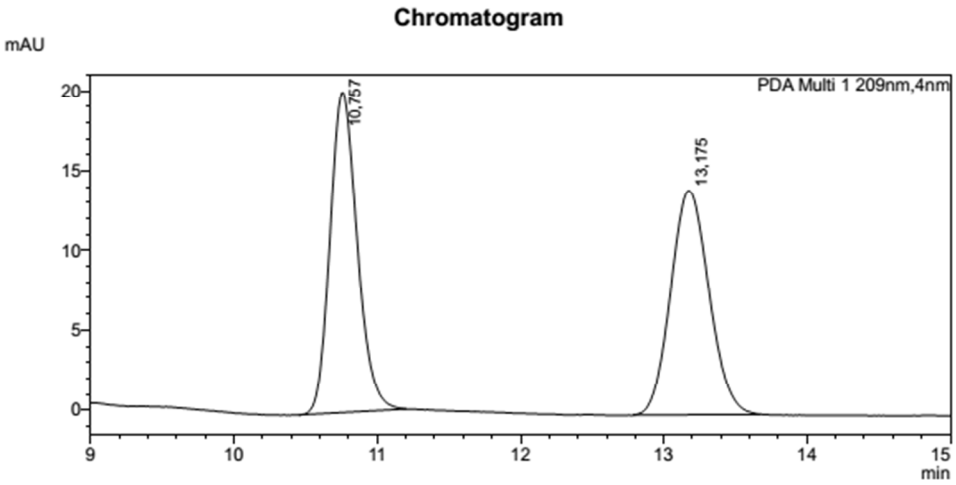
HPLC: Chiracel-OBH, *n*-heptane/*i*-PrOH 90:10, 0.5 mL/min, 40 °C, detection at 209 nm. Retention time (min): 10.7 (major) and 13.1 (minor).



Peak Table

PDA Ch1 209nm

Peak#	Ret. Time	Area	Height	Conc.
1	10,705	20228294	1306007	96,933
2	13,147	640032	34873	3,067
Total		20868325	1340880	

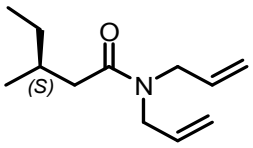


Peak Table

PDA Ch1 209nm

Peak#	Ret. Time	Area	Height	Conc.
1	10,757	264624	20024	50,278
2	13,175	261697	14067	49,722
Total		526321	34092	

***(S)*-*N*,*N*-Diallyl-3-methyl-pentanamide (2c)**



2c

The reaction was performed with 0.2 mmol **1c**, $CuBr{\cdot}SMe_2$ (2.06 mg, 0.01 mmol, 5 mol%), ligand **L1** (7.68 mg, 0.012 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (50 μL, 0.4 mmol), EtMgBr (0.4 mmol, 3.0 M in Et_2O), 2.0 mL of DCM at −78 °C. Product **2c** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 5:1) [52% yield, 98% *ee*].

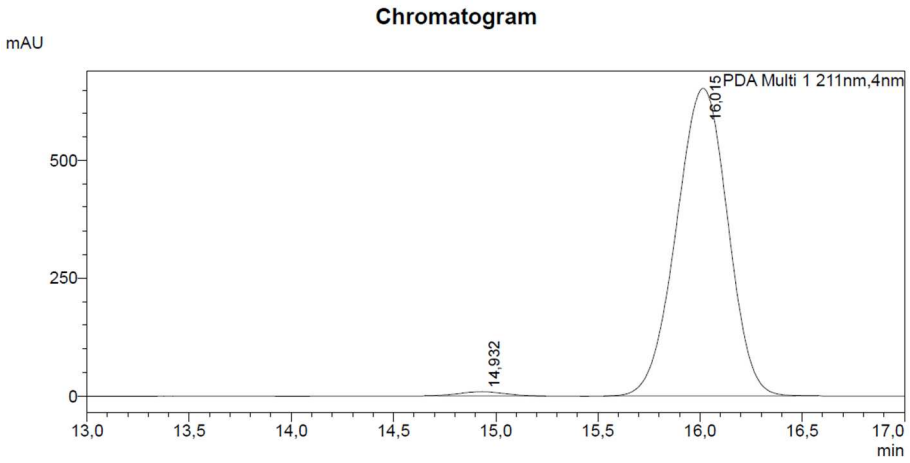
^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.80-5.70 (m, 2H, C*H*=CH_2), 5.20-5.08 (m, 4H, CH=CH_2), 4.00 (dd, *J* = 15.3, 5.9 Hz, 1H, NC*H*HCH=CH_2), 3.96 (dd, *J* = 15.3, 5.9 Hz, 1H, NCH*H*CH=CH_2), 3.87 (dt, *J* = 4.8, 1.8 Hz, 2H, NCH_2CH=CH_2), 2.28 (dd, *J* = 14.9, 5.9 Hz, 1H, C*H*HCO), 2.10 (dd, *J* = 14.9, 8.0 Hz, 1H,

CH*H*CO), 2.02-1.90 (m, 1H, C*H*CH_2), 1.43-1.33 (m, 1H, CH_3C*H*H), 1.22-1.13 (m, 1H, CH_3CH*H*), 0.91 (d, *J* = 6.6 Hz, 3H, CH_3CH), 0.88 (t, *J* = 7.5 Hz, 3H, C$H_3$$CH_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.8, 133.6, 133.2, 117.1, 116.6, 49.3, 47.9, 40.1, 32.0, 29.7, 19.6, 11.6.

HRMS (ESI+, m/Z): calcd for $C_{12}H_{22}NO$ $[M+H]^+$: 196.16959, found: 196.16933.

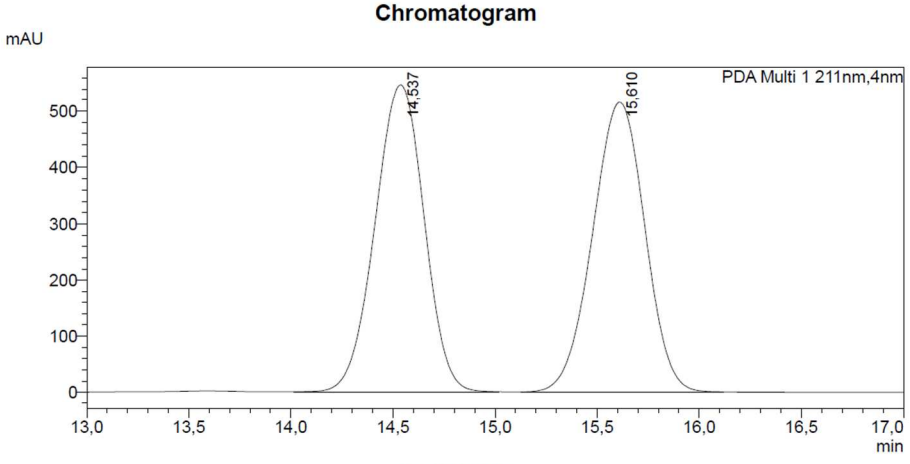
HPLC: Chiracel-ODH, *n*-heptane/*i*-PrOH 99:01, 0.5 mL/min, 40 °C, detection at 211 nm. Retention time (min): 14.9 (minor) and 16.0 (major).



Peak Table

PDA Ch1 211nm

Peak#	Ret. Time	Area	Height	Conc.
1	14,932	136632	8764	1,185
2	16,015	11394875	653622	98,815
Total		11531507	662385	

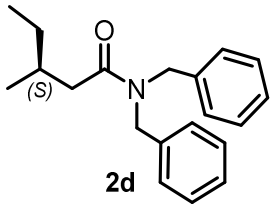


Peak Table

PDA Ch1 211nm

Peak#	Ret. Time	Area	Height	Conc.
1	14,537	9133797	546961	49,854
2	15,610	9187223	514678	50,146
Total		18321020	1061639	

***(S)*-*N*,*N*-Dibenzyl-3-methyl-pentanamide (2d)**



2d

The reaction was performed with 0.2 mmol **1d**, $CuBr{\cdot}SMe_2$ (2.06 mg, 0.01 mmol, 5 mol%), ligand **L1** (7.68 mg, 0.012 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (50 μL, 0.4 mmol), EtMgBr (0.4 mmol, 3.0 M in Et_2O), 2.0 mL of DCM at −78 °C. Product **2d** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 5:1) [78% yield, 97% *ee*].

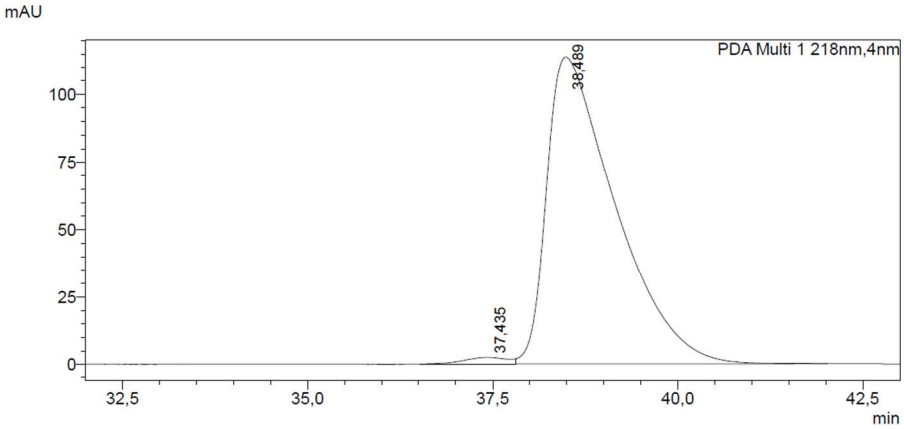
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.39-7.27 (m, 6H, C*H*$_{Ar}$), 7.23 (d, *J* = 7.4 Hz, 2H, C*H*$_{Ar}$), 7.16 (d, *J* = 7.4 Hz, 2H, C*H*$_{Ar}$), 4.65 (d, *J* = 14.7 Hz, 1H, NC*H*H), 4.58 (d, *J* = 14.7 Hz, 1H, NCH*H*), 4.46 (s, 2H, NC*H*$_2$), 2.42 (dd, *J* = 15.0, 5.8 Hz, 1H, C*H*HCO), 2.24 (dd, *J* = 15.0, 8.0 Hz, 1H, CH*H*CO), 2.11-2.02 (m, 1H, C*H*), 1.45-1.40 (m, 1H, CH_3C*H*H), 1.24-1.19 (m, 1H, CH_3CH*H*), 0.97 (d, *J* = 6.6 Hz, 3H, C*H*$_3$CH), 0.90 (t, *J* = 7.4 Hz, 3H, C*H*$_3$$CH_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.3, 137.8, 136.8, 129.0, 128.7, 128.4, 127.7, 127.4, 126.5, 50.0, 48.1, 40.3, 32.2, 29.7, 19.6, 11.6.

HRMS (ESI+, m/Z): calcd for $C_{20}H_{26}NO$ $[M+H]^+$: 296.20089, found: 296.20084.

HPLC: Chiracel-ODH, *n*-heptane/*i*-PrOH 99.5:0.5, 0.8 mL/min, 40 °C, detection at 218 nm. Retention time (min): 37.4 (minor) and 38.5 (major).

Chromatogram

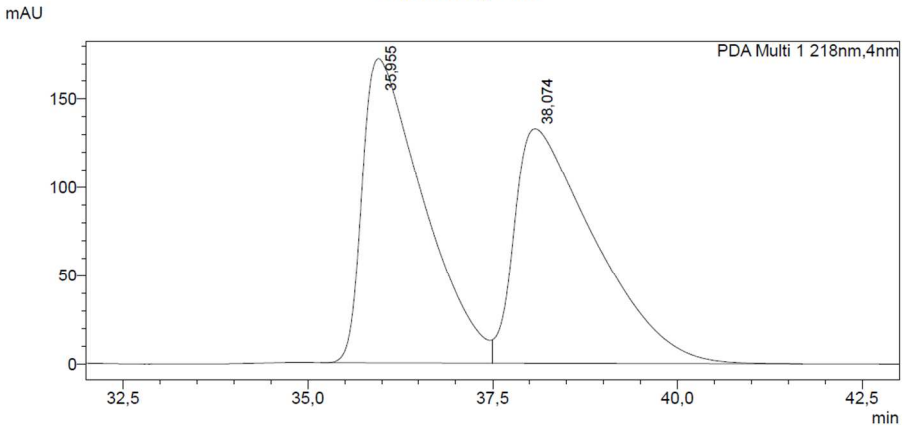


Peak Table

PDA Ch1 218nm

Peak#	Ret. Time	Area	Height	Conc.
1	37,435	98705	2376	1,330
2	38,489	7322151	113555	98,670
Total		7420856	115931	

Chromatogram

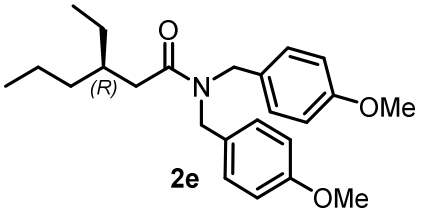


Peak Table

PDA Ch1 218nm

Peak#	Ret. Time	Area	Height	Conc.
1	35,955	9924418	172365	49,575
2	38,074	10094393	132682	50,425
Total		20018811	305048	

***(R)*-*N*,*N*-Bis(4-methoxybenzyl)-3-ethyl-hexanamide (2e)**



2e

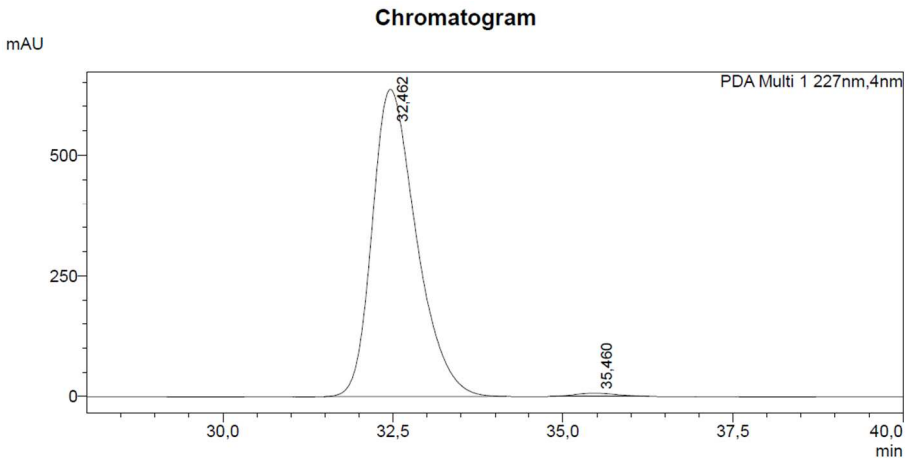
The reaction was performed with 0.1 mmol **1e**, $CuBr{\cdot}SMe_2$ (1.03 mg, 0.005 mmol, 5 mol%), ligand **L1** (3.84 mg, 0.006 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (38 μL, 0.3 mmol), EtMgBr (0.2 mmol, 3.0 M in Et_2O), 1.0 mL of DCM at −78 °C. Product **2e** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 4:1) [72% yield, 98% *ee*].

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.15 (d, *J* = 8.6 Hz, 2H, C*H*$_{Ar}$), 7.07 (d, *J* = 8.6 Hz, 2H, C*H*$_{Ar}$), 6.89 (d, *J* = 8.6 Hz, 2H, C*H*$_{Ar}$), 6.84 (d, *J* = 8.6 Hz, 2H, C*H*$_{Ar}$), 4.51 (s, 2H, NC*H*$_2$), 4.37 (s, 2H, NC*H*$_2$), 3.81 (s, 3H, OC*H*$_3$), 3.79 (s, 3H, OC*H*$_3$), 2.33 (dd, *J* = 15.4, 7.1 Hz, 1H, C*H*HCO), 2.31 (dd, *J* = 15.4, 6.7 Hz, 1H, CH*H*CO), 2.00-1.97 (m, 1H, C*H*), 1.40-1.28 (m, 6H, CH_3CH_2, $CH_3CH_2CH_2$), 0.90-0.84 (m, 6H, CH_3CH_2).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.3, 159.1, 159.0, 129.9, 129.8, 128.7, 127.8, 114.3, 114.0, 55.4, 55.4, 49.2, 47.2, 37.8, 36.3, 35.8, 26.4, 19.9, 14.5, 11.0.

HRMS (ESI+, m/Z): calcd for $C_{24}H_{34}NO_3$ $[M+H]^+$: 384.25332, found: 384.25366.

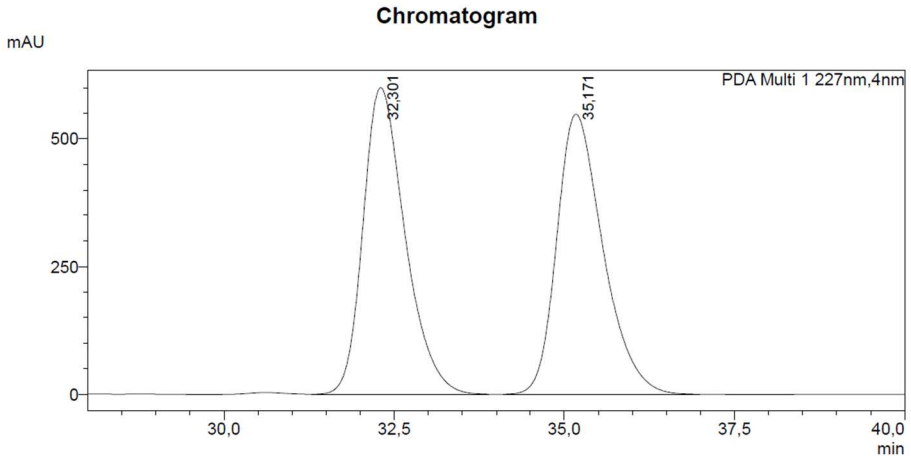
HPLC: Chiracel-ADH, *n*-heptane/*i*-PrOH 95:5, 0.5 mL/min, 40 °C, detection at 227 nm. Retention time (min): 32.5 (major) and 35.5 (minor).



Peak Table

PDA Ch1 227nm

Peak#	Ret. Time	Area	Height	Conc.
1	32,462	28833022	637371	99,044
2	35,460	278425	6743	0,956
Total		29111447	644113	

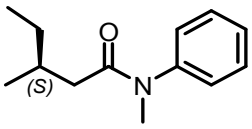


Peak Table

PDA Ch1 227nm

Peak#	Ret. Time	Area	Height	Conc.
1	32,301	25771746	600523	49,885
2	35,171	25890368	547079	50,115
Total		51662114	1147602	

***(S)*-*N*-Methyl-*N*-phenyl-3-methyl-pentanamide (2f)**



2f

The reaction was performed with 0.2 mmol **1f**, $CuBr{\cdot}SMe_2$ (2.06 mg, 0.01 mmol, 5 mol%), ligand **L1** (7.68 mg, 0.012 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (50 μL, 0.4 mmol), EtMgBr (0.4 mmol, 3.0 M in Et_2O), 2.0

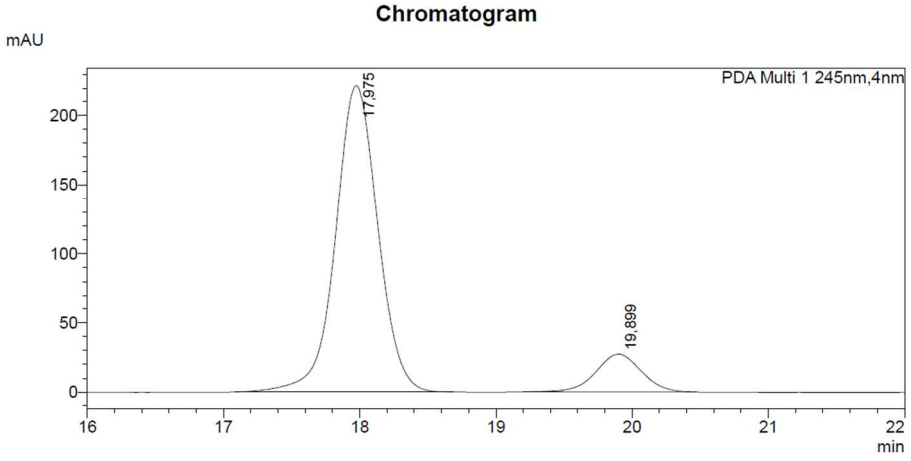
mL of DCM at −78 °C. Product **2f** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 3:1) [66% yield, 77% *ee*].

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.40 (t, *J* = 7.6 Hz, 2H, CH_{Ar}), 7.32 (t, *J* = 7.3 Hz, 1H, CH_{Ar}), 7.15 (d, *J* = 7.5 Hz, 2H, CH_{Ar}), 3.25 (s, 3H, NCH_3), 2.08-2.06 (m, 1H, C*H*HCO), 1.91-1.83 (m, 2H, CH*H*CO, C*H*), 1.24-1.20 (m, 1H, CH_3C*H*H), 1.06-1.03 (m, 1H, CH_3CH*H*), 0.81 (d, *J* = 6.0 Hz, 3H, CH_3CH), 0.75 (t, *J* = 7.4 Hz, 3H, CH_3CH_2).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.9, 144.5, 129.8, 127.7, 127.6, 41.0, 37.5, 32.3, 29.5, 19.5, 11.5.

HRMS (ESI+, m/Z): calcd for $C_{13}H_{20}NO$ $[M+H]^+$: 206.15394, found: 206.15401.

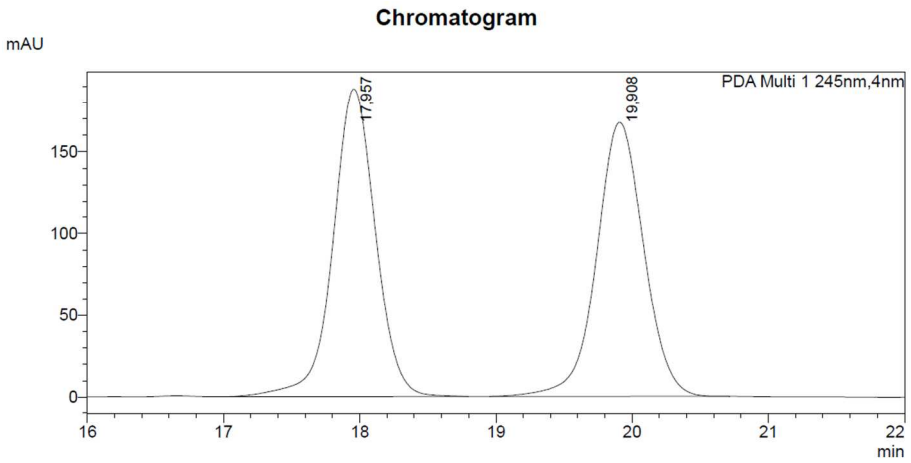
HPLC: Chiracel-OZH, *n*-heptane/*i*-PrOH 95:5, 0.5 mL/min, 40 °C, detection at 245 nm. Retention time (min): 18.0 (major) and 19.9 (minor).



Peak Table

PDA Ch1 245nm

Peak#	Ret. Time	Area	Height	Conc.
1	17,975	4787286	221909	88,357
2	19,899	630834	27026	11,643
Total		5418120	248935	

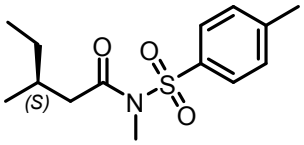


Peak Table

PDA Ch1 245nm

Peak#	Ret. Time	Area	Height	Conc.
1	17,957	4078662	187675	50,266
2	19,908	4035524	167194	49,734
Total		8114186	354869	

***(S)*-*N*-Methyl-*N*-tosyl-3-methyl-pentanamide (2g)**



2g

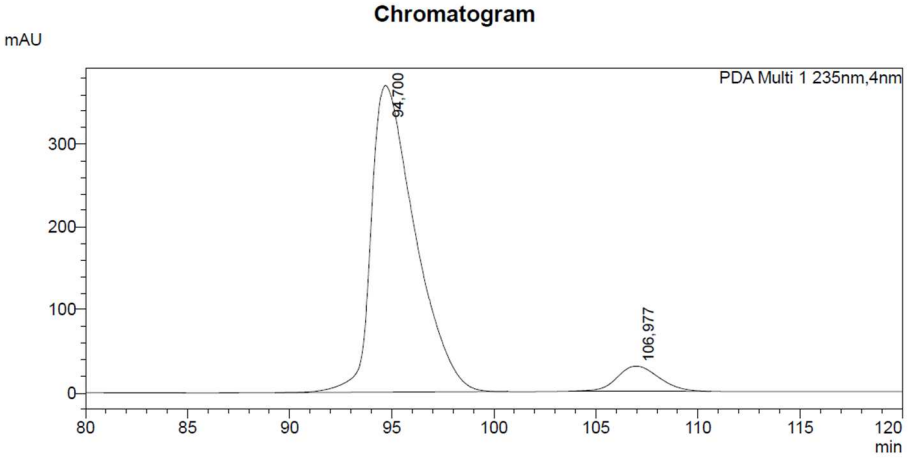
The reaction was performed with 0.1 mmol **1g**, $CuBr{\cdot}SMe_2$ (2.06 mg, 0.01 mmol, 10 mol%), ligand **L1** (7.68 mg, 0.012 mmol, 12 mol%), $BF_3{\cdot}Et_2O$ (25 μL, 0.2 mmol), EtMgBr (0.2 mmol, 3.0 M in Et_2O), 1.0 mL of DCM at −78 °C. Product **2g** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 10:1) [83% yield, 86% *ee*]. *Note: When the reaction was carried out in the absence of Lewis acid the product **2g** was obtained in 60% yield and 36% ee.*

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.76 (d, J = 8.3 Hz, 2H, CH_{Ar}), 7.33 (d, J = 8.0 Hz, 2H, CH_{Ar}), 3.29 (s, 3H, NCH_3), 2.61 (dd, J = 16.3, 5.7 Hz, 1H, C*H*HCO), 2.46 (dd, J = 16.3, 7.9 Hz, 1H, CH*H*CO), 2.43 (s, 3H, PhCH_3), 1.98-1.86 (m, 1H, CH_3C*H*), 1.35-1.25 (m, 1H, CH_3C*H*H), 1.19-1.08 (m, 1H, CH_3CH*H*), 0.83 (d, J = 6.6 Hz, 3H, CH_3CH), 0.82 (t, J = 7.4 Hz, 3H, C$H_3$$CH_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.1, 144.9, 136.6, 129.9, 127.5, 43.4, 33.2, 31.6, 29.4, 21.8, 19.3, 11.4.

HRMS (ESI+, m/Z): calcd for $C_{14}H_{23}N_3OS$ $[M+H]^+$: 284.13149, found: 284.13154.

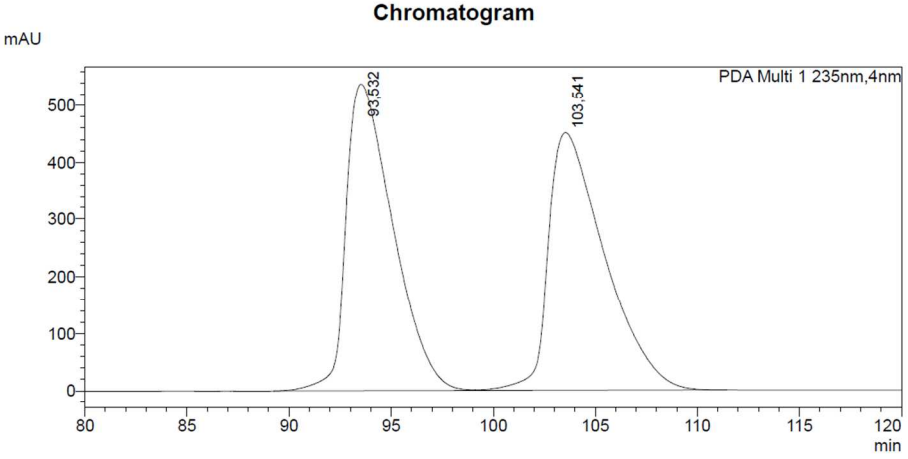
HPLC: Chiracel-OZH, *n*-heptane/*i*-PrOH 99.2:0.8, 0.5 mL/min, 40 °C, detection at 235 nm. Retention time (min): 94.7 (major) and 107.0 (minor).



Peak Table

PDA Ch1 235nm

Peak#	Ret. Time	Area	Height	Conc.
1	94,700	55248018	370230	92,854
2	106,977	4251673	29966	7,146
Total		59499691	400196	

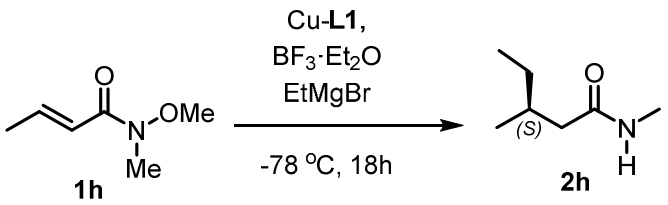


Peak Table

PDA Ch1 235nm

Peak#	Ret. Time	Area	Height	Conc.
1	93,532	85991452	537967	49,790
2	103,541	86715601	451024	50,210
Total		172707054	988991	

***(S)*-*N*-Methyl-3-methyl-pentanamide (2h)**



The reaction was performed with 0.2 mmol **1h**, $CuBr{\cdot}SMe_2$ (2.06 mg, 0.01 mmol, 5 mol%), ligand **L1** (7.68 mg, 0.012 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (50 μL, 0.4 mmol), EtMgBr (0.4 mmol, 3.0 M in Et_2O), 2.0 mL of DCM at −78 °C. Product **2h** was obtained as a colorless oil after column chromatography (SiO_2, Et_2O) [65% yield, 95% *ee*].

Note: Only demethoxylated product **2h,** most likely promoted by the Grignard reagent, was obtained. Decreasing the amount of Grignard reagent to 0.2 mmol led to decrease in the substrate conversion (which was also demthoxylated) and once again **2h** was the major product.

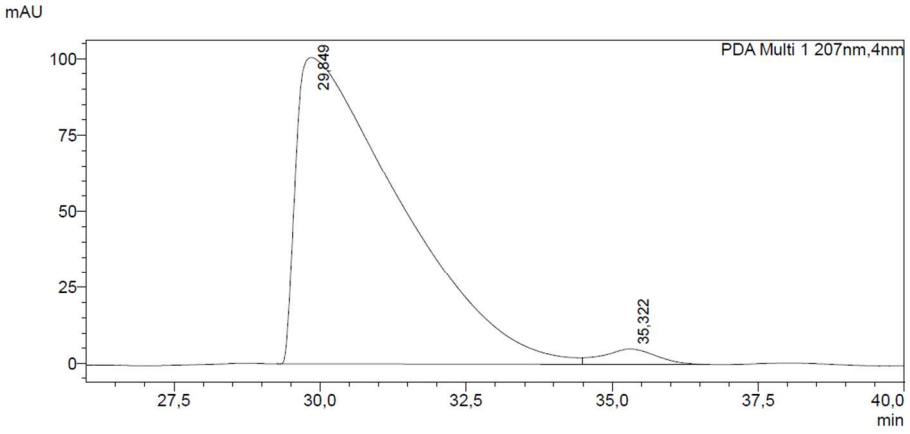
^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.61 (br s, 1H, N*H*), 2.79 (d, *J* = 4.9 Hz, 3H, NC*H*$_3$), 2.20-2.13 (m, 1H, C*H*HCO), 1.94-1.82 (m, 2H, CH*H*CO, C*H*), 1.40-1.30 (m, 1H, CH_3C*H*H), 1.24-1.12 (m, 1H, CH_3CH*H*), 0.90 (d, *J* = 6.2 Hz, 3H, C*H*$_3$CH), 0.87 (t, *J* = 7.4 Hz, 3H, C*H*$_3$$CH_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.6, 44.3, 32.4, 29.6, 26.3, 19.3, 11.4.

HRMS (ESI+, m/Z): calcd for $C_7H_{16}NO$ $[M+H]^+$: 130.12264, found: 130.12266.

HPLC: Chiracel-ASH, *n*-heptane/*i*-PrOH 98:2, 0.5 mL/min, 40 °C, detection at 207 nm. Retention time (min): 29.8 (major) and 35.3 (minor).

<Chromatogram>

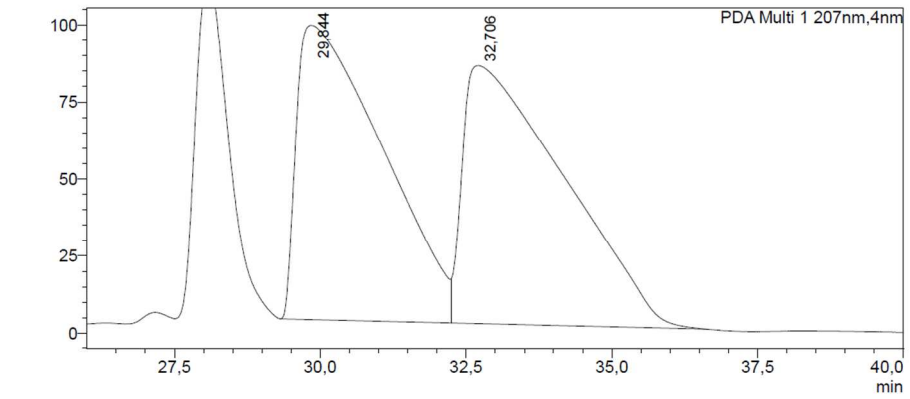


Peak Table

PDA Ch1 207nm

Peak#	Ret. Time	Area	Height	Conc.
1	29,849	12482944	100609	97,509
2	35,322	318904	4979	2,491
Total		12801848	105588	

Chromatogram

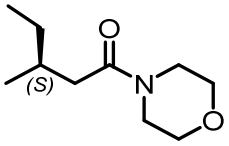


Peak Table

PDA Ch1 207nm

Peak#	Ret. Time	Area	Height	Conc.
1	29,844	9815559	95488	49,279
2	32,706	10102927	83645	50,721
Total		19918486	179133	

***(S)*-3-Methyl-1-(4-morpholinyl)-pentan-1-one (2i)**



2i

The reaction was performed with 0.2 mmol **1i**, $CuBr{\cdot}SMe_2$ (2.06 mg, 0.01 mmol, 5 mol%), ligand **L1** (7.68 mg, 0.012 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (50 μL, 0.4 mmol), EtMgBr (0.4 mmol, 3.0 M in Et_2O), 2.0 mL of DCM at −78 °C. Product **2i** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 1:1 [75% yield, 96% *ee*].

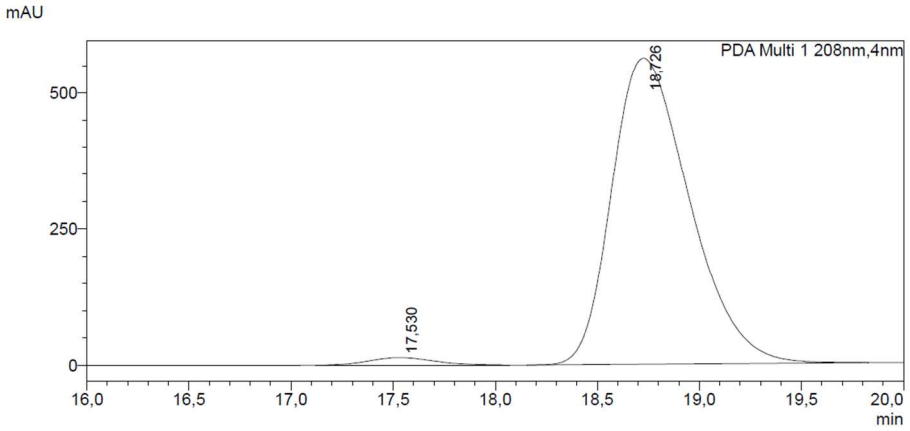
^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.68-3.49 (m, 8H, NC*H*$_2$C*H*$_2$O), 2.31 (dd, *J* = 14.6, 5.9 Hz, 1H, C*H*HCO), 2.12 (dd, *J* = 14.6, 8.2 Hz, 1H, CH*H*CO), 1.94-1.85 (m, 1H, C*H*), 1.43-1.37 (m, 1H, CH_3C*H*H), 1.25-1.20 (m, 1H, CH_3CH*H*), 0.94 (d, *J* = 6.6 Hz, 3H, C*H*$_3$CH), 0.90 (t, *J* = 7.4 Hz, 3H, C*H*$_3$CH$_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.6, 67.1, 66.8, 46.4, 42.0, 40.1, 32.1, 29.7, 19.5, 11.5.

HRMS (ESI+, m/Z): calcd for $C_{10}H_{20}NO_2$ $[M+H]^+$: 186.14886, found: 186.14893.

HPLC: Chiracel-OBH, *n*-heptane/*i*-PrOH 95:5, 0.5 mL/min, 40 °C, detection at 208 nm. Retention time (min): 17.5 (minor) and 18.7 (major).

Chromatogram

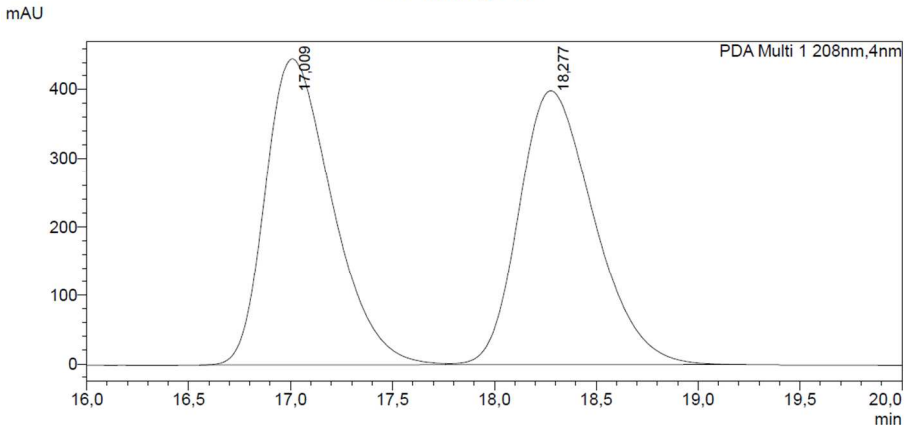


Peak Table

PDA Ch1 208nm

Peak#	Ret. Time	Area	Height	Conc.
1	17,530	300198	13745	1,976
2	18,726	14892120	563258	98,024
Total		15192318	577002	

Chromatogram

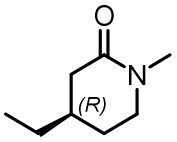


Peak Table

PDA Ch1 208nm

Peak#	Ret. Time	Area	Height	Conc.
1	17,009	10189441	446410	49,898
2	18,277	10230956	398335	50,102
Total		20420397	844745	

***(R)*-4-Ethyl-1-methylpiperidin-2-one (2j)**



2j

The reaction was performed with 0.2 mmol **1j**, $CuBr{\cdot}SMe_2$ (2.06 mg, 0.01 mmol, 5 mol%), ligand **L1** (7.68 mg, 0.012 mmol, 6 mol%), EtMgBr (0.4 mmol, 3.0 M in Et_2O) in 2.0 mL of DCM at −50 °C. Product **2j** was obtained as a pale yellow oil after column chromatography (SiO_2, Et_2O) [75% yield, 93% *ee*].

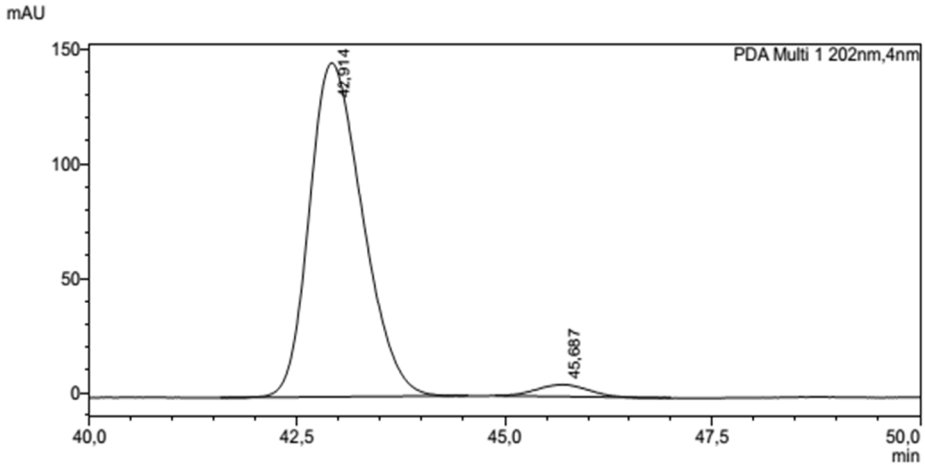
^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.30-3.27 (m, 2H, CH_2N), 2.93 (s, 3H, NCH_3), 2.54-2.48 (m, 1H, C*H*), 2.00-1.88 (m, 2H, CH_2CO), 1.75-1.64 (m, 1H, CH_2C*H*HCH), 1.49-1.39 (m, 1H, CH_2CH*H*CH), 1.33 (dq, *J* = 14.5, 7.3, Hz, 2H, C$H_2$$CH_3$), 0.91 (t, *J* = 7.3 Hz, 3H, C$H_3$$CH_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.1, 49.4, 38.6, 34.9, 34.6, 28.9, 28.6, 11.2.

HRMS (ESI+, m/Z): calcd for $C_8H_{16}NO$ $[M+H]^+$: 142.12264, found: 142.12263.

HPLC: Chiracel-ODH, *n*-heptane/*i*-PrOH 98:02, 0.5 mL/min, 40 °C, detection at 202 nm. Retention time (min): 43.0 (major) and 45.7 (minor).

Chromatogram

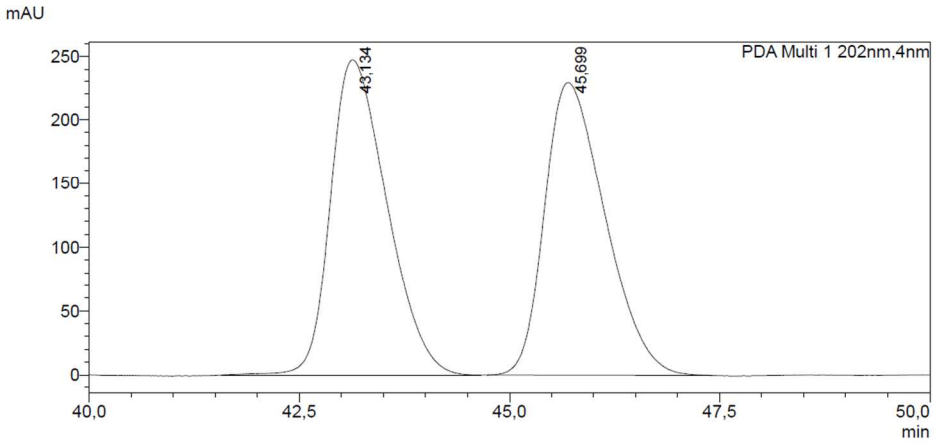


Peak Table

PDA Ch1 202nm

Peak#	Ret. Time	Area	Height	Conc.
1	42,914	6486680	145799	96,727
2	45,687	219477	5161	3,273
Total		6706157	150960	

Chromatogram

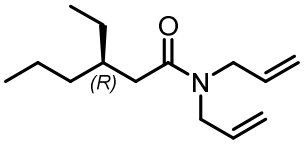


Peak Table

PDA Ch1 202nm

Peak#	Ret. Time	Area	Height	Conc.
1	43,134	11554476	247557	50,134
2	45,699	11492915	229038	49,866
Total		23047391	476594	

***(R)*-*N*,*N*-Diallyl-3-ethylhexanamide (2k)**



2k

The reaction was performed with 0.2 mmol **1k**, $CuBr{\cdot}SMe_2$ (2.06 mg, 0.01 mmol, 5 mol%), ligand **L1** (7.68 mg, 0.012 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (50 μL, 0.4 mmol), EtMgBr (0.4 mmol, 3.0 M in Et_2O), 2.0 mL of DCM at −78 °C. Product **2k** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 5:1) [71% yield, 98% *ee*].

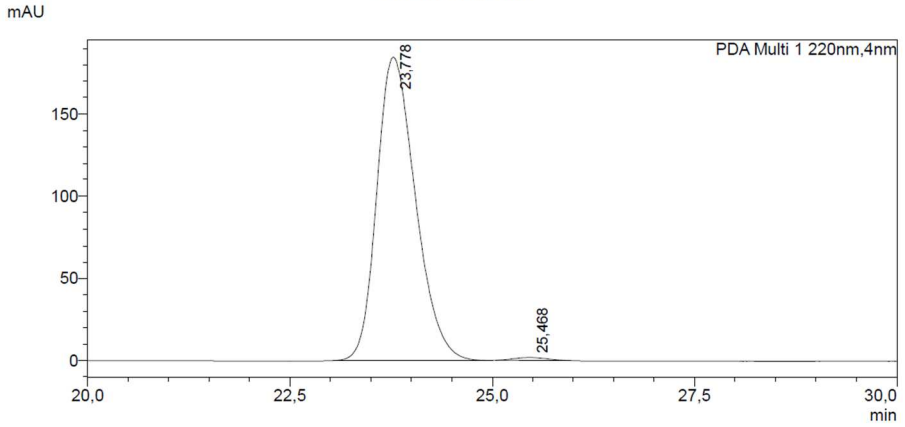
^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.80-5.70 (m, 2H, C*H*=CH_2), 5.20-5.07 (m, 4H, CH=C*H*$_2$), 3.98 (dt, *J* = 6.0, 1.4 Hz, 2H, NC*H*$_2$CH=CH_2), 3.86 (dt, *J* = 4.8, 1.8 Hz, 2H, NC*H*$_2$CH=CH_2), 2.21 (dd, *J* = 15.2, 7.2 Hz, 1H, C*H*HCO), 2.20 (dd, *J* = 15.2, 6.6 Hz, 1H, CH*H*CO), 1.95-1.86 (m, 1H, C*H*CH_2), 1.36-1.21 (m, 6H, C*H*$_2$), 0.88 (t, *J* = 6.8 Hz, 3H, C*H*$_3$), 0.85 (t, *J* = 7.4 Hz, 3H, C*H*$_3$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.0, 133.6, 133.2, 117.1, 116.6, 49.3, 48.0, 37.5, 36.1, 35.6, 26.4, 19.9, 14.5, 11.0.

HRMS (ESI+, m/Z): calcd for $C_{14}H_{26}NO$ $[M-H]^+$: 224.20089, found: 224.20105.

HPLC: Chiracel-ADH, *n*-heptane/*i*-PrOH 99.2:2, 0.5 mL/min, 40 °C, detection at 220 nm. Retention time (min): 23.8 (major) and 25.5 (minor).

Chromatogram

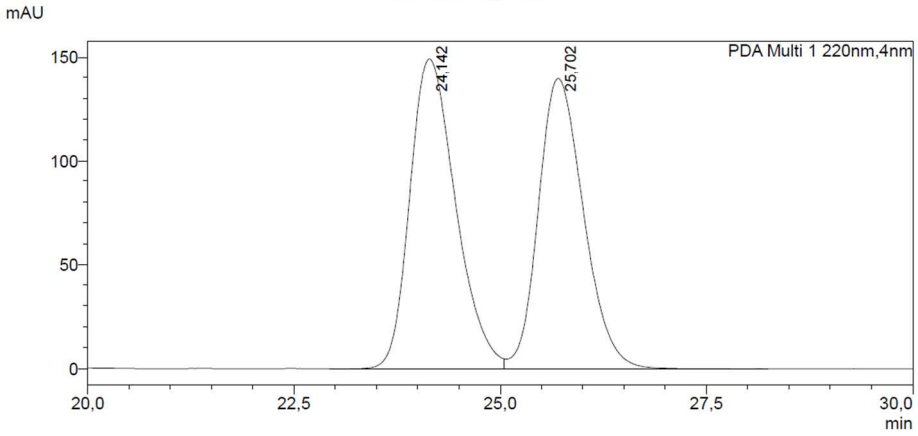


Peak Table

PDA Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.
1	23,778	6122919	184791	99,193
2	25,468	49793	1809	0,807
Total		6172712	186600	

Chromatogram

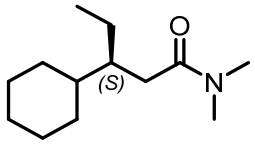


Peak Table

PDA Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.
1	24,142	5741742	149285	51,979
2	25,702	5304468	139387	48,021
Total		11046210	288672	

***(S)*-*N*,*N*-Dimethyl-3-cyclohexyl-pentanamide (2l)**



2l

The reaction was performed with 0.1 mmol **1l**, $CuBr{\cdot}SMe_2$ (1.03 mg, 0.005 mmol, 5 mol%), ligand **L1** (3.84 mg, 0.006 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (25 μL, 0.2 mmol), EtMgBr (0.2 mmol, 3.0 M in Et_2O), 1.0 mL of DCM at −78 °C. Product **2l** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 1:1) [73% yield, 93% *ee*].

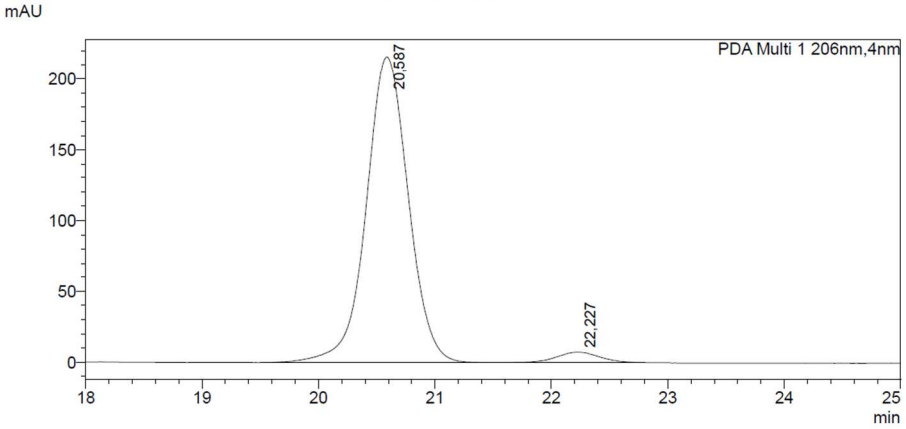
^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.01 (s, 3H, NC*H*$_3$), 2.94 (s, 3H, NC*H*$_3$), 2.30 (dd, *J* = 15.1, 5.7 Hz, 1H, C*H*HCO), 2.13 (dd, *J* = 15.1, 7.8 Hz, 1H, CH*H*CO), 1.77-1.57 (m, 6H, C*H*$_2$, C*H*), 1.42-0.96 (m, 8H, C*H*$_2$, C*H*), 0.86 (t, *J* = 7.4 Hz, 3H, C*H*$_3$CH$_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.5, 41.8, 40.0, 37.6, 35.7, 34.7, 30.2, 29.4, 27.00, 26.96 (2C), 23.8, 12.0.

HRMS (ESI+, m/Z): calcd for $C_{13}H_{26}NO$ $[M+H]^+$: 212.20089, found: 212.20080.

HPLC: Chiracel-OZH, *n*-heptane/*i*-PrOH 95:5, 0.5 mL/min, 40 °C, detection at 206 nm. Retention time (min): 20.6 (major) and 22.2 (minor).

Chromatogram

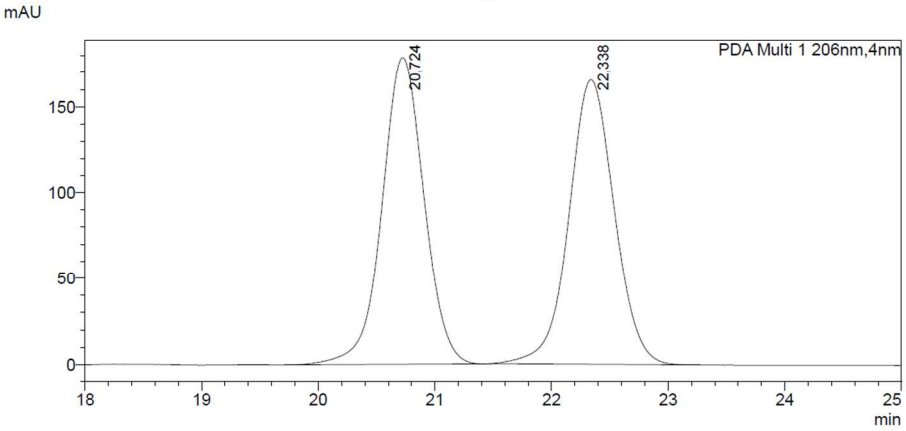


Peak Table

PDA Ch1 206nm

Peak#	Ret. Time	Area	Height	Conc.
1	20,587	5429559	215927	96,682
2	22,227	186315	7329	3,318
Total		5615874	223257	

Chromatogram

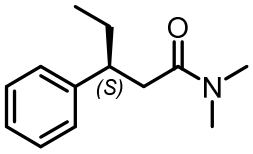


Peak Table

PDA Ch1 206nm

Peak#	Ret. Time	Area	Height	Conc.
1	20,724	4466284	178591	49,972
2	22,338	4471287	165274	50,028
Total		8937571	343865	

***(S)*-*N*,*N*-Dimethyl-3-phenylpentanamide (2m)**



2m

The reaction was performed with 0.1 mmol **1m**, $CuBr{\cdot}SMe_2$ (1.03 mg, 0.005 mmol, 5 mol%), ligand **L1** (3.84 mg, 0.006 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (25 μL, 0.2 mmol), EtMgBr (0.2 mmol, 3.0 M in Et_2O), 1.0 mL of DCM at −78 °C. Product **2m** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 1:2) [70% yield, 94% *ee*].

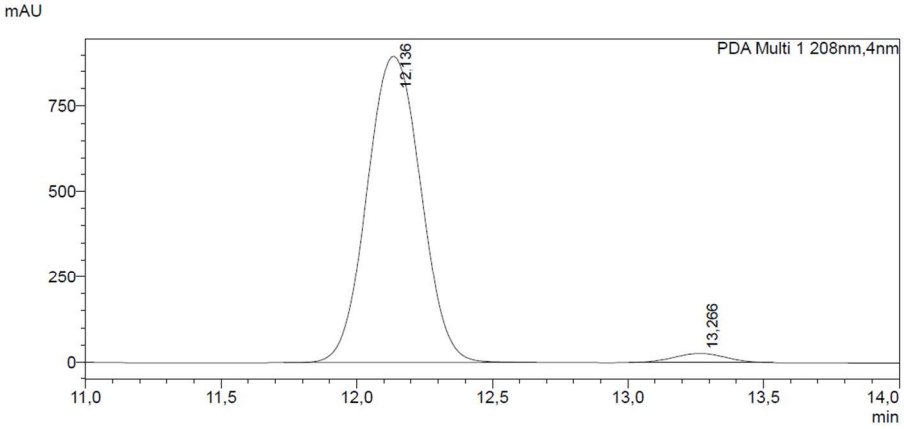
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.30-7.26 (m, 2H, C*H*$_{Ar}$), 7.21-7.17 (m, 3H, C*H*$_{Ar}$), 3.08 (ddt, *J* = 9.9, 7.1, 5.2 Hz, 1H, C*H*), 2.87 (s, 3H, NC*H*$_3$), 2.83 (s, 3H, NC*H*$_3$), 2.60 (dd, *J* = 15.1, 6.9 Hz, 1H, C*H*HCO), 2.56 (dd, *J* = 15.1, 7.2 Hz, 1H, CH*H*CO), 1.79 (dqd, *J* = 13.5, 7.4, 5.1 Hz, 1H, C*H*HCH$_3$), 1.61 (ddq, *J* = 13.5, 9.5, 7.4 Hz, 1H, CH*H*CH$_3$), 0.79 (t, *J* = 7.4 Hz, 3H, C*H*$_3$CH$_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.0, 144.9, 128.5, 127.8, 126.4, 44.2, 40.6, 37.5, 35.5, 28.9, 12.3.

HRMS (ESI+, m/Z): calcd for $C_{13}H_{20}NO$ $[M+H]^+$: 206.15394, found: 206.15400.

HPLC: Chiracel-ODH, *n*-heptane/*i*-PrOH 90:10, 0.5 mL/min, 40 °C, detection at 208 nm. Retention time (min): 12.1 (major) and 13.3 (minor).

Chromatogram

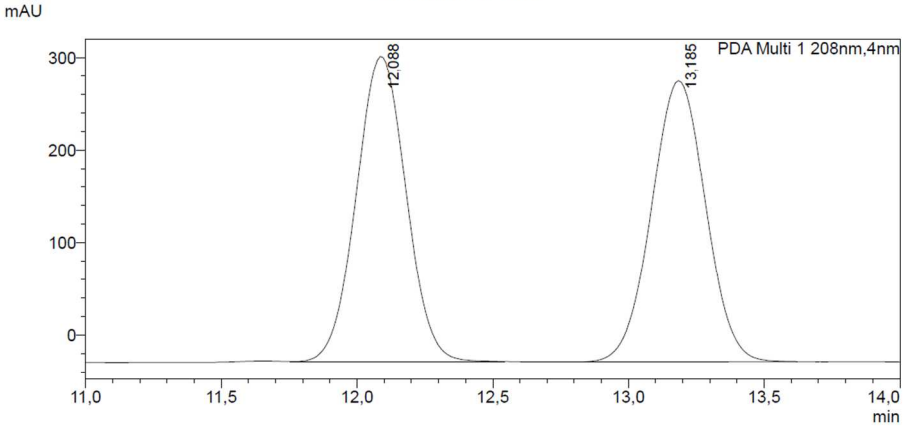


Peak Table

PDA Ch1 208nm

Peak#	Ret. Time	Area	Height	Conc.
1	12,136	12354791	897209	97,197
2	13,266	356346	26637	2,803
Total		12711136	923846	

Chromatogram

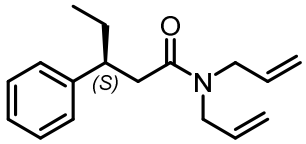


Peak Table

PDA Ch1 208nm

Peak#	Ret. Time	Area	Height	Conc.
1	12,088	4198974	329626	49,949
2	13,185	4207513	303029	50,051
Total		8406486	632655	

***(S)*-*N*,*N*-Diallyl-3-phenylpentanamide (2n)**



2n

The reaction was performed with 0.1 mmol **1n**, $CuBr{\cdot}SMe_2$ (2.06 mg, 0.01 mmol, 10 mol%), ligand **L1** (7.68 mg, 0.012 mmol, 12 mol%), $BF_3{\cdot}Et_2O$ (25 μL, 0.2 mmol), in 1.0 mL of DCM at −78 °C and slow addition of a solution of EtMgBr (0.2 mmol, 3.0 M in Et_2O) in 0.5 mL of toluene and added dropwise to the reaction mixture during 2 hours using a syringe pump. Product **2n** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 5:1) [63% yield, 93% *ee*].

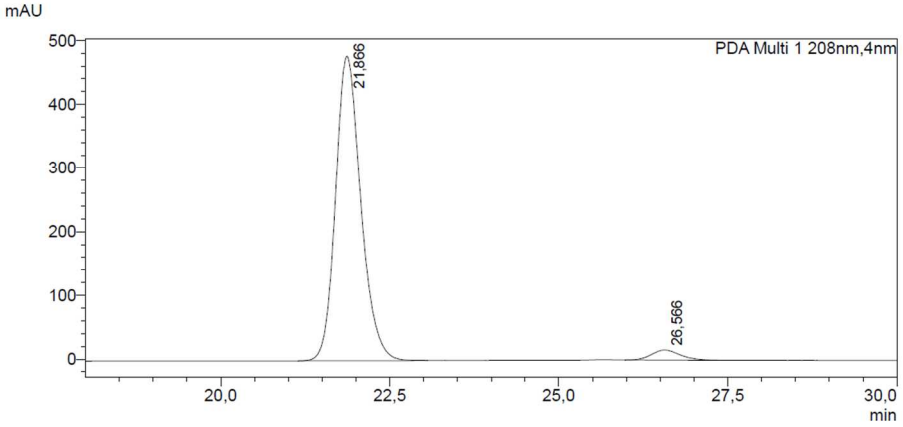
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.30-7.28 (m, 2H, C*H*$_{Ar}$), 7.20-7.17 (m, 3H, C*H*$_{Ar}$), 5.70-5.60 (m, 2H, C*H*=CH_2), 5.14 (dq, *J* = 10.4, 1.5 Hz, 1H, C*H*H=CH), 5.06 (dq, *J* = 10.3, 1.4 Hz, 1H, C*H*H=CH), 5.03 (dq, *J* = 17.1, 1.7 Hz, 1H, CH*H*=CH), 4.94 (dq, *J* = 17.1, 1.6 Hz, 1H, CH*H*=CH), 4.00 (dd, *J* = 15.3, 5.7, 1H, C*H*HCH=), 3.82 (dd, *J* = 15.3, 5.9, 1H, CH*H*CH=), 3.78-3.65 (m, 2H, C*H*$_2$CH=), 3.13 (dtd, *J* = 9.8, 7.2, 5.2 Hz, 1H, C*H*), 2.57 (d, *J* = 7.2 Hz, 2H, C*H*$_2$CO), 1.82-1.72 (m, 1H, C*H*HCH_3), 1.65-1.54 (m, 1H, CH*H*CH_3), 0.79 (t, *J* = 7.3 Hz, 3H, C*H*$_3$$CH_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.0, 144.7, 133.4, 133.0, 128.5, 127.9, 126.4, 117.0, 116.6, 49.2, 48.0, 44.2, 40.2, 29.0, 12.3.

HRMS (ESI+, m/Z): calcd for $C_{17}H_{24}NO$ $[M+H]^+$: 258.18549, found: 258.18524.

HPLC: Chiracel-ADH, *n*-heptane/*i*-PrOH 98:2, 0.5 mL/min, 40 °C, detection at 208 nm. Retention time (min): 21.9 (major) and 26.6 (minor).

Chromatogram

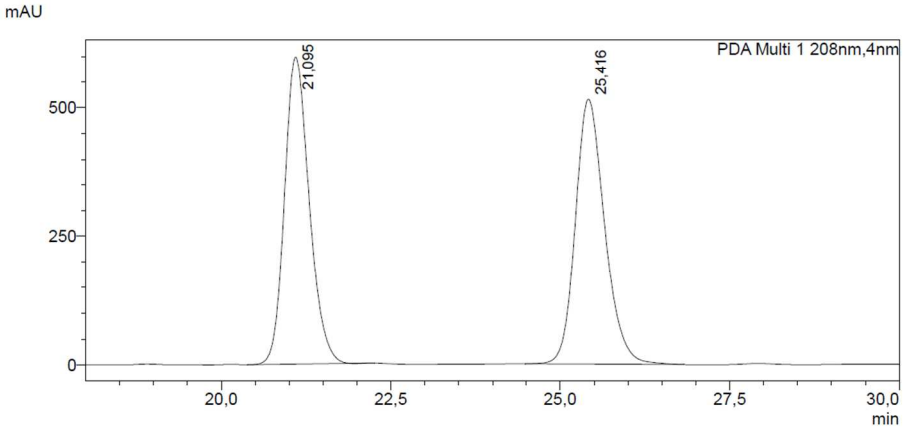


Peak Table

PDA Ch1 208nm

Peak#	Ret. Time	Area	Height	Conc.
1	21,866	12443048	478839	96,377
2	26,566	467788	15844	3,623
Total		12910836	494684	

Chromatogram

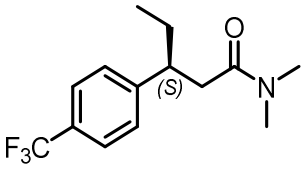


Peak Table

PDA Ch1 208nm

Peak#	Ret. Time	Area	Height	Conc.
1	21,095	15118330	597199	49,437
2	25,416	15462949	513992	50,563
Total		30581279	1111191	

***(S)*-*N*,*N*-Dimethyl-3-(4-(trifluoromethyl)phenyl)pentanamide (2o)**



2o

The reaction was performed with 0.1 mmol **1o**, $CuBr{\cdot}SMe_2$ (1.03 mg, 0.005 mmol, 5 mol%), ligand **L1** (3.84 mg, 0.006 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (25 μL, 0.2 mmol), EtMgBr (0.2 mmol, 3.0 M in Et_2O), 1.0 mL of DCM at −78 °C. Product **2o** was obtained as a colorless oil after column chromatography (SiO_2, Et_2O) [81% yield, 96% *ee*].

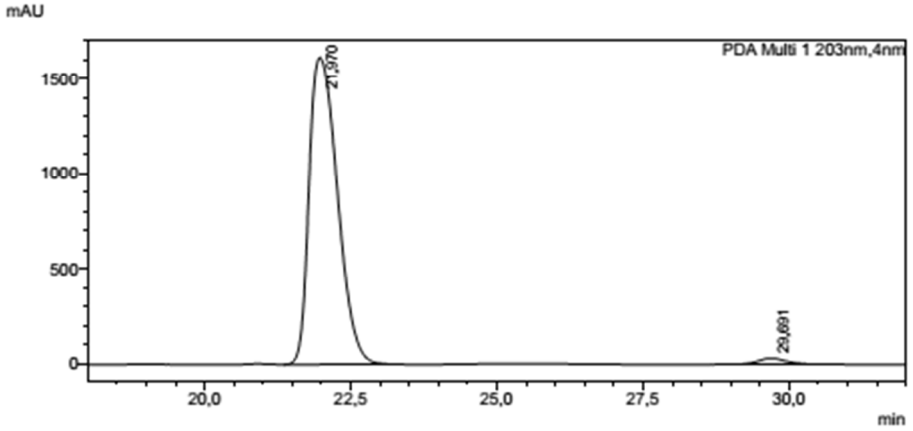
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.54 (d, *J* = 8.1 Hz, 2H, C*H*$_{Ar}$), 7.33 (d, *J* = 8.1 Hz, 2H, C*H*$_{Ar}$), 3.19 (dtd, *J* = 9.6, 7.0, 5.3 Hz, 1H, C*H*), 2.89 (s, 3H, NC*H*$_3$), 2.88 (s, 3H, NC*H*$_3$), 2.60 (d, *J* = 7.0 Hz, 2H, C*H*$_2$CO), 1.80 (ddq, *J* = 13.4, 5.3, 7.3 Hz, 1H, C*H*HCH$_3$), 1.61 (ddq, *J* = 13.4, 9.6, 7.3 Hz, 1H, CH*H*CH$_3$), 0.79 (t, *J* = 7.3 Hz, 3H, C*H*$_3$CH$_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.4, 149.2 (q, *J* = 1.1 Hz), 128.6 (q, *J* = 32.2 Hz), 128.1, 125.4 (q, *J* = 3.8 Hz), 124.4 (q, *J* = 272.0 Hz), 43.9, 40.1, 37.4, 35.6, 29.0, 12.1.

HRMS (ESI+, m/Z): calcd for $C_{14}H_{19}F_3NO$ $[M+H]^+$: 274.14133, found: 274.14140.

HPLC: Chiracel-ADH, *n*-heptane/*i*-PrOH 98:2, 0.5 mL/min, 40 °C, detection at 203 nm. Retention time (min): 21.9 (major) and 29.7 (minor).

Chromatogram

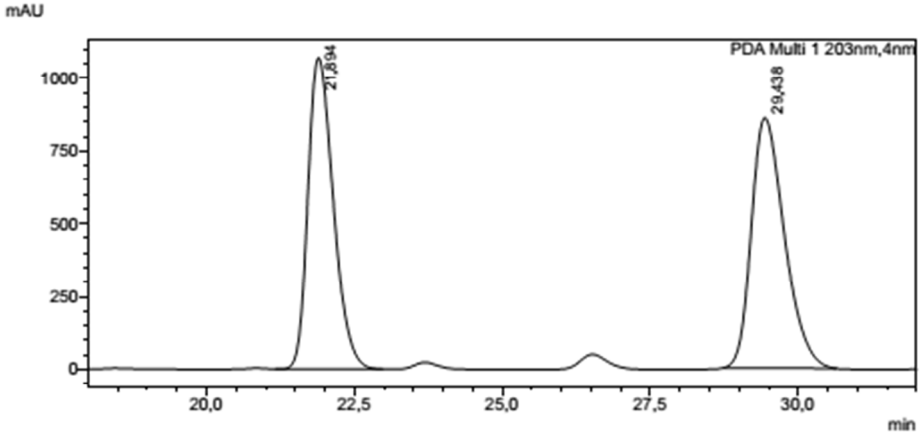


Peak Table

PDA Ch1 203nm

Peak#	Ret. Time	Area	Height	Conc.
1	21,970	54400969	1613896	98,109
2	29,691	1048684	31286	1,891
Total		55449653	1645182	

Chromatogram

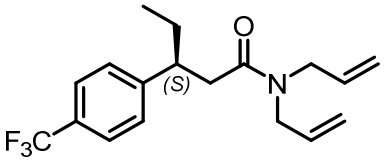


Peak Table

PDA Ch1 203nm

Peak#	Ret. Time	Area	Height	Conc.
1	21,894	31940760	1068861	48,894
2	29,438	33386436	857427	51,106
Total		65327196	1926288	

***(S)*-*N*,*N*-Diallyl-3-(4-trifluoromethyl)phenyl)pentanamide (2p)**



2p

The reaction was performed with 0.1 mmol **1p**, $CuBr{\cdot}SMe_2$ (2.06 mg, 0.01 mmol, 10 mol%), ligand **L1** (7.68 mg, 0.012 mmol, 12 mol%), $BF_3{\cdot}Et_2O$ (25 μL, 0.2 mmol), in 1.0 mL of DCM at −78 °C and slow addition of a solution of EtMgBr (0.2 mmol, 3.0 M in Et_2O) in 0.5 mL of toluene and added dropwise to the reaction mixture during 2 hours using a syringe pump. Product **2p** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 5:1) [67% yield, 90% *ee*].

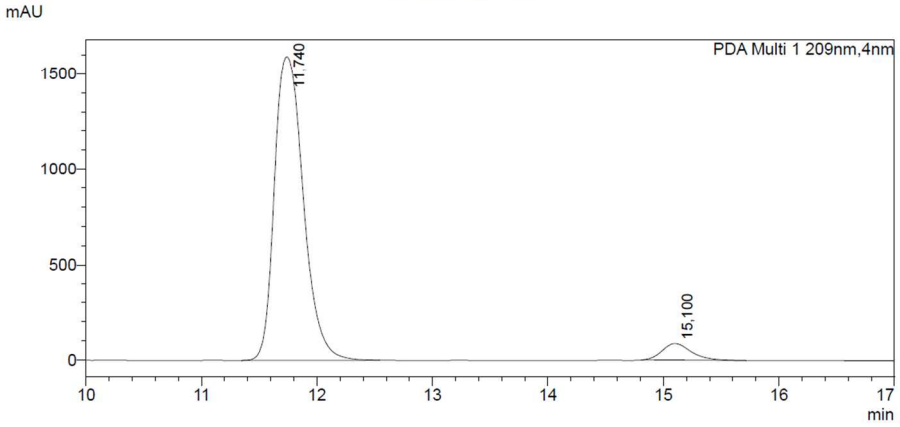
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.53 (d, *J* = 7.8 Hz, 2H, CH_{Ar}), 7.31 (d, *J* = 7.8 Hz, 2H, CH_{Ar}), 5.72-5.59 (m, 2H, C*H*=CH_2), 5.15 (dd, *J* = 10.1, 1.5 Hz, 1H, C*H*H=CH), 5.06 (dd, *J* = 10.2, 1.4 Hz, 1H, C*H*H=CH), 5.01 (dd, *J* = 17.1, 1.8 Hz, 1H, CH*H*=CH), 4.94 (dd, *J* = 17.1, 1.6 Hz, 1H, CH*H*=CH), 3.93 (ddt, *J* = 15.3, 5.8, 1.5 Hz, 1H, C*H*HCH=), 3.87 (ddt, *J* = 15.3, 5.9, 1.4 Hz, 1H, CH*H*CH=), 3.76 (dt, *J* = 4.8, 1.7 Hz, 2H, CH_2CH=), 3.24 (dtd, *J* = 9.6, 7.2, 5.3 Hz, 1H, C*H*), 2.59 (dd, *J* = 15.6, 6.9 Hz, 1H, CH*H*CO), 2.59 (dd, *J* = 15.6, 7.4 Hz, 1H, C*H*HCO), 1.77 (dqd, *J* = 13.3, 7.3, 5.3 Hz, 1H, C*H*HCH_3), 1.77 (ddq, *J* = 13.3, 9.6, 7.3 Hz, 1H, CH*H*CH_3), 0.78 (t, *J* = 7.3 Hz, 3H, CH_3CH_2).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.4, 149.0, 133.2, 132.8, 129.0 (q, *J* = 30.7 Hz), 128.2, 125.4 (q, *J* = 3.7 Hz), 124.4 (q, *J* = 272.1 Hz), 117.1, 116.6, 49.2, 48.2, 43.9, 39.7, 29.0, 12.2.

HRMS (ESI+, m/Z): calcd for $C_{18}H_{23}F_3NO$ $[M+H]^+$: 326.17263, found: 326.17300.

HPLC: Chiracel-ADH, *n*-heptane/*i*-PrOH 95:5, 0.5 mL/min, 40 °C, detection at 209 nm. Retention time (min): 11.7 (major) and 15.1 (minor).

Chromatogram

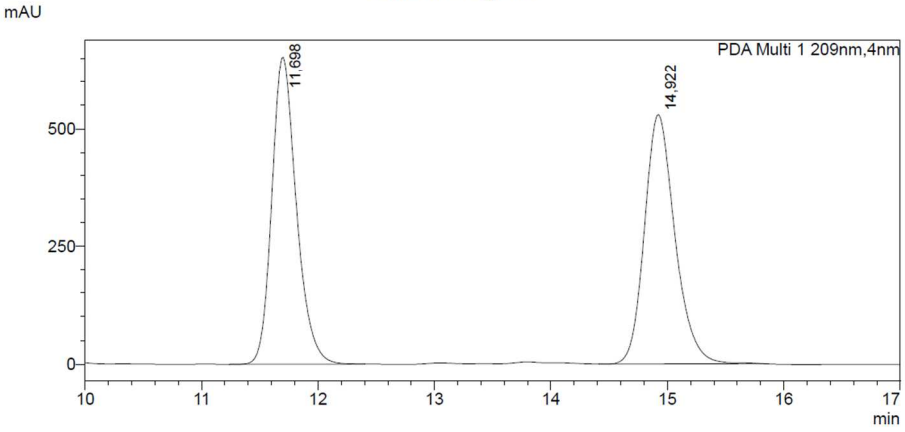


Peak Table

PDA Ch1 209nm

Peak#	Ret. Time	Area	Height	Conc.
1	11,740	27774942	1591595	94,880
2	15,100	1498729	86438	5,120
Total		29273671	1678033	

Chromatogram

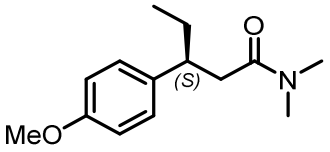


Peak Table

PDA Ch1 209nm

Peak#	Ret. Time	Area	Height	Conc.
1	11,698	9562547	653296	49,836
2	14,922	9625463	529518	50,164
Total		19188010	1182814	

***(S)*-*N*,*N*-Dimethyl-3-(4-methoxyphenyl)pentanamide (2q)**



2q

The reaction was performed with 0.1 mmol **1q**, $CuBr{\cdot}SMe_2$ (1.03 mg, 0.005 mmol, 5 mol%), ligand **L1** (3.84 mg, 0.006 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (25 μL, 0.2 mmol), EtMgBr (0.2 mmol, 3.0 M in Et_2O), 1.0 mL of DCM at −78 °C. Product **2q** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 1:10) [70% yield, 97% *ee*].

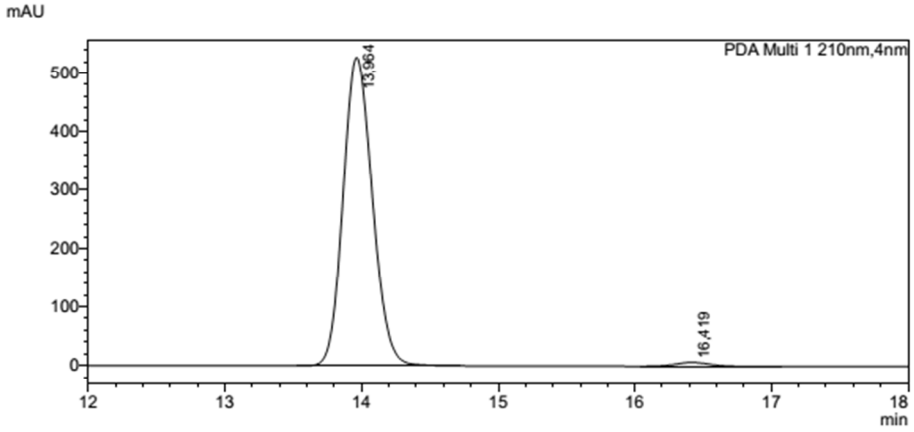
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.12 (d, *J* = 8.6 Hz, 2H, CH_{Ar}), 6.83 (d, *J* = 8.6 Hz, 2H, CH_{Ar}), 3.78 (s, 3H, OCH_3), 3.03 (dtd, *J* = 9.8, 7.1, 5.2 Hz, 1H, C*H*), 2.87 (s, 3H, NCH_3), 2.84 (s, 3H, NCH_3), 2.55 (dd, *J* = 15.5, 7.1 Hz, 1H, C*H*HCO) 2.54 (dd, *J* = 15.5, 7.1 Hz, 1H, CH*H*CO), 1.76 (dqd, *J* = 14.6, 7.2, 5.2 Hz, 1H, C*H*HCH$_3$), 1.57 (ddq, *J* = 14.6, 9.8, 7.2 Hz, 1H, CH*H*CH$_3$), 0.78 (t, *J* = 7.3 Hz, 3H, CH_3CH$_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.2, 158.1, 136.9, 128.6, 113.8, 55.3, 43.5, 40.9, 37.5, 35.6, 29.1, 12.3.

HRMS (ESI+, m/Z): calcd for $C_{14}H_{22}NO_2$ $[M+H]^+$: 236.16451, found: 236.16450.

HPLC: Chiracel-OJH, *n*-heptane/*i*-PrOH 90:10, 0.5 mL/min, 40 °C, detection at 210 nm. Retention time (min): 14.0 (major) and 16.4 (minor).

Chromatogram

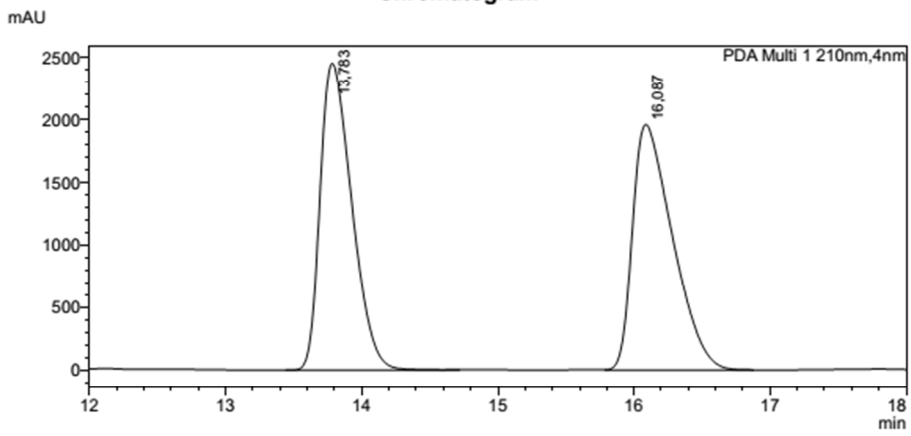


Peak Table

PDA Ch1 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	13,964	7850822	528047	98,523
2	16,419	117709	6702	1,477
Total		7968531	534748	

Chromatogram

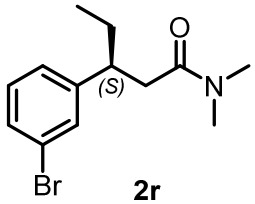


Peak Table

PDA Ch1 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	13,783	39665936	2454329	49,783
2	16,087	40011474	1958244	50,217
Total		79677409	4412573	

***(S)*-*N*,*N*-Dimethyl-3-(3-bromophenyl)pentanamide (2r)**



2r

The reaction was performed with 0.1 mmol **1r**, $CuBr{\cdot}SMe_2$ (1.03 mg, 0.005 mmol, 5 mol%), ligand **L1** (3.84 mg, 0.006 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (25 μL, 0.2 mmol), EtMgBr (0.2 mmol, 3.0 M in Et_2O), 1.0 mL of DCM at −78 °C. Product **2r** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 1:2) [74% yield, 95% *ee*].

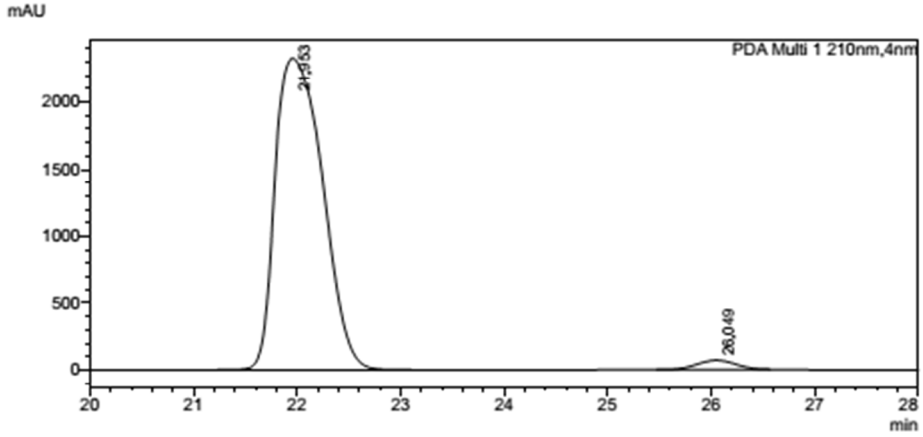
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.34-7.30 (m, 2H, CH_{Ar}), 7.15-7.14 (m, 2H, CH_{Ar}), 3.07 (dtd, J = 9.8, 7.1, 5.1 Hz, 1H, C*H*), 2.88 (s, 6H, NCH_3), 2.55 (d, J = 7.0 Hz, 2H, CH_2CO), 1.77 (dqd, J = 14.7, 7.3, 5.1 Hz, 1H, C*H*HCH$_3$), 1.57 (ddq, J = 14.7, 9.8, 7.3 Hz, 1H, CH*H*CH$_3$), 0.78 (t, J = 7.4 Hz, 3H, CH_3CH$_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.5, 147.5, 130.6, 130.0, 129.5, 126.8, 122.6, 43.9, 40.2, 37.4, 35.6, 29.0, 12.2.

HRMS (ESI+, m/Z): calcd for $C_{13}H_{19}BrNO$ $[M+H]^+$: 284.06445, found: 284.06469.

HPLC: Chiracel-ODH, *n*-heptane/*i*-PrOH 97:3, 0.5 mL/min, 40 °C, detection at 210 nm. Retention time (min): 22.0 (major) and 26.0 (minor).

Chromatogram

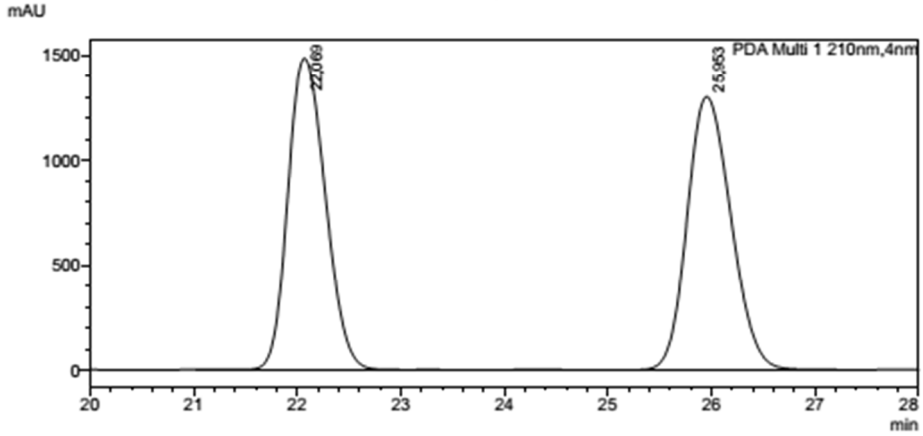


Peak Table

PDA Ch1 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	21,953	74443452	2327134	97,606
2	26,049	1825778	69430	2,394
Total		76269229	2396564	

Chromatogram

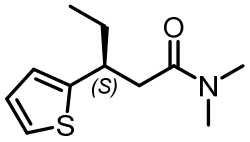


Peak Table

PDA Ch1 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	22,069	37665334	1486350	49,455
2	25,953	38495669	1301772	50,545
Total		76161003	2788122	

***(S)*-*N*,*N*-Dimethyl-3-(thiophen-2-yl)pentanamide (2s)**



2s

The reaction was performed with 0.1 mmol **1s**, $CuBr{\cdot}SMe_2$ (1.03 mg, 0.005 mmol, 5 mol%), ligand **L1** (3.84 mg, 0.006 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (25 μL, 0.2 mmol), EtMgBr (0.2 mmol, 3.0 M in Et_2O), 1.0 mL of DCM at −78 °C. Product **2s** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 1:5) [85% yield, 95% *ee*].

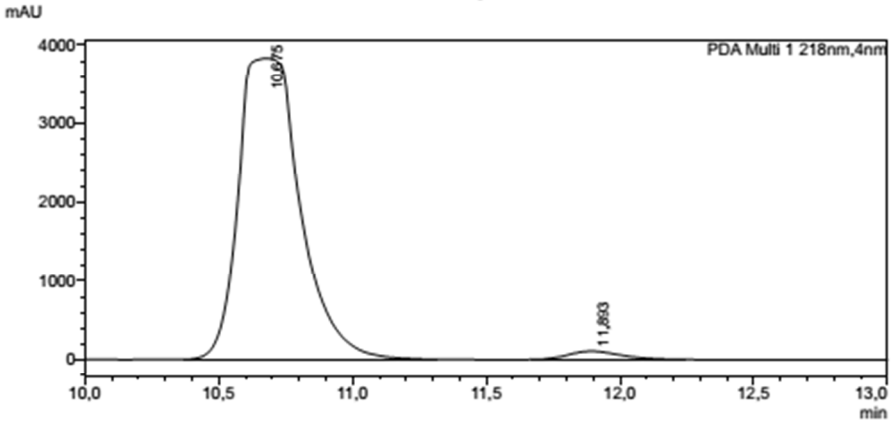
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.13 (d, *J* = 5.1 Hz, 1H, C*H*$_{Ar}$), 6.91 (dd, *J* = 5.1, 3.4 Hz, 1H, C*H*$_{Ar}$), 6.83 (d, *J* = 3.4 Hz, 1H, C*H*$_{Ar}$), 3.49-3.42 (m, 1H, C*H*), 2.90 (s, 3H, NC*H*$_3$), 2.89 (s, 3H, NC*H*$_3$), 2.64 (dd, *J* = 15.2, 7.1, Hz, 1H, C*H*HCO), 2.58 (dd, *J* = 15.2, 6.9, Hz, 1H, CH*H*CO), 1.82 (dqd, *J* = 14.4, 7.3, 5.1 Hz, 1H, C*H*HCH$_3$), 1.61 (ddq, *J* = 14.4, 9.3, 7.3 Hz, 1H, CH*H*CH$_3$), 0.88 (t, *J* = 7.2 Hz, 3H, C*H*$_3$CH$_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.6, 148.9, 126.7, 124.2, 123.0, 41.4, 39.6, 37.4, 35.6, 30.3, 12.2.

HRMS (ESI+, m/Z): calcd for $C_{11}H_{18}NOS$ $[M+H]^+$: 212.11036, found: 212.11043.

HPLC: Chiracel-ADH, *n*-heptane/*i*-PrOH 90:10, 0.5 mL/min, 40 °C, detection at 218 nm. Retention time (min): 10.7 (major) and 11.9 (minor).

Chromatogram

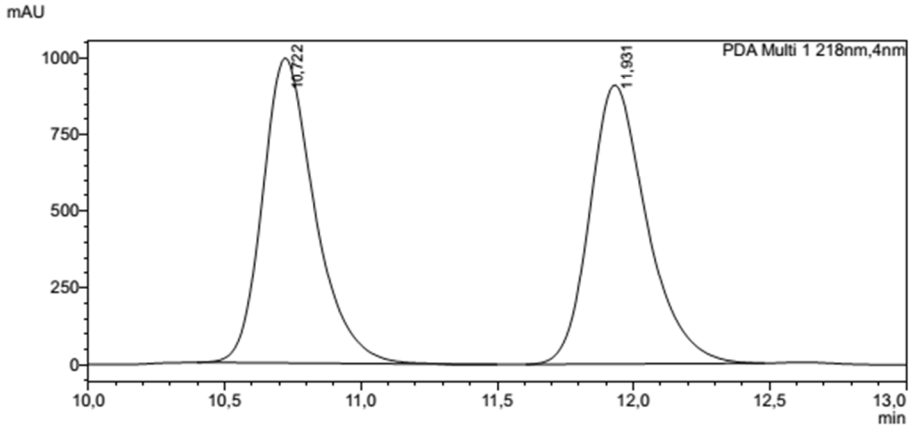


Peak Table

PDA Ch1 218nm

Peak#	Ret. Time	Area	Height	Conc.
1	10,675	61580191	3829489	97,636
2	11,893	1490738	108543	2,364
Total		63070929	3938032	

Chromatogram

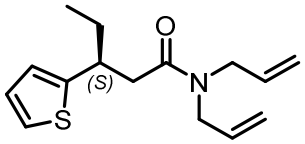


Peak Table

PDA Ch1 218nm

Peak#	Ret. Time	Area	Height	Conc.
1	10,722	13192277	994164	49,986
2	11,931	13199894	906279	50,014
Total		26392172	1900443	

***(S)*-*N*,*N*-Diallyl-3-(thiophen-2-yl)pentanamide (2t)**



2t

The reaction was performed with 0.1 mmol **1t**, $CuBr{\cdot}SMe_2$ (2.06 mg, 0.01 mmol, 10 mol%), ligand **L1** (7.68 mg, 0.012 mmol, 12 mol%), $BF_3{\cdot}Et_2O$ (25 μL, 0.2 mmol), in 1.0 mL of DCM at −78 °C and slow addition of a solution of EtMgBr (0.2 mmol, 3.0 M in Et_2O) in 0.5 mL of toluene and added dropwise to the reaction mixture during 2 hours using a syringe pump. Product **2t** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 5:1) [63% yield, 91% *ee*].

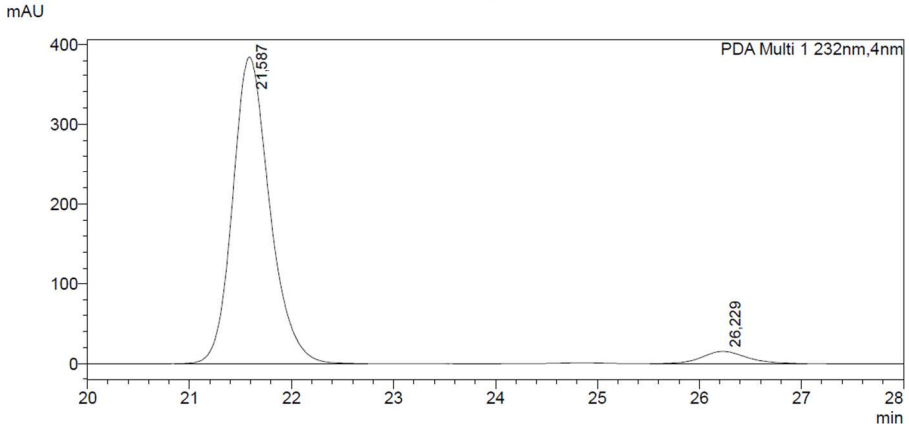
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.13 (d, *J* = 5.0 Hz, 1H, C*H*$_{Ar}$), 6.91 (dd, *J* = 5.0, 3.4 Hz, 1H, C*H*$_{Ar}$), 6.83 (d, *J* = 3.4 Hz, 1H, C*H*$_{Ar}$), 5.74-5.63 (m, 2H, C*H*=CH$_2$), 5.16 (d, *J* = 10.4, 1H, CH*H*=CH), 5.10-5.04 (m, 2H, C*H*$_2$=CH), 4.99 (d, *J* = 17.1, 1H, CH*H*=CH), 4.04 (dd, *J* = 15.3, 5.5 Hz, 1H, C*H*HCH=), 3.84 (dd, *J* = 15.3, 6.0 Hz, 1H, CH*H*CH=), 3.83-3.69 (m, 2H, C*H*$_2$CH=), 3.73 (dd, *J* = 17.5, 4.7 Hz, 2H, C*H*$_2$CH=), 3.54-3.47 (m, 1H, C*H*), 2.62 (dd, *J* = 15.1, 7.3 Hz, 1H, C*H*HCO), 2.57 (dd, *J* = 15.1, 6.8 Hz, 1H, CH*H*CO), 1.85-1.75 (m, 1H, C*H*HCH$_3$), 1.66-1.54 (m, 1H, CH*H*CH$_3$), 0.87 (t, *J* = 7.3 Hz, 3H, C*H*$_3$CH$_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.5, 148.7, 133.4, 132.9, 126.6, 124.4, 123.0, 117.1, 116.6, 49.2, 48.2, 41.1, 39.6, 30.3, 12.2.

HRMS (ESI+, m/Z): calcd for $C_{15}H_{22}NOS$ $[M+H]^+$: 264.14166, found: 264.14193.

HPLC: Chiracel-ADH, *n*-heptane/*i*-PrOH 98:2, 0.5 mL/min, 40 °C, detection at 232 nm. Retention time (min): 21.6 (major) and 26.2 (minor).

Chromatogram

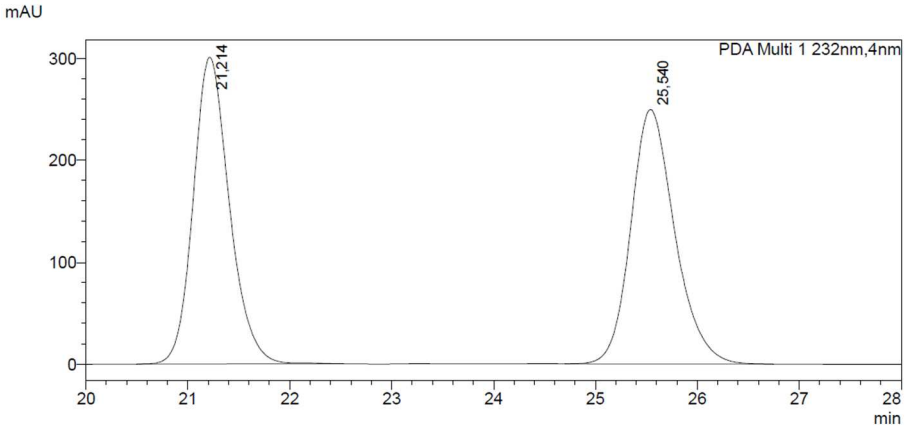


Peak Table

PDA Ch1 232nm

Peak#	Ret. Time	Area	Height	Conc.
1	21,587	9695979	384425	95,492
2	26,229	457782	15181	4,508
Total		10153761	399606	

Chromatogram

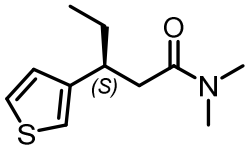


Peak Table

PDA Ch1 232nm

Peak#	Ret. Time	Area	Height	Conc.
1	21,214	7405436	301200	49,782
2	25,540	7470289	249171	50,218
Total		14875725	550371	

***(S)*-*N*,*N*-Dimethyl-3-(thiophen-2-yl)pentanamide (2u)**



2u

The reaction was performed with 0.1 mmol **1u**, $CuBr{\cdot}SMe_2$ (1.03 mg, 0.005 mmol, 5 mol%), ligand **L1** (3.84 mg, 0.006 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (25 μL, 0.2 mmol), EtMgBr (0.2 mmol, 3.0 M in Et_2O), 1.0 mL of DCM at −78 °C. Product **2u** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 1:5) [63% yield, 96% *ee*].

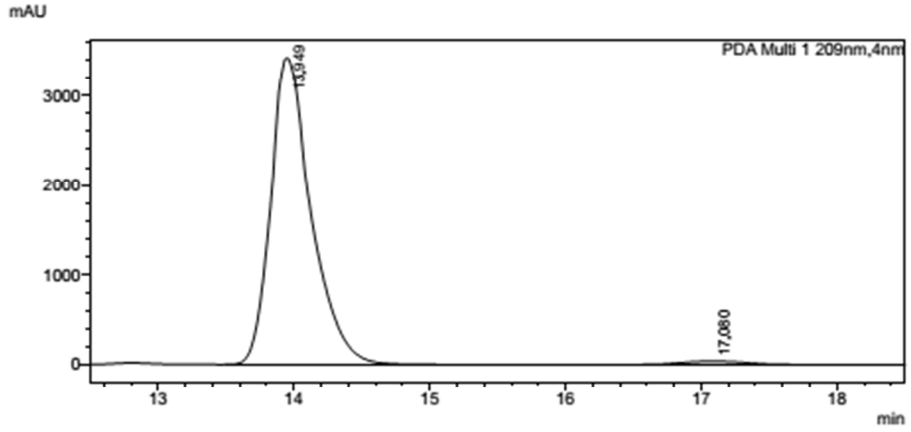
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.24 (dd, *J* = 5.0, 3.0 Hz, 1H, CH_{Ar}), 6.98 (ddd, *J* = 3.0, 1.3, 0.5 Hz, 1H, CH_{Ar}), 6.98 (dd, *J* = 5.0, 1.3 Hz, 1H, CH_{Ar}) 3.24 (dtd, *J* = 9.5, 7.0, 5.0 Hz, 1H, C*H*), 2.89 (s, 3H, NCH_3), 2.84 (s, 3H, NCH_3), 2.56 (dd, *J* = 14.9, 7.0, Hz, 1H, C*H*HCO), 2.53 (dd, *J* = 14.9, 7.0, Hz, 1H, CH*H*CO), 1.76 (dqd, *J* = 13.3, 7.3, 5.0 Hz, 1H, C*H*HCH$_3$), 1.60 (ddq, *J* = 13.3, 9.5, 7.3 Hz, 1H, CH*H*CH$_3$), 0.82 (t, *J* = 7.4 Hz, 3H, CH_3CH$_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.1, 145.7, 126.9, 125.4, 120.3, 40.3, 39.5, 37.4, 35.6, 29.0, 12.2.

HRMS (ESI+, m/Z): calcd for $C_{11}H_{18}NOS$ $[M+H]^+$: 212.11036, found: 212.11035.

HPLC: Chiracel-OBH, *n*-heptane/*i*-PrOH 90:10, 0.5 mL/min, 40 °C, detection at 209 nm. Retention time (min): 13.9 (major) and 17.1 (minor).

Chromatogram

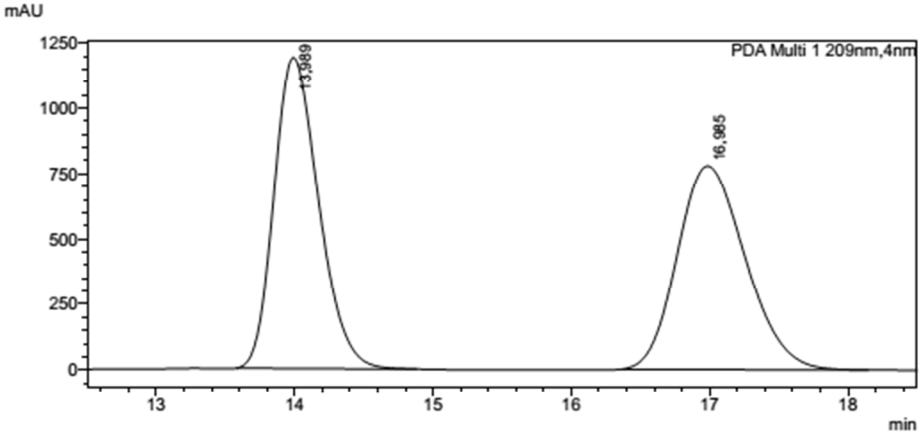


Peak Table

PDA Ch1 209nm

Peak#	Ret. Time	Area	Height	Conc.
1	13,949	70888601	3417676	98,169
2	17,080	1321822	40020	1,831
Total		72210423	3457696	

Chromatogram

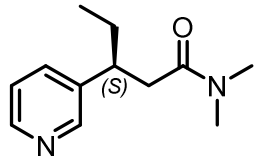


Peak Table

PDA Ch1 209nm

Peak#	Ret. Time	Area	Height	Conc.
1	13,989	26693908	1188704	50,046
2	16,985	26645038	778613	49,954
Total		53338946	1967317	

***(S)*-*N*,*N*-Dimethyl-3-(3-pyridinyl)pentanamide (2v)**



2v

The reaction was performed with 0.1 mmol **1v**, $CuBr{\cdot}SMe_2$ (1.03 mg, 0.005 mmol, 5 mol%), ligand **L1** (3.84 mg, 0.006 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (25 μL, 0.2 mmol), EtMgBr (0.2 mmol, 3.0 M in Et_2O), 1.0 mL of DCM at −78 °C. Product **2v** was obtained as a colorless oil after column chromatography (SiO_2 previously treated with NEt_3 (10%), Et_2O:MeOH 30:1) [74% yield, 95% *ee*]. *Note: In this case the reaction was quenched with 2 M NaOH solution.*

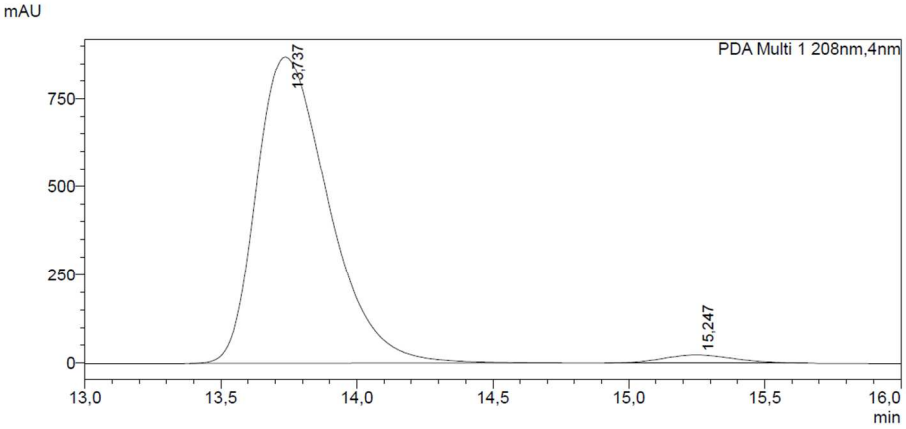
^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.44 (s, 1H, CH_{Ar}), 8.41 (d, *J* = 4.8 Hz, 1H, CH_{Ar}), 7.51 (dt, *J* = 7.8, 1.9 Hz, 1H, CH_{Ar}), 7.19 (dd, *J* = 7.8, 4.8 Hz, 1H, CH_{Ar}), 3.11 (dtd, *J* = 9.6, 7.1, 5.2 Hz, 1H, C*H*), 2.87 (s, 3H, NCH_3), 2.84 (s, 3H, NCH_3), 2.59 (dd, *J* = 15.4, 6.7 Hz, 1H, C*H*HCO), 2.57 (dd, *J* = 15.4, 7.4 Hz, 1H, CH*H*CO), 1.79 (dqd, *J* = 13.6, 7.4, 5.1 Hz, 1H, C*H*HCH$_3$), 1.59 (ddq, *J* = 13.6, 9.6, 7.4 Hz, 1H, CH*H*CH$_3$), 0.77 (t, *J* = 7.4 Hz, 3H, CH_3CH$_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.2, 149.5, 147.9, 140.2, 135.5, 123.5, 41.7, 40.0, 37.4, 35.6, 28.9, 12.1.

HRMS (ESI+, m/Z): calcd for $C_{12}H_{19}N_2O$ $[M+H]^+$: 207.14919, found: 207.14865.

HPLC: Chiracel-ODH, *n*-heptane/*i*-PrOH 80:20, 0.5 mL/min, 40 °C, detection at 208 nm. Retention time (min): 13.7 (major) and 15.2 (minor).

Chromatogram

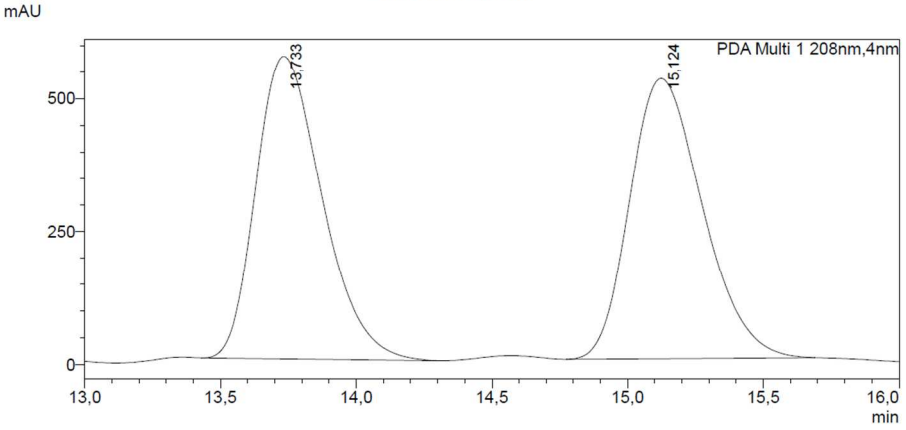


Peak Table

PDA Ch1 208nm

Peak#	Ret. Time	Area	Height	Conc.
1	13,737	16026694	871396	97,451
2	15,247	419248	22914	2,549
Total		16445942	894310	

Chromatogram

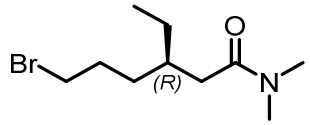


Peak Table

PDA Ch1 208nm

Peak#	Ret. Time	Area	Height	Conc.
1	13,733	9636544	568196	49,572
2	15,124	9802781	526242	50,428
Total		19439326	1094438	

***(R)*-*N*,*N*-Dimethyl-6-bromo-3-ethyl-hexanamide (2w)**



2w

The reaction was performed with 0.1 mmol **1w**, $CuBr{\cdot}SMe_2$ (1.03 mg, 0.005 mmol, 5 mol%), ligand **L1** (3.84 mg, 0.006 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (25 μL, 0.2 mmol), EtMgBr (0.2 mmol, 3.0 M in Et_2O), 1.0 mL of DCM at −78 °C. Product **2w** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 1:1) [76% yield, 97% *ee*].

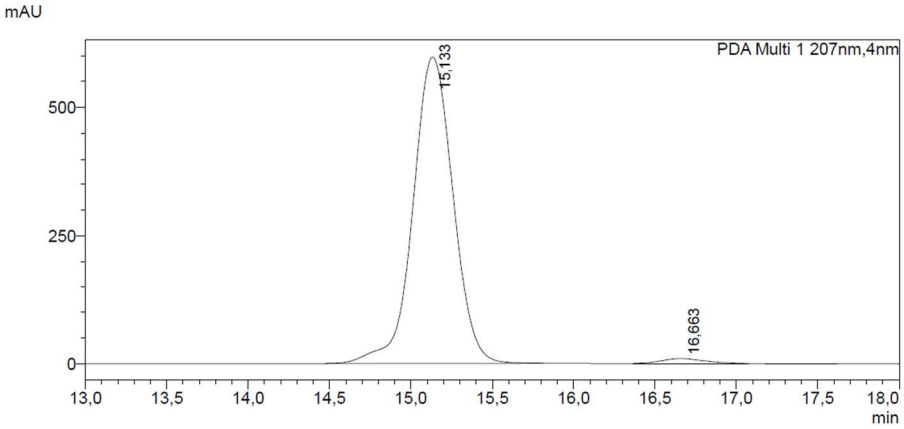
^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.40 (dt, *J* = 12.0, 6.8 Hz, 1H, C*H*HBr), 3.38 (dt, *J* = 12.0, 6.8 Hz, 1H, CH*H*Br), 3.00 (s, 3H, NCH_3), 2.94 (s, 3H, NCH_3), 2.28 (dd, *J* = 15.3, 6.5 Hz, 1H, C*H*HCO), 2.18 (dd, *J* = 15.3, 7.1 Hz, 1H, CH*H*CO), 1.97-1.82 (m, 3H, C*H*CH_2, CH_2CH_2Br), 1.46-1.32 (m, 4H, CH_2CH_3, C$H_2CH_2CH_2$Br), 0.88 (t, *J* = 7.4 Hz, 3H, CH_3CH_2).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.6, 37.6, 35.6, 34.3, 32.3, 30.3, 26.5, 11.0.

HRMS (ESI+, m/Z): calcd for $C_{10}H_{21}BrNO$ $[M+H]^+$: 250.08010, found: 250.08049.

HPLC: Chiracel-ODH, *n*-heptane/*i*-PrOH 95:5, 0.5 mL/min, 40 °C, detection at 207 nm. Retention time (min): 15.1 (major) and 16.7 (minor).

Chromatogram

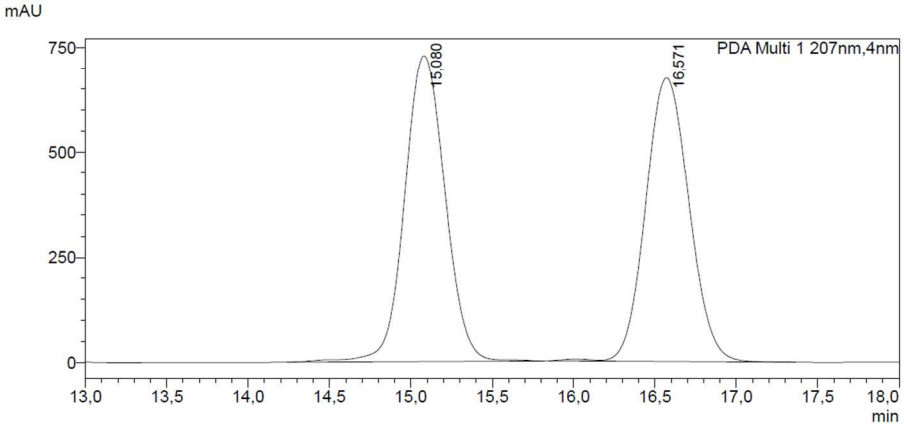


Peak Table

PDA Ch1 207nm

Peak#	Ret. Time	Area	Height	Conc.
1	15,133	10258204	597629	98,303
2	16,663	177119	9541	1,697
Total		10435323	607170	

Chromatogram

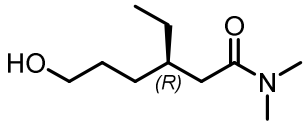


Peak Table

PDA Ch1 207nm

Peak#	Ret. Time	Area	Height	Conc.
1	15,080	12574536	727078	50,137
2	16,571	12505652	672469	49,863
Total		25080188	1399547	

***(R)*-*N*,*N*-Dimethyl-6-hydroxy-3-ethyl-hexanamide (2x)**



2x

The reaction was performed with 0.1 mmol **1x**, $CuBr{\cdot}SMe_2$ (1.03 mg, 0.005 mmol, 5 mol%), ligand **L1** (3.84 mg, 0.006 mmol, 6 mol%), TMSOTf (54 μL, 0.3 mmol), EtMgBr (0.3 mmol, 3.0 M in Et_2O), 1.0 mL of DCM at −50 °C. Product **2x** was obtained as a colorless oil after column chromatography (SiO_2, Et_2O:MeOH 30:1) [71% yield, 93% *ee*].

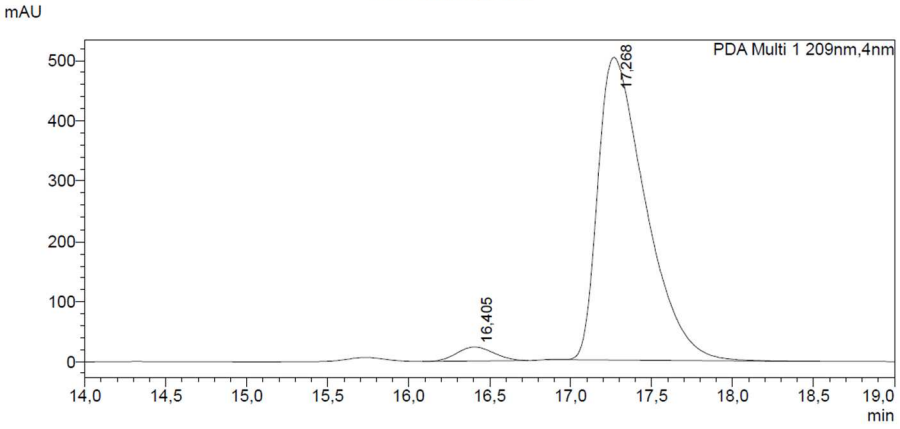
^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.69-3.58 (m, 2H, C*H*$_2$OH), 3.00 (s, 3H, NC*H*$_3$), 2.93 (s, 3H, NC*H*$_3$), 2.30 (dd, *J* = 15.5, 5.4 Hz, 1H, C*H*HCO), 2.15 (dd, *J* = 15.5, 8.4 Hz, 1H, CH*H*CO), 1.93-1.86 (m, 1H, C*H*), 1.65-1.35 (m, 2H, C*H*$_2$CH$_2$OH), 1.46-1.35 (m, 2H, C*H*$_2$CH$_2$CH$_2$OH), 1.34-1.22 (m, 2H, C*H*$_2$CH$_3$), 0.87 (t, *J* = 7.4 Hz, 3H, C*H*$_3$CH$_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.2, 62.5, 37.7, 37.5, 35.6, 35.1, 29.7, 29.4, 26.6, 11.2.

HRMS (ESI+, m/Z): calcd for $C_{10}H_{22}NO_2$ $[M+H]^+$: 188.16451, found: 188.16425.

HPLC: Chiracel-OJH, *n*-heptane/*i*-PrOH 95:5, 0.5 mL/min, 40 °C, detection at 209 nm. Retention time (min): 16.4 (minor) and 17.3 (major).

Chromatogram

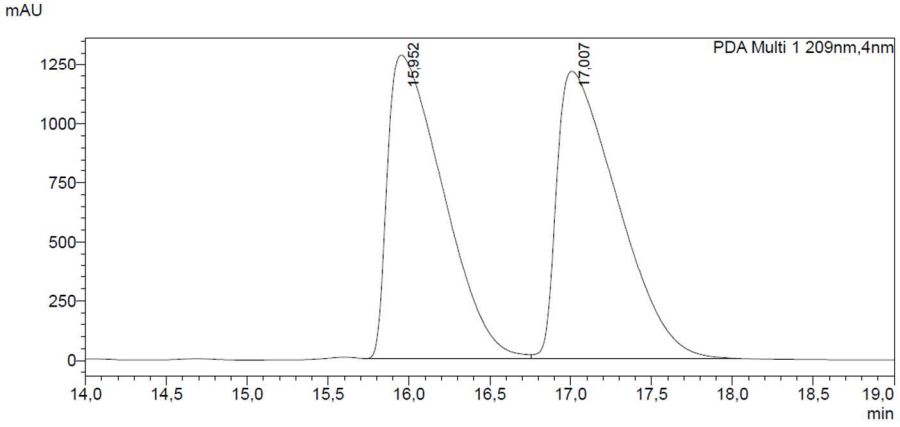


Peak Table

PDA Ch1 209nm

Peak#	Ret. Time	Area	Height	Conc.
1	16,405	366220	23060	3,440
2	17,268	10279931	502723	96,560
Total		10646151	525783	

Chromatogram

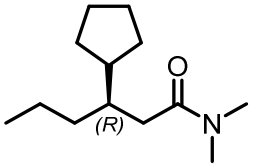


Peak Table

PDA Ch1 209nm

Peak#	Ret. Time	Area	Height	Conc.
1	15,952	30543999	1282872	49,095
2	17,007	31670290	1211003	50,905
Total		62214289	2493875	

***(R)*-*N*,*N*-Dimethyl-3-cyclopentyl-hexanamide (3a)**



3a

The reaction was performed with 0.2 mmol **1a**, $CuBr{\cdot}SMe_2$ (2.06 mg, 0.01 mmol, 5 mol%), ligand **L1** (7.68 mg, 0.012 mmol, 6 mol%), TMSOTf (72 μL, 0.4 mmol), cyclopentylMgBr (0.4 mmol, 2.0 M in Et_2O), 2.0 mL of DCM at −50 °C. Product **3a** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 2:1) [78% yield, 87% *ee*].

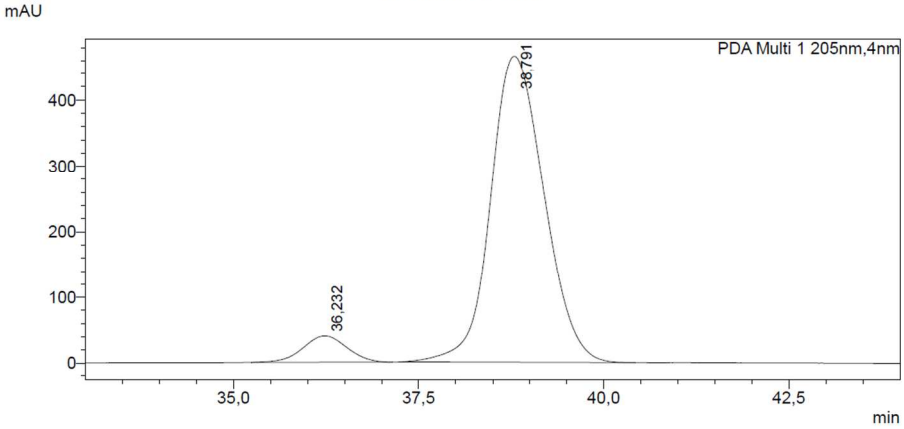
^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.01 (s, 3H, NC*H*$_3$), 2.93 (s, 3H, NC*H*$_3$), 2.28 (dd, *J* = 15.2, 5.6 Hz, 1H, C*H*HCO), 2.22 (dd, *J* = 15.2, 7.5 Hz, 1H, CH*H*CO), 1.96-1.44 (m, 8H, C*H*CH$_2$, C*H*$_2$), 1.38-1.09 (m, 6H, C*H*$_2$), 0.87 (t, *J* = 6.9 Hz, 3H, C*H*$_3$CH$_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.3, 43.9, 39.1, 37.6, 36.4, 35.6, 35.1, 30.1, 30.0, 25.6, 25.5, 19.8, 14.7.

HRMS (ESI+, m/Z): calcd for $C_{13}H_{26}NO$ $[M+H]^+$: 212.20089, found: 212.20077.

HPLC: Chiracel-OZH, *n*-heptane/*i*-PrOH 98:2, 0.5 mL/min, 40 °C, detection at 205 nm. Retention time (min): 36.2 (minor) and 38.8 (major).

Chromatogram

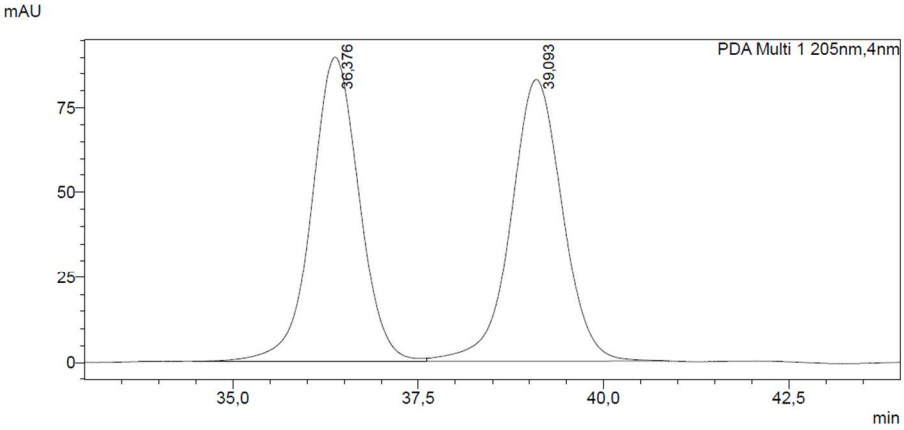


Peak Table

PDA Ch1 205nm

Peak#	Ret. Time	Area	Height	Conc.
1	36,232	1642501	39917	6,554
2	38,791	23418422	465250	93,446
Total		25060923	505167	

Chromatogram

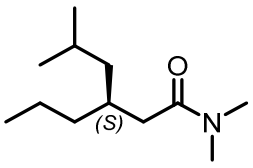


Peak Table

PDA Ch1 205nm

Peak#	Ret. Time	Area	Height	Conc.
1	36,376	3988931	89780	49,854
2	39,093	4012230	82857	50,146
Total		8001161	172638	

***(S)*-*N*,*N*-Dimethyl-5-methy-3-propyl-hexanamide (3b)**



3b

The reaction was performed with 0.2 mmol **1a**, $CuBr{\cdot}SMe_2$ (2.06 mg, 0.01 mmol, 5 mol%), ligand **L1** (7.68 mg, 0.012 mmol, 6 mol%), TMSOTf (72 μL, 0.4 mmol), cyclopentylMgBr (0.4 mmol, 2.0 M in Et_2O), 2.0 mL of DCM at −50 °C. Product **3b** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 2:1) [84% yield, 95% *ee*].

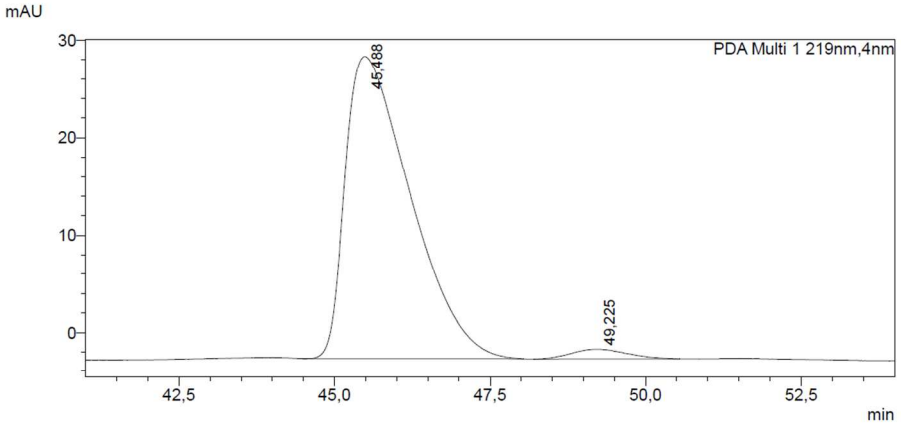
^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.99 (s, 3H, NC*H*$_3$), 2.93 (s, 3H, NC*H*$_3$), 2.22 (dd, *J* = 15.1, 7.3 Hz, 1H, C*H*HCO), 2.17 (dd, *J* = 15.1, 6.4 Hz, 1H, CH*H*CO), 2.03-1.93 (m, 1H, $CH_3CH_2CH_2CH$), 1.67-1.59 (dhept, *J*=13.3, 6.6 Hz, 1H, CH_3CH), 1.34-1.21 (m, 4H, CH_3CH_2, $CH_3CH_2CH_2$), 1.19-1.04 (m, 2H, CH_3CHCH_2), 0.87 (t, *J* = 6.9 Hz, 3H, CH_3CH_2), 0.87 (d, *J* = 6.6 Hz, 3H, CH_3CH), 0.86 (d, *J* = 6.6 Hz, 3H, CH_3CH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.1, 44.1, 38.6, 37.6, 36.8, 35.6, 32.5, 25.5, 23.1, 22.9, 19.7, 14.6.

HRMS (ESI+, m/Z): calcd for $C_{12}H_{26}NO$ $[M+H]^+$: 200.20089, found: 200.20066.

HPLC: Chiracel-ADH, *n*-heptane/*i*-PrOH 95.5:0.5, 0.5 mL/min, 40 °C, detection at 219 nm. Retention time (min): 45.5 (major) and 49.2 (minor).

Chromatogram

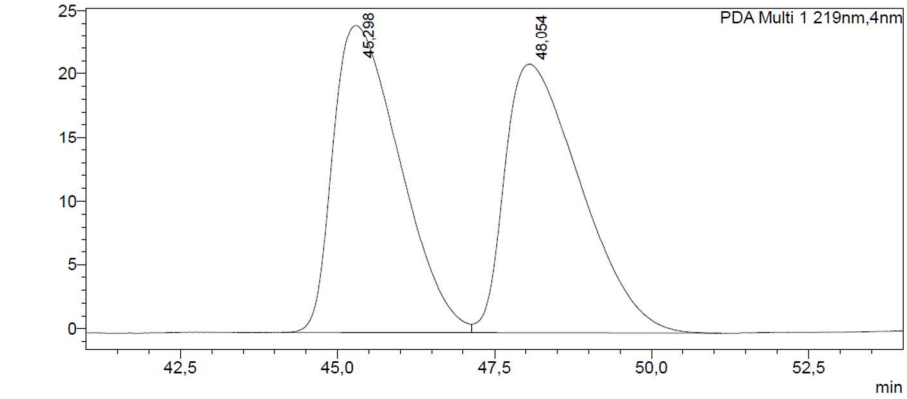


Peak Table

PDA Ch1 219nm

Peak#	Ret. Time	Area	Height	Conc.
1	45,488	2263494	30996	97,365
2	49,225	61265	1002	2,635
Total		2324759	31998	

Chromatogram

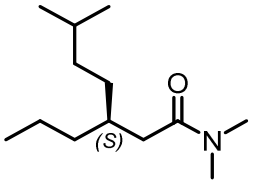


Peak Table

PDA Ch1 219nm

Peak#	Ret. Time	Area	Height	Conc.
1	45,298	1780403	24126	50,090
2	48,054	1774024	21055	49,910
Total		3554427	45181	

***(S)*-*N*,*N*-Dimethyl-6-methy-3-propyl-heptanamide (3c)**



3c

The reaction was performed with 0.2 mmol **1a**, $CuBr{\cdot}SMe_2$ (2.06 mg, 0.01 mmol, 5 mol%), ligand **L1** (7.68 mg, 0.012 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (50 μL, 0.4 mmol), *i*-pentylMgBr (0.4 mmol, 2.0 M in Et_2O), 2.0 mL of DCM at −78 °C. Product **3c** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 2:1) [77% yield, 97% *ee*].

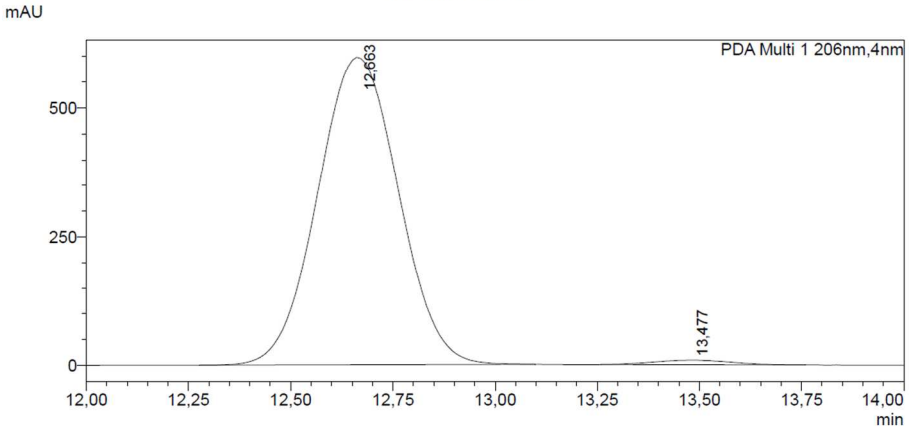
^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.99 (s, 3H, NC*H*$_3$), 2.93 (s, 3H, NC*H*$_3$), 2.21 (d, *J* = 6.9 Hz, 2H, C*H*$_2$CO), 1.94-1.84 (m, 1H, $CH_3CH_2CH_2CH$), 1.52-1.41 (m, 1H, CH_3CH), 1.34-1.19 (m, 6H, C*H*$_2$), 1.17-1.11 (m, 2H, CH_3CHCH_2), 0.87 (t, *J* = 6.7 Hz, 3H, C*H*$_3$CH$_2$), 0.85 (d, *J* = 6.6 Hz, 6H, C*H*$_3$CH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.1, 38.2, 37.6, 36.4, 35.9, 35.6, 34.9, 31.8, 28.4, 22.8, 22.7, 19.9, 14.5.

HRMS (ESI+, m/Z): calcd for $C_{13}H_{28}NO$ $[M+H]^+$: 214.21654, found: 214.21645.

HPLC: Chiracel-ODH, *n*-heptane/*i*-PrOH 98:2, 0.5 mL/min, 40 °C, detection at 206 nm. Retention time (min): 12.7 (major) and 13.5 (minor).

Chromatogram

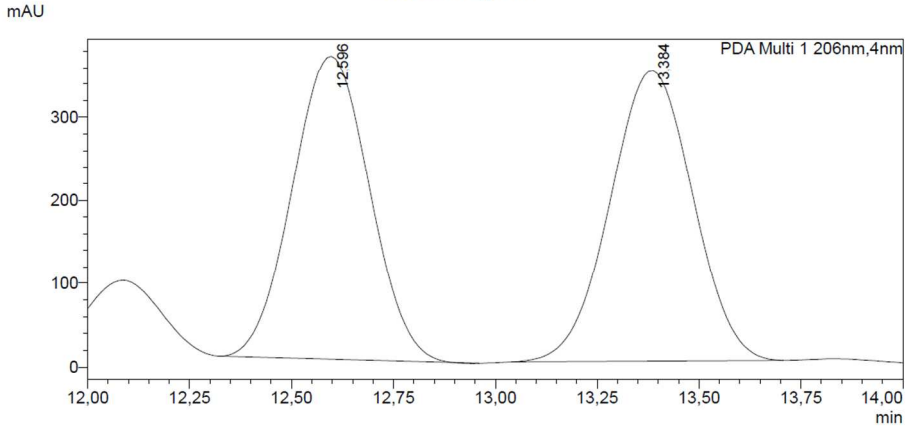


Peak Table

PDA Ch1 206nm

Peak#	Ret. Time	Area	Height	Conc.
1	12,663	8225074	597393	98,620
2	13,477	115054	8816	1,380
Total		8340128	606210	

Chromatogram

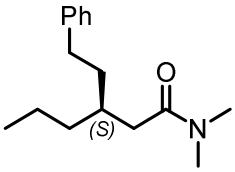


Peak Table

PDA Ch1 206nm

Peak#	Ret. Time	Area	Height	Conc.
1	12,596	4779960	364348	49,311
2	13,384	4913457	348288	50,689
Total		9693417	712637	

***(S)*-*N*,*N*-Dimethyl-3-phenethylhexanamide (3d)**



3d

The reaction was performed with 0.2 mmol **1a**, $CuBr{\cdot}SMe_2$ (2.06 mg, 0.01 mmol, 5 mol%), ligand **L1** (7.68 mg, 0.012 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (50 μL, 0.4 mmol), phenylethylMgBr (0.4 mmol, 2.6 M in Et_2O), 2.0 mL of DCM at −78 °C. Product **3d** was obtained as a orange oil after column chromatography (SiO_2, pentane:Et_2O 1:1) [73% yield, 97% *ee*].

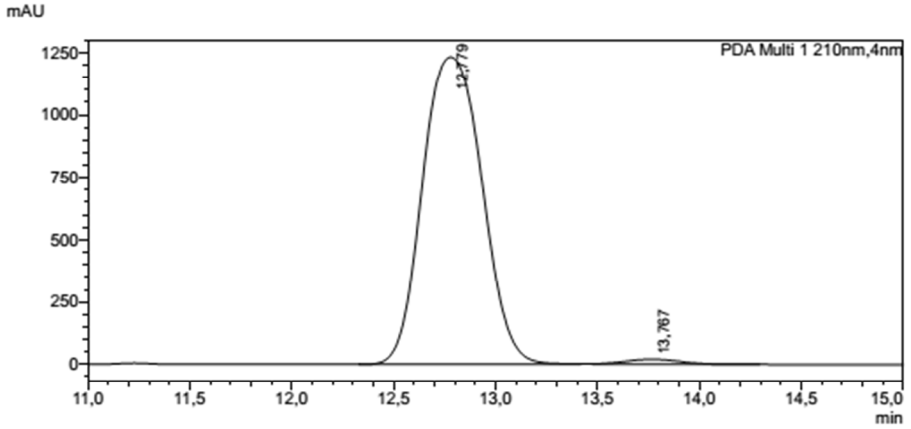
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.28-7.25 (m, 2H, CH_{Ar}), 7.19-7.14 (m, 3H, CH_{Ar}), 2.96 (s, 3H, NCH_3), 2.94 (s, 3H, NCH_3), 2.67-2.55 (m, 2H, CH_2Ph), 2.30 (dd, *J* = 15.9, 7.0 Hz, 1H, C*H*HCO), 2.28 (dd, *J* = 15.9, 6.8 Hz, 1H, CH*H*CO), 2.07-1.97 (m, 1H, C*H*), 1.66-1.60 (m, 2H, CH_2CH_3), 1.38-1.28 (m, 4H, C$H_2CH_2CH_3$ and CH_2CH_2Ph), 0.90 (t, *J* = 6.9 Hz, 3H, CH_3CH_2).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.8, 142.9, 128.5, 128.4, 125.8, 38.2, 37.6, 36.4, 36.0, 35.6, 34.6, 33.3, 19.9, 14.6.

HRMS (ESI+, m/Z): calcd for $C_{16}H_{26}NO$ $[M+H]^+$: 248.20089, found: 248.20103.

HPLC: Chiracel-OJH, *n*-heptane/*i*-PrOH 95:5, 0.5 mL/min, 40 °C, detection at 210 nm. Retention time (min): 12.8 (major) and 13.8 (minor).

Chromatogram

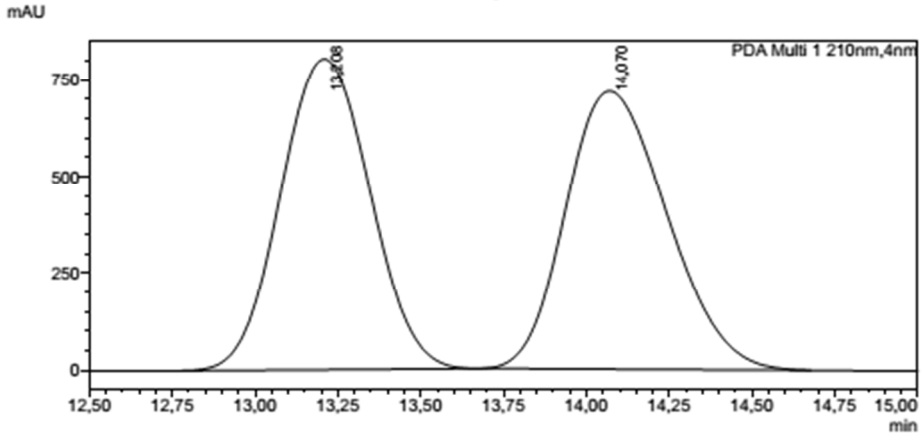


Peak Table

PDA Ch1 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	12,779	24992848	1230790	98,622
2	13,767	349340	19382	1,378
Total		25342188	1250172	

Chromatogram

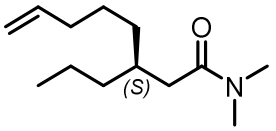


Peak Table

PDA Ch1 210nm

Peak#	Ret. Time	Area	Height	Conc.
1	13,208	15054037	802655	49,697
2	14,070	15237642	717338	50,303
Total		30291679	1519993	

***(S)*-*N*,*N*-Dimethyl-3-propyl-oct-7-enamide (3e)**



3e

The reaction was performed with 0.2 mmol **1a**, $CuBr{\cdot}SMe_2$ (2.06 mg, 0.01 mmol, 5 mol%), ligand **L1** (7.68 mg, 0.012 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (50 μL, 0.4 mmol), pent-4-en-1-ylMgBr (0.4 mmol, 1.7 M in Et_2O), 2.0 mL of DCM at −78 °C. Product **3e** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 1:1) [80% yield, 97% *ee*].

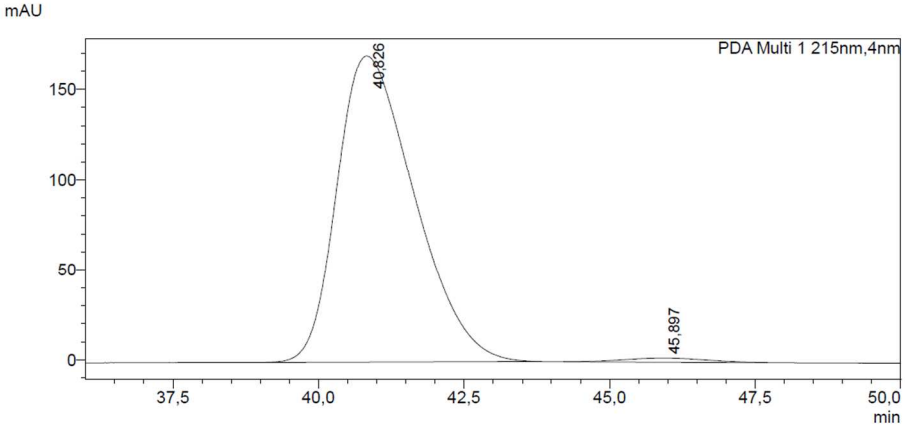
^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.79 (ddt, *J* = 17.1, 10.3, 6.7 Hz, 1H, C*H*=CH_2), 4.97 (dc, *J* = 17.1, 1.9 Hz, 1H, CH=C*H*H), 4.91 (ddt, *J* = 10.3, 2.0, 1.1 Hz, 1H, CH=CH*H*), 2.99 (s, 3H, NC*H*$_3$), 2.93 (s, 3H, NC*H*$_3$), 2.23 (dd, *J* = 15.4, 6.9 Hz, 1H, C*H*HCO), 2.19 (dd, *J* = 15.4, 6.9 Hz, 1H, CH*H*CO), 2.05-1.99 (m, 2H, C*H*$_2$CH=CH_2), 1.97-1.90 (m, 1H, C*H*CH_2CO), 1.41-1.24 (m, 8H, C*H*$_2$), 0.87 (t, *J* = 6.6 Hz, 3H, C*H*$_3CH_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.0, 139.1, 114.4, 38.2, 37.6, 36.4, 35.6, 34.6, 34.2, 33.6, 26.1, 19.9, 14.5.

HRMS (ESI+, m/Z): calcd for $C_{13}H_{26}NO$ $[M+H]^+$: 212.20089, found: 212.20081.

HPLC: Chiracel-OBH, *n*-heptane/*i*-PrOH 99.7:0.3, 0.5 mL/min, 40 °C, detection at 215 nm. Retention time (min): 40.8 (major) and 45.9 (minor).

Chromatogram

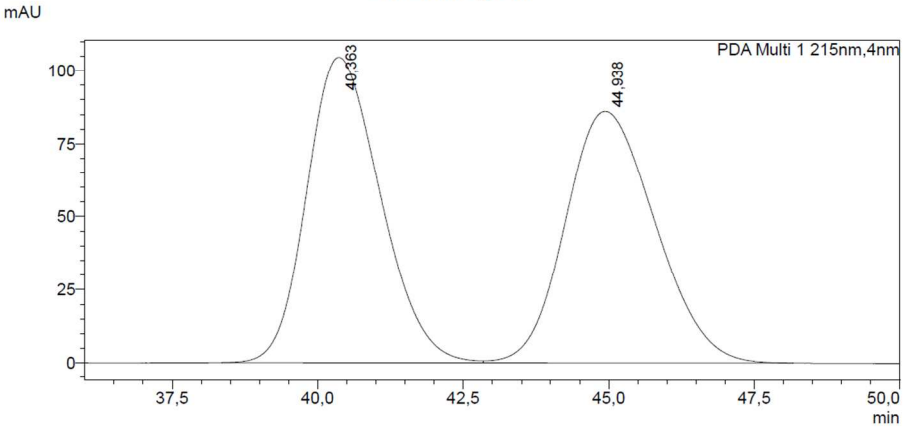


Peak Table

PDA Ch1 215nm

Peak#	Ret. Time	Area	Height	Conc.
1	40,826	15705271	169852	98,618
2	45,897	220089	2241	1,382
Total		15925360	172093	

Chromatogram

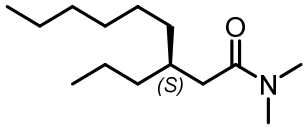


Peak Table

PDA Ch1 215nm

Peak#	Ret. Time	Area	Height	Conc.
1	40,363	9207269	104536	49,937
2	44,938	9230333	86039	50,063
Total		18437601	190575	

***(S)*-*N*,*N*-Dimethyl-3-propyl-nonanamide (3f)**



3f

The reaction was performed with 0.2 mmol **1a**, $CuBr{\cdot}SMe_2$ (2.06 mg, 0.01 mmol, 5 mol%), ligand **L1** (7.68 mg, 0.012 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (50 μL, 0.4 mmol), HexMgBr (0.4 mmol, 2.0 M in Et_2O), 2.0 mL of DCM at −78 °C. Product **3f** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 1:1) [82% yield, 97% *ee*].

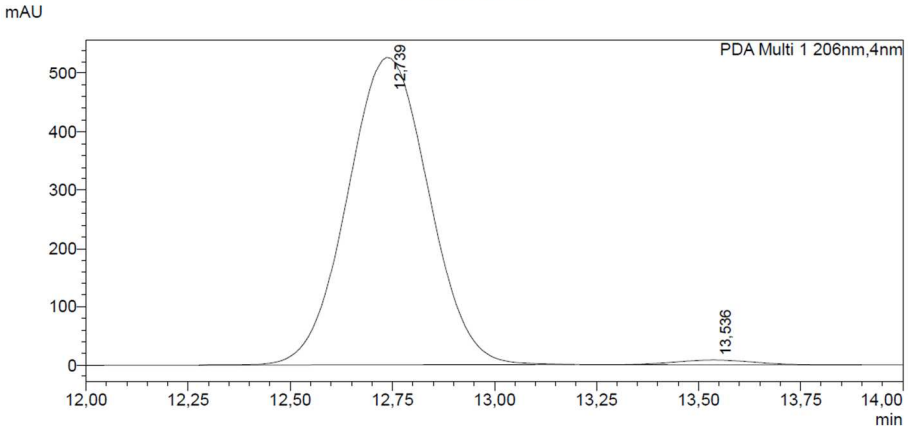
^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.99 (s, 3H, NC*H*$_3$), 2.93 (s, 3H, NC*H*$_3$), 2.21 (d, *J* = 6.9 Hz, 2H, C*H*$_2$CO), 1.92-1.89 (m, 1H, C*H*), 1.32-1.17 (m, 14H, C*H*$_2$), 0.87 (t, *J* = 6.6 Hz, 3H, C*H*$_3$), 0.86 (t, *J* = 6.9 Hz, 3H, C*H*$_3$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.1, 38.2, 37.6, 36.5, 35.6, 34.8, 34.1, 32.0, 29.8, 26.7, 22.8, 19.9, 14.5, 14.2.

HRMS (ESI+, m/Z): calcd for $C_{14}H_{30}NO$ $[M+H]^+$: 228.23219, found: 228.23209.

HPLC: Chiracel-ODH, *n*-heptane/*i*-PrOH 98:2, 0.5 mL/min, 40 °C, detection at 206 nm. Retention time (min): 12.7 (major) and 13.5 (minor).

Chromatogram

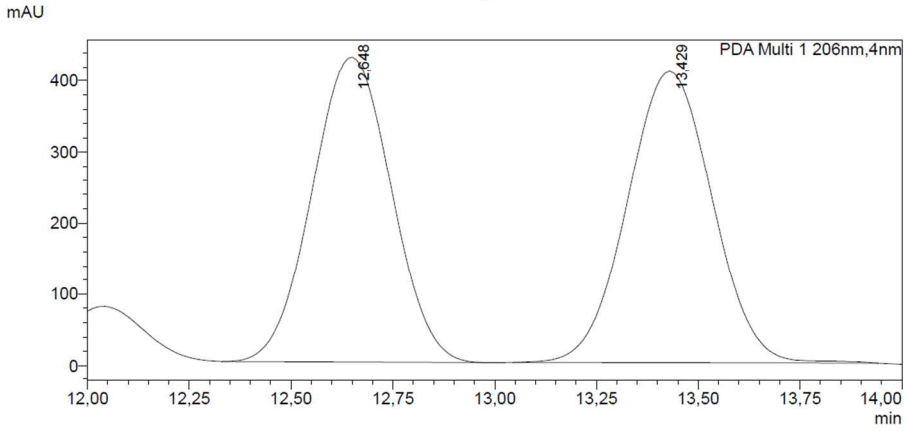


Peak Table

PDA Ch1 206nm

Peak#	Ret. Time	Area	Height	Conc.
1	12,739	7280697	526858	98,531
2	13,536	108550	8152	1,469
Total		7389247	535011	

Chromatogram

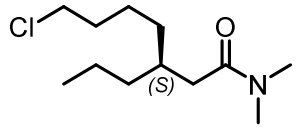


Peak Table

PDA Ch1 206nm

Peak#	Ret. Time	Area	Height	Conc.
1	12,648	5800398	429019	49,462
2	13,429	5926658	408653	50,538
Total		11727056	837672	

***(S)*-*N*,*N*-Dimethyl-7-chloro-3-propyl-heptanamide (3g)**



3g

The reaction was performed with 0.2 mmol **1a**, $CuBr{\cdot}SMe_2$ (2.06 mg, 0.01 mmol, 5 mol%), ligand **L1** (7.68 mg, 0.012 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (50 μL, 0.4 mmol), (4-chlorobutyl)MgBr (0.4 mmol, 1.3 M in Et_2O), 2.0 mL of DCM at −78 °C. Product **3g** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 1:1) [41% yield, 98% *ee*].

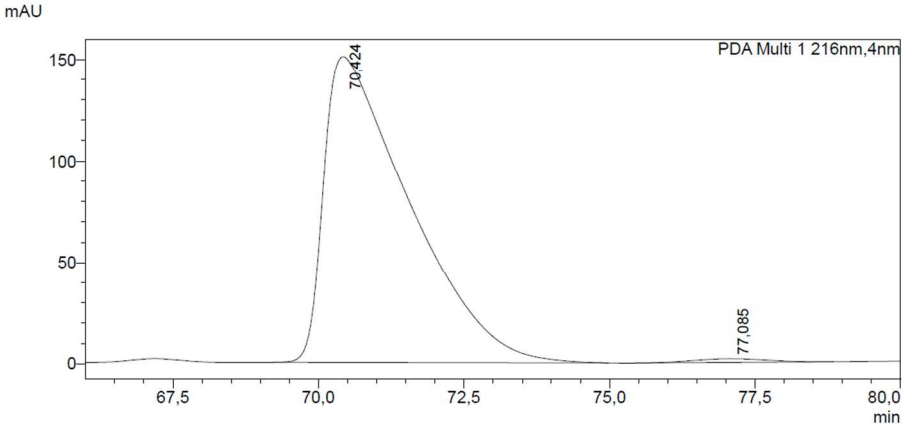
^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.54 (t, *J* = 6.6 Hz, 2H, C*H*$_2$Cl), 3.01 (s, 3H, NC*H*$_3$), 2.95 (s, 3H, NC*H*$_3$), 2.26 (dd, *J* = 15.2, 6.7 Hz, 1H, C*H*HCO), 2.20 (dd, *J* = 15.2, 7.0 Hz, 1H, CH*H*CO), 1.98-1.94 (m, 1H, C*H*), 1.80-1.73 (m, 2H, C*H*$_2$CH$_2$Cl), 1.48-1.40 (m, 2H, C*H*$_2$CH$_2$CH$_2$Cl), 1.35-1.25 (m, 6H, C*H*$_2$), 0.89 (t, *J* = 6.7 Hz, 3H, C*H*$_3$CH$_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.9, 45.2, 38.0, 37.6, 36.4, 35.6, 34.5, 33.3, 32.9, 24.0, 19.9, 14.5.

HRMS (ESI+, m/Z): calcd for $C_{12}H_{25}ClNO$ $[M+H]^+$: 234.16192, found: 234.16222.

HPLC: Chiracel-ODH, *n*-heptane/*i*-PrOH 99.5:0.5, 0.5 mL/min, 40 °C, detection at 216 nm. Retention time (min): 70.4 (major) and 77.1 (minor).

Chromatogram

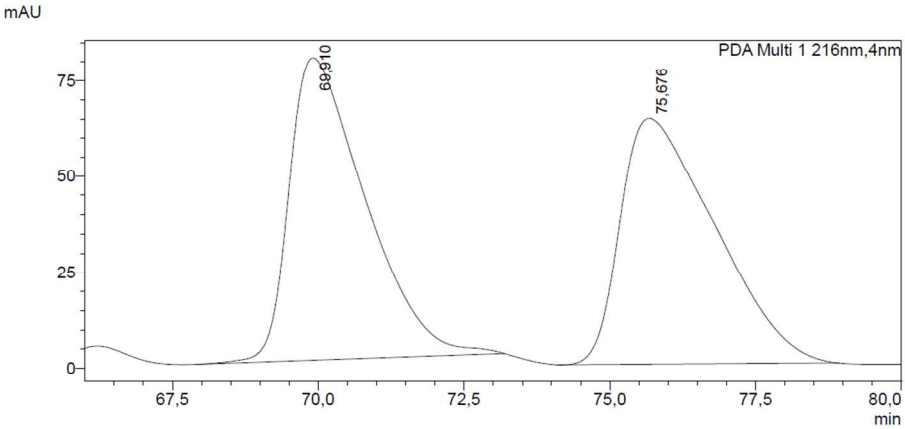


Peak Table

PDA Ch1 216nm

Peak#	Ret. Time	Area	Height	Conc.
1	70,424	15401682	150739	98,980
2	77,085	158655	1816	1,020
Total		15560338	152556	

Chromatogram

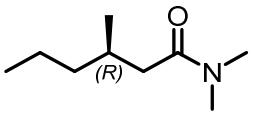


Peak Table

PDA Ch1 216nm

Peak#	Ret. Time	Area	Height	Conc.
1	69,910	7161957	79017	49,771
2	75,676	7227734	64129	50,229
Total		14389691	143145	

***(R)*-*N*,*N*-Dimethyl-3-methyl-hexanamide (3h)**



3h

The reaction was performed with 0.2 mmol **1a**, $CuBr{\cdot}SMe_2$ (2.06 mg, 0.01 mmol, 5 mol%), ligand **L1** (7.68 mg, 0.012 mmol, 6 mol%), TMSOTf (72 μL, 0.4 mmol), MeMgBr (0.4 mmol, 3.0 M in Et_2O), 2.0 mL of DCM at −50 °C. Product **3h** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 1:1) [93% yield, 99% *ee*]. *Note: different temperatures and reactions scales, LA have been tried providing the corresponding product with nearly similar outcome. For details see Table S2 , entries 13, 14, 17, 20, 23*

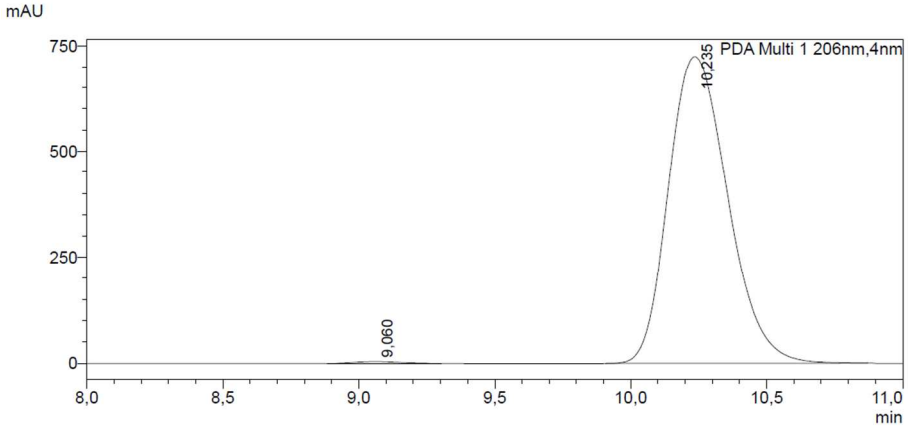
^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.00 (s, 3H, NC*H*$_3$), 2.95 (s, 3H, NC*H*$_3$), 2.29 (dd, *J* = 14.6, 5.8 Hz, 1H, C*H*HCO), 2.12 (dd, *J* = 14.6, 8.1 Hz, 1H, CH*H*CO), 2.05-1.97 (m, 1H, C*H*CH_2), 1.43-1.24 (m, 3H, C*H*$_2CH_3$, C*H*HCH_2CH_3), 1.19-1.10 (m, 1H, CH*H*CH_2CH_3), 0.93 (d, *J* = 6.6 Hz, 3H, C*H*$_3$CH), 0.89 (t, *J* = 7.0 Hz, 3H, C*H*$_3CH_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.9, 40.8, 39.5, 37.6, 35.5, 30.2, 20.3, 20.0, 14.4.

HRMS (ESI+, m/Z): calcd for $C_9H_{20}NO$ $[M+H]^+$: 158.15394, found: 158.15384.

HPLC: Chiracel-OBH, *n*-heptane/*i*-PrOH 90:10, 0.5 mL/min, 40 °C, detection at 206 nm. Retention time (min): 9.1 (minor) and 10.2 (major).

Chromatogram

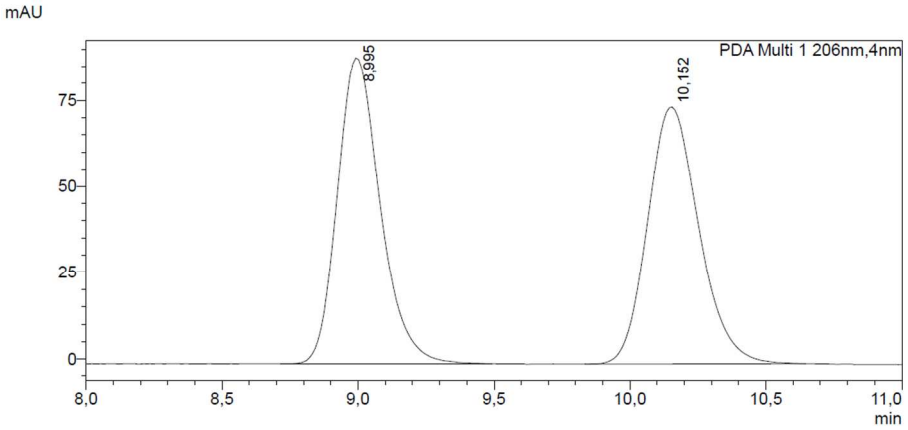


Peak Table

PDA Ch1 206nm

Peak#	Ret. Time	Area	Height	Conc.
1	9,060	47641	4345	0,432
2	10,235	10974951	724084	99,568
Total		11022592	728429	

Chromatogram

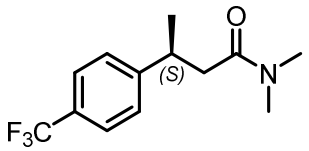


Peak Table

PDA Ch1 206nm

Peak#	Ret. Time	Area	Height	Conc.
1	8,995	972588	88794	49,971
2	10,152	973703	74508	50,029
Total		1946291	163302	

***(S)*-*N*,*N*-Dimethyl-3-(4-(trifluoromethyl)phenyl)butanamide (3i)**



3i

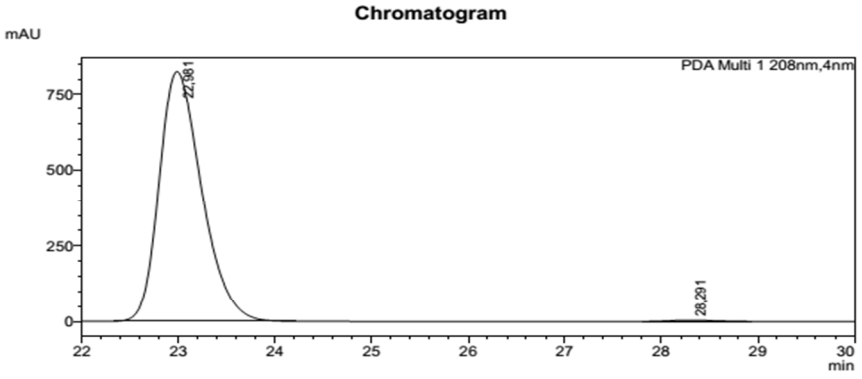
The reaction was performed with 0.1 mmol **1o**, $CuBr{\cdot}SMe_2$ (1.03 mg, 0.005 mmol, 5 mol%), ligand **L1** (3.84 mg, 0.006 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (25 μL, 0.2 mmol), MeMgBr (0.2 mmol, 3.0 M in Et_2O), 1.0 mL of DCM at −78 °C. Product **3i** was obtained as a colorless oil after column chromatography (SiO_2, Et_2O) [54% yield, 99% *ee*].

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.54 (d, *J* = 8.1 Hz, 2H, C*H*$_{Ar}$), 7.36 (d, *J* = 8.1 Hz, 2H, C*H*$_{Ar}$), 3.45 (sex (qt), *J* = 6.9 Hz, 1H, C*H*), 2.91 (s, 6H, NC*H*$_3$), 2.62 (dd, *J* = 15.3, 6.7 Hz, 1H, C*H*HCO), 2.54 (dd, *J* = 15.3, 7.3 Hz, 1H, CH*H*CO), 1.33 (d, *J* = 6.9 Hz, 3H, C*H*$_3$CH$_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.3, 150.9, 128.7 (q, *J* = 32.3 Hz), 127.4, 125.5 (q, *J* = 3.8 Hz), 124.4 (q, *J* = 272.4 Hz), 41.5, 37.4, 36.4, 35.7, 21.8.

HRMS (ESI+, m/Z): calcd for $C_{13}H_{17}F_3NO$ $[M+H]^+$: 260.12568, found: 260.12609.

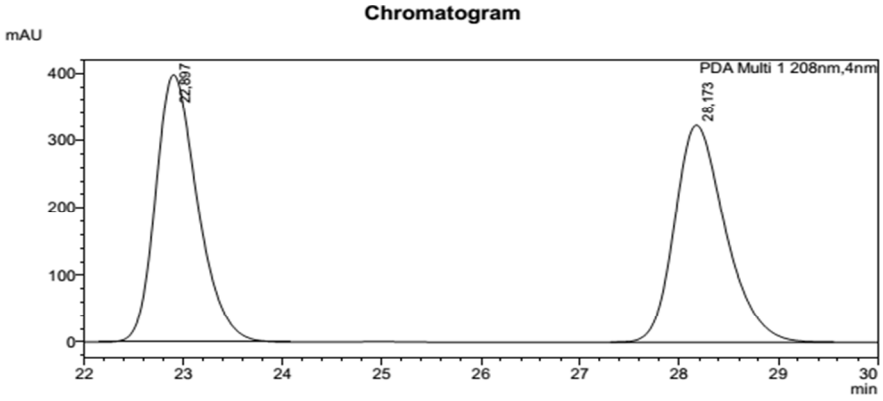
HPLC: Chiracel-ADH, *n*-heptane/*i*-PrOH 98:2, 0.5 mL/min, 40 °C, detection at 208 nm. Retention time (min): 23.0 (major) and 28.3 (minor).



Peak Table

PDA Ch1 208nm

Peak#	Ret. Time	Area	Height	Conc.
1	22,981	25270631	824055	99,449
2	28,291	140013	4380	0,551
Total		25410644	828435	

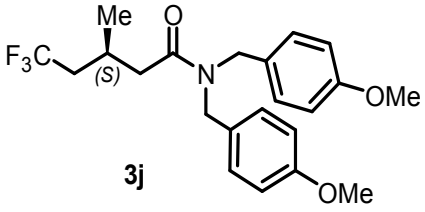


Peak Table

PDA Ch1 208nm

Peak#	Ret. Time	Area	Height	Conc.
1	22,897	11754995	398184	50,460
2	28,173	11540592	322553	49,540
Total		23295586	720738	

(*S*)-5,5,5-trifluoro-N,N-bis(4-methoxybenzyl)-3-methylpentanamide (3j)



3j

The reaction was performed with 0.1 mmol **1y**, $CuBr{\cdot}SMe_2$ (1.03 mg, 0.005 mmol, 5 mol%), ligand **L1** (3.84 mg, 0.006 mmol, 6 mol%), $BF_3{\cdot}Et_2O$ (37 μL, 0.3 mmol), MeMgBr (0.3 mmol, 3.0 M in Et_2O), 1.0

mL of DCM at -78 °C. Product **3j** was obtained as a colorless oil after column chromatography (SiO_2, Et_2O) [62% yield, 99% *ee*].

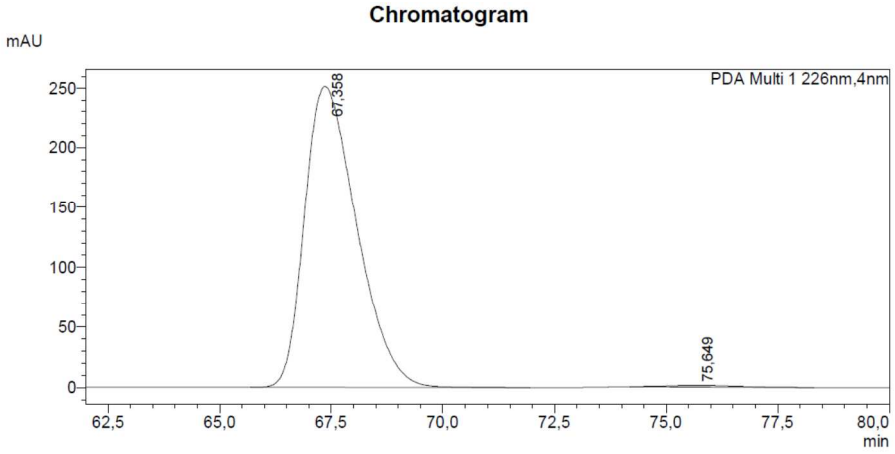
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.14 (d, *J* = 8.4 Hz, 2H, C*H*$_{Ar}$), 7.04 (d, *J* = 8.5 Hz, 2H, C*H*$_{Ar}$), 6.90 (d, *J* = 8.5 Hz, 2H, C*H*$_{Ar}$), 6.85 (d, *J* = 8.4 Hz, 2H, C*H*$_{Ar}$), 4.52 (s, 2H, NC*H*$_2$), 4.35 (s, 2H, NC*H*$_2$), 3.82 (s, 3H, OC*H*$_3$), 3.80 (s, 3H, OC*H*$_3$), 2.58-2.24 (m, 4H, C*H*$_2$), 2.08-1.94 (m, 1H, C*H*), 1.10 (d, *J* = 6.6 Hz, 3H, C*H*$_3$).

^{19}F NMR ($CDCl_3$, 377 MHz): δ -63.0 (t, *J* = 11.3 Hz).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.5, 159.3, 159.1, 129.8, 129.6, 128.3, 127.7, 127.2 (q, *J* = 277.8 Hz), 114.5, 114.1, 55.5, 55.4, 49.2, 47.5, 39.8, 29.8, 25.4 (q, *J* = 2.4 Hz), 20.3.

HRMS (ESI+, m/Z): calcd for $C_{22}H_{27}F_3NO_3$ $[M+H]^+$: 410.19375, found: 410.19382.

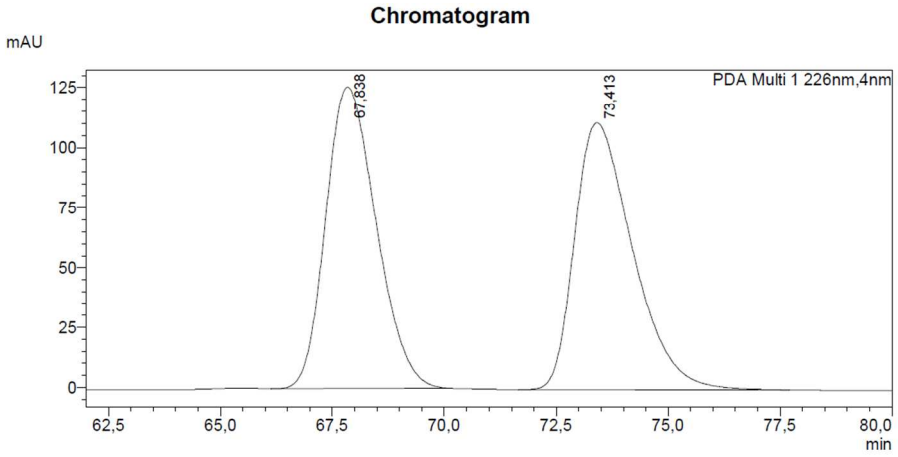
HPLC: Chiracel-ODH, *n*-heptane/*i*-PrOH 99:1, 0.5 mL/min, 40 °C, detection at 226 nm. Retention time (min): 67.4 (major) and 75.6 (minor).



Peak Table

PDA Ch1 226nm

Peak#	Ret. Time	Area	Height	Conc.
1	67,358	20388212	251811	99,346
2	75,649	134315	1415	0,654
Total		20522527	253226	

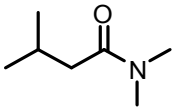


Peak Table

PDA Ch1 226nm

Peak#	Ret. Time	Area	Conc.	Height
1	67,838	9872325	49,555	125697
2	73,413	10049432	50,445	111187
Total		19921757		236884

***N*,*N*-Dimethyl-3-methyl-butanamide (3k)**[1]



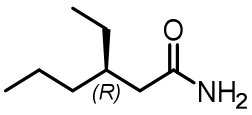
3k

The reaction was performed with 0.2 mmol **1b**, $CuBr{\cdot}SMe_2$ (2.06 mg, 0.01 mmol, 5 mol%), TMSOTf (72 µL, 0.4 mmol), MeMgBr (0.4 mmol, 3.0 M in Et_2O), 2.0 mL of DCM at −10 °C. Product **3k** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 1:1) [63% yield].

^{1}H NMR (CD_2Cl_2, 400 MHz): δ 2.93 (s, 3H, NCH_3), 2.84 (s, 3H, NCH_3), 2.12 (d, J = 7.0 Hz, 2H, CH_2CO), 2.00 (nonuplet, J = 6.7 Hz, 1H, CH_2CH), 0.87 (d, J = 6.6 Hz, 6H, (CH_3)$_2$CH).

9. Deprotection of protecting group at the Nitrogen

***(R)*-3-Ethyl-hexanamide (4)**



4

The product **4** was prepared by a literature procedure.[16] **2e** (0.2 mmol) was dissolved in trifluoroacetic acid (4.0 mL) and heated to reflux for 17 h at 90 °C. The product solution was concentrated under reduced pressure. After the addition of DCM (4 mL), the organic layer was washed with saturated aqueous $NaHCO_3$ (4 mL). The aqueous layer was extracted with DCM (10 mL × 3) and the combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (SiO_2, Et_2O) to afford product **4** as a white powder [92% yield, 98% ee].

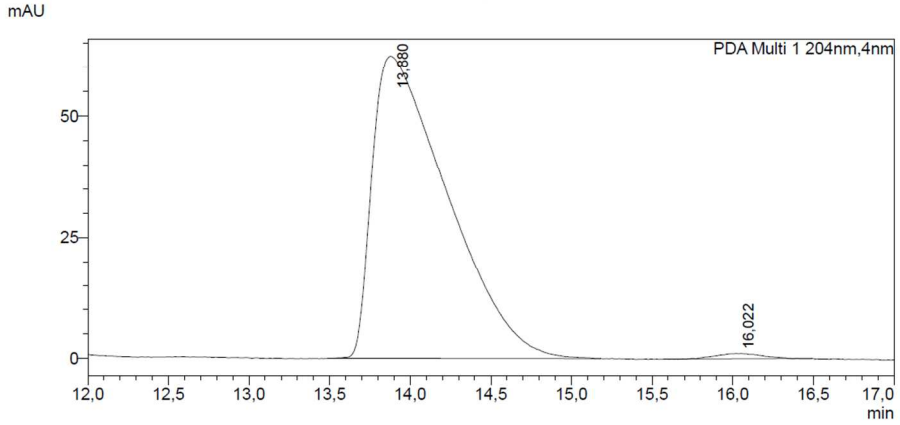
^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.37 (br s, 2H, N*H*$_2$), 2.14 (dd, *J* = 14.5, 7.5 Hz, 1H, C*H*HCO), 2.13 (dd, *J* = 14.5, 6.9 Hz, 1H, CH*H*CO), 1.85-1.80 (m, 1H, C*H*), 1.43-1.25 (m, 6H, C*H*$_2$), 0.90 (t, *J* = 6.6 Hz, 3H, C*H*$_3$), 0.88 (t, *J* = 7.4 Hz, 3H, C*H*$_3$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.0, 40.8, 36.5, 35.6, 26.2, 19.8, 14.5, 10.8.

HRMS (ESI+, m/Z): calcd for $C_8H_{18}NO$ $[M+H]^+$: 144.13829, found: 144.13828.

HPLC: Chiracel-ASH, *n*-heptane/*i*-PrOH 90:10, 0.5 mL/min, 40 °C, detection at 204 nm. Retention time (min): 13.9 (major) and 16.0 (minor).

Chromatogram

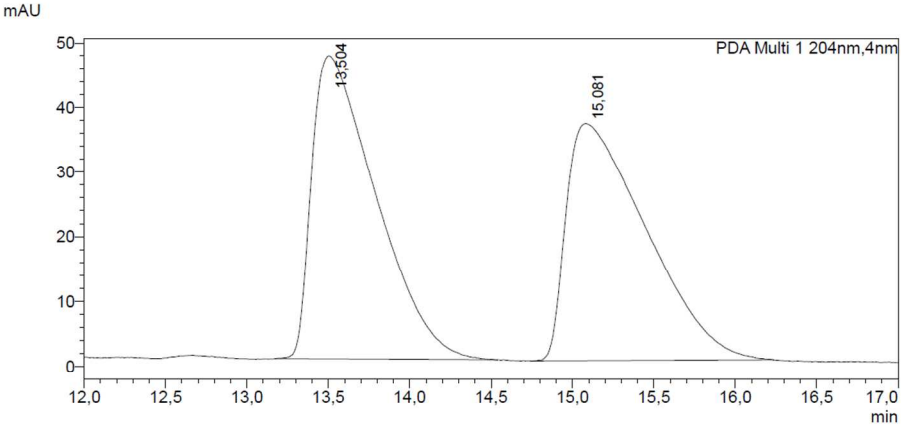


Peak Table

PDA Ch1 204nm

Peak#	Ret. Time	Area	Height	Conc.
1	13,880	2023839	62325	98,978
2	16,022	20904	1085	1,022
Total		2044744	63410	

Chromatogram



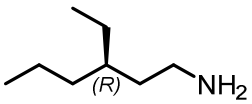
Peak Table

PDA Ch1 204nm

Peak#	Ret. Time	Area	Height	Conc.
1	13,504	1281122	46806	50,686
2	15,081	1246450	36537	49,314
Total		2527572	83343	

10. Transformation of amide into *β*- and *γ*-branched amines

_(R)_-3-Ethyl-hexan-1-amine (5)



5

A solution of **4** (50.1 mg, 0.35 mmol, 97% *ee*) in anhydrous THF (3.5 mL) cooled at 0 °C was added under nitrogen a solution of $LiAlH_4$ (1.0 M in Et_2O, 0.7 mL, 0.7 mmol). The resulting mixture was stirred at ambient temperature (1 h) and then heated to 60 °C for 18 h. The reaction was quenched with NaOH (2 M, 2.0 mL) and extracted with DCM (10 mL × 3). The organic layer was then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was redissolved in Et_2O (5 mL), filtered and concentrated under reduced pressure to afford product **5** as a light yellow oil [85% yield, 97% ee].

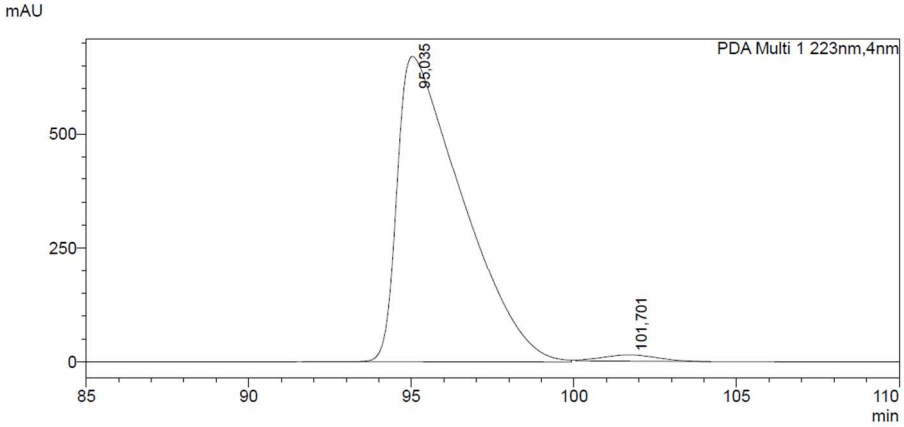
^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.68 (t, 2H, *J* = 7.4 Hz, C*H*$_2$NH$_2$), 1.43-1.13 (m, 11H, C*H*, C*H*$_2$, N*H*$_2$), 0.88 (t, *J* = 6.7 Hz, 3H, C*H*$_3$), 0.84 (t, *J* = 7.4 Hz, 3H, C*H*$_3$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 40.1, 37.8, 36.5, 35.7, 26.0, 19.8, 14.6, 10.8.

HRMS (ESI+, m/Z): calcd for $C_8H_{20}N$ $[M+H]^+$: 130.15903, found: 130.15904.

The *ee* of this compound was determined from the corresponding *N*-benzoyl derivate: HPLC: Chiracel-ODH, *n*-heptane/*i*-PrOH 98:2, 0.5 mL/min, 40 °C, detection at 223 nm. Retention time (min): 95.0 (major) and 101.7 (minor).

Chromatogram

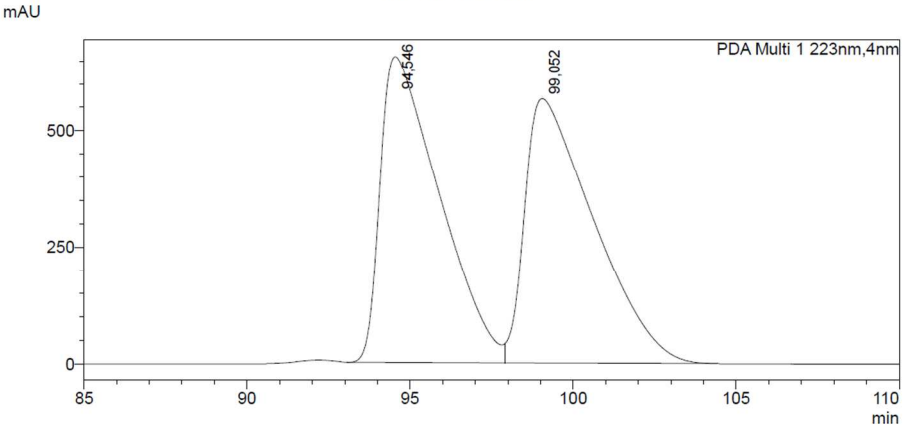


Peak Table

PDA Ch1 223nm

Peak#	Ret. Time	Area	Height	Conc.
1	95,035	93360356	671522	98,299
2	101,701	1615940	13675	1,701
Total		94976296	685197	

Chromatogram

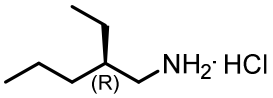


Peak Table

PDA Ch1 223nm

Peak#	Ret. Time	Area	Height	Conc.
1	94,546	82717020	655920	49,874
2	99,052	83133367	566070	50,126
Total		165850387	1221990	

***(R)*-2-Ethylpentan-1-amine hydrochloride (6)**



6

The compound was prepared following the literature procedure.[20] *m*-Chloroperbenzoic acid (72% purity, 290 mg, 1.2 mmol) was dried under vacuum for 15 min at room temperature prior to use. To a stirred solution of *m*-CPBA in DCM (1 mL) and water (99 μl) was added a 48% aqueous solution of tetrafluoroboric acid (155 μL, 1.2 mmol), a 0.89 M DCM solution of iodobenzene (55 μL, 0.05 mmol) and then **4** (143.1 mg, 1.0 mmol, 97% *ee*) at 25 °C under nitrogen and the mixture was stirred for 48 h. A 10% aqueous HCl solution (2 mL) was added and the reaction mixture was extracted with DCM four times. Combined organic phase was extracted with 10% aqueous HCl solution two times. Combined aqueous phase was concentrated under reduced pressure. Product **6** was obtained as a white solid in 91% yield and 97% *ee*.

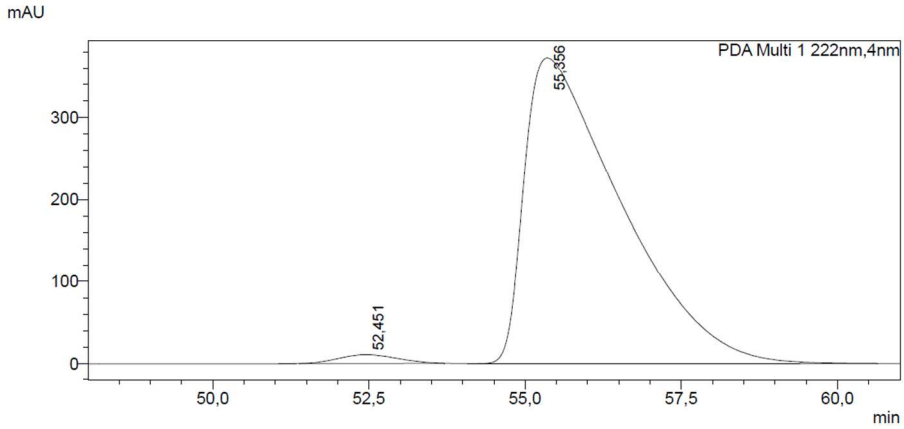
^{1}H NMR (D_2O, 400 MHz): δ 2.84 (d, J = 6.1 Hz, 2H, CH_2NH$_2$), 1.61-1.51 (m, 1H, CH), 1.32-1.15 (m, 6H, CH_2), 0.80-0.76 (m, 6H, CH_3).

^{13}C NMR (D_2O, 100 MHz): δ 45.0, 39.3, 34.5, 25.3, 21.3, 15.9, 12.1.

HRMS (ESI+, m/Z): calcd for $C_7H_{18}N$ $[M+H]^+$: 116.14338, found: 116.14317.

The *ee* of this compound was determined from the corresponding *N*-benzoyl derivate: HPLC: Chiracel-OBH, *n*-heptane/*i*-PrOH 99:1, 0.5 mL/min, 40 °C, detection at 222 nm. Retention time (min): 52.5 (minor) and 55.4 (major).

Chromatogram

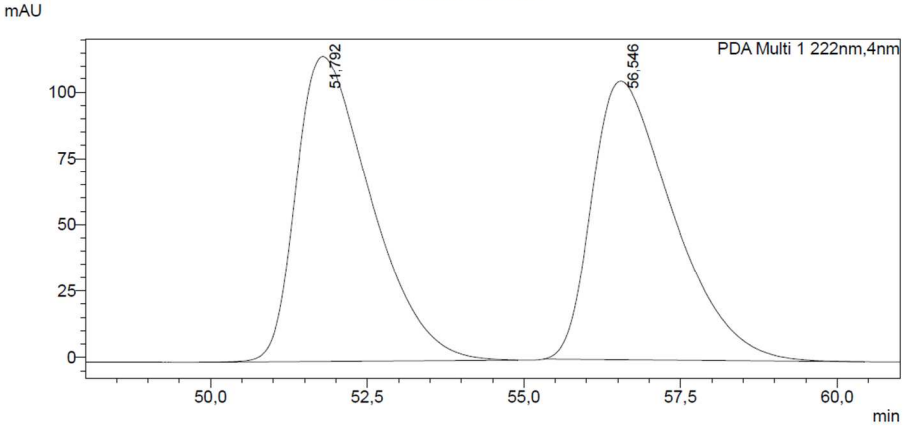


Peak Table

PDA Ch1 222nm

Peak#	Ret. Time	Area	Height	Conc.
1	52,451	692661	10613	1,696
2	55,356	40153969	372474	98,304
Total		40846630	383086	

Chromatogram



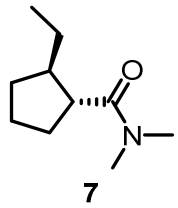
Peak Table

PDA Ch1 222nm

Peak#	Ret. Time	Area	Height	Conc.
1	51,792	9577222	115215	50,288
2	56,546	9467523	104978	49,712
Total		19044745	220193	

11. Catalytic ACA followed by intramolecular trapping

(1*R*,2*R*)-2-ethyl-*N*,*N*-dimethylcyclopentane-1-carboxamide (7)



7

In a flame-dried Schlenk tube equipped with septum and magnetic stirring bar, $CuBr \cdot SMe_2$ (2.06 mg, 0.01 mmol, 5 mol%), and ligand **L1** (7.68 mg, 0.012 mmol, 6 mol%) were dissolved in DCM (2 mL) and stirred under nitrogen atmosphere for 20 min. Amide **1v** (0.2 mmol) was added at once. After stirring for 5 min. at RT the reaction mixture was cooled to −78 °C and EtMgBr (0.4 mmol, 3.0 M in Et_2O) was added. Immediately after TMSOTf (72 μL, 0.4 mmol) was added. After stirring at −78 °C for 18 h, the reaction was warmed up to RT and stirred for 8 h. The resulting reaction mixture was quenched with saturated aqueous NH_4Cl solution and extracted with DCM (10 mL × 3). Combined organic phases were dried over $MgSO_4$, filtered and solvents were evaporated on rotary evaporator. Product **7** was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O 1:1) [66% yield, 92% *ee*]. Relative configuration was determined by NOE experiments (Figure S35).

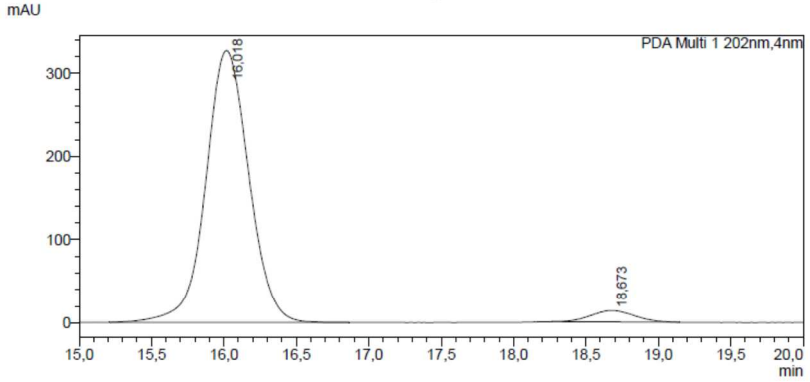
^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.05 (s, 3H, NC*H*$_3$), 2.96 (s, 3H, NC*H*$_3$) 2.53 (q (dt), *J* = 8.3 Hz, 1H, C*H*CO), 2.24 (ttd, *J* = 8.6, 8.6, 5.5 Hz, 1H, C*H*CHCO), 1.99-1.84 (m, 2H, C*H*$_2$), 1.78-1.61 (m, 3H, C*H*$_2$), 1.52-1.41 (m, 1H, C*H*$_2$), 1.29-1.13 (m, 2H, C*H*$_2$), 0.88 (t, *J* = 7.4 Hz, 3H, C*H*$_3$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.3, 47.6, 45.8, 37.4, 35.8, 31.9, 30.7, 28.0, 24.7, 12.9.

HRMS (ESI+, m/Z): calcd for $C_{10}H_{20}NO$ $[M+H]^+$:170.15449, found:170.15379.

HPLC: Chiracel-OZH, *n*-heptane/*i*-PrOH 95:5, 0.5 mL/min, 40 °C, detection at 202 nm. Retention time (min): 16.0 (major) and 18.7 (minor).

Chromatogram

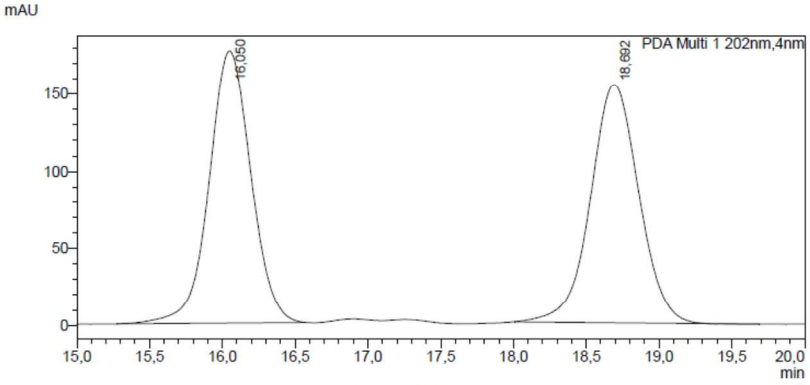


Peak Table

PDA Ch1 202nm

Peak#	Ret. Time	Area	Height	Conc.
1	16,018	6752737	326541	95,871
2	18,673	290809	13683	4,129
Total		7043547	340224	

Chromatogram



Peak Table

PDA Ch1 202nm

Peak#	Ret. Time	Area	Height	Conc.
1	16,050	3549085	176667	49,796
2	18,692	3578234	154526	50,204
Total		7127318	331193	

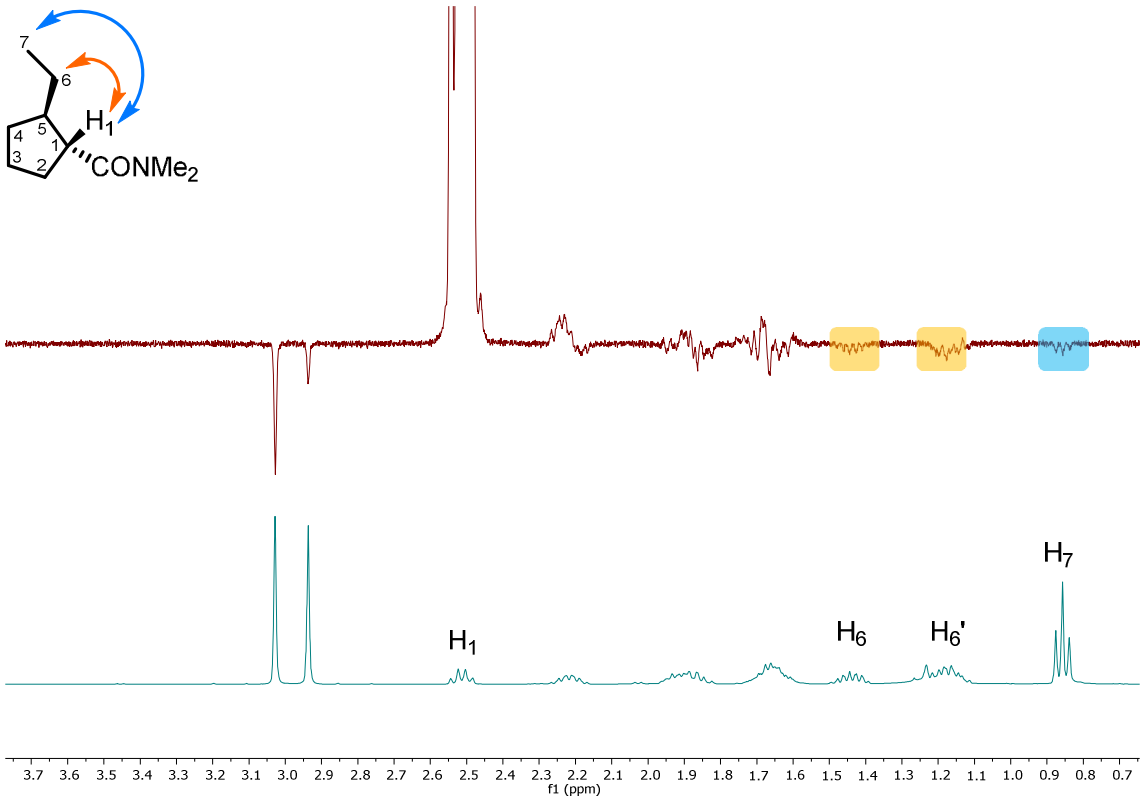


Figure S35. ^{1}H NMR and 1D NOE experiment of **7**. Selective irradiation on H_1 showed NOE with ethyl moiety (H_6 and H_7, highlighted) which are positioned on the same side of the ring.

12. References

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