Supplementary Information

Highly enantioselective organocatalytic formation of quaternary carbon center via chiral Brønsted acid catalyzed self-coupling of enamides

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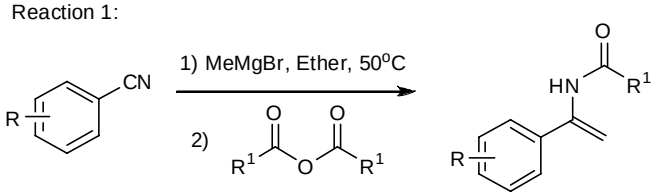
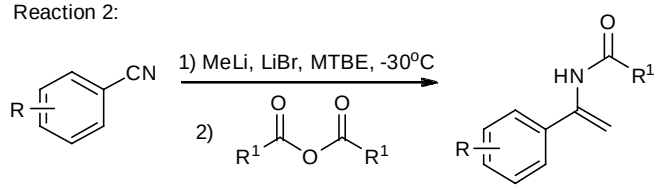
General: All solvents were purified by standard procedures and distilled prior to use.
Reagents obtained from commercial sources were used without further purification. TLC chromatography was performed on precoated aluminium silica gel SIL G/UV254 plates (Marcherey, Nagel & Co.) or silica gel 60-F254 precoated glass plates (Merck). ^{1}H NMR spectra were recorded with a Varian Unity 300. ESI mass spectra were recorded with a LCQ Finnigan spectrometer. High-resolution mass spectra were measured with a Bruker APEX IV 7T FT-ICR instrument. A Perkin-Elmer 241 polarimeter was used for optical rotation measurements.

Synthesis of enamides:

Reaction 1:



Reaction 2:



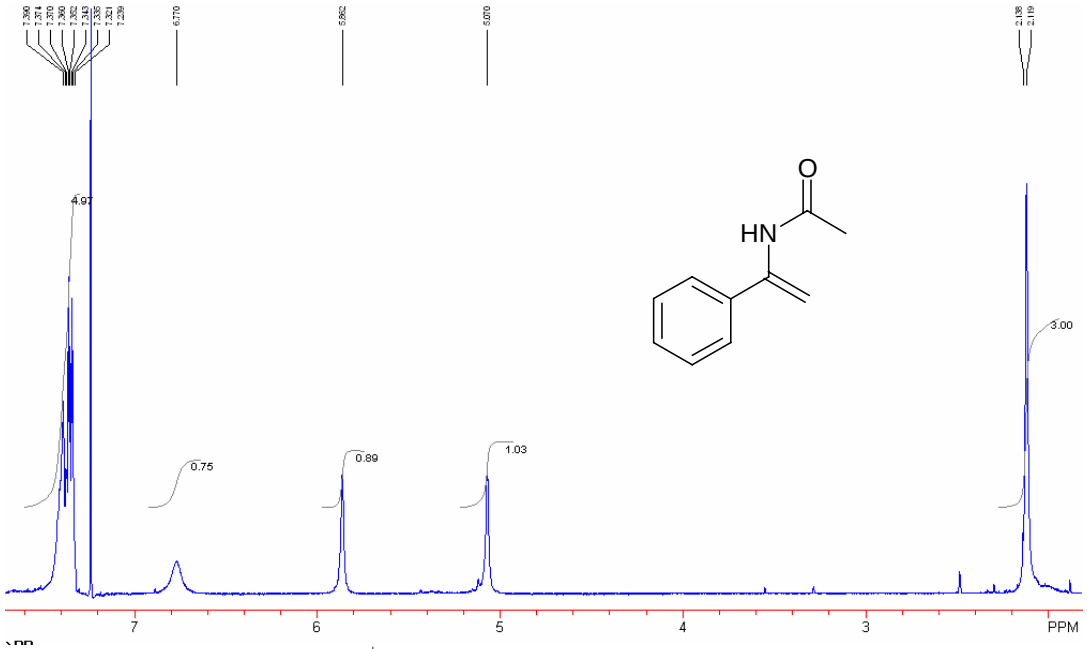
Enamides used for Table 2, entries **1**, **2**, **5**, **6** and **7** were synthesized via reaction 1, according to the literature known procedure.[1]
Enamides used for Table 2, entries **3** and **4** were synthesized via reaction 2, according to the literature known procedure.[2]

[1] M. J. Burk, Y. M. Wang, J. R. Lee, *J. Am. Chem. Soc.*, **1996**, *118*, 5142–5143.
[2] C. G. Savarin, G. N. Boice, J. A. Murry, E. Corley, L. DiMichele, D. Hughes, *Org. Lett.*, **2006**, *8*, 3903-3906.

General procedure for the self-coupling reaction of enamides

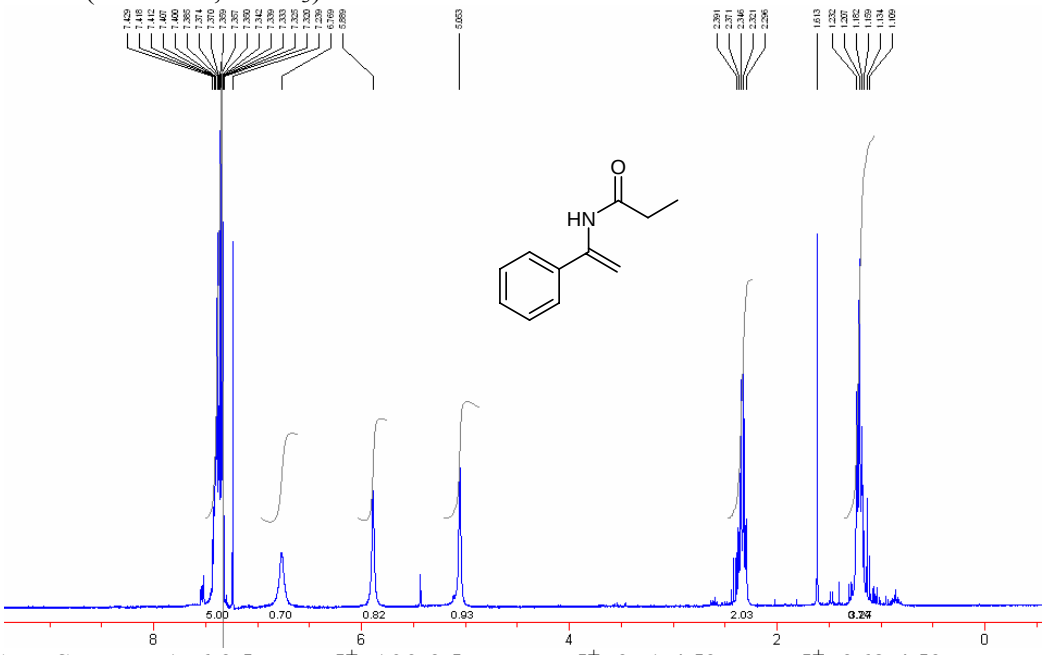
To a 10 mL argon flushed two-neck round bottom flask the enamide (0.158 mmol), the catalyst (0.1 eq) and 1.5 mL toluene was added. The mixture was allowed to stir for 3 days at room temperature. The reaction was quenched with a saturated $NaHCO_3$ solution and the aqueous phase was extracted 3 times with dichloromethane. The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure at 40°C. The product was purified by flash chromatography (*n*-Hexane/EA 1:1).

^{1}H-NMR (300 MHz, $CDCl_3$):



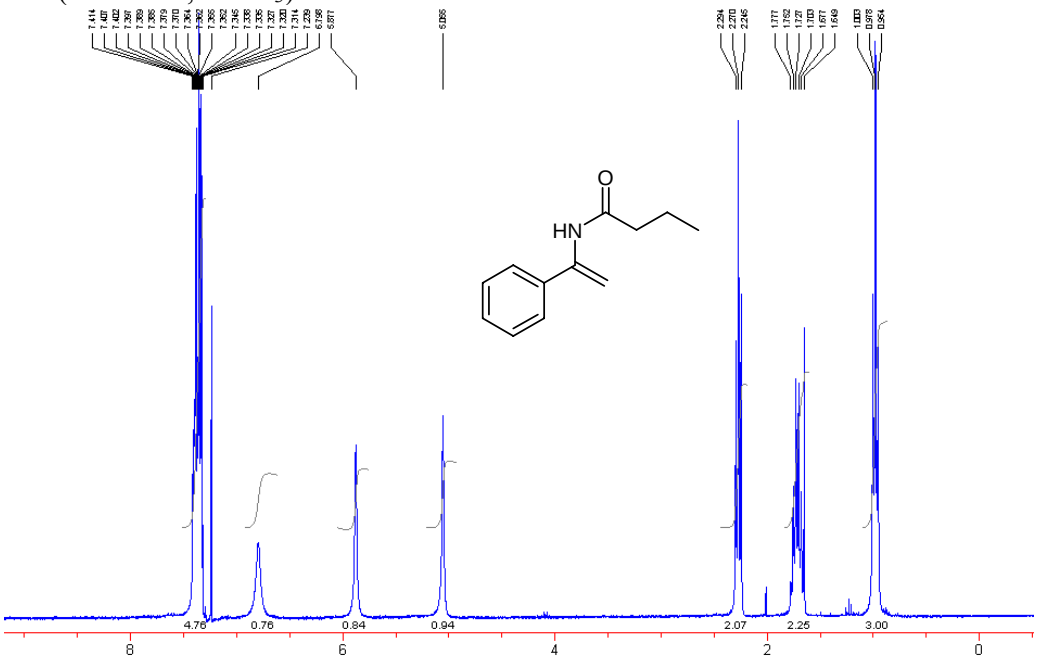
DCI-MS: *m/z* = 162.2 $[M + H]^+$.

^{1}H-NMR (300 MHz, $CDCl_3$):



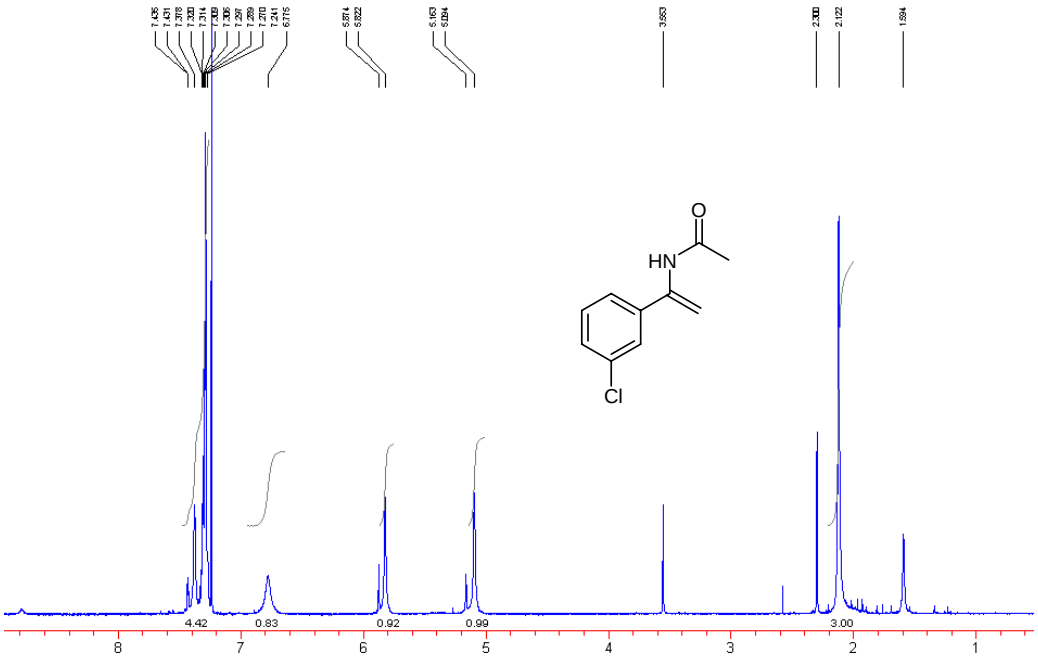
DCI-MS: *m/z* = 176.2 $[M + H]^+$, 193.2 $[M + NH_4]^+$, 351.4 $[2M + H]^+$, 368.4 $[2M + NH_4]^+$.

^{1}H-NMR (300 MHz, $CDCl_3$):



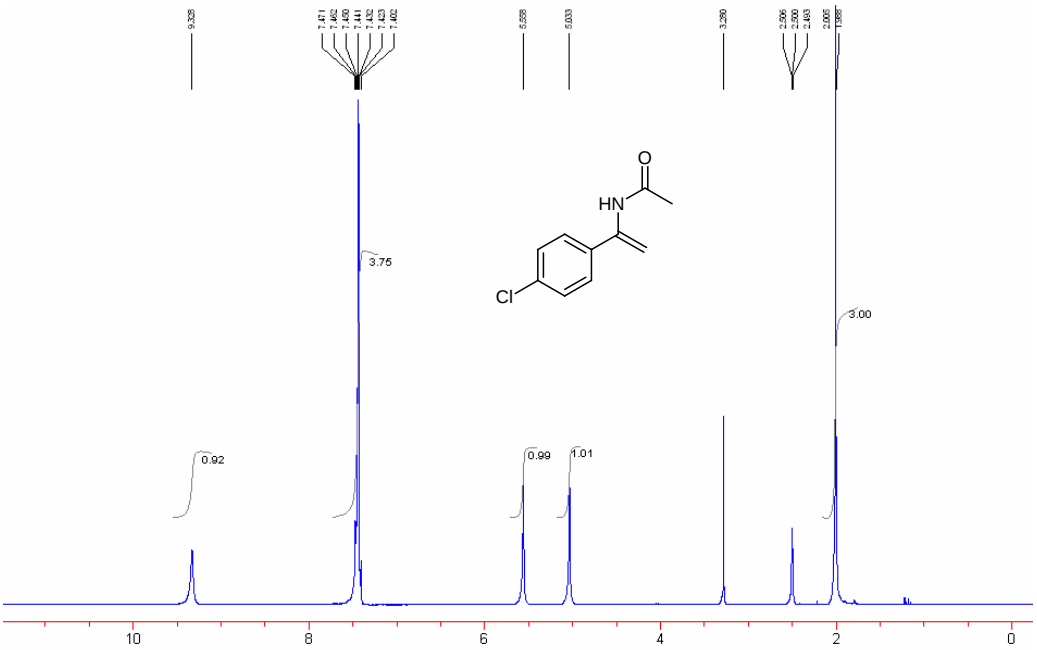
ESI-MS: *m/z* = 212 $[M + Na]^+$, 401 $[2M + Na]^+$.

^{1}H-NMR (300 MHz, $CDCl_3$):



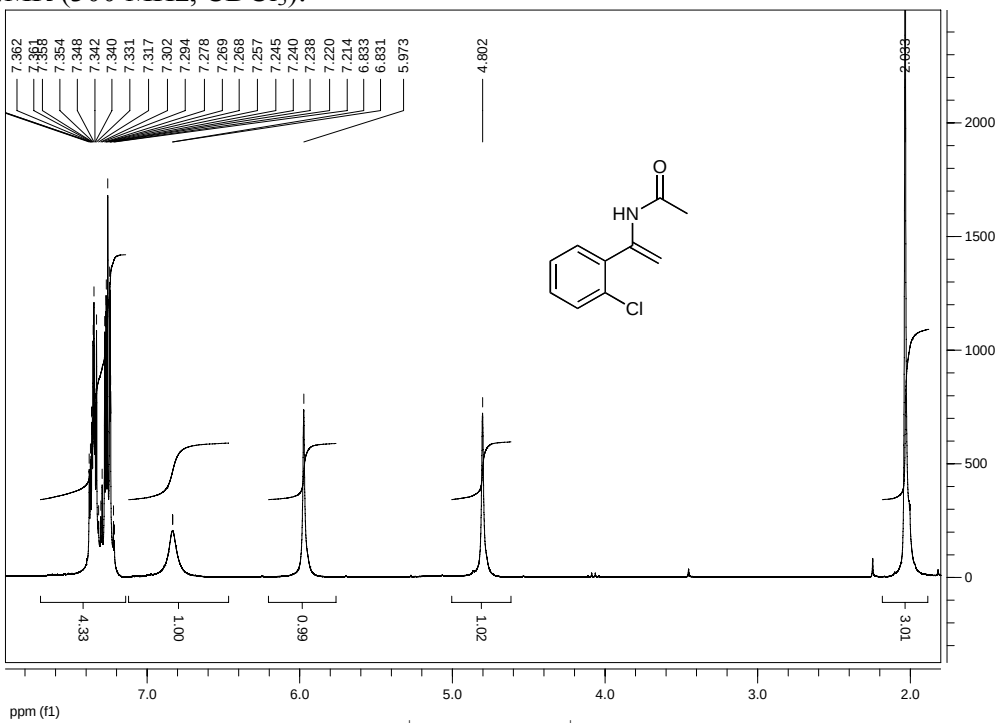
ESI-MS: *m/z* = 196.1 $[M + H]^+$, 213.2 $[M + NH_4]^+$.

^{1}H-NMR (300 MHz, $CDCl_3$):



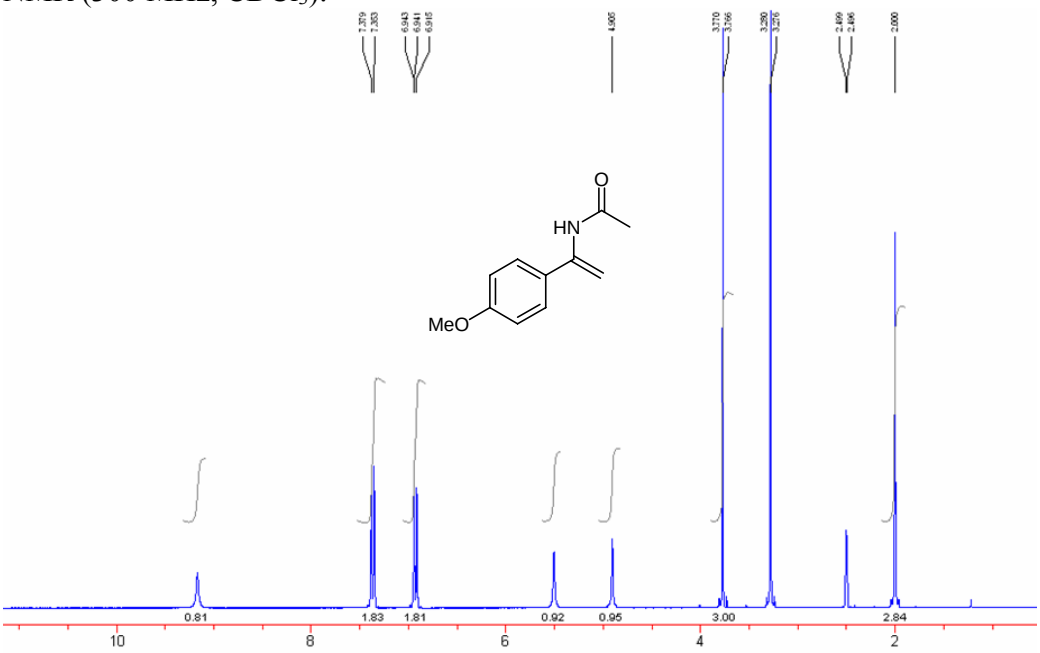
DCI-MS: *m/z* = 196.1 $[M + H]^+$, 213.2 $[M + NH_4]^+$, 391.3 $[2M + H]^+$, 408.3 $[2M + NH_4]^+$.

^{1}H-NMR (300 MHz, $CDCl_3$):



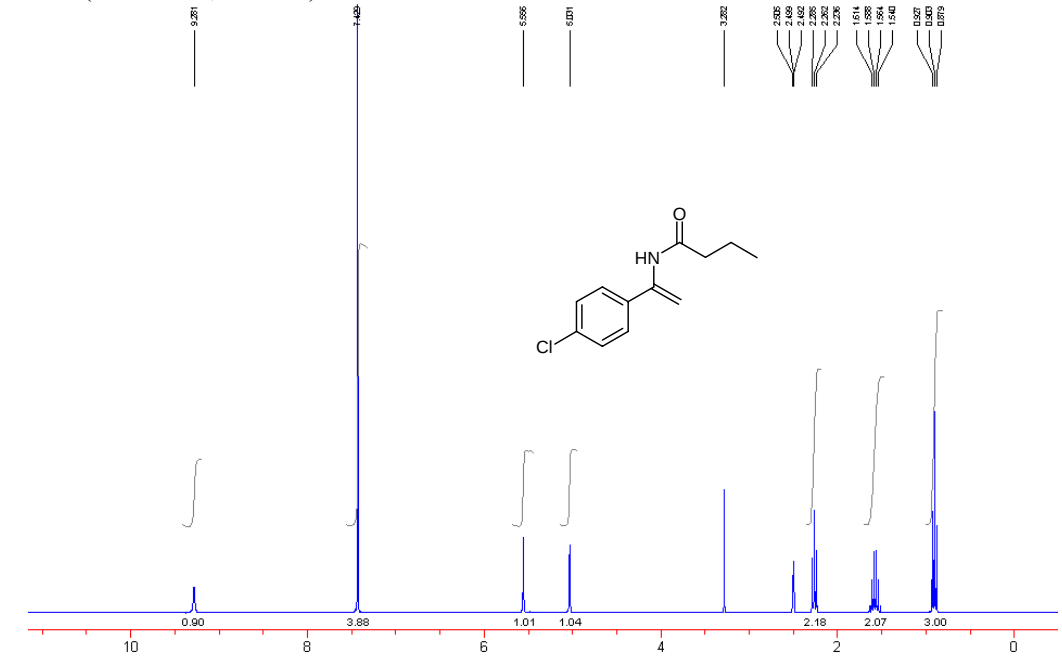
MALDI-TOF-MS : *m/z* = 196 $[M + H]^+$, 218 $[M+Na]^+$.

^{1}H-NMR (300 MHz, $CDCl_3$):



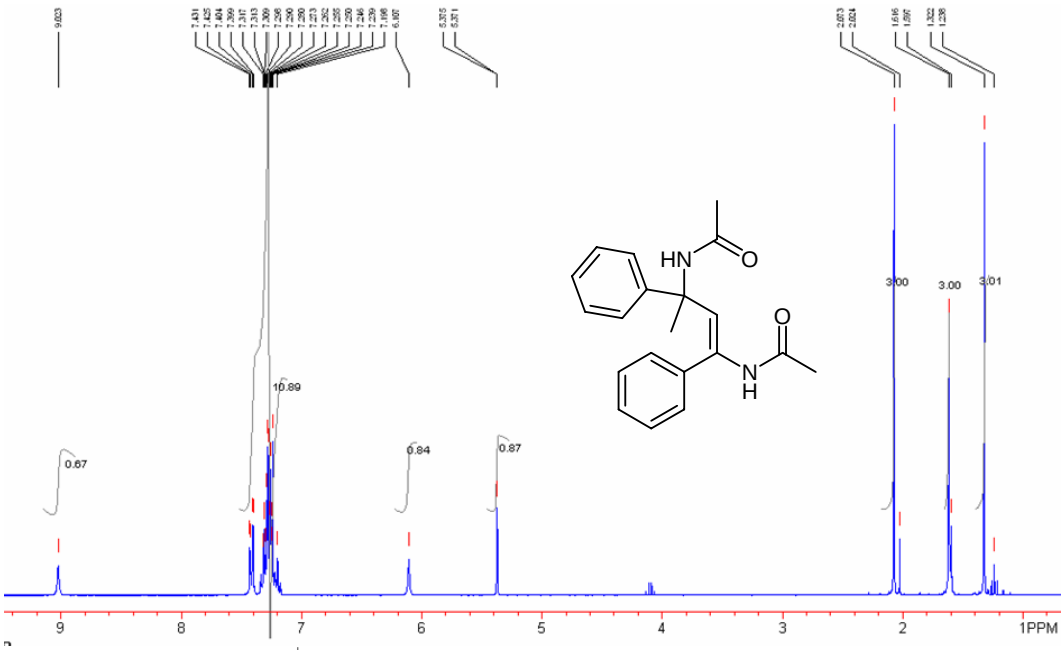
ESI-MS: *m/z* = 192 $[M + H]^+$.

^{1}H-NMR (300 MHz, $CDCl_3$):



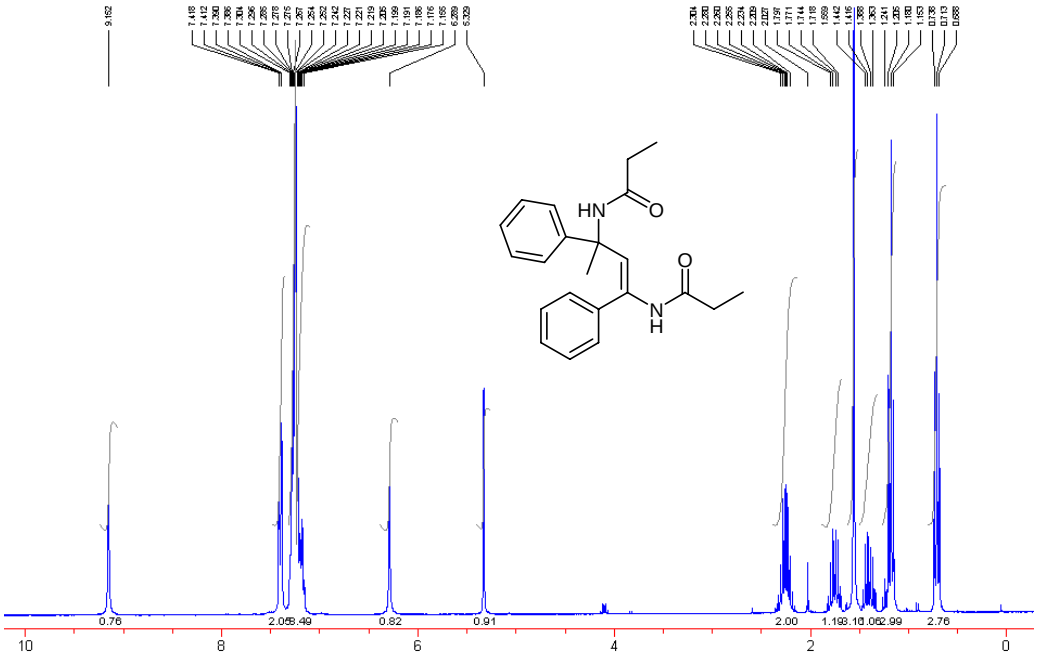
ESI-MS: *m/z* = 246 $[M + Na]^+$, 278 $[M + Na + CH_3OH]^+$.

^{1}H-NMR (300 MHz, $CDCl_3$):



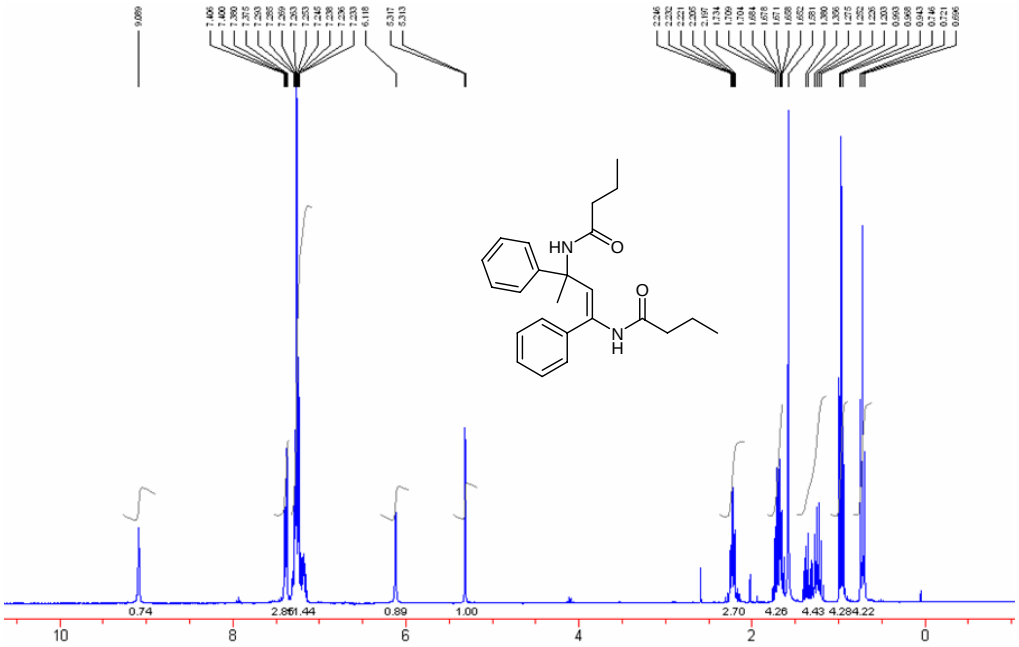
ESI-MS: *m/z* = 345 $[M + Na]^+$.

^{1}H-NMR (300 MHz, $CDCl_3$):



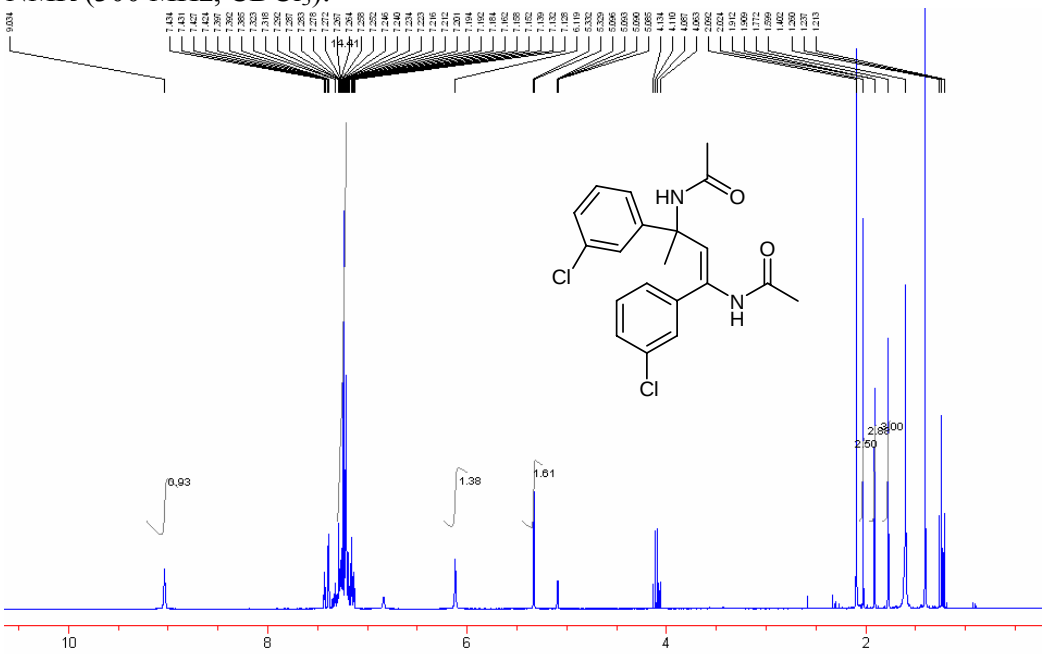
ESI-MS: *m/z* = 373 $[M + Na]^+$, 723 $[2M + Na]^+$.

^{1}H-NMR (300 MHz, $CDCl_3$):



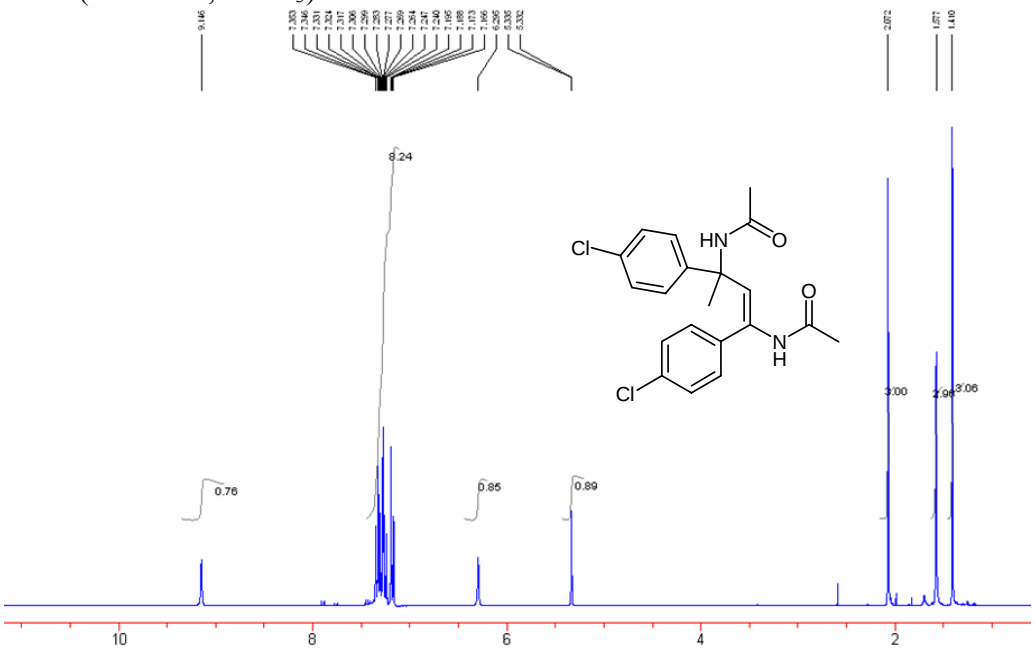
ESI-MS: *m/z* = 379 $[M + H]^+$, 401 $[M + Na]^+$, 757 $[2M + H]^+$, 779 $[2M + Na]^+$.

^{1}H-NMR (300 MHz, $CDCl_3$):



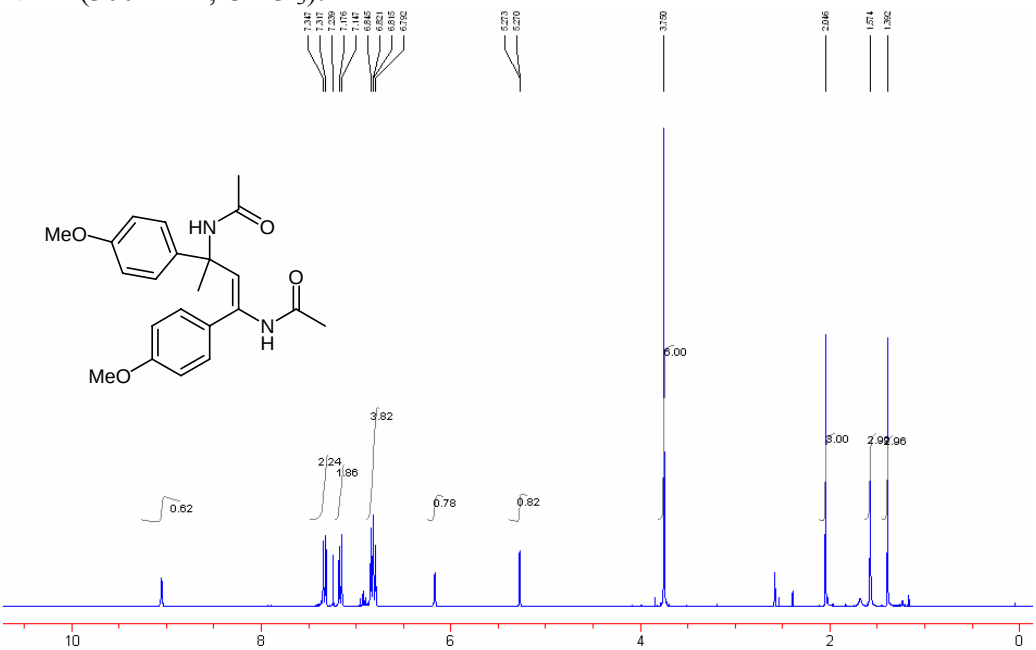
ESI-MS: *m/z* = 413 $[M + Na]^+$, 803 $[2M + Na]^+$.

^{1}H-NMR (300 MHz, $CDCl_3$):



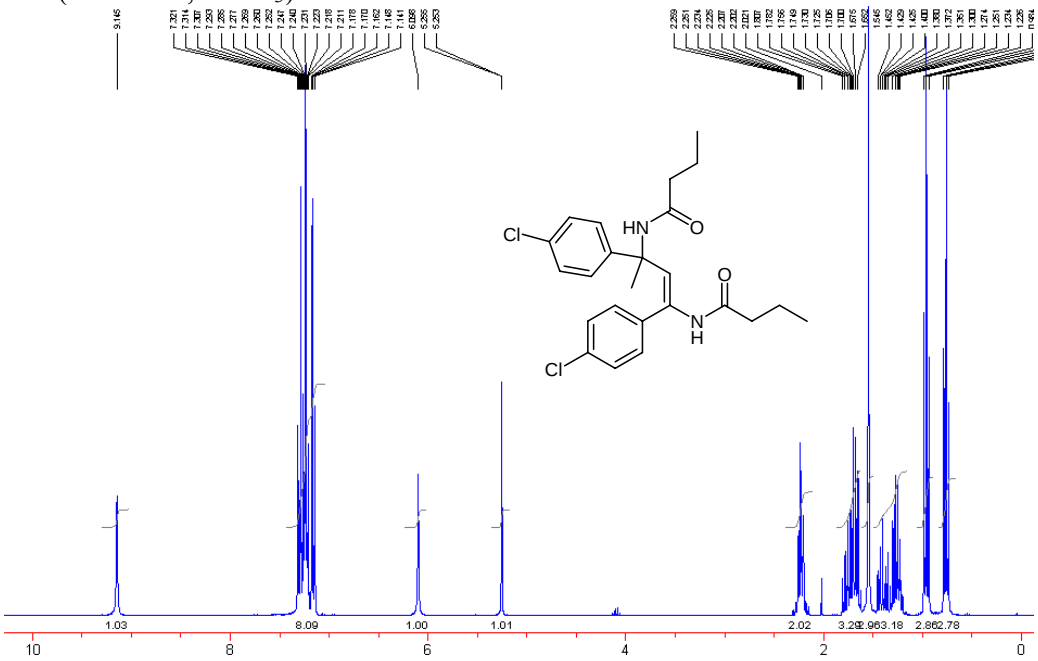
ESI-MS: *m/z* = 413 $[M + Na]^+$, 805 $[2M + Na]^+$.

^{1}H-NMR (300 MHz, $CDCl_3$):



ESI-MS: *m/z* = 405 $[M + Na]^+$, 787 $[2M + Na]^+$.

^{1}H-NMR (300 MHz, $CDCl_3$):



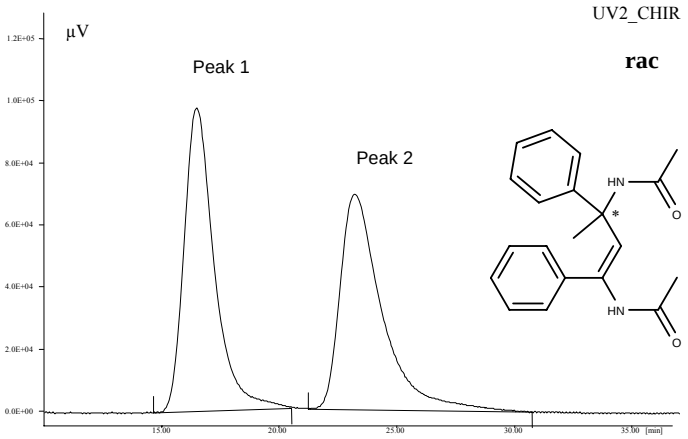
ESI-MS: *m/z* = 447 $[M + H]^+$, 469 $[M + Na]^+$.

HPLC Analysis

Table 2, entry 1: **racemic product**
HPLC Diacel Chiralcel OD
Control method: 90-10-1M *n*-hexane / 2-propanol = 90 : 10, flow rate 1 mL/min, λ = 254 nm

	Name	Rt	Area	%Area
1	Peak 1	16,40	8386645,500	50,278
2	Peak 2	23,04	8294050,500	49,722

Total Area of Peak = 16680696.00



Chiral product
HPLC Diacel Chiralcel OD
Control method: 90_10_1M *n*-hexane / 2-propanol = 90 : 10, flow rate 1 mL/min, λ = 254 nm

	Name	Rt	Area	%Area
1	Peak 1	15,98	42095075,25	98,75
2	Peak 2	23,33	532945,50	1,25

Total Area of Peak = 42628020.75

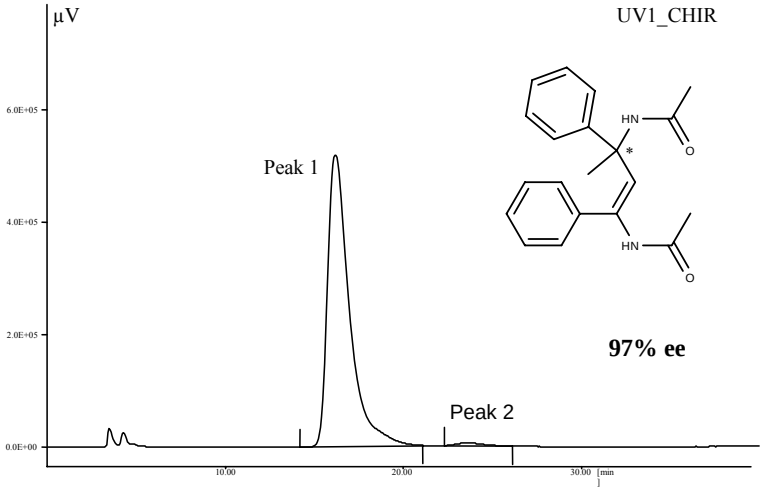
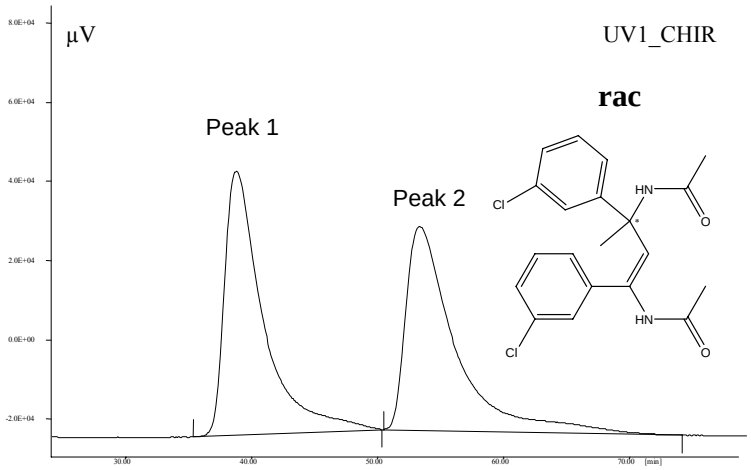


Table 2, entry 3: **racemic product**
HPLC Diacel Chiralcel OD
Control method: 95_5_1M *n*-hexane / 2-propanol = 95 : 5, flow rate 1 mL/min, λ = 210 nm

	Name	Rt	Area	%Area
1	Peak 1	38,61	13892937,76	50,28
2	Peak 2	52,99	13740184,49	49,72

Total Area of Peak = 27633122.25



Chiral product
HPLC Diacel Chiralcel OD
Control method: 95_5_1M *n*-hexane / 2-propanol = 95 : 5, flow rate 1 mL/min, λ = 210 nm

	Name	Rt	Area	%Area
1	Peak 1	38,21	9851722,75	94,16
2	Peak 2	54,64	610579,25	5,84

Total Area of Peak = 10462302.00

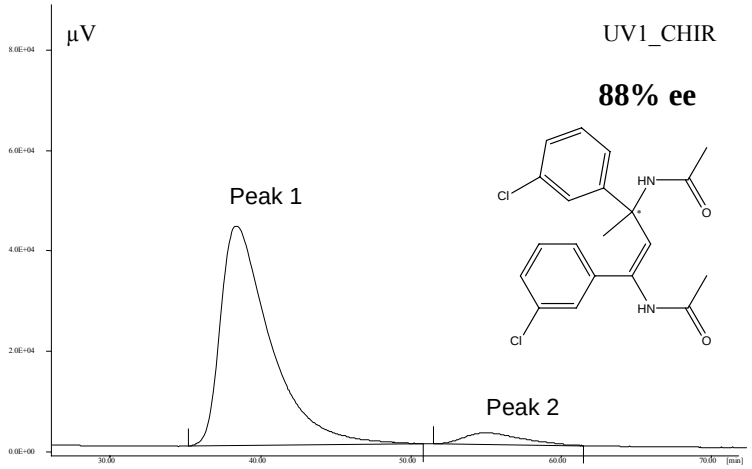
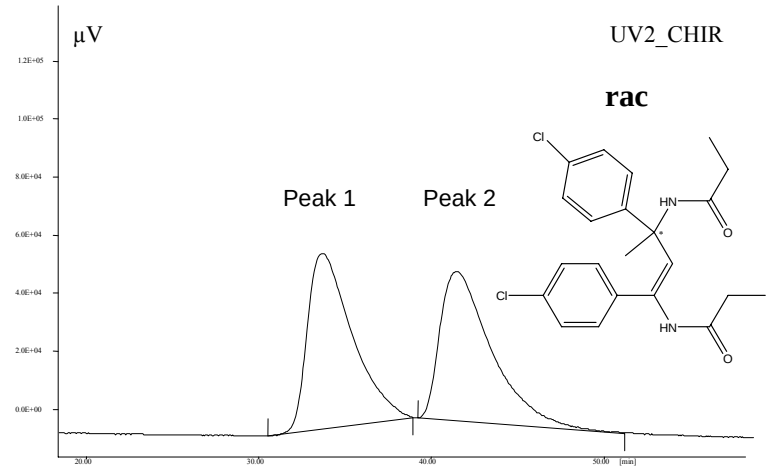


Table 2, entry 4: **racemic product**
HPLC Diacel Chiralcel OD
Control method: 95_5_1M *n*-hexane / 2-propanol = 95 : 5, flow rate 1 mL/min, λ = 254 nm

	Name	Rt	Area	%Area
1	Peak 1	33,48	10626177,50	50,51
2	Peak 2	41,19	10409748,50	49,49

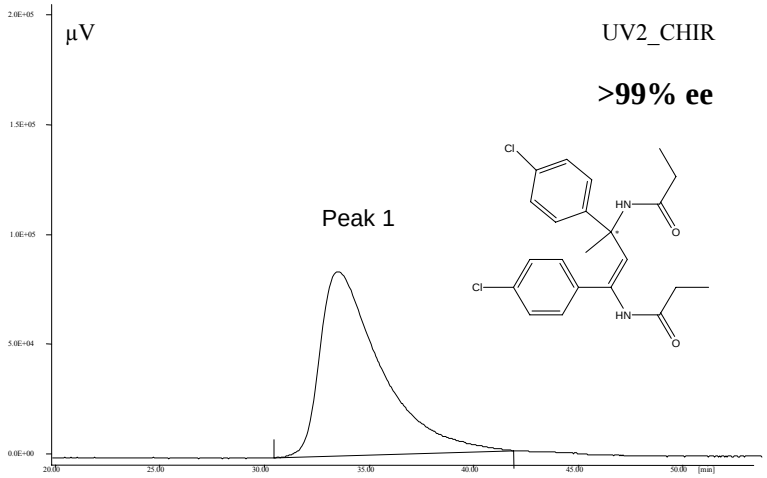
Total Area of Peak = 21035926.00



Chiral product
HPLC Diacel Chiralcel OD
Control method: 95_5_1M *n*-hexane / 2-propanol = 95 : 5, flow rate 1 mL/min, λ = 254 nm

	Name	Rt	Area	%Area
1	Peak 1	33,34	16489886,00	>99%

Total Area of Peak = 16489886.00

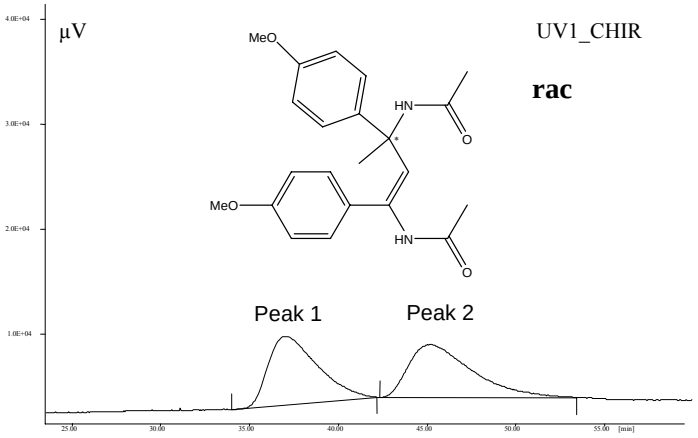


$[\alpha]_D^{25} = -365$; $c = 0.1$, CH_2Cl_2

Table 2, entry 5: **racemic product**
HPLC Diacel Chiralcel OD
Control method: 90_10_1M *n*-hexane / 2-propanol = 90 : 10, flow rate 1 mL/min, λ = 210 nm

	Name	Rt	Area	%Area
1	Peak 1	36,82	1241478,75	50,36
2	Peak 2	44,98	1223537,00	49,64

Total Area of Peak = 2465015.75



Chiral product
HPLC Diacel Chiralcel OD
Control method: 90_10_1M *n*-hexane / 2-propanol = 90 : 10, flow rate 1 mL/min, λ = 210 nm

	Name	Rt	Area	%Area
1	Peak 1	36,40	1151145,00	6,02
2	Peak 2	42,19	17980090,75	93,98

Total Area of Peak = 19131235.75

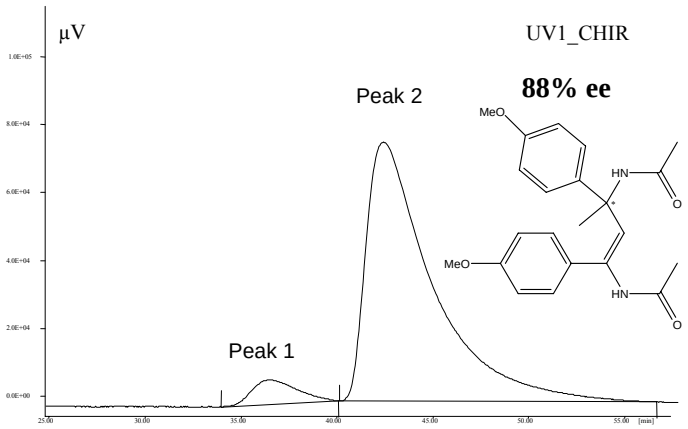
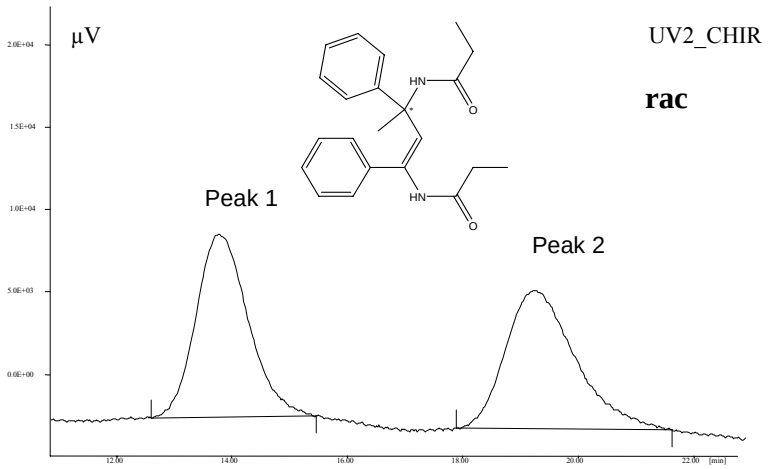


Table 2, entry 6: **racemic product**
HPLC Diacel Chiralcel OD
Control method: 90_10_1M *n*-hexane / 2-propanol = 90 : 10, flow rate 1 mL/min, λ = 254 nm

	Name	Rt	Area	%Area
1	Peak 1	13,73	678320,25	49,62
2	Peak 2	19,11	688610,50	50,38

Total Area of Peak = 1366930.75



Chiral product
HPLC Diacel Chiralcel OD
Control method: 90_10_1M *n*-hexane / 2-propanol = 90 : 10, flow rate 1 mL/min, λ = 254 nm

	Name	Rt	Area	%Area
1	Peak 1	13,33	14076569,50	92,52
2	Peak 2	19,03	1137986,50	7,48

Total Area of Peak = 15214556.00

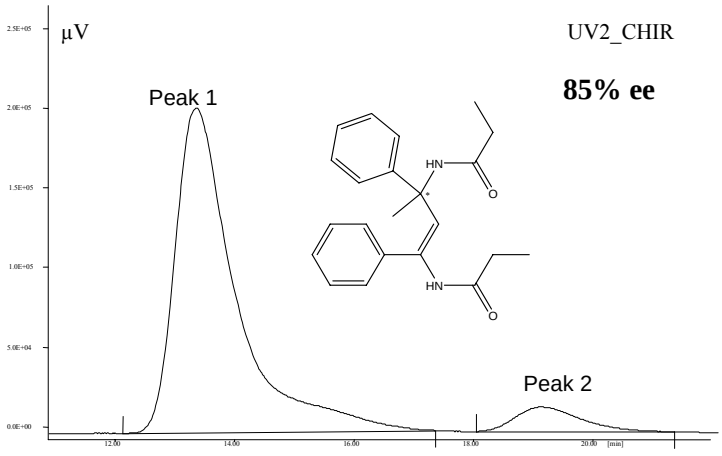
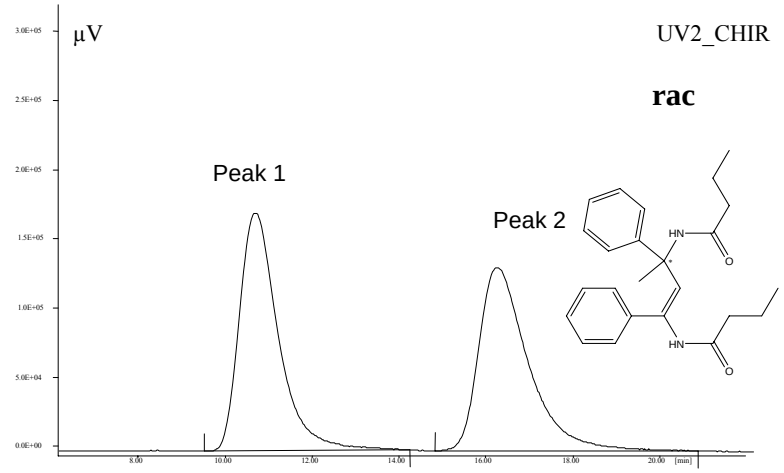


Table 2, entry 7: **racemic product**
HPLC Diacel Chiralcel OD
Control method: 90_10_1M *n*-hexane / 2-propanol = 90 : 10, flow rate 1 mL/min, λ=254 nm

	Name	Rt	Area	%Area
1	Peak 1	10,63	10369171,50	50,51
2	Peak 2	16,13	10160049,00	49,49

Total Area of Peak = 20529220.50



Chiral product
HPLC Diacel Chiralcel OD
Control method: 90-10-1M *n*-hexane / 2-propanol = 90 : 10, flow rate 1 mL/min, λ=254 nm

	Name	Rt	Area	%Area
1	Peak 1	10,61	16612964,50	98,43
2	Peak 2	16,26	265117,00	1,57

Total Area of Peak = 16878081.50

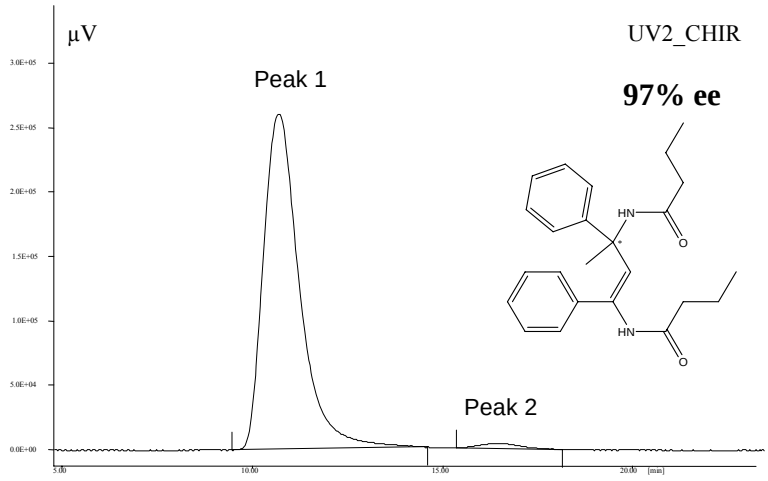
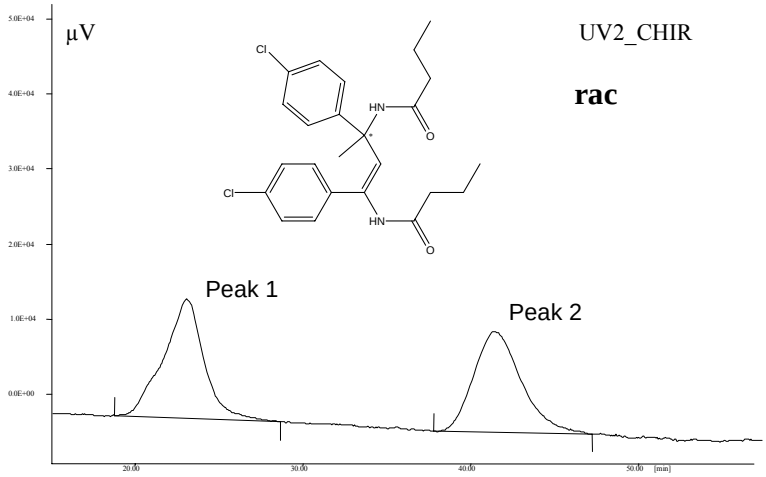


Table 2, entry 8: racemic product
HPLC Diacel Chiralpak IA
Control method: 97_3_1M *n*-hexane / 2-propanol = 97 : 3, flow rate 1 mL/min, λ = 254 nm

	Name	Rt	Area	%Area
1	Peak 1	22,91	2582215,250	49,893
2	Peak 2	41,11	2593342,499	50,107

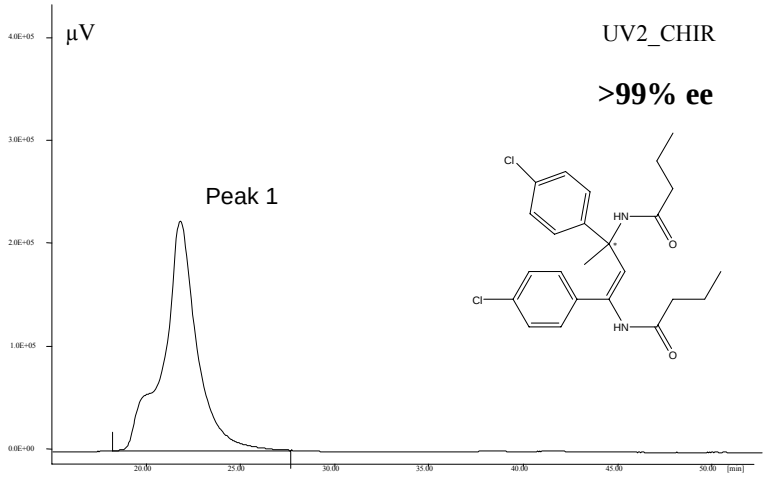
Total Area of Peak = 5175557.75



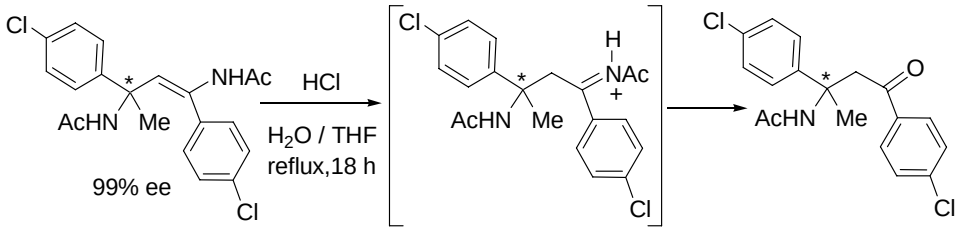
Chiral product
HPLC Diacel Chiralpak IA
Control method: 97_3_1M *n*-hexane / 2-propanol = 97 : 3, flow rate 1 mL/min, λ = 254 nm

	Name	Rt	Area	%Area
1	Peak 1	21,73	26482661,50	>99%

Total Area of Peak = 26482661.50

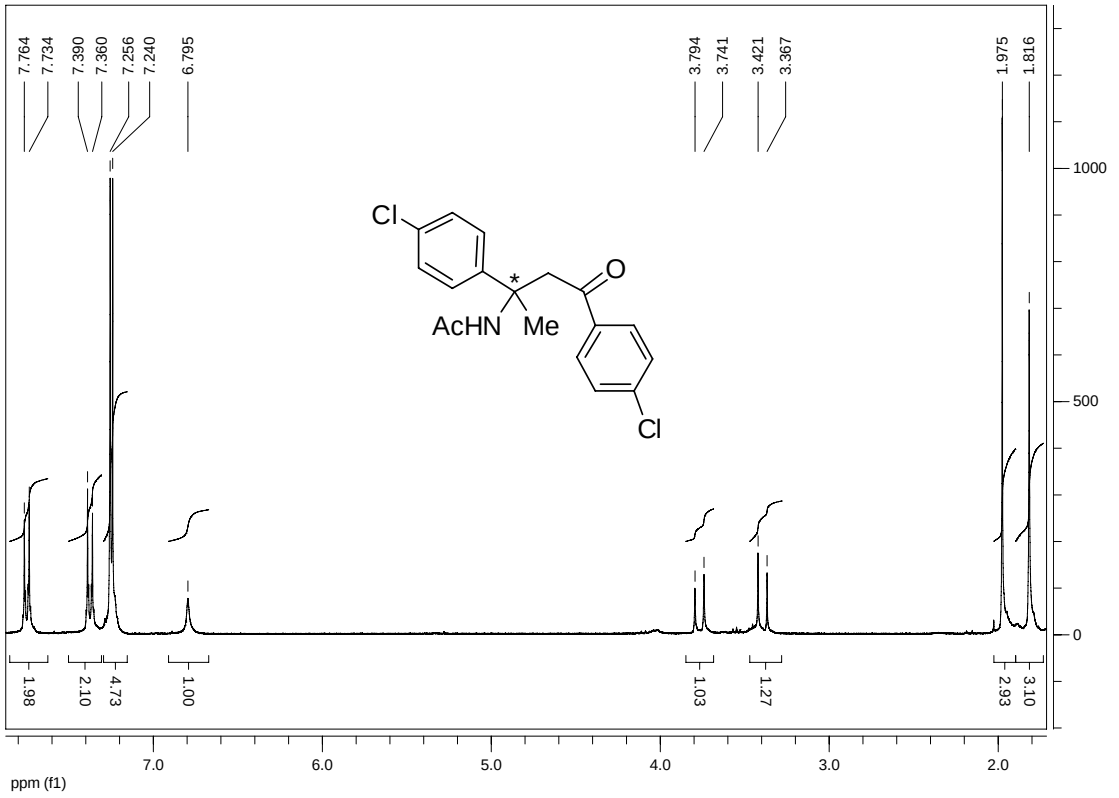


Conversion to β-aminoketone with the quaternary carbon center bonded to nitrogen:

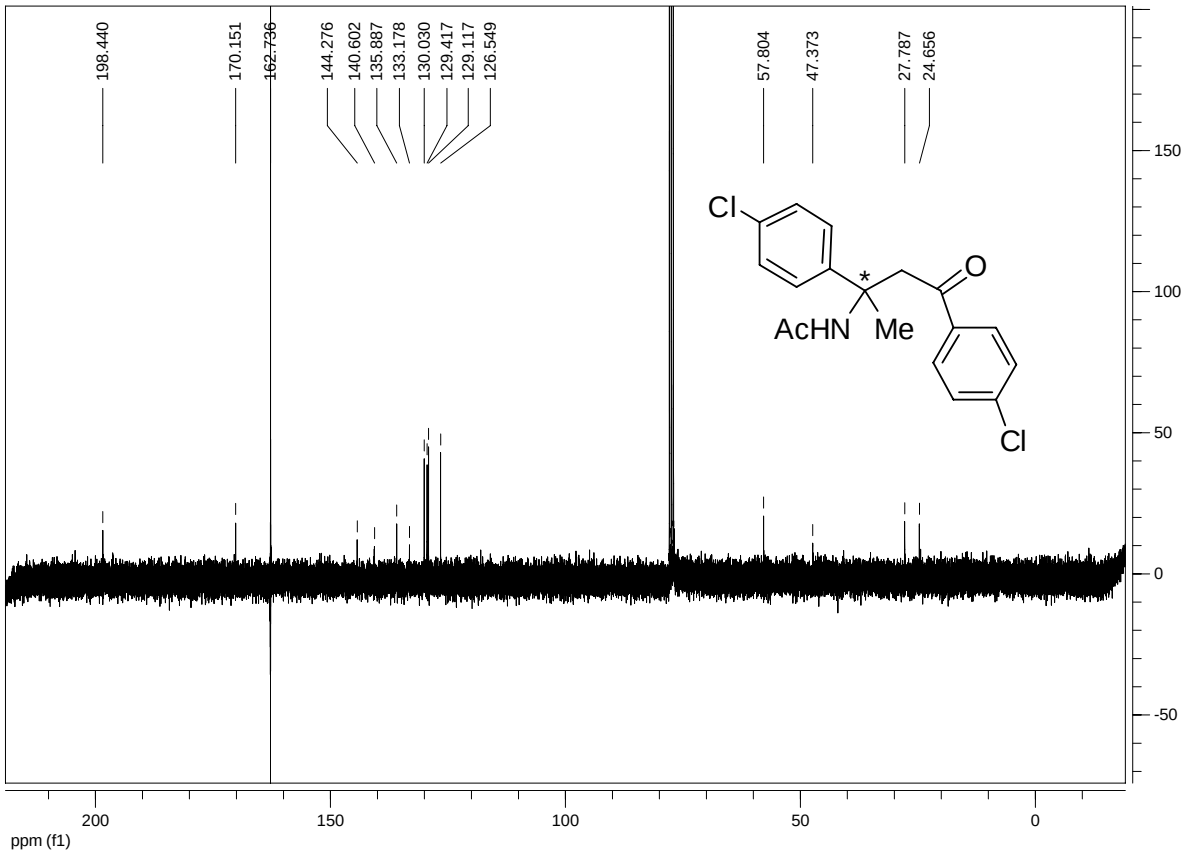


Experimental procedure:

The product of the self-coupling reaction (30 mg, 0.07672 mmol) was dissolved in 1.5 mL THF. 2 mL of 2N HCl was added and the reaction mixture was refluxed for 18 h, followed by neutralization with a saturated $NaHCO_3$ solution and extraction with dichloromethane (3 times). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure at 40°C. The product was purified by flash chromatography (Petrolether/EA 1:1). Yield: 95%, $[\alpha]_D^{25} = -22$; $c = 0.1$, CH_2Cl_2.



^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.82 (s, 3H, CH_3), 1.97 (s, 3H, CH_3), 3.39 (d, 1H, J = 16 Hz), 3.76 (d, 1H, J = 16 Hz) (diastereotopic CH_2 protons), 6.79 (br.s, 1H, NH), 7.23-7.26 (m, 4H, H_{arom}), 7.35-7.39 (m, 2H, H_{arom}), 7.73-7.76 (m, 2H) ppm.



^{13}C NMR (150.8 MHz, $CDCl_3$) δ = 24.65 (CH_3), 27.78 (CH_3), 47.37 (CH_2), 57.81 (CN), 126.55, 129.12, 129.42, 130.03, 133.10, 135.88, 140.65, 144.27, 170.15 (C=O, amide), 198.44 (C=O) ppm.

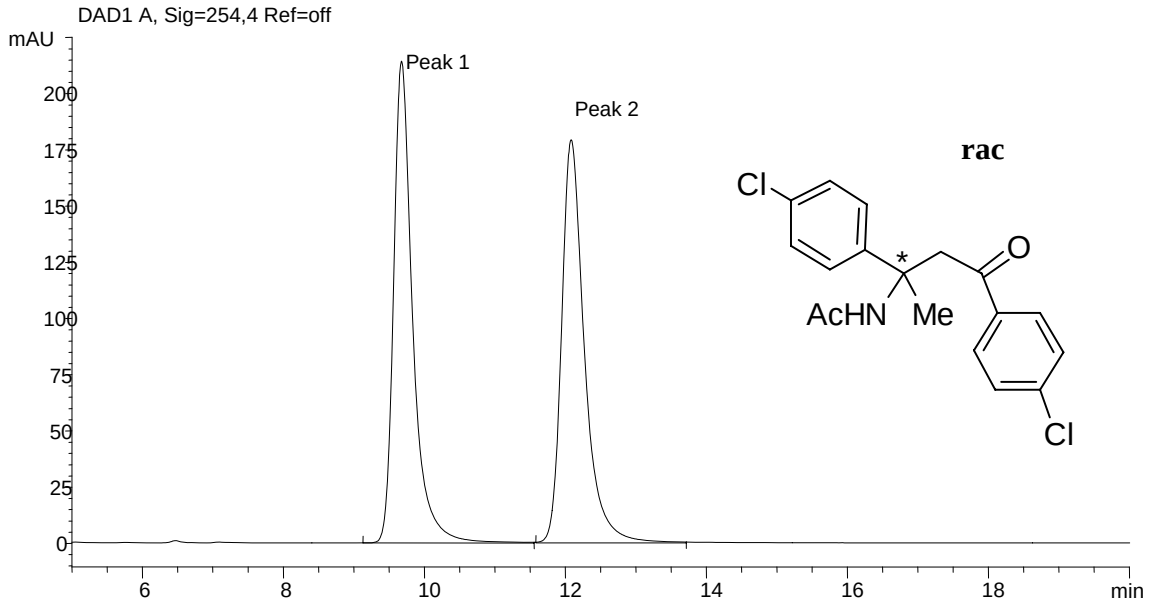
MALDI-TOF-MS : *m/z* = 350 $[M]^+$, 373 $[M+Na]^+$, 389 $[M+K]^+$.

HPLC Diacel Chiralpak IA
Control method: 85-15-1M

n-hexane / 2-propanol = 85 : 15, flow rate 1 mL/min, λ = 254 nm

	Name	**Rt**	**Area**	**%Area**
1	Peak 1	9,675	4039,9	50.082
2	Peak 2	12,081	4026,6	49,918

Total Area of Peak = 8066,5



HPLC Diacel Chiralpak IA
Control method: 85-15-1M

n-hexane / 2-propanol = 85 : 15, flow rate 1 mL/min, λ = 254 nm

	Name	**Rt**	**Area**	**%Area**
1	Peak 1	9,629	3246,3	98,886
2	Peak 2	12,056	36,6	1,114

Total Area of Peak = 3282,9