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Supporting Information

Construction of enantioenriched polysubstituted hexahydropyridazines via a sequential multicatalytic process merging palladium catalysis and aminocatalysis

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General Remarks

^{1}H NMR (200 or 300 MHz) and ^{13}C (50 or 75 MHz) spectra were recorded with Brüker Avance 200, or 300 MHz spectrometers using tetramethylsilane as an internal standard. Chemical shifts (δ) are given in parts per million and coupling constants are given as absolute values expressed in Hertz.

Infrared spectra were recorded with a Nicolet iS10 Infrared FT ATR spectrometer. Optical rotation values were measured at room temperature with a Perkin-Elmer 241 polarimeter.

Electrospray ionization (ESI) mass spectra were collected using a Q-TOF instrument supplied by WATERS. Samples (solubilized in ACN at 1mg/mL and then diluted by 1000) were introduced into the MS *via* an UPLC system whilst a Leucine Enkephalin solution was co-injected *via* a micro pump.

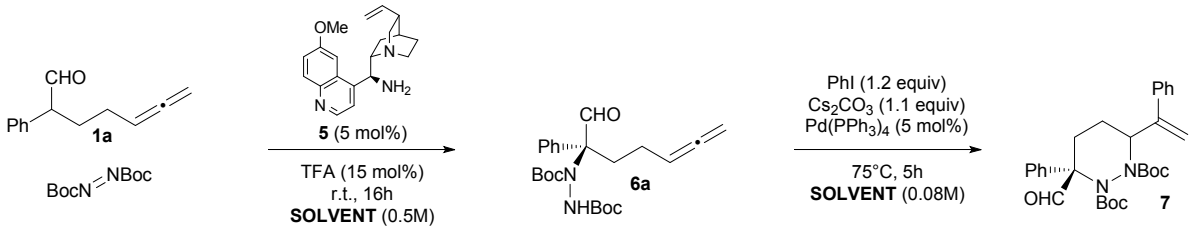
Thin-layer chromatography (TLC) was carried out on aluminium sheets precoated with silica gel 60 F_{254} (Merck). Column chromatography separations were performed using Merck Kieselgel 60 (0.040-0.060 mm).

HPLC analyses were performed with a JASCO machine equipped with a UV/Vis detector at 30°C employing chiral AD column. HPLC grade heptane and isopropyl alcohol were used as the eluting solvents. HPLC traces were compared to racemic samples prepared by using benzylamine as the catalyst.

Tetrahydrofuran and dichloromethane were dried prior to use by distillation from standard drying agents.

Screening results

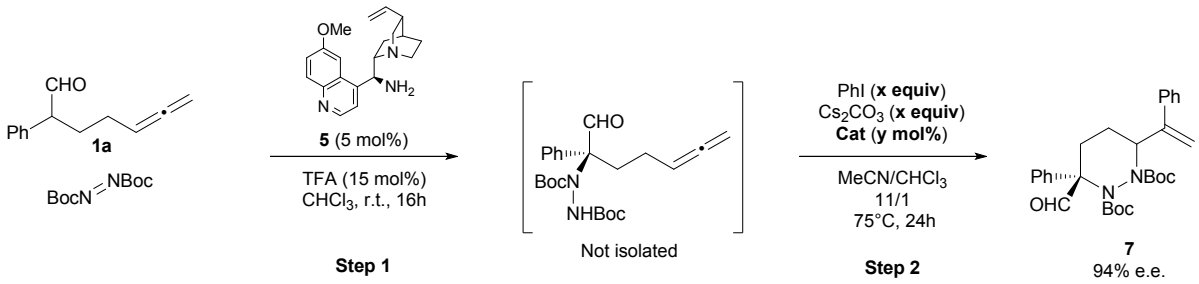
Two-step procedure



SOLVENT	YIELD
$CHCl_3$	82%
CH_2Cl_2	53%
CH_3CN	< 10%

SOLVENT	YIELD
$CHCl_3$	< 30%
CH_2Cl_2	< 10%
CH_3CN	66%
$CHCl_3/CH_3CN$ 6/1	30%
$CHCl_3/CH_3CN$ 11/1	52%

Sequential multicatalysis



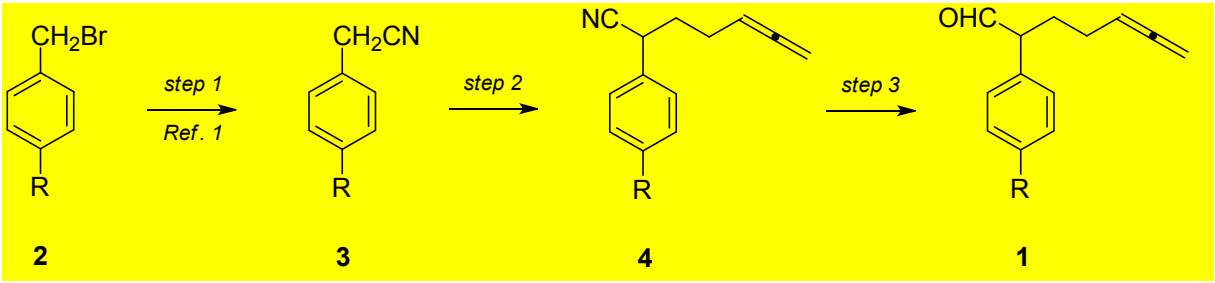
Cat (Palladium catalyst)	$Pd(PPh_3)_4$ **Cat I**	$Pd(OAC)_2$ *(R)*-BINAP **Cat II**	$Pd(OAC)_2$ *(S)*-BINAP **Cat III**

Entry	$[C]_{Step\ 1}$	$[C]_{Step\ 2}$	cat.	x	y	yield	d.r.
1	1 M	0,08 M	**Cat I**	1.2	5	57%	3/1
2	1 M	0,08 M	**Cat I**	1.4	5	67%	3/1
3	0,8 M	0,07 M	**Cat I**	1.4	5	55%	2.8/1
4	0,8 M	0,07 M	**Cat I**	1.4	10	69%	2.3/1
5	1 M	0,08 M	**Cat II**	1.4	5	66%	2.5/1
6	1 M	0,08 M	**Cat III**	1.4	5	70%	2.5/1

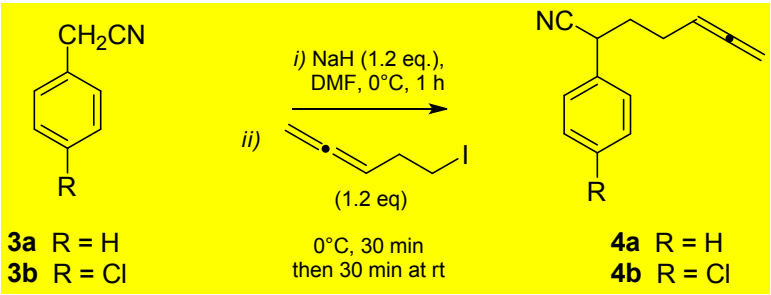
Experimental Procedure

Procedure for the synthesis of (1)

Aldehyde **1** was synthetized according to the three-step sequence depicted below.



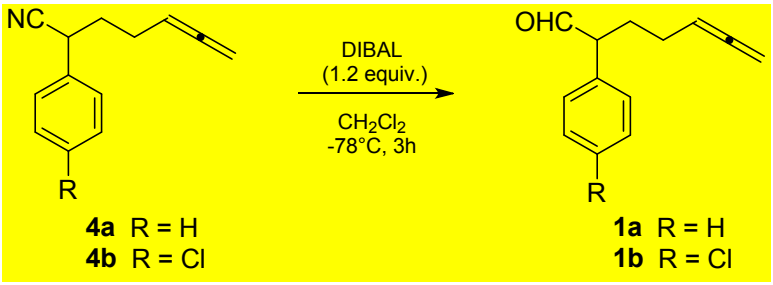
General procedure for the synthesis of compounds **4**



To a suspension NaH (60% in oil, 3.17 mmol, 1.2 equiv.) in DMF (7 mL) was added a solution of benzyl cyanide derivatives **3**[1] (2.64 mmol, 1 equiv.) in DMF (7 mL) at 0°C. The solution was stirred for 1h a solution of 5-iodopentan-1,2-diene[2] (3.17mmol, 1.2 equiv.) in DMF (5 mL) was added at this temperature. The reaction mixture was stirred at 0°C for 0.5h and an additional 0.5h at room temperature. The reaction mixture was quenched by addition of a saturated aqueous NH_4Cl solution and the mixture was extracted with EtOAc. The organic layers were combined, washed twice with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography (petroleum ether/ Et_2O, 95/5) to afford the aldehyde **1a** (160 mg, 33%) or aldehyde **1b** (153mg, 27%)

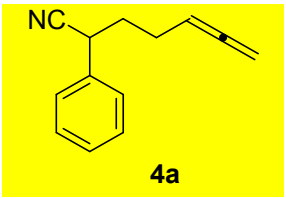
1 O. Yabe, H. Mizufune and T. Ikemoto, *Synlett*, 2009, **8**, 1291-1294.
2 W. G. Dauben and G. Shapiro, *J. Org. Chem.*, 1984, **49**, 4252-4258.

General procedure for the synthesis of aldehydes **1**



Compound **4** (0.7 mmol) was dissolved in DCM (4 mL). The solution was cooled down to -78°C and a solution of DIBAL (1M in cyclohexane, 0.84 mL, 0.84 mmol, 1.2 equiv.) was added dropwise. The reaction mixture was stirred at -78°C for 3h, quenched by addition of MeOH. The mixture was treated with an aqueous HCl solution (1N) and extracted with EtOAc. The organic layers were combined, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography (petroleum ether/ Et_2O, 95/5) to afford the aldehyde **1a** (40 mg, 40%) or **1b** (60 mg, 40%).

2-phenylhepta-5,6-dienenitrile **4a**



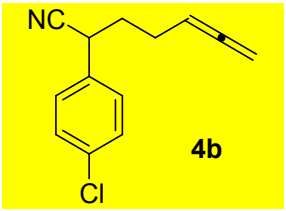
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) = 7.44-7.29 (m, 5H), 5.13 (quint, *J* = 6.4 Hz, 1H), 4.76 (dt, *J* = 6.4 and 3.3 Hz, 2H), 3.88 (dd, *J* = 8.3 and 6.4 Hz, 1H), 2.23-1.92 (m, 4H).

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) = 208.7, 135.7, 129.1 (2C), 128.1, 127.3 (2C), 120.8, 88.2, 76.2, 36.4, 34.8, 25.2.

IR (neat) υ□□ (cm^{-1}) = 3031.4, 2929.7, 2859.1, 2239.8, 1954.6.

HRMS (ESI) Calcd for $C_{13}H_{14}N$ $[M + H]^+$: 184.1126, Found: 184.1132.

2-(4chlorophenyl)-hepta-5,6-dienenitrile **4b**



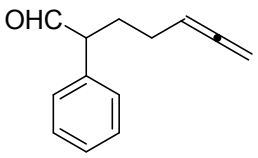
4b

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) = 7.44-7.29 (m, 5H), 5.13 (quint, *J* = 6.4 Hz, 1H), 4.76 (dt, *J* = 6.4 and 3.3 Hz, 2H), 3.88 (dd, *J* = 8.3 and 6.4 Hz, 1H), 2.23-1.92 (m, 4H).

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) = 208.8, 134.3, 129.5 (2C), 128.8 (2C), 127.4, 120.4, 88.1, 76.4, 36.0, 34.8, 25.1.

IR (neat) υ□□ (cm^{-1}) = 2926.6, 2859.5, 2240.0, 1954.4.

2-phenylhepta-5,6-dienal **1a**



1a

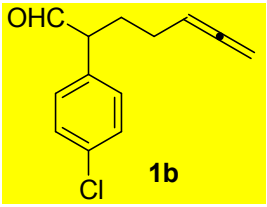
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) = 9.69 (d, *J* = 1.5 Hz, 1H), 7.40-7.28 (m, 3H), 7.21-7.18 (m, 2H), 5.08 (quint, *J* = 6.6 Hz, 1H), 4.70 (dt, *J* = 6.6 and 3 Hz, 1H), 4.69 (dd, *J* = 6.6 and 3 Hz, 1H), 3.62-3.57 (m, 1H), 2.25-2.16 (m, 1H), 2.03-1.79 (m, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) = 208.8, 200.8, 136.2, 129.2 (2C), 129.1 (2C), 127.8, 89.2, 75.6, 58.4, 29.0, 25.5.

IR (neat) υ□□ (cm^{-1}) = 3027.7, 2928.5, 2857.3, 2815.9, 2713.2, 1954.9, 1720.0.

HRMS (ESI) Calcd for $C_{13}H_{14}ONa$ $[M + Na]^+$: 209.0942, Found: 209.0939.

2-(4-chlorophenyl)-hepta-5,6-dienal **1b**



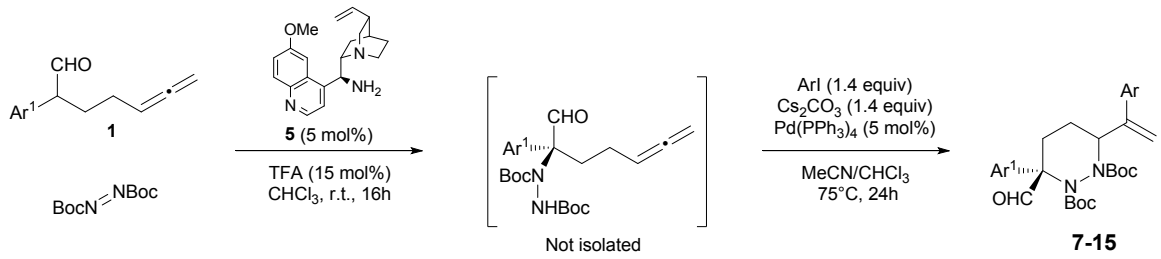
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) = 9.67 (d, *J* = 1.6 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.12 (d, *J* = 8.4 Hz, 2H), 5.07 (quint, *J* = 6.6 Hz, 1H), 4.70 (dt, *J* = 6.6 and 3.2 Hz, 1H), 3.59 (ddd, *J* = 7.8, 6.2 and 1.6 Hz, 1H), 2.25-2.14 (m, 1H), 2.04-1.75 (m, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) = 208.8, 200.2, 134.7, 133.8, 130.4 (2C), 129.4 (2C), 89.0, 75.7, 58.7, 29.0, 25.4.

IR (neat) υ□□ (cm^{-1}) = 2923.5, 2857.0, 2815.8, 2714.5, 1955.1, 1721.0.

HRMS (ESI) Calcd for $C_{13}H_{14}OCl$ $[M + H]^+$: 221.0733, Found: 221.0741.

General procedure for the multicatalytic access to cyclic hydrazines 7-15

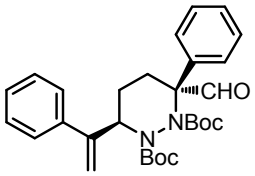


Aldehyde **1** (1.2 equiv) was dissolved in chloroform (1 M). Catalyst **5** (5 mol%), DtBAD (1 equiv) and TFA (15 mol%) were respectively added and the solution was stirred at room temperature for 16h. After purging with argon, cesium carbonate (1.4 equiv), $Pd(PPh_3)_4$ (5 mol%), acetonitrile (0.08 M) and iodoaryl compound (1.4 equiv) were respectively added. Reaction mixture was heated at 75°C for 24h then filtered on a pad of celite and washed with DCM. The organic layer was concentrated under reduced pressure. The residue was purified by column chromatography (DCM/ Et_2O, 98/2) to afford a mixture of diastereomers which were separated by a second column chromatography (petroleum ether/EtO_2, 85/15).

Enantiomeric excess was determined for the minor diastereomer of compound **7** (94%) or **15** (93%).

The ee values of the compounds **8-14** were assigned by analogy with **7** (minor diastereomer) as the formation of the quaternary stereocenter (organocatalytic electrophilic amination) was conducted under the same conditions than **7**.

Compound **7** (major diastereomer)



^{1}H NMR (300 MHz, $(CD_3)_2SO$, 80°C) δ = 10.03 (s, 1H), 7.42-7.25 (m, 8H), 7.21-7.19 (m, 2H), 5.93 (bs, 1H), 5.47-5.37 (m, 1H), 5.34 (bs, 1H), 1.96 (td, *J*= 13.8 and 2.4 Hz, 1H), 1.86-1.79 (m, 1H), 1.59 (bd, *J* = 13.8 Hz, 1H), 1.57 (bs, 1H), 1.47 (bs, 9H), 1.28 (bs, 9H).

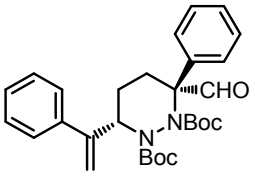
^{13}C NMR (75 MHz, $(CD_3)_2SO$, 80°C) δ = 198.6, 155.6, 153.6, 149.0, 140.2, 138.2, 128.7 (2C), 128.5 (2C), 128.0, 127.6, 127.3 (2C), 125.9 (2C), 113.0, 82.5 (2C), 82.1, 72.8, 30.7, 28.2 (3C), 28.1 (3C), 21.3.

IR (neat) υ□□ (cm^{-1}) = 2971.0, 2933.0, 2869.7, 1705.3, 1366.5, 1158.2.

HRMS (ESI) Calcd for $C_{29}H_{36}N_2O_5Na$ $[M + Na]^+$: 515.2522, Found: 515.2526.

$[\alpha]_D^{20}$ = +5.0 (*c* 1.0, $CHCl_3$).

Compound **7** (minor diastereomer)



^{1}H NMR (300 MHz, $CHCl_3$, r.t., mixture of rotamers**)** δ = 9.73 (s, 1H), 7.69-7.31 (m, 10H), 6.16-5.83 (m, 1H), 5.34-4.91 (m, 2H), 2.46-1.73 (m, 4H), 1.53-1.47 (m, 9H), 1.38-1.30 (m, 9H).

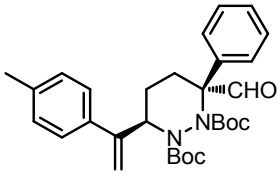
^{13}C NMR (75 MHz, $CHCl_3$, r.t., mixture of rotamers**)** δ = 194.8, 155.1, 154.7, 147.8, 140.4, 138.0, 128.4 (2C), 128.0 (2C), 127.6 (2C), 127.3, 126.9 (2C), 126.7, 113.4, 82.9, 81.9, 81.6, 71.5, 28.9, 28.2 (3C), 28.0 (3C), 23.8.

IR (neat) υ□□ (cm^{-1}) = 2977.3, 2926.6, 1723.2, 1705.7, 1689.4, 1380.2, 1366.8, 1164.2.

HRMS (ESI) Calcd for $C_{29}H_{36}N_2O_5Na$ $[M + Na]^+$: 515.2522, Found: 515.2526.

$[\alpha]_D^{20}$ = +10.0 (*c* 1.0, $CHCl_3$).

Compound **8** (major diastereomer)



^{1}H NMR (300 MHz, $(CD_3)_2SO$, 80°C) δ = 10.02 (s, 1H), 7.39-7.28 (m, 5H), 7.20-7.13 (m, 4H), 5.89 (bs, 1H), 5.43-5.34 (m, 1H), 5.30 (s, 1H), 2.29 (s, 3H), 1.95 (bt, *J* = 14.1 Hz,1H), 1.88-1.78 (m, 1H), 1.59 (bd, *J* = 14.1 Hz, 1H), 1.50 (bs, 1H), 1.47 (bs, 9H), 1.28 (bs, 9H).

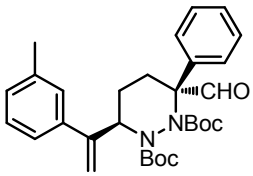
^{13}C NMR (75 MHz, $(CD_3)_2SO$, 80°C) δ = 198.6, 155.6, 153.3, 148.8, 138.4, 137.4, 137.3, 129.3 (2C), 128.5 (2C), 127.6, 127.1 (2C), 125.9 (2C), 112.2, 82.4 (2C), 82.1, 72.8, 30.8, 28.2 (3C), 28.1 (3C), 21.4, 21.0.

IR (neat) υ□□ (cm^{-1}) = 2977.3, 2933.0, 2869.7, 1709.6, 1367.7, 1161.9.

HRMS (ESI) Calcd for $C_{30}H_{38}N_2O_5Na$ $[M + Na]^+$: 529.2678, Found: 529.2673.

$[\alpha]_D^{20}$ = +26.0 (*c* 1.0, $CHCl_3$).

Compound **9** (major diastereomer)



^{1}H NMR (300 MHz, $(CD_3)_2SO$, 80°C) δ = 10.02 (s, 1H), 7.39-7.34 (m, 2H), 7.30-7.28 (m, 1H), 7.21-7.19 (m, 5H), 7.10-7.08 (m, 1H), 5.90 (bs, 1H), 5.44-5.35 (m, 1H), 5.32 (s, 1H), 2.31 (s, 3H), 1.95 (bt, *J* = 14.4 Hz, 1H), 1.86-1.79 (m, 1H), 1.59 (bd, *J* = 14.4 Hz, 1H), 1.50 (bs, 1H), 1.47 (bs, 9H), 1.27 (bs, 9H).

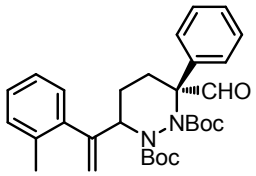
^{13}C NMR (75 MHz, $(CD_3)_2SO$, 80°C) δ = 198.6, 155.7, 153.5, 149.1, 140.2, 138.3, 137.9, 128.7, 128.6, 128.5 (2C), 127.8, 127.6, 125.9 (2C), 124.4, 112.7, 82.4 (2C), 82.1, 72.8, 30.8, 28.2 (3C), 28.1 (3C), 21.4 (2C).

IR (neat) υ□□ (cm^{-1}) = 2971.0, 2924.8, 2865.4, 1707.1, 1367.4, 1161.0.

HRMS (ESI) Calcd for $C_{30}H_{38}N_2O_5Na$ $[M + Na]^+$: 529.2678, Found: 529.2675.

$[\alpha]_D^{20}$ = +20.0 (*c* 1.0, $CHCl_3$).

Compound **10**



Mixture of diastereomers (9/1)

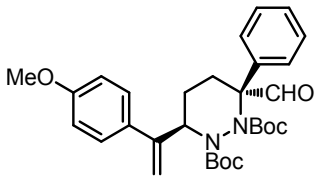
^{1}H NMR (300 MHz, $CDCl_3$, r.t.) δ = 10.24-9.77 (m, 1H), 7.40-7.31 (m, 3H), 7.23-7.12 (m, 6H), 6.26-6.07 (m, 1H), 5.26-4.90 (m, 2H), 2.40-2.35 (m, 3H), 2.05-1.89 (m, 1H), 1.61-1.43 (m, 18H), 1.16 (bs, 3H).

IR (neat) υ□□ (cm^{-1}) = 2977.3, 2926.7, 2869.7, 1707.0, 1366.7, 1156.7.

HRMS (ESI) Calcd for $C_{30}H_{38}N_2O_5Na$ $[M + Na]^+$: 529.2678, Found: 529.2679.

The product, obtained in low yield as a mixture of diastereomers (9/1) has not been characterized by ^{13}C NMR.

Compound **11** (major diastereomer)



^{1}H NMR (300 MHz, $(CD_3)_2SO$, 80°C) δ = 10.01 (s, 1H), 7.39-7.28 (m, 5H), 7.21-7.19 (m, 2H), 6.91-6.88 (m, 2H), 5.86 (bs, 1H), 5.34 (bs, 1H), 5.27 (s, 1H), 3.76 (s, 3H), 1.96 (td, *J* = 14.1 and 2.7 Hz, 1H), 1.88-1.80 (m, 1H), 1.60 (bd, *J* = 14.1 Hz, 1H), 1.52 (bs, 1H), 1.47 (bs, 9H), 1.28 (bs, 9H).

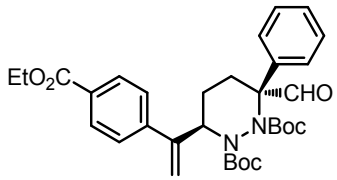
^{13}C NMR (75 MHz, $(CD_3)_2SO$, 80°C) δ = 198.6, 159.6, 155.6, 153.5, 148.4, 138.3, 132.6, 128.4 (2C), 128.3, 127.5 (2C), 125.9 (2C), 114.4 (2C), 111.6, 82.4 (2C), 82.1, 72.9, 55.7, 30.8, 28.2 (3C), 28.1 (3C), 21.5.

IR (neat) υ□□ (cm^{-1}) = 2977.3, 2933.0, 2869.7, 1705.7, 1367.2, 1159.7.

HRMS (ESI) Calcd for $C_{30}H_{38}N_2O_6Na$ $[M + Na]^+$: 545.2628, Found: 545.2628.

$[\alpha]_D^{20}$ = +16.0 (*c* 1.0, $CHCl_3$)

Compound **12** (major diastereomer)



^{1}H NMR (300 MHz, $(CD_3)_2SO$, 80°C) δ = 10.02 (s, 1H), 7.92 (d, *J* = 8.1 Hz, 2H), 7.56 (d, *J* = 8.1 Hz, 2H), 7.39-7.34 (m, 2H), 7.30-7.26 (m, 1H), 7.20-7.17 (m, 2H), 6.00 (bs, 1H), 5.47 (bs, 1H), 5.45-5.37 (m, 1H), 4.33 (q, *J* = 7.2 Hz, 2H), 2.02-1.83 (m, 2H), 1.61 (bd, *J* = 13.8 Hz, 1H), 1.50 (bs, 1H), 1.47 (bs, 9H), 1.33 (t, *J* = 7.2 Hz, 3H), 1.26 (bs, 9H).

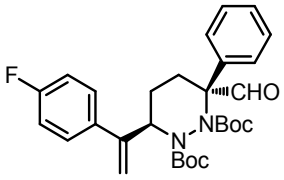
^{13}C NMR (75 MHz, $(CD_3)_2SO$, 80°C) δ = 198.5, 166.0, 155.5, 153.5, 148.2, 144.9, 138.2, 129.9, 129.6 (2C), 128.5 (2C), 127.7, 127.6 (2C), 125.8 (2C), 114.8, 82.6 (2C), 82.2, 72.8, 61.0, 30.9, 28.1 (3C), 28.1 (3C), 21.2, 14.6.

IR (neat) υ□□ (cm^{-1}) = 2977.3, 2929.8, 2869.7, 1708.1, 1367.0, 1159.9.

HRMS (ESI) Calcd for $C_{32}H_{40}N_2O_7Na$ $[M + Na]^+$: 587.2733, Found: 587.2736.

$[\alpha]_D^{20}$ = -11.0 (*c* 1.0, $CHCl_3$)

Compound **13** (major diastereomer)



^{1}H NMR (300 MHz, $(CD_3)_2SO$, 80°C) δ = 10.02 (s, 1H), 7.48-7.43 (m, 2H), 7.39-7.34 (m, 2H), 7.31-7.26 (m, 1H), 7.20-7.10 (m, 4H), 5.90 (bs, 1H), 5.43-5.31 (m, 2H), 1.96 (td, *J* = 14.1 and 2.7 Hz, 1H), 1.89-1.78 (m, 1H), 1.61 (bd, *J* = 14.1 Hz, 1H), 1.51-1.49 (m, 1H), 1.46 (bs, 9H), 1.27 (bs, 9H).

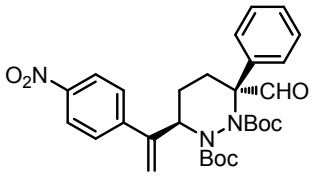
^{13}C NMR (75 MHz, $(CD_3)_2SO$, 80°C) δ = 198.6, 162.3 (d, *J* = 243.8 Hz), 155.6, 153.4, 147.9, 138.3, 136.6, 129.3 (d, *J* = 8.3 Hz, 2C), 128.5, 127.6 (2C), 125.9 (2C), 115.5 (d, *J*= 21.8 Hz, 2C), 113.4, 82.5 (2C), 82.1, 72.8, 30.7, 28.1 (3C), 28.1 (3C), 21.2.

IR (neat) υ□□ (cm^{-1}) = 2977.3, 2933.0, 2879.2, 1705.6, 1367.5, 1157.9.

HRMS (ESI) Calcd for $C_{29}H_{35}N_2O_5FNa$ $[M + Na]^+$: 533.2428, Found: 533.2431.

$[\alpha]_D^{20}$ = +10.0 (*c* 1.0, $CHCl_3$).

Compound **14** (major diastereomer)



^{1}H NMR (300 MHz, $(CD_3)_2SO$, 80°C) δ = 10.01 (s, 1H), 8.18 (d, *J* = 8.7 Hz, 2H), 7.72 (d, *J* = 8.7 Hz, 2H), 7.40-7.35 (m, 2H), 7.32-7.27 (m, 1H), 7.20-7.17 (m, 2H), 6.05 (bs, 1H), 5.57 (s, 1H), 5.45 (bs, 1H), 2.03-1.87 (m, 2H), 1.63 (bd, *J* = 13.8 Hz, 1H), 1.50 (bs, 1H), 1.46 (bs, 9H), 1.25 (bs, 9H).

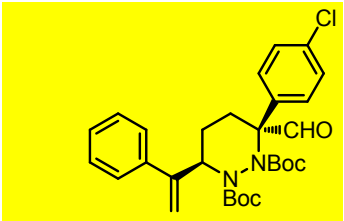
^{13}C NMR (75 MHz, $(CD_3)_2SO$, 80°C) δ = 198.5, 155.6, 153.5, 147.6, 147.5, 147.0, 138.1, 128.7 (2C), 128.6 (2C), 127.7, 125.8 (2C), 123.8 (2C), 116.5, 82.8 (2C), 82.3, 72.8, 30.6, 28.1 (3C), 28.0 (3C), 21.1.

IR (neat) υ□□ (cm^{-1}) = 2977.5, 2926.9, 2847.8, 1709.4, 1345.6, 1163.2.

HRMS (ESI) Calcd for $C_{29}H_{35}N_3O_7Na$ $[M + Na]^+$: 560.2373, Found: 560.2374.

$[\alpha]_D^{20}$ = -10.0 (*c* 1.0, $CHCl_3$)

Compound **15** (major diastereomer)



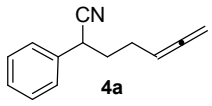
^{1}H NMR (300 MHz, $(CD_3)_2SO$, 80°C) δ = 9.99 (s, 1H), 7.43-7.28 (m, 7H), 7.22-7.19 (m, 2H), 5.88 (bs, 1H), 5.40 (m, 1H), 5.33 (s, 1H), 1.98-1.82 (m, 2H), 1.61 (bd, *J* = 14.1 Hz, 1H), 1.49 (bs, 1H), 1.47 (bs, 9H), 1.30 (bs, 9H).

^{13}C NMR (75 MHz, $(CD_3)_2SO$, 80°C) δ = 198.0, 148.5, 139.9, 136.8, 132.2, 128.4 (2C), 128.1 (2C), 127.7, 127.6 (2C), 127.0 (2C), 112.7, 82.3 (2C), 82.1, 72.2, 30.4, 27.9 (3C), 27.8 (3C), 21.1. (Two peaks corresponding to the C=O carbamates are missing)

IR (neat) υ□□ (cm^{-1}) = 2977.5, 2926.9, 2847.8, 1709.4, 1345.6, 1163.2.

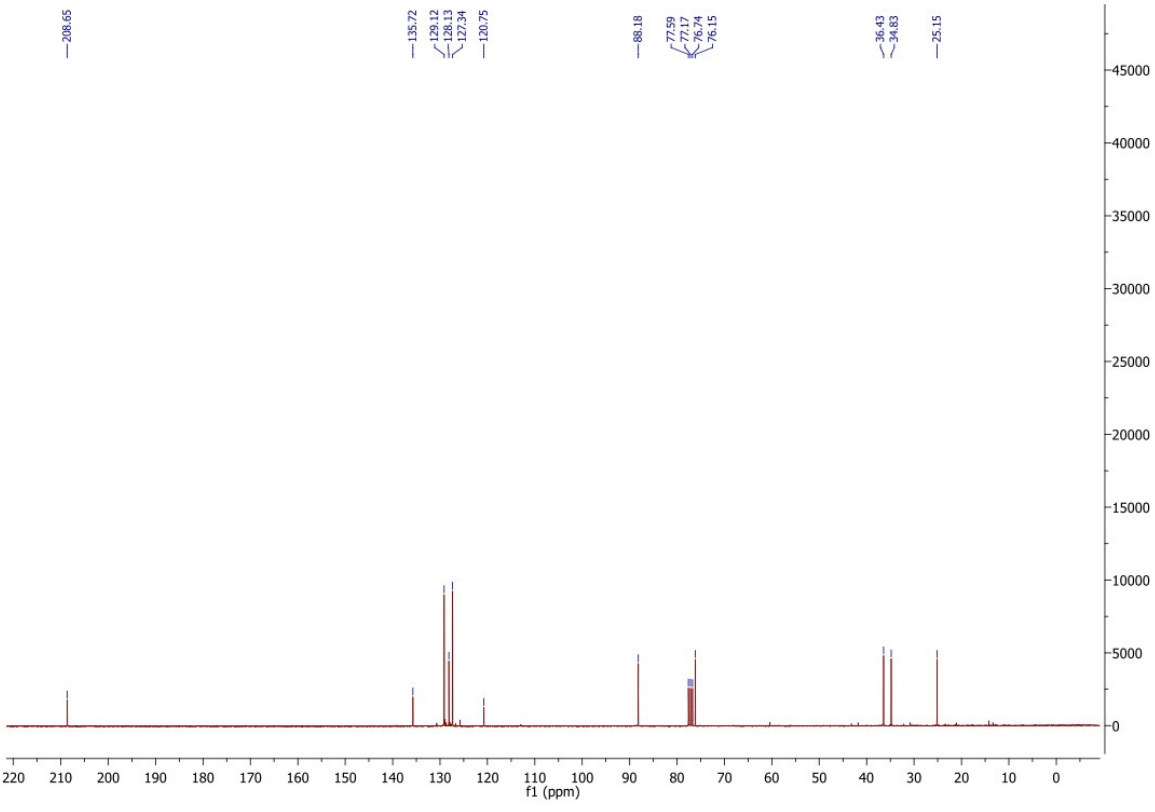
HRMS (ESI) Calcd for $C_{29}H_{35}N_2O_5ClNa$ $[M + Na]^+$: 549.2132, Found: 549.2133.

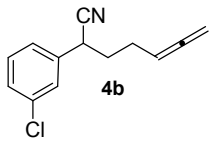
$[\alpha]_D^{20}$ = +15.0 (*c* 1.0, $CHCl_3$)


CN

4a

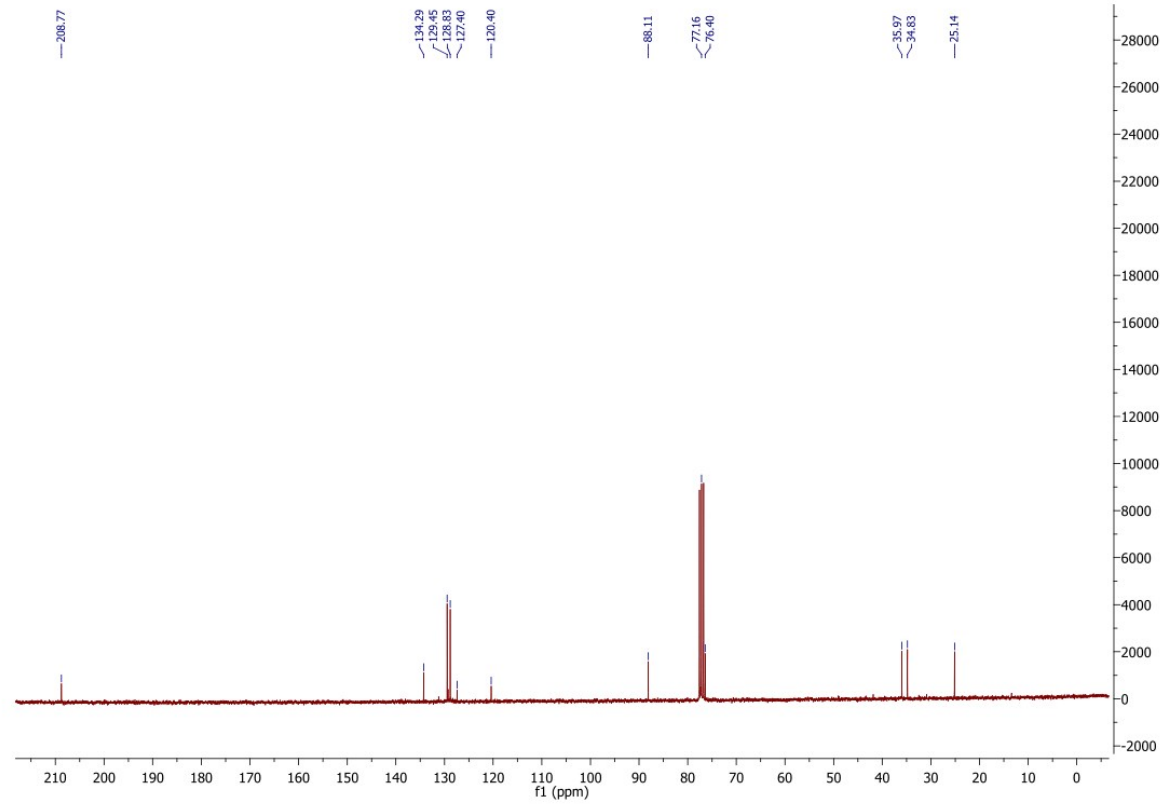
7.44
7.29
5.17
5.15
5.13
5.11
5.09
4.78
4.77
4.76
4.75
4.74
3.91
3.89
3.88
3.86
2.23
1.92
5.30
0.99
1.99
1.00
4.30
f1 (ppm)

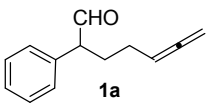

208.65
135.72
129.12
128.13
127.34
120.75
88.18
77.59
77.17
76.74
76.15
36.43
34.83
25.15
f1 (ppm)


CN
Cl

4b

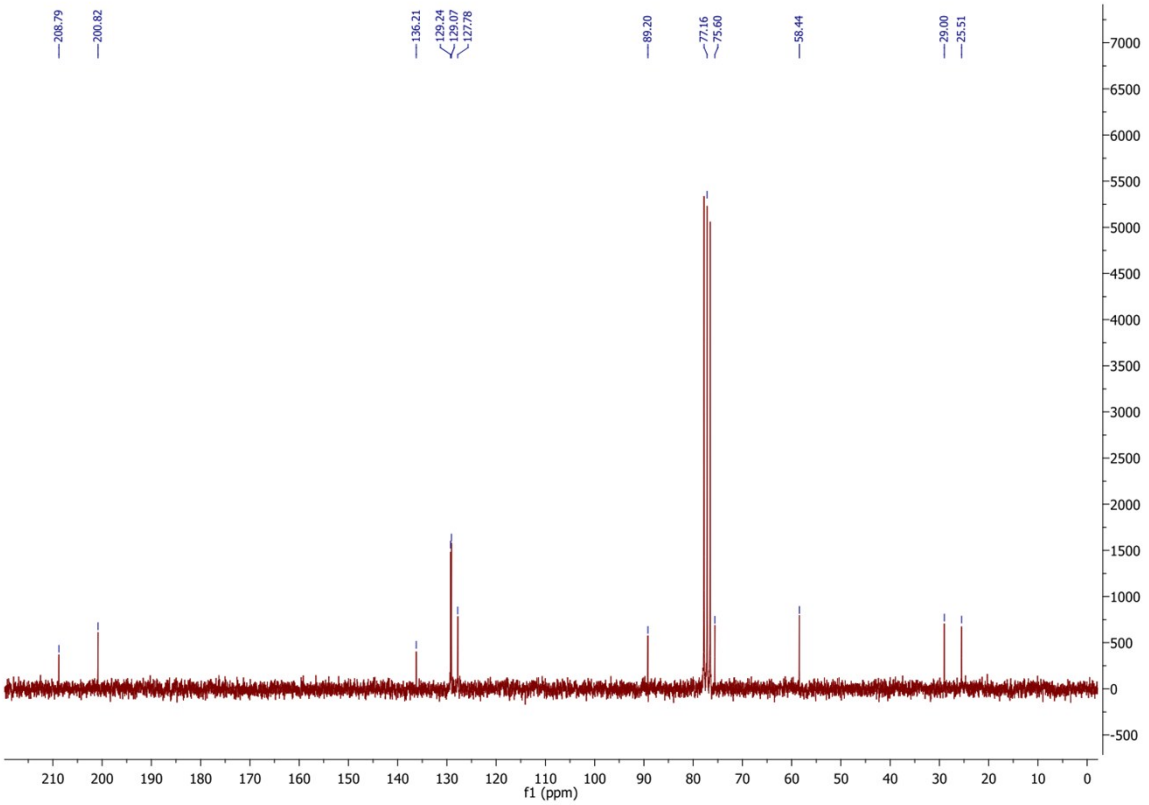
7.39
7.37
7.31
7.28
5.18
5.16
5.14
5.12
5.10
4.81
4.80
4.78
4.77
4.76
3.91
3.89
3.86
2.25
1.92
2.16
2.51
1.00
1.93
0.98
4.28
f1 (ppm)

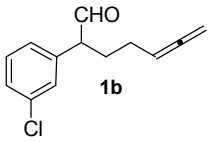

208.77
134.29
129.45
128.83
127.40
120.40
88.11
77.16
76.40
35.97
34.83
25.14
f1 (ppm)


CHO

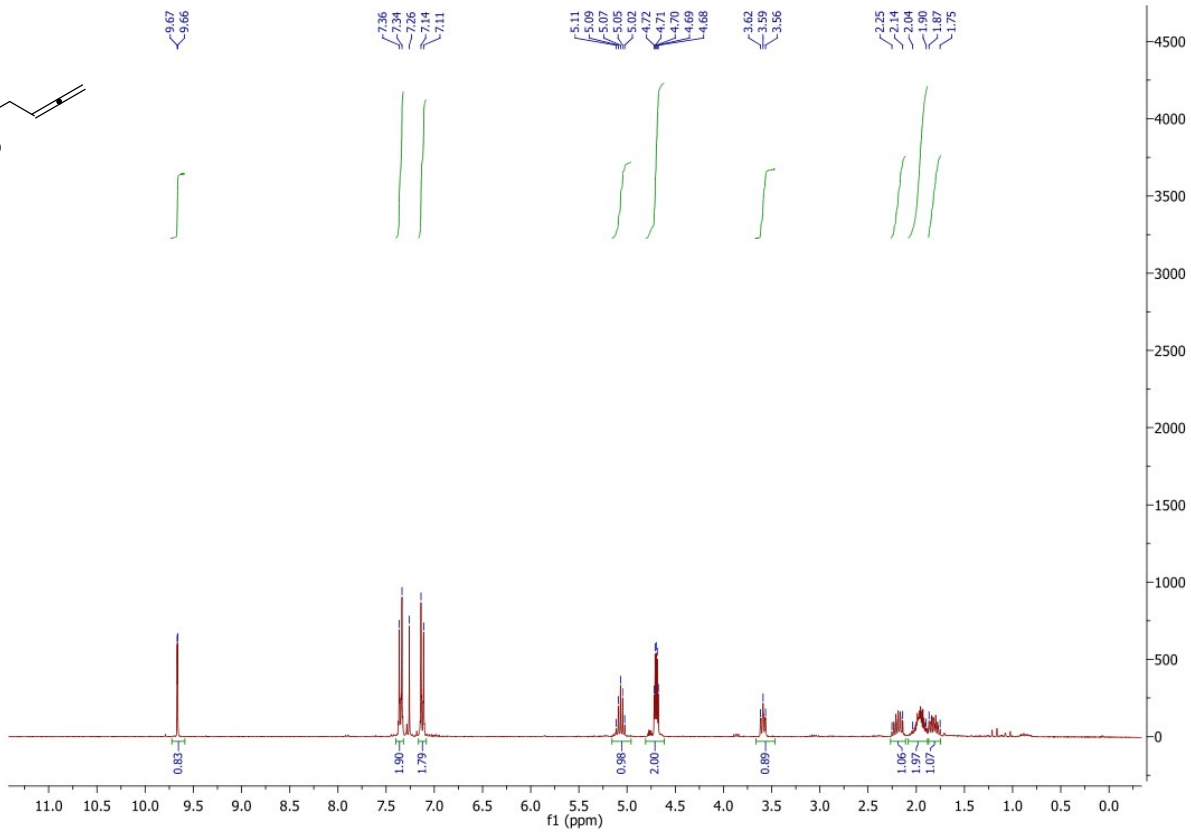
1a

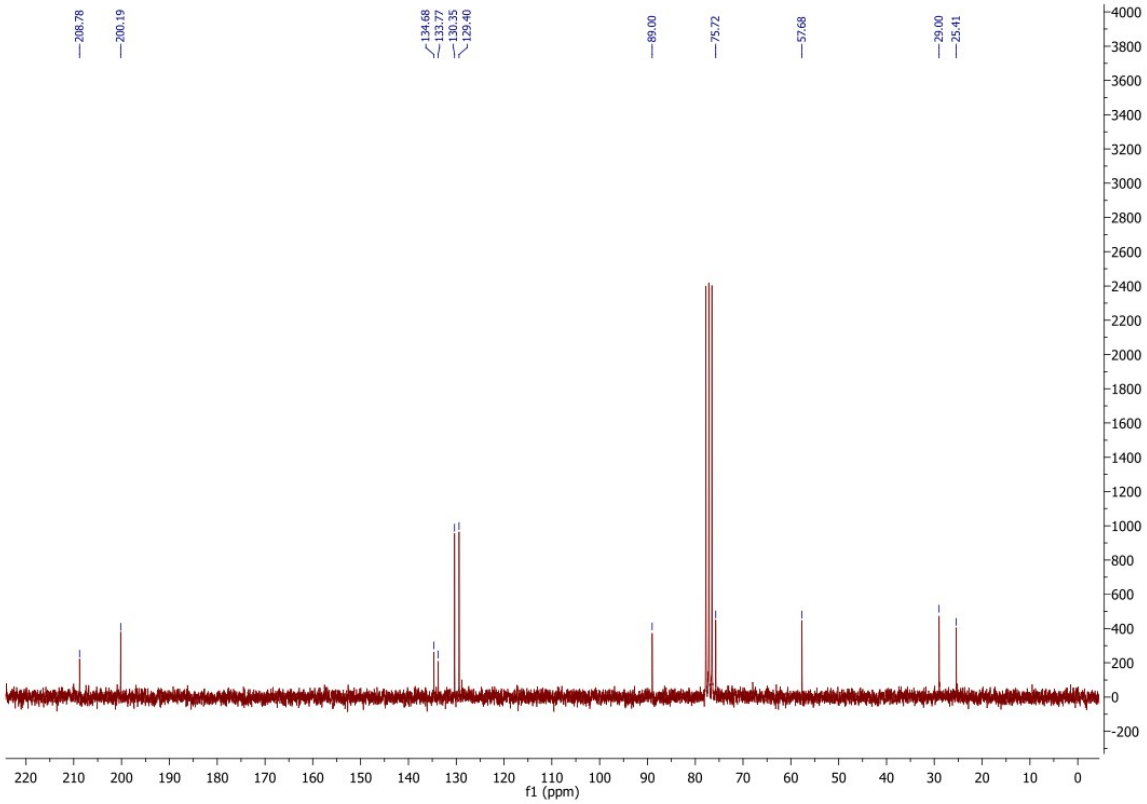
9.70
9.69
7.40
7.28
7.26
7.21
7.18
5.13
5.10
5.08
5.06
5.04
4.72
4.71
4.70
4.68
4.67
3.62
3.57
2.25
2.16
2.03
1.79
0.94
3.05
1.99
0.96
1.00
0.95
1.00
1.02
3.10
f1 (ppm)


208.79
200.82
136.21
129.24
129.07
127.78
89.20
77.16
75.60
58.44
29.00
25.51
f1 (ppm)

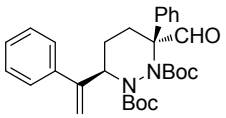

CHO
Cl

1b

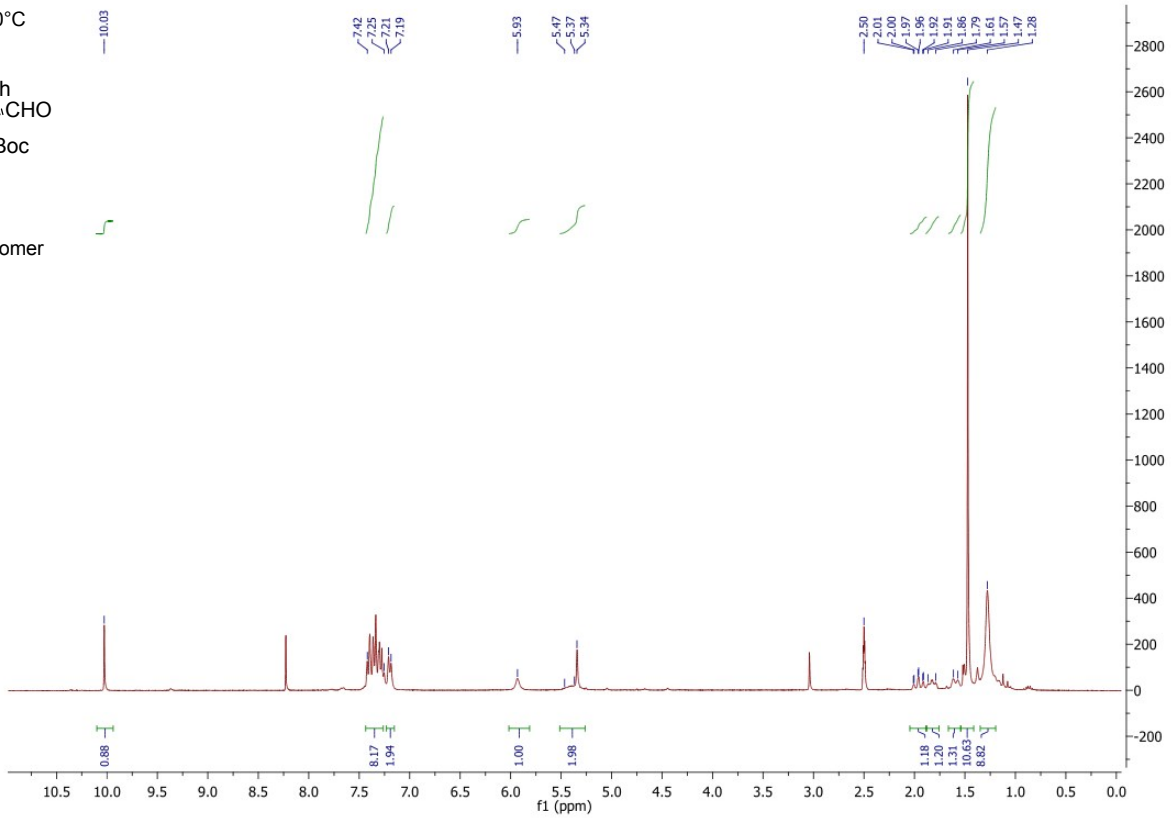

9.67
9.66
7.36
7.34
7.26
7.14
7.11
5.11
5.09
5.07
5.05
5.02
4.72
4.71
4.70
4.69
4.68
3.62
3.59
3.56
2.25
2.14
2.04
1.90
1.87
1.75
0.83
1.90
1.79
0.98
2.00
0.89
1.06
1.97
1.07
f1 (ppm)

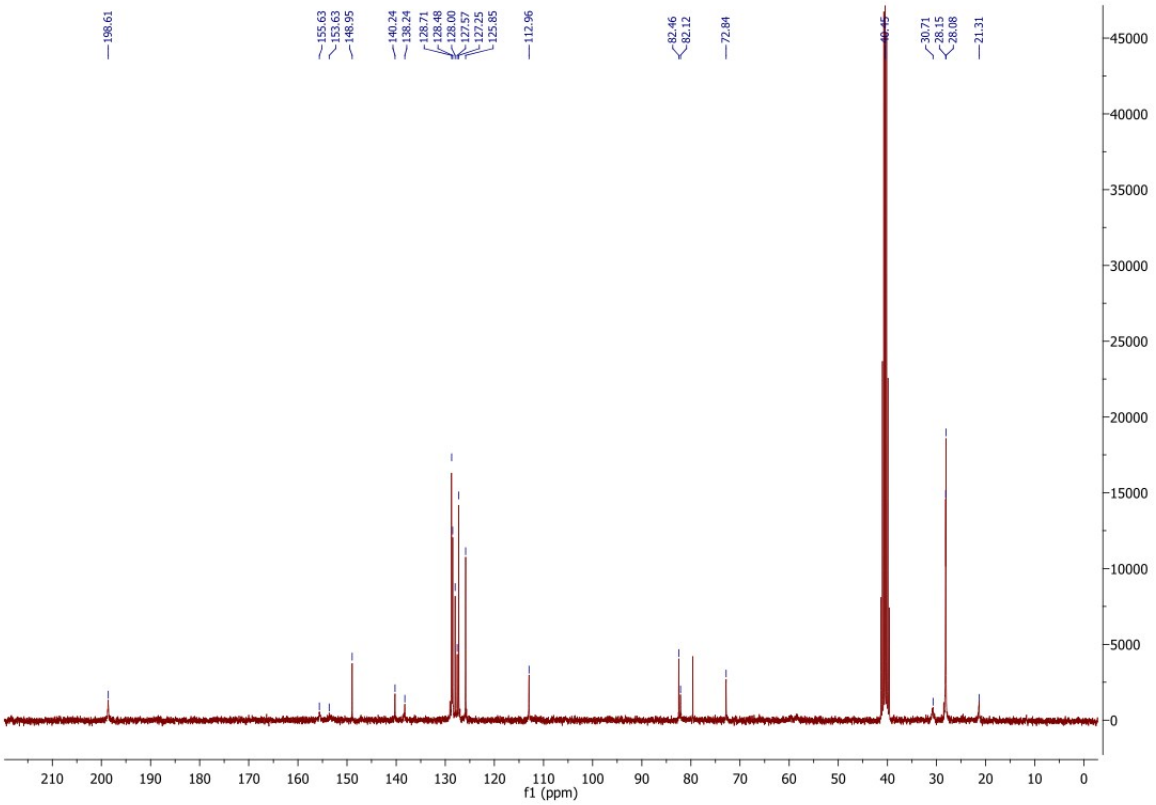

208.78
200.19
134.68
133.77
130.35
129.40
89.00
75.72
57.68
29.00
25.41
f1 (ppm)

DMSO-d_6, 80°C

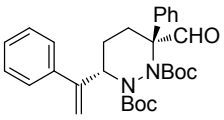


7
Major diastereomer

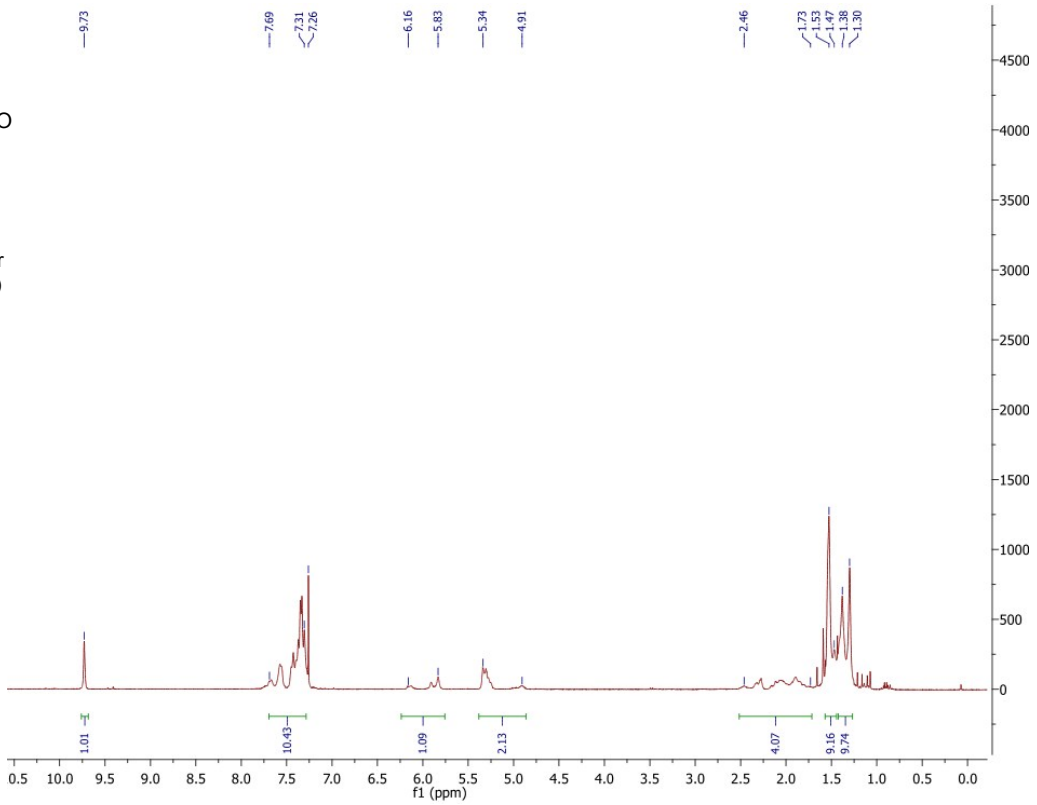


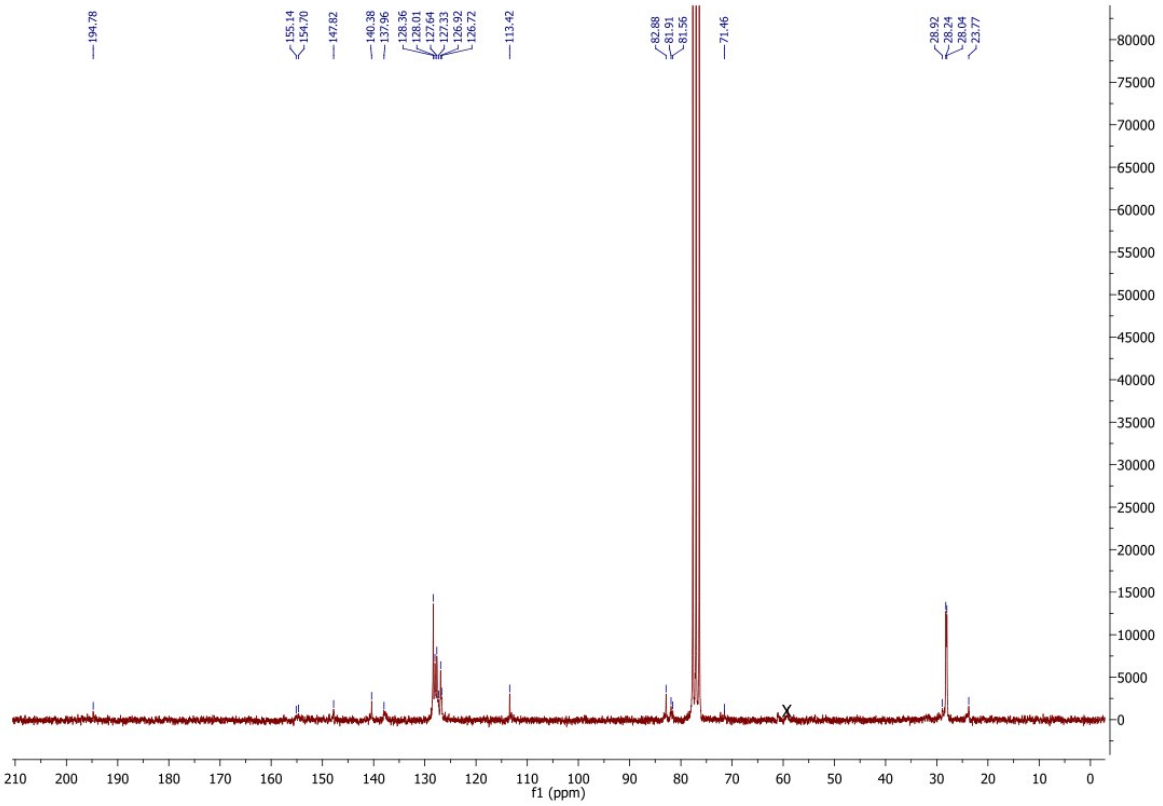


$CHCl_3$, r.t.

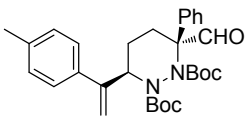


7
Minor diastereomer
(rotameric mixture)

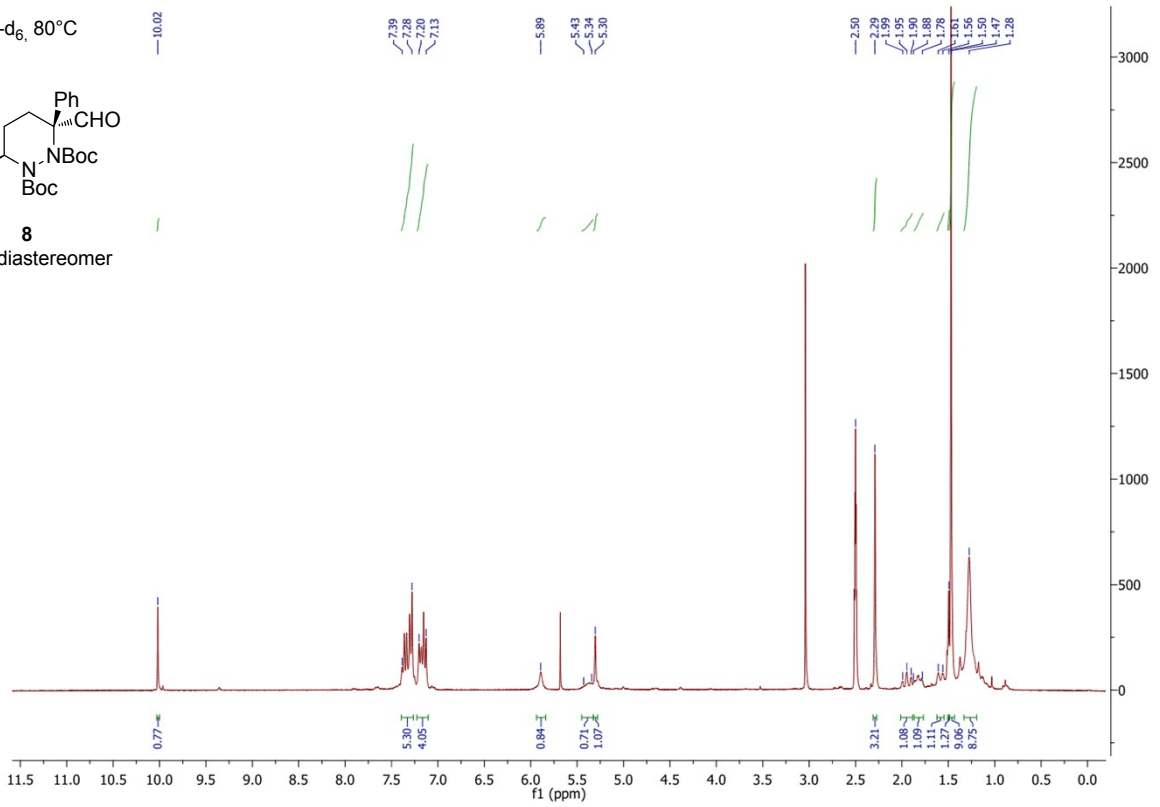


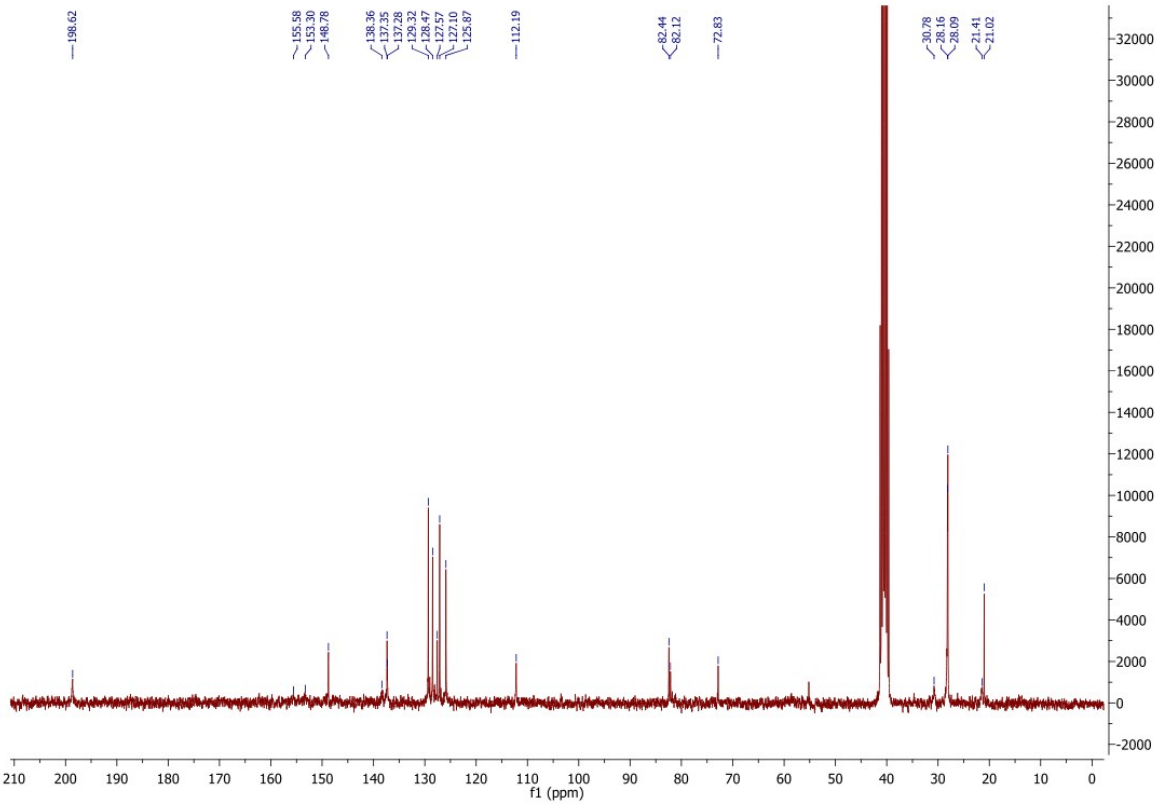


DMSO-d_6, 80°C

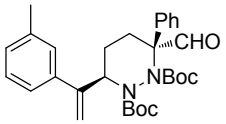


8
Major diastereomer

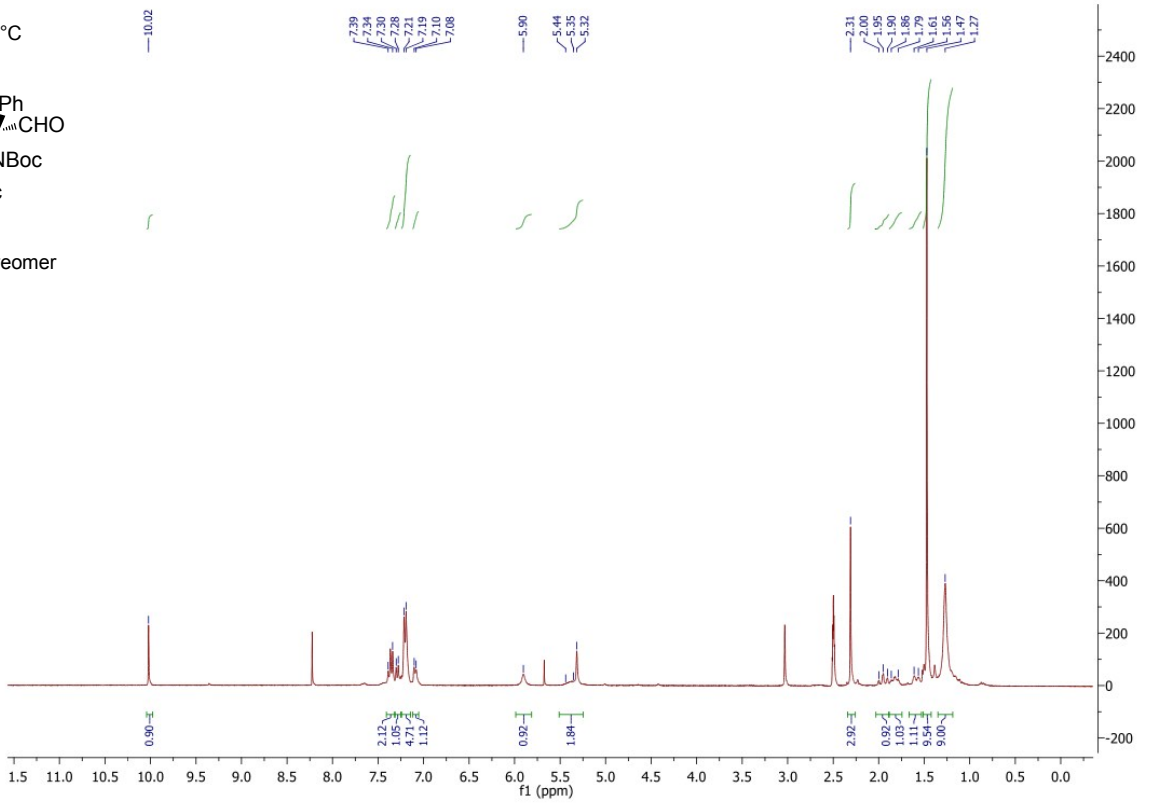


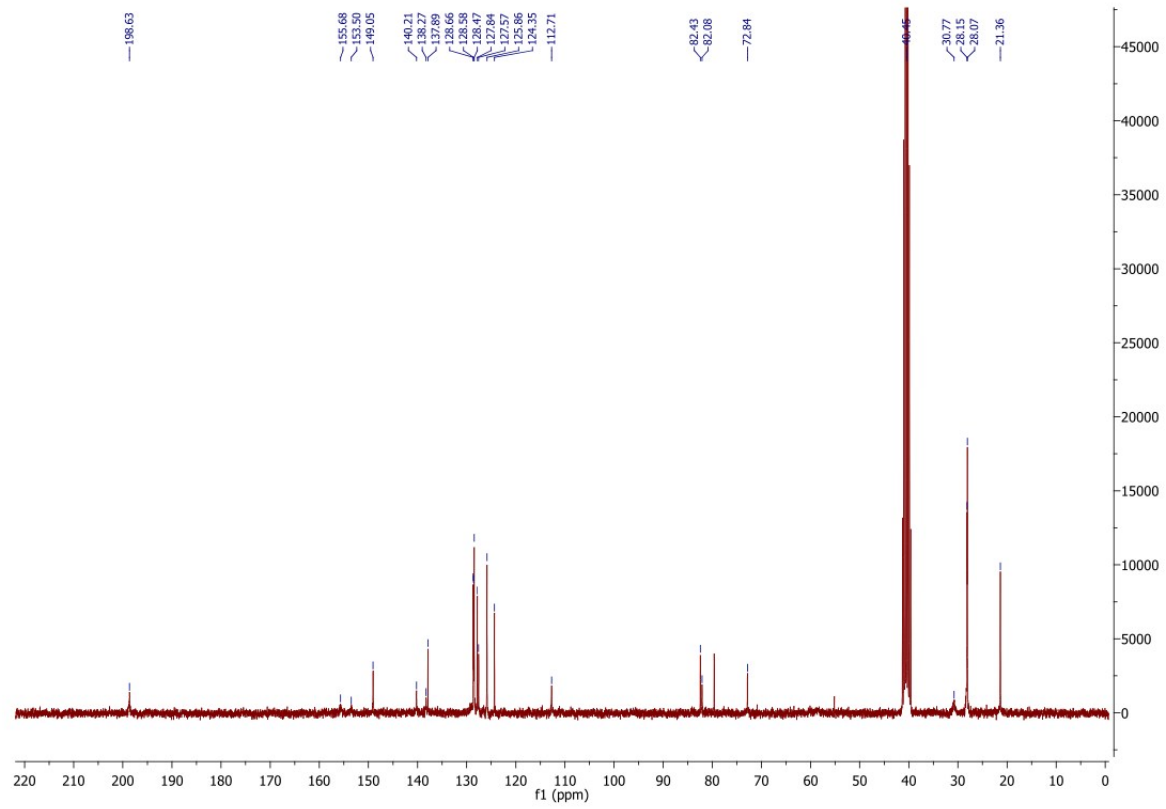


DMSO-d_6, 80°C

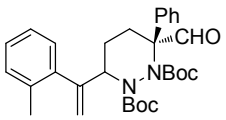


9
Major diastereomer

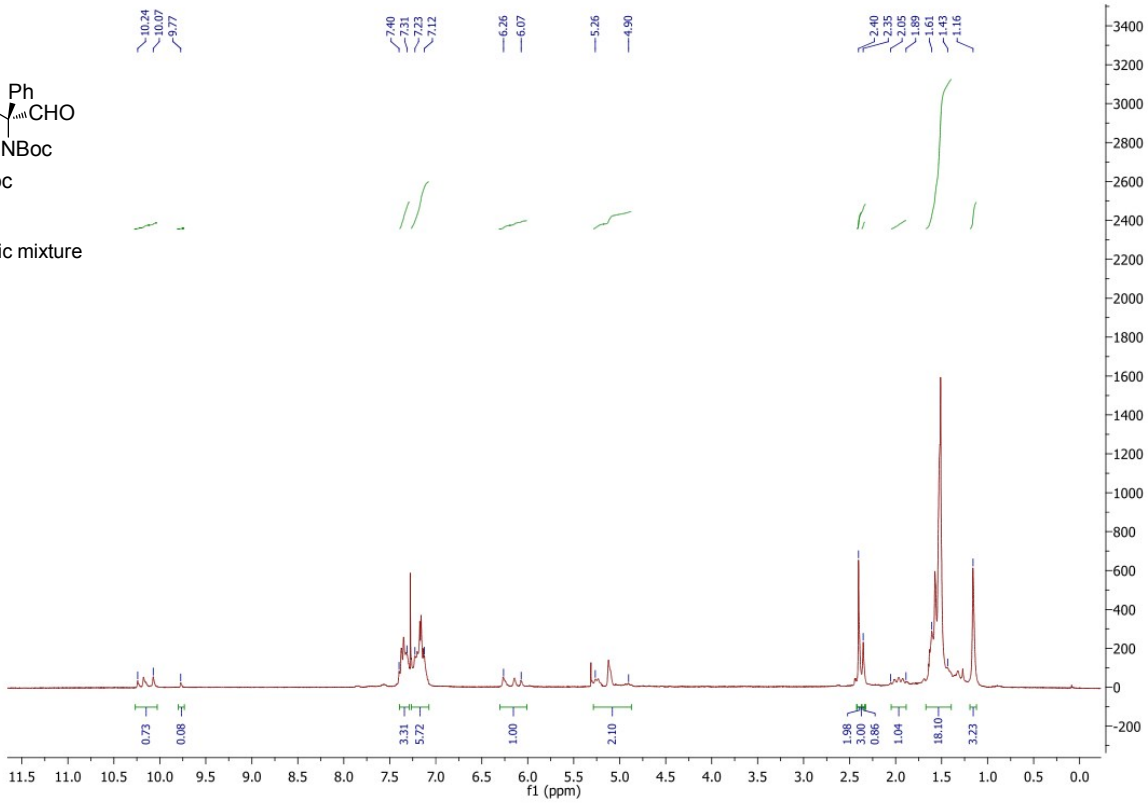




$CHCl_3$, r.t.



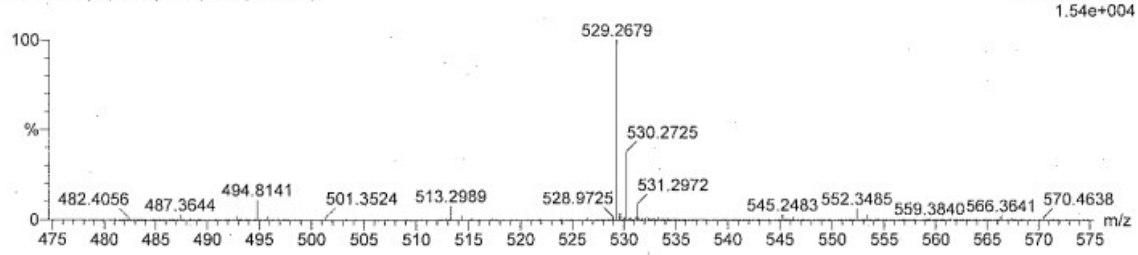
10
diastereomeric mixture
9/1



Single Mass Analysis
Tolerance = 2.0 PPM / DBE: min = -1.5, max = 500.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

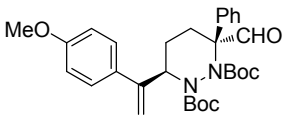
Monoisotopic Mass, Even Electron Ions
4893 formula(e) evaluated with 8 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-150 H: 0-150 N: 0-50 O: 0-50 Na: 0-1
Anne-Sophie MARQUES
LCMS - dilution 100
ASM-080-(01) 792 (5.531) Cm (790:792)

10-Jul-2015
1: TOF MS ES+
1.54e+004

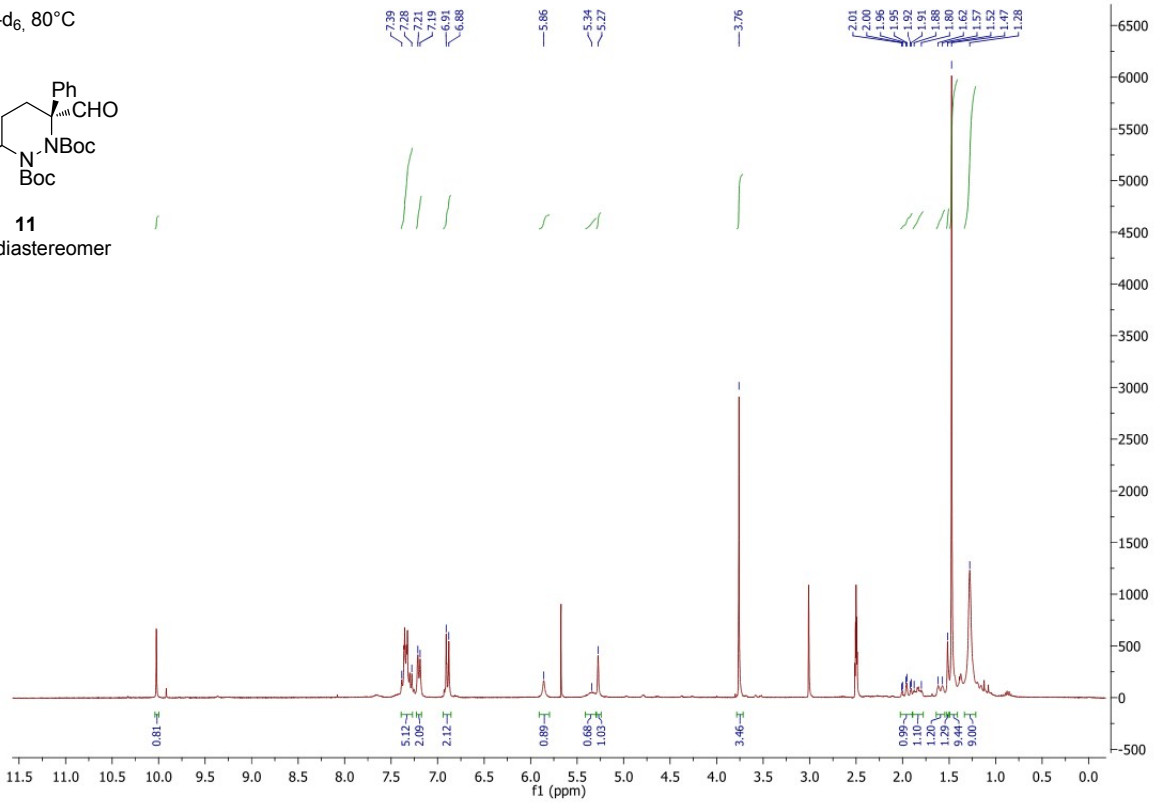


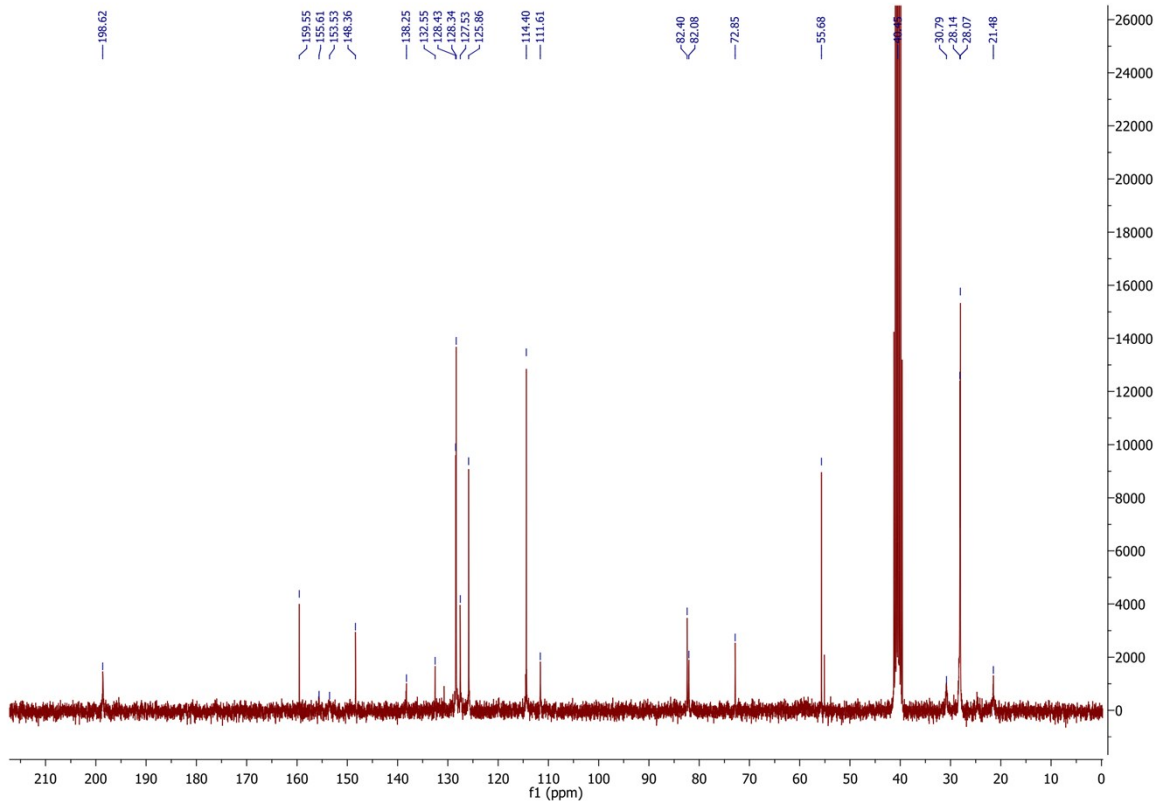
Minimum:				-1.5			
Maximum:		10.0	2.0	500.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
529.2679	529.2678	0.1	0.2	12.5	196.7	0.4	C30 H38 N2 O5 Na

DMSO-d_6, 80°C

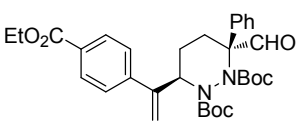


11
Major diastereomer

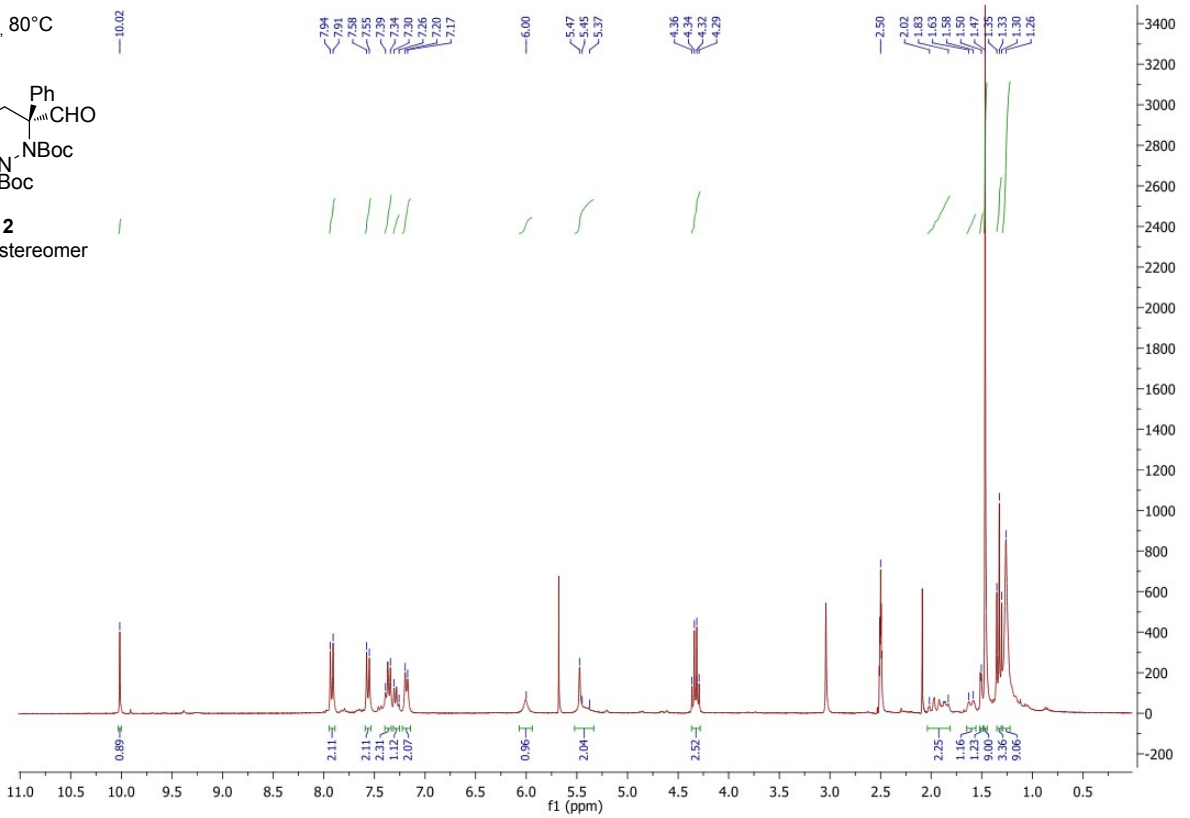


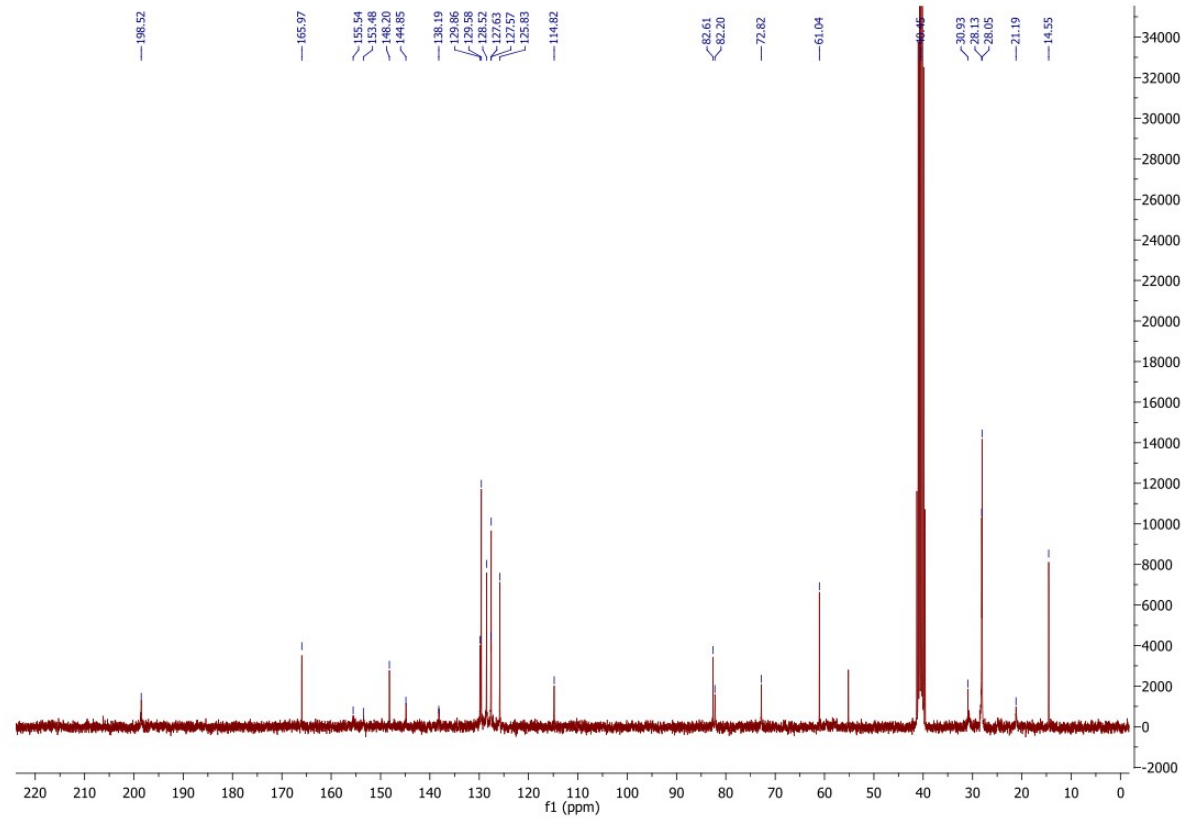


DMSO-d_6, 80°C

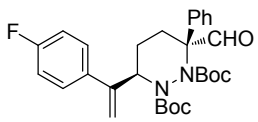


12
Major diastereomer

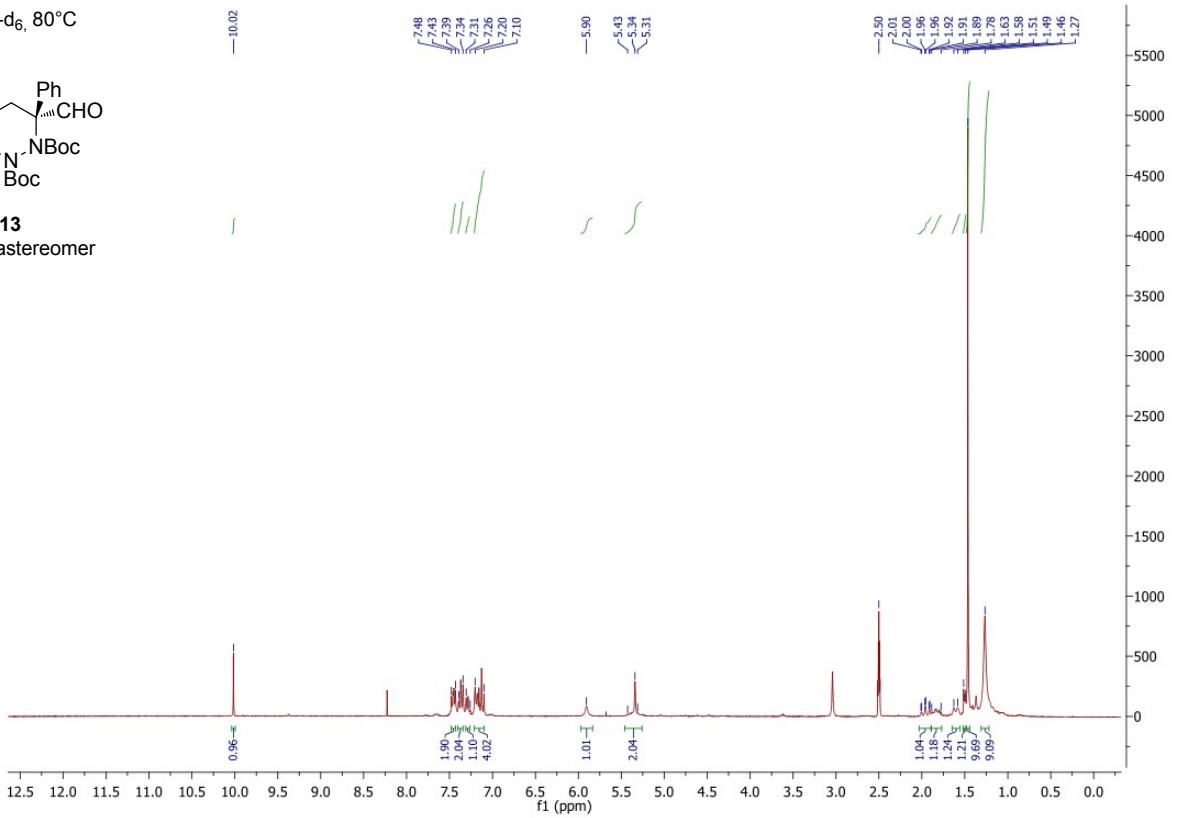


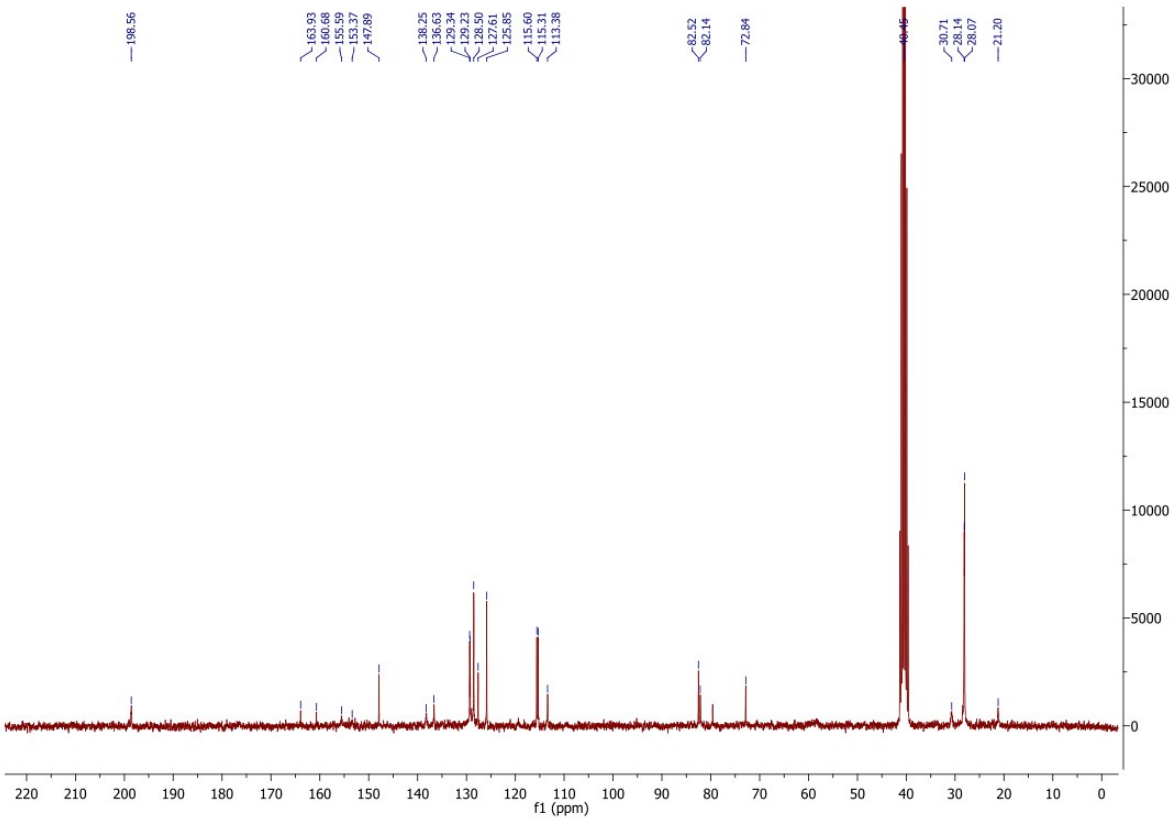


DMSO-d_6, 80°C

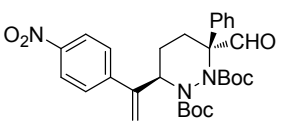


13
Major diastereomer

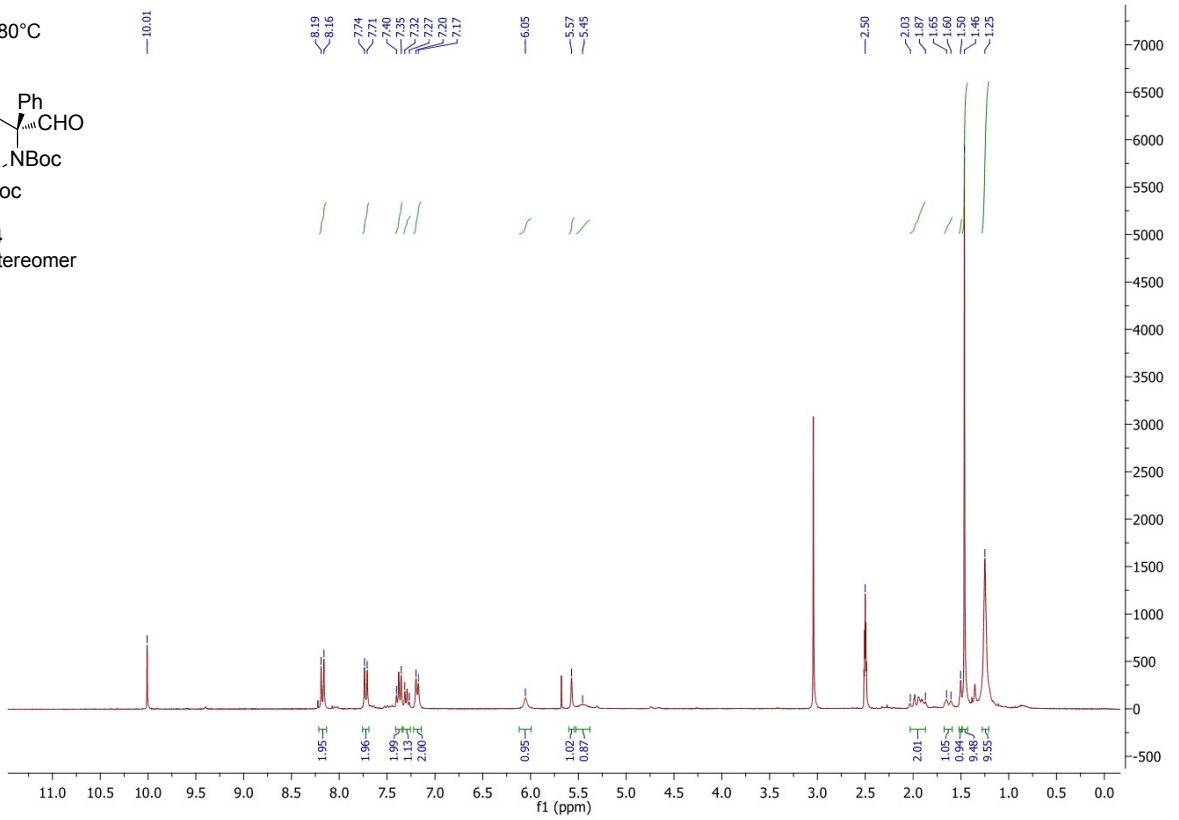


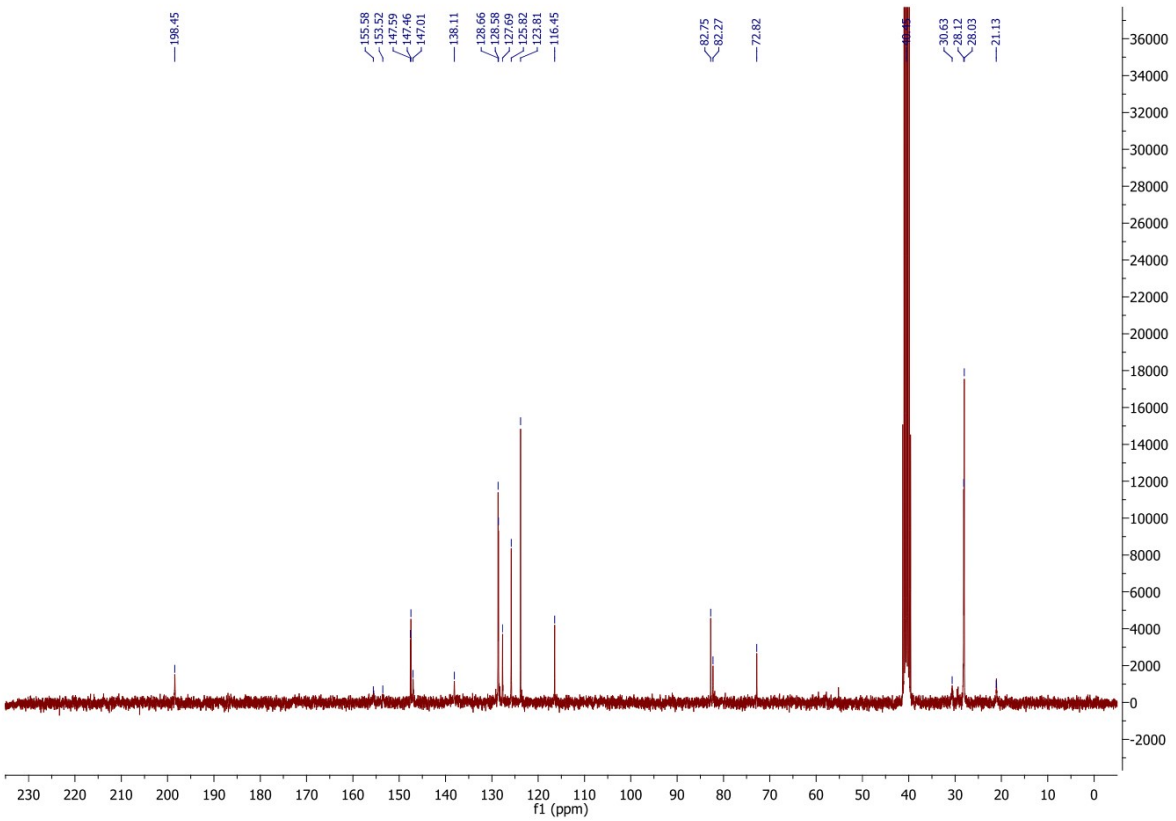


DMSO-d_6, 80°C

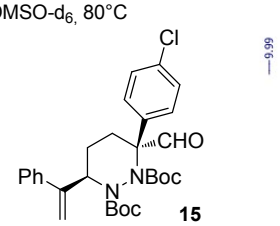


14
Major diastereomer



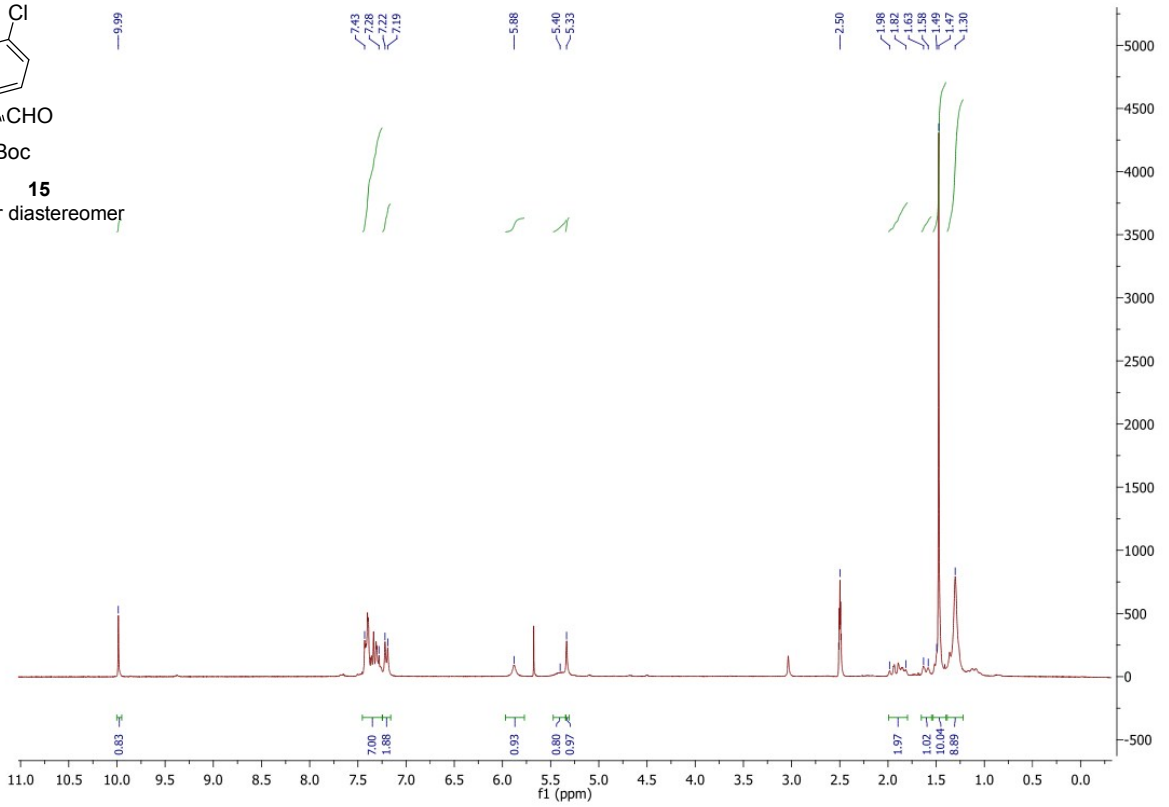


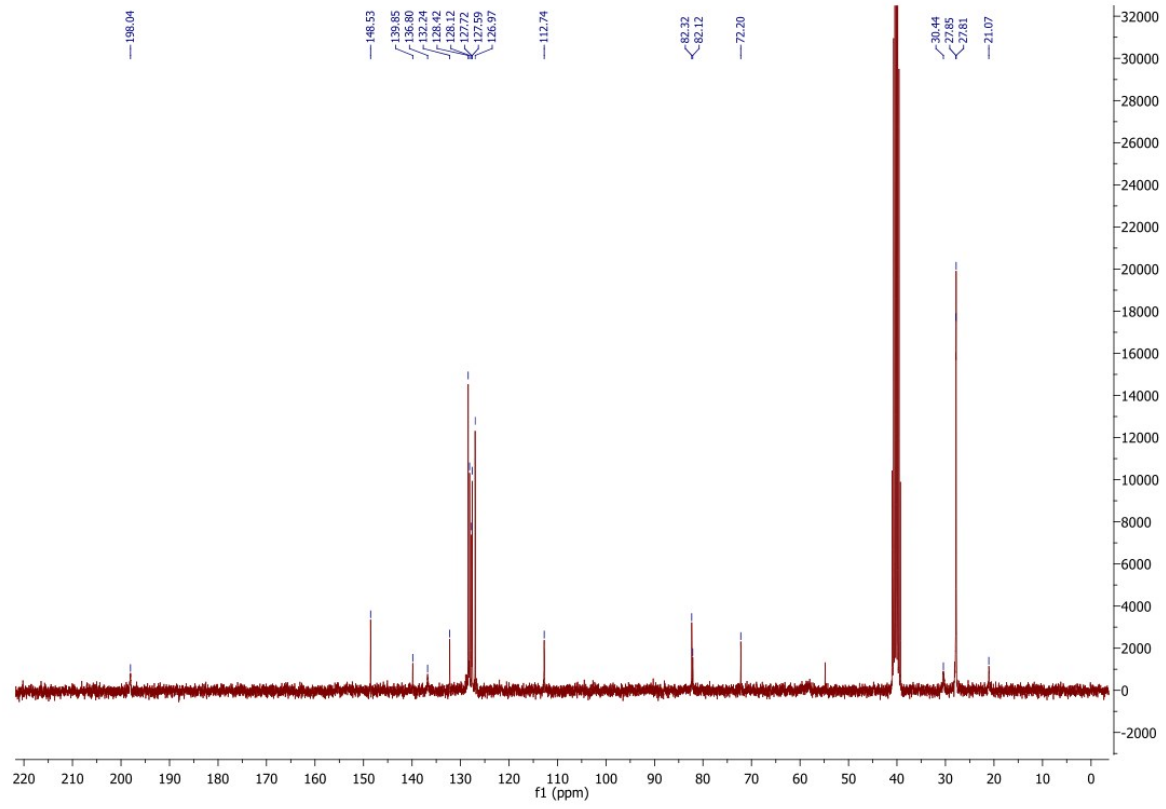
DMSO-d_6, 80°C

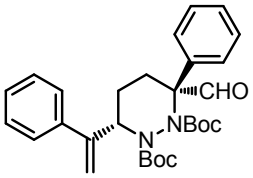


15

Major diastereomer

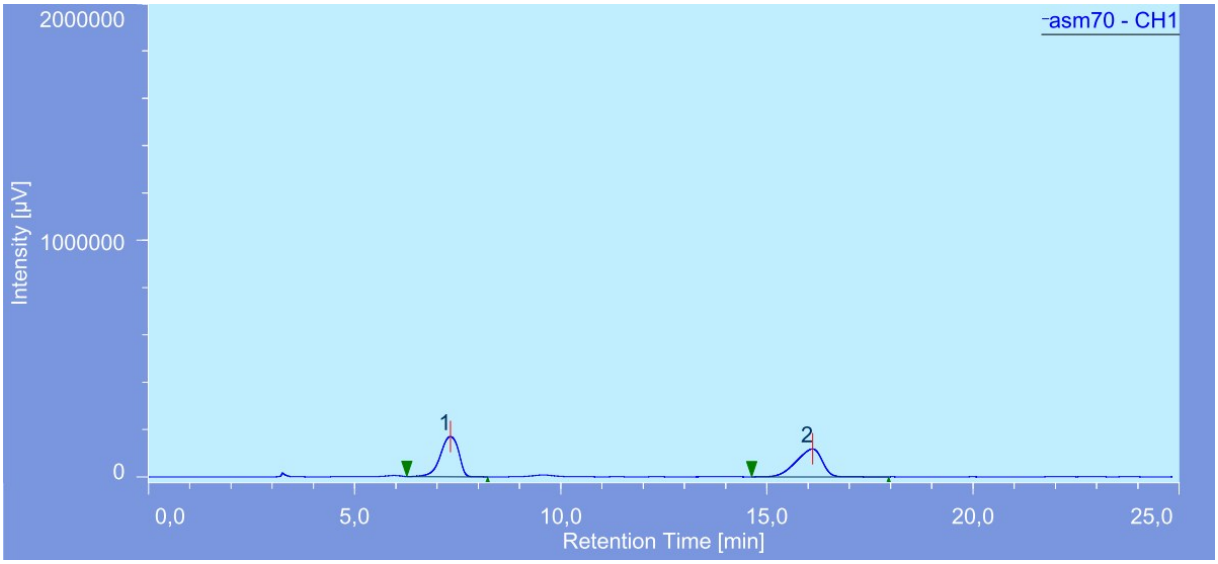






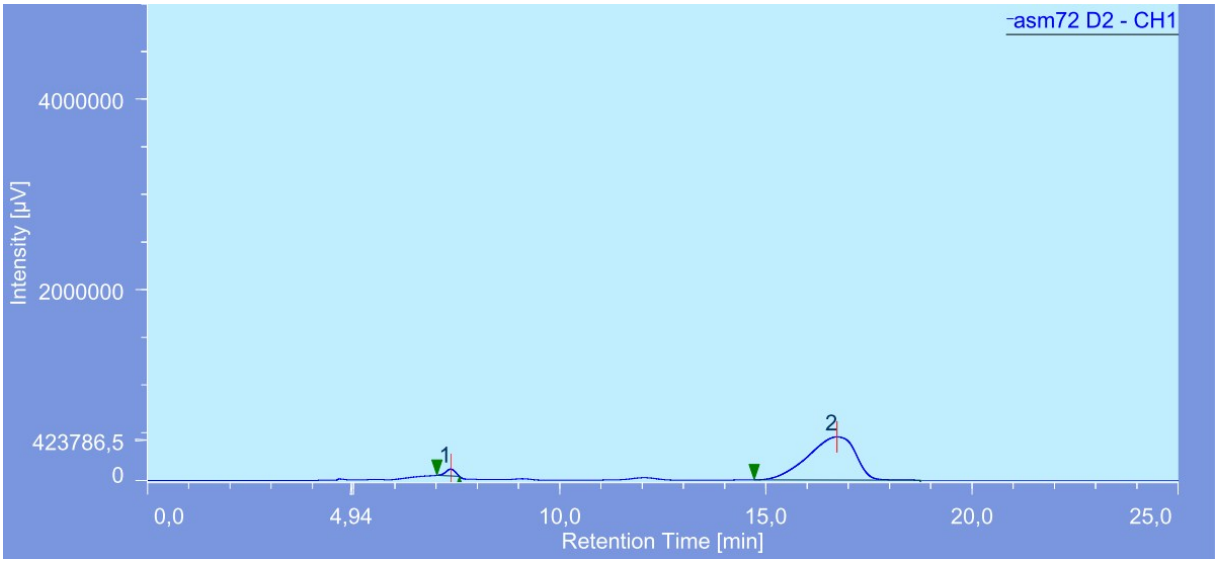
7
(minor diastereomer)

Racemic sample (chiral AD column, 30°C, heptane/2-propanol, 98/2, 1.0 mL/min)

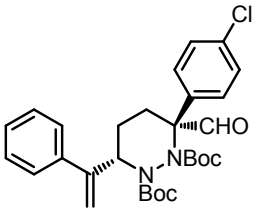


#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%
1	Unknown	1	7,318	5209968	169489	50,422	58,963
2	Unknown	1	16,103	5122833	117958	49,578	41,037

Enantioenriched sample (chiral AD column, 30°C, heptane/2-propanol, 98/2, 1.0 mL/min)

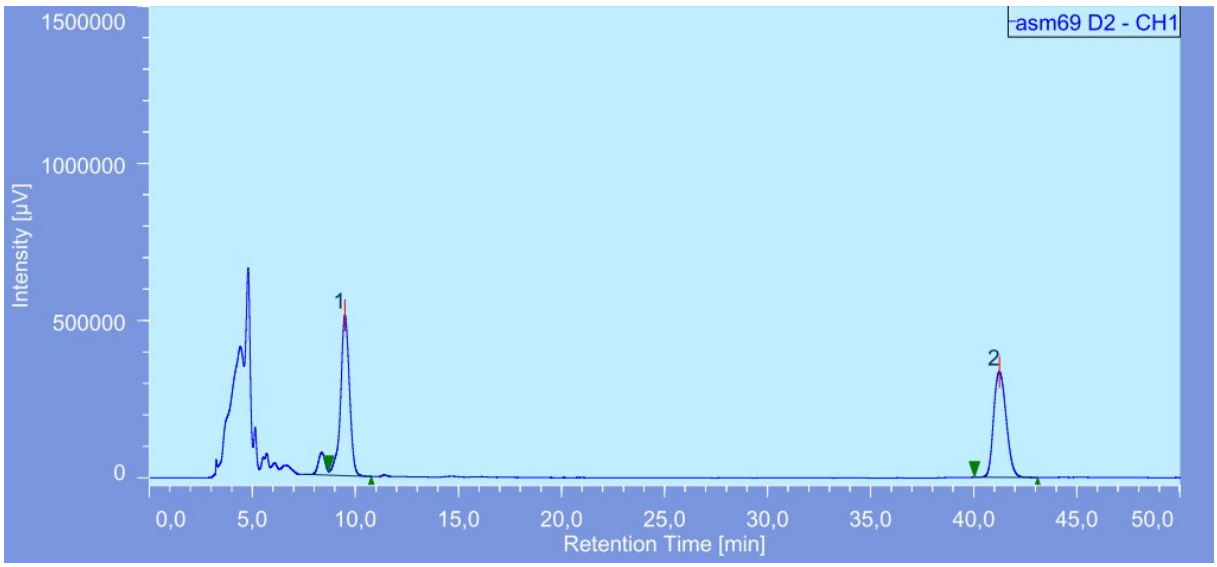


#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%
1	Unknown	1	7,353	1122325	71402	3,015	13,645
2	Unknown	1	16,725	36108403	451879	96,985	86,355



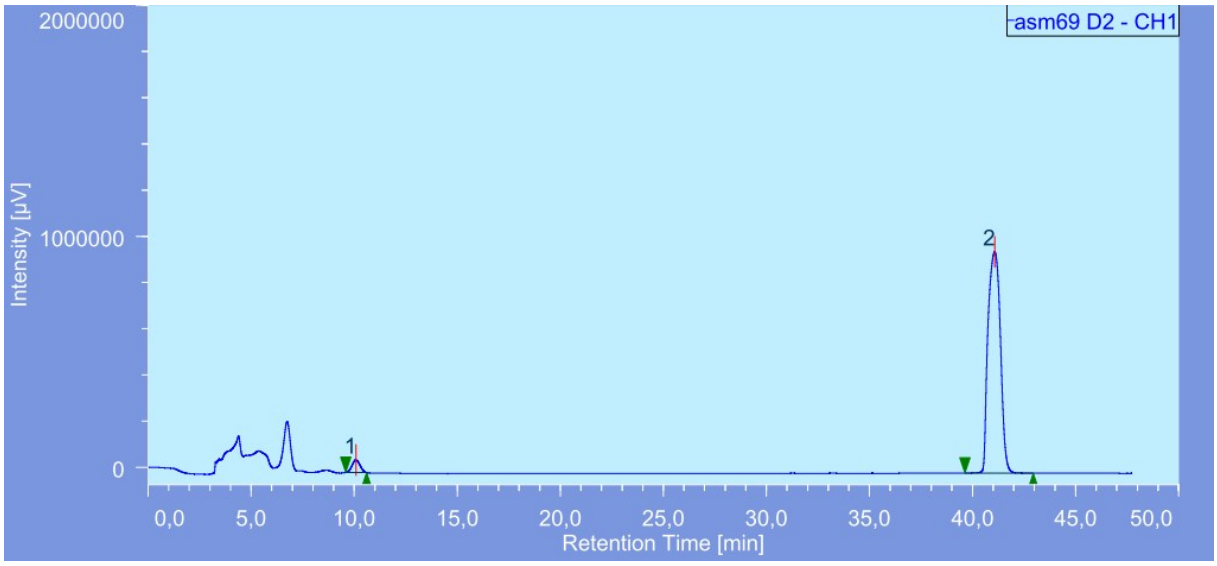
15
(minor diastereomer)

Racemic sample (chiral OD-H column, 30°C, heptane/2-propanol, 98/2, 1.0 mL/min)



#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%
1	Unknown	1	9,488	15325319	510617	51,863	60,353
2	Unknown	1	41,232	14224123	335433	48,137	39,647

Enantioenriched sample (chiral OD-H column, 30°C, heptane/2-propanol, 98/2, 1.0 mL/min)



#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%
1	Unknown	1	10,078	1452636	54022	3,510	5,347
2	Unknown	1	41,062	39930886	956277	96,490	94,653