Electronic Supplementary Information

Trapping of chiral enolates generated by Lewis acid promoted conjugate addition of Grignard reagents to unreactive Michael acceptors by various electrophiles

D. Vargová, J. M. Pérez, S. R. Harutyunyan, R. Šebesta*

Contents

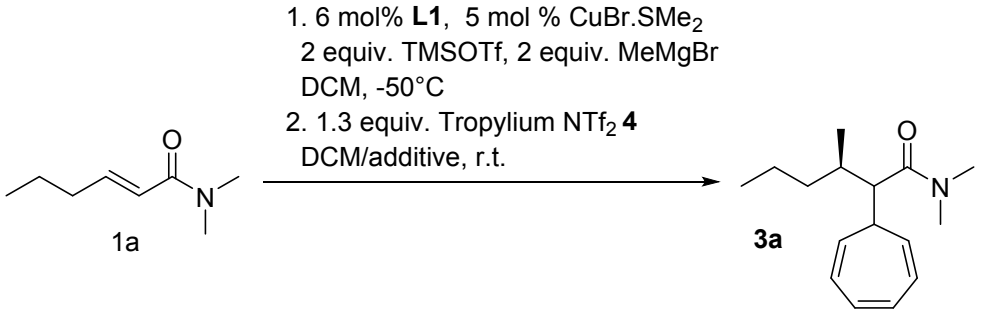
General experimental information

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 and GC-MS. (GC, HP6890: MS HP5973) with an HP5 column (Agilent Technologies, Palo Alto, CA). Purification of the products was performed by column chromatography using Merck 60 A 230-400 mesh silica gel. Components were visualized by UV and $KMnO_4$ staining. NMR data was collected on Agilent MR 400 with Varian 5mm OneNMR probe (^{1}H at 400.0 MHz; ^{13}C at 100.58 MHz) and or Varian Mercury Plus 300 with Varian 5 mm PFG AutoSW probe (^{1}H at 300.0 MHz; ^{19}F at 282 MHz). 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). 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). When possible, signals of minor diastereomers are in italic. 1D ^{19}F spectra were acquired with inverse-gated ^{1}H decoupling. Assignments of peaks were performed with the assistance of 2D NMR experiments including COSY, HSQC and HMBC. 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.

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. Diisopropyl amine was dried over CaH_2 and distilled 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 (3.0 M in Et_2O), *i*BuMgBr, cyclopentylMgBr (2.0 M in Et_2O). *n*BuLi was purchased from Sigma-Aldrich as a 1.6 M solution in hexanes. Enamides and heteroarene substrates were available from previous research.[7–9] Chiral ligands (**L1**, **L2**) were purchased from Solvias. (*R*)-BINAP was purchased from TCI. The BF_4 salts of tropylium and benzo[1,3]dithiol-1-ium were purchased from TCI. The cations were characterized by ^1H and ^{19}F NMR and compared with literature data. *Benzo[1,3]dithiol-1-ium bis((trifluoromethyl)sulfonyl)amide is stable in a nitrogen-flushed flask at -23 °C for several months. 5,6-Dihydro-4H-1,3-dithiin-1-ium bis((trifluoromethyl)sulfonyl)amide was only used freshly prepared. Tropylium bis((trifluoromethyl)sulfonyl)amide was stored up to one week at -23 °C in a nitrogen flushed flask. After more than two weeks a drop in the yields was observed.* All new compounds were fully characterized by ^1H and ^{13}C NMR and HRMS techniques. Enantiomeric ratios of the conjugated addition products were determined, and are assumed to be the same, as for the tandem products. For the same CA products one representative HPLC chromatogram is shown.

Optimization of trapping reaction

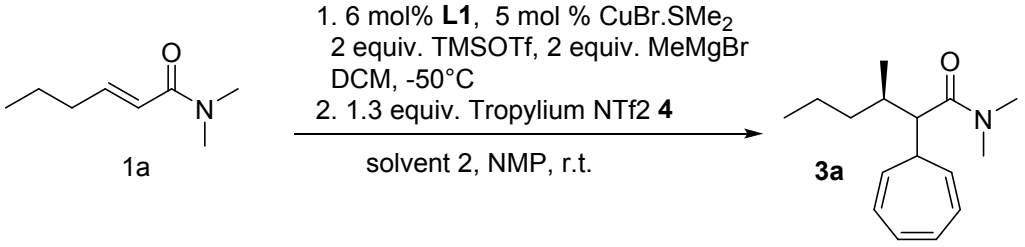
Table S1: Screening of additives in the trapping reaction:



Entry	Additive 4.4 equiv.	Conversion (%)	Yield **3a** (%)	dr
1	-	25	19[a]	59:41
2	DMF	32	6	nd
3	DMPU	37	9	nd
4	NMP	33	21	59:41
5	DMEU	45	27	54:46

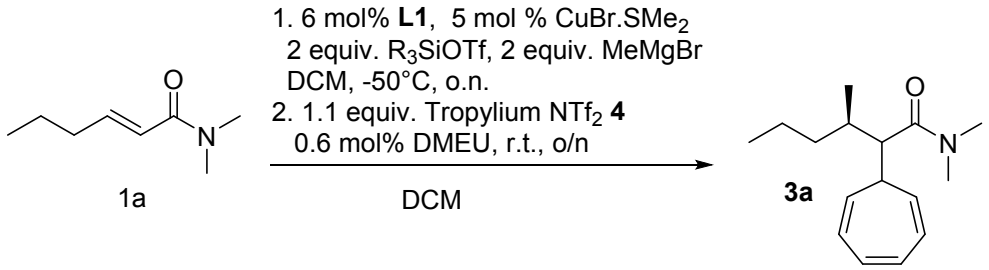
[a] 1.1 equiv. of tropylium NTf_2 **4** added.

Table S2: Screening of solvents in the trapping reaction:



Entry	Solvent 2	Additive	Conversion (%)	Yield **3a** (%)	dr
1	DCM	Y	28	19	53:47
2	THF	Y	11	0	n.d.
3	Trifluorotoluene	Y	0	0	-
4	2-Me-THF	Y	0	0	-
5	THF	N	37	15	53:47
6	2-Me-THF	N	11	n.d.	n.d.

Table S3: The effect of different silyl triflates on the dr of **3a** in the trapping reaction:

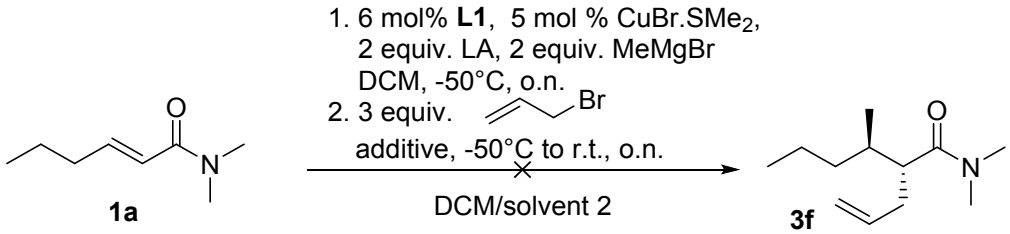


Entry	R_3SiOTf	Conversion (%)	Yield **3a**	dr
1	TMSOTf	75	59	56:44
2	TESOTf	75	48	56:44
3	TIPSOTf	69	57	56:44
4	TBSOTf	56	23	55:45
5	TBDPSOTf	49	33	n.d.[a]

[a]Due to the large amount of TBDPSOTf residue it is not clear from the crude.

Presumably, the ee of the reaction is also affected, the ee's were not determined.

Table S4: Screening of conditions for trapping of Pd-allyl cation **9**:



Entry	LA	Additive	Solvent 2
1	TMSOTf	$Pd(PPh_3)_4$[a]	DCM
2	TMSOTf	DMPU	DCM
3	TMSOTf	DMPU	THF
4	TMSOTf[b]	DMPU	PhMe
5	$BF_3.Et_2O$[c]	DMEU	DCM
6	$BF_3.Et_2O$[c]	-	DCM
7	TMSOTf	MeLi, LiCl, $Pd(PPh_3)_4$[a]	THF

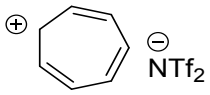
[a] 5 mol % CuI was used; [b] Reaction was performed without ligand; [c] EtMgBr was used.

Synthesis of cations

The cations were prepared according to the procedure reported previously.[1]

Carbenium tetrafluorborate (1.0 mmol) and $LiNTf_2$ (1.0 mmol, 287 mg) were combined in a mixture of H_2O (2.5 mL) and EtOAc (2.5 mL) and then stirred for 2 h. After separation of layers, organic phase was dried over anhydrous $MgSO_4$, filtered and solvent was evaporated under reduced pressure. The crude product was dried at high vacuum overnight.

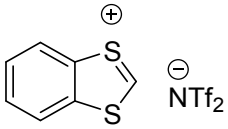
Cyclohepta-2,4,6-trien-1-ylium bis((trifluoromethyl)sulfonyl)amide **4**



91% yield, red-brown solid

^{1}H NMR (300 MHz, CD_2Cl_2) δ 9.32 (s, 7H).
^{19}F NMR (282 MHz, CD_2Cl_2) δ -79.5.
Spectral data are in agreement with literature data.[1a]

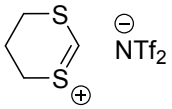
Benzo[d][1,3]dithiol-1-ium bis((trifluoromethyl)sulfonyl)amide **5**



85% yield, red solid

^{1}H NMR (300 MHz, CD_2Cl_2) δ 11.71 (s, 1H), 8.72 (dd, J = 5.9, 2.9 Hz, 3H), 8.16 (dd, J = 6.4, 3.2 Hz, 3H).
^{19}F NMR (282 MHz, CD_2Cl_2) δ -79.5.
Spectral data are in agreement with literature data.[1a]

5,6-Dihydro-4H-1,3-dithiin-1-ium bis((trifluoromethyl)sulfonyl)amide **6**



55% yield after two steps, orange slurry

^{1}H NMR (300 MHz, CD_2Cl_2) δ 5.91 (br s, 1H), 3.84 – 2.91 (m, 2H), 2.86 – 1.80 (m, 4H).

^{19}F NMR (282 MHz, CD_2Cl_2) δ -79.3.
Spectral data are in agreement with literature data.[1b]

Trapping of enamides

Procedure A: With tropylium cation

In a flame-dried Schlenk tube equipped with septum and magnetic stirring bar, CuBr.SMe_2 (5 mol%) and **L1** (6 mol%) were dissolved in DCM (1.0 mL), and stirred under nitrogen atmosphere for 20 min. The substrate (0.212 mmol, 1.0 equiv.) was added at once. After stirring for 5 min at r.t. the reaction mixture was cooled down to -50 °C (or -78 °C), and TMSOTf (2.0 equiv) was added. After 20 min, RMgBr (2.0 equiv, 3M or 2M in Et_2O) was added and stirred for 18 h at the same temperature. Cation (1.1 equiv) was dissolved in DCM (0.07 M), and DMEU (15 µL per 0.233 mmol of tropylium cation) (*takes about 5 minutes to dissolve*) and added to the reaction mixture at -50 °C and stirred overnight at ambient temperature in the absence of light. The reaction was quenched by 2 mL of NH_4Cl, extracted to DCM (3 x 10 mL), dried over $MgSO_4$, filtered and the solvent was evaporated. The products were obtained after column chromatography on SiO_2 with pentane/Et_2O. All the trapping products stain yellow with $KMnO_4$, while the CA products stain white. The trapping product has always a higher R_f value, than the CA product.

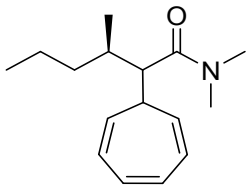
Procedure B: With benzoditiolium cation

The same procedure was used for CA as in procedure A. Benzo[*d*][1,3]dithiol-1-ium bis((trifluoromethyl)sulfonyl)amide **5** was dissolved in DCM (0.07M) and added to the reaction mixture at -50 °C and stirred overnight at ambient temperature in the absence of light. The work-up follows the same procedure as in A.

HPLC of the CA product isolated from the trapping reaction mixture was measured. The enantiomeric excesses were compared with the data reported in the literature.[2] Since the values are comparable, within experimental error, it was shown, that the enantiomeric ratios do not change during the course of the trapping reaction. For products, where the conjugate addition step follows the same procedure one representative HPLC is given.

The absolute configurations on the carbons in position 3 were assigned configurations as reported previously. The relative stereochemistry was assigned by X-ray crystallography (see details below). The stereogenic center on carbon 2 for products with nearly 1:1 diastereomeric ratio is not indicated.

(3R)-2-(cyclohepta-2,4,6-trien-1-yl)-N,N,3-trimethylhexanamide **3a**



CA was performed at -50°C. Column chromatography on SiO_2 with pentane/Et_2O 5:1.

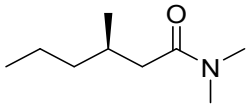
59% yield, *er* 99:1, yellow oil, major diastereomer was obtained pure, minor only as mixture inseparable from major.

Major diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.72 – 6.51 (m, 2H), 6.18 (ddd, *J* = 9.9, 6.0, 4.0 Hz, 2H), 5.54 (dd, *J* = 9.5, 6.4 Hz, 1H), 5.21 (dd, *J* = 9.5, 6.6 Hz, 1H), 3.08 (s, 3H), 3.00 (s, 3H), 2.89 (t, *J* = 7.8 Hz, 1H), 2.25 (q, *J* = 7.1 Hz, 1H), 2.03 (dtd, *J* = 9.6, 6.8, 2.6 Hz, 1H), 1.44 – 1.31 (m, 2H), 1.22 – 1.03 (m, 2H), 0.91 – 0.81 (m, 6H).

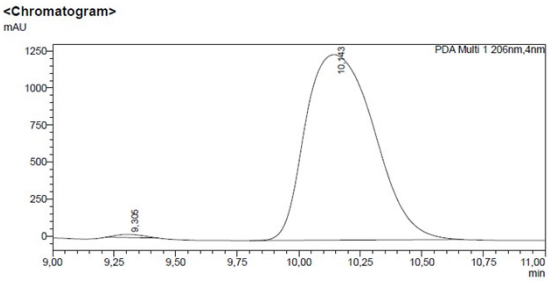
Major diastereomer: ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.5, 133.5, 132.9, 127.7, 127.5, 126.9, 125.9, 48.9, 42.3, 40.8, 38.8, 38.2, 36.8, 23.2, 19.7, 16.9.

HRMS (ESI+, *m/z*): calcd for $C_{16}H_{26}NO$ $[M+H]^+$: 248.2009, found: 248.2010.

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

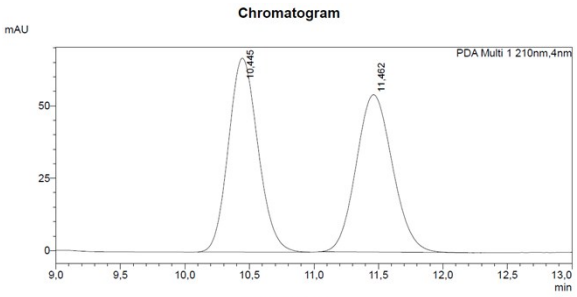


HPLC: Chiracel-OBH, *n*-heptane/*i*-PrOH 95:5, 0.5 mL/min, 40 °C, detection at 210 nm. Retention time (min): 10.4 (minor) and 11.5 (major).



<Peak Table>
PDA Ch1 206nm

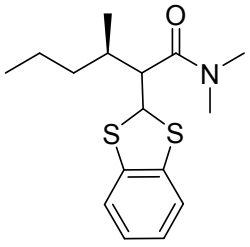
Name	Area	Ret. Time	Area%	Height
	162659	9,305	0,663	21336
	24357843	10,143	99,337	1253018
	24520502		100,000	1274354



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	

(3R)-2-(Benzo[d][1,3]dithiol-2-yl)-N,N,3-trimethylhexanamide **3b**



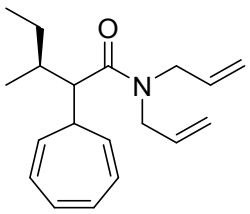
CA was performed at -50°C. Column chromatography on SiO_2 with pentane/Et_2O 10:1.
25% yield, *er* 99:1, red solid, inseparable mixture of diastereomers

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 – 7.15 (m, 2H), 7.12 – 6.95 (m, 2H), 5.23 (dd, *J* = 17.7, 10.8 Hz, 1H), 3.29 (ddd, *J* = 10.9, 4.0, 2.0 Hz, 1H), 3.01 – 2.93 (overlapping singlets, 6H), 2.13 (s, 1H), 1.53 – 1.25 (m, 2H), 1.25 – 1.05 (m, 2H), 1.01 – 0.81 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.9, 174.9, 140.2, 140.1, 139.8, 139.7, 128.2, 128.2, 128.1, 128.1, 125.3, 125.2, 125.1, 125.1, 58.3, 57.9, 55.6, 54.7, 40.9, 40.9, 39.9, 38.4, 36.9, 36.4, 23.5, 23.3, 20.3, 17.0, 16.8, 16.8.

HRMS (ESI+, m/Z): calcd for $C_{16}H_{24}NOS_2$ $[M+H]^+$: 310.1294, found: 310.1291.

(3S)-N,N-Diallyl-2-(cyclohepta-2,4,6-trien-1-yl)-3-methylpentanamide **3f**



CA was performed at -50°C. Column chromatography on SiO_2 with pentane/Et_2O 3:1.

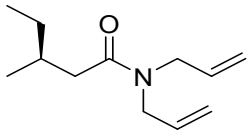
25% yield, *er* 79:21, yellow oil, inseparable mixture of diastereomers

Mixture of diastereomers: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.63 – 6.52 (m, 2H), 6.12 (dt, *J* = 9.8, 3.1 Hz, 2H), 5.80 – 5.63 (m, 2H), 5.52 – 5.39 (m, 1H), 5.22 – 5.05 (m, 5H), 4.08 – 3.83 (m, 4H), 2.81 (dt, *J* = 11.6, 7.2 Hz, 1H), 2.25 – 2.06 (m, 1H), 1.91 (ttd, *J* = 10.4, 6.9, 3.7 Hz, 1H), 1.44 (dddd, *J* = 25.0, 13.2, 7.4, 3.8 Hz, 1H), 1.04 (ddd, *J* = 17.2, 8.6, 5.2 Hz, 1H), 0.88 – 0.74 (m, 6H).

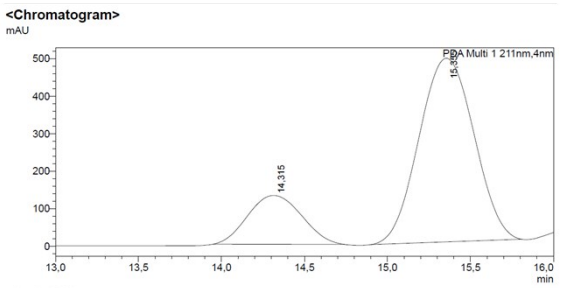
Mixture of diastereomers: ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.0, 176.8, 136.19, 136.17, 136.12, 136.1, 133.6, 133.5, 133.0, 132.9, 127.7, 127.6, 127.5, 127.4, 127.1, 126.8, 125.9, 125.7, 120.5, 120.4, 120.18, 120.15, 52.5, 52.4, 50.3, 50.3, 48.9, 48.0, 42.7, 42.4, 39.0, 38.4, 30.0, 29.6, 19.1, 18.9, 14.9, 14.2.

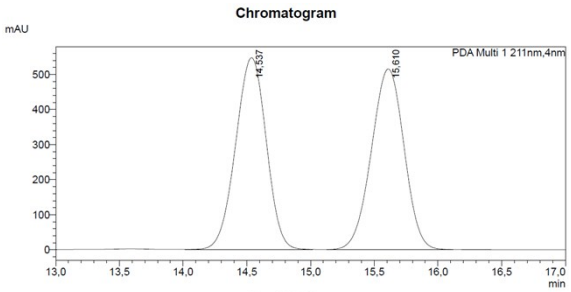
HRMS (ESI+, m/Z): calcd for $C_{19}H_{27}NO$ $[M+H]^+$: 286.2165, found: 286.2160.

(S)-N,N-Diallyl-3-methyl-pentanamide



HPLC: Chiracel-ODH, *n*-heptane/*i*-PrOH 99:01, 0.5 mL/min, 40 °C, detection at 211 nm. Retention time (min): 14.5 (minor) and 15.6 (major).





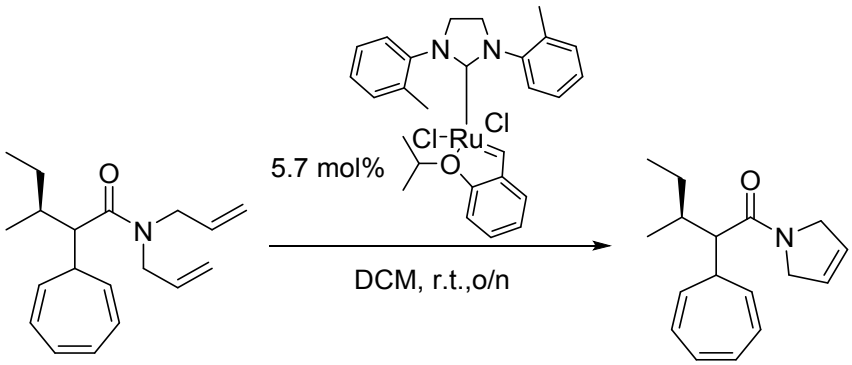
<Peak Table>
PDA Ch1 211nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	14,315	2928762	130170	20,603		M	
2	15,355	11286689	489529	79,397		M	
Total		14215451	619699				

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	

(3S)-2-(Cyclohepta-2,4,6-trien-1-yl)-1-(2,5-dihydro-1H-pyrrol-1-yl)-3-methylpentan-1-one **9**



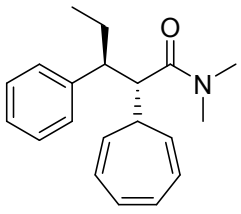
Hoveyda-Grubbs catalyst (1.7 mg, 0.003 mmol, 5.7 mol%) was dissolved in 1mL of dry DCM, and the substrate (15.0 mg, 0.053 mmol) was added in dry DCM (2 mL) and left to stir overnight. The solvent was evaporated, and the reaction mixture was filtered through a small pad of silica gel in hexane/Et_2O 1:1 to get rid of the catalyst. Evaporation of the solvent afforded the crude product.

95% yield, *er* 79:21, yellow oil

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.72 – 6.56 (m, 2H), 6.20 (dt, *J* = 10.7, 5.8 Hz, 2H), 5.89 (dd, *J* = 5.3, 3.1 Hz, 1H), 5.79 (dd, *J* = 6.5, 3.4 Hz, 1H), 5.59 (ddd, *J* = 22.1, 9.5, 6.4 Hz, 1H), 5.22 (td, *J* = 10.0, 6.6 Hz, 1H), 4.39 – 4.20 (m, 4H), 2.67 (dt, *J* = 12.3, 7.6 Hz, 1H), 2.35 (q, *J* = 6.9 Hz, 1H), 2.21 (q, *J* = 6.9 Hz, 1H), 2.08 – 1.91 (m, 1H), 1.57 – 1.31 (m, 1H), 1.24 – 1.01 (m, 1H), 0.94 – 0.80 (m, 6H).

HRMS (ESI+, m/Z): calcd for $C_{17}H_{24}NO$ $[M+H]^+$: 258.1852, found: 258.1850.

(2R,3S)-2-(Cyclohepta-2,4,6-trien-1-yl)-N,N-dimethyl-3-phenylpentanamide **3g**



CA was performed at -50°C. Column chromatography on SiO_2 with pentane/Et_2O 3:1.

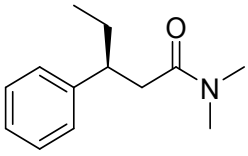
24% yield, *er* 77:23, white solid

Major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (t, *J* = 7.2 Hz, 2H), 7.09 (t, *J* = 7.2 Hz, 1H), 7.03 (d, *J* = 7.0 Hz, 2H), 6.50 – 6.41 (m, 2H), 6.03 (dtd, *J* = 15.7, 5.8, 2.3 Hz, 2H), 5.47 – 5.39 (m, 1H), 5.08 – 4.99 (m, 1H), 3.09 (t, *J* = 8.0 Hz, 1H), 2.93 (td, *J* = 9.2, 7.6, 3.3 Hz, 1H), 2.86 (s, 3H), 2.57 (s, 3H), 2.24 (q, *J* = 6.8 Hz, 1H), 1.66 (ddq, *J* = 25.2, 13.5, 6.6 Hz, 2H), 0.59 (t, *J* = 7.2 Hz, 3H).

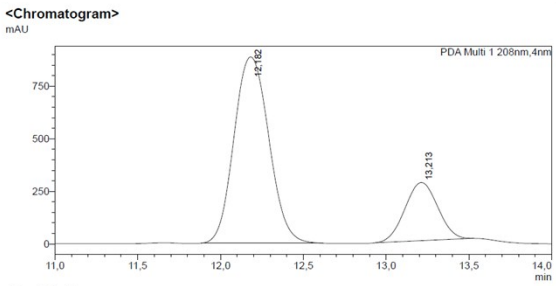
Major diastereomer: ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.3, 133.3, 132.8, 131.1, 130.8 (2C), 129.0, 127.7, 127.7, 126.8, 125.7, 51.3, 49.4, 43.0, 40.2, 38.2, 26.3, 15.0.

HRMS (ESI+, *m/z*): calcd for $C_{20}H_{25}NONa$ $[M+Na]^+$: 318.1828, found: 318.1828.

(S)-N,N-Dimethyl-3-phenylpentanamide

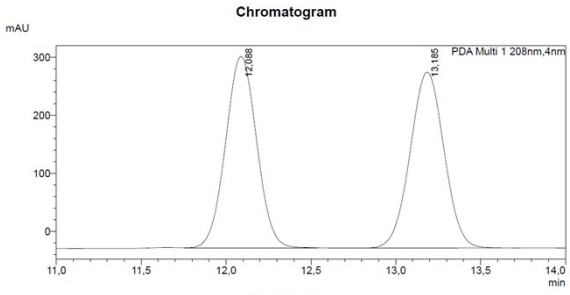


HPLC: Chiracel-ODH, *n*-heptane/*i*-PrOH 90:10, 0.5 mL/min, 40 °C, detection at 208 nm. Retention time (min): 12.1 (major) and 13.3 (minor).



<Peak Table>
PDA Ch1 208nm

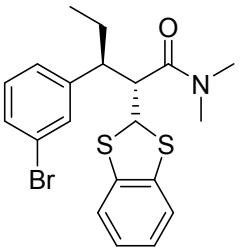
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	12,182	12981773	885590	77,277		M	
2	13,213	3817161	276448	22,723		M	
Total		16798934	1162037				



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	

(2R,3S)-2-(Benzo[d][1,3]dithiol-2-yl)-3-(3-bromophenyl)-N,N-dimethylpentanamide **3h**



CA was performed at -78°C, 2 equiv. of cation were used in this case. Column chromatography on SiO_2 with pentane/Et_2O 3:1.

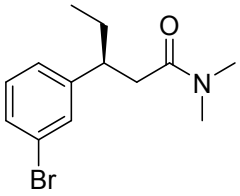
40% yield, *er* 65:35, white crystals, inseparable mixture of diastereomers

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (d, *J* = 7.7 Hz, 1H), 7.24 (s, 1H), 7.19 – 7.09 (m, 2H), 7.07 (d, *J* = 7.6 Hz, 1H), 7.02 (d, *J* = 7.5 Hz, 1H), 7.00 – 6.94 (m, 2H), 5.20 (d, *J* = 10.4 Hz, 1H), *4.83 (d, J = 10.0 Hz, 1H)*, *3.49 (dd, J = 9.9, 7.2 Hz, 1H),* 3.31 (dd, *J* = 10.3, 5.2 Hz, 1H), 3.15 (dt, *J* = 11.7, 4.4 Hz, 1H), 2.79 (s, 3H), *2.74 (s, 1H),* 2.18 (s, 3H), 1.90 – 1.67 (m, 2H), *0.87 (t, J = 7.3 Hz, 3H),* 0.64 (t, *J* = 7.3 Hz, 3H).

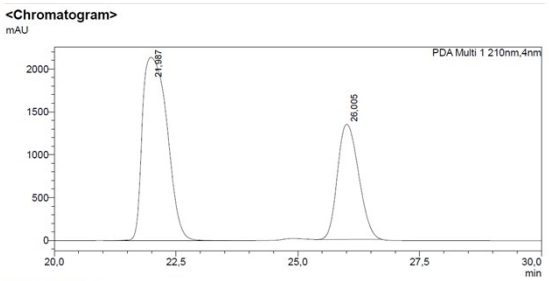
^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 146.8, *142.3*, 139.9, 139.4, *134.9*, 134.0, 132.65, 132.61, *132.56*, *132.2*, *130.9*, 130.0, 128.3, 128.2, 125.3, *125.2*, 125.1, *124.9*, *58.1,* 57.8, 56.5, *56.2, 51.5,* 50.7, *40.8*, 39.9, 38.2, *37.4*, 24.0, *15.1,* 14.9.

HRMS (ESI+, *m/z*): calcd for $C_{20}H_{25}NONa$ $[M+Na]^+$: 318.1828, found: 318.1828.

(S)-N,N-Dimethyl-3-(3-bromophenyl)pentanamide

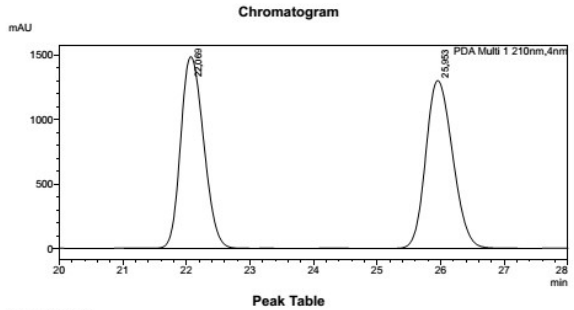


HPLC: Chiracel-ODH, *n*-heptane/*i*-PrOH 97:2, 0.5 mL/min, 40 °C, detection at 210 nm. Retention time (min): 22.0 (major) and 26.0 (minor).



<Peak Table>
PDA Ch1 210nm

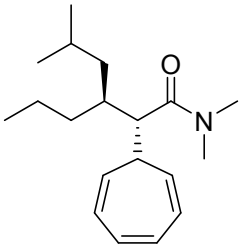
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	21,987	75807070	2136703	65,083		V	
2	26,005	40670613	1342665	34,917		M	
Total		116477683	3479368				



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	

(2S,3S)-2-(Cyclohepta-2,4,6-trien-1-yl)-N,N,5-trimethyl-3-propylhexanamide **3i**



CA was performed at -50°C. Column chromatography on SiO_2 with pentane/Et_2O 10:1.

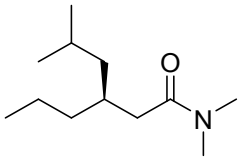
59% yield, *er* 97:3, yellow oil

Major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.67 – 6.55 (m, 2H), 6.22 (dd, *J* = 9.4, 4.2 Hz, 1H), 6.18 – 6.13 (m, 1H), 5.50 – 5.41 (m, 1H), 5.26 (q, *J* = 7.5 Hz, 1H), 3.02 (q, *J* = 8.2, 7.2 Hz, 1H), 3.00 (s, 3H), 2.96 (s, 3H), 2.63 – 2.54 (m, 1H), 1.89 – 1.76 (m, 1H), 1.66 – 1.58 (m, 1H), 1.57 – 1.46 (m, 1H), 1.34 – 1.15 (m, 2H), 1.06 (dt, *J* = 13.4, 6.5 Hz, 2H), 0.88 (*overlapping t*, *J* = 7.2 Hz, 3H), 0.84 (d, *J* = 4.2 Hz, 3H), 0.83 (d, *J* = 4.4 Hz, 3H).

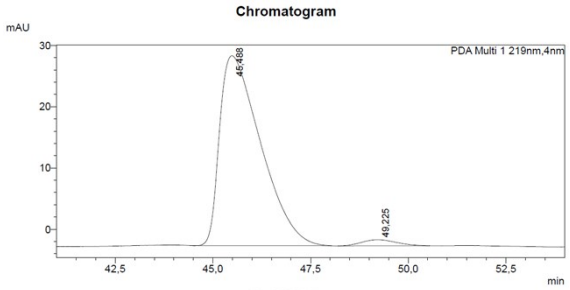
Mixture of diastereomers: ^{13}C NMR (101 MHz, $CDCl_3$) δ *177.07*, 177.01, *133.35,* 133.30, 132.93, *132.90*, 128.02, 127.95, 127.73, *127.69*, 127.63, *127.51*, 126.48, *126.41*, 44.92, *44.80*, 43.86, *42.50*, *42.23*, 42.12, *40.66*, 40.59, *38.88*, 38.81, *38.28*, 38.25, 36.24, 35.57, *28.34*, 28.29, *26.74*, 25.56, 25.46, *24.44*, 23.22, *22.39*, 17.12, 17.07.

HRMS (ESI+, *m/z*): calcd for $C_{19}H_{32}NO$ $[M+H]^+$: 290.2478, found: 290.2479.

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



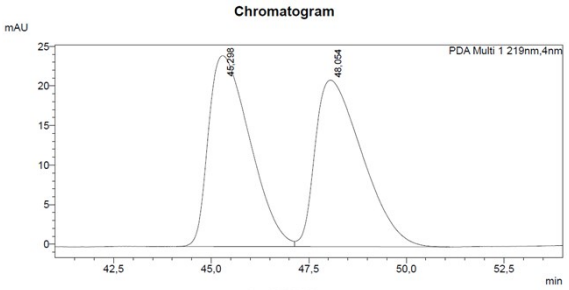
HPLC: Chiracel-ADH, *n*-heptane/*i*-PrOH 95.5:0.5, 0.5 mL/min, 40 °C, detection at 219 nm. Retention time (min): 45.5 (major) and 59.2 (minor).



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	

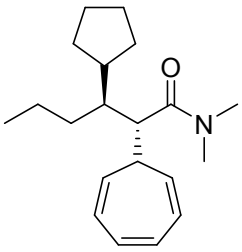


Peak Table

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	

(2S,3S)-2-(Cyclohepta-2,4,6-trien-1-yl)-3-cyclopentyl-N,N-dimethylhexanamide **3j**



CA was performed at -50°C. Column chromatography on SiO_2 with pentane/Et_2O 10:1.

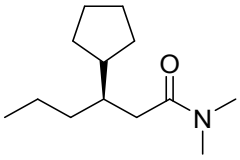
44% yield, *er* 99:1, yellow oil, mixture of diastereomers

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.61 – 6.51 (m, 2H), 6.11 (ddd, *J* = 14.5, 9.3, 4.8 Hz, 2H), 5.51 (dd, *J* = 9.5, 6.5 Hz, 1H), *5.38 (dd, J = 9.6, 6.7 Hz, 1H)*, *5.23 – 5.19 (m, 1H)*, 5.16 (dd, *J* = 9.5, 6.8 Hz, 1H), 2.99 (s, 3H), 3.04 – 2.92 (m, 1H), 2.89 (s, 3H), *2.50 – 2.42 (m, 1H)*, 2.32 (q, *J* = 7.2 Hz, 1H), 1.92 (ddt, *J* = 17.2, 10.1, 7.1 Hz, 1H), 1.78 (p, *J* = 5.4 Hz, 1H), 1.75 – 1.63 (m, 1H), 1.61 – 1.33 (m, 4H), 1.30 – 0.95 (m, 6H), 0.76 (t, *J* = 6.9 Hz, 3H).

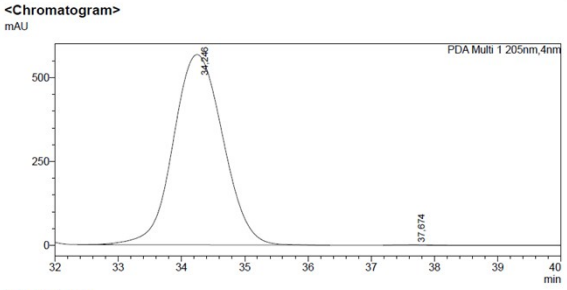
^{13}C NMR (101 MHz, $CDCl_3$) δ 177.4, 133.5, *133.3*, *132.9*, 132.8, *127.9*, 127.8, *127.4*, 127.1, *126.7*, 125.9, *46.0*, 45.9, 45.4, 44.9, *42.9*, 42.5, *40.8*, 40.7, 38.4, *38.3*, 34.5, 34.3, *34.2*, *33.8*, *32.0*, 31.8, *28.3*, 28.1, 28.0, *27.7*, *26.1*, 24.2, *17.4*, 17.2.

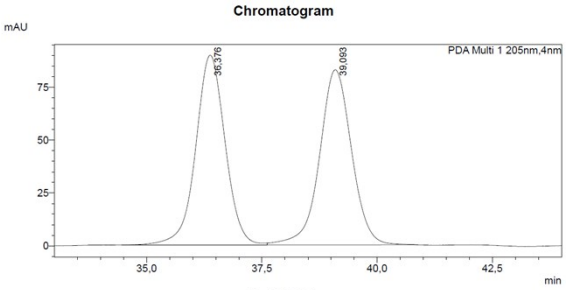
HRMS (ESI+, *m/z*): calcd for $C_{20}H_{32}NO$ $[M+H]^+$:302.2478, found: 302.2478.

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



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).





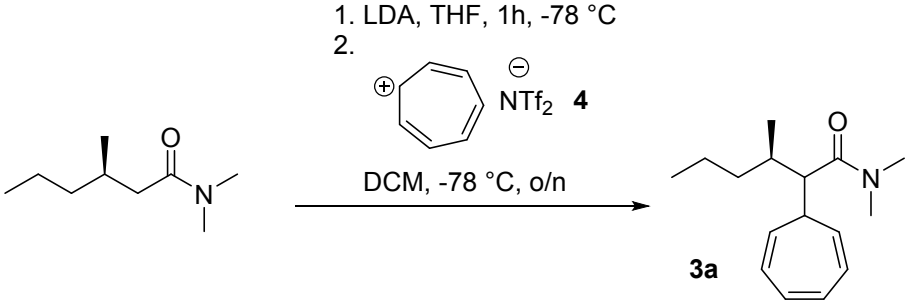
<Peak Table>
PDA Ch1 205nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	34,246	30969457	566884	99,868		S	
2	37,674	40922	974	0,132		V	
Total		31010379	567858				

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	

Synthesis of **3a** via Li-**2**:



Diisopropyl amine (0.031 mL, 0.219 mmol, 1.15 equiv.) was dissolved in THF (0.1 mL) and cooled down to -78 °C. *n*BuLi (0.131 mL, 0.210 mmol, 1.1 equiv, 1.6 M in hexane) was added dropwise, and the reaction was stirred for 30 min. (*R*)-*N*,*N*-Dimethyl-3-methyl-hexanamide

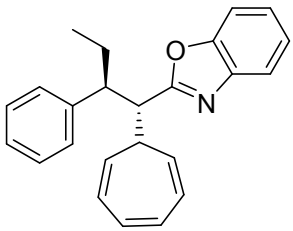
(30.0 mg, 0.191 mmol, 1.0 equiv) was dissolved in THF (0.3 mL) and added dropwise to the solution. The reaction was stirred at - 78 °C for 1 h, before tropylium NTf_2 **4** (77.9 mg, 0.210 mmol, 1.1 equiv) dissolved in DCM (2.6 mL) and DMEU (15 µL) was added dropwise, and let to stir overnight at -78 °C. The reaction was quenched with 0.1 mL of MeOH, followed by 2 mL NH_4Cl and let to warm to room temperature. The reaction was extracted with DCM (3 x 10 mL), dried over $MgSO_4$, filtered, and the solvent was evaporated. The crude mixture was analyzed by GC-MS.

Trapping of heteroarenes

Conditions A: In a heat-dried Schlenk tube equipped with septum and magnetic stirring bar, CuBr·SMe_2 (5 mol %), and ligand **L2** (6 mol %) were dissolved in Et_2O (0.1 M) and stirred under nitrogen atmosphere for 15 min. The substrate (1.0 equiv.) was added at once. After stirring for 5 min. at r.t. the reaction mixture was cooled to −78 °C and $BF_3.Et_2O$ (1.2 equiv.) was added followed by EtMgBr (1.2 equiv.). The reaction was stirred at −78 °C for 4 h. Cation (1.5 equiv.) was dissolved in DCM (0.07 M), and DMEU (only for tropylium cation) (15 µL per 0.233 mmol of tropylium cation) (*takes about 5 minutes to dissolve*) and added to the reaction mixture at -78 °C and stirred overnight at ambient temperature in the absence of light. The reaction was quenched by 2 mL of NH_4Cl, extracted to DCM (3x10 mL), dried over $MgSO_4$, filtered and the solvent was evaporated. The products were obtained after column chromatography on SiO_2 with pentane/Et_2O. All the trapping products stain yellow with $KMnO_4$, while the CA products stain white. The trapping product has a higher R_f value, than the CA product in most cases.

Conditions B: In a heat dried Schlenk tube equipped with septum and magnetic stirring bar, CuBr·SMe_2 (10 mol %), and ligand **L2** (12 mol %) were dissolved in DCM (0.1 M) and stirred under nitrogen atmosphere for 15 min. The substrate (1.0 equiv) was added at once. After stirring for 5 min. at r.t. the reaction mixture was cooled to −78 °C and TMSOTf (3.0 equiv) was added followed by RMgBr (3.0 equiv). The reaction was stirred at −78 °C for 16 h. The addition of cation and work-up follows the same procedure are in A.

2-((1R,2S)-1-(Cyclohepta-2,4,6-trien-1-yl)-2-phenylbutyl)benzo[d]oxazole **12a**



Prepared using conditions A. Column chromatography on SiO_2 with pentane/Et_2O 20:1.

64% yield, *er* 99:1, colorless crystals.

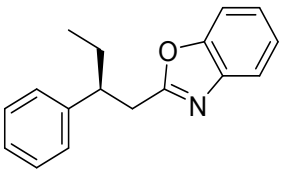
Major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.71 (m, 1H), 7.58 – 7.50 (m, 1H), 7.39 – 7.29 (m, 2H), 7.24 (ddd, *J* = 7.6, 5.2, 1.6 Hz, 3H), 7.16 – 7.11 (m, 2H), 6.54 – 6.43 (m, 2H), 6.14 (dt, *J* = 9.6, 4.7 Hz, 1H), 6.00 (dd, *J* = 9.6, 5.0 Hz, 1H), 5.69 (dd, *J* = 9.6, 5.9 Hz, 1H), 5.12 (dd, *J* = 9.5, 5.9 Hz, 1H), 3.64 (dd, *J* = 10.3, 6.1 Hz, 1H), 3.34 (td, *J* = 10.8, 3.6 Hz,

1H), 1.78 (q, *J* = 6.0 Hz, 1H), 1.65 (ddd, *J* = 13.6, 6.7, 4.3 Hz, 1H), 1.50 (dqd, *J* = 14.4, 7.3, 3.5 Hz, 1H), 0.64 (t, *J* = 7.3 Hz, 3H).

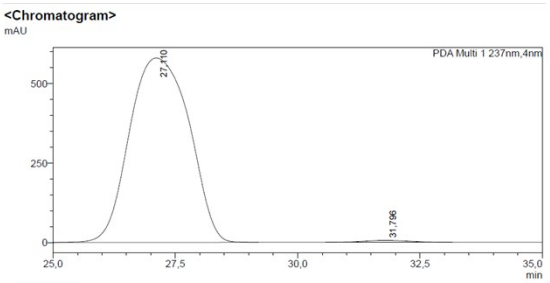
^{13}C NMR (101 MHz, $CDCl_3$) δ *165.64*, 166.61, 149.6, *149.4*, 140.6, 140.1, *140.0*, *139.9*, *130.2*, 129.8, *129.6*, 129.5, 127.38, *127.36*, 127.2, *126.9*, 125.7, *125.5*, *124.27*, *124.25*, 124.1, 123.62, 123.61, *123.3*, 123.2 *122.9*, 122.2, *122.1*, *122.0*, 121.1, 118.9, *118.7*, 109.5, 109.3, 48.1, *47.4*, 47.2, *45.7*, 39.4, *38.5*, 25.7, *25.3*, *11.2*, 11.0.

HRMS (ESI+, *m/z*): calcd for $C_{24}H_{24}NO$ $[M+H]^+$: 342.1852, found: 342.1858.

(S)-2-(2-phenylbutyl)benzoxazole

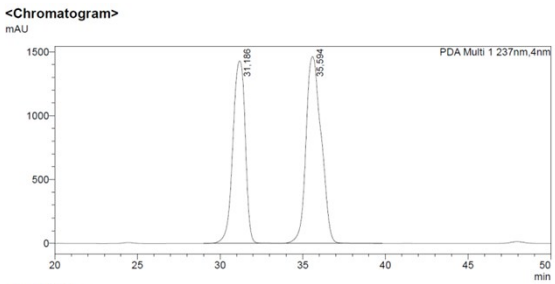


HPLC: Chiracel-OZH, *n*-heptane/*i*-PrOH 99.5:0.5, 0.5 mL/min, 40 °C, detection at 237 nm. Retention time (min): 31.2 (major) and 36.0 (minor).



<Peak Table>
PDA Ch1 237nm

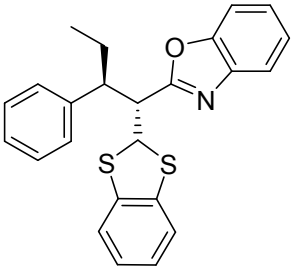
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	27,110	49224077	579573	99,163			
2	31,796	415624	6115	0,837			
Total		49639700	585688				



<Peak Table>
PDA Ch1 237nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	31,186	74615772	1428286	44,336			
2	35,594	93680623	1461716	55,664		SV	
Total		168296396	2890002				

2-((1R,2S)-1-(Benzo[d][1,3]dithiol-2-yl)-2-phenylbutyl)benzo[d]oxazole **12b**



Prepared using conditions B. Column chromatography on SiO_2 with pentane/Et_2O 10:1.

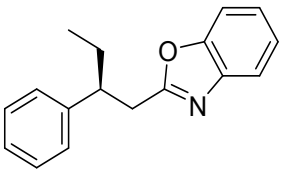
46% yield, *er* 55: 45, white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 – 7.48 (m, 1H), 7.35 – 7.26 (m, 2H), 7.23 – 7.12 (m, 6H), 7.02 (d, *J* = 7.7 Hz, 1H), 6.79 (d, *J* = 7.7 Hz, 1H), 6.65 (t, *J* = 7.6 Hz, 1H), 6.53 (t, *J* = 7.6 Hz, 1H), 4.80 (d, *J* = 4.8 Hz, 1H), 3.57 (dd, *J* = 9.8, 5.1 Hz, 1H), 3.44 (td, *J* = 10.3, 3.8 Hz, 1H), 1.62 – 1.40 (m, 2H), 0.59 (t, *J* = 7.3 Hz, 3H).

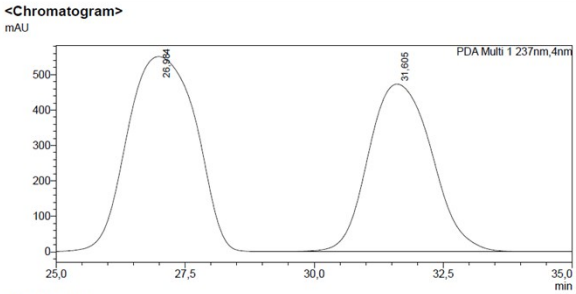
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.9, 152.9, 143.4, 143.3, 139.7, 139.0, 131.7, 130.9, 129.9, 127.8, 127.5, 127.2, 126.6, 124.7, 124.6, 122.3, 112.9, 57.6, 56.9, 50.8, 28.9, 14.5.

HRMS (ESI+, *m/z*): calcd for $C_{24}H_{22}NOS_2$ $[M+H]^+$: 404.1137, found: 404.1130.

(S)-2-(2-phenylbutyl)benzoxazole



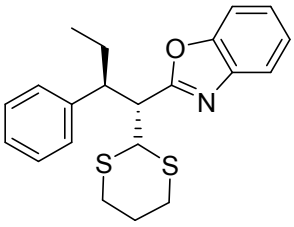
HPLC: Chiracel-OZH, *n*-heptane/*i*-PrOH 99.5:0.5, 0.5 mL/min, 40 °C, detection at 237 nm. Retention time (min): 31.2 (major) and 36.0 (minor).



<Peak Table>
PDA Ch1 237nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	26,984	50733191	550042	55,711			
2	31,605	40330994	472258	44,289			
Total		91064185	1022301				

2-((1R,2S)-1-(1,3-Dithian-2-yl)-2-phenylbutyl)benzo[d]oxazole **12c**



Prepared using conditions B. Column chromatography on SiO_2 with pentane/Et_2O 2:1.

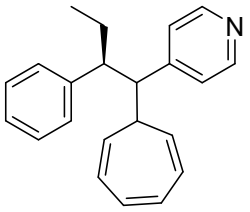
32% yield, *er* 55: 45, yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 – 7.74 (m, 1H), 7.57 (ddd, *J* = 8.0, 5.0, 3.3 Hz, 1H), 7.39 – 7.24 (m, 7H), 3.92 (d, *J* = 4.7 Hz, 1H), 3.70 (dd, *J* = 10.4, 4.7 Hz, 1H), 3.48 (td, *J* = 11.0, 3.3 Hz, 1H), 2.79 – 2.60 (m, 4H), 2.56 – 2.45 (m, 1H), 1.92 (d, *J* = 14.3 Hz, 1H), 1.79 – 1.66 (m, 1H), 1.58 (tdd, *J* = 7.3, 5.2, 2.7 Hz, 1H), 0.62 (t, *J* = 8.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 153.3, 143.7, 143.6 131.3, 131.0, 129.6, 127.5, 126.9, 122.9, 113.4, 54.1, 52.4, 50.5, 33.5, 33.0, 32.3, 28.9, 28.2, 14.5.

HRMS (ESI+, *m/z*): calcd for $C_{21}H_{24}NOS_2$ $[M+H]^+$: 370.1294, found: 370.1291.

4-((2S)-1-(Cyclohepta-2,4,6-trien-1-yl)-2-phenylbutyl)pyridine **12d**



Prepared using conditions B. Column chromatography on SiO_2 with pentane/Et_2O 10:1.

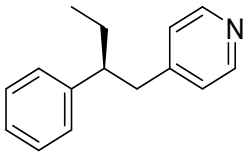
16% yield, *er* 99:1, white solid, mixture of diastereomers dr 1:1

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 5.5 Hz, 2H), *8.36 (d, J = 5.6 Hz, 2H)*, 7.20 (dq, *J* = 12.1, 6.8 Hz, 6H), 7.13 – 7.03 (m, 2H), 6.94 (d, *J* = 6.5 Hz, 1H), *6.84 (d, J = 6.0 Hz, 2H)*, *6.75 (dd, J = 10.9, 5.6 Hz, 1H)*, 6.62 (dd, *J* = 9.8, 5.9 Hz, 3H), 6.57 (d, *J* = 5.3 Hz, 2H), *6.38 (dd, J = 9.3, 5.6 Hz, 1H)*, 6.13 (dd, *J* = 9.4, 5.3 Hz, 1H), 6.00 (ddd, *J* = 14.2, 9.3, 5.5 Hz, 2H), *5.48 (dd, J = 9.3, 5.9 Hz, 1H)*, 5.18 (dd, *J* = 9.4, 6.0 Hz, 1H), 4.85 (dd, *J* = 9.3, 6.1 Hz, 1H), *4.78 (dd, J = 9.3, 6.0 Hz, 1H)*, *3.30 – 3.19 (m, 2H)*, 3.17 – 3.05 (m, 2H), 1.94 (dt, *J* = 11.0, 6.0 Hz, 1H), *1.89 – 1.72 (m, 2H)*, *1.67 (ddd, J = 13.3, 9.4, 7.0 Hz, 1H)*, 1.54 (ddt, *J* = 14.7, 7.4, 4.0 Hz, 1H), 1.47 – 1.31 (m, 1H), *0.86 (t, J = 7.3 Hz, 3H)*, 0.64 (t, *J* = 7.3 Hz, 3H).

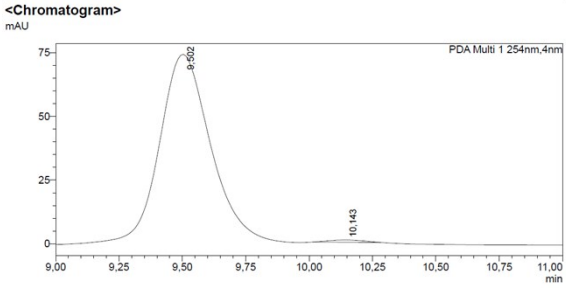
^{13}C NMR (101 MHz, $CDCl_3$) δ 153.0, 151.9, 151.5, 145.0, 142.2, 133.7, 133.4, 133.34, 133.33, 132.0, 131.3, 130.8, 130.2, 129.1, 129.1, 128.4, 127.8, 127.7, 127.2, 127.1, 127.0, 126.7, 126.6, 125.7, 125.5, 56.8, 54.8, 52.9, 51.7, 43.8, 43.3, 29.1, 25.7, 15.1, 14.9.

HRMS (ESI+, *m/z*): calcd for $C_{22}H_{24}N$ $[M+H]^+$: 302.1903, found: 302.1901.

(S)-4-(2-phenylbutyl)pyridine

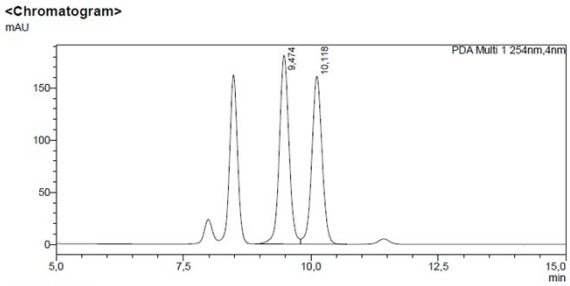


HPLC**:** (254 nm, Chiralcel OZ-H, *n*-heptane:*i*PrOH = 95:5, 40 °C, 1.0 ml/min.), t_R = 9.47 min (major), t_R = 10.11 min (minor).



<Peak Table>
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9,502	1045634	74242	99,192			
2	10,143	8519	902	0,808		M	
Total		1054153	75143				



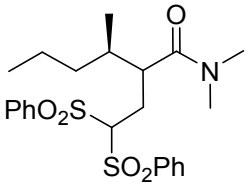
<Peak Table>
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9,474	2378298	180990	51,450			
2	10,118	2244221	160770	48,550		V	
Total		4622519	341760				

Trapping of enamides by activated alkenes

The conjugate addition step was performed in the same way, as described for the trapping of enamides above. Alkene (2.0 equiv) was dissolved in DCM (0.1M) and added to the reaction and stirred overnight at -50 °C. (Similar outcome was achieved, if the reaction was stirred at ambient temperature after the addition of alkene). The reaction was quenched by aq. NH_4Cl (2 mL), extracted to DCM (3 x 10 mL) and dried over $MgSO_4$, filtered and the solvent was evaporated.

(3R)-2-(2,2-bis(phenylsulfonyl)ethyl)-N,N,3-trimethylhexanamide **15a**



Column chromatography on SiO_2 with pentane/Et_2O 5:1.

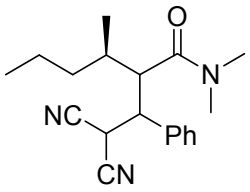
65% yield, *er* 99:1, yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 – 7.95 (m, 2H), 7.91 – 7.82 (m, 2H), 7.73 – 7.63 (m, 2H), 7.61 – 7.49 (m, 4H), 4.68 (dd, *J* = 11.0, 2.6 Hz, 1H), *4.57 (dd, J = 10.6, 2.6 Hz, 1H)*, 3.47 – 3.27 (m, 1H), 3.08 (2 s, 3H), 2.91 (s, 3H), 2.45 (ddt, *J* = 14.0, 11.2, 2.8 Hz, 1H), 2.22 – 2.01 (m, 1H), 1.66 (m, 1H), 1.38 – 1.20 (m, 3H), 1.24 – 1.05 (m, 1H), 0.93 – 0.80 (m, 3H), 0.75 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.91, 175.89, 140.7, 140.62, 140.58, 140.5, 140.3, 137.3, 137.3, 137.2, 137.1, 137.0, 132.6, 132.5, 131.95, 131.93, 131.84, 131.83, 131.77, 131.73, 131.61, 131.59, 84.5, 84.4, 46.4, 45.4, 40.4, 40.1, 39.7, 38.5, 38.42, 38.37, 37.7, 37.3, 28.1, 26.3, 23.3, 22.8, 20.0, 17.7, 16.84, 16.80.

HRMS (ESI+, *m/z*): calcd for $C_{23}H_{31}NO_5S_2$ $[M+H]^+$: 466.1716, found: 466.1715.

(3R)-2-(2,2-Dicyano-1-phenylethyl)-N,N,3-trimethylhexanamide **15b**



Trapping reaction performed at -78 °C. Column chromatography on SiO_2 with pentane/Et_2O 5:1.

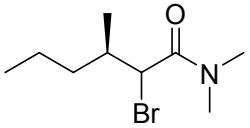
20% yield, *er* 99:1, white solid.

^{1}H NMR (400 MHz, $CDCl_3$, *signals of diastereomers are in italic*) δ 7.42 – 7.24 (m, 5H), *4.39 (d, J = 5.4 Hz), 4.32 (d, J = 5.2 Hz), 4.11 (d, J = 5.1 Hz), 4.06 (d, J = 5.1 Hz),* 3.68 (dddd, *J* = 20.6, 15.5, 10.8, 5.2 Hz, 1H), 3.48 – 3.32 (m, 1H), *3.10 (s, 1H), 3.09 (s, 1H), 2.97 (s, 1H), 2.83 (s, 2H), 2.80 (s, 1H), 2.59 (s, 2H), 2.57 (s, 1H),* 1.73 (tt, *J* = 6.7, 3.0 Hz, 1H), 1.61 – 1.10 (m, 4H), 1.01 (dd, *J* = 28.1, 6.8 Hz, 3H), 0.93 – 0.62 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 205.4, 174.5, 173.0, 138.9, 138.4, 131.9, 131.8, 131.6, 131.6, 131.1, 131.0, 131.0, 114.6, 114.4, 114.3, 50.6, 50.5, 49.4, 48.8, 48.7, 48.4, 41.0, 40.6, 40.6, 40.1, 38.6, 38.1, 38.1, 37.0, 36.6, 36.4, 35.9, 32.3, 30.5, 29.5, 29.4, 23.7, 23.3, 23.2, 20.5, 20.4, 17.0, 16.9, 16.7, 16.5.

HRMS (ESI-, *m/z*): calcd for $C_{19}H_{24}N_3O$ $[M-H]^-$: 310.1914, found: 310.1933.

(3R)-2-Bromo-N,N,3-trimethylhexanamide **15c**



The conjugate addition step was performed in the same way, as described above. NBS (41.5 mg, 0.233 mmol, 1.1 equiv.) was dissolved in DCM (3.0 mL) and added to the reaction mixture at -50 °C and stirred overnight at ambient temperature. The reaction was quenched with saturated NH_4Cl, and extracted to DCM, dried over anhydrous $MgSO_4$, and filtered through a pad of Celite, and the solvent was evaporated.

(*Using 3 equiv. of NBS led to a less clean reaction, with 40% conversion.)*

Column chromatography on SiO_2 with pentane/Et_2O 5:1.

22% yield, *er* 99:1, yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.20 (d, *J* = 8.9 Hz, 1H), 3.02 (s, 3H), 2.93 (s, 3H), 2.22 – 2.07 (m, 1H), 1.40 – 1.29 (m, 2H), 1.29 – 1.16 (m, 2H), 1.07 (d, *J* = 6.6 Hz, 3H), 0.82 (t, *J* = 6.9 Hz, 3H).

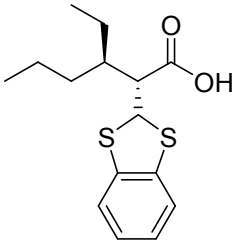
^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 54.3, 40.3, 39.0, 39.0, 38.9, 23.0, 20.3, 16.8.

HRMS (ESI+, m/Z): calcd for $C_9H_{19}BrNO$ $[M+H]^+$: 236.0645, found: 236.0646.

Trapping of carboxylic acids

In a flame-dried Schlenk tube equipped with septum and magnetic stirring bar, (*E*)-hexenoic acid (30.0 mg, 0.263 mmol, 1.0 equiv), $CuBr{\cdot}SMe_2$ (2.7 mg, 0.013 mmol, 5 mol%) and ligand (*R*)-Tol-Binap **L3** (10.7 mg, 0.016 mmol, 6 mol%) were dissolved in MTBE (2.6 mL) and stirred under nitrogen atmosphere for 20 min. at r.t. The mixture was cooled to −78 °C and *n*BuLi (0.164 mL, 0.263 mmol, 1.0 equiv) was added. After 5 min., TMSOTf (0.1 mL, 0.578 mmol, 2.2 equiv) was added, and the mixture was allowed to stir for 5 min before EtMgBr (0.13 mL, 0.394 mmol, 1.5 equiv) was added dropwise. The reaction mixture was stirred under nitrogen atmosphere for 2 h. A solution of tropylium NTf_2 (107.0 mg, 0.288 mmol, 1.1 equiv) in DCM (3.8 mL) and DMEU (20 µL) was added dropwise. After stirring for 16 h at ambient temperature, the reaction mixture was quenched by HCl aqueous solution (2.0 mL, 1.0 M) and extracted with DCM (3 x 10 mL). The combined organic phase was dried over $MgSO_4$, filtered and evaporated. The products were obtained after column chromatography on SiO_2 pentane to pentane/Et_2O 10:1. Precipitation by pentane followed by filtration removed most of the catalyst.

(3R)-2-(Benzo[d][1,3]dithiol-2-yl)-3-ethylhexanoic acid **18a**



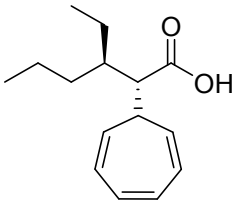
Yellow oil, *er* 99:1, 20% (small amount of BINAP present in the product)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 – 7.11 (m, 2H), 7.00 – 6.94 (m, 2H), 5.00 (d, *J* = 11.2 Hz, 1H), 2.99 (td, *J* = 11.5, 2.4 Hz, 1H), 1.92 – 1.81 (m, 1H), 1.58 – 1.45 (m, 1H), 1.42 – 1.33 (m, 2H), 1.17 – 1.13 (m, 2H), 1.12 – 0.93 (m, 1H), 0.90 – 0.79 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 177.3, 137.2, 136.2, 125.8, 125.7, 122.8, 122.6, 55.0, 53.5, 32.3, 31.1, 25.2, 23.0, 14.4, 14.1.

HRMS (ESI-, *m/z*): calcd for $C_{15}H_{19}O_2S_2$ $[M-H]^-$: 295.0821, found: 295.0835.

(3R)-2-(Cyclohepta-2,4,6-trien-1-yl)-3-ethylhexanoic acid **18b**



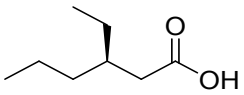
Yellow oil, *er* 99:1, 15% yield, the product was obtained as a mixture with the conjugate addition product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.66 – 6.55 (m, 2H), 6.16 (dd, *J* = 8.4, 3.9 Hz, 2H), 5.38 – 5.30 (m, 1H), 5.18 (dd, *J* = 9.2, 6.4 Hz, 1H), 2.77 (dt, *J* = 10.8, 5.6 Hz, 1H), 2.05 (dt, *J* = 15.9, 6.5 Hz, 1H), 1.38 – 1.14 (m, 5H), 0.85 – 0.77 (m, 6H).

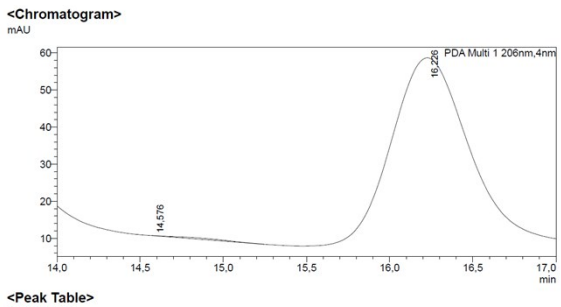
^{13}C NMR (101 MHz, $CDCl_3$) δ 178.4, 129.9, 129.5, 124.1, 123.9, 122.6, 121.3, 47.3, 37.2, 33.4, 31.1, 29.8, 18.5, 13.1, 9.6.

HRMS (ESI-, *m/z*): calcd for $C_{15}H_{21}O_2$ $[M-H]^-$: 233.1536, found: 233.1553.

(R)-3-Ethylhexanoic acid

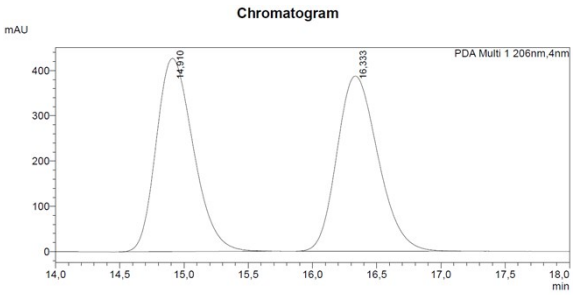


The *ee* of this compound was determined from the corresponding *N,N*-dimethyl amide derivate. HPLC: Chiracel-OBH, *n*-heptane/*i*-PrOH 98:2, 0.5 mL/min., 40 °C, detection at 206 nm. Retention time (min): 14.6 (minor) and 16.3 (major).



<Peak Table>
PDA Ch1 206nm

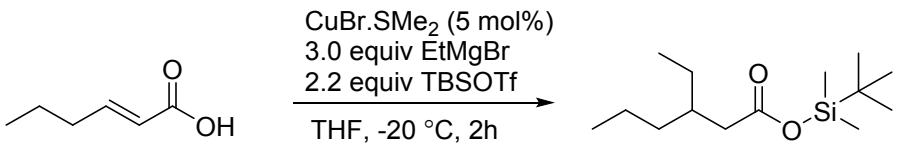
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	14,576	6454	19	0,405		M	
2	16,226	1587412	49968	99,595			
Total		1593867	49987				



Peak Table
PDA Ch1 206nm

Peak#	Ret. Time	Area	Height	Conc.
1	14,910	8571570	426940	49,943
2	16,333	8591130	386997	50,057
Total		17162699	813937	

Synthesis of TBS-ester intermediate



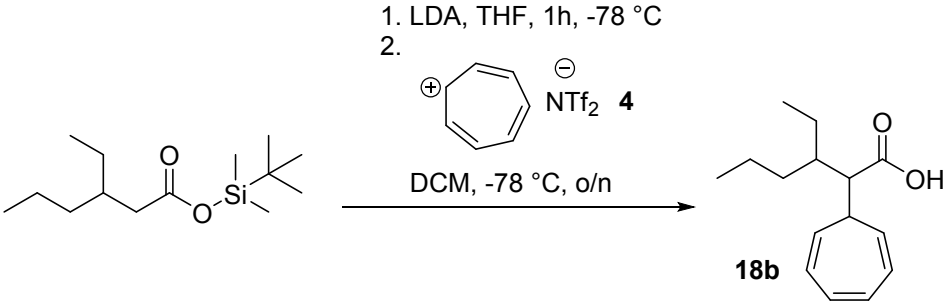
In a flame-dried Schlenk tube equipped with septum and magnetic stirring bar, hexenoic acid (70.0 mg, 0.613 mmol, 1.0 equiv.), $CuBr{\cdot}SMe_2$ (6.3 mg, 0.031 mmol, 5 mol%) and THF (6.1

mL) were added. The mixture was cooled to -20 °C and TBSOTf (0.313 mL, 1.363 mmol, 2.2 equiv.) was added. After 20 min., EtMgBr (0.613 mL, 1.840 mmol, 3.0 eq) was added dropwise, and the reaction mixture was allowed to stir for 2 h. The reaction was quenched with saturated $NaHCO_3$ aqueous solution (4.3 mL) and warmed to room temperature. The mixture was extracted with Et_2O (10.0 mL × 3). The combined organic phase was dried over $MgSO_4$, filtered and evaporated. Product was obtained as a colorless oil after column chromatography (SiO_2, pentane:Et_2O = 100:1) 30 mg, 19% yield.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.23 (d, J = 6.8 Hz, 2H), 1.84-1.72 (m, 1H), 1.43-1.18 (m, 6H), 0.93 (s, 9H), 0.91-0.85 (m, 6H), 0.26 (s, 6H).

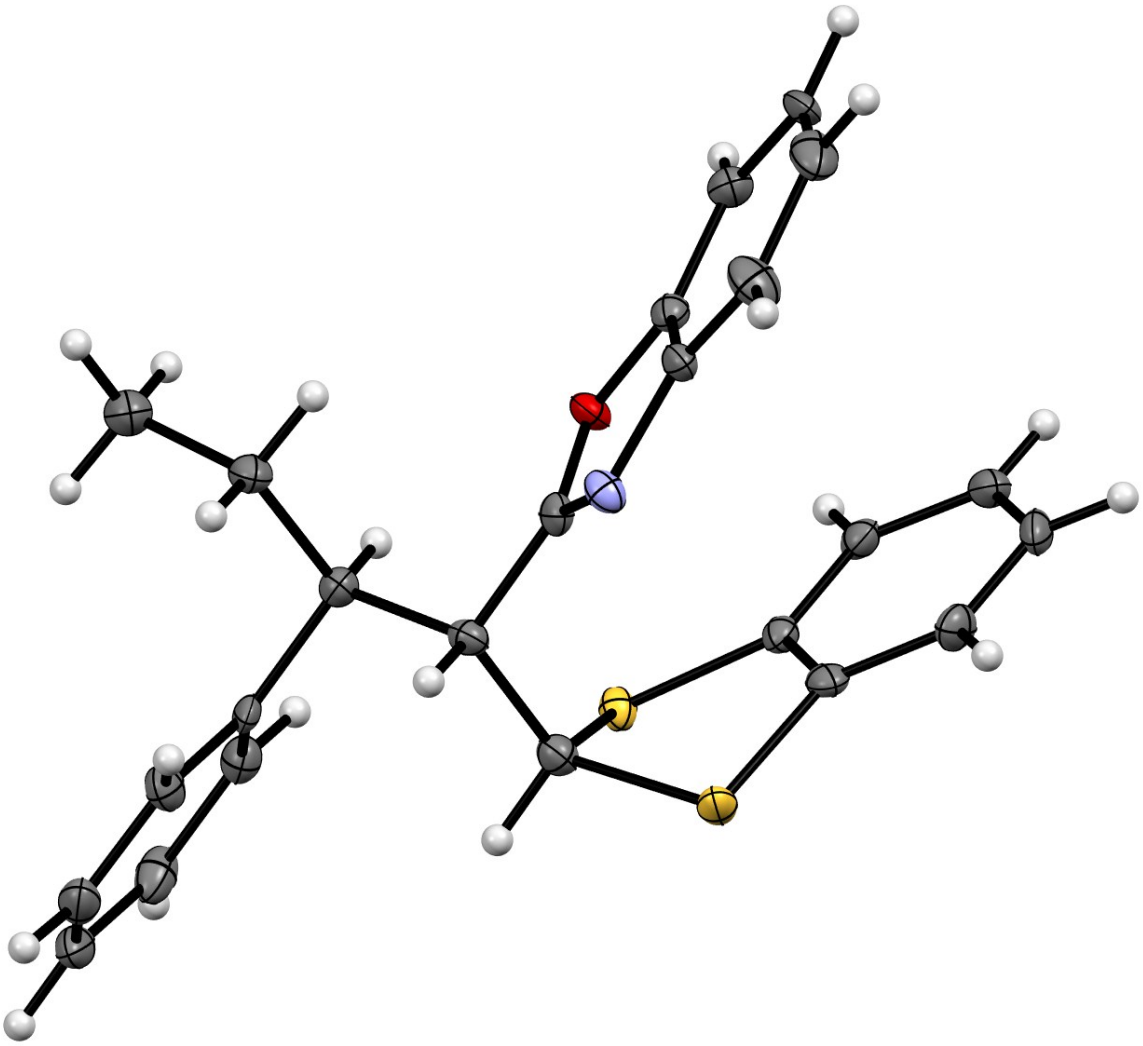
Spectral data are in agreement with literature data.[2d]

Synthesis of **18b** via lithiation of TBS-ester intermediate:



Diisopropyl amine (0.019 mL, 0.133 mmol, 1.15 equiv.) was dissolved in THF (0.1ml) and cooled down to -78 °C. *n*BuLi (0.080 mL, 0.128 mmol, 1.1 equiv., 1.6 M in hexane) was added dropwise, and the reaction was stirred for 30 min. TBS-ester intermediate (30.0 mg, 0.116 mmol, 1.0 equiv.) was dissolved in THF (0.4 ml) and added dropwise to the solution. The reaction was stirred at - 78 °C for 1 h, before tropylium **4** (47.4 mg, 0.128 mmol, 1.1 equiv.) dissolved in DCM (1.6 mL) and DMEU (9 µL) was added dropwise, and let to stir overnight. The reaction was quenched with 0.1ml of MeOH, followed by 2 ml NH_4Cl and let to warm to room temperature. The reaction was extracted with DCM (3x10 mL), dried over $MgSO_4$, filtered, and the solvent was evaporated. The crude mixture was analyzed by GC-MS.

X-ray crystallography



A suitable crystal of compound **12b** was mounted on top of a cryoloop and transferred into the cold (100 K) nitrogen stream of a Bruker D8 Venture diffractometer. Data collection and reduction was done using the Bruker software suite APEX3.[1] The final unit cell was obtained from the xyz centroids of 9944 reflections after integration. A multiscan absorption correction was applied, based on the intensities of symmetry-related reflections measured at different angular settings (*SADABS*).[1] The structures were solved by dual space methods using *SHELXT,*[2] and refinement of the structure was performed using *SHELXL*.[3] During the refinement, warning signs of twinning appeared and this was checked using PLATON/TWINROTMAT.[4] Data reduction was repeated using two components of which the orientation matrices were identified with program CELL_NOW.[5] Integration was done using SAINT and the data was corrected for absorption using TWINABS.[6] The structure was refined as described above (hklf4), except for the final refinements which were done using the hklf5 routine, which resulted in a BASF value of 0.134. The hydrogen atoms were generated by geometrical considerations, constrained to idealized geometries and allowed to ride on their carrier atoms with an isotropic displacement parameter related to the equivalent displacement parameter of their carrier atoms. The absolute configuration at C8 (R) was inferred from

[1] Bruker (2016) APEX3, SAINT and SADABS. Bruker AXS Inc., Madison, Wisconsin, USA.

[2] Sheldrick, G. M. (2015) Acta Cryst. A, 71, 3-8.

[3] Sheldrick, G. M. (2015) Acta Cryst. C, 71, 3-8.

[4] A. L. Spek, Acta Cryst. 2015, C71, 9–18.

[5] Sheldrick, G. M. (2008). CELL_NOW. Version 2008/4. Georg-August-Universität Göttingen, Göttingen, Germany.

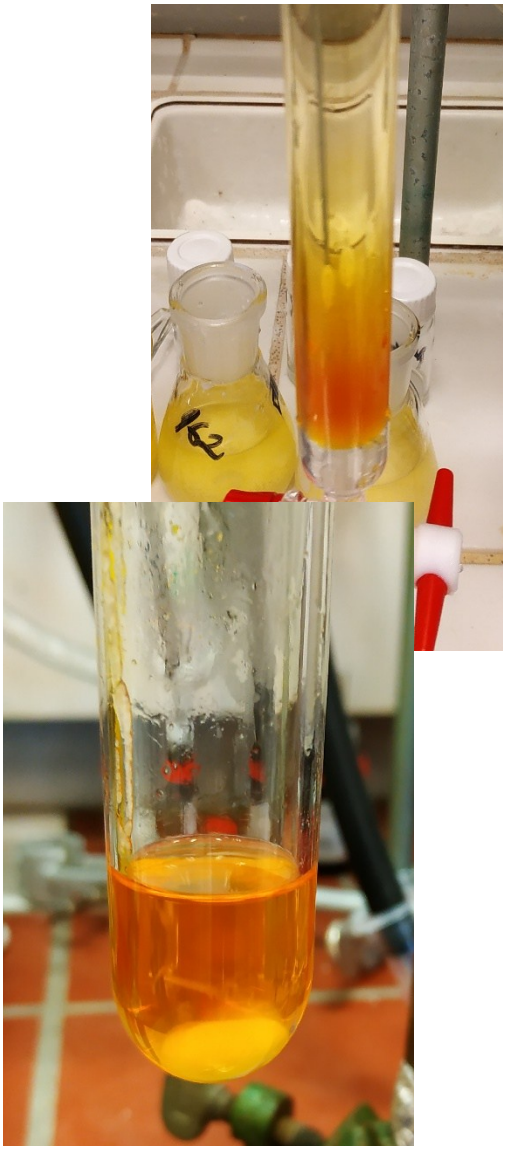
[6] Sheldrick, G. M. (2012). TWINABS. Version 2012/1. Georg-August-Universität Göttingen, Göttingen, Germany.

the known configuration at C16 (S). Crystal data and details on data collection and refinement are presented in Table S1.

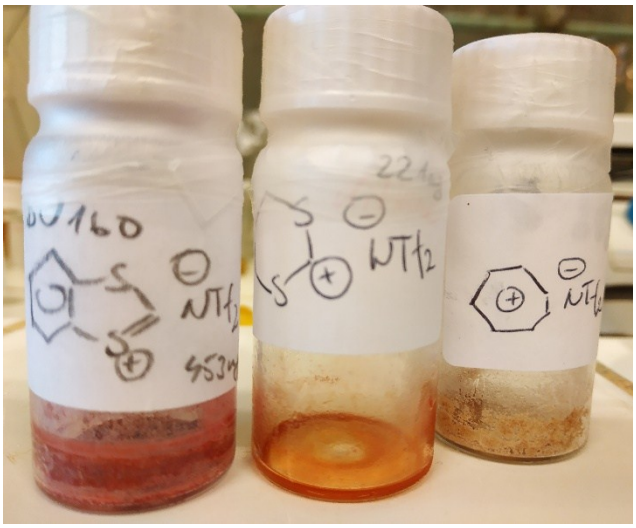
Table S1. Crystallographic data for compound **12b**

chem formula	$C_{24}H_{21}NOS_2$
M_r	403.54
cryst syst	monoclinic
color, habit	colourless, block
size (mm)	0.347 x 0.214 x 0.176
space group	$P2_1c$
a (Å)	14.3601(5)
b (Å)	8.9695(3)
c (Å)	15.4933(5)
β (°)	98.9420(10)
V (Å^3)	1971.33(11)
Z	4
ρ_{calc}, g.cm^{-3}	1.360
Radiation [Å]	Cu K_α 1.54178
μ(Mo K_α), mm^{-1}	2.554
F(000)	848
temp (K)	100(2)
θ range (°)	3.115 – 66.584
data collected (h,k,l)	-17:16; 0:10; 0:18
no. of rflns collected	43522
no. of indpndt reflns	3495
observed reflns $F_o \geq 2.0\ \sigma(F_o)$	3219
R(F) (%)	4.40
wR(F^2) (%)	10.99
GooF	1.117
weighting a,b	0.0275, 4.5660
params refined	255
min, max resid dens	-0.300, 0.340

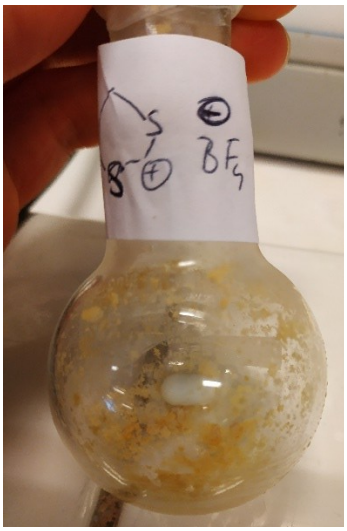
a) b) c)



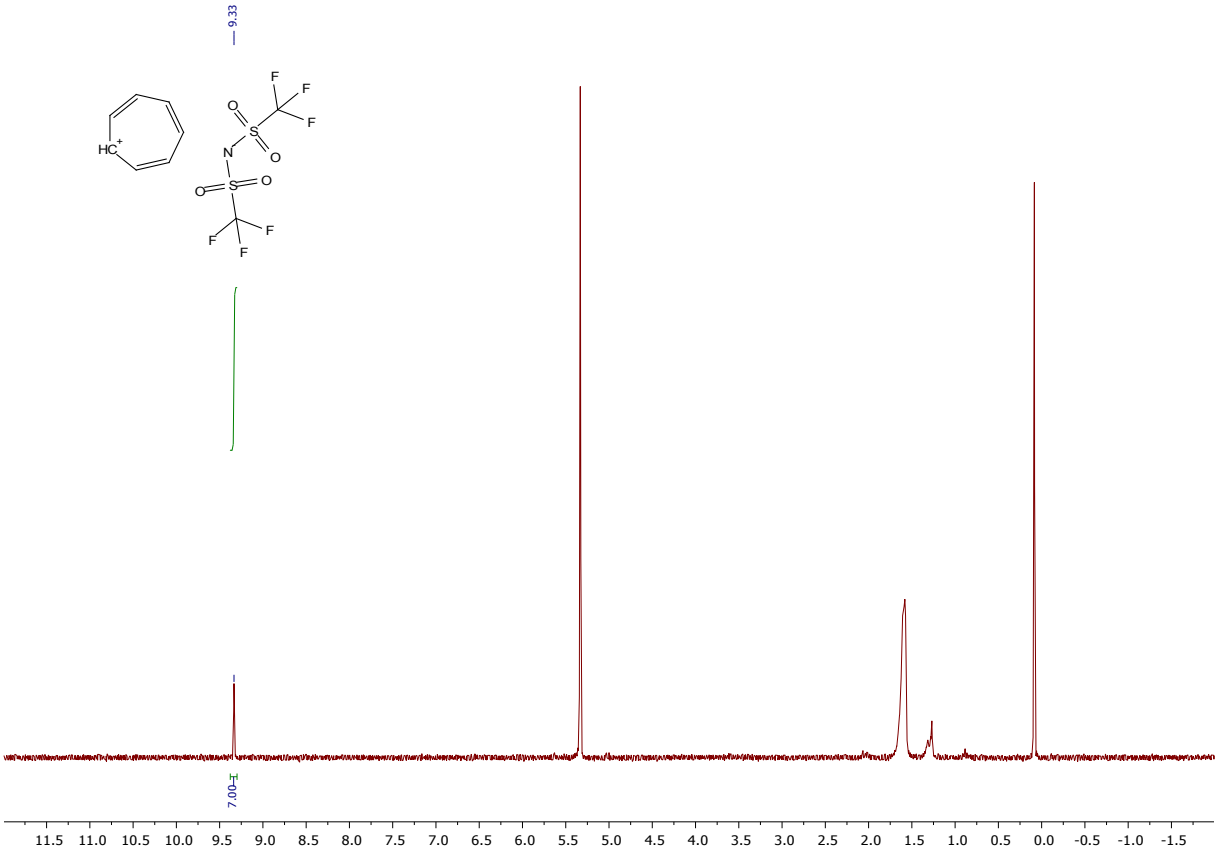
The trapping reaction of tropylium cation should be bright yellow in most cases. A black, or darker color is usually a sign of a failed experiment and is mostly due to a problem with the conjugate addition step, if older chemicals were used. a) Reaction with tropylium cation after work-up. b) Reaction with benzoditiolium. c) Reaction with ditianium.



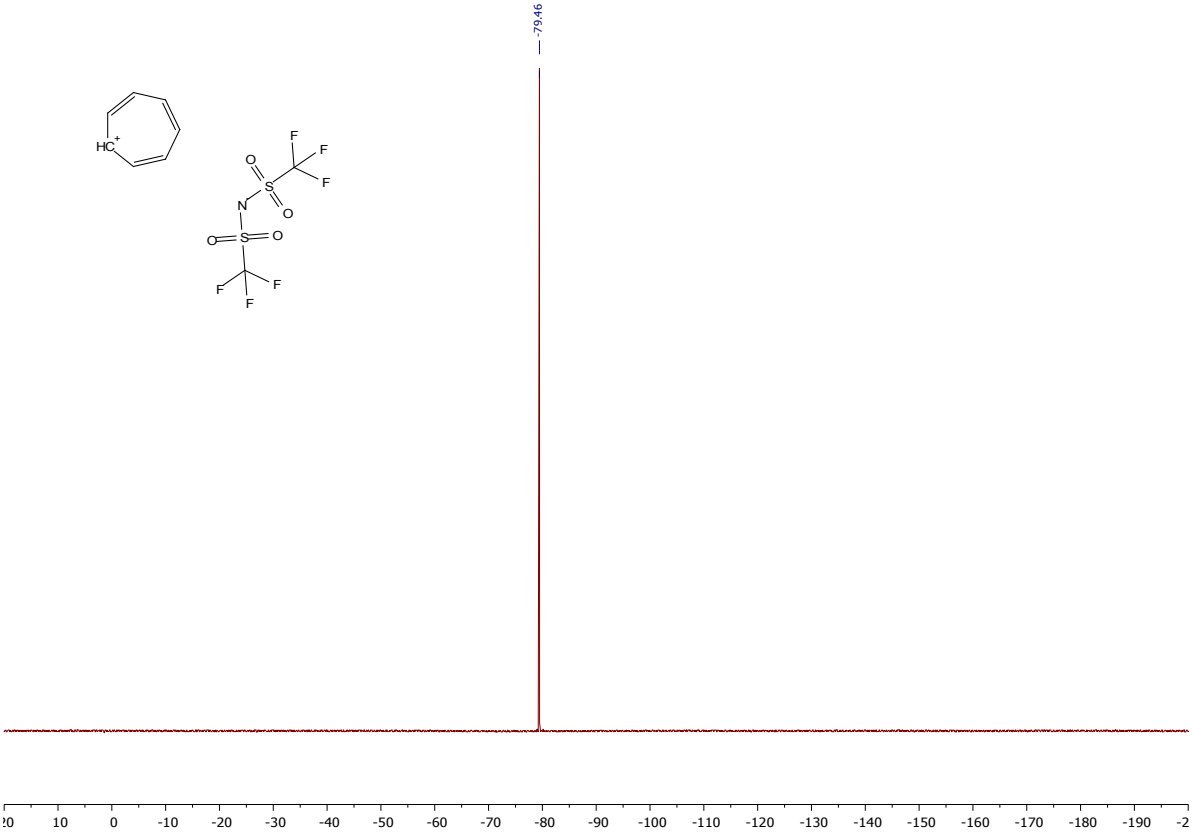
Cations.



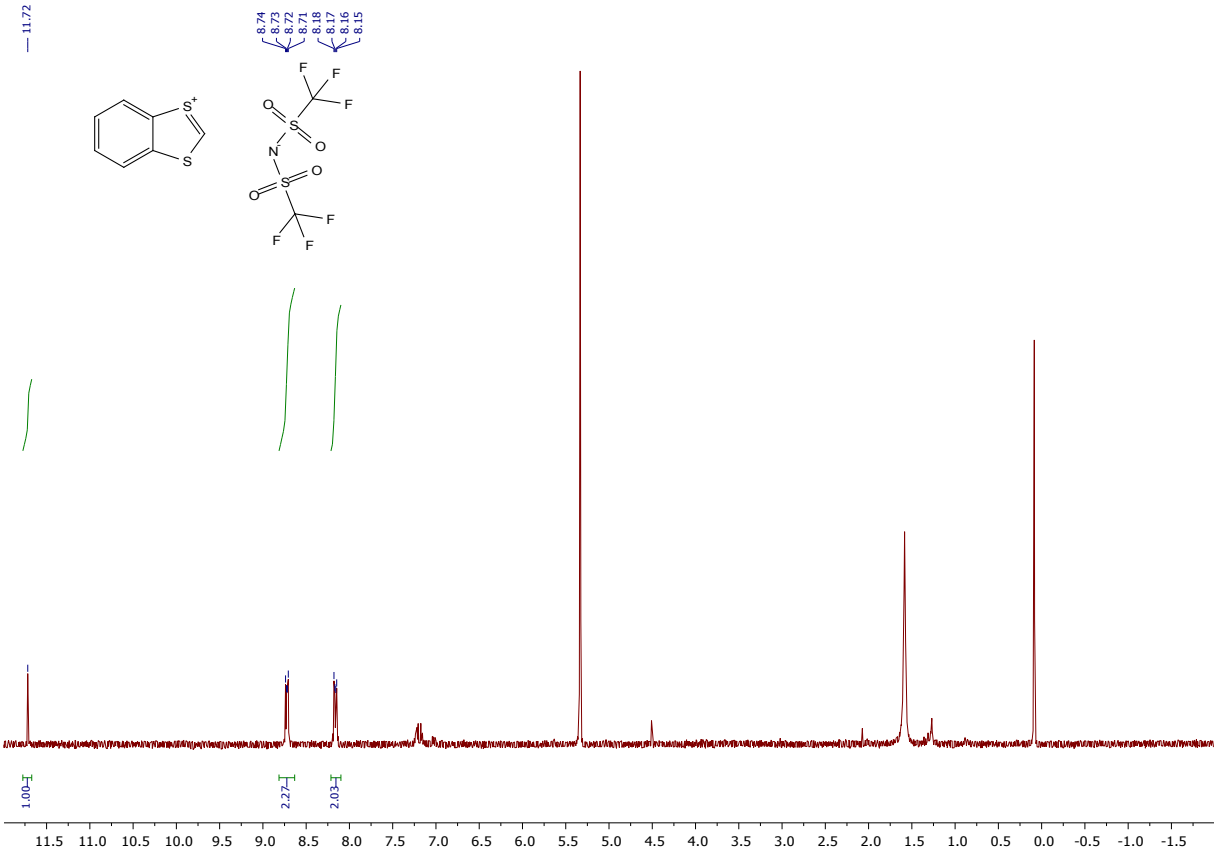
Pictures of ^{1}H, ^{13}C, and ^{19}F NMR spectra



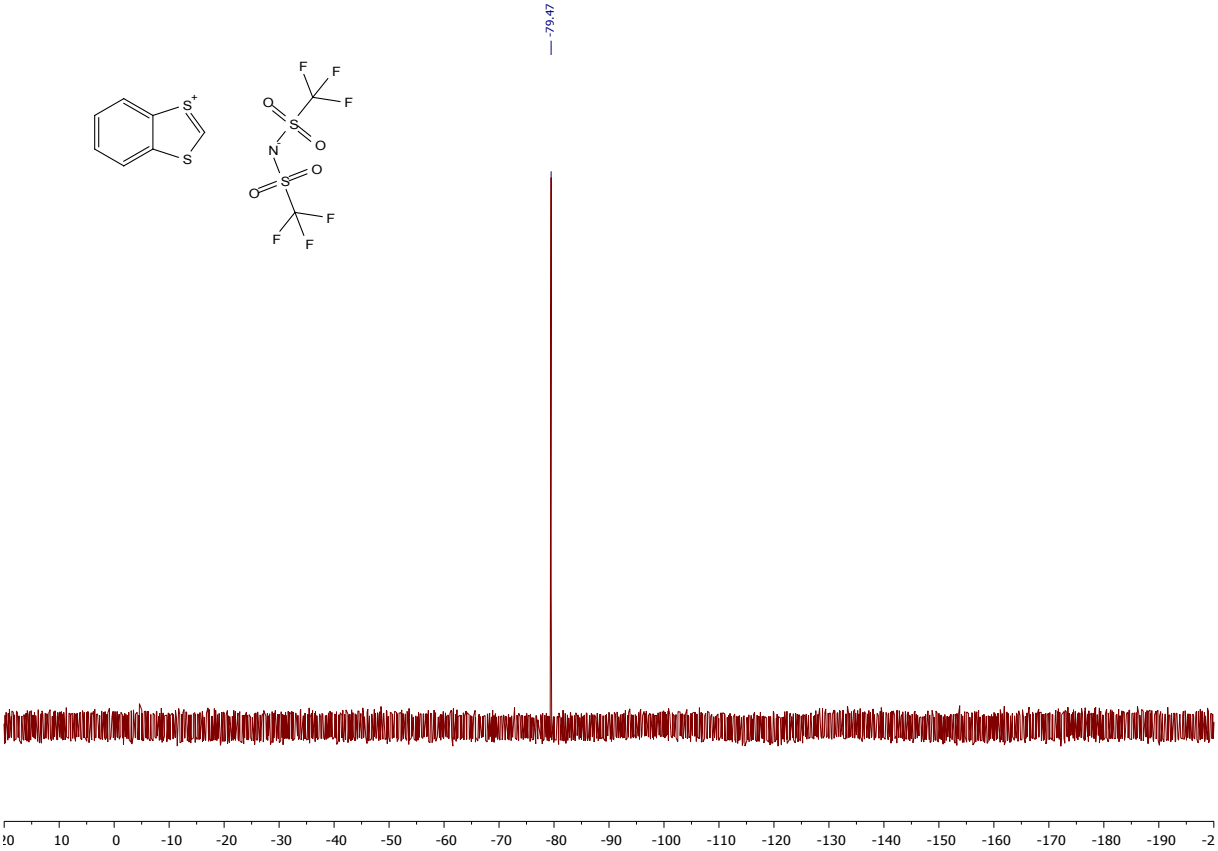
^{1}H-NMR (300 MHz, CD_2Cl_2) of **4**



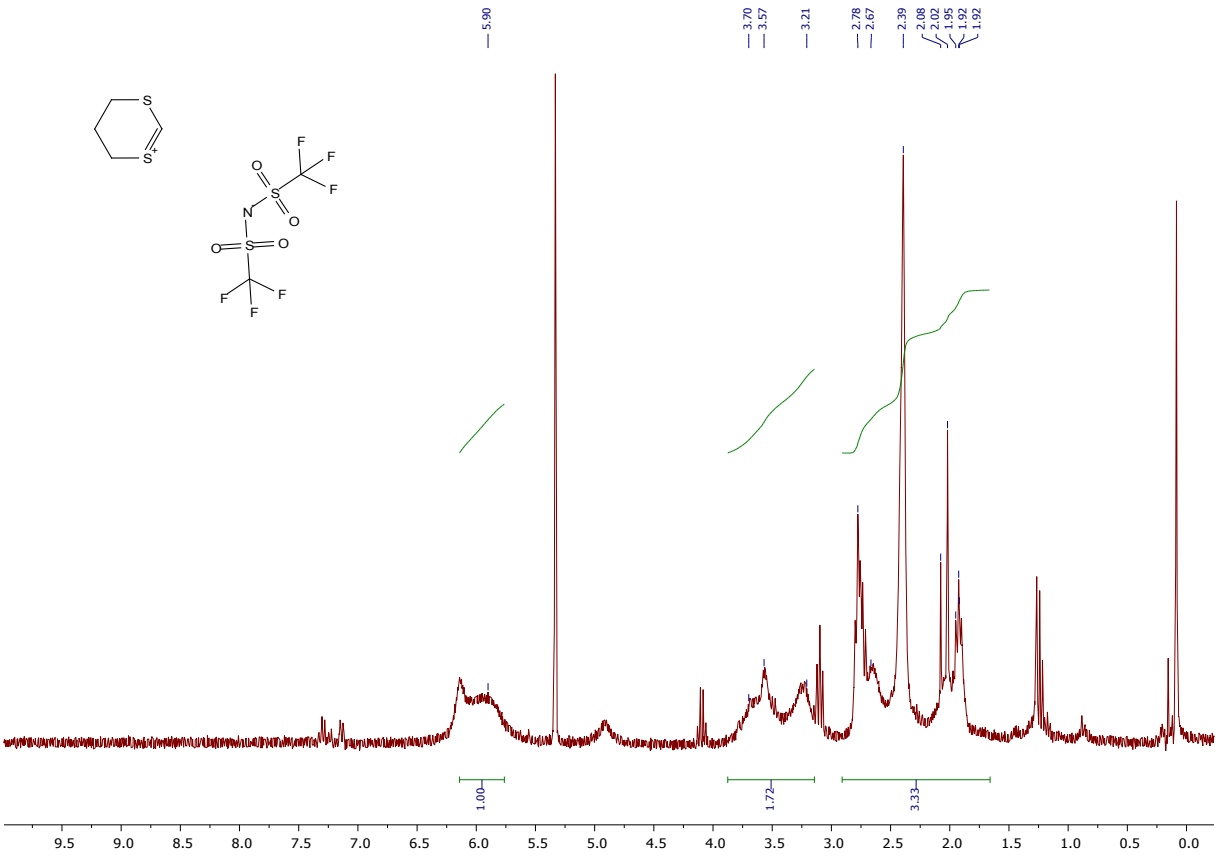
^{19}F-NMR (282 MHz, CD_2Cl_2) of **4**



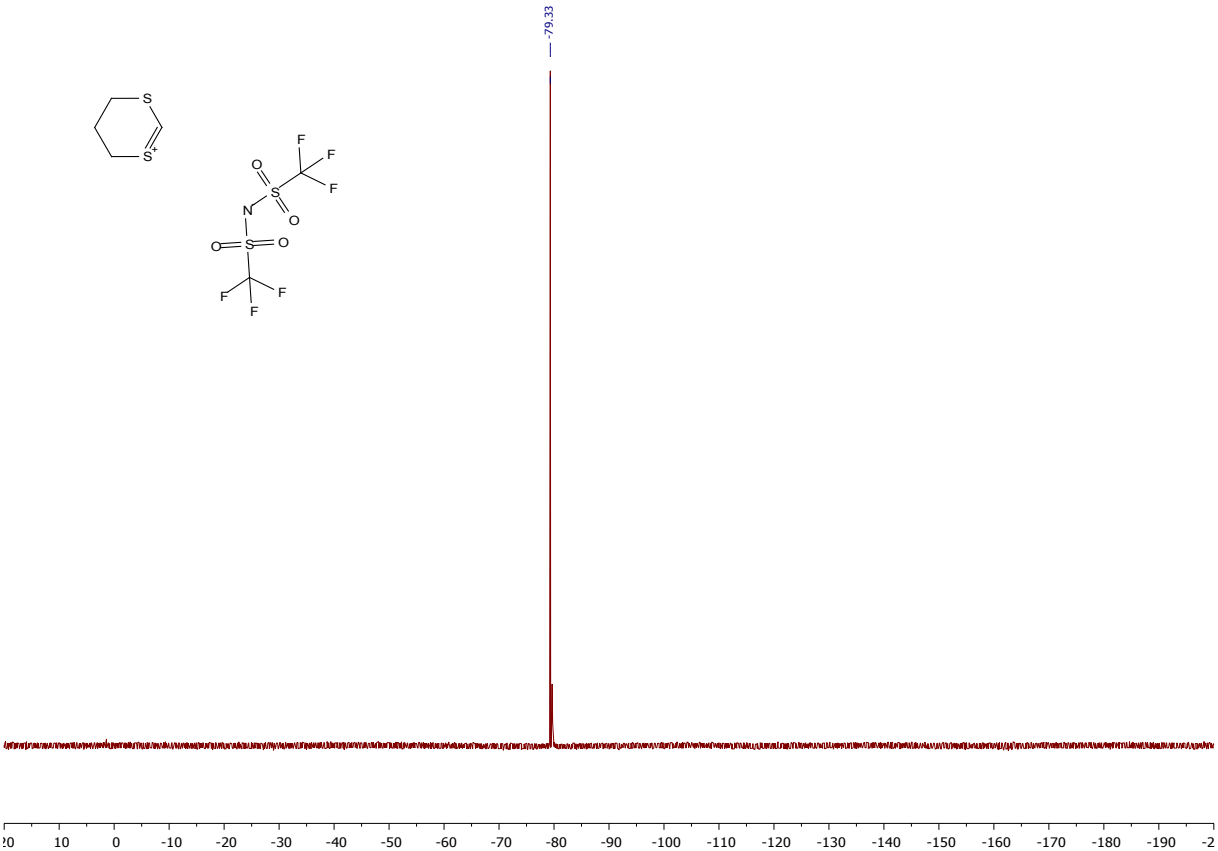
^{1}H-NMR (282 MHz, CD_2Cl_2) of **5**



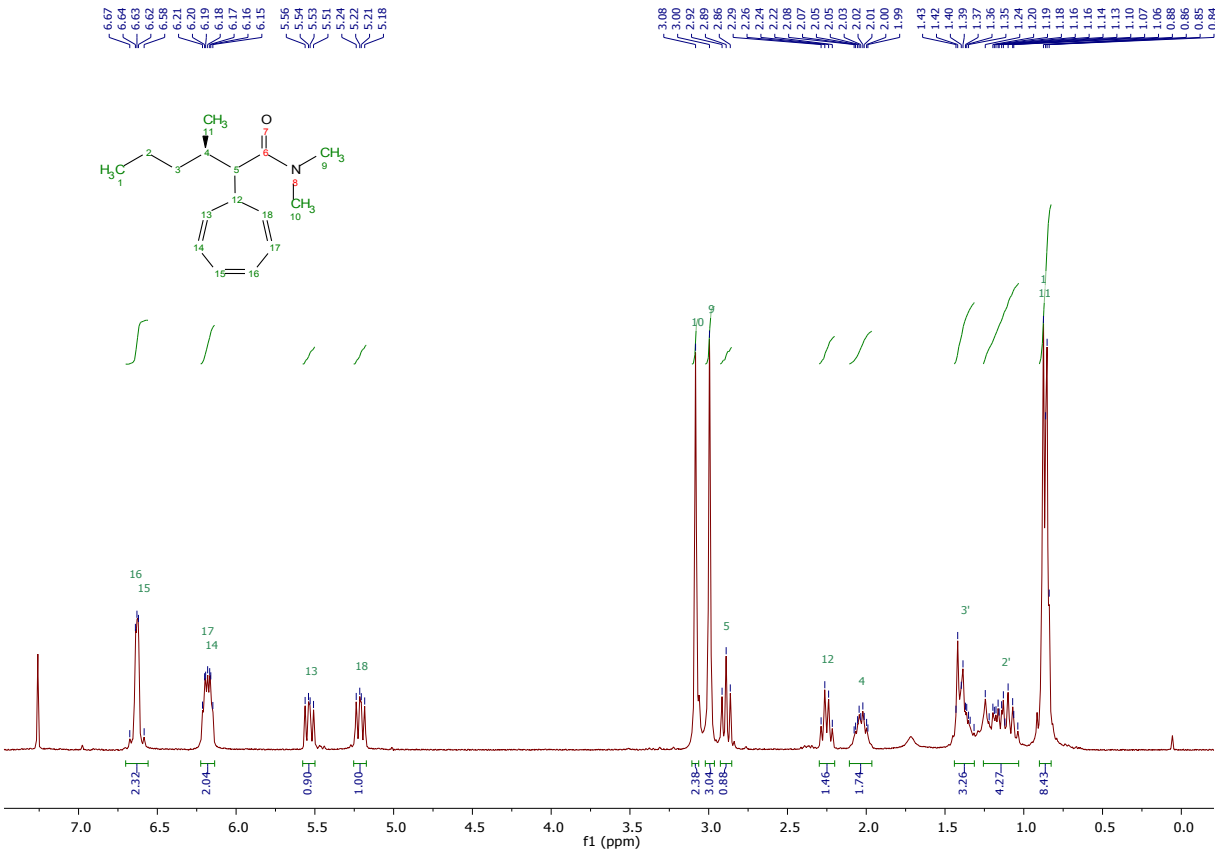
^{19}F-NMR (282 MHz, CD_2Cl_2) of **5**



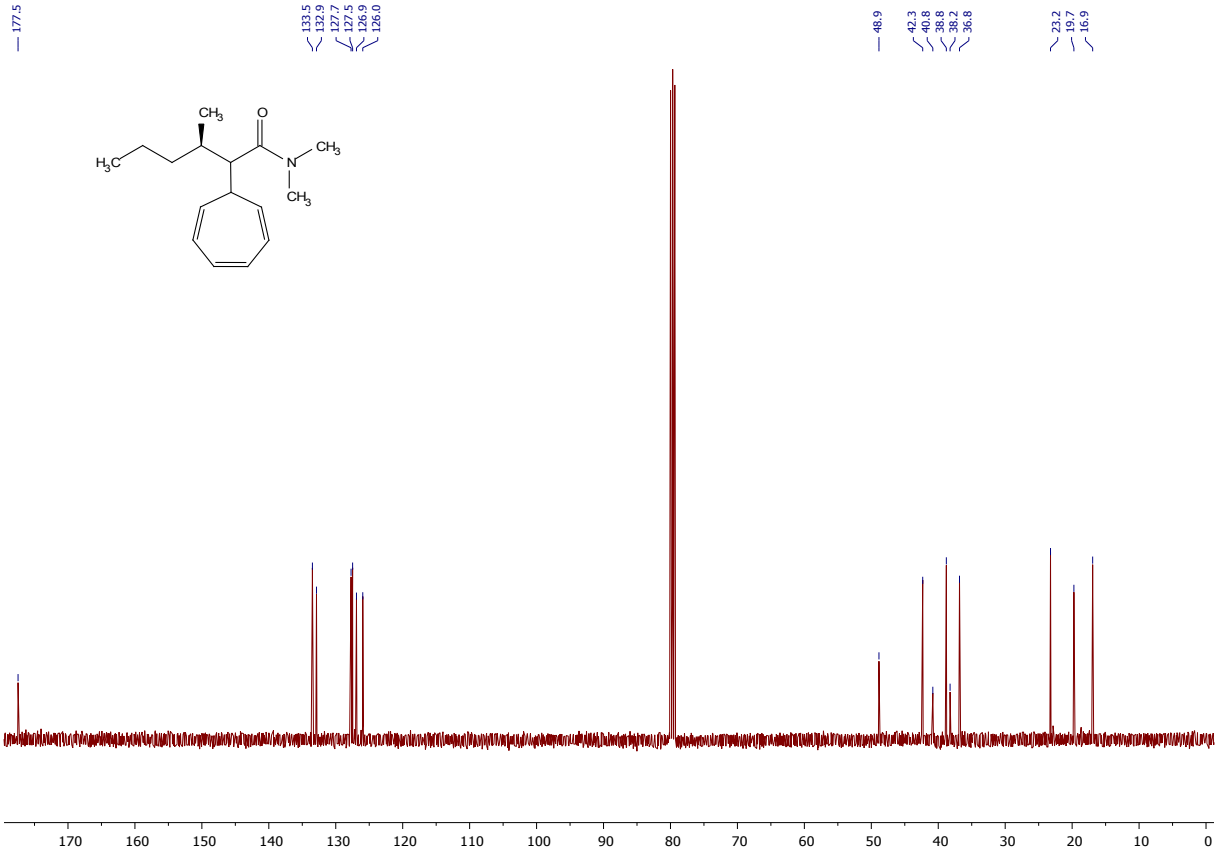
^{1}H-NMR (282 MHz, CD_2Cl_2) of **6**



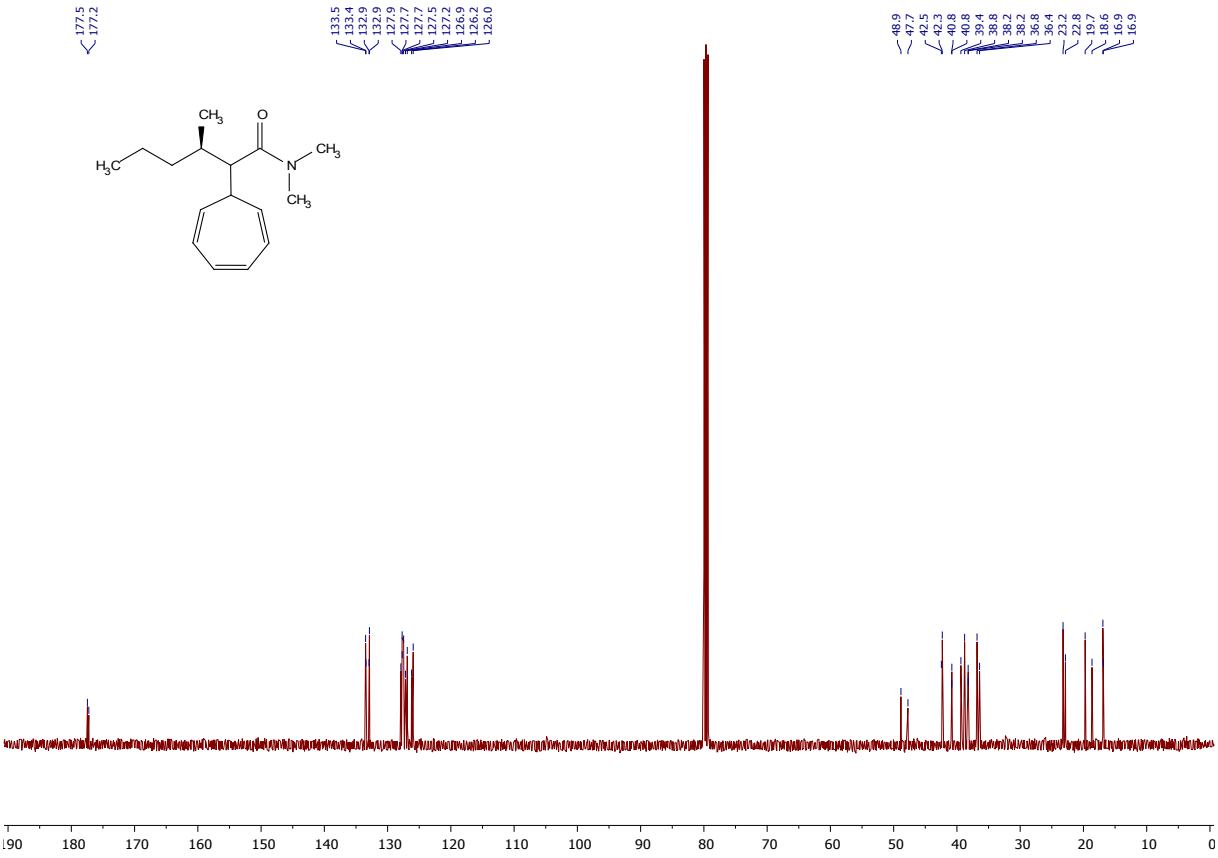
^{19}F-NMR (282 MHz, CD_2Cl_2) of **6**



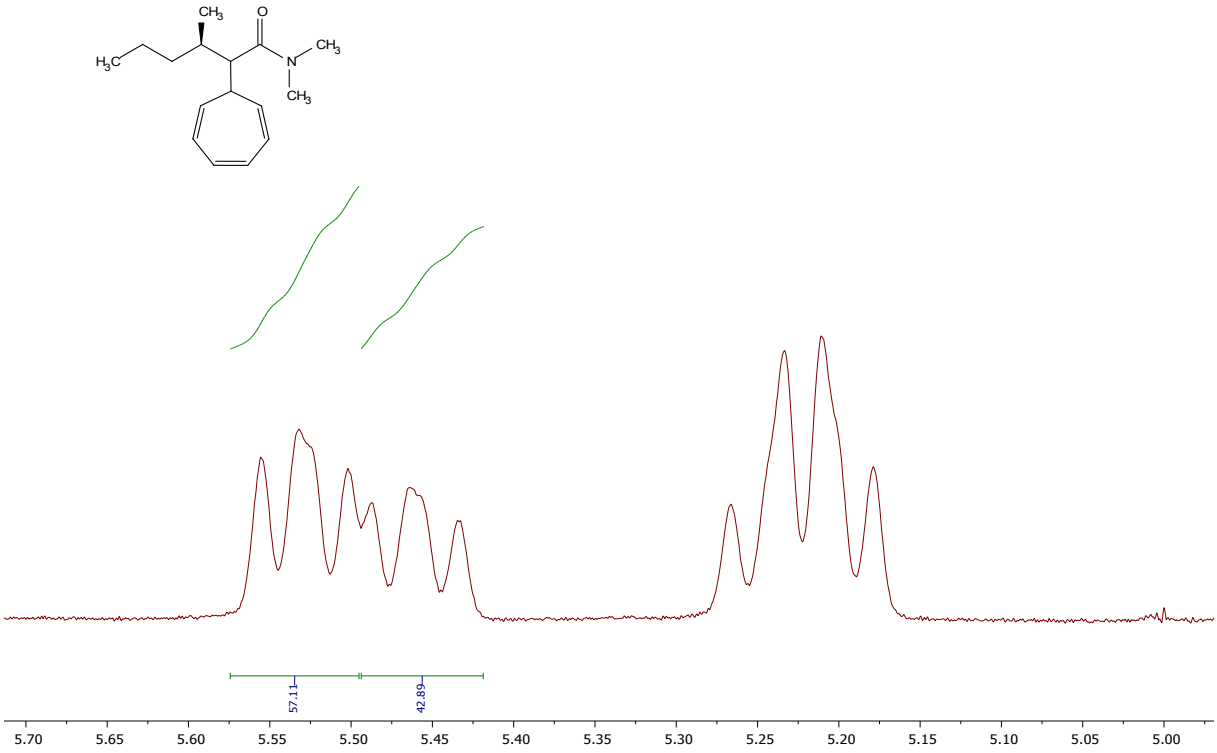
^{1}H-NMR (300 MHz, $CDCl_3$) of major diastereomer of **3a**



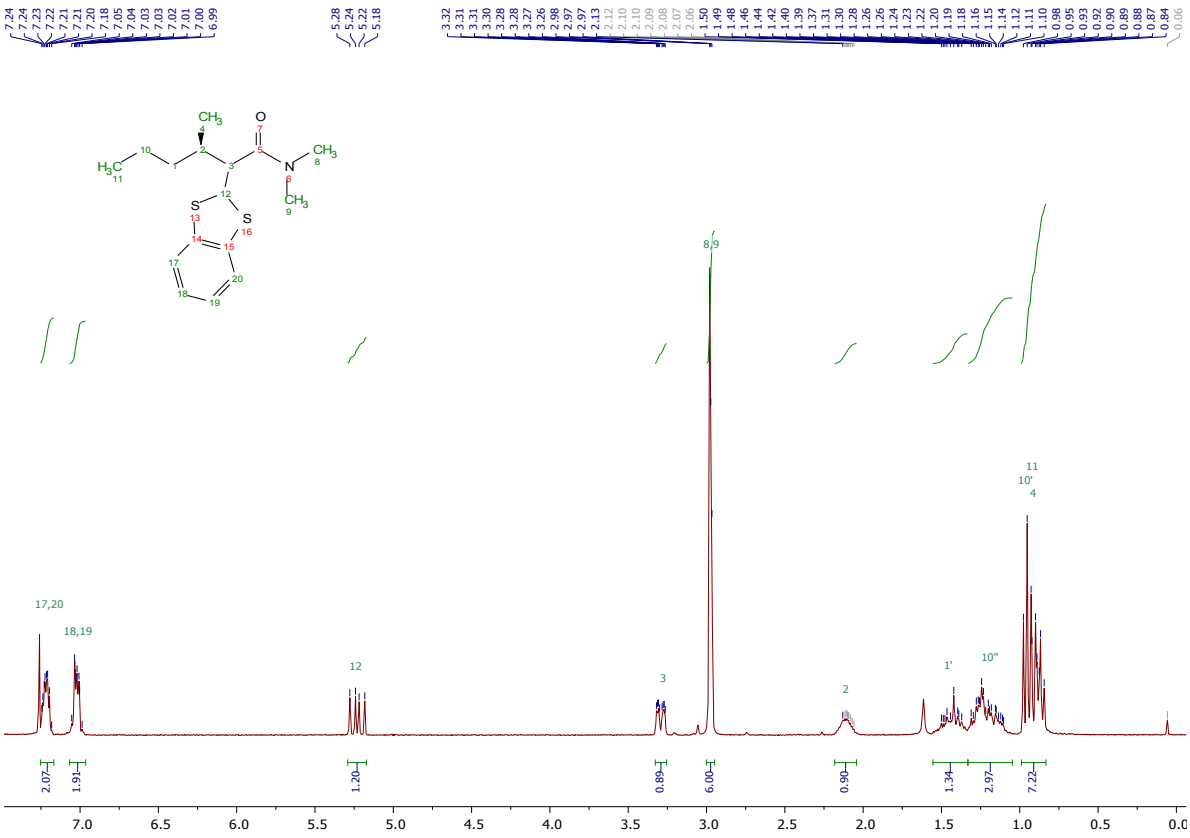
^{13}C-NMR (101 MHz, $CDCl_3$) of major diastereomer of **3a**



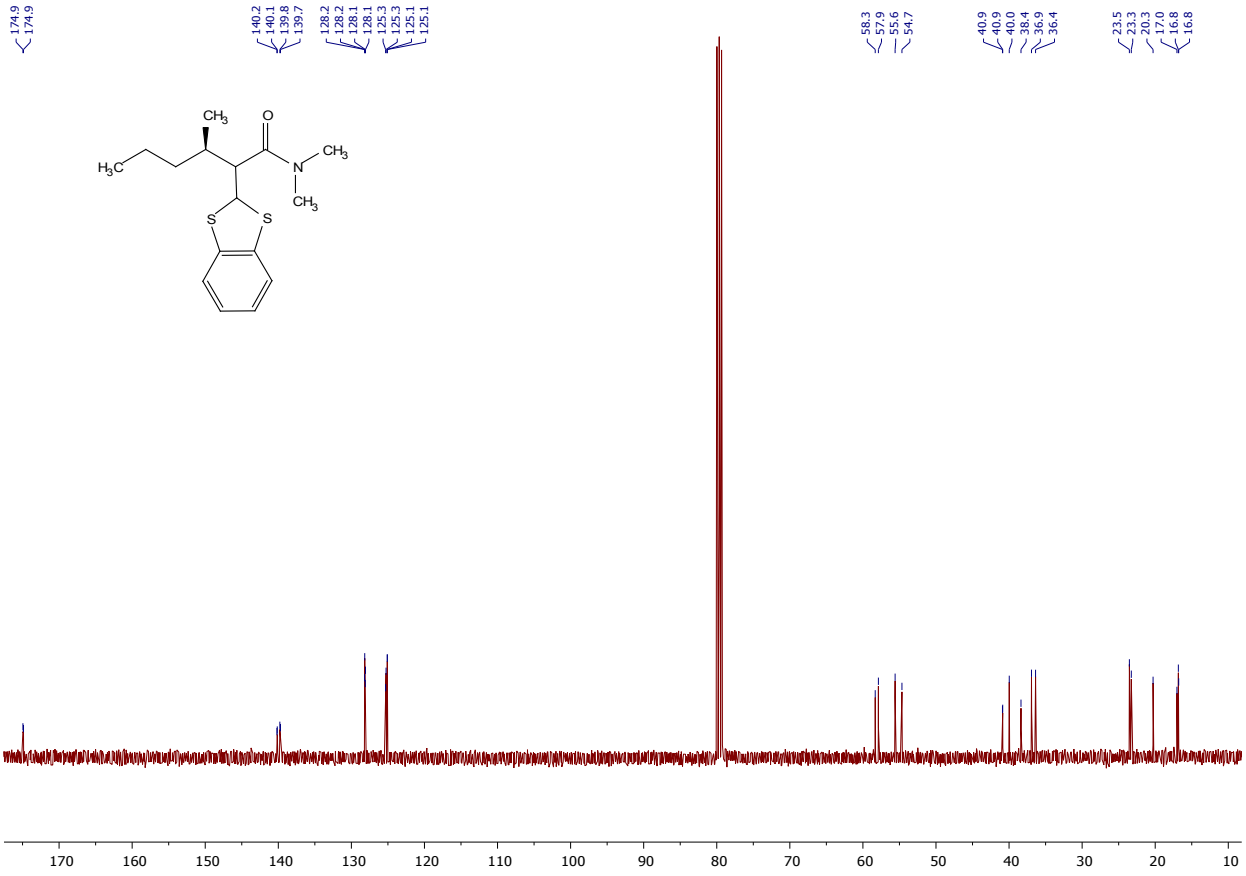
^{13}C-NMR (101 MHz, $CDCl_3$) of mixture of diastereomers of **3a**



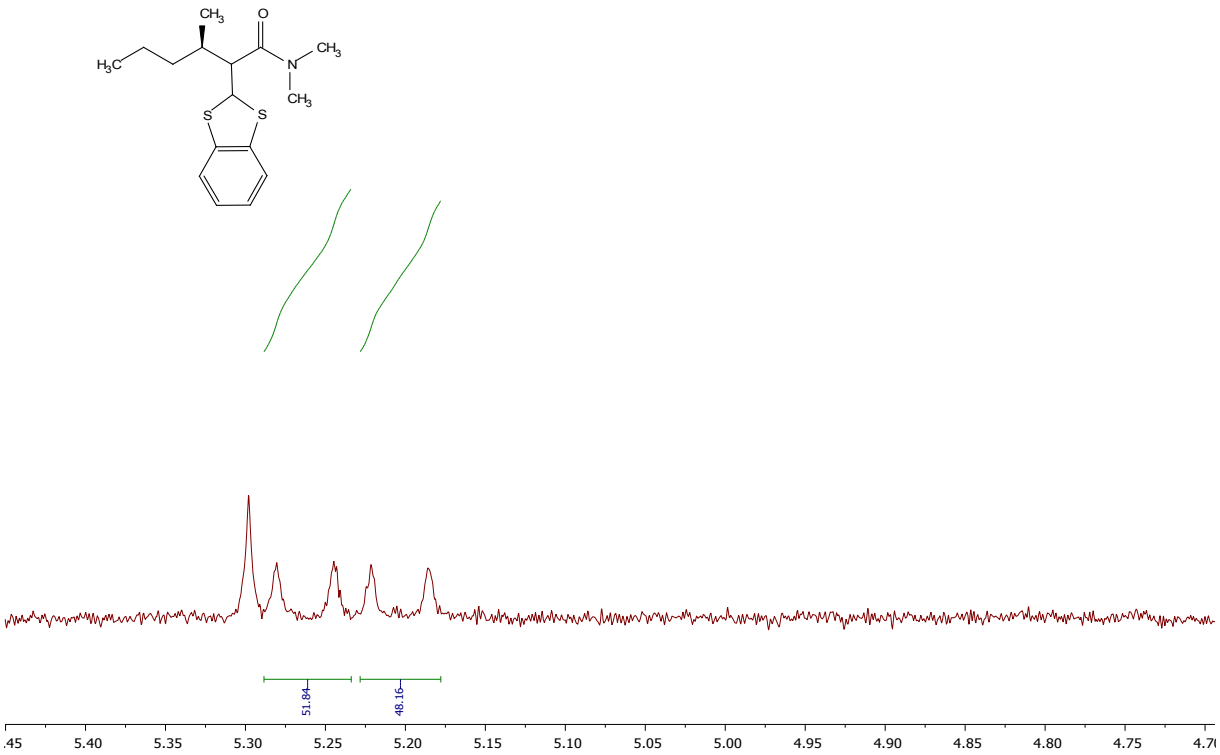
^{1}H-NMR (300 MHz, $CDCl_3$) of the crude mixture for dr determination of **3a**



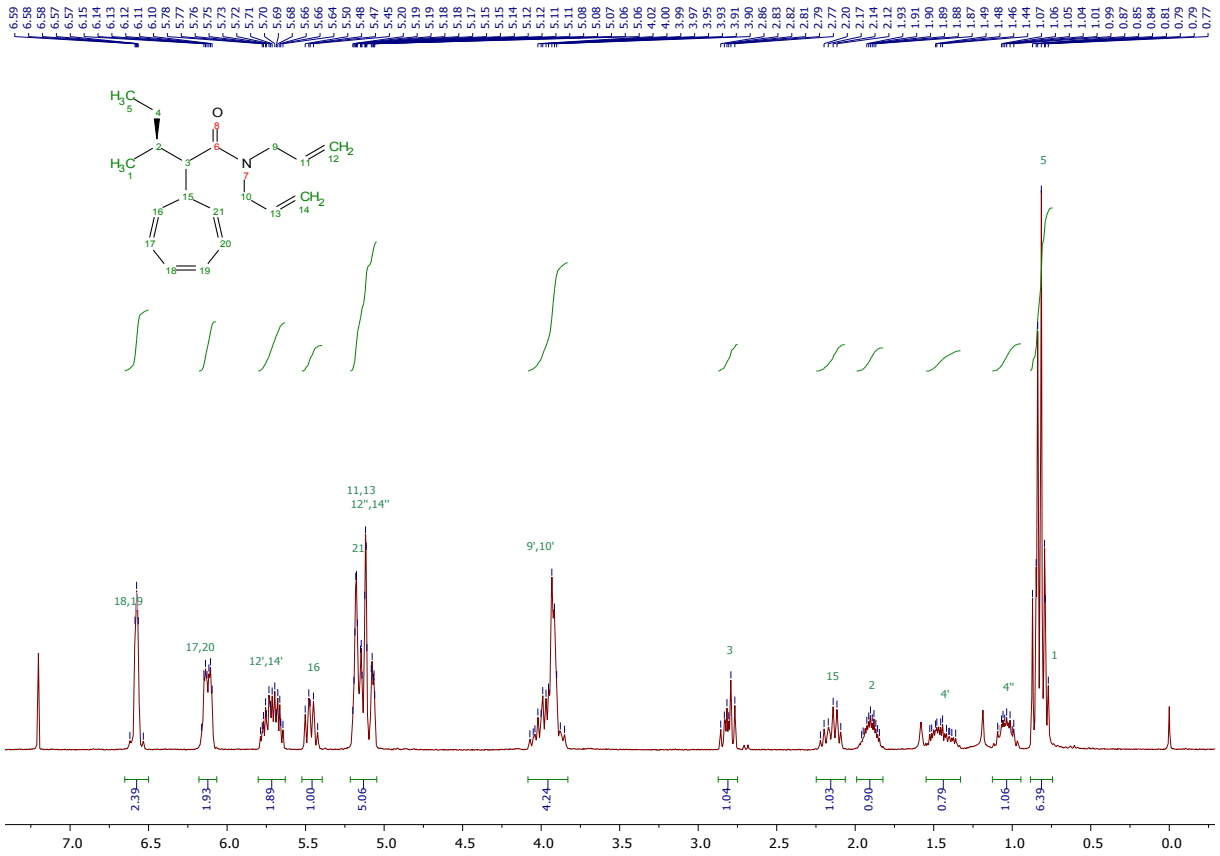
^{1}H-NMR (300 MHz, $CDCl_3$) of mixture of diastereomers of **3b**



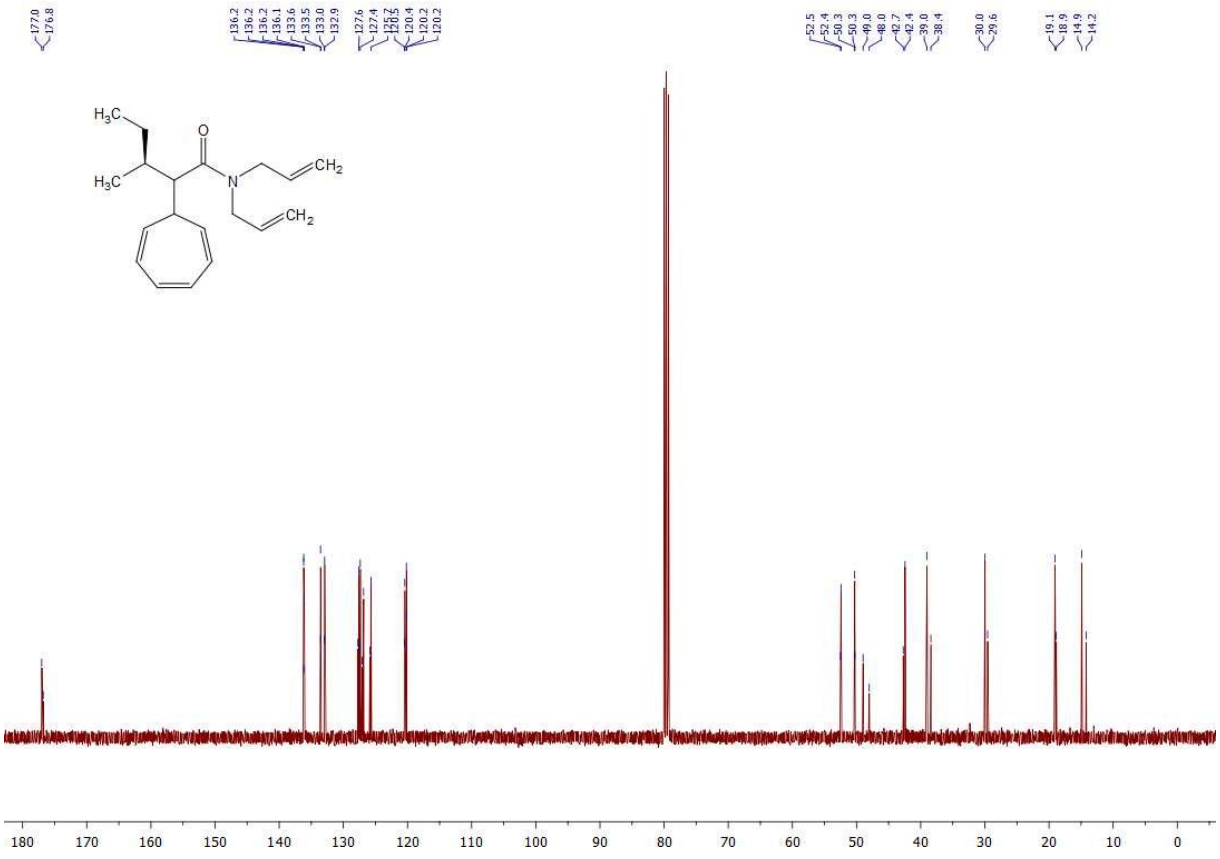
^{13}C-NMR (101 MHz, $CDCl_3$) of mixture of diastereomers of **3b**



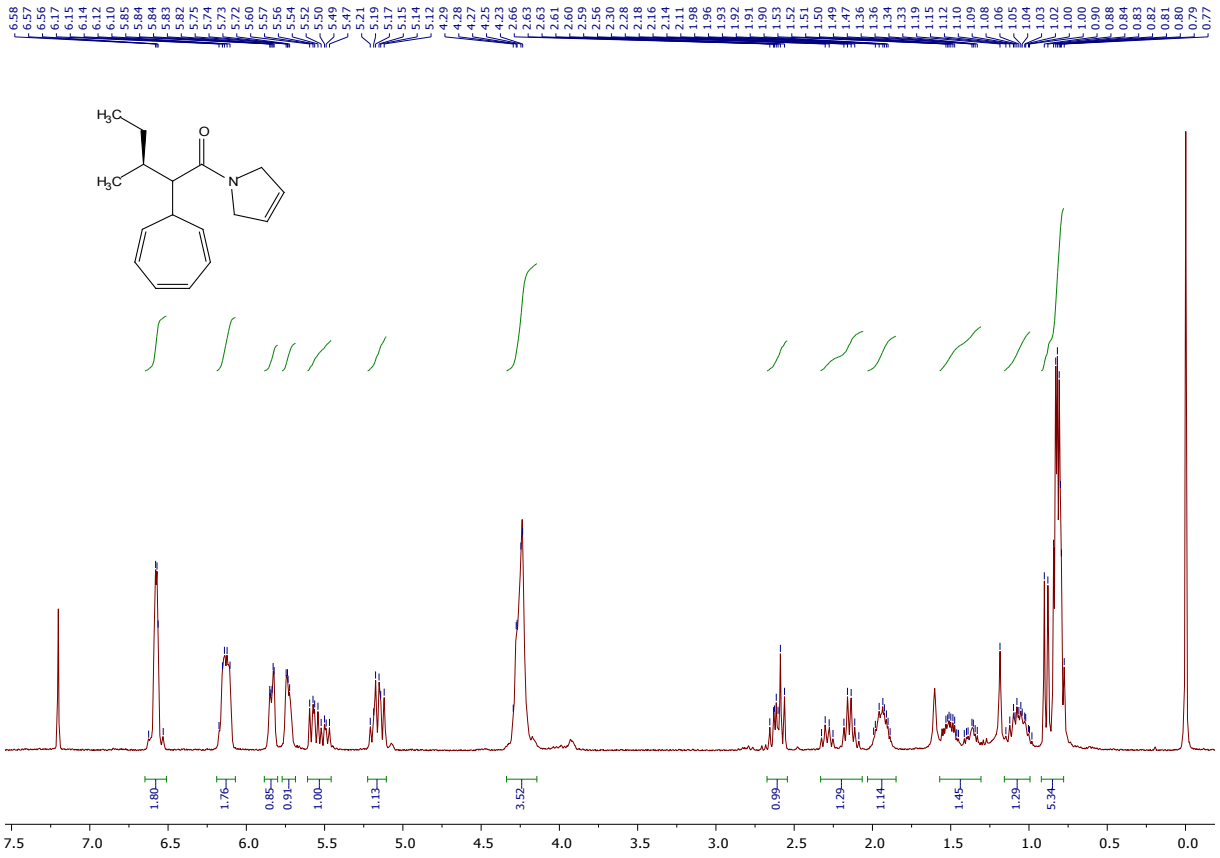
^{1}H-NMR (300 MHz, $CDCl_3$) of the crude mixture for dr determination of **3b**



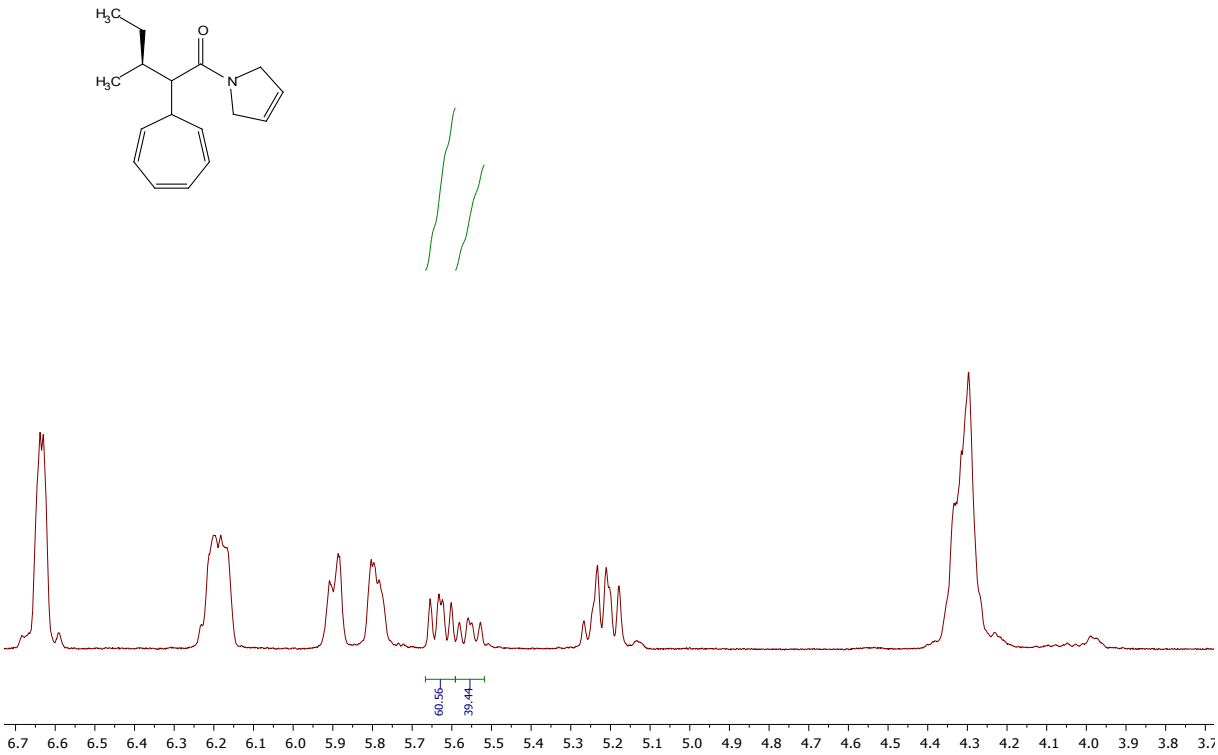
^{1}H-NMR (300 MHz, $CDCl_3$) of mixture of diastereomers of **3k**



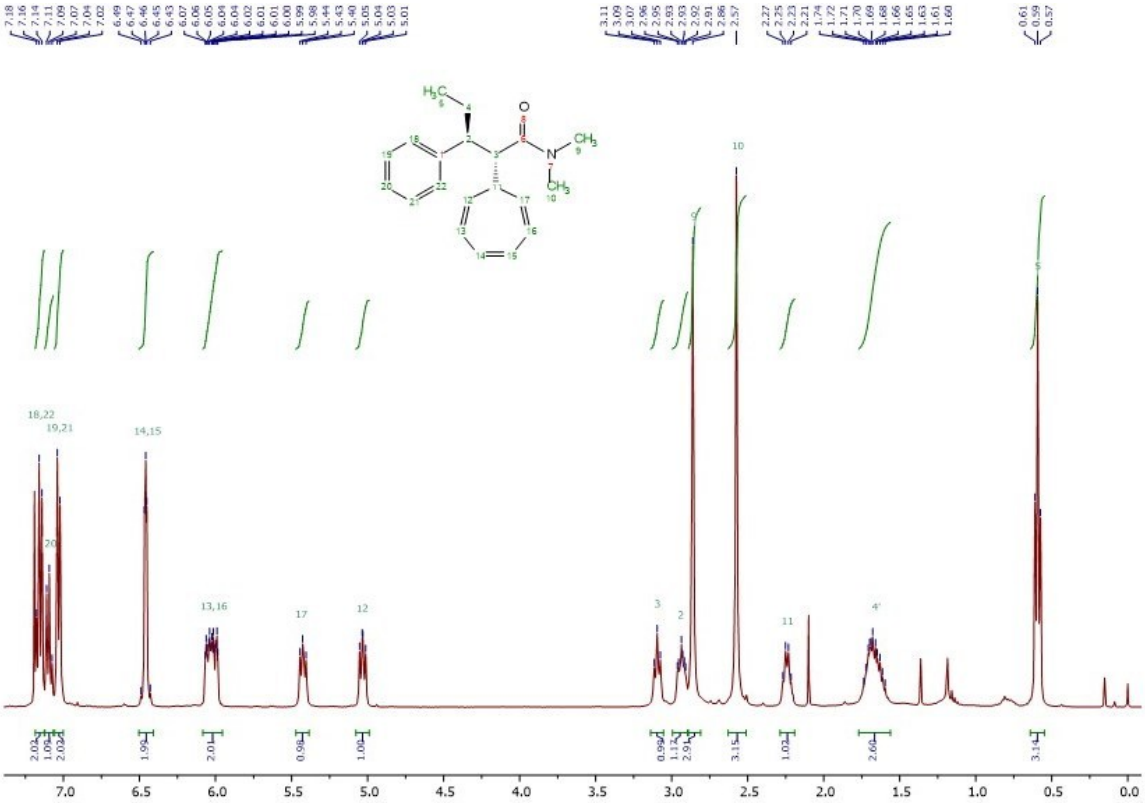
^{13}C-NMR (101 MHz, $CDCl_3$) of mixture of diastereomers of **3k**



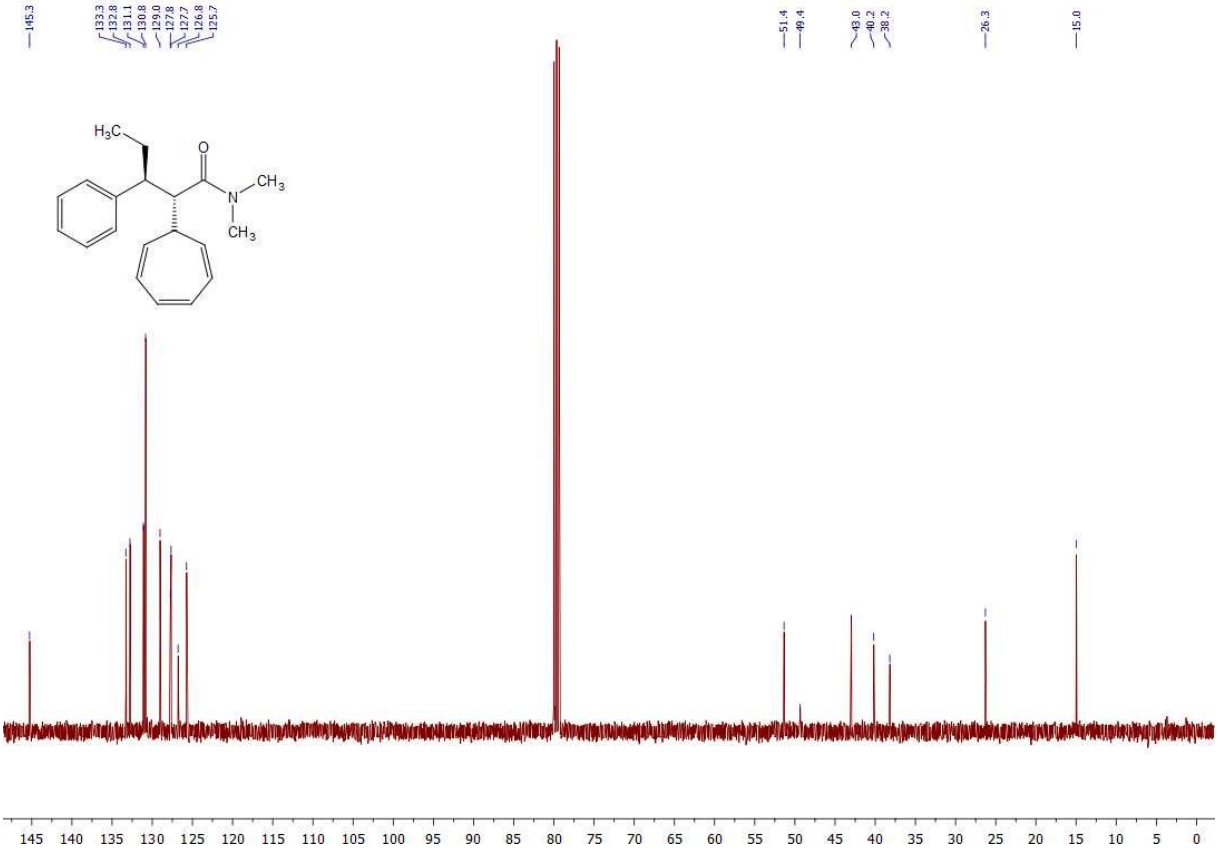
^{1}H-NMR (300 MHz, $CDCl_3$) of mixture of diastereomers of **10**



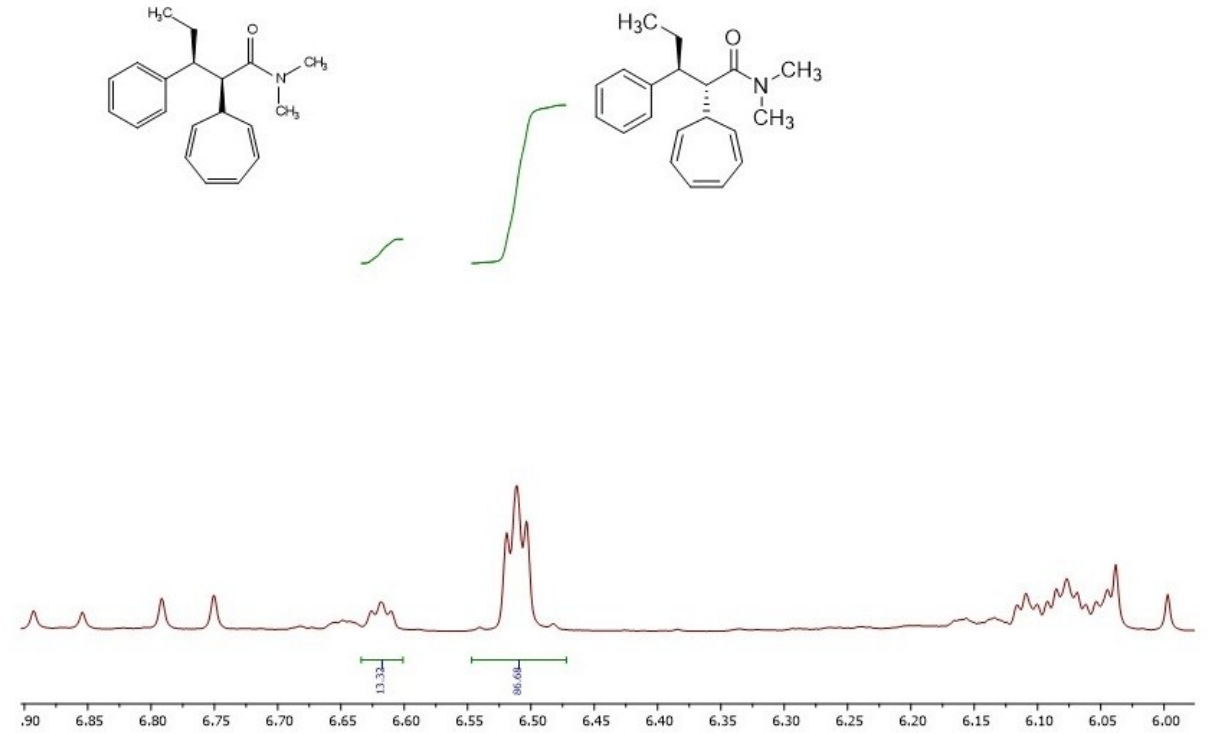
^{1}H-NMR (300 MHz, $CDCl_3$) of the crude mixture for dr determination of **10**



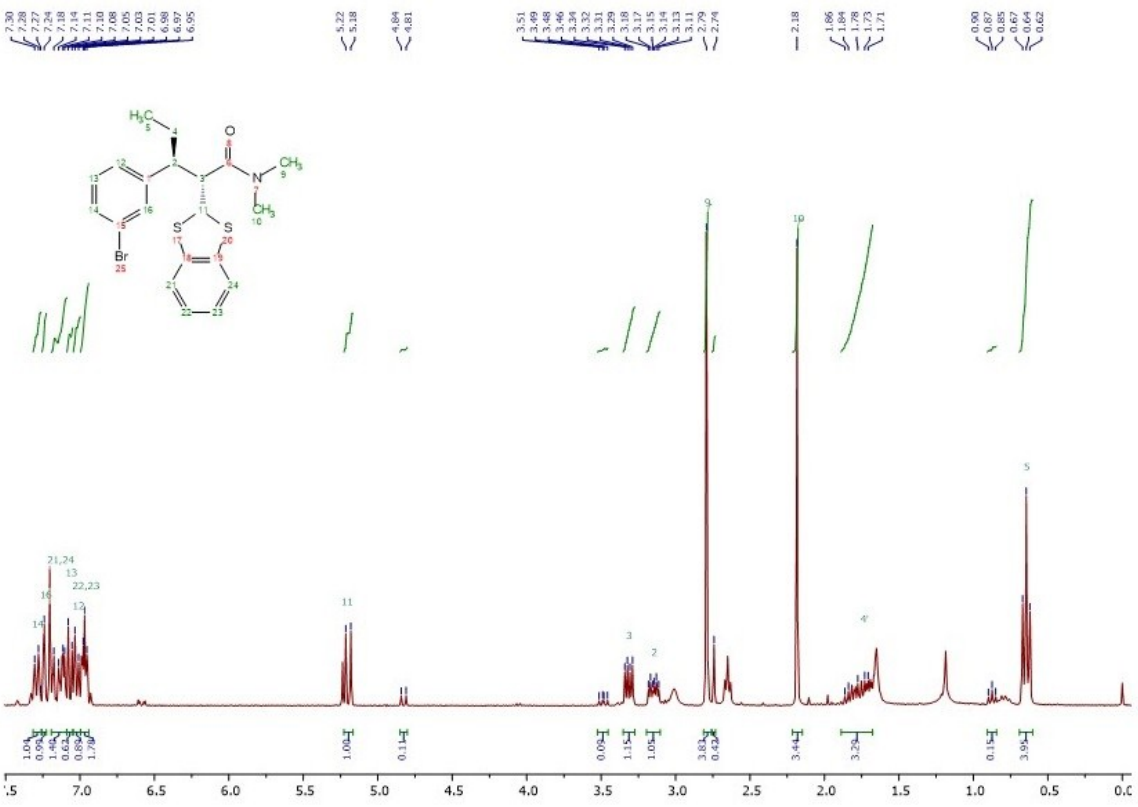
^{1}H-NMR (400 MHz, $CDCl_3$) of major of diastereomer of **3g**



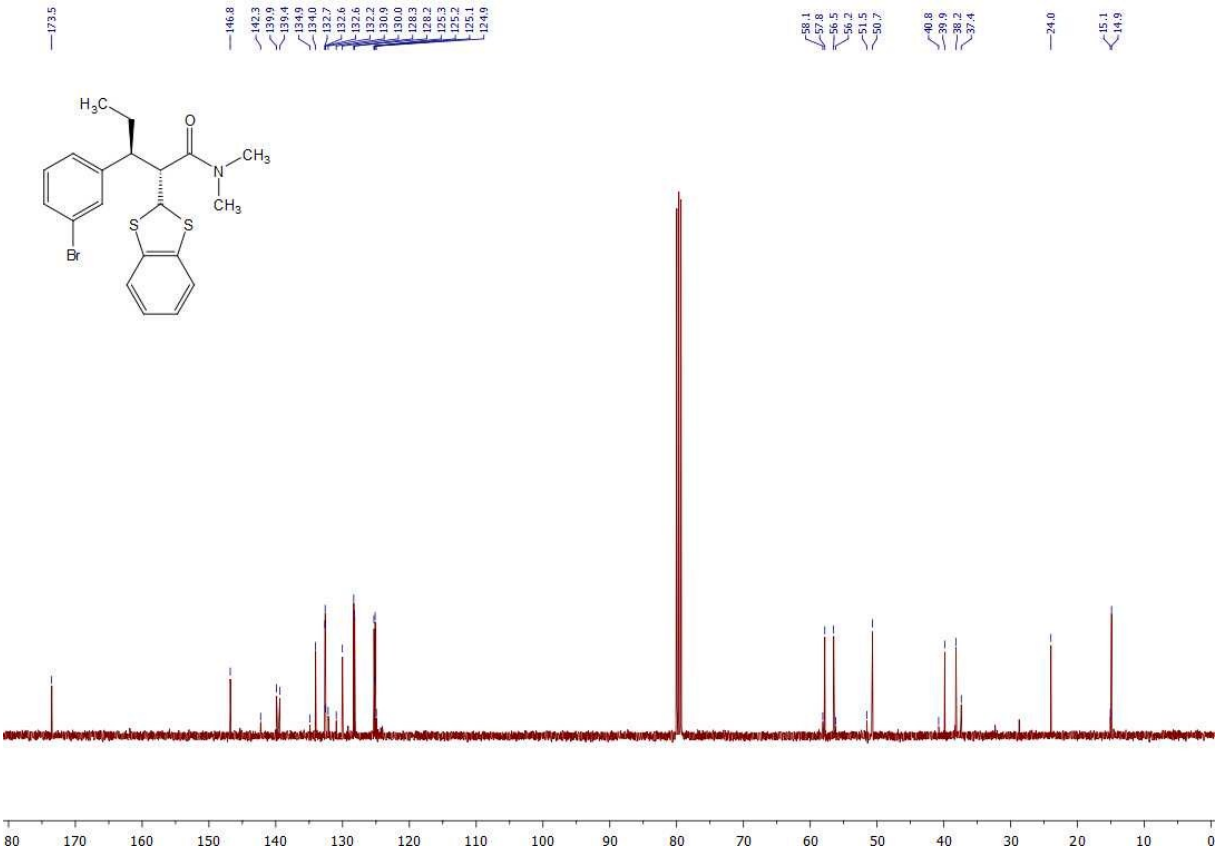
^{13}C-NMR (101 MHz, $CDCl_3$) of mixture of diastereomers of **3g**



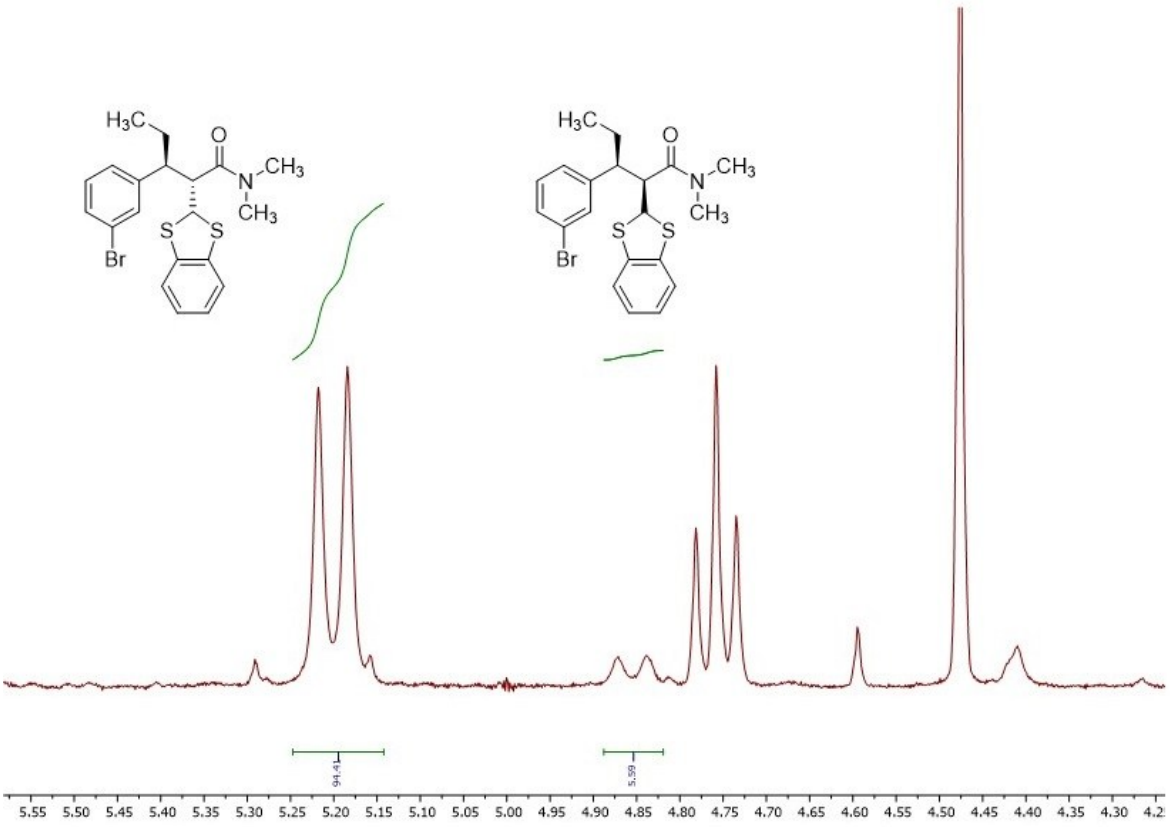
^{1}H-NMR (400 MHz, $CDCl_3$) of the crude mixture for dr determination of **10**



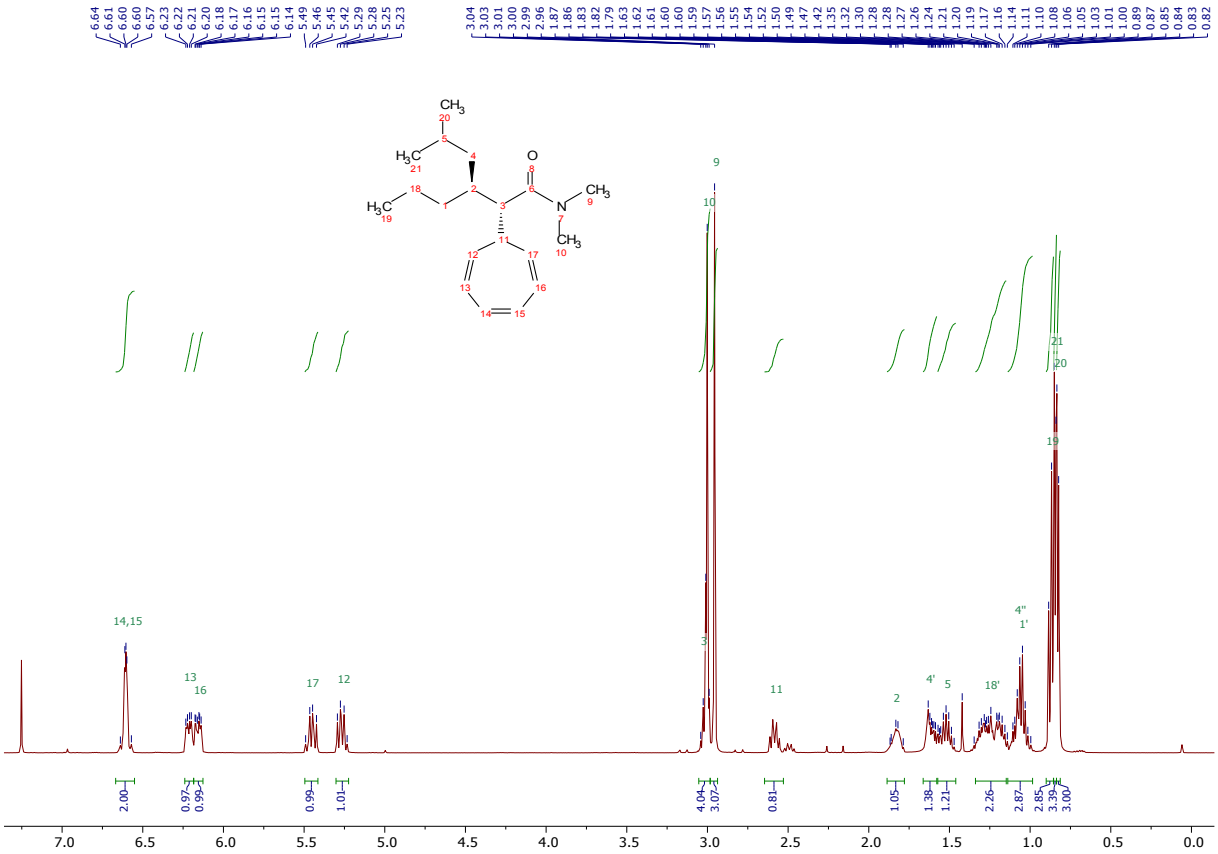
^{1}H-NMR (300 MHz, $CDCl_3$) of mixture of diastereomers of **3h**



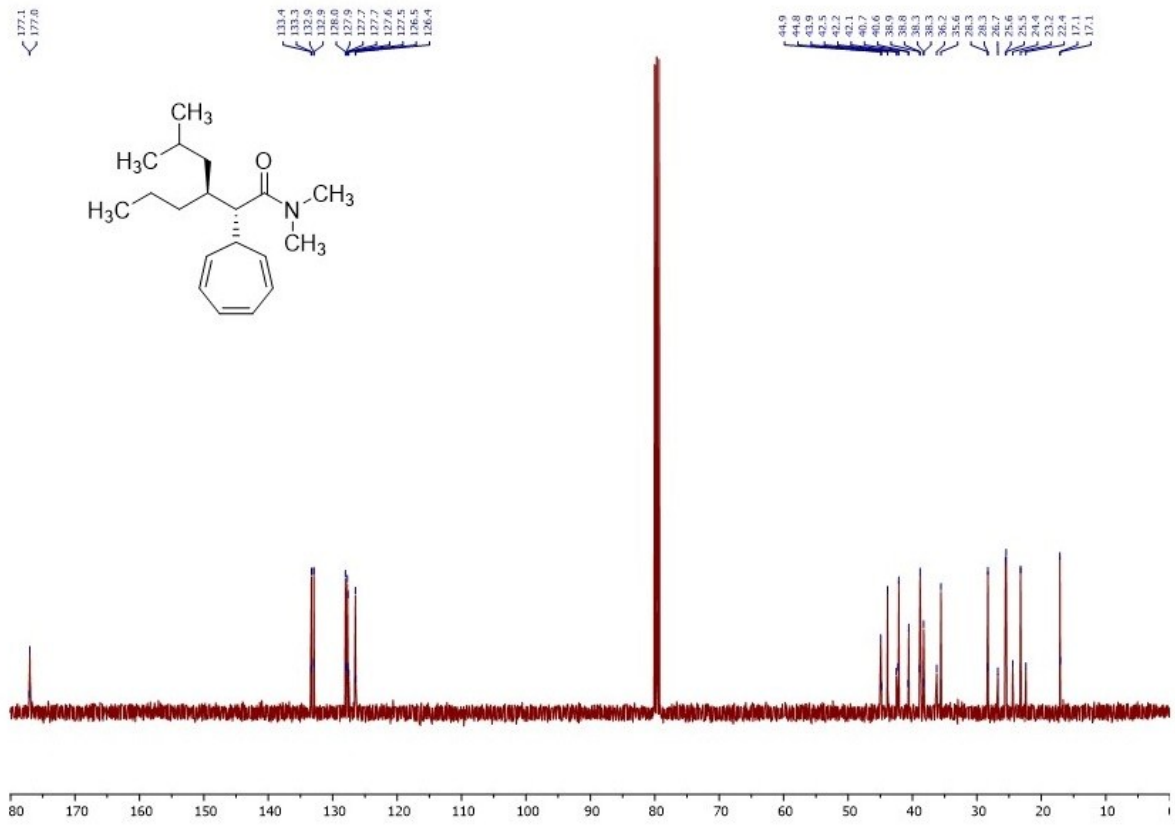
^{13}C-NMR (101 MHz, $CDCl_3$) of mixture of diastereomers of **3h**



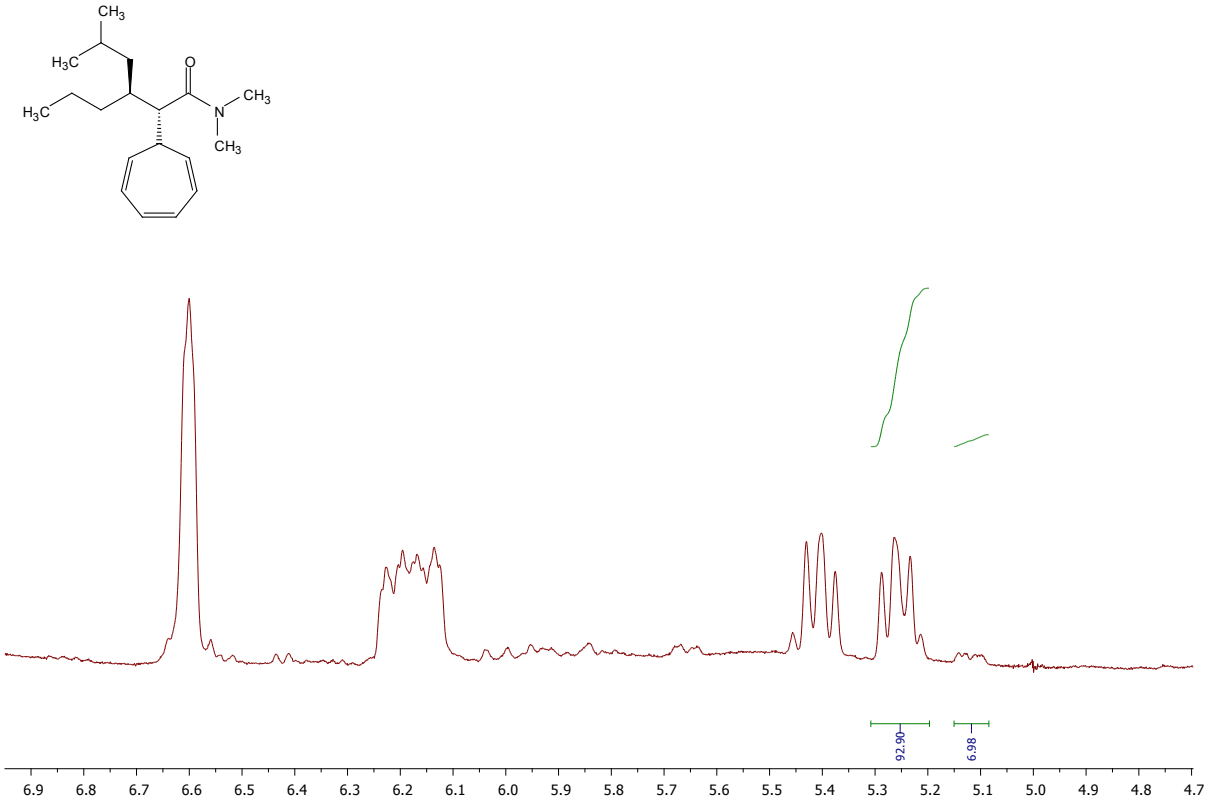
^{1}H-NMR (300 MHz, $CDCl_3$) of the crude mixture for dr determination of **3h**



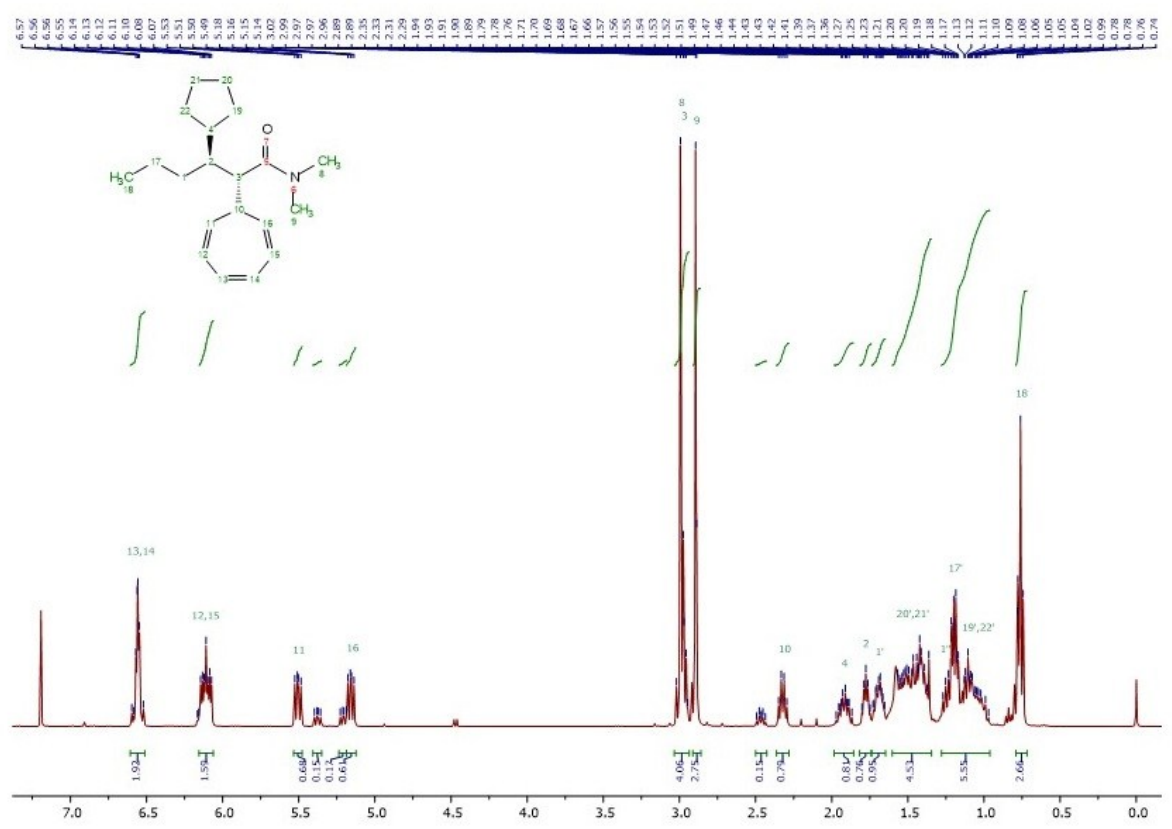
^{1}H-NMR (400 MHz, $CDCl_3$) of major diastereomer of **3i**



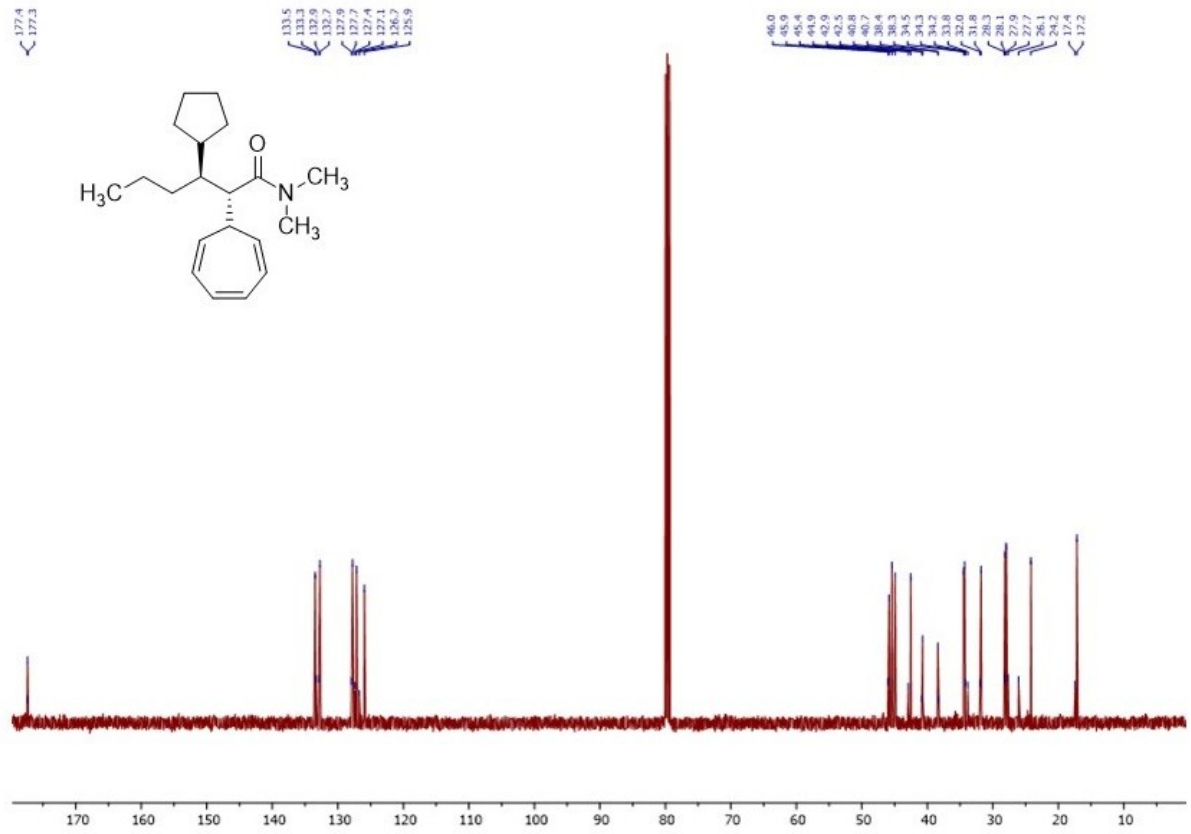
^{13}C-NMR (101 MHz, $CDCl_3$) of mixture of diastereomers of **3i**



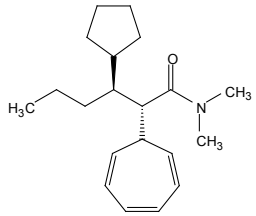
^{1}H-NMR (300 MHz, $CDCl_3$) of the crude mixture for dr determination of **3i**

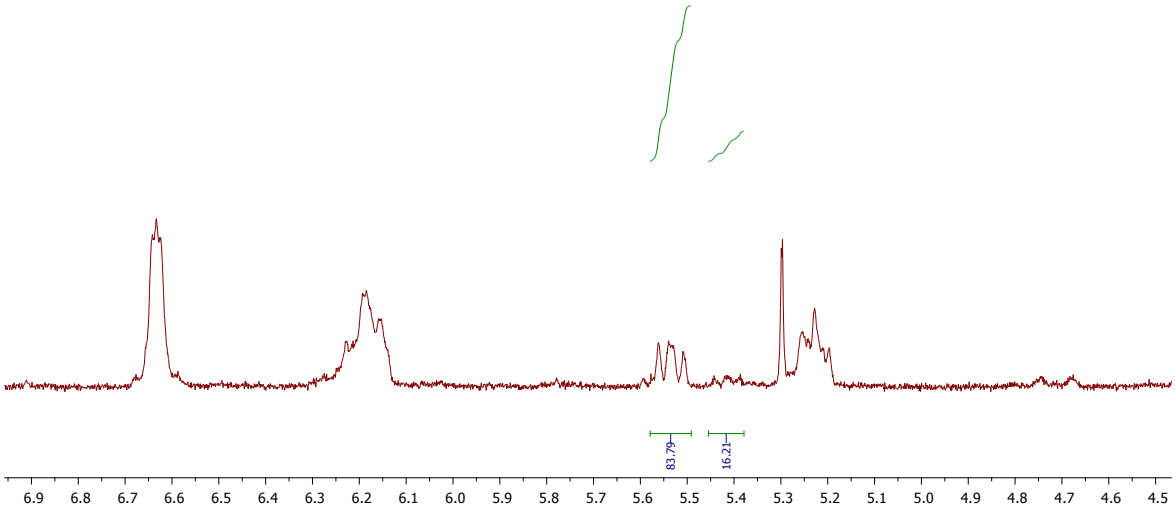


^{1}H-NMR (400 MHz, $CDCl_3$) of mixture of diastereomers of **3j**

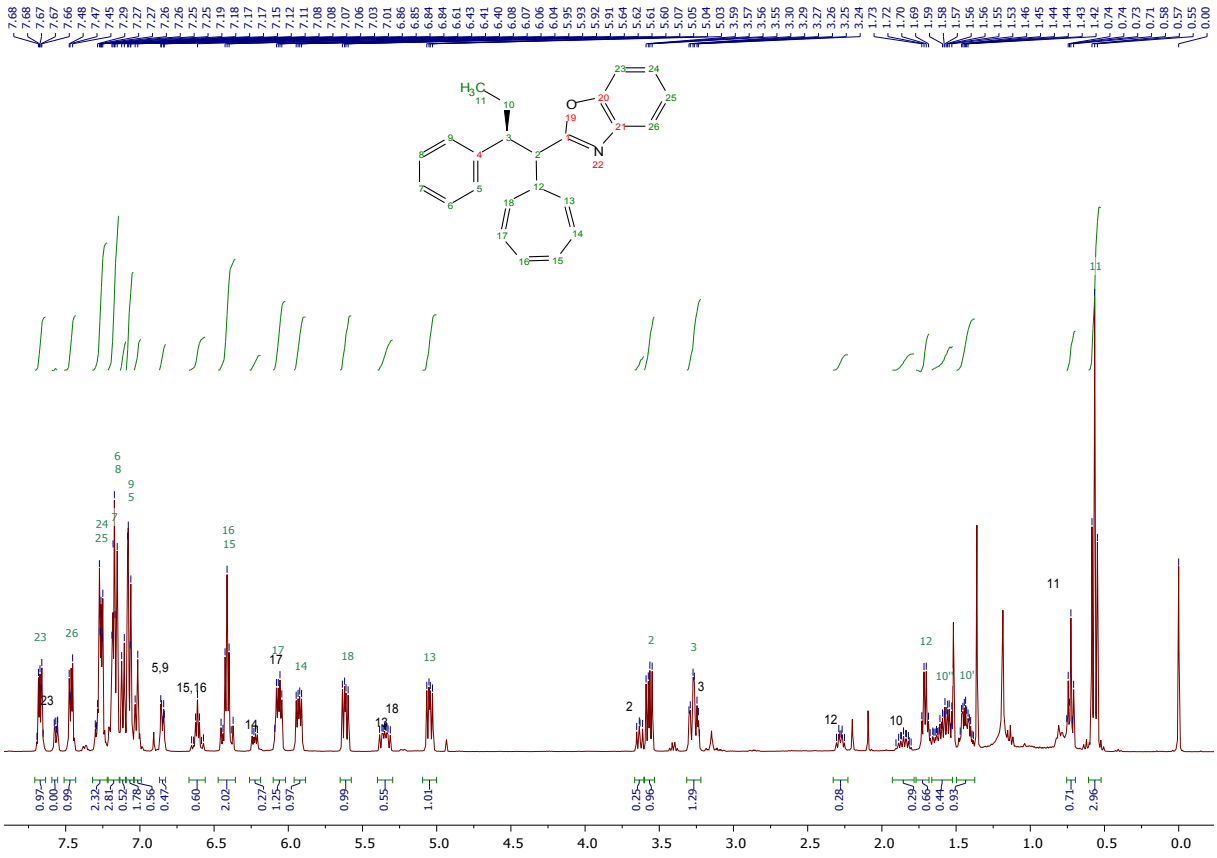


^{13}C-NMR (101 MHz, $CDCl_3$) of mixture of diastereomers of **3j**

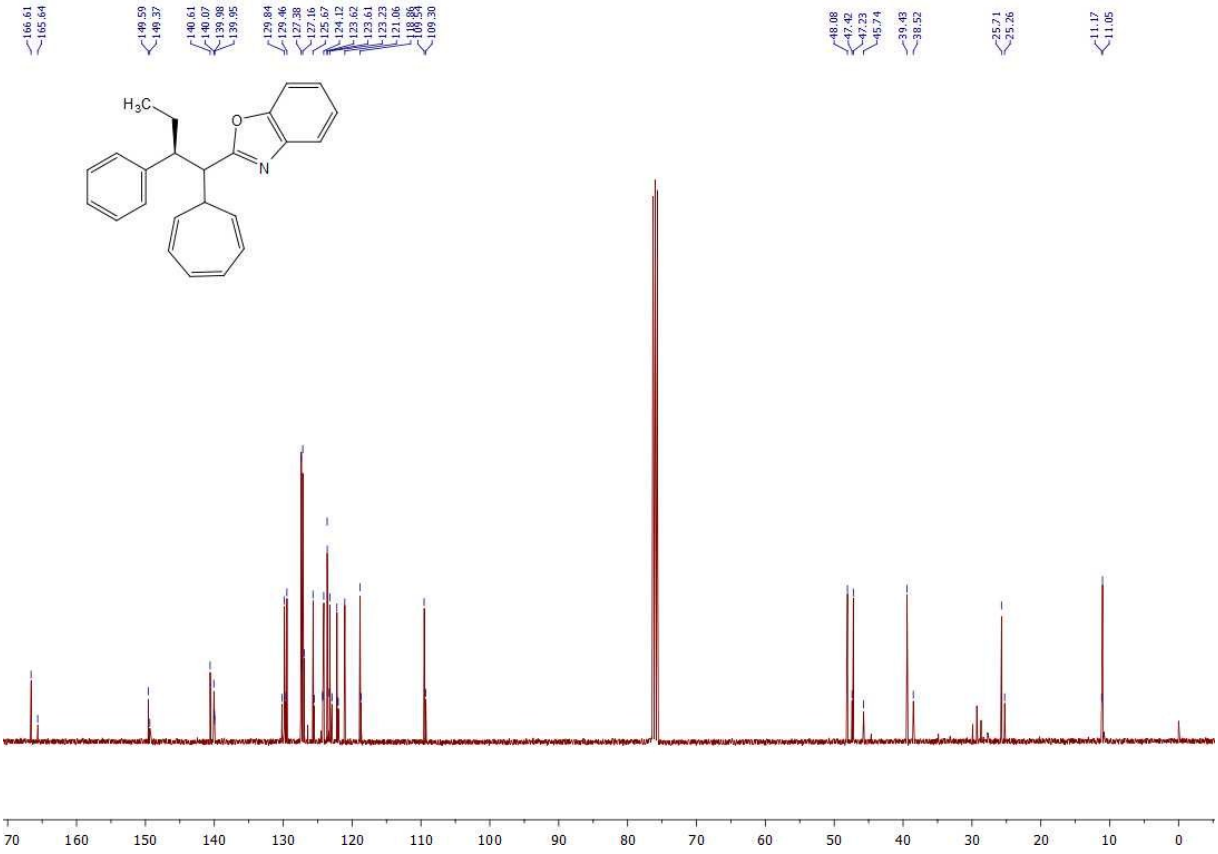




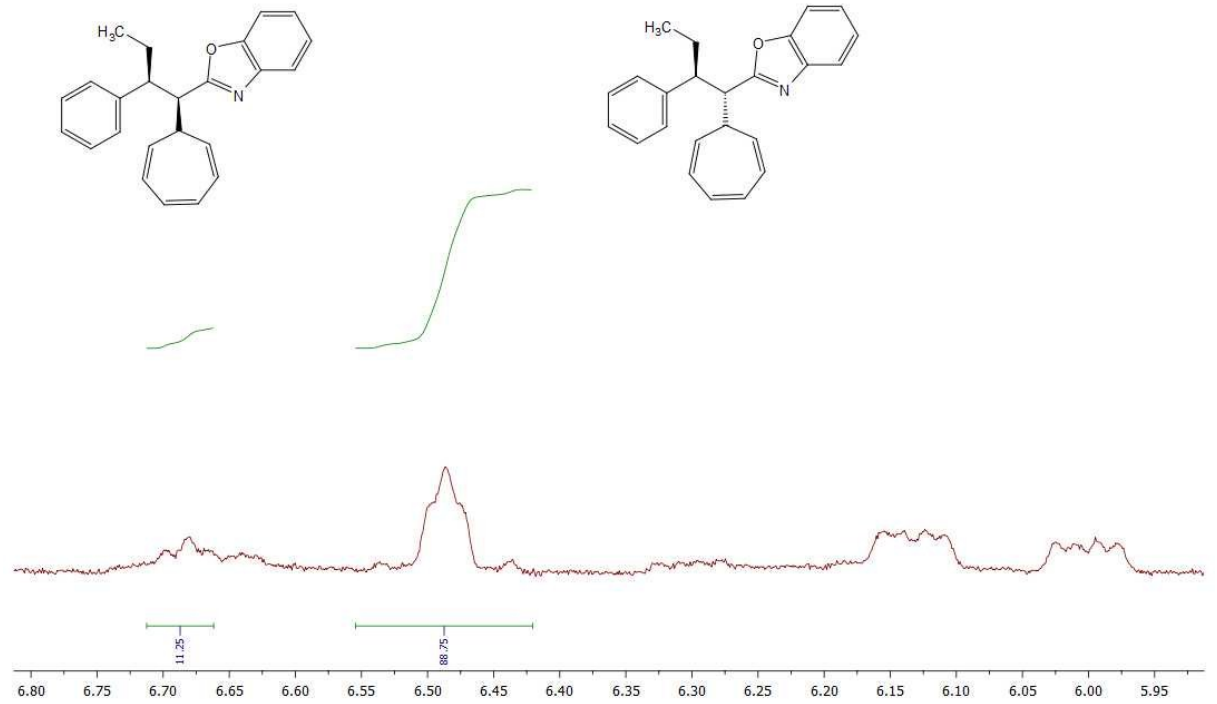
^{1}H-NMR (300 MHz, $CDCl_3$) of the crude mixture for dr determination of **3j**



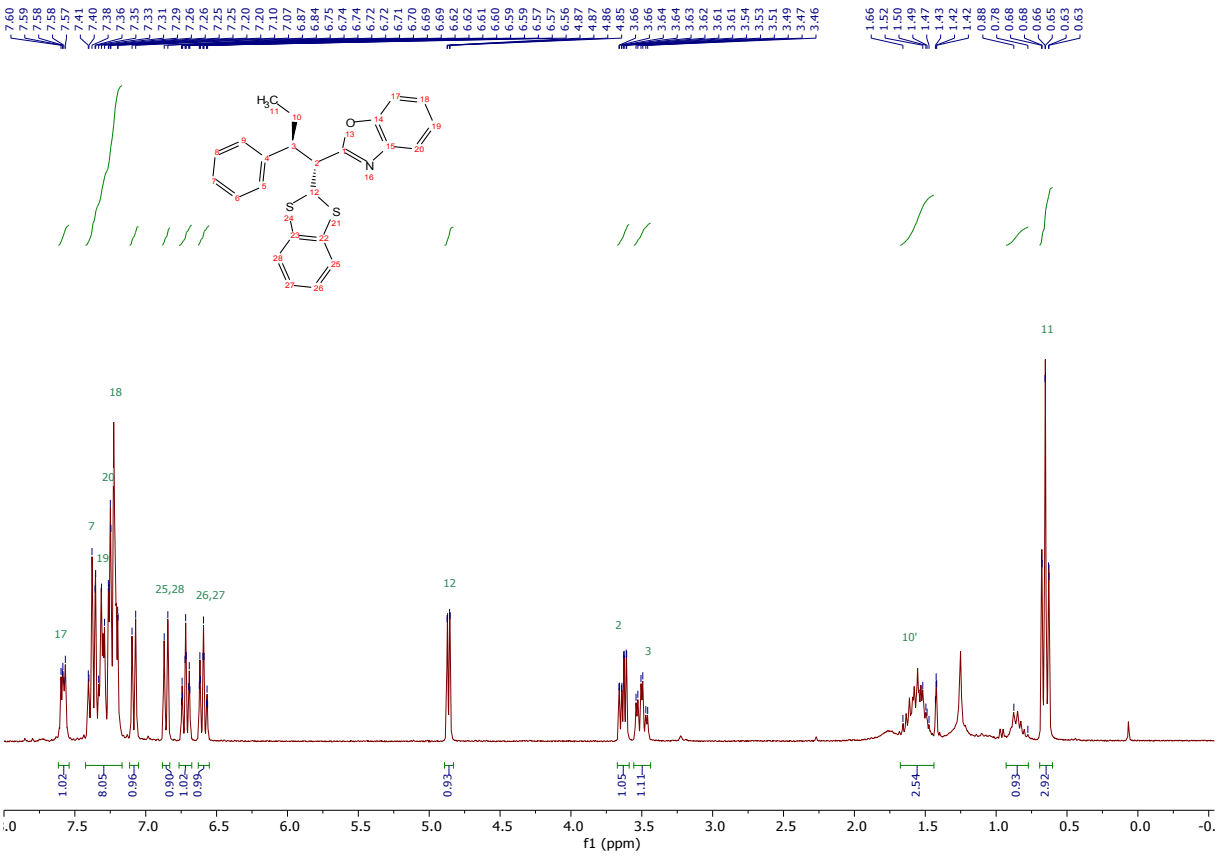
^{1}H-NMR (400 MHz, $CDCl_3$) of mixture of diastereomers of **12a**



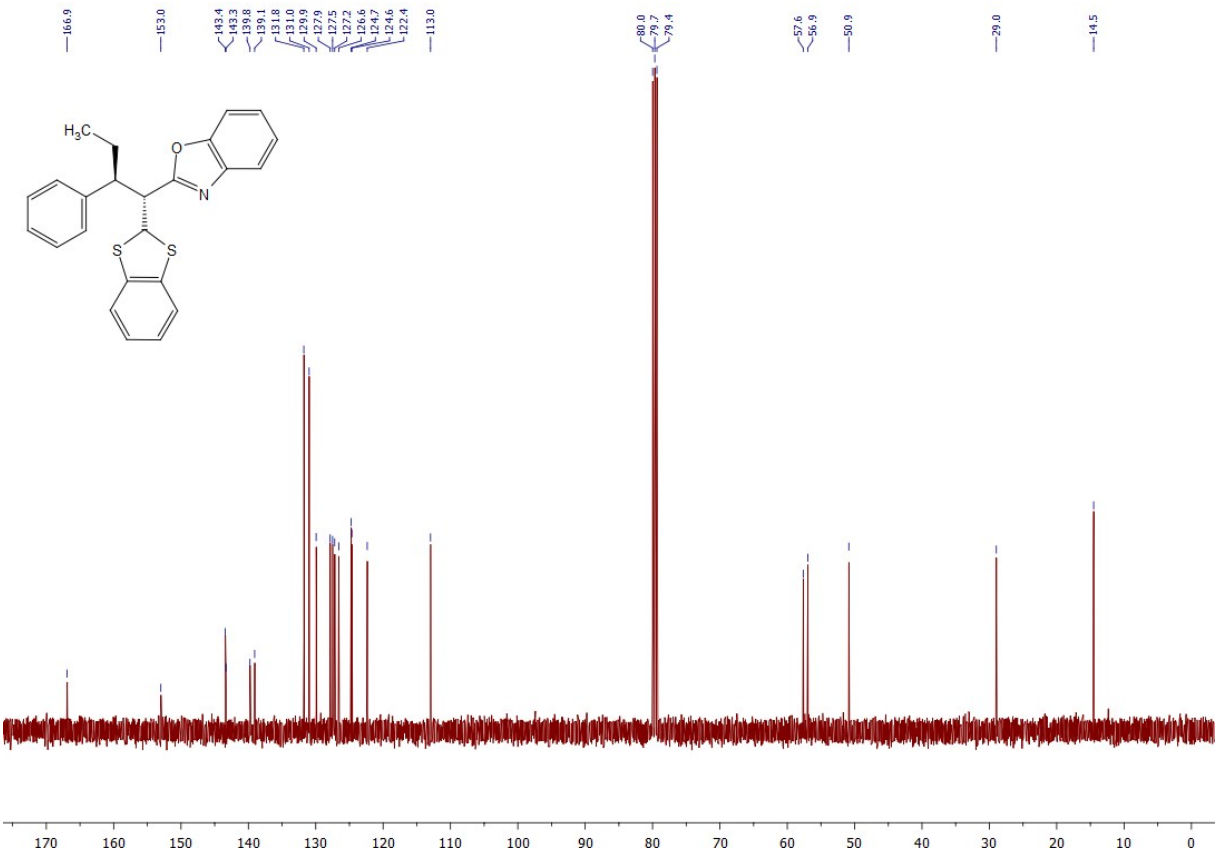
^{13}C-NMR (101 MHz, $CDCl_3$) of mixture of diastereomers of **12a**



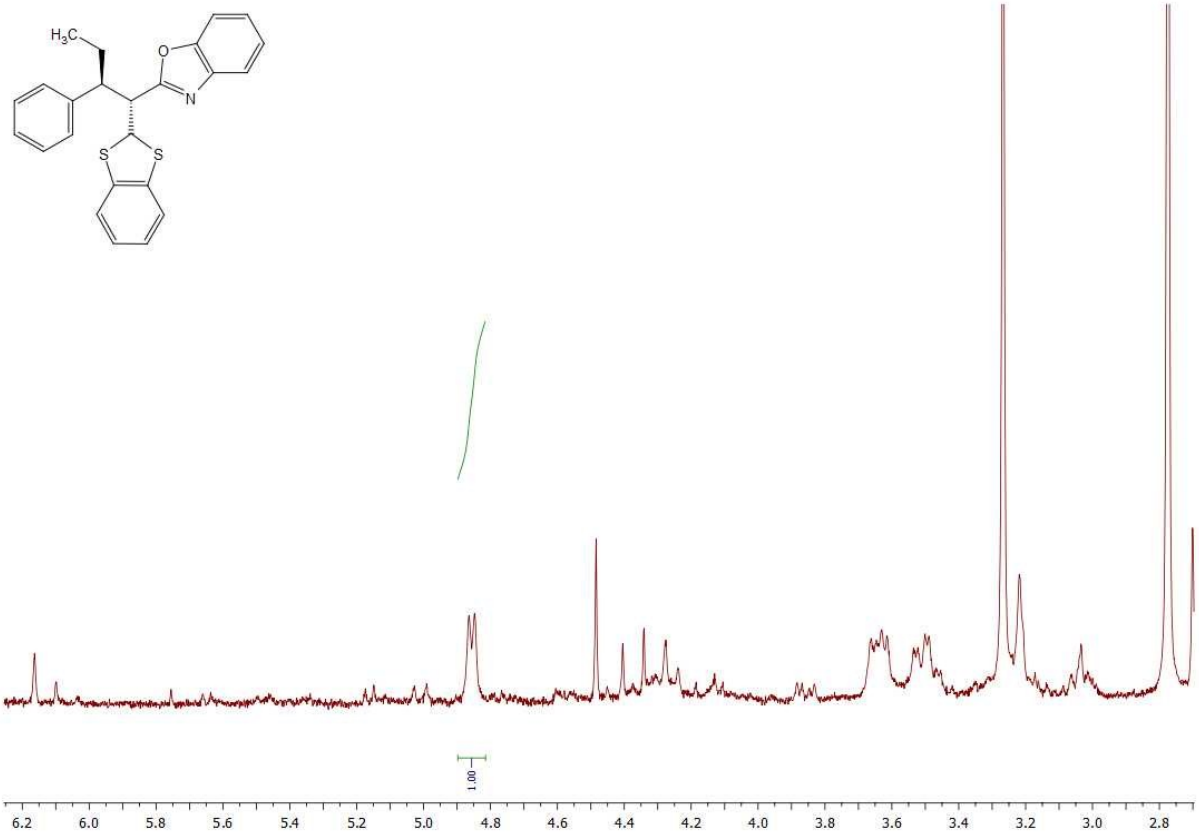
^{1}H-NMR (300 MHz, $CDCl_3$) of the crude mixture for dr determination of **12a**



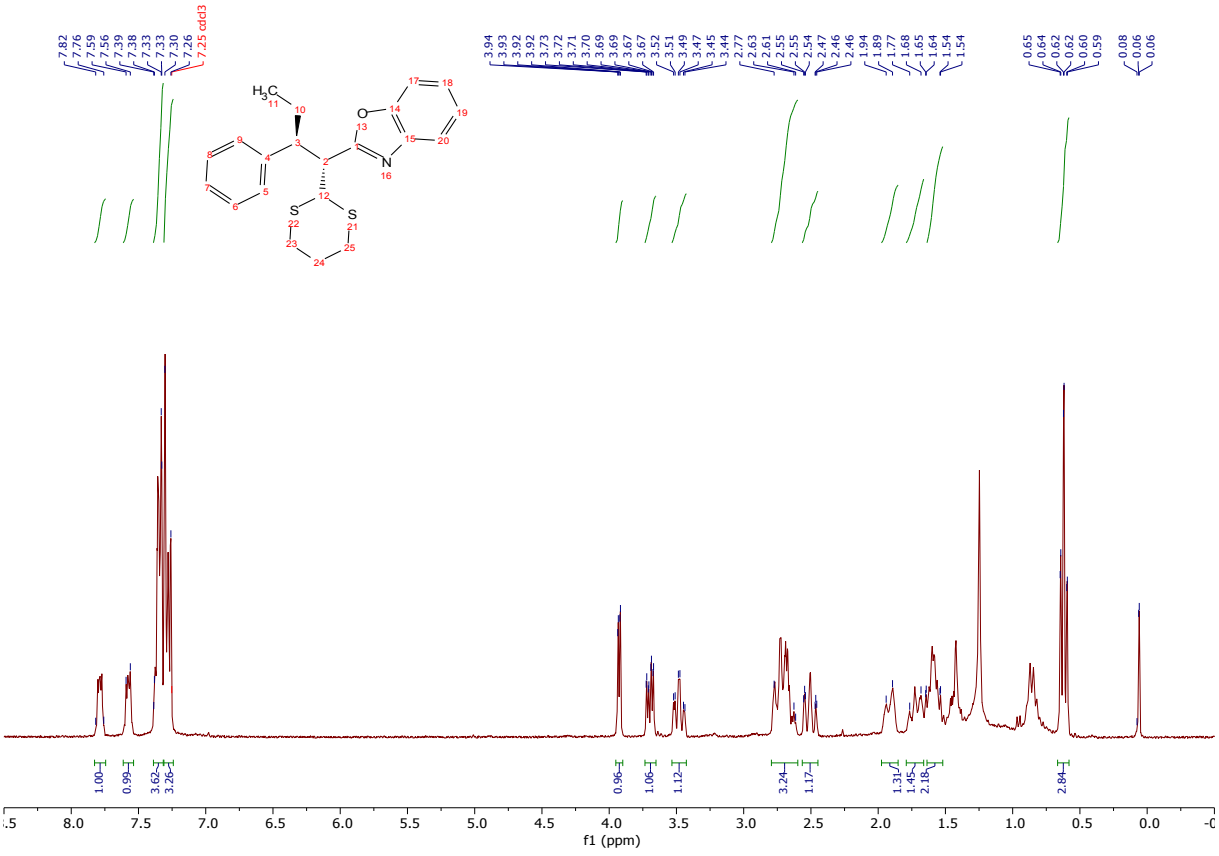
^{1}H-NMR (300 MHz, $CDCl_3$) of major diastereomer of **12b**



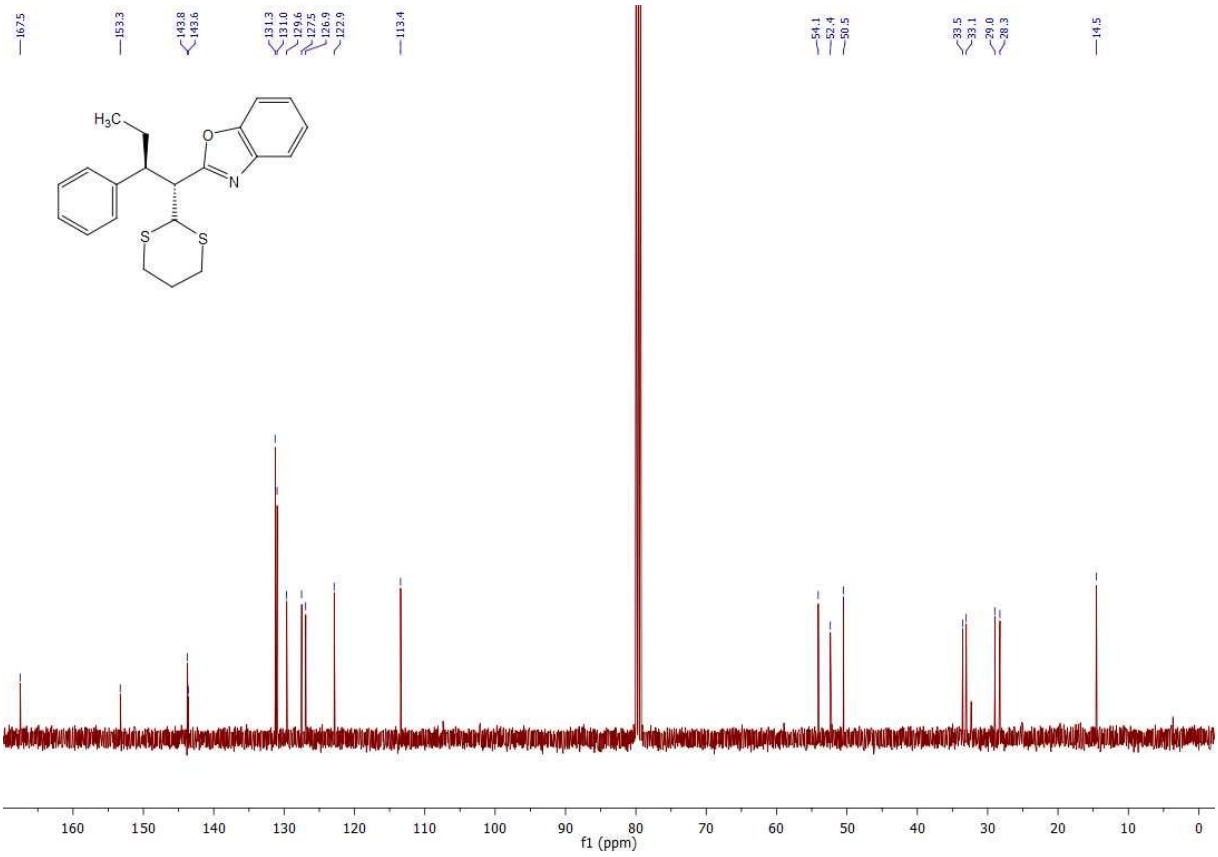
^{13}C-NMR (101 MHz, $CDCl_3$) of major diastereomer of **12b**



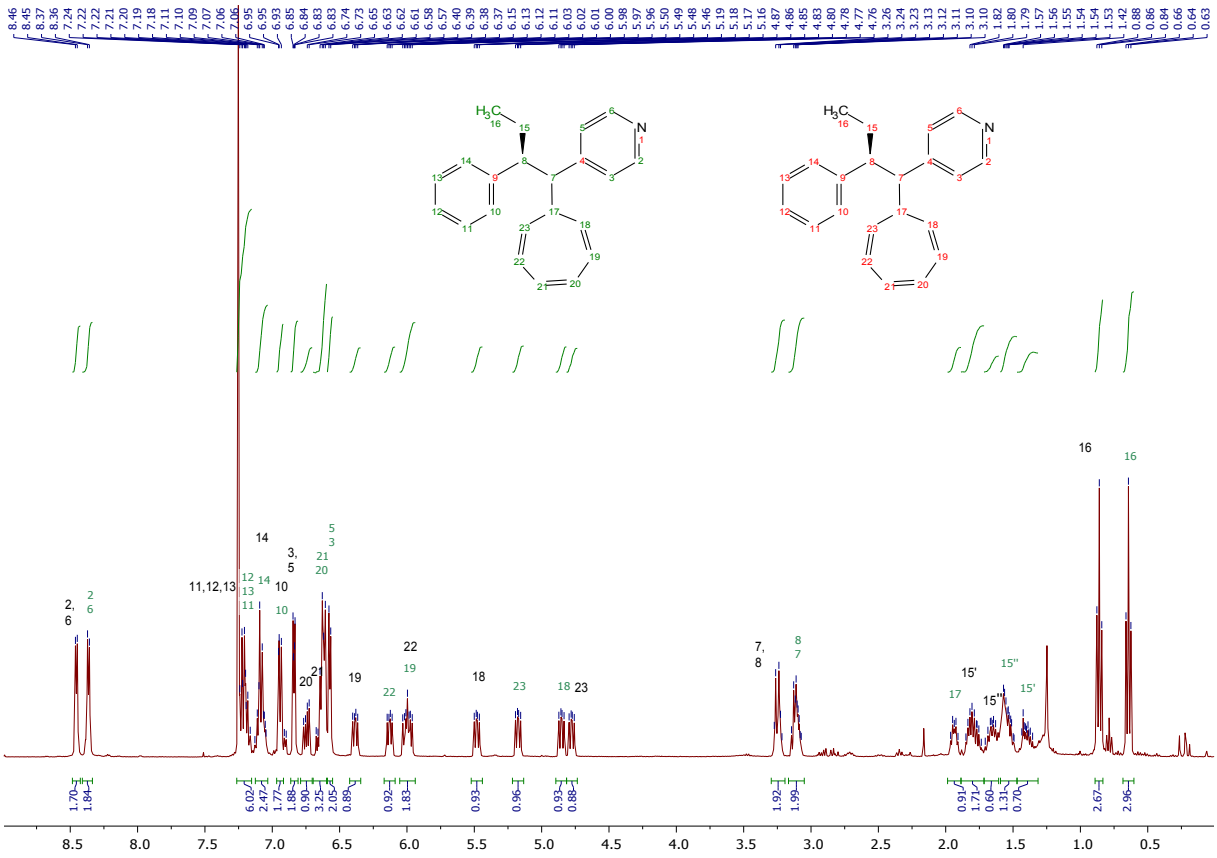
^{1}H-NMR (300 MHz, $CDCl_3$) of the crude mixture for dr determination of **12b**



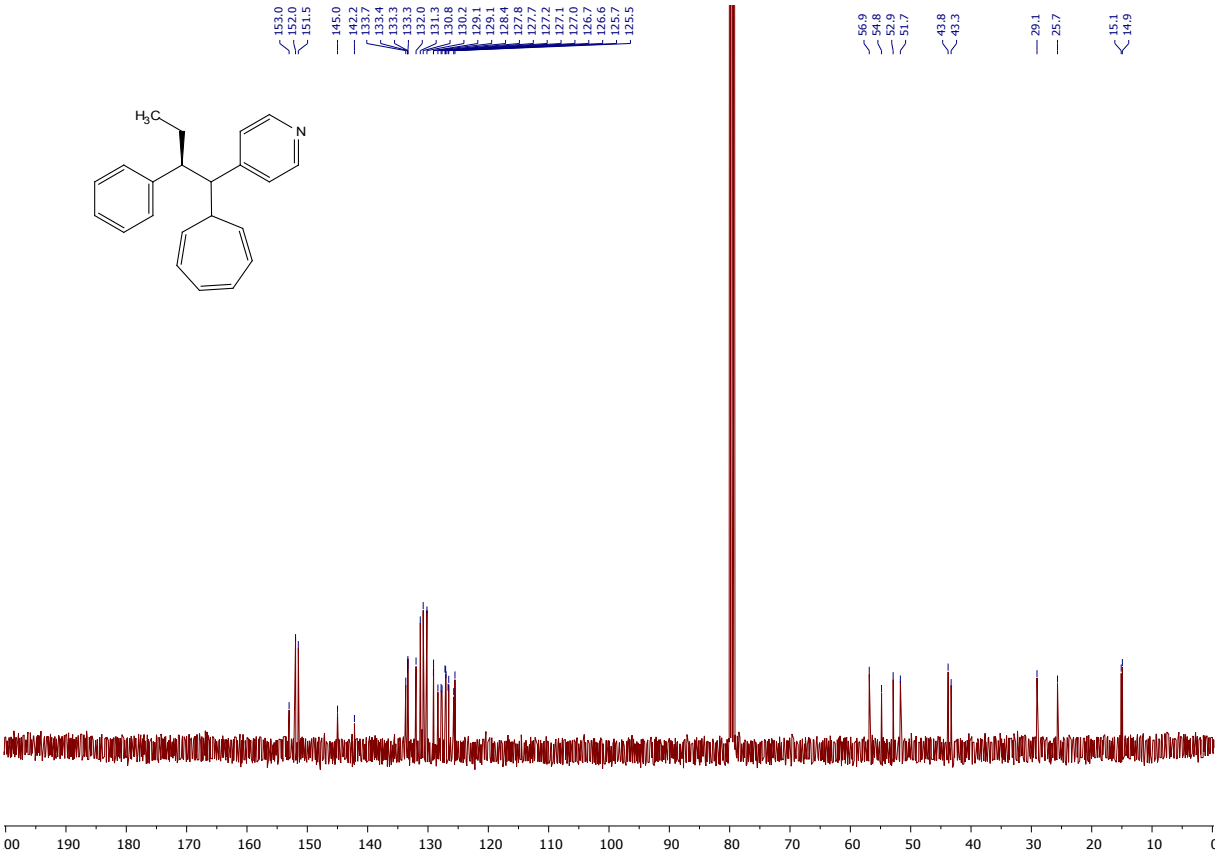
^{1}H-NMR (300 MHz, $CDCl_3$) of major diastereomer of **12c**



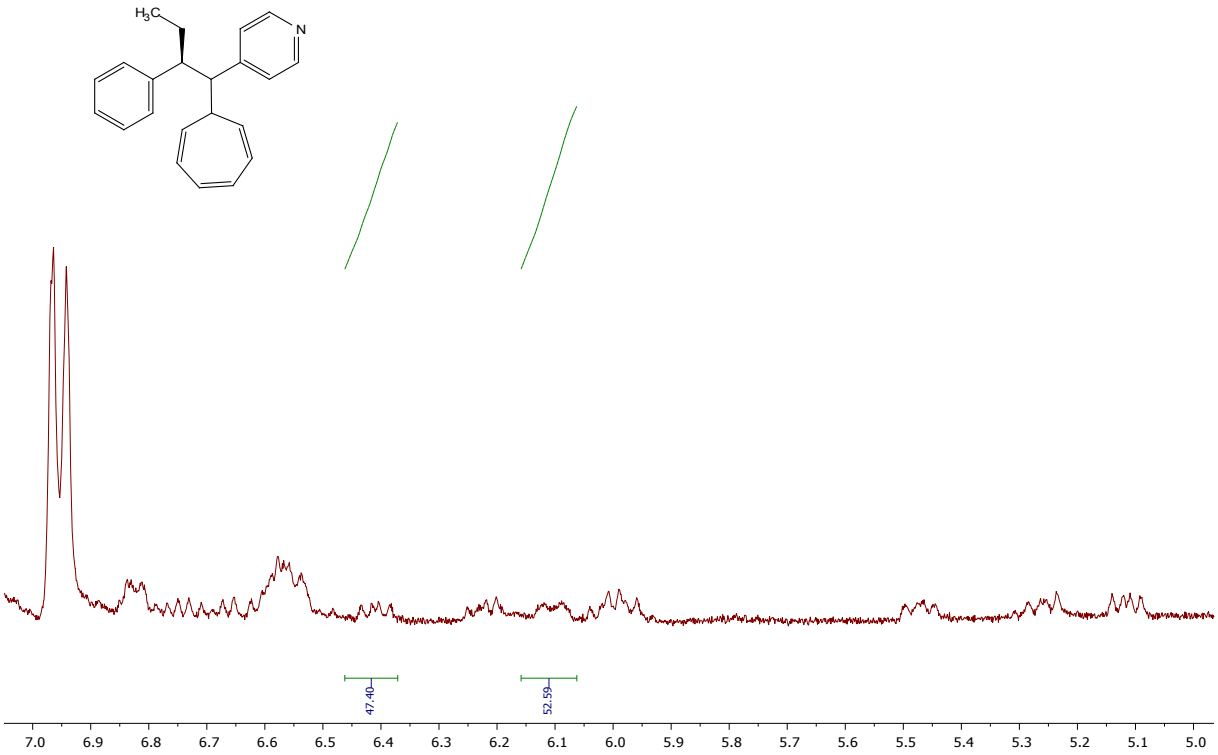
^{13}C-NMR (101 MHz, $CDCl_3$) of major diastereomer of **12c**



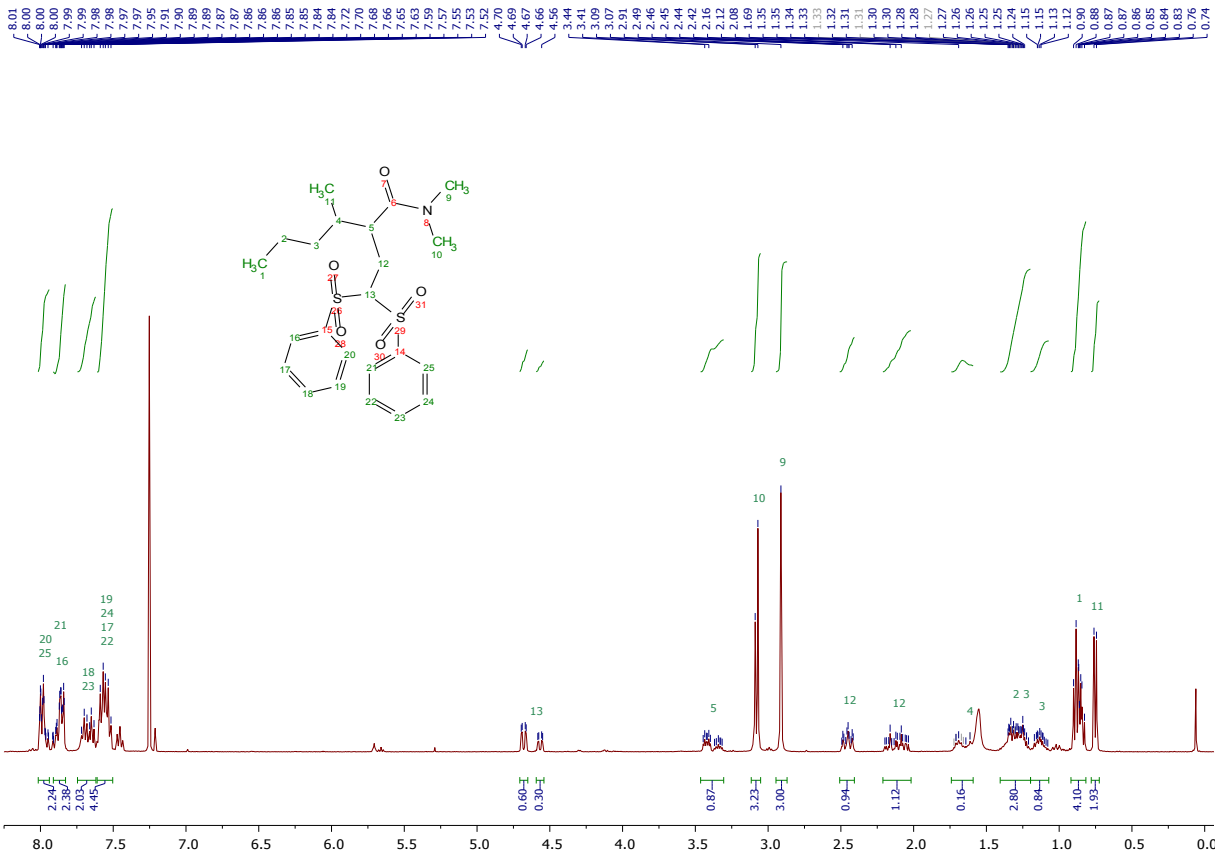
^{1}H-NMR (400 MHz, $CDCl_3$) of mixture of diastereomers of **12d**



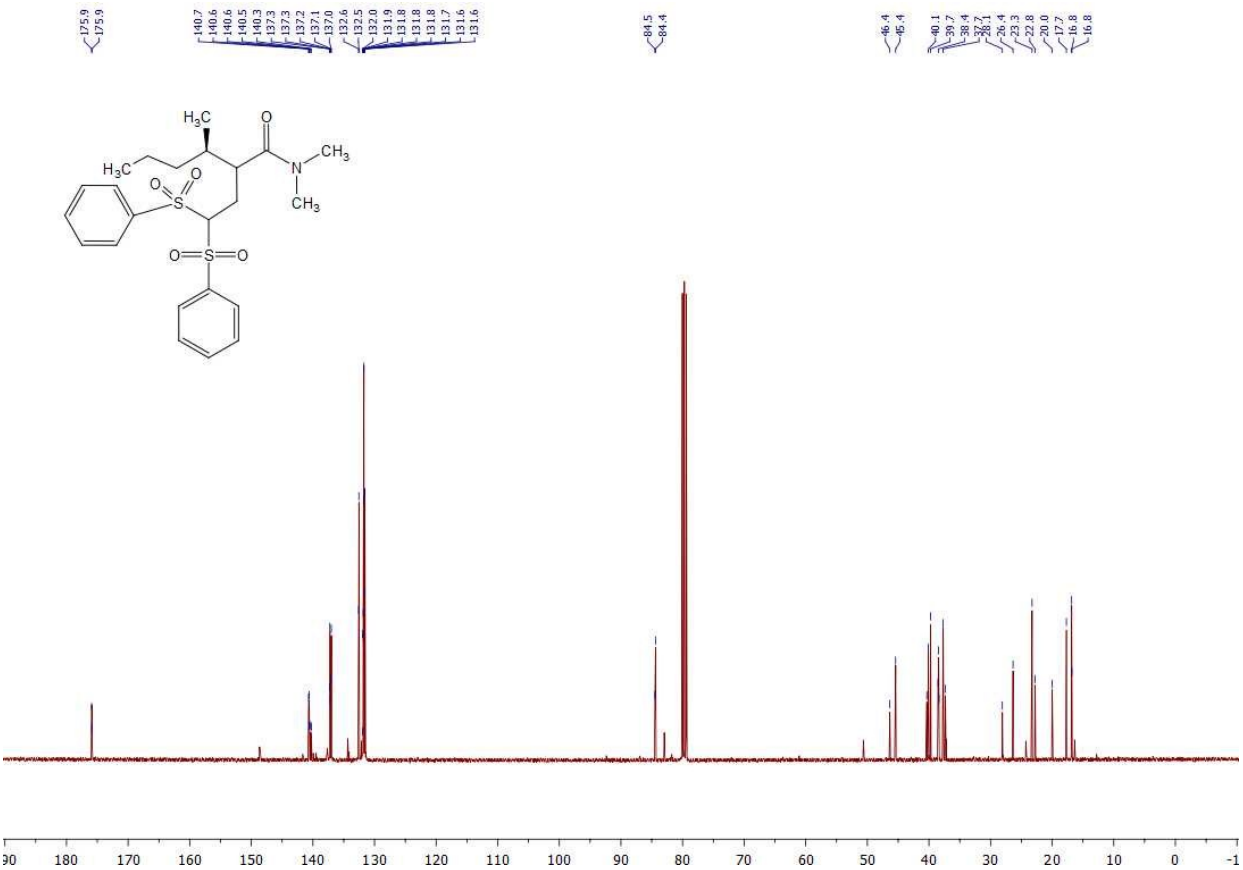
^{13}C-NMR (101 MHz, $CDCl_3$) of mixture of diastereomers of **12d**



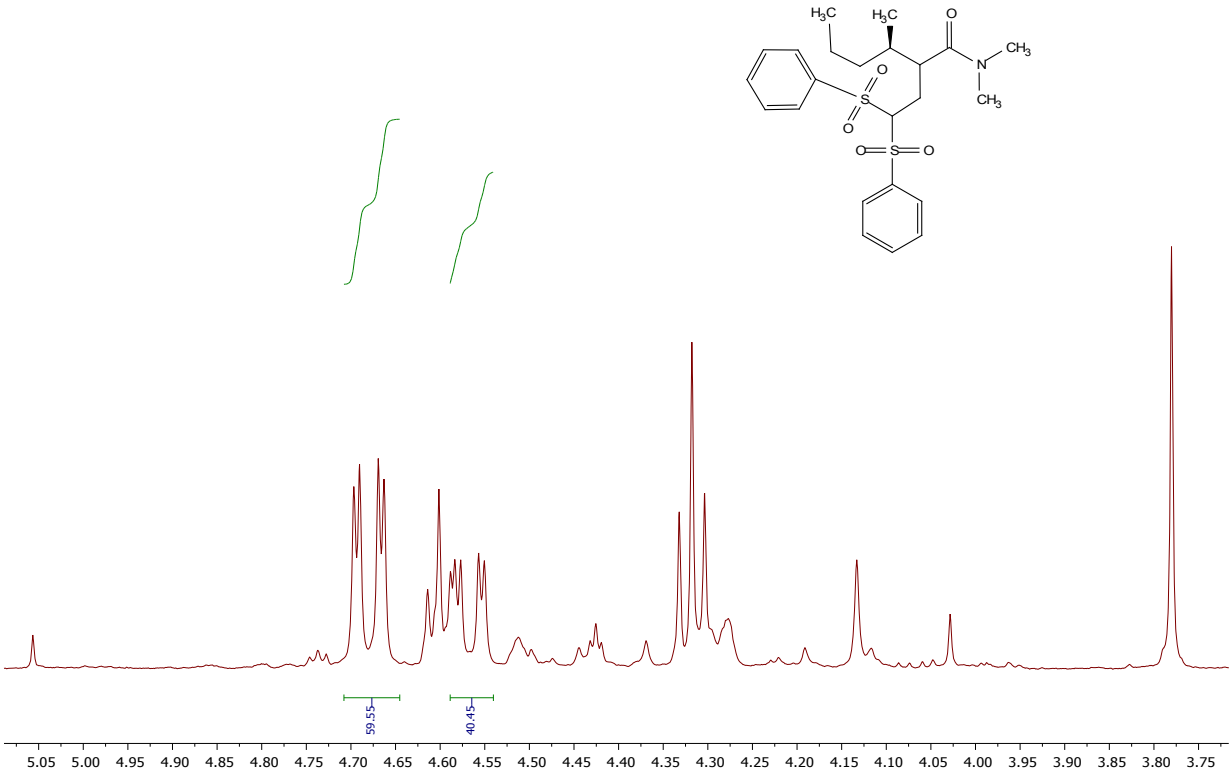
^{1}H-NMR (300 MHz, $CDCl_3$) of the crude mixture for dr determination of **12d**



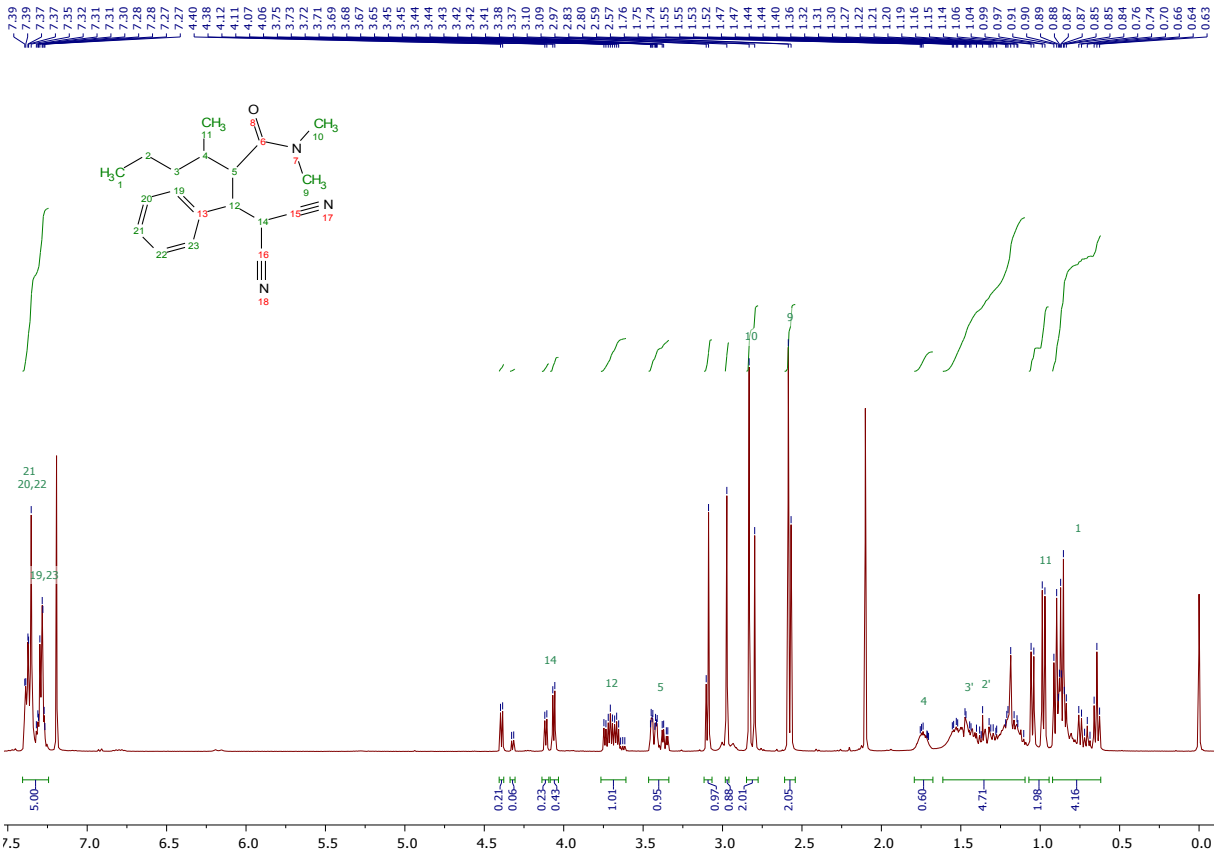
^{1}H-NMR (400 MHz, $CDCl_3$) of mixture of diastereomers of **15a**



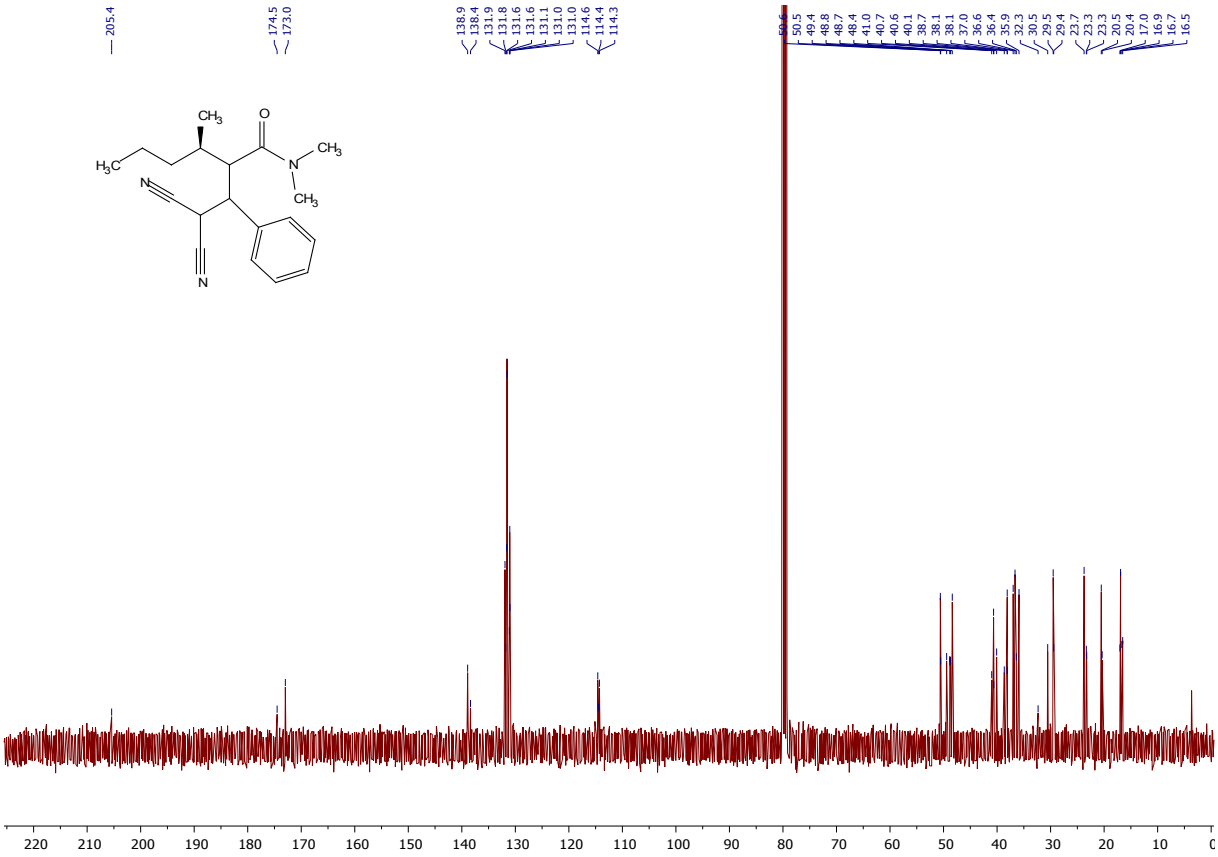
^{13}C-NMR (101 MHz, $CDCl_3$) of mixture of diastereomers of **15a**



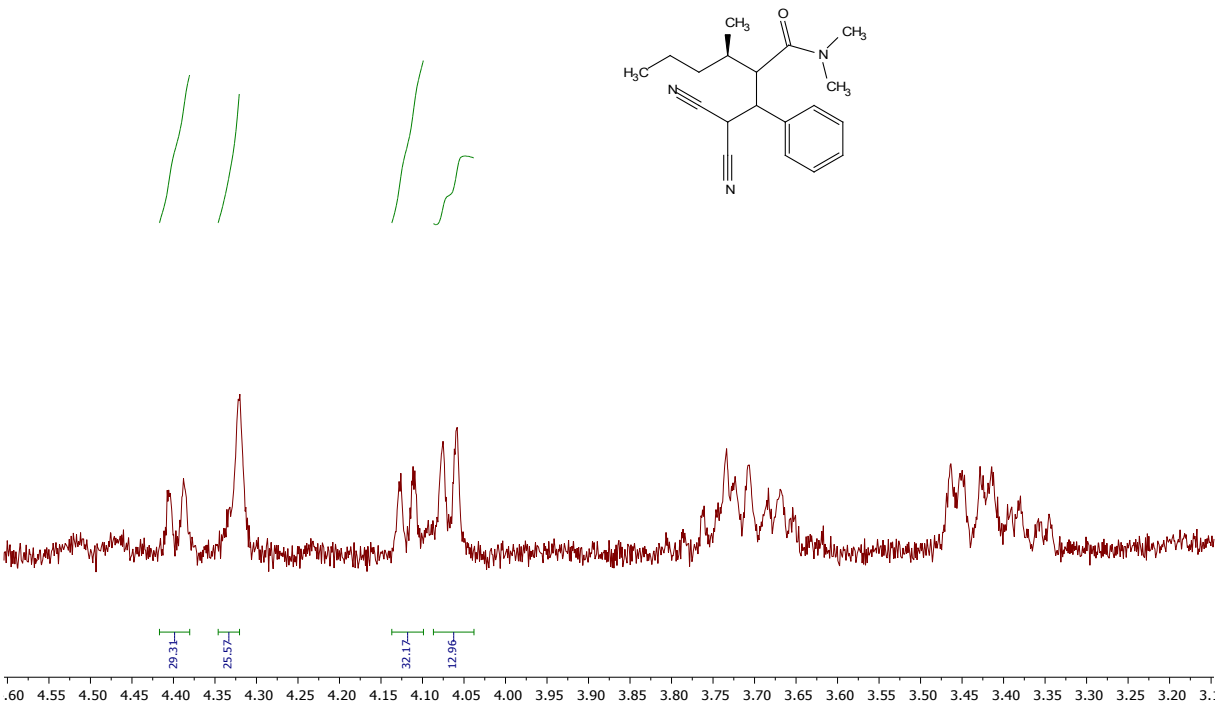
^{1}H-NMR (400 MHz, $CDCl_3$) of the crude mixture for dr determination of **15a**



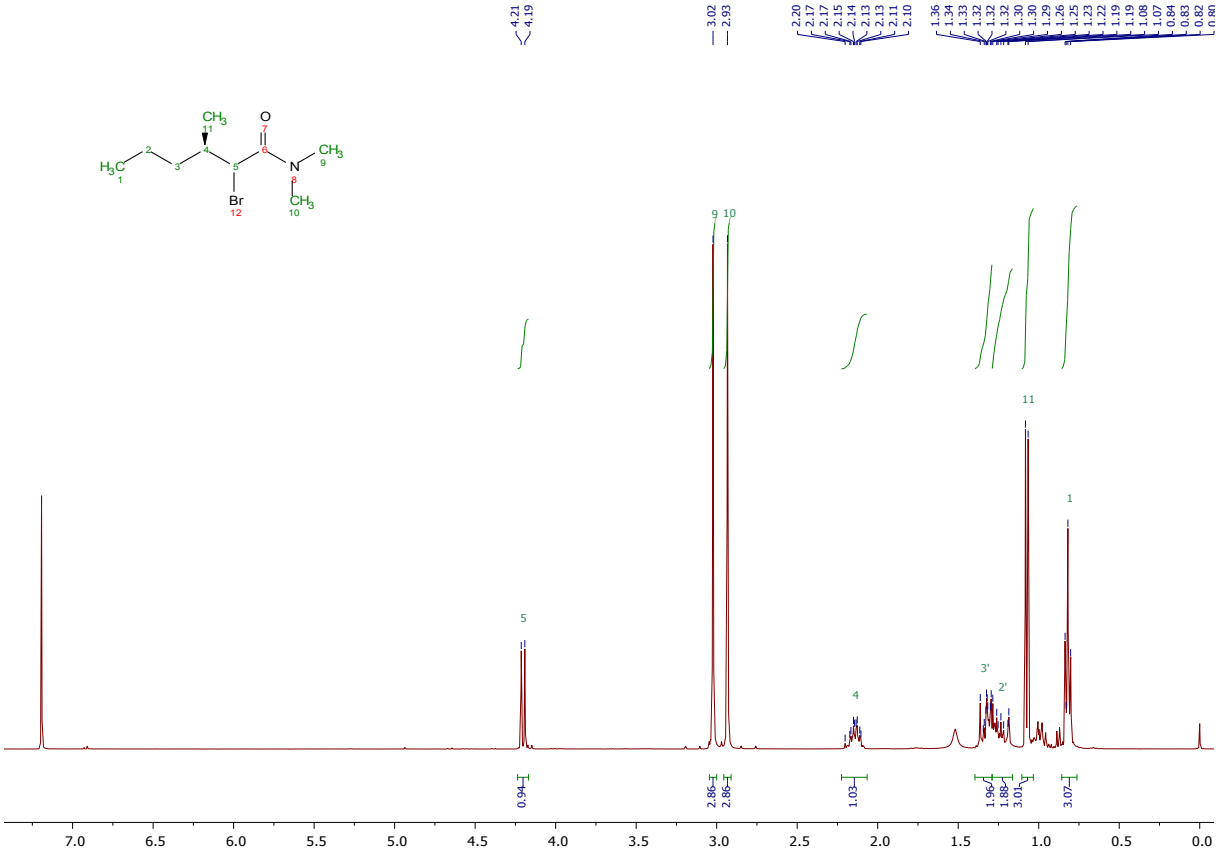
^{1}H-NMR (400 MHz, $CDCl_3$) of mixture of diastereomers of **15b**



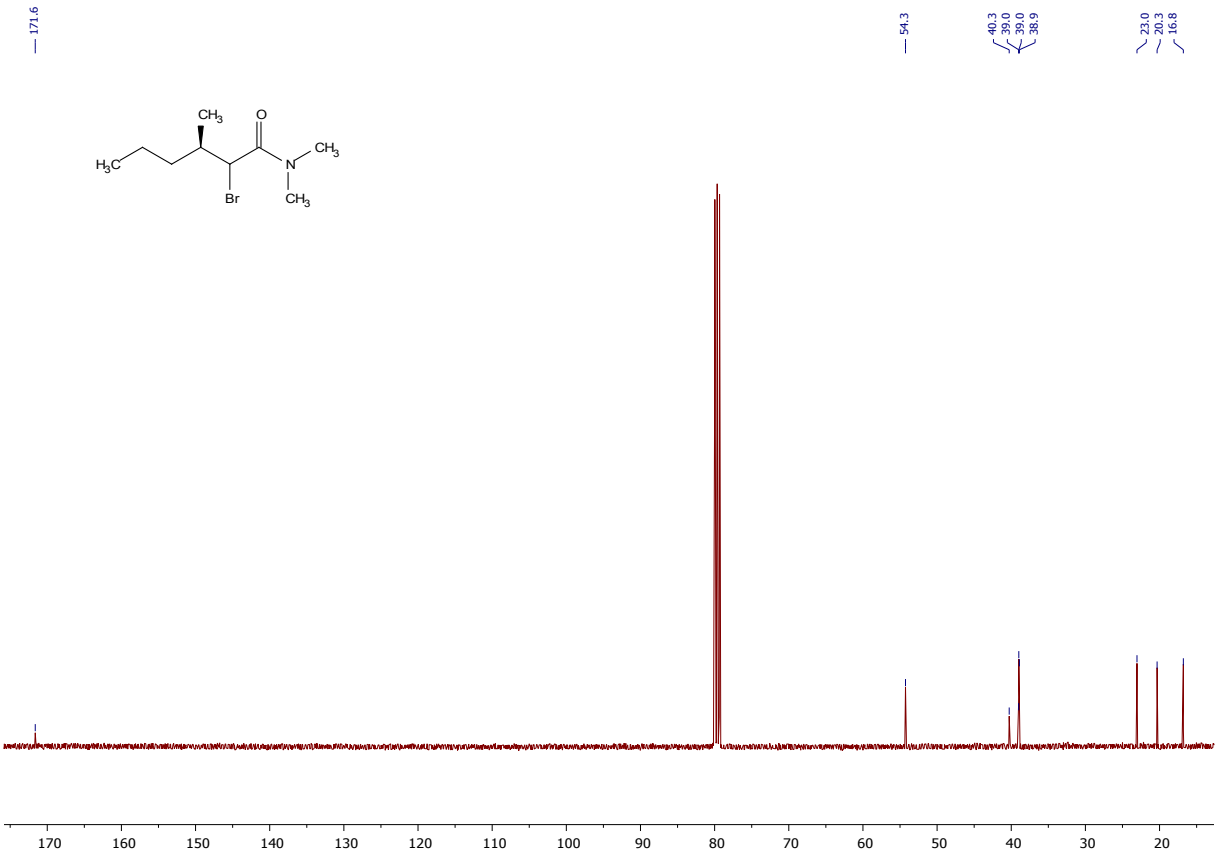
^{13}C-NMR (101 MHz, $CDCl_3$) of mixture of diastereomers of **15b**



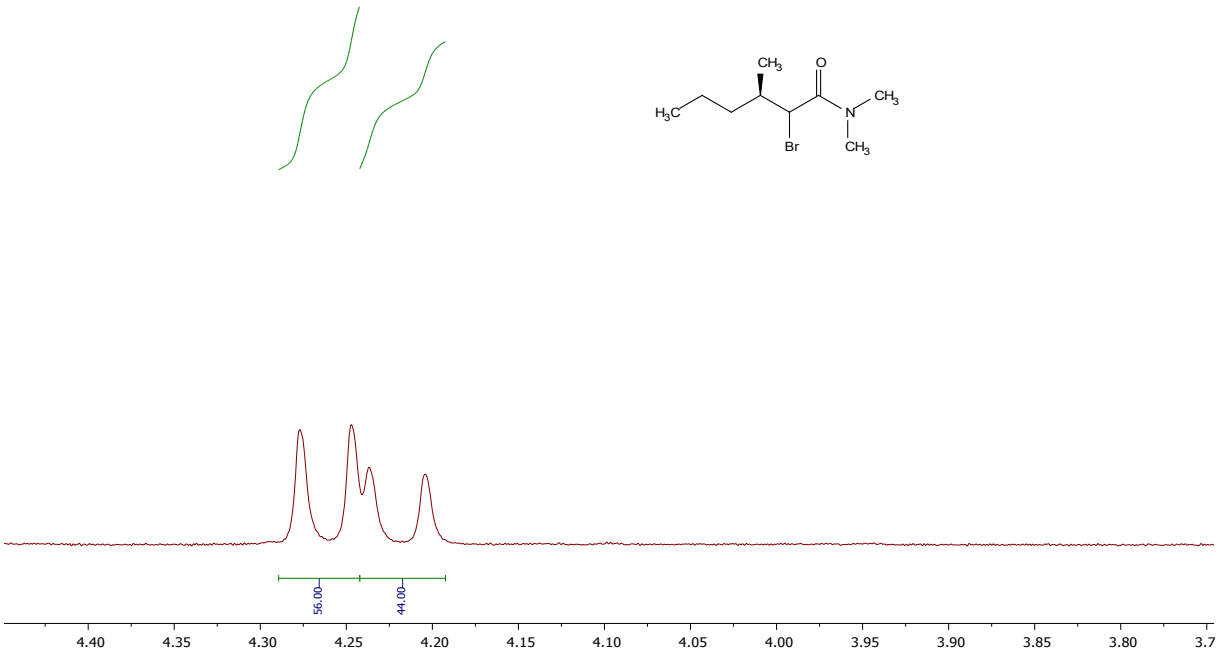
^{1}H-NMR (300 MHz, $CDCl_3$) of the crude mixture for dr determination of **15b**



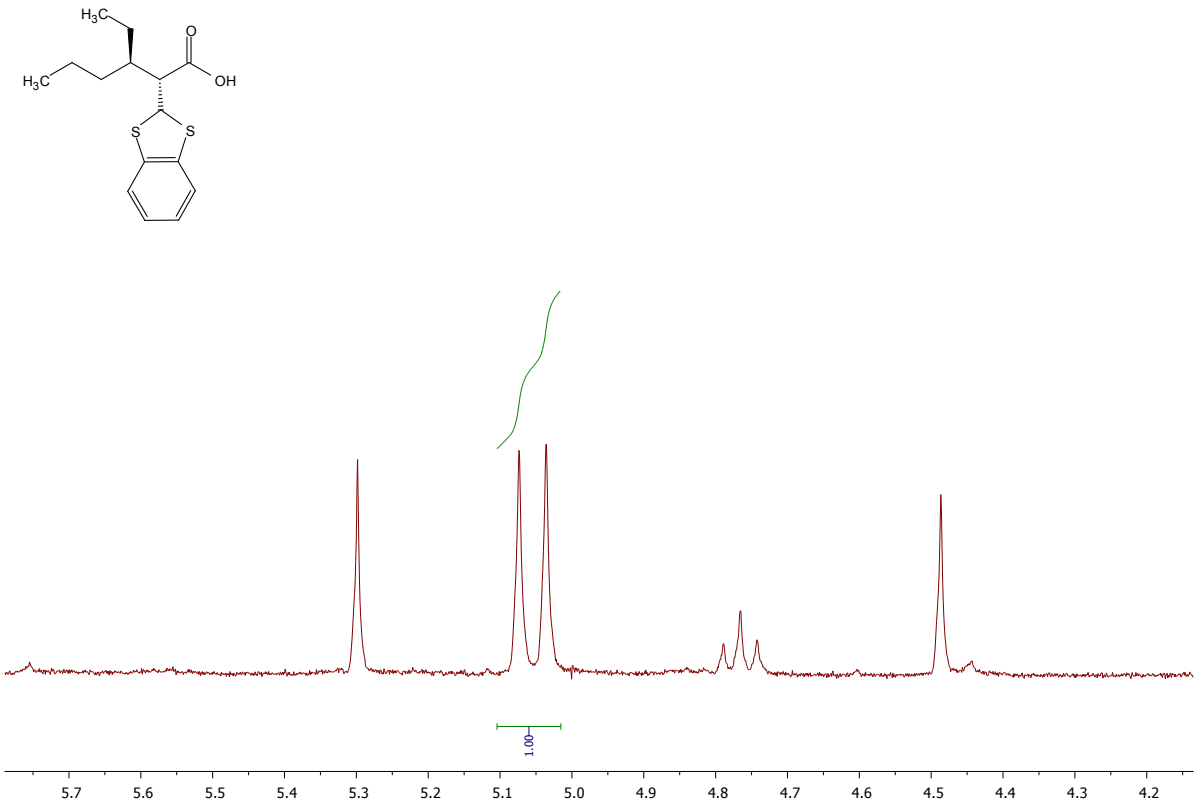
^{1}H-NMR (400 MHz, $CDCl_3$) of mixture of diastereomers of **15c**



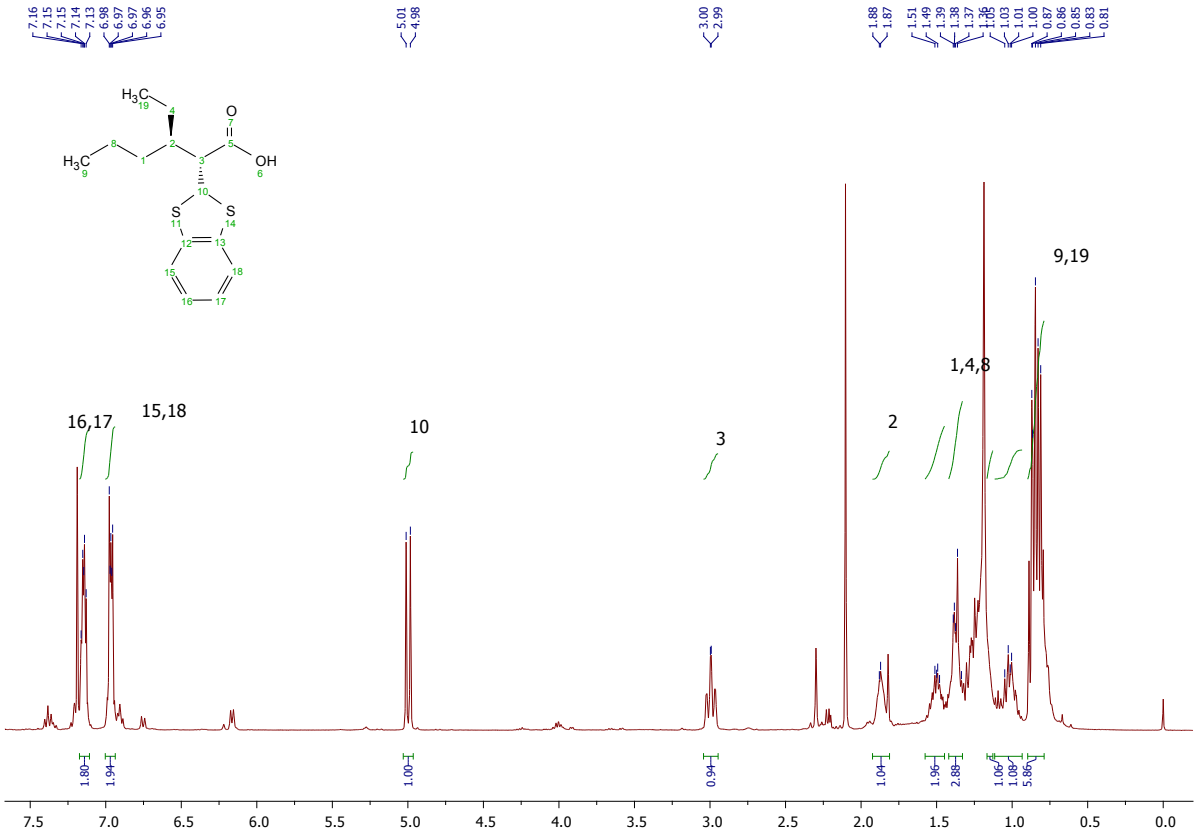
^{13}C-NMR (101 MHz, $CDCl_3$) of mixture of diastereomers of **15c**



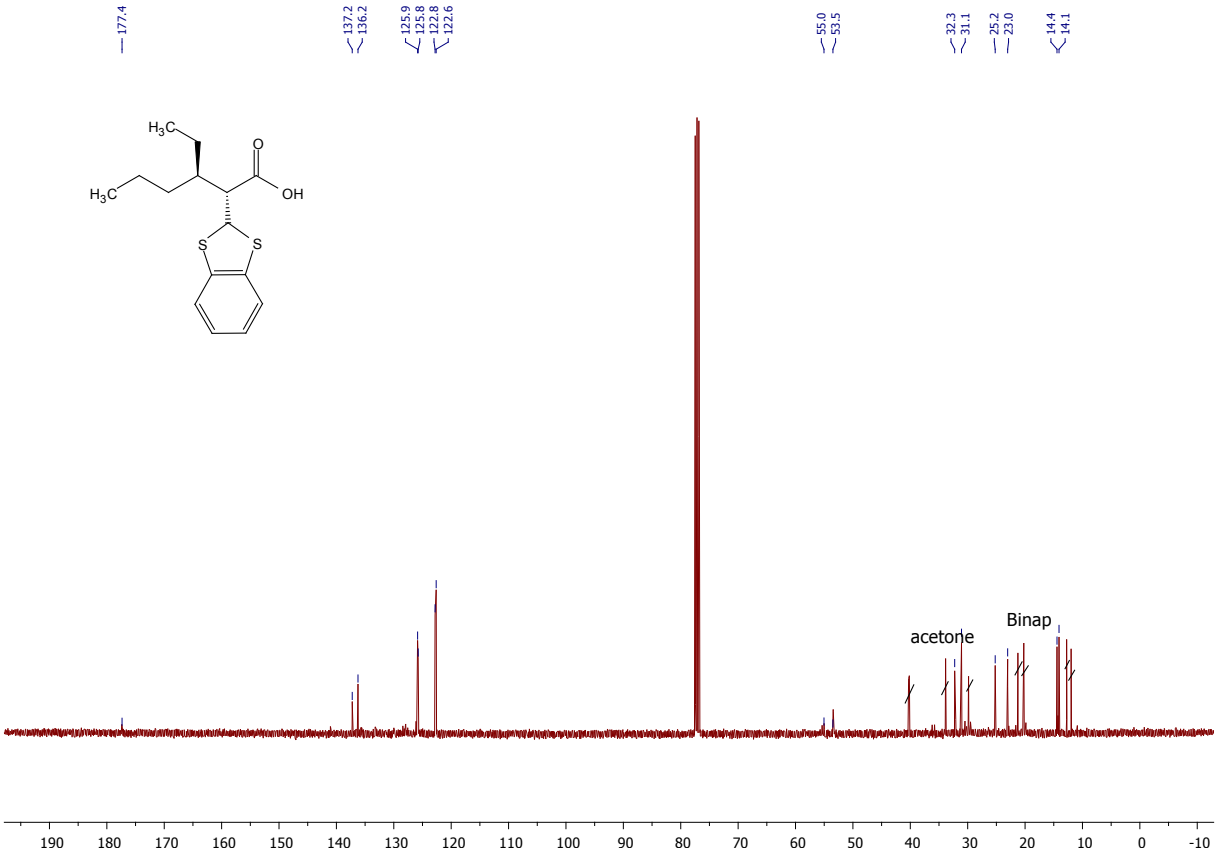
^{1}H-NMR (300 MHz, $CDCl_3$) of the crude mixture for dr determination of **15c**



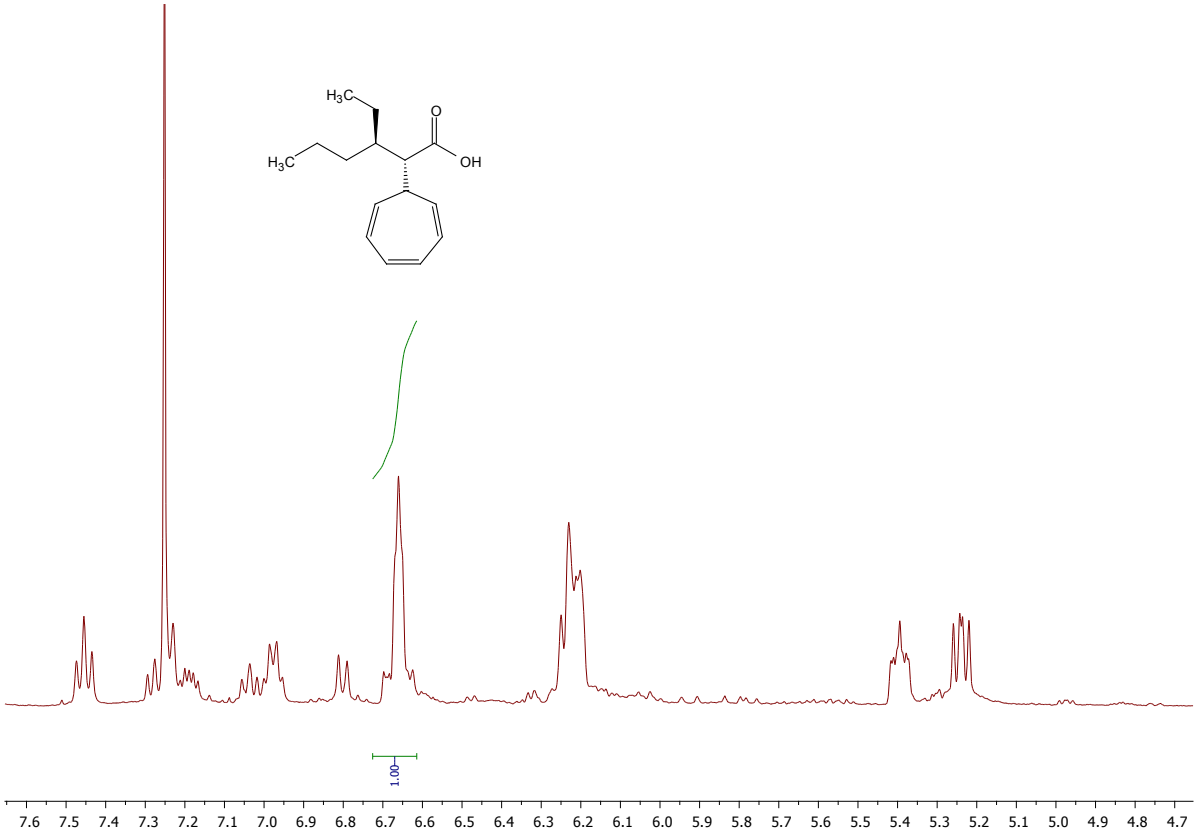
^{1}H-NMR (300 MHz, $CDCl_3$) of the crude mixture of **18a**



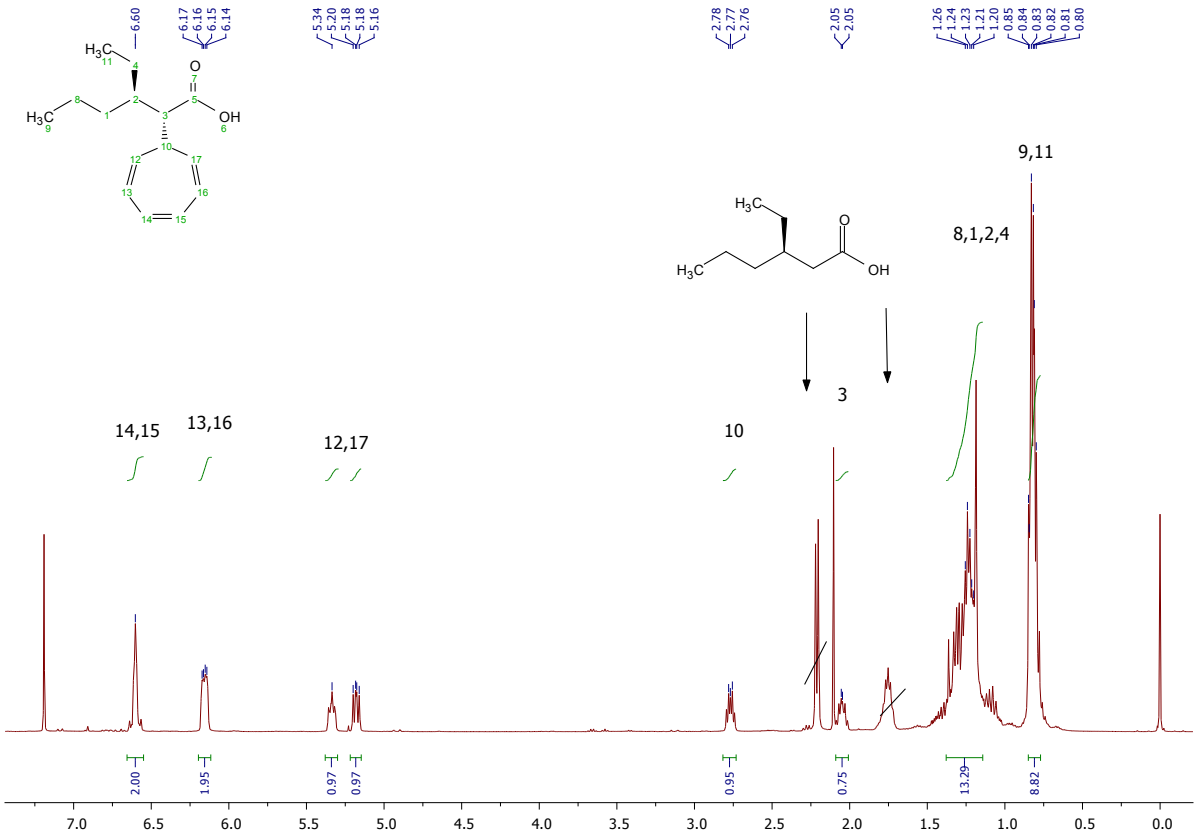
^{1}H-NMR (400 MHz, $CDCl_3$) of **18a**



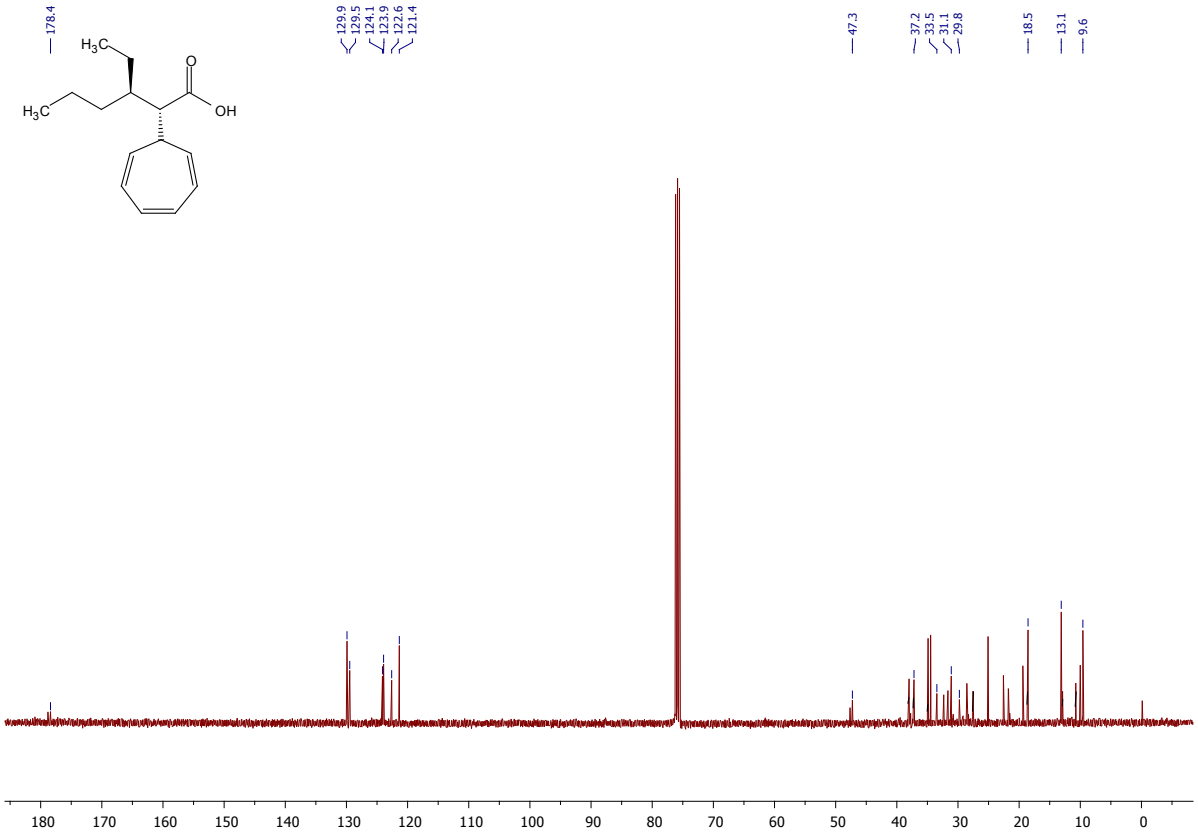
^{13}C-NMR (101 MHz, $CDCl_3$) of **18a**



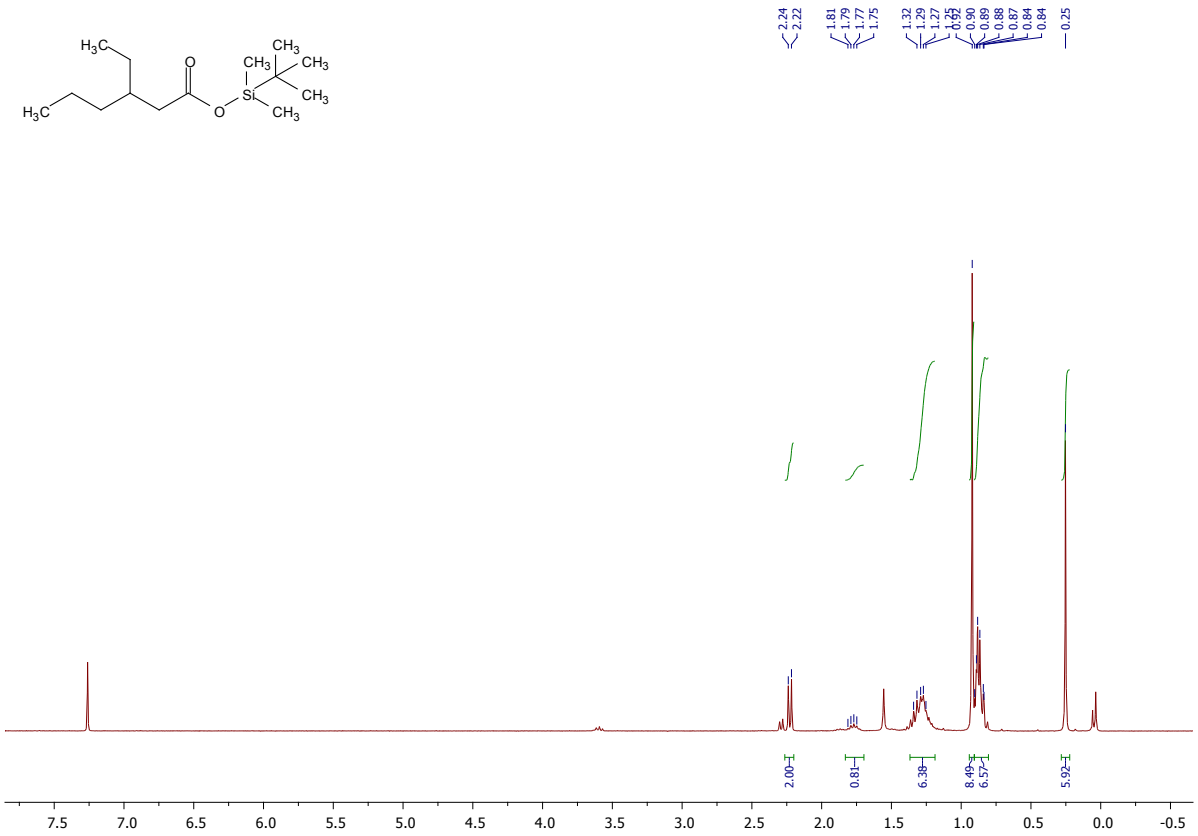
^{1}H-NMR (300 MHz, $CDCl_3$) of the crude mixture for dr determination of **18b**



^{1}H-NMR (400 MHz, $CDCl_3$) of **18b**



^{13}C-NMR (101 MHz, $CDCl_3$) of **18b**

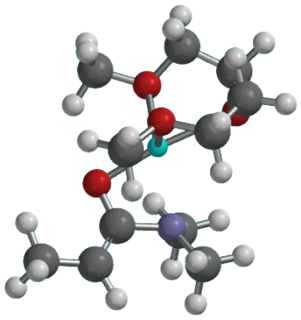


^{1}H-NMR (300 MHz, $CDCl_3$) of TBS-ester intermediate

Computational details

The molecular models were build and optimized by AM1 method in Spartan 18 program package.[3] From the conformer distribution, ten most stable conformers were selected and pre-optimized in Spartan at HF/3-21G level and then fully geometrically optimized at ωB97X-D/6-31G* level and energies were then refined by single point calculations at M06-2X/6-311+G** level.[4]

Z-Me-Li(diglyme)-ketene-aminal

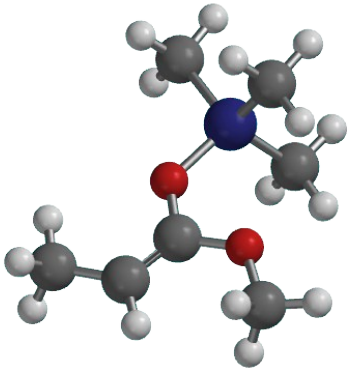


Geometry optimization: ωB97X-D/6-31G*
Single point energy calculation: M06-2X/6-311+G**
Energy:-796.702572 hartrees
HOMO energy: -5.35 eV

Cartesian coordinates

C	2.426595	1.683071	-1.293866
C	1.813458	0.626927	-0.703679
O	1.698697	0.371735	0.561984
N	1.069653	-0.354330	-1.508484
C	0.742751	0.002983	-2.874019
C	1.677900	-1.681706	-1.442534
Li	0.021034	-0.428409	0.378068
C	3.086269	2.765152	-0.489631
H	2.496193	1.738554	-2.375446
H	2.827580	2.650246	0.567573
H	4.183811	2.736861	-0.560865
H	2.776386	3.770067	-0.811897
H	0.022969	-0.721825	-3.273463
H	1.622637	0.010054	-3.539697
H	0.296036	1.000887	-2.894892
H	0.963910	-2.439079	-1.787734
H	2.587193	-1.744408	-2.063924
H	1.953741	-1.892731	-0.406544
O	-0.173853	-1.561444	2.027463
C	0.458950	-0.914452	3.119964
C	-1.509087	-1.939513	2.259462
O	-1.888033	-1.539947	-0.097365
C	-2.036591	-2.488942	0.944468
C	-2.909936	-0.558691	-0.180385
O	-1.383848	1.088875	0.517403
C	-2.272980	0.768313	-0.529225
C	-0.730749	2.342289	0.340602
H	1.415772	-0.555182	2.740510
H	-2.094978	-1.065785	2.585585
H	-1.573783	-2.708397	3.044183
H	0.600241	-1.616396	3.951763
H	-1.466589	3.156656	0.370667
H	-0.170040	2.360883	-0.601968
H	-3.051689	1.538721	-0.634431
H	-1.724865	0.689707	-1.479753
H	-3.638922	-0.846362	-0.948765
H	-3.433438	-0.461734	0.779304
H	-3.083076	-2.805060	1.048515
H	-1.440653	-3.355185	0.645833
H	-0.142112	-0.059520	3.458268
H	-0.016555	2.437116	1.156948

Z-Me-TMS-ketene-acetal

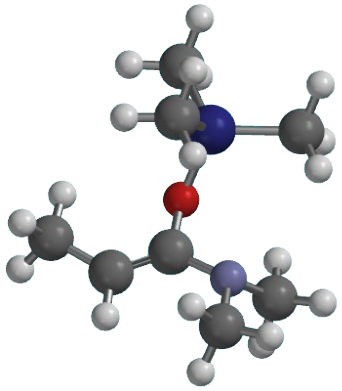


Geometry optimization: ωB97X-D/6-31G*
Single point energy calculation: M06-2X/6-311+G**
Energy:-716.287318 hartrees
HOMO energy: -7.02 eV

Cartesian coordinates

C	-0.832357	0.000001	2.347249
C	-0.148079	-0.000001	1.197281
O	-0.741420	-0.000003	-0.005387
O	1.207785	-0.000002	1.063989
C	1.983557	-0.000000	2.241045
Si	0.003194	0.000000	-1.532159
C	-1.462106	0.000001	-2.696843
C	1.029266	-1.551694	-1.765188
C	1.029266	1.551692	-1.765186
C	-2.330655	0.000002	2.420910
H	-0.285049	0.000001	3.282170
H	-2.703261	-0.882508	2.955857
H	-2.703261	0.882511	2.955858
H	-2.774992	0.000002	1.423218
H	1.863909	-1.579884	-1.059165
H	1.437247	-1.595912	-2.782043
H	1.863907	1.579885	-1.059163
H	1.437247	1.595912	-2.782040
H	0.420103	-2.448750	-1.609440
H	1.783068	-0.894009	2.843858
H	1.783068	0.894011	2.843855
H	3.024895	-0.000001	1.917397
H	-2.088259	0.884857	-2.542782
H	0.420100	2.448747	-1.609440
H	-1.128925	0.000008	-3.741059
H	-2.088250	-0.884864	-2.542793

Z-Me-TMS-ketene-aminal

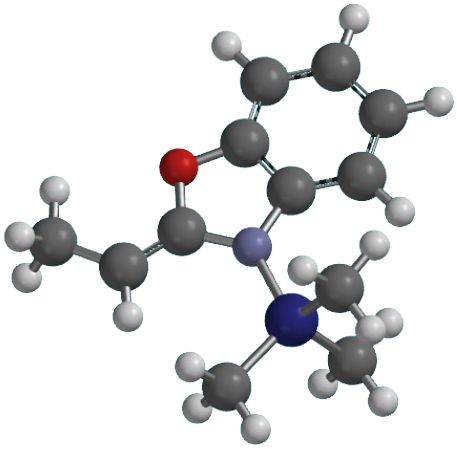


Geometry optimization: ωB97X-D/6-31G*
Single point energy calculation: M06-2X/6-311+G**
Energy:-735.717270 hartrees
HOMO energy: -6.87 eV

Cartesian coordinates

C	-1.787950	1.281485	0.404747
C	-0.814903	0.392513	0.642800
O	-0.673555	-0.724694	-0.126772
N	0.173917	0.498722	1.639962
C	0.256825	1.764434	2.335111
C	0.258032	-0.641582	2.543522
Si	0.647714	-0.911573	-1.169094
C	0.036658	-2.096555	-2.484063
C	2.117407	-1.644671	-0.260896
C	1.080439	0.764001	-1.891232
C	-2.719752	1.215349	-0.768439
H	-1.915951	2.107878	1.095868
H	-3.765988	1.162306	-0.443035
H	-2.628800	2.105060	-1.404730
H	-2.516005	0.333449	-1.381922
H	2.467959	-0.959689	0.517895
H	2.948685	-1.830927	-0.951772
H	1.395118	1.457848	-1.104203
H	1.898240	0.678992	-2.615898
H	1.859168	-2.598092	0.213728
H	-0.605395	1.952255	2.998770
H	0.320283	2.580161	1.609514
H	1.163442	1.768722	2.948706
H	1.227349	-0.631651	3.053538
H	-0.540109	-0.622260	3.304014
H	-0.813440	-1.673917	-3.029674
H	0.218636	1.205253	-2.402226
H	0.828082	-2.321282	-3.209065
H	-0.289347	-3.043677	-2.040188
H	0.173244	-1.567858	1.975034

Z-Me-TMS-N-benzoxazol



Geometry optimization: ωB97X-D/6-31G*
Single point energy calculation: M06-2X/6-311+G**
Energy:-886.912213 hartrees
HOMO energy: -6.13 eV

Cartesian coordinates

C	-0.678782	-0.000000	-3.954912
C	-0.954709	-0.000000	-2.479071
C	0.004561	-0.000000	-1.548384
O	1.337016	0.000000	-1.919376
N	-0.065640	-0.000000	-0.136370
Si	-1.464833	0.000000	0.972288
C	-1.359079	-1.552207	2.025331
C	-1.359076	1.552207	2.025331
C	-3.104546	0.000000	0.064544
C	3.215375	0.000000	1.704032
C	2.092531	0.000000	-0.785695
C	1.817115	-0.000000	1.601193
C	4.026564	0.000001	0.575929
C	3.465263	0.000001	-0.708564
C	1.258944	-0.000000	0.331085
H	-3.244473	-0.889491	-0.556644
H	-3.244475	0.889491	-0.556644
H	-1.537440	2.440870	1.410139
H	-0.383101	1.675194	2.504228
H	3.667133	0.000000	2.691384
H	5.106215	0.000001	0.685280
H	4.073793	0.000001	-1.605772
H	0.393954	0.000001	-4.161884
H	-1.985994	-0.000001	-2.158330
H	-2.120069	1.531700	2.814309
H	1.209744	-0.000001	2.499118
H	-2.120074	-1.531698	2.814307
H	-3.897445	-0.000001	0.822871
H	-1.537442	-2.440871	1.410140
H	-0.383106	-1.675196	2.504230

H	-1.113960	-0.881982	-4.442047
H	-1.113962	0.881981	-4.442047

References

1. (a) M. Drusan, E. Rakovský, J. Marek and R. Šebesta, *Adv. Synth. Catal.*, 2015, **357**, 1493-1498; (b) I. Némethová, Z. Sorádová and R. Šebesta, *Synthesis*, 2017, **49**, 2461-2469.
2. (a) M. Rodríguez-Fernández, X. Yan, J. F. Collados, P. B. White and S. R. Harutyunyan, *J. Am. Chem. Soc.*, 2017, **139**, 14224-14231; (b) R. P. Jumde, F. Lanza, M. J. Veenstra and S. R. Harutyunyan, *Science*, 2016, **352**, 433-437; (c) R. P. Jumde, F. Lanza, T. Pellegrini and S. R. Harutyunyan, *Nat. Commun.*, 2017, **8**, 2058; (d) X. Yan and S. R. Harutyunyan, *Nat. Commun.*, 2019, **10**, 3402.
3. Spartan ´18, Wavefunction, Inc., Irvine, CA.
4. Y. Shao, Z. Gan, E. Epifanovsky, A. T. B. Gilbert, M. Wormit, J. Kussmann, A. W. Lange, A. Behn, J. Deng, X. Feng, D. Ghosh, M. Goldey, P. R. Horn, L. D. Jacobson, I. Kaliman, R. Z. Khaliullin, T. Kuś, A. Landau, J. Liu, E. I. Proynov, Y. M. Rhee, R. M. Richard, M. A. Rohrdanz, R. P. Steele, E. J. Sundstrom, H. L. Woodcock, P. M. Zimmerman, D. Zuev, B. Albrecht, E. Alguire, B. Austin, G. J. O. Beran, Y. A. Bernard, E. Berquist, K. Brandhorst, K. B. Bravaya, S. T. Brown, D. Casanova, C.-M. Chang, Y. Chen, S. H. Chien, K. D. Closser, D. L. Crittenden, M. Diedenhofen, R. A. DiStasio, H. Do, A. D. Dutoi, R. G. Edgar, S. Fatehi, L. Fusti-Molnar, A. Ghysels, A. Golubeva-Zadorozhnaya, J. Gomes, M. W. D. Hanson-Heine, P. H. P. Harbach, A. W. Hauser, E. G. Hohenstein, Z. C. Holden, T.-C. Jagau, H. Ji, B. Kaduk, K. Khistyaev, J. Kim, J. Kim, R. A. King, P. Klunzinger, D. Kosenkov, T. Kowalczyk, C. M. Krauter, K. U. Lao, A. D. Laurent, K. V. Lawler, S. V. Levchenko, C. Y. Lin, F. Liu, E. Livshits, R. C. Lochan, A. Luenser, P. Manohar, S. F. Manzer, S.-P. Mao, N. Mardirossian, A. V. Marenich, S. A. Maurer, N. J. Mayhall, E. Neuscamman, C. M. Oana, R. Olivares-Amaya, D. P. O'Neill, J. A. Parkhill, T. M. Perrine, R. Peverati, A. Prociuk, D. R. Rehn, E. Rosta, N. J. Russ, S. M. Sharada, S. Sharma, D. W. Small, A. Sodt, T. Stein, D. Stück, Y.-C. Su, A. J. W. Thom, T. Tsuchimochi, V. Vanovschi, L. Vogt, O. Vydrov, T. Wang, M. A. Watson, J. Wenzel, A. White, C. F. Williams, J. Yang, S. Yeganeh, S. R. Yost, Z.-Q. You, I. Y. Zhang, X. Zhang, Y. Zhao, B. R. Brooks, G. K. L. Chan, D. M. Chipman, C. J. Cramer, W. A. Goddard, M. S. Gordon, W. J. Hehre, A. Klamt, H. F. Schaefer, M. W. Schmidt, C. D. Sherrill, D. G. Truhlar, A. Warshel, X. Xu, A. Aspuru-Guzik, R. Baer, A. T. Bell, N. A. Besley, J.-D. Chai, A. Dreuw, B. D. Dunietz, T. R. Furlani, S. R. Gwaltney, C.-P. Hsu, Y. Jung, J. Kong, D. S. Lambrecht, W. Liang, C. Ochsenfeld, V. A. Rassolov, L. V. Slipchenko, J. E. Subotnik, T. Van Voorhis, J. M. Herbert, A. I. Krylov, P. M. W. Gill and M. Head-Gordon, *Mol. Phys.*, 2015, **113**, 184-215.