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Supporting Information

Sustainable Asymmetric Organolithium Chemistry: Enantio- and Chemoselective Acylations through Recycling of Solvent, Sparteine, and Weinreb "Amine"

Serena Monticelli,[a] Wolfgang Holzer,[a] Thierry Langer,[a] Alexander Roller,[b] Berit Olofsson,*[c] and Vittorio Pace*[a]

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Table of Contents

1. Instrumentation and General Analytical Methods 2
2. General Procedures and Recovery Tables for sparteine, CPME and Weinreb amine 3
3. Synthesis of ketones from lithiated 3-phenylpropyl diisopropylcarbamate **1** 7 - 40
4. Synthesis of ketones from lithiated *R*/*S*-1-phenylethyl diisopropylcarbamate **18** 41 - 53 54 - 59
5. Stereoselective Michael addition to α,β-unsaturated Weinreb amides 60 - 61
6. Trapping of tetrahedral intermediate from lithiated 3-phenylpropyl diisopropylcarbamate **1** to Weinreb amide as *O-TMS* hemiaminal 62 - 67
7. Synthesis of highly stable carbinol from lithiated 3-phenylpropyl diisopropylcarbamate **1** to *N*-acyl pyrrole 68 - 83
8. Synthesis of ketones from lithiated *N*-Boc Pyrrolidine **32** 84 - 98
9. Synthetic manipulation of α-oxyketones 99 - 109
10. X-ray Structural Analyses 110
11. References 111-157
12. Copies of NMR Spectra (^{1}H and ^{13}C) for All the Synthesized Compounds

Instrumentation and General Analytical Methods

Melting points were determined on a Reichert–Kofler hot-stage microscope and are uncorrected. HRMS spectra were recorded on a Bruker maXis 4G instrument (ESI-TOF, APCI). Optical rotations were obtained on a Perkin-Elmer 241 polarimeter. Chiral HPLC separations were done on Shimadzu Prominence LC-20AD. Chiralpak columns IA, IB, IC, IG (150 x 2.1 mm) were used for normal phase separations.

^{1}H, ^{13}C, ^{15}N, ^{19}F NMR spectra were recorded with a Bruker Avance III 400 spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C, 40 MHz for ^{15}N, 377 MHz for ^{19}F). The center of the (residual) solvent signal was used as an internal standard with δ 7.26 ppm (^{1}H in $CDCl_3$), 7.16 ppm (^{1}H in C_6D_6), δ 5.32 ppm (^{1}H in CD_2D_2), δ 4.78 ppm (^{1}H in CD_3OD), δ 77.00 ppm (^{13}C in $CDCl_3$), δ 128.06 ppm (^{13}C in C_6D_6), δ 54.00 ppm (^{13}C in CD_2D_2), and δ 49.15 ppm (^{13}C in CD_3OD). ^{15}N NMR spectra (gsHMBC) were referenced against neat, external nitromethane, Absolute referencing was used for the ^{19}F NMR spectra. Spin-spin coupling constants (*J*) are given in Hz. As far as possible, full and unambiguous assignment of all resonances was performed by combined application of standard NMR techniques, such as APT, HSQC, HMBC, COSY and NOESY experiments.

CPME was distilled over Na/benzophenone. Light petroleum refers to the fraction of bp 40-60 °C. *N,N,N,N*-Tetramethylethylenediamine (TMEDA), (-)-sparteine and (+)-sparteine were distilled over CaH_2 prior to use.

3-Phenylpropyl diisopropylcarbamate and *R*/*S*-1-phenylethyl diisopropylcarbamate were synthesized from the respective alcohols according to literature procedures.[1]

Weinreb amides were synthesized from the respective acyl chloride according to literature procedures.[2]

Chemicals were purchased from Sigma-Aldrich, Acros, Alfa Aesar, Fluorochem and TCI Europe unless otherwise specified. Solutions were evaporated under reduced pressure with a rotary evaporator. TLC was carried out on aluminium sheets precoated with silica gel 60F254 (Macherey-Nagel, Merck); the spots were visualized under UV light (λ = 254 nm) and/or $KMnO_4$ (aq.) was used as revealing system.

General Procedure 1 (GP1), used with 1.

A solution of 3-phenylpropyl diisopropylcarbamate **1** (0.294 mmol, 1.5 equiv) and (-) or (+)-sparteine (0.313 mmol, 1.6 equiv) under argon in anhydrous CPME (2 mL) was cooled to -78 °C. A solution of *s*-BuLi (1.3 M in cyclohexane/hexane 92:8, 0.313 mmol, 1.6 equiv) was added dropwise and the reaction mixture was stirred for 30 min, then Weinreb amide (0.196 mmol, 1.0 equiv) in CPME (1 mL) was slowly added. The reaction mixture was quenched after 3 h with HCl (1M solution, 5 mL) and stirred 1-2 min before the two phases were separated. The organic layer was washed with water, dried over anhydrous Na_2SO_4, filtered and distilled. The distillation afforded CPME (ca. 80% - for full details see Table S3) and, a saturated solution of ketone (ca. 0.5 mL) which was crystallized by cooling from the residual CPME appropriately left. The acidic aqueous layer was basified with NaOH (20% *aq.*) and extracted with CPME (5 mL). The organic layer was distilled to recover *N,O*-dimethylhydroxylamine (bp 43 °C, see table 2), CPME (bp 106 °C, see table 3) and sparteine (137-138 °C, 1.33 mbar, see table 1). Racemic ketone has been prepared using TMEDA as HPLC reference.

General Procedure 2 (GP2), used with 18.

A solution of (*R*) or (*S*)-1-phenylethyl diisopropylcarbamate **18** (0.294 mmol, 1.5 equiv) under argon in anhydrous CPME (2 mL) was cooled to -78 °C. A solution of *s*-BuLi (1.3 M in cyclohexane/hexane 92:8, 0.313 mmol, 1.6 equiv) was added dropwise and the reaction mixture was stirred for 5 min, then Weinreb amide (0.196 mmol, 1.0 equiv) in CPME (1 mL) was added slowly. The reaction mixture was quenched after 3 h with HCl (1M solution, 5 mL) and stirred 1-2 min before the two phases were separated. The organic layer was washed with water, dried over anhydrous Na_2SO_4, filtered and distilled. The distillation afforded CPME (ca. 80% - for full details see Table S3) and a saturated solution of ketone (ca. 0.5 mL) which was crystallized by cooling from the residual CPME appropriately left. The acidic aqueous layer were basified with NaOH (20% *aq.*) and extracted with CPME (5 mL). The organic layer was distilled for recovering *N,O*-dimethylhydroxylamine (bp 43 °C) and CPME (bp 106 °C). Racemic ketone has been prepared using racemic 1-phenylethyl diisopropylcarbamate **18**.

General Procedure 3 (GP3), used with 32.

A solution of *N*-Boc-pyrrolidine **32** (0.454 mmol, 1.5 equiv) and (-)or(+)-sparteine (0.485 mmol, 1.6 equiv) under argon in anhydrous CPME (3 mL) was cooled to -78 °C. A solution of *s*-BuLi (1.3 M in cyclohexane/hexane 92:8, 0.485 mmol, 1.6 equiv) was added dropwise and the reaction mixture was stirred for 30 min, then Weinreb amide (0.303 mmol, 1.0 equiv) in CPME (1 mL) was added slowly. The reaction mixture was quenched after 3 h with HCl (1M solution, 5 mL) and stirred 1-2 min before the two phases were separated. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered and distilled. The distillation afforded CPME (ca. 80% - for full details see Table S3) and a

saturated solution of ketone (ca. 0.7 mL) which was crystallized by cooling from the residual CPME appropriately left. The acidic aqueous layer was basified with NaOH (20% *aq.*) and extracted with CPME (5 mL). The organic layer was distilled for recovering *N,O*-dimethylhydroxylamine (bp 43 °C), CPME (bp 106 °C) and sparteine (137-138 °C, 1.33 mbar). Racemic ketone has been prepared using TMEDA as HPLC reference.

Recovery procedure for (-)- and (+)-sparteine, Weinreb amine and CPME

Experiments in which sparteine, Weinreb amine and CPME were amenable for recovery were run at larger scale as indicated in the appropriate experimental section. Subsequent distillations afforded each single component which could be reused in additional experiments as detailed.

Because of the very limited amount of sparteine used in some cases, the recovery was realized collecting together the basified water phases of a set of different reactions, estracting with CPME and distilling the organic phase.

Table S1. Recovery of sparteine.

Synthesis of compound	Sparteine used (g)	Sparteine recovered (g)	Recovery yield (%)
(***R***)-**3**	1.5 [a]	1.2	80
(***S***)-**3**	1.5 [b]	1.25	83
(***R***)-**5**	1.5 [a]	1.21	81
(***R***)-**8**	1.5 [a]	1.24	83
(***S***)-**11**	1.5 [b]	1.2	80
(***R***)-**12**	1.5 [a]	1.15	70
(***R***)-**15**	1.5 [a]	1.24	83
(***R***)-**33**	1.5 [a]	1.2	80
(***S***)-**33**	1.5 [b]	1.18	79
(***R***)-**36**	1.5 [a]	1.17	78
(***S***)-**36**	1.5 [b]	1.22	81
Others [a,c]	1.88	1.5	80
Others [b,d]	0.81	0.57	70

[a] (-)-sparteine. [b] (+)-sparteine. [c] The basic water phases corresponding to the preparation of compounds: **(*R*)-3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,33,34,35,36,37,38,39** were collected together, extracted with CPME and then distilled**.** [d] The basic water phases corresponding to the preparation of compounds: **(*S*)-3,9,11,14,16,33, 34, 36, 37** were collected together, extracted with CPME and then distilled.

Table S2. Recovery of Weinreb amine.

Synthesis of compound	Weinreb amide used (mmol)	Weinreb "amine" recovered (mmol) / g	Recovery yield (%)
(*R*)-3	4	2.8 / 0.171	70
(*S*)-3	4	3.0 / 0.183	75
(*R*)-5	4	3.1 / 0.189	77
(*R*)-8	4	2.8 / 0.171	70
(*S*)-11	4	2.6 / 0.159	65
(*R*)-12	4	2.6 / 0.159	65
(*R*)-15	4	2.8 / 0.171	70
(*R*)-33	4	3.0 / 0.183	75
(*S*)-33	4	2.4 / 0.147	60
(*R*)-36	4	2.5 / 0.153	62
(*S*)-36	4	2.6 / 0.159	64
Others[a]	5.06	3.59 / 0.219	71
Others[b]	4.93	3.45/ 0.211	70

[a] The basic water phases corresponding to the preparation of compounds: **(*R*)-3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,33,34,35,36,37,38,39** were collected together, extracted with CPME and then distilled.

[b] The basic water phases corresponding to the preparation of compounds: **(*S*)-3,9,11,14,16,33, 34, 36, 37; (*R*)-19,20,21,22,23; (*R,R*)-24,25; (*S*)-19,20,21,22,23; (*S,S*)-24,25** were collected together, extracted with CPME and then distilled.

Table S3. Recovery of CPME.

Synthesis of compound	CPME used (mL)	CPME recovered (mL)	Recovery yield (%)
(*R*)-3	27[a]	23.0	85
	30[b]	27.5	92
(*S*)-3	27[a]	23.0	85
	30[b]	25.8	86
(*R*)-5	27[a]	24.3	90
	30[b]	28.2	94
(*R*)-8	27[a]	24.0	89
	30[b]	27.0	90
(*S*)-11	27[a]	23.2	86
	30[b]	28.3	94
(*R*)-12	27[a]	24.4	90
	30[b]	27.7	92
(*R*)-15	27[a]	24.7	91
	30[b]	28.0	93
(*R*)-33	27[a]	22.9	85
	30[b]	26.4	88
(*S*)-33	27[a]	24.3	90
	30[b]	27.3	91
(*R*)-36	27[a]	24.7	91
	30[b]	28.1	94
(*S*)-36	27[a]	24.0	89
	30[b]	27.0	90
Others [b,c]	110	93.5	85
Others [b,d]	115[d]	95.5	83

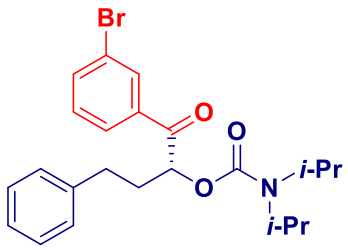
[a] Solvent used for running reaction.

[b] Solvent used for work-up procedure.

[c] CPME employed for the extraction of the basic aqueous phases collected from the work-up followed for the preparation of compounds: **(*R*)-3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,33,34,35,36,37,38,39.**

[d] CPME employed for the extraction of the basic aqueous phases collected from the work-up followed for the preparation of compounds **(*S*)-3,9,11,14,16,33, 34, 36, 37; (*R*)-19,20,21,22,23; (*R,R*)-24,25; (*S*)-19,20,21,22,23; (*S,S*)-24,25**.

(*R*)-1-(3-Bromophenyl)-1-oxo-4-phenyl-2-butanyl diisopropylcarbamate, ((*R*)-3)



Synthesized according to **GP1** using **1** (0.077 g, 0.294 mmol, 1.5 equiv); (-)-sparteine (0.073 g, 0.313 mmol, 1.6 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and 3-bromo-*N*-methoxy-*N*-methylbenzamide (0.048 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*)-3** was obtained in 95% yield (0.082 g) as a white solid; mp 75-82 °C. Reaction run in larger scale starting from **1** (1.58 g, 6 mmol, 1.5 equiv); (-)-sparteine (1.5 g, 6.4 mmol, 1.6 equiv); *s*-BuLi 1.4 M (4.57 mL, 6.4 mmol, 1.6 equiv) and 3-bromo-*N*-methoxy-*N*-methylbenzamide (0.972 g, 4 mmol, 1.0 equiv) in CPME (27 mL) allowed to recover CPME (85%, 23 mL) and prepare **(*R*)-3** in comparable yield (90%, 1.6 g). The organic layer from the basic extraction with CPME (30 mL) afforded upon distillation (-)-sparteine (80%, 1.2 g, 1.18 mL), *N*-methyl-*N*-methoxyamine (70%, 2.8 mmol, 0.21 mL) and CPME (92%, 27.5 mL). (Entry 5, optimization table)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (m, 1H, *m*-Br Ph H-2), 7.76 (m, 1H, *m*-Br Ph H-6), 7.66 (m, 1H, *m*-Br Ph H-4), 7.30 (m, 2H, Ph H-3,5), 7.29 (m, 1H, *m*-Br Ph H-5), 7.22 (m, 1H, Ph H-4), 7.17 (m, 2H, Ph H-2,6), 5.77 (m, 1H, C<u>H</u>C=O), 4.02 (br s, 1H, C<u>H</u>CH_3), 3.86 (br s, 1H, C<u>H</u>CH_3), 2.89-2.74 (m, 2H, Ph$C\underline{H}_2$), 2.13-2.20 (m, 2H, $C\underline{H}_2$CH), 1.33 (br, 6H, $C\underline{H}_3$), 1.20 (br, 6H, $C\underline{H}_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ 196.5 (*m*-Br Ph<u>C</u>=O), 154.7 (N<u>C</u>=O), 140.5 (Ph C-1), 136.8 (*m*-Br Ph C-1), 136.0 (*m*-Br Ph C-4), 131.4 (*m*-Br Ph C-2), 130.2 (*m*-Br Ph C-5), 128.6 (Ph C-3,5), 128.4 (Ph C-2,6), 126.9 (*m*-Br Ph C-6), 126.3 (Ph C-4), 122.9 (*m*-Br Ph C-3), 74.5 (<u>C</u>HC=O), 46.8 (br <u>C</u>HCH_3), 45.7 (br <u>C</u>HCH_3), 32.9 ($\underline{C}H_2$CH), 31.8 (Ph$\underline{C}H_2$), 21.8 (br, $\underline{C}H_3$), 21.4 (br, $\underline{C}H_3$), 20.4 (br, 2×$\underline{C}H_3$).

HRMS (ESI), *m/z*: calcd. for $C_{23}H_{29}BrNO_3$ 446.1325$[M+H]^+$; found 446.1324.

$[\alpha]_D$ -41 (*c* 0.5, $CHCl_3$).

HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 1 mL/min

E-factor calculation

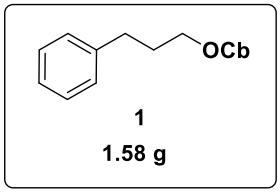
Total amount of reactants: 1.58 g + 0.972 g + 1.5 g + 31.08 g + 36.6 g + 3.514 g + 49.02 g = 124.27 g

Amount of final products: 0.170 g + 1.6 g + 43.43 g + 1.2 g = 46.4 g

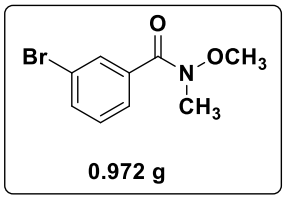
Amount of waste: 124.27 g - 46.4 g = 77.87 g

E-factor = amount of waste/ amount of final products = 77.87 g/46.4 g = **1.68**

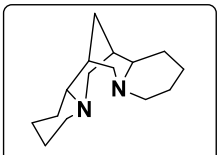
Reactants



1
1.58 g



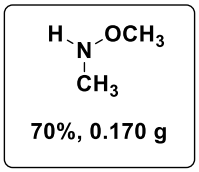
0.972 g



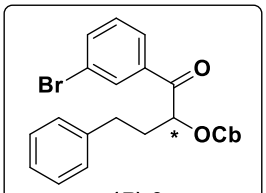
(-)-sparteine
1.5 g

CPME (27 mL + 30 mL) = 57 mL density: 0.86 g/mL = 49.02 g
HCl (1M solution, density 1.036 g/mL, 30 mL) = 31.08 g
NaOH (20% aq. density 1.22 g/mL, 30 mL) = 36.6 g
***s*-BuLi 1.4 M in cyclohexane (4.57 mL, density: 0.769 g/mL) = 3.514 g**

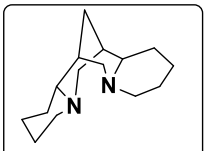
Products



70%, 0.170 g



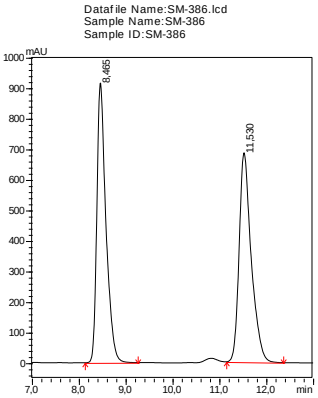
(*R*)-3
90%, 1.6 g



80%, 1.2 g

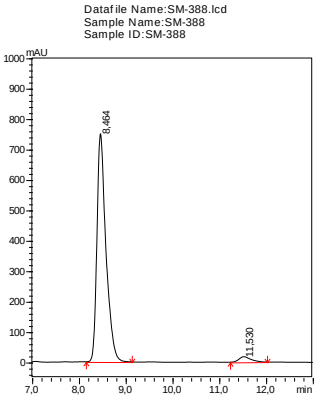
CPME (23 mL + 27.5 mL) = 50.5 mL 43.43 g

Racemate



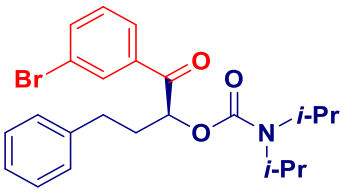
Peaks	Retention time (min)	Area	Area%
1	8,465	12371983	50,205
2	11,530	12270746	49,795
Total		24642729	100,000

***Enantioenriched* (*R*)-3**



Peaks	Retention time (min)	Area	Area%
1	8,464	10041535	97,006
2	11,530	309944	2,994
Total		10351480	100,000

(*S*)-1-(3-Bromophenyl)-1-oxo-4-phenyl-2-butanyl diisopropylcarbamate, ((*S*)-3)

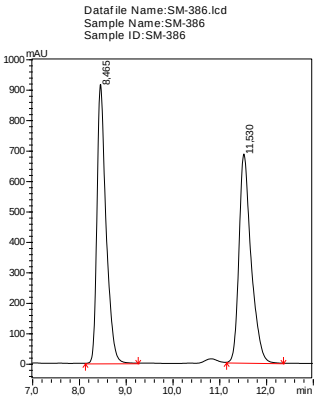


Synthesized according to **GP1** using **1** (0.077 g, 0.294 mmol, 1.5 equiv); (+)-sparteine (0.073 g, 0.313 mmol, 1.6 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and 3-bromo-*N*-methoxy-*N*-methylbenzamide (0.048 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*S*)-3** was obtained in 87% yield (0.076 g) as a white solid; mp 75-82 °C. Reaction run in larger scale starting from **1** (1.58 g, 6 mmol, 1.5 equiv); (+)-sparteine (1.5 g, 6.4 mmol, 1.6 equiv); *s*-BuLi 1.4 M (4.57 mL, 6.4 mmol, 1.6 equiv) and 3-bromo-*N*-methoxy-*N*-methylbenzamide (0.972 g, 4 mmol, 1.0 equiv) in CPME (27 mL) allowed to recover CPME (85%, 23 mL) and prepare **(*S*)-3** in comparable yield (83%, 1.48 g). The organic layer from the basic extraction with CPME (30 mL) afforded upon distillation (+)-sparteine (83%, 1.25 g, 1.22 mL), *N*-methyl-*N*-methoxyamine (75%, 3.0 mmol, 0.23 mL) and CPME (92%, 25.8 mL).

$[\alpha]_D$ +14 (*c* 0.5, $CHCl_3$).

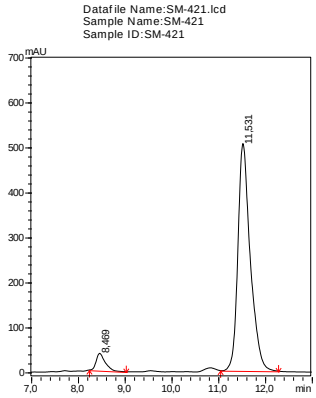
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 1 mL/min

Racemate



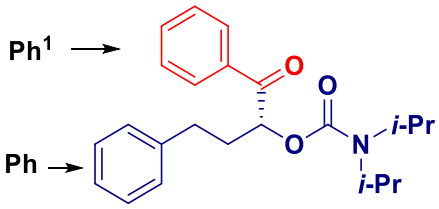
Peaks	Retention time (min)	Area	Area%
1	8,465	12371983	50,205
2	11,530	12270746	49,795
Total		24642729	100,000

***Enantioenriched* (*S*)-3**



Peaks	Retention time (min)	Area	Area%
1	8,469	503918	5,159
2	11,531	9264670	94,841
Total		9768588	100,000

(*R*)-1-Oxo-1,4-diphenyl-2-butanyl diisopropylcarbamate, ((*R*)-4)



Synthesized according to **GP1** using **1** (0.077g, 0.294 mmol, 1.5 equiv); (-)-sparteine (0.073 g, 0.313 mmol, 1.6 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and *N*-methoxy-*N*-methylbenzamide (0.032 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*)-4** was obtained in 90% yield (0.065 g) as a white solid; mp 91-94 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (m, 2H, Ph^1 H-2,6), 7.54 (m, 1H, Ph^1 H-4), 7.42 (m, 2H, Ph^1 H-3,5), 7.29 (m, 2H, Ph H-3,5), 7.21 (m, 1H, Ph H-4), 7.17 (m, 2H, Ph H-2,6), 5.92 (dd, *J* = 7.6 Hz, 4.8 Hz, 1H, C<u>H</u>C=O), 4.06 (br s, 1H, C<u>H</u>CH_3), 3.87 (br s, 1H, C<u>H</u>CH_3), 2.75-2.89 (m, 2H, Ph$C\underline{H}_2$), 2.14-2.21 (m, 2H, $C\underline{H}_2$CH), 1.34 (br , 6H, $C\underline{H}_3$), 1.22 (br , 6H, $C\underline{H}_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ 197.6 (Ph<u>C</u>=O), 154.9 (N<u>C</u>=O), 140.8 (Ph C-1), 135.1 (Ph^1 C-1), 133.2 (Ph^1 C-4), 128.6 (Ph^1 C-3,5), 128.5 (Ph C-3,5), 128.40 (Ph C-2,6), 128.36 (Ph^1 C-2,6), 126.2 (Ph C-4), 74.5 (<u>C</u>HC=O), 46.7 (<u>C</u>HCH_3), 45.6 (<u>C</u>HCH_3), 33.1 ($\underline{C}H_2CH$), 31.9 (Ph$\underline{C}H_2$), 21.8 ($\underline{C}H_3$ via HSQC), 21.4 ($\underline{C}H_3$ via HSQC), 20.5 ($\underline{C}H_3$ br).

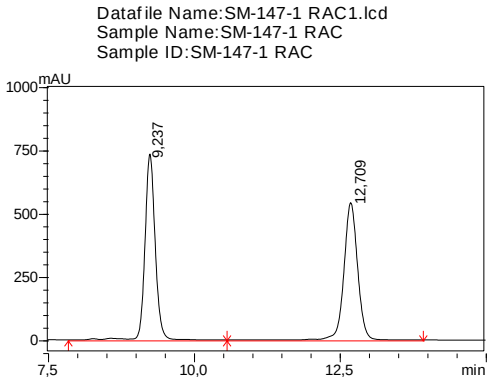
HRMS (ESI), *m/z*: calcd. for $C_{23}H_{29}NNaO_3$ 390.2040[M+Na]$^+$; found 390.2045.

$[\alpha]_D$ -56 (*c* 0.5, $CHCl_3$).

HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow:

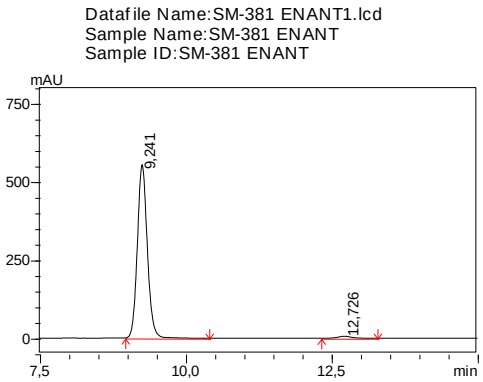
1 mL/min

Racemate



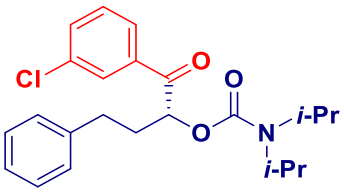
Peaks	Retention time (min)	Area	Area%
1	9,237	8970193	50,564
2	12,709	8770233	49,436
Total		17740426	100,000

***Enantioenriched* (*R*)-4**



Peaks	Retention time (min)	Area	Area%
1	9,241	6558728	98,624
2	12,726	91509	1,376
Total		6650238	100,000

(*R*)-1-(3-Chlorophenyl)-1-oxo-4-phenyl-2-butanyl diisopropylcarbamate, ((*R*)-5)



Synthesized according to **GP1** using **1** (0.077 g, 0.294 mmol, 1.5 equiv); (-)-sparteine (0.073 g, 0.313 mmol, 1.6 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and 3-chloro-*N*-methoxy-*N*-methylbenzamide (0.039 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*)-5** was obtained in 89% yield (0.070 g) as a white solid; mp 70-74 °C. Reaction run in larger scale starting from **1** (1.58 g, 6 mmol, 1.5 equiv); (-)-sparteine (1.5 g, 6.4 mmol, 1.6 equiv); *s*-BuLi 1.4 M (4.57 mL, 6.4 mmol, 1.6 equiv) and 3-chloro-*N*-methoxy-*N*-methylbenzamide (0.796 g, 4 mmol, 1.0 equiv) in CPME (27 mL) allowed to recover CPME (85%, 24.3 mL) and prepare **(*R*)-5** in comparable yield (85%, 1.36 g). The organic layer from the basic extraction with CPME (30 mL) afforded upon distillation (-)-sparteine (81%, 1.21 g, 1.19 mL), *N*-methyl-*N*-methoxyamine (77%, 3.1 mmol, 0.24 mL) and CPME (94%, 28.2 mL).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (m, 1H, *m*-Cl Ph H-2), 7.71 (m, 1H, *m*-Cl Ph H-6), 7.50 (m, 1H, *m*-Cl Ph H-4), 7.35 (m, 1H, *m*-Cl Ph H-5), 7.30 (m, 2H, Ph H-3,5), 7.22 (m, 1H, Ph H-4), 7.18 (m, 2H, Ph H-2,6), 5.77 (m, 1H, C<u>H</u>C=O), 4.02 (br s, 1H, C<u>H</u>CH_3), 3.87 (br s, 1H, C<u>H</u>CH_3), 2.74-2.90 (m, 2H, PhC<u>H</u>$_2$), 2.13-2.20 (m, 2H, C<u>H</u>$_2$CH), 1.33 (br s, 6H, C<u>H</u>$_3$), 1.20 (br s, 6H, C<u>H</u>$_3$).

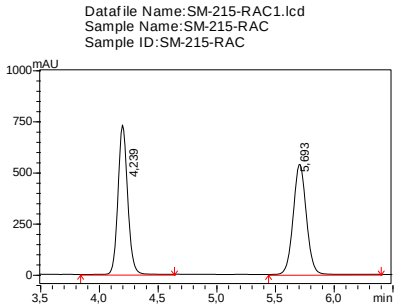
^{13}C NMR (100 MHz, $CDCl_3$): δ 196.6 (Ph<u>C</u>=O), 154.7 (N<u>C</u>=O), 140.5 (Ph C-1), 136.6 (*m*-Cl Ph C-1), 134.9 (*m*-Cl Ph C-3), 133.4 (*m*-Cl Ph C-4), 130.0 (*m*-Cl Ph C-5), 128.6 (Ph C-3,5), 128.44 (*m*-Cl Ph C-2), 128.39 (Ph C-2,6), 126.4 (*m*-Cl Ph C-6), 126.3 (Ph C-4), 74.5 (<u>C</u>HC=O), 46.7 (<u>C</u>HCH_3), 45.7 (<u>C</u>HCH_3), 32.9 (<u>C</u>H$_2$CH), 31.8 (Ph<u>C</u>H$_2$), 21.8 (<u>C</u>H$_3$ br), 21.4 (<u>C</u>H$_3$ br), 20.5 (<u>C</u>H$_3$ br).

HRMS (ESI), *m/z*: calcd. for $C_{23}H_{28}ClNNaO_3$ 424.1650 $[M+Na]^+$; found 424.1650.

[α]$_D$ -42 (*c* 0.5, $CHCl_3$).

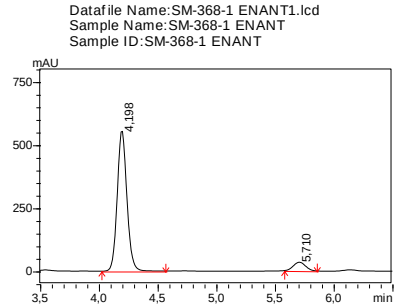
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 1 mL/min

Racemate



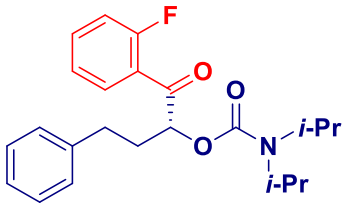
Peaks	Retention time (min)	Area	Area%
1	4,239	4175534	49,872
2	5,693	4197049	50,128
Total		8372583	100,000

***Enantioenriched* (*R*)-5**



Peaks	Retention time (min)	Area	Area%
1	4,198	3192526	92,849
2	5,710	245864	7,151
Total		3438390	100,000

(*R*)-1-(2-Fluorophenyl)-1-oxo-4-phenyl-2-butanyl diisopropylcarbamate, ((*R*)-6)



Synthesized according to **GP1** using **1** (0.077 g, 0.294 mmol, 1.5 equiv); (-)-sparteine (0.073 g, 0.313 mmol, 1.6 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and 2-fluoro-*N*-

methoxy-*N*-methylbenzamide (0.036 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*)-6** was obtained in 85% yield (0.064 g) as a white solid; mp 85-87 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (ddd, *J* = 7.9 Hz, 1.8 Hz, $^{4}J_{H,F}$ = 7.1 Hz, 1H, *o*-F Ph H-6), 7.51 (dddd, *J* = 8.3 Hz, 7.3 Hz, 1.8 Hz, $^{4}J_{H,F}$ = 5.1 Hz, 1H, *o*-F Ph H-4), 7.28 (m, 2H, Ph H-3,5), 7.22 (ddd, *J* = 7.9 Hz, 7.3 Hz, 1.8 Hz, 1H, *o*-F Ph H-5), 7.19 (m, 1H, Ph H-4), 7.17 (m, 2H, Ph H-2,6), 7.12 (ddd, $^{3}J_{H,F}$ = 11.1 Hz, *J* = 8.3 Hz, 1.0 Hz, 1H, *o*-F Ph H-3), 5.79 (ddd, *J* = 8.7 Hz, 3.5 Hz, $J_{H,F}$ = 1.3 Hz, 1H, C<u>H</u>C=O), 4.03 (br s, 1H, C<u>H</u>CH_3), 3.87 (br s, 1H, C<u>H</u>CH_3), 2.84 (m, 2H, PhC<u>H_2</u>), 2.22 (m, 1H, C<u>H_2</u>CH), 2.11 (m, 1H, C<u>H_2</u>CH), 1.33 (br s, 6H, C<u>H_3</u>), 1.21 (br s, 6H, C<u>H_3</u>).

^{13}C NMR (100 MHz, $CDCl_3$): δ 195.0 (d, *J* = 4.6 Hz, *o*-F PhC=O), 161.2 (d, *J* = 254.4 Hz, *o*-F Ph C-2), 154.8 (NC=O), 140.9 (Ph C-1), 134.6 (d, *J* = 9.0 Hz, *o*-F Ph C-4), 131.3 (d, *J* = 2.9 Hz, *o*-F Ph C-6), 128.4 (Ph C-3,5), 128.3 (Ph C-2,6), 126.1 (Ph C-4), 124.6 (d, *J* = 3.3 Hz, *o*-F Ph C-5), 123.8 (d, *J* = 13.9 Hz, *o*-F Ph C-1), 116.5 (d, *J* = 23.7 Hz, *o*-F Ph C-3), 78.0 (d, *J* = 7.7 Hz, CHC=O), 46.6 (br CHCH$_3$), 45.6 (br CHCH$_3$), 32.36 (d, *J* = 1.5 Hz, CH_2CH), 32.29 (PhCH_2), 21.7 (br, CH_3), 21.3 (br, CH_3), 20.5 (br, 2×CH_3).

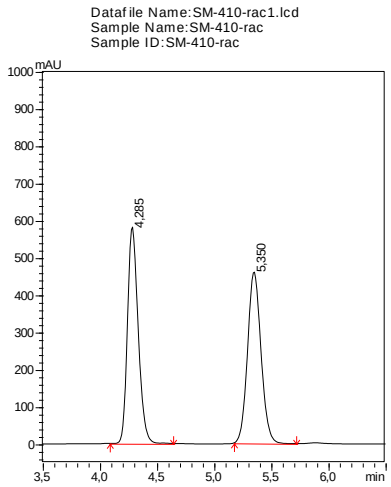
^{19}F NMR (376 MHz, $CDCl_3$): δ -108.8 (m).

HRMS (ESI), *m/z*: calcd. for $C_{23}H_{29}FNO_3$ 386.2126 $[M+H]^+$; found 386.2128.

$[\alpha]_D$ -39 (*c* 0.5, $CHCl_3$).

HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 1 mL/min

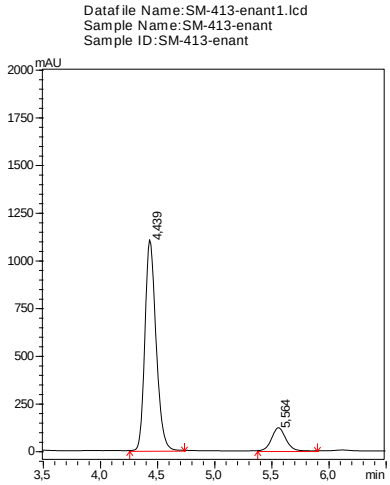
Racemate



Peaks	Retention time (min)	Area	Area%
1	4,285	3778060	50,143
2	5,350	3756581	49,857

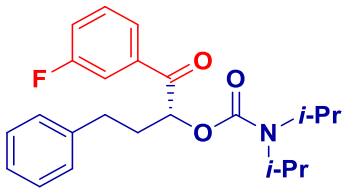
Total		7534642	100,000

***Enantioenriched* (*R*)-6**



Peaks	Retention time (min)	Area	Area%
1	4,439	7463243	87,988
2	5,564	1018858	12,012
Total		8482101	100,000

(*R*)-1-(3-Fluorophenyl)-1-oxo-4-phenyl-2-butanyl diisopropylcarbamate, ((*R*)-7)



Synthesized according to **GP1** using **1** (0.077 g, 0.294 mmol, 1.5 equiv); (-)-sparteine (0.073 g, 0.313 mmol, 1.6 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and 3-fluoro-*N*-methoxy-*N*-methylbenzamide (0.036 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*)-7** was obtained in 91% yield (0.069 g) as a white solid; mp 57-60 °C. Reaction run with (-)-sparteine recovered from preparation of **(*R*)-5.**

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (m, 1H, *m*-F Ph H-6), 7.55 (m, 1H, *m*-F Ph H-2), 7.39 (m, 1H, *m*-F Ph H-5), 7.30 (m, 2H, Ph H-3,5), 7.24 (m, 1H, *m*-F Ph H-4), 7.22 (m, 1H, Ph H-4), 7.17 (m, 2H, Ph H-2,6), 5.80 (m, 1H, C<u>H</u>C=O), 4.03 (br s, 1H, C<u>H</u>CH_3), 3.86 (br s, 1H, C<u>H</u>CH_3), 2.84 (m, 1H, Ph$C\underline{H}_2$), 2.80 (m, 1H, Ph$C\underline{H}_2$), 2.18 (m, 1H, $C\underline{H}_2$CH), 2.15 (m, 1H, $C\underline{H}_2$CH), 1.33 (br, 6H, $C\underline{H}_3$), 1.20 (br, 6H, $C\underline{H}_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ 196.5 (d, ^4J = 2.2 Hz, PhC=O), 162.8 (d, ^1J = 248.1 Hz, *m*-F Ph C-3), 154.7 (NC=O), 140.5 (Ph C-1), 137.1 (d, ^3J = 6.3 Hz, *m*-F Ph C-1), 130.3 (d, ^3J = 7.7 Hz, *m*-F Ph C-5), 128.6 (Ph C-3,5), 128.4 (Ph C-2,6), 126.3 (Ph C-4), 124.1 (d, ^4J = 3.1 Hz, *m*-F Ph C-6), 120.2 (d, ^2J = 21.5 Hz, *m*-F Ph C-4), 115.2 (d, ^2J = 22.6 Hz, *m*-F Ph C-2), 74.5 (CHC=O), 46.8 $CHCH_3$, 45.7 $CHCH_3$, 33.0 (CH_2CH), 31.9 ($PhCH_2$), 22.0-20.0 (CH_3).

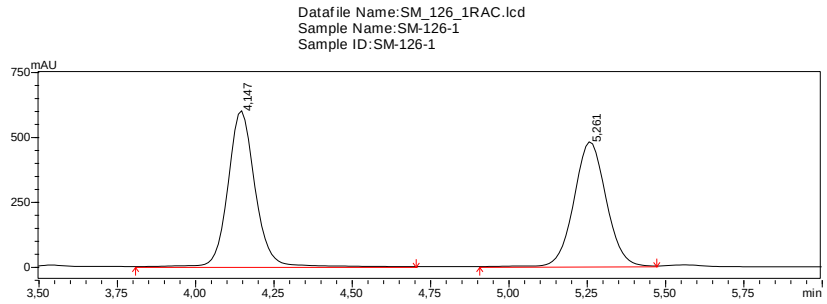
^{19}F NMR (376 MHz, $CDCl_3$): δ -111.6 (m).

HRMS (ESI), *m/z*: calcd. for $C_{23}H_{28}FNNaO_3$ 408.1945 $[M+Na]^+$; found 408.1951

$[\alpha]_D$ -76 (*c* 0.5, $CHCl_3$).

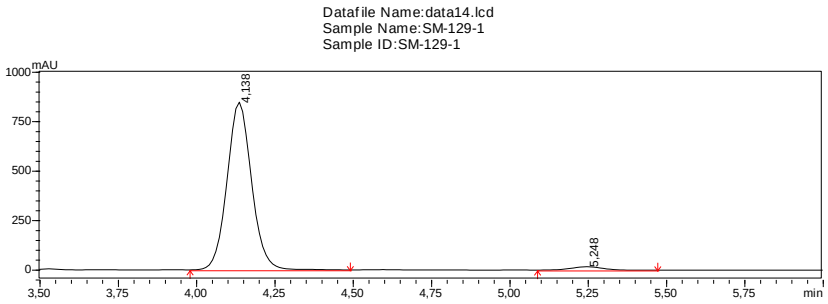
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 1 mL/min

Racemate



Peaks	Retention time (min)	Area	Area%
1	4,147	3582812	51,322
2	5,261	3398295	48,678
total		6981108	100,000

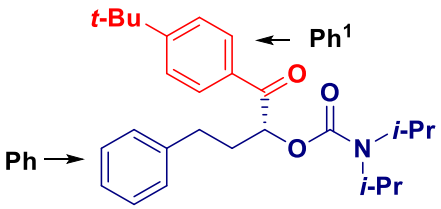
***Enantioenriched* (*R*)-7**



Peaks	Retention time (min)	Area	Area%

1	4,138	4606403	97,532
2	5,248	116582	2,468
total		4722985	100,000

(*R*)-1-[4-(2-Methyl-2-propanyl)phenyl]-1-oxo-4-phenyl-2-butanyl diisopropylcarbamate ((*R*)-8)



Synthesized according to **GP1** using **1** (0.077 g, 0.294 mmol, 1.5 equiv); (-)-sparteine (0.073 g, 0.313 mmol, 1.6 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and 4-(tert-butyl)-*N*-methoxy-*N*-methyl-benzamide (0.043 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*)-8** was obtained in 95% yield (0.079 g) as a white solid; mp 70-74 °C. Reaction run in larger scale starting from **1** (1.58 g, 6 mmol, 1.5 equiv); (-)-sparteine (1.5 g, 6.4 mmol, 1.6 equiv); *s*-BuLi 1.4 M (4.57 mL, 6.4 mmol, 1.6 equiv) and 4-(tert-butyl)-*N*-methoxy-*N*-methyl-benzamide (0.885 g, 4 mmol, 1.0 equiv) in CPME (27 mL) allowed to recover CPME (89%, 24.0 mL) and prepare **(*R*)-8** in comparable yield (89%, 1.51 g). The organic layer from the basic extraction with CPME (30 mL) afforded upon distillation (-)-sparteine (83%, 1.24 g, 1.22 mL), *N*-methyl-*N*-methoxyamine (70%, 2.8 mmol, 0.21 mL) and CPME (90%, 27.0 mL).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (m, 2H, Ph^1 H-2,6), 7.43 (m, 2H, Ph^1 H-3,5), 7.29 (m, 2H, Ph H-3,5), 7.20 (m, 1H, Ph H-4), 7.17 (m, 2H, Ph H-2,6), 5.91 (dd, *J* = 8.0 Hz, 4.6 Hz, 1H, C<u>H</u>C=O), 4.06 (br s, 1H, C<u>H</u>CH_3), 3.86 (br s, 1H, C<u>H</u>CH_3), 2.75-2.89 (m, 2H, Ph$C\underline{H}_2$), 2.13-2.22 (m, 2H, $C\underline{H}_2$CH), 1.34-1.21 (br, 12H, $C\underline{H}_3$), 1.32 (s, 9H, $C(C\underline{H}_3)_3$).

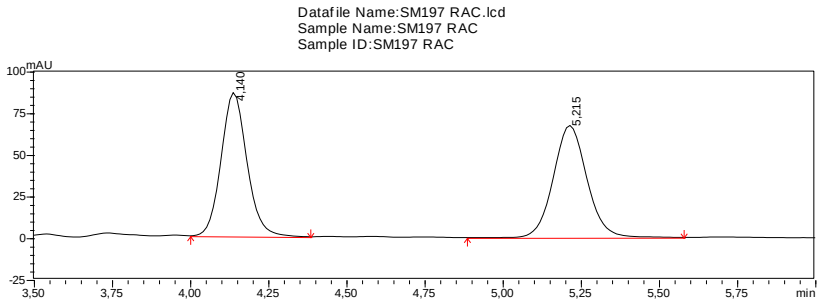
^{13}C NMR (100 MHz, $CDCl_3$): δ 197.2 (Ph<u>C</u>=O), 157.0 (Ph^1 C-4), 154.9 (N<u>C</u>=O), 140.9 (Ph C-1), 132.3 (Ph^1 C-1), 128.5 (Ph C-3,5), 128.4 (Ph C-2,6), 128.3 (Ph^1 C-2,6), 126.2 (Ph C-4), 125.6 (Ph^1 C-3,5), 74.4 (<u>C</u>HC=O), 46.6 (<u>C</u>HCH_3), 45.6 (<u>C</u>HCH_3), 35.1 ($\underline{C}(CH_3)_3$), 33.2 ($\underline{C}H_2CH$), 32.0 (Ph$\underline{C}H_2$), 31.0 ($C(\underline{C}H_3)_3$), 21.7 ($\underline{C}H_3$), 21.4 ($\underline{C}H_3$), 20.5 ($\underline{C}H_3$).

HRMS (ESI), *m/z*: calcd. for $C_{27}H_{38}NO_3$ 424.2846 $[M+H]^+$; found 424.2854.

$[\alpha]_D$ -17 (*c* 0.5, $CHCl_3$).

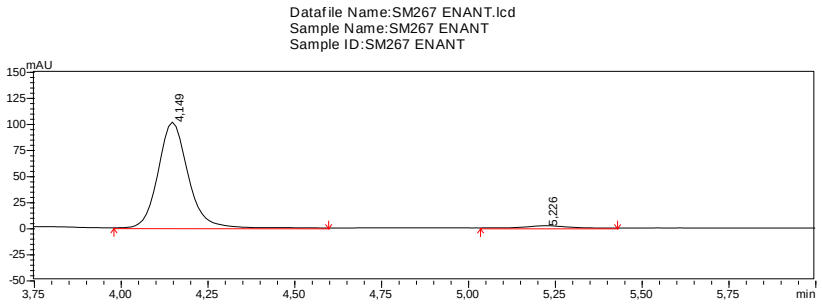
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 1 mL/min

Racemate



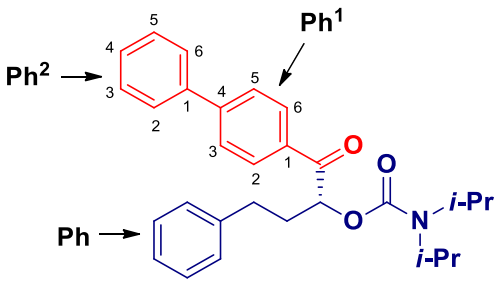
Peaks	Retention time (min)	Area	Area%
1	4,140	493830	49,575
2	5,215	502306	50,425
Total		996136	100,000

***Enantioenriched* (*R*)-8**



Peaks	Retention time (min)	Area	Area%
1	4,149	602309	97,519
2	5,226	15327	2,481
Total		617636	100,000

(*R*)-1-(4-Biphenylyl)-1-oxo-4-phenyl-2-butanyl diisopropylcarbamate, ((*R*)-9)



Synthesized according to **GP1** using **1** (0.077 g, 0.294 mmol, 1.5 equiv); (-)-sparteine (0.073 g, 0.313 mmol, 1.6 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and *N*-methoxy-*N*-methyl-4-biphenylcarboxamide (0.047 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*)-9** was obtained in 92% yield (0.080g) as a white solid; mp 132-135 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (m, 2H, Ph^1 H-2,6), 7.64 (m, 2H, Ph^1 H-3,5), 7.61 (m, 2H, Ph^2 H-2,6), 7.47 (m, 2H, Ph^2 H-3,5), 7.40 (m, 1H, Ph^2 H-4), 7.30 (m, 2H, Ph H-3,5), 7.22 (m, 1H, Ph H-4), 7.19 (m, 2H, Ph H-2,6), 5.94 (dd, *J* = 7.5Hz, 5.1 Hz, 1H, C<u>H</u>C=O), 4.06 (br s, 1H, C<u>H</u>CH_3), 3.88 (br s, 1H, C<u>H</u>CH_3), 2.76-2.92 (m, 2H, PhC<u>H_2</u>), 2.15-2.27 (m, 2H, C<u>H_2</u>CH), 1.35 (br s, 6H, C<u>H_3</u>), 1.22 (br s, 6H, C<u>H_3</u>).

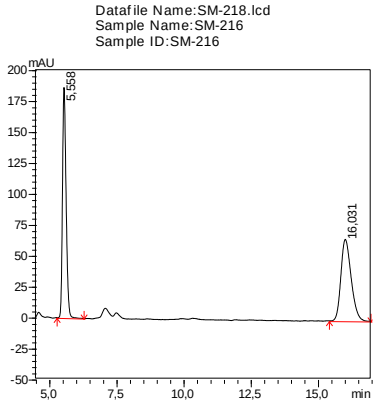
^{13}C NMR (100 MHz, $CDCl_3$): δ 197.2 (Ph<u>C</u>=O), 154.9 (N<u>C</u>=O), 145.9 (Ph^1 C-4), 140.8 (Ph C-1), 139.9 (Ph^2 C-1), 133.7 (Ph^1 C-1), 129.0 (Ph^1 C-2,6), 128.9 (Ph^2 C-3,5), 128.6 (Ph C-3,5), 128.4 (Ph C-2,6), 128.2 (Ph^2 C-4), 127.3 (Ph^1 C-3,5), 127.3 (Ph^2 C-2,6), 126.2 (Ph C-4), 74.4 (<u>C</u>HC=O), 46.7 (<u>C</u>HCH_3), 45.7 (<u>C</u>HCH_3), 33.2 (<u>C</u>H_2CH), 32.0 (Ph<u>C</u>H_2), 21.9 (<u>C</u>H_3 br s), 21.4 (<u>C</u>H_3 br s), 20.5 (<u>C</u>H_3 br s).

HRMS (ESI), *m/z*: calcd. for $C_{29}H_{34}NO_3$ 444.2533 [M+H]; found 444.2536.

$[\alpha]_D$ -69 (*c* 0.5, $CHCl_3$).

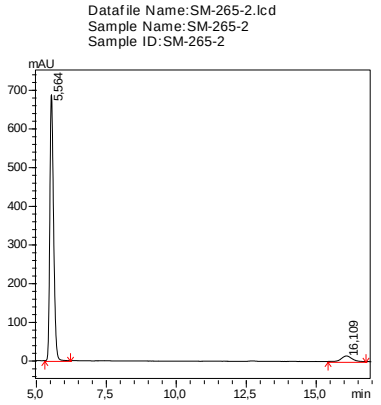
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 1 mL/min

Racemate



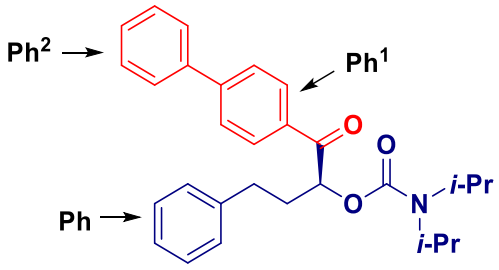
Peaks	Retention time (min)	Area	Area%
1	5,558	1727879	49,916
2	16,031	1733678	50,084
Total		3461556	100,000

***Enantioenriched* (*R*)-9**



Peaks	Retention time (min)	Area	Area%
1	5,564	6393887	94,571
2	16,109	367067	5,429
Total		6760955	100,000

(*S*)-1-(4-Biphenylyl)-1-oxo-4-phenyl-2-butanyl diisopropylcarbamate, ((*S*)-9)

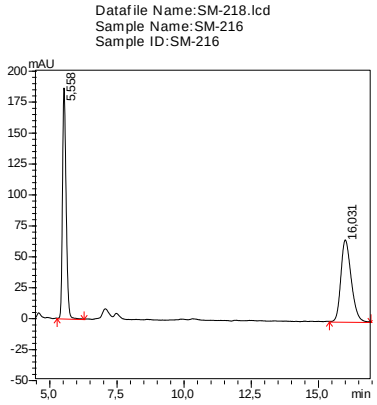


Synthesized according to **GP1** using **1** (0.077 g, 0.294 mmol, 1.5 equiv); (+)-sparteine (0.073 g, 0.313 mmol, 1.6 equiv); s-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and *N*-methoxy-*N*-methyl-4-biphenylcarboxamide (0.047 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*S*)-9** was obtained in 88% yield (0.076 g) as a white solid; mp 132-135 °C. Reaction run with (+)-sparteine recovered from preparation of **(*S*)-3.**

$[\alpha]_D$ +65 (*c* 0.5, $CHCl_3$).

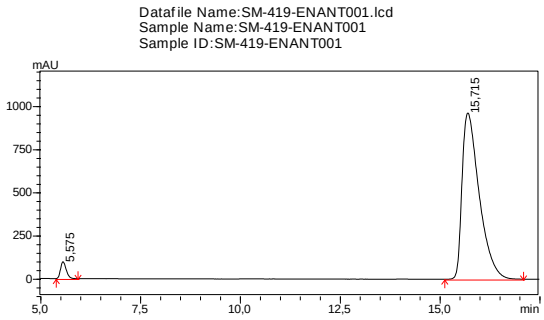
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 1 mL/min

Racemate



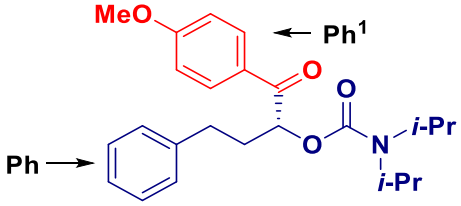
Peaks	Retention time (min)	Area	Area%
1	5,558	1727879	49,916
2	16,031	1733678	50,084
Total		3461556	100,000

***Enantioenriched* (*S*)-9**



Peaks	Retention time (min)	Area	Area%
1	5,575	964729	3,245
2	15,715	28761124	96,755
Total		29725853	100,000

(*R*)-1-(4-Methoxyphenyl)-1-oxo-4-phenyl-2-butanyl diisopropylcarbamate, ((*R*)-10)



Synthesized according to **GP1** using **1** (0.077 g, 0.294 mmol, 1.5 equiv); (-)-sparteine (0.073 g, 0.313 mmol, 1.6 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and N,4-dimethoxy-*N*-methylbenzamide (0.038 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*)-10** was obtained in 81% yield (0.063 g) as a white solid; mp 77-80 °C. Reaction run with (-)-sparteine recovered from preparation of **(*R*)-8.**

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (m, 2H, Ph^1 H-2,6), 7.29 (m, 2H, Ph H-3,5), 7.20 (m, 1H, Ph H-4), 7.17 (m, 2H, Ph H-2,6), 6.89 (m, 2H, Ph^1 H-3,5), 5.90 (m, 1H, C<u>H</u>C=O), 4.07 (br s, 1H, C<u>H</u>CH_3), 3.86 (br s, 1H, C<u>H</u>CH_3), 3.85 (s, 3H, OCH_3), 2.74-2.88 (m, 2H, Ph$C\underline{H}_2$), 2.13-2.20 (m, 2H, $C\underline{H}_2$CH), 1.34-1.21 (br, 12H, $C\underline{H}_3$).

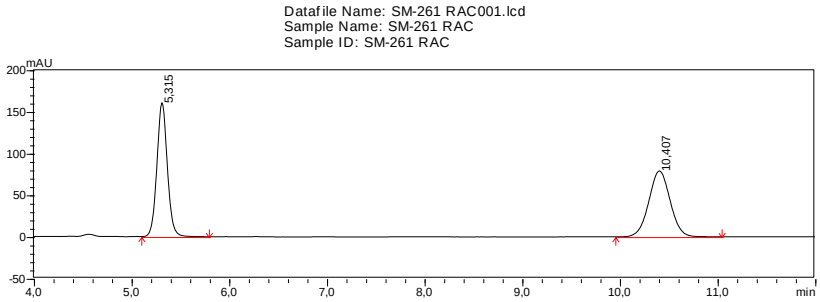
^{13}C NMR (100 MHz, $CDCl_3$): δ 195.9 (Ph<u>C</u>=O), 163.6 (Ph^1 C-4), 154.9 (N<u>C</u>=O), 140.8 (Ph C-1), 130.7 (Ph^1 C-2,6), 128.5 (Ph C-3,5), 128.4 (Ph C-2,6), 127.9 (Ph^1 C-1), 126.1 (Ph C-4), 113.8 (Ph^1 C-3,5), 74.1 (<u>C</u>HC=O), 55.4 (OCH_3), 46.6 (<u>C</u>HCH_3), 45.6 (<u>C</u>HCH_3), 33.4 ($\underline{C}H_2$CH), 31.9 (Ph$\underline{C}H_2$), 21.8 ($\underline{C}H_3$), 21.3 ($\underline{C}H_3$), 20.5 ($\underline{C}H_3$).

HRMS (ESI), *m/z*: calcd. for $C_{24}H_{32}NO_4$ 398.2326 $[M+H]^+$; found 398.2330.

$[\alpha]_D$ -73 (*c* 0.5, $CHCl_3$).

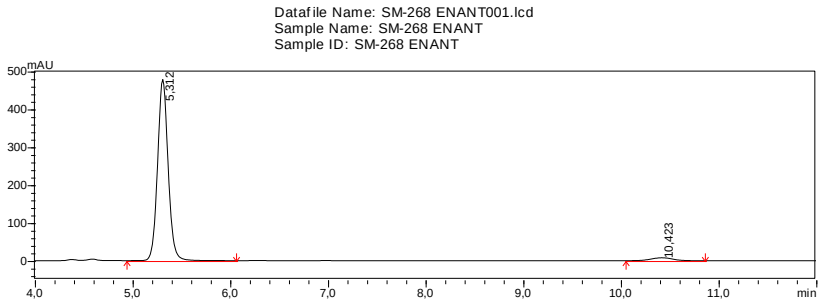
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 1 mL/min

Racemate



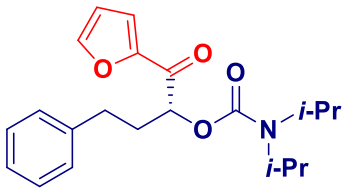
Peaks	Retention time (min)	Area	Area%
1	5,315	1195643	49,879
2	10,407	1201452	50,121
Total		2397095	100,000

***Enantioenriched* (*R*)-10**



Peaks	Retention time (min)	Area	Area%
1	5,312	3595139	96,859
2	10,423	116568	3,141
Total		3711707	100,000

(*R*)-1-(2-Furyl)-1-oxo-4-phenyl-2-butanyl diisopropylcarbamate, ((*R*)-11)



Synthesized according to **GP1** using **1** (0.077 g, 0.294 mmol, 1.5 equiv); (-)-sparteine (0.073 g, 0.313 mmol, 1.6 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and *N*-methoxy-*N*-methyl-2-furamide (0.030 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*)-11** was obtained in 85% yield (0.059 g) as a white solid; mp 147-150 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (m, dd, *J* = 1.7 Hz, 0.8 Hz, 1H, Furyl H-5), 7.29 (m, 2H, Ph H-3,5), 7.22 (m, 1H, Ph H-4), 7.17 (m, 2H, Ph H-2,6), 7.18 (m, dd, *J* = 3.6 Hz, 0.8 Hz, 1H, Furyl H-3), 6.51 (m, dd, *J* = 3.6 Hz, 1.7 Hz, 1H, Furyl H-4), 5.69 (m, 1H, C<u>H</u>C=O), 4.04 (br s, 1H, C<u>H</u>CH_3), 3.87 (br s, 1H, C<u>H</u>CH_3), 2.74-2.90 (m, 2H, PhC<u>H</u>$_2$), 2.13-2.27 (m, 2H, C<u>H</u>$_2$CH), 1.15-1.40 (2 br s, 12H, C<u>H</u>$_3$).

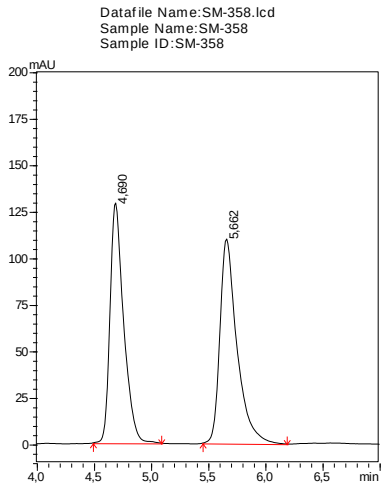
^{13}C NMR (100 MHz, $CDCl_3$): δ 186.1 (Furyl <u>C</u>=O), 154.7 (N<u>C</u>=O), 150.8 (Furyl C-2), 146.6 (Furyl C-5), 140.8 (Ph C-1), 128.5 (Ph C-3,5), 128.4 (Ph C-2,6), 126.2 (Ph C-4), 118.1 (Furyl C-3), 112.2 (Furyl C-4), 74.7 (<u>C</u>HC=O), 46.7 (<u>C</u>HCH_3), 45.6 (<u>C</u>HCH_3), 33.1 (<u>C</u>H$_2$CH), 31.8 (Ph<u>C</u>H$_2$), 21.8 (<u>C</u>H$_3$), 21.4 (<u>C</u>H$_3$), 20.4 (<u>C</u>H$_3$ 2x).

HRMS (ESI), *m/z*: calcd. for $C_{21}H_{28}NO_4$ 358.2013 $[M+H]^+$; found 358.2014.

[α]$_D$ -110 (*c* 0.5, $CHCl_3$).

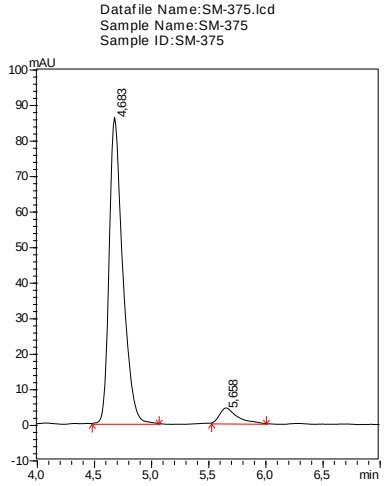
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 1 mL/min

Racemate



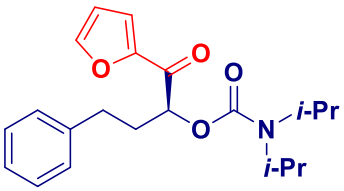
Peaks	Retention time (min)	Area	Area%
1	4,690	1067464	48,416
2	5,662	1137305	51,584
Total		2204769	100,000

***Enantioenriched* (*R*)-11**



Peaks	Retention time (min)	Area	Area%
1	4,683	708800	94,039
2	5,658	44932	5,961
Total		753733	100,000

(*S*)-1-(2-Furyl)-1-oxo-4-phenyl-2-butanyl diisopropylcarbamate, ((*S*)-11)

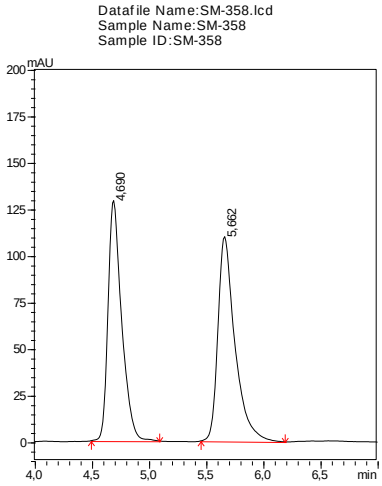


Synthesized according to **GP1** using **1** (0.077 g, 0.294 mmol, 1.5 equiv); (+)-sparteine (0.073 g, 0.313 mmol, 1.6 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and *N*-methoxy-*N*-methyl-2-furamide (0.030 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*S*)-11** was obtained in 90% yield (0.063 g) as a white solid; mp 147-150 °C. Reaction run in larger scale starting from **1** (1.58 g, 6 mmol, 1.5 equiv); (+)-sparteine (1.5 g, 6.4 mmol, 1.6 equiv); *s*-BuLi 1.4 M (4.57 mL, 6.4 mmol, 1.6 equiv) and *N*-methoxy-*N*-methyl-2-furamide (0.620 g, 4 mmol, 1.0 equiv) in CPME (27 mL) allowed to recover CPME (86%, 23.2 mL) and prepare **(*S*)-11** in comparable yield (83%, 1.18 g). The organic layer from the basic extraction with CPME (30 mL) afforded upon distillation (+)-sparteine (80%, 1.2 g, 1.18 mL), *N*-methyl-*N*-methoxyamine (65%, 2.6 mmol, 0.20 mL) and CPME (94%, 28.3 mL).

$[\alpha]_D$ +35 (*c* 0.5, $CHCl_3$).

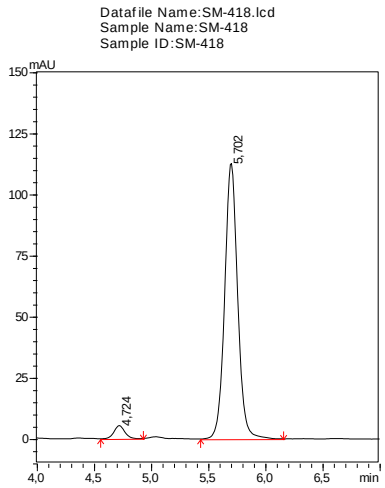
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 1 mL/min

Racemate



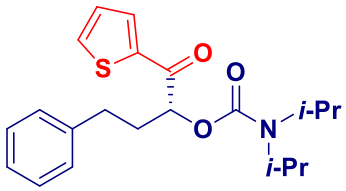
Peaks	Retention time (min)	Area	Area%
1	4,690	1067464	48,416
2	5,662	1137305	51,584
Total		2204769	100,000

***Enantioenriched* (*S*)-11**



Peaks	Retention time (min)	Area	Area%
1	4,724	34349	3,713
2	5,702	890792	96,287
Total		925141	100,000

(*R*)-1-Oxo-4-phenyl-1-(2-thienyl)-2-butanyl diisopropylcarbamate, ((*R*)-12)



Synthesized according to **GP1** using **1** (0.144 g, 0.546 mmol, 1.5 equiv); (-)-sparteine (0.136 g, 0.582 mmol, 1.6 equiv); *s*-BuLi 1.3 M (0.45 mL, 0.582 mmol, 1.6 equiv) in CPME (2 mL); and *N*-methoxy-*N*-methyl-2-thiophenecarboxamide (0.062 g, 0.364 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*)-12** was obtained in 88% yield (0.119 g) as a white solid; mp 124-127 °C. Reaction run in larger scale starting from **1** (1.58 g, 6 mmol, 1.5 equiv); (-)-sparteine (1.5 g, 6.4 mmol, 1.6 equiv); *s*-BuLi 1.4 M (4.57 mL, 6.4 mmol, 1.6 equiv) and *N*-methoxy-*N*-methyl-2-thiophenecarboxamide (0.684 g, 4 mmol, 1.0 equiv) in CPME (27 mL) allowed to recover CPME (90%, 24.4 mL) and prepare **(*R*)-12** in comparable yield (80%, 1.19 g). The organic layer from the basic extraction with CPME (30 mL) afforded upon distillation (-)-sparteine (70%, 1.15 g, 1.13 mL), *N*-methyl-*N*-methoxyamine (65%, 2.6 mmol, 0.20 mL) and CPME (92%, 27.7 mL).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (m, 2H, Th H-3,5), 7.30 (m, 2H, Ph H-3,5), 7.21 (m, 1H, Ph H-4), 7.19 (m, 2H, Ph H-2,6), 7.09 (m, 1H, Th H-4), 5.69 (m, 1H, C<u>H</u>C=O), 4.03 (br s, 1H, C<u>H</u>CH_3), 3.88 (br s, 1H, C<u>H</u>CH_3), 2.75-2.91 (m, 2H, PhC<u>H</u>$_2$), 2.20-2.26 (m, 2H, C<u>H</u>$_2$CH), 1.34-1.21 (br, 12H, C<u>H</u>$_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ 190.2 (Th<u>C</u>=O), 154.7 (N<u>C</u>=O), 141.2 (Th C-2), 140.7 (Ph C-1), 133.9 (Th C-5), 132.2 (Th C-3), 128.6 (Ph C-3,5), 128.4 (Ph C-2,6), 128.1 (Th C-4), 126.2 (Ph C-4), 75.2 (<u>C</u>HC=O), 46.7 (<u>C</u>HCH_3), 45.7 (<u>C</u>HCH_3), 33.7 (<u>C</u>H_2CH), 31.9 (Ph<u>C</u>H_2), 21.8 (<u>C</u>H_3 via HSQC), 21.4 (<u>C</u>H_3 via HSQC), 20.5 (<u>C</u>H_3 br).

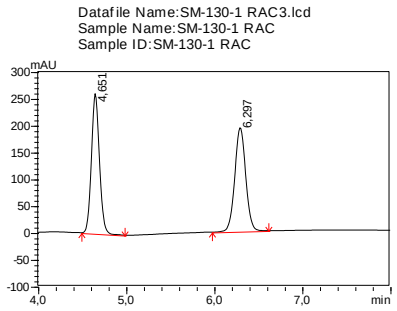
HRMS (ESI), *m/z*: calcd. for $C_{21}H_{27}NNaO_3S$ 396.1604 $[M+Na]^+$; found 396.1607.

[α]$_D$ -41 (*c* 0.5, $CHCl_3$).

HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 1 mL/min

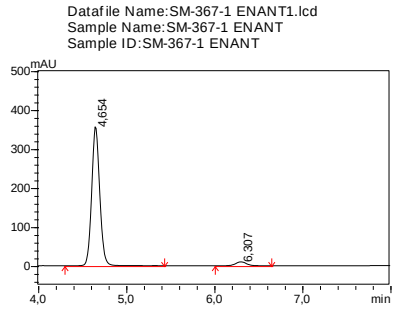
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 1 mL/min

Racemate



Peaks	Retention time (min)	Area	Area%
1	4,651	1640815	49,638
2	6,297	1664745	50,362
Total		3305560	100,000

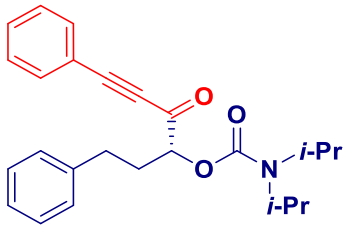
***Enantioenriched* (*R*)-12**



Peaks	Retention time (min)	Area	Area%
1	4,654	2266034	96,224

2	6,307	88926	3,776
Total		2354960	100,000

(*R*)-4-Oxo-1,6-diphenyl-5-hexyn-3-yl diisopropylcarbamate, ((*R*)-13)



Synthesized according to **GP1** using **1** (0.077 g, 0.294 mmol, 1.5 equiv); (-)-sparteine (0.073 g, 0.313 mmol, 1.6 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and *N*-methoxy-*N*-methyl-3-phenyl-2-propynamide (0.037 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*)-13** was obtained in 77% yield (0.059 g) as a white solid; mp 73-74 °C. Reaction run with (-)-sparteine recovered from preparation of **(*R*)-12.**

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (m, 2H, Ph^1 H-2,6), 7.46 (m, 1H, Ph^1 H-4), 7.37 (m, 2H, Ph^1 H-3,5), 7.30 (m, 2H, Ph H-3,5), 7.22 (m, 2H, Ph H-2,6), 7.21 (m, 1H, Ph H-4), 5.17 (m, 1H, C<u>H</u>C=O), 4.08 (br s, 1H, C<u>H</u>CH_3), 3.89 (br s, 1H, C<u>H</u>CH_3), 2.89-2.76 (m, 2H, Ph$C\underline{H}_2$), 2.35-2.18 (m, 2H, $C\underline{H}_2$CH), 1.40 -1.20 (br, 12H, CH_3).

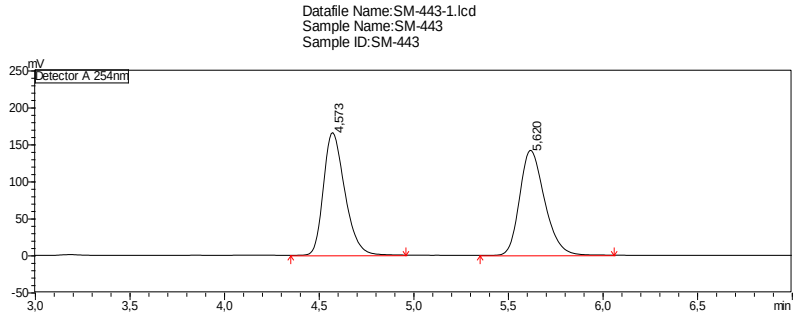
^{13}C NMR (100 MHz, $CDCl_3$): δ 185.6 (<u>C</u>=O), 154.6 (N<u>C</u>=O), 140.7 (Ph C-1), 132.9 (Ph^1 C-2,6), 130.8 (Ph^1 C-4), 128.6 (Ph^1 C-3,5), 128.5 (Ph C-3,5), 128.4 (Ph C-2,6), 126.2 (Ph C-4), 119.8 (Ph^1 C-1), 93.6 (C=OC≡<u>C</u>), 85.8 (C=O<u>C</u>≡C), 78.8 (<u>C</u>HC=O), 46.7 (br <u>C</u>HCH_3), 45.7 (br <u>C</u>HCH_3), 32.6 ($C\underline{H}_2$CH), 31.6 (Ph$C\underline{H}_2$), 21.7 (br <u>C</u>H_3), 21.5 (<u>C</u>H_3 br), 20.4 (br, 2×<u>C</u>H_3).

HRMS (ESI), *m/z*: calcd. for $C_{25}H_{30}NO_3$ 392.2219 $[M+H]^+$; found 392.2220.

[α]$_D$ -44 (*c* 0.5, $CHCl_3$).

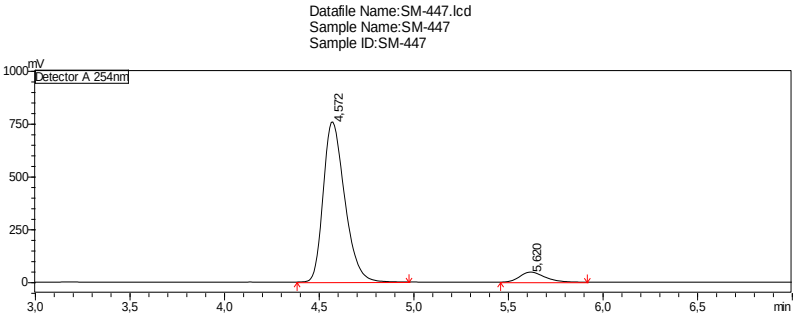
HPLC analysis: Chiralpak IA Column, λ 254 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 1 mL/min

Racemate



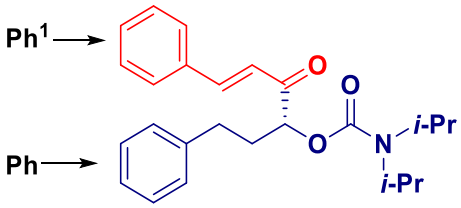
Peaks	Retention time (min)	Area	Area%
1	4,573	1299951	50,035
2	5,620	1298135	49,965
Total		2598086	100,000

***Enantioenriched* (*R*)-13**



Peaks	Retention time (min)	Area	Area%
1	4,572	5975193	93,295
2	5,620	429434	6,705
Total		6404627	100,000

(*R*)-(5*E*)-4-Oxo-1,6-diphenyl-5-hexen-3-yl diisopropylcarbamate, ((*R*)-14)



Synthesized according to **GP1** using **1** (0.077 g, 0.294 mmol, 1.5 equiv); (-)-sparteine (0.073 g, 0.313 mmol, 1.6 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and (2*E*)-*N*-methoxy-

N-methyl-3-phenylacrylamide (0.038 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*)-14** was obtained in 78% yield (0.060 g) as a white solid; mp 77-80 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, *J* = 16.0 Hz, 1H, CH=C<u>H</u>Ph), 7.52 (m, 2H, Ph^{1} H-2,6), 7.39 (m, 3H, Ph^{1} H-3,4,5), 7.30 (m, 2H, Ph H-3,5), 7.21 (m, 3H, Ph H-2,4,6), 6.86 (d, *J* = 16.0 Hz, 1H, C<u>H</u>=CHPh), 5.30 (dd, *J* = 7.8 Hz, 5.2 Hz, 1H, C<u>H</u>C=O), 4.08 (br s, 1H, C<u>H</u>CH_3), 3.89 (br s, 1H, C<u>H</u>CH_3), 2.74-2.88 (m, 2H, PhC<u>H</u>$_2$), 2.10-2.24 (m, 2H, C<u>H</u>$_2$CH), 1.15-1.45 (br, 12H, C<u>H</u>$_3$).

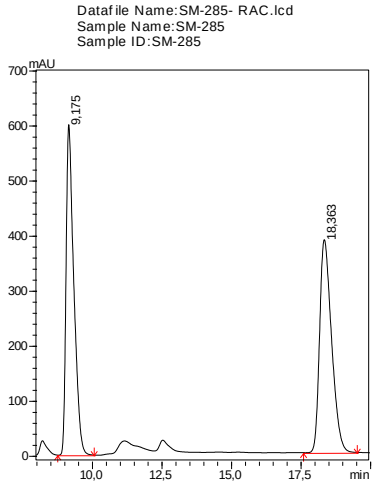
^{13}C NMR (100 MHz, $CDCl_3$): δ 197.0 (CH=CH<u>C</u>=O), 154.8 (N<u>C</u>=O), 143.9 (CH=<u>C</u>HPh), 140.9 (Ph C-1), 134.5 (Ph^{1} C-1), 130.6 (Ph^{1} C-4), 128.9 (Ph^{1} C-3,5), 128.5 (Ph C-3,5), 128.4 (Ph C-2,6; Ph^{1} C-2,6), 126.2 (Ph C-4), 121.4 (<u>C</u>H=CHPh), 77.4 (O<u>C</u>HC=O), 46.7 (<u>C</u>HCH_3), 45.6 (<u>C</u>HCH_3), 32.8 (<u>C</u>H$_2$CH), 31.8 (Ph<u>C</u>H$_2$), 20.1-22.1 (<u>C</u>H$_3$).

HRMS (ESI), *m/z*: calcd. for $C_{25}H_{32}NO_3$ 394.2377 $[M+H]^+$; found 394.2380.

[α]$_D$ -20 (*c* 0.5, $CHCl_3$).

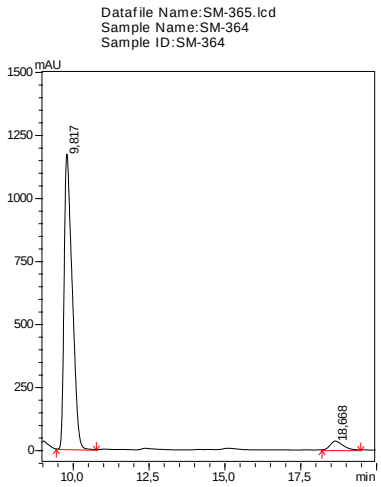
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 1 mL/min

Racemate



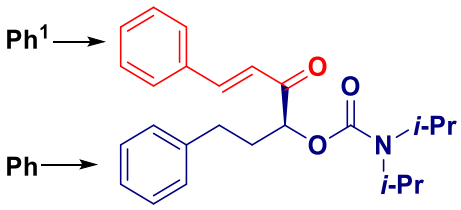
Peaks	Retention time (min)	Area	Area%
1	9,175	11611457	50,143
2	18,363	11545028	49,857
Total		23156486	100,000

***Enantioenriched* (*R*)-14**



Peaks	Retention time (min)	Area	Area%
1	9,817	21600332	95,648
2	18,668	982877	4,352
Total		22583208	100,000

(*S*)-(5*E*)-4-Oxo-1,6-diphenyl-5-hexen-3-yl diisopropylcarbamate, ((*S*)-14)

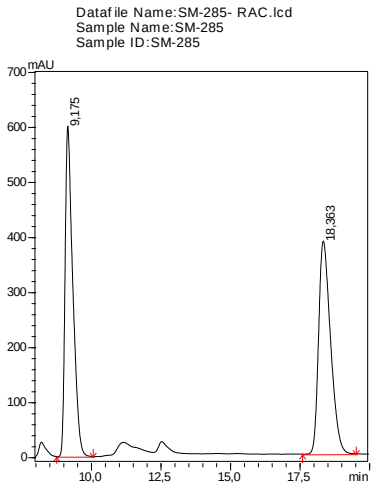


Synthesized according to **GP1** using **1** (0.077 g, 0.294 mmol, 1.5 equiv); (+)-sparteine (0.073 g, 0.313 mmol, 1.6 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and (2*E*)-*N*-methoxy-*N*-methyl-3-phenylacrylamide (0.038 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*S*)-14** was obtained in 75% yield (0.058 g) as a white solid; mp 77-80 °C. Reaction run with (+)-sparteine recovered from preparation of **(*S*)-11.**

$[\alpha]_D$ +43 (*c* 0.5, $CHCl_3$).

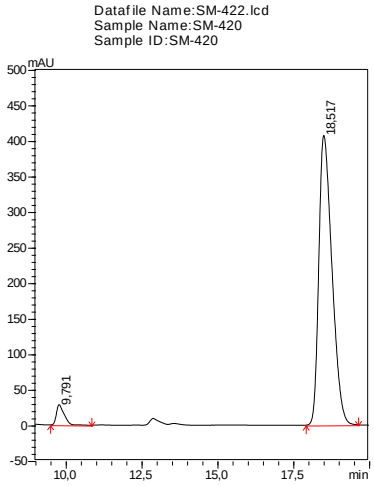
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 1 mL/min

Racemate



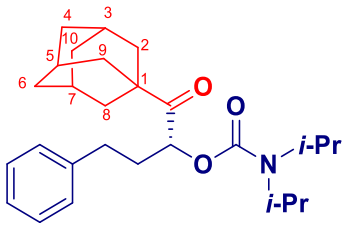
Peaks	Retention time (min)	Area	Area%
1	9,175	11611457	50,143
2	18,363	11545028	49,857
Total		23156486	100,000

***Enantioenriched* (*S*)-14**



Peaks	Retention time (min)	Area	Area%
1	9,791	499382	3,911
2	18,517	12270734	96,089
Total		12770116	100,000

(*R*)-1-(Adamantan-1-yl)-1-oxo-4-phenyl-2-butanyl diisopropylcarbamate, ((*R*)-15)



Synthesized according to **GP1** using **1** (0.077 g, 0.294 mmol, 1.5 equiv); (-)-sparteine (0.073 g, 0.313 mmol, 1.6 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and *N*-methoxy-*N*-methyl-1-adamantanecarboxamide (0.044 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*)-15** was obtained in 83% yield (0.069 g) as a white solid; mp 60-63 °C. Reaction run in larger scale starting from **1** (1.58 g, 6 mmol, 1.5 equiv); (-)-sparteine (1.5 g, 6.4 mmol, 1.6 equiv); *s*-BuLi 1.4 M (4.57 mL, 6.4 mmol, 1.6 equiv) and *N*-methoxy-*N*-methyl-1-adamantanecarboxamide (0.893 g, 4 mmol, 1.0 equiv) in CPME (27 mL) allowed to recover CPME (91%, 24.7 mL) and prepare **(*R*)-15** in comparable yield (78%, 1.32 g). The organic layer from the basic extraction with CPME (30 mL) afforded upon distillation (-)-sparteine (83%, 1.24 g, 1.22 mL), *N*-methyl-*N*-methoxyamine (70%, 2.8 mmol, 0.21 mL) and CPME (93%, 28.0 mL).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (m, 2H, Ph H-3,5), 7.20 (m, 1H, Ph H-4), 7.19 (m, 2H, Ph H-2,6), 5.42 (dd, *J* = 8.1 Hz, 3.7 Hz, 1H, C<u>H</u>C=O), 4.10 (br s, 1H, C<u>H</u>CH_3), 3.75 (br s, 1H, C<u>H</u>CH_3), 2.66-2.84 (m, 2H, Ph$C\underline{H}_2$), 1.93-2.06 (m, 2H, $C\underline{H}_2$CH), 2.01 (m, 3H, Adam H-3,5,7), 1.92 (m, 3H, Adam H-2,8,9), 1.82 (m, 3H, Adam H-2,8,9), 1.69 (m, 6H, Adam H-4,6,10), 1.38 (br s, 6H, $C\underline{H}_3$), 1.15 (br s, 6H, $C\underline{H}_3$).

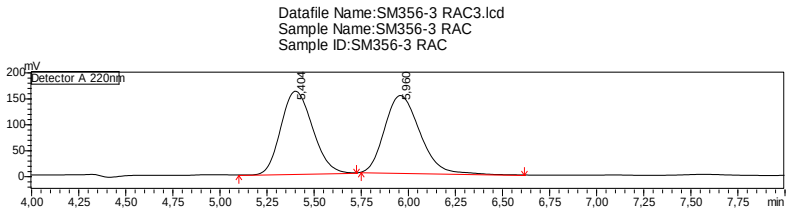
^{13}C NMR (100 MHz, $CDCl_3$): δ 211.9 (Adam <u>C</u>=O), 154.8 (N<u>C</u>=O), 141.1 (Ph C-1), 128.5 (Ph C-3,5), 128.4 (Ph C-2,6), 126.2 (Ph C-4), 73.0 (<u>C</u>HC=O), 46.7 (<u>C</u>HCH_3), 45.7 (Adam C-1), 45.3 (<u>C</u>HCH_3), 38.4 (Adam C-2,8,9), 36.4 (Adam C-4,6,10), 33.0 (<u>C</u>H_2CH), 32.1 (Ph<u>C</u>H_2), 27.9 (Adam C-3,5,7), 21.9 (<u>C</u>H_3 br), 21.4 (<u>C</u>H_3 br), 20.5 (br, 2×<u>C</u>H_3).

HRMS (ESI), *m/z*: calcd. for $C_{27}H_{40}NO_3$ 426.3003$[M+H]^+$; found 426.3004.

$[\alpha]_D$ -30 (*c* 0.5, $CHCl_3$).

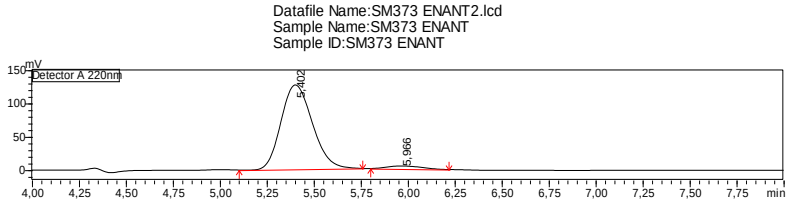
HPLC analysis: Chiralpak IG Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 95/5. Flow: 1 mL/min

Racemate



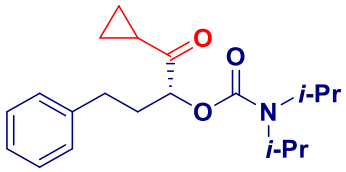
Peaks	Retention time (min)	Area	Area%
1	5,404	1858480	49,114
2	5,960	1925501	50,886
Total		3783980	100,000

***Enantioenriched* (*R*)-15**



Peaks	Retention time (min)	Area	Area%
1	5,402	1468079	96,404
2	5,966	54762	3,596
Total		1522841	100,000

(*R*)-1-Cyclopropyl-1-oxo-4-phenyl-2-butanyl diisopropylcarbamate, ((*R*)-16)



Synthesized according to **GP1** using **1** (0.077 g, 0.294 mmol, 1.5 equiv); (-)-sparteine (0.073 g, 0.313 mmol, 1.6 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and *N*-methoxy-*N*-methylcyclopropanecarboxamide (0.025g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*)-16** was obtained by chromatography purification on silica gel (pentane/CPME 95:5) in 80% yield (0.052 g) as an oil. Reaction run with (-)-sparteine recovered from preparation of **(*R*)-15.**

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (m, 2H, Ph H-3,5), 7.21 (m, 1H, Ph H-4), 7.20 (m, 2H, Ph H-2,6), 5.77 (m, 1H, C<u>H</u>C=O), 4.07 (br s, 1H, C<u>H</u>CH_3), 3.86 (br s, 1H, C<u>H</u>CH_3), 2.82-2.71 (m, 2H, Ph$C\underline{H}_2$), 2.24-2.06 (m, 2H, $C\underline{H}_2CH$), 1.96-2.03 (m, 1H, Cycprop H-1), 1.40-1.18 (br, 3H, CH_3), 1.15-1.10 (m, 1H, Cycprop H-2), 1.06-0.99 (m, 1H, Cycprop H-3), 0.95-0.88 (m, 2H, Cycprop H-2,3).

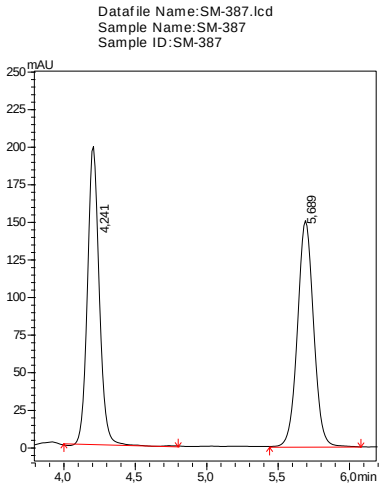
^{13}C NMR (100 MHz, $CDCl_3$): δ 208.0 (<u>C</u>=O), 154.8 (N<u>C</u>=O), 141.0 (Ph C-1), 128.5 (Ph C-3,5), 128.3 (Ph C-2,6), 126.1 (Ph C-4), 78.7 (<u>C</u>HC=O), 46.7 (<u>C</u>HCH_3), 45.6 (<u>C</u>HCH_3), 32.7 ($\underline{C}H_2CH$), 31.9 (Ph$\underline{C}H_2$), 21.8 (br, <u>C</u>H_3), 21.5 (br, <u>C</u>H_3), 20.5 (br, 2×<u>C</u>H_3), 17.0 (Cycprop C-1), 11.4 (Cycprop C-3), 11.0 (Cycprop C-2).

HRMS (ESI), *m/z*: calcd. for $C_{20}H_{30}NO_3$ 332.2220 $[M+H]^+$; found 332.2222.

[α]$_D$ -28 (*c* 0.5, $CHCl_3$).

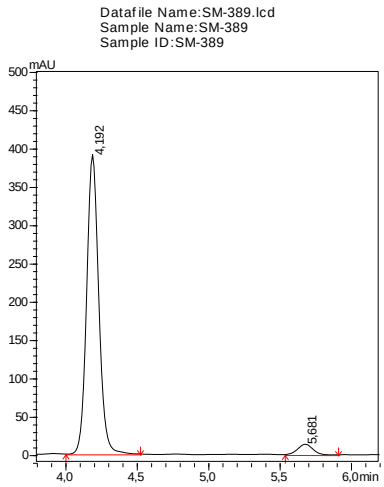
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 1 mL/min

Racemate



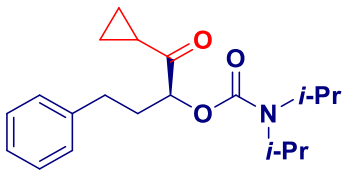
Peaks	Retention time (min)	Area	Area%
1	4,241	1121284	48,987
2	5,689	1167639	51,013
Total		2288923	100,000

***Enantioenriched* (*R*)-16**



Peaks	Retention time (min)	Area	Area%
1	4,192	2321047	95,964
2	5,681	97623	4,036
Total		2418670	100,000

(*S*)-1-Cyclopropyl-1-oxo-4-phenyl-2-butanyl diisopropylcarbamate, ((*S*)-16)

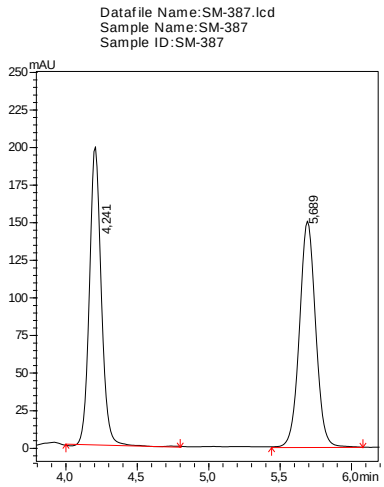


Synthesized according to **GP1** using **1** (0.077 g, 0.294 mmol, 1.5 equiv); (+)-sparteine (0.073 g, 0.313 mmol, 1.6 equiv); s-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and *N*-methoxy-*N*-methylcyclopropanecarboxamide (0.025 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*S*)-16** was obtained by chromatography purification on silica gel (pentane/CPME 95:5) in 88% yield (0.057 g) as an oil.

$[\alpha]_D$ +14 (*c* 0.5, $CHCl_3$).

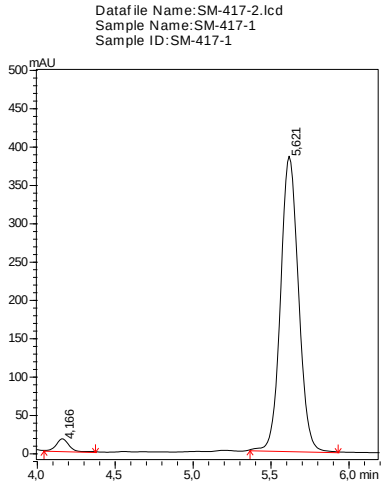
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 1 mL/min

Racemate



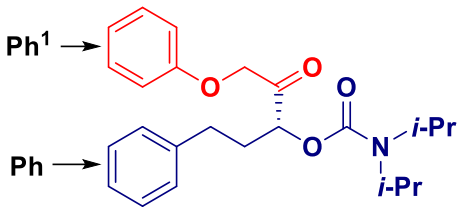
Peaks	Retention time (min)	Area	Area%
1	4,241	1121284	48,987
2	5,689	1167639	51,013
Total		2288923	100,000

***Enantioenriched* (*S*)-16**



Peaks	Retention time (min)	Area	Area%
1	4,166	80762	97,420
2	5,621	3049329	2,580
Total		3130090	100,000

(*R*)-2-Oxo-1-phenoxy-5-phenyl-3-pentanyl diisopropylcarbamate, ((*R*)-17)



Synthesized according to **GP1** using **1** (0.077 g, 0.294 mmol, 1.5 equiv); (-)-sparteine (0.073 g, 0.313 mmol, 1.6 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and *N*-methoxy-*N*-methyl-2-phenoxyacetamide (0.038 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*)-17** was obtained in 79% yield (0.061 g) as a white solid; mp 62-65 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (m, 2H, Ph H-3,5), 7.28 (m, 2H, Ph^1 H-3,5), 7.22 (m, 1H, Ph H-4), 7.18 (m, 2H, Ph H-2,6), 6.98 (m, 1H, Ph^1 H-4), 6.87 (m, 2H, Ph^1 H-2,6), 5.29 (dd, *J* = 8.5 Hz, 4.1 Hz, 1H, C<u>H</u>C=O), 4.76 (s, 2H, C<u>H</u>$_2$O), 4.03 (br s, 1H, C<u>H</u>CH$_3$), 3.88 (br s, 1H, C<u>H</u>CH$_3$), 2.73-2.88 (m, 2H, PhC<u>H</u>$_2$), 2.08-2.26 (m, 2H, C<u>H</u>$_2$CH), 1.40-1.20 (br s, 12H, C<u>H</u>$_3$).

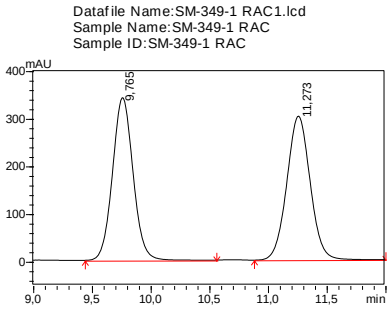
^{13}C NMR (100 MHz, $CDCl_3$): δ 203.9 ($CH_2\underline{C}$=O), 157.7 (Ph^1 C-1), 154.7 (N<u>C</u>=O), 140.5 (Ph C-1), 129.5 (Ph^1 C-3,5), 128.6 (Ph C-3,5), 128.4 (Ph C-2,6), 126.3 (Ph C-4), 121.6 (Ph^1 C-4), 114.5 (Ph^1 C-2,6), 76.0 (<u>C</u>HC=O), 70.9 (<u>C</u>H$_2$O), 46.8 (<u>C</u>HCH$_3$), 45.8 (<u>C</u>HCH$_3$), 32.3 (<u>C</u>H$_2$CH), 31.8 (Ph<u>C</u>H$_2$), 21.7 (<u>C</u>H$_3$ br), 21.4 (<u>C</u>H$_3$ br), 20.5 (2×<u>C</u>H$_3$, br).

HRMS (ESI), *m/z*: calcd. for $C_{24}H_{32}NO_4$ 398.2326 $[M+H]^+$; found 398.2328.

$[\alpha]_D$ -11 (*c* 0.5, $CHCl_3$).

HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 0.5 mL/min

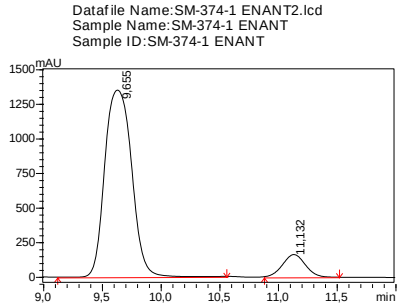
Racemate



Peaks	Retention time (min)	Area	Area%
1	9,765	4146476	49,914

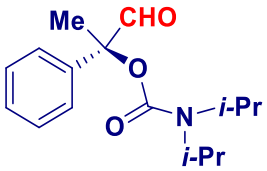
2	11,273	4160751	50,086
Total		8307227	100,000

***Enantioenriched* (*R*)-17**



Peaks	Retention time (min)	Area	Area%
1	9,655	21423564	90,818
2	11,132	2166087	9,182
Total		23589651	100,000

(*R*)-1-Oxo-2-phenyl-2-propanyl diisopropylcarbamate, ((*R*)-19)



Synthesized according to **GP2** using **(*R*)-18** (0.073 g, 0.294 mmol, 1.5 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and *N*-methoxy-*N*-methylformamide (0.017 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*)-19** was obtained in 75% yield (0.041 g) as a white solid; mp 100-103 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.47 (s, 1H, CHO), 7.46 (m, 2H, Ph H-2,6), 7.40 (m, 2H, Ph H-3,5), 7.33 (m, 1H, Ph H-4), 4.01 (sept, *J* = 6.9 Hz, 2H, C<u>H</u>CH_3), 1.84 (s, 3H, CH_3), 1.33 (br s,6H, CHC<u>H</u>$_3$), 1.27 (br, 6H, CHC<u>H</u>$_3$).

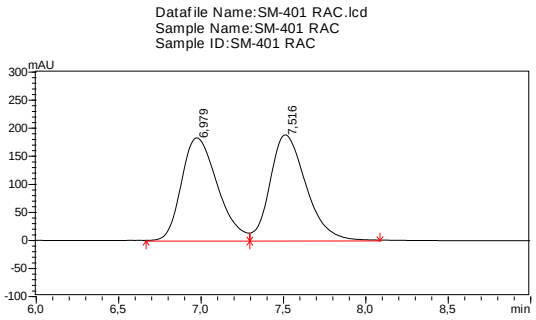
^{13}C NMR (100 MHz, $CDCl_3$): δ 194.3 (<u>C</u>HO), 154.1 (N<u>C</u>=O), 137.1 (Ph C-1), 128.7 (Ph C-3,5), 128.2 (Ph C-4), 125.8 (Ph C-2,6), 85.3 (Ph<u>C</u>), 46.8 (<u>C</u>HCH_3), 46.2 (<u>C</u>HCH_3), 21.6 (CH<u>C</u>H$_3$), 21.4 (CH<u>C</u>H$_3$), 21.2 (CH_3), 20.5 (CH<u>C</u>H$_3$), 20.3 (CH<u>C</u>H$_3$).

HRMS (ESI), *m/z*: calcd. for $C_{16}H_{23}NNaO_3$ 300.1570$[M+Na]^+$; found 300.1575.

$[\alpha]_D$ +75 (*c* 0.5, $CHCl_3$).

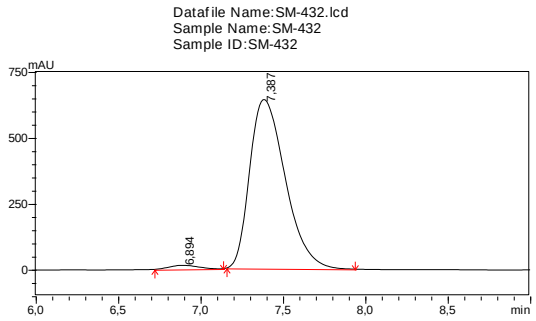
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 99/1. Flow: 1 mL/min

Racemate



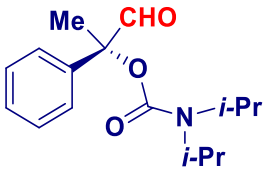
Peaks	Retention time (min)	Area	Area%
1	6,979	2757914	49,461
2	7,516	2818041	50,539
Total		5575955	100,000

***Enantioenriched* (*R*)-19**



Peaks	Retention time (min)	Area	Area%
1	6,894	165705	1,696
2	7,387	9606305	98,304
Total		9772010	100,000

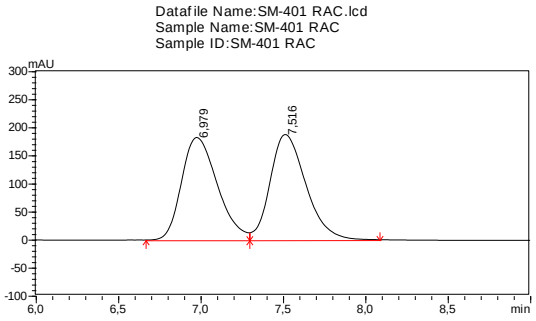
(*S*)-1-Oxo-2-phenyl-2-propanyl diisopropylcarbamate, ((*S*)-19)



Synthesized according to **GP2** using **(*S*)-18** (0.073 g, 0.294 mmol, 1.5 equiv); s-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and *N*-methoxy-*N*-methylformamide (0.017 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*S*)-19** was obtained in 95% yield (0.052g) as a white solid; mp 100-103 °C (lit. [3] 105 °C)

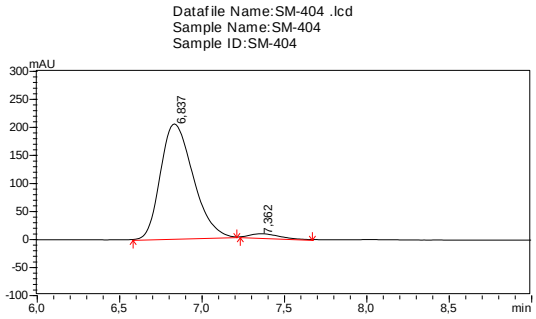
[α]$_D$ -103 (*c* 0.5, $CHCl_3$). *Lit.*[3] -116.1 (*c* 0.7, CH_2Cl_2). *Retention of configuration.*

Racemate



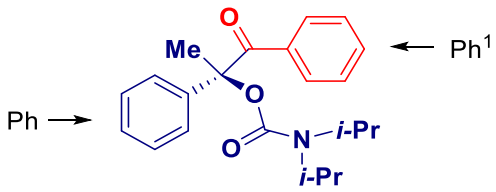
Peaks	Retention time (min)	Area	Area%
1	6,979	2757914	49,461
2	7,516	2818041	50,539
Total		5575955	100,000

***Enantioenriched* (*S*)-19**



Peaks	Retention time (min)	Area	Area%
1	6,837	2807938	97,289
2	7,362	78253	2,711
Total		2886191	100,000

(*R*)-1-Oxo-1,2-diphenyl-2-propanyl diisopropylcarbamate, ((*R*)-20)



Synthesized according to **GP2** using **(*R*)-18** (0.073 g, 0.294 mmol, 1.5 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and *N*-methoxy-*N*-methylbenzamide (0.032 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*)-20** was obtained in 98% yield (0.068 g) as a white solid; mp 95-99 °C.(lit. [3] 105 °C)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (m, 2H, Ph^1 H-2,6), 7.54 (m, 2H, Ph H-2,6), 7.39 (m, 2H, Ph H-3,5), 7.33 (m, 1H, Ph^1 H-4), 7.31 (m, 1H, Ph H-4), 7.21 (m, 2H, Ph^1 H-3,5), 4.22 (m, 1H, C<u>H</u>CH_3), 3.52 (m, 1H, C<u>H</u>CH_3), 1.98 (s, 3H, CH_3), 1.29 (d, *J* = 6.7 Hz, 3H, CHC<u>H</u>$_3$), 1.23 (d, *J* = 6.7 Hz, 3H, CHC<u>H</u>$_3$), 1.10 (d, *J* = 6.7 Hz, 3H, CHC<u>H</u>$_3$), 0.79 (d, *J* = 6.7 Hz, 3H, CHC<u>H</u>$_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ 197.3 (Ph<u>C</u>=O), 152.6 (N<u>C</u>=O), 141.2 (Ph C-1), 136.1 (Ph^1 C-1), 131.3 (Ph^1 C-4), 129.0 (Ph^1 C-2,6), 128.9 (Ph C-3,5), 127.7 (Ph C-4), 127.6 (Ph^1 C-3,5), 124.4 (Ph C-2,6), 86.6 (Ph<u>C</u>), 46.6 (<u>C</u>HCH_3), 45.8 (<u>C</u>HCH_3), 27.8 (CH_3), 21.3 (CH<u>C</u>H_3), 21.0 (CH<u>C</u>H_3), 20.5 (CH<u>C</u>H_3), 19.6 (CH<u>C</u>H_3).

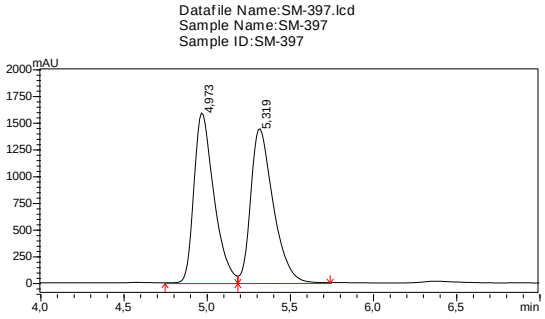
^{15}N NMR (40 MHz, $CDCl_3$): δ -267.7.

HRMS (ESI), *m/z*: calcd. for $C_{22}H_{27}NNaO_3$ 376.1883 $[M+Na]^+$; found 376.1892.

$[\alpha]_D$ +86 (*c* 0.5, $CHCl_3$). *Lit*.[3] +113 (*c* 1.1, CH_2Cl_2).

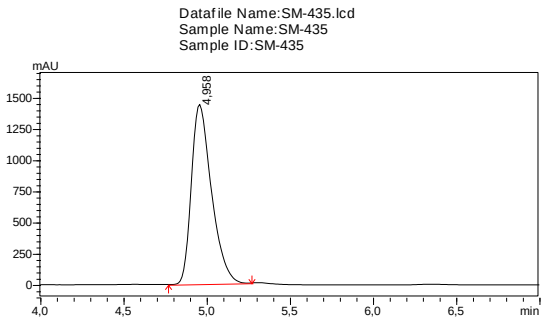
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 95/5. Flow: 1 mL/min

Racemate



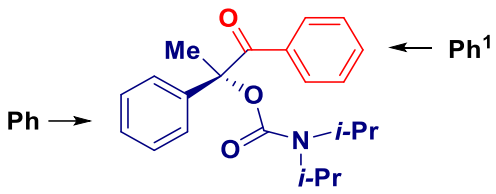
Peaks	Retention time (min)	Area	Area%
1	4,973	13268363	49,603
2	5,319	13480496	50,397
Total		26748860	100,000

***Enantioenriched* (*R*)-20**



Peaks	Retention time (min)	Area	Area%
1	4,958	12065873	100,000
Total		12065873	100,000

(*S*)-1-Oxo-1,2-diphenyl-2-propanyl diisopropylcarbamate, ((*S*)-20)

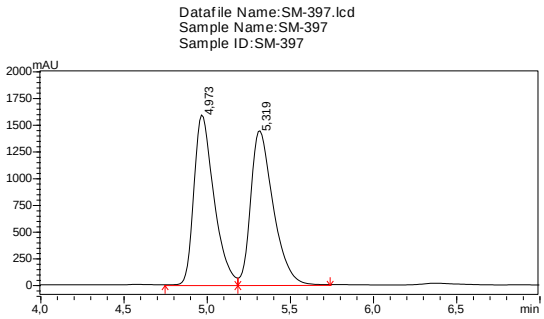


Synthesized according to **GP2** using **(*S*)-18** (0.073 g, 0.294 mmol, 1.5 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and *N*-methoxy-*N*-methylbenzamide (0.032 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*S*)-20** was obtained in 98% yield (0.068 g) as a white solid; mp 95-99 °C (lit. [3] 105 °C)

[α]$_D$ -99 (*c* 0.5, $CHCl_3$). *Lit*.[3] -104.7 (*c* 1.1, CH_2Cl_2). *Retention of configuration*.

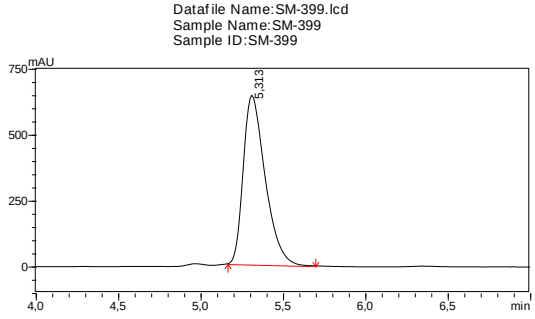
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 95/5. Flow: 1 mL/min

Racemate



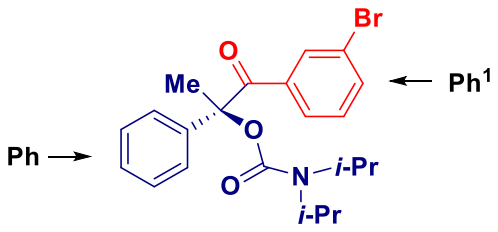
Peaks	Retention time (min)	Area	Area%
1	4,973	13268363	49,603
2	5,319	13480496	50,397
Total		26748860	100,000

***Enantioenriched* (*S*)-20**



Peaks	Retention time (min)	Area	Area%
1	5,313	5905695	100,000
Total		5905695	100,000

(*R*)-1-(3-Bromophenyl)-1- oxo-2-phenyl-2-propanyl diisopropylcarbamate, ((*R*)-21)



Synthesized according to **GP2** using **(*R*)-18** (0.073 g, 0.294 mmol, 1.5 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and 3-bromo-*N*-methoxy-*N*-methylbenzamide (0.048 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*)-21** was obtained in 95% yield (0.080 g) as a white solid; mp 94-98 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (m, 1H, Ph^1 H-2), 7.64 (m, 1H, Ph^1 H-6), 7.51 (m, 2H, Ph H-2,6), 7.46 (m, 1H, Ph^1 H-4), 7.40 (m, 2H, Ph H-3,5), 7.32 (m, 1H, Ph H-4), 7.11 (m, 2H, Ph^1 H-5), 4.21 (br sept, 1H, C<u>H</u>CH$_3$), 3.57 (br sept, 1H, C<u>H</u>CH$_3$), 1.97 (s, 3H, CH$_3$), 1.32 (d, *J*= 6.7 Hz, 3H, CHC<u>H</u>$_3$), 1.28 (d, *J* = 6.8 Hz, 3H, CHC<u>H</u>$_3$), 1.12 (d, *J* = 6.7 Hz, 3H, CHC<u>H</u>$_3$), 0.85 (d, *J* = 6.7 Hz, 3H, CHC<u>H</u>$_3$).

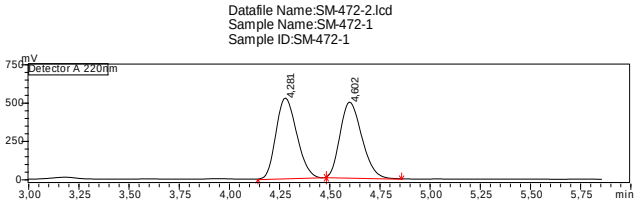
^{13}C NMR (100 MHz, $CDCl_3$): δ 195.7 (Ph<u>C</u>=O), 152.6 (N<u>C</u>=O), 140.5 (Ph C-1), 137.8 (Ph^1 C-1), 134.2 (Ph^1 C-4), 131.9 (Ph^1 C-2), 129.3 (Ph^1 C-5), 129.0 (Ph C-3,5), 127.9 (Ph C-4), 127.5 (Ph^1 C-6), 124.4 (Ph C-2,6), 121.7 (Ph^1 C-3), 86.6 (Ph<u>C</u>), 46.7 (<u>C</u>HCH$_3$), 46.0 (<u>C</u>HCH$_3$), 27.6 (CH$_3$), 21.4, 21.2, 20.5, 19.7 (4×CH<u>C</u>H$_3$).

HRMS (ESI), *m/z*: calcd. for $C_{22}H_{26}BrNNaO_3$ 454.0988[M+Na]$^+$; found 454.0997.

[α]$_D$ +55 (*c* 0.5, $CHCl_3$).

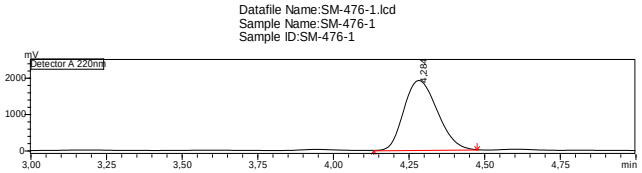
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 90/10. Flow: 1 mL/min

Racemate



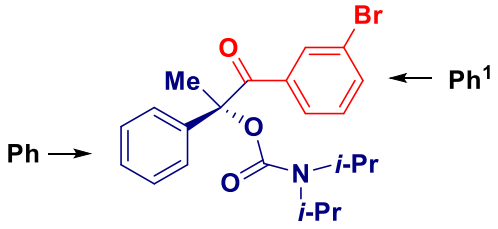
Peak	Retention time (min)	Area	Area%
1	4,281	3745557	50,283
2	4,602	3703466	49,717
tot		7449023	100,000

***Enantioenriched* (*R*)-21**



Peak	Retention time (min)	Area	Area%
1	4,284	14722873	100,000
tot		14722873	100,000

(*S*)-1-(3-Bromophenyl)-1- oxo-2-phenyl-2-propanyl diisopropylcarbamate, ((*S*)-21)

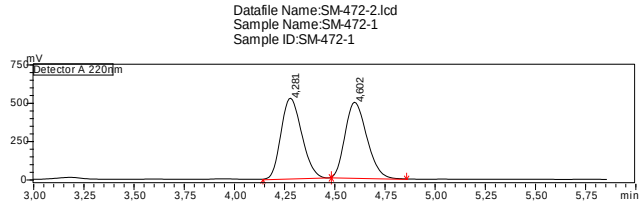


Synthesized according to **GP2** using **(*S*)-18** (0.073 g, 0.294 mmol, 1.5 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and 3-bromo-*N*-methoxy-*N*-methylbenzamide (0.048 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*S*)-21** was obtained in 95% yield (0.080 g) as a white solid; mp 94-98 °C.

[α]$_D$ -78 (*c* 0.5, $CHCl_3$).

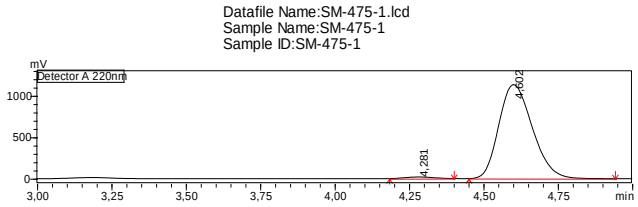
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 90/10. Flow: 1 mL/min

Racemate



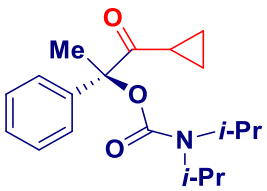
Peak	Retention time (min)	Area	Area%
1	4,281	3745557	50,283
2	4,602	3703466	49,717
tot		7449023	100,000

***Enantioenriched* (*S*)-21**



Peak	Retention time (min)	Area	Area%
1	4,281	125956	1,399
2	4,602	8874975	98,601
tot		9000931	100,000

(*R*)-1-Cyclopropyl-1-oxo-2-phenyl-2-propanyl diisopropylcarbamate, ((*R*)-22)



Synthesized according to **GP2** using **(*R*)-18** (0.073 g, 0.294 mmol, 1.5 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and *N*-methoxy-*N*-methylcyclopropanecarboxamide (0.025 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*)-22** was obtained in 80% yield (0.050 g) as a white solid; mp 100-102 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (m, 2H, Ph H-2,6),7.37 (m, 2H, Ph H-3,5), 7.30 (m, 1H, Ph H-4), 4.20 (br m, 1H, C<u>H</u>CH_3), 3.89 (br m,1H, C<u>H</u>CH_3), 1.93 (m, 1H, Cycprop C-1), 1.86 (s, 3H, CH_3), 1.35 (br s, 6H, CHC<u>H</u>$_3$), 1.29 (br s, 6H, CHC<u>H</u>$_3$), 1.08 (m, 1H, Cycprop H-2), 0.86 (m, 1H, Cycprop H-3), 0.80 (m, 1H, Cycprop H-2), 0.59 (m, 1H, Cycprop H-3).

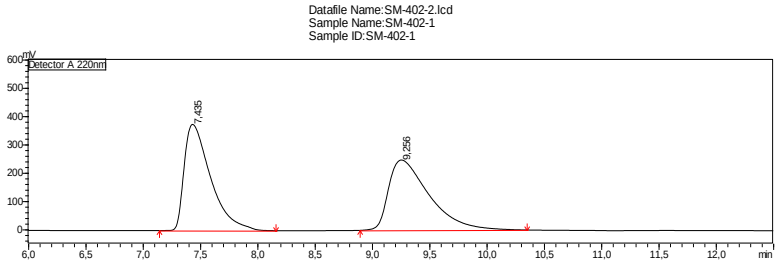
^{13}C NMR (100 MHz, $CDCl_3$): δ 206.6 (<u>C</u>=O), 153.3 (N<u>C</u>=O), 140.4 (Ph C-1), 128.5 (Ph C-3,5), 127.1 (Ph C-4), 125.1 (Ph C-2,6), 87.0 (Ph<u>C</u>), 46.4 (<u>C</u>HCH_3), 46.3 (<u>C</u>HCH_3), 24.3 (CH_3), 21.4 (CH<u>C</u>H$_3$ 2x), 20.6 (CH<u>C</u>H$_3$), 20.4 (CH<u>C</u>H$_3$), 16.0 (Cycprop C-1), 11.8 (Cycprop C-3), 10.9 (Cycprop C-2).

HRMS (ESI), *m/z*: calcd. for $C_{19}H_{28}NO_3$ 318.2064$[M+H]^+$; found 318.2069.

$[\alpha]_D$ +93 (*c* 0.5, $CHCl_3$).

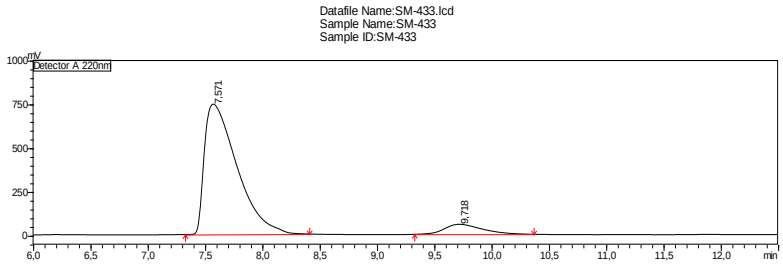
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-heptane / *MTBE* 80/20. Flow: 1 mL/min

Racemate



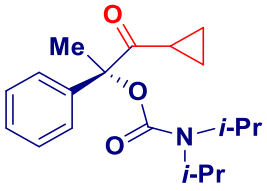
Peaks	Retention time (min)	Area	Area%
1	7,435	6023582	49,660
2	9,256	6106021	50,340
Total		12129604	100,000

***Enantioenriched* (*R*)-22**



Peaks	Retention time (min)	Area	Area%
1	7,571	14716518	91,831
2	9,718	1309054	8,169
Total		16025572	100,000

(*S*)-1-Cyclopropyl-1-oxo-2-phenyl-2-propanyl diisopropylcarbamate, ((*S*)-22)

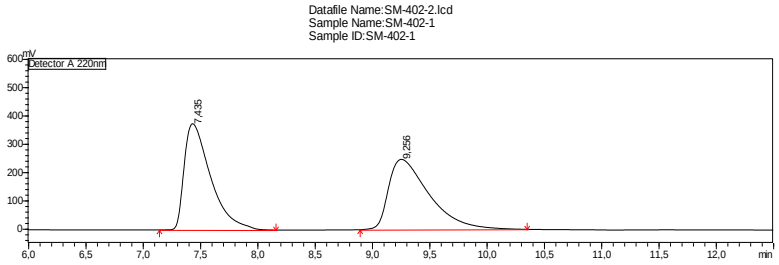


Synthesized according to **GP2** using **(*S*)-18** (0.073 g, 0.294 mmol, 1.5 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and *N*-methoxy-*N*-methylcyclopropanecarboxamide (0.025 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*S*)-22** was obtained in 78% yield (0.048 g) as a white solid; mp 100-102 °C.

$[\alpha]_D$ -85 (*c* 0.5, $CHCl_3$).

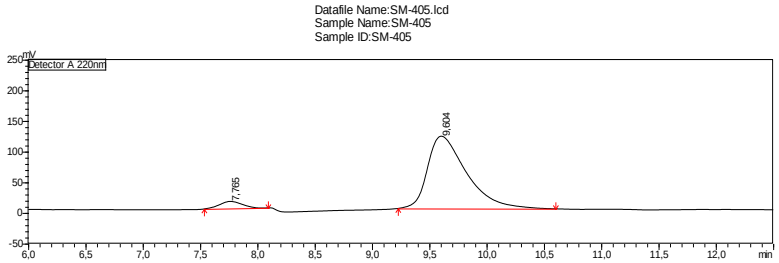
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-heptane / MTBE 80/20. Flow: 1 mL/min

Racemate



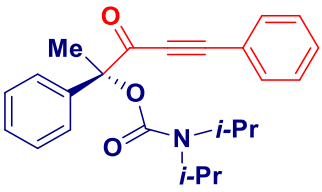
Peaks	Retention time (min)	Area	Area%
1	7,435	6023582	49,660
2	9,256	6106021	50,340
Total		12129604	100,000

***Enantioenriched* (*S*)-22**



Peaks	Retention time (min)	Area	Area%
1	7,765	157785	5,357
2	9,604	2787352	94,643
Total		2945138	100,000

(*S*)-1-Oxo-1,2-diphenyl-2-propanyl diisopropylcarbamate, ((*S*)-23)



Synthesized according to **GP2** using **(*R*)-18** (0.073 g, 0.294 mmol, 1.5 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and *N*-methoxy-*N*-methyl-3-phenyl-2-propynamide (0.037 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*S*)-23** was obtained in 93% yield (0.069 g) as a white solid; mp 96-99 °C.

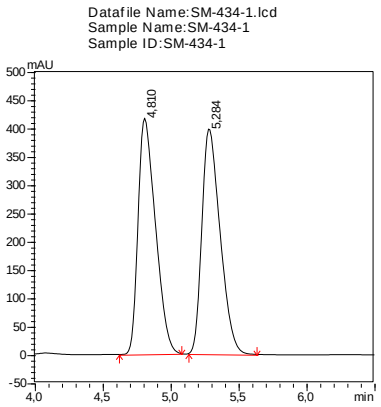
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (m, 2H, Ph H-2,6), 7.42 (m, 2H, Ph^1 H-2,6), 7.40 (m, 2H, Ph H-3,5), 7.38 (m, 1H, Ph^1 H-4), 7.32 (m, 1H, Ph H-4), 7.31 (m, 2H, Ph^1 H-3,5), 4.13 (br m, 1H, C<u>H</u>CH_3), 3.96 (br m, 1H, C<u>H</u>CH_3), 2.01 (s, 3H, CH_3), 1.37 (m, 6H, CH<u>C</u>H_3), 1.25 (m, 3H, CH<u>C</u>H_3), 1.24 (m, 3H, CH<u>C</u>H_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ 184.1 (Ph<u>C</u>=O), 153.6 (N<u>C</u>=O), 138.8 (Ph C-1), 132.6 (Ph^1 C-2,6), 130.2 (Ph^1 C-4), 128.6 (Ph C-3,5), 128.4 (Ph^1 C-3,5), 128.1 (Ph C-4), 125.6 (Ph C-2,6), 120.4 (Ph^1 C-1), 91.9 (Ph<u>C</u>≡C), 86.4 (CH_3-<u>C</u>), 85.6 (PhC≡<u>C</u>), 46.5 (<u>C</u>HCH_3), 46.2 (<u>C</u>HCH_3), 23.27 (CH_3), 21.4 (2×CH<u>C</u>H_3), 20.8 (CH<u>C</u>H_3), 20.4 (CH<u>C</u>H_3).

HRMS (ESI), *m/z*: calcd. for $C_{19}H_{28}NO_3$ 378.2064 $[M+H]^+$; found 378.2066.

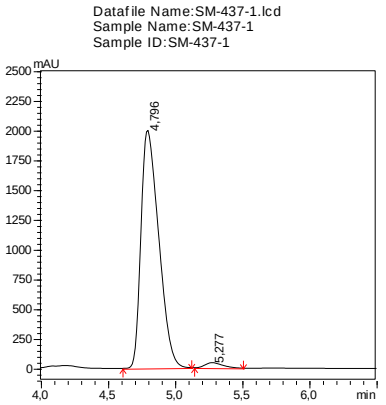
$[\alpha]_D$ -73 (*c* 0.5, $CHCl_3$). *Inversion of configuration*. The absolute configuration has been assigned based on the crystal structure of **(*S,S*)-24** togheter with the trend observed in signs of optical rotation of **19**, **20**, **21** and **22**.

Racemate



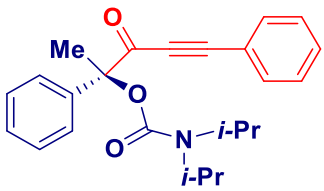
Peaks	Retention time (min)	Area	Area%
1	4,810	3704234	49,979
2	5,284	3707346	50,021
Total		7411580	100,000

***Enantioenriched* (*S*)-23**



Peaks	Retention time (min)	Area	Area%
1	4,796	18384539	97,925
2	5,277	389507	2,075
total		18774046	100,000

(*R*)-1-Oxo-1,2-diphenyl-2-propanyl diisopropylcarbamate, ((*R*)-23)

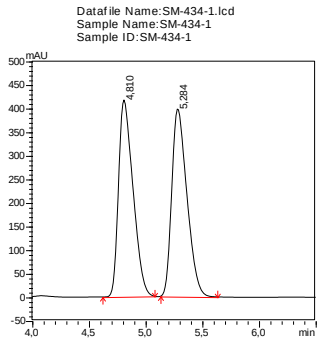


Synthesized according to **GP2** using **(*S*)-18** (0.073 g, 0.294 mmol, 1.5 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and *N*-methoxy-*N*-methyl-3-phenyl-2-propynamide (0.037 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*)-23** was obtained in 90% yield (0.067 g) as a white solid; mp 96-99 °C.

$[\alpha]_D$ +94 (*c* 0.5, $CHCl_3$). *Inversion of configuration.* The absolute configuration has been assigned based on the crystal structure of **(*R*,*R*)-24** togheter with the trend observed in signs of optical rotation of **19**, **20**, **21** and **22**.

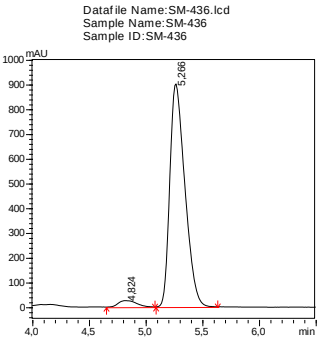
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 1 mL/min

Racemate



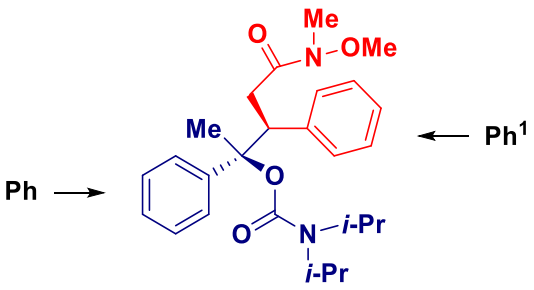
Peaks	Retention time (min)	Area	Area%
1	4,810	3704234	49,979
2	5,284	3707346	50,021
total		7411580	100,000

***Enantioenriched* (*R*)-23**



Peaks	Retention time (min)	Area	Area%
1	4,824	281017	3,258
2	5,266	8343898	96,742
total		8624915	100,000

(2*S*,3*S*)-5-[Methoxy(methyl)amino]-5-oxo-2,3-diphenyl-2-pentanyl diisopropylcarbamate, ((*S*,*S*)-24)



Synthesized according to **GP2** using **(*R*)-18** (0.073 g, 0.294 mmol, 1.5 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and (2*E*)-*N*-methoxy-*N*-methyl-3-phenylacrylamide (0.037 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*S*,*S*)-24** was obtained in 98% yield (0.085 g) as a white solid; mp 110-115 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (m, 2H, Ph H-3,5), 7.20 (m, 1H, Ph H-4), 7.19 (m, 1H, Ph^1 H-4), 7.18 (m, 4H, Ph^1 H-3,5; Ph H-2,6), 7.06 (m, 2H, Ph^1 H-2,6), 4.15 (br s, 1H, C<u>H</u>CH_3), 3.81 (dd, 1H, *J* = 11.3 Hz, 3.4 Hz, C<u>H</u>Ph^1), 3.58 (br s, 1H, C<u>H</u>CH_3), 3.49 (s, 3H, OCH_3), 2.96 (dd, 1H, *J* = 15.8 Hz, 11.3 Hz, CH_2C=O), 2.95 (s, 3H, NCH_3), 2.67 (dd, 1H, *J* = 15.8 Hz, 3.4 Hz, CH_2C=O), 1.96 (s, 3H, CH_3), 1.16-1.18 (br, 12H, CH(<u>C</u>H_3)$_2$).

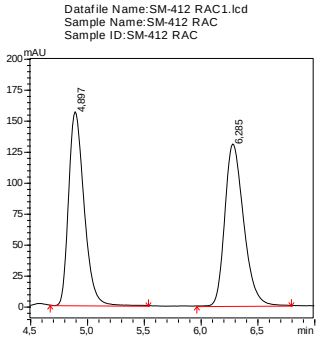
^{13}C NMR (100 MHz, $CDCl_3$): δ 172.4 (CH_2<u>C</u>=O), 152.9 (N<u>C</u>=O), 143.9 (Ph C-1), 139.6 (Ph^1 C-1), 130.2 (Ph^1 C-2,6), 127.6 (Ph C-3,5), 127.4 (Ph^1 C-3,5), 126.7 (Ph C-4; Ph^1 C-4), 125.7 (Ph C-2,6), 84.4 (Ph-<u>C</u>), 61.0 (O<u>C</u>H_3), 53.1 (Ph^1<u>C</u>H), 46.3 (<u>C</u>HCH_3), 45.2 (<u>C</u>HCH_3), 32.7 (<u>C</u>H_2C=O), 32.0 (N<u>C</u>H_3), 22.3 (C<u>C</u>H_3), 21.1 (2×<u>C</u>H_3), 20.7 (<u>C</u>H_3), 20.5 (<u>C</u>H_3).

HRMS (ESI), *m/z*: calcd. for $C_{26}H_{36}N_2NaO_4$ 463.2567 $[M+Na]^+$; found 463.2571.

[α]$_D$ +12 (*c* 0.5, $CHCl_3$). *Inversion of configuration*

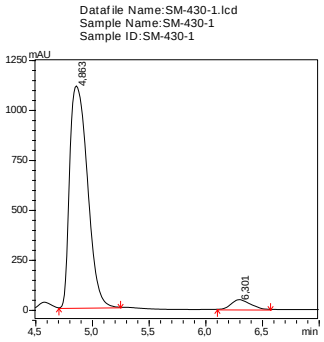
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 1 mL/min

Diastereoisomeric mixture



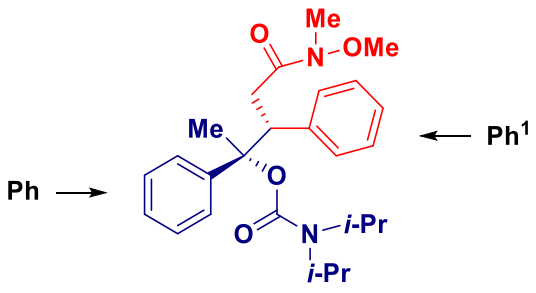
Peaks	Retention time (min)	Area	Area%
1	4,897	1466979	49,441
2	6,285	1500171	50,559
Total		2967151	100,000

***Diasteroisomer* (*S*,*S*)-24**



Peaks	Retention time (min)	Area	Area%
1	4,863	12125322	95,636
2	6,301	553349	4,364
Total		12678671	100,000

(2*R*,3*R*)-5-[Methoxy(methyl)amino]-5-oxo-2,3-diphenyl-2-pentanyl diisopropylcarbamate, ((*R*,*R*)-24)

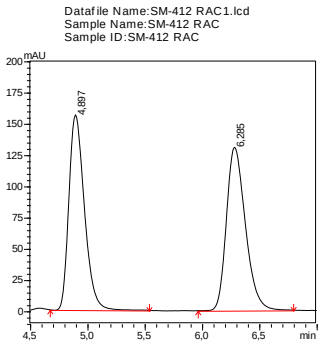


Synthesized according to **GP2** using **(*S*)-18** (0.073 g, 0.294 mmol, 1.5 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and (2*E*)-*N*-methoxy-*N*-methyl-3-phenylacrylamide (0.037 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*,*R*)-24** was obtained in 98% yield (0.085 g) as a white solid; mp 115-118 °C.

[α]$_D$ -6 (*c* 0.5, $CHCl_3$).

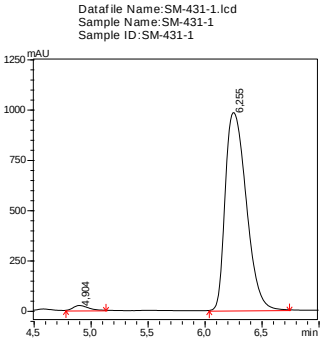
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 1 mL/min

Diastereoisomeric mixture



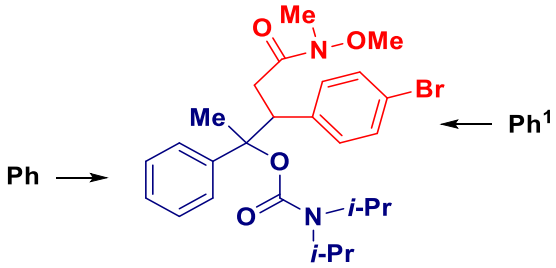
Peaks	Retention time (min)	Area	Area%
1	4,897	1466979	49,441
2	6,285	1500171	50,559
Total		2967151	100,000

***Diasteroisomer* (*R*,*R*)-24**



Peaks	Retention time (min)	Area	Area%
1	4,904	213573	1,665
2	6,255	12614540	98,335
Total		12828113	100,000

(2*S*,3*S*)-3-(4-Bromophenyl)-5-[methoxy(methyl)amino]-5-oxo-2-phenyl-2-pentanyl diisopropylcarbamate, ((*S*,*S*)-25)



Synthesized according to **GP2** using **(*R*)-18** (0.073 g, 0.294 mmol, 1.5 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and (2*E*)-3-(4-bromophenyl)-*N*-methoxy-*N*-methylacrylamide (0.053 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*S*,*S*)-25** was obtained in 98% yield (0.100g) as a white solid; mp 122-140 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (m, 2H, Ph^1 H-3,5), 7.26 (m, 2H, Ph H-3,5), 7.20 (m, 1H, Ph H-4), 7.14 (m, 2H, Ph H-2,6), 6.90 (m, 2H, Ph^1 H-2,6), 4.14 (br s, 1H, C<u>H</u>CH_3), 3.77 (dd, H, *J* = 11.4 Hz, 3.3 Hz, C<u>H</u>Ph^1), 3.77 (m, 1H, C<u>H</u>$_2$C=O), 3.59 (br s, 1H, C<u>H</u>CH_3), 3.51 (s, 3H, OCH_3), 2.96 (s, 3H, NCH_3), 2.68 (dd, 1H, *J* = 16.0 Hz, 3.3 Hz, C<u>H</u>$_2$C=O), 1.94 (s, 3H, CH_3), 1.17-1.18 (br, 12H, CH(<u>C</u>H_3)$_2$).

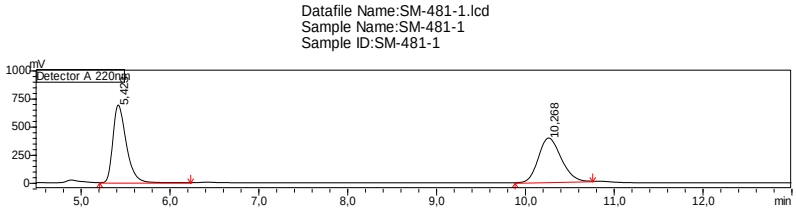
^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1 (CH_2<u>C</u>=O), 152.7 (N<u>C</u>=O), 143.5 (Ph C-1), 138.7 (Ph^1 C-1), 131.8 (Ph^1 C-2,6), 130.5 (Ph^1 C-3,5), 127.7 (Ph C-3,5), 126.8 (Ph C-4), 125.6 (Ph C-2,6), 120.7 (Ph^1 C-4), 84.6 (Ph<u>C</u>), 61.1 (O<u>C</u>H_3), 52.6 (Ph^1<u>C</u>H), 46.4 (<u>C</u>HCH_3), 45.3 (<u>C</u>HCH_3), 32.5 (<u>C</u>H_2C=O), 32.0 (N<u>C</u>H_3), 22.4 (C<u>C</u>H_3), 21.2 (2×<u>C</u>H_3), 20.7 (<u>C</u>H_3), 20.4 (<u>C</u>H_3).

HRMS (ESI), *m/z*: calcd. for $C_{26}H_{35}BrN_2NaO_4$ 541.1672[M+Na]$^+$; found 541.1664.

[α]$_D$ +56 (*c* 0.5, $CHCl_3$).

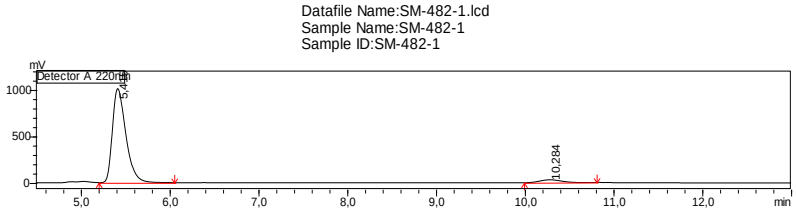
HPLC analysis: Chiralpak IA Column, λ 220 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 1 mL/min

Diastereoisomeric mixture



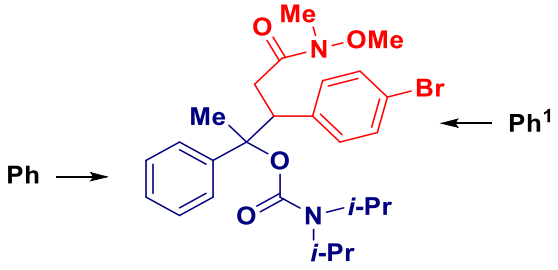
Peaks	Retention time (min)	Area	Area%
1	5,423	691695	51,012
2	10,268	391880	48,988
Total		1083574	100,000

***Diastereoisomer* (*S*,*S*)-25**



Peaks	Retention time (min)	Area	Area%
1	5,415	1011734	95,486
2	10,284	30599	4,514
Total		1042333	100,000

(2*R*,3*R*)-3-(4-Bromophenyl)-5-[methoxy(methyl)amino]-5-oxo-2-phenyl-2-pentanyl diisopropylcarbamate, ((*R*,*R*)-25)

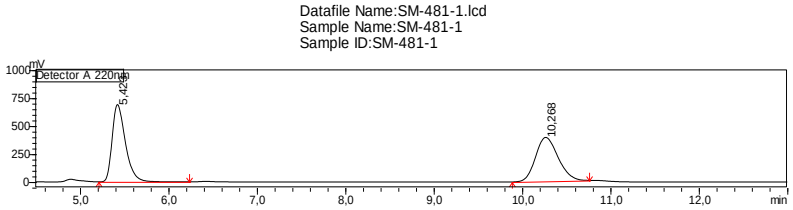


Synthesized according to **GP2** using **(*S*)-18** (0.073 g, 0.294 mmol, 1.5 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and (2*E*)-3-(4-bromophenyl)-*N*-methoxy-*N*-methylacrylamide (0.053 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*,*R*)-25** was obtained in 98% yield (0.100 g) as a white solid; mp 122-140 °C.

[α]$_D$ -18 (*c* 0.5, $CHCl_3$)

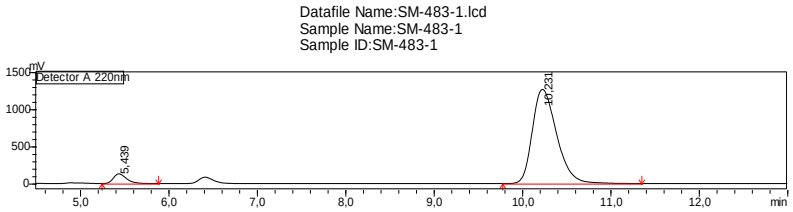
HPLC analysis: Chiralpak IA Column, λ 220 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 1 mL/min

Diastereoisomeric mixture



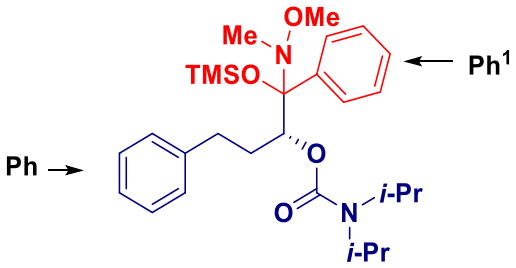
Peaks	Retention time (min)	Area	Area%
1	5,423	691695	51,012
2	10,268	391880	48,988
Total		1083574	100,000

***Diastereoisomer* (*R*,*R*)-25**



Peaks	Retention time (min)	Area	Area%
1	5,439	130421	5,299
2	10,231	1265716	94,701
Total		1396136	100,000

(2*R*)-1-[Methoxy(methyl)amino]-1,4-diphenyl-1-[(trimethylsilyl)oxy]-2-butanyldiisopropyl carbamate, (27)



By following the **GP1**, a solution of **1** (0.200 g, 0.76 mmol, 1.5 equiv) and (-)-sparteine (0.190 g, 0.811 mmol, 1.6 equiv) was cooled at -78 °C under argon in CPME (4 mL). A solution of *s*-BuLi (1.3 M, 0.62 mL, 0.811 mmol, 1.6 equiv) was added dropwise; the reaction mixture was stirred for 30 min, then *N*-methoxy-*N*-methylbenzamide (0.083 g, 0.506 mmol, 1.0 equiv) in CPME was added slowly; After 2 hours a solution of Im-TMS (1-(trimethylsilyl)imidazole) (0.107 g, 0.76 mmol, 1.5 equiv) was added and the reaction mixture was allowed to reach room temperature over 2 hours and then quenched with $NaHCO_3$ 5% solution (5 mL). The crude was purified by chromatography on allumina III grade (hexane/AcOEt) to obtain the pure product as mixture of two stereoisomers. Compound **27** was obtained in 55% yield (0.139 g) as transparent oil.

Major diastereoisomers:

^{1}H NMR (400 MHz, C_6D_6): δ 7.81 (m, 1H, Ph^1 H-2), 7.63 (m, 1H, Ar), 7.30-6.95 (m, 8H, Ar), 5.88 (m, 1H, C<u>H</u>CH_2), 3.98 (m, 1H, C<u>H</u>CH_3), 3.39 (m, 1H, C<u>H</u>CH_3), 3.17 (s, 3H, O<u>C</u>H_3), 2.80 (m, 1H, Ph<u>C</u>H_2), 2.71 (m, 1H, Ph<u>C</u>H_2), 2.39 (m, 1H, <u>C</u>H_2CH), 2.30 (s, 3H, N<u>C</u>H_3), 1.78 (m, 1H, <u>C</u>H_2CH), 1.45-0.76 (m, 12H, CH<u>C</u>H_3), 0.49 (s, 9H, Si(<u>C</u>$H_3)_3$).

^{13}C NMR (100 MHz, C_6D_6): δ 154.4 (N<u>C</u>=O), 143.0 (Ph C-1), 141.3 (Ph^1 C-1), 129.2 (Ar), 128.7 (Ar), 128.34 (Ar), 127.2 (Ar), 126.1 (Ph C-4), 128.7 (Ph^1 C-2), 97.7 (<u>C</u>OTMS), 76.8 (<u>C</u>HCH_2), 58.4 (O<u>C</u>H_3), 46.1 (<u>C</u>HCH_3), 45.4 (<u>C</u>HCH_3), 36.1 (N<u>C</u>H_3), 35.3 (<u>C</u>H_2CH), 33.0 (Ph<u>C</u>H_2), 21.1, 21.0, 20.8 (CH(<u>C</u>$H_3)_2$), 2.92 (Si(<u>C</u>$H_3)_3$).

^{15}N NMR (40 MHz, $CDCl_3$): δ -212.0.

Minor diastereoisomers:

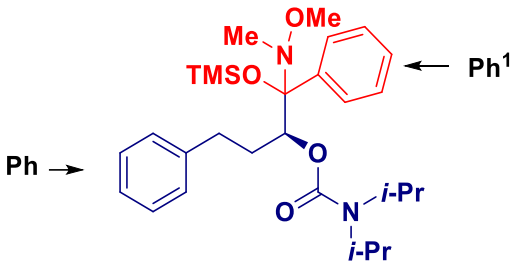
^{1}H NMR (400 MHz, C_6D_6): δ 7.86 (m, 1H, Ar), 7.63 (m, 1H, Ar), 7.30-6.95 (m, 8H, Ar), 6.05 (m, 1H, C<u>H</u>CH_2), 4.37 (m, 1H, C<u>H</u>CH_3), 3.39 (m, 1H, C<u>H</u>CH_3), 3.55 (s, 3H, O<u>C</u>H_3), 2.82 (m, 1H, Ph<u>C</u>H_2), 2.61 (m, 1H, Ph<u>C</u>H_2), 2.37 (s, 3H, N<u>C</u>H_3), 2.23 (m, 1H, <u>C</u>H_2CH), 1.50 (m, 1H, <u>C</u>H_2CH), 1.45-0.76 (m, 12H, CH<u>C</u>H_3), 0.37 (s, 9H, Si(<u>C</u>$H_3)_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ 154.1 (N<u>C</u>=O), 142.8 (Ph C-1), 141.2 (Ph^1 C-1), 129.0 (Ar), 128.8 (Ar), 127.9 (Ar), 127.5 (Ar), 126.0 (Ph C-4), 97.3 (<u>C</u>OTMS), 73.6 (<u>C</u>HCH$_2$), 59.2 (O<u>C</u>H$_3$), 46.6 (<u>C</u>HCH$_3$), 45.3 (<u>C</u>HCH$_3$), 36.3 (N<u>C</u>H$_3$), 34.8 (<u>C</u>H$_2$CH), 32.8 (Ph<u>C</u>H$_2$), 21.1, 21.0, 20.8 (CH(<u>C</u>H$_3$)$_2$), 2.86 (Si(<u>C</u>H$_3$)$_3$).

^{15}N NMR (40 MHz, $CDCl_3$): δ -212.1.

HRMS (ESI), *m/z*: calcd. for $C_{28}H_{44}N_2NaO_4Si$ 523.2963 $[M+Na]^+$; found 523.2974.

(2*S*)-1-[Methoxy(methyl)amino]-1,4-diphenyl-1-[(trimethylsilyl)oxy]-2-butanyl diisopropylcarbamate, (28)

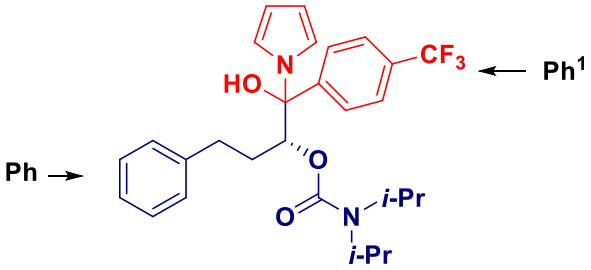


By following the **GP1**, a solution of **1** (0.200 g, 0.76 mmol, 1.5 equiv) and (+)-sparteine (0.190 g, 0.811 mmol, 1.6 equiv) was cooled at -78 °C under argon in CPME (4 mL). A solution of *s*-BuLi (1.3 M, 0.62 mL, 0.811 mmol, 1.6 equiv) was added dropwise; the reaction mixture was stirred for 30 min, then *N*-methoxy-*N*-methylbenzamide (0.083 g, 0.506 mmol, 1.0 equiv) in CPME was added slowly; After 2 hours a solution of Im-TMS (1-(trimethylsilyl)imidazole) (0.107 g, 0.76 mmol, 1.5 equiv) was added and the reaction mixture was allowed to reach room temperature over 2 hours and then quenched with $NaHCO_3$ 5% solution (5 mL). The crude was purified by chromatography on allumina III grade (hexane/AcOEt) to obtain the pure product as mixture of two stereoisomers**.** Compound **28** was obtained in 59% yield (0.149 g) as transparent oil.

Spectroscopic data are corresponding to compound **27.**

NO HPLC analysis available.

(2*R*)-1-Hydroxy-4-phenyl-1-(1H-pyrrol-1-yl)-1-[4-(trifluoromethyl)phenyl]-butan-2-yl diisopropylcarbamate, (30)



By following the **GP1**, a solution of **1** (0.153 g, 0.583 mmol, 1.5 equiv) and (-)-sparteine (0.146 g, 0.622 mmol, 1.6 equiv) was cooled at -78 °C under argon in CPME (3.3 mL). A solution of *s*-BuLi (1.3 M, 0.48 mL, 0.622 mmol, 1.6 equiv) was added dropwise; the reaction mixture was stirred for 30 min, then (1H-pyrrol-1-yl)(4-(trifluoromethyl)phenyl)methanone **29** (0.093 g, 0.389 mmol, 1.0 equiv) in CPME was added slowly; After 3 hours the reaction mixture was quenched with acetic acid (0.05 mL). The crude was purified by chromatography on silica gel (hexane/AcOEt) to obtain the pure product**.** Compound **30a** was obtained in 40% yield (0.078 g) as transparent oil and **30b** was obtained in 42% yield (0.082 g) as transparent oil.

30a

^{1}H NMR (400 MHz, C_6D_6): δ 7.32 (m, 2H, Ph^{1} H-2,6), 7.22 (m, 2H, Ph^{1} H-3,5), 7.07 (m, 2H, Ph H-3,5), 7.05 (m, 2H, Py H-2,5), 7.00 (m, 1H, Ph H-4), 6.98 (m, 2H, Ph H-2,6), 6.30 (m, 2H, Py H-3,4), 5.78 (d, *J* = 9.3 Hz, 1H, C<u>H</u>CH$_2$), 4.82 (br s, 1H, OH), 3.56 (m, 2H, C<u>H</u>CH$_3$), 2.67 (m, 1H, PhC<u>H</u>$_2$), 2.57 (m, 1H, PhC<u>H</u>$_2$), 2.11 (m, 1H, C<u>H</u>$_2$CH), 1.84 (m, 1H, C<u>H</u>$_2$CH), 1.09 (br s, 6H, C<u>H</u>$_3$), 0.76 (br s, 6H, C<u>H</u>$_3$).

^{13}C NMR (100 MHz, C_6D_6): δ 154.8 (N<u>C</u>=O), 145.5 (Ph^{1} C-1), 141.3 (Ph C-1), 130.6 (q, *J* = 32.3 Hz, Ph^{1} C-4), 128.8 (Ph C-3,5), 128.7 (Ph C-2,6), 126.9 (Ph^{1} C-2,6), 126.5 (Ph C-4), 125.3 (q, *J* = 3.8 Hz, Ph^{1} C-3,5), 124.7 (q, *J* = 272.2 Hz, <u>C</u>F$_3$), 119.3 (Pyr C-2,5), 109.5 (Pyr C-3,4), 89.7 (<u>C</u>OH), 77.8 (<u>C</u>HCH$_2$), 46.5 (<u>C</u>H(CH$_3$)$_2$), 46.5 (<u>C</u>H(CH$_3$)$_2$), 32.5 (Ph<u>C</u>H$_2$), 32.0 (<u>C</u>H$_2$CH), 21.0, 20.8, 20.5, 20.4 (4×CH(<u>C</u>H$_3$)$_2$).

^{15}N NMR (40 MHz, C_6D_6): δ -202.9 (Py N).

^{19}F NMR (376 MHz, C_6D_6): δ -62.3 (CF_3).

HRMS (ESI), *m/z*: calcd. for $C_{28}H_{33}F_3N_2NaO_3$ 525.2335 $[M+Na]^+$; found 525.2341

[α]$_D$ + 112 (*c* 0.5, CH_2Cl_2).

30b

^{1}H NMR (400 MHz, C_6D_6): δ 7.40 (m, 2H, Ph^1 H-2,6), 7.29 (m, 2H, Ph^1 H-3,5), 7.12 (m, 2H, Ph H-3,5), 7.05 (m, 2H, Ph H-2,6), 7.04 (m, 1H, Ph H-4), 6.90 (m, 2H, Py H-2,5), 6.29 (m, 2H, Py H-3,4), 5.79 (br d, *J* = 9.8 Hz, 1H, C<u>H</u>CH_2), 4.41 (br s, 1H, OH), 3.72 (m, 1H, C<u>H</u>CH_3), 3.36 (m, 1H, C<u>H</u>CH_3), 2.71-2.54 (m, 2H, Ph<u>C</u>H_2), 1.99-1.80 (m, 2H, <u>C</u>H_2CH), 1.11 (d, *J* = 6.0 Hz, 3H, C<u>H</u>$_3$), 1.07 (d, *J* = 6.6 Hz, 3H, C<u>H</u>$_3$), 0.76 (m, *J* = 6.0 Hz, 6H, C<u>H</u>$_3$).

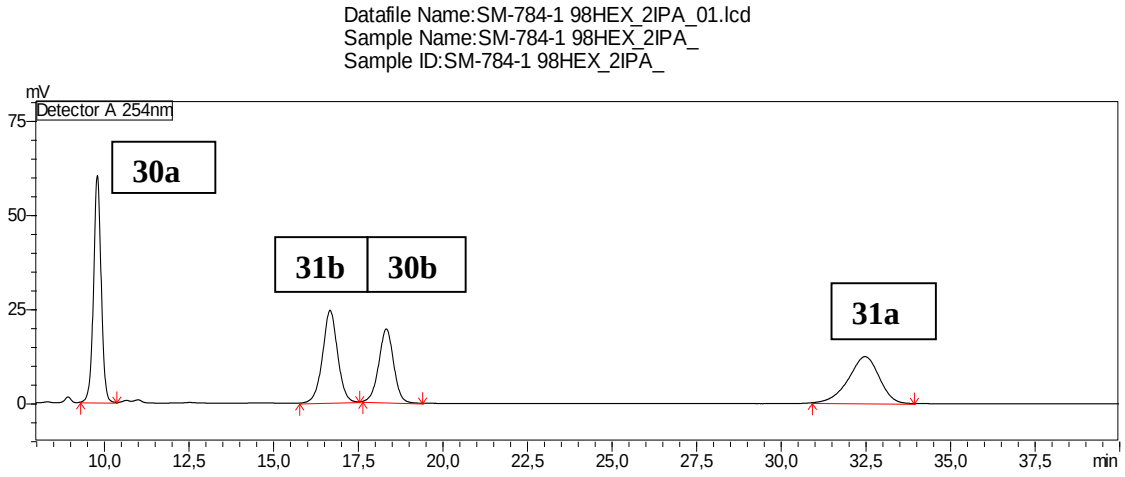
^{13}C NMR (100 MHz, C_6D_6): δ 154.6 (N<u>C</u>=O), 146.0 (Ph^1 C-1), 141.3 (Ph C-1), 130.5 (q, *J* = 32.3 Hz, Ph^1 C-4), 128.9 (Ph C-3,5), 128.8 (Ph C-2,6), 127.7 (Ph^1 C-2,6), 126.5 (Ph C-4), 125.0 (q, *J* = 3.8 Hz, Ph^1 C-3,5), 124.8 (q, *J* = 272.0 Hz, <u>C</u>F_3), 119.6 (Py C-2,5), 109.4 (Py C-3,4), 89.2 (<u>C</u>OH), 77.2 (<u>C</u>HCH_2), 46.5 (<u>C</u>H$(CH_3)_2$), 46.1 (<u>C</u>H$(CH_3)_2$), 32.7 (Ph<u>C</u>H_2), 32.5 (<u>C</u>H_2CH), 20.8 (2× CH(<u>C</u>$H_3)_2$), 20.5, 20.3 (2×CH(<u>C</u>$H_3)_2$).

^{15}N NMR (40 MHz, C_6D_6): δ -204.3 (Py N).

^{19}F NMR (376 MHz, C_6D_6): δ -62.3 (CF_3).

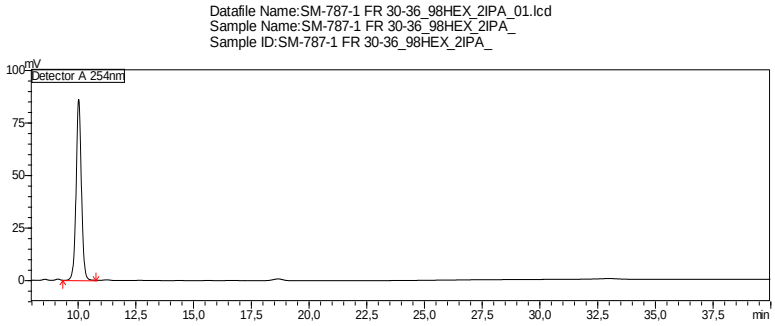
HRMS (ESI), *m/z*: calcd. for $C_{28}H_{33}F_3N_2NaO_3$ 525.2335 $[M+Na]^+$; found 525.2341.

HPLC analysis: Chiralpak IA Column, λ 254 nm, eluent: *n*-hexane / *i*-propanol 98/02. Flow:1 mL/min



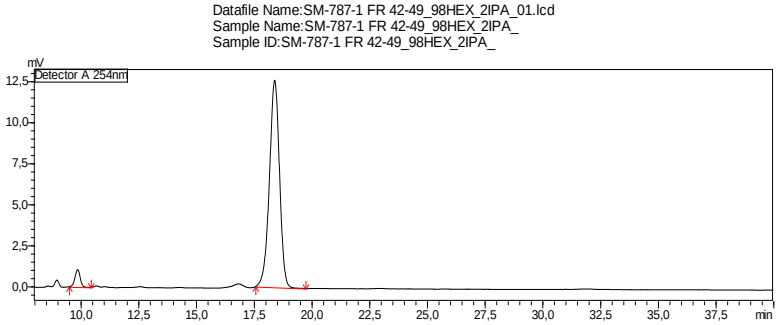
Peaks	Ret.T	Area	Area%
1	9,812	941572	30,775
2	16,689	751662	24,568
3	18,350	586898	19,183
4	32,497	779407	25,475
Total		3059539	100,000

30a



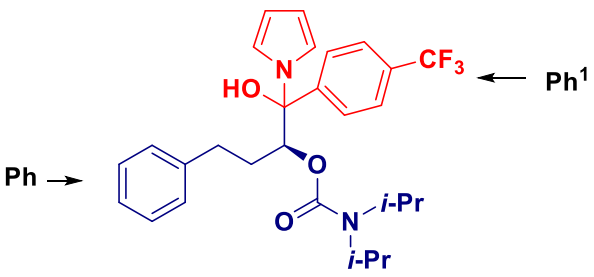
Peaks	Ret.T	Area	Area%
1	10,046	1371801	100,000
total		1371801	100,000

30b



Peaks	Ret.T	Area	Area%
1	9,871	16606	4,146
2	18,406	383957	95,854
total		400563	100,000

(2*S*)-1-Hydroxy-4-phenyl-1-(1H-pyrrol-1-yl)-1-[4-(trifluoromethyl)phenyl]-butan-2-yl diisopropylcarbamate, (31)



By following the **GP1**, a solution of **1** (0.153 g, 0.583 mmol, 1.5 equiv) and (+)-sparteine (0.146 g, 0.622 mmol, 1.6 equiv) was cooled at -78 °C under argon in CPME (3.3 mL). A solution of *s*-BuLi (1.3 M, 0.48

mL, 0.622 mmol, 1.6 equiv) was added dropwise; the reaction mixture was stirred for 30 min, then (1H-pyrrol-1-yl)(4-(trifluoromethyl)phenyl)methanone **29** (0.093 g, 0.389 mmol, 1.0 equiv) in CPME was added slowly; After 3 hours the reaction mixture was quenched with acetic acid (0.05 mL). The crude was purified by chromatography on silica gel (hexane/AcOEt) to obtain the pure product. Compound **31a** was obtained in 37% yield (0.071 g) as transparent oil and **31b** was obtained in 40% yield (0.078 g) as transparent oil.

31a

^{1}H NMR (400 MHz, C_6D_6): δ 7.32 (m, 2H, Ph^1 H-2,6), 7.22 (m, 2H, Ph^1 H-3,5), 7.07 (m, 2H, Ph H-3,5), 7.05 (m, 2H, Py H-2,5), 7.00 (m, 1H, Ph H-4), 6.98 (m, 2H, Ph H-2,6), 6.30 (m, 2H, Py H-3,4), 5.78 (d, *J* = 9.3 Hz, 1H, C<u>H</u>CH_2), 4.82 (br s, 1H, OH), 3.56 (m, 2H, C<u>H</u>CH_3), 2.67 (m, 1H, PhC<u>H</u>$_2$), 2.57 (m, 1H, PhC<u>H</u>$_2$), 2.11 (m, 1H, C<u>H</u>$_2$CH), 1.84 (m, 1H, C<u>H</u>$_2$CH), 1.09 (br s, 6H, C<u>H</u>$_3$), 0.76 (br s, 6H, C<u>H</u>$_3$).

^{13}C NMR (100 MHz, C_6D_6): δ 154.8 (N<u>C</u>=O), 145.5 (Ph^1 C-1), 141.3 (Ph C-1), 130.6 (q, *J* = 32.3 Hz, Ph^1 C-4), 128.8 (Ph C-3,5), 128.7 (Ph C-2,6), 126.9 (Ph^1 C-2,6), 126.5 (Ph C-4), 125.3 (q, *J* = 3.8 Hz, Ph^1 C-3,5), 124.7 (q, *J* = 272.2 Hz, <u>C</u>F_3), 119.3 (Pyr C-2,5), 109.5 (Pyr C-3,4), 89.7 (<u>C</u>OH), 77.8 (<u>C</u>HCH_2), 46.5 (<u>C</u>H$(CH_3)_2$), 46.5 (<u>C</u>H$(CH_3)_2$), 32.5 (Ph<u>C</u>H_2), 32.0 (<u>C</u>H_2CH), 21.0, 20.8, 20.5, 20.4, (4×CH(<u>C</u>$H_3)_2$).

^{15}N NMR (40 MHz, C_6D_6): δ -202.9 (Py N).

^{19}F NMR (376 MHz, C_6D_6): δ -62.3 (CF_3).

HRMS (ESI), *m/z*: calcd. for $C_{28}H_{33}F_3N_2NaO_3$ 525.2335 $[M+Na]^+$; found 525.2341.

[α]$_D$ - 164 (*c* 0.5, CH_2Cl_2).

31b

^{1}H NMR (400 MHz, C_6D_6): δ 7.40 (m, 2H, Ph^1 H-2,6), 7.29 (m, 2H, Ph^1 H-3,5), 7.12 (m, 2H, Ph H-3,5), 7.05 (m, 2H, Ph H-2,6), 7.04 (m, 1H, Ph H-4), 6.90 (m, 2H, Py H-2,5), 6.29 (m, 2H, Py H-3,4), 5.79 (br d, *J* = 9.8 Hz, 1H, C<u>H</u>CH_2), 4.41 (br s, 1H, OH), 3.72 (m, 1H, C<u>H</u>CH_3), 3.36 (m, 1H, C<u>H</u>CH_3), 2.71-2.54 (m, 2H, PhC<u>H</u>$_2$), 1.99-1.80 (m, 2H, C<u>H</u>$_2$CH), 1.11 (d, *J* = 6.0 Hz, 3H, C<u>H</u>$_3$), 1.07 (d, *J* = 6.6 Hz, 3H, C<u>H</u>$_3$), 0.76 (m, *J* = 6.0 Hz, 6H, C<u>H</u>$_3$).

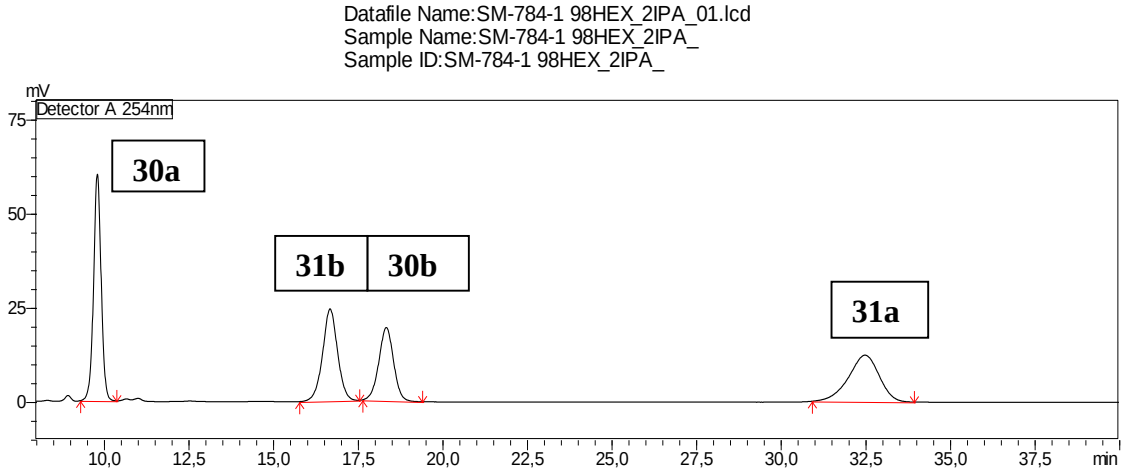
^{13}C NMR (100 MHz, C_6D_6): δ 154.6 (N<u>C</u>=O), 146.0 (Ph^1 C-1), 141.3 (Ph C-1), 130.5 (q, *J* = 32.3 Hz, Ph^1 C-4), 128.9 (Ph C-3,5), 128.8 (Ph C-2,6), 127.7 (Ph^1 C-2,6), 126.5 (Ph C-4), 125.0 (q, *J* = 3.8 Hz, Ph^1 C-3,5), 124.8 (q, *J* = 272.0 Hz, <u>C</u>F_3), 119.6 (Py C-2,5), 109.4 (Py C-3,4), 89.2 (<u>C</u>OH), 77.2 (<u>C</u>HCH_2), 46.5 (<u>C</u>H$(CH_3)_2$), 46.1 (<u>C</u>H$(CH_3)_2$), 32.7 (Ph<u>C</u>H_2), 32.5 (<u>C</u>H_2CH), 20.8 (2×CH(<u>C</u>$H_3)_2$), 20.5, 20.3 (2×CH(<u>C</u>$H_3)_2$).

^{15}N NMR (40 MHz, C_6D_6): δ -204.3 (Py N).

^{19}F NMR (376 MHz, C_6D_6): δ -62.3 (CF_3).

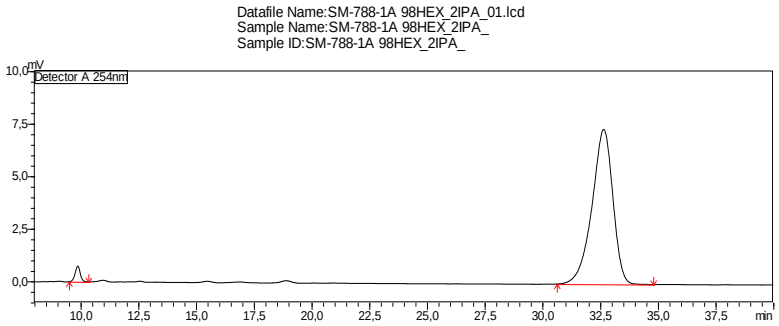
HRMS (ESI), *m/z*: calcd. for $C_{28}H_{33}F_3N_2NaO_3$ 525.2335 $[M+Na]^+$; found 525.2341

HPLC analysis: Chiralpak IA Column, λ 254 nm, eluent: *n*-hexane / *i*-propanol 98/02. Flow:1 mL/min



Peaks	Ret.T	Area	Area%
1	9,812	941572	30,775
2	16,689	751662	24,568
3	18,350	586898	19,183
4	32,497	779407	25,475
Total		3059539	100,000

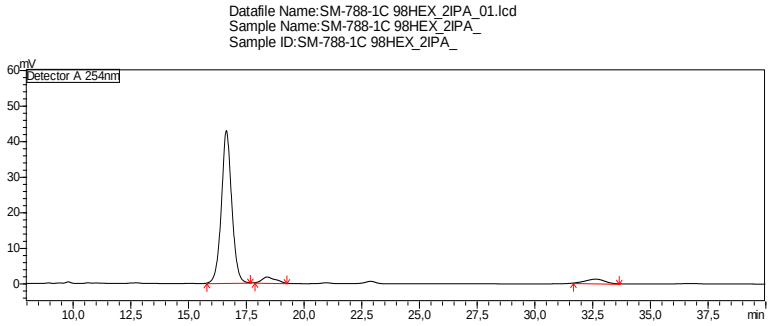
31a



Peaks	Ret.T	Area	Area%
1	9,877	11567	2,434

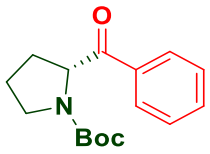
2	32,655	463702	97,566
total		475269	100,000

31b



Peaks	Ret.T	Area	Area%
1	16,660	1337061	90,920
2	18,428	65906	4,482
3	32,654	67626	4,599
total		1470593	100,000

(2*R*)-2-Methyl-2-propanyl-2-benzoyl-1-pyrrolidinecarboxylate, ((*R*)-33)



Synthesized according to **GP3** using **32** (0.078 g, 0.454 mmol, 1.5 equiv); (-)-sparteine (0.112 g, 0.485 mmol, 1.6 equiv); *s*-BuLi 1.3 M (0.37 ml, 0.485 mmol, 1.6 equiv) in CPME (3 mL); and *N*-methoxy-*N*-methyl-benzamide (0.050 g, 0.303 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*)-33** was obtained in 85% yield (0.071 g) as a pale yellow solid; mp 64-70 °C. Reaction run in larger scale starting from **32** (1.27 g, 6 mmol, 1.5 equiv); (-)-sparteine (1.5 g, 6.4 mmol, 1.6 equiv); *s*-BuLi 1.4 M (4.57 mL, 6.4 mmol, 1.6 equiv) and *N*-methoxy-*N*-methyl-benzamide (0.660 g, 4 mmol, 1.0 equiv) in CPME (27 mL) allowed to recover CPME (85%, 22.9 mL) and prepare **(*R*)-33** in comparable yield (80%, 0.880 g). The organic layer from the basic extraction with CPME (30 mL) afforded upon distillation (-)-sparteine (80%, 1.20 g, 1.18 mL), *N*-methyl-*N*-methoxyamine (75%, 3.0 mmol, 0.23 mL) and CPME (88%, 26.4 mL).

Rotamers ratio = 60:40

Major rotamer:

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (m, 2H, Ph H-2,6), 7.58 (m, 1H, Ph H-4), 7.48 (m, 2H, Ph H-3,5), 5.19 (dd, *J* = 8.9, 4.0 Hz, 1H, Pyr H-2), 3.72-3.43 (m, 2H, Pyr H-5), 2.32 (m, 1H, Pyr H-3), 1.99-1.87 (m, 2H, Pyr H-4), 1.92 (m, 1H, Pyr H-3), 1.25 (s, 9H, $(CH_3)_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ 198.9 (C=O), 153.8 (N-C(=O)-O), 135.3 (Ph C-1), 133.2 (Ph C-4), 128.7 (Ph C-3,5), 128.2 (Ph C-2,6), 79.8 ($(CH_3)_3\underline{C}O$), 61.3 (Pyr C-2), 46.6 (Pyr C-5), 30.8 (Pyr C-3), 28.2 ($(CH_3)_3$), 23.5 (Pyr C-4).

Minor rotamer:

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (m, 2H, Ph H-2,6), 7.55 (m, 1H, Ph H-4), 7.44 (m, 2H, Ph H-3,5), 5.33 (m, 1H, Pyr H-2), 3.71-3.44 (m, 2H, Pyr H-5), 2.28 (m, 1H, Pyr H-3), 1.99-1.87 (m, 2H, Pyr H-4), 1.91 (m, 1H, Pyr H-3), 1.46 (s, 9H, $(CH_3)_3$).

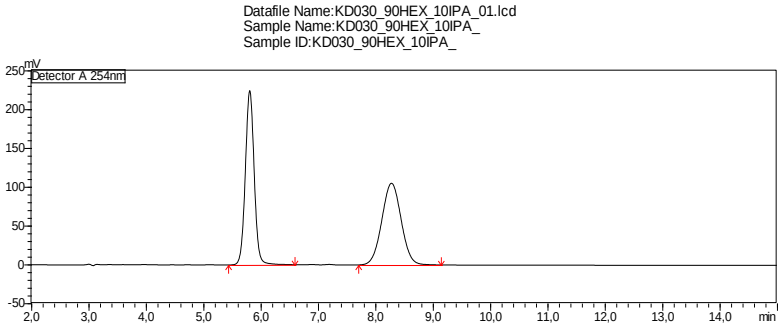
^{13}C NMR (100 MHz, $CDCl_3$): δ 198.4 (C=O), 154.4 (N-C(=O)-O), 135.1 (Ph C-1), 133.1 (Ph C-4), 128.6 (Ph C-3,5), 128.5 (Ph C-2,6), 79.6 ($(CH_3)_3\underline{C}O$), 61.1 (Pyr C-2), 46.8 (Pyr C-5), 29.8 (Pyr C-3), 28.5 ($(CH_3)_3$), 24.1 (Pyr C-4).

HRMS (ESI), *m/z*: calcd. for $C_{16}H_{21}NNaO_3$: 298.1414 $[M+Na]^+$; found: 298.1415.

[α]$_D$ = +26.50 (*c* 0.5, $CHCl_3$) *lit.*[4] +28.10 (*c* 1.35, $CHCl_3$).

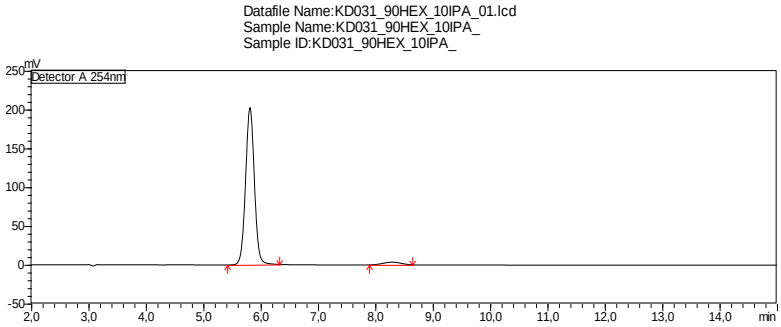
HPLC analysis: Chiralpak IA Column, λ 254 nm, eluent: *n*-hexane / *i*-propanol 90/10. Flow: 1 mL/min

Racemate



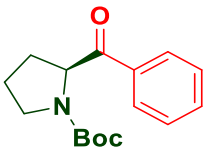
Peaks	Retention time (min)	Area	Area%
1	5,810	2410041	49,432
2	8,282	2465392	50,568
total		4875433	100,000

***Enantioenriched* (*R*)-33**



Peaks	Retention time (min)	Area	Area%
1	5,814	2158925	96,697
2	8,295	73753	3,303
total		2232678	100,000

(2*S*)-2-Methyl-2-propanyl 2-benzoyl-1-pyrrolidinecarboxylate, ((*S*)-33)



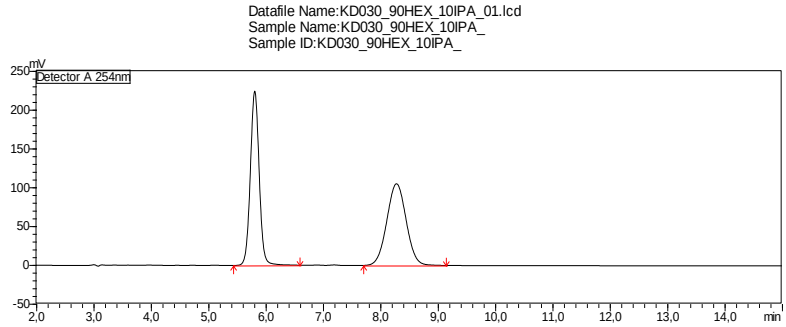
Synthesized according to **GP3** using **32** (0.078 g, 0.454 mmol, 1.5 equiv); (+)-sparteine (0.112 g, 0.485 mmol, 1.6 equiv); *s*-BuLi 1.3 M (0.37 ml, 0.485 mmol, 1.6 equiv) in CPME (3 mL); and *N*-methoxy-*N*-

methyl-benzamide (0.050 g, 0.303 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*S*)-33** was obtained in 88% yield (0.073 g) as a pale yellow solid; mp 64-70 °C. Reaction run in larger scale starting from **32** (1.27 g, 6 mmol, 1.5 equiv); (+)-sparteine (1.5 g, 6.4 mmol, 1.6 equiv); *s*-BuLi 1.4 M (4.57 mL, 6.4 mmol, 1.6 equiv) and *N*-methoxy-*N*-methyl-benzamide (0.660 g, 4 mmol, 1.0 equiv) in CPME (27 mL) allowed to recover CPME (90%, 24.3 mL) and prepare **(*S*)-33** in comparable yield (82%, 0.902 g). The organic layer from the basic extraction with CPME (30 mL) afforded upon distillation (+)-sparteine (79%, 1.18 g, 1.16 mL), *N*-methyl-*N*-methoxyamine (60%, 2.4 mmol, 0.15 mL) and CPME (91%, 27.3 mL).

$[\alpha]_D$ = -34.90 (*c* 0.5, $CHCl_3$) *lit*.[5] -63.1 (*c* 1.02, $CHCl_3$)

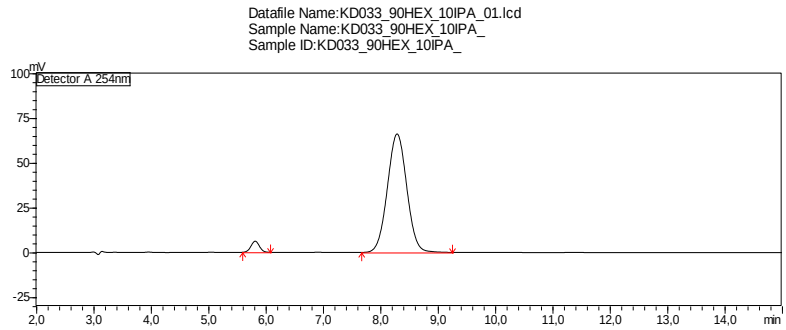
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 90/10. Flow: 1 mL/min

Racemate



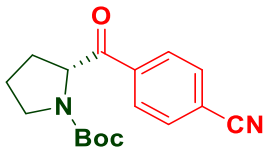
Peaks	Retention time (min)	Area	Area%
1	5,810	2410041	49,432
2	8,282	2465392	50,568
total		4875433	100,000

***Enantioenriched* (*S*)-33**



Peaks	Retention time (min)	Area	Area%
1	5,818	63844	3,948
2	8,292	1553393	96,052
total		1617236	100,000

(2*R*)-2-Methyl-2-propanyl 2-(4-cyanobenzoyl)-1-pyrrolidinecarboxylate, ((*R*)-34)



Synthesized according to **GP3** using **32** (0.078 g, 0.454 mmol, 1.5 equiv); (-)-sparteine (0.112 g, 0.485 mmol, 1.6 equiv); *s*-BuLi 1.3 M (0.37 ml, 0.485 mmol, 1.6 equiv) in CPME (3 mL); and 4-cyano-*N*-methoxy-*N*-methyl-benzamide (0.056 g, 0.303 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*)-34** was obtained in 75% yield (0.068 g) as a yellow solid, mp 64-67 °C. Reaction run with (-)-sparteine recovered from preparation of **(*R*)-33.**

Rotamers ratio = 51:49

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07-8.02 (m, 2H, Ph H-2,6), 7.80-7.74 (m, 2H, Ph H-3,5), 5.25 (dd, *J* = 9.1, 3.8 Hz, 0.49H, Pyr H-2), 5.13 (dd, *J* = 9.3, 4.5 Hz, 0.51H, Pyr H-2), 3.70-3.44 (m, 2H, Pyr H-5), 2.34-2.28 (m, 1H, Pyr H-3), 2.00-1.87 (m, 2H, Pyr H-4), 1.90-1.86 (m, 1H, Pyr H-3), 1.44 (s, 4.5H, $(CH_3)_3$), 1.24 (s, 4.5H, $(CH_3)_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ 197.79 (C=O), 197.76 (C=O), 154.4 (NC=O), 153.4 (NC=O), 138.4 (Ph C-1), 138.3 (Ph C-1), 132.6 (Ph C-3,5), 132.4 (Ph C-3,5), 128.8 (Ph C-2,6), 128.5 (Ph C-2,6), 117.9 (C≡N), 117.7 (C≡N), 116.5 (Ph C-4), 116.3 (Ph C-4), 80.1 ($(CH_3)_3\underline{C}O$), 80.0 ($(CH_3)_3\underline{C}O$), 61.5 (Pyr C-2), 61.1 (Pyr C-2), 46.7 (Pyr C-5), 46.6 (Pyr C-5), 30.6 (Pyr C-3), 29.5 (Pyr C-3), 28.4 ($(CH_3)_3$), 28.1 ($(CH_3)_3$), 24.3 (Pyr C-4), 23.5 (Pyr C-4).

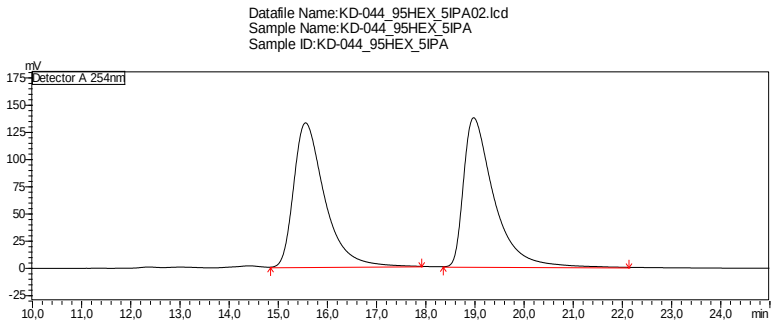
HRMS (ESI), *m/z*: calcd. for $C_{17}H_{20}N_2NaO_3$ 323.1366 $[M+Na]^+$; found: 323.1368.

$[\alpha]_D$ = +8.00 (*c* 0.5, $CHCl_3$)

HPLC analysis: Chiralpak IB Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 95/05. Flow:

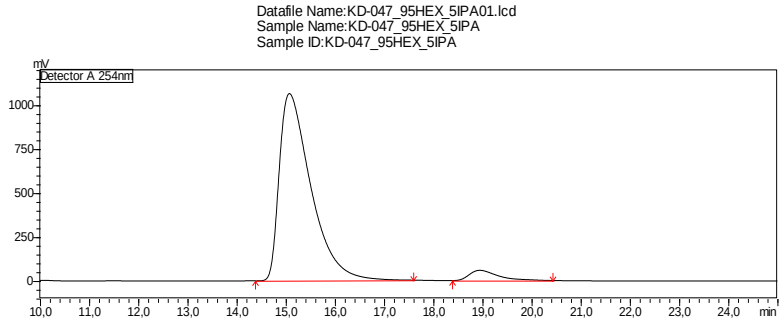
1 mL/min

Racemate



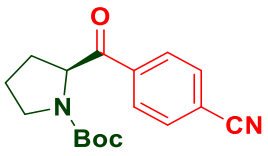
Peaks	Retention time (min)	Area	Area%
1	15,566	5774381	49,599
2	18,985	5867752	50,401
total		11642134	100,000

***Enantioenriched* (*R*)-34**



Peaks	Retention time (min)	Area	Area%
1	15,075	47467160	95,234
2	18,947	2375422	4,766
total		49842581	100,000

(2*S*)-2-Methyl-2-propanyl 2-(4-cyanobenzoyl)-1-pyrrolidinecarboxylate, ((*S*)-34)



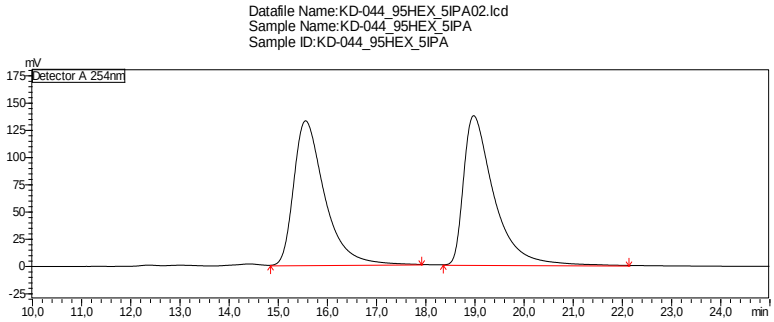
Synthesized according to **GP3** using **32** (0.078 g, 0.454 mmol, 1.5 equiv); (+)-sparteine (0.112 g, 0.485 mmol, 1.6 equiv); *s*-BuLi 1.3 M (0.37 ml, 0.485 mmol, 1.6 equiv) in CPME (3 mL); and 4-cyano-*N*-methoxy-*N*-methyl-benzamide (0.056 g, 0.303 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*S*)-34** was obtained in 81% yield (0.074 g) as a yellow solid, mp 64-67 °C. Reaction run with (+)-sparteine recovered from preparation of **(*S*)-33.**

$[\alpha]_D$ = -18.66 (*c* 0.5, $CHCl_3$)

HPLC analysis: Chiralpak IB Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 95/05. Flow:

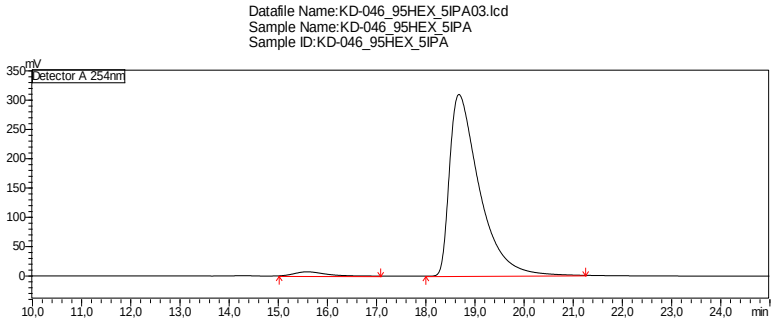
1 mL/min

Racemate



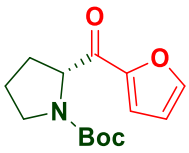
Peaks	Retention time (min)	Area	Area%
1	15,566	5774381	49,599
2	18,985	5867752	50,401
total		11642134	100,000

***Enantioenriched* (*S*)-34**



Peaks	Retention time (min)	Area	Area%
1	15,601	293721	2,206
2	18,686	13020658	97,794
total		13314379	100,000

(*2R)-2*-Methyl-2-propanyl 2-(furan-2-ylcarbonyl)pyrrolidine-1-carboxylate, ((*R)*-35)



Synthesized according to **GP3** using **32** (0.078 g, 0.454 mmol, 1.5 equiv); (-)-sparteine (0.112 g, 0.485 mmol, 1.6 equiv); *s*-BuLi 1.3 M (0.37 ml, 0.485 mmol, 1.6 equiv) in CPME (3 mL); and *N*-methoxy-*N*-methylfuran-2-carboxamide (0.047 g, 0.303 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R)*-35** was obtained in 75% yield (0.060 g) as a brownish solid, mp 68 °C.

Rotamers ratio = 61:39

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61-7.58 (m, 1H, Fur H-5), 7.26-7.22 (m, 1H, Fur H-3), 6.56-6.52 (m, 1H, Fur H-4), 5.08 (dd, *J* = 8.6, 3.1 Hz, 0.39H, Pyr H-2), 4.90 (dd, *J* = 8.6, 4.6 Hz, 0.61H, Pyr H-2), 3.67-3.42 (m, 2H, Pyr H-5), 2.33-2.23 (m, 1H, Pyr H-3), 2.01-1.88 (m, 3H, Pyr H-3, H-4) 1.45 (s, 3.5H, $(CH_3)_3$), 1.26 (s, 5.5H, $(CH_3)_3$).

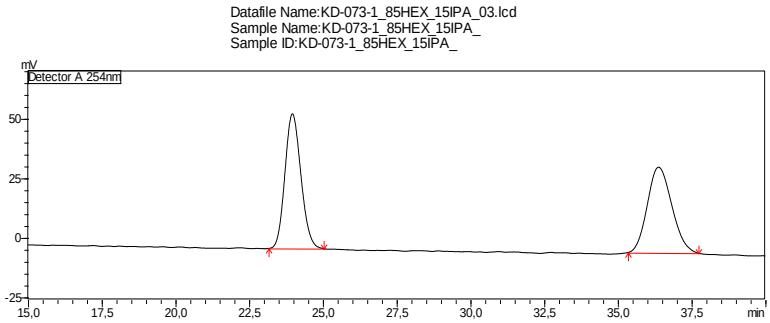
^{13}C NMR (100 MHz, $CDCl_3$): δ 188.5 (C=O), 187.8 (C=O), 154.4 (NC=O), 153.7 (NC=O), 151.2 (Fur C-2), 146.5 (Fur C-5), 117.9 (Fur C-3), 117.5 (Fur C-3), 112.2 (Fur C-4), 79.9 ($(CH_3)_3\underline{C}O$), 79.7 ($(CH_3)_3\underline{C}O$), 61.8 (Pyr C-2), 61.3 (Pyr C-2), 46.9 (Pyr C-5), 46.7 (Pyr C-5), 30.9 (Pyr C-3), 29.8 (Pyr C-3), 28.4 ($(CH_3)_3$), 28.1 ($(CH_3)_3$), 24.2 (Pyr C-4), 23.7 (Pyr C-4).

HRMS (ESI), *m/z*: calcd. for $C_{14}H_{19}NNaO_4$ 288.1206 $[M+Na]^+$; found: 288.1210.

$[\alpha]_D$ = +50.30 (*c* 0.5, $CHCl_3$).

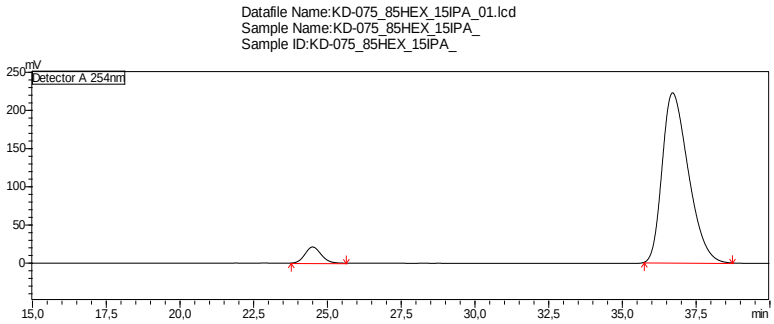
HPLC analysis: Chiralpak IC Column, λ 254 nm, eluent: *n*-hexane / *i*-propanol 85/15. Flow: 1 mL/min

Racemate



Peaks	Retention time (min)	Area	Area%
1	23,965	2135782	50,697
2	36,383	2077028	49,303
total		4212810	100,000

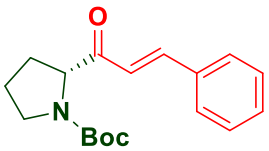
***Enantioenriched* (*R*)-35**



Peaks	Retention time (min)	Area	Area%

1	24,516	799349	5,509
2	36,719	13709425	94,491
total		14508774	100,000

(*2R*)-2-Methyl-2-propanyl 2-((2*E*)-3-phenyl-prop-2-enoyl)pyrrolidine-1-carboxylate, ((*R*)-36)



Synthesized according to **GP3** using **32** (0.078 g, 0.454 mmol, 1.5 equiv); (-)-sparteine (0.112 g, 0.485 mmol, 1.6 equiv); *s*-BuLi 1.3 M (0.37 ml, 0.485 mmol, 1.6 equiv) in CPME (3 mL); and (2*E*)-*N*-methoxy-*N*-methyl-3-phenyl-2-propenamide (0.058 g, 0.303 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*)-36** was obtained in 85% yield (0.077 g) as a yellow solid, mp 91-93 °C. Reaction run in larger scale starting from **32** (1.27 g, 6 mmol, 1.5 equiv); (-)-sparteine (1.5 g, 6.4 mmol, 1.6 equiv); *s*-BuLi 1.4 M (4.57 mL, 6.4 mmol, 1.6 equiv) and (2*E*)-*N*-methoxy-*N*-methyl-3-phenyl-2-propenamide (0.764 g, 4 mmol, 1.0 equiv) in CPME (27 mL) allowed to recover CPME (91%, 24.7 mL) and prepare **(*R*)-36** in comparable yield (80%, 0.964 g). The organic layer from the basic extraction with CPME (30 mL) afforded upon distillation (-)-sparteine (78%, 1.17 g, 1.15 mL), *N*-methyl-*N*-methoxyamine (62%, 2.5 mmol, 0.19 mL) and CPME (94%, 28.1 mL).

Rotamers ratio = 66:34

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72-7.65 (m, 1H, PhCH=C<u>H</u>), 7.56-7.54 (m, 2H, Ph H-2,6), 7.40-7.37 (m, 3H, Ph H-3,4,5), 6.85 (d, *J* = 16.0 Hz, 1H, PhC<u>H</u>=CH), 4.68-4.66 (m, 0.34H, Pyr H-2), 4.47 (dd, d, *J* = 8.2, 5.2 Hz, 0.66H, Pyr H-2), 3.61-3.45 (m, 2H, Pyr), 2.29-2.18 (m, 1H, Pyr), 1.94-1.87 (m, 3H, Pyr) 1.48 (s, 3.0H, $(CH_3)_3$), 1.39 (s, 6H, $(CH_3)_3$).

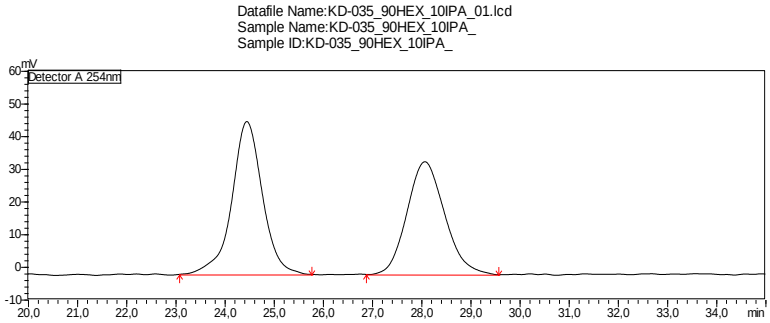
^{13}C NMR (100 MHz, $CDCl_3$): δ 199.1 (C=O), 198.5 (C=O), 154.5 (NC=O), 154.0 (NC=O), 143.7 (Ph-<u>C</u>=C), 134.6 (Ph C-1), 134.4 (Ph C-1), 130.6 (Ph), 130.4 (Ph), 128.9 (Ph), 128.8 (Ph) 128.3 (PhC=<u>C</u>), 80.1 ($(CH_3)_3$<u>C</u>O), 79.7 ($(CH_3)_3$<u>C</u>O), 64.8 (Pyr C-2), 63.8 (Pyr C-2), 46.9 (Pyr), 46.8 (Pyr), 30.5 (Pyr C-4), 29.2 (Pyr), 28.4 ($(CH_3)_3$), 28.1 ($(CH_3)_3$), 24.3 (Pyr), 23.8 (Pyr).

HRMS (ESI), *m/z*: calcd. for $C_{18}H_{23}NNaO_3$ 324.1570 $[M+Na]^+$; found: 324.1574.

$[\alpha]_D$ = +75.10 (*c* 0.5, $CHCl_3$).

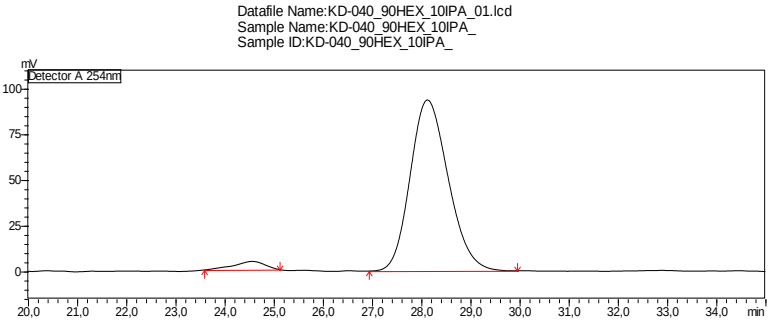
HPLC analysis: Chiralpak IC Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 95/05. Flow: 1 mL/min

Racemate



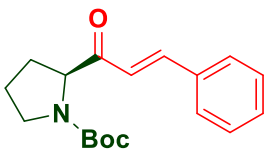
Peaks	Retention time (min)	Area	Area%
1	24,452	2021480	52,378
2	28,075	1837906	47,622
total		3859386	100,000

***Enantioenriched* (*R*)-36**



Peaks	Retention time (min)	Area	Area%
1	24,561	201734	3,857
2	28,126	5028918	96,143
total		5230653	100,000

(*2S*)-2-Methyl-2-propanyl 2-((2E)-3-phenyl-prop-2-enoyl)pyrrolidine-1-carboxylate, ((*S*)-36)



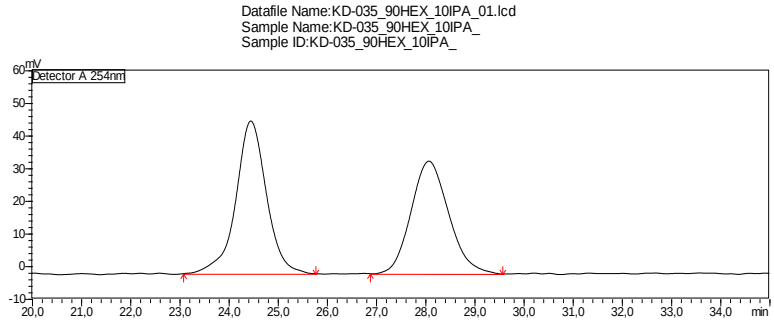
Synthesized according to **GP3** using **32** (0.078 g, 0.454 mmol, 1.5 equiv); (+)-sparteine (0.112 g, 0.485 mmol, 1.6 equiv); *s*-BuLi 1.3 M (0.37 ml, 0.485 mmol, 1.6 equiv) in CPME (3 mL); and *N*-methoxy-*N*-methyl-3-phenyl-2-propenamide (0.058 g, 0.303 mmol, 1.0 equiv) dissolved in CPME (1 mL); Compound **(*S*)-36** was obtained in 83% yield (0.075 g), mp 91-93 °C. Reaction run in larger scale starting from **32** (1.27 g, 6 mmol, 1.5 equiv); (+)-sparteine (1.5 g, 6.4 mmol, 1.6 equiv); *s*-BuLi 1.4 M (4.57 mL,

6.4 mmol, 1.6 equiv) and *N*-methoxy-*N*-methyl-3-phenyl-2-propenamide (0.764 g, 4 mmol, 1.0 equiv) in CPME (27 mL) allowed to recover CPME (89%, 24.0 mL) and prepare **(*S*)-36** in comparable yield (75%, 0.903 g). The organic layer from the basic extraction with CPME (30 mL) afforded upon distillation (+)-sparteine (81%, 1.22 g, 1.2 mL), *N*-methyl-*N*-methoxyamine (64%, 2.6 mmol, 0.2 mL) and CPME (90%, 27.0 mL).

$[\alpha]_D$ = -53.35 (*c* 0.5, $CHCl_3$)

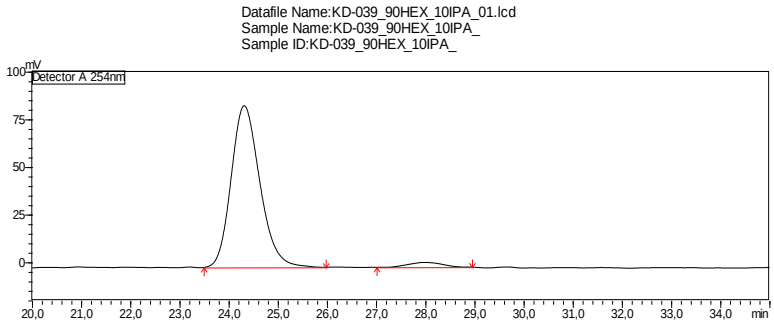
HPLC analysis: Chiralpak IC Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 95/05. Flow: 1 mL/min

Racemate



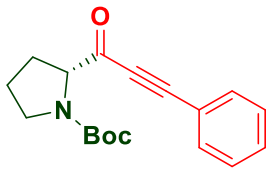
Peaks	Retention time (min)	Area	Area%
1	24,452	2021480	52,378
2	28,075	1837906	47,622
total		3859386	100,000

***Enantioenriched* (*S*)-36**



Peaks	Retention time (min)	Area	Area%
1	24,317	3441466	96,748
2	27,993	115676	3,252
total		3557143	100,000

(2*R*)-2-Methyl-2-propanyl 2-(3-phenyl-2-propynoyl)-1-pyrrolidinecarboxylate, ((*R*)-37)



Synthesized according to **GP3** using **32** (0.078 g, 0.454 mmol, 1.5 equiv); (-)-sparteine (0.112 g, 0.485 mmol, 1.6 equiv); *s*-BuLi 1.3 M (0.37 ml, 0.485 mmol, 1.6 equiv) in CPME (3 mL); and *N*-methoxy-*N*-methyl-3-phenyl-2-propynamide (0.057 g, 0.303 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*)-37** was obtained in 80% yield (0.072 g) as a yellow solid, mp 74-75 °C. Reaction run with (-)-sparteine recovered from preparation of **(*R*)-36.**

Rotamers ratio = 74:26

Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58-7.52 (m, 2H, Ph H-2,6), 7.48-7.41 (m, 1H, Ph H-4), 7.39-7.33 (m, 2H, Ph H-3,5), 4.30 (dd, *J* = 8.5, 5.3 Hz, 1H, Pyr H-2), 3.60 (m, 2H, Pyr H-5), 2.28 (m, 1H, Pyr H-3), 2.07 (m, 1H, Pyr H-3), 2.02-1.84 (m, 2H, Pyr H-4), 1.40 (s, 9H, $(CH_3)_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ 188.6 (C=O), 153.7 (NC=O), 133.3 (Ph C-2,6), 130.9 (Ph C-4), 128.6 (Ph C-3,5), 119.6 (Ph C-1), 93.5 (C≡CPh), 85.6 (C≡CPh), 80.4 ($(CH_3)_3CO$), 66.7 (Pyr C-2), 46.6 (Pyr C-5), 30.7 (Pyr C-3), 28.1 ($(CH_3)_3$), 23.7 (Pyr C-4).

Minor isomer:

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58-7.52 (m, 2H, Ph H-2,6), 7.48-7.41 (m, 1H, Ph H-4), 7.39-7.33 (m, 2H, Ph H-3,5), 4.49 (dd, *J* = 8.7, 4.4 Hz, 1H, Pyr H-2), 3.47 (m, 2H, Pyr H-5), 2.22 (m, 1H, Pyr H-3), 2.09 (m, 1H, Pyr H-3), 2.02-1.84 (m, 2H, Pyr H-4), 1.44 (s, 9H, $(CH_3)_3$).

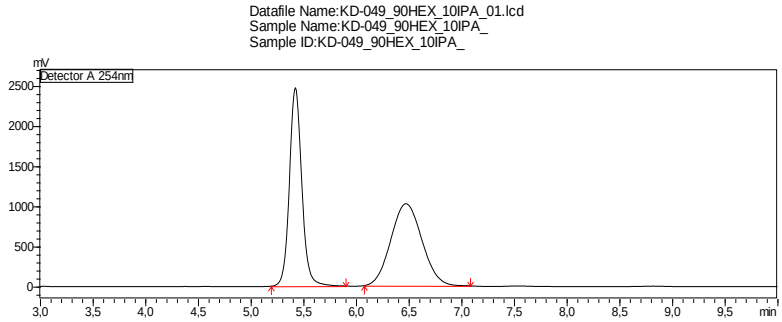
^{13}C NMR (100 MHz, $CDCl_3$): δ 187.8 (C=O), 154.5 (NC=O), 133.0 (Ph C-2,6), 130.7 (Ph C-4), 128.5 (Ph C-3,5), 119.9 (Ph C-1), 92.9 (C≡CPh), 86.1 (C≡CPh), 79.9 ($(CH_3)_3CO$), 66.5 (Pyr C-2), 46.8 (Pyr C-5), 29.2 (Pyr C-3), 28.4 ($(CH_3)_3$), 24.3 (Pyr C-4).

HRMS (ESI), *m/z*: calcd. for $C_{18}H_{21}NNaO_3$ 322.1414 $[M+Na]^+$; found: 322.1415.

$[\alpha]_D$ = +116.25 (*c* 0.5, $CHCl_3$).

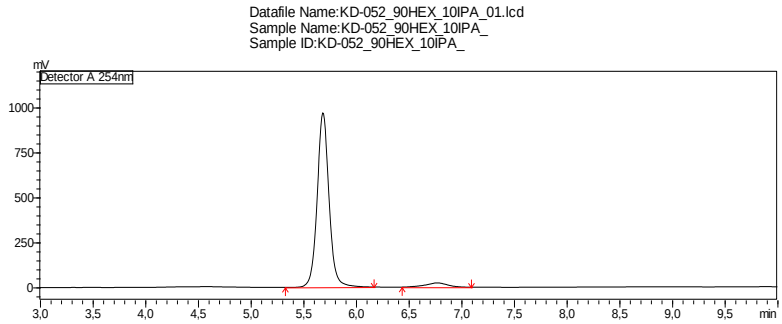
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 95/05. Flow: 1 mL/min

Racemate



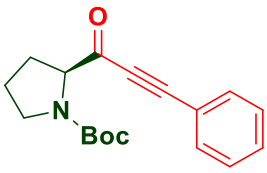
Peaks	Retention time (min)	Area	Area%
1	5,424	20217455	49,028
2	6,474	21018735	50,972
total		41236189	100,000

***Enantioenriched* (*R*)-37**



Peaks	Retention time (min)	Area	Area%
1	5,686	7572598	95,668
2	6,773	342926	4,332
total		7915524	100,000

(*2S)-2*-Methyl-2-propanyl 2-(3-phenyl-2-propynoyl)-1-pyrrolidinecarboxylate, ((*S)*-37)

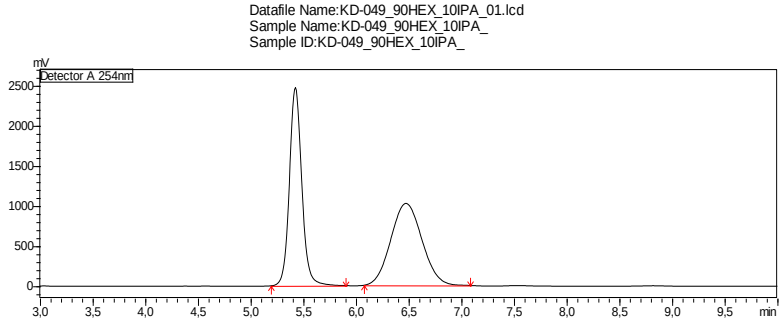


Synthesized according to **GP3** using **32** (0.078 g, 0.454 mmol, 1.5 equiv); (+)-sparteine (0.112 g, 0.485 mmol, 1.6 equiv); *s*-BuLi 1.3 M (0.37 ml, 0.485 mmol, 1.6 equiv) in CPME (3 mL); and *N*-methoxy-*N*-methyl-3-phenyl-2-propynamide (0.057 g, 0.303 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*S)*-37** was obtained in 81% yield (73 mg) as a yellow solid, mp 74-75 °C. Reaction run with (+)-sparteine recovered from preparation of **(*S*)-36.**

$[\alpha]_D$ = -118.65 (*c* 0.5, $CHCl_3$)

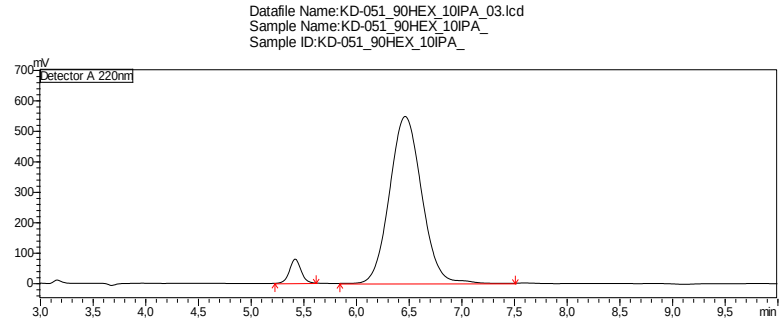
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 95/05. Flow: 1 mL/min

Racemate



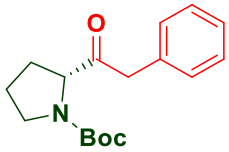
Peaks	Retention time (min)	Area	Area%
1	5,424	20217455	49,028
2	6,474	21018735	50,972
total		41236189	100,000

***Enantioenriched* (*S*)-37**



Peaks	Retention time (min)	Area	Area%
1	5,423	596986	4,899
2	6,467	342926	95,101
total		12187016	100,000

(*2R*)-2-Methyl-2-propanyl 2-(phenylacetyl)pyrrolidine-1-carboxylate, ((*R*)-38)



Synthesized according to **GP3** using **32** (0.078 g, 0.454 mmol, 1.5 equiv); (-)-sparteine (0.112 g, 0.485 mmol, 1.6 equiv); *s*-BuLi 1.3 M (0.37 ml, 0.485 mmol, 1.6 equiv) in CPME (3 mL); and *N*-methoxy-*N*-methyl-2-phenylacetamide (0.054 g, 0.303 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound ***(R)*-38** was obtained in 79% yield (0.069 g) as a light brown solid, mp 54°C.

Rotamers ratio = 59:41

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.21 (m, 5H, Ph), 4.44 (dd, *J* = 8.0, 3.6 Hz, 0.41H, Pyr H-2), 4.36-4.33 (m, 0.59H, Pyr H-2), 3.83 (s, 0.82H, CH_2), 3.75 (s, 1.16H, CH_2), 3.56-3.38 (m, 2H, Pyr), 2.14-2.07 (m, 0.59H, Pyr), 1.99-1.92 (m, 0.41H, Pyr), 1.81-1.74 (m, 3H, Pyr) 1.48 (s, 3.6H, $(CH_3)_3$), 1.39 (s, 5.4H, $(CH_3)_3$).

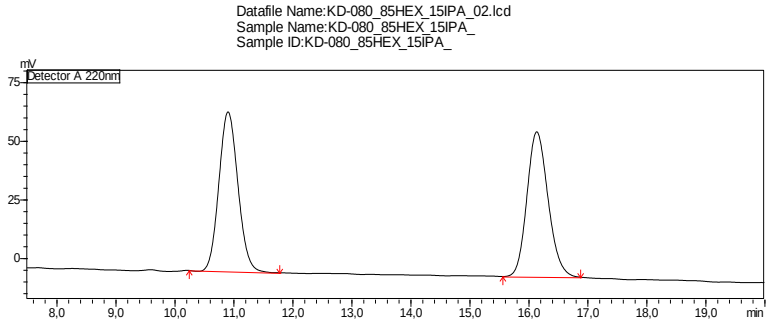
^{13}C NMR (100 MHz, $CDCl_3$): δ 207.7 (C=O), 207.2 (C=O), 153.9 (NC=O), 133.9 (Ph C-1), 133.5 (Ph C-1), 129.7 (Ph), 129.6 (Ph), 128.6 (Ph), 128.5 (Ph), 127.0 (Ph), 126.8 (Ph), 80.2 ($(CH_3)_3\underline{C}O$), 79.8 ($(CH_3)_3\underline{C}O$), 65.1 (Pyr C-2), 64.5 (Pyr C-2), 46.9 (Pyr), 46.8 (Pyr), 46.7 (Ph$\underline{C}H_2$C=O). 45.8 (Ph$\underline{C}H_2$C=O), 30.2 (Pyr), 29.2 (Pyr), 28.5 ($(CH_3)_3$), 28.3 ($(CH_3)_3$), 24.4 (Pyr), 23.6 (Pyr).

HRMS (ESI), *m/z*: calcd. for $C_{17}H_{23}NNaO_3$ 312.1570 $[M+Na]^+$; found: 312.1577.

$[\alpha]_D$ = +24.80 (*c* 0.5, $CHCl_3$).

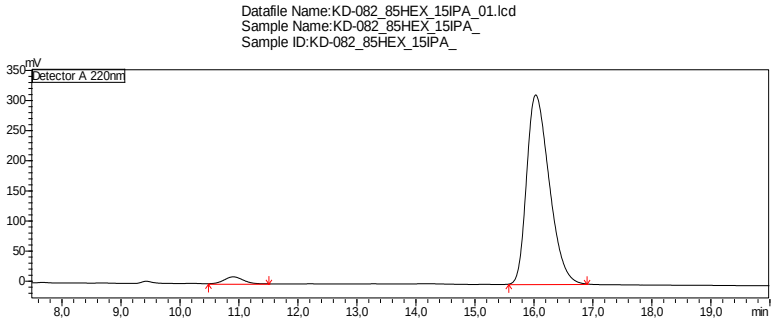
HPLC analysis: Chiralpak IC Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 85/15. Flow: 1 mL/min

Racemate



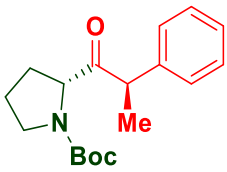
Peaks	Retention time (min)	Area	Area%
1	10,909	1521977	49,697
2	16,142	1540530	50,303
total		3062507	100,000

***Enantioenriched* (*R*)-38**



Peaks	Retention time (min)	Area	Area%
1	10,914	252948	2,939
2	16,040	8354130	97,061
total		8607078	100,000

(*R*,*R*)-2-Methyl-2-propanyl 2-(2-phenylpropanoyl)pyrrolidine-1-carboxylate, ((*R*,*R*)-39)



Synthesized according to **GP3** using **32** (0.078 g, 0.454 mmol, 1.5 equiv); (-)-sparteine (0.112 g, 0.485 mmol, 1.6 equiv); *s*-BuLi 1.3 M (0.37 ml, 0.485 mmol, 1.6 equiv) in CPME (3 mL); and (2*R*)-*N*-methoxy-*N*-methyl-2-phenylpropanamide (0.058 g, 0.303 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **(*R*,*R*)-39** was obtained in 85% yield (0.078 g) as a white solid, mp 95-97 °C

The racemic reference has been synthesized starting from *rac*-*N*-methoxy-*N*-methyl-2-phenylpropanamide, using TMEDA instead of (-)-sparteine and comprises a mixture of 4 stereoisomers.

Rotamers ratio = 65:35

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.19 (m, 5H, Ph), 4.36 (dd, *J* = 8.8, 4.1 Hz, 0.39H, Pyr H-2), 4.32 (dd, *J* = 9.2, 4.5 Hz, 0.61H, Pyr H-2), 4.07 (q, *J* = 7.2 Hz, 0.39H, CH), 4.01 (q, *J* = 7.1 Hz, 0.61H, CH), 3.46-3.40 (m, 0.61H, Pyr), 3.32-3.19 (m, 1H, Pyr), 2.91-2.85 (m, 0.39H, Pyr), 2.14-2.05 (m, 0.61H, Pyr), 1.91-1.59 (m, 3H, Pyr) 1.50 (s, 3H, $(CH_3)_3$), 1.42-1.40 (m, 3H, CH_3), 1.31 (s, 6H, $(CH_3)_3$).

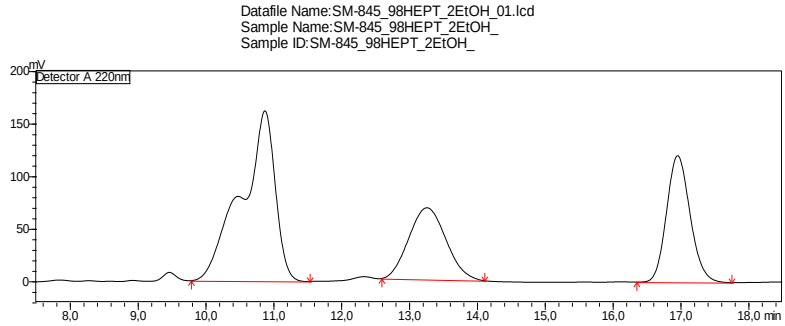
^{13}C NMR (100 MHz, $CDCl_3$): δ 211.1 (C=O), 210.0 (C=O), 154.2 (NC=O), 140.2 (Ph C-1), 139.9 (Ph C-1), 128.9 (Ph), 128.6 (Ph), 128.1 (Ph), 128.1 (Ph), 127.2 (Ph), 126.9 (Ph), 80.0 ($(CH_3)_3\underline{C}O$), 79.7 ($(CH_3)_3\underline{C}O$), 65.3 (Pyr C-2), 65.1 (Pyr C-2), 49.0 (CH), 48.0 (CH), 46.7 (Pyr), 46.6 (Pyr), 29.7 (Pyr), 29.3 (Pyr C-3), 28.5 ($(CH_3)_3$), 28.2 ($(CH_3)_3$), 24.0 (Pyr), 23.1 (Pyr), 18.7 (CH_3), 18.7 (CH_3).

HRMS (ESI), *m/z*: calcd. for $C_{18}H_{25}NNaO_3$ 326.1727 $[M+Na]^+$; found: 326.1732.

$[\alpha]_D$ = -72.45 (*c* 0.5, $CHCl_3$).

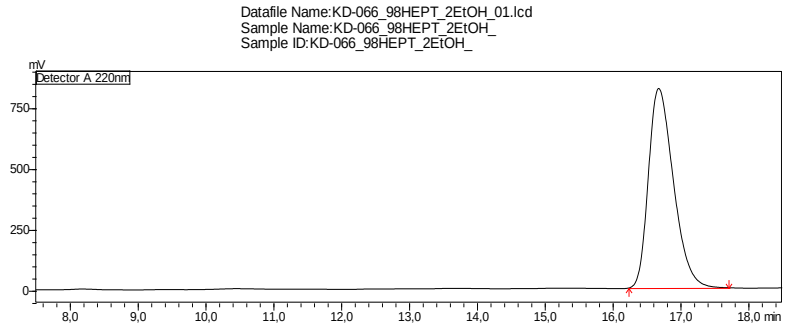
HPLC analysis: Chiralpak IC Column, λ 220 nm, eluent: *n*-heptane / ethanol 98/02. Flow: 1 mL/min

Mixture of steroisomers



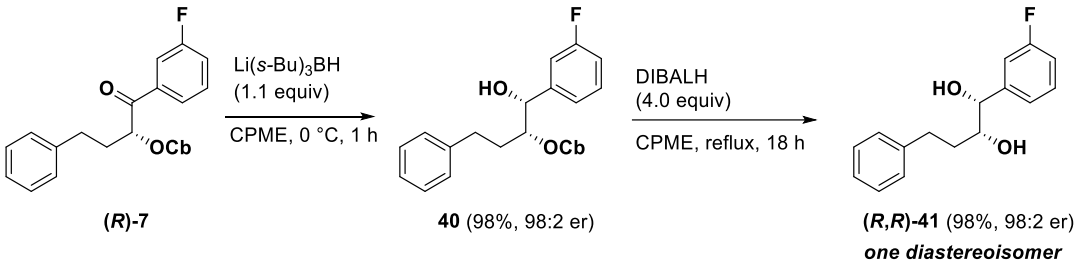
Peaks	Retention time (min)	Area	Area%
1 + 2	10,467 + 10,875	5644174	50,589
3	13,263	2605175	23,350
4	16,959	2907573	26,061
total		11156922	100,000

***One steroisomer* (*R*,*R*)-39**



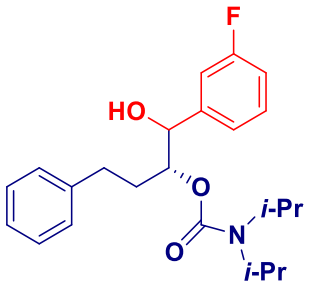
Peaks	Retention time (min)	Area	Area%
1	16,680	21001961	100
total		21001961	100,000

Synthetic manipulation of chiral α-oxyketones:



(*R*)-7 **40** (98%, 98:2 er) **(*R*,*R*)-41** (98%, 98:2 er)
one diastereoisomer

(2*R*)-1-(3-Fluorophenyl)-1-hydroxy-4-phenyl-2-butanyl diisopropylcarbamate, ((*R*)-40)



L-selectride 1M in THF (0.135 mL, 0.135 mmol, 2.0 equiv) was added dropwise to a stirred solution of **(*R*)-7** (0.026 g, 0.067 mmol, 1.0 equiv) in dry CPME (1 mL) at 0 °C for 1h. Then aqueos NaOH 10% was added and stirred 5 min before CPME was added and the phases were separated. Purification by column chromatography on silica gel (80:20 hexane/EtOAc). Compound **(*R*)-40** was obtained in 98% yield (0.025 g) as transparent oil.

Racemic reference was prepared from racemic ketone using $NaBH_4$ as reducing agent (4 stereoisomers).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (m, 1H, Ph^{1} H-5), 7.25 (m, 2H, Ph H-3,5), 7.17 (m, 1H, Ph H-4), 7.10 (m, 2H, Ph H-2), 7.08 (m, 3H, Ph H-2,6; Ph^{1} H-2), 6.97 (m, 1H, Ph^{1} H-4), 4.97 (m, 1H, C<u>H</u>OC=O), 4.73 (d, *J* = 6.7 Hz, 1H, C<u>H</u>OH), 3.93 (br s, 2H, C<u>H</u>CH_3), 3.83 (br, 1H, CHO<u>H</u>), 2.71-2.59 (m, 2H, PhC<u>H</u>$_2$), 1.92-1.74 (m, 2H, C<u>H</u>$_2$CH), 1.27-1.20 (br s, 12H, C<u>H</u>$_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ 162.8 (d, *J* = 246.0 Hz, Ph^{1} C-3), 156.1 (N<u>C</u>=O), 143.8 (d, *J* = 6.8 Hz, Ph^{1} C-1), 141.2 (Ph C-1), 129.8 (d, *J* = 8.1 Hz, Ph^{1} C-5), 128.3 (Ph C-3,5), 128.2 (Ph C-2,6), 126.0 (Ph C-4), 122.5 (d, *J* = 2.9 Hz, Ph^{1} C-6), 114.7 (d, *J* = 21.7 Hz, Ph^{1} C-4), 113.9 (d, *J* = 21.9 Hz, Ph^{1} C-2), 78.3 (<u>C</u>HOC=O), 46.4 (br <u>C</u>HCH_3), 45.9 (br <u>C</u>HCH_3), 32.6 (<u>C</u>$_2$CH), 31.9 (Ph<u>C</u>$_2$),), 21.4 (2×<u>C</u>H_3), 20.5 (<u>C</u>H_3), 20.4 (<u>C</u>H_3).

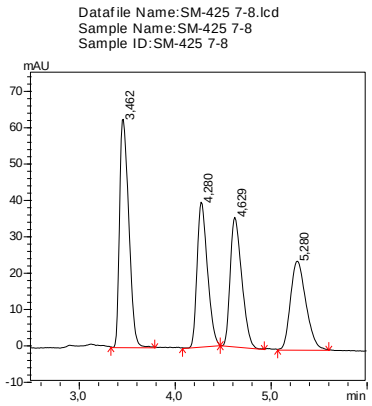
^{19}F NMR (376 MHz, $CDCl_3$): δ -113.0 (m).

HRMS (ESI), *m/z*: calcd. for $C_{23}H_{31}FNO_3$ 388.2282$[M+H]^+$; found 388.2281.

[α]$_D$ +34 (*c* 0.5, $CHCl_3$).

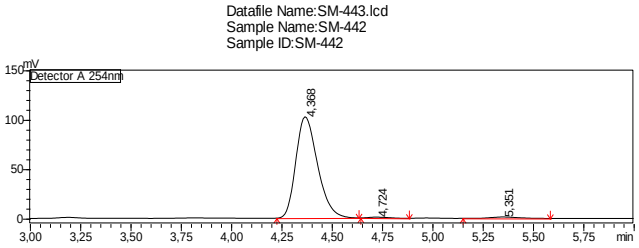
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 80/20. Flow: 1 mL/min

Stereoisomers mixture



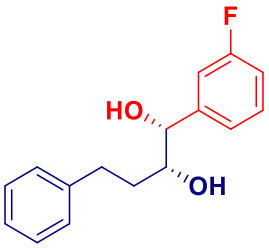
Peaks	Retention time (min)	Area	Area%
1	3,462	414231	32,698
2	4,280	292889	23,120
3	4,629	290898	22,963
4	5,280	268821	21,220
total		1266838	100,000

***Diastereoisomer* (*R*)-40**



Peaks	Retention time (min)	Area	Area%
1	4,368	770182	97,597
2	4,724	6009	0,761
3	5,351	12958	1,642
total		789149	100,000

(1*R,2R*)-1-(3-Fluorophenyl)-4-phenyl-1,2-butanediol, ((*R,R*)-41)



DIBAL-H (1M in THF, 0.66 mL, 0.66 mmol, 10 equiv) was added dropwise to a stirred solution of **(*R*)-40** (0.025 g, 0.066 mmol, 1.0 equiv) in dry CPME (2 mL) at room temperature. The reaction mixture refluxed for 18 h at 70 °C. Then aqueos NaOH 20% was added and stirred 5 min before CPME was added and the phases separated. Compound **(*R,R*)-41** was obtained by crystallization from CPME in 98% yield (0.016 g) as a white solid; mp 90-94 °C

Racemic reference was prepared from stereoisomeric mixture.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.07 (m, 1H, *m*-F Ph H-6), 7.04 (m, 1H, *m*-F Ph H-2), 7.30 (m, 1H, *m*-F Ph H-5), 7.26 (m, 2H, Ph H-3,5), 7.17 (m, 1H, Ph H-4), 7.12 (m, 2H, Ph H-2,6), 6.99 (m, 1H, *m*-F Ph H-4), 4.47 (d, *J* = 6.5 Hz, 1H, PhC<u>H</u>OH), 3.68 (m, 1H, CH_2C<u>H</u>OH), 2.84 (m, 1H, PhC<u>H_2</u>), 2.62 (m, 1H, PhC<u>H_2</u>), 2.44 (br s,2H, CHO<u>H</u>), 1.79-1.61 (m, 1H, C<u>H_2</u>CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ 162.9 (d, *J* = 246.5 Hz, *m*-F Ph C-3), 143.7 (d, *J* = 6.8 Hz, *m*-F Ph C-1), 141.5 (Ph C-1), 130.0 (d, *J* = 8.2 Hz, *m*-F Ph C-5), 128.4 (Ph C-3,5), 128.3 (Ph C-2,6), 125.9 (Ph C-4), 122.4 (d, *J* = 2.9 Hz, *m*-F Ph C-6), 115.0 (d, *J* = 21.2 Hz, *m*-F Ph C-4), 113.7 (d, *J* = 21.9 Hz, *m*-F Ph C-2), 77.2 (d, *J* = 1.7 Hz, PhC<u>H</u>OH), 75.1 (CH_2<u>C</u>HOH), 34.3 (<u>C</u>H_2CH), 31.9 (Ph<u>C</u>H_2).

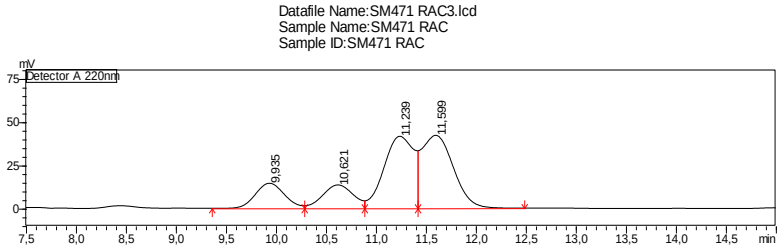
^{19}F NMR (376 MHz, $CDCl_3$): δ -112.5 (m).

HRMS (ESI), *m/z*: calcd. for $C_{16}H_{17}FNaO_2$ 283.1105 $[M+Na]^+$; found 283.1099.

$[\alpha]_D$ +22 (*c* 0.5, $CHCl_3$).

HPLC analysis: Chiralpak IG Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 90/10. Flow: 1 mL/min

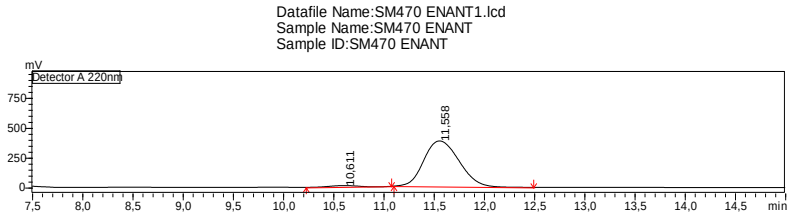
Mixture 4 stereoisomers



Peaks	Retention time (min)	Area	Area%

1	9,935	291194	12,305
2	10,621	284508	12,023
3	11,239	862553	36,450
4	11,599	928158	39,222
total		2366413	100,000

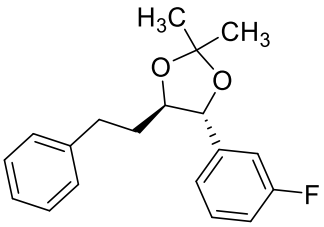
***Diasteroisomer* (*R,R*)-41**



Peaks	Retention time (min)	Area	Area%
1	10,611	142042	1,510
2	11,558	9266134	98,490
total		9408176	100,000

Proof of configuration at C1 center through transformation of 1,2-diol **41** into corresponding acetonide :

(4*R*,5*R*)-4-(3-Fluorophenyl)-2,2-dimethyl-5-(2-phenethyl)-1,3-dioxolane:



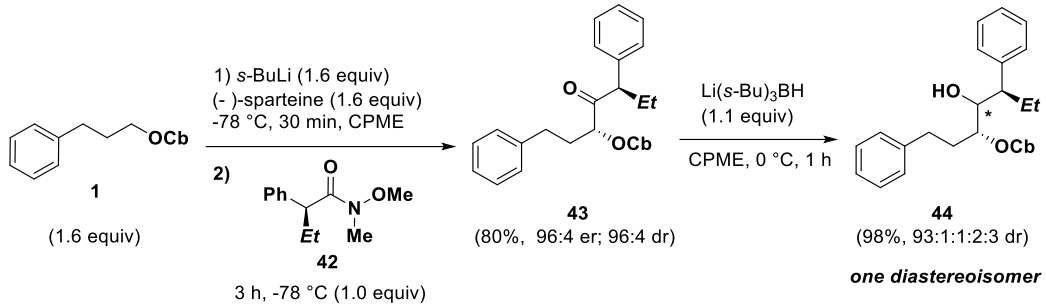
Compound **41** *syn* (0.007 g, 0.027 mmol, 1.0 equiv), 10-camphorsulfonic acid (0.006 g, 27 x 10^{-4} mmol, 10 mol%), MS3A (0.600 g), and 2,2-dimethoxypropane (10 μL, 0.081 mmol, 3.0 equiv), were added to dichloromethane (1.0 mL) at RT under argon. The reaction mixture was stirred for 1 h, then saturated aqueous $NaHCO_3$ was added. MS3A was removed from the reaction mixture by filtration and the aqueous layer was extracted twice with dichloromethane. The combined organic layer was washed with brine, dried over Na_2SO_4, and evaporated. The residue was purified by silica-gel column chromatography (hexane/EtOAc = 95:5) to give acetonide in 80 % yield (0.006 g) as a transparent oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.31 (m, 1H, *m*-F Ph H-5), 7.26 (m, 2H, Ph H-3,5), 7.18 (m, 1H, Ph H-4), 7.14 (m, 2H, Ph H-2,6), 7.11 (m, 1H, *m*-F Ph H-6), 7.09 (m, 1H, *m*-F Ph H-2), 7.0 (m, 1H, *m*-F Ph H-4), 4.56 (d, *J* = 8.5 Hz, 1H, *m*-F Ph C<u>H</u>), 3.77 (m, 1H, C<u>H</u>CH_2), 2.83 (m, 1H, PhC<u>H</u>$_2$), 2.63 (m, 1H, PhC<u>H</u>$_2$), 1.91 (m, 2H, C<u>H</u>$_2$CH), 1.57 (s, 3H, C<u>H</u>$_3$), 1.54 (s, 3H, C<u>H</u>$_3$).

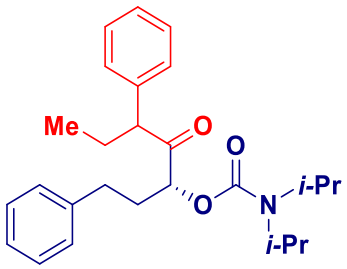
^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.0 (^1J= 246.3 Hz, *m*-F Ph C-3), 141.5 (Ph C-1), 140.7 (^3J= 7.1 Hz, *m*-F Ph C-1), 130.1 (^3J= 8.2 Hz, *m*-F Ph C-5), 128.4 (Ph C-3,5), 128.3 (Ph C-2,6), 125.9 (Ph C-4), 122.3 (^4J= 2.9 Hz, *m*-F Ph C-6), 115.2 (^2J= 21.2 Hz, *m*-F Ph C-4), 113.5 (^2J= 22.2 Hz, *m*-F Ph C-2), 109.0 (<u>C</u>$(CH_3)_2$), 82.6 (*m*-F Ph <u>C</u>H), 82.5 (<u>C</u>HCH_2), 33.3 (CH<u>C</u>H$_2$), 32.2 (<u>C</u>H$_2$Ph), 27.4 (<u>C</u>H$_3$), 26.9 (<u>C</u>H$_3$).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -112.7 (m)

HRMS (ESI), *m/z*: calcd. For $C_{19}H_{21}FNaO_2$ 323.1418 $[M+Na]^+$; found 323.1416



(2*R*)-4-Oxo-1,5-diphenyl-3-heptanyl diisopropylcarbamate, (*rac*-43)



Synthesized according to **GP1** using **1** (0.077g, 0.294 mmol, 1.5 equiv); (-)-sparteine (0.073 g, 0.313 mmol, 1.6 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and *N*-methoxy-*N*-methyl-2-phenylbutanamide (0.047 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound ***rac*-43** was obtained in 75% yield (0.060 g) as a white solid; mp 132-135 °C.

Major diastereoisomer:

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (m, 2H, Ph^1 H-3,5), 7.25 (m, 3H, Ph^1 H-4), 7.24 (m, 3H, Ph^1 H-2,6), 7.21 (m, 2H, Ph H-3,5), 7.15 (m, 1H, Ph H-4), 6.89 (m, 2H, Ph H-2,6), 5.09 (dd, *J* = 7.7 Hz, 4.0 Hz, 1H, C<u>H</u>C=O), 4.04 (br s, 1H, C<u>H</u>CH_3), 3.84 (br s, 1H, C<u>H</u>CH_3), 3.76 (dd, *J* = 8.2 Hz, 6.7 Hz,1H, CHPh), 2.53 (m,

1H, PhC$\underline{H}_2$), 2.40 (m, 1H, PhC$\underline{H}_2$), 1.77 (m, 2H, C$\underline{H}_2$CH), 2.10 (m, 1H, C$\underline{H}_2$CH$_3$), 1.74 (m, 1H, C$\underline{H}_2$CH$_3$), 1.37-1.17 (br, 12H, C$\underline{H}_3$), 0.82 (t, *J* = 7.4 Hz, 3H, CH$_2$C$\underline{H}_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ 207.6 (C=O), 154.7 (N$\underline{C}$=O), 140.9 (Ph C-1), 138.0 (Ph^1 C-1), 128.8 (Ph^1 C-3,5), 128.6 (Ph^1 C-2,6), 128.25 (Ph C-2,6), 128.4 (Ph C-3,5), 127.3 (Ph^1 C-4), 126.0 (Ph C-4), 77.6 ($\underline{C}$HC=O), 57.4 ($\underline{C}$HPh), 46.7 (br $\underline{C}$HCH$_3$), 45.6 (br $\underline{C}$HCH$_3$), 32.3 ($\underline{C}$H$_2$CH), 31.5 (Ph$\underline{C}$H$_2$), 26.4 ($\underline{C}$H$_2$CH$_3$), 21.7 (br $\underline{C}$H$_3$), 21.5 (br, $\underline{C}$H$_3$), 20.5 (br 2×$\underline{C}$H$_3$), 11.9 (CH$_2\underline{C}$H$_3$).

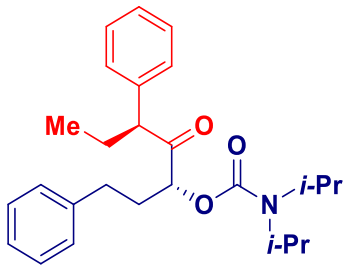
Minor diastereoisomer:

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (m, 2H, Ph^1 H-3,5), 7.28 (m, 3H, Ph^1 H-4), 7.24 (m, 3H, Ph^1 H-2,6), 7.21 (m, 2H, Ph H-3,5), 7.15 (m, 1H, Ph H-4), 7.01 (m, 2H, Ph H-2,6), 4.99 (dd, *J* = 8.3 Hz, 5.0 Hz, 1H, C$\underline{H}$C=O), 4.04 (br s, 1H, C$\underline{H}$CH$_3$), 3.84 (br s, 1H, C$\underline{H}$CH$_3$), 2.53-2.40 (m, 2H, PhC$\underline{H}_2$), 3.69 (dd, *J* = 8.3 Hz, 6.5 Hz,1H, CHPh), 2.10-1.74 (m, 2H, C$\underline{H}_2$CH$_3$), 1.77 (m, 2H, C$\underline{H}_2$CH), 1.37-1.17 (br, 12H, C$\underline{H}_3$), 0.78 (t, *J* = 7.4 Hz, 3H, CH$_2$C$\underline{H}_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ 208.3 (C=O), 154.4 (N$\underline{C}$=O), 140.9 (Ph C-1), 138.3 (Ph^1 C-1), 128.7 (Ph^1 C-3,5), 128.6 (Ph^1 C-2,6), 128.41 (Ph C-3,5), 128.27 (Ph C-2,6), 127.2 (Ph^1 C-4), 126.1 (Ph C-4), 78.6 ($\underline{C}$HC=O), 55.5 ($\underline{C}$HPh), 46.7 (br $\underline{C}$HCH$_3$), 45.6 (br $\underline{C}$HCH$_3$), 31.5 (Ph$\underline{C}$H$_2$), 32.3 ($\underline{C}$H$_2$CH), 26.1 ($\underline{C}$H$_2$CH$_3$), 21.7 (br $\underline{C}$H$_3$), 21.5 (br $\underline{C}$H$_3$), 20.5 (br 2 $\underline{C}$H$_3$), 12.0 (CH$_2\underline{C}$H$_3$).

HRMS (ESI), *m/z*: calcd. for $C_{26}H_{35}NNaO_3$ 432.2509[M+Na]$^+$; found 432.2513.

(3*R*, 5*S*)-4-Oxo-1,5-diphenyl-3-heptanyl diisopropylcarbamate, (43)



Synthesized according to **GP1** using **1** (0.077g, 0.294 mmol, 1.5 equiv); (-)-sparteine (0.073 g, 0.313 mmol, 1.6 equiv); *s*-BuLi 1.4 M (0.022 mL, 0.313 mmol, 1.6 equiv) in CPME (2 mL); and (*S*)-*N*-methoxy-*N*-methyl-2-phenylbutanamide (0.047 g, 0.196 mmol, 1.0 equiv) dissolved in CPME (1 mL); compound **43** was obtained in 80% NMR yield (calculated on the crude). The compound could not be purified and was directly used in the synthesis of **44** as mixture with Hoppe carbamate.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (m, 2H, Ph^1 H-3,5), 7.25 (m, 3H, Ph^1 H-4), 7.24 (m, 3H, Ph^1 H-2,6), 7.21 (m, 2H, Ph H-3,5), 7.15 (m, 1H, Ph H-4), 6.89 (m, 2H, Ph H-2,6), 5.09 (dd, *J* = 7.7 Hz, 4.0 Hz, 1H,

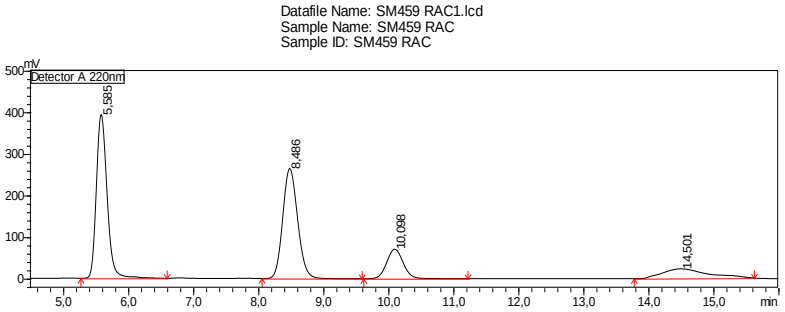
C<u>H</u>C=O), 4.04 (br s, 1H, C<u>H</u>CH$_3$), 3.84 (br s, 1H, C<u>H</u>CH$_3$), 3.76 (dd, *J* = 8.2 Hz, 6.7 Hz,1H, CHPh), 2.53 (m, 1H, PhC<u>H</u>$_2$), 2.40 (m, 1H, PhC<u>H</u>$_2$), 1.77 (m, 2H, C<u>H</u>$_2$CH), 2.10 (m, 1H, C<u>H</u>$_2$CH$_3$), 1.74 (m, 1H, C<u>H</u>$_2$CH$_3$), 1.37-1.17 (br, 12H, C<u>H</u>$_3$), 0.82 (t, *J* = 7.4 Hz, 3H, CH$_2$C<u>H</u>$_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ 207.6 (C=O), 154.7 (N<u>C</u>=O), 140.9 (Ph C-1), 138.0 (Ph^1 C-1), 128.8 (Ph^1 C-3,5), 128.6 (Ph^1 C-2,6), 128.25 (Ph C-2,6), 128.4 (Ph C-3,5), 127.3 (Ph^1 C-4), 126.0 (Ph C-4), 77.6 (<u>C</u>HC=O), 57.4 (<u>C</u>HPh), 46.7 (br <u>C</u>HCH$_3$), 45.6 (br <u>C</u>HCH$_3$), 32.3 (<u>C</u>H$_2$CH), 31.5 (PhC<u>H</u>$_2$), 26.4 (<u>C</u>H$_2$CH$_3$), 21.7 (br <u>C</u>H$_3$), 21.5 (br <u>C</u>H$_3$), 20.5 (br 2 <u>C</u>H$_3$), 11.9 (CH$_2$<u>C</u>H$_3$).

HRMS (ESI), *m/z*: calcd. for $C_{26}H_{35}NNaO_3$ 432.2509[M+Na]$^+$; found 432.2513.

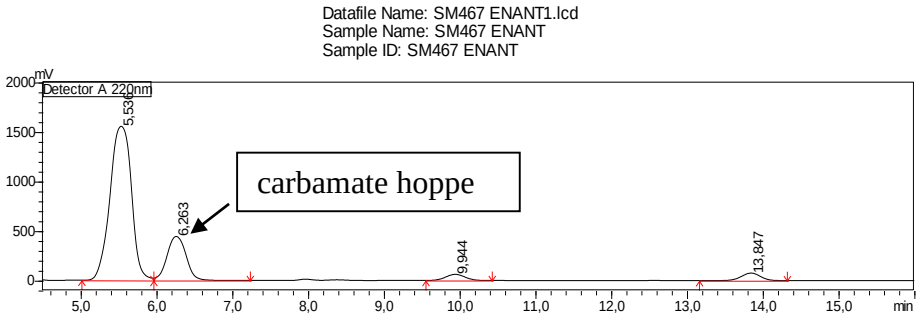
HPLC analysis: Chiralpak IG Column, λ220 nm, eluent: *n*-hexane / *i*-propanol 90/10. Flow: 1 mL/min

***Stereoisomers mixture rac*-43**



Peaks	Retention time (min)	Area	Area%
1	5,585	4506660	40,792
2	8,486	4181966	37,853
3	10,098	1248517	11,301
4	14,501	1110834	10,055
total		11047976	100

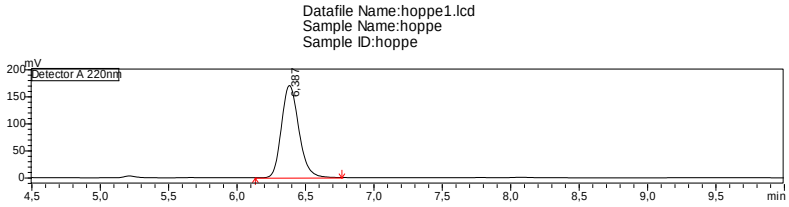
***Diastereoisomer* 43**



Peaks	Retention time (min)	Area	Area%
1	5,536	30548094	75,164
2	6,263	7706102	18,961
3	9,944	1082946	2,665
4	13,847	1304667	3,210
total		40641809	100,000

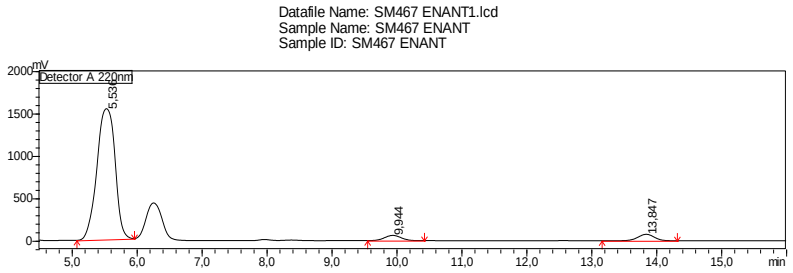
The ketone was reduced to alcohol althought the co-presence of carbamate precursor.

Carbamate Hoppe



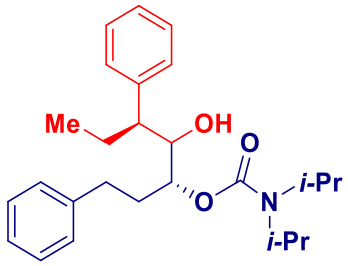
Peaks	Retention time (min)	Area	Area%
1	6,387	1504959	100,000
total		1504959	100,000

***Diastereoisomer* 43**



Peaks	Retention time (min)	Area	Area%
1	5,536	29939624	92,614
2	9,944	1082946	3,350
3	13,847	1304667	4,036
total		32327237	100,000

(3*R*, 5*S*)-4-Hydroxy-1,5-diphenyl-3-heptanyl diisopropylcarbamate (44)



L-selectride (1M in THF, 0.158 mL, 0.158 mmol, 2.0 equiv) was added dropwise to a stirred solution of **43** (0.032 g, 0.079 mmol, 1.0 equiv) in dry CPME (3 mL) at 0 °C for 1h. Then aqueos NaOH 10% was added and stirred 5 min before CPME was added and the phases were separated. Purification by column chromatography on alumina II grade (95:05 hexane/EtOAc). Compound **44** was obtained in 98% yield (0.031 g) as a transparent oil.

Racemic reference was prepared from stereoisomers mixture ***rac*-43** using $NaBH_4$ as reducing agent (four stereoisomers).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (m, 2H, Ph^1 H-3,5), 7.28 (m, 2H, Ph H-3,5), 7.23 (m, 3H, Ph^1 H-2,4,6), 7.19 (m, 1H, Ph H-4), 7.18 (m, 2H, Ph H-2,6), 4.98 (m, 1H, C<u>H</u>OC=O), 4.02 (br s, 1H, C<u>H</u>CH_3), 3.96 (m,1H, C<u>H</u>OH), 3.80 (br s, 1H, C<u>H</u>CH_3), 2.77 (m, 1H, PhC<u>H</u>$_2$), 2.63 (m, 1H, PhC<u>H</u>$_2$), 2.58 (m, 1H, CHPh), 2.08 (m, 1H, C<u>H</u>$_2$CH), 1.86 (m, 1H, C<u>H</u>$_2$CH), 1.72 (m, 2H, C<u>H</u>$_2$$CH_3$), 1.25 (br s, 6H, C<u>H</u>$_3$), 1.24 (br s, 6H, C<u>H</u>$_3$), 0.71 (t, *J* = 7.4 Hz, 3H, CH_2C<u>H</u>$_3$).

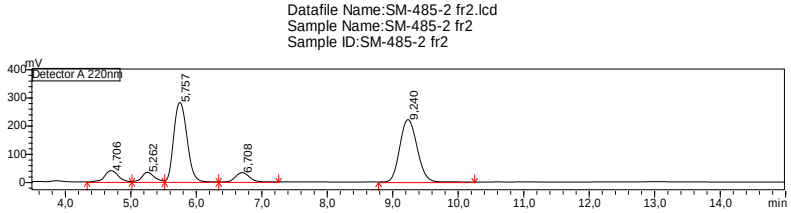
^{13}C NMR (100 MHz, $CDCl_3$): δ 155.2 (N<u>C</u>=O), 141.9 (Ph C-1), 141.0 (Ph^1 C-1), 129.0 (Ph^1 C-2,6), 128.43 (Ph^1 C-3,5), 128.37 (Ph C-3,5), 128.35 (Ph C-2,6), 126.7 (Ph^1 C-4), 125.9 (Ph C-4), 76.1 (<u>C</u>HOH), 75.8 (<u>C</u>HOC=O), 50.4 (<u>C</u>HPh^1), 46.3 (br <u>C</u>HCH_3), 45.5 (br <u>C</u>HCH_3), 32.2 (Ph<u>C</u>H$_2$), 31.0 (<u>C</u>H$_2$CH), 25.2 (<u>C</u>H$_2$$CH_3$), 21.6 (br, 2<u>C</u>H$_3$), 20.6 (br, 2×<u>C</u>H$_3$), 12.1 ($CH_2$<u>C</u>H$_3$).

HRMS (ESI), *m/z*: calcd. for $C_{26}H_{38}NO_3$ 412.2846 $[M+H]^+$; found 412.2855.

[α]$_D$ +27 (*c* 0.5, $CHCl_3$).

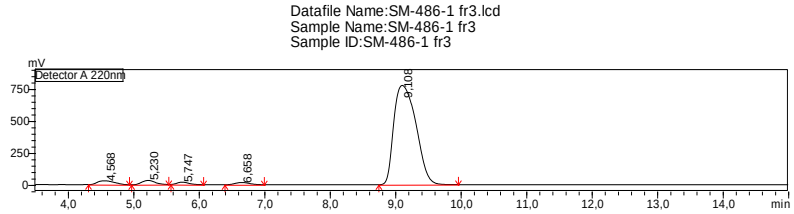
HPLC analysis: Chiralpak IC Column, λ 220 nm, eluent: *n*-hexane / *i*-propanol 95/5. Flow: 1 mL/min

diastereoisomers mixture *rac*-44

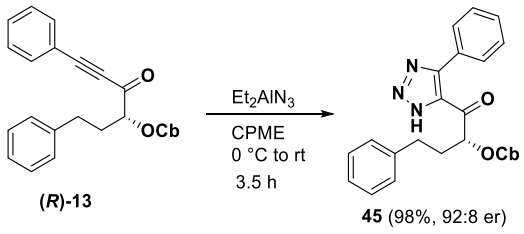


Peaks	Retention time (min)	Area	Area%
1	4,706	572997	6,031
2	5,262	449569	4,732
3	5,757	3973453	41,825
4	6,708	479884	5,051
5	9,240	4024297	42,360
total		9500202	100,000

***Diastereoisomer* 44**



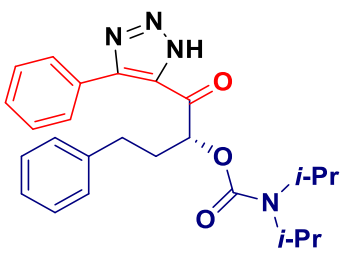
Peaks	Retention time (min)	Area	Area%
1	4,568	524039	2,656
2	5,230	456115	2,312
3	5,747	232549	1,179
4	6,658	255756	1,296
5	9,108	18261636	92,557
total		19730096	100,000



(*R*)-13

45 (98%, 92:8 er)

(*R*)-1-Oxo-4-phenyl-1-(4-phenyl-1H-1,2,3-triazol-5-yl)-2-butanyl diisoproprylcarbamate, ((*R*)-45)



An oven-dried flask was charged with sodium azide (0.027 g, 0.041 mmol, 4.0 equiv) and diethylaluminum chloride 0.9 M (0.45 mL, 0.041 mmol, 4.0 equiv) in CPME (1.0 mL) at 0 °C under argon and stirred for 15 min. The white heterogeneous mixture was then warmed to room temperature and stirred for 6 hours. During the formation of the reagent, a suspension of sodium chloride was formed. A solution of **(*R*)-13** (0.040 g, 0.102 mmol, 1.0 equiv) in CPME (0.5 mL) was added at 0 °C. The mixture was gradually heated to room temperature and stirred for 3.5 hours. The reaction mixture was cooled to 0 °C and it was quenched with water. The two resulting phases were separated, and the organic phase was dried over anhydrous $NaSO_4$ and filtered. Compound **(*R*)-45** was obtained by crystallization from CPME in 98% yield (0.043 g) as a white solid; mp 133-135 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ 13.92 (br s, 1H, triazole NH), 7.76 (m, 2H, Ph^1 H-2,6), 7.34 (m, 3H, Ph^1 H-3,4,5), 7.25 (m, 2H, Ph H-3,5), 7.17 (m, 2H, Ph H-2,6), 7.16 (m, 1H, Ph H-4), 6.21 (dd, *J* = 8.9 Hz, 3.9 Hz, 1H, C<u>H</u>C=O), 4.10 (m, 1H, C<u>H</u>CH_3), 3.92 (m, 1H, C<u>H</u>CH_3), 2.84 (m, 2H, Ph$C\underline{H}_2$), 2.31-2.21 (m, 2H, $C\underline{H}_2$CH), 1.27 (br m, 6H, $C\underline{H}_3$), 1.40 (br m, 3H, $C\underline{H}_3$), 1.37 (br m, 3H, $C\underline{H}_3$).

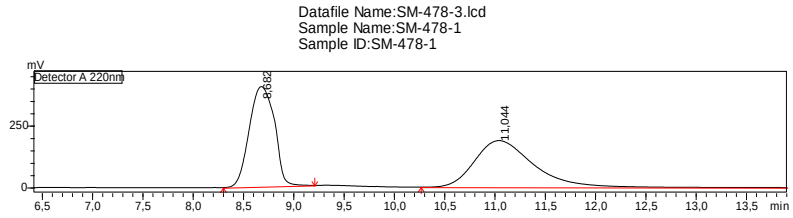
^{13}C NMR (100 MHz, $CDCl_3$): δ 191.4 (triazole-<u>C</u>=O), 155.5 (N<u>C</u>=O), 141.1 (Ph C-1), 139.2 (Ph^1 C-1), 129.4 (Ph^1 C-4), 128.9 (Ph^1 C-2,6), 128.4 (Ph C-3,5), 128.3 (Ph C-2,6), 128.2 (Ph^1 C-3,5), 126.0 (Ph C-4), 76.9 (<u>C</u>HC=O), 46.9 (<u>C</u>HCH_3), 46.1 (<u>C</u>HCH_3), 33.0 ($\underline{C}H_2CH$), 32.0 (Ph$\underline{C}H_2$), 21.7, 21.3, 20.5 (4×$\underline{C}H_3$).

HRMS (ESI), *m/z*: calcd. for $C_{25}H_{30}N_4NaO_3$ 457.2210 $[M+Na]^+$; found 457.2215.

$[\alpha]_D$ -39 (*c* 0.5, $CHCl_3$).

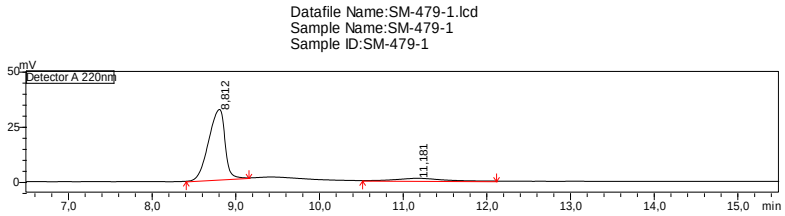
HPLC analysis: Chiralpak IC Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 95/5. Flow: 1 mL/min

Racemate

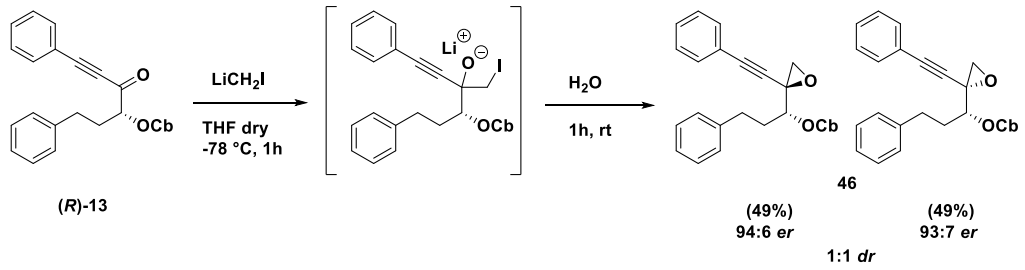


Peaks	Retention time (min)	Area	Area%
1	8,682	404103	47,896
2	11,044	188490	52,104
total		592593	100,000

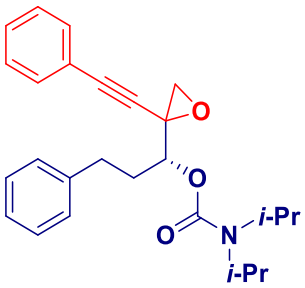
***Enantioenriched* (*R*)-45**



Peaks	Retention time (min)	Area	Area%
1	8,812	31708	91,810
2	11,181	8,190	8,190
total		32851	100,000



(2*R*)-4,5-Anhydro-1,2-dideoxy-3-0-(diisopropylcarbamoyl)-1-phenyl-4-(phenylethynyl)pentitol, (46)



A solution of **(*R*)-13** (0.030 mg, 0.076 mmol, 1.0 equiv) in THF (0.38 mL) was cooled at −78 °C. Diiodomethane (0.062 g, 0.23 mmol, 3.0 equiv) was first added, followed by MeLi−LiBr complex 1.5 M solution in diethyl ether (0.14 mL, 0.21 mmol, 2.8 equiv). The resulting solution was stirred at that temperature for 1 h and at r.t. overnight. Water was added and the mixture was washed with Et_2O and brine. The two resulting phases were separated, and the organic phase was dried over anhydrous $NaSO_4$, filtered, and removed in vacuo to give the desired product as a mixture of two stereoisomers. Purification by column chromatography on alumina II grade a (95:5 hexane/EtOAc) allowed the separation of them. Compound **46a** and **46b** were obtained in 49% yield (0.015 g) as a transparent oils.

46a

^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.47-7.15 (m, 8H, Ph H, Ph^1 H-3,4,5), 7.45 (m, 2H, Ph^1 H-2,6), 4.85 (m, 1H, C<u>H</u>OC=O), 4.15 (br, 1H, C<u>H</u>CH_3), 3.73 (br, 1H, C<u>H</u>CH_3), 3.12 (d, *J* = 5.4 Hz, CH-epoxide), 2.93 (d, *J* = 5.4 Hz, CH-epoxide), 2.82-2.68 (m, 2H, PhC<u>H_2</u>), 2.24-2.17 (m, 2H, C<u>H_2</u>CH), 1.40-1.13 (br, 12H, CH_3).

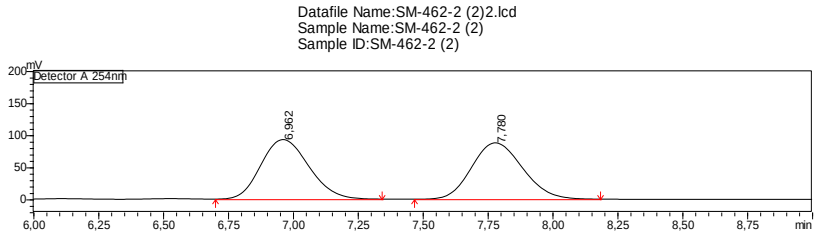
^{13}C NMR (100 MHz, CD_2Cl_2): δ 155.2 (N<u>C</u>=O), 142.0 (Ph C-1), 132.3 (Ph^1 C-2,6), 129.3 (Ar), 128.8 (Ph C(2x)), 128.7 (Ar), 126.4 (Ph C-4), 122.3 (Ph^1 C-1), 85.7 (<u>C</u>≡CPh), 84.7 (C≡<u>C</u>Ph), 75.3 (<u>C</u>HOC=O), 53.3 (CH_2-epoxide), 53.3 (C-epoxide), 47.3 (br, <u>C</u>HCH_3), 45.7 (br, <u>C</u>HCH_3), 34.2 (<u>C</u>H_2CH), 32.1 (Ph<u>C</u>H_2), 21.8 (br, <u>C</u>H_3), 20.6 (br, <u>C</u>H_3).

HRMS (ESI), *m/z*: calcd. for$C_{26}H_{32}NO_3$ 406.2377 $[M+H]^+$; found 406.2376.

[α]$_D$ +5 (*c* 0.5, $CHCl_3$).

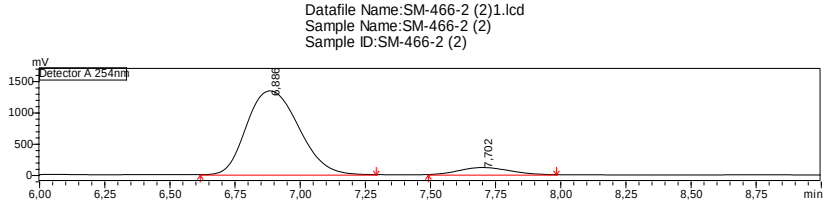
HPLC analysis: Chiralpak IA Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 95/5. Flow: 1 mL/min

two stereoisomers



Peaks	Retention time (min)	Area	Area%
1	6,962	1192874	49,849
2	7,780	1200081	50,151
total		2392955	100,000

***Stereoisomer* 46a**



Peak	Retention time (min)	Area	Area%
1	6,886	18567220	92,582
2	7,702	1487636	7,418
total		20054856	100,000

46b

^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.45-7.16 (m, 8H, Ph H, Ph^1 H-3,4,5), 7.44 (m, 2H, Ph^1 H-2,6), 4.59 (m, 1H, C<u>H</u>OC=O), 4.10 (br, 1H, C<u>H</u>CH_3), 3.76 (br, 1H, C<u>H</u>CH_3), 3.12 (A-part of an AB-system, $^2J_{AB}$ = 5.8 Hz, CH-epoxide), 3.09 (B-part of an AB-system, $^2J_{AB}$ = 5.4 Hz, CH-epoxide), 2.85-2.71 (m, 2H, Ph<u>C</u>H_2), 2.26-2.20 (m, 2H, <u>C</u>H_2CH), 1.38-1.13 (br, 12H, CH_3).

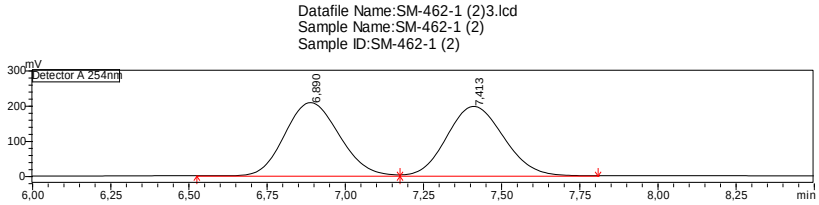
^{13}C NMR (100 MHz, CD_2Cl_2): δ 155.0 (N<u>C</u>=O), 142.1 (Ph C-1), 132.2 (Ph^1 C-2,6), 129.2 (Ph^1 C-4), 128.81 (Ar), 128.76 (Ar), 128.75 (Ar), 126.3 (Ph C-4), 122.4 (Ph^1 C-1), 85.8 (<u>C</u>≡CPh), 84.7 (C≡<u>C</u>Ph), 75.1 (<u>C</u>HOC=O), 54.8 (CH_2-epoxide), 52.2 (C-epoxide) 33.9 (<u>C</u>H_2CH), 32.0 (Ph<u>C</u>H_2), 21.8 (br <u>C</u>H_3), 20.7 (br, <u>C</u>H_3), <u>C</u>HCH_3 not unambiguously identified.

HRMS (ESI), *m/z*: calcd. for $C_{26}H_{32}NO_3$ 406.2377 $[M+H]^+$; found 406.2376.

[α]$_D$+12 (*c* 0.5, $CHCl_3$).

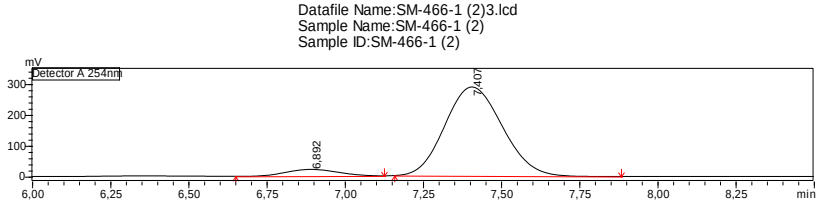
HPLC analysis: Chiralpak IC Column, λ 250 nm, eluent: *n*-hexane / *i*-propanol 95/5. Flow: 1 mL/min

two stereoisomers



Peaks	Retention time (min)	Area	Area%
1	6,890	2508428	50,229
2	7,413	2485573	49,771
total		4994001	100,000

***Stereoisomer* 46b**



Peaks	Retention time (min)	Area	Area%
1	6,892	246347	6,279

2	7,407	3677268	93,721
total		3923615	100,000

X-ray Analysis

The X-ray intensity data were measured on Bruker D8 Venture and X8 APEXII diffractometer equipped with multilayer monochromator, Mo and Cu K/α INCOATEC micro focus sealed tubes, Oxford and Kryoflex 2 cooling systems. The structure was solved by *direct methods* and refined by *full-matrix least-squares techniques*. Non-hydrogen atoms were refined with *anisotropic displacement parameters*. Hydrogen atoms were inserted at calculated positions and refined with riding model. The following software was used: *Bruker SAINT software package*[6] using a narrow-frame algorithm for frame integration, *SADABS*[7]for absorption correction, *OLEX2*[8] for structure solution, refinement, molecular diagrams and graphical user-interface, *Shelxle*[9] for refinement and graphical user-interface *SHELXS-2015*[10] for structure solution, *SHELXL-2015*[10] for refinement*, Platon*[11] for symmetry check. Experimental data and CCDC-Codes Experimental data and CCDC-Code (Available online: http://www.ccdc.cam.ac.uk/conts/retrieving.html) can be found in Table 1. Crystal data, data collection parameters, and structure refinement details are given in Tables 2 to 11. Crystal structures are visualized in Figures 1 to 5.

Table 1 Experimental parameter and CCDC-Code.

Sample	**Machine**	**Source**	**Temp.**	**Detector Distance**	**Time/ Frame**	**#Frames**	**Frame width**	**CCDC**
	Bruker		[K]	[mm]	[s]		[°]	
[(R,R)-24]	X8	MO	130	40	15	759	0.500	1871505
[(S,S)-24]	D8	CU	100	40	14	9624	0.500	1571506
[(R,R)-39]	X8	MO	100	35	4.4	6792	0.500	1871509
[(S)-3]	X8	MO	100	35	6	5208	0.500	1871507
[(R)-3]	D8	MO	100	40	60	6737	0.700	1871508

(2R,3R)-5-[methoxy(methyl)amino]-5-oxo-2,3-diphenyl-2-pentanyl diisopropylcarbamate, [(*R*,*R*)-24]

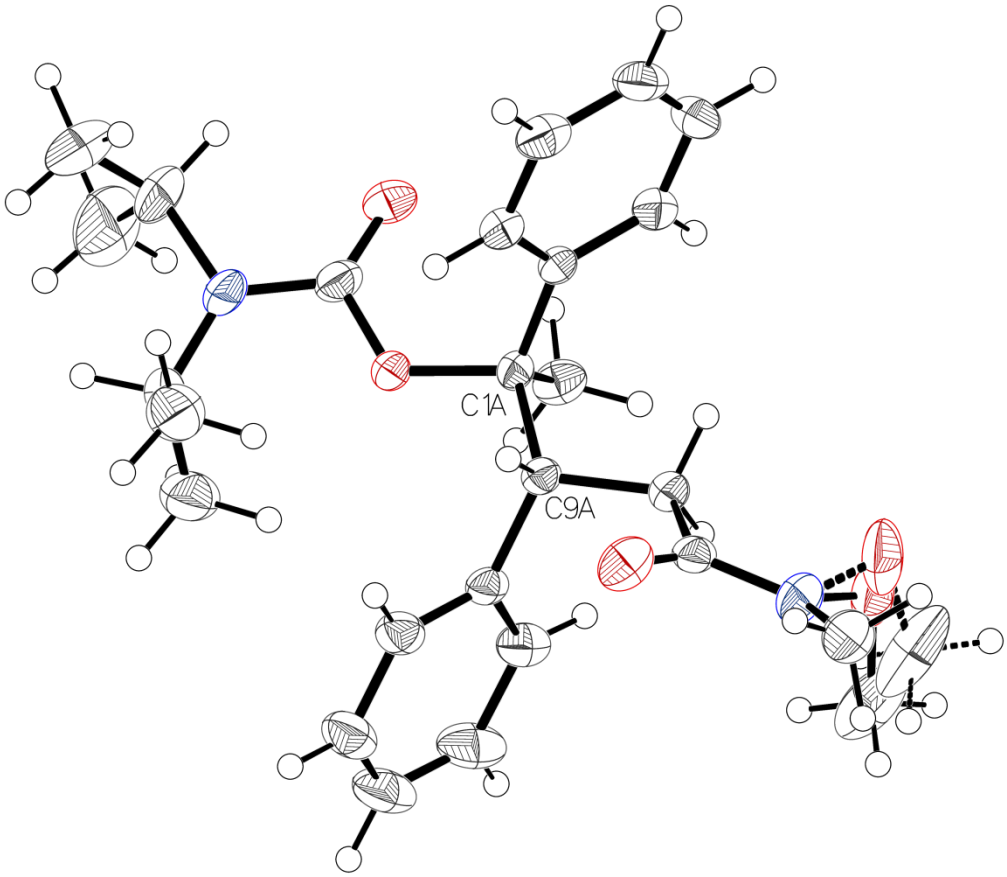


Figure 1 Crystal structure of **[(R,R)-24].** Anisotropic displacement ellipsoids visualized with 50% probability, second independent molecule of the asymmetric unit omitted for clarity. Chiral centres are proofed by Flack and Hooft parameter (-0.2(6)/ -0.3(4)). C1A, C9A (mol A), C1B, C9B (mol B) are in R-conformation. Bond precision: C-C = 0.0052 A. Degree of disorder in mol A is 6%, in mol B 28%.

Table 2 Sample and crystal data of **[(R,R)-24].**

Chemical formula	C26H36N2O4	**Crystal system**	monoclinic	
Formula weight [g/mol]	440.57	**Space group**	*C2*	
Temperature [K]	130	**Z**	8	
Measurement method	\f and \w scans	**Volume [Å^3]**	4961.2(5)	
Radiation (Wavelength [Å])	MoKα (λ = 0.71073)	**Unit cell dimensions [Å] and [°]**	40.480(3)	90
Crystal size / [mm^3]	0.4 × 0.15 × 0.06		6.4588(4)	115.105(2)
Crystal habit	clear colourless block		20.9553(11)	90

Density (calculated) / [g/cm^3]	1.18	**Absorption coefficient / [mm^{-1}]**	0.079
Abs. correction Tmin	0.6485	**Abs. correction Tmax**	0.746
Abs. correction type	multiscan	**F(000) [e$^-$]**	1904

Table 3 Data collection and structure refinement of **[(R,R)-24].**

Index ranges	-56 ≤ h ≤ 55, -9 ≤ k ≤ 8, -29 ≤ l ≤ 29	**Theta range for data collection [°]**	2.146 to 60.182	
Reflections number	23848	**Data / restraints / parameters**	14311/6/672	
Refinement method	Least squares	**Final R indices**	all data	R1 = 0.0865, wR2 = 0.1583
Function minimized	$\Sigma\, w(F_o^2 - F_c^2)^2$		I>2σ(I)	R1 = 0.0599, wR2 = 0.1409
Goodness-of-fit on F^2	1.033	**Weighting scheme**	$w=1/[\sigma^2(F_o^2)+(0.0700P)^2+1.9888P]$	
Largest diff. peak and hole [e Å^{-3}]	0.36/-0.36		where $P=(F_o^2+2F_c^2)/3$	

(2*S*,3*S*)-5-[methoxy(methyl)amino]-5-oxo-2,3-diphenyl-2-pentanyl diisopropylcarbamate, [(S,S)-24]

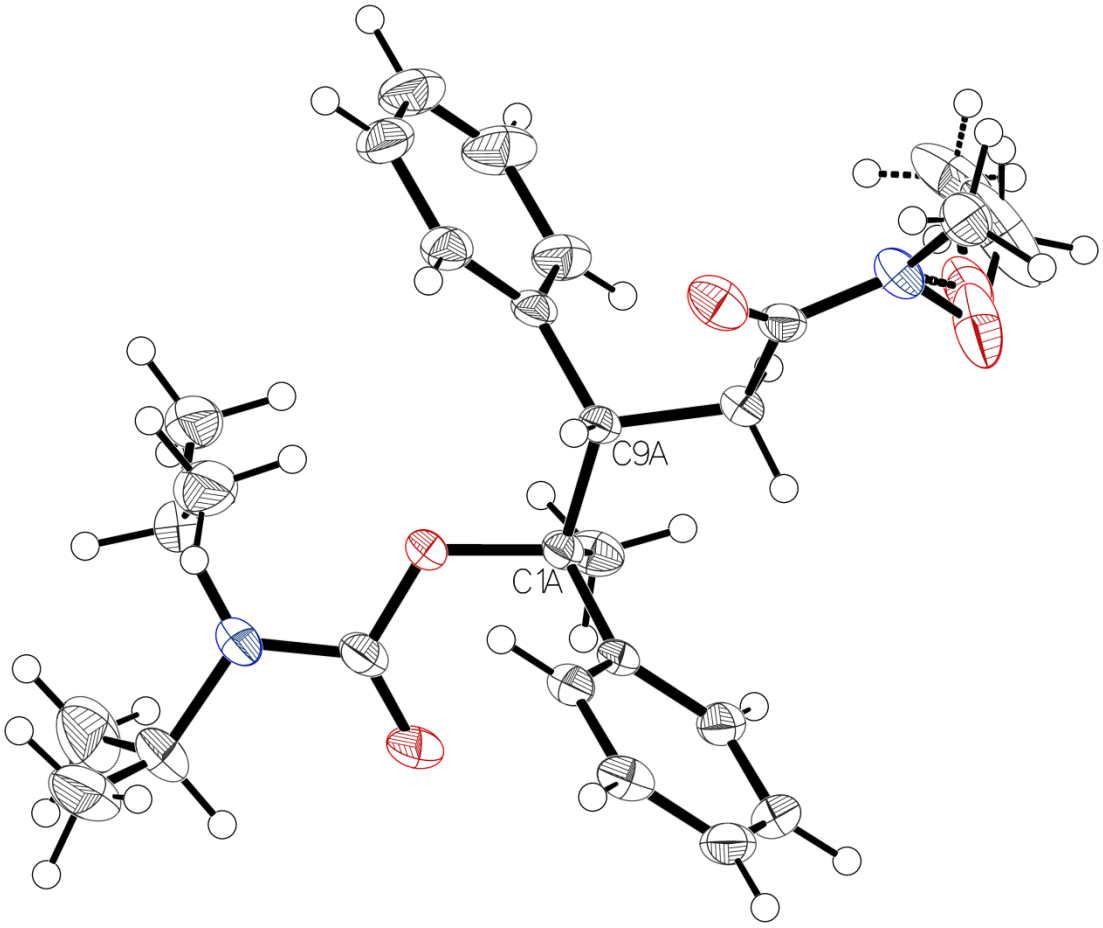


Figure 2 Crystal structure of **[(S,S)-24]**. Anisotropic displacement ellipsoids visualized with 50% probability, second independent molecule of the asymmetric unit omitted for clarity. Chiral centres are proofed by Flack and Hooft parameter (-0.06(9)/ -0.03(2)). C1A, C9A (mol A), C1B, C9B (mol B) are in S-conformation. Bond precision: C-C = 0.0041 A. Degree of disorder in mol A is 6%, in mol B 28% (identical as in **[(R,R)-24],** also the unit cell is very close).

Table 4 Sample and crystal data of **[(S,S)-24].**

Chemical formula	C26H36N2O4	**Crystal system**	monoclinic	
Formula weight [g/mol]	440.57	**Space group**	*C2*	
Temperature [K]	100	**Z**	8	
Measurement method	\f and \w scans	**Volume [Å^3]**	4958.3(3)	
Radiation (Wavelength [Å])	CuKα (λ = 1.54178)	**Unit cell dimensions [Å] and [°]**	40.5119(12)	90
Crystal size / [mm^3]	0.538 × 0.252 × 0.146		6.4473(2)	115.1286(11)

Crystal habit	clear colourless block		20.9677(6)	90
Density (calculated) / [g/cm^3]	1.18	**Absorption coefficient / [mm^{-1}]**	0.633	
Abs. correction Tmin	0.5632	**Abs. correction Tmax**	0.7542	
Abs. correction type	multiscan	**F(000) [e$^-$]**	1904	

Table 5 Data collection and structure refinement of **[(S,S)-24].**

Index ranges	$-51 \le h \le 50$, $-8 \le k \le 7$, $-26 \le l \le 26$	**Theta range for data collection [°]**	4.654 to 158.346	
Reflections number	87898	**Data / restraints / parameters**	10343/37/684	
Refinement method	Least squares	**Final R indices**	all data	R1 = 0.0518, wR2 = 0.1392
Function minimized	$\Sigma\, w(F_o^2 - F_c^2)^2$		$I>2\sigma(I)$	R1 = 0.0516, wR2 = 0.1388
Goodness-of-fit on F^2	1.012	**Weighting scheme**	$w=1/[\sigma^2(F_o^2)+(0.0927P)^2+3.0127P]$	
Largest diff. peak and hole [e Å^{-3}]	0.40/-0.33		where $P=(F_o^2+2F_c^2)/3$	

tert-butyl (2R)-2-[(2R)-2-phenylpropanoyl]pyrrolidine-1-carboxylate, [(R,R)-39]

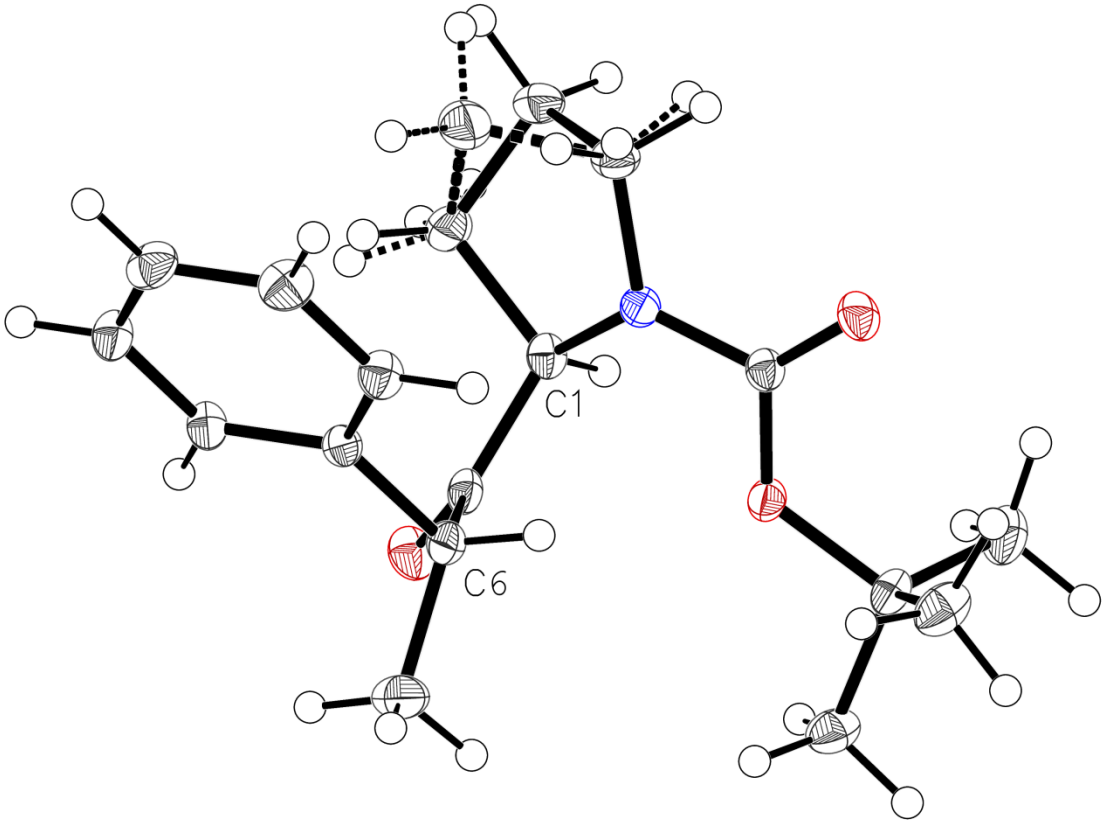


Figure 3 Asymmetric Unit of **[(R,R)-39]**. Anisotropic displacement ellipsoids visualized with 50% probability, second independent molecule of the asymmetric unit omitted for clarity. Chiral centres are proofed by Flack and Hooft parameter (--0.2(4)/ -0.1(3)). C1, C6 are in S-conformation. Bond precision: C-C = 0.0041 A. Degree of disorder is 6%.

Table 6 Sample and crystal data of **[(R,R)-39]**.

Chemical formula	C18H25NO3	**Crystal system**	monoclinic	
Formula weight [g/mol]	303.39	**Space group**	*P21*	
Temperature [K]	100	**Z**	2	
Measurement method	\f and \w scans	**Volume [Å^3]**	830.69(18)	
Radiation (Wavelength [Å])	MoKα (λ = 0.71073)	**Unit cell dimensions [Å] and [°]**	5.9751(7)	90
Crystal size / [mm^3]	0.4 × 0.1 × 0.1		17.5321(18)	104.061(6)
Crystal habit	clear colourless block		8.1747(12)	90
Density (calculated) / [g/cm^3]	1.213	**Absorption coefficient / [mm^{-1}]**	0.082	

Abs. correction Tmin	0.7579	**Abs. correction Tmax**	0.8879
Abs. correction type	multiscan	**F(000) [e^-]**	328

Table 7 Data collection and structure refinement of **[(R,R)-39]**.

Index ranges	$-8 \le h \le 8$, $-24 \le k \le 24$, $-11 \le l \le 11$	**Theta range for data collection [°]**	4.646 to 60.062	
Reflections number	60880	**Data / restraints / parameters**	4872/1/212	
Refinement method	Least squares	**Final R indices**	all data	R1 = 0.0388, wR2 = 0.0940
Function minimized	$\Sigma\, w(F_o^2 - F_c^2)^2$		I>2σ(I)	R1 = 0.0361, wR2 = 0.0921
Goodness-of-fit on F^2	1.035	**Weighting scheme**	$w=1/[\sigma^2(F_o^2)+(0.0465P)^2+0.1757P]$	
Largest diff. peak and hole [e $Å^{-3}$]	0.22/-0.20		where $P=(F_o^2+2F_c^2)/3$	

(S)-1-(3-bromophenyl)-1-oxo-4-phenyl-2-butanyl diisopropylcarbamate, [(S)-3]

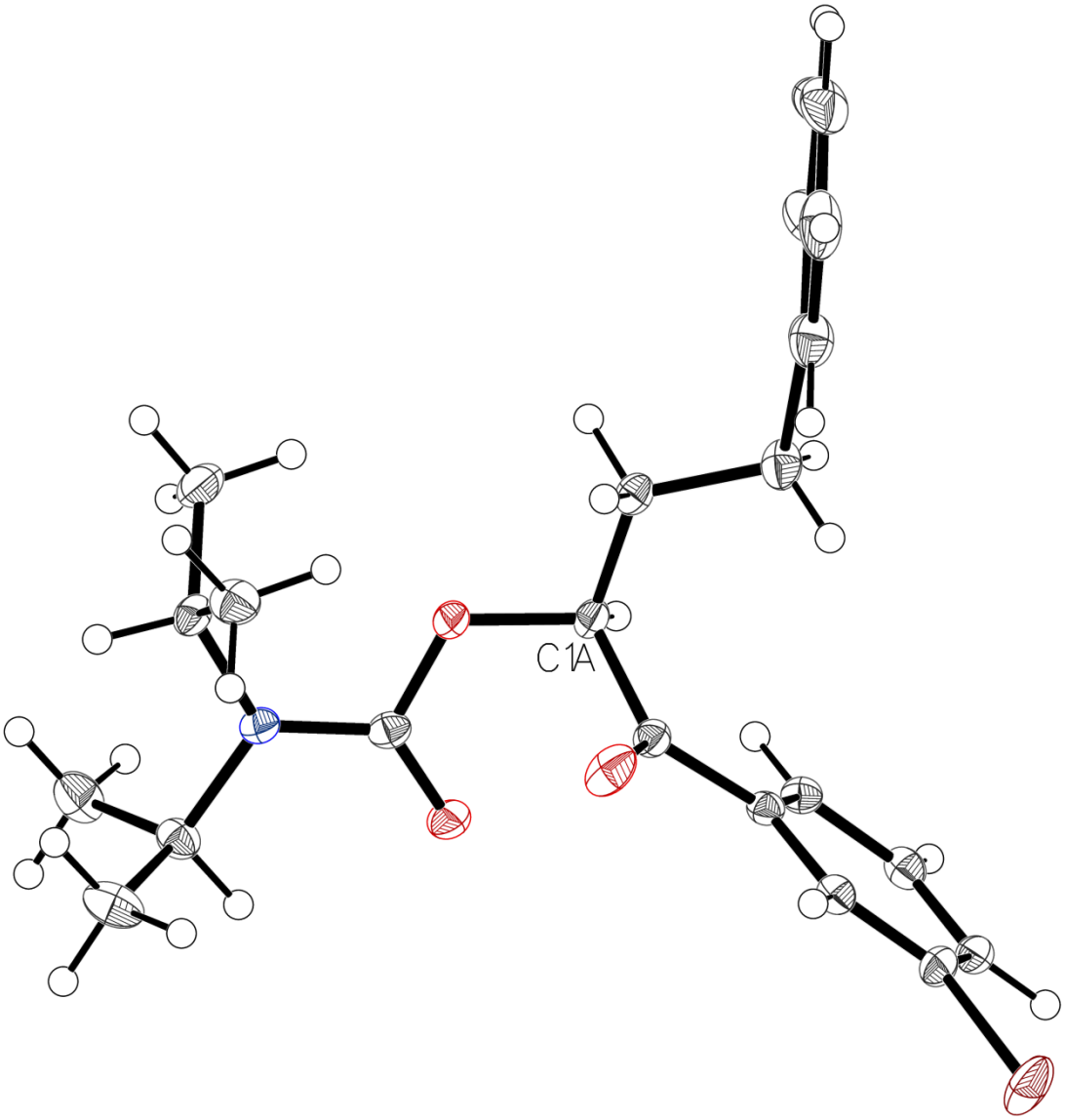


Figure 4 Asymmetric Unit of **[(S)-3]**. Anisotropic displacement ellipsoids visualized with 50% probability, second independent molecule of the asymmetric unit omitted for clarity. Chiral centres are proofed by Flack and Hooft parameter (0.022(3) / 0.034(3)). C1A (mol A), C1B (mol B) are in S-conformation. Bond precision: C-C = 0.0043 A.

Table 8 Sample and crystal data of **[(S)-3]**

Chemical formula	C23H28BrNO3	**Crystal system**	triclinic	
Formula weight [g/mol]	446.37	**Space group**	*P1*	
Temperature [K]	100	**Z**	2	
Measurement method	\f and \w scans	**Volume [Å³]**	1083.53(10)	
Radiation (Wavelength [Å])	MoKα (λ = 0.71073)	**Unit cell dimensions [Å] and [°]**	5.7959(3)	99.170(3)

Crystal size / [mm^3]	0.2 × 0.03 × 0.03		13.0795(7)	98.366(3)
Crystal habit	clear colourless block		14.8490(8)	98.188(3)
Density (calculated) / [g/cm^3]	1.368	**Absorption coefficient / [mm^{-1}]**	1.919	
Abs. correction Tmin	0.546	**Abs. correction Tmax**	0.746	
Abs. correction type	multiscan	**F(000) [e$^-$]**	464	

Table 9 Data collection and structure refinement of **[(S)-3]**

Index ranges	-8 ≤ h ≤ 8, -18 ≤ k ≤ 18, -21 ≤ l ≤ 20	**Theta range for data collection [°]**	4.64 to 61.108	
Reflections number	72072	**Data / restraints / parameters**	12925/3/513	
Refinement method	Least squares	**Final R indices**	all data	R1 = 0.0433, wR2 = 0.0691
Function minimized	$\Sigma\, w(F_o^2 - F_c^2)^2$		I>2σ(I)	R1 = 0.0323, wR2 = 0.0658
Goodness-of-fit on F^2	1.037	**Weighting scheme**	$w=1/[\sigma^2(F_o^2)+(0.0218P)^2]$	
Largest diff. peak and hole [e Å^{-3}]	0.46/-0.58		where $P=(F_o^2+2F_c^2)/3$	

(R)-1-(3-bromophenyl)-1-oxo-4-phenyl-2-butanyl diisopropylcarbamate, [(R)-3]

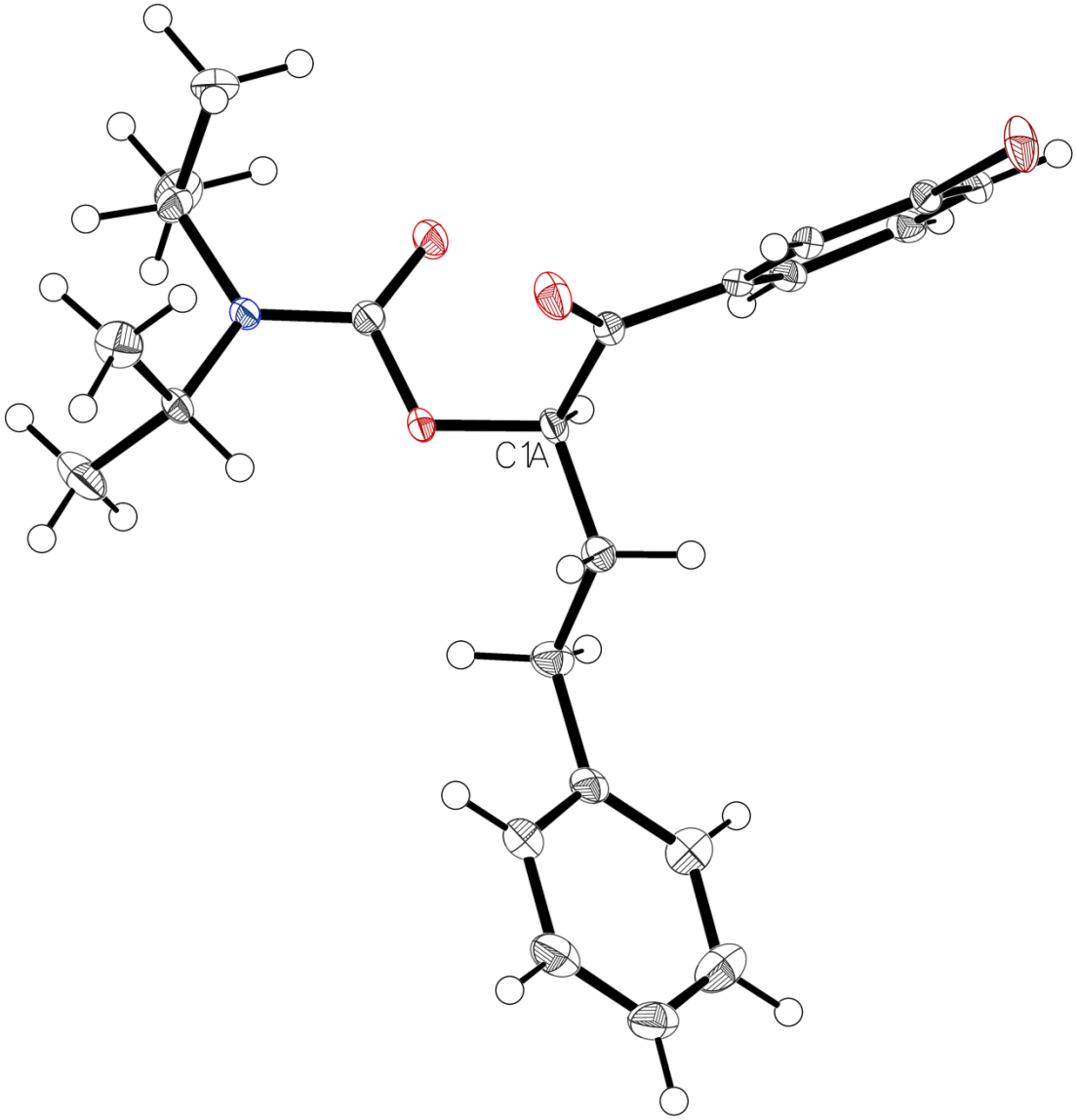


Figure 5 Crystal structure of **[(R)-3]**. Anisotropic displacement ellipsoids visualized with 50% probability, second independent molecule of the asymmetric unit omitted for clarity. Chiral centres are proofed by Flack and Hooft parameter (-0.009(6)/ -0.0086(19)). C1A (mol A), C1B (mol B) are in R-conformation. Bond precision: C-C = 0.0049 A. The unit cell of **[(S)-3]** is very close.

Table 10 Sample and crystal data of **[(R)-3]**

Chemical formula	C23H28BrNO3	**Crystal system**	triclinic	
Formula weight [g/mol]	446.37	**Space group**	*P1*	
Temperature [K]	100	**Z**	2	
Measurement method	\f and \w scans	**Volume [Å^3]**	1084.98(16)	
Radiation (Wavelength [Å])	MoKα (λ = 0.71073)	**Unit cell dimensions [Å] and [°]**	5.7915(5)	99.147(3)
Crystal size / [mm^3]	0.446 × 0.041 × 0.028		13.0931(11)	98.283(3)
Crystal habit	clear colourless block		14.8582(13)	98.156(3)
Density (calculated) / [g/cm^3]	1.366	**Absorption coefficient / [mm^{-1}]**	1.917	
Abs. correction Tmin	0.4964	**Abs. correction Tmax**	0.746	
Abs. correction type	multiscan	**F(000) [e$^-$]**	464	

Table 11 Data collection and structure refinement of **[(R)-3]**

Index ranges	-8 ≤ h ≤ 8, -18 ≤ k ≤ 18, -20 ≤ l ≤ 20	**Theta range for data collection [°]**	4.632 to 60.134	
Reflections number	45166	**Data / restraints / parameters**	12477/3/513	
Refinement method	Least squares	**Final R indices**	all data	R1 = 0.0433, wR2 = 0.0981
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$		I>2σ(I)	R1 = 0.0394, wR2 = 0.0959
Goodness-of-fit on F^2	1.076	**Weighting scheme**	$w=1/[\sigma^2(F_o^2)+(0.0608P)^2+0.2722P]$	
Largest diff. peak and hole [e Å^{-3}]	0.67/-0.67		where $P=(F_o^2+2F_c^2)/3$	

References.

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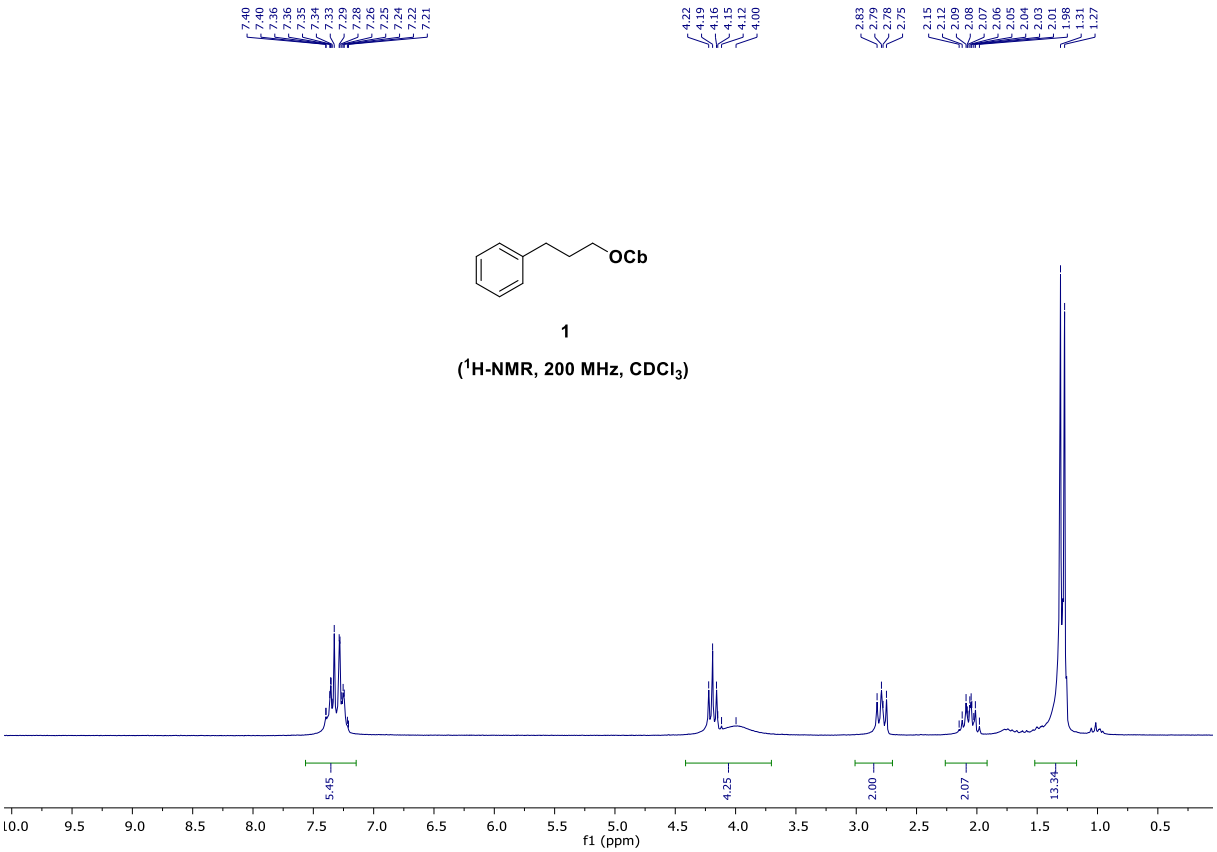
Copies of NMR Spectra (^{1}H and ^{13}C)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7.40
7.36
7.36
7.35
7.34
7.33
7.29
7.28
7.26
7.25
7.24
7.22
7.21
4.22
4.19
4.16
4.15
4.12
4.00
2.83
2.79
2.78
2.75
2.15
2.12
2.09
2.08
2.07
2.06
2.05
2.04
2.03
2.01
1.98
1.31
1.27
OCb
1
(1H-NMR, 200 MHz, CDCl3)
5.45
4.25
2.00
2.07
13.34
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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3.0
2.5
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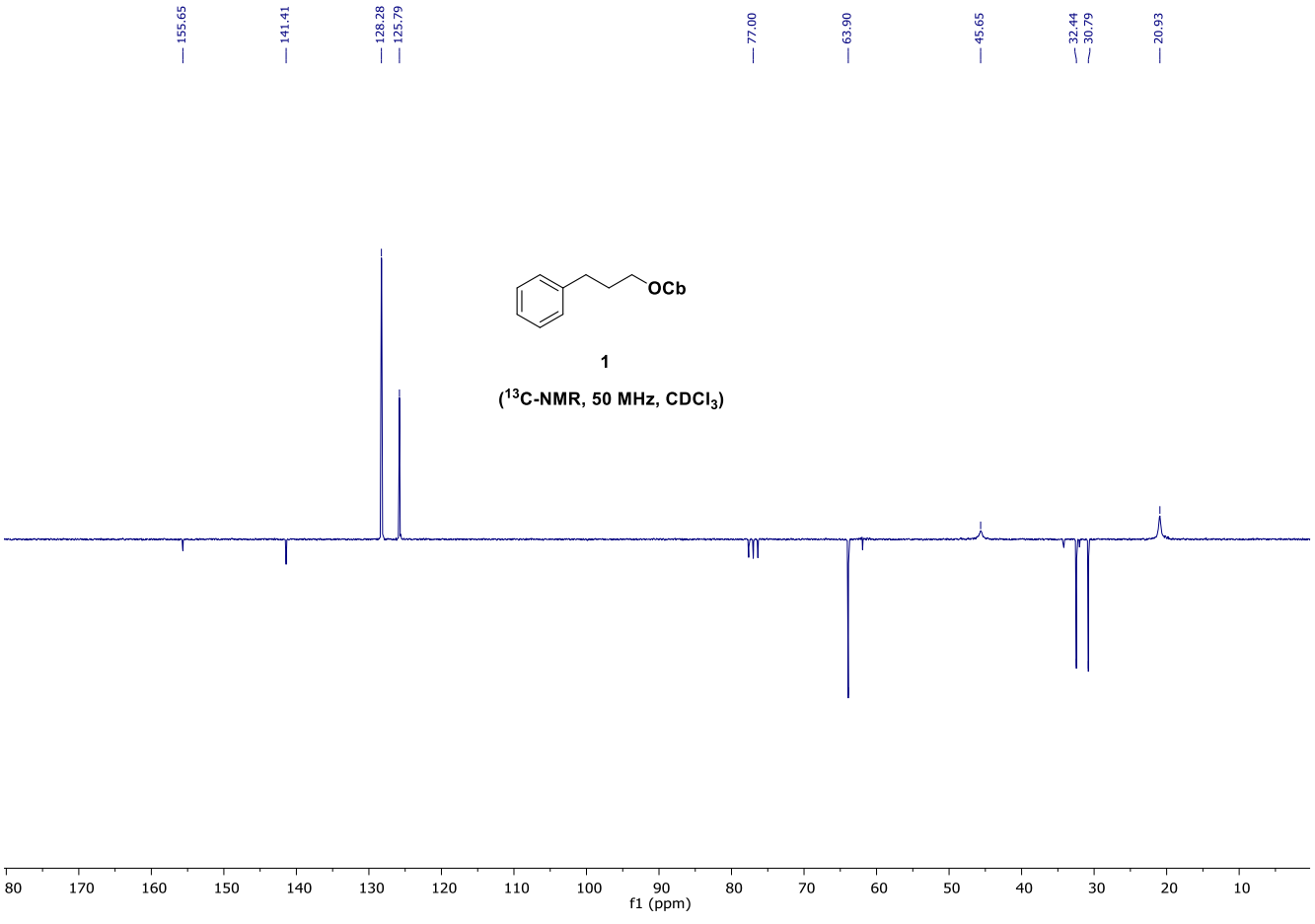
0.5
f1 (ppm)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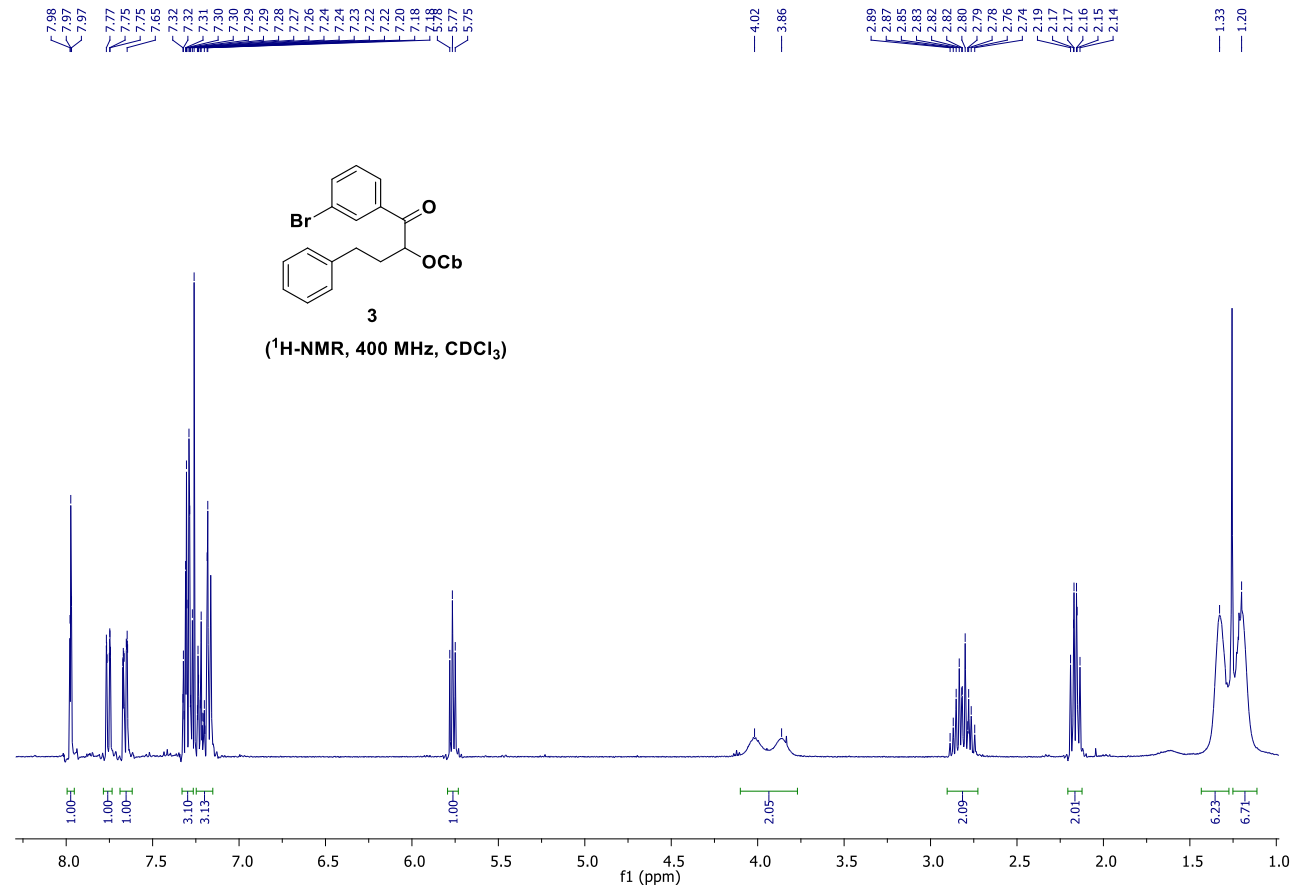
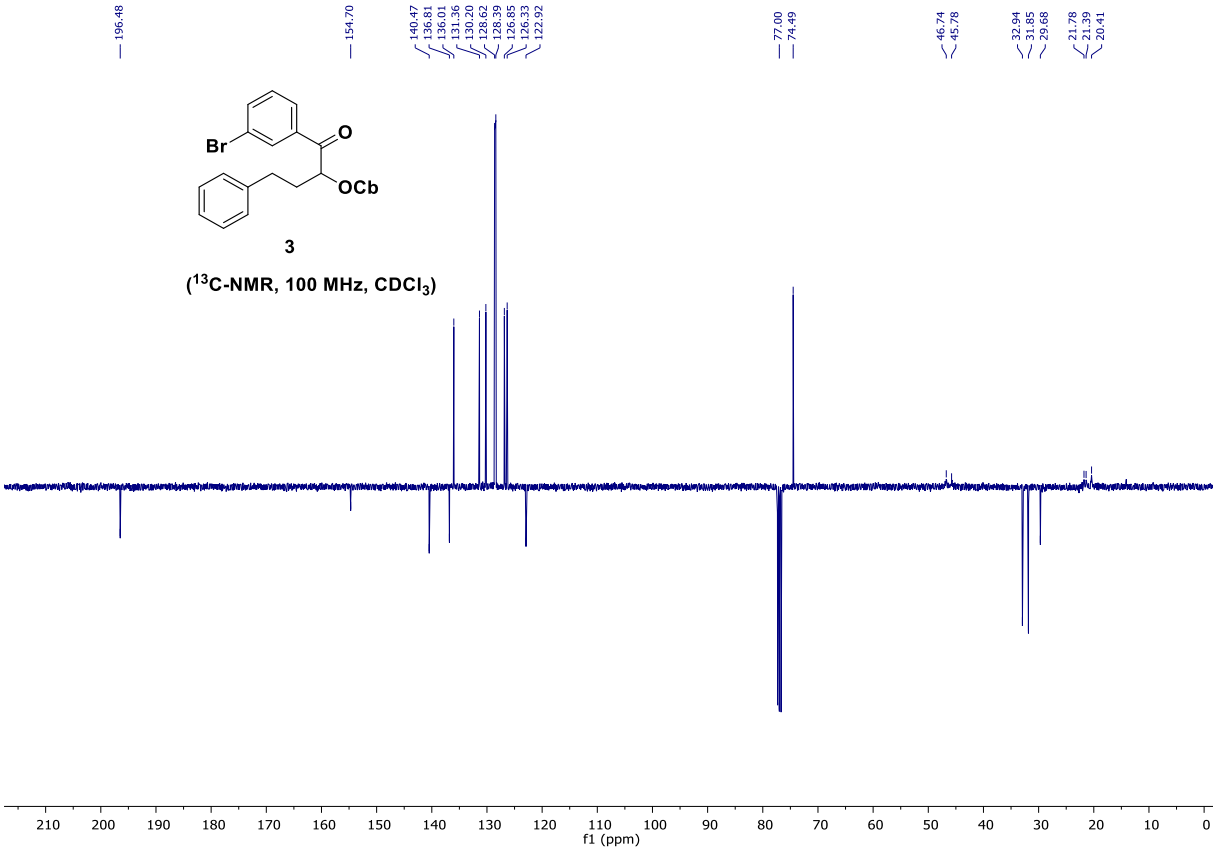
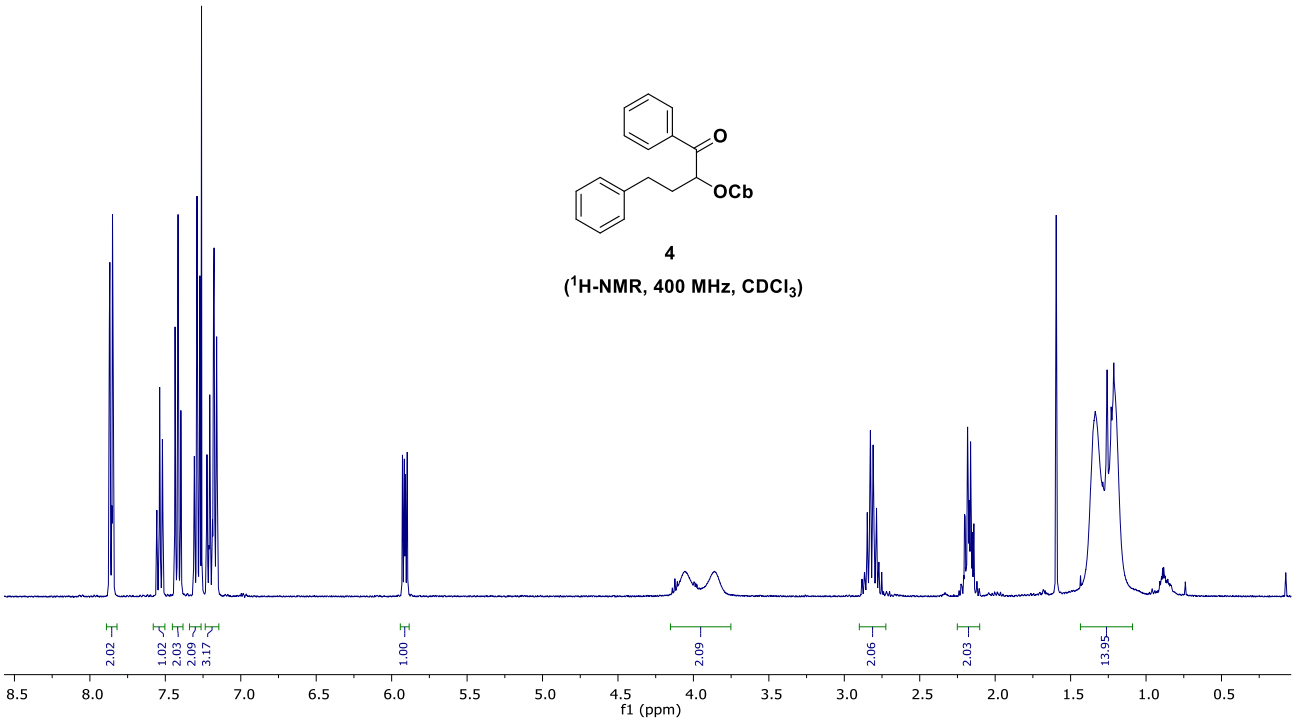
128.28
125.79
77.00
63.90
45.65
32.44
30.79
20.93
OCb
1
(13C-NMR, 50 MHz, CDCl3)
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


7.98 7.97 7.97 7.77 7.75 7.75 7.65 7.32 7.31 7.30 7.30 7.29 7.28 7.27 7.26 7.24 7.24 7.23 7.22 7.22 7.20 7.18 5.77 5.75
4.02 3.86
2.89 2.87 2.85 2.83 2.82 2.82 2.80 2.79 2.78 2.76 2.74 2.19 2.17 2.17 2.16 2.15 2.14
1.33 1.20
Br
O
OCb
3
(1H-NMR, 400 MHz, CDCl3)
1.00 1.00 1.00 3.10 3.13 1.00 2.05 2.09 2.01 6.23 6.71
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
f1 (ppm)


196.48
154.70
140.47 136.81 136.01 131.36 130.20 128.62 128.39 126.85 126.33 122.92
77.00 74.49
46.74 45.78
32.94 31.85 29.68
21.78 21.39 20.41
Br
O
OCb
3
(13C-NMR, 100 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



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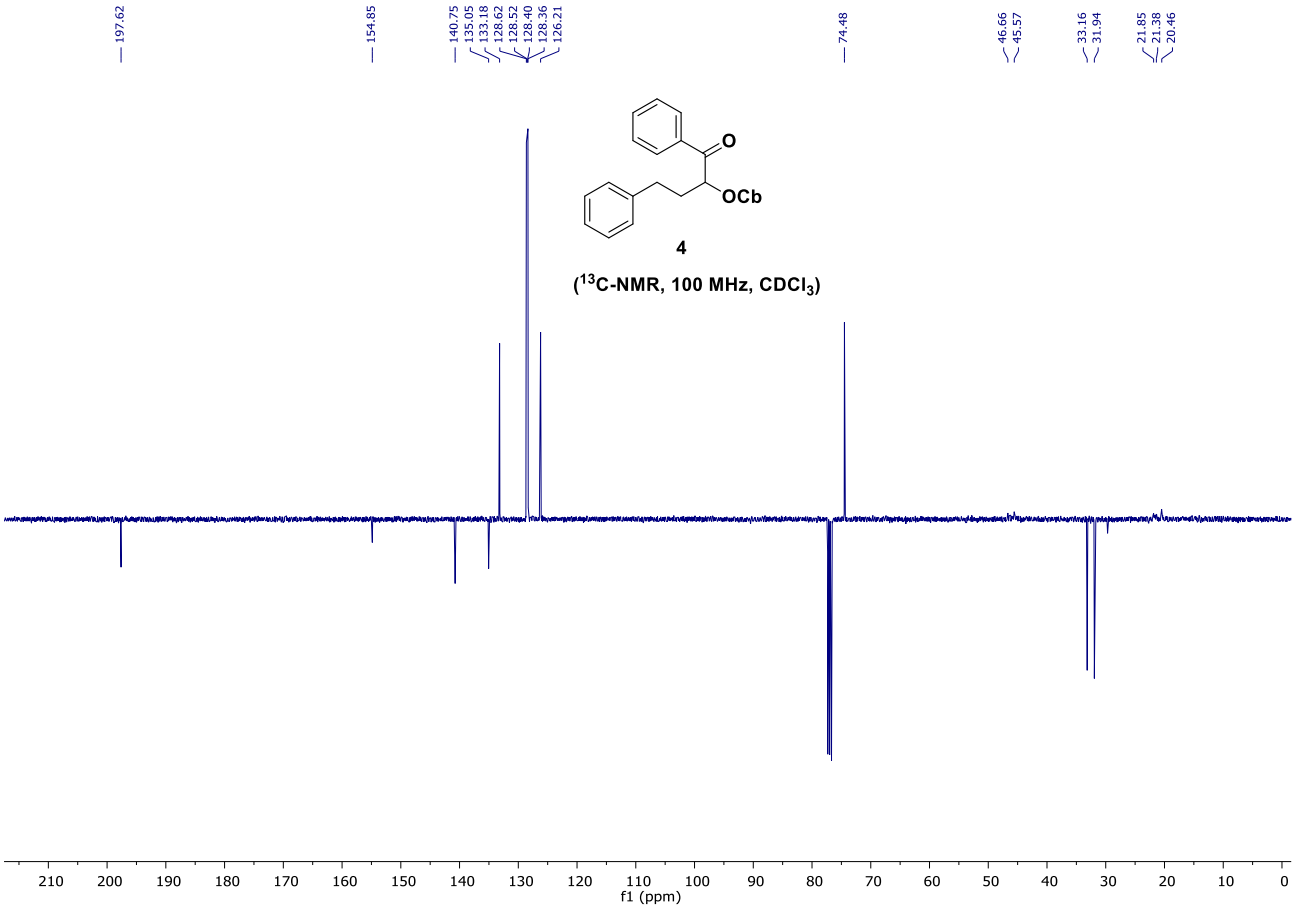
(^{1}H-NMR, 400 MHz, $CDCl_3$)



4

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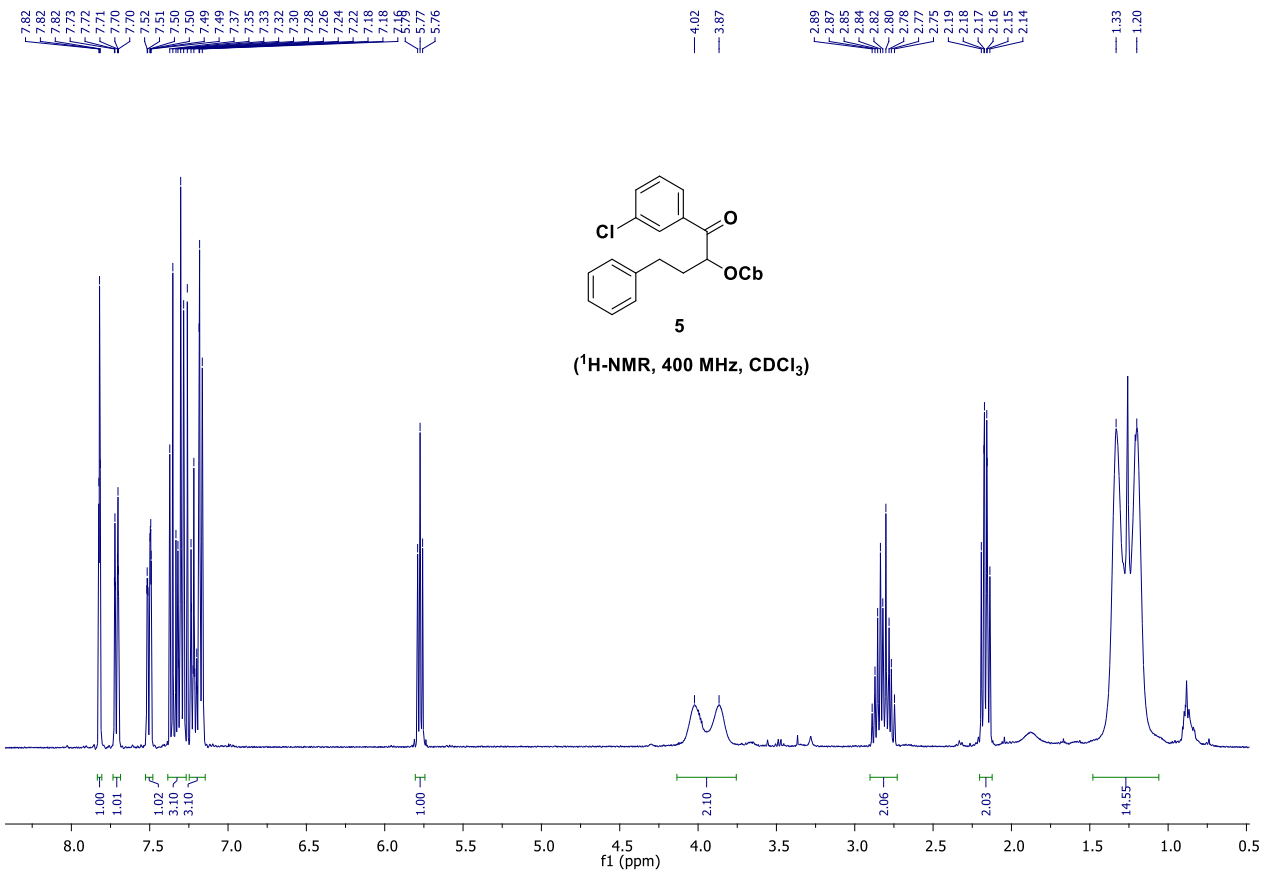
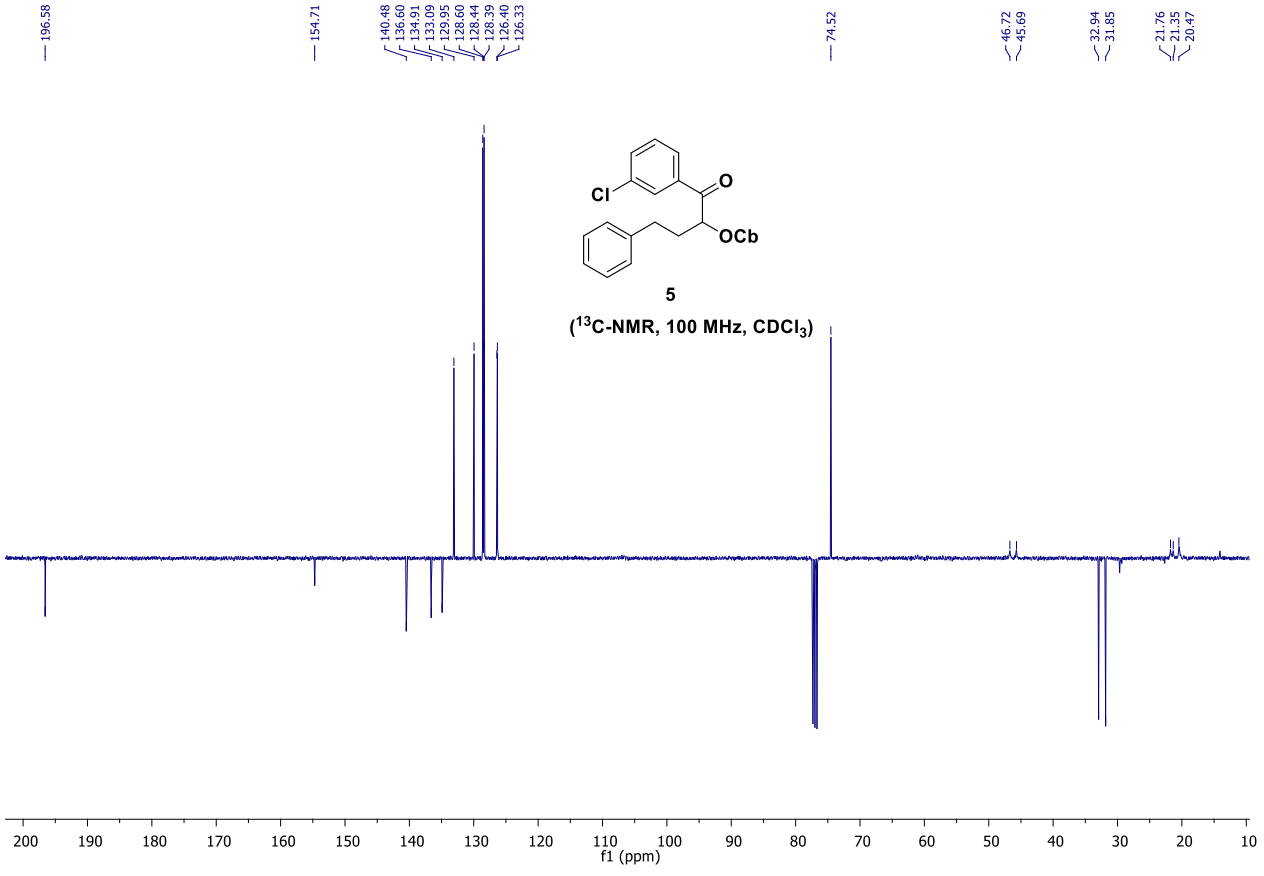

7.82
7.82
7.82
7.73
7.72
7.71
7.70
7.70
7.52
7.51
7.50
7.50
7.49
7.49
7.37
7.35
7.33
7.32
7.30
7.28
7.26
7.24
7.22
7.18
7.16
5.77
5.76
4.02
3.87
2.89
2.87
2.85
2.84
2.82
2.80
2.78
2.77
2.75
2.19
2.18
2.17
2.16
2.15
2.14
1.33
1.20
Cl
O
OCb
5
(1H-NMR, 400 MHz, CDCl3)
1.00
1.01
1.02
3.10
3.10
1.00
2.10
2.06
2.03
14.55
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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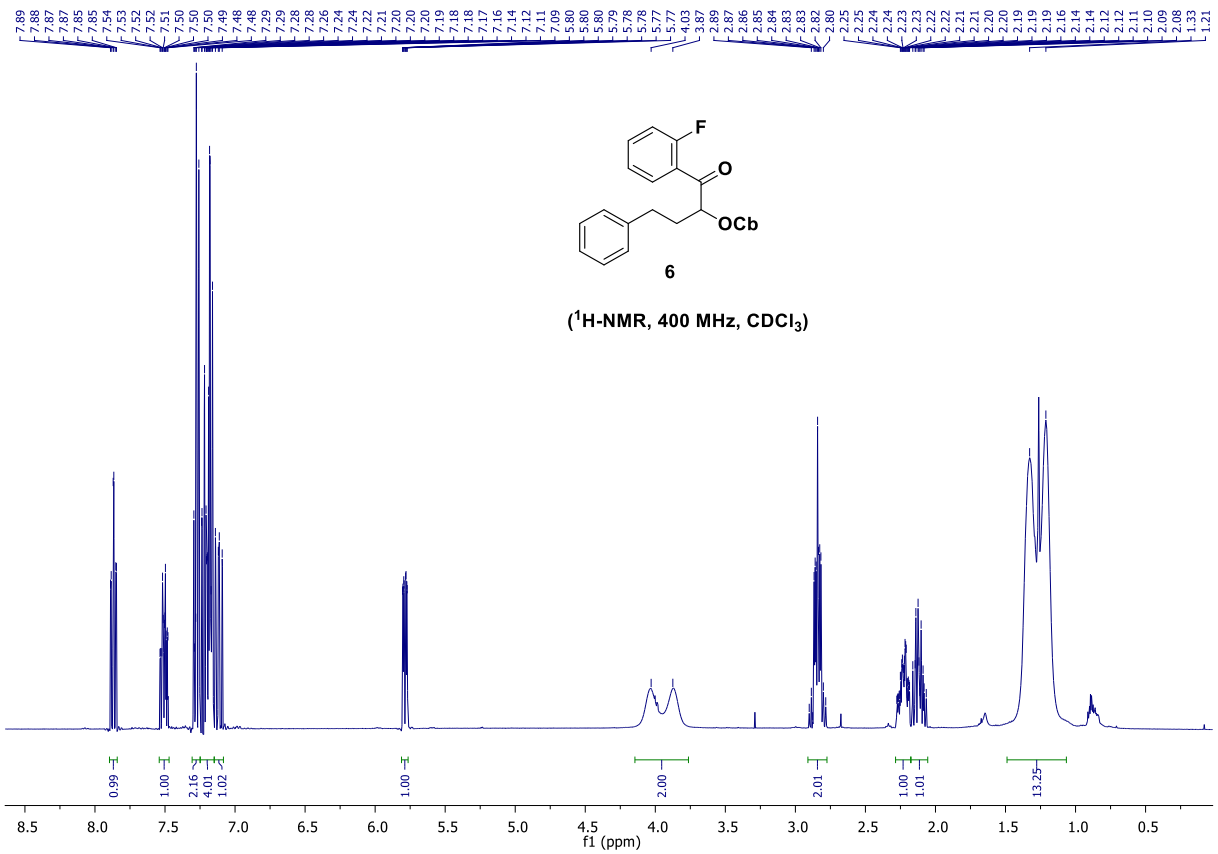
134.91
133.09
129.95
128.60
128.44
128.39
126.40
126.33
74.52
46.72
45.69
32.94
31.85
21.76
21.35
20.47
Cl
O
OCb
5
(13C-NMR, 100 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)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O
OCb
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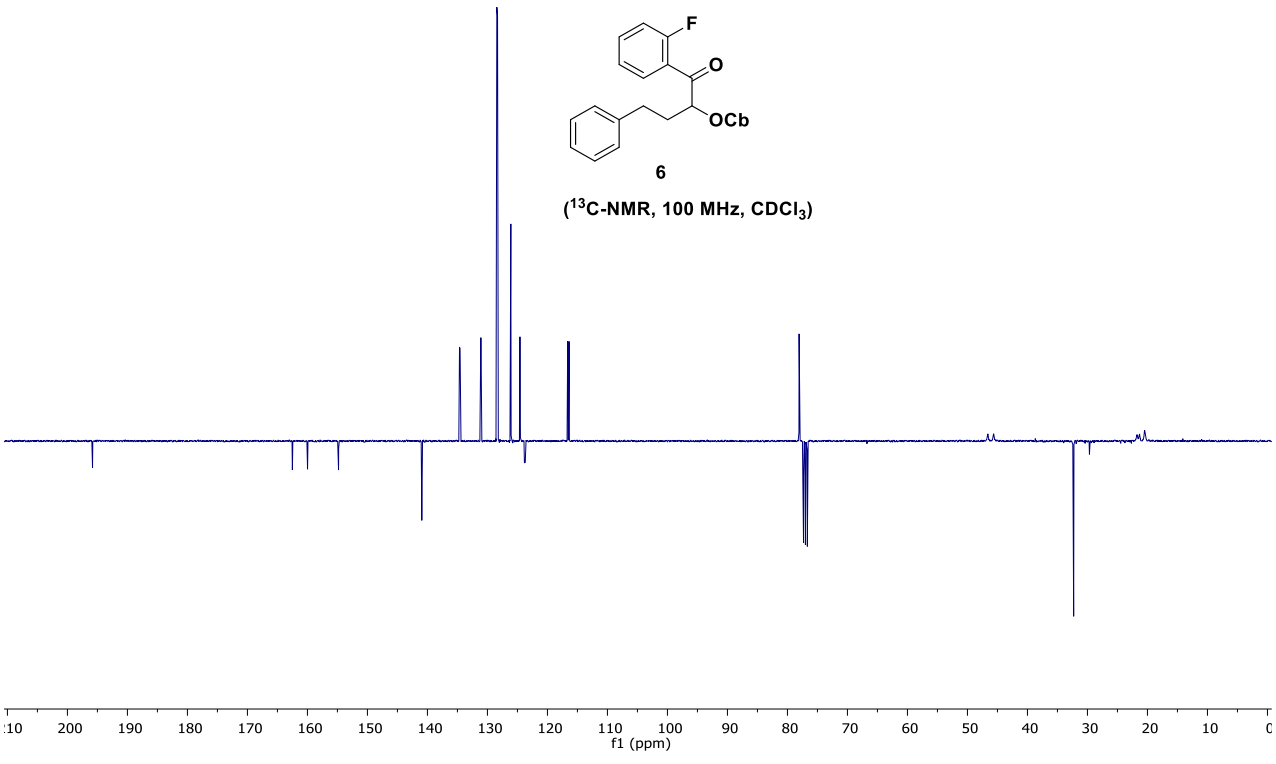
f1 (ppm)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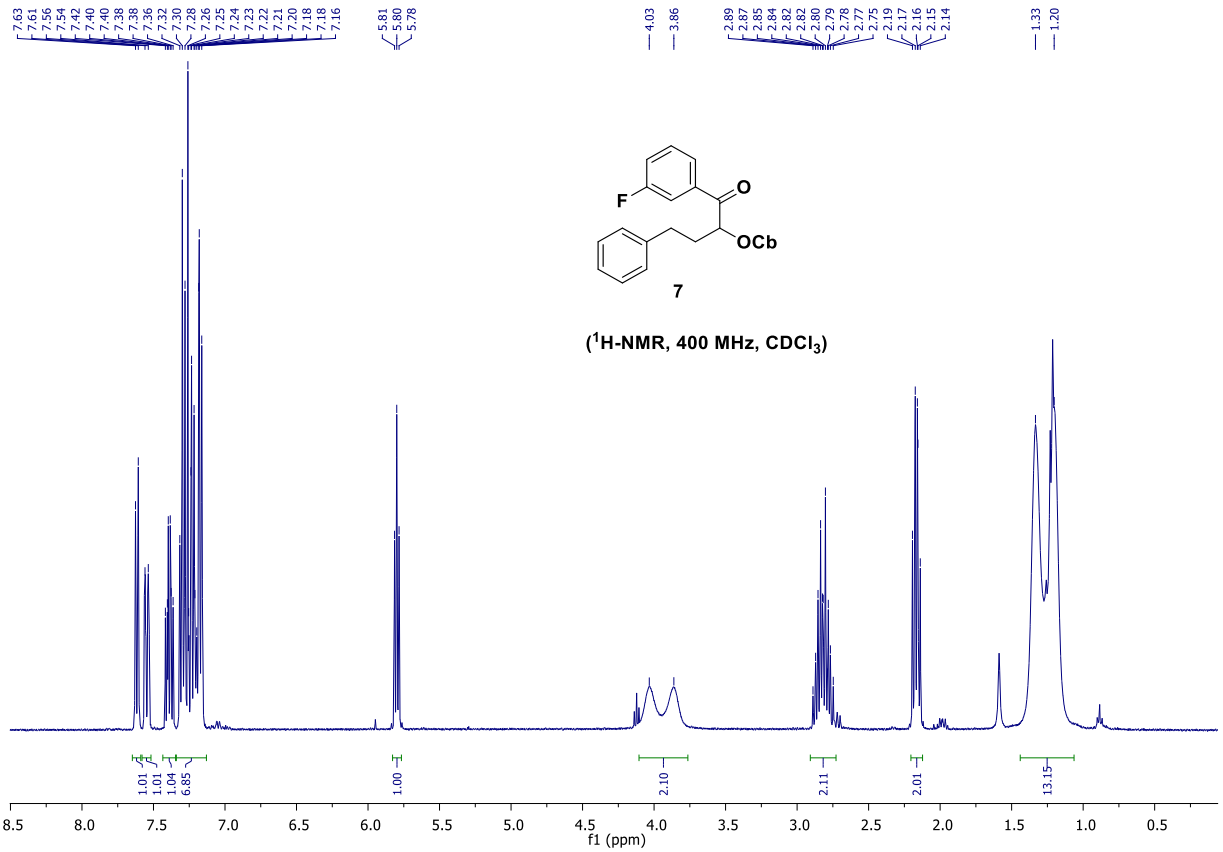
O
OCb
6
(13C-NMR, 100 MHz, CDCl3)
f1 (ppm)



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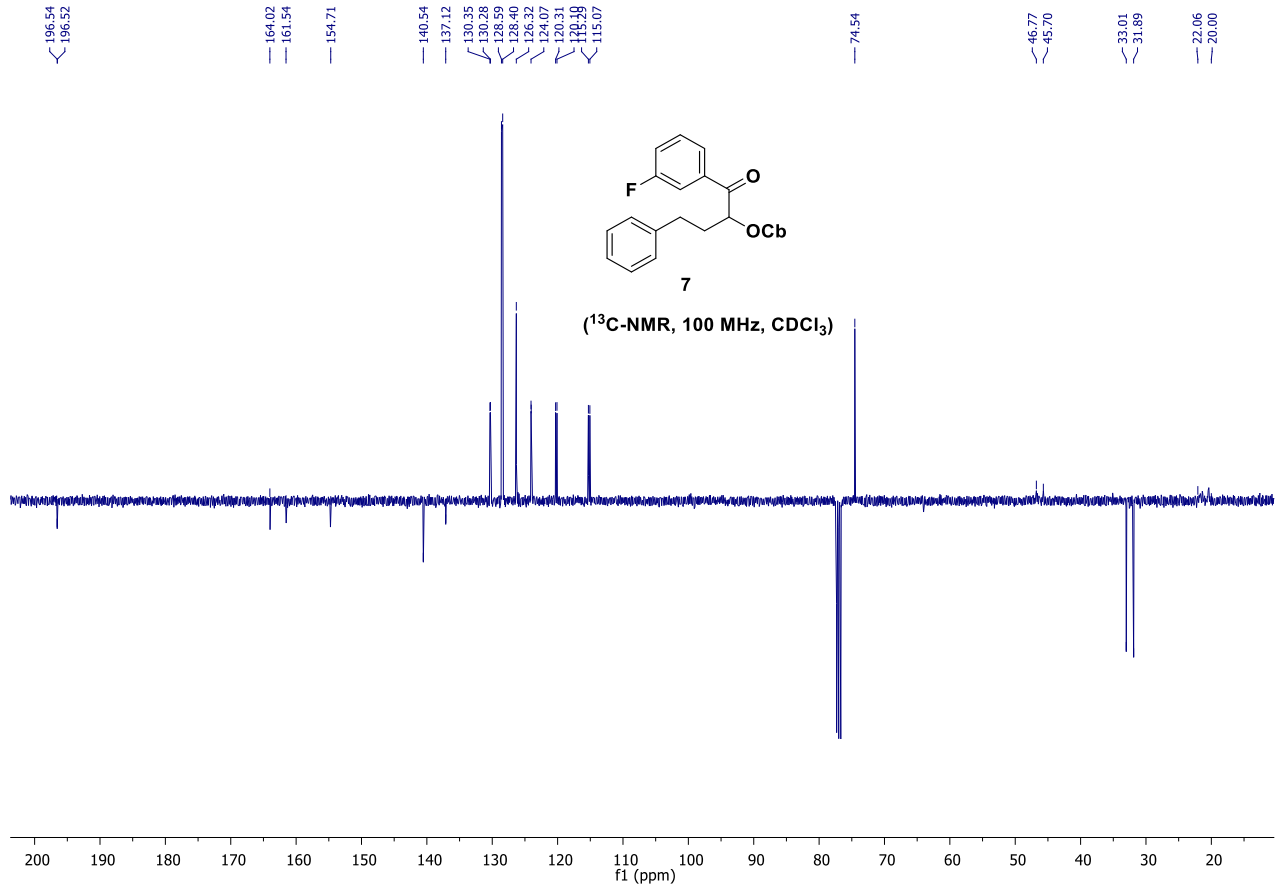
(¹H-NMR, 400 MHz, $CDCl_3$)



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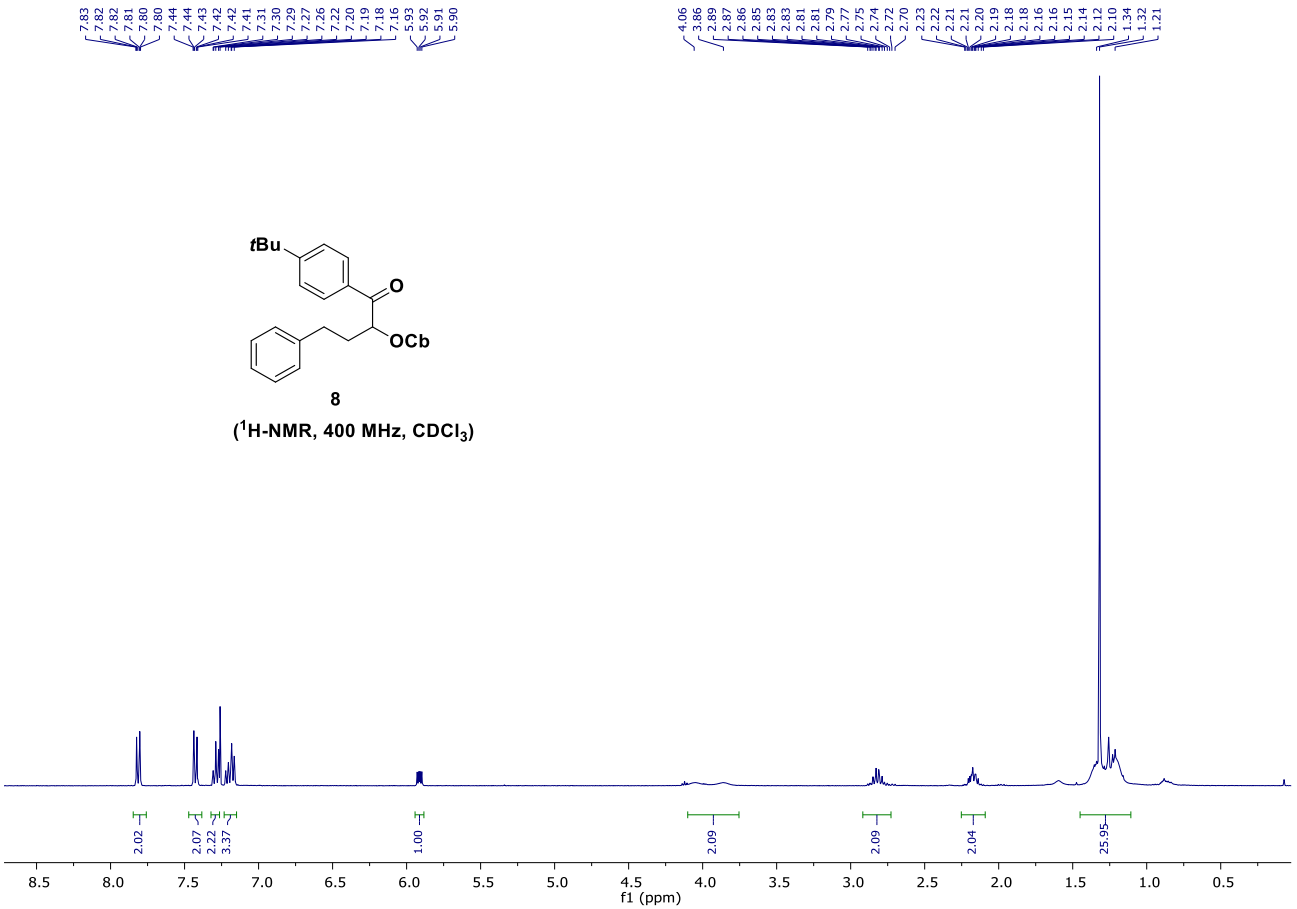

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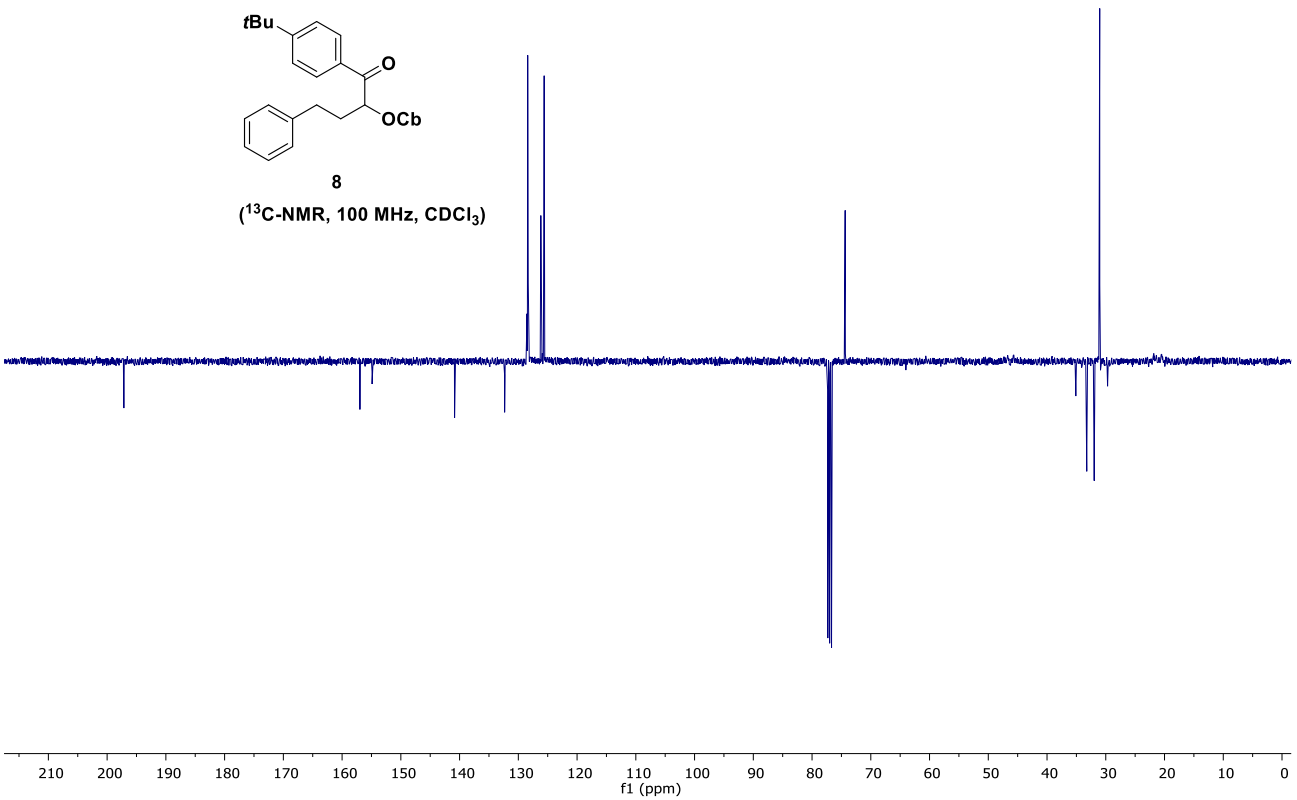

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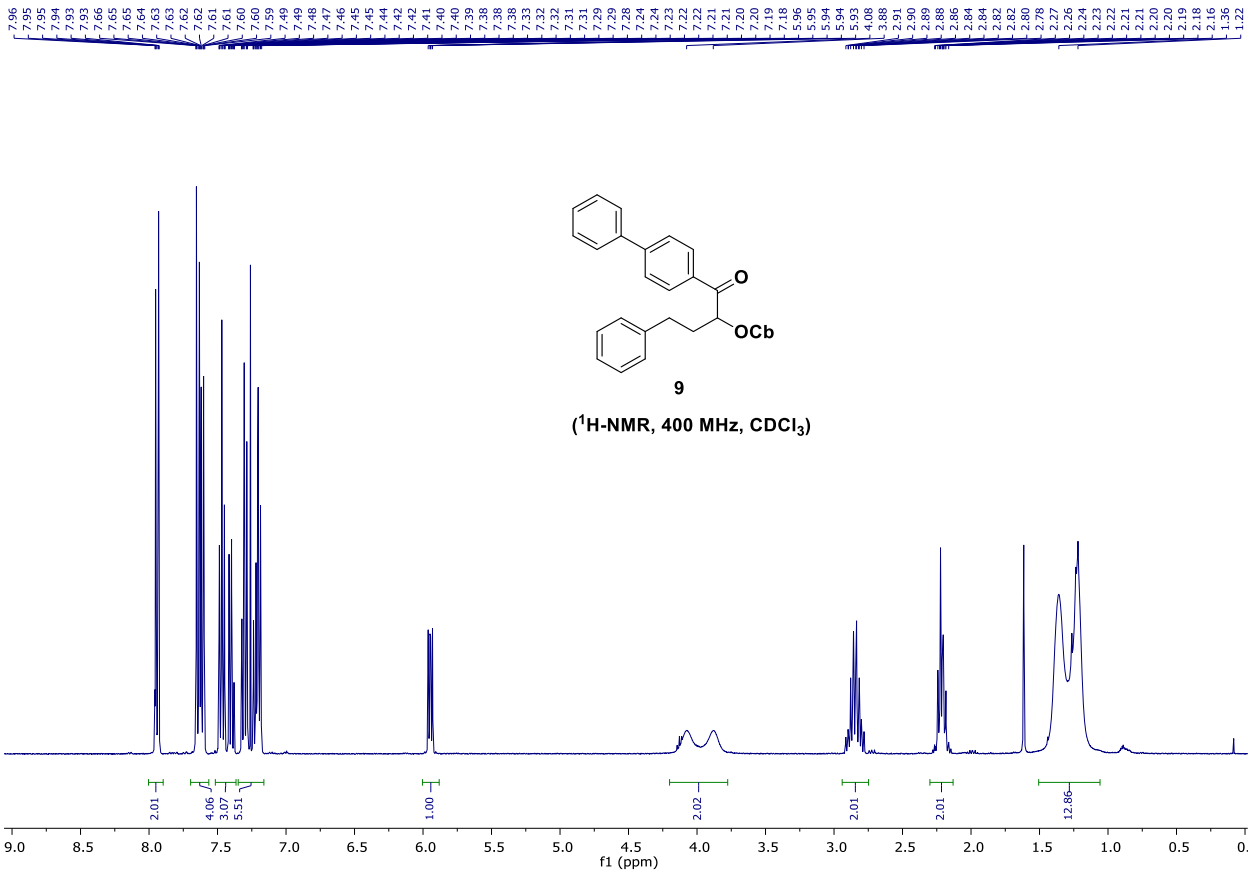
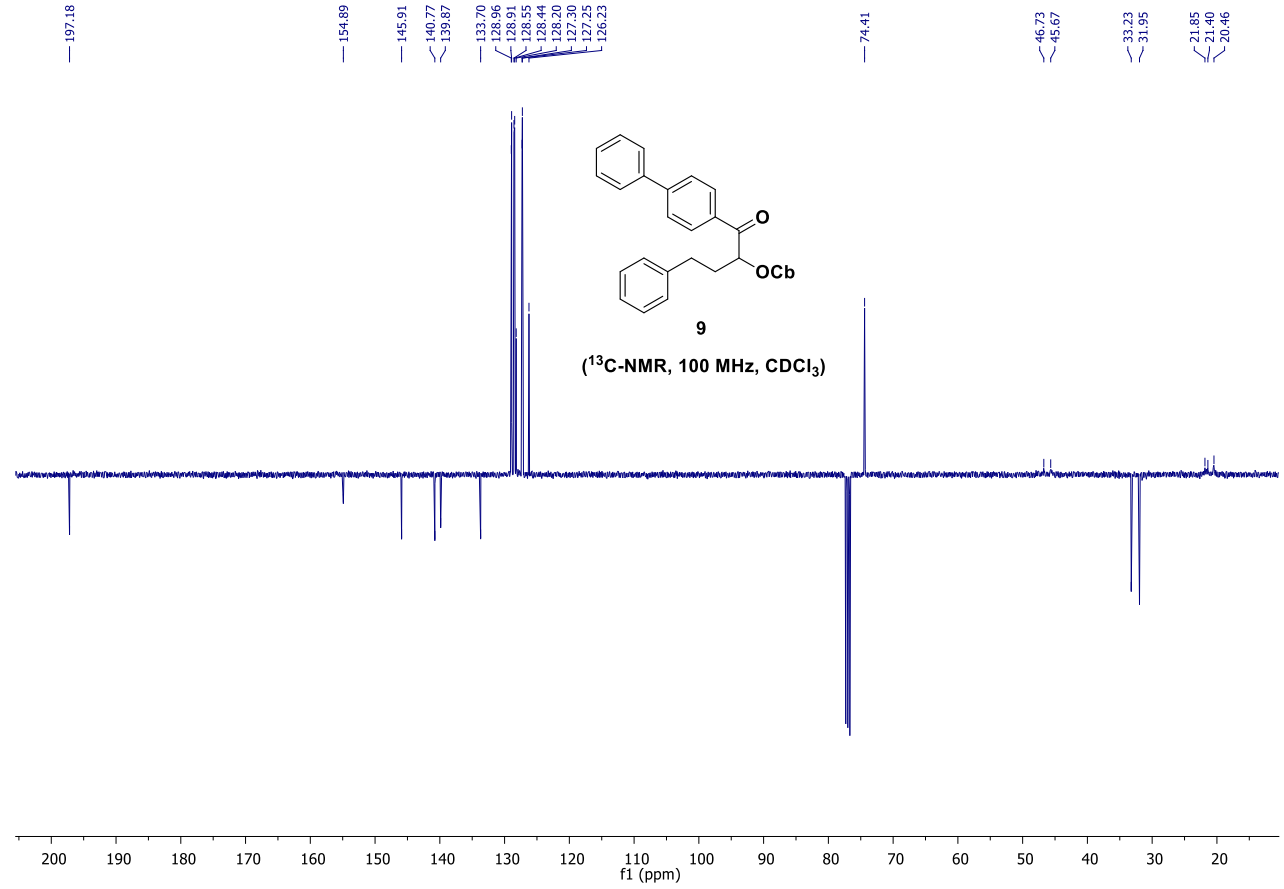
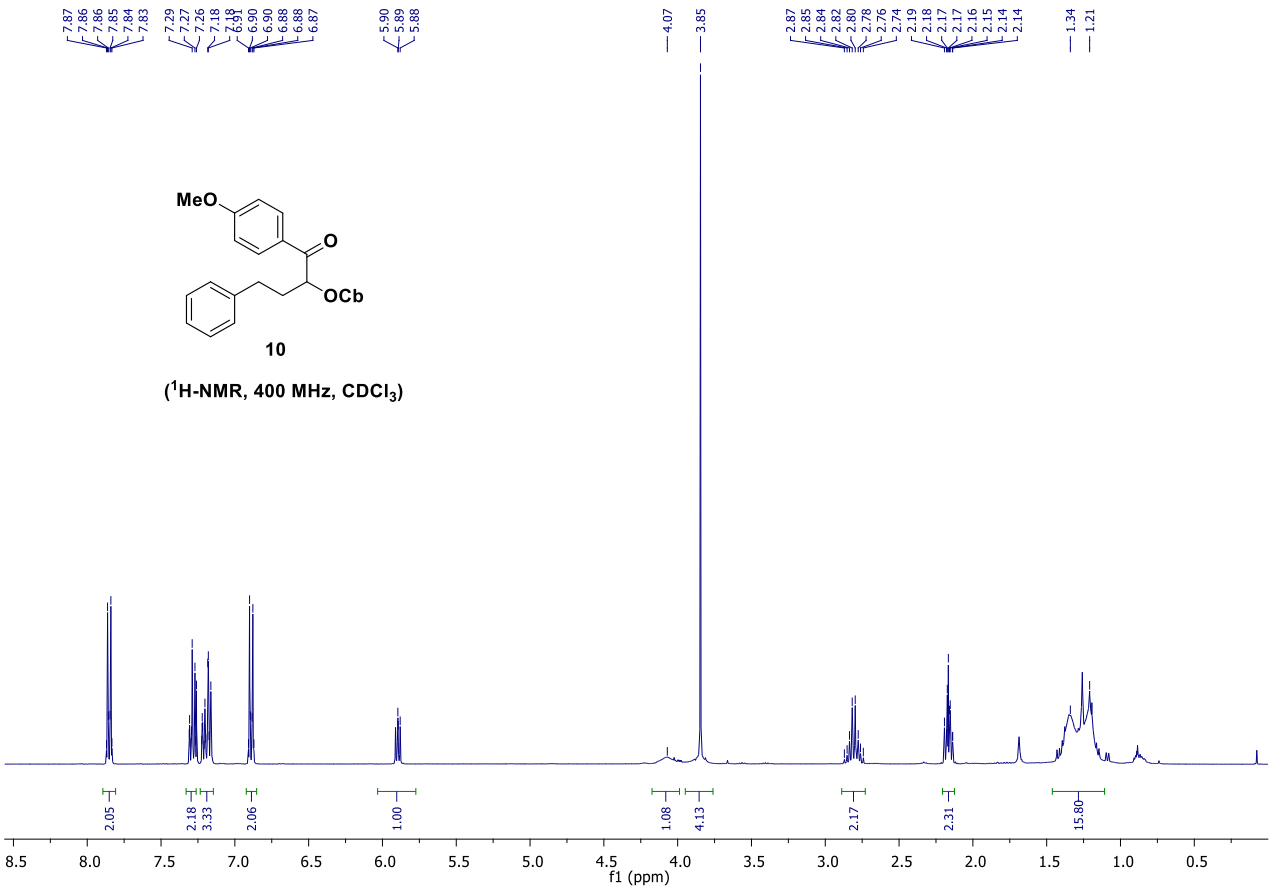
(^{13}C-NMR, 100 MHz, $CDCl_3$)


O
OCb
9
(1H-NMR, 400 MHz, CDCl3)
f1 (ppm)


O
OCb
9
(13C-NMR, 100 MHz, CDCl3)
f1 (ppm)


MeO
O
OCb
10
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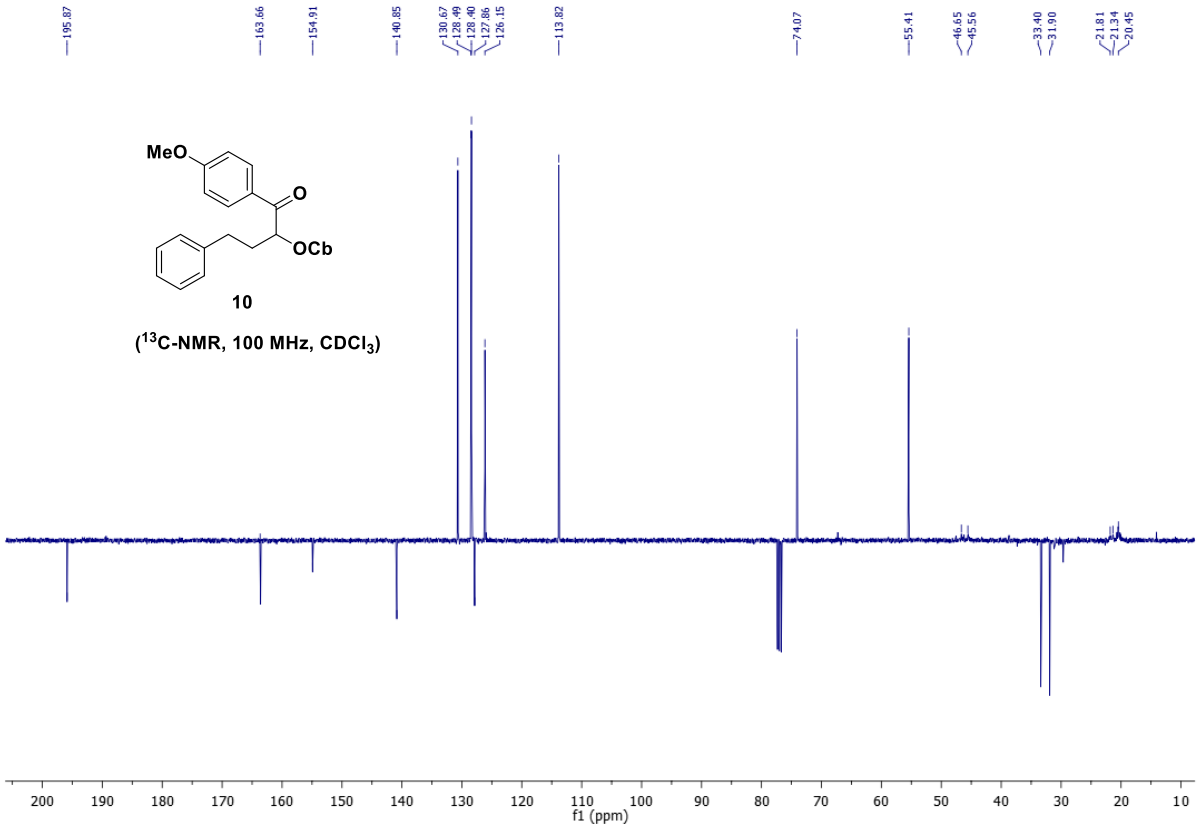
f1 (ppm)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O
OCb
10
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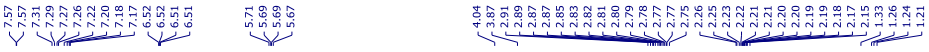
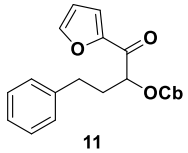
f1 (ppm)





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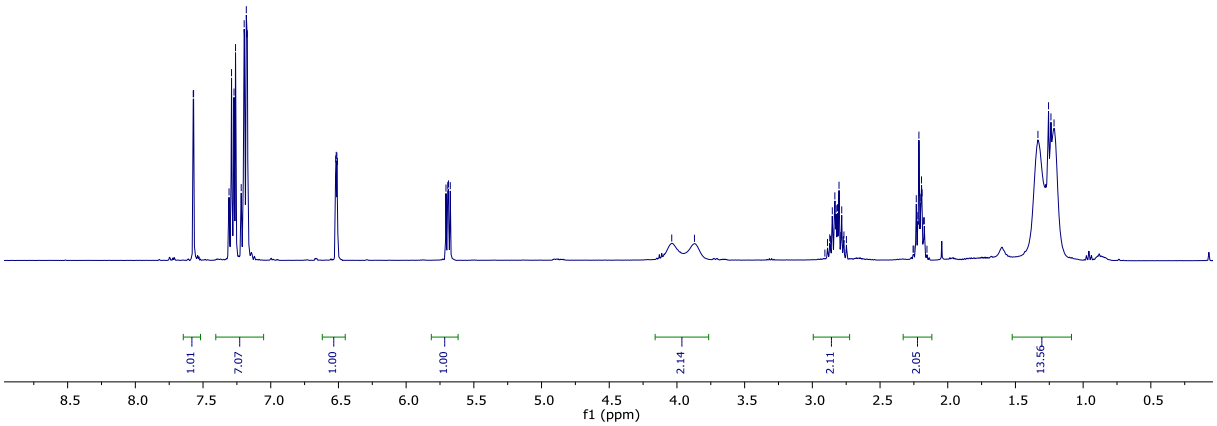
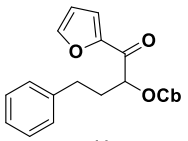
(^{1}H-NMR, 400 MHz, $CDCl_3$)





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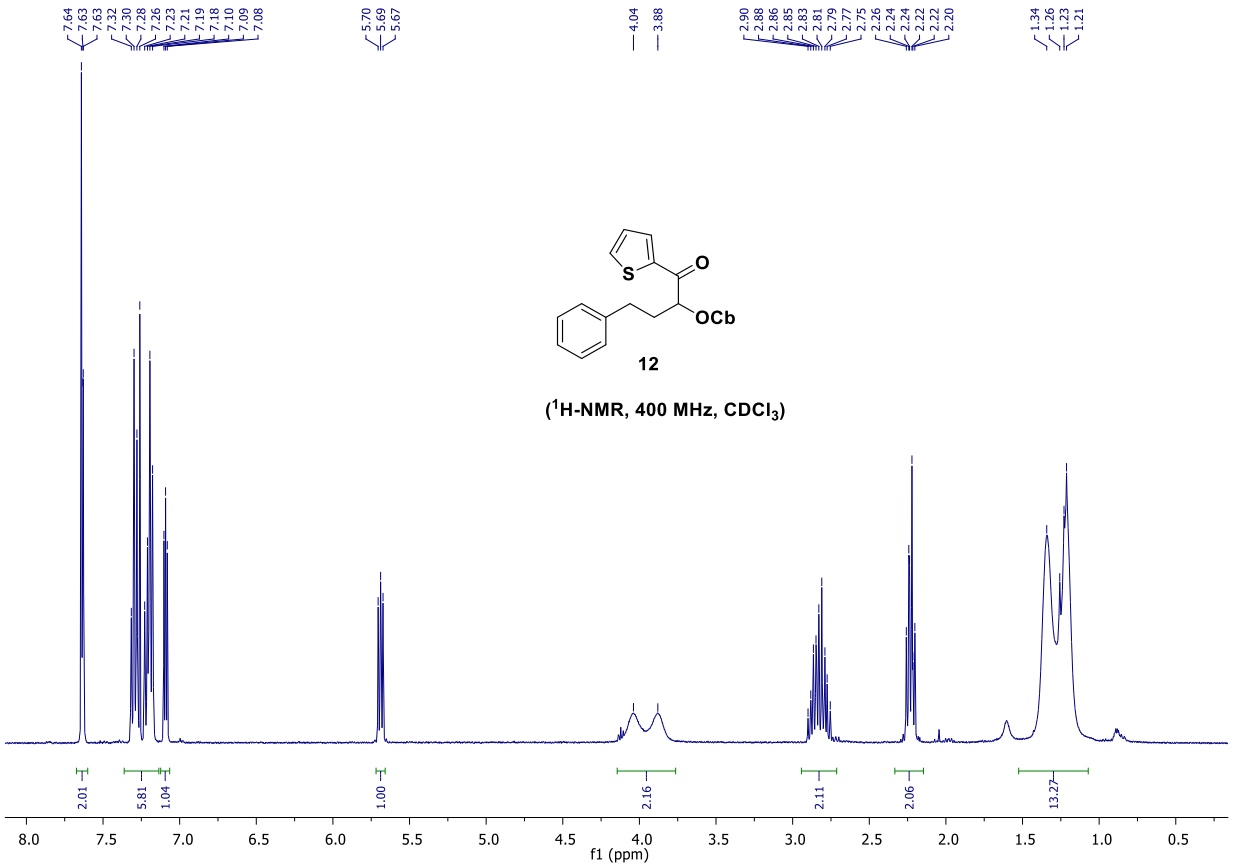

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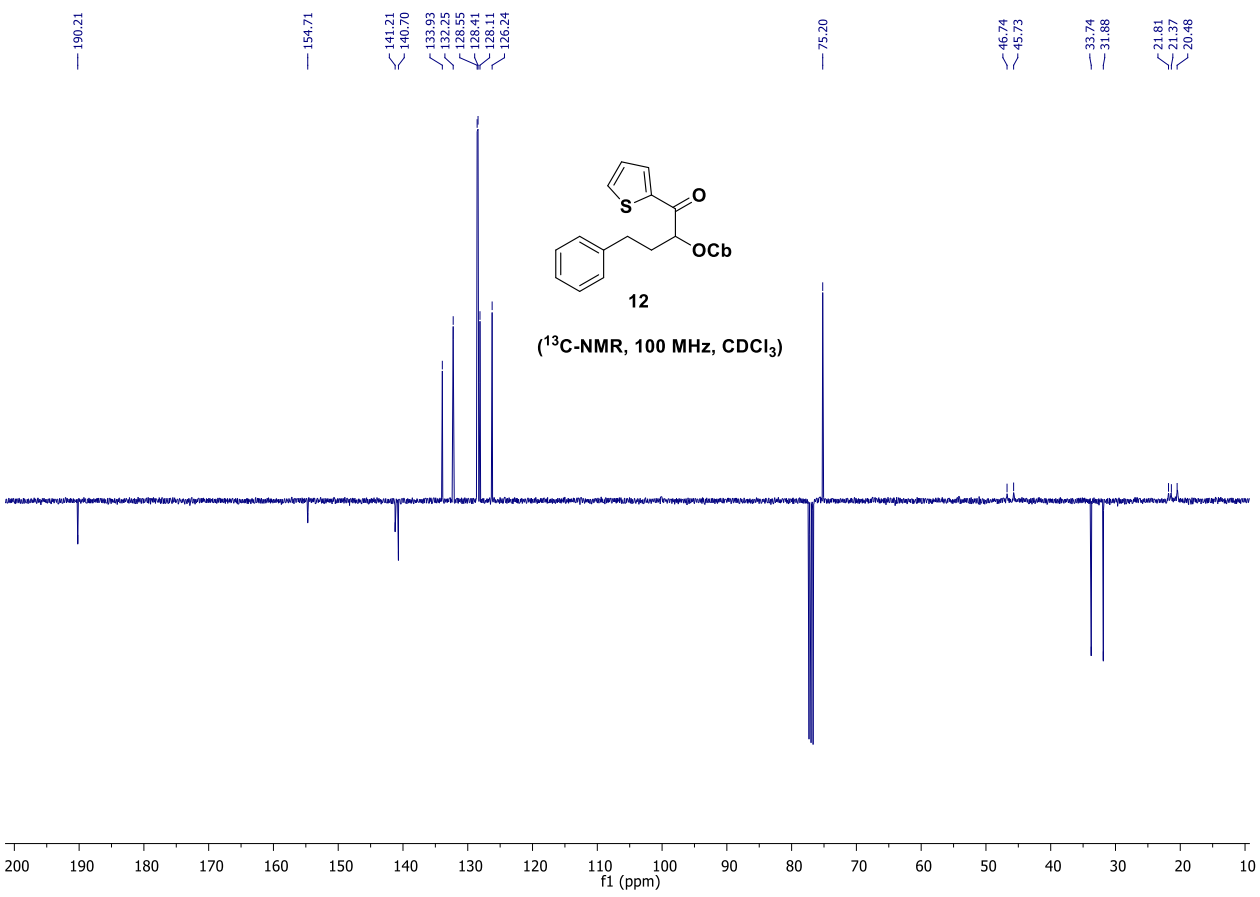

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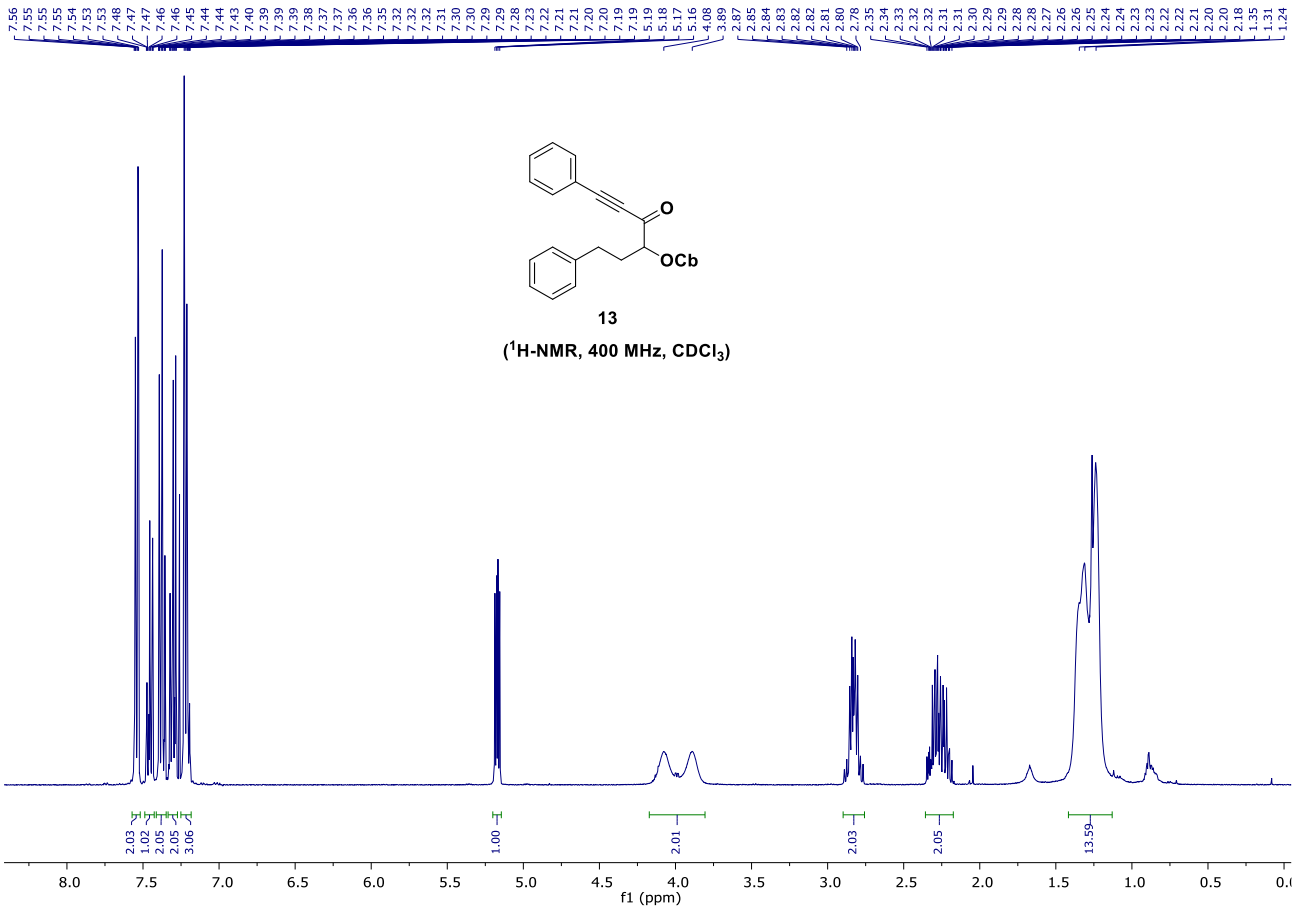
(^{13}C-NMR, 100 MHz, $CDCl_3$)



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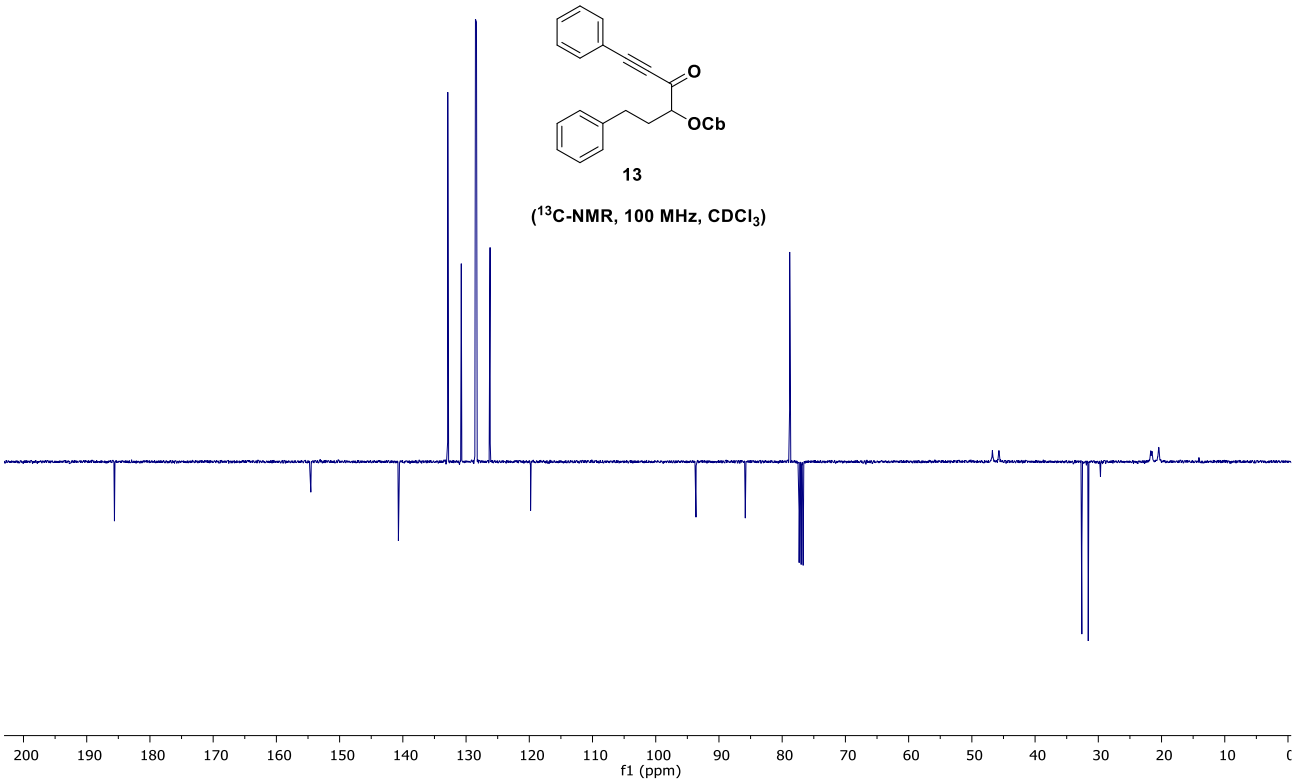

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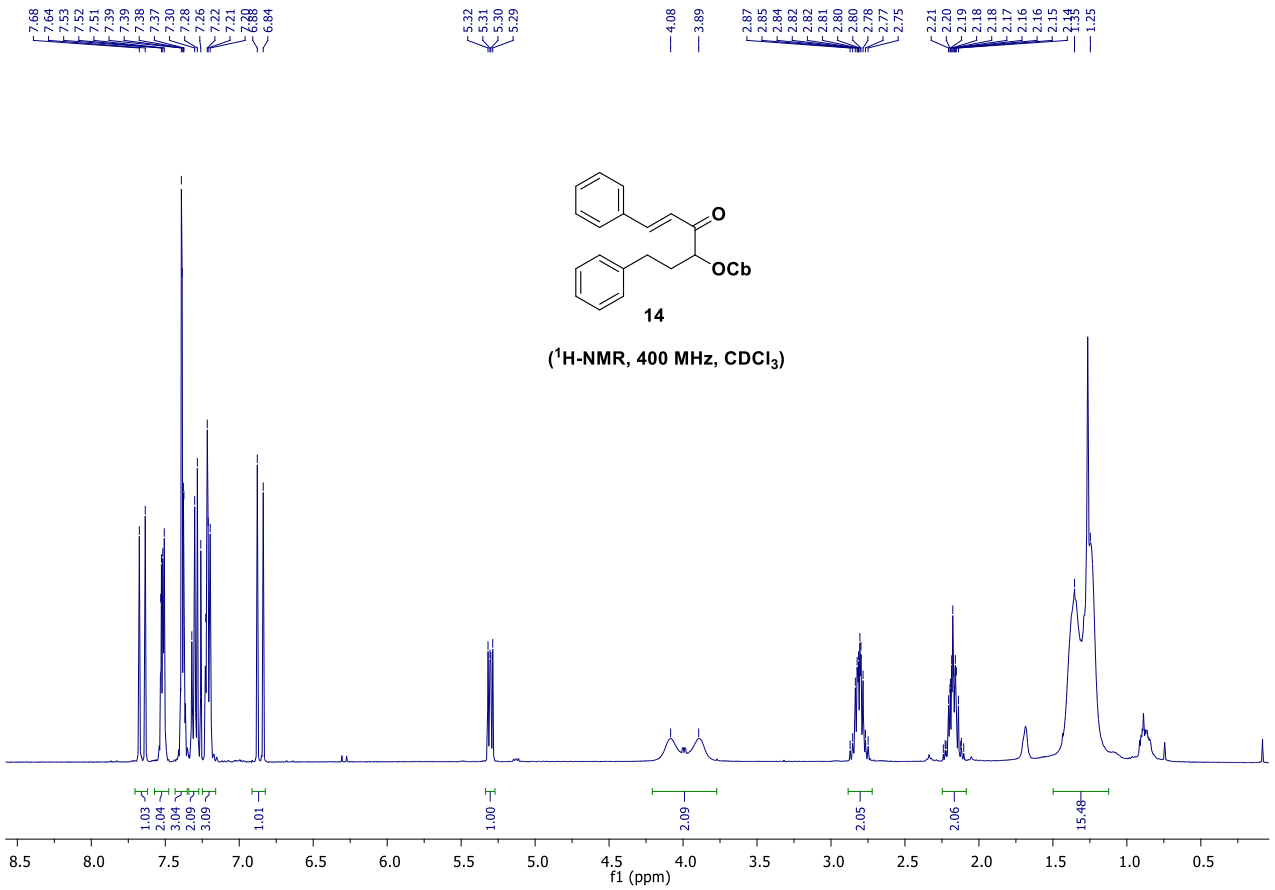

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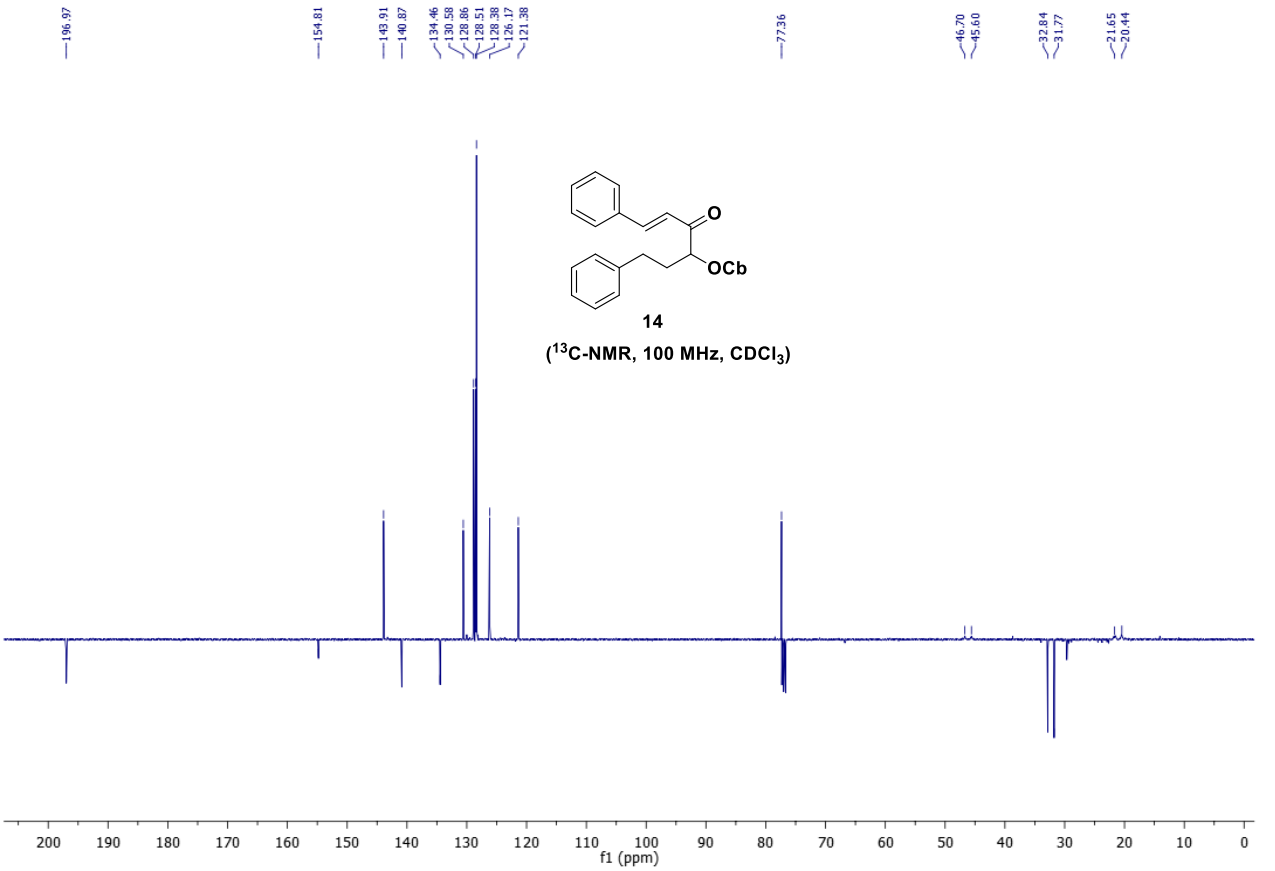

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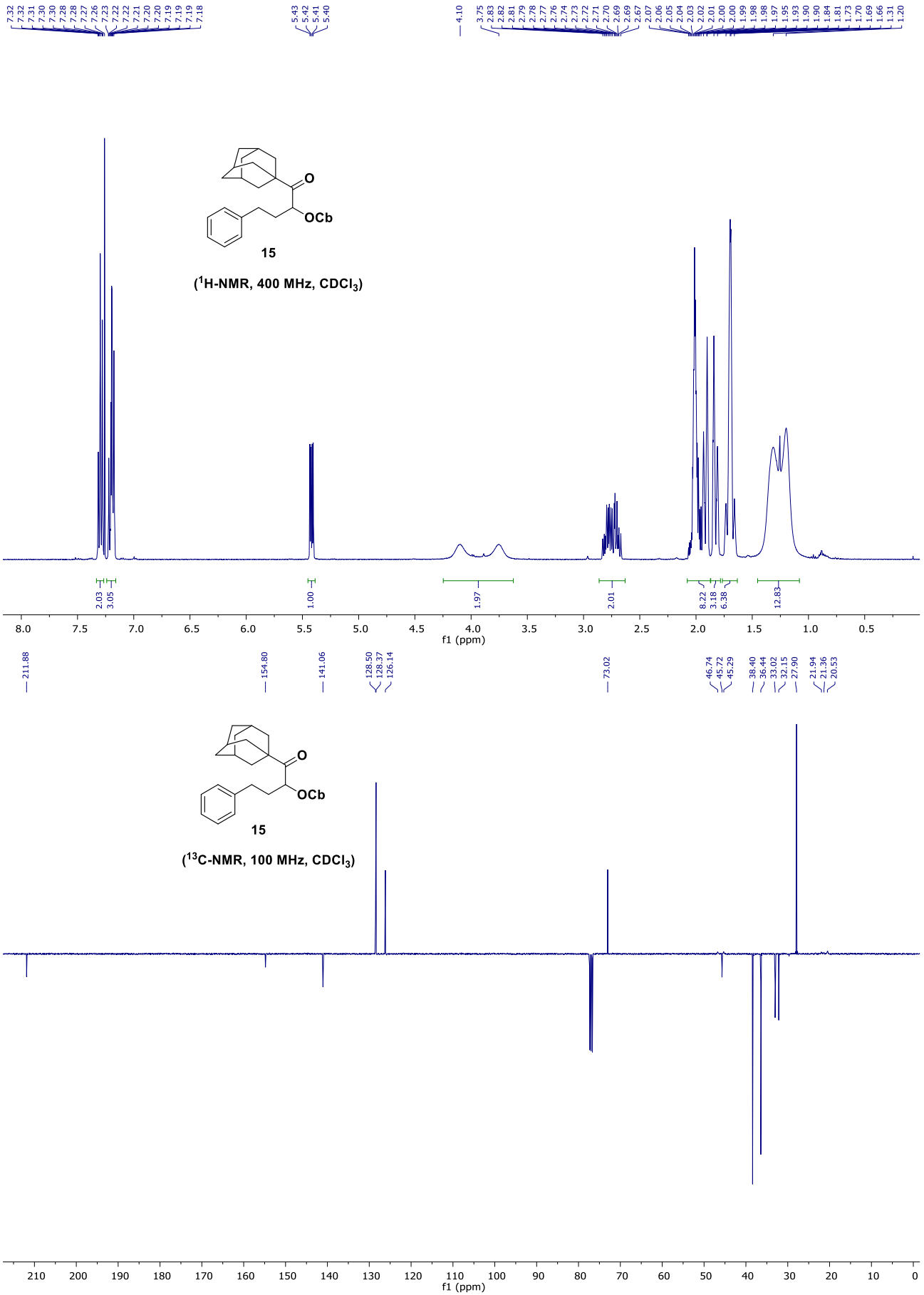
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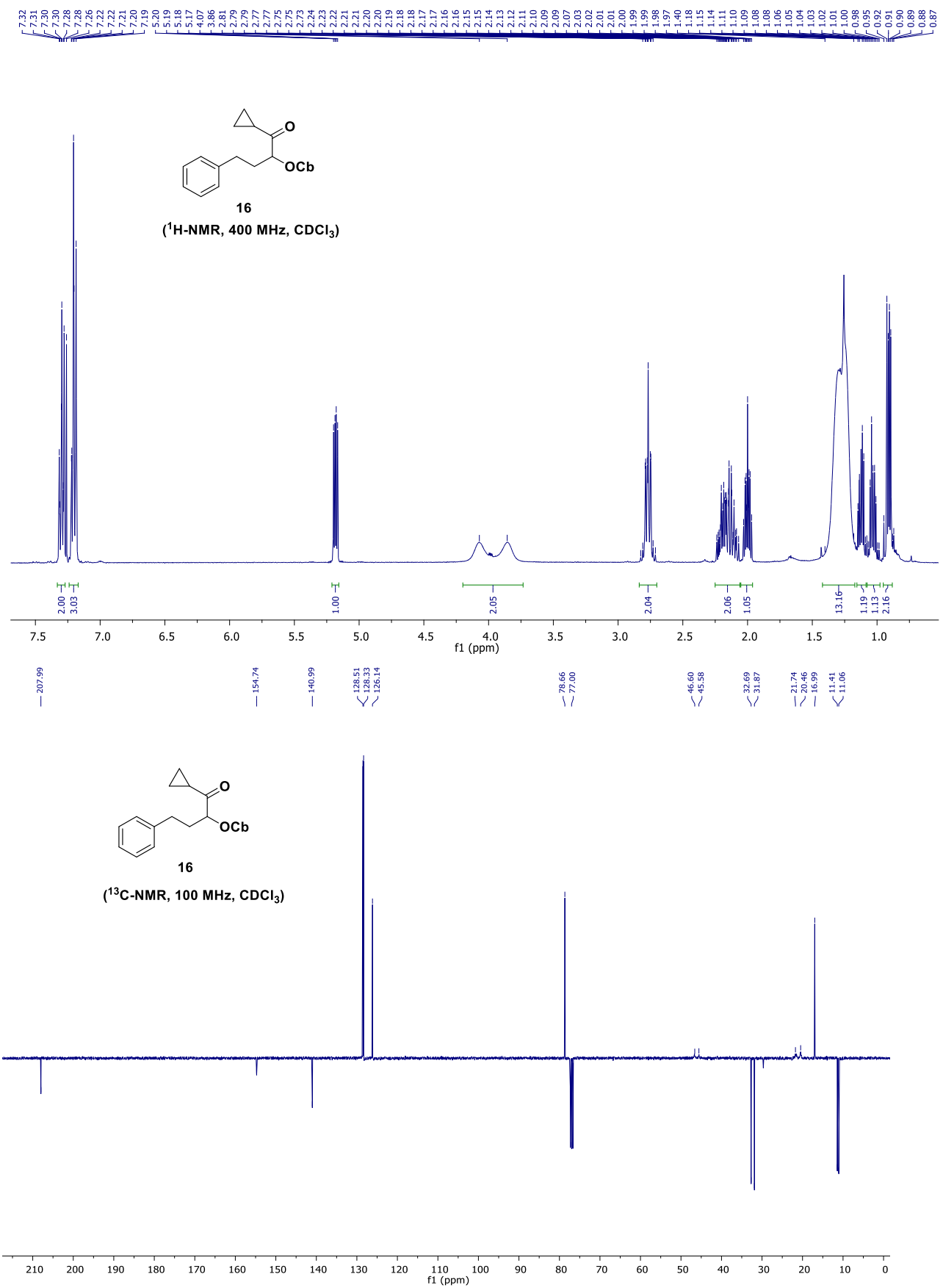
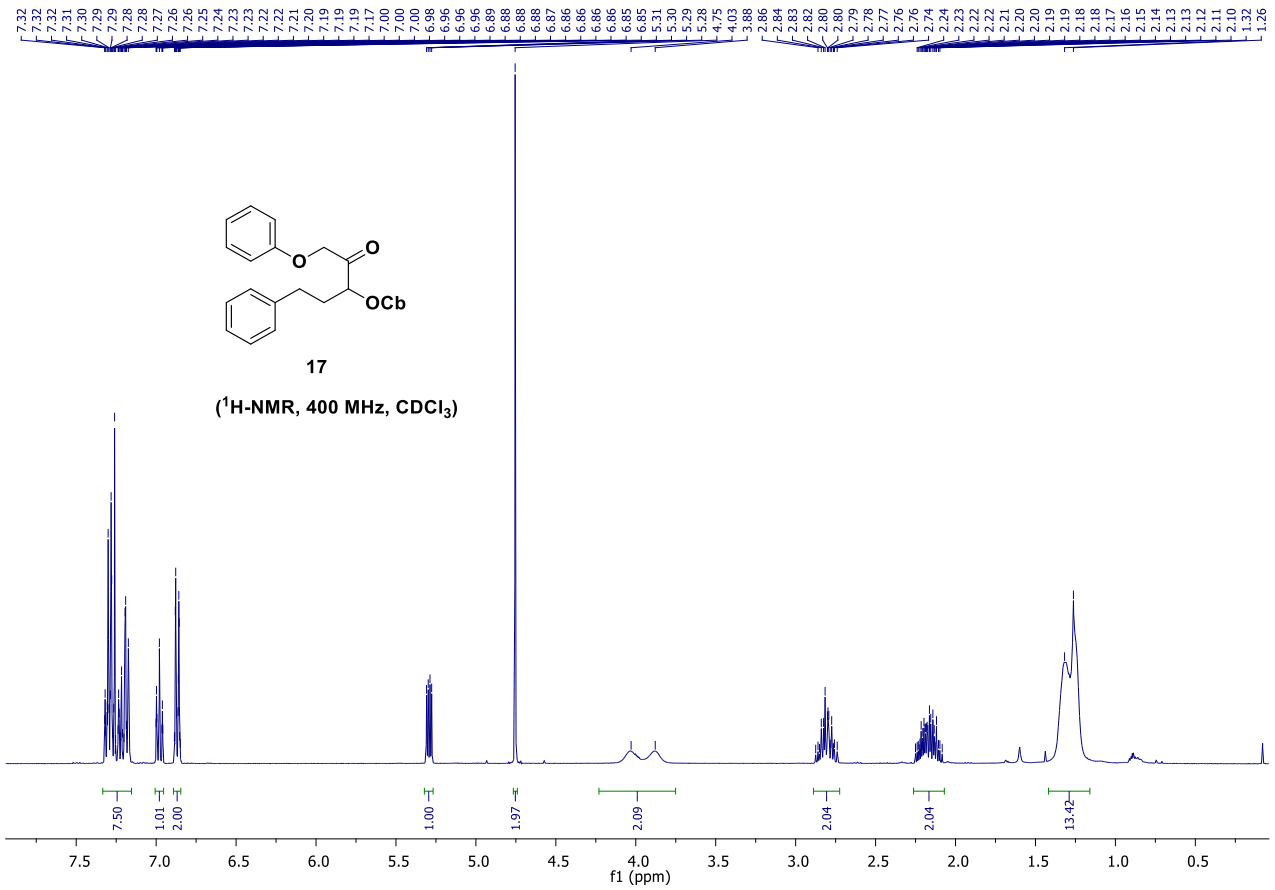
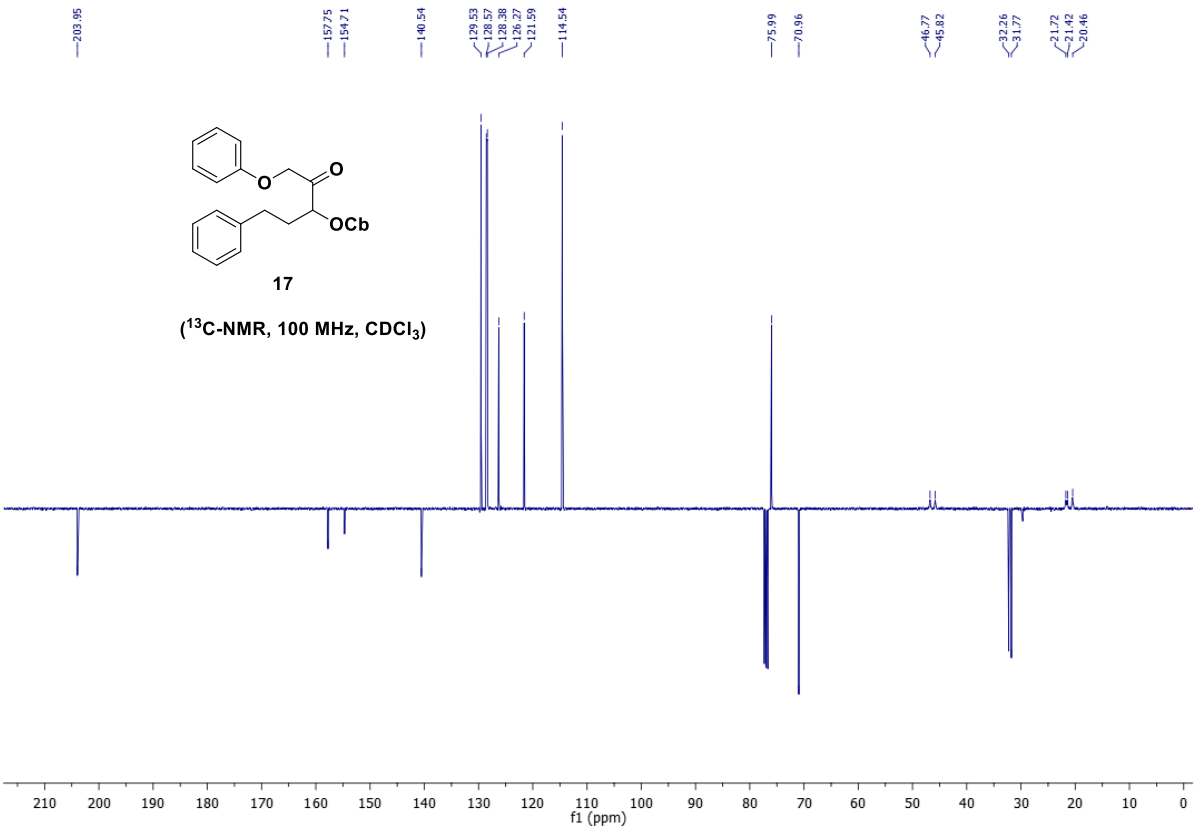
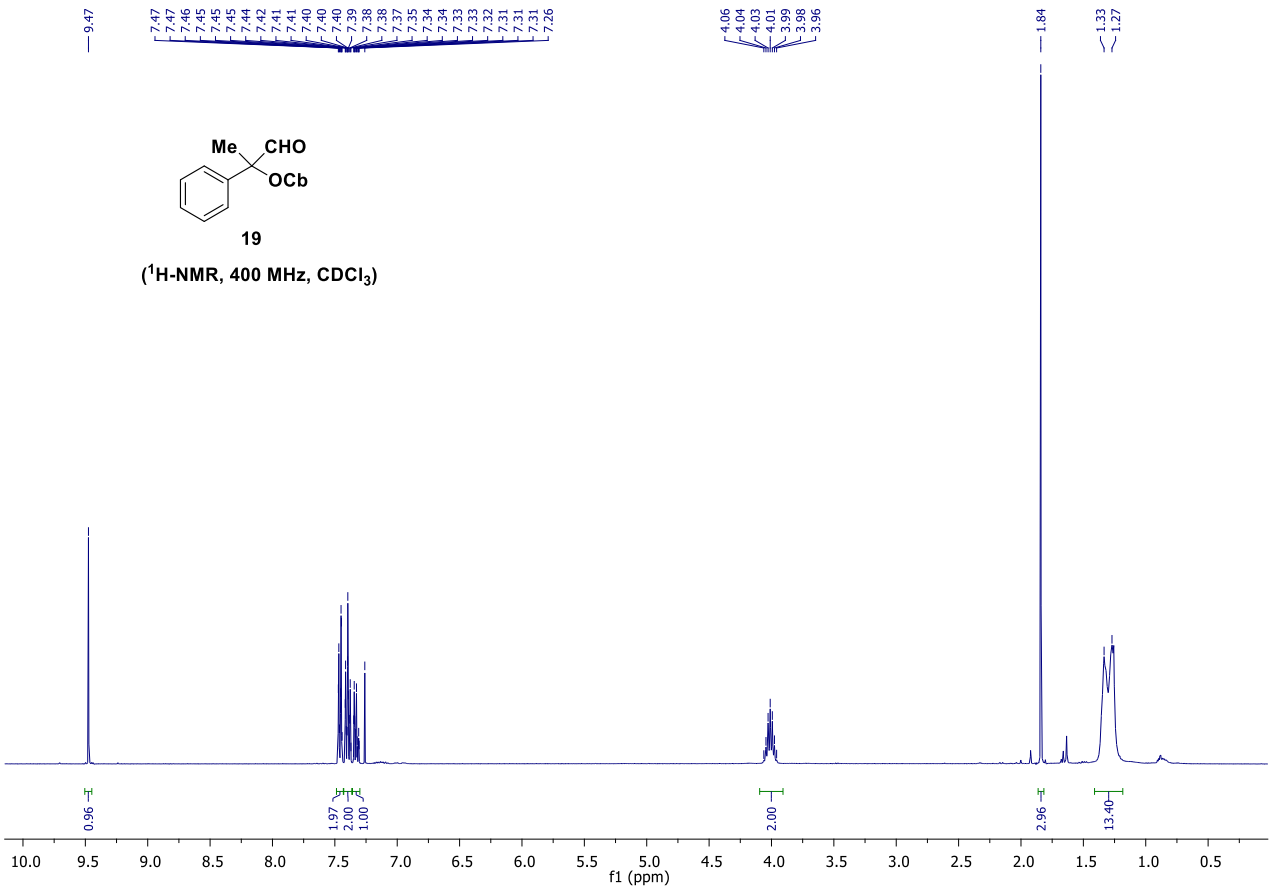
5.43 5.42 5.41 5.40
4.10
3.75 2.83 2.82 2.81 2.79 2.78 2.77 2.76 2.74 2.73 2.72 2.71 2.70 2.69 2.69 2.67 2.07 2.06 2.05 2.04 2.03 2.02 2.01 2.00 2.00 1.99 1.98 1.98 1.97 1.95 1.93 1.90 1.90 1.84 1.81 1.73 1.70 1.69 1.66 1.31 1.20
O
OCb
15
(1H-NMR, 400 MHz, CDCl3)
2.03 3.05 1.00 1.97 2.01 8.22 3.18 6.38 12.83
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)
211.88 154.80 141.06 128.50 128.37 126.14 73.02 46.74 45.72 45.29 38.40 36.44 33.02 32.15 27.90 21.94 21.36 20.53
O
OCb
15
(13C-NMR, 100 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


O
OCb
16
(1H-NMR, 400 MHz, CDCl3)
f1 (ppm)
O
OCb
16
(13C-NMR, 100 MHz, CDCl3)
f1 (ppm)

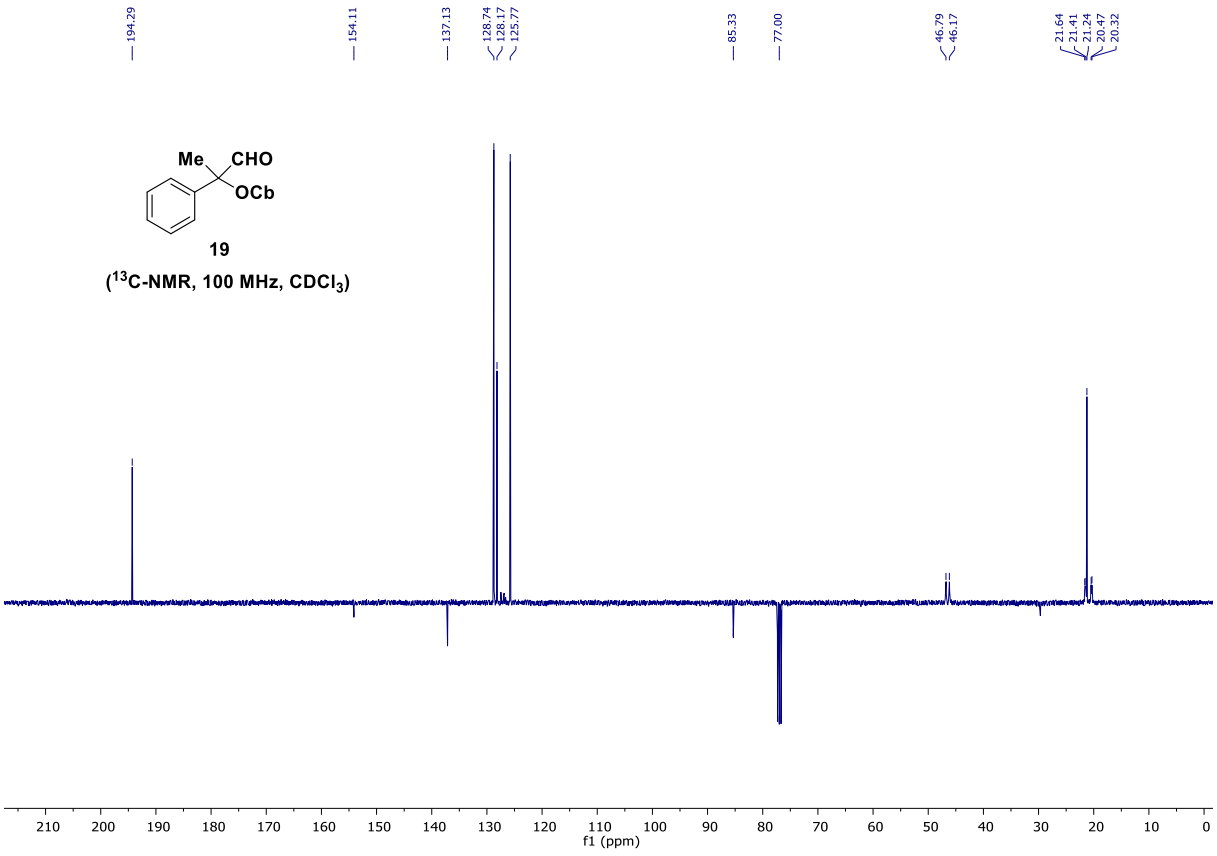

OCb
17
(1H-NMR, 400 MHz, CDCl3)
f1 (ppm)


OCb
17
(13C-NMR, 100 MHz, CDCl3)
f1 (ppm)



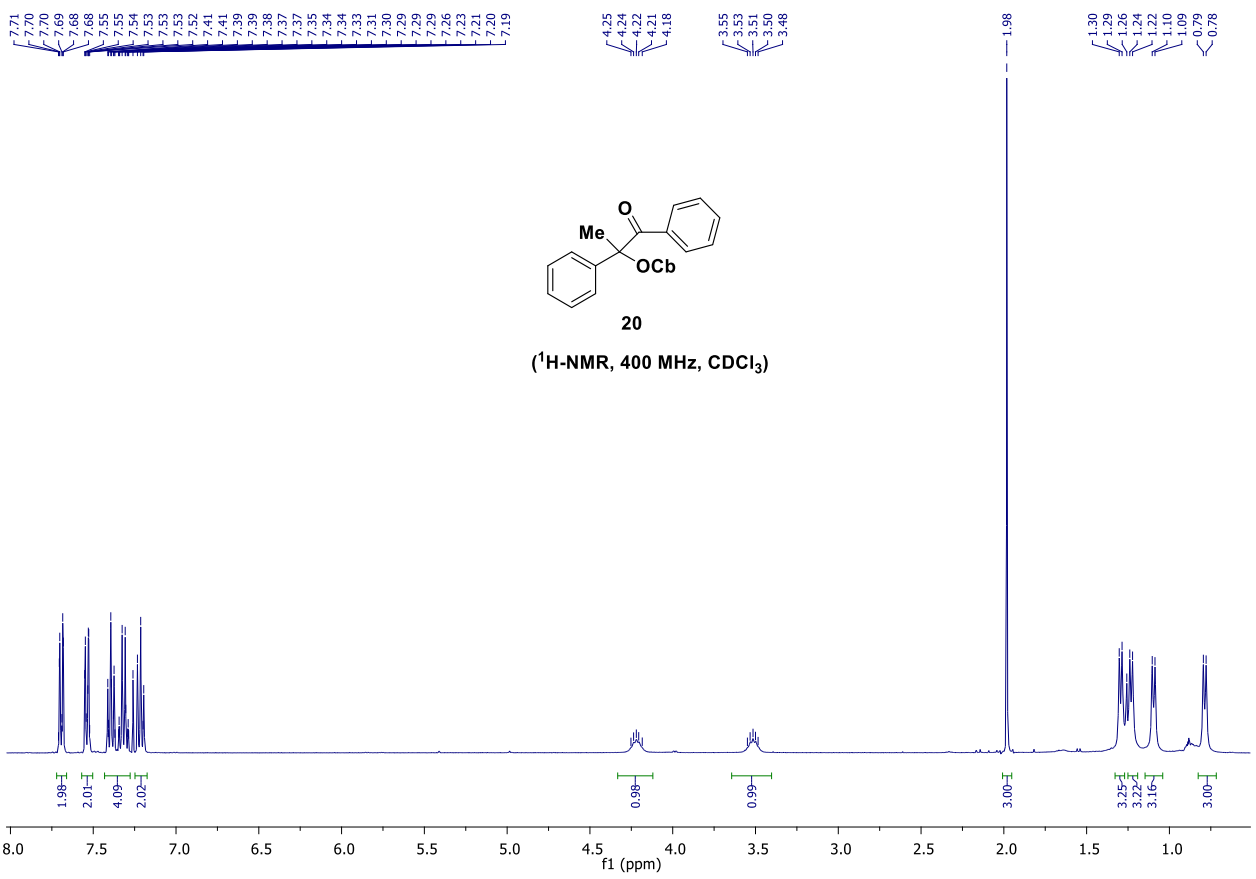
19

(^{1}H-NMR, 400 MHz, $CDCl_3$)



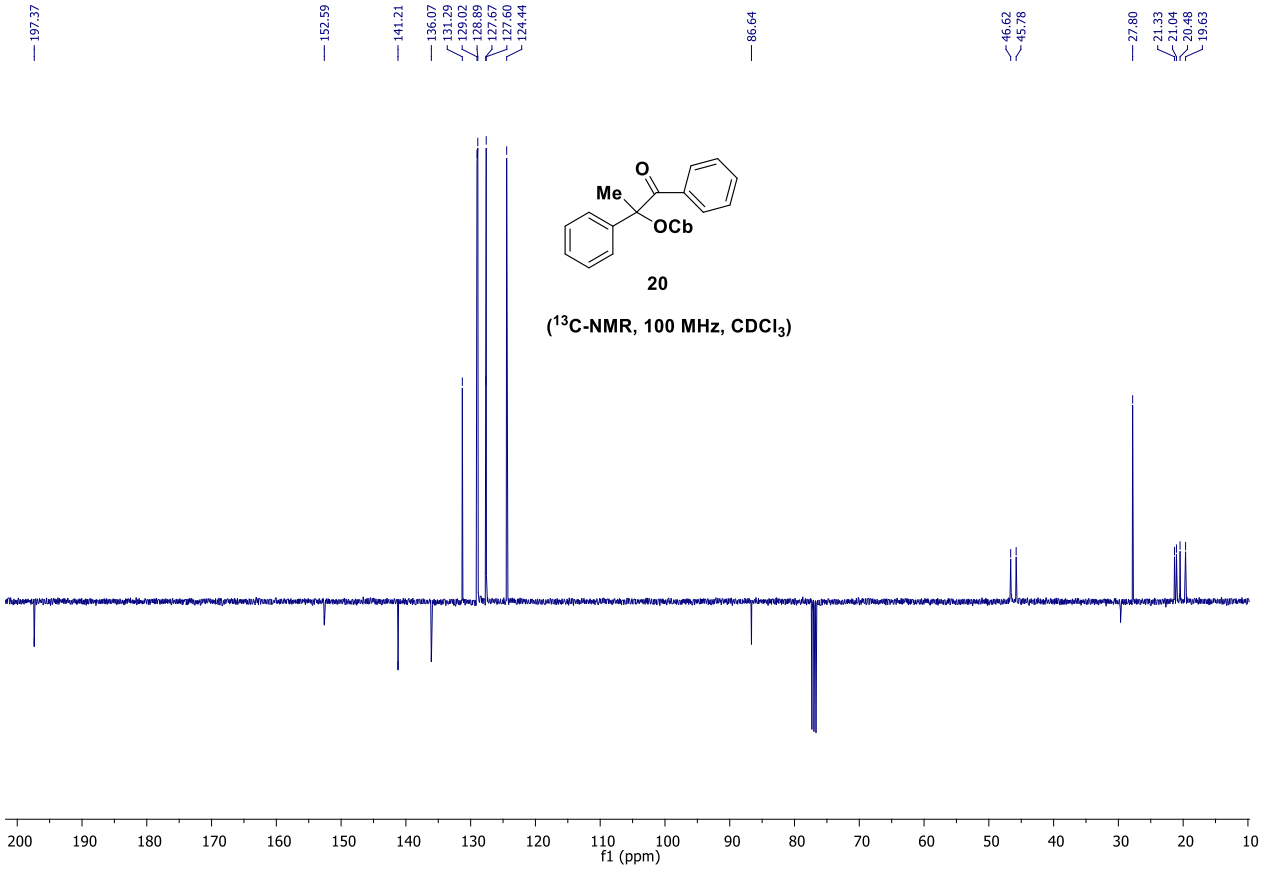
19

(^{13}C-NMR, 100 MHz, $CDCl_3$)



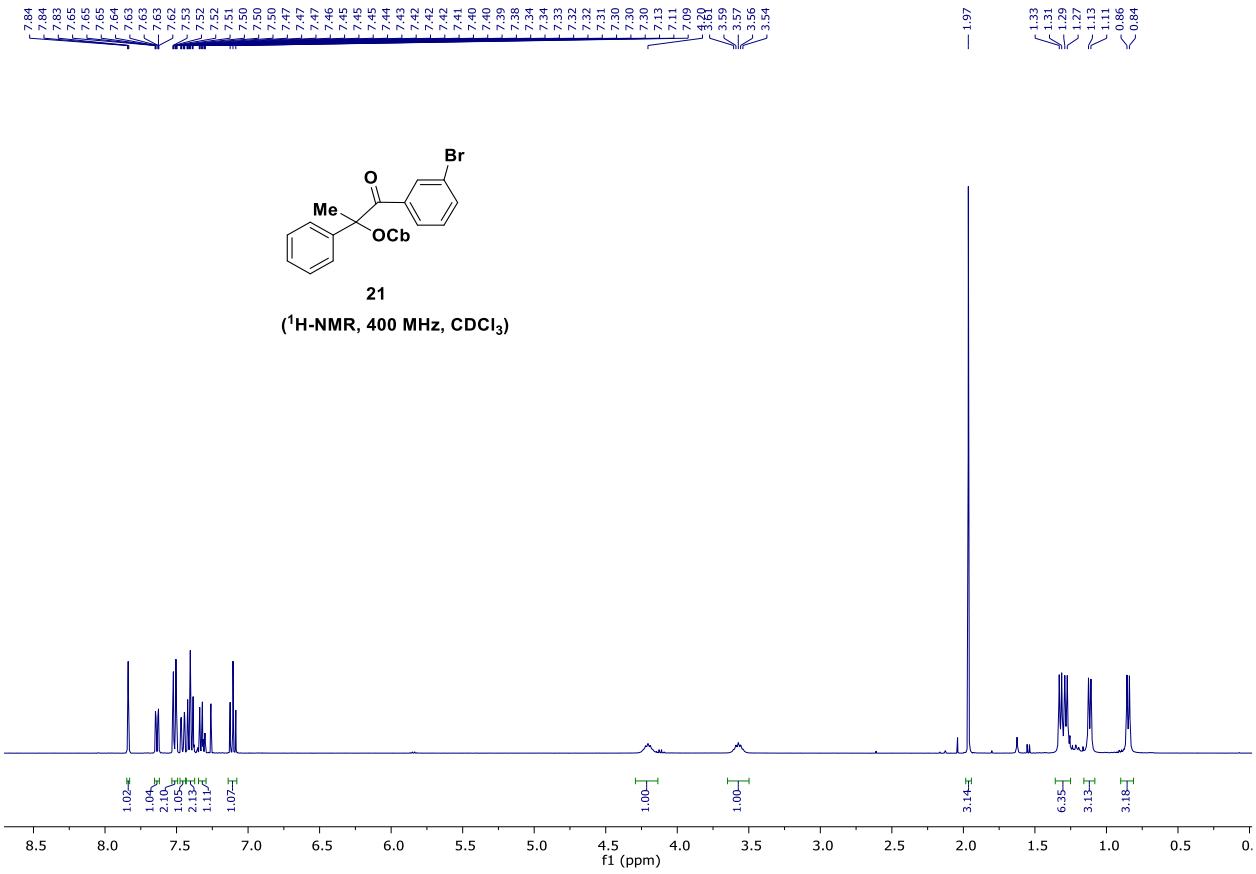
20

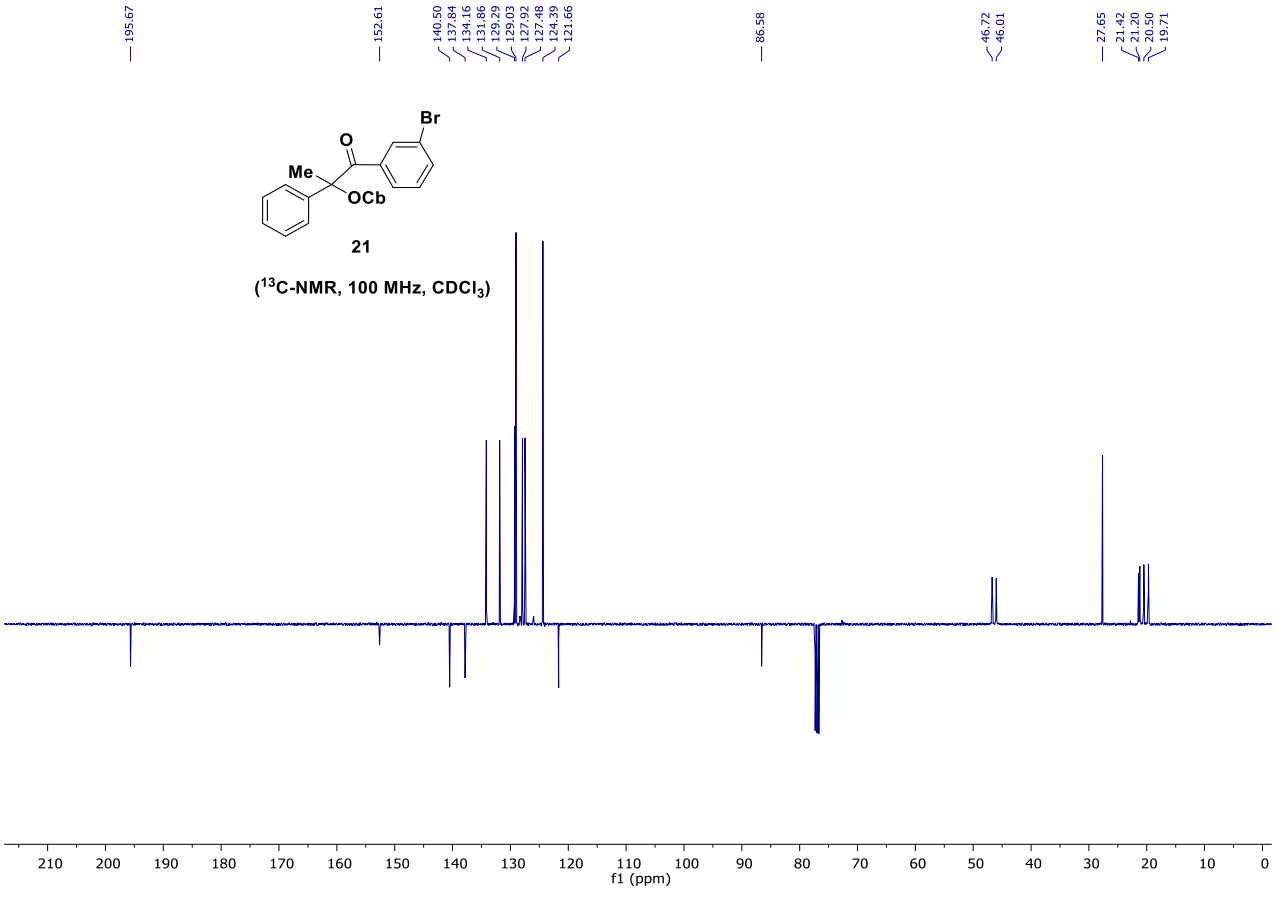
(^{1}H-NMR, 400 MHz, $CDCl_3$)

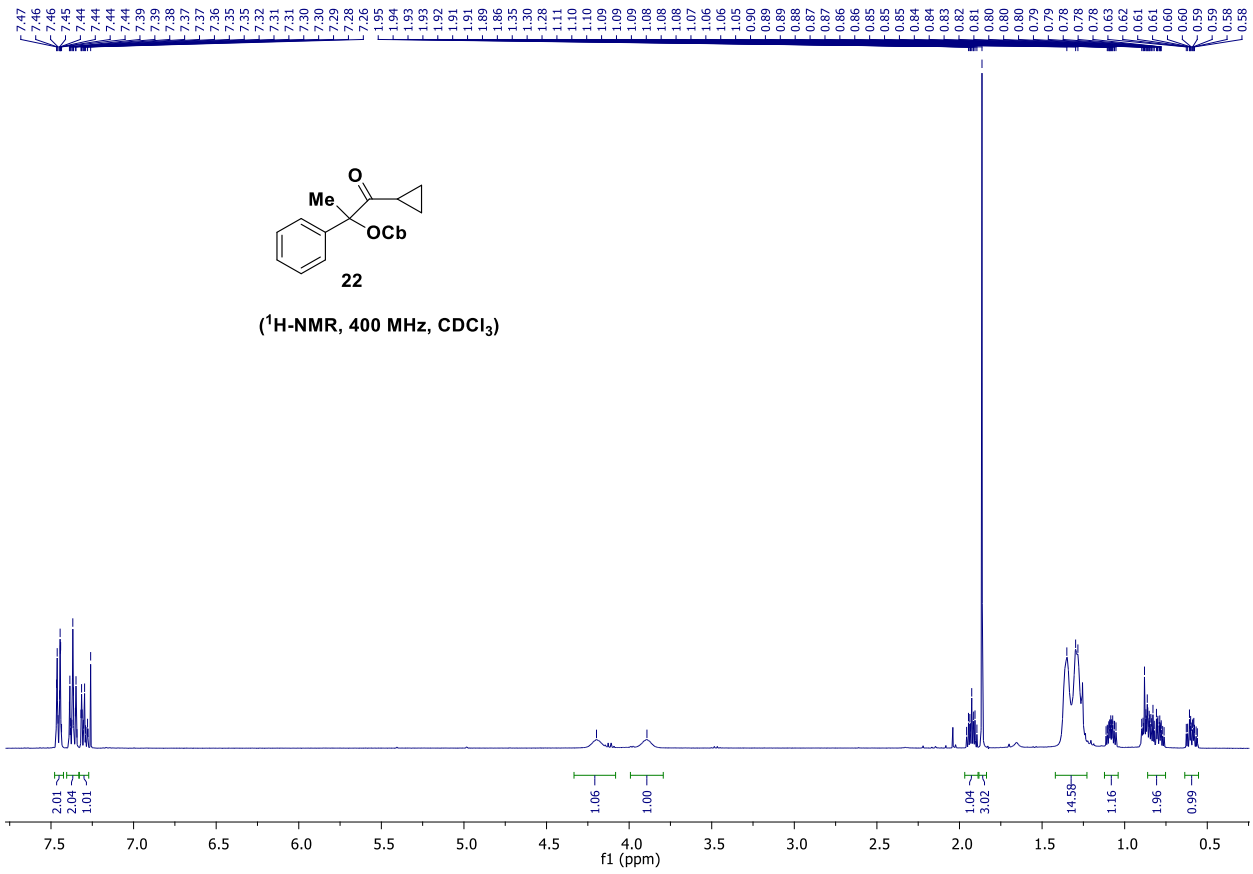


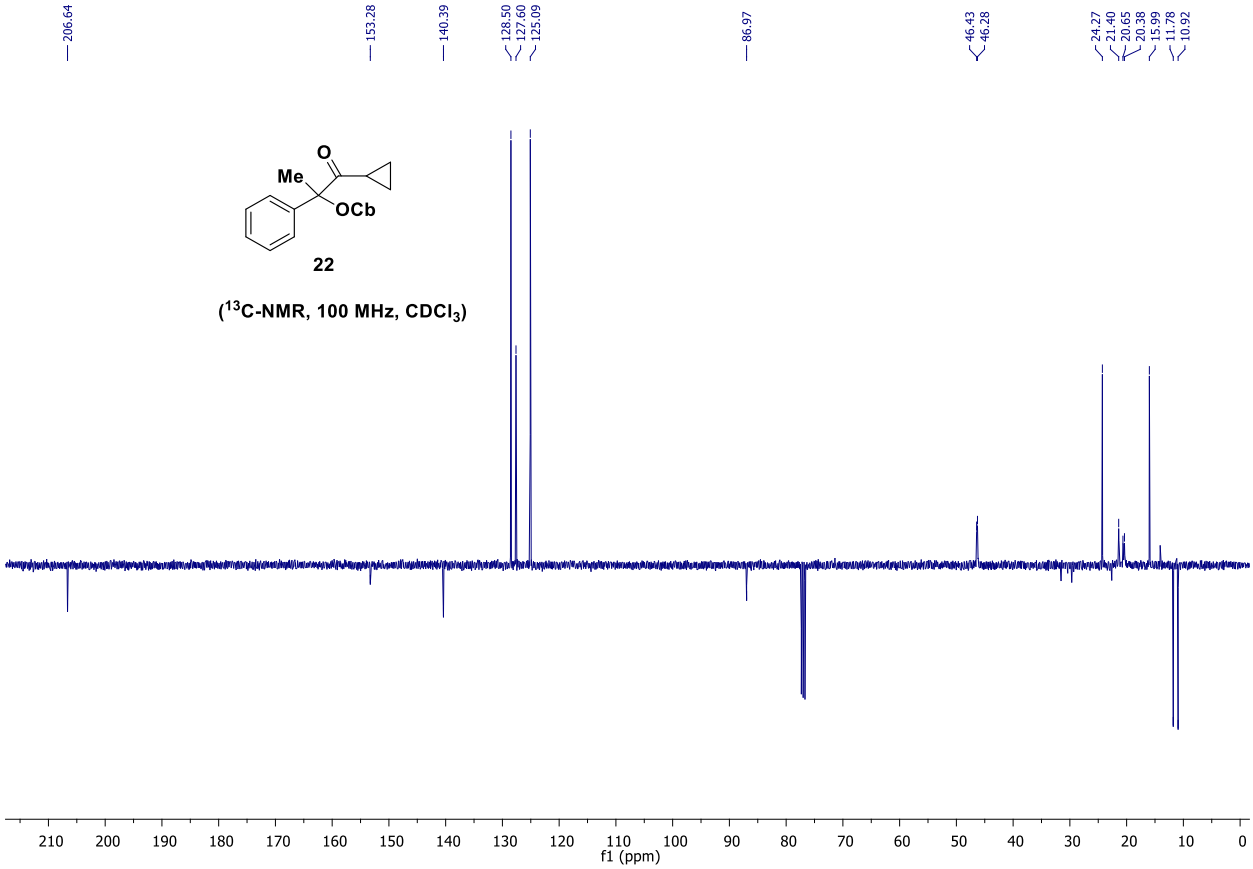
20

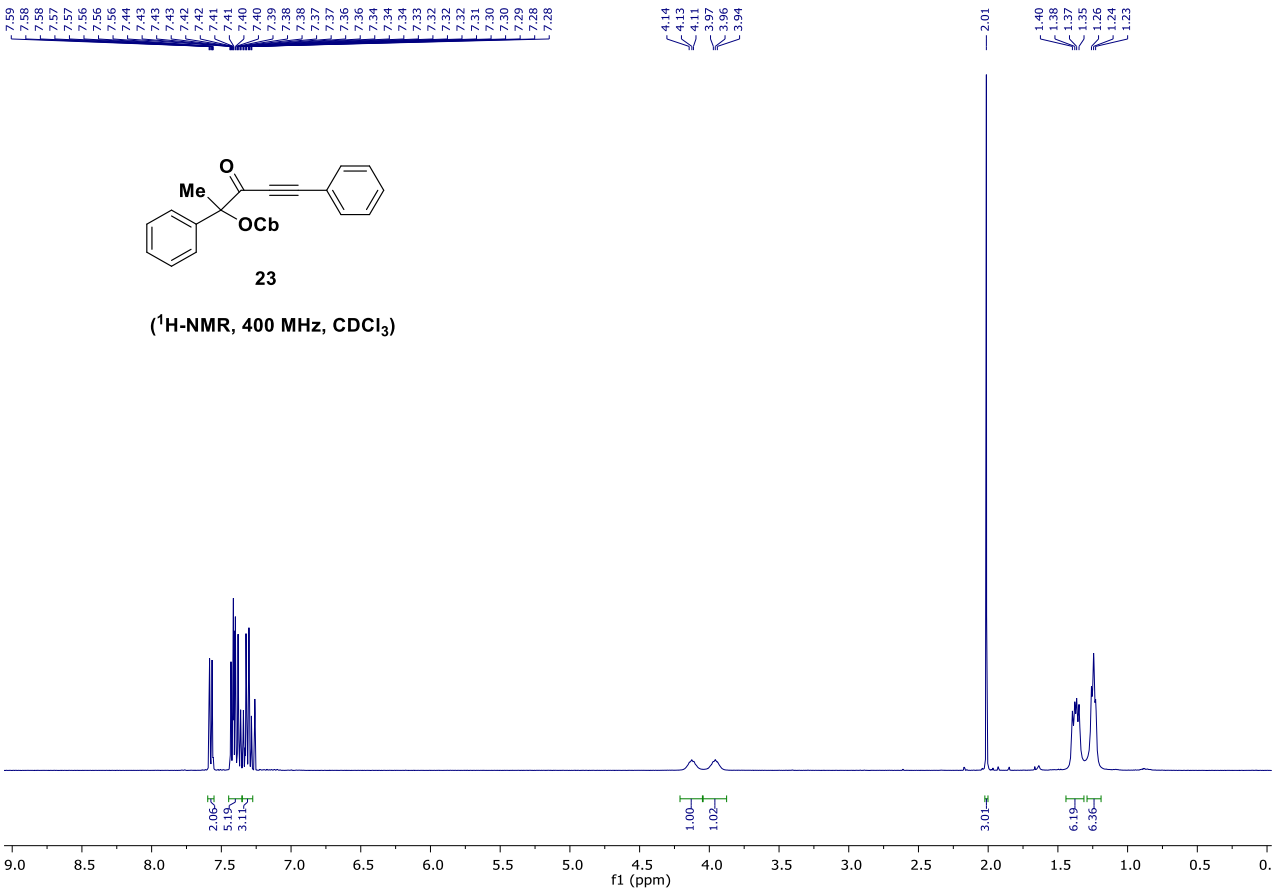
(^{13}C-NMR, 100 MHz, $CDCl_3$)


Br
O
Me
OCb
21
(1H-NMR, 400 MHz, CDCl3)
f1 (ppm)


Br
O
Me
OCb
21
(13C-NMR, 100 MHz, CDCl3)
f1 (ppm)

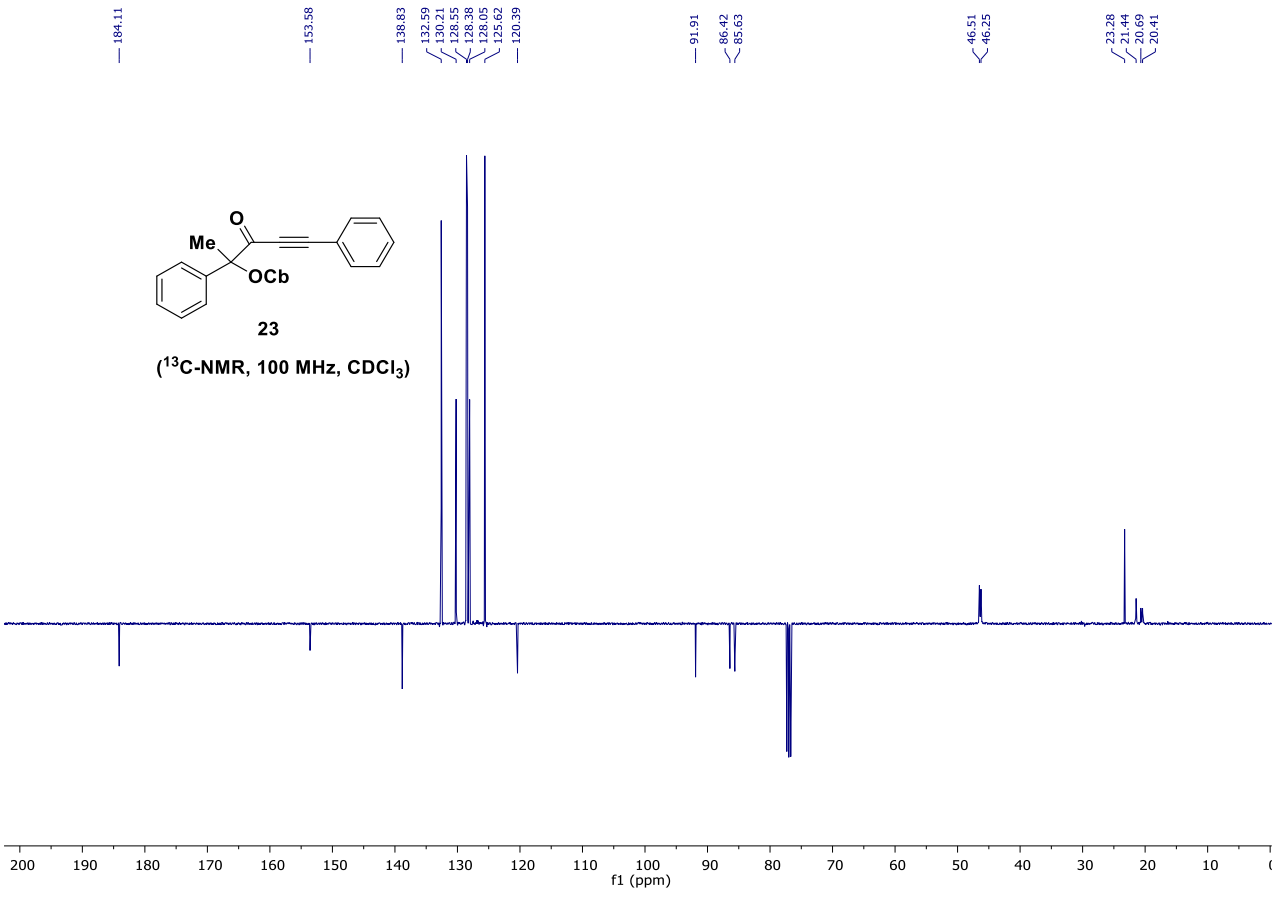

O
Me
OCb
22
(1H-NMR, 400 MHz, CDCl3)
f1 (ppm)


O
Me
OCb
22
(13C-NMR, 100 MHz, CDCl3)
f1 (ppm)



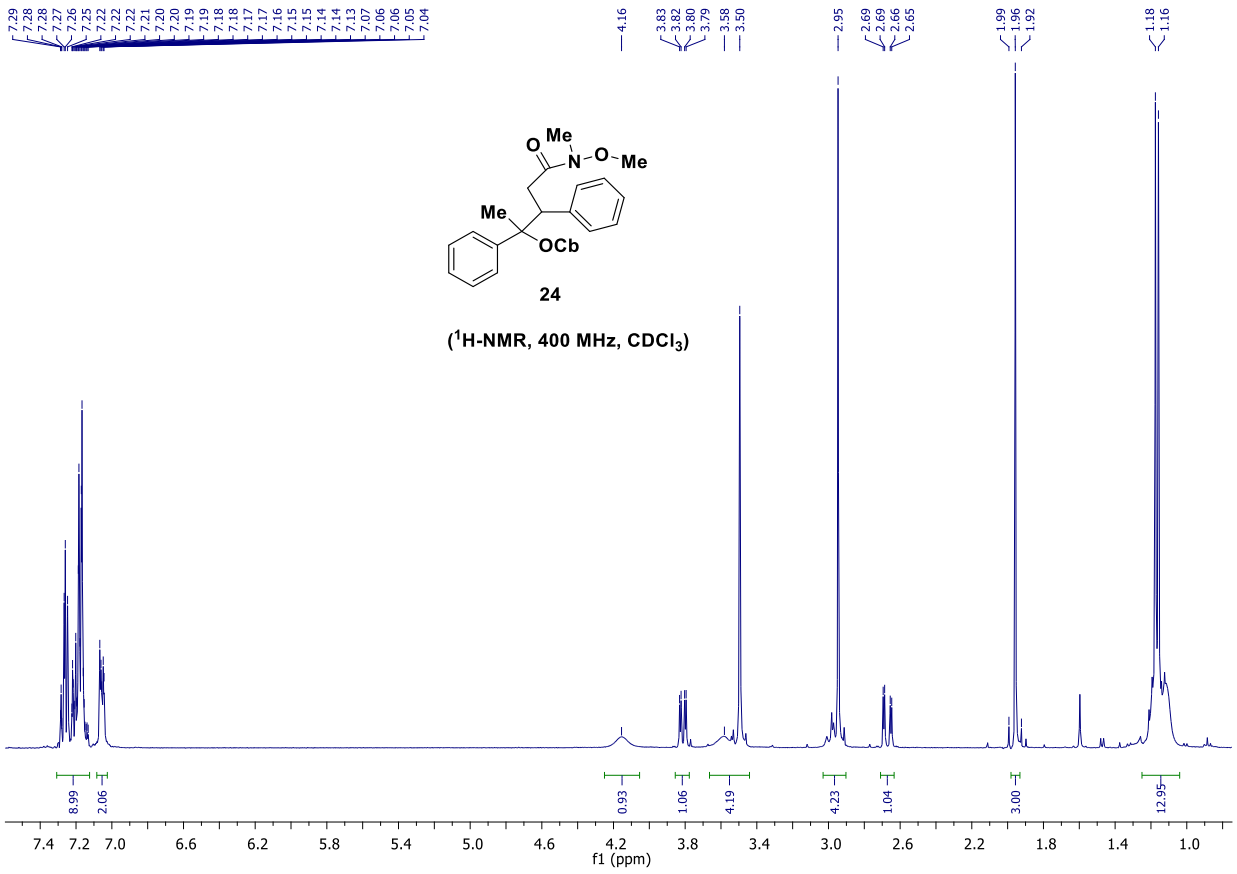
23

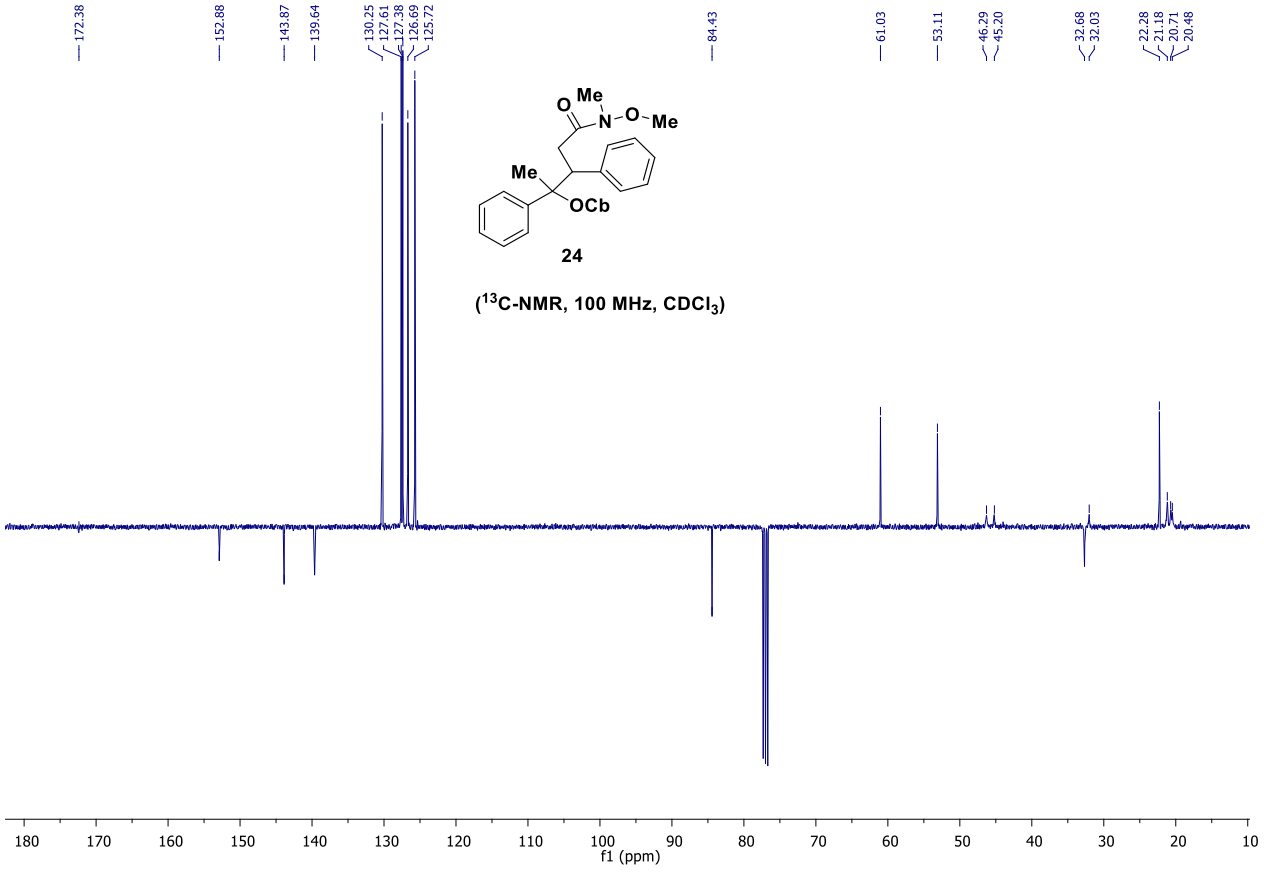
(^{1}H-NMR, 400 MHz, $CDCl_3$)

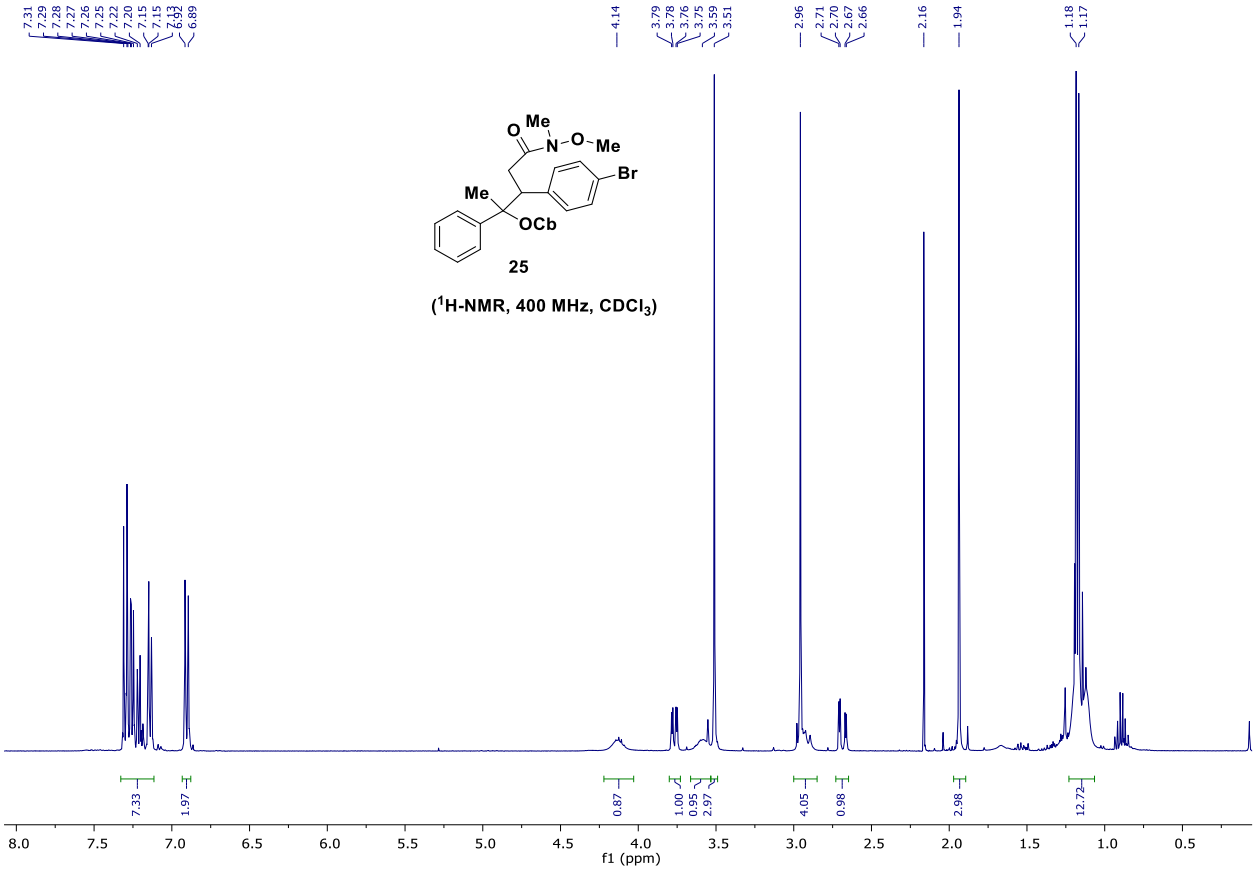


23

(^{13}C-NMR, 100 MHz, $CDCl_3$)

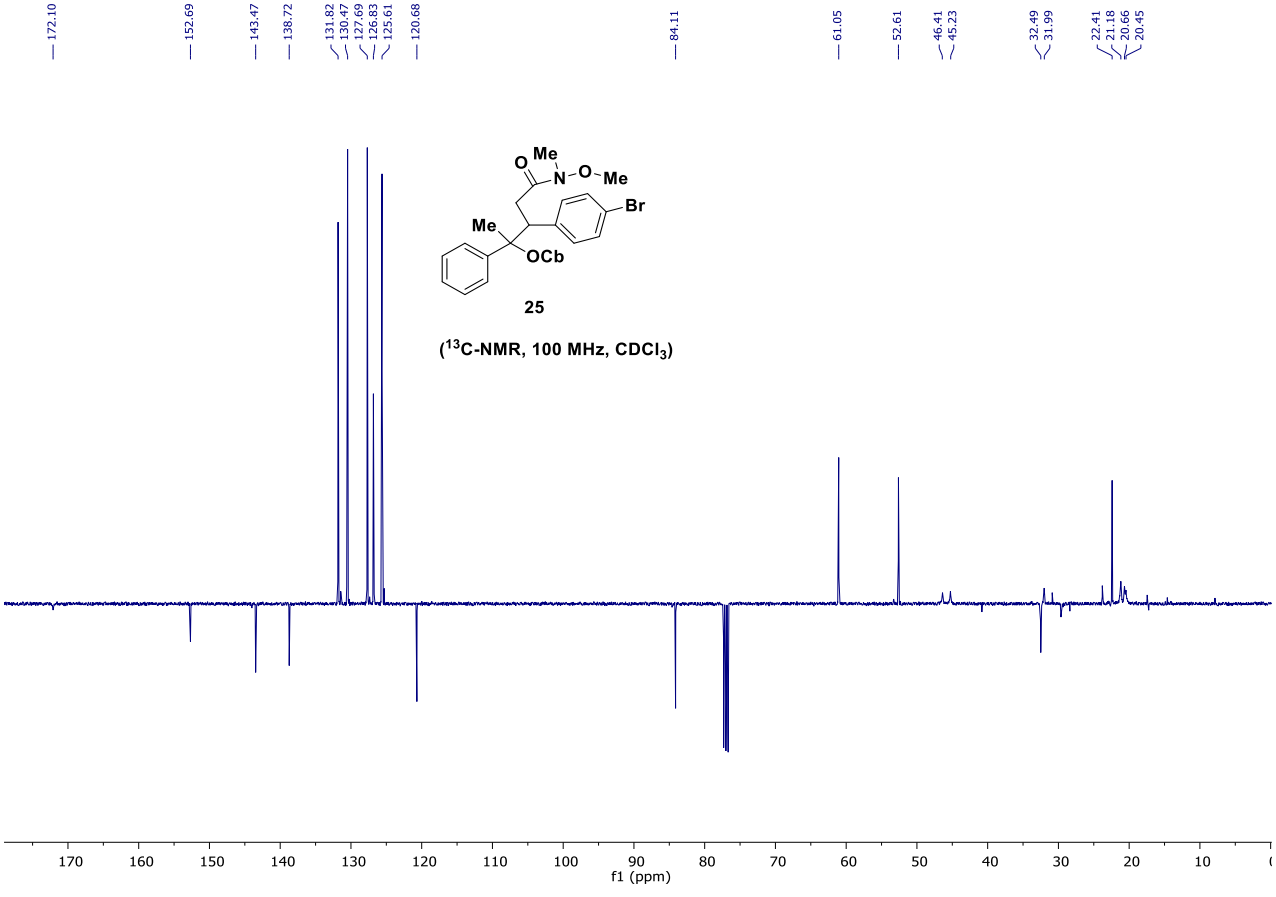

Me
O
N
O
Me
Me
OCb
24
(1H-NMR, 400 MHz, CDCl3)
f1 (ppm)


Me
O
N
O
Me
Me
OCb
24
(13C-NMR, 100 MHz, CDCl3)
f1 (ppm)



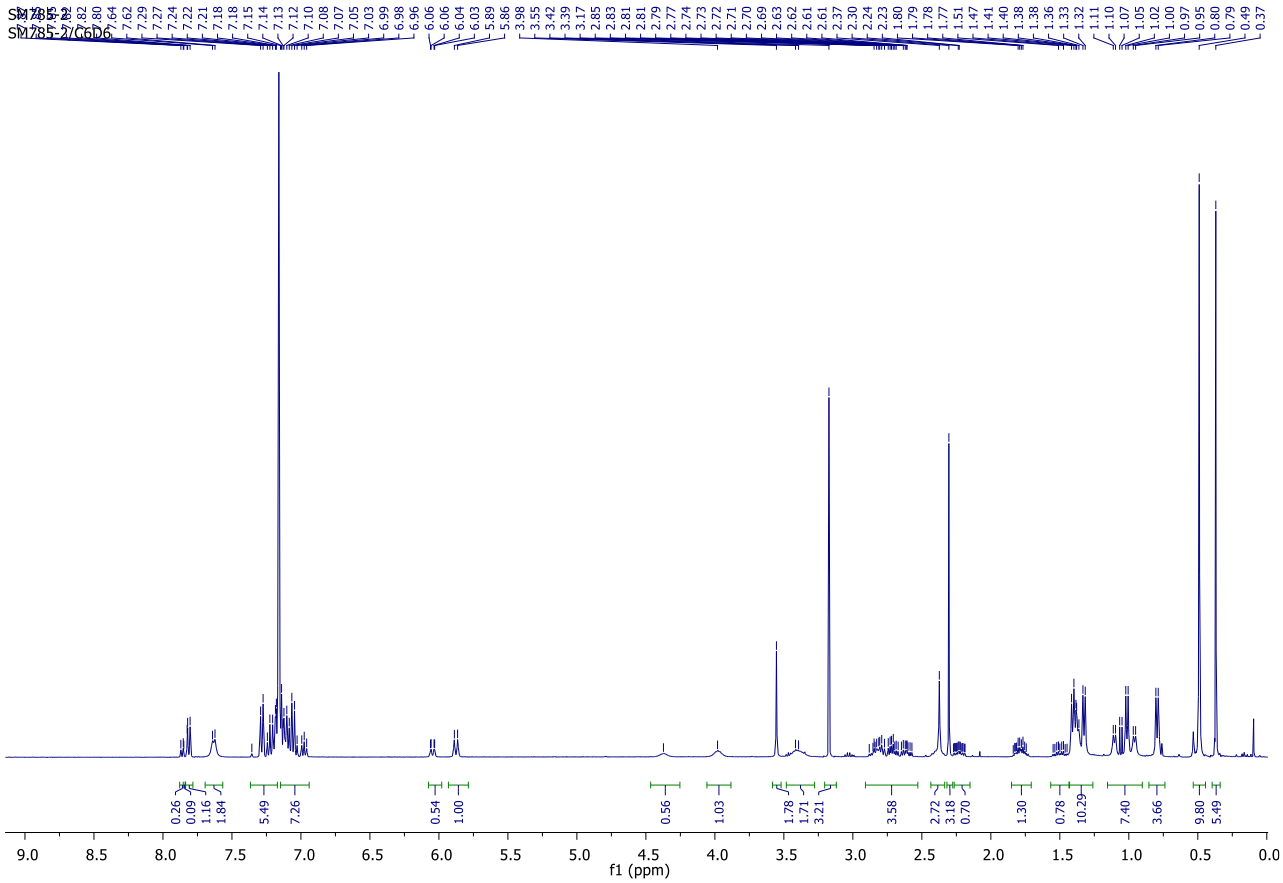
25

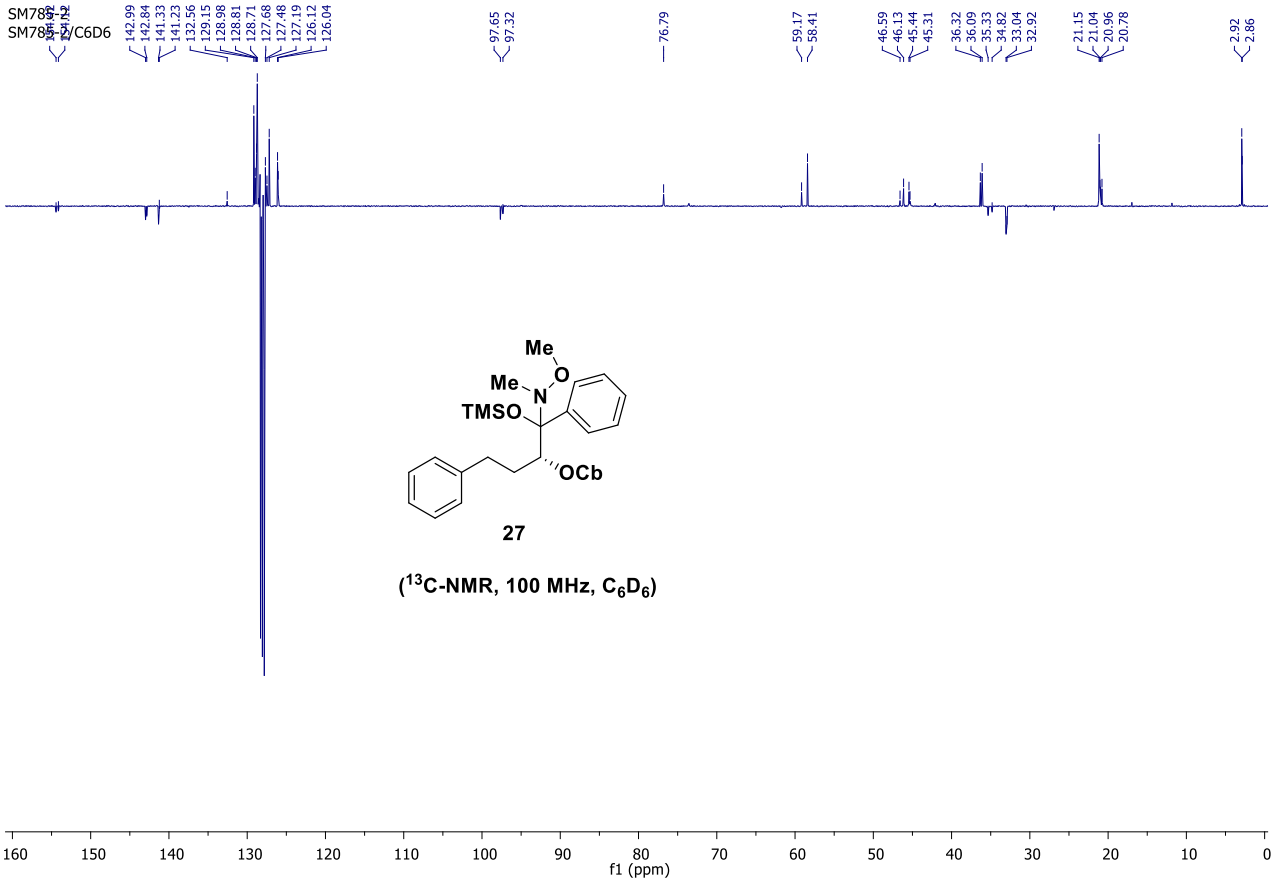
(^{1}H-NMR, 400 MHz, $CDCl_3$)



25

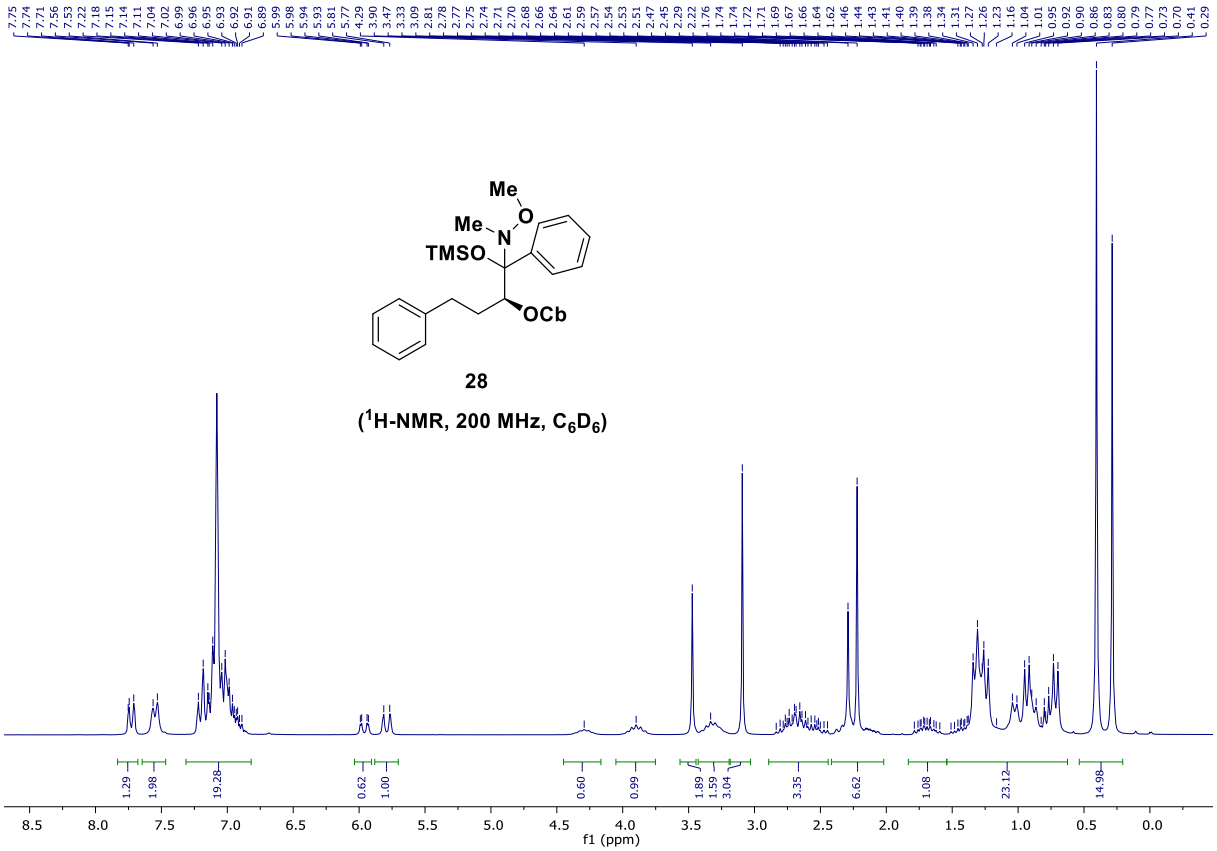
(^{13}C-NMR, 100 MHz, $CDCl_3$)

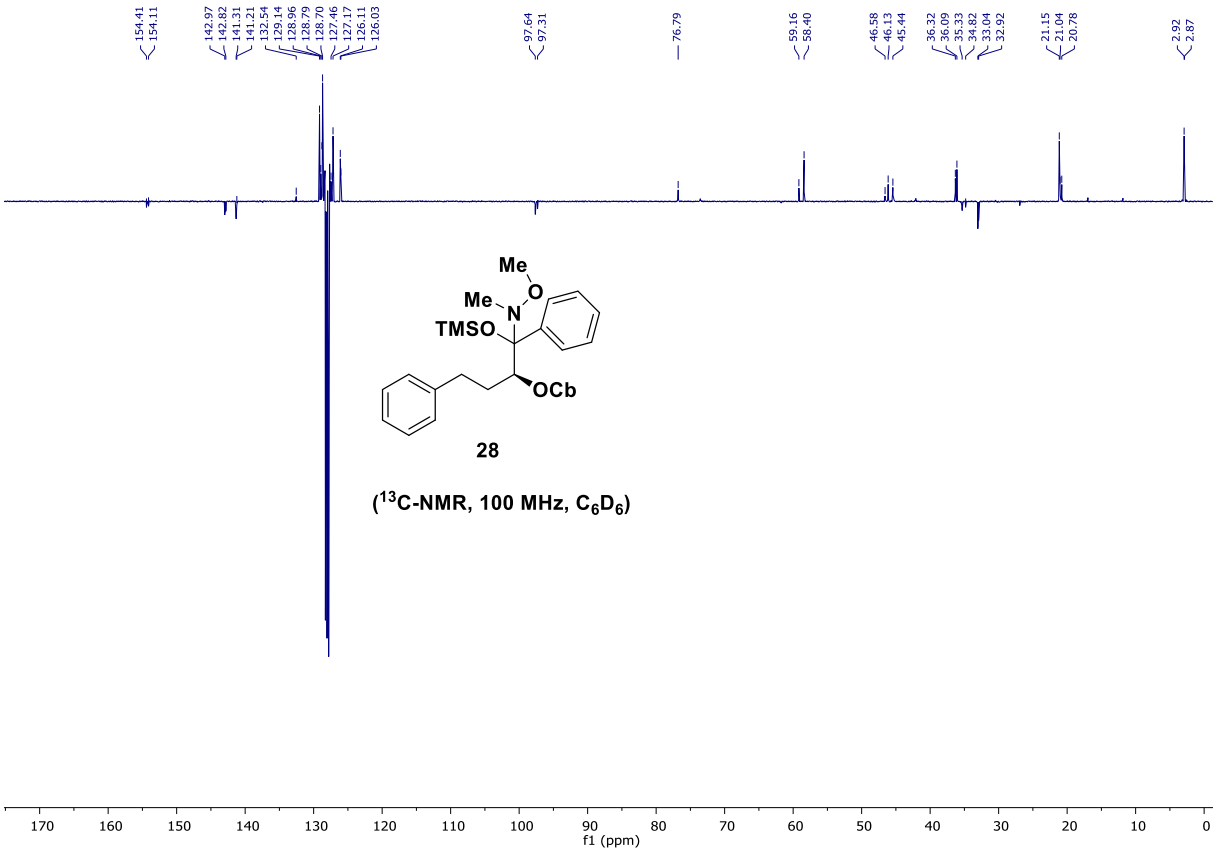


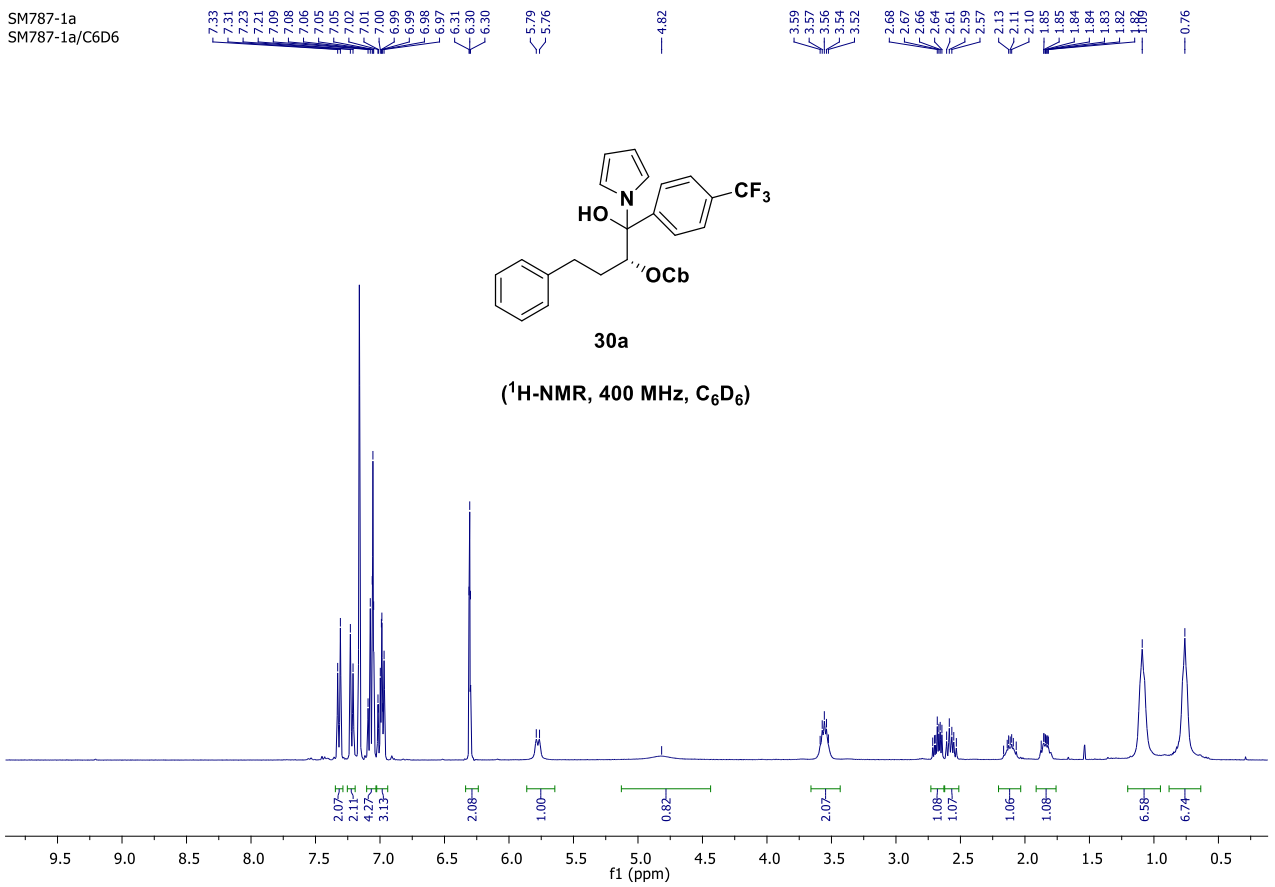


27

(^{13}C-NMR, 100 MHz, C_6D_6)

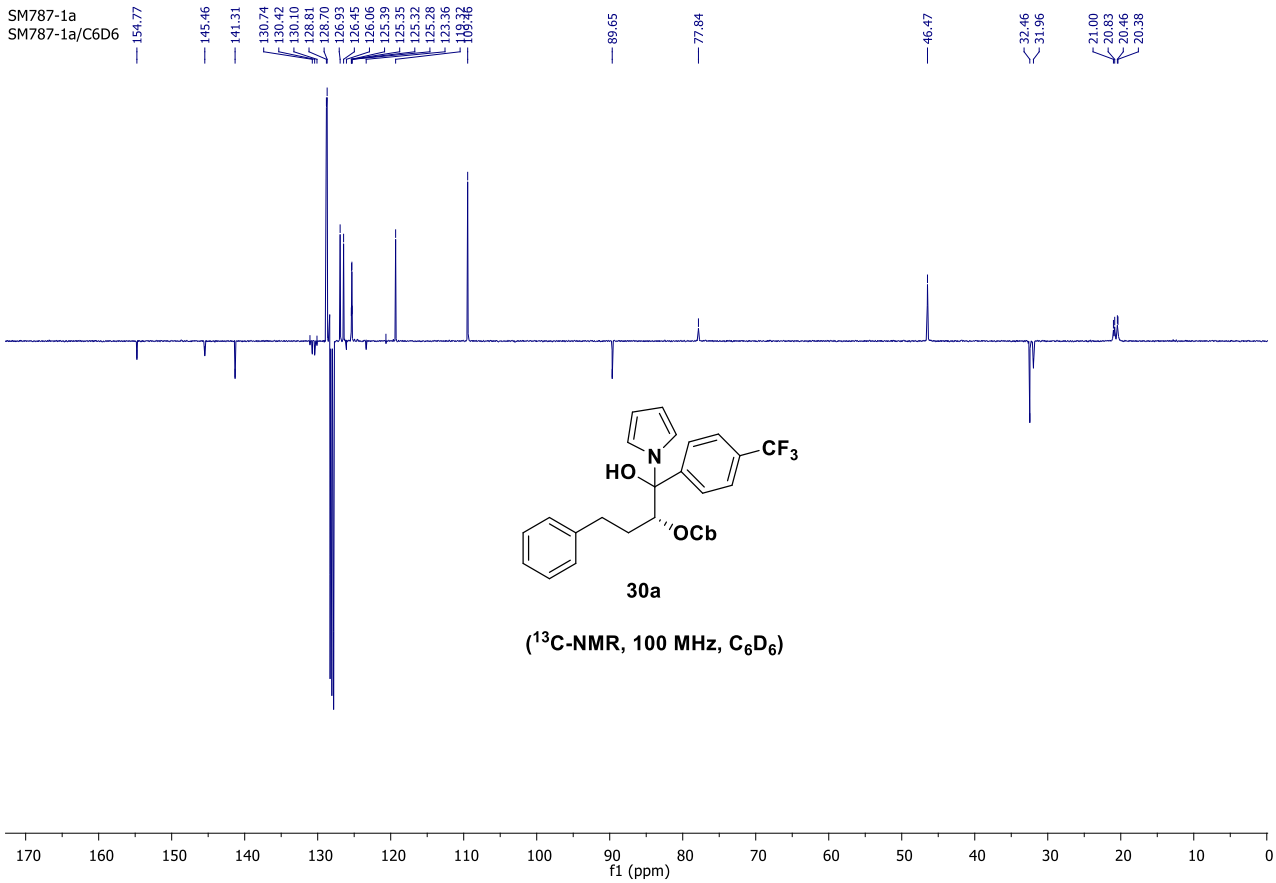

Me
O
Me
N
TMSO
OCb
28
(1H-NMR, 200 MHz, C6D6)
f1 (ppm)


Me
O
Me
N
TMSO
OCb
28
(13C-NMR, 100 MHz, C6D6)
f1 (ppm)



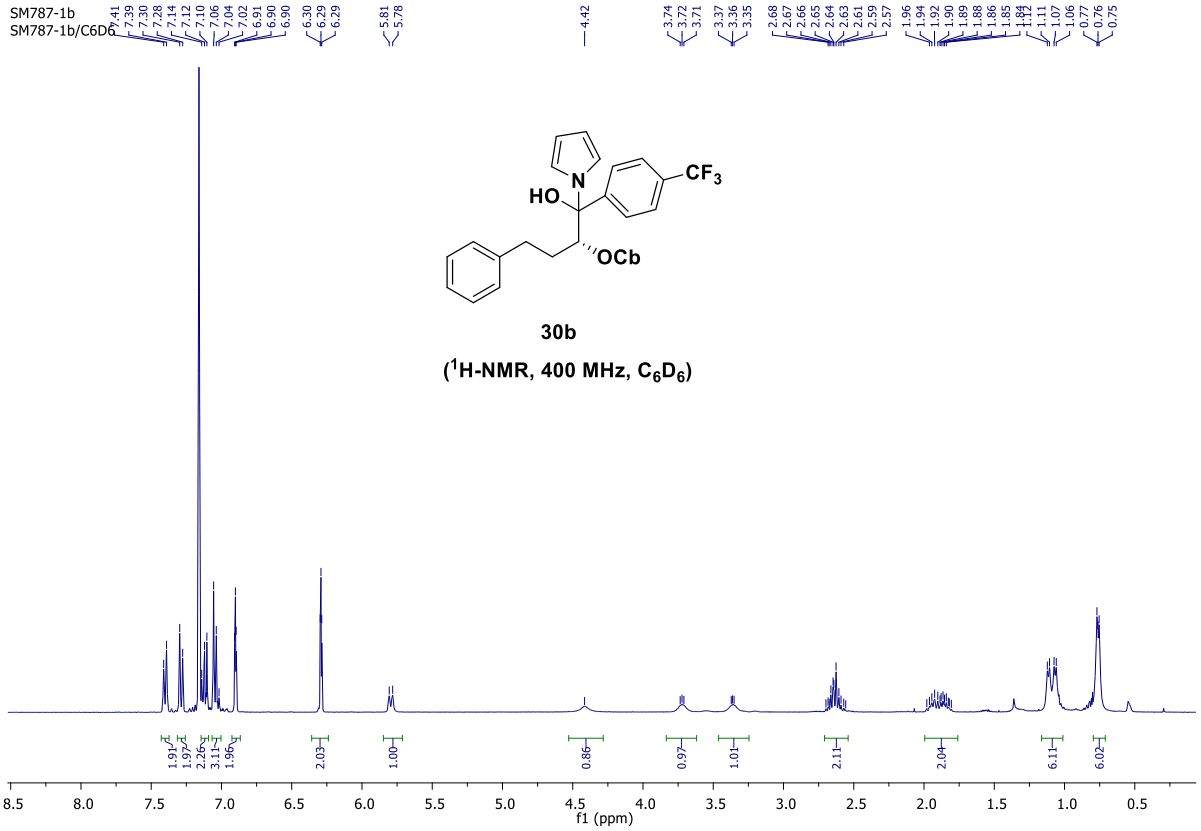
30a

(^{1}H-NMR, 400 MHz, C_6D_6)



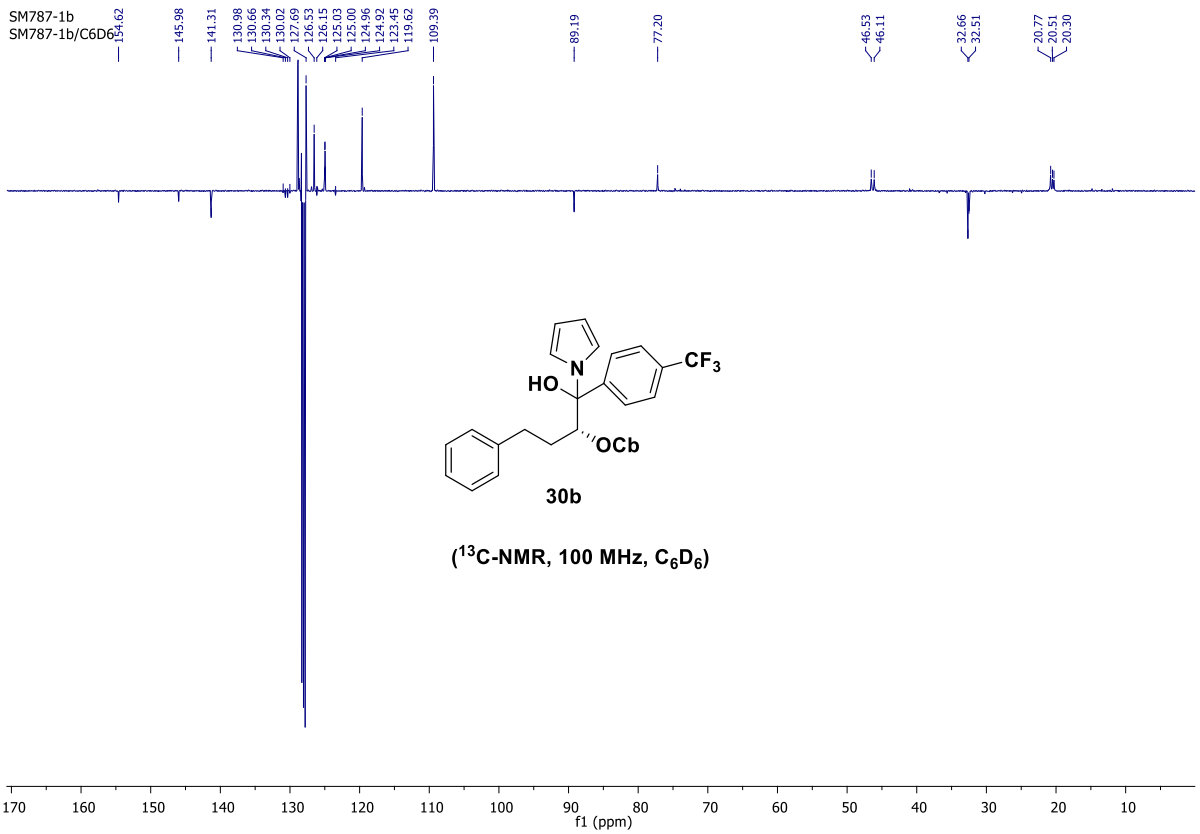
30a

(^{13}C-NMR, 100 MHz, C_6D_6)



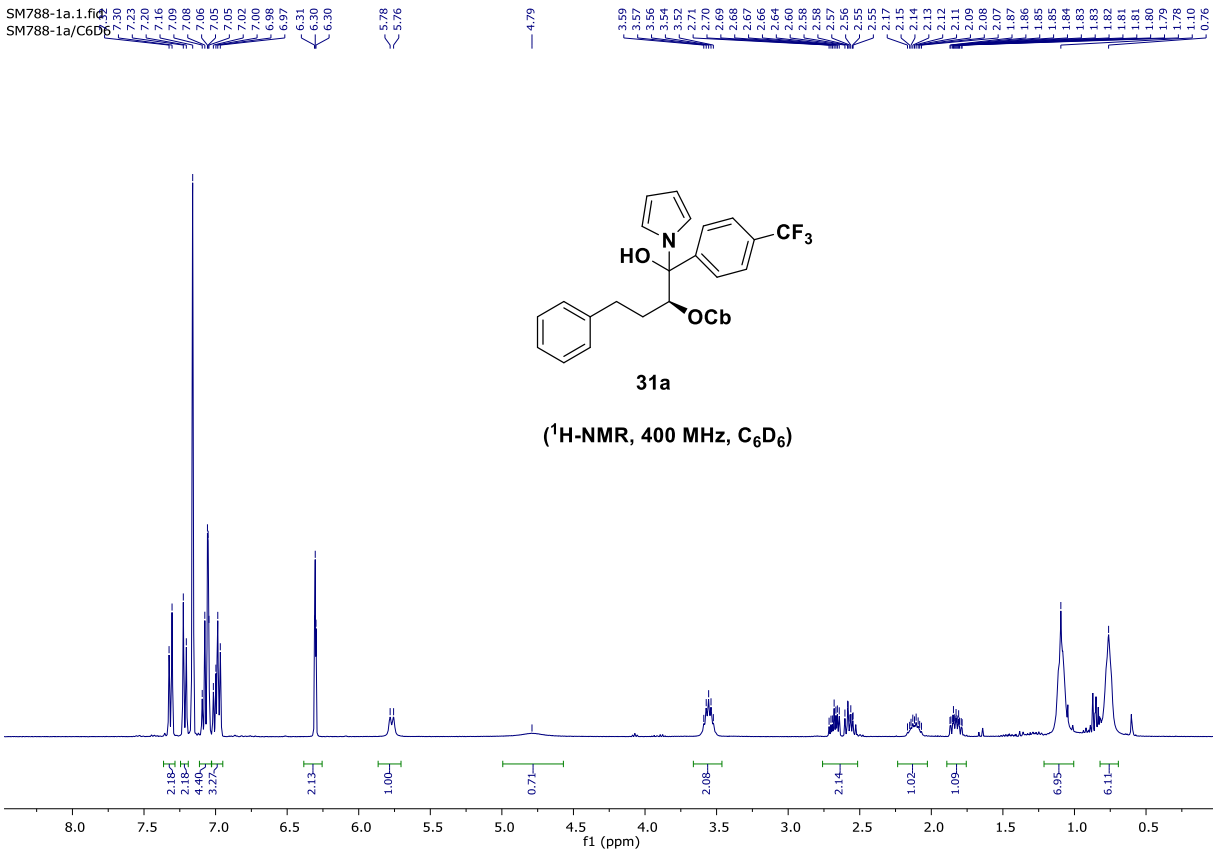
30b

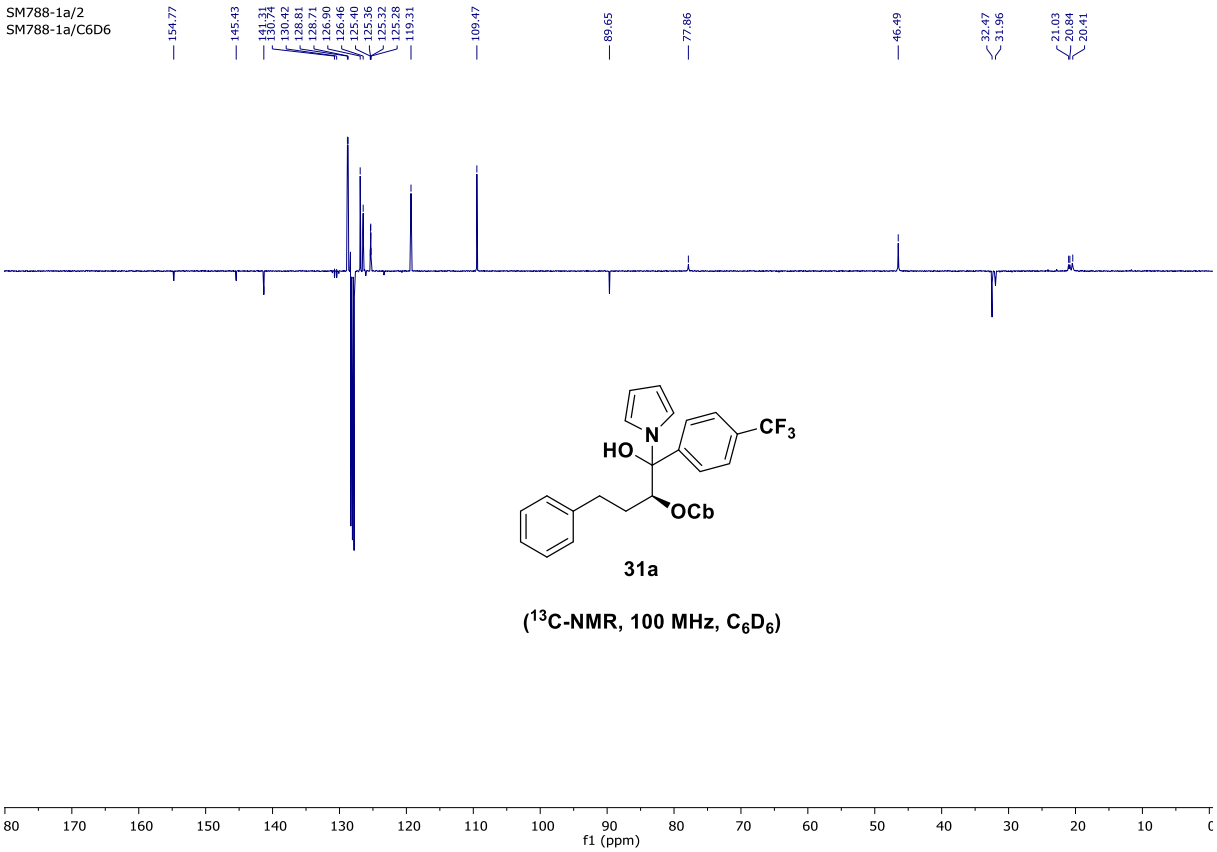
(^{1}H-NMR, 400 MHz, C_6D_6)

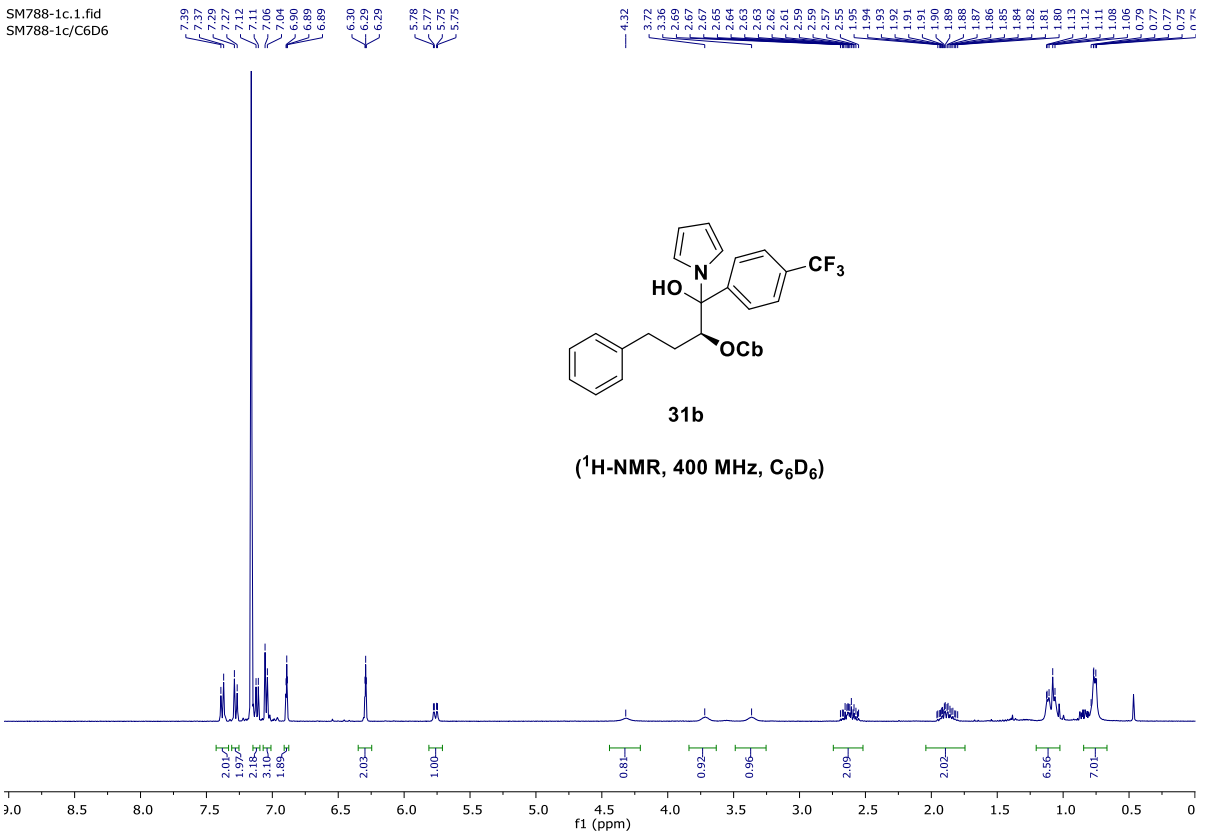


30b

(^{13}C-NMR, 100 MHz, C_6D_6)

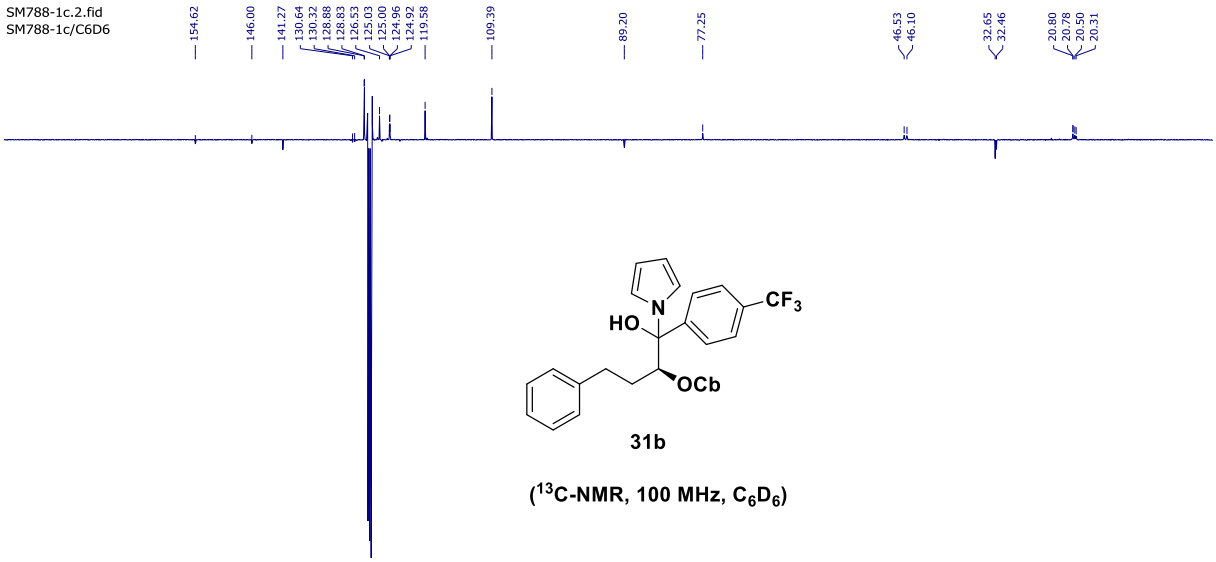

SM788-1a.1.fid
SM788-1a/C6D6
HO
N
CF3
OCb
31a
(1H-NMR, 400 MHz, C6D6)
f1 (ppm)


SM788-1a/2
SM788-1a/C6D6
HO
N
CF3
OCb
31a
(13C-NMR, 100 MHz, C6D6)
f1 (ppm)



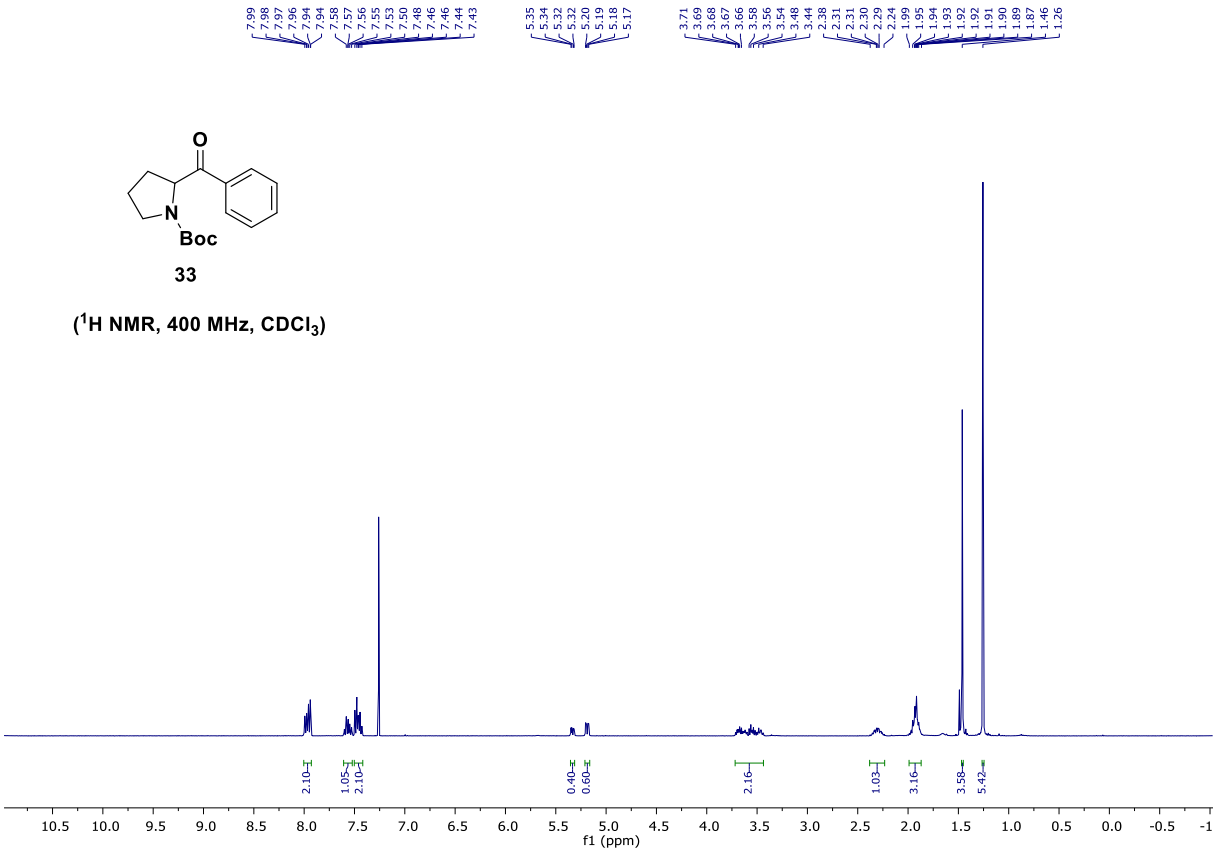
31b

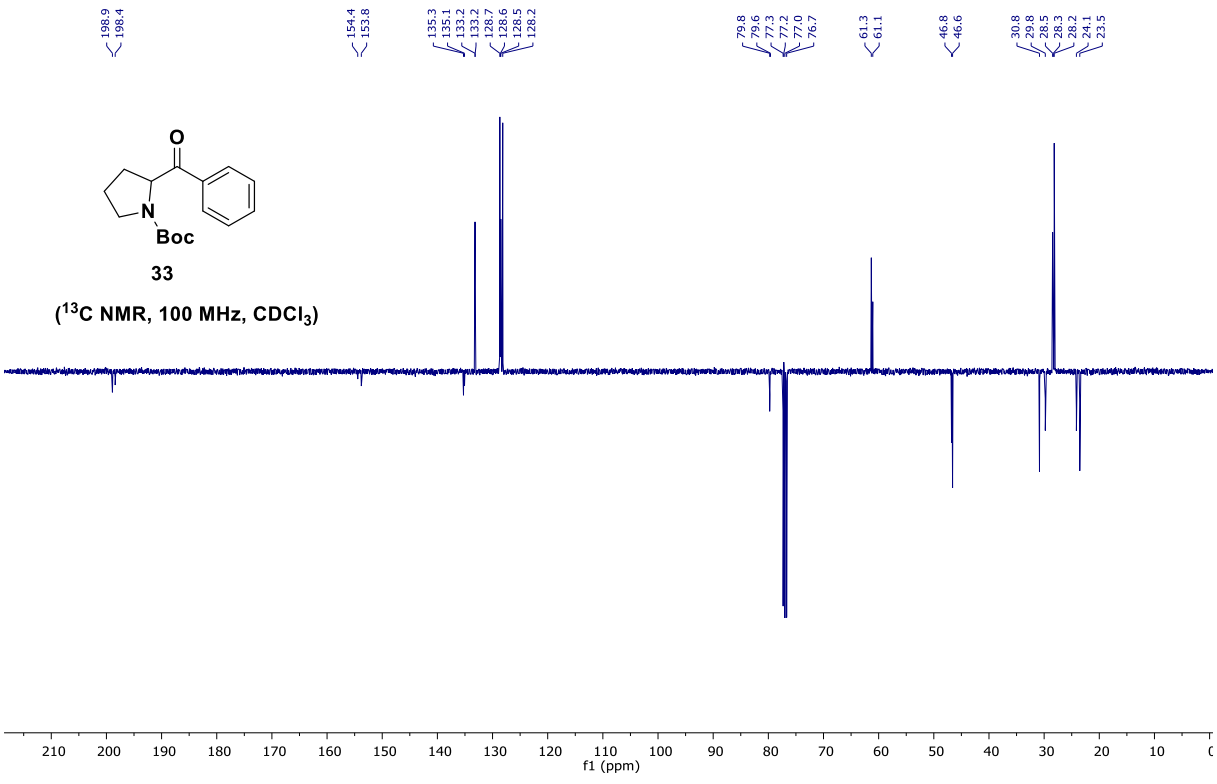
(^{1}H-NMR, 400 MHz, C_6D_6)

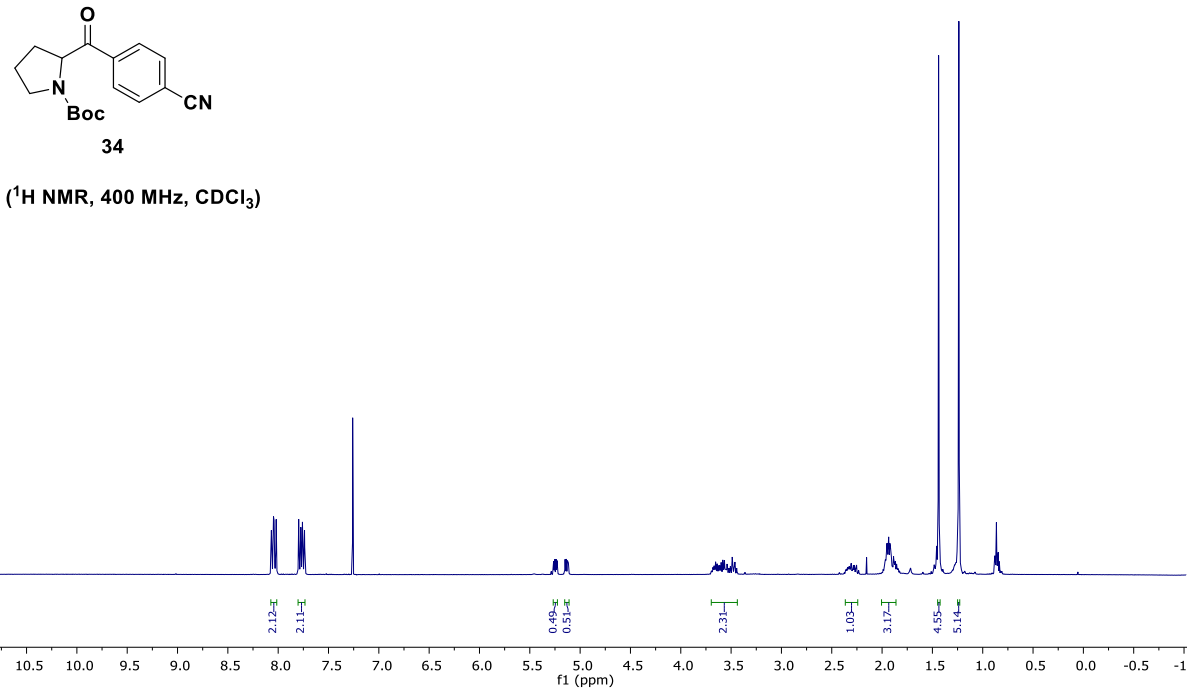


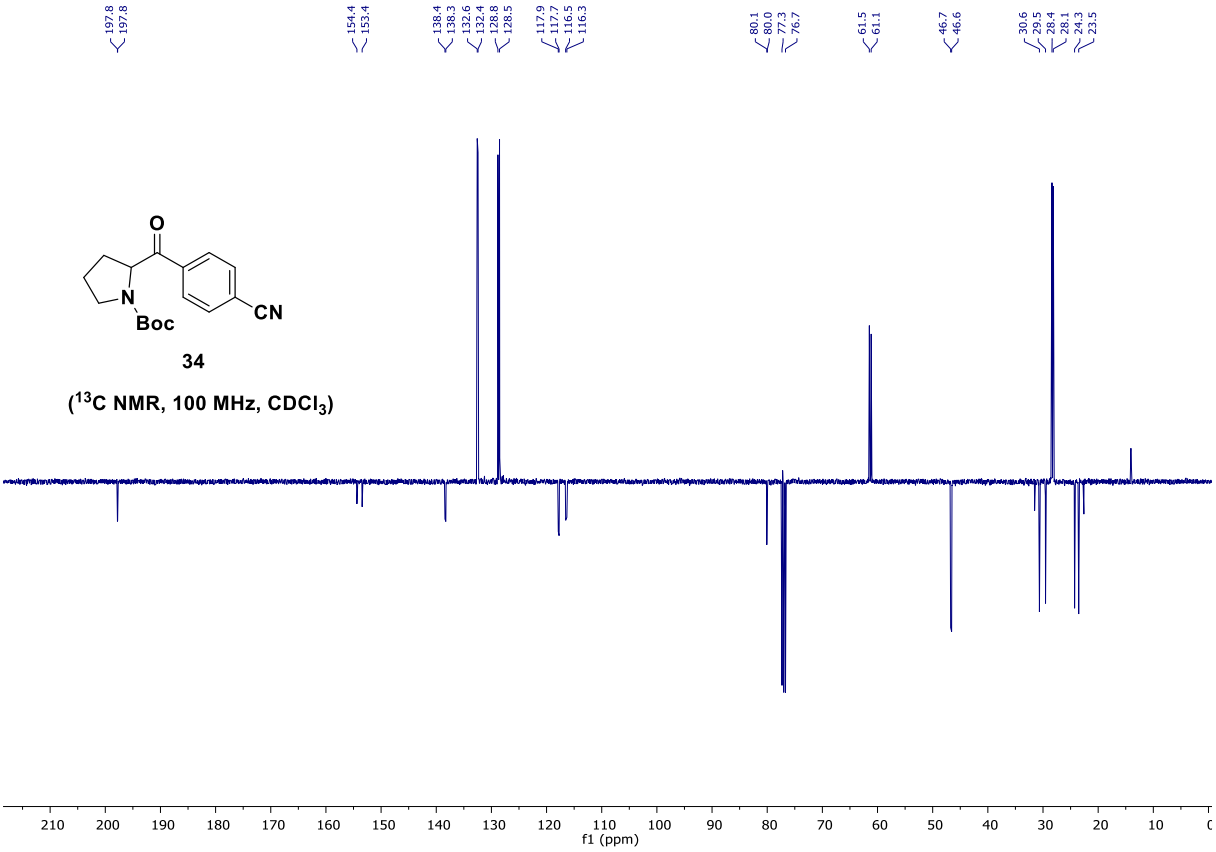
31b

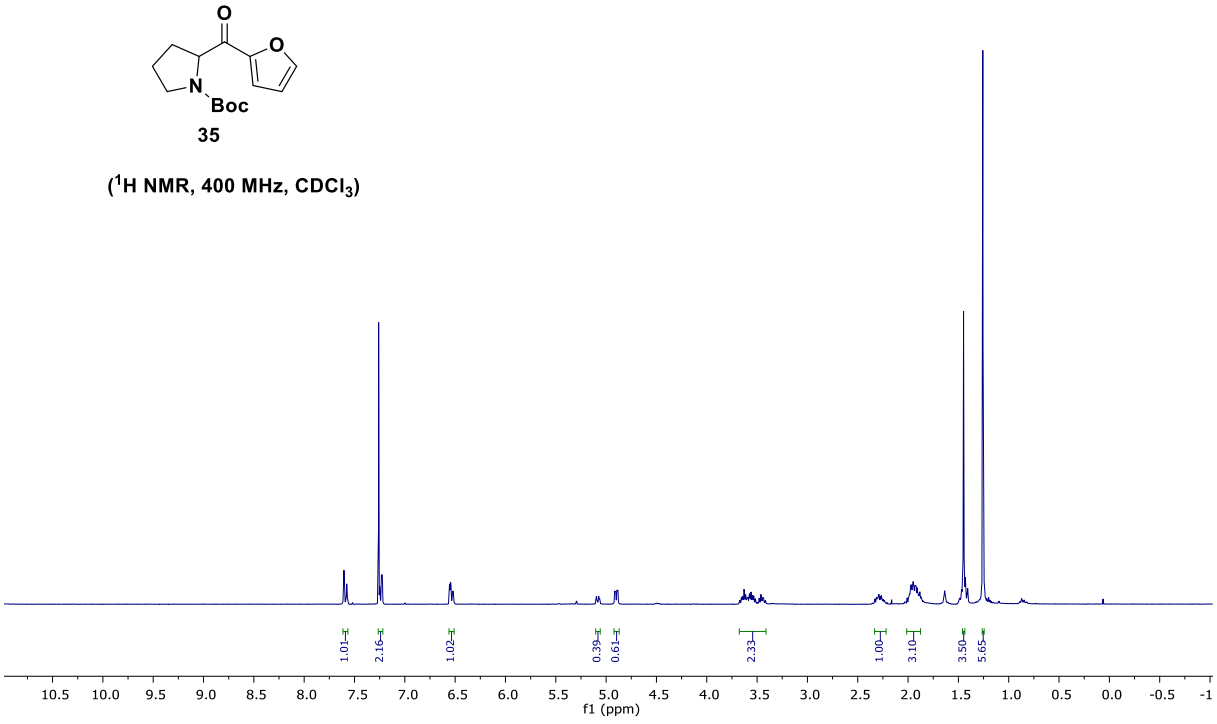
(^{13}C-NMR, 100 MHz, C_6D_6)

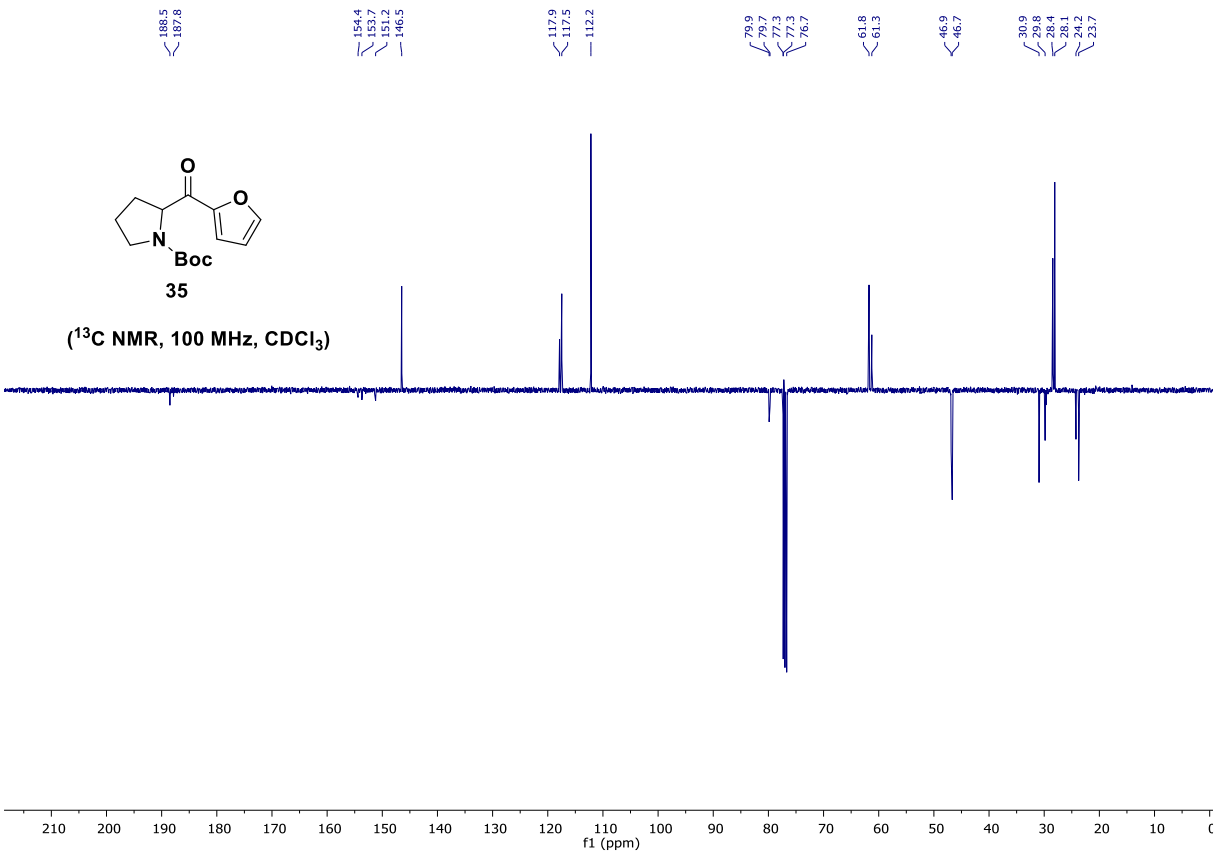

7.99 7.98 7.97 7.96 7.94 7.94 7.58 7.57 7.56 7.55 7.53 7.50 7.48 7.46 7.46 7.44 7.43
5.35 5.34 5.32 5.32 5.20 5.19 5.18 5.17
3.71 3.69 3.68 3.67 3.66 3.58 3.56 3.54 3.48 3.44 2.38 2.31 2.31 2.30 2.29 2.24 1.99 1.95 1.94 1.93 1.92 1.92 1.91 1.90 1.89 1.87 1.46 1.26
O
N
Boc
33
(1H NMR, 400 MHz, CDCl3)
2.10 1.05 2.10 0.40 0.60 2.16 1.03 3.16 3.58 5.42
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

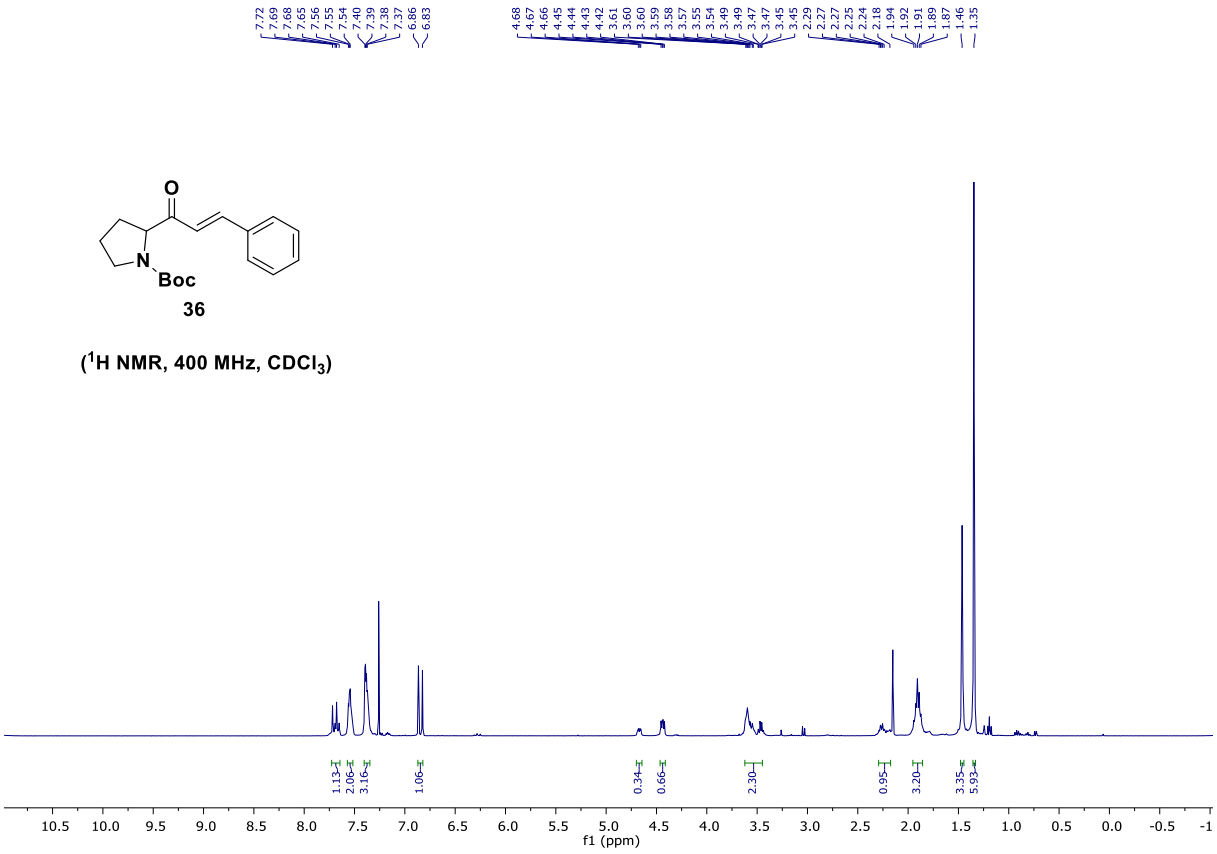

198.9 198.4
154.4 153.8
135.3 135.1 133.2 133.2 128.7 128.6 128.5 128.2
79.8 79.6 77.3 77.2 77.0 76.7
61.3 61.1
46.8 46.6
30.8 29.8 28.5 28.3 28.2 24.1 23.5
O
N
Boc
33
(13C NMR, 100 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


8.07
8.05
8.04
8.02
7.80
7.78
7.76
7.74
5.26
5.25
5.24
5.23
5.15
5.14
5.13
5.12
3.70
3.65
3.64
3.60
3.58
3.57
3.54
3.49
3.47
3.46
3.44
2.31
2.28
2.25
2.00
1.97
1.96
1.95
1.94
1.93
1.92
1.91
1.90
1.89
1.88
1.87
1.86
1.44
1.24
O
N
Boc
CN
34
(1H NMR, 400 MHz, CDCl3)
2.12
2.11
0.49
0.51
2.31
1.03
3.17
4.55
5.14
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


197.8
197.8
154.4
153.4
138.4
138.3
132.6
132.4
128.8
128.5
117.9
117.7
116.5
116.3
80.1
80.0
77.3
76.7
61.5
61.1
46.7
46.6
30.6
29.5
28.4
28.1
24.3
23.5
O
N
Boc
CN
34
(13C NMR, 100 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

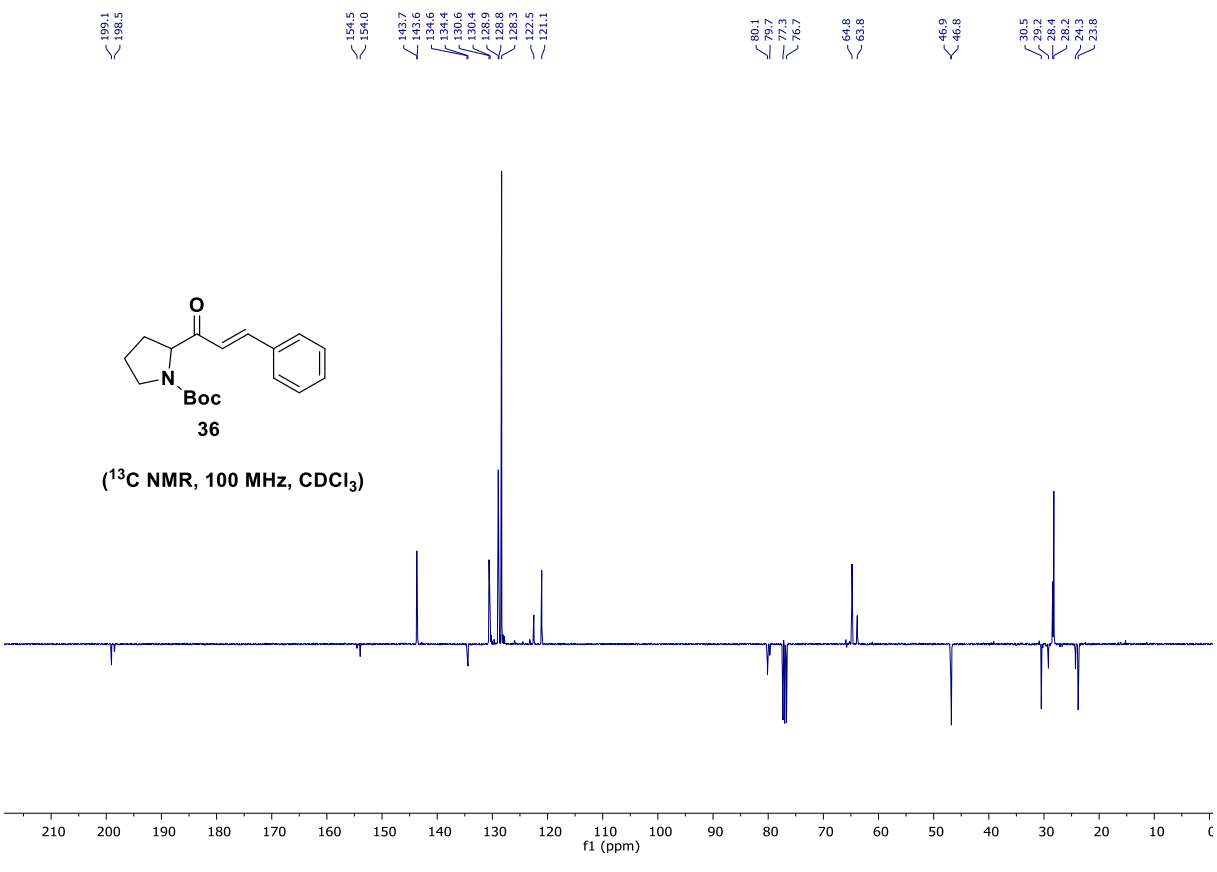

7.61
7.61
7.58
7.25
7.23
7.22
6.56
6.55
6.55
6.54
6.53
6.52
6.52
6.52
5.10
5.09
5.07
4.92
4.90
4.89
4.88
3.67
3.63
3.61
3.58
3.56
3.55
3.54
3.53
3.46
3.42
2.33
2.29
2.27
2.23
2.01
1.98
1.98
1.97
1.96
1.96
1.94
1.93
1.92
1.91
1.90
1.89
1.88
1.45
1.26
O
O
N
Boc
35
(1H NMR, 400 MHz, CDCl3)
1.01
2.16
1.02
0.39
0.61
2.33
1.00
3.10
3.50
5.65
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


188.5
187.8
154.4
153.7
151.2
146.5
117.9
117.5
112.2
79.9
79.7
77.3
77.3
76.7
61.8
61.3
46.9
46.7
30.9
29.8
28.4
28.1
24.2
23.7
O
O
N
Boc
35
(13C NMR, 100 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)



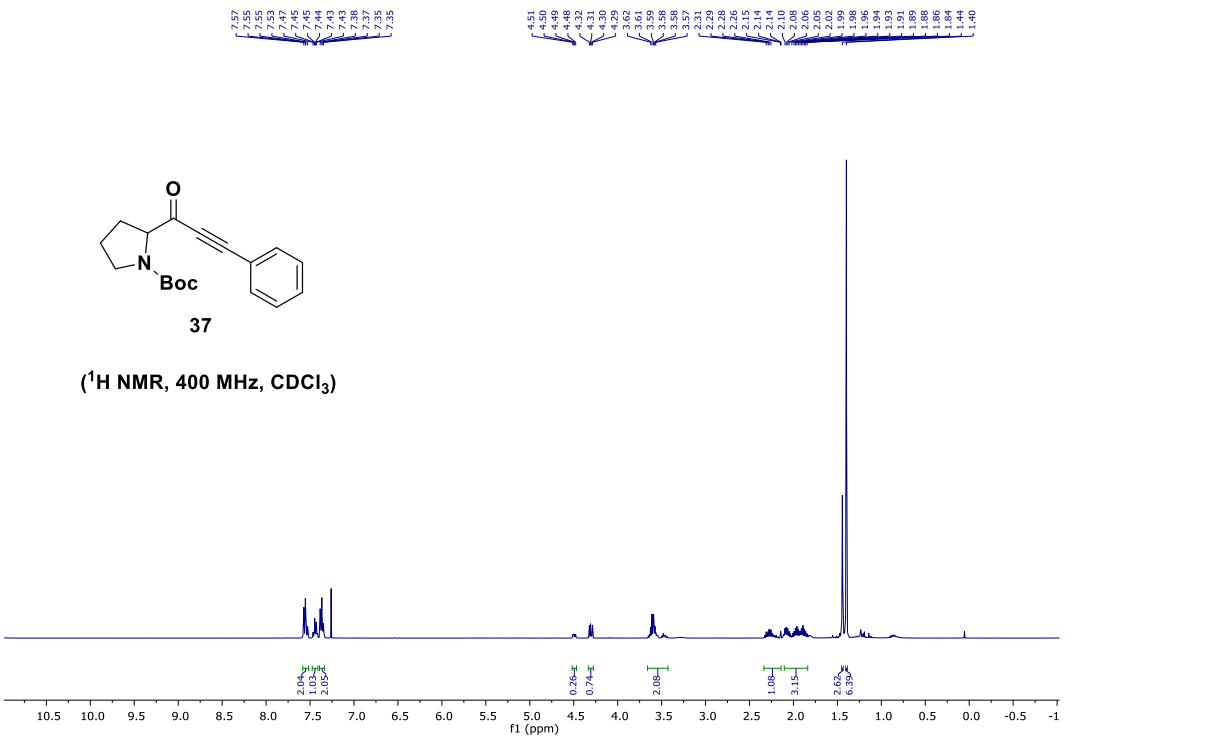
36

(^{1}H NMR, 400 MHz, $CDCl_3$)



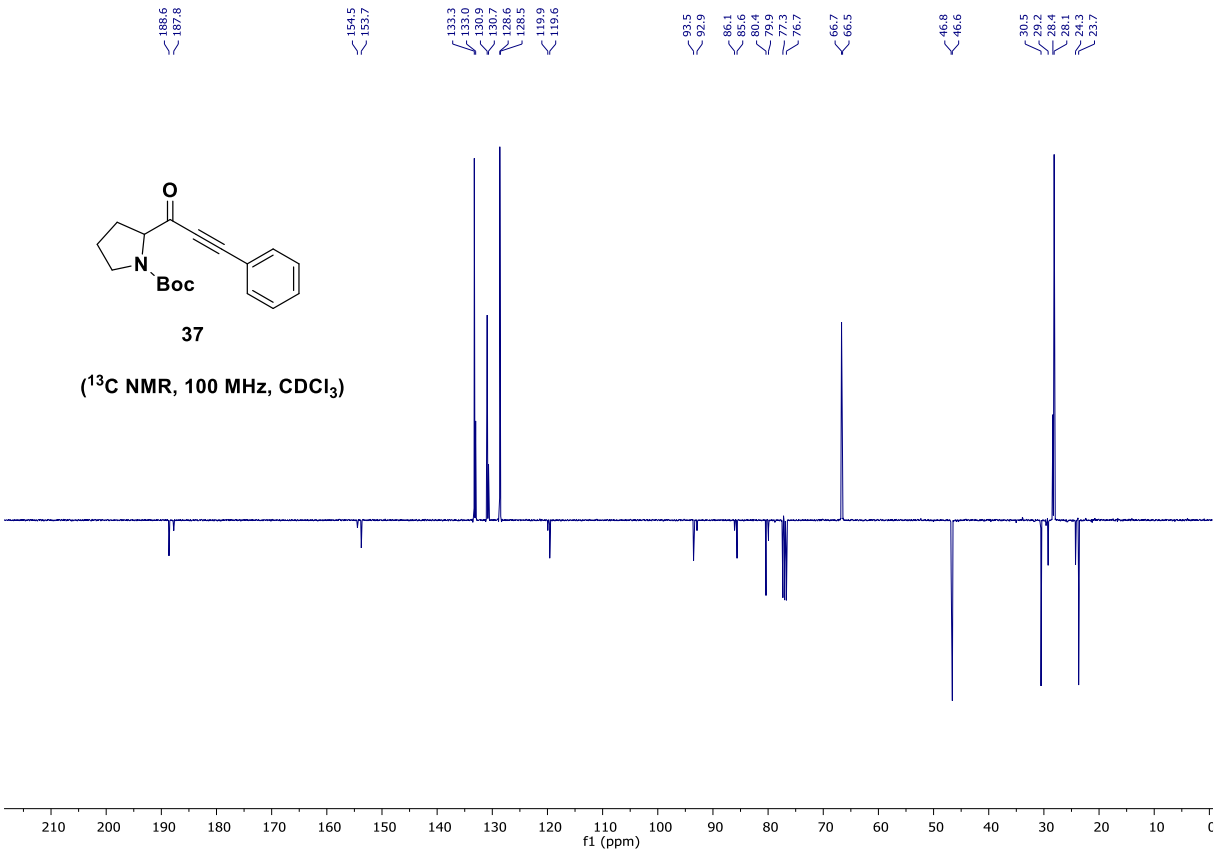
36

(^{13}C NMR, 100 MHz, $CDCl_3$)



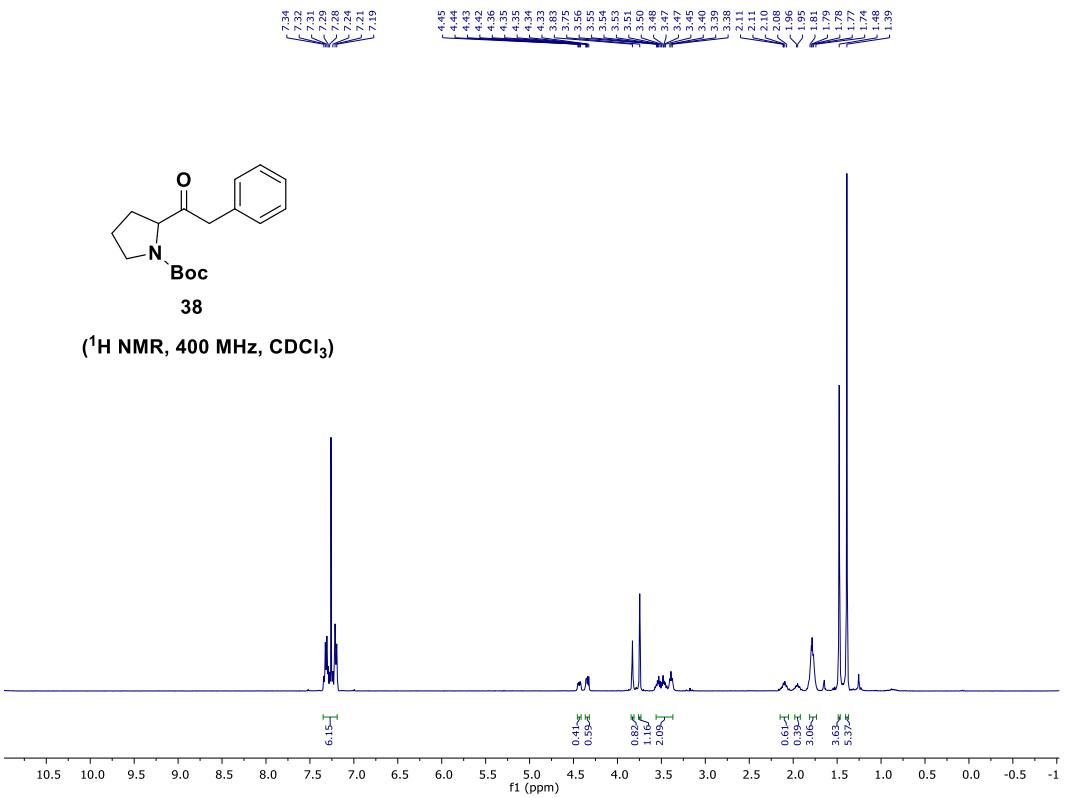
37

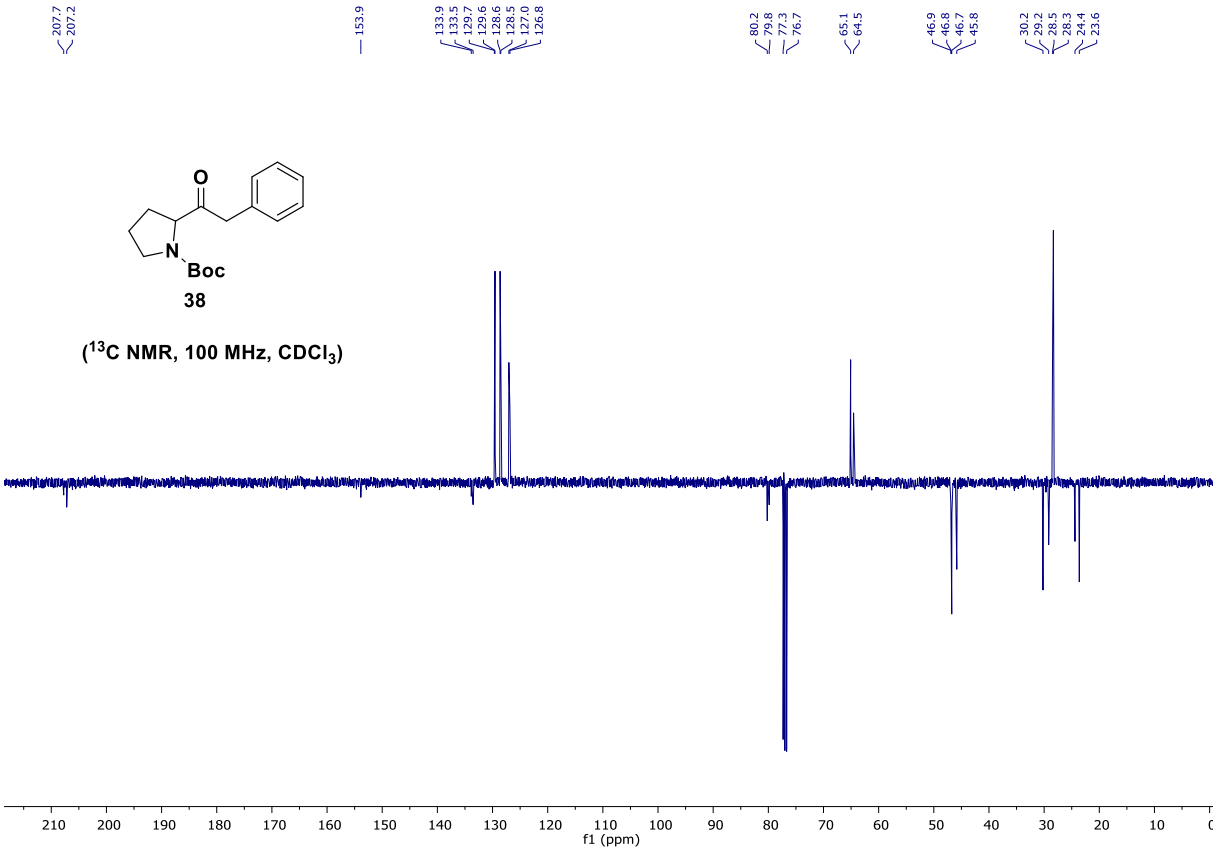
(^{1}H NMR, 400 MHz, $CDCl_3$)

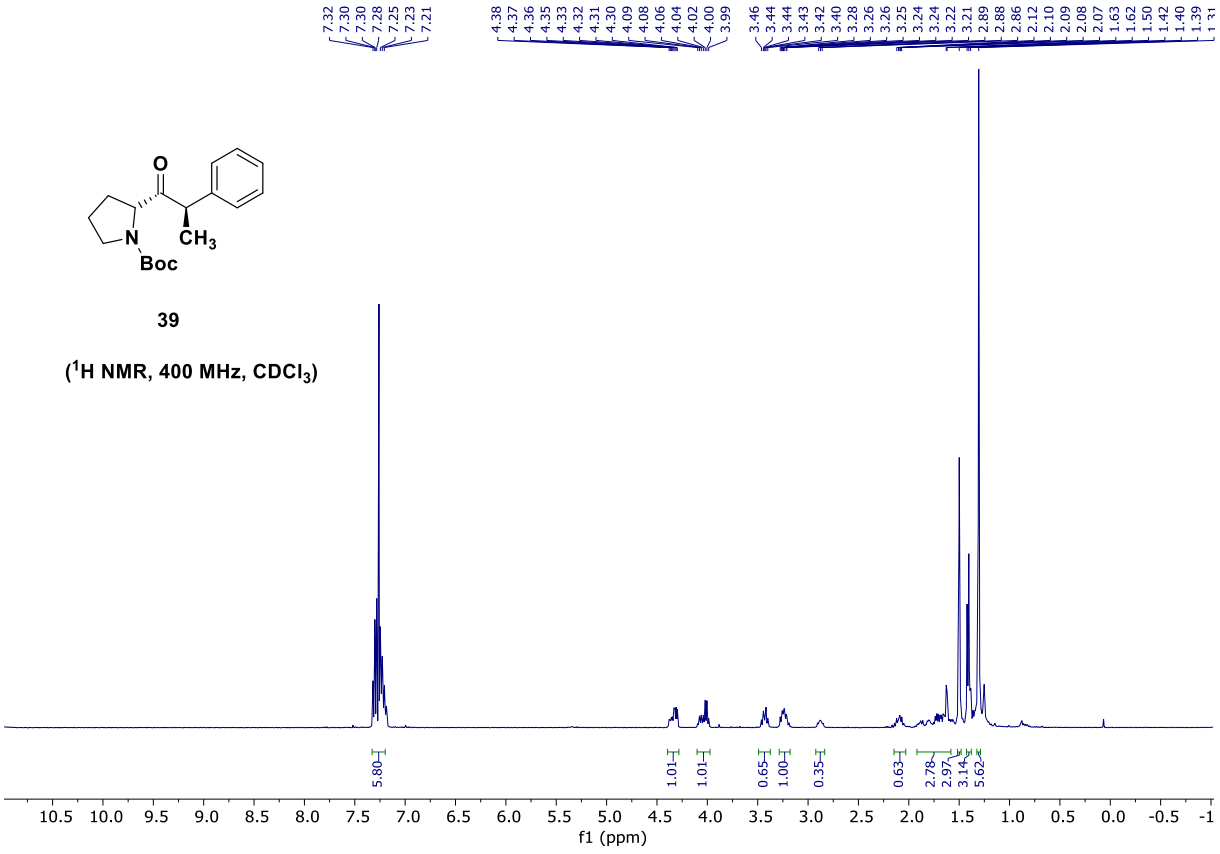


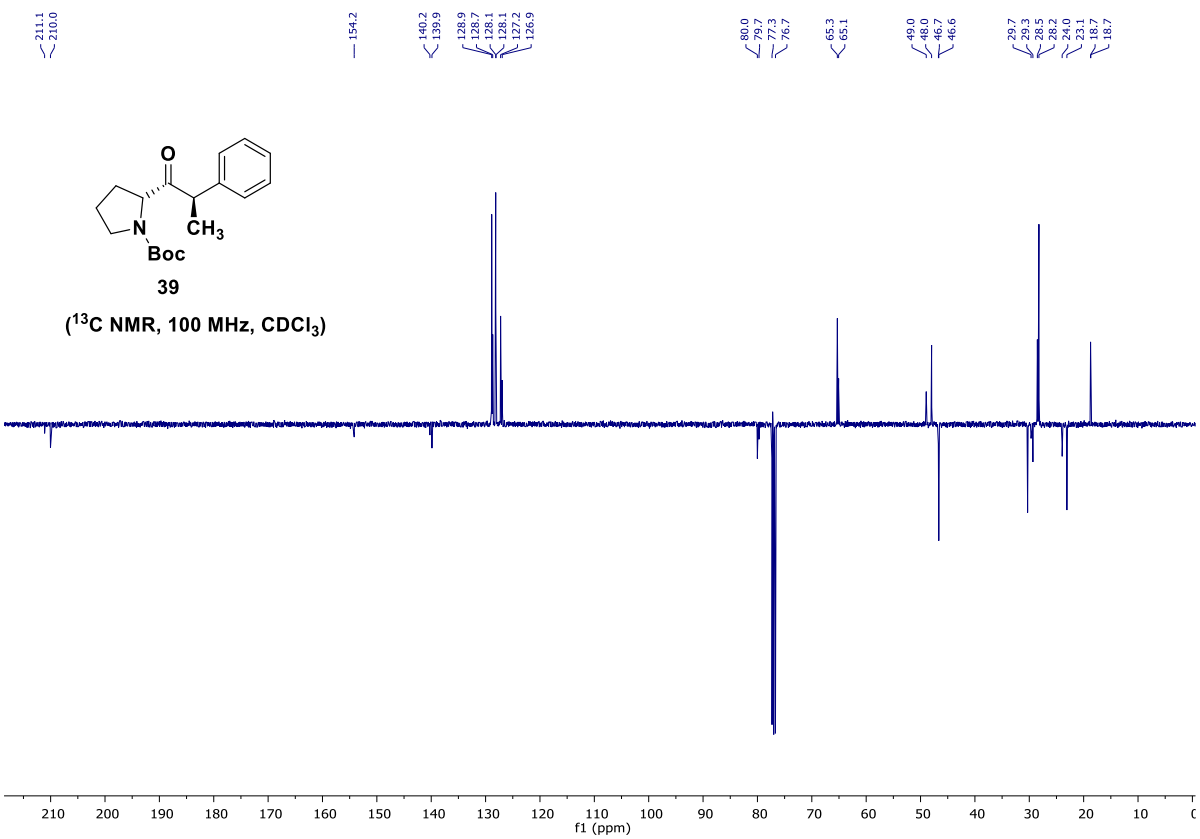
37

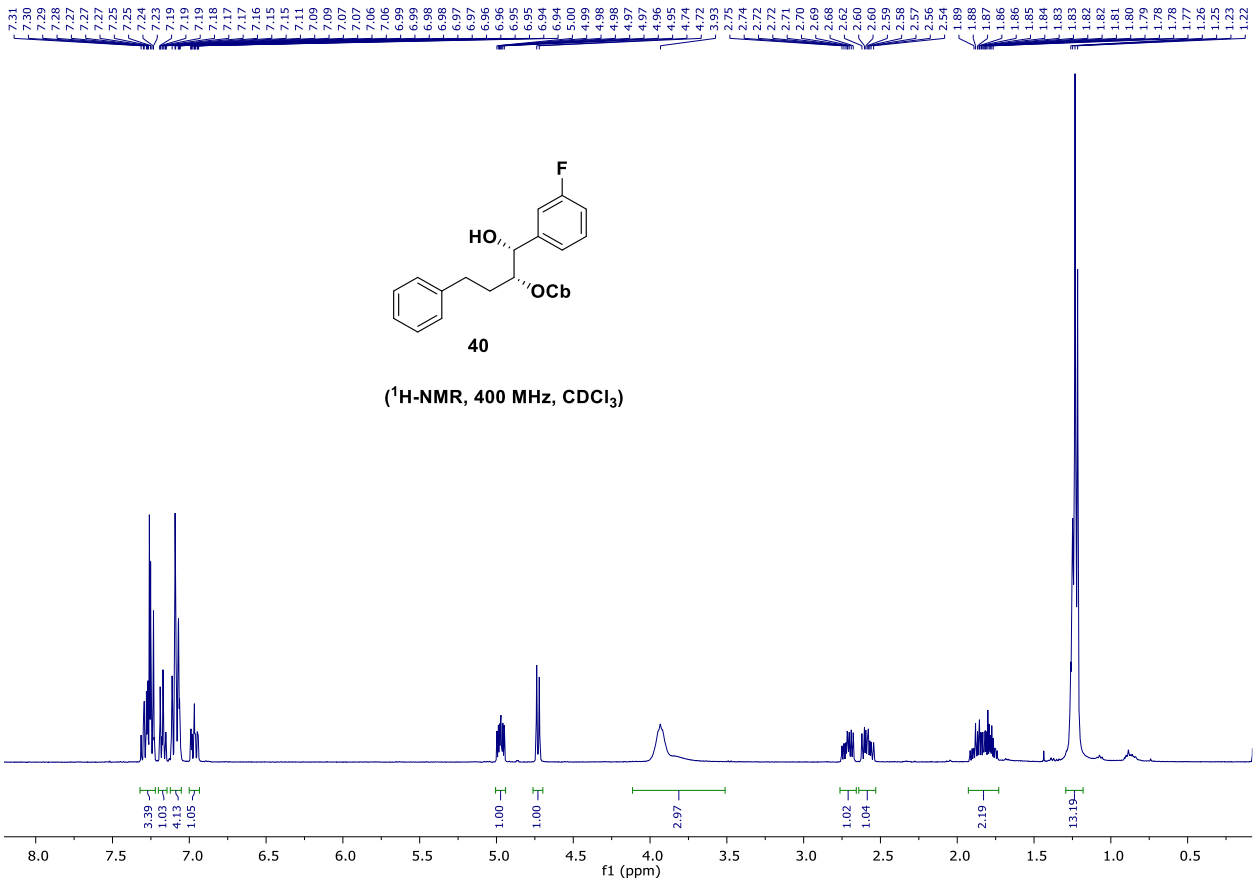
(^{13}C NMR, 100 MHz, $CDCl_3$)

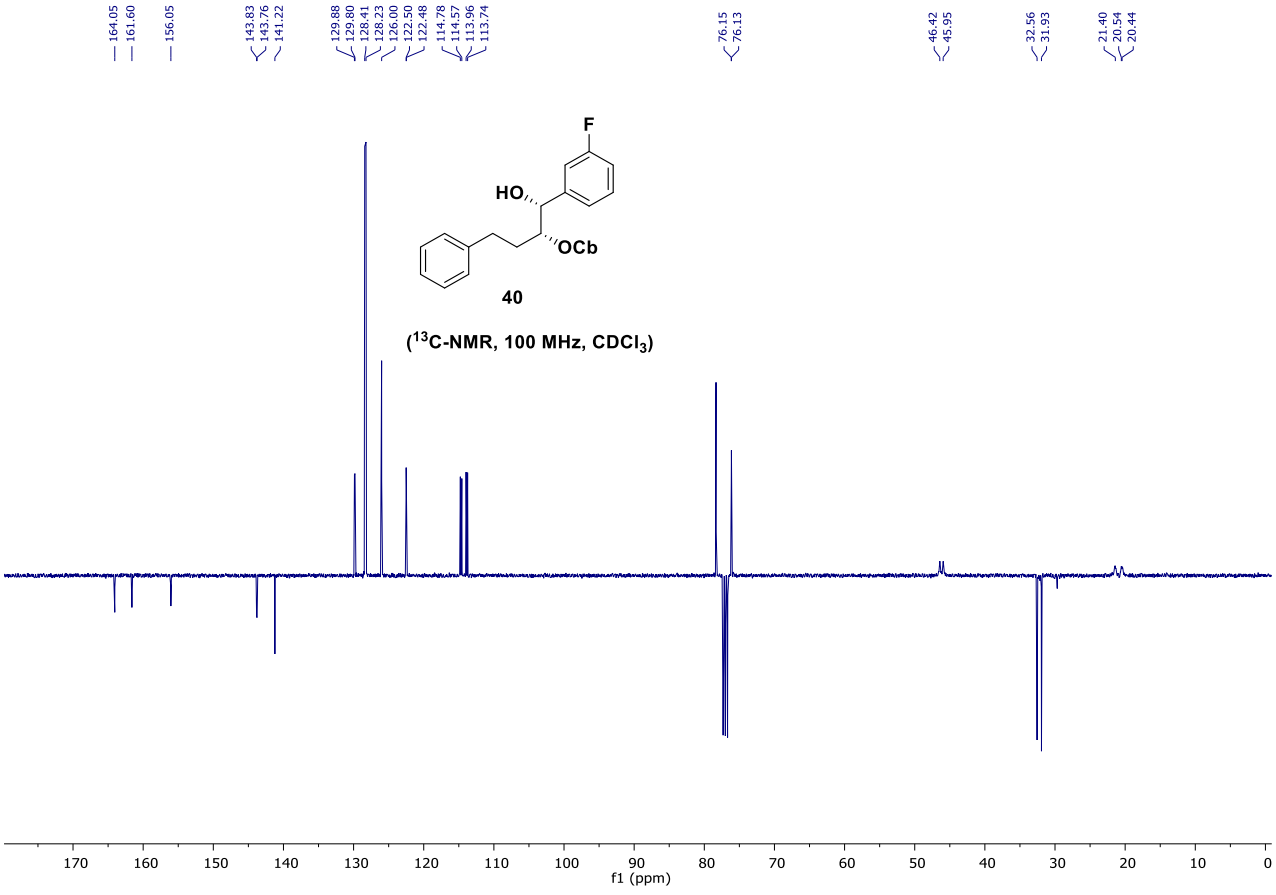

7.34
7.32
7.31
7.29
7.28
7.24
7.21
7.19
4.45
4.44
4.43
4.42
4.36
4.35
4.35
4.34
4.33
3.83
3.75
3.56
3.55
3.54
3.53
3.51
3.50
3.48
3.47
3.47
3.45
3.40
3.39
3.38
2.11
2.11
2.10
2.08
1.96
1.95
1.81
1.79
1.78
1.77
1.74
1.48
1.39
O
N
Boc
38
(1H NMR, 400 MHz, CDCl3)
6.15
0.41
0.59
0.82
1.16
2.09
0.61
0.39
3.06
3.63
5.37
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

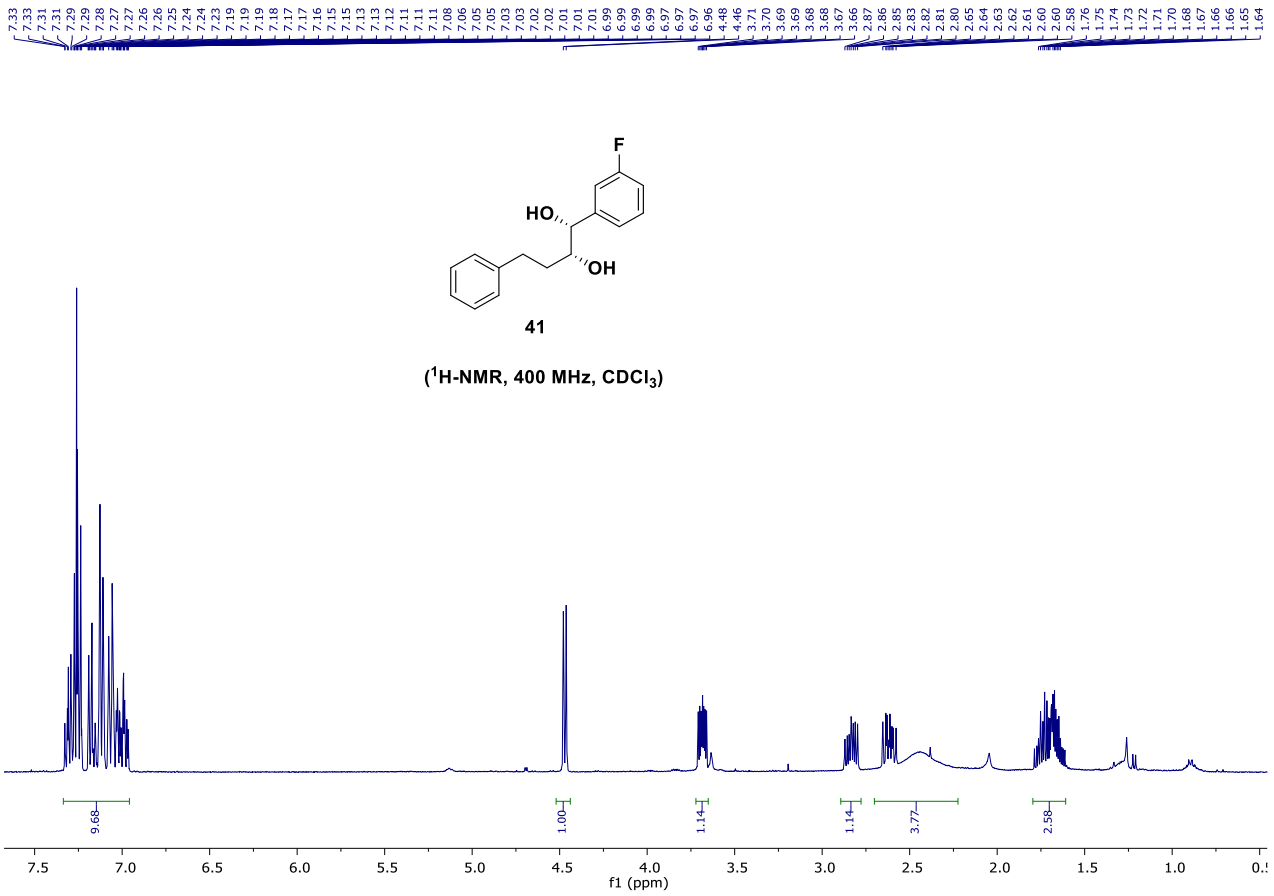

207.7
207.2
153.9
133.9
133.5
129.7
129.6
128.6
128.5
127.0
126.8
80.2
79.8
77.3
76.7
65.1
64.5
46.9
46.8
46.7
45.8
30.2
29.2
28.5
28.3
24.4
23.6
O
N
Boc
38
(13C NMR, 100 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

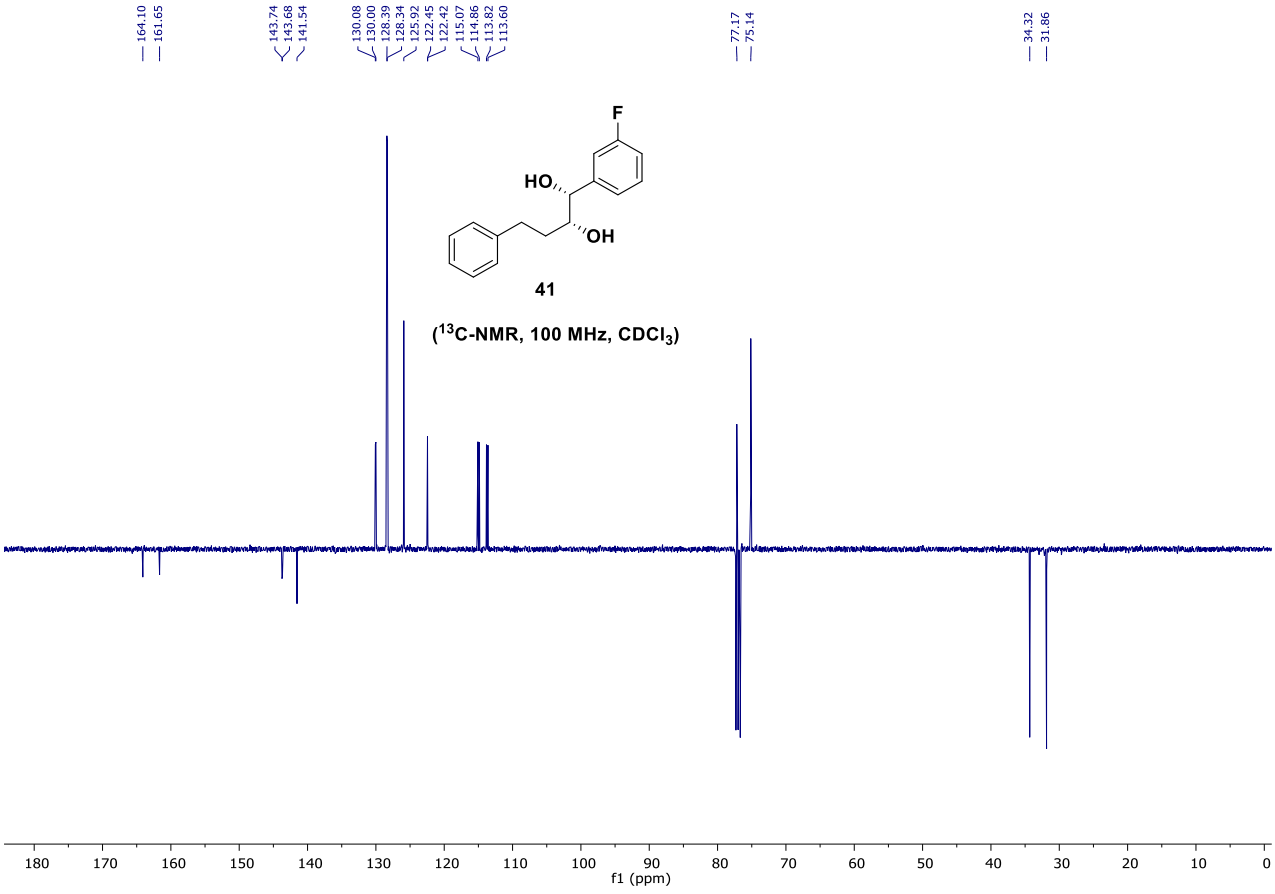

O
N
CH3
Boc
39
(1H NMR, 400 MHz, CDCl3)
f1 (ppm)


O
N
CH3
Boc
39
(13C NMR, 100 MHz, CDCl3)
f1 (ppm)

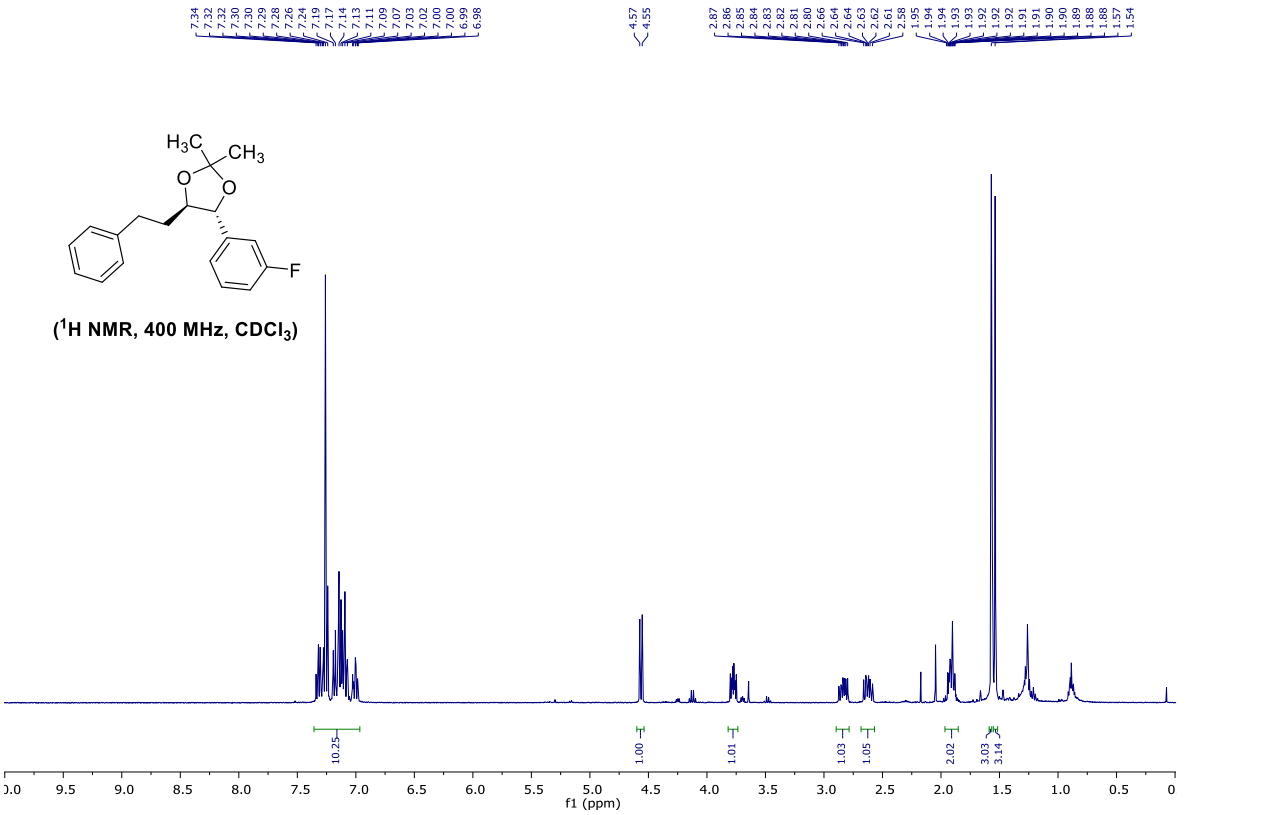

F
HO
OCb
40
(1H-NMR, 400 MHz, CDCl3)
f1 (ppm)

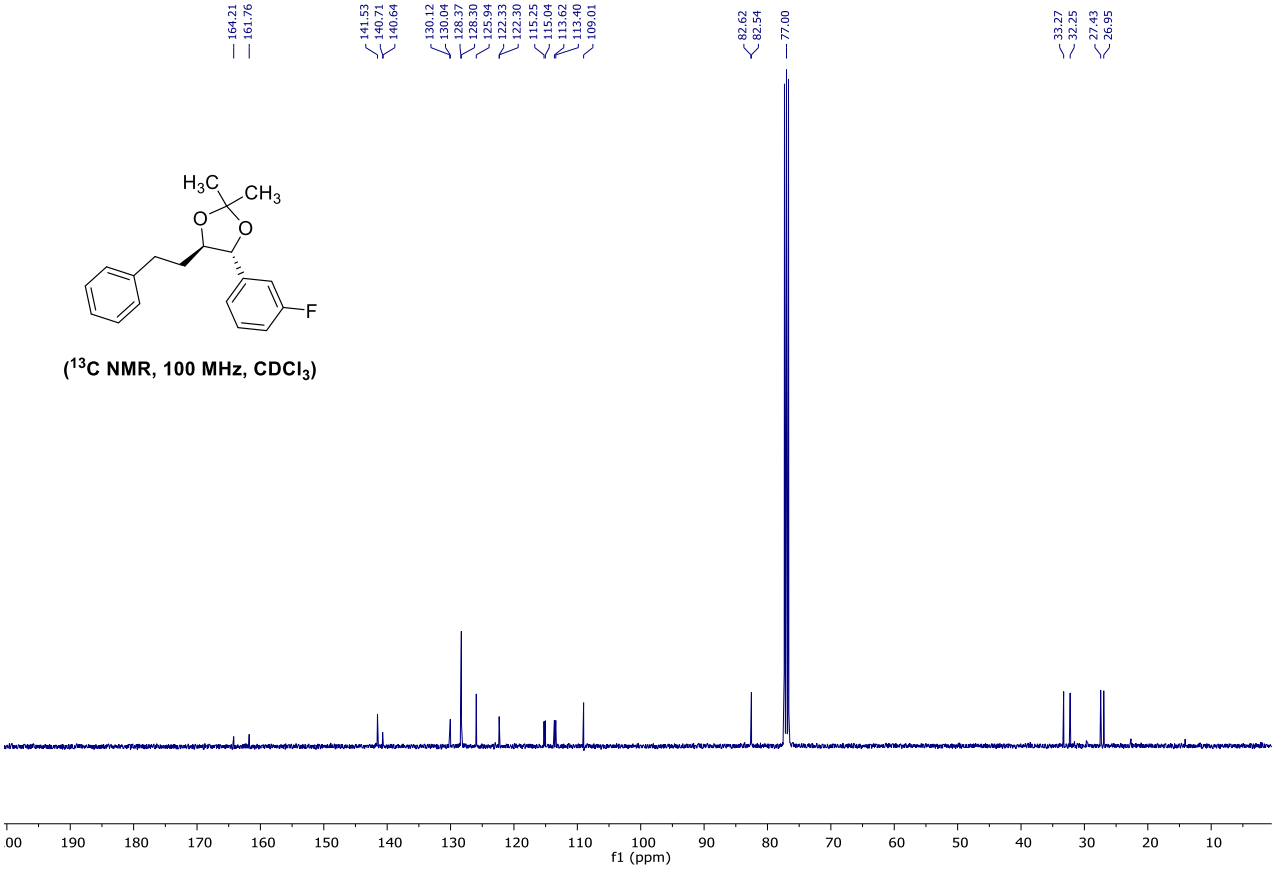

F
HO
OCb
40
(13C-NMR, 100 MHz, CDCl3)
f1 (ppm)



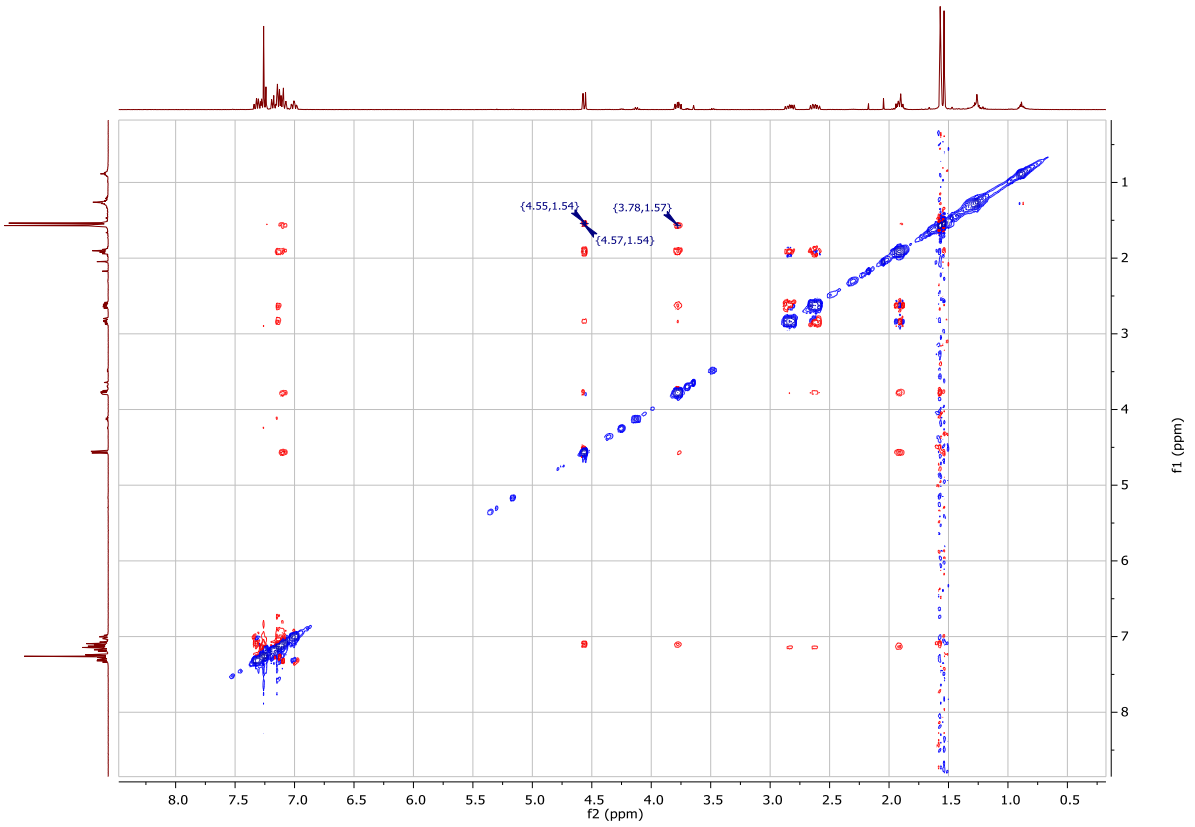


Proof of ***syn*** orientation of 1,2-diol **42** via NOESY experiment on the derived acetonide:

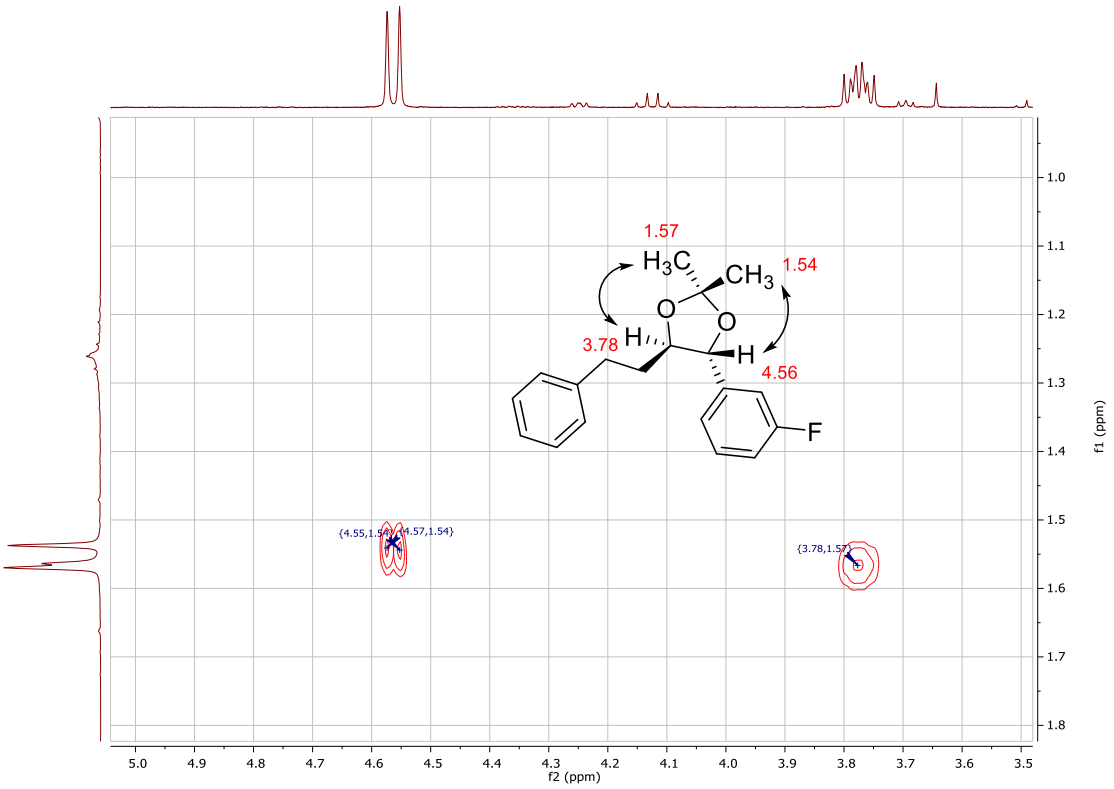


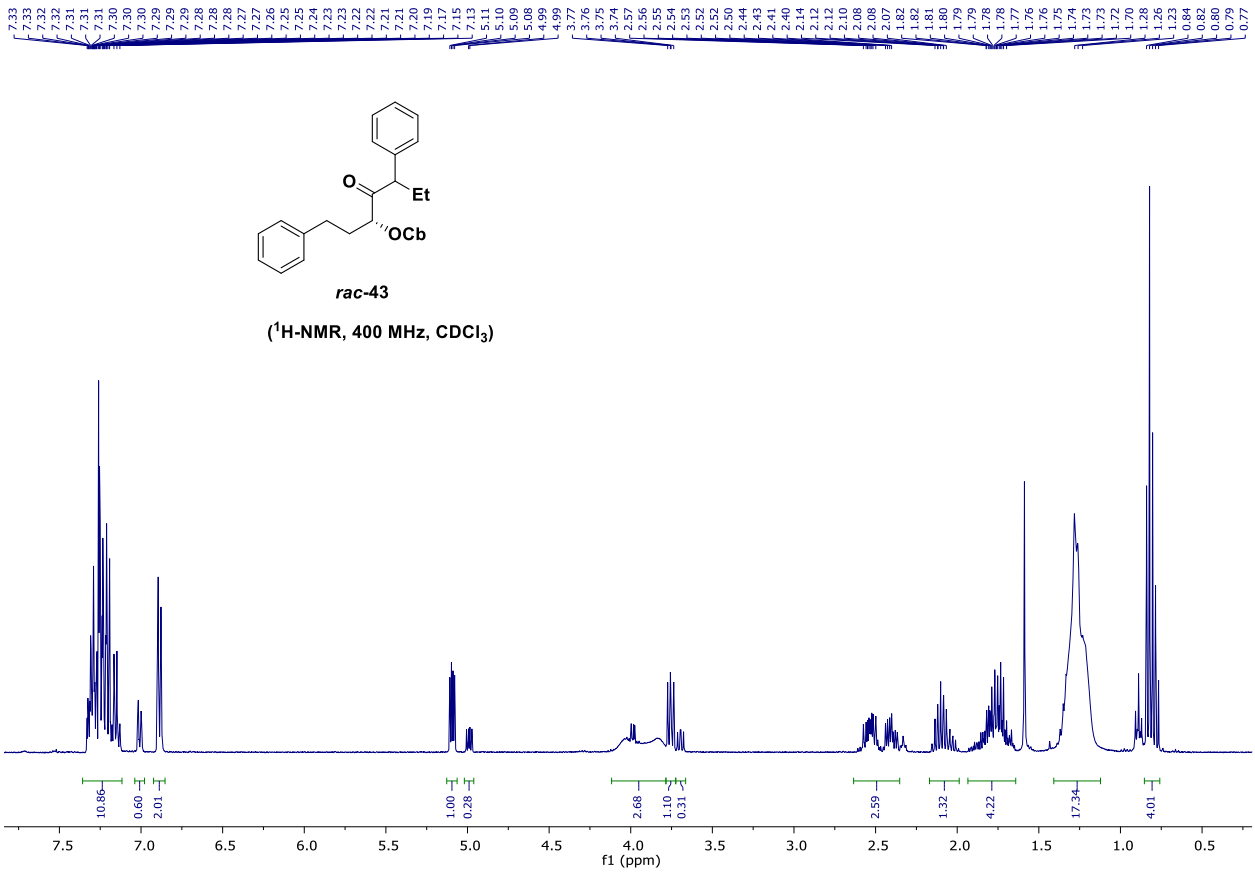


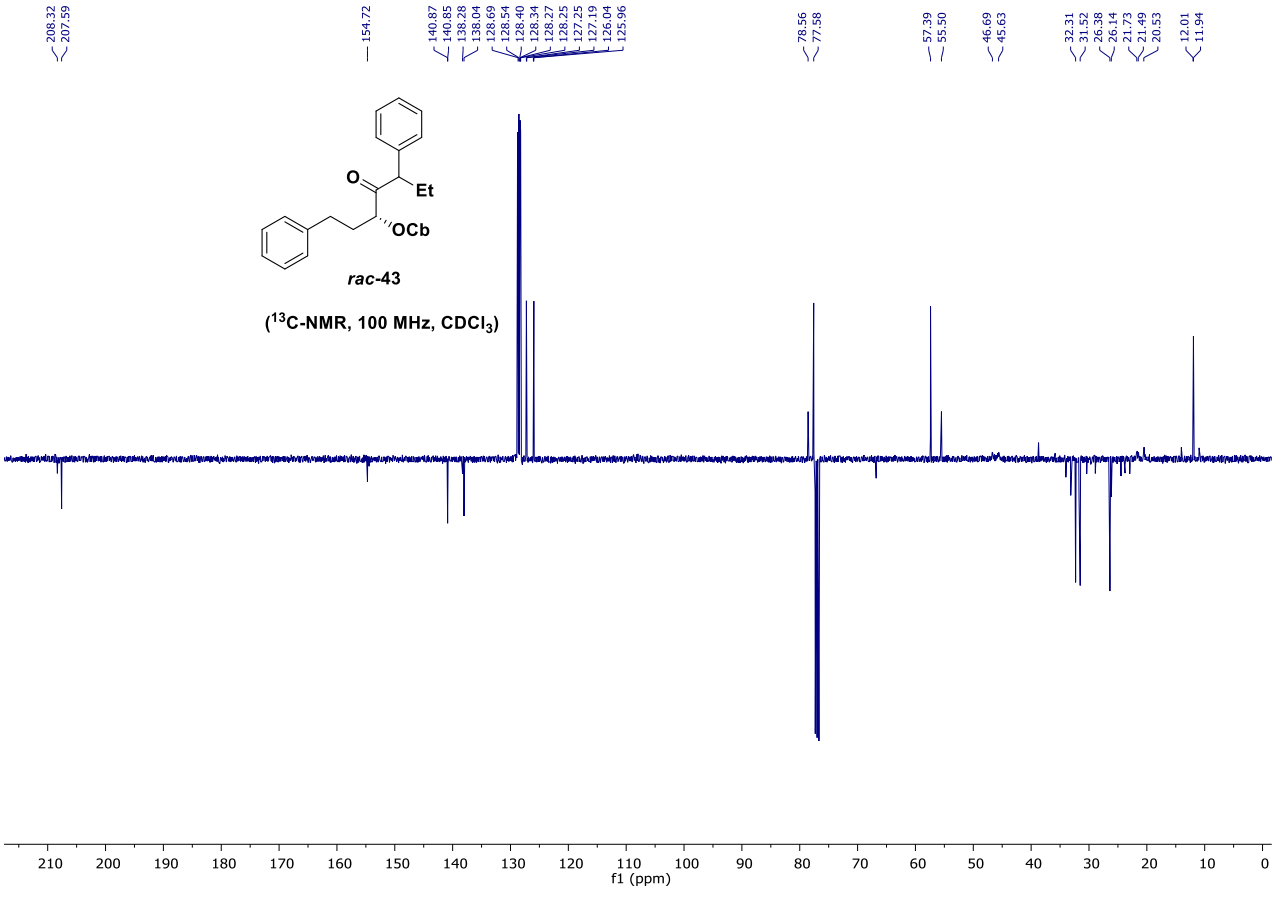
NOESY spectrum of acetonide (400 MHz, CDCl3)

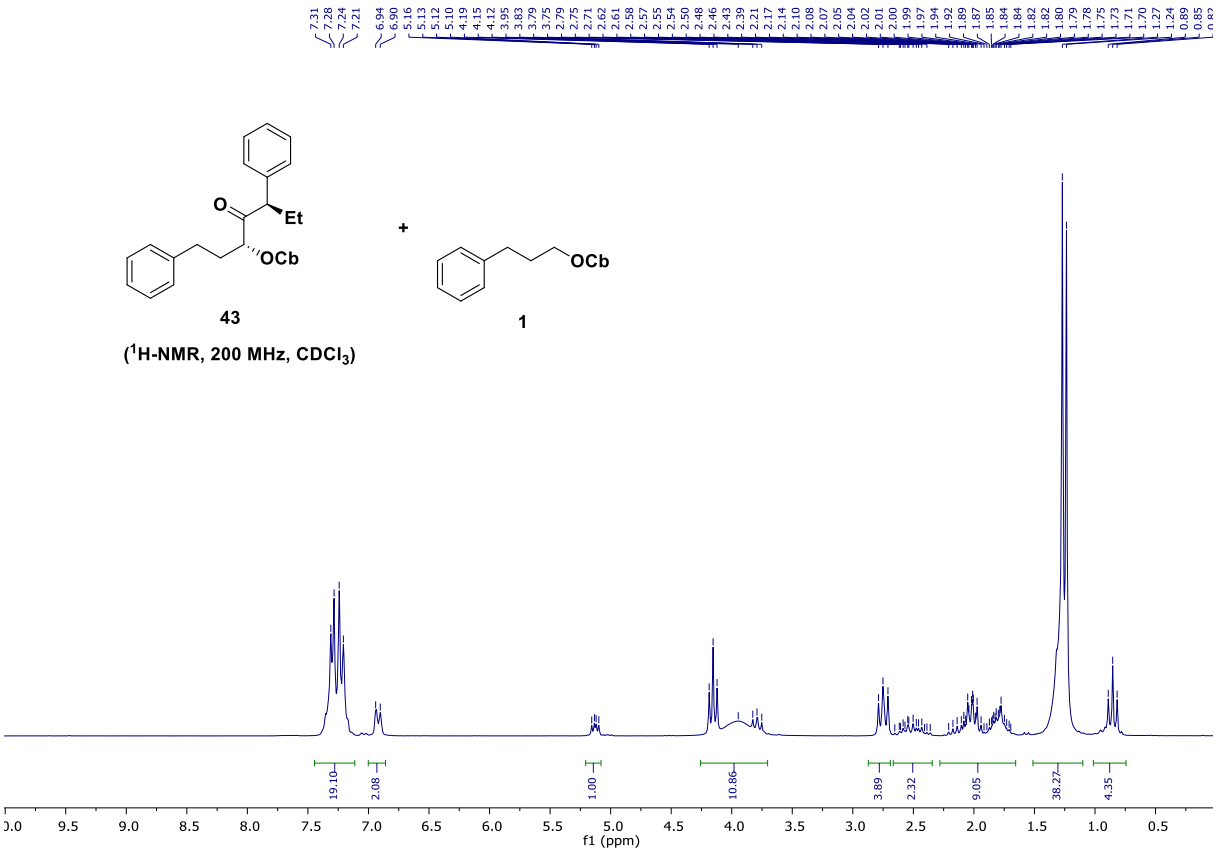


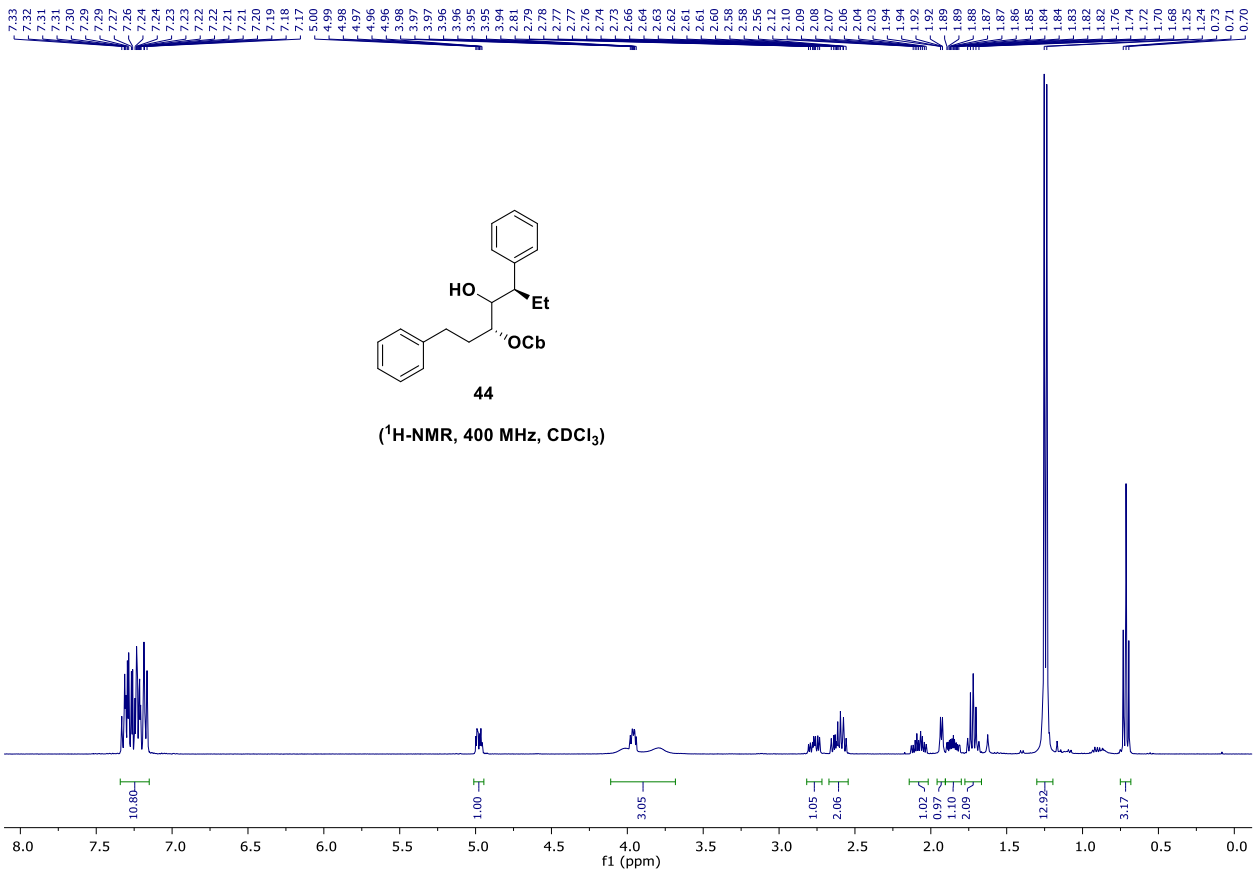
Enlarged view

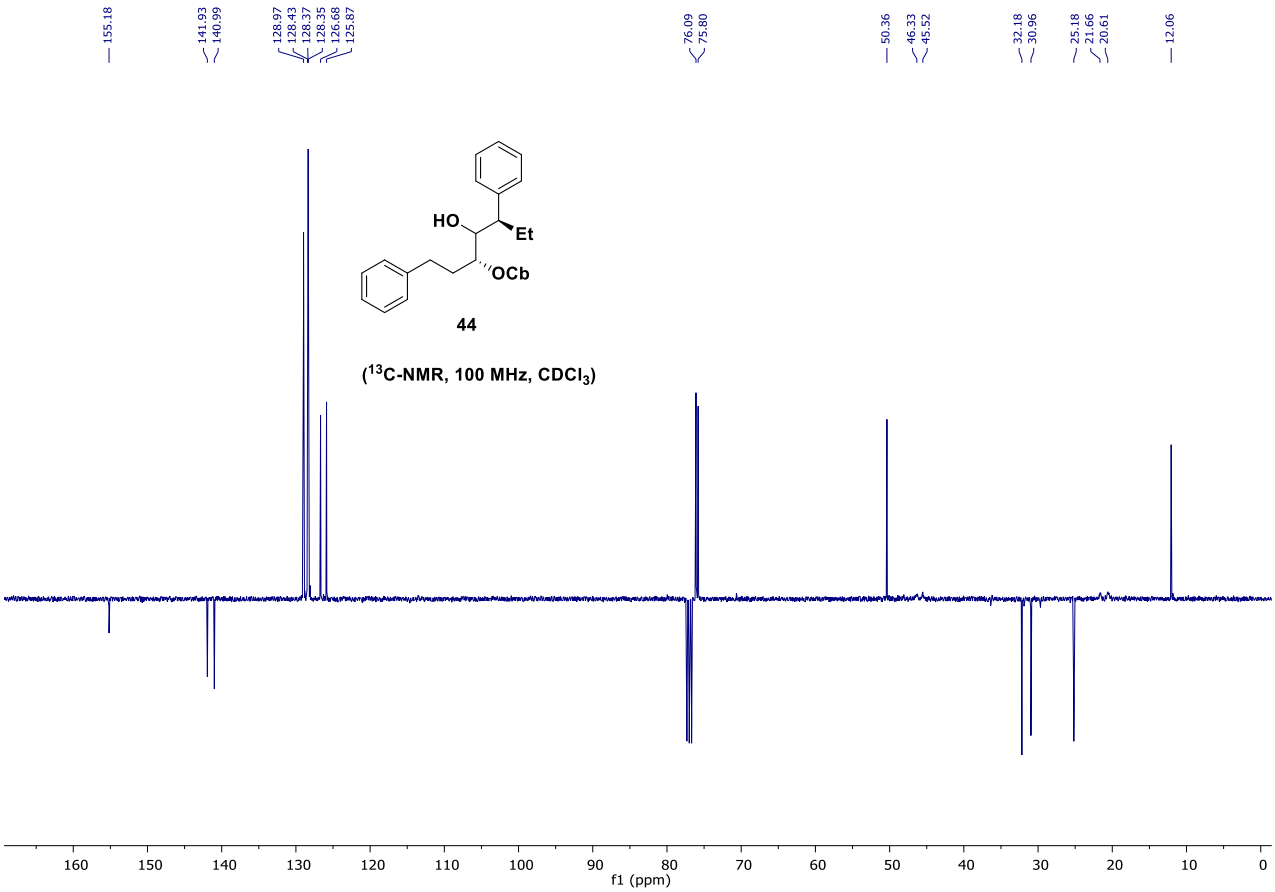



O
Et
OCb
rac-43
(1H-NMR, 400 MHz, CDCl3)
f1 (ppm)


O
Et
OCb
rac-43
(13C-NMR, 100 MHz, CDCl3)
f1 (ppm)

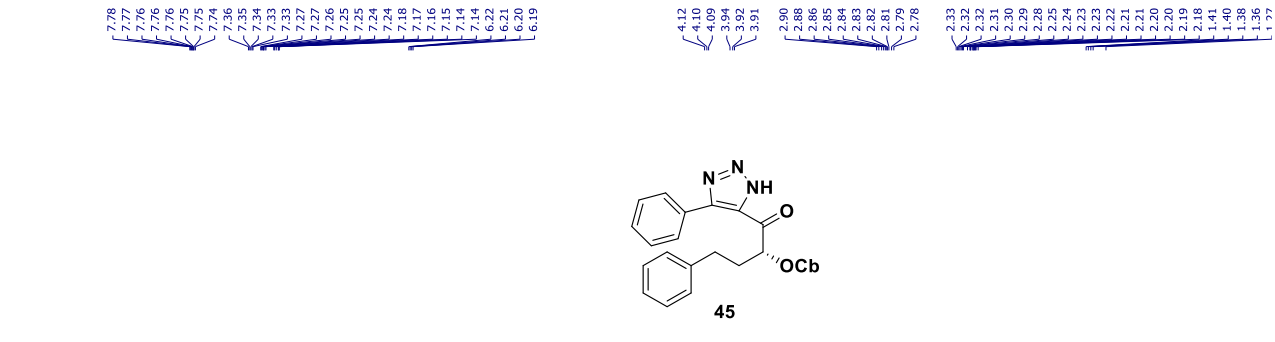

O
Et
OCb
43
+
OCb
1
(1H-NMR, 200 MHz, CDCl3)
19.10
2.08
1.00
10.86
3.89
2.32
9.05
38.27
4.35
f1 (ppm)


HO
Et
OCb
44
(1H-NMR, 400 MHz, CDCl3)
10.80
1.00
3.05
1.05
2.06
1.02
0.97
1.10
2.09
12.92
3.17
f1 (ppm)



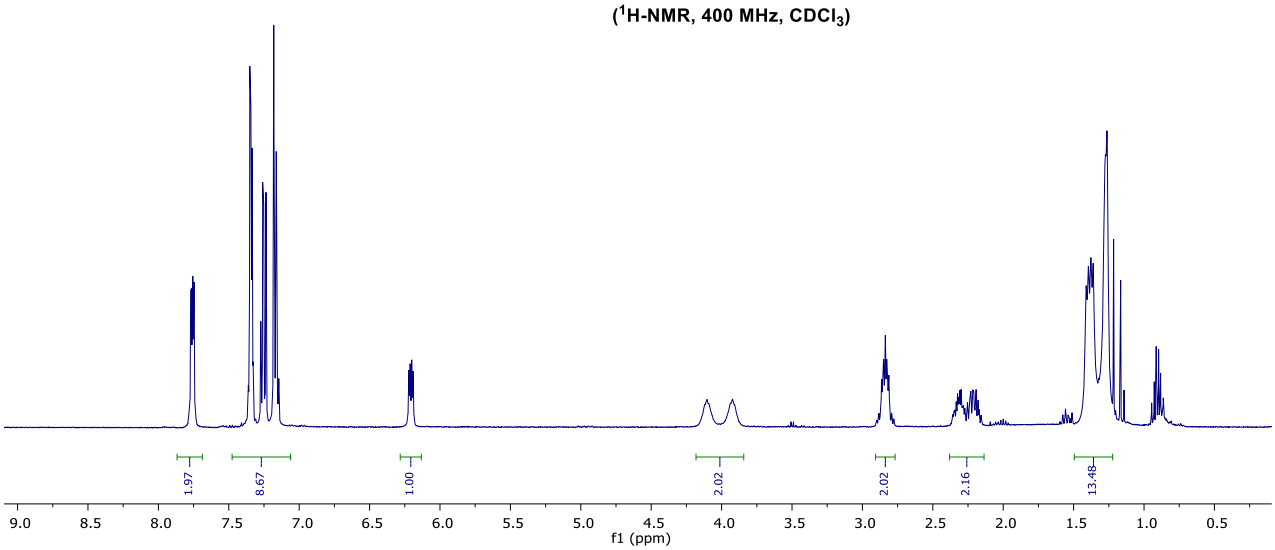
44

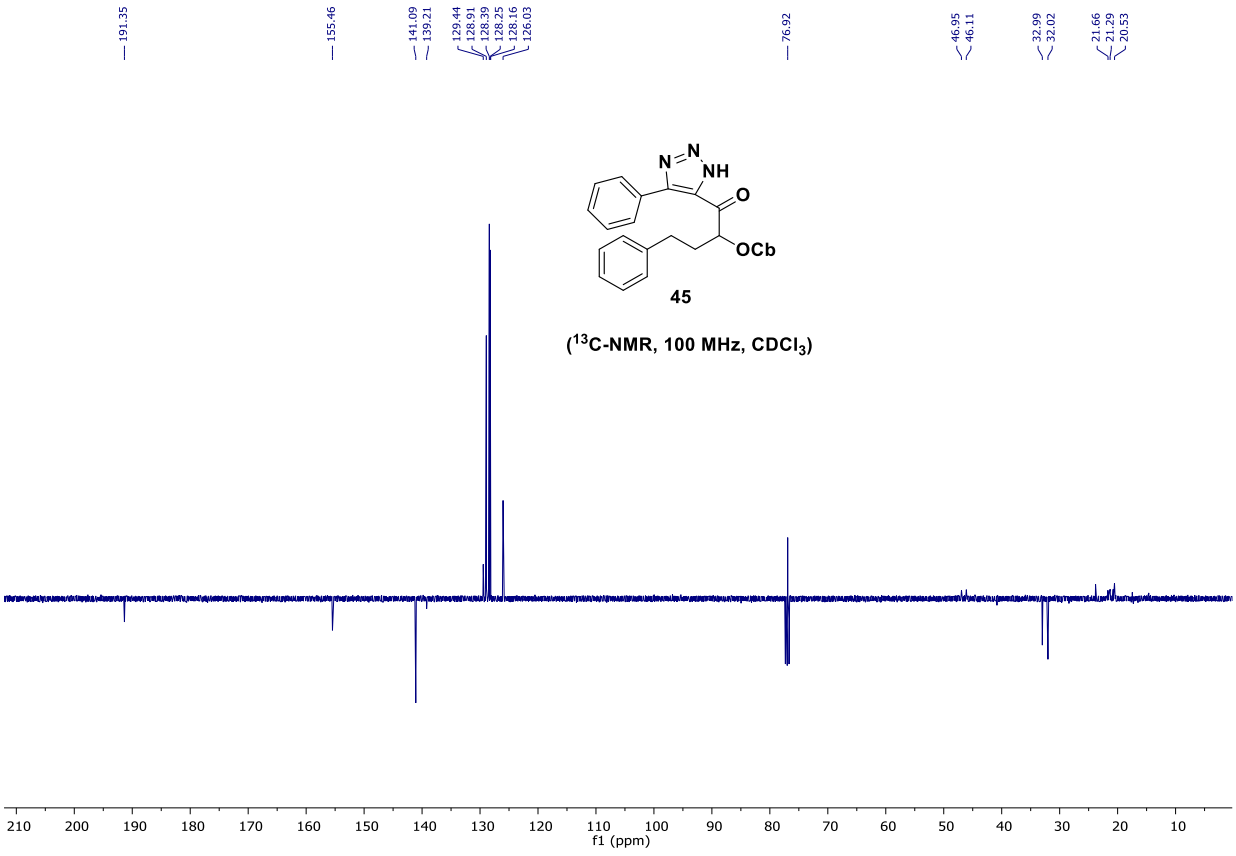
(^{13}C-NMR, 100 MHz, $CDCl_3$)



45

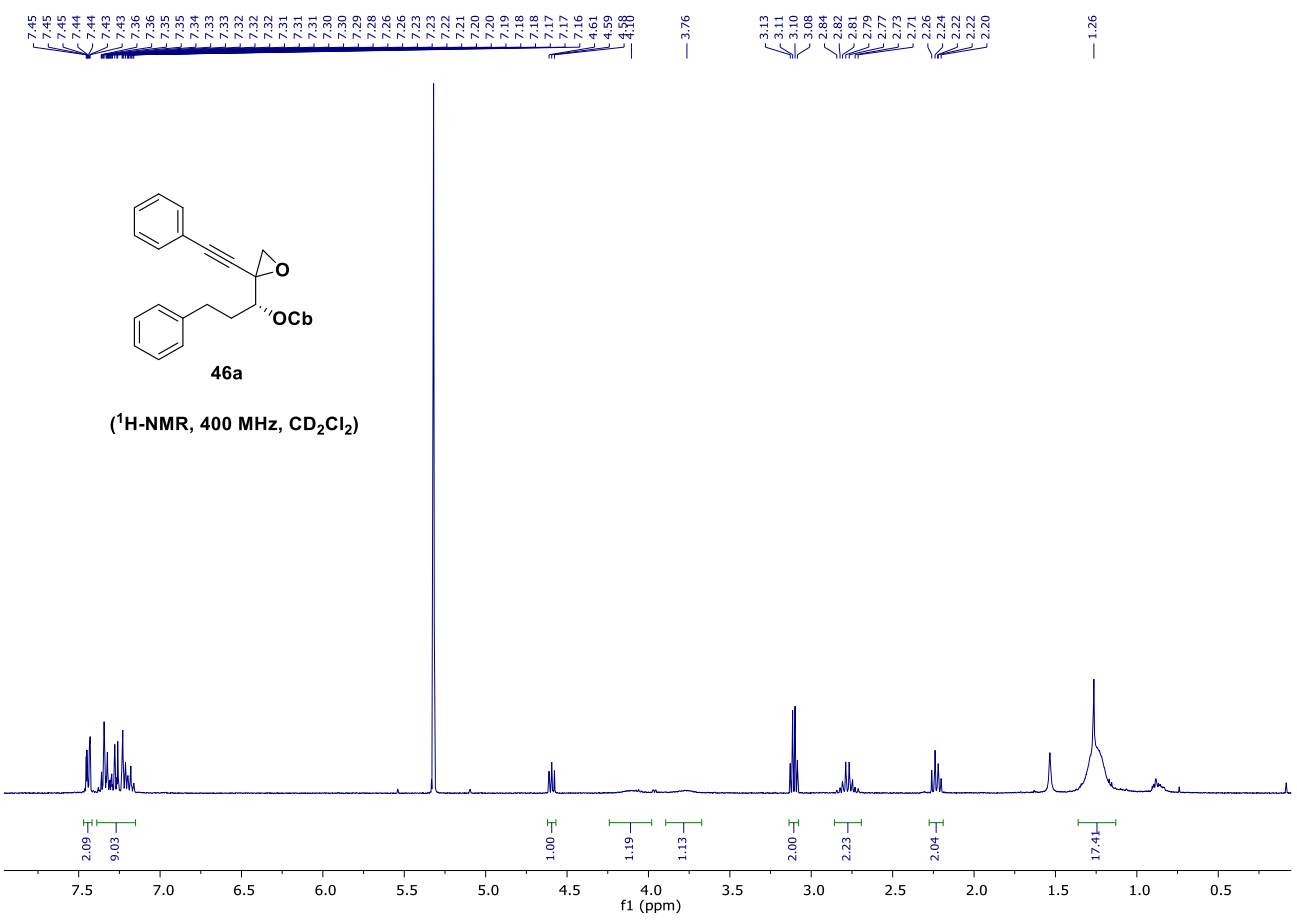
(^{1}H-NMR, 400 MHz, $CDCl_3$)





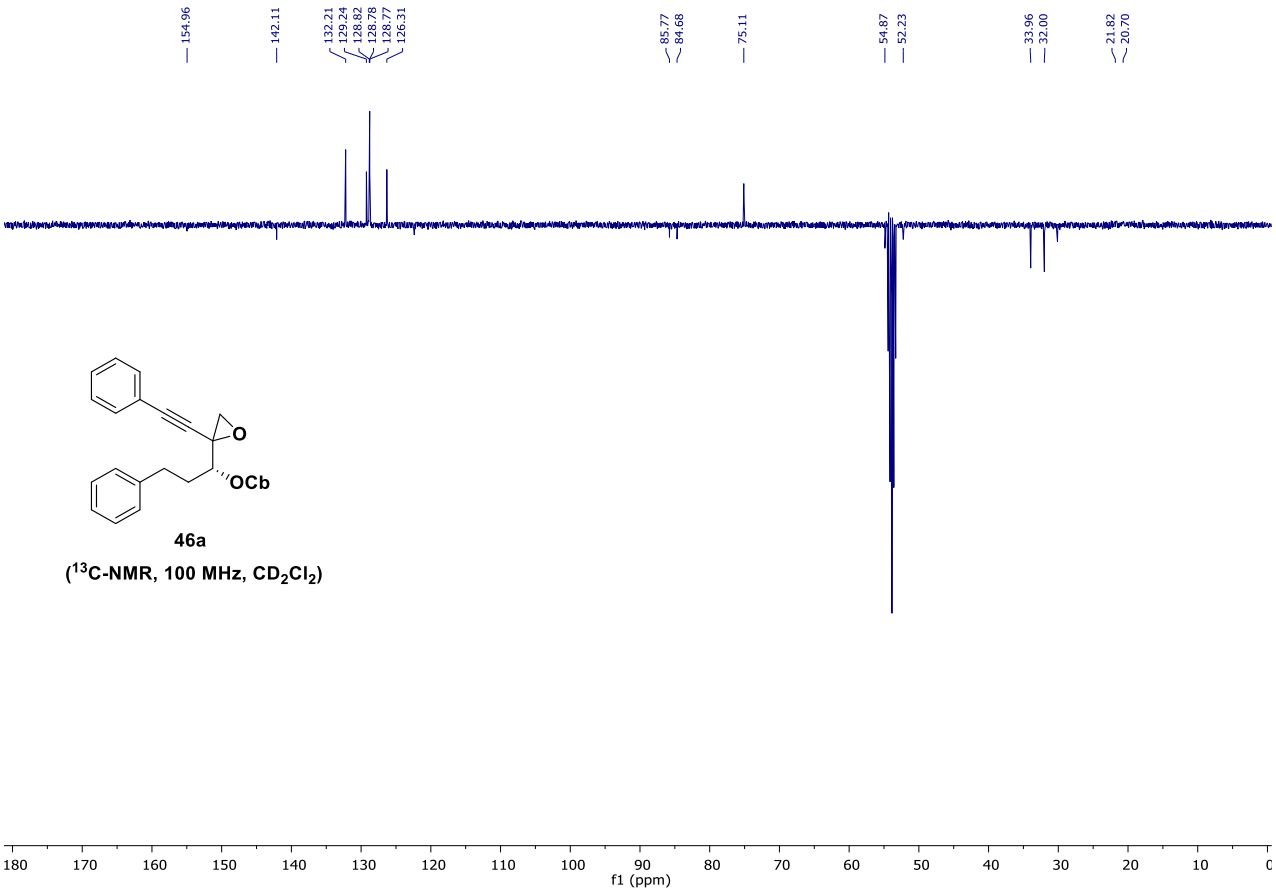
45

(^{13}C-NMR, 100 MHz, $CDCl_3$)



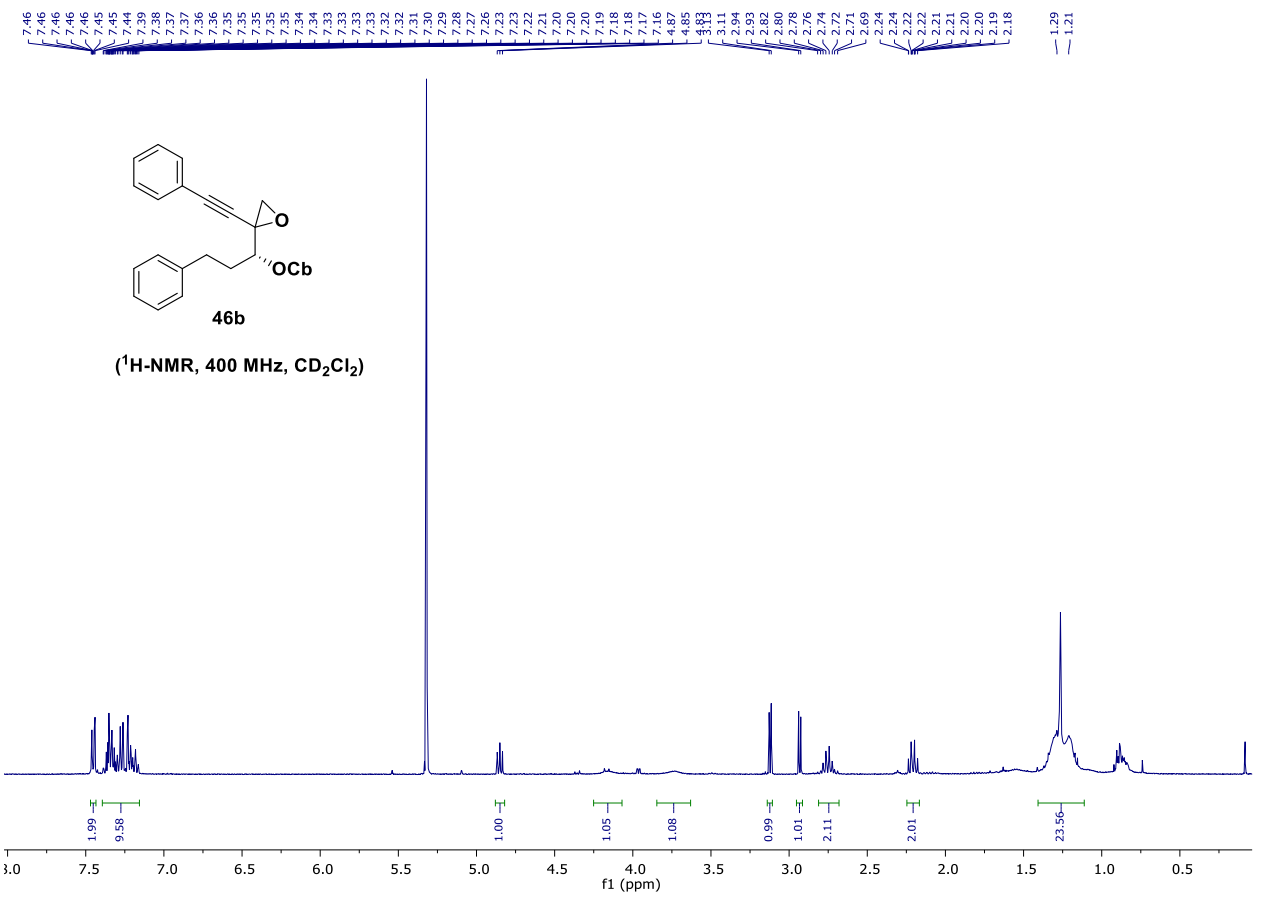
46a

(^{1}H-NMR, 400 MHz, CD_2Cl_2)



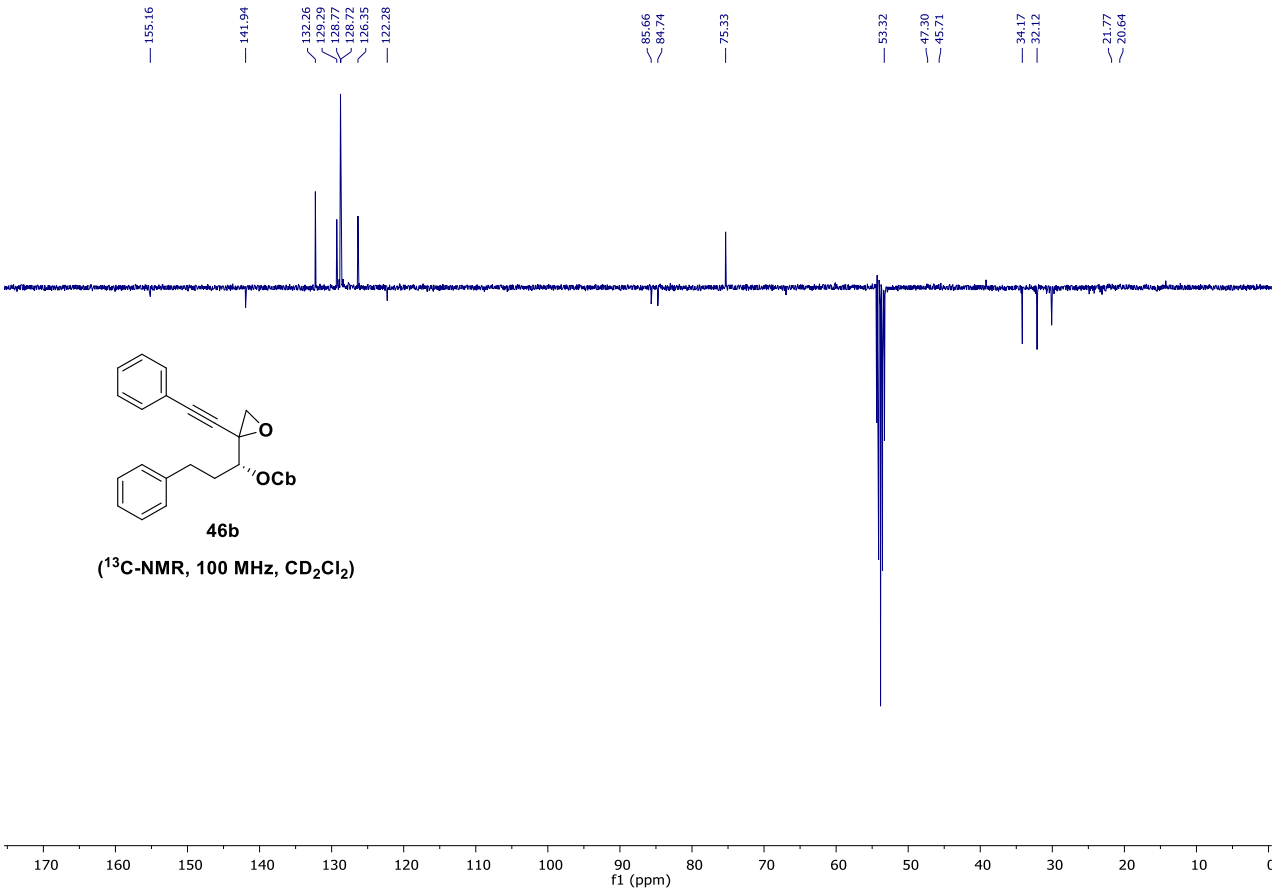
46a

(^{13}C-NMR, 100 MHz, CD_2Cl_2)



46b

(^{1}H-NMR, 400 MHz, CD_2Cl_2)



46b

(^{13}C-NMR, 100 MHz, CD_2Cl_2)